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Conformational studies of long chain arylpiperazines using NMR techniques

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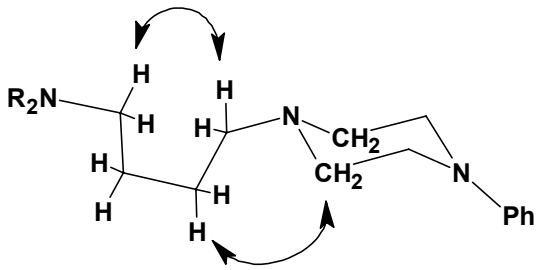
NMR spectroscopy is one of the most powerful techniques for the conformational analysis of small organic compounds. Recently it was applied to study a flexible, complex arylpiperazine derivatives to determine how structural features influenced their conformation in solution. Arylpiperazines constitute functionally diversified class of 5-HT_{1A} serotonin receptor ligands, since among them, agonists, partial agonists or antagonists can be found. We hope that the results of extensive NMR investigations together with biological data may help in determination of bioactive conformation of studied compounds.

Preliminary results obtained from the analysis of 2D NOESY spectra of various arylpiperazines containing flexible 4-carbon chain showed that small changes in the structure can express in large changes in conformation. We have found two types of conformations of investigated compounds. First is, the most expected for alkyl chain, maximally extended conformation, in which we can not observe any NOE interactions between protons of the two ending methylene groups. Further the plane of the aryl moiety connected to piperazine is twisted against the plane of piperazine ring. The second is characterised by strong NOE interactions between all protons in alkyl chain. Such set of signals indicate that these protons have to be much closer in space than it can be achieved in extended conformation. Therefore we have proposed “kinked” or folded conformation to explain spectral properties of these derivatives.



Proposed folded conformation of investigated arylpiperazine derivatives. Arrows indicate important NOE interactions observed for this structure.

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