(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) **EP 3 707 143 B9**

(12) **CORRECTED EUROPEAN PATENT SPECIFICATION**

(15) Correction information:
Corrected version no 1 (W1 B1)
Corrections, see
Claims EN 13

(48) Corrigendum issued on:
12.04.2023 Bulletin 2023/15

(45) Date of publication and mention of the grant of the patent:
28.12.2022 Bulletin 2022/52

(21) Application number: **18795687.5**

(22) Date of filing: **06.11.2018**

(51) International Patent Classification (IPC):
C07D 495/04 *(2006.01)* ***A61P 35/00*** *(2006.01)*
A61P 5/00 *(2006.01)* ***A61K 31/4422*** *(2006.01)*

(52) Cooperative Patent Classification (CPC):
C07D 495/04; A61P 5/00; A61P 35/00

(86) International application number:
PCT/EP2018/080367

(87) International publication number:
WO 2019/086720 (09.05.2019 Gazette 2019/19)

(54) **NEW ANALOGS AS ANDROGEN RECEPTOR AND GLUCOCORTICOID RECEPTOR MODULATORS**

NEUE ANALOGA ALS ANDROGEN-REZEPTOR UND GLUCOCORTICOID-REZEPTOR-MODULATOREN

NOUVEAUX ANALOGUES EN TANT QUE MODULATEURS DES RÉCEPTEURS D'ANDROGÈNE ET DES RÉCEPTEURS DES GLUCOCORTICOÏDES

(84) Designated Contracting States:
AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HR HU IE IS IT LI LT LU LV MC MK MT NL NO PL PT RO RS SE SI SK SM TR
Designated Extension States:
BA ME

(30) Priority: **06.11.2017 EP 17382741**

(43) Date of publication of application:
16.09.2020 Bulletin 2020/38

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WO-A2-2017/059401 US-A- 4 659 717

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Description

Field of the invention

[0001] This invention relates to novel pharmaceutically-useful, optionally substituted dihydropyridines derivatives which are useful as modulators of nuclear receptors, such as receptors selected from androgen receptor and glucocorticoid receptor. The compounds are of potential utility in the treatment of diseases and conditions mediated by the nuclear receptors selected from androgen receptor and glucocorticoid receptor, such as cancer. The invention also relates to the use of such compounds as medicaments, to pharmaceutical compositions containing them, and to synthetic routes for their production.

Background of the invention

[0002] Nuclear receptors constitute a large superfamily of ligand-dependent transcription factors that are involved in many physiologic and developmental processes and are linked to a wide range of human diseases. That makes them attractive targets for drug discovery. In fact, approximately 13% of all FDA-approved drugs act on nuclear receptors. (Mangelsdorf DJ. et al, The nuclear receptor superfamily: the second decade, Cell 1995, 83, 835-839).

[0003] Nuclear receptors bind specific DNA elements in the regulatory regions of genes via a highly-conserved DNA-binding domain (DBD) and specific ligands via another highly conserved domain, the ligand binding domain (LBD), which consists of a series of approximately 12 helices that form a hydrophobic pocket. The binding of ligands in the pocket induces conformational changes in the receptor that affect the recruitment of coregulatory molecules (cofactors) that stimulate (co-activators) or repress (corepressors) transcription. (Huang P. et al, Structural overview of the nuclear receptor superfamily: Insights into physiology and therapeutics, Annu Rev Physiol 2010, 72, 247-272).

[0004] The androgen receptor (AR) belongs to the subfamily of steroid hormone-activated nuclear receptors which include also the estrogen, glucocorticoid, minerocorticoid and progesterone receptors (ER, GR, MR and PR). In the cytoplasm, unliganded AR is stabilized by heat shock proteins. Upon ligand binding of testosterone or dihydrotestosterone (DHT), a conformational change arises in the AR causing dissociation of specific chaperones, dimerization and phosphorylation of AR, and AR translocation to the nucleus. The DNA-binding domain (DBD) in AR binds to androgen response elements (AREs) inside the nucleus, causing recruitment of DNA transcriptional machinery and gene transcription. AR is found in a variety of tissues throughout the human body including prostate, scalp, skin and muscle.

[0005] Androgen receptor is the primary therapeutic target in prostate cancer which is a major health problem in industrialized countries, as it represents the second main cause of death from cancer in men. In newly diagnosed patients, the tumor is frequently confined to the prostate where it can be removed surgically or treated by radiotherapy. When metastases are detected or rising prostate-specific antigen (PSA) biomarker levels indicate disease progression, the first course of treatment is lowering the supply of androgens to the tumor (androgen deprivation therapy, ADT) because, in the primary stage, prostate tumor growth is androgen-dependent. Androgen levels can be decreased by surgical castration (elimination of testosterone production in the testis) or by medical treatment with antiandrogens (deactivation of AR), LHRH (luteinizing hormone-releasing hormone) agonists or antagonists (suppression of testosterone production in the testis) and CYP17 or 5alpha-reductase inhibitors (inhibition of androgen biosynthesis).

[0006] Initially ADT is effective in controlling the disease, but within a few years tumor cells usually evolve mechanisms for continued growth under conditions of androgen depletion and the cancer becomes what is known as recurrent or castration-resistant prostate cancer (CRPC). Most of the mechanisms promoting CRPC are still AR-dependent and include intratumoral androgen synthesis, increased expression of AR through gene amplification or overexpression, upregulation of coactivator proteins that augment AR activity, acquisition of mutations within the AR protein that increase its activity in response to antagonists or other steroid hormones, constitutively active AR splice variants, and signaling through alternative pathways (e.g. induced by glucocorticoid receptor overexpression). (Watson PA. et al, Emerging mechanisms of resistance to AR inhibitors in prostate cancer, Nat Rev Cancer 2015, 15, 701-711).

[0007] There is no cure for CRPC and current medication provides only a modest overall survival benefit of 4 to 5 months. The median survival of patients with advanced metastatic prostate cancer, who have failed androgen deprivation therapy, was typically 16 to 20 months in 2009. (Thoreson GR. et al, Emerging therapies in castration resistant prostate cancer, Can J Urol 2014, 21, 98-105).

[0008] Nonsteroidal antiandrogens have been preferred over steroidal compounds for prostate cancer because they are more selective and have fewer side effects. (Elancheran R, Recent discoveries and developments of androgen receptor based therapy for prostate cancer, Med Chem Commun 2015, 6, 746-768).

[0009] Therefore, there is still a great need for new treatment options including improved, non-steroidal AR antagonists that could be useful for the treatment of both primary and especially castrate-resistant prostate cancer.

[0010] AR antagonists may also be useful for the treatment of other conditions, disorders and diseases which are regulated by the androgen receptor including but not limited to breast cancer (Hickey TE et al, Expression of androgen

receptor splice variants in clinical breast cancer, Oncotarget 2015, advanced publication Nov 5), epithelial ovarian cancer, benign prostate hyperplasia, alopecia and acne (Jie JL, et al, Rational design and synthesis of 4-((1R,2R)-2-hydroxycyclohexyl)-2(trifluoromethyl)benzonitrile (PF-998425), a novel, nonsteroidal androgen receptor antagonist devoid of phototoxicity for dermatological indications, J Med Chem 2008, 51, 7010-7014), hirsutism and polycystic ovary syndrome.

[0011] As has been pointed out previously, glucocorticoid receptor might play a role in one of the mechanisms promoting CRPC. At first, the hypothesis that GR can confer resistance may seem inconsistent with clinical evidence that glucocorticoid administration can be beneficial to some patients with CRPC. This apparent contradiction is explained by the fact that glucocorticoids inhibit adrenocorticotropic hormone (ACTH) production by the pituitary gland, which results in reduced androgen levels. This androgen-lowering activity explains the decline in serum PSA levels that is observed in men taking prednisone alone, which was documented in the comparator arm of the Phase III clinical trial that led to approval of abiraterone for chemotherapy-naive CRPC. However, in men with prostate cancers that express high levels of GR, this androgen-lowering benefit would be counteracted by GR activation in tumour cells. In this setting, a more effective treatment strategy could be combined inhibition of AR and GR, as is currently being explored in an early-phase clinical trial of enzalutamide in combination with the GR antagonist mifepristone/RU486 (ClinicalTrials.gov identifier: NCT02012296). One potential confounder of this study is the fact that mifepristone also has a high binding affinity for AR and can function as an AR agonist. Therefore, mifepristone treatment could unintentionally result in AR activation through agonism by displacing the potent antagonism of enzalutamide. (Watson PA. et al, Emerging mechanisms of resistance to androgen receptor inhibitors in prostate cancer, Nature Reviews Cancer | AOP, published online 13 November 2015, and references therein).

[0012] There are studies showing that GR agonists, such as dexamethasone, are sufficient to induce enzalutamide resistance, whereas a GR antagonist could restore sensitivity. Currently, with the widespread use of enzalutamide, resistance is increasing as a clinical problem, in which activation of the glucocorticoid signalling pathway seems to have an important role. These findings suggest the role that glucocorticoids might have in promoting tumour growth. A major implication of these studies is that glucocorticoids might promote tumour growth and progression in men whose cancers express the GR. Thus, new strategies that block both AR signalling and GR signalling might be necessary and efforts to develop GR-specific antagonists that do not have off-target effects on the AR would be useful to prevent or overcome enzalutamide resistance. As opposed to AR inhibition, which can cause unpleasant but tolerable adverse effects, total GR inhibition can be lethal. (Narayanan S, et al, Androgen-glucocorticoid interactions in the era of novel prostate cancer therapy, NATURE REVIEWS | UROLOGY, doi:10.1038/nrurol.2015.254, Published online 8 Dec 2015, and references therein).

[0013] Glucocorticoids (GR agonists) are strong immunosuppressive and antiinflammatory agents that are widely used as co-medication in cancer therapy of solid tumors to alleviate adverse effects, reduce toxicity and protect normal tissue. However, glucocorticoids may interfere with therapeutic efficacy of anti-cancer medication, e.g. by inhibiting apoptosis and promoting proliferation. Therefore, there have been suggestions to minimize the use of glucocorticoids in anti-cancer therapy. Mechanistically, dexamethasone (an important glucocorticoid drug) has been found to suppress immune response by enhancing expression of the T cell checkpoint proteins PD-1 and CTLA-4. GR antagonist mifepristone has been shown to reverse this effect (K. Xing et al., Dexamethasone enhances programmed cell death 1 (PD-1) expression during T cell activation: an insight into the optimum application of glucocorticoids in anti-cancer therapy, BMC Immunology 2015, 16, 39; M. Xia et al., Dexamethasone enhances CTLA-4 expression during T cell activation, Cell Mol Life Sci 1999, 55, 1649-1659) .

[0014] GR antagonists that have the opposite effect to glucocorticoids might therefore be useful as activators of the immune system for the treatment of solid tumors as a single agent and in combination with checkpoint inhibitors. Currently, Mifepristone is being studied in cancer patients, wherein stress-response mechanisms including the hypothalamic-pituitary-adrenal (HPA) axis are frequently activated and dysregulated.

[0015] High levels and altered diurnal rhythms of cortisol, a glucocorticoid hormone involved in stress signaling, inflammation and metabolism, have been correlated with poor prognosis of terminal cancer patients, e.g. lung, breast, colorectal and ovarian cancer (H.M. Kimet al., Random serum cortisol as a predictor for survival of terminally ill patients with cancer, Am J Hosp Pall Med 2016, 33, 281-285; A. Schrepf et al., Diurnal cortisol and survival in epithelial ovarian cancer, Psychoneuroendocrinology 2015, 53, 256-267).

[0016] Recently it was shown that cortisol production is a common feature of a broad spectrum of malignant cells and that cancer-derived cortisol inhibits tumor-specific CD8+ T cell proliferation in a GR-specific fashion. The effect was inhibited in the presence of GR antagonist mifepristone/RU486. These data suggest that the production of cortisol by tumor cells may have an important immunoregulatory function and that GR antagonists may have a therapeutic potential as reactivators of the immune system (N. Cirillo et al., Characterisation of the cancer-associated glucocorticoid system: key role of 11b-hydroxysteroid dehydrogenase type 2, Br. J. Cancer 2017, advanced online publication 1-10, doi: 10.1038/bjc.2017.243).

[0017] Currently, there are few glucocorticoid receptor antagonists marketed and in clinical assays. Among them is mifepristone, a synthetic steroid compound which has been investigated as an antiglucocorticoid drug in the treatment

of persistent or recurrent Cushing's disease. Its affinity to the progesterone receptor is a main drawback. (Schteingart D.E., Drugs in the medical treatment of Cushing's syndrome, Expert Opin. Emerging Drugs (2009) 14(4):661-671). Other glucocorticoid receptor antagonists are in (pre)clinical development (Kach J. et al, Selective glucocorticoid receptor modulators (SGRMs) delay castrate-resistant prostate cancer growth, mct.aacrjournals.org on April 21, 2017; Hunt H.J. et al, The Identification of the Clinical Candidate (R)-(1-(4-fluorophenyl)-6-((1-methyl-1Hpyrazol-4-yl)sulfonyl)-4,4a, 5, 6,7,8-hexahydro-1H-pyrazolo[3,4-g]isoquinolin-4a-yl) (4-(trifluoromethyl)pyridin-2-yl)methanone (CORT125134): A Selective Glucocorticoid Receptor (GR) Antagonist, J. Med. Chem, DOI: 10.1021/acs.jmedchem.7b00162 • Publication Date (Web): 03 Apr 2017).

[0018] The listing or discussion of an apparently prior-published document in this specification should not necessarily be taken as an acknowledgement that the document is part of the state of the art or is common general knowledge.

[0019] 1,4-dihydropyridines are an important class of cardiovascular drugs such as nifedipine, nitrendipine, amlodipine and many other analogs which exert their antihypertensive and antianginal actions by blocking L-type calcium channels. The 1,4-dihydropyridine nucleus is also a privileged scaffold that can, when appropriately substituted, interact at diverse receptors and ion channels, providing a wide range of biological activities (P. loan et al., 1,4-Dihydropyridine scaffold in medicinal chemistry, The story so far and perspectives. (Part 1): Action in Ion Channels and GPCRs. Curr. Med. Chem. 2011, 18, 4901-4922; E. Carosati et al., 1,4-Dihydropyridine Scaffold in Medicinal Chemistry, The story so far and perspectives (Part 2): Action in Other Targets and Antitargets, Curr. Med. Chem. 2012, 19, 4306-4323).

[0020] International patent application WO 2005/016885 A2 discloses various dihydropyridines with inhibitory activity against beta-adrenergic receptors and L-type calcium channels that may be useful for the treatment of heart disease. However, there is no mention that these compounds may be useful for the treatment of cancer.

[0021] European patent application EP 0 217 530 A1 discloses dihydropyridines derivatives as vasodilators useful in the treatment of stroke, angina and migraine. In addition, the compounds are useful as antiasthma agents. Among the disclosed compounds there are 4-benzothiophene-1,4-dihydropyridine-3,5-diester derivatives which are not active as modulators of androgen receptor, therefore are not included in the scope of the present invention.

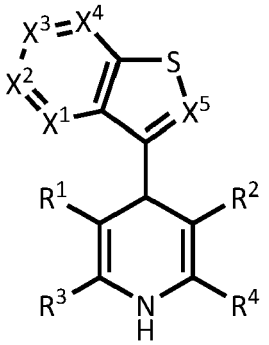
[0022] Patent application US 2016/0151388 A1 dislcoses a method and compositions related to glucocorticoid receptor antagonist in prostate cancer, alone or in combination with an androgen receptor antagonist. The prostate cancer may be one that has become resitant to androgen deprivation therapy, for example, by increase in glucocorticoid receptor expression and /or activity.

[0023] Patent application WO 2017 059401 A2 discloses derivatives of dihydropyridine with an annellated ring as ligands on the androgen receptor whereby the dihydropyridine ring is fused to an aromatic ring and a non-aromatic ring. The disclosed compounds are useful for treating hormone refractory prostate cancer.

[0024] The problem to be solved by the present invention is to provide compounds as modulators of nuclear receptors selected from androgen receptor and glucocorticoid receptor.

SUMMARY OF THE INVENTION

[0025] In one of its aspects (aspect 1), the present invention refers to dihydropyridine derivative of formula (I):



(I)

wherein:

- R^1 is a group selected from:

  a) $-COR^5$,

b) -$COOR^5$,

c) -CN,

d) -$C(O)NH_2$,

- R^5 is a group selected from:

  a) linear or branched C_1-C_6 alkyl optionally substituted by 1, 2 or 3 substituents selected from -$N(R^6)R^7$ and -OR^6, halogen atom, C_3-C_6 cycloalkyl and alkynyl,

  b) C_3-C_6 cycloalkyl,

- R^2 is a group selected from:

  a) -$COOR^8$,

  b) -COR^8,

  c) -$C(O)N(R^8)R^9$,

  d) -CN,

  e) -$S(O)_nR^8$, wherein n is an integer from 1 to 2,

- R^8 and R^9 are independently selected from:

  a) linear or branched C_1-C_6 alkyl optionally substituted by 1, 2 or 3 substituents selected from A^1 or B^2,

  b) A^1 group,

  c) hydrogen atom,
  or

- R^8 and R^9 together with the nitrogen atom to which they are attached form a 5-6 membered heterocycle which optionally comprises 1 heteroatom selected from O and N, and said heterocycle being optionally substituted by 1 or 2 groups independently selected from linear or branched C_1-C_4 alkyl,

- R^3 is a group selected from:

  a) linear or branched C_1-C_6 alkyl optionally substituted by 1, 2 or 3 substituents selected from halogen atom, -$N(R^6)R^7$, and -OR^6,

  b) C_3-C_6 cycloalkyl optionally substituted by 1, 2 or 3 halogen atoms,

  c) hydrogen atom,

  d) -NH_2,

  e) -CN,

- R^4 is a group selected from:

  a) A^1 group,

  b) linear or branched C_1-C_6 alkyl optionally substituted by 1, 2 or 3 substituents selected from A^1 or B^2,

  c) -$N(R^6)R^7$,

d) -CN,

e) -CO-H,

f) -CO-Me,

g) -CO-OMe

h) hydrogen atom,

- X^1, X^2, X^3, X^4, and X^5 are independently selected from C-B^1, N and C-H,
- A^1 is selected from:

  a) C_3-C_6 cycloalkyl which ring is optionally substituted by 1, 2, 3 or 4 substituents selected from =0 and B^3;

  b) a 3 to 6 membered saturated heterocyclyl ring comprising 1, 2 or 3 heteroatoms selected from O, S and N, and which ring is optionally substituted by 1, 2 or 3 substituents selected from =O and B^3;

  c) phenyl or 5 to 6 membered heteroaryl group, either ones are optionally substituted by 1, 2 or 3 substituents selected from B^1;

- each B^1 is independently selected from halogen atom, -CF_3 group, 5 to 6 membered heteroaryl, linear or branched C_1-C_6 alkyl, -CN, -N(R^6)R^7, -OR^6, -C(=O)R^6, -C(=O)OR^6, -C(=O)N(R^6)R^7, -OC(=O)-R^6, -N(R^6)C(=O)R^7, -N$R^7$$SO_2$$R^6$, -$SO_2$N($R^6$)$R^7$, -S$R^6$, -S(O)$R^6$ and -$S(O)_2$$R^6$,
- each B^2 is independently selected from halogen atom, -CN, -N(R^6)R^7, -OR^6, -C(=O)R^6, -C(=O)OR^6, -C(=O)N(R^6)R^7, -OC(=O)-R^s, -N(R^6)C(=O)R^7, -N$R^7$$SO_2$$R^6$, -$SO_2$N($R^6$)$R^7$, -S$R^6$, -S(O)$R^6$, -$S(O)_2$$R^6$, and alkynyl group,
- each B^3 is independently selected from halogen atom, linear or branched C_1-C_6 alkyl, -CN, -N(R^6)R^7, -OR^6, -C(=O)R^6, -C(=O)OR^6, -C(=O)N(R^6)R^7, -OC(=O)-R^6, -N(R^6)C(=O)R^7, -N$R^7$$SO_2$$R^6$, -$SO_2$N($R^6$)$R^7$, -S$R^6$, -S(O)$R^6$, -$S(O)_2$$R^6$,

each R^6 and R^7 independently represents:

- hydrogen atom,
- linear or branched C_1-C_{12} alkyl, C_3-C_6 cycloalkyl and C_4-C_6 heterocycloalkyl, which are optionally substituted by 1, 2 or 3 substituents selected from =O (oxo), halogen atom, hydroxy, phenyl, C_3-C_6 cycloalkyl, linear or branched C_1-C_6 alkoxy, amino, alkylamino, dialkylamino, linear or branched C_1-C_6 alkylcarbonyl,
- phenyl or 5 to 6 membered heteroaryl group, which are optionally substituted by 1, 2 or 3 substituents selected from halogen atom, cyano group, linear or branched C_1-C_6 alkyl, linear or branched C_1-C_6 haloalkyl, hydroxy, linear or branched C_1-C_6 alkoxy, amino, alkylamino, dialkylamino;
- R^6 and R^7 form together with the nitrogen atom to which they are attached, a 3-to 8 membered ring which optionally contains a further heteroatom selected from O, N and S, and which ring is optionally substituted by 1, 2 or 3 substituents selected from =O (oxo), linear or branched C_1-C_6 alkyl, linear or branched C_1-C_6 haloalkyl, linear or branched C_1-C_6 alkylcarbonyl;
- with the proviso that when R^1 is -COOR^5 and R^2 is -COOR^8 then R^4 is not a methyl group,

and pharmaceutically acceptable salts thereof.

[0026] Other aspects of the present invention are:
In a second aspect, the present invention refers to processes for the preparation of the compounds defined in the first aspect.

[0027] In a third aspect, the present invention refers to pharmaceutical compositions comprising an effective amount of a compound defined in the first aspect.

[0028] In a fourth, the present invention refers to a combination product comprising a compound as defined in the first

aspect and another therapeutic agent selected from agents for treating prostate cancer, castration-resistant prostate cancer, pancreatic cancer, bladder cancer, renal cancer, gastric cancer, lung cancer, breast cancer, colon cancer, colorectal cancer, ovarian cancer, and other solid tumours, melanoma, metastasizing cancers, benign prostate hyperplasia, polycystic ovary syndrome (PCOS), hair loss, hirsutism, acne, hypogonadism, muscle wasting diseases, cachexia and Cushing's syndrome, anti-psychotic drug induced weight gain, obesity, post-traumatic stress disorder and alcoholism.

[0029] In a fifth aspect, the present invention relates to a compound as defined in the first aspect for use as a medicament.

[0030] In a sixth aspect the present invention relates to a compound as defined in the first aspect for use in the treatment of a disease or pathological condition selected from the group consisting of cancer, prostate cancer, castration-resistant prostate cancer, pancreatic cancer, bladder cancer, renal cancer, gastric cancer, lung cancer, breast cancer, colon cancer, colorectal cancer, ovarian cancer, and other solid tumours, melanoma, metastasizing cancers, benign prostate hyperplasia, polycystic ovary syndrome (PCOS), hair loss, hirsutism, acne, hypogonadism, muscle wasting diseases and cachexia, and Cushing's syndrome, anti-psychotic drug induced weight gain, obesity, post-traumatic stress disorder and alcoholism.

[0031] In a seventh aspect, the present invention relates to a pharmaceutical composition comprising a compound as defined the first aspect of the invention and a pharmaceutically acceptable diluent or carrier.

[0032] As it is said before, the invention relates to dihydropyridine derivatives for use in the treatment or prevention of diseases known to be susceptible to amelioration by treating with modulators of nuclear receptors, in particular by modulators of nuclear receptors selected from androgen receptor and glucocorticoid receptor. Such diseases are, for example cancer, prostate cancer, castration-resistant prostate cancer, pancreatic cancer, bladder cancer, renal cancer, gastric cancer, lung cancer, breast cancer, colon cancer, colorectal cancer, ovarian cancer, and other solid tumours, melanoma, metastasizing cancers, benign prostate hyperplasia, polycystic ovary syndrome (PCOS), hair loss, hirsutism, acne, hypogonadism, muscle wasting diseases and cachexia, and Cushing's syndrome, anti-psychotic drug induced weight gain, obesity, post-traumatic stress disorder and alcoholism.

[0033] Accordingly, the invention relates to compounds according to the first aspect, and pharmaceutically acceptable salts thereof, and pharmaceutical compositions comprising such compounds and / or salts thereof for use in the treatment of pathological conditions or disease of human body which comprises administering to a subject in need of said treatment, an effective amount of the dihydropyridine derivatives of the invention or a pharmaceutically acceptable salt thereof.

[0034] As used herein, the term halogen atom is used to designate an atom selected from the group consisting of chlorine, fluorine, bromine or iodine atom, preferably bromine, fluorine or chlorine atom.

[0035] As used herein the term alkyl is used to designate linear or branched hydrocarbon radicals (C_nH_{2n+1}) having 1 to 12 carbon atoms. Examples include methyl, ethyl, n-propyl, i-propyl, n-butyl, sec-butyl, tert-butyl, n-pentyl, 1-methylbutyl, 2-methyl-butyl, isopentyl, 1-ethylpropyl, 1,1-dimethylpropyl, 1,2-dimethylpropyl, n-hexyl, 1-ethylbutyl, 2-ethylbutyl, 1,1-dimethylbutyl, 1,2-dimethylbutyl, 1,3dimethylbutyl, 2,2-dimethylbutyl, 2,3-dimethylbutyl, 2-methylpentyl and 3-methylpentyl, n-heptyl, 3-methylheptyl, n-octyl, 2,2-dimethyloctyl radicals. In a preferred embodiment said alkyl groups have 1 to 6 carbon atoms.

[0036] As used herein, the term haloalkyl is used to designate C_1-C_6 alkyl substituted by one or more halogen atoms, preferably one, two or three halogen atoms. The haloalkyl groups may be linear or branched. Preferably, the halogen atoms are selected from the group consisting of fluorine or chlorine atoms. In a preferred embodiment, the haloalkyl group is a linear or branched C_1-C_4 alkyl substituted by one, two or three fluorine or chlorine atoms.

[0037] As used herein, the term cycloalkyl is used to designate hydrocarbon cyclic groups (C_nH_{2n-1}) having 3 to 6 carbon atoms. Such cycloalkyl groups include, by way of example, single ring structures such as cyclopropyl, cyclobutyl, cyclopentyl, cyclooctyl, and the like.

[0038] As used herein, the term heterocyclyl is used to designate saturated rings comprising 3 to 6 carbon atoms and 1, 2 or 3 heteroatoms selected from O, S and N as part of the ring. The heterocyclyl groups include, for example, azetidinyl, pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl.

[0039] As used herein, the term C_1-C_6 alkoxy is used to designate radicals which contain a linear or branched C_1-C_6 alkyl group linked to an oxygen atom (C_nH_{2n+1}-O-). Preferred alkoxy radicals include methoxy, ethoxy, n-propoxy, i-propoxy, n-butoxy, sec-butoxy, t-butoxy, trifluoromethoxy, difluoromethoxy, hydroxymethoxy, 2-hydroxyethoxy or 2-hydroxypropoxy.

[0040] As used herein, the term carbonyl group is used to designate a group C=O. As used herein, when the term oxo (=O) is used to designate a subsitutent in a ring, it means that a carbon atom of said ring is present in the form of a carbonyl (C=O) group.

[0041] As used herein, the term heteroaryl group is used to designate a 5 or 6-membered heteroaromatic ring containing carbon, hydrogen and one or more atoms selected from O, N and S. Said groups may optionally be substituted by 1, 2 or 3 substituents selected from the group consisting of halogen atom, cyano group, linear or branched C_1-C_6 haloalkyl, linear or branched C_1-C_6 alkyl, hydroxy, linear or branched C_1-C_6 alkoxy, amino, alkylamino and dialkylamino. The heteroaryl groups may optionally be substituted by substituents such as those defined under R^6 and B^1. The preferred

groups are optionally substituted pyridyl and pyrimidinyl. When a heteroaryl radical carries 2 or more substituents, the substituents may be the same or different.

[0042] As used herein, the term alkylamino is used to designate radicals which contain a linear or branched C_1-C_6 alkyl group linked to a group -NH-. Preferred alkylamino radicals include methylamino, ethylamino, n-propylamino, i-propylamino, n-butylamino, sec-butylamino, t-butylamino, trifluoromethylamino, difluoromethylamino, hydroxymethylamino, 2-hydroxyetylamino or 2-hydroxypropylamino.

[0043] As used herein, the term dialkylamino is used to designate radicals which contain two linear or branched C_1-C_6 alkyl groups linked to a group nitrogen atom which alkyl groups may be identical or different. Preferred dialkylamino radicals include di(methyl)amino, di(ethyl)amino, di-(n-propyl)amino, di-(i-propyl)amino, di-(n-butyl)amino, di-(sec-butyl)amino, di-(t-butyl)amino, di-(trifluoromethyl)amino, di(hydroxymethyl)amino,di(2-hydroxyetyl)amino, di(2-hydroxypropyl)amino, methylethylamino, methyl-i-propylamino and ethyl-n-propylamino.

[0044] As used herein, some of the atoms, radicals, chains or cycles present in the general structures of the invention are "optionally substituted". This means that these atoms, radicals, chains or cycles can be either unsubstituted or substituted in any position by one or more, for example 1, 2, 3 or 4, substituents, whereby the hydrogen atoms bound to the unsubstituted atoms, radicals, chains or cycles are replaced by chemically acceptable atoms, radicals, chains or cycles. When two or more substituents are present, each substituent may be the same or different.

[0045] As used herein, the term pharmaceutically acceptable salt is used to designate salts with a pharmaceutically acceptable acid or base. Pharmaceutically acceptable acids include both inorganic acids, for example hydrochloric, sulphuric, phosphoric, diphosphoric, hydrobromic, hydroiodic and nitric acid and organic acids, for example citric, fumaric, maleic, malic, mandelic, ascorbic, oxalic, succinic, tartaric, benzoic, acetic, methanesulphonic, ethanesulphonic, benzenesulphonic or p-toluenesulphonic acid. Pharmaceutically acceptable bases include alkali metal (e.g. sodium or potassium), alkali earth metal (e.g. calcium or magnesium) hydroxides, and organic bases, for example alkyl amines, phenylalkyl amines and heterocyclic amines.

[0046] Other preferred salts according to the invention are quaternary ammonium compounds wherein an equivalent of an anion (X^{-n}), wherein "-n" indicates the negative charge of the anion and is typically -1, -2 or -3, is associated with the positive charge of the N atom. X^{-n} may be an anion of various mineral acids such as, for example, chloride, bromide, iodide, sulphate, nitrate, phosphate, or an anion of an organic acid such as, for example, acetate, maleate, fumarate, citrate, oxalate, succinate, tartrate, malate, mandelate, trifluoroacetate, methanesulphonate and ptoluenesulphonate. X^{-n} is preferably an anion selected from chloride, bromide, iodide, sulphate, nitrate, acetate, maleate, oxalate, succinate or trifluoroacetate. More preferably, X- is chloride, bromide, trifluoroacetate or methanesulphonate.

[0047] According to one embodiment of the present invention in the compounds of formula (I), X^1, X^2, X^3 and X^5 represent C-H or C-B^1 group. In a preferred embodiment B^1 represents a halogen atom. In a more preferred embodiment X^1, X^3 and X^5 represent C-H and X^2 is C-B^1, wherein B^1 represents a halogen atom.

[0048] According to another embodiment of the present invention in the compounds of formula (I), X^4 represents a group selected from C-B^1 and N atom. In a preferred embodiment X^4 represents C-B^1. In a more preferred embodiment B^1 is selected from -CN group and halogen atom.

[0049] According to another embodiment of the present invention in the compounds of formula (I), R^1 is a group selected from -COR^5, -$COOR^5$ and -CN group. In a preferred embodiment, R^5 is independently selected from C_3-C_5 cycloalkyl, -C_1-C_3 alkyl wherein the terminal methyl is unsubstituted or substituted by three fluorine atoms (-CF_3) and C_1-C_3 alkyl optionally substituted at any position by an alkynyl group. In a more preferred embodiment, each R^5 is independently selected from -C_1-C_3 alkyl and -C_3-C_5 cycloalkyl.

[0050] According to one embodiment of the present invention in the compounds of formula (I), R^2 is a group selected from -COR^8 and -$COOR^8$ preferably -$COOR^8$. In a preferred embodiment, R^8 is independently selected from:

- linear or branched C_1-C_6 alkyl optionally substituted by 1, 2 or 3 substituents selected from A^1 or B^2, preferably A^1 wherein A^1 represents a group selected from phenyl, C_3-C_6 cycloalkyl, which is optionally substituted by 1, 2 or 3 C_1-C_3 alkyl and 3 to 6 membered saturated heterocyclyl rings comprising 1, 2 or 3 heteroatoms selected from O, S and N, and which ring is optionally substituted by 1, 2 or 3 C_1-C_3 alkyl groups; and B^2 represents a halogen atom.

[0051] In a more preferred embodiment R^2 represents -$COOR^8$, wherein R^8 represents independently:

- linear or branched C_1-C_6 alkyl optionally substituted by 1, 2 or 3 substituents selected from fluorine atoms and C_3-C_5 cycloalkyl optionally substituted by 1, 2 or 3 fluorine atoms, or
- A^1 group, which represents C_3-C_6 cycloalkyl which is optionally substituted by 1, 2 or 3 substituents selected from the group consisting of fluorine atoms and C_1-C_3 alkyl groups.

[0052] According to another embodiment of the present invention in the compounds of formula (I), R^2 represents a -CN group.

[0053] According to another embodiment of the present invention in the compounds of formula (I), R^3 is a group selected from C_3-C_6 cycloalkyl optionally substituted by 1, 2 or 3 halogen atoms; and linear or branched C_1-C_4 alkyl optionally substituted by 1, 2 or 3 substituents selected from halogen atom, -$N(R^6)R^7$, and -OR^6. In a preferred embodiment, R^6 and R^7 are selected from hydrogen atom and a linear or branched C_1-C_6 alkyl.

[0054] In a more preferred embodiment R^3 is selected from linear or branched C_1-C_4 alkyl and C_3-C_6 cycloalkyl. In a more preferred embodiment R^3 is selected from methyl or cyclopropyl group, said groups being optionally substituted by 1, 2 or 3 fluorine atoms.

[0055] According to another embodiment of the present invention in the compounds of formula (I), R^4 represents a linear or branched C_1-C_6 alkyl optionally substituted by 1, 2 or 3 substituents selected from A^1 or B^2. In a more preferred embodiment A^1 represents C_3-C_6 cycloalkyl and B^2 represents a group selected from halogen atom, -$N(R^6)R^7$, and-OR^6. In a more preferred embodiment, R^6 and R^7 are selected from hydrogen atom and a linear or branched C_1-C_6 alkyl. In a more preferred embodiment R^4 represents a linear or branched C_1-C_3 alkyl optionally substituted by 1, 2 or 3 substituents selected from 1, 2 or 3 fluorine atoms and hydroxyl group.

[0056] According to another embodiment of the present invention in the compounds of formula (I), R^4 represents an A^1 group. In a more preferred embodiment, A^1 represents C_3-C_6 cycloalkyl which optionally contains 1, 2 or 3 heteroatoms selected from O, S and N, and which ring is optionally substituted by C_1-C_3 alkyl. In a more preferred embodiment R^4 represents an A^1 group, which represents C_3-C_6 cycloalkyl.

[0057] According to one embodiment of the present invention in the compounds of formula (I), R^4 represents a -$N(R^6)R^7$ group. In a more preferred embodiment, R^6 and R^7 are selected from a hydrogen atom and a linear or branched C_1-C_4 alkyl.

[0058] In a more preferred embodiment R^4 is a group selected from:

- $N(R^6)R^7$, wherein R^6 and R^7 are independently selected from a hydrogen atom and a linear or branched C_1-C_3 alkyl,
- A^1 group, which represents C_3-C_6 cycloalkyl,
- linear or branched C_1-C_6 alkyl optionally substituted by 1, 2 or 3 substituents selected from 1, 2 or 3 fluorine atoms or 1 hydroxyl group,

[0059] According to one embodiment of the present invention in the compounds of formula (I), X^1, X^2, X^3 and X^5 represent -CH, X^4 represents C-B^1, wherein B^1 represents -CN group or bromine atom, R^1 is a group selected from -$C(O)CH_3$, -$C(O)OCH_3$, -$C(O)OCH_2$-alkynyl and CN, R^2 is a group selected from -C(O)OCH-lineal or branched C_1-C_5 alkyl group optionally substituted by 1, 2 or 3 fluorine atoms and $C(O)OCH_2$-cyclopropyl optionally substituted by 1, 2 or 3 fluorine atoms, R^3 is a group selected from linear or branched C_1-C_3 alkyl and C_3-C_4 cycloalkyl and R^4 is a group selected from a linear or branched C_1-C_3 alkyl, C_3-C_4 cycloalkyl and -NH_2.

[0060] Compound according to claim 1 wherein X^1, X^2, X^3 and X^5 represent a -CH, X^4 represents a C-B^1, wherein B^1 represents -CN group, R^1 is a group selected from - $C(O)CH_3$, -$C(O)OCH_3$, R^2 is a group selected from -$C(O)OCH_2$ -cyclopropyl optionally substituted by 1, 2 or 3 fluorine atoms, and -$C(O)OCH_2$-CF_3 , R^3 is a group selected from methyl and cyclopropyl and R^4 is a group selected from cyclopropyl and -NH_2.

[0061] According to another embodiment of the present invention in the compounds of formula (I), X^1, X^3, X^4 and X^5 represent a -CH and X^2 represents a C-B^1 group. In a more preferred embodiment B^1 represents a halogen atom.

[0062] According to another embodiment of the present invention in the compounds of formula (I), X^1, X^2, X^3, X^4 and X^5 represent a -CH.

[0063] Individual compounds of the present invention include:

Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1 ,4-dihydro-pyridine-3-carboxylate

Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1 ,4-dihydro-pyridine-3-carboxylate (Enantiomer 1)

Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1 ,4-dihydro-pyridine-3-carboxylate (Enantiomer 2)

5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxamide 1-(4-(benzo[b]thiophen-3-yl)-5-benzoyl-2,6-dimethyl-1,4-dihydropyridin-3-yl)ethan-1-one

Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-6-methyl-2-phenyl-1,4-dihydropyridine-3-carboxylate

1-(4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-5-nicotinoyl-1,4-dihydro pyridin-3-yl)ethan-1-one

Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-6-methyl-1,4-dihydro-[2,3'-bipyridine]-3-carboxylate

2,2,2-trifluoroethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

5-Acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylic acid

1-(4-(Benzo[b]thiophen-3-yl)-2,6-dimethyl-5-(4-methylpiperazine-1-carbonyl)-1,4-di hydropyridin-3-yl)ethan-1-one

5-Acetyl-4-(benzo[b]thiophen-3-yl)-N,N-diethyl-2,6-dimethyl-1,4-dihydropyridine-3-carboxamide

1-(4-(Benzo[b]thiophen-3-yl)-2,6-dimethyl-5-(morpholine-4-carbonyl)-1,4-dihydropyridin-3-yl)ethan-1-one

2-Methoxyethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

3-Acetamidopropyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

Benzyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydro-pyridine-3-carboxylate

2-Morpholinoethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

2-(Dimethylamino)ethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

2-Acetamidoethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2-(methoxymethyl)-6-methyl-1,4-dihydropyridine-3-carboxylate

Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2-((dimethylamino)methyl)-6-methyl-1,4-dihydropyridine-3-carboxylate

Pyridin-4-ylmethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

4-Methoxybenzyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

Pyridin-2-ylmethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-6-methyl-2-(morpholino-methyl)-1,4-dihydropyridine-3-carboxylate

Dimethyl 4-(benzo[b]thiophen-3-yl)-2,6-bis(morpholinomethyl)-1,4-dihydropyridine-3,5-dicarboxylate

2-Hydroxyethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

1-(4-(Benzo[b]thiophen-3-yl)-5-(cyclopropanecarbonyl)-6-cyclopropyl-2-methyl-1,4-di hydropyridin-3-yl)ethan-1-one

Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2-(1-(tert-butoxycarbonyl) azetidin-3-yl)-6-methyl-1 ,4-di hydropyridine-3-carboxylate

(1-(tert-Butoxycarbonyl)piperidin-4-yl)methyl 5-acetyl-4-(benzo[b] thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

Cyclohexylmethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

Methyl 4-(benzo[b]thiophen-3-yl)-5-(cyclopropanecarbonyl)-2,6-dicyclopropyl-1,4-dihydropyridine-3-carboxylate

5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-N-phenyl-1,4-dihydropyridine-3-carboxamide

Tetrahydro-2H-pyran-4-yl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

(Tetrahydro-2H-pyran-4-yl)methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

Cyclohexyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2-(2-methoxy-2-oxoethyl)-6-methyl-1,4-dihydropyridine-3-carboxylate

Methyl 5-acetyl-2,6-dimethyl-4-(2-methylbenzo[b]thiophen-3-yl)-1,4-dihydropyridine-3-carboxylate

Cyclopropylmethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2-(2-methoxyethyl)-6-methyl-1,4-dihydropyridine-3-carboxylate

Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2-((benzyloxy)methyl)-6-methyl-1,4-dihydropyridine-3-carboxylate

Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-6-methyl-2-(phenoxymethyl)-1,4-dihydropyridine-3-carboxylate

Phenethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

Methyl 4-(benzo[b]thiophen-3-yl)-5-(cyclopropanecarbonyl)-6-cyclopropyl-2-methyl-1,4-dihydropyridine-3-carboxylate

Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-6-methyl-2-(trifluoromethyl)-1,4-dihydropyridine-3-carboxylate

Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-6-benzyl-2-methyl-1,4-dihydropyridine-3-carboxylate

Methyl 4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-5-(2-phenylacetyl)-1,4-dihydropyridine-3-carboxylate

Methyl 4-(benzo[b]thiophen-3-yl)-5-(2-methoxyacetyl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-6-(methoxymethyl)-2-methyl-1,4-dihydropyridine-3-carboxylate

Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2-(fluoromethyl)-6-methyl-1,4-dihydropyridine-3-carboxylate

Cyclopropylmethyl 5-acetyl-4-(5-fluorobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

1-(tert-Butoxycarbonyl)piperidin-4-yl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

Cyclopentylmethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

Cyclopropylmethyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

1-methylpiperidin-4-yl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

Cyclopentyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

4,4-dimethylcyclohexyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

Cyclobutyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

Methyl 5-acetyl-4-(5-fluorobenzo[b]thiophen-3-yl)-6-methyl-2-(trifluoromethyl)-1,4-dihydropyridine-3-carboxylate

Methyl 5-acetyl-2,6-dimethyl-4-(thieno[3,2-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2-methyl-6-(trifluoromethyl)-1,4-dihydropyridine-3-carboxylate

Cyclopropylmethyl 5-acetyl-4-(5-chlorobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

Cyclohexylmethyl 5-acetyl-4-(5-chlorobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

Cyclohexylmethyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

Cyclopentylmethyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

Cyclohexyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

Cyclopentyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

Methyl 5-acetyl-4-(5-chlorobenzo[b]thiophen-3-yl)-6-methyl-2-(trifluoromethyl)-1,4-dihydropyridine-3-carboxylate

Benzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

(Tetrahydro-2H-pyran-4-yl)methyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

Benzyl 5-acetyl-4-(5-fluorobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

Benzyl 5-acetyl-4-(5-chlorobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

(Tetrahydro-2H-pyran-4-yl)methyl 5-acetyl-4-(5-chlorobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

(Tetrahydro-2H-pyran-4-yl)methyl 5-acetyl-4-(5-fluorobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

Benzyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-6-methyl-2-(trifluoromethyl)-1,4-dihydropyridine-3-carboxylate

Pyridin-4-ylmethyl 5-acetyl-4-(5-fluorobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

4-Fluorobenzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

Pyridin-3-ylmethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

1,1'-(4-(benzo[b]thiophen-3-yl)-2-benzyl-6-methyl-1,4-dihydropyridine-3,5-diyl)bis(ethan-1-one)

1-(5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3-yl)-2-phenylethan-1-one

Methyl 5-acetyl-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-2-(trifluoromethyl)-1,4-dihydropyridine-3-carboxylate

1-(2-methyl-5-(piperidine-1-carbonyl)-4-(thieno[2,3-b]pyridin-3-yl)-6-(trifluoromethyl)-1,4-dihydropyridin-3-yl)ethan-1-one

4-(((5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydro-pyridine-3-carbonyl)oxy)methyl)benzoic acid

Benzyl 5-acetyl-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-2-(trifluoromethyl)-1,4-dihydropyridine-3-carboxylate

Pyridin-3-ylmethyl 5-acetyl-4-(5-fluorobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

Pyridin-3-ylmethyl 5-acetyl-4-(7-bromobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

Pyridin-3-ylmethyl 5-acetyl-4-(7-cyanobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

Pyridin-3-ylmethyl 5-acetyl-4-(5-chlorobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

Pyridin-3-ylmethyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

Pyridin-4-ylmethyl 5-acetyl-4-(5-chlorobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

4-(Cyclopropylcarbamoyl)benzyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

Pyridin-4-ylmethyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4dihydropyridine-3-carboxylate

4-Bromobenzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

3-Bromobenzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

2-Bromobenzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

(3-Fluoropyridin-4-yl)methyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

Pyrimidin-5-ylmethyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

(5-Bromopyridin-3-yl)methyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

2-Phenylpropan-2-yl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

3-cyanobenzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

4-cyanobenzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

(6-Chloropyridin-3-yl)methyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

3-Morpholinobenzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

4,4-Dimethylcyclohexyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

(2-Chloropyridin-4-yl)methyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

Tetrahydro-2H-pyran-4-yl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

4,4-Difluorocyclohexyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

5-Acetyl-N-benzyl-N,2,6-trimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxamide

Oxetan-3-yl 5-acetyl-4-(7-bromobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate

Isopropyl 5-acetyl-4-(7-bromobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate

Methyl 5-acetyl-4-(7-bromobenzo[b]thiophen-3-yl)-6-methyl-2-(trifluoromethyl)-1,4-dihydropyridine-3-carboxylate

Cyclopropylmethyl 5-acetyl-4-(7-bromobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate

Methyl 5-acetyl-2-cyclopropyl-6-methyl-4-(7-(2,2,2-trifluoroacetyl) benzo[b]thiophen-3-yl)-1 ,4-di hydropyridine-3-carboxylate

2-Phenylpropan-2-yl 5-acetyl-4-(7-bromobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

Methyl 5-acetyl-2-amino-4-(benzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

Methyl 2-amino-4-(benzo[b]thiophen-3-yl)-5-(cyclopropanecarbonyl)-6-methyl-1,4-dihydropyridine-3-carboxylate

Methyl 5-acetyl-2-amino-4-(5-fluorobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

Methyl 5-acetyl-2-amino-4-(7-bromobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

Methyl 5-acetyl-2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

Cyclopentyl 5-acetyl-2-amino-4-(7-bromobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

Dimethyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

Cyclopentyl 5-acetyl-2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

Dimethyl 2,6-diamino-4-(benzo[b]thiophen-3-yl)-1,4-dihydropyridine-3,5-dicarboxylate cyclopropylmethyl 5-acetyl-2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

4,4-difluorocyclohexyl 5-acetyl-2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

methyl 2-amino-5-cyano-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

4-fluorobenzyl 5-acetyl-2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

methyl 5-acetyl-2-amino-4-(5-fluorothieno[2,3-b]pyridin-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

methyl 2-acetamido-5-acetyl-4-(5-fluorothieno[2,3-b]pyridin-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

cyclopentylmethyl 5-acetyl-2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

3-(cyclopropylmethyl) 5-methyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

dimethyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-cyclopropyl-1,4-dihydropyridine-3,5-dicarboxylate

3-(cyclopropylmethyl) 5-methyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-cyclopropyl-1,4-dihydropyridine-3,5-dicarboxylate

dimethyl 2,6-diamino-4-(7-cyanobenzo[b]thiophen-3-yl)-1,4-dihydropyridine-3,5-dicarboxylate

5-(cyclopropylmethyl) 3-methyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-cyclopropyl-1,4-dihydropyridine-3,5-dicarboxylate

3-(4-fluorobenzyl) 5-methyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

3-(4-fluorobenzyl) 5-methyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-cyclopropyl-1,4-dihydropyridine-3,5-dicarboxylate

Cyclopropylmethyl 2-amino-5-cyano-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

4-Fluorobenzyl 2-amino-5-cyano-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

Cyclopropylmethyl 6-amino-5-cyano-4-(7-cyanobenzo[b]thiophen-3-yl)-2-cyclopropyl-1,4-dihydropyridine-3-carboxylate

3-Cyclopentyl 5-methyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

Cyclopropylmethyl 5-acetyl-2-amino-4-(6-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

Cyclohexyl 5-acetyl-2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

Cyclohexylmethyl 5-acetyl-2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

Cyclopropylmethyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-5-(cyclopropanecarbonyl)-6-methyl-1,4-dihydropyridine-3-carboxylate 3-Fluorobenzyl 5-acetyl-2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

3-(Cyclobutylmethyl) 5-methyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

3-((3,3-Difluorocyclobutyl)methyl) 5-methyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1 ,4-dihydropyridine-3, 5-dicarboxylate

Cyclopropylmethyl 2-amino-5-carbamoyl-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

3-((2,2-Difluorocyclopropyl)methyl) 5-methyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

5-Cyclopropyl 3-(cyclopropylmethyl) 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

3-((2,2-Difluorocyclopropyl)methyl) 5-methyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-cyclopropyl-1,4-dihydropyridine-3,5-dicarboxylate

3-(Cyclopropylmethyl) 5-methyl 2-amino-4-(7-cyano-5-fluorobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

3-(cyclopropylmethyl) 5-methyl 2-amino-4-(7-cyano-4-fluorobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

3-Isopropyl 5-methyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

3-((2,2-Difluoro-3,3-dimethylcyclopropyl)methyl) 5-methyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

5-Methyl 3-neopentyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

3-(Cyclopropylmethyl) 5-methyl 2-amino-4-(7-cyanothieno[3,2-b]pyridin-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

5-Methyl 3-neopentyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-cyclopropyl-1,4-dihydropyridine-3,5-dicarboxylate

Bis(cyclopropylmethyl) 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

3-(Cyclopropylmethyl) 5-(prop-2-yn-1-yl) 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

3-(Cyclopropylmethyl) 5-methyl 2-amino-4-(5,7-dicyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

5-(But-2-yn-1-yl) 3-(cyclopropylmethyl) 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

5-Methyl 3-(2,2,2-trifluoroethyl) 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

3-(Cyclopropylmethyl) 5-(2,2,2-trifluoroethyl) 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyri-

dine-3,5-dicarboxylate

3-(Cyclopropylmethyl) 5-methyl 2-amino-4-(6-chloro-7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

3-(2-Fluoro-2-methylpropyl) 5-methyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

3-(Cyclopropylmethyl) 5-methyl 2-amino-4-(7-cyano-6-(trifluoromethyl)benzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

5-Methyl 3-prop-2-yn-1-yl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

3-(Cyclopropylmethyl) 5-methyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-(trifluoromethyl)-1,4-dihydropyridine-3,5-dicarboxylate

4-(Benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarbonitrile

4-(6-hydroxybenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarbonitrile

4-(6-methoxybenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarbonitrile

2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3,5-dicarbonitrile

4-(benzo[b]thiophen-3-yl)-2-methyl-6-phenyl-1,4-dihydropyridine-3,5-dicarbonitrile

4-(benzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3,5-dicarbonitrile 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carbonitrile

Ethyl 4-(benzo[b]thiophen-3-yl)-5-cyano-2,6-dimethyl-1,4-dihydropyridine -3-carboxylate

Ethyl 4-(benzo[b]thiophen-3-yl)-5-cyano-2-methyl-6-phenyl-1,4-dihydropyridine-3-carboxylate

Ethyl 4-(benzo[b]thiophen-3-yl)-5-cyano-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate

Methyl 4-(benzo[b]thiophen-3-yl)-5-cyano-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate

1,1'-(4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-diyl)diethanone

1,1'-(4-(6-hydroxybenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-diyl)bis(ethan-1-one)

1,1'-(4-(6-Methoxybenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-diyl)diethanone

1,1'-(4-(Benzo[b]thiophen-3-yl)-2,6-dicyclopropyl-1,4-dihydropyridine-3,5-diyl)diethanone

1,1'-(4-(5-chlorobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-diyl)diethanone

1,1'-(4-(5-bromobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-diyl)diethanone

1,1'-(4-(5-fluorobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-diyl)bis(ethan-1-one)

1,1'-(2,6-dimethyl-4-(5-morpholinobenzo[b]thiophen-3-yl)-1,4-dihydropyridine-3,5-diyl)bis(ethan-1-one)

1,1'-(2,6-dimethyl-4-(5-(4-methylpiperazin-1-yl)benzo[b]thiophen-3-yl)-1,4-dihydropyridine-3,5-diyl)bis(ethan-1-one)

1,1'-(4-(5-(benzylamino)benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-diyl)bis(ethan-1-one)

3-(3,5-diacetyl-2,6-dimethyl-1,4-dihydropyridin-4-yl)benzo[b]thiophene-5-carbonitrile

3-(3,5-diacetyl-2,6-dimethyl-1,4-dihydropyridin-4-yl)benzo[b]thiophene-5-carboxylic acid

N-cyclopropyl-3-(3,5-diacetyl-2,6-dimethyl-1,4-dihydropyridin-4-yl)benzo[b]thiophene-5-carboxamide

N-(cyclopropylmethyl)-3-(3,5-diacetyl-2,6-dimethyl-1,4-dihydropyridin-4-yl)benzo[b]thiophene-5-carboxamide

1,1'-(2,6-Dimethyl-4-(5-(4-methylpiperazine-1-carbonyl)benzo[b]thiophen-3-yl)-1,4-dihydropyridine-3,5-diyl)bis(ethan- 1 -one)

1,1'-(2 ,6-Dimethyl-4-(5-(morpholine-4-carbonyl)benzo[b]thiophen-3-yl)-1 ,4-dihydropyridine-3,5-diyl)bis(ethan-1-one)

1,1'-(2,6-Dimethyl-4-(thieno[3,2-c]pyridin-3-yl)-1,4-dihydropyridine-3,5-diyl)bis(ethan-1-one)

1,1'-(2,6-Dimethyl-4-(thieno[2,3-c]pyridin-3-yl)-1,4-dihydropyridine-3,5-diyl)bis(ethan-1-one)

1,1'-(2,6-Dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3,5-diyl)bis(ethan-1-one)

Dimethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-2,3-dicarboxylate

Dimethyl 5-acetyl-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-2,3-dicarboxylate

Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate

Dimethyl 4-(benzo[b]thiophen-3-yl)-2,6-dicyclopropyl-1,4-dihydropyridine-3,5-dicarboxylate

Ethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

Methyl 5-acetyl-4-(5-chlorobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

1,1'-(4-(benzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydro-pyridine-3,5-diyl)diethanone

1-(4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-5-(methylsulfonyl)-1,4-dihydro-pyridin-3-yl)ethanone

Methyl 5-acetyl-4-(5-fluorobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

Methyl 5-acetyl-4-(5-bromobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

methyl 5-acetyl-4-(5-cyanobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

3-(3-acetyl-5-(methoxycarbonyl)-2,6-dimethyl-1,4-dihydropyridin-4-yl)benzo[b]thiophene-5-carboxylic acid

methyl 5-acetyl-4-(5-(cyclopropylcarbamoyl)benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

Methyl 5-acetyl-4-(5-((cyclopropylmethyl)carbamoyl)benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

Methyl 5-acetyl-2,6-dimethyl-4-(5-(4-methylpiperazine-1-carbonyl)benzo[b]thiophen-3-yl)-1 ,4-di hydropyridine-3-carboxylate

Methyl 5-acetyl-2,6-dimethyl-4-(5-(morpholine-4-carbonyl)benzo[b]thiophen-3-yl)-1,4-dihydropyridine-3-carboxylate

Methyl 5-acetyl-2,6-dimethyl-4-(thieno[3,2-c]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

Methyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-c]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

Methyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

Methyl 5-acetyl-2-cyclopropyl-4-(5-fluorobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

Dimethyl 2,6-dicyclopropyl-4-(5-fluorobenzo[b]thiophen-3-yl)-1,4-dihydropyridine-3,5-dicarboxylate

Methyl 5-acetyl-2-cyclopropyl-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

Dimethyl 2,6-dicyclopropyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3,5-dicarboxylate

Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dicyclopropyl-1,4-dihydropyridine-3-carboxylate

Methyl 5-acetyl-4-(5-chlorobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate

Dimethyl 4-(5-chlorobenzo[b]thiophen-3-yl)-2,6-dicyclopropyl-1,4-dihydropyridine-3,5-dicarboxylate

Methyl 5-acetyl-4-(7-bromobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate

Methyl 5-acetyl-2-cyclopropyl-4-(7-(cyclopropylcarbamoyl)benzo[b] thiophen-3-yl)-6-methyl-1 ,4-di hydropyridine-3-carboxylate

Methyl 5-acetyl-4-(7-cyanobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate

Dimethyl 4-(7-cyanobenzo[b]thiophen-3-yl)-2,6-dicyclopropyl-1,4-dihydropyridine-3,5-dicarboxylate

Methyl 5-acetyl-2-cyclopropyl-4-(7-(methoxycarbonyl) benzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

Dimethyl 2,6-dicyclopropyl-4-(7-(methoxycarbonyl)benzo[b]thiophen-3-yl)-1,4-dihydropyridine-3,5-dicarboxylate

3-(3-Acetyl-6-cyclopropyl-5-(methoxycarbonyl)-2-methyl-1,4-dihydropyridin-4-yl)benzo[b]thiophene-7-carboxylic acid

Benzyl 5-acetyl-2-cyclopropyl-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

Pyridin-4-ylmethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate

bis(pyridin-4-ylmethyl) 2,6-dicyclopropyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3,5-dicarboxylate

Pyridin-4-ylmethyl 5-acetyl-4-(7-bromobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

Pyridin-4-ylmethyl 5-acetyl-4-(5-chlorobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate

Pyridin-4-ylmethyl 5-acetyl-4-(7-cyanobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate

Pyridin-4-ylmethyl 5-acetyl-2-cyclopropyl-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

Benzyl 5-acetyl-2-cyclopropyl-4-(7-(methoxycarbonyl)benzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

Dibenzyl 2,6-dicyclopropyl-4-(7-(methoxycarbonyl)benzo[b]thiophen-3-yl)-1,4-dihydropyridine-3,5-dicarboxylate

Benzyl 5-acetyl-4-(7-(methoxycarbonyl)benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

Methyl 3-(3,5-diacetyl-2,6-dimethyl-1,4-dihydropyridin-4-yl)benzo[b]thiophene-7-carboxylate

3-(3,5-Diacetyl-2,6-dimethyl-1,4-dihydropyridin-4-yl)benzo[b]thiophene-7-carbonitrile

Pyridin-4-ylmethyl 5-acetyl-4-(7-bromobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate

4-Fluorobenzyl 5-acetyl-2-cyclopropyl-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

bis(4-fluorobenzyl) 2,6-dicyclopropyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3,5-dicarboxylate

4-cyanobenzyl 5-acetyl-2-cyclopropyl-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

Methyl 5-acetyl-4-(7-chlorobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate

methyl 5-acetyl-2-cyclopropyl-6-methyl-4-(7-(trifluoromethyl)benzo[b]thiophen-3-yl)-1,4-dihydropyridine-3-carboxylate

3-chlorobenzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

2-phenylpropan-2-yl 5-acetyl-4-(7-bromobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate

Cyclohexyl 5-acetyl-2-cyclopropyl-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

2-Phenylpropan-2-yl 5-acetyl-2-cyclopropyl-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

1-(4-(7-Bromobenzo[b]thiophen-3-yl)-5-(cyclopropanecarbonyl)-6-cyclopropyl-2-methyl-1,4-dihydropyridin-3-yl)ethan-1-one

3-chlorobenzyl 5-acetyl-2-cyclopropyl-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

2-(4-Fluorophenyl)propan-2-yl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

2-(4-fluorophenyl)propan-2-yl 5-acetyl-4-(7-bromobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate

2-(4-fluorophenyl)propan-2-yl 5-acetyl-2-cyclopropyl-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

Methyl 5-acetyl-2-cyclopropyl-4-(7-fluorobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

Cyclopropylmethyl 5-acetyl-2-cyclopropyl-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

Cyclopentyl 5-acetyl-2-cyclopropyl-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

Cyclopropylmethyl 5-acetyl-4-(7-cyanobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate

Methyl 5-acetyl-4-(7-bromobenzo[b]thiophen-3-yl)-2-cyclobutyl-6-methyl-1,4-dihydropyridine-3-carboxylate

Dimethyl 4-(7-cyanobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

Methyl 5-cyano-4-(7-cyanobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate

Methyl 5-acetyl-4-(7-bromobenzo[b]thiophen-3-yl)-2-cyclopentyl-6-methyl-1,4-dihydropyridine-3-carboxylate

Methyl 5-acetyl-4-(7-bromobenzo[b]thiophen-3-yl)-2-cyclohexyl-6-methyl-1,4-dihydropyridine-3-carboxylate

Methyl 5-cyano-4-(7-cyanobenzo[b]thiophen-3-yl)-2,6-dicyclopropyl-1,4-dihydropyridine-3-carboxylate

3-((4-Methylpiperazin-1-yl)methyl)benzyl 5-acetyl-4-(7-bromobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

3-(cyclopropylmethyl) 5-methyl 4-(7-cyanobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

3-(cyclopropylmethyl) 5-methyl 4-(7-cyanobenzo[b]thiophen-3-yl)-2,6-dicyclopropyl-1,4-dihydropyridine-3,5-dicarboxylate

cyclopropylmethyl 5-cyano-4-(7-cyanobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate

dimethyl 2-cyano-4-(7-cyanobenzo[b]thiophen-3-yl)-6-cyclopropyl-1,4-dihydropyridine-3,5-dicarboxylate

dimethyl 2-cyano-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

methyl 5-acetyl-2-((2-aminoethoxy)methyl)-4-(benzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

methyl 5-acetyl-2-((2-aminoethoxy)methyl)-4-(7-bromobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

methyl 5-acetyl-2-((2-aminoethoxy)methyl)-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

Dimethyl 4-(7-cyanobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-formyl-1,4-dihydropyridine-3,5-dicarboxylate

Dimethyl 4-(7-cyanobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-(hydroxymethyl)-1,4-dihydropyridine-3,5-dicarboxylate

Dimethyl 4-(7-cyanobenzo[b]thiophen-3-yl)-2-formyl-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

Dimethyl 4-(7-cyanobenzo[b]thiophen-3-yl)-2-(hydroxymethyl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

Dimethyl 2-cyano-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3,5-dicarboxylate

Cyclopropylmethyl 5-acetyl-4-(6-cyanobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate

Cyclopropylmethyl 2,5-diacetyl-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

Methyl 5-acetyl-2-amino-4-(benzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate hydrochloride

Methyl 5-acetyl-2-amino-4-(benzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate trifluoromethanesulfonate

4-(Pyridin-4-yl)benzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4 dihydropyridine-3-carboxyl ate

4-(Pyridin-3-yl)benzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxyl ate

3-(Pyridin-4-yl)benzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

3-(Pyridin-3-yl)benzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

2-(Pyridin-4-yl)benzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

2-(pyridin-3-yl)benzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[3,4'-Bipyridin]-5-ylmethyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[3,3'-Bipyridin]-5-ylmethyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[2,4'-Bipyridin]-5-ylmethyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[2,3'-Bipyridin]-5-ylmethyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[2,3'-Bipyridin]-4-ylmethyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[2,4'-Bipyridin]-4-ylmethyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

Methyl 5-acetyl-2-cyclopropyl-6-methyl-4-(7-(pyridin-4-yl)benzo[b]thiophen-3-yl)-1,4-dihydropyridine-3-carboxylate

Methyl 5-acetyl-2-cyclopropyl-4-(7-cyclopropylbenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

3-(Pyridin-4-yl)benzyl 5-acetyl-2-cyclopropyl-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

1,1'-(2 ,6-Dimethyl-4-(5-(pyridin-3-yl)benzo[b]thiophen-3-yl)-1 ,4-dihydro-pyridine-3,5-diyl)diethanone

Methyl 5-acetyl-2-cyclopropyl-6-methyl-4-(7-phenylbenzo[b]thiophen-3-yl)-1,4-dihydropyridine-3-carboxylate

[0064] When the compounds of the present invention are combined with other therapeutic agents, said other therapeutic agents are selected from the group consisting of:

A - hormone therapy agents such as:

1- gonadotropin-releasing hormone (GnRH) receptor agonists or antagonists;
2- androgen receptor antagonists and CYP17 inhibitors;

B - blockers of oncogenic kinases signaling pathways such as:

1- inhibitors of Vascular Endothelial Growth Factor (VEGF),
2- inhibitors of Epidermal Growth Factor Receptor (EGFR),
3- inhibitors of phosphoinositide 3-kinase (PI3K),
4- Protein kinase B, also known as AKT,
5- mechanistic target of rapamycin (mTOR),
6- c-Met, also called MET or hepatocyte growth factor receptor (HGFR)
7- Src, (nonreceptor tyrosine kinases)
8- poly(ADP-ribose) polymerase (PARP),
9- angiopoietin,
10-Anaplastic lymphoma kinase also known as ALK tyrosine kinase receptor, and
11-anti-Insulin-like growth factors (IGF) antibodies;

C - cancer chemotherapy agents such as:

1- taxane anti-neoplastic agents,
2- topoisomerase II inhibitors,
3- anti-tumor antibiotics;
4- HSP90 (heat shock protein 90) inhibitors;

D - agents targeting neuroendocrine differentiation such as:

1- Aurora kinase inhibitors;

E - agents targeting immune evasion such as Prostate Specific Antigen (PSA) -directed vaccines
F - agents or natural extracts known to promote hair growth;
G - agents or natural extracts known to treat acne;
H - agents or natural extracts known to treat hirsutism;
I - agents known to treat conditions caused by elevated levels of cortisol such as:

1- GR antagonists,
2- 11-beta HSD inhibitors; and

J - one or more immunotherapeutic agent selected from the group consisting of antibodies anti-CTLA4, antibodies anti-PD1 and antibodies anti-PDL1; more preferably, the immunotherapeutic agent is selected from the group consisting of ipilimumab, tremelimumab, nivolumab, pembrolizumab, CT-011, AMP-224, MPDL3280A, MEDI4736 and MDX-1105.

[0065] Examples of gonadotropin-releasing hormone (GnRH) receptor agonists include, but are not limited to leuprolide, goserelin, and buserelin. Examples of gonadotropin-releasing hormone (GnRH) receptor antagonist include, but are not limited to degarelix and abarelix, among others.

[0066] Examples of androgen receptor antagonists include but are not limited to nilutamide, bicalutamide, flutamide and enzalutamide.

[0067] Examples of CYP17 inhibitors include but are not limited to abiraterone and gleterone.

[0068] Examples of VEGF receptor inhibitors include, but are not limited to bevacizumab, axitinib and brivanib alaninate.

[0069] Examples of EGFR inhibitors include, but are not limited to gefitinib, afatinib, cetuximab and panitumumab.

[0070] Examples of PI3K inhibitors include, but are not limited to pictilisib (also known as GDC 0941) and BKM120.

[0071] Examples of mTOR inhibitors include, but are not limited to temsirolimus, ridaforolimus and everolimus.

[0072] Examples of dual PI3K and mTOR inhibitors include, but are not limited to Apitolisib (GDC-0980), dactolisib (BEZ235) and LY3023414.

[0073] Examples of AKT inhibitors include, but are not limited to A-443654, perifosine and ipatasertib.

[0074] Examples of c-Met inhibitors include, but are not limited to tivantinib, JNJ-38877605, cabozantinib and capmatinib.

[0075] Examples of Src blockers include, but are not limited to dasatinib, saracatinib, bosutinib, and KX01, which are in clinical development.

[0076] Examples of PARP inhibitors include, but are not limited to olaparib and veliparib.

[0077] Examples of ALK inhibitors include, but are not limited to X-396, alectinib, ceritinib, lorlatinib and crizotinib (dual ALK and ROS-1 inhibitor).

[0078] Examples of anti-IGF antibodies include, but are not limited to figitumumab, ganitumab and BI836845.

[0079] Examples of taxane anti-neoplastic agents include, but are not limited to cabazitaxel and larotaxel.

[0080] Examples of topoisomerase II inhibitors include, but are not limited to etoposide and teniposide.

[0081] Examples of anti-tumor antibiotics include, but are not limited to doxorubicin, bleomycin, daunorubicin, daunorubicin liposomal, mitoxantrone, epirubicin, idarubicin, and mitomycin C.

[0082] Examples of HSP90 (heat shock protein 90) inhibitors include, but are not limited to Debio 0932, MPC-3100, IPI-504, NVP-AUY922.

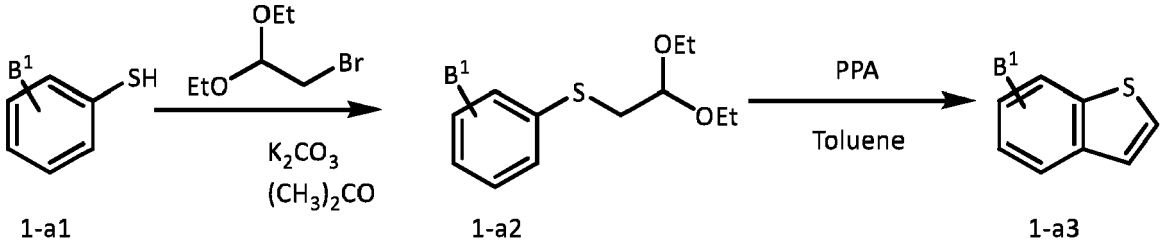
[0083] Examples of Aurora kinase inhibitors include, but are not limited to alisertib, tozasertib, danusertib and barasertib.

[0084] Examples of PSA-directed vaccine include, but are not limited to ProstVac-VF.

[0085] The compounds of this invention can be prepared by using the procedures described below. To facilitate the description of the procedures, concrete examples have been used in some cases, however they do not restrict in any way the scope of the present invention.

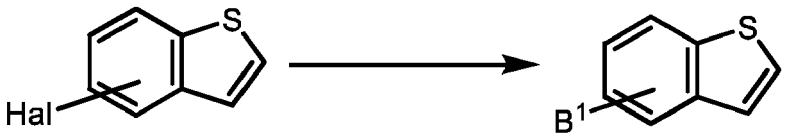
[0086] When one of X^1, X^2, X^3, X^4 and X^5 represents C-B^1 and the rest of X^1, X^2, X^3, X^4 and X^5 represent C-H the compounds of formula (I) are benzothiophenes of formula (1-a3), as depicted in Scheme 1-a and can be obtained be reacting thiophenol precursor (1-a1), where B^1 is selected from halogen, alkyl, haloalkyl, cycloalkyl, heterocycloalkyl and aryl, with 2-bromo-1,1-diethoxyethane and potassium carbonate in acetone affording intermediates (1-a2) which are cyclized to benzothiophenes (1-a3) by heating with polyphosphoric acid in toluene.

Scheme 1-a



[0087] When one of X^1, X^2, X^3, X^4 and X^5 represents C-B^1 and the rest of X^1, X^2, X^3, X^4 and X^5 represent C-H the compounds of formula (I) are benzothiophene intermediates of formula (III), as depicted in Scheme 1-b, can be obtained from halogen precursor (II), where halogen (Hal) is selected from chloro, iodo or preferentially bromo.

Scheme 1-b



(II) (III)

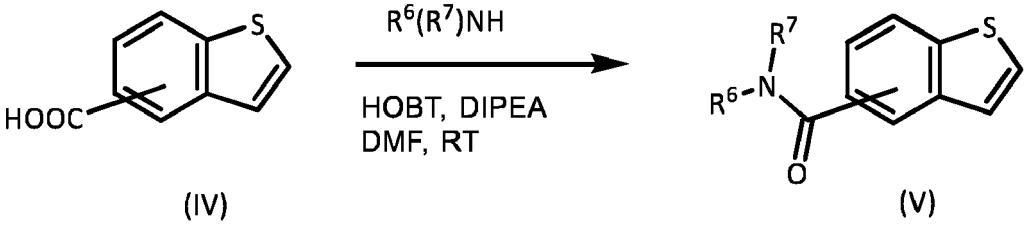
[0088] More specifically, when B^1 represents -C(O)CF_3, one way to synthesize benzothiophene derivatives of formula (III) is by reacting the halogen precursor (II), specifically bromo precursor, with n-butyllithium and 2,2,2-trifluoro-1-morpholinoethan-1-one in diethyl ether at -60°C.

[0089] When B^1 represents -CN, the cyano group can be introduced by heating the halogen precursor (II), specifically bromo precursor, with zinc cyanide and tetrakis(triphenylphosphine)palladium(0) in a sealed tube at 90°C. The cyano derivative (III) can be converted into the carboxylic acid by heating with potassium hydroxide in methanol and water at 80°C, which can be further transformed into the methyl ester by refluxing in saturated HCl in methanol.

[0090] When B^1 represents mono- or dialkylamino, one way to synthesize benzothiophene derivatives of formula (III) is by refluxing the halogen precursor (II), specifically bromo precursor, with the corresponding amine, $Pd_2(dba)_3$, tricyclohexylphosphine and NaOtBu in dry toluene.

[0091] When B^1 represents mono- or dialkylaminocarbonyl, benzothiophene intermediates of formula (V) can be obtained by reacting carboxylic acid precursor (IV) with the corresponding amine, HOBT and DIPEA in DMF at room temperature, as depicted in Scheme 2.

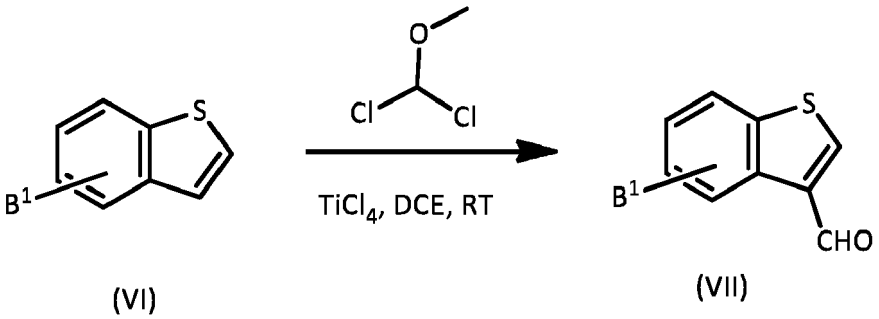
Scheme 2



(IV) (V)

[0092] 3-formylbenzo[b]thiophenes of formula (VII) can be obtained by reacting precursor (VI) with dichloro(methoxy)methane and titanium tetrachloride in dichloroethane at room temperature as represented in reaction Scheme 3.

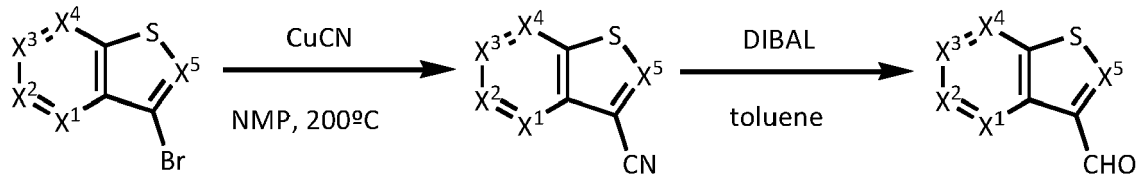
Scheme 3



(VI) (VII)

[0093] Another way of introducing a formyl group in position 3 of the bicyclic heterocycle (X), as depicted in reaction Scheme 4, is by heating the 3-bromo derivative (VIII) with copper(I) cyanide in NMP at 200°C and subsequent reduction with DIBAL in toluene.

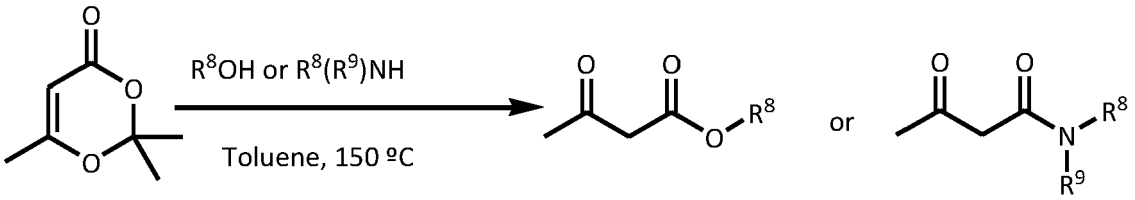
Scheme 4



(VIII) (IX) (X)

[0094] One way to synthesize dicarbonyl intermediates of formula (XI) and (XII) (used in the synthesis of compounds of formula (I) wherein R^2 represents -$COOR^8$ or - $C(O)N(R^8)R^9$) is by heating commercially available 2,2,6-trimethyl-4H-1,3-dioxin-4-one and the corresponding alcohol or amine in toluene at 150 °C, as represented by the acetoacetylation reaction depicted in reaction Scheme 5.

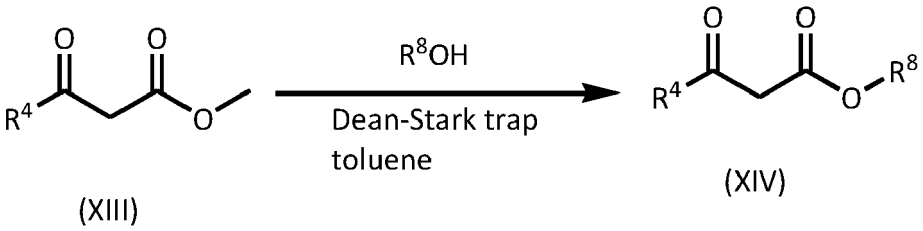
Scheme 5



(XI) (XII)

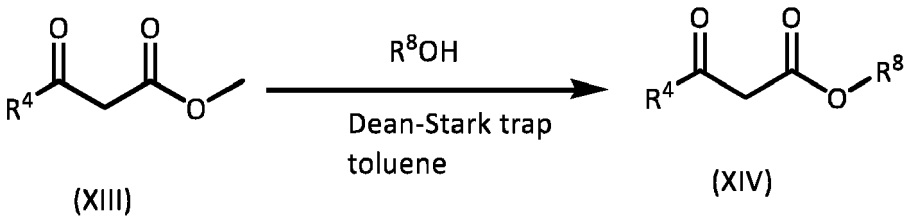
[0095] One way to synthetize dicarbonyl intermediates (XIV) (used in the synthesis of compounds of formula (I) wherein R^4 represents alkyl, cycloalkyl, phenyl or heteroaryl) is by reesterification in which methyl ester (XIII) and an alcohol are refluxed in dry toluene using a Dean-Stark trap, as shown in Scheme 6.

Scheme 6



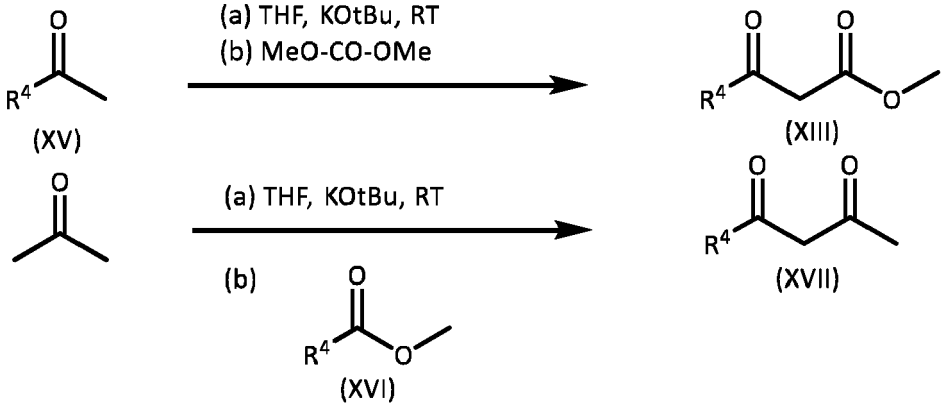
[0096] Another reesterification method affords dicarbonyl intermediates (XIV) by refluxing methyl ester (XIII) and an alcohol in dry toluene in a sealed tube using 10 mol-% trichlorobismuthane and molecular sieves, as represented in Scheme 7.

Scheme 7



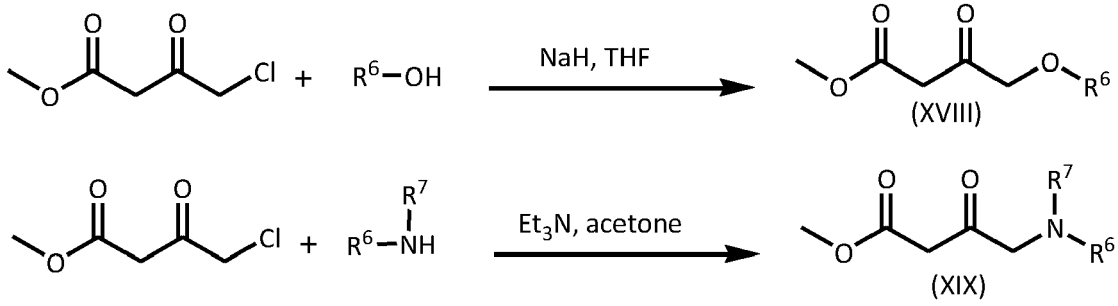
[0097] Dicarbonyl intermediates of formula (XIII) and (XVII) (used in the synthesis of compounds of formula (I) wherein R^2 represents -COR^8 or -$COOR^8$) can be synthesized via Claysen condensation by treating a methylketone derivative (XV) or acetone with potassium tert-butoxide in THF and reacting the mixture with either dimethyl carbonate or a methyl or ethyl ester (XVI), as represented in reaction Scheme 8.

Scheme 8



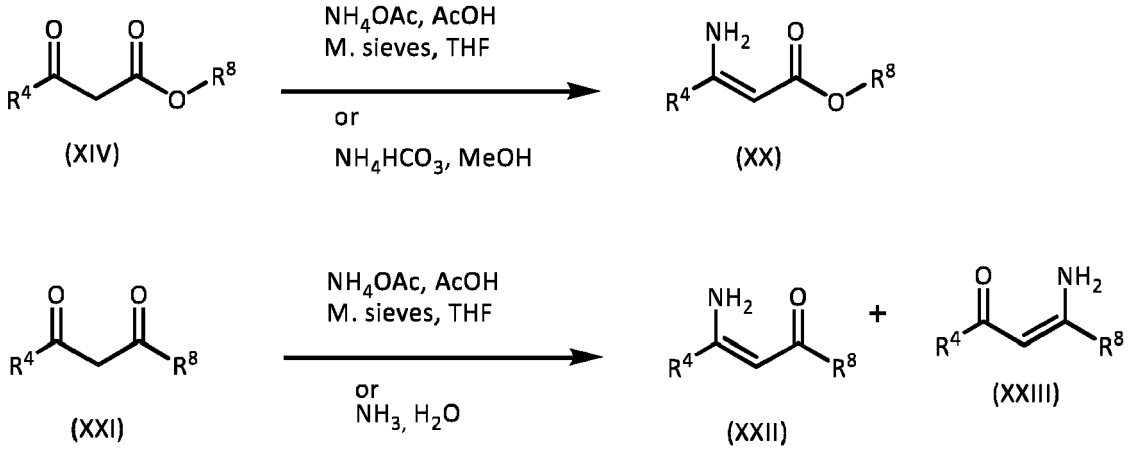
[0098] Ketoester intermediates of formula (XVIII) (used in the synthesis of compounds of formula (I) wherein R^2 represents -$COOR^8$ and R^4 represent -CH_2OR^6 or-$CH_2N(R^6)R^7$) can be synthesized by deprotonating an alcohol with sodium hydride in THF and treating the mixture with methyl 4-chloro-3-oxobutanoate, as represented in reaction Scheme 9. Ketoester intermediates of formula (XIX) can be synthesized accordingly by heating methyl 4-chloro-3-oxobutanoate with an amine in acetone and trimethylamine.

Scheme 9



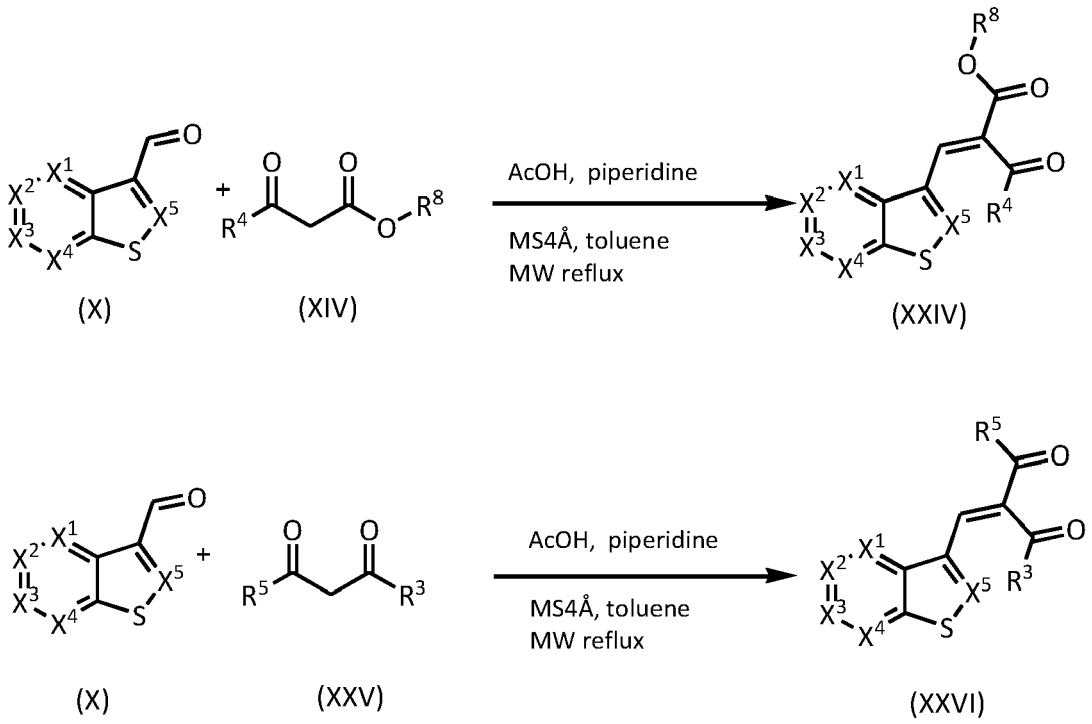
[0099] 1,3-ketoester intermediates of formula (XIV) can be transformed into enamines (XX) either by heating with ammonium acetate, acetic acid and molecular sieves in THF or by reacting with ammonium bicarbonate in methanol, as represented in reaction Scheme 10. Accordingly, 1,3-diketones (XXI) can be converted into a mixture of enamines (XXII) and (XXIII) using the procedure described above or, alternatively, by reaction in aqueous ammonia.

Scheme 10



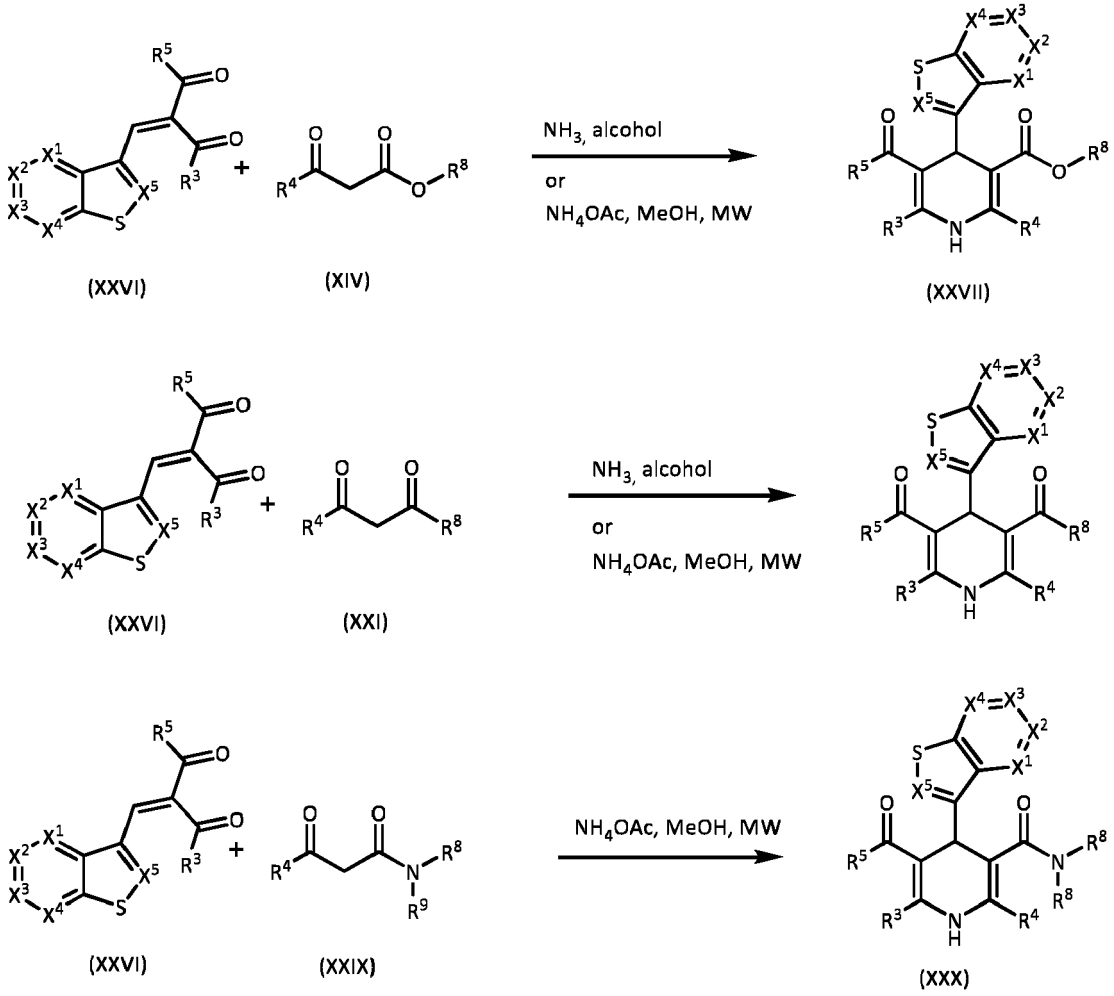
[0100] Knoevenagel products of formula (XXIV) and (XXVI) can be prepared by reacting aldehydes (X) (e.g. benzo[b]thiophene-3-carbaldehyde) and 1,3-dicarbonyl intermediates (XIV) or (XXV), respectively, with acetic acid, piperidine and molecular sieves in toluene in the microwave oven, as adapted from Liu & Zhang, Angew. Chem. Int. Ed. 2009, 48, 6093-6 and represented in reaction Scheme 11.

Scheme 11



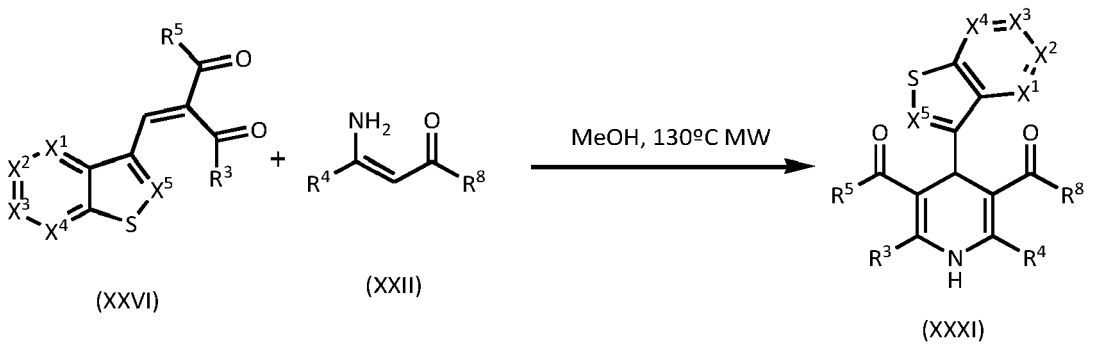
[0101] Dihydropyridines of formula (XXVII) and (XXVIII) can be prepared in a 3-component Hantzsch synthesis by heating Knoevenagel products (XXVI) with 1,3-dicarbonyl compounds (XIV), (XXI) or (XXIX) and ammonia in alcohols such as e.g. isopropanol, ethanol or 2,2,2-trifluoroethanol, as represented in reaction Scheme 12. Instead of ammonia, NH_4OAc in MeOH under microwave conditions can be used to synthesize dihydropyridines of formula (XXVII), (XXVIII) and (XXX).

Scheme 12

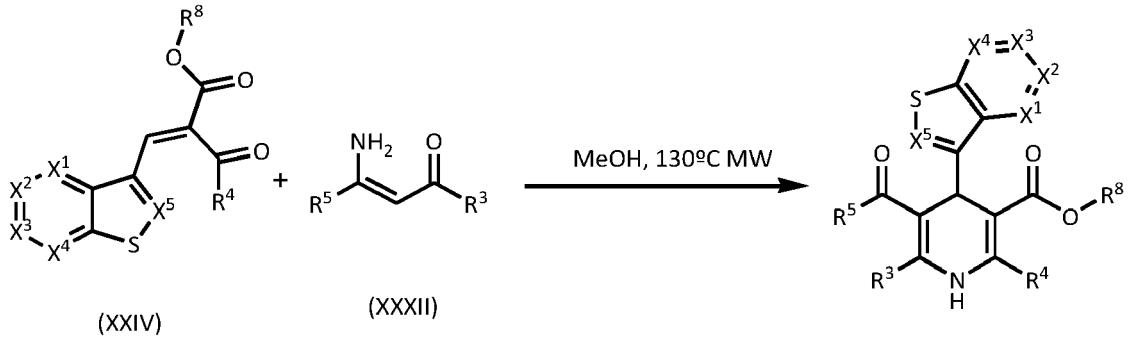


[0102] Another way of preparing dihydropyridines (XXXI) and (XXXIII) is by heating Knoevenagel products (XXVI) or (XXIV) with enamines (XXII) or (XXXII), respectively, in methanol under microwave conditions (Scheme 13).

Scheme 13



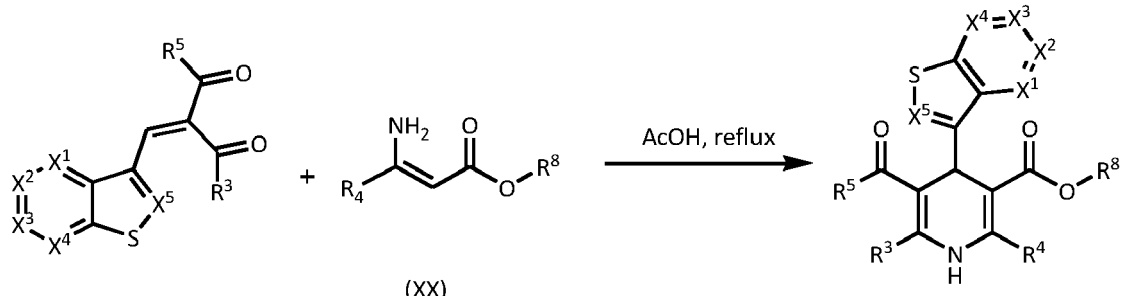
(XXVI) (XXII) (XXXI)



(XXIV) (XXXII) (XXXIII)

[0103] Dihydropyridines of formula (XXXIII) can also be prepared by heating Knoevenagel products (XXVI) and enamines (XX) in AcOH, as represented in reaction Scheme 14.

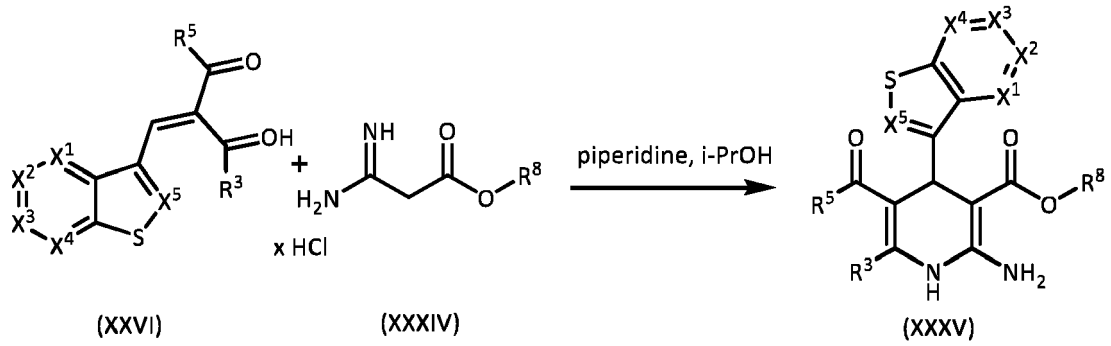
Scheme 14



(XXVI) (XX) (XXXIII)

[0104] Dihydropyridines of formula (XXXV) (which are used as intermediates in the synthesis of compounds of formula (I) wherein R^4 represents $-NH_2$) can be synthesized by heating Knoevenagel product (XXVI) and amidine (XXXIV) with piperidine in isopropanol, as represented in reaction Scheme 15.

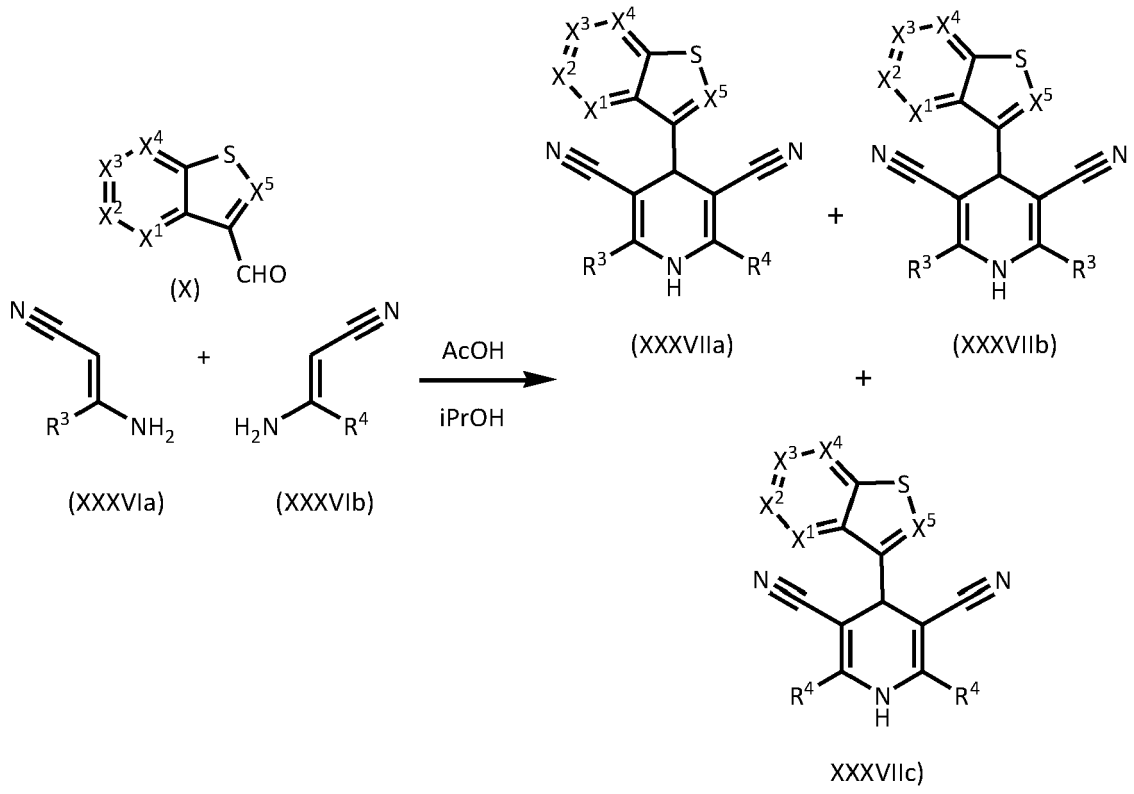
Scheme 15



(XXVI) (XXXIV) (XXXV)

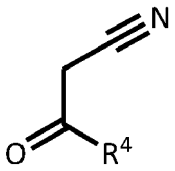
[0105] The dihydropyridine scaffold can be assembled without prior formation of a Knoevenagel product. For example, compounds of formula (I) in which R^1 and R^2 both represent -CN, can be synthesized by heating aldehyde (X) and enamines (XXXVIa) and (XXXVIb) with acetic acid in isopropanol, as represented in reaction Scheme 16. When R^3 is not equal to R^4, mixtures of dihydropyridines (XXXVIIa), (XXXVIIb) and (XXXVIIc) are obtained that need to be separated, e.g. by column chromatography.

Scheme 16



(X) (XXXVIa) (XXXVIb) (XXXVIIa) (XXXVIIb) XXXVIIc)

[0106] In a variation of the method described above, one of the enamines, e.g. (XXXVIb), can be replaced by a ketone, e.g. (XXXVIc), to prepare the same mixture of dihydropyridines (XXXVIIa), (XXXVIIb) and (XXXVIIc).



(XXXVIc)

[0107] The reaction conditions described above in Scheme 16 (heating with acetic acid in alcohols such as e.g. isopropanol, optionally in the presence of substoichiometric amounts of piperidine) can be utilized in a wider scope to synthesize dihydropyridines of formula (I), in which R^1 represents either -CHO, -COR^5 or -CN and R^2 is selected from -COR^8, -$S(O)_nR^8$ (wherein n is 1 or 2), -$COOR^8$ and -$C(O)N(R^8)R^9$, provided that an aldehyde (X) (e.g. benzo[b]thiophene-3-carbaldehyde) is reacted with:

(a) two enamines as exemplified by, but not limited to, the compounds of formulae (XX), (XXII), (XXIII), (XXXII) or (XXXVIa/b), or

(b) one enamine as exemplified by, but not limited to, the compounds of formulae (XX), (XXII), (XXIII), (XXXII) or (XXXVIa/b) and a 1,3-dicarbonyl compound as exemplified by, but not limited to, the compounds of formulae (XIV), (XXV) or (XXIX).

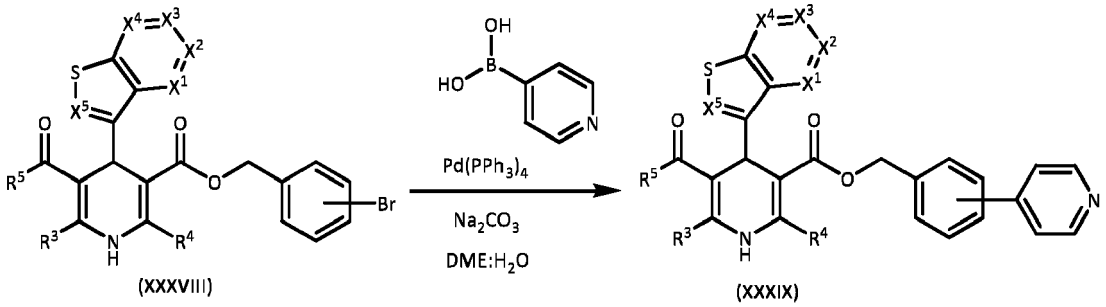
[0108] The enamines described above can also be formed in situ giving rise to yet another variation of the Hantzsch synthesis of the dihydropyridine scaffold in which compounds of formula (I) are prepared in a 4-component reaction by heating an aldehyde (e.g. benzo[b]thiophene-3-carbaldehyde), two 1,3-dicarbonyl compounds (e.g. compounds of formula (XIV), (XXV) or (XXIX)) and aqueous ammonia in alcohols (e.g. ethanol).

[0109] The methods for synthesizing the 1,4-dihydropyridine scaffold, as described above, are variations of the well documented Hantzsch Reaction that has been reviewed, for example, in "Hantzsch reaction: Recent advances in Hantzsch 1,4-dihydropyridines", A. Saini et al., J Scient Indust Res 2008, 67, 95-111.

[0110] Dihydropyridines of formula (I) bearing halogen atoms, such as -Br, on an aromatic ring, can be further derivatized by metal-catalyzed coupling reactions in which the halogen atom is replaced by e.g. aryl, heteroaryl or small alkyl groups (Suzuki coupling), by amines (Buchwald coupling) or by a cyano group (Zn coupling).

[0111] For example, halogen-substituted benzyl esters of formula (XXXVIII) can be coupled with pyridinylboronic acid (or other heteroaryl, phenyl or alkyl boronic acids) by heating both components with a palladium catalyst, e.g. palladium-tetrakis(triphenylphosphine), and a base, e.g. potassium carbonate, in a 3:1 mixture of DME and water to afford dihydropyridine (XXXIX) as represented in Scheme 17.

Scheme 17

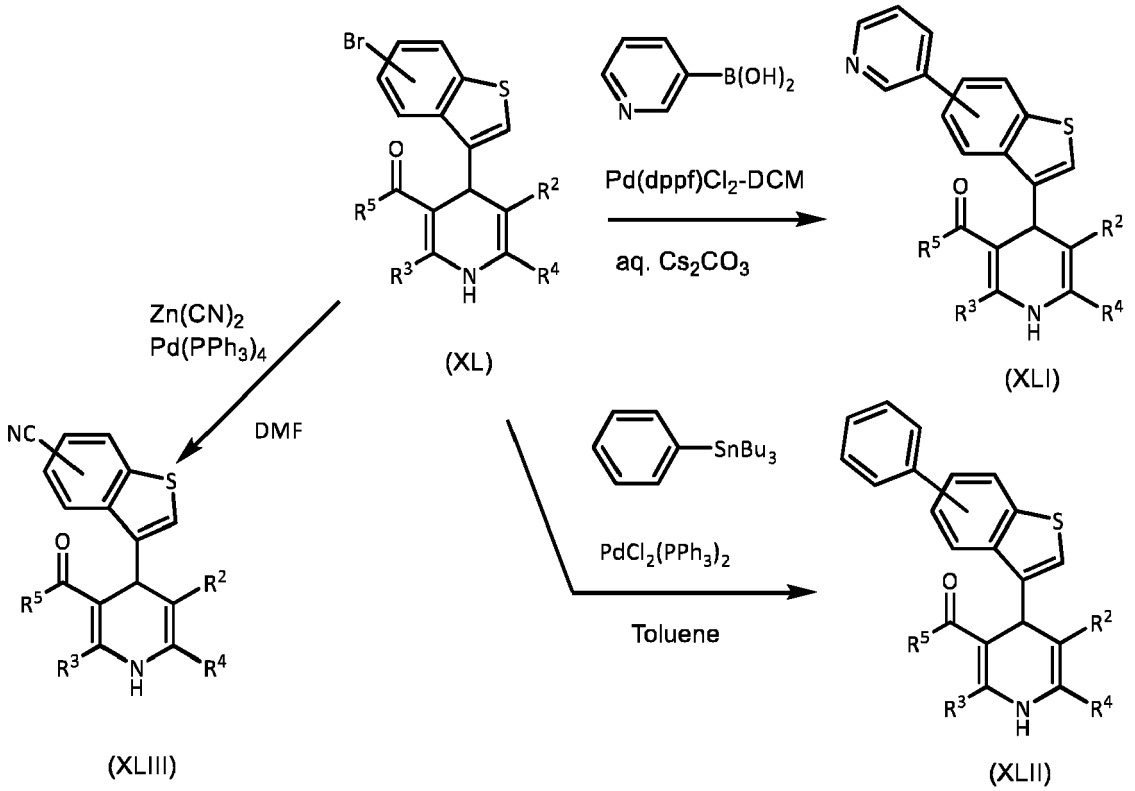


[0112] In another example, benzothiophenes of formula (XL) that are substitued with halogen atoms as depicted in Scheme 18, can be converted into compounds of formula (XLI) by Suzuki coupling with pyridylboronic acid utilizing a catalyst (e.g. Pd(dppf)Cl_2*DCM) and aqueous CS_2CO_3 in dichloromethane at reflux temperature. In yet another example, coupling of halogen-substituted benzothiophenes (XL) with stannanes, like e.g. tributyl(phenyl) stannane, using catalysts such as palladium(II)bis(triphenylphosphine)dichloride in hot toluene (2 mL) afford compounds of formula (XLII).

[0113] The bromine atom of benzothiophenes (XL) shown in Scheme 18 can be displaced by a cyano group by heating

with $Zn(CN)_2$ and $Pd(PPh_3)_4$ in DMF to afford dihydropyridines of formula (XLIII).

Scheme 18



Pharmacological activity

Rat androgen receptor binding

[0114] The assay was carried out following the instructions of polarscreen AR competitor assay green kit (*Life Technologies,* Cat#.: A15880). Briefly, the test is based on measuring the changes of fluorescence polarization shown by the Fluormone AL Green. Thus, when the Fluormone is bound to the receptor, a fluorescence polarization is observed that diminishes when a ligand competes for the receptor binding site and the Fluormone gets displaced.

[0115] The inhibition values for each of the compounds are measured in duplicate at 1 and 10 μM) and the plate is incubated for 4 hours at RT. Fluorescence polarization is the measured in a Tecan Infinite M1000 Pro reader (Aexc=485 nm, λem=535 nm). In order to obtain a dose-response curve and calculate the potency of inhibition (expressed as IC_{50}) for AR, a series of 1:10 dilutions in test in 1 X buffer from 10 μM) to 0.1 nM for each compound was carried out.

Human androgen receptor binding

[0116] Radioligand binding studies were carried out on endogenously expressed human androgen receptor using the LnCap prostate cancer cell line. The test is based on measuring radioactively labelled AR ligand [^{3}H]-methyltrienolone that gets displaced by increasing concentrations of test compound. The test is performed in 96-well plates (Falcon, #353072). Positive and negative controls are also required in each analyzed plate to evaluate the total and non-specific binding binding of the radioligand to the receptor. Cells (60000 per well) were incubated for 24 hours before executing the experiment at 37°C and in a 5% CO_2 atmosphere. Medium was replaced by assay buffer (RPMI-640 (ATCC #30-2001) supplemented with 0.1% bovine serum albumin (Sigma #8806-56) and Triamcinolone acetonide (Sigma #T6501)). The compounds at the desired concentrations and [^{3}H]methyltrienolone (Perkin Elmer #NET590) were added to the wells.

Table 1: Test conditions

	Sample	Non-specific binding	Total binding
Assay buffer	80 μL	80 μL	90 μL
Compound (10x)	10 μL		
[^{3}H]methyltrienolone (20 nM)	10 μL	10 μL	10 μL
Testosterone (200 μM)		10 μL	

[0117] In order to obtain a dose-response curve and calculate the potency of inhibition (expressed as IC_{50}) for AR, a series of 1:10 dilutions in test in 1 X buffer from 10 μM) to 0.1 nM for each compound was carried out.

[0118] Cells were incubated for 2 hours at 37°C in a 5% CO_2 atmosphere and then washed twice with ice-cold HBSS. Then cells were lysed with solubilization buffer (Hank's Balanced Salt Solution (HBSS, Sigma # H6648), 0.5% Sodium dodecyl sulfate 0.5% (SDS, Sigma #L7390-500G, Lote: 078K0102) and 20% Glycerol (Sigma Aldrich, #G2025) for 30 minutes at RT. 75 μL aliquots were taken from each well and transferred to a 96-well flexiplate (Perkin Elmer #1450-401) and mixed with 100 μL of scintillation cocktail (Optiphase supermix, PerkinElmer, # 1200-439). Plates are shaken for 60 minutes and radioactivity was measured in a beta scintillation counter (Microbeta Trilux, Perkin Elmer).

Competition binding in IM-9 human glucocorticoid receptor (GR IM-9)

[0119] Glucocorticoid receptor competition binding assays were carried out in a polypropilene 96-well plate. In each well was incubated 100 μg of cytosol from IM-9 cell line, 1.5 nM [3H]-Dexamethasone (71 Ci/mmol, 1 mCi/ml, Perkin Elmer NET1192001MC) and compounds studied and standard. Non-specific binding was determined in the presence of Triamcinolone 10μM (Sigma Aldrich T6376).

[0120] The reaction mixture (Vt: 200 μl/well) was incubated at 4°C for 6 hours, 180 μL was transfered to GF/B 96-well plate (Millipore, Madrid, Spain) pretreated with 0.5% of PEI and treated with binding buffer (TES 10mM, sodium molybdate 10mM, EDTA 1 mM, pH 7.4, 2-mercaptoethanol 20 mM,Glycerol 10%) after was filtered and washed six times with 250 μl wash buffer (TES 10mM, sodium molybdate 10mM, EDTA 1 mM, pH 7.4, 2-mercaptoethanol 20 mM ,Glycerol 10%), before measuring in a microplate beta scintillation counter (Microbeta Trilux, PerkinElmer, Madrid, Spain).

Functional Assay AR-receptor

[0121] MDA-MB-453 cells were cultured in DMEM (ATCC, ref 30-2002), 10% FBS, 1% penicillin, 1% streptomycin, 75 μg/ml gentamycin.

[0122] The day before performing assay, the cells were trypsinized and seeded in a 384-well plate (Greiner, ref 781098) (8000 cells/well) in 50 μl of complete culture medium. Cells were stores at 37°C in a 5% CO_2 atmosphere overnight.

[0123] The medium was replaced by 50 μl complete growth medium with 0.1% FBS. Compounds were dispensed with Echo 550 (Labcyte) and incubated for 24 h at 37°C in a 5% CO_2 atmosphere. Antagonist effect was measured in the presence of DHT 1nM.

[0124] After incubation, assay medium removed and 20 μl of 1× Promega lysis buffer were added to each well. The plate was incubated 15 minutes at RT and quick-frozen to -80°C and the thaw to room temperature. 50 μl of luciferase substrate (E4550, Promega) were added to each well and luminescence (integration time 1000 msec) was read in an EnSpire multilabel reader (Perkin Elmer).

Results

[0125] Table shows the binding of some compounds of the present invention in the differents assays.

Example	AR rat-fluorimetric	AR LNCaP	GR IM-9	AR antag KB
A1	A			
A2	B			
A3	A			
A10	A			

(continued)

Example	AR rat-fluorimetric	AR LNCaP	GR IM-9	AR antag KB
B6	B	C	B	B
B12	C	C		A
B18	A			
B21	B	C		B
C1	B			
C2	B	C	B	B
C3	A			
C6	B	B	A	
C7	B			
C10	C			B
C14	B	A	B	
C19	C			
C20	B	B		
C21	A			
C23	A			
C24	A	A	A	C
C26	A			
C27	C			
C28	B			
C29	A			
C32		C		
C34		C	A	
C35	B		A	
C36		B	A	C
C37		A	A	
C38		A		
C39		B	A	C
C41		C	B	B
C42		C	A	A
C43		C	B	A
C44		C	B	B
C45		C		
C46		B	A	B
C47		B	A	
C48		C	B	B
C52	B			B
C53		A		
C56		B	A	

(continued)

Example	AR rat-fluorimetric	AR LNCaP	GR IM-9	AR antag KB
C57				B
C58		A	A	B
C60				B
C61			C	B
C62				B
C64			C	B
C65		C	A	B
C66		B	A	A
C67		A	A	A
C68			C	
C71		C	A	C
C72		C	A	C
C73		C	A	C
C74			B	C
C75			B	C
C76		C	A	
C77			B	
C78		C	B	
C79			A	C
C80			C	C
C81			A	
C82			A	
C83			B	
C84			A	
C85			C	
C86			B	
C91			A	
C92			A	
C93			B	
C94			A	
C95			A	
C96			B	
C97			A	
C98			B	
C99			B	
C100			A	
C101			A	
C102			B	

(continued)

Example	AR rat-fluorimetric	AR LNCaP	GR IM-9	AR antag KB
C103			A	
C104			A	
C105			B	
C106			B	
C107			A	C
C108			A	C
C109			A	
C110			A	
C111			A	
C112		B	A	
C113		B	A	
C114			C	
C115			C	
C116			B	
C117		B	A	B
C118		A	A	B
C119		C	A	B
C120		B	A	
C121		C	B	
C122			B	A
C123		A	A	
D1	A	B	C	
D2	C			
D3	A			
D5			A	
D6			B	C
D7			A	C
D8			A	
D10			A	
D11			A	
D12			A	
D13			A	
D14			C	
D15			B	
D16			A	
D17			A	
D18			A	
D19			A	

(continued)

Example	AR rat-fluorimetric	AR LNCaP	GR IM-9	AR antag KB
D20			B	
D21			A	
D22		C	A	
D23		B	A	
D24		B	A	B
D25		C	A	
D26		B	B	
D27		B	A	B
D28			B	
D29		B	A	
D30		B	A	B
D31		B	A	B
D32		B	A	B
D33		B	A	
D34		B	A	
D35		B	B	
D36		B	A	
D37		B	A	B
D38		B	A	
D39		B	A	B
D40		B	A	
D41		B	A	A
D42		B	A	
D43		B	A	C
D44			A	
D45		B	A	
D46		C	A	C
D47		B	A	C
D48			A	
D49		A	A	
D50			A	
D51			A	
D52			A	
D53			A	
D54			A	
D55			A	
D56			A	
E1	A	A		

(continued)

Example	AR rat-fluorimetric	AR LNCaP	GR IM-9	AR antag KB
G1	A	A		
G2	C			
G3	C			
G4	C			
H1	A			
H2	A			
H3	C			
H4	C			
H5	C			
H6	C			
H7	C			
H8	C			
H9	C			
H10	C			
H11	C			
H12	C			
H13	C			
H14	C			
H15	A	B		
I2		B	B	
J1	A			
J2	A			
J3	B			
J6	C			
J10	B			
J11	A			
J12	A			
J13	C			
J14	C			
J15	C			
J16	C			
J17	C			
J18	C			
J19	C			
J20	B			
J21	A	A		
J22	A	A	A	
J23	A	A	B	C

(continued)

Example	AR rat-fluorimetric	AR LNCaP	GR IM-9	AR antag KB
J24	C			
J25		B		
J25-a			B	
J26		A	A	B
J27		C	C	
J28		A	A	
J28-a		B	A	
J29		B		
J30		C		
J31		C	A	
J32		C		B
J33		B		B
J34				B
J36			C	
J38				B
J40		C		
J41		A	A	B
J42		B	A	A
J42-a			B	
J43			A	B
K1	B			
K2	C			
L1		C	A	B
L2		C	A	B
L3		A	A	B
L4		A	A	B
L5			A	C
L7			B	C
L8	C			
L9				B
L12			B	
L13			B	
L14			C	
M1	C			
N1			C	

Range:

[0126]

A: IC_{50} < 100 nM

B: 100 nM =< IC_{50} < 1 μM

C: IC_{50} >= 1 μM

[0127] As can be seen from the results described in Table 1, the compounds of the present invention are modulators of nuclear receptor selected from androgen receptor and glucocorticoid receptor.

[0128] The invention thus also relates to a compound as defined in the first aspect for use in the treatment or prevention of diseases known to be susceptible to improvement by treatment with a modulator of androgen receptor and glucocorticoid receptor said diseases being selected from prostate cancer, castration-resistant prostate cancer, pancreatic cancer, bladder cancer, renal cancer, gastric cancer, lung cancer, breast cancer, colon cancer, colorectal cancer, ovarian cancer, and other solid tumours, melanoma, metastasizing cancers, benign prostate hyperplasia, polycystic ovary syndrome (PCOS), hair loss, hirsutism, acne, hypogonadism, muscle wasting diseases and cachexia, and Cushing's syndrome, anti-psychotic drug induced weight gain, obesity, post-traumatic stress disorder and alcoholism. Accordingly, the invention also relates to the derivatives of the first aspect and pharmaceutically acceptable salts thereof, and pharmaceutical compositions comprising such compounds and/or salts thereof, for use in the treatment of disorders of the human body which comprises administering to a subject requiring such treatment an effective amount of the dihydropyridine derivative of the invention or a pharmaceutically acceptable salt thereof.

[0129] The present invention also provides pharmaceutical compositions which comprise, as an active ingredient, at least a dihydropyridine derivative of formula (I) or a pharmaceutically acceptable salt thereof in association with other therapeutics agents, as have been mentioned above, and with a pharmaceutically acceptable excipient such as a carrier or diluent. The active ingredient may comprise 0.001% to 99% by weight, preferably 0.01% to 90% by weight of the composition depending upon the nature of the formulation and whether further dilution is to be made prior to application. Preferably, the compositions are made up in a form suitable for oral, topical, nasal, rectal, percutaneous or injectable administration.

[0130] The pharmaceutically acceptable excipients, which are admixed with the active compound or salts of such compound, to form the compositions of this invention, are well known *per se* and the actual excipients used depend inter alia on the intended method of administering the compositions.

[0131] Compositions of this invention are preferably adapted for injectable and oral (per os) administration. In this case, the compositions for oral administration may take the form of tablets, sustained release tablets, sublingual tablets, capsules, inhalation aerosols, inhalation solutions, dry powder inhalation, or liquid preparations, such as mixtures, elixirs, syrups or suspensions, all containing the compound of the invention; such preparations may be made by methods well-known in the art.

[0132] The diluents, which may be used in the preparation of the compositions, include those liquid and solid diluents, which are compatible with the active ingredient, together with colouring or flavouring agents, if desired. Tablets or capsules may conveniently contain between 2 and 500 mg of active ingredient or the equivalent amount of a salt thereof.

[0133] The liquid composition adapted for oral use may be in the form of solutions or suspensions. The solutions may be aqueous solutions of a soluble salt or other derivative of the active compound in association with, for example, sucrose to form syrup. The suspensions may comprise an insoluble active compound of the invention or a pharmaceutically acceptable salt thereof in association with water, together with a suspending agent or flavouring agent.

[0134] Compositions for parenteral injection may be prepared from soluble salts, which may or may not be freeze-dried and which may be dissolved in pyrogen free aqueous media or other appropriate parenteral injection fluid.

[0135] Effective doses are normally in the range of 2-2000 mg of active ingredient per day. Daily dosage may be administered in one or more treatments, preferably from 1 to 4 treatments, per day.

[0136] The present invention will be further illustrated by the following examples. The following are given by way of illustration and do not limit the scope of the invention in any way. The synthesis of the compounds of the invention is illustrated by the following examples including the preparation of the intermediates, which do not limit the scope of the invention in any way.

EXAMPLES

General

[0137] Reagents, solvents and starting products were acquired from commercial sources and used without further purification. All reactions were performed under an atmosphere of air and with anhydrous solvents unless otherwise stated. The term "concentration" refers to the vacuum evaporation using a Büchi rotavapor. When indicated, the reaction products were purified by "flash" chromatography on silica gel (40-63 μm) with the indicated solvent system. Yields refer

to isolated compounds estimated to be > 95% pure as determined by ^{1}H NMR. All the dihydropyridines were obtained as racemic mixtures.

[0138] Mass spectrometry was carried out on a Varian MAT-711 spectrometer employing EI and ESI methods. HPLC experiments were carried out on a LaChrom Elite L-2350 instrument (Sunfire silica gel column 5 μm, 4.6 mmx150 mm) equipped with an L-2455 diode array detector. HPLC-MS analysis was performed on a Gilson instrument equipped with a Gilson 321 piston pump, a Gilson 864 vacuum degasser, a Gilson 189 injection module, a 1/1000 Gilson splitter, a Gilson 307 pump, a Gilson 170 detector, and a Thermoquest Fennigan aQa detector.

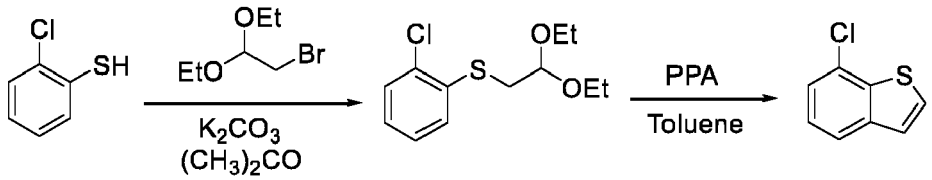
[0139] ^{1}H and ^{13}C nuclear magnetic resonance experiments were carried out using either a Varian Inova 500 MHz or Varian Mercury 300 or 400 MHz NMR spectrometers. Chemical shifts are reported relative to the deuterated solvent signal or tetramethylsilane as an internal reference. Coupling constants *J* are given in Hertz (Hz) and multiplicities as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet or as a combination of them.

PREPARATION OF INTERMEDIATES

General procedure aa

Intermediate 1: 7-chlorobenzo[b]thiophene

[0140]



[0141] To a solution of 2-chlorobenzenethiol (1.53 g, 10.58 mmol, 1.0 eq.) and 2-bromo-1,1-diethoxyethane (2.4 mL, 15.87 mmol, 1.5 eq.) in acetone (10 ml) was added potassium carbonate (3.65 g, 26.45 mmol, 2.5 eq). The mixture was refluxed for 90 minutes and then 0,5 eq of 2-bromo-1,1-diethoxyethanewas added. The mixture was refluxed for another 2 hours, cooled to room temperature and concentrated. The resulting residue was purified by flash column chromatography on silica gel using hexane/diethyl ether (2%) as eluent to afford (2-chlorophenyl)(2,2-diethoxyethyl)sulfane as a light yellow oil (2.71 g, 97%).

[0142] To a solution of polyphosphoric acid (6.0 g, 51.97 mmol, 9 eq.) in toluene (15 ml) was added under vigorous stirring a solution of (2-chlorophenyl)(2,2-diethoxyethyl)sulfane (1.5 g, 5.77 mmol, 1 eq) in toluene (5 mL). The mixture was stirred at reflux temperature for 5 hours and was then poured into ice cold water (30 mL) and stirred for 10 minutes. The mixture was washed with toluene, sat. aq. bicarbonate solution and brine, dried (Na_2SO_4) and concentrated. The resulting residue was purified by flash column chromatography on silica gel using hexane as eluent (as described in WO 2009/008992 A2) to afford 7-chlorobenzo[b]thiophene as a light-yellow oil (0.68 g, 70%).

[0143] ^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 7.77 - 7.71 (m, 1H), 7.50 (d, *J* = 5.4 Hz, 1H), 7.41 - 7.30 (m, 3H).

Intermediate 2: 7-(trifluoromethyl)benzo[b]thiophene

[0144] General procedure aa yielded the title compound as a light-yellow oil (0.44 g, 41 %). ^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 8.00 (d, *J* = 7.9 Hz, 1H), 7.66 (d, *J* = 7.3 Hz, 1H), 7.57 (d, *J* = 5.5 Hz, 1H), 7.51 - 7.37 (m, 2H).

[0145] ^{19}F NMR (282 MHz, $CDCl_3$-*d*) δ (ppm): -63.13 (CF_3).

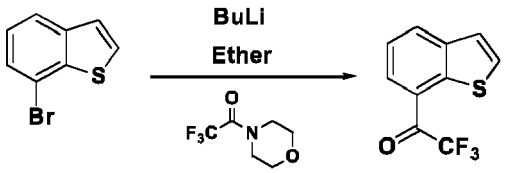
Intermediate 3: 7-fluorobenzo[b]thiophene

[0146] General procedure aa yielded the title compound as a yellow oil (1.78 g, 52 %). ^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm) δ 7.63 (d, *J* = 8.0 Hz, 1H), 7.49 (d, *J* = 5.3 Hz, 1H), 7.41 - 7.30 (m, 2H), 7.07 (dd, *J* = 9.8, 8.0 Hz, 1H).

[0147] ^{19}F NMR (282 MHz, $CDCl_3$-*d*) δ (ppm): -115.37 (CF).

Intermediate 4: 1-(Benzo[b]thiophen-7-yl)-2,2,2-trifluoroethan-1-one

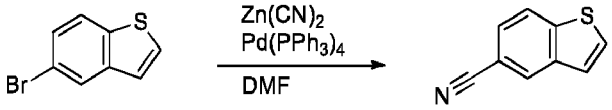
[0148]



[0149] This compound was synthetized using a modified procedure of J. Med. Chem. 2002, 45, 4038-4046. 7-bromobenzo[b]thiophene (1.0 g, 4.69 mmol, 1.0 eq.) was dissolved in diethyl ether (25 ml) and cooled at -40°C. Then n-butyllithium 1.6 M (3.23 ml, 5.16 mmol, 1.1 eq) was added dropwise and the solution was warmed to 0°C over a 1 h period. The solution was cooled to -60°C and a solution of 2,2,2-trifluoro-1-morpholinoethan-1-one (0.86 g, 4.69 mmol, 1.0 eq) in diethyl ether (5 ml) was added in portions. The resultant mixture was stirred at -60°C for 7 h and then warmed up to room temperature. The solution was hydrolyzed with saturated NH_4Cl (5 ml), washed with NH_4Cl (3 $\times$ 5 ml) and water (3 $\times$ 5 ml), dried (Na_2SO_4) and concentrated. The resulting residue was purified by flash column chromatography on silica gel using ethyl hexane: ethyl acetate (10:1) as eluent to afford a light-yellow solid (0.98 g, 91%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.20 (ddd, J = 7.9, 4.5, 1.4 Hz, 2H), 7.70 (d, J = 5.5 Hz, 1H), 7.58 (t, J = 7.9 Hz, 1H), 7.49 (d, J = 5.5 Hz, 1H). ^{19}F NMR (282 MHz, $CDCl_3$) δ = - 69.54 (s, CF_3).

Intermediate 5: Benzo[b]thiophene-5-carbonitrile

[0150]



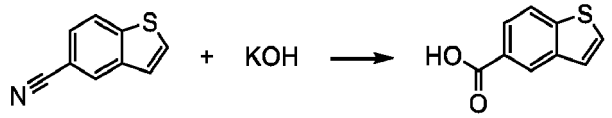
[0151] Nitrogen gas was bubbled through a mixture of 5-bromobenzo[b]thiophene (510 mg, 2.34 mmol) and zinc cyanide (299 mg, 2.49 mmol) in dry DMF (3 mL) for 5 minutes. Tetrakis(triphenylphosphine)palladium(0) (153 mg, 0.13 mmol) was added, the tube sealed and the mixture stirred at 90°C for 7h. The reaction mixture was filtered over Celite, and the filtrate was extracted using AcOEt and $NaHCO_3$. The organic phase was concentrated and the residue purified by column chromatography (Yield: 82%).
^{1}H-NMR (400 MHz, DMSO-d_6) δ = 7.58 (dd, 1H), 7.72 (m, 1H), 7.99 (d, 1H), 8.26 (m, 1H), 8.43 (d, 1H).

Intermediate 6: Benzo[b]thiophene-7-carbonitrile

[0152] The title compound was synthesized according to the method described above for benzo[b]thiophene-5-carbonitrile.
^{1}H-NMR (400 MHz, DMSO) δ= 7.59 (dd, 1H), 7.65 (d, 1H), 7.96 (dd, 1H), 8.01 (d, 1H), 8.26 (dd, 1H).

Intermediate 7: Benzo[b]thiophene-5-carboxylic acid

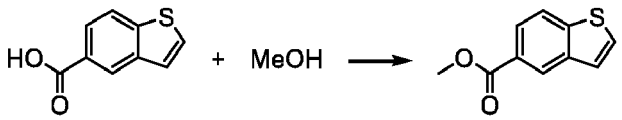
[0153]



[0154] To a solution of benzo[b]thiophene-5-carbonitrile (400 mg, 2.51 mmol) in MeOH (40 mL), KOH (2.0 g, 35 mmol) and water 10 mL were added in portions, and the mixture was stirred at 80°C for 36 hours. After acidification with 2N HCl (pH 4-5), the solid was filtered off and washed with pentane to yield the title compound as an offwhite solid (390 mg, 87%).
^{1}H-NMR (400 MHz, DMSO-d_6) δ= 7.58 (dd, 1H), 7.72 (m, 1H), 8.01 (d, 1H), 8.29 (m, 1H), 8.46 (d, 1H), 12.11 (s, 1H).

Intermediate 8: Methyl benzo[b]thiophene-5-carboxylate

[0155]



[0156] Benzo[b]thiophene-5-carboxylic acid (390 mg, 2.19 mmol) was refluxed in sat. HCl in MeOH (30 mL) for 24 hours. The methyl ester was obtained after evaporation of the solvent (340 mg, 76%).
^{1}H-NMR (400 MHz, DMSO-d_6) δ= 3.85 (s, 3H), 7.59 (dd, 1H), 7.73 (m, 1H), 7.98 (d, 1H), 8.27 (m, 1H), 8.44 (d, 1H).

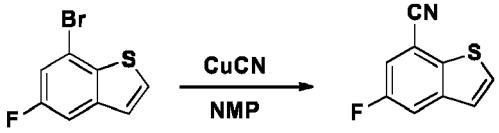
Intermediate 9: 5-Fluorobenzo[b]thiophene-7-carbonitrile

Synthesis of 7-Bromo-5-fluorobenzo[b]thiophene

[0157] General procedure **aa** afforded the title compound as a light-yellow oil (1.02 g) that was used as such in the next step.

Synthesis of 5-Fluorobenzo[b]thiophene-7-carbonitrile

[0158]



[0159] A solution of 7-bromo-5-fluorobenzo[b]thiophene (1.02 g, 4.41 mmol, 1.0 eq.) and copper cyanide (0.590 g, 6.62 mmol, 1.5 eq.) in N-methyl-2-pirrolydone (12 ml) was stirred for 2 days in a sealed tube at 200 °C. The mixture was cooled to room temperature, poured into sat. aq. $NaHCO_3$ (30 mL) and kept at 4 °C for 60 min. The solid was filtered off and dissolved in a mixture of 40 mL NH_4OH(28%)/NH_4Cl(sat) (1:1) and ethyl acetate (60 mL) and stirred for 1h. Then, it was washed with ethyl acetate (x3), dried (Na_2SO_4), concentrated and purified by flash column chromatography on silica gel using hexane/diethyl ether (2%) as eluent to afford 5-fluoro-3-formylbenzo[b]thiophene-7-carbonitrile as a white solid (0.23 g, 29%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm): 7.73 (dd, *J* = 8.8, 2.3 Hz, 1H), 7.69 (d, *J* = 5.5 Hz, 1H), 7.47 (dd, *J* = 8.1, 2.2 Hz, 1H), 7.39 (d, *J* = 5.5 Hz, 1H).

Intermediate 10: 4-Fluorobenzo[b]thiophene-7-carbonitrile

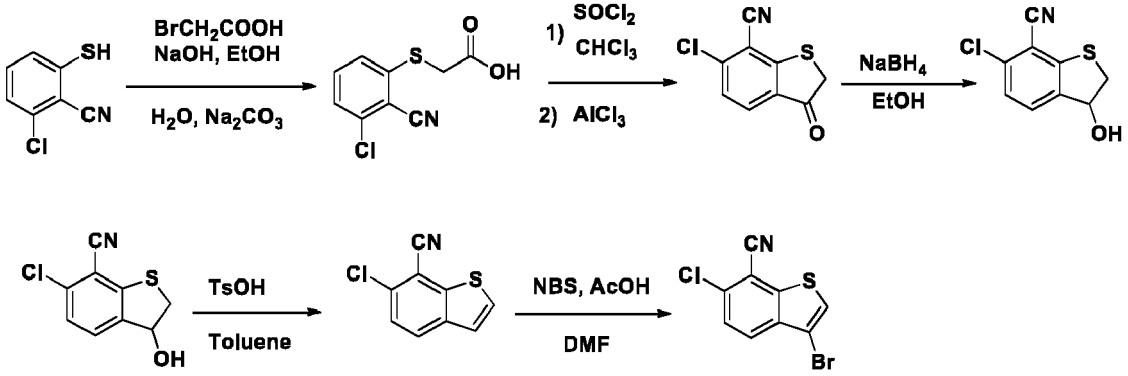
[0160] The title compound was prepared in a 2-step synthesis as described above for Intermediate 9 and was afforded as a white solid (0.33 g).
^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm): 7.70 (dd, *J* = 8.2, 4.5 Hz, 1H), 7.61 (d, *J* = 5.5 Hz, 1H), 7.53 (d, *J* = 5.5 Hz, 1H), 7.13 (t, *J* = 8.8 Hz, 1H).

Intermediate 11: 5,7-Dichlorobenzo[b]thiophene

[0161] General procedure **aa** afforded the title compound as a light-yellow oil (1.57 g). ^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm): 7.78 (dd, J = 8.0, 0.8 Hz, 1H), 7.52 (s, 1H), 7.50 (s, 1H), 7.46 - 7.42 (m, 1H).

Intermediate 12: 3-Bromo-6-chlorobenzo[b]thiophene-7-carbonitrile

[0162]



[0163] To a solution of 2-chloro-6-mercaptobenzonitrile (1.5 g, 8.84 mmol, 1.0 eq.) in ethanol (20 ml) was added a solution of sodium hydroxide (0.35 g, 8.84 mmol, 1.0 eq.) in water (7 ml). Then, a solution of 2-bromoacetic acid (1.35 g, 9.73 mmol, 1.1 eq.), sodium carbonate (0.51 g, 4.86 mmol, 0.5 eq.) in water (8 mL) was added, and the mixture was stirred for 2 hours. The pH of the mixture was adjusted (~ 2) with HCl (2N) and extracted with ethyl acetate (x2) and DCM (x2). The organic phase was dried (Na_2SO_4) and concentrated affording 2-((3-chloro-2-cyanophenyl) thio) acetic acid as a yellow oil. This product was used in the next step without further purification.

^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm): 7.51 - 7.44 (m, 2H), 7.42 - 7.35 (m, 1H), 3.79 (s, 2H), 2.83 (bs, 1H).

[0164] To a solution of 2-((3-chloro-2-cyanophenyl) thio) acetic acid (2.0 g, 8.78 mmol, 1.0 eq.) in chloroform (60 ml), thionyl chloride (0.96 mL, 13.18 mmol, 1.5 eq.) was dropwise added. The mixture was refluxed for 1 hour and then cooled to 0 °C, when aluminum chloride (10.54 g, 79.06 mmol, 9 eq.) was added in portions. The mixture was stirred at RT overnight, cooled to 0 °C before adding water, and then extracted with ethyl acetate (x3). The organic phase was dried (Na_2SO_4), concentrated and purified by flash column chromatography on silica gel using hexane/ethyl acetate (4:1) as eluent to afford 6-chloro-3-oxo-2,3-dihydrobenzo[b]thiophene-7-carbonitrile (1.53 g, 83%).

^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm): 7.48 (d, *J* = 8.5 Hz, 1H), 7.35 (d, *J* = 8.5 Hz, 1H), 3.95 (s, 2H).

[0165] A solution of 6-chloro-3-oxo-2,3-dihydrobenzo[b]thiophene-7-carbonitrile (1.53 g, 7.79 mmol, 1.0 eq.) and sodium borohydride (0.32 g, 8.57 mmol, 1.1 eq.) in ethanol (60 ml) was stirred for 1 hour at RT, concentrated, redissolved in ethyl acetate and washed with water. The organic phase was dried over Na_2SO_4 and concentrated to afford 6-chloro-3-hydroxy-2,3-dihydrobenzo[b]thiophene-7-carbonitrile which was used in the next step without further purification.

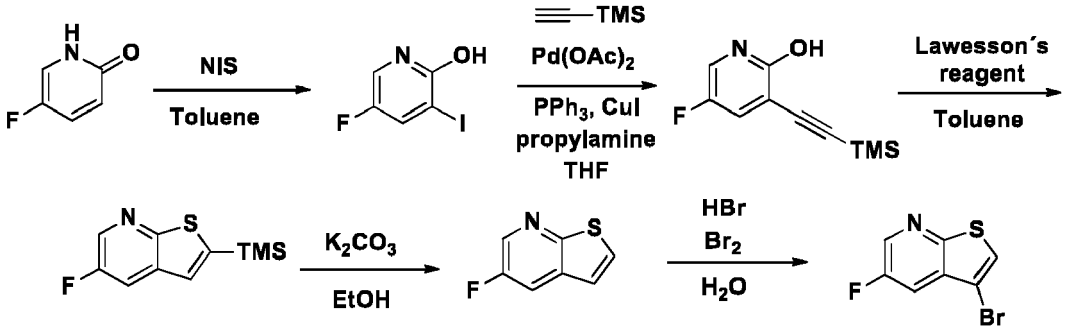
[0166] A solution of 6-chloro-3-hydroxy-2,3-dihydrobenzo[b]thiophene-7-carbonitrile (7.79 mmol, 1.0 eq.) and p-toluensulfonic acid (0.15 g, 78 mmol, 0.1 eq.) in toluene (20 ml) was refluxed for 1 hour, concentrated and purified by flash column chromatography on silica gel using hexane/ethyl acetate (6:1) as eluent to afford 6-chlorobenzo[b]thiophene-7-carbonitrile (1.26 g, 83%).

^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm): 7.93 (d, *J* = 8.6 Hz, 1H), 7.60 (d, *J* = 5.4 Hz, 1H), 7.47 (d, *J* = 8.6 Hz, 1H), 7.39 (d, *J* = 5.5 Hz, 1H).

[0167] A solution of 6-chlorobenzo[b]thiophene-7-carbonitrile (1.26 g, 6.50 mmol, 1.0 eq.), N-Bromo succinimide (1.74 g, 9.76 mmol, 1.5 eq.), acetic acid (0.04 mL, 0.64 mmol, 0.1 eq.), in N, N-dimethylformamide (10 ml) was heated at 130 °C for 1h in a microwave reactor. Then water was added, and the mixture was extracted with ethyl acetate (x3). The organic phase was dried (Na_2SO_4), concentrated and purified by flash column chromatography on silica gel using hexane/ethyl acetate (8:1) as eluent to afford 3-bromo-6-chlorobenzo[b]thiophene-7-carbonitrile (1.33 g, 75%).

Intermediate 13: 3-Bromo-5-fluorothieno[2,3-b]pyridine

[0168]



[0169] To a solution of 5-fluoropyridin-2(1H)-one (1.0 g, 8.84 mmol, 1.0 eq.) in dry toluene (20 ml) was added N-iodosuccinimide (1.99 g, 8.84 mmol, 1.0 eq). The resultant mixture was stirred for 30 minutes at 90 °C, then cooled to RT and concentrated. The residue was purified by flash column chromatography on silica gel using hexane/ethyl acetate (2:1) as eluent to afford 5-fluoro-3-iodopyridin-2-ol as a yellow solid (1.4 g, 65%).

^{1}H-NMR (300 MHz, DMSO-d_6) δ (ppm): 11.81 (s, 1H), 10.99 (bs, 1H), 8.18 (dd, J= 7.2, 3.1 Hz, 1H), 7.65 (t, J = 3.1 Hz, 1H).

[0170] A solution of 5-fluoro-3-iodopyridin-2-ol (0.5 g, 2.06 mmol, 1 eq.), palladium acetate (0.005 g, 0.02 mmol, 0.01 eq.), triphenylphosphine (0.011 g, 0.041 mmol, 0.02 eq.), copper iodide (0.008 g, 0.041 mmol, 0.02 eq.) in dry tetrahydrofuran (15 ml) was purged with argon gas for 5 minutes. Then, trimethylsilylacetylene (0.43 mL, 3.10 mmol, 1.5 eq) and propylamine (0.34 mL, 4.13 mmol, 2 eq) was added, and the mixture was stirred at 38 °C for 60 minutes, concentrated, taken up in ethyl acetate and washed with Rochelle salt (x2), hydrochloride acid 0.1 N (x2) and saturated sodium bicarbonate (x2). The organic phase was dried (Na_2SO_4), filtered, concentrated and purified by flash column chromatography on silica gel using hexane/ ethyl acetate (2:1) as eluent to afford 5-fluoro-3-((trimethylsilyl)ethynyl)pyridin-2-ol as a light yellow oil (0.263 g, 61%).

^{1}H-NMR (300 MHz, DMSO-d_6) δ (ppm): 13.57 (bs, 1H), 7.60 (dd, J = 7.6, 3.1 Hz, 1H), 7.39 (t, J = 3.1 Hz, 1H), 0.26 (s, 9H).

[0171] To a solution of 5-fluoro-3-((trimethylsilyl)ethynyl)pyridin-2-ol (0.26 g, 1.25 mmol, 1 eq.) in dry toluene (10 ml) was added Lawesson's reagent (0.0.25 mL, 0.63 mmol, 0.5 eq). The mixture was stirred at 120 °C for 60 minutes, concentrated and purified by flash column chromatography on silica gel using ethyl hexane: ethyl acetate (7:1) as eluent to afford 5-fluoro-2-(trimethylsilyl)thieno[2,3-b]pyridine as a yellow solid (0.22 g, 76%).

^{1}H-NMR (300 MHz, DMSO-d_6) δ (ppm): 3.68 (d, J = 2.4 Hz, 1H), 2.95 (dd, J = 9.0, 2.4 Hz, 1H), 2.58 (s, 1H), -4.37 (s, 9H).

[0172] To a solution of 5-fluoro-2-(trimethylsilyl)thieno[2,3-b]pyridine 0.22 g, 0.96 mmol, 1 eq.) in ethanol (4 ml) was added potassium carbonate (0.332 g, 2.40 mmol, 2.5 eq.). The mixture was stirred at 65 °C for 60 minutes. Then, the solid was filtered off and washed with dichloromethane. The filtrate was concentrated, taken up in ethyl acetate, washed with water ($\times$2) and brine ($\times$2), dried (Na_2SO_4) and concentrated, and the residue was purified by flash column chromatography on silica gel using hexane/ ethyl acetate (20:1) as eluent to afford 5-fluorothieno[2,3-b]pyridine as a light yellow oil (0.111 g, 75%).

^{1}H-NMR (300 MHz, CDCL) δ (ppm): 8.47 (d, J = 2.4 Hz, 1H), 7.75 (dd, J = 8.9, 2.7 Hz, 1H), 7.63 (d, J = 6.0 Hz, 1H), 7.24 (d, J = 6.0 Hz, 1H).

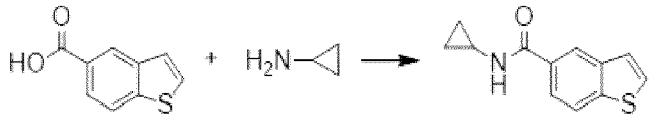
[0173] To a solution of 5-fluorothieno[2,3-b]pyridine 0.78 g, 5.12 mmol, 1 eq.) in water (8mL) was added hydrobromic acid (5.22 mL, 46.09 mmol, 9 eq.) and bromine (0.39 g, 7.68 mmol, 1.5 eq.) and this mixture was stirred at 55 °C for 20 hours. The solid was filtered off and washed with saturated sodium bicarbonate, then taken up in ethyl acetate, washed with saturated sodium bicarbonate ($\times$2), dried (Na SO_4), concentrated and purified by flash column chromatography on silica gel using hexane/ ethyl acetate (20:1) as eluent to afford 3-bromo-5-fluorothieno[2,3-b]pyridine as a light yellow oil (0.73 g, 62%).

^{1}H-NMR (300 MHz, CDCL) δ (ppm): 8.51 (s, 1H), 7.76 (dd, J = 8.5, 2.5 Hz, 1H), 7.64 (s, 1H).

General procedure a

Intermediate a1: N-Cyclopropylbenzo[b]thiophene-5-carboxamide

[0174]



[0175] To a solution of benzo[b]thiophene-5-carboxylic acid (700 mg, 3.93 mmol), EDC*HCl (1130 mg, 5.89 mmol), HOBT (601 mg, 3.93 mmol) in 15 mL of DMF at 5°C, were added cyclopropyl amine (336 mg, 5.89 mmol) and DIPEA (1270 g, 9.89 mmol). The reaction mixture was stirred for 18 hours at room temperature. The solution was poured into NaHCO saturated and the precipitate was washed with three times of cold water and one time of pentane to obtain the desired amide derivative (700 mg, 82%).

^{1}H-NMR (400 MHz, DMSO-d_6) δ= 0.60 (m, 2H), 0.71 (m, 2H), 2.93 (m, 1H), 7.56 (dd, 1H), 7.67 (d, 1H), 7.93 (d, 1H), 8.22 (dd, 1H), 8.46 (d, 1H).

[0176] The following derivatives were synthesized according to General procedure **a** as described above and were used in the next step without further purification.

Intermediate a2: N-(Cyclopropylmethyl)benzo[b] thiophene-5-carboxamide

[0177] ^{1}H-NMR (400 MHz, DMSO-d_6) δ= 0.20 (m, 2H), 0.47 (m, 2H), 1.05 (m, 1H), 3.14 (m, 2H), 7.49 (dd, 1H), 7.63 (d, 1H), 7.89 (d, 1H), 8.18 (dd, 1H), 8.30 (t, 1H), 8.42 (d, 1H).

Intermediate a3: Benzo[b]thiophen-5-yl(4-methylpiperazin-1-yl)methanone

[0178] ^{1}H-NMR (400 MHz, DMSO-d_6) δ= 2.15 (s, 3H), 2.29 (m, 4H), 3.41 (m, 4H), 7.47 (dd, 1H), 7.61 (d, 1H), 7.97 (d, 1H), 8.15 (dd, 1H), 8.50 (d, 1H).

Intermediate a4: Benzo[b]thiophen-5-yl(morpholino)methanone

[0179] ^{1}H-NMR (400 MHz, DMSO-d_6) δ= 3.49 (m, 4H), 3.65 (m, 4H), 7.47 (dd, 1H), 7.61 (d, 1H), 7.97 (d, 1H), 8.15 (dd, 1H), 8.50 (d, 1H).

Intermediate a5: N-Cyclopropylbenzo[b]thiophene-7-carboxamide

[0180] ^{1}H-NMR (400 MHz, DMSO) δ= 0.62 (m, 2H), 0.74 (m, 2H), 2.91 (m, 1H), 7.47 (dd, 2H), 7.81 (d,1H), 7.92 (d, 1H), 8.04 (dd, 1H), 8.69 (d, 1H).

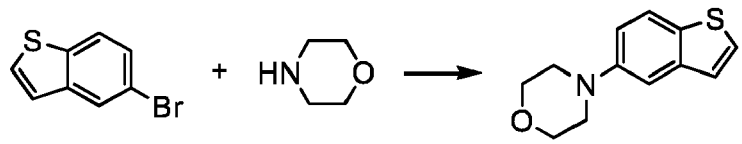
Intermediate a6: Benzo[b]thiophen-7-yl(4-methylpiperazin-1-yl)methanone

[0181] ^{1}H-NMR (400 MHz, DMSO) δ= 2.19 (s, 3H), 2.28 (d, 4H), 3.42 (t, 4H), 7.37 (d, 1H), 7.46 (dd, 1H), 7.51 (d, 1H), 7.83 (d, 1H), 7.96 (dd, 1H).

General procedure b

Intermediate b1: 4-(Benzo[b]thiophen-5-yl)morpholine

[0182]



[0183] A solution of 5-bromobenzo[b]thiophene (600 mg, 2.82 mmol), morpholine (368 mg, 4.23 mmol), $Pd_2(dba)_3$ (129 mg, 0.14 mmol), tricyclohexylphosphine (119 mg, 0.42 mmol) and NatButO (541 mg, 8.46 mmol) in dry toluene (20 mL) under N_2 atmosphere was refluxed for 24 hours. After cooling, the muxture was poured into sat. aq. $NaHCO_3$, extracted with AcOEt (3X), dried over Na_2SO_4, filtered over and concentrated. The product was isolated as grey solid after flash column chromatography (230 mg, 37%).
^{1}H-NMR (400 MHz, DMSO-d_6) δ= 3.45 (m, 4H), 3.23 (m,4H), 6.94 (d, 1H), 7.42 (d, 1H), 7.54 (dd, 1H), 7.66 (d, 1H), 7.71 (d, 1H).

[0184] The following derivatives were synthesized according to General procedure **b** as described above and were used in the next step without further purification:

Intermediate b2: 1-(Benzo[b]thiophen-5-yl)-4-methylpiperazine

[0185] ^{1}H-NMR (400 MHz, DMSO-d_6) δ= 2.25 (s, 3H), 2.53 (m, 4H), 3.16 (m,4H), 6.93 (d, 1H), 7.39 (d, 1H), 7.61 (d, 1H), 7.51 (dd, 1H), 7.68 (d, 1H).

Intermediate b3: N-Benzylbenzo[b]thiophen-5-amine

[0186] ^{1}H-NMR (400 MHz, DMSO-d_6) δ= 5.06 (d, 2H), 6.91 (d, 1H), 7.17 (m, 1H), 7.24 (m, 2H), 7.27 (m, 2H) 7.32 (d, 1H), 7.49 (d, 1H), 7.51 (dd, 1H), 7.74 (t, 1H), 7.81 (d, 1H).

Intermediate b4: 1-(Benzo[b]thiophen-7-yl)-4-methylpiperazine

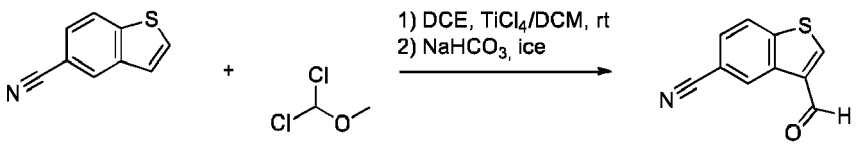
[0187] ^{1}H-NMR (400 MHz, DMSO-d_6) δ= 2.27 (s, 3H), 2.54 (m, 4H), 3.14 (m, 4H), 6.97 (d, 1H),7.33 (t, 1H),7.43 (d, 1H), 7.55 (d, 1H), 7.71 (d, 1H).

PREPARATION OF 3-FORMYLBENZO[b]THIOPHENE INTERMEDIATES

General procedure c

Intermediate c1: 3-Formylbenzo[b]thiophene-5-carbonitrile

[0188]



[0189] 5-cyanebenzo[b]thiophene (320 mg, 2 mmol) was dissolved in dry dichloroethane (4 mL) under a nitrogen atmosphere. Dichloro(methoxy)methane (0.277 mL, 3 mmol) and titanium tetrachloride (0.33 mL) were added dropwise. The mixture was stirred at RT for 20h, then poured onto a mixture of $NaHCO_3$ solution and ice and extracted with DCM. The organic phases were combined and concentrated, and the residue was filtered off and rinsed with diethyl ether. (Yield: 32 %).
^{1}H-NMR (400 MHz, DMSO-d_6) δ= 7.89 (dd, 1H), 8.39 (m, 1H), 8.86 (m, 1H), 9.16 (s, 1H), 10.16 (d, 1H).
[0190] The following derivatives were synthesized according to General procedure **c** as described above and were used in the next step without further purification:

Intermediate c2: 5-Fluorobenzo[b]thiophene-3-carbaldehyde

[0191] 535 mg, 90%.
[0192] ^{1}H-NMR (400 MHz, DMSO-d_6) δ= 7.42 (m, 1H) 8.21 (m, 2H), 9.09 (s, 1H), 10.11 (s, 1H).

Intermediate c3: 5-Morpholinobenzo[b]thiophene-3-carbaldehyde

[0193] ^{1}H-NMR (400 MHz, DMSO-d_6) δ= 3.46 (m, 4H), 3.23 (m,4H), 6.95 (d, 1H), 7.55 (dd, 1H), 7.73 (d, 1H), 9.05 (s, 1H), 10.16 (s, 1H).

Intermediate c4: 5-(4-Methylpiperazin-1-yl)benzo[b]thiophene-3-carbaldehyde

[0194] ^{1}H-NMR (400 MHz, DMSO-d_6) δ= 2.19 (s, 3H), 2.49 (m, 4H), 3.25 (m,4H), 7.23 (d, 1H), 7.89 (d, 1H), 8.05 (d, 1H), 8.31 (s, 1H), 10.11 (s, 1H).

Intermediate c5: 5-(Benzylamino)benzo[b]thiophene-3-carbaldehyde

[0195] ^{1}H-NMR (400 MHz, DMSO-d_6) δ= 4.98 (d, 2H), 6.98 (d, 1H), 7.23 (dd, 1H), 7.17 (m, 1H), 7.24 (m, 2H), 7.27 (m, 2H), 7.99 (d, 1H),8.24 (t, 1H) 8.51 (s, 1H), 10.12 (s, 1H).

Intermediate c6: N-Cyclopropyl-3-formylbenzo[b]thiophene-5-carboxamide

[0196] ^{1}H-NMR (400 MHz, DMSO-d_6) δ= 0.60 (m, 2H), 0.71 (m, 2H), 2.93 (m, 1H), 7.68 (t, 1H), 7.97 (d, 1H), 8.16 (d, 1H), 8.56 (dd, 1H), 9.09 (s, 1H), 10.15 (s, 1H).

Intermediate c7: N-(Cyclopropylmethyl)-3-formylbenzo[b]thiophene-5-carboxamide

[0197] ^{1}H-NMR (400 MHz, DMSO-d_6) δ= 0.27 (m, 2H), 0.52 (m, 2H), 2.26 (m, 1H), 3.27 (m, 2H), 7.95 (d, 1H), 8.18 (dd, 1H), 8.48 (t, 1H), 8.53 (d, 1H) 9.04 (s, 1H), 10.12 (s, 1H).

Intermediate c8: 5-(4-Methylpiperazine-1-carbonyl)benzo[b]thiophene-3-carbaldehyde

[0198] ^{1}H-NMR (400 MHz, DMSO-d_6) δ= 2.16 (s, 3H), 2.29 (m, 4H), 3.41 (m, 4H), 7.97 (d, 1H), 8.17 (d, 1H), 8.50 (d, 1H), 9.06 (s, 1H), 10.11 (s, 1H).

Intermediate c9: 5-(morpholine-4-carbonyl)benzo[b]thiophene-3-carbaldehyde

[0199] ^{1}H-NMR (400 MHz, DMSO-d_6) δ= 3.51 (m, 4H), 3.66 (m, 4H), 7.96 (d, 1H), 8.18 (d, 1H), 8.51 (d, 1H), 9.08 (s, 1H), 10.13 (s, 1H).

Intermediate c10: 3-Formylbenzo[b]thiophene-7-carbonitrile

[0200] ^{1}H-NMR (400 MHz, DMSO-d_6) δ= 7.70 (t, 1H), 8.16 (d, 1H), 8.81 (d, 1H), 9.08 (s, 1H), 10.16 (s, 1H).

Intermediate c11: 7-(4-Methylpiperazin-1-yl)benzo[b]thiophene-3-carbaldehyde

[0201] ^{1}H-NMR (400 MHz, DMSO-d_6) δ= 2.91 (s, 4H), 3.30 (s, 6H), 3.49 (s, 9H),7.16 (d, 1H), 7.35 (t, 1H),7.97 (d, 1H), 8.04 (d, 1H), 8.30 (d, 1H),10.10 (s, 1H).

Intermediate c12: 7-(4-methylpiperazine-1-carbonyl)benzo[b]thiophene-3-carbaldehyde

[0202] ^{1}H-NMR (400 MHz, DMSO-d_6) δ= 3.41 (dd, 4H), 3.49 (dd, 4H), 3.90 (s, 3H), 7.66 (m, 1H), 8.23 (s, 2H), 9.08 (s, 1H), 10.15 (s, 1H).

Intermediate c13: N-Cyclopropyl-3-formylbenzo[b]thiophene-7-carboxamide

[0203] ^{1}H-NMR (400 MHz, DMSO-d_6) δ= 0.64 (dt, 2H), 0.75 (td, 2H), 2.93 (m, 1H), 7.64 (t, 1H), 8.08 (dd, 1H), 8.72 (dd, 1H), 8.84 (d, 1H), 9.04 (s, 1H), 10.14 (s, 1H).

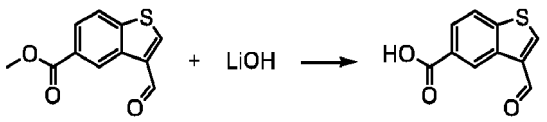
Intermediate c14: Methyl 3-formylbenzo[b]thiophene-5-carboxylate

[0204] The title compound was synthesized according to General procedure **c** and purified by trituration with n-pentane to yield a pale brown solid (320 mg, 83%). ^{1}H-NMR (400 MHz, DMSO-d_6) δ= 3.97 (s, 3H), 7.73 (m, 1H), 8.20 (m, 1H), 8.85 (dd, 1H), 9.08 (s, 1H), 10.15 (s, 1H).

[0205] The ester was hydrolysed as follows:

Intermediate c15: 3-Formylbenzo[b]thiophene-5-carboxylic acid

[0206]



[0207] To a solution of methyl 3-formylbenzo[b]thiophene-5-carboxylate (320 mg, 1.45 mmol) in EtOH (15 mL) and water (5 mL), litium hydroxide (230 mg, 9.6 mmol) was added at 0°C. The mixture was stirred for 24 hours at room temperature. The product was isolated as a pale yellow solid after acidification (pH 4-5) with 2N HCl, followed by filtration and pentane washing (260 mg, 92% yield).
^{1}H-NMR (400 MHz, DMSO-d_6) δ= 7.81 (m, 1H), 8.23 (m, 1H), 8.88 (dd, 1H), 9.08 (s, 1H), 10.15 (s, 1H), 12.45 (s, 1H).

Intermediate c16: 7-(2,2,2-Trifluoroacetyl)benzo[b]thiophene-3-carbaldehyde

[0208] The title compound was synthesized according to General procedure **c** and purified by flash column chromatography yielding a yellow solid (0.31 g, 91%). ^{1}H-NMR (300 MHz, $CDCl_3$) δ= 10.22 (s, 1H), 9.20 (s, 1H), 9.03 (d, J = 8.0 Hz, 1H), 8.34 (d, J = 7.0 Hz, 1H), 7.88 (t, J = 7.9 Hz, 1H). ^{19}F NMR (282 MHz, $CDCl_3$) δ = - 68.92 (s, CF_3).

Intermediate c17: 7-Chlorobenzo[b]thiophene-3-carbaldehyde

[0209] The title compound was synthesized according to General procedure **c** and purified by flash column chromatography yielding a yellow solid (0.38 g, 48 %). ^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm) δ 10.13 (s, 1H), 8.66 - 8.51 (m, 1H), 8.35 (s, 1H), 7.53 - 7.41 (m, 2H).

Intermediate c18: 7-(Trifluoromethyl)benzo[b]thiophene-3-carbaldehyde

[0210] The title compound was synthesized according to General procedure **c** and purified by flash column chromatography yielding a yellow solid (0.081 g, 16 %).
^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 10.18 (s, 1H), 8.92 (d, *J* = 8.0 Hz, 1H), 8.43 (s, 1H), 7.78 (d, *J* = 7.5 Hz, 1H), 7.63 (t, *J* = 8.0 Hz, 1H).
^{19}F NMR (282 MHz, $CDCl_3$-*d*) δ (ppm): -62.56 (CF_3).

Intermediate c19: 7-Fluorobenzo[b]thiophene-3-carbaldehyde

[0211] The title compound was synthesized according to General procedure **c** and purified by flash column chromatography yielding a yellow solid (0.27 g, 19 %). ^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 10.15 (s, 1H), 8.45 (d, *J* = 8.1 Hz, 1H), 8.34 (s, 1H), 7.48 (td, *J* = 8.1, 5.1 Hz, 1H), 7.22 - 7.09 (m, 1H).
^{19}F NMR (282 MHz, $CDCl_3$-*d*) δ (ppm): -115.33 (CF).

Intermediate c20: Thieno[2,3-b]pyridine-3-carbaldehyde

[0212] Step 1: 3-Bromo-thieno[2,3-b]pyridine (500 mg, 2.35 mmol) and copper (I) cyanide (315 mg, 3.53 mmol) were suspended in NMP (10 mL) and stirred at 200°C for 20 hours under N_2 atmosphere. The solution was poured into sat. aq. $NaHCO_3$, filtered and washed with water to afford thieno[2,3-b]pyridine-3-carbonitrile as a grey solid (376 mg, 95% yield).
^{1}H-NMR (400 MHz, DMSO-d_6) δ= 7.65 (m, 1H), 8.39 (dd, 1H), 8.75 (m, 1H), 9.04 (d, 1H).
[0213] Step 2: To a solution of diisobutylaluminum hydride (DIBAL) (25%w in toluene, 2.7 mL, 4.1 mmol) in toluene (45 mL) at -78°C under N_2 atmosphere, a solution of thieno[2,3-b]pyridine-3-carbonitrile (660 mg, 4.1 mmol) in toluene (4 mL) was added dropwise. The temperature was allowed to rise to 0°C and the mixture was stirred until completion. Then, water (30 mL) was added slowly and the product was extracted with AcOEt (3X), dried over Na_2SO_4, filtered over silica gel and concentrated. The title compound was obtained as a brown solid and used in the next step without further purification (569 mg, 85% yield).
^{1}H-NMR (400 MHz, DMSO-d_6) δ= 7.60 (m, 1H), 8.68 (t, 1H), 8.80 (d, 1H), 9.08 (d, 1H), 10.06 (s, 1H).

Intermediate c21: 5-Fluoro-3-formylbenzo[b]thiophene-7-carbonitrile

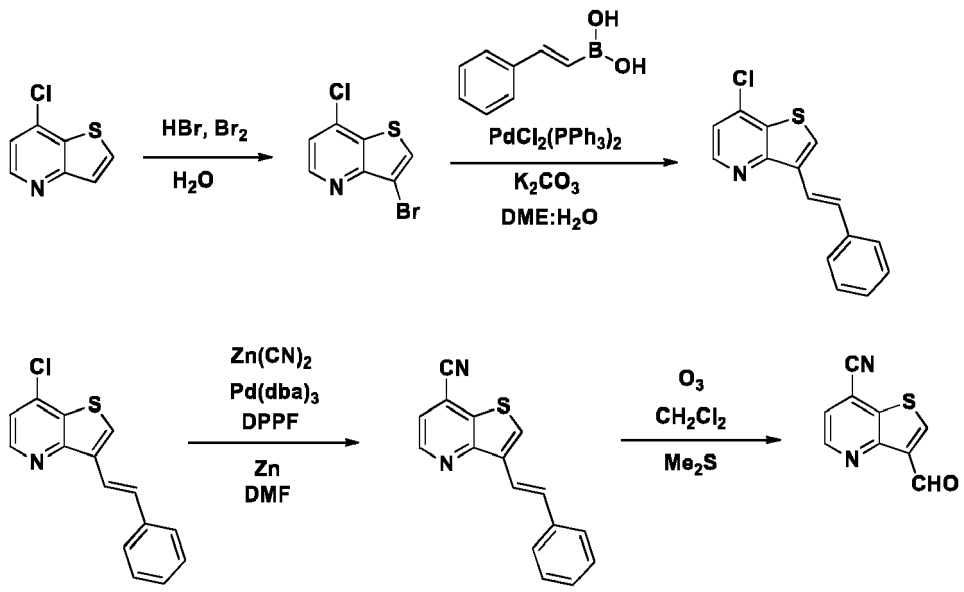
[0214] General procedure **c** gave the title compound as a yellow solid (0.153 g, 58 %).
^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 10.14 (s, 1H), 8.68 (d, *J* = 9.1 Hz, 1H), 8.53 (s, 1H), 7.59 (d, *J* = 9.1 Hz, 1H).

Intermediate c22: 4-Fluoro-3-formylbenzo[b]thiophene-7-carbonitrile

[0215] General procedure **c** gave the title compound as a yellow solid (0.125 g, 33 %).
^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 10.40 (s, 1H), 8.57 (s, 1H), 7.82 (dd, *J* = 8.1, 4.4 Hz, 1H), 7.40 - 7.28 (m, 1H).

Intermediate c23: 3-Formylthieno[3,2-b]pyridine-7-carbonitrile

[0216]



[0217] This aldehyde was prepared in 4 steps using a different method.

[0218] First step: A solution of 7-chlorothieno[3,2-b]pyridine (3.0 g, 17.68 mmol, 1.0 eq.), hydrobromic acid (30 mL, 265.28 mmol, 15 eq.) and bromine (2.28 mL, 44.20 mmol, 2.5 eq.) in water (40 ml) was stirred at 80°C for 2 days. The mixture was cooled to room temperature and $NaHCO_3$ was added until pH 8. The mixture was washed with ethyl acetate (x3) and dichloromethane (x2), dried over Na_2SO_4, concentrated and purified by flash column chromatography on silica gel using hexane/ethyl acetate (15:1) as eluent to afford 3-bromo-7-chlorothieno[3,2-b]pyridine as a yellow solid (3.45 g, 79%).

^{1}H-NMR (300 MHz, $CDCl_3$-*d*) 5 (ppm): 8.74 (dd, *J* = 5.0, 0.4 Hz, 1H), 7.84 (s, 1H), 7.44 - 7.30 (m, 1H).

[0219] Second step: To a solution of 3-bromo-7-chlorothieno[3,2-b]pyridine (1.2 g, 4.82 mmol, 1.0 eq.), bis(triphenylphosphine)palladium (II) dichloride (0.338 g, 0.48 mmol, 0.1 eq.) and potassium carbonate (2.0 g, 14.48 mmol, 3 eq.) in a mixture of dimethylether and water (3:1) (32 mL) was added (E)-styrylboronic acid (0.92 g, 6.28 mmol, 1.3 eq). The resultant mixture was stirred at 110 °C for 1 hour. The mixture was cooled to RT, filtered over celite, washed with DCM, concentrated and purified by flash column chromatography on silica gel using hexane/ethyl acetate (10:1) as eluent to afford (E)-7-chloro-3-styrylthieno[3,2-b]pyridine as a yellow oil (0.870 g, 66%).

^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 8.69 (d, *J* = 5.6 Hz, 1H), 7.83 (s, 1H), 7.76 (d, *J* = 16.4 Hz, 1H), 7.61 (d, *J* = 8.2 Hz, 2H), 7.53 (d, *J* = 16.4 Hz, 1H), 7.42 - 7.33 (m, 3H), 7.29 (d, *J* = 7.1 Hz, 1H).

[0220] Third step: A solution of (E)-7-chloro-3-styrylthieno[3,2-b]pyridine (0.870 g, 3.20 mmol, 1.0 eq.), zinc cyanide (0.75 g, 6.40 mmol, 2 eq.), tris(benzylideneacetone)dipalladium (0) (0.092 g, 0.16 mmol, 0.05 eq.), 1,1'ferrocenediyl-bis-(diphenylphosphine) (0.234 g, 0.32 mmol, 0.1 eq.) and zinc (0.063 mL, 0.96 mmol, 0.3 eq.) in N,N-dimethylformamide (7 ml) was stirred at 160°C for 90 min. The mixture was cooled to RT, filtered over celite, washed with DCM, concentrated and purified by flash column chromatography on silica gel using hexane/ethyl acetate (7:1) as eluent to afford (E)-3-styrylthieno[3,2-b]pyridine-7-carbonitrile as a light yellow solid (0.38 g, 47%).

[0221] Fourth step: A mixture of (E)-3-styrylthieno[3,2-b]pyridine-7-carbonitrile (0.370 g, 1.47 mmol, 1 eq.) and DCM (10 mL) at -78 °C was purged with N_2 for 5 min. Then, ozone was bubbled into the mixture for 15 min and dimethyl sulphide (1.1 mL, 14.78 mmol, 10 eq.) was added. The mixture was stirred at -78 °C with a nitrogen current for 30 min, concentrated and purified by flash column chromatography on silica gel using hexane/ethyl acetate (7:1) as eluent to afford 3-formylthieno[3,2-b]pyridine-7-carbonitrile as a light yellow solid (0.125 g, 45%).

^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 10.53 (s, 1H), 9.01 (d, *J* = 4.7 Hz, 1H), 8.78 (s, 1H), 7.67 (d, *J* = 4.7 Hz, 1H).

Intermediate c24: 3-Formylbenzo[b]thiophene-5,7-dicarbonitrile

[0222] This aldehyde was prepared starting from 5,7-dichlorobenzo[b]thiophene following the 4-step synthesis described for Intermediate **c23**, except that the cyanation reaction was done before the bromination step.

[0223] Yellow solid (0.22 g).

[0224] ^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 10.18 (s, 1H), 9.28 (d, *J* = 1.2 Hz, 1H), 8.60 (s, 1H), 8.04 (d, *J* = 1.2 Hz, 1H).

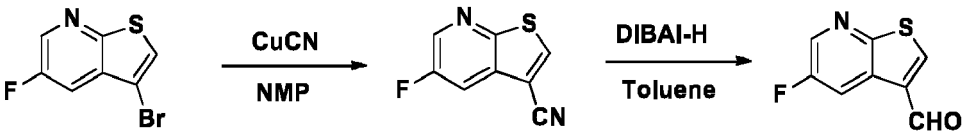
Intermediate c25: 6-Chloro-3-formylbenzo[b]thiophene-7-carbonitrile

[0225] This aldehyde was prepared starting from 3-bromo-6-chlorobenzo[b]thiophene-7-carbonitrile following Steps 2 and 4 of the synthesis described for Intermediate **c23.** Yellow solid (0.29 g).

[0226] ^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 10.13 (s, 1H), 8.84 (d, *J* = 8.8 Hz, 1H), 8.44 (s, 1H), 7.63 (d, *J* = 8.8 Hz, 1H).

Intermediate c26: 5-Fluorothieno[2,3-b]pyridine-3-carbaldehyde

[0227]



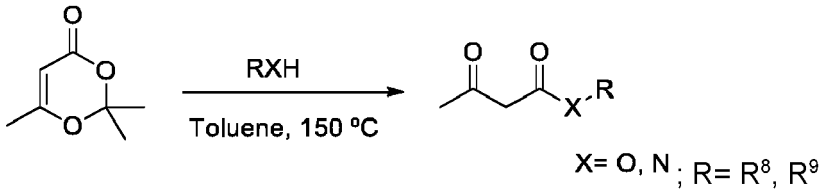
[0228] A solution of 3-bromo-5-fluorothieno[2,3-b]pyridine (0.73 g, 3.14 mmol, 1.0 eq.) and copper cyanide (0.42 g, 4.72 mmol, 1.5 eq.) in N-methyl-2-pirrolydone (18 ml) was stirred for 2 days in a sealed tube at 200 °C, then cooled to RT and poured into saturated aqueous $NaHCO_3$ (30 mL). This mixture was stirred at 4 °C for 60 min. The solid was filtered off and dissolved in a mixture of 40 mL of $NH_4OH_{(28\%)}$/$NH_4Cl_{(sat)}$ (1:1) and ethyl acetate (60 mL) which was stirred for 1h and then extracted with ethyl acetate (x3). The organic phase was dried over Na_2SO_4, filtered, concentrated and purified by flash column chromatography on silica gel using hexane/ethyl acetate (20:1) as eluent to afford 5-fluorothieno[2,3-b]pyridine-3-carbonitrile as a white solid (0.32 g, 56%).
^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 8.61 (d, *J* = 2.4 Hz, 1H), 8.32 (s, 1H), 7.96 (dd, J = 8.1, 2.7 Hz, 1H).

[0229] To a solution of 5-fluorothieno[2,3-b]pyridine-3-carbonitrile (0.32 g, 1.77 mmol, 1 eq.) in toluene (30 ml) at -78 °C was dropwise added a solution of DIBAl-H (1.98 mL, 1.94 mmol, 1.1 eq) in toluene. This mixture was stirred at -78 °C for 5 minutes, then at - 40 °C for 6 hours, and finally it was allowed to warm up to RT. After the addition of water the mixture was extracted with ethyl acetate (x2) which was dried (Na_2SO_4), concentrated and the residue purified by flash column chromatography on silica gel using hexane/ ethyl acetate (10:1) as eluent to afford 5-fluorothieno[2,3-b]pyridine-3-carbaldehyde as a light yellow oil (0.149 g, 47%).
^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 10.05 (s, 1H), 8.63 (dd, J = 8.8, 2.6 Hz, 1H), 8.56 (d, *J* = 2.6 Hz, 1H), 8.50 (s, 1H).

PREPARATION OF DICARBONYL INTERMEDIATES

[0230] Dicarbonyl compounds were synthesized according to the literature as described in the general procedures below.

[0231] **General procedure d**(adapted from Haibin Mao et al., Chem. Int. Ed. 2013, 52, 6288-6291)



[0232] To a solution of 2,2,6-trimethyl-4H-1,3-dioxin-4-one (1 eq) in toluene (5 M) at room temperature, the corresponding alcohol or amine (1 eq) was added. The mixture was heated at 150 °C for 6 hours, then allowed to cool to room temperature and concentrated in vacuum. The remaining residue was purified by flash column chromatography on silica gel using ethyl acetate/hexane as eluent to afford the dicarbonyl compound.

[0233] The following dicarbonyl compounds were synthesized following General procedure **d**.

Intermediate d1: 2,2,2-Trifluoroethyl 3-oxobutanoate

[0234] Light brown oil (8.93 g, 70 %).

[0235] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 4.53 (q, J = 8.4 Hz, 1H), 3.57 (s, 1H), 2.28 (s, 1H). ^{19}F NMR (282 MHz, $CDCl_3$) δ = -73.92.

Intermediate d2: N,N-Diethyl-3-oxobutanamide

[0236] Yellow oil (1.5 g, 91%).
[0237] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 3.49 (s, 2H), 3.39 (q, J = 7.1 Hz, 2H), 3.28 (q, J = 7.2 Hz, 2H), 2.28 (s, 3H), 1.15 (dt, J = 10.6, 7.1 Hz, 6H).

Intermediate d3: 1-(4-Methylpiperazin-1-yl)butane-1,3-dione

[0238] Yellow oil (1.8 g, 91 %).
[0239] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 3.69 - 3.61 (m, 2H), 3.55 (s, 2H), 3.47 - 3.38 (m, 2H), 2.44 - 2.33 (m, 4H), 2.30 (s, 3H), 2.27 (s, 3H).

Intermediate d4: 1-Morpholinobutane-1,3-dione

[0240] Dark yellow oil (1.6 g, 88 %).
[0241] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 3.72 - 3.58 (m, 6H), 3.56 (s, 2H), 3.50 - 3.35 (m, 2H), 2.28 (s, 3H).

Intermediate d5: 2-Methoxyethyl 3-oxobutanoate

[0242] Yellow oil (1.5 g, 91 %).
[0243] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 4.34 - 4.24 (m, 2H), 3.65 - 3.55 (m, 2H), 3.49 (s, 2H), 3.38 (s, 3H), 2.27 (s, 3H).

Intermediate d6: 3-Acetamidopropyl 3-oxobutanoate

[0244] General procedure **d** using N-(3-hydroxypropyl)acetamide (prepared according to K. Veejendra et al., J. Org. Chem. 2004, 69, 577-580) yielded light yellow oil (2.1 g, 92 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 5.96 (bs, 1H), 4.22 (t, J = 6.0 Hz, 2H), 3.50 (s, 2H), 3.33 (q, J = 6.3 Hz, 2H), 2.28 (s, 3H), 1.98 (s, 3H), 1.93 - 1.80 (m, 2H).

Intermediate d7: Benzyl 3-oxobutanoate

[0245] Light yellow oil (2 g, 98 %).
[0246] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.36 (s, 5H), 5.18 (s, 2H), 3.50 (s, 2H), 2.25 (s, 3H).

Intermediate d8: 2-Morpholinoethyl 3-oxobutanoate

[0247] Light yellow oil (2 g, 98 %).
[0248] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 4.27 (t, J = 5.8 Hz, 2H), 3.73 - 3.64 (m, 4H), 3.47 (s, 2H), 2.63 (t, J = 5.8 Hz, 2H), 2.51 - 2.44 (m, 4H), 2.28 (s, 3H).

Intermediate d9: 2-(Dimethylamino)ethyl 3-oxobutanoate

[0249] Light yellow oil (2.1 g, 92 %).
[0250] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 4.24 (t, J = 5.7 Hz, 2H), 3.48 (s, 2H), 2.57 (t, J= 5.7 Hz, 2H), 2.27 (s, 9H).

Intermediate d10: 2-Acetamidoethyl 3-oxobutanoate

[0251] Yellow oil (1.1 g, 91%).
[0252] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 4.26 (t, J = 4.6 Hz, 2H), 3.56 - 3.51 (m, 4H), 2.28 (s, 3H), 2.00 (s, 3H).

Intermediate d11: Cyclohexylmethyl 3-oxobutanoate

[0253] Light yellow oil (1.4 g, 67%).
[0254] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 3.95 (d, J = 6.4 Hz, 2H), 3.44 (s, 2H), 2.27 (s, 3H), 1.78 - 1.56 (m, 6H), 1.33 - 1.09 (m, 3H), 1.06 - 0.83 (m, 2H).

Intermediate d12: Pyridin-4-ylmethyl 3-oxobutanoate

[0255] Yellow oil (1.2 g, 89%).
[0256] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.61 (d, J = 5.6 Hz, 2H), 7.25 (d, J = 4.1 Hz, 2H), 5.19 (s, 2H), 3.57 (s, 2H), 2.28 (s, 3H).

Intermediate d13: Pyridin-2-ylmethyl 3-oxobutanoate

[0257] Yellow oil (1.0 g, 74%).
[0258] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.58 (ddd, J = 4.9, 1.8, 1.0 Hz, 1H), 7.71 (td, J = 7.7, 1.8 Hz, 1H), 7.38 (ddt, J = 7.8, 1.1, 0.6 Hz, 1H), 7.26 - 7.20 (m, 1H), 5.29 (s, 2H), 3.57 (s, 2H), 2.28 (s, 3H).

Intermediate d14: 4-Methoxybenzyl 3-oxobutanoate

[0259] Light yellow oil (1.0 g, 43%).
[0260] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.29 (d, J = 8.5 Hz, 2H), 6.88 (d, J = 8.5 Hz, 2H), 5.10 (s, 2H), 3.80 (s, 3H), 3.46 (s, 2H), 2.22 (s, 3H).

Intermediate d15: 2-((tert-Butoxycarbonyl)oxy)ethyl 3-oxobutanoate

[0261] Colorless oil (1.2 g, 46%).
[0262] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 4.32 (dd, J = 19.8, 5.3 Hz, 4H), 3.47 (s, 2H), 2.27 (s, 2H), 1.49 (s, 9H).

Intermediate d16: tert-butyl 4-(((3-oxobutanoyl)oxy)methyl)piperidine-1-carboxylate Yellow oil (0.46 g, 67%).

[0263] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 4.12 (d, J = 14.5 Hz, 2H), 4.00 (d, J = 6.5 Hz, 2H), 3.46 (s, 2H), 2.69 (t, J = 12.5 Hz, 2H), 2.27 (s, 3H), 1.82 (s, 1H), 1.68 (d, J = 13.6 Hz, 2H), 1.45 (s, 9H), 1.31 - 1.05 (m, 2H).

Intermediate d17: Tetrahydro-2H-(pyran-4-yl)methyl-3-oxobutanoate

[0264] Colorless oil (0.58 g, 83%).
[0265] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 4.05 - 3.92 (m, 4H), 3.47 (d, J = 0.4 Hz, 2H), 3.39 (td, J = 11.9, 2.3 Hz, 2H), 2.27 (s, 3H), 2.03 - 1.83 (m, 1H), 1.63 (ddd, J = 12.8, 3.9, 1.9 Hz, 2H), 1.37 (dtd, J = 13.3, 11.8, 4.5 Hz, 2H).

Intermediate d18: Cyclohexyl 3-oxobutanoate

[0266] Colorless oil (1.08 g, 84%).
[0267] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 4.81 (td, J = 8.8, 3.8 Hz, 1H), 3.42 (s, 2H), 2.26 (s, 3H), 1.91 - 1.80 (m, 2H), 1.77 - 1.66 (m, 2H), 1.61 - 1.49 (m, 2H), 1.47 - 1.29 (m, 4H).

Intermediate d19: Tetrahydro-2H-(pyran-4-yl)-3-oxobutanoate

[0268] Colorless oil (0.6 g, 92%).
[0269] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 5.07 - 4.96 (m, 1H), 3.90 (dt, J = 11.9, 4.6 Hz, 2H), 3.54 (ddd, J = 11.9, 8.9, 3.0 Hz, 2H), 3.46 (s, 2H), 2.27 (s, 3H), 1.97 - 1.91 (m, 2H), 1.70 (dtd, J = 13.0, 8.9, 4.0 Hz, 2H).

Intermediate d20: Cyclopropylmethyl 3-oxobutanoate

[0270] Colorless oil (0.9 g, 82%).
[0271] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 3.97 (d, J = 7.3 Hz, 2H), 3.46 (s, 2H), 2.28 (s, 3H), 1.23 - 1.06 (m, 1H), 0.63 - 0.52 (m, 2H), 0.33 - 0.25 (m, 2H).

Intermediate d21: tert-Butyl 4-(((3-oxobutanoyl)oxy)methyl)piperidine-1-carboxylate Colorless oil (0.45 g, 71%).

[0272] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 4.13 (bs, 2H), 4.00 (d, J = 6.5 Hz, 2H), 3.46 (s, 2H), 2.69 (t, J = 12.7 Hz, 2H), 2.27 (s, 3H), 1.82 (tdd, J = 15.2, 6.5, 3.5 Hz, 1H), 1.68 (d, J = 12.7 Hz, 2H), 1.45 (s, 9H), 1.19 (dtd, J = 12.7, 12.3, 5.7 Hz, 2H).

Intermediate d22: phenethyl 3-oxobutanoate

[0273] Yellow oil (0.97 g, 58%).
[0274] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.34 - 7.27 (m, 2H), 7.25 - 7.17 (m, 3H), 4.37 (t, J = 7.0 Hz, 2H), 3.43 (s, 2H), 2.97 (t, J = 7.0 Hz, 2H), 2.20 (s, 3H).

Intermediate d23: 1,3-dicyclopropylpropane-1,3-dione

[0275] Colorless oil (1.3 g, 87%).
[0276] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 3.78 (s, 2H), 1.56 (td, J = 8.0, 4.1 Hz, 2H), 1.15 - 1.03 (m, 4H), 0.98 - 0.85 (m, 4H).

Intermediate d24: methyl 3-cyclopropyl-3-oxopropanoate

[0277] Light-yellow oil (2.01 g, 79%).
[0278] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 3.74 (d, J = 1.5 Hz, 3H), 3.58 (d, J = 1.2 Hz, 2H), 2.17 - 1.95 (m, 1H), 1.28 - 1.07 (m, 2H), 1.07 - 0.82 (m, 2H).

Intermediate d25: methyl 4-fluoro-3-oxobutanoate

[0279] Light-yellow oil (2.8 g, 78%).
[0280] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 4.91 (d, J = 47.5 Hz, 2H), 3.76 (s, 3H), 3.61 (d, J = 3.7 Hz, 2H). ^{19}F NMR (282 MHz, $CDCl_3$) δ = 123.96 (t, J = 47.5 Hz).

Intermediate d26: Methyl 4-(benzyloxy)-3-oxobutanoate

[0281] Yellow oil (0.75 g, 51%).
[0282] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.41 - 7.29 (m, 5H), 4.59 (s, 2H), 4.14 (s, 2H), 3.71 (s, 3H), 3.56 (s, 2H).

Intermediate d27: Methyl 3-oxo-4-phenoxybutanoate

[0283] Yellow oil (47%).
[0284] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.53 - 7.31 (m, 5H), 4.32 (s, 2H), 3.69 (s, 3H), 3.55 (s, 2H).

Intermediate d28: 3-oxo-N-phenylbutanamide

[0285] Yellow oil (0.98 g, 79%).
[0286] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 9.08 (bs, 1H), 7.54 (dt, J = 8.8, 1.7 Hz, 2H), 7.38 - 7.28 (m, 2H), 7.12 (tt, J = 7.1, 1.1 Hz, 1H), 3.59 (s, 2H), 2.33 (s, 3H).

Intermediate d29: tert-butyl 4-((3-oxobutanoyl)oxy)piperidine-1-carboxylate

[0287] Light yellow oil (1.3 g, 89%).
[0288] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 4.99 (tt, J = 8.5, 3.6 Hz, 1H), 3.77 - 3.61 (m, 2H), 3.46 (s, 2H), 3.24 (ddd, J = 13.3, 8.5, 3.6 Hz, 2H), 2.27 (s, 3H), 1.87 (ddt, J = 12.9, 6.5, 3.4 Hz, 2H), 1.63 (dp, J = 12.9, 4.3 Hz, 2H), 1.46 (s, 9H).

Intermediate d30: Cyclopentylmethyl 3-oxobutanoate

[0289] Colorless oil (1.63 g, 84%).
[0290] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 4.03 (d, J = 7.1 Hz, 2H), 3.45 (s, 2H), 2.27 (s, 3H), 2.24 - 2.15 (m, 1H), 1.81 - 1.69 (m, 2H), 1.64 - 1.51 (m, 4H), 1.34 - 1.17 (m, 2H).

Intermediate d31: 1-Methylpiperidin-4-yl 3-oxobutanoate

[0291] Yellow oil (1.2 g, 57%).
[0292] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 4.84 (tt, J = 7.9, 3.8 Hz, 1H), 3.44 (s, 2H), 2.70 - 2.55 (m, 2H), 2.34 - 2.18 (m, 8H), 2.02 - 1.86 (m, 2H), 1.73 (dtd, J = 12.7, 8.6, 3.8 Hz, 2H).

Intermediate d32: Cyclopentyl 3-oxobutanoate

[0293] Colorless oil (1.25 g, 70%).
[0294] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 5.28 - 5.16 (m, 1H), 3.40 (s, 2H), 2.26 (s, 3H), 1.92-1.81 (m, 2H), 1.76-1.66 (m, 4H), 1.63-1.54 (m, 2H).

Intermediate d33: 4,4-Dimethylcyclohexyl 3-oxobutanoate

[0295] Light yellow oil (0.42 g, 57%).
[0296] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 4.80 (tt, J = 8.8, 4.1 Hz, 1H), 3.42 (s, 2H), 2.27 (s, 3H), 1.82 - 1.70 (m, 2H), 1.65 - 1.52 (m, 2H), 1.48 - 1.38 (m, 2H), 1.25 (ddd, J = 14.0, 10.4, 4.1 Hz, 2H), 0.93 (s, 3H), 0.91 (s, 3H).

Intermediate d34: Cyclobutyl 3-oxobutanoate

[0297] Colorless oil (1.06 g, 51%).
[0298] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 5.09 - 4.96 (m, 1H), 3.41 (s, 2H), 2.42 - 2.29 (m, 2H), 2.26 (s, 3H), 2.14 - 2.00 (m, 2H), 1.86 - 1.54 (m, 2H).

Intermediate d35: 4-Fluorobenzyl 3-oxobutanoate

[0299] Colorless oil (1.32 g, 89%).
[0300] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.41 - 7.28 (m, 2H), 7.13 - 6.96 (m, 2H), 5.14 (s, 2H), 3.49 (s, 2H), 2.24 (s, 3H). ^{19}F NMR (282 MHz, $CDCl_3$) δ = -113.31.

Intermediate d36: Pyridin-3-ylmethyl 3-oxobutanoate

[0301] Light-yellow oil (0.95 g, 70%).
[0302] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.62 (d, J = 2.2 Hz, 1H), 8.59 (dd, J = 4.8, 1.6 Hz, 1H), 7.76 - 7.65 (m, 1H), 7.31 (ddd, J = 7.9, 4.8, 0.9 Hz, 1H), 5.19 (s, 2H), 3.51 (s, 2H), 2.25 (s, 3H).

Intermediate d37: tert-butyl 4-(((3-oxobutanoyl)oxy)methyl)benzoate

[0303] Light-yellow solid (0.59 g, 79%).
[0304] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.96 (d, J = 8.0 Hz, 2H), 7.39 (d, J = 8.0 Hz, 2H), 5.15 (s, 2H), 1.93 (s, 2H), 1.93 (s, 3H), 1.59 (s, 9H).

Intermediate d38: 4-(Cyclopropylcarbamoyl)benzyl 3-oxobutanoate

[0305] General procedure **d** using N-cyclopropyl-4-(hydroxymethyl)benzamide (J.Med. Chem., **2001**, 44, 1491-1508) yielded yellow oil (0.14 g, 76%).
[0306] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.73 (d, J = 8.2 Hz, 2H), 7.40 (d, J = 8.2 Hz, 2H), 6.23 (bs, 1H), 5.20 (s, 2H), 3.52 (s, 2H), 2.90 (dq, J = 7.2, 3.5 Hz, 1H), 2.25 (s, 3H), 0.88 (q, J = 6.5 Hz, 2H), 0.67 - 0.52 (m, 2H).

Intermediate d39: 4-bromobenzyl 3-oxobutanoate

[0307] Yellow oil (0.5 g, 34%).
[0308] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.49 (d, J = 8.0 Hz, 2H), 7.23 (d, J = 8.0 Hz, 2H), 5.12 (s, 2H), 3.50 (s, 2H), 2.24 (s, 3H).

Intermediate d40: 3-bromobenzyl 3-oxobutanoate

[0309] Yellow oil (1.5 g, 69%).
[0310] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.50 (d, J = 1.8 Hz, 1H), 7.46 (dt, J = 7.5, 1.8 Hz, 1H), 7.29 - 7.21 (m, 2H), 5.13 (s, 2H), 3.51 (s, 2H), 2.25 (s, 3H).

Intermediate d41: 2-bromobenzyl 3-oxobutanoate

[0311] Yellow oil (1.2 g, 83%).

[0312] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.56 (dd, J = 7.8, 1.1 Hz, 1H), 7.41 (dd, J = 7.5, 1.6 Hz, 1H), 7.31 (td, J = 7.5, 1.1 Hz, 1H), 7.18 (td, J = 7.8, 1.6 Hz, 1H), 5.25 (s, 2H), 3.52 (s, 2H), 2.26 (s, 3H).

Intermediate d42: (3-Fluoropyridin-4-yl)methyl 3-oxobutanoate Yellow oil (0.305 g, 41%).

[0313] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.54 - 8.38 (m, 2H), 7.46 - 7.31 (m, 1H), 5.29 (s, 2H), 3.57 (s, 2H), 2.29 (s, 3H). ^{19}F NMR (282 MHz, $CDCl_3$) δ = -132.13 (s, CF).

Intermediate d43: Pyrimidin-5-ylmethyl 3-oxobutanoate

[0314] Yellow oil (0.65 g, 96%).
[0315] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 9.20 (s, 1H), 8.77 (s, 2H), 5.20 (s, 2H), 3.53 (s, 2H), 2.26 (s, 3H).

Intermediate d44: (5-Bromopyridin-3-yl)methyl 3-oxobutanoate Yellow oil (0.5 g, 63%).

[0316] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.65 (d, J = 2.0 Hz, 1H), 8.53 (s, 1H), 7.87 (s, 1H), 5.17 (s, 2H), 3.53 (s, 2H), 2.26 (s, 3H).

Intermediate d45: 3-cyanobenzyl 3-oxobutanoate

[0317] Yellow oil (0.57 g, 75%).
[0318] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.68 - 7.57 (m, 3H), 7.53 - 7.45 (m, 1H), 5.20 (s, 2H), 3.54 (s, 2H), 2.27 (s, 3H).

Intermediate d46: 4-cyanobenzyl 3-oxobutanoate

[0319] Yellow oil (0.62 g, 82%).
[0320] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.66 (d, J = 8.1 Hz, 2H), 7.46 (d, J = 8.1 Hz, 2H), 5.22 (s, 2H), 3.54 (s, 2H), 2.26 (s, 3H).

Intermediate d47: (6-chloropyridin-3-yl)methyl 3-oxobutanoate Yellow oil (0.69 g, 87%).

[0321] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.31 (s, 1H), 7.79 - 7.52 (m, 1H), 7.26 (d, J = 8.2 Hz, 1H), 5.09 (s, 2H), 3.45 (s, 2H), 2.17 (s, 3H).

Intermediate d48: 3-morpholinobenzyl 3-oxobutanoate

[0322] Yellow oil (0.71 g, 92%).
[0323] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.30 (d, J = 7.9 Hz, 1H), 6.94 - 6.86 (m, 3H), 5.16 (s, 2H), 3.90 - 3.86 (m, 4H), 3.51 (s, 2H), 3.21 - 3.17 (m, 4H), 2.27 (s, 3H).

Intermediate d49: (2-Chloropyridin-4-yl)methyl 3-oxobutanoate

[0324] Yellow oil (0.50 g, 63%).
[0325] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.41 - 8.33 (m, 1H), 7.32 (s, 1H), 7.19 (d, J = 5.1 Hz, 1H), 5.17 (s, 2H), 3.58 (s, 2H), 2.28 (s, 3H).

Intermediate d50: 4,4-Difluorocyclohexyl 3-oxobutanoate

[0326] Yellow oil (0.35 g, 91%).
[0327] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 4.93 (s, 1H), 4.53 (s, 2H), 2.04 (d, J = 1.1 Hz, 3H), 1.89 - 1.78 (m, 8H). ^{19}F NMR (282 MHz, $CDCl_3$) δ = -94.48 (d, J = 252.2 Hz, CF), -100.51 (d, J = 235.8 Hz, CF).

Intermediate d51: N-benzyl-N-methyl-3-oxobutanamide

[0328] Yellow oil (2.50 g, 86%).
[0329] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.38 - 7.23 (m, 5H), 4.56 (d, J = 32.5 Hz, 3H), 3.60 (d, J = 12.5 Hz, 2H), 2.89 (s, 2H), 2.29 (s, 3H).

Intermediate d52: 4-chlorobenzyl 3-oxobutanoate

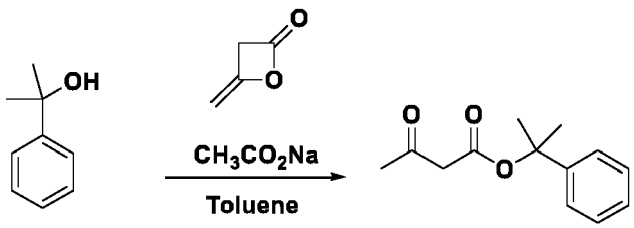
[0330] Yellow oil (0.5 g, 34%).
[0331] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.49 (d, J = 8.0 Hz, 2H), 7.23 (d, J = 8.0 Hz, 2H), 5.12 (s, 2H), 3.50 (s, 2H), 2.24 (s, 3H).

Intermediate d53: 3-chlorobenzyl 3-oxobutanoate

[0332] Yellow oil (0.119 g, 75 %).
[0333] ^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 7.35 (s, 1H), 7.33 - 7.27 (m, 2H), 7.25 - 7.19 (m, 1H), 5.14 (s, 2H), 3.52 (s, 2H), 2.26 (s, 3H).

Intermediate d54: 2-phenylpropan-2-yl 3-oxobutanoate

[0334]



[0335] Modified procedure d using 4-methyleneoxetan-2-one (1 eq) and sodium acetate (0.1 eq) yielded the title compound as yellow oil (2.46 g, 76%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.41 - 7.27 (m, 5H), 3.42 (s, 2H), 2.25 (s, 3H), 1.80 (s, 6H).

Intermediate d55: 2-(4-Fluorophenyl)propan-2-yl 3-oxobutanoate

[0336] Modified procedure **d** using 4-methyleneoxetan-2-one (1 eq) yielded the title compound as yellow oil (0.52 g, 34 %).
^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 7.40 - 7.31 (m, 2H), 7.05 - 6.95 (m, 2H), 3.41 (s, 2H), 2.23 (s, 3H), 1.78 (s, 6H).
^{19}F NMR (282 MHz, $CDCl_3$-*d*) δ (ppm): -115.79 (CF).

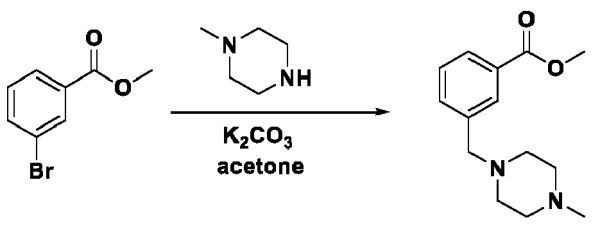
Intermediate d56: 2H-thiopyran-3,5(4H,6H)-dione

[0337] Synthesis according to literature procedure J. Org.Chem. 1977, 42, 1163-1169 yielded yellow oil (2.1 g, 52%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 3.57 (s, 2H), 3.39 (s, 4H).

Intermediate d57: 3-((4-Methylpiperazin-1-yl)methyl)benzyl 3-oxobutanoate

Step 1: Synthesis of 3-((4-methylpiperazin-1-yl)methyl)benzoate

[0338]

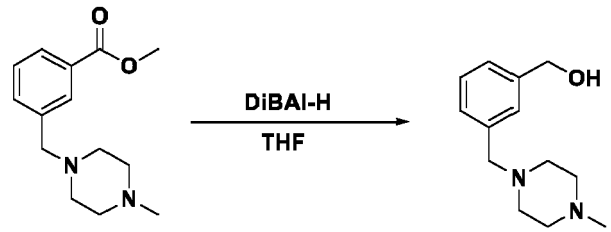


[0339] To a solution of 1-methylpiperazine (3.0 mL, 26.89 mmol, 3.08 eq.) in acetone (35 ml) was added potassium carbonate (2.41 g, 17.46 mmol, 2 eq). The mixture was stirred for 10 minutes. Then methyl 3-bromobenzoate (2.0 g, 8.73 mmol, 1.0 eq.) was added, and the mixture was stirred at room temperature overnight. The solid was removed by

filtration, and the filtrate was concentrated and purified by flash column chromatography on silica gel using dichloromethane / 3% methanol as eluent to afford methyl 3-((4-methylpiperazin-1-yl)methyl)benzoate as a yellow oil (2.1 g, 97%).
^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 7.97 (s, 1H), 7.92 (dt, *J* = 7.7, 1.4 Hz, 1H), 7.53 (d, *J* = 7.7 Hz, 1H), 7.38 (t, *J* = 7.7 Hz, 1H), 3.91 (s, 3H), 3.55 (s, 2H), 2.48 (bs, 8H), 2.29 (s, 3H).

Step 2: Synthesis of (3-((4-methylpiperazin-1-yl)methyl)phenyl)metanol

[0340]



[0341] To a solution of methyl 3-((4-methylpiperazin-1-yl)methyl)benzoate (2.02 g, 8.13 mmol, 1 eq.) in tetrahydrofurane (60 ml) was added under vigorous stirring diisobutylaluminium hydride (18.73 mL, 18.73 mmol, 2.26 eq). The mixture was stirred at room temperature for 5 hours. Then Rochele's salt solution (105 mL) and dichloromethane (105 mL) were added. The mixture was stirred at room temperature for 60 minutes and then extracted with dichloromethane (x3) and dried (Na_2SO_4). The solvent was removed under reduced pressure, and the resulting residue was purified by flash column chromatography on silica gel using dichloromethane / 7% methanol as eluent to afford (3-((4-methylpiperazin-1-yl)methyl)phenyl)methanol as a yellow oil (1.75 g, 98%).
^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 7.32 - 7.15 (m, 4H), 4.62 (s, 2H), 3.71 (t, *J* = 6.2 Hz, 1H), 3.45 (s, 2H), 2.37 (bs, 8H), 2.20 (s, 3H).

Step 3: Synthesis of 3-((4-Methylpiperazin-1-yl)methyl)benzyl 3-oxobutanoate

[0342] Transformation of (3-((4-methylpiperazin-1-yl)methyl)phenyl)methanol using General procedure **d** yielded the title compound as a yellow oil (0.55 g, 81%). ^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 7.36 - 7.28 (m, 3H), 7.24 - 7.20 (m, 1H), 5.17 (s, 2H), 3.52 (s, 2H), 3.50 (s, 2H), 2.53 (bs, 8H), 2.34 (s, 3H), 2.25 (s, 3H).

Intermediate d58: Cyclopropyl 3-oxobutanoate

[0343] Modified procedure **d** using 4-methyleneoxetan-2-one (1 eq) and sodium acetate (0.1 eq) yielded the title compound as a yellow oil (1.99 g, 81 %).
[0344] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 4.19 - 4.04 (m, 1H), 3.39 (s, 2H), 2.22 (s, 3H), 0.79 - 0.58 (m, 4H).

Intermediate d59: Prop-2-yn-1-yl 3-oxobutanoate

[0345] General procedure **d** yielded the title compound as a yellow oil (2.5 g, 91 %).
[0346] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 4.74 (d, *J* = 2.5 Hz, 2H), 3.50 (s, 2H), 2.50 (t, *J* = 2.5 Hz, 1H), 2.28 (s, 3H).

Intermediate d60: But-2-yn-1-yl 3-oxobutanoate

[0347] General procedure **d** yielded the title compound as a yellow oil (3.0 g, 92 %).
[0348] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 4.65 (q, *J* = 2.2 Hz, 2H), 3.44 (s, 2H), 2.22 (s, 3H), 1.80 (t, *J* = 2.2 Hz, 3H).

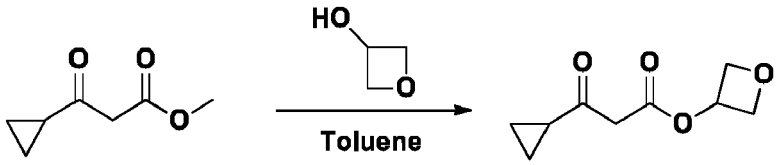
Intermediate d61: 2,2,2-Trifluoroethyl 3-oxobutanoate

[0349] General procedure **d** yielded the title compound as a yellow oil (2.1 g, 81 %).
[0350] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 4.53 (q, *J* = 7.6, 6.9 Hz, 2H), 3.57 (s, 2H), 2.29 (s, 3H).

General procedure e

Intermediate e1: Oxetan-3-yl 3-cyclopropyl-3-oxopropanoate

[0351]



[0352] To a solution of methyl 3-cyclopropyl-3-oxopropanoate (1 g, 7.03 mmol, 1.2 eq.) in toluene (5 ml) was added oxetan-3-ol (0.37 ml, 5.87 mmol, 1 eq). The resultant mixture was refluxed using a Dean-Stark trap for 12 hours, cooled to RT and concentrated. The resulting residue was purified by flash column chromatography on silica gel using ethyl acetate/hexane (1:3) as eluent to afford the title compound as a light-yellow oil (0.52 g, 44%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 5.50 (p, J = 5.8 Hz, 1H), 4.99-4.81 (m, 2H), 4.66 (dd, J = 7.8, 5.8 Hz, 2H), 3.63 (s, 2H), 2.02 (tt, J = 7.8, 4.5 Hz, 1H), 1.17-1.08 (m, 2H), 1.05-0.93 (m, 2H).

Intermediate e2: Isopropyl 3-cyclopropyl-3-oxopropanoate

[0353] General procedure **e** yielded the title compound as a light-yellow oil (0.9 g, 75%). ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 5.06 (hept, J = 6.4 Hz, 1H), 3.52 (s, 2H), 2.14 - 1.93 (m, 1H), 1.26 (s, 3H), 1.24 (s, 3H), 1.15 - 1.06 (m, 2H), 1.00 - 0.90 (m, 2H).

Intermediate e3: Benzyl 4,4,4-trifluoro-3-oxobutanoate

[0354] General procedure **e** yielded the title compound as a red oil (1.8 g, 62%).
[0355] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.37 (s, 5H), 5.24 (s, 2H), 2.86 (s, 2H). ^{19}F NMR (282 MHz, $CDCl_3$) δ = -87.15.

Intermediate e4: 2-Phenylpropan-2-yl 3-cyclopropyl-3-oxopropanoate

[0356] General procedure **e** using 1 eq of DMAP yielded the title compound as a yellow oil (0.41 g, 29 %).
[0357] ^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 7.40 - 7.31 (m, 4H), 7.23 (d, *J* = 6.9 Hz, 1H), 3.53 (s, 2H), 2.03 - 1.99 (m, 1H), 1.80 (s, 6H), 1.15 - 1.09 (m, 2H), 1.00 - 0.89 (m, 2H).

Intermediate e5: Cyclohexyl 3-cyclopropyl-3-oxopropanoate

[0358] General procedure **e** yielded the title compound as a light-yellow solid (1.2 g, 85 %).
[0359] ^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 4.91 - 4.75 (m, 1H), 3.52 (s, 2H), 2.12 - 1.95 (m, 1H), 1.93 - 1.79 (m, 2H), 1.78 - 1.60 (m, 2H), 1.53 - 1.23 (m, 6H), 1.18 - 1.04 (m, 2H), 1.03 - 0.88 (m, 2H).

Intermediate e6: 3-Chlorobenzyl 3-cyclopropyl-3-oxopropanoate

[0360] General procedure **e** yielded the title compound as a yellow oil (0.69 g, 78 %).
^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 7.35 (s, 1H), 7.32 - 7.27 (m, 2H), 7.25 - 7.20 (m, 1H), 5.15 (s, 2H), 3.63 (s, 2H), 2.09 - 1.92 (m, 1H), 1.20 - 1.05 (m, 2H), 1.03 - 0.87 (m, 2H).

Intermediate e7: 2-(4-Fluorophenyl)propan-2-yl 3-cyclopropyl-3-oxopropanoate

[0361] General procedure **e** yielded the title compound as a yellow oil (0.52 g, 35 %).
^{1}H-NMR (300 MHz, CDCl -d) δ (ppm): 7.40 - 7.31 (m, 2H), 7.05 - 6.96 (m, 2H), 3.53 (s, 2H), 2.01 (tt, *J* = 7.7, 4.4 Hz, 1H), 1.78 (s, 6H), 1.12 (pd, *J* = 3.5, 1.4 Hz, 2H), 0.96 (dt, *J* = 7.7, 3.5 Hz, 2H).
^{19}F NMR (282 MHz, CDCl -d) δ (ppm): -115.92 (CF).

Intermediate e8: Cyclopropylmethyl 3-cyclopropyl-3-oxopropanoate

[0362] General procedure **e** using 1 eq DMAP yielded the title compound as a light-yellow oil (2.2 g, 34 %).
^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm) 3.98 (d, *J* = 7.3 Hz, 2H), 3.58 (s, 2H), 2.05 (tt, *J* = 7.9, 4.6 Hz, 1H), 1.24 - 1.04 (m, 3H), 1.02 - 0.91 (m, 2H), 0.61 - 0.51 (m, 2H), 0.29 (dt, *J* = 6.4, 4.6 Hz, 2H).

Intermediate e): 3-Bromobenzyl 3-cyclopropyl-3-oxopropanoate

[0363] General procedure **e** yielded the title compound as a yellow oil (0.28 g, 27 %).
^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 7.51 (s, 1H), 7.45 (dt, *J* = 7.5, 1.7 Hz, 1H), 7.31 - 7.21 (m, 2H), 5.14 (s, 2H), 3.63 (s, 2H), 2.01 (tt, *J* = 7.7, 4.5 Hz, 1H), 1.21 - 1.06 (m, 2H), 1.01 - 0.87 (m, 2H).

Intermediate e10: Cyclopentyl 3-cyclopropyl-3-oxopropanoate

[0364] General procedur **e** yielded the title compound as a light-yellow oil (0.54 g, 79 %).
^{1}H-NMR (300 MHz, CDCl -d) δ (ppm): 5.22 (tt, *J* = 6.0, 2.7 Hz, 1H), 3.51 (s, 2H), 2.02 (tt, *J* = 7.8, 4.5 Hz, 1H), 1.92 - 1.78 (m, 2H), 1.77 - 1.65 (m, 4H), 1.64 - 1.53 (m, 2H), 1.16 - 1.04 (m, 2H), 0.95 (dt, *J* = 7.8, 3.2 Hz, 2H).

Intermediate e11: Cyclopentyl 2-cyanoacetate

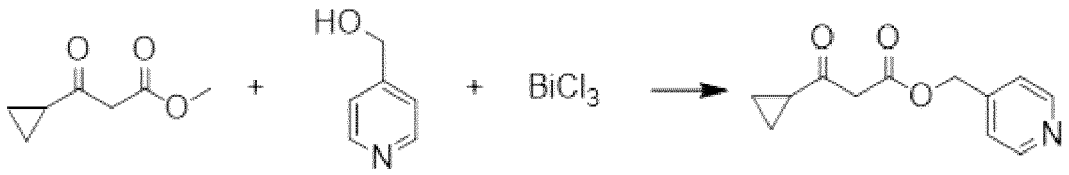
[0365] General procedure **e** yielded the title compound as a light-yellow oil (2.34 g, 50 %).
^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 5.25 (td, *J* = 5.8, 2.9 Hz, 1H), 3.41 (s, 2H), 1.96 - 1.82 (m, 2H), 1.81 - 1.68 (m, 4H), 1.67 - 1.55 (m, 2H).

General procedure f

[0366] The synthetic method was adapted from Sabitha-G et al., Bismuth(III)Chloride-Catalyzed Highly Efficient Transeterification of β-Keto Esters, Helvetica Chimica Acta, Vol. 94. 2011.

Intermediate f1: Pyridin-4-ylmethyl 3-cyclopropyl-3-oxopropanoate

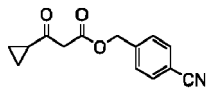
[0367]



[0368] In a sealed flask, a mixture of 2.0 g of molecular sieves, 500 mg (4.58 mmol) of pyridin-4-ylmethanol, 0.83 mL (6.87 mmol) of methyl 3-cyclopropyl-3-oxopropanoate and 10% (0.45 mmol) of trichlorobismuthane in 10 mL of dry toluene was stirred at reflux for 36 hours. The reaction mixture was filtered and the filtrate concentrated, the remaining solid was purified by silica gel chromatography column (cyclohexane/ethyl acetate) to yield the desired β-keto ester (455 mg, 45%).
^{1}H-NMR (400 MHz, DMSO-d_6) δ = 0.94 (m, 4H), 2.12 (ddd, 1H), 3.86 (s, 2H), 5.20 (s, 2H), 7.36 (d, 2H), 8.56 (d, 2H).
HPLC-MS: Rt 3.040; m/z 220.1 (MH^+).
[0369] The following intermediates were synthesized according to General procedure **f. Intermediate f2:** 4-Fluorobenzyl 3-cyclopropyl-3-oxopropanoate
^{1}H-NMR (400 MHz, DMSO-d_6) δ = 0.91 (m, 4H), 2.08 (m, 1H), 3.77 (s, 2H), 5.12 (s, 2H), 7.21 (t, 2H), 7.43 (dd, 2H).

Intermediate f3: 4-Cyanobenzyl 3-cyclopropyl-3-oxopropanoate

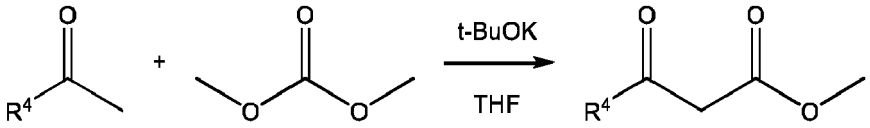
[0370]



[0371] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 0.93 (m, 4H), 2.10 (ddd, 1H), 3.83 (s, 2H), 5.24 (s, 2H), 7.56 (d, 2H), 7.86 (d, 2H).
[0372] HPLC-MS: Rt 4.133; m/z 244.0 (MH^+).

General procedure g (adapted from M. A. Walker et al, Bioorg. Med. Chem. Lett. 2006, 16, 2920-2924)

[0373]



[0374] An aromatic ketone (1 eq) was dissolved in THF (0.5 M) at room temperature, and potassium tert-butoxide (3 eq) was added. The mixture was stirred for 5 minutes before dimethyl carbonate (10 eq) was added. The reaction mixture was stirred at RT for 5 hours, concentrated and quenched by the addition of water. The mixture was extracted with dichloromethane (x3), and the combined organic layers were washed with brine, dried (Na_2SO_4), filtered and concentrated. The crude product was purified by flash column chromatography on silica gel using ethyl acetate/hexane as eluent to afford the corresponding dicarbonyl compound.
[0375] The following intermediates were synthesized according to General procedure **g**.

Intermediate g1: Methyl 3-oxo-3-phenylpropanoate

[0376] Yellow oil (1.11 g, 66%).
[0377] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.95 (d, *J* = 7.8 Hz, 2H), 7.65 - 7.41 (m, 3H), 4.01 (s, 2H), 3.76 (s, 3H).

Intermediate g2: Methyl 3-oxo-3-(pyridin-3-yl)propanoate

[0378] Yellow oil (1.22 g, 83%).
[0379] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 9.15 (dd, *J* = 2.3, 1 Hz, 1H), 8.81 (dd, *J* = 4.8, 1.7 Hz, 1H), 8.23 (ddd, *J* = 8.0, 2.3, 1.7 Hz, 1H), 7.45 (ddd, *J* = 8.0, 4.8, 0.9 Hz, 1H), 4.02 (s, 2H), 3.76 (s, 3H).

Intermediate g3: 1-Phenylpentane-2,4-dione

[0380] Yellow oil (1.11 g, 66%).
[0381] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.37 - 7.26 (m, 5H), 3.59 (s, 4H), 2.02 (s, 3H).

Intermediate g4: 1,3-Dicyclopropylpropane-1,3-dione

[0382] Light-yellow oil (1.3 g, 87%).
[0383] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 3.78 (s, 2H), 2.03 (td, *J* = 7.9, 3.9 Hz, 2H), 1.14 - 1.04 (m, 8H).

Intermediate g5: tert-Butyl 3-(3-methoxy-3-oxopropanoyl)azetidine-1-carboxylate

[0384] Yellow oil (0.4 g, 63%).
[0385] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 4.11 - 3.98 (m, 4H), 3.73 (s, 3H), 3.66 - 3.53 (m, 1H), 3.47 (s, 2H), 1.42 (s, 9H).

Intermediate g6: 1-(Pyridin-3-yl)butane-1,3-dione

[0386] Yellow oil (0.20 g, 30%).
[0387] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 15.95 (s, 1H), 9.05 (d, *J* = 2.1 Hz, 1H), 8.71 (dd, *J* = 4.8, 1.6 Hz, 1H), 8.14 (dt, *J* = 8.0, 2.0 Hz, 1H), 7.38 (ddd, *J* = 8.0, 4.9, 0.9 Hz, 1H), 6.17 (s, 1H), 2.21 (s, 3H).

Intermediate g7: Methyl 3-cyclobutyl-3-oxopropanoate

Colorless oil (1.97 g, 62 %).

[0388] ^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 3.71 (s, 3H), 3.45 - 3.31 (m, 3H), 2.32 - 2.06 (m, 4H), 2.05 - 1.74 (m, 2H).

Intermediate g8: Methyl 3-cyclopentyl-3-oxopropanoate

Colorless oil (0.51 g, 67 %).

[0389] ^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 3.73 (s, 3H), 3.50 (s, 2H), 2.98 (p, *J* = 7.9 Hz, 1H), 1.89 - 1.73 (m, 4H), 1.68 - 1.57 (m, 4H).

Intermediate g9: Methyl 3-cyclohexyl-3-oxopropanoate

Colorless oil (1.14 g, 78 %).

[0390] ^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 3.71 (s, 3H), 3.48 (s, 2H), 2.44 (tt, *J* = 11.1, 3.4 Hz, 1H), 1.91 - 1.83 (m, 2H), 1.84 - 1.71 (m, 2H), 1.44 - 1.13 (m, 6H).

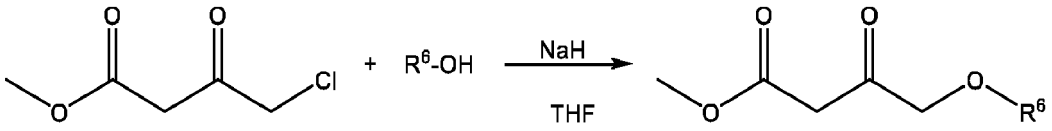
Intermediate g10: (Z)-3-Amino-3-cyclopropylacrylonitrile

[0391] Colorless oil (1.3 g, 81 %).

[0392] ^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 4.63 (bs, 2H), 3.78 (s, 1H), 1.54 - 1.35 (m, 1H), 1.00 - 0.81 (m, 2H), 0.81 - 0.60 (m, 2H).

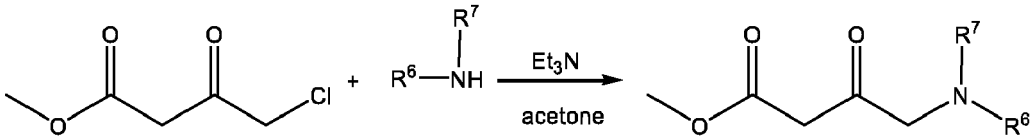
General procedure h (adapted from S. Mitsuhashi et al, J. Am. Chem. Soc. 2008, 130, 4140).

[0393] Preparation of keto ethers:



[0394] To a suspension of sodium hydride (2.2 eq) in THF (0.5 M) at RT, an alcohol (1.1 eq) was added dropwise. The mixture was stirred for 5 min before methyl 4-chloro-3-oxobutanoate (1 eq) was dropwise added. This mixture was stirred for 30 min and then concentrated in vacuum. Water was added, and the pH was adjusted to 6-7 by the addition of 2N aq. HCl. The resulting mixture was extracted with dichloromethane (x2) and ethyl acetate (x2), and the combined organic layers were washed with brine, dried (Na_2SO_4), filtered and concentrated. The resulting residue was purified by flash column chromatography on silica gel using ethyl acetate/hexane as eluent to afford the corresponding dicarbonyl compound.

[0395] Preparation of keto amines:



[0396] Methyl 4-chloro-3-oxobutanoate (1 eq) was dissolved in acetone (0.5 M) at RT, and an amine (1.1 eq) was added. The mixture was stirred for 5 min before trimethylamine (2 eq) was added. This mixture was stirred at 100° C for 3h and then concentrated under vacuum. The residue was taken up in water and extracted with dichloromethane (x2) and ethyl acetate (x2). The combined organic layers were washed with brine, dried (Na_2SO_4), filtered and concentrated. The resulting residue was purified by flash column chromatography on silica gel using ethyl acetate/hexane as eluent to afford the corresponding dicarbonyl compound.

[0397] The following intermediates were synthesized according to General procedure **h**.

Intermediate h1: Methyl 4-methoxy-3-oxobutanoate

[0398] Colorless oil (0.9 g, 93%).
[0399] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 4.10 (s, 2H), 3.75 (s, 3H), 3.50 (s, 2H), 3.40 (s, 3H).

Intermediate h2: Methyl 4-(dimethylamino)-3-oxobutanoate

[0400] Light-yellow oil (0.37 g, 35%).
[0401] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 3.73 (s, 3H), 3.51 (s, 2H), 3.20 (s, 2H), 2.28 (s, 6H).

Intermediate h3: Methyl 4-morpholino-3-oxobutanoate

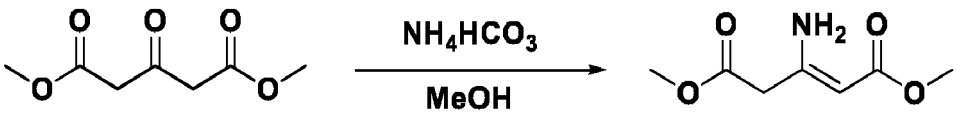
[0402] Light-yellow oil (0.5 g, 37%).
[0403] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 3.76 - 3.78 (m, 7H), 3.51 (s, 2H), 3.25 (s, 2H), 2.55 - 2.43 (m, 4H).

PREPARATION OF ENAMINE INTERMEDIATES

General procedure i

Intermediate i1: Dimethyl (Z)-3-aminopent-2-enedioate

[0404]



[0405] To a round bottom flask containing a dimethyl 3-oxopentanedioate (0.83 ml, 5.74 mmol, 1 eq.) in MeOH (10 ml) at room temperature was added ammonium bicarbonate (1.13 g, 14.35 mmol, 2.5 eq). The mixture was stirred at room temperature overnight and then concentrated. The resulting residue was purified by flash column chromatography on silica gel using ethyl acetate/hexane (1:3) as eluent to afford dimethyl (Z)-3-aminopent-2-enedioate as a yellow oil (0.8 g, 81%).
[0406] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.81 (bs, 1H), 5.50 (bs, 1H). 4.58 (s, 1H), 3.73 (s, 3H), 3.65 (s, 3H), 3.15 (s, 2H).
[0407] The following intermediates were synthesized according to General procedure **i**.

Intermediate i2: Cyclopropylmethyl (Z)-3-aminobut-2-enoate

[0408] White solid (0.45 g, 53%).
[0409] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.91 (bs, 2H), 4.56 (s, 1H), 3.88 (d, *J* = 7.2 Hz, 2H), 1.90 (s, 3H), 1.19 - 1.07 (m, 1H), 0.58 - 0.50 (m, 2H), 0.32 - 0.23 (m, 2H).

Intermediate i3: Methyl (Z)-3-amino-5-methoxypent-2-enoate

[0410] Light-yellow oil (0.93 g, 94%).
[0411] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.83 (bs, 1H), 5.50 (bs, 1H), 4.49 (s, 1H), 3.63 (s, 3H), 3.59 - 3.54 (m, 2H), 3.36 (s, 3H), 2.37 (t, *J* = 5.7 Hz, 2H).

Intermediate i4: Methyl (Z)-3-amino-4-(benzyloxy)but-2-enoate

[0412] Orange oil (0.55 g, 76%).
[0413] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.41 - 7.36 (m, 1H), 7.36 - 7.30 (m, 4H), 6.61 (bs, 1H), 5.27 (bs, 1H), 4.58 - 4.54 (m, 1H), 4.52 (s, 2H), 4.07 (d, *J* = 0.7 Hz, 2H), 3.66 (s, 3H).

Intermediate i5: Methyl (Z)-3-amino-4-phenoxybut-2-enoate

[0414] Yellow solid (0.11 g, 65%).
[0415] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.35 - 7.27 (m, 2H), 7.05 - 6.87 (m, 3H), 5.86 (bs, 2H), 4.74 - 4.67 (m, 1H), 4.59

(d, *J* = 0.8 Hz, 2H), 3.68 (s, 3H).

Intermediate i6: 5-Amino-2H-thiopyran-3(6H)-one

[0416] Brown solid (0.05 g, 35%).
[0417] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 6.97 (bs, 2H), 4.94 (s, 1H), 3.31 (s, 2H), 3.03 (s, 2H).

Intermediates i7 and i8: (Z)-4-amino-1-methoxypent-3-en-2-one and (Z)-4-amino-5-methoxypent-3-en-2-one

[0418] General procedure **i** yielded a mixture of the title compounds that were separated by flash chromatography.

i7: (Z)-4-amino-1-methoxypent-3-en-2-one; light yellow oil, 0.703 g, 74%.

[0419] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 9.56 (bs, 1H), 5.72 (bs, 1H), 5.00 (s, 1H), 3.97 (s, 2H), 3.38 (s, 3H), 2.05 (s, 3H).

i8: (Z)-4-amino-5-methoxypent-3-en-2-one; light yellow oil, 0.25 g, 26%.

[0420] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 9.85 (bs, 1H), 5.31 (s, 1H), 5.12 (bs, 1H), 3.89 (s, 2H), 3.41 (s, 3H), 1.97 (s, 3H).

Intermediate i9: Methyl (Z)-3-amino-4-fluorobut-2-enoate

[0421] Yellowish solid (0.22 g, 55%).
[0422] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 6.35 (bs, 2H), 4.89 (d, J = 46.9 Hz, 2H), 4.59 (s, 1H), 3.67 (s, 3H). ^{19}F NMR (282 MHz, $CDCl_3$) δ = 122.24 (t, *J* = 46.9 Hz).

Intermediate i10: Cyclohexylmethyl (Z)-3-aminobut-2-enoate

[0423] Yellowish oil (0.8 g, 73%).
[0424] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.88 (s, 2H), 4.53 (s, 1H), 3.86 (d, J= 6.6 Hz, 2H), 1.90 (s, 3H), 1.87 - 1.47 (m, 6H), 1.38 - 1.12 (m, 3H), 1.08 - 0.76 (m, 2H).

Intermediate i11: Cyclopentylmethyl (Z)-3-aminobut-2-enoate

[0425] Yellowish oil (0.3 g, 55%).
[0426] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.92 (s, 2H), 4.54 (s, 1H), 3.93 (d, *J* = 7.1 Hz, 2H), 2.20 (p, *J* = 7.5 Hz, 1H), 1.90 (s, 3H), 1.74 (dtdd, J= 13.6, 7.5, 5.2, 3.4 Hz, 2H), 1.67 - 1.46 (m, 4H), 1.34 - 1.18 (m, 2H).

Intermediate i12: Cyclohexyl (Z)-3-aminobut-2-enoate

[0427] Yellowish oil (0.75 g, 63%).
[0428] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.90 (s, 2H), 4.73 (tt, *J* = 8.8, 4.3 Hz, 1H), 4.52 (s, 1H), 2.27 (s, 3H), 1.72 (d, *J* = 10.3 Hz, 4H), 1.61 - 1.49 (m, 4H), 1.49 - 1.35 (m, 2H).

Intermediate i13: Cyclopentyl (Z)-3-aminobut-2-enoate

[0429] Yellowish oil (0.17 g, 24%).
[0430] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.90 (s, 2H), 4.73 (tt, *J* = 8.8, 4.3 Hz, 1H), 4.52 (s, 1H), 2.27 (s, 3H), 1.72 (d, *J* = 10.3 Hz, 2H), 1.61 - 1.49 (m, 4H), 1.49 - 1.35 (m, 2H).

Intermediate i14: Benzyl (Z)-3-aminobut-2-enoate

[0431] Yellowish oil (0.203 g, 68%).
[0432] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.91 (s, 2H), 7.36 - 7.28 (m, 5H), 5.12 (s, 2H), 4.61 (s, 1H), 1.91 (s, 3H).

Intermediate i15: (Tetrahydro-2H-pyran-4-yl)methyl (Z)-3-aminobut-2-enoate

[0433] Yellowish oil (0.23 g, 77%).
[0434] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.85 (s, 2H), 4.51 (s, 1H), 4.05 - 3.85 (m, 4H), 3.37 (td, *J* = 11.8, 2.2 Hz, 2H),

1.96 - 1.86 (m, 4H), 1.62 (ddt, *J* = 10.8, 4.3, 2.2 Hz, 2H), 1.35 (dtd, *J* = 13.3, 11.8, 4.5 Hz, 2H).

Intermediate i16: (Tetrahydro-2H-pyran-4-yl)methyl (Z)-3-aminobut-2-enoate

[0435] Yellowish oil (0.23 g, 77%).
[0436] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.85 (s, 2H), 4.51 (s, 1H), 4.05 - 3.85 (m, 4H), 3.37 (td, *J* = 11.8, 2.2 Hz, 2H), 1.96 - 1.86 (m, 4H), 1.62 (ddt, *J* = 10.8, 4.3, 2.2 Hz, 2H), 1.35 (dtd, *J* = 13.3, 11.8, 4.5 Hz, 2H).

Intermediate i17: Pyridin-4-ylmethyl (Z)-3-aminobut-2-enoate

[0437] Yellow oil (0.19 g, 69%).
[0438] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.71 - 8.39 (m, 2H), 7.89 (s, 2H), 7.29 - 7.23 (m, 2H), 5.13 (s, 2H), 4.64 (s, 1H), 1.94 (s, 3H).

Intermediate i18: 4-Fluorobenzyl (Z)-3-aminobut-2-enoate

[0439] Yellow oil (0.72 g, 96%).
[0440] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.96 (s, 2H), 7.40 - 7.30 (m, 2H), 7.11 - 6.89 (m, 2H), 5.07 (s, 2H), 4.58 (s, 1H), 1.97 - 1.81 (m, 3H).

Intermediate i19: tert-Butyl (Z)-4-(((3-aminobut-2-enoyl)oxy)methyl)benzoate

[0441] Yellow oil (0.40 g, 89%).
[0442] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.98 - 7.92 (m, 2H), 7.42 - 7.33 (m, 2H), 5.15 (s, 2H), 4.61 (s, 1H), 1.92 (s, 3H), 1.58 (s, 9H) 1.28 (s, 2H).

Intermediate i20: Pyridin-3-ylmethyl (Z)-3-aminobut-2-enoate

[0443] Yellowish oil (0.50 g, 71%).
[0444] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.62 (d, *J* = 1.7 Hz, 1H), 8.54 (dd, *J* = 4.8, 1.6 Hz, 1H), 7.94 (s, 2H), 7.70 (dt, *J* = 7.8, 1.9 Hz, 1H), 7.31 - 7.27 (m, 1H), 5.12 (s, 2H), 4.58 (s, 1H), 1.92 (s, 3H).

Intermediate i21: 4-Bromobenzyl (Z)-3-aminobut-2-enoate

[0445] Light-yellow oil (0.48 g, 95%).
[0446] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.85 (s, 2H), 7.46 (d, *J* = 8.4 Hz, 2H), 7.23 (d, *J* = 8.4 Hz, 2H), 5.05 (s, 2H), 4.58 (s, 1H), 1.91 (s, 3H).

Intermediate i22: 3-Bromobenzyl (Z)-3-aminobut-2-enoate

[0447] Light-yellow oil (0.2 g, 69%).
[0448] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.92 (s, 2H), 7.51 (s, 1H), 7.44 (m, 2H), 7.24 - 7.18 (m, 1H), 5.07 (s, 2H), 3.52 (s, 1H), 1.92 (s, 3H).

Intermediate i23: 2-Bromobenzyl (Z)-3-aminobut-2-enoate

[0449] Light-yellow oil (0.45 g, 90%).
[0450] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.95 (bs, 2H), 7.61 - 7.44 (m, 1H), 7.41 (d, *J* = 7.6 Hz, 1H), 7.33 - 7.22 (m, 1H), 7.22 - 7.06 (m, 1H), 5.19 (s, 2H), 4.64 (s, 1H), 1.93 (s, 3H).

Intermediate i24: (3-Fluoropyridin-4-yl)methyl (Z)-3-aminobut-2-enoate

[0451] Light-yellow oil (0.207 g, 69%).
[0452] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.55-8.30 (m, 2H), 7.92 (bs, 2H), 7.35 (t, *J* = 5.6 Hz, 1H), 5.22 (s, 2H), 4.64 (s, 1H), 1.95 (s, 3H). ^{19}F NMR (282 MHz, $CDCl_3$) δ = -132.71 (s, F).

Intermediate i25: Pyrimidin-5-ylmethyl (Z)-3-aminobut-2-enoate

[0453] Light-yellow oil (0.415 g, 64%).
[0454] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 9.16 (s, 1H), 8.77 (d, *J* = 4.8 Hz, 2H), 7.94 (bs, 2H), 5.12 (s, 2H), 3.53 (s, 1H), 1.93 (s, 3H).

Intermediate i26: (5-Bromopyridin-3-yl)methyl (Z)-3-aminobut-2-enoate

[0455] Light-yellow oil (0.364 g, 73%).
[0456] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 9.16 (d, *J* = 4.8 Hz, 1H), 8.77 (d, *J* = 4.8 Hz, 1H), 7.94 (s, 3H), 5.12 (s, 2H), 3.53 (s, 1H), 1.93 (s, 3H).

Intermediate i27: 2-Phenylpropan-2-yl (Z)-3-aminobut-2-enoate

[0457] Light-yellow oil (0.20 g, 69%).
[0458] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.74 (bs, 1H), 7.41 - 7.29 (m, 5H), 4.61 (s, 1H), 4.34 (bs, 2H), 1.88 (s, 3H), 1.76 (s, 6H).

Intermediate i28: 3-cyanobenzyl (Z)-3-aminobut-2-enoate

[0459] Light-yellow oil (0.52 g, 93%).
[0460] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.92 (bs, 2H), 7.66 (s, 1H), 7.57 (d, *J* = 7.9 Hz, 2H), 7.51 - 7.36 (m, 1H), 5.12 (s, 2H), 4.60 (s, 1H), 1.93 (s, 3H).

Intermediate i29: 4-cyanobenzyl (Z)-3-aminobut-2-enoate

[0461] Light-yellow oil (0.56 g, 90%).
[0462] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.92 (bs, 2H), 7.67 - 7.61 (m, 2H), 7.44 (d, *J* = 7.9 Hz, 2H), 5.15 (s, 2H), 4.61 (s, 1H), 1.93 (s, 3H).

Intermediate i30: 4-cyanobenzyl (Z)-3-aminobut-2-enoate

[0463] Light-yellow oil (0.22 g, 75%).
[0464] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.37 (s, 1H), 7.90 (s, 2H), 7.65 (dd, *J* = 8.2, 2.4 Hz, 1H), 7.30 (dd, *J* = 12.8, 8.2 Hz, 1H), 5.07 (s, 2H), 4.54 (s, 1H), 1.90 (s, 3H).

Intermediate i31: 3-Morpholinobenzyl (Z)-3-aminobut-2-enoate

[0465] Light-yellow oil (0.69 g, 97%).
[0466] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.92 (s, 2H), 7.31 - 7.20 (m, 1H), 6.88 (dd, *J* = 16.4, 8.5 Hz, 3H), 5.07 (s, 2H), 4.60 (s, 1H), 3.86 (t, *J* = 4.8 Hz, 4H), 3.16 (t, *J* = 4.8 Hz, 4H), 1.91 (s, 3H).

Intermediate i32: 4,4-Dimethylcyclohexyl (Z)-3-aminobut-2-enoate

[0467] Light-yellow oil (0.55 g, 81%).
[0468] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.85 (bs, 2H), 4.71 (tt, *J* = 8.9, 4.2 Hz, 1H), 4.52 (s, 1H), 1.90 (s, 3H), 1.82 - 1.70 (m, 2H), 1.58 (dt, *J* = 9.3, 5.8 Hz, 2H), 1.49 - 1.39 (m, 2H), 1.26 (ddd, *J* = 13.7, 10.8, 4.1 Hz, 2H), 0.93 (s, 3H), 0.91 (s, 3H).

Intermediate i33: (2-chloropyridin-4-yl)methyl (Z)-3-aminobut-2-enoate

[0469] Light-yellow oil (0.25 g, 83%).
[0470] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.33 (d, *J* = 5.4 Hz, 1H), 7.92 (bs, 2H), 7.30 (s, 1H), 7.17 (d, *J* = 5.4 Hz, 1H), 5.10 (s, 2H), 4.64 (s, 1H), 1.95 (s, 3H).

Intermediate i34: 4,4-difluorocyclohexyl (Z)-3-aminobut-2-enoate

[0471] Light-yellow oil (0.30 g, 94%).

[0472] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.86 (bs, 2H), 5.16 - 4.75 (m, 1H), 4.53 (s, 1H), 2.16 - 1.98 (m, 3H), 2 - 1,78 (m, 8H). ^{19}F NMR (282 MHz, $CDCl_3$) δ = -94.48 (d, *J* = 252.2 Hz), -100.51 (d, *J* = 235.8 Hz).

Intermediate i35: (Z)-3-Amino-N-benzyl-N-methylbut-2-enamide

[0473] Light-yellow oil (0.70 g, 71%).
[0474] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.54 - 6.96 (m, 7H), 4.72 (s, 1H), 4.56 (m, 2H), 2.92 (s, 3H), 1.90 (s, 3H).

Intermediate i36: oxetan-3-yl (Z)-3-aminobut-2-enoate

[0475] Light-yellow oil (0.04 g, 17%).
[0476] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 6.33 (s, 2H), 5.42 (tt, *J* = 6.4, 5.6 Hz, 1H), 4.87 (td, *J* = 6.8, 1.0 Hz, 2H), 4.66 (ddd, *J* = 6.9, 5.6, 1.0 Hz, 2H), 4.50 (s, 1H), 1.48 - 1.38 (m, 1H), 0.98 - 0.83 (m, 2H), 0.83 - 0.70 (m, 2H).

Intermediate i37: 3-Chlorobenzyl (Z)-3-aminobut-2-enoate

[0477] Light-yellow oil (0.198 g, 99 %).
[0478] ^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 7.93 (bs, 1H), 7.36 (s, 1H), 7.33 - 7.26 (m, 1H), 7.24 (s, 2H), 5.08 (s, 2H), 4.89 - 4.39 (m, 2H), 1.93 (s, 3H).

Intermediate i38: 2-Phenylpropan-2-yl (Z)-3-amino-3-cyclopropylacrylate

[0479] Light-yellow solid (0.38 g, 93 %).
[0480] ^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 7.40 - 7.31 (m, 4H), 7.24 - 7.17 (m, 1H), 6.19 (s, 2H), 4.56 (s, 1H), 1.76 (s, 6H), 1.47 - 1.31 (m, 1H), 0.87 - 0.79 (m, 2H), 0.78 - 0.70 (m, 2H).

Intermediate i39: Cyclohexyl (Z)-3-amino-3-cyclopropylacrylate

[0481] Light-yellow solid (0.22 g, 43 %).
[0482] ^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 6.22 (bs, 2H), 4.80 - 4.58 (m, 1H), 4.46 (s, 1H), 1.97 - 1.77 (m, 2H), 1.80 - 1.61 (m, 2H), 1.56 - 1.18 (m, 7H), 0.90 - 0.78 (m, 2H), 0.78 - 0.68 (m, 2H).

Intermediate i40: (Z)-3-Amino-1,3-dicyclopropylprop-2-en-1-one

[0483] Light-yellow solid (0.22 g, 44 %).
[0484] ^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 9.82 (bs, 1H), 5.12 (s, 1H), 4.83 (bs, 1H), 1.75 - 1.59 (m, 1H), 1.49 - 1.32 (m, 1H), 1.01 - 0.84 (m, 4H), 0.84 - 0.76 (m, 2H), 0.76 - 0.63 (m, 2H).

Intermediate i41: 3-Chlorobenzyl (Z)-3-amino-3-cyclopropylacrylate

[0485] Light-yellow solid (0.14 g, 70 %).
[0486] ^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 7.37 - 7.29 (m, 1H), 7.23 - 7.17 (m, 3H), 6.25 (bs, 2H), 5.03 (s, 1H), 4.65 (s, 2H), 1.19 - 1.03 (m, 1H), 0.92 - 0.75 (m, 2H), 0.78 - 0.63 (m, 2H).

Intermediate i42: 2-(4-Fluorophenyl)propan-2-yl (Z)-3-aminobut-2-enoate

[0487] Light-yellow solid (0.20 g, 80 %).
[0488] ^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 7.77 (bs, 1H), 7.39 - 7.27 (m, 2H), 7.08 - 6.93 (m, 2H), 4.58 (s, 1H), 4.36 (bs, 1H), 1.88 (s, 3H), 1.74 (s, 6H).
[0489] ^{19}F NMR (282 MHz, $CDCl_3$-*d*) δ (ppm): -117.11 (CF).

Intermediate i43: 2-(4-Fluorophenyl)propan-2-yl (Z)-3-amino-3-cyclopropylacrylate

[0490] Yellow solid (0.43 g, 96 %).
[0491] ^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 7.41 - 7.28 (m, 2H), 7.09 - 6.89 (m, 2H), 6.11 (bs, 2H), 4.54 (s, 1H), 1.73 (s, 6H), 1.40 (qt, *J* = 8.1, 5.0 Hz, 1H), 0.89 - 0.81 (m, 2H), 0.73 (dt, *J* = 8.1, 5.0 Hz, 2H).
[0492] ^{19}F NMR (282 MHz, $CDCl_3$-*d*) δ (ppm): -117.14 (CF).

Intermediate i44: 3-Bromobenzyl (Z)-3-amino-3-cyclopropylacrylate

[0493] Light-yellow solid (0.15 g, 54 %).
[0494] ^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 7.57 - 7.48 (m, 1H), 7.46 - 7.37 (m, 1H), 7.33 - 7.24 (m, 1H), 7.25 - 7.18 (m, 1H), 6.10 (bs, 2H), 5.06 (s, 1H), 3.75 (s, 2H), 2.10 - 1.93 (m, 1H), 1.18 - 1.03 (m, 2H), 1.03 - 0.92 (m, 2H).

Intermediate i45: Methyl (Z)-3-amino-3-cyclobutylacrylate

[0495] Light-yellow solid (0.35 g, 70 %).
[0496] ^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 6.98 (bs, 2H), 4.53 (s, 1H), 3.64 (s, 3H), 3.05 (p, *J* = 8.4 Hz, 1H), 2.22 - 1.95 (m, 4H), 1.94 - 1.57 (m, 2H).

Intermediate i46: Methyl (Z)-3-amino-3-cyclopentylacrylate

[0497] Light-yellow solid (0.42 g, 83 %).
[0498] ^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 7.52 (bs, 2H), 4.59 (s, 1H), 3.63 (s, 3H), 2.49 (p, *J* = 8.5 Hz, 1H), 2.07 - 1.85 (m, 2H), 1.85 - 1.40 (m, 6H).

Intermediate i47: Methyl (Z)-3-amino-3-cyclohexylacrylate

[0499] Light-yellow solid (0.45 g, 92 %).
[0500] ^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 17.57 (bs, 2H), 4.54 (s, 1H), 3.63 (s, 3H), 1.98 - 1.60 (m, 6H), 1.35 - 1.13 (m, 5H).

Intermediate i48: 3-((4-Methylpiperazin-1-yl)methyl)benzyl (Z)-3-aminobut-2-enoate

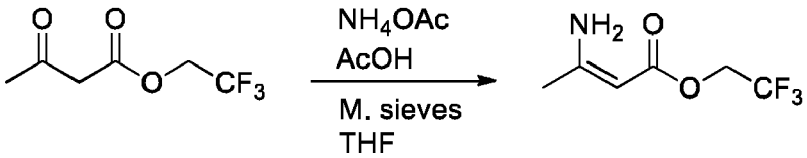
[0501] Yellow solid (0.54 g, 98%).
[0502] ^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 7.91 (s, 2H), 7.29 (s, 4H), 5.09 (s, 2H), 4.60 (s, 1H), 3.51 (s, 2H), 2.52 (bs, 8H), 2.33 (s, 3H), 1.91 (s, 3H).

Other methods of enamine preparation:

[0503] The following enamines have been prepared by alternative procedures:

Intermediate i49: 2,2,2-trifluoroethyl (Z)-3-aminobut-2-enoate

[0504]



[0505] 2,2,2-trifluoroethyl 3-oxobutanoate (1 g, 5.43 mmol, 1 eq) was dissolved in THF (1.2 M) at RT, and molecular sieves (2 g), ammonium acetate (0.83 g, 10.87 mmol, 2 eq) and acetic acid (0,310 ml, 5.43 mmol, 1 eq) were added. The reaction mixture was heated at 110 °C for 6 hours and then allowed to cool to RT. Water was addded, and the mixture was extracted with ethyl acetate (×3). The combined organic layers were washed with brine, dried (Na_2SO_4), filtered and concentrated. The residue was purified by flash column chromatography on silica gel using ethyl acetate/hexane (1:3) as eluent to afford 2,2,2-trifluoroethyl (Z)-3-aminobut-2-enoate (0.5 g, 56%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.89 (bs, 1H), 4.84 (bs, 1H), 4.59 (s, 1H), 4.44 (q, *J* = 8.7 Hz, 2H), 1.93 (s, 3H). ^{19}F NMR (282 MHz, $CDCl_3$) δ = -73.40 (t, *J* = 8.6 Hz, 3F).

Intermediate i50: Methyl (Z)-3-amino-3-(pyridin-3-yl)acrylate

[0506] The procedure described for 2,2,2-trifluoroethyl (Z)-3-aminobut-2-enoate (see above) was followed to obtain the title compound (0.7 g, 72%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.80 (s, 1H), 8.66 (s, 1H), 7.82 (d, *J* = 7.8 Hz, 1H), 7.40 - 7.30 (m, 1H), 4.96 (s, 1H),

3.72 (s, 3H).

Intermediate i51: Mixture of (Z)-4-amino-5-phenylpent-3-en-2-one and (Z)-4-amino-1-phenylpent-3-en-2-one

[0507] The procedure described for 2,2,2-trifluoroethyl (Z)-3-aminobut-2-enoate (see above) was followed to obtain a mixture of (Z)-4-amino-5-phenylpent-3-en-2-one and (Z)-4-amino-1-phenylpent-3-en-2-one as a yellow oil (0.5 g, 79%) that was used as such in the subsequent step.

Intermediate i52: (Z)-4-Aminopent-3-en-2-one

[0508] Prepared according to the process described in US 8,030,302 (3.7 g, 74%). ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 9.70 (bs, 1H), 5.04 (bs, 1H), 4.92 (s, 1H), 2.03 (s, 3H), 1.91 (s, 3H).

Intermediate i53: 5-Amino-2H-pyran-3(6H)-one

[0509] Literature procedure Synth. Comm. 2004, 34, 557-565 yielded the title compound as a dark orange solid (0.35 g, 90%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.03 (bs, 2H), 5.01 (s, 1H), 4.18 (s, 2H), 3.80 (s, 2H).

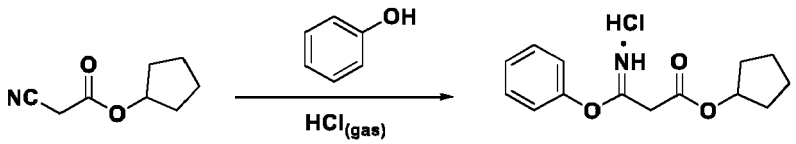
PREPARATION OF AMIDINE INTERMEDIATES

General procedure y

Intermediate y1: Cyclopentyl 3-amino-3-iminopropanoate hydrochloride

Step 1: Synthesis of cyclopentyl 3-imino-3-phenoxypropanoate hydrochloride

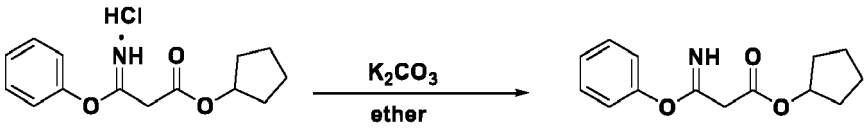
[0510]



[0511] A mixture of cyclopentyl 2-cyanoacetate (2.81 g, 18.34 mmol, 1.15 eq) and phenol (1.50 g, 15.95 mmol, 1.3 eq) was stirred at -20°C, when HCl gas was bubbled into the mixture for 90 min. Then, the mixture was left at 4°C for two days without stirring. Cold ether was added, and the mixture was stirred at 0°C. The solid formed and was filtered off and washed with cold ether to afford cyclopentyl 3-imino-3-phenoxypropanoate hydrochloride as a white solid (2.76 g, 61%).
^{1}H-NMR (300 MHz, DMSO-d_6) δ (ppm): 7.55 - 7.41 (m, 1H), 7.20 - 7.09 (m, 2H), 6.80 - 6.70 (m, 2H), 5.10 - 5.01 (m, 1H), 3.95 (s, 4H), 1.94 - 1.69 (m, 2H), 1.68 - 1.47 (m, 6H).

Step 2: Synthesis of cyclopentyl 3-imino-3-phenoxypropanoate

[0512]

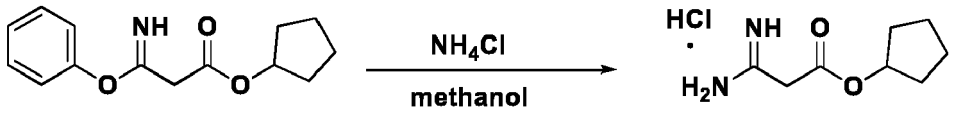


[0513] To a suspension of cyclopentyl 3-imino-3-phenoxypropanoate hydrochloride (1.0 g, 3.53 mmol, 1.0 eq.) in ether (25 ml) was added a solution of potassium carbonate (0.73 g, 5.30 mmol, 1.5 eq) in water (11 mL) at 0°C. The resultant mixture was stirred until the solid had dissolved and was then washed with ether, dried (Na_2SO_4) and concentrated to afford cyclopentyl 3-imino-3-phenoxypropanoate as light yellow oil (0.86 g, 99%).
^{1}H-NMR (300 MHz, DMSO-d6) δ (ppm): 7.66 (bs, 2H), 7.51 - 7.39 (m, 2H), 7.35 - 7.23 (m, 1H), 7.20 - 7.10 (m, 2H), 4.97

(dq, *J* = 5.7, 3.1 Hz, 1H), 3.46 (s, 1H), 1.89 - 1.65 (m, 2H), 1.64 - 1.25 (m, 6H).

Step 3: Synthesis of cyclopentyl 3-amino-3-iminopropanoate hydrochloride

[0514]

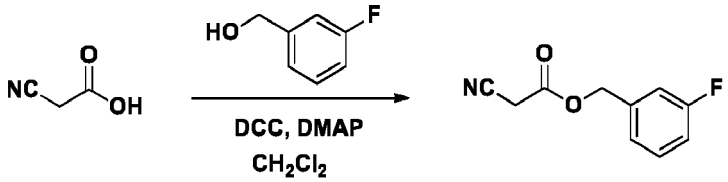


[0515] To a solution of cyclopentyl 3-imino-3-phenoxypropanoate (0.86 g, 3.49 mmol, 1.0 eq.) in methanol (5 ml) was added ammonium chloride (0.21 g, 3.84 mmol, 1.1 eq). The mixture was stirred at room temperature overnight and concentrated. The remaining solid was triturated with diethyl ether and filtered off to afford cyclopentyl 3-amino-3-iminopropanoate hydrochloride as a white solid (0.61 g, 84%).
^{1}H-NMR (300 MHz, DMSO-d_6) δ (ppm): 9.12 (bs, 2H), 8.82 (bs, 2H), 5.12 (tt, *J* = 4.9, 2.2 Hz, 1H), 3.55 (s, 2H), 1.81 (t, *J* = 7.5 Hz, 2H), 1.76 - 1.47 (m, 6H).

[0516] The cyclopentyl 2-cyanoacetate precursor used in *Step 1* of the synthesis of Intermediate y1 was purchased from commercial vendors. Other alkyl 2-cyanoacetates were synthesized using the following ester formation method (*Step 0*), as shown for 3-fluorobenzyl 2-cyanoacetate, a precursor of Intermediate y2:

Step 0: Synthesis of 3-fluorobenzyl 2-cyanoacetate

[0517]



[0518] To a solution of 2-cyanoacetic acid (4.45 g, 52.32 mmol, 1.0 eq.) in DCM (34 ml) was added (3-fluorophenyl)methanol (5.67 mL, 52.32 mmol, 1.0 eq) and cooled at 0°C. Then, a solution of N,N- dicylohexylcarbodiimide (10.79 g, 52.32 mmol, 1.0 eq) and dimethylaminopyridine (0.32 g, 2.62 mmol, 0.05 eq) in DCM (16 mL) was dropwise added, and the mixture was stirred at RT overnight. The solid was filtered off and washed with DCM. The filtrate was concentrated and purified by flash column chromatography on silica gel using ethyl acetate/hexane (1:3) as eluent to afford 3-fluorobenzyl 2-cyanoacetate as a light-yellow oil (7.2 g, 66%).
^{1}H-NMR (300 MHz, DMSO-d_6) δ (ppm): 7.45 - 7.27 (m, 1H), 7.20 - 7.01 (m, 3H), 5.22 (s, 2H), 3.51 (s, 2H).

[0519] The following amidine intermediates were prepared according to *General Procedure* ***y*** (Steps 0 to 3).

Intermediate y2: 3-Fluorobenzyl 3,3-diaminoacrylate hydrochloride

[0520] White solid (0.550 g).

[0521] ^{1}H-NMR (300 MHz, DMSO-d_6) δ (ppm): 9.36 (bs, 2H), 9.05 (bs, 2H), 7.64 - 7.43 (m, 4H), 5.21 (s, 2H), 3.78 (s, 2H).

Intermediate y3: Cyclobutylmethyl 3,3-diaminoacrylate hydrochloride

[0522] White solid (0.542 g).

[0523] ^{1}H-NMR (300 MHz, DMSO-d_6) δ (ppm): 9.27 (bs, 2H), 8.99 (bs, 2H), 4.19 - 3.85 (m, 2H), 3.67 (s, 2H), 2.67 - 2.53 (m, 1H), 2.11 - 1.54 (m, 6H).

Intermediate y4: 3,3-Difluorocyclobutyl)methyl 3,3-diaminoacrylate

[0524] White solid (0.450 g).

[0525] ^{1}H-NMR (300 MHz, DMSO-d_6) δ (ppm): 9.33 (bs, 2H), 9.01 (bs, 2H), 4.17 (d, *J* = 5.1 Hz, 2H), 3.71 (s, 2H), 2.79 - 2.53 (m, 3H), 2.44 - 2.29 (m, 2H).

Intermediate y5: 2,2-Difluorocyclopropyl)methyl 3,3-diaminoacrylate hydrochloride White solid (0.36 g).

[0526] ^{1}H-NMR (300 MHz, DMSO-d_6) δ (ppm): 9.33 (bs, 2H), 9.05 (bs, 2H), 4.42 - 4.21 (m, 1H), 4.14 - 3.90 (m, 1H), 3.73 (s, 2H), 2.20 - 2.00 (m, 1H), 1.82 - 1.61 (m, 1H), 1.61 - 1.36 (m, 1H).

Intermediate y6: Isopropyl 3,3-diaminoacrylate hydrochloride

[0527] White solid (0.47 g).

[0528] ^{1}H-NMR (300 MHz, DMSO-d_6) δ (ppm): 9.28 (bs, 2H), 9.00 (bs, 2H), 4.95 (pd, J = 6.3, 1.5 Hz, 1H), 3.62 (s, 2H), 1.22 (d, J = 6.3 Hz, 6H).

Intermediate y7: 2,2-Difluoro-3,3-dimethylcyclopropyl)methyl 3,3-diaminoacrylate hydrochloride

[0529] White solid (0.132 g).

[0530] ^{1}H-NMR (300 MHz, DMSO-d_6) δ (ppm): 9.31 (s, 2H), 9.03 (s, 2H), 4.21 (d, J = 8.8 Hz, 2H), 3.70 (s, 2H), 1.82 - 1.56 (m, 1H), 1.34 - 0.94 (m, 6H).

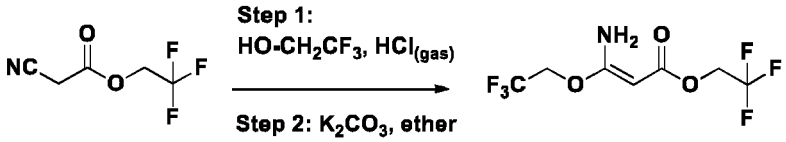
Intermediate y8: Neopentyl 3,3-diaminoacrylate hydrochloride

[0531] White solid (0.791 g).

[0532] ^{1}H-NMR (300 MHz, DMSO-d_6) δ (ppm): 9.25 (s, 2H), 8.97 (s, 2H), 3.79 (s, 2H), 3.66 (s, 2H), 0.89 (s, 9H).

Intermediate y9: 2,2,2-Trifluoroethyl (E)-3-amino-3-(2,2,2-trifluoroethoxy)acrylate

[0533] The title compound was prepared following Step 0 of *General Procedure* ***y*** and a slightly modified version of Steps 1 and 2, as outlined below.



[0534] Step 1: Into a mixture of 2,2,2-trifluoroethyl 2-cyanoacetate (3.5 g, 20.94 mmol, 1.15 eq) and 2,2,2-trifluoroethyl-1-ol (1.32 mL, 18.21 mmol, 1 eq) that was stirred at - 20°C, HCl gas was bubbled for 60 min. Then, the mixture was left at 4°C for two days without stirring. After that time the mixture was stirred again, and cold ether was added at 0°C. The solid was filtered off and washed with cold ether to afford 2,2,2-trifluoroethyl (E)-3-amino-3-(2,2,2-trifluoroethoxy)acrylate hydrochloride as a white solid (2.5 g, 40%).
^{1}H-NMR (300 MHz, DMSO-d_6) δ (ppm): 7.70 (s, 1H), 5.83 (s, 2H), 4.73 (ddq, J = 37.4, 18.4, 9.0 Hz, 4H), 3.89 (s, 1H).

[0535] Step 2: To a mixture of 2,2,2-trifluoroethyl (E)-3-amino-3-(2,2,2-trifluoroethoxy) acrylate hydrochloride (0.13 g, 0.43 mmol, 1.0 eq.) and ether (5 ml) was added a solution of potassium carbonate (0.088 g, 0.64 mmol, 1.5 eq) in water (1.5 mL) at 0°C. The resultant mixture was stirred until the solid dissolved. The mixture was extracted with ether, and the organic phase was dried (Na_2SO_4) and concentrated to afford 2,2,2-trifluoroethyl (E)-3-amino-3-(2,2,2-trifluoroethoxy) acrylate as colorless oil (0.12 g, 98%) which was used as such in the next step.

Intermediate y10: 2-Fluoro-2-methylpropyl 3-amino-3-iminopropanoate hydrochloride

[0536] General Procedure **y** (Steps 0 to 3) afforded the title compound as white solid (0.28 g). ^{1}H-NMR (300 MHz, DMSO-d_6) δ (ppm): 9.33 (s, 2H), 9.04 (s, 2H), 4.19 (d, J = 21.1 Hz, 2H), 3.76 (s, 2H), 1.41-1.34 (m, 6H).

Intermediate y11: Cyclopropylmethyl 3,3-diaminoacrylate hydrochloride

[0537] General Procedure **y** (Steps 0 to 3) afforded the title compound as white solid (0.48 g).
^{1}H-NMR (300 MHz, DMSO-d_6) δ (ppm): 9.13 (bs, 3H), 8.83 (bs, 2H), 5.13 (t, J = 6.0 Hz, 1H), 3.57 (s, 2H), 1.86 - 1.80 (m, 1H), 1.68 - 1.58 (m, 4H).

Intermediate y12: 4,4-Difluorocyclohexyl 3-amino-3-iminopropanoate hydrochloride

[0538] General Procedure **y** (Steps 0 to 3) afforded title compound as white solid (0.098 g).
^{1}H-NMR (300 MHz, DMSO-d_6) δ (ppm): δ 9.32 (s, 2H), 9.02 (s, 2H), 4.96 - 4.66 (m, 1H), 3.41 (s, 2H), 2.10 - 1.76 (m, 8H).

Intermediate y13: 4-Fluorobenzyl 3-amino-3-iminopropanoate hydrochloride

[0539] General Procedure **y** (Steps 0 to 3) afforded title compound as white solid (0.45 g).
^{1}H-NMR (300 MHz, DMSO-d_6) δ (ppm): 9.30 (bs, 2H), 9.01 (bs, 2H), 7.49 - 7.43 (m, 2H), 7.26 - 7.17 (m, 2H), 5.17 (s, 2H), 3.73 (s, 2H).

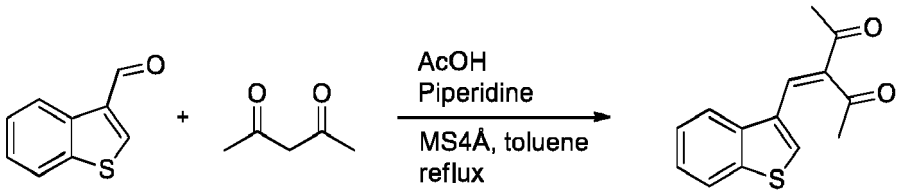
Intermediate y14: Cyclopentylmethyl 3-amino-3-iminopropanoate hydrochloride

[0540] General Procedure **y** (Steps 0 to 3) afforded title compound as white solid (0.22 g).
^{1}H-NMR (300 MHz, DMSO-d_6) δ (ppm): 9.31 (bs, 2H), 9.03 (bs, 2H), 3.96 (d, 2H), 3.76 (s, 2H), 2.2 - 2.1 (m, 1H), 1:8 - 1.6 (m, 2H), 1.6 - 1.4 (m, 4H), 1.4 - 1.1 (m, 2H).

PREPARATION OF KNOEVENAGEL INTERMEDIATES

General procedure j (adapted from Lu Liu et al, Chem. Int. Ed. 2009, 48, 6093-6096) **Intermediate j1:** 3-(benzo[*b*]thiophen-3-ylmethylene)pentane-2,4-dione

[0541]



[0542] Benzo[*b*]thiophene-3-carbaldehyde (1 g, 6.16 mmol, 1 eq) was dissolved in toluene (0.5 M) at RT, and acetic acid (0.176 ml, 3.08 mmol, 0.5 eq), piperidine (0.061 ml, 0,61 mmol, 0.1 eq), molecular sieves (6 g) and 2,4-pentanedione (0.95 ml, 9.24 mmol, 1.5 eq) were added. The reaction mixture was heated in a microwave oven at 111 °C until the disappearance of starting material (4 h). The mixture was allowed to cool to RT and then concentrated. The resulting residue was purified by flash column chromatography on silica gel using ethyl acetate/hexane (1:6) as eluent to afford the Knoevenagel product as a yellow solid (1.8 g, 60%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.89 (t, *J* = 7.5 Hz, 2H), 7.76 (s, 1H), 7.72 (s, 1H), 7.48 (p, *J* = 7.4 Hz, 2H), 2.49 (s, 3H), 2.30 (s, 3H).
[0543] The following intermediates were synthesized according to General procedure j.

Intermediate j2: (E)-2-(benzo[*b*]thiophen-3-ylmethylene)-1-(pyridin-3-yl)butane-1,3-dione

[0544] Yellow solid (0.25 g, 33%).
[0545] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 9.03 (s, 1H), 8.72 (d, *J* = 3.6 Hz, 1H), 8.20 (ddd, J= 8.0, 2.3, 1.7 Hz, 1H), 8.14 (d, *J* = 0.9 Hz, 1H), 7.96 (dt, *J* = 8.1, 1.0 Hz, 1H), 7.83 (ddd, *J* = 7.9, 1.2, 0.7 Hz, 1H), 7.53 (s, 1H), 7.52 - 7.32 (m, 3H), 2.52 (s, 3H).

Intermediate j3: Methyl (Z)-2-(benzo[*b*]thiophen-3-ylmethylene)-4-chloro-3-oxobutanoate

[0546] Yellow solid (0.4 g, 32%).
[0547] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.16 (s, 1H), 8.03 - 7.86 (m, 2H), 7.82 (s, 1H), 7.60 - 7.39 (m, 2H), 4.34 (s, 2H), 3.90 (s, 3H).

Intermediate j4: (E)-2-(Benzo[*b*]thiophen-3-ylmethylene)-1-cyclopropylbutane-1,3-dione

[0548] Yellow oil (0.4 g, 63%).

[0549] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.96 - 7.84 (m, 3H), 7.75 (d, *J* = 1.1 Hz, 1H), 7.56 - 7.38 (m, 2H), 2.45 (s, 3H), 2.03 (dt, *J* = 7.9, 3.6 Hz, 1H), 1.28 - 1.08 (m, 2H), 1.04 - 0.83 (m, 2H).

Intermediate j5: Tetrahydro-2H-pyran-4-yl (Z)-3-oxo-2-(thieno[2,3-b]pyridin-3-ylmethylene)butanoate

[0550] Yellow oil (0.04 g, 25%).
[0551] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.63 (d, *J* = 4.6 Hz, 1H), 8.14 (d, *J* = 8.1 Hz, 1H), 7.94 (s, 1H), 7.76 (s, 1H), 7.40 (dd, *J* = 8.1, 4.6 Hz, 1H), 5.16 (tt, *J* = 8.6, 4.1 Hz, 1H), 3.81 (dt, *J* = 11.8, 4.6 Hz, 2H), 3.49 (ddd, *J* = 11.8, 8.8, 3.0 Hz, 2H) , 2.46 (s, 3H), 1.91 (dp, *J* = 8.5, 4.1 Hz, 2H), 1.63 (dtd, *J* = 13.0, 8.5, 4.1 Hz, 2H).

Intermediate j6: Isopropyl (Z)-3-(7-bromobenzo[b]thiophen-3-yl)-2-(cyclopropanecarbonyl)acrylate

[0552] Yellow oil (0.13 g, 32%).
[0553] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.88 (s, 2H), 7.85 (s, 1H), 7.57 - 7.53 (m, 1H), 7.38 - 7.31 (m, 1H), 5.19 (p, *J* = 6.3 Hz, 1H), 2.08 (tt, *J* = 7.8, 4.6 Hz, 1H), 1.35 (s, 3H), 1.32 (s, 3H), 1.21 - 1.11 (m, 2H), 1.02 - 0.91 (m, 2H).

Intermediate j7: Methyl (Z)-2-((7-bromobenzo[b]thiophen-3-yl)methylene)-4,4,4-trifluoro-3-oxobutanoate

[0554] Yellow solid (0.040 g, 10%).
[0555] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.22 (d, *J* = 1.0 Hz, 1H), 7.87 (t, *J* = 1.3 Hz, 1H), 7.78 - 7.75 (m, 1H), 7.69 (d, *J* = 5.0 Hz, 1H), 7.38 - 7.34 (m, 1H), 3.92 (s, 3H). ^{19}F NMR (282 MHz, $CDCl_3$) δ = - 75.69 (s, CF_3).

Intermediate j8: Cyclopropylmethyl (Z)-3-(7-bromobenzo[b]thiophen-3-yl)-2-(cyclopropanecarbonyl)acrylate

[0556] Yellow solid (0.25 g, 59%).
[0557] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.96 - 7.84 (m, 3H), 7.58 (d, *J* = 7.6 Hz, 1H), 7.40 - 7.33 (m, 1H), 4.13 (d, *J* = 7.5 Hz, 2H), 2.10 (tt, *J* = 7.5, 4.6 Hz, 1H), 1.25 - 1.18 (m, 3H), 0.99 (dt, *J* = 7.9, 3.5 Hz, 2H), 0.71 - 0.46 (m, 2H), 0.41 - 0.23 (m, 2H).

Intermediate j9: Cyclopropylmethyl (Z)-3-(7-bromobenzo[b]thiophen-3-yl)-2-(cyclopropanecarbonyl)acrylate

[0558] Yellow solid (0.13 g, 50%).
[0559] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.33 - 8.24 (m, 2H), 7.93 (s, 1H), 7.78 (s, 1H), 7.72 (t, *J* = 7.8 Hz, 1H), 2.50 (s, 3H), 2.30 (s, 3H). ^{19}F NMR (282 MHz, $CDCl_3$) δ = - 69.81 (s, CF_3).

Intermediate j10: 3-((7-Chlorobenzo[b]thiophen-3-yl)methylene)pentane-2,4-dione Yellow solid (0.158 g, 56 %).

[0560] ^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 7.77 (d, *J* = 7.1 Hz, 2H), 7.69 (s, 1H), 7.45 (d, *J* = 5.0 Hz, 2H), 2.48 (s, 3H), 2.29 (s, 3H).

Intermediate j11: 3-((7-(Trifluoromethyl)benzo[b]thiophen-3-yl)methylene)pentane-2,4-dione

[0561] Yellow solid (0.052 g, 50 %).
[0562] ^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 8.06 (d, *J* = 8.0 Hz, 1H), 7.82 (s, 1H), 7.80 - 7.73 (m, 2H), 7.61 (t, *J* = 8.0 Hz, 1H), 2.50 (s, 3H), 2.30 (s, 3H).
[0563] ^{19}F NMR (282 MHz, $CDCl_3$-*d*) δ (ppm): -62.87 (CF_3).

Intermediate j12: 3-(2-Acetyl-3-oxobut-1-en-1-yl)benzo[b]thiophene-7-carbonitrile Dark-yellow solid (0.132 g, 68 %).

[0564] ^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 8.10 (d, *J* = 8.1 Hz, 1H), 7.85 (s, 1H), 7.81 (d, *J* = 7.5 Hz, 1H), 7.69 (s, 1H), 7.60 (td, *J* = 8.1, 7.4, 1.0 Hz, 1H), 2.49 (s, 3H), 2.31 (s, 3H).

Intermediate j13: Cyclopropylmethyl (Z)-2-(cyclopropanecarbonyl)-3-(thieno[2,3-b]pyridin-3-yl)acrylate

[0565] Yellow solid (0.146 g, 61 %).
[0566] ^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 8.63 (d, *J* = 4.6 Hz, 1H), 8.20 (d, *J* = 8.4 Hz, 1H), 7.91 (s, 1H), 7.90 (s, 1H), 7.40 (ddd, *J* = 8.4, 4.6, 0.8 Hz, 1H), 4.12 (d, *J* = 7.2 Hz, 2H), 2.21 - 2.04 (m, 1H), 1.29 - 1.13 (m, 3H), 1.11 - 0.93 (m, 2H), 0.67 - 0.54 (m, 2H), 0.43 - 0.27 (m, 2H).

Intermediate j14: Cyclopentyl (Z)-2-(cyclopropanecarbonyl)-3-(thieno[2,3-b]pyridin-3-yl)acrylate

[0567] Light-yellow solid (0.21 g, 90 %).
[0568] ^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 8.63 (dd, *J* = 4.6, 1.4 Hz, 1H), 8.19 (dd, J= 8.2, 1.4 Hz, 1H), 7.89 (s, 1H), 7.86 (s, 1H), 7.40 (dd, *J* = 8.2, 4.6 Hz, 1H), 5.36 (tt, *J* = 5.7, 2.5 Hz, 1H), 2.10 (tt, *J* = 8.0, 4.6 Hz, 1H), 1.98 - 1.86 (m, 2H), 1.86 - 1.70 (m, 4H), 1.69 - 1.57 (m, 2H), 1.19 (dt, *J* = 6.9, 3.5 Hz, 2H), 0.99 (dt, *J* = 8.0, 3.5 Hz, 2H).

Intermediate j15: Cyclopropylmethyl (Z)-3-(7-cyanobenzo[b]thiophen-3-yl)-2-(cyclopropanecarbonyl)acrylate

[0569] Yellow solid (0.23 g, 69 %).
[0570] ^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 8.19 - 8.09 (m, 1H), 7.95 (s, 1H), 7.92 (s, 1H), 7.81 - 7.74 (m, 1H), 7.62 - 7.53 (m, 1H), 4.13 (d, *J* = 7.2 Hz, 2H), 2.12 (tt, *J* = 7.8, 4.6 Hz, 1H), 1.29 - 1.13 (m, 3H), 1.07 - 0.93 (m, 2H), 0.67 - 0.55 (m, 2H), 0.35 (dt, *J* = 6.2, 4.6 Hz, 2H).

Intermediate j16: Methyl (Z)-3-(7-cyanobenzo[b]thiophen-3-yl)-2-(cyclopropanecarbonyl)acrylate

[0571] Yellow solid (0.21 g, 80 %).
[0572] ^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 8.13 (t, *J* = 9.1 Hz, 1H), 8.02 - 7.86 (m, 2H), 7.79 (d, *J* = 7.7 Hz, 1H), 7.57 (td, *J* = 7.7, 2.7 Hz, 1H), 3.89 (s, 3H), 2.13 - 2.01 (m, 1H), 1.28 - 1.16 (m, 2H), 1.14 - 0.93 (m, 2H).

Intermediate j17: Methyl (Z)-2-((7-cyanobenzo[b]thiophen-3-yl)methylene)-3-oxobutanoate

[0573] Yellow solid (0.11 g, 60 %).
[0574] ^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 8.11 (d, *J* = 8.2 Hz, 1H), 7.99 (s, 1H), 7.84 (s, 1H), 7.80 (d, *J* = 7.4 Hz, 1H), 7.62 - 7.54 (m, 1H), 3.87 (s, 3H), 2.47 (s, 3H).

Intermediate j18: (E)-2-((7-cyanobenzo[b]thiophen-3-yl)methylene)-3-oxobutanamide Yellow solid (0.17 g, 58 %).

[0575] ^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 8.35 (s, 1H), 8.14 - 8.07 (m, 1H), 7.88 - 7.73 (m, 2H), 7.63 - 7.54 (m, 1H), 6.08 (bs, 1H), 5.87 (bs, 1H), 2.55 (s, 3H).

Intermediate j19: Cyclopropyl (E)-2-((7-cyanobenzo[b]thiophen-3-yl)methylene)-3-oxobutanoate

[0576] Yellow solid (0.104 g, 30 %).
[0577] ^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 8.09 (d, *J* = 8.2 Hz, 1H), 8.02 (s, 1H), 7.80 (d, *J* = 7.3 Hz, 2H), 7.63 - 7.51 (m, 1H), 4.43 - 4.31 (m, 1H), 2.46 (s, 3H), 0.85 - 0.74 (m, 2H), 0.73 - 0.61 (m, 2H).

Intermediate j20: Methyl (E)-2-((7-cyano-5-fluorobenzo[b]thiophen-3-yl)methylene)-3-oxobutanoate

[0578] Yellow solid (0.136 g, 60 %).
[0579] ^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 8.07 (s, 1H), 7.79 (d, *J* = 8.7 Hz, 1H), 7.72 (s, 1H), 7.56 (d, *J* = 7.7 Hz, 1H), 3.87 (s, 3H), 2.47 (s, 3H).

Intermediate j21: Methyl (E)-2-((7-cyano-4-fluorobenzo[b]thiophen-3-yl)methylene)-3-oxobutanoate

[0580] Yellow solid (0.116 g, 63 %).
[0581] ^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 8.11 (s, 1H), 7.85 (s, 1H), 7.76 (dd, *J* = 8.2, 4.3 Hz, 1H), 7.24 - 7.16 (m, 1H), 3.89 (s, 3H), 2.35 (s, 3H).

Intermediate j22: Methyl (E)-2-((7-cyanothieno[3,2-b]pyridin-3-yl)methylene)-3-oxobutanoate

[0582] Yellow solid (0.77 g, 40 %).
[0583] ^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 8.91 (d, *J* = 4.7 Hz, 1H), 8.32 (s, 1H), 8.15 (s, 1H), 7.63 (d, *J* = 4.7 Hz, 1H), 3.90 (s, 3H), 2.53 (s, 3H).

Intermediate j23: Cyclopropylmethyl (E)-2-((7-cyanobenzo[b]thiophen-3-yl)methylene)-3-oxobutanoate

[0584] Yellow solid (0.45 g, 52 %).

[0585] ^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 8.11 (dd, *J* = 8.2, 0.9 Hz, 1H), 8.06 (s, 1H), 7.83 (d, *J* = 0.9 Hz, 1H), 7.79 (d, *J* = 7.5 Hz, 1H), 7.57 (dd, *J* = 8.2, 7.5 Hz, 1H), 4.13 (d, *J* = 7.4 Hz, 2H), 2.48 (s, 3H), 1.26 - 1.04 (m, 1H), 0.66 - 0.51 (m, 2H), 0.38 - 0.21 (m, 2H).

Intermediate j24: Prop-2-yn-1-yl (E)-2-((7-cyanobenzo[b]thiophen-3-yl)methylene)-3-oxobutanoate

[0586] Yellow solid (0.7 g, 85 %).
[0587] ^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 8.13 (dd, *J* = 8.2, 0.9 Hz, 1H), 7.99 (s, 1H), 7.96 (s, 1H), 7.80 (d, *J* = 7.1 Hz, 1H), 7.62 - 7.55 (m, 1H), 4.89 (d, *J* = 2.5 Hz, 2H), 2.55 (t, *J* = 2.5 Hz, 1H), 2.40 (s, 3H).

Intermediate j25: Methyl (E)-2-((5,7-dicyanobenzo[b]thiophen-3-yl)methylene)-3-oxobutanoate

[0588] Yellow solid (0.135 g, 59 %).
[0589] ^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 8.31 (d, *J* = 1.4 Hz, 1H), 7.96 - 7.87 (m, 2H), 7.49 (s, 1H), 4.13 (d, *J* = 1.0 Hz, 3H), 2.04 (d, *J* = 1.0 Hz, 3H).

Intermediate j26: But-2-yn-1-yl (E)-2-((7-cyanobenzo[b]thiophen-3-yl) methylene)-3-oxobutanoate

[0590] Yellow solid (0.125 g, 36 %).
[0591] ^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 8.11 (td, *J* = 4.4, 0.8 Hz, 2H), 7.86 (d, *J* = 0.8 Hz, 1H), 7.80 (d, *J* = 7.4 Hz, 1H), 7.58 (dd, *J* = 8.2, 7.4 Hz, 1H), 4.86 (q, *J* = 2.3 Hz, 2H), 2.48 (s, 3H), 1.89 (t, *J* = 2.3 Hz, 3H).

Intermediate j27: (2,2,2-Trifluoroethyl) -2-((7-cyanobenzo[b]thiophen-3-yl) methylene)-3-oxobutanoate

[0592] Yellow solid (0.079 g, 38 %).
[0593] ^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 8.15 - 7.98 (m, 2H), 7.95 - 7.88 (m, 1H), 7.86 - 7.72 (m, 2H), 4.66 (dq, *J* = 11.7, 8.3 Hz, 2H), 2.53 - 2.40 (m, 3H).

Intermediate j28: Methyl (E)-2-((6-chloro-7-cyanobenzo[b]thiophen-3-yl) methylene)-3-oxobutanoate

[0594] Yellow solid (0.24 g, 56 %).
[0595] ^{1}H-NMR (300 MHz, $CDCl_3$-*d*) δ (ppm): 8.01 (d, *J* = 8.7 Hz, 1H), 7.91 (d, *J* = 0.9 Hz, 1H), 7.84 (d, *J* = 0.9 Hz, 1H), 7.58 (d, *J* = 8.7 Hz, 1H), 3.90 (s, 3H), 2.36 (s, 3H).

Intermediate j29: (E)-3-(2-Cyano-3-oxobut-1-en-1-yl)benzo[b]thiophene-7-carbonitrile

[0596] General procedure **j** using 3-oxobutanenitrile gave title compound as yellow solid (0.23 g, 69 %).
[0597] ^{1}H-NMR (300 MHz, DMSO-d_6) δ (ppm): 9.07 (s, 1H), 8.47 (s, 1H), 8.22 (d, *J* = 8.2 Hz, 1H), 7.85 (d, *J* = 7.4 Hz, 1H), 7.64 (t, *J* = 7.8 Hz, 1H), 2.63 (s, 3H).

Intermediate j30: 3-((5-Fluorothieno[2,3-b]pyridin-3-yl)methylene)pentane-2,4-dione

[0598] General procedure j gave title compound as yellow solid (0.132 g, 61 %).
^{1}H-NMR (300 MHz, DMSO-d_6) δ (ppm): 8.56 (d, *J* = 2.4 Hz, 1H), 7.90 (s, 1H), 7.83 (dd, *J* = 8.7, 2.4 Hz, 1H), 7.55 (s, 1H), 2.48 (s, 3H), 2.32 (s, 3H).

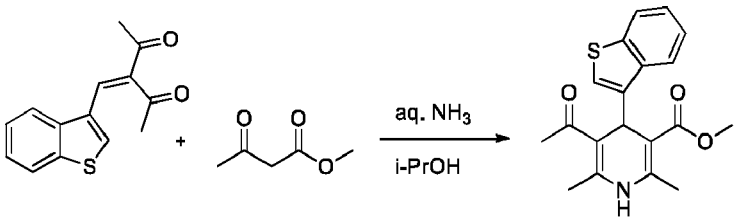
EXAMPLES

PREPARATION OF DIHYDROPYRIDINES

Method A (Rampa, A et al, Forsch. 1992, 42, 1284).

Example A1: Methyl 5-acetyl-4-(benzo[*b*]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

[0599]



[0600] A mixture of 3-(benzo[*b*]thiophen-3-ylmethylene)pentane-2,4-dione (0.24 g, 0.98 mmol, 1 eq), methyl 3-oxobutanoate (0.158 ml, 1.47 mmol, 1.5 eq) and 30% aqueous ammonium (0.62 ml, 9.8 mmol, 10 eq) in *i*-PrOH (2 ml) was heated at reflux teperature for 12 h. The solvent was removed under reduced pressure. The residue was taken up in water and extracted with dichloromethane and ethyl acetate. The combined organic layers were washed with brine, dried (Na_2SO_4), filtered and concentrated, and the crude product was purified by flash column chromatography on silica gel using CH_2Cl_2/MeOH (1%) as eluent to afford the title compound as a yellow solid (114 mg, 25%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.10 (d, *J* = 8.0 Hz, 1H), 7.79 (d, *J* = 7.9 Hz, 1H), 7.34 (dt, *J* = 24.0, 7.1 Hz, 2H), 7.13 (s, 1H), 6.27 (bs, 1H), 5.47 (s, 1H), 3.64 (s, 3H), 2.34 (s, 3H), 2.27 (s, 3H), 2.14 (s, 3H).

HRMS (IE) m/z calculated $C_{19}H_{19}NO_3S$ [M^+]: 341.1086, found: 341.1069.

[0601] Example A1 is a racemic mixture of two stereoisomers that have been separated by semi-preparative chiral HPLC (column: ChiralPak IA, 5 μm, 4.6 x 250 mm, eluent: n- hexane/iPrOH 95:5) affording **Example A2** (Enantiomer 1, Tr= 22,54 min, 95,60 % ee; 96,46% purity) and **Example A3** (Enantiomer 2, Tr= 18,10 min, 99,88 % ee; 92,87 % purity). Purity has been determined on a RP-C18 analytical column (Gemini-NX C18 5 μm, 4,6 x 150 mm; eluents: ACN/water/100 mM ammonium acetate, pH 7). The absolute stereochemistry has not been determined.

Example A4: 5-acetyl-4-(benzo[*b*]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxamide

[0602] Method A yielded the title compound as a yellow solid (73 mg, 22%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.05 (d, *J* = 7.7 Hz, 1H), 7.76 (d, *J* = 7.6 Hz, 1H), 7.29 (dt, *J* = 15.0, 7.0 Hz, 2H), 7.09 (s, 1H), 6.76 (s, 1H), 5.65 (bs, 2H), 5.34 (s, 1H), 2.25 (s, 3H), 2.08 (s, 6H).
HRMS (IE) m/z calculated $C_{18}H_{18}N_2O_2S$: 326.0910, found: 326.1011.

Example A5: 1-(4-(benzo[b]thiophen-3-yl)-5-benzoyl-2,6-dimethyl-1,4-dihydropyridin-3-yl)ethan-1-one

[0603] Method A yielded the title compound as a dark yellow solid (63 mg, 16%). ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.79 - 7.70 (m, 1H), 7.65 - 7.56 (m, 1H), 7.53 - 7.31 (m, 5H), 7.25 - 7.18 (m, 2H), 7.06 (s, 1H), 5.72 (bs, 1H), 5.56 (s, 1H), 2.48 (s, 3H), 2.07 (s, 3H), 1.77 (s, 3H).
HRMS (IE): m/z calculated $C_{24}H_{21}NO_2S$ [M^+]: 387.1293, found: 387.1286.

Example A6: Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-6-methyl-2-phenyl-1,4-dihydropyridine-3-carboxylate

[0604] Method A in MeOH yielded the title compound as a dark yellow solid (15 mg, 5%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.21 (d, *J* = 8.2 Hz, 1H), 7.83 (d, J= 7.9 Hz, 1H), 7.45-7.31 (m, 5H), 7.30 - 7.24 (m, 3H), 6.02 (bs, 1H), 5.59 (s, 1H), 3.38 (s, 3H), 2.41 (s, 3H), 2.17 (s, 3H).
HRMS (IE): m/z calculated $C_{24}H_{21}NO_3S$ [M^+]: 403.1242, found: 403.1252.
[0605] In the Hantzsch synthesis of the following examples, preformed enamines have been used instead of mixtures of 1,3-dicarbonyl compounds and ammonia:

Example A8: 1-(4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-5-nicotinoyl-1,4-dihydro pyridin-3-yl)ethan-1-one

[0606] Method A using (E)-4-aminopent-3-en-2-one in EtOH yielded the title compound as a dark yellow solid (60 mg, 19%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.64 (d, J = 11.7 Hz, 2H), 7.84 - 7.60 (m, 3H), 7.35 - 7.21 (m, 3H), 7.08 (s, 1H), 5.97 (bs, 1H), 5.56 (s, 1H), 2.45 (s, 3H), 2.10 (s, 3H), 1.77 (s, 3H).
HRMS (IE): m/z calculated $C_{23}H_{20}N_2O_2S$ [M^+]: 388.1245, found: 388.1229.

Example A9: Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-6-methyl-1,4-dihydro-[2,3'-bipyridine]-3-carboxylate

[0607] Method A using methyl (Z)-3-amino-3-(pyridin-3-yl)acrylate in acetic acid yielded the title compound as a yellow solid (31 mg, 16%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.49 (s, 1H), 8.42 (s, 1H), 8.18 (d, *J* = 8.0 Hz, 1H), 7.83 (d, *J* = 8.0 Hz, 1H), 7.55 (d, *J* = 7.9 Hz, 1H), 7.41 (t, *J* = 7.5 Hz, 1H), 7.33 (t, *J* = 7.2 Hz, 1H), 7.26 - 7.16 (m, 2H), 6.68 (bs, 1H), 5.59 (s, 1H), 3.37 (s, 3H), 2.41 (s, 3H), 2.15 (s, 3H).
HRMS (IE) m/z calculated $C_{23}H_{20}N_2O_3S$ [M^+]: 404.1195, found: 404.1179.

Example A10: 2,2,2-trifluoroethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

[0608] Method A using 2,2,2-trifluoroethyl (E)-3-aminobut-2-enoate in 2,2,2-trifluoroethanol yielded the title compound as a yellow solid (190 mg, 58%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.08 (d, *J* = 7.9 Hz, 1H), 7.81 (d, *J* = 8.0 Hz, 1H), 7.35 (dt, *J* = 21.4, 7.1 Hz, 2H), 7.17 (s, 1H), 6.10 (bs, 1H), 5.47 (s, 1H), 4.58 - 4.27 (m, 2H), 2.37 (s, 3H), 2.31 (s, 3H), 2.16 (s, 2H). ^{19}F-NMR (300 MHz, $CDCl_3$) δ = -73.39 (t, *J* = 8.1 Hz).
HRMS (IE) m/z calculated $C_{20}H_{18}F_3NO_3S$ [M^+]: 409.0960, found: 409.0943.

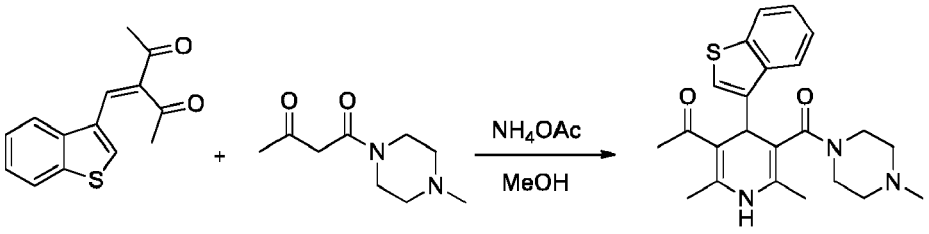
Example A10 was hydrolyzed to afford the carboxylic acid Example A11: **Example A11:** 5-Acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylic acid

[0609] 2,2,2-trifluoroethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate (0.05 g, 0.14 mmol, 1 eq.) was dissolved in dioxane (3 ml) at room temperature. Sodium hydroxide (0.42 ml, 0.84 mmol, 6 eq) was added, and the reaction mixture was heated at 130 °C for 4 hours. The solvent was removed under reduced pressure, and water and 2N HCl was added (pH 6-7). The mixture was extracted with dichloromethane and ethyl acetate, and the combined organic layers were washed with brine, dried (Na_2SO_4), filtered and concentrated. The crude product was purified by flash column chromatography on silica gel using CH_2Cl_2/MeOH (4%) as eluent to afford the title compound (15 mg, 38%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 11.82 (s, 1H), 8.95 (s, 1H), 8.14 (dd, *J* = 6.9, 1.3 Hz, 1H), 7.89 (dd, *J* = 7.0, 1.6 Hz, 1H), 7.32 (td, *J* = 7.6, 1.5 Hz, 2H), 7.18 (s, 1H), 5.40 (s, 1H), 2.32 (s, 3H), 2.24 (s, 3H), 2.10 (s, 3H).
HRMS (IE) m/z calculated $C_{18}H_{17}NO_3S$ [M^+]: 327.0929, found: 327.0937.

Method B (adapted from WO2006047537)

Example B1: 1-(4-(Benzo[b]thiophen-3-yl)-2,6-dimethyl-5-(4-methylpiperazine-1-carbonyl)-1,4-dihydropyridin-3-yl)ethan-1-one

[0610]



[0611] A mixture of 3-(benzo[b]thiophen-3-ylmethylene)pentane-2,4-dione (0.12 g, 0.49 mmol, 1 eq), 1-(4-methylpiperazin-1-yl)butane-1,3-dione (0.1 g, 0.54 mmol, 1.1 eq), ammonium acetate (0.06 g, 0.73 mmol, 1.5 eq) in MeOH (2 ml) was heated in a microwave reactor at 130°C for 15 min. The reaction mixture was allowed to cool to RT and then concentrated. The residue was purified by flash column chromatography on silica gel using CH_2Cl_2/MeOH (5%) as eluent to afford the title compound as a yellow solid (30 mg, 16%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.87 (d, *J* = 7.6 Hz, 1H), 7.80 (d, *J* = 7.3 Hz, 1H), 7.34 (dt, *J* = 14.8, 6.7 Hz, 2H), 7.09 (s, 1H), 5.91 (bs, 1H), 5.38 (s, 1H), 3.90 (d, *J* = 11.6 Hz, 1H), 3.11 - 2.92 (m, 1H), 2.91 - 2.73 (m, 1H), 2.68 - 2.55 (m, 1H), 2.37 (s, 3H), 2.33 - 2.19 (m, 2H), 1.90 (s, 3H), 1.85 (s, 3H), 1.69 (s, 3H), 1.55 - 1.36 (m, 1H), 0.40 - 0.17 (m, 1H).
HRMS (IE): m/z calculated $C_{23}H_{27}N_3O_2S$ [M^+]: 409.1824, found: 409.1834.

Example B2: 5-Acetyl-4-(benzo[b]thiophen-3-yl)-N,N-diethyl-2,6-dimethyl-1,4-dihydropyridine-3-carboxamide

[0612] Method B yielded the title compound as a yellow solid (30 mg, 16%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.86 (d, *J* = 7.3 Hz, 1H), 7.78 (d, *J* = 7.8 Hz, 1H), 7.35-7.28 (m, 2H), 7.11 (s, 1H), 5.68 (bs, 1H), 5.37 (s, 1H), 3.50 - 3.28 (m, 1H), 3.23 - 2.94 (m, 1H), 2.86 - 2.75 (m, 1H), 2.70 - 2.45 (m, 1H), 2.37 (s, 3H), 1.93 (s, 3H), 1.71 (s, 3H), 0.94 (t, *J* = 6.0 Hz, 3H), 0.20 (s, 3H).
HRMS (IE) m/z calculated $C_{22}H_{26}N_2O_2S$ [M^+]: 382.1715, found: 382.1724.

Example B3: 1-(4-(Benzo[b]thiophen-3-yl)-2,6-dimethyl-5-(morpholine-4-carbonyl)-1,4-dihydropyridin-3-yl)ethan-1-one

[0613] Method B yielded the title compound as a yellow solid (18 mg, 12%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.89 (d, *J* = 7.3 Hz, 1H), 7.83 (d, *J* = 7.9 Hz, 1H), 7.45-7.28 (m, 2H), 7.11 (s, 1H), 5.66 (bs, 1H), 5.39 (s, 1H), 3.84 (d, *J* = 11.8 Hz, 1H), 3.54 - 3.36 (m, 2H), 3.14 - 2.97 (m, 2H), 2.90 - 2.79 (m, 2H), 2.66 - 2.45 (m, 1H), 2.38 (s, 3H), 1.93 (s, 3H), 1.70 (s, 3H).
HRMS (IE): m/z calculated $C_{22}H_{24}N_2O_3S$ [M^+]: 396.1508, found: 396.1494.

Example B4: 2-Methoxyethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

[0614] Method B yielded the title compound as a yellow solid (30 mg, 16%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.13 (d, *J* = 8.0 Hz, 1H), 7.80 (d, *J* = 7.9 Hz, 1H), 7.45-7.29 (m, 2H), 7.17 (s, 1H), 5.90 (bs, 1H), 5.49 (s, 1H), 4.20 (t, *J* = 4.8 Hz, 2H), 3.57 - 3.50 (m, 2H), 3.33 (s, 3H), 2.37 (s, 3H), 2.30 (s, 3H), 2.14 (s, 3H).
HRMS (IE): m/z calculated $C_{21}H_{23}NO_4S$ [M^+]: 385.1348, found: 385.1335.

Example B5: 3-Acetamidopropyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

[0615] Method B yielded the title compound as a yellow solid (22 mg, 11%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.14 (d, *J* = 8.0 Hz, 1H), 7.79 (d, *J* = 8.0 Hz, 1H), 7.38 (t, *J* = 7.6 Hz, 1H), 7.34 - 7.25 (m, 1H), 7.14 (s, 1H), 5.56 (bs, 1H), 5.46 (s, 1H), 4.24 - 3.95 (m, 2H), 3.06 - 2.71 (m, 2H), 2.32 (s, 3H), 2.30 (s, 3H), 2.16 (s, 3H), 2.04 - 1.94 (m, 1H), 1.85 (s, 3H), 1.81 - 1.43 (m, 2H).
HRMS (IE): m/z calculated $C_{23}H_{26}N_2O_4S$ [M^+]: 426.1613, found: 426.1603.

Example B6: Benzyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydro-pyridine-3-carboxylate

[0616] Method B yielded the title compound as a yellow solid (19 mg, 10%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.01 (d, *J* = 8.7 Hz, 1H), 7.79 (d, *J* = 8.5 Hz, 1H), 7.41 - 7.26 (m, 5H), 7.26 - 7.19 (m, 2H), 7.09 (s, 1H), 5.87 (bs, 1H), 5.49 (s, 1H), 5.19 - 5.01 (m, 2H), 2.36 (s, 3H), 2.30 (s, 3H), 2.12 (s, 3H).
HRMS (IE): m/z calculated $C_{25}H_{23}NO_3S$ [M^+]: 417.1399, found: 417.1399.

Example B7: 2-Morpholinoethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

[0617] Method B yielded the title compound as a yellow solid (30 mg, 11%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.11 (d, J= 9.1 Hz, 1H), 7.79 (d, J= 7.1 Hz, 1H), 7.42 - 7.25 (m, 2H), 7.15 (s, 1H), 6.07 (bs, 1H), 5.49 (s, 1H), 4.29 - 4.07 (m, 2H), 3.59 (t, *J* = 4.6 Hz, 4H), 2.51 (t, *J* = 5.7 Hz, 2H), 2.38 - 2.33 (m, 7H), 2.31 (s, 3H), 2.16 (s, 3H).
HRMS (IE) m/z calculated $C_{24}H_{28}N_2O_4S$ [M^+]: 440.1770, found: 440.1783.

Example B8: 2-(Dimethylamino)ethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

[0618] Method B yielded the title compound as a yellow solid (15 mg, 7%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.12 (d, *J* = 8.0 Hz, 1H), 7.79 (d, *J* = 7.9 Hz, 1H), 7.43-7.23 (m, 2H), 7.15 (s, 1H), 5.97 (bs, 1H), 5.48 (s, 1H), 4.19 (h, *J* = 5.8 Hz, 2H), 2.59 (q, *J* = 6.2 Hz, 2H), 2.36 (s, 3H), 2.30 (s, 3H), 2.23 (s, 6H), 2.15 (s, 3H).
HRMS (IE): m/z calculated $C_{22}H_{26}N_2O_3S$ [M^+]: 398.1664, found: 398.1663.

Example B9: 2-Acetamidoethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

[0619] Method B yielded the title compound as a yellow solid (34 mg, 14%).

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.19 (d, *J* = 8.0 Hz, 1H), 7.82 (d, *J* = 7.9 Hz, 1H), 7.43 (t, *J* = 7.4 Hz, 1H), 7.34 (t, *J* = 7.4 Hz, 1H), 7.20 (s, 1H), 5.84 (bs, 1H), 5.47 (s, 1H), 4.86 (bs, 1H), 4.25 - 4.09 (m, 1H), 4.07 - 3.86 (m, 1H), 3.60 - 3.38 (m, 1H), 3.24 - 3.08 (m, 1H), 2.37 (s, 3H), 2.34 (s, 3H), 2.20 (s, 3H), 1.61 (s, 3H).
HRMS (IE): m/z calculated $C_{22}H_{24}N_2O_4S$ [M^+]: 412.1457, found: 412.1458.

Example B10: Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2-(methoxymethyl)-6-methyl-1,4-dihydropyridine-3-carboxylate

[0620] Method B yielded the title compound as a light-yellow solid (25 mg, 14%). ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.10 (d, *J* = 8.0 Hz, 1H), 7.80 (d, *J* = 7.9 Hz, 1H), 7.42 - 7.27 (m, 3H), 7.15 (s, 1H), 5.46 (s, 1H), 4.59 (dd, *J* = 26.8 Hz, 2H), 3.63 (s, 3H), 3.47 (s, 3H), 2.41 (s, 3H), 2.14 (s, 3H).
HRMS (IE): m/z calculated $C_{20}H_{21}NO_4S$ [M^+]: 371.1191, found: 371.1176.

Example B11: Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2-((dimethylamino)methyl)-6-methyl-1,4-dihydropyridine-3-carboxylate

[0621] Method B yielded the title compound as a yellow solid (25 mg, 11%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.18 (s, 1H), 8.10 (d, *J* = 8.2 Hz, 1H), 7.80 (d, *J* = 7.6 Hz, 1H), 7.43 - 7.28 (m, 2H), 7.14 (s, 1H), 5.47 (s, 1H), 3.73 - 3.50 (m, 5H), 2.42 (s, 3H), 2.29 (s, 6H), 2.14 (s, 3H).
HRMS (IE) m/z calculated $C_{21}H_{24}N_2O_3S$ [M^+]: 384.1508, found: 384.1506.

Example B12: Pyridin-4-ylmethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

[0622] Method B yielded the title compound as a yellow solid (25 mg, 13%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.49 - 8.34 (m, 2H), 8.03 (d, *J* = 6.8 Hz, 1H), 7.80 (d, *J* = 8.5 Hz, 1H), 7.35 - 7.20 (m, 2H), 7.14 (s, 1H), 6.93 (s, 1H), 6.91 (s, 1H), 6.33 (s, 1H), 5.52 (s, 1H), 5.08 (q, *J* = 13.7 Hz, 2H), 2.35 (s, 3H), 2.33 (s, 3H), 2.16 (s, 3H).
HRMS (IE): m/z calculated $C_{24}H_{22}N_2O_3S$ [M^+]: 418.1351, found: 418.1360.

Example B13: 4-Methoxybenzyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

[0623] Method B yielded the title compound as a yellow solid (28 mg, 13%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.00 (d, *J* = 8.6 Hz, 1H), 7.78 (d, *J* = 8.5 Hz, 1H), 7.32 - 7.20 (m, 2H), 7.16 (d, *J* = 8.5 Hz, 2H), 7.08 (s, 1H), 6.83 (d, *J* = 8.6 Hz, 2H), 5.93 (s, 1H), 5.47 (s, 1H), 5.02 (d, *J* = 2.8 Hz, 2H), 3.81 (s, 3H), 2.35 (s, 3H), 2.28 (s, 3H), 2.11 (s, 3H).
HRMS (IE): m/z calculated $C_{26}H_{25}NO_4S$ [M^+]: 447.1504, found: 447.1506.

Example B15: Pyridin-2-ylmethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

[0624] Method B yielded the title compound as a yellow solid (35 mg, 14%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.53 (d, *J* = 4.0 Hz, 1H), 8.04 (d, *J* = 8.5 Hz, 1H), 7.78 (d, *J* = 8.5 Hz, 1H), 7.52 - 7.43 (m, 1H), 7.31 - 7.21 (m, 2H), 7.15 (d, *J* = 5.4 Hz, 2H), 6.91 (d, *J* = 7.8 Hz, 1H), 6.22 (s, 1H), 5.55 (s, 1H), 5.22 (d, *J* = 3.8 Hz, 2H), 2.34 (s, 3H), 2.31 (s, 3H), 2.14 (s, 3H).
HRMS (IQ) m/z calculated $C_{24}H_{23}N_2O_3S$ [M^{+1}]: 419.1429, found: 419.1436.

Example B16: Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-6-methyl-2-(morpholinomethyl)-1,4-dihydropyridine-3-carboxylate

[0625] Method B yielded the title compound as a yellow solid (25 mg, 10%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.16 - 7.97 (m, 2H), 7.80 (d, *J* = 8.0 Hz, 1H), 7.42 - 7.17 (m, 2H), 7.11 (s, 1H), 5.47 (s, 1H), 3.82 - 3.69 (m, 5H), 3.64 (s, 4H), 2.52 (t, *J* = 4.6 Hz, 4H), 2.42 (s, 3H), 2.13 (s, 3H).
HRMS (IE) m/z calculated $C_{23}H_{26}N_2O_4S$ [M^+]: 426.1613, found: 426.1604.

Example B16-a: Dimethyl 4-(benzo[b]thiophen-3-yl)-2,6-bis(morpholinomethyl)-1,4-dihydropyridine-3,5-dicarboxylate

[0626] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 9.52 (s, 1H), 8.06 (d, J = 8.4 Hz, 1H), 7.79 (d, J = 7.8 Hz, 1H), 7.47 - 7.14 (m, 2H), 7.05 (s, 1H), 5.48 (s, 1H), 3.80 (d, J = 4.6 Hz, 12H), 3.55 (d, J = 1.7 Hz, 6H), 2.56 (tq, J = 11.7, 5.9, 4.9 Hz, 8H).
[0627] HRMS (IE) m/z calculated $C_{27}H_{33}N_3O_6S$ [M^+]: 527.2090, found: 527.2064.

Example B17: 2-Hydroxyethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

[0628] Method B yielded the title compound as a yellow solid (25 mg, 10%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.14 (d, *J* = 8.1 Hz, 1H), 7.81 (d, *J* = 7.9 Hz, 1H), 7.35 (dt, *J* = 25.8, 7.3 Hz, 2H), 7.17 (s, 1H), 6.07 (s, 1H), 5.48 (s, 1H), 4.25 - 4.05 (m, 2H), 3.68 (s, 2H), 2.34 (s, 3H), 2.32 (s, 3H), 2.16 (s, 3H), 1.83 (bs, 1H).
HRMS (IE): m/z calculated $C_{20}H_{21}NO_4S$ [M^+]: 371.1191, found: 371.1190.

Example B18: 1-(4-(Benzo[b]thiophen-3-yl)-5-(cyclopropanecarbonyl)-6-cyclopropyl-2-methyl-1,4-dihydropyridin-3-yl)ethan-1-one

[0629] Method B yielded the title compound as a yellow solid (15 mg, 10%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.07 (d, *J* = 8.0 Hz, 1H), 7.78 (d, *J* = 8.0 Hz, 1H), 7.45-7.26 (m, 2H), 7.04 (s, 1H), 5.78 (s, 1H), 5.57 (s, 1H), 2.39 (s, 3H), 2.37 - 2.23 (m, 1H), 2.13 (s, 4H), 1.27 (s, 1H), 1.11 (tdd, *J* = 5.6, 4.3, 2.7 Hz, 1H), 1.05 - 0.88 (m, 3H), 0.86 - 0.75 (m, 1H), 0.70 (d, *J* = 5.5 Hz, 2H).
HRMS (IE) m/z calculated $C_{23}H_{23}NO_2S$ [M^+]: 377.1424, found: 377.1428.

Example B19: Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2-(1-(tert-butoxycarbonyl) azetidin-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

[0630] Method B yielded the title compound as a light-yellow solid (0.065 mg, 19%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.06 (d, *J* = 8.1 Hz, 1H), 7.80 (d, *J* = 7.8 Hz, 1H), 7.50-7.22 (m, 2H), 7.14 (s, 1H), 6.69 (s, 1H), 5.48 (s, 1H), 4.68 (tt, *J* = 8.8, 4.6 Hz, 1H), 4.22 (td, *J* = 8.9, 3.6 Hz, 2H), 3.82 (ddd, *J* = 14.7, 9.0, 5.0 Hz, 2H), 3.63 (s, 3H), 2.45 (s, 3H), 2.14 (s, 3H), 1.46 (s, 9H).
HRMS (IE): m/z calculated $C_{26}H_{30}N_2O_5S$ [M^+]: 482.1875, found: 482.1874.

Example B20: (1-(tert-Butoxycarbonyl)piperidin-4-yl)methyl 5-acetyl-4-(benzo[b] thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

[0631] Method B yielded the title compound as a yellow solid (0.06 mg, 26%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.12 (d, *J* = 7.9 Hz, 1H), 7.78 (d, *J* = 7.9 Hz, 1H), 7.32 (ddd, *J* = 23.7, 11.3, 4.4 Hz, 2H), 7.12 (s, 1H), 6.23 (s, 1H), 5.47 (s, 1H), 4.11 - 3.79 (m, 4H), 2.72 - 2.44 (m, 2H), 2.34 (s, 3H), 2.30 (s, 3H), 2.17 (s, 3H), 1.71 - 1.58 (m, 1H), 1.44 (s, 10H), 1.38 - 1.21 (m, 1H), 0.99 (td, *J* = 11.8, 4.2 Hz, 2H).
HRMS (IE) m/z calculated $C_{29}H_{36}N_2O_5S$ [M^+]: 524.2345, found: 524.2349.

Example B21: Cyclohexylmethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

[0632] Method B yielded the title compound as a light-yellow solid (35 mg, 17%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.13 (d, J= 7.9 Hz, 1H), 7.79 (d, J= 8.0 Hz, 1H), 7.43-7.19 (m, 2H), 7.12 (s, 1H), 5.96 (s, 1H), 5.49 (s, 1H), 3.87 (d, *J* = 6.2 Hz, 2H), 2.36 (s, 3H), 2.30 (s, 3H), 2.16 (s, 3H), 1.70 - 1.46 (m, 6H), 1.27 - 1.01 (m, 4H), 1.01 - 0.75 (m, 1H).
HRMS (IE) m/z calculated $C_{25}H_{29}NO_3S$ [M^+]: 423.1868, found: 423.1876.

Example B22: Methyl 4-(benzo[b]thiophen-3-yl)-5-(cyclopropanecarbonyl)-2,6-dicyclopropyl-1,4-dihydropyridine-3-carboxylate

[0633] Method B yielded the title compound as a light-yellow solid (0.030 g, 11 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.09 (ddd, *J* = 8.1, 1.1, 0.7 Hz, 1H), 7.78 (ddd, *J* = 7.8, 1.1, 0.7 Hz, 1H), 7.45 - 7.27 (m, 2H), 7.03 (s, 1H), 5.66 (bs, 1H), 5.59 (s, 1H), 3.64 (s, 3H), 2.73 (tt, *J* = 8.5, 5.5 Hz, 1H), 2.37 (tt, *J* = 8.5, 5.5 Hz, 1H), 2.22 (tt, *J* = 7.8, 4.6 Hz, 1H), 1.13 - 0.86 (m, 6H), 0.80 - 0.52 (m, 6H).
HRMS (IE) m/z calculated $C_{25}H_{25}NO_3S$ [M^+]: 419.1555, found: 419.1543.
HPLC (98.4%): Rt 11.68 min.

Example B23: 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-N-phenyl-1,4-dihydropyridine-3-carboxamide

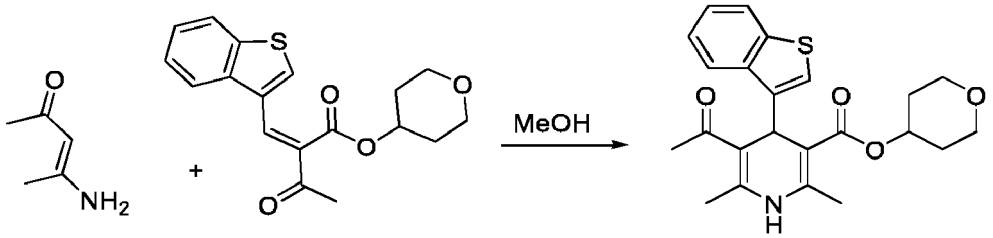
[0634] Method B yielded the title compound as a yellow solid (0.04 g, 23 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.11 - 8.04 (m, 1H), 7.89 - 7.81 (m, 1H), 7.41 - 7.27 (m, 3H), 7.25 - 6.98 (m, 6H), 5.66 (bs, 1H), 5.44 (s, 1H), 2.38 (s, 3H), 2.22 (s, 3H), 2.16 (s, 3H).
HRMS (IE) m/z calculated $C_{24}H_{22}N_2O_2S$ [M^+]: 402.1402, found: 402.1403.

HPLC (96.5%): Rt 24.12 min.

Method C

Example C1: Tetrahydro-2H-pyran-4-yl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

[0635]



[0636] A mixture of tetrahydro-2H-pyran-4-yl (Z)-2-(benzo[b]thiophen-3-ylmethylene)-3-oxobutanoate (0.056 g, 0.17 mmol) and (E)-4-aminopent-3-en-2-one (0.017 g, 0.17 mmol) in methanol (1 mL) was heated in a microwave reactor at 130°C for 60 min. The mixture was allowed to cool to RT and the solvent was removed under reduced pressure. The residue was purified by column chromatography (2:1 hexane: ethyl acetate) affording a light yellow solid (0.07 g, 43%). ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.13 (d, *J* = 7.8 Hz, 1H), 7.80 (d, *J* = 7.8 Hz, 1H), 7.42 - 7.26 (m, 2H), 7.13 (s, 1H), 5.77 (bs, 1H), 5.49 (s, 1H), 4.94 (tt, *J* = 8.9, 4.5 Hz, 1H), 3.84 (ddd, *J* = 15.8, 12.0, 4.5 Hz, 2H), 3.46 (dddd, *J* = 12.0, 8.9, 6.2, 3.0 Hz, 2H), 2.38 (s, 3H), 2.32 (s, 3H), 2.16 (s, 3H), 1.96 - 1.56 (m, 4H).
HRMS (IE) m/z calculated $C_{23}H_{25}NO_4S$ [M^+]: 411.1504, found: 411.1503.
HPLC (99.4%): Rt 22.96 min.
[0637] The following examples have been prepared according to Method C:

Example C2: (Tetrahydro-2H-pyran-4-yl)methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

[0638] Light-yellow solid (0.018 g, 28%).
[0639] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.12 (d, *J* = 8.1 Hz, 1H), 7.79 (d, *J* = 8.1 Hz, 1H), 7.44-7.23 (m, 2H), 7.13 (s, 1H), 5.87 (bs, 1H), 5.48 (s, 1H), 4.09 - 3.57 (m, 4H), 3.53 - 3.08 (m, 2H), 2.36 (s, 3H), 2.32 (s, 3H), 2.16 (s, 3H), 1.88 - 1.52 (m, 1H), 1.52 - 1.08 (m, 4H).
[0640] HRMS (IE) m/z calculated $C_{24}H_{27}NO_4S$ [M^+]: 425.1661, found: 425.1661.
[0641] HPLC (98.8%): Rt 17.86 min.

Example C3: Cyclohexyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

[0642] Light-yellow solid (0.07 g, 36%).
[0643] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.19 - 8.11 (m, 1H), 7.85 - 7.72 (m, 1H), 7.40 - 7.28 (m, 2H), 7.12 (s, 1H), 5.77 (bs, 1H), 5.49 (s, 1H), 4.77 (dt, *J* = 9.2, 5.0 Hz, 1H), 2.38 (s, 3H), 2.30 (s, 3H), 2.16 (s, 3H), 1.92 - 1.61 (m, 4H), 1.47 - 1.13 (m, 6H).
[0644] HRMS (IE) m/z calculated $C_{24}H_{27}NO_3S$ [M^+]: 409.1712, found: 409.1714.
[0645] HPLC (98.4%): Rt 20.63 min.

Example C4: Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2-(2-methoxy-2-oxoethyl)-6-methyl-1,4-dihydropyridine-3-carboxylate

[0646] Light-yellow solid (0.148 g, 45%).
[0647] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.08 (d, *J* = 8.1 Hz, 1H), 7.80 (d, *J* = 8.1 Hz, 1H), 7.42 - 7.26 (m, 2H), 7.21 (s, 1H), 6.96 (bs, 1H), 5.50 (s, 1H), 4.02 - 3.76 (m, 2H), 3.73 (s, 3H), 3.63 (s, 3H), 2.39 (s, 3H), 2.15 (s, 3H).
[0648] HRMS (IE) m/z calculated $C_{21}H_{21}NO_5S$ [M^+]: 399.1140, found: 399.1148. HPLC (95.2%): Rt 20.91 min.

Example C5: Methyl 5-acetyl-2,6-dimethyl-4-(2-methylbenzo[b]thiophen-3-yl)-1,4-dihydropyridine-3-carboxylate

[0649] Light-yellow solid (0.065 g, 25%).
[0650] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.83 (d, *J* = 8.1 Hz, 1H), 7.67 (d, *J* = 8.1 Hz, 1H), 7.35-7.14 (m, 2H), 5.63 (bs, 1H), 5.59 (s, 1H), 3.49 (s, 3H), 2.50 (s, 3H), 2.29 (s, 3H), 2.25 (s, 3H), 2.07 (s, 3H).
[0651] HRMS (IE) m/z calculated $C_{20}H_{21}NO_3S$ [M^+]: 355.1242, found: 355.1241.
[0652] HPLC (98.43%): Rt 18.11 min.

Example C6: Cyclopropylmethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

[0653] Light-yellow solid (0.065 g, 25%).
[0654] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.15 (d, *J* = 8.0 Hz, 1H), 7.79 (d, *J* = 8.0 Hz, 1H), 7.34 (dt, *J* = 13.1, 7.4 Hz, 2H), 7.16 (s, 1H), 5.78 (bs, 1H), 5.51 (s, 1H), 3.88 (dd, *J* = 7.6, 3.9 Hz, 2H), 2.39 (s, 3H), 2.32 (s, 3H), 2.15 (s, 3H), 1.08 (ddt, *J* = 10.9, 7.6, 3.9 Hz, 1H), 0.51 (d, *J* = 7.6 Hz, 2H), 0.20 (d, *J* = 4.9 Hz, 2H).
[0655] HRMS (IE) m/z calculated $C_{22}H_{23}NO_3S$ [M^+]: 381.1399, found: 381.1399.
[0656] HPLC (98.9%): Rt 17.72 min.

Example C7: Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2-(2-methoxyethyl)-6-methyl-1,4-dihydropyridine-3-carboxylate

[0657] Light-yellow solid (0.16 g, 64%).
[0658] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.09 (d, *J* = 8.0 Hz, 1H), 7.80 (d, *J* = 8.0 Hz, 1H), 7.43-7.27 (m, 2H), 7.21 (bs, 1H), 7.16 (s, 1H), 5.49 (s, 1H), 3.63 (s, 3H), 3.61 (d, *J* = 5.1 Hz, 2H), 3.40 (s, 3H), 3.26 - 3.11 (m, 1H), 3.10 - 2.97 (m, 1H), 2.36 (s, 3H), 2.15 (s, 3H). HRMS (IE) m/z calculated $C_{21}H_{23}NO_4S$ [M^+]: 385.1348, found: 385.1347.
[0659] HPLC (99.7%): Rt 19.65 min.

Example C8: Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2-((benzyloxy)methyl)-6-methyl-1,4-dihydropyridine-3-carboxylate

[0660] Yellow solid (0.18 g, 64%).
[0661] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.09 (d, *J* = 8.0 Hz, 1H), 7.85 - 7.76 (m, 1H), 7.45 - 7.24 (m, 8H), 7.13 (s, 1H), 5.45 (s, 1H), 4.85 - 4.66 (m, 2H), 4.62 (s, 2H), 3.61 (s, 3H), 2.37 (s, 3H), 2.13 (s, 3H).
[0662] HRMS (IE) m/z calculated $C_{26}H_{25}NO_4S$ [M^+]: 447.1504, found: 447.1490.
[0663] HPLC (95.6%): Rt 11.55 min.

Example C9: Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-6-methyl-2-(phenoxymethyl)-1,4-dihydropyridine-3-carboxylate

[0664] Yellow solid (0.11 g, 52%).
[0665] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.15 - 8.07 (m, 1H), 7.86 - 7.76 (m, 1H), 7.43 - 7.27 (m, 4H), 7.17 (s, 1H), 7.14 (bs, 1H), 7.07 - 6.93 (m, 3H), 5.50 (s, 1H), 5.36 - 5.12 (m, 2H), 3.67 (d, *J* = 0.6 Hz, 3H), 2.40 (s, 3H), 2.15 (d, 3H).
[0666] HRMS (IE) m/z calculated $C_{25}H_{23}NO_4S$ [M^+]: 433.1348, found: 433.1346.
[0667] HPLC (96.0%): Rt 10.20 min.

Example C10: Phenethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

[0668] Yellow solid (0.075 g, 21%).
[0669] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.98 - 7.89 (m, 1H), 7.81 - 7.75 (m, 1H), 7.35 - 7.26 (m, 3H), 7.24 - 7.13 (m, 4H), 7.00 (s, 1H), 5.75 (bs, 1H), 5.40 (s, 1H), 4.38 (dt, *J* = 10.9, 6.6 Hz, 1H), 4.21 (dt, *J* = 10.9, 7.2 Hz, 1H), 2.88 (t, *J* = 6.6 Hz, 2H), 2.37 (s, 3H), 2.23 (s, 3H), 2.10 (s, 3H).
[0670] HRMS (IE) m/z calculated $C_{26}H_{25}NO_3S$ [M^+]: 431.1555, found: 431.1549.
[0671] HPLC (97.6%): Rt 17.80 min.

Example C11: Methyl 4-(benzo[b]thiophen-3-yl)-5-(cyclopropanecarbonyl)-6-cyclopropyl-2-methyl-1,4-dihydropyridine-3-carboxylate

[0672] Yellow solid (0.080 g, 40 %).
[0673] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.53 (s, 1H), 8.09 - 7.91 (m, 1H), 7.91 - 7.79 (m, 1H), 7.37 - 7.16 (m, 2H), 7.03

(s, 1H), 5.28 (s, 1H), 3.51 (s, 3H), 2.47 - 2.39 (m, 1H), 2.28 (s, 3H), 2.28 - 2.20 (m, 1H), 1.00 - 0.59 (m, 8H).
[0674] HRMS (IE) m/z calculated $C_{23}H_{23}NO_3S$ [M^+]: 393.1399, found: 393.1403.
[0675] HPLC (98.3%): Rt 16.05 min.

Example C14: Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-6-methyl-2-(trifluoromethyl)-1,4-dihydropyridine-3-carboxylate

[0676] Yellow solid (0.012 g, 6%).
[0677] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.00 (ddd, *J* = 8.1, 1.3, 0.7 Hz, 1H), 7.83 (ddd, *J* = 7.8, 1.3, 0.7 Hz, 1H), 7.46 - 7.30 (m, 2H), 7.17 (s, 1H), 6.22 (bs, 1H), 5.51 (s, 1H), 3.65 (s, 3H), 2.43 (s, 3H), 2.11 (s, 3H). ^{19}F-NMR (300 MHz, $CDCl_3$) δ = -63.89 (3F).
[0678] HRMS (IE) m/z calculated $C_{19}H_{16}F_3NO_3S$ [M^+]: 395.0803, found: 395.0792.
[0679] HPLC (99.5%): Rt 12.57 min.

Example C15 and Example C16: Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-6-benzyl-2-methyl-1,4-dihydropyridine-3-carboxylate and methyl 4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-5-(2-phenylacetyl)-1,4-dihydropyridine-3-carboxylate

[0680] Method C afforded Examples C15 and C16 which were separated by column chromatography.

Example C15: Yellow solid (0.02 g, 6%).

[0681] ^{1}H-NMR (500 MHz, $CDCl_3$) δ = 8.07 (d, J= 8.2 Hz, 1H), 7.81 (d, J= 8.2 Hz, 1H), 7.41 - 7.26 (m, 7H), 7.14 (s, 1H), 5.70 (bs, 1H), 5.53 (s, 1H), 4.35 (d, *J* = 16.1 Hz, 1H), 4.11 (d, *J* = 16.1 Hz, 1H), 3.64 (s, 3H), 2.20 (s, 3H), 2.14 (s, 3H).
[0682] HRMS (IE) m/z calculated $C_{25}H_{23}NO_3S$ [M^+]: 417.1399, found: 417.1400.
[0683] HPLC (98.6%): Rt 12.86 min.

Example C16: Yellow solid (0.078 g, 24%).

[0684] ^{1}H-NMR (500 MHz, $CDCl_3$) δ = 8.13 (d, *J* = 8.0 Hz, 1H), 7.84 (d, *J* = 8.0 Hz, 1H), 7.40 (ddd, *J* = 8.2, 7.0, 1.3 Hz, 1H), 7.33 (ddd, *J* = 8.2, 7.0, 1.3 Hz, 1H), 7.26 - 7.20 (m, 2H), 7.20 - 7.15 (m, 2H), 7.00 (s, 1H), 6.99 (s, 1H), 5.82 (bs, 1H), 5.60 (s, 1H), 3.91 (d, *J* = 15.9 Hz, 1H), 3.67 (s, 3H), 3.58 (d, *J* = 15.9 Hz, 1H), 2.40 (s, 3H), 2.29 (s, 3H).
[0685] HRMS (IE) m/z calculated $C_{25}H_{23}NO_3S$ [M^+]: 417.1399, found: 417.1396.
[0686] HPLC (95.4%): Rt 15.69 min.

Example C18: Methyl 4-(benzo[b]thiophen-3-yl)-5-(2-methoxyacetyl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

[0687] Yellow solid (0.03 g, 23%).
[0688] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.10 (d, *J* = 8.7 Hz, 1H), 7.82 (d, *J* = 8.7 Hz, 1H), 7.41 (t, *J* = 7.6 Hz, 1H), 7.33 (t, *J* = 7.6 Hz, 1H), 7.16 (s, 1H), 5.96 (s, 1H), 5.44 (s, 1H), 4.32 (d, *J* = 16.1 Hz, 1H), 3.92 (d, *J* = 16.6 Hz, 1H), 3.66 (s, 3H), 3.28 (s, 3H), 2.43 (s, 3H), 2.31 (s, 3H).
[0689] HRMS (IE) m/z calculated $C_{20}H_{21}NO_4S$ [M^+]: 371.1191, found: 371.1183.
[0690] HPLC (97.4%): Rt 22.72 min.

Example C19: Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-6-(methoxymethyl)-2-methyl-1,4-dihydropyridine-3-carboxylate

[0691] Yellow solid (0.062 g, 36%).
[0692] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.08 (d, *J* = 8.0 Hz, 1H), 7.81 (d, *J* = 8.0 Hz, 1H), 7.42 - 7.36 (m, 2H), 7.31 (t, *J* = 7.5 Hz, 1H), 7.17 (s, 1H), 5.47 (s, 1H), 4.71 (s, 2H), 3.65 (s, 3H), 3.52 (s, 3H), 2.32 (s, 3H), 2.07 (s, 3H).
[0693] HRMS (IE) m/z calculated $C_{20}H_{21}NO_4S$ [M^+]: 371.1191, found: 371.1187.
[0694] HPLC (96.0%): Rt 26.61 min.

Example C20: Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2-(fluoromethyl)-6-methyl-1,4-dihydropyridine-3-carboxylate

[0695] Yellow solid (0.015 g, 7%).
[0696] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.09 (d, *J* = 8.0 Hz, 1H), 7.81 (d, *J* = 8.0 Hz, 1H), 7.36 (dt, *J* = 24.7, 7.3 Hz, 2H), 7.18 (s, 1H), 6.72 (d, *J* = 6.5 Hz, 1H), 5.65 (dd, *J* = 47.7, 16.3 Hz, 2H), 5.44 (s, 1H), 3.63 (s, 3H), 2.43 (s, 3H), 2.14 (s, 3H). ^{19}F NMR (282 MHz, $CDCl_3$) δ = 122.68 (td, *J* = 47.7, 6.5 Hz).

[0697] HRMS (IE) m/z calculated $C_{19}H_{18}FNO_3S$ [M^+]: 359.0991, found: 359.0977.
[0698] HPLC (96.8%): Rt 13.25 min.

Example C21: Cyclopropylmethyl 5-acetyl-4-(5-fluorobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

[0699] Yellow solid (0.055 g, 52%).
[0700] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.82 (dd, *J* = 10.5, 2.3 Hz, 1H), 7.70 (dd, *J* = 8.7, 5.0 Hz, 1H), 7.24 (s, 1H), 7.06 (td, *J* = 8.7, 2.3 Hz, 1H), 5.95 (s, 1H), 5.43 (s, 1H), 3.97 - 3.80 (m, 2H), 2.37 (s, 3H), 2.32 (s, 3H), 2.16 (s, 3H), 1.19 - 1.02 (m, 1H), 0.62 - 0.43 (m, 2H), 0.28 - 0.15 (m, 2H). ^{19}F NMR (282 MHz, $CDCl_3$) δ = -118.91 (s).
[0701] HRMS (IE) m/z calculated $C_{22}H_{22}FNO_3S$ [M^+]: 399.1304, found: 399.1318.
[0702] HPLC (98.9%): Rt 17.97 min.

Example C22: 1-(tert-Butoxycarbonyl)piperidin-4-yl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

[0703] Method C using ammonium acetate (1.5 eq) in methanol afforded the title compound as a yellow solid (0.085 g, 21%).
[0704] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.12 (d, *J* = 7.8 Hz, 1H), 7.79 (d, *J* = 7.8 Hz, 1H), 7.34 (dt, *J* = 12.9, 7.2 Hz, 2H), 7.12 (s, 1H), 5.80 (s, 1H), 5.48 (s, 1H), 4.91 (dt, *J* = 8.6, 4.4 Hz, 1H), 3.67 (dd, *J* = 15.3, 7.8 Hz, 2H), 3.07 (dt, *J* = 10.2, 5.2 Hz, 2H), 2.38 (s, 3H), 2.31 (s, 3H), 2.16 (s, 3H), 1.62 - 1.52 (m, 4H), 1.45 (s, 9H).
[0705] HRMS (IE) m/z calculated $C_{28}H_{34}N_2O_5S$ [M^+]: 510.2188, found: 510.2182.
[0706] HPLC (99.0%): Rt 21.85 min.

Example C23: Cyclopentylmethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

[0707] Method C using ammonium acetate (1.5 eq) in methanol afforded the title compound as a yellow solid (0.035 g, 14%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.13 (d, *J* = 7.9 Hz, 1H), 7.79 (d, *J* = 7.4 Hz, 1H), 7.43-7.29 (m, 2H), 7.13 (s, 1H), 5.84 (bs, 1H), 5.50 (s, 1H), 3.95 (d, *J* = 7.3 Hz, 2H), 2.38 (s, 3H), 2.31 (s, 3H), 2.22 - 2.09 (m, 4H), 1.77 - 1.45 (m, 6H), 1.18 - 1.11 (m, 2H). HRMS (IE) m/z calculated $C_{24}H_{27}NO_3S$ [M^+]: 409.1712, found: 409.1712.
HPLC (99.4%): Rt 16.93 min.

Example C24 Cyclopropylmethyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[0708] Yellow solid (0.035 g, 43%).
[0709] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.53 - 8.46 (m, 2H), 7.30 (dd, *J* = 7.9, 4.6 Hz, 1H), 7.23 (s, 1H), 6.53 (s, 1H), 5.47 (s, 1H), 3.95 - 3.73 (m, 2H), 2.37 (s, 3H), 2.32 (s, 3H), 2.17 (s, 3H), 1.03 (ddd, *J* = 12.7, 8.0, 5.0 Hz, 1H), 0.48 (d, *J* = 8.0 Hz, 2H), 0.17 (d, *J* = 4.4 Hz, 2H).
[0710] HRMS (IE) m/z calculated $C_{21}H_{22}N_2O_3S$ [M^+]: 382.1351, found: 382.1346.
[0711] HPLC (97.9%): Rt 25.95 min.

Example C25: 1-methylpiperidin-4-yl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

[0712] Method C using ammonium acetate (1.5 eq) in methanol afforded the title compound as a yellow solid (0.025 g, 10%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.13 (d, *J* = 8.0 Hz, 1H), 7.78 (d, *J* = 8.0 Hz, 1H), 7.34 (dt, *J* = 15.9, 7.3 Hz, 2H), 7.11 (s, 1H), 6.03 (s, 1H), 5.49 (s, 1H), 4.78 (tt, *J* = 8.5, 4.1 Hz, 1H), 2.67 - 2.50(d, *J* = 17.6 Hz, 2H), 2.35 (s, 3H), 2.30 (s, 3H), 2.27 (d, *J* = 2.3 Hz, 1H), 2.20 (s, 3H), 2.16 (s, 3H), 2.12 (bs, 1H), 1.96 - 1.83 (m, 2H), 1.80 - 1.59 (m, 2H). HRMS (IE) m/z calculated $C_{24}H_{28}N_2O_3S$ [M^+]: 424.1821, found: 424.1827.
HPLC (96.8%): Rt 33.18 min.

Example C26: Cyclopentyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

[0713] Method C using ammonium acetate (1.5 eq) in methanol afforded the title compound as a yellow solid (0.04 g, 17%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.14 (d, *J* = 8.2 Hz, 1H), 7.79 (d, *J* = 7.7 Hz, 1H), 7.42 - 7.28 (m, 2H), 7.11 (s, 1H), 5.81

(s, 1H), 5.48 (s, 1H), 5.27 - 5.11 (m, 1H), 2.38 (s, 3H), 2.29 (s, 3H), 2.16 (s, 3H), 1.90 - 1.47 (m, 8H).
HRMS (IE) m/z calculated $C_{23}H_{25}NO_3S$ [M^+]: 395.1555, found: 395.1558.
HPLC (97.1%): Rt 17.56 min.

Example C27: 4,4-dimethylcyclohexyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

[0714] Method C using ammonium acetate (1.5 eq) in methanol afforded the title compound as a light yellow solid (0.03 g, 11 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.15 (ddd, *J* = 8.1, 1.3, 0.7 Hz, 1H), 7.79 (ddd, *J* = 7.8, 1.3, 0.7 Hz, 1H), 7.40 - 7.28 (m, 2H), 7.13 (s, 1H), 5.78 (bs, 1H), 5.50 (s, 1H), 4.74 (tt, *J* = 8.8, 4.2 Hz, 1H), 2.37 (s, 3H), 2.31 (s, 3H), 2.16 (s, 3H), 1.80 - 1.66 (m, 1H), 1.66 - 1.50 (m, 3H), 1.46 - 1.27 (m, 3H), 1.27 - 1.16 (m, 1H), 0.88 (s, 3H), 0.88 (s, 3H). HRMS (IE) m/z calculated $C_{26}H_{31}NO_3S$ [M^+]: 437.2025, found: 437.2028.
HPLC (98.3%): Rt 16.78 min.

Example C28: Cyclobutyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

[0715] Method C using ammonium acetate (1.5 eq) in methanol afforded the title compound as a light yellow solid (0.02 g, 9%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.14 (d, *J* = 7.9 Hz, 1H), 7.79 (d, *J* = 7.9 Hz, 1H), 7.35-7.31 (m, 2H), 7.13 (s, 1H), 6.09 (s, 1H), 5.47 (s, 1H), 5.00 - 4.89 (m, 1H), 2.36 (s, 3H), 2.32 - 2.23 (m, 5H), 2.15 (s, 3H), 2.12 - 1.99 (m, 1H), 1.99 - 1.85 (m, 1H), 1.82 - 1.66 (m, 1H), 1.66 - 1.51 (m, 1H).
HRMS (IE) m/z calculated $C_{22}H_{23}NO_3S$ [M^+]: 381.1399, found: 381.1408.
HPLC (99.0%): Rt 17.42 min.

Example C29: Methyl 5-acetyl-4-(5-fluorobenzo[b]thiophen-3-yl)-6-methyl-2-(trifluoromethyl)-1,4-dihydropyridine-3-carboxylate

[0716] Method C using trifluoroacetic acid (1.5 eq) in methanol afforded the title compound as a yellow solid (0.035 g, 37%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.71 (dd, *J* = 9.6, 3.6 Hz, 2H), 7.24 (s, 1H), 7.11 (td, *J* = 8.7, 2.4 Hz, 1H), 6.30 (s, 1H), 5.43 (s, 1H), 3.69 (s, 3H), 2.43 (s, 3H), 2.13 (s, 3H). ^{19}F-NMR (282 MHz, $CDCl_3$) δ = -63.84 (s, CF_3), -118.19 (td, J= 9.6, 4.9 Hz, F).
HRMS (IE) m/z calculated $C_{19}H_{15}NO_3SF_4$ [M^+]: 413.0709, found: 413.0702.
HPLC (99.1%): Rt 13.51 min.

Example C30: Methyl 5-acetyl-2,6-dimethyl-4-(thieno[3,2-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[0717] Yellow solid (0.015 g, 24%).
[0718] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.66 (dd, *J* = 4.5, 1.5 Hz, 1H), 8.07 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.29 (s, 1H), 7.18 (dd, *J* = 8.2, 4.5 Hz, 1H), 5.97 (s, 1H), 5.72 (s, 1H), 3.63 (s, 3H), 2.45 (s, 3H), 2.36 (s, 3H), 2.24 (s, 3H).
[0719] HRMS (IE) m/z calculated $C_{18}H_{18}N_2O_3S$ [M^+]: 342.1038, found: 342.1034.
[0720] HPLC (98.8%): Rt 22.75 min.

Example C31: Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2-methyl-6-(trifluoromethyl)-1,4-dihydropyridine-3-carboxylate

[0721] Method C using trifluoroacetic acid (1.5 eq) in methanol afforded the title compound as a yellow solid (0.035 g, 24%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.97 - 7.91 (m, 1H), 7.83 (ddd, *J* = 7.7, 1.4, 0.7 Hz, 1H), 7.44 - 7.30 (m, 2H), 7.24 (s, 1H), 5.94 (s, 1H), 5.40 (s, 1H), 3.58 (s, 3H), 2.39 (s, 3H), 1.99 (q, *J* = 0.7 Hz, 3H). ^{19}F-NMR (282 MHz, $CDCl_3$) δ = -63.65. (s, CF3).
HRMS (IE) m/z calculated $C_{19}H_{16}NO_3SF_3$ [M^+]: 395.0803, found: 395.0810.
HPLC (98.5%): Rt 10.44 min.

Example C32: Cyclopropylmethyl 5-acetyl-4-(5-chlorobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

[0722] Yellow solid (0.075 g, 50%).

[0723] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.12 (d, *J* = 2.0 Hz, 1H), 7.70 (d, *J* = 9.0 Hz, 1H), 7.28 (d, *J* = 2.5 Hz, 1H), 7.21 (s, 1H), 5.78 (s, 1H), 5.44 (s, 1H), 3.90 (d, *J* = 7.3 Hz, 2H), 2.39 (s, 3H), 2.33 (s, 3H), 2.16 (s, 3H), 1.29 - 1.13 (m, 1H), 0.59 - 0.46 (m, 2H), 0.21 (dd, *J* = 4.8, 1.8 Hz, 2H).

[0724] HRMS (IE) m/z calculated $C_{22}H_{22}NO_3SCl$ [M^+]: 415.1009, found: 415.0997.

[0725] HPLC (99.6%): Rt 18.43 min.

Example C33: Cyclohexylmethyl 5-acetyl-4-(5-chlorobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

[0726] Yellow solid (0.080 g, 61%).

[0727] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.10 (bs, 1H), 7.68 (d, *J* = 8.5 Hz, 1H), 7.31 - 7.21 (m, 1H), 7.17 (s, 1H), 6.05 (bs, 1H), 5.42 (s, 1H), 3.90 (ddd, *J* = 27.5, 10.8, 6.6 Hz, 2H), 2.36 (s, 3H), 2.30 (s, 3H), 2.17 (s, 3H), 1.85 - 1.43 (m, 6H), 1.32 - 1.01 (m, 3H), 1.01 - 0.78 (m, 2H).

[0728] HRMS (IE) m/z calculated $C_{25}H_{28}NO_3SCl$ [M^+]: 457.1478, found: 457.1477.

[0729] HPLC (99.1%): Rt 18.16 min.

Example C34: Cyclohexylmethyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[0730] Yellow solid (0.075 g, 58%).

[0731] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.57 - 8.44 (m, 2H), 7.32 (dd, *J* = 8.2, 4.6 Hz, 1H), 7.20 (s, 1H), 6.40 (s, 1H), 5.46 (s, 1H), 3.86 (dd, *J* = 6.1, 3.5 Hz, 2H), 2.37 (s, 3H), 2.33 (s, 3H), 2.18 (s, 3H), 1.70 - 1.44 (m, 6H), 1.16 (d, *J* = 40.3 Hz, 3H), 0.91 - 0.74 (m, 2H). HRMS (IE) m/z calculated $C_{24}H_{28}N_2O_3S$ [M^+]: 424.1821, found: 424.1833.

[0732] HPLC (98.9%): Rt 25.30 min.

Example C35: Cyclopentylmethyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[0733] Yellow solid (0.095 g, 75%).

[0734] ^{1}H-NMR (300 MHz, $CDCl_3$) 5 = 8.49 (d, *J* = 8.2 Hz, 2H), 7.31 (dd, J= 8.1, 4.6 Hz, 1H), 7.20 (s, 1H), 6.44 (s, 1H), 5.46 (s, 1H), 4.01 - 3.86 (m, 2H), 2.37 (s, 3H), 2.32 (s, 3H), 2.17 (s, 3H), 2.14 - 2.02 (m, 1H), 1.67 - 1.44 (m, 6H), 1.21 - 1.05 (m, 2H).

[0735] HRMS (IE) m/z calculated $C_{23}H_{26}N_2O_3S$ [M^+]: 410.1664, found: 410.1665.

[0736] HPLC (98.4%): Rt 25.14 min.

Example C36: Cyclohexyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[0737] Yellow solid (0.028 g, 48%).

[0738] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.59 - 8.40 (m, 2H), 7.31 (dd, *J* = 8.2, 4.6 Hz, 1H), 7.19 (s, 1H), 6.47 (s, 1H), 5.46 (s, 1H), 4.75 (tt, *J* = 8.8, 3.9 Hz, 1H), 2.37 (s, 3H), 2.31 (s, 3H), 2.17 (s, 3H), 1.87 - 1.74 (m, 1H), 1.75 - 1.55 (m, 3H), 1.56 - 1.45 (m, 1H), 1.45 - 1.13 (m, 5H).

[0739] HRMS (IE) m/z calculated $C_{23}H_{26}N_2O_3S$ [M^+]: 410.1664, found: 410.1665.

[0740] HPLC (98.2%): Rt 24.87 min.

Example C37: Cyclopentyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[0741] Yellow solid (0.034 g, 59%).

[0742] ^{1}H-NMR (300 MHz, $CDCl_3$) 5 = 8.53 - 8.42 (m, 2H), 7.31 (dd, *J* = 8.2, 4.6 Hz, 1H), 7.17 (s, 1H), 5.85 (s, 1H), 5.44 (s, 1H), 5.16 (dq, *J* = 6.1, 3.0 Hz, 1H), 2.38 (s, 3H), 2.31 (s, 3H), 2.17 (s, 3H), 1.80 (td, *J* = 15.9, 14.5, 6.1 Hz, 2H), 1.67 - 1.46 (m, 6H).

[0743] HRMS (IE) m/z calculated $C_{22}H_{24}N_2O_3S$ [M^+]: 396.1508, found: 396.1505.

[0744] HPLC (98.9%): Rt 25.70 min.

Example C38: Methyl 5-acetyl-4-(5-chlorobenzo[b]thiophen-3-yl)-6-methyl-2-(trifluoromethyl)-1,4-dihydropyridine-3-carboxylate

[0745] Method C using trifluoroacetic acid (1.5 eq) in methanol afforded the title compound as a yellow solid (0.022 g, 51%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.00 (d, *J* = 1.6 Hz, 1H), 7.73 (d, *J* = 8.6 Hz, 1H), 7.31 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.20 (s, 1H), 6.29 (s, 1H), 5.45 (s, 1H), 3.71 (s, 3H), 2.44 (s, 3H), 2.13 (s, 3H). ^{19}F-NMR (282 MHz, $CDCl_3$) δ = -63.85 (s, CF_3). HRMS (IE) m/z calculated $C_{19}H_{15}NO_3SF_3Cl$ [M^+]: 429.0413, found: 429.0413.
HPLC (95.7%): Rt 13.94 min.

Example C39: Benzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[0746] Yellow solid (0.070 g, 69%).
[0747] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.50 - 8.44 (m, 1H), 8.26 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.34 - 7.24 (m, 2H), 7.26 (d, *J* = 0.8 Hz, 1H), 7.20 - 7.16 (m, 2H), 7.16 - 7.10 (m, 2H), 5.95 (s, 1H), 5.44 (s, 1H), 5.07 (s, 2H), 2.37 (s, 3H), 2.33 (s, 3H), 2.13 (s, 3H).
[0748] HRMS (IE) m/z calculated $C_{24}H_{22}N_2O_3S$ [M^+]: 418.1351, found: 418.1358.
[0749] HPLC (99.4%): Rt 26.38 min.

Example C40: (Tetrahydro-2H-pyran-4-yl)methyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[0750] Yellow solid (0.029 g, 45%).
[0751] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.55-8.43 (m, 2H), 7.32 (dd, *J* = 8.1, 4.6 Hz, 1H), 7.19 (s, 1H), 6.18 (s, 1H), 5.45 (s, 1H), 3.99 - 3.77 (m, 4H), 3.24 (dtd, *J* = 20.2, 11.6, 2.5 Hz, 2H), 2.37 (s, 3H), 2.34 (s, 3H), 2.18 (s, 3H), 1.47 - 1.15 (m, 5H).
[0752] HRMS (IE) m/z calculated $C_{23}H_{26}N_2O_4S$ [M^+]: 426.1613, found: 426.1600.
[0753] HPLC (99.5%): Rt 32.56 min.

Example C41: Benzyl 5-acetyl-4-(5-fluorobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

[0754] Yellow solid (0.018 g, 11%).
[0755] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.75 - 7.63 (m, 2H), 7.33 - 7.17 (m, 5H), 7.16 (s, 1H), 7.04 (td, *J* = 8.9, 8.5, 2.0 Hz, 1H), 5.92 (s, 1H), 5.42 (s, 1H), 5.10 (q, *J* = 12.3 Hz, 2H), 2.35 (s, 3H), 2.31 (s, 3H), 2.13 (s, 3H). ^{19}F-NMR (282 MHz, $CDCl_3$) δ = -118.53 (s, CF). HRMS (IE) m/z calculated $C_{25}H_{22}NO_3SF$ [M^+]: 435.1304, found: 435.1307.
[0756] HPLC (97.1%): Rt 18.43 min.

Example C42: Benzyl 5-acetyl-4-(5-chlorobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

[0757] Yellow solid (0.065 g, 60%).
[0758] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.06 (d, *J* = 1.7 Hz, 1H), 7.68 (d, *J* = 8.6 Hz, 1H), 7.39-7.18 (m, 6H), 7.13 (s, 1H), 6.00 (s, 1H), 5.44 (s, 1H), 5.27 - 4.96 (m, 2H), 2.35 (s, 3H), 2.30 (s, 3H), 2.13 (s, 3H).
[0759] HRMS (IE) m/z calculated $C_{25}H_{22}NO_3SCl$ [M^+]: 451.1011, found: 451.1011.
[0760] HPLC (97.4%): Rt 18.38 min.

Example C43: (Tetrahydro-2H-pyran-4-yl)methyl 5-acetyl-4-(5-chlorobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

[0761] Yellow solid (0.076 g, 46%).
[0762] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.10 (d, *J* = 1.8 Hz, 1H), 7.68 (d, *J* = *8.1* Hz, 1H), 7.27-7.24 (m, 1H), 7.18 (s, 1H), 6.15 (bs, 1H), 5.39 (s, 1H), 3.93 - 3.82 (m, 4H), 3.50 - 3.19 (m, 2H), 2.35 (s, 3H), 2.17 (s, 3H), 2.03 (s, 3H), 1.89 - 1.63 (m, 2H), 1.51 - 1.47 (m, 1H), 1.35 - 1.17 (m, 2H).
[0763] HRMS (IE) m/z calculated $C_{24}H_{26}NO_4SCl$ [M^+]: 459.1271, found: 459.1272.
[0764] HPLC (99.4%): Rt 24.50 min.

Example C44: (Tetrahydro-2H-pyran-4-yl)methyl 5-acetyl-4-(5-fluorobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

[0765] Yellow solid (0.097 g, 57%).

[0766] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.79 (d, *J* = 9.7 Hz, 1H), 7.70 (dd, *J* = 8.3, 5.1 Hz, 1H), 7.21 (s, 1H), 7.06 (t, *J* = 8.3 Hz, 1H), 6.02 (s, 1H), 5.40 (s, 1H), 3.99 - 3.73 (m, 4H), 3.28 (dt, *J* = 25.5, 12.5 Hz, 2H), 2.36 (s, 3H), 2.32 (s, 3H), 2.17 (s, 3H), 1.81 (s, 1H), 1.54 - 1.13 (m, 4H). ^{19}F-NMR (282 MHz, $CDCl_3$) δ = -118.74 (s, CF).

[0767] HRMS (IE) m/z calculated $C_{24}H_{26}NO_4SF$ [M^+]: 443.1567, found: 443.1574.

[0768] HPLC (99.6%): Rt 24.69 min

Example C45: Benzyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-6-methyl-2-(trifluoromethyl)-1,4-dihydropyridine-3-carboxylate

[0769] Method C using trifluoroacetic acid (1.5 eq) in methanol afforded the title compound as a yellow solid (0.015 g, 27%).

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.97 - 7.90 (m, 1H), 7.85 - 7.77 (m, 1H), 7.35 - 7.29 (m, 2H), 7.29 - 7.22 (m, 3H), 7.16 - 7.07 (m, 3H), 6.18 (s, 1H), 5.53 (s, 1H), 5.07 (q, *J* = 12.2 Hz, 2H), 2.42 (s, 3H), 2.10 (s, 3H). ^{19}F-NMR (282 MHz, $CDCl_3$) δ = -63.64 (s, CF_3).

HRMS (IE) m/z calculated $C_{25}H_{20}NO_3SF_3$ [M^+]: 471.1116, found: 471.1117.

HPLC (99.3%): Rt 12.46 min

Example C46: Pyridin-4-ylmethyl 5-acetyl-4-(5-fluorobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

[0770] Yellow solid (0.091 g, 55%).

[0771] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.50 - 8.42 (m, 2H), 7.76 - 7.63 (m, 2H), 7.21 (s, 1H), 7.04 (td, *J* = 8.7, 2.5 Hz, 1H), 6.96 (d, *J* = 5.2 Hz, 2H), 6.13 (s, 1H), 5.45 (s, 1H), 5.11 (q, *J* = 13.7 Hz, 2H), 2.36 (s, 3H), 2.35 (s, 3H), 2.17 (s, 3H). ^{19}F-NMR (282 MHz, $CDCl_3$) δ = -118.54 (s, CF).

[0772] HRMS (IE) m/z calculated $C_{24}H_{21}N_2O_3SF$ [M^+]: 436.1257, found: 436.1255.

[0773] HPLC (99.5%): Rt 26.10 min.

Example C47: 4-Fluorobenzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[0774] Yellow solid (0.050 g, 43%).

[0775] ^{1}H-NMR (300 MHz, $CDCl_3$) **5** = 8.49 (d, *J* = 4.5 Hz, 1H), 8.28 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.21 - 7.07 (m, 4H), 6.95 (t, *J* = 8.6 Hz, 2H), 6.06 (s, 1H), 5.43 (s, 1H), 5.11 - 4.93 (m, 2H), 2.37 (s, 3H), 2.33 (s, 3H), 2.14 (s, 3H). ^{19}F-NMR (282 MHz, $CDCl_3$) δ = -113.87 (s, CF).

[0776] HRMS (IE) m/z calculated $C_{24}H_{21}N_2O_3SF$ [M^+]: 436.1257, found: 436.1259.

[0777] HPLC (98.5%): Rt 20.40 min.

Example C48: Pyridin-3-ylmethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

[0778] Method C using ammonium acetate (1.5 eq) in methanol afforded the title compound as a yellow solid (0.025 g, 15%).

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.50 (d, *J* = 11.7 Hz, 2H), 8.01 - 7.96 (m, 1H), 7.85 - 7.66 (m, 1H), 7.40 (d, *J* = 7.9 Hz, 1H), 7.32 - 7.21 (m, 2H), 7.17 (t, *J* = 6.5 Hz, 1H), 7.10 (s, 1H), 6.14 (s, 1H), 5.46 (s, 1H), 5.08 (d, *J* = 3.1 Hz, 2H), 2.34 (s, 3H), 2.30 (s, 3H), 2.12 (s, 3H).

HRMS (IE) m/z calculated $C_{24}H_{22}N_2O_3S$ [M^+]: 418.1351, found: 418.1346.

HPLC (98.0%): Rt 24.79 min.

Example C51: 1,1'-(4-(benzo[b]thiophen-3-yl)-2-benzyl-6-methyl-1,4-dihydropyridine-3,5-diyl)bis(ethan-1-one)

[0779] Yield: 8 % (18 mg, yellow solid).

[0780] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.12 (d, *J* = 7.8 Hz, 1H), 7.80 (d, *J* = 8.5 Hz, 1H), 7.45-7.28 (m, 5H), 7.32 - 7.19 (m, 2H), 7.09 (s, 1H), 5.85 (s, 1H), 5.66 (s, 1H), 4.15 (dd, *J* = 16.5 Hz, *J* = 41.8 Hz, 1H), 2.26 (s, 3H), 2.24 (s, 3H), 2.17 (s, 3H).

[0781] HRMS (IE) m/z calculated $C_{25}H_{23}NO_2S$ [M^+]: 401.1450, found: 401.1442

Example C52: 1-(5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3-yl)-2-phenylethan-1-one

[0782] Light-yellow solid (35 mg, 15%).
[0783] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.12 (d, *J* = 8.1 Hz, 1H), 7.80 (d, *J* = 7.9 Hz, 1H), 7.47-7.25 (m, 5H), 7.22 (d, *J* = 8.3 Hz, 2H), 7.09 (s, 1H), 5.85 (s, 1H), 5.66 (s, 1H), 4.15 (dd, *J* = 94.6, 16.2 Hz, 2H), 2.26 (s, 3H), 2.24 (s, 3H), 2.17 (s, 3H).
[0784] HRMS (IE) m/z calculated $C_{25}H_{23}NO_2S$ [M$^+$]: 401.1450, found: 401.1437.

Example C53: Methyl 5-acetyl-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-2-(trifluoromethyl)-1,4-dihydropyridine-3-carboxylate

[0785] Method C using 1.5 eq of TFA yielded the title compound as a yellow solid (30 mg, 26%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.56 (bs, 1H), 8.36 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.36 (dd, *J* = 8.2, 4.5 Hz, 1H), 7.23 (s, 1H), 6.52 (bs, 1H), 5.49 (s, 1H), 3.66 (s, 3H), 2.44 (s, 3H), 2.16 (s, 3H). ^{19}F-NMR (282 MHz, $CDCl_3$) δ = -63.72 (CF_3).
HRMS (IE) m/z calculated $C_{18}H_{15}N_2O_3SF_3$ [M$^+$]: 396.0755, found: 396.0768.

Example C54: 1-(2-methyl-5-(piperidine-1-carbonyl)-4-(thieno[2,3-b]pyridin-3-yl)-6-(trifluoromethyl)-1,4-dihydropyridin-3-yl)ethan-1-one

[0786] Method C using 1.5 eq of TFA yielded the title compound as a yellow solid (10 mg, 15%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.60 (dd, *J* = 4.6, 1.6 Hz, 1H), 8.13 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.42 - 7.31 (m, 2H), 5.65 (s, 1H), 5.47 (s, 1H), 3.35 - 3.14 (m, 2H), 2.80 - 2.65 (m, 1H), 2.41 (s, 3H), 2.26 - 2.12 (m, 1H), 1.93 (s, 3H), 1.39 - 1.22 (m, 2H), 1.23 - 1.04 (m, 2H), 1.06 - 0.82 (m, 2H). ^{19}F-NMR (282 MHz, $CDCl_3$) δ = -67.14 (CF_3).
HRMS (IE) m/z calculated $C_{22}H_{22}N_3O_2SF_3$ [M$^+$]: 449.1385, found: 449.1378.

Example C55: 4-(((5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carbonyl)oxy)methyl)benzoic acid

[0787] Method C gave 4-(tert-butoxycarbonyl)benzyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate (yellow solid, 30 mg, 66%). ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.00 (d, *J* = 8.1 Hz, 1H), 7.88 (d, *J* = 8.6 Hz, 2H), 7.79 (d, *J* = 8.1 Hz, 1H), 7.32 - 7.22 (m, 3H), 7.19 (d, *J* = 7.9 Hz, 2H), 5.86 (s, 1H), 5.49 (s, 1H), 5.11 (s, 2H), 2.37 (s, 3H), 2.31 (s, 3H), 2.13 (s, 3H), 1.60 (s, 9H).
[0788] Hydrolysis of the ester: A mixture of 4-(tert-butoxycarbonyl)benzyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate (0.05 g, 0.09 mmol) in dichloromethane (3 mL) was stirred at 0 °C. Trifluoroacetic acid (0,5 mL) in dichloromethane (2 mL) was dropwise added at the same temperature during 60 min. The mixture was allowed to warm up to RT and the solvent was removed under reduced pressure. The residue was purified by column chromatography (5% DCM in methanol) affording a yellow solid (0.012 g, 27%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 17.14 (s, 1H), 9.14 (s, 1H), 8.02 (dd, *J* = 4.8, 3.0 Hz, 1H), 7.89 (dd, *J* = 6.2, 3.0 Hz, 1H), 7.81 (d, *J* = 7.9 Hz, 2H), 7.30 - 7.24 (m, 2H), 7.20 (s, 1H), 7.12 (d, *J* = 7.9 Hz, 2H), 5.46 (s, 1H), 5.05 (s, 2H), 2.31 (s, 3H), 2.27 (s, 3H), 2.11 (s, 3H).
HRMS (IE) m/z calculated $C_{26}H_{23}NO_5SNa$ [M^{+Na}]: 484.1189, found: 484.1188.

Example C56: Benzyl 5-acetyl-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-2-(trifluoromethyl)-1,4-dihydropyridine-3-carboxylate

[0789] Method C using 1.5 eq of TFA in dioxane yielded the title compound as a yellow solid (35 mg, 12%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.51 (s, 1H), 8.23 (d, *J* = 8.1 Hz, 1H), 7.32 - 7.07 (m, 7H), 6.45 (s, 1H), 5.49 (s, 1H), 5.09 (d, *J* = 2.6 Hz, 2H), 2.43 (s, 3H), 2.14 (s, 3H). ^{19}F-NMR (282 MHz, $CDCl_3$) δ = -63.44 (CF_3).
HRMS (IE) m/z calculated $C_{24}H_{19}N_2O_3SF_3$ [M$^+$]: 472.1068, found: 472.1067.

Example C57: Pyridin-3-ylmethyl 5-acetyl-4-(5-fluorobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

[0790] Method C yielded the title compound as a yellow solid (60 mg, 50%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.52 (d, *J* = 4.3 Hz, 1H), 8.48 (s, 1H), 7.72 - 7.63 (m, 2H), 7.46 (d, *J* = 7.8 Hz, 1H), 7.24 - 7.18 (m, 1H), 7.17 (s, 1H), 7.04 (td, *J* = 8.7, 2.5 Hz, 1H), 6.27 (s, 1H), 5.39 (s, 1H), 5.11 (s, 2H), 2.34 (s, 3H), 2.30 (s, 3H), 2.14 (s, 3H). ^{19}F-NMR (282 MHz, $CDCl_3$) δ = -118.51 (q, *J* = 9.2 Hz, CF).
HRMS (IE) m/z calculated $C_{24}H_{21}N_2O_3SF$ [M$^+$]: 436.1257, found: 436.1252

Example C58: Pyridin-3-ylmethyl 5-acetyl-4-(7-bromobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

[0791] Method C yielded the title compound as a yellow solid (68 mg, 49%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.52 (s, 2H), 7.98 (d, *J* = 7.9 Hz, 1H), 7.44 (d, *J* = 7.5 Hz, 1H), 7.36 (d, *J* = 7.1 Hz, 1H), 7.23 - 7.10 (m, 3H), 5.93 (s, 1H), 5.41 (s, 1H), 5.08 (q, *J* = 12.8 Hz, 2H), 2.36 (s, 3H), 2.32 (s, 3H), 2.13 (s, 3H).
HRMS (IE) m/z calculated $C_{24}H_{21}N_2O_3SBr$ [M^+]: 496.0456, found: 496.0462.

Example C59: Pyridin-3-ylmethyl 5-acetyl-4-(7-cyanobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

[0792] Method C yielded the title compound as a yellow solid (30 mg, 31%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.52 (d, *J* = 15.9 Hz, 2H), 8.29 (d, *J* = 8.2 Hz, 1H), 7.64 (d, *J* = 8.2 Hz, 1H), 7.43 - 7.29 (m, 2H), 7.25 - 7.14 (m, 2H), 6.00 (s, 1H), 5.48 (s, 1H), 5.07 (q, *J* = 13.7, 13.0 Hz, 2H), 2.38 (s, 3H), 2.36 (s, 3H), 2.15 (s, 3H).
HRMS (IE) m/z calculated $C_{25}H_{21}N_3O_3S$ [M^+]: 443.1304, found: 443.1288.

Example C60: Pyridin-3-ylmethyl 5-acetyl-4-(5-chlorobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

[0793] Method C yielded the title compound as a yellow solid (68 mg, 35%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.52 (s, 2H), 8.04 (s, 1H), 7.69 (d, *J* = 8.6 Hz, 1H), 7.49 (d, *J* = 7.8 Hz, 1H), 7.29-7.19 (m, 2H), 7.15 (s, 1H), 6.00 (s, 1H), 5.41 (s, 1H), 5.13 (s, 2H), 2.36 (s, 3H), 2.32 (s, 3H), 2.14 (s,3H).
HRMS (IE) m/z calculated $C_{24}H_{21}N_2O_3SCl$ [M^+]: 452.0961, found: 452.0959.

Example C61: Pyridin-3-ylmethyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[0794] Method C yielded the title compound as a yellow solid (35 mg, 34%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.62 - 8.40 (m, 3H), 8.29 (d, *J* = 8.0 Hz, 1H), 7.40 (d, *J* = 8.0 Hz, 1H), 7.23 - 7.14 (m, 3H), 6.05 (s, 1H), 5.43 (s, 1H), 5.09 (q, *J* = 12.6 Hz, 2H), 2.38 (s, 3H), 2.35 (s, 3H), 2.15 (s, 3H).
HRMS (IE) m/z calculated $C_{23}H_{21}N_3O_3S$ [M^+]: 419.1304, found: 419.1306.

Example C62: Pyridin-4-ylmethyl 5-acetyl-4-(5-chlorobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

[0795] Method C yielded the title compound as a yellow solid (35 mg, 48%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.46 (d, *J* = 4.7 Hz, 2H), 8.04 (s, 1H), 7.70 (d, *J* = 8.5 Hz, 1H), 7.23 - 7.16 (m, 2H), 6.99 (d, *J* = 5.0 Hz, 2H), 6.00 (s, 1H), 5.46 (s, 1H), 5.22 - 5.03 (m, 2H), 2.38 (s, 3H), 2.35 (s, 3H), 2.17 (s, 3H).
HRMS (IE) m/z calculated $C_{24}H_{21}N_2O_3SCl$ [M^+]: 452.0961, found: 452.0954.

Example C63: 4-(cyclopropylcarbamoyl)benzyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

[0796] Method C yielded the title compound as a yellow solid (30 mg, 13%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.00 (dd, *J* = 6.9, 2.4 Hz, 1H), 7.84 - 7.75 (m, 1H), 7.61 (d, *J* = 8.2 Hz, 2H), 7.34 - 7.24 (m, 1H), 7.28 - 7.20 (m, 1H), 7.18 (d, *J* = 8.2 Hz, 2H), 7.10 (s, 1H), 6.18 (bs, 1H), 5.87 (bs, 1H), 5.49 (s, 1H), 5.10 (s, 2H), 2.90 (dt, *J* = 6.9, 3.6 Hz, 1H), 2.37 (s, 3H), 2.31 (s, 3H), 2.13 (s, 3H), 0.93 - 0.82 (m, 2H), 0.67 - 0.57 (m, 2H).
HRMS (IE) m/z calculated $C_{29}H_{29}N_2O_4S$ [M^{+1}]: 501.1843, found: 501.1841.

Example C64: Pyridin-4-ylmethyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4dihydropyridine-3-carboxylate

[0797] Method C yielded the title compound as a yellow solid (28 mg, 40%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.51 - 8.41 (m, 3H), 8.37 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.22 - 7.15 (m, 2H), 6.96 (d, *J* = 5.5 Hz, 2H), 5.49 (s, 1H), 5.28 (s, 1H), 5.04 (q, *J* = 15.0 Hz, 2H), 2.35 (s, 6H), 2.18 (s, 3H).
HRMS (IE) m/z calculated $C_{23}H_{21}N_3O_3S$ [M^+]: 419.1304, found: 419.1304.

Example C65: 4-bromobenzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[0798] Method C yielded the title compound as a yellow solid (131 mg, 72%).

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.50 (d, *J* = 4.7 Hz, 1H), 8.34 (s, 1H), 7.38 (d, *J* = 8.0 Hz, 2H), 7.18 (s, 2H), 6.99 (d, *J* = 8.0 Hz, 2H), 6.00 (s, 1H), 5.43 (s, 1H), 4.99 (q, *J* = 12.5 Hz, 2H), 2.39 (s, 3H), 2.36 (s, 3H), 2.16 (s, 3H).
HRMS (IE) m/z calculated $C_{24}H_{21}N_2O_3SBr$ [M^+]: 496.0456, found: 496.0441.

Example C66: 3-bromobenzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[0799] Method C yielded the title compound as a yellow solid (115 mg, 54%). ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.50 (dd, *J* = 4.6, 1.5 Hz, 1H), 8.31 (d, *J* = 8.1 Hz, 1H), 7.48 - 7.37 (m, 1H), 7.33 (t, *J* = 1.5 Hz, 1H), 7.23 - 7.01 (m, 4H), 5.97 (s, 1H), 5.44 (s, 1H), 5.02 (q, *J* = 12 Hz, 2H), 2.38 (s,3), 2.36 (s, 3H), 2.15 (s, 3H).
HRMS (IE) m/z calculated $C_{24}H_{21}N_2O_3SBr$ [M^+]: 496.0456, found: 496.0456.

Example C67: 2-bromobenzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[0800] Method C yielded the title compound as a yellow solid (127 mg, 74%). ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.46 (dd, *J* = 4.7, 1.6 Hz, 1H), 8.32 (d, *J* = 8.2 Hz, 1H), 7.57 - 7.48 (m, 1H), 7.23 - 7.05 (m, 5H), 6.04 (s, 1H), 5.47 (s, 1H), 5.14 (q, *J* = 15 Hz, 2H), 2.39 (s, 3H), 2.38 (s, 3H), 2.16 (s, 3H).
HRMS (IE) m/z calculated $C_{24}H_{21}N_2O_3SBr$ [M^+]: 496.0456, found: 496.0446.

Example C68: (3-fluoropyridin-4-yl)methyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[0801] Method C yielded the title compound as a yellow solid (30 mg, 47%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.50 (d, *J* = 4.6 Hz, 1H), 8.44 - 8.30 (m, 2H), 8.23 (s, 1H), 7.20 (q, *J* = 4.9 Hz, 2H), 6.88 (t, *J* = 5.4 Hz, 1H), 6.18 (s, 1H), 5.47 (s, 1H), 5.24 - 5.09 (m, 2H), 2.38 (s, 3H), 2.37 (s, 3H), 2.18 (s, 3H). ^{19}F-NMR (282 MHz, $CDCl_3$) δ = - 132.30 (s, CF).
HRMS (IE) m/z calculated $C_{23}H_{20}N_3O_3SF$ [M^+]: 437.1209, found: 437.1215.

Example C69: Pyrimidin-5-ylmethyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[0802] Method C yielded the title compound as a yellow solid (35 mg, 58%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 9.13 (s, 1H), 8.56 (s, 2H), 8.50 (dd, *J* = 4.6, 1.6 Hz, 1H), 8.33 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.23 (dd, *J* = 8.3, 4.6 Hz, 1H), 7.18 (s, 1H), 6.51 (s, 1H), 5.42 (s, 1H), 5.08 (q, *J* = 12 Hz, 2H), 2.36 (s, 3H), 2.33 (s, 3H), 2.16 (s, 3H).
HRMS (IE) m/z calculated $C_{22}H_{20}N_4O_3S$ [M^+]: 420.1256, found: 420.1262.

Example C70: (5-bromopyridin-3-yl)methyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[0803] Method C yielded the title compound as a yellow solid (84 mg, 63%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.58 (s, 1H), 8.50 (d, *J* = 4.3 Hz, 1H), 8.38 (s, 1H), 8.32 (d, *J* = 7.8 Hz, 1H), 7.54 (s, 1 H), 7.22 (dd, *J* = 4.3, 7.8 Hz, 1H), 7.18 (s, 1H), 6.32 (bs, 1H), 5.43 (s, 1H), 5.04 (q, *J* = 13 Hz, 2H), 2.37 (s, 3H), 2.35 (s, 3H), 2.16 (s, 3H).
HRMS (IE) m/z calculated $C_{23}H_{20}N_3O_3SBr$ [M^+]: 497.0409, found: 497.0412.

Example C71: 2-phenylpropan-2-yl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[0804] Method C yielded the title compound as a yellow solid (17 mg, 27%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.60 - 8.47 (m, 1H), 8.36 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.23 - 7.09 (m, 5H), 7.08 - 6.99 (m, 2H), 6.02 (s, 1H), 5.49 (s, 1H), 2.38 (s, 3H), 2.31 (s, 3H), 2.15 (s, 3H), 1.70 (s, 3H), 1.64 (s, 3H).
HRMS (IE) m/z calculated $C_{26}H_{27}N_2O_3S$ [M^{+1}]: 447.1737, found: 447.1736.

Example C72: 3-Cyanobenzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[0805] Method C yielded the title compound as a yellow solid (38 mg, 58%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.55 - 8.45 (m, 1H), 8.34 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.54 (dt, *J* = 7.4, 1.5 Hz, 1H), 7.45 (s, 1H), 7.37 - 7.27 (m, 2H), 7.24 - 7.20 (m, 1H), 7.19 (s, 1H), 6.40 (s, 1H), 5.45 (s, 1H), 5.06 (q, *J* = 12 Hz, 2H), 2.37

(s, 3H), 2.35 (s, 3H), 2.17 (s, 3H).
HRMS (IE) m/z calculated $C_{25}H_{21}N_3O_3S$ [M^+]: 443.1304, found: 443.1310.

Example C73: 4-cyanobenzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[0806] Method C yielded the title compound as a yellow solid (25 mg, 40%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.55 - 8.45 (m, 1H), 8.34 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.54 (dt, *J* = 7.4, 1.5 Hz, 1H), 7.45 (s, 1H), 7.37 - 7.27 (m, 2H), 7.24 - 7.20 (m, 1H), 7.19 (s, 1H), 6.40 (s, 1H), 5.45 (s, 1H), 5.19 - 4.93 (q, *J* = 12 Hz, 2H), 2.37 (s, 3H), 2.35 (s, 3H), 2.17 (s, 3H).
HRMS (IE) m/z calculated $C_{25}H_{21}N_3O_3S$ [M^+]: 443.1304, found: 443.1306.

Example C74: (6-chloropyridin-3-yl)methyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[0807] Method C yielded the title compound as a yellow solid (80 mg, 54%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.57 - 8.46 (m, 1H), 8.37 (d, *J* = 8.2 Hz, 1H), 8.26 (d, *J* = 2.4 Hz, 1H), 7.28 (d, *J* = 2.7 Hz, 1H), 7.22 (d, *J* = 4.6 Hz, 1H), 7.20 - 7.12 (m, 2H), 6.16 (s, 1H), 5.41 (s, 1H), 5.13 - 4.93 (q, *J* = 12 Hz, 2H), 2.38 (s, 3H), 2.36 (s, 3H), 2.17 (s, 3H).
HRMS (IE) m/z calculated $C_{23}H_{20}N_3O_3SCl$ [M^+]: 453.0914, found: 453.0894.

Example C75: 3-morpholinobenzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[0808] Method C yielded the title compound as a yellow solid (50 mg, 69%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.51 - 8.45 (m, 1H), 8.32 (d, *J* = 8.1 Hz, 1H), 7.24 - 7.11 (m, 3H), 6.89 (d, *J* = 8.1 Hz, 1H), 6.74 (d, *J* = 6.9 Hz, 2H), 5.92 (s, 1H), 5.45 (s, 1H), 5.04 (d, *J* = 3.0 Hz, 2H), 3.88 (d, *J* = 4.8 Hz, 4H), 3.09 (t, *J* = 4.8 Hz, 4H), 2.39 (s, 3H), 2.35 (s, 3H), 2.14 (s, 3H).
HRMS (IE) m/z calculated $C_{28}H_{29}N_3O_4S$ [M^+]: 503.1879, found: 503.1878.

Example C76: 4,4-dimethylcyclohexyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[0809] Method C yielded the title compound as a yellow solid (45 mg, 73%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.57 - 8.45 (m, 2H), 7.31 (dd, *J* = 8.1, 4.7 Hz, 1H), 7.20 (s, 1H), 6.90 (s, 1H), 5.46 (s, 1H), 4.71 (tt, *J* = 8.8, 4.1 Hz, 1H), 2.35 (s, 3H), 2.31 (s, 3H), 2.17 (s, 3H), 1.70 - 1.49 (m, 3H), 1.35 - 1.17 (m, 5H), 0.86 (s, 3H), 0.83 (s, 3H).
HRMS (IE) m/z calculated $C_{25}H_{30}N_2O_3S$ [M^+]: 438.1977, found: 438.1967.

Example C77: (2-chloropyridin-4-yl)methyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[0810] Method C yielded the title compound as a yellow solid (117 mg, 75%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.53 (s, 1H), 8.41 (d, *J* = 8.2 Hz, 1H), 8.22 (d, *J* = 5.1 Hz, 1H), 7.22 (s, 2H), 7.01 (d, *J* = 7.4 Hz, 1H), 6.85 (d, *J* = 5.1 Hz, 1H), 6.14 (s, 1H), 5.49 (s, 1H), 5.13 - 4.96 (q, *J* = 12 Hz, 2H), 2.40 (s, 6H), 2.19 (s, 3H).
HRMS (IE) m/z calculated $C_{23}H_{20}N_3O_3SCl$ [M^+]: 453.0914, found: 453.0927.

Example C78: Tetrahydro-2H-pyran-4-yl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[0811] Method C yielded the title compound as a yellow solid (25 mg, 51%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.50 (d, *J* = 8.1 Hz, 2H), 7.33 (dd, *J* = 8.1, 4.7 Hz, 1H), 7.24 - 7.17 (m, 1H), 6.70 (s, 1H), 5.46 (s, 1H), 4.92 (tt, *J* = 8.9, 4.2 Hz, 1H), 3.81 (ddt, *J* = 16.6, 11.5, 4.2 Hz, 2H), 3.46 (ddt, *J* = 12.0, 5.3, 2.9 Hz, 2H), 2.36 (s, 3H), 2.33 (s, 3H), 2.18 (s, 3H), 1.92 - 1.83 (m, 1H), 1.80 - 1.71 (m, 1H), 1.69 - 1.57 (m, 1H), 1.53 - 1.40 (m, 1H).
HRMS (IE) m/z calculated $C_{22}H_{24}N_2O_4S$ [M^+]: 412.1457, found: 412.1457.

Example C79: 4,4-difluorocyclohexyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[0812] Method C yielded the title compound as a yellow solid (45 mg, 83%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.57 - 8.48 (m, 2H), 7.33 (dd, *J* = 7.9, 4.8 Hz, 1H), 7.20 (s, 1H), 6.96 (s, 1H), 5.46 (s, 1H), 4.90 (s, 1H), 2.35 (s, 3H), 2.32 (s, 3H), 2.19 (s, 3H), 1.96 - 1.58 (m, 8H). ^{19}F-NMR (282 MHz, $CDCl_3$) δ = -95.77 (d, *J* = 247.3 Hz CF).
HRMS (IE) m/z calculated $C_{23}H_{24}N_2O_3SF_2$ [M^+]: 446.1476, found: 446.1475.

Example C80: 5-Acetyl-N-benzyl-N,2,6-trimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxamide

[0813] Method C yielded the title compound as a yellow solid (37 mg, 67%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.51 (d, *J* = 4.6 Hz, 1H), 8.16 - 8.06 (m, 1H), 7.25 - 7.15 (m, 5H), 7.08 - 6.98 (m, 2H), 6.12 (s, 1H), 5.37 (s, 1H), 4.65 (d, *J* = 14.1 Hz, 1H), 4.07 (d, *J* = 14.1 Hz, 1H), 2.36 (s, 3H), 2.13 (s, 3H), 1.98 (s, 3H), 1.68 (s, 3H).
HRMS (IE) m/z calculated $C_{25}H_{25}N_3O_2S$ [M^+]: 431.1667, found: 431.1675.

Example C81: Oxetan-3-yl 5-acetyl-4-(7-bromobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate

[0814] Method C yielded the title compound as a yellow solid (5.2 mg, 6%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.12 (d, *J* = 8.0 Hz, 1H), 7.48 (d, *J* = 7.9 Hz, 1H), 7.30 (d, *J* = 7.9 Hz, 1H), 7.18 (s, 1H), 5.73 (s, 1H), 5.45 (s, 1H), 5.40 (q, *J* = 5.9 Hz, 1H), 4.89 - 4.80 (m, 2H), 4.61 - 4.49 (m, 2H), 2.55 (tt, *J* = 8.6, 5.7 Hz, 1H), 2.36 (s, 3H), 2.16 (s, 3H), 1.01 (ddp, *J* = 18.2, 8.6, 4.6 Hz, 2H), 0.69 (dq, *J* = 7.4, 4.6, 4.0 Hz, 2H).
HRMS (IE) m/z calculated $C_{23}H_{22}NO_4SBr$ [M^+]: 487.0453, found: 487.0439.

Example C82: Isopropyl 5-acetyl-4-(7-bromobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate

[0815] Method C yielded the title compound as a yellow solid (21 mg, 14%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.14 (d, *J* = 8.1 Hz, 1H), 7.46 (d, *J* = 7.6 Hz, 1H), 7.30 (s, 1H), 7.24 (s, 1H), 7.15 (s, 1H), 5.68 (s, 1H), 5.44 (s, 1H), 5.03 (p, *J* = 6.2 Hz, 1H), 2.53 (ddd, *J* = 8.8, 5.7, 3.4 Hz, 1H), 2.36 (s, 3H), 2.14 (s, 3H), 1.21 (d, *J* = 6.2 Hz, 3H), 1.12 (d, *J* = 6.2 Hz, 3H), 1.01 - 0.88 (m, 2H), 0.67 (dqd, *J* = 11.1, 5.7, 3.4 Hz, 2H).
HRMS (IE) m/z calculated $C_{23}H_{24}NO_3SBr$ [M^+]: 473.0660, found: 473.0677.

Example C83: Methyl 5-acetyl-4-(7-bromobenzo[b]thiophen-3-yl)-6-methyl-2-(trifluoromethyl)-1,4-dihydropyridine-3-carboxylate

[0816] Method C using 1.5 eq of TFA in MeOH yielded the title compound as a yellow solid (8 mg, 18%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.00 (d, *J* = 8.1 Hz, 1H), 7.51 (d, *J* = 7.5 Hz, 1H), 7.35-7.28 (m, 1H), 7.24 (s, 1H), 6.20 (bs, 1H), 5.47 (s, 1H), 3.65 (s, 3H), 2.44 (s, 3H), 2.12 (s, 3H). ^{19}F-NMR (282 MHz, $CDCl_3$) δ = 63.85 (s, CF_3).
HRMS (IE) m/z calculated $C_{19}H_{15}NO_3SF_3Br$ [M^+]: 472.9908, found: 472.9915.

Example C84: Cyclopropylmethyl 5-acetyl-4-(7-bromobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate

[0817] Method C in dioxane yielded the title compound as a yellow solid (20 mg, 13%). ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.15 (d, *J* = 8.1 Hz, 1H), 7.46 (d, *J* = 7.6 Hz, 1H), 7.29-7.23 (m, 1H), 7.17 (s, 1H), 5.70 (bs, 1H), 5.47 (bs, 1H), 3.95 - 3.86 (m, 2H), 2.59 (tt, *J* = 8.7, 5.7 Hz, 1H), 2.36 (s, 3H), 2.14 (s, 3H), 1.12 - 0.87 (m, 3H), 0.73 - 0.59 (m, 2H), 0.57 - 0.44 (m, 2H), 0.26 - 0.14 (m, 2H).
HRMS (IE) m/z calculated $C_{24}H_{24}NO_3SBr$ [M^+]: 485.0660, found: 485.0676.

Example C85: Methyl 5-acetyl-2-cyclopropyl-6-methyl-4-(7-(2,2,2-trifluoroacetyl) benzo[b]thiophen-3-yl)-1,4-dihydropyridine-3-carboxylate

[0818] Method C yielded the title compound as a yellow solid (42 mg, 44%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.64 (d, *J* = 8.1 Hz, 1H), 8.17 (d, *J* = 7.4 Hz, 1H), 7.62 (t, *J* = 7.8 Hz, 1H), 7.32 (s, 1H), 5.89 (bs, 1H), 5.54 (s, 1H), 3.64 (s, 3H), 2.59 (tt, *J* = 8.7, 5.6 Hz, 1H), 2.36 (s, 3H), 2.14 (s, 3H), 1.06 - 0.85 (m, 2H),

0.81 - 0.58 (m, 2H).
HRMS (IE) m/z calculated $C_{23}H_{20}NO_4SF_3$ [M^+]: 463.1065, found: 463.1054.

Example C86: 2-phenylpropan-2-yl 5-acetyl-4-(7-bromobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

[0819] Method C yielded the title compound as a yellow solid (18 mg, 18%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.06 (d, *J* = 8.1 Hz, 1H), 7.46 (d, *J* = 7.6 Hz, 1H), 7.21 - 7.10 (m, 5H), 7.07 - 6.98 (m, 2H), 5.87 (bs, 1H), 5.49 (s, 1H), 2.36 (s, 3H), 2.28 (s, 3H), 2.14 (s, 3H), 1.72 (s, 3H), 1.64 (s, 3H).
HRMS (ESI) m/z calculated $C_{27}H_{26}NO_3SBr$ [M^+]: 546.0709, found: 546.0711.
HPLC (98.2%): Rt 18.30 min.

Example C87: Methyl 5-acetyl-4-(7-chlorobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate

[0820] Method C yielded the title compound as a yellow solid (80 mg, 69%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.07 - 7.99 (m, 1H), 7.39 - 7.28 (m, 2H), 7.15 (d, *J* = 1.7 Hz, 1H), 5.67 (s, 1H), 5.45 (s, 1H), 3.66 (s, 3H), 2.59 (tt, *J* = 8.4, 5.7 Hz, 1H), 2.35 (s, 3H), 2.13 (s, 3H), 1.04 - 0.90 (m, 2H), 0.66 (dtt, *J* = 9.0, 5.7, 3.4 Hz, 2H).
HRMS (IE) m/z calculated $C_{21}H_{20}NO_3SCl$ [M^+]: 401.0852, found: 401.0855.
HPLC (99.1%): Rt 18.66 min.

Example C88: methyl 5-acetyl-2-cyclopropyl-6-methyl-4-(7-(trifluoromethyl)benzo[b]thiophen-3-yl)-1,4-dihydropyridine-3-carboxylate

[0821] Method C yielded the title compound as a yellow solid (55 mg, 80%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.35 (d, *J* = 8.2 Hz, 1H), 7.62 (d, *J* = 7.5 Hz, 1H), 7.49 (t, *J* = 7.9 Hz, 1H), 7.20 (s, 1H), 5.66 (bs, 1H), 5.51 (s, 1H), 3.65 (s, 3H), 2.59 (h, *J* = 6.9, 6.2 Hz, 1H), 2.36 (s, 3H), 2.13 (s, 3H), 1.09 - 0.84 (m, 2H), 0.7509 - 0.57 (m, 2H). ^{19}F-NMR (282 MHz, $CDCl_3$) δ (ppm): -62.96 (s, CF_3).
HRMS (IE) m/z calculated $C_{22}H_{20}NO_3SF_3$ [M^+]: 435.1116, found: 435.1129.
HPLC (99.4%): Rt 19.68 min.

Example C89: 3-chlorobenzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[0822] Method C yielded the title compound as a yellow solid (78 mg, 53%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.49 (dd, *J* = 4.6, 1.6 Hz, 1H), 8.29 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.28 - 7.23 (m, 1H), 7.22 - 7.13 (m, 4H), 7.01 (dt, *J* = 7.6, 1.6 Hz, 1H), 6.26 (s, 1H), 5.44 (s, 1H), 5.09 - 4.97 (m, 2H), 2.37 (s, 3H), 2.34 (s, 6H), 2.15 (s, 3H).
HRMS (IE) m/z calculated $C_{24}H_{21}N_2O_3SCl$ [M^+]: 452.0961, found: 452.0966.
HPLC (98.6%): Rt 19.83 min.

Example C90: 2-phenylpropan-2-yl 5-acetyl-4-(7-bromobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate

[0823] Method C yielded the title compound as a yellow solid (20 mg, 17%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.05 (d, *J* = 8.0 Hz, 1H), 7.52 - 7.40 (m, 1H), 7.22 - 7.13 (m, 4H), 7.12 (s, 1H), 7.10 - 7.04 (m, 2H), 5.67 (bs, 1H), 5.50 (s, 1H), 2.63 - 2.47 (m, 1H), 2.35 (s, 3H), 2.13 (s, 3H), 1.72 (s, 3H), 1.67 (s, 3H), 1.03 - 0.77 (m, 2H), 0.76 - 0.57 (m, 2H).
HRMS (ESI) m/z calculated $C_{29}H_{28}NO_3SBrNa$ [M^{+Na}]: 572.0865, found: 572.0865.
HPLC (98.82%): Rt 17.16 min.

Example C91: Cyclohexyl 5-acetyl-2-cyclopropyl-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[0824] Method C yielded the title compound as a yellow solid (70 mg, 79%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.52 (s, 1H), 8.46 (d, *J* = 8.1 Hz, 1H), 7.31 (dd, *J* = 8.1, 4.7 Hz, 1H), 7.13 (s, 1H), 5.69 (bs, 1H), 5.47 (s, 1H), 4.83 - 4.71 (m, 1H), 2.64 - 2.47 (m, 1H), 2.36 (s, 3H), 2.16 (s, 3H), 1.90 - 1.70 (m, 2H), 1.68 - 1.50 (m, 4H), 1.35 - 1.19 (m, 4H), 1.08 - 0.87 (m, 2H), 0.78 - 0.58 (m, 2H).

HRMS (IE) m/z calculated $C_{25}H_{28}N_2O_3S$ [M^+]: 436.1821, found: 436.1841.
HPLC (99.3%): Rt 18.47 min.

Example C92: 2-phenylpropan-2-yl 5-acetyl-2-cyclopropyl-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[0825] Method C yielded the title compound as a yellow solid (15 mg, 16 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.50 (dd, *J* = 4.6, 1.6 Hz, 1H), 8.33 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.23 - 7.12 (m, 4H), 7.11 (s, 1H), 7.12 - 7.02 (m, 2H), 5.71 (s, 1H), 5.49 (s, 1H), 2.65 - 2.49 (m, 1H), 2.36 (s, 3H), 2.13 (s, 3H), 1.70 (s, 3H), 1.67 (s, 3H), 1.03 - 0.83 (m, 2H), 0.76 - 0.58 (m, 2H).
HRMS (ESI) m/z calculated $C_{28}H_{29}N_2O_3S$ [M^{+1}]: 473.1893, found: 473.1891.
HPLC (95.7%): Rt 25.13 min.

Example C93: 1-(4-(7-Bromobenzo[b]thiophen-3-yl)-5-(cyclopropanecarbonyl)-6-cyclopropyl-2-methyl-1,4-dihydropyridin-3-yl)ethan-1-one

[0826] Method C yielded the title compound as a yellow solid (80 mg, 56 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.09 (d, *J* = 8.1 Hz, 1H), 7.46 (d, *J* = 7.6 Hz, 1H), 7.28 (d, *J* = 8.1 Hz, 1H), 7.10 (s, 1H), 5.84 (bs, 1H), 5.50 (s, 1H), 2.41 (s, 3H), 2.38 - 2.27 (m, 1H), 2.20 - 2.01 (m, 4H), 1.41 - 1.22 (m, 1H), 1.20 - 1.06 (m, 1H), 1.07 - 0.90 (m, 3H), 0.84 - 0.65 (m, 3H).
HRMS (IE) m/z calculated $C_{23}H_{22}NO_2SBr$ [M^+]: 455.0555, found: 455.0540.
HPLC (99.1%): Rt 22.48 min

Example C94: 3-chlorobenzyl 5-acetyl-2-cyclopropyl-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[0827] Method C yielded the title compound as a yellow solid (16 mg, 13 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.53 (d, *J* = 4.6 Hz, 1H), 8.32 (d, *J* = 8.1 Hz, 1H), 7.32 - 7.28 (m, 1H), 7.25 - 7.18 (m, 3H), 7.16 (s, 1H), 7.07 (d, *J* = 7.4 Hz, 1H), 5.79 (bs, 1H), 5.50 (s, 1H), 5.16 - 5.04 (m, 2H), 2.73 - 2.51 (m, 1H), 2.39 (s, 3H), 2.19 (s, 3H), 1.08 - 0.87 (m, 2H), 0.83 - 0.61 (m, 2H).
HRMS (IE) m/z calculated $C_{26}H_{23}N_2O_3SCl$ [M^+]: 478.1118, found: 478.1118.
HPLC (96.7%): Rt 19.79 min.

Example C95: 2-(4-fluorophenyl)propan-2-yl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[0828] Method C yielded the title compound as a yellow solid (10 mg, 7 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm): 8.52 (d, *J* = 3.9 Hz, 1H), 8.35 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.21 (dd, *J* = 8.2, 4.6 Hz, 1H), 7.16 (s, 1H), 7.00 - 6.91 (m, 2H), 6.87 - 6.75 (m, 2H), 5.90 (s, 1H), 5.48 (s, 1H), 2.38 (s, 3H), 2.30 (s, 3H), 2.15 (s, 3H), 1.68 (s, 3H), 1.61 (s, 3H). ^{19}F-NMR (282 MHz, $CDCl_3$) δ (ppm): -116.44 (CF).
HRMS (IE) m/z calculated $C_{26}H_{25}N_2O_3SF$ [M^+]: 464.1570, found: 464.1570.
HPLC (98.2%): Rt 19.52 min.

Example C96: 2-(4-fluorophenyl)propan-2-yl 5-acetyl-4-(7-bromobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate

[0829] Method C yielded the title compound as a yellow solid (30 mg, 17 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm): 8.03 (d, *J* = 8.1 Hz, 1H), 7.47 (d, *J* = 7.6 Hz, 1H), 7.17 (t, *J* = 7.9 Hz, 1H), 7.12 (s, 1H), 6.98 (dd, *J* = 8.7, 5.4 Hz, 2H), 6.80 (t, *J* = 8.7 Hz, 2H), 5.61 (s, 1H), 5.48 (s, 1H), 2.62 - 2.45 (m, 1H), 2.35 (s, 3H), 2.13 (s, 3H), 1.69 (s, 3H), 1.65 (s, 3H), 1.04 - 0.82 (m, 2H), 0.76 - 0.59 (m, 2H). ^{19}F-NMR (282 MHz, $CDCl_3$) δ (ppm): -116.65 (CF).
HRMS (IE) m/z calculated $C_{29}H_{27}N_2O_3SBrFNa$ [M^{+Na}]: 590.0771, found: 590.0772.
HPLC (98.0%): Rt 18.52 min.

Example C97: 2-(4-fluorophenyl)propan-2-yl 5-acetyl-2-cyclopropyl-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[0830] Method C yielded the title compound as a yellow solid (38 mg, 24 %).

^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm): 8.55 - 8.44 (m, 1H), 8.33 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.19 (dd, *J* = 8.2, 4.6 Hz, 1H), 7.10 (s, 1H), 7.03 - 6.93 (m, 2H), 6.79 (t, *J* = 8.7 Hz, 2H), 5.97 (bs, 1H), 5.46 (s, 1H), 2.60 - 2.43 (m, 1H), 2.34 (s, 3H), 2.12 (s, 3H), 1.66 (s, 3H), 1.63 (s, 3H), 1.00 - 0.80 (m, 2H), 0.78 - 0.56 (m, 2H). ^{19}F-NMR (282 MHz, $CDCl_3$) δ (ppm): -116.53 (CF).
HRMS (IE) m/z calculated $C_{28}H_{28}N_2O_3SF$ [M^+]: 491.1799, found: 491.1800.
HPLC (98.9%): Rt 19.26 min.

Example C98: Methyl 5-acetyl-2-cyclopropyl-4-(7-fluorobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

[0831] Method C yielded the title compound as a yellow solid (94 mg, 71 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm): 7.89 (d, *J* = 8.2 Hz, 1H), 7.35 (td, *J* = 8.0, 5.2 Hz, 1H), 7.13 (s, 1H), 7.01 (dd, *J* = 9.7, 8.0 Hz, 1H), 5.63 (bs, 1H), 5.47 (s, 1H), 3.67 (s, 3H), 2.60 (tt, *J* = 8.7, 5.7 Hz, 1H), 2.36 (s, 3H), 2.14 (s, 3H), 1.08 - 0.85 (m, 2H), 0.74 - 0.56 (m, 2H). ^{19}F-NMR (282 MHz, $CDCl_3$) δ (ppm): -116.08 (CF).
HRMS (IE) m/z calculated $C_{21}H_{20}NO_3SF$ [M^+]: 385.1148, found: 385.1132.
HPLC (99.3%): Rt 22.58 min.

Example C99: Cyclopropylmethyl 5-acetyl-2-cyclopropyl-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[0832] Method C in dioxane yielded the title compound as a yellow solid (12 mg, 26 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm): 8.53 - 8.50 (m, 1H), 8.46 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.29 (dd, *J* = 8.2, 4.6 Hz, 1H), 7.17 (s, 1H), 5.71 (bs, 1H), 5.48 (s, 1H), 3.90 (dd, *J* = 7.3, 2.7 Hz, 2H), 2.60 (tt, *J* = 8.6, 5.7 Hz, 1H), 2.37 (s, 3H), 2.16 (s, 3H), 1.05 - 0.91 (m, 3H), 0.72 - 0.61 (m, 2H), 0.55 - 0.43 (m, 2H), 0.27 - 0.12 (m, 2H).
HRMS (IE) m/z calculated $C_{23}H_{24}N_2O_3S$ [M^+]: 408.1508, found: 408.1509.
HPLC (99.7%): Rt 30.16 min.

Example C100: Cyclopentyl 5-acetyl-2-cyclopropyl-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[0833] Method C in dioxane yielded the title compound as a yellow solid (27 mg, 14 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm): 8.52 (dd, *J* = 4.6, 1.5 Hz, 1H), 8.46 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.30 (dd, *J* = 8.2, 4.6 Hz, 1H), 7.12 (s, 1H), 5.71 (bs, 1H), 5.45 (s, 1H), 5.24 - 5.11 (m, 1H), 2.62 - 2.45 (m, 1H), 2.36 (s, 3H), 2.16 (s, 3H), 1.92 - 1.72 (m, 2H), 1.64 - 1.44 (m, 6H), 1.07 - 0.85 (m, 2H), 0.76 - 0.56 (m, 2H).
HRMS (IE) m/z calculated $C_{24}H_{26}N_2O_3S$ [M^+]: 422.1664, found: 422.1662.
HPLC (99.7%): Rt 30.24 min.

Example C101: Cyclopropylmethyl 5-acetyl-4-(7-cyanobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate

[0834] Method C in dioxane yielded the title compound as a yellow solid (9 mg, 26 %). ^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm): 8.56 - 8.41 (m, 1H), 7.66 (d, *J* = 7.5 Hz, 1H), 7.46 (t, *J* = 7.5 Hz, 1H), 7.24 (s, 1H), 5.71 (bs, 1H), 5.53 (s, 1H), 3.98 - 3.77 (m, 2H), 2.70 - 2.52 (m, 1H), 2.37 (s, 3H), 2.16 (s, 3H), 1.09 - 0.92 (m, 3H), 0.77 - 0.58 (m, 2H), 0.53 - 0.39 (m, 2H), 0.27 - 0.10 (m, 2H).
HRMS (IE) m/z calculated $C_{25}H_{24}N_2O_3S$ [M^+]: 432.1508, found: 432.1516.
HPLC (97.8%): Rt 22.16 min.

Example C102: Methyl 5-acetyl-4-(7-bromobenzo[b]thiophen-3-yl)-2-cyclobutyl-6-methyl-1,4-dihydropyridine-3-carboxylate

[0835] Method C yielded the title compound as a yellow solid (41 mg, 29 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm): 8.09 (d, *J* = 8.8 Hz, 1H), 7.47 (d, *J* = 7.5 Hz, 1H), 7.29 (d, *J* = 8.0 Hz, 1H), 7.18 (s, 1H), 6.10 (bs, 1H), 5.41 (s, 1H), 3.63 (s, 3H), 2.42 (s, 3H), 2.33 - 2.17 (m, 2H), 2.14 (s, 3H), 2.06 - 1.78 (m, 5H).
HRMS (IE) m/z calculated $C_{22}H_{22}NO_3SBr$ [M^+]: 459.0504, found: 459.0505.
HPLC (95.2%): Rt 18.21 min.

Example C103: Dimethyl 4-(7-cyanobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

[0836] Method C yielded the title compound as a yellow solid (80 mg, 65 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm): 8.36 (d, *J* = 9.2 Hz, 1H), 7.66 (d, *J* = 7.3 Hz, 1H), 7.46 (dd, *J* = 9.2, 7.3 Hz, 1H), 7.24 (s, 1H), 5.64 (bs, 1H), 5.47 (s, 1H), 3.56 (s, 3H), 3.54 (s, 3H), 2.77 - 2.67 (m, 1H), 2.34 (s, 3H), 1.07 - 0.96 (m, 2H), 0.77 - 0.65 (m, 2H).
HRMS (IE) m/z calculated $C_{22}H_{20}N_2O_4S$ [M^+]: 408.1144, found: 408.1153.
HPLC (99.2%): Rt 12.64 min.

Example C104: Methyl 5-cyano-4-(7-cyanobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate

[0837] Method C yielded the title compound as a yellow solid (40 mg, 48 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm): 8.24 (d, *J* = 9.1 Hz, 1H), 7.71 (d, *J* = 7.3 Hz, 1H), 7.56 - 7.44 (m, 1H), 7.23 (s, 1H), 5.73 (bs, 1H), 5.14 (s, 1H), 3.55 (s, 3H), 2.87 - 2.71 (m, 1H), 2.09 (s, 3H), 1.13 - 0.99 (m, 2H), 0.82 - 0.65 (m, 2H).
HRMS (IE) m/z calculated $C_{21}H_{17}N_3O_2S$ [M^+]: 375.1041, found: 375.1046.
HPLC (99.0%): Rt 21.27 min.

Example C105: Methyl 5-acetyl-4-(7-bromobenzo[b]thiophen-3-yl)-2-cyclopentyl-6-methyl-1,4-dihydropyridine-3-carboxylate

[0838] Method C yielded the title compound as a yellow solid (59 mg, 40 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm): 8.06 (d, *J* = 8.0 Hz, 1H), 7.47 (d, *J* = 7.4 Hz, 1H), 7.29 (d, *J* = 8.0 Hz, 1H), 7.19 (s, 1H), 5.88 (bs, 1H), 5.45 (s, 1H), 4.26 - 4.02 (m, 1H), 3.63 (s, 3H), 2.38 (s, 3H), 2.15 (s, 3H), 2.04 - 1.90 (m, 2H), 1.78 - 1.69 (m, 4H), 1.53 - 1.38 (m, 2H).
HRMS (IE) m/z calculated $C_{23}H_{24}NO_3SBr$ [M^+]: 473.0660, found: 473.0647.
HPLC (97.4%): Rt 12.81 min.

Example C106: Methyl 5-acetyl-4-(7-bromobenzo[b]thiophen-3-yl)-2-cyclohexyl-6-methyl-1,4-dihydropyridine-3-carboxylate

[0839] Method C yielded the title compound as a yellow solid (89 mg, 59 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm): 8.05 (d, *J* = 8.8 Hz, 1H), 7.46 (d, *J* = 7.5 Hz, 1H), 7.28 (d, *J* = 7.5 Hz, 1H), 7.18 (s, 1H), 6.00 (bs, 1H), 5.44 (s, 1H), 3.80 - 3.66 (m, 1H), 3.62 (s, 3H), 2.38 (s, 3H), 2.15 (s, 3H), 1.92 - 1.69 (m, 5H), 1.44 - 1.20 (m, 5H). HRMS (IE) m/z calculated $C_{24}H_{26}NO_3SBr$ [M^+]: 487.0817, found: 487.0801.
HPLC (96.7%): Rt 11.94 min.

Example C107: Methyl 5-cyano-4-(7-cyanobenzo[b]thiophen-3-yl)-2,6-dicyclopropyl-1,4-dihydropyridine-3-carboxylate

[0840] Method C yielded the title compound as a yellow solid (15 mg, 13 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm): 8.25 (dd, *J* = 8.2, 0.9 Hz, 1H), 7.71 (d, *J* = 7.3 Hz, 1H), 7.55 - 7.45 (m, 1H), 7.20 (s, 1H), 5.57 (bs, 1H), 5.14 (s, 1H), 3.56 (s, 3H), 2.87 - 2.70 (m, 1H), 1.93 - 1.78 (m, 1H), 1.16 - 0.83 (m, 5H), 0.80 - 0.63 (m, 3H).
HRMS (IE) m/z calculated $C_{23}H_{19}N_3O_2S$ [M^+]: 401.1198, found: 401.1199.
HPLC (96.5%): Rt 15.42 min.

Example C108: 3-((4-methylpiperazin-1-yl)methyl)benzyl 5-acetyl-4-(7-bromobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

[0841] Method C yielded the title compound as a yellow solid (33 mg, 18 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm): 7.98 (d, *J* = 8.2 Hz, 1H), 7.43 (d, *J* = 7.6 Hz, 1H), 7.27 - 7.04 (m, 6H), 5.80 (bs, 1H), 5.44 (s, 1H), 5.07 (s, 2H), 3.44 (s, 2H), 2.48 - 2.41 (m, 4H), 2.37 (s, 3H), 2.32 (s, 3H), 2.28 (s, 3H), 2.12 (s, 3H), 1.73 - 1.60 (m, 4H). HRMS (IE) m/z calculated $C_{31}H_{34}N_3O_3SBr$ [M^+]: 607.1504, found: 607.1491.
HPLC (98.4%): Rt 9.94 min.

Example C109: 3-(cyclopropylmethyl) 5-methyl 4-(7-cyanobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

[0842] The title compound was prepared using a variation of Method C by heating in dioxane in a sealed tube at 130 °C overnight yielding a yellow solid (35 mg, 28 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm): 8.40 (d, *J* = 8.2 Hz, 1H), 7.65 (d, *J* = 7.0 Hz, 1H), 7.44 (t, *J* = 7.7 Hz, 1H), 7.26 (s, 1H), 5.61 (bs, 1H), 5.49 (s, 1H), 3.84 - 3.73 (m, 2H), 3.55 (s, 3H), 2.81 - 2.65 (m, 1H), 2.34 (s, 3H), 1.02 (dd, *J* = 8.9, 5.5 Hz, 2H), 0.95 - 0.80 (m, 1H), 0.72 (d, *J* = 6.1 Hz, 2H), 0.38 (t, *J* = 9.7 Hz, 2H), 0.06 (s, 2H).
HRMS (IE) m/z calculated $C_{25}H_{24}N_2NaO_4S$ [M^+]: 471.1349, found: 471.1347.

Example C110: 3-(cyclopropylmethyl) 5-methyl 4-(7-cyanobenzo[b]thiophen-3-yl)-2,6-dicyclopropyl-1,4-dihydropyridine-3,5-dicarboxylate

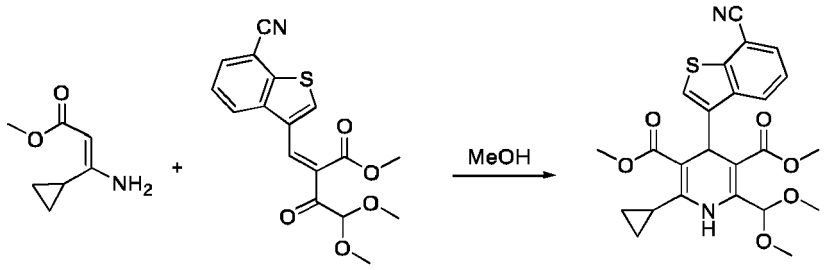
[0843] The title compound was prepared using a variation of Method C by heating in dioxane in a sealed tube at 130 °C overnight yielding a yellow solid (20 mg, 15 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm): 8.41 (d, *J* = 8.3 Hz, 1H), 7.65 (d, *J* = 7.4 Hz, 1H), 7.44 (t, *J* = 7.8 Hz, 1H), 7.23 (s, 1H), 5.56 (bs, 1H), 5.51 (s, 1H), 3.79 (d, *J* = 7.3 Hz, 2H), 3.57 (s, 3H), 2.85 - 2.61 (m, 2H), 1.09 - 0.84 (m, 5H), 0.75 - 0.55 (m, 4H), 0.47 - 0.29 (m, 2H), 0.15 - -0.02 (m, 2H).
HRMS (IE) m/z calculated $C_{27}H_{26}N_2NaO_4S$ [M^{+Na}]: 497.1505, found: 497.1503.

Example C111: Cyclopropylmethyl 5-cyano-4-(7-cyanobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate

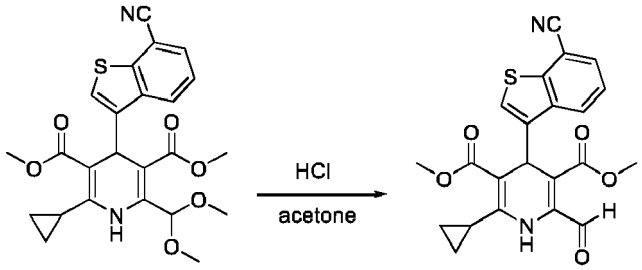
[0844] The title compound was prepared using a variation of Method C by heating the reaction mixture in MeOH in a sealed tube at 130 °C for 7h yielding a yellow solid (8 mg, 7%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm): 8.24 (d, *J* = 8.3 Hz, 1H), 7.70 (d, *J* = 7.4 Hz, 1H), 7.48 (t, *J* = 7.8 Hz, 1H), 7.27 (s, 1H), 5.73 (bs, 1H), 5.19 (s, 1H), 3.75 (d, *J* = 7.3 Hz, 2H), 2.92 - 2.70 (m, 1H), 2.09 (s, 3H), 1.14 - 0.97 (m, 2H), 0.88 - 0.66 (m, 3H), 0.40 - 0.12 (m, 2H), 0.08 - -0.17 (m, 2H)
HRMS (IE) m/z calculated $C_{24}H_{21}N_3NaO_2S$ [M^{+Na}]: 438.1247, found: 438.1245.

Example C112: Dimethyl 2-cyano-4-(7-cyanobenzo[b]thiophen-3-yl)-6-cyclopropyl-1,4-dihydropyridine-3,5-dicarboxylate

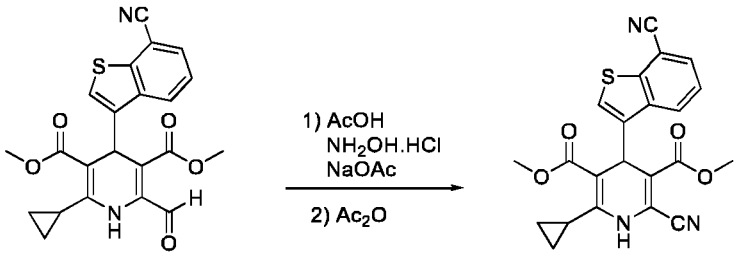
[0845] The title compound was prepared in three steps following Y. Satoh et al., Chem. Pharm. Bull. 1991, 39, 3189-3201.



[0846] In a first step, dimethyl 4-(7-cyanobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-(dimethoxymethyl)-1,4-dihydropyridine-3,5-dicarboxylate was prepared using a variation of Method C by heating the reaction mixture in methanol in a sealed tube at 130 °C for 90 min yielding a yellow solid (130 mg, 48 %).



[0847] In a second step, dimethyl 4-(7-cyanobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-(dimethoxymethyl)-1,4-dihydropyridine-3,5-dicarboxylate (0.100 g, 0.21 mmol) was stirred in acetone (4 mL) and hydrochloride acid 4N (0.53 mL, 2.13 mmol) at room temperature for 60 minutes. The solvent was removed under reduced pressure, and the residue was dissolved in ethyl acetate and washed with toluene, saturated bicarbonate solution and brine. The organic phase was dried (Na_2SO_4), filtered and concentrated yielding dimethyl 4-(7-cyanobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-formyl-1,4-dihydropyridine-3,5-dicarboxylate that was used in the next step without further purification.



[0848] In a third step, a mixture of dimethyl 4-(7-cyanobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-formyl-1,4-dihydropyridine-3,5-dicarboxylate, sodium acetate (0.026 g, 0.32 mmol) and hydroxylamine hydrochloride (0.018 g, 0.25 mmol) in acetic acid (1 mL) was stirred at room temperature for 60 minutes. Acetic anhydride (0.142 mL, 1.48 mmol) was added and stirred at room temperature for 60 minutes and then at 95°C for 120 minutes. The solvent was removed under reduced pressure, and the residue was taken up in ethyl acetate and washed with toluene, saturated bicarbonate solution and brine. The organic phase was dried (Na_2SO_4), filtered and concentrated and the residue purified by column chromatography (4:1 hexane: ethyl acetate) affording the title compound dimethyl 2-cyano-4-(7-cyanobenzo[b]thiophen-3-yl)-6-cyclopropyl-1,4-dihydropyridine-3,5-dicarboxylate as a yellow solid (0.030 g, 34%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm): 8.33 (d, *J* = 8.3 Hz, 1H), 7.72 (d, *J* = 7.3 Hz, 1H), 7.58 - 7.49 (m, 1H), 7.35 (s, 1H), 6.73 (bs, 1H), 5.52 (s, 1H), 3.69 (s, 3H), 3.64 (s, 1H), 3.55 (s, 3H), 3.03 - 2.86 (m, 2H), 2.21 - 2.07 (m, 2H).
HRMS (IE) m/z calculated $C_{22}H_{18}N_3O_4S$ [M^{+1}]: 420.1013, found: 420.1012.

Example C113: Dimethyl 2-cyano-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

[0849] Following the 3-step procedure described above for the synthesis of Example C112, the title compound was obtained as a yellow solid (0.046 g, 41 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm): 8.35 (d, *J* = 8.3 Hz, 1H), 7.71 (d, *J* = 7.3 Hz, 1H), 7.58 - 7.47 (m, 1H), 7.36 (s, 1H), 6.70 (bs, 1H), 5.52 (s, 1H), 3.69 (s, 3H), 3.56 (s, 3H), 2.42 (s, 3H).
HRMS (IE) m/z calculated $C_{20}H_{14}N_3O_4S$ [M^{+1}]: 392.0700, found: 392.0698.

Example C114: Methyl 5-acetyl-2-((2-aminoethoxy)methyl)-4-(benzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

[0850] In a first step, methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2-((2-(1,3-dioxoisoindolin-2-yl)ethoxy)methyl)-6-methyl-1,4-dihydropyridine-3-carboxylate was prepared using a variation of Method C by heating in methanol in a sealed tube at 130 °C for 7h yielding a yellow solid (120 mg, 60 %).

[0851] Deprotection: In a second step, methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2-((2-(1,3-dioxoisoindolin-2-yl)ethoxy)methyl)-6-methyl-1,4-dihydropyridine-3-carboxylate (0.060 g, 0.11 mmol) and hydrazine monohydrate (0.018 g, 0.56 mmol) were heated in ethanol (3 mL) at 78°C for 5 minutes. The mixture was allowed to cool to RT and after addition of hydrazine monohydrate (0.018 g, 0.56 mmol) was stirred at room temperature overnight. The mixture was filtered, concentrated and the residue purified by column chromatography (dichloromethane: methanol 10%) affording

a yellow solid (0.020 g, 44%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm): 8.15 - 8.01 (m, 2H), 7.80 (d, *J* = 7.6 Hz, 1H), 7.34 (dt, *J* = 24.5, 6.8 Hz, 2H), 7.15 (bs, 1H), 5.45 (bs, 1H), 4.85 - 4.49 (m, 2H), 3.62 (s, 3H), 3.57 (t, *J* = 5.0 Hz, 2H), 2.97 (bs, 2H), 2.42 (s, 3H), 2.13 (s, 3H), 1.78 (bs, 3H).

Example C115: Methyl 5-acetyl-2-((2-aminoethoxy)methyl)-4-(7-bromobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

[0852] Following the 2-step procedure described above for the synthesis of Example C114, the title compound was obtained as a yellow solid (0.030 g, 33 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm): 8.10 (d, *J* = 7.5 Hz, 2H), 7.46 (d, *J* = 7.3 Hz, 1H), 7.31 - 7.25 (m, 1H), 7.22 (s, 1H), 5.40 (s, 1H), 4.85 - 4.56 (m, 2H), 3.60 (s, 5H), 2.99 (s, 2H), 2.42 (s, 5H), 2.13 (s, 3H).

Example C116: Methyl 5-acetyl-2-((2-aminoethoxy)methyl)-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

[0853] Following the 2-step procedure described above for the synthesis of Example C114, the title compound was obtained as a yellow solid (0.035 g, 51 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm): 8.41 (d, *J* = 8.2 Hz, 1H), 8.27 (bs, 1H), 7.66 (d, *J*= 7.2 Hz, 1H), 7.47 (t, *J* = 7.8 Hz, 1H), 7.27 (s, 1H), 5.47 (s, 1H), 4.85 - 4.56 (m, 2H), 3.59 (s, 5H), 2.98 (s, 2H), 2.42 (s, 3H), 2.15 (s, 3H), 1.83 (s, 2H).
HRMS (IE) m/z calculated $C_{22}H_{24}N_3O_4S$ [M^{+1}]: 426.1482, found: 426.1480.
[0854] Examples C117 and C118 have been prepared according to the following 3-step synthesis:

Example C117: Dimethyl 4-(7-cyanobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-formyl-1,4-dihydropyridine-3,5-dicarboxylate

[0855] In a first step, dimethyl 4-(7-cyanobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-(dimethoxymethyl)-1,4-dihydropyridine-3,5-dicarboxylate was prepared using a variation of Method C by heating in methanol in a sealed tube at 130°C for 1,5h yielding a yellow solid (0.130 g, 48%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm): 8.36 (d, *J* = 8.3 Hz, 1H), 7.67 (d, *J* = 7.4 Hz, 1H), 7.47 (t, *J* = 7.8 Hz, 1H), 7.30 (s, 1H), 6.80 (s, 1H), 5.98 (s, 1H), 5.52 (s, 1H), 3.59 (s, 3H), 3.58 (s, 3H), 3.44 (s, 3H), 3.43 (s, 3H), 2.89 - 2.79 (m, 1H), 1.11 - 0.89 (m, 2H), 0.91 - 0.58 (m, 2H).
[0856] Deprotection: In a second step, a mixture of dimethyl 4-(7-cyanobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-(dimethoxymethyl)-1,4-dihydropyridine-3,5-dicarboxylate (0.100 g, 0.21 mmol) and hydrochloride acid 4N (0.53 mL, 2.13 mmol) in acetone (4 mL) was stirred at room temperature for 60 minutes. The solvent was removed under reduced pressure and the residue was taken up in ethyl acetate, washed with toluene, saturated bicarbonate solution and brine and then dried (Na_2SO_4) and concentrated yielding the title compound that was used without further purification.
^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm): 10.50 (s, 1H), 8.33 (d, *J* = 8.3 Hz, 1H), 7.71 (d, *J* = 7.0 Hz, 1H), 7.51 (t, *J* = 7.8 Hz, 1H), 7.32 (s, 1H), 7.26 (s, 1H), 5.59 (s, 1H), 3.68 (s, 3H), 3.62 (d, *J* = 6.2 Hz, 1H), 3.57 (s, 3H), 2.98 (t, *J* = 7.6 Hz, 2H), 2.17 - 2.05 (m, 2H).
HRMS (APCI) m/z calculated $C_{22}H_{19}N_2O_5S$ [M^{+1}]: 423.1009, found: 423.1007.

Example C118: Dimethyl 4-(7-cyanobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-(hydroxymethyl)-1,4-dihydropyridine-3,5-dicarboxylate

[0857] Reduction: In a third step, sodium borohydride (0.005 g, 0.13 mmol) was added to a mixture of dimethyl 4-(7-cyanobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-formyl-1,4-dihydropyridine-3,5-dicarboxylate (0.047 g, 0.11 mmol) in ethanol (3 mL) at 0°C which was stirred at same temperature for 1h. Then water was added, and the mixture was extracted with ethyl acetate. The organic phase was separated, dried (Na_2SO_4), filtered and concentrated, and the resulting residue was purified by column chromatography (2:1 hexane: ethyl acetate) affording the title compound as a yellow solid (0.026 g, 56%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm): 8.33 (d, *J* = 7.9 Hz, 1H), 7.67 (d, *J* = 7.2 Hz, 1H), 7.52 - 7.45 (m, 2H), 7.30 (s, 1H), 5.46 (s, 1H), 4.82 (bs, 2H), 3.61 (t, *J* = 6.2 Hz, 2H), 3.54 (s, 3H), 3.53 (s, 3H), 2.93 (t, *J* = 7.4 Hz, 2H), 2.86 (bs, 1H), 2.17 - 2.05 (m, 2H).

Example C119: Dimethyl 4-(7-cyanobenzo[b]thiophen-3-yl)-2-formyl-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

[0858] The title compound was prepared following the synthesis described for Example C117 yielding a solid that was

used without further purification.
^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm): 10.50 (s, 1H), 8.35 (d, *J* = 8.3 Hz, 1H), 7.70 (d, *J* = 7.3 Hz, 1H), 7.55 - 7.46 (m, 1H), 7.33 (s, 1H), 7.10 (bs, 1H), 5.58 (s, 1H), 3.67 (s, 3H), 3.57 (s, 3H), 2.45 (s, 3H).
HRMS (APCI) m/z calculated $C_{20}H_{17}N_2O_5S$ [M^{+1}]: 397.0853, found: 397.0853.

Example C120: Dimethyl 4-(7-cyanobenzo[b]thiophen-3-yl)-2-(hydroxymethyl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

[0859] The title compound was prepared following the synthesis described for Example C118 yielding a yellow solid (0.007 g, 16%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm): 8.35 (d, *J* = 8.5 Hz, 1H), 7.66 (d, *J* = 7.2 Hz, 1H), 7.47 (t, *J* = 7.7 Hz, 1H), 7.30 (s, 1H), 7.24 (bs, 1H), 5.45 (s, 1H), 4.83 (d, *J* = 2.1 Hz, 2H), 3.54 (s, 3H), 3.53 (s, 3H), 2.41 (s, 3H), 1.61 (s, 1H).
HRMS (APCI) m/z calculated $C_{20}H_{19}N_2O_5S$ [M^{+1}]: 399.1009, found: 399.1010.

Example C121: Dimethyl 2-cyano-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3,5-dicarboxylate

[0860] The title compound was prepared from methyl (Z)-4,4-dimethoxy-3-oxo-2-(thieno[2,3-b]pyridin-3-ylmethylene)butanoate following the 3-step synthesis described for Examples C117 and C118 yielding a yellow solid (0.025 g).
^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm): 8.33 (d, *J* = 8.3 Hz, 1H), 7.72 (d, *J* = 7.3 Hz, 1H), 7.58 - 7.49 (m, 1H), 7.35 (s, 1H), 6.73 (bs, 1H), 5.52 (s, 1H), 3.69 (s, 3H), 3.64 (s, 1H), 3.55 (s, 3H), 3.03 - 2.86 (m, 2H), 2.21 - 2.07 (m, 2H).
HRMS (APCI) m/z calculated $C_{22}H_{18}N_3O_4S$ [M^{+1}]: 420.1013, found: 420.1012.

Example C122: Cyclopropylmethyl 5-acetyl-4-(6-cyanobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate

[0861] The title compound was prepared using a variation of Method C by heating in dioxane in a sealed tube at 130 °C for 2 h yielding a yellow solid (0.010 g, 10%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm): 8.30 (d, *J* = 9.1 Hz, 1H), 8.11 (s, 1H), 7.59 (d, *J* = 9.1 Hz, 1H), 7.36 (s, 1H), 5.71 (bs, 1H), 5.54 (s, 1H), 3.88 (dd, *J* = 7.3, 2.1 Hz, 2H), 2.68 - 2.54 (m, 1H), 2.36 (s, 3H), 2.15 (s, 3H), 1.08 - 0.93 (m, 3H), 0.74 - 0.64 (m, 2H), 0.54 - 0.42 (m, 2H), 0.22 - 0.12 (m, 2H).
HRMS (APCI) m/z calculated $C_{25}H_{25}N_2O_3S$ [M^{+1}]: 433.1580, found: 433.1581.

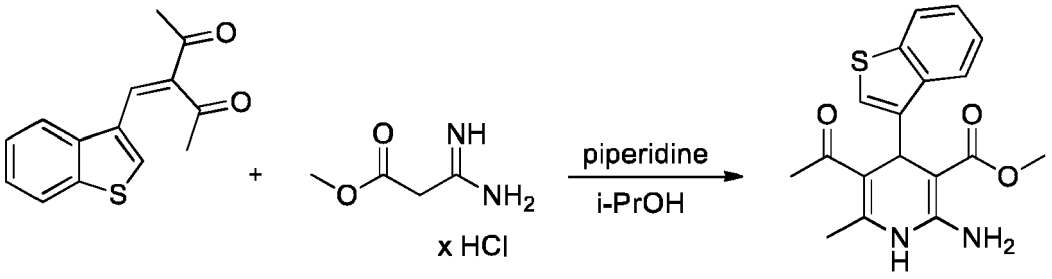
Example C123: Cyclopropylmethyl 2,5-diacetyl-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

[0862] The title compound was prepared using a variation of Method C by heating in dioxane in a sealed tube at 130 °C for 2 h yielding a yellow solid (0.006 g, 11%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm): 8.47 (d, *J* = 8.2 Hz, 1H), 7.66 (d, *J* = 7.3 Hz, 1H), 7.46 (t, *J* = 7.6 Hz, 1H), 7.29 (s, 1H), 5.86 (bs, 1H), 5.52 (s, 1H), 3.91 - 3.78 (m, 2H), 2.40 (s, 3H), 2.35 (s, 3H), 2.16 (s, 3H), 0.26 - 0.07 (m, 1H), 1.09 - 0.95 (m, 2H), 0.57 - 0.38 (m, 2H).

Method D

Example D1: Methyl 5-acetyl-2-amino-4-(benzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

[0863]



[0864] A mixture of 3-(benzo[b]thiophen-3-ylmethylene)pentane-2,4-dione (0.15 g, 0.61 mmol, 1 eq), methyl 3-amino-

3-iminopropanoate (0.093 g, 0.61 mmol, 1 eq) and piperidine (0.073 g, 0.74 mmol, 1.2 eq) in *i*-PrOH (5 ml) was stirred at reflux temperature for 4 hours. The reaction mixture was concentrated in vacuum, and the precipitate that formed was filtered off, washed with methanol, dichloromethane and ether and dried affording the title compound as a yellow solid (65 mg, 31%).

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.00 (s, 1H), 7.22 (d, *J* = 7.8 Hz, 1H), 7.06 (d, *J* = 7.9 Hz, 1H), 6.63 - 6.43 (m, 2H), 6.40 (s, 1H), 5.80 (s, 2H), 4.46 (s, 1H), 2.66 (s, 3H), 1.46 (s, 3H), 1.24 (s, 3H).
HRMS (IE) m/z calculated $C_{18}H_{18}N_2O_3S$ [M^+]: 342.1038, found: 342.1044.

Example D2: Methyl 2-amino-4-(benzo[b]thiophen-3-yl)-5-(cyclopropanecarbonyl)-6-methyl-1,4-dihydropyridine-3-carboxylate

[0865] Method D yielded the title compound as a light-yellow solid (40 mg, 48 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.02 (d, *J* = 7.7 Hz, 1H), 7.78 (d, *J* = 7.5 Hz, 1H), 7.40-7.19 (m, 3H), 7.10 (s, 1H), 6.23 (s, 2H), 5.51 (s, 1H), 3.61 (s, 3H), 2.23 - 1.97 (m, 4H), 0.96 (dq, *J* = 6.9, 2.1 Hz, 1H), 0.82 (td, *J* = 7.2, 6.3, 3.5 Hz, 2H), 0.68 (dt, *J* = 8.6, 4.2 Hz, 1H).
HRMS (IE) m/z calculated $C_{20}H_{20}N_2O_3S$ [M^+]: 368.1195, found: 368.1183.

Example D3: Methyl 5-acetyl-2-amino-4-(5-fluorobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

[0866] Method D yielded the title compound as a yellow solid (0.075 g, 44%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.75 - 7.67 (m, 2H), 7.48 (s, 1H), 7.19 (s, 1H), 7.05 (t, *J* = 7.7 Hz, 1H), 6.27 (s, 2H), 5.29 (s, 1H), 3.66 (s, 3H), 2.20 (s, 3H), 2.17 (s, 3H). ^{19}F-NMR (282 MHz, $CDCl_3$) δ = -119.10 (s).
HRMS (IE) m/z calculated $C_{18}H_{17}FN_2O_3S$ [M^+]: 360.0944, found: 360.0943.

Example D4: Methyl 5-acetyl-2-amino-4-(7-bromobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

[0867] Method D in methanol yielded the title compound as a yellow solid (0.031 g, 24%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.82 (s, 1H), 8.06 (d, *J* = 8.0 Hz, 1H), 7.54 (d, *J* = 7.5 Hz, 1H), 7.39 - 7.27 (m, 2H), 6.61 (bs, 2H), 5.22 (s, 1H), 3.45 (s, 3H), 2.27 (s, 3H), 2.05 (s, 3H).
HRMS (IE) m/z calculated $C_{18}H_{17}N_2O_3SBr$ [M^+]: 420.0143, found: 420.0130.
HPLC (98.4%): Rt 16.46 min.

Example D5: Methyl 5-acetyl-2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

[0868] Method D in methanol yielded the title compound as a yellow solid (0.075 g, 64%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm): 8.35 (d, *J* = 8.2 Hz, 1H), 7.66 (d, *J* = 7.3 Hz, 1H), 7.46 (t, *J* = 7.8 Hz, 1H), 7.27 (s, 1H), 6.33 (bs, 1H), 6.03 (bs, 2H), 5.39 (s, 1H), 3.61 (s, 3H), 2.35 (s, 3H), 2.14 (s, 3H).
HRMS (IE) m/z calculated $C_{19}H_{18}N_3O_3S$ [M^+]: 368.1063, found: 368.1064.
HPLC (98.4%): Rt 20.05 min.

Example D6: Cyclopentyl 5-acetyl-2-amino-4-(7-bromobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

[0869] Method D in methanol yielded the title compound as a yellow solid (0.070 g, 46 %).
^{1}H-NMR (300 MHz, DMSO) δ (ppm): 8.83 (bs, 1H), 8.11 - 8.01 (m, 1H), 7.55 (d, *J* = 7.5 Hz, 1H), 7.39 - 7.26 (m, 2H), 6.65 (bs, 2H), 5.21 (s, 1H), 5.03 - 4.89 (m, 1H), 2.26 (s, 3H), 2.11 (s, 3H), 1.86 - 1.71 (m, 1H), 1.69 - 1.52 (m, 3H), 1.54 - 1.33 (m, 3H), 1.33 - 1.19 (m, 1H).
HRMS (IE) m/z calculated $C_{22}H_{23}N_2O_3SBr$ [M^+]: 474.0613, found: 474.0605.
HPLC (95.5%): Rt 13.81 min.

Example D7: Dimethyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

[0870] Method D in methanol yielded the title compound as a yellow solid (0.045 g, 34 %).
^{1}H-NMR (300 MHz, DMSO) δ (ppm): 8.33 (d, *J* = 8.0 Hz, 1H), 7.65 (d, *J* = 7.3 Hz, 1H), 7.43 (t, *J* = 8.0 Hz, 1H), 7.27 (s, 1H), 6.91 (bs, 1H), 6.20 (bs, 2H), 5.37 (s, 1H), 3.53 (s, 3H), 3.51 (s, 3H), 2.27 (s, 3H).
[0871] HRMS (IE) m/z calculated $C_{19}H_{17}N_3O_4S$ [M^+]: 383.0940, found: 383.0947.
[0872] HPLC (97.5%): Rt 14.58 min.

Example D8: Cyclopentyl 5-acetyl-2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

[0873] Method D in methanol yielded the title compound as a yellow solid (0.048 g, 31 %).
^{1}H-NMR (300 MHz, DMSO) δ (ppm): 8.35 - 8.20 (m, 1H), 7.57 (d, *J* = 7.8 Hz, 1H), 7.35 (t, *J* = 7.8 Hz, 1H), 7.18 (bs, 2H), 6.16 (bs, 2H), 5.30 (s, 1H), 5.11 - 4.95 (m, 1H), 2.17 (s, 3H), 2.12 (s, 3H), 1.86 - 1.73 (m, 1H), 1.71 - 1.51 (m, 3H), 1.52 - 1.36 (m, 3H), 1.35 - 1.24 (m, 1H).
HRMS (IE) m/z calculated $C_{23}H_{23}N_3O_3S$ [M^+]: 421.1460, found: 421.1453.
HPLC (98.4%): Rt 17.10 min.

Example D9: Dimethyl 2,6-diamino-4-(benzo[b]thiophen-3-yl)-1,4-dihydropyridine-3,5-dicarboxylate

[0874] Method D using benzo[b]thiophene-3-carbaldehyde and methyl 3-amino-3-iminopropanoate (2 eq) yielded the title compound as a yellow solid (0.115 g, 53 %). ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.13-7.90 (m, 2H), 7.86 (d, *J* = 8.0 Hz, 1H), 7.58 - 7.34 (m, 3H), 7.19 (s, 1H), 6.98 (s, 1H), 6.54 (s, 1H), 4.74 (s, 1H), 3.72 (s, 3H), 3.60 (s, 1H), 3.37 (s, 3H).

Example D10: Cyclopropylmethyl 5-acetyl-2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

[0875] Method D using morpholine (1.2 eq.) in isopropanol yielded the title compound as a yellow solid (0.038 g, 51 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.43 (d, *J* = 8.3 Hz, 1H), 7.66 (d, *J* = 7.3 Hz, 1H), 7.43 (t, *J* = 7.8 Hz, 1H), 7.30 (s, 1H), 6.51 (bs, 1H), 6.08 (bs, 2H), 5.43 (s, 1H), 3.83 (d, *J* = 7.3 Hz, 2H), 2.33 (s, 3H), 2.17 (s, 3H), 1.10 - 0.95 (m, 1H), 0.60 - 0.40 (m, 2H), 0.27 - 0.03 (m, 2H).

Example D11: 4,4-difluorocyclohexyl 5-acetyl-2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

[0876] Method D using morpholine (1.2 eq.) in isopropanol yielded the title compound as a yellow solid (0.053 g, 30 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.35 (d, *J* = 8.2 Hz, 1H), 7.67 (d, *J* = 7.3 Hz, 1H), 7.45 (t, *J* = 7.8 Hz, 1H), 7.28 (s, 1H), 6.05 (bs, 2H), 5.42 (s, 1H), 4.82 (bs, 1H), 2.32 (s, 3H), 2.20 (s, 3H), 2.02 - 1.80 (m, 3H), 1.76 - 1.58 (m, 5H), 1.53 - 1.38 (m, 1H). ^{19}F-NMR (282 MHz, $CDCl_3$) δ (ppm): -97.60 (CF), -98.46 (CF).

Example D12: Methyl 2-amino-5-cyano-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

[0877] Method D using morpholine (1.2 eq.) in isopropanol yielded the title compound as a yellow solid (0.022 g, 15 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.24 - 8.16 (m, 1H), 7.74 - 7.67 (m, 1H), 7.47 (t, *J* = 7.8 Hz, 1H), 7.31 (s, 1H), 6.89 (bs, 1H), 6.26 (bs, 2H), 5.03 (s, 1H), 3.49 (s, 3H), 2.04 (s, 3H).

Example D13: 4-fluorobenzyl 5-acetyl-2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

[0878] Method D using morpholine (1.2 eq.) in isopropanol yielded the title compound as a yellow solid (0.074 g, 43 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.14 (d, *J* = 7.9 Hz, 1H), 7.60 (d, *J* = 7.0 Hz, 1H), 7.20 (s, 2H), 7.13 - 7.02 (m, 2H), 6.95 (t, *J* = 8.2 Hz, 2H), 6.48 (bs, 1H), 6.12 (bs, 2H), 5.37 (s, 1H), 4.98 (s, 2H), 2.31 (s, 3H), 2.12 (s, 3H). ^{19}F-NMR (282 MHz, $CDCl_3$) δ (ppm): - 113.91 (CF).

Example D14: Methyl 5-acetyl-2-amino-4-(5-fluorothieno[2,3-b]pyridin-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

[0879] Method D in methanol yielded the title compound as a yellow solid (0.012 g, 67 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.90 (s, 1H), 8.55 (d, *J* = 2.6 Hz, 1H), 8.16 (dd, *J* = 10.5, 2.6 Hz, 1H), 7.48 (s, 1H), 6.65 (bs, 2H), 5.20 (s, 1H), 3.48 (s, 3H), 2.30 (s, 3H), 2.11 (s, 3H). ^{19}F-NMR (282 MHz, $CDCl_3$) δ (ppm): -129.28 (d, *J* = 10.4 Hz).
[0880] Example D14 was further modified to render Example D15:

Example D15: Methyl 2-acetamido-5-acetyl-4-(5-fluorothieno[2,3-b]pyridin-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

[0881] A mixture of methyl 5-acetyl-2-amino-4-(5-fluorothieno[2,3-b]pyridin-3-yl)-6-methyl-1,4-dihydropyridine-3-car-

boxylate (0.025 g, 0.07 mmol) and acetyl chloride (0.005 mL, 0.07 mmol) in pyridine (1 mL) was stirred at 75 °C for 3 hours. The mixture was allowed to cool to RT and the solvent was removed under reduced pressure. The residue was purified by column chromatography (DCM:MeOH 2%) affording a yellow solid (0.017 g, 61%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 11.71 (bs, 1H), 10.50 (s, 1H), 8.43 (d, *J* = 2.4 Hz, 1H), 8.02 (dd, *J* = 9.8, 2.7 Hz, 1H), 7.34 (s, 1H), 5.33 (s, 1H), 3.66 (s, 3H), 2.39 (s, 3H), 2.21 (s, 3H), 2.18 (s, 3H). ^{19}F-NMR (282 MHz, $CDCl_3$) δ (ppm): -133.66 (d, *J* = 9.5 Hz).

Example D16: Cyclopentylmethyl 5-acetyl-2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

[0882] Method D using morpholine (1.2 eq.) in isopropanol yielded the title compound as a yellow solid (0.066 g, 51 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.36 (d, *J* = 8.2 Hz, 1H), 7.65 (d, *J* = 7.4 Hz, 1H), 7.43 (t, *J* = 7.8 Hz, 1H), 7.26 (s, 1H), 6.25 (bs, 1H), 6.02 (bs, 2H), 5.42 (s, 1H), 3.90 (dd, *J* = 7.2, 1.8 Hz, 2H), 2.32 (s, 3H), 2.18 (s, 3H), 1.58 (d, *J* = 34.3 Hz, 7H), 1.28 - 1.04 (m, 2H).

Example D17: 3-(cyclopropylmethyl) 5-methyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

[0883] Method D using morpholine (1.2 eq.) in isopropanol yielded the title compound as a yellow solid (0.070 g, 47 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.36 (d, *J* = 8.7 Hz, 1H), 7.64 (d, *J* = 7.1 Hz, 1H), 7.47 - 7.37 (m, 1H), 7.32 (s, 1H), 5.99 (bs, 2H), 5.87 (bs, 1H), 5.41 (s, 1H), 3.71 (d, *J* = 7.2 Hz, 2H), 3.52 (s, 3H), 2.35 (s, 3H), 0.91 - 0.75 (m, 1H), 0.44 - 0.24 (m, 2H), 0.13 - - 0.10 (m, 2H).

Example D18: Dimethyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-cyclopropyl-1,4-dihydropyridine-3,5-dicarboxylate

[0884] Method D in methanol yielded the title compound as a yellow solid (0.054 g, 41 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.32 (d, *J* = 8.2 Hz, 1H), 7.65 (d, *J* = 7.3 Hz, 1H), 7.44 (t, *J* = 7.8 Hz, 1H), 7.24 (s, 1H), 6.18 (bs, 2H), 6.15 (bs, 1H), 5.39 (s, 1H), 3.56 (s, 3H), 3.52 (s, 3H), 2.81 - 2.64 (m, 1H), 1.01 - 0.84 (m, 2H), 0.83 - 0.60 (m, 2H).

Example D19: 3-(cyclopropylmethyl) 5-methyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-cyclopropyl-1,4-dihydropyridine-3,5-dicarboxylate

[0885] Method D yielded the title compound as a yellow solid (0.017 g, 12 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.37 (d, *J* = 8.2 Hz, 1H), 7.64 (d, *J* = 7.3 Hz, 1H), 7.42 (t, *J* = 7.8 Hz, 1H), 7.28 (s, 1H), 6.15 (bs, 2H), 6.02 (bs, 1H), 5.42 (s, 1H), 3.72 (d, *J* = 7.2 Hz, 2H), 3.55 (s, 3H), 2.78 - 2.62 (m, 1H), 1.01 - 0.77 (m, 3H), 0.79 - 0.62 (m, 2H), 0.47 - 0.24 (m, 2H), 0.12 - -0.09 (m, 2H).

Example D20: dimethyl 2,6-diamino-4-(7-cyanobenzo[b]thiophen-3-yl)-1,4-dihydropyridine-3,5-dicarboxylate

[0886] Method D in methanol yielded the title compound as a yellow solid (0.135 g, 66 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.14 (d, *J* = 7.9 Hz, 1H), 7.98 (d, *J* = 7.2 Hz, 1H), 7.69 (t, *J* = 7.9 Hz, 1H), 7.47 (bs, 1H), 7.21 (s, 1H), 7.16 (bs, 1H), 6.60 (bs, 2H), 4.74 (s, 1H), 3.70 (s, 3H), 3.56 (s, 1H), 3.35 (s, 3H).

Example D21: 5-(cyclopropylmethyl) 3-methyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-cyclopropyl-1,4-dihydropyridine-3,5-dicarboxylate

[0887] Method D using morpholine in isopropanol yielded the title compound as a yellow solid (0.040 g, 31 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.35 (d, *J* = 8.2 Hz, 1H), 7.64 (d, *J* = 7.2 Hz, 1H), 7.42 (t, *J* = 7.7 Hz, 1H), 7.26 (s, 1H), 6.26 (bs, 3H), 5.41 (s, 1H), 3.77 (d, *J* = 7.2 Hz, 2H), 3.52 (s, 3H), 2.84 - 2.66 (m, 1H), 0.97 - 0.80 (m, 3H), 0.81 - 0.61 (m, 2H), 0.48 - 0.25 (m, 2H), 0.15 - -0.08 (m, 2H).

Example D22: 3-(4-fluorobenzyl) 5-methyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

[0888] Method D using morpholine in isopropanol yielded the title compound as a yellow solid (0.035 g, 25 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.11 (d, *J* = 8.3 Hz, 1H), 7.59 (d, *J* = 7.3 Hz, 1H), 7.30-7.15 (m, 2H), 6.97 - 6.77 (m, 4H),

6.68 (s, 1H), 6.22 (bs, 2H), 5.34 (s, 1H), 5.04 - 4.75 (m, 2H), 3.50 (s, 3H), 2.26 (s, 3H). ^{19}F-NMR (282 MHz, $CDCl_3$) δ (ppm): -114.23 (CF).

Example D23: 3-(4-fluorobenzyl) 5-methyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-cyclopropyl-1,4-dihydropyridine-3,5-dicarboxylate

[0889] Method D using morpholine in isopropanol yielded the title compound as a yellow solid (0.035 g, 25 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.10 (d, *J* = 8.2 Hz, 1H), 7.60 (d, *J* = 7.3 Hz, 1H), 7.25-7.13 (m, 2H), 6.87 (q, *J* = 8.7, 7.6 Hz, 4H), 6.29 (s, 2H), 6.20 (s, 1H), 5.36 (s, 1H), 5.00 - 4.77 (m, 2H), 3.52 (s, 3H), 2.83 - 2.53 (m, 1H), 0.99 - 0.82 (m, 2H), 0.79 - 0.62 (m, 2H). ^{19}F-NMR (282 MHz, $CDCl_3$) δ (ppm): -114.26 (CF).

Example D24: cyclopropylmethyl 2-amino-5-cyano-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

[0890] Method D using piperidine in dioxane yielded the title compound as a yellow solid (0.035 g, 23 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.20 (d, *J* = 8.3 Hz, 1H), 7.69 (d, *J* = 7.4 Hz, 1H), 7.45 (t, *J* = 7.8 Hz, 1H), 7.35 (s, 1H), 7.04 (bs, 1H), 6.27 (bs, 2H), 5.08 (s, 1H), 3.69 (dt, *J* = 7.2, 3.8 Hz, 2H), 2.02 (s, 3H), 0.83 - 0.64 (m, 1H), 0.35 - 0.11 (m, 2H), 0.06 - -0.29 (m, 2H).
HRMS (APCI) m/z calculated $C_{21}H_{19}N_4O_2S$ [M^{+1}]: 391.1223, found: 391.1223.

Example D25: 4-Fluorobenzyl 2-amino-5-cyano-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

[0891] Method D using morpholine in dioxane yielded the title compound as a yellow solid (0.010 g, 8 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.08 (d, *J* = 8.2 Hz, 1H), 7.69 (d, *J* = 7.1 Hz, 1H), 7.38 (t, *J* = 7.8 Hz, 1H), 7.28 (s, 1H), 6.79 (s, 2H), 6.77 (s, 2H), 6.46 (bs, 1H), 6.28 (s, 2H), 5.05 (s, 1H), 4.98 - 4.75 (m, 2H), 2.09 (s, 3H). ^{19}F-NMR (282 MHz, $CDCl_3$) δ (ppm): - 114.12 (CF).
HRMS (APCI) m/z calculated $C_{24}H_{18}N_4O_2S$ [M^{+1}]: 445.1129, found: 445.1126.

Example D26: Cyclopropylmethyl 6-amino-5-cyano-4-(7-cyanobenzo[b]thiophen-3-yl)-2-cyclopropyl-1,4-dihydropyridine-3-carboxylate

[0892] Method D run at room temperature overnight yielded the title compound as a yellow solid (0.060 g, 51 %).
^{1}H-NMR (300 MHz, DMSO-d_6) δ = 8.20 (d, *J* = 8.3 Hz, 1H), 7.95 (d, *J* = 7.3 Hz, 1H), 7.76 (bs, 1H), 7.61 (t, *J* = 7.8 Hz, 1H), 6.77 (s, 1H), 5.51 (bs, 2H), 5.21 (s, 1H), 4.60 - 4.35 (m, 1H), 3.56 (d, *J* = 7.2 Hz, 2H), 1.23 - 1.10 (m, 1H), 0.81 - 0.64 (m, 1H),0.64 - 0.47 (m, 1H), 0.39 - 0.29 (m, 2H), 0.27 - 0.12 (m, 2H), 0.04 - -0.20 (m, 2H).
HRMS (APCI) m/z calculated $C_{23}H_{21}N_4O_2S$ [M^{+1}]: 417.1380, found: 417.1382.

Example D27: 3-Cyclopentyl 5-methyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

[0893] Method D using morpholine at room temperature overnight yielded the title compound as a yellow solid (0.082 g, 51 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.30 (d, *J* = 8.7 Hz, 1H), 7.65 (d, *J* = 7.3 Hz, 1H), 7.43 (t, *J* = 7.8 Hz, 1H), 7.30 (s, 1H), 6.07 (s, 2H), 6.03 (s, 1H), 5.32 (s, 1H), 5.07 - 4.92 (m, 1H), 3.54 (s, 3H), 2.32 (s, 3H), 1.87 - 1.74 (m, 1H), 1.71 - 1.57 (m, 2H), 1.54 - 1.40 (m, 3H), 1.39 - 1.29 (m, 1H), 1.24 - 1.11 (m, 1H).
HRMS (APCI) m/z calculated $C_{23}H_{24}N_3O_4S$ [M^{+1}]: 438.1482, found: 438.1481.

Example D28: Cyclopropylmethyl 5-acetyl-2-amino-4-(6-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

[0894] Method D using morpholine at room temperature overnight yielded the title compound as a yellow solid (0.062 g, 45 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.93 (bs, 1H), 8.53 (s, 1H), 8.25 (d, *J* = 8.4 Hz, 1H), 7.75 (d, *J* = 8.4 Hz, 1H), 7.59 (s, 1H), 6.69 (bs, 2H), 5.32 (s, 1H), 3.79 - 3.62 (m, 2H), 2.30 (s, 3H), 2.09 (s, 3H), 1.06 - 0.87 (m, 1H), 0.40 (d, *J* = 8.0 Hz, 2H), 0.20 - 0.02 (m, 2H).
HRMS (APCI) m/z calculated $C_{22}H_{22}N_3O_3S$ [M^{+1}]: 408.1376, found: 408.1378.

Example D29: Cyclohexyl 5-acetyl-2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

[0895] Method D using morpholine at room temperature overnight yielded the title compound as a yellow solid (0.066 g, 43 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.37 (d, *J* = 8.0 Hz, 1H), 7.66 (d, *J* = 7.1 Hz, 1H), 7.43 (t, *J* = 7.8 Hz, 1H), 7.27 (s, 1H), 6.25 (bs, 1H), 6.03 (bs, 2H), 5.40 (s, 1H), 4.77 - 4.56 (m, 1H), 2.32 (s, 3H), 2.17 (s, 3H), 1.99 - 1.86 (m, 1H), 1.78 - 1.67 (m, 1H), 1.63 - 1.49 (m, 3H), 1.39 - 1.07 (m, 5H).
HRMS (APCI) m/z calculated $C_{24}H_{26}N_3O_3S$ [M^{+1}]: 436.1689, found: 436.1690.

Example D30: Cyclohexylmethyl 5-acetyl-2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

[0896] Method D using morpholine at room temperature overnight yielded the title compound as a yellow solid (0.077 g, 46 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.37 (d, *J* = 8.1 Hz, 1H), 7.66 (d, *J* = 7.3 Hz, 1H), 7.45 (t, *J* = 7.8 Hz, 1H), 7.28 (s, 1H), 6.38 (bs, 1H), 6.06 (bs, 2H), 5.41 (s, 1H), 3.81 (d, *J* = 6.6 Hz, 2H), 2.31 (s, 3H), 2.18 (s, 3H), 1.69 - 1.53 (m, 4H), 1.51 - 1.37 (m, 2H), 1.16 - 0.96 (m, 3H), 0.87 - 0.73 (m, 2H).
HRMS (APCI) m/z calculated $C_{25}H_{28}N_3O_3S$ [M^{+1}]: 450.1846, found: 450.1849.

Example D31: Cyclopropylmethyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-5-(cyclopropanecarbonyl)-6-methyl-1,4-dihydropyridine-3-carboxylate

[0897] Method D using morpholine at room temperature overnight yielded the title compound as a yellow solid (0.120 g, 40 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.38 (d, *J* = 8.2 Hz, 1H), 7.66 (d, *J* = 7.3 Hz, 1H), 7.42 (t, *J* = 7.8 Hz, 1H), 7.32 (s, 1H), 6.54 (bs, 1H), 6.14 (bs, 2H), 5.56 (s, 1H), 3.82 (d, *J* = 7.3 Hz, 2H), 2.25 (s, 3H), 2.13 - 1.98 (m, 1H), 1.04 - 0.94 (m, 2H), 0.91 - 0.69 (m, 3H), 0.50 - 0.38 (m, 2H), 0.21 - 0.05 (m, 2H).
HRMS (APCI) m/z calculated $C_{24}H_{24}N_3O_3S$ [M^{+1}]: 434.1533, found: 421.1537.

Example D32: 3-Fluorobenzyl 5-acetyl-2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

[0898] Method D using morpholine at room temperature overnight yielded the title compound as a yellow solid (0.058 g, 34 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.17 (d, *J* = 8.5 Hz, 1H), 7.60 (d, *J* = 7.3 Hz, 1H), 7.23 (s, 3H), 6.96 (t, *J* = 8.5 Hz, 1H), 6.86 (d, *J* = 7.3 Hz, 1H), 6.74 (d, *J* = 11.4 Hz, 1H), 6.41 (bs, 1H), 6.12 (bs, 2H), 5.39 (s, 1H), 5.06 - 4.92 (m, 2H), 2.32 (s, 3H), 2.13 (s, 3H).
^{19}F-NMR (282 MHz, $CDCl_3$) δ (ppm): -112.76 (s, CF).
HRMS (APCI) m/z calculated $C_{25}H_{21}N_3O_3SF$ [M^{+1}]: 462.1282, found: 462.1278.

Example D33: 3-(Cyclobutylmethyl) 5-methyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

[0899] Method D using morpholine at room temperature overnight yielded the title compound as a yellow solid (0.040 g, 33 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.31 (d, *J* = 8.1 Hz, 1H), 7.66 (d, *J* = 7.2 Hz, 1H), 7.44 (t, *J* = 7.8 Hz, 1H), 7.29 (s, 1H), 6.82 (s, 1H), 6.22 (bs, 2H), 5.35 (s, 1H), 3.89 (t, *J* = 7.2 Hz, 2H), 3.54 (s, 3H), 2.41 - 2.29 (m, 1H), 2.26 (s, 3H), 1.93 - 1.63 (m, 4H), 1.58 - 1.27 (m, 2H).
HRMS (APCI) m/z calculated $C_{23}H_{24}N_3O_4S$ [M^+]:438.1482, found: 438.1483.

Example D34: 3-((3,3-Difluorocyclobutyl)methyl) 5-methyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

[0900] Method D using morpholine at room temperature overnight yielded the title compound as a yellow solid (0.035 g, 22 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.28 (d, *J* = 8.2 Hz, 1H), 7.67 (d, *J* = 7.2 Hz, 1H), 7.46 (t, *J* = 7.8 Hz, 1H), 7.31 (s, 1H), 6.19 (s, 1H), 6.14 (bs, 2H), 5.35 (s, 1H), 4.00 - 3.81 (m, 2H), 3.55 (s, 3H), 2.35 (m, 1H), 2.32 (s, 3H), 2.26 - 1.93 (m, 4H).

^{19}F-NMR (282 MHz, $CDCl_3$) δ (ppm): -83.87 (d, *J* = 193.0 Hz), -93.31 (d, *J* = 193.0 Hz).
HRMS (APCI) m/z calculated $C_{23}H_{22}N_3O_4SF_2$ [M^+]:474.1294, found: 474.1295.

Example D35: Cyclopropylmethyl 2-amino-5-carbamoyl-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

[0901] Method D using morpholine at room temperature overnight yielded the title compound as a yellow solid (0.011 g, 11 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.28 (d, *J* = 8.2 Hz, 1H), 7.66 (d, *J* = 7.3 Hz, 1H), 7.46-7.33 (m, 2H), 6.93 (bs, 1H), 6.28 (bs, 2H), 5.37 (bs, 2H), 5.21 (s, 1H), 3.76 (d, *J* = 7.2 Hz, 2H), 2.16 (s, 3H), 0.95 - 0.85 (m, 1H), 0.53 - 0.27 (m, 2H), 0.23 - -0.06 (m, 2H). HRMS (APCI) m/z calculated $C_{21}H_{21}N_4O_3S$ [M^{+1}]: 409.1329, found: 409.1324.

Example D36: 3-((2,2-Difluorocyclopropyl)methyl) 5-methyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

[0902] Method D using morpholine at room temperature overnight yielded the title compound as a yellow solid (0.065 g, 40 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.31 (dd, *J* = 7.7, 2.8 Hz, 1H), 7.65 (d, *J* = 7.0 Hz, 1H), 7.52 - 7.38 (m, 1H), 7.31 (d, *J* = 3.3 Hz, 1H), 6.07 (bs, 3H), 5.37 (s, 1H), 4.16 - 3.95 (m, 1H), 3.91 - 3.71 (m, 1H), 3.52 (s, 3H), 2.35 (s, 3H), 1.71 - 1.60 (m, 1H), 1.29 - 1.16 (m, 1H), 0.90 (s, 1H). ^{19}F-NMR (282 MHz, $CDCl_3$) δ (ppm): -129.21 (ddt, *J* = 160.2, 70.2, 10.9 Hz), -143.62 (ddd, *J* = 160.2, 51.3, 10.9 Hz).
HRMS (APCI) m/z calculated $C_{22}H_{20}N_3O_4SF_2$ [M^+]: 460.1137, found: 460.1137.

Example D37: 5-Cyclopropyl 3-(cyclopropylmethyl) 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

[0903] Method D using morpholine at room temperature overnight yielded the title compound as a yellow solid (0.008 g, 5 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.32 (d, *J* = 8.2 Hz, 1H), 7.65 (d, *J* = 7.2 Hz, 1H), 7.47 - 7.36 (m, 1H), 7.28 (s, 1H), 6.35 (bs, 1H), 6.11 (bs, 2H), 5.31 (s, 1H), 4.03 - 3.89 (m, 1H), 3.71 (d, *J* = 7.2 Hz, 2H), 2.33 (s, 3H), 1.25 (s, 1H), 1.00 - 0.69 (m, 2H), 0.60 - 0.28 (m, 4H), 0.22 - -0.03 (m, 2H).
HRMS (APCI) m/z calculated $C_{24}H_{24}N_3O_4S$ [M^{+1}]: 450.1482, found: 450.1481.

Example D38: 3-((2,2-Difluorocyclopropyl)methyl) 5-methyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-cyclopropyl-1,4-dihydropyridine-3,5-dicarboxylate

[0904] Method D using morpholine at room temperature overnight yielded the title compound as a yellow solid (0.004 g, 26 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.32 (d, *J* = 8.3 Hz, 1H), 7.65 (d, *J* = 7.2 Hz, 1H), 7.44 (t, *J* = 7.8 Hz, 1H), 7.27 (s, 1H), 6.30 (bs, 3H), 5.38 (s, 1H), 4.15 - 3.95 (m, 1H), 3.91 - 3.73 (m, 1H), 3.55 (s, 3H), 2.77 - 2.62 (m, 1H), 1.84 - 1.40 (m, 1H), 1.28 - 1.17 (m, 2H), 1.03 - 0.52 (m, 4H). ^{19}F-NMR (282 MHz, $CDCl_3$) δ (ppm): -129.11 (ddt, *J* = 160.0, 62.6, 11.7 Hz), -143.52 (ddd, *J* = 160.0, 35.4, 11.7 Hz).
HRMS (APCI) m/z calculated $C_{24}H_{22}N_3O_4SF_2$ [M^{+1}]: 486.1294, found: 486.1292.

Example D39: 3-(Cyclopropylmethyl) 5-methyl 2-amino-4-(7-cyano-5-fluorobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

[0905] Method D using morpholine at room temperature overnight yielded the title compound as a yellow solid (0.020 g, 28 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.05 (dd, *J* = 10.0, 2.3 Hz, 1H), 7.46 - 7.36 (m, 2H), 6.14 (s, 1H), 6.08 (bs, 2H), 5.32 (s, 1H), 3.73 (d, *J* = 7.3 Hz, 2H), 3.55 (s, 3H), 2.35 (s, 3H), 0.94 - 0.78 (m, 1H), 0.53 - 0.25 (m, 2H), 0.17 - -0.11 (m, 2H).
^{19}F-NMR (282 MHz, $CDCl_3$) δ (ppm): -117.83 (d, *J* = 7.7 Hz).
HRMS (APCI) m/z calculated $C_{22}H_{21}N_3O_4SF$ [M^{+1}]: 442.1231, found: 442.1231.

Example D40: 3-(cyclopropylmethyl) 5-methyl 2-amino-4-(7-cyano-4-fluorobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

[0906] Method D using morpholine at room temperature overnight yielded the title compound as a yellow solid (0.015

g, 16 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.62 (dd, *J* = 8.2, 4.0 Hz, 1H), 7.33 (s, 1H), 7.09 (dd, *J* = 11.0, 8.2 Hz, 1H), 6.15 - 6.01 (m, 3H), 5.66 (d, *J* = 4.0 Hz, 1H), 3.76 - 3.57 (m, 2H), 3.48 (s, 3H), 2.32 (s, 3H), 0.91 - 0.59 (m, 1H), 0.39 - 0.02 (m, 2H), 0.02 - -0.25 (m, 2H). ^{19}F-NMR (282 MHz, $CDCl_3$) δ (ppm): -104.35 (d, *J* = 11.0 Hz).
HRMS (APCI) m/z calculated $C_{22}H_{21}N_3O_4SF$ [M^{+1}]: 442.1231, found: 442.1229.

Example D41: 3-Isopropyl 5-methyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

[0907] Method D using morpholine at room temperature overnight yielded the title compound as a yellow solid (0.045 g, 26 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.34 (d, *J* = 8.2 Hz, 1H), 7.65 (d, *J* = 7.2 Hz, 1H), 7.43 (t, *J* = 7.8 Hz, 1H), 7.29 (s, 1H), 6.91 (bs, 1H), 6.25 (bs, 2H), 5.34 (s, 1H), 4.95 - 4.76 (m, 1H), 3.53 (s, 3H), 2.26 (s, 3H), 1.18 (d, *J* = 6.1 Hz, 3H), 0.70 (d, *J* = 6.1 Hz, 3H).
HRMS (APCI) m/z calculated $C_{21}H_{22}N_3O_4S$ [M^{+1}]: 412.1326, found: 412.1335.

Example D42: 3-((2,2-Difluoro-3,3-dimethylcyclopropyl)methyl) 5-methyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

[0908] Method D using morpholine at room temperature overnight yielded the title compound as a yellow solid (0.052 g, 31 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.32 (ddd, *J* = 8.3, 5.3, 1.0 Hz, 1H), 7.65 (d, *J* = 7.4 Hz, 1H), 7.50 - 7.39 (m, 1H), 7.31 (s, 1H), 6.12 (d, *J* = 3.4 Hz, 1H), 6.08 (d, *J* = 2.2 Hz, 2H), 5.37 (s, 1H), 4.16 - 4.02 (m, 1H), 3.97 - 3.81 (m, 1H), 3.55 (d, *J* = 1.5 Hz, 3H), 2.33 (d, *J* = 2.9 Hz, 3H), 1.40 - 1.21 (m, 1H), 1.15 (dd, *J* = *2.4,* 1.5 Hz, 2H), 1.01 - 0.92 (m, 3H), 0.90 (dd, *J* = 2.9, 1.4 Hz, 1H). ^{19}F-NMR (282 MHz, $CDCl_3$) δ (ppm): -137.08 (ddd, *J* = 156.1, 65.1, 13.6 Hz), -148.04 (dd, *J* = 155.7, 19.2 Hz)
HRMS (APCI) m/z calculated $C_{24}H_{24}N_3O_4SF_2$ [M^{+1}]: 488.1450, found: 488.1468.

Example D43: 5-Methyl 3-neopentyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

[0909] Method D using morpholine at room temperature overnight yielded the title compound as a yellow solid (0.061 g, 40 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.34 (d, *J* = 8.2 Hz, 1H), 7.63 (d, *J* = 7.1 Hz, 1H), 7.45-7.36 (m, 1H), 7.32 (s, 1H), 6.10 (bs, 3H), 5.44 (s, 1H), 3.80 - 3.53 (m, 5H), 2.30 (s, 3H), 0.74 (s, 9H).
HRMS (APCI) m/z calculated $C_{23}H_{26}N_3O_4S$ [M^{+1}]: 440.1639, found: 440.1638.

Example D44: 3-(Cyclopropylmethyl) 5-methyl 2-amino-4-(7-cyanothieno[3,2-b]pyridin-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

[0910] Method D using morpholine at room temperature overnight yielded the title compound as a yellow solid (0.048 g, 42 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.77 (d, *J* = 4.7 Hz, 1H), 7.64 (s, 1H), 7.42 (d, *J* = 4.7 Hz, 1H), 6.34 (s, 1H), 6.13 (s, 2H), 5.54 (s, 1H), 3.83 - 3.62 (m, 2H), 3.56 (s, 3H), 2.26 (s, 3H), 0.92 - 0.75 (m, 1H), 0.39 - 0.17 (m, 2H), 0.10 - -0.13 (m, 2H).
HRMS (APCI) m/z calculated $C_{21}H_{21}N_4O_4S$ [M^{+1}]: 425.1278, found: 425.1280.

Example D45: 5-Methyl 3-neopentyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-cyclopropyl-1,4-dihydropyridine-3,5-dicarboxylate

[0911] Method D using morpholine at room temperature overnight yielded the title compound as a yellow solid (0.063 g, 35 %). ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.33 (dd, *J* = 8.3, 1.0 Hz, 1H), 7.64 (dd, *J* = 7.6, 0.8 Hz, 1H), 7.41 (dd, *J* = 8.3, 7.4 Hz, 1H), 7.28 (s, 1H), 6.13 (bs, 2H), 5.91 (bs, 1H), 5.46 (s, 1H), 3.75 - 3.56 (m, 5H), 2.68 - 2.51 (m, 1H), 0.94 - 0.84 (m, 2H), 0.75 (s, 9H), 0.72 - 0.64 (m, 2H).
HRMS (APCI) m/z calculated $C_{25}H_{28}N_3O_4S$ [M^{+1}]: 466.1795, found: 466.1798.

Example D46: Bis(cyclopropylmethyl) 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

[0912] Method D using morpholine at room temperature overnight yielded the title compound as a yellow solid (0.120 g, 56 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.40 (d, *J* = 7.3 Hz, 1H), 7.63 (d, *J* = 8.4 Hz, 1H), 7.39 (dd, *J* = 8.2, 7.4 Hz, 1H), 7.34 (s, 1H), 6.02 (bs, 3H), 5.44 (s, 1H), 3.83 - 3.64 (m, 4H), 2.36 (s, 3H), 0.97 - 0.75 (m, 2H), 0.51 - 0.23 (m, 4H), 0.16 - -0.07 (m, 4H).
HRMS (APCI) m/z calculated $C_{25}H_{26}N_3O_4S$ [M^{+1}]: 464.1639, found: 464.11638.

Example D47: 3-(Cyclopropylmethyl) 5-(prop-2-yn-1-yl) 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

[0913] Method D using morpholine at room temperature overnight yielded the title compound as a yellow solid (0.112 g, 52 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.39 (dd, *J* = 8.3, 1.0 Hz, 1H), 7.64 (dd, *J* = 7.1, 1.2 Hz, 1H), 7.41 (dd, *J* = 8.2, 7.4 Hz, 1H), 7.34 (s, 1H), 6.02 (bs, 3H), 5.44 (s, 1H), 4.63 - 4.42 (m, 2H), 3.71 (d, *J* = 7.3 Hz, 2H), 2.46 - 2.26 (m, 4H), 0.91 - 0.73 (m, 1H), 0.49 - 0.20 (m, 2H), 0.12 - -0.14 (m, 2H).
HRMS (APCI) m/z calculated $C_{24}H_{22}N_3O_4S$ [M^{+1}]: 448.1326, found: 448.1327.

Example D48: 3-(Cyclopropylmethyl) 5-methyl 2-amino-4-(5,7-dicyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

[0914] Method D using morpholine at room temperature overnight yielded the title compound as a yellow solid (0.005 g, 8 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.64 (s, 1H), 7.85 (s, 1H), 7.49 (s, 1H), 6.07 (bs, 2H), 5.97 (bs, 1H), 5.40 (s, 1H), 3.72 (d, J = 7.3 Hz, 2H), 3.55 (s, 3H), 2.37 (s, 3H), 0.87-0.82 (m, 1H), 0.58 - 0.29 (m, 2H), 0.16 - -0.11 (m, 2H).
HRMS (APCI) m/z calculated $C_{23}H_{21}N_4O_4S$ [M^{+1}]: 449.1278, found: 449.1277.

Example D49: 5-(But-2-yn-1-yl) 3-(cyclopropylmethyl) 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

[0915] Method D using morpholine at room temperature overnight yielded the title compound as a yellow solid (0.007 g, 4 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.39 (dd, *J* = 8.3, 1.0 Hz, 1H), 7.64 (dd, *J* = 7.1, 1.2 Hz, 1H), 7.41 (dd, *J* = 8.2, 7.4 Hz, 1H), 7.34 (s, 1H), 6.02 (bs, 3H), 5.44 (s, 1H), 4.63 - 4.42 (m, 2H), 3.71 (d, *J* = 7.3 Hz, 2H), 2.46 - 2.26 (m, 4H), 0.91 - 0.73 (m, 1H), 0.49 - 0.20 (m, 2H), 0.12 - -0.14 (m, 2H).
HRMS (APCI) m/z calculated $C_{25}H_{24}N_3O_4S$ [M^{+1}]: 462.1482, found: 462.1480.

Example D50: 5-Methyl 3-(2,2,2-trifluoroethyl) 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

[0916] The title compound was prepared using a variation of Method D: A mixture of methyl (Z)-2-((7-cyanobenzo[b]thiophen-3-yl)methylene)-3-oxobutanoate (0.123 g, 0.43 mmol), 2,2,2-trifluoroethyl 3-amino-3-iminopropanoate (0.115 g, 0.43 mmol), ammonium acetate (0.033 g, 0.43 mmol) in trifluoroethanol (3 mL) was stirred at room temperature overnight and then concentrated. The residue was purified by column chromatography (1:1 hexane: ethyl acetate) affording a yellow solid (0.019 g, 10%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.30 (d, *J* = 8.3 Hz, 1H), 7.68 (d, *J* = 7.2 Hz, 1H), 7.46 (t, *J* = 7.7 Hz, 1H), 7.34 (s, 1H), 6.55 (bs, 1H), 6.24 (bs, 2H), 5.41 (s, 1H), 4.54 - 4.38 (m, 1H), 4.23 - 4.07 (m, 1H), 3.57 (s, 3H), 2.35 (s, 3H). ^{19}F-NMR (282 MHz, $CDCl_3$) δ (ppm): -73.93 (t, *J* = 9.8 Hz).
HRMS (APCI) m/z calculated $C_{20}H_{17}N_3O_4SF_3$ [M^{+1}]: 452.0886, found: 452.0885.

Example D51: 3-(Cyclopropylmethyl) 5-(2,2,2-trifluoroethyl) 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

[0917] Method D using morpholine at room temperature overnight yielded the title compound as a yellow solid (0.0065 g, 7 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.34 (d, J = 8.3 Hz, 1H), 7.65 (d, J = 7.2 Hz, 1H), 7.44-7.38 (m, 1H), 7.34 (s, 1H), 6.16 (bs, 1H), 6.04 (bs, 2H), 5.42 (s, 1H), 4.41 (dq, J = 12.7, 8.5 Hz, 1H), 4.20 (dt, J = 12.7, 8.5 Hz, 1H), 3.73 (d, J = 7.3 Hz,

2H), 2.38 (s, 3H), 0.90 - 0.82 (m, 1H), 0.47 - 0.29 (m, 2H), 0.10 - -0.04 (m, 2H). ^{19}F-NMR (282 MHz, $CDCl_3$) δ (ppm): -73.88 (t, *J* = 9.1 Hz).
HRMS (APCI) m/z calculated $C_{23}H_{21}N_3O_4SF_3$ [M^{+1}]: 492.1199, found: 492.1197.

Example D52: 3-(Cyclopropylmethyl) 5-methyl 2-amino-4-(6-chloro-7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

[0918] Method D using morpholine at room temperature overnight yielded the title compound as a yellow solid (0.060 g, 39 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.27 (d, *J* = 8.8 Hz, 1H), 7.44 (d, *J* = 8.8 Hz, 1H), 7.29 (s, 1H), 6.14 - 5.94 (m, 3H), 5.35 (s, 1H), 3.76 - 3.67 (m, 2H), 3.54 (s, 3H), 2.34 (s, 3H), 0.93 - 0.75 (m, 1H), 0.48 - 0.24 (m, 2H), 0.12 - -0.09 (m, 2H)
HRMS (APCI) m/z calculated $C_{22}H_{21}N_3O_4SCl$ [M^{+1}]: 458.0936, found: 458.0938.

Example D53: 3-(2-Fluoro-2-methylpropyl) 5-methyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

[0919] Method D using morpholine at room temperature overnight yielded the title compound as a yellow solid (0.060 g, 39 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.34 (d, *J* = 9.0 Hz, 1H), 7.64 (d, *J* = 7.4 Hz, 1H), 7.47-7.37 (m, 1H), 7.32 (s, 1H), 6.63 (bs, 1H), 6.20 (bs, 2H), 5.43 (s, 1H), 4.12 - 3.79 (m, 2H), 3.56 (s, 3H), 2.30 (s, 3H), 1.27 - 1.03 (m, 6H). ^{19}F-NMR (282 MHz, $CDCl_3$) δ (ppm): (-142.28) - (-148.26) (m, CF).
HRMS (APCI) m/z calculated $C_{22}H_{23}N_3O_4SF$ [M^{+1}]: 444.1388, found: 444.1388.

Example D54: 3-(Cyclopropylmethyl) 5-methyl 2-amino-4-(7-cyano-6-(trifluoromethyl)benzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

[0920] Method D using morpholine at room temperature overnight yielded the title compound as a yellow solid (0.003 g, 3 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.09 (d, J = 8.4 Hz, 1H), 7.44 (d, J = 8.2 Hz, 1H), 7.35 (s, 1H), 6.03 - 5.91 (m, 3H), 5.24 (s, 1H), 3.84 (d, J = 7.0 Hz, 2H), 3.58 (s, 3H), 2.22 (s, 3H), 0.88 - 0.77 (m, 1H), 0.50 - 0.22 (m, 2H), 0.14 - -0.10 (m, 2H).

Example D55: 5-Methyl 3-prop-2-yn-1-yl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

[0921] Method D using morpholine at room temperature overnight yielded the title compound as a yellow solid (0.005 g, 4 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.34 (d, 1H), 7.63 (d, 1H), 7.49 (t, 1H), 7.31 (s, 1H), 6.1 (bs, 3H), 5.44 (s, 1H), 4.44 - 4.26 (m, 2H), 3.59 (s, 3H), 2.42-2.24 (m, 4H).

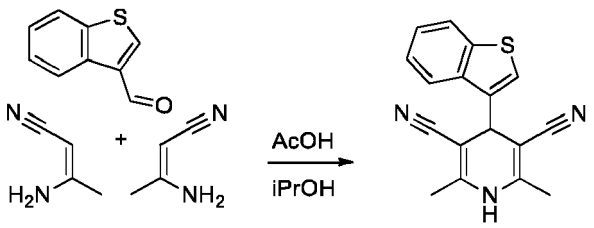
Example D56: 3-(Cyclopropylmethyl) 5-methyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-(trifluoromethyl)-1,4-dihydropyridine-3,5-dicarboxylate

[0922] Method D using morpholine at room temperature overnight yielded the title compound as a yellow solid (0.007 g, 5 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.33 (d, 1H), 7.65 (d, 1H), 7.44 - 7.35 (m, 1H), 7.31 (s, 1H), 6.09 (bs, 2H), 5.96 (bs, 1H), 5.48 (s, 1H), 3.76 (d, 2H), 2.38 (s, 3H), 0.98 - 0.81 (m, 1H), 0.46 - 0.26 (m, 2H), 0.14 - -0.11 (m, 2H).

Method E:

Example E1: 4-(Benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarbonitrile

[0923]



[0924] A mixture of thianaphthene-3-carboxaldehyde (0.5 g, 3.08 mmol), 3-aminocrotonitrile (0.554 mL, 6.74 mmol) and acetic acid (0.076 mL, 3.08 mmol) in isopropyl alcohol (10 mL) was stirred at 100°C for 18 hours. The mixture was allowed to cool to RT and concentrated. The residue was basified with aq. sodium bicarbonate, and the resulting solid was filtered off and washed with cold water and ethyl ether. The desired product was obtained as a light-yellow solid (0.738 g, 82 %).
^{1}H-NMR (400 MHz, DMSO-d_6) δ = 2.06 (s, 6H), 5.00 (s, 1H), 7.36-7.46 (m, 1H), 7.65 (s, 1H), 7.89 (d, 1H), 8.03 (d, 1H), 9.67 (s, 1H).
HPLC-MS: Rt 3.878 min, m/z 292.0 (MH^+).
[0925] The following examples were synthesized according to Method E:

Example E2: 4-(6-hydroxybenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarbonitrile

[0926] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 2.05 (s, 6H), 4.80 (s, 1H), 6.86 (dd, 1H), 7.13 (s, 1H), 7.24 (d, 1H), 7.61 (d, 1H), 9.64 (s, 2H).
[0927] HPLC-MS: Rt 3.285 min, m/z 308.0 (MH^+).

Example E3: 4-(6-methoxybenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarbonitrile

[0928] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 2.06 (s, 6H), 3.81 (s, 3H), 4.84 (s, 1H), 7.00 (d, 1H), 7.20 (s, 1H), 7.50 (d, 1H), 7.71 (d, 1H), 9.69 (s, 1H).
[0929] HPLC-MS: Rt 3.962 min, m/z 322.0 (MH^+).

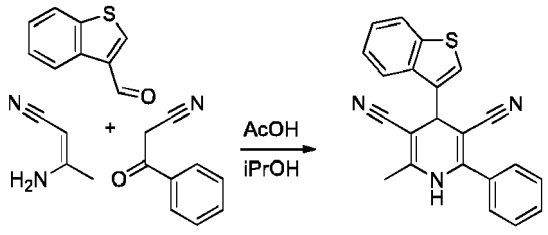
Example E4: 2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3,5-dicarbonitrile

[0930] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 8.90 (s, 1H), 8.47 (s, 1H), 7.78 (s, 1H), 7.72 (d, 1H), 6.91 (t, 1H), 6.17 (s, 1H), 2.65 (s, 6H).
[0931] HPLC-MS: Rt 2.735; m/z 229.9 (MH^+).

Method F:

Example F1: 4-(benzo[b]thiophen-3-yl)-2-methyl-6-phenyl-1,4-dihydropyridine-3,5-dicarbonitrile

[0932]



[0933] A mixture of thianaphthene-3-carboxaldehyde (0.104 g, 0.64 mmol), 3-aminocrotonitrile (0.052 g, 0.64 mmol), benzoylacetonitrile (0.0897 g, 0.62 mmol) and acetic acid (0.035 mL, 0.64 mmol) in isopropyl alcohol (3.5 mL) was heated to 100°C and left to stir for 16 hours. The mixture was allowed to cool to RT and concentrated. The residue was basified with aq. sodium bicarbonate, and the resulting solid was filtered off and purified by column chromatography (3:1 Hexane: Ethyl acetate) rendering a light-yellow solid (0.0162 g, 7 %).
^{1}H-NMR (400 MHz, DMSO-d_6) δ = 2.12 (s, 3H), 5.17 (s, 1H), 7.39-7.49 (m, 2H), 7.50-7.59 (m 5H), 7.78 (s, 1H), 8.01

(dd, 1H), 8.06 (dd, 1H), 9.92 (s, 1H).
HPLC-MS: Rt 4.329 min, m/z 354.1 (MH^+).
[0934] The following examples were synthesized according to Method F.

Example F2: 4-(benzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3,5-dicarbonitrile

[0935] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 0.95 (s, 4H), 2.06 (s, 3H), 4.98 (s, 1H), 7.41 (s, 2H), 7.64 (s 1H), 7.84 (s, 1H), 8.03 (s, 1H), 8.82 (s, 1H).
[0936] HPLC-MS: Rt 4.138 min, m/z 318.0 (MH^+).

Example F3: 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carbonitrile

[0937] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 2.00 (s, 6H), 2.31 (s, 3H), 5.16 (s, 1H), 7.30-7.48 (m, 3H), 7.97 (d 1H), 8.04 (d, 1H), 9.30 (s, 1H).
[0938] HPLC-MS: Rt 3.816 min, m/z 175.1 (MH^+-134).

Example F4: Ethyl 4-(benzo[b]thiophen-3-yl)-5-cyano-2,6-dimethyl-1,4-dihydropyridine -3-carboxylate

[0939] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 0.90 (t, 3H), 2.02 (s, 3H), 2.30 (s, 3H), 3.85 (dd, 2H), 5.02 (s, 1H), 7.31-7.45 (m 3H), 7.91 (d, 1H), 7.96 (d, 1H), 9.30 (s, 1H).
[0940] HPLC-MS: Rt 4.418 min, m/z 205.1 (MH^+-134).

Example F5: Ethyl 4-(benzo[b]thiophen-3-yl)-5-cyano-2-methyl-6-phenyl-1,4-dihydropyridine-3-carboxylate

[0941] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 0.98 (t, 3H), 2.37 (s, 3H), 3.92 (q, 2H), 5.17 (s, 1H), 7.41 (ddd 2H), 7.49 (d, 5H), 8.00 (t, 2H), 9.60 (s, 1H).
[0942] HPLC-MS: Rt 4.946 min, m/z 267.1 (MH^+-134).

Example F6: Ethyl 4-(benzo[b]thiophen-3-yl)-5-cyano-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate

[0943] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 0.80-0.98 (m, 6H), 0.96 -1.06 (m, 1H), 2.03 (s, 3H), 2.73-2.84 (m, 1H), 3.82-3.95 (m, 2H), 5.02 (s, 1H), 7.32 (s, 1H), 7.33-7.44 (m, 2H), 7.90 (d, 1H), 7.96 (d, 1H), 8.23 (s, 1H).
[0944] HPLC-MS: Rt 4.693 min, m/z 231.1 (MH^+-134).

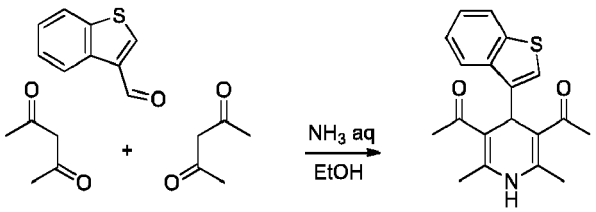
Example F7: Methyl 4-(benzo[b]thiophen-3-yl)-5-cyano-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate

[0945] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 0.79-0.95 (m, 3H), 1.02 (ddd, 1H), 2.03 (s, 3H), 2.78 (dq, 1H), 3.45 (s, 3H), 5.01 (s,1H), 7.30 (s, 1H), 7.39 (dt, 2H), 7.90 (d, 1H),7.96 (dd, 1H), 8.28 (s, 1H).
[0946] HPLC-MS: Rt 4.438 min, m/z 217.1 (MH^+-134).

Method G:

Example G1: 1,1'-(4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-diyl)diethanone

[0947]



[0948] A mixture of thianaphthene-3-carboxaldehyde (0.2 g, 1.23 mmol), acetylacetone (0.25 mL, 2.47 mmol) and aqueous ammonium hydroxide solution (38-40%, 0.12 mL) in ethanol (1 mL) was heated to 90°C and left to stir for 16 hours. The mixture was allowed to cool to RT and was then poured into 10 ml of cold water. The precipitate formed was filtered off, dried and washed with cold diethyl ether. The desired product was obtained as a strongly yellow solid (0.193

g, 48 %).
^{1}H-NMR (400 MHz, DMSO-d_6) δ = 2.17 (s, 6H), 2.29 (s, 6H), 5.52 (s, 1H), 7.23 (s, 1H), 7.33 (dt 2H), 7.88 (d, 1H), 8.12 (d, 1H), 9.08 (s, 1H).
HPLC-MS: Rt 3.668 min, m/z 192.1 (MH^+-134).

[0949] The following examples were synthesized according to Method G.

Example G2: 1,1'-(4-(6-hydroxybenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-diyl)bis(ethan-1-one)

[0950] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 2.28 (s, 12H), 5.29 (s, 1H), 6.76 (d, 2H), 7.10 (s 1H), 7.45 (d, 1H), 9.10 (s, 1H), 9.40 (s, 1H).
[0951] HPLC-MS: Rt 2.950 min, m/z 192.1(MH^+-150).

Example G3: 1,1'-(4-(6-Methoxybenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-diyl)diethanone

[0952] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 2.29 (d, 12H), 3.75 (s, 3H), 5.32 (s, 1H), 6.86 (d 1H), 6.89 (dd, 1H), 7.36 (d, 1H), 7.55 (d, 1H), 9.12 (s, 1H).
[0953] HPLC-MS: Rt 3.676 min, m/z 192 (MH^+-164).

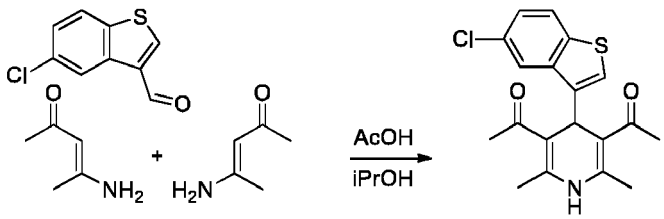
Example G4: 1,1'-(4-(Benzo[b]thiophen-3-yl)-2,6-dicyclopropyl-1,4-dihydropyridine-3,5-diyl)diethanone

[0954] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 0.69 (dd, 2H), 0.74 (dd, 4H), 0.78-0.84 (m, 2H), 2.18-2.25 (m, 2H), 2.27 (s, 6H), 5.69 (s, 1H), 7.21 (s 1H), 7.26-7.36 (m, 2H), 7.89 (d, 1H), 7.97 (d, 1H), 83.99 (s, 1H).

Method H:

Example H1: 1,1'-(4-(5-chlorobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-diyl)diethanone

[0955]



[0956] A mixture of 5-chlorobenzo[b]thiophene-3-carbaldehyde (0.05 g, 0.26 mmol), 4-amino-3-penten-2-one (0.60 g, 0.52 mmol) and acetic acid (0.015 mL) in isopropanol (1.5 mL) was heated to 100°C and left to stir for 16 hours. The mixture was allowed to cool to RT and was then treated with saturated aqueous sodium bicarbonate solution (10 mL). The solid was filtered off, washed with water, dried and purified by column chromatography (3:1 hexane: ethyl acetate) affording a fine yellow solid (8.8 mg, 9.5%).
^{1}H-NMR (400 MHz, DMSO-d_6) δ = 2.17 (s, 6H), 2.31 (s, 6H), 5.44 (s, 1H), 7.33 (d, 2H), 7.92 (d, 1H), 8.23 (s, 1H), 9.15 (s, 1H).
HPLC-MS: Rt 4.072 min, m/z 192.1 (MH^+-168).
[0957] The following examples were synthesized according to Method H.

Example H2: 1,1'-(4-(5-bromobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-diyl)diethanone

[0958] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 2.17 (s, 6H), 2.31 (s, 6H), 5.44 (s, 1H), 7.30 (d, 1H), 7.44 (d, 1H), 7.86 (d, 1H), 8.38 (s, 1H), 9.16 (s, 1H).

Example H3: 1,1'-(4-(5-fluorobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-diyl)bis(ethan-1-one)

[0959] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 9.15 (s, 1H), 7.92 (dd, J = 8.1, 4.2 Hz, 2H), 7.34 (s, 1H), 7.20 (td, J = 8.8, 2.3 Hz, 1H), 5.44 (s, 1H), 2.32 (s, 6H), 2.18 (s, 6H).

Example H4: 1,1'-(2,6-dimethyl-4-(5-morpholinobenzo[b]thiophen-3-yl)-1,4-dihydropyridine-3,5-diyl)bis(ethan-1-one)

[0960] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 9.11 (s, 1H), 7.70 (d, 1H), 7.49 (d, 1H), 7.20 (s, 1H), 7.09 (dd, 1H), 5.48 (s, 1H), 3.80 (t, 4H), 3.12 (t, 4H), 2.27 (s, 6H), 2.19 (s, 6H).

Example H5: 1,1'-(2,6-dimethyl-4-(5-(4-methylpiperazin-1-yl)benzo[b]thiophen-3-yl)-1,4-dihydropyridine-3,5-diyl)bis(ethan-1-one)

[0961] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 9.12 (s, 1H), 7.67 (d, 1H), 7.48 (d, 1H), 7.19 (s, 1H), 5.48 (s, 1H), 3.80 (t, 4H), 3.12 (t, 4H), 2.27 (s, 6H), 2.19 (s, 6H).

Example H6: 1,1'-(4-(5-(benzylamino)benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-diyl)bis(ethan-1-one)

[0962] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 8.98 (s, 1H), 7.50 (d, 1H), 7.43 (d, 2H), 7.32 (t, 2H), 7.23 (t, 1H), 7.14 (d, 1H), 7.08 (s, 1H), 6,77 (dd, 1H), 6.21 (t, 1H), 5.33 (s, 1H), 4.30 (d, 2H), 2.22 (s, 6H), 2.09 (s, 6H).

Example H7: 3-(3,5-diacetyl-2,6-dimethyl-1,4-dihydropyridin-4-yl)benzo[b]thiophene-5-carbonitrile

[0963] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 2.17 (s, 6H), 2.33 (s, 6H), 5.49 (s, 1H), 7.43 (s, 1H), 7.67 (dd, 1H), 8.13 (d, 1H), 8.66 (s, 1H), 9.20 (s, 1H).
[0964] HPLC-MS: Rt 3.563; m/z 351.1 (MH^+).

Example H8: 3-(3,5-diacetyl-2,6-dimethyl-1,4-dihydropyridin-4-yl)benzo[b]thiophene-5-carboxylic acid

[0965] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 9.13 (s, 1H), 8.82 (s, 1H), 7.96 (d, 1H), 7.85 (d, 1H), 7.33 (s, 1H), 5.54 (s, 1H), 2.30 (s, 6H), 2.18 (s, 6H).

Example H9: N-cyclopropyl-3-(3,5-diacetyl-2,6-dimethyl-1,4-dihydropyridin-4-yl)benzo[b]thiophene-5-carboxamide

[0966] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 9.13 (s, 1H), 8.64 (s, 1H), 8.42 (d, 1H), 7.93 (d, 1H), 7.72 (d, 1H), 7.32 (s, 1H), 5.53 (s, 1H), 2.89 (m, 1H), 2.29 (s, 6H), 2.18 (s, 6H), 0.73 (m, 2H), 0.61 (m, 2H).

Example H10: N-(cyclopropylmethyl)-3-(3,5-diacetyl-2,6-dimethyl-1,4-dihydropyridin-4-yl)benzo[b]thiophene-5-carboxamide

[0967] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 9.12 (s, 1H), 8.68 (s, 1H), 8.50 (d, 1H), 7.95 (d, 1H), 7.78 (d, 1H), 7.32 (s, 1H), 5.53 (s, 1H), 3.26 (t, 2H), 2.29 (s, 6H), 2.18 (s, 6H), 1.08 (m, 1H), 0.45 (m, 2H), 0.28 (m, 2H).

Example H11: 1,1'-(2,6-Dimethyl-4-(5-(4-methylpiperazine-1-carbonyl)benzo[b]thiophen-3-yl)-1,4-dihydropyridine-3,5-diyl)bis(ethan-1-one)

[0968] ^{1}H-NMR (400 MHz, $CDCl_3$) δ = 8.21 (s, 1H), 7.82 (d, 1H), 7.42 (d, 1H), 7.21 (d, 1H), 6.17 (s, 1H), 5.61 (s, 1H), 3.77 (d, 4H), 2.54 (m, 4H), 2.38 (s, 3H), 2.34 (s, 3H), 2.22 (s, 3H), 2.08 (s, 3H).

Example H12: 1,1'-(2,6-Dimethyl-4-(5-(morpholine-4-carbonyl)benzo[b]thiophen-3-yl)-1,4-dihydropyridine-3,5-diyl)bis(ethan-1-one)

[0969] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 9.15 (s, 1H), 8.21 (s, 1H), 7.97 (d, 1H), 7.35 (dd, 1H), 7.32 (s, 1H), 5.50 (s, 1H), 3.67 (m, 8H), 2.31 (s, 6H), 2.16 (s, 6H).

Example H13: 1,1'-(2,6-Dimethyl-4-(thieno[3,2-c]pyridin-3-yl)-1,4-dihydropyridine-3,5-diyl)bis(ethan-1-one)

[0970] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 9.35 (s, 1H), 9.18 (s, 1H), 8.36 (d, 1H), 7.95 (d,1H), 7.34 (s, 1H), 5.58 (s, 1H), 2.31 (s, 6H), 2.19 (s, 6H).

Example H14: 1,1'-(2,6-Dimethyl-4-(thieno[2,3-c]pyridin-3-yl)-1,4-dihydropyridine-3,5-diyl)bis(ethan-1-one)

[0971] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 9.17 (s, 1H), 9.13 (d, 1H), 8.44 (d, 1H), 8.05 (dd, 1H), 7.57 (s, 1H), 5.51 (s, 1H), 2.31 (s, 6H), 2.17 (s, 6H).

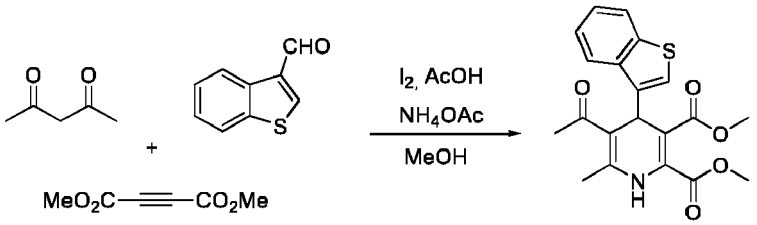
Example H15: 1,1'-(2,6-Dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3,5-diyl)bis(ethan-1-one)

[0972] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 9.15 (s, 1H), 8.49 (d, 2H), 7.43 (s, 1H), 7.33 (s, 1H), 5.47 (s, 1H), 2.32 (s, 6H), 2.18 (s, 6H).

Method I:

Example I1: Dimethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-2,3-dicarboxylate

[0973]



[0974] A mixture of benzo[b]thiophene-3-carbaldehyde (0.20 g, 1.23 mmol), pentane-2,4-dione (0.123 g, 1.23 mmol), dimethyl but-2-ynedioate (0.182 mL, 1.48 mmol), ammonium acetate (0.143 g, 1.85 mmol), iodine (0.094 g, 0.37 mmol) and two drops of acetic acid were stirred in methanol (3 mL) at 60°C for 12h. The solvent was removed under reduced pressure. The residue was dissolved in ethyl acetate and the organic layer was washed twice with saturated NaS_2O_3 solution and brine, dried (Na_2SO_4), filtered and concentrated. The residue was purified by column chromatography (2:1 hexane: ethyl acetate) affording a yellow solid (0.028 g, 6%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.94 - 7.80 (m, 2H), 7.46 - 7.29 (m, 2H), 7.19 (s, 1H), 6.38 (bs, 1H), 5.38 (s, 1H), 3.81 (s, 3H), 3.52 (s, 3H), 2.43 (s, 3H), 2.04 (s, 3H).
HRMS (APCI) m/z calculated $C_{20}H_{20}NO_5S$ [M^{+1}]: 386.1056, found: 386.1058.

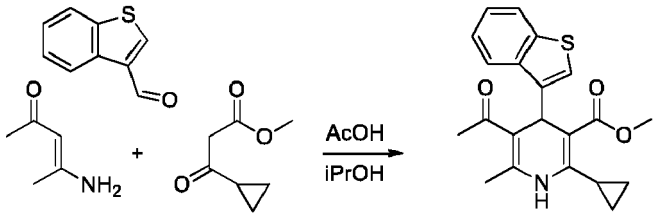
Example I2: Dimethyl 5-acetyl-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-2,3-dicarboxylate

[0975] The title compound was prepared according to Method I affording a yellow solid (0.04 g, 2%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.24 (d, J = 7.9 Hz, 1H), 7.70 (d, J = 7.2 Hz, 1H), 7.50 (t, J = 7.9 Hz, 1H), 7.34 (s, 1H), 6.43 (bs, 1H), 5.41 (s, 1H), 3.84 (s, 3H), 3.55 (s, 3H), 2.44 (s, 3H), 2.11 (s, 3H).
HRMS (APCI) m/z calculated $C_{21}H_{19}N_2O_5S$ [M^{+1}]: 411.1009, found: 411.1006.

Method J:

Example J1: Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate

[0976]



[0977] A mixture of thianaphthene-3-carboxaldehyde (0.106 g, 0.65 mmol), methyl 3-cyclopropyl-3-oxopropanoate (0.071 g, 0.72 mmol) and 4-amino-3-penten-2-one (0.088 g, 0.61 mmol) and acetic acid (0.035 mL) in isopropylalcohol

(1.5 mL) was heated to 100°C and left to stir for 19 hours. The mixture was allowed to cool to RT and was then treated with saturated aqueous sodium bicarbonate solution (10 mL). The solid was filtered off, washed with water, dried and purified by column chromatography (4:1 hexane: ethyl acetate) affording a fine yellow solid (0.075 g, 44 %).
^{1}H-NMR (400 MHz, DMSO-d_6) δ = 0.76 (s, 2H), 0.96 (d, 2H), 2.12 (s, 3H), 2.33 (s, 3H), 2.69 (s, 1H), 3.58 (s, 3H), 5.43 (s, 1H), 7.15 (s, 1H), 7.31 (s, 1H), 7.38 (s, 1H), 7.90 (s, 2H), 8.05 (d, 1H).
HPLC-MS: Rt 4.302 min, m/z 234.1 (MH^+-133).

[0978] A second reaction product was isolated by column chromatography:

Example J1-a: Dimethyl 4-(benzo[b]thiophen-3-yl)-2,6-dicyclopropyl-1,4-dihydropyridine-3,5-dicarboxylate

[0979] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 0.56 (s, 2H), 0.82 (s, 2H), 0.90 (d, 2H), 1.04 (s, 2H), 2.56 (m, 2H), 3.55 (s, 5H), 5.37 (s, 1H), 7.05 (s, 1H), 7.11 (s 1H), 7.32 (t, 1H), 7.39 (t, 1H), 7.90 (d, 1H), 7.98 (s, 1H).

[0980] HPLC-MS: Rt 4.935; m/z 276.1 (MH^+).

[0981] The following examples were synthesized according to Method J.

Example J2: Ethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

[0982] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 1.1 (t, 3H), 2.11 (s, 3H), 2.25 (s, 3H), 2.31 (s, 3H), 3.99 (d, 2H), 5.40 (s, 1H), 7.23 (s, 1H), 7.31 (t 1H), 7.37 (m, 1H), 7.89 (d, 1H), 8.08 (d, 1H), 9.02 (s, 1H).

[0983] HPLC-MS: Rt 4.284 min, m/z 222.1 (MH^+-134).

Example J3: Methyl 5-acetyl-4-(5-chlorobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

[0984] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 2.13 (s, 3H), 2.25 (s, 3H), 2.33 (s, 3H), 3.54 (s, 3H), 5.33 (s, 1H), 7.33 (s, 1H), 7.93 (d, 1H), 8.11 (d, 1H), 8.52 (s, 1H), 9.11 (s, 1H). HPLC-MS: Rt 4.431 min, m/z 208.1 (MH^+-168).

Example J6: 1,1'-(4-(benzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3,5-diyl)diethanone

[0985] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 0.72 (m, 2H), 0.80 (m, 2H), 2.16 (s, 3H), 2.26 (d, 1H), 2.33 (s, 6H), 5.60 (s, 1H), 7.21 (s, 1H), 7.32 (dd, 2H), 7.89 (d, 1H), 8.04 (d, 1H), 9.02 (s, 1H).

[0986] HPLC-MS: Rt 4.692; m/z 352.0 (MH^+).

Example J10: 1-(4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-5-(methylsulfonyl)-1,4-dihydro-pyridin-3-yl)ethanone

[0987] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 2.16 (s, 3H), 2.29 (d, 6H), 2.47 (s, 3H), 5.47 (s, 1H), 7.33 (t, 1H), 7.43 - 7.37 (m, 2H), 7.93 (d, 1H), 8.07 (d, 1H), 9.26 (s, 1H).

[0988] HPLC-MS: Rt 3.395 min, m/z 228.0 (MH^+-134).

Example J11: Methyl 5-acetyl-4-(5-fluorobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

[0989] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 9.10 (s, 1H), 7.93 (dd, J = 8.8, 5.2 Hz, 1H), 7.81 (dd, J = 11.0, 2.5 Hz, 1H), 7.35 (s, 1H), 7.20 (td, J = 8.8, 2.6 Hz, 1H), 5.33 (s, 1H), 3.54 (s, 3H), 2.32 (s, 3H), 2.26 (s, 3H), 2.12 (s, 3H).

[0990] HPLC-MS: Rt 4.345; m/z 360.0 (MH^+).

Example J12: Methyl 5-acetyl-4-(5-bromobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

[0991] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 9.11 (s, 1H), 8.26 (d, 1H), 7.88 (d, 1H), 7.45 (d, 1H), 7.31 (s, 1H), 5.34 (s, 1H), 3.58 (s, 3H), 2.34 (s, 3H), 2.25 (s, 3H), 2.16 (s, 3H).

Example J13: Methyl 5-acetyl-4-(5-cyanobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

[0992] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 9.16 (s, 1H), 8.53 (s, 1H), 8.15 (d, 1H), 7.67 (d, 1H), 7.46 (s, 1H), 5.40 (s, 1H), 3.55 (s, 3H), 2.35 (s, 3H), 2.27 (s, 3H), 2.17 (s, 3H).

Example J14: 3-(3-acetyl-5-(methoxycarbonyl)-2,6-dimethyl-1,4-dihydropyridin-4-yl)benzo[b]thiophene-5-carboxylic acid

[0993] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 12.94 (s, 1H), 9.12 (s, 1H), 8.77 (s, 1H), 8.00 (d, 1H), 7.85 (d, 1H), 7.32 (s,

1H), 5.52 (s, 1H), 3.56 (s, 3H), 2.35 (s, 3H), 2.24 (s, 3H), 2.12 (s, 3H).

Example J15: Methyl 5-acetyl-4-(5-(cyclopropylcarbamoyl)benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

[0994] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 9.06 (s, 1H), 8.59 (s, 1H), 8.45 (d, 1H), 7.91 (d, 1H), 7.72 (dd, 1H), 7.26 (s, 1H), 5.39 (s, 1H), 3.53 (s, 3H), 2.85 (m, 1H), 2.37 (s, 3H), 2.19 (s, 3H), 2.06 (s, 3H), 0.69 (m, 2H), 0.58 (m, 2H).

Example J16: Methyl 5-acetyl-4-(5-((cyclopropylmethyl)carbamoyl)benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

[0995] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 9.10 (s, 1H), 8.66 (s, 1H), 8.60 (d, 1H), 7.97 (d, 1H), 7.81 (d, 1H), 7.30 (s, 1H), 5.43 (s, 1H), 3.57 (s, 3H), 3.20 (m, 2H), 2.85 (m, 1H), 2.34 (s, 3H), 2.22 (s, 3H), 2.10 (s, 3H), 0.45 (m, 2H), 0.26 (m, 2H).

Example J17: Methyl 5-acetyl-2,6-dimethyl-4-(5-(4-methylpiperazine-1-carbonyl)benzo[b]thiophen-3-yl)-1,4-dihydropyridine-3-carboxylate

^{1}H-NMR (400 MHz, $CDCl_3$) δ = 8.22 (s, 1H), 7.82 (d, 1H), 7.36 (dd, 1H), 7.22 (d, 1H), 5.94 (s, 1H), 5.46 (s, 1H), 3.77 (d, 4H), 3.65 (s, 3H), 2.53 (m, 4H), 2.38 (s, 3H), 2.36 (s, 3H), 2.32 (s, 3H), 2.12 (s, 3H).

Example J18: Methyl 5-acetyl-2,6-dimethyl-4-(5-(morpholine-4-carbonyl)benzo[b]thiophen-3-yl)-1,4-dihydropyridine-3-carboxylate

[0996] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 9.11 (s, 1H), 8.13 (s, 1H), 7.97 (d, 1H), 7.35 (d, 1H), 7.32 (s, 1H), 5.39 (s, 1H), 3.64 (m, 8H), 3.36 (s, 3H), 2.32 (s, 3H), 2.25 (s, 3H), 2.12 (s, 3H).

Example J19: Methyl 5-acetyl-2,6-dimethyl-4-(thieno[3,2-c]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[0997] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 9.27 (d, 1H), 9.13 (s, 1H), 8.36 (d, 1H), 7.97 (dd,1H), 7.35 (s, 1H), 5.48 (s, 1H), 3.52 (s, 3H), 2.32 (s, 3H), 2.27 (s, 3H), 2.14 (s, 3H).

Example J20: Methyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-c]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[0998] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 9.15 (s, 1H), 9.12 (s, 1H), 8.46 (d, 1H), 7.97 (dd,1H), 7.59 (s, 1H), 5.41 (s, 1H), 3.52 (s, 3H), 2.32 (s, 3H), 2.27 (s, 3H), 2.12 (s, 3H).

Example J21: Methyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[0999] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 9.10 (s, 1H), 8.50 (dd, 1H), 8.40 (dd, 1H), 7.45 (dd,1H), 7.35 (s, 1H), 5.36 (s, 1H), 3.52 (s, 3H), 2.32 (s, 3H), 2.27 (s, 3H), 2.13 (s, 3H).

Example J22: Methyl 5-acetyl-2-cyclopropyl-4-(5-fluorobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

[1000] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 0.76 (m, 1H), 0.87 (m, 2H), 1.05 (m, 1H), 2.14 (s, 3H), 2.33 (s, 3H), 2.70 (m, 1H), 3.57 (s, 3H), 5.34 (s, 1H), 7.21 (t, 1H), 7.27 (s, 1H), 7.80 (s, 1H), 7.93 (dd, 1H), 7.96 (s, 1H).
[1001] HPLC-MS: Rt 4.645 m/z 234.1 (MH^+).
[1002] A second reaction product was isolated by column chromatography:

Example J22-a: Dimethyl 2,6-dicyclopropyl-4-(5-fluorobenzo[b]thiophen-3-yl)-1,4-dihydropyridine-3,5-dicarboxylate

[1003] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 0.60 (m, 2H), 0.68 (m, 2H), 1.00 (m, 4H), 2.76 (m, 2H), 3.61 (s, 6H), 5.42 (s, 1H), 5.54 (s, 1H), 7.05 (t, 1H), 7.14 (s, 1H), 7.71 (m, 1H).
[1004] HPLC-MS: Rt 5.256; m/z 428.1 (MH^+).

Example J23: Methyl 5-acetyl-2-cyclopropyl-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[1005] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 8.51 (dd, 1H), 8.39 (dd, 1H), 7.95 (s, 1H), 7.44 (dd, 1H), 7.27 (s, 1H), 5.38

(s, 1H), 3.56 (s, 3H), 2.71 (dd, 1H), 2.34 (s, 3H), 2.14 (s, 3H), 0.84 (t, 4H).
[1006] A second reaction product was isolated by column chromatography:

Example J23-a: Dimethyl 2,6-dicyclopropyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3,5-dicarboxylate

[1007] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 0.57 (q, 2H), 0.83 (m, 2H), 0.91 (t, 2H), 1.04 (q, 2H), 2.57 (td, 2H), 3.54 (s, 6H), 5.31 (s, 1H), 7.09 (s, 1H), 7.26 (s, 1H), 7.45 (dd, 1H), 8.30 (dd, 1H),8.52 (m, 1H).
[1008] HPLC-MS: Rt 4.848; m/z 411.0 (MH^+).

Example J24: Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dicyclopropyl-1,4-dihydropyridine-3-carboxylate

[1009] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 0.81 (m, 7H), 1.07 (dt, 1H), 2.14 (m, 1H), 2.28 (s, 3H), 2.74 (m, 1H), 3.57 (s, 3H), 5.49 (s, 1H), 7.14 (s, 1H), 7.31 (t, 1H), 7.36 (t, 1H), 7.90 (m, 2H), 7.98 (d, 1H).
[1010] HPLC-MS: Rt 4.670; m/z 260.1 (MH^+).

Example J25: Methyl 5-acetyl-4-(5-chlorobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate

[1011] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 0.84 (m, 3H), 1.05 (m, 1H), 2.15 (s, 3H), 2.34 (s, 3H), 2.70 (ddd, 1H), 3.58 (s, 3H), 5.35 (s, 1H), 7.26 (s, 1H), 7.35 (dd, 1H), 7.94 (d, 1H), 7.97 (s, 1H), 8.08 (d, 1H).
[1012] HPLC-MS: Rt 5.312; m/z 402.9 (MH^+).
[1013] A second reaction product was isolated by column chromatography:

Example J25-a: Dimethyl 4-(5-chlorobenzo[b]thiophen-3-yl)-2,6-dicyclopropyl-1,4-dihydropyridine-3,5-dicarboxylate

[1014] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 2.28 (s, 6H), 3.50 (s, 6H), 5.26 (s, 1H), 7.33 (s, 2H), 7.93 (d, 1H), 8.00 (s, 1H), 9.10 (s, 1H).
[1015] HPLC-MS: Rt 4.773; m/z 224.1 (MH^+).

Example J26: Methyl 5-acetyl-4-(7-bromobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate

[1016] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 0.82 (m, 3H), 1.05 (dq, 1H), 2.13 (s, 3H), 2.33 (s, 3H), 2.69 (m, 1H), 3.56 (s, 3H), 5.38 (s, 1H), 7.28 (s, 1H), 7.37 (t, 1H), 7.57 (d, 1H), 7.93 (s, 1H), 8.10 (d, 1H).
[1017] HPLC-MS: Rt 5.355; m/z 448.8 (MH^+).

Example J27: Methyl 5-acetyl-2-cyclopropyl-4-(7-(cyclopropylcarbamoyl)benzo[b] thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

[1018] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 0.59 (m, 2H), 0.71 (m, 2H), 0.84 (dd, 4H), 2.10 (s, 3H), 2.33 (s, 3H), 2.68 (m, 1H), 2.88 (m, 1H), 3.55 (s, 3H), 5.40 (s, 1H), 7.21 (s, 1H), 7.47 (m, 1H), 7.86 (d, 1H), 7.89 (s, 1H), 8.23 (d, 1H), 8.63 (d, 1H).
[1019] HPLC-MS: Rt 4.354; m/z 451.0 (MH^+).

Example J28: Methyl 5-acetyl-4-(7-cyanobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate

[1020] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 0.85 (m, 3H), 1.06 (m, 1H), 2.14 (s, 2H), 2.34 (s, 3H), 2.70 (t, 1H), 3.54 (s, 3H), 5.42 (d, 1H), 7.60 (dd, 1H), 7.38 (s, 1H), 7.91 (d, 1H), 7.98 (s, 1H), 8.42 (dd, 1H).
[1021] HPLC-MS: Rt 4.848; m/z 393.0 (MH^+).

Example J28-a: Dimethyl 4-(7-cyanobenzo[b]thiophen-3-yl)-2,6-dicyclopropyl-1,4-dihydropyridine-3,5-dicarboxylate

[1022] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 0.58 (td, 2H), 0.88 (m, 4H), 1.03 (q, 2H), 2.56 (m, 2H), 3.53 (s, 6H), 5.36 (s, 1H), 7.10 (s, 1H), 7.38 (s, 1H), 7.62 (m, 1H), 7.92 (d, 1H), 8.32 (d, 1H).
[1023] HPLC-MS: Rt 5.493; m/z 435.0 (MH^+).

Example J29: Methyl 5-acetyl-2-cyclopropyl-4-(7-(methoxycarbonyl) benzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

[1024] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 0.76 (m, 1H), 0.87 (m, 2H), 1.06 (dt, 1H), 2.12 (s, 3H), 2.34 (s, 3H), 2.69 (m, 1H), 3.55 (s, 3H), 3.93 (s, 3H), 5.43 (s, 1H), 7.28 (s, 1H), 7.57 (t, 1H), 7.92 (s, 1H), 8.04 (d, 1H), 8.39 (d, 1H).
[1025] HPLC-MS: Rt 4.875; m/z 426.1 (MH^+).
[1026] A second reaction product was isolated by column chromatography:

Example J29-a: Dimethyl 2,6-dicyclopropyl-4-(7-(methoxycarbonyl)benzo[b]thiophen-3-yl)-1,4-dihydropyridine-3,5-dicarboxylate

[1027] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 0.56 (td, 2H), 0.87 (m, 4H), 1.05 (td, 2H), 2.57 (m, 2H), 3.53 (s, 6H), 3.93 (s, 3H), 5.38 (s, 1H), 7.06 (s, 1H), 7.27 (s, 1H), 7.58 (t, 1H), 8.05 (d, 1H), 8.30 (d, 1H).
[1028] HPLC-MS: Rt 5.520; m/z 468.1 (MH^+).
[1029] The ester functionality on the benzothiophene ring of methyl 5-acetyl-2-cyclopropyl-4-(7-(methoxycarbonyl) benzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate (Example J29) was hydrolyzed as follows:

Example J30: 3-(3-Acetyl-6-cyclopropyl-5-(methoxycarbonyl)-2-methyl-1,4-dihydropyridin-4-yl)benzo[b]thiophene-7-carboxylic acid

[1030] A mixture of methyl 5-acetyl-2-cyclopropyl-4-(7-(methoxycarbonyl)benzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate (0.004 g, 0.094 mmol) and 1M NaOH (0.47 mL, 0.470 mmol) in 1 mL THF was stirred at 40 °C over the weekend. The reaction mixture was diluted with 0.1 M NaOH and washed with DCM. The aqueous layer was cooled to 0°C and 4M HCl were added until a solid started to precipitate. Then 1M HCl was dropwise added until the pH reached 2-3. The precipitate was filtered off, washed with water and purified by column chromatography (DCM/MeoH) to give the title compound (0.0116 g, 30%).
^{1}H-NMR (400 MHz, DMSO-d_6) δ = 0.83 (m, 2H), 1.06 (m, 2H), 2.12 (s, 3H), 2.34 (s, 3H), 2.69 (m, 1H), 3.56 (s, 3H), 5.43 (s, 1H), 7.24 (s, 1H), 7.54 (t, 1H), 7.91 (s, 1H), 8.01 (d, 1H), 8.34 (d, 1H), 13.46 (s, 1H).
HPLC-MS: Rt 3.039; m/z 410.0 (MH^+).

Example J31: Benzyl 5-acetyl-2-cyclopropyl-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[1031] The title compound was obtained following Method J.
^{1}H-NMR (400 MHz, DMSO-d_6) δ = 0.81 (m, 3H), 1.08 (m, 1H), 2.15 (s, 3H), 2.34 (s, 3H), 2.72 (dt, 1H), 5.06 (d, 2H), 5.41 (s, 1H), 7.17 (dd, 2H), 7.24 (s, 1H), 7.27 (m, 2H), 7.30 (dd, 2H), 8.00 (s, 1H), 8.31 (d, 1H), 8.47 (d, 1H).
HPLC-MS: Rt 4.976; m/z 445.1 (MH^+).

Example J32: Pyridin-4-ylmethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate

[1032] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 0.83 (m, 3H), 1.09 (m, 1H), 2.16 (s, 3H), 2.33 (s, 3H), 2.73 (m, 1H), 5.11 (q, 2H), 5.51 (s, 1H), 7.08 (d, 2H), 7.18 (s, 1H), 7.28 (m, 2H), 7.90 (d, 1H), 8.02 (d, 2H), 8.41 (d, 2H).
[1033] HPLC-MS: Rt 4.673; m/z 445.1 (MH^+).
[1034] A second reaction product was isolated by column chromatography:

Example J32-a: bis(pyridin-4-ylmethyl) 2,6-dicyclopropyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3,5-dicarboxylate

[1035] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 0.62 (m, 2H), 0.86 (dd, 4H) 1.06 (dt, 2H), 2.57 (m, 2H), 5.08 (m, 4H), 5.42 (s, 1H), 7.06 (d, 4H), 7.19 (dd, 1H), 7.28 (s, 1H), 7.33 (s, 1H), 8.15 (dd, 1H), 8.40 (d, 4H), 8.46 (dd, 1H).
[1036] HPLC-MS: Rt 4.445; m/z 565.2 (MH^+).

Example J33: Pyridin-4-ylmethyl 5-acetyl-4-(7-bromobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

[1037] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 2.15 (s, 3H), 2.31 (d, 6H), 5.06 (dd, 2H), 5.43 (s, 1H), 7.00 (d, 2H), 7.24 (t, 1H), 7.39 (s, 1H), 7.53 (d, 1H), 8.08 (d, 1H), 8.38 (d, 2H), 9.18 (s, 1H).
[1038] HPLC-MS: Rt 4.799; m/z 497.0 (MH^+).

Example J34: Pyridin-4-ylmethyl 5-acetyl-4-(5-chlorobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate

[1039] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 0.86 (m, 3H), 1.09 (dd, 1H), 2.18 (s, 3H), 2.34 (s, 3H), 2.75 (ddd, 1H), 5.11 (d, 2H), 5.44 (s, 1H), 7.05 (d, 2H),7.30 (s, 1H) 7.32 (dd, 1H),7.94 (d, 1H), 8.07 (s, 1H), 8.10 (d, 1H), 8.40 (d, 2H).
[1040] HPLC-MS: Rt 5.002; m/z 479.0 (MH^+).

Example J35: Pyridin-4-ylmethyl 5-acetyl-4-(7-cyanobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate

[1041] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 0.86 (m, 3H), 1.10 (m, 1H), 2.18 (s, 3H), 2.35 (s, 3H), 2.75 (t, 1H), 5.08 (dd, 2H), 5.50 (s, 1H), 7.03 (d, 2H), 7.42 (s, 1H), 7.46 (t, 1H), 7.87 (d, 1H), 8.08 (s, 1H), 8.39 (dd, 3H).
[1042] HPLC-MS: Rt 4.603; m/z 470.1 (MH^+).

Example J36: Pyridin-4-ylmethyl 5-acetyl-2-cyclopropyl-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[1043] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 0.85 (dt, 3H), 1.10 (m, 1H), 2.18 (s, 2H), 2.34 (s, 2H), 2.75 (dd, 1H), 5.10 (dd, 2H), 5.45 (s, 1H), 7.06 (d, 2H), 7.32 (m, 2H), 8.06 (s, 1H), 8.36 (d, 1H), 8.40 (d, 2H), 8.48 (d, 1H).
[1044] HPLC-MS: Rt 3.943; m/z 446.1 (MH^+).

Example J37: Benzyl 5-acetyl-2-cyclopropyl-4-(7-(methoxycarbonyl)benzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

[1045] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 0.80 (dd, 3H), 1.08 (d, 1H), 2.13 (s, 3H), 2.34 (s, 3H), 2.71 (t, 1H), 3.93 (s, 3H), 5.05 (s, 2H), 5.47 (s, 1H), 7.18 (d, 2H), 7.26 (s, 4H), 7.42 (t, 1H), 8.00 (m, 2H), 8.32 (d, 1H).
[1046] HPLC-MS: Rt 5.546; m/z 502.2 (MH^+).
[1047] A second reaction product was isolated by column chromatography:

Example J37-a: Dibenzyl 2,6-dicyclopropyl-4-(7-(methoxycarbonyl)benzo[b]thiophen-3-yl)-1,4-dihydropyridine-3,5-dicarboxylate

[1048] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 0.55 (dd, 2H), 0.82 (dd, 4H), 1.05 (m, 2H), 2.57 (m, 2H), 3.93 (s, 3H), 5.01 (q, 4H), 5.44 (s, 1H), 7.15 (d, 4H), 7.26 (m, 8H), 7.99 (d, 1H), 8.12 (d, 1H).
[1049] HPLC-MS: Rt 6.574; m/z 621.3 (MH^+).

Example J38: Benzyl 5-acetyl-4-(7-(methoxycarbonyl)benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

[1050] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 2.11 (s, 3H), 2.28 (s, 3H), 2.32 (s, 3H), 3.92 (s, 3H), 5.00 (s, 2H), 5.44 (s, 1H), 7.14 (d, 2H), 7.24 (d, 3H), 7.33 (s, 1H), 7.41 (dd, 1H), 8.00 (d, 1H), 8.33 (d, 1H), 9.12 (s, 1H).
[1051] HPLC-MS: Rt 5.546; m/z 502.2 (MH^+).

Example J39: Methyl 3-(3,5-diacetyl-2,6-dimethyl-1,4-dihydropyridin-4-yl)benzo[b]thiophene-7-carboxylate

[1052] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 2.16 (s, 6H), 2.31 (s, 6H), 3.92 (s, 3H), 5.52 (s, 1H), 7.34 (s, 1H), 7.55 (t, 1H), 8.03 (d, 1H), 8.50 (d, 1H), 9.13 (s, 1H).
[1053] HPLC-MS: Rt 4.224; m/z 384.1 (MH^+).

Example J40: 3-(3,5-diacetyl-2,6-dimethyl-1,4-dihydropyridin-4-yl)benzo[b]thiophene-7-carbonitrile

[1054] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 2.17 (s, 5H), 2.32 (s, 5H), 5.52 (s, 1H), 7.43 (s, 1H), 7.59 (m, 1H), 7.90 (d, 1H), 8.54 (d, 1H), 9.19 (s, 1H).
[1055] HPLC-MS: Rt 4.212; m/z 351.1 (MH^+).

Example J41: Pyridin-4-ylmethyl 5-acetyl-4-(7-bromobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate

[1056] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 0.85 (m, 3H) 1.09 (t, 1H), 2.16 (s, 3H), 2.34 (s, 3H), 2.73 (m, 1H), 5.10 (d, 2H), 5.45 (s, 1H), 7.05 (d, 2H), 7.24 (m, 1H), 7.31 (s, 1H), 7.54 (d, 1H), 8.06 (m, 2H), 8.40 (d, 2H).
[1057] HPLC-MS: Rt 5.143; m/z 523.1 (MH^+).

Example J42: 4-fluorobenzyl 5-acetyl-2-cyclopropyl-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[1058] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 0.80 (m, 8H), 1.05 (d, 3H), 2.15 (s, 7H), 2.33 (s, 8H), 5.04 (q, 5H), 5.39 (d, 2H), 7.08 (t, 4H), 7.24 (m, 7H), 7.30 (dd, 3H), 7.99 (s, 2H), 8.29 (dd, 2H), 8.48 (dd, 2H).
[1059] HPLC-MS: Rt 5.056; m/z 463.1 (MH^+).
[1060] A second reaction product was isolated by column chromatography:

Example J42-a: bis(4-fluorobenzyl) 2,6-dicyclopropyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3,5-dicarboxylate

[1061] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 0.57 (dd, 2H), 0.82 (m, 6H), 1.02 (d, 2H), 5.01 (d, 4H), 5.34 (d, 1H), 7.19 (m, 8H), 8.05 (dd, 2H), 8.46 (m, 2H).
[1062] HPLC-MS: Rt 6.223; m/z 599.2 (MH^+).

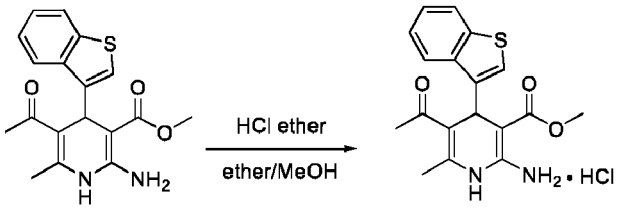
Example J43: 4-cyanobenzyl 5-acetyl-2-cyclopropyl-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[1063] ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 0.83 (m, 3H), 1.09 (m, 1H), 2.16 (s, 3H), 2.34 (s, 3H), 2.73 (m, 1H), 5.14 (dd, 2H), 5.41 (s, 1H), 7.31 (m, 4H), 7.70 (d, 2H), 8.03 (s, 1H), 8.32 (d, 1H), 8.47 (d, 1H).
[1064] HPLC-MS: Rt 4.766; m/z 470.1 (MH^+).

Method K

Example K1: Methyl 5-acetyl-2-amino-4-(benzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate hydrochloride

[1065]



[1066] To a mixture of methyl 5-acetyl-2-amino-4-(benzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate (0.07 g, 0,20 mmol) in DCM/MeOH (1:1, 2 mL), 2M HCl in ether (0.21 mL, 0.40 mmol) was added dropwise at 0°C. The mixture was allowed to warm up to RT and stirred at RT overnight. The solvent was removed under reduced pressure, and the remaining solid was washed with ether and dichloromethane affording a white solid (0.055 g, 71 %). Anal. calculated $C_{18}H_{19}ClN_2O_3S$ (378.08): C, 57.06; H, 5.06; N, 7.39; S, 8.46. Found: C, 56,14; H,5,25; N7.05; S,8.22.
^{1}H-NMR (300 MHz, DMSO-d_6) δ = 12.36 (s, 1H), 10.27 (s, 1H), 9.60 (s, 1H), 8.06 (d, J = 8.0 Hz, 1H), 7.90 (d, J = 8.0 Hz, 1H), 7.63 - 7.40 (m, 2H), 7.40 - 7.14 (m, 1H), 4.98 (s, 1H), 4.34 (s, 1H), 3.81 (s, 3H), 2.44 (s, 3H), 2.17 (s, 3H).

Example K2: Methyl 5-acetyl-2-amino-4-(benzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate trifluoromethanesulfonate

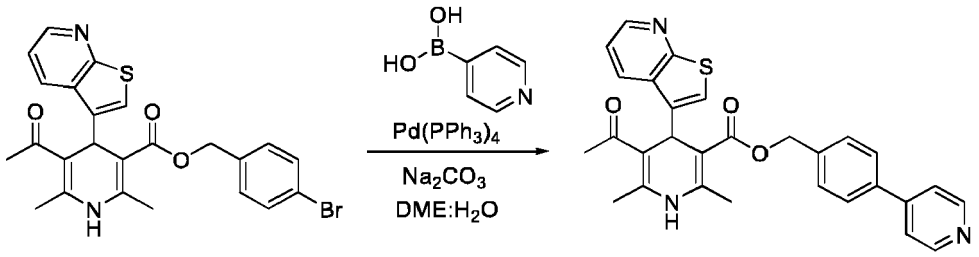
[1067] Method K yielded the title compound as a white solid (0.091 g, 89 %). Anal. calculated $C_{19}H_{19}F_3N_2O_6S_2$ (492.06): C, 46.34; H, 3.89; N, 5.69; S, 13.02. Found: C, 46.28; H, 4.21; N, 5.53; S, 13.15.
^{1}H-NMR (300 MHz, DMSO-d_6) δ = 11.67 (s, 1H), 10.04 (s, 1H), 9.34 (s, 1H), 8.06 (d, *J* = 8.0 Hz, 1H), 7.92 (d, *J* = 7.9

Hz, 1H), 7.65 - 7.46 (m, 2H), 7.41 - 7.17 (m, 1H), 4.99 (s, 1H), 4.24 (s, 1H), 3.81 (s, 3H), 2.42 (s, 3H), 2.17 (s, 3H).

Method L

Example L1: 4-(pyridin-4-yl)benzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4 dihydropyridine-3-carboxylate

[1068]



[1069] A mixture of 4-bromobenzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate (0.030 g, 0.06 mmol), pyridin-4-ylboronic acid (0.011 g, 0.09 mmol), Palladium-tetrakis(triphenylphosphine) (0.003 g, 0.003 mmol) and potassium carbonate (0.019 g, 0.18 mmol) in DME:H_2O (3:1, 1 mL) was heated at 110°C for 3h. The mixture was allowed to cool to RT, filtered over Celite and the solvent was removed under reduced pressure. The residue was purified by column chromatography (dichloromethane: methanol 2%) affording a yellow solid (0.036 g, 61%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.67 (s, 2H), 8.45 (dd, *J* = 4.5, 1.6 Hz, 1H), 8.32 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.54 - 7.47 (m, 4H), 7.25 - 7.17 (m, 3H), 7.13 (dd, *J* = 8.2, 4.6 Hz, 1H), 6.48 (bs, 1H), 5.48 (s, 1H), 5.09 (q, *J* = 15.0 Hz, 2H), 2.36 (s, 6H), 2.16 (s, 3H).
HRMS (IE) m/z calculated $C_{29}H_{25}N_3O_3S$ [M^+]: 495.1617, found: 495.1636.
[1070] The following Examples were prepared following Method L.

Example L2: 4-(pyridin-3-yl)benzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[1071] Yellow solid (0.025 g, 51%).
[1072] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.83 (s, 1H), 8.65 - 8.54 (m, 1H), 8.45 (dd, *J* = 4.6, 1.6 Hz, 1H), 8.33 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.87 (dt, *J* = 8.0, 1.8 Hz, 1H), 7.50 - 7.43 (m, 2H), 7.38 (dd, *J* = 7.9, 4.8 Hz, 1H), 7.26 - 7.20 (m, 2H), 7.18 (s, 1H), 7.15 (dd, *J* = 8.2, 4.6 Hz, 1H), 6.61 (s, 1H), 5.48 (s, 1H), 5.12 (q, *J* = 15.0 Hz, 2H), 2.36 (s, 3H), 2.36 (s, 3H), 2.16 (s, 3H).
[1073] HRMS (IE) m/z calculated $C_{29}H_{25}N_3O_3S$ [M+]: 495.1617, found: 495.1619.

Example L3: 3-(pyridin-4-yl)benzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[1074] Yellow solid (0.037 g, 78%).
[1075] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.65 (d, *J* = 4.8 Hz, 2H), 8.42 (dd, *J* = 4.8, 1.6 Hz, 1H), 8.31 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.55 (dt, *J* = 7.7, 1.5 Hz, 1H), 7.46 - 7.33 (m, 4H), 7.22 (dt, *J* = 7.7, 1.5 Hz, 1H), 7.17 (s, 1H), 7.14 - 7.05 (m, 1H), 6.76 (s, 1H), 5.48 (s, 1H), 5.23 - 5.04 (m, 2H), 2.36 (s, 3H), 2.35 (s, 3H), 2.15 (s, 3H).
[1076] HRMS (IE) m/z calculated $C_{29}H_{25}N_3O_3S$ [M^+]: 495.1566, found: 495.1541.

Example L4: 3-(pyridin-3-yl)benzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[1077] Yellow solid, 0.26 g, 62%).
[1078] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.77 (s, 1H), 8.60 (d, *J* = 4.9 Hz, 1H), 8.42 (dd, *J* = 4.9, 1.6 Hz, 1H), 8.31 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.77 (dt, *J* = 7.9, 1.9 Hz, 1H), 7.49 (dt, *J* = 7.7, 1.5 Hz, 1H), 7.43 - 7.32 (m, 3H), 7.20 (dt, *J* = 7.5, 1.5 Hz, 1H), 7.17 (s, 1H), 7.10 (dd, *J* = 8.2, 4.5 Hz, 1H), 6.62 (s, 1H), 5.47 (s, 1H), 5.15 (q, *J* = 12.5 Hz, 2H), 2.36 (s, 3H), 2.35 (s, 3H), 2.14 (s, 3H).
[1079] HRMS (IE) m/z calculated $C_{29}H_{25}N_3O_3S$ [M^+]: 495.1566, found: 495.1565.

Example L5: 2-(pyridin-4-yl)benzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[1080] Yellow solid (0.023 g, 45%).
[1081] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.75 (s, 1H), 8.52 (s, 1H), 8.41 (dd, *J* = 4.6, 1.6 Hz, 1H), 8.13 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.54 (d, *J* = 5.3 Hz, 1H), 7.48 - 7.31 (m, 2H), 7.19 (dd, *J* = 7.3, 1.6 Hz, 1H), 7.13 (s, 1H), 7.08 - 6.94 (m, 3H), 6.37 (s, 1H), 5.36 (s, 1H), 4.97 (q, *J* = 7.3 Hz, 2H), 2.35 (s, 3H), 2.29 (s, 3H), 2.15 (s, 3H).
[1082] HRMS (IE) m/z calculated $C_{29}H_{26}N_3O_3S$ [M^{+1}]: 496.1689, found: 496.1689.

Example L6: 2-(pyridin-3-yl)benzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[1083] Yellow solid (0.018 g, 48%).
[1084] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.53 (s, 1H), 8.42 (dd, *J* = 4.7, 1.6 Hz, 2H), 8.16 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.45 - 7.27 (m, 4H), 7.25 - 7.16 (m, 2H), 7.14 (s, 1H), 7.09 - 6.94 (m, 1H), 6.42 (s, 1H), 5.38 (s, 1H), 4.97 (q, *J* = 12 Hz, 2H), 2.35 (s, 3H), 2.28 (s, 3H), 2.15 (s, 3H).
[1085] HRMS (IE) m/z calculated $C_{29}H_{26}N_3O_3S$ [M^{+1}]: 496.1689, found: 496.1687.

Example L7: [3,4'-bipyridin]-5-ylmethyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[1086] Yellow solid (0.025 g, 64%).
[1087] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.81 - 8.68 (m, 3H), 8.58 - 8.52 (m, 1H), 8.42 (dd, *J* = 4.6, 1.6 Hz, 1H), 8.32 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.60 (t, *J* = 2.2 Hz, 1H), 7.37 (d, *J* = 5.2 Hz, 2H), 7.17 (s, 1H), 7.14 (dd, *J* = 8.2, 4.6 Hz, 1H), 6.38 (s, 1H), 5.46 (s, 1H), 5.17 (q, *J* = 12 Hz, 2H), 2.36 (s, 6H), 2.16 (s, 3H).
[1088] HRMS (IE) m/z calculated $C_{28}H_{24}N_4O_3S$ [M^+]: 496.1569, found: 496.1556.

Example L8: [3,3'-bipyridin]-5-ylmethyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[1089] Yellow solid (0.022 g, 57%).
[1090] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.77 - 8.62 (m, 3H), 8.55 - 8.50 (m, 1H), 8.41 (dd, *J* = 4.6, 1.6 Hz, 1H), 8.33 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.73 (dt, *J* = 8.1, 1.8 Hz, 1H), 7.56 (t, *J* = 2.1 Hz, 1H), 7.43 (dd, *J* = 8.0, 4.8 Hz, 1H), 7.17 (s, 1H), 7.14 (dd, *J* = 8.2, 4.6 Hz, 1H), 6.54 (s, 1H), 5.45 (s, 1H), 5.26 - 5.04 (m, 2H), 2.36 (s, 6H), 2.15 (s, 3H).
[1091] HRMS (IE) m/z calculated $C_{28}H_{24}N_4O_3S$ [M^+]: 496.1569, found: 496.1580.

Example L9: [2,4'-bipyridin]-5-ylmethyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[1092] Yellow solid (0.014 g, 23%).
[1093] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.73 (d, *J* = 5.1 Hz, 2H), 8.59 (d, *J* = 2.2 Hz, 1H), 8.44 (dd, *J* = 4.6, 1.6 Hz, 1H), 8.31 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.92 - 7.86 (m, 2H), 7.61 (d, *J* = 8.1 Hz, 1H), 7.40 (dd, *J* = 8.1, 2.2 Hz, 1H), 7.18 (s, 1H), 7.14 (dd, *J* = 8.2, 4.6 Hz, 1H), 6.38 (s, 1H), 5.45 (s, 1H), 5.26 - 5.01 (q, *J* = 15 Hz, 2H), 2.36 (s, 6H), 2.16 (s, 3H).
[1094] HRMS (IE) m/z calculated $C_{28}H_{24}N_4O_3S$ [M^+]: 496.1569, found: 496.1563.

Example L10: [2,3'-bipyridin]-5-ylmethyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[1095] Yellow solid (0.032 g, 72%).
[1096] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 9.19 (s, 1H), 8.78 - 8.63 (m, 1H), 8.59 (d, *J* = 2.3 Hz, 1H), 8.45 (dd, *J* = 4.6, 1.6 Hz, 1H), 8.31 (dt, *J* = 8.0, 1.6 Hz, 2H), 7.59 (dd, *J* = 8.0, 0.9 Hz, 1H), 7.47 - 7.36 (m, 2H), 7.18 (s, 1H), 7.17 - 7.11 (m, 1H), 6.31 (s, 1H), 5.45 (s, 1H), 5.22 - 5.04 (q, *J* = 12 Hz, 2H), 2.36 (s, 6H), 2.15 (s, 3H).
[1097] HRMS (IE) m/z calculated $C_{28}H_{24}N_4O_3S$ [M^+]: 496.1569, found: 496.1563.

Example L11: [2,3'-bipyridin]-4-ylmethyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[1098] Yellow solid (0.040 g, 82%).

[1099] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 9.11 - 9.01 (m, 1H), 8.64 (dd, *J* = 5.0, 1.5 Hz, 1H), 8.56 (dd, *J* = 5.0, 0.9 Hz, 1H), 8.43 (dt, *J* = 4.6, 1.2 Hz, 1H), 8.36 (dt, *J* = 8.2, 1.2 Hz, 1H), 8.16 (dq, *J* = 8.0, 1.5, 1.0 Hz, 1H), 7.46 - 7.37 (m, 2H), 7.21 (s, 1H), 7.15 (ddd, *J* = 8.2, 4.6, 0.9 Hz, 1H), 6.96 (dt, *J* = 5.1, 1.2 Hz, 1H), 6.76 (s, 1H), 5.51 (s, 1H), 5.27 - 5.03 (q, *J* = 15 Hz, 2H), 2.38 (d, *J* = 0.9 Hz, 3H), 2.37 - 2.35 (m, 3H), 2.17 (d, *J* = 1.0 Hz, 3H).

[1100] HRMS (IE) m/z calculated $C_{28}H_{24}N_4O_3S$ [M^+]: 496.1569, found: 496.1570.

Example L12: [2,4'-bipyridin]-4-ylmethyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[1101] Yellow solid (0.024 g, 50%).

[1102] ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.78 - 8.62 (m, 2H), 8.57 (d, *J* = 5.0 Hz, 1H), 8.44 (dd, *J* = 4.6, 1.6 Hz, 1H), 8.36 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.84 - 7.66 (m, 2H), 7.45 (s, 1H), 7.21 (s, 1H), 7.15 (dd, *J* = 8.2, 4.6 Hz, 1H), 7.00 (dd, *J* = 5.0, 1.5 Hz, 1H), 6.60 (s, 1H), 5.52 (s, 1H), 5.12 (q, *J* = 12 Hz, 2H), 2.39 (s, 3H), 2.37 (s, 3H), 2.19 (s, 3H).

[1103] HRMS (IE) m/z calculated $C_{28}H_{24}N_4O_3S$ [M^+]: 496.1569, found: 496.1545.

Example L13: Methyl 5-acetyl-2-cyclopropyl-6-methyl-4-(7-(pyridin-4-yl)benzo[b]thiophen-3-yl)-1,4-dihydropyridine-3-carboxylate

[1104] Method L in dioxane/water 3:1 gave the title compound as a yellow solid (0.018 g, 64%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.72 (bs, 2H), 8.21 (dd, *J* = 8.2, 1.1 Hz, 1H), 7.69 - 7.59 (m, 2H), 7.53 (t, *J* = 7.7 Hz, 1H), 7.42 - 7.35 (m, 1H), 7.15 (s, 1H), 5.72 (bs, 1H), 5.52 (s, 1H), 3.69 (s, 3H), 2.61 (tt, *J* = 8.6, 5.7 Hz, 1H), 2.37 (s, 3H), 2.16 (s, 3H), 0.98 (dtq, *J* = 17.6, 8.6, 4.1 Hz, 2H), 0.79 - 0.56 (m, 2H).
HRMS (IE) m/z calculated $C_{26}H_{24}N_2O_3S$ [M^+]: 444.1508, found: 444.1526.

Example L14: Methyl 5-acetyl-2-cyclopropyl-4-(7-cyclopropylbenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

[1105] Method L in toluene/water 19:1 gave the title compound as a yellow solid (0.030 g, 66%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.92 (d, *J* = 8.1 Hz, 1H), 7.32 (t, *J* = 7.7 Hz, 1H), 7.11 (s, 1H), 6.96 (d, *J* = 7.7 Hz, 1H), 5.63 (bs, 1H), 5.47 (s, 1H), 3.67 (d, *J* = 1.4 Hz, 3H), 2.59 (tt, *J* = 8.6, 5.7 Hz, 1H), 2.36 (s, 3H), 2.13 (s, 3H), 2.11 - 2.03 (m, 1H), 1.07 - 0.86 (m, 4H), 0.85 - 0.75 (m, 2H), 0.73 - 0.57 (m, 2H).
HRMS (IE) m/z calculated $C_{24}H_{25}NO_3S$ [M^+]: 407.1555, found: 407.1551.

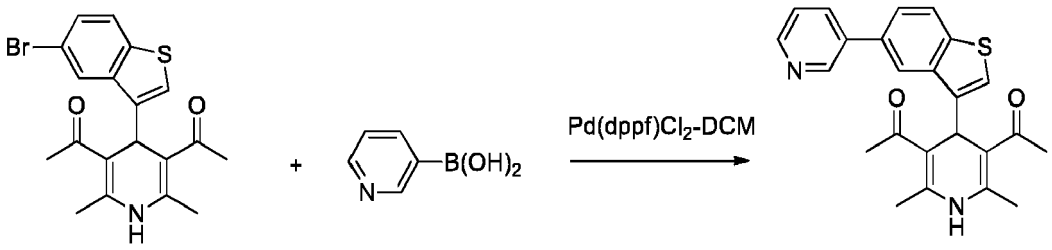
Example L15: 3-(pyridin-4-yl)benzyl 5-acetyl-2-cyclopropyl-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[1106] Method L gave the title compound as a yellow solid (0.018 g, 42 %).
^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm): 8.66 (d, *J* = 4.7 Hz, 2H), 8.44 (dd, *J* = 4.7, 1.4 Hz, 1H), 8.29 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.56 (d, *J* = 7.8 Hz, 1H), 7.46 (s, 1H), 7.44 - 7.35 (m, 3H), 7.23 (d, *J* = 1.4 Hz, 1H), 7.14 - 7.06 (m, 2H), 5.79 (bs, 1H), 5.49 (s, 1H), 5.24 - 5.10 (m, 2H), 2.71 - 2.55 (m, 1H), 2.35 (s, 3H), 2.14 (s, 3H), 1.01 - 0.84 (m, 2H), 0.80 - 0.55 (m, 2H).
HRMS (IE) m/z calculated $C_{31}H_{27}N_3O_3S$ [M^+]: 521.1773, found: 521.1783.
HPLC (95.0%): Rt 31.35 min

Method M

Example M1: 1,1'-(2,6-dimethyl-4-(5-(pyridin-3-yl)benzo[b]thiophen-3-yl)-1,4-dihydropyridine-3,5-diyl)diethanone

[1107]

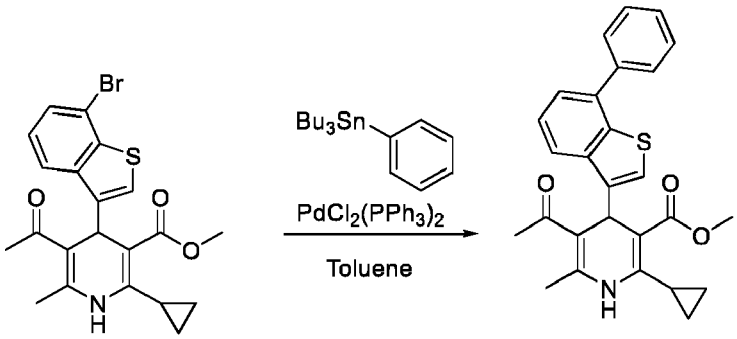


[1108] To a mixture of 1,1'-(4-(5-bromobenzo[*b*]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-diyl)diethanone (53 mg, 0.13 mmol), 3-pyridylboronic acid (24.8 mg, 0.20 mmol) and [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II) complex with dichloromethane (4.6 mg, 0.0056 mmol) in dry DCM (3 mL) under nitrogen atmosphere at RT, aq 2M Cs_2CO_3 (0.40 mmol) was added dropwise. The mixture was then refluxed for 24h under a N_2 stream, cooled to RT, filtered to remove the catalyst and concentrated in vacuum. Column chromatography afforded the title compound.
^{1}H-NMR (400 MHz, DMSO-d_6) δ = 2.20 (s, 6H), 2.32 (s, 6H), 5.60 (s, 1H), 7.30 (s, 1H), 7.56 (dd, 1H), 7.68 (dd, 1H), 8.02 (d, 1H), 8.13 (dd, 1H), 8.52 (d, 1H), 8.61 (s, 1H), 8.97 (s, 1H), 9.17 (s, 1H).
HPLC-MS: Rt 3.645 min, m/z 403.1 (MH^+).

Method N

Example N1: Methyl 5-acetyl-2-cyclopropyl-6-methyl-4-(7-phenylbenzo[b]thiophen-3-yl)-1,4-dihydropyridine-3-carboxylate

[1109]



[1110] A mixture of methyl 5-acetyl-4-(7-bromobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate (0.050 g, 0.11 mmol), tributyl(phenyl) stannane (0.073 mL, 0.22 mmol) and palladium(II)bis(triphenylphosphine)dichloride (0.008 g, 0.011 mmol) in toluene (2 mL) was heated at 90°C for 12 h. The mixture was allowed to cool to RT, filtered over Celite, concentrated and purified by column chromatography (5:1 hexane: ethyl acetate) affording a yellow solid (0.025 g, 50%).
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.15 - 8.06 (m, 1H), 7.72 - 7.64 (m, 2H), 7.53 - 7.29 (m, 5H), 7.12 (s, 1H), 5.62 (s, 1H), 5.51 (s, 1H), 3.70 (s, 3H), 2.61 (tt, *J* = 8.7, 5.7 Hz, 1H), 2.37 (s, 3H), 2.17 (s, 3H), 1.03 - 0.84 (m, 2H), 0.74 - 0.57 (m, 2H).
HRMS (IE) m/z calculated $C_{27}H_{25}NO_3S$ [M^+]: 443.1555, found: 443.1557.

ABBREVIATIONS

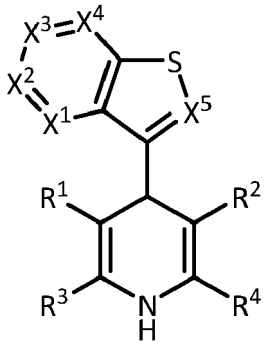
[1111] The followiing abbreviations have been used along the present specification:

ACN:	Acetonitrile
Ac:	Acetyl
Dba:	dibenzylideneacetone
DCM:	Dichloromethane
DIBAL:	Diisobutylaluminium hydride
DIPEA:	N,N-Diisopropylethylamine
DMAP:	4-Dimethylaminopyridine
DME:	1,2-Dimethoxyethane
DMEM:	Dulbecco's Modified Eagle's Medium
DMF:	Dimethylformamide
DMSO:	Dimethylsulfoxide
dppf:	1,1'-bis(diphenylphosphino)ferrocene
EDTA:	Ethylenediaminetetraacetic acid
ESI:	Electrospray ionization
EtOH:	Ethanol
FBS:	Fetal bovine serum
HBSS:	Hank's Balanced Solution

HOBT:	Benzotriazol-1-ol
HPLC:	High performance liquid chromatography
HRMS:	High ressolution mass spectrometry
IE:	Electron ionization
i-PrOH:	Isopropanol
MeOH:	Methanol
MS4A:	4Å Molecular sieves
MW:	molecular weight
NMP:	N-methylpyrrolidone
NMR:	Nuclear magnetic resonance
PEI:	Polyethyleneimine
Ph:	Phenyl
PPA:	Polyphosphoric acid
RT:	Room temperature
Rt:	Retention time
tBut:	ter-butyl
TES:	N-[tris(hydroxymethyl)methyl]-2-aminoethanesulfonic acid
TFA:	Trifluoroacetic acid
THF:	Tetrahydrofurane

Claims

1. A compound of formula (I):



(I)

wherein:

- R^1 is a group selected from:

  a) $-COR^5$,
  b) $-COOR^5$,
  c) -CN,
  d) $-C(O)NH_2$

- R^5 is a group selected from:

  a) linear or branched C_1-C_6 alkyl optionally substituted by 1, 2 or 3 substituents selected from $-N(R^6)R^7$ and $-OR^6$, halogen atom, C_3-C_6 cycloalkyl and alkynyl group,
  b) C_3-C_6 cycloalkyl,

- R^2 is a group selected from:

  a) $-COOR^8$,
  b) $-COR^8$,

c) -C(O)N(R^8)R^9,
d) -CN,
e) -S(O)$_n$$R^8$, wherein n is an integer from 1 to 2,

- R^8 and R^9 are independently selected from:

a) linear or branched C_1-C_6 alkyl optionally substituted by 1, 2 or 3 substituents selected from A^1 or B^2,
b) A^1 group,
c) hydrogen atom,
or

- R^8 and R^9 together with the nitrogen atom to which they are attached form a 5-6 membered heterocycle which optionally comprises 1 heteroatom selected from O and N, and said heterocycle being optionally substituted by 1 or 2 groups independently selected from linear or branched C_1-C_4 alkyl
- R^3 is a group selected from:

a) linear or branched C_1-C_6 alkyl optionally substituted by 1, 2 or 3 substituents selected from halogen atom, - N(R^6)R^7, and -OR^6,
b) C_3-C_6 cycloalkyl optionally substituted by 1, 2 or 3 halogen atoms,
c) hydrogen atom,
d) -NH_2,
e) -CN,

- R^4 is a group selected from:

a) A^1 group,
b) linear or branched C_1-C_6 alkyl optionally substituted by 1, 2 or 3 substituents selected from A^1 or B^2,
c) -N(R^6)R^7,
d) -CN,
e) -CO-H;
f) -CO-Me and
g) CO-OMe
h) hydrogen atom,

- X^1, X^2, X^3, X^4, and X^5 are independently selected from C-B^1, N and C-H,
- A^1 is selected from:

a) C_3-C_6 cycloalkyl which ring is optionally substituted by 1, 2, 3 or 4 substituents selected from =O and B^3;
b) a 3 to 6 membered saturated heterocyclyl ring comprising 1, 2 or 3 heteroatoms selected from O, S and N, and which ring is optionally substituted by 1, 2 or 3 substituents selected from =O and B^3;
c) phenyl or 5 to 6 membered heteroaryl group, either ones are optionally substituted by 1, 2 or 3 substituents selected from B^1;

- each B^1 is independently selected from halogen atom, -CF_3 group, 5 to 6 membered heteroaryl, linear or branched C_1-C_6 alkyl, -CN, -N(R^6)R^7, -OR^6, -C(=O)R^6, -C(=O)OR^6, -C(=O)N(R^6)R^7, -OC(=O)-R^6, -N(R^6)C(=O)R^7, -N$R^7$$SO_2$$R^6$, -$SO_2$N($R^6$)$R^7$, -S$R^6$, -S(O)$R^6$ and -S(O)$_2$$R^6$,
- each B^2 is independently selected from halogen atom, -CN, -N(R^6)R^7, -OR^6, -C(=O)R^6, -C(=O)OR^6, -C(=O)N(R^6)R^7, -OC(=O)-R^6, -N(R^6)C(=O)R^7, -N$R^7$$SO_2$$R^6$, -$SO_2$N($R^6$)$R^7$, -S$R^6$, -S(O)$R^6$, -S(O)$_2$$R^6$, and alkynyl group,- each B^3 is independently selected from halogen atom, linear or branched C_1-C_6 alkyl, -CN, -N(R^6)R^7, -OR^6, -C(=O)R^6, -C(=O)OR^6, -C(=O)N(R^6)R^7, -OC(=O)-R^6, -N(R^6)C(=O)R^7, -N$R^7$$SO_2$$R^6$, -$SO_2$N($R^6$)$R^7$, -S$R^6$, -S(O)$R^6$, -S(O)$_2$$R^6$,

each R^6 and R^7 independently represents:

- hydrogen atom,
- linear or branched C_1-C_{12} alkyl, C_3-C_6 cycloalkyl and C_4-C_6 heterocycloalkyl, which are optionally substituted by 1, 2 or 3 substituents selected from =O (oxo), halogen atom, hydroxy, phenyl, C_3-C_6 cycloalkyl, linear or branched C_1-C_6 alkoxy, amino, alkylamino, dialkylamino, linear or branched C_1-C_6 alkylcarbonyl,

- phenyl or 5 to 6 membered heteroaryl group, which are optionally substituted by 1, 2 or 3 substituents selected from halogen atom, cyano group, linear or branched C_1-C_6 alkyl, linear or branched C_1-C_6 haloalkyl, hydroxy, linear or branched C_1-C_6 alkoxy, amino, alkylamino, dialkylamino;
- R^6 and R^7 form together with the nitrogen atom to which they are attached, a 3-to 8 membered ring which optionally contains a further heteroatom selected from O, N and S, and which ring is optionally substituted by 1, 2 or 3 substituents selected from =O (oxo), linear or branched C_1-C_6 alkyl, linear or branched C_1-C_6 haloalkyl, linear or branched C_1-C_6 alkylcarbonyl;
- with the proviso that when R^1 is -$COOR^5$ and R^2 is -$COOR^8$ then R^4 is not a methyl group,

and pharmaceutically acceptable salts thereof.

2. Compound according to claim 1 wherein X^1, X^2, X^3 and X^5 represent C-H or C-B^1, wherein B^1 represents halogen atom.

3. Compound according to claim 2 wherein X^4 is a group selected from C-B^1 and N.

4. Compound according to claim 3 wherein B^1 is selected from -CN group and halogen atom.

5. Compound according to any one of claims 2 to 4 wherein R^1 is a group selected from -COR^5, -$COOR^5$ and -CN group.

6. Compound according to claim 5 wherein R^5 is selected from:

- C_1-C_4 alkyl wherein the terminal methyl is unsubstituted or substituted by three fluorine atoms (-CF_3)
- C_1-C_3 alkyl optionally substituted at any position by an alkynyl group, and
- C_3-C_5 cycloalkyl,

7. Compound according to any one of claims 2 to 6 wherein R^2 represents -$COOR^8$.

8. Compound according to claim 7 wherein R^8 represents independently:

- linear or branched C_1-C_6 alkyl optionally substituted by 1, 2 or 3 substituents selected from fluorine atoms and C_3-C_5 cycloalkyl optionally substituted by 1, 2 or 3 fluorine atoms, or
- A^1 group, which represents C_3-C_6 cycloalkyl which is optionally substituted by 1, 2 or 3 substituents selected from the group consisting of fluorine atoms and C_1-C_3 alkyl groups.

9. Compound according to any one of claims 2 to 8 wherein R^3 is a group selected from linear or branched C_1-C_4 alkyl and C_3-C_4 cycloalkyl, said groups being optionally substituted by 1, 2 or 3 fluorine atoms.

10. Compound according to any one of claims 2 to 9 wherein R^4 is a group selected from:

- -$N(R^6)R^7$, wherein R^6 and R^7 are independently selected from a hydrogen atom and a linear or branched C_1-C_3 alkyl,
- A^1 group, which represents C_3-C_6 cycloalkyl,
- linear or branched C_1-C_3 alkyl optionally substituted by 1, 2 or 3 substituents selected from 1, 2 or 3 fluorine atoms or 1 hydroxyl group.

11. Compound according to claim 1 wherein X^1, X^2, X^3 and X^5 represent -CH, X^4 represents C-B^1, wherein B^1 represents -CN group or bromine atom, R^1 is a group selected from -$C(O)CH_3$, -$C(O)OCH_3$, -$C(O)OCH_2$-alkynyl and CN, R^2 is a group selected from -C(O)O-lineal or branched C_1-C_5 alkyl group optionally substituted by 1, 2 or 3 fluorine atoms and $C(O)OCH_2$-cyclopropyl optionally substituted by 1, 2 or 3 fluorine atoms, R^3 is a group selected from linear or branched C_1-C_3 alkyl and C_3-C_4 cycloalkyl and R^4 is a group selected from a linear or branched C_1-C_3 alkyl, C_3-C_4 cycloalkyl and -NH_2.

12. Compound according to claim 1 wherein X^1, X^2, X^3 and X^5 represent a -CH, X^4 represents C-B^1, wherein B^1 represents -CN group, R^1 is a group selected from - $C(O)CH_3$, -$C(O)OCH_3$, R^2 is a group selected from -$C(O)OCH_2$-cyclopropyl optionally substituted by 1, 2 or 3 fluorine atoms, and -$C(O)OCH_2$-CF_3, R^3 is a group selected from methyl and cyclopropyl and R^4 is a group selected from cyclopropyl and -NH_2.

13. A compound according to claim 1, which is selected from the group consisting of:

Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydro-pyridine-3-carboxylate
Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydro-pyridine-3-carboxylate (Enantiomer 1)
Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydro-pyridine-3-carboxylate (Enantiomer 2)
5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxamide
1-(4-(benzo[b]thiophen-3-yl)-5-benzoyl-2,6-dimethyl-1,4-dihydropyridin-3-yl)ethan-1-one
Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-6-methyl-2-phenyl-1,4-dihydropyridine-3-carboxylate
1-(4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-5-nicotinoyl-1,4-dihydro pyridin-3-yl)ethan-1-one
Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-6-methyl-1,4-dihydro-[2,3'-bipyridine]-3-carboxylate
2,2,2-trifluoroethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate
5-Acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylic acid
1-(4-(Benzo[b]thiophen-3-yl)-2,6-dimethyl-5-(4-methylpiperazine-1-carbonyl)-1,4-dihydropyridin-3-yl)ethan-1-one
5-Acetyl-4-(benzo[b]thiophen-3-yl)-N,N-diethyl-2,6-dimethyl-1,4-dihydropyridine-3-carboxamide
1-(4-(Benzo[b]thiophen-3-yl)-2,6-dimethyl-5-(morpholine-4-carbonyl)-1,4-dihydropyridin-3-yl)ethan-1-one
2-Methoxyethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate
3-Acetamidopropyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate
Benzyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydro-pyridine-3-carboxylate
2-Morpholinoethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate
2-(Dimethylamino)ethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate
2-Acetamidoethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate
Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2-(methoxymethyl)-6-methyl-1,4-dihydropyridine-3-carboxylate
Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2-((dimethylamino)methyl)-6-methyl-1,4-dihydropyridine-3-carboxylate
Pyridin-4-ylmethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate
4-Methoxybenzyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate
Pyridin-2-ylmethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate
Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-6-methyl-2-(morpholino-methyl)-1,4-dihydropyridine-3-carboxylate
Dimethyl 4-(benzo[b]thiophen-3-yl)-2,6-bis(morpholinomethyl)-1,4-dihydropyridine-3,5-dicarboxylate
2-Hydroxyethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate
1-(4-(Benzo[b]thiophen-3-yl)-5-(cyclopropanecarbonyl)-6-cyclopropyl-2-methyl-1,4-dihydropyridin-3-yl)ethan-1-one
Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2-(1-(tert-butoxycarbonyl) azetidin-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate
(1-(tert-Butoxycarbonyl)piperidin-4-yl)methyl 5-acetyl-4-(benzo[b] thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate
Cyclohexylmethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate
Methyl 4-(benzo[b]thiophen-3-yl)-5-(cyclopropanecarbonyl)-2,6-dicyclopropyl-1,4-dihydropyridine-3-carboxylate
5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-N-phenyl-1,4-dihydropyridine-3-carboxamide
Tetrahydro-2H-pyran-4-yl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate
(Tetrahydro-2H-pyran-4-yl)methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate
Cyclohexyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate
Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2-(2-methoxy-2-oxoethyl)-6-methyl-1,4-dihydropyridine-3-carboxylate
Methyl 5-acetyl-2,6-dimethyl-4-(2-methylbenzo[b]thiophen-3-yl)-1,4-dihydropyridine-3-carboxylate
Cyclopropylmethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate
Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2-(2-methoxyethyl)-6-methyl-1,4-dihydropyridine-3-carboxylate
Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2-((benzyloxy)methyl)-6-methyl-1,4-dihydropyridine-3-carboxylate
Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-6-methyl-2-(phenoxymethyl)-1,4-dihydropyridine-3-carboxylate
Phenethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate
Methyl 4-(benzo[b]thiophen-3-yl)-5-(cyclopropanecarbonyl)-6-cyclopropyl-2-methyl-1,4-dihydropyridine-3-carboxylate
Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-6-methyl-2-(trifluoromethyl)-1,4-dihydropyridine-3-carboxylate
Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-6-benzyl-2-methyl-1,4-dihydropyridine-3-carboxylate
Methyl 4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-5-(2-phenylacetyl)-1,4-dihydropyridine-3-carboxylate

Methyl 4-(benzo[b]thiophen-3-yl)-5-(2-methoxyacetyl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate
Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-6-(methoxymethyl)-2-methyl-1,4-dihydropyridine-3-carboxylate
Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2-(fluoromethyl)-6-methyl-1,4-dihydropyridine-3-carboxylate
Cyclopropylmethyl 5-acetyl-4-(5-fluorobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate
1-(tert-Butoxycarbonyl)piperidin-4-yl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate
Cyclopentylmethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate
Cyclopropylmethyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate
1-methylpiperidin-4-yl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate
Cyclopentyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate
4,4-dimethylcyclohexyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate
Cyclobutyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate
Methyl 5-acetyl-4-(5-fluorobenzo[b]thiophen-3-yl)-6-methyl-2-(trifluoromethyl)-1,4-dihydropyridine-3-carboxylate
Methyl 5-acetyl-2,6-dimethyl-4-(thieno[3,2-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate
Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2-methyl-6-(trifluoromethyl)-1,4-dihydropyridine-3-carboxylate
Cyclopropylmethyl 5-acetyl-4-(5-chlorobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate
Cyclohexylmethyl 5-acetyl-4-(5-chlorobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate
Cyclohexylmethyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate
Cyclopentylmethyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate
Cyclohexyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate
Cyclopentyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate
Methyl 5-acetyl-4-(5-chlorobenzo[b]thiophen-3-yl)-6-methyl-2-(trifluoromethyl)-1,4-dihydropyridine-3-carboxylate
Benzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate
(Tetrahydro-2H-pyran-4-yl)methyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate
Benzyl 5-acetyl-4-(5-fluorobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate
Benzyl 5-acetyl-4-(5-chlorobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate
(Tetrahydro-2H-pyran-4-yl)methyl 5-acetyl-4-(5-chlorobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate
(Tetrahydro-2H-pyran-4-yl)methyl 5-acetyl-4-(5-fluorobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate
Benzyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-6-methyl-2-(trifluoromethyl)-1,4-dihydropyridine-3-carboxylate
Pyridin-4-ylmethyl 5-acetyl-4-(5-fluorobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate
4-Fluorobenzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate
Pyridin-3-ylmethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate
1,1'-(4-(benzo[b]thiophen-3-yl)-2-benzyl-6-methyl-1,4-dihydropyridine-3,5-diyl)bis(ethan-1-one)
1-(5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3-yl)-2-phenylethan-1-one
Methyl 5-acetyl-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-2-(trifluoromethyl)-1,4-dihydropyridine-3-carboxylate
1-(2-methyl-5-(piperidine-1-carbonyl)-4-(thieno[2,3-b]pyridin-3-yl)-6-(trifluoromethyl)-1,4-dihydropyridin-3-yl)ethan-1-one
4-(((5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydro-pyridine-3-carbonyl)oxy)methyl)benzoic acid
Benzyl 5-acetyl-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-2-(trifluoromethyl)-1,4-dihydropyridine-3-carboxylate
Pyridin-3-ylmethyl 5-acetyl-4-(5-fluorobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate
Pyridin-3-ylmethyl 5-acetyl-4-(7-bromobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate
Pyridin-3-ylmethyl 5-acetyl-4-(7-cyanobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate
Pyridin-3-ylmethyl 5-acetyl-4-(5-chlorobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate
Pyridin-3-ylmethyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate
Pyridin-4-ylmethyl 5-acetyl-4-(5-chlorobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate
4-(Cyclopropylcarbamoyl)benzyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate
Pyridin-4-ylmethyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4dihydropyridine-3-carboxylate
4-Bromobenzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate
3-Bromobenzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate
2-Bromobenzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate
(3-Fluoropyridin-4-yl)methyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

Pyrimidin-5-ylmethyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate
(5-Bromopyridin-3-yl)methyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate
2-Phenylpropan-2-yl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate
3-cyanobenzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate
4-cyanobenzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate
(6-Chloropyridin-3-yl)methyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate
3-Morpholinobenzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate
4,4-Dimethylcyclohexyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate
(2-Chloropyridin-4-yl)methyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate
Tetrahydro-2H-pyran-4-yl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate
4,4-Difluorocyclohexyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate
5-Acetyl-N-benzyl-N,2,6-trimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxamide
Oxetan-3-yl 5-acetyl-4-(7-bromobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate
Isopropyl 5-acetyl-4-(7-bromobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate
Methyl 5-acetyl-4-(7-bromobenzo[b]thiophen-3-yl)-6-methyl-2-(trifluoromethyl)-1,4-dihydropyridine-3-carboxylate
Cyclopropylmethyl 5-acetyl-4-(7-bromobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate
Methyl 5-acetyl-2-cyclopropyl-6-methyl-4-(7-(2,2,2-trifluoroacetyl) benzo[b]thiophen-3-yl)-1,4-dihydropyridine-3-carboxylate
2-Phenylpropan-2-yl 5-acetyl-4-(7-bromobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate
Methyl 5-acetyl-2-amino-4-(benzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate
Methyl 2-amino-4-(benzo[b]thiophen-3-yl)-5-(cyclopropanecarbonyl)-6-methyl-1,4-dihydropyridine-3-carboxylate
Methyl 5-acetyl-2-amino-4-(5-fluorobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate
Methyl 5-acetyl-2-amino-4-(7-bromobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate
Methyl 5-acetyl-2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate
Cyclopentyl 5-acetyl-2-amino-4-(7-bromobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate
Dimethyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate
Cyclopentyl 5-acetyl-2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate
Dimethyl 2,6-diamino-4-(benzo[b]thiophen-3-yl)-1,4-dihydropyridine-3,5-dicarboxylate
cyclopropylmethyl 5-acetyl-2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate
4,4-difluorocyclohexyl 5-acetyl-2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate
methyl 2-amino-5-cyano-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate
4-fluorobenzyl 5-acetyl-2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate
methyl 5-acetyl-2-amino-4-(5-fluorothieno[2,3-b]pyridin-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate
methyl 2-acetamido-5-acetyl-4-(5-fluorothieno[2,3-b]pyridin-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate
cyclopentylmethyl 5-acetyl-2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate
3-(cyclopropylmethyl) 5-methyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate
dimethyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-cyclopropyl-1,4-dihydropyridine-3,5-dicarboxylate
3-(cyclopropylmethyl) 5-methyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-cyclopropyl-1,4-dihydropyridine-3,5-dicarboxylate
dimethyl 2,6-diamino-4-(7-cyanobenzo[b]thiophen-3-yl)-1,4-dihydropyridine-3,5-dicarboxylate
5-(cyclopropylmethyl) 3-methyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-cyclopropyl-1,4-dihydropyridine-3,5-dicarboxylate
3-(4-fluorobenzyl) 5-methyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

3-(4-fluorobenzyl) 5-methyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-cyclopropyl-1,4-dihydropyridine-3,5-dicarboxylate

Cyclopropylmethyl 2-amino-5-cyano-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

4-Fluorobenzyl 2-amino-5-cyano-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

Cyclopropylmethyl 6-amino-5-cyano-4-(7-cyanobenzo[b]thiophen-3-yl)-2-cyclopropyl-1,4-dihydropyridine-3-carboxylate

3-Cyclopentyl 5-methyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

Cyclopropylmethyl 5-acetyl-2-amino-4-(6-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

Cyclohexyl 5-acetyl-2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

Cyclohexylmethyl 5-acetyl-2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

Cyclopropylmethyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-5-(cyclopropanecarbonyl)-6-methyl-1,4-dihydropyridine-3-carboxylate

3-Fluorobenzyl 5-acetyl-2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

3-(Cyclobutylmethyl) 5-methyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

3-((3,3-Difluorocyclobutyl)methyl) 5-methyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

Cyclopropylmethyl 2-amino-5-carbamoyl-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

3-((2,2-Difluorocyclopropyl)methyl) 5-methyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

5-Cyclopropyl 3-(cyclopropylmethyl) 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

3-((2,2-Difluorocyclopropyl)methyl) 5-methyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-cyclopropyl-1,4-dihydropyridine-3,5-dicarboxylate

3-(Cyclopropylmethyl) 5-methyl 2-amino-4-(7-cyano-5-fluorobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

3-(cyclopropylmethyl) 5-methyl 2-amino-4-(7-cyano-4-fluorobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

3-Isopropyl 5-methyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

3-((2,2-Difluoro-3,3-dimethylcyclopropyl)methyl) 5-methyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

5-Methyl 3-neopentyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

3-(Cyclopropylmethyl) 5-methyl 2-amino-4-(7-cyanothieno[3,2-b]pyridin-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

5-Methyl 3-neopentyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-cyclopropyl-1,4-dihydropyridine-3,5-dicarboxylate

Bis(cyclopropylmethyl) 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

3-(Cyclopropylmethyl) 5-(prop-2-yn-1-yl) 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

3-(Cyclopropylmethyl) 5-methyl 2-amino-4-(5,7-dicyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

5-(But-2-yn-1-yl) 3-(cyclopropylmethyl) 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

5-Methyl 3-(2,2,2-trifluoroethyl) 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

3-(Cyclopropylmethyl) 5-(2,2,2-trifluoroethyl) 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

3-(Cyclopropylmethyl) 5-methyl 2-amino-4-(6-chloro-7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyri-

dine-3,5-dicarboxylate
3-(2-Fluoro-2-methylpropyl) 5-methyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate
3-(Cyclopropylmethyl) 5-methyl 2-amino-4-(7-cyano-6-(trifluoromethyl)benzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate
5-Methyl 3-prop-2-yn-1-yl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate
3-(Cyclopropylmethyl) 5-methyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-(trifluoromethyl)-1,4-dihydropyridine-3,5-dicarboxylate
4-(Benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarbonitrile
4-(6-hydroxybenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarbonitrile
4-(6-methoxybenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarbonitrile
2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3,5-dicarbonitrile
4-(benzo[b]thiophen-3-yl)-2-methyl-6-phenyl-1,4-dihydropyridine-3,5-dicarbonitrile
4-(benzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3,5-dicarbonitrile
5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carbonitrile
Ethyl 4-(benzo[b]thiophen-3-yl)-5-cyano-2,6-dimethyl-1,4-dihydropyridine -3-carboxylate
Ethyl 4-(benzo[b]thiophen-3-yl)-5-cyano-2-methyl-6-phenyl-1,4-dihydropyridine-3-carboxylate
Ethyl 4-(benzo[b]thiophen-3-yl)-5-cyano-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate
Methyl 4-(benzo[b]thiophen-3-yl)-5-cyano-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate
1,1'-(4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-diyl)diethanone
1,1'-(4-(6-hydroxybenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-diyl)bis(ethan-1-one)
1,1'-(4-(6-Methoxybenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-diyl)diethanone
1,1'-(4-(Benzo[b]thiophen-3-yl)-2,6-dicyclopropyl-1,4-dihydropyridine-3,5-diyl)diethanone
1,1'-(4-(5-chlorobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-diyl)diethanone
1,1'-(4-(5-bromobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-diyl)diethanone
1,1'-(4-(5-fluorobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-diyl)bis(ethan-1-one)
1,1'-(2,6-dimethyl-4-(5-morpholinobenzo[b]thiophen-3-yl)-1,4-dihydropyridine-3,5-diyl)bis(ethan-1-one)
1,1'-(2,6-dimethyl-4-(5-(4-methylpiperazin-1-yl)benzo[b]thiophen-3-yl)-1,4-dihydropyridine-3,5-diyl)bis(ethan-1-one)
1,1'-(4-(5-(benzylamino)benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-diyl)bis(ethan-1-one)
3-(3,5-diacetyl-2,6-dimethyl-1,4-dihydropyridin-4-yl)benzo[b]thiophene-5-carbonitrile
3-(3,5-diacetyl-2,6-dimethyl-1,4-dihydropyridin-4-yl)benzo[b]thiophene-5-carboxylic acid
N-cyclopropyl-3-(3,5-diacetyl-2,6-dimethyl-1,4-dihydropyridin-4-yl)benzo[b]thiophene-5-carboxamide
N-(cyclopropylmethyl)-3-(3,5-diacetyl-2,6-dimethyl-1,4-dihydropyridin-4-yl)benzo[b]thiophene-5-carboxamide
1,1'-(2,6-Dimethyl-4-(5-(4-methylpiperazine-1-carbonyl)benzo[b]thiophen-3-yl)-1,4-dihydropyridine-3,5-diyl)bis(ethan-1-one)
1,1'-(2,6-Dimethyl-4-(5-(morpholine-4-carbonyl)benzo[b]thiophen-3-yl)-1,4-dihydropyridine-3,5-diyl)bis(ethan-1-one)
1,1'-(2,6-Dimethyl-4-(thieno[3,2-c]pyridin-3-yl)-1,4-dihydropyridine-3,5-diyl)bis(ethan-1-one)
1,1'-(2,6-Dimethyl-4-(thieno[2,3-c]pyridin-3-yl)-1,4-dihydropyridine-3,5-diyl)bis(ethan-1-one)
1,1'-(2,6-Dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3,5-diyl)bis(ethan-1-one)
Dimethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-2,3-dicarboxylate
Dimethyl 5-acetyl-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-2,3-dicarboxylate
Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate
Dimethyl 4-(benzo[b]thiophen-3-yl)-2,6-dicyclopropyl-1,4-dihydropyridine-3,5-dicarboxylate
Ethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate
Methyl 5-acetyl-4-(5-chlorobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate
1,1'-(4-(benzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydro-pyridine-3,5-diyl)diethanone
1-(4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-5-(methylsulfonyl)-1,4-dihydro-pyridin-3-yl)ethanone
Methyl 5-acetyl-4-(5-fluorobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate
Methyl 5-acetyl-4-(5-bromobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate
methyl 5-acetyl-4-(5-cyanobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate
3-(3-acetyl-5-(methoxycarbonyl)-2,6-dimethyl-1,4-dihydropyridin-4-yl)benzo[b]thiophene-5-carboxylic acid
methyl 5-acetyl-4-(5-(cyclopropylcarbamoyl)benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate
Methyl 5-acetyl-4-(5-((cyclopropylmethyl)carbamoyl)benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

Methyl 5-acetyl-2,6-dimethyl-4-(5-(4-methylpiperazine-1-carbonyl)benzo[b]thiophen-3-yl)-1,4-dihydropyridine-3-carboxylate

Methyl 5-acetyl-2,6-dimethyl-4-(5-(morpholine-4-carbonyl)benzo[b]thiophen-3-yl)-1,4-dihydropyridine-3-carboxylate

Methyl 5-acetyl-2,6-dimethyl-4-(thieno[3,2-c]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

Methyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-c]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

Methyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

Methyl 5-acetyl-2-cyclopropyl-4-(5-fluorobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

Dimethyl 2,6-dicyclopropyl-4-(5-fluorobenzo[b]thiophen-3-yl)-1,4-dihydropyridine-3,5-dicarboxylate

Methyl 5-acetyl-2-cyclopropyl-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

Dimethyl 2,6-dicyclopropyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3,5-dicarboxylate

Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dicyclopropyl-1,4-dihydropyridine-3-carboxylate

Methyl 5-acetyl-4-(5-chlorobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate

Dimethyl 4-(5-chlorobenzo[b]thiophen-3-yl)-2,6-dicyclopropyl-1,4-dihydropyridine-3,5-dicarboxylate

Methyl 5-acetyl-4-(7-bromobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate

Methyl 5-acetyl-2-cyclopropyl-4-(7-(cyclopropylcarbamoyl)benzo[b] thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

Methyl 5-acetyl-4-(7-cyanobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate

Dimethyl 4-(7-cyanobenzo[b]thiophen-3-yl)-2,6-dicyclopropyl-1,4-dihydropyridine-3,5-dicarboxylate

Methyl 5-acetyl-2-cyclopropyl-4-(7-(methoxycarbonyl) benzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

Dimethyl 2,6-dicyclopropyl-4-(7-(methoxycarbonyl)benzo[b]thiophen-3-yl)-1,4-dihydropyridine-3,5-dicarboxylate

3-(3-Acetyl-6-cyclopropyl-5-(methoxycarbonyl)-2-methyl-1,4-dihydropyridin-4-yl)benzo[b]thiophene-7-carboxylic acid

Benzyl 5-acetyl-2-cyclopropyl-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

Pyridin-4-ylmethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate

bis(pyridin-4-ylmethyl) 2,6-dicyclopropyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3,5-dicarboxylate

Pyridin-4-ylmethyl 5-acetyl-4-(7-bromobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

Pyridin-4-ylmethyl 5-acetyl-4-(5-chlorobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate

Pyridin-4-ylmethyl 5-acetyl-4-(7-cyanobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate

Pyridin-4-ylmethyl 5-acetyl-2-cyclopropyl-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

Benzyl 5-acetyl-2-cyclopropyl-4-(7-(methoxycarbonyl)benzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate

Dibenzyl 2,6-dicyclopropyl-4-(7-(methoxycarbonyl)benzo[b]thiophen-3-yl)-1,4-dihydropyridine-3,5-dicarboxylate

Benzyl 5-acetyl-4-(7-(methoxycarbonyl)benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate

Methyl 3-(3,5-diacetyl-2,6-dimethyl-1,4-dihydropyridin-4-yl)benzo[b]thiophene-7-carboxylate

3-(3,5-Diacetyl-2,6-dimethyl-1,4-dihydropyridin-4-yl)benzo[b]thiophene-7-carbonitrile

Pyridin-4-ylmethyl 5-acetyl-4-(7-bromobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate

4-Fluorobenzyl 5-acetyl-2-cyclopropyl-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

bis(4-fluorobenzyl) 2,6-dicyclopropyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3,5-dicarboxylate

4-cyanobenzyl 5-acetyl-2-cyclopropyl-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

Methyl 5-acetyl-4-(7-chlorobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate

methyl 5-acetyl-2-cyclopropyl-6-methyl-4-(7-(trifluoromethyl)benzo[b]thiophen-3-yl)-1,4-dihydropyridine-3-carboxylate

3-chlorobenzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

2-phenylpropan-2-yl 5-acetyl-4-(7-bromobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate

Cyclohexyl 5-acetyl-2-cyclopropyl-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

2-Phenylpropan-2-yl 5-acetyl-2-cyclopropyl-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

1-(4-(7-Bromobenzo[b]thiophen-3-yl)-5-(cyclopropanecarbonyl)-6-cyclopropyl-2-methyl-1,4-dihydropyridin-3-

yl)ethan-1-one
3-chlorobenzyl 5-acetyl-2-cyclopropyl-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate
2-(4-Fluorophenyl)propan-2-yl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate
2-(4-fluorophenyl)propan-2-yl 5-acetyl-4-(7-bromobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate
2-(4-fluorophenyl)propan-2-yl 5-acetyl-2-cyclopropyl-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate
Methyl 5-acetyl-2-cyclopropyl-4-(7-fluorobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate
Cyclopropylmethyl 5-acetyl-2-cyclopropyl-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate
Cyclopentyl 5-acetyl-2-cyclopropyl-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate
Cyclopropylmethyl 5-acetyl-4-(7-cyanobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate
Methyl 5-acetyl-4-(7-bromobenzo[b]thiophen-3-yl)-2-cyclobutyl-6-methyl-1,4-dihydropyridine-3-carboxylate
Dimethyl 4-(7-cyanobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate
Methyl 5-cyano-4-(7-cyanobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate
Methyl 5-acetyl-4-(7-bromobenzo[b]thiophen-3-yl)-2-cyclopentyl-6-methyl-1,4-dihydropyridine-3-carboxylate
Methyl 5-acetyl-4-(7-bromobenzo[b]thiophen-3-yl)-2-cyclohexyl-6-methyl-1,4-dihydropyridine-3-carboxylate
Methyl 5-cyano-4-(7-cyanobenzo[b]thiophen-3-yl)-2,6-dicyclopropyl-1,4-dihydropyridine-3-carboxylate
3-((4-Methylpiperazin-1-yl)methyl)benzyl 5-acetyl-4-(7-bromobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate
3-(cyclopropylmethyl) 5-methyl 4-(7-cyanobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate
3-(cyclopropylmethyl) 5-methyl 4-(7-cyanobenzo[b]thiophen-3-yl)-2,6-dicyclopropyl-1,4-dihydropyridine-3,5-dicarboxylate
cyclopropylmethyl 5-cyano-4-(7-cyanobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate
dimethyl 2-cyano-4-(7-cyanobenzo[b]thiophen-3-yl)-6-cyclopropyl-1,4-dihydropyridine-3,5-dicarboxylate
dimethyl 2-cyano-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate
methyl 5-acetyl-2-((2-aminoethoxy)methyl)-4-(benzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate
methyl 5-acetyl-2-((2-aminoethoxy)methyl)-4-(7-bromobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate
methyl 5-acetyl-2-((2-aminoethoxy)methyl)-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate
Dimethyl 4-(7-cyanobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-formyl-1,4-dihydropyridine-3,5-dicarboxylate
Dimethyl 4-(7-cyanobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-(hydroxymethyl)-1,4-dihydropyridine-3,5-dicarboxylate
Dimethyl 4-(7-cyanobenzo[b]thiophen-3-yl)-2-formyl-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate
Dimethyl 4-(7-cyanobenzo[b]thiophen-3-yl)-2-(hydroxymethyl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate
Dimethyl 2-cyano-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3,5-dicarboxylate
Cyclopropylmethyl 5-acetyl-4-(6-cyanobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridine-3-carboxylate
Cyclopropylmethyl 2,5-diacetyl-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate
Methyl 5-acetyl-2-amino-4-(benzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate hydrochloride
Methyl 5-acetyl-2-amino-4-(benzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate trifluoromethanesulfonate
4-(Pyridin-4-yl)benzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4 dihydropyridine-3-carboxylate
4-(Pyridin-3-yl)benzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate
3-(Pyridin-4-yl)benzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate
3-(Pyridin-3-yl)benzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate
2-(Pyridin-4-yl)benzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate
2-(pyridin-3-yl)benzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate
[3,4'-Bipyridin]-5-ylmethyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate
[3,3'-Bipyridin]-5-ylmethyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate
[2,4'-Bipyridin]-5-ylmethyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate
[2,3'-Bipyridin]-5-ylmethyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate

[2,3'-Bipyridin]-4-ylmethyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate
[2,4'-Bipyridin]-4-ylmethyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate
Methyl 5-acetyl-2-cyclopropyl-6-methyl-4-(7-(pyridin-4-yl)benzo[b]thiophen-3-yl)-1,4-dihydropyridine-3-carboxylate
Methyl 5-acetyl-2-cyclopropyl-4-(7-cyclopropylbenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridine-3-carboxylate
3-(Pyridin-4-yl)benzyl 5-acetyl-2-cyclopropyl-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate
1,1'-(2,6-Dimethyl-4-(5-(pyridin-3-yl)benzo[b]thiophen-3-yl)-1,4-dihydro-pyridine-3,5-diyl)diethanone
Methyl 5-acetyl-2-cyclopropyl-6-methyl-4-(7-phenylbenzo[b]thiophen-3-yl)-1,4-dihydropyridine-3-carboxyl ate

14. Compound as defined in any one of claims 1 to 13 for use in the treatment of a disease or pathological condition susceptible of improvement by antagonism of androgen receptor and/or glucocorticoid receptor selected from prostate cancer, castration-resistant prostate cancer, pancreatic cancer, bladder cancer, renal cancer, gastric cancer, lung cancer, breast cancer, colon cancer, colorectal cancer, ovarian cancer, and other solid tumours, melanoma, metastasizing cancers, benign prostate hyperplasia, polycystic ovary syndrome (PCOS), hair loss, hirsutism, acne, hypogonadism, muscle wasting diseases and cachexia, and Cushing's syndrome, anti-psychotic drug induced weight gain, obesity, post-traumatic stress disorder and alcoholism.

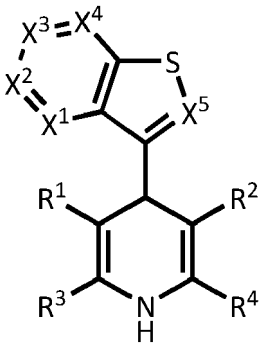
15. A pharmaceutical composition comprising a compound as defined in any one of claims 1 to 13 and a pharmaceutically acceptable diluent or carrier.

16. A pharmaceutical composition according to claim 15 further comprising a therapeutically effective amount of a therapeutic agent selected from agents for treating prostate cancer, castration-resistant prostate cancer, pancreatic cancer, bladder cancer, renal cancer, gastric cancer, lung cancer, breast cancer, colon cancer, colorectal cancer, ovarian cancer, and other solid tumours, melanoma, metastasizing cancers, benign prostate hyperplasia, polycystic ovary syndrome (PCOS), hair loss, hirsutism, acne, hypogonadism, muscle wasting diseases and cachexia, and Cushing's syndrome, anti-psychotic drug induced weight gain, obesity, post-traumatic stress disorder and alcoholism.

17. A combination product comprising a compound according to any one claims 1 to 13 and a therapeutic agent used for the treatment of prostate cancer, castration-resistant prostate cancer, pancreatic cancer, bladder cancer, renal cancer, gastric cancer, lung cancer, breast cancer, colon cancer, colorectal cancer, ovarian cancer, and other solid tumours, melanoma, metastasizing cancers, benign prostate hyperplasia, polycystic ovary syndrome (PCOS), hair loss, hirsutism, acne, hypogonadism, muscle wasting diseases and cachexia, and Cushing's syndrome, anti-psychotic drug induced weight gain, obesity, post-traumatic stress disorder and alcoholism, in particular a therapeutic agent selected from gonadotropin-releasing hormone (GnRH) receptor agonist or antagonist, androgen receptor antagonist, CYP17 inhibitor, VEGF inhibitor, EGFR inhibitor, PI3K inhibitor, AKT inhibitor, mTOR inhibitor, c-Met inhibitor, Src, inhibitor, PARP inhibitor, angiopoietin, ALK inhibitor, ROS-1 inhibitor, anti-(IGF) antibodies, taxane anti-neoplastic agent, topoisomerase II inhibitor, anti-tumor antibiotic, HSP90 inhibitor, aurora kinase inhibitor, PSA-directed vaccine, GR antagonists, 11-beta HSD inhibitors, one or more immunotherapeutic agent selected from the group consisting of antibodies anti-CTLA4, antibodies anti-PD1 and antibodies anti-PDL1, in particular an antibody selected from the group consisting of ipilimumab, tremelimumab, nivolumab, pembrolizumab, CT-011, AMP-224, MPDL3280A, MEDI4736 and MDX-1105.

Patentansprüche

1. Eine Verbindung mit der Formel (I):



(I)

worin:

- R^1 eine Gruppe ist ausgewählt aus:

  a) $-COR^5$,
  b) $-COOR^5$,
  c) -CN,
  d) $-C(O)NH_2$

- R^5 eine Gruppe ist ausgewählt aus:

  a) linearem oder verzweigtem C_1-C_6-Alkyl optional substituiert durch 1, 2 oder 3 Substituenten ausgewählt aus $-N(R^6)R^7$ und $-OR^6$, Halogenatom, C_3-C_6-Cycloalkyl und Alkynylgruppe,
  b) C_3-C_6-Cycloalkyl,

- R^2 eine Gruppe ist ausgewählt aus:

  a) $-COOR^8$,
  b) $-COR^8$,
  c) $-C(O)N(R^8)R^9$,
  d) -CN,
  e) $-S(O)_nR^8$, wobei n eine ganze Zahl von 1 bis 2 ist,

- R^8 und R^9 unabhängig voneinander ausgewählt sind:

  a) linearem oder verzweigtem C_1-C_6-Alkyl optional substituiert durch 1, 2 oder 3 Substituenten ausgewählt aus A^1 oder B^2,
  b) A^1-Gruppe,
  c) Wasserstoffatom,
  oder

- R^8 und R^9 zusammen mit dem Stickstoffatom, an das sie gebunden sind, einen 5- bis 6-gliedrigen Heterozcyklus bilden, der optional 1 Heteroatom ausgewählt aus O und N enthält, und wobei der Heterocyclus optional substituiert ist durch 1 oder 2 Gruppen unabhängig voneinander ausgewählt aus linearem oder verzweigtem C_1-C_4-Alkyl
- R^3 eine Gruppe ist ausgewählt aus:

  a) linearem oder verzweigtem C_1-C_6-Alkyl optional substituiert durch 1, 2 oder 3 Substituenten ausgewählt aus Halogenatom, $-N(R^6)R^7$, und $-OR^6$,
  b) C_3-C_6-Cycloalkyl optional substituiert durch 1, 2 oder 3 Halogenatome,
  c) Wasserstoffatom,
  d) $-NH_2$,
  e) -CN,

- R^4 eine Gruppe ist ausgewählt aus:

  a) A^1-Gruppe,
  b) linearem oder verzweigtem C_1-C_6-Alkyl optional substituiert durch 1, 2 oder 3 Substituenten ausgewählt aus A^1 oder B^2,
  c) -$N(R^6)R^7$,
  d) -CN,
  e) -CO-H;
  f) -CO-Me und
  g) CO-OMe
  h) Wasserstoffatom,

- X^1, X^2, X^3, X^4, und X^5 unabhängig voneinander ausgewählt aus C-B^1, N und C-H,
- A^1 ausgewählt ist aus:

  a) C_3-C_6-Cycloalkyl dessen Ring optional substituiert ist durch 1, 2, 3 oder 4 Substituenten ausgewählt aus =O und B^3;
  b) einem 3- bis 6-gliedrigen gesättigten Heterocyclylring enthaltend 1, 2 oder 3 Heteroatome ausgewählt aus O, S und N, und wobei der Ring optional substituiert ist durch 1, 2 oder 3 Substituenten ausgewählt aus =O und B^3;
  c) Phenyl oder einer 5- bis 6-gliedrigen Heteroarylgruppe, wobei beide Gruppen optional substituiert sind durch 1, 2 oder 3 Substituenten ausgewählt aus B^1;

- wobei jedes B^1 unabhängig ausgewählt ist aus Halogenatom, -CF_3-Gruppe, 5- bis 6-gliedrigem Heteroaryl, linearem oder verzweigtem C_1-C_6-Alkyl, -CN, -$N(R^6)R^7$, -OR^6, -$C(=O)R^6$, -$C(=O)OR^6$, -$C(=O)N(R^6)R^7$, -$OC(=O)$-R^6, -$N(R^6)C(=O)R^7$, -$NR^7SO_2R^6$, -$SO_2N(R^6)R^7$, -SR^6, -$S(O)R^6$ und -$S(O)_2R^6$,
- jedes B^2 unabhängig ausgewählt ist aus Halogenatom, -CN, -$N(R^6)R^7$, -OR^6, -$C(=O)R^6$, -$C(=O)OR^6$, -$C(=O)N(R^6)R^7$,-$OC(=O)$-R^6, -$N(R^6)C(=O)R^7$, -$NR^7SO_2R^6$, -$SO_2N(R^6)R^7$, -SR^6, -$S(O)R^6$, -$S(O)_2R^6$,und Alkynylgruppe,
- jedes B^3 unabhängig ausgewählt ist aus Halogenatom, linearem oder verzweigtem C_1-C_6-Alkyl, -CN, -$N(R^6)R^7$, -OR^6, -$C(=O)R^6$, -$C(=O)OR^6$, -$C(=O)N(R^6)R^7$, -$OC(=O)$-R^6, -$N(R^6)C(=O)R^7$, -$NR^7SO_2R^6$, -$SO_2N(R^6)R^7$, -SR^6, -$S(O)R^6$, -$S(O)_2R^6$,

jedes R^6 und R^7 unabhängig voneinander darstellt:

- Wasserstoffatom,
- lineares oder verzweigtes C_1-C_{12}-Alkyl, C_3-C_6-Cycloalkyl und C_4-C_6-Heterocycloalkyl, die optional substituiert sind durch 1, 2 oder 3 Substituenten ausgewählt aus =O (Oxo), Halogenatom, Hydroxyl, Phenyl, C_3-C_6-Cycloalkyl, linearem oder verzweigtem C_1-C_6-Alkoxy, Amino, Alkylamino, Dialkylamino, linearem oder verzweigtem C_1-C_6-Alkylcarbonyl,
- Phenyl oder 5- bis 6-gliedrige Heteroarylgruppe, die optional substituiert sind durch 1, 2 oder 3 Substituenten ausgewählt aus Halogenatom, Cyanogruppe, linearem oder verzweigtem C_1-C_6-Alkyl, linearem oder verzweigtem C_1-C_6-Haloalkyl, Hydroxyl, linearem oder verzweigtem C_1-C_6-Alkoxy, Amino, Alkylamino, Dialkylamino;
- R^6 und R^7 zusammen mit dem Stickstoffatom, an das sie gebunden sind, einen 3- bis 8-gliedrigen Ring bilden, der optional ein weiteres Heteroatom enthält ausgewählt aus O, N und S, und wobei der Ring optional substituiert ist durch 1, 2 oder 3 Substituentens ausgewählt aus =O (Oxo), linearem oder verzweigtem C_1-C_6-Alkyl, linearem oder verzweigtem C_1-C_6-Haloalkyl, linearem oder verzweigtem C_1-C_6-Alkylcarbonyl;
- mit der Maßgabe, dass, wenn R^1 -$COOR^5$ ist und R^2 -$COOR^8$ ist, dann R^4 keine Methylgruppe darstellt.

und pharmazeutisch annehmbare Salze davon.

2. Verbindung gemäß Anspruch 1, wobei X^1, X^2, X^3 und X^5 C-H oder C-B^1 darstellen, wobei B^1 Halogenatom darstellt.

3. Verbindung gemäß Anspruch 2, wobei X^4 eine Gruppe ist ausgewählt aus C-B^1 und N.

4. Verbindung gemäß Anspruch 3, wobei B^1 ausgewählt ist aus -CN-Gruppe und Halogenatom.

5. Verbindung gemäß irgendeinem der Ansprüche 2 bis 4, wobei R^1 eine Gruppe ist ausgewählt aus -COR^5, -$COOR^5$

und -CN-Gruppe.

6. Verbindung gemäß Anspruch 5, wobei R^5 ausgewählt ist aus:

- C_1-C_4-Alkyl, wobei das endständige Methyl unsubstituiert ist oder durch drei Fluoratome (-CF_3) substituiert ist
- C_1-C_3-Alkyl optional substituiert an irgendeiner Position durch eine Alkynylgruppe, und
- C_3-C_5-Cycloalkyl.

7. Verbindung gemäß irgendeinem der Ansprüche 2 bis 6, wobei R^2 - $COOR^8$ darstellt.

8. Verbindung gemäß Anspruch 7, wobei R^8 unabhängig darstellt:

- lineares oder verzweigtes C_1-C_6-Alkyl optional substituiert durch 1, 2 oder 3 Substituenten ausgewählt aus Fluoratomen und C_3-C_5-Cycloalkyl optional substituiert durch 1, 2 oder 3 Fluoratom, oder
- A^1-Gruppe, die C_3-C_6-Cycloalkyl darstellt, das optional substituiert ist durch 1, 2 oder 3 Substituenten ausgewählt aus der Gruppe bestehend aus Fluoratomen und C_1-C_3-Alkylgruppen.

9. Verbindung gemäß irgendeinem der Ansprüche 2 bis 8, wobei R^3 eine Gruppe ist ausgewählt aus linearem oder verzweigtem C_1-C_4-Alkyl und C_3-C_4-Cycloalkyl, wobei die Gruppen optional substituiert sind durch 1, 2 oder 3 Fluoratome.

10. Verbindung gemäß irgendeinem der Ansprüche 2 bis 9, wobei R^4 eine Gruppe ist ausgewählt aus:

- -$N(R^6)R^7$, wobei R^6 und R^7 unabhängig voneinander ausgewählt sind aus Wasserstoffatom und einem linearen oder verzweigten C_1-C_3-Alkyl,
- A^1-Gruppe, die C_3-C_6-Cycloalkyl darstellt,
- linearem oder verzweigtem C_1-C_3-Alkyl optional substituiert durch 1, 2 oder 3 Substituenten ausgewählt aus 1, 2 oder 3 Fluoratomen oder 1 Hydroxylgruppe.

11. Verbindung gemäß Anspruch 1, wobei X^1, X^2, X^3 und X^5 -CH darstellen, X^4 C-B^1 darstellt, wobei B^1 -CN-Gruppe oder Bromatom darstellt, R^1 eine Gruppe ist ausgewählt aus -$C(O)CH_3$, -$C(O)OCH_3$ -$C(O)OCH_2$-Alkynyl und CN, R^2 eine Gruppe ist ausgewählt aus -C(O)O-linearer oder verzweigter C_1-C_5-Alkylgruppe optional substituiert durch 1, 2 oder 3 Fluoratome und $C(O)OCH_2$-Cyclopropyl optional substituiert durch 1, 2 oder 3 Fluoratome, R^3 eine Gruppe ist ausgewählt aus linearem oder verzweigtem C_1-C_3-Alkyl und C_3-C_4-Cycloalkyl und R^4 eine Gruppe ist ausgewählt aus linearem oder verzweigtem C_1-C_3-Alkyl, C_3-C_4-Cycloalkyl und -NH_2.

12. Verbindung gemäß Anspruch 1, wobei X^1, X^2, X^3 und X^5 -CH darstellt, X^4 C-B^1 darstellt, wobei B^1 -CN-Gruppe darstellt, R^1 eine Gruppe ist ausgewählt aus -$C(O)CH_3$, -$C(O)OCH_3$, R^2 eine Gruppe ist ausgewählt aus -$C(O)OCH_2$-Cyclopropyl optional substituiert durch 1, 2 oder 3 Fluoratome, und -$C(O)OCH_2$-CF_3, R^3 eine Gruppe ist ausgewählt aus Methyl und Cyclopropyl und R^4 eine Gruppe ist ausgewählt aus Cyclopropyl und -NH_2.

13. Eine Verbindung gemäß Anspruch 1, die ausgewählt ist aus der Gruppe bestehend aus:

Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydro-pyridin-3-carboxylat
Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydro-pyridin-3-carboxylat (Enantiomer 1)
Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydro-pyridin-3-carboxylat (Enantiomer 2)
5-Acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3-carboxamid
1-(4-(Benzo[b]thiophen-3-yl)-5-benzoyl-2,6-dimethyl-1,4-dihydropyridin-3-yl)ethan-1-on
Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-6-methyl-2-phenyl-1,4-dihydropyridin-3-carboxylat
1-(4-(Benzo[b]thiophen-3-yl)-2,6-dimethyl-5-nicotinoyl-1,4-dihydro pyridin-3-yl)ethan-1-on
Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-6-methyl-1,4-dihydro-[2,3'-bipyridin]-3-carboxylat
2,2,2-Trifluorethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3-carboxylat
5-Acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3-carbonsäure
1-(4-(Benzo[b]thiophen-3-yl)-2,6-dimethyl-5-(4-methylpiperazin-1-carbonyl)-1,4-dihydropyridin-3-yl)ethan-1-on
5-Acetyl-4-(benzo[b]thiophen-3-yl)-N,N-diethyl-2,6-dimethyl-1,4-dihydropyridin-3-carboxamid
1-(4-(Benzo[b]thiophen-3-yl)-2,6-dimethyl-5-(morpholin-4-carbonyl)-1,4-dihydropyridin-3-yl)ethan-1-on
2-Methoxyethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3-carboxylat

3-Acetamidopropyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3-carboxylat
Benzyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydro-pyridin-3-carboxylat
2-Morpholinoethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3-carboxylat
2-(Dimethylamino)ethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3-carboxylat
2-Acetamidoethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3-carboxylat
Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2-(methoxymethyl)-6-methyl-1,4-dihydropyridin-3-carboxylat
Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2-((dimethylamino)methyl)-6-methyl-1,4-dihydropyridin-3-carboxylat
Pyridin-4-ylmethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3-carboxylat
4-Methoxybenzyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3-carboxylat
Pyridin-2-ylmethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3-carboxylat
Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-6-methyl-2-(morpholino-methyl)-1,4-dihydropyridin-3-carboxylat
Dimethyl 4-(benzo[b]thiophen-3-yl)-2,6-bis(morpholinomethyl)-1,4-dihydropyridin-3,5-dicarboxylat
2-Hydroxyethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3-carboxylat
1-(4-(Benzo[b]thiophen-3-yl)-5-(cyclopropancarbonyl)-6-cyclopropyl-2-methyl-1,4-dihydropyridin-3-yl)ethan-1-on
Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2-(1-(tert-butoxycarbonyl) azetidin-3-yl)-6-methyl-1,4-dihydropyridin-3-carboxylat
(1-(tert-Butoxycarbonyl)piperidin-4-yl)methyl 5-acetyl-4-(benzo[b] thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3-carboxylat
Cyclohexylmethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3-carboxylat
Methyl 4-(benzo[b]thiophen-3-yl)-5-(cyclopropancarbonyl)-2,6-dicyclopropyl-1,4-dihydropyridin-3-carboxylat
5-Acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-N-phenyl-1,4-dihydropyridin-3-carboxamid
Tetrahydro-2H-pyran-4-yl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3-carboxylat
(Tetrahydro-2H-pyran-4-yl)methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3-carboxylat
Cyclohexyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3-carboxylat
Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2-(2-methoxy-2-oxoethyl)-6-methyl-1,4-dihydropyridin-3-carboxylat
Methyl 5-acetyl-2,6-dimethyl-4-(2-methylbenzo[b]thiophen-3-yl)-1,4-dihydropyridin-3-carboxylat
Cyclopropylmethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3-carboxylat
Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2-(2-methoxyethyl)-6-methyl-1,4-dihydropyridin-3-carboxylat
Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2-((benzyloxy)methyl)-6-methyl-1,4-dihydropyridin-3-carboxylat
Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-6-methyl-2-(phenoxymethyl)-1,4-dihydropyridin-3-carboxylat
Phenethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3-carboxylat
Methyl 4-(benzo[b]thiophen-3-yl)-5-(cyclopropancarbonyl)-6-cyclopropyl-2-methyl-1,4-dihydropyridin-3-carboxylat
Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-6-methyl-2-(trifluormethyl)-1,4-dihydropyridin-3-carboxylat
Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-6-benzyl-2-methyl-1,4-dihydropyridin-3-carboxylat
Methyl 4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-5-(2-phenylacetyl)-1,4-dihydropyridin-3-carboxylat
Methyl 4-(benzo[b]thiophen-3-yl)-5-(2-methoxyacetyl)-2,6-dimethyl-1,4-dihydropyridin-3-carboxylat
Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-6-(methoxymethyl)-2-methyl-1,4-dihydropyridin-3-carboxylat
Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2-(fluormethyl)-6-methyl-1,4-dihydropyridin-3-carboxylat
Cyclopropylmethyl 5-acetyl-4-(5-fluorbenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3-carboxylat
1-(tert-Butoxycarbonyl)piperidin-4-yl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3-carboxylat
Cyclopentylmethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3-carboxylat
Cyclopropylmethyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3-carboxylat
1-Methylpiperidin-4-yl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3-carboxylat
Cyclopentyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3-carboxylat
4,4-Dimethylcyclohexyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3-carboxylat
Cyclobutyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3-carboxylat
Methyl 5-acetyl-4-(5-fluorbenzo[b]thiophen-3-yl)-6-methyl-2-(trifluormethyl)-1,4-dihydropyridin-3-carboxylat
Methyl 5-acetyl-2,6-dimethyl-4-(thieno[3,2-b]pyridin-3-yl)-1,4-dihydropyridin-3-carboxylat
Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2-methyl-6-(trifluormethyl)-1,4-dihydropyridin-3-carboxylat
Cyclopropylmethyl 5-acetyl-4-(5-chlorbenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3-carboxylat
Cyclohexylmethyl 5-acetyl-4-(5-chlorbenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3-carboxylat
Cyclohexylmethyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3-carboxylat
Cyclopentylmethyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3-carboxylat

Cyclohexyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3-carboxylat
Cyclopentyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3-carboxylat
Methyl 5-acetyl-4-(5-chlorbenzo[b]thiophen-3-yl)-6-methyl-2-(trifluormethyl)-1,4-dihydropyridin-3-carboxylat
Benzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3-carboxylat
(Tetrahydro-2H-pyran-4-yl)methyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3-carboxylat
Benzyl 5-acetyl-4-(5-fluorbenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3-carboxylat
Benzyl 5-acetyl-4-(5-chlorbenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3-carboxylat
(Tetrahydro-2H-pyran-4-yl)methyl 5-acetyl-4-(5-chlorbenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3-carboxylat
(Tetrahydro-2H-pyran-4-yl)methyl 5-acetyl-4-(5-fluorbenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3-carboxylat
Benzyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-6-methyl-2-(trifluormethyl)-1,4-dihydropyridin-3-carboxylat
Pyridin-4-ylmethyl 5-acetyl-4-(5-fluorbenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3-carboxylat
4-Fluorbenzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3-carboxylat
Pyridin-3-ylmethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3-carboxylat
1,1'-(4-(Benzo[b]thiophen-3-yl)-2-benzyl-6-methyl-1,4-dihydropyridin-3,5-diyl)bis(ethan-1-on)
1-(5-Acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3-yl)-2-phenylethan-1-on
Methyl 5-acetyl-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-2-(trifluormethyl)-1,4-dihydropyridin-3-carboxylat
1-(2-Methyl-5-(piperidin-1-carbonyl)-4-(thieno[2,3-b]pyridin-3-yl)-6-(trifluormethyl)-1,4-dihydropyridin-3-yl)ethan-1-on
4-(((5-Acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydro-pyridin-3-carbonyl)oxy)methyl)benzoesäure
Benzyl 5-acetyl-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-2-(trifluormethyl)-1,4-dihydropyridin-3-carboxylat
Pyridin-3-ylmethyl 5-acetyl-4-(5-fluorbenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3-carboxylat
Pyridin-3-ylmethyl 5-acetyl-4-(7-brombenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3-carboxylat
Pyridin-3-ylmethyl 5-acetyl-4-(7-cyanobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3-carboxylat
Pyridin-3-ylmethyl 5-acetyl-4-(5-chlorbenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3-carboxylat
Pyridin-3-ylmethyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3-carboxylat
Pyridin-4-ylmethyl 5-acetyl-4-(5-chlorbenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3-carboxylat
4-(Cyclopropylcarbamoyl)benzyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3-carboxylat
Pyridin-4-ylmethyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3-carboxylat
4-Brombenzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3-carboxylat
3-Brombenzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3-carboxylat
2-Brombenzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3-carboxylat
(3-Fluorpyridin-4-yl)methyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3-carboxylat
Pyrimidin-5-ylmethyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3-carboxylat
(5-Brompyridin-3-yl)methyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3-carboxylat
2-Phenylpropan-2-yl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3-carboxylat
3-Cyanobenzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3-carboxylat
4-Cyanobenzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3-carboxylat
(6-Chlorpyridin-3-yl)methyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3-carboxylat
3-Morpholinobenzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3-carboxylat
4,4-Dimethylcyclohexyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3-carboxylat
(2-Chlorpyridin-4-yl)methyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3-carboxylat
Tetrahydro-2H-pyran-4-yl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3-carboxylat
4,4-Difluorcyclohexyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3-carboxylat
5-Acetyl-N-benzyl-N,2,6-trimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3-carboxamid
Oxetan-3-yl 5-acetyl-4-(7-brombenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridin-3-carboxylat
Isopropyl 5-acetyl-4-(7-brombenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridin-3-carboxylat
Methyl 5-acetyl-4-(7-brombenzo[b]thiophen-3-yl)-6-methyl-2-(trifluormethyl)-1,4-dihydropyridin-3-carboxylat
Cyclopropylmethyl 5-acetyl-4-(7-brombenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridin-3-carboxylat
Methyl 5-acetyl-2-cyclopropyl-6-methyl-4-(7-(2,2,2-trifluoracetyl) benzo[b]thiophen-3-yl)-1,4-dihydropyridin-3-carboxylat
2-Phenylpropan-2-yl 5-acetyl-4-(7-brombenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3-carboxylat
Methyl 5-acetyl-2-amino-4-(benzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridin-3-carboxylat
Methyl 2-amino-4-(benzo[b]thiophen-3-yl)-5-(cyclopropancarbonyl)-6-methyl-1,4-dihydropyridin-3-carboxylat

Methyl 5-acetyl-2-amino-4-(5-fluorbenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridin-3-carboxylat
Methyl 5-acetyl-2-amino-4-(7-brombenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridin-3-carboxylat
Methyl 5-acetyl-2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridin-3-carboxylat
Cyclopentyl 5-acetyl-2-amino-4-(7-brombenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridin-3-carboxylat
Dimethyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridin-3,5-dicarboxylat
Cyclopentyl 5-acetyl-2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridin-3-carboxylat
Dimethyl 2,6-diamino-4-(benzo[b]thiophen-3-yl)-1,4-dihydropyridin-3,5-dicarboxylat
Cyclopropylmethyl 5-acetyl-2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridin-3-carboxylat
4,4-Difluorcyclohexyl 5-acetyl-2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridin-3-carboxylat
Methyl 2-amino-5-cyano-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridin-3-carboxylat
4-Fluorbenzyl 5-acetyl-2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridin-3-carboxylat
Methyl 5-acetyl-2-amino-4-(5-fluorthieno[2,3-b]pyridin-3-yl)-6-methyl-1,4-dihydropyridin-3-carboxylat
Methyl 2-acetamido-5-acetyl-4-(5-fluorthieno[2,3-b]pyridin-3-yl)-6-methyl-1,4-dihydropyridin-3-carboxylat
Cyclopentylmethyl 5-acetyl-2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridin-3-carboxylat
3-(Cyclopropylmethyl) 5-methyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridin-3,5-dicarboxylat
Dimethyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-cyclopropyl-1,4-dihydropyridin-3,5-dicarboxylat
3-(Cyclopropylmethyl) 5-methyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-cyclopropyl-1,4-dihydropyridin-3,5-dicarboxylat
Dimethyl 2,6-diamino-4-(7-cyanobenzo[b]thiophen-3-yl)-1,4-dihydropyridin-3,5-dicarboxylat
5-(Cyclopropylmethyl) 3-methyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-cyclopropyl-1,4-dihydropyridin-3,5-dicarboxylat
3-(4-Fluorbenzyl) 5-methyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridin-3,5-dicarboxylat
3-(4-Fluorbenzyl) 5-methyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-cyclopropyl-1,4-dihydropyridin-3,5-dicarboxylat
Cyclopropylmethyl 2-amino-5-cyano-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridin-3-carboxylat
4-Fluorbenzyl 2-amino-5-cyano-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridin-3-carboxylat
Cyclopropylmethyl 6-amino-5-cyano-4-(7-cyanobenzo[b]thiophen-3-yl)-2-cyclopropyl-1,4-dihydropyridin-3-carboxylat
3-Cyclopentyl 5-methyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridin-3,5-dicarboxylat
Cyclopropylmethyl 5-acetyl-2-amino-4-(6-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridin-3-carboxylat
Cyclohexyl 5-acetyl-2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridin-3-carboxylat
Cyclohexylmethyl 5-acetyl-2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridin-3-carboxylat
Cyclopropylmethyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-5-(cyclopropancarbonyl)-6-methyl-1,4-dihydropyridin-3-carboxylat
3-Fluorbenzyl 5-acetyl-2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridin-3-carboxylat
3-(Cyclobutylmethyl) 5-methyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridin-3,5-dicarboxylat
3-((3,3-Difluorcyclobutyl)methyl) 5-methyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridin-3,5-dicarboxylat
Cyclopropylmethyl 2-amino-5-carbamoyl-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridin-3-carboxylat
3-((2,2-Difluorcyclopropyl)methyl) 5-methyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridin-3,5-dicarboxylat
5-Cyclopropyl 3-(cyclopropylmethyl) 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridin-3,5-dicarboxylat
3-((2,2-Difluorcyclopropyl)methyl) 5-methyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-cyclopropyl-1,4-dihydropyridin-3,5-dicarboxylat
3-(Cyclopropylmethyl) 5-methyl 2-amino-4-(7-cyano-5-fluorbenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridin-3,5-dicarboxylat

3-(Cyclopropylmethyl) 5-methyl 2-amino-4-(7-cyano-4-fluorbenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridin-3,5-dicarboxylat 3-Isopropyl 5-methyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridin-3,5-dicarboxylat

3-((2,2-Difluor-3,3-dimethylcyclopropyl)methyl) 5-methyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridin-3,5-dicarboxylat

5-Methyl 3-neopentyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridin-3,5-dicarboxylat

3-(Cyclopropylmethyl) 5-methyl 2-amino-4-(7-cyanothieno[3,2-b]pyridin-3-yl)-6-methyl-1,4-dihydropyridin-3,5-dicarboxylat

5-Methyl 3-neopentyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-cyclopropyl-1,4-dihydropyridin-3,5-dicarboxylat

Bis(cyclopropylmethyl) 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridin-3,5-dicarboxylat

3-(Cyclopropylmethyl) 5-(prop-2-yn-1-yl) 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridin-3,5-dicarboxylat

3-(Cyclopropylmethyl) 5-methyl 2-amino-4-(5,7-dicyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridin-3,5-dicarboxylat

5-(But-2-yn-1-yl) 3-(cyclopropylmethyl) 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridin-3,5-dicarboxylat

5-Methyl 3-(2,2,2-trifluorethyl) 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridin-3,5-dicarboxylat

3-(Cyclopropylmethyl) 5-(2,2,2-trifluorethyl) 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridin-3,5-dicarboxylat

3-(Cyclopropylmethyl) 5-methyl 2-amino-4-(6-chlor-7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridin-3,5-dicarboxylat

3-(2-Fluor-2-methylpropyl) 5-methyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridin-3,5-dicarboxylat

3-(Cyclopropylmethyl) 5-methyl 2-amino-4-(7-cyano-6-(trifluormethyl)benzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridin-3,5-dicarboxylat

5-Methyl 3-prop-2-yn-1-yl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridin-3,5-dicarboxylat

3-(Cyclopropylmethyl) 5-methyl 2-amino-4-(7-cyanobenzo[b]thiophen-3-yl)-6-(trifluormethyl)-1,4-dihydropyridin-3,5-dicarboxylat

4-(Benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3,5-dicarbonitril 4-(6-Hydroxybenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3,5-dicarbonitril

4-(6-Methoxybenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3,5-dicarbonitril

2,6-Dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3,5-dicarbonitril 4-(Benzo[b]thiophen-3-yl)-2-methyl-6-phenyl-1,4-dihydropyridin-3,5-dicarbonitril

4-(Benzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridin-3,5-dicarbonitril

5-Acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3-carbonitril

Ethyl 4-(benzo[b]thiophen-3-yl)-5-cyano-2,6-dimethyl-1,4-dihydropyridin -3-carboxylat

Ethyl 4-(benzo[b]thiophen-3-yl)-5-cyano-2-methyl-6-phenyl-1,4-dihydropyridin-3-carboxylat

Ethyl 4-(benzo[b]thiophen-3-yl)-5-cyano-2-cyclopropyl-6-methyl-1,4-dihydropyridin-3-carboxylat

Methyl 4-(benzo[b]thiophen-3-yl)-5-cyano-2-cyclopropyl-6-methyl-1,4-dihydropyridin-3-carboxylat

1,1'-(4-(Benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3,5-diyl)diethanon

1,1 '-(4-(6-Hydroxybenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3,5-diyl)bis(ethan-1-on)

1,1 '-(4-(6-Methoxybenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3,5-diyl)diethanon

1,1'-(4-(Benzo[b]thiophen-3-yl)-2,6-dicyclopropyl-1,4-dihydropyridin-3,5-diyl)diethanon

1,1'-(4-(5-Chlorbenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3,5-diyl)diethanon

1,1'-(4-(5-Brombenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3,5-diyl)diethanon

1,1'-(4-(5-Fluorbenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3,5-diyl)bis(ethan-1-on)

1,1'-(2,6-Dimethyl-4-(5-morpholinobenzo[b]thiophen-3-yl)-1,4-dihydropyridin-3,5-diyl)bis(ethan-1-on)

1,1'-(2,6-Dimethyl-4-(5-(4-methylpiperazin-1-yl)benzo[b]thiophen-3-yl)-1,4-dihydropyridin-3,5-diyl)bis(ethan-1-on)

1,1'-(4-(5-(Benzylamino)benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3,5-diyl)bis(ethan-1-on)

3-(3,5-Diacetyl-2,6-dimethyl-1,4-dihydropyridin-4-yl)benzo[b]thiophen-5-carbonitril

3-(3,5-Diacetyl-2,6-dimethyl-1,4-dihydropyridin-4-yl)benzo[b]thiophen-5-carbonsäure

N-Cyclopropyl-3-(3,5-diacetyl-2,6-dimethyl-1,4-dihydropyridin-4-yl)benzo[b]thiophen-5-carboxamid

N-(Cyclopropylmethyl)-3-(3,5-diacetyl-2,6-dimethyl-1,4-dihydropyridin-4-yl)benzo[b]thiophen-5-carboxamid

1,1'-(2,6-Dimethyl-4-(5-(4-methylpiperazin-1-carbonyl)benzo[b]thiophen-3-yl)-1,4-dihydropyridin-3,5-diyl)bis(ethan-1-on)
1,1'-(2,6-Dimethyl-4-(5-(morpholin-4-carbonyl)benzo[b]thiophen-3-yl)-1,4-dihydropyridin-3,5-diyl)bis(ethan-1-on)
1,1'-(2,6-Dimethyl-4-(thieno[3,2-c]pyridin-3-yl)-1,4-dihydropyridin-3,5-diyl)bis(ethan-1-on)
1,1'-(2,6-Dimethyl-4-(thieno[2,3-c]pyridin-3-yl)-1,4-dihydropyridin-3,5-diyl)bis(ethan-1-on)
1,1'-(2,6-Dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3,5-diyl)bis(ethan-1-on)
Dimethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridin-2,3-dicarboxylat
Dimethyl 5-acetyl-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridin-2,3-dicarboxylat
Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridin-3-carboxylat
Dimethyl 4-(benzo[b]thiophen-3-yl)-2,6-dicyclopropyl-1,4-dihydropyridin-3,5-dicarboxylat
Ethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3-carboxylat
Methyl 5-acetyl-4-(5-chlorbenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3-carboxylat
1,1'-(4-(Benzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydro-pyridin-3,5-diyl)diethanon
1-(4-(Benzo[b]thiophen-3-yl)-2,6-dimethyl-5-(methylsulfonyl)-1,4-dihydropyridin-3-yl)ethanon
Methyl 5-acetyl-4-(5-fluorbenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3-carboxylat
Methyl 5-acetyl-4-(5-brombenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3-carboxylat
Methyl 5-acetyl-4-(5-cyanobenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3-carboxylat
3-(3-Acetyl-5-(methoxycarbonyl)-2,6-dimethyl-1,4-dihydropyridin-4-yl)benzo[b]thiophen-5-carbonsäure
Methyl 5-acetyl-4-(5-(cyclopropylcarbamoyl)benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3-carboxylat
Methyl 5-acetyl-4-(5-((cyclopropylmethyl)carbamoyl)benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3-carboxylat
Methyl 5-acetyl-2,6-dimethyl-4-(5-(4-methylpiperazin-1-carbonyl)benzo[b]thiophen-3-yl)-1,4-dihydropyridin-3-carboxylat
Methyl 5-acetyl-2,6-dimethyl-4-(5-(morpholin-4-carbonyl)benzo[b]thiophen-3-yl)-1,4-dihydropyridin-3-carboxylat
Methyl 5-acetyl-2,6-dimethyl-4-(thieno[3,2-c]pyridin-3-yl)-1,4-dihydropyridin-3-carboxylat
Methyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-c]pyridin-3-yl)-1,4-dihydropyridin-3-carboxylat
Methyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3-carboxylat
Methyl 5-acetyl-2-cyclopropyl-4-(5-fluorbenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridin-3-carboxylat
Dimethyl 2,6-dicyclopropyl-4-(5-fluorbenzo[b]thiophen-3-yl)-1,4-dihydropyridin-3,5-dicarboxylat
Methyl 5-acetyl-2-cyclopropyl-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3-carboxylat
Dimethyl 2,6-dicyclopropyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3,5-dicarboxylat
Methyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2,6-dicyclopropyl-1,4-dihydropyridin-3-carboxylat
Methyl 5-acetyl-4-(5-chlorbenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridin-3-carboxylat
Dimethyl 4-(5-chlorbenzo[b]thiophen-3-yl)-2,6-dicyclopropyl-1,4-dihydropyridin-3,5-dicarboxylat
Methyl 5-acetyl-4-(7-brombenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridin-3-carboxylat
Methyl 5-acetyl-2-cyclopropyl-4-(7-(cyclopropylcarbamoyl)benzo[b] thiophen-3-yl)-6-methyl-1,4-dihydropyridin-3-carboxylat
Methyl 5-acetyl-4-(7-cyanobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridin-3-carboxylat
Dimethyl 4-(7-cyanobenzo[b]thiophen-3-yl)-2,6-dicyclopropyl-1,4-dihydropyridin-3,5-dicarboxylat
Methyl 5-acetyl-2-cyclopropyl-4-(7-(methoxycarbonyl) benzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridin-3-carboxylat
Dimethyl 2,6-dicyclopropyl-4-(7-(methoxycarbonyl)benzo[b]thiophen-3-yl)-1,4-dihydropyridin-3,5-dicarboxylat
3-(3-Acetyl-6-cyclopropyl-5-(methoxycarbonyl)-2-methyl-1,4-dihydropyridin-4-yl)benzo[b]thiophen-7-carbonsäure
Benzyl 5-acetyl-2-cyclopropyl-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3-carboxylat
Pyridin-4-ylmethyl 5-acetyl-4-(benzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridin-3-carboxylat
Bis(pyridin-4-ylmethyl) 2,6-dicyclopropyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3,5-dicarboxylat
Pyridin-4-ylmethyl 5-acetyl-4-(7-brombenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3-carboxylat
Pyridin-4-ylmethyl 5-acetyl-4-(5-chlorbenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridin-3-carboxylat
Pyridin-4-ylmethyl 5-acetyl-4-(7-cyanobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridin-3-carboxylat
Pyridin-4-ylmethyl 5-acetyl-2-cyclopropyl-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3-carboxylat
Benzyl 5-acetyl-2-cyclopropyl-4-(7-(methoxycarbonyl)benzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridin-3-

carboxylat
Dibenzyl 2,6-dicyclopropyl-4-(7-(methoxycarbonyl)benzo[b]thiophen-3-yl)-1,4-dihydropyridin-3,5-dicarboxylat
Benzyl 5-acetyl-4-(7-(methoxycarbonyl)benzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3-carboxylat
Methyl 3-(3,5-diacetyl-2,6-dimethyl-1,4-dihydropyridin-4-yl)benzo[b]thiophen-7-carboxylat
3-(3,5-Diacetyl-2,6-dimethyl-1,4-dihydropyridin-4-yl)benzo[b]thiophen-7-carbonitril
Pyridin-4-ylmethyl 5-acetyl-4-(7-brombenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridin-3-carboxylat
4-Fluorbenzyl 5-acetyl-2-cyclopropyl-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3-carboxylat
Bis(4-fluorbenzyl) 2,6-dicyclopropyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3,5-dicarboxylat
4-Cyanobenzyl 5-acetyl-2-cyclopropyl-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3-carboxylat
Methyl 5-acetyl-4-(7-chlorbenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridin-3-carboxylat
Methyl 5-acetyl-2-cyclopropyl-6-methyl-4-(7-(trifluormethyl)benzo[b]thiophen-3-yl)-1,4-dihydropyridin-3-carboxylat
3-Chlorbenzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3-carboxylat
2-Phenylpropan-2-yl 5-acetyl-4-(7-brombenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridin-3-carboxylat
Cyclohexyl 5-acetyl-2-cyclopropyl-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3-carboxylat
2-Phenylpropan-2-yl 5-acetyl-2-cyclopropyl-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3-carboxylat
1-(4-(7-Brombenzo[b]thiophen-3-yl)-5-(cyclopropancarbonyl)-6-cyclopropyl-2-methyl-1,4-dihydropyridin-3-yl)ethan-1 -on
3-Chlorbenzyl 5-acetyl-2-cyclopropyl-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3-carboxylat
2-(4-Fluorphenyl)propan-2-yl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3-carboxylat
2-(4-Fluorphenyl)propan-2-yl 5-acetyl-4-(7-brombenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridin-3-carboxylat
2-(4-Fluorphenyl)propan-2-yl 5-acetyl-2-cyclopropyl-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3-carboxylat
Methyl 5-acetyl-2-cyclopropyl-4-(7-fluorbenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridin-3-carboxylat
Cyclopropylmethyl 5-acetyl-2-cyclopropyl-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3-carboxylat
Cyclopentyl 5-acetyl-2-cyclopropyl-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3-carboxylat
Cyclopropylmethyl 5-acetyl-4-(7-cyanobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridin-3-carboxylat
Methyl 5-acetyl-4-(7-brombenzo[b]thiophen-3-yl)-2-cyclobutyl-6-methyl-1,4-dihydropyridin-3-carboxylat
Dimethyl 4-(7-cyanobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridin-3,5-dicarboxylat
Methyl 5-cyano-4-(7-cyanobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridin-3-carboxylat
Methyl 5-acetyl-4-(7-brombenzo[b]thiophen-3-yl)-2-cyclopentyl-6-methyl-1,4-dihydropyridin-3-carboxylat
Methyl 5-acetyl-4-(7-brombenzo[b]thiophen-3-yl)-2-cyclohexyl-6-methyl-1,4-dihydropyridin-3-carboxylat
Methyl 5-cyano-4-(7-cyanobenzo[b]thiophen-3-yl)-2,6-dicyclopropyl-1,4-dihydropyridin-3-carboxylat
3-((4-Methylpiperazin-1-yl)methyl)benzyl 5-acetyl-4-(7-brombenzo[b]thiophen-3-yl)-2,6-dimethyl-1,4-dihydropyridin-3-carboxylat
3-(Cyclopropylmethyl) 5-methyl 4-(7-cyanobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridin-3,5-dicarboxylat
3-(Cyclopropylmethyl) 5-methyl 4-(7-cyanobenzo[b]thiophen-3-yl)-2,6-dicyclopropyl-1,4-dihydropyridin-3,5-dicarboxylat
Cyclopropylmethyl 5-cyano-4-(7-cyanobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridin-3-carboxylat
Dimethyl 2-cyano-4-(7-cyanobenzo[b]thiophen-3-yl)-6-cyclopropyl-1,4-dihydropyridin-3,5-dicarboxylat
Dimethyl 2-cyano-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridin-3,5-dicarboxylat
Methyl 5-acetyl-2-((2-aminoethoxy)methyl)-4-(benzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridin-3-carboxylat
Methyl 5-acetyl-2-((2-aminoethoxy)methyl)-4-(7-brombenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridin-3-carboxylat
Methyl 5-acetyl-2-((2-aminoethoxy)methyl)-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridin-3-carboxylat
Dimethyl 4-(7-cyanobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-formyl-1,4-dihydropyridin-3,5-dicarboxylat
Dimethyl 4-(7-cyanobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-(hydroxymethyl)-1,4-dihydropyridin-3,5-dicarbo-

xylat
Dimethyl 4-(7-cyanobenzo[b]thiophen-3-yl)-2-formyl-6-methyl-1,4-dihydropyridin-3,5-dicarboxylat
Dimethyl 4-(7-cyanobenzo[b]thiophen-3-yl)-2-(hydroxymethyl)-6-methyl-1,4-dihydropyridin-3,5-dicarboxylat
Dimethyl 2-cyano-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3,5-dicarboxylat
Cyclopropylmethyl 5-acetyl-4-(6-cyanobenzo[b]thiophen-3-yl)-2-cyclopropyl-6-methyl-1,4-dihydropyridin-3-carboxylat
Cyclopropylmethyl 2,5-diacetyl-4-(7-cyanobenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridin-3-carboxylat
Methyl 5-acetyl-2-amino-4-(benzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridin-3-carboxylat hydrochlorid
Methyl 5-acetyl-2-amino-4-(benzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridin-3-carboxylat trifluormethansulfonat
4-(Pyridin-4-yl)benzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4 dihydropyridin-3-carboxylat
4-(Pyridin-3-yl)benzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3-carboxylat
3-(Pyridin-4-yl)benzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3-carboxylat
3-(Pyridin-3-yl)benzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3-carboxylat
2-(Pyridin-4-yl)benzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3-carboxylat
2-(Pyridin-3-yl)benzyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3-carboxylat
[3,4'-Bipyridin]-5-ylmethyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3-carboxylat
[3,3'-Bipyridin]-5-ylmethyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3-carboxylat
[2,4'-Bipyridin]-5-ylmethyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3-carboxylat
[2,3'-Bipyridin]-5-ylmethyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3-carboxylat
[2,3'-Bipyridin]-4-ylmethyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3-carboxylat
[2,4'-Bipyridin]-4-ylmethyl 5-acetyl-2,6-dimethyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3-carboxylat
Methyl 5-acetyl-2-cyclopropyl-6-methyl-4-(7-(pyridin-4-yl)benzo[b]thiophen-3-yl)-1,4-dihydropyridin-3-carboxylat
Methyl 5-acetyl-2-cyclopropyl-4-(7-cyclopropylbenzo[b]thiophen-3-yl)-6-methyl-1,4-dihydropyridin-3-carboxylat
3-(Pyridin-4-yl)benzyl 5-acetyl-2-cyclopropyl-6-methyl-4-(thieno[2,3-b]pyridin-3-yl)-1,4-dihydropyridin-3-carboxylat
1,1'-(2,6-Dimethyl-4-(5-(pyridin-3-yl)benzo[b]thiophen-3-yl)-1,4-dihydropyridin-3,5-diyl)diethanon
Methyl 5-acetyl-2-cyclopropyl-6-methyl-4-(7-phenylbenzo[b]thiophen-3-yl)-1,4-dihydropyridin-3-carboxylat.

14. Verbindung wie in irgendeinem der Ansprüche 1 bis 13 definiert zur Verwendung bei der Behandlung einer Erkrankung oder eines pathologischen Zustands, empfänglich für eine Verbesserung durch Antagonismus des Androgenrezeptors und/oder Glucocorticoidrezeptors, ausgewählt aus Prostatakrebs, kastrationsresistentem Prostatakrebs, Bauchspeicheldrüsenkrebs, Blasenkrebs, Nierenkrebs, Magenkrebs, Lungenkrebs, Brustkrebs, Darmkrebs, Kolorektalkrebs, Eierstockkrebs und anderen festen Tumoren, Melanom, Metastasierungskrebs, benigner Prostatahyperplasie, polyzystischem Ovarialsyndrom (PCOS), Haarverlust, Hirsutismus, Akne, Hypogonadismus, Muskelschwunderkrankungen und Kachexie und Cushing-Syndrom, durch antipsychotische Arzneimittel induzierter Gewichtszunahme, Fettleibigkeit, posttraumatischer Belastungsstörung und Alkoholismus.

15. Eine pharmazeutische Zusammensetzung, umfassend eine Verbindung wie in irgendeinem der Ansprüche 1 bis 13 definiert und ein pharmazeutisch annehmbares Verdünnungsmittel oder einen pharmazeutisch annehmbaren Träger.

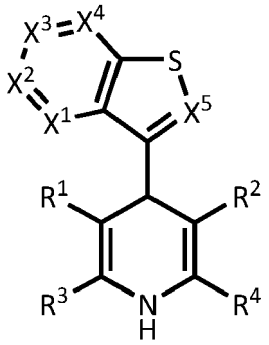
16. Eine pharmazeutische Zusammensetzung gemäß Anspruch 15, ferner umfassend eine therapeutisch wirksame Menge eines therapeutischen Mittels, ausgewählt aus Mitteln zur Behandlung von Prostatakrebs, kastrationsresistentem Prostatakrebs, Bauchspeicheldrüsenkrebs, Blasenkrebs, Nierenkrebs, Magenkrebs, Lungenkrebs, Brustkrebs, Darmkrebs, Kolorektalkrebs, Eierstockkrebs und anderen festen Tumoren, Melanom, Metastasierungskrebs, benigner Prostatahyperplasie, polyzystischem Eierstocksyndrom (PCOS), Haarverlust, Hirsutismus, Akne, Hypogonadismus, Muskelschwunderkrankungen und Kachexie und Cushing-Syndrom, durch antipsychotische Arzneimittel induzierter Gewichtszunahme, Fettleibigkeit, posttraumatischer Belastungsstörung und Alkoholismus.

17. Ein Kombinationsprodukt, umfassend eine Verbindung gemäß irgendeinem der Ansprüche 1 bis 13 und ein therapeutisches Mittel, das für die Behandlung von Prostatakrebs, kastrationsresistentem Prostatakrebs, Bauchspeicheldrüsenkrebs, Blasenkrebs, Nierenkrebs, Magenkrebs, Lungenkrebs, Brustkrebs, Darmkrebs, Kolorektalkrebs, Eierstockkrebs und anderen festen Tumoren, Melanom, Metastasierungskrebs, benigner Prostatahyperplasie, polyzystischem Ovarialsyndrom (PCOS), Haarverlust, Hirsutismus, Akne, Hypogonadismus, Muskelschwunderkrankungen und Kachexie und Cushing-Syndrom, durch antipsychotische Arzneimittel induzierter Gewichtszunahme,

Fettleibigkeit, posttraumatischer Belastungsstörung und Alkoholismus verwendet wird, insbesondere ein therapeutisches Mittel ausgewählt aus Gonadotropin-Releasing Hormon (GnRH)-Rezeptoragonisten oder -Antagonisten, Androgenrezeptorantagonisten, CYP17-Inhibitor, VEGF-Inhibitor, EGFR-Inhibitor, P13K-Inhibitor, AKT-Inhibitor, mTOR-Inhibitor, c-Met-Inhibitor, Src-Inhibitor, PARP-Inhibitor, Angiopoietin, ALK-Inhibitor, ROS-1-Inhibitor, Anti-(IGF)-Antikörpern, Taxan-Antineoplastikum, Topoisomerase II-Inhibitor, Anti-Tumor-Antibiotikum, HSP90-Inhibitor, Aurora-Kinase-Inhibitor, einem auf PSA gerichteten Impfstoff, GR-Antagonisten, 11-beta-HSD-Inhibitoren, einem oder mehreren immuntherapeutischen Mitteln, ausgewählt aus der Gruppe bestehend aus Anti-CTLA4- Antikörpern, Anti-PD1-Antikörpern und Anti-PDL1-Antikörpern, insbesondere einem Antikörper ausgewählt aus der Gruppe bestehend aus Ipilimumab, Tremelimumab, Nivolumab, Pembrolizumab, CT-011, AMP-224, MPDL3280A, MEDI4736 und MDX-1105.

Revendications

1. Composé de formule (I) :



(I)

où :

- R^1 est un groupe choisi parmi :

  a) $-COR^5$,
  b) $-COOR^5$,
  c) -CN,
  d) $-C(O)NH_2$

- R^5 est un groupe choisi parmi :

  a) alkyle en C_1-C_6 linéaire ou ramifié éventuellement substitué par 1, 2 ou 3 substituants choisis parmi $-N(R^6)R^7$ et $-OR^6$, un atome d'halogène, cycloalkyle en C_3-C_6 et alcynyle,
  b) cycloalkyle en C_3-C_6,

- R^2 est un groupe choisi parmi :

  a) $-COOR^8$,
  b) $-COR^8$,
  c) $-C(O)N(R^8)R^9$,
  d) -CN,
  e) $-S(O)_nR^8$, où n est un nombre entier de 1 à 2,

- R^8 et R^9 sont indépendamment choisis parmi :

  a) alkyle en C_1-C_6 linéaire ou ramifié éventuellement substitué par 1, 2 ou 3 substituants choisis parmi A^1 ou B^2,
  b) groupe A^1,

c) atome d'hydrogène,
ou

- R^8 et R^9 ensemble avec l'atome d'azote auquel ils sont attachés forment un hétérocycle à 5-6 éléments qui comprend éventuellement 1 hétéroatome choisi parmi 0 et N, et ledit hétérocycle étant éventuellement substitué par 1 ou 2 groupes indépendamment choisis parmi un alkyle en C_1-C_4 linéaire ou ramifié
- R^3 est un groupe choisi parmi :

a) alkyle en C_1-C_6 linéaire ou ramifié éventuellement substitué par 1, 2 ou 3 substituants choisis parmi un atome d'halogène, $-N(R^6)R^7$, et $-OR^6$,
b) cycloalkyle en C_3-C_6 éventuellement substitué par 1, 2 ou 3 atomes d'halogène,
c) atome d'hydrogène,
d) $-NH_2$,
e) -CN,

- R^4 est un groupe choisi parmi :

a) groupe A^1,
b) alkyle en C_1-C_6 linéaire ou ramifié éventuellement substitué par 1, 2 ou 3 substituants choisis parmi A^1 ou B^2,
c) $-N(R^6)R^7$,
d) -CN,
e) -CO-H ;
f) -CO-Me et
g) CO-OMe
h) atome d'hydrogène,

- X^1, X^2, X^3, X^4, et X^5 sont indépendamment choisis parmi C-B^1, N et C-H,
- A^1 est choisi parmi :

a) cycloalkyle en C_3-C_6 lequel noyau est éventuellement substitué par 1, 2, 3 ou 4 substituants choisis parmi =0 et B^3;
b) un noyau hétérocyclyle saturé à de 3 à 6 éléments comprenant 1, 2 ou 3 hétéroatomes choisis parmi 0, S et N, et lequel noyau est éventuellement substitué par 1, 2 ou 3 substituants choisis parmi =0 et B^3 ;
c) groupe phényle ou hétéroaryle à de 5 à 6 éléments, l'un ou l'autre est éventuellement substitué par 1, 2 ou 3 substituants choisis parmi B^1 ;

- chaque B^1 est indépendamment choisi parmi un atome d'halogène, groupe $-CF_3$, hétéroaryle à de 5 à 6 éléments, alkyle en C_1-C_6 linéaire ou ramifié, -CN, $-N(R^6)R^7$, $-OR^6$, $-C(=O)R^6$, $-C(=O)OR^6$, $-C(=O)N(R^6)R^7$, $-OC(=O)-R^6$, $-N(R^6)C(=O)R^7$, $-NR^7SO_2R^6$, $-SO_2N(R^6)R^7$, $-SR^6$, $-S(O)R^6$ et $-S(O)_2R^6$,
- chaque B^2 est indépendamment choisi parmi un atome d'halogène, -CN, $-N(R^6)R^7$, $-OR^6$, $-C(=O)R^6$, $-C(=O)OR^6$, $-C(=O)N(R^6)R^7$, $-OC(=O)-R^6$,$-N(R^6)C(=O)R^7$, $-NR^7SO_2R^6$, $-SO_2N(R^6)R^7$, $-SR^6$, $-S(O)R^6$, $-S(O)_2R^6$, et groupe alcynyle,
- chaque B^3 est indépendamment choisi parmi un atome d'halogène, groupe alkyle en C_1-C_6 linéaire ou ramifié, -CN, $-N(R^6)R^7$, $-OR^6$, $-C(=O)R^6$, $-C(=O)OR^6$, $-C(=O)N(R^6)R^7$, $-OC(=O)-R^6$, $-N(R^6)C(=O)R^7$, $-NR^7SO_2R^6$, $-SO_2N(R^6)R^7$, $-SR^6$, $-S(O)R^6$, $-S(O)_2R^6$,

chaque R^6 et R^7 représente indépendamment :

- un atome d'hydrogène,
- alkyle en C_1-C_{12} linéaire ou ramifié, cycloalkyle en C_3-C_6 et hétérocycloalkyle en C_4-C_6, lesquels sont éventuellement substitués par 1, 2 ou 3 substituants choisis parmi =O (oxo), un atome d'halogène, hydroxy, phényle, cycloalkyle en C_3-C_6, alcoxy en C_1-C_6 linéaire ou ramifié, amino, alkylamino, dialkylamino, alkylcarbonyle en C_1-C_6 linéaire ou ramifié,
- phényle ou hétéroaryle à de 5 à 6 éléments, lesquels sont éventuellement substitués par 1, 2 ou 3 substituants choisis parmi un atome d'halogène, groupe cyano, alkyle en C_1-C_6 linéaire ou ramifié, haloalkyle en C_1-C_6 linéaire ou ramifié, hydroxy, alcoxy en C_1-C_6 linéaire ou ramifié, amino, alkylamino, dialkylamino ;
- R^6 et R^7 forment avec l'atome d'azote auquel ils sont fixés, un noyau à de 3 à 8 éléments qui contient

éventuellement un autre hétéroatome choisi parmi O, N et S, et lequel noyau est éventuellement substitué par 1, 2 ou 3 substituants choisis parmi =0 (oxo), alkyle en C_1-C_6 linéaire ou ramifié, haloalkyle en C_1-C_6 linéaire ou ramifié, alkylcarbonyle en C_1-C_6 linéaire ou ramifié ;
- à condition que lorsque R^1 est -$COOR^5$ et R^2 est -$COOR^8$ alors R^4 n'est pas un groupe méthyle,

et sels pharmaceutiquement acceptables de celui-ci.

2. Composé selon la revendication 1, où X^1, X^2, X^3 et X^5 représentent C-H ou C-B^1, où B^1 représente un atome d'halogène.

3. Composé selon la revendication 2, où X^4 est un groupe choisi parmi C-B^1 et N.

4. Composé selon la revendication 3, où B^1 est choisi parmi un groupe -CN et un atome d'halogène.

5. Composé selon l'une quelconque des revendications 2 à 4, où R^1 est un groupe choisi parmi -COR^5, -$COOR^5$ et -CN.

6. Composé selon la revendication 5, où R^5 est choisi parmi :

- un groupe alkyle en C_1-C_4 où le méthyle terminal est non substitué ou substitué par trois atomes de fluor (-CF_3)
- un groupe alkyle en C_1-C_3 éventuellement substitué à une position quelconque par un groupe alcynyle, et
- un groupe cycloalkyle en C_3-C_5.

7. Composé selon l'une quelconque des revendications 2 à 6, où R^2 représente -$COOR^8$.

8. Composé selon la revendication 7, où R^8 représente indépendamment :

- alkyle en C_1-C_6 linéaire ou ramifié éventuellement substitué par 1, 2 ou 3 substituants choisis parmi des atomes de fluor et cycloalkyle en C_3-C_5 éventuellement substitué par 1, 2 ou 3 atomes de fluor, ou
- groupe A^1, qui représente un cycloalkyle en C_3-C_6 qui est éventuellement substitué par 1, 2 ou 3 substituants choisis dans le groupe consistant en atomes de fluor et groupes alkyle en C_1-C_3.

9. Composé selon l'une quelconque des revendications 2 à 8, où R^3 est un groupe choisi parmi un alkyle en C_1-C_4 linéaire ou ramifié et cycloalkyle en C_3-C_4, lesdits groupes étant éventuellement substitués par 1, 2 ou 3 atomes de fluor.

10. Composé selon l'une quelconque des revendications 2 à 9, où R^4 est un groupe choisi parmi :

- -$N(R^6)R^7$, où R^6 et R^7 sont indépendamment choisis parmi un atome d'hydrogène et un alkyle en C_1-C_3 linéaire ou ramifié,
- un groupe A^1, qui représente un cycloalkyle en C_3-C_6,
- alkyle en C_1-C_3 linéaire ou ramifié, éventuellement substitué par 1, 2 ou 3 substituants choisis parmi 1, 2 ou 3 atomes de fluor ou 1 groupe hydroxyle.

11. Composé selon la revendication 1, où X^1, X^2, X^3 et X^5 représentent -CH, X^4 représente C-B^1, où B^1 représente un groupe -CN ou atome de brome, R^1 est un groupe choisi parmi -$C(O)CH_3$, -$C(O)OCH_3$, -$C(O)OCH_2$-alcynyle et CN, R^2 est un groupe choisi parmi un -C(O)O-groupe alkyle en C_1-C_5 linéaire ou ramifié éventuellement substitué par 1, 2 ou 3 atomes de fluor et $C(O)OCH_2$-cyclopropyle éventuellement substitué par 1, 2 ou 3 atomes de fluor, R^3 est un groupe choisi parmi un groupe alkyle en C_1-C_3 linéaire ou ramifié et cycloalkyle en C_3-C_4 et R^4 est un groupe choisi parmi un alkyle en C_1-C_3 linéaire ou ramifié, cycloalkyle en C_3-C_4 et -NH_2.

12. Composé selon la revendication 1, où X^1, X^2, X^3 et X^5 représentent un -CH, X^4 représente C-B^1, où B^1 représente un groupe -CN, R^1 est un groupe choisi parmi -$C(O)CH_3$, -$C(O)OCH_3$, R^2 est un groupe choisi parmi -$C(O)OCH_2$-cyclopropyle éventuellement substitué par 1, 2 ou 3 atomes de fluor, et -$C(O)OCH_2$-CF_3, R^3 est un groupe choisi parmi méthyle et cyclopropyle et R^4 est un groupe choisi parmi cyclopropyle et -NH_2.

13. Composé selon la revendication 1, qui est choisi dans le groupe consistant en :

5-acétyl-4-(benzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydro-pyridine-3-carboxylate de méthyle

5-acétyl-4-(benzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydro-pyridine-3-carboxylate de méthyle (Enantiomère 1)

5-acétyl-4-(benzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydro-pyridine-3-carboxylate de méthyle (Enantiomère 2)

5-acétyl-4-(benzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydropyridine-3-carboxamide

1-(4-(benzo[b]thiophén-3-yl)-5-benzoyl-2,6-diméthyl-1,4-dihydropyridin-3-yl)éthan-1-one

5-acétyl-4-(benzo[b]thiophén-3-yl)-6-méthyl-2-phényl-1,4-dihydropyridine-3-carboxylate de méthyle

1-(4-(benzo[b]thiophén-3-yl)-2,6-diméthyl-5-nicotinoyl-1,4-dihydro pyridin-3-yl)éthan-1-one

5-acétyl-4-(benzo[b]thiophén-3-yl)-6-méthyl-1,4-dihydro-[2,3'-bipyridine]-3-carboxylate de méthyle

5-acétyl-4-(benzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydropyridine-3-carboxylate de 2,2,2-trifluoroéthyle

acide 5-acétyl-4-(benzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydro-pyridine-3-carboxylique

1-(4-(Benzo[b]thiophén-3-yl)-2,6-diméthyl-5-(4-méthylpipérazine-1-carbonyl)-1,4-dihydropyridin-3-yl)éthan-1-one

5-Acétyl-4-(benzo[b]thiophén-3-yl)-N,N-diéthyl-2,6-diméthyl-1,4-dihydropyridine-3-carboxamide

1-(4-(benzo[b]thiophén-3-yl)-2,6-diméthyl-5-(morpholine-4-carbonyl)-1,4-dihydropyridin-3-yl)éthan-1-one

5-acétyl-4-(benzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydropyridine-3-carboxylate de 2-méthoxyéthyle

5-acétyl-4-(benzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydropyridine-3-carboxylate de 3-acétamidopropyle

5-acétyl-4-(benzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydro-pyridine-3-carboxylate de benzyle

5-acétyl-4-(benzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydropyridine-3-carboxylate de 2-morpholinoéthyle

5-acétyl-4-(benzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydropyridine-3-carboxylate de 2-(diméthylamino)éthyle

5-acétyl-4-(benzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydropyridine-3-carboxylate de 2-acétamidoéthyle

5-acétyl-4-(benzo[b]thiophén-3-yl)-2-(méthoxyméthyl)-6-méthyl-1,4-dihydropyridine-3-carboxylate de méthyle

5-acétyl-4-(benzo[b]thiophén-3-yl)-2-((diméthylamino)méthyl)-6-méthyl-1,4-dihydropyridine-3-carboxylate de méthyle

5-acétyl-4-(benzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydropyridine-3-carboxylate de pyridine-4-ylméthyle

5-acétyl-4-(benzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydropyridine-3-carboxylate de 4-méthoxybenzyle

5-acétyl-4-(benzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydropyridine-3-carboxylate de pyridine-2-ylméthyle

5-acétyl-4-(benzo[b]thiophén-3-yl)-6-méthyl-2-(morpholino-méthyl)-1,4-dihydropyridine-3-carboxylate de méthyle

4-(benzo[b]thiophén-3-yl)-2,6-bis(morpholinométhyl)-1,4-dihydropyridine-3,5-dicarboxylate de diméthyle

5-acétyl-4-(benzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydropyridine-3-carboxylate de 2-hydroxyéthyle

1-(4-(benzo[b]thiophén-3-yl)-5-(cyclopropanecarbonyl)-6-cyclopropyl-2-méthyl-1,4-dihydropyridin-3-yl)éthan-1-one

5-acétyl-4-(benzo[b]thiophén-3-yl)-2-(1-(tert-butoxycarbonyl) azétidin-3-yl)-6-méthyl-1,4-dihydropyridine-3-carboxylate de méthyle

5-acétyl-4-(benzo[b] thiophén-3-yl)-2,6-diméthyl-1,4-dihydropyridine-3-carboxylate de (1-(tert-butoxycarbonyl)pipéridin-4-yl)méthyle

5-acétyl-4-(benzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydropyridine-3-carboxylate de cyclohexylméthyle

4-(benzo[b]thiophén-3-yl)-5-(cyclopropanecarbonyl)-2,6-dicyclopropyl-1,4-dihydropyridine-3-carboxylate de méthyle

5-acétyl-4-(benzo[b]thiophén-3-yl)-2,6-diméthyl-N-phényl-1,4-dihydropyridine-3-carboxamide

5-acétyl-4-(benzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydropyridine-3-carboxylate de tétrahydro-2H-pyran-4-yle

5-acétyl-4-(benzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydropyridine-3-carboxylate de (tétrahydro-2H-pyran-4-yl)méthyle

5-acétyl-4-(benzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydropyridine-3-carboxylate de cyclohexyle

5-acétyl-4-(benzo[b]thiophén-3-yl)-2-(2-méthoxy-2-oxoéthyl)-6-méthyl-1,4-dihydropyridine-3-carboxylate de méthyle

5-acétyl-2,6-diméthyl-4-(2-méthylbenzo[b]thiophén-3-yl)-1,4-dihydropyridine-3-carboxylate de méthyle

5-acétyl-4-(benzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydropyridine-3-carboxylate de cyclopropylméthyle

5-acétyl-4-(benzo[b]thiophén-3-yl)-2-(2-méthoxyéthyl)-6-méthyl-1,4-dihydropyridine-3-carboxylatedeméthyle

5-acétyl-4-(benzo[b]thiophén-3-yl)-2-((benzyloxy)méthyl)-6-méthyl-1,4-dihydropyridine-3-carboxylate de méthyle

5-acétyl-4-(benzo[b]thiophén-3-yl)-6-méthyl-2-(phénoxyméthyl)-1,4-dihydropyridine-3-carboxylate de méthyle

5-acétyl-4-(benzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydropyridine-3-carboxylate de phénéthyle

4-(benzo[b]thiophén-3-yl)-5-(cyclopropanecarbonyl)-6-cyclopropyl-2-méthyl-1,4-dihydropyridine-3-carboxylate de méthyle

5-acétyl-4-(benzo[b]thiophén-3-yl)-6-méthyl-2-(trifluorométhyl)-1,4-dihydropyridine-3-carboxylate de méthyle

5-acétyl-4-(benzo[b]thiophén-3-yl)-6-benzyl-2-méthyl-1,4-dihydropyridine-3-carboxylate de méthyle
4-(benzo[b]thiophén-3-yl)-2,6-diméthyl-5-(2-phénylacétyl)-1,4-dihydropyridine-3-carboxylate de méthyle
4-(benzo[b]thiophén-3-yl)-5-(2-méthoxyacétyl)-2,6-diméthyl-1,4-dihydropyridine-3-carboxylate de méthyle
5-acétyl-4-(benzo[b]thiophén-3-yl)-6-(méthoxyméthyl)-2-méthyl-1,4-dihydropyridine-3-carboxylate de méthyle
5-acétyl-4-(benzo[b]thiophén-3-yl)-2-(fluorométhyl)-6-méthyl-1,4-dihydropyridine-3-carboxylate de méthyle
5-acétyl-4-(5-fluorobenzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydropyridine-3-carboxylate de cyclopropylméthyle
5-acétyl-4-(benzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydropyridine-3-carboxylate de 1-(tert-butoxycarbonyl)pipéridin-4-yle
5-acétyl-4-(benzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydropyridine-3-carboxylate de cyclopentylméthyle
5-acétyl-2,6-diméthyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate de cyclopropylméthyle
5-acétyl-4-(benzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydropyridine-3-carboxylate de 1-méthylpipéridin-4-yle
5-acétyl-4-(benzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydropyridine-3-carboxylate de cyclopentyle
5-acétyl-4-(benzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydropyridine-3-carboxylate de 4,4-diméthylcyclohexyle
5-acétyl-4-(benzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydropyridine-3-carboxylate de cyclobutyle
5-acétyl-4-(5-fluorobenzo[b]thiophén-3-yl)-6-méthyl-2-(trifluorométhyl)-1,4-dihydropyridine-3-carboxylate de méthyle
5-acétyl-2,6-diméthyl-4-(thiéno[3,2-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate de méthyle
5-acétyl-4-(benzo[b]thiophén-3-yl)-2-méthyl-6-(trifluorométhyl)-1,4-dihydropyridine-3-carboxylate de méthyle
5-acétyl-4-(5-chlorobenzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydropyridine-3-carboxylate de cyclopropylméthyle
5-acétyl-4-(5-chlorobenzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydropyridine-3-carboxylate de cyclohexylméthyle
5-acétyl-2,6-diméthyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate de cyclohexylméthyle
5-acétyl-2,6-diméthyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate de cyclopentylméthyle
5-acétyl-2,6-diméthyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate de cyclohexyle
5-acétyl-2,6-diméthyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate de cyclopentyle
5-acétyl-4-(5-chlorobenzo[b]thiophén-3-yl)-6-méthyl-2-(trifluorométhyl)-1,4-dihydropyridine-3-carboxylate de méthyle
5-acétyl-2,6-diméthyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate de benzyle
5-acétyl-2,6-diméthyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate de (tétrahydro-2H-pyran-4-yl)méthyle
5-acétyl-4-(5-fluorobenzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydropyridine-3-carboxylate de benzyle
5-acétyl-4-(5-chlorobenzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydropyridine-3-carboxylate de benzyle
5-acétyl-4-(5-chlorobenzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydropyridine-3-carboxylate de (tétrahydro-2H-pyran-4-yl)méthyle
5-acétyl-4-(5-fluorobenzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydropyridine-3-carboxylate de (tétrahydro-2H-pyran-4-yl)méthyle
5-acétyl-4-(benzo[b]thiophén-3-yl)-6-méthyl-2-(trifluorométhyl)-1,4-dihydropyridine-3-carboxylate de benzyle
5-acétyl-4-(5-fluorobenzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydropyridine-3-carboxylate de pyridine-4-ylméthyle
5-acétyl-2,6-diméthyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate de 4-fluorobenzyle
5-acétyl-4-(benzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydropyridine-3-carboxylate de pyridin-3-ylméthyle
1,1'-(4-(benzo[b]thiophén-3-yl)-2-benzyl-6-méthyl-1,4-dihydropyridine-3,5-diyl)bis(éthan-1-one)
1-(5-acétyl-4-(benzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydropyridin-3-yl)-2-phényléthan-1-one
5-acétyl-6-méthyl-4-(thiéno[2,3-b]pyridin-3-yl)-2-(trifluorométhyl)-1,4-dihydropyridine-3-carboxylate de méthyle
1-(2-méthyl-5-(pipéridine-1-carbonyl)-4-(thiéno[2,3-b]pyridin-3-yl)-6-(trifluorométhyl)-1,4-dihydropyridin-3-yl)éthan-1-one
acide 4-(((5-acétyl-4-(benzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydro-pyridine-3-carbonyl)oxy)méthyl)benzoïque
5-acétyl-6-méthyl-4-(thiéno[2,3-b]pyridin-3-yl)-2-(trifluorométhyl)-1,4-dihydropyridine-3-carboxylate de benzyle
5-acétyl-4-(5-fluorobenzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydropyridine-3-carboxylate de pyridin-3-ylméthyle
5-acétyl-4-(7-bromobenzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydropyridine-3-carboxylate de pyridin-3-ylméthyle
5-acétyl-4-(7-cyanobenzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydro-pyridine-3-carboxylate de pyridin-3-ylméthyle
5-acétyl-4-(5-chlorobenzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydro-pyridine-3-carboxylate de pyridin-3-ylméthyle

5-acétyl-2,6-diméthyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate de pyridin-3-ylméthyle
5-acétyl-4-(5-chlorobenzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydro-pyridine-3-carboxylate de pyridin-4-ylméthyle
5-acétyl-4-(benzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydropyridine-3-carboxylate de 4-(cyclopropylcarbamoyl)benzyle
5-acétyl-2,6-diméthyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate de pyridin-4-ylméthyle
5-acétyl-2,6-diméthyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate de 4-bromobenzyle
5-acétyl-2,6-diméthyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate de 3-bromobenzyle
5-acétyl-2,6-diméthyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate de 2-bromobenzyle
5-acétyl-2,6-diméthyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate de (3-fluoropyridin-4-yl)méthyle
5-acétyl-2,6-diméthyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate de pyrimidin-5-ylméthyle
5-acétyl-2,6-diméthyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate de (5-bromopyridin-3-yl)méthyle
5-acétyl-2,6-diméthyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate de 2-phénylpropan-2-yle
5-acétyl-2,6-diméthyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate de 3-cyanobenzyle
5-acétyl-2,6-diméthyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate de 4-cyanobenzyle
5-acétyl-2,6-diméthyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate de (6-chloropyridin-3-yl)méthyle
5-acétyl-2,6-diméthyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate de 3-morpholinobenzyle
5-acétyl-2,6-diméthyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate de 4,4-diméthylcyclohexyle
5-acétyl-2,6-diméthyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate de (2-chloropyridin-4-yl)méthyle
5-acétyl-2,6-diméthyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate de tétrahydro-2H-pyran-4-yle
5-acétyl-2,6-diméthyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate de 4,4-difluorocyclohexyle
5-acétyl-N-benzyl-N,2,6-triméthyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxamide
5-acétyl-4-(7-bromobenzo[b]thiophén-3-yl)-2-cyclopropyl-6-méthyl-1,4-dihydropyridine-3-carboxylate d'oxétan-3-yle
5-acétyl-4-(7-bromobenzo[b]thiophén-3-yl)-2-cyclopropyl-6-méthyl-1,4-dihydropyridine-3-carboxylate d'isopropyle
5-acétyl-4-(7-bromobenzo[b]thiophén-3-yl)-6-méthyl-2-(trifluorométhyl)-1,4-dihydropyridine-3-carboxylate de méthyle
5-acétyl-4-(7-bromobenzo[b]thiophén-3-yl)-2-cyclopropyl-6-méthyl-1,4-dihydropyridine-3-carboxylate de cyclopropylméthyle
5-acétyl-2-cyclopropyl-6-méthyl-4-(7-(2,2,2-trifluoroacétyl) benzo[b]thiophén-3-yl)-1,4-dihydropyridine-3-carboxylate de méthyle
5-acétyl-4-(7-bromobenzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydropyridine-3-carboxylate de 2-phénylpropan-2-yle
5-acétyl-2-amino-4-(benzo[b]thiophén-3-yl)-6-méthyl-1,4-dihydropyridine-3-carboxylate de méthyle
2-amino-4-(benzo[b]thiophén-3-yl)-5-(cyclopropanecarbonyl)-6-méthyl-1,4-dihydropyridine-3-carboxylate de méthyle
5-acétyl-2-amino-4-(5-fluorobenzo[b]thiophén-3-yl)-6-méthyl-1,4-dihydropyridine-3-carboxylate de méthyle
5-acétyl-2-amino-4-(7-bromobenzo[b]thiophén-3-yl)-6-méthyl-1,4-dihydropyridine-3-carboxylate de méthyle
5-acétyl-2-amino-4-(7-cyanobenzo[b]thiophén-3-yl)-6-méthyl-1,4-dihydropyridine-3-carboxylate de méthyle
5-acétyl-2-amino-4-(7-bromobenzo[b]thiophén-3-yl)-6-méthyl-1,4-dihydropyridine-3-carboxylate de cyclopentyle
2-amino-4-(7-cyanobenzo[b]thiophén-3-yl)-6-méthyl-1,4-dihydropyridine-3,5-dicarboxylate de diméthyle
5-acétyl-2-amino-4-(7-cyanobenzo[b]thiophén-3-yl)-6-méthyl-1,4-dihydropyridine-3-carboxylate de cyclopentyle
2,6-diamino-4-(benzo[b]thiophén-3-yl)-1,4-dihydropyridine-3,5-dicarboxylate de diméthyle
5-acétyl-2-amino-4-(7-cyanobenzo[b]thiophén-3-yl)-6-méthyl-1,4-dihydropyridine-3-carboxylate de cyclopropylméthyle
5-acétyl-2-amino-4-(7-cyanobenzo[b]thiophén-3-yl)-6-méthyl-1,4-dihydropyridine-3-carboxylate de 4,4-difluorocyclohexyle
2-amino-5-cyano-4-(7-cyanobenzo[b]thiophén-3-yl)-6-méthyl-1,4-dihydropyridine-3-carboxylate de méthyle

5-acétyl-2-amino-4-(7-cyanobenzo[b]thiophén-3-yl)-6-méthyl-1,4-dihydropyridine-3-carboxylate de 4-fluorobenzyle
5-acétyl-2-amino-4-(5-fluorothiéno[2,3-b]pyridin-3-yl)-6-méthyl-1,4-dihydropyridine-3-carboxylate de méthyle
2-acétamido-5-acétyl-4-(5-fluorothiéno[2,3-b]pyridin-3-yl)-6-méthyl-1,4-dihydropyridine-3-carboxylate de méthyle
5-acétyl- 2-amino-4-(7-cyanobenzo[b]thiophén-3-yl)-6-méthyl-1,4-dihydropyridine-3-carboxylate de cyclopentylméthyle
2-amino-4-(7-cyanobenzo[b]thiophén-3-yl)-6-méthyl-1,4-dihydropyridine-3,5-dicarboxylate de 3-(cyclopropylméthyl) 5-méthyle
2-amino-4-(7 -cyanobenzo[b]thiophén-3-yl)-6-cyclopropyl-1,4-dihydropyridine-3,5-dicarboxylate de diméthyle
2-amino-4-(7 -cyanobenzo[b]thiophén-3-yl)-6-cyclopropyl-1,4-dihydropyridine-3,5-dicarboxylate de 3-(cyclopropylméthyl) 5-méthyle
2,6-diamino-4-(7-cyanobenzo[b]thiophén-3-yl)-1,4-dihydropyridine-3,5-dicarboxylate de diméthyle
2-amino-4-(7 -cyanobenzo[b]thiophén-3-yl)-6-cyclopropyl-1,4-dihydropyridine-3,5-dicarboxylate de 5-(cyclopropylméthyl) 3-méthyle
2-amino-4-(7-cyanobenzo[b]thiophén-3-yl)-6-méthyl-1,4-dihydropyridine-3,5-dicarboxylate de 3-(4-fluorobenzyl) 5-méthyle
2-amino-4-(7 -cyanobenzo[b]thiophén-3-yl)-6-cyclopropyl-1,4-dihydropyridine-3,5-dicarboxylate de 3-(4-fluorobenzyl) 5-méthyle
2-amino-5-cyano-4-(7-cyanobenzo[b]thiophén-3-yl)-6-méthyl-1,4-dihydropyridine-3-carboxylate de cyclopropylméthyle
2-amino-5-cyano-4-(7-cyanobenzo[b]thiophén-3-yl)-6-méthyl-1,4-dihydropyridine-3-carboxylate de 4-fluorobenzyle
6-amino-5-cyano-4-(7-cyanobenzo[b]thiophén-3-yl)-2-cyclopropyl-1,4-dihydropyridine-3-carboxylate de cyclopropylméthyle
5-méthyl 2-amino-4-(7-cyanobenzo[b]thiophén-3-yl)-6-méthyl-1,4-dihydropyridine-3,5-dicarboxylate de 3-cyclopentyle
5-acétyl-2-amino-4-(6-cyanobenzo[b]thiophén-3-yl)-6-méthyl-1,4-dihydropyridine-3-carboxylate de cyclopropylméthyle
5-acétyl-2-amino-4-(7-cyanobenzo[b]thiophén-3-yl)-6-méthyl-1,4-dihydropyridine-3-carboxylate de cyclohexyle
5-acétyl-2-amino-4-(7-cyanobenzo[b]thiophén-3-yl)-6-méthyl-1,4-dihydropyridine-3-carboxylate de cyclohexylméthyle
2-amino-4-(7-cyanobenzo[b]thiophén-3-yl)-5-(cyclopropanecarbonyl)-6-méthyl-1,4-dihydropyridine-3-carboxylate de cyclopropylméthyle
5-acétyl-2-amino-4-(7-cyanobenzo[b]thiophén-3-yl)-6-méthyl-1,4-dihydropyridine-3-carboxylate de 3-fluorobenzyle
2-amino-4-(7-cyanobenzo[b]thiophén-3-yl)-6-méthyl-1,4-dihydropyridine-3,5-dicarboxylate de 3-(cyclobutylméthyl) 5-méthyle
2-amino-4-(7-cyanobenzo[b]thiophén-3-yl)-6-méthyl-1,4-dihydropyridine-3,5-dicarboxylate de 3-((3,3-difluorocyclobutyl)méthyl) 5-méthyle
2-amino-5-carbamoyl-4-(7-cyanobenzo[b]thiophén-3-yl)-6-méthyl-1,4-dihydropyridine-3-carboxylate de cyclopropylméthyle
2-amino-4-(7-cyanobenzo[b]thiophén-3-yl)-6-méthyl-1,4-dihydropyridine-3,5-dicarboxylate de 3-((2,2-difluorocyclopropyl)méthyl) 5-méthyle
2-amino-4-(7-cyanobenzo[b]thiophén-3-yl)-6-méthyl-1,4-dihydropyridine-3,5-dicarboxylate de 5-cyclopropyl 3-(cyclopropylméthyle)
2-amino-4-(7 -cyanobenzo[b]thiophén-3-yl)-6-cyclopropyl-1,4-dihydropyridine-3,5-dicarboxylate de 3-((2,2-difluorocyclopropyl)méthyl) 5-méthyle
2-amino-4-(7-cyano-5-fluorobenzo[b]thiophén-3-yl)-6-méthyl-1,4-dihydropyridine-3,5-dicarboxylate de 3-(cyclopropylméthyl) 5-méthyle
2-amino-4-(7-cyano-4-fluorobenzo[b]thiophén-3-yl)-6-méthyl-1,4-dihydropyridine-3,5-dicarboxylate de 3-(cyclopropylméthyl) 5-méthyle
2-amino-4-(7-cyanobenzo[b]thiophén-3-yl)-6-méthyl-1,4-dihydropyridine-3,5-dicarboxylate de 3-isopropyl 5-méthyle
2-amino-4-(7-cyanobenzo[b]thiophén-3-yl)-6-méthyl-1,4-dihydropyridine-3,5-dicarboxylate de 3-((2,2-difluoro-3,3-diméthylcyclopropyl)méthyl) 5-méthyle
2-amino-4-(7-cyanobenzo[b]thiophén-3-yl)-6-méthyl-1,4-dihydropyridine-3,5-dicarboxylate de 5-méthyl 3-néo-

pentyle
2-amino-4-(7-cyanothiéno[3,2-b]pyridin-3-yl)-6-méthyl-1,4-dihydropyridine-3,5-dicarboxylate de 3-(cyclopropylméthyl) 5-méthyle
2-amino-4-(7-cyanobenzo[b]thiophén-3-yl)-6-cyclopropyl-1,4-dihydro-pyridine-3,5-dicarboxylate de 5-méthyl 3-néopentyle
2-amino-4-(7-cyanobenzo[b]thiophén-3-yl)-6-méthyl-1,4-dihydropyridine-3,5-dicarboxylate de bis(cyclopropylméthyle)
2-amino-4-(7-cyanobenzo[b]thiophén-3-yl)-6-méthyl-1,4-dihydropyridine-3,5-dicarboxylate de 3-(cyclopropylméthyl) 5-(prop-2-yn-1-yle)
2-amino-4-(5,7-dicyanobenzo[b]thiophén-3-yl)-6-méthyl-1,4-dihydropyridine-3,5-dicarboxylate de 3-(cyclopropylméthyl) 5-méthyle
2-amino-4-(7-cyanobenzo[b]thiophén-3-yl)-6-méthyl-1,4-dihydropyridine-3,5-dicarboxylate de 5-(but-2-yn-1-yl) 3-(cyclopropylméthyle)
2-amino-4-(7-cyanobenzo[b]thiophén-3-yl)-6-méthyl-1,4-dihydropyridine-3,5-dicarboxylate de 5-méthyl 3-(2,2,2-trifluoroéthyle)
2-amino-4-(7-cyanobenzo[b]thiophén-3-yl)-6-méthyl-1,4-dihydropyridine-3,5-dicarboxylate de 3-(cyclopropylméthyl) 5-(2,2,2-trifluoroéthyle)
2-amino-4-(6-chloro-7-cyanobenzo[b]thiophén-3-yl)-6-méthyl-1,4-dihydropyridine-3,5-dicarboxylate de 3-(cyclopropylméthyl) 5-méthyle
2-amino-4-(7-cyanobenzo[b] thiophén-3-yl)-6-méthyl-1,4-dihydropyridine-3,5-dicarboxylate de 3-(2-fluoro-2-méthylpropyl) 5-méthyle
2-amino-4-(7-cyano-6-(trifluorométhyl)benzo[b]thiophén-3-yl)-6-méthyl-1,4-dihydropyridine-3,5-dicarboxylate de 3-(cyclopropylméthyl) 5-méthyle
2-amino-4-(7-cyanobenzo[b]thiophén-3-yl)-6-méthyl-1,4-dihydropyridine-3,5-dicarboxylate de 5-méthyl 3-prop-2-yn-1-yle
2-amino-4-(7 -cyanobenzo[b]thiophén-3-yl)-6-(trifluorométhyl)-1,4-dihydropyridine-3,5-dicarboxylate de 3-(cyclopropylméthyl) 5-méthyle
4-(benzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydropyridine-3,5-dicarbonitrile
4-(6-hydroxybenzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydropyridine-3,5-dicarbonitrile
4-(6-méthoxybenzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydropyridine-3,5-dicarbonitrile
2,6-diméthyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3,5-dicarbonitrile
4-(benzo[b]thiophén-3-yl)-2-méthyl-6-phényl-1,4-dihydropyridine-3,5-dicarbonitrile
4-(benzo[b]thiophén-3-yl)-2-cyclopropyl-6-méthyl-1,4-dihydropyridine-3,5-dicarbonitrile
5-acétyl-4-(benzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydropyridine-3-carbonitrile
4-(benzo[b]thiophén-3-yl)-5-cyano-2,6-diméthyl-1,4-dihydropyridine-3-carboxylate d'éthyle
4-(benzo[b]thiophén-3-yl)-5-cyano-2-méthyl-6-phényl-1,4-dihydropyridine-3-carboxylate d'éthyle
4-(benzo[b]thiophén-3-yl)-5-cyano-2-cyclopropyl-6-méthyl-1,4-dihydropyridine-3-carboxylate d'éthyle
4-(benzo[b]thiophén-3-yl)-5-cyano-2-cyclopropyl-6-méthyl-1,4-dihydropyridine-3-carboxylate de méthyle
1,1'-(4-(benzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydropyridine-3,5-diyl)diéthanone
1,1'-(4-(6-hydroxybenzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydro-pyridine-3,5-diyl)bis(éthan-1-one)
1,1'-(4-(6-méthoxybenzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydro-pyridine-3,5-diyl)diéthanone
1,1'-(4-(benzo[b]thiophén-3-yl)-2,6-dicyclopropyl-1,4-dihydropyridine-3,5-diyl)diéthanone
1,1'-(4-(5-chlorobenzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydropyridine-3,5-diyl)diéthanone
1,1'-(4-(5-bromobenzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydropyridine-3,5-diyl)diéthanone
1,1'-(4-(5-fluorobenzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydropyridine-3,5-diyl)bis(éthan-1-one)
1,1'-(2,6-diméthyl-4-(5-morpholinobenzo[b]thiophén-3-yl)-1,4-dihydropyridine-3,5-diyl)bis(éthan-1-one)
1,1'-(2,6-diméthyl-4-(5-(4-méthylpipérazin-1-yl)benzo[b]thiophén-3-yl)-1,4-dihydropyridine-3,5-diyl)bis(éthan-1-one)
1,1'-(4-(5-(benzylamino)benzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydropyridine-3,5-diyl)bis(éthan-1-one)
3-(3,5-diacétyl-2,6-diméthyl-1,4-dihydropyridin-4-yl)benzo[b]thiophène-5-carbonitrile
acide 3-(3,5-diacétyl-2,6-diméthyl-1,4-dihydropyridin-4-yl)benzo[b]thiophène-5-carboxylique
N-cyclopropyl-3-(3,5-diacétyl-2,6-diméthyl-1,4-dihydropyridin-4-yl)benzo[b]thiophène-5-carboxamide
N-(cyclopropylméthyl)-3-(3,5-diacétyl-2,6-diméthyl-1,4-dihydropyridin-4-yl)benzo[b]thiophène-5-carboxamide
1,1'-(2,6-diméthyl-4-(5-(4-méthylpipérazine-1-carbonyl)benzo[b]thiophén-3-yl)-1,4-dihydropyridine-3,5-diyl)bis(éthan-1-one)
1,r-(2,6-diméthyl-4-(5-(morpholine-4-carbonyl)benzo[b]thiophén-3-yl)-1,4-dihydropyridine-3,5-diyl)bis(éthan-1-one)
1,1'-(2,6-diméthyl-4-(thiéno[3,2-c]pyridin-3-yl)-1,4-dihydropyridine-3,5-diyl)bis(éthan-1-one)

1,1'-(2,6-diméthyl-4-(thiéno[2,3-c]pyridin-3-yl)-1,4-dihydropyridine-3,5-diyl)bis(éthan-1-one)
1,1'-(2,6-diméthyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3,5-diyl)bis(éthan-1-one)
5-acétyl-4-(benzo[b]thiophén-3-yl)-6-méthyl-1,4-dihydropyridine-2,3-dicarboxylate de diméthyle
5-acétyl-4-(7-cyanobenzo[b]thiophén-3-yl)-6-méthyl-1,4-dihydropyridine-2,3-dicarboxylate de diméthyle
5-acétyl-4-(benzo[b]thiophén-3-yl)-2-cyclopropyl-6-méthyl-1,4-dihydropyridine-3-carboxylate de méthyle
4-(benzo[b]thiophén-3-yl)-2,6-dicyclopropyl-1,4-dihydropyridine-3,5-dicarboxylate de diméthyle
5-acétyl-4-(benzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydropyridine-3-carboxylate d'éthyle
5-acétyl-4-(5-chlorobenzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydropyridine-3-carboxylate de méthyle
1,1'-(4-(benzo[b]thiophén-3-yl)-2-cyclopropyl-6-méthyl-1,4-dihydro-pyridine-3,5-diyl)diéthanone
1-(4-(benzo[b]thiophén-3-yl)-2,6-diméthyl-5-(méthylsulfonyl)-1,4-dihydro-pyridin-3-yl)éthanone
5-acétyl-4-(5-fluorobenzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydropyridine-3-carboxylate de méthyle
5-acétyl-4-(5-bromobenzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydropyridine-3-carboxylate de méthyle
5-acétyl-4-(5-cyanobenzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydropyridine-3-carboxylate de méthyle
acide 3-(3-acétyl-5-(méthoxycarbonyl)-2,6-diméthyl-1,4-dihydropyridin-4-yl)benzo[b]thiophène-5-carboxylique
5-acétyl-4-(5-(cyclopropylcarbamoyl)benzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydropyridine-3-carboxylate de méthyle
5-acétyl-4-(5-((cyclopropylméthyl)carbamoyl)benzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydropyridine-3-carboxylate de méthyle
5-acétyl-2,6-diméthyl-4-(5-(4-méthylpipérazine-1-carbonyl)benzo[b] thiophén-3-yl)-1,4-dihydropyridine-3-carboxylate de méthyle
5-acétyl-2,6-diméthyl-4-(5-(morpholine-4-carbonyl)benzo[b]thiophén-3-yl)-1,4-dihydropyridine-3-carboxylate de méthyle
5-acétyl-2,6-diméthyl-4-(thiéno[3,2-c]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate de méthyle
5-acétyl-2,6-diméthyl-4-(thiéno[2,3-c]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate de méthyle
5-acétyl-2,6-diméthyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate de méthyle
5-acétyl-2-cyclopropyl-4-(5-fluorobenzo[b]thiophén-3-yl)-6-méthyl-1,4-dihydropyridine-3-carboxylate de méthyle
2,6-dicyclopropyl-4-(5-fluorobenzo[b]thiophén-3-yl)-1,4-dihydropyridine-3,5-dicarboxylate de diméthyle
5-acétyl-2-cyclopropyl-6-méthyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate de méthyle
2,6-dicyclopropyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3,5-dicarboxylate de diméthyle
5-acétyl-4-(benzo[b]thiophén-3-yl)-2,6-dicyclopropyl-1,4-dihydropyridine-3-carboxylate de méthyle
5-acétyl-4-(5-chlorobenzo[b]thiophén-3-yl)-2-cyclopropyl-6-méthyl-1,4-dihydropyridine-3-carboxylate de méthyle
4-(5-chlorobenzo[b]thiophén-3-yl)-2,6-dicyclopropyl-1,4-dihydropyridine-3,5-dicarboxylate de diméthyle
5-acétyl-4-(7-bromobenzo[b]thiophén-3-yl)-2-cyclopropyl-6-méthyl-1,4-dihydropyridine-3-carboxylate de méthyle
5-acétyl-2-cyclopropyl-4-(7-(cyclopropylcarbamoyl)benzo[b] thiophén-3-yl)-6-méthyl-1,4-dihydropyridine-3-carboxylate de méthyle
5-acétyl-4-(7-cyanobenzo[b]thiophén-3-yl)-2-cyclopropyl-6-méthyl-1,4-dihydropyridine-3-carboxylate de méthyle
4-(7-cyanobenzo[b]thiophén-3-yl)-2,6-dicyclopropyl-1,4-dihydropyridine-3,5-dicarboxylate de diméthyle
5-acétyl-2-cyclopropyl-4-(7-(méthoxycarbonyl) benzo[b]thiophén-3-yl)-6-méthyl-1,4-dihydropyridine-3-carboxylate de méthyle
2,6-dicyclopropyl-4-(7-(méthoxycarbonyl)benzo[b]thiophén-3-yl)-1,4-dihydropyridine-3,5-dicarboxylate de diméthyle
acide 3-(3-acétyl-6-cyclopropyl-5-(méthoxycarbonyl)-2-méthyl-1,4-dihydropyridin-4-yl)benzo[b]thiophène-7-carboxylique
5-acétyl-2-cyclopropyl-6-méthyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate de benzyle
5-acétyl-4-(benzo[b]thiophén-3-yl)-2-cyclopropyl-6-méthyl-1,4-dihydropyridine-3-carboxylate de pyridin-4-ylméthyle
2,6-dicyclopropyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3,5-dicarboxylate de bis(pyridin-4-ylméthyle)
5-acétyl-4-(7-bromobenzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydropyridine-3-carboxylate de pyridin-4-ylméthyle
5-acétyl-4-(5-chlorobenzo[b]thiophén-3-yl)-2-cyclopropyl-6-méthyl-1,4-dihydropyridine-3-carboxylate de pyridin-4-ylméthyle
5-acétyl-4-(7-cyanobenzo[b]thiophén-3-yl)-2-cyclopropyl-6-méthyl-1,4-dihydropyridine-3-carboxylate de pyridin-4-ylméthyle

5-acétyl-2-cyclopropyl-6-méthyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate de pyridin-4-ylméthyle

5-acétyl-2-cyclopropyl-4-(7-(méthoxycarbonyl)benzo[b]thiophén-3-yl)-6-méthyl-1,4-dihydropyridine-3-carboxylate de benzyle

2,6-dicyclopropyl-4-(7-(méthoxycarbonyl)benzo[b]thiophén-3-yl)-1,4-dihydropyridine-3,5-dicarboxylate de dibenzyle

5-acétyl-4-(7-(méthoxycarbonyl)benzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydropyridine-3-carboxylate de benzyle

3-(3,5-diacétyl-2,6-diméthyl-1,4-dihydropyridin-4-yl)benzo[b]thiophène-7-carboxylate de méthyle

3-(3,5-diacétyl-2,6-diméthyl-1,4-dihydropyridin-4-yl)benzo[b]thiophène-7-carbonitrile

5-acétyl-4-(7-bromobenzo[b]thiophén-3-yl)-2-cyclopropyl-6-méthyl-1,4-dihydropyridine-3-carboxylate de pyridin-4-ylméthyle

5-acétyl-2-cyclopropyl-6-méthyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate de 4-fluorobenzyle

2,6-dicyclopropyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3,5-dicarboxylate de bis(4-fluorobenzyle)

5-acétyl-2-cyclopropyl-6-méthyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate de 4-cyanobenzyle

5-acétyl-4-(7-chlorobenzo[b]thiophén-3-yl)-2-cyclopropyl-6-méthyl-1,4-dihydropyridine-3-carboxylate de méthyle

5-acétyl-2-cyclopropyl-6-méthyl-4-(7-(trifluorométhyl)benzo[b]thiophén-3-yl)-1,4-dihydropyridine-3-carboxylate de méthyle

5-acétyl-2,6-diméthyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate de 3-chlorobenzyle

5-acétyl-4-(7-bromobenzo[b]thiophén-3-yl)-2-cyclopropyl-6-méthyl-1,4-dihydropyridine-3-carboxylate de 2-phénylpropan-2-yle

5-acétyl-2-cyclopropyl-6-méthyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate de cyclohexyle

5-acétyl-2-cyclopropyl-6-méthyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate de 2-phénylpropan-2-yle

1-(4-(7-bromobenzo[b]thiophén-3-yl)-5-(cyclopropanecarbonyl)-6-cyclopropyl-2-méthyl-1,4-dihydropyridin-3-yl)éthan-1-one

5-acétyl-2-cyclopropyl-6-méthyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate de 3-chlorobenzyle

5-acétyl-2,6-diméthyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate de 2-(4-fluorophényl)propan-2-yle

5-acétyl-4-(7-bromobenzo[b]thiophén-3-yl)-2-cyclopropyl-6-méthyl-1,4-dihydropyridine-3-carboxylate de 2-(4-fluorophényl)propan-2-yle

5-acétyl-2-cyclopropyl-6-méthyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate de 2-(4-fluorophényl)propan-2-yle

5-acétyl-2-cyclopropyl-4-(7-fluorobenzo[b]thiophén-3-yl)-6-méthyl-1,4-dihydropyridine-3-carboxylate de méthyle

5-acétyl-2-cyclopropyl-6-méthyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate de cyclopropylméthyle

5-acétyl-2-cyclopropyl-6-méthyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate de cyclopentyle

5-acétyl-4-(7-cyanobenzo[b]thiophén-3-yl)-2-cyclopropyl-6-méthyl-1,4-dihydropyridine-3-carboxylate de cyclopropylméthyle

5-acétyl-4-(7-bromobenzo[b]thiophén-3-yl)-2-cyclobutyl-6-méthyl-1,4-dihydropyridine-3-carboxylate de méthyle

4-(7-cyanobenzo[b]thiophén-3-yl)-2-cyclopropyl-6-méthyl-1,4-dihydro-pyridine-3,5-dicarboxylate de diméthyle

5-cyano-4-(7-cyanobenzo[b]thiophén-3-yl)-2-cyclopropyl-6-méthyl-1,4-dihydropyridine-3-carboxylate de méthyle

5-acétyl-4-(7-bromobenzo[b]thiophén-3-yl)-2-cyclopentyl-6-méthyl-1,4-dihydropyridine-3-carboxylate de méthyle

5-acétyl-4-(7-bromobenzo[b]thiophén-3-yl)-2-cyclohexyl-6-méthyl-1,4-dihydropyridine-3-carboxylate de méthyle

5-cyano-4-(7-cyanobenzo[b]thiophén-3-yl)-2,6-dicyclopropyl-1,4-dihydropyridine-3-carboxylate de méthyle

5-acétyl-4-(7-bromobenzo[b]thiophén-3-yl)-2,6-diméthyl-1,4-dihydro-pyridine-3-carboxylate de 3-((4-méthylpipérazin-1-yl)méthyl)benzyle

4-(7-cyanobenzo[b]thiophén-3-yl)-2-cyclopropyl-6-méthyl-1,4-dihydropyridine-3,5-dicarboxylate de 3-(cyclo-

propylméthyl) 5-méthyle
4-(7-cyanobenzo[b]thiophén-3-yl)-2,6-dicyclopropyl-1,4-dihydropyridine-3,5-dicarboxylate de 3-(cyclopropylméthyl) 5-méthyle
5-cyano-4-(7-cyanobenzo[b]thiophén-3-yl)-2-cyclopropyl-6-méthyl-1,4-dihydropyridine-3-carboxylate de cyclopropylméthyle
2-cyano-4-(7-cyanobenzo[b]thiophén-3-yl)-6-cyclopropyl-1,4-dihydro-pyridine-3,5-dicarboxylate de diméthyle
2-cyano-4-(7-cyanobenzo[b]thiophén-3-yl)-6-méthyl-1,4-dihydropyridine-3,5-dicarboxylate de diméthyle
5-acétyl-2-((2-aminoéthoxy)méthyl)-4-(benzo[b]thiophén-3-yl)-6-méthyl-1,4-dihydropyridine-3-carboxylate de méthyle
5-acétyl-2-((2-aminoéthoxy)méthyl)-4-(7-bromobenzo[b]thiophén-3-yl)-6-méthyl-1,4-dihydropyridine-3-carboxylate de méthyle
5-acétyl-2-((2-aminoéthoxy)méthyl)-4-(7-cyanobenzo[b]thiophén-3-yl)-6-méthyl-1,4-dihydropyridine-3-carboxylate de méthyle
4-(7-cyanobenzo[b]thiophén-3-yl)-2-cyclopropyl-6-formyl-1,4-dihydropyridine-3,5-dicarboxylate de diméthyle
4-(7-cyanobenzo[b]thiophén-3-yl)-2-cyclopropyl-6-(hydroxyméthyl)-1,4-dihydropyridine-3,5-dicarboxylate de diméthyle
4-(7-cyanobenzo[b]thiophén-3-yl)-2-formyl-6-méthyl-1,4-dihydropyridine-3,5-dicarboxylate de diméthyle
4-(7-cyanobenzo[b]thiophén-3-yl)-2-(hydroxyméthyl)-6-méthyl-1,4-dihydropyridine-3,5-dicarboxylate de diméthyle
2-cyano-6-méthyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3,5-dicarboxylate de diméthyle
5-acétyl-4-(6-cyanobenzo[b]thiophén-3-yl)-2-cyclopropyl-6-méthyl-1,4-dihydropyridine-3-carboxylate de cyclopropylméthyle
2,5-diacétyl-4-(7-cyanobenzo[b]thiophén-3-yl)-6-méthyl-1,4-dihydro-pyridine-3-carboxylate de cyclopropylméthyle
5-acétyl-2-amino-4-(benzo[b]thiophén-3-yl)-6-méthyl-1,4-dihydropyridine-3-carboxylate hydrochlorure de méthyle
5-acétyl-2-amino-4-(benzo[b]thiophén-3-yl)-6-méthyl-1,4-dihydropyridine-3-carboxylate trifluorométhanesulfonate de méthyle
5-acétyl-2,6-diméthyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate de 4-(pyridin-4-yl)benzyle
5-acétyl-2,6-diméthyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate de 4-(pyridin-3-yl)benzyle
5-acétyl-2,6-diméthyl-4-(thiéno[2,3-b]pyridin-3-yl)-l,4-dihydropyridine-3-carboxylate de 3-(pyridin-4-yl)benzyle
5-acétyl-2,6-diméthyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate de 3-(pyridin-4-yl)benzyle
5-acétyl-2,6-diméthyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate de 2-(pyridin-4-yl)benzyle
5-acétyl-2,6-diméthyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate de 2-(pyridin-3-yl)benzyle
5-acétyl-2,6-diméthyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate de [3,4'-bipyridin]-5-ylméthyle
5-acétyl-2,6-diméthyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate de [3,3'-bipyridin]-5-ylméthyle
5-acétyl-2,6-diméthyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate de [2,4'-bipyridin]-5-ylméthyle
5-acétyl-2,6-diméthyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate de [2,3'-bipyridin]-5-ylméthyle
5-acétyl-2,6-diméthyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate de [2,3'-bipyridin]-4-ylméthyle
5-acétyl-2,6-diméthyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate de [2,4'-bipyridin]-4-ylméthyle
5-acétyl-2-cyclopropyl-6-méthyl-4-(7-(pyridin-4-yl)benzo[b]thiophén-3-yl)-1,4-dihydropyridine-3-carboxylate de méthyle
5-acétyl-2-cyclopropyl-4-(7-cyclopropylbenzo[b]thiophén-3-yl)-6-méthyl-1,4-dihydropyridine-3-carboxylate de méthyle
5-acétyl-2-cyclopropyl-6-méthyl-4-(thiéno[2,3-b]pyridin-3-yl)-1,4-dihydropyridine-3-carboxylate de 3-(pyridin-4-yl)benzyle
1,1'-(2,6-diméthyl-4-(5-(pyridin-3-yl)benzo[b]thiophén-3-yl)-1,4-dihydro-pyridine-3,5-diyl)diéthanone
5-acétyl-2-cyclopropyl-6-méthyl-4-(7-phénylbenzo[b]thiophén-3-yl)-1,4-dihydropyridine-3-carboxylate de méthyle.

14. Composé comme défini dans l'une quelconque des revendications 1 à 13 pour une utilisation dans le traitement d'une maladie ou d'un état pathologique susceptible d'amélioration par antagonisme du récepteur d'androgène

et/ou récepteur de glucocorticoïde choisi parmi le cancer de la prostate, cancer de la prostate résistant à la castration, cancer du pancréas, cancer de la vessie, cancer du rein, cancer gastrique, cancer du poumon, cancer du sein, cancer du colon, cancer colorectal, cancer des ovaires, et d'autres tumeurs solides, mélanome, cancers métastasés, hyperplasie de la prostate bénigne, syndrome de l'ovaire polycystique (PCOS), perte des cheveux, hirsutisme, acné, hypogonadisme, maladies atrophiant les muscles et cachexie, et syndrome de Cushing, prise de poids induite par des anti-psychotiques, obésité, trouble du stress post-traumatique et alcoolisme.

15. Composition pharmaceutique comprenant un composé selon l'une quelconque des revendications 1 à 13 et un diluant ou support pharmaceutiquement acceptable.

16. Composition pharmaceutique selon la revendication 15 comprenant de plus une quantité thérapeutiquement efficace d'un agent thérapeutique choisi parmi des agents pour traiter le cancer de la prostate, cancer de la prostate résistant à la castration, cancer du pancréas, cancer de la vessie, cancer du rein, cancer gastrique, cancer du poumon, cancer du sein, cancer du colon, cancer colorectal, cancer des ovaires, et d'autres tumeurs solides, mélanome, cancers métastasés, hyperplasie de la prostate bénigne, syndrome de l'ovaire polycystique (PCOS), perte des cheveux, hirsutisme, acné, hypogonadisme, maladies atrophiant les muscles et cachexie, et syndrome de Cushing, prise de poids induite par des anti-psychotiques, obésité, trouble du stress post-traumatique et alcoolisme.

17. Produit de combinaison comprenant un composé selon l'une quelconque des revendications 1 à 13 et un agent thérapeutique utilisé pour le traitement du cancer de la prostate, cancer de la prostate résistant à la castration, cancer du pancréas, cancer de la vessie, cancer du rein, cancer gastrique, cancer du poumon, cancer du sein, cancer du colon, cancer colorectal, cancer des ovaires, et d'autres tumeurs solides, mélanome, cancers métastasés, hyperplasie de la prostate bénigne, syndrome de l'ovaire polycystique (PCOS), perte des cheveux, hirsutisme, acné, hypogonadisme, maladies atrophiant les muscles et cachexie, et syndrome de Cushing, prise de poids induite par des anti-psychotiques, obésité, trouble du stress post-traumatique et alcoolisme, en particulier un agent thérapeutique choisi parmi un agoniste ou antagoniste du récepteur de l'hormone libérant de la gonadotropine (GnRH), antagoniste du récepteur d'androgène, inhibiteur de CYP17, inhibiteur de VEGF, inhibiteur de EGFR, inhibiteur de PI3K, inhibiteur de AKT, inhibiteur de mTOR, inhibiteur de c-Met, inhibiteur de Src, inhibiteur de PARP, angiopoïétine, inhibiteur de ALK, inhibiteur de ROS-1, anticorps anti-(IGF), agent anti-néoplastique de taxane, inhibiteur de topoisomérase II, antibiotique anti-tumoral, inhibiteur de HSP90, inhibiteur de kinase Aurora, vaccin ciblant le PSA, antagonistes de GR, inhibiteurs de 11-bêta HSD, un ou pluieurs agents immunothérapeutiques choisis dans le groupe consistant en anticorps anti-CTLA4, anticorps anti-PD1 et anticorps anti-PDL1, en particulier un anticorps choisi dans le groupe consistant en ipilimumab, tremelimumab, nivolumab, pembrolizumab, CT-011, AMP-224, MPDL3280A, MEDI4736 et MDX-1105.

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