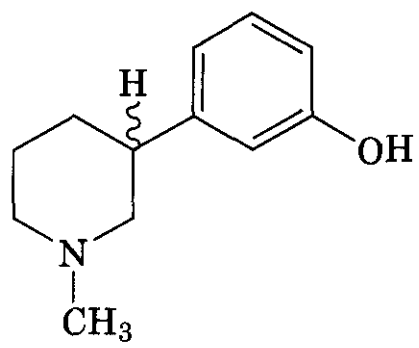


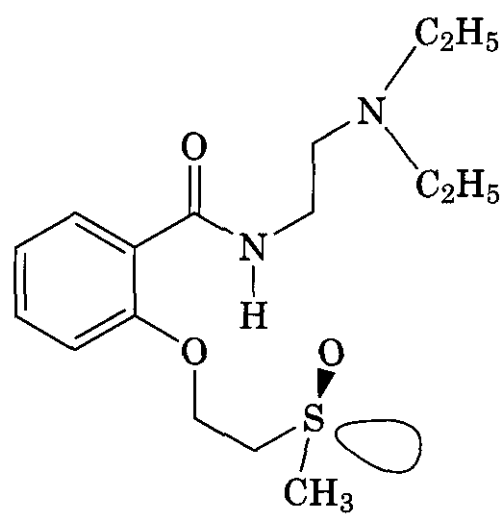
(92)

tors. Thus, this enantiomer exhibits a bifunctional mode of doparninergic attenuation: that of presynaptic agonism and postsynaptic antagonism. The observed pharmacological effects of the racemic modification are the sum total of the complex activities of the two enantiomers, and the pharmacology of racemic 3-PPP is not an accurate reflection of the pharmacological properties of the individual enantiomers. The contemporary literature strongly reflects the philosophy that pharmacological testing only of a racemic mixture is inadequate and may be misleading.

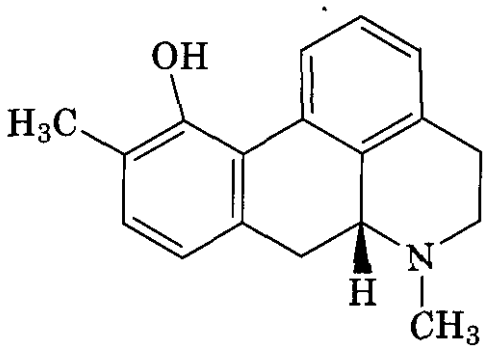
(*R*)-(−)-11-Hydroxy-10-methylaporphine **(93)** is a highly selective serotonergic 5-HT$_{1A}$ agonist (60).

Remarkably, the (*S*)-enantiomer (94) is a potent antagonist at this same subpopulation of serotonin receptors (guinea pig ileum preparation) (61). Both enantiomers bind strongly to 5-HT$_{1A}$ receptors from rat forebrain membrane. The phenomenon of enantiomers that possess opposite effects (agonist-antagonist) at the same receptor, once considered to be extremely rare, has recently been noted more often, probably because of the increasing recognition by medicinal chemists and pharmacologists that each member of an enantiomeric pair may possess its own unique and unpredictable pharmacology.

In addition to stereochemistry about a carbon center, other potentially chiral atoms offer possibilities for pharmacological significance. A gastroprokinetic compound (95) with



(95)



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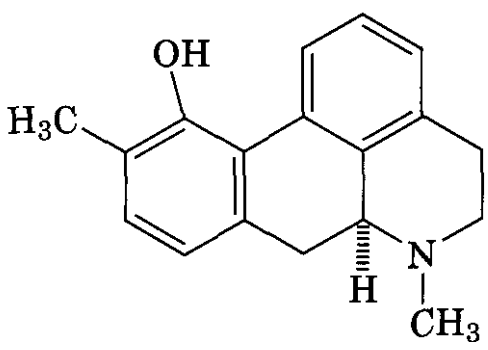
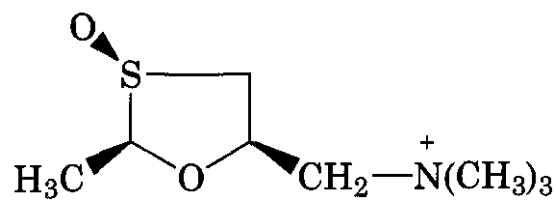


(94)

serotonergic activity bears a chiral sulfoxide moiety (62). The enantiomers are equipotent, but the (*S*)-enantiomer demonstrates a greater intrinsic activity than that of the (*R*)-enantiomer.

Casy **(63)** cited pharmacological differences between stereoisomers of chiral sulfoxide moieties in cholinergic oxathiolane congeners (96–99) of muscarine.



(96)

cis- and trans-4-Aminocrotonic acids (100) and (101) were prepared (64) as congeners of γ-aminobutyric acid (GABA) (6).