

The Enzyme List

Class 6 — Ligases

Nomenclature Committee
of the
International Union of Biochemistry and Molecular Biology
(NC-IUBMB)

L^AT_EX version prepared by Andrew McDonald,
School of Biochemistry and Immunology, Trinity College Dublin, Ireland

Generated from the [ExplorEnz](#) database, March 2019

© 2019 IUBMB

Contents

| | |
|--|-----------|
| EC 6.1 Forming carbon-oxygen bonds | 1 |
| EC 6.1.1 Ligases forming aminoacyl-tRNA and related compounds | 2 |
| EC 6.1.2 Acidalcohol ligases (ester synthases) | 7 |
| EC 6.1.3 Cyclo-ligases | 8 |
| EC 6.2 Forming carbon-sulfur bonds | 8 |
| EC 6.2.1 Acid-thiol ligases | 8 |
| EC 6.3 Forming carbon-nitrogen bonds | 22 |
| EC 6.3.1 Acid—ammonia (or amine) ligases (amide synthases) | 22 |
| EC 6.3.2 Acid—amino-acid ligases (peptide synthases) | 26 |
| EC 6.3.3 Cyclo-ligases | 39 |
| EC 6.3.4 Other carbon-nitrogen ligases | 41 |
| EC 6.3.5 Carbon-nitrogen ligases with glutamine as amido-N-donor | 47 |
| EC 6.4 Forming carbon-carbon bonds | 50 |
| EC 6.4.1 Ligases that form carbon-carbon bonds (only sub-subclass identified to date) | 50 |
| EC 6.5 Forming phosphoric-ester bonds | 52 |
| EC 6.5.1 Ligases that form phosphoric-ester bonds (only sub-subclass identified to date) | 52 |
| EC 6.6 Forming nitrogen—metal bonds | 57 |
| EC 6.6.1 Forming coordination complexes | 57 |
| References | 59 |
| Index | 84 |

EC 6.1 Forming carbon-oxygen bonds

This subclass contains a single sub-subclass for enzymes that acylate a tRNA with the corresponding amino acid, forming a carbon-oxygen bond (amino-acid—tRNA ligases; EC 6.1.1).

EC 6.1.1 Ligases forming aminoacyl-tRNA and related compounds

EC 6.1.1.1

Accepted name: tyrosine—tRNA ligase
Reaction: $\text{ATP} + \text{L-tyrosine} + \text{tRNA}^{\text{Tyr}} = \text{AMP} + \text{diphosphate} + \text{L-tyrosyl-tRNA}^{\text{Tyr}}$
Systematic name: L-tyrosine:tRNA^{Tyr} ligase (AMP-forming)
References: [7, 74, 162, 383, 43]

[EC 6.1.1.1 created 1961, modified 2002]

EC 6.1.1.2

Accepted name: tryptophan—tRNA ligase
Reaction: $\text{ATP} + \text{L-tryptophan} + \text{tRNA}^{\text{Trp}} = \text{AMP} + \text{diphosphate} + \text{L-tryptophyl-tRNA}^{\text{Trp}}$
Other name(s): tryptophanyl-tRNA synthetase; L-tryptophan-tRNA^{Trp} ligase (AMP-forming); tryptophanyl-transfer ribonucleate synthetase; tryptophanyl-transfer ribonucleic acid synthetase; tryptophanyl-transfer RNA synthetase; tryptophanyl ribonucleic synthetase; tryptophanyl-transfer ribonucleic synthetase; tryptophanyl-tRNA synthase; tryptophan translase; TrpRS
Systematic name: L-tryptophan:tRNA^{Trp} ligase (AMP-forming)
References: [83, 338, 470]

[EC 6.1.1.2 created 1961, modified 2002]

EC 6.1.1.3

Accepted name: threonine—tRNA ligase
Reaction: $\text{ATP} + \text{L-threonine} + \text{tRNA}^{\text{Thr}} = \text{AMP} + \text{diphosphate} + \text{L-threonyl-tRNA}^{\text{Thr}}$
Other name(s): threonyl-tRNA synthetase; threonyl-transfer ribonucleate synthetase; threonyl-transfer RNA synthetase; threonyl-transfer ribonucleic acid synthetase; threonyl ribonucleic synthetase; threonine-transfer ribonucleate synthetase; threonine translase; threonyl-tRNA synthetase; TRS
Systematic name: L-threonine:tRNA^{Thr} ligase (AMP-forming)
References: [7, 162]

[EC 6.1.1.3 created 1961]

EC 6.1.1.4

Accepted name: leucine—tRNA ligase
Reaction: $\text{ATP} + \text{L-leucine} + \text{tRNA}^{\text{Leu}} = \text{AMP} + \text{diphosphate} + \text{L-leucyl-tRNA}^{\text{Leu}}$
Other name(s): leucyl-tRNA synthetase; leucyl-transfer ribonucleate synthetase; leucyl-transfer RNA synthetase; leucyl-transfer ribonucleic acid synthetase; leucine-tRNA synthetase; leucine translase
Systematic name: L-leucine:tRNA^{Leu} ligase (AMP-forming)
References: [7, 32, 33]

[EC 6.1.1.4 created 1961]

EC 6.1.1.5

Accepted name: isoleucine—tRNA ligase
Reaction: $\text{ATP} + \text{L-isoleucine} + \text{tRNA}^{\text{Ile}} = \text{AMP} + \text{diphosphate} + \text{L-isoleucyl-tRNA}^{\text{Ile}}$
Other name(s): isoleucyl-tRNA synthetase; isoleucyl-transfer ribonucleate synthetase; isoleucyl-transfer RNA synthetase; isoleucine-transfer RNA ligase; isoleucine-tRNA synthetase; isoleucine translase
Systematic name: L-isoleucine:tRNA^{Ile} ligase (AMP-forming)
References: [7, 32, 33]

[EC 6.1.1.5 created 1961]

EC 6.1.1.6

Accepted name: lysine—tRNA ligase
Reaction: $\text{ATP} + \text{L-lysine} + \text{tRNA}^{\text{Lys}} = \text{AMP} + \text{diphosphate} + \text{L-lysyl-tRNA}^{\text{Lys}}$
Other name(s): lysyl-tRNA synthetase; lysyl-transfer ribonucleate synthetase; lysyl-transfer RNA synthetase; L-lysine-transfer RNA ligase; lysine-tRNA synthetase; lysine translase
Systematic name: L-lysine:tRNA^{Lys} ligase (AMP-forming)
References: [7, 62, 216, 405]

[EC 6.1.1.6 created 1961]

EC 6.1.1.7

Accepted name: alanine—tRNA ligase
Reaction: $\text{ATP} + \text{L-alanine} + \text{tRNA}^{\text{Ala}} = \text{AMP} + \text{diphosphate} + \text{L-alanyl-tRNA}^{\text{Ala}}$
Other name(s): alanyl-tRNA synthetase; alanyl-transfer ribonucleate synthetase; alanyl-transfer RNA synthetase; alanyl-transfer ribonucleic acid synthetase; alanine-transfer RNA ligase; alanine transfer RNA synthetase; alanine tRNA synthetase; alanine translase; alanyl-transfer ribonucleate synthase; AlaRS; Ala-tRNA synthetase
Systematic name: L-alanine:tRNA^{Ala} ligase (AMP-forming)
References: [163, 457]

[EC 6.1.1.7 created 1961]

[6.1.1.8 Deleted entry. D-alanine-sRNA synthetase]

[EC 6.1.1.8 created 1961, deleted 1965]

EC 6.1.1.9

Accepted name: valine—tRNA ligase
Reaction: $\text{ATP} + \text{L-valine} + \text{tRNA}^{\text{Val}} = \text{AMP} + \text{diphosphate} + \text{L-valyl-tRNA}^{\text{Val}}$
Other name(s): valyl-tRNA synthetase; valyl-transfer ribonucleate synthetase; valyl-transfer RNA synthetase; valyl-transfer ribonucleic acid synthetase; valine transfer ribonucleate ligase; valine translase
Systematic name: L-valine:tRNA^{Val} ligase (AMP-forming)
References: [32, 33]

[EC 6.1.1.9 created 1961]

EC 6.1.1.10

Accepted name: methionine—tRNA ligase
Reaction: $\text{ATP} + \text{L-methionine} + \text{tRNA}^{\text{Met}} = \text{AMP} + \text{diphosphate} + \text{L-methionyl-tRNA}^{\text{Met}}$
Other name(s): methionyl-tRNA synthetase; methionyl-transfer ribonucleic acid synthetase; methionyl-transfer ribonucleate synthetase; methionyl-transfer RNA synthetase; methionine translase; MetRS
Systematic name: L-methionine:tRNA^{Met} ligase (AMP-forming)
Comments: In those organisms producing *N*-formylmethionyl-tRNA^{fMet} for translation initiation, this enzyme also recognizes the initiator tRNA^{fMet} and catalyses the formation of L-methionyl-tRNA^{fMet}, the substrate for EC 2.1.2.9, methionyl-tRNA formyltransferase.
References: [33, 223]

[EC 6.1.1.10 created 1961, modified 2002]

EC 6.1.1.11

Accepted name: serine—tRNA ligase

Reaction: $\text{ATP} + \text{L-serine} + \text{tRNA}^{\text{Ser}} = \text{AMP} + \text{diphosphate} + \text{L-seryl-tRNA}^{\text{Ser}}$
Other name(s): seryl-tRNA synthetase; SerRS; seryl-transfer ribonucleate synthetase; seryl-transfer RNA synthetase; seryl-transfer ribonucleic acid synthetase; serine transase
Systematic name: L-serine:tRNA^{Ser} ligase (AMP-forming)
Comments: This enzyme also recognizes tRNA^{Sec}, the special tRNA for selenocysteine, and catalyses the formation of L-seryl-tRNA^{Sec}, the substrate for EC 2.9.1.1, L-seryl-tRNA^{Sec} selenium transferase.
References: [193, 249, 459, 314]

[EC 6.1.1.11 created 1961, modified 2002]

EC 6.1.1.12

Accepted name: aspartate—tRNA ligase
Reaction: $\text{ATP} + \text{L-aspartate} + \text{tRNA}^{\text{Asp}} = \text{AMP} + \text{diphosphate} + \text{L-aspartyl-tRNA}^{\text{Asp}}$
Other name(s): aspartyl-tRNA synthetase; aspartyl ribonucleic synthetase; aspartyl-transfer RNA synthetase; aspartic acid transase; aspartyl-transfer ribonucleic acid synthetase; aspartyl ribonucleate synthetase
Systematic name: L-aspartate:tRNA^{Asp} ligase (AMP-forming)
References: [126, 311]

[EC 6.1.1.12 created 1965]

EC 6.1.1.13

Accepted name: D-alanine—poly(phosphoribitol) ligase
Reaction: $\text{ATP} + \text{D-alanine} + \text{poly(ribitol phosphate)} = \text{AMP} + \text{diphosphate} + \text{O-D-alanyl-poly(ribitol phosphate)}$
Other name(s): D-alanyl-poly(phosphoribitol) synthetase; D-alanine: membrane acceptor ligase; D-alanine-D-alanyl carrier protein ligase; D-alanine-membrane acceptor ligase; D-alanine-activating enzyme
Systematic name: D-alanine:poly(phosphoribitol) ligase (AMP-forming)
Comments: A thioester bond is formed transiently between D-alanine and the sulfhydryl group of the 4'-phosphopantetheine prosthetic group of D-alanyl carrier protein during the activation of the alanine. Involved in the synthesis of teichoic acids.
References: [21, 355, 329, 152, 87]

[EC 6.1.1.13 created 1965, modified 2001]

EC 6.1.1.14

Accepted name: glycine—tRNA ligase
Reaction: $\text{ATP} + \text{glycine} + \text{tRNA}^{\text{Gly}} = \text{AMP} + \text{diphosphate} + \text{glycyl-tRNA}^{\text{Gly}}$
Other name(s): glycyl-tRNA synthetase; glycyl-transfer ribonucleate synthetase; glycyl-transfer RNA synthetase; glycyl-transfer ribonucleic acid synthetase; glycyl transase
Systematic name: glycine:tRNA^{Gly} ligase (AMP-forming)
References: [117, 307]

[EC 6.1.1.14 created 1972]

EC 6.1.1.15

Accepted name: proline—tRNA ligase
Reaction: $\text{ATP} + \text{L-proline} + \text{tRNA}^{\text{Pro}} = \text{AMP} + \text{diphosphate} + \text{L-prolyl-tRNA}^{\text{Pro}}$
Other name(s): prolyl-tRNA synthetase; prolyl-transfer RNA synthetase; prolyl-transfer ribonucleate synthetase; proline transase; prolyl-transfer ribonucleic acid synthetase; prolyl-s-RNA synthetase; prolinyl-tRNA ligase
Systematic name: L-proline:tRNA^{Pro} ligase (AMP-forming)
References: [310, 332]

[EC 6.1.1.15 created 1972]

EC 6.1.1.16

Accepted name: cysteine—tRNA ligase
Reaction: $\text{ATP} + \text{L-cysteine} + \text{tRNA}^{\text{Cys}} = \text{AMP} + \text{diphosphate} + \text{L-cysteinyl-tRNA}^{\text{Cys}}$
Other name(s): cysteinyl-tRNA synthetase; cysteinyl-transferRNA synthetase; cysteinyl-transfer ribonucleate synthetase; cysteine translase
Systematic name: L-cysteine:tRNA^{Cys} ligase (AMP-forming)
References: [266]

[EC 6.1.1.16 created 1972]

EC 6.1.1.17

Accepted name: glutamate—tRNA ligase
Reaction: $\text{ATP} + \text{L-glutamate} + \text{tRNA}^{\text{Glu}} = \text{AMP} + \text{diphosphate} + \text{L-glutamyl-tRNA}^{\text{Glu}}$
Other name(s): glutamyl-tRNA synthetase; glutamyl-transfer ribonucleate synthetase; glutamyl-transfer RNA synthetase; glutamyl-transfer ribonucleic acid synthetase; glutamate-tRNA synthetase; glutamic acid translase
Systematic name: L-glutamate:tRNA^{Glu} ligase (AMP-forming)
References: [350]

[EC 6.1.1.17 created 1972]

EC 6.1.1.18

Accepted name: glutamine—tRNA ligase
Reaction: $\text{ATP} + \text{L-glutamine} + \text{tRNA}^{\text{Gln}} = \text{AMP} + \text{diphosphate} + \text{L-glutaminy-tRNA}^{\text{Gln}}$
Other name(s): glutaminy-tRNA synthetase; glutaminy-transfer RNA synthetase; glutaminy-transfer ribonucleate synthetase; glutamine-tRNA synthetase; glutamine translase; glutamate-tRNA ligase; glutaminy ribonucleic acid; GlnRS
Systematic name: L-glutamine:tRNA^{Gln} ligase (AMP-forming)
References: [350]

[EC 6.1.1.18 created 1972]

EC 6.1.1.19

Accepted name: arginine—tRNA ligase
Reaction: $\text{ATP} + \text{L-arginine} + \text{tRNA}^{\text{Arg}} = \text{AMP} + \text{diphosphate} + \text{L-arginyl-tRNA}^{\text{Arg}}$
Other name(s): arginyl-tRNA synthetase; arginyl-transfer ribonucleate synthetase; arginyl-transfer RNA synthetase; arginyl transfer ribonucleic acid synthetase; arginine-tRNA synthetase; arginine translase
Systematic name: L-arginine:tRNA^{Arg} ligase (AMP-forming)
References: [9, 269, 284]

[EC 6.1.1.19 created 1972]

EC 6.1.1.20

Accepted name: phenylalanine—tRNA ligase
Reaction: $\text{ATP} + \text{L-phenylalanine} + \text{tRNA}^{\text{Phe}} = \text{AMP} + \text{diphosphate} + \text{L-phenylalanyl-tRNA}^{\text{Phe}}$
Other name(s): phenylalanyl-tRNA synthetase; phenylalanyl-transfer ribonucleate synthetase; phenylalanine-tRNA synthetase; phenylalanyl-transfer RNA synthetase; phenylalanyl-tRNA ligase; phenylalanyl-transfer RNA ligase; L-phenylalanyl-tRNA synthetase; phenylalanine translase
Systematic name: L-phenylalanine:tRNA^{Phe} ligase (AMP-forming)
References: [408]

[EC 6.1.1.20 created 1972]

EC 6.1.1.21

Accepted name: histidine—tRNA ligase
Reaction: $\text{ATP} + \text{L-histidine} + \text{tRNA}^{\text{His}} = \text{AMP} + \text{diphosphate} + \text{L-histidyl-tRNA}^{\text{His}}$
Other name(s): histidyl-tRNA synthetase; histidyl-transfer ribonucleate synthetase; histidine transase
Systematic name: L-histidine:tRNA^{His} ligase (AMP-forming)
References: [430]

[EC 6.1.1.21 created 1972]

EC 6.1.1.22

Accepted name: asparagine—tRNA ligase
Reaction: $\text{ATP} + \text{L-asparagine} + \text{tRNA}^{\text{Asn}} = \text{AMP} + \text{diphosphate} + \text{L-asparaginyl-tRNA}^{\text{Asn}}$
Other name(s): asparaginyl-tRNA synthetase; asparaginyl-transfer ribonucleate synthetase; asparaginyl transfer RNA synthetase; asparaginyl transfer ribonucleic acid synthetase; asparagyl-transfer RNA synthetase; asparagine transase
Systematic name: L-asparagine:tRNA^{Asn} ligase (AMP-forming)
References: [84]

[EC 6.1.1.22 created 1976]

EC 6.1.1.23

Accepted name: aspartate—tRNA^{Asx} ligase
Reaction: $\text{ATP} + \text{L-aspartate} + \text{tRNA}^{\text{Asx}} = \text{AMP} + \text{diphosphate} + \text{L-aspartyl-tRNA}^{\text{Asx}}$
Other name(s): nondiscriminating aspartyl-tRNA synthetase
Systematic name: L-aspartate:tRNA^{Asx} ligase (AMP-forming)
Comments: When this enzyme acts on tRNA^{Asp}, it catalyses the same reaction as EC 6.1.1.12, aspartate—tRNA ligase. It has, however, diminished discrimination, so that it can also form aspartyl-tRNA^{Asn}. This relaxation of specificity has been found to result from the absence of a loop in the tRNA that specifically recognizes the third position of the anticodon [174]. This accounts for the ability of this enzyme in, for example, *Thermus thermophilus*, to recognize both tRNA^{Asp} (GUC anticodon) and tRNA^{Asn} (GUU anticodon). The aspartyl-tRNA^{Asn} is not used in protein synthesis until it is converted by EC 6.3.5.6, asparaginyl-tRNA synthase (glutamine-hydrolysing), into asparaginyl-tRNA^{Asn}.
References: [174, 381, 25]

[EC 6.1.1.23 created 2002]

EC 6.1.1.24

Accepted name: glutamate—tRNA^{Gln} ligase
Reaction: $\text{ATP} + \text{L-glutamate} + \text{tRNA}^{\text{Gln}} = \text{AMP} + \text{diphosphate} + \text{L-glutamyl-tRNA}^{\text{Gln}}$
Other name(s): nondiscriminating glutamyl-tRNA synthetase
Systematic name: L-glutamate:tRNA^{Gln} ligase (AMP-forming)
Comments: When this enzyme acts on tRNA^{Glu}, it catalyses the same reaction as EC 6.1.1.17, glutamate—tRNA ligase. It has, however, diminished discrimination, so that it can also form glutamyl-tRNA^{Gln}. This relaxation of specificity has been found to result from the absence of a loop in the tRNA that specifically recognizes the third position of the anticodon [174]. This accounts for the ability of this enzyme in, for example, *Bacillus subtilis*, to recognize both tRNA₁^{Gln} (UUG anticodon) and tRNA^{Glu} (UUC anticodon) but not tRNA₂^{Gln} (CUG anticodon). The ability of this enzyme to recognize both tRNA^{Glu} and one of the tRNA^{Gln} isoacceptors derives from their sharing a major identity element, a hypermodified derivative of U³⁴ (5-methylaminomethyl-2-thiouridine). The glutamyl-tRNA^{Gln} is not used in protein synthesis until it is converted by EC 6.3.5.7, glutaminyl-tRNA synthase (glutamine-hydrolysing), into glutaminyl-tRNA^{Gln}.
References: [174, 381, 200]

[EC 6.1.1.24 created 2002]

[6.1.1.25 Deleted entry. lysine—tRNA^{Pyl} ligase. The tRNA^{Pyl} is now known only to be charged with pyrrolysine (cf. EC 6.1.1.26).]

[EC 6.1.1.25 created 2002, deleted 2012]

EC 6.1.1.26

Accepted name: pyrrolysine—tRNA^{Pyl} ligase
Reaction: ATP + L-pyrrolysine + tRNA^{Pyl} = AMP + diphosphate + L-pyrrolysyl-tRNA^{Pyl}
Other name(s): PylS; pyrrolysyl-tRNA synthetase
Systematic name: L-pyrrolysine:tRNA^{Pyl} ligase (AMP-forming)
Comments: In organisms such as *Methanosarcina barkeri* that incorporate the modified amino acid pyrrolysine (Pyl) into certain methylamine methyltransferases, an unusual tRNA^{Pyl}, with a CUA anticodon, can be charged directly with pyrrolysine by this class II aminoacyl—tRNA ligase. The enzyme is specific for pyrrolysine as substrate as it cannot be replaced by lysine or any of the other natural amino acids [38].
References: [38, 336, 379]

[EC 6.1.1.26 created 2007]

EC 6.1.1.27

Accepted name: *O*-phospho-L-serine—tRNA ligase
Reaction: ATP + *O*-phospho-L-serine + tRNA^{Cys} = AMP + diphosphate + *O*-phospho-L-seryl-tRNA^{Cys}
Other name(s): *O*-phosphoseryl-tRNA ligase; non-canonical *O*-phosphoseryl-tRNA synthetase; SepRS
Systematic name: *O*-phospho-L-serine:tRNA^{Cys} ligase (AMP-forming)
Comments: In organisms like *Archaeoglobus fulgidus* lacking EC 6.1.1.16 (cysteine—tRNA ligase) for the direct Cys-tRNA^{Cys} formation, Cys-tRNA^{Cys} is produced by an indirect pathway, in which EC 6.1.1.27 (*O*-phosphoseryl-tRNA ligase) ligates *O*-phosphoserine to tRNA^{Cys}, and EC 2.5.1.73 (*O*-phospho-L-seryl-tRNA: Cys-tRNA synthase) converts the produced *O*-phospho-L-seryl-tRNA^{Cys} to Cys-tRNA^{Cys}. The SepRS/SepCysS pathway is the sole route for cysteine biosynthesis in the organism [123]. *Methanosarcina mazei* can use both pathways, the direct route using EC 6.1.1.16 (cysteine—tRNA ligase) and the indirect pathway with EC 6.1.1.27 and EC 2.5.1.73 (*O*-phospho-L-seryl-tRNA: Cys-tRNA synthase) [150].
References: [123, 150]

[EC 6.1.1.27 created 2009]

[6.1.1.28 Deleted entry. proline/cysteinetRNA ligase. Later published work having demonstrated that this was not a genuine enzyme, EC 6.1.1.28 was withdrawn at the public-review stage before being made official.]

[EC 6.1.1.28 created 2014, deleted 2014]

EC 6.1.2 Acidalcohol ligases (ester synthases)

EC 6.1.2.1

Accepted name: D-alanine—(*R*)-lactate ligase
Reaction: D-alanine + (*R*)-lactate + ATP = D-alanyl-(*R*)-lactate + ADP + phosphate
Other name(s): VanA; VanB; VanD
Systematic name: D-alanine:(*R*)-lactate ligase (ADP-forming)
Comments: The product of this enzyme, the depsipeptide D-alanyl-(*R*)-lactate, can be incorporated into the peptidoglycan pentapeptide instead of the usual D-alanyl-D-alanine dipeptide, which is formed by EC 6.3.2.4, D-alanine—D-alanine ligase. The resulting peptidoglycan does not bind the glycopeptide antibiotics vancomycin and teicoplanin, conferring resistance on the bacteria.
References: [47, 278, 331]

[EC 6.1.2.1 created 2010]

EC 6.1.2.2

- Accepted name:** nebramycin 5' synthase
- Reaction:** (1) tobramycin + carbamoyl phosphate + ATP + H₂O = nebramycin 5' + AMP + diphosphate + phosphate (overall reaction)
(1a) carbamoyl phosphate + ATP + H₂O = diphosphate + *O*-carbamoyladenylate + phosphate
(1b) *O*-carbamoyladenylate + tobramycin = AMP + nebramycin 5'
(2) kanamycin A + carbamoyl phosphate + ATP + H₂O = 6''-*O*-carbamoylkanamycin A + AMP + diphosphate + phosphate (overall reaction)
(2a) carbamoyl phosphate + ATP + H₂O = diphosphate + *O*-carbamoyladenylate + phosphate
(2b) *O*-carbamoyladenylate + kanamycin A = AMP + 6''-*O*-carbamoylkanamycin A
- Other name(s):** tobramycin carbamoyltransferase; TobZ
- Systematic name:** tobramycin:carbamoyl phosphate ligase (AMP,phosphate-forming)
- Comments:** Requires Fe(III). The enzyme from the bacterium *Streptoalloteichus tenebrarius* catalyses the activation of carbamoyl phosphate to *O*-carbamoyladenylate and the subsequent carbamoylation of kanamycin and tobramycin.
- References:** [326]

[EC 6.1.2.2 created 2014]

EC 6.1.3 Cyclo-ligases

EC 6.1.3.1

- Accepted name:** olefin β-lactone synthetase
- Reaction:** ATP + a (2*R*,3*S*)-2-alkyl-3-hydroxyalkanoate = AMP + diphosphate + a *cis*-3-alkyl-4-alkyloxetan-2-one
- Other name(s):** *oleC* (gene name)
- Systematic name:** (2*R*,3*S*)-2-alkyl-3-hydroxyalkanoate ligase (β-lactone,AMP-forming)
- Comments:** The enzyme, found in certain bacterial species, participates in a pathway for the production of olefins. It forms a β-lactone. The alkyl group at C² of the substrate ends up as the 3-alkyl group of the product.
- References:** [411, 119, 191, 65]

[EC 6.1.3.1 created 2017]

EC 6.2 Forming carbon-sulfur bonds

This subclass contains enzymes that use the energy from NTP hydrolysis to catalyse the attachment of an acyl group to the sulfur atom of 4'-phosphopantetheine groups in coenzyme A and acyl-binding proteins, or of a cysteine residue, forming a carbon-sulfur bond.

EC 6.2.1 Acid-thiol ligases

EC 6.2.1.1

- Accepted name:** acetate—CoA ligase
- Reaction:** ATP + acetate + CoA = AMP + diphosphate + acetyl-CoA
- Other name(s):** acetyl-CoA synthetase; acetyl activating enzyme; acetate thiokinase; acyl-activating enzyme; acetyl coenzyme A synthetase; acetic thiokinase; acetyl CoA ligase; acetyl CoA synthase; acetyl-coenzyme A synthase; short chain fatty acyl-CoA synthetase; short-chain acyl-coenzyme A synthetase; ACS

Systematic name: acetate:CoA ligase (AMP-forming)
Comments: Also acts on propanoate and propenoate.
References: [64, 104, 154, 280]

[EC 6.2.1.1 created 1961]

EC 6.2.1.2

Accepted name: medium-chain acyl-CoA ligase
Reaction: ATP + a medium-chain fatty acid + CoA = AMP + diphosphate + a medium-chain acyl-CoA
Other name(s): *fadK* (gene name); *lvaE* (gene name); butyryl-CoA synthetase; fatty acid thiokinase (medium chain); acyl-activating enzyme; fatty acid elongase; fatty acid activating enzyme; fatty acyl coenzyme A synthetase; butyrate—CoA ligase; butyryl-coenzyme A synthetase; L-(+)-3-hydroxybutyryl CoA ligase; short-chain acyl-CoA synthetase; medium-chain acyl-CoA synthetase; butanoate:CoA ligase (AMP-forming)
Systematic name: medium-chain fatty acid:CoA ligase (AMP-forming)
Comments: Acts on fatty acids from C₄ to C₁₁ and on the corresponding 3-hydroxy and 2,3- or 3,4-unsaturated acids. The enzyme from the bacterium *Pseudomonas putida* also acts on 4-oxo and 4-hydroxy derivatives.
References: [248, 257, 460, 290, 344]

[EC 6.2.1.2 created 1961, modified 2011, modified 2018]

EC 6.2.1.3

Accepted name: long-chain-fatty-acid—CoA ligase
Reaction: ATP + a long-chain fatty acid + CoA = AMP + diphosphate + an acyl-CoA
Other name(s): acyl-CoA synthetase; fatty acid thiokinase (long chain); acyl-activating enzyme; palmitoyl-CoA synthase; lignoceroyl-CoA synthase; arachidonyl-CoA synthetase; acyl coenzyme A synthetase; acyl-CoA ligase; palmitoyl coenzyme A synthetase; thiokinase; palmitoyl-CoA ligase; acyl-coenzyme A ligase; fatty acid CoA ligase; long-chain fatty acyl coenzyme A synthetase; oleoyl-CoA synthetase; stearoyl-CoA synthetase; long chain fatty acyl-CoA synthetase; long-chain acyl CoA synthetase; fatty acid elongase; LCFA synthetase; pristanoyl-CoA synthetase; ACS3; long-chain acyl-CoA synthetase I; long-chain acyl-CoA synthetase II; fatty acyl-coenzyme A synthetase; long-chain acyl-coenzyme A synthetase; FAA1
Systematic name: long-chain fatty acid:CoA ligase (AMP-forming)
Comments: Acts on a wide range of long-chain saturated and unsaturated fatty acids, but the enzymes from different tissues show some variation in specificity. The liver enzyme acts on acids from C₆ to C₂₀; that from brain shows high activity up to C₂₄.
References: [22, 168, 296, 423]

[EC 6.2.1.3 created 1961, modified 1989, modified 2011]

EC 6.2.1.4

Accepted name: succinate—CoA ligase (GDP-forming)
Reaction: GTP + succinate + CoA = GDP + phosphate + succinyl-CoA
Other name(s): succinyl-CoA synthetase (GDP-forming); succinyl coenzyme A synthetase (guanosine diphosphate-forming); succinate thiokinase; succinic thiokinase; succinyl coenzyme A synthetase; succinate-phosphorylating enzyme; P-enzyme; SCS; G-STK; succinyl coenzyme A synthetase (GDP-forming); succinyl CoA synthetase; succinyl coenzyme A synthetase
Systematic name: succinate:CoA ligase (GDP-forming)
Comments: Itaconate can act instead of succinate, and ITP instead of GTP.
References: [146, 196, 263, 372]

[EC 6.2.1.4 created 1961]

EC 6.2.1.5

Accepted name: succinate—CoA ligase (ADP-forming)
Reaction: ATP + succinate + CoA = ADP + phosphate + succinyl-CoA
Other name(s): succinyl-CoA synthetase (ADP-forming); succinic thiokinase; succinate thiokinase; succinyl-CoA synthetase; succinyl coenzyme A synthetase (adenosine diphosphate-forming); succinyl coenzyme A synthetase; A-STK (adenin nucleotide-linked succinate thiokinase); STK; A-SCS
Systematic name: succinate:CoA ligase (ADP-forming)
References: [146, 194, 195]

[EC 6.2.1.5 created 1961]

EC 6.2.1.6

Accepted name: glutarate—CoA ligase
Reaction: ATP + glutarate + CoA = ADP + phosphate + glutaryl-CoA
Other name(s): glutaryl-CoA synthetase; glutaryl coenzyme A synthetase
Systematic name: glutarate:CoA ligase (ADP-forming)
Comments: GTP or ITP can act instead of ATP.
References: [274]

[EC 6.2.1.6 created 1961]

EC 6.2.1.7

Accepted name: cholate—CoA ligase
Reaction: (1) ATP + cholate + CoA = AMP + diphosphate + choloyl-CoA
(2) ATP + (25*R*)-3 α ,7 α ,12 α -trihydroxy-5 β -cholestan-26-oate + CoA = AMP + diphosphate + (25*R*)-3 α ,7 α ,12 α -trihydroxy-5 β -cholestanoyl-CoA
Other name(s): BAL; bile acid CoA ligase; bile acid coenzyme A ligase; choloyl-CoA synthetase; choloyl coenzyme A synthetase; cholic thiokinase; cholate thiokinase; cholic acid:CoA ligase; 3 α ,7 α ,12 α -trihydroxy-5 β -cholestanoyl coenzyme A synthetase; 3 α ,7 α ,12 α -trihydroxy-5 β -cholestanoyl-CoA synthetase; THCA-CoA ligase; 3 α ,7 α ,12 α -trihydroxy-5 β -cholestanate—CoA ligase; 3 α ,7 α ,12 α -trihydroxy-5 β -cholestanate:CoA ligase (AMP-forming); cholyl-CoA synthetase; trihydroxycoprostanoyl-CoA synthetase
Systematic name: cholate:CoA ligase (AMP-forming)
Comments: Requires Mg²⁺ for activity. The mammalian enzyme is membrane-bound and catalyses the first step in the conjugation of bile acids with amino acids, converting bile acids into their acyl-CoA thioesters. Chenodeoxycholate, deoxycholate, lithocholate and trihydroxycoprostanoyl-CoA can also act as substrates [109]. The bacterial enzyme is soluble and participates in an anaerobic bile acid 7 α -dehydroxylation pathway [250].
References: [106, 107, 339, 378, 250, 463, 109]

[EC 6.2.1.7 created 1961 (EC 6.2.1.29 created 1992, incorporated 2005), modified 2005]

EC 6.2.1.8

Accepted name: oxalate—CoA ligase
Reaction: ATP + oxalate + CoA = AMP + diphosphate + oxalyl-CoA
Other name(s): oxalyl-CoA synthetase; oxalyl coenzyme A synthetase
Systematic name: oxalate:CoA ligase (AMP-forming)
References: [134]

[EC 6.2.1.8 created 1972]

EC 6.2.1.9

Accepted name: malate—CoA ligase

Reaction: ATP + malate + CoA = ADP + phosphate + malyl-CoA
Other name(s): malyl-CoA synthetase; malyl coenzyme A synthetase; malate thiokinase
Systematic name: malate:CoA ligase (ADP-forming)
References: [293]

[EC 6.2.1.9 created 1972]

EC 6.2.1.10

Accepted name: carboxylic acid—CoA ligase (GDP-forming)
Reaction: GTP + a carboxylate + CoA = GDP + phosphate + acyl-CoA
Other name(s): acyl-CoA synthetase (GDP-forming); acyl coenzyme A synthetase (guanosine diphosphate forming)
Systematic name: carboxylic acid:CoA ligase (GDP-forming)
References: [366]

[EC 6.2.1.10 created 1972, modified 2011]

EC 6.2.1.11

Accepted name: biotin—CoA ligase
Reaction: ATP + biotin + CoA = AMP + diphosphate + biotinyl-CoA
Other name(s): biotinyl-CoA synthetase; biotin CoA synthetase; biotinyl coenzyme A synthetase
Systematic name: biotin:CoA ligase (AMP-forming)
References: [66]

[EC 6.2.1.11 created 1972]

EC 6.2.1.12

Accepted name: 4-coumarate—CoA ligase
Reaction: ATP + 4-coumarate + CoA = AMP + diphosphate + 4-coumaroyl-CoA
Other name(s): 4-coumaroyl-CoA synthetase; *p*-coumaroyl CoA ligase; *p*-coumaryl coenzyme A synthetase; *p*-coumaryl-CoA synthetase; *p*-coumaryl-CoA ligase; feruloyl CoA ligase; hydroxycinnamoyl CoA synthetase; 4-coumarate:coenzyme A ligase; caffeoyl coenzyme A synthetase; *p*-hydroxycinnamoyl coenzyme A synthetase; feruloyl coenzyme A synthetase; sinapoyl coenzyme A synthetase; 4-coumaryl-CoA synthetase; hydroxycinnamate:CoA ligase; *p*-coumaryl-CoA ligase; *p*-hydroxycinnamic acid:CoA ligase; 4CL
Systematic name: 4-coumarate:CoA ligase (AMP-forming)
References: [141, 235]

[EC 6.2.1.12 created 1976]

EC 6.2.1.13

Accepted name: acetate—CoA ligase (ADP-forming)
Reaction: ATP + acetate + CoA = ADP + phosphate + acetyl-CoA
Other name(s): acetyl-CoA synthetase (ADP-forming); acetyl coenzyme A synthetase (adenosine diphosphate-forming); acetate thiokinase
Systematic name: acetate:CoA ligase (ADP-forming)
Comments: Also acts on propanoate and, very slowly, on butanoate.
References: [352]

[EC 6.2.1.13 created 1978]

EC 6.2.1.14

Accepted name: 6-carboxyhexanoate—CoA ligase

Reaction: ATP + 6-carboxyhexanoate + CoA = AMP + diphosphate + 6-carboxyhexanoyl-CoA
Other name(s): 6-carboxyhexanoyl-CoA synthetase; pimelyl-CoA synthetase
Systematic name: 6-carboxyhexanoate:CoA ligase (AMP-forming)
References: [181, 182]

[EC 6.2.1.14 created 1983]

EC 6.2.1.15

Accepted name: arachidonate—CoA ligase
Reaction: ATP + arachidonate + CoA = AMP + diphosphate + arachidonoyl-CoA
Other name(s): arachidonoyl-CoA synthetase
Systematic name: arachidonate:CoA ligase (AMP-forming)
Comments: Not identical with EC 6.2.1.3 long-chain-fatty-acid—CoA ligase. Icosa-8,11,14-trienoate, but not the other long-chain fatty acids, can act in place of arachidonate.
References: [467]

[EC 6.2.1.15 created 1984]

EC 6.2.1.16

Accepted name: acetoacetate—CoA ligase
Reaction: ATP + acetoacetate + CoA = AMP + diphosphate + acetoacetyl-CoA
Other name(s): acetoacetyl-CoA synthetase
Systematic name: acetoacetate:CoA ligase (AMP-forming)
Comments: Also acts, more slowly, on L-3-hydroxybutanoate.
References: [122]

[EC 6.2.1.16 created 1984]

EC 6.2.1.17

Accepted name: propionate—CoA ligase
Reaction: ATP + propanoate + CoA = AMP + diphosphate + propanoyl-CoA
Other name(s): propionyl-CoA synthetase
Systematic name: propanoate:CoA ligase (AMP-forming)
Comments: Propenoate can act instead of propanoate. Not identical with EC 6.2.1.1 (acetate—CoA ligase) or EC 6.2.1.2 (butyrate—CoA ligase).
References: [357]

[EC 6.2.1.17 created 1984]

EC 6.2.1.18

Accepted name: citrate—CoA ligase
Reaction: ATP + citrate + CoA = ADP + phosphate + (3S)-citryl-CoA
Other name(s): citryl-CoA synthetase; citrate:CoA ligase; citrate thiokinase
Systematic name: citrate:CoA ligase (ADP-forming)
Comments: The enzyme is a component of EC 2.3.3.8 ATP citrate synthase.
References: [233, 16]

[EC 6.2.1.18 created 1986]

EC 6.2.1.19

Accepted name: long-chain-fatty-acid—protein ligase
Reaction: ATP + a long-chain fatty acid + [protein]-L-cysteine = AMP + diphosphate + a [protein]-S-(long-chain-acyl)-L-cysteine

Other name(s): *luxE* (gene name); acyl-protein synthetase; long-chain-fatty-acid—luciferin-component ligase
Systematic name: long-chain-fatty-acid:protein ligase (AMP-forming)
Comments: Together with a hydrolase component (EC 3.1.2.2/EC 3.1.2.14) and a reductase component (EC 1.2.1.50), this enzyme forms a multienzyme fatty acid reductase complex that produces the long-chain aldehyde substrate of the bacterial luciferase enzyme (EC 1.14.14.3). The enzyme activates free long-chain fatty acids, generated by the action of the transferase component, forming a fatty acyl-AMP intermediate, followed by the transfer of the acyl group to an internal L-cysteine residue. It then transfers the acyl group to EC 1.2.1.50, long-chain acyl-protein thioester reductase.
References: [358, 360, 452, 395, 234]

[EC 6.2.1.19 created 1986, modified 2011, modified 2016]

EC 6.2.1.20

Accepted name: long-chain-fatty-acid—[acyl-carrier-protein] ligase
Reaction: ATP + a long-chain fatty acid + an [acyl-carrier protein] = AMP + diphosphate + a long-chain acyl-[acyl-carrier protein]
Other name(s): acyl-[acyl-carrier-protein] synthetase (ambiguous); acyl-ACP synthetase (ambiguous); stearyl-ACP synthetase; acyl-acyl carrier protein synthetase (ambiguous); long-chain-fatty-acid:[acyl-carrier-protein] ligase (AMP-forming)
Systematic name: long-chain-fatty-acid:[acyl-carrier protein] ligase (AMP-forming)
Comments: The enzyme ligates long chain fatty acids (with aliphatic chain of 13-22 carbons) to an acyl-carrier protein. Not identical with EC 6.2.1.3 long-chain-fatty-acid—CoA ligase.
References: [431, 187]

[EC 6.2.1.20 created 1986]

[6.2.1.21 Deleted entry. phenylacetate—CoA ligase. Activity covered by EC 6.2.1.30, phenylacetate—CoA ligase]

[EC 6.2.1.21 created 1986, deleted 2001]

EC 6.2.1.22

Accepted name: [citrate (*pro*-3*S*)-lyase] ligase
Reaction: ATP + acetate + holo-[citrate (*pro*-3*S*)-lyase] = AMP + diphosphate + acetyl-[citrate (*pro*-3*S*)-lyase]
Other name(s): citrate lyase ligase; citrate lyase synthetase; acetate: SH-[acyl-carrier-protein] enzyme ligase (AMP); acetate:HS-citrate lyase ligase; acetate:citrate-(*pro*-3*S*)-lyase(thiol-form) ligase (AMP-forming); acetate:[citrate-(*pro*-3*S*)-lyase](thiol-form) ligase (AMP-forming)
Systematic name: acetate:holo-[citrate-(*pro*-3*S*)-lyase] ligase (AMP-forming)
Comments: Both this enzyme and EC 2.3.1.49,deacetyl-[citrate-(*pro*-3*S*)-lyase] *S*-acetyltransferase, acetylate and activate EC 4.1.3.6, citrate (*pro*-3*S*)-lyase.
References: [12, 13, 340, 380]

[EC 6.2.1.22 created 1989]

EC 6.2.1.23

Accepted name: dicarboxylate—CoA ligase
Reaction: ATP + an α,ω -dicarboxylate + CoA = AMP + diphosphate + an ω -carboxyacyl-CoA
Other name(s): carboxylyl-CoA synthetase; dicarboxylyl-CoA synthetase
Systematic name: ω -dicarboxylate:CoA ligase (AMP-forming)
Comments: Acts on dicarboxylic acids of chain length C₅ to C₁₆; the best substrate is dodecanedioic acid.
References: [441]

[EC 6.2.1.23 created 1989, modified 2011]

EC 6.2.1.24

Accepted name: phytanate—CoA ligase
Reaction: ATP + phytanate + CoA = AMP + diphosphate + phytanoyl-CoA
Other name(s): phytanoyl-CoA ligase
Systematic name: phytanate:CoA ligase (AMP-forming)
Comments: Not identical with EC 6.2.1.20 long-chain-fatty-acid—[acyl-carrier-protein] ligase.
References: [295]

[EC 6.2.1.24 created 1989]

EC 6.2.1.25

Accepted name: benzoate—CoA ligase
Reaction: ATP + benzoate + CoA = AMP + diphosphate + benzoyl-CoA
Other name(s): benzoate—coenzyme A ligase; benzoyl-coenzyme A synthetase; benzoyl CoA synthetase (AMP forming)
Systematic name: benzoate:CoA ligase (AMP-forming)
Comments: Also acts on 2-, 3- and 4-fluorobenzoate, but only very slowly on the corresponding chlorobenzoates.
References: [171, 377]

[EC 6.2.1.25 created 1989]

EC 6.2.1.26

Accepted name: *o*-succinylbenzoate—CoA ligase
Reaction: ATP + 2-succinylbenzoate + CoA = AMP + diphosphate + 4-(2-carboxyphenyl)-4-oxobutanoyl-CoA
Other name(s): *o*-succinylbenzoyl-coenzyme A synthetase; *o*-succinylbenzoate:CoA ligase (AMP-forming)
Systematic name: 2-succinylbenzoate:CoA ligase (AMP-forming)
References: [153, 205, 268]

[EC 6.2.1.26 created 1992]

EC 6.2.1.27

Accepted name: 4-hydroxybenzoate—CoA ligase
Reaction: ATP + 4-hydroxybenzoate + CoA = AMP + diphosphate + 4-hydroxybenzoyl-CoA
Other name(s): 4-hydroxybenzoate-CoA synthetase; 4-hydroxybenzoate—coenzyme A ligase (AMP-forming); 4-hydroxybenzoyl coenzyme A synthetase; 4-hydroxybenzoyl-CoA ligase
Systematic name: 4-hydroxybenzoate:CoA ligase (AMP-forming)
References: [275]

[EC 6.2.1.27 created 1992]

EC 6.2.1.28

Accepted name: 3 α ,7 α -dihydroxy-5 β -cholestanate—CoA ligase
Reaction: ATP + (25*R*)-3 α ,7 α -dihydroxy-5 β -cholestan-26-oate + CoA = AMP + diphosphate + (25*R*)-3 α ,7 α -dihydroxy-5 β -cholestanoyl-CoA
Other name(s): 3 α ,7 α -dihydroxy-5 β -cholestanoyl coenzyme A synthetase; DHCA-CoA ligase; 3 α ,7 α -dihydroxy-5 β -cholestanate:CoA ligase (AMP-forming)
Systematic name: (25*R*)-3 α ,7 α -dihydroxy-5 β -cholestan-26-oate:CoA ligase (AMP-forming)
References: [339]

[EC 6.2.1.28 created 1992]

[6.2.1.29 Deleted entry. 3 α ,7 α ,12 α -trihydroxy-5 β -cholestanate—CoA ligase. The enzyme is identical to EC 6.2.1.7, cholate—CoA ligase]

[EC 6.2.1.29 created 1992, deleted 2005]

EC 6.2.1.30

- Accepted name:** phenylacetate—CoA ligase
Reaction: ATP + phenylacetate + CoA = AMP + diphosphate + phenylacetyl-CoA
Other name(s): phenacyl coenzyme A synthetase; phenylacetyl-CoA ligase; PA-CoA ligase; phenylacetyl-CoA ligase (AMP-forming)
Systematic name: phenylacetate:CoA ligase (AMP-forming)
Comments: Also acts, more slowly, on acetate, propanoate and butanoate, but not on hydroxy derivatives of phenylacetate and related compounds.
References: [255]

[EC 6.2.1.30 created 1992 (EC 6.2.1.21 created 1986, incorporated 2001)]

EC 6.2.1.31

- Accepted name:** 2-furoate—CoA ligase
Reaction: ATP + 2-furoate + CoA = AMP + diphosphate + 2-furoyl-CoA
Other name(s): 2-furoyl coenzyme A synthetase
Systematic name: 2-furoate:CoA ligase (AMP-forming)
References: [204]

[EC 6.2.1.31 created 1992]

EC 6.2.1.32

- Accepted name:** anthranilate—CoA ligase
Reaction: ATP + anthranilate + CoA = AMP + diphosphate + anthraniloyl-CoA
Other name(s): anthraniloyl coenzyme A synthetase; 2-aminobenzoate—CoA ligase; 2-aminobenzoate—coenzyme A ligase; 2-aminobenzoate coenzyme A ligase
Systematic name: anthranilate:CoA ligase (AMP-forming)
References: [10]

[EC 6.2.1.32 created 1992]

EC 6.2.1.33

- Accepted name:** 4-chlorobenzoate—CoA ligase
Reaction: 4-chlorobenzoate + CoA + ATP = 4-chlorobenzoyl-CoA + AMP + diphosphate
Systematic name: 4-chlorobenzoate:CoA ligase
Comments: Requires Mg²⁺. This enzyme is part of the bacterial 2,4-dichlorobenzoate degradation pathway.
References: [99, 239, 57]

[EC 6.2.1.33 created 1999]

EC 6.2.1.34

- Accepted name:** *trans*-feruloyl-CoA synthase
Reaction: ferulic acid + CoA + ATP = feruloyl-CoA + products of ATP breakdown
Other name(s): *trans*-feruloyl-CoA synthetase; *trans*-ferulate:CoASH ligase (ATP-hydrolysing); ferulate:CoASH ligase (ATP-hydrolysing)
Systematic name: ferulate:CoA ligase (ATP-hydrolysing)
Comments: Requires Mg²⁺. It has not yet been established whether AMP + diphosphate or ADP + phosphate are formed in this reaction.
References: [302, 337]

[EC 6.2.1.34 created 2000]

EC 6.2.1.35

- Accepted name:** acetate—[acyl-carrier protein] ligase
Reaction: ATP + acetate + an [acyl-carrier protein] = AMP + diphosphate + an acetyl-[acyl-carrier protein]
Other name(s): HS-acyl-carrier protein:acetate ligase; [acyl-carrier protein]:acetate ligase; MadH; ACP-SH:acetate ligase
Systematic name: acetate:[acyl-carrier-protein] ligase (AMP-forming)
Comments: This enzyme, from the anaerobic bacterium *Malonomonas rubra*, is a component of the multienzyme complex EC 7.2.4.4, biotin-dependent malonate decarboxylase. The enzyme uses the energy from hydrolysis of ATP to convert the thiol group of the acyl-carrier-protein-bound 2'-(5-phosphoribosyl)-3'-dephospho-CoA prosthetic group into its acetyl thioester [30].
References: [157, 30, 31, 94]

[EC 6.2.1.35 created 2008, modified 2018]

EC 6.2.1.36

- Accepted name:** 3-hydroxypropionyl-CoA synthase
Reaction: 3-hydroxypropanoate + ATP + CoA = 3-hydroxypropanoyl-CoA + AMP + diphosphate
Other name(s): 3-hydroxypropionyl-CoA synthetase (AMP-forming); 3-hydroxypropionate—CoA ligase
Systematic name: hydroxypropanoate:CoA ligase (AMP-forming)
Comments: Catalyses a step in the 3-hydroxypropanoate/4-hydroxybutanoate cycle, an autotrophic CO₂ fixation pathway found in some thermoacidophilic archaea [29, 6]. The enzymes from *Metallosphaera sedula* and *Sulfolobus tokodaii* can also use propionate, acrylate, acetate, and butanoate as substrates [6], and are thus different from EC 6.2.1.17 (propionate—CoA ligase), which does not accept acetate or butanoate.
References: [29, 6]

[EC 6.2.1.36 created 2009]

EC 6.2.1.37

- Accepted name:** 3-hydroxybenzoate—CoA ligase
Reaction: ATP + 3-hydroxybenzoate + CoA = AMP + diphosphate + 3-hydroxybenzoyl-CoA
Other name(s): 3-hydroxybenzoyl-CoA synthetase; 3-hydroxybenzoate—coenzyme A ligase (AMP-forming); 3-hydroxybenzoyl coenzyme A synthetase; 3-hydroxybenzoyl-CoA ligase
Systematic name: 3-hydroxybenzoate:CoA ligase (AMP-forming)
Comments: The enzyme works equally well with 4-hydroxybenzoate but shows low activity towards benzoate, 4-aminobenzoate, 3-aminobenzoate, 3-fluorobenzoate, 4-fluorobenzoate, 3-chlorobenzoate, and 4-chlorobenzoate. There is no activity with 3,4-dihydroxybenzoate, 2,3-dihydroxybenzoate, and 2-hydroxybenzoate as substrates.
References: [214]

[EC 6.2.1.37 created 2011]

EC 6.2.1.38

- Accepted name:** (2,2,3-trimethyl-5-oxocyclopent-3-enyl)acetyl-CoA synthase
Reaction: [(1R)-2,2,3-trimethyl-5-oxocyclopent-3-enyl]acetate + ATP + CoA = AMP + diphosphate + [(1R)-2,2,3-trimethyl-5-oxocyclopent-3-enyl]acetyl-CoA
Other name(s): 2-oxo- Δ^3 -4,5,5-trimethylcyclopentenylacetyl-CoA synthetase
Systematic name: [(1R)-2,2,3-trimethyl-5-oxocyclopent-3-enyl]acetate:CoA ligase (AMP-forming)
Comments: Isolated from *Pseudomonas putida*. Forms part of the pathway of camphor catabolism.
References: [318]

[EC 6.2.1.38 created 2012]

EC 6.2.1.39

- Accepted name:** [butirosin acyl-carrier protein]—L-glutamate ligase
- Reaction:** (1) ATP + L-glutamate + BtrI acyl-carrier protein = ADP + phosphate + L-glutamyl-[BtrI acyl-carrier protein]
(2) ATP + L-glutamate + 4-amino butanoyl-[BtrI acyl-carrier protein] = ADP + phosphate + 4-(γ -L-glutamylamino)butanoyl-[BtrI acyl-carrier protein]
- Other name(s):** [BtrI acyl-carrier protein]—L-glutamate ligase; BtrJ
- Systematic name:** [BtrI acyl-carrier protein]:L-glutamate ligase (ADP-forming)
- Comments:** Catalyses two steps in the biosynthesis of the side chain of the aminoglycoside antibiotics of the butirosin family. The enzyme adds one molecule of L-glutamate to a dedicated acyl-carrier protein, and following decarboxylation of the product by EC 4.1.1.95, L-glutamyl-[BtrI acyl-carrier protein] decarboxylase, adds a second L-glutamate molecule. Requires Mg²⁺ or Mn²⁺, and activity is enhanced in the presence of Mn²⁺.
- References:** [230]

[EC 6.2.1.39 created 2012]

EC 6.2.1.40

- Accepted name:** 4-hydroxybutyrate—CoA ligase
- Reaction:** ATP + 4-hydroxybutanoate + CoA = AMP + diphosphate + 4-hydroxybutanoyl-CoA
- Other name(s):** 4-hydroxybutyrate-CoA synthetase; 4-hydroxybutyrate:CoA ligase (AMP-forming)
- Systematic name:** 4-hydroxybutanoate:CoA ligase (AMP-forming)
- Comments:** Isolated from the archaeon *Metallosphaera sedula*. Involved in the 3-hydroxypropanoate/4-hydroxybutanoate cycle.
- References:** [343, 151]

[EC 6.2.1.40 created 2014]

EC 6.2.1.41

- Accepted name:** 3-[(3a*S*,4*S*,7a*S*)-7a-methyl-1,5-dioxo-octahydro-1*H*-inden-4-yl]propanoate—CoA ligase
- Reaction:** ATP + 3-[(3a*S*,4*S*,7a*S*)-7a-methyl-1,5-dioxo-octahydro-1*H*-inden-4-yl]propanoate + CoA = AMP + diphosphate + 3-[(3a*S*,4*S*,7a*S*)-7a-methyl-1,5-dioxo-octahydro-1*H*-inden-4-yl]propanoyl-CoA
- Other name(s):** *fadD3* (gene name); HIP—CoA ligase
- Systematic name:** 3-[(3a*S*,4*S*,7a*S*)-7a-methyl-1,5-dioxo-octahydro-1*H*-inden-4-yl]propanoate:CoA ligase (AMP-forming)
- Comments:** The enzyme, characterized from actinobacterium *Mycobacterium tuberculosis*, catalyses a step in the degradation of cholesterol and cholate. The enzyme is very specific for its substrate, and requires that the side chain at C¹⁷ is completely removed.
- References:** [166, 51]

[EC 6.2.1.41 created 2014]

EC 6.2.1.42

- Accepted name:** 3-oxocholest-4-en-26-oate—CoA ligase
- Reaction:** ATP + (2*S*)-3-oxocholest-4-en-26-oate + CoA = AMP + diphosphate + (2*S*)-3-oxocholest-4-en-26-oyl-CoA
- Other name(s):** *fadD19* (gene name)
- Systematic name:** (2*S*)-3-oxocholest-4-en-26-oate:CoA ligase (AMP-forming)
- Comments:** The enzyme, characterized from actinobacterium *Mycobacterium tuberculosis*, catalyses a step in the degradation of cholesterol. It is responsible for the activation of the C₈ side chain. 3 β -hydroxycholest-5-en-26-oate can also be used as substrate.
- References:** [465, 52]

[EC 6.2.1.42 created 2014]

EC 6.2.1.43

- Accepted name:** 2-hydroxy-7-methoxy-5-methyl-1-naphthoate—CoA ligase
Reaction: ATP + 2-hydroxy-7-methoxy-5-methyl-1-naphthoate + CoA = AMP + diphosphate + 2-hydroxy-7-methoxy-5-methyl-1-naphthoyl-CoA
Other name(s): NcsB2
Systematic name: 2-hydroxy-7-methoxy-5-methyl-1-naphthoate:CoA ligase
Comments: The enzyme from the bacterium *Streptomyces carzinostaticus* is involved in the attachment of the 2-hydroxy-7-methoxy-5-methyl-1-naphthoate moiety of the antibiotic neocarzinostatin. *In vitro* the enzyme also catalyses the activation of other 1-naphthoic acid analogues, e.g. 2-hydroxy-5-methyl-1-naphthoate or 2,7-dihydroxy-5-methyl-1-naphthoate.
References: [71]

[EC 6.2.1.43 created 2014]

EC 6.2.1.44

- Accepted name:** 3-(methylthio)propionyl—CoA ligase
Reaction: ATP + 3-(methylsulfanyl)propanoate + CoA = AMP + diphosphate + 3-(methylsulfanyl)propanoyl-CoA
Other name(s): DmdB; MMPA-CoA ligase; methylmercaptopropionate-coenzyme A ligase; 3-methylmercaptopropionyl-CoA ligase; 3-(methylthio)propanoate:CoA ligase (AMP-forming)
Systematic name: 3-(methylsulfanyl)propanoate:CoA ligase (AMP-forming)
Comments: The enzyme is part of a dimethylsulfoniopropionate demethylation pathway in the marine bacteria *Ruegeria pomeroyi* and *Pelagibacter ubique*. It also occurs in some nonmarine bacteria capable of metabolizing dimethylsulfoniopropionate (e.g. *Burkholderia thailandensis*, *Pseudomonas aeruginosa*, and *Silicibacter lacuscaerulensis*). It requires Mg²⁺ [48].
References: [354, 48]

[EC 6.2.1.44 created 2014]

EC 6.2.1.45

- Accepted name:** E1 ubiquitin-activating enzyme
Reaction: ATP + ubiquitin + [E1 ubiquitin-activating enzyme]-L-cysteine = AMP + diphosphate + S-ubiquitinyl-[E1 ubiquitin-activating enzyme]-L-cysteine
Other name(s): ubiquitin activating enzyme; E1; ubiquitin-activating enzyme E1
Systematic name: ubiquitin:[E1 ubiquitin-activating enzyme] ligase (AMP-forming)
Comments: Catalyses the ATP-dependent activation of ubiquitin through the formation of a thioester bond between the C-terminal glycine of ubiquitin and the sulfhydryl side group of a cysteine residue in the E1 protein. The two-step reaction consists of the ATP-dependent formation of an E1-ubiquitin adenylate intermediate in which the C-terminal glycine of ubiquitin is bound to AMP via an acyl-phosphate linkage, then followed by the conversion to an E1-ubiquitin thioester bond via the cysteine residue on E1 in the second step.
References: [145, 173, 482, 50]

[EC 6.2.1.45 created 2015]

EC 6.2.1.46

- Accepted name:** L-*allo*-isoleucine—holo-[CmaA peptidyl-carrier protein] ligase
Reaction: ATP + L-*allo*-isoleucine + holo-[CmaA peptidyl-carrier protein] = AMP + diphosphate + L-*allo*-isoleucyl-[CmaA peptidyl-carrier protein]
Other name(s): CmaA
Systematic name: L-*allo*-isoleucine:holo-[CmaA peptidyl-carrier protein] ligase (AMP-forming)

Comments: This two-domain protein from the bacterium *Pseudomonas syringae* contains an adenylation domain (A domain) and a thiolation domain (T domain). It catalyses the adenylation of L-*allo*-isoleucine and its attachment to the T domain. The enzyme is involved in the biosynthesis of the toxin coronatine, which mimics the plant hormone jasmonic acid isoleucine. Coronatine promotes opening of the plant stomata allowing bacterial invasion, which is followed by bacterial growth in the apoplast, systemic susceptibility, and disease.

References: [73]

[EC 6.2.1.46 created 2015]

EC 6.2.1.47

Accepted name: medium-chain-fatty-acid—[acyl-carrier-protein] ligase

Reaction: ATP + a medium-chain fatty acid + a holo-[acyl-carrier protein] = AMP + diphosphate + a medium-chain acyl-[acyl-carrier protein]

Other name(s): *jamA* (gene name)

Systematic name: medium-chain-fatty-acid:[acyl-carrier protein] ligase (AMP-forming)

Comments: The enzyme ligates medium chain fatty acids (with aliphatic chain of 6-12 carbons) to an acyl-carrier protein.

References: [102, 484]

[EC 6.2.1.47 created 2016]

EC 6.2.1.48

Accepted name: carnitine—CoA ligase

Reaction: ATP + L-carnitine + CoA = AMP + diphosphate + L-carnitiny-CoA

Other name(s): *caiC* (gene name)

Systematic name: L-carnitine:CoA ligase (AMP-forming)

Comments: The enzyme, originally characterized from the bacterium *Escherichia coli*, can catalyse the transfer of CoA to L-carnitine, crotonobetaine and γ -butyrobetaine. *In vitro* the enzyme also exhibits the activity of EC 2.8.3.21, L-carnitine CoA-transferase.

References: [103, 34]

[EC 6.2.1.48 created 2017]

EC 6.2.1.49

Accepted name: long-chain fatty acid adenylyltransferase FadD28

Reaction: ATP + a long-chain fatty acid + holo-[mycocerosate synthase] = AMP + diphosphate + a long-chain acyl-[mycocerosate synthase] (overall reaction)

(1a) ATP + a long-chain fatty acid = diphosphate + a long-chain acyl-adenylate ester

(1b) a long-chain acyl-adenylate ester + holo-[mycocerosate synthase] = AMP + a long-chain acyl-[mycocerosate synthase]

Other name(s): *fadD28* (gene name)

Systematic name: long-chain fatty acid:holo-[mycocerosate synthase] ligase (AMP-forming)

Comments: The enzyme, found in certain mycobacteria, activates long-chain fatty acids by adenylation and transfers them to EC 2.3.1.111, mycocerosate synthase. The enzyme participates in the biosynthesis of the virulent lipids dimycocerosates (DIM) and dimycocerosyl triglycosyl phenolphthiocerol (PGL).

References: [114, 137, 19, 272, 444]

[EC 6.2.1.49 created 2016 as EC 2.7.7.95, transferred 2017 to EC 6.2.1.49]

EC 6.2.1.50

Accepted name: 4-hydroxybenzoate adenylyltransferase FadD22

Reaction: ATP + 4-hydroxybenzoate + holo-[4-hydroxyphenylalkanoate synthase] = AMP + diphosphate + 4-hydroxybenzoyl-[4-hydroxyphenylalkanoate synthase] (overall reaction)

(1a) $\text{ATP} + 4\text{-hydroxybenzoate} = 4\text{-hydroxybenzoyl-adenylate} + \text{diphosphate}$

(1b) $4\text{-hydroxybenzoyl-adenylate} + \text{holo-[4-hydroxyphenylalkanoate synthase]} = \text{AMP} + 4\text{-hydroxybenzoyl-[4-hydroxyphenylalkanoate synthase]}$

Other name(s): *fadD22* (gene name); 4-hydroxybenzoate adenylase

Systematic name: 4-hydroxybenzoate:holo-[4-hydroxyphenylalkanoate synthase] ligase (AMP-forming)

Comments: This mycobacterial enzyme participates in the biosynthesis of phenolphthiocerols. Following the substrate's activation by adenylation, it is transferred to an acyl-carrier protein domain within the enzyme, from which it is transferred to EC 2.3.1.261, 4-hydroxyphenylalkanoate synthase.

References: [391, 444]

[EC 6.2.1.50 created 2017 as EC 2.7.7.98, transferred 2017 to EC 6.2.1.50]

EC 6.2.1.51

Accepted name: 4-hydroxyphenylalkanoate adenyltransferase FadD29

Reaction: (1) $\text{ATP} + 17\text{-(4-hydroxyphenyl)heptadecanoate} + \text{holo-[(phenol)carboxyphthiodienone synthase]} = \text{AMP} + \text{diphosphate} + 17\text{-(4-hydroxyphenyl)heptadecanoyl-[(phenol)carboxyphthiodienone synthase]}$

(1a) $\text{ATP} + 17\text{-(4-hydroxyphenyl)heptadecanoate} = \text{diphosphate} + 17\text{-(4-hydroxyphenyl)heptadecanoyl-adenylate}$

(1b) $17\text{-(4-hydroxyphenyl)heptadecanoyl-adenylate} + \text{holo-[(phenol)carboxyphthiodienone synthase]} = \text{AMP} + 17\text{-(4-hydroxyphenyl)heptadecanoyl-[(phenol)carboxyphthiodienone synthase]}$

(2) $\text{ATP} + 19\text{-(4-hydroxyphenyl)nonadecanoate} + \text{holo-[(phenol)carboxyphthiodienone synthase]} = \text{AMP} + \text{diphosphate} + 19\text{-(4-hydroxyphenyl)nonadecanoyl-[(phenol)carboxyphthiodienone synthase]}$

(2a) $\text{ATP} + 19\text{-(4-hydroxyphenyl)nonadecanoate} = \text{diphosphate} + 19\text{-(4-hydroxyphenyl)nonadecanoyl-adenylate}$

(2b) $19\text{-(4-hydroxyphenyl)nonadecanoyl-adenylate} + \text{holo-[(phenol)carboxyphthiodienone synthase]} = \text{AMP} + 19\text{-(4-hydroxyphenyl)nonadecanoyl-[(phenol)carboxyphthiodienone synthase]}$

Other name(s): *fadD29* (gene name); 4-hydroxyphenylalkanoate adenylase

Systematic name: 4-hydroxyphenylalkanoate:holo-[(phenol)carboxyphthiodienone synthase] ligase

Comments: The mycobacterial enzyme participates in the biosynthesis of phenolphthiocerols. Following the substrate's activation by adenylation, it is transferred to an acyl-carrier protein domain within the enzyme, from which it is transferred to the phenolphthiocerol/phthiocerol polyketide synthase.

References: [391, 444]

[EC 6.2.1.51 created 2016 as EC 2.7.7.94, transferred 2017 to EC 6.2.1.51]

EC 6.2.1.52

Accepted name: L-firefly luciferin—CoA ligase

Reaction: $\text{ATP} + \text{L-firefly luciferin} + \text{CoA} = \text{AMP} + \text{diphosphate} + \text{L-firefly luciferyl-CoA}$

Other name(s): LUC

Systematic name: (R)-4,5-dihydro-2-(6-hydroxy-1,3-benzothiazol-2-yl)thiazole-4-carboxylate:CoA ligase (AMP-forming)

Comments: This is an alternative activity of the firefly luciferase (EC 1.13.12.7), which the enzyme exhibits under normal conditions only when acting on the L-enantiomer of its substrate. The D-isomer can act as a substrate for the CoA—ligase activity *in vitro* only under low oxygen conditions that are not found *in vivo*. The activation of L-firefly luciferin to a CoA ester is a step in a recycling pathway that results in its epimerization to the D enantiomer, which is the only substrate whose oxygenation results in light emission.

References: [116, 298, 446, 247]

[EC 6.2.1.52 created 2017]

EC 6.2.1.53

- Accepted name:** L-proline—[L-prolyl-carrier protein] ligase
- Reaction:** ATP + L-proline + holo-[L-prolyl-carrier protein] = AMP + diphosphate + L-prolyl-[L-prolyl-carrier protein] (overall reaction)
(1a) ATP + L-proline = diphosphate + (L-prolyl)adenylate
(1b) (L-prolyl)adenylate + holo-[L-prolyl-carrier protein] = AMP + L-prolyl-[L-prolyl-carrier protein]
- Other name(s):** *pltF* (gene name); *bmp4* (gene name); *pigI* (gene name)
- Systematic name:** L-proline:[L-prolyl-carrier protein] ligase (AMP-forming)
- Comments:** The enzyme participates in the biosynthesis of several pyrrole-containing compounds, such as undecylprodigiosin, prodigiosin, pyoluteorin, and coumermycin A1. It catalyses the activation of L-proline to an adenylate form, followed by its transfer to the 4'-phosphopanthoine moiety of an L-prolyl-carrier protein.
- References:** [429, 147, 466]

[EC 6.2.1.53 created 2018]

EC 6.2.1.54

- Accepted name:** D-alanine—[D-alanyl-carrier protein] ligase
- Reaction:** ATP + D-alanine + holo-[D-alanyl-carrier protein] = AMP + diphosphate + D-alanyl-[D-alanyl-carrier protein] (overall reaction)
(1a) ATP + D-alanine = (D-alanyl)adenylate + diphosphate
(1b) (D-alanyl)adenylate + holo-[D-alanyl-carrier protein] = AMP + D-alanyl-[D-alanyl-carrier protein]
- Other name(s):** *dltA* (gene name); Dcl
- Systematic name:** D-alanine:[D-alanyl-carrier protein] ligase
- Comments:** The enzyme is involved in the modification of wall teichoic acids, as well as type I and IV lipoteichoic acids, with D-alanine residues. It activates D-alanine using ATP to form a high-energy (D-alanyl)adenylate intermediate and subsequently transfers the alanyl moiety to the phosphopantheinyl prosthetic group of a D-alanyl-carrier protein (DltC).
- References:** [329, 476, 98, 316]

[EC 6.2.1.54 created 2018]

EC 6.2.1.55

- Accepted name:** E1 SAMP-activating enzyme
- Reaction:** ATP + [SAMP]-Gly-Gly + [E1 SAMP-activating enzyme]-L-cysteine = S-[[SAMP]-Gly-Gly]-[[E1 SAMP-activating enzyme]-L-cysteine] + AMP + diphosphate (overall reaction)
(1a) ATP + [SAMP]-Gly-Gly = diphosphate + [SAMP]-Gly-Gly-AMP
(1b) [SAMP]-Gly-Gly-AMP + [E1 SAMP-activating enzyme]-L-cysteine = S-[[SAMP]-Gly-Gly]-[[E1 SAMP-activating enzyme]-L-cysteine] + AMP
- Other name(s):** UbaA; SAMP-activating enzyme E1
- Systematic name:** [SAMP]:[E1 SAMP-activating enzyme] ligase (AMP-forming)
- Comments:** Contains Zn²⁺. The enzyme catalyses the activation of SAMPs (Small Archaeal Modifier Proteins), which are ubiquitin-like proteins found only in the Archaea. SAMPs are involved in protein degradation, and also act as sulfur carriers involved in thiolation of tRNA and other metabolites such as molybdopterin. The enzyme catalyses the ATP-dependent formation of a SAMP adenylate intermediate in which the C-terminal glycine of SAMP is bound to AMP via an acyl-phosphate linkage (reaction 1). This intermediate can accept a sulfur atom to form a thiocarboxylate moiety in a mechanism that is not yet understood. Alternatively, the E1 enzyme can transfer SAMP from its activated form to an internal cysteine residue, releasing AMP (reaction 2). In this case SAMP is subsequently transferred to a lysine residue in a target protein in a process termed SAMPylation. Auto-SAMPylation (attachment of SAMP to lysine residues within the E1 enzyme) has been observed. *cf.* EC 2.7.7.100, SAMP-activating enzyme.
- References:** [283, 261, 282, 155]

[EC 6.2.1.55 created 2018]

EC 6.3 Forming carbon-nitrogen bonds

This subclass contains enzymes that form carbon-nitrogen bonds. Sub-subclasses are: acid—ammonia (or amine) ligases (amide synthases; EC 6.3.1), acid—amino-acid ligases (peptide synthases; EC 6.3.2), enzymes forming heterocyclic rings (cyclo-ligases; EC 6.3.3), enzymes using glutamine as amido-N-donor (EC 6.3.5) and other carbon-nitrogen ligases (EC 6.3.4).

EC 6.3.1 Acid—ammonia (or amine) ligases (amide synthases)

EC 6.3.1.1

Accepted name: aspartate—ammonia ligase
Reaction: $\text{ATP} + \text{L-aspartate} + \text{NH}_3 = \text{AMP} + \text{diphosphate} + \text{L-asparagine}$
Other name(s): asparagine synthetase; L-asparagine synthetase
Systematic name: L-aspartate:ammonia ligase (AMP-forming)
References: [349, 458]

[EC 6.3.1.1 created 1961]

EC 6.3.1.2

Accepted name: glutamine synthetase
Reaction: $\text{ATP} + \text{L-glutamate} + \text{NH}_3 = \text{ADP} + \text{phosphate} + \text{L-glutamine}$
Other name(s): glutamate—ammonia ligase; glutamylhydroxamic synthetase; L-glutamine synthetase; GS
Systematic name: L-glutamate:ammonia ligase (ADP-forming)
Comments: Glutamine synthetase, which catalyses the incorporation of ammonium into glutamate, is a key enzyme of nitrogen metabolism found in all domains of life. Several types have been described, differing in their oligomeric structures and cofactor requirements.
References: [105, 120, 217, 270, 471, 208, 237, 256]

[EC 6.3.1.2 created 1961, modified 2016]

[6.3.1.3 *Transferred entry. phosphoribosyl-glycinamide synthetase. Now EC 6.3.4.13, phosphoribosylamine—glycine ligase*]

[EC 6.3.1.3 created 1961, deleted 1972]

EC 6.3.1.4

Accepted name: aspartate—ammonia ligase (ADP-forming)
Reaction: $\text{ATP} + \text{L-aspartate} + \text{NH}_3 = \text{ADP} + \text{phosphate} + \text{L-asparagine}$
Other name(s): asparagine synthetase (ADP-forming); asparagine synthetase (adenosine diphosphate-forming)
Systematic name: L-aspartate:ammonia ligase (ADP-forming)
References: [297]

[EC 6.3.1.4 created 1972]

EC 6.3.1.5

Accepted name: NAD⁺ synthase
Reaction: $\text{ATP} + \text{deamido-NAD}^+ + \text{NH}_3 = \text{AMP} + \text{diphosphate} + \text{NAD}^+$
Other name(s): NAD synthetase; NAD synthase; nicotinamide adenine dinucleotide synthetase; diphosphopyridine nucleotide synthetase
Systematic name: deamido-NAD⁺:ammonia ligase (AMP-forming)

Comments: L-Glutamine also acts, more slowly, as amido-donor [*cf.* EC 6.3.5.1].

References: [397]

[EC 6.3.1.5 created 1972]

EC 6.3.1.6

Accepted name: glutamate—ethylamine ligase

Reaction: ATP + L-glutamate + ethylamine = ADP + phosphate + *N*⁵-ethyl-L-glutamine

Other name(s): *N*⁵-ethyl-L-glutamine synthetase; theanine synthetase; *N*⁵-ethylglutamine synthetase

Systematic name: L-glutamate:ethylamine ligase (ADP-forming)

References: [373, 374, 375]

[EC 6.3.1.6 created 1976]

EC 6.3.1.7

Accepted name: 4-methyleneglutamate—ammonia ligase

Reaction: ATP + 4-methylene-L-glutamate + NH₃ = AMP + diphosphate + 4-methylene-L-glutamine

Other name(s): 4-methyleneglutamine synthetase

Systematic name: 4-methylene-L-glutamate:ammonia ligase (AMP-forming)

Comments: Glutamine can act instead of NH₃, but more slowly.

References: [469]

[EC 6.3.1.7 created 1986]

EC 6.3.1.8

Accepted name: glutathionylspermidine synthase

Reaction: glutathione + spermidine + ATP = glutathionylspermidine + ADP + phosphate

Other name(s): glutathione:spermidine ligase (ADP-forming)

Systematic name: γ -L-glutamyl-L-cysteinyl-glycine:spermidine ligase (ADP-forming) [spermidine is numbered so that atom *N*-1 is in the amino group of the aminopropyl part of the molecule]

Comments: Requires magnesium ions. Involved in the synthesis of trypanothione in trypanosomatids. The enzyme from *Escherichia coli* is bifunctional and also catalyses the glutathionylspermidine amidase (EC 3.5.1.78) reaction, resulting in a net hydrolysis of ATP.

References: [393, 41]

[EC 6.3.1.8 created 1999]

EC 6.3.1.9

Accepted name: trypanothione synthase

Reaction: (1) glutathione + spermidine + ATP = glutathionylspermidine + ADP + phosphate

(2) glutathione + glutathionylspermidine + ATP = *N*¹,*N*⁸-bis(glutathionyl)spermidine + ADP + phosphate

Other name(s): glutathionylspermidine:glutathione ligase (ADP-forming)

Systematic name: spermidine/glutathionylspermidine:glutathione ligase (ADP-forming)

Comments: The enzyme, characterized from several trypanosomatids (e.g. *Trypanosoma cruzi*) catalyses two subsequent reactions, leading to production of trypanothione from glutathione and spermidine. Some trypanosomatids (e.g. Crithidia species and some *Leishmania* species) also contain an enzyme that only carries out the first reaction (*cf.* EC 6.3.1.8, glutathionylspermidine synthase). The enzyme is bifunctional, and also catalyses the hydrolysis of glutathionylspermidine and trypanothione (*cf.* EC 3.5.1.78, glutathionylspermidine amidase).

References: [393, 321, 70, 320, 124]

[EC 6.3.1.9 created 1999, modified 2014]

EC 6.3.1.10

- Accepted name:** adenosylcobinamide-phosphate synthase
Reaction: (1) ATP + adenosylcobyrinic acid + (*R*)-1-aminopropan-2-yl phosphate = ADP + phosphate + adenosylcobinamide phosphate
(2) ATP + adenosylcobyrinic acid + (*R*)-1-aminopropan-2-ol = ADP + phosphate + adenosylcobinamide
Other name(s): CbiB
Systematic name: adenosylcobyrinic acid:(*R*)-1-aminopropan-2-yl phosphate ligase (ADP-forming)
Comments: One of the substrates for this reaction, (*R*)-1-aminopropan-2-yl phosphate, is produced by CobD (EC 4.1.1.81, threonine-phosphate decarboxylase).
References: [60, 455]

[EC 6.3.1.10 created 2004]

EC 6.3.1.11

- Accepted name:** glutamate—putrescine ligase
Reaction: ATP + L-glutamate + putrescine = ADP + phosphate + γ -L-glutamylputrescine
Other name(s): γ -glutamylputrescine synthetase; YcjK
Systematic name: L-glutamate:putrescine ligase (ADP-forming)
Comments: Forms part of a novel bacterial putrescine utilization pathway in *Escherichia coli*.
References: [213]

[EC 6.3.1.11 created 2005]

EC 6.3.1.12

- Accepted name:** D-aspartate ligase
Reaction: ATP + D-aspartate + [β -GlcNAc-(1 \rightarrow 4)-Mur2Ac(oyl-L-Ala- γ -D-Glu-L-Lys-D-Ala-D-Ala)]_n = [β -GlcNAc-(1 \rightarrow 4)-Mur2Ac(oyl-L-Ala- γ -D-Glu-6-*N*-(β -D-Asp)-L-Lys-D-Ala-D-Ala)]_n + ADP + phosphate
Other name(s): Asl_{fm}; UDP-MurNAc-pentapeptide:D-aspartate ligase; D-aspartic acid-activating enzyme
Systematic name: D-aspartate:[β -GlcNAc-(1 \rightarrow 4)-Mur2Ac(oyl-L-Ala- γ -D-Glu-L-Lys-D-Ala-D-Ala)]_n ligase (ADP-forming)
Comments: This enzyme forms part of the peptidoglycan assembly pathway of Gram-positive bacteria grown in medium containing D-Asp. Normally, the side chains acylate the 6-amino group of the L-lysine residue contain L-Ala-L-Ala but these amino acids are replaced by D-Asp when D-Asp is included in the medium. Hybrid chains containing L-Ala-D-Asp, L-Ala-L-Ala-D-Asp or D-Asp-L-Ala are not formed [27]. The enzyme belongs in the ATP-grasp protein superfamily [125, 27]. The enzyme is highly specific for D-aspartate, as L-aspartate, D-glutamate, D-alanine, D-iso-asparagine and D-malic acid are not substrates [27]. In *Enterococcus faecium*, the substrate D-aspartate is produced by EC 5.1.1.13, aspartate racemase [27]
References: [400, 401, 125, 27]

[EC 6.3.1.12 created 2006]

EC 6.3.1.13

- Accepted name:** L-cysteine:1D-*myo*-inositol 2-amino-2-deoxy- α -D-glucopyranoside ligase
Reaction: 1-*O*-(2-amino-2-deoxy- α -D-glucopyranosyl)-1D-*myo*-inositol + L-cysteine + ATP = 1-*O*-[2-(L-cysteinamido)-2-deoxy- α -D-glucopyranosyl]-1D-*myo*-inositol + AMP + diphosphate
Other name(s): MshC; MshC ligase; Cys:GlcN-Ins ligase; mycothiol ligase
Systematic name: L-cysteine:1-*O*-(2-amino-2-deoxy- α -D-glucopyranosyl)-1D-*myo*-inositol ligase (AMP-forming)
Comments: This enzyme is a key enzyme in the biosynthesis of mycothiol, a small molecular weight thiol found in *Mycobacteria* spp. and other actinomycetes. Mycothiol plays a fundamental role in these organisms by helping to provide protection from the effects of reactive oxygen species and electrophiles, including many antibiotics. The enzyme may represent a novel target for new classes of antituberculars [144].

References: [110, 144, 433]

[EC 6.3.1.13 created 2009]

EC 6.3.1.14

Accepted name: diphthine—ammonia ligase
Reaction: ATP + diphthine-[translation elongation factor 2] + NH₃ = AMP + diphosphate + diphthamide-[translation elongation factor 2]
Other name(s): diphthamide synthase; diphthamide synthetase; DPH6 (gene name); ATPBD4 (gene name); diphthine:ammonia ligase (AMP-forming)
Systematic name: diphthine-[translation elongation factor 2]:ammonia ligase (AMP-forming)
Comments: This amidase catalyses the last step in the conversion of an L-histidine residue in the translation elongation factor EF2 to diphthamide. This factor is found in all archaea and eukaryota, but not in eubacteria, and is the target of bacterial toxins such as the diphtheria toxin and the *Pseudomonas* exotoxin A (see EC 2.4.2.36, NAD⁺—diphthamide ADP-ribosyltransferase). The substrate of the enzyme, diphthine, is produced by EC 2.1.1.98, diphthine synthase.
References: [289, 288, 409]

[EC 6.3.1.14 created 1990 as EC 6.3.2.22, transferred 2010 to EC 6.3.1.14, modified 2013]

EC 6.3.1.15

Accepted name: 8-demethylnovobiocic acid synthase
Reaction: ATP + 3-dimethylallyl-4-hydroxybenzoate + 3-amino-4,7-dihydroxycoumarin = AMP + diphosphate + 8-demethylnovobiocic acid
Other name(s): *novL* (gene name); novobiocin ligase; novobiocic acid synthetase (misleading); 8-desmethyl-novobiocic acid synthetase; 8-demethylnovobiocic acid synthetase
Systematic name: 3-dimethylallyl-4-hydroxybenzoate:3-amino-4,7-dihydroxycoumarin ligase (AMP-forming)
Comments: The enzyme is involved in the biosynthesis of the aminocoumarin antibiotic novobiocin.
References: [402, 334, 322]

[EC 6.3.1.15 created 2013]

[6.3.1.16 *Transferred entry. carbapenam-3-carboxylate synthetase. The enzyme was discovered at the public-review stage to have been misclassified and so was withdrawn. See EC 6.3.3.6, carbapenam-3-carboxylate synthase*]

[EC 6.3.1.16 created 2013, deleted 2013]

EC 6.3.1.17

Accepted name: β-citrylglutamate synthase
Reaction: ATP + citrate + L-glutamate = ADP + phosphate + β-citryl-L-glutamate
Other name(s): NAAG synthetase I; NAAGS-I; RIMKLB (gene name) (ambiguous)
Systematic name: citrate:L-glutamate ligase (ADP-forming)
Comments: The enzyme, found in animals, also has the activity of EC 6.3.2.41, *N*-acetylaspartylglutamate synthase.
References: [69]

[EC 6.3.1.17 created 2014]

EC 6.3.1.18

Accepted name: γ-glutamylanilide synthase
Reaction: ATP + L-glutamate + aniline = ADP + phosphate + *N*⁵-phenyl-L-glutamine
Other name(s): *atdA1* (gene name); *tdnQ* (gene name); *dcaQ* (gene name)
Systematic name: L-glutamate:aniline ligase (ADP-forming)

Comments: Requires Mg^{2+} . The enzyme, characterized from the bacterium *Acinetobacter* sp. YAA, catalyses the first step in the degradation of aniline. It can also accept chlorinated and methylated forms of aniline, preferably in the *o*- and *p*-positions.

References: [418]

[EC 6.3.1.18 created 2014]

EC 6.3.1.19

Accepted name: prokaryotic ubiquitin-like protein ligase

Reaction: ATP + [prokaryotic ubiquitin-like protein]-L-glutamate + [protein]-L-lysine = ADP + phosphate + N^6 -([prokaryotic ubiquitin-like protein]- γ -L-glutamyl)-[protein]-L-lysine

Other name(s): PafA (ambiguous); Pup ligase; proteasome accessory factor A

Systematic name: [prokaryotic ubiquitin-like protein]:[protein]-L-lysine

Comments: The enzyme has been characterized from the bacteria *Mycobacterium tuberculosis* and *Corynebacterium glutamicum*. It catalyses the ligation of the prokaryotic ubiquitin-like protein (Pup) to a target protein by forming a bond between an ϵ -amino group of a lysine residue of the target protein and the γ -carboxylate of the C-terminal glutamate of the ubiquitin-like protein (Pup). The attachment of Pup, also known as Pupylation, marks proteins for proteasomal degradation.

References: [414, 143, 313, 23, 407]

[EC 6.3.1.19 created 2015]

EC 6.3.1.20

Accepted name: lipoate—protein ligase

Reaction: ATP + (*R*)-lipoate + a [lipoyl-carrier protein]-L-lysine = a [lipoyl-carrier protein]- N^6 -(lipoyl)lysine + AMP + diphosphate (overall reaction)

(1a) ATP + (*R*)-lipoate = lipoyl-AMP + diphosphate

(1b) lipoyl-AMP + a [lipoyl-carrier protein]-L-lysine = a [lipoyl-carrier protein]- N^6 -(lipoyl)lysine + AMP

Other name(s): *lplA* (gene name); *lplJ* (gene name); lipoate protein ligase; lipoate-protein ligase A; LPL; LPL-B

Systematic name: [lipoyl-carrier protein]-L-lysine:lipoate ligase (AMP-forming)

Comments: Requires Mg^{2+} . This enzyme participates in lipoate salvage, and is responsible for lipoylation in the presence of exogenous lipoic acid [330]. The enzyme attaches lipoic acid to the lipoyl domains of certain key enzymes involved in oxidative metabolism, including pyruvate dehydrogenase (E_2 domain), 2-oxoglutarate dehydrogenase (E_2 domain), the branched-chain 2-oxoacid dehydrogenases and the glycine cleavage system (H protein) [416]. Lipoylation is essential for the function of these enzymes. The enzyme can also use octanoate instead of lipoate.

References: [291, 138, 480, 95, 121, 416, 330]

[EC 6.3.1.20 created 2006 as EC 2.7.7.63, transferred 2016 to EC 6.3.1.20]

EC 6.3.2 Acid—amino-acid ligases (peptide synthases)

EC 6.3.2.1

Accepted name: pantoate— β -alanine ligase (AMP-forming)

Reaction: ATP + (*R*)-pantoate + β -alanine = AMP + diphosphate + (*R*)-pantothenate

Other name(s): pantothenate synthetase; pantoate activating enzyme; pantoic-activating enzyme; D-pantoate: β -alanine ligase (AMP-forming); pantoate— β -alanine ligase (ambiguous)

Systematic name: (*R*)-pantoate: β -alanine ligase (AMP-forming)

References: [133, 243, 244]

[EC 6.3.2.1 created 1961, modified 2014]

EC 6.3.2.2

Accepted name: glutamate—cysteine ligase
Reaction: ATP + L-glutamate + L-cysteine = ADP + phosphate + γ -L-glutamyl-L-cysteine
Other name(s): γ -glutamylcysteine synthetase; γ -glutamyl-L-cysteine synthetase; γ -glutamylcysteinyl synthetase
Systematic name: L-glutamate:L-cysteine γ -ligase (ADP-forming)
Comments: Can use L-aminohexanoate in place of glutamate.
References: [245, 394, 251]

[EC 6.3.2.2 created 1961]

EC 6.3.2.3

Accepted name: glutathione synthase
Reaction: ATP + γ -L-glutamyl-L-cysteine + glycine = ADP + phosphate + glutathione
Other name(s): glutathione synthetase; GSH synthetase
Systematic name: γ -L-glutamyl-L-cysteine:glycine ligase (ADP-forming)
References: [222, 246]

[EC 6.3.2.3 created 1961]

EC 6.3.2.4

Accepted name: D-alanine—D-alanine ligase
Reaction: ATP + 2 D-alanine = ADP + phosphate + D-alanyl-D-alanine
Other name(s): MurE synthetase [ambiguous]; alanine:alanine ligase (ADP-forming); alanylalanine synthetase
Systematic name: D-alanine:D-alanine ligase (ADP-forming)
Comments: Involved with EC 6.3.2.7 (UDP-*N*-acetylmuramoyl-L-alanyl-D-glutamate—L-lysine ligase) or EC 6.3.2.13 (UDP-*N*-acetylmuramoyl-L-alanyl-D-glutamate—2,6-diaminopimelate ligase), EC 6.3.2.8 (UDP-*N*-acetylmuramate—L-alanine ligase), EC 6.3.2.9 (UDP-*N*-acetylmuramoyl-L-alanine—D-glutamate ligase) and EC 6.3.2.10 (UDP-*N*-acetylmuramoyl-tripeptide—D-alanyl-D-alanine ligase) in the synthesis of a cell-wall peptide (click here for diagram).
References: [180, 306, 442]

[EC 6.3.2.4 created 1961, modified 2002]

EC 6.3.2.5

Accepted name: phosphopantothenate—cysteine ligase (CTP)
Reaction: CTP + (*R*)-4'-phosphopantothenate + L-cysteine = CMP + diphosphate + *N*-[(*R*)-4'-phosphopantothenoyl]-L-cysteine
Other name(s): phosphopantothenoylcysteine synthetase (ambiguous); phosphopantothenate—cysteine ligase (ambiguous)
Systematic name: (*R*)-4'-phosphopantothenate:L-cysteine ligase
Comments: A key enzyme in the production of coenzyme A. The bacterial enzyme requires CTP, in contrast to the eukaryotic enzyme, EC 6.3.2.51, which requires ATP. Cysteine can be replaced by some of its derivatives.
References: [46, 406, 211]

[EC 6.3.2.5 created 1961, modified 2003, modified 2017]

EC 6.3.2.6

Accepted name: phosphoribosylaminoimidazolesuccinocarboxamide synthase
Reaction: ATP + 5-amino-1-(5-phospho-D-ribosyl)imidazole-4-carboxylate + L-aspartate = ADP + phosphate + (*S*)-2-[5-amino-1-(5-phospho-D-ribosyl)imidazole-4-carboxamido]succinate

Other name(s): phosphoribosylaminoimidazole-succinocarboxamide synthetase; PurC; SAICAR synthetase; 4-(*N*-succinocarboxamide)-5-aminoimidazole synthetase; 4-[(*N*-succinylamino)carbonyl]-5-aminoimidazole ribonucleotide synthetase; SAICARs; phosphoribosylaminoimidazolesuccinocarboxamide synthetase; 5-aminoimidazole-4-*N*-succinocarboxamide ribonucleotide synthetase
Systematic name: 5-amino-1-(5-phospho-*D*-ribosyl)imidazole-4-carboxylate:L-aspartate ligase (ADP-forming)
Comments: Forms part of the purine biosynthesis pathway.
References: [241, 324, 101, 58, 312, 304]

[EC 6.3.2.6 created 1961, modified 2000, modified 2006]

EC 6.3.2.7

Accepted name: UDP-*N*-acetylmuramoyl-L-alanyl-*D*-glutamate—L-lysine ligase
Reaction: ATP + UDP-*N*-acetyl- α -*D*-muramoyl-L-alanyl-*D*-glutamate + L-lysine = ADP + phosphate + UDP-*N*-acetyl- α -*D*-muramoyl-L-alanyl- γ -*D*-glutamyl-L-lysine
Other name(s): MurE synthetase; UDP-*N*-acetylmuramoyl-L-alanyl-*D*-glutamyl-L-lysine synthetase; uridine diphospho-*N*-acetylmuramoylalanyl-*D*-glutamyllysine synthetase; UPD-MurNAc-L-Ala-*D*-Glu:L-Lys ligase; UDP-*N*-acetylmuramoyl-L-alanyl-*D*-glutamate:L-lysine γ -ligase (ADP-forming)
Systematic name: UDP-*N*-acetyl- α -*D*-muramoyl-L-alanyl-*D*-glutamate:L-lysine γ -ligase (ADP-forming)
Comments: Involved in the synthesis of a cell-wall peptide in bacteria. This enzyme adds lysine in some Gram-positive organisms; in others and in Gram-negative organisms EC 6.3.2.13 (UDP-*N*-acetylmuramoyl-L-alanyl-*D*-glutamate—2,6-diaminopimelate ligase) adds 2,6-diaminopimelate instead.
References: [179, 442]

[EC 6.3.2.7 created 1961, modified 2002]

EC 6.3.2.8

Accepted name: UDP-*N*-acetylmuramate—L-alanine ligase
Reaction: ATP + UDP-*N*-acetyl- α -*D*-muramate + L-alanine = ADP + phosphate + UDP-*N*-acetyl- α -*D*-muramoyl-L-alanine
Other name(s): MurC synthetase; UDP-*N*-acetylmuramoyl-L-alanine synthetase; uridine diphospho-*N*-acetylmuramoylalanine synthetase; UDP-*N*-acetylmuramoylalanine synthetase; L-alanine-adding enzyme; UDP-acetylmuramyl-L-alanine synthetase; UDPMurNAc-L-alanine synthetase; L-Ala ligase; uridine diphosphate *N*-acetylmuramate:L-alanine ligase; uridine 5'-diphosphate-*N*-acetylmuramyl-L-alanine synthetase; uridine-diphosphate-*N*-acetylmuramate:L-alanine ligase; UDP-MurNAc:L-alanine ligase; alanine-adding enzyme; UDP-*N*-acetylmuramyl:L-alanine ligase; UDP-*N*-acetylmuramate:L-alanine ligase (ADP-forming)
Systematic name: UDP-*N*-acetyl- α -*D*-muramate:L-alanine ligase (ADP-forming)
Comments: Involved in the synthesis of a cell-wall peptide in bacteria.
References: [179, 303, 442]

[EC 6.3.2.8 created 1965, modified 2002]

EC 6.3.2.9

Accepted name: UDP-*N*-acetylmuramoyl-L-alanine—*D*-glutamate ligase
Reaction: ATP + UDP-*N*-acetyl- α -*D*-muramoyl-L-alanine + *D*-glutamate = ADP + phosphate + UDP-*N*-acetyl- α -*D*-muramoyl-L-alanyl-*D*-glutamate
Other name(s): MurD synthetase; UDP-*N*-acetylmuramoyl-L-alanyl-*D*-glutamate synthetase; uridine diphospho-*N*-acetylmuramoylalanyl-*D*-glutamate synthetase; *D*-glutamate-adding enzyme; *D*-glutamate ligase; UDP-Mur-NAC-L-Ala:*D*-Glu ligase; UDP-*N*-acetylmuramoyl-L-alanine:glutamate ligase (ADP-forming); UDP-*N*-acetylmuramoylalanine—*D*-glutamate ligase; UDP-*N*-acetylmuramoyl-L-alanine:*D*-glutamate ligase (ADP-forming)
Systematic name: UDP-*N*-acetyl- α -*D*-muramoyl-L-alanine:*D*-glutamate ligase (ADP-forming)
Comments: Involved in the synthesis of a cell-wall peptide in bacteria.
References: [179, 442]

[EC 6.3.2.9 created 1965, modified 2002]

EC 6.3.2.10

- Accepted name:** UDP-*N*-acetylmuramoyl-tripeptide—D-alanyl-D-alanine ligase
- Reaction:** ATP + UDP-*N*-acetylmuramoyl-L-alanyl- γ -D-glutamyl-L-lysine + D-alanyl-D-alanine = ADP + phosphate + UDP-*N*-acetylmuramoyl-L-alanyl- γ -D-glutamyl-L-lysyl-D-alanyl-D-alanine
- Other name(s):** MurF synthetase; UDP-*N*-acetylmuramoyl-L-alanyl-D-glutamyl-L-lysyl-D-alanyl-D-alanine synthetase; UDP-*N*-acetylmuramoylalanyl-D-glutamyl-lysine-D-alanyl-D-alanine ligase; uridine diphosphoacetylmuramoylpentapeptide synthetase; UDPacetylmuramoylpentapeptide synthetase; UDP-MurNAc-L-Ala-D-Glu-L-Lys:D-Ala-D-Ala ligase
- Systematic name:** UDP-*N*-acetylmuramoyl-L-alanyl-D-glutamyl-L-lysine:D-alanyl-D-alanine ligase (ADP-forming)
- Comments:** Involved with EC 6.3.2.4 (D-alanine—D-alanine ligase), EC 6.3.2.7 (UDP-*N*-acetylmuramoyl-L-alanyl-D-glutamate—L-lysine ligase) or EC 6.3.2.13 (UDP-*N*-acetylmuramoyl-L-alanyl-D-glutamate—2,6-diaminopimelate ligase), EC 6.3.2.8 (UDP-*N*-acetylmuramate—L-alanine ligase) and EC 6.3.2.9 (UDP-*N*-acetylmuramoyl-L-alanine—D-glutamate ligase) in the synthesis of a cell-wall peptide (click here) for diagram. This enzyme also catalyses the reaction when the C-terminal residue of the tripeptide is *meso*-2,4-diaminoheptanedioate (acylated at its L-centre), linking the D-Ala-D-Ala to the carboxy group of the L-centre. This activity was previously attributed to EC 6.3.2.15, which has since been deleted.
- References:** [180, 442]

[EC 6.3.2.10 created 1965, modified 2002]

EC 6.3.2.11

- Accepted name:** carnosine synthase
- Reaction:** ATP + L-histidine + β -alanine = ADP + phosphate + carnosine
- Other name(s):** carnosine synthetase; carnosine-anserine synthetase; homocarnosine-carnosine synthetase; carnosine-homocarnosine synthetase; L-histidine: β -alanine ligase (AMP-forming) (incorrect)
- Systematic name:** L-histidine: β -alanine ligase (ADP-forming)
- Comments:** This enzyme was thought to form AMP [189, 404], but studies with highly purified enzyme proved that it forms ADP [97]. Carnosine is a dipeptide that is present at high concentrations in skeletal muscle and the olfactory bulb of vertebrates [77]. It is also found in the skeletal muscle of some invertebrates. The enzyme can also catalyse the formation of homocarnosine from 4-aminobutanoate and L-histidine, with much lower activity [97].
- References:** [189, 404, 77, 97]

[EC 6.3.2.11 created 1965, modified 2010]

EC 6.3.2.12

- Accepted name:** dihydrofolate synthase
- Reaction:** ATP + 7,8-dihydropteroate + L-glutamate = ADP + phosphate + 7,8-dihydropteroylglutamate
- Other name(s):** dihydrofolate synthetase; 7,8-dihydrofolate synthetase; H₂-folate synthetase; 7,8-dihydropteroate:L-glutamate ligase (ADP); dihydropteroate:L-glutamate ligase (ADP-forming); DHFS
- Systematic name:** 7,8-dihydropteroate:L-glutamate ligase (ADP-forming)
- Comments:** In some bacteria, a single protein catalyses both this activity and that of EC 6.3.2.17, tetrahydrofolate synthase [40], the combined activity of which leads to the formation of the coenzyme polyglutamated tetrahydropteroate (H₄PteGlu_{*n*}), i.e. various tetrahydrofolates. In contrast, the activities are located on separate proteins in most eukaryotes studied to date [348]. This enzyme is responsible for attaching the first glutamate residue to dihydropteroate to form dihydrofolate and is present only in those organisms that have the ability to synthesize tetrahydrofolate *de novo*, e.g. plants, most bacteria, fungi and protozoa [348].
- References:** [140, 40, 348, 61, 72]

[EC 6.3.2.12 created 1972, modified 2005]

EC 6.3.2.13

- Accepted name:** UDP-*N*-acetylmuramoyl-L-alanyl-D-glutamate—2,6-diaminopimelate ligase
- Reaction:** ATP + UDP-*N*-acetyl- α -D-muramoyl-L-alanyl-D-glutamate + *meso*-2,6-diaminoheptanedioate = ADP + phosphate + UDP-*N*-acetyl- α -D-muramoyl-L-alanyl- γ -D-glutamyl-*meso*-2,6-diaminoheptanedioate
- Other name(s):** MurE synthetase [ambiguous]; UDP-*N*-acetylmuramoyl-L-alanyl-D-glutamate:*meso*-2,6-diaminoheptanedioate ligase (ADP-forming); UDP-*N*-acetylmuramoyl-L-alanyl-D-glutamyl-*meso*-2,6-diaminopimelate synthetase; UDP-*N*-acetylmuramoylalanyl-D-glutamate—2,6-diaminopimelate ligase; UDP-*N*-acetylmuramoyl-L-alanyl-D-glutamate:*meso*-2,6-diaminoheptanedioate γ -ligase (ADP-forming)
- Systematic name:** UDP-*N*-acetyl- α -D-muramoyl-L-alanyl-D-glutamate:*meso*-2,6-diaminoheptanedioate γ -ligase (ADP-forming)
- Comments:** Involved in the synthesis of a cell-wall peptide in bacteria. This enzyme adds diaminopimelate in Gram-negative organisms and in some Gram-positive organisms; in others EC 6.3.2.7 (UDP-*N*-acetylmuramoyl-L-alanyl-D-glutamate—L-lysine ligase) adds lysine instead. It is the amino group of the L-centre of the diaminopimelate that is acylated.
- References:** [285, 442]

[EC 6.3.2.13 created 1972, modified 2002, modified 2010]

EC 6.3.2.14

- Accepted name:** enterobactin synthase
- Reaction:** 6 ATP + 3 2,3-dihydroxybenzoate + 3 L-serine = enterobactin + 6 AMP + 6 diphosphate
- Other name(s):** *N*-(2,3-dihydroxybenzoyl)-serine synthetase; 2,3-dihydroxybenzoylserine synthetase; 2,3-dihydroxybenzoate—serine ligase
- Systematic name:** 2,3-dihydroxybenzoate:L-serine ligase
- Comments:** This enzyme complex catalyses the conversion of three molecules each of 2,3-dihydroxybenzoate and L-serine to form the siderophore enterobactin. In *Escherichia coli* the complex is formed by EntB (an aryl carrier protein that has to be activated by 4'-phosphopantetheine), EntD (a phosphopantetheinyl transferase that activates EntB), EntE (catalyses the ATP-dependent condensation of 2,3-dihydroxybenzoate and holo-EntB to form the covalently arylated form of EntB), and EntF (a four domain protein that catalyses the activation of L-serine by ATP, the condensation of the activated L-serine with the activated 2,3-dihydroxybenzoate, and the trimerization of three such moieties to a single enterobactin molecule).
- References:** [44, 368, 369, 370, 127, 387]

[EC 6.3.2.14 created 1972, modified 2012]

[6.3.2.15 Deleted entry. UDP-*N*-acetylmuramoylalanyl-D-glutamyl-2,6-diaminopimelate-D-alanyl-D-alanine ligase. The activity observed is due to EC 6.3.2.10, UDP-*N*-acetylmuramoyl-tripeptide—D-alanyl-D-alanine ligase]

[EC 6.3.2.15 created 1976, deleted 2002]

EC 6.3.2.16

- Accepted name:** D-alanine—alanyl-poly(glycerolphosphate) ligase
- Reaction:** ATP + D-alanine + alanyl-poly(glycerolphosphate) = ADP + phosphate + D-alanyl-alanyl-poly(glycerolphosphate)
- Other name(s):** D-alanyl-alanyl-poly(glycerolphosphate) synthetase; D-alanine:membrane-acceptor ligase; D-alanylalanylpoly(phosphoglycerol) synthetase; D-alanyl-poly(phosphoglycerol) synthetase; D-alanine-membrane acceptor-ligase
- Systematic name:** D-alanine:alanyl-poly(glycerolphosphate) ligase (ADP-forming)
- Comments:** Involved in the synthesis of teichoic acids.
- References:** [355]

[EC 6.3.2.16 created 1976]

EC 6.3.2.17

- Accepted name:** tetrahydrofolate synthase
Reaction: $\text{ATP} + \text{tetrahydropteroyl-}[\gamma\text{-Glu}]_n + \text{L-glutamate} = \text{ADP} + \text{phosphate} + \text{tetrahydropteroyl-}[\gamma\text{-Glu}]_{n+1}$
Other name(s): foylpolylglutamate synthase; folate polyglutamate synthetase; formyltetrahydropteroyldiglutamate synthetase; N^{10} -formyltetrahydropteroyldiglutamate synthetase; foylpolyl- γ -glutamate synthase; foylpolylglutamyl synthetase; foylpolyl(γ -glutamate) synthase; foylpolylglutamate synthetase; FPGS; tetrahydrofoylpolylglutamate synthase; tetrahydrofolate:L-glutamate γ -ligase (ADP-forming); tetrahydropteroyl- $[\gamma\text{-Glu}]_n$:L-glutamate γ -ligase (ADP-forming)
Systematic name: tetrahydropteroyl- γ -polyglutamate:L-glutamate γ -ligase (ADP-forming)
Comments: In some bacteria, a single protein catalyses both this activity and that of EC 6.3.2.12, dihydrofolate synthase [40], the combined activity of which leads to the formation of the coenzyme polyglutamated tetrahydropteroyl (H₄PteGlu_n), i.e. various tetrahydrofolates (H₄folate). In contrast, the activities are located on separate proteins in most eukaryotes studied to date [348]. In *Arabidopsis thaliana*, this enzyme is present as distinct isoforms in the mitochondria, the cytosol and the chloroplast. Each isoform is encoded by a separate gene, a situation that is unique among eukaryotes [348]. As the affinity of folate-dependent enzymes increases markedly with the number of glutamic residues, the tetrahydropteroyl polyglutamates are the preferred coenzymes of C₁ metabolism. (reviewed in [72]). The enzymes from different sources (particularly eukaryotes versus prokaryotes) have different substrate specificities with regard to one-carbon substituents and the number of glutamate residues present on the tetrahydrofolates.
References: [67, 267, 40, 348, 72, 61]

[EC 6.3.2.17 created 1984, modified 2003, modified 2005]

EC 6.3.2.18

- Accepted name:** γ -glutamylhistamine synthase
Reaction: $\text{ATP} + \text{L-glutamate} + \text{histamine} = \text{products of ATP breakdown} + N^\alpha\text{-}\gamma\text{-L-glutamylhistamine}$
Other name(s): γ -glutaminylhistamine synthetase; γ -GHA synthetase
Systematic name: L-glutamate:histamine ligase
References: [403]

[EC 6.3.2.18 created 1986]

[6.3.2.19 Deleted entry. ubiquitin—protein ligase. The ubiquitinylation process is now known to be performed by several enzymes in sequence, starting with EC 6.2.1.45 (ubiquitin-activating enzyme E1) and followed by several transfer reactions, including those of EC 2.3.2.23 (E2 ubiquitin-conjugating enzyme) and EC 2.3.2.27 (RING-type E3 ubiquitin transferase)]

[EC 6.3.2.19 created 1986, deleted 2015]

EC 6.3.2.20

- Accepted name:** indoleacetate—lysine synthetase
Reaction: $\text{ATP} + (\text{indol-3-yl})\text{acetate} + \text{L-lysine} = \text{ADP} + \text{phosphate} + N^6\text{-}[(\text{indol-3-yl})\text{acetyl}]\text{-L-lysine}$
Other name(s): indoleacetate:L-lysine ligase (ADP-forming)
Systematic name: (indol-3-yl)acetate:L-lysine ligase (ADP-forming)
References: [135, 172]

[EC 6.3.2.20 created 1989]

[6.3.2.21 Deleted entry. ubiquitin—calmodulin ligase. The reaction is performed by the sequential action of EC 6.2.1.45 (ubiquitin-activating enzyme E1), several ubiquitin transferases and finally by EC 2.3.2.27 [ubiquitin transferase RING E3 (calmodulin-selective)]]

[EC 6.3.2.21 created 1990, deleted 2015]

[6.3.2.22 Transferred entry. diphthine—ammonia ligase. Now EC 6.3.1.14, diphthine—ammonia ligase.]

[EC 6.3.2.22 created 1990, deleted 2010]

EC 6.3.2.23

Accepted name: homoglutathione synthase
Reaction: ATP + γ -L-glutamyl-L-cysteine + β -alanine = ADP + phosphate + γ -L-glutamyl-L-cysteinyl- β -alanine
Other name(s): homoglutathione synthetase; β -alanine specific hGSH synthetase
Systematic name: γ -L-glutamyl-L-cysteine: β -alanine ligase (ADP-forming)
Comments: Not identical with EC 6.3.2.3 glutathione synthase.
References: [246]

[EC 6.3.2.23 created 1990]

EC 6.3.2.24

Accepted name: tyrosine—arginine ligase
Reaction: ATP + L-tyrosine + L-arginine = AMP + diphosphate + L-tyrosyl-L-arginine
Other name(s): tyrosyl-arginine synthase; kyotorphin synthase; kyotorphin-synthesizing enzyme; kyotorphin synthetase
Systematic name: L-tyrosine:L-arginine ligase (AMP-forming)
References: [437]

[EC 6.3.2.24 created 1992]

EC 6.3.2.25

Accepted name: tubulin—tyrosine ligase
Reaction: ATP + detyrosinated α -tubulin + L-tyrosine = α -tubulin + ADP + phosphate
Systematic name: α -tubulin:L-tyrosine ligase (ADP-forming)
Comments: L-Tyrosine is linked via a peptide bond to the C-terminus of de-tyrosinated α -tubulin (des-Tyr⁰- α -tubulin). The enzyme is highly specific for α -tubulin and moderately specific for ATP and L-tyrosine. L-Phenylalanine and 3,4-dihydroxy-L-phenylalanine are transferred but with higher K_m values.
References: [461, 367]

[EC 6.3.2.25 created 1999]

EC 6.3.2.26

Accepted name: *N*-(5-amino-5-carboxypentanoyl)-L-cysteinyl-D-valine synthase
Reaction: 3 ATP + L-2-aminohexanedioate + L-cysteine + L-valine + H₂O = 3 AMP + 3 diphosphate + *N*-[L-5-amino-5-carboxypentanoyl]-L-cysteinyl-D-valine
Other name(s): L- δ -(α -aminoadipoyl)-L-cysteinyl-D-valine synthetase; ACV synthetase; L- α -aminoadipyl-cysteinyl-valine synthetase;
Systematic name: L-2-aminohexanedioate:L-cysteine:L-valine ligase (AMP-forming, valine-inverting)
Comments: Requires Mg²⁺. The enzyme contains 4'-phosphopantetheine, which may be involved in the mechanism of the reaction. Forms part of the penicillin biosynthesis pathway (for pathway, click here).
References: [49, 426]

[EC 6.3.2.26 created 2002]

[6.3.2.27 Deleted entry. The activity is covered by two independent enzymes, EC 6.3.2.38 *N*²-citryl-*N*⁶-acetyl-*N*⁶-hydroxylysine synthase, and EC 6.3.2.39, aerobactin synthase]

[EC 6.3.2.27 created 2002, modified 2006, deleted 2012]

[6.3.2.28 Transferred entry. L-amino-acid α -ligase. Now EC 6.3.2.49, L-alanine-L-anticapsin ligase]

[EC 6.3.2.28 created 2006, deleted 2015]

EC 6.3.2.29

Accepted name: cyanophycin synthase (L-aspartate-adding)
Reaction: $\text{ATP} + [\text{L-Asp}(4\text{-L-Arg})]_n + \text{L-Asp} = \text{ADP} + \text{phosphate} + [\text{L-Asp}(4\text{-L-Arg})]_{n+1}\text{-L-Asp}$
Other name(s): CphA (ambiguous); CphA1 (ambiguous); CphA2 (ambiguous); cyanophycin synthetase (ambiguous); multi-L-arginyl-poly-L-aspartate synthase (ambiguous)
Systematic name: cyanophycin:L-aspartate ligase (ADP-forming)
Comments: Requires Mg^{2+} for activity. Both this enzyme and EC 6.3.2.30, cyanophycin synthase (L-arginine-adding), are required for the elongation of cyanophycin, which is a protein-like cell inclusion that is unique to cyanobacteria and acts as a temporary nitrogen store [4]. Both enzymes are found in the same protein but have different active sites [4, 28]. Both L-Asp and L-Arg must be present before either enzyme will display significant activity [4].
References: [3, 4, 8, 28, 485, 486]

[EC 6.3.2.29 created 2007]

EC 6.3.2.30

Accepted name: cyanophycin synthase (L-arginine-adding)
Reaction: $\text{ATP} + [\text{L-Asp}(4\text{-L-Arg})]_n\text{-L-Asp} + \text{L-Arg} = \text{ADP} + \text{phosphate} + [\text{L-Asp}(4\text{-L-Arg})]_{n+1}$
Other name(s): CphA (ambiguous); CphA1 (ambiguous); CphA2 (ambiguous); cyanophycin synthetase (ambiguous); multi-L-arginyl-poly-L-aspartate synthase (ambiguous)
Systematic name: cyanophycin:L-arginine ligase (ADP-forming)
Comments: Requires Mg^{2+} for activity. Both this enzyme and EC 6.3.2.29, cyanophycin synthase (L-aspartate-adding), are required for the elongation of cyanophycin, which is a protein-like cell inclusion that is unique to cyanobacteria and acts as a temporary nitrogen store [4]. Both enzymes are found in the same protein but have different active sites [4, 28]. Both L-Asp and L-Arg must be present before either enzyme will display significant activity [4]. Canavanine and lysine can be incorporated into the polymer instead of arginine [4].
References: [3, 4, 8, 28, 485, 486]

[EC 6.3.2.30 created 2007]

EC 6.3.2.31

Accepted name: coenzyme $\text{F}_{420}\text{-0}$:L-glutamate ligase
Reaction: $\text{GTP} + \text{coenzyme } \text{F}_{420}\text{-0} + \text{L-glutamate} = \text{GDP} + \text{phosphate} + \text{coenzyme } \text{F}_{420}\text{-1}$
Other name(s): CofE-AF; MJ0768; CofE
Systematic name: L-glutamate:coenzyme $\text{F}_{420}\text{-0}$ ligase (GDP-forming)
Comments: This protein catalyses the successive addition of two glutamate residues to cofactor F_{420} by two distinct and independent reactions. In the reaction described here the enzyme attaches a glutamate via its α -amine group to $\text{F}_{420}\text{-0}$. In the second reaction (EC 6.3.2.34, coenzyme $\text{F}_{420}\text{-1}$ — γ -L-glutamate ligase) it catalyses the addition of a second L-glutamate residue to the γ -carboxyl of the first glutamate.
References: [228, 308]

[EC 6.3.2.31 created 2010]

EC 6.3.2.32

Accepted name: coenzyme $\gamma\text{-F}_{420}\text{-2}$: α -L-glutamate ligase
Reaction: $\text{ATP} + \text{coenzyme } \gamma\text{-F}_{420}\text{-2} + \text{L-glutamate} = \text{ADP} + \text{phosphate} + \text{coenzyme } \alpha\text{-F}_{420}\text{-3}$
Other name(s): MJ1001; CofF protein; $\gamma\text{-F}_{420}\text{-2}$: α -L-glutamate ligase
Systematic name: L-glutamate:coenzyme $\gamma\text{-F}_{420}\text{-2}$ (ADP-forming)
Comments: The enzyme caps the γ -glutamyl tail of the hydride carrier coenzyme F_{420} [229].
References: [229]

[EC 6.3.2.32 created 2010]

EC 6.3.2.33

Accepted name: tetrahydrosarcinapterin synthase
Reaction: ATP + tetrahydromethanopterin + L-glutamate = ADP + phosphate + 5,6,7,8-tetrahydrosarcinapterin
Other name(s): H₄MPT:α-L-glutamate ligase; MJ0620; MptN protein
Systematic name: tetrahydromethanopterin:α-L-glutamate ligase (ADP-forming)
Comments: This enzyme catalyses the biosynthesis of 5,6,7,8-tetrahydrosarcinapterin, a modified form of tetrahydromethanopterin found in the Methanosarcinales. It does not require K⁺, and does not discriminate between ATP and GTP [229].
References: [229]

[EC 6.3.2.33 created 2010]

EC 6.3.2.34

Accepted name: coenzyme F₄₂₀-1:γ-L-glutamate ligase
Reaction: GTP + coenzyme F₄₂₀-1 + L-glutamate = GDP + phosphate + coenzyme γ-F₄₂₀-2
Other name(s): F₄₂₀:γ-glutamyl ligase; CofE-AF; MJ0768; CofE
Systematic name: L-glutamate:coenzyme F₄₂₀-1 ligase (GDP-forming)
Comments: This protein catalyses the successive addition of two glutamate residues to cofactor F₄₂₀ by two distinct and independent reactions. In the first reaction (EC 6.3.2.31, coenzyme F₄₂₀-0—L-glutamate ligase) the enzyme attaches a glutamate via its α-amine group to F₄₂₀-0. In the second reaction, which is described here, the enzyme catalyses the addition of a second L-glutamate residue to the γ-carboxyl of the first glutamate.
References: [228, 308]

[EC 6.3.2.34 created 2010]

EC 6.3.2.35

Accepted name: D-alanine—D-serine ligase
Reaction: D-alanine + D-serine + ATP = D-alanyl-D-serine + ADP + phosphate
Other name(s): VanC; VanE; VanG
Systematic name: D-alanine:D-serine ligase (ADP-forming)
Comments: The product of this enzyme, D-alanyl-D-serine, can be incorporated into the peptidoglycan pentapeptide instead of the usual D-alanyl-D-alanine dipeptide, which is formed by EC 6.3.2.4, D-alanine—D-alanine ligase. The resulting peptidoglycan does not bind the glycopeptide antibiotics vancomycin and teicoplanin, conferring resistance on the bacteria.
References: [100, 323, 113, 90, 456]

[EC 6.3.2.35 created 2010]

EC 6.3.2.36

Accepted name: 4-phosphopantoate—β-alanine ligase
Reaction: ATP + (R)-4-phosphopantoate + β-alanine = AMP + diphosphate + (R)-4'-phosphopantothenate
Other name(s): phosphopantothenate synthetase; TK1686 protein
Systematic name: (R)-4-phosphopantoate:β-alanine ligase (AMP-forming)
Comments: The conversion of (R)-pantoate to (R)-4'-phosphopantothenate is part of the pathway leading to biosynthesis of 4'-phosphopantetheine, an essential cofactor of coenzyme A and acyl-carrier protein. In bacteria and eukaryotes this conversion is performed by condensation with β-alanine, followed by phosphorylation (EC 6.3.2.1 [pantoate—β-alanine ligase] and EC 2.7.1.33 [pantothenate kinase], respectively). In archaea the order of these two steps is reversed, and phosphorylation precedes condensation with β-alanine. The two archaeal enzymes that catalyse this conversion are EC 2.7.1.169, pantoate kinase, and this enzyme.
References: [475]

[EC 6.3.2.36 created 2011]

EC 6.3.2.37

- Accepted name:** UDP-*N*-acetylmuramoyl-L-alanyl-D-glutamate—D-lysine ligase
Reaction: ATP + UDP-*N*-acetyl- α -D-muramoyl-L-alanyl-D-glutamate + D-lysine = ADP + phosphate + UDP-*N*-acetyl- α -D-muramoyl-L-alanyl- γ -D-glutamyl-*N*^ε-D-lysine
Other name(s): UDP-MurNAc-L-Ala-D-Glu:D-Lys ligase; D-lysine-adding enzyme
Systematic name: UDP-*N*-acetyl- α -D-muramoyl-L-alanyl-D-glutamate:D-lysine γ -ligase (ADP-forming)
Comments: Involved in the synthesis of cell-wall peptidoglycan. The D-lysine is attached to the peptide chain at the *N*⁶ position. The enzyme from *Thermotoga maritima* also performs the reaction of EC 6.3.2.7, UDP-*N*-acetylmuramoyl-L-alanyl-D-glutamate—L-lysine ligase.
References: [42]

[EC 6.3.2.37 created 2011, modified 2015]

EC 6.3.2.38

- Accepted name:** *N*²-citryl-*N*⁶-acetyl-*N*⁶-hydroxylysine synthase
Reaction: 2 ATP + citrate + *N*⁶-acetyl-*N*⁶-hydroxy-L-lysine + H₂O = 2 ADP + 2 phosphate + *N*²-citryl-*N*⁶-acetyl-*N*⁶-hydroxy-L-lysine
Other name(s): *N*^α-citryl-*N*^ε-acetyl-*N*^ε-hydroxylysine synthase; *iucA* (gene name)
Systematic name: citrate:*N*⁶-acetyl-*N*⁶-hydroxy-L-lysine ligase (ADP-forming)
Comments: Requires Mg²⁺. Aerobactin is one of a group of high-affinity iron chelators known as siderophores and is produced under conditions of iron deprivation [56]. It is a dihydroxamate comprising two molecules of *N*⁶-acetyl-*N*⁶-hydroxy-L-lysine and one molecule of citrate. This enzyme catalyses the first of two synthase reactions to link *N*⁶-acetyl-*N*⁶-hydroxy-L-lysine and citrate [85, 56].
References: [17, 132, 262, 85, 56]

[EC 6.3.2.38 created 2012]

EC 6.3.2.39

- Accepted name:** aerobactin synthase
Reaction: 2 ATP + *N*²-citryl-*N*⁶-acetyl-*N*⁶-hydroxy-L-lysine + *N*⁶-acetyl-*N*⁶-hydroxy-L-lysine + H₂O = 2 ADP + 2 phosphate + aerobactin
Other name(s): *iucC* (gene name)
Systematic name: *N*²-citryl-*N*⁶-acetyl-*N*⁶-hydroxy-L-lysine:*N*⁶-acetyl-*N*⁶-hydroxy-L-lysine ligase (ADP-forming)
Comments: Requires Mg²⁺. Aerobactin is one of a group of high-affinity iron chelators known as siderophores and is produced under conditions of iron deprivation [56]. It is a dihydroxamate comprising two molecules of *N*⁶-acetyl-*N*⁶-hydroxy-L-lysine and one molecule of citric acid. This enzyme catalyses the second of two synthase reactions to link *N*⁶-acetyl-*N*⁶-hydroxy-L-lysine and citrate [3,4,5].
References: [17, 132, 262, 85, 86, 56]

[EC 6.3.2.39 created 2012]

EC 6.3.2.40

- Accepted name:** cyclopeptide synthase
Reaction: 2 ATP + *S*-adenosyl-L-methionine + anthranilate + L-phenylalanine = cyclopeptide + 2 AMP + 2 diphosphate + *S*-adenosyl-L-homocysteine
Systematic name: *S*-adenosyl-L-methionine:anthranilate:L-phenylalanine ligase (cyclopeptide forming)
Comments: Cyclopeptide synthase is the key enzyme of benzodiazepine alkaloid biosynthesis in the fungus *Penicillium cyclopium*. The enzyme is a non-ribosomal peptide synthase.
References: [224, 130]

[EC 6.3.2.40 created 2013]

EC 6.3.2.41

Accepted name: *N*-acetylaspartylglutamate synthase
Reaction: ATP + *N*-acetyl-L-aspartate + L-glutamate = ADP + phosphate + *N*-acetyl-L-aspartyl-L-glutamate
Other name(s): *N*-acetylaspartylglutamate synthetase; NAAG synthetase; NAAGS; RIMKLA (gene name) (ambiguous); RIMKLB (gene name) (ambiguous)
Systematic name: *N*-acetyl-L-aspartate:L-glutamate ligase (ADP, *N*-acetyl-L-aspartyl-L-glutamate-forming)
Comments: The enzyme, found in animals, produces the neurotransmitter *N*-acetyl-L-aspartyl-L-glutamate. One isoform also has the activity of EC 6.3.1.17, β -citrylglutamate synthase [69], while another isoform has the activity of EC 6.3.2.42, *N*-acetylaspartylglutamylglutamate synthase [238].
References: [26, 69, 238]

[EC 6.3.2.41 created 2014]

EC 6.3.2.42

Accepted name: *N*-acetylaspartylglutamylglutamate synthase
Reaction: 2 ATP + *N*-acetyl-L-aspartate + 2 L-glutamate = 2 ADP + 2 phosphate + *N*-acetyl-L-aspartyl-L-glutamyl-L-glutamate
Other name(s): *N*-acetylaspartylglutamylglutamate synthetase; NAAG(2) synthase; NAAG synthetase II; NAAGS-II; RIMKLA (gene name) (ambiguous)
Systematic name: *N*-acetyl-L-aspartate:L-glutamate ligase (ADP, *N*-acetyl-L-aspartyl-L-glutamyl-L-glutamate-forming)
Comments: The enzyme, found in mammals, also has the activity of EC 6.3.2.41, *N*-acetylaspartylglutamate synthase.
References: [238]

[EC 6.3.2.42 created 2014]

EC 6.3.2.43

Accepted name: [lysine-biosynthesis-protein LysW]—L-2-aminoadipate ligase
Reaction: ATP + [lysine-biosynthesis-protein LysW]-C-terminal-L-glutamate + L-2-aminoadipate = ADP + phosphate + [lysine-biosynthesis-protein LysW]-C-terminal- γ -(L-2-aminoadip-2-yl)-L-glutamate
Other name(s): α -aminoadipate-lysW ligase *lysX* (gene name); LysX (ambiguous); AAA—LysW ligase
Systematic name: [lysine-biosynthesis-protein LysW]-C-terminal-L-glutamate:L-2-aminoadipate ligase (ADP-forming)
Comments: The enzymes from the thermophilic bacterium *Thermus thermophilus* and the thermophilic archaea *Sulfolobus acidocaldarius* and *Sulfolobus tokodaii* protect the amino group of L-2-aminoadipate by conjugation to the carrier protein LysW. This reaction is part of the lysine biosynthesis pathway in these organisms.
References: [443, 165, 317]

[EC 6.3.2.43 created 2014]

EC 6.3.2.44

Accepted name: pantoate— β -alanine ligase (ADP-forming)
Reaction: ATP + (*R*)-pantoate + β -alanine = ADP + phosphate + (*R*)-pantothenate
Other name(s): pantothenate synthetase (ambiguous); pantoate— β -alanine ligase (ambiguous)
Systematic name: (*R*)-pantoate: β -alanine ligase (ADP-forming)
Comments: The enzyme, characterized from the archaeon *Methanosarcina mazei*, is involved in the biosynthesis of pantothenate. It is different from EC 6.3.2.1, the AMP-forming pantoate- β -alanine ligase found in bacteria and eukaryota.
References: [363]

[EC 6.3.2.44 created 2014]

EC 6.3.2.45

Accepted name: UDP-*N*-acetylmuramate—L-alanyl- γ -D-glutamyl-*meso*-2,6-diaminoheptanedioate ligase

Reaction: ATP + UDP-*N*-acetyl- α -D-muramate + L-alanyl- γ -D-glutamyl-*meso*-2,6-diaminoheptanedioate = ADP + phosphate + UDP-*N*-acetylmuramoyl-L-alanyl- γ -D-glutamyl-*meso*-2,6-diaminoheptanedioate

Other name(s): murein peptide ligase; Mpl; *yjfG* (gene name); UDP-MurNAc:L-Ala- γ -D-Glu-*meso*-A2pm ligase; UDP-*N*-acetylmuramate:L-alanyl- γ -D-glutamyl-*meso*-diaminopimelate ligase

Systematic name: UDP-*N*-acetylmuramate:L-alanyl- γ -D-glutamyl-*meso*-2,6-diaminoheptanedioate ligase2015

Comments: The enzyme catalyses the reincorporation into peptidoglycan of the tripeptide L-alanyl- γ -D-glutamyl-2,6-*meso*-diaminoheptanedioate released during the maturation and constant remodeling of this bacterial cell wall polymer that occur during cell growth and division. The enzyme can also use the tetrapeptide L-alanyl- γ -D-glutamyl-*meso*-2,6-diaminoheptanedioyl-D-alanine or the pentapeptide L-alanyl- γ -D-glutamyl-*meso*-2,6-diaminoheptanedioyl-D-alanyl-D-alanine *in vivo* and *in vitro*. Requires Mg²⁺.

References: [273, 156]

[EC 6.3.2.45 created 2014]

EC 6.3.2.46

Accepted name: fumarate—(*S*)-2,3-diaminopropanoate ligase

Reaction: ATP + fumarate + L-2,3-diaminopropanoate = AMP + diphosphate + *N*³-fumaroyl-L-2,3-diaminopropanoate

Other name(s): DdaG; fumarate:(*S*)-2,3-diaminopropanoate ligase (AMP-forming)

Systematic name: fumarate:L-2,3-diaminopropanoate ligase (AMP-forming)

Comments: The enzyme, characterized from the bacterium *Enterobacter agglomerans*, is involved in biosynthesis of dapidamide tripeptide antibiotics, a family of fumaramoyl- and epoxysuccinamoyl-peptides named for the presence of an L-2,3-diaminopropanoate (DAP) moiety and two amide linkages in their scaffold.

References: [161]

[EC 6.3.2.46 created 2015]

EC 6.3.2.47

Accepted name: dapidamide synthase

Reaction:

- (1) ATP + 3-[(2*E*)-4-amino-4-oxobut-2-enoyl]amino-L-alanine + L-valine = ADP + phosphate + 3-[(2*E*)-4-amino-4-oxobut-2-enoyl]amino-L-alanyl-L-valine
- (2) ATP + 3-[(2*E*)-4-amino-4-oxobut-2-enoyl]amino-L-alanine + L-isoleucine = ADP + phosphate + 3-[(2*E*)-4-amino-4-oxobut-2-enoyl]amino-L-alanyl-L-isoleucine
- (3) ATP + 3-[(2*E*)-4-amino-4-oxobut-2-enoyl]amino-L-alanine + L-leucine = ADP + phosphate + 3-[(2*E*)-4-amino-4-oxobut-2-enoyl]amino-L-alanyl-L-leucine
- (4) ATP + 3-([(2*R*,3*R*)-3-carbamoyloxiran-2-yl]carbonylamino)-L-alanine + L-valine = ADP + phosphate + 3-([(2*R*,3*R*)-3-carbamoyloxiran-2-yl]carbonylamino)-L-alanyl-L-valine

Other name(s): DdaF; dapidamide A synthase

Systematic name: 3-[(2*E*)-4-amino-4-oxobut-2-enoyl]amino-L-alanine:L-valine ligase (ADP-forming)

Comments: The enzyme, characterized from the bacterium *Pantoea agglomerans*, is involved in biosynthesis of dapidamide tripeptide antibiotics, a family of fumaramoyl- and epoxysuccinamoyl-peptides named for the presence of an (*S*)-2,3-diaminopropanoate (DAP) moiety and two amide linkages in their scaffold.

References: [161, 160]

[EC 6.3.2.47 created 2015, modified 2016]

EC 6.3.2.48

Accepted name: L-arginine-specific L-amino acid ligase

Reaction: ATP + L-arginine + an L-amino acid = ADP + phosphate + an L-arginyl-L-amino acid

Other name(s): RizA; L-amino acid ligase RizA

Systematic name: L-arginine:L-amino acid ligase (ADP-forming)

Comments: The enzyme, characterized from the bacterium *Bacillus subtilis*, requires Mn^{2+} for activity. It shows strict substrate specificity toward L-arginine as the first (N-terminal) amino acid of the product. The second amino acid could be any standard protein-building amino acid except for L-proline.

References: [202]

[EC 6.3.2.48 created 2015]

EC 6.3.2.49

Accepted name: L-alanine—L-anticapsin ligase
Reaction: ATP + L-alanine + L-anticapsin = ADP + phosphate + bacilysin
Other name(s): BacD; alanine-anticapsin ligase; L-Ala-L-anticapsin ligase; *ywfE* (gene name)
Systematic name: L-alanine:L-anticapsin ligase (ADP-forming)
Comments: The enzyme, characterized from the bacterium *Bacillus subtilis*, is involved in the biosynthesis of the nonribosomally synthesized dipeptide antibiotic bacilysin, composed of L-alanine and L-anticapsin. The enzyme requires Mg^{2+} or Mn^{2+} for activity, and has a broad substrate specificity *in vitro* [417].
References: [417, 435, 388, 325]

[EC 6.3.2.49 created 2006 as EC 6.3.2.28, transferred 2015 to EC 6.3.2.49]

EC 6.3.2.50

Accepted name: tenuazonic acid synthetase
Reaction: ATP + L-isoleucine + acetoacetyl-CoA = AMP + diphosphate + tenuazonic acid + CoA
Other name(s): TAS1 (gene name)
Systematic name: L-isoleucine:acetoacetyl-CoA ligase (tenuazonic acid-forming)
Comments: This fungal enzyme, isolated from *Magnaporthe oryzae*, is a non-ribosomal peptide synthetase (NRPS)-polyketide synthase (PKS) hybrid protein that consists of condensation (C), adenylation (A) and peptidyl-carrier protein (PCP) domains in the NRPS portion and a ketosynthase (KS) domain in the PKS portion. ATP is required for activation of isoleucine, which is then condensed with acetoacetyl-CoA. Cyclization and release from the enzyme are catalysed by the KS domain.
References: [477]

[EC 6.3.2.50 created 2017]

EC 6.3.2.51

Accepted name: phosphopantothenate—cysteine ligase (ATP)
Reaction: ATP + (R)-4'-phosphopantothenate + L-cysteine = AMP + diphosphate + N-[(R)-4'-phosphopantothenoyl]-L-cysteine
Other name(s): phosphopantothenoylcysteine synthetase (ambiguous); PPCS (gene name)
Systematic name: (R)-4'-phosphopantothenate:L-cysteine ligase (ATP-utilizing)
Comments: A key enzyme in the production of coenzyme A. The eukaryotic enzyme requires ATP, in contrast to the bacterial enzyme, EC 6.3.2.5, phosphopantothenate—cysteine ligase, which requires CTP.
References: [81, 252, 212]

[EC 6.3.2.51 created 2017]

EC 6.3.2.52

Accepted name: jasmonoyl—L-amino acid synthetase
Reaction: ATP + jasmonate + an L-amino acid = AMP + diphosphate + a jasmonoyl-L-amino acid
Other name(s): JAR1 (gene name); JAR4 (gene name); JAR6 (gene name)
Systematic name: jasmonate:L-amino acid ligase

Comments: Two jasmonoyl-L-amino acid synthetases have been described from *Nicotiana attenuata* [453] and one from *Arabidopsis thaliana* [399]. The *N. attenuata* enzymes generate jasmonoyl-L-isoleucine, jasmonoyl-L-leucine, and jasmonoyl-L-valine. The enzyme from *A. thaliana* could catalyse the addition of many different amino acids to jasmonate *in vitro* [1,4,5]. While the abundant form of jasmonate in plants is (–)-jasmonate, the active form of jasmonoyl-L-isoleucine is (+)-7-iso-jasmonoyl-L-isoleucine.

References: [399, 192, 453, 142, 415]

[EC 6.3.2.52 created 2018]

EC 6.3.2.53

Accepted name: UDP-*N*-acetylmuramoyl-L-alanine—L-glutamate ligase

Reaction: ATP + UDP-*N*-acetyl- α -D-muramoyl-L-alanine + L-glutamate = ADP + phosphate + UDP-*N*-acetyl- α -D-muramoyl-L-alanyl-L-glutamate

Other name(s): *murD2* (gene name); UDP-*N*-acetyl- α -D-muramoyl-L-alanyl-L-glutamate synthetase; UDP-MurNAc-L-Ala-L-Glu synthetase

Systematic name: UDP-*N*-acetylmuramoyl-L-alanine—L-glutamate ligase (ADP-forming)

Comments: The enzyme, characterized from the bacterium *Xanthomonas oryzae*, catalyses the ligation of a terminal L-glutamate to UDP-*N*-acetyl- α -D-muramoyl-L-alanine. The combined activity of this enzyme and EC 5.1.1.23, UDP-*N*-acetyl- α -D-muramoyl-L-alanyl-L-glutamate epimerase, provides an alternative route for incorporating D-glutamate into peptidoglycan, replacing the more common combination of EC 5.1.1.3, glutamate racemase, and EC 6.3.2.9, UDP-*N*-acetylmuramoyl-L-alanine—D-glutamate ligase.

References: [111]

[EC 6.3.2.53 created 2018]

EC 6.3.3 Cyclo-ligases

EC 6.3.3.1

Accepted name: phosphoribosylformylglycinamide cyclo-ligase

Reaction: ATP + 2-(formamido)-*N*¹-(5-phospho-D-ribosyl)acetamide = ADP + phosphate + 5-amino-1-(5-phospho-D-ribosyl)imidazole

Other name(s): phosphoribosylaminoimidazole synthetase; AIR synthetase; 5'-aminoimidazole ribonucleotide synthetase; 2-(formamido)-1-*N*-(5-phosphoribosyl)acetamide cyclo-ligase (ADP-forming)

Systematic name: 2-(formamido)-*N*¹-(5-phosphoribosyl)acetamide cyclo-ligase (ADP-forming)

References: [226, 225]

[EC 6.3.3.1 created 1961, modified 2000]

EC 6.3.3.2

Accepted name: 5-formyltetrahydrofolate cyclo-ligase

Reaction: ATP + 5-formyltetrahydrofolate = ADP + phosphate + 5,10-methenyltetrahydrofolate

Other name(s): 5,10-methenyltetrahydrofolate synthetase; formyltetrahydrofolic cyclodehydrase; 5-formyltetrahydrofolate cyclodehydrase

Systematic name: 5-formyltetrahydrofolate cyclo-ligase (ADP-forming)

References: [139]

[EC 6.3.3.2 created 1972]

EC 6.3.3.3

Accepted name: dethiobiotin synthase

Reaction: ATP + 7,8-diaminononanoate + CO₂ = ADP + phosphate + dethiobiotin
Other name(s): dethiobiotin synthase
Systematic name: 7,8-diaminononanoate:carbon-dioxide cyclo-ligase (ADP-forming)
Comments: CTP has half the activity of ATP.
References: [207, 472]

[EC 6.3.3.3 created 1976]

EC 6.3.3.4

Accepted name: (carboxyethyl)arginine β-lactam-synthase
Reaction: ATP + L-N²-(2-carboxyethyl)arginine = AMP + diphosphate + deoxyamidinoproclavaminatate
Other name(s): L-2-N-(2-carboxyethyl)arginine cyclo-ligase (AMP-forming)
Systematic name: L-N²-(2-carboxyethyl)arginine cyclo-ligase (AMP-forming)
Comments: Forms part of the pathway for the biosynthesis of the β-lactamase inhibitor clavulanate in *Streptomyces clavuligerus*. It has been proposed [20] that L-N²-(2-carboxyethyl)arginine is first converted into an acyl-AMP by reaction with ATP and loss of diphosphate, and that the β-lactam ring is then formed by the intramolecular attack of the β-nitrogen on the activated carboxy group.
References: [483, 432, 20]

[EC 6.3.3.4 created 2003]

EC 6.3.3.5

Accepted name: O-ureido-D-serine cyclo-ligase
Reaction: O-ureido-D-serine + ATP + H₂O = D-cycloserine + CO₂ + NH₃ + ADP + phosphate
Other name(s): *dcsG* (gene name)
Systematic name: O-ureido-D-serine cyclo-ligase (D-cycloserine-forming)
Comments: The enzyme participates in the biosynthetic pathway of D-cycloserine, an antibiotic substance produced by several *Streptomyces* species.
References: [209, 436]

[EC 6.3.3.5 created 2013]

EC 6.3.3.6

Accepted name: carbapenam-3-carboxylate synthase
Reaction: ATP + (2*S*,5*S*)-5-carboxymethylproline = AMP + diphosphate + (3*S*,5*S*)-carbapenam 3-carboxylate
Other name(s): CarA (ambiguous); CPS (ambiguous); carbapenam-3-carboxylate ligase; 6-methyl-(2*S*,5*S*)-5-carboxymethylproline cyclo-ligase (AMP-forming)
Systematic name: (2*S*,5*S*)-5-carboxymethylproline cyclo-ligase (AMP-forming)
Comments: The enzyme is involved in the biosynthesis of the carbapenem β-lactam antibiotic (5*R*)-carbapen-2-em-3-carboxylate in the bacterium *Pectobacterium carotovorum*.
References: [131, 279, 341, 18]

[EC 6.3.3.6 created 2013 as 6.3.1.16, transferred 2013 to EC 6.3.3.6]

EC 6.3.3.7

Accepted name: Ni-sirohydrochlorin *a,c*-diamide reductive cyclase
Reaction: ATP + Ni-sirohydrochlorin *a,c*-diamide + **3** reduced electron acceptor + H₂O = ADP + phosphate + 15,17³-seco-F₄₃₀-17³-acid + **3** electron acceptor
Other name(s): *cfbC* (gene name); *cfbD* (gene name)
Systematic name: Ni-sirohydrochlorin *a,c*-diamide reductive cyclo-ligase (ADP-forming)
Comments: The enzyme, studied from the methanogenic archaeon *Methanosarcina acetivorans*, participates in the biosynthesis of the nickel-containing tetrapyrrole cofactor coenzyme F₄₃₀, which is required by EC 2.8.4.1, coenzyme-B sulfoethylthiotransferase.
References: [333, 481]

[EC 6.3.3.7 created 2017]

EC 6.3.4 Other carbon-nitrogen ligases

[6.3.4.1 *Transferred entry. GMP synthase. Now included in EC 6.3.5.2, GMP synthase (glutamine-hydrolysing)*]

[EC 6.3.4.1 created 1961, deleted 2013]

EC 6.3.4.2

- Accepted name:** CTP synthase (glutamine hydrolysing)
Reaction: ATP + UTP + L-glutamine = ADP + phosphate + CTP + L-glutamate (overall reaction)
(1a) L-glutamine + H₂O = L-glutamate + NH₃
(1b) ATP + UTP + NH₃ = ADP + phosphate + CTP
Other name(s): UTP—ammonia ligase; cytidine triphosphate synthetase; uridine triphosphate aminase; cytidine 5'-triphosphate synthetase; CTPS (gene name); *pyrG* (gene name); CTP synthase; UTP:ammonia ligase (ADP-forming)
Systematic name: UTP:L-glutamine amido-ligase (ADP-forming)
Comments: The enzyme contains three functionally distinct sites: an allosteric GTP-binding site, a glutaminase site where glutamine hydrolysis occurs (*cf.* EC 3.5.1.2, glutaminase), and the active site where CTP synthesis takes place. The reaction proceeds via phosphorylation of UTP by ATP to give an activated intermediate 4-phosphoryl UTP and ADP [447, 227]. Ammonia then reacts with this intermediate generating CTP and a phosphate. The enzyme can also use ammonia from the surrounding solution [1, 448].
References: [231, 240, 1, 447, 227, 448]

[EC 6.3.4.2 created 1961, modified 2013]

EC 6.3.4.3

- Accepted name:** formate—tetrahydrofolate ligase
Reaction: ATP + formate + tetrahydrofolate = ADP + phosphate + 10-formyltetrahydrofolate
Other name(s): formyltetrahydrofolate synthetase; 10-formyltetrahydrofolate synthetase; tetrahydrofolic formylase; tetrahydrofolate formylase
Systematic name: formate:tetrahydrofolate ligase (ADP-forming)
Comments: In eukaryotes occurs as a trifunctional enzyme also having methylenetetrahydrofolate dehydrogenase (NADP⁺) (EC 1.5.1.5) and methenyltetrahydrofolate cyclohydrolase (EC 3.5.4.9) activity.
References: [183, 240, 342, 464]

[EC 6.3.4.3 created 1961]

EC 6.3.4.4

- Accepted name:** adenylosuccinate synthase
Reaction: GTP + IMP + L-aspartate = GDP + phosphate + N⁶-(1,2-dicarboxyethyl)-AMP
Other name(s): IMP—aspartate ligase; adenylosuccinate synthetase; succinoadenylic kinosynthetase; succino-AMP synthetase
Systematic name: IMP:L-aspartate ligase (GDP-forming)
References: [82, 232, 473]

[EC 6.3.4.4 created 1961]

EC 6.3.4.5

- Accepted name:** argininosuccinate synthase
Reaction: ATP + L-citrulline + L-aspartate = AMP + diphosphate + 2-(N⁰-L-arginino)succinate

Other name(s): citrulline—aspartate ligase; argininosuccinate synthetase; arginine succinate synthetase; argininosuccinic acid synthetase; arginosuccinate synthetase
Systematic name: L-citrulline:L-aspartate ligase (AMP-forming)
References: [345, 382]

[EC 6.3.4.5 created 1961]

EC 6.3.4.6

Accepted name: urea carboxylase
Reaction: $\text{ATP} + \text{urea} + \text{HCO}_3^- = \text{ADP} + \text{phosphate} + \text{urea-1-carboxylate}$
Other name(s): urease (ATP-hydrolysing); urea carboxylase (hydrolysing); ATP—urea amidolyase; urea amidolyase; UALase; UCA
Systematic name: urea:carbon-dioxide ligase (ADP-forming)
Comments: A biotinyl-protein. The yeast enzyme (but not that from green algae) also catalyses the reaction of EC 3.5.1.54 allophanate hydrolase, thus bringing about the hydrolysis of urea to CO_2 and NH_3 . Previously also listed as EC 3.5.1.45. The enzyme from the prokaryotic bacterium *Oleomonas sagaranensis* can also use acetamide and formamide as substrates [190].
References: [364, 365, 412, 190]

[EC 6.3.4.6 created 1972, modified 1986 (EC 3.5.1.45 created 1978, incorporated 1986)]

EC 6.3.4.7

Accepted name: ribose-5-phosphate—ammonia ligase
Reaction: $\text{ATP} + \text{ribose 5-phosphate} + \text{NH}_3 = \text{ADP} + \text{phosphate} + \text{5-phosphoribosylamine}$
Other name(s): 5-phosphoribosylamine synthetase; ribose 5-phosphate aminotransferase; ammonia-ribose 5-phosphate aminotransferase
Systematic name: ribose-5-phosphate:ammonia ligase (ADP-forming)
References: [351]

[EC 6.3.4.7 created 1972]

EC 6.3.4.8

Accepted name: imidazoleacetate—phosphoribosyldiphosphate ligase
Reaction: $\text{ATP} + \text{imidazole-4-acetate} + \text{5-phosphoribosyl diphosphate} = \text{ADP} + \text{phosphate} + \text{1-(5-phosphoribosyl)imidazole-4-acetate} + \text{diphosphate}$
Other name(s): 5-phosphoribosylimidazoleacetate synthetase
Systematic name: imidazoleacetate:5-phosphoribosyl-diphosphate ligase (ADP- and diphosphate-forming)
References: [76]

[EC 6.3.4.8 created 1972]

EC 6.3.4.9

Accepted name: biotin—[methylmalonyl-CoA-carboxyltransferase] ligase
Reaction: $\text{ATP} + \text{biotin} + \text{apo-[methylmalonyl-CoA:pyruvate carboxyltransferase]} = \text{AMP} + \text{diphosphate} + \text{[methylmalonyl-CoA:pyruvate carboxyltransferase]}$
Other name(s): biotin-[methylmalonyl-CoA-carboxyltransferase] synthetase; biotin-methylmalonyl coenzyme A carboxyltransferase synthetase; biotin-transcarboxylase synthetase; methylmalonyl coenzyme A holotranscarboxylase synthetase; biotin—[methylmalonyl-CoA-carboxyltransferase] ligase; biotin:apo[methylmalonyl-CoA:pyruvate carboxyltransferase] ligase (AMP-forming)
Systematic name: biotin:apo[methylmalonyl-CoA:pyruvate carboxyltransferase] ligase (AMP-forming)
References: [220]

[EC 6.3.4.9 created 1972]

EC 6.3.4.10

Accepted name: biotin—[propionyl-CoA-carboxylase (ATP-hydrolysing)] ligase
Reaction: ATP + biotin + apo-[propionyl-CoA:carbon-dioxide ligase (ADP-forming)] = AMP + diphosphate + [propionyl-CoA:carbon-dioxide ligase (ADP-forming)]
Other name(s): biotin-[propionyl-CoA-carboxylase (ATP-hydrolysing)] synthetase; biotin-propionyl coenzyme A carboxylase synthetase; propionyl coenzyme A holocarboxylase synthetase
Systematic name: biotin:apo-[propanoyl-CoA:carbon-dioxide ligase (ADP-forming)] ligase (AMP-forming)
References: [389]

[EC 6.3.4.10 created 1972]

EC 6.3.4.11

Accepted name: biotin—[methylcrotonoyl-CoA-carboxylase] ligase
Reaction: ATP + biotin + apo-[3-methylcrotonoyl-CoA:carbon-dioxide ligase (ADP-forming)] = AMP + diphosphate + [3-methylcrotonoyl-CoA:carbon-dioxide ligase (ADP-forming)]
Other name(s): biotin-[methylcrotonoyl-CoA-carboxylase] synthetase; biotin- β -methylcrotonyl coenzyme A carboxylase synthetase; β -methylcrotonyl coenzyme A holocarboxylase synthetase; holocarboxylase synthetase
Systematic name: biotin:apo-[3-methylcrotonoyl-CoA:carbon-dioxide ligase (ADP-forming)] ligase (AMP-forming)
References: [164]

[EC 6.3.4.11 created 1972]

EC 6.3.4.12

Accepted name: glutamate—methylamine ligase
Reaction: ATP + L-glutamate + methylamine = ADP + phosphate + N^5 -methyl-L-glutamine
Other name(s): γ -glutamylmethylamide synthetase
Systematic name: L-glutamate:methylamine ligase (ADP-forming)
References: [210]

[EC 6.3.4.12 created 1972]

EC 6.3.4.13

Accepted name: phosphoribosylamine—glycine ligase
Reaction: ATP + 5-phospho-D-ribosylamine + glycine = ADP + phosphate + N^1 -(5-phospho-D-ribosyl)glycinamide
Other name(s): phosphoribosylglycinamide synthetase; glycinamide ribonucleotide synthetase; phosphoribosylglycineamide synthetase; glycineamide ribonucleotide synthetase; 2-amino- N -ribosylacetamide 5'-phosphate kinosynthase; 5'-phosphoribosylglycinamide synthetase; GAR
Systematic name: 5-phospho-D-ribosylamine:glycine ligase (ADP-forming)
References: [136, 148]

[EC 6.3.4.13 created 1961 as EC 6.3.1.3, transferred 1972 to EC 6.3.4.13, modified 2000]

EC 6.3.4.14

Accepted name: biotin carboxylase
Reaction: ATP + [biotin carboxyl-carrier protein]-biotin- N^6 -L-lysine + hydrogencarbonate- = ADP + phosphate + [biotin carboxyl-carrier protein]-carboxybiotin- N^6 -L-lysine
Other name(s): *accC* (gene name); biotin-carboxyl-carrier-protein:carbon-dioxide ligase (ADP-forming)
Systematic name: [biotin carboxyl-carrier protein]-biotin- N^6 -L-lysine:hydrogencarbonate ligase (ADP-forming)

Comments: This enzyme, part of an acetyl-CoA carboxylase complex, acts on a biotin carboxyl-carrier protein (BCCP) that has been biotinylated by EC 6.3.4.15, biotin—[biotin carboxyl-carrier protein] ligase. In some organisms the enzyme is part of a multi-domain polypeptide that also includes the carrier protein (e.g. mycobacteria). Yet in other organisms (e.g. mammals) this activity is included in a single polypeptide that also catalyses the transfer of the carboxyl group from biotin to acetyl-CoA (see EC 6.4.1.2, acetyl-CoA carboxylase).

References: [93, 309, 184, 63, 45]

[EC 6.3.4.14 created 1976, modified 2014, modified 2018]

EC 6.3.4.15

Accepted name: biotin—[biotin carboxyl-carrier protein] ligase

Reaction: ATP + biotin + [biotin carboxyl-carrier protein]-L-lysine = AMP + diphosphate + [biotin carboxyl-carrier protein]-N⁶-biotinyl-L-lysine

Other name(s): *birA* (gene name); HLCS (gene name); HCS1 (gene name); biotin-[acetyl-CoA carboxylase] synthetase; biotin-[acetyl coenzyme A carboxylase] synthetase; acetyl coenzyme A holocarboxylase synthetase; acetyl CoA holocarboxylase synthetase; biotin:apocarboxylase ligase; Biotin holoenzyme synthetase; biotin:apo-[acetyl-CoA:carbon-dioxide ligase (ADP-forming)] ligase (AMP-forming); biotin—[acetyl-CoA-carboxylase] ligase

Systematic name: biotin:apo-[carboxyl-carrier protein] ligase (AMP-forming)

Comments: The enzyme biotinylates a biotin carboxyl-carrier protein that is part of an acetyl-CoA carboxylase complex, enabling its subsequent carboxylation by EC 6.3.4.14, biotin carboxylase. The carboxyl group is eventually transferred to acetyl-CoA by EC 2.1.3.15, acetyl-CoA carboxytransferase. In some organisms the carrier protein is part of EC 6.4.1.2, acetyl-CoA carboxylase.

References: [218, 468, 305]

[EC 6.3.4.15 created 1978, modified 2018]

EC 6.3.4.16

Accepted name: carbamoyl-phosphate synthase (ammonia)

Reaction: 2 ATP + NH₃ + hydrogencarbonate = 2 ADP + phosphate + carbamoyl phosphate (overall reaction)
(1a) ATP + hydrogencarbonate = ADP + carboxyphosphate
(1b) NH₃ + carboxyphosphate = carbamate + phosphate
(1c) ATP + carbamate = ADP + carbamoyl phosphate

Other name(s): carbon-dioxide—ammonia ligase; carbamoylphosphate synthase; carbamylphosphate synthetase; carbamoylphosphate synthase (ammonia); carbamoylphosphate synthetase; carbamylphosphate synthetase I; CPSI (gene name); carbon-dioxide:ammonia ligase (ADP-forming, carbamate-phosphorylating)

Systematic name: hydrogencarbonate:ammonia ligase (ADP-forming, carbamate-phosphorylating)

Comments: The enzyme catalyses the first committed step in the urea cycle. The reaction proceeds via three separate chemical reactions: phosphorylation of hydrogencarbonate to carboxyphosphate; a nucleophilic attack of ammonia on carboxyphosphate yielding carbamate; and the phosphorylation of carbamate forming carbamoyl phosphate. Two moles of ATP are utilized for the synthesis of one molecule of carbamyl phosphate, making the reaction essentially irreversible. The enzyme requires the allosteric activator *N*-acetyl-L-glutamate. *cf.* EC 6.3.5.5, carbamoyl-phosphate synthase (glutamine-hydrolysing).

References: [108, 186, 253, 254, 335, 328]

[EC 6.3.4.16 created 1965 as EC 2.7.2.5, transferred 1978 to EC 6.3.4.16]

EC 6.3.4.17

Accepted name: formate—dihydrofolate ligase

Reaction: ATP + formate + dihydrofolate = ADP + phosphate + 10-formyldihydrofolate

Other name(s): formyltransferase, dihydrofolate; dihydrofolate formyltransferase; formyl dihydrofolate synthase

Systematic name: formate:dihydrofolate ligase (ADP-forming)
Comments: Not identical with EC 6.3.4.3 (formate—tetrahydrofolate ligase).
References: [96]

[EC 6.3.4.17 created 1992]

EC 6.3.4.18

Accepted name: 5-(carboxyamino)imidazole ribonucleotide synthase
Reaction: ATP + 5-amino-1-(5-phospho-D-ribosyl)imidazole + HCO₃⁻ = ADP + phosphate + 5-carboxyamino-1-(5-phospho-D-ribosyl)imidazole
Other name(s): N⁵-CAIR synthetase; N⁵-carboxyaminoimidazole ribonucleotide synthetase; PurK
Systematic name: 5-amino-1-(5-phospho-D-ribosyl)imidazole:carbon-dioxide ligase (ADP-forming)
Comments: In *Escherichia coli*, this enzyme, along with EC 5.4.99.18, 5-(carboxyamino)imidazole ribonucleotide mutase, is required to carry out the single reaction catalysed by EC 4.1.1.21, phosphoribosylaminoimidazole carboxylase, in vertebrates. Belongs to the ATP grasp protein superfamily [428]. Carboxyphosphate is the putative acyl phosphate intermediate. Involved in the late stages of purine biosynthesis.
References: [276, 294, 428]

[EC 6.3.4.18 created 2006]

EC 6.3.4.19

Accepted name: tRNA^{Ile}-lysidine synthase
Reaction: [tRNA^{Ile2}]-cytidine³⁴ + L-lysine + ATP = [tRNA^{Ile2}]-lysidine³⁴ + AMP + diphosphate + H₂O
Other name(s): Tils; *mesJ* (gene name); *yacA* (gene name); isoleucine-specific transfer ribonucleate lysidine synthetase; tRNA^{Ile}-lysidine synthetase
Systematic name: L-lysine:[tRNA^{Ile2}]-cytidine³⁴ ligase (AMP-forming)
Comments: The bacterial enzyme modifies the wobble base of the CAU anticodon of tRNA^{Ile} at the oxo group in position 2 of cytidine³⁴. This modification determines both codon and amino acid specificities of tRNA^{Ile}.
References: [176, 371, 300, 396, 299]

[EC 6.3.4.19 created 2011]

EC 6.3.4.20

Accepted name: 7-cyano-7-deazaguanine synthase
Reaction: 7-carboxy-7-carbaguanine + NH₃ + ATP = 7-cyano-7-carbaguanine + ADP + phosphate + H₂O
Other name(s): preQ₀ synthase; 7-cyano-7-carbaguanine synthase; *queC* (gene name)
Systematic name: 7-carboxy-7-carbaguanine:ammonia ligase (ADP-forming)
Comments: Binds Zn²⁺. The reaction is part of the biosynthesis pathway of queuosine.
References: [264, 68]

[EC 6.3.4.20 created 2012]

EC 6.3.4.21

Accepted name: nicotinate phosphoribosyltransferase
Reaction: nicotinate + 5-phospho- α -D-ribose 1-diphosphate + ATP + H₂O = β -nicotinate D-ribonucleotide + diphosphate + ADP + phosphate
Other name(s): niacin ribonucleotidase; nicotinic acid mononucleotide glycohydrolase; nicotinic acid mononucleotide pyrophosphorylase; nicotinic acid phosphoribosyltransferase; nicotinate-nucleotide:diphosphate phospho- α -D-ribosyltransferase
Systematic name: 5-phospho- α -D-ribose 1-diphosphate:nicotinate ligase (ADP, diphosphate-forming)

Comments: The enzyme, which is involved in pyridine nucleotide recycling, can form β -nicotinate D-ribonucleotide and diphosphate from nicotinate and 5-phospho- α -D-ribose 1-diphosphate (PRPP) in the absence of ATP. However, when ATP is available the enzyme is phosphorylated resulting in a much lower K_m for nicotinate. The phospho-enzyme is hydrolysed during the transferase reaction, regenerating the low affinity form. The presence of ATP shifts the products/substrates equilibrium from 0.67 to 1100 [445].

References: [177, 178, 206, 445]

[EC 6.3.4.21 created 1961 as EC 2.4.2.11, transferred 2013 to EC 6.3.4.21]

EC 6.3.4.22

Accepted name: tRNA^{Ile2}-agmatinylcytidine synthase

Reaction: ATP + agmatine + [tRNA^{Ile2}]-cytidine³⁴ + H₂O = [tRNA^{Ile2}]-2-agmatinylcytidine³⁴ + AMP + 2 phosphate

Other name(s): TiaS; AF2259; tRNA^{Ile}-2-agmatinylcytidine synthetase; tRNA^{Ile}-agm²C synthetase; tRNA^{Ile}-agmatidine synthetase

Systematic name: agmatine:[tRNA^{Ile}]-cytidine³⁴ ligase

Comments: The enzyme from the archaeon *Archaeoglobus fulgidus* modifies the wobble base of the CAU anticodon of the archaeal tRNA^{Ile2} at the oxo group in position 2 of cytidine³⁴. This modification is crucial for accurate decoding of the genetic code. In bacteria EC 6.3.4.19, tRNA^{Ile}-lysine synthase, catalyses the modification of [tRNA^{Ile2}]-cytidine³⁴ to [tRNA^{Ile2}]-lysine³⁴.

References: [175, 424, 315]

[EC 6.3.4.22 created 2013]

EC 6.3.4.23

Accepted name: formate—phosphoribosylaminoimidazolecarboxamide ligase

Reaction: ATP + formate + 5-amino-1-(5-phospho-D-ribosyl)imidazole-4-carboxamide = ADP + phosphate + 5-formamido-1-(5-phospho-D-ribosyl)imidazole-4-carboxamide

Other name(s): 5-formaminoimidazole-4-carboxamide ribonucleotide synthetase; 5-formaminoimidazole-4-carboxamide-1- β -D-ribofuranosyl 5'-monophosphate synthetase; *purP* (gene name)

Systematic name: formate:5-amino-1-(5-phospho-D-ribosyl)imidazole-4-carboxamide ligase (ADP-forming)

Comments: This archaeal enzyme, characterized from the methanogen *Methanocaldococcus jannaschii*, catalyses a step in the synthesis of purine nucleotides. It differs from the orthologous bacterial/eukaryotic enzymes, which utilize 10-formyltetrahydrofolate rather than formate and ATP. *cf.* EC 2.1.2.3, phosphoribosylaminoimidazolecarboxamide formyltransferase.

References: [319, 479]

[EC 6.3.4.23 created 2013]

EC 6.3.4.24

Accepted name: tyramine—L-glutamate ligase

Reaction: ATP + tyramine + L-glutamate = ADP + phosphate + γ -glutamyltyramine

Other name(s): *mfnD* (gene name)

Systematic name: tyramine:L-glutamate γ -ligase (ADP-forming)

Comments: The enzyme, which has been characterized from the archaea *Methanocaldococcus fervens*, participates in the biosynthesis of the cofactor methanofuran. Requires a divalent cation for activity, with Mn²⁺ giving the highest activity, followed by Mg²⁺, Co²⁺, Zn²⁺, and Fe²⁺.

References: [454]

[EC 6.3.4.24 created 2014]

EC 6.3.5 Carbon-nitrogen ligases with glutamine as amido-N-donor

EC 6.3.5.1

- Accepted name:** NAD⁺ synthase (glutamine-hydrolysing)
Reaction: ATP + deamido-NAD⁺ + L-glutamine + H₂O = AMP + diphosphate + NAD⁺ + L-glutamate
Other name(s): NAD synthetase (glutamine-hydrolysing); nicotinamide adenine dinucleotide synthetase (glutamine); desamidonicotinamide adenine dinucleotide amidotransferase; DPN synthetase
Systematic name: deamido-NAD⁺:L-glutamine amido-ligase (AMP-forming)
Comments: NH₃ can act instead of glutamine (*cf.* EC 6.3.1.5 NAD⁺ synthase).
References: [177, 178]

[EC 6.3.5.1 created 1961]

EC 6.3.5.2

- Accepted name:** GMP synthase (glutamine-hydrolysing)
Reaction: ATP + XMP + L-glutamine + H₂O = AMP + diphosphate + GMP + L-glutamate (overall reaction)
(1a) L-glutamine + H₂O = L-glutamate + NH₃
(1b) ATP + XMP + NH₃ = AMP + diphosphate + GMP
Other name(s): GMP synthetase (glutamine-hydrolysing); guanylate synthetase (glutamine-hydrolyzing); guanosine monophosphate synthetase (glutamine-hydrolyzing); xanthosine 5'-phosphate amidotransferase; guanosine 5'-monophosphate synthetase
Systematic name: xanthosine-5'-phosphate:L-glutamine amido-ligase (AMP-forming)
Comments: Involved in the *de novo* biosynthesis of guanosine nucleotides. An N-terminal glutaminase domain binds L-glutamine and generates ammonia, which is transferred by a substrate-protective tunnel to the ATP-pyrophosphatase domain. The enzyme can catalyse the second reaction alone in the presence of ammonia.
References: [215, 5, 478, 2]

[EC 6.3.5.2 created 1961, modified 2013]

EC 6.3.5.3

- Accepted name:** phosphoribosylformylglycinamide synthase
Reaction: ATP + N²-formyl-N¹-(5-phospho-D-ribosyl)glycinamide + L-glutamine + H₂O = ADP + phosphate + 2-(formamido)-N¹-(5-phospho-D-ribosyl)acetamide + L-glutamate
Other name(s): phosphoribosylformylglycinamide synthetase; formylglycinamide ribonucleotide amidotransferase; phosphoribosylformylglycineamide synthetase; FGAM synthetase; FGAR amidotransferase; 5'-phosphoribosylformylglycinamide:L-glutamine amido-ligase (ADP-forming); 2-N-formyl-1-N-(5-phospho-D-ribosyl)glycinamide:L-glutamine amido-ligase (ADP-forming)
Systematic name: N²-formyl-N¹-(5-phospho-D-ribosyl)glycinamide:L-glutamine amido-ligase (ADP-forming)
References: [271]

[EC 6.3.5.3 created 1961, modified 2000]

EC 6.3.5.4

- Accepted name:** asparagine synthase (glutamine-hydrolysing)
Reaction: ATP + L-aspartate + L-glutamine + H₂O = AMP + diphosphate + L-asparagine + L-glutamate (overall reaction)
(1a) L-glutamine + H₂O = L-glutamate + NH₃
(1b) ATP + L-aspartate + NH₃ = AMP + diphosphate + L-asparagine
Other name(s): asparagine synthetase (glutamine-hydrolysing); glutamine-dependent asparagine synthetase; asparagine synthetase B; AS; AS-B
Systematic name: L-aspartate:L-glutamine amido-ligase (AMP-forming)

Comments: The enzyme from *Escherichia coli* has two active sites [221] that are connected by an intramolecular ammonia tunnel [170, 425]. The enzyme catalyses three distinct chemical reactions: glutamine hydrolysis to yield ammonia takes place in the N-terminal domain. The C-terminal active site mediates both the synthesis of a β -aspartyl-AMP intermediate and its subsequent reaction with ammonia. The ammonia released is channeled to the other active site to yield asparagine [425].

References: [327, 39, 356, 221, 170, 425]

[EC 6.3.5.4 created 1972, modified 2006]

EC 6.3.5.5

Accepted name: carbamoyl-phosphate synthase (glutamine-hydrolysing)

Reaction: $2 \text{ ATP} + \text{L-glutamine} + \text{hydrogencarbonate} + \text{H}_2\text{O} = 2 \text{ ADP} + \text{phosphate} + \text{L-glutamate} + \text{carbamoyl phosphate}$ (overall reaction)

(1a) $\text{L-glutamine} + \text{H}_2\text{O} = \text{L-glutamate} + \text{NH}_3$

(1b) $\text{ATP} + \text{hydrogencarbonate} = \text{ADP} + \text{carboxyphosphate}$

(1c) $\text{NH}_3 + \text{carboxyphosphate} = \text{carbamate} + \text{phosphate}$

(1d) $\text{ATP} + \text{carbamate} = \text{ADP} + \text{carbamoyl phosphate}$

Other name(s): carbamoyl-phosphate synthetase (glutamine-hydrolysing); carbamyl phosphate synthetase (glutamine); carbamoylphosphate synthetase II; glutamine-dependent carbamyl phosphate synthetase; carbamoyl phosphate synthetase; CPS; carbon-dioxide:L-glutamine amido-ligase (ADP-forming, carbamate-phosphorylating); *carA* (gene name); *carB* (gene name); CAD (gene name); hydrogencarbonate:L-glutamine amido-ligase (ADP-forming, carbamate-phosphorylating)

Systematic name: hydrogencarbonate:L-glutamine amido-ligase (ADP-forming, carbamate-phosphorylating)

Comments: The product carbamoyl phosphate is an intermediate in the biosynthesis of arginine and the pyrimidine nucleotides [398]. The enzyme from *Escherichia coli* has three separate active sites, which are connected by a molecular tunnel that is almost 100 Å in length [427]. The amidotransferase domain within the small subunit of the enzyme hydrolyses glutamine to ammonia via a thioester intermediate. The ammonia migrates through the interior of the protein, where it reacts with carboxyphosphate to produce the carbamate intermediate. The carboxyphosphate intermediate is formed by the phosphorylation of hydrogencarbonate by ATP at a site contained within the N-terminal half of the large subunit. The carbamate intermediate is transported through the interior of the protein to a second site within the C-terminal half of the large subunit, where it is phosphorylated by another ATP to yield the final product, carbamoyl phosphate [347]. *cf.* EC 6.3.4.16, carbamoyl-phosphate synthase (ammonia).

References: [11, 188, 474, 398, 159, 347, 346, 427]

[EC 6.3.5.5 created 1972 as EC 2.7.2.9, transferred 1978 to EC 6.3.5.5, modified 2006]

EC 6.3.5.6

Accepted name: asparaginyl-tRNA synthase (glutamine-hydrolysing)

Reaction: $\text{ATP} + \text{L-aspartyl-tRNA}^{\text{Asn}} + \text{L-glutamine} + \text{H}_2\text{O} = \text{ADP} + \text{phosphate} + \text{L-asparaginyl-tRNA}^{\text{Asn}} + \text{L-glutamate}$

Other name(s): Asp-AdT; Asp-tRNA^{Asn} amidotransferase; aspartyl-tRNA^{Asn} amidotransferase; Asn-tRNA^{Asn}:L-glutamine amido-ligase (ADP-forming); aspartyl-tRNA^{Asn}:L-glutamine amido-ligase (ADP-forming)

Systematic name: L-aspartyl-tRNA^{Asn}:L-glutamine amido-ligase (ADP-forming)

Comments: This reaction forms part of a two-reaction system for producing asparaginyl-tRNA in *Deinococcus radiodurans* and other organisms lacking a specific enzyme for asparagine synthesis. In the first step, a non-discriminating ligase (EC 6.1.1.23, aspartate—tRNA^{Asn} ligase) mischarges tRNA^{Asn} with aspartate, leading to the formation of Asp-tRNA^{Asn}. The aspartyl-tRNA^{Asn} is not used in protein synthesis until the present enzyme converts it into asparaginyl-tRNA^{Asn} (aspartyl-tRNA^{Asp} is not a substrate for this reaction). Ammonia or asparagine can substitute for the preferred substrate glutamine.

References: [281, 78, 174]

[EC 6.3.5.6 created 2002, modified 2012]

EC 6.3.5.7

- Accepted name:** glutaminyl-tRNA synthase (glutamine-hydrolysing)
- Reaction:** $\text{ATP} + \text{L-glutamyl-tRNA}^{\text{Gln}} + \text{L-glutamine} = \text{ADP} + \text{phosphate} + \text{L-glutaminyl-tRNA}^{\text{Gln}} + \text{L-glutamate}$
- Other name(s):** Glu-AdT; Glu-tRNA^{Gln} amidotransferase; glutamyl-tRNA^{Gln} amidotransferase; Glu-tRNA^{Gln}:L-glutamine amido-ligase (ADP-forming)
- Systematic name:** L-glutamyl-tRNA^{Gln}:L-glutamine amido-ligase (ADP-forming)
- Comments:** In systems lacking discernible glutamine—tRNA ligase (EC 6.1.1.18), glutaminyl-tRNA^{Gln} is formed by a two-enzyme system. In the first step, a nondiscriminating ligase (EC 6.1.1.24, glutamate—tRNA^{Gln} ligase) mischarges tRNA^{Gln} with glutamate, forming glutamyl-tRNA^{Gln}. The glutamyl-tRNA^{Gln} is not used in protein synthesis until the present enzyme converts it into glutaminyl-tRNA^{Gln} (glutamyl-tRNA^{Glu} is not a substrate for this reaction). Ammonia or asparagine can substitute for the preferred substrate glutamine.
- References:** [167, 78, 174]

[EC 6.3.5.7 created 2002]

[6.3.5.8 *Transferred entry. aminodeoxychorismate synthase. Now EC 2.6.1.85, aminodeoxychorismate synthase. As ATP is not hydrolysed during the reaction, the classification of the enzyme as a ligase was incorrect*]

[EC 6.3.5.8 created 2003, deleted 2007]

EC 6.3.5.9

- Accepted name:** hydrogenobyric acid *a,c*-diamide synthase (glutamine-hydrolysing)
- Reaction:** $2 \text{ATP} + \text{hydrogenobyric acid } a,c\text{-diamide} + 2 \text{L-glutamine} + 2 \text{H}_2\text{O} = 2 \text{ADP} + 2 \text{phosphate} + \text{hydrogenobyric acid } a,c\text{-diamide} + 2 \text{L-glutamate}$
- Other name(s):** CobB
- Systematic name:** hydrogenobyric-acid:L-glutamine amido-ligase (AMP-forming)
- Comments:** This step in the aerobic biosynthesis of cobalamin generates hydrogenobyric acid *a,c*-diamide, the substrate required by EC 6.6.1.2, cobaltochelataase, which adds cobalt to the macrocycle.
- References:** [89, 455]

[EC 6.3.5.9 created 2004]

EC 6.3.5.10

- Accepted name:** adenosylcobyric acid synthase (glutamine-hydrolysing)
- Reaction:** $4 \text{ATP} + \text{adenosylcobyric acid } a,c\text{-diamide} + 4 \text{L-glutamine} + 4 \text{H}_2\text{O} = 4 \text{ADP} + 4 \text{phosphate} + \text{adenosylcobyric acid } a,c\text{-diamide} + 4 \text{L-glutamate}$
- Other name(s):** CobQ; cobyric acid synthase; 5'-deoxy-5'-adenosylcobyric-acid-*a,c*-diamide:L-glutamine amido-ligase; Ado-cobyric acid synthase [glutamine hydrolyzing]
- Systematic name:** adenosylcobyric-acid-*a,c*-diamide:L-glutamine amido-ligase (ADP-forming)
- Comments:** Requires Mg²⁺. NH₃ can act instead of glutamine. This enzyme catalyses the four-step amidation sequence from cobyric acid *a,c*-diamide to cobyric acid via the formation of cobyric acid triamide, tetraamide and pentaamide intermediates.
- References:** [37, 455]

[EC 6.3.5.10 created 2004]

EC 6.3.5.11

- Accepted name:** cobyriate *a,c*-diamide synthase
- Reaction:** $2 \text{ATP} + \text{cobyriate } a,c\text{-diamide} + 2 \text{L-glutamine} + 2 \text{H}_2\text{O} = 2 \text{ADP} + 2 \text{phosphate} + \text{cobyriate } a,c\text{-diamide} + 2 \text{L-glutamate}$ (overall reaction)
(1a) $\text{ATP} + \text{cobyriate } a,c\text{-diamide} + \text{L-glutamine} + \text{H}_2\text{O} = \text{ADP} + \text{phosphate} + \text{cobyriate } c\text{-monamide} + \text{L-glutamate}$

(1b) $\text{ATP} + \text{cobyrinate } c\text{-monamide} + \text{L-glutamine} + \text{H}_2\text{O} = \text{ADP} + \text{phosphate} + \text{cobyrinate } a,c\text{-diamide} + \text{L-glutamate}$

Other name(s): cobyrinic acid *a,c*-diamide synthetase; CbiA
Systematic name: cobyrinate:L-glutamine amido-ligase (ADP-forming)
Comments: This enzyme is the first glutamine amidotransferase that participates in the anaerobic (early cobalt insertion) biosynthetic pathway of adenosylcobalamin, and catalyses the ATP-dependent synthesis of cobyrinate *a,c*-diamide from cobyrinate using either L-glutamine or ammonia as the nitrogen source. It is proposed that the enzyme first catalyses the amidation of the *c*-carboxylate, and then the intermediate is released into solution and binds to the same catalytic site for the amidation of the *a*-carboxylate. The K_m for ammonia is substantially higher than that for L-glutamine.
References: [118]

[EC 6.3.5.11 created 2010]

EC 6.3.5.12

Accepted name: Ni-sirohydrochlorin *a,c*-diamide synthase
Reaction: $2 \text{ATP} + \text{Ni-sirohydrochlorin} + 2 \text{L-glutamine} + 2 \text{H}_2\text{O} = 2 \text{ADP} + 2 \text{phosphate} + \text{Ni-sirohydrochlorin } a,c\text{-diamide} + 2 \text{L-glutamate}$
Other name(s): *cfbB* (gene name)
Systematic name: Ni-sirohydrochlorin:L-glutamine amido-ligase (ADP-forming)
Comments: The enzyme, studied from the methanogenic archaeon *Methanosarcina acetivorans*, participates in the biosynthesis of the nickel-containing tetrapyrrole cofactor coenzyme F₄₃₀, which is required by EC 2.8.4.1, coenzyme-B sulfoethylthiotransferase.
References: [481]

[EC 6.3.5.12 created 2017]

EC 6.4 Forming carbon-carbon bonds

This subclass contains a single sub-subclass (EC 6.4.1) for enzymes that form carbon-carbon bonds. These are the carboxylating enzymes, which are mostly biotinyl-proteins.

EC 6.4.1 Ligases that form carbon-carbon bonds (only sub-subclass identified to date)

EC 6.4.1.1

Accepted name: pyruvate carboxylase
Reaction: $\text{ATP} + \text{pyruvate} + \text{HCO}_3^- = \text{ADP} + \text{phosphate} + \text{oxaloacetate}$
Other name(s): pyruvic carboxylase
Systematic name: pyruvate:carbon-dioxide ligase (ADP-forming)
Comments: A biotinyl-protein containing manganese (animal tissues) or zinc (yeast). The animal enzyme requires acetyl-CoA.
References: [265, 384, 386, 439]

[EC 6.4.1.1 created 1961]

EC 6.4.1.2

Accepted name: acetyl-CoA carboxylase
Reaction: $\text{ATP} + \text{acetyl-CoA} + \text{hydrogencarbonate} = \text{ADP} + \text{phosphate} + \text{malonyl-CoA}$
Other name(s): HFA1 (gene name); ACC1 (gene name); acetyl coenzyme A carboxylase; acetyl-CoA:carbon-dioxide ligase (ADP-forming)
Systematic name: acetyl-CoA:hydrogencarbonate ligase (ADP-forming)

Comments: This enzyme is a multi-domain polypeptide that catalyses three different activities - a biotin carboxyl-carrier protein (BCCP), a biotin carboxylase that catalyses the transfer of a carboxyl group from hydrogencarbonate to the biotin molecule carried by the carrier protein, and the transfer of the carboxyl group from biotin to acetyl-CoA, forming malonyl-CoA. In some organisms these activities are catalysed by separate enzymes (see EC 6.3.4.14, biotin carboxylase, and EC 2.1.3.15, acetyl-CoA carboxytransferase). The carboxylation of the carrier protein requires ATP, while the transfer of the carboxyl group to acetyl-CoA does not.

References: [449, 149, 259, 258, 440, 434, 59, 199]

[EC 6.4.1.2 created 1961, modified 2018]

EC 6.4.1.3

Accepted name: propionyl-CoA carboxylase
Reaction: $\text{ATP} + \text{propanoyl-CoA} + \text{HCO}_3^- = \text{ADP} + \text{phosphate} + (S)\text{-methylmalonyl-CoA}$
Other name(s): propionyl coenzyme A carboxylase
Systematic name: propanoyl-CoA:carbon-dioxide ligase (ADP-forming)
Comments: A biotinyl-protein. Also carboxylates butanoyl-CoA and catalyses transcarboxylation.
References: [197, 219, 277, 292, 440]

[EC 6.4.1.3 created 1961, modified 1983]

EC 6.4.1.4

Accepted name: methylcrotonoyl-CoA carboxylase
Reaction: $\text{ATP} + 3\text{-methylcrotonoyl-CoA} + \text{HCO}_3^- = \text{ADP} + \text{phosphate} + 3\text{-methylglutaconyl-CoA}$
Other name(s): methylcrotonyl coenzyme A carboxylase; β -methylcrotonyl coenzyme A carboxylase; β -methylcrotonyl CoA carboxylase; methylcrotonoyl-CoA carboxylase
Systematic name: 3-methylcrotonoyl-CoA:carbon-dioxide ligase (ADP-forming)
Comments: A biotinyl-protein.
References: [203, 242, 359, 440]

[EC 6.4.1.4 created 1961]

EC 6.4.1.5

Accepted name: geranoyl-CoA carboxylase
Reaction: $\text{ATP} + \text{geranoyl-CoA} + \text{HCO}_3^- = \text{ADP} + \text{phosphate} + 3\text{-(4-methylpent-3-en-1-yl)pent-2-enedioyl-CoA}$
Other name(s): geranoyl coenzyme A carboxylase; geranyl-CoA carboxylase
Systematic name: geranoyl-CoA:carbon-dioxide ligase (ADP-forming)
Comments: A biotinyl-protein. Also carboxylates dimethylpropenoyl-CoA and farnesoyl-CoA.
References: [385]

[EC 6.4.1.5 created 1972]

EC 6.4.1.6

Accepted name: acetone carboxylase
Reaction: $\text{acetone} + \text{CO}_2 + \text{ATP} + 2 \text{H}_2\text{O} = \text{acetoacetate} + \text{AMP} + 2 \text{phosphate}$
Systematic name: acetone:carbon-dioxide ligase (AMP-forming)
Comments: Requires Mg^{2+} and ATP. The enzyme from *Xanthobacter* sp. strain Py2 also carboxylates butan-2-one to 3-oxopentanoate.
References: [392]

[EC 6.4.1.6 created 2001]

EC 6.4.1.7

Accepted name: 2-oxoglutarate carboxylase

Reaction: $\text{ATP} + 2\text{-oxoglutarate} + \text{HCO}_3^- = \text{ADP} + \text{phosphate} + \text{oxalosuccinate}$

Other name(s): oxalosuccinate synthetase; carboxylating factor for ICDH (incorrect); CFI; OGC

Comments: A biotin-containing enzyme that requires Mg^{2+} for activity. It was originally thought [15] that this enzyme was a promoting factor for the carboxylation of 2-oxoglutarate by EC 1.1.1.41, isocitrate dehydrogenase (NAD^+), but this has since been disproved [14]. The product of the reaction is unstable and is quickly converted into isocitrate by the action of EC 1.1.1.41 [14].

References: [15, 14]

[EC 6.4.1.7 created 2006]

EC 6.4.1.8

Accepted name: acetophenone carboxylase

Reaction: $2 \text{ATP} + \text{acetophenone} + \text{HCO}_3^- + \text{H}_2\text{O} + \text{H}^+ = 2 \text{ADP} + 2 \text{phosphate} + 3\text{-oxo-3-phenylpropanoate}$

Systematic name: acetophenone:carbon-dioxide ligase (ADP-forming)

Comments: The enzyme is involved in anaerobic degradation of ethylbenzene. No activity with acetone, butanone, 4-hydroxy-acetophenone or 4-amino-acetophenone.

References: [185]

[EC 6.4.1.8 created 2011]

EC 6.4.1.9

Accepted name: coenzyme F_{430} synthetase

Reaction: $\text{ATP} + 15,17^3\text{-seco-F}_{430}\text{-}17^3\text{-acid} = \text{ADP} + \text{phosphate} + \text{coenzyme F}_{430}$

Other name(s): *cfbE* (gene name)

Systematic name: 15,17³-seco-F₄₃₀-17³-acid cyclo-ligase (ADP-forming)

Comments: The enzyme, studied from the methanogenic archaeon *Methanosarcina acetivorans*, catalyses the last step in the biosynthesis of the nickel-containing tetrapyrrole cofactor coenzyme F_{430} , which is required by EC 2.8.4.1, coenzyme-B sulfoethylthiotransferase.

References: [481]

[EC 6.4.1.9 created 2017]

EC 6.5 Forming phosphoric-ester bonds

This subclass contains enzymes that restore broken phosphodiester bonds in nucleic acids (often called repair enzymes) in a single sub-subclass (EC 6.5.1).

EC 6.5.1 Ligases that form phosphoric-ester bonds (only sub-subclass identified to date)

EC 6.5.1.1

Accepted name: DNA ligase (ATP)

Reaction: $\text{ATP} + (\text{deoxyribonucleotide})_n\text{-}3'\text{-hydroxyl} + 5'\text{-phospho-(deoxyribonucleotide)}_m = (\text{deoxyribonucleotide})_{n+m} + \text{AMP} + \text{diphosphate (overall reaction)}$

(1a) $\text{ATP} + [\text{DNA ligase}]\text{-L-lysine} = [\text{DNA ligase}]\text{-}N^6\text{-(}5'\text{-adenylyl)-L-lysine} + \text{diphosphate}$

(1b) $[\text{DNA ligase}]\text{-}N^6\text{-(}5'\text{-adenylyl)-L-lysine} + 5'\text{-phospho-(deoxyribonucleotide)}_m = 5'\text{-(}5'\text{-diphosphoadenosine)-}(\text{deoxyribonucleotide})_m + [\text{DNA ligase}]\text{-L-lysine}$

(1c) $(\text{deoxyribonucleotide})_n\text{-}3'\text{-hydroxyl} + 5'\text{-(}5'\text{-diphosphoadenosine)-}(\text{deoxyribonucleotide})_m = (\text{deoxyribonucleotide})_{n+m} + \text{AMP}$

Other name(s): polydeoxyribonucleotide synthase (ATP); polynucleotide ligase (ambiguous); sealase; DNA repair enzyme (ambiguous); DNA joinase (ambiguous); DNA ligase (ambiguous); deoxyribonucleic ligase (ambiguous); deoxyribonucleate ligase (ambiguous); DNA-joining enzyme (ambiguous); deoxyribonucleic-joining enzyme (ambiguous); deoxyribonucleic acid-joining enzyme (ambiguous); deoxyribonucleic repair enzyme (ambiguous); deoxyribonucleic joinase (ambiguous); deoxyribonucleic acid ligase (ambiguous); deoxyribonucleic acid joinase (ambiguous); deoxyribonucleic acid repair enzyme (ambiguous); poly(deoxyribonucleotide):poly(deoxyribonucleotide) ligase (AMP-forming)

Systematic name: poly(deoxyribonucleotide)-3'-hydroxyl:5'-phospho-poly(deoxyribonucleotide) ligase (ATP)

Comments: The enzyme catalyses the ligation of DNA strands with 3'-hydroxyl and 5'-phosphate termini, forming a phosphodiester and sealing certain types of single-strand breaks in duplex DNA. Catalysis occurs by a three-step mechanism, starting with the activation of the enzyme by ATP, forming a phosphoramidate bond between adenylate and a lysine residue. The adenylate group is then transferred to the 5'-phosphate terminus of the substrate, forming the capped structure 5'-(5'-diphosphoadenosine)-[DNA]. Finally, the enzyme catalyses a nucleophilic attack of the 3'-OH terminus on the capped terminus, which results in formation of the phosphodiester bond and release of the adenylate. RNA can also act as substrate, to some extent. *cf.* EC 6.5.1.2, DNA ligase (NAD⁺), EC 6.5.1.6, DNA ligase (ATP or NAD⁺), and EC 6.5.1.7, DNA ligase (ATP, ADP or GTP).

References: [24, 35, 462, 169]

[EC 6.5.1.1 created 1972, modified 1976, modified 2016]

EC 6.5.1.2

Accepted name: DNA ligase (NAD⁺)

Reaction: NAD⁺ + (deoxyribonucleotide)_n-3'-hydroxyl + 5'-phospho-(deoxyribonucleotide)_m = (deoxyribonucleotide)_{n+m} + AMP + β-nicotinamide D-nucleotide (overall reaction)

(1a) NAD⁺ + [DNA ligase]-L-lysine = [DNA ligase]-N⁶-(5'-adenylyl)-L-lysine + β-nicotinamide D-nucleotide

(1b) [DNA ligase]-N⁶-(5'-adenylyl)-L-lysine + 5'-phospho-(deoxyribonucleotide)_m = 5'-(5'-diphosphoadenosine)-(deoxyribonucleotide)_m + [DNA ligase]-L-lysine

(1c) (deoxyribonucleotide)_n-3'-hydroxyl + 5'-(5'-diphosphoadenosine)-(deoxyribonucleotide)_m = (deoxyribonucleotide)_{n+m} + AMP

Other name(s): polydeoxyribonucleotide synthase (NAD⁺); polynucleotide ligase (NAD⁺); DNA repair enzyme (ambiguous); DNA joinase (ambiguous); polynucleotide synthetase (nicotinamide adenine dinucleotide); deoxyribonucleic-joining enzyme (ambiguous); deoxyribonucleic ligase (ambiguous); deoxyribonucleic repair enzyme (ambiguous); deoxyribonucleic joinase (ambiguous); DNA ligase (ambiguous); deoxyribonucleate ligase (ambiguous); polynucleotide ligase (ambiguous); deoxyribonucleic acid ligase (ambiguous); polynucleotide synthetase (ambiguous); deoxyribonucleic acid joinase (ambiguous); DNA-joining enzyme (ambiguous); polynucleotide ligase (nicotinamide adenine dinucleotide); poly(deoxyribonucleotide):poly(deoxyribonucleotide) ligase (AMP-forming, NMN-forming)

Systematic name: poly(deoxyribonucleotide)-3'-hydroxyl:5'-phospho-poly(deoxyribonucleotide) ligase (NAD⁺)

Comments: The enzyme, typically found in bacteria, catalyses the ligation of DNA strands with 3'-hydroxyl and 5'-phosphate termini, forming a phosphodiester and sealing certain types of single-strand breaks in duplex DNA. Catalysis occurs by a three-step mechanism, starting with the activation of the enzyme by NAD⁺, forming a phosphoramidate bond between adenylate and a lysine residue. The adenylate group is then transferred to the 5'-phosphate terminus of the substrate, forming the capped structure 5'-(5'-diphosphoadenosine)-[DNA]. Finally, the enzyme catalyses a nucleophilic attack of the 3'-OH terminus on the capped terminus, which results in formation of the phosphodiester bond and release of the adenylate. RNA can also act as substrate, to some extent. *cf.* EC 6.5.1.1, DNA ligase (ATP), EC 6.5.1.6, DNA ligase (ATP or NAD⁺), and EC 6.5.1.7, DNA ligase (ATP, ADP or GTP).

References: [487, 236, 286, 287, 438]

[EC 6.5.1.2 created 1972, modified 1976, modified 2016]

EC 6.5.1.3

Accepted name: RNA ligase (ATP)
Reaction: $\text{ATP} + (\text{ribonucleotide})_n\text{-}3'\text{-hydroxyl} + 5'\text{-phospho-}(\text{ribonucleotide})_m = (\text{ribonucleotide})_{n+m} + \text{AMP} + \text{diphosphate}$ (overall reaction)
 (1a) $\text{ATP} + [\text{RNA ligase}]\text{-L-lysine} = [\text{RNA ligase}]\text{-}N^6\text{-(5'-adenylyl)}\text{-L-lysine} + \text{diphosphate}$
 (1b) $[\text{RNA ligase}]\text{-}N^6\text{-(5'-adenylyl)}\text{-L-lysine} + 5'\text{-phospho-}(\text{ribonucleotide})_m = 5'\text{-(5'-diphosphoadenosine)-}(\text{ribonucleotide})_m + [\text{RNA ligase}]\text{-L-lysine}$
 (1c) $(\text{ribonucleotide})_n\text{-}3'\text{-hydroxyl} + 5'\text{-(5'-diphosphoadenosine)-}(\text{ribonucleotide})_m = (\text{ribonucleotide})_{n+m} + \text{AMP}$
Other name(s): polyribonucleotide synthase (ATP); RNA ligase; polyribonucleotide ligase; ribonucleic ligase; poly(ribonucleotide):poly(ribonucleotide) ligase (AMP-forming)
Systematic name: poly(ribonucleotide)-3'-hydroxyl:5'-phospho-poly(ribonucleotide) ligase (ATP)
Comments: The enzyme catalyses the ligation of RNA strands with 3'-hydroxyl and 5'-phosphate termini, forming a phosphodiester and sealing certain types of single-strand breaks in RNA. Catalysis occurs by a three-step mechanism, starting with the activation of the enzyme by ATP, forming a phosphoramidate bond between adenylylate and a lysine residue. The adenylylate group is then transferred to the 5'-phosphate terminus of the substrate, forming the capped structure 5'-(5'-diphosphoadenosine)-[RNA]. Finally, the enzyme catalyses a nucleophilic attack of the 3'-OH terminus on the capped terminus, which results in formation of the phosphodiester bond and release of the adenylylate.
References: [390, 75, 410, 362, 158, 301]

[EC 6.5.1.3 created 1976, modified 2016]

EC 6.5.1.4

Accepted name: RNA 3'-terminal-phosphate cyclase (ATP)
Reaction: $\text{ATP} + [\text{RNA}]\text{-}3'\text{-(3'-phospho-ribonucleoside)} = \text{AMP} + \text{diphosphate} + [\text{RNA}]\text{-}3'\text{-(2',3'-cyclophospho-ribonucleoside)}$ (overall reaction)
 (1a) $\text{ATP} + [\text{RNA 3'-phosphate cyclase}]\text{-L-histidine} = [\text{RNA 3'-phosphate cyclase}]\text{-}N^{\tau}\text{-(5'-adenylyl)}\text{-L-histidine} + \text{diphosphate}$
 (1b) $[\text{RNA 3'-phosphate cyclase}]\text{-}N^{\tau}\text{-(5'-adenylyl)}\text{-L-histidine} + [\text{RNA}]\text{-}3'\text{-(3'-phospho-ribonucleoside)} = [\text{RNA 3'-phosphate cyclase}]\text{-L-histidine} + [\text{RNA}]\text{-}3'\text{-ribonucleoside-}3'\text{-(5'-diphosphoadenosine)}$
 (1c) $[\text{RNA}]\text{-}3'\text{-ribonucleoside-}3'\text{-(5'-diphosphoadenosine)} = [\text{RNA}]\text{-}3'\text{-(2',3'-cyclophospho-ribonucleoside)} + \text{AMP}$
Other name(s): *rtcA* (gene name); RNA cyclase (ambiguous); RNA-3'-phosphate cyclase (ambiguous)
Systematic name: RNA-3'-phosphate:RNA ligase (cyclizing, AMP-forming)
Comments: The enzyme converts the 3'-terminal phosphate of various RNA substrates into the 2',3'-cyclic phosphodiester in an ATP-dependent reaction. Catalysis occurs by a three-step mechanism, starting with the activation of the enzyme by ATP, forming a phosphoramidate bond between adenylylate and a histidine residue [36, 421]. The adenylylate group is then transferred to the 3'-phosphate terminus of the substrate, forming the capped structure [RNA]-3'-(5'-diphosphoadenosine). Finally, the enzyme catalyses an attack of the vicinal O-2' on the 3'-phosphorus, which results in formation of cyclic phosphate and release of the adenylylate. The enzyme also has a polynucleotide 5' adenylylation activity [53]. *cf.* EC 6.5.1.5, RNA 3'-terminal-phosphate cyclase (GTP).
References: [112, 353, 128, 129, 36, 421, 53, 80]

[EC 6.5.1.4 created 1986, modified 1989, modified 2013, modified 2016]

EC 6.5.1.5

Accepted name: RNA 3'-terminal-phosphate cyclase (GTP)
Reaction: $\text{GTP} + [\text{RNA}]\text{-}3'\text{-(3'-phospho-ribonucleoside)} = \text{GMP} + \text{diphosphate} + [\text{RNA}]\text{-}3'\text{-(2',3'-cyclophospho-ribonucleoside)}$ (overall reaction)
 (1a) $\text{GTP} + [\text{RNA 3'-phosphate cyclase}]\text{-L-histidine} = 5'\text{-guanosyl } [\text{RNA 3'-phosphate cyclase}]\text{-}N^{\tau}\text{-phosphono-L-histidine} + \text{diphosphate}$

(1b) 5'-guanosyl [RNA 3'-phosphate cyclase]-N^ε-phosphono-L-histidine + [RNA]-3'-(3'-phosphoribonucleoside) = [RNA 3'-phosphate cyclase]-L-histidine + [RNA]-3'-ribonucleoside-3'-(5'-diphosphoguanosine)

(1c) [RNA]-3'-ribonucleoside-3'-(5'-diphosphoguanosine) = [RNA]-3'-(2',3'-cyclophospho)-ribonucleoside + GMP

Other name(s): Pf-Rtc; RNA-3'-phosphate cyclase (GTP)

Systematic name: RNA-3'-phosphate:RNA ligase (cyclizing, GMP-forming)

Comments: The enzyme, which is specific for GTP, was characterized from the archaeon *Pyrococcus furiosus*. The enzyme converts the 3'-terminal phosphate of various RNA substrates into the 2',3'-cyclic phosphodiester in a GTP-dependent reaction. Catalysis occurs by a three-step mechanism, starting with the activation of the enzyme by GTP, forming a phosphoramidate bond between guanylate and a histidine residue. The guanylate group is then transferred to the 3'-phosphate terminus of the substrate, forming the capped structure [RNA]-3'-(5'-diphosphoguanosine). Finally, the enzyme catalyses an attack of the vicinal O-2' on the 3'-phosphorus, which results in formation of cyclic phosphate and release of the guanylate. *cf.* EC 6.5.1.4, RNA-3'-phosphate cyclase (ATP).

References: [376]

[EC 6.5.1.5 created 2013, modified 2016]

EC 6.5.1.6

Accepted name: DNA ligase (ATP or NAD⁺)

Reaction: (1) ATP + (deoxyribonucleotide)_n-3'-hydroxyl + 5'-phospho-(deoxyribonucleotide)_m = (deoxyribonucleotide)_{n+m} + AMP + diphosphate (overall reaction)

(1a) ATP + [DNA ligase]-L-lysine = 5'-adenosyl [DNA ligase]-N^ε-phosphono-L-lysine + diphosphate

(1b) 5'-adenosyl [DNA ligase]-N^ε-phosphono-L-lysine + 5'-phospho-(deoxyribonucleotide)_m = 5'-(5'-diphosphoadenosine)-(deoxyribonucleotide)_m + [DNA ligase]-L-lysine

(1c) (deoxyribonucleotide)_n-3'-hydroxyl + 5'-(5'-diphosphoadenosine)-(deoxyribonucleotide)_m = (deoxyribonucleotide)_{n+m} + AMP

(2) NAD⁺ + (deoxyribonucleotide)_n-3'-hydroxyl + 5'-phospho-(deoxyribonucleotide)_m = (deoxyribonucleotide)_{n+m} + AMP + β-nicotinamide D-nucleotide (overall reaction)

(2a) NAD⁺ + [DNA ligase]-L-lysine = 5'-adenosyl [DNA ligase]-N^ε-phosphono-L-lysine + β-nicotinamide D-nucleotide

(2b) 5'-adenosyl [DNA ligase]-N^ε-phosphono-L-lysine + 5'-phospho-(deoxyribonucleotide)_m = 5'-(5'-diphosphoadenosine)-(deoxyribonucleotide)_m + [DNA ligase]-L-lysine

(2c) (deoxyribonucleotide)_n-3'-hydroxyl + 5'-(5'-diphosphoadenosine)-(deoxyribonucleotide)_m = (deoxyribonucleotide)_{n+m} + AMP

Systematic name: poly(deoxyribonucleotide)-3'-hydroxyl:5'-phospho-poly(deoxyribonucleotide) ligase (ATP or NAD⁺)

Comments: The enzymes from the archaea *Thermococcus fumicolans* and *Thermococcus onnurineus* show high activity with either ATP or NAD⁺, and significantly lower activity with TTP, GTP, and CTP. The enzyme catalyses the ligation of DNA strands with 3'-hydroxyl and 5'-phosphate termini, forming a phosphodiester and sealing certain types of single-strand breaks in duplex DNA. Catalysis occurs by a three-step mechanism, starting with the activation of the enzyme by ATP or NAD⁺, forming a phosphoramidate bond between adenylate and a lysine residue. The adenylate group is then transferred to the 5'-phosphate terminus of the substrate, forming the capped structure 5'-(5'-diphosphoadenosine)-[DNA]. Finally, the enzyme catalyses a nucleophilic attack of the 3'-OH terminus on the capped terminus, which results in formation of the phosphodiester bond and release of the adenylate. Different from EC 6.5.1.1, DNA ligase (ATP), EC 6.5.1.2, DNA ligase (NAD⁺) and EC 6.5.1.7, DNA ligase (ATP, ADP or GTP).

References: [361, 201]

[EC 6.5.1.6 created 2014, modified 2016]

EC 6.5.1.7

Accepted name: DNA ligase (ATP, ADP or GTP)

- Reaction:** (1) $\text{ATP} + (\text{deoxyribonucleotide})_{n-3'}\text{-hydroxyl} + 5'\text{-phospho-}(\text{deoxyribonucleotide})_m = (\text{deoxyribonucleotide})_{n+m} + \text{AMP} + \text{diphosphate}$ (overall reaction)
 (1a) $\text{ATP} + [\text{DNA ligase}]\text{-L-lysine} = 5'\text{-adenosyl} [\text{DNA ligase}]\text{-N}^{\epsilon}\text{-phosphono-L-lysine} + \text{diphosphate}$
 (1b) $5'\text{-adenosyl} [\text{DNA ligase}]\text{-N}^{\epsilon}\text{-phosphono-L-lysine} + 5'\text{-phospho-}(\text{deoxyribonucleotide})_m = 5'\text{-(5'-diphosphoadenosine)-}(\text{deoxyribonucleotide})_m + [\text{DNA ligase}]\text{-L-lysine}$
 (1c) $(\text{deoxyribonucleotide})_{n-3'}\text{-hydroxyl} + 5'\text{-(5'-diphosphoadenosine)-}(\text{deoxyribonucleotide})_m = (\text{deoxyribonucleotide})_{n+m} + \text{AMP}$
 (2) $\text{ADP} + (\text{deoxyribonucleotide})_{n-3'}\text{-hydroxyl} + 5'\text{-phospho-}(\text{deoxyribonucleotide})_m = (\text{deoxyribonucleotide})_{n+m} + \text{AMP} + \text{phosphate}$ (overall reaction)
 (2a) $\text{ADP} + [\text{DNA ligase}]\text{-L-lysine} = 5'\text{-adenosyl} [\text{DNA ligase}]\text{-N}^{\epsilon}\text{-phosphono-L-lysine} + \text{phosphate}$
 (2b) $5'\text{-adenosyl} [\text{DNA ligase}]\text{-N}^{\epsilon}\text{-phosphono-L-lysine} + 5'\text{-phospho-}(\text{deoxyribonucleotide})_m = 5'\text{-(5'-diphosphoadenosine)-}(\text{deoxyribonucleotide})_m + [\text{DNA ligase}]\text{-L-lysine}$
 (2c) $(\text{deoxyribonucleotide})_{n-3'}\text{-hydroxyl} + 5'\text{-(5'-diphosphoadenosine)-}(\text{deoxyribonucleotide})_m = (\text{deoxyribonucleotide})_{n+m} + \text{AMP}$
 (3) $\text{GTP} + (\text{deoxyribonucleotide})_{n-3'}\text{-hydroxyl} + 5'\text{-phospho-}(\text{deoxyribonucleotide})_m = (\text{deoxyribonucleotide})_{n+m} + \text{GMP} + \text{diphosphate}$ (overall reaction)
 (3a) $\text{GTP} + [\text{DNA ligase}]\text{-L-lysine} = 5'\text{-guanosyl} [\text{DNA ligase}]\text{-N}^{\epsilon}\text{-phosphono-L-lysine} + \text{diphosphate}$
 (3b) $5'\text{-guanosyl} [\text{DNA ligase}]\text{-N}^{\epsilon}\text{-phosphono-L-lysine} + 5'\text{-phospho-}(\text{deoxyribonucleotide})_m = 5'\text{-(5'-diphosphoguanosine)-}(\text{deoxyribonucleotide})_m + [\text{DNA ligase}]\text{-L-lysine}$
 (3c) $(\text{deoxyribonucleotide})_{n-3'}\text{-hydroxyl} + 5'\text{-(5'-diphosphoguanosine)-}(\text{deoxyribonucleotide})_m = (\text{deoxyribonucleotide})_{n+m} + \text{GMP}$

Other name(s): poly(deoxyribonucleotide):poly(deoxyribonucleotide) ligase (ATP, ADP or GTP)
Systematic name: poly(deoxyribonucleotide)-3'-hydroxyl:5'-phospho-poly(deoxyribonucleotide) ligase (ATP, ADP or GTP)

Comments: The enzymes from the archaea *Hyperthermus butylicus* and *Sulfophobococcus zilligii* are active with ATP, ADP or GTP. They show no activity with NAD^+ . The enzyme catalyses the ligation of DNA strands with 3'-hydroxyl and 5'-phosphate termini, forming a phosphodiester and sealing certain types of single-strand breaks in duplex DNA. Catalysis occurs by a three-step mechanism, starting with the activation of the enzyme by ATP, ADP, or GTP, forming a phosphoramidate bond between adenylylate/guanylate and a lysine residue. The nucleotide is then transferred to the 5'-phosphate terminus of the substrate, forming the capped structure 5'-(5'-diphosphoadenosine/guanosine)-[DNA]. Finally, the enzyme catalyses a nucleophilic attack of the 3'-OH terminus on the capped terminus, which results in formation of the phosphodiester bond and release of the nucleotide. Different from EC 6.5.1.1, DNA ligase (ATP), and EC 6.5.1.6, DNA ligase (ATP or NAD^+), which cannot utilize GTP.

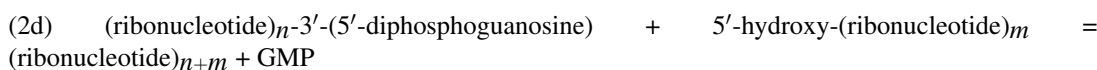
References: [413, 198]

[EC 6.5.1.7 created 2014, modified 2016]

EC 6.5.1.8

Accepted name: 3'-phosphate/5'-hydroxy nucleic acid ligase

- Reaction:** (1) $(\text{ribonucleotide})_{n-3'}\text{-phosphate} + 5'\text{-hydroxy-}(\text{ribonucleotide})_m + \text{GTP} = (\text{ribonucleotide})_{n+m} + \text{GMP} + \text{diphosphate}$ (overall reaction)
 (1a) $\text{GTP} + [\text{RNA ligase}]\text{-L-histidine} = [\text{RNA ligase}]\text{-N}^{\tau}\text{-(5'-guanosyl-phosphono)-L-histidine} + \text{diphosphate}$
 (1b) $[\text{RNA ligase}]\text{-N}^{\tau}\text{-(5'-guanosyl-phosphono)-L-histidine} + (\text{ribonucleotide})_{n-3'}\text{-phosphate} = (\text{ribonucleotide})_{n-3'}\text{-(5'-diphosphoguanosine)} + [\text{RNA ligase}]\text{-L-histidine}$
 (1c) $(\text{ribonucleotide})_{n-3'}\text{-(5'-diphosphoguanosine)} + 5'\text{-hydroxy-}(\text{ribonucleotide})_m = (\text{ribonucleotide})_{n+m} + \text{GMP}$
 (2) $(\text{ribonucleotide})_{n-2',3'}\text{-cyclophosphate} + 5'\text{-hydroxy-}(\text{ribonucleotide})_m + \text{GTP} + \text{H}_2\text{O} = (\text{ribonucleotide})_{n+m} + \text{GMP} + \text{diphosphate}$ (overall reaction)
 (2a) $(\text{ribonucleotide})_{n-2',3'}\text{-cyclophosphate} + \text{H}_2\text{O} = (\text{ribonucleotide})_{n-3'}\text{-phosphate}$
 (2b) $\text{GTP} + [\text{RNA ligase}]\text{-L-histidine} = [\text{RNA ligase}]\text{-N}^{\tau}\text{-(5'-guanosyl-phosphono)-L-histidine} + \text{diphosphate}$
 (2c) $[\text{RNA ligase}]\text{-N}^{\tau}\text{-(5'-guanosyl-phosphono)-L-histidine} + (\text{ribonucleotide})_{n-3'}\text{-phosphate} = (\text{ribonucleotide})_{n-3'}\text{-(5'-diphosphoguanosine)} + [\text{RNA ligase}]\text{-L-histidine}$



- Other name(s):** *rtcB* (gene name)
- Systematic name:** poly(ribonucleotide)-3'-phosphate:5'-hydroxy-poly(ribonucleotide) ligase (GMP-forming)
- Comments:** The enzyme is a GTP- and Mn^{2+} -dependent 3'-5' nucleic acid ligase with the ability to join RNA with 3'-phosphate or 2',3'-cyclic-phosphate ends to RNA with 5'-hydroxy ends. It can also join DNA with 3'-phosphate ends to DNA with 5'-hydroxy ends, provided the DNA termini are unpaired [54]. The enzyme is found in members of all three kingdoms of life, and is essential in metazoa for the splicing of intron-containing tRNAs. The reaction follows a three-step mechanism with initial activation of the enzyme by GTP hydrolysis, forming a phosphoramidate bond between the guanylate and a histidine residue. The guanylate group is transferred to the 3'-phosphate terminus of the substrate, forming the capped structure [DNA/RNA]-3'-(5'-diphosphoguanosine). When a suitable 5'-OH end is available, the enzyme catalyses an attack of the 5'-OH on the capped end to form a 3'-5' phosphodiester splice junction, releasing the guanylate. When acting on an RNA 2',3'-cyclic-phosphate, the enzyme catalyses an additional reaction, hydrolysing the cyclic phosphate to a 3'-phosphate [260]. The metazoan enzyme requires activating cofactors in order to achieve multiple turnover catalysis [91].
- References:** [420, 422, 419, 92, 55, 54, 79, 91, 260]

[EC 6.5.1.8 created 2017]

EC 6.6 Forming nitrogen—metal bonds

This subclass contains a single sub-subclass for enzymes that form coordination complexes, i.e. form nitrogen—metal bonds (EC 6.6.1).

EC 6.6.1 Forming coordination complexes

EC 6.6.1.1

- Accepted name:** magnesium chelatase
- Reaction:** $\text{ATP} + \text{protoporphyrin IX} + \text{Mg}^{2+} + \text{H}_2\text{O} = \text{ADP} + \text{phosphate} + \text{Mg-protoporphyrin IX} + 2 \text{H}^+$
- Other name(s):** protoporphyrin IX magnesium-chelatase; protoporphyrin IX Mg-chelatase; magnesium-protoporphyrin IX chelatase; magnesium-protoporphyrin chelatase; magnesium-chelatase; Mg-chelatase; Mg-protoporphyrin IX magnesio-lyase
- Systematic name:** Mg-protoporphyrin IX magnesium-lyase
- Comments:** This is the first committed step of chlorophyll biosynthesis and is a branchpoint of two major routes in the tetrapyrrole pathway.
- References:** [450, 451, 115]

[EC 6.6.1.1 created 2003]

EC 6.6.1.2

- Accepted name:** cobaltochelataase
- Reaction:** $\text{ATP} + \text{hydrogenobyric acid } a,c\text{-diamide} + \text{Co}^{2+} + \text{H}_2\text{O} = \text{ADP} + \text{phosphate} + \text{cob(II)yrinic acid } a,c\text{-diamide} + \text{H}^+$
- Other name(s):** hydrogenobyric acid *a,c*-diamide cobaltochelataase; CobNST; CobNCobST
- Systematic name:** hydrogenobyric-acid-*a,c*-diamide:cobalt cobalt-ligase (ADP-forming)

Comments: This enzyme, which forms part of the aerobic cobalamin biosynthesis pathway, is a type I chelatase, being heterotrimeric and ATP-dependent. It comprises two components, one of which corresponds to CobN and the other is composed of two polypeptides, specified by *cobS* and *cobT* in *Pseudomonas denitrificans*, and named CobST [88]. Hydrogenobyric acid is a very poor substrate. ATP can be replaced by dATP or CTP but the reaction proceeds more slowly. CobN exhibits a high affinity for hydrogenobyric acid *a,c*-diamide. The oligomeric protein CobST possesses at least one sulfhydryl group that is essential for ATP-binding. Once the Co²⁺ is inserted, the next step in the pathway ensures that the cobalt is ligated securely by reducing Co(II) to Co(I). This step is carried out by EC 1.16.8.1, cob(II)yrinic acid *a,c*-diamide reductase.

References: [88, 455]

[EC 6.6.1.2 created 2004]

References

- [1] A., Koshland Levitzki, , and Jr. Ligand-induced dimer-to-tetramer transformation in cytosine triphosphate synthetase. *Biochemistry*, 11:247–253, 1972.
- [2] J.L. Abbott, J.M. Newell, C.M. Lightcap, M.E. Olanich, D.T. Loughlin, M.A. Weller, G. Lam, S. Pollack, and W.A. Patton. The effects of removing the GAT domain from *E. coli* GMP synthetase. *Protein J.*, 25:483–491, 2006.
- [3] E. Aboulmagd, F.B. Oppermann-Sanio, and A. Steinbüchel. Molecular characterization of the cyanophycin synthetase from *Synechocystis* sp. strain PCC6308. *Arch. Microbiol.*, 174:297–306, 2000.
- [4] E. Aboulmagd, F.B. Oppermann-Sanio, and A. Steinbüchel. Purification of *Synechocystis* sp. strain PCC6308 cyanophycin synthetase and its characterization with respect to substrate and primer specificity. *Appl. Environ. Microbiol.*, 67:2176–2182, 2001.
- [5] R. Abrams and M. Bentley. Biosynthesis of nucleic acid purines. III. Guanosine 5'-phosphate formation from xanthosine 5'-phosphate and L-glutamine. *Arch. Biochem. Biophys.*, 79:91–110, 1959.
- [6] B.E. Alber, J.W. Kung, and G. Fuchs. 3-Hydroxypropionyl-coenzyme A synthetase from *Metallosphaera sedula*, an enzyme involved in autotrophic CO₂ fixation. *J. Bacteriol.*, 190:1383–1389, 2008.
- [7] E.H. Allen, E. Glassman, and R.S. Schweet. Incorporation of amino acids into ribonucleic acid. I. The role of activating enzymes. *J. Biol. Chem.*, 235:1061–1067, 1960.
- [8] M.M. Allen, F. Hutchison, and P.J. Weathers. Cyanophycin granule polypeptide formation and degradation in the cyanobacterium *Aphanocapsa* 6308. *J. Bacteriol.*, 141:687–693, 1980.
- [9] C.C. Allende and J.E. Allende. Purification and substrate specificity of arginyl-ribonucleic acid synthetase from rat liver. *J. Biol. Chem.*, 239:1102–1106, 1964.
- [10] U. Altenschmidt, C. Eckerskorn, and G. Fuchs. Evidence that enzymes of a novel aerobic 2-amino-benzoate metabolism in denitrifying *Pseudomonas* are coded on a small plasmid. *Eur. J. Biochem.*, 194:647–653, 1990.
- [11] P.M. Anderson and A. Meister. Evidence for an activated form of carbon dioxide in the reaction catalysed by *Escherichia coli* carbamyl phosphate synthetase. *Biochemistry*, 4:2803–2809, 1965.
- [12] G. Antranikian and G. Gottschalk. Copurification of citrate lyase and citrate lyase ligase from *Rhodospseudomonas gelatinosa* and subsequent separation of the two enzymes. *Eur. J. Biochem.*, 126:43–47, 1982.
- [13] G. Antranikian, C. Herzberg, and G. Gottschalk. Covalent modification of citrate lyase ligase from *Clostridium sphenoides* by phosphorylation/dephosphorylation. *Eur. J. Biochem.*, 153:413–420, 1985.
- [14] M. Aoshima and Y. Igarashi. A novel oxalosuccinate-forming enzyme involved in the reductive carboxylation of 2-oxoglutarate in *Hydrogenobacter thermophilus* TK-6. *Mol. Microbiol.*, 62:748–759, 2006.
- [15] M. Aoshima, M. Ishii, and Y. Igarashi. A novel biotin protein required for reductive carboxylation of 2-oxoglutarate by isocitrate dehydrogenase in *Hydrogenobacter thermophilus* TK-6. *Mol. Microbiol.*, 51:791–798, 2004.
- [16] M. Aoshima, M. Ishii, and Y. Igarashi. A novel enzyme, citryl-CoA synthetase, catalysing the first step of the citrate cleavage reaction in *Hydrogenobacter thermophilus* TK-6. *Mol. Microbiol.*, 52:751–761, 2004.
- [17] D.L. Appanna, B.J. Grundy, E.W. Szczepan, and T. Viswanatha. Aerobactin synthesis in a cell-free system of *Aerobacter aerogenes* 62-1. *Biochim. Biophys. Acta*, 801:437–443, 1984.
- [18] S.O. Arnett, B. Gerratana, and C.A. Townsend. Rate-limiting steps and role of active site Lys⁴⁴³ in the mechanism of carbapenam synthetase. *Biochemistry*, 46:9337–9345, 2007.
- [19] P. Arora, A. Goyal, V.T. Natarajan, E. Rajakumara, P. Verma, R. Gupta, M. Yousuf, O.A. Trivedi, D. Mohanty, A. Tyagi, R. Sankaranarayanan, and R.S. Gokhale. Mechanistic and functional insights into fatty acid activation in *Mycobacterium tuberculosis*. *Nat. Chem. Biol.*, 5:166–173, 2009.
- [20] B.O. Bachmann, R. Li, and C.A. Townsend. β -Lactam synthetase: a new biosynthetic enzyme. *Proc. Natl. Acad. Sci. USA*, 95:9082–9086, 1998.

- [21] J. Baddiley and F.C. Neuhaus. The enzymic activation of D-alanine. *Biochem. J.*, 75:579–579, 1960.
- [22] A.M. Bakken and M. Farstad. Identical subcellular distribution of palmitoyl-CoA and arachidonoyl-CoA synthetase activities in human blood platelets. *Biochem. J.*, 261:71–76, 1989.
- [23] J. Barandun, C.L. Delley, N. Ban, and E. Weber-Ban. Crystal structure of the complex between prokaryotic ubiquitin-like protein and its ligase PafA. *J. Am. Chem. Soc.*, 135:6794–6797, 2013.
- [24] A. Becker, G. Lyn, M. Gefter, and J. Hurwitz. The enzymatic repair of DNA. II. Characterization of phage-induced sealase. *Proc. Natl. Acad. Sci. USA*, 58:1996–2003, 1967.
- [25] H.D. Becker and D. Kern. *Thermus thermophilus*: a link in evolution of the tRNA-dependent amino acid amidation pathways. *Proc. Natl. Acad. Sci. USA*, 95:12832–12837, 1998.
- [26] I. Becker, J. Lodder, V. Gieselmann, and M. Eckhardt. Molecular characterization of *N*-acetylaspartylglutamate synthetase. *J. Biol. Chem.*, 285:29156–29164, 2010.
- [27] S. Bellais, M. Arthur, L. Dubost, J.E. Hugonnet, L. Gutmann, J. van Heijenoort, R. Legrand, J.P. Brouard, L. Rice, and J.L. Mainardi. *Asl_{fm}*, the D-aspartate ligase responsible for the addition of D-aspartic acid onto the peptidoglycan precursor of *Enterococcus faecium*. *J. Biol. Chem.*, 281:11586–11594, 2006.
- [28] H. Berg, K. Ziegler, K. Piotukh, K. Baier, W. Lockau, and R. Volkmer-Engert. Biosynthesis of the cyanobacterial reserve polymer multi-L-arginyl-poly-L-aspartic acid (cyanophycin): mechanism of the cyanophycin synthetase reaction studied with synthetic primers. *Eur. J. Biochem.*, 267:5561–5570, 2000.
- [29] I.A. Berg, D. Kockelkorn, W. Buckel, and G. Fuchs. A 3-hydroxypropionate/4-hydroxybutyrate autotrophic carbon dioxide assimilation pathway in *Archaea*. *Science*, 318:1782–1786, 2007.
- [30] M. Berg, H. Hilbi, and P. Dimroth. The acyl carrier protein of malonate decarboxylase of *Malonomonas rubra* contains 2'-(5''-phosphoribosyl)-3'-dephosphocoenzyme A as a prosthetic group. *Biochemistry*, 35:4689–4696, 1996.
- [31] M. Berg, H. Hilbi, and P. Dimroth. Sequence of a gene cluster from *Malonomonas rubra* encoding components of the malonate decarboxylase Na⁺ pump and evidence for their function. *Eur. J. Biochem.*, 245:103–115, 1997.
- [32] P. Berg, F.H. Bergmann, E.J. Ofengand, and M. Dieckmann. The enzymic synthesis of amino acyl derivatives of ribonucleic acid. I. The mechanism of leucyl-, valyl-, isoleucyl- and methionyl ribonucleic acid formation. *J. Biol. Chem.*, 236:1726–1734, 1961.
- [33] F.H. Bergmann, P. Berg, and M. Dieckmann. The enzymic synthesis of amino acyl derivatives of ribonucleic acid. II. The preparation of leucyl-, valyl-, isoleucyl- and methionyl ribonucleic acid synthetases from *Escherichia coli*. *J. Biol. Chem.*, 236:1735–1740, 1961.
- [34] V. Bernal, P. Areense, V. Blatz, M.A. Mandrand-Berthelot, M. Canovas, and J.L. Iborra. Role of betaine:CoA ligase (CaiC) in the activation of betaines and the transfer of coenzyme A in *Escherichia coli*. *J. Appl. Microbiol.*, 105:42–50, 2008.
- [35] U. Bertazzoni, M. Mathelet, and F. Campagnari. Purification and properties of a polynucleotide ligase from calf thymus glands. *Biochim. Biophys. Acta*, 287:404–414, 1972.
- [36] E. Billy, D. Hess, J. Hofsteenge, and W. Filipowicz. Characterization of the adenylation site in the RNA 3'-terminal phosphate cyclase from *Escherichia coli*. *J. Biol. Chem.*, 274:34955–34960, 1999.
- [37] F. Blanche, M. Couder, L. Debussche, D. Thibaut, B. Cameron, and J. Crouzet. Biosynthesis of vitamin B₁₂: stepwise amidation of carboxyl groups b, d, e, and g of cobyrinic acid *a,c*-diamide is catalyzed by one enzyme in *Pseudomonas denitrificans*. *J. Bacteriol.*, 173:6046–6051, 1991.
- [38] S.K. Blight, R.C. Larue, A. Mahapatra, D.G. Longstaff, E. Chang, G. Zhao, P.T. Kang, K.B. Green-Church, M.K. Chan, and J.A. Krzycki. Direct charging of tRNA(CUA) with pyrrolysine in vitro and in vivo. *Nature*, 431:333–335, 2004.
- [39] S.K. Boehlein, N.G. Richards, and S.M. Schuster. Glutamine-dependent nitrogen transfer in *Escherichia coli* asparagine synthetase B. Searching for the catalytic triad. *J. Biol. Chem.*, 269:7450–7457, 1994.

- [40] A.L. Bognar, C. Osborne, B. Shane, S.C. Singer, and R. Ferone. Folylpoly- γ -glutamate synthetase-dihydrofolate synthetase. Cloning and high expression of the *Escherichia coli* folC gene and purification and properties of the gene product. *J. Biol. Chem.*, 260:5625–5630, 1985.
- [41] J.M. Bollinger, D.S. Kwon, G.W. Huisman, R. Kolter, , and C.T. Glutathionylspermidine metabolism in *E. coli*. Purification, cloning, overproduction and characterization of a bifunctional glutathionylspermidine synthetase/amidase. *J. Biol. Chem.*, 270:14031–14041, 1995.
- [42] A. Boniface, A. Bouhss, D. Mengin-Lecreulx, and D. Blanot. The MurE synthetase from *Thermotoga maritima* is endowed with an unusual D-lysine adding activity. *J. Biol. Chem.*, 281:15680–15686, 2006.
- [43] P. Brick, T.N. Bhat, and D.M. Blow. Structure of tyrosyl-tRNA synthetase refined at 2.3 Å resolution. Interaction of the enzyme with the tyrosyl adenylate intermediate. *J. Mol. Biol.*, 208:83–98, 1989.
- [44] N. Brot and J. Goodwin. Regulation of 2,3-dihydroxybenzoylserine synthetase by iron. *J. Biol. Chem.*, 243:510–513, 1968.
- [45] T.C. Broussard, S. Pakhomova, D.B. Neau, R. Bonnot, and G.L. Waldrop. Structural analysis of substrate, reaction intermediate, and product binding in *Haemophilus influenzae* biotin carboxylase. *Biochemistry*, 54:3860–3870, 2015.
- [46] G.M. Brown. The metabolism of pantothenic acid. *J. Biol. Chem.*, 234:370–378, 1959.
- [47] T.D. Bugg, G.D. Wright, S. Dutka-Malen, M. Arthur, P. Courvalin, and C.T. Walsh. Molecular basis for vancomycin resistance in *Enterococcus faecium* BM4147: biosynthesis of a depsipeptide peptidoglycan precursor by vancomycin resistance proteins VanH and VanA. *Biochemistry*, 30:10408–10415, 1991.
- [48] H.A. Bullock, C.R. Reisch, A.S. Burns, M.A. Moran, and W.B. Whitman. Regulatory and functional diversity of methylmercaptopropionate coenzyme A ligases from the dimethylsulfoniopropionate demethylation pathway in *Ruegeria pomeroyi* DSS-3 and other proteobacteria. *J. Bacteriol.*, 196:1275–1285, 2014.
- [49] M.F. Byford, J.E. Baldwin, C.-Y. Shiau, and C.J. Schofield. The mechanism of ACV synthetase. *Chem. Rev.*, 97:2631–2649, 1997.
- [50] A.F. Carvalho, M.P. Pinto, C.P. Grou, R. Vitorino, P. Domingues, F. Yamao, C. Sa-Miranda, and J.E. Azevedo. High-yield expression in *Escherichia coli* and purification of mouse ubiquitin-activating enzyme E1. *Mol Biotechnol*, 51:254–261, 2012.
- [51] I. Casabon, A.M. Crowe, J. Liu, and L.D. Eltis. FadD3 is an acyl-CoA synthetase that initiates catabolism of cholesterol rings C and D in actinobacteria. *Mol. Microbiol.*, 87:269–283, 2013.
- [52] I. Casabon, K. Swain, A.M. Crowe, L.D. Eltis, and W.W. Mohn. Actinobacterial acyl coenzyme a synthetases involved in steroid side-chain catabolism. *J. Bacteriol.*, 196:579–587, 2014.
- [53] A.K. Chakravarty and S. Shuman. RNA 3'-phosphate cyclase (RtcA) catalyzes ligase-like adenylation of DNA and RNA 5'-monophosphate ends. *J. Biol. Chem.*, 286:4117–4122, 2011.
- [54] A.K. Chakravarty and S. Shuman. The sequential 2',3'-cyclic phosphodiesterase and 3'-phosphate/5'-OH ligation steps of the RtcB RNA splicing pathway are GTP-dependent. *Nucleic Acids Res.*, 40:8558–8567, 2012.
- [55] A.K. Chakravarty, R. Subbotin, B.T. Chait, and S. Shuman. RNA ligase RtcB splices 3'-phosphate and 5'-OH ends via covalent RtcB-(histidiny)-GMP and polynucleotide-(3')pp(5')G intermediates. *Proc. Natl. Acad. Sci. USA*, 109:6072–6077, 2012.
- [56] G.L. Challis. A widely distributed bacterial pathway for siderophore biosynthesis independent of nonribosomal peptide synthetases. *ChemBioChem*, 6:601–611, 2005.
- [57] K.H. Chang, P.H. Liang, W. Beck, J.D. Scholten, , and D. Isolation and characterization of the three polypeptide components of 4-chlorobenzoate dehalogenase from *Pseudomonas* sp. strain CBS-3. *Biochemistry*, 31:5605–5610, 1992.
- [58] Z.D. Chen, J.E. Dixon, and H. Zalkin. Cloning of a chicken liver cDNA encoding 5-aminoimidazole ribonucleotide carboxylase and 5-aminoimidazole-4-N-succinocarboxamide ribonucleotide synthetase by functional complementation of *Escherichia coli pur* mutants. *Proc. Natl. Acad. Sci. USA*, 87:3097–3101, 1990.

- [59] D. Cheng, C.H. Chu, L. Chen, J.N. Feder, G.A. Mintier, Y. Wu, J.W. Cook, M.R. Harpel, G.A. Locke, Y. An, and J.K. Tamura. Expression, purification, and characterization of human and rat acetyl coenzyme A carboxylase (ACC) isozymes. *Protein Expr. Purif.*, 51:11–21, 2007.
- [60] C.G. Cheong, C.B. Bauer, K.R. Brushaber, J.C. Escalante-Semerena, and I. Rayment. Three-dimensional structure of the L-threonine-*O*-3-phosphate decarboxylase (CobD) enzyme from *Salmonella enterica*. *Biochemistry*, 41:4798–4808, 2002.
- [61] H. Cherest, D. Thomas, and Y. Surdin-Kerjan. Polyglutamylation of folate coenzymes is necessary for methionine biosynthesis and maintenance of intact mitochondrial genome in *Saccharomyces cerevisiae*. *J. Biol. Chem.*, 275:14056–14063, 2000.
- [62] V. Chiumecka, M. von Tigerstrom, P. D’Obrenan, and C.J. Smith. Purification and properties of lysyl transfer ribonucleic acid synthetase from bakers’ yeast. *J. Biol. Chem.*, 244:5481–5488, 1969.
- [63] C.Y. Chou, L.P. Yu, and L. Tong. Crystal structure of biotin carboxylase in complex with substrates and implications for its catalytic mechanism. *J. Biol. Chem.*, 284:11690–11697, 2009.
- [64] T.C. Chou and F. Lipmann. Separation of acetyl transfer enzymes in pigeon liver extract. *J. Biol. Chem.*, 196:89–103, 1952.
- [65] J.K. Christenson, J.E. Richman, M.R. Jensen, J.Y. Neufeld, C.M. Wilmot, and L.P. Wackett. β -Lactone synthetase found in the olefin biosynthesis pathway. *Biochemistry*, 56:348–351, 2017.
- [66] J.E. Christner, M.J. Schlesinger, and M.J. Coon. Enzymatic activation of biotin. Biotinyl adenylate formation. *J. Biol. Chem.*, 239:3997–4005, 1964.
- [67] D. Cichowicz, S.K. Foo, and B. Shane. Folylpoly- γ -glutamate synthesis by bacteria and mammalian cells. *Mol. Cell. Biochem.*, 39:209–228, 1981.
- [68] N. Cicmil and R.H. Huang. Crystal structure of QueC from *Bacillus subtilis*: an enzyme involved in preQ₁ biosynthesis. *Proteins*, 72:1084–1088, 2008.
- [69] F. Collard, V. Stroobant, P. Lamosa, C.N. Kapanda, D.M. Lambert, G.G. Muccioli, J.H. Poupaert, F. Opperdoes, and E. Van Schaftingen. Molecular identification of *N*-acetylaspartylglutamate synthase and β -citrylglutamate synthase. *J. Biol. Chem.*, 285:29826–29833, 2010.
- [70] M. Comini, U. Menge, J. Wissing, and L. Flohe. Trypanothione synthesis in crithidia revisited. *J. Biol. Chem.*, 280:6850–6860, 2005.
- [71] H.A. Cooke, J. Zhang, M.A. Griffin, K. Nonaka, S.G. Van Lanen, B. Shen, and S.D. Bruner. Characterization of NcsB2 as a promiscuous naphthoic acid/coenzyme A ligase integral to the biosynthesis of the enediyne antitumor antibiotic neocarzinostatin. *J. Am. Chem. Soc.*, 129:7728–7729, 2007.
- [72] E.A. Cossins and L. Chen. Foliates and one-carbon metabolism in plants and fungi. *Phytochemistry*, 45:437–452, 1997.
- [73] R. Couch, S.E. O’Connor, H. Seidle, C.T. Walsh, and R. Parry. Characterization of CmaA, an adenylation-thiolation didomain enzyme involved in the biosynthesis of coronatine. *J. Bacteriol.*, 186:35–42, 2004.
- [74] J.R. Cowles and J.L. Key. Demonstration of two tyrosyl-tRNA synthetases of pea roots. *Biochim. Biophys. Acta*, 281:33–44, 1972.
- [75] J.W. Cranston, R. Silber, V.G. Malathi, and J. Hurwitz. Studies on ribonucleic acid ligase. Characterization of an adenosine triphosphate-inorganic pyrophosphate exchange reaction and demonstration of an enzyme-adenylate complex with T4 bacteriophage-induced enzyme. *J. Biol. Chem.*, 249:7447–7456, 1974.
- [76] G.M. Crowley. The enzymatic synthesis of 5’-phosphoribosylimidazoleacetic acid. *J. Biol. Chem.*, 239:2593–2601, 1964.
- [77] K.G. Crush. Carnosine and related substances in animal tissues. *Comp. Biochem. Physiol.*, 34:3–30, 1970.
- [78] A.W. Curnow, D.L. Tumbula, J.T. Pelaschier, B. Min, and D. Söll. Glutamyl-tRNA^{Gln} amidotransferase in *Deinococcus radiodurans* may be confined to asparagine biosynthesis. *Proc. Natl. Acad. Sci. USA*, 95:12838–12843, 1998.
- [79] U. Das, A.K. Chakravarty, B.S. Remus, and S. Shuman. Rewriting the rules for end joining via enzymatic splicing of DNA 3’-PO₄ and 5’-OH ends. *Proc. Natl. Acad. Sci. USA*, 110:20437–20442, 2013.

- [80] U. Das and S. Shuman. 2'-Phosphate cyclase activity of RtcA: a potential rationale for *the* operon organization of RtcA with an RNA repair ligase RtcB in *Escherichia coli* and other bacterial taxa. *RNA*, 19:1355–1362, 2013.
- [81] M. Daugherty. Complete reconstitution of the human coenzyme A biosynthetic pathway via comparative genomics. *J. Biol. Chem.*, 277:21431–21439, 2002.
- [82] C.L. Davey. Synthesis of adenylosuccinic acid in preparations of mammalian skeletal muscle. *Nature*, 183:995–996, 1959.
- [83] E.W. Davie, V.V. Koningsberger, and F. Lipmann. The isolation of a tryptophan-activating enzyme from pancreas. *Arch. Biochem. Biophys.*, 65:21–28, 1956.
- [84] M.R. Davies and R.D. Marshall. Partial purification of L-asparaginyl-tRNA synthetase from rabbit liver. *Biochem. Biophys. Res. Commun.*, 47:1386–1395, 1972.
- [85] V. de Lorenzo, A. Bindereif, B.H. Paw, and J.B. Neilands. Aerobactin biosynthesis and transport genes of plasmid ColV-K30 in *Escherichia coli* K-12. *J. Bacteriol.*, 165:570–578, 1986.
- [86] V. de Lorenzo and J.B. Neilands. Characterization of *iucA* and *iucC* genes of the aerobactin system of plasmid ColV-K30 in *Escherichia coli*. *J. Bacteriol.*, 167:350–355, 1986.
- [87] D.V. Debabov, M.P. Heaton, Q. Zhang, K.D. Stewart, R.H. Lambalot, and F.C. Neuhaus. The D-alanyl carrier protein in *Lactobacillus casei*: cloning, sequencing and expression of *dltC*. *J. Bacteriol.*, 178:3869–3876, 1996.
- [88] L. Debussche, M. Couder, D. Thibaut, B. Cameron, J. Crouzet, and F. Blanche. Assay, purification, and characterization of cobaltochelataase, a unique complex enzyme catalyzing cobalt insertion in hydrogenobyric acid *a,c*-diamide during coenzyme B₁₂ biosynthesis in *Pseudomonas denitrificans*. *J. Bacteriol.*, 174:7445–7451, 1992.
- [89] L. Debussche, D. Thibaut, B. Cameron, J. Crouzet, and F. Blanche. Purification and characterization of cobyrinic acid *a,c*-diamide synthase from *Pseudomonas denitrificans*. *J. Bacteriol.*, 172:6239–6244, 1990.
- [90] F. Depardieu, M.G. Bonora, P.E. Reynolds, and P. Courvalin. The *vanG* glycopeptide resistance operon from *Enterococcus faecalis* revisited. *Mol. Microbiol.*, 50:931–948, 2003.
- [91] K.K. Desai, A.L. Beltrame, and R.T. Raines. Coevolution of RtcB and Archease created a multiple-turnover RNA ligase. *RNA*, 21:1866–1872, 2015.
- [92] K.K. Desai and R.T. Raines. tRNA ligase catalyzes the GTP-dependent ligation of RNA with 3'-phosphate and 5'-hydroxyl termini. *Biochemistry*, 51:1333–1335, 2012.
- [93] P. Dimroth, R.B. Guchhait, E. Stoll, and M.D. Lane. Enzymatic carboxylation of biotin: molecular and catalytic properties of a component enzyme of acetyl CoA carboxylase. *Proc. Natl. Acad. Sci. USA*, 67:1353–1360, 1970.
- [94] P. Dimroth and H. Hilbi. Enzymic and genetic basis for bacterial growth on malonate. *Mol. Microbiol.*, 25:3–10, 1997.
- [95] J. Kim do, K.H. Kim, H.H. Lee, S.J. Lee, J.Y. Ha, H.J. Yoon, and S.W. Suh. Crystal structure of lipoate-protein ligase A bound with the activated intermediate: insights into interaction with lipoyl domains. *J. Biol. Chem.*, 280:38081–38089, 2005.
- [96] J.C. Drake, J. Baram, and C.J. Allegra. Isolation and characterization of a novel dihydrofolate formylating enzyme from human MCF-7 breast cancer cells. *Biochem. Pharmacol.*, 39:615–618, 1990.
- [97] J. Drozak, M. Veiga da Cunha, D. Vertommen, V. Stroobant, and E. Van Schaftingen. Molecular identification of carnosine synthase as ATP-grasp domain-containing protein 1 (ATPGD1). *J. Biol. Chem.*, 285:9346–9356, 2010.
- [98] L. Du, Y. He, and Y. Luo. Crystal structure and enantiomer selection by D-alanyl carrier protein ligase DltA from *Bacillus cereus*. *Biochemistry*, 47:11473–11480, 2008.
- [99] D. Dunaway-Mariano, , and P.C. On the origins and functions of the enzymes of the 4-chlorobenzoate to 4-hydroxybenzoate converting pathway. *Biodegradation*, 5:259–276, 1994.
- [100] S. Dutka-Malen, C. Molinas, M. Arthur, and P. Courvalin. Sequence of the *vanC* gene of *Enterococcus gallinarum* BM4174 encoding a D-alanine:D-alanine ligase-related protein necessary for vancomycin resistance. *Gene*, 112:53–58, 1992.

- [101] D.J. Ebbole and H. Zalkin. Cloning and characterization of a 12-gene cluster from *Bacillus subtilis* encoding nine enzymes for de novo purine nucleotide synthesis. *J. Biol. Chem.*, 262:8274–8287, 1987.
- [102] D.J. Edwards, B.L. Marquez, L.M. Nogle, K. McPhail, D.E. Goeger, M.A. Roberts, and W.H. Gerwick. Structure and biosynthesis of the jamaicamides, new mixed polyketide-peptide neurotoxins from the marine cyanobacterium *Lyngbya majuscula*. *Chem. Biol.*, 11:817–833, 2004.
- [103] K. Eichler, F. Bourgis, A. Buchet, H.P. Kleber, and M.A. Mandrand-Berthelot. Molecular characterization of the *cai* operon necessary for carnitine metabolism in *Escherichia coli*. *Mol. Microbiol.*, 13:775–786, 1994.
- [104] M.A. Eisenberg. The acetate-activating enzyme of *Rhodospirillum rubrum*. *Biochim. Biophys. Acta*, 16:58–65, 1955.
- [105] W.H. Elliott. Isolation of glutamine synthetase and glutamotransferase from green peas. *J. Biol. Chem.*, 201:661–672, 1953.
- [106] W.H. Elliott. The enzymic activation of cholic acid by guinea-pig-liver microsomes. *Biochem. J.*, 62:427–433, 1956.
- [107] W.H. Elliott. The breakdown of adenosine triphosphate accompanying cholic acid activation by guinea-pig liver microsomes. *Biochem. J.*, 65:315–321, 1957.
- [108] L.A. Fahien and P.P. Cohen. A kinetic study of carbamyl phosphate synthetase. *J. Biol. Chem.*, 239:1925–1934, 1964.
- [109] C.N. Falany, X. Xie, J.B. Wheeler, J. Wang, M. Smith, D. He, and S. Barnes. Molecular cloning and expression of rat liver bile acid CoA ligase. *J. Lipid Res.*, 43:2062–2071, 2002.
- [110] F. Fan, A. Luxenburger, G.F. Painter, and J.S. Blanchard. Steady-state and pre-steady-state kinetic analysis of *Mycobacterium smegmatis* cysteine ligase (MshC). *Biochemistry*, 46:11421–11429, 2007.
- [111] R. Feng, Y. Satoh, Y. Ogasawara, T. Yoshimura, and T. Dairi. A glycopeptidyl-glutamate epimerase for bacterial peptidoglycan biosynthesis. *J. Am. Chem. Soc.*, 139:4243–4245, 2017.
- [112] W. Filipowicz, M. Konarska, H.J. Gross, and A.J. Shatkin. RNA 3'-terminal phosphate cyclase activity and RNA ligation in HeLa cell extract. *Nucleic Acids Res.*, 11:1405–1418, 1983.
- [113] M. Fines, B. Perichon, P. Reynolds, D.F. Sahn, and P. Courvalin. VanE, a new type of acquired glycopeptide resistance in *Enterococcus faecalis* BM4405. *Antimicrob. Agents Chemother.*, 43:2161–2164, 1999.
- [114] A.M. Fitzmaurice and P.E. Kolattukudy. Open reading frame 3, which is adjacent to the mycocerosic acid synthase gene, is expressed as an acyl coenzyme A synthase in *Mycobacterium bovis* BCG. *J. Bacteriol.*, 179:2608–2615, 1997.
- [115] M.N. Fodje, A. Hansson, M. Hansson, J.G. Olsen, S. Gough, R.D. Willows, and S. Al-Karadaghi. Interplay between an AAA module and an integrin I domain may regulate the function of magnesium chelatase. *J. Mol. Biol.*, 311:111–122, 2001.
- [116] H. Fraga, J.C. Esteves da Silva, and R. Fontes. Identification of luciferyl adenylate and luciferyl coenzyme A synthesized by firefly luciferase. *Chembiochem*, 5:110–115, 2004.
- [117] M.J. Fraser. Glycyl-RNA synthetase of rat liver: partial purification and effects of some metal ions on its activity. *Can. J. Biochem. Physiol.*, 41:1123–1233, 1963.
- [118] V. Fresquet, L. Williams, and F.M. Raushel. Mechanism of cobyrinic acid *a,c*-diamide synthetase from *Salmonella typhimurium* LT2. *Biochemistry*, 43:10619–10627, 2004.
- [119] J.A. Frias, B.R. Goblirsch, L.P. Wackett, and C.M. Wilmot. Cloning, purification, crystallization and preliminary X-ray diffraction of the OleC protein from *Stenotrophomonas maltophilia* involved in head-to-head hydrocarbon biosynthesis. *Acta Crystallogr. Sect. F Struct. Biol. Cryst. Commun.*, 66:1108–1110, 2010.
- [120] B.A. Fry. Glutamine synthesis by *Micrococcus pyogenes* var. *aureus*. *Biochem. J.*, 59:579–589, 1955.
- [121] K. Fujiwara, S. Toma, K. Okamura-Ikeda, Y. Motokawa, A. Nakagawa, and H. Taniguchi. Crystal structure of lipoate-protein ligase A from *Escherichia coli*. Determination of the lipoic acid-binding site. *J. Biol. Chem.*, 280:33645–33651, 2005.

- [122] T. Fukui, M. Ito, and K. Tomita. Purification and characterization of acetoacetyl-CoA synthetase from *Zoogloea ramigera* I-16-M. *Eur. J. Biochem.*, 127:423–428, 1982.
- [123] R. Fukunaga and S. Yokoyama. Structural insights into the first step of RNA-dependent cysteine biosynthesis in archaea. *Nat. Struct. Mol. Biol.*, 14:272–279, 2007.
- [124] P.K. Fyfe, S.L. Oza, A.H. Fairlamb, and W.N. Hunter. *Leishmania* trypanothione synthetase-amidase structure reveals a basis for regulation of conflicting synthetic and hydrolytic activities. *J. Biol. Chem.*, 283:17672–17680, 2008.
- [125] M.Y. Galperin and E.V. Koonin. A diverse superfamily of enzymes with ATP-dependent carboxylate-amine/thiol ligase activity. *Protein Sci.*, 6:2639–2643, 1997.
- [126] J. Gangloff and G. Dirheimer. Studies on aspartyl-tRNA synthetase from baker's yeast. I. Purification and properties of the enzyme. *Biochim. Biophys. Acta*, 294:263–272, 1973.
- [127] A.M. Gehring, I. Mori, and C.T. Walsh. Reconstitution and characterization of the *Escherichia coli* enterobactin synthetase from EntB, EntE, and EntF. *Biochemistry*, 37:2648–2659, 1998.
- [128] P. Genschik, E. Billy, M. Swianiewicz, and W. Filipowicz. The human RNA 3'-terminal phosphate cyclase is a member of a new family of proteins conserved in Eucarya, Bacteria and Archaea. *EMBO J.*, 16:2955–2967, 1997.
- [129] P. Genschik, K. Drabikowski, and W. Filipowicz. Characterization of the *Escherichia coli* RNA 3'-terminal phosphate cyclase and its σ^{54} -regulated operon. *J. Biol. Chem.*, 273:25516–25526, 1998.
- [130] M Gerlach, N. Schwelle, W. Lerbs, and M. Luckner. Enzymatic synthesis of cyclopeptide intermediates in *Penicillium cyclopium*. *Phytochemistry*, 24:1935–1939, 1985.
- [131] B. Gerratana, A. Stapon, and C.A. Townsend. Inhibition and alternate substrate studies on the mechanism of carbapenam synthetase from *Erwinia carotovora*. *Biochemistry*, 42:7836–7847, 2003.
- [132] F. Gibson and D.I. Magrath. The isolation and characterization of a hydroxamic acid (aerobactin) formed by *Aerobacter aerogenes* 62-I. *Biochim. Biophys. Acta*, 192:175–184, 1969.
- [133] H.S. Ginoza and R.A. Altenbern. The pantothenate-synthesizing enzyme cell-free extracts of *Brucella abortus*, strain 19. *Arch. Biochem. Biophys.*, 56:537–541, 1955.
- [134] J. Giovanelli. Oxalyl-coenzyme A synthetase from pea seeds. *Biochim. Biophys. Acta*, 118:124–143, 1966.
- [135] N.L. Glass and T. Kosuge. Cloning of the gene for indoleacetic acid-lysine synthetase from *Pseudomonas syringae* subsp. savastanoi. *J. Bacteriol.*, 166:598–598, 1986.
- [136] D.A. Goldthwait, R.A. Peabody, and G.R. Greenberg. On the mechanism of synthesis of glycinamide ribotide and its formyl derivative. *J. Biol. Chem.*, 221:569–577, 1956.
- [137] A. Goyal, M. Yousuf, E. Rajakumara, P. Arora, R.S. Gokhale, and R. Sankaranarayanan. Crystallization and preliminary X-ray crystallographic studies of the N-terminal domain of FadD28, a fatty-acyl AMP ligase from *Mycobacterium tuberculosis*. *Acta Crystallogr. Sect. F Struct. Biol. Cryst. Commun.*, 62:350–352, 2006.
- [138] D.E. Green, T.W. Morris, J. Green, J.E. Cronan, Guest Jr., and J.R. Purification and properties of the lipoate protein ligase of *Escherichia coli*. *Biochem. J.*, 309:853–862, 1995.
- [139] D.M. Greenberg, L.K. Wynston, and A. Nagabhushanan. Further studies on N^5 -formyltetrahydrofolic acid cyclodehydrase. *Biochemistry*, 4:1872–1878, 1965.
- [140] M.J. Griffin and G.M. Brown. The biosynthesis of folic acid. III. Enzymatic formation of dihydrofolic acid from dihydropterotic acid and of tetrahydropteroylpolyglutamic acid compounds from tetrahydrofolic acid. *J. Biol. Chem.*, 239:310–316, 1964.
- [141] G.G. Gross and M.H. Zenk. Isolation and properties of hydroxycinnamate: CoA ligase from lignifying tissue of *Forsythia*. *Eur. J. Biochem.*, 42:453–459, 1974.
- [142] A. Guranowski, O. Miersch, P.E. Staswick, W. Suza, and C. Wasternack. Substrate specificity and products of side-reactions catalyzed by jasmonate:amino acid synthetase (JAR1). *FEBS Lett.*, 581:815–820, 2007.

- [143] E. Guth, M. Thommen, and E. Weber-Ban. Mycobacterial ubiquitin-like protein ligase PafA follows a two-step reaction pathway with a phosphorylated pup intermediate. *J. Biol. Chem.*, 286:4412–4419, 2011.
- [144] M.T. Gutierrez-Lugo, G.L. Newton, R.C. Fahey, and C.A. Bewley. Cloning, expression and rapid purification of active recombinant mycothiol ligase as B1 immunoglobulin binding domain of streptococcal protein G, glutathione-S-transferase and maltose binding protein fusion proteins in *Mycobacterium smegmatis*. *Protein Expr. Purif.*, 50:128–136, 2006.
- [145] A.L. Haas, J.V. Warms, A. Hershko, and I.A. Rose. Ubiquitin-activating enzyme. Mechanism and role in protein-ubiquitin conjugation. *J. Biol. Chem.*, 257:2543–2548, 1982.
- [146] L.P. Hager. Succinyl CoA synthetase. In P.D. Boyer, H. Lardy, and K. Myrback, editors, *The Enzymes*, volume 6, pages 387–399. Academic Press, New York, 2nd edition, 1962.
- [147] A.K. Harris, N.R. Williamson, H. Slater, A. Cox, S. Abbasi, I. Foulds, H.T. Simonsen, F.J. Leeper, and G.P. Salmond. The *Serratia* gene cluster encoding biosynthesis of the red antibiotic, prodigiosin, shows species- and strain-dependent genome context variation. *Microbiology*, 150:3547–3560, 2004.
- [148] S.C. Hartman and J.M. Buchanan. Biosynthesis of the purines. XXII. 2-Amino-*N*-ribosylacetamide-5'-phosphate kinosynthase. *J. Biol. Chem.*, 233:456–461, 1958.
- [149] M.D. Hatch and P.K. Stumpf. Fat metabolism in higher plants. XVI. Acetyl coenzyme A carboxylase and acyl coenzyme A-malonyl coenzyme A transcarboxylase from wheat germ. *J. Biol. Chem.*, 236:2879–2885, 1961.
- [150] S.I. Hauenstein and J.J. Perona. Redundant synthesis of cysteinyl-tRNA^{Cys} in *Methanosarcina mazei*. *J. Biol. Chem.*, 283:22007–22017, 2008.
- [151] A.S. Hawkins, Y. Han, R.K. Bennett, M.W. Adams, and R.M. Kelly. Role of 4-hydroxybutyrate-CoA synthetase in the CO₂ fixation cycle in thermoacidophilic archaea. *J. Biol. Chem.*, 288:4012–4022, 2013.
- [152] M.P. Heaton and F.C. Neuhaus. Role of D-alanyl carrier protein in the biosynthesis of D-alanyl-lipoteichoic acid. *J. Bacteriol.*, 176:681–690, 1994.
- [153] L. Heide, S. Arendt, and E. Leistner. Enzymatic-synthesis, characterization, and metabolism of the coenzyme-A ester of *o*-succinylbenzoic acid, an intermediate in menaquinone (vitamin K₂) biosynthesis. *J. Biol. Chem.*, 257:7396–7400, 1982.
- [154] P. Hele. The acetate activating enzyme of beef heart. *J. Biol. Chem.*, 206:671–676, 1954.
- [155] N.L. Hepowit, I.M. de Vera, S. Cao, X. Fu, Y. Wu, S. Uthandi, N.E. Chavarria, M. Englert, D. Su, D. Söll, D.J. Kojetin, and J.A. Maupin-Furlow. Mechanistic insight into protein modification and sulfur mobilization activities of noncanonical E1 and associated ubiquitin-like proteins of Archaea. *FEBS J.*, 283:3567–3586, 2016.
- [156] M. Herve, A. Boniface, S. Gobec, D. Blanot, and D. Mengin-Lecreulx. Biochemical characterization and physiological properties of *Escherichia coli* UDP-*N*-acetylmuramate:L-alanyl- γ -D-glutamyl-*meso*-diaminopimelate ligase. *J. Bacteriol.*, 189:3987–3995, 2007.
- [157] H. Hilbi, I. Dehning, B. Schink, and P. Dimroth. Malonate decarboxylase of *Malonomonas rubra*, a novel type of biotin-containing acetyl enzyme. *Eur. J. Biochem.*, 207:117–123, 1992.
- [158] C.K. Ho, L.K. Wang, C.D. Lima, and S. Shuman. Structure and mechanism of RNA ligase. *Structure*, 12:327–339, 2004.
- [159] H.M. Holden, J.B. Thoden, and F.M. Raushel. Carbamoyl phosphate synthetase: a tunnel runs through it. *Curr. Opin. Struct. Biol.*, 8:679–685, 1998.
- [160] M.A. Hollenhorst, S.B. Bumpus, M.L. Matthews, J.M. Bollinger, Kelleher Jr., Walsh N.L., and C.T. The nonribosomal peptide synthetase enzyme DdaD tethers N(β)-fumaramoyl-L-2,3-diaminopropionate for Fe(II)/ α -ketoglutarate-dependent epoxidation by DdaC during daptiamide antibiotic biosynthesis. *J. Am. Chem. Soc.*, 132:15773–15781, 2010.
- [161] M.A. Hollenhorst, J. Clardy, and C.T. Walsh. The ATP-dependent amide ligases DdaG and DdaF assemble the fumaramoyl-dipeptide scaffold of the daptiamide antibiotics. *Biochemistry*, 48:10467–10472, 2009.
- [162] R.W. Holley, E.F. Brunngraber, F. Saad, and H.H. Williams. Partial purification of the threonine- and tyrosine-activating enzymes from rat liver, and the effect of potassium ions on the activity of the tyrosine enzyme. *J. Biol. Chem.*, 236:197–199, 1961.

- [163] R.W. Holley and J. Goldstein. An alanine-dependent, ribonuclease-inhibited conversion of adenosine 5'-phosphate to adenosine triphosphate. *J. Biol. Chem.*, 234:1765–1768, 1959.
- [164] T. Höpner and J. Knappe. Einbau von Biotin in β -methylcrotonyl-CoA-carboxylase urch Holocarboxylase-synthetase. *Biochem. Z.*, 342:190–206, 1965.
- [165] A. Horie, T. Tomita, A. Saiki, H. Kono, H. Taka, R. Mineki, T. Fujimura, C. Nishiyama, T. Kuzuyama, and M. Nishiyama. Discovery of proteinaceous *N*-modification in lysine biosynthesis of *Thermus thermophilus*. *Nat. Chem. Biol.*, 5:673–679, 2009.
- [166] M. Horinouchi, T. Hayashi, H. Koshino, and T. Kudo. ORF18-disrupted mutant of *Comamonas testosteroni* TA441 accumulates significant amounts of 9,17-dioxo-1,2,3,4,10,19-hexanorandrostano-5-oic acid and its derivatives after incubation with steroids. *J. Steroid Biochem. Mol. Biol.*, 101:78–84, 2006.
- [167] K.Y. Horiuchi, M.R. Harpel, L. Shen, Y. Luo, K.C. Rogers, and R.A. Copeland. Mechanistic studies of reaction coupling in Glu-tRNA^{Gln} amidotransferase. *Biochemistry*, 40:6450–6457, 2001.
- [168] K. Hosaka, M. Mishima, T. Tanaka, T. Kamiryo, and S. Numa. Acyl-coenzyme-A synthetase I from *Candida lipolytica*. Purification, properties and immunochemical studies. *Eur. J. Biochem.*, 93:197–203, 1979.
- [169] T.R. Howes and A.E. Tomkinson. DNA ligase I, the replicative DNA ligase. *Subcell. Biochem.*, 62:327–341, 2012.
- [170] X. Huang, H.M. Holden, and F.M. Raushel. Channeling of substrates and intermediates in enzyme-catalyzed reactions. *Annu. Rev. Biochem.*, 70:149–180, 2001.
- [171] G.N. Hutber and D.W. Ribbons. Involvement of coenzyme-A esters in the metabolism of benzoate and cyclohexanecarboxylate by *Rhodospseudomonas palustris*. *J. Gen. Microbiol.*, 129:2413–2420, 1983.
- [172] O. Hutzinger and T. Kosuge. Microbial synthesis and degradation of indole-3-acetic acid. 3. The isolation and characterization of indole-3-acetyl- ϵ -L-lysine. *Biochemistry*, 7:601–605, 1968.
- [173] J.T. Huzil, R. Pannu, C. Ptak, G. Garen, and M.J. Ellison. Direct catalysis of lysine 48-linked polyubiquitin chains by the ubiquitin-activating enzyme. *J. Biol. Chem.*, 282:37454–37460, 2007.
- [174] M. Ibba and D. Söll. Aminoacyl-tRNA synthesis. *Annu. Rev. Biochem.*, 69:617–650, 2000.
- [175] Y. Ikeuchi, S. Kimura, T. Numata, D. Nakamura, T. Yokogawa, T. Ogata, T. Wada, T. Suzuki, and T. Suzuki. Agmatine-conjugated cytidine in a tRNA anticodon is essential for AUA decoding in archaea. *Nat. Chem. Biol.*, 6:277–282, 2010.
- [176] Y. Ikeuchi, A. Soma, T. Ote, J. Kato, Y. Sekine, and T. Suzuki. molecular mechanism of lysidine synthesis that determines tRNA identity and codon recognition. *Mol. Cell*, 19:235–246, 2005.
- [177] J. Imsande. Pathway of diphosphopyridine nucleotide biosynthesis in *Escherichia coli*. *J. Biol. Chem.*, 236:1494–1497, 1961.
- [178] J. Imsande and P. Handler. Biosynthesis of diphosphopyridine nucleotide. III. Nicotinic acid mononucleotide pyrophosphorylase. *J. Biol. Chem.*, 236:525–530, 1961.
- [179] E. Ito and J.L. Strominger. Enzymatic synthesis of the peptide in bacterial uridine nucleotides. I. Enzymatic addition of L-alanine, D-glutamic acid, and L-lysine. *J. Biol. Chem.*, 237:2689–2695, 1962.
- [180] E. Ito and J.L. Strominger. Enzymatic synthesis of the peptide in bacterial uridine nucleotides. II. Enzymatic synthesis and addition of D-alanyl-D-alanine. *J. Biol. Chem.*, 237:2696–2703, 1962.
- [181] Y. Izumi, H. Morita, K. Sato, Y. Tani, and K. Ogata. Synthesis of biotin-vitimers from pimelic acid and coenzyme A by cell-free extracts of various bacteria. *Biochim. Biophys. Acta*, 264:210–213, 1972.
- [182] Y. Izumi, H. Morita, Y. Tani, and K. Ogata. The pimelyl-CoA synthetase responsible for the first step in biotin biosynthesis by microorganisms. *Agric. Biol. Chem.*, 38:2257–2262, 1974.
- [183] L. Jaenicke and E. Brode. Untersuchungen über Einkohlenstoffkörper. I. Die Tetrahydrofolatformylase aus Taubenleber. Rinigung und Mechanismus. *Biochem. Z.*, 334:108–132, 1961.

- [184] K. Janiyani, T. Bordelon, G.L., Cronan Waldrop, , and Jr. Function of *Escherichia coli* biotin carboxylase requires catalytic activity of both subunits of the homodimer. *J. Biol. Chem.*, 276:29864–29870, 2001.
- [185] B. Jobst, K. Schuhle, U. Linne, and J. Heider. ATP-dependent carboxylation of acetophenone by a novel type of carboxylase. *J. Bacteriol.*, 192:1387–1394, 2010.
- [186] M.E. Jones and L. Spector. The pathway of carbonate in the biosynthesis of carbamyl phosphate. *J. Biol. Chem.*, 235:2897–2901, 1960.
- [187] D. Kaczmarzyk and M. Fulda. Fatty acid activation in cyanobacteria mediated by acyl-acyl carrier protein synthetase enables fatty acid recycling. *Plant Physiol.*, 152:1598–1610, 2010.
- [188] S.M. Kalman, P.H. Duffield, and T. Brzozowski. Purification and properties of a bacterial carbamyl phosphate synthetase. *J. Biol. Chem.*, 241:1871–1877, 1966.
- [189] G.D. Kalyankar and A. Meister. Enzymatic synthesis of carnosine and related β -alanyl and γ -aminobutyryl peptides. *J. Biol. Chem.*, 234:3210–3218, 1959.
- [190] T. Kanamori, N. Kanou, H. Atomi, and T. Imanaka. Enzymatic characterization of a prokaryotic urea carboxylase. *J. Bacteriol.*, 186:2532–2539, 2004.
- [191] P. Kancharla, S.A. Bonnett, and K.A. Reynolds. *Stenotrophomonas maltophilia* OleC-catalyzed ATP-dependent formation of long-chain Z-olefins from 2-alkyl-3-hydroxyalkanoic acids. *Chembiochem*, 17:1426–1429, 2016.
- [192] J.H. Kang, L. Wang, A. Giri, and I.T. Baldwin. Silencing threonine deaminase and JAR4 in *Nicotiana attenuata* impairs jasmonic acid-isoleucine-mediated defenses against *Manduca sexta*. *Plant Cell*, 18:3303–3320, 2006.
- [193] J.R. Katze and W. Konigsberg. Purification and properties of seryl transfer ribonucleic acid synthetase from *Escherichia coli*. *J. Biol. Chem.*, 245:923–930, 1970.
- [194] S. Kaufman. Studies on the mechanism of the reaction catalyzed by the phosphorylating enzyme. *J. Biol. Chem.*, 216:153–164, 1955.
- [195] S. Kaufman and S.G.A. Alivasatos. Purification and properties of the phosphorylating enzyme from spinach. *J. Biol. Chem.*, 216:141–152, 1955.
- [196] S. Kaufman, C. Gilvarg, O. Cori, and S. Ochoa. Enzymatic oxidation of α -ketoglutarate and coupled phosphorylation. *J. Biol. Chem.*, 203:869–888, 1953.
- [197] Y. Kaziro, S. Ochoa, R.C. Warner, and J.-Y. Chen. Metabolism of propionic acid in animal tissues. VIII. Crystalline propionyl carboxylase. *J. Biol. Chem.*, 236:1917–1923, 1961.
- [198] J.H. Kim, K.K. Lee, Y. Sun, G.J. Seo, S.S. Cho, S.H. Kwon, and S.T. Kwon. Broad nucleotide cofactor specificity of DNA ligase from the hyperthermophilic crenarchaeon *Hyperthermus butylicus* and its evolutionary significance. *Extremophiles*, 17:515–522, 2013.
- [199] K.W. Kim, H. Yamane, J. Zondlo, J. Busby, and M. Wang. Expression, purification, and characterization of human acetyl-CoA carboxylase 2. *Protein Expr. Purif.*, 53:16–23, 2007.
- [200] S.I. Kim and D. Söll. Major identity element of glutamine tRNAs from *Bacillus subtilis* and *Escherichia coli* in the reaction with *B. subtilis* glutamyl-tRNA synthetase. *Mol. Cells*, 8:459–465, 1998.
- [201] Y.J. Kim, H.S. Lee, S.S. Bae, J.H. Jeon, S.H. Yang, J.K. Lim, S.G. Kang, S.T. Kwon, and J.H. Lee. Cloning, expression, and characterization of a DNA ligase from a hyperthermophilic archaeon *Thermococcus* sp. *Biotechnol. Lett.*, 28:401–407, 2006.
- [202] K. Kino, Y. Kotanaka, T. Arai, and M. Yagasaki. A novel L-amino acid ligase from *Bacillus subtilis* NBRC3134, a microorganism producing peptide-antibiotic rhizocitin. *Biosci. Biotechnol. Biochem.*, 73:901–907, 2009.
- [203] J. Knappe, H.-G. Schlegel, and F. Lynen. Zur biochemischen Funktion des Biotins. I. Die Beteilligung der β -Methylcrotonyl-Carboxylase an der Bildung von β -Hydroxy- β -methyl-glutaryl-CoA from β -Hydroxy-isovaleryl-CoA. *Biochem. Z.*, 335:101–122, 1961.

- [204] K. Koenig and J.R. Andreessen. Molybdenum involvement in aerobic degradation of 2-furoic acid by *Pseudomonas putida* FU1. *Appl. Environ. Microbiol.*, 55:1829–1834, 1989.
- [205] R. Kolkman and E. Leistner. 4-(2'-Carboxyphenyl)-4-oxobutyryl coenzyme A ester, an intermediate in vitamin K₂ (menaquinone) biosynthesis. *Z. Naturforsch. C: Sci.*, 42:1207–1214, 1987.
- [206] A. Kosaka, H.O. Spivey, and R.K. Gholson. Nicotinate phosphoribosyltransferase of yeast. Purification and properties. *J. Biol. Chem.*, 246:3277–3283, 1971.
- [207] K. Krell and M.A. Eisenberg. The purification and properties of dethiobiotin synthetase. *J. Biol. Chem.*, 245:6558–6566, 1970.
- [208] Y. Kumada, D.R. Benson, D. Hillemann, T.J. Hosted, D.A. Rochefort, C.J. Thompson, W. Wohlleben, and Y. Tateno. Evolution of the glutamine synthetase gene, one of the oldest existing and functioning genes. *Proc. Natl. Acad. Sci. USA*, 90:3009–3013, 1993.
- [209] T. Kumagai, Y. Koyama, K. Oda, M. Noda, Y. Matoba, and M. Sugiyama. Molecular cloning and heterologous expression of a biosynthetic gene cluster for the antitubercular agent D-cycloserine produced by *Streptomyces lavendulae*. *Antimicrob. Agents Chemother.*, 54:1132–1139, 2010.
- [210] H.-F. Kung and C. Wagner. γ -Glutamylmethylamide. A new intermediate in the metabolism of methylamine. *J. Biol. Chem.*, 244:4136–4140, 1969.
- [211] T. Kupke. Molecular characterization of the 4'-phosphopantothenoylecysteine synthetase domain of bacterial Dfp flavo-proteins. *J. Biol. Chem.*, 277:36137–36145, 2002.
- [212] T. Kupke, P. Hernandez-Acosta, and F.A. Cuiñez-Macia. 4'-phosphopantetheine and coenzyme A biosynthesis in plants. *J. Biol. Chem.*, 278:38229–38237, 2003.
- [213] S. Kurihara, S. Oda, K. Kato, H.G. Kim, T. Koyanagi, H. Kumagai, and H. Suzuki. A novel putrescine utilization pathway involves γ -glutamylated intermediates of *Escherichia coli* K-12. *J. Biol. Chem.*, 280:4602–4608, 2005.
- [214] D. Laempe, M. Jahn, K. Breese, H. Schägger, and G. Fuchs. Anaerobic metabolism of 3-hydroxybenzoate by the denitrifying bacterium *Thauera aromatica*. *J. Bacteriol.*, 183:968–979, 2001.
- [215] U. Lagerkvist. Biosynthesis of guanosine 5'-phosphate. II. Amination of xanthosine 5'-phosphate by purified enzyme from pigeon liver. *J. Biol. Chem.*, 233:143–149, 1958.
- [216] U. Lagerkvist, L. Rymo, O. Lindqvist, and E. Andersson. Some properties of crystals of lysine transfer ribonucleic acid ligase from yeast. *J. Biol. Chem.*, 247:3897–3899, 1972.
- [217] A. Lajtha, P. Mela, and H. Waelsch. Manganese-dependent glutamotransferase. *J. Biol. Chem.*, 205:553–564, 1953.
- [218] A.D. Landman and K. Dakshinamurti. Acetyl-Coenzyme A carboxylase. Role of the prosthetic group in enzyme polymerization. *Biochem. J.*, 145:545–548, 1975.
- [219] M.D. Lane, D.R. Halenz, D.P. Kosow, and C.S. Hegre. Further studies on mitochondrial propionyl carboxylase. *J. Biol. Chem.*, 235:3082–3086, 1960.
- [220] M.D. Lane, D.L. Young, and F. Lynen. The enzymatic synthesis of holotranscarboxylase from apotranscarboxylase and (+)-biotin. I. Purification of the apoenzyme and synthetase; characteristics of the reaction. *J. Biol. Chem.*, 239:2858–2864, 1964.
- [221] T.M. Larsen, S.K. Boehlein, S.M. Schuster, N.G. Richards, J.B. Thoden, H.M. Holden, and I. Rayment. Three-dimensional structure of *Escherichia coli* asparagine synthetase B: a short journey from substrate to product. *Biochemistry*, 38:16146–16157, 1999.
- [222] M.Y. Law and B. Halliwell. Purification and properties of glutathione synthetase from (*Spinacia oleracea*) leaves. *Plant Sci.*, 43:185–191, 1986.
- [223] C.P. Lee, M.R. Dyson, N. Mandal, U. Varshney, B. Bahramian, and U.L. RajBhandary. Striking effects of coupling mutations in the acceptor stem on recognition of tRNAs by *Escherichia coli* Met-tRNA synthetase and Met-tRNA transformylase. *Proc. Natl. Acad. Sci. USA*, 89:9262–9266, 1992.

- [224] W. Lerbs and M. Luckner. Cyclopeptide synthetase activity in surface cultures of *Penicillium cyclopium*. *J. Basic Microbiol.*, 25:387–391, 1985.
- [225] B. Levenberg and J.M. Buchanan. Biosynthesis of the purines. XIII. Structure, enzymatic synthesis, and metabolism of (α -*N*-formyl)-glycinamide ribotide. *J. Biol. Chem.*, 224:1018–1027, 1957.
- [226] B. Levenberg and J.M. Buchanan. Properties of the purines. XII. Structure, enzymatic synthesis, and metabolism of 5-aminoimidazole ribotide. *J. Biol. Chem.*, 224:1005–1018, 1957.
- [227] D.A. Lewis and J.J. Villafranca. Investigation of the mechanism of CTP synthetase using rapid quench and isotope partitioning methods. *Biochemistry*, 28:8454–8459, 1989.
- [228] H. Li, M. Graupner, H. Xu, and R.H. White. CofE catalyzes the addition of two glutamates to F₄₂₀-O in F₄₂₀ coenzyme biosynthesis in *Methanococcus jannaschii*. *Biochemistry*, 42:9771–9778, 2003.
- [229] H. Li, H. Xu, D.E. Graham, and R.H. White. Glutathione synthetase homologs encode α -L-glutamate ligases for methanogenic coenzyme F₄₂₀ and tetrahydrosarcinapterin biosyntheses. *Proc. Natl. Acad. Sci. USA*, 100:9785–9790, 2003.
- [230] Y. Li, N.M. Llewellyn, R. Giri, F. Huang, and J.B. Spencer. Biosynthesis of the unique amino acid side chain of butirosin: possible protective-group chemistry in an acyl carrier protein-mediated pathway. *Chem. Biol.*, 12:665–675, 2005.
- [231] I. Lieberman. Enzymatic amination of uridine triphosphate to cytidine triphosphate. *J. Biol. Chem.*, 222:765–775, 1956.
- [232] I. Lieberman. Enzymatic synthesis of adenosine-5'-phosphate from inosine-5'-phosphate. *J. Biol. Chem.*, 223:327–339, 1956.
- [233] U. Lill, A. Schreil, and H. Eggerer. Isolation of enzymically active fragments formed by limited proteolysis of ATP citrate lyase. *Eur. J. Biochem.*, 125:645–650, 1982.
- [234] J.W. Lin, Y.F. Chao, and S.F. Weng. Nucleotide sequence and functional analysis of the *luxE* gene encoding acyl-protein synthetase of the *lux* operon from *Photobacterium leiognathi*. *Biochem. Biophys. Res. Commun.*, 228:764–773, 1996.
- [235] T. Lindl, F. Kreuzaler, and F. Hahlbrock. Synthesis of *p*-coumaroyl coenzyme A with a partially purified *p*-coumarate:CoA ligase from cell suspension cultures of soybean (*Glycine max*). *Biochim. Biophys. Acta*, 302:457–464, 1973.
- [236] J.W. Little, S.B. Zimmerman, C.K. Oshinsky, and M. Gellert. Enzymatic joining of DNA strands, II. An enzyme-adenylate intermediate in the *dpn*-dependent DNA ligase reaction. *Proc. Natl. Acad. Sci. USA*, 58:2004–2011, 1967.
- [237] O. Llorca, M. Betti, J.M. Gonzalez, A. Valencia, A.J. Marquez, and J.M. Valpuesta. The three-dimensional structure of an eukaryotic glutamine synthetase: functional implications of its oligomeric structure. *J. Struct. Biol.*, 156:469–479, 2006.
- [238] J. Lodder-Gadaczek, I. Becker, V. Gieselmann, L. Wang-Eckhardt, and M. Eckhardt. *N*-acetylaspartylglutamate synthetase II synthesizes *N*-acetylaspartylglutamylglutamate. *J. Biol. Chem.*, 286:16693–16706, 2011.
- [239] F. Löffler, R. Müller, , and F. Purification and properties of 4-halobenzoate-coenzyme A ligase from *Pseudomonas* sp. CBS3. *Biol. Chem. Hoppe-Seyler*, 373:1001–1007, 1992.
- [240] C.W. Long, A. Levitzki, L.L. Koshland Houston, , and Jr. Subunit structures and interactions of CTP synthetase. *Fed. Proc.*, 28:342–342, 1969.
- [241] L.N. Lukens and J.M. Buchanan. Biosynthesis of purines. XXIV. The enzymatic synthesis of 5-amino-1-ribosyl-4-imidazolecarboxylic acid 5'-phosphate from 5-amino-1-ribosylimidazole 5'-phosphate and carbon dioxide. *J. Biol. Chem.*, 234:1799–1805, 1959.
- [242] F. Lynen, J. Knappe, E. Lorch, G. Jütting, E. Ringelmann, and J.-P. Lachance. Zur biochemischen Funktion des Biotins. II. Reinigung und Wirkungsweise der β -Methyl-crotonyl-Carboxylase. *Biochem. Z.*, 335:123–166, 1961.
- [243] W.K. Maas. Pantothenate studies. III. Description of the extracted pantothenate-synthesizing enzyme of *Escherichia coli*. *J. Biol. Chem.*, 198:23–32, 1952.
- [244] W.K. Maas. Mechanism of the enzymatic synthesis of pantothenate from β -alanine and pantoate. *Fed. Proc.*, 15:305–306, 1956.

- [245] C.M. MacKinnon, P.E. Carter, S.J. Smyth, B. Dunbar, and J.E. Fothergill. Molecular cloning of cDNA for human complement component C1s. The complete amino acid sequence. *Eur. J. Biochem.*, 169:547–553, 1987.
- [246] P.K. Macnicol. Homogluthathione and glutathione synthetases of legume seedlings - partial-purification and substrate-specificity. *Plant Sci.*, 53:229–235, 1987.
- [247] J. Maeda, D.I. Kato, M. Okuda, M. Takeo, S. Negoro, K. Arima, Y. Ito, and K. Niwa. Biosynthesis-inspired deracemizative production of D-luciferin by combining luciferase and thioesterase. *Biochim. Biophys. Acta*, 1861:2112–2118, 2017.
- [248] H.R. Mahler, S.J. Wakil, and R.M. Bock. Studies on fatty acid oxidation. I. Enzymatic activation of fatty acids. *J. Biol. Chem.*, 204:453–468, 1953.
- [249] M.H. Makman and G.L. Cantoni. Isolation of seryl and phenylalanyl ribonucleic acid synthetases from baker's yeast. *Biochemistry*, 4:1434–1442, 1965.
- [250] D.H. Mallonee, J.L. Adams, and P.B. Hylemon. The bile acid-inducible *baiB* gene from *Eubacterium* sp. strain VPI 12708 encodes a bile acid-coenzyme A ligase. *J. Bacteriol.*, 174:2065–2071, 1992.
- [251] S. Mandeles and K. Bloch. Enzymatic synthesis of γ -glutamylcysteine. *J. Biol. Chem.*, 214:639–646, 1955.
- [252] N. Manoj, E. Strauss, T.P. Begley, and S.E. Ealick. Structure of human phosphopantothienoylcysteine synthetase at 2.3 Å Resolution. *Structure*, 11:927–936, 2003.
- [253] M. Marshall, R.L. Metzenberg, and P.P. Cohen. Purification of carbamyl phosphate synthetase from frog liver. *J. Biol. Chem.*, 233:102–105, 1958.
- [254] M. Marshall, R.L. Metzenberg, and P.P. Cohen. Physical and kinetic properties of carbamyl phosphate synthetase from frog liver. *J. Biol. Chem.*, 236:2229–2237, 1961.
- [255] H. Martinez-Blanco, A. Reglero, L.B. Rodriguez-Asparicio, and J.M. Luengo. Purification and biochemical characterization of phenylacetyl-CoA ligase from *Pseudomonas putida*. A specific enzyme for the catabolism of phenylacetic acid. *J. Biol. Chem.*, 265:7084–7090, 1990.
- [256] R.M. Martinez-Espinosa, J. Esclapez, V. Bautista, and M.J. Bonete. An octameric prokaryotic glutamine synthetase from the haloarchaeon *Haloferax mediterranei*. *FEMS Microbiol. Lett.*, 264:110–116, 2006.
- [257] E.J. Massaro and W.J. Lennarz. The partial purification and characterization of a bacterial fatty acyl coenzyme A synthetase. *Biochemistry*, 4:85–90, 1965.
- [258] M. Matsushashi, S. Matsushashi, and F. Lynen. Zur Biosynthese der Fettsäuren. V. Die Acetyl-CoA Carboxylase aus Rattenleber und ihre Aktivierung durch Citronensäure. *Biochem. Z.*, 340:263–289, 1964.
- [259] M. Matsushashi, S. Matsushashi, S. Numa, and F. Lynen. Zur Biosynthese der Fettsäuren. IV Acetyl CoA Carboxylase aus Hefe. *Biochem. Z.*, 340:243–262, 1964.
- [260] W.P. Maughan and S. Shuman. Distinct contributions of enzymic functional groups to the 2',3'-cyclic phosphodiesterase, 3'-phosphate guanylation, and 3'-ppG/5'-OH ligation steps of the *Escherichia coli* RtcB nucleic acid splicing pathway. *J. Bacteriol.*, 198:1294–1304, 2016.
- [261] J.A. Maupin-Furlow. Ubiquitin-like proteins and their roles in archaea. *Trends Microbiol.*, 21:31–38, 2013.
- [262] P.J. Maurer and M. Miller. Microbial iron chelators: total synthesis of aerobactin and its constituent amino acid, N⁶-acetyl-N⁶-hydroxylysine. *J. Am. Chem. Soc.*, 104:3096–3101, 1982.
- [263] R. Mazumder, D.R. Sanadi, and W.V. Rodwell. Purification and properties of hog kidney succinic thiokinase. *J. Biol. Chem.*, 235:2546–2550, 1960.
- [264] R.M. McCarty, A. Somogyi, G. Lin, N.E. Jacobsen, and V. Bandarian. The deazapurine biosynthetic pathway revealed: *in vitro* enzymatic synthesis of preQ₀ from guanosine 5'-triphosphate in four steps. *Biochemistry*, 48:3847–3852, 2009.
- [265] W.R. McClure, H.A. Lardy, and H.P. Kneifel. Rat liver pyruvate carboxylase. I. Preparation, properties, and cation specificity. *J. Biol. Chem.*, 246:3569–3578, 1971.

- [266] D.J. McCorquodale. The separation and partial purification of aminoacyl-RNA synthetases from *Escherichia coli*. *Biochim. Biophys. Acta*, 91:541–548, 1964.
- [267] J.J. McGuire and J.R. Bertino. Enzymatic synthesis and function of folylpolyglutamates. *Mol. Cell. Biochem.*, 38:19–48, 1981.
- [268] R. Meganathan and R. Bentley. Menaquinone (vitamin K₂) biosynthesis: conversion of *o*-succinylbenzoic acid to 1,4-dihydroxy-2-naphthoic acid by *Mycobacterium phlei* enzymes. *J. Bacteriol.*, 140:92–98, 1979.
- [269] A.H. Mehler and S.K. Mitra. The activation of arginyl transfer ribonucleic acid synthetase by transfer ribonucleic acid. *J. Biol. Chem.*, 242:5495–5499, 1967.
- [270] A. Meister. Glutamine synthesis. In P.D. Boyer, H. Lardy, and K. Myrbäck, editors, *The Enzymes*, volume 6, pages 443–468. Academic Press, New York, 2nd edition, 1962.
- [271] I. Melnick and J.M. Buchanan. Biosynthesis of the purines. I. Conversion of (α -*N*-formyl)glycinamide ribotide to (α -*N*-formyl)glycinamide ribotide; purification and requirements of the enzyme system. *J. Biol. Chem.*, 225:157–162, 1957.
- [272] S. Menendez-Bravo, S. Comba, M. Sabatini, A. Arabolaza, and H. Gramajo. Expanding the chemical diversity of natural esters by engineering a polyketide-derived pathway into *Escherichia coli*. *Metab. Eng.*, 24:97–106, 2014.
- [273] D. Mengin-Lecreulx, J. van Heijenoort, and J.T. Park. Identification of the *mpl* gene encoding UDP-*N*-acetylmuramate: L-alanyl- γ -D-glutamyl-*meso*-diaminopimelate ligase in *Escherichia coli* and its role in recycling of cell wall peptidoglycan. *J. Bacteriol.*, 178:5347–5352, 1996.
- [274] G.K.K. Menon, D.L. Friedman, and J.R. Stern. Enzymic synthesis of glutaryl-coenzyme A. *Biochim. Biophys. Acta*, 44:375–377, 1960.
- [275] S.M. Merkel, A.E. Eberhard, J. Gibson, and C.S. Harwood. Involvement of coenzyme A thioesters in anaerobic metabolism of 4-hydroxybenzoate by *Rhodospseudomonas palustris*. *J. Bacteriol.*, 171:1–7, 1989.
- [276] E. Meyer, N.J. Leonard, B. Bhat, J. Stubbe, and J.M. Smith. Purification and characterization of the *purE*, *purK*, and *purC* gene products: identification of a previously unrecognized energy requirement in the purine biosynthetic pathway. *Biochemistry*, 31:5022–5032, 1992.
- [277] H. Meyer, B. Nevaldine, and F. Meyer. Acyl-coenzyme A carboxylase of the free-living nematode *Turbatrix aceti*. 1. Its isolation and molecular characteristics. *Biochemistry*, 17:1822–1827, 1978.
- [278] D. Meziane-Cherif, M.A. Badet-Denisot, S. Evers, P. Courvalin, and B. Badet. Purification and characterization of the VanB ligase associated with type B vancomycin resistance in *Enterococcus faecalis* V583. *FEBS Lett.*, 354:140–142, 1994.
- [279] M.T. Miller, B. Gerratana, A. Stapon, C.A. Townsend, and A.C. Rosenzweig. Crystal structure of carbapenam synthetase (CarA). *J. Biol. Chem.*, 278:40996–41002, 2003.
- [280] A. Millerd and J. Bonner. Acetate activation and acetoacetate formation in plant systems. *Arch. Biochem. Biophys.*, 49:343–355, 1954.
- [281] B. Min, J.T. Pelaschier, D.E. Graham, D. Tumbula-Hansen, and D. Söll. Transfer RNA-dependent amino acid biosynthesis: an essential route to asparagine formation. *Proc. Natl. Acad. Sci. USA*, 99:2678–2683, 2002.
- [282] H.V. Miranda, H. Antelmann, N. Hepowit, N.E. Chavarria, D.J. Krause, J.R. Pritz, K. Basell, D. Becher, M.A. Humbard, L. Brocchieri, and J.A. Maupin-Furlow. Archaeal ubiquitin-like SAMP3 is isopeptide-linked to proteins via a UbaA-dependent mechanism. *Mol. Cell. Proteomics*, 13:220–239, 2014.
- [283] H.V. Miranda, N. Nembhard, D. Su, N. Hepowit, D.J. Krause, J.R. Pritz, C. Phillips, D. Soll, and J.A. Maupin-Furlow. E1- and ubiquitin-like proteins provide a direct link between protein conjugation and sulfur transfer in archaea. *Proc. Natl. Acad. Sci. USA*, 108:4417–4422, 2011.
- [284] S.K. Mitra and A.H. Mehler. The arginyl transfer ribonucleic acid synthetase of *Escherichia coli*. *J. Biol. Chem.*, 242:5491–5494, 1967.

- [285] Y. Mizuno and E. Ito. Purification and properties of uridine diphosphate *N*-acetylmuramyl-L-alanyl-D-glutamate:*meso*-2,6-diaminopimelate ligase. *J. Biol. Chem.*, 243:2665–2672, 1968.
- [286] P. Modrich and I.R. Lehman. Deoxyribonucleic acid ligase. A steady state kinetic analysis of the reaction catalyzed by the enzyme from *Escherichia coli*. *J. Biol. Chem.*, 248:7502–7511, 1973.
- [287] P. Modrich, Y. Anraku, and I.R. Lehman. Deoxyribonucleic acid ligase. Isolation and physical characterization of the homogeneous enzyme from *Escherichia coli*. *J. Biol. Chem.*, 248:7495–7501, 1973.
- [288] J.M. Moehring and T.J. Moehring. The post-translational trimethylation of diphthamide studied in vitro. *J. Biol. Chem.*, 263:3840–3844, 1988.
- [289] T.J. Moehring and J.M. Moehring. Mutant cultured cells used to study the synthesis of diphthamide. *UCLA Symp. Mol. Cell. Biol. New Ser.*, 45:53–63, 1987.
- [290] R.M. Morgan-Kiss and J.E. Cronan. The *Escherichia coli fadK* (*ydiD*) gene encodes an anaerobically regulated short chain acyl-CoA synthetase. *J. Biol. Chem.*, 279:37324–37333, 2004.
- [291] T.W. Morris, K.E., Cronan Reed, , and Jr. Identification of the gene encoding lipoate-protein ligase A of *Escherichia coli*. Molecular cloning and characterization of the *lplA* gene and gene product. *J. Biol. Chem.*, 269:16091–16100, 1994.
- [292] J. Moss and M.D. Lane. The biotin-dependent enzymes. *Adv. Enzymol. Relat. Areas Mol. Biol.*, 35:321–442, 1971.
- [293] S. Mue, S. Tuboi, and G. Kikuchi. On malyl-coenzyme A synthetase. *J. Biochem. (Tokyo)*, 56:545–551, 1964.
- [294] E.J. Mueller, E. Meyer, J. Rudolph, V.J. Davisson, and J. Stubbe. *N*⁵-Carboxyaminoimidazole ribonucleotide: evidence for a new intermediate and two new enzymatic activities in the de novo purine biosynthetic pathway of *Escherichia coli*. *Biochemistry*, 33:2269–2278, 1994.
- [295] F.N. Muralidharan and V.B. Muralidharan. Phytanoyl-CoA ligase activity in rat liver. *Biochem. Int.*, 13:123–130, 1986.
- [296] K. Nagamatsu, S. Soeda, M. Mori, and Y. Kishimoto. Lignoceroyl-coenzyme A synthetase from developing rat brain: partial purification, characterization and comparison with palmitoyl-coenzyme A synthetase activity and liver enzyme. *Biochim. Biophys. Acta*, 836:80–88, 1985.
- [297] P.M. Nair. Asparagine synthetase from γ -irradiated potatoes. *Arch. Biochem. Biophys.*, 133:208–215, 1969.
- [298] M. Nakamura, S. Maki, Y. Amano, Y. Ohkita, K. Niwa, T. Hirano, Y. Ohmiya, and H. Niwa. Firefly luciferase exhibits bimodal action depending on the luciferin chirality. *Biochem. Biophys. Res. Commun.*, 331:471–475, 2005.
- [299] K. Nakanishi, L. Bonnefond, S. Kimura, T. Suzuki, R. Ishitani, and O. Nureki. Structural basis for translational fidelity ensured by transfer RNA lysidine synthetase. *Nature*, 461:1144–1148, 2009.
- [300] K. Nakanishi, S. Fukai, Y. Ikeuchi, A. Soma, Y. Sekine, T. Suzuki, and O. Nureki. Structural basis for lysidine formation by ATP pyrophosphatase accompanied by a lysine-specific loop and a tRNA-recognition domain. *Proc. Natl. Acad. Sci. USA*, 102:7487–7492, 2005.
- [301] J. Nandakumar, S. Shuman, and C.D. Lima. RNA ligase structures reveal the basis for RNA specificity and conformational changes that drive ligation forward. *Cell*, 127:71–84, 2006.
- [302] A. Narbad and M.J. Gasson. Metabolism of ferulic acid via vanillin using a novel CoA-dependent pathway in a newly isolated strain of *Pseudomonas fluorescens*. *Microbiology*, 144:1397–1405, 1998.
- [303] S.G. Nathenson, J.L. Strominger, and E. Ito. Enzymatic synthesis of the peptide in bacterial uridine nucleotides. IV. Purification and properties of D-glutamic acid-adding enzyme. *J. Biol. Chem.*, 239:1773–1776, 1964.
- [304] S.W. Nelson, D.J. Binkowski, R.B. Honzatko, and H.J. Fromm. Mechanism of action of *Escherichia coli* phosphoribosylaminoimidazolesuccinocarboxamide synthetase. *Biochemistry*, 44:766–774, 2005.
- [305] E. Nenortas and D. Beckett. Purification and characterization of intact and truncated forms of the *Escherichia coli* biotin carboxyl carrier subunit of acetyl-CoA carboxylase. *J. Biol. Chem.*, 271:7559–7567, 1996.
- [306] F.C. Neuhaus. Kinetic studies on D-Ala-D-Ala synthetase. *Fed. Proc.*, 21:229–229, 1962.

- [307] B. Niyomporn, J.L. Dahl, and J.L. Strominger. Biosynthesis of the peptidoglycan of bacterial cell walls. IX. Purification and properties of glycyl transfer ribonucleic acid synthetase from *Staphylococcus aureus*. *J. Biol. Chem.*, 243:773–778, 1968.
- [308] B. Nocek, E. Evdokimova, M. Proudfoot, M. Kudritska, L.L. Grochowski, R.H. White, A. Savchenko, A.F. Yakunin, A. Edwards, and A. Joachimiak. Structure of an amide bond forming F₄₂₀: γ -glutamyl ligase from *Archaeoglobus fulgidus* — a member of a new family of non-ribosomal peptide synthases. *J. Mol. Biol.*, 372:456–469, 2007.
- [309] E. Norman, K.A. De Smet, N.G. Stoker, C. Ratledge, P.R. Wheeler, and J.W. Dale. Lipid synthesis in mycobacteria: characterization of the biotin carboxyl carrier protein genes from *Mycobacterium leprae* and *M. tuberculosis*. *J. Bacteriol.*, 176:2525–2531, 1994.
- [310] S.J. Norton. Purification and properties of the prolyl RNA synthetase of *Escherichia coli*. *Arch. Biochem. Biophys.*, 106:147–152, 1964.
- [311] S.J. Norton, J.M. Ravel, C. Lee, and W. Shive. Purification and properties of the aspartyl ribonucleic acid synthetase of *Lactobacillus arabinosus*. *J. Biol. Chem.*, 238:269–274, 1963.
- [312] A.F. O'Donnell, S. Tiong, D. Nash, and D.V. Clark. The *Drosophila melanogaster ade5* gene encodes a bifunctional enzyme for two steps in the de novo purine synthesis pathway. *Genetics*, 154:1239–1253, 2000.
- [313] N. Ofer, N. Forer, M. Korman, M. Vishkautzan, I. Khalaila, and E. Gur. Allosteric transitions direct protein tagging by PafA, the prokaryotic ubiquitin-like protein (Pup) ligase. *J. Biol. Chem.*, 288:11287–11293, 2013.
- [314] T. Ohama, D.C. Yang, and D.L. Hatfield. Selenocysteine tRNA and serine tRNA are aminoacylated by the same synthetase, but may manifest different identities with respect to the long extra arm. *Arch. Biochem. Biophys.*, 315:293–301, 1994.
- [315] T. Osawa, H. Inanaga, S. Kimura, N. Terasaka, T. Suzuki, and T. Numata. Crystallization and preliminary X-ray diffraction analysis of an archaeal tRNA-modification enzyme, TiaS, complexed with tRNA(Ile²) and ATP. *Acta Crystallogr. Sect. F Struct. Biol. Cryst. Commun.*, 67:1414–1416, 2011.
- [316] K.T. Osman, L. Du, Y. He, and Y. Luo. Crystal structure of *Bacillus cereus* D-alanyl carrier protein ligase (DltA) in complex with ATP. *J. Mol. Biol.*, 388:345–355, 2009.
- [317] T. Ouchi, T. Tomita, A. Horie, A. Yoshida, K. Takahashi, H. Nishida, K. Lassak, H. Taka, R. Mineki, T. Fujimura, S. Kosono, C. Nishiyama, R. Masui, S. Kuramitsu, S.V. Albers, T. Kuzuyama, and M. Nishiyama. Lysine and arginine biosyntheses mediated by a common carrier protein in *Sulfolobus*. *Nat. Chem. Biol.*, 9:277–283, 2013.
- [318] H.J. Ougham, D.G. Taylor, and P.W. Trudgill. Camphor revisited: involvement of a unique monooxygenase in metabolism of 2-oxo- Δ^3 -4,5,5-trimethylcyclopentenylacetic acid by *Pseudomonas putida*. *J. Bacteriol.*, 153:140–152, 1983.
- [319] K. Ownby, H. Xu, and R.H. White. A *Methanocaldococcus jannaschii* archaeal signature gene encodes for a 5-formaminoimidazole-4-carboxamide-1- β -D-ribofuranosyl 5'-monophosphate synthetase. A new enzyme in purine biosynthesis. *J. Biol. Chem.*, 280:10881–10887, 2005.
- [320] S.L. Oza, M.P. Shaw, S. Wyllie, and A.H. Fairlamb. Trypanothione biosynthesis in *Leishmania major*. *Mol. Biochem. Parasitol.*, 139:107–116, 2005.
- [321] S.L. Oza, E. Tetaud, M.R. Ariyanayagam, S.S. Warnon, and A.H. Fairlamb. A single enzyme catalyses formation of trypanothione from glutathione and spermidine in *Trypanosoma cruzi*. *J. Biol. Chem.*, 277:35853–35861, 2002.
- [322] M. Pacholec, J. Tao, and C.T. Walsh. CouO and NovO: C-methyltransferases for tailoring the aminocoumarin scaffold in coumermycin and novobiocin antibiotic biosynthesis. *Biochemistry*, 44:14969–14976, 2005.
- [323] I.S. Park, C.H. Lin, and C.T. Walsh. Bacterial resistance to vancomycin: overproduction, purification, and characterization of VanC2 from *Enterococcus casseliflavus* as a D-Ala-D-Ser ligase. *Proc. Natl. Acad. Sci. USA*, 94:10040–10044, 1997.
- [324] J. Parker. Identification of the *purC* gene product of *Escherichia coli*. *J. Bacteriol.*, 157:712–717, 1984.
- [325] J.B. Parker and C.T. Walsh. Action and timing of BacC and BacD in the late stages of biosynthesis of the dipeptide antibiotic bacilysin. *Biochemistry*, 52:889–901, 2013.

- [326] C. Parthier, S. Gorlich, F. Jaenecke, C. Breithaupt, U. Brauer, U. Fandrich, D. Clausnitzer, U.F. Wehmeier, C. Bottcher, D. Scheel, and M.T. Stubbs. The *O*-carbamoyltransferase TobZ catalyzes an ancient enzymatic reaction. *Angew. Chem. Int. Ed. Engl.*, 51:4046–4052, 2012.
- [327] M.K. Patterson, Orr Jr., and G.R. Asparagine biosynthesis by the Novikoff hepatoma. Isolation, purification, property, and mechanism studies of the enzyme system. *J. Biol. Chem.*, 243:376–380, 1968.
- [328] S. Pekkala, A.I. Martinez, B. Barcelona, J. Gallego, E. Bendala, I. Yefimenko, V. Rubio, and J. Cervera. Structural insight on the control of urea synthesis: identification of the binding site for *N*-acetyl-L-glutamate, the essential allosteric activator of mitochondrial carbamoyl phosphate synthetase. *Biochem. J.*, 424:211–220, 2009.
- [329] M. Perego, P. Glaser, A. Minutello, M.A. Strauch, K. Leopold, and W. Fischer. Incorporation of D-alanine into lipoteichoic acid and wall teichoic acid in *Bacillus subtilis*. Identification of genes and regulation. *J. Biol. Chem.*, 270:15598–15606, 1995.
- [330] R.N. Perham. Swinging arms and swinging domains in multifunctional enzymes: catalytic machines for multistep reactions. *Annu. Rev. Biochem.*, 69:961–1004, 2000.
- [331] B. Perichon, P. Reynolds, and P. Courvalin. VanD-type glycopeptide-resistant *Enterococcus faecium* BM4339. *Antimicrob. Agents Chemother.*, 41:2016–2018, 1997.
- [332] P.J. Peterson and L. Fowden. Purification, properties and comparative specificities of the enzyme prolyl-transfer ribonucleic acid synthetase from *Phaseolus aureus* and *Polygonatum multiflorum*. *Biochem. J.*, 97:112–124, 1965.
- [333] A. Pfaltz, A. Kobelt, R. Huster, and R.K. Thauer. Biosynthesis of coenzyme F₄₃₀ in methanogenic bacteria. Identification of 15,17³-seco-F₄₃₀-17³-acid as an intermediate. *Eur. J. Biochem.*, 170:459–467, 1987.
- [334] N. Pi, C.L. Meyers, M. Pacholec, C.T. Walsh, and J.A. Leary. Mass spectrometric characterization of a three-enzyme tandem reaction for assembly and modification of the novobiocin skeleton. *Proc. Natl. Acad. Sci. USA*, 101:10036–10041, 2004.
- [335] D.L. Pierson and J.M. Brien. Human carbamylphosphate synthetase I. Stabilization, purification, and partial characterization of the enzyme from human liver. *J. Biol. Chem.*, 255:7891–7895, 1980.
- [336] C. Polycarpo, A. Ambrogelly, A. Bérubé, S.M. Winbush, J.A. McCloskey, P.F. Crain, J.L. Wood, and D. Söll. An aminoacyl-tRNA synthetase that specifically activates pyrrolysine. *Proc. Natl. Acad. Sci. USA*, 101:12450–12454, 2004.
- [337] A.L. Pometto and D.L. Crawford. Whole-cell bioconversion of vanillin to vanillic acid by *Streptomyces viridosporus*. *Appl. Environ. Microbiol.*, 45:1582–1585, 1983.
- [338] E.C. Preddie. Tryptophanyl transfer ribonucleic acid synthetase from bovine pancreas. II. The chemically different subunits. *J. Biol. Chem.*, 244:3958–3968, 1969.
- [339] K. Prydz, B.F. Kase, I. Björkhem, and J.I. Pedersen. Subcellular localization of 3 α ,7 α -dihydroxy- and 3 α ,7 α ,12 α -trihydroxy-5 β -cholestanoyl-coenzyme A ligase(s) in rat liver. *J. Lipid Res.*, 29:997–1004, 1988.
- [340] A. Quentmeier and G. Antranikian. Characterization of citrate lyase from *Clostridium sporosphaeroides*. *Arch. Microbiol.*, 141:85–90, 1985.
- [341] M.L. Raber, S.O. Arnett, and C.A. Townsend. A conserved tyrosyl-glutamyl catalytic dyad in evolutionarily linked enzymes: carbapenam synthetase and β -lactam synthetase. *Biochemistry*, 48:4959–4971, 2009.
- [342] J.C. Rabinowitz and W.E. Pricer. Formyltetrahydrofolate synthetase. I. Isolation and crystallization of the enzyme. *J. Biol. Chem.*, 237:2898–2902, 1962.
- [343] W.H. Ramos-Vera, M. Weiss, E. Strittmatter, D. Kockelkorn, and G. Fuchs. Identification of missing genes and enzymes for autotrophic carbon fixation in crenarchaeota. *J. Bacteriol.*, 193:1201–1211, 2011.
- [344] J.M. Rand, T. Pisithkul, R.L. Clark, J.M. Thiede, C.R. Mehrer, D.E. Agnew, C.E. Campbell, A.L. Markley, M.N. Price, J. Ray, K.M. Wetmore, Y. Suh, A.P. Arkin, A.M. Deutschbauer, D. Amador-Noguez, and B.F. Pfleger. A metabolic pathway for catabolizing levulinic acid in bacteria. *Nat Microbiol*, 2:1624–1634, 2017.

- [345] S. Ratner. Urea synthesis and metabolism of arginine and citrulline. *Adv. Enzymol. Relat. Subj. Biochem.*, 15:319–387, 1954.
- [346] F.M. Raushel, J.B. Thoden, and H.M. Holden. The amidotransferase family of enzymes: molecular machines for the production and delivery of ammonia. *Biochemistry*, 38:7891–7899, 1999.
- [347] F.M. Raushel, J.B. Thoden, G.D. Reinhart, and H.M. Holden. Carbamoyl phosphate synthetase: a crooked path from substrates to products. *Curr. Opin. Chem. Biol.*, 2:624–632, 1998.
- [348] S. Ravel, H. Cherest, S. Jabrin, D. Grunwald, Y. Surdin-Kerjan, R. Douce, and F. Rébeillé. Tetrahydrofolate biosynthesis in plants: molecular and functional characterization of dihydrofolate synthetase and three isoforms of folylpolyglutamate synthetase in *Arabidopsis thaliana*. *Proc. Natl. Acad. Sci. USA*, 98:15360–15365, 2001.
- [349] J.M. Ravel, S.J. Norton, J.S. Humphreys, and W. Shive. Asparagine biosynthesis in *Lactobacillus arabinosus* and its control by asparagine through enzyme inhibition and repression. *J. Biol. Chem.*, 237:2845–2849, 1962.
- [350] J.M. Ravel, S. Wang, C. Heinemeyer, and W. Shive. Glutamyl and glutaminyl ribonucleic acid synthetases of *Escherichia coli* W. Separation, properties, and stimulation of adenosine triphosphate-pyrophosphate exchange by acceptor ribonucleic acid. *J. Biol. Chem.*, 240:432–438, 1965.
- [351] G.H. Reem. Enzymatic synthesis of 5'-phosphoribosylamine from ribose 5-phosphate and ammonia, an alternate first step in purine biosynthesis. *J. Biol. Chem.*, 243:5695–5701, 1968.
- [352] R.E. Reeves, L.G. Warren, B. Susskind, and H.-S. Lo. An energy-conserving pyruvate-to-acetate pathway in *Entamoeba histolytica*. Pyruvate synthase and a new acetate thiokinase. *J. Biol. Chem.*, 252:726–731, 1977.
- [353] D. Reinberg, J. Arenas, and J. Hurwitz. The enzymatic conversion of 3'-phosphate terminated RNA chains to 2',3'-cyclic phosphate derivatives. *J. Biol. Chem.*, 260:6088–6097, 1985.
- [354] C.R. Reisch, M.J. Stoudemayer, V.A. Varaljay, I.J. Amster, M.A. Moran, and W.B. Whitman. Novel pathway for assimilation of dimethylsulphoniopropionate widespread in marine bacteria. *Nature*, 473:208–211, 2011.
- [355] V.M. Reusch and F.C. Neuhaus. D-Alanine:membrane acceptor ligase from *Lactobacillus casei*. *J. Biol. Chem.*, 246:6136–6143, 1971.
- [356] N.G. Richards and S.M. Schuster. Mechanistic issues in asparagine synthetase catalysis. *Adv. Enzymol. Relat. Areas Mol. Biol.*, 72:145–198, 1998.
- [357] C.A. Ricks and R.M. Cook. Regulation of volatile fatty acid uptake by mitochondrial acyl CoA synthetases of bovine liver. *J. Dairy Sci.*, 64:2324–2335, 1981.
- [358] D. Riendeau, A. Rodrigues, and E. Meighen. Resolution of the fatty acid reductase from *Photobacterium phosphoreum* into acyl protein synthetase and acyl-CoA reductase activities. Evidence for an enzyme complex. *J. Biol. Chem.*, 257:6908–6915, 1982.
- [359] H.C. Rilling and M.J. Coon. The enzymatic isomerization of α -methylvinylacetyl coenzyme A and the specificity of a bacterial α -methylcrotonyl coenzyme A carboxylase. *J. Biol. Chem.*, 235:3087–3092, 1960.
- [360] A. Rodriguez and E. Meighen. Fatty acyl-AMP as an intermediate in fatty acid reduction to aldehyde in luminescent bacteria. *J. Biol. Chem.*, 260:771–774, 1985.
- [361] J.L. Rolland, Y. Gueguen, C. Persillon, J.M. Masson, and J. Dietrich. Characterization of a thermophilic DNA ligase from the archaeon *Thermococcus fumicolans*. *FEMS Microbiol. Lett.*, 236:267–273, 2004.
- [362] P.J. Romaniuk and O.C. Uhlenbeck. Joining of RNA molecules with RNA ligase. *Methods Enzymol.*, 100:52–59, 1983.
- [363] S. Ronconi, R. Jonczyk, and U. Genschel. A novel isoform of pantothenate synthetase in the Archaea. *FEBS J.*, 275:2754–2764, 2008.
- [364] R.J. Roon and B. Levenberg. ATP-Urea amidolyase (ADP) (*Candida utilis*). *Methods Enzymol.*, 17A:317–324, 1970.
- [365] R.J. Roon and B. Levenberg. Urea amidolyase. I. Properties of the enzyme from *Candida utilis*. *J. Biol. Chem.*, 247:4107–4113, 1972.

- [366] C.R. Rossi and D.M. Gibson. Activation of fatty acids by a guanosine triphosphate-specific thiokinase from liver mitochondria. *J. Biol. Chem.*, 239:1694–1699, 1964.
- [367] M. Rudiger, J. Wehland, , and K. The carboxy-terminal peptide of detyrosinated α tubulin provides a minimal system to study the substrate specificity of tubulin-tyrosine ligase. *Eur. J. Biochem.*, 220:309–320, 1994.
- [368] F. Rusnak, W.S. Faraci, and C.T. Walsh. Subcloning, expression, and purification of the enterobactin biosynthetic enzyme 2,3-dihydroxybenzoate-AMP ligase: demonstration of enzyme-bound (2,3-dihydroxybenzoyl)adenylate product. *Biochemistry*, 28:6827–6835, 1989.
- [369] F. Rusnak, J. Liu, N. Quinn, G.A. Berchtold, and C.T. Walsh. Subcloning of the enterobactin biosynthetic gene *entB*: expression, purification, characterization, and substrate specificity of isochorismatase. *Biochemistry*, 29:1425–1435, 1990.
- [370] F. Rusnak, M. Sakaitani, D. Drucekhammer, J. Reichert, and C.T. Walsh. Biosynthesis of the *Escherichia coli* siderophore enterobactin: sequence of the *entF* gene, expression and purification of EntF, and analysis of covalent phosphopantetheine. *Biochemistry*, 30:2916–2927, 1991.
- [371] S.P. Salowe, J. Wiltsie, J.C. Hawkins, and L.M. Sonatore. The catalytic flexibility of tRNA^{Ile}-lysine synthetase can generate alternative tRNA substrates for isoleucyl-tRNA synthetase. *J. Biol. Chem.*, 284:9656–9662, 2009.
- [372] D.R. Sanadi, D.M. Gibson, and P. Ayengar. Guanosine triphosphate, the primary product of phosphorylation coupled to the breakdown of succinyl coenzyme A. *Biochim. Biophys. Acta*, 14:434–436, 1954.
- [373] K. Sasaoka and M. Kito. Synthesis of theanine by tea seedling homogenate. *Agric. Biol. Chem.*, 28:313–317, 1964.
- [374] K. Sasaoka, M. Kito, and H. Inagaki. Studies on the biosynthesis of theanine in tea seedlings. Synthesis of theanine by the homogenate of tea seedlings. *Agric. Biol. Chem.*, 27:467–468, 1963.
- [375] K. Sasaoka, M. Kito, and Y. Onishi. Some properties of the theanine synthesizing enzyme in tea seedlings. *Agric. Biol. Chem.*, 29:984–988, 1965.
- [376] A. Sato, T. Soga, K. Igarashi, K. Takesue, M. Tomita, and A. Kanai. GTP-dependent RNA 3'-terminal phosphate cyclase from the hyperthermophilic archaeon *Pyrococcus furiosus*. *Genes Cells*, 16:1190–1199, 2011.
- [377] U. Schennen, K. Braun, and H.-J. Knackmuss. Anaerobic degradation of 2-fluorobenzoate by benzoate-degrading, denitrifying bacteria. *J. Bacteriol.*, 161:321–325, 1985.
- [378] L. Schepers, M. Casteels, K. Verheyden, G. Parmentier, S. Asselberghs, H.J. Eyssen, and G.P. Mannaerts. Subcellular distribution and characteristics of trihydroxycoprostanoyl-CoA synthetase in rat liver. *Biochem. J.*, 257:221–229, 1989.
- [379] P. Schimmel and K. Beebe. Molecular biology: genetic code seizes pyrrolysine. *Nature*, 431:257–258, 2004.
- [380] H. Schmellenkamp and H. Eggerer. Mechanism of enzymic acetylation of des-acetyl citrate lyase. *Proc. Natl. Acad. Sci. USA*, 71:1987–1991, 1974.
- [381] E. Schmitt, L. Moulinier, S. Fujiwara, T. Imanaka, J.C. Thierry, and D. Moras. Crystal structure of aspartyl-tRNA synthetase from *Pyrococcus kodakaraensis* KOD: archaeon specificity and catalytic mechanism of adenylate formation. *EMBO J.*, 17:5227–5237, 1998.
- [382] A. Schuegraf, S. Ratner, and R.C. Warner. Free energy changes of the argininosuccinate synthetase reaction and of the hydrolysis of the inner pyrophosphate bond of adenosine triphosphate. *J. Biol. Chem.*, 235:3597–3602, 1960.
- [383] R.S. Schweet and E.H. Allen. Purification and properties of tyrosine-activating enzyme of hog pancreas. *J. Biol. Chem.*, 233:1104–1108, 1958.
- [384] M.C. Scrutton, M.R. Young, and M.F. Utter. Pyruvate carboxylase from baker's yeast. The presence of bound zinc. *J. Biol. Chem.*, 245:6220–6227, 1970.
- [385] W. Seubert, E. Fass, and U. Remberger. Untersuchungen über den bakteriellen Abbau von Isoprenoiden. III. Reinigung und Eigenschaften der Geranylcarboxylase. *Biochem. Z.*, 338:265–275, 1963.
- [386] W. Seubert and U. Remberger. Reinigung und Wirkungsweise der Pyruvatcarboxylase aus *Pseudomonas citronellolis*. *Biochem. Z.*, 334:401–414, 1961.

- [387] C.A. Shaw-Reid, N.L. Kelleher, H.C. Losey, A.M. Gehring, C. Berg, and C.T. Walsh. Assembly line enzymology by multimodular nonribosomal peptide synthetases: the thioesterase domain of *E. coli* EntF catalyzes both elongation and cyclolactonization. *Chem. Biol.*, 6:385–400, 1999.
- [388] Y. Shomura, E. Hinokuchi, H. Ikeda, A. Senoo, Y. Takahashi, J. Saito, H. Komori, N. Shibata, Y. Yonetani, and Y. Higuchi. Structural and enzymatic characterization of BacD, an L-amino acid dipeptide ligase from *Bacillus subtilis*. *Protein Sci.*, 21:707–716, 2012.
- [389] L. Siegel, J.L. Foote, and M.J. Coon. The enzymatic synthesis of propionyl coenzyme A holocarboxylase from *d*-biotinyl 5'-adenylate and the apocarboxylase. *J. Biol. Chem.*, 240:1025–1031, 1965.
- [390] R. Silber, V.G. Malathi, and J. Hurwitz. Purification and properties of bacteriophage T₄-induced RNA ligase. *Proc. Natl. Acad. Sci. USA*, 69:3009–3013, 1972.
- [391] R. Simeone, M. Leger, P. Constant, W. Malaga, H. Marrakchi, M. Daffe, C. Guilhot, and C. Chalut. Delineation of the roles of FadD22, FadD26 and FadD29 in the biosynthesis of phthiocerol dimycocerosates and related compounds in *Mycobacterium tuberculosis*. *FEBS J.*, 277:2715–2725, 2010.
- [392] M.K. Sluis and S.A. Ensign. Purification and characterization of acetone carboxylase from *Xanthobacter* strain Py2. *Proc. Natl. Acad. Sci. USA*, 94:8456–8461, 1997.
- [393] K. Smith, K. Nadeau, M. Bradley, C.T. Walsh, , and A.H. Purification of glutathionylspermidine and trypanothione synthase from *Crithidia fasciculata*. *Protein Sci.*, 1:874–883, 1992.
- [394] J.E. Snoke, S. Yanari, and K. Bloch. Synthesis of glutathione from γ -glutamylcysteine. *J. Biol. Chem.*, 201:573–586, 1953.
- [395] R.R. Soly and E.A. Meighen. Identification of the acyl transfer site of fatty acyl-protein synthetase from bioluminescent bacteria. *J. Mol. Biol.*, 219:69–77, 1991.
- [396] A. Soma, Y. Ikeuchi, S. Kanemasa, K. Kobayashi, N. Ogasawara, T. Ote, J. Kato, K. Watanabe, Y. Sekine, and T. Suzuki. An RNA-modifying enzyme that governs both the codon and amino acid specificities of isoleucine tRNA. *Mol. Cell*, 12:689–698, 2003.
- [397] R.L. Spencer and J. Preiss. Biosynthesis of diphosphopyridine nucleotide. The purification and the properties of diphosphopyridine nucleotide synthetase from *Escherichia coli* B. *J. Biol. Chem.*, 242:385–392, 1967.
- [398] M.A. Stapleton, F. Javid-Majd, M.F. Harmon, B.A. Hanks, J.L. Grahmann, L.S. Mullins, and F.M. Raushel. Role of conserved residues within the carboxy phosphate domain of carbamoyl phosphate synthetase. *Biochemistry*, 35:14352–14361, 1996.
- [399] P.E. Staswick and I. Tiryaki. The oxylipin signal jasmonic acid is activated by an enzyme that conjugates it to isoleucine in *Arabidopsis*. *Plant Cell*, 16:2117–2127, 2004.
- [400] W. Staudenbauer and J.L. Strominger. Activation of D-aspartic acid for incorporation into peptidoglycan. *J. Biol. Chem.*, 247:5095–5102, 1972.
- [401] W. Staudenbauer, E. Willoughby, and J.L. Strominger. Further studies of the D-aspartic acid-activating enzyme of *Streptococcus faecalis* and its attachment to the membrane. *J. Biol. Chem.*, 247:5289–5296, 1972.
- [402] M. Steffensky, S.M. Li, and L. Heide. Cloning, overexpression, and purification of novobiocin acid synthetase from *Streptomyces spheroides* NCIMB 11891. *J. Biol. Chem.*, 275:21754–21760, 2000.
- [403] C. Stein and D. Weinreich. An in vitro characterization of γ -glutamylhistamine synthetase: a novel enzyme catalyzing histamine metabolism in the central nervous system of the marine mollusk, *Aplysia californica*. *J. Neurochem.*, 38:204–214, 1982.
- [404] J.J. Stenesh and T. Winnick. Carnosine-anserine synthetase of muscle. 4. Partial purification of the enzyme and further studies of β -alanyl peptide synthesis. *Biochem. J.*, 77:575–581, 1960.
- [405] R. Stern and A.H. Mehler. Lysyl-sRNA synthetase from *Escherichia coli*. *Biochem. Z.*, 342:400–409, 1965.

- [406] E. Strauss, C. Kinsland, Y. Ge, F.W. McLafferty, and T.P. Begley. Phosphopantothoenoylcysteine synthetase from *Escherichia coli*. Identification and characterization of the last unidentified Coenzyme A biosynthetic enzymes in bacteria. *J. Biol. Chem.*, 276:13513–13516, 2001.
- [407] F. Striebel, F. Imkamp, D. Özcelik, and E. Weber-Ban. Pupylation as a signal for proteasomal degradation in bacteria. *Biochim. Biophys. Acta*, 1843:103–113, 2014.
- [408] M.P. Stulberg. The isolation and properties of phenylalanyl ribonucleic acid synthetase from *Escherichia coli* B. *J. Biol. Chem.*, 242:1060–1064, 1967.
- [409] X. Su, Z. Lin, W. Chen, H. Jiang, S. Zhang, and H. Lin. Chemogenomic approach identified yeast YLR143W as diphthamide synthetase. *Proc. Natl. Acad. Sci. USA*, 109:19983–19987, 2012.
- [410] A. Sugino, T.J. Snoper, and N.R. Cozzarelli. Bacteriophage T₄ RNA ligase. Reaction intermediates and interaction of substrates. *J. Biol. Chem.*, 252:1732–1738, 1977.
- [411] D.J. Sukovich, J.L. Seffernick, J.E. Richman, K.A. Hunt, J.A. Gralnick, and L.P. Wackett. Structure, function, and insights into the biosynthesis of a head-to-head hydrocarbon in *Shewanella oneidensis* strain MR-1. *Appl. Environ. Microbiol.*, 76:3842–3849, 2010.
- [412] R.A. Sumrada and T.G. Cooper. Urea carboxylase and allophanate hydrolase are components of a multifunctional protein in yeast. *J. Biol. Chem.*, 257:9119–9127, 1982.
- [413] Y. Sun, M.S. Seo, J.H. Kim, Y.J. Kim, G.A. Kim, J.I. Lee, J.H. Lee, and S.T. Kwon. Novel DNA ligase with broad nucleotide cofactor specificity from the hyperthermophilic crenarchaeon *Sulfolobococcus zilligii*: influence of ancestral DNA ligase on cofactor utilization. *Environ Microbiol.*, 10:3212–3224, 2008.
- [414] M. Sutter, F.F. Damberger, F. Imkamp, F.H. Allain, and E. Weber-Ban. Prokaryotic ubiquitin-like protein (Pup) is coupled to substrates via the side chain of its C-terminal glutamate. *J. Am. Chem. Soc.*, 132:5610–5612, 2010.
- [415] W.P. Suza and P.E. Staswick. The role of JAR1 in jasmonoyl-L-isoleucine production during *Arabidopsis* wound response. *Planta*, 227:1221–1232, 2008.
- [416] S.W., Cronan Jordan, , and Jr. A new metabolic link. The acyl carrier protein of lipid synthesis donates lipoic acid to the pyruvate dehydrogenase complex in *Escherichia coli* and mitochondria. *J. Biol. Chem.*, 272:17903–17906, 1997.
- [417] K. Tabata, H. Ikeda, and S. Hashimoto. *ywfE* in *Bacillus subtilis* codes for a novel enzyme, L-amino acid ligase. *J. Bacteriol.*, 187:5195–5202, 2005.
- [418] M. Takeo, A. Ohara, S. Sakae, Y. Okamoto, C. Kitamura, D. Kato, and S. Negoro. Function of a glutamine synthetase-like protein in bacterial aniline oxidation via γ -glutamylanilide. *J. Bacteriol.*, 195:4406–4414, 2013.
- [419] N. Tanaka, A.K. Chakravarty, B. Maughan, and S. Shuman. Novel mechanism of RNA repair by RtcB via sequential 2',3'-cyclic phosphodiesterase and 3'-phosphate/5'-hydroxyl ligation reactions. *J. Biol. Chem.*, 286:43134–43143, 2011.
- [420] N. Tanaka, B. Meineke, and S. Shuman. RtcB, a novel RNA ligase, can catalyze tRNA splicing and HAC1 mRNA splicing *in vivo*. *J. Biol. Chem.*, 286:30253–30257, 2011.
- [421] N. Tanaka and S. Shuman. Structure-activity relationships in human RNA 3'-phosphate cyclase. *RNA*, 15:1865–1874, 2009.
- [422] N. Tanaka and S. Shuman. RtcB is the RNA ligase component of an *Escherichia coli* RNA repair operon. *J. Biol. Chem.*, 286:7727–7731, 2011.
- [423] T. Tanaka, K. Hosaka, M. Hoshimaru, and S. Numa. Purification and properties of long-chain acyl-coenzyme-A synthetase from rat liver. *Eur. J. Biochem.*, 98:165–172, 1979.
- [424] N. Terasaka, S. Kimura, T. Osawa, T. Numata, and T. Suzuki. Biogenesis of 2-*agmatinyl*cytidine catalyzed by the dual protein and RNA kinase TiaS. *Nat. Struct. Mol. Biol.*, 18:1268–1274, 2011.
- [425] A.R. Tesson, T.S. Soper, M. Ciustea, and N.G. Richards. Revisiting the steady state kinetic mechanism of glutamine-dependent asparagine synthetase from *Escherichia coli*. *Arch. Biochem. Biophys.*, 413:23–31, 2003.

- [426] H.B. Theilgaard, K.N. Kristiansen, C.M. Henriksen, and J. Nielsen. Purification and characterization of δ -(L- α -aminoadipyl)-L-cysteinyl-D-valine synthetase from *Penicillium chrysogenum*. *Biochem. J.*, 327:185–191, 1997.
- [427] J.B. Thoden, X. Huang, F.M. Raushel, and H.M. Holden. Carbamoyl-phosphate synthetase. Creation of an escape route for ammonia. *J. Biol. Chem.*, 277:39722–39727, 2002.
- [428] J.B. Thoden, T.J. Kappock, J. Stubbe, and H.M. Holden. Three-dimensional structure of N^5 -carboxyaminoimidazole ribonucleotide synthetase: a member of the ATP grasp protein superfamily. *Biochemistry*, 38:15480–15492, 1999.
- [429] M.G. Thomas, M.D. Burkart, and C.T. Walsh. Conversion of L-proline to pyrrolyl-2-carboxyl-S-PCP during undecylprodigiosin and pyoluteorin biosynthesis. *Chem. Biol.*, 9:171–184, 2002.
- [430] M.V. Tigerstrom and G.M. Tener. Histidyl transfer ribonucleic acid synthetase from bakers' yeast. *Can. J. Biochem.*, 45:1067–1074, 1967.
- [431] T.K., Cronan Ray, , and Jr. Activation of long chain fatty acids with acyl carrier protein: demonstration of a new enzyme, acyl-acyl carrier protein synthetase, in *Escherichia coli*. *Proc. Natl. Acad. Sci. USA*, 73:4374–4378, 1976.
- [432] C.A. Townsend. New reactions in clavulanic acid biosynthesis. *Curr. Opin. Chem. Biol.*, 6:583–589, 2002.
- [433] L.W. Tremblay, F. Fan, M.W. Vetting, and J.S. Blanchard. The 1.6 Å crystal structure of *Mycobacterium smegmatis* MshC: the penultimate enzyme in the mycothiol biosynthetic pathway. *Biochemistry*, 47:13326–13335, 2008.
- [434] G.E. Trumble, M.A. Smith, and W.W. Winder. Purification and characterization of rat skeletal muscle acetyl-CoA carboxylase. *Eur. J. Biochem.*, 231:192–198, 1995.
- [435] T. Tsuda, T. Suzuki, and S. Kojima. Crystallization and preliminary X-ray diffraction analysis of *Bacillus subtilis* YwfE, an L-amino-acid ligase. *Acta Crystallogr. Sect. F Struct. Biol. Cryst. Commun.*, 68:203–206, 2012.
- [436] N. Uda, Y. Matoba, T. Kumagai, K. Oda, M. Noda, and M. Sugiyama. Establishment of an *in vitro* D-cycloserine-synthesizing system by using *O*-ureido-L-serine synthase and D-cycloserine synthetase found in the biosynthetic pathway. *Antimicrob. Agents Chemother.*, 57:2603–2612, 2013.
- [437] H. Ueda, Y. Yoshihara, N. Fukushima, H. Shiomi, A. Nakamura, and H. Takagi. Kyotorphin (tyrosine-arginine) synthetase in rat brain synaptosomes. *J. Biol. Chem.*, 262:8165–8173, 1987.
- [438] S. Uphoff, R. Reyes-Lamothe, F. Garza de Leon, D.J. Sherratt, and A.N. Kapanidis. Single-molecule DNA repair in live bacteria. *Proc. Natl. Acad. Sci. USA*, 110:8063–8068, 2013.
- [439] M.F. Utter and D.B. Keech. Pyruvate carboxylase. I. Nature of the reaction. *J. Biol. Chem.*, 238:2603–2608, 1963.
- [440] P. Vagelos. Regulation of fatty acid biosynthesis. *Curr. Top. Cell. Regul.*, 4:119–166, 1971.
- [441] J. Vamecq, E. de Hoffmann, and F. van Hoof. The microsomal dicarboxyl-CoA synthetase. *Biochem. J.*, 230:683–693, 1985.
- [442] J. van Heijenoort. Recent advances in the formation of the bacterial peptidoglycan monomer unit. *Nat. Prod. Rep.*, 18:503–519, 2001.
- [443] M.N. Vassilyeva, H. Sakai, T. Matsuura, S. Sekine, M. Nishiyama, T. Terada, M. Shirouzu, S. Kuramitsu, D.G. Vassylyev, and S. Yokoyama. Cloning, expression, purification, crystallization and initial crystallographic analysis of the lysine-biosynthesis LysX protein from *Thermus thermophilus* HB8. *Acta Crystallogr. D Biol. Crystallogr.*, 59:1651–1652, 2003.
- [444] O. Vergnolle, S.S. Chavadi, U.R. Edupuganti, P. Mohandas, C. Chan, J. Zeng, M. Kopylov, N.G. Angelo, J.D. Warren, C.E. Soll, and L.E. Quadri. Biosynthesis of cell envelope-associated phenolic glycolipids in *Mycobacterium marinum*. *J. Bacteriol.*, 197:1040–1050, 2015.
- [445] A. Vinitzky and C. Grubmeyer. A new paradigm for biochemical energy coupling. *Salmonella typhimurium* nicotinate phosphoribosyltransferase. *J. Biol. Chem.*, 268:26004–26010, 1993.
- [446] V.R. Viviani, V. Scorsato, R.A. Prado, J.G. Pereira, K. Niwa, Y. Ohmiya, and J.A. Barbosa. The origin of luciferase activity in *Zophobas* mealworm AMP/CoA-ligase (protoluciferase): luciferin stereoselectivity as a switch for the oxygenase activity. *Photochem Photobiol Sci*, 9:1111–1119, 2010.

- [447] W. von der Saal, P.M. Anderson, and J.J. Villafranca. Mechanistic investigations of *Escherichia coli* cytidine-5'-triphosphate synthetase. Detection of an intermediate by positional isotope exchange experiments. *J. Biol. Chem.*, 260:14993–14997, 1985.
- [448] S.L. Wadskov-Hansen, M. Willemoes, J. Martinussen, K. Hammer, J. Neuhard, and S. Larsen. Cloning and verification of the *Lactococcus lactis* *pyrG* gene and characterization of the gene product, CTP synthase. *J. Biol. Chem.*, 276:38002–38009, 2001.
- [449] S.J. Wakil. A malonic acid derivative as an intermediate in fatty acid synthesis. *J. Am. Chem. Soc.*, 80:6465–6465, 1958.
- [450] C.J. Walker and J.D. Weinstein. In vitro assay of the chlorophyll biosynthetic enzyme Mg-chelatase: resolution of the activity into soluble and membrane-bound fractions. *Proc. Natl. Acad. Sci. USA*, 88:5789–5793, 1991.
- [451] C.J. Walker and R.D. Willows. Mechanism and regulation of Mg-chelatase. *Biochem. J.*, 327:321–333, 1997.
- [452] L. Wall and E.A. Meighen. Subunit structure of the fatty-acid reductase complex from *Photobacterium phosphoreum*. *Biochemistry*, 25:4315–4321, 1986.
- [453] L. Wang, R. Halitschke, J.H. Kang, A. Berg, F. Harnisch, and I.T. Baldwin. Independently silencing two JAR family members impairs levels of trypsin proteinase inhibitors but not nicotine. *Planta*, 226:159–167, 2007.
- [454] Y. Wang, H. Xu, K.C. Harich, and R.H. White. Identification and characterization of a tyramine-glutamate ligase (MfnD) Involved in methanofuran biosynthesis. *Biochemistry*, 53:6220–6230, 2014.
- [455] M.J. Warren, E. Raux, H.L. Schubert, and J.C. Escalante-Semerena. The biosynthesis of adenosylcobalamin (vitamin B₁₂). *Nat. Prod. Rep.*, 19:390–412, 2002.
- [456] S. Watanabe, N. Kobayashi, D. Quinones, S. Hayakawa, S. Nagashima, N. Uehara, and N. Watanabe. Genetic diversity of the low-level vancomycin resistance gene *vanC-2/vanC-3* and identification of a novel *vanC* subtype (*vanC-4*) in *Enterococcus casseliflavus*. *Microb. Drug Resist.*, 15:1–9, 2009.
- [457] G.C. Webster. Isolation of an alanine-activating enzyme from pig liver. *Biochim. Biophys. Acta*, 49:141–152, 1961.
- [458] G.C. Webster and J.E. Varner. Aspartate metabolism and asparagine synthesis in plant systems. *J. Biol. Chem.*, 215:91–99, 1955.
- [459] L.T. Webster and E.W. Davie. Purification and properties of serine-activating enzyme from beef pancreas. *J. Biol. Chem.*, 236:479–484, 1961.
- [460] J.R. Websterlt, L.D. Gerowin, and L. Rakita. Purification and characteristics of a butyryl coenzyme A synthetase from bovine heart mitochondria. *J. Biol. Chem.*, 240:29–33, 1965.
- [461] J. Wehland, H.C. Schröder, , and K. Isolation and purification of tubulin-tyrosine ligase. *Methods Enzymol.*, 134:170–179, 1986.
- [462] B. Weiss and C.C. Richardson. Enzymatic breakage and joining of deoxyribonucleic acid. I. Repair of single-strand breaks in DNA by an enzyme system from *Escherichia coli* infected with T4 bacteriophage. *Proc. Natl. Acad. Sci. USA*, 57:1021–1028, 1967.
- [463] J.B. Wheeler, D.R. Shaw, and S. Barnes. Purification and characterization of a rat liver bile acid coenzyme A ligase from rat liver microsomes. *Arch. Biochem. Biophys.*, 348:15–24, 1997.
- [464] H.R. Whiteley, M.J. Osborn, and F.M. Huennekens. Purification and properties of the formate-activating enzyme from *Micrococcus aerogenes*. *J. Biol. Chem.*, 234:1538–1543, 1959.
- [465] M.H. Wilbrink, M. Petrusma, L. Dijkhuizen, and R. van der Geize. FadD19 of *Rhodococcus rhodochrous* DSM43269, a steroid-coenzyme A ligase essential for degradation of C-24 branched sterol side chains. *Appl. Environ. Microbiol.*, 77:4455–4464, 2011.
- [466] N.R. Williamson, H.T. Simonsen, R.A. Ahmed, G. Goldet, H. Slater, L. Woodley, F.J. Leeper, and G.P. Salmond. Biosynthesis of the red antibiotic, prodigiosin, in *Serratia*: identification of a novel 2-methyl-3-n-amylo-pyrrole (MAP) assembly pathway, definition of the terminal condensing enzyme, and implications for undecylprodigiosin biosynthesis in *Streptomyces*. *Mol. Microbiol.*, 56:971–989, 2005.

- [467] D.B. Wilson, S.M. Prescott, and P.W. Majerus. Discovery of an arachidonoyl coenzyme A synthetase in human platelets. *J. Biol. Chem.*, 257:3510–3515, 1982.
- [468] K.P. Wilson, L.M. Shewchuk, R.G. Brennan, A.J. Otsuka, and B.W. Matthews. *Escherichia coli* biotin holoenzyme synthetase/bio repressor crystal structure delineates the biotin- and DNA-binding domains. *Proc. Natl. Acad. Sci. USA*, 89:9257–9261, 1992.
- [469] H.C. Winter, T.-Z. Su, and E.E. Dekker. 4-Methyleneglutamine synthetase: a new amide synthetase present in germinating peanuts. *Biochem. Biophys. Res. Commun.*, 111:484–489, 1983.
- [470] K.K. Wong, A. Meister, and K. Moldave. Enzymic formation of ribonucleic acid-amino acid from synthetic aminoacyl-adenylate and ribonucleic acid. *Biochim. Biophys. Acta*, 36:531–533, 1959.
- [471] C.A. Woolfolk, B. Shapiro, and E.R. Stadtman. Regulation of glutamine synthetase. I. Purification and properties of glutamine synthetase from *Escherichia coli*. *Arch. Biochem. Biophys.*, 116:177–192, 1966.
- [472] H.-C. Yang, Y. Tani, and K. Ogata. Synthesis of biotin vitamers from biotin diamino-carboxylic acid or 7,8-diaminopelargonic acid by a purified enzyme of *Pseudomonas graveolens*. *Agric. Biol. Chem.*, 34:1748–1750, 1970.
- [473] E.F. Yefimochkina and A.E. Braunstein. The amination of inosinic acid to adenylic acid in muscle extracts. *Arch. Biochem. Biophys.*, 83:350–352, 1959.
- [474] M.C.M. Yip and W.E. Knox. Glutamine-dependent carbamyl phosphate synthetase. Properties and distribution in normal and neoplastic rat tissues. *J. Biol. Chem.*, 245:2199–2204, 1970.
- [475] Y. Yokooji, H. Tomita, H. Atomi, and T. Imanaka. Pantoate kinase and phosphopantothenate synthetase, two novel enzymes necessary for CoA biosynthesis in the *Archaea*. *J. Biol. Chem.*, 284:28137–28145, 2009.
- [476] H. Yonus, P. Neumann, S. Zimmermann, J.J. May, M.A. Marahiel, and M.T. Stubbs. Crystal structure of DltA. Implications for the reaction mechanism of non-ribosomal peptide synthetase adenylation domains. *J. Biol. Chem.*, 283:32484–32491, 2008.
- [477] C.S. Yun, T. Motoyama, and H. Osada. Biosynthesis of the mycotoxin tenuazonic acid by a fungal NRPS-PKS hybrid enzyme. *Nat Commun*, 6:8758–8758, 2015.
- [478] H. Zalkin, P. Argos, S.V. Narayana, A.A. Tiedeman, and J.M. Smith. Identification of a *trpG*-related glutamine amide transfer domain in *Escherichia coli* GMP synthetase. *J. Biol. Chem.*, 260:3350–3354, 1985.
- [479] Y. Zhang, R.H. White, and S.E. Ealick. Crystal structure and function of 5-formaminoimidazole-4-carboxamide ribonucleotide synthetase from *Methanocaldococcus jannaschii*. *Biochemistry*, 47:205–217, 2008.
- [480] X. Zhao, J.R. Miller, Y. Jiang, M.A. Marletta, and J.E. Cronan. Assembly of the covalent linkage between lipoic acid and its cognate enzymes. *Chem. Biol.*, 10:1293–1302, 2003.
- [481] K. Zheng, P.D. Ngo, V.L. Owens, X.P. Yang, and S.O. Mansoorabadi. The biosynthetic pathway of coenzyme F₄₃₀ in methanogenic and methanotrophic archaea. *Science*, 354:339–342, 2016.
- [482] M. Zheng, J. Liu, Z. Yang, X. Gu, F. Li, T. Lou, C. Ji, and Y. Mao. Expression, purification and characterization of human ubiquitin-activating enzyme, UBE1. *Mol. Biol. Rep.*, 37:1413–1419, 2010.
- [483] J. Zhou, W.L. Kelly, B.O. Bachmann, M. Gunsior, C.A. Townsend, and E.I. Solomon. Spectroscopic studies of substrate interactions with clavaminic synthase 2, a multifunctional α -KG-dependent non-heme iron enzyme: Correlation with mechanisms and reactivities. *J. Am. Chem. Soc.*, 123:7388–7398, 2001.
- [484] X. Zhu, J. Liu, and W. Zhang. *De novo* biosynthesis of terminal alkyne-labeled natural products. *Nat. Chem. Biol.*, 11:115–120, 2015.
- [485] K. Ziegler, R. Deutzmann, and W. Lockau. Cyanophycin synthetase-like enzymes of non-cyanobacterial eubacteria: characterization of the polymer produced by a recombinant synthetase of *Desulfitobacterium hafniense*. *Z. Naturforsch. [C]*, 57:522–529, 2002.

- [486] K. Ziegler, A. Diener, C. Herpin, R. Richter, R. Deutzmann, and W. Lockau. Molecular characterization of cyanophycin synthetase, the enzyme catalyzing the biosynthesis of the cyanobacterial reserve material multi-L-arginyl-poly-L-aspartate (cyanophycin). *Eur. J. Biochem.*, 254:154–159, 1998.
- [487] S.B. Zimmerman, J.W. Little, C.K. Oshinsky, and M. Gellert. Enzymatic joining of DNA strands: a novel reaction of diphosphopyridine nucleotide. *Proc. Natl. Acad. Sci. USA*, 57:1841–1848, 1967.

Index

- N*-(5-amino-5-carboxypentanoyl)-L-cysteinyl-D-valine synthase, 32
- L-*allo*-isoleucine—holo-[CmaA peptidyl-carrier protein] ligase, 18
- 3-[(3*aS*,4*S*,7*aS*)-7*a*-methyl-1,5-dioxo-octahydro-1*H*-inden-4-yl]propanoic acid—CoA ligase (GDP-forming), 11
- CoA ligase, 17
- acetate—[acyl-carrier protein] ligase, 16
- acetate—CoA ligase, 8
- acetate—CoA ligase (ADP-forming), 11
- acetoacetate—CoA ligase, 12
- acetone carboxylase, 51
- acetophenone carboxylase, 52
- acetyl-CoA carboxylase, 50
- N*-acetylaspartylglutamate synthase, 36
- N*-acetylaspartylglutamylglutamate synthase, 36
- adenosylcobinamide-phosphate synthase, 24
- adenosylcobyrinic acid synthase (glutamine-hydrolysing), 49
- adenylosuccinate synthase, 41
- aerobactin synthase, 35
- D-alanine—(*R*)-lactate ligase, 7
- D-alanine—D-alanine ligase, 27
- D-alanine—[D-alanyl-carrier protein] ligase, 21
- D-alanine—D-serine ligase, 34
- L-alanine—L-anticapsin ligase, 38
- D-alanine—alanyl-poly(glycerolphosphate) ligase, 30
- D-alanine—poly(phosphoribitol) ligase, 4
- alanine—tRNA ligase, 3
- anthranilate—CoA ligase, 15
- arachidonate—CoA ligase, 12
- arginine—tRNA ligase, 5
- L-arginine-specific L-amino acid ligase, 37
- argininosuccinate synthase, 41
- asparagine synthase (glutamine-hydrolysing), 47
- asparagine—tRNA ligase, 6
- asparaginyl-tRNA synthase (glutamine-hydrolysing), 48
- D-aspartate ligase, 24
- aspartate—ammonia ligase, 22
- aspartate—ammonia ligase (ADP-forming), 22
- aspartate—tRNA ligase, 4
- aspartate—tRNA^{Asn} ligase, 6
- benzoate—CoA ligase, 14
- biotin carboxylase, 43
- biotin—[biotin carboxyl-carrier protein] ligase, 44
- biotin—CoA ligase, 11
- biotin—[methylcrotonoyl-CoA-carboxylase] ligase, 43
- biotin—[methylmalonyl-CoA-carboxytransferase] ligase, 42
- biotin—[propionyl-CoA-carboxylase (ATP-hydrolysing)] ligase, 43
- [butirosin acyl-carrier protein]—L-glutamate ligase, 17
- carbamoyl-phosphate synthase (ammonia), 44
- carbamoyl-phosphate synthase (glutamine-hydrolysing), 48
- carbapenam-3-carboxylate synthase, 40
- 5-(carboxyamino)imidazole ribonucleotide synthase, 45
- (carboxyethyl)arginine β -lactam-synthase, 40
- 6-carboxyhexanoate—CoA ligase, 11
- phenylacetic acid—CoA ligase (GDP-forming), 11
- carnitine—CoA ligase, 19
- carnosine synthase, 29
- 4-chlorobenzoate—CoA ligase, 15
- cholate—CoA ligase, 10
- [citrate (*pro*-3*S*)-lyase] ligase, 13
- citrate—CoA ligase, 12
- N*²-citryl-*N*⁶-acetyl-*N*⁶-hydroxylysine synthase, 35
- β -citrylglutamate synthase, 25
- cobaltochelataase, 57
- cobyrinate *a,c*-diamide synthase, 49
- coenzyme γ -F₄₂₀-2: α -L-glutamate ligase, 33
- coenzyme F₄₂₀-0:L-glutamate ligase, 33
- coenzyme F₄₂₀-1: γ -L-glutamate ligase, 34
- coenzyme F₄₃₀ synthetase, 52
- 4-coumarate—CoA ligase, 11
- CTP synthase (glutamine hydrolysing), 41
- 7-cyano-7-deazaguanine synthase, 45
- cyanophycin synthase (L-arginine-adding), 33
- cyanophycin synthase (L-aspartate-adding), 33
- cyclopeptine synthase, 35
- cysteine—tRNA ligase, 5
- L-cysteine:1*D*-*myo*-inositol 2-amino-2-deoxy- α -*D*-glucopyranoside ligase, 24
- dapdiamide synthase, 37
- 8-demethylnovobiocic acid synthase, 25
- dethiobiotin synthase, 39
- dicarboxylate—CoA ligase, 13
- dihydrofolate synthase, 29
- 3 α ,7 α -dihydroxy-5 β -cholestanate—CoA ligase, 14
- diphthine—ammonia ligase, 25
- DNA ligase (ATP), 52
- DNA ligase (ATP or NAD⁺), 55
- DNA ligase (ATP, ADP or GTP), 55
- DNA ligase (NAD⁺), 53
- E1 SAMP-activating enzyme, 21
- E1 ubiquitin-activating enzyme, 18
- enterobactin synthase, 30
- trans*-feruloyl-CoA synthase, 15
- L-firefly luciferin—CoA ligase, 20
- formate—dihydrofolate ligase, 44
- formate—phosphoribosylaminoimidazolecarboxamide ligase, 46
- formate—tetrahydrofolate ligase, 41
- 5-formyltetrahydrofolate cyclo-ligase, 39
- fumarate—(*S*)-2,3-diaminopropanoate ligase, 37
- 2-furoate—CoA ligase, 15

geranoyl-CoA carboxylase, 51
glutamate—cysteine ligase, 27
glutamate—ethylamine ligase, 23
glutamate—methylamine ligase, 43
glutamate—putrescine ligase, 24
glutamate—tRNA ligase, 5
glutamate—tRNA^{Gln} ligase, 6
glutamine synthetase, 22
glutamine—tRNA ligase, 5
glutamyl-tRNA synthase (glutamine-hydrolysing), 49
 γ -glutamylanilide synthase, 25
 γ -glutamylhistamine synthase, 31
glutarate—CoA ligase, 10
glutathione synthase, 27
glutathionylspermidine synthase, 23
glycine—tRNA ligase, 4
GMP synthase (glutamine-hydrolysing), 47

histidine—tRNA ligase, 6
homoglutathione synthase, 32
hydrogenobyrinic acid *a,c*-diamide synthase (glutamine-hydrolysing), 49
2-hydroxy-7-methoxy-5-methyl-1-naphthoate—CoA ligase, 18
4-hydroxybenzoate adenyltransferase FadD22, 19
3-hydroxybenzoate—CoA ligase, 16
4-hydroxybenzoate—CoA ligase, 14
4-hydroxybutyrate—CoA ligase, 17
4-hydroxyphenylalkanoate adenyltransferase FadD29, 20
3-hydroxypropionyl-CoA synthase, 16

imidazoleacetate—phosphoribosyldiphosphate ligase, 42
indoleacetate—lysine synthetase, 31
isoleucine—tRNA ligase, 2

jasmonoyl—L-amino acid synthetase, 38

leucine—tRNA ligase, 2
lipoate—protein ligase, 26
long-chain fatty acid adenyltransferase FadD28, 19
long-chain-fatty-acid—[acyl-carrier-protein] ligase, 13
long-chain-fatty-acid—CoA ligase, 9
long-chain-fatty-acid—protein ligase, 12
lysine—tRNA ligase, 3
[lysine-biosynthesis-protein LysW]—L-2-aminoadipate ligase, 36

magnesium chelatase, 57
malate—CoA ligase, 10
medium-chain acyl-CoA ligase, 9
medium-chain-fatty-acid—[acyl-carrier-protein] ligase, 19
methionine—tRNA ligase, 3
methylcrotonoyl-CoA carboxylase, 51
4-methyleneglutamate—ammonia ligase, 23
3-(methylthio)propionyl—CoA ligase, 18

NAD⁺ synthase, 22
NAD⁺ synthase (glutamine-hydrolysing), 47

nebramycin 5' synthase, 8
Ni-sirohydrochlorin *a,c*-diamide reductive cyclase, 40
Ni-sirohydrochlorin *a,c*-diamide synthase, 50
nicotinate phosphoribosyltransferase, 45

olefin β -lactone synthetase, 8
oxalate—CoA ligase, 10
3-oxocholest-4-en-26-oate—CoA ligase, 17
2-oxoglutarate carboxylase, 52

pantoate— β -alanine ligase (ADP-forming), 36
pantoate— β -alanine ligase (AMP-forming), 26
phenylacetate—CoA ligase, 15
phenylalanine—tRNA ligase, 5
3'-phosphate/5'-hydroxy nucleic acid ligase, 56
O-phospho-L-serine—tRNA ligase, 7
4-phosphopantoate— β -alanine ligase, 34
phosphopantothenate—cysteine ligase (ATP), 38
phosphopantothenate—cysteine ligase (CTP), 27
phosphoribosylamine—glycine ligase, 43
phosphoribosylaminoimidazolesuccinocarboxamide synthase, 27
phosphoribosylformylglycinamide cyclo-ligase, 39
phosphoribosylformylglycinamide synthase, 47
phytanate—CoA ligase, 14
prokaryotic ubiquitin-like protein ligase, 26
L-proline—[L-prolyl-carrier protein] ligase, 21
proline—tRNA ligase, 4
propionate—CoA ligase, 12
propionyl-CoA carboxylase, 51
pyrrolysine—tRNA^{Pyl} ligase, 7
pyruvate carboxylase, 50

ribose-5-phosphate—ammonia ligase, 42
RNA 3'-terminal-phosphate cyclase (ATP), 54
RNA 3'-terminal-phosphate cyclase (GTP), 54
RNA ligase (ATP), 54

serine—tRNA ligase, 3
succinate—CoA ligase (ADP-forming), 10
succinate—CoA ligase (GDP-forming), 9
o-succinylbenzoate—CoA ligase, 14

tenuazonic acid synthetase, 38
tetrahydrofolate synthase, 31
tetrahydrosarcapterin synthase, 34
threonine—tRNA ligase, 2
(2,2,3-trimethyl-5-oxocyclopent-3-enyl)acetyl-CoA synthase, 16
tRNA^{Ile2}-agmatinylcytidine synthase, 46
tRNA^{Ile}-lysidine synthase, 45
trypanothione synthase, 23
tryptophan—tRNA ligase, 2
tubulin—tyrosine ligase, 32
tyramine—L-glutamate ligase, 46
tyrosine—arginine ligase, 32
tyrosine—tRNA ligase, 2

UDP-*N*-acetylmuramate—L-alanine ligase, 28

UDP-*N*-acetylmuramate—L-alanyl- γ -D-glutamyl-*meso*-2,6-diaminoheptanedioate
ligase, 36

UDP-*N*-acetylmuramoyl-L-alanine—D-glutamate ligase, 28

UDP-*N*-acetylmuramoyl-L-alanine—L-glutamate ligase, 39

UDP-*N*-acetylmuramoyl-L-alanyl-D-glutamate—2,6-diaminopimelate
ligase, 30

UDP-*N*-acetylmuramoyl-L-alanyl-D-glutamate—D-lysine ligase,
35

UDP-*N*-acetylmuramoyl-L-alanyl-D-glutamate—L-lysine ligase,
28

UDP-*N*-acetylmuramoyl-tripeptide—D-alanyl-D-alanine ligase,
29

urea carboxylase, 42

O-ureido-D-serine cyclo-ligase, 40

valine—tRNA ligase, 3