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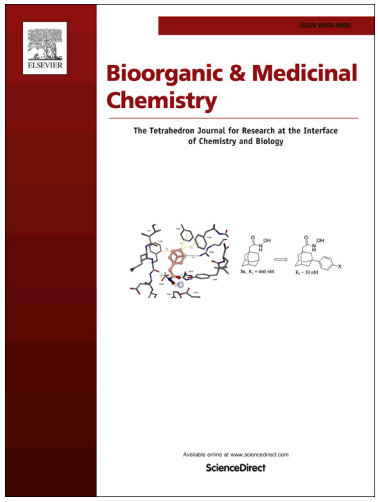

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Development of 1,3-diphenyladamantane derivatives as nonsteroidal progesterone receptor antagonists

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Abstract

Nonsteroidal progesterone receptor (PR) full antagonists are needed as tools for elucidating the physiological functions of PR and as candidates for treatment of various diseases. We designed and synthesized 1,3-diphenyladamantane derivatives, and investigated their PR-antagonistic activity in comparison with our recently developed boron cluster-based PR antagonists. Among the synthesized adamantane derivatives, compound **9a** exhibited the most potent PR-antagonistic activity (IC_{50}: 25 nM) and showed high binding affinity for the PR ligand-binding domain, comparable with that of the boron cluster-based PR antagonists. These results suggest that disubstituted adamantane, like the boron cluster *m*-carborane, is a promising hydrophobic pharmacophore for further structural development of nonsteroidal PR antagonists.

Keyword

progesterone, antagonist, adamantane, hydrophobic pharmacophore