MW SYSTEMATIC STUDY OF ALKALOIDS: THE DISTORTED TROPANE OF SCOPOLINE

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Tropane alkaloids have diverse pharmacological uses and are well-known for their neurostimulant activity. Previous structure-activity-relationship established correlations between bioactivity and several aspects of ligand conformation and stereochemistry, including delicate intramolecular effects like nitrogen inversion[a]. We have initiated a series of structural studies on tropane alkaloids[b], aimed to discerning their intrinsic stereochemical properties using rotational spectroscopy in supersonic jets[c]. Here we extend these studies to the epoxytropanes, initially motivated to interrogate the influence of the epoxy group on nitrogen inversion and ring conformation. The rotational spectrum evidences a single structure in the gas phase, providing a first description of the (three ring) structurally-distorted tropane in scopoline. The determined rotational parameters of scopoline reveal the structural consequences of the intramolecular cyclation of scopine, which breaks the original epoxy group and creates a new ether bridge and a 7β-hydroxytropane configuration. The hydroxyl group further stabilizes the molecule by an $O-H\cdots N$ intramolecular hydrogen bond, which, in turn, forces the N-methyl group to the less stable axial form[b]. The experimental work was supported by ab initio and DFT calculations.

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[b] E.J. Cocinero, A. Lesarri, P. Écija, J.-U. Grabow, J.A. Fernández, F. Castaño, *Phys. Chem. Chem. Phys.* 12, 6076 (2010).
[c] E.J. Cocinero, A. Lesarri, P. Écija, J.-U. Grabow, J.A. Fernández, F. Castaño, *Phys. Chem. Chem. Phys.* 12, 12486 (2010).