

Table S4. List of reactions in the metabolic network we build for *B. cicadellinicola* and the evidences used to assign the direction of the reactions. The metabolites kept in the reactions after filtering appear in bold. **M**: MetaCyc pathways evidence; **T**: topological evidence

Reaction BioCyc ID	Name	Formula	Evidence to assign the direction
RXNI-3	NA	menaquinone-8 + malate → menaquinol + oxaloacetate	M
6PGLUCONOLACT-RXN	6-phospho gluconolactonase	H ₂ O + D-glucono-delta-lactone-6-phosphate → 6-phospho-D-gluconate	M
DEPHOSPHOCOAKIN-RXN	Dephospho-CoA kinase	dephospho-CoA + ATP → ADP + coenzyme A	M
PGLUCISOM-RXN	Glucose-6-phosphate isomerase	beta-D-glucose-6-phosphate → fructose-6-phosphate	T
DIHYDROFOLATESYNT H-RXN	dihydrofolate synthetase	7,8-dihydropteroate + L-glutamate + ATP → ADP + phosphate + 7,8-dihydrofolate	M
HOMOCYSMET-RXN	5-methyl tetrahydropteroyl triglutamate--homocysteine S-methyltransferase	L-homocysteine + 5-methyltetrahydropteroyltri-L-glutamate → L-methionine + tetrahydropteroyltri-L-glutamate	M
THI-P-SYN-RXN	Thiamine-phosphate pyrophosphorylase	4-amino-5-hydroxymethyl-2-methylpyrimidine-pyrophosphate + 4-methyl-5-(beta-hydroxyethyl)thiazole phosphate → diphosphate + thiamine-phosphate	M
F16ALDOLASE-RXN	Fructose-bisphosphate aldolase	fructose-1,6-bisphosphate → dihydroxy-acetone phosphate + D-glyceraldehyde-3-phosphate	T
UDPREDUCT-RXN	NA	UDP + a reduced thioredoxin → H ₂ O + dUDP + an oxidized thioredoxin	M
METHYLENETHFDEHYDROG-NADP-RXN	Methylene tetrahydrofolate dehydrogenase (NADP+)	5,10-methylene-THF + NADP ⁺ ↔ 5,10-methenyltetrahydrofolate + NADPH	
GMP-SYN-NH3-RXN	GMP synthetase	ammonia + xanthosine-5-phosphate + ATP → GMP + diphosphate + AMP	M
RIBULP3EPIM-RXN	ribulose phosphate 3-epimerase	D-ribulose-5-phosphate → D-xylulose-5-phosphate	T
P-PANTOCYSLIG-RXN	Phospho pantothenate--cysteine ligase	D-4'-phosphopantothenate + L-cysteine + CTP → diphosphate + R-4'-phosphopantothenoyl-L-cysteine + CMP	M
GLUTRACE-RXN	Glutamate racemase	L-glutamate → D-glutamate	M
RIBOFLAVINKIN-RXN	Riboflavin kinase	ATP + riboflavin → FMN + ADP	M
3-DEHYDROQUINATE-DEHYDRATASE-RXN	3-dehydroquinate dehydratase	3-dehydroquinate → H ₂ O + 3-dehydro-shikimate	M
SIROHEME-FERROCHELAT-RXN	Sirohydrochlorin ferrochelatase	sirohydrochlorin + Fe ²⁺ → H ⁺ + siroheme	M

Reaction BioCyc ID	Name	Formula	Evidence to assign the direction
1.5.1.20-RXN	Methylene tetrahydrofolate reductase (NADPH)	$H^+ + 5,10\text{-methylene-THF} + NAD(P)H \rightarrow NAD(P)^+ + 5\text{-methyl-THF}$	M
DIHYDROOROTOX-RXN	Dihydroorotate oxidase	dihydroorotate + oxygen \rightarrow H ₂ O ₂ + orotate	T
CHORISMATE-SYNTHASE-RXN	Chorismate synthase	5-enolpyruvyl-shikimate-3-phosphate \rightarrow phosphate + chorismate	M
PHOSACETYLTRANS-RXN	Phosphate acetyltransferase	phosphate + acetyl-CoA \leftrightarrow coenzyme A + acetylphosphate	
CDPREDUCT-RXN	NA	a reduced thioredoxin + CDP \rightarrow H ₂ O + dCDP + an oxidized thioredoxin	M
PANTEPADENYLYLTRAN-RXN	Pantetheine-phosphate adenylyl transferase	pantetheine 4'-phosphate + ATP \rightarrow dephospho-CoA + diphosphate	M
RXN-8972TER	UDP-N-acetylmuramoylalanyl-D-glutamate--2,6-diaminopimelate ligase	UDP-N-acetylmuramoyl-L-alanyl-D-glutamate + meso-diaminopimelate + ATP \rightarrow a UDP-N-acetylmuramoyl-tripeptide + ADP + phosphate	M
7KAPSYN-RXN	8-amino-7-oxononanoate synthase	L-alanine + pimeloyl-CoA \rightarrow 7-keto-8-aminopelargonate + coenzyme A + CO ₂	M
H2PTEROATESYNTH-RXN	Dihydropteroate synthase	(2-amino-4-hydroxy-7,8-dihydropteridin-6-yl)methyl diphosphate + p-aminobenzoate \rightarrow diphosphate + 7,8-dihydropteroate	M
GPPSYN-RXN	Dimethyl allyltransferase	dimethylallyl-diphosphate + isopentenyl diphosphate \rightarrow geranyl-diphosphate + diphosphate	M
5-FORMYL-THF-CYCLO-LIGASE-RXN	5-formyl tetrahydrofolate cyclo-ligase	5-formyl-tetrahydrofolate + ATP \leftrightarrow 5,10-methenyltetrahydrofolate + ADP + phosphate	
POLY-RXN	polymerisation	a UDP-N-acetylmuramoyl-pentapeptide \rightarrow UDP-N-acetylmuramoyl-L-alanyl-D-glutamyl-meso-2,6-diaminoheptanedioate- D-alanyl-D-alanine	M
TRANSALDOL-RXN	Transaldolase	D-sedoheptulose-7-phosphate + D-glyceraldehyde-3-phosphate \rightarrow D-erythrose-4-phosphate + fructose-6-phosphate	T
QUINOLINATE-SYNTHA-RXN	NA	dihydroxy-acetone phosphate + iminoaspartate \rightarrow H ₂ O + phosphate + quinolinate	M
RXN-6102	NA	L-glutamate + tetrahydrofolate + ATP \rightarrow tetrahydrofolate-L-glutamate + ADP + phosphate	M
PABSYNMULTI-RXN	synthesis of p-aminobenzoic acid	L-glutamine + chorismate \rightarrow pyruvate + L-glutamate + p-aminobenzoate + H ⁺	T
TRIOSEPIISOMERIZATIO-RXN	Triosephosphate isomerase	D-glyceraldehyde-3-phosphate \leftrightarrow dihydroxy-acetone phosphate	T

Reaction BioCyc ID	Name	Formula	Evidence to assign the direction
SAICARSYN-RXN	Phosphoribosyl aminoimidazole-succino carboxamide synthetase	4-carboxyaminoimidazole ribonucleotide + ATP + L-aspartate → ADP + phosphate + 5'- phosphoribosyl-4-(N-succinocarboxamide)-5-aminoimidazole	M
RXN0-302	2-C-methyl-D-erythritol 2,4-cyclodiphosphate synthase	2-phospho-4-(cytidine 5'-diphospho)-2-C-methyl-D-erythritol → 2-C-methyl-D-erythritol-2,4-cyclodiphosphate + CMP	M
ATPPHOSPHORIBOSYLTRANS-RXN	ATP phosphoribosyl transferase	5-phosphoribosyl 1-pyrophosphate + ATP → phosphoribosyl-ATP + diphosphate	M
PSERTRANSAMPYR-RXN	NA	2-oxo-3-hydroxy-4-phosphobutanoate + L-glutamate → 4-(phosphonoxy)-threonine + 2-ketoglutarate	M
FADSYN-RXN	FMN adenylyl transferase	FMN + ATP → diphosphate + FAD	M
H2NEOPTERINALDOL-RXN	Dihydroneopterin aldolase	7,8-dihydro-D-neopterin → 6-hydroxymethyl-7,8-dihydropterin + glycolaldehyde	M
PRPPAMIDOTRANS-RXN	Amido phosphoribosyl transferase	L-glutamine + H ₂ O + 5-phosphoribosyl 1-pyrophosphate → diphosphate + L-glutamate + 5-phospho-beta-D-ribosyl-amine	M
4.2.3.12-RXN	6-pyruvoyl tetrahydropterin synthase	7,8-dihydroneopterin triphosphate → PPPi + 6-pyruvoyl tetrahydropterin	M
PEPDEPHOS-RXN	Pyruvate kinase	ADP + phosphoenolpyruvate → pyruvate + ATP	M
DIMETHUROPORDEHYDROG-RXN	NA	NAD ⁺ + precorrin-2 → sirohydrochlorin + NADH	M
OROTPDECARB-RXN	Orotidine-5'-phosphate decarboxylase	orotidine-5'-phosphate → UMP + CO₂	M
GDPKIN-RXN	NA	GDP + ATP → ADP + GTP	M
AICARSYN-RXN	Adenylosuccinate lyase	5'-phosphoribosyl-4-(N-succinocarboxamide)-5-aminoimidazole → fumarate + aminoimidazole carboxamide ribonucleotide	M
DIHYDROOROT-RXN	Dihydroorotase	N-carbamoyl-L-aspartate → dihydroorotate + H₂O	M
PHOSNACMURPENTATRANS-RXN	Phospho-N-acetylmuramoyl-pentapeptide-transferase	undecaprenyl phosphate + UDP-N-acetylmuramoyl-L-alanyl-D-glutamyl-meso-2,6-diaminoheptanedioate-D-alanyl-D-alanine → UMP + N-acetylmuramoyl-L-alanyl-D-glutamyl-meso-2,6-diaminoheptane-D-alanyl-D-alanine-diphosphoundecaprenol	T
IMPCYCLOHYDROLASE-RXN	IMP cyclohydrolase	phosphoribosyl-formamido-carboxamide → inosine-5'-phosphate + H₂O	M
GLU6PDEHYDROG-RXN	Glucose-6-phosphate 1-dehydrogenase	beta-D-glucose-6-phosphate + NADP⁺ → H ⁺ + NADPH + D-glucono-&delta;-lactone-6-phosphate	M
UDPKIN-RXN	NA	UDP + ATP → ADP + UTP	M

Reaction BioCyc ID	Name	Formula	Evidence to assign the direction
PABASYN-RXN	Amino deoxychorismate synthase	L-glutamine + chorismate → 4-amino-4-deoxychorismate + L-glutamate	M
P-PANTOCYSDECARB-RXN	Phospho pantothenoyl cysteine decarboxylase	R-4'-phosphopantothenoyl-L-cysteine → panetheine 4'-phosphate + CO ₂	M
UMPKI-RXN	NA	UMP + ATP → UDP + ADP	M
H2PTERIDINEPYROPHOSPHOKIN-RXN	2-amino-4-hydroxy-6-hydroxy methyl dihydro pteridine pyrophospho kinase	6-hydroxymethyl-7,8-dihydropterin + ATP → (2-amino-4-hydroxy-7,8-dihydropteridin-6-yl)methyl diphosphate + AMP	M
S-ADENMETSYN-RXN	Methionine adenosyl transferase	H ₂ O + L-methionine + ATP → diphosphate + phosphate + S-adenosyl-L-methionine	M
2-DEHYDROPANTOATE-REDUCT-RXN	2-dehydropantoate 2-reductase	2-dehydropantoate + NADPH → L-pantoate + NADP ⁺	M
HISTALDEHYD-RXN	Histidinol dehydrogenase	H ₂ O + NAD ⁺ + histidinal → NADH + L-histidine	M
GLUTATHIONE-SYN-RXN	glutathione synthetase	L-γ-glutamylcysteine + ATP + glycine → ADP + phosphate + glutathione	M
FGAMSYN-RXN	Phosphoribosyl formyl glycinamide synthetase	L-glutamine + H ₂ O + 5'-phosphoribosyl-N-formylglycineamide + ATP → 5-phosphoribosyl-N-formylglycineamidine + ADP + phosphate + L-glutamate	M
NAD-SYNTH-NH3-RXN	NAD(+) synthetase	ammonia + deamido-NAD + ATP → diphosphate + NAD⁺ + AMP	M
GTP-CYCLOHYDRO-II-RXN	GTP cyclohydrolase II	H ₂ O + GTP → formate + diphosphate + 2,5-diamino-6-(ribosylamino)-4-(3H)-pyrimidinone 5'-phosphate	M
UDP-NACMURALA-GLU-LIG-RXN	UDP-N-acetylmuramoylalanine--D-glutamate ligase	D-glutamate + ATP + UDP-N-acetylmuramoyl-L-alanine → ADP + phosphate + UDP-N-acetylmuramoyl-L-alanyl-D-glutamate	M
PHOSPHASERDECARB-RXN	Phosphatidyl serine decarboxylase	an L-1-phosphatidylserine → an L-1-phosphatidylethanolamine + CO ₂	M
THYMIDYLATESYN-RXN	Thymidylate synthase	5,10-methylene-THF + dUMP → dTMP + 7,8-dihydrofolate	T
L-ASPARTATE-OXID-RXN	NA	oxygen + L-aspartate → H₂O₂ + iminoaspartate	M
DTDPKIN-RXN	NA	ATP + dTDP → dTTP + ADP	M

Reaction BioCyc ID	Name	Formula	Evidence to assign the direction
1.1.1.262-RXN	4-hydroxythreonine-4-phosphate dehydrogenase	4-(phosphonoxy)-threonine + NAD ⁺ → NADH + (2S)-2-amino-3-oxo-4-phosphonoxybutanoate	M
PGPPHOSPHA-RXN	Phosphatidylglycero phosphatase	H ₂ O + an L-1-phosphatidylglycerol-phosphate → phosphate + an L-1-phosphatidyl-glycerol	M
ASPARTASE-RXN	Aspartate ammonia-lyase	L-aspartate → ammonia + fumarate	M
PDXJ-RXN	NA	1-amino-propan-2-one-3-phosphate + 1-deoxy-D-xylulose 5-phosphate → pyridoxine-5'-phosphate + H ₂ O + phosphate	M
CARDIOLIPSYN-RXN	NA	an L-1-phosphatidyl-glycerol → glycerol + cardiolipin	M
3-DEHYDROQUINATE-SYNTHASE-RXN	3-dehydroquinate synthase	3-deoxy-D-arabino-heptulosonate-7-phosphate → phosphate + 3-dehydroquinate	M
GLUTAMIDOTRANS-RXN	NA	L-glutamine + phosphoribulosylformimino-AICAR-P → D-erythro-imidazole-glycerol-phosphate + L-glutamate + aminoimidazole carboxamide ribonucleotide	M
RIBOFLAVIN-SYN-RXN	Riboflavin synthase	6,7-dimethyl-8-(1-D-ribityl)lumazine → riboflavin + 5-amino-6-ribitylamino-2,4(1H,3H)-pyrimidinedione	M
DUDPKIN-RXN	NA	dUDP + ATP → dUTP + ADP	M
RXN-8447	NA	H ⁺ + (2S)-2-amino-3-oxo-4-phosphonoxybutanoate → 1-amino-propan-2-one-3-phosphate + CO ₂	M
NAG1P-URIDYLTRANS-RXN	UDP-N-acetylglucosamine pyrophosphorylase	N-acetyl-glucosamine-1-phosphate + UTP → diphosphate + UDP-N-acetyl-D-glucosamine	M
RXN0-2921	NA	L-glutamate + ATP + a 5,10-methylene-tetrahydrofolate → ADP + phosphate + a 5,10-methylene-tetrahydrofolate	M
ADENOSYLHOMOCYSTEINE-NUCLEOSIDASE-RXN	Adenosyl homocysteine nucleosidase	S-adenosyl-L-homocysteine + H ₂ O → S-ribosyl-L-homocysteine + adenine	T
ACETATEKIN-RXN	Acetate kinase	acetate + ATP ↔ ADP + acetylphosphate	
ERYTH4PDEHYDROG-RXN	Erythrose-4-phosphate dehydrogenase	H ₂ O + NAD ⁺ + D-erythrose-4-phosphate → H ⁺ + NADH + erythronate-4-phosphate	M
THI-P-KIN-RXN	Thiamine-phosphate kinase	ATP + thiamine-phosphate → ADP + thiamine diphosphate	M
DTMPKI-RXN	Thymidylate kinase	dTMP + ATP → ADP + dTDP	M
5.4.2.10-RXN	Phosphoglucosamine mutase	D-glucosamine-6-phosphate → D-glucosamine 1-phosphate	M

Reaction BioCyc ID	Name	Formula	Evidence to assign the direction
RXN0-5180	NA	isopentenyl diphosphate + (E,E)-farnesyl diphosphate → diphosphate + 2-cis,6-trans,10-trans-geranylgeranyl diphosphate	M
ASPCARBTRANS-RXN	Aspartate carbamoyl transferase	carbamoyl-phosphate + L-aspartate → phosphate + N-carbamoyl-L-aspartate	M
L-ASPARTATE-OXIDASE-RXN	L-aspartate oxidase	H ₂ O + oxygen + L-aspartate → H ₂ O ₂ + ammonia + iminoaspartate	T
ERYTHRON4PDEHYDROG-RXN	NA	NAD ⁺ + erythronate-4-phosphate → 2-oxo-3-hydroxy-4-phosphobutanoate + NADH	M
GARTRANSFORMYL2-RXN	NA	formate + 5-phospho-ribosyl-glycineamide + ATP → 5'-phosphoribosyl-N-formylglycineamide + ADP + phosphate	M
HISTAMINOTRANS-RXN	Histidinol-phosphate aminotransferase	imidazole acetol-phosphate + L-glutamate → L-histidinol-phosphate + 2-ketoglutarate	M
AIRCARBOXY-RXN	Phosphoribosyl aminoimidazole carboxylase	5-aminoimidazole ribonucleotide + CO ₂ → 4-carboxyaminoimidazole ribonucleotide	M
DALADALALIG-RXN	D-alanine--D-alanine ligase	D-alanine + ATP → ADP + D-alanyl-D-alanine + phosphate	M
UDPNACETYLGLUCOSAMENOLPYRTRANS-RXN	UDP-N-acetyl glucosamine 1-carboxyvinyl transferase	phosphoenolpyruvate + UDP-N-acetyl-D-glucosamine → UDP-GlcNAc-enolpyruvate + phosphate	M
ADENYL-KIN-RXN	Adenylate kinase	ATP + AMP → ADP	M
CARBPSYN-RXN	carbamoyl-phosphate synthetase (glutamine-hydrolysing)	L-glutamine + H ₂ O + HCO₃⁻ + ATP → carbamoyl-phosphate + ADP + phosphate + L-glutamate	M
NACGLCTRANS-RXN	Undecaprenyl diphospho-muramoyl pentapeptide beta-N- acetyl glucosaminyl transferase	N-acetylmuramoyl-L-alanyl-D-glutamyl-meso-2,6-diaminoheptane-D-alanyl-D-alanine-diphosphoundecaprenol + UDP-N-acetyl-D-glucosamine → UDP + N-acetylmuramoyl-L-alanyl-D-glutamyl-meso-2,6-diaminoheptane-D-alanyl-D-alanine-diphosphoundecaprenyl-N-acetylglucosamine	M
L-GLN-FRUCT-6-P-AMINOTRANS-RXN	Glucosamine--fructose-6-phosphate aminotransferase (isomerizing)	L-glutamine + fructose-6-phosphate → D-glucosamine-6-phosphate + L-glutamate	M
DXS-RXN	NA	pyruvate + D-glyceraldehyde-3-phosphate → 1-deoxy-D-xylulose 5-phosphate + CO ₂	M
HEMEOSYN-RXN	heme o biosynthesis	H ₂ O + protoheme IX + (E,E)-farnesyl diphosphate → diphosphate + heme o	T
GLYOHMETRANS-RXN	glycine hydroxy methyltransferase	L-serine + tetrahydrofolate ↔ H ₂ O + 5,10-methylene-THF + glycine	

Reaction BioCyc ID	Name	Formula	Evidence to assign the direction
GLUTCYSLIG-RXN	Glutamate--cysteine ligase	L-glutamate + L-cysteine + ATP → ADP + L-γ-glutamylcysteine + phosphate	M
METBALT-RXN	NA	ammonia + succinate + 2-oxobutanoate ← O-succinyl-L-homoserine + H2O	T
RXN-8675	Uroporphyrinogen-III C-methyltransferase	precorrin-1 + S-adenosyl-L-methionine → S-adenosyl-L-homocysteine + precorrin-2	M
AMPSYN-RXN	Adenylosuccinate lyase	adenylo-succinate → fumarate + AMP	M
UROGENIIISYN-RXN	uroporphyrinogen-III synthase	hydroxymethylbilane → H2O + uroporphyrinogen-III	M
ADCLY-RXN	Amino deoxychorismate lyase	4-amino-4-deoxychorismate → pyruvate + p-aminobenzoate	M
GTP-CYCLOHYDRO-I-RXN	GTP cyclohydrolase I	H2O + GTP → formate + 7,8-dihydroneopterin triphosphate	M
DIHYDROFOLATEREDUCT-RXN	Dihydrofolate reductase	NADPH + 7,8-dihydrofolate → tetrahydrofolate + NADP+	M
2.7.7.60-RXN	2-C-methyl-D-erythritol 4-phosphate cytidylyl transferase	2-C-methyl-D-erythritol-4-phosphate + CTP → 4-(cytidine 5'-diphospho)-2-C-methyl-D-erythritol + diphosphate	M
HOMSUCTRAN-RXN	Homoserine O-succinyl transferase	homoserine + succinyl-CoA → O-succinyl-L-homoserine + coenzyme A	M
DCTP-DEAM-RXN	dCTP deaminase	H2O + dCTP → ammonia + dUTP	M
PYRIMSYN3-RXN	Phosphomethylpyrimidine kinase	hydroxymethylpyrimidine phosphate + ATP → ADP + 4-amino-5-hydroxymethyl-2-methylpyrimidine-pyrophosphate	M
RXN-1381	NA	sn-glycerol-3-phosphate + a fatty acyl CoA → coenzyme A + a 2-lysophosphatidate	M
PEPCARBOXYKIN-RXN	Phosphoenolpyruvate carboxykinase (ATP)	oxaloacetate + ATP → ADP + phosphoenolpyruvate + CO2	M
RIBOFLAVINSYNDEAM-RXN	NA	H2O + 2,5-diamino-6-(ribosylamino)-4-(3H)-pyrimidinone 5'-phosphate → ammonia + 5-amino-6-(5'-phosphoribosylamino)uracil	M
RXN-1623	NA	a 2-lysophosphatidate + a fatty acyl CoA → coenzyme A + an L-phosphatidate	M
THIAZOLSYN2-RXN	NA	L-tyrosine + a ThiS-ThiF acyl-disulfide + 1-deoxy-D-xylulose 5-phosphate → a ThiS sulfur-carrier protein + 4-hydroxybenzyl alcohol + a ThiF protein + CO2 + 4-methyl-5-(beta-hydroxyethyl)thiazole phosphate	M
DUTP-PYROP-RXN	dUTP pyrophosphatase	dUTP + H2O → diphosphate + dUMP	M

Reaction BioCyc ID	Name	Formula	Evidence to assign the direction
ACETYL-COA-CARBOXYLTRANSFER-RXN	Acetyl-CoA carboxylase	$H^+ + HCO_3^- + \text{acetyl-CoA} + ATP \rightarrow \text{malonyl-CoA} + ADP + \text{phosphate}$	M
DCDPKIN-RXN	NA	$dCDP + ATP \rightarrow ADP + dCTP$	M
RXN-5985	NA	$9\text{-mercaptodethiobiotin} \rightarrow \text{biotin}$	M
RXN-5984	NA	a sulfurated sulfur donor + dethiobiotin + a sulfur donor \rightarrow 9-mercaptodethiobiotin + an unsulfurated sulfur acceptor	M
DAHPSYN-RXN	2-dehydro-3-deoxyphosphoheptonate aldolase	$H_2O + \text{phosphoenolpyruvate} + \text{D-erythrose-4-phosphate} \rightarrow \text{3-deoxy-D-arabino-heptulosonate-7-phosphate} + \text{phosphate}$	M
ADENYLOSUCCINATE-SYNTHASE-RXN	adenylosuccinate synthetase	$\text{inosine-5'-phosphate} + GTP + \text{L-aspartate} \rightarrow \text{phosphate} + GDP + \text{adenylo-succinate}$	M
HISTPRATPHYD-RXN	Phosphoribosyl-ATP pyrophosphatase	$H_2O + \text{phosphoribosyl-ATP} \rightarrow \text{phosphoribosyl-AMP} + \text{diphosphate}$	M
PYRIMSYN1-RXN	NA	$5\text{-aminoimidazole ribonucleotide} \rightarrow \text{hydroxymethylpyrimidine phosphate}$	M
PNPOXI-RXN	NA	$\text{pyridoxine-5'-phosphate} + \text{oxygen} \rightarrow H_2O_2 + \text{pyridoxal 5'-phosphate}$	M
DETHIOBIOTIN-SYN-RXN	dethiobiotin synthetase	$7,8\text{-diaminopelargonate} + ATP + CO_2 \rightarrow ADP + \text{phosphate} + \text{dethiobiotin}$	M
IMIDPHOSDEHYD-RXN	Imidazoleglycerol-phosphate dehydratase	$\text{D-erythro-imidazole-glycerol-phosphate} \rightarrow \text{imidazole acetol-phosphate} + H_2O$	M
RXN-6282	NA	$H_2O + 5,10\text{-methenyl-tetrahydropteroyl-}[\gamma\text{-Glu}](n) \rightarrow \text{an N10-formyl-tetrahydrofolate}$	M
PRPPSYN-RXN	ribose-phosphate diphosphokinase	$\text{D-ribose-5-phosphate} + ATP \rightarrow 5\text{-phosphoribosyl 1-pyrophosphate} + AMP$	M
GMP-SYN-GLUT-RXN	GMP synthetase (glutamine-hydrolysing)	$L\text{-glutamine} + H_2O + \text{xanthosine-5-phosphate} + ATP \rightarrow \text{GMP} + \text{diphosphate} + L\text{-glutamate} + AMP$	M
DAPASYN-RXN	Adenosylmethionine--8-amino-7-oxononanoate aminotransferase	$7\text{-keto-8-aminopelargonate} + S\text{-adenosyl-L-methionine} \rightarrow 7,8\text{-diaminopelargonate} + S\text{-adenosyl-4-methylthio-2-oxobutanoate}$	M
FPPSYN-RXN	Geranyl transtransferase	$\text{geranyl-diphosphate} + \text{isopentenyl diphosphate} \rightarrow \text{diphosphate} + (E,E)\text{-farnesyl diphosphate}$	T
RXN-8001	NA	$NAD^+ + \text{histidinol} \rightarrow H^+ + NADH + \text{L-histidine}$	T
PANTOATE-BETA-ALANINE-LIG-RXN	Pantoate--beta-alanine ligase	$\text{beta-alanine} + ATP + \text{L-pantoate} \rightarrow \text{pantothenate} + \text{diphosphate} + AMP$	M
ACSERLY-RXN	Cysteine synthase	$O\text{-acetyl-L-serine} + \text{hydrogen sulfide} \rightarrow \text{acetate} + \text{L-cysteine}$	M
O-SUCCHOMOSERLYASE-RXN	O-succinyl homoserine (thiol)-lyase	$O\text{-succinyl-L-homoserine} + \text{L-cysteine} \rightarrow \text{cystathionine} + \text{succinate}$	M

Reaction BioCyc ID	Name	Formula	Evidence to assign the direction
CDPKIN-RXN	NA	CDP + ATP ↔ ADP + CTP	
RIB5PISOM-RXN	Ribose 5-phosphate epimerase	D-ribose-5-phosphate ← D-ribulose-5-phosphate	T
2.8.1.6-RXN	biotin synthase	a sulfurated sulfur donor + dethiobiotin + S-adenosyl-L-methionine + a sulfur donor → biotin + 5'- deoxyadenosine + an unsulfurated sulfur acceptor + L-methionine	M
SERINE-O-ACETTRAN-RXN	Serine O-acetyltransferase	L-serine + acetyl-CoA → coenzyme A + O-acetyl-L-serine	M
QUINOPRIBOTRANS-RXN	Nicotinate-nucleotide pyrophosphorylase (carboxylating)	diphosphate + nicotinate nucleotide + CO ₂ ← quinolinate + 5-phosphoribosyl 1-pyrophosphate	T
RIBOFLAVINSYNREDUC-RXN	NA	H ⁺ + NADPH + 5-amino-6-(5'- phosphoribosylamino)uracil → 5-amino-6-(5'- phosphoribitylamino)uracil + NADP ⁺	M
HISTOLDEHYD-RXN	Histidinol dehydrogenase	NAD ⁺ + histidinol → histidinal + NADH	M
RXN-3742	NA	L-glutamate + ATP + a folylpolyglutamate(n) → ADP + phosphate + a folylpolyglutamate(n)	M
SHIKIMATE-KINASE-RXN	shikimate-kinase	ATP + shikimate → ADP + shikimate-3-phosphate	M
GLYC3PDEHYDROGBIOSYN-RXN	Glycerol-3-phosphate dehydrogenase (NAD(P) ⁺)	H ⁺ + dihydroxy-acetone phosphate + NAD(P)H → NAD(P) ⁺ + sn-glycerol-3-phosphate	M
METHENYLTHFCYCLOHYDRO-RXN	Methenyl tetrahydrofolate cyclohydrolase	5,10-methenyltetrahydrofolate + H ₂ O ↔ 10-formyl-tetrahydrofolate	
PHOSGLYPHOS-RXN	Phosphoglycerate kinase	3-phosphoglycerate + ATP ← ADP + 1,3-diphosphateglycerate	T
6PGLUCONDEHYDROGRXN	Phosphogluconate dehydrogenase (decarboxylating)	NAD(P) ⁺ + 6-phospho-D-gluconate → D-ribulose-5-phosphate + NAD(P)H + CO ₂	M
2PGADEHYDRAT-RXN	Phosphopyruvate hydratase	2-phosphoglycerate → H ₂ O + phosphoenolpyruvate	T
CTPSYN-RXN	CTP synthetase	L-glutamine + H ₂ O + ATP + UTP → ADP + phosphate + L-glutamate + CTP	M
UROPORIIIMETHYLTRANSA-RXN	NA	uroporphyrinogen-III + S-adenosyl-L-methionine → S-adenosyl-L-homocysteine + precorrin-1	M
NAD-SYNTH-GLN-RXN	NAD(+) synthetase (glutamine-hydrolysing)	L-glutamine + H ₂ O + deamido-NAD + ATP → diphosphate + NAD⁺ + L-glutamate + AMP	M
FORMYLTHFGLUSYNTH-RXN	NA	L-glutamate + ATP + an N10-formyl-tetrahydrofolate → ADP + phosphate + an N10-formyl-tetrahydrofolate	M

Reaction BioCyc ID	Name	Formula	Evidence to assign the direction
HISTIDPHOS-RXN	Histidinol-phosphatase	H ₂ O + L-histidinol-phosphate → phosphate + histidinol	M
1TRANSKETO-RXN	Transketolase	D-xylulose-5-phosphate + D-ribose-5-phosphate → D-sedoheptulose-7-phosphate + D-glyceraldehyde-3-phosphate	T
NAD-KIN-RXN	NAD(+) kinase	NAD⁺ + ATP → ADP + NADP⁺	M
PHOSPHASERSYN-RXN	CDP-diacylglycerol--serine O-phosphatidyltransferase	a CDP-diacylglycerol + L-serine → an L-1-phosphatidylserine + CMP	M
GUANYL-KIN-RXN	Guanylate kinase	GMP + ATP → ADP + GDP	M
RXN0-5234	NA	threonine ↔ acetaldehyde + glycine	
RXN-8973	UDP-N-acetylmuramoyl alanyl-D-glutamyl-2,6-diaminopimelate--D-alanyl- D-alanine ligase	a UDP-N-acetylmuramoyl-tripeptide + D-alanyl-D-alanine + ATP → ADP + phosphate + a UDP-N-acetylmuramoyl-pentapeptide	M
RXN-8972BIS	UDP-N-acetylmuramoyl alanyl-D-glutamate--2,6-diaminopimelate ligase	L-lysine + UDP-N-acetylmuramoyl-L-alanyl-D-glutamate + ATP → a UDP-N-acetylmuramoyl-tripeptide + ADP + phosphate	M
IMP-DEHYDROG-RXN	IMP dehydrogenase	inosine-5'-phosphate + H₂O + NAD⁺ → xanthosine-5-phosphate + NADH	M
UNDECAPRENYL-DIPHOSPHATASE-RXN	Undecaprenyl-diphosphatase	H ₂ O + di-trans,poly-cis-undecaprenyl diphosphate → phosphate + undecaprenyl phosphate	M
RXN0-5240	NA	D-alanine + pyridoxal 5'-phosphate → pyruvate + pyridoxamine 5'-phosphate	T
DIOHBUTANONEPSYN-RXN	NA	D-ribulose-5-phosphate → formate + 3,4-dihydroxy-2-butanone-4-P	M
DGDPKIN-RXN	NA	dGDP + ATP → dGTP + ADP	M
3PGAREARR-RXN	Phosphoglycerate mutase	3-phosphoglycerate → 2-phosphoglycerate	T
SHIKIMATE-5-DEHYDROGENASE-RXN	Shikimate 5-dehydrogenase	3-dehydro-shikimate + NADPH → shikimate + NADP⁺	M
NICONUCADENYLYLTRAN-RXN	Nicotinate-nucleotide adenylyl transferase	nicotinate nucleotide + ATP → diphosphate + deamido-NAD	M
DIAMINOPIMEPIM-RXN	Diaminopimelate epimerase	L,L-diaminopimelate → meso-diaminopimelate	M
GLYRIBONUCSYN-RXN	Phosphoribosyl amine--glycine ligase	ATP + glycine + 5-phospho-beta-D-ribosyl-amine → ADP + phosphate + 5-phospho-ribosyl-glycineamide	M

Reaction BioCyc ID	Name	Formula	Evidence to assign the direction
CDPDIGLYSYN-RXN	phosphatidate cytidylyl transferase	an L-phosphatidate + CTP → a CDP-diacylglycerol + diphosphate	M
RXN-6321	NA	5,10-methenyltetrahydrofolate + H ₂ O → 5-formyl-tetrahydrofolate	M
UDPNACETYLMURAMA TEDEHYDROG-RXN	UDP-N-acetylmuramate dehydrogenase	NADPH + UDP-GlcNAc-enolpyruvate → UDP-N-acetylmuramate + NADP ⁺	M
FUMHYDR-RXN	Fumarate hydratase	Malate ← H ₂ O + fumarate	T
OHMETHYLBILANESYN-RXN	Hydroxy methylbilane synthase	H ₂ O + porphobilinogen → ammonia + hydroxymethylbilane	M
RXN-8998	NA	di-trans,poly-cis-nonaprenyl diphosphate + isopentenyl diphosphate → di-trans,poly-cis-decaprenyl diphosphate + diphosphate	M
RXN-8997	NA	isopentenyl diphosphate + di-trans,poly-cis-octaprenyl diphosphate → di-trans,poly-cis-nonaprenyl diphosphate + diphosphate	M
RXN-8999	NA	di-trans,poly-cis-decaprenyl diphosphate + isopentenyl diphosphate → diphosphate + di-trans,poly-cis-undecaprenyl diphosphate	M
RXN-8994	NA	isopentenyl diphosphate + di-trans,poly-cis-pentaprenyl diphosphate → diphosphate + di-trans,poly-cis-hexaprenyl diphosphate	M
PRIBFAICARPISOM-RXN	N-(5'-phospho-D-riboseylformimino)-5-amino-1-(5"-phosphoribosyl)-4-imidazole carboxamide isomerase	phosphoribosylformiminoAICAR-phosphate → phosphoribulosylformimino-AICAR-P	M
RXN-8993	NA	isopentenyl diphosphate + 2-cis,6-trans,10-transgeranylgeranyl diphosphate → diphosphate + di-trans,poly-cis-pentaprenyl diphosphate	M
RXN-8996	NA	isopentenyl diphosphate + di-trans,poly-cis-heptaprenyl diphosphate → diphosphate + di-trans,poly-cis-octaprenyl diphosphate	M
6PFRUCTPHOS-RXN	6-phospho fructokinase	fructose-6-phosphate + ATP → ADP + fructose-1,6-bisphosphate	M
CYSTATIONINE-BETA-LYASE-RXN	Cystathionine beta-lyase	cystathionine + H ₂ O → ammonia + pyruvate + L-homocysteine	M
RXN-8995	NA	isopentenyl diphosphate + di-trans,poly-cis-hexaprenyl diphosphate → diphosphate + di-trans,poly-cis-heptaprenyl diphosphate	M
CMPKI-RXN	Cytidylate kinase	ATP + CMP → ADP + CDP	M
2.3.1.157-RXN	Glucosamine-1-phosphate N-acetyltransferase	acetyl-CoA + D-glucosamine 1-phosphate → coenzyme A + N-acetyl-glucosamine-1-phosphate	M

Reaction BioCyc ID	Name	Formula	Evidence to assign the direction
PHOSPHAGLYPSYN-RXN	CDP-diacylglycerol--glycerol-3-phosphate 3-phosphatidyl transferase	a CDP-diacylglycerol + sn-glycerol-3-phosphate → an L-1-phosphatidylglycerol-phosphate + CMP	M
ISPH2-RXN	NA	H⁺ + 1-hydroxy-2-methyl-2-(E)-butenyl 4-diphosphate + NAD(P)H → NAD(P)⁺ + H₂O + isopentenyl diphosphate	M
AIRS-RXN	Phosphoribosyl formyl glycinamide cyclo-ligase	5-phosphoribosyl-N-formylglycineamide + ATP → ADP + phosphate + 5-aminoimidazole ribonucleotide	M
OROPRIBTRANS-RXN	Orotate phosphoribosyl transferase	orotate + 5-phosphoribosyl 1-pyrophosphate → diphosphate + orotidine-5'-phosphate	M
2.5.1.19-RXN	3-phosphoshikimate 1-carboxyvinyl transferase	phosphoenolpyruvate + shikimate-3-phosphate → phosphate + 5-enolpyruvyl-shikimate-3-phosphate	M
PYRUVDEH-RXN	NA	coenzyme A + NAD ⁺ + pyruvate → NADH + acetyl-CoA + CO ₂	M
FOLYLPOLYGLUTAMAT ESYNTH-RXN	Folyl polyglutamate synthetase	L-glutamate + ATP + a tetrahydrofolate polyglutamate → ADP + phosphate + a tetrahydrofolate polyglutamate	M
PANTOTHENATE-KIN-RXN	Pantothenate kinase	pantothenate + ATP → D-4'-phosphopantothenate + ADP	M
AICARTRANSFORM-RXN	Phosphoribosyl aminoimidazole carboxamide formyltransferase	10-formyl-tetrahydrofolate + aminoimidazole carboxamide ribonucleotide → phosphoribosyl-formamido-carboxamide + tetrahydrofolate	M
GDPREDUCT-RXN	NA	GDP + a reduced thioredoxin → dGDP + H ₂ O + an oxidized thioredoxin	M
RXN0-884	NA	H⁺ + 1-hydroxy-2-methyl-2-(E)-butenyl 4-diphosphate + NAD(P)H → NAD(P)⁺ + H₂O + dimethylallyl-diphosphate	M
DXPREDISOM-RXN	NA	NADPH + 1-deoxy-D-xylulose 5-phosphate → 2-C-methyl-D-erythritol-4-phosphate + NADP ⁺	M
RXN0-882	NA	2-C-methyl-D-erythritol-2,4-cyclodiphosphate + a protein dithiol → H ₂ O + 1-hydroxy-2-methyl-2-(E)-butenyl 4-diphosphate + a protein disulfide	M
2TRANSKETO-RXN	Transketolase	D-xylulose-5-phosphate + D-erythrose-4-phosphate → D-glyceraldehyde-3-phosphate + fructose-6-phosphate	T
GART-RXN	Phosphoribosyl glycinamide formyltransferase	5-phospho-ribosyl-glycineamide + 10-formyl-tetrahydrofolate → 5'-phosphoribosyl-N-formylglycineamide + tetrahydrofolate	M

Reaction BioCyc ID	Name	Formula	Evidence to assign the direction
2.7.1.148-RXN	4-(cytidine 5'-diphospho)-2-C-methyl-D-erythritol kinase	4-(cytidine 5'-diphospho)-2-C-methyl-D-erythritol + ATP → ADP + 2-phospho-4-(cytidine 5'-diphospho)-2-C-methyl-D-erythritol	M
LUMAZINESYN-RXN	NA	3,4-dihydroxy-2-butanone-4-P + 5-amino-6-ribitylamino-2,4(1H,3H)-pyrimidinedione → H ₂ O + phosphate + 6,7-dimethyl-8-(1-D-ribityl)lumazine	M
3-CH3-2-OXOBUTANOATE-OH-CH3-XFER-RXN	3-methyl-2-oxobutanoate hydroxy methyltransferase	H ₂ O + 5,10-methylene-THF + 2-keto-isovalerate → 2-dehydropantoate + tetrahydrofolate	M
GAPOXNPHOSPHN-RXN	Glyceraldehyde 3-phosphate dehydrogenase (phosphorylating)	phosphate + NAD ⁺ + D-glyceraldehyde-3-phosphate → NADH + 1,3-diphosphateglycerate	T
HISTCYCLOHYD-RXN	Phosphoribosyl-AMP cyclohydrolase	H ₂ O + phosphoribosyl-AMP → phosphoribosylformiminoAICAR-phosphate	M
RXN0-742	NA	HCO ₃ ⁻ + 5-aminoimidazole ribonucleotide + ATP → ADP + phosphate + N5-carboxyaminoimidazole ribonucleotide	M
UDP-NACMUR-ALA-LIG-RXN	UDP-N-acetylmuramate--alanine ligase	UDP-N-acetylmuramate + L-alanine + ATP → ADP + phosphate + UDP-N-acetylmuramoyl-L-alanine	M
RXN0-743	NA	N5-carboxyaminoimidazole ribonucleotide → 4-carboxyaminoimidazole ribonucleotide	M
SULITE-REDUCT-RXN	Sulfite reductase (NADPH)	sulfite → hydrogen sulfide	M
HYDROGENSULFITE__45__REDUCTASE__45__RXN	Hydrogen sulfite reductase	bisulfite → trithionate + OH ⁻	M
RXN__45__8315	NA	sulfite → bisulfite	M
ADENYLYLSULFKIN__45__RXN	Adenylyl sulfate kinase	adenosine 5'-phosphosulfate → phosphoadenosine-5'-phosphosulfate	M
_1__46__8__46__4__46__8__45__RXN	Phospho adenylyl-sulfate reductase (thioredoxin)	phosphoadenosine-5'-phosphosulfate → adenosine-3',5'-bisphosphate + sulfite	M
ADENYLYLSULFKIN__45__RXN	Adenylyl sulfate kinase	adenosine 5'-phosphosulfate → phosphoadenosine-5'-phosphosulfate	M
SULFATE__45__ADENYLYLTRANS__45__RXN	Sulfate adenylyl transferase	sulfate + ATP → adenosine 5'-phosphosulfate	M
_325__45__BISPHOSPHATE__45__NUCLEOTIDASE__45__RXN	3'(2'),5'-bisphosphate nucleotidase	adenosine-3',5'-bisphosphate → AMP	M
SUPEROX__45__DISMUT__45__RXN	Superoxide dismutase	O ₂ ⁻ → H ₂ O ₂	M
RXN0__45__1241	NA	L-glutamine → N5-methyl-L-glutamine	M

Reaction BioCyc ID	Name	Formula	Evidence to assign the direction
PMPOXI_45_RXN	Pyridoxamine-phosphate oxidase	pyridoxamine 5'-phosphate → H ₂ O ₂ + pyridoxal 5'-phosphate	M