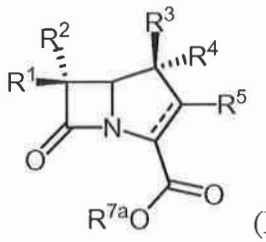
Claims

What is claimed is:

1. A cell lysate comprising a group of enzymes capable of generating a compound of the Formula (I–a):



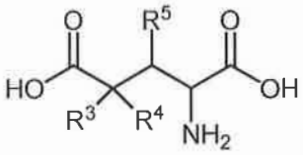
(I–a)

or a salt or tautomer thereof, or a combination thereof;

from:

glucose and glycine or salts thereof; and/or

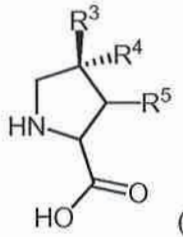
glucose and an optionally substituted glutamate of formula (i):



(i)

or salts thereof; and/or

glucose and a proline compound of formula (iv):



(iv)

or salts thereof;

wherein:

the dashed line ==== represents a single or double bond;

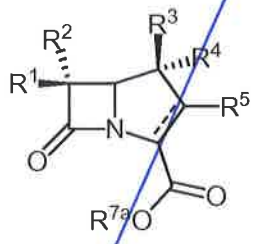
each instance of R^1, R^2, R^3, and R^4 is independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted heteroalkyl, optionally substituted heteroalkenyl, optionally substituted heteroalkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, and optionally substituted heteroaryl;

R^5 is selected from the group consisting of hydrogen, $–OR^8$, $–SR^8$, and $–N(R^8)_2$;

each instance of R^8 is independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted heteroalkyl, optionally substituted heteroalkenyl, optionally substituted heteroalkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, $-C(=O)R^{8a}$, $-C(=O)OR^{8a}$, $-C(=O)SR^{8a}$, $-C(=O)N(R^{8b})_2$, $-C(=NR^{8b})R^{8a}$, $-C(=NR^{8b})OR^{8a}$, $-C(=NR^{8b})SR^{8a}$, $-C(=NR^{8b})N(R^{8b})_2$, $-C(=S)R^{8a}$, $-C(=S)OR^{8a}$, $-C(=S)SR^{8a}$, $-C(=S)N(R^{8b})_2$, $-C(=O)NR^{8b}SO_2R^{8a}$, $-S(=O)R^{8a}$, $-SO_2R^{8a}$, $-SO_2N(R^{8a})_2$, $-Si(R^{8a})_3$, $-P(=O)(R^{8a})_2$, $-P(=O)(OR^{8a})_2$, $-P(=O)(R^{8a})(OR^{8a})$, $-P(=O)(R^{8a})(N(R^{8b})_2)$, $-P(=O)(N(R^{8b})_2)_2$, $-P(=O)_2R^{8a}$, $-P(=O)_2OR^{8a}$, $-P(=O)_2N(R^{8b})_2$, $-B(R^{8a})_2$, $-B(OR^{8a})_2$, and $-BR^{8a}(OR^{8a})$, wherein R^{8a} is selected from the group consisting of optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted heteroalkyl, optionally substituted heteroalkenyl, optionally substituted heteroalkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, if attached to an oxygen atom an oxygen protecting group, and if attached to a sulfur atom a sulfur protecting group, or two R^{8a} groups or an R^{8a} and R^{8b} group are joined to form an optionally substituted heterocyclic ring; and each instance of R^{8b} is independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted heteroalkyl, optionally substituted heteroalkenyl, optionally substituted heteroalkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, and a nitrogen protecting group, or two R^{8b} are joined to form an optionally substituted heterocyclic ring; and

R^{7a} is hydrogen.

2. A method of generating a compound of Formula (I–a):



(I–a)

or a salt or tautomer thereof, or a combination thereof;

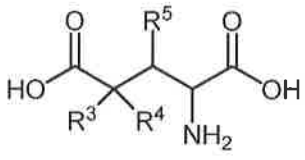
the method comprising:

providing a cell lysate of claim 1 comprising one or more enzymes, wherein the one or more enzymes are selected from the group consisting of gamma–glutamyl kinase, Glu–5–P dehydrogenase, glycolysis/Acetyl-CoA biosynthesis multi–enzyme, an Acetyl-CoA acetyltransferase, a beta–oxidation multienzyme, a Crotonyl–CoA reductase, an Acetyl-CoA carboxylase, a Malonyl-CoA reductase, a threonine aldolase, a beta–alanine transferase, a proline 3-hydroxylase, a proline oxidase, a carboxymethyl–Pro synthase, a carbapenam synthetase, a beta–lactam synthetase, a carbapenem synthase, a transferase, an oxygenase, and a methyltransferase, and isozymes thereof;

wherein the one or more cell lysates are contacted with:

(1) glucose and glycine or salts thereof; and/or

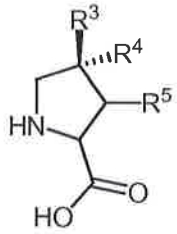
(2) glucose and an optionally substituted glutamate of the formula (i):



(i)

or salts thereof, and/or

(3) glucose and a proline compound of formula (iv):



(iv)

or salts thereof;

wherein:

the dashed line ==== represents a single or double bond;

each instance of R^1, R^2, R^3, and R^4 is independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted heteroalkyl, optionally substituted heteroalkenyl, optionally substituted heteroalkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, and optionally substituted heteroaryl; and

R^5 is selected from the group consisting of hydrogen, $–OR^8$, $–SR^8$, and $–N(R^8)_2$;

each instance of R^8 is independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted heteroalkyl, optionally substituted heteroalkenyl, optionally substituted heteroalkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl,

optionally substituted aryl, optionally substituted heteroaryl, $-C(=O)R^{8a}$, $-C(=O)OR^{8a}$, $-C(=O)SR^{8a}$, $-C(=O)N(R^{8b})_2$, $-C(=NR^{8b})R^{8a}$, $-C(=NR^{8b})OR^{8a}$, $-C(=NR^{8b})SR^{8a}$, $-C(=NR^{8b})N(R^{8b})_2$, $-C(=S)R^{8a}$, $-C(=S)OR^{8a}$, $-C(=S)SR^{8a}$, $-C(=S)N(R^{8b})_2$, $-C(=O)NR^{8b}SO_2R^{8a}$, $-S(=O)R^{8a}$, $-SO_2R^{8a}$, $-SO_2N(R^{8a})_2$, $-Si(R^{8a})_3$, $-P(=O)(R^{8a})_2$, $-P(=O)(OR^{8a})_2$, $-P(=O)(R^{8a})(OR^{8a})$, $-P(=O)(R^{8a})(N(R^{8b})_2)$, $-P(=O)(N(R^{8b})_2)_2$, $-P(=O)_2R^{8a}$, $-P(=O)_2OR^{8a}$, $-P(=O)_2N(R^{8b})_2$, $-B(R^{8a})_2$, $-B(OR^{8a})_2$, and $-BR^{8a}(OR^{8a})$, wherein R^{8a} is selected from the group consisting of optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted heteroalkyl, optionally substituted heteroalkenyl, optionally substituted heteroalkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, if attached to an oxygen atom an oxygen protecting group, and if attached to a sulfur atom a sulfur protecting group, or two R^{8a} groups or an R^{8a} and R^{8b} group are joined to form an optionally substituted heterocyclic ring; and each instance of R^{8b} is independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted heteroalkyl, optionally substituted heteroalkenyl, optionally substituted heteroalkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, and a nitrogen protecting group, or two R^{8b} are joined to form an optionally substituted heterocyclic ring; and

R^{7a} is hydrogen.

3. The lysate or method of claims 1 or 2, wherein R^1 is hydrogen.

4. The lysate or method of claims 1 or 2, wherein R^3 is hydrogen or $-CH_3$.

5. The lysate or method of claims 1 or 2, wherein R^2 is hydrogen, $-CH_3$ or $-CH_2CH_3$.

6. The lysate or method of claims 1 or 2, wherein R^4 is hydrogen.

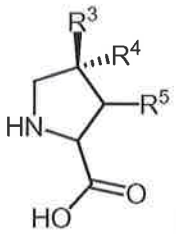
7. The lysate or method of claims 1 or 2, wherein one or more enzymes selected from the group consisting of gamma–glutamyl kinase, Glu–5–P dehydrogenase, glycolysis/Acetyl-CoA biosynthesis multi–enzyme, an Acetyl-CoA acetyltransferase, a beta–oxidation multienzyme, a Crotonyl–CoA reductase, an Acetyl-CoA carboxylase, a Malonyl-CoA

reductase, a threonine aldolase, a beta–alanine transferase, a proline 3-hydroxylase, a proline oxidase, and isozymes thereof, were present in the cell cytoplasm prior to lysing.

8. The lysate or method of claims 1 or 2, wherein one or more enzymes selected from the group consisting of a carboxymethyl–Pro synthase, a carbapenam synthetase, a beta–lactam synthetase, a carbapenem synthase, a transferase, an oxygenase, and a methyltransferase, and isozymes thereof, were sequestered in the periplasmic space of the cell prior to lysing.

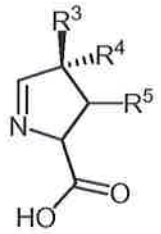
9. The lysate or method of claims 1 or 2, wherein the cell lysate is a lysate of an *E.coli* organism engineered to overexpress the group of enzymes.

10. The lysate or method of claims 1 or 2, wherein the proline compound of formula (iv):



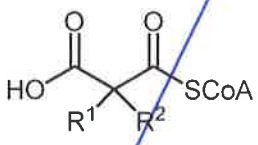
(iv)

or salt thereof, is enzymatically converted to a pyrrole compound of formula:



(v)

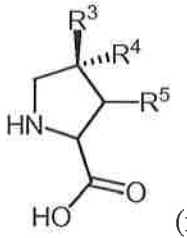
or salt thereof; upon contact with a proline oxidase; and wherein glucose or salt thereof is enzymatically converted to an optionally substituted CoA compound of formula (iii):



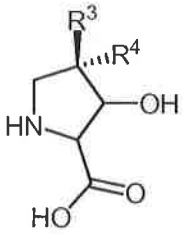
(iii)

or salt thereof; wherein –SCoA is Coenzyme A monoradical.

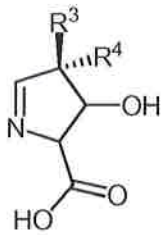
11. The lysate or method of claims 1 or 2, wherein the proline compound of formula (iv):


(iv)

or salt thereof, wherein R^5 is hydrogen, is enzymatically converted to a 3-hydroxylated proline compound of formula:

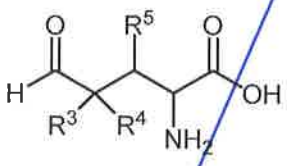

(iv-a)

or salt thereof; upon contact with a proline-3-hydroxylase, and the 3-hydroxylated proline compound of formula (iv-a) or salt thereof, is enzymatically converted to a 3-hydroxylated pyrrole compound of formula:


(v-a)

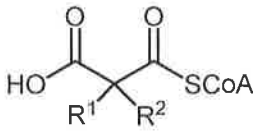
upon contact with a proline oxidase.

12. The lysate or method of claims 1 or 2, wherein the glucose and glycine or salts thereof are enzymatically converted to an optionally substituted glutamate semialdehyde of formula (ii):


(ii)

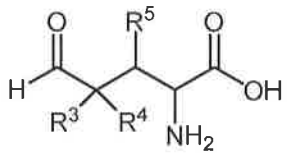
or salt thereof, upon contact with one or more enzymes selected from the group consisting of glycolysis/Acetyl-CoA biosynthesis multienzyme, Acetyl-CoA carboxylase, Malonyl-CoA reductase, threonine aldolase, gamma–glutamyl kinase, and Glu–5–P dehydrogenase, and isozymes thereof; and

wherein glucose or salt thereof is enzymatically converted to an optionally substituted CoA compound of formula (iii):


(iii)

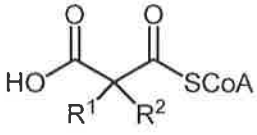
or salt thereof; wherein –SCoA is Coenzyme A monoradical.

13. The lysate or method of claims 1 or 2, wherein the optionally substituted glutamate of formula (i) or salt thereof is converted to an optionally substituted glutamate semialdehyde compound of formula (ii):


(ii)

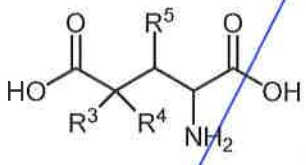
or salt thereof; upon contact with gamma–glutamyl kinase and Glu–5–P dehydrogenase; and

wherein glucose or salt thereof is enzymatically converted to an optionally substituted CoA compound of formula (iii):


(iii)

or salt thereof; wherein –SCoA is Coenzyme A monoradical.

14. The lysate or method of claims 1 or 2, wherein the optionally substituted glutamate of formula (i):


(i)

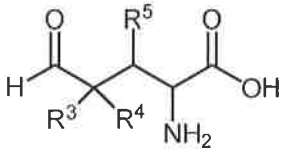
or salt thereof, is enzymatically converted to a proline compound of formula (iv):


(iv)

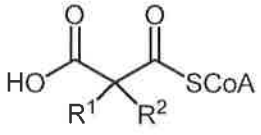
or salt thereof; upon contact with an γ-glutamyl kinase-GP-reductase multienzyme complex.

15. The lysate or method of claims 1 or 2, wherein the cell converts the combination of glucose and glycine, or salts thereof, or the combination of glucose and an optionally

substituted glutamate of the formula (i), or salts thereof, to an optionally substituted CoA compound of formula (iii), or salt thereof, and an optionally substituted glutamate semialdehyde of formula (ii), or salt thereof:



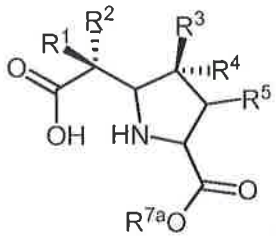
(ii)



(iii)

wherein –SCoA is Coenzyme A monoradical; and

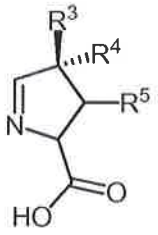
wherein the optionally substituted glutamate semialdehyde of formula (ii) or salt thereof and the optionally substituted CoA compound of formula (iii) or salt thereof generate a pyrrolidinyl compound of Formula (II–a):



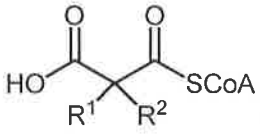
(II–a)

or salt thereof, upon contact with a carboxymethyl–Pro synthase or an isozyme thereof.

16. The lysate or method of claims 1 or 2, wherein the cell converts the combination of glucose or salt thereof and the proline compound of formula (iv) or salt thereof to an optionally substituted CoA compound of formula (iii), or salt thereof, and an pyrrole compound of formula (v), or salt thereof:



(v)



(iii)

wherein –SCoA is Coenzyme A monoradical; and

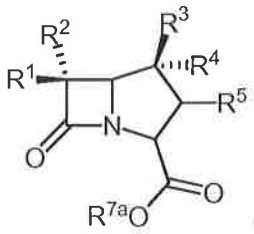
wherein optionally substituted CoA compound of formula (iii), or salt thereof, and an pyrrole compound of formula (v), or salt thereof generate a pyrrolidinyl compound of Formula (II–a):



(II–a)

or salt thereof, upon contact with a carboxymethyl–Pro synthase or an isozyme thereof.

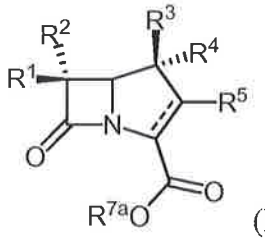
17. The lysate or method of claim 15 or 16, wherein the pyrrolidinyl compound (II–a) or salt thereof generates a β–lactam compound of Formula (III–a):



(III–a)

or salt thereof, upon contact with a carbapenam synthetase, a beta–lactam synthetase, or an isozyme thereof.

18. The lysate or method of claim 17, wherein the β–lactam compound of Formula (III–a) or salt thereof generates a compound of Formula (I–a):

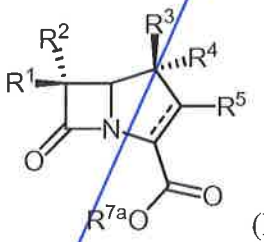


(I–a)

or salt thereof, wherein ==== represents a double bond, upon contact with a carbapenem synthase or isozyme thereof.

19. The lysate or method of claim 18, wherein R^5 is hydrogen.

20. The lysate or method of claim 19, further comprising contacting the compound of Formula (I–a):



(I–a)

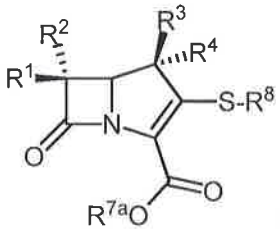
or a salt thereof, wherein ==== represents a double bond;

with a transferase enzyme and a compound of the formula:

HSR^8

wherein R^8 is selected from the group consisting of optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted heteroalkyl, optionally substituted heteroalkenyl, optionally substituted heteroalkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, and optionally substituted heteroaryl;

to provide a thiol–containing compound of Formula (I–c):

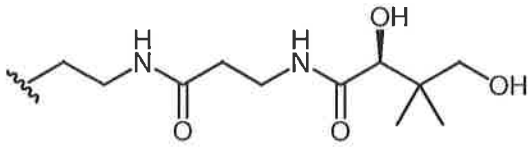


(I–c)

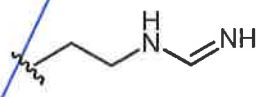
or salt thereof.

21. The lysate or method of claim 20, wherein R^8 is an optionally substituted alkyl, optionally substituted heteroalkyl, or optionally substituted heterocyclyl.

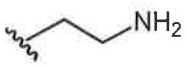
22. The lysate or method of claim 21, wherein R^8 is selected from the group consisting of:



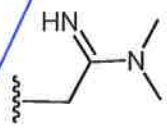
(a)



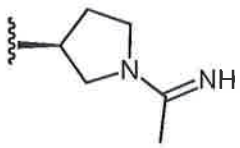
(b)



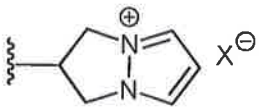
(c)



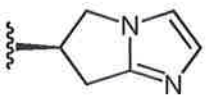
(d)



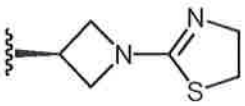
(e)



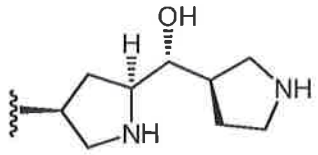
(f)



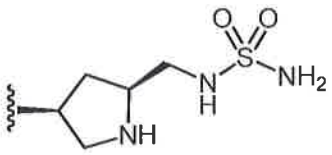
(g)



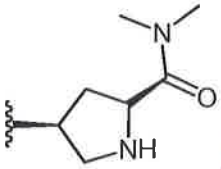
(h)



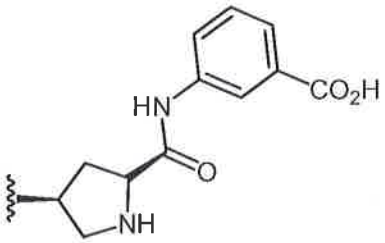
(i)



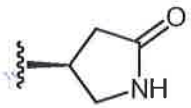
(j)



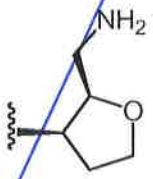
(k)



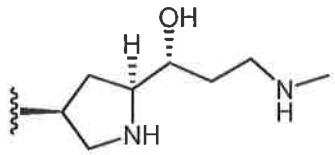
(l)



(m)



(n)



(o)

wherein X^- is a counterion.

23. The lysate or method of claim 18, wherein R^5 is –OH.

24. The lysate or method of claim 23, wherein the compound of Formula (I–a):



(I–a)

or a salt or tautomer thereof, or a combination thereof, wherein ==== represents a double bond;

is contacted with a compound of the formula:

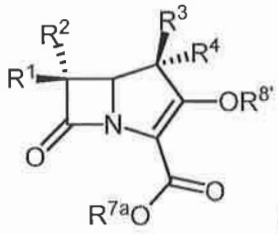
$R^{8'}$–X

wherein:

X is a leaving group; and

$R^{8'}$ is selected from the group consisting of $-C(=O)R^{8a}$, $-C(=O)OR^{8a}$, $-C(=O)SR^{8a}$, $-C(=O)N(R^{8b})_2$, $-C(=NR^{8b})R^{8a}$, $-C(=NR^{8b})OR^{8a}$, $-C(=NR^{8b})SR^{8a}$, $-C(=NR^{8b})N(R^{8b})_2$, $-C(=S)R^{8a}$, $-C(=S)OR^{8a}$, $-C(=S)SR^{8a}$, $-C(=S)N(R^{8b})_2$, $-C(=O)NR^{8b}SO_2R^{8a}$, $-S(=O)R^{8a}$, $-SO_2R^{8a}$, $-SO_2N(R^{8a})_2$, $-Si(R^{8a})_3$, $-P(=O)(R^{8a})_2$, $-P(=O)(OR^{8a})_2$, $-P(=O)(R^{8a})(OR^{8a})$, $-P(=O)(R^{8a})(N(R^{8b})_2)$, $-P(=O)(N(R^{8b})_2)_2$, $-P(=O)_2R^{8a}$, $-P(=O)_2OR^{8a}$, $-P(=O)_2N(R^{8b})_2$, $-B(R^{8a})_2$, $-B(OR^{8a})_2$, and $-BR^{8a}(OR^{8a})$, wherein R^{8a} is selected from the group consisting of optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted heteroalkyl, optionally substituted heteroalkenyl, optionally substituted heteroalkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, if attached to an oxygen atom an oxygen protecting group, and if attached to a sulfur atom a sulfur protecting group, or two R^{8a} groups or an R^{8a} and R^{8b} group are joined to form an optionally substituted heterocyclic ring; and each instance of R^{8b} is independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted heteroalkyl, optionally substituted heteroalkenyl, optionally substituted heteroalkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, and a nitrogen protecting group, or two R^{8b} are joined to form an optionally substituted heterocyclic ring;

to provide a compound of Formula (I–e):



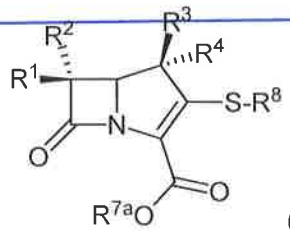
(I–e)

or salt thereof.

25. The lysate or method of claim 24, wherein the compound of Formula (I–e) is contacted with a compound of the formula $HS–R^8$,

wherein R^8 is selected from the group consisting of optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted heteroalkyl, optionally substituted heteroalkenyl, optionally substituted heteroalkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, and optionally substituted heteroaryl;

to provide a thiol–containing compound of Formula (I–c):



(I–c)

or salt thereof.

26. The lysate or method of any one of claims 15 to 25, wherein R^2 is $-CH_2CH_3$.

27. The lysate or method of claim 26, further comprising contacting the compound with an oxygenase enzyme to provide a hydroxylated compound wherein R^2 is $-CH(OH)CH_3$.

28. The lysate or method of any one of claims 15 to 25, wherein R^1 and R^2 are both hydrogen.

29. The lysate or method of claim 28, further comprising contacting the compound with an methyltransferase enzyme to provide a compound wherein R^1 is hydrogen and R^2 is $-CH_3$ or $-CH_2CH_3$.

30. The lysate or method of claim 29, further comprising contacting the compound wherein R^2 is $-CH_2CH_3$ with an oxygenase enzyme to provide a hydroxylated compound wherein R^2 is $-CH(OH)CH_3$.

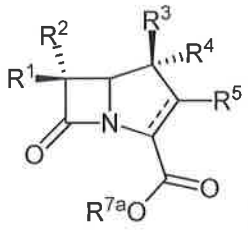
31. A pharmaceutical composition comprising a compound or salt thereof prepared by the method of any one of claims 2–30 and a pharmaceutically acceptable excipient.

32. Use of a compound or salt thereof prepared by a method of any one of claims 2–30 or a pharmaceutical composition of claim 31 in the manufacture of a medicament for treating a bacterial infection.

Claims

What is claimed is:

1. A combination of one or more cell lysates comprising a group of enzymes capable of generating a compound of the Formula (I–a):



(I–a)

or a salt or tautomer thereof, or a combination thereof,

wherein:

the dashed line ==== represents a double bond;

R^1 is hydrogen;

R^2 is $–CH_2CH_3$;

R^3 is hydrogen;

R^4 is hydrogen;

R^5 is –OH; and

R^{7a} is hydrogen;

from glucose and glycine or salts thereof; wherein the group of enzymes is:

a. ProA and ProB, or γ-glutamyl kinase-GP-reductase multienzyme complex;
b. Glk;
c. Pgi;
d. PfkA;
e. Fba;
f. TpiA;
g. GapA;
h. Pgk;
i. GpmA;
j. Eno;
k. PykA;
l. PykF;

m. AceE;

n. AceF;

o. acetyl-CoA acetyltransferase;

p. S-hydratase and 3-hydroxyacyl-CoA dehydrogenase and crotonyl–CoA reductase, or beta–oxidation multienzyme and crotonyl–CoA reductase, or beta-alanine transaminase;

q. acetyl-CoA carboxylase;

r. malonyl-CoA reductase;

s. threonine aldolase;

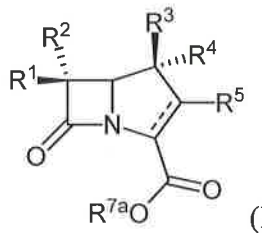
t. carboxymethyl–Pro synthase;

u. carbapenam synthetase or beta–lactam synthetase; and

v. carbapenem synthase;

or isozymes thereof.

2. A combination of one or more cell lysates comprising a group of enzymes capable of generating a compound of the Formula (I–a):



(I–a)

or a salt or tautomer thereof, or a combination thereof,

wherein:

the dashed line ==== represents a double bond;

R^1 is hydrogen;

R^2 is hydrogen;

R^3 is hydrogen;

R^4 is hydrogen;

R^5 is –OH; and

R^{7a} is hydrogen;

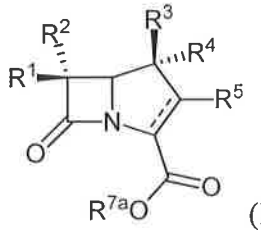
from glucose and glycine or salts thereof;

wherein the group of enzymes is:

a. ProA and ProB, or γ-glutamyl kinase-GP-reductase multienzyme complex;
b. Glk;
c. Pgi;
d. PfkA;
e. Fba;
f. TpiA;
g. GapA;
h. Pgk;
i. GpmA;
j. Eno;
k. PykA;
l. PykF;
m. AceE;
n. AceF;
o. S-hydratase and 3-hydroxyacyl-CoA dehydrogenase and crotonyl–CoA reductase, or beta–oxidation multienzyme and crotonyl–CoA reductase, or beta-alanine transaminase;
p. threonine aldolase;
q. carboxymethyl–Pro synthase;
r. carbapenam synthetase or beta–lactam synthetase;
and
s. carbapenem synthase;

or isozymes thereof.

3. A combination of one or more cell lysates comprising a group of enzymes capable of generating a compound of the Formula (I–a):



(I–a)

or a salt or tautomer thereof, or a combination thereof,

wherein:

the dashed line ==== represents a double bond;

R^1 is hydrogen;

R^2 is $-CH_2CH_3$;

each instance of R^3 and R^4 is independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted heteroalkyl, optionally substituted heteroalkenyl, optionally substituted heteroalkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, and optionally substituted heteroaryl;

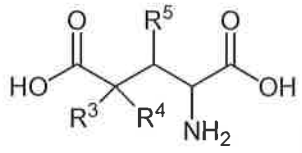
R^5 is hydrogen or $-OR^8$;

each instance of R^8 is independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted heteroalkyl, optionally substituted heteroalkenyl, optionally substituted heteroalkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, $-C(=O)R^{8a}$, $-C(=O)OR^{8a}$, $-C(=O)SR^{8a}$, $-C(=O)N(R^{8b})_2$, $-C(=NR^{8b})R^{8a}$, $-C(=NR^{8b})OR^{8a}$, $-C(=NR^{8b})SR^{8a}$, $-C(=NR^{8b})N(R^{8b})_2$, $-C(=S)R^{8a}$, $-C(=S)OR^{8a}$, $-C(=S)SR^{8a}$, $-C(=S)N(R^{8b})_2$, $-C(=O)NR^{8b}SO_2R^{8a}$, $-S(=O)R^{8a}$, $-SO_2R^{8a}$, $-SO_2N(R^{8a})_2$, $-Si(R^{8a})_3$, $-P(=O)(R^{8a})_2$, $-P(=O)(OR^{8a})_2$, $-P(=O)(R^{8a})(OR^{8a})$, $-P(=O)(R^{8a})(N(R^{8b})_2)$, $-P(=O)(N(R^{8b})_2)_2$, $-P(=O)_2R^{8a}$, $-P(=O)_2OR^{8a}$, $-P(=O)_2N(R^{8b})_2$, $-B(R^{8a})_2$, $-B(OR^{8a})_2$, and $-BR^{8a}(OR^{8a})$, wherein R^{8a} is selected from the group consisting of optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted heteroalkyl, optionally substituted heteroalkenyl, optionally substituted heteroalkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, if attached to an oxygen atom an oxygen protecting group, and if attached to a sulfur atom a sulfur protecting group, or two R^{8a} groups or an R^{8a} and R^{8b} group are joined to form an optionally substituted heterocyclic ring; and each instance of R^{8b} is independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted heteroalkyl, optionally substituted heteroalkenyl, optionally substituted heteroalkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally

substituted heteroaryl, and a nitrogen protecting group, or two R^{8b} are joined to form an optionally substituted heterocyclic ring; and

R^{7a} is hydrogen;

from glucose and an optionally substituted glutamate of formula (i):



(i)

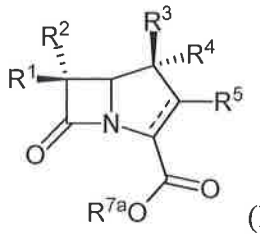
or salts thereof;

wherein the group of enzymes is:

a. ProA and ProB, or γ-glutamyl kinase-GP-reductase multienzyme complex;
b. Glk;
c. Pgi;
d. PfkA;
e. Fba;
f. TpiA;
g. GapA;
h. Pgk;
i. GpmA;
j. Eno;
k. PykA;
l. PykF;
m. AceE;
n. AceF;
o. acetyl-CoA acetyltransferase;
p. acetyl-CoA carboxylase;
q. malonyl-CoA reductase,
r. carboxymethyl–Pro synthase;
s. carbapenam synthetase or beta–lactam synthetase; and
t. carbapenem synthase;

or isozymes thereof.

4. A combination of one or more cell lysates comprising a group of enzymes capable of generating a compound of the Formula (I–a):



(I–a)

or a salt or tautomer thereof, or a combination thereof,

wherein:

the dashed line ---- represents a double bond;

R^1 is hydrogen;

R^2 is hydrogen;

each instance of R^3 and R^4 is independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted heteroalkyl, optionally substituted heteroalkenyl, optionally substituted heteroalkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, and optionally substituted heteroaryl;

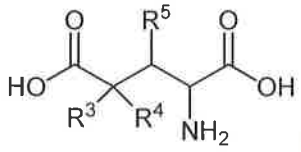
R^5 is hydrogen or $-OR^8$;

each instance of R^8 is independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted heteroalkyl, optionally substituted heteroalkenyl, optionally substituted heteroalkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, $-C(=O)R^{8a}$, $-C(=O)OR^{8a}$, $-C(=O)SR^{8a}$, $-C(=O)N(R^{8b})_2$, $-C(=NR^{8b})R^{8a}$, $-C(=NR^{8b})OR^{8a}$, $-C(=NR^{8b})SR^{8a}$, $-C(=NR^{8b})N(R^{8b})_2$, $-C(=S)R^{8a}$, $-C(=S)OR^{8a}$, $-C(=S)SR^{8a}$, $-C(=S)N(R^{8b})_2$, $-C(=O)NR^{8b}SO_2R^{8a}$, $-S(=O)R^{8a}$, $-SO_2R^{8a}$, $-SO_2N(R^{8a})_2$, $-Si(R^{8a})_3$, $-P(=O)(R^{8a})_2$, $-P(=O)(OR^{8a})_2$, $-P(=O)(R^{8a})(OR^{8a})$, $-P(=O)(R^{8a})(N(R^{8b})_2)$, $-P(=O)(N(R^{8b})_2)_2$, $-P(=O)_2R^{8a}$, $-P(=O)_2OR^{8a}$, $-P(=O)_2N(R^{8b})_2$, $-B(R^{8a})_2$, $-B(OR^{8a})_2$, and $-BR^{8a}(OR^{8a})$, wherein R^{8a} is selected from the group consisting of optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted heteroalkyl, optionally substituted heteroalkenyl, optionally substituted heteroalkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, if attached to an oxygen atom an oxygen protecting group, and if attached

to a sulfur atom a sulfur protecting group, or two R^{8a} groups or an R^{8a} and R^{8b} group are joined to form an optionally substituted heterocyclic ring; and each instance of R^{8b} is independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted heteroalkyl, optionally substituted heteroalkenyl, optionally substituted heteroalkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, and a nitrogen protecting group, or two R^{8b} are joined to form an optionally substituted heterocyclic ring; and

R^{7a} is hydrogen;

from glucose and an optionally substituted glutamate of formula (i):



(i)

or salts thereof;

wherein the group of enzymes is:

a. ProA and ProB, or γ-glutamyl kinase-GP-reductase multienzyme complex;
b. Glk;
c. Pgi;
d. PfkA;
e. Fba;
f. TpiA;
g. GapA;
h. Pgk;
i. GpmA;
j. Eno;
k. PykA;
l. PykF;
m. AceE;
n. AceF;
o. S-hydratase and 3-hydroxyacyl-CoA dehydrogenase, or beta–oxidation multienzyme;

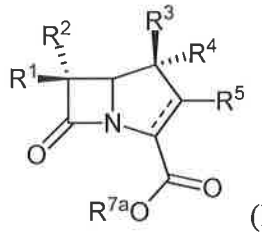
p. carboxymethyl–Pro synthase;

q. carbapenam synthetase or beta–lactam synthetase; and

r. carbapenem synthase;

or isozymes thereof.

5. A combination of one or more cell lysates comprising a group of enzymes capable of generating a compound of the Formula (I–a):



(I–a)

or a salt or tautomer thereof, or a combination thereof,

wherein:

the dashed line ==== represents a double bond;

R^1 is hydrogen;

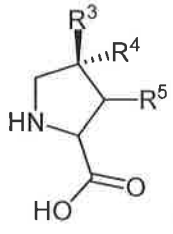
R^2 is $–CH_2CH_3$;

each instance of R^3 and R^4 is independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted heteroalkyl, optionally substituted heteroalkenyl, optionally substituted heteroalkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, and optionally substituted heteroaryl;

R^5 is -OH; and

R^{7a} is hydrogen;

from glucose and a proline compound of formula (iv):



(iv)

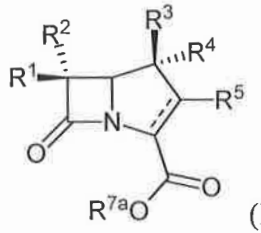
or salts thereof, wherein R^5 is hydrogen;

wherein the group of enzymes is:

a. Glk;
b. Pgi;
c. PfkA;
d. Fba;
e. TpiA;
f. GapA;
g. Pgk;
h. GpmA;
i. Eno;
j. PykA;
k. PykF;
l. AceE;
m. AceF;
n. acetyl-CoA acetyltransferase;
o. acetyl-CoA carboxylase;
p. malonyl-CoA reductase,
q. proline 3-hydroxylase;
r. proline oxidase;
s. carboxymethyl–Pro synthase;
t. carbapenam synthetase or beta–lactam synthetase; and
u. carbapenem synthase;

or isozymes thereof.

6. A combination of one or more cell lysates comprising a group of enzymes capable of generating a compound of the Formula (I–a):



(I–a)

or a salt or tautomer thereof, or a combination thereof,

wherein:

the dashed line ==== represents a double bond;

R^1 is hydrogen;

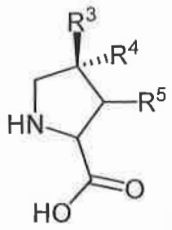
R^2 is hydrogen;

each instance of R^3 and R^4 is independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted heteroalkyl, optionally substituted heteroalkenyl, optionally substituted heteroalkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, and optionally substituted heteroaryl;

R^5 is -OH; and

R^{7a} is hydrogen;

from glucose and a proline compound of formula (iv):



(iv)

or salts thereof, wherein R^5 is hydrogen;

wherein the group of enzymes is:

a. Glk;
b. Pgi;
c. PfkA;
d. Fba;
e. TpiA;
f. GapA;
g. Pgk;
h. GpmA;
i. Eno;
j. PykA;
k. PykF;
l. AceE;
m. AceF;

n. S-hydratase and 3-hydroxyacyl-CoA dehydrogenase, or beta–oxidation multienzyme;

o. proline 3-hydroxylase;

p. proline oxidase;

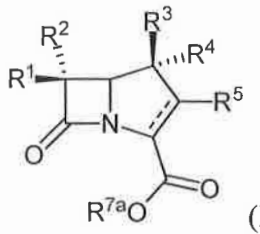
q. carboxymethyl–Pro synthase;

r. carbapenam synthetase or beta–lactam synthetase; and

s. carbapenem synthase;

or isozymes thereof.

7. A combination of one or more cell lysates comprising a group of enzymes capable of generating a compound of the Formula (I–a):



(I–a)

or a salt or tautomer thereof, or a combination thereof,

wherein:

the dashed line ---- represents a double bond;

R^1 is hydrogen;

R^2 is $–CH_2CH_3$;

each instance of R^3 and R^4 is independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted heteroalkyl, optionally substituted heteroalkenyl, optionally substituted heteroalkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, and optionally substituted heteroaryl;

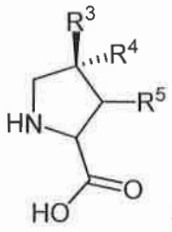
R^5 is hydrogen or $–OR^8$;

each instance of R^8 is independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted heteroalkyl, optionally substituted heteroalkenyl, optionally substituted heteroalkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally

substituted aryl, optionally substituted heteroaryl, –C(=O)R^{8a}, –C(=O)OR^{8a}, –C(=O)SR^{8a}, –C(=O)$N(R^{8b})_2$, –C(=NR^{8b})R^{8a}, –C(=NR^{8b})OR^{8a}, –C(=NR^{8b})SR^{8a}, –C(=NR^{8b})$N(R^{8b})_2$, –C(=S)R^{8a}, –C(=S)OR^{8a}, –C(=S)SR^{8a}, –C(=S)$N(R^{8b})_2$, –C(=O)$NR^{8b}SO_2R^{8a}$, –S(=O)R^{8a}, –SO_2R^{8a}, –$SO_2N(R^{8a})_2$, –$Si(R^{8a})_3$, –P(=O)$(R^{8a})_2$, –P(=O)$(OR^{8a})_2$, –P(=O)$(R^{8a})(OR^{8a})$, –P(=O)$(R^{8a})(N(R^{8b})_2)$, –P(=O)$(N(R^{8b})_2)_2$, –$P(=O)_2R^{8a}$, –$P(=O)_2OR^{8a}$, –$P(=O)_2N(R^{8b})_2$, –$B(R^{8a})_2$, –$B(OR^{8a})_2$, and –$BR^{8a}(OR^{8a})$, wherein R^{8a} is selected from the group consisting of optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted heteroalkyl, optionally substituted heteroalkenyl, optionally substituted heteroalkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, if attached to an oxygen atom an oxygen protecting group, and if attached to a sulfur atom a sulfur protecting group, or two R^{8a} groups or an R^{8a} and R^{8b} group are joined to form an optionally substituted heterocyclic ring; and each instance of R^{8b} is independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted heteroalkyl, optionally substituted heteroalkenyl, optionally substituted heteroalkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, and a nitrogen protecting group, or two R^{8b} are joined to form an optionally substituted heterocyclic ring; and

R^{7a} is hydrogen;

from glucose and a proline compound of formula (iv):



(iv)

or salts thereof;

wherein the group of enzymes is:

a. Glk;

b. Pgi;

c. PfkA;

d. Fba;

e. TpiA;

f. GapA;

g. Pgk;

h. GpmA;

i. Eno;

j. PykA;

k. PykF;

l. AceE;

m. AceF;

n. acetyl-CoA acetyltransferase;

o. acetyl-CoA carboxylase;

p. malonyl-CoA reductase,

q. proline oxidase;

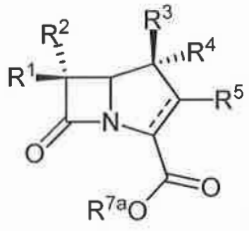
r. carboxymethyl–Pro synthase;

s. carbapenam synthetase or beta–lactam synthetase; and

t. carbapenem synthase;

or isozymes thereof.

8. A combination of one or more cell lysates comprising a group of enzymes capable of generating a compound of the Formula (I–a):



(I–a)

or a salt or tautomer thereof, or a combination thereof,

wherein:

the dashed line ---- represents a double bond;

R^1 is hydrogen;

R^2 is hydrogen;

each instance of R^3 and R^4 is independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted

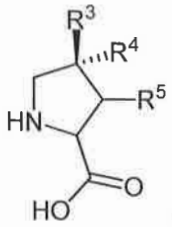
alkynyl, optionally substituted heteroalkyl, optionally substituted heteroalkenyl, optionally substituted heteroalkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, and optionally substituted heteroaryl;

R^5 is hydrogen or $-OR^8$;

each instance of R^8 is independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted heteroalkyl, optionally substituted heteroalkenyl, optionally substituted heteroalkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, $-C(=O)R^{8a}$, $-C(=O)OR^{8a}$, $-C(=O)SR^{8a}$, $-C(=O)N(R^{8b})_2$, $-C(=NR^{8b})R^{8a}$, $-C(=NR^{8b})OR^{8a}$, $-C(=NR^{8b})SR^{8a}$, $-C(=NR^{8b})N(R^{8b})_2$, $-C(=S)R^{8a}$, $-C(=S)OR^{8a}$, $-C(=S)SR^{8a}$, $-C(=S)N(R^{8b})_2$, $-C(=O)NR^{8b}SO_2R^{8a}$, $-S(=O)R^{8a}$, $-SO_2R^{8a}$, $-SO_2N(R^{8a})_2$, $-Si(R^{8a})_3$, $-P(=O)(R^{8a})_2$, $-P(=O)(OR^{8a})_2$, $-P(=O)(R^{8a})(OR^{8a})$, $-P(=O)(R^{8a})(N(R^{8b})_2)$, $-P(=O)(N(R^{8b})_2)_2$, $-P(=O)_2R^{8a}$, $-P(=O)_2OR^{8a}$, $-P(=O)_2N(R^{8b})_2$, $-B(R^{8a})_2$, $-B(OR^{8a})_2$, and $-BR^{8a}(OR^{8a})$, wherein R^{8a} is selected from the group consisting of optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted heteroalkyl, optionally substituted heteroalkenyl, optionally substituted heteroalkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, if attached to an oxygen atom an oxygen protecting group, and if attached to a sulfur atom a sulfur protecting group, or two R^{8a} groups or an R^{8a} and R^{8b} group are joined to form an optionally substituted heterocyclic ring; and each instance of R^{8b} is independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted heteroalkyl, optionally substituted heteroalkenyl, optionally substituted heteroalkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, and a nitrogen protecting group, or two R^{8b} are joined to form an optionally substituted heterocyclic ring; and

R^{7a} is hydrogen;

from glucose and a proline compound of formula (iv):



(iv)

or salts thereof;

wherein the group of enzymes is:

a. Glk;
b. Pgi;
c. PfkA;
d. Fba;
e. TpiA;
f. GapA;
g. Pgk;
h. GpmA;
i. Eno;
j. PykA;
k. PykF;
l. AceE;
m. AceF;
n. S-hydratase and 3-hydroxyacyl-CoA dehydrogenase, or beta–oxidation multienzyme;
o. proline oxidase;
p. carboxymethyl–Pro synthase;
q. carbapenam synthetase or beta–lactam synthetase; and
r. carbapenem synthase;

or isozymes thereof.

9. A method of generating a compound of Formula (I–a):



(I–a)

or a salt or tautomer thereof, or a combination thereof;

the method comprising:

providing the one or more cell lysates of claim 1 comprising:

a. ProA and ProB, or γ-glutamyl kinase-GP-reductase multienzyme complex;
b. Glk;
c. Pgi;
d. PfkA;
e. Fba;
f. TpiA;
g. GapA;
h. Pgk;
i. GpmA;
j. Eno;
k. PykA;
l. PykF;
m. AceE;
n. AceF;
o. acetyl-CoA acetyltransferase;
p. S-hydratase and 3-hydroxyacyl-CoA dehydrogenase and crotonyl–CoA reductase, or beta–oxidation multienzyme and crotonyl–CoA reductase, or beta-alanine transaminase;
q. acetyl-CoA carboxylase;
r. malonyl-CoA reductase;
s. threonine aldolase;
t. carboxymethyl–Pro synthase;
u. carbapenam synthetase or beta–lactam synthetase;

and

v. carbapenem synthase;

or isozymes thereof;

wherein the one or more cell lysates are contacted with glucose and glycine, or salts thereof, to provide a compound of Formula (I-a) or a salt or tautomer thereof, or a combination thereof, wherein:

the dashed line ---- represents a double bond;

R^1 is hydrogen;

R^2 is $-CH_2CH_3$;

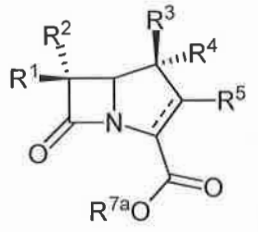
R^3 is hydrogen;

R^4 is hydrogen;

R^5 is –OH; and

R^{7a} is hydrogen.

10. A method of generating a compound of Formula (I–a):



(I–a)

or a salt or tautomer thereof, or a combination thereof;

the method comprising:

providing the one or more cell lysates of claim 2 comprising:

a. ProA and ProB, or γ-glutamyl kinase-GP-reductase multienzyme complex;
b. Glk;
c. Pgi;
d. PfkA;
e. Fba;
f. TpiA;
g. GapA;
h. Pgk;
i. GpmA;
j. Eno;

k. PykA;

l. PykF;

m. AceE;

n. AceF;

o. S-hydratase and 3-hydroxyacyl-CoA dehydrogenase and crotonyl–CoA reductase, or beta–oxidation multienzyme and crotonyl–CoA reductase, or beta-alanine transaminase;

p. threonine aldolase;

q. carboxymethyl–Pro synthase;

r. carbapenam synthetase or beta–lactam synthetase; and

s. carbapenem synthase;

or isozymes thereof;

wherein the one or more cell lysates are contacted with glucose and glycine, or salts thereof, to provide a compound of Formula (I-a) or a salt or tautomer thereof, or a combination thereof, wherein:

the dashed line ==== represents a double bond;

R^1 is hydrogen;

R^2 is hydrogen;

R^3 is hydrogen;

R^4 is hydrogen;

R^5 is –OH; and

R^{7a} is hydrogen.

11. A method of generating a compound of Formula (I–a):



(I–a)

or a salt or tautomer thereof, or a combination thereof;

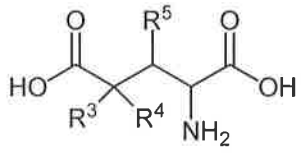
the method comprising:

providing the one or more cell lysates of claim 3 comprising:

a. ProA and ProB, or γ-glutamyl kinase-GP-reductase multienzyme complex;
b. Glk;
c. Pgi;
d. PfkA;
e. Fba;
f. TpiA;
g. GapA;
h. Pgk;
i. GpmA;
j. Eno;
k. PykA;
l. PykF;
m. AceE;
n. AceF;
o. acetyl-CoA acetyltransferase;
p. acetyl-CoA carboxylase;
q. malonyl-CoA reductase,
r. carboxymethyl–Pro synthase;
s. carbapenam synthetase or beta–lactam synthetase; and
t. carbapenem synthase;

or isozymes thereof;

wherein the one or more cell lysates are contacted with glucose and an optionally substituted glutamate of the formula (i):



(i)

or salts thereof, to provide a compound of Formula (I-a) or a salt or tautomer thereof, or a combination thereof, wherein:

the dashed line ==== represents a double bond;

R^1 is hydrogen;

R^2 is $-CH_2CH_3$;

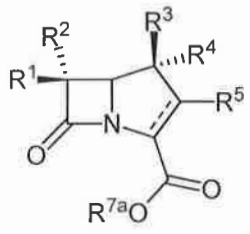
each instance of R^3 and R^4 is independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted heteroalkyl, optionally substituted heteroalkenyl, optionally substituted heteroalkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, and optionally substituted heteroaryl;

R^5 is hydrogen or $-OR^8$;

each instance of R^8 is independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted heteroalkyl, optionally substituted heteroalkenyl, optionally substituted heteroalkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, $-C(=O)R^{8a}$, $-C(=O)OR^{8a}$, $-C(=O)SR^{8a}$, $-C(=O)N(R^{8b})_2$, $-C(=NR^{8b})R^{8a}$, $-C(=NR^{8b})OR^{8a}$, $-C(=NR^{8b})SR^{8a}$, $-C(=NR^{8b})N(R^{8b})_2$, $-C(=S)R^{8a}$, $-C(=S)OR^{8a}$, $-C(=S)SR^{8a}$, $-C(=S)N(R^{8b})_2$, $-C(=O)NR^{8b}SO_2R^{8a}$, $-S(=O)R^{8a}$, $-SO_2R^{8a}$, $-SO_2N(R^{8a})_2$, $-Si(R^{8a})_3$, $-P(=O)(R^{8a})_2$, $-P(=O)(OR^{8a})_2$, $-P(=O)(R^{8a})(OR^{8a})$, $-P(=O)(R^{8a})(N(R^{8b})_2)$, $-P(=O)(N(R^{8b})_2)_2$, $-P(=O)_2R^{8a}$, $-P(=O)_2OR^{8a}$, $-P(=O)_2N(R^{8b})_2$, $-B(R^{8a})_2$, $-B(OR^{8a})_2$, and $-BR^{8a}(OR^{8a})$, wherein R^{8a} is selected from the group consisting of optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted heteroalkyl, optionally substituted heteroalkenyl, optionally substituted heteroalkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, if attached to an oxygen atom an oxygen protecting group, and if attached to a sulfur atom a sulfur protecting group, or two R^{8a} groups or an R^{8a} and R^{8b} group are joined to form an optionally substituted heterocyclic ring; and each instance of R^{8b} is independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted heteroalkyl, optionally substituted heteroalkenyl, optionally substituted heteroalkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, and a nitrogen protecting group, or two R^{8b} are joined to form an optionally substituted heterocyclic ring; and

R^{7a} is hydrogen.

12. A method of generating a compound of Formula (I–a):



(I–a)

or a salt or tautomer thereof, or a combination thereof;

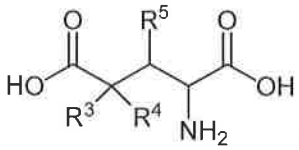
the method comprising:

providing the one or more cell lysates of claim 4 comprising:

a. ProA and ProB, or γ-glutamyl kinase-GP-reductase multienzyme complex;
b. Glk;
c. Pgi;
d. PfkA;
e. Fba;
f. TpiA;
g. GapA;
h. Pgk;
i. GpmA;
j. Eno;
k. PykA;
l. PykF;
m. AceE;
n. AceF;
o. S-hydratase and 3-hydroxyacyl-CoA dehydrogenase, or beta–oxidation multienzyme;
p. carboxymethyl–Pro synthase;
q. carbapenam synthetase or beta–lactam synthetase; and
r. carbapenem synthase;

or isozymes thereof;

wherein the one or more cell lysates are contacted with glucose and an optionally substituted glutamate of the formula (i):



(i),

or salts thereof, to provide a compound of Formula (I-a) or a salt or tautomer thereof, or a combination thereof, wherein:

the dashed line ==== represents a double bond;

R^1 is hydrogen;

R^2 is hydrogen;

each instance of R^3 and R^4 is independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted heteroalkyl, optionally substituted heteroalkenyl, optionally substituted heteroalkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, and optionally substituted heteroaryl;

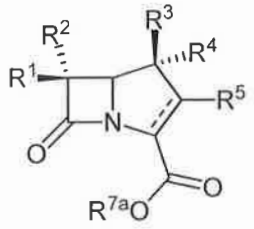
R^5 is hydrogen or $-OR^8$;

each instance of R^8 is independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted heteroalkyl, optionally substituted heteroalkenyl, optionally substituted heteroalkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, $-C(=O)R^{8a}$, $-C(=O)OR^{8a}$, $-C(=O)SR^{8a}$, $-C(=O)N(R^{8b})_2$, $-C(=NR^{8b})R^{8a}$, $-C(=NR^{8b})OR^{8a}$, $-C(=NR^{8b})SR^{8a}$, $-C(=NR^{8b})N(R^{8b})_2$, $-C(=S)R^{8a}$, $-C(=S)OR^{8a}$, $-C(=S)SR^{8a}$, $-C(=S)N(R^{8b})_2$, $-C(=O)NR^{8b}SO_2R^{8a}$, $-S(=O)R^{8a}$, $-SO_2R^{8a}$, $-SO_2N(R^{8a})_2$, $-Si(R^{8a})_3$, $-P(=O)(R^{8a})_2$, $-P(=O)(OR^{8a})_2$, $-P(=O)(R^{8a})(OR^{8a})$, $-P(=O)(R^{8a})(N(R^{8b})_2)$, $-P(=O)(N(R^{8b})_2)_2$, $-P(=O)_2R^{8a}$, $-P(=O)_2OR^{8a}$, $-P(=O)_2N(R^{8b})_2$, $-B(R^{8a})_2$, $-B(OR^{8a})_2$, and $-BR^{8a}(OR^{8a})$, wherein R^{8a} is selected from the group consisting of optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted heteroalkyl, optionally substituted heteroalkenyl, optionally substituted heteroalkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, if attached to an oxygen atom an oxygen protecting group, and if attached to a sulfur atom a sulfur protecting group, or two R^{8a} groups or an R^{8a} and R^{8b} group are joined to form an optionally substituted heterocyclic ring; and each instance of R^{8b} is independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally

substituted alkenyl, optionally substituted alkynyl, optionally substituted heteroalkyl, optionally substituted heteroalkenyl, optionally substituted heteroalkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, and a nitrogen protecting group, or two R^{8b} are joined to form an optionally substituted heterocyclic ring; and

R^{7a} is hydrogen.

13. A method of generating a compound of Formula (I–a):



(I–a)

or a salt or tautomer thereof, or a combination thereof;

the method comprising:

providing the one or more cell lysates of claim 5 comprising:

a. Glk;
b. Pgi;
c. PfkA;
d. Fba;
e. TpiA;
f. GapA;
g. Pgk;
h. GpmA;
i. Eno;
j. PykA;
k. PykF;
l. AceE;
m. AceF;
n. acetyl-CoA acetyltransferase;
o. acetyl-CoA carboxylase;
p. malonyl-CoA reductase,

q. proline 3-hydroxylase;

r. proline oxidase;

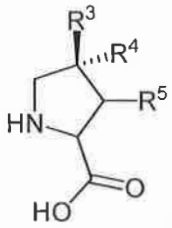
s. carboxymethyl–Pro synthase;

t. carbapenam synthetase or beta–lactam synthetase; and

u. carbapenem synthase;

or isozymes thereof;

wherein the one or more cell lysates are contacted with glucose and a proline compound of formula (iv):



(iv),

or salts thereof, wherein R^5 is hydrogen, to provide a compound of Formula (I-a) or a salt or tautomer thereof, or a combination thereof, wherein:

the dashed line ==== represents a double bond;

R^1 is hydrogen;

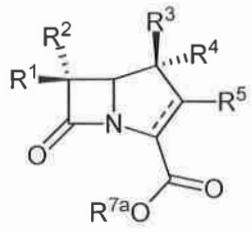
R^2 is $-CH_2CH_3$;

each instance of R^3 and R^4 is independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted heteroalkyl, optionally substituted heteroalkenyl, optionally substituted heteroalkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, and optionally substituted heteroaryl;

R^5 is -OH; and

R^{7a} is hydrogen.

14. A method of generating a compound of Formula (I–a):



(I–a)

or a salt or tautomer thereof, or a combination thereof;

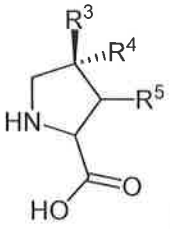
the method comprising:

providing the one or more cell lysates of claim 6 comprising:

a. Glk;
b. Pgi;
c. PfkA;
d. Fba;
e. TpiA;
f. GapA;
g. Pgk;
h. GpmA;
i. Eno;
j. PykA;
k. PykF;
l. AceE;
m. AceF;
n. S-hydratase and 3-hydroxyacyl-CoA dehydrogenase, or beta–oxidation multienzyme;
o. proline 3-hydroxylase;
p. proline oxidase;
q. carboxymethyl–Pro synthase;
r. carbapenam synthetase or beta–lactam synthetase; and
s. carbapenem synthase;

or isozymes thereof;

wherein the one or more cell lysates are contacted with glucose and a proline compound of formula (iv):



(iv),

or salts thereof, wherein R^5 is hydrogen, to provide a compound of Formula (I-a) or a salt or tautomer thereof, or a combination thereof, wherein:

the dashed line ---- represents a double bond;

R^1 is hydrogen;

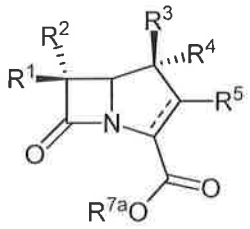
R^2 is hydrogen;

each instance of R^3 and R^4 is independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted heteroalkyl, optionally substituted heteroalkenyl, optionally substituted heteroalkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, and optionally substituted heteroaryl;

R^5 is -OH; and

R^{7a} is hydrogen.

15. A method of generating a compound of Formula (I–a):



(I–a)

or a salt or tautomer thereof, or a combination thereof;

the method comprising:

providing the one or more cell lysates of claim 7 comprising:

a. Glk;
b. Pgi;
c. PfkA;
d. Fba;
e. TpiA;

f. GapA;

g. Pgk;

h. GpmA;

i. Eno;

j. PykA;

k. PykF;

l. AceE;

m. AceF;

n. acetyl-CoA acetyltransferase;

o. acetyl-CoA carboxylase;

p. malonyl-CoA reductase,

q. proline oxidase;

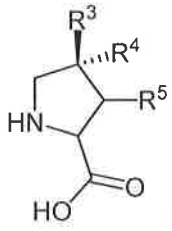
r. carboxymethyl–Pro synthase;

s. carbapenam synthetase or beta–lactam synthetase; and

t. carbapenem synthase;

or isozymes thereof;

wherein the one or more cell lysates are contacted with glucose and a proline compound of formula (iv):



(iv),

or salts thereof, to provide a compound of Formula (I-a) or a salt or tautomer thereof, or a combination thereof, wherein:

the dashed line ---- represents a double bond;

R^1 is hydrogen;

R^2 is $-CH_2CH_3$;

each instance of R^3 and R^4 is independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted heteroalkyl, optionally substituted heteroalkenyl, optionally

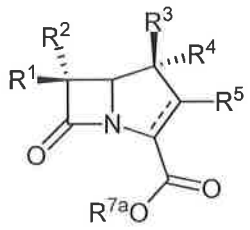
substituted heteroalkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, and optionally substituted heteroaryl;

R^5 is hydrogen or $-OR^8$;

each instance of R^8 is independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted heteroalkyl, optionally substituted heteroalkenyl, optionally substituted heteroalkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, $-C(=O)R^{8a}$, $-C(=O)OR^{8a}$, $-C(=O)SR^{8a}$, $-C(=O)N(R^{8b})_2$, $-C(=NR^{8b})R^{8a}$, $-C(=NR^{8b})OR^{8a}$, $-C(=NR^{8b})SR^{8a}$, $-C(=NR^{8b})N(R^{8b})_2$, $-C(=S)R^{8a}$, $-C(=S)OR^{8a}$, $-C(=S)SR^{8a}$, $-C(=S)N(R^{8b})_2$, $-C(=O)NR^{8b}SO_2R^{8a}$, $-S(=O)R^{8a}$, $-SO_2R^{8a}$, $-SO_2N(R^{8a})_2$, $-Si(R^{8a})_3$, $-P(=O)(R^{8a})_2$, $-P(=O)(OR^{8a})_2$, $-P(=O)(R^{8a})(OR^{8a})$, $-P(=O)(R^{8a})(N(R^{8b})_2)$, $-P(=O)(N(R^{8b})_2)_2$, $-P(=O)_2R^{8a}$, $-P(=O)_2OR^{8a}$, $-P(=O)_2N(R^{8b})_2$, $-B(R^{8a})_2$, $-B(OR^{8a})_2$, and $-BR^{8a}(OR^{8a})$, wherein R^{8a} is selected from the group consisting of optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted heteroalkyl, optionally substituted heteroalkenyl, optionally substituted heteroalkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, if attached to an oxygen atom an oxygen protecting group, and if attached to a sulfur atom a sulfur protecting group, or two R^{8a} groups or an R^{8a} and R^{8b} group are joined to form an optionally substituted heterocyclic ring; and each instance of R^{8b} is independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted heteroalkyl, optionally substituted heteroalkenyl, optionally substituted heteroalkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, and a nitrogen protecting group, or two R^{8b} are joined to form an optionally substituted heterocyclic ring; and

R^{7a} is hydrogen.

16. A method of generating a compound of Formula (I–a):



(I–a)

or a salt or tautomer thereof, or a combination thereof;

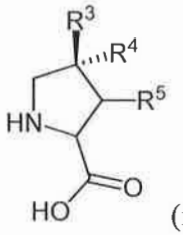
the method comprising:

providing the one or more cell lysates of claim 8 comprising:

a. Glk;
b. Pgi;
c. PfkA;
d. Fba;
e. TpiA;
f. GapA;
g. Pgk;
h. GpmA;
i. Eno;
j. PykA;
k. PykF;
l. AceE;
m. AceF;
n. S-hydratase and 3-hydroxyacyl-CoA dehydrogenase, or beta–oxidation multienzyme;
o. proline oxidase;
p. carboxymethyl–Pro synthase;
q. carbapenam synthetase or beta–lactam synthetase; and
r. carbapenem synthase;

or isozymes thereof;

wherein the one or more cell lysates are contacted with glucose and a proline compound of formula (iv):



(iv),

or salts thereof, to provide a compound of Formula (I-a) or a salt or tautomer thereof, or a combination thereof, wherein:

the dashed line ==== represents a double bond;

R^1 is hydrogen;

R^2 is hydrogen;

each instance of R^3 and R^4 is independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted heteroalkyl, optionally substituted heteroalkenyl, optionally substituted heteroalkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, and optionally substituted heteroaryl;

R^5 is hydrogen or $-OR^8$;

each instance of R^8 is independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted heteroalkyl, optionally substituted heteroalkenyl, optionally substituted heteroalkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, $-C(=O)R^{8a}$, $-C(=O)OR^{8a}$, $-C(=O)SR^{8a}$, $-C(=O)N(R^{8b})_2$, $-C(=NR^{8b})R^{8a}$, $-C(=NR^{8b})OR^{8a}$, $-C(=NR^{8b})SR^{8a}$, $-C(=NR^{8b})N(R^{8b})_2$, $-C(=S)R^{8a}$, $-C(=S)OR^{8a}$, $-C(=S)SR^{8a}$, $-C(=S)N(R^{8b})_2$, $-C(=O)NR^{8b}SO_2R^{8a}$, $-S(=O)R^{8a}$, $-SO_2R^{8a}$, $-SO_2N(R^{8a})_2$, $-Si(R^{8a})_3$, $-P(=O)(R^{8a})_2$, $-P(=O)(OR^{8a})_2$, $-P(=O)(R^{8a})(OR^{8a})$, $-P(=O)(R^{8a})(N(R^{8b})_2)$, $-P(=O)(N(R^{8b})_2)_2$, $-P(=O)_2R^{8a}$, $-P(=O)_2OR^{8a}$, $-P(=O)_2N(R^{8b})_2$, $-B(R^{8a})_2$, $-B(OR^{8a})_2$, and $-BR^{8a}(OR^{8a})$, wherein R^{8a} is selected from the group consisting of optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted heteroalkyl, optionally substituted heteroalkenyl, optionally substituted heteroalkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, if attached to an oxygen atom an oxygen protecting group, and if attached to a sulfur atom a sulfur protecting group, or two R^{8a} groups or an R^{8a} and R^{8b} group are joined to form an optionally substituted heterocyclic ring; and each instance of R^{8b} is independently

selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted heteroalkyl, optionally substituted heteroalkenyl, optionally substituted heteroalkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, and a nitrogen protecting group, or two R^{8b} are joined to form an optionally substituted heterocyclic ring; and

R^{7a} is hydrogen.

17. The lysate or method of any one of claims 3-8 or 11-16, wherein R^3 is hydrogen or $-CH_3$.

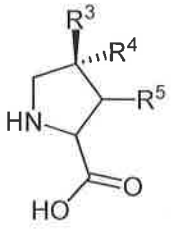
18. The lysate or method of any one of claims 3-8 or 11-16, wherein R^4 is hydrogen.

19. The lysate or method of any one of claims 1-18, wherein one or more enzymes selected from the group consisting of ProA, ProB, γ-glutamyl kinase-GP-reductase multienzyme complex, Glk, Pgi, PfkA, Fba, TpiA, GapA, Pgk, GpmA, Eno, PykA, PykF, AceE, and AceF, acetyl-CoA acetyltransferase, beta–oxidation multienzyme, S-hydratase, 3-hydroxyacyl-CoA dehydrogenase, crotonyl–CoA reductase, acetyl-CoA carboxylase, malonyl-CoA reductase, threonine aldolase, beta–alanine transaminase, proline 3-hydroxylase, proline oxidase, and isozymes thereof, were present in the cell cytoplasm prior to lysing.

20. The lysate or method of any one of claims 1-18, wherein one or more enzymes selected from the group consisting of carboxymethyl–Pro synthase, carbapenam synthetase, beta–lactam synthetase, carbapenem synthase, and isozymes thereof,were sequestered in the periplasmic space of the cell prior to lysing.

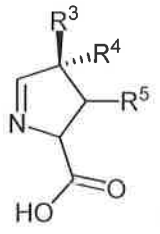
21. The lysate or method of any one of claims 1-18, wherein the cell lysate is a lysate of an *E.coli* organism engineered to overexpress the group of enzymes.

22. The lysate or method of any one of claims 5-8 or 13-16, wherein R^5 is hydrogen or –OH, and the proline compound of formula (iv):



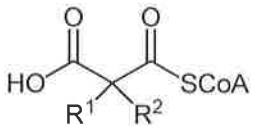
(iv)

or salt thereof, is enzymatically converted to a compound of formula:



(v)

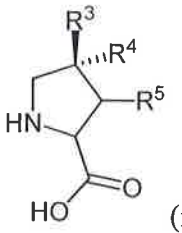
or salt thereof; upon contact with a proline oxidase; and wherein glucose or salt thereof is enzymatically converted to an optionally substituted CoA compound of formula (iii):



(iii)

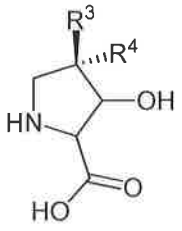
or salt thereof; wherein –SCoA is Coenzyme A monoradical.

23. The lysate or method of any one of claims 5-8 or 13-16, wherein the proline compound of formula (iv):



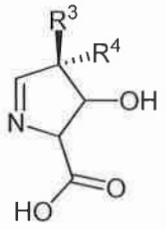
(iv)

or salt thereof, wherein R^5 is hydrogen, is enzymatically converted to a 3-hydroxylated proline compound of formula:



(iv-a)

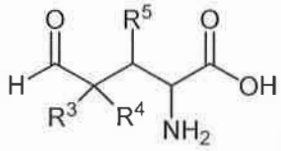
or salt thereof; upon contact with proline-3-hydroxylase, and the 3-hydroxylated proline compound of formula (iv-a) or salt thereof, is enzymatically converted to a 3-hydroxylated compound of formula:



(v-a)

upon contact with proline oxidase.

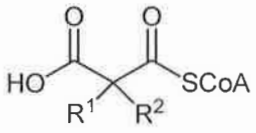
24. The lysate or method of any one of claims 1, 2, 9, or 10, wherein R^5 is –OH, and the glucose and glycine or salts thereof are enzymatically converted to an optionally substituted glutamate semialdehyde of formula (ii):



(ii)

or salt thereof, upon contact with(i) ProA and ProB, or γ-glutamyl kinase-GP-reductase multienzyme complex; (ii) beta–oxidation multienzyme and crotonyl–CoA reductase, or S-hydratase and 3-hydroxyacyl-CoA dehydrogenase and crotonyl–CoA reductase, or a beta-alanine transaminase; (iii) Glk, Pgi, PfkA, Fba, TpiA, GapA, Pgk, GpmA, Eno, PykA, PykF, AceE, and AceF; (iv) threonine aldolase; or isozymes thereof; and

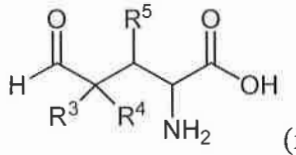
wherein glucose or salt thereof is enzymatically converted to an optionally substituted CoA compound of formula (iii):



(iii)

or salt thereof; wherein –SCoA is Coenzyme A monoradical.

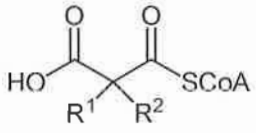
25. The lysate or method of any one of claims 3, 4, 12, or 13, wherein R^5 is hydrogen or –OH and the optionally substituted glutamate of formula (i) or salt thereof is enzymatically converted to an optionally substituted glutamate semialdehyde compound of formula (ii):



(ii)

or salt thereof; upon contact withProA and ProB, or γ-glutamyl kinase-GP-reductase multienzyme complex; and

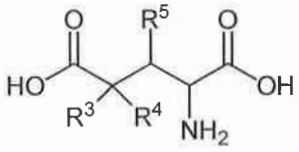
wherein glucose or salt thereof is enzymatically converted to an optionally substituted CoA compound of formula (iii):



(iii)

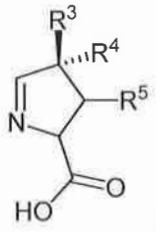
or salt thereof; wherein –SCoA is Coenzyme A monoradical.

26. The lysate or method of any one of claims 3, 4, 12, or 13, wherein R^5 is hydrogen or –OH and the optionally substituted glutamate of formula (i):



(i)

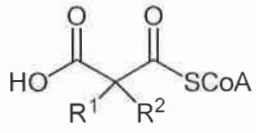
or salt thereof, is enzymatically converted to a compound of formula (v):



(v)

or salt thereof; upon contact with ProA and ProB, or γ-glutamyl kinase-GP-reductase multienzyme complex,

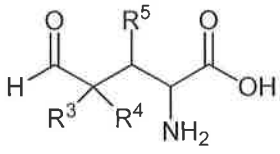
and wherein glucose or salt thereof is enzymatically converted to an optionally substituted CoA compound of formula (iii):



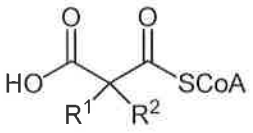
(iii)

or salt thereof; wherein –SCoA is Coenzyme A monoradical.

27. The lysate or method of any one of claims 1-4 or 9-12, wherein R^5 is hydrogen or –OH and the combination of glucose and glycine, or salts thereof, or the combination of glucose and an optionally substituted glutamate of the formula (i), or salts thereof, is enzymatically converted to an optionally substituted CoA compound of formula (iii), or salt thereof, and an optionally substituted glutamate semialdehyde of formula (ii), or salt thereof:



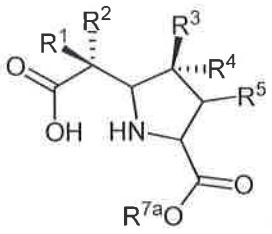
(ii)



(iii)

wherein –SCoA is Coenzyme A monoradical; and

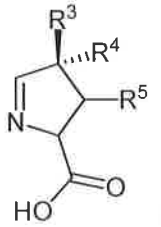
wherein the optionally substituted glutamate semialdehyde of formula (ii) or salt thereof and the optionally substituted CoA compound of formula (iii) or salt thereof is enzymatically converted to a pyrrolidinyl compound of Formula (II–a):



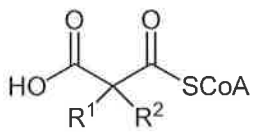
(II–a)

or salt thereof, upon contact with a carboxymethyl–Pro synthase or an isozyme thereof.

28. The lysate or method of any one of claims 5-8 or 13-16, wherein the R^5 is hydrogen or –OH and the combination of glucose or salt thereof and the proline compound of formula (iv) or salt thereof is enzymatically converted to an optionally substituted CoA compound of formula (iii), or salt thereof, and a compound of formula (v), or salt thereof:



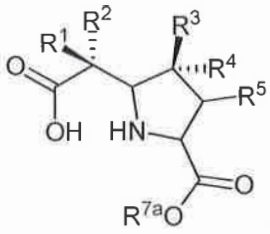
(v)



(iii)

wherein –SCoA is Coenzyme A monoradical; and

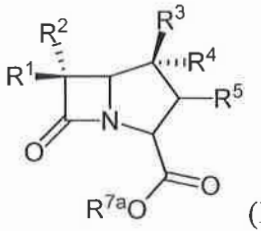
wherein optionally substituted CoA compound of formula (iii), or salt thereof, and a compound of formula (v), or salt thereof is enzymatically converted to a pyrrolidinyl compound of Formula (II–a):



(II–a)

or salt thereof, upon contact with a carboxymethyl–Pro synthase or an isozyme thereof.

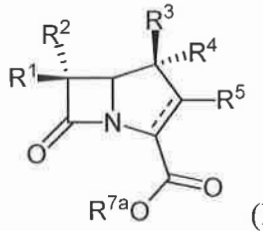
29. The lysate or method of any one of claims 27 or 28, wherein the pyrrolidinyl compound (II–a) or salt thereof is enzymatically converted to a β–lactam compound of Formula (III–a):



(III–a)

or salt thereof, upon contact with carbapenam synthetase, beta–lactam synthetase, or an isozyme thereof.

30. The lysate or method of claim 29, wherein the β–lactam compound of Formula (III–a) or salt thereof is enzymatically converted to a compound of Formula (I–a):

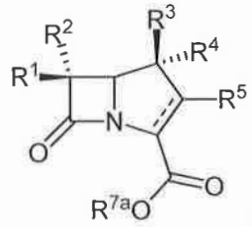


(I–a)

or salt thereof, wherein ==== represents a double bond, upon contact with carbapenem synthase or isozyme thereof.

31. The lysate or method of claim 30, wherein R^5 is hydrogen.

32. The lysate or method of claim 31, further comprising contacting the compound of Formula (I–a):



(I–a)

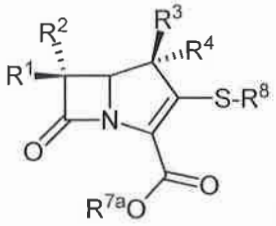
or a salt thereof, wherein ==== represents a double bond;

with a transferase enzyme and a compound of the formula:

HSR^8

wherein R^8 is selected from the group consisting of optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted heteroalkyl, optionally substituted heteroalkenyl, optionally substituted heteroalkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, and optionally substituted heteroaryl;

to provide a thiol–containing compound of Formula (I–c):

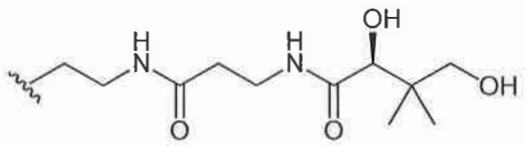


(I–c)

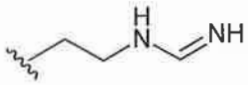
or salt thereof.

33. The lysate or method of claim 32, wherein R^8 is an optionally substituted alkyl, optionally substituted heteroalkyl, or optionally substituted heterocyclyl.

34. The lysate or method of claim 33, wherein R^8 is selected from the group consisting of:



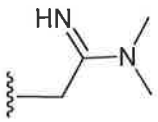
(a)



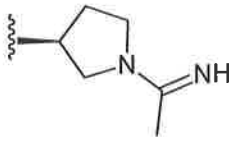
(b)



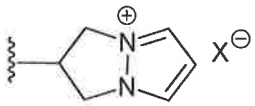
(c)



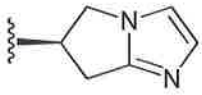
(d)



(e)



(f)



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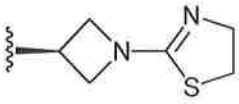
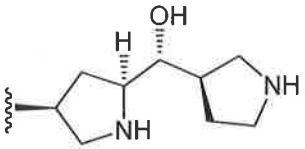
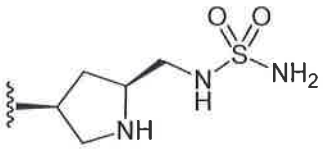


(h)



(i)



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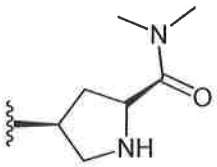
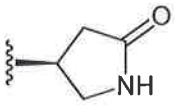


(k)



(l)



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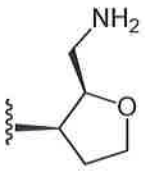

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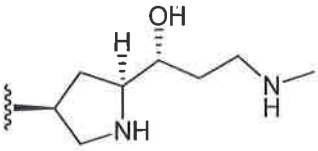


(o)

wherein X^- is a counterion.

35. The lysate or method of claim 30, wherein R^5 is –OH.

36. The lysate or method of claim 35, wherein the compound of Formula (I–a):



(I–a)

or a salt or tautomer thereof, or a combination thereof, wherein ==== represents a double bond; is contacted with a compound of the formula:

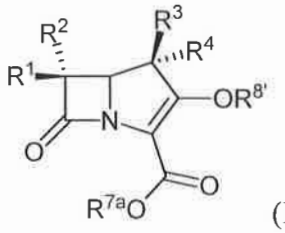
$$R^{8'}–X$$

wherein:

X is a leaving group; and

$R^{8'}$ is selected from the group consisting of $–C(=O)R^{8a}$, $–C(=O)OR^{8a}$, $–C(=O)SR^{8a}$, $–C(=O)N(R^{8b})_2$, $–C(=NR^{8b})R^{8a}$, $–C(=NR^{8b})OR^{8a}$, $–C(=NR^{8b})SR^{8a}$, $–C(=NR^{8b})N(R^{8b})_2$, $–C(=S)R^{8a}$, $–C(=S)OR^{8a}$, $–C(=S)SR^{8a}$, $–C(=S)N(R^{8b})_2$, $–C(=O)NR^{8b}SO_2R^{8a}$, $–S(=O)R^{8a}$, $–SO_2R^{8a}$, $–SO_2N(R^{8a})_2$, $–Si(R^{8a})_3$, $–P(=O)(R^{8a})_2$, $–P(=O)(OR^{8a})_2$, $–P(=O)(R^{8a})(OR^{8a})$, $–P(=O)(R^{8a})(N(R^{8b})_2)$, $–P(=O)(N(R^{8b})_2)_2$, $–P(=O)_2R^{8a}$, $–P(=O)_2OR^{8a}$, $–P(=O)_2N(R^{8b})_2$, $–B(R^{8a})_2$, $–B(OR^{8a})_2$, and $–BR^{8a}(OR^{8a})$, wherein R^{8a} is selected from the group consisting of optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted heteroalkyl, optionally substituted heteroalkenyl, optionally substituted heteroalkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, if attached to an oxygen atom an oxygen protecting group, and if attached to a sulfur atom a sulfur protecting group, or two R^{8a} groups or an R^{8a} and R^{8b} group are joined to form an optionally substituted heterocyclic ring; and each instance of R^{8b} is independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted heteroalkyl, optionally substituted heteroalkenyl, optionally substituted heteroalkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, and a nitrogen protecting group, or two R^{8b} are joined to form an optionally substituted heterocyclic ring;

to provide a compound of Formula (I–e):



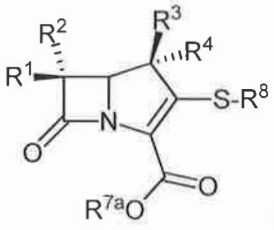
(I–e)

or salt thereof.

37. The lysate or method of claim 36, wherein the compound of Formula (I–e) is contacted with a compound of the formula HS–R^8,

wherein R^8 is selected from the group consisting of optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted heteroalkyl, optionally substituted heteroalkenyl, optionally substituted heteroalkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, and optionally substituted heteroaryl;

to provide a thiol–containing compound of Formula (I–c):



(I–c)

or salt thereof.

38. The lysate or method of any one of claims 1, 3, 5, 7, 9, 11, 13, or 15, wherein R^2 is –CH_2CH_3, further comprising contacting the compound with an oxygenase enzyme to provide a hydroxylated compound wherein R^2 is –$CH(OH)CH_3$.

39. The lysate or method of any one of claims 2, 4, 6, 8, 10, 12, 14, or 16, wherein R^1 and R^2 are both hydrogen, further comprising contacting the compound with an methyltransferase enzyme to provide a compound wherein R^1 is hydrogen and R^2 is –CH_3 or -CH_2CH_3.

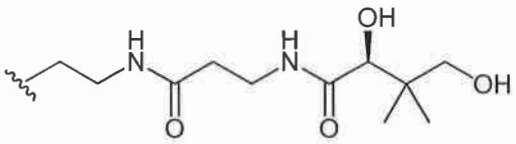
40. The lysate or method of claim 39, further comprising contacting the compound wherein R^2 is $-CH_2CH_3$ with an oxygenase enzyme to provide a hydroxylated compound wherein R^2 is $-CH(OH)CH_3$.

41. A pharmaceutical composition comprising a compound or salt thereof prepared by the method of any one of claims 9-40 and a pharmaceutically acceptable excipient.

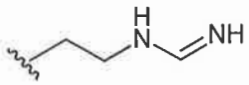
42. Use of a compound or salt thereof prepared by a method of any one of claims 9-40 or a pharmaceutical composition of claim 41 in the manufacture of a medicament for treating a bacterial infection.

43. The method of claim 37,wherein R^8 is an optionally substituted alkyl, optionally substituted heteroalkyl, or optionally substituted heterocyclyl.

44. The method of claim 43,wherein R^8 is selected from the group consisting of:



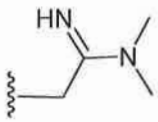
(a)



(b)



(c)



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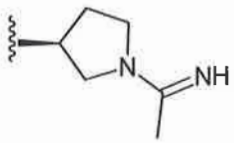

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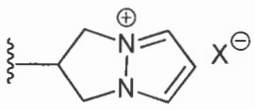

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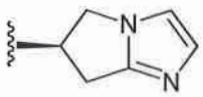

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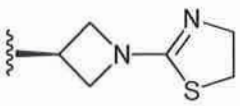

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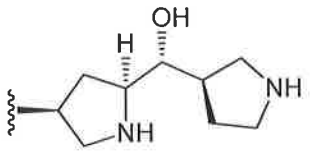

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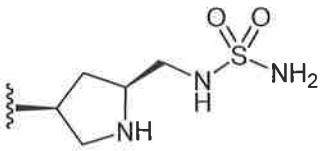

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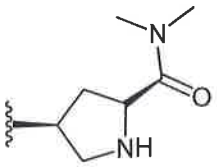

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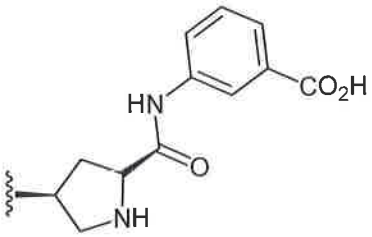

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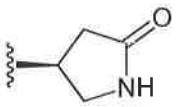

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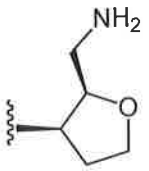

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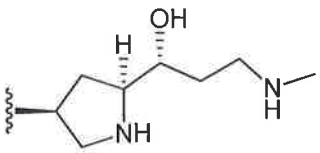

(o)

wherein X^- is a counterion.