Public Abstract
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Title:Synthesis and Structure-Activity Relationships of a Series of Sigma Receptor Ligands

Sigma receptors are involved in several biological processes, and sigma ligands might be promising as cancer treatment agents, cocaine abuse medicines, and valuable psychiatric drugs. In an attempt to elucidate effectual structure-activity relationships, a series of N-phenylpropyl-Nâ€™-benzylpiperazine and N-phenylpropyl-4-benzylpiperidine analogs systematically substituted on both phenyl rings was synthesized. These ligands were specifically designed to have certain substituents and substitution pattern representing three physico-chemical parameters denoting size, hydrophobicity, and electronic characteristics, in order to study the effect of those properties on the biological activity.

Structure-activity relationships (SAR) were evaluated qualitatively to describe the effect of the systematic benzyl substitution in comparison to the phenylpropyl substitution. High quality mathematical equations were derived to quantitatively express the statistical correlation between the biological activity and the physico-chemical parameters associated with the benzyl ring substitution. Finally, the effect of the piperidine moiety was compared to the piperazine in a systematic and coherent fashion. This SAR study will result in a better comprehension of the interaction between the sigma protein receptors and the ligands, a better understanding of the pharmacophore profile, and a more effective design for future potent sigma receptor ligands.