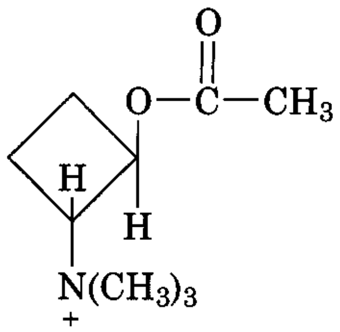
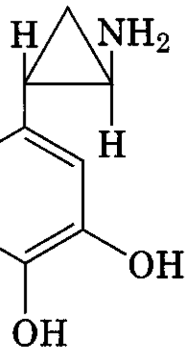


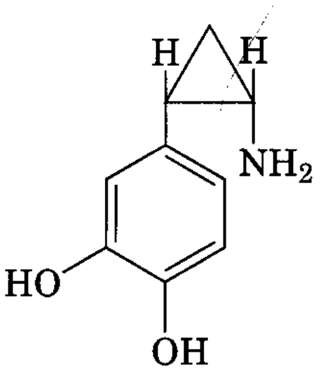
(40)

as differences in extraneous molecular bulk seem insufficient to account for the dramatic difference in pharmacological potencies between the three- and the four-membered ring systems.

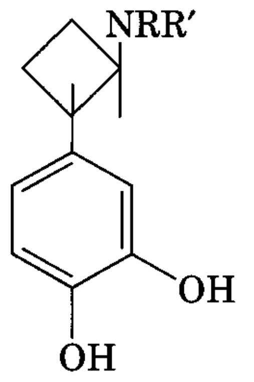
The cyclopropane ring was employed to impart a degree of rigidity to the side chain of **dopamine** (structures 41 and **42**) (30).



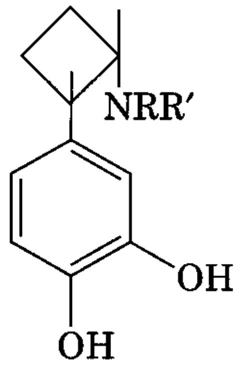
(41)



(42)



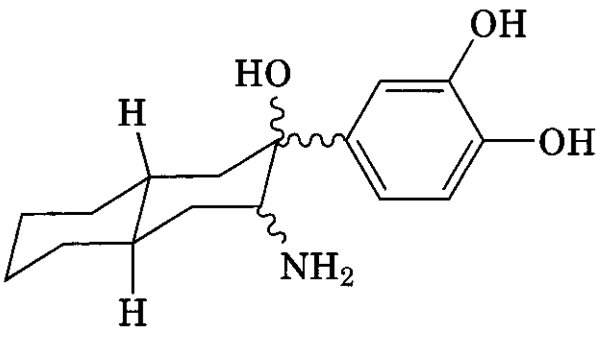
(43a) R = R′ = CH_3
(43b) R = R′ = H



(44a) R = R′ = CH_3
(44b) R = R′ = H

Neither isomer displayed effects at **dopamine** receptors, but both were a-adrenoceptor agonists, with the (±)-*trans*-**isomer** (41) being approximately five times more potent than the (±)-*cis*-**isomer** (42). It was suggested (31) that these findings may contribute to determining the preferred conformation of **β-phenethylamines** at the a-adrenoceptor. The racemic trans-cyclobutane congeners (**43a**) and (**43b**) are more potent than their racemic *cis*-**isomers** (**44a**) and (**44b**) in binding studies on rat corpus striatum tissue, but the binding affinities for (**43a**) and (**43b**) are much less than that of **dopamine** (32). Racemic *trans*-(**43a**) was more potent than the trans-primary amine (**43b**), but it was still much less potent, than dopamine. The racemic cis-isomer of (**44b**) demonstrated very low **affinity** for the receptor.

A **β-phenethylamine** moiety was incorporated into the trans-decalin ring system (45)



(45)

and the racemic modifications of all four possible isomers were prepared as "frozen" analogs of possibly significant conformations of the flexible norepinephrine molecule (33). All four compounds displayed approximately equal (extremely low) potency. This result il-