

Carboxylases for CO2 Biotransformation

Subjects: [Biochemistry & Molecular Biology](#)

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The rapid growth of atmospheric CO₂ concentration by continuous consumption of fossil fuels is one of the main causes of global warming. Turning CO₂ into fuels and chemicals through biotransformation offers a win-win strategy to both decrease atmospheric CO₂ and efficiently exploit carbon resources. The overall efficiency of CO₂ biotransformation in vitro and CO₂ assimilation in vivo is generally determined by the biochemical properties of carboxylases. Herein, we summarized carboxylases based on catalytic mechanism and CO₂ biotransformation in vitro and CO₂ assimilation in vivo based on newly mined or designed carboxylases.

C1 resource utilization

carboxylases

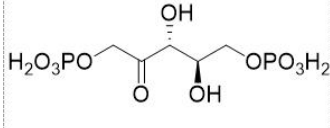
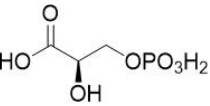
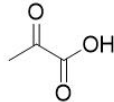
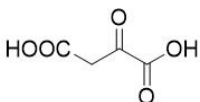
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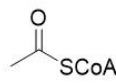
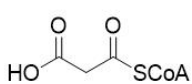
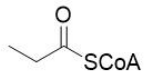
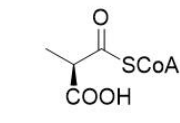
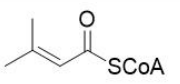
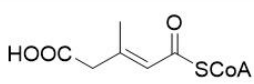
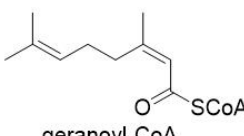
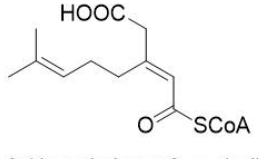

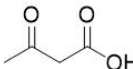
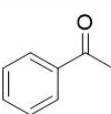
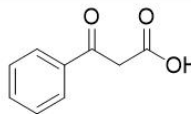
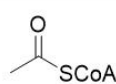
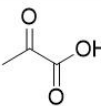
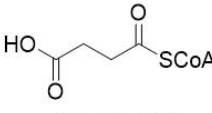
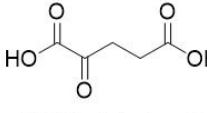
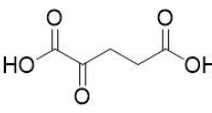
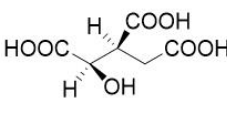
designed pathway

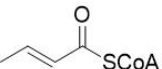
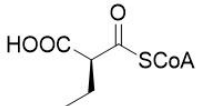
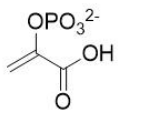
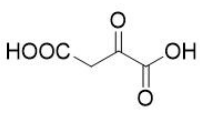
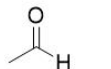
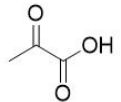
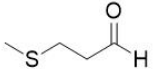
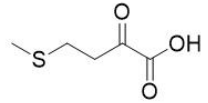
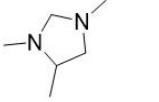
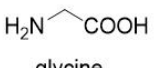
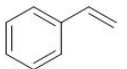
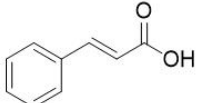

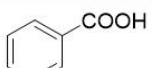
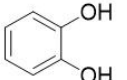
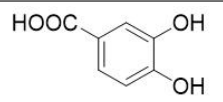

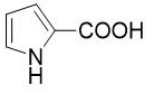
1. Carboxylases for CO₂ Biotransformation

CO₂ is a poor electrophile and usually exists as bicarbonate in an aqueous solution. Therefore, the carboxylation reaction often requires energy (adenosine triphosphate (ATP), nicotinamide adenine dinucleotide phosphate (NADPH), or ferredoxin) or the assistance of coenzymes (metal ion, ThDP, and prenylated flavin mononucleotide (prFMN), etc.) [24]. We divide carboxylases into seven categories: (1) Only divalent metal-dependent carboxylases, (2) ATP-dependent carboxylases, (3) redox equivalents-dependent carboxylases, (4) substrate-activated carboxylases, (5) ThDP-dependent carboxylases, (6) multi-enzyme complex constructed carboxylase, (7) prFMN-dependent carboxylases. Representative carboxylases are shown in Table 1.

Table 1. Representative carboxylases for CO₂ fixation.

Aliphatic Substrates	Products	Enzyme and Category	Pathway
<div></div> <div>D-ribulose 1,5-bisphosphate</div>	<div></div> <div>3-phosphoglycerate</div>	<div>Rubisco</div> <div>EC-4.1.1.39</div> <div>Only divalent metal-dependent carboxylases</div>	Calvin-Benson-Bassham (CBB) cycle
<div></div> <div>pyruvate</div>	<div></div> <div>oxaloacetate</div>	<div>PC</div> <div>EC-6.4.1.1</div> <div>ATP-dependent carboxylases</div>	/

 <p>acetyl-CoA</p>	 <p>malonyl-CoA</p>	<p>ACC</p> <p>EC-6.4.1.2</p> <p>ATP-dependent carboxylase</p>	<p>3-hydroxypropionate-cycle (HP)</p> <p>and</p> <p>3-HP/4-hydroxybutyrate-cycle (HB)</p>
 <p>propionyl-CoA</p>	 <p>(S)-methylmalonyl-CoA</p>	<p>PCC</p> <p>EC-6.4.1.3</p> <p>ATP-dependent carboxylase</p>	<p>3-HP</p> <p>and</p> <p>3-HP/4-HB</p>
 <p>3-methylcrotonyl-CoA</p>	 <p>3-methylglutaconyl-CoA</p>	<p>MCC</p> <p>EC-6.4.1.4</p> <p>ATP-dependent carboxylase</p>	<p>/</p>
 <p>geranyl-CoA</p>	 <p>3-(4-methylpent-3-en-1-yl)pent-2-enedioyl-CoA</p>	<p>GCC</p> <p>EC-6.4.1.5</p> <p>ATP-dependent carboxylase</p>	<p>/</p>
 <p>acetone</p>	 <p>acetoacetate</p>	<p>AC</p> <p>EC-6.4.1.6</p> <p>ATP-dependent carboxylase</p>	<p>/</p>
 <p>acetophenone</p>	 <p>3-oxo-3-phenylpropanoate</p>	<p>APC</p> <p>EC-6.4.1.8</p> <p>ATP-dependent carboxylase</p>	<p>/</p>
 <p>acetyl-CoA</p>	 <p>pyruvate</p>	<p>PS</p> <p>EC-1.2.7.1</p> <p>Redox-equivalents-dependent carboxylase</p>	<p>4-HB</p>
 <p>succinyl-CoA</p>	 <p>2-Ketoglutaric acid</p>	<p>OGS</p> <p>EC-1.2.7.3</p> <p>Redox-equivalents-dependent carboxylase</p>	<p><u>cTCA</u></p>
 <p>2-Ketoglutaric acid</p>	 <p>isocitrate</p>	<p>IDH</p> <p>EC-1.1.1.41/42</p> <p>Redox-equivalents-dependent carboxylase</p>	<p><u>cTCA</u></p>

 crotonyl-CoA ₁	 (2S)-ethylmalonyl-CoA ₁	CCR¶ EC-1.3.1.85¶ Redox-equivalents-dependent-carboxylases	CETCH-pathway¶
 phosphoenolpyruvate ₁	 oxaloacetate ₁	PEPC¶ EC-4.1.1.31¶ Substrate-activated-carboxylases	4-HB-and¶ MCG¶ pathways
 acetaldehyde ₁	 pyruvate ₁	PDC¶ EC-4.1.1.1¶ <u>ThDP</u> -dependent-carboxylases	/¶
 methional ₁	 4-methylthio-2-oxobutanoate	<u>KdcA</u> ¶ from <i>Lactococcus lactis</i> ¶ <u>ThDP</u> -dependent-carboxylases	/¶
 5,10-methylene-THF ₁	 glycine ₁	GCS¶ Multi-enzyme-complex-constructed-carboxylases	reductive-glycine- pathway¶ ₁
 styrene ₁	 cinnamic acid ₁	Ferulic-acid-decarboxylase-(FDC1)¶ <u>prFMN</u> -dependent-carboxylases	/¶
 benzene ₁	 benzoic acid ₁	Benzene-carboxylase¶ <u>prFMN</u> -dependent-carboxylases	/¶
 catechol ₁	 3,4-dihydroxybenzoic acid ₁	3,4-dihydroxybenzoic-acid-decarboxylase-from- <i>E. cloacae</i> -(<u>EcAroY</u>)¶ <u>prFMN</u> -dependent-carboxylases	/¶
 pyrrole ₁	 pyrrole-2-carboxylic acid ₁	Pyrrole-2-carboxylic-acid-decarboxylase¶ <u>prFMN</u> -dependent-carboxylases	/¶

2. ATP-Dependent Carboxylases

Biotin-dependent carboxylases include pyruvate carboxylase (PC, EC 6.4.1.1), acetyl-CoA carboxylase (ACC, EC 6.4.1.2), propionyl-CoA carboxylase (PCC, EC 6.4.1.3), 3-methylcrotonoyl-CoA carboxylase (MCC, EC 6.4.1.4), and geranoyl-CoA carboxylase (GCC, EC 6.4.1.5). They are widely distributed in nature and can be found in archaea, bacteria, algae, fungi, plants, and animals^[1]. The catalytic process of biotin-dependent carboxylases can be divided into two steps (Figure 2). First, the biotin carboxylase (BC) domain catalyzes the ATP-dependent

carboxylation of the N1' atom of the biotin cofactor, using bicarbonate as the CO₂ donor. Second, the carboxyltransferase (CT) domain transfers the CO₂ from carboxy-biotin to the substrates^{[2][3][4]}. The site for carboxylation is on the α-carbon of saturated substrates (pyruvate, acetyl-CoA, and propionyl-CoA) or the γ-carbon of α, β-unsaturated substrates (3-methylcrotonyl-CoA, geranyl-CoA). Acetyl-CoA carboxylase and propionyl-CoA carboxylase are two carboxylases of 3-hydroxypropionate/malyl-CoA cycle and 3-hydroxypropionate/4-hydroxybutyrate cycle^{[5][6]}.

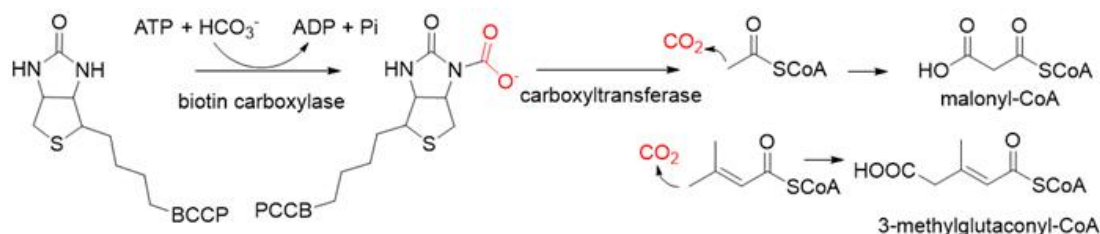


Figure 2. The catalytic process of biotin-dependent carboxylases^{[2][3][4]}.

Acetone carboxylases (AC, EC 6.4.1.6) are soluble cytoplasmic enzymes, and can be found in many species of aerobic, anaerobic phototrophic bacteria, and even microaerobic gastric human pathogenic species *Helicobacter pylori*. They catalyze the carboxylation of acetone to form acetoacetate at the expense of ATP^[7]. There are two different types of acetone carboxylases. One requires 2 ATP equivalents as an energy supply for the carboxylation reaction, while another requires 4 ATP equivalents. The main difference in catalytic mechanism lies in the processes of substrate activation. The catalytic mechanism proposed for acetone carboxylase of *Xanthobacter/Rhodobacter* is that one ATP is sequentially hydrolyzed to ADP and AMP to activate acetone and bicarbonate, respectively. While the catalytic mechanism of acetone carboxylase from *Aromatoleum* is that 2 ATP are hydrolyzed to 2 AMP to activate two substrates^[8]. Acetoacetate can be activated by a CoA ligase to form acetoacetyl-CoA, which is cleaved to form 2 acetyl-CoA by thiolase. Therefore, a new pathway from isopropanol and CO₂ to acetyl-CoA can be constructed. Acetophenone carboxylase (APC, EC 6.4.1.8) catalyzes the carboxylation of acetophenone to benzoylacetate^[9]. Different from the above two activation processes of acetone carboxylases, acetophenone and bicarbonate are all activated by hydrolyzing ATP to ADP.

3. Redox Equivalents-Dependent Carboxylases

Pyruvate synthase (PS, EC 1.2.7.1) and 2-oxoglutarate synthase (OGS, EC 1.2.7.3) are a class of enzymes sharing a similar catalytic mechanism^{[10][11]}. They belong to strictly anaerobic enzymes and show low catalytic activity. Acetyl-CoA can be reductively carboxylated by pyruvate synthase at the expense of two equivalents of ferredoxin to generate pyruvate. Similarly, succinyl-CoA can be converted to 2-oxoglutarate by 2-oxoglutarate synthase^[12]. Different from the above two enzymes, isocitrate dehydrogenase (IDH, EC 1.1.1.41/42) converts 2-oxoglutarate to isocitrate at the expense of NAD(P)H^[13]. The carboxylation process of isocitrate dehydrogenase is assumed to proceed via the enolate intermediate of 2-oxoglutarate, which is formed with the assistance of divalent metal ions Mg²⁺ or Mn²⁺. After the addition of CO₂, the unstable keto-tricarboxylic acid intermediate is immediately

reduced by NAD(P)H to yield stable isocitrate (Figure 3A). 2-oxoglutarate synthase and isocitrate dehydrogenase are carboxylases of the reductive tricarboxylic acid (rTCA) cycle.

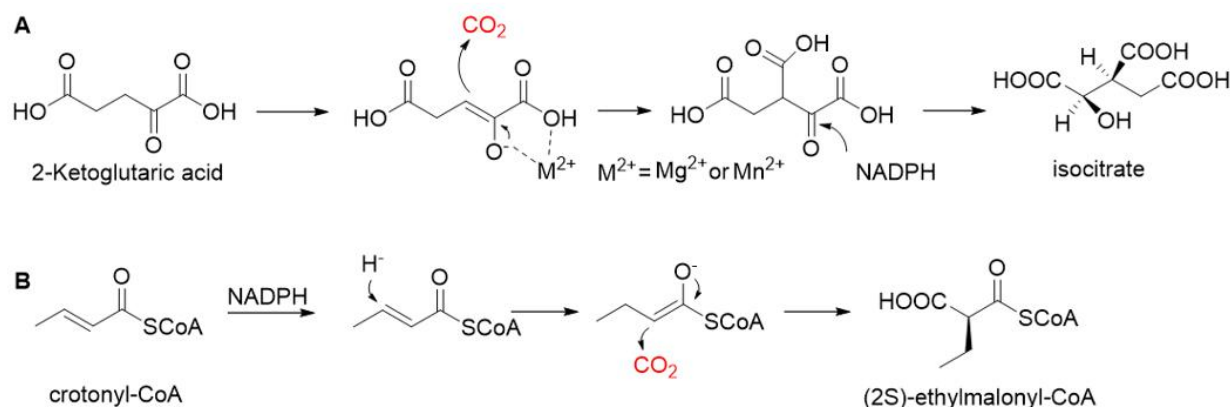


Figure 3. The catalytic mechanism of isocitrate dehydrogenase and crotonyl-CoA carboxylase/reductase. **(A)** The catalytic mechanism of isocitrate dehydrogenase^[13]. **(B)** The catalytic mechanism of crotonyl-CoA carboxylase/reductase^[14].

Enoyl-CoA carboxylases/reductases (ECRs) are a class of carboxylases that exist in secondary metabolism, as well as in central carbon metabolism of α -proteobacteria and *Streptomyces*^[14]. The best-studied ECR is crotonyl-CoA carboxylase/reductase (CCR, EC 1.3.1.85) that catalyzes NADPH-dependent reductive carboxylation of crotonyl-CoA into (2S)-ethylmalonyl-CoA. The mechanism of CCR is assumed to proceed via nucleophilic hydride attack at β -carbon of the enoyl-CoA ester; the forming enolate is trapped by CO_2 to generate (2S)-ethylmalonyl-CoA (Figure 3B). Recently, combining experimental biochemistry, protein crystallography, and advanced computer simulations, Gabriele M. M. Stoffel et al. determined the CO_2 -binding residues at the active site of crotonyl-CoA carboxylase/reductase from *Kitasatospora setae*^[15]. Propionyl-CoA synthase from *Erythrobacter* sp. NAP1, as well as an acrylyl-CoA reductase from *Nitrosopumilus maritimus*, have almost no carboxylation activity. Based on the determined CO_2 -binding residues, they used rational design to engineer two enzymes into carboxylases by increasing interactions of the proteins with CO_2 and suppressing diffusion of water to the active site^[16].

Relative to Rubisco, CCR is oxygen-insensitive, does not react with O_2 , requires only the NADPH, and catalyzes CO_2 fixation with higher efficiency ($K_{cat}/K_m = 1642.6 \text{ s}^{-1} \text{ mM}^{-1}$)^{[17][18]}. All of these characteristics make CCR a good candidate enzyme for the fixation of CO_2 . Based on CCR, Tobias J. Erb research group constructed a crotonyl-CoA/ethylmalonyl-CoA/hydroxybutyryl-CoA (CETCH) cycle in vitro^[19], which consists of 17 enzymes and can convert CO_2 into organic molecules at a rate of 5 nanomoles of CO_2 per minute per milligram of protein (Figure 4). Recently, they successfully encapsulated thylakoids isolated from the spinach plant along with all enzymes of the CETCH pathway within water-in-oil droplets^[20]. The encapsulated system could use light energy to produce glycolate from CO_2 , while also phosphorylating ADP to ATP.

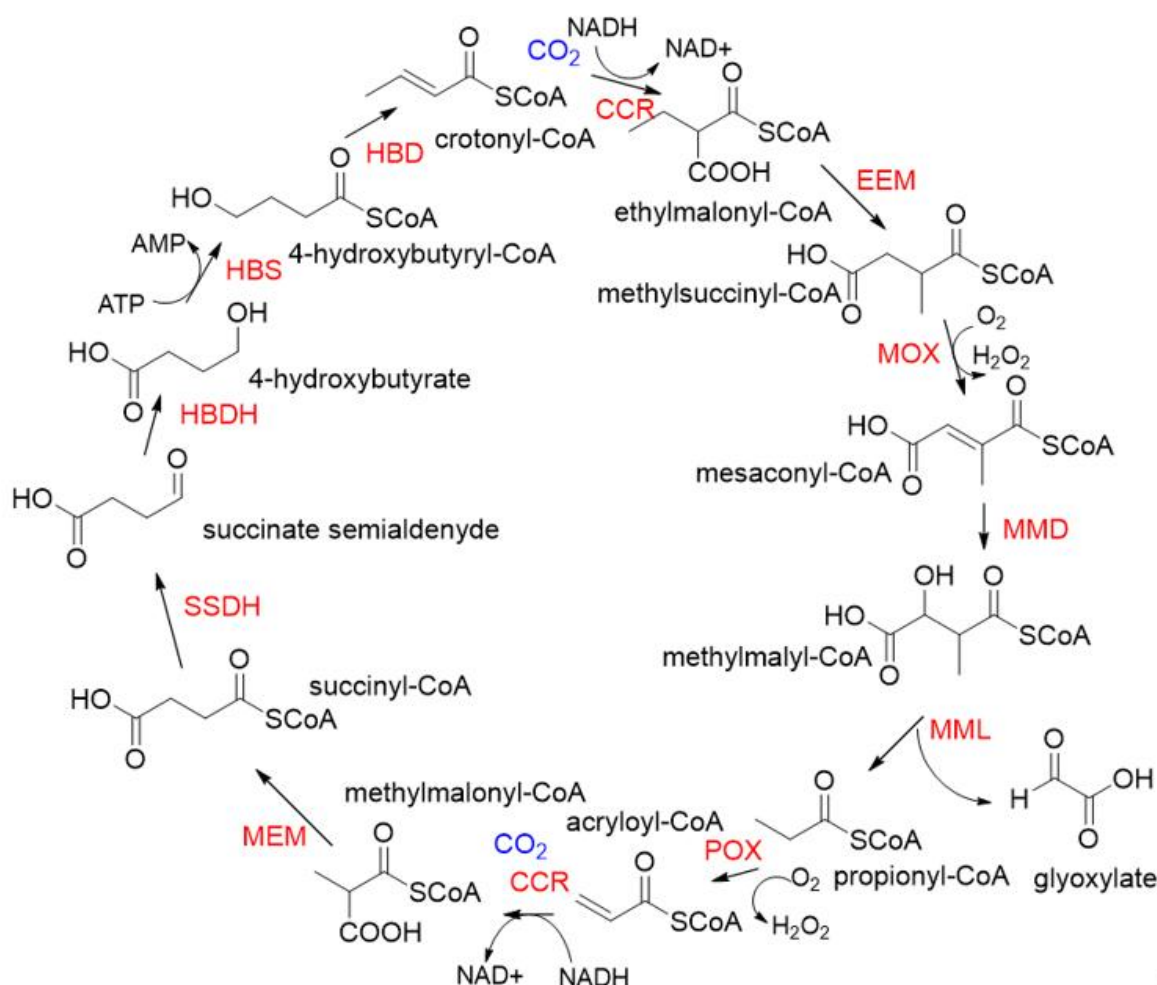


Figure 4. The crotonyl-CoA/ethylmalonyl-CoA/hydroxybutyryl-CoA cycle pathway (CETCH pathway)^[19]. CCR, crotonyl-CoA carboxylase/reductase; EEM, ethylmalonyl-CoA epimerase, and mutase; MOX, methylsuccinyl-CoA oxidase; MMD, methylmalyl-CoA dehydratase; MML, methylmalyl-CoA lyase; POX, propionyl-CoA oxidase; MEM, methylmalonyl-CoA epimerase, and mutase; SSDH, succinate semialdehyde dehydrogenase; HBDH, 4-hydroxybutyrate dehydrogenase; HBS, 4-hydroxybutyryl-CoA synthetase; HBD, 4-hydroxybutyryl-CoA dehydratase.

4. Substrate-Activated Carboxylases

Phosphoenolpyruvate (PEP) carboxylase (PEPC, EC 4.1.1.31) catalyzes the irreversible carboxylation of PEP to form oxaloacetate (OAA) using Mg²⁺ or Mn²⁺ as a cofactor^[21]. This kind of enzyme is present in most photosynthetic organisms^[22]. PEPC is used to replenish intermediates of the TCA cycle for amino acid biosynthesis, or to shuttle CO₂ between the mesophyll and bundle sheath cells in C₄ plants. The catalytic mechanism of PEPC has been well studied (Figure 5). First, bicarbonate act as a nucleophile to attack phosphate groups in PEP, yielding carboxyphosphate and enolates of pyruvate, which is stabilized by metal ions Mn²⁺. Next, carboxyphosphate decomposes into inorganic phosphate and CO₂, which is attacked by enolates of pyruvate to form OAA^[23].

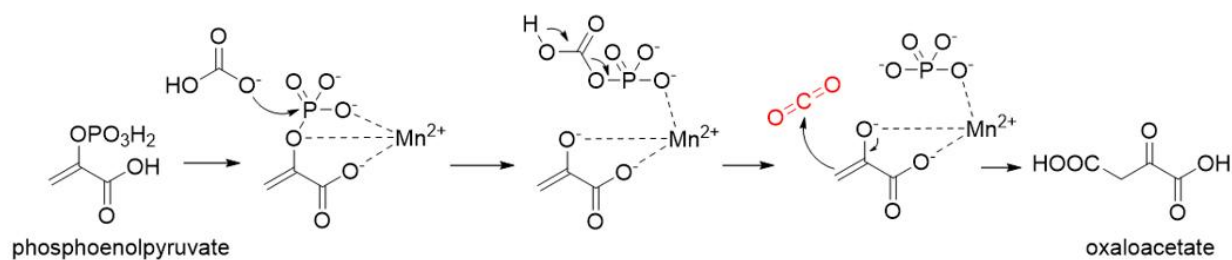


Figure 5. The catalytic mechanism of phosphoenolpyruvate carboxylase^[23].

PEPC is known to be one of the most active carboxylases ($K_{cat}/K_m = 23,792 \text{ s}^{-1} \text{ mM}^{-1}$)^[24]. Based on PEPC, Hong Yu et al. constructed a synthetic malyl-CoA-glycerate (MCG) pathway^[25], which is capable of converting one C3 sugar to two acetyl-CoA via fixation of one CO₂ equivalent, or assimilating glyoxylate, a photorespiration intermediate, to produce acetyl-CoA without carbon loss (Figure 6). Coupling the MCG pathway with the CBB cycle, photosynthetic organisms utilize only 5.5 ATP and 1.5 Rubisco turnovers to produce one acetyl-CoA from CO₂ equivalents, while the native pathway requires 7 ATP and 3 Rubisco turnovers. When transferring the MCG pathway into a photosynthetic organism *Synechococcus elongates* PCC7942, the intracellular acetyl-CoA level increased, and bicarbonate assimilation was improved by roughly 2-fold.

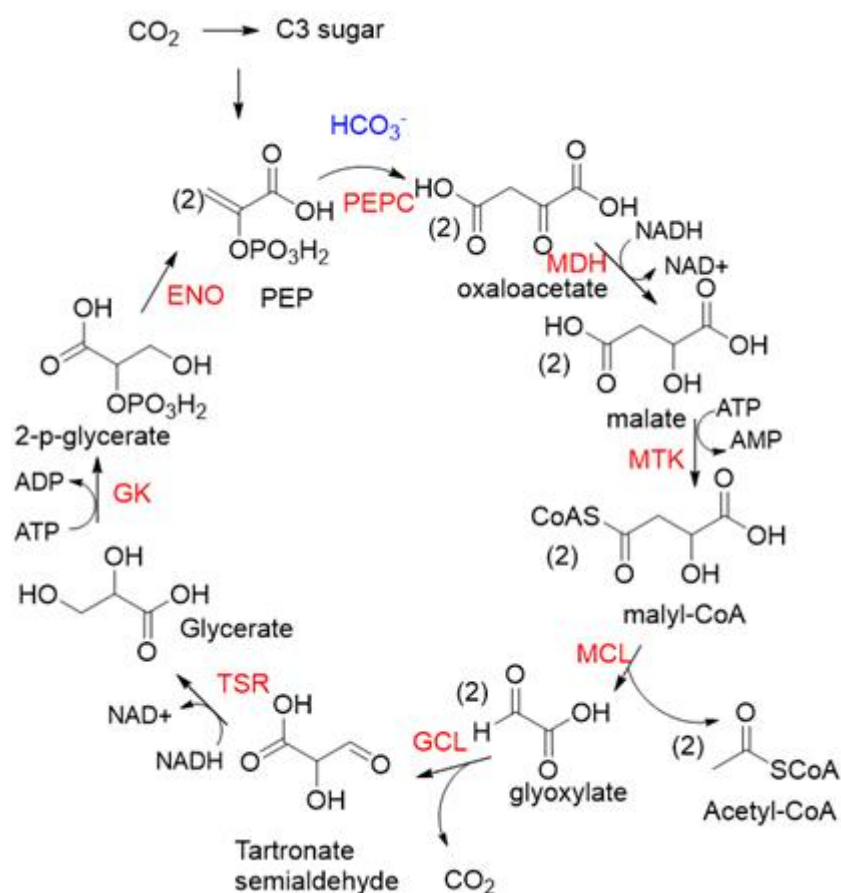


Figure 6. The synthetic malyl-CoA-glycerate (MCG) pathway^[25]. PEPC, PEP carboxylase; MDH, malate dehydrogenase; MTK, malate thiokinase; MCL, malyl-CoA lyase; GCL, glyoxylate carboligase; TSR, tartronate semialdehyde reductase; GK, glycerate kinase; ENO, enolase.

5. ThDP-Dependent Carboxylases

Pyruvate decarboxylase (PDC, EC 4.1.1.1) is a key enzyme of carbon metabolism at the branching point between aerobic respiration and anaerobic alcoholic fermentation, and can be found in some bacteria, yeasts, and plants^[26]. PDC catalyzes the decarboxylation of pyruvate by using ThDP and Mg²⁺ as cofactors (Figure 7). This enzyme has been successfully applied to yield pyruvic acid through the reverse carboxylation reaction. To favor the carboxylation, high pH and high bicarbonate concentration are needed^[27]. In addition to using a high concentration of bicarbonate solution as a CO₂ source, elevated CO₂ pressure is also an effective way to drive the direction of carboxylation. Combining branched-chain α -keto acid decarboxylase (KdcA) from *Lactococcus lactis* with transaminase or amino acid dehydrogenase, Julia Martin et al. achieved the synthesis of L-methionine from the abundant industrial intermediate methional under a 2 bar CO₂ atmosphere^[28].

Figure 7. The catalytic mechanism of pyruvate decarboxylase^{[26][27]}.

6. Multi-Enzyme Complex Constructed Carboxylase

The glycine cleavage system (GCS) is common among many organisms because of its involvement in glycine and serine catabolism^[29]. The GCS converts glycine to CO₂, NH₄⁺, and methylene-THF. GCS is composed of four proteins, a carrier protein, and three enzymes. They are lipoic acid-containing protein (GcvH), glycine dehydrogenase (GcvP), aminomethyltransferase (GcvT), and lipoamide dehydrogenase (Lpd), respectively. The glycine cleavage process can be divided into three steps. The first step is the decarboxylation of glycine by the glycine dehydrogenase. The decarboxylated moiety is then further degraded by the aminomethyl transferase with the aid of tetrahydrofolate. The last step is the reoxidation of the two sulfhydryl groups to form lipoic acid-generating NADH by dihydrolipomide dehydrogenase. Two sulfhydryl groups or lipoate attached to the lipoic acid-containing protein act as intermediate shuttles.

Now, GCS is confirmed to be reversible (rGCS) and can condense the C1 moiety of methylene-THF with CO₂ and ammonia to produce glycine^[30], which shows great application potential for reductive glycine pathway (RGP). Arren Bar-Even's research group has made a series of encouraging progress^{[31][32]}. Especially, they redesigned the central carbon metabolism of the model bacterium *E. coli* for growth on one-carbon compounds (formate and methanol) using the RGP^[32] (Figure 8). Recently, Irene Sánchez-Andrea et al. demonstrated that sulfate-reducing bacterium *Desulfovibrio desulfuricans* (strain G11) could grow autotrophically via the RGP using hydrogen and sulfate as energy substrates^[33]. This work first demonstrates that autotrophic microbial growth can be fully supported by RGP, which is a highly ATP-efficient CO₂ fixation pathway.

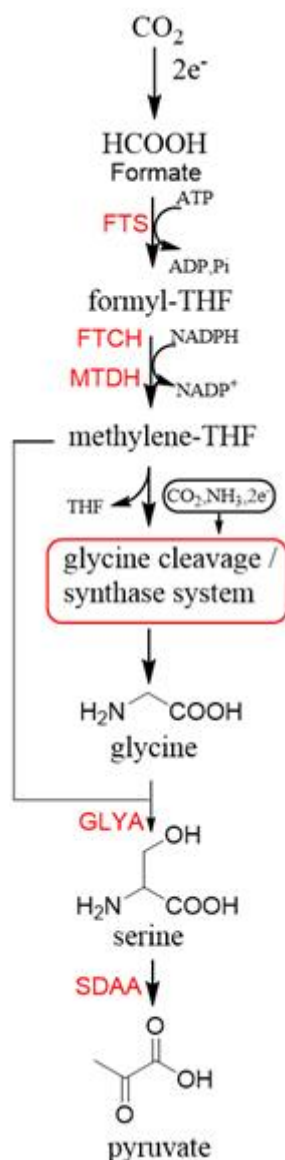


Figure 8. The reductive glycine pathway (RGP)^[32]. FTS, formyl-THF synthase; FTCH, formyl-THF cyclohydrolase; MTDH, methylene-THF dehydrogenase; GLYA, L-serine hydroxymethyltransferase; SDAA, L-serine dehydratase.

7. prFMN-Dependent Carboxylases

prFMN-dependent decarboxylases catalyze the non-oxidative reversible decarboxylation of aromatic substrates, and play a pivotal role in bacterial ubiquinone (coenzyme Q) biosynthesis and microbial biodegradation of aromatic compounds^{[34][35]}. The prFMN cofactor is provided by an associated prenyltransferase (UbiX), which extends the isoalloxazine FMN ring system through prenylation with a fourth non-aromatic ring. The catalytically active iminium species of the cofactor (prFMN^{iminium}) is obtained by oxidizing the reduced prFMN with O_2 . There are two different catalytic reaction mechanisms for the prFMN-assisted (de)carboxylation reaction. For α , β -unsaturated carboxylic acids, the reaction proceeds through the intermolecular 1, 3-dipolar cycloaddition step. While for protocatechuic acid-type substrates, the electrophilic character of the iminium ion of prFMN^{iminium} enables reversible (de)carboxylation via a mono-covalently bound quinoid-cofactor intermediate. prFMN-dependent decarboxylases

encompass a wide range of substrates^[36], including non-aromatic α , β -unsaturated (acrylic) acid derivatives, catechol, and 4-hydroxybenzoic acid derivatives, polycyclic aromatic hydrocarbons (PAHs), and heterocyclic substrates. Recently, combining ferulic acid decarboxylase (FDC, prFMN-dependent) with carboxylic acid reductase (CAR), alcohol dehydrogenase (ADH), or imine reductase (IREC), Godwin A. Aleku et al. designed cascade reactions to enable efficient functionalization of terminal alkenes to the corresponding aldehyde, alcohol, amide or amine derivatives through ambient CO₂ fixation^[37].

References

1. Tong, L. Structure and function of biotin-dependent carboxylases. *Cell Mol. Life Sci.* 2013, 70, 863–891.
2. Sarawut, J.; John, C.W. The Biotin Enzyme Family: Conserved Structural Motifs and Domain Rearrangements. *Protein Pept. Sci.* 2003, 4, 217–229.
3. Maurice, M.; Reinhardt, L.; Surinya, K.H.; Attwood, P.V.; Wallace, J.C.; Cleland, W.W.; Rayment, I. Domain architecture of pyruvate carboxylase, a biotin-dependent multifunctional enzyme. *Science* 2007, 317, 1076–1079.
4. Huang, C.S.; Sadre-Bazzaz, K.; Shen, Y.; Deng, B.; Zhou, Z.H.; Tong, L. Crystal structure of the $\alpha_6\beta_6$ holoenzyme of propionyl-coenzyme A carboxylase. *Nature* 2010, 466, 1001–1005.
5. Tong, L. Acetyl-coenzyme A carboxylase: Crucial metabolic enzyme and attractive target for drug discovery. *Mol. life Sci. CMLS* 2005, 62, 1784–1803.
6. Wongkittichote, P.; Ah Mew, N.; Chapman, K.A. Propionyl-CoA carboxylase—A review. *Genet. Metab.* 2017, 122, 145–152.
7. Heider, J.; Schuhle, K.; Frey, J.; Schink, B. Activation of Acetone and Other Simple Ketones in Anaerobic Bacteria. *J. Mol. Microbiol. Biotechnol.* 2016, 26, 152–164.
8. Boyd, J.M.; Ensign, S.A. ATP-Dependent Enolization of Acetone by Acetone Carboxylase from *Rhodobacter capsulatus*. *Biochemistry* 2005, 44, 8543–8553.
9. Weidenweber, S.; Schühle, K.; Demmer, U.; Warkentin, E.; Ermler, U.; Heider, J. Structure of the acetophenone carboxylase core complex: Prototype of a new class of ATP-dependent carboxylases/hydrolases. *Rep.* 2017, 7, 39674.
10. Mai, X.; Adams, M.W. Characterization of a fourth type of 2-keto acid-oxidizing enzyme from a hyperthermophilic archaeon: 2-ketoglutarate ferredoxin oxidoreductase from *Thermococcus litoralis*. *J. Bacteriol.* 1996, 178, 5890–5896.
11. Menon, A.L.; Hendrix, H.; Hutchins, A.; Verhagen, M.F.J.M.; Adams, M.W.W. The δ -Subunit of Pyruvate Ferredoxin Oxidoreductase from *Pyrococcus furiosus* Is a Redox-Active, Iron–Sulfur

- Protein: Evidence for an Ancestral Relationship with 8Fe-Type Ferredoxins. *Biochemistry* 1998, 37, 12838–12846.
12. Ragsdale, S.W. Pyruvate Ferredoxin Oxidoreductase and Its Radical Intermediate. *Rev.* 2003, 103, 2333–2346.
 13. Soundar, S.; O'Hagan, M.; Fomulu, K.S.; Colman, R.F. Identification of Mn²⁺-binding Aspartates from α , β , and γ Subunits of Human NAD-dependent Isocitrate Dehydrogenase. *Biol. Chem.* 2006, 281, 21073–21081.
 14. Erb, T.J.; Berg, I.A.; Brecht, V.; Müller, M.; Fuchs, G.; Alber, B.E. Synthesis of C₅-dicarboxylic acids from C₂-units involving crotonyl-CoA carboxylase/reductase: The ethylmalonyl-CoA pathway. *Natl. Acad. Sci. USA* 2007, 104, 10631.
 15. Stoffel, G.M.M.; Saez, D.A.; DeMirici, H.; Vögeli, B.; Rao, Y.; Zarzycki, J.; Yoshikuni, Y.; Wakatsuki, S.; Vöhringer-Martinez, E.; Erb, T.J. Four amino acids define the CO₂ binding pocket of enoyl-CoA carboxylases/reductases. *Natl. Acad. Sci. USA* 2019, 116, 13964.
 16. Bernhardsgrutter, I.; Schell, K.; Peter, D.M.; Borjian, F.; Saez, D.A.; Vöhringer-Martinez, E.; Erb, T.J. Awakening the Sleeping Carboxylase Function of Enzymes: Engineering the Natural CO₂-Binding Potential of Reductases. *J. Am. Chem. Soc.* 2019, 141, 9778–9782.
 17. Erb, T.J.; Brecht, V.; Fuchs, G.; Müller, M.; Alber, B.E. Carboxylation mechanism and stereochemistry of crotonyl-CoA carboxylase/reductase, a carboxylating enoyl-thioester reductase. *Natl. Acad. Sci. USA* 2009, 106, 8871.
 18. Peter, D.M.; Schada von Borzyskowski, L.; Kiefer, P.; Christen, P.; Vorholt, J.A.; Erb, T.J. Screening and Engineering the Synthetic Potential of Carboxylating Reductases from Central Metabolism and Polyketide Biosynthesis. *Angewandte Chemie* 2015, 54, 13457–13461.
 19. Schwander, T.; Schada von Borzyskowski, L.; Burgener, S.; Cortina, N.S.; Erb, T.J. A synthetic pathway for the fixation of carbon dioxide in vitro. *Science* 2016, 354, 900–904.
 20. Miller, T.; Beneyton, T.; Schwander, T.; Diehl, C.; Girault, M.; McLean, R.; Chotel, T.; Claus, P.; Cortina, N.; Baret, J.-C.; et al. Light-powered CO₂ fixation in a chloroplast mimic with natural and synthetic parts. *Science* 2020, 368, 649–654.
 21. Kai, Y.; Matsumura, H.; Izui, K. Phosphoenolpyruvate carboxylase: Three-dimensional structure and molecular mechanisms. *Biochem. Biophys.* 2003, 414, 170–179.
 22. Hatch, M.D. C₄ photosynthesis: A unique blend of modified biochemistry, anatomy and ultrastructure. *Biophys. Acta Rev. Bioenerg.* 1987, 895, 81–106.
 23. Chollet, R.; Vidal, J.; O'Leary, M.H. PHOSPHOENOLPYRUVATE CARBOXYLASE: A Ubiquitous, Highly Regulated Enzyme in Plants. *Rev. Plant Physiol. Plant Mol. Biol.* 1996, 47, 273–298.

24. Cotton, C.A.; Edlich-Muth, C.; Bar-Even, A. Reinforcing carbon fixation: CO₂ reduction replacing and supporting carboxylation. *Opin. Biotechnol.* 2018, 49, 49–56.
25. Yu, H.; Li, X.; Duchoud, F.; Chuang, D.S.; Liao, J.C. Augmenting the Calvin-Benson-Bassham cycle by a synthetic malyl-CoA-glycerate carbon fixation pathway. *Commun.* 2018, 9, 2008.
26. Kutter, S.; Wille, G.; Relle, S.; Weiss, M.S.; Hubner, G.; Konig, S. The crystal structure of pyruvate decarboxylase from *Kluyveromyces lactis*. Implications for the substrate activation mechanism of this enzyme. *FEBS J.* 2006, 273, 4199–4209.
27. Miyazaki, M.; Shibue, M.; Ogino, K.; Nakamura, H.; Maeda, H. Enzymatic synthesis of pyruvic acid from acetaldehyde and carbon dioxide. *Commun.* 2001, 18, 1800–1801.
28. Martin, J.; Eisoldt, L.; Skerra, A. Fixation of gaseous CO₂ by reversing a decarboxylase for the biocatalytic synthesis of the essential amino acid L-methionine. *Catal.* 2018, 1, 555–561.
29. Gonzales, J.N.; Matson, M.M.; Atsumi, S. Nonphotosynthetic Biological CO₂ Biochemistry 2019, 58, 1470–1477.
30. Tashiro, Y.; Hirano, S.; Matson, M.M.; Atsumi, S.; Kondo, A. Electrical-biological hybrid system for CO₂ Metab. Eng. 2018, 47, 211–218.
31. Yishai, O.; Bouzon, M.; Doring, V.; Bar-Even, A. In Vivo Assimilation of One-Carbon via a Synthetic Reductive Glycine Pathway in *Escherichia coli*. *ACS Synth. Biol.* 2018, 7, 2023–2028.
32. Kim, S.; Lindner, S.N.; Aslan, S.; Yishai, O.; Wenk, S.; Schann, K.; Bar-Even, A. Growth of *coli* on formate and methanol via the reductive glycine pathway. *Nat. Chem. Biol.* 2020, 16, 538–545.
33. Sánchez-Andrea, I.; Guedes, I.A.; Hornung, B.; Boeren, S.; Lawson, C.E.; Sousa, D.Z.; Bar-Even, A.; Claassens, N.J.; Stams, A.J.M. The reductive glycine pathway allows autotrophic growth of *Desulfovibrio desulfuricans*. *Commun.* 2020, 11, 5090.
34. Payne, K.A.; White, M.D.; Fisher, K.; Khara, B.; Bailey, S.S.; Parker, D.; Rattray, N.J.; Trivedi, D.K.; Goodacre, R.; Beveridge, R.; et al. New cofactor supports α , β -unsaturated acid decarboxylation via 1,3-dipolar cycloaddition. *Nature* 2015, 522, 497–501.
35. White, M.D.; Payne, K.A.; Fisher, K.; Marshall, S.A.; Parker, D.; Rattray, N.J.; Trivedi, D.K.; Goodacre, R.; Rigby, S.E.; Scrutton, N.S.; et al. UbiX is a flavin prenyltransferase required for bacterial ubiquinone biosynthesis. *Nature* 2015, 522, 502–506.
36. Payer, S.E.; Faber, K.; Glueck, S.M. Non-Oxidative Enzymatic (De)Carboxylation of (Hetero)Aromatics and Acrylic Acid Derivatives. *Synth. Catal.* 2019, 361, 2402–2420.
37. Aleku, G.A.; Saaret, A.; Bradshaw-Allen, R.T.; Derrington, S.R.; Titchiner, G.R.; Gostimskaya, I.; Gahloth, D.; Parker, D.A.; Hay, S.; Leys, D. Enzymatic C-H activation of aromatic compounds through CO₂ fixation. *Nat. Chem. Biol.* 2020, 16, 1255–1260.

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