ACS Medicinal Chemistry Letters

PATENT HIGHLIGHT

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Substituted Benzylspiroindolin-2-one Analogues as Positive Allosteric Modulators of the Muscarinic Acetylcholine Receptor M1

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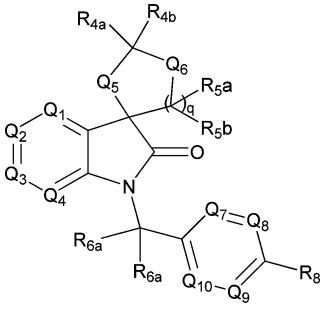
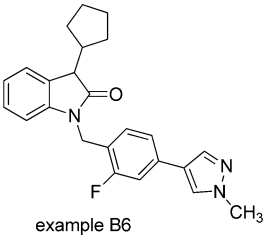
Title:	Substituted Benzylspiroindolin-2-one Analogues as Positive Allosteric Modulators of the Muscarinic Acetylcholine Receptor M1		
Application Number:	WO 2013071201A1	**Publication date:**	16 May 2013
Priority Application:	61/558,849	**Priority date:**	11 November 2001
Inventors:	Craig W. Lindsley, Jeffrey P. Conn, Michael R. Wood, Corey R. Hopkins, Bruce J. Melancon, Michael S. Poslusney		
Assignee Company:	N/A		
Disease Area:	Cognition	**Biological Target:**	Muscarinic M1 Receptor

Summary: This patent application describes the synthesis and evaluation of novel benzylspiroindolinones as potential positive allosteric modulators of the muscarinic M1 receptor. These compounds have potential use in the treatment of cognitive disorders such as Alzheimer's Disease and as adjuncts in the treatment of schizophrenia. Allosteric receptor modulators enhance the affinity of endogenous ligands and can provide symptomatic relief for diseases where the receptor may be involved. Selective enhancement of muscarinic M1 function is hypothesized to be a useful approach for cognitive enhancement. Since design of orthosteric M1 ligands with sufficient receptor selectivity is very difficult, allosteric ligands represent an alternative approach with promise.

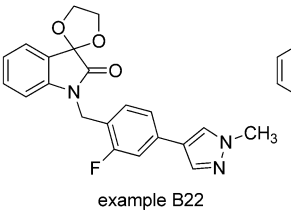
Primary Markush:



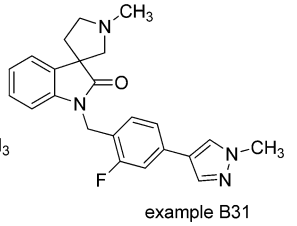
Notable substructures:



example B6



example B22



example B31

Biological Data:
Example B1M1 EC_{50} 1800 nM, E_{max} 80%
Example B22 M1 EC_{50} 3200 nM, E_{max} 86%
Example B31 M1 EC_{50} 3800 nM, E_{max} 76%

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Notes

The authors declare no competing financial interest.

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