

USPATFULL

Subject Coverage	U. S. patents and applications in all areas of technology					
File Type	Full text					
Features	Thesaurus	National Patent Classification fields International Patent Classification fields				
	Alerts (SDIs)	Every update (twice a week), Weekly, or Monthly (Weekly is the default)				
	CAS Registry Numbers®	<input checked="" type="checkbox"/>	Page Images	<input type="checkbox"/>	STN AnaVist	<input checked="" type="checkbox"/>
	Keep & Share	<input checked="" type="checkbox"/>	SLART	<input checked="" type="checkbox"/>	STN Easy	<input checked="" type="checkbox"/>
	Learning Database	<input type="checkbox"/>	Structures	<input type="checkbox"/>	STN Viewer	<input checked="" type="checkbox"/>
Record Content	<ul style="list-style-type: none"> • Full text and classifications for the latest publications of U.S. patents and applications issued by the U.S. Patent and Trademark Office since 1975 • Complete Chemical Abstracts indexing for one equivalent U.S. chemical patent may also be included in a record 					
File Size	More than 6.3 million records (10/11)					
Coverage	1975-present Partial coverage of selected technologies 1971-1974 Defensive publications from 1976-present U.S. applications from 2001-present					
Updates	Twice a week U.S. Patent Classifications - bimonthly					
Language	English					
Database Producer	U.S. Patent and Trademark Office Office of Data Base Administration Data Maintenance Division 2011 Jefferson-Davis Highway, CP2-9C18 Arlington, VA 22202 USA					
Sources	U.S. patents issued by the U.S. Patent and Trademark Office					
User Aids	<ul style="list-style-type: none"> • Online Helps (HELP DIRECTORY lists all help messages available) • STNGUIDE 					

Clusters

- AEROTECH
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 - AUTHORS
 - BIOSCIENCE
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 - CONSTRUCTION
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 - ENGINEERING
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 - HANAVIST
 - HEALTH
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Search and Display Field Codes

Fields that allow left truncation are marked with an asterisk (*).

Search Field Name	Search Code	Search Examples	Display Codes
Basic Index * (contains single words from the title (TI), abstract (AB), claims (CLM), detailed description (DETD), summary (SUMM), drawing description (DRWD), parent case data (PARN), and government interest (GOVI) fields)	None (or /BI)	S GROWTH REGUL? S NAPHTHALENE? S ?VECTOR?	AB, CLM, DETD, DRWD, GOVI, PARN, SUMM, TI
Abstract *	/AB	S COBALT CATALYST?/AB	AB
Accession Number	/AN	S 94:1112/AN S 2001:100195/AN	AN
Application Country	/AC	S US/AC AND L1	AI
Application Date (1)	/AD	S NOV 23 1998/AD S 19981123/AD	AI
Application Number (2)	/AP	S US1977-851992/AP	AI
Application Year (1)	/AY	S 1997/AY	AI
Art Unit (1)	/ARTU (or /ART)	S 126/ARTU	ARTU
CAS Registry Number (RN) (CAS data)	/RN	S 67111-72-2/RN	IT, RN
Claim Text *	/CLM	S COBALT (S) SALT#/CLM	CLM
Classification Code (CAS data) (code and text) (3)	/CC	S 27/CC S HETEROCYCLIC/CC	CC
Controlled Term (CAS data)	/CT	S ANIMAL GROWTH SUBSTANCES/CT	CT, IT
Disclaimer Date (1)	/DCD	S 19940111/DCD S JAN 11 1994/DCD	DCD
Document Type (code and text)	/DT (or /TC)	S REISSUE/DT	DT
Entry Date (1)	/ED	S L1 AND ED>JAN 1, 2001	Not displayed
Examiner Name	/EXNAM	S SIEGEL ALAN M/EXNAM	EXNAM
Examiner's Field of Search	/EXF	S 564/EXF;S 564/48/EXF	EXF
Exemplary Claim Text *	/ECLM	S COBALT (S) MIXTURE/ECLM	CLM, ECLM
Field Availability (code and text)	/FA	S PARENT CASE DATA/FA S PARN/FA	Not displayed
File Segment (code and text)	/FS	S GRANTED/FS S APPLICATION/FS S OS/FS S PS/FS	FS
Government Interest	/GOVI	S W-7405-ENG-48/GOVI	GOVI
Index Term (CAS data)	/IT	S REACTION OF/IT S 61895-14-5P/IT	IT
Inventor	/IN (or /AU)	S BENTLEY TERENCE J?/IN	IN
Inventor Address, City	/IN.CTY	S CRANBURY/IN.CTY	IN, INA
Inventor Address, Country	/IN.CNY	S JAPAN/IN.CNY	IN, INA
Inventor Address, State	/IN.ST	S NJ/IN.ST	IN, INA
Inventor Address, ZIP code (1)	/IN.ZIP	S 43017/IN.ZIP	IN, INA
International Patent Classification (Main and Secondary) (4,5)	/IC	S C07C125/IC S C07C125-06/IC S A01B-001-00-A01B-003-00/IC S ENZYMES/IC	IC

Search and Display Field Codes (cont'd)

Search Field Name	Search Code	Search Examples	Display Codes
International Patent Classification, Action Date	/IPC.ACD	S 20010529/IPC.ACD	IPC
International Patent Classification, Keyword terms	/IPC.KW	S INITIAL/IPC.KW	IPC
International Patent Classification, Main (4,5)	/ICM	S C07D/ICM S C07D-209/ICM S C07D-209-34/ICM S C07C-125/06/ICM S A01B001-00-A01B003-00/ICM S ENZYMES/ICM	ICM
International Patent Classification, Main Group Range-Searchable (1)	/MGR /ICS	S 200-209/MGR S C07C125-06/ICS	ICM ICS
International Patent Classification, Secondary (4,5)		S C07C125/ICS S A01B001/00-A01B003/00/ICS S ENZYMES/ICS	
International Patent Classification, Subgroup Range-Searchable (1)	/SGR	S 400-600/SGR	IC
International Patent Classification, Version(s) (1)	/IPC.VER	S 7/IPC.VER	IPC
Language (code and text) Legal Representative (3)	/LA /LREP (or /AG)	S L1 AND EN/LA S JACKSON H G/LREP	LA LREP
Line Count (1)	/LN.CNT	S 1000-1500/LN.CNT	LN.CNT
National Patent Classification, Current, Main and Secondary (4,6)	/NCL	S 106035000/NCL S 106/035.000/NCL S 106/35/NCL S ZEOLITES+NT/NCL	NCL
National Patent Classification, Current, Main (4,6)	/NCLM	S 423308000/NCLM S 423/NCLM S ZEOLITES+NT/NCLM	NCLM
National Patent Classification, Current, Secondary (4,6)	/NCLS	S 106038000/NCLS S 106/NCLS S ZEOLITES+NT/NCLS	NCLS
National Patent Classification, Issue, Main and Secondary (4,6)	/INCL	S 433228000/INCL S 433/INCL S 433/227-433/229/INCL S ZEOLITES+NT/INCL	INCL
National Patent Classification, Issue, Main (4,6)	/INCLM	S 523118000/INCLM S 523/INCLM S ZEOLITES+NT/INCLM	INCLM
National Patent Classification, Issue, Secondary (4,6)	/INCLS	S 106035000/INCLS S 106/INCLS S ZEOLITES+NT/INCLS	INCLS
Number of Claims (1)	/CLMN	S CLMN>20	CLMN
Other Source	/OS	S 99:9994/OS	OS
Patent Assignee (3)	/PA (or /CS)	S AMERICAN CYANAMID/PA	PA
Patent Assignee Address, City	/PA.CTY	S STAMFORD/PA.CTY	PA
Patent Assignee Address, Country	/PA.CNY	S UNITED KINGDOM/PA.CNY	PA
Patent Assignee Address, State	/PA.ST	S CT/PA.ST	PA
Patent Assignee Address, ZIP code (1)	/PA.ZIP	S 53201/PA.ZIP	PA
Patent Assignee Type	/PAT	S U S CORPORATION/PAT	PAT
Patent Assignee, Original	/PAO	S ABBOTT/PAO	PAO, RAI

Search and Display Field Codes (cont'd)

Search Field Name	Search Code	Search Examples	Display Codes
Patent Country	/PC	S US/PC AND L2	PI
Patent Kind (7)	/PK	S USA1/PK	PI
Patent Number (2)	/PN	S US5933861/PN S US2001008908/PN	PI
Patent Number/Kind Code	PNK	S US20050136407/PNK	PNK
Priority Country	/PRC	S DE/PRC	PRAI
Priority Date (1)	/PRD	S 19981213/PRD S PRD>=DEC 13 1998	PRAI
Priority Number (2,8)	/PRN	S DE1990-4041295/PRN	PRAI
Priority Year (1)	/PRY	S PRY>=1997	PRAI
Publication Date (1)	/PD	S JUNE 1 1999/PD	PI
Publication Year (1)	/PY	S PY>=1998	PI
Reassignment Agent	/RAA	S BAKER BOTTS/RAA	RAA, RAI
Reassignment Company	/RAC	S ABBOTT/RAC	RAC, RAI
Reassignment Date (1)	/RAD	S 20070411/RAD	RAD, RAI
Reassignment Execution Date (1)	/RAXD	S 20080324/RAXD	RAXD, RAI
Reassignment Kind	/RAK	S CABLE/RAK	RAK, RAI
Reassignment Update Date (1)	/RAUP	S 20071004/RAUP	RAUP, RAI
Reference Non-Patent Information	/REN	S HOUSE/REN S SYNTH? REACTION#/REN	REN
Reference Patent Classification (4,6)	/RPCL	S 100003000/RPCL	REP
Reference Patent Country	/RPC	S L7 AND US/RPC	REP
Reference Patent Inventor	/RPIN	S ASATO/RPIN	REP
Reference Patent IPC	/RPIC	S A01B/RPIC S A01B069/RPIC S A01B069-04/RPIC	REP
Reference Patent Number (2)	/RPN	S US5174198/RPN	REP
Reference Patent Publication Date (1)	/RPD	S DEC 1992/RPD	REP
Reference Patent Publication Year (1)	/RPY	S 1970/RPY	REP
Related Application Country	/RLC	S US/RLC	RLI
Related Application Date (1)	/RLD	S 12 AUG 1976/RLD	RLI
Related Application Number (2)	/RLN	S US76-713768/RLN	RLI
Related Application Year (1)	/RLY	S RLY<1976	RLI
Related Patent Number (2)	/RLPN	S US13887504/RLPN	RLI
Related Patent Publication Year (1)	/RLPY	S 1973/RLPY	RLI
Related Publication Indicator	/RLP	S ABANDONED/RLP	RLI
Section Cross-reference (CAS data) (3)	/SX	S 11/CC,SX S PLANT BIOCHEMISTRY/CC,SX	CC
Supplementary Term (CAS data) Term of Patent (1)	/ST	S GROWTH PROMOT?/ST	ST
Title *	/PTERM	S 1-4/PTERM	PTERM
	/TI	S THIOPHEN?/TI	TI
Update Date (1)	/UP	S L2 AND UP>NOV 1 2001	Not displayed
Update Date of CA Indexing (1)	/UPCA	S UPCA>=20011106	Not displayed

(1) Numeric search field that may be searched with numeric operators or ranges.

(2) Either STN format or Derwent format may be used.

(3) Search with implied (S) proximity is available in this field.

(4) An online thesaurus is available for this field.

(5) This field contains the classifications and catchwords for main classification subject headings and subheadings from the current (7th) edition of the WIPO International Patent Classifications (IPC) manual. To search the classifications from any of the specific editions (1-8) of the IPC manual, use the field code followed by the edition number, e.g., /IC2, ICM2, /ICS2 for the 2nd edition. Catchwords are included only in the fields for the 7th, 6th, and 5th editions of the IPC manual.

(6) This field is range-searchable in Manual of Classification order. However, it is not a numeric field and may not be searched using numeric operators.

(7) Available for patent documents published starting in 2001.

(8) U.S. provisional priority numbers are searched only with the P appended, e.g., US1999-121903P/PRN.

Super Search Fields

Enter a super search code to execute a search in one or more fields that may contain the desired information. Super search fields facilitate crossfile and multifile searching. EXPAND may not be used with super search fields. Use EXPAND with the individual field codes instead.

Search Field Name	Search Code	Fields Searched	Search Examples	Display Codes
International Patent Classifications (2,3)	/IPC	/IC, /ICM, /ICS, /IPCI /IPCR	S A01B/IPC S A01B001/IPC	IPC
International Patent Classification (Old IPC)	/IPC.OLD		S A01?/IPC.OLD	IPC
Application Number Group (1)	/APPS	/AP, /PRN, /RLN	S US56-626454/APPS S 56US-0626454/APPS	AI, PRAI, RLI
Patent Country Group	/PCS	/PC, /PC. /RPC, /RPC	S US/PCS AND L1	PI, REP, RLI
Patent Number Group (1)	/PATS	/PN, /RLPN, /RPN	S US102601/PATS S US0102601/PATS	PI, REP, RLI

- (1) Either STN format or Derwent format may be used.
 (2) A thesaurus is available for this field.
 (3) EXPAND and SELECT work with this field.

Thesaurus Fields

A thesaurus is present for the National Patent Classification fields (/INCL, /INCLM, /INCLS, /NCL, /NCLM, /NCLS, /RPCL) and the International Patent Classification fields. The classifications and catchwords for the main headings and subheadings from the 7th edition of the WIPO International Patent Classification (IPC) manual are available in the following fields: /IC, /ICM, /ICS, /IPCI, and /IPCR. The classifications from the previous editions (1-7) are also available as separate thesauri. To EXPAND and SEARCH in the thesauri for editions 1-8, use the field code followed by the edition number, e.g., /IC2, /ICM2, /ICS2 for the 2nd edition. Catchwords are included only in the thesauri for the 8th, 7th, 6th, and 5th editions.

Code	Content	Example
ALL	All associated terms	E 135100000+ALL/INCL E A01N025-04+ALL/IPC
AUTO (1)	Automatic Relationship (BT, SELF)	E A01N025-06/IC REL=ON
ED	Validity Range	E A01B001-00+ED/IPC
HIE	Hierarchy (Broader and Narrower Terms (all Broader and Narrower Terms) (BT, SELF, NT)	E 523523000+HIE/NCL E A01B001-06+HIE/IPC
INDEX	IPC Index Terms	E A01B001-00+INDEX/IPC
TI	Complete Title of the SELF Term	E 135+TI/NCLM E A01B001-04+TI/IPC
BT	Broader Terms (BT, SELF)	E 135120400+BT/NCLS E A01N029-12+BT/IPC
KT	Keyword Terms (2) (SELF, KT)	E ZEOLITES+KT/NCL
NT	Narrower Terms (SELF, NT)	E 126001**1+NT/INCL E A01N025-00+NT/IPC
NEXT	Next Classification	E 135086000+NEXT15/INCL E A01B001-20+NEXT3/ICS
PREV	Previous Classification	E 523523000+PREV3/NCLS E A01B001-20+PREV5/IPC
BRO	Complete Class	E 135019000+BRO5/INCL E A01B001-20+BRO3/IPC
RT	Related Terms	E A01B001-16+RT/IPC

- (1) AUTOMATIC relationship is SET OFF. If you SET RELATION ON, the result of EXPAND without any relationship code is the same as described for AUTO.
 (2) Keyword terms are the catchwords corresponding to the USPTO Manual of Classifications subject index headings and subheadings.

DISPLAY and PRINT Formats

Any combination of formats may be used to display or print answers. Multiple codes must be separated by spaces or commas, e.g., D L3 1-10 TI,AB or D L3 1-10 TI AB. The fields are displayed or printed in the order requested.

Hit-term highlighting is available in all fields except DRWN and ECL. Highlighting must be on when a SEARCH is performed to use the FHITSTR, HIT, HITRN, HITSTR, KWIC, and OCC formats.

Format	Content	Examples
AB	Abstract	D 1-3 AB
AI (AP) (1)	Application Information	D 4 9 AI
AN (2)	Accession Number	D AN
ARTU	Art Unit	D L3 5-7 ARTU
CC (SX)	Classification Code and Section cross-reference (CAS data)	D L3 CC 1-5
CLM	Patent Claim Text	D CLM L8
CLM(n) (3)	Patent Claim Text for Claim n	D CLM(2)
CLMN	Number of Claims	D CLMN
CT (2)	Controlled Term (CAS data)	D 4 CT
DCD	Disclaimer Date	D L3 6,8 DCD
DETD	Detailed Description	D 1-4 DETD
DRWD	Drawing Description	D L9 DRWD 3-6
DRWN	Number of Drawings	D DRWN
DT (TC)	Document Type	D DT 2,6-10
ECL	Exemplary Claim Number	D 7 L3 ECL
ECLM (3)	Exemplary Claim Text	D 1-5, 10 ECLM
EXF (2)	Examiner's Field of Search	D 1,5,8 EXF
EXNAM	Examiner Name	D EXNAM 4-8,11
FS (2)	File Segment	D FS
GOVI	Government Interest	D 3,5,7 GOVI
ICM (2)	IPC, Main	D 5-6 L1 ICM
ICS (2)	IPC, Secondary	D L4 1-6 ICS
IN (AU)	Inventor (includes INA)	D IN
INA (3)	Inventor Address	D L5 1-4 INA
INCLM (2)	Issue Main National Patent Classification Code	D 2,5 INCLM
INCLS (2)	Issue Secondary National Patent Classification Code	D L2 1-3 INCLS
IPCI (2,5)	IPC, Initial Classification	D IPCI
IPCR (2)	IPC, Reclassification	D IPCR
IT	Index Term (CAS data)	D 1,5,10 IT
LA (3)	Language	D LA
LN.CNT	Line Count	D LN.CNT
LREP (AG)	Legal Representative	D 2 7 LREP
MFN	Microfilm Frame Number of document at the U.S. Patent and Trademark Office	D MFN
MRN	Microfilm Reel Number of document at the USPTO	D MRN
NCLM (2)	Current Main National Patent Classification Code	D 1-2 NCLM
NCLS (2)	Current Secondary National Patent Classification Code	D 1-5 NCLS
OS	Other Source Chemical Abstracts	D OS
PA (CS)	Patent Assignee (includes PAA and PAT)	D 1-3 PA
PAA (3)	Patent Assignee Address	D 4 9 PAA
PAO	Patent Assignee, Original	D PAO
PARN	Parent Case Data	D L3 5-7 PARN
PAT (3)	Patent Assignee Type	D L3 PAT 1-5
PI (PN) (1)	Patent Information	D PI L8
PNK	Patent Number/Kind Code	D PNK
PRAI (PRN) (1)	Priority Information	D PRAI
PTERM	Term of Patent	D 4 PTERM
RAA	Reassignment Agent	D RAA
RAC	Reassignment Company	D RAC
RAD	Reassignment Date	D RAD
RAK	Reassignment Kind	D RAK
RAUP	Reassignment Update Date	D RAUP
RAXD	Reassignment Execution Date	D RAXD
REN	Reference Non-Patent Information	D L3 6,8 REN

DISPLAY and PRINT Formats (cont'd)

REP (RPN) RLI (RLN) (1) RN (3) ST SUMM TI (2)	Reference Patent Information Related Application Information CAS Registry Number (CAS data) Supplementary Terms (CAS data) Summary of the Invention Title	D 1-4 REP D L9 RLI 3-6 D RN 2,6-10 D ST D L5 1-4 SUMM D 2,5 TI
ABS ALL (1) APPS (1) BIB (1) CAS CBIB DALL (1) IABS IALL (1) IBIB (1) IC (2) IMAX (1) INCL (2) IND IPC (2,5) IPC.TAB (2,5) IPC.UNIQ IRAI (PA.HIST) ISTD (1) MAX (1) NCL (2) PATS (1) RAI (LSUS) SBIB (1) SCAN (2,4) STD (1) TRIAL (2)	AB AN, TI, IN, PA, PI, AI, PTERM, DCD, RLI, PRAI, DT, FS, REP, REN, EXNAM, LREP, CLMN, ECL, DRWN, AB, GOVI, PARN, SUMM, DRWD, DETD, CLM, INCL (INCLM, INCLS), NCL (NCLM, NCLS), IC (IPC.VER, ICM, ICS, IPCI, IPC), EXF, ARTU AI, PRAI, RLI AN, TI, IN, PA, PI, AI, PTERM, DCD, RLI, PRAI, DT, FS, EXNAM, LREP, CLMN, ECL, DRWN, LN.CNT OS, CC, ST, IT Compressed bibliographic information ALL, delimited for postprocessing ABS, with a text label ALL, indented with text labels BIB, indented with text labels International Patent Classifications (IPC.VER, ICM, ICS) MAX, indented with text labels Issue National Patent Classification Code (INCLM, INCLS) INCL (INCLM, INCLS), NCL (NCLM, NCLS), IC (IPC.VER, ICM, ICS, IPCI, IPC), EXF, ARTU, OS, CC, ST, IT International Patent Classifications (IPC.VER, ICM, ICS, IPCI, IPCR) IPC in Tabular Format Unique IPC codes for a basic and equivalents RAI, indented with text labels STD, indented with text labels AN, TI, IN, PA, PI, AI, PTERM, DCD, RLI, PRAI, DT, FS, REP, REN, EXNAM, LREP, CLMN, ECL, DRWN, AB, GOVI, PARN, SUMM, DRWD, DETD, CLM, INCL (INCLM, INCLS), NCL (NCLM, NCLS), IC (IPC.VER, ICM, ICS, IPCI, IPCR), EXF, ARTU, OS, CC, ST, IT Current National Patent Classification Code (NCLM, NCLS) PI, REP, RLI RAD, RAUP, RAK, PAO, RAXD, RAC, RAA, MRN, MFN AN, TI, IN, PA, PI, AI, RLI, PRAI, DT, FS, LN.CNT AN, TI, NCL (NCLM, NCLS), IC (IPC.VER, ICM, ICS, IPCI, IPCR)), GI (random answer display, no answer) AN, TI, IN, PA, PI, AI, RLI, PRAI, DT, FS, LN.CNT, INCL (INCLM, INCLS), NCL (NCLM, NCLS), IC (IPC.VER, ICM, ICS, IPCI, IPCR), EXF (STD is the default) AN, TI, INCL (INCLM, INCLS), NCL (NCLM, NCLS), IC (IPC.VER, ICM, ICS, IPCI, IPCR)), GI	D L3 1-5 ABS D 3 ALL D APPS D BIB D CAS 3 L2 D CBIB D 1-15 DALL D 1-4 IABS D IALL 2 D IBIB 4-10 D 1-4 L2 IC D IMAX 1 D 1,5 L4 INCL D L2 IND 1-4 D 1-4 L2 IPC D IPC.TAB D IPC.UNIQ D IRAI 1, D PA.HIST D ISTD 1,5 D MAX L1 1 D 6,12 L1 NCL D PATS 1-3 D RAI, D LSUS D SBIB D SCAN D STD 1, 8 D TRIAL
FP (1) FPALL (1) FPBIB (1)	Front page format for: PI, TI, IN, PA, PTERM, DCD, AI, RLI, PRAI, IC (IPC.VER, ICM, ICS, IPCI, IPCR), INCL (INCLM, INCLS), NCL (NCLM, NCLS), EXF, REP, REN, ARTU, EXNAM, LREP, CLMN, DRWN, AB Front page format for: PI, TI, IN, PA, PTERM, DCD, AI, RLI, PRAI, IC (IPC.VER, ICM, ICS, IPCI, IPCR), INCL (INCLM, INCLS), NCL (NCLM, NCLS), REP, REN, EXF, ARTU, EXNAM, LREP, CLMN, DRWN, AB, PARN, SUMM, DRWD, DETD, CLM Front page format for: PI, TI, IN, PA, PTERM, DCD, AI, RLI, PRAI, REP, REN, EXNAM, LREP, CLMN, DRWN	D FP D FPALL L10 1 D 1-10 FPBIB

DISPLAY and PRINT Formats (cont'd)

Format	Content	Examples
FHITSTR HIT HITRN HITSTR	First hit CAS Registry Number, its role, Fields containing hit terms Hit CAS Registry Number and its text modification Hit CAS Registry Number, its text modification, its CA index name, and its structure diagram	D CBIB FHITSTR D HIT D HITRN D HITSTR
KWIC OCC (2)	Up to 20 words before and after hit terms (KeyWord-In-Context) Number of occurrences of hit terms and fields in which they occur	D KWIC D OCC

- (1) By default, patent numbers, application and priority numbers are displayed in STN format. To display them in Derwent format, enter SET PATENT DERWENT at an arrow prompt. To reset display to STN format, enter SET PATENT STN.
- (2) No online display fee for the format.
- (3) Custom display only.
- (4) SCAN must be specified on the command line, i.e., D SCAN or DISPLAY SCAN.
- (5) IPCI-2 is a display label relating to the most recent publication of the patent document. It is part of the IPCI display field.

Extended DISPLAY and PRINT formats

Use the extended display formats to display not only the publication from the USPATFULL file, i.e., the original publication, but also the latest publication for the invention, if available, from the USPAT2 file.

Format	Content	Examples
BIB.EX	BIB for the original plus BIB for the latest publication	D 1-5 BIB.EX
CLM.EX	CLM for the original plus CLM for the latest publication	DIS L2 CLM.EX
FP.EX	FP for the original plus FP for the latest publication	D FP.EX 1-
IBIB.EX	IBIB for the original plus BIB for the latest publication	D IBIB.EX 1-3 L5
IMAX.EX	IMAX for the original plus IMAX for the latest publication	D IMAX.EX 1
MAX.EX	MAX for the original plus MAX for the latest publication	DISPLAY L1 1 MAX.EX
STD.EX	STD for the original plus STD for the latest publication	D STD.EX L5 3, 6

Full-Text Browsing

User Request	Example	System Response
DISPLAY BROWSE	=> DISPLAY BROWSE ENTER (L1) OR L#: ENTER (DIS), ANSWER NUMBERS, OR END:	NOVICE version
D BRO Answer number(s) Answer number(s) and format Format only *Format Forward n fields Backward n fields Search forward for a character string Search backward for a character string End DISPLAY BROWSE	=> D BRO L1 : :1-3 : :4 HIT :TI TX :*KWIC :F3 :B1 :S GROWTH REGUL :S :S- ALKANOIC ACID :S- :END =>	EXPERT version display answers 1, 2, and 3 in default format display next answer in default format display answer 4 in HIT format display title and text of last answer displayed change default to KWIC; no answer displayed move forward 3 fields move backward 1 field search forward within record for 'growth regul' repeat search forward for the current string search backward within record for 'alkanoic acid.' repeat search backward for the current string exit DISPLAY BROWSE and return to => prompt

SELECT, ANALYZE, and SORT Fields

The SELECT command is used to create E-numbers containing terms taken from the specified field in an answer set.

The ANALYZE command is used to create an L-number containing terms taken from the specified field in an answer set.

The SORT command is used to rearrange the search results in either alphabetic or numeric order of the specified field(s).

Field Name	Field Code	ANALYZE/ SELECT (1)	SORT
Abstract	AB	Y	N
Accession Number	AN	Y	N
Application Country	AC	Y (2)	Y
Application Date	AD	Y (2)	Y
Application Information	AI	Y (2,3,4)	Y
Application Number	AP	Y (2,3)	Y
Application Number Group	APPS	Y (2,3,5)	N
Application Year	AY	Y (2)	Y
Art Unit	ARTU	Y	Y
Author (Inventor)	AU	Y (6)	Y
CAS Registry Number (CAS data)	RN	Y (2)	N
Citation	CIT	Y (2,7)	N
Classification Code (CAS data)	CC	Y	Y
Controlled Term	CT	Y (2)	N
Corporate Source (Patent Assignee)	CS	Y (8)	Y
Current Main National Patent Classification Code	NCLM	Y	Y
Current National Patent Classification Code, Main and Secondary	NCL	Y	Y
Current Secondary National Patent Classification Code	NCLS	Y	N

SELECT, ANALYZE, and SORT Fields (cont'd)

Field Name	Field Code	ANALYZE/ SELECT (1)	SORT
Detailed Description	DETD	Y (9)	N
Disclaimer Date	DCD	Y	Y
Document Type	DT	Y	Y
Drawing Description	DRWD	Y (9)	N
Examiner Name	EXNAM	Y	Y
Examiner's Field of Search	EXF	Y	Y
Exemplary Claim Text	ECLM	Y	N
Government Interest	GOVI	Y	N
Index Term (CAS data)	IT	Y (2)	N
International Patent Classifications, All codes	IPC	Y (10)	N
International Patent Classifications, Main and Secondary	IC	Y	Y
Inventor	IN	Y	Y
Inventor Address	INA	N	Y
Inventor Address, City	IN.CTY	Y	Y
Inventor Address, Country	IN.CNY	Y	Y
Inventor Address, State	IN.ST	Y	Y
Inventor Address, ZIP Code	IN.ZIP	Y	Y
IPC Advanced Level	IPC.A	Y (10)	N
IPC Advanced Level for invention	IPC.AI	Y (10)	N
IPC Core Level	IPC.C	Y (10)	N
IPC Core Level for invention	IPC.CI	Y (10)	N
IPC Pre IPC-8 from ICM and 1st IPC-8	IPC.F	Y (10)	N
IPC, Main	ICM	Y	Y
IPC, Secondary	ICS	Y	Y
IPC Initial Classification	IPCI	Y (10)	N
IPC Reclassification	IPCR	Y (10)	N
Issue Main National Patent Classification Code	INCLM	Y	Y
Issue National Patent Classification Code, Main and Secondary	INCL	Y	Y
Issue Secondary National Patent Classification	INCLS	Y	N
Language	LA	Y	Y
Legal Representative	LREP	Y	N
	AG	Y (11)	N
Line Count	LN.CNT	N	Y
Number of Claims	CLMN	N	Y
Occurrence Count of Hit Terms	OCC	N	Y
Other Source Chemical Abstracts	OS	Y (2)	N
Other Source Patent Number	OSPN	Y (2,12)	N
Parent Case Data	PARN	Y (9)	N
Patent Assignee	PA	Y	Y
Patent Assignee Address	PAA	N	Y
Patent Assignee Address, City	PA.CTY	Y	Y
Patent Assignee Address, Country	PA.CNY	Y	Y
Patent Assignee Address, State	PA.ST	Y	Y
Patent Assignee Address, ZIP Code	PA.ZIP	Y	Y
Patent Assignee Type	PAT	Y	Y
Patent Assignee, Original	PAO	Y	N
Patent Claim Text	CLM	Y	N
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Patent Country Group	PCS	Y (2,13)	N
Patent Date	PD	Y (2)	Y
Patent Information	PI	Y (2,3,14)	Y
Patent Kind	PK	Y	Y
Patent Number	PN	Y (2,3)	Y
Patent Number Group	PATS	Y (2,3,15)	N
Patent Number/Kind Code	PNK	Y	N

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Field Name	Field Code	ANALYZE/ SELECT (1)	SORT
Patent Year	PY	Y (2)	Y
Priority Country	PRC	Y (2)	Y
Priority Date	PRD	Y (2)	Y
Priority Information	PRAI	Y (2,3,16)	Y
Priority Number	PRN	Y (2,3)	Y
Priority Year	PRY	Y (2)	Y
Reassignment Agent	RAA	Y	N
Reassignment Company	RAC	Y	N
Reassignment Date	RAD	Y	N
Reassignment Execution Date	RAXD	Y	N
Reassignment Kind	RAK	Y	N
Reassignment Update Date	RAUP	Y	N
Reference Patent Classification	RPCL	Y (2)	N
Reference Patent Country	RPC	Y (2)	N
Reference Patent Information	REP	Y (2,3,17)	N
Reference Patent Inventor	RPIN	Y (2)	N
Reference Patent IPC	RPIC	Y (2,3)	N
Reference Patent Number	RPN	Y (2,3)	N
Reference Patent Publication Date	RPD	Y (2)	N
Reference Patent Publication Year	RPY	Y (2)	N
Related Application Country	RLC	Y (2)	N
Related Application Date	RLD	Y	N
Related Application Information	RLI	Y (3,18)	N
Related Application Number	RLN	Y (3)	N
Related Application Type	RLT	Y	N
Related Application Year	RLY	Y	N
Related Patent Number	RLPN	Y (3)	N
Related Patent Publication Year	RLPY	Y	N
Section Cross-reference (CAS data)	SX	Y	Y
Summary of the Invention	SUMM	Y (9)	N
Supplementary Term (CAS data)	ST	Y	N
Term of Patent	PTERM	N	Y
Title	TI	Y (default)	Y
Treatment Code	TC	Y (19)	Y

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- (4) Selects or analyzes the application number with /AP appended to the terms created by SELECT.
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- (18) Selects or analyzes the RLN and appends /RLN to the terms created by SELECT.
- (19) Appends /DT to the terms created by SELECT.

Sample Records

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ACCESSION NUMBER: 2005:44303 USPATFULL
TITLE: Treatment of bipolar disorders and associated symptoms
INVENTOR(S): Romano, Steven Joseph, New York, NY, UNITED STATES
Giller, Earl L., Madison, CT, UNITED STATES
Harrigan, Edmund P., Old Lyme, CT, UNITED STATES
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PATENT ASSIGNEE(S): Pfizer Inc (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US-20050038036	A1	20050217
APPLICATION INFO.:	2004US-000843915	A1	20040512 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	2003US-000471450P	20030516 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	PFIZER INC, 150 EAST 42ND STREET, 5TH FLOOR - STOP 49, NEW YORK, NY, 10017-5612	

ASSIGNMENT HISTORY FOR US 20050038036
<no data available>

NUMBER OF CLAIMS: 13
EXEMPLARY CLAIM: 1
ABSTRACT:

The present invention relates to a method for treatments relating to bipolar disorder in a mammal, including a human, the treatments including treatment of rapid-cycling bipolar disorder, treatment of symptoms of bipolar disorder selected from the group consisting of acute mania and depression, treatment for effecting mood stabilization; treatment for preventing relapse into bipolar episodes, and for the treatment of suicidal thoughts and tendencies associated with bipolar disorder, comprising administering to said mammal an effective amount of a compound of the formula I: ##STR1##

or a pharmaceutically acceptable acid addition salt thereof, wherein Ar, n, X, and Y are as defined.

[0001] This application claims priority under 35 U.S.C. 119 of U.S. Provisional 60/471,450, filed May 16, 2003. The entire contents of the prior application are incorporated herein by reference.

FIELD OF THE INVENTION

[0002] The present invention relates to the treatment of bipolar disorder in a mammal, including a human. More specifically, the present invention is directed to the treatment in a mammal, including a human, of rapid-cycling bipolar disorder, and for the treatment of symptoms of bipolar disorder, such symptoms selected from the group consisting of acute mania and depression. The present invention is also directed to a treatment method for effecting mood stabilization in a person afflicted with bipolar disorder. The present invention further relates to a method of preventing relapse into bipolar episodes in a person afflicted with bipolar disorder. The present invention is further directed to the treating suicidal thoughts and tendencies in a person afflicted with bipolar disorder. The present invention also relates to new therapeutic uses for piperazinyl-heterocyclic compounds of the formula I, as defined below, for example ziprasidone.

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BACKGROUND OF THE INVENTION

[0003] The piperazinyl-heterocyclic compounds of formula I of this invention are disclosed in U.S. Pat. Nos. 4,831,031 and 4,883,795, both of which are assigned in common with the present application. Certain treatments for such compounds are disclosed in U.S. Pat. Nos. 6,127,373, 6,245,766, and 6,387,904, all of which are also assigned in common with the present application. The patents listed in this paragraph are incorporated by reference in their entireties into the present disclosure.

SUMMARY OF THE INVENTION

[0004] The present invention relates to the use of piperazinyl-heterocyclic compounds of the formula I, as defined below, in methods for the treatment of bipolar disorder in a mammal, including a human. Specifically, the present invention is directed to a method for the treatment in a mammal, including a human, of rapid-cycling bipolar disorder, a method for the treatment of symptoms of bipolar disorder, such symptoms selected from the group consisting of acute mania and depression; a method for a treatment that effects mood stabilization in a person afflicted with bipolar disorder; a method for a treatment that prevents relapse into bipolar episodes in a person afflicted with bipolar disorder; a method for the treatment of suicidal thoughts and tendencies in a person afflicted with bipolar disorder; such treatments comprising administering a pharmaceutically effective amount of a compound of the formula I: ##STR2##

[0005] or a pharmaceutically acceptable acid addition salt thereof, wherein Ar is benzoisothiazolyl or an oxide or dioxide thereof each optionally substituted by one fluoro, chloro, trifluoromethyl, methoxy, cyano, nitro or naphthyl optionally substituted by fluoro, chloro, trifluoromethyl, methoxy, cyano or nitro; quinolyl; 6-hydroxy-8-quinolyl; isoquinolyl; quinazolyl; benzothiazolyl; benzothiadiazolyl; benzotriazolyl; benzoxazolyl; benzoxazolonyl; indolyl; indanyl optionally substituted by one or two fluoro, 3-indazolyl optionally substituted by 1-trifluoromethylphenyl; or phthalazinyl; n is 1 or 2; and X and Y together with the phenyl to which they are attached form quinolyl; 2-hydroxyquinolyl; benzothiazolyl; 2-aminobenzothiazolyl; benzoisothiazolyl; indazolyl; 2-hydroxyindazolyl; indolyl; spiro; oxindolyl optionally substituted by one to three of (C.sub.1-C.sub.3) alkyl, or one of chloro, fluoro or phenyl, said phenyl optionally substituted by one chloro or fluoro; benzoxazolyl; 2-aminobenzoxazolyl; benzoxazolonyl; 2-aminobenzoxazolonyl; benzothiazolonyl; bezoimidazolonyl; or benzotriazolyl.

[0006] In one specific embodiment, the present invention is directed to a method for the treatment in a mammal, including a human, of rapid-cycling bipolar disorder, a method for the treatment of symptoms of bipolar disorder, such symptoms selected from the group consisting of acute mania and depression; a method for a treatment that effects mood stabilization in a person afflicted with bipolar disorder; a method for a treatment that prevents relapse into bipolar episodes in a person afflicted with bipolar disorder; a method for the treatment of suicidal thoughts and tendencies in a mammal afflicted with bipolar disorder; such treatments comprising administering to said mammal an effective amount of ziprasidone: 5-(2-(4-(1,2-benzisothiazol-3-yl)piperazinyl)ethyl)chlorooxindole, or a pharmaceutically acceptable acid addition salt thereof.

[0007] The term "ziprasidone", as used herein, unless otherwise indicated, encompasses the free base of the compound ziprasidone (named in the preceding paragraph) and all pharmaceutically acceptable salts thereof.

[0008] Pharmaceutically acceptable addition salts include, but are not limited to, salts of the compounds of formula 1, such as mesylate, esylate, and hydrochloride, among others, and may also include polymorphic forms of such salts.

[0009] In yet another aspect of the present invention, the treatments described above improve the condition of a person afflicted with bipolar disorder, or as the case may be the symptoms associated with bipolar disorder as described above, within about 96 hours from the first administration of a compound of formula 1, such as for example, Ziprasidone.

[0010] However, such improvements can be realized more rapidly, that is within about 24 to about 96 hours after administering a compound of formula 1, such as for example, Ziprasidone.

[0011] The term "treating", as used herein, refers to reversing, alleviating, inhibiting the progress of, or preventing the disorder or condition to which such term applies, or one or more symptoms of such disorder or condition. The term "treatment", as used herein, refers to the act of treating, as "treating" is defined immediately above.

[0012] The term "pharmaceutically effective amount", as used herein, refers to an amount of the compound sufficient to treat, in a mammal, including a human, as the case may be, rapid-cycling bipolar disorder, symptoms of bipolar disorder selected from the group consisting of acute mania and depression; to effect mood stabilization; to prevent relapse into bipolar episodes; and to a treat suicidal thoughts and tendencies.

[0013] As provided in the DSM-IV, the specifier of bipolar disorder with rapid cycling can be applied to Bipolar I Disorder or Bipolar II Disorder. The essential feature of a rapid-cycling Bipolar Disorder is the occurrence of four or more mood episodes during the previous 12 months.

[0014] The "symptoms of bipolar disorder selected from the group consisting of acute mania and depression" refer to, respectively, one or more symptoms that may be associated with a manic episode or a depressive episode, as the case may be, of bipolar disorder.

[0015] "Mood stabilization", as used herein, refers to the suppression of manic symptoms and depressive symptoms in order to maintain a euthymic state in the subject of the treatment.

[0016] As used herein, the term "relapse prevention" refers to preventing the recurrence of a kind of episode in a subject who previously experienced at least one of that same kind of episode. An example of "relapse prevention" is preventing a recurrence of a manic episode in a subject who previously experienced one or more manic episodes.

[0017] The treatment of "suicidal thoughts and tendencies" refers to the suppression of suicidal ideation in a subject afflicted with bipolar disorder, with the further goal of suppressing suicide attempts.

[0018] In practicing the inventive methods, the treatment preferably comprise administering a compound of formula I wherein Ar is benzoisothiazolyl and n is 1.

[0019] Preferably X and Y, together with the phenyl to which they are attached, form an oxindole optionally substituted by chloro, fluoro or phenyl.

[0020] In yet another, more specific embodiment of the inventive methods, the compound administered is one wherein Ar is naphthyl and n is 1.

[0021] The psychiatric disorders and conditions referred to herein are known to those of skill in the art and are defined in art-recognized medical texts such as the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, American Psychiatric Association, 1994 (DSM-IV), which is incorporated herein by reference in its entirety.

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DETAILED DESCRIPTION OF THE INVENTION

[0022] The piperazinyheterocyclic compounds of formula I can be prepared by one or more of the synthetic methods described and referred to in U.S. Pat. Nos. 4,831,031 and 4,883,795. U.S. Pat. Nos. 4,831,031 and 4,883,795 are incorporated herein by reference in their entireties.

[0023] The compounds of formula I may be prepared by reacting piperazines of formula II with compounds of formula III as follows: ##STR3##

[0024] wherein Hal is fluoro, chloro, bromo or iodo. This coupling reaction is generally conducted in a polar solvent such as a lower alcohol, for instance ethanol, dimethylformamide or methylisobutylketone, and in the presence of a weak base such as a tertiary amine base, for instance triethylamine or diisopropylethylamine. Preferably, the reaction is in the further presence of a catalytic amount of sodium iodide, and a neutralizing agent for hydrochloride such as sodium carbonate. The reaction is preferably conducted at the reflux temperature of the solvent used. The piperazine derivatives of formula II may be prepared by methods known in the art. For instance, preparation may be effected by reacting an arylhalide of the formula ArHal wherein Ar is as defined above and Hal is fluoro, chloro, bromo or iodo, with piperazine in a hydrocarbon solvent such as toluene at about room temperature to reflux temperature for about half an hour to 24 hours. Alternatively, the compounds of formula II may be prepared by heating an amino-substituted aryl compound of the formula ArNH.sub.2 wherein Ar is as defined above with a secondary amine to allow cyclization to form the piperazine ring attached to the aryl group Ar.

[0025] The compounds of formula III may be prepared by known methods. For instance, compounds (III) may be prepared by reacting a halo-acetic acid or halo-butyric acid wherein the halogen substituted is fluoro, chloro, bromo or iodo with a compound of the formula IV as follows: ##STR4##

[0026] wherein X and Y are as defined above and m is 1 or 3. The compounds (V) are then reduced, e.g. with triethylsilane and trifluoroacetic acid in a nitrogen atmosphere, to form compounds (111).

[0027] When Ar is the oxide or dioxide of benzoisothiazolyl, the corresponding benzoisothiazolyl is oxidized under acid conditions at low temperatures. The acid used is advantageously a mixture of sulphuric acid and nitric acid.

[0028] The pharmaceutically acceptable acid addition salts of the compounds of formula I may be prepared in a conventional manner by treating a solution or suspension of the free base (I) with about one chemical equivalent of a pharmaceutically acceptable acid. Conventional concentration and recrystallization techniques may be employed in isolating the salts. Illustrative of suitable acids are acetic, lactic, succinic, maleic, tartaric, citric, gluconic, ascorbic, benzoic, cinnamic, fumaric, sulfuric, phosphoric, hydrochloric, hydrobromic, hydroiodic, sulfamic, sulfonic such as methanesulfonic, benzenesulfonic, and related acids.

[0029] Compounds of formula I, and their pharmaceutically acceptable salts (referred to collectively hereinafter, as "the active compounds of this invention"), can be administered to a human subject either alone, or, preferably, in combination with pharmaceutically-acceptable carriers or diluents, in a pharmaceutical composition. Such compounds can be administered orally or parenterally. Parenteral administration includes especially intravenous and intramuscular administration. Treatments of the present invention may be delivered in an injectable depot formulation, such as the depot formulations disclosed in U.S. Provisional Patent Application No. 60/421,295 filed on Oct. 25, 2002, which application is incorporated herein by reference in its entirety.

[0030] Additionally, in a pharmaceutical composition comprising an active compound of this invention, the weight ratio of active ingredient to carrier will normally be in the range from 1:6 to 2:1, and preferably 1:4 to 1:1. However, in any given case, the ratio chosen will depend on such factors as the solubility of the active component, the dosage contemplated and the precise route of administration.

[0031] For oral use in treating psychiatric conditions whose manifestations include psychiatric symptoms or behavioral disturbance, the active compounds of this invention can be administered, for example, in the form of tablets or capsules, or as an aqueous solution or suspension. In the case of tablets for oral use, carriers that can be used include lactose and cornstarch, and lubricating agents, such as magnesium stearate, can be added. For oral administration in capsule form, useful diluents are lactose and dried cornstarch. When aqueous suspensions are required for oral use, the active ingredient can be combined with emulsifying and suspending agents. If desired, certain sweetening and/or flavoring agents can be added. For intramuscular, parenteral and intravenous use, sterile solutions of the active ingredient can be prepared, and the pH of the solutions should be suitably adjusted and buffered. For intravenous use, the total concentration of solutes should be controlled to render the preparation isotonic.

[0032] When an active compound of this invention is to be used in a human subject to treat psychiatric conditions whose manifestations include psychiatric symptoms or behavioral disturbance, the prescribing physician will normally determine the daily dosage. Moreover, the dosage will vary according to the age, weight and response of the individual patient as well as the severity of the patient's symptoms. However, in most instances, an effective amount for treating the psychiatric conditions described herein, will be a daily dosage in the range from about 0.5 to about 500 mg, more specifically about 10 mg a day to about 200 mg a day, relatively more specifically about 20 mg a day to about 180 mg a day, relatively still more specifically about 30 mg a day to about 170 mg a day, and relatively even more specifically from about 40 to about 160 mg a day, in single or divided doses, orally or parenterally. In some instances it may be necessary to use dosages outside these limits. The receptor binding and neurotransmitter uptake inhibition profile for Ziprasidone, 5-(2-(4-(1,2-benzisothiazol-3-yl)piperazinyl)ethyl)chloroindole, was described in The Journal of Pharmacology and Experimental Therapeutics, 275, 101-113 (1995), which is incorporated herein by reference in its entirety. A summary of its affinity for various receptors in the central nervous system tissue is presented in Table 1.

TABLE 1

Ziprasidone

Receptor (Ligand)	
DA D1([.sup.3H]SCH23390)	6.28 + 0.17 (3)
DA D2([.sup.3H]spiperone)	8.32 + 0.04 (6)
DA D3([.sup.3H]raclopride)	8.14 + 0.03 (3)
DA D4([.sup.3 H]spiperone)	7.49 + 0.11 (3)
5-HT2A([.sup.3H]ketanserin)	9.38 + 0.03 (5)
5-HT1A([.sup.3H]-80H-DPAT)	8.47 + 0.05 (4)
5-HT-2C- ([.sup.3H]mesulergine)	8.88 + 0.05 (6)
5-HT1D- ([.sup.3H]-5-HT)	8.69 + 0.04 (6)
Alpha-1 ([.sup.3H]prazosin)	7.98 + 0.03 (3)
Histamine H1 ([.sup.3H]mepyramine)	7.33 + 0.07 (3)
Neurotransmitter Reuptake Blockade:	
Norpinephrine	7.30 + 0.01 (4)
5-HT	7.29 + 0.06 (3)
DA	6.58 + 0.02 (3)

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[0033] The following examples illustrate methods of preparing various compounds of formula I.

EXAMPLE 1

[0034] 6-(2-(4-(1-Naphthyl)piperazinyl)ethyl)-benzoxazolone

[0035] A. To a 500 ml three-necked round-bottomed flask equipped with mechanical stirrer and nitrogen inlet were added 200 grams of polyphosphoric acid, 13.51 grams (0.1 mole) of benzoxazolone, and 13.89 g (0.1 mole) of bromoacetic acid. The reaction was heated with stirring at 115.degree. C. for 2.5 hours and poured into 1 kg ice. The mixture was stirred mechanically for 1 hour to form a purple solid, which was then filtered off and washed with water. The solid was slurried with acetone for 30 minutes, a small amount of purple solid filtered off, and the brown filtrate evaporated. The resulting dark brown gum was slurried with 150 ml ethanol for 30 minutes, and the brown solid filtered off and washed with ethanol. This solid has a m.p. of 192.degree.-194.degree. C.

[0036] The solid (6.6 grams, 0.0257 mole) was placed in a 100 ml three-necked round-bottomed flask equipped with magnetic stirrer, dropping funnel, thermometer, and nitrogen inlet and 19.15 ml (0.257 mole) of trifluoroacetic acid added. Triethylsilane (9.44 ml, 0.0591 mole) was added dropwise to the stirring slurry over 30 minutes. The reaction was stirred overnight at room temperature, then poured into 150 grams ice. The mixture was stirred for 15 minutes, and the brown gum filtered off. The gum was dissolved in 100 ml ethyl acetate, and 125 ml cyclohexane added, giving a brown precipitate, which was filtered and washed with cyclohexane. The filtrate was evaporated and the resulting yellow solid slurried with 50 ml isopropyl ether the pale yellow solid was filtered off and dried to give 2.7 g 6-(2-bromoethyl)-benzoxazolone (11% yield for two steps), m.p. 148'-151.degree. C.

[0037] B. To a 100 ml round-bottomed flask equipped with magnetic stirrer, condenser, and nitrogen inlet were added 0.618 g (2.10 mmol) of N-(1-naphthyl)piperazine 0.472 g (1.95 mmol) of 6-(2-bromoethyl)-benzoxazolone, 0.411 ml (2.92 mmol) of triethylamine, 50 ml ethanol, and a catalytic amount of sodium iodide. The reaction was refluxed for 3 days, cooled, and evaporated to a brown gum. The gum was partitioned between 50 ml water and 75 ml methylene chloride, the pH adjusted with aqueous 1 N sodium hydroxide solution, and a little methanol added to facilitate phase separation. The methylene chloride layer was dried over sodium sulfate and evaporated, then chromatographed on silica gel. Fractions containing the product were combined and evaporated, the residue taken up in ethyl acetate, treated with hydrochloride gas, and the resulting hydrochloride salt of the product filtered off to give the white solid title compound, m.p. 282.degree.-285.degree. C., 213 mg (23% yield).

EXAMPLE 2

[0038] 6-(2-(4-(1-Naphthyl)piperazinyl)ethyl)-benzimidazolone

[0039] A. To a 500 ml three-necked round-bottomed flask equipped with mechanical stirrer and nitrogen inlet were added 100 grams of polyphosphoric acid, 6.7 grams (0.05 mole) of benzoxazolone, and 6.95 grams (0.05 mole) of bromoacetic acid. The reaction was heated with stirring at 115.degree. C. for 1.5 hours and poured into 1 kg ice. The mixture was stirred mechanically for 1 hour to form a gray solid, which was then filtered off and washed with water. The solid was slurried with acetone for 30 minutes, a small amount of purple solid filtered off, and the brown filtrate evaporated. The resulting dark brown gum was taken up in ethyl acetate/water, and the organic layer washed with water and brine, dried, and evaporated to solid, 6.5 grams (51%). NMR (d, DMSO-d.sub.6): 5.05 (s, 2H), 7.4 (m, 1H), 7.7-8.05 (m, 2H).

[0040] The solid (6.0 grams, 0.0235 mole) was placed in a 100 ml three-necked round-bottomed flask equipped with magnetic stirrer, dropping funnel, thermometer, and nitrogen inlet and 18.2 ml (0.235 mole) of trifluoroacetic acid added. Triethylsilane (8.64 ml, 0.0541 mole) was added dropwise to the stirring slurry over 30 minutes. The reaction was stirred overnight at room a temperature, then poured into 150 grams ice. The mixture was stirred for 14 minutes, and the pink solid 6-(2-bromoethyl)-benzimidazolone filtered off to give 5.0 grams (42% yield for two steps), m.p. 226.degree.-220.degree. C.

[0041] B. To a 100 ml round-bottomed flask equipped with magnetic stirrer, condenser, and nitrogen inlet were added 2.64 grams (12.4 mmol) of N-(1-naphthyl)-piperazine, 3.0 grams (12.4 mmol) of 6-(2-bromoethyl)-benzimidazolone, 1.31 grams (12.4 mmol) sodium carbonate, 50 ml methylisobutylketone, and a catalytic amount of sodium iodide. The reaction was refluxed for 3 days, cooled, and evaporated to a brown gum. The gum was partitioned between 50 ml water and 75 ml ethyl acetate, and the ethyl acetate layer washed with brine, dried over sodium sulfate, and evaporated, then chromatographed on silica gel. Fractions containing the product were combined and evaporated, the residue taken up in tetrahydrofuran, treated with hydrochloric acid gas, and the resulting hydrochloride salt of the product filtered off to give a white solid, m.p. 260.degree.-262.degree. C., 716 mg (14% yield).

EXAMPLE 3

[0042] 6-(2-(4-(8-Quinolyl)piperazinyl)ethyl)-benzoxazolone

[0043] To a 35 ml round-bottomed flask equipped with condenser and nitrogen inlet were added 0.36 grams (1.5 mmol) of 6-bromoethyl benzoxazolone, 0.32 grams (1.5 mmol) of 8-piperazinyl quinoline, 0.2 grams (1.9 mmol) of sodium carbonate, 50 mg of sodium iodide, and 5 ml of ethanol. The reaction was refluxed for 20 hours, cooled, diluted with water, and the pH adjusted to 4 with 1 N Sodium hydroxide, and the product extracted into ethyl acetate. The ethyl acetate layer was washed with brine, dried, and evaporated to give 0.3 grams of a yellow oil. The oil was dissolved in ethyl acetate, ethyl acetate saturated with hydrochloric acid gas added, and the mixture concentrated to dryness. The residue was crystallized from isopropanol to give 0.18 grams (32%) of a yellow salt, m.p. 2000 NMR (d, CDCl.sub.3): 2.74 (m, 2H), 2.89 (m, 6H), 3.44 (m, 4H), 6.76-7.42 (m, 7H), 8.07 (m, 1H), 8.83 (m, 1H).

EXAMPLE 4

[0044] 6-(2-(4-(6-Quinolyl)piperazinyl)ethyl)-benzoxazolone

[0045] To a 35 ml round-bottomed flask equipped with condenser and nitrogen inlet were added 0.36 grams (1.5 mmol) of 6bromoethylbenzoxazolone, 0.32 g (1.5 mmol) of 8-piperazinylquinazoline, 0.85 grams (8.0 mmol) of sodium carbonate, 2 mg of sodium iodide, and 35 ml of ethanol. The reaction was refluxed for 3 days, cooled, diluted with water, and the pH adjusted to 4 with 1 N HCl. The aqueous layer was separated, the pH adjusted to 7 with 1 N Sodium hydroxide, and the product extracted into ethyl acetate. The ethyl acetate layer was washed with brine, dried, and evaporated to give 1.3 grams of a yellow oil. The oil was crystallized from chloroform (1.1 g), dissolved in ethyl acetate, ethyl acetate saturated with hydrochloric acid gas added, and the mixture concentrated to dryness. The residue gave 0.9 grams (58%) of a yellow salt, m.p. 200.degree. C. NMR (d, CDCl.sub.3):

[0046] 2.72 (m, 6H), 2.86 (m, 2H), 3.83 (m, 4H), 6.9-7.9 (m, 7H), 8.72 (s, 1H).

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EXAMPLE 5

[0047] 6-(2-(4-(4-Phthalazinyl)piperazinyl)ethyl)-benzoxazolone

[0048] To a 35 ml round-bottomed flask equipped with condenser and nitrogen inlet were added 1.13 grams (4.7 mmol) of 6-bromoethyl benzoxazolone, 1.0 gram (4.7 mmol) of 4-piperazinyl phthalazine, 0.64 grams (6.0 mmol) of sodium carbonate, and 30 ml of ethanol. The reaction was refluxed for 20 hours, cooled, diluted with water, and the pH adjusted to 4 with 1 N HCl. The aqueous layer was separated, the pH adjusted to 7 with 1 N Sodium hydroxide, and the product extracted into ethyl acetate. The ethyl acetate layer was washed with brine, dried, and evaporated to give 0.5 grams of a red oil. The oil was chromatographed on silica gel using chloroform/methanol as eluent to give 0.2 grams of a pink oil. The oil was dissolved in ethyl acetate, ethyl acetate saturated with hydrochloric acid gas added and the mixture concentrated to give 0.37 grams (11%) of a yellow salt, m.p. 200.degree. C. NMR (d, CDCl.sub.3): 2.78 (m, 2H), 2.88 (m, 6H), 3.65 (m, 4H), 7.0-8.1 (m, 7H), 9.18 (s, 1H).

EXAMPLE 6

[0049] 6-(2-(4-(4-Methoxy-1-naphthyl)piperazinyl)ethyl)-benzoxazolone

[0050] To a 35 ml round-bottomed flask equipped with condenser and nitrogen inlet were added 0.24 grams (1.0 mmol) of 6-bromoethylbenzoxazolone, 0.24 grams (1.0 mmol) of 4-methoxy-1-piperazinyl naphthalene, 0.13 grams (1.2 mmol) of sodium carbonate, and 25 ml of ethanol. The reaction was refluxed for 36 hours, cooled, diluted with water, and the product extracted into ethyl acetate. The ethyl acetate layer was washed with brine, dried, and evaporated to give 0.49 grams of a yellow oil. The oil was chromatographed on silica gel using chloroform as eluent to give 0.36 grams of yellow crystals. The solid was dissolved in ethyl acetate, ethyl acetate saturated with hydrochloric acid gas added, and the mixture concentrated to dryness to give 0.26 grams (55%) of white salt crystals, m.p. 2000 C. NMR (d, CDCl.sub.3): 2.8-3.2 (m, 12H), 4.01 (s, 3H), 6.7-7.6 (m, 7H), 8.26 (m, 2H).

EXAMPLE 7

[0051] 6-(2-(4-(5-Tetralinyl)piperazinyl)ethyl)-benzoxazolone

[0052] To a 35 ml round-bottomed flask equipped with condenser and nitrogen inlet were added 1.0 gram (3.9 mmol) of 6-bromoethylbenzoxazolone, 0.85 grams (3.9 mmol) of 5-piperazinyl tetralin, 0.4 grams (3.9 mmol) of sodium carbonate, 2 mg of sodium iodide, and 30 ml of isopropanol. The reaction was refluxed for 18 hours, cooled, evaporated to dryness, and the residue dissolved in ethyl acetate/water. The pH was adjusted to 2.0 with 1 N HCl, and the precipitate which had formed collected by filtration. The precipitate was suspended in ethyl acetate/water, the pH adjusted to 8.5 with 1 N Sodium hydroxide, and the ethyl acetate layer separated. The ethyl acetate layer was washed with brine, dried, and evaporated to give 0.7 grams of a solid. The solid was dissolved in ethyl acetate, ethyl acetate saturated with hydrochloric acid gas added, and the mixture concentrated to dryness to give 0.70 grams (40%) of a yellow salt, m.p. 200.degree. C. NMR (d, CDCl.sub.3): 1.9 (m, 4H), 2.95 (m, 16H), 6.8-7.2 (m, 6H).

EXAMPLE 8

[0053] 6-(2-(4-(6-Hydroxy-8-quinolyl)piperazinyl)ethyl)-benzoxazolone

[0054] To a 35 ml round-bottomed flask equipped with condenser and nitrogen inlet were added 0.84 grams (3.5 mmol) of 6-bromoethylbenzoxazolone, 0.80 grams (3.5 mmol) of 6-hydroxy-8-piperazinyl quinoline, 0.37 grams (3.5 mmol) of sodium carbonate, 2 mg of sodium iodide, and 30 ml of isopropanol. The reaction was refluxed for 18 hours, cooled, evaporated, and the residue dissolved in ethyl acetate/water. The pH was adjusted to 2.0 with 1 N HCl, and the phases separated. The aqueous phase was adjusted to pH 8.5 and extracted with ethyl acetate. The ethyl acetate layer was washed with brine, dried, and evaporated to give 0.33 grams of a yellow solid. The solid was dissolved in ethyl acetate, ethyl acetate saturated with hydrochloric acid gas added, and the mixture concentrated to dryness. The residue was crystallized from isopropanol to give 0.32 grams (20%) of a yellow salt, m.p. 200.degree. C. NMR (d, CDCl.sub.3): 2.8 (m, 8H), 3.4 (m, 4H), 6.7-7.3 (m, 7H), 7.7-7.9 (m, 1H).

EXAMPLE 9

[0055] 6-(2-(4-(1-(6-Fluoro)naphthyl)piperazinyl)ethyl)-benzoxazolone

[0056] A. To a round-bottomed flask equipped with condenser and nitrogen inlet were added 345 ml (3.68 mol) of fluorebenzene and 48 grams (0.428 mol) of furoic acid. To the stirring suspension was added in portion 120 grams (0.899 mol) of aluminum chloride. The reaction was then stirred at 950 C. for 16 hours and then quenched by addition to ice/water/1 N HCl. After stirring 1 hour, the aqueous layer was decanted off, and benzene and a saturated aqueous solution of sodium bicarbonate added. After stirring 1 hour, the layers were separated, the aqueous layer washed with benzene, acidified, and extracted into ethyl acetate. The ethyl acetate layer was washed with water and brine, dried over sodium sulfate, and evaporated to a solid. The solid was triturated with isopropyl ether to give 5.0 grams (6.1%) of white solid 6-fluoro-1-naphthoic acid, NMR (d, DMSO-d.sub.6): 7.0-8.0 (m, 5H), 8.6 (m, 1H).

[0057] B. To a 125 ml round-bottomed flask equipped with condenser, addition funnel, and nitrogen inlet were added 5.0 grams (26.3 mmol) of 6-fluoro-1-naphthoic acid and 50 ml acetone. To the stirring suspension were added dropwise 6.25 ml (28.9 mmol) of diphenyl phosphoryl azide and 4 ml (28.9 mmol) of triethylamine. The reaction was refluxed 1 hour, poured into water/ethyl acetate, and filtered. The filtrate was washed with water and brine, dried over sodium sulfate, and evaporated. The residue was further treated with hydrochloric acid to form the hydrochloride salt and then liberated with sodium hydroxide to afford the free base 6-fluoro-1-amino-naphthalene as an oil, 1.0 gram (24%).

[0058] C. To a 125 ml round-bottomed flask equipped with condenser and nitrogen inlet were added 1.0 gram (6.21 mmol) of 6-fluoro-1-amino naphthalene, 1.8 grams (7.76 mmol) of N-benzyl bis(2-chloroethyl)amine hydrochloride, 3.3 ml (19.2 mmol) of diisopropylethylamine, and 50 ml isopropanol. The reaction was refluxed 24 hours, cooled, and evaporated to an oil. The oil was taken up in ethyl acetate, washed with water and brine, dried over sodium sulfate, and evaporated to an oil. The oil was chromatographed on silica gel using methylene chloride as eluent to afford 1.5 grams (75.5%) of an oil, 1-benzyl-4-(6-fluoronaphthyl)-piperazine.

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[0059] D. To a 125 ml round-bottomed flask equipped with nitrogen inlet were added 1.5 grams (4.69 mmol) of 1-benzyl-4-(6-fluoronaphthyl)-piperazine, 1.2 ml (31.3 mmol) of formic acid, 3.0 grams 5% palladium on carbon, 50 ml ethanol. The reaction was stirred at room temperature for 16 hours, the catalyst filtered under N.sub.2, and the solvent evaporated. The oil, N-(1-(6-fluoro)naphthyl)-piperazine (0.420 grams, 39%), was used directly in the following step.

[0060] E. To a 100 ml round-bottomed flask equipped with magnetic stirrer, condenser, and nitrogen inlet were added 0.420 grams (1.83 mmol) of N-(1-naphthyl)piperazine, 0.440 grams (1.83 mmol) of 6-(2-bromoethyl)-benzoxazolone, 194 mg (1.83 mmol) of sodium carbonate, 50 ml methylisobutylketone, and a catalytic amount of sodium iodide. The reaction was refluxed for 3 days, cooled, and evaporated to a brown gum. The gum was partitioned between 50 ml water and 75 ml ethyl acetate, the pH adjusted with aqueous 1 N Sodium hydroxide solution, the layers separated, and the ethyl acetate layer washed with water and brine. The ethyl acetate layer was dried over sodium sulphate and evaporated, then chromatographed on silica gel. Fractions containing the product were combined and evaporated, the residue taken up in ether/methylene chloride, treated with hydrochloric acid gas, and the resulting hydrochloride salt of the product filtered off to give a white solid, m.p. 295.degree.-300.degree. C., 214 mg (22% yield).

EXAMPLE 10

[0061] 6-(4-(4-(1-Naphthyl)piperazinyl)butyl)-benzoxazolone

[0062] A. To a 500 ml round-bottomed flask equipped with mechanical stirrer and nitrogen inlet were added 200 grams polyphosphoric acid, 16.7 grams (0.1 mol) 4-bromobutyric acid, and 13.51 grams (0.1 mol) benzoxazolone. The reaction was heated at 115.degree. C. for 1 hour and 60.degree. C. for 1.5 hours. It was then poured onto ice, stirred for 45 minutes and the solid filtered and washed with water. The solid was suspended in acetone, stirred for 20 minutes, filtered, washed with petroleum ether, and dried to give 12.3 grams (43%) of white solid 6-(4-bromobutyl)-benzoxazolone NMR (d, DMSO-d.sub.6): 1.77 (quin, 2H), 3.00 (t, 2H), 3.45 (t, 2H), 7.0-7.8 (m, 3H).

[0063] B. To a 100 ml three-necked round-bottomed flask equipped with dropping funnel, thermometer, and nitrogen inlet were added 10 grams (0.035 mol) 6-(4-bromobutyl)-benzoxazolone and 26.08 ml (0.35 mol) trifluoroacetic acid. To the stirring suspension was added dropwise 12.93 ml (0.080 mol) triethylsilane, and the reaction stirred at room temperature for 16 hours. The reaction was then poured into water, and the resulting white solid filtered and washed with water. It was then suspended in isopropyl ether, stirred, and filtered to afford white solid 6-(4-trifluoroacetoxybutyl)-benzoxazolone, m.p. 100.degree.-103.degree. C., 10.47 grams (98.7%).

[0064] C. To a 250 ml round-bottomed flask equipped with nitrogen inlet were added 5.0 grams (0.0164 mol) 6-(trifluoroacetoxybutyl)-benzoxazolone, 100 ml methanol, and 1 gram sodium carbonate. The reaction was stirred at room temperature for 1 hour, evaporated, and the residue taken up in methylene chloride/methanol, washed with aqueous HCl, dried over sodium sulfate, and evaporated to white solid 6-(4-chlorobutyl)-benzoxazolone, m.p. 130.degree.-133.degree. C., 2.57 grams (75.7%).

[0065] E. To a 100 ml round-bottom flask equipped with condenser and nitrogen inlet were added 0.658 grams (3.10 mmol) of 6-(4-chlorobutyl)-benzoxazolone, 0.7 grams (3.10 mmol) of N-(1-naphthyl)piperazine, 0.328 grams sodium carbonate, 2 mg sodium iodide, and 50 ml isopropanol. The reaction was refluxed for 3 days, evaporated, taken up in methylene chloride, washed with water, dried over sodium sulfate, and evaporated. The residue was chromatographed on silica gel using ethyl acetate as eluent, and the product dissolved in acetone, precipitated with ethereal HCl, and the white solid filtered, washed with acetone, and dried to afford 6.76 grams (46.0%) of a white solid, m.p. 231.degree.-233.degree. C.

EXAMPLE 11

[0066] 6-(2-(4-(3-(N-(3-Trifluoromethyl)phenyl)indazolyl)-piperazinyl)ethyl)benzoxazolone

[0067] To a 125 ml round-bottomed flask equipped with condenser were added 1.0 gram (2.89 mmol) of N-(3-tri-fluoromethylphenyl)indazolyl)piperazine, 0.70 grams (2.89 mol) of 6-(2-bromoethyl)benzoxazolone, 0.31 grams (2.89 mmol) of sodium carbonate, and 50 ml of methyl isobutyl ketone, and the mixture refluxed 18 hours. The reaction was cooled and partitioned between ethyl acetate and water. The ethyl acetate layer was isolated, washed with water and saturated aqueous sodium chloride solution, dried over sodium sulfate, and evaporated to an oil. The oil was chromatographed on silica gel using ethyl acetate/methylene chloride as eluent, and the product fractions collection and dissolved in ether, precipitated with hydrochloride gas, and the solid collected to give the hydrochloride salt of the title compound, m.p. 280.degree.-282.degree. C., 0.75 grams (47%).

EXAMPLE 12

[0068] 5-(2-(4-(1-Naphthyl)piperazinyl)ethyl)oxindole

[0069] A. To a 250 ml round-bottomed flask equipped with condenser and nitrogen inlet were added 30.7 grams (230 mmol) aluminum chloride, 150 ml carbon disulfide, and 3.8 ml (48 mmol) chloroacetyl chloride. To the stirring mixture was added 5.0 grams (37 mmol) of oxindole portionwise over 15 minutes. The reaction was stirred a further 10 minutes, then refluxed 2 hours. The reaction was cooled, added to ice, stirred thoroughly, and the beige precipitate filtered, washed with water, and dried to afford 7.67 grams (97%) of 5-chloroacetyl-oxindole. NMR (d, DMSO-d.sub.6): 3.40 (s, 2H), 5.05 (s, 2H), 6.8-7.9 (m, 3H).

[0070] B. To a 100 ml round-bottomed flask equipped with condenser and nitrogen inlet were added 5.0 grams (23.9 mmol) of 5-chloroacetyl oxindole and 18.5 ml trifluoroacetic acid. To the stirring solution was added 8.77 ml (54.9 mmol) of triethylsilane while cooling to prevent exotherm, and the reaction stirred 16 hours at room temperature. The reaction was then poured into ice water, stirred and the beige solid filtered, washed with water and hexane, and dried to give 5-(2-chloroethyl)oxindole, m.p. 168.degree.-170.degree. C., 3.0 grams (64%).

[0071] C. To a 50 ml round bottomed flask equipped with condenser and nitrogen inlet were added 370 mg (1.69 mmol) 5-(2-chloroethyl)oxindole, 400 mg (1.69 mmol) N-(1-naphthyl)piperazine hydrochloride, 200 mg (1.69 mmol) sodium carbonate, 2 mg sodium iodide, and 50 ml methylisobutylketone. The reaction was refluxed 24 hours, cooled, and evaporated. The residue was taken up in ethyl acetate, washed with water and brine, dried over sodium sulfate, and evaporated. The residue was chromatographed on silica gel with ethyl acetate, and the product fractions collected and evaporated to give a foam. The foam was dissolved in ether, treated with hydrochloric acid gas, and the precipitate collected, washed with ether, and dried to afford a white solid, m.p. 303.degree.-305.degree. C., 603 mg (84%).

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EXAMPLE 13

[0072] 6-(2-(4-(4-(2-,1,3-Benzothiadiazolyl)piperazinyl)ethyl)-benzoxazolone

[0073] A. To a 125 ml round-bottomed flask equipped with condenser and nitrogen inlet were added 2.0 grams (13.2 mmol) 4-amino-2,1,3-benzothiadiazole, 2.54 grams (13.2 mmol) mechlorethamine hydrochloride, 4.19 grams (39.6 mmol) sodium carbonate, 2 mg sodium iodide, and 50 ml ethanol. The reaction was refluxed 2 days, cooled, and evaporated. The residue was taken up in methylene chloride, washed in water, dried over sodium sulfate, and evaporated. The residue was chromatographed on silica gel using ethyl acetate/methanol as eluent, and the product fractions collected and evaporated to an oil of 4-(2,1,3-benzothiadiazolyl)-N-methylpiperazine, 628 mg (20%). NMR (d, CDCl.sub.3): 2.5 (s, 3H), 2.8 (m, 4H), 3.6 (m, 4H), 6.8 (m, 1H), 7.5 (m, 2H).

[0074] B. To a 25 ml round-bottomed flask equipped with condenser and nitrogen inlet were added 620 mg (2.64 mmol) of 4-(2,1,3-benzothiadiazolyl)-N-methylpiperazine, 0.224 ml (2.64 mmol) vinyl chloroformate, and 15 ml dichloroethane. The reaction was refluxed 16 hours, cooled, and evaporated. The residue was chromatographed on silica gel using methylene chloride/ethyl acetate as eluent, and the product fractions collected to give yellow solid 4-(2,1,3-benzothiadiazolyl)-N-vinylloxycarbonylpiperazine, 530 mg (69%). NMR (d, CDCl.sub.3): 3.6 (m, 4H), 3.8 (m, 4H). 4.4-5.0 (m, 2H), 6.6-7.6 (m, 4H).

[0075] C. To a 50 ml round-bottomed flask equipped with condenser and nitrogen inlet were added 530 mg (1.83 mmol) 4-(2,1,3-benzothiadiazolyl)-N-vinylloxycarbonylpiperazine and 25 ml ethanol, and the suspension saturated with hydrochloric acid gas. The reaction was refluxed 2.75 hours, cooled and evaporated. The residue was triturated with acetone to give a yellow solid N-(2,1,3-benzothiadiazolyl)-piperazine, m.p. 240.degree.-244.degree. C., 365 mg (62%).

[0076] D. To a 125 ml round-bottomed flask equipped with condenser and nitrogen inlet were added 365 mg (1.13 mmol) N-(2,1,3-benzothiadiazolyl)-piperazine, 275 mg (1.13 mmol) 6-(2-bromoethyl)benzoxazolone, 359 mg (3.39 mmol) sodium carbonate, 2 mg sodium iodide and 40 ml ethanol. The reaction was heated at reflux for 2 days, cooled and evaporated. The residue was taken up in methylene chloride, washed with water, dried over sodium sulfate, and evaporated. The residue was chromatographed on silica gel using ethyl acetate/methanol as eluent and the product fractions collected, dissolved in methylene chloride/methanol, precipitated by addition of and ethereal solution of HCl, and the solid filtered, washed with ether, and dried to give 228 mg (45%), m.p. 166.degree.-170.degree. C.

EXAMPLE 14

[0077] 6-(2-(4-(1-Naphthyl)-piperazinyl)ethyl)benzothiazolone

[0078] To a 100 ml round-bottomed flask with condenser and nitrogen inlet were added 1.0 gram (3.88 mmol) of 6-(2-bromoethyl)benzothiazolone, 822 mg (3.88 mmol) N-(1-naphthyl)piperazine, 410 mg (3.88 mmol) sodium carbonate, and 50 ml methylisobutylketone. The reaction was refluxed for 24 hours, cooled, and evaporated. The residue was taken up in ethyl acetate, washed with water and brine, dried over sodium sulfate, and evaporated. The resulting solid was treated with hot ethyl acetate to afford a white solid, m.p. 198.degree.-220.degree. C., 540 mg (36%).

EXAMPLE 15

[0079] 6-(2-(4-(3-benzisothiazolyl)piperazinyl)ethyl)benzoxazolone

[0080] To a 125 ml round-bottomed flask equipped with condenser were added 4.82 grams (0.022 mol) of N-(3-benzisothiazolyl)piperazine (prepared according to the procedure given in U.S. Pat. No. 4,411,901), 5.32 grams (0.022 mol) of 6-(2-bromo)ethylbenzoxazolone, 2.33 grams (0.022 mol) of sodium carbonate, and 50 ml of methyl isobutyl ketone. The mixture was refluxed for 18 hours. The reaction was cooled and partitioned between ethyl acetate and water. The ethyl acetate layer was isolated, washed with water and saturated aqueous sodium chloride solution dried over sodium sulfate, and evaporated to an oil. The oil was chromatographed on silica gel using ethyl acetate as eluent, and the product fractions collected and triturated with methylene chloride/isopropyl ether to give a white solid, m.p. 185.degree.-187.degree. C. NMR (CDCl₃): 1.7 (bs, 1H), 2.8 (m, 8H), 3.6 (m, 4H), 6.9-8.0 (m, 7H).

EXAMPLE 16

[0081] 5-(2-(4-(1,2-benzisothiazol-3-yl)-piperazinyl)ethyl)oxindole

[0082] To a 125 ml round-bottom flask equipped with nitrogen inlet and condenser were added 0.62 grams (3.20 mmol) 5-(2-chloroethyl)-oxindole, 0.70 grams (3.20 mmol) sodium carbonate, 2 mg sodium iodide, and 30 ml methylisobutyl ketone. The reaction was refluxed 40 hours, cooled, filtered, and evaporated. The residue was chromatographed on silica gel, eluting the byproducts with ethyl acetate (1 l) and the product with 4% methanol in ethyl acetate (1.5 l). The product fractions (R_f=0.2 in 5% methanol in ethyl acetate) were evaporated, taken up in methylene chloride, and precipitated by addition of ether saturated with HCl; the solid was filtered and washed with ether, dried, and washed with acetone. The latter was done by slurrying the solid acetone and filtering. The title compound was obtained as a high melting, non-hygroscopic solid product, m.p. 288.degree.-288.5.degree. C., 0.78 (59%).

[0083] In a manner analogous to that for preparing 5-(2-(4-(1,2-benzisothiazol-3-yl)piperazinyl)ethyl)-oxindole, the following compounds were made:

[0084] 5-(2-(4-(1,2-benzisothiazol-3-yl)piperazinyl)ethyl)-1-ethyloxindole hydrochloride, 25%, m.p. 278.degree.-279.degree. C.;

[0085] 5-(2-(4-(1,2-benzisothiazol-3-yl)piperazinyl)ethyl)-1-methyloxindolehydrochloride hemihydrate, 42%, m.p. 283.degree.-285.degree. C.; MS(%): 392(1), 232(100), 177(31); Anal. for C₂₂H₂₄N₄OS.HCl._{1/2}H₂O: C, 60.33; H, 5.98; N, 12.79. Found: C, 60.37; H, 5.84; N, 12.77;

[0086] 5-(2-(4-(1,2-benzisothiazol-3-yl)piperazinyl)ethyl)-1-(3-chlorophenyl)oxindole hydrochloride hydrate, 8%, m.p. 221.degree.-223.degree. C.; MS(%): 488(1), 256(4), 232(100), 177 (15); Anal. for C₂₇H₂₅ClN₄OS.HCl.H₂O: C, 59.67; H, 5.19; N, 10.31. Found: C 59.95, H 5.01, N 10.14;

[0087] 5-(2-(4-(1,2-benzisothiazol-3-yl)piperazinyl)ethyl)-3,3-dimethyloxindole hydrochloride hemihydrate, 40%, m.p. 289.degree.-291.degree. C.; MS(%): 406(1), 232(100), 177(42); Anal. for C₂₃H₂₆N₄OS.HCl._{1/2}H₂O: C 61.11, H 6.24, N 12.39. Found: C, 61.44; H, 6.22; N, 12.01;

[0088] 5-(2-(4-(1,2-benzisothiazol-3-yl)piperazinyl)ethyl)-1,3-dimethyloxindole, 76%, m.p. 256.degree. C.;

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[0089] 5'-(2-(4-(1,2-benzisothiazol-3-yl)piperazinyl)ethyl)-spiro[cyclopentane-1,3'-indoline]-2'-one hydrochloride hemihydrate, 50%, m.p. 291.degree.-293.degree. C. (dec.); MS(%): 432(1) 232(100), 200(11), 177(36); Anal. for C.sub.25H.sub.28N.sub.4 OS.HCl.sub.1/2H.sub.2O: C, 62.81; H, 6.33; N, 11.72. Found: C 63.01, H, 6.32, N 11.34;

[0090] 5-(2-(4-(1,2-benzisothiazol-3-yl)piperazinyl)ethyl)-1,3,3-trimethyloxindole hydrochloride hemihydrate, 63%, m.p. 225.degree.-257.degree. C.; MS(%): 420(1), 232(100), 177(37); Anal. for C.sub.24H.sub.28N.sub.4 OS.HCl.sub.1/2H.sub.2O: C, 61.85; H, 6.49; N, 12.02. Found: C, 61.97; H, 6.34; N, 11.93;

[0091] 5-(2-(4-(1,2-benzisothiazol-3-yl)piperazinyl)ethyl)-6-fluorooxindole hydrochloride hydrate, 18%, m.p. 291.degree.-293.degree. C.; MS(%): 396(1), 232(100), 177(53); Anal. for C.sub.2H.sub.2, H.sub.2, H.sub.4FOS.HCl.sub.1/2H.sub.2O: C, 55.93; H, 5.36; N, 12.42. Found: C, 56.39; H, 5.30; N, 12.19;

[0092] 5-(2-(4-(1,2-benzisothiazol-3-yl)piperazinyl)ethyl)-7-fluorooxindole hydrochloride, 9%, m.p. 2530 C.;

[0093] 5-(2-(4-(1,2-benzisothiazol-3-yl)piperazinyl)ethyl)-6-chlorooxindole hydrochloride, 20%, m.p.>300.degree. C.; MS(%): 488(1), 256(4), 232(100), 177(15); Analysis for C.sub.2, H.sub.2ClN.sub.4 OS.HCl.sub.1/2H.sub.2O: C, 52.50; H, 4.71; N, 11.39. Found: C, 52.83; H, 4.93; N, 11.42;

[0094] 5-(2-(4-(1,2-benzisothiazol-3-yl)piperazinyl)ethyl)-6-fluoro-3,3-dimethyloxindole hydrochloride, 35%, m.p. 284.degree.-2860 C.; Anal. for C.sub.23H.sub.25FN.sub.4 OS.HCl.H.sub.2O: C 57.67, H 5.89, N 11.70. Found: C, 58.03; H, 5.79; N, 11.77;

[0095] 5-(2-(4-(1,2-benzisothiazol-3-yl)piperazinyl)butyl)oxindole hemihydrate, 26%, m.p. 131.degree.-1350 C.; MS(%): 406(2), 270(8), 243(65), 232(23), 177(45), 163(100); Anal. for C.sub.23H.sub.26N.sub.4 OS.sub.1/2H.sub.2O: C, 66.48; H, 6.55; N, 13.48. Found: C, 66.83; H, 6.30; N, 13.08;

[0096] 5-(2-(4-(1,2-benzisothiazol-3-yl)piperazinyl)butyl)-7-fluorooxindole hydrate, 7%, m.p. 126.degree.-129.degree. C.; MS(%): 424(3); Anal. for C.sub.23H.sub.25 FN.sub.4 OS.H.sub.2O: C, 57.67; H, 5.89; N, 11.70. Found: C, 57.96; H, 5.62; N, 11.47; 5-(2-(4-(1,2-benzisothiazol-3-yl)piperazinyl)butyl)-1-ethyloxindole hemihydrate, 25%, m.p. 1260-1280 C.; MS(%): 434(2), 298(10), 271(55), 232(34), 177(53), 163(100); Anal. for C.sub.25H.sub.30N.sub.4 OS.sub.1/2H.sub.2O: C, 67.69; H, 7.04; N, 12.63. Found: C, 67.94; H, 6.73; N, 12.21;

[0097] 5-(2-(4-(naphthalen-1-yl)piperazinyl)ethyl)-1-ethyloxindole hydrochloride hydrate, 21%, m.p.>300.degree. C.; MS(%): 399(1), 225(96), 182(30), 70(100); Anal. for C.sub.26H.sub.29N.sub.3 O.HCl.H.sub.2O: C, 68.78; H, 7.10; N, 9.26. Found: C, 69.09; H, 6.72; N, 9.20;

[0098] 5-(2-(4-(naphthalen-1-yl)piperazinyl)ethyl)-6-fluorooxindole hydrochloride, 23%, m.p. 2890-2910 C.; MS(%): 389(1), 232(3), 225(100), 182(32), 70(84); Anal. for C.sub.24H.sub.24FN.sub.3 O.HCl.sub.1/2 CH.sub.2 Cl.sub.2; C, 62.82; H, 5.60; N, 8.97. Found: C, 62.42; H, 5.82; N, 8.77;

[0099] 5-(2-(4-(naphthalen-1-yl)piperazinyl)ethyl)-7-fluorooxindole hydrochloride, 22%, m.p. 308.degree. C. (dec.); MS(%): 389(1), 225(100); Anal. for C.sub.24H.sub.24FN.sub.3 O.HCl.CH.sub.2 Cl.sub.2; C 58.78, H 5.93, N 8.23. Found: C, 58.82; H, 5.80; N, 8.27;

EXAMPLE 17

[0100] 6-(4-(2-(3-Benzisothiazolyl)piperazinyl)ethyl)phenyl)benzothiazolone

[0101] To a 100 ml round-bottomed flask equipped with condenser and nitrogen inlet were added 1.03 grams (4 mmol) 6-(2-bromoethyl)-benzothiazolone, 0.88 grams (4 mmol) N-benzisothiazolylpiperazine, 0.84 grams (8 mmol) sodium carbonate, 2 mg sodium iodide, and 40 ml methylisobutyl ketone. The reaction was refluxed 36 hours, cooled, filtered, and the filtrate evaporated. The residue was chromatographed on silica gel using ethyl acetate as eluent to afford an oil, which was taken up in methylene chloride and precipitated by addition of ether saturated with HCl. The solid was filtered, washed with ether, dried briefly, washed with a minimal amount of acetone and dried to afford a white solid, m.p. 288.degree.-290.degree. C., 1.44 grams (76.7%).

EXAMPLE A

[0102] A. Following the general procedure for the preparation of 5-(chloroacetyl)oxindole in Example 12A, the following intermediates were prepared from the appropriate oxindoles:

[0103] 5-(chloroacetyl)-1-ethyl-oxindole (81%, m.p. 1570-1590 C., NMR(CDCl.sub.3); 1.30(t,3H), 3.60(s,2H), 3.85(q,2H), 4.70(s,2H), 6.85-8.15(m,2H);

[0104] 5-(chloroacetyl)-1-methyloxindole(C.sub.1, H.sub.10ClNO.sub.2, 92%, m.p. 2010-2020 C.;

[0105] 1(3-chlorophenyl)-5(chloroacetyl)oxindole, 98% m.p. 143.degree.-145.degree. C., NMR(DMSO-d.sub.6): 3.85(br s,2H), 5.10(s,2H), 6.8(d,1H), 7.4-7.6(m,4H), 7.9 (s+d,2H); MS(%): 319(17, 270(100), 179(46), 178(38);

[0106] 1,3-dimethyl-5-(chloroacetyl)oxindole, 97% m.p. 206.degree.-207.degree.

[0107] 5-(chloroacetyl)-spirocyclopentane[1,3']-indolone, 99%, m.p. 203.degree.-204.degree. C.(dec).; NMR(DMSO-d.sub.6): 2.0(brs,8H), 4.95(s,2H), 6.9(d,1H), 7.8(d+s,2H), 10.6(brs, 1H);

[0108] 5-(chloroacetyl)-1,3,3-trimethyloxindole, 82%, m.p. 1820-185.degree. C., NMR(CDCl.sub.3): 1.45(s,6H), 3.25(s,3H), 4.65(s,2H), 6.9(d, 1H), 7.9(s,1H), 8.0(d,1H);

[0109] 6-fluoro-5-(chloroacetyl)oxindole, 96%, m.p. 1780-1800 C.; NMR(DMSO-d.sub.6): 3.5(s,2H), 4.8(d,2H), 6.7-7.2(m,2H), 7.8(d,1H);

[0110] 7-fluoro-5-(chloroacetyl)oxindole, 91%, m.p. 1940-1960 C., NMR(DMSO-d.sub.6): 3.68(s,2H), 5.13(s,2H) 7.65-7.9(dd,2H);

[0111] 6-chloro-5-(chloroacetyl)oxindole, 99%, m.p. 206.degree.-207.degree. C.;

[0112] 5-(chloroacetyl)-3,3-dimethyl-6-fluorooxindole, 89%, m.p. 185.degree.-1880 C.;

[0113] 5-(γ -chlorobutyryl)oxindole, 84%, oil, MS(%): 239, 237(55);

[0114] 1-ethyl-5-(γ -chlorobutyryl)oxindole, 99%, oil, NMR(CDCl.sub.3): 1.2(t,3H), 1.5-2.7(m,5H), 3.0-3.2(m,2H), 3.5-4.0(m,3H), 6.8-7.0(d,1H), 7.9(s,1H), 7.95(d,1H), and

[0115] 5-(γ -chlorobutyryl)-7-fluorooxindole, 53%, m.p. 156.degree.-160.degree. C.

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EXAMPLE B

[0116] By the same procedure as that used to prepare 5-(2-chloroethyl)oxindole in Example 12B, the following were prepared:

[0117] 5-(2-chloroethyl)-1-ethyloxindole, 93%, m.p. 120.degree.-122.degree. C.; NMR (CDCl₃): 1.30(t,2H), 3.55(s,2H), 3.65-4.0(m,4H), 6.8-7.3(m,3H);

[0118] 5-(2-chloroethyl)-1-methyloxindole, 99%, m.p. 127.degree.-130.degree. C.; NMR (CDCl₃): 3.1(t,2H), 3.2(s,2H), 3.5(s,2H), 3.75(t,2H), 6.8(d,1H), 7.15(s,1H), 7.3(d,1H);

[0119] 5-(2-chloroethyl)-1-(3-chlorophenyl)oxindole, 83%, m.p. 75.degree.-76.degree. C.;

[0120] 5-(2-chloroethyl)-1,3-dimethyloxindole, 58%, m.p. 73.degree.-75 C., NMR CDCl₃: 1.45-1.55(d,3H), 3.03-3.2(t,2H), 3.25(s,3H), 3.30-3.60(q,1H), 3.65-3.90(t,2H), 6.85-6.90(d,1H), 7.15(s,1H), 7.15-7.30(d,1H);

[0121] 5'-(2-chloroethyl)-spiro[cyclopentane-1,3'-indoline]-2'-one, 92%, m.p. 140.degree.-142.degree. C.; NMR(DMSO-d₆): 2.8(brs,8H), 2.90(t,2H), 3.7(t,2H), 6.6-7.1(m,3H), 10.2(brs,1H);

[0122] 5-(2-chloroethyl)-,3,3-trimethyloxindole, 83%, oil;

[0123] 5-(2-chloroethyl)-6-fluorooxindole 62%, m.p. 1880-190.degree. C.; NMR(DMSO-d₆) 3.05(t,2H), 3.5(2,2H), 3.85(t,2H), 6.6-7.3(m,2H);

[0124] 5-(2-chloroethyl)-7-fluorooxindole, 79%, m.p. 176.degree.-179 C.; MS(%); 213(50), 180(20), 164(100), 136(76);

[0125] 5-(2-chloroethyl)-6-chlorooxindole, 94%, m.p. 210.degree.-211.degree. C.;

[0126] 5-(2-chloroethyl)-3,3-dimethyl-6-fluorooxindole (C₁₂H₁₃ClFNO), 84%, m.p. 195.degree.-196 C., NMR(DMSO-d₆): 1.3(s,6H), 3.05(t,2H), 3.7(t,2H), 6.65(d,1H), 7.1(d,1H), 10.1(br s,1H);

[0127] 5-(4-chlorobutyl)oxindole, 40%, oil, NMR(CDCl₃): 1.6-2.0(m,4H), 2.6(m,2H), 3.6(m,4H), 6.8-7.15(m,3H), 9.05(br s, 1H);

[0128] 5-(4-chlorobutyl)-ethyloxindole, 48%, oil, NMR(CDCl₃): 1.25(t,3H), 1.5-1.95(m,4H), 2.6(m,2H), 3.5(s,2H), 3.55(t,2H), 3.75(q,2H), 6.7-7.2(m,3H); and

[0129] 5-(4-chlorobutyl)-7-fluorooxindole, 71%, m.p. 1680-173.degree. C.

What is claimed is:

1. A method for treating rapid-cycling bipolar disorder in a mammal in need thereof comprising administering to said mammal a pharmaceutically effective amount of a compound of formula ##STR5## or a pharmaceutically acceptable acid addition salt thereof, wherein Ar is benzoisothiazolyl or an oxide or dioxide thereof each optionally substituted by one fluoro, chloro, trifluoromethyl, methoxy, cyano, nitro or naphthyl optionally substituted by fluoro, chloro, trifluoromethyl, methoxy, cyano or nitro; quinolyl; 6-hydroxy-8-quinolyl; isoquinolyl; quinazolyl; benzothiazolyl; benzothiadiazolyl; benzotriazolyl; benzoxazolyl; benzoxazolonyl; indolyl; indanyl optionally substituted by one or two fluoro, 3-indazolyl optionally substituted by 1-trifluoromethylphenyl; or phthalazinyl; n is 1 or 2; and X and Y together with the phenyl to which they are attached form quinolyl; 2-hydroxyquinolyl; benzothiazolyl; 2-aminobenzothiazolyl; benzoisothiazolyl; indazolyl; 2-hydroxyindazolyl; indolyl; spiro; oxindolyl optionally substituted by one to three of (C₁-C₃) alkyl, or one of chloro, fluoro or phenyl, said phenyl optionally substituted by one chloro or fluoro; benzoxazolyl; 2-aminobenzoxazolyl; benzoxazolonyl; 2-aminobenzoxazolonyl; benzothiazolonyl; bezoimidazolonyl; or benzotriazolyl.

2. A method of treating in a mammal in need thereof a symptom of bipolar disorder selected from the group consisting of acute mania, depression, and suicidal thoughts or suicidal tendencies, which method comprises administering to said mammal a pharmaceutically effective amount of a compound of formula ##STR6## or a pharmaceutically acceptable acid addition salt thereof, wherein Ar is benzoisothiazolyl or an oxide or dioxide thereof each optionally substituted by one fluoro, chloro, trifluoromethyl, methoxy, cyano, nitro or naphthyl optionally substituted by fluoro, chloro, trifluoromethyl, methoxy, cyano or nitro; quinolyl; 6-hydroxy-8-quinolyl; isoquinolyl; quinazolyl; benzothiazolyl; benzothiadiaazolyl; benzotriazolyl; benzoxazolyl; benzoxazolonyl; indolyl; indanyl optionally substituted by one or two fluoro, 3-indazolyl optionally substituted by 1-trifluoromethylphenyl; or phthalazinyl; n is 1 or 2; and X and Y together with the phenyl to which they are attached form quinolyl; 2-hydroxyquinolyl; benzothiazolyl; 2-aminobenzothiazolyl; benzoisothiazolyl; indazolyl; 2-hydroxyindazolyl; indolyl; spiro; oxindolyl optionally substituted by one to three of (C.sub.1-C.sub.3) alkyl, or one of chloro, fluoro or phenyl, said phenyl optionally substituted by one chloro or fluoro; benzoxazolyl; 2-aminobenzoxazolyl; benzoxazolonyl; 2-aminobenzoxazolonyl; benzothiazolonyl; bezoimidazolonyl; or benzotriazolyl.

3. The method of claim 2 wherein the symptom is selected from the group consisting of acute mania and depression.

4. The method of claim 2 wherein the symptom is suicidal thoughts or tendencies.

5. A method of stabilizing mood or of preventing relapse into a bipolar episode in a mammal afflicted with bipolar disorder, which method comprises administering to said mammal a pharmaceutically effective amount of a compound of formula ##STR7## or a pharmaceutically acceptable acid addition salt thereof, wherein Ar is benzoisothiazolyl or an oxide or dioxide thereof each optionally substituted by one fluoro, chloro, trifluoromethyl, methoxy, cyano, nitro or naphthyl optionally substituted by fluoro, chloro, trifluoromethyl, methoxy, cyano or nitro; quinolyl; 6-hydroxy-8-quinolyl; isoquinolyl; quinazolyl; benzothiazolyl; benzothiadiaazolyl; benzotriazolyl; benzoxazolyl; benzoxazolonyl; indolyl; indanyl optionally substituted by one or two fluoro, 3-indazolyl optionally substituted by 1-trifluoromethylphenyl; or phthalazinyl; n is 1 or 2; and X and Y together with the phenyl to which they are attached form quinolyl; 2-hydroxyquinolyl; benzothiazolyl; 2-aminobenzothiazolyl; benzoisothiazolyl; indazolyl; 2-hydroxyindazolyl; indolyl; spiro; oxindolyl optionally substituted by one to three of (C.sub.1-C.sub.3) alkyl, or one of chloro, fluoro or phenyl, said phenyl optionally substituted by one chloro or fluoro; benzoxazolyl; 2-aminobenzoxazolyl; benzoxazolonyl; 2-aminobenzoxazolonyl; benzothiazolonyl; bezoimidazolonyl; or benzotriazolyl.

6. The method of claim 5, for stabilizing mood.

7. The method of claim 5, for preventing relapse into a bipolar episode.

8. The method of any preceding claim wherein the compound is ziprasidone.

9. The method of claim 1, 2, or 5 wherein the compound is ziprasidone and is administered in dosages of about 0.5 mg to about 500 mg per day.

10. The method of claim 1, 2, or 5 wherein the compound is ziprasidone and the administration is oral.

11. The method of claim 1, 2, or 5 wherein the compound is ziprasidone and the administration is parenteral.

12. The method of claim 1, 2, or 5 wherein the treatments effect improvement in the mammal within about 96 hours after administrating the compound.

13. The method of claim 1, 2, or 5 wherein the treatments effect improvement in the mammal within about 24 to about 96 hours after administering the compound.

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ISSUE U.S. PATENT CLASSIF.:

MAIN: 514/253.060
 SECONDARY: 514/254.020; 514/254.060

CURRENT U.S. PATENT CLASSIF.:

MAIN: 514/253.060
 SECONDARY: 514/254.020; 514/254.060

INT. PATENT CLASSIF.:

[7]
 MAIN: A61K-0031/496
 INITIAL: A61K0031-496 [ICM,7]
 RECLASS: A61K0031-496 [I,C*]; A61K0031-496 [I,A]

CHEMICAL ABSTRACTS INDEXING COPYRIGHT 2010 ACS on STN

 PATENT KIND DATE

 OS CA 141:420463 * WO 2004100957 A1 20041125
 * CA Indexing for this record included
 CA CLASSIF.: 1-11 (Pharmacology)
 Section cross-reference(s): 28
 SUPPL. TERM: bipolar disorder treatment piperazinyl heterocyclic compd;
 ziprasidone treatment acute mania depression mood
 stabilization; suicide thought treatment ziprasidone
 INDEX TERM: Dopamine receptors
 (D1, ziprasidone affinity for, in central nervous system
 tissue; treatment of bipolar disorders and assocd.
 symptoms using piperazinyl-heterocyclic compds., esp.
 ziprasidone)
 INDEX TERM: Dopamine receptors
 (D1A, ziprasidone affinity for, in central nervous
 system tissue; treatment of bipolar disorders and
 assocd. symptoms using piperazinyl-heterocyclic
 compds., esp. ziprasidone)
 INDEX TERM: Dopamine receptors
 (D2, ziprasidone affinity for, in central nervous system
 tissue; treatment of bipolar disorders and assocd.
 symptoms using piperazinyl-heterocyclic compds., esp.
 ziprasidone)
 INDEX TERM: Dopamine receptors
 (D3, ziprasidone affinity for, in central nervous system
 tissue; treatment of bipolar disorders and assocd.
 symptoms using piperazinyl-heterocyclic compds., esp.
 ziprasidone)
 INDEX TERM: Dopamine receptors
 (D4, ziprasidone affinity for, in central nervous system
 tissue; treatment of bipolar disorders and assocd.
 symptoms using piperazinyl-heterocyclic compds., esp.
 ziprasidone)
 INDEX TERM: Histamine receptors
 (H1, ziprasidone affinity for, in central nervous system
 tissue; treatment of bipolar disorders and assocd.
 symptoms using piperazinyl-heterocyclic compds., esp.
 ziprasidone)
 INDEX TERM: Mental disorder
 (bipolar disorder, rapid-cycling; treatment of bipolar
 disorders and assocd. symptoms using
 piperazinyl-heterocyclic compds., esp. ziprasidone)
 INDEX TERM: Nervous system
 (central, ziprasidone affinity for receptors in tissue
 of; treatment of bipolar disorders and assocd. symptoms
 using piperazinyl-heterocyclic compds., esp.
 ziprasidone)
 INDEX TERM: Mental disorder
 (depression, as symptom of bipolar disorder, treatment
 of; treatment of bipolar disorders and assocd. symptoms
 using piperazinyl-heterocyclic compds., esp.
 ziprasidone)

INDEX TERM: Mental disorder
(mania, as symptom of bipolar disorder, treatment of;
treatment of bipolar disorders and assocd. symptoms
using piperazinyl-heterocyclic compds., esp.
ziprasidone)

INDEX TERM: Nervous system agents
(noradrenaline reuptake inhibitors; treatment of bipolar
disorders and assocd. symptoms using
piperazinyl-heterocyclic compds., esp. ziprasidone)

INDEX TERM: Drug delivery systems
(oral; treatment of bipolar disorders and assocd.
symptoms using piperazinyl-heterocyclic compds., esp.
ziprasidone)

INDEX TERM: Drug delivery systems
(parenterals; treatment of bipolar disorders and assocd.
symptoms using piperazinyl-heterocyclic compds., esp.
ziprasidone)

INDEX TERM: Emotion
(stabilization of swings in; treatment of bipolar
disorders and assocd. symptoms using
piperazinyl-heterocyclic compds., esp. ziprasidone)

INDEX TERM: Death
(suicide, thoughts of or tendencies for, as symptom of
bipolar disorder, treatment of; treatment of bipolar
disorders and assocd. symptoms using
piperazinyl-heterocyclic compds., esp. ziprasidone)

INDEX TERM: 5-HT reuptake inhibitors
Human
Mammalia
(treatment of bipolar disorders and assocd. symptoms
using piperazinyl-heterocyclic compds., esp.
ziprasidone)

INDEX TERM: 5-HT receptors
(type 5-HT1A, ziprasidone affinity for, in central
nervous system tissue; treatment of bipolar disorders
and assocd. symptoms using piperazinyl-heterocyclic
compds., esp. ziprasidone)

INDEX TERM: 5-HT receptors
(type 5-HT1D, ziprasidone affinity for, in central
nervous system tissue; treatment of bipolar disorders
and assocd. symptoms using piperazinyl-heterocyclic
compds., esp. ziprasidone)

INDEX TERM: 5-HT receptors
(type 5-HT2A, ziprasidone affinity for, in central
nervous system tissue; treatment of bipolar disorders
and assocd. symptoms using piperazinyl-heterocyclic
compds., esp. ziprasidone)

INDEX TERM: 5-HT receptors
(type 5-HT2C, ziprasidone affinity for, in central
nervous system tissue; treatment of bipolar disorders
and assocd. symptoms using piperazinyl-heterocyclic
compds., esp. ziprasidone)

INDEX TERM: Biological transport
(uptake, reuptake, of norepinephrine, 5-HT, and
dopamine, ziprasidone blockade of; treatment of bipolar
disorders and assocd. symptoms using
piperazinyl-heterocyclic compds., esp. ziprasidone)

INDEX TERM: Neurotransmitters
(ziprasidone blockade of reuptake of; treatment of
bipolar disorders and assocd. symptoms using
piperazinyl-heterocyclic compds., esp. ziprasidone)

INDEX TERM: Adrenoceptors
(.alpha.1, ziprasidone affinity for, in central nervous
system tissue; treatment of bipolar disorders and
assocd. symptoms using piperazinyl-heterocyclic
compds., esp. ziprasidone)

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INDEX TERM: 110-85-0D, Piperazine, heterocyclic compds. 146939-27-7, Ziprasidone
(treatment of bipolar disorders and assocd. symptoms using piperazinyl-heterocyclic compds., esp. ziprasidone)

INDEX TERM: 118289-56-8P 118289-57-9P 118289-80-8P 118289-81-9P
118289-84-2P 118289-85-3P 118289-86-4P 118289-88-6P
118289-89-7P 118289-90-0P 118289-91-1P 118289-93-3P
118289-94-4P 118289-95-5P 118305-72-9P 118306-70-0P
118306-71-1P 118306-81-3P 122883-69-6P 122883-72-1P
122883-74-3P 122883-75-4P 122883-76-5P 122883-77-6P
122883-78-7P 122883-80-1P 122883-83-4P 122883-85-6P
122883-86-7P 122883-87-8P 122883-88-9P 122883-89-0P
122883-90-3P 122883-91-4P 122883-92-5P 122883-93-6P
122883-94-7P 122883-95-8P 122883-96-9P 122883-97-0P
221377-24-8P 795313-43-8P 795313-62-1P 795313-65-4P
(treatment of bipolar disorders and assocd. symptoms using piperazinyl-heterocyclic compds., esp. ziprasidone)

INDEX TERM: 55-86-7, Mechlorethamine hydrochloride 59-48-3, Oxindole
59-49-4, 2(3H)-Benzoxazolone 76-05-1, Trifluoroacetic acid, reactions 79-04-9, Chloroacetyl chloride 79-08-3, Bromoacetic acid 462-06-6, Fluorobenzene 767-64-6, 4-Amino-2,1,3-benzothiadiazole 2623-87-2, 4-Bromobutyric acid 5130-24-5, Vinyl chloroformate 10429-82-0, N-Benzylbis(2-chloroethyl)amine hydrochloride 26386-88-9, Diphenyl phosphoryl azide 26447-28-9, Furoic acid 57536-84-2 57536-86-4, N-(1-Naphthyl)piperazine 87691-87-0 98223-97-3 104113-71-5 118306-75-5 118306-80-2, 6-(2-Bromoethyl)benzothiazolone 118306-90-4 118306-91-5 118306-92-6 221377-26-0
(treatment of bipolar disorders and assocd. symptoms using piperazinyl-heterocyclic compds., esp. ziprasidone)

INDEX TERM: 575-08-6P, 6-Fluoro-1-naphthoic acid 62078-78-8P, 6-Fluoro-1-aminonaphthalene 65435-04-3P, 5-Chloroacetyloxindole 92584-74-2P, 6-(2-Bromoethyl)benzoxazolone 117922-85-7P 117922-86-8P 118289-70-6P 118306-76-6P, 5-(2-Chloroethyl)oxindole 118306-77-7P 118306-78-8P 118306-79-9P 118306-87-9P 118306-94-8P 118306-96-0P, 6-(4-Chlorobutyl)benzoxazolone 118306-97-1P 118306-98-2P 118306-99-3P 118307-00-9P 118307-01-0P 118307-02-1P 118307-03-2P 118307-04-3P 118307-05-4P 118307-06-5P 118307-07-6P 118307-08-7P 199387-17-2P
(treatment of bipolar disorders and assocd. symptoms using piperazinyl-heterocyclic compds., esp. ziprasidone)

INDEX TERM: 118289-51-3P 118289-52-4P 118289-53-5P 118289-54-6P 118289-55-7P, 5-(2-Chloroethyl)-6-chlorooxindole 118306-83-5P 118306-84-6P 118306-85-7P 118306-86-8P 118307-09-8P 118307-10-1P 118307-11-2P 118307-12-3P
(treatment of bipolar disorders and assocd. symptoms using piperazinyl-heterocyclic compds., esp. ziprasidone)

INDEX TERM: 50-67-9, 5-HT, biological studies 51-41-2, Norepinephrine 51-61-6, Dopamine, biological studies
(ziprasidone blockade of reuptake of; treatment of bipolar disorders and assocd. symptoms using piperazinyl-heterocyclic compds., esp. ziprasidone)

D CLM.EX

-- Original Publication -- (APPLICATION - A1)

CLM What is claimed is:

1. A method, comprising: receiving mean glucose value information of a patient based on a predetermined time period; receiving an HbA1C level of the patient; determining a correlation between the received mean glucose value information and the HbA1C level; and determining a target HbA1C level based on the determined correlation.
2. The method of claim 1 wherein receiving mean glucose value information includes: receiving monitored glucose level information over the predetermined time period; and applying a weighting function to the received monitored glucose level information.
3. The method of claim 2 wherein the weighting function is based on a time of day information associated with the received monitored glucose level information.
4. The method of claim 2 wherein the weighting function is based on a time period associated with the received monitored glucose level information.
5. The method of claim 1 wherein determining the target HbA1C level includes: receiving one or more patient specific parameters; and applying the received one or more patient specific parameters to the determined correlation between the received mean glucose value information and the received HbA1C level.
6. The method of claim 5 wherein the one or more patient specific parameters includes an age of the patient, a history of hypoglycemia, an activity level of the patient, a medication intake information of the patient, or a risk associated with high or low blood glucose levels of the patient.
7. The method of claim 1 wherein the determined correlation between the received mean glucose value information and the received HbA1C level includes a rate of glycation of the patient.
8. The method of claim 1 wherein the predetermined time period includes one of approximately 30 days, approximately 45 days, or approximately 90 days.
9. The method of claim 1 including outputting the determined target HbA1C level.
10. The method of claim 1 including storing one or more of the mean glucose value information, the received HbA1C level, the determined correlation between the received mean glucose value information and the HbA1C level, and the determined target HbA1C level.
11. An apparatus, comprising: a communication interface; one or more processors operatively coupled to the communication interface; and a memory for storing instructions which, when executed by the one or more processors, causes the one or more processors to receive mean glucose value information of a patient based on a predetermined time period, receive a HbA1C level of the patient, determine a correlation between the received mean glucose value information and the HbA1C level, and to determine a target HbA1C level based on the determined correlation.
12. The apparatus of claim 11 wherein the memory for storing instructions which, when executed by the one or more processors, causes the one or more processors to receive monitored glucose level information over the predetermined time period, and to apply a weighting function to the received monitored glucose level information.

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13. The apparatus of claim 12 wherein the weighting function is based on a time of day information associated with the received monitored glucose level information.

14. The apparatus of claim 12 wherein the weighting function is based on a time period associated with the received monitored glucose level information.

15. The apparatus of claim 11 wherein the memory for storing instructions which, when executed by the one or more processors, causes the one or more processors to receive one or more patient specific parameters, and to apply the received one or more patient specific parameters to the determined correlation between the received mean glucose value information and the received HbA1C level.

16. The apparatus of claim 15 wherein the one or more patient specific parameters includes an age of the patient, a history of hypoglycemia, an activity level of the patient, a medication intake information of the patient, or a risk associated with high or low blood glucose levels of the patient.

17. The apparatus of claim 11 wherein the determined correlation between the received mean glucose value information and the received HbA1C level includes a rate of glycation of the patient.

18. The apparatus of claim 11 wherein the predetermined time period includes one of approximately 30 days, approximately 45 days, or approximately 90 days.

19. The apparatus of claim 11 including an output unit operatively coupled to the one or more processors for outputting the determined target HbA1C level.

20. The apparatus of claim 11 wherein the memory for storing instructions which, when executed by the one or more processors, causes the one or more processors to store one or more of the mean glucose value information, the received HbA1C level, the determined correlation between the received mean glucose value information and the HbA1C level, and the determined target HbA1C level.

DISPLAY BIB.EX

-- Original Publication -- (APPLICATION - A1)

AN 2009:31807 USPATFULL
TI HIGHLY WATER REPELLENT FLUOROPOLYMER COATING
IN Jing, Naiyong, Woodbury, MN, UNITED STATES
Chen, Lisa P., Saint Paul, MN, UNITED STATES
PA 3M Innovative Properties Company (U.S. corporation)
PI US-20090029177 A1 20090129
AI 2006US-000091855 A1 20061220 (12)
2006WO-US0048636 20061220
20080724 PCT 371 date
PRAI 2005US-000752527P 20051221 (60)
DT Utility
FS APPLICATION
LREP 3M INNOVATIVE PROPERTIES COMPANY, PO BOX 33427, ST. PAUL, MN,
55133-3427, US
CLMN Number of Claims: 20
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1102
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

In North America

CAS
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CAS Customer Center:
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