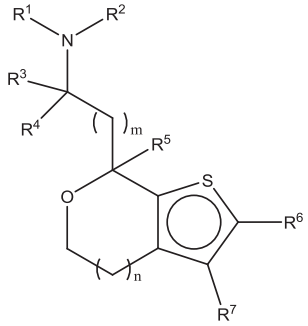
IV. SUMMARY

[0010] In one aspect, the present disclosure refers to a method of preparing a compound of formula (IVa): [Chem. 1]

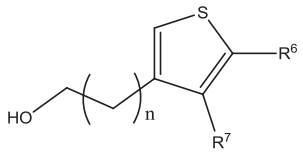


(IVa),

or a pharmaceutically acceptable salt or stereoisomer thereof, the method comprising:

(a) treating a hydroxyalkyl thiophene of formula (i):

[Chem. 2]



(i),

with an amino-aldehyde acetal and an acid to produce a compound of formula (IVa), wherein:

m is 0;

n is 1;

R^1 and R^2 are each independently hydrogen or C_1-C_4 alkyl;

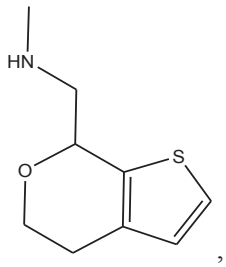
R^3 and R^4 are each independently hydrogen or C_1-C_4 alkyl;

R^5 is hydrogen; and

R^6 and R^7 are each independently hydrogen, halo, or C_1-C_4 alkyl.

[0010a] In another aspect, the present disclosure refers to a method of preparing a compound of formula

[Chem. 8]

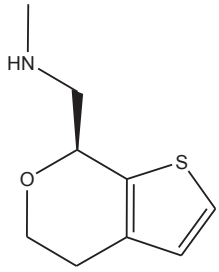


,

or a pharmaceutically acceptable salt or stereoisomer thereof, comprising combining 2-(Thiophen-3-yl)ethanol, *N*-methyl-2,2-dimethoxyethanamine and triflic acid and isolating said compound.

[0010b] In yet another aspect, the present disclosure refers to a method of preparing a compound of formula

[Chem. 12]

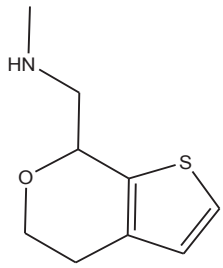


,

or a pharmaceutically acceptable salt or stereoisomer thereof, comprising:

combining 2-(Thiophen-3-yl)ethanol, *N*-methyl-2,2-dimethoxyethanamine, and triflic acid; isolating

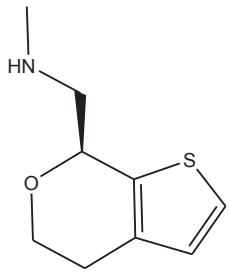
[Chem. 13]



; and

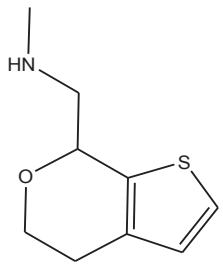
resolving

[Chem. 15]



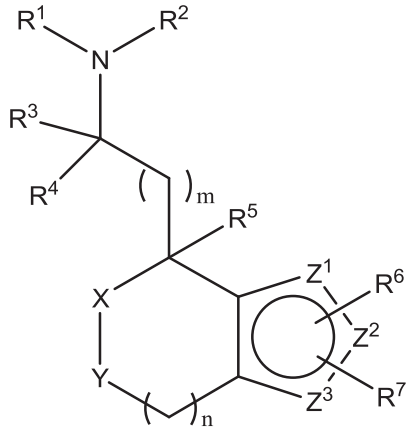
from

[Chem. 14]



.

Provided herein are compounds of formula (I), or pharmaceutically acceptable salts or stereoisomers thereof:



(I),

wherein R^1, R^2, R^3, R^4, R^5, R^6, R^7, X, Y, Z^1, Z^2, Z^3, m, and n are defined herein elsewhere. The compounds are useful for treating various disorders, such as neurological disorders including, but not limited to, psychosis and schizophrenia.

[0011] Also provided herein are compositions and dosage forms, comprising a compound provided herein, and one or more pharmaceutically acceptable excipients. Compositions and dosage forms provided herein may further comprise one or more additional active ingredients.

[0012] Also provided herein are methods for the treatment, prevention, and/or management of various neurological disorders, including those of the central nervous system (CNS) using the compounds and compositions provided herein. In one example, provided herein is a method of treating or managing one or more symptoms of a neurological disorder provided herein. Such neurological disorders include, but are not limited to, schizophrenia, schizophrenia spectrum disorder, acute schizophrenia, chronic schizophrenia, NOS schizophrenia, schizoid personality disorder, schizotypal personality disorder, delusional disorder, psychosis, psychotic disorder, brief psychotic disorder, shared psychotic disorder, psychotic disorder due to a general medical condition, drug-induced psychosis (*e.g.*, cocaine, alcohol, amphetamine), psychoaffective disorder, aggression, delirium, Parkinson's psychosis, excitative psychosis, Tourette's syndrome, organic or NOS psychosis, seizure, agitation, post-traumatic stress disorder, behavior disorder, neurodegenerative disease, Alzheimer's disease, Parkinson's disease, dyskinesias, Huntington's disease, dementia, mood disorder, anxiety, affective disorders (*e.g.*, depression, *e.g.*, major depressive disorder and dysthymia; bipolar disorder, *e.g.*, bipolar depressive disorder; manic disorder; seasonal affective disorder; and attention deficit disorder (ADD) and attention deficit hyperactivity disorder (ADHD)), obsessive-compulsive disorder, vertigo, epilepsy, pain (*e.g.*, neuropathic pain, sensitization accompanying neuropathic pain, and inflammatory pain), fibromyalgia, migraine, cognitive impairment, movement disorder, restless leg syndrome (RLS), multiple sclerosis, sleep disorder, sleep apnea, narcolepsy, excessive daytime sleepiness, jet lag, drowsy side effect of medications, insomnia, substance abuse or dependency (*e.g.*, nicotine,

cocaine), addiction, eating disorder, sexual dysfunction, hypertension, emesis, Lesche-Nyhane disease, Wilson's disease, autism, Huntington's chorea, and premenstrual dysphoria.

[0013] In one example, provided herein is a method of treating, preventing, and/or managing psychosis or schizophrenia. In one example, provided herein is a method of treating or managing one or more symptoms of psychosis or schizophrenia. In one example, provided herein is a method of treating, preventing, and/or managing psychosis or schizophrenia in a subject, such as a mammal, such as, *e.g.*, human, rodent (such as, *e.g.*, mice and rats), cat, dog, non-human primate, among others. In one example, the method comprises contacting a compound provided herein with one or more receptors of the central nervous system. In one example, the method comprises contacting a cell with a compound provided herein. In an exemplary example, the cell is a brain cell, such as, *e.g.*, a neuronal cell or a glial cell.

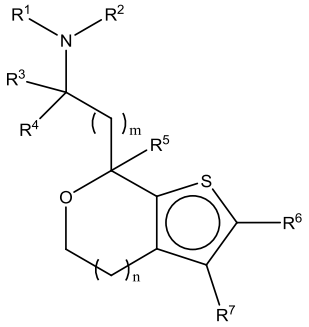
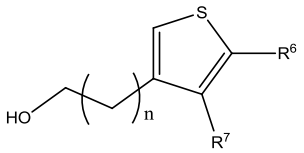
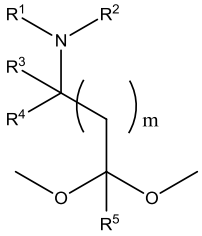
V. DETAILED DESCRIPTION

[0014] Unless defined otherwise, all technical and scientific terms used herein have the same meaning as those commonly understood by one of ordinary skill in the art. In certain embodiments, abbreviations are as defined in *J. Org. Chem*. 2007, *72*, 23A. All publications and patents referred to herein are incorporated by reference herein in their entireties.

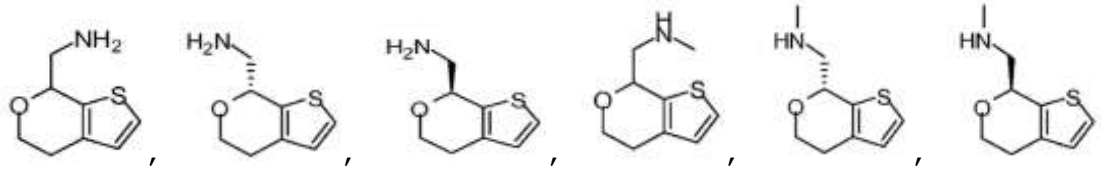
A. Definitions

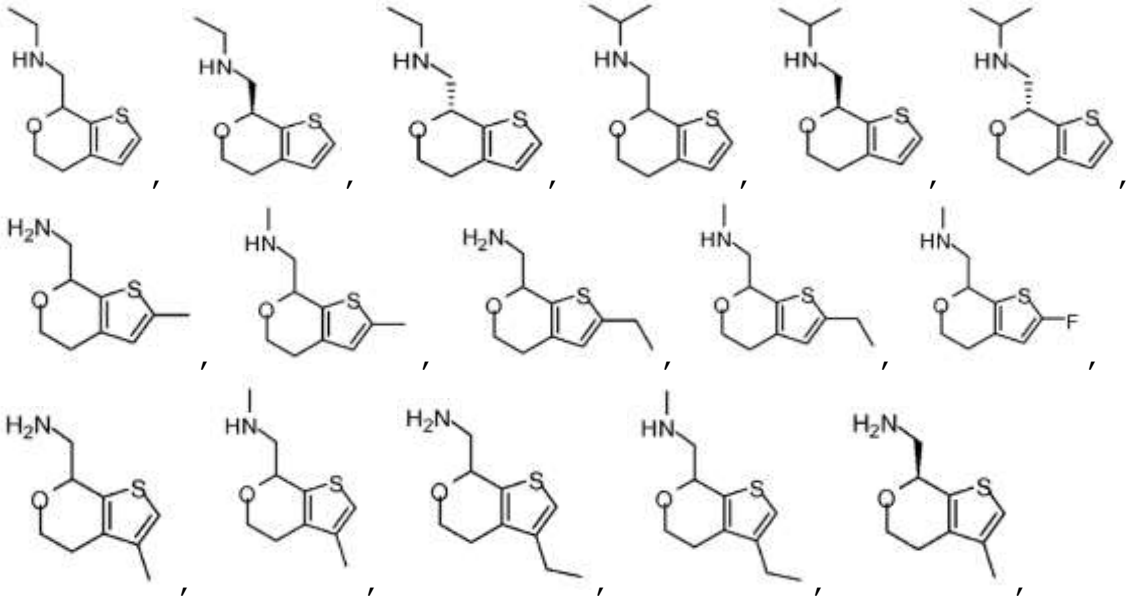
[0015] As used in the specification and the accompanying claims, the indefinite articles "a" and "an" and the definite article "the" include plural as well as singular referents, unless the context clearly dictates otherwise.

[0016] As used herein, and unless otherwise indicated, the term "alkyl" refers to a linear or branched saturated monovalent hydrocarbon radical, wherein the alkyl may optionally be substituted with one or more substituents. In certain embodiments, the alkyl is a linear saturated monovalent hydrocarbon radical that has 1 to 20 (C_{1-20}), 1 to 15 (C_{1-15}), 1 to 12 (C_{1-12}), 1 to 10 (C_{1-10}), or 1 to 6 (C_{1-6}) carbon atoms, or branched saturated monovalent hydrocarbon radical of 3 to 20 (C_{3-20}), 3 to 15 (C_{3-15}), 3 to 12 (C_{3-12}), 3 to 10 (C_{3-10}), or 3 to 6 (C_{3-6}) carbon atoms. As used herein, linear C_{1-6} and branched C_{3-6} alkyl groups are also referred as "lower alkyl." Examples of alkyl groups include, but are not limited to, methyl, ethyl, propyl (including all isomeric forms, *e.g.*, *n*-propyl and isopropyl), butyl (including all isomeric forms, *e.g*, *n*-butyl, isobutyl, and *t*-butyl), pentyl (including all isomeric forms), and hexyl (including all isomeric forms). For example, C_{1-6} alkyl refers to a linear saturated monovalent hydrocarbon radical of 1 to 6 carbon

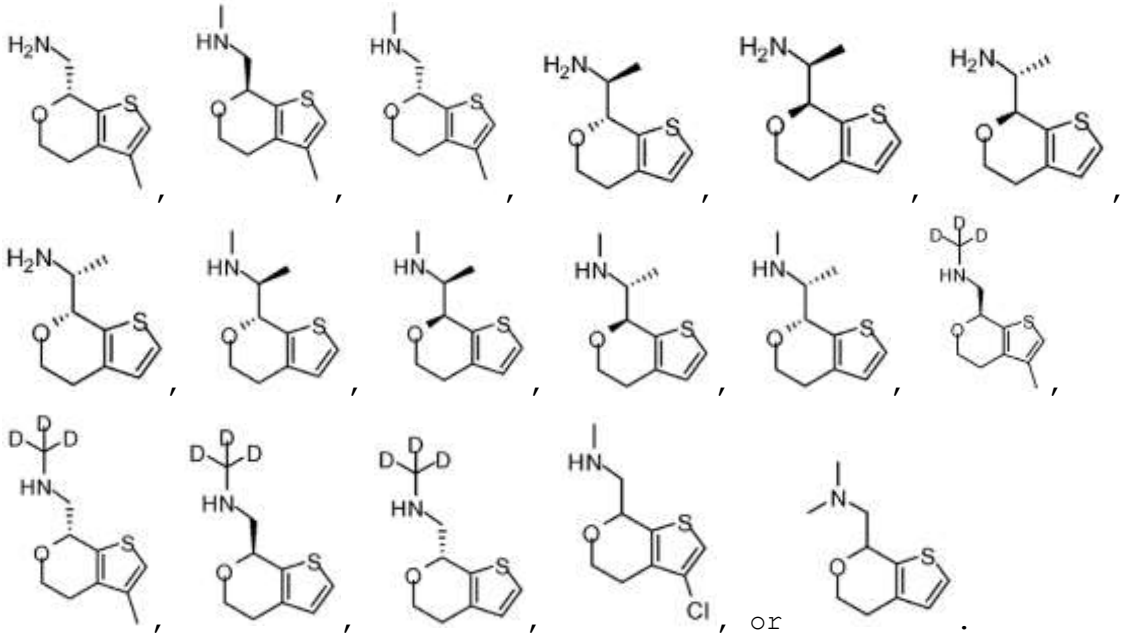
[Claims]
[Claim 1]
A method of preparing a compound of formula (IVa):
[Chem. 1]

(IVa),
or a pharmaceutically acceptable salt or stereoisomer thereof, the method comprising:
(a) treating a hydroxyalkyl thiophene of formula (i):
[Chem. 2]

(i),
with an amino-aldehyde acetal and an acid to produce a compound of formula (IVa), wherein:
m is 0;
n is 1;
R^1 and R^2 are each independently hydrogen or C_1-C_4 alkyl;
R^3 and R^4 are each independently hydrogen or C_1-C_4 alkyl;
R^5 is hydrogen; and
R^6 and R^7 are each independently hydrogen, halo, or C_1-C_4 alkyl.
[Claim 2]
The method of claim 1, wherein the amino-aldehyde acetal is an amino-aldehyde dimethyl acetal of formula (ii):
[Chem. 3]

(ii),
wherein R^1 to R^5 and m are defined as in claim 1.
[Claim 3]
The method of claim 1, wherein the amino-aldehyde acetal comprises an amino-aldehyde diethyl acetal.
[Claim 4]
The method of any one of claims 1-3, wherein the acid comprises trifluoromethyl sulfonic acid.
[Claim 5]
The method of any one of claims 1-4, wherein the treating of the hydroxyalkyl thiophene with an amino-aldehyde acetal and an acid is carried out in an ether solvent.
[Claim 6]
The method of claim 5, wherein the ether solvent is 1,4-dioxane.

[Claim 7]
The method of any one of claims 1-6, further comprising the step of (b) treating the product of step (a) with a base.
[Claim 8]
The method of claim 7, wherein the base comprises potassium hydroxide.
[Claim 9]
The method of claim 8, wherein the base is aqueous potassium hydroxide.
[Claim 10]
The method of any one of claims 1-9, wherein the method produces at least one stereoisomer of the compound of formula (IVa), or a pharmaceutically acceptable salt thereof.
[Claim 11]
The method of claim 10, wherein the method produces a mixture comprising more than one stereoisomer of the compound of formula (IVa), or a pharmaceutically acceptable salt thereof.
[Claim 12]
The method of claim 11, wherein the method further comprises the step of (c) isolating one stereoisomer of the compound of formula (IVa) or a pharmaceutically acceptable salt thereof by resolution of the mixture.
[Claim 13]
The method of claim 12, wherein the resolution comprises at least one of chiral chromatography, recrystallization, diastereomeric salt formation, or derivatization of the more than one stereoisomer of the compound of formula (IVa) into diastereomeric adducts followed by separation.
[Claim 14]
The method of claim 13, wherein the resolution comprises diastereomeric salt formation.
[Claim 15]
The method of any one of claims 1-14, wherein the compound of formula (IVa) or a pharmaceutically acceptable salt thereof comprises a pharmaceutically acceptable salt.
[Claim 16]
The method of claim 15, wherein the compound of formula (IVa) or a pharmaceutically acceptable salt or stereoisomer thereof comprises a hydrochloride salt.
[Claim 17]
The method of any one of claims 1-16, wherein R^3 and R^4 are each hydrogen and R^6 and R^7 are each independently hydrogen or C_1-C_4 alkyl.
[Claim 18]
The method of any one of claims 1-17, wherein the compound of formula (IVa) or a pharmaceutically acceptable salt or stereoisomer thereof is selected from the following compounds or pharmaceutically acceptable salts or stereoisomers thereof:
[Chem. 4]





[Chem. 5]



[Claim 19]

The method of any one of claims 1-17, wherein R^2, R^3, R^4, R^5, R^6, and R^7 are each hydrogen.

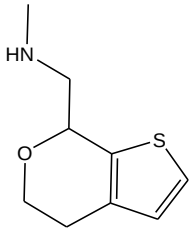
[Claim 20]

The method of claim 19, wherein R^1 is methyl.

[Claim 21]

The method of any one of claims 1-20, wherein the compound of formula (IVa) is

[Chem. 6]

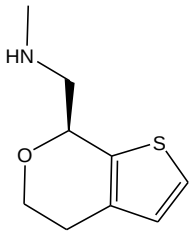


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[Claim 22]

The method of any one of claims 1-21, wherein the compound of formula (IVa) is

[Chem. 7]

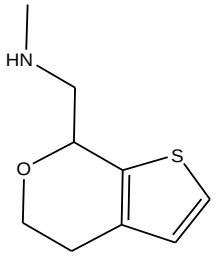


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[Claim 23]

A method of preparing a compound of formula

[Chem. 8]



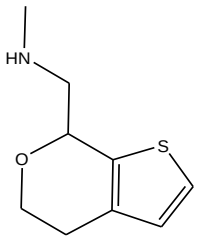
,

or a pharmaceutically acceptable salt or stereoisomer thereof, comprising combining 2-(Thiophen-3-yl)ethanol, *N*-methyl-2,2-dimethoxyethanamine and triflic acid and isolating said compound.

[Claim 24]

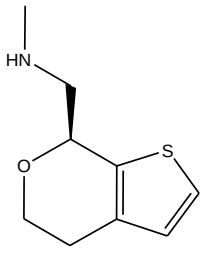
The method of claim 23, further comprising resolving

[Chem. 9]

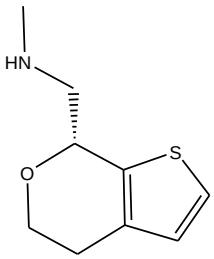


into

[Chem. 10]



and

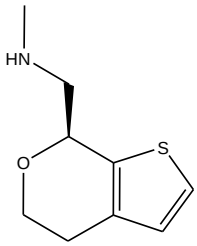


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[Claim 25]

The method of claim 24, further comprising isolating

[Chem. 11]



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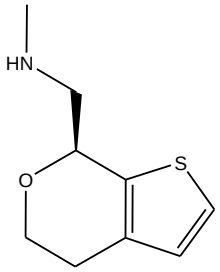
[Claim 26]

The method of claim 25, wherein said resolving is accomplished using chiral chromatography.

[Claim 27]

A method of preparing a compound of formula

[Chem. 12]

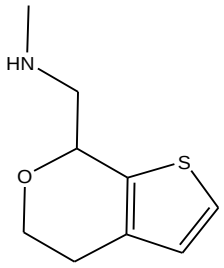


,

or a pharmaceutically acceptable salt or stereoisomer thereof, comprising:

combining 2-(Thiophen-3-yl)ethanol, *N*-methyl-2,2-dimethoxyethanamine, and triflic acid; isolating

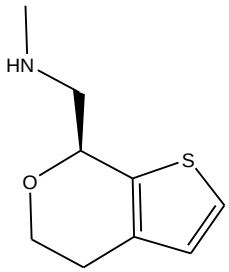
[Chem. 13]



; and

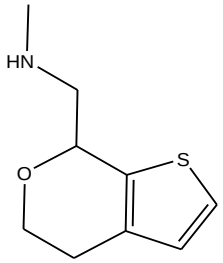
resolving

[Chem. 15]



from

[Chem. 14]



.

[Claim 28]

The method of claim 27, wherein said resolving is accomplished using chiral chromatography.