Example 3
Synthesis of [2-(3-fluoro-5-methanesulfonylphenoxy)ethyl](propyl)amine hemi-L-tartrate:

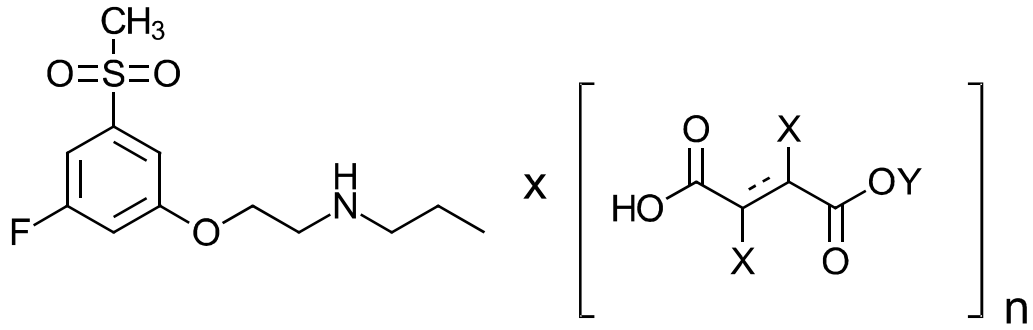
The EtOH-solution of [2-(3-fluoro-5-methanesulfonylphenoxy)ethyl](propyl)amine from Example 2 (estimated amount: 24.5 g, 88.9 mmol) was diluted with EtOH until the concentration was 0.40 M. A solution of L-tartaric acid (6.81 g, 45.4 mmol) in water (20 mL) was added. The formed slurry was heated to reflux temperature and additional amounts of EtOH (50 mL) and water (5 mL) were added. The heating was continued until all solids dissolved. After allowing the mixture to cool to room temperature, the formed slurry was stirred at room temperature overnight, and then at 5 to 10°C for 5 h. The precipitate was isolated by filtration and the filter cake was washed with EtOH (3 x 35 mL). The product was dried by pulling air through it for 20 min. There was obtained 29.9 g (96%) of [2-(3-fluoro-5-methanesulfonylphenoxy)ethyl](propyl)amine hemi-L-tartrate as a solid with an LC-purity of 99.9%. ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.89 (t, 3H), 1.55 (m, 2H), 2.74 (t, 2H), 3.13 (t, 2H), 3.28 (s, 3H), 3.89 (s, 1H), 4.27 (t, 2H), 7.25 (m, 1H), 7.3-7.4 (m, 2H).

X-ray powder diffraction analysis was performed on a sample of the crystals of the hemi-L-tartrate salt of [2-(3-fluoro-5-methanesulfonylphenoxy)ethyl](propyl)amine as prepared above according to standard methods using the instrument, equipment and the conditions described in the general description. The analysis provided the diffractogram depicted in Figure 1. The main characteristic peaks, with positions and relative intensities, have been extracted from the diffractogram in Figure 1 and is given below in Table 1.

It will be understood that the relative intensities of peaks may vary according to the orientation of the sample under test and on the type and setting of the instrument used so that the intensities in the XRD traces included herein are illustrative and not intended to be used for absolute comparison.

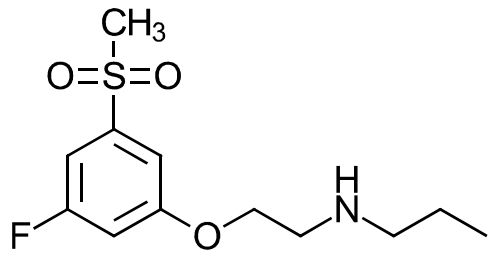
CLAIMS

1. A salt of Formula III:

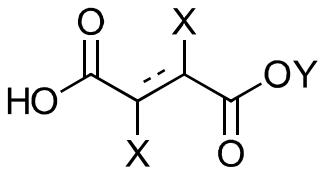


Formula III ,

said salt being a combination of a compound of Formula I and an acid of Formula II:



Formula I



Formula II

in a ratio of 1:n,

wherein

X is H or OH,

Y is H or a cation selected from the group consisting of Li, Na and K,

 is a single bond or a double bond, and

n is 0.5 or 1.

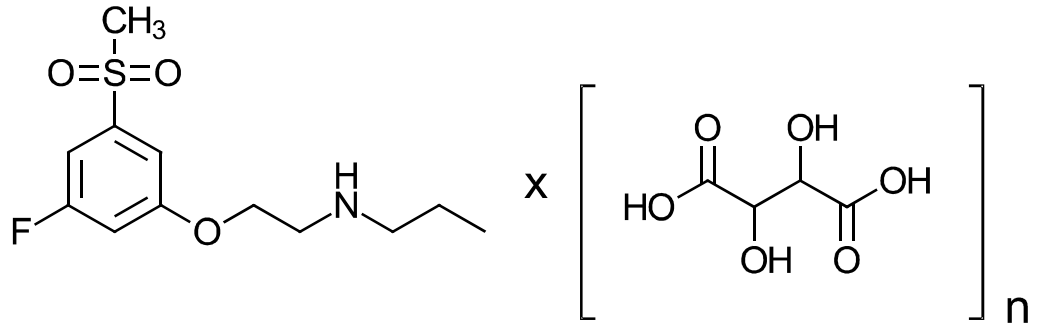
2. The salt of Formula III according to claim 1, wherein

X is OH,

Y is H, and

 is a single bond,

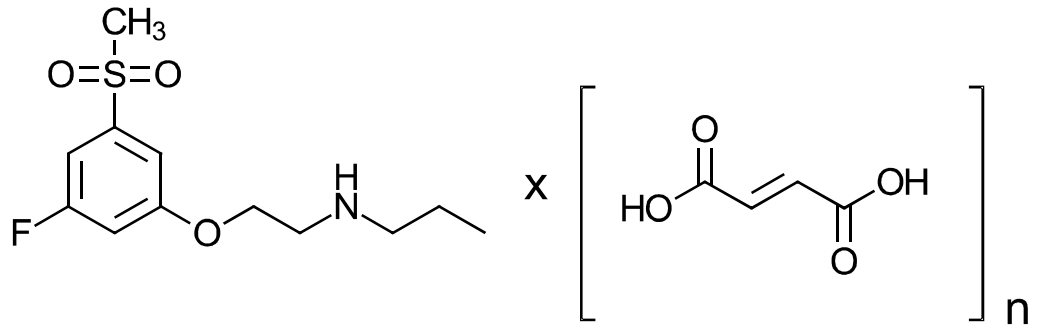
thereby providing a salt of Formula IV being a combination of a compound of Formula I and tartaric acid:



Formula IV .

3. The salt of Formula III according to claim 1 or 2, wherein the tartaric acid is L-(+)-tartaric acid and/or D-(-)-tartaric acid.

4. The salt of Formula III according to claim 1, wherein
X is H,
Y is H, and
--- is a double bond,
thereby providing a salt of Formula V being a combination of a compound of Formula V and fumaric acid:



Formula V .

5. The salt of Formula III according to any one of the preceding claims, wherein n is 0.5.

6. The salt of Formula III according to any one of claims 1-4, wherein
n is 1.

7. The salt of Formula III according to any one of the preceding claims, wherein one or more of the hydrogen atoms of the compound of Formula I is/are replaced with deuterium.

8. The salt of Formula III according to any one of the preceding claims, characterized by being crystalline.

9. The salt of Formula III according to
any one of claims 1-3, 5 or 7, characterized by an XRP diffractogram as shown in Figure 1, or
any one of claims 1, 4, 5 or 7, characterized by an XRP diffractogram as shown in Figure 2.

10. The salt of Formula III according to any one of claims 1-3, 5 or 7, characterized by an XRP diffractogram comprising a peak at 13.0 2θ and one or more peaks selected from the following: 12.4, 14.4, 21.1, 24.4 2θ.

11. The salt of Formula III according to any one of claims 1, 4, 5 or 7, characterized by an XRP diffractogram comprising a peak at 15.3 2θ and one or more peaks selected from the following:7.6, 13.0, 21.8, 23.0 2θ.

12. A pharmaceutical composition comprising a salt of Formula III according to any one of the preceding claims in admixture with a pharmaceutically acceptable excipient, carrier and/or diluent.

13. The pharmaceutical composition according to claim 12 comprising the compound of Formula I in an amount from 2.0 mg up to 10.0 mg.

14. The pharmaceutical composition according to claim 12 or 13, wherein the amount of the compound of Formula I is 2.5 mg, 5.0 mg or 7.5 mg.

15. The pharmaceutical composition according to claim 13 or 14, wherein the pharmaceutical composition is provided in a single dosage form.

16. The salt of Formula III according to any one of claims 1-11 or the pharmaceutical composition according to any one of claims 12-15 for use as a medicament.

17. The salt according to any one of claims 1-11 or the pharmaceutical composition according to any one of claims 12-15 for use in the treatment and/or prevention of a disease, disorder and/or condition selected from the group consisting of psychosis, schizophrenia, schizophreniform disorder, bipolar disorder, psychotic disorder, drug induced psychotic disorder, mood disorder, anxiety disorder, depression, obsessive-compulsive disease, dementia, age-related cognitive impairment, Autism spectrum disorders, ADHD, cerebral Palsy, Gilles de la Tourette's syndrome, brain injury, sleep disorder, sexual disorder, eating disorder, obesita, headache, pains in conditions characterized by increased muscular tone, Parkinson's disease, parkinsonian syndrome, dyskinesia, L-DOPA induced dyskinesias, Tardive dyskinesias, dystonia, tics and tremor dementia, Huntington's disease, movement disorder induced by drugs, restless legs, narcolepsy, Alzheimer’s disease and disorder(s) related to Alzheimer's disease.

18. The salt or the pharmaceutical composition for use according to claim 17, wherein the disease, disorder and or condition is schizophrenia, L-DOPA induced dyskinesias and/or Huntington's disease.

19. The salt or the pharmaceutical composition for use according to claim 17 or 18, wherein the disease, disorder and/or condition is L-DOPA induced dyskinesias.

20. The salt or the pharmaceutical composition for use according to any one of claims 17-19, wherein the salt or the pharmaceutical composition is administered to a patient in a dosage from 2.0 mg up to 10.0 mg such as 2.5 mg, 5.0 mg or 7.5 mg.

21. The salt or the pharmaceutical composition for use according to claim 20, wherein the disease, disorder and/or condition, or
symptoms associated with said disease, disorder and/or condition
is/are alleviated and/or reduced to a greater extent as compared to administration of the salt or the pharmaceutical composition to a patient in a dosage equal to or greater than 10 mg

22. The salt or the pharmaceutical composition for use according to claim 21, wherein the administration of the dosage equal to or greater than 10 mg and the administration of the dosage from 2.0 up to 10.0 mg take place an equal number of times such as an equal number of times daily.

23. Use of a salt according to any one of claims 1-11 or a pharmaceutical composition according to any one of claims 12-15 for the manufacture of a medicament for the treatment and/or prevention of a disease, disorder and/or condition selected from the group consisting of psychosis, schizophrenia, schizophreniform disorder, bipolar disorder, psychotic disorder, drug induced psychotic disorder, mood disorder, anxiety disorder, depression, obsessive-compulsive disease, dementia, age-related cognitive impairment, Autism spectrum disorders, ADHD, cerebral Palsy, Gilles de la Tourette's syndrome, brain injury, sleep disorder, sexual disorder, eating disorder, obesita, headache, pains in conditions characterized by increased muscular tone, Parkinson's disease, parkinsonian syndrome, dyskinesia, L-DOPA induced dyskinesias, Tardive dyskinesias, dystonia, tics and tremor dementia, Huntington's disease, movement disorder induced by drugs, restless legs, narcolepsy, Alzheimer’s disease and disorder(s) related to Alzheimer's disease.

24. The use according to claim 23, wherein the disease, disorder and or condition is schizophrenia, L-DOPA induced dyskinesias and/or Huntington's disease.

25. The use according to claim 23 or 24, wherein the disease, disorder and/or condition is L-DOPA induced dyskinesias.

26. The use according to any one of claims 23-25, wherein the salt or the pharmaceutical composition is administered to a patient in a dosage from 2.0 mg up to 10.0 mg such as 2.5 mg, 5.0 mg or 7.5 mg.

27. The use according to claim 26, wherein
the disease, disorder and/or condition, or
symptoms associated with said disease, disorder and/or condition
is/are alleviated and/or reduced to a greater extent as compared to administration of the salt or the pharmaceutical composition to a patient in a dosage equal to or

greater than 10 mg.

28. The use according to claim 27, wherein the administration of the dosage equal to or greater than 10 mg and the administration of the dosage from 2.0 mg up to 10.0 mg take place an equal number of times such as an equal number of times daily.

29. A method for preparing a salt of Formula III according to any one of claims 1-11, said method comprising the steps of:
- providing a compound of Formula I and an acid of Formula II in a ratio of 1:0.5 or 1:1,
- combining said compound of Formula I with said acid of Formula II in a solvent to form a solution, and
- allowing said solution to stand until a precipitate forms, and
- isolating said precipitate by filtration thereby providing the salt of Formula III.

30. The method according to claim 29, wherein said solvent is a mixture of solvents.