

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

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Application
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Priority

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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.

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