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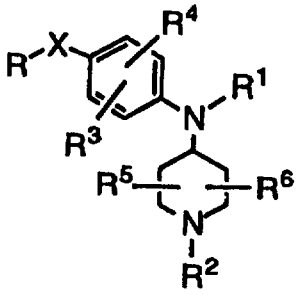
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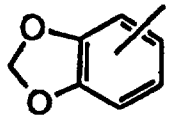
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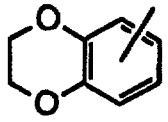
(54) Title: 1,4-DI-SUSTITUTED PIPERIDINES AS MUSCARINIC ANTAGONISTS



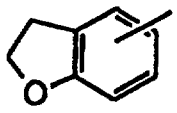
(I)



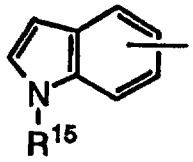
(a)



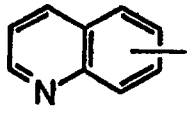
(b)



(c)



(d)



(e)

(57) Abstract

1,4-Di-substituted piperidine muscarinic antagonists of formula (I) or a pharmaceutically acceptable salt, ester, or solvate thereof, wherein X is a bond, -O-, -S-, -SO-, $-SO_2-$, -CO-, $-C(OR^7)_2-$, $-CH_2-O-$, $-O-CH_2-$, -CH=CH-, $-CH_2-$, $-CH(C_1-C_6$ alkyl)-, $-C(C_1-C_6$ alkyl$)_2-$, $-CONR^{17}-$, $-NR^{17}CO-$, $-SO_2NR^{17}-$ or $-NR^{17}SO_2-$; R is C_3-C_6 cycloalkyl, (a), (b), (c), (d), (e), optionally substituted phenyl or optionally substituted pyridyl; R^1 is H, -CN, $-CF_3$, alkyl, cycloalkyl, cycloalkenyl, alkenyl, $-COR^{15}$, -COO(alkyl, aryl, heteroaryl, alkylaryl or alkylheteroaryl), alkylaryl, alkylheteroaryl or $-CON(R^{13})_2$; R^2 is cycloalkyl, cycloalkenyl, t-butoxycarbonyl or optionally substituted 4-piperidinyl; R^3 and R^4 are H, halo, $-CF_3$, alkyl, alkoxy or -OH; R^5 and R^6 are H, alkyl, $-CF_3$, alkoxy, -OH, alkylcarbonyl, alkoxycarbonyl, $R^{13}CONH-$, $R^{14}OCONH-$, $R^{13}NHCONH-$ or $NH_2CONR^{13}-$; R^7 is H or alkyl, or the two R^7 groups may form $-(CH_2)_{2-4}$; R^{13} is H, alkyl, cycloalkyl, -(alkyl)$COOR^{15}$, aryl, heteroaryl, alkylaryl, alkylheteroaryl and adamantyl; R^{14} is H or alkyl; R^{15} is H, C_1-C_{20} alkyl, C_1-C_6 cycloalkyl, aryl or heteroaryl; and R^{17} is H, C_1-C_6 alkyl, aryl or heteroaryl; useful for treating cognitive disorders such as Alzheimer's disease are disclosed, as well as pharmaceutical compositions and methods of preparation. Also disclosed are combinations of compounds of formula (I) capable of enhancing ACh release with ACh'ase inhibitors.