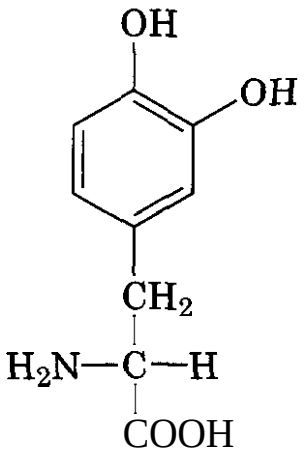

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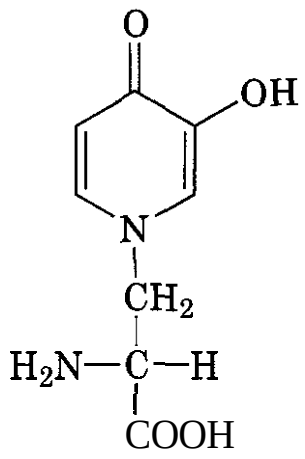

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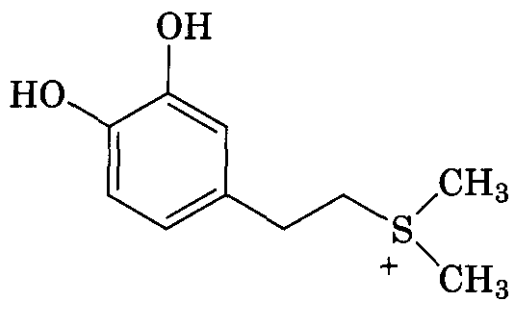

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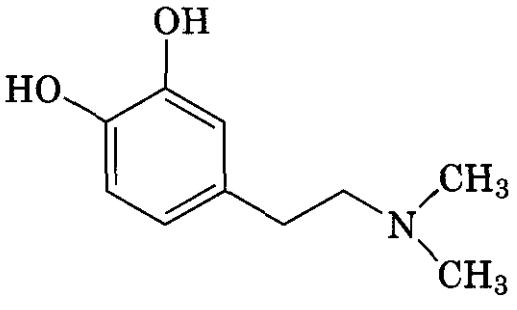
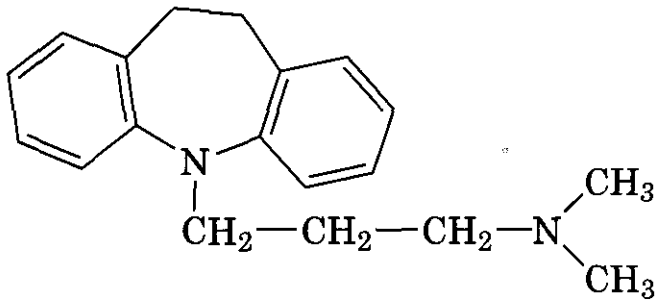


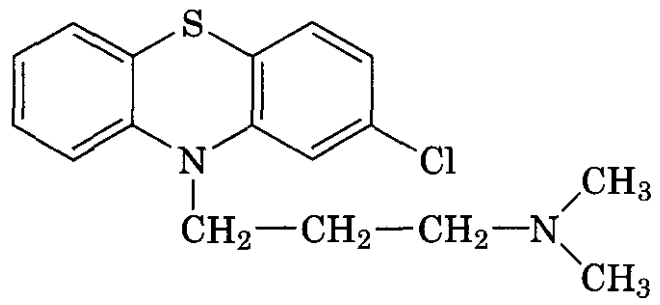
(7)

esis that β-phenethylamines such as (7) interact with dopamine receptors in their protonated (cationic) form.

Bioisosteric replacement strategy has been fruitful in design of psychoactive agents, by use of the antidepressant dibenzazepine derivative imipramine (8) as the lead. The structural similarity between imipramine and the phenothiazine antipsychotics [typified by chlorpromazine (9)] is apparent. Although these two

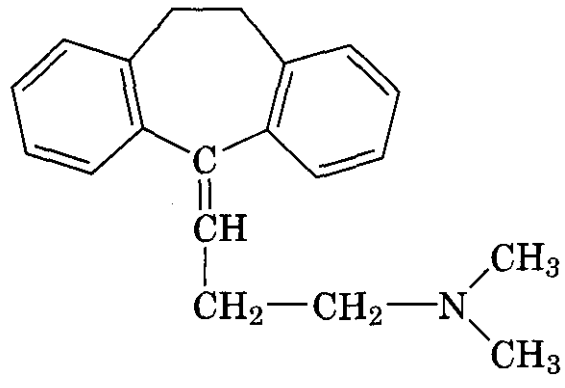


(8)



(9)

bioisosteric molecules have different pharmacological properties and therapeutic uses and likely have different mechanisms and sites of action in the central nervous system (9), they share the property of being psychotropic agents. They illustrate the observation that bioisosteric manipulation of a molecule may change its mode of action. In the antidepressant dibenzocycloheptene derivative amitriptyline (10), the ring nitrogen of imipramine is



(10)

replaced by an exocyclic olefin moiety. Demexiptiline (11), doxepin (12), and dothiepin (13) represent other bioisosteric modifications of imipramine that possess antidepressant ac-