

## Title (en)

TETRACYCLIC TERPENE SERIES COMPOUNDS, METHODS FOR PREPARING SAME, USES THEREOF AS MEDICINES AND PHARMACEUTICAL COMPOUNDS CONTAINING SAME

## Title (de)

TETRACYCLISCHE VERBINDUNGEN DER TERPENREIHE, VERFAHREN ZU IHRER HERSTELLUNG, IHRE VERWENDUNG ALS MEDIZIN UND PHARMAZEUTISCHE VERBINDUNGEN, DIE SIE ENTHALTEN

## Title (fr)

COMPOSÉS EN SÉRIE TRITERPÈNES TÉTRACYCLIQUES, LEURS PROCÉDÉS DE PRÉPARATION, LEURS APPLICATIONS COMME MÉDICAMENTS ET LES COMPOSÉS PHARMACEUTIQUES LES RENFERMANT

## Publication

**EP 1846435 A1 20071024 (FR)**

## Application

**EP 06707715 A 20060113**

## Priority

- EP 2006050200 W 20060113
- FR 0501029 A 20050202

## Abstract (en)

[origin: FR2881428A1] Triterpenic alkaloids (I) and their addition salts, isomers, enantiomers and/or diastereomers are new. Triterpenic alkaloids of formula (I) and their addition salts, isomers, enantiomers and/or diastereomers are new. R 1-CH 2X 1R 7, -CH=NR 5or -CH=O; X 1-X 3O, NH or S; R 7, R 8H, 1-10C alkyl, 1-10C alkyl-phenyl, 1-10C alkyl-carbonyl or SO 2R 9; R 91-10C alkyl or 1-10C alkyl-phenyl; either R ,R 3H or -C(=X)-R 10; or R 10H, 1-10C alkyl, (1-10C alkyl)phenyl, 3-10C cycloalkyl; R 4H, 10C alkyl or -X 3-R 12; R 12H (preferred), 1-10C alkylcarbonyl, 1-10C alkyl-phenyl or 1-10C alkyl-sulfonyl; R 5N-oxide-N +>OCH 3R 13or NCH 3R 13; R 13H, 3-10C cycloalkyl, 1-10C alkyl, phenyl or phthalimide (preferably CH 3); R 6=O or -OR 14; and R 14H, 1-10C alkyl, 1-10C alkylcarbonyl, 1-10C alkyl-phenyl or 1-10C alkyl-sulfonyl. Provided that: when X 1is S, R 7is not SO 2R 9; at least one of R 2and R 3is H. Provided that: when R 2is absent, then R 1is -CH 2X 1R 7, and NR 7and X 1R 7together forms -N=C(R 11)-X 1- (where R 11is H, 1= 1-C alkyl, (1-C alkyl)phenyl) or 3-10C cycloalkyl); when R 2= H, then R 1is -CH 2X 1R 7, and NR 7and X 1R 7together forms -N-CH(R 11)-X 1-. Provided that (I) is not: N-(16-Hydroxy-4-hydroxymethyl-17-isopropyl-4,13,14-trimethyl-11-oxo-tetradecahydro-cyclopropa[9,10]cyclopenta[a]phenanthren-3-yl)-isobutyramide; N-[3-(1-dimethylamino-ethyl)-2-hydroxy-10-hydroxymethyl-3a,10,12b-trimethyl-5-oxo-1,2,3,3a,4,5,5a,6,8,9,10,10a,11,12,12a,12b-hexadecahydro-benzo[4,5]cyclohepta[1,2-e]inden-9-yl]-isobutyramide; N-[17-(1-dimethylamino-ethyl)-16-hydroxy-4-hydroxymethyl-4,13,14-trimethyl-11-oxo-tetradecahydro-cyclopropa[9,10]cyclopenta[a]phenanthren-3-yl]-benzamide; acetic acid 4-acetoxymethyl-17-(1-dimethylamino-ethyl)-3-isobutyrylamino-4,13,14-trimethyl-11-oxo-tetradecahydro-cyclopropa[9,10]cyclopenta[a]phenanthren-16-yl ester; 3-(1-dimethylamino-ethyl)-2-hydroxy-10-isopropyl-3a,12a,14b-trimethyl-2,3,3a,5a,6,8,8a,12,12a,12b,13,14,14a,14b-tetradecahydro-1H,4H-11-oxa-9-aza-indeno[5',4':4,5]cyclohepta[1,2-a]naphthalen-5-one; acetic acid 3-(1-dimethylamino-ethyl)-10-isopropyl-3a,12a,14b-trimethyl-5-oxo-2,3,3a,4,5,5a,6,8,8a,12,12a,12b,13,14,14a,14b-hexadecahydro-1H-11-oxa-9-aza-indeno[5',4':4,5]cyclohepta[1,2-a]naphthalen-2-yl ester, 3-(1-dimethylamino-ethyl)-2-hydroxy-10-isopropyl-3a,12a,14b-trimethyl-2,3,3a,5a,6,8,8a,9,10,12,12a,12b,13,14,14a,14b-hexadecahydro-1H,4H-11-oxa-9-aza-indeno[5',4':4,5]cyclohepta[1,2-a]naphthalen-5-one; N-[3-(1-dimethylamino-ethyl)-2-hydroxy-10-hydroxymethyl-3a,10,12b-trimethyl-5-oxo-1,2,3,3a,4,5,5a,6,8,9,10,10a,11,12,12a,12b-hexadecahydro-benzo[4,5]cyclohepta[1,2-e]inden-9-yl]-isobutyramide; N-[16-hydroxy-4-hydroxymethyl-4,13,14-trimethyl-17-(1-methylamino-ethyl)-11-oxo-tetradecahydro-cyclopropa[9,10]cyclopenta[a]phenanthren-3-yl]-isobutyramide; methanesulfonic acid 17-(1-dimethylamino-ethyl)-3-isobutyrylamino-16-methanesulfonyloxy-4,13,14-trimethyl-11-oxo-tetradecahydro-cyclopropa[9,10]cyclopenta[a]phenanthren-4-ylmethyl ester; acetic acid 16-acetoxy-17-[1-(acetyl-methyl-amino)-ethyl]-3-isobutyrylamino-4,13,14-trimethyl-11-oxo-tetradecahydro-cyclopropa[9,10]cyclopenta[a]phenanthren-4-ylmethyl ester or alkaloid compound of formula (Ic), where all the above compounds are in their stereo isomeric form. Independent claims are included for: (1) the preparations of (I); and (2) the preparation of intermediate N-(16-hydroxy-4-hydroxymethyl-17-isopropyl-4,13,14-trimethyl-11-oxo-tetradecahydro-cyclopropa[9,10]cyclopenta[a]phenanthren-3-yl)-isobutyramide of formula (X). [Image] [Image] [Image] ACTIVITY : CNS-Gen.; Neuroprotective; Nootropic; Antiparkinsonian; Vasotropic; Tranquilizer; Vulnerary; Muscular-Gen. MECHANISM OF ACTION : Acetylcholinesterase inhibitor. The ability of (I) to inhibit acetylcholinesterase was tested using in vitro assay in human. The results showed (20S)-3beta -isobutyrylamino-9,19-cyclo-4alpha -hydroxymethyl-4beta , 14alpha -dimethyl-20-dimethylamino-5alpha ,9beta -pregnan-16alpha -ol-11-one exhibited IC 50value of 31 nM.

## IPC 8 full level

**C07J 53/00** (2006.01); **C07J 41/00** (2006.01); **C07J 71/00** (2006.01)

## CPC (source: EP US)

**A61P 21/04** (2017.12 - EP); **A61P 25/00** (2017.12 - EP); **A61P 25/02** (2017.12 - EP); **A61P 25/16** (2017.12 - EP); **A61P 25/28** (2017.12 - EP); **C07J 41/0005** (2013.01 - EP US); **C07J 63/004** (2013.01 - EP US)

## Citation (search report)

See references of WO 2006082126A1

## Designated contracting state (EPC)

AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IS IT LI LT LU LV MC NL PL PT RO SE SI SK TR

## DOCDB simple family (publication)

**FR 2881428 A1 20060804**; **FR 2881428 B1 20081219**; CA 2601724 A1 20060810; EP 1846435 A1 20071024; JP 2008528656 A 20080731; US 2012040930 A1 20120216; WO 2006082126 A1 20060810

## DOCDB simple family (application)

**FR 0501029 A 20050202**; CA 2601724 A 20060113; EP 06707715 A 20060113; EP 2006050200 W 20060113; JP 2007553576 A 20060113; US 81524806 A 20060113