What is claimed is:

1. A method of preparing the zwitterion of 5-({[2-amino-3-(4-carbamoyl-2,6-dimethyl-phenyl)-propionyl]-[1-(4-phenyl-1h-imidazol-2-yl)-ethyl]-amino}-methyl)-2-methoxy-benzoic acid comprising the steps of:
combining a strong ionizable acid with 5-({[2-tert-butoxycarbonylamino-3-(4-carbamoyl-2,6-dimethyl-phenyl)-propionyl]-[1-(4-phenyl-1H-imidazol-2-yl)-ethyl]-amino}-methyl)-2-methoxy-benzoic acid to prepare a salt of 5-({[2-amino-3-(4-carbamoyl-2,6-dimethyl-phenyl)-propionyl]-[1-(4-phenyl-1h-imidazol-2-yl)-ethyl]-amino}-methyl)-2-methoxy-benzoic acid; and
washing said salt of 5-({[2-amino-3-(4-carbamoyl-2,6-dimethyl-phenyl)-propionyl]-[1-(4-phenyl-1h-imidazol-2-yl)-ethyl]-amino}-methyl)-2-methoxy-benzoic acid an inorganic base to obtain the zwitterion of 5-({[2-amino-3-(4-carbamoyl-2,6-dimethyl-phenyl)-propionyl]-[1-(4-phenyl-1h-imidazol-2-yl)-ethyl]-amino}-methyl)-2-methoxy-benzoic acid.

2. The method of claim 1, further comprising the step of washing said zwitterion of 5-({[2-amino-3-(4-carbamoyl-2,6-dimethyl-phenyl)-propionyl]-[1-(4-phenyl-1h-imidazol-2-yl)-ethyl]-amino}-methyl)-2-methoxy-benzoic acid with water.

3. The method of claim 1, wherein said inorganic base is sodium hydroxide.

4. The method of claim 1, wherein said ionizable acid is hydrochloric acid and wherein said salt is the hydrochloride salt of 5-({[2-amino-3-(4-carbamoyl-2,6-dimethyl-phenyl)-propionyl]-[1-(4-phenyl-1h-imidazol-2-yl)-ethyl]-amino}-methyl)-2-methoxy-benzoic acid.

5. Crystalline zwitterion of 5-({[2-amino-3-(4-carbamoyl-2,6-dimethyl-phenyl)-propionyl]-[1-(4-phenyl-1h-imidazol-2-yl)-ethyl]-amino}-methyl)-2-methoxy-benzoic acid prepared by the process of claim 1.

6. A method of preparing the zwitterion of 5-({[2-amino-3-(4-carbamoyl-2,6-dimethyl-phenyl)-propionyl]-[1-(4-phenyl-1h-imidazol-2-yl)-ethyl]-amino}-methyl)-2-methoxy-benzoic acid comprising the steps of:
combining hydrochoric acid with 5-({[2-tert-butoxycarbonylamino-3-(4-carbamoyl-2,6-dimethyl-phenyl)-propionyl]-[1-(4-phenyl-1H-imidazol-2-yl)-ethyl]-amino}-methyl)-2-methoxy-benzoic acid to prepare the hydrochloride salt of 5-({[2-amino-3-(4-carbamoyl-2,6-dimethyl-phenyl)-propionyl]-[1-(4-phenyl-1h-imidazol-2-yl)-ethyl]-amino}-methyl)-2-methoxy-benzoic acid;
washing said salt of 5-({[2-amino-3-(4-carbamoyl-2,6-dimethyl-phenyl)-propionyl]-[1-(4-phenyl-1h-imidazol-2-yl)-ethyl]-amino}-methyl)-2-methoxy-benzoic acid with sodium hydroxide to obtain the zwitterion of 5-({[2-amino-3-(4-carbamoyl-2,6-dimethyl-phenyl)-propionyl]-[1-(4-phenyl-1h-imidazol-2-yl)-ethyl]-amino}-methyl)-2-methoxy-benzoic acid; and
washing said zwitterion of 5-({[2-amino-3-(4-carbamoyl-2,6-dimethyl-phenyl)-propionyl]-[1-(4-phenyl-1h-imidazol-2-yl)-ethyl]-amino}-methyl)-2-methoxy-benzoic acid with water.

7. Crystalline zwitterion of 5-({[2-amino-3-(4-carbamoyl-2,6-dimethyl-phenyl)-propionyl]-[1-(4-phenyl-1h-imidazol-2-yl)-ethyl]-amino}-methyl)-2-methoxy-benzoic acid prepared by the process of claim 1.

8. A Form α crystal of 5-({[2-amino-3-(4-carbamoyl-2,6-dimethyl-phenyl)-propionyl]-[1-(4-phenyl-1h-imidazol-2-yl)-ethyl]-amino}-methyl)-2-methoxy-benzoic acid

9. The α crystal of claim 8, wherein said crystal is characterized by a powder X-ray diffraction pattern having powder X-ray diffraction peaks at about 14.0, 14.3, and 14.7 degrees 2-theta.

10. The α crystal of claim 8, wherein said crystal is characterized by a powder X-ray diffraction pattern having powder X-ray diffraction peaks at about 10.2, 11.3, 14.0, 14.3, and 14.7 degrees 2-theta.

11. The α crystal of claim 8, wherein said crystal is characterized by a powder X-ray diffraction pattern having powder X-ray diffraction peaks at about 10.2, 11.3, 11.8, 14.0, 14.3, 14.7, 16.1, and 18.3 degrees 2-theta.

12. The α crystal of claim 8, wherein said crystal is characterized by a powder X-ray diffraction pattern having powder X-ray diffraction peaks substantially as shown in Table 1.

13. The α crystal of claim 8, wherein said crystal is characterized by a powder X-ray diffraction pattern having powder X-ray diffraction peaks substantially similar to the powder X-ray diffraction peaks of Figure 1.

14. The α crystal of claim 8, wherein said crystal is characterized by a thermal gravimetric analysis (TGA) substantially similar to the TGA in Figure 2.

15. The α crystal of claim 8, wherein said crystal is characterized by a differential scanning calorimetry (DSC) measurement substantially similar to the DSC in Figure 3.

16. A method of treating a mammal suffering from irritable bowel syndrome, pain or another opioid receptor disorder comprising administering to said mammal an effective amount of a

Form α crystal of 5-({[2-amino-3-(4-carbamoyl-2,6-dimethyl-phenyl)-propionyl]-[1-(4-phenyl-1h-imidazol-2-yl)-ethyl]-amino}-methyl)-2-methoxy-benzoic acid.

17. A Form β crystal of 5-({[2-amino-3-(4-carbamoyl-2,6-dimethyl-phenyl)-propionyl]-[1-(4-phenyl-1h-imidazol-2-yl)-ethyl]-amino}-methyl)-2-methoxy-benzoic acid.

18. The β crystal of claim 17, wherein said crystal is characterized by a powder X-ray diffraction pattern having powder X-ray diffraction peaks at about 11.0, 12.4, and 15.2 degrees 2-theta.

19. The β crystal of claim 17, wherein said crystal is characterized by a powder X-ray diffraction pattern having powder X-ray diffraction peaks at about 11.0, 12.4, 14.9, 15.2, and 22.1 degrees 2-theta.

20. The β crystal of claim 17, wherein said crystal is characterized by a powder X-ray diffraction pattern having powder X-ray diffraction peaks at about 11.0, 12.4, 14.9, 15.2, 22.1, 25.6, 27.4, and 30.4 degrees 2-theta.

21. The β crystal of claim 17, wherein said crystal is characterized by a powder X-ray diffraction pattern having powder X-ray diffraction peaks substantially as shown in Table 2.

22. The β crystal of claim 17, wherein said crystal is characterized by a powder X-ray diffraction pattern having powder X-ray diffraction peaks substantially similar to the powder X-ray diffraction peaks of Figure 1.

23. The β crystal of claim 17, wherein said crystal is characterized by a thermal gravimetric analysis (TGA) substantially similar to the TGA in Figure 4.

24. The β crystal of claim 17, wherein said crystal is characterized by a differential scanning calorimetry (DSC) measurement substantially similar to the DSC in Figure 5.

25. A method of treating a mammal suffering from irritable bowel syndrome, pain or another opioid receptor disorder comprising administering to said mammal an effective amount of a Form β crystal of 5-({[2-amino-3-(4-carbamoyl-2,6-dimethyl-phenyl)-propionyl]-[1-(4-phenyl-1h-imidazol-2-yl)-ethyl]-amino}-methyl)-2-methoxy-benzoic acid.

CLAIMS

1. A method of preparing a crystalline zwitterion of 5-({[2-amino-3-(4-carbamoyl-2,6-dimethyl-phenyl)-propionyl]-[1-(4-phenyl-1H-imidazol-2-yl)-ethyl]-amino}-methyl)-2-methoxy-benzoic acid comprising the steps of:

combining a strong ionizable acid with 5-({[2-tert-butoxycarbonylamino-3-(4-carbamoyl-2,6-dimethyl-phenyl)-propionyl]-[1-(4-phenyl-1H-imidazol-2-yl)-ethyl]-amino}-methyl)-2-methoxy-benzoic acid to prepare a salt of 5-({[2-amino-3-(4-carbamoyl-2,6-dimethyl-phenyl)-propionyl]-[1-(4-phenyl-1H-imidazol-2-yl)-ethyl]-amino}-methyl)-2-methoxy-benzoic acid; and

washing said salt of 5-({[2-amino-3-(4-carbamoyl-2,6-dimethyl-phenyl)-propionyl]-[1-(4-phenyl-1H-imidazol-2-yl)-ethyl]-amino}-methyl)-2-methoxy-benzoic acid with an inorganic base to obtain a zwitterion of 5-({[2-amino-3-(4-carbamoyl-2,6-dimethyl-phenyl)-propionyl]-[1-(4-phenyl-1H-imidazol-2-yl)-ethyl]-amino}-methyl)-2-methoxy-benzoic acid; and crystallizing the zwitterion.

2. The method of claim 1, further comprising the step of washing said zwitterion of 5-({[2-amino-3-(4-carbamoyl-2,6-dimethyl-phenyl)-propionyl]-[1-(4-phenyl-1H-imidazol-2-yl)-ethyl]-amino}-methyl)-2-methoxy-benzoic acid with water.

3. The method of claim 1 or claim 2, wherein said inorganic base is sodium hydroxide.

4. The method of any one of the preceding claims, wherein said ionizable acid is hydrochloric acid and wherein said salt is the hydrochloride salt of 5-({[2-amino-3-(4-carbamoyl-2,6-dimethyl-phenyl)-propionyl]-[1-(4-phenyl-1H-imidazol-2-yl)-ethyl]-amino}-methyl)-2-methoxy-benzoic acid.

5. Crystalline zwitterion of 5-({[2-amino-3-(4-carbamoyl-2,6-dimethyl-phenyl)-propionyl]-[1-(4-phenyl-1H-imidazol-2-yl)-ethyl]-amino}-methyl)-2-methoxy-benzoic acid prepared by the method of claim 1.

6. A method of preparing a crystalline zwitterion of 5-({[2-amino-3-(4-carbamoyl-2,6-dimethyl-phenyl)-propionyl]-[1-(4-phenyl-1H-imidazol-2-yl)-ethyl]-amino}-methyl)-2-methoxy-benzoic acid comprising the steps of:

combining hydrochloric acid with 5-({[2-tert-butoxycarbonylamino-3-(4-carbamoyl-2,6-dimethyl-phenyl)-propionyl]-[1-(4-phenyl-1H-imidazol-2-yl)-ethyl]-amino}-methyl)-2-methoxy-benzoic acid to prepare the hydrochloride salt of 5-({[2-amino-3-(4-carbamoyl-2,6-dimethyl-phenyl)-propionyl]-[1-(4-phenyl-1H-imidazol-2-yl)-ethyl]-amino}-methyl)-2-methoxy-benzoic acid;

washing said salt of 5-({[2-amino-3-(4-carbamoyl-2,6-dimethyl-phenyl)-propionyl]-[1-(4-phenyl-1H-imidazol-2-yl)-ethyl]-amino}-methyl)-2-methoxy-benzoic acid with sodium hydroxide to obtain the zwitterion of 5-({[2-amino-3-(4-carbamoyl-2,6-dimethyl-phenyl)-propionyl]-[1-(4-phenyl-1H-imidazol-2-yl)-ethyl]-amino}-methyl)-2-methoxy-benzoic acid;

washing said zwitterion of 5-({[2-amino-3-(4-carbamoyl-2,6-dimethyl-phenyl)-propionyl]-[1-(4-phenyl-1H-imidazol-2-yl)-ethyl]-amino}-methyl)-2-methoxy-benzoic acid with water; and crystallizing the zwitterion.

7. Crystalline zwitterion of 5-({[2-amino-3-(4-carbamoyl-2,6-dimethyl-phenyl)-propionyl]-[1-(4-phenyl-1H-imidazol-2-yl)-ethyl]-amino}-methyl)-2-methoxy-benzoic acid prepared by the method of claim 6.

8. A Form α crystal of 5-({[2-amino-3-(4-carbamoyl-2,6-dimethyl-phenyl)-propionyl]-[1-(4-phenyl-1H-imidazol-2-yl)-ethyl]-amino}-methyl)-2-methoxy-benzoic acid.

9. The α crystal of claim 8, wherein said crystal is characterized by a powder X-ray diffraction pattern having powder X-ray diffraction peaks at about 14.0, 14.3, and 14.7 degrees 2-theta.

10. The α crystal of claim 8, wherein said crystal is characterized by a powder X-ray diffraction pattern having powder X-ray diffraction peaks at about 10.2, 11.3, 14.0, 14.3, and 14.7 degrees 2-theta.

11. The α crystal of claim 8, wherein said crystal is characterized by a powder X-ray diffraction pattern having powder X-ray diffraction peaks at about 10.2, 11.3, 11.8, 14.0, 14.3, 14.7, 16.1, and 18.3 degrees 2-theta.

12. The α crystal of claim 8, wherein said crystal is characterized by a powder X-ray diffraction pattern having powder X-ray diffraction peaks substantially as shown in Table 1.

13. The α crystal of claim 8, wherein said crystal is characterized by a powder X-ray diffraction pattern having powder X-ray diffraction peaks substantially similar to the powder X-ray diffraction peaks of Figure 1.

14. The α crystal of claim 8, wherein said crystal is characterized by a thermal gravimetric analysis (TGA) substantially similar to the TGA in Figure 2.

15. The α crystal of claim 8, wherein said crystal is characterized by a differential scanning calorimetry (DSC) measurement substantially similar to the DSC in Figure 3.

16. A Form β crystal of 5-({[2-amino-3-(4-carbamoyl-2,6-dimethyl-phenyl)-propionyl]-[1-(4-phenyl-1H-imidazol-2-yl)-ethyl]-amino}-methyl)-2-methoxy-benzoic acid.

17. The β crystal of claim 16, wherein said crystal is characterized by a powder X-ray diffraction pattern having powder X-ray diffraction peaks at about 11.0, 12.4 and 15.2 degrees 2-theta.

18. The β crystal of claim 16, wherein said crystal is characterized by a powder X-ray diffraction pattern having powder X-ray diffraction peaks at about 11.0, 12.4, 14.9, 15.2 and 22.1 degrees 2-theta.

19. The β crystal of claim 16, wherein said crystal is characterized by a powder X-ray diffraction pattern having powder X-ray diffraction peaks at about 11.0, 12.4, 14.9, 15.2, 22.1, 25.6, 27.4 and 30.4 degrees 2-theta.

20. The β crystal of claim 16, wherein said crystal is characterized by a powder X-ray diffraction pattern having powder X-ray diffraction peaks substantially as shown in Table 2.

21. The β crystal of claim 16, wherein said crystal is characterized by a powder X-ray diffraction pattern having powder X-ray diffraction peaks substantially similar to the powder X-ray diffraction peaks of Figure 1.

22. The β crystal of claim 16, wherein said crystal is characterized by a a thermal gravimetric analysis (TGA) substantially similar to the TGA in Figure 4.

23. The β crystal of claim 16, wherein said crystal is characterized by a differential scanning calorimetry (DSC) measurement substantially similar to the DSC in Figure 5.

24. Use of a Form α crystal of 5-({[2-amino-3-(4-carbamoyl-2,6-dimethyl-phenyl)-propionyl]-[1-(4-phenyl-1H-imidazol-2-yl)-ethyl]-amino}-methyl)-2-methoxy-benzoic acid in the manufacture of a medicament for treating irritable bowel syndrome, pain or another opioid receptor disorder.

25. Use of a Form β crystal of 5-({[2-amino-3-(4-carbamoyl-2,6-dimethyl-phenyl)-propionyl]-[1-(4-phenyl-1H-imidazol-2-yl)-ethyl]-amino}-methyl)-2-methoxy-benzoic acid in the manufacture of a medicament for treating irritable bowel syndrome, pain or another opioid receptor disorder.

26. A method of preparing a crystalline zwitterion of 5-({[2-amino-3-(4-carbamoyl-2,6-dimethyl-phenyl)-propionyl]-[1-(4-phenyl-1H-imidazol-2-yl)-ethyl]-amino}-methyl)-2-methoxy-benzoic acid; Crystalline zwitterion of 5-({[2-amino-3-(4-carbamoyl-2,6-dimethyl-phenyl)-propionyl]-[1-(4-phenyl-1H-imidazol-2-yl)-ethyl]-amino}-methyl)-2-methoxy-benzoic acid prepared by the process of claim 1 or claim 6; Form α crystal of 5-({[2-amino-3-(4-carbamoyl-2,6-dimethyl-phenyl)-propionyl]-[1-(4-phenyl-1H-imidazol-2-yl)-ethyl]-amino}-methyl)-2-methoxy-benzoic acid; Form β crystal of 5-({[2-amino-3-(4-carbamoyl-2,6-dimethyl-phenyl)-propionyl]-[1-(4-phenyl-1H-imidazol-2-yl)-ethyl]-amino}-methyl)-2-methoxy-benzoic acid; A method of treating a mammal suffering from irritable bowel syndrome, pain or another opioid receptor disorder comprising administering to said mammal an effective amount of a Form α crystal of 5-({[2-amino-3-(4-carbamoyl-2,6-dimethyl-phenyl)-propionyl]-[1-(4-phenyl-1H-imidazol-2-yl)-ethyl]-amino}-methyl)-2-methoxy-benzoic acid or Form β crystal of 5-({[2-amino-3-(4-carbamoyl-2,6-dimethyl-phenyl)-propionyl]-[1-(4-phenyl-1H-imidazol-2-yl)-ethyl]-amino}-methyl)-2-methoxy-benzoic acid; Use of a Form α crystal of 5-({[2-amino-3-(4-carbamoyl-2,6-dimethyl-phenyl)-propionyl]-[1-(4-phenyl-1H-imidazol-2-yl)-ethyl]-amino}-methyl)-2-methoxy-benzoic acid or a Form β crystal of 5-({[2-amino-3-(4-carbamoyl-2,6-dimethyl-phenyl)-propionyl]-[1-(4-phenyl-1H-imidazol-2-yl)-ethyl]-amino}-methyl)-2-methoxy-benzoic acid in the manufacture of a medicament; substantially as herein described with reference to any one or more of the examples but excluding any comparatives.