

Figure 5-32 shows TGA/DSC curves of Type J.

Figure 5-33 shows ^1H NMR of Type J.

Figure 5-34 shows XRPD pattern of Type K.

Figure 5-35 shows TGA/DSC curves of Type K.

5 Figure 5-36 shows ^1H NMR of Type K.

Figure 5-37 shows XRPD pattern of Type L.

Figure 5-38 shows TGA/DSC curves of Type L.

Figure 5-39 shows ^1H NMR of Type L.

Figure 5-40 shows XRPD pattern of Type M.

10 Figure 5-41 shows TGA/DSC curves of Type M.

Figure 5-42 shows ^1H NMR of Type M.

Figure 5-43 shows XRPD pattern of Type N.

Figure 5-44 shows TGA/DSC curves of Type N.

Figure 5-45 shows ^1H NMR of Type N.

15 Figure 5-46 shows XRPD pattern of Type O.

Figure 5-47 shows TGA/DSC curves of Type O.

Figure 5-48 shows ^1H NMR of Type O.

Figure 5-49 shows XRPD pattern of Type P.

Figure 5-50 shows TGA/DSC curves of Type P.

20 Figure 5-51 shows ^1H NMR of Type P.

Figure 5-52 shows XRPD pattern of Type Q.

Figure 5-53 shows TGA/DSC curves of Type Q.

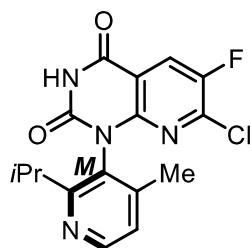
Figure 5-54 shows ^1H NMR of Type Q.

25 Figure 6-1 shows HPLC of M-5 from resolution with 1,3-diphenyl-3-oxopropanesulfonic acid.

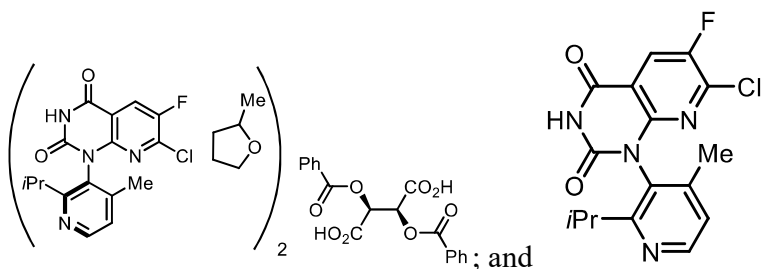
Figure 6-2 shows HPLC of 5 (P-atropisomer excess) from resolution with 1,3-diphenyl-3-oxopropanesulfonic acid.

SUMMARY

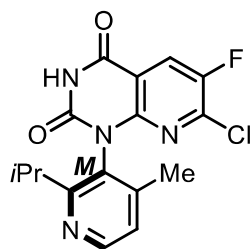
30 The present invention disclosure relates to improved preparation of a compound having the following chemical structure:



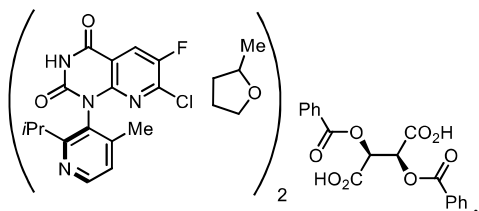
and key intermediates thereof, i.e., compositions and compounds comprising the following chemical structures:



5 The present inventiondisclosure additionally relates to a method of preparing Compound 5M having the following chemical structure

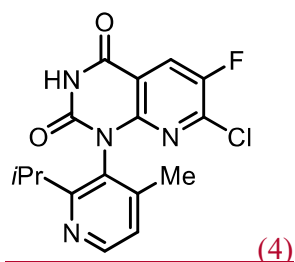


The present inventiondisclosure additionally relates to a composition comprising a structure

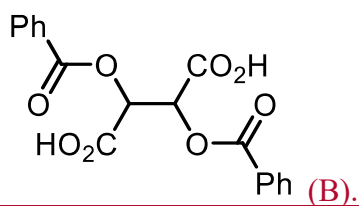


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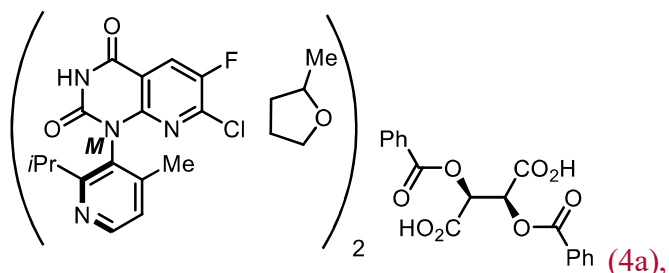
In one aspect, the present disclosure relates to a composition, the composition comprising a compound of Formula 4



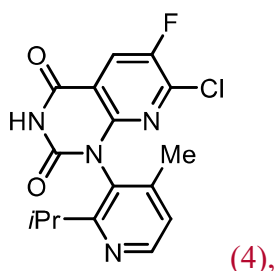
and a compound of Formula B



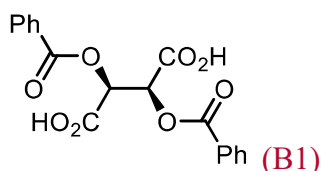
In another aspect, the present disclosure relates to a method of making a composition of Formula 4a



5 the method comprising reacting a compound of Formula 4

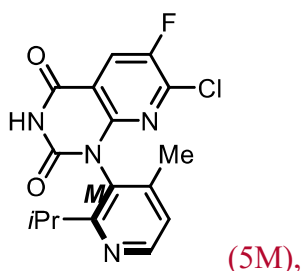


with a compound of Formula B1



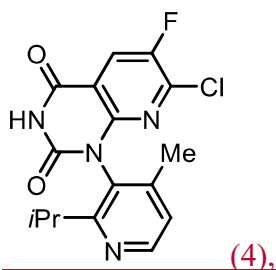
in the presence of 2-methyltetrahydrofuran to form the composition of Formula 4a.

10 In yet another aspect, the present disclosure relates to a method of making a compound of Formula 5M

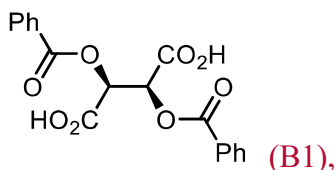


the method comprising:

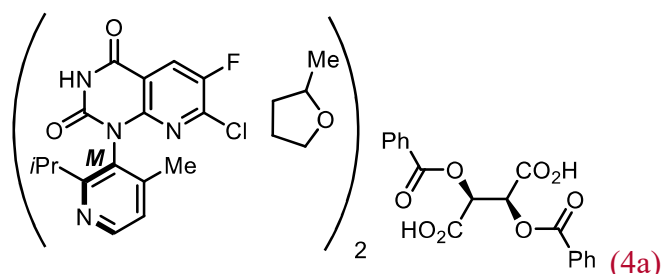
a) reacting a compound of Formula 4



with a compound of Formula B1



5 in the presence of 2-methyltetrahydrofuran to form a composition of Formula 4a



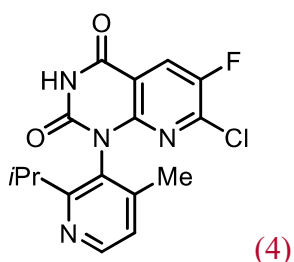
as crystals;

b) isolating the composition of Formula 4a, and

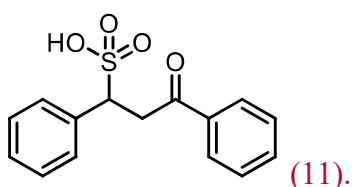
c) treating the isolated composition of Formula 4a with a base to produce the compound

10 of Formula 5M.

In yet another aspect, the present disclosure relates to a composition, the composition comprising a compound of Formula 4



and a compound of Formula 11

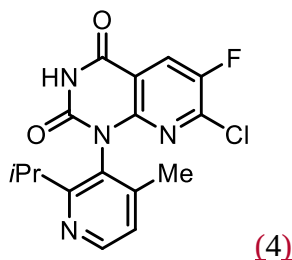


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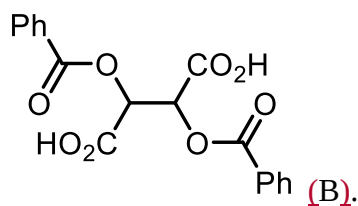
CLAIMS

What is claimed is:

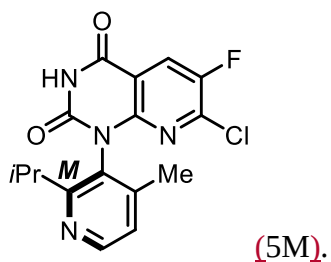
1. A composition, the composition comprising a compound of Formula 4:



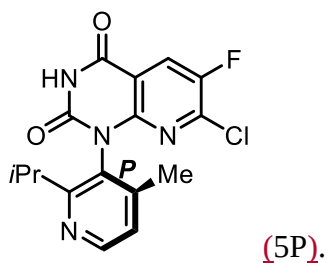
and a compound of Formula B:



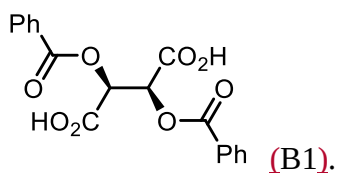
2. The composition of claim 1, wherein the compound of Formula 4 is a compound of Formula 5M:



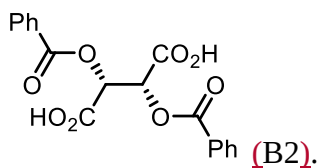
3. The composition of claim 1, wherein the compound of Formula 4 is a compound of Formula 5P:



4. The composition of any one of claims 1-3, wherein the compound of Formula B is a compound of ~~Formula~~ ~~formula~~ B1:

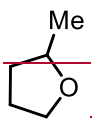


5. The composition of any one of claims 1-3, wherein the compound of Formula B is a compound of ~~Formula~~ ~~formula~~ B2:



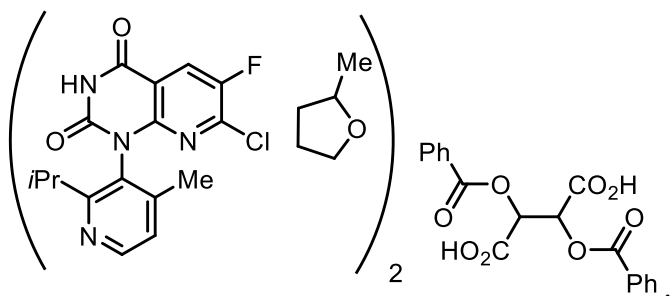
6. The composition of any one of claims 1-3, wherein the composition comprises a 2 to 1 ratio of the compound of Formula 4 to the compound of Formula B.

7. The composition of any one of claims 1-3, wherein the composition further comprises 2-methyltetrahydrofuran, ~~having the formula:~~

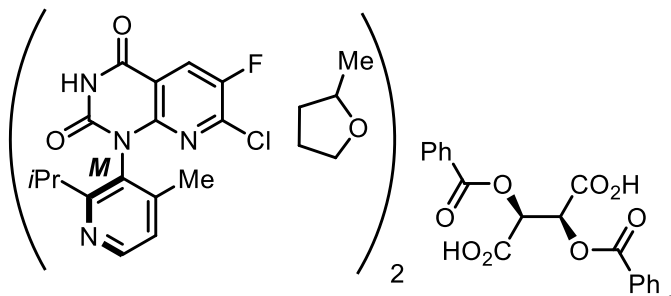


8. The composition of any one of claims 1-3, wherein the ratio of the 2-methyltetrahydrofuran to the compound of ~~formula~~ ~~Formula~~ B is 2 to 1.

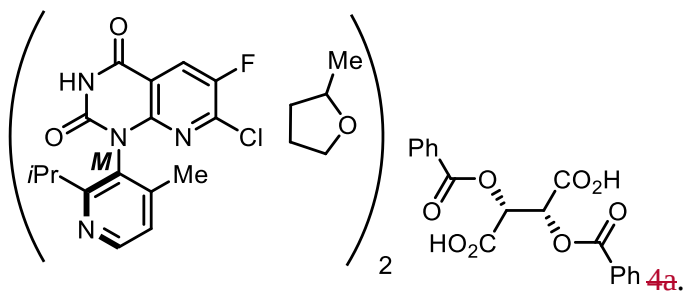
9. The composition of claim 1, wherein the composition ~~is~~ ~~has the formula:~~



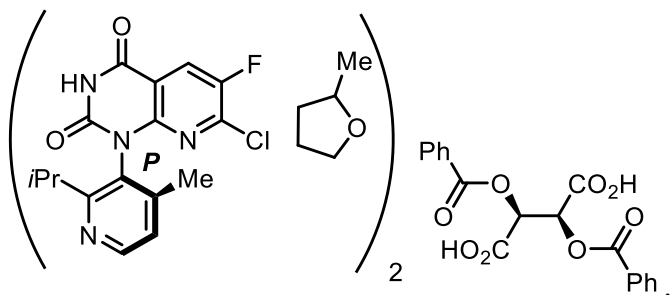
10. The composition of claim 9, wherein the composition ~~is~~ ~~has the formula:~~



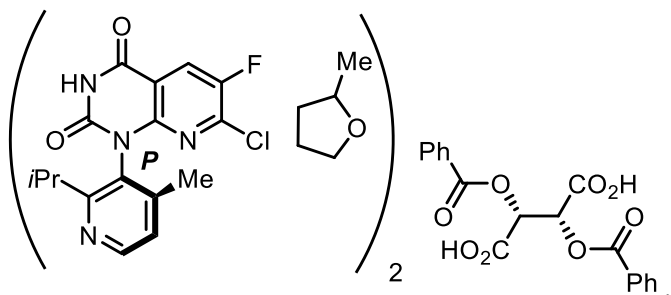
11. The composition of claim 9, wherein the composition ~~is has the formula:~~



12. The composition of claim 9, wherein the composition ~~is has the formula:~~

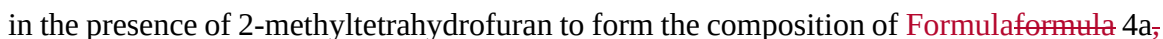
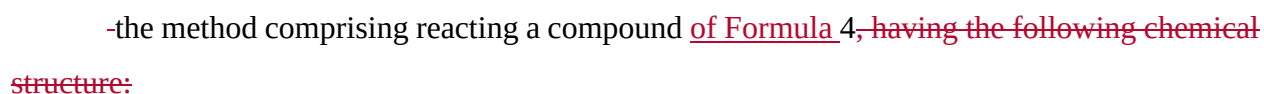


13. The composition of claim 9, wherein the composition ~~is has the formula:~~



14. The composition of any one of claims 1-13, wherein the composition is in a crystalline state.

15. A method of making a composition of ~~formula-Formula~~ 4a

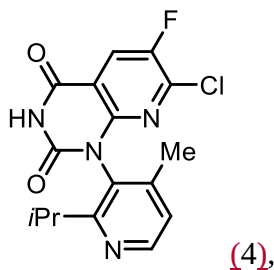


16. A method of ~~making~~obtaining a compound of ~~Formula~~formula 5M, ~~having the following chemical structure:~~

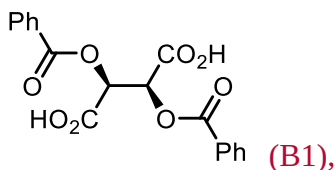


the method comprising:

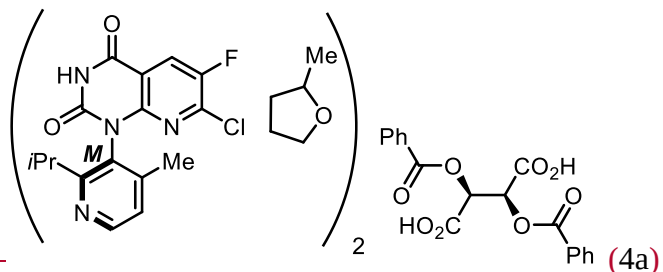
a) reacting a compound of Formula 4, ~~having the following chemical structure:~~



with a compound of Formula B1, ~~having the formula:~~



in the presence of 2-methyltetrahydrofuran to form a composition of Formula~~formula~~ 4a,



~~having the structure:-~~

-as crystals;

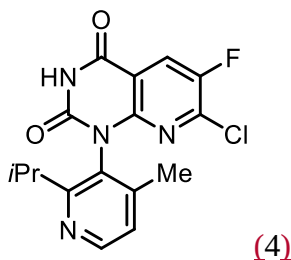
b) isolating the composition of Formula 4a, and

c) treating the isolated composition of Formula 4a with a base to produce the compound of Formula~~formula~~ 5M.

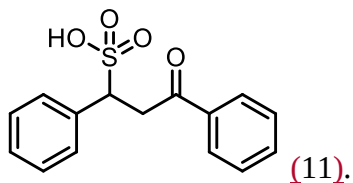
17. The method according to Claim 16, wherein the base is Na₂HPO₄.

18. The method according to Claim 16, wherein the base is NaHCO₃.

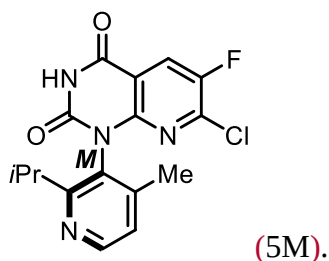
19. A composition, the composition comprising a compound of Formula 4~~:~~



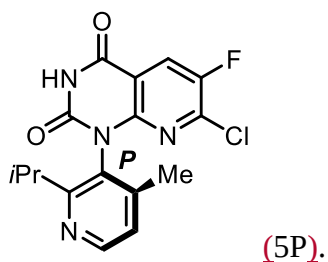
and a compound of Formula 11:



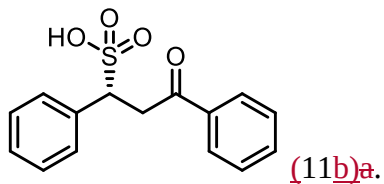
20. The composition of claim 19, wherein the compound of Formula 4 is a compound of Formula 5M:



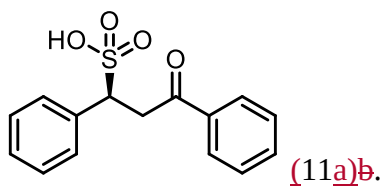
21. The composition of claim 19, wherein the compound of Formula 4 is a compound of Formula 5P:



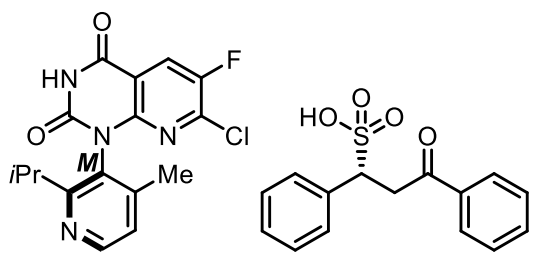
22. The composition of any one of claims 19-21, wherein the compound of Formula 11 is a compound of ~~Formula~~ Formula 11b:



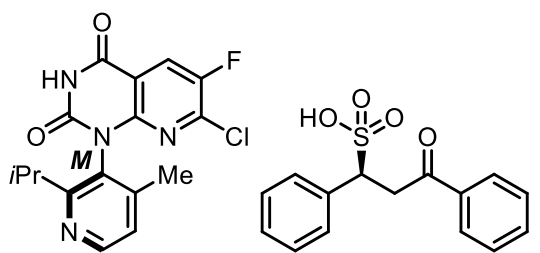
23. The composition of any one of claims 19-21, wherein the compound of Formula 11 is a compound of ~~Formula~~ Formula 11a:



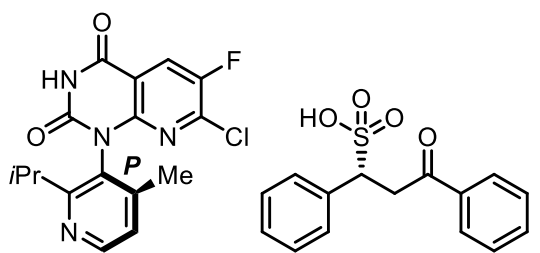
24. The composition of claim 19, wherein the composition ~~is~~has the formula:



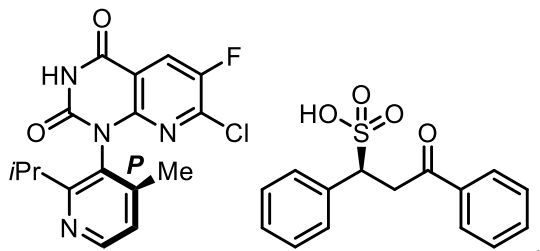
25. The composition of claim 19, wherein the composition ~~is~~has the formula:



26. The composition of claim 19, wherein the composition ~~is~~has the formula:

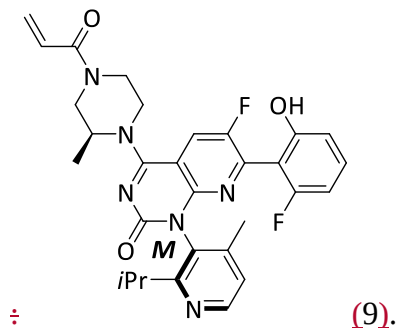


27. The composition of claim 19, wherein the composition ~~is~~has the formula:



28. The composition of any one of claims 19-27, wherein the composition comprises a 1 to 1 ratio of the compound of Formula 4 to the compound of Formula 11.

29. The method of claim 16, wherein the compound of ~~Formula~~formula 5M is used to generate a compound ~~of having the~~ Formula 9



30. The method of claim 29, wherein the method further comprises mixing the compound of Formula 9 with at least one pharmaceutically acceptable excipient to form a pharmaceutical composition.