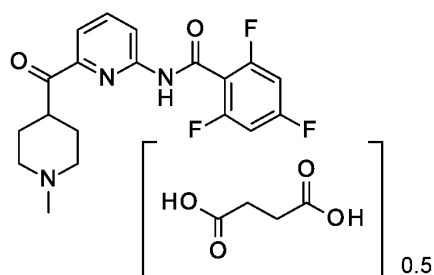


WE CLAIM:

1. A process for preparing a compound of the formula:



5 comprising the steps of:

- i.) Treatment of piperidine-4-carboxylic acid under reductive amination conditions comprising formaldehyde and formic acid in water with subsequent treatment with aqueous HCl followed by water distillation and acetonitrile addition, with repeated dilution/distillation until the water content is not more than 0.2% by Karl-Fischer analysis, to obtain solid 1-methylpiperidine-4-carboxylic acid hydrochloride;
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- ii.) Treatment of 1-methylpiperidine-4-carboxylic acid hydrochloride with a chlorinating agent such as thionyl chloride in chlorobenzene to obtain 1-methylpiperidine-4-carboxylic acid chloride;
- 15
- iii.) Treatment of 1-methylpiperidine-4-carboxylic acid chloride with N,N-diethylamine in chlorobenzene containing triethylamine with subsequent base wash and subsequent treatment with aqueous HCl in isopropanol to obtain solid N,N-diethyl-1-methyl-piperidine-4-carboxamide hydrate hydrochloride;
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- iv.) Treatment of N,N-diethyl-1-methyl-piperidine-4-carboxamide hydrate hydrochloride with a mineral base such as aqueous NaOH in a non-polar

solvent such as methyl-tert-butyl ether with subsequent water wash, phase separation, and distillation of the organic solvent until the water content is not more than 0.1 weight t% by Karl Fischer analysis to obtain N,N-diethyl-1-methyl-piperidine-4-carboxamide;

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v.) Subsequent treatment of N,N-diethyl-1-methyl-piperidine-4-carboxamide with (6-bromo-2-pyridyl)lithium in a non-polar organic solvent such as methyl-tert-butyl ether with subsequent extraction of the resulting mixture with water and a suitable organic solvent such as *n*-butanol, phase separation, and repeated distillation of the organic solvent until the water content is not more than 0.2 weight % by Karl-Fischer analysis, to obtain (6-bromo-2-pyridyl)-(1-methyl-4-piperidyl)methanone;

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vi.) Treatment of (6-bromo-2-pyridyl)-(1-methyl-4-piperidyl)methanone with aqueous HBr and subsequent extraction with *n*-butanol followed by repeated distillation of the organic solvent until the water content is not more than 0.3% by Karl-Fischer analysis, to obtain solid (6-bromo-2-pyridyl)-(1-methyl-4-piperidyl)methanone hydrobromide;

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vii.) Treatment of (6-bromo-2-pyridyl-1-methyl-4-piperidyl)methanone hydrobromide with a solution of NH₃ in ethylene glycol in the presence of Cu₂O catalyst at about 80 °C for about 2 hr, with subsequent washes with water, saturated aqueous NaCl, and 20% aqueous NaOH and subsequent extraction with a non-polar aprotic solvent such as methyl-tert-butyl ether, phase separation, and treatment of the organic phase with 5 weight % carbon;

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viii.) Filtration of the above mixture, dilution with a suitable polar alcoholic solvent such as isopropanol, and repeated distillation of the organic solvent until the water content is not more than 0.2% by Karl-Fischer analysis,

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with subsequent treatment of the resulting residue with isopropanol, water, and 20 weight % HCl, wherein the water concentration of the resulting slurry is at least 2%, filtration of the resulting slurry, and drying under vacuum at 40 °C for 16-24 hr to obtain solid (6-amino-2-pyridyl)-(1-methyl-4-piperidyl)methanone dihydrate dihydrochloride;

ix.) Treatment of (6-amino-2-pyridyl)-(1-methyl-4-piperidyl)methanone dihydrate dihydrochloride in chlorobenzene with 6 weight/weight % NaOH in water at about 54 °C for about 30 min, with subsequent phase separation and vacuum distillation of the aqueous solution to obtain (6-amino-2-pyridyl)-(1-methyl-4-piperidyl)methanone;

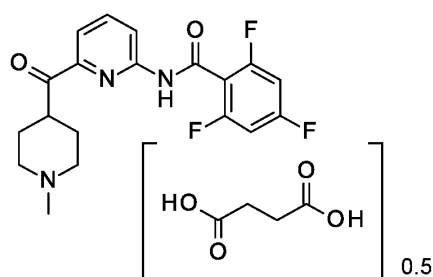
x.) Subsequent treatment of (6-amino-2-pyridyl)-(1-methyl-4-piperidyl)methanone with 2,4,6-trifluorobenzoic acid chloride in chlorobenzene at about 100 °C for about 4 hr, with subsequent cooling, charging with acetonitrile and heating the resulting slurry to 80 °C for about 1 hr, and subsequent collection of the resulting solid by filtration, to obtain solid 2,4,6-trifluoro-N-[6-(1-methylpiperidine-4-carbonyl)-2-pyridyl]benzamide hydrochloride;

xi.) Treatment of 2,4,6-trifluoro-N-[6-(1-methylpiperidine-4-carbonyl)-2-pyridyl]benzamide hydrochloride with saturated aqueous Na₂CO₃ in methyl-tert-butyl ether;

xii.) Treatment of the mixture of step xi above with SiO₂ with subsequent filtration, treatment with carbon, filtration, and evaporation, dilution with ethanol, and distillation until the water content is not more than 1% by Karl-Fischer analysis, to obtain 2,4,6-trifluoro-N-[6-(1-methylpiperidine-4-carbonyl)-2-pyridyl]benzamide;

- xiii.) Treatment of 2,4,6-trifluoro-N-[6-(1-methylpiperidine-4-carbonyl)-2-pyridyl]benzamide in ethanol with a solution of 0.5 equivalents succinic acid in ethanol at about 55 °C for not less than 3 hr at RT, and subsequent collection of the solid by filtration, to obtain solid 2,4,6-trifluoro-N-[6-(1-methylpiperidine-4-carbonyl)-2-pyridyl]benzamide hemisuccinate.

2. A process for preparing a compound of the formula:



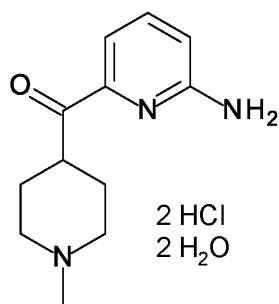
comprising the steps of:

- i.) Treatment of piperidine-4-carboxylic acid under reductive amination conditions comprising formaldehyde and formic acid in water with subsequent treatment with aqueous HCl followed by water distillation and acetonitrile addition, with repeated dilution/distillation until the water content is not more than 0.2% by Karl-Fischer analysis, to obtain solid 1-methylpiperidine-4-carboxylic acid hydrochloride;
- ii.) Treatment of 1-methylpiperidine-4-carboxylic acid hydrochloride with a chlorinating agent such as thionyl chloride in chlorobenzene obtain 1-methylpiperidine-4-carboxylic acid chloride;
- iii.) Treatment of 1-methylpiperidine-4-carboxylic acid chloride with N,N-diethylamine in chlorobenzene containing triethylamine with subsequent base wash and subsequent treatment with aqueous HCl in isopropanol to

obtain solid N,N-diethyl-1-methyl-piperidine-4-carboxamide hydrate hydrochloride;

- iv.) Treatment of N,N-diethyl-1-methyl-piperidine-4-carboxamide hydrate hydrochloride with a mineral base such as aqueous NaOH in a non-polar solvent such as methyl-tert-butyl ether with subsequent water wash, phase separation, and distillation of the organic solvent until the water content is not more than 0.1 weight % by Karl Fischer analysis to obtain N,N-diethyl-1-methyl-piperidine-4-carboxamide;
- v.) Subsequent treatment of N,N-diethyl-1-methyl-piperidine-4-carboxamide with (6-bromo-2-pyridyl)lithium in a non-polar organic solvent such as methyl-tert-butyl ether with subsequent extraction of the resulting mixture with water and a suitable organic solvent such as *n*-butanol, phase separation, and repeated distillation of the organic solvent until the water content is not more than 0.2 weight % by Karl-Fischer analysis, to obtain (6-bromo-2-pyridyl)-(1-methyl-4-piperidyl)methanone;
- vi.) Treatment of (6-bromo-2-pyridyl)-(1-methyl-4-piperidyl)methanone with aqueous HBr and subsequent extraction with *n*-butanol followed by repeated distillation of the organic solvent until the water content is not more than 0.3% by Karl-Fischer analysis, to obtain solid (6-bromo-2-pyridyl)-(1-methyl-4-piperidyl)methanone hydrobromide;
- vii.) Treatment of (6-bromo-2-pyridyl-1-methyl-4-piperidyl)methanone hydrobromide in a biphasic mixture of water and toluene with solid KOH for about 3 hr with subsequent separation of the organic layer and evaporation of the solvent to obtain of (6-bromo-2-pyridyl-1-methyl-4-piperidyl)methanone;

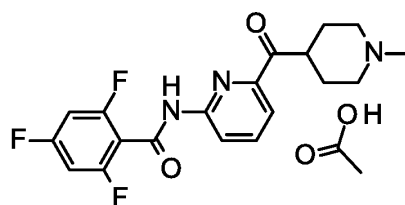
- viii.) Treatment of (6-bromo-2-pyridyl-1-methyl-4-piperidyl)methanone with 2,4,6-trifluorobenzamide in toluene containing K_2CO_3 , water, $Pd(OAc)_2$, and Xantphos at about 70 °C for about 12 hr, until the (6-bromo-2-pyridyl)-(1-methyl-4-piperidyl)methanone content is not more than 0.1% by HPLC, with subsequent dilution of the reaction mixture with water and EtOAc, subsequent treatment with thiourea-modified silica gel at 60 °C for about 8 hr, with subsequent filtration to obtain a solution of 2,4,6-trifluoro-N-[6-(1-methylpiperidine-4-carbonyl)-2-pyridyl]benzamide;
- ix.) Treatment of a solution of 2,4,6-trifluoro-N-[6-(1-methylpiperidine-4-carbonyl)-2-pyridyl]benzamide in EtOAc with a solution of about 0.5 equivalents of succinic acid dissolved in EtOH at 55 °C for about 3 hr, with subsequent cooling to RT over about 10 hr, and collection of the resulting solids by filtration, to obtain solid 2,4,6-trifluoro-N-[6-(1-methylpiperidine-4-carbonyl)-2-pyridyl]benzamide hemisuccinate.
3. A process of Claim 1 or 2 wherein the reactions are performed using batch processing methodology.
4. A process of Claim 3 wherein the batch produced is at process scale.
5. A process of Claim 4 wherein the batch produced is at least 1 kilogram.
6. A process of Claim 4 wherein the batch produced is at least 10 kilograms.
7. A process of Claim 4 wherein the batch produced is at least 100 kilograms.
8. A tablet produced by the process of any one of claims 1 - 7 wherein the tablet comprises 50 mg of 2,4,6-trifluoro-N-[6-(1-methylpiperidine-4-carbonyl)-2-pyridyl]benzamide hemisuccinate.
9. A tablet produced by the process of any one of claims 1 - 7 wherein the tablet comprises 100 mg of 2,4,6-trifluoro-N-[6-(1-methylpiperidine-4-carbonyl)-2-pyridyl]benzamide hemisuccinate.
10. A compound of the formula:



11. The compound of Claim 10 which is crystalline.

12. The compound according to claim 11 characterized by an X-ray powder
5 diffraction pattern using CuK α radiation having an intense peak at diffraction
angle 2-theta of 8.3° in combination with one or more of the peaks selected from
the group consisting of 16.6°, 23.5°, and 33.7° ($\pm$ 0.2° respectively).

13. A compound of the formula:



14. A crystalline form of the compound according to claim 13.

15. The compound according to claim 14 characterized by an X-ray powder
15 diffraction pattern using CuK α radiation having an intense peak at diffraction
angle 2-theta of 26.2° in combination with one or more of the peaks selected from
the group consisting of 20.4°, 14.0°, and 17.9° ($\pm$ 0.2° respectively).

16. A pharmaceutical composition comprising a compound according to any one of claims 13 to 15 with one or more pharmaceutically acceptable carriers, diluents, or excipients.

5 17. The pharmaceutical composition of claim 16 further comprising acetic acid.

18. A method of treating migraine in a patient comprising administering to a patient in need of such treatment an effective amount of a compound according to any one of claims 13 to 15.

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19. A compound according to any one of claims 13 to 15 for use in therapy.

20. A compound according to any one of claims 13 to 15 for use in the treatment of migraine.

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