Synthesis and Study of Biological Activity of tetrahydro-1*H*-[3]-benzazepines

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The 3-Benzazepines are an important class of compounds in drug discovery due to their biological activity such as analgesic, antihypertensive or anticancer properties as well as dopaminergic or antidopaminergic activity. In particular, the tetrahydro-1*H*-[3]-benzazepine is a common skeleton in a number of natural and pharmaceutical products. As consequence of the interesting biological properties, derivatives of the tetrahydro-1*H*-[3]-benzazepines, especially the 1-aryl substituted have been synthesized by different routes and evaluated their pharmacologic activity. [1,2]

The stereoselective synthetic approaches of tetrahydro-1*H*-[3]-benzazepine have focused on ring enlargements, as the Stevens rearrangement (SR) which is a good regio- and diastereoselective synthetic methodology. In my research group, the reaction conditions to synthesize tetrahydro-1*H*-[3]-benzazepines 1,2-disubstituted by via SR from tetrahydroisoquinolinium salts conveniently functionalized have been optimized. [3,4]

This methodology allowed us to obtain a wide variety of tetrahydro-1*H*-[3]-benzazepines 1,2-disubstituted with different substituents at A-ring (Cl, OMe) and the C-1 (-C_6H_4X, X = H, OMe, Cl, NO_2, NMe_2, NH_2, SMe) and C-2 (Electron-withdrawing groups) positions. The demethylation of the synthesized tetrahydroisoquinolines and tetrahydro-1*H*-[3]-benzazepines 1,2-disubstituted, lead us to get catechol structure, an important requirement for their dopaminergic activity.

We have studied the dopaminergic activity of the synthesized compounds by radioligand binding assays, establishing a structure-activity relationships.

Literature:

[1] A. Gini, Adv. Synth. Catal. 2016, 358, 4049. [2] H. Damsen, Eur. J. Org. Chem. 2015, 36, 7880. [3] M. Valpuesta, Eur. J. Org. Chem. 2010, 23, 4393. [4] M. Ariza, Eur. J. Org. Chem. 2011, 32, 6507.