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Benzenesulfonyl and Benzenesulfonamide as Modulators of the 5-HT$_6$ Receptor

Patent Highlight

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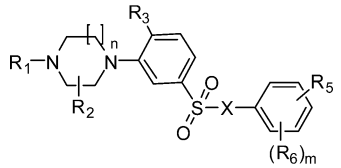
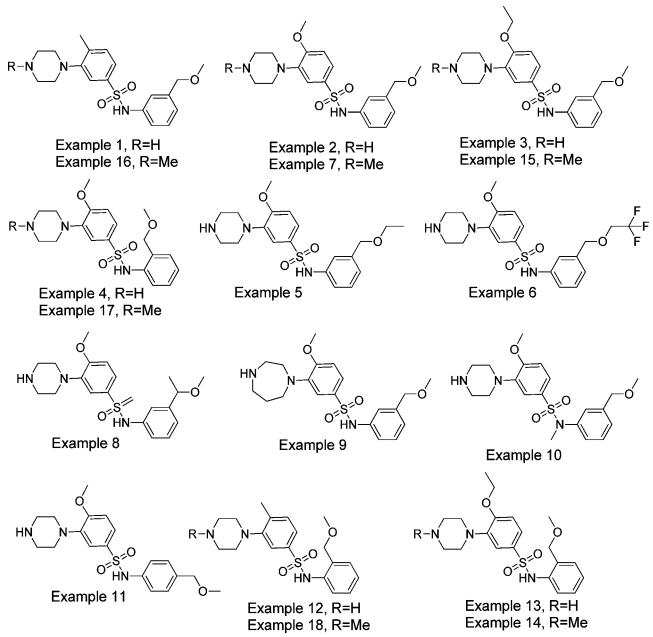
Title:	Benzenesulfonyl and Benzenesulfonamide as Modulators of the 5-HT$_6$ Receptor		
Patent/Patent Application Number:	WO 2012059432 A1	**Publication Date:**	May 12, 2012
Priority Application:	US 2010-408714P	**Priority Date:**	November 1, 2010
Inventors:	Haupt, A.; Pohlki, F.; Unger, L.; Relo, A. L.; Wicke, K.; Zhang, M.		
Assignee Company:	Abbott GMBH & Co., Germany, and Abbott Laboratories, USA		
Disease Area:	Central nervous system, addiction, obesity	**Biological Target:**	5-HT$_6$ receptor

Summary: A series of benzenesulfone and benzensulfonamide analogues of piperazine/homopiperazine as modulators of the 5-HT$_6$ receptor is claimed. The modulation of the 5-HT$_6$ receptor is expected to improve certain disorders including anxiety, feeding disorders, and cognitive dysfunction associated with Alzheimer's disease or schizophrenia.

Important Compound Classes:



Key Structures:



Recent Review Articles:

1. Marazziti, D.; Baroni, S.; Catena Dell'Osso, M.; Bordi, F.; Borsini, F. Serotonin receptors of type 6 (5-HT$_6$): What can we expect from them? *Curr. Med. Chem.* **2011**, *18* (18), 2783−2790.
2. Rosse, G.; Schaffhauser, H. 5-HT$_6$ receptor antagonists as potential therapeutics for cognitive impairment. *Curr. Top. Med. Chem.* **2010**, *10* (2), 207−221.
3. Liu, K. G.; Robichaud, A. J. 5-HT$_6$ medicinal chemistry. *Int. Rev. Neurobiol.* **2010**, *94*, 1−34.

Biological Assay: Human recombinant 5-HT$_6$ receptor binding assay using [^{3}H]-lysergic acid diethylamine ligand

Special Issue: Alzheimer's Disease

Published: October 26, 2012

Biological Data: Description of 5-HT_6 receptor binding data for 18 compounds. Compounds were also tested for affinity against the D_2, α_1-adrenergic, and H_1 receptors.

Example	h5-HT_6 K_i	Example	h5-HT_6 K_i	Example	h5-HT_6 K_i
1	<10 nM	7	<10 nM	13	<10 nM
2	<10 nM	8	<20 nM	14	<10 nM
3	<10 nM	9	<20 nM	15	<10 nM
4	<10 nM	10	<100 nM	16	<100 nM
5	<10 nM	11	<100 nM	17	<10 nM
6	<10 nM	12	<100 nM	18	<100 nM

Synthesis: Preparation of 18 compounds

Claims: Claims 25−29: Use of compounds for the preparation of a medicament for treating diseases of the central nervous system, addiction, and obesity.

Additional Information: SB-742457 and LU-AE58054 have both completed phase II clinical trials and showed potential in improving cognitive function as well as in treating Alzheimer's disease.

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Notes

The authors declare no competing financial interest.