Comparative study of dopaminergic activity of tetrahydro-1H-[3]-benzazepines and their precursors

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SUMMARY:

The discovery of the tetrahydro-1*H*-[3]-benzazepine SCH23390 [1], represented one of the most important advances in the study of dopaminergic receptors due to their behavior as a selective D1 receptor antagonist. The high affinity and selectivity of this tetrahydro-1*H*-[3]-benzazepine has led to the search for new structures because of their potential dopaminergic activity, especially 1-aryl-substituted tetrahydro-1*H*-[3]-benzazepines. Furthermore, their precursors, the tetrahydroisoquinolines 1-substituted have shown to have activity for D1 and D2 dopaminergic receptors.[2]

We have carried out the synthesis of tetrahydro-1*H*-[3]-benzazepines 1,2-di-substituted by Stevens rearrangement (SR) on tetrahydroisoquinolinium salts. Stevens rearrangement is an efficient regio- and diastereoselective synthetic methodology. [3a,b] As part of our studies, we have performed the synthesis of benzazepines with modifications at the C-1 and C-2 positions with chlorine and hydroxyl groups at A-ring which is an important factor to modulate affinity at dopaminergic receptors.

The interaction of these molecules with D1 and D2 dopaminergic receptors have been studied to establish a structure-activity relationship by radioligand binding assays.

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