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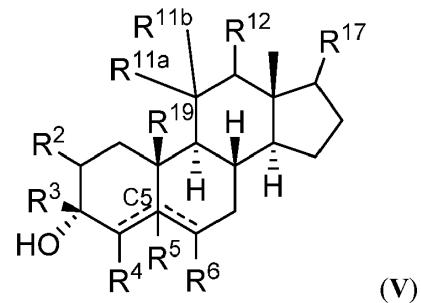
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(54)	Title	C7, C12, AND C16 SUBSTITUTED NEUROACTIVE STEROIDS AND THEIR METHODS OF USE
(56)	References Cited:	US-A1- 2016 108 080 WO-A2-2010/003391 WO-A1-2015/180679 WO-A1-98/05337 BARBORA SLAVÍKOVÁ ET AL: "Allopregnanolone (3[alpha]-Hydroxy-5[alpha]-pregnan-20-one) Derivatives with a Polar Chain in Position 16[alpha]: Synthesis and Activity", JOURNAL OF MEDICINAL CHEMISTRY, vol. 52, no. 7, 9 April 2009 (2009-04-09), pages 2119-2125, XP055406982, ISSN: 0022-2623, DOI: 10.1021/jm801454a

- STASTNA E ET AL: "Synthesis of C3, C5, and C7 pregnane derivatives and their effect on NMDA receptor responses in cultured rat hippocampal neurons", STEROIDS, ELSEVIER SCIENCE PUBLISHERS, NEW YORK, NY, US, vol. 74, no. 2, 24 November 2008 (2008-11-24), pages 256-263, XP025894826, ISSN: 0039-128X, DOI: 10.1016/J.STEROIDS.2008.11.011 [retrieved on 2008-11-24]
- KRAFFT ET AL: "Synthesis of the C/D/E and A/B Rings of Xestobergsterol-(A)", THE JOURNAL OF ORGANIC CHEMISTRY, AMERICAN CHEMICAL SOCIETY ETC., vol. 64, no. 7, 18 March 1999 (1999-03-18) , pages 2475-2485, XP002216916, ISSN: 0022-3263, DOI: 10.1021/JO982319W
- HANA CHODOUNSKÁ ET AL: "Epalons: Synthesis of 3[alpha],7[alpha]-Dihydroxy-5[alpha]-pregn an-20-one", COLLECTION SYMPOSIUM SERIES (XIIITH SYMPOSIUM ON CHEMISTRY OF NUCLEIC ACID COMPONENTS SPINDLERUV MLYN, CZECH REPUBLIC; SEPTEMBER 03 -09, 2005), vol. 63, no. 10, 1998, pages 1543-1548, XP055406876, XX ISSN: 0010-0765, DOI: 10.1135/cccc19981543 ISBN: 978-80-86241-25-8
- PATRICE C PEART ET AL: "Hydroxylation of steroids by, and", STEROIDS, ELSEVIER SCIENCE PUBLISHERS, NEW YORK, NY, US, vol. 76, no. 12, 7 July 2011 (2011-07-07), pages 1317-1330, XP028286807, ISSN: 0039-128X, DOI: 10.1016/J.STEROIDS.2011.06.010 [retrieved on 2011-07-07]
- Monica E Deluca ET AL: "98. Synthesis of 3P-Hydro~y[Zl-'~C]-5/?-pregn-8(14)-en-20-one from Chenodeoxycholic Acid", , 1986, XP055407089, Retrieved from the Internet: URL:http://onlinelibrary.wiley.com/store/1/0.1002/hlca.19860690810/asset/19860690810_ftp.pdf?v=1&t=j7lpx7ms&s=1fe8c4e128f3e8367 9125527ed5551f9d1640064
- LEHMANN G ET AL: "Schweinegallensauren. V. Der Abbau von Hyocholsaure zu Pregnanderivaten. [Swine bile acids. V. Degradation of hyocholic acid into pregnanone derivatives]", JOURNAL FÜR PRAKТИSCHE CHEMIE : PRACTICAL APPLICATIONS AND APPLIED CHEMISTRY : COVERING ALL ASPECTS OF APPLIED CHEMISTRY, WILEY, DE, vol. 32, no. 3-4, 1 July 1966 (1966-07-01) , pages 217-224, XP009500206, ISSN: 0021-8383, DOI: 10.1002/PRAC.19660320316 [retrieved on 2004-11-08]
- JUNGMANN R ET AL: "7-Keto-5-[beta]-ätiensäure-Derivate. Über Gallensäuren und verwandte Stoffe, 51. Mitteilung [Bile acids and related substances. LI. 7-Oxo-5.bet.a.-etianic acid derivatives]", HELVETICA CHIMICA ACTA, VERLAG HELVETICA CHIMICA ACTA, CH, vol. 41, no. 5, 1958, pages 1206-1233, XP009500207, ISSN: 0018-019X, DOI: 10.1002/HLCA.19580410507 [retrieved on 2004-10-24]
- SLAVIKOVA BARBORA ET AL: "3.ALPHA.-FLUORO ANALOGUES OF ALLOPREGNANOLONE AND THEIR BINDING TO GABAARECEPTORS", COLLECTION SYMPOSIUM SERIES (XIIITH SYMPOSIUM ON CHEMISTRY OF NUCLEIC ACID COMPONENTS SPINDLERUV MLYN, CZECH REPUBLIC; SEPTEMBER 03 -09, 2005); [COLLECTION SYMPOSIUM SERIES / INSTITUTE OF ORGANIC CHEMISTRY AND BIOCHEMISTRY, ACADEMY OF SCIENCES OF THE, vol. 67, no. 1, 1 January 2002 (2002-01-01), pages 30-46, XP008073174, ISSN: 0010-0765, DOI: 10.1135/CCCC20020030 ISBN: 978-80-86241-25-8
- PURDY R H ET AL: "Synthesis, Metabolism, and Pharmacological Activity of 3.alpha.-Hydroxy Steroids Which Potentiate GABA-Receptor-Mediated Chloride Ion Uptake in Rat Cerebral Cortical Synaptoneuroosomes", JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY, US, vol. 33, no. 6, 1 January 1990 (1990-01-01), pages 1572-1581, XP002012635, ISSN: 0022-2623, DOI: 10.1021/JM00168A008
- BARBORA SLAV?KOV? ET AL: "Allopregnanolone and Pregnanolone Analogues Modified in the C Ring: Synthesis and Activity", JOURNAL OF MEDICINAL CHEMISTRY, vol. 56, no. 6, 28 March 2013 (2013-03-28) , pages 2323-2336, XP055406860, US ISSN: 0022-2623, DOI: 10.1021/jm3016365
- CRISTINA SUÑOL ET AL: "Activity of B-Nor Analogues of Neurosteroids on the GABA A Receptor in Primary Neuronal Cultures", JOURNAL OF MEDICINAL CHEMISTRY, vol. 49, no. 11, 1 June 2006 (2006-06-01), pages 3225-3234, XP055570705, US ISSN: 0022-2623, DOI: 10.1021/jm060002f
- ZENG C-M ET AL: "Neurosteroid Analogues. 10. The Effect of Methyl Group Substitution at the C-6 and C-7 Positions on the GABA Modulatory and Anesthetic Actions of (3alpha,5alpha)- and (3alpha,5beta)-3-Hydroxypregn-20-one", JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY, vol. 48, no. 8, 25 March 2005 (2005-03-25) , pages 3051-3059, XP003021562, ISSN: 0022-2623, DOI: 10.1021/JM049027+

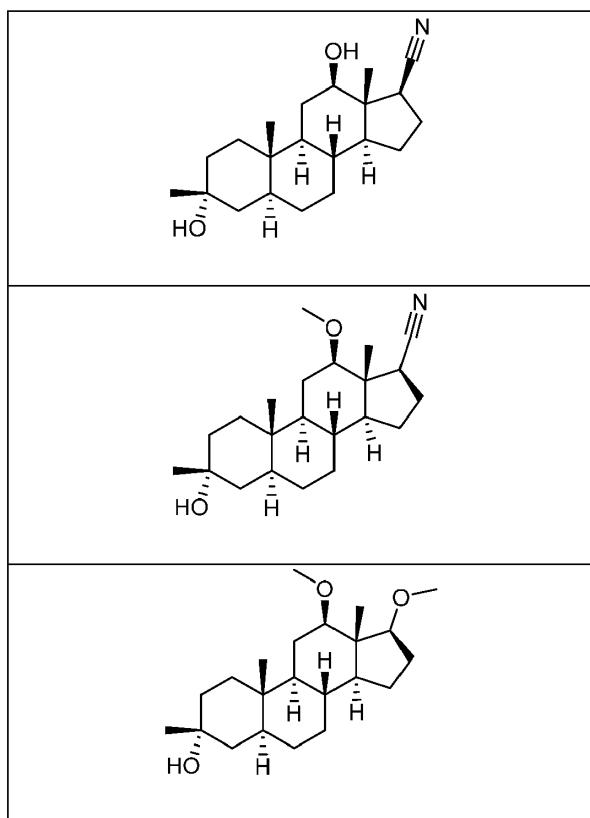
Enclosed is a translation of the patent claims in Norwegian. Please note that as per the Norwegian Patents Acts, section 66i the patent will receive protection in Norway only as far as there is agreement between the translation and the language of the application/patent granted at the EPO. In matters concerning the validity of the patent, language of the application/patent granted at the EPO will be used as the basis for the decision. The patent documents published by the EPO are available through Espacenet (<http://worldwide.espacenet.com>) or via the search engine on our website here: <https://search.patentstyret.no/>

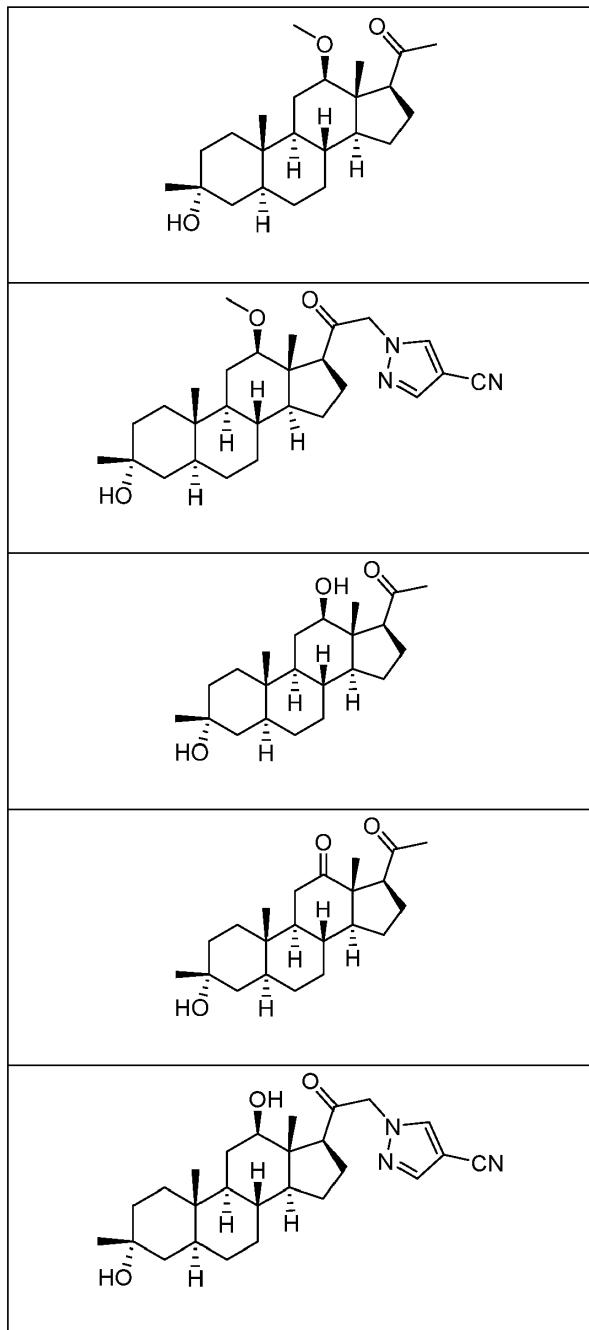
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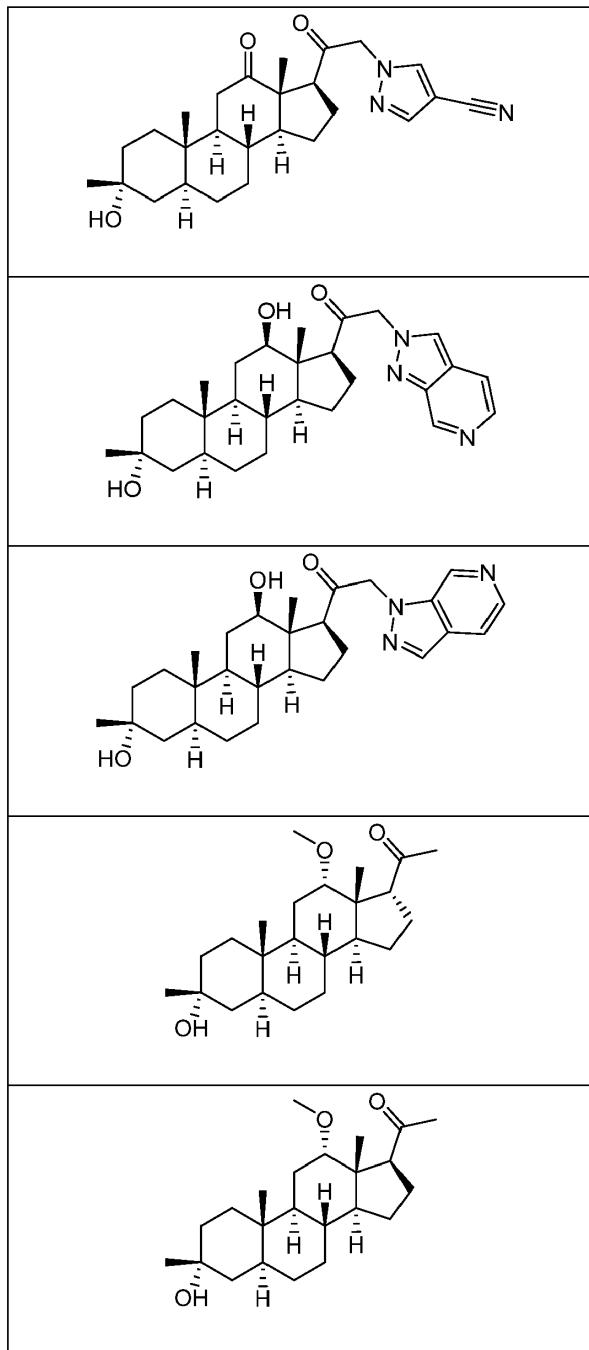
1. Forbindelse av formel (V):

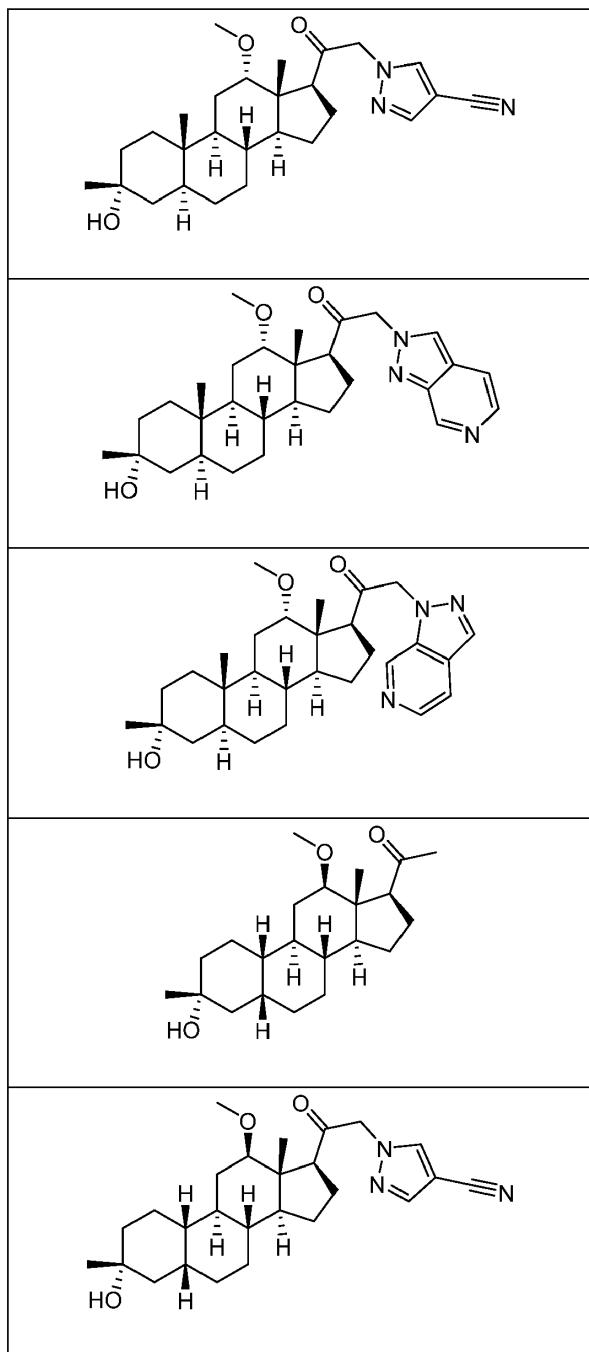


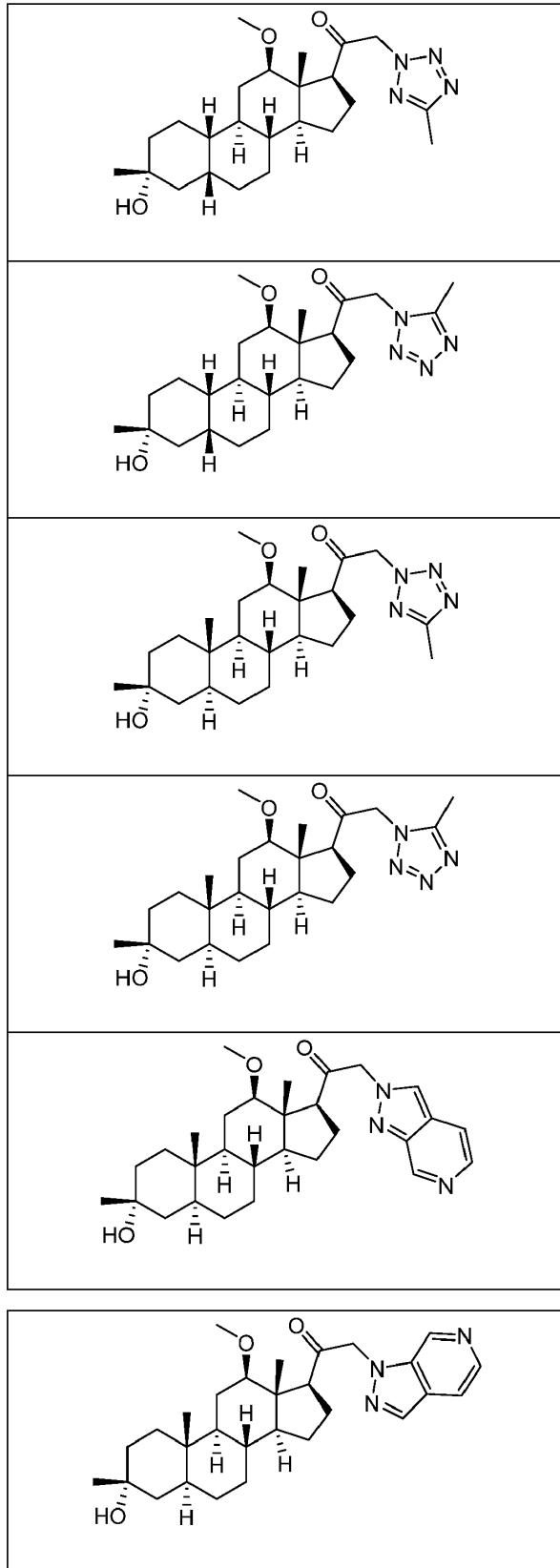
eller et farmasøytisk akseptabelt salt derav,
hvorfor forbindelsen velges fra gruppen som består av:



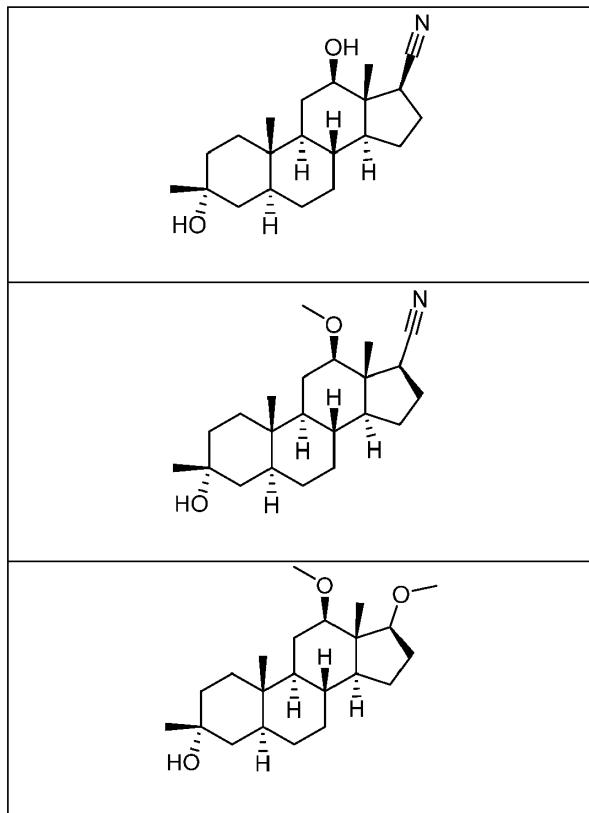


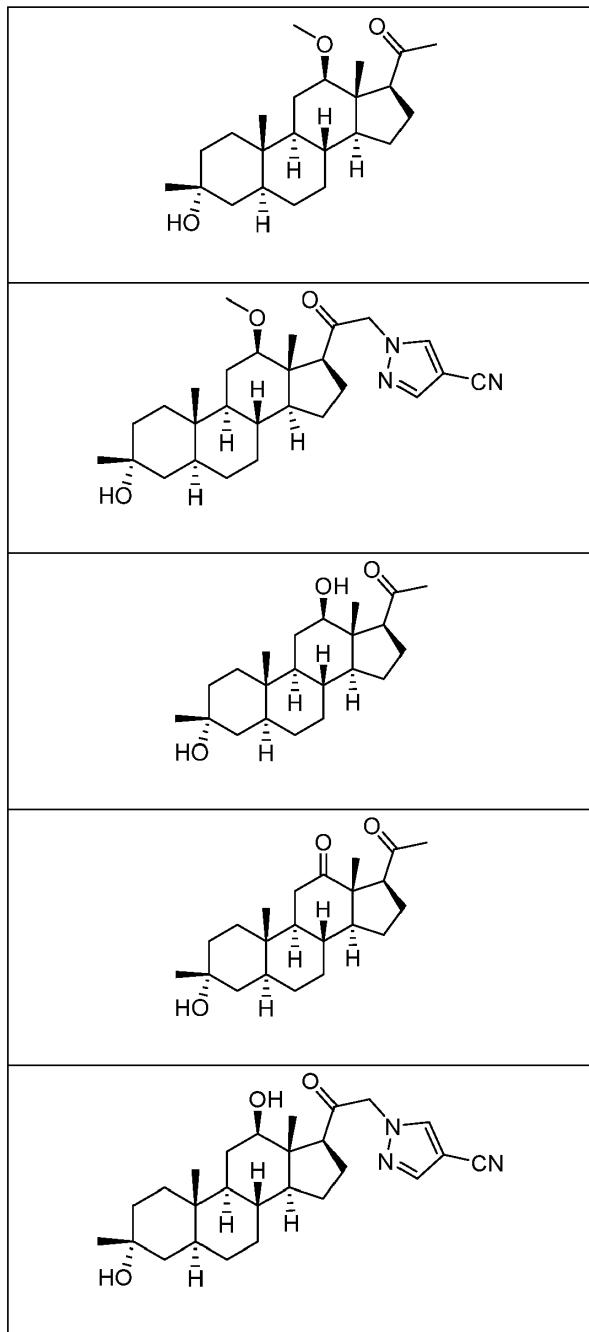


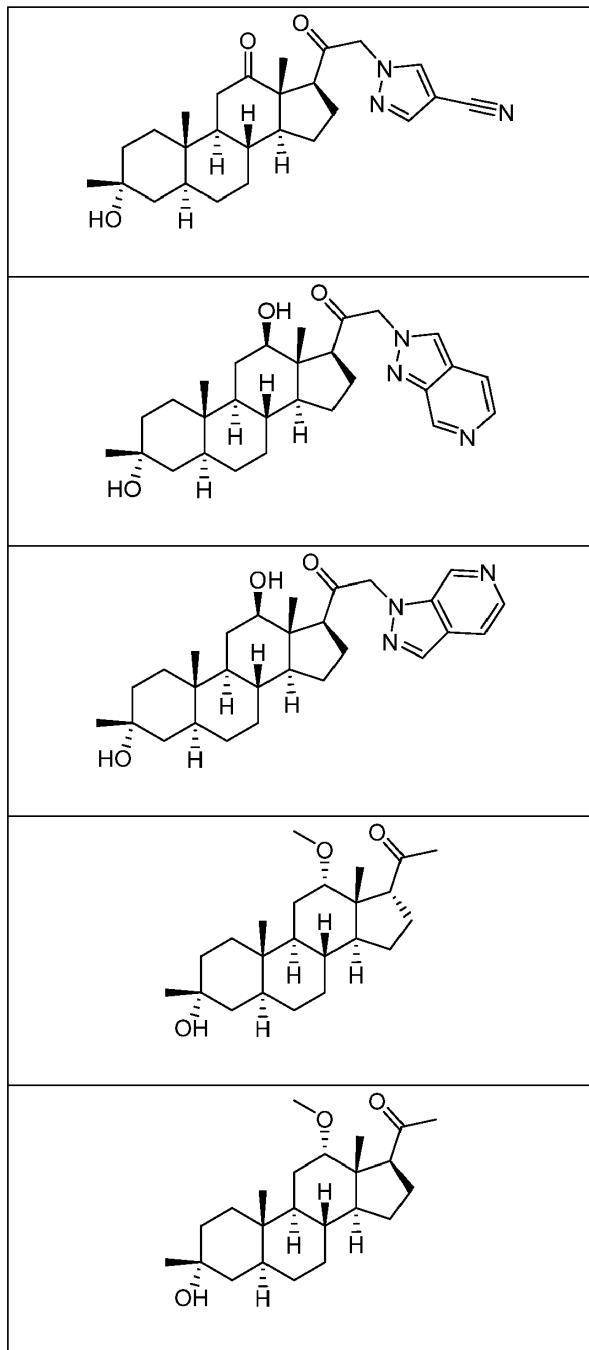


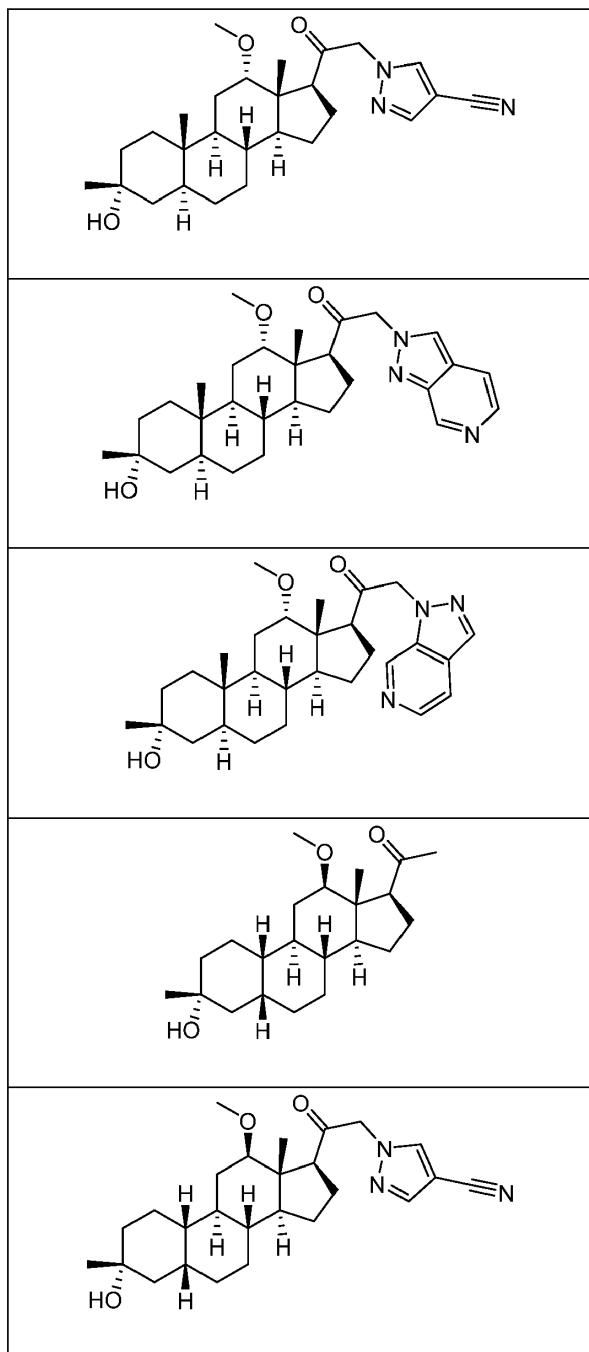


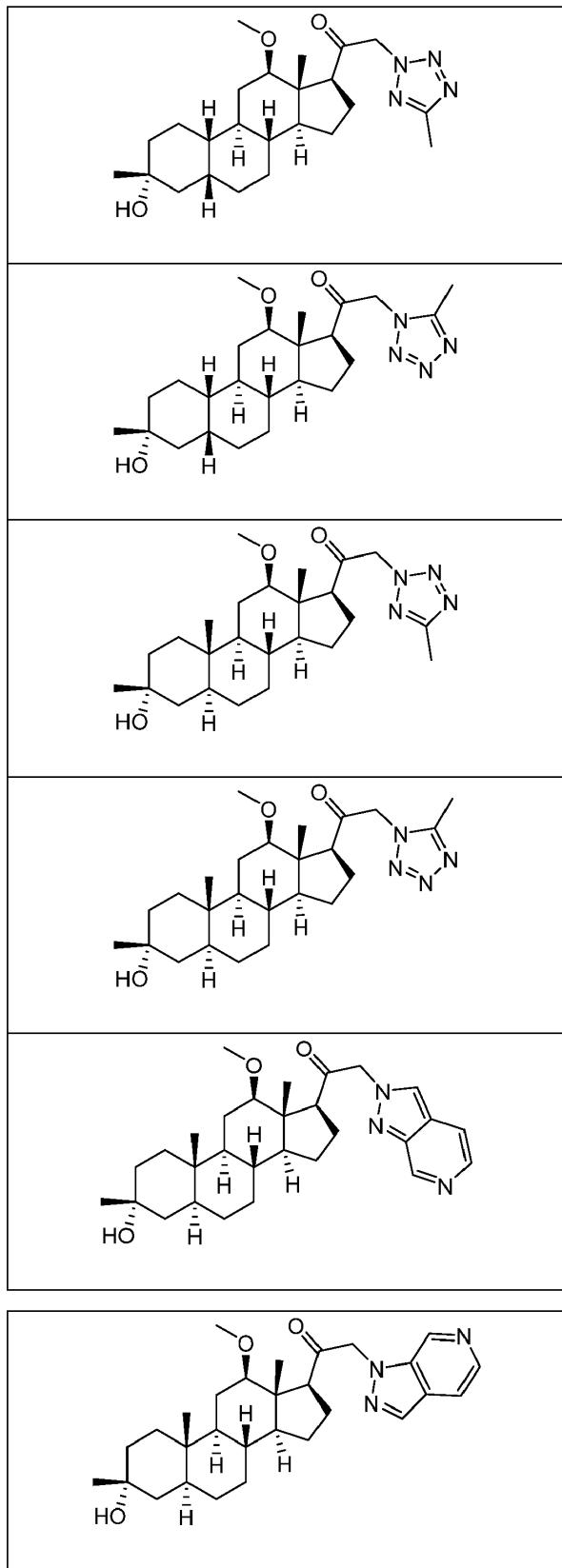
eller et farmasøytisk akseptabelt salt av en forbindelse valgt fra gruppen som består av:











2. Farmasøytisk sammensetning omfattende en forbindelse ifølge krav 1, eller et farmasøytisk akseptabelt salt derav, og en farmasøytisk akseptabel eksipiens.

3. Forbindelse ifølge krav 1 eller en sammensetning ifølge krav 2, for anvendelse i en fremgangsmåte for:

å indusere sedasjon og/eller anestesi hos et menneske, eventuelt hvori

- (i) det humane individet opplever sedasjon og/eller anestesi innen to timer etter administrering, eventuelt hvori det humane individet opplever sedasjon og/eller anestesi innen én time etter administrering; eventuelt hvori det humane individet opplever sedasjon og/eller anestesi øyeblikkelig; og/eller
- (ii) forbindelsen administreres ved intravenøs administrering; og/eller
- (iii) forbindelsen administreres kronisk; og/eller
- (iv) forbindelsen administreres i kombinasjon med et annet terapeutisk middel.

4. Forbindelse ifølge krav 1 eller en sammensetning ifølge krav 2, for anvendelse i en fremgangsmåte for behandling av anfall hos et menneske.

5. Forbindelse ifølge krav 1 eller en sammensetning ifølge krav 2, for anvendelse i en fremgangsmåte for behandling av epilepsi eller status epilectus hos et menneske.

6. Forbindelse ifølge krav 1 eller en sammensetning ifølge krav 2, for anvendelse i en fremgangsmåte for behandling av en nevroendokrin forstyrrelse eller dysfunksjon hos et menneske.

7. Forbindelse ifølge krav 1 eller en sammensetning ifølge krav 2, for anvendelse i en fremgangsmåte for behandling av en nevrodegenerativ sykdom eller forstyrrelse hos et menneske.

8. Forbindelse ifølge krav 1 eller en sammensetning ifølge krav 2, for anvendelse i en fremgangsmåte for behandling av en bevegelsesforstyrrelse eller skjelving hos et menneske.

9. Forbindelse ifølge krav 1 eller en sammensetning ifølge krav 2, for anvendelse i en fremgangsmåte for behandling av en stemningsforstyrrelse eller angstforstyrrelse hos et menneske.

10. Forbindelse ifølge krav 1 eller en sammensetning ifølge krav 2, for anvendelse i en fremgangsmåte for behandling av en CNS-relatert forstyrrelse hos et menneske med behov derav.

11. Forbindelse ifølge krav 1 eller en sammensetning ifølge krav 2, for anvendelse ifølge krav 10, hvori den CNS-relaterte forstyrrelsen er en søvnforstyrrelse, en humørforstyrrelse, en schizofrenispektrumforstyrrelse, en krampeforstyrrelse, en forstyrrelse av hukommelse og/eller kognisjon, en bevegelsesforstyrrelse, en personlighetsforstyrrelse, autismespektrumforstyrrelse, smerte, traumatisk hjerneskade, en vaskulær sykdom, en stoffmisbruksforstyrrelse og/eller bortfallssyndrom eller tinnitus; og/eller hvori individet er et individ med Retts syndrom, fragilt X-syndrom eller Angelmans syndrom.