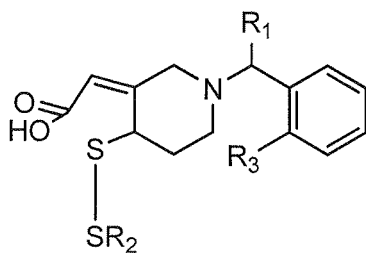
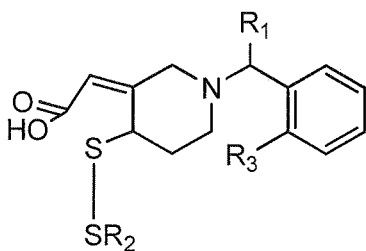


of developing embodiments for the present disclosure demonstrated that the mixed disulfide conjugates of thienopyridine compounds of the present disclosure are capable of producing active thienopyridine metabolites (e.g., active thienopyridine metabolites capable of antiplatelet activity) in the presence of endogenous glutathione (GSH) without the need for bioactivation by P450s. This approach not only bypasses the oxidative bioactivation process by P450s, but circumvents many of the drawbacks associated with thienopyridinyl drugs. For example, the mixed disulfide conjugates of thienopyridine compounds of the present disclosure improve dosing consistency because production of the active metabolite from the conjugates is predictable. In addition, use of the mixed disulfide conjugates of thienopyridine compounds of the present disclosure as antiplatelet agents reduce the toxicity as toxic reactive metabolites are not produced by the thiol-exchange reaction. In addition, the therapeutic onset time for the mixed disulfide conjugates of thienopyridine compounds of the present disclosure is shortened, which greatly benefits patients who experience acute cardiovascular events. For example, the standard regimen for thienopyridines requires continuously dosing patients for 3-5 days as only a small percentage of ingested thienopyridines are converted to the active metabolite. In contrast, the mixed disulfide conjugates of thienopyridine compounds of the present disclosure release the active metabolites with high yields in less than 30 min. In addition, the mixed disulfide conjugates of thienopyridine compounds of the present disclosure have superior stability over the active metabolites and therefore they can be used to quantitatively generate the active metabolites for basic and clinical research in vitro. Accordingly, in certain embodiments, the present disclosure provides mixed disulfide conjugates of thienopyridine compounds capable of overcoming such drawbacks associated with thienopyridinyl compounds widely used as antiplatelet agents (e.g., Clopidogrel (Plavix), ticlopidine (Ticlid) and prasugrel (Effient)). The present disclosure is not limited to particular mixed disulfide conjugates of thienopyridine compounds. In a first aspect, the present disclosure, there is provided a compound having Formula I:



Formula I: \_\_\_\_\_, including pharmaceutically acceptable salts, solvates, and/or prodrugs thereof; wherein R1, R2, and R3 independently include any chemical moiety that renders the resulting compound capable of producing active thienopyridine metabolites upon interaction with endogenous glutathione (GSH).

5 In an aspect, there is provided a compound having Formula I:



Formula I: \_\_\_\_\_, or a pharmaceutically acceptable salt or solvate

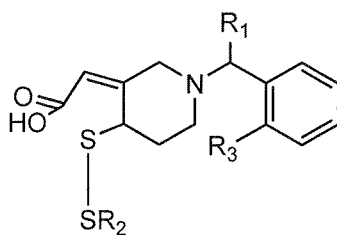
thereof; wherein R<sub>1</sub> is selected from the group consisting of H, -CO-OCH<sub>3</sub>, and ;

R<sub>2</sub> is selected from the group consisting of , , ,

and ; and

10 R<sub>3</sub> is Chlorine or Fluorine.

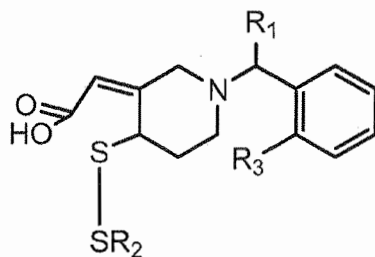
In some embodiments, the mixed disulfide conjugates of thienopyridine compounds



are described by Formula I: \_\_\_\_\_, including pharmaceutically acceptable salts, solvates, and/or prodrugs thereof; wherein R1, R2, and R3 independently include any chemical moiety

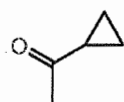
## What Is Claimed Is:

1. A compound having Formula I:



Formula I: \_\_\_\_\_, including pharmaceutically acceptable salts, solvates, and/or prodrugs thereof; wherein R1, R2, and R3 independently include any chemical moiety that renders the resulting compound capable of producing active thienopyridine metabolites upon interaction with endogenous glutathione (GSH).

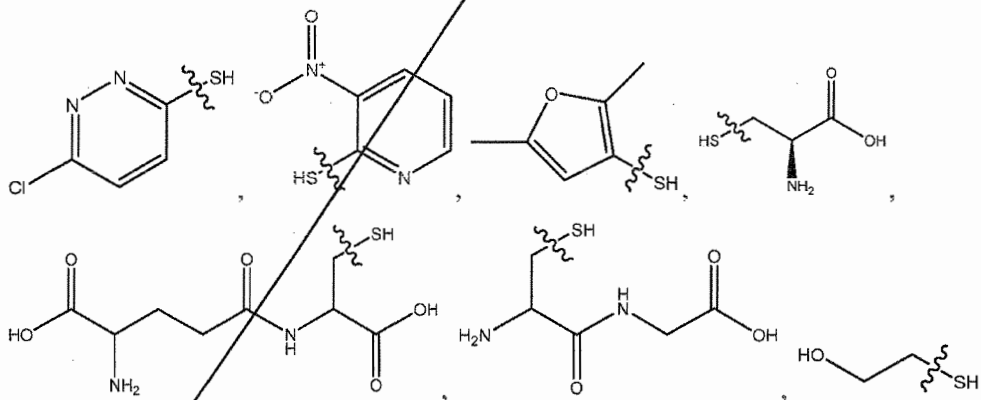
2. The compound of claim 1, wherein R1 is selected from the group consisting of H, -

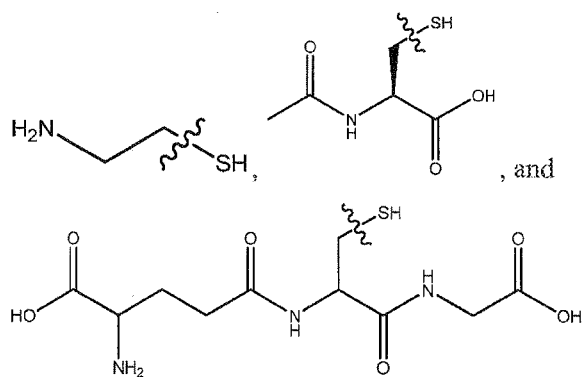


CO-OCH3, and

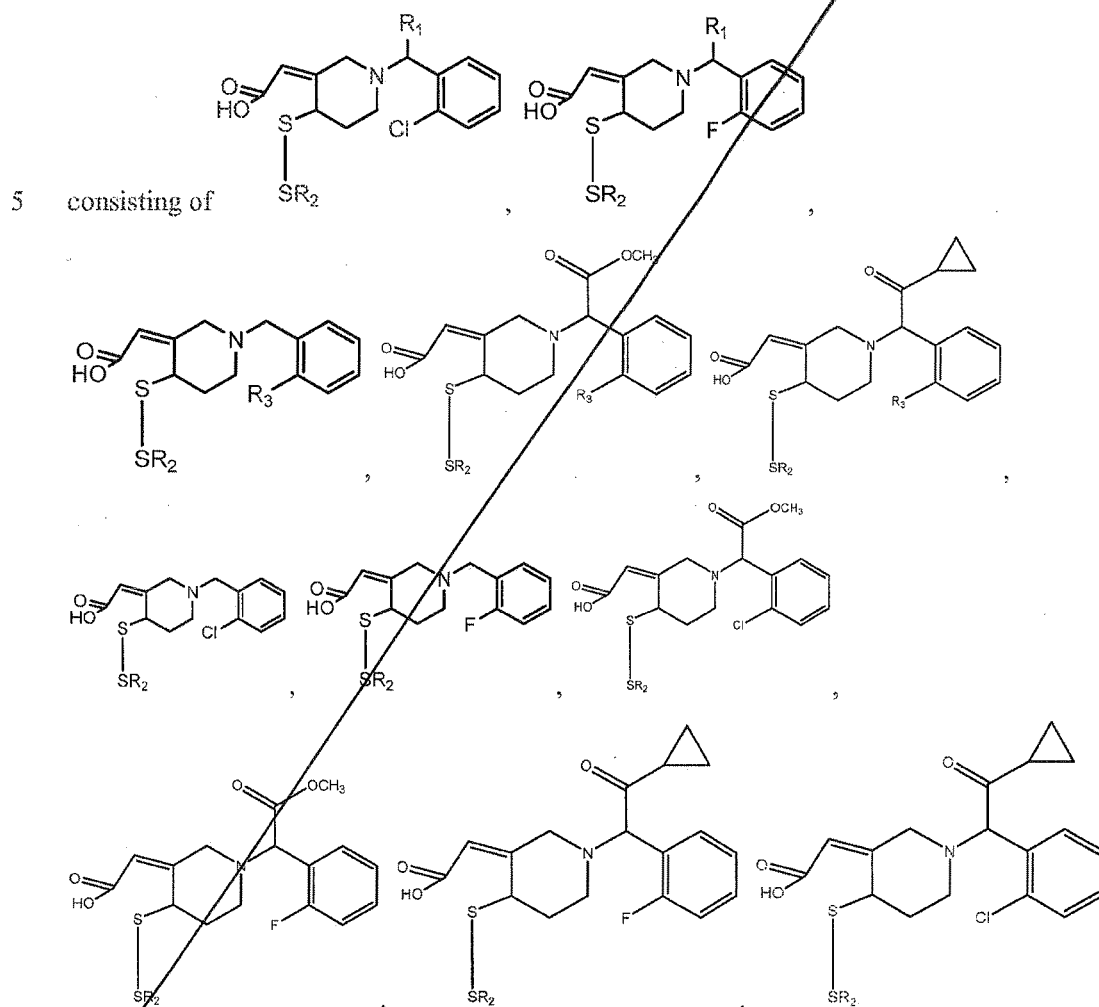
3. The compound of claim 1, wherein R3 is Chlorine or Fluorine.

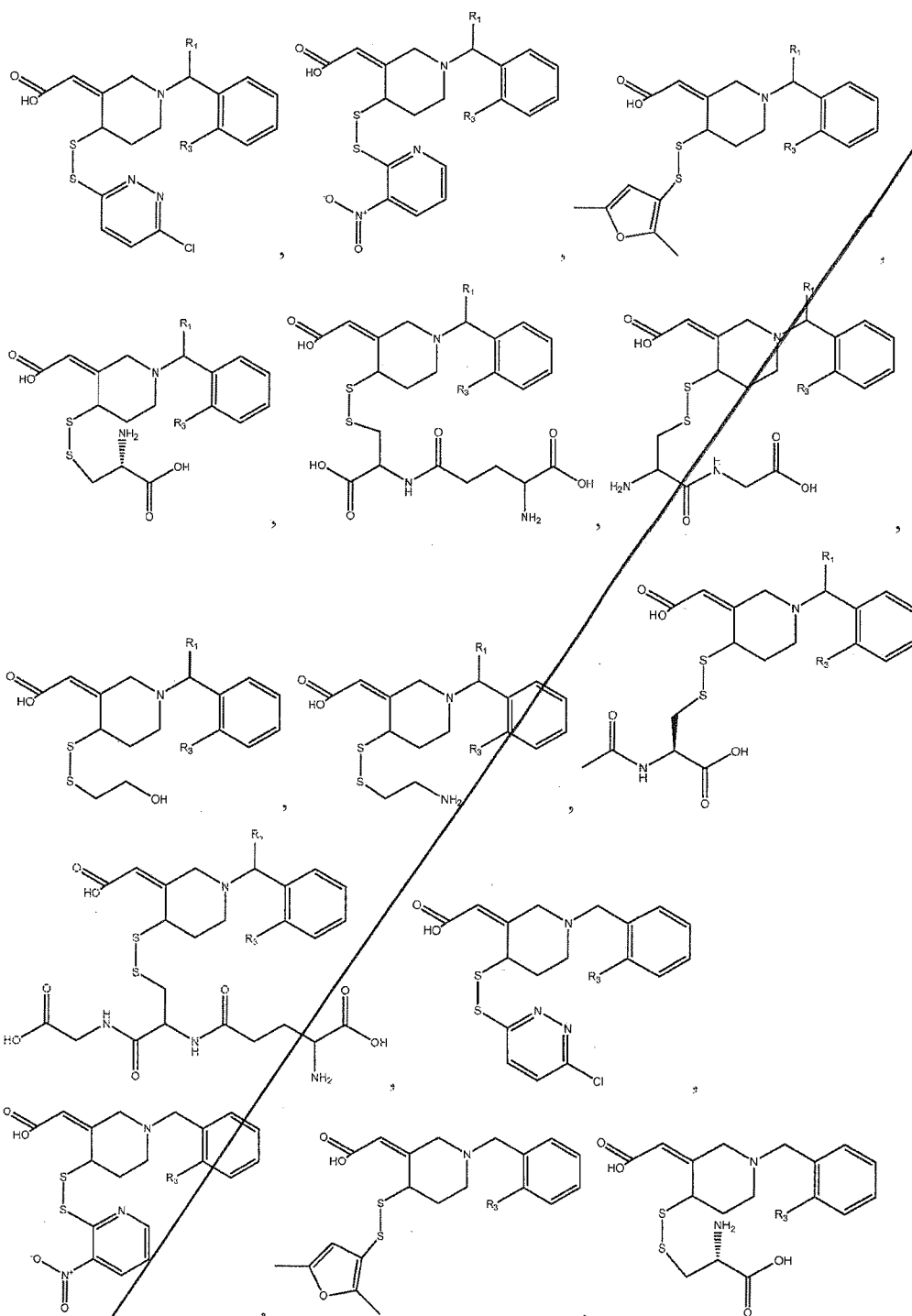
4. The compound of claim 1, wherein R2 is selected from the group consisting of

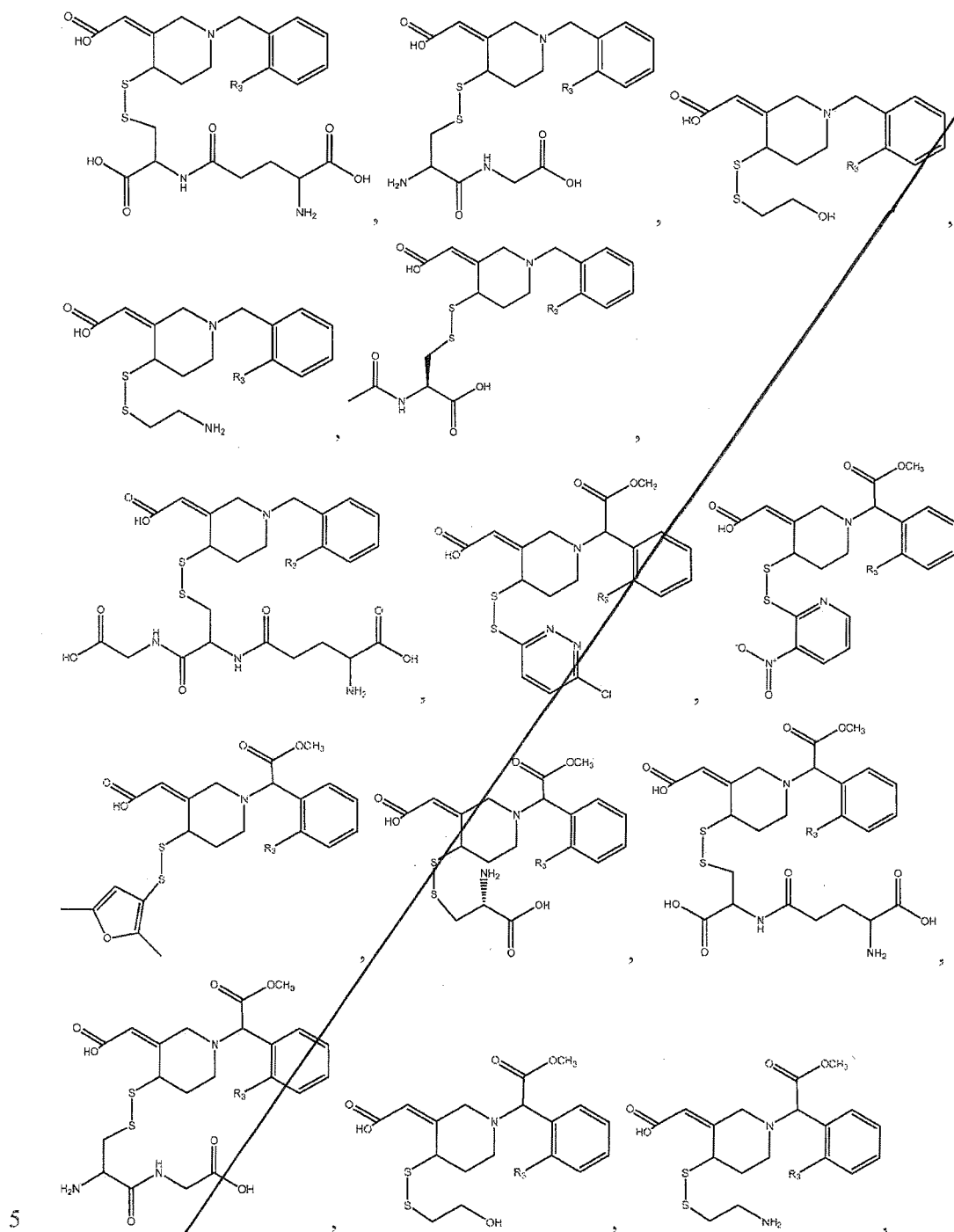


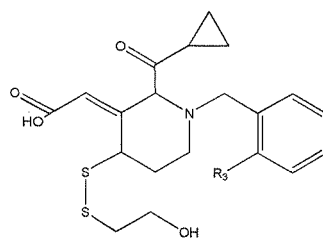
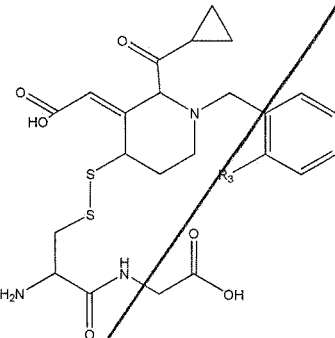
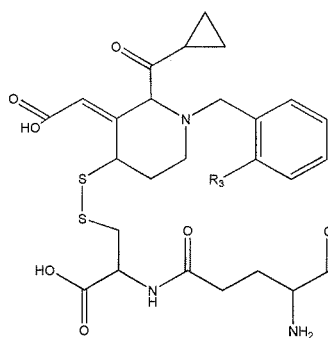
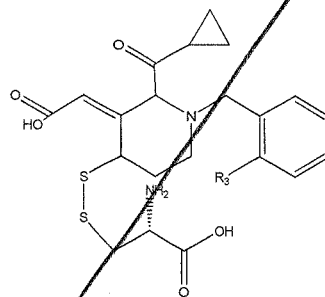
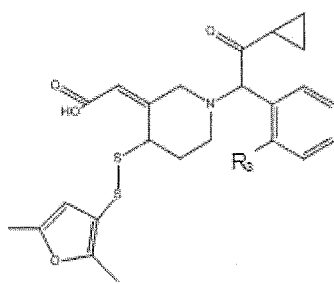
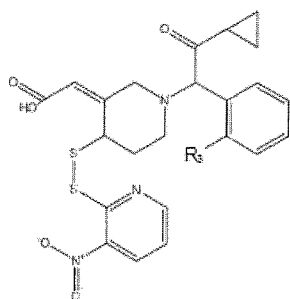
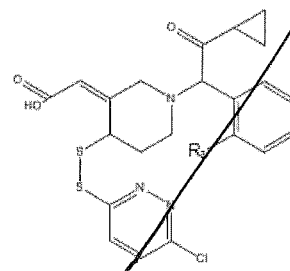
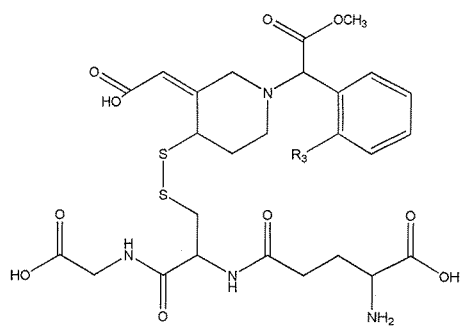
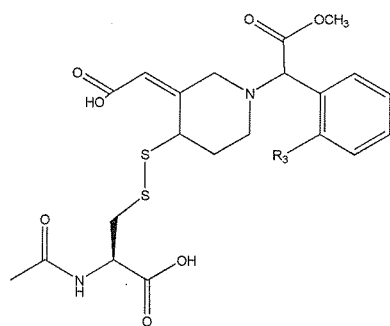


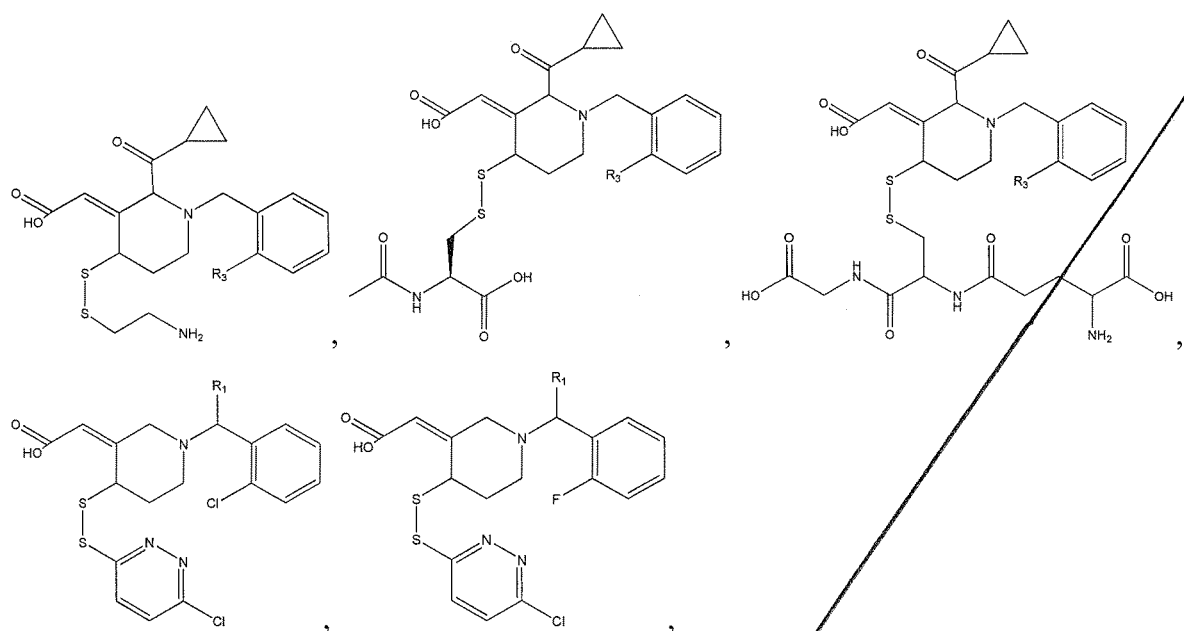
5. The compound of claim 1, wherein said compound is selected from the group

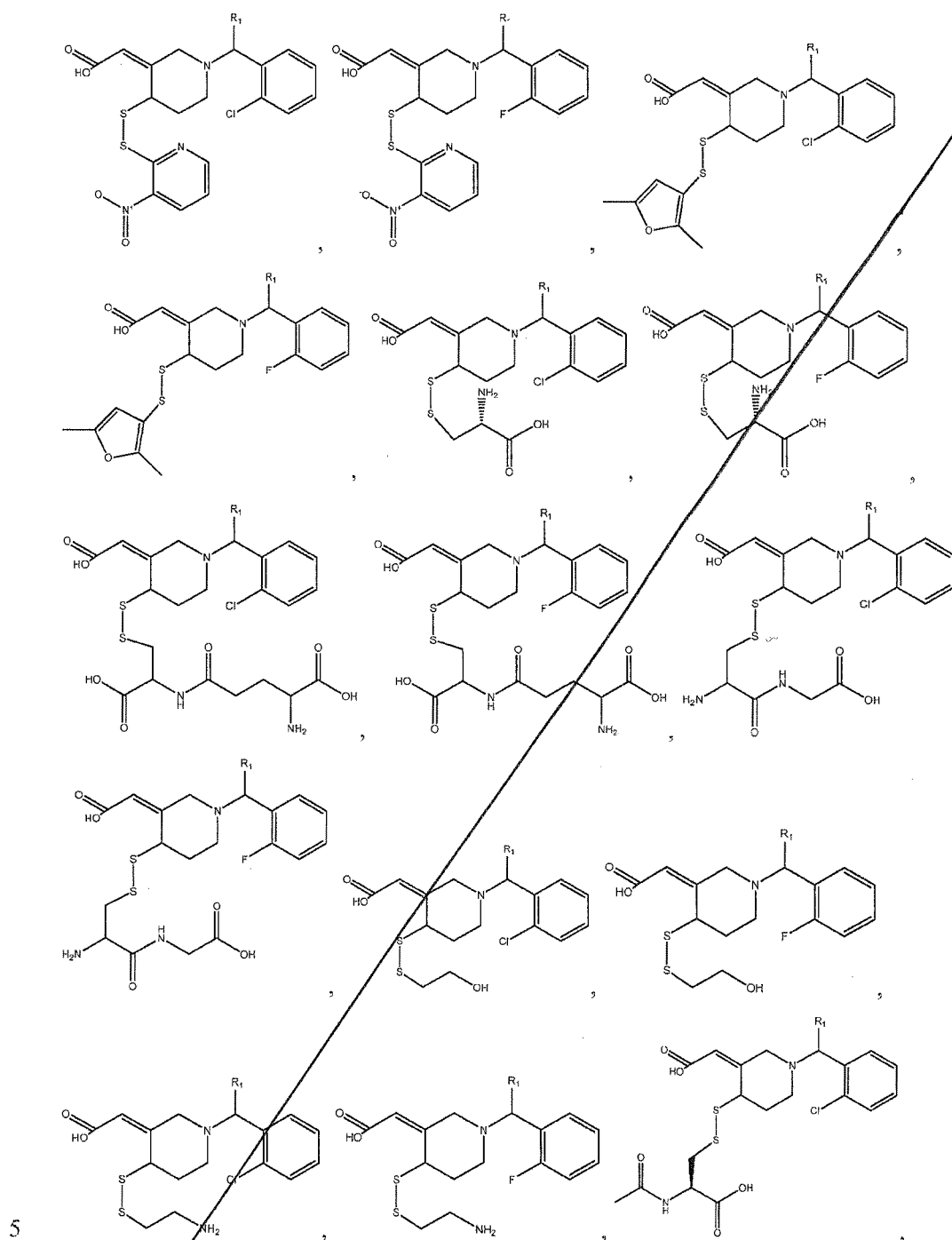


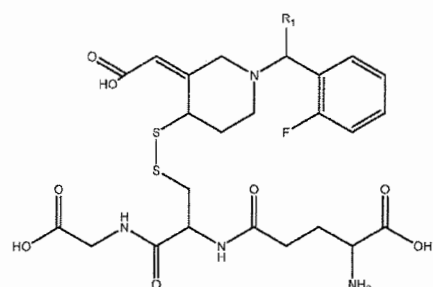
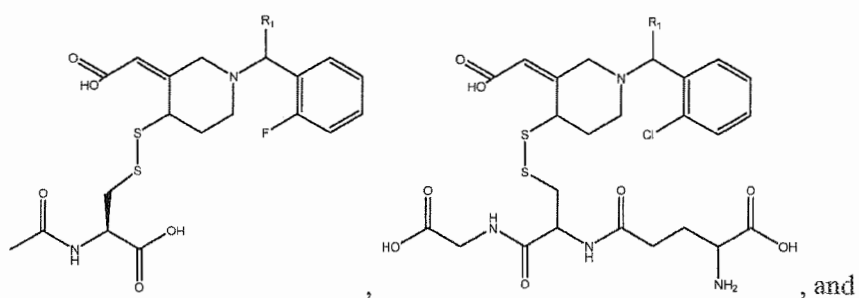






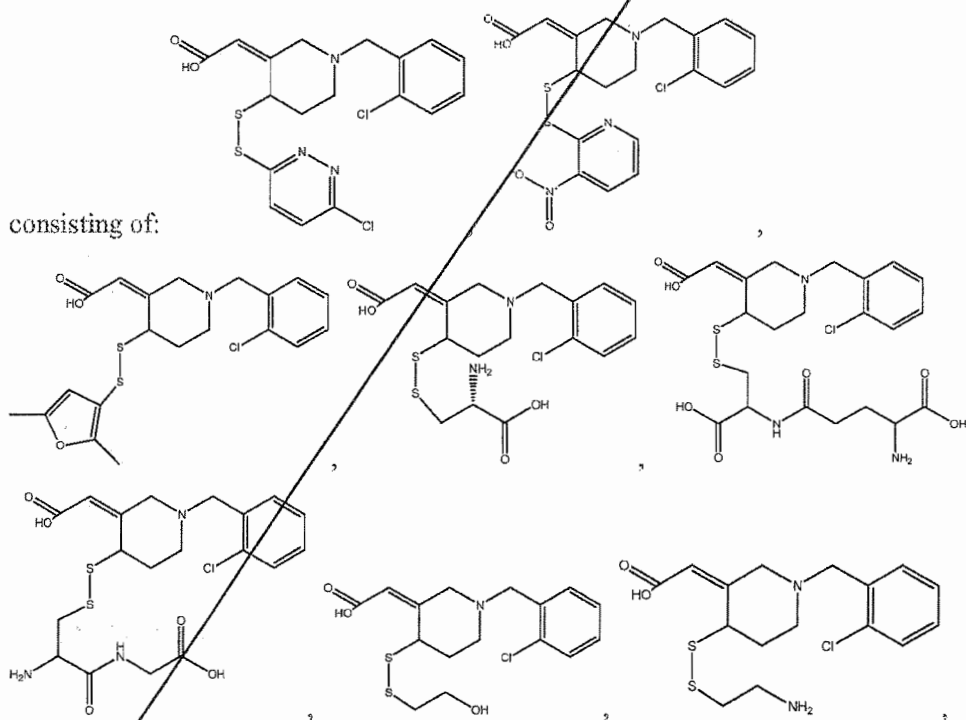


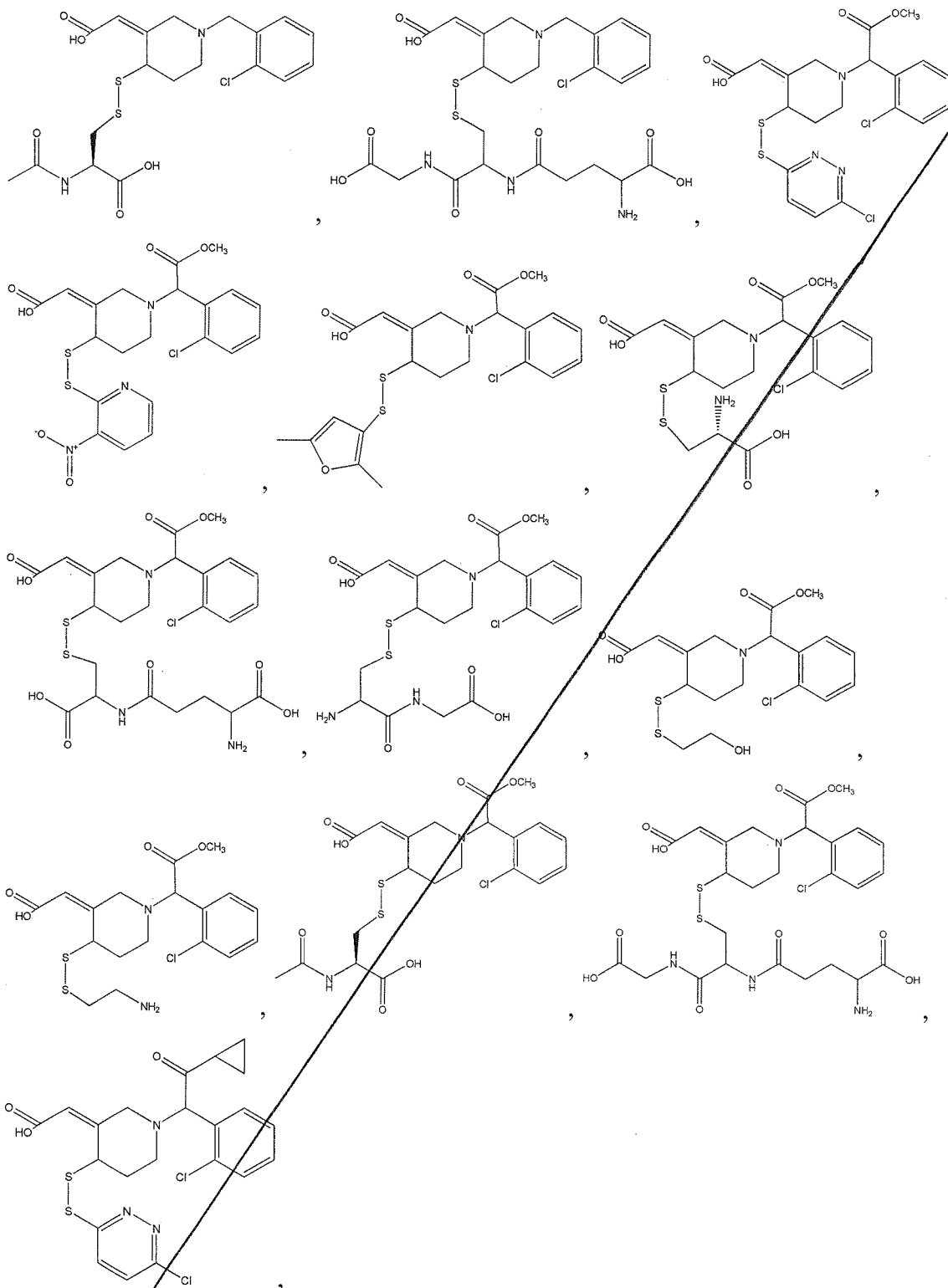


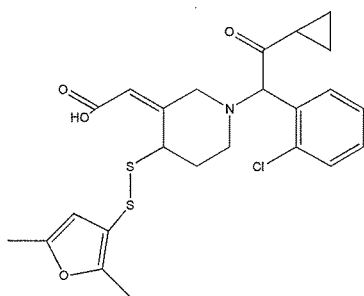
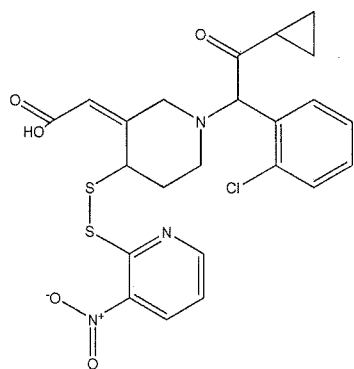


6. The compound of claim 1, wherein said compound is selected from the group

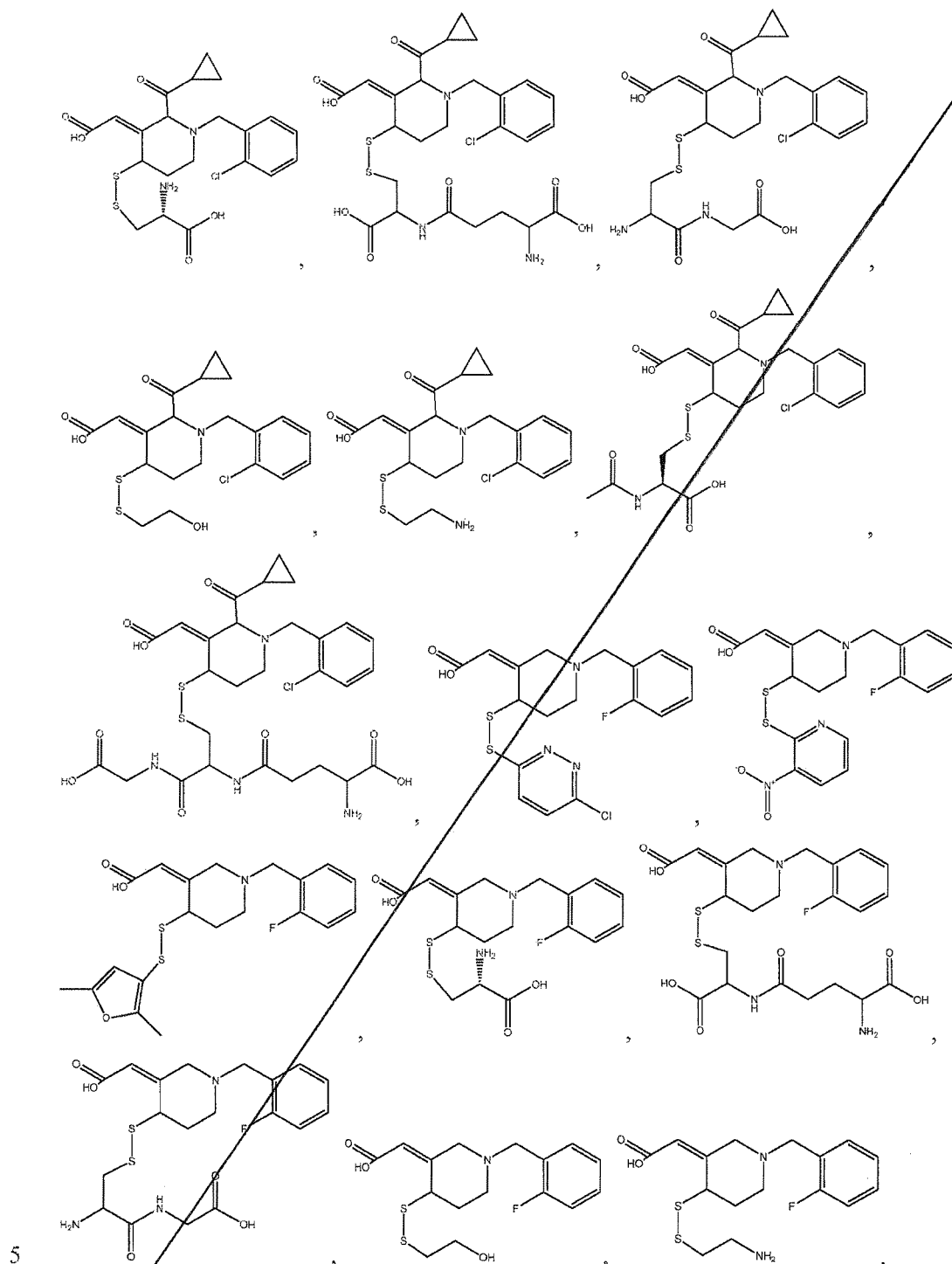
5 consisting of:

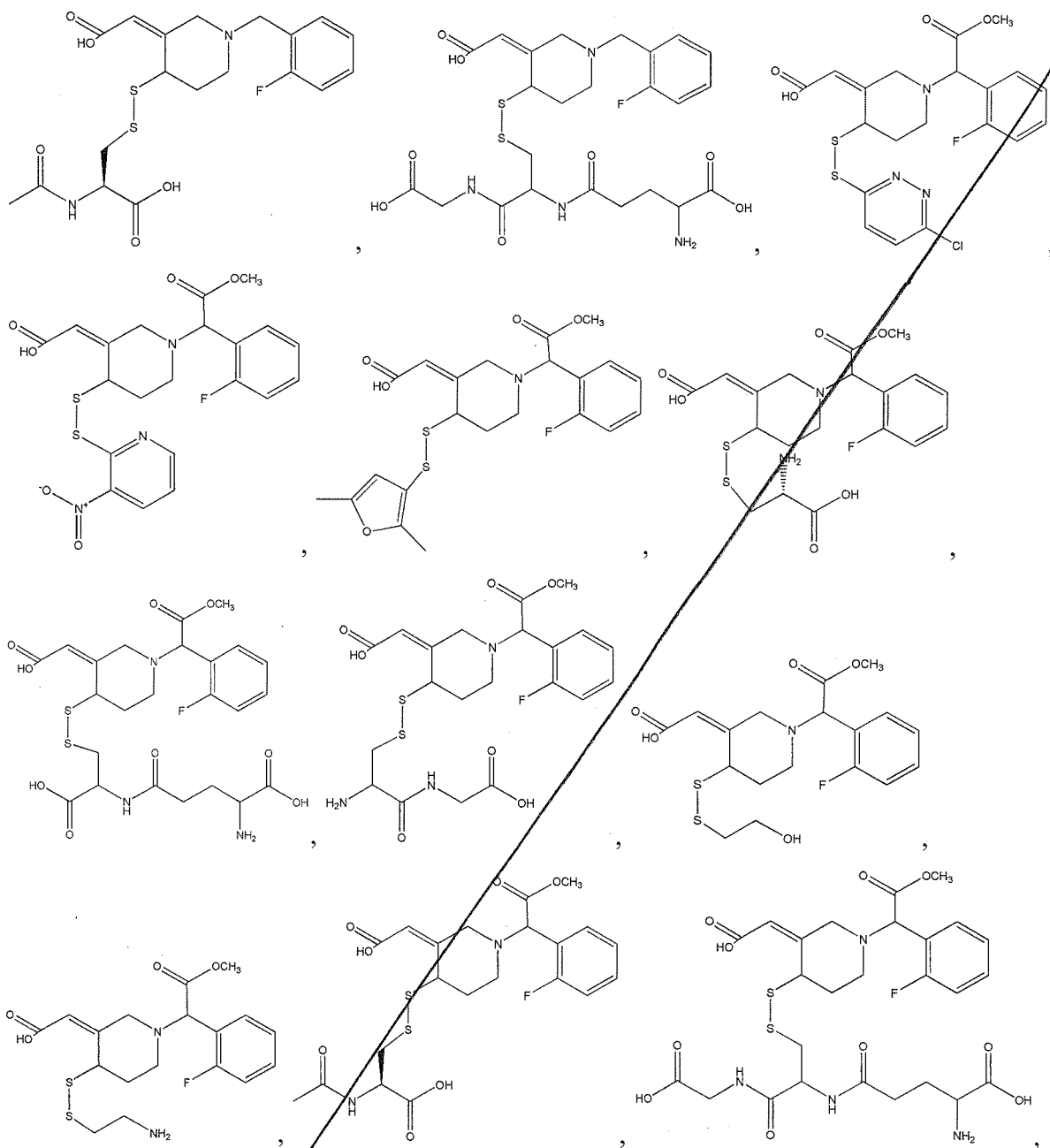


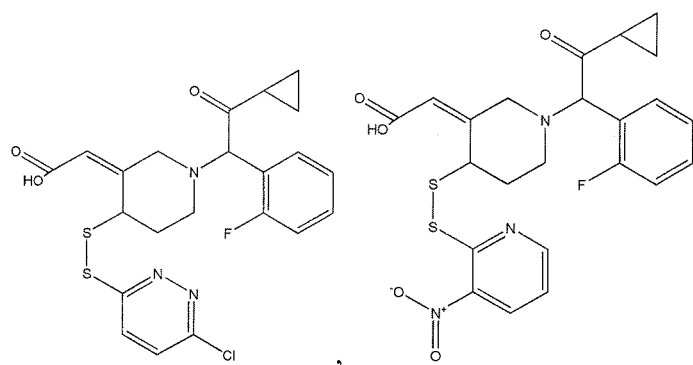




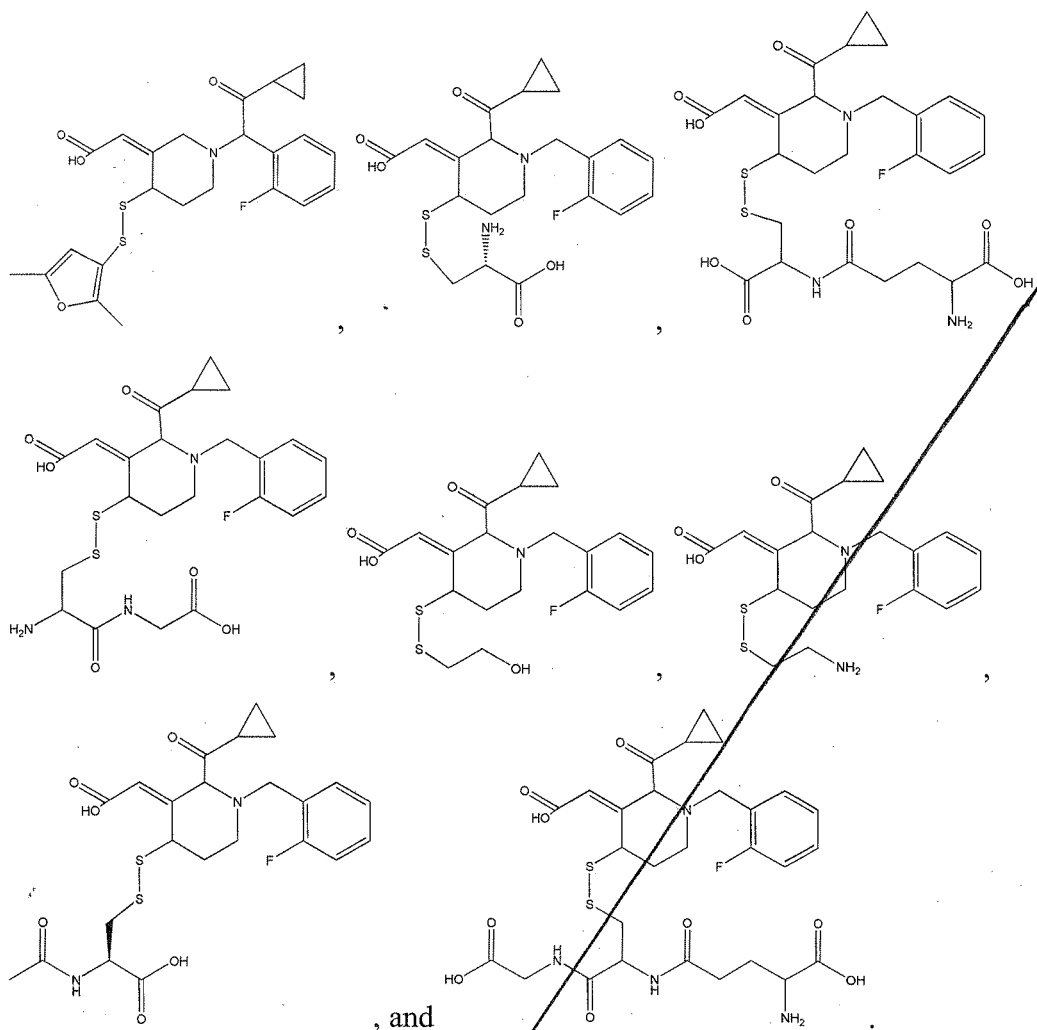
56a







58a



7. A pharmaceutical composition comprising a compound of any one of claims 1-6 and a pharmaceutically acceptable carrier.
8. The pharmaceutical composition of claim 7, wherein said pharmaceutical composition is configured for intravenous administration.
9. Use of a compound of claim 1 for the manufacture of a medicament for the treatment, amelioration, or prevention of a cardiovascular disease in a patient.

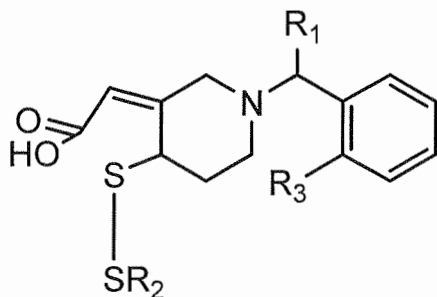
10. The use of claim 9, wherein said medicament is formulated for oral administration and intravenous administration.
11. The use of claim 9, wherein said cardiovascular disease is selected from the group consisting of coronary artery disease, peripheral vascular disease, atherothrombosis, and cerebrovascular disease.
12. The use of claim 9, wherein said compound reduces aggregation of platelets.
13. The use of claim 12, wherein said reduces aggregation of said platelets occurs through irreversible binding to P2Y<sub>12</sub> receptors.
14. The use of claim 12, wherein said reduces aggregation of said platelets occurs through blocking ADP receptors.
15. The use of claim 12, wherein said compound is capable of producing active thienopyridine metabolites in the presence of endogenous glutathione without the need for bioactivation by P450s.
16. The use of claim 12, further comprising at least one agent selected from the group consisting of a HMG-CoA reductase inhibitor, an ACE Inhibitor, a Calcium Channel Blocker, a Platelet Aggregation Inhibitor, a Polyunsaturated Fatty Acid, Fibrin Acid Derivative, a Bile Acid Sequestrant, an Antioxidant, a Thrombolytic Agent, and an Antianginal Agent.
17. Use of a compound of claim 1 for the manufacture of a medicament for the treatment, amelioration, or prevention of aggregation of platelets onto blood vessels in a patient.
18. The use of claim 17, wherein said medicament is formulated for oral administration and intravenous administration.

19. The use of claim 18, wherein said treating, ameliorating, or preventing said aggregation of said platelets occurs through irreversible binding to P2Y<sub>12</sub> receptors.

20. The use of claim 18, wherein said treating, ameliorating, or preventing said aggregation of said platelets occurs through blocking ADP receptors.

**What Is Claimed Is:**

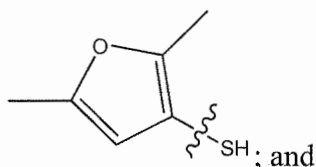
1. A compound having Formula I:



Formula I: , or a pharmaceutically acceptable salt or solvate

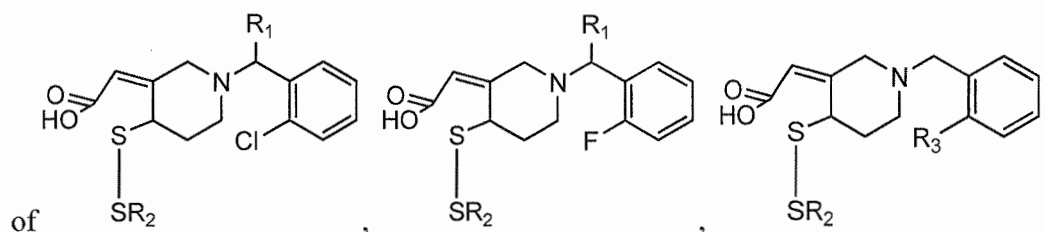
thereof; wherein  $R_1$  is selected from the group consisting of H,  $-\text{CO}-\text{OCH}_3$ , and ;

$R_2$  is selected from the group consisting of , , , and

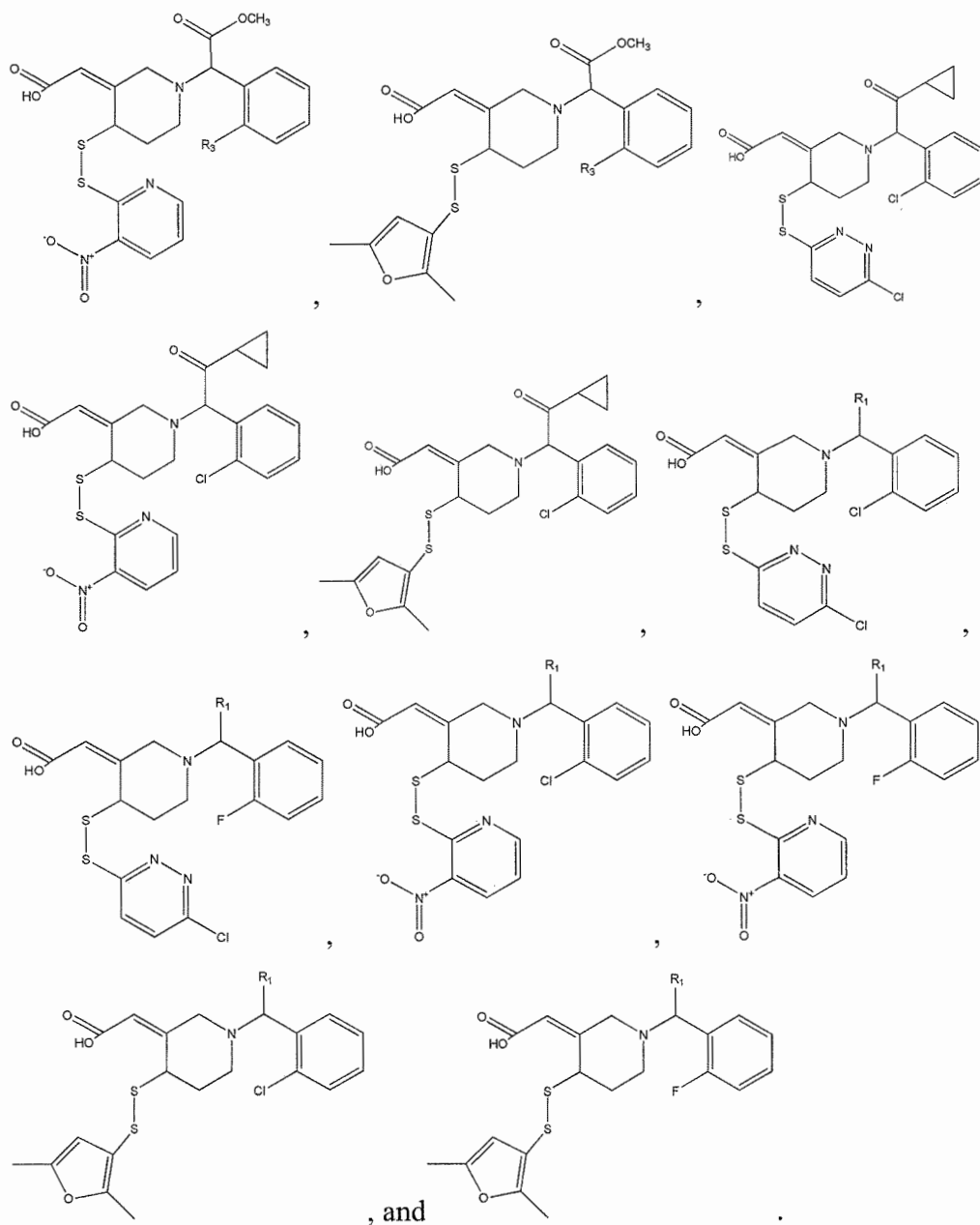


$R_3$  is Chlorine or Fluorine.

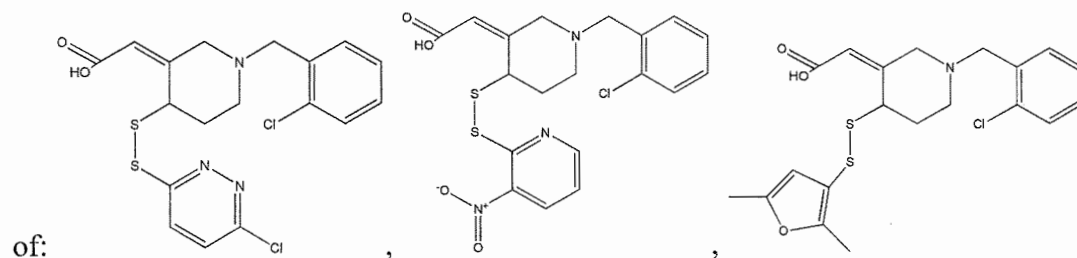
2. The compound of claim 1, wherein said compound is selected from the group consisting

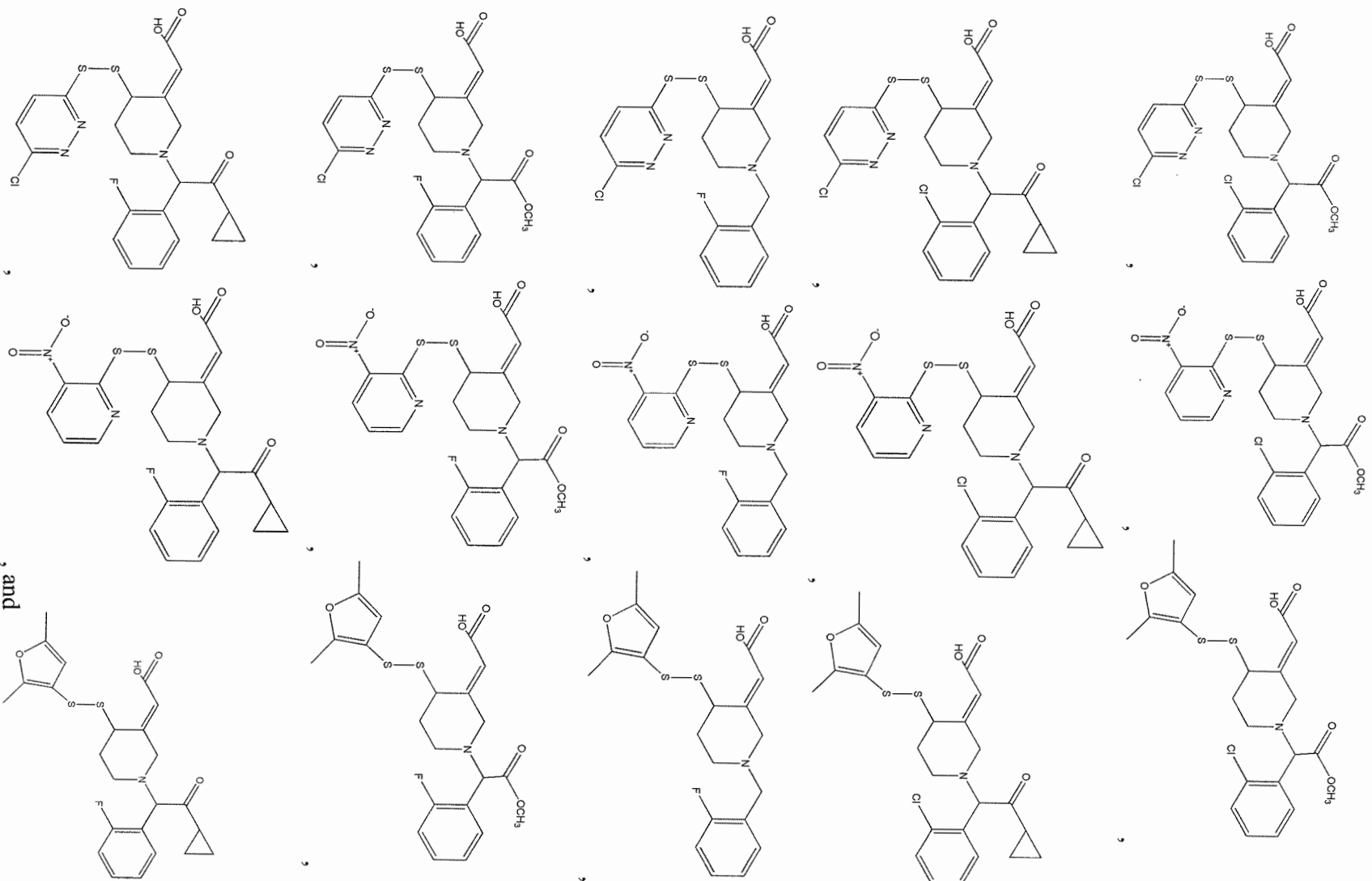






3. The compound of claim 1, wherein said compound is selected from the group consisting





, and

4. A pharmaceutical composition comprising a compound of any one of claims 1 to 3, and a pharmaceutically acceptable carrier.
5. The pharmaceutical composition of claim 4, wherein said pharmaceutical composition is configured for intravenous administration.
6. Use of a compound of claim 1 for the manufacture of a medicament for the treatment, amelioration, or prevention of a cardiovascular disease in a patient.
7. The use of claim 6, wherein said medicament is formulated for oral administration or intravenous administration.
8. The use of claim 6, wherein said cardiovascular disease is selected from the group consisting of coronary artery disease, peripheral vascular disease, atherothrombosis, and cerebrovascular disease.
9. The use of claim 6, wherein said compound reduces aggregation of platelets.
10. The use of claim 9, wherein said compound reduces aggregation of said platelets occurs through irreversible binding to P2Y<sub>12</sub> receptors.
11. The use of claim 9, wherein said compound reduces aggregation of said platelets occurs through blocking ADP receptors.
12. The use of claim 9, wherein said compound is capable of producing active thienopyridine metabolites in the presence of endogenous glutathione without the need for bioactivation by P450s.
13. The use of claim 9, further comprising co-administration of at least one agent selected from the group consisting of a HMG-CoA reductase inhibitor, an ACE Inhibitor, a Calcium Channel Blocker, a Platelet Aggregation Inhibitor, a Polyunsaturated Fatty Acid, Fibrin Acid

Derivative, a Bile Acid Sequestrant, an Antioxidant, a Thrombolytic Agent, and an Antianginal Agent.

14. Use of a compound of claim 1 for the manufacture of a medicament for the treatment, amelioration, or prevention of aggregation of platelets onto blood vessels in a patient.
15. The use of claim 14, wherein said medicament is formulated for oral administration or intravenous administration.
16. The use of claim 15, wherein said treatment, amelioration, or prevention of aggregation of platelets occurs through irreversible binding of said compound to P2Y<sub>12</sub> receptors.
17. The use of claim 15, wherein said treatment, amelioration, or prevention of aggregation of platelets occurs through blocking ADP receptors by said compound.