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(12) **United States Patent**
Gano

(10) **Patent No.: US 8,039,627 B2**
(45) **Date of Patent: Oct. 18, 2011**

(54) **SUBSTITUTED 3-ISOBUTYL-9,10-DIMETHOXY-1,3,4,6,7,11B-HEXAHYDRO-2H-PYRIDO[2,1-A]ISOQUINOLIN-2-OL COMPOUNDS AND METHODS RELATING THERETO**

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(22) Filed: **Nov. 8, 2007**

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(51) **Int. Cl.**
C07D 455/06 (2006.01)
A01N 43/42 (2006.01)

(52) **U.S. Cl.** **546/95**; 514/294

(58) **Field of Classification Search** 546/95; 514/294

See application file for complete search history.

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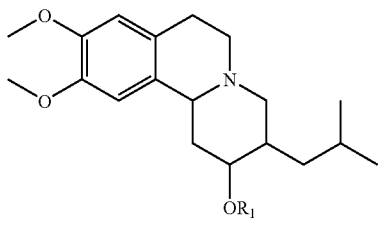
(57) **ABSTRACT**

Substituted 3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-2-ol compounds are disclosed that are inhibitors of the vesicular monoamine transporter 2 (VMAT2). The compounds of this invention have the structure:



wherein R_1 is as defined herein, including stereoisomers and pharmaceutically acceptable salts and solvates thereof. Also disclosed are compositions containing a compound of this invention in combination with a pharmaceutically acceptable carrier, as well as methods relating to the use in a subject in need thereof.

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Figure 1a

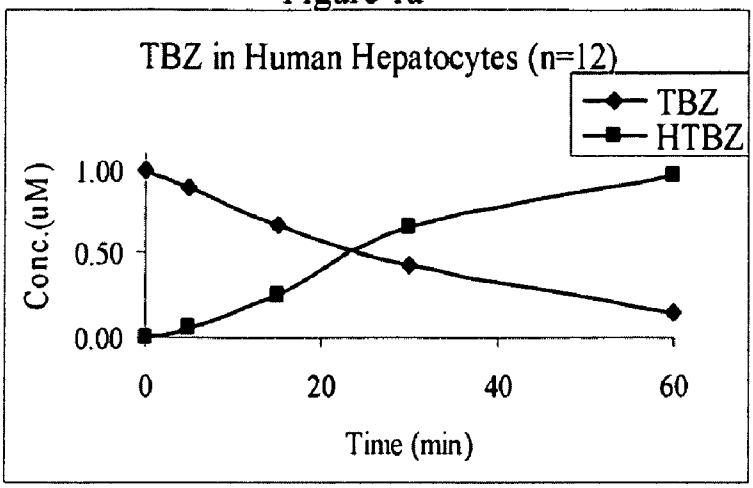


Figure 1b

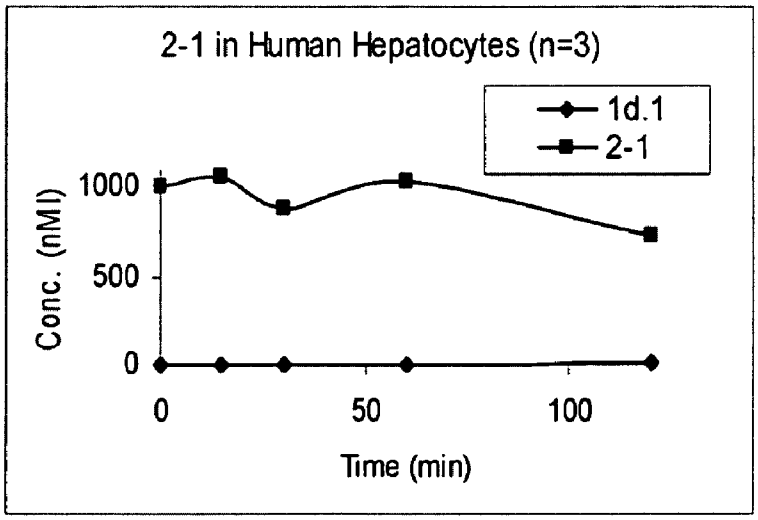


Figure 1c

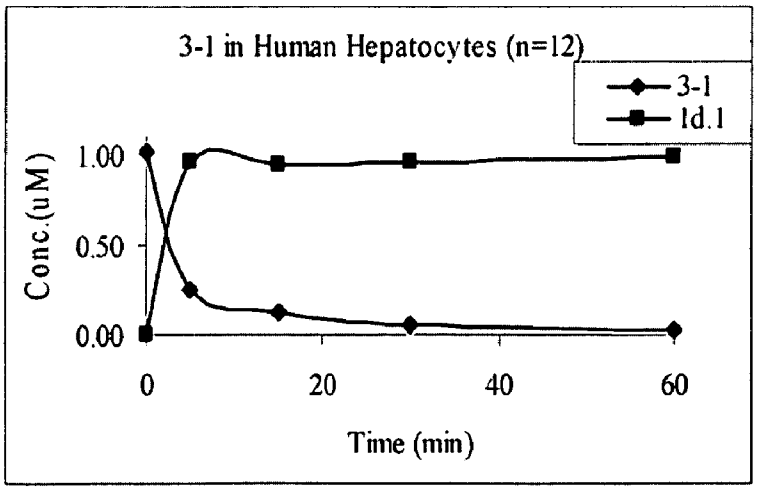


Figure 2a (rat)

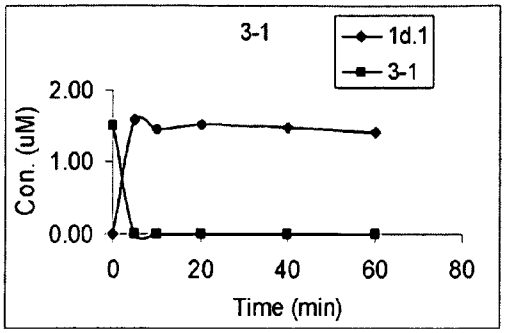


Figure 2b (rat)

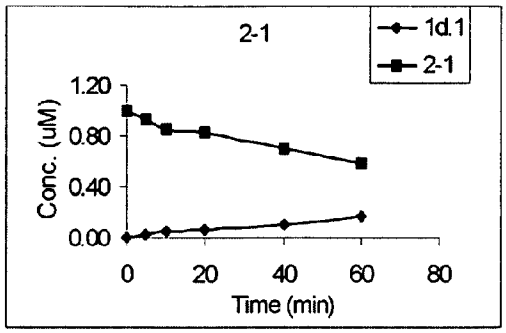


Figure 2c (dog)

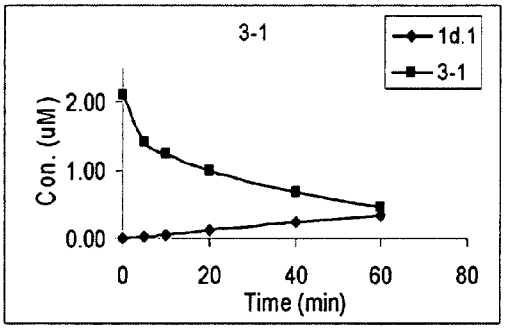


Figure 2d (dog)

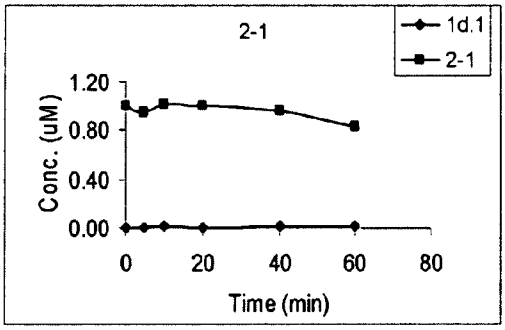


Figure 2e (human)

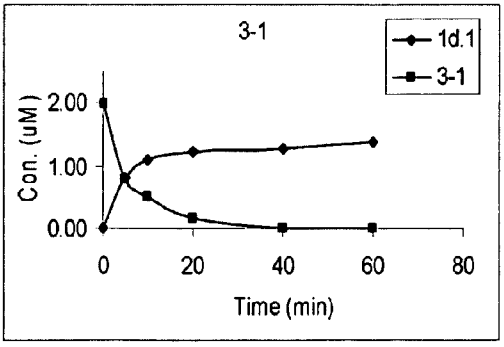


Figure 2f (human)

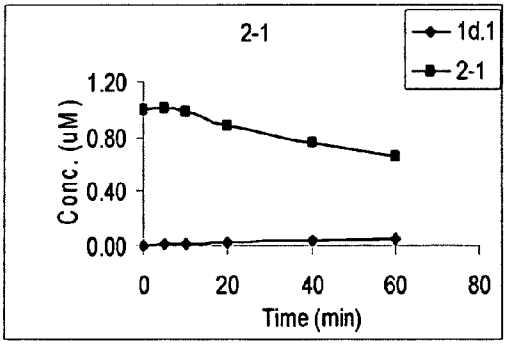


Figure 3a
Plasma Concentration-Time Profile of 10 mg/kg PO of 3-1 and 10 mg/kg PO of 1d.1 to male rats (N=3)

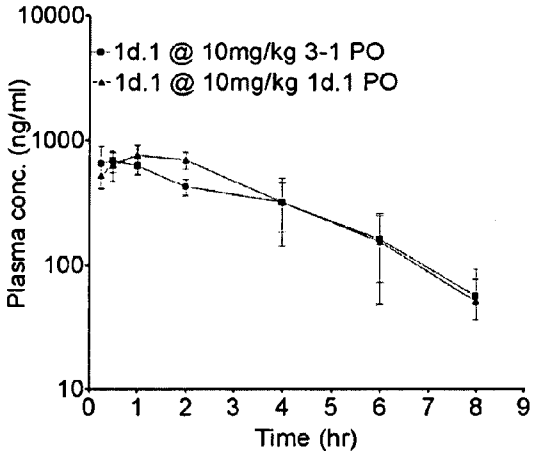


Figure 3b
Plasma Concentration-Time Profile of 10 mg/kg PO of 2-1 to Male Rats (N=3)

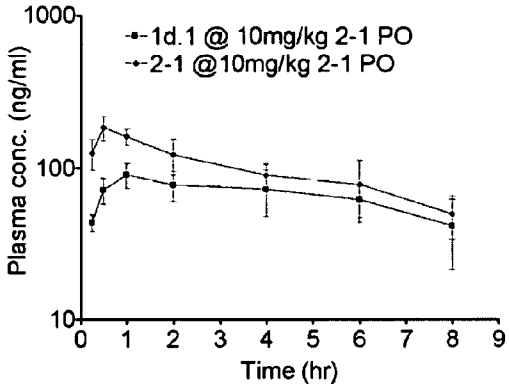


Figure 3c
Plasma Concentration-Time Profile of 6.1 mg/kg PO of 3-1 to Male Dogs (N=3)

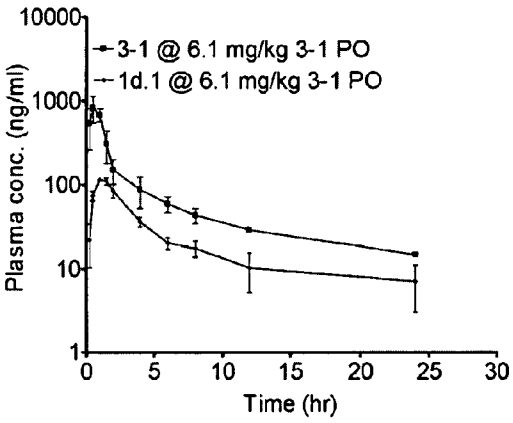
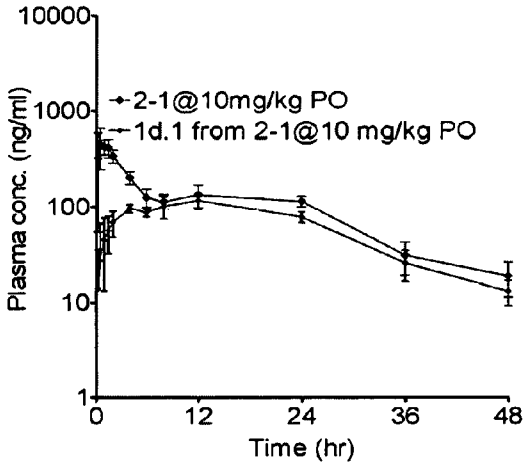


Figure 3d
Plasma Concentration-Time Profile of 10 mg/kg PO of 2-1 to Male Dogs (N=3)



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