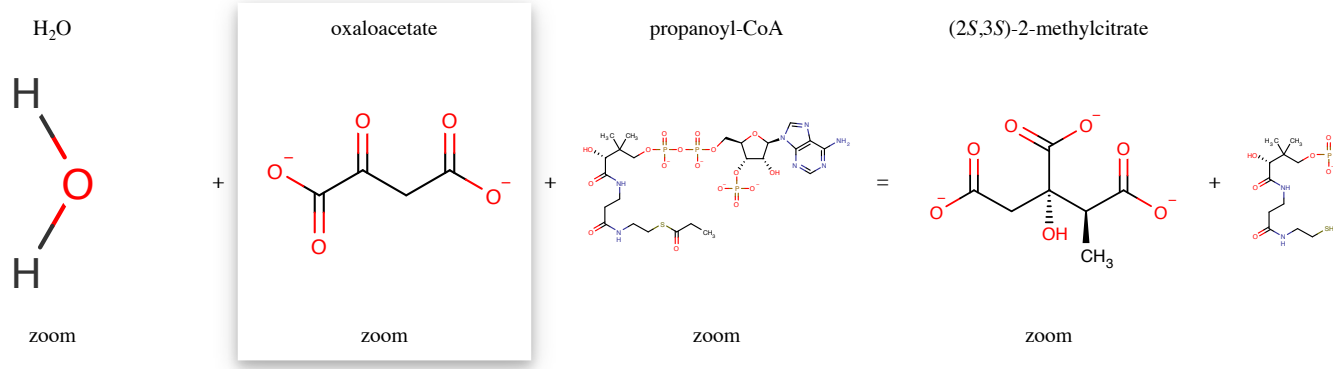
RHEA:23780

- Reaction information
- Reaction participants
- Cross-references
- Related reactions
- Publications



Enzymes

UniProtKB *help_outline*	15 proteins
Enzyme class *help_outline*	EC 2.3.3.5 2-methylcitrate synthase
GO Molecular Function *help_outline*	• GO:0050440 2-methylcitrate synthase activity

Reaction participants << Hide

- Name *help_outline* H_2O Identifier CHEBI:15377 (Beilstein: 3587155; CAS: 7732-18-5) *help_outline* Charge 0 Formula H2O InChIKey*help_outline* XLYOFNOQVPJJNP-UHFFFAOYSA-N SMILES*help_outline* [H]O[H] 2D coordinates Mol file for the small molecule Search links Involved in 5,958 reaction(s) Find molecules that contain or resemble this structure Find proteins in UniProtKB for this molecule
- Name *help_outline* oxaloacetate Identifier CHEBI:16452 (Beilstein: 3605372; CAS: 149-63-3) *help_outline* Charge -2 Formula C4H2O5 InChIKey*help_outline* KHPXUQMNIQBQEV-UHFFFAOYSA-L SMILES*help_outline* [O-]C(=O)CC(=O)C([O-])=O 2D coordinates Mol file for the small molecule Search links Involved in 54 reaction(s) Find molecules that contain or resemble this structure Find proteins in UniProtKB for this molecule
- Name *help_outline* propanoyl-CoA Identifier CHEBI:57392 Charge -4 Formula C24H36N7O17P3S InChIKey*help_outline* QAQREVBBADEHPA-IEXPHMLFSA-J SMILES*help_outline* CCC(=O)SCCNC(=O)CCNC(=O)[C@H](O)C(C)(C)COP([O-])(=O)OP([O-])(=O)OC[C@H]1O[C@H]([C@H](O)[C@@H]1OP([O-])([O-])=O)n1cnc2c(N)ncnc12 2D coordinates Mol file for the small molecule Search links Involved in 44 reaction(s) Find molecules that contain or resemble this structure Find proteins in UniProtKB for this molecule
- Name *help_outline* (2*S*,3*S*)-2-methylcitrate Identifier CHEBI:58853 Charge -3 Formula C7H7O7 InChIKey*help_outline* YNOXCRMFGMSKIJ-NFNCENRGSA-K SMILES*help_outline* C[C@H](C([O-])=O)[C@@](O)(CC([O-])=O)C([O-])=O 2D coordinates Mol file for the small molecule Search links Involved in 3 reaction(s) Find molecules that contain or resemble this structure Find proteins in UniProtKB for this molecule
- Name *help_outline* CoA Identifier CHEBI:57287 (Beilstein: 11604429) *help_outline* Charge -4 Formula C21H32N7O16P3S InChIKey*help_outline* RGJOEKWQDUBAIZ-IBOSZNHHSA-J SMILES*help_outline* CC(C)(COP([O-])(=O)OP([O-])(=O)OC[C@H]1O[C@H]([C@H](O)[C@@H]1OP([O-])([O-])=O)n1cnc2c(N)ncnc12)[C@@H](O)C(=O)NCCC(=O)NCCS 2D coordinates Mol file for the small molecule Search links Involved in 1,426 reaction(s) Find molecules that contain or resemble this structure Find proteins in UniProtKB for this molecule
- Name *help_outline* H^+ Identifier CHEBI:15378 Charge 1 Formula H InChIKey*help_outline* GPRLSGONYQIRFK-UHFFFAOYSA-N SMILES*help_outline* [H+] 2D coordinates Mol file for the small molecule Search links Involved in 9,087 reaction(s) Find molecules that contain or resemble this structure Find proteins in UniProtKB for this molecule

Cross-references

	RHEA:23780	RHEA:23781	RHEA:23782	RHEA:23783
Reaction direction *help_outline*	undefined	left-to-right	right-to-left	bidirectional
UniProtKB *help_outline*	• 15 proteins		•	

	RHEA:23780	RHEA:23781	RHEA:23782	RHEA:23783
EC numbers *help_outline*	• 2.3.3.5			
Gene Ontology *help_outline*	• GO:0050440			
KEGG *help_outline*				• R00931
MetaCyc *help_outline*				• 2-METHYLCITRATE-SYNTHASE-RXN
EcoCyc *help_outline*		• 2-METHYLCITRATE-SYNTHASE-RXN		

Related reactions *help_outline*

More general form(s) of this reaction

- RHEA:57492
  H_2O + oxaloacetate + propanoyl-CoA = 2-methylcitrate + CoA + H^+

Publications

- **Identification of two prpDBC gene clusters in Corynebacterium glutamicum and their involvement in propionate degradation via the 2-methylcitrate cycle.**

  Claes W.A., Puehler A., Kalinowski J.

  Genome sequencing revealed that the Corynebacterium glutamicum genome contained, besides gltA, two additional citrate synthase homologous genes (prpC) located in two different prpDBC gene clusters, which were designated prpD1B1C1 and prpD2B2C2. The coding regions of the two gene clusters as well a ... >> More

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  J. Bacteriol. 184:2728-2739(2002) [PubMed] [EuropePMC]

- **Methylcitrate cycle activation during adaptation of Fusarium solani and Fusarium verticillioides to propionyl-CoA-generating carbon sources.**

  Domin N., Wilson D., Brock M.

  Propionyl-CoA is an inhibitor of both primary and secondary metabolism in Aspergillus species and a functional methylcitrate cycle is essential for the efficient removal of this potentially toxic metabolite. Although the genomes of most sequenced fungal species appear to contain genes coding for e ... >> More

  Propionyl-CoA is an inhibitor of both primary and secondary metabolism in Aspergillus species and a functional methylcitrate cycle is essential for the efficient removal of this potentially toxic metabolite. Although the genomes of most sequenced fungal species appear to contain genes coding for enzymes of the methylcitrate cycle, experimental confirmation of pathway activity in filamentous fungi has only been provided for Aspergillus nidulans and Aspergillus fumigatus. In this study we demonstrate that pathogenic Fusarium species also possess a functional methylcitrate cycle. Fusarium solani appears highly adapted to saprophytic growth as it utilized propionate with high efficiency, whereas Fusarium verticillioides grew poorly on this carbon source. In order to elucidate the mechanisms of propionyl-CoA detoxification, we first identified the genes coding for methylcitrate synthase from both species. Despite sharing 96 % amino acid sequence identity, analysis of the two purified enzymes demonstrated that their biochemical properties differed in several respects. Both methylcitrate synthases exhibited low K(m) values for propionyl-CoA, but that of F. verticillioides displayed significantly higher citrate synthase activity and greater thermal stability. Activity determinations from cell-free extracts of F. solani revealed a strong methylcitrate synthase activity during growth on propionate and to a lesser extent on Casamino acids, whereas activity by F. verticillioides was highest on Casamino acids. Further phenotypic analysis confirmed that these biochemical differences were reflected in the different growth behaviour of the two species on propionyl-CoA-generating carbon sources. << Less

  Microbiology 155:3903-3912(2009) [PubMed] [EuropePMC]

- **The methylcitric acid pathway in Ralstonia eutropha: new genes identified involved in propionate metabolism.**

  Bramer C.O., Steinbuchel A.

  From Ralstonia eutropha HF39 null-allele mutants were created by Tn5 mutagenesis and by homologous recombination which were impaired in growth on propionic acid and levulinic acid. From the molecular, physiological and enzymic analysis of these mutants it was concluded that in this bacterium propi ... >> More

From Ralstonia eutropha HF39 null-allele mutants were created by Tn5 mutagenesis and by homologous recombination which were impaired in growth on propionic acid and levulinic acid. From the molecular, physiological and enzymic analysis of these mutants it was concluded that in this bacterium propionic acid is metabolized via the methylcitric acid pathway. The genes encoding enzymes of this pathway are organized in a cluster in the order prpR, prpB, prpC, acnM, ORF5 and prpD, with prpR transcribed divergently from the other genes. (i) prpC encodes a 2-methylcitric acid synthase (42720 Da) as shown by the measurement of the respective enzyme activity, complementation of a prpC mutant of Salmonella enterica serovar Typhimurium and high sequence similarity. (ii) For the translational product of acnM the function of a 2-methyl-cis-aconitic acid hydratase (94726 Da) is proposed. This protein and also the ORF5 translational product are essential for growth on propionic acid, as revealed by the propionic-acid-negative phenotype of Tn5-insertion mutants, and are required for the conversion of 2-methylcitric acid into 2-methylisocitric acid as shown by the accumulation of the latter, which could be purified as its calcium salt from the supernatants of these mutants. In contrast, inactivation of prpD did not block the ability of the cell to use propionic acid as carbon and energy source, as shown by the propionic acid phenotype of a null-allele mutant. It is therefore unlikely that prpD from R. eutropha encodes a 2-methyl-cis-aconitic acid dehydratase as proposed recently for the homologous prpD gene from S. enterica. (iii) The translational product of prpB encodes 2-methylisocitric acid lyase (32314 Da) as revealed by measurement of the respective enzyme activity and by demonstrating accumulation of methylisocitric acid in the supernatant of a prpB null-allele mutant. (iv) The expression of prpC and probably also of the other enzymes is regulated and is induced during cultivation on propionic acid or levulinic acid. The putative translational product of prpR (70895 Da) exhibited high similarities to PrpR of Escherichia coli and S. enterica, and might represent a transcriptional activator of the sigma-54 family involved in the regulation of the other prp genes. Since the prp locus of R. eutropha was very different from those of E. coli and S. enterica, an extensive comparison of prp loci available from databases and literature was done, revealing two different classes of prp loci. << Less

Microbiology 147:2203-2214(2001) [PubMed] [EuropePMC]

This publication is cited by 1 other entry.

- **Propionate oxidation in Escherichia coli: evidence for operation of a methylcitrate cycle in bacteria.**

  Textor S., Wendisch V.F., de Graaf A.A., Mueller U., Linder M.I., Linder D., Buckel W.

  Escherichia coli grew in a minimal medium on propionate as the sole carbon and energy source. Initially a lag phase of 4-7 days was observed. Cells adapted to propionate still required 1-2 days before growth commenced. Incorporation of (2-13C), (3-13C) or (2H3)propionate into alanine revealed by N ... >> More

  Escherichia coli grew in a minimal medium on propionate as the sole carbon and energy source. Initially a lag phase of 4-7 days was observed. Cells adapted to propionate still required 1-2 days before growth commenced. Incorporation of (2-13C), (3-13C) or (2H3)propionate into alanine revealed by NMR that propionate was oxidized to pyruvate without randomisation of the carbon skeleton and excluded pathways in which the methyl group was transiently converted to a methylene group. Extracts of propionate-grown cells contained a specific enzyme that catalyses the condensation of propionyl-CoA with oxaloacetate, most probably to methylcitrate. The enzyme was purified and identified as the already-known citrate synthase II. By 2-D gel electrophoresis, the formation of a second propionate-specific enzyme with sequence similarities to isocitrate lyases was detected. The genes of both enzymes were located in a putative operon with high identities (at least 76% on the protein level) with the very recently discovered prp operon from Salmonella typhimurium. The results indicate that E. coli oxidises propionate to pyruvate via the methylcitrate cycle known from yeast. The 13C patterns of aspartate and glutamate are consistent with the further oxidation of pyruvate to acetyl-CoA. Oxaloacetate is predominantly generated via the glyoxylate cycle rather than by carboxylation of phosphoenolpyruvate. << Less

  Arch. Microbiol. 168:428-436(1997) [PubMed] [EuropePMC]

- **Citrate synthase and 2-methylcitrate synthase: structural, functional and evolutionary relationships.**

  Gerike U., Hough D.W., Russell N.J., Dyall-Smith M.L., Danson M.J.

  Following the complete sequencing of the Escherichia coli genome, it has been shown that the proposed second citrate synthase of this organism, recently described by the authors, is in fact a 2-methylcitrate synthase that possesses citrate synthase activity as a minor component. Whereas the hexame ... >> More

  Following the complete sequencing of the Escherichia coli genome, it has been shown that the proposed second citrate synthase of this organism, recently described by the authors, is in fact a 2-methylcitrate synthase that possesses citrate synthase activity as a minor component. Whereas the hexameric citrate synthase is constitutively produced, the 2-methylcitrate synthase is induced during growth on propionate, and the catabolism of propionate to succinate and pyruvate via 2-methylcitrate is proposed. The citrate synthases of the psychrotolerant eubacterium DS2-3R, and of the thermophilic archaea Thermoplasma acidophilum and Pyrococcus furiosus, are approximately 40% identical in sequence to the Escherichia coli 2-methylcitrate synthase and also possess 2-methylcitrate synthase activity. The data are discussed with respect to the structure, function and evolution of citrate synthase and 2-methylcitrate synthase. << Less

  Microbiology 144:929-935(1998) [PubMed] [EuropePMC]

- **Oxidation of propionate to pyruvate in Escherichia coli. Involvement of methylcitrate dehydratase and aconitase.**

  Brock M., Maerker C., Schuetz A., Voelker U., Buckel W.

  The pathway of the oxidation of propionate to pyruvate in Escherichia coli involves five enzymes, only two of which, methylcitrate synthase and 2-methylisocitrate lyase, have been thoroughly characterized. Here we report that the isomerization of (2S,3S)-methylcitrate to (2R,3S)-2-methylisocitrate ... >> More

  The pathway of the oxidation of propionate to pyruvate in Escherichia coli involves five enzymes, only two of which, methylcitrate synthase and 2-methylisocitrate lyase, have been thoroughly characterized. Here we report that the isomerization of (2S,3S)-methylcitrate to (2R,3S)-2-methylisocitrate requires a novel enzyme, methylcitrate dehydratase (PrpD), and the well-known enzyme, aconitase (AcnB), of the tricarboxylic acid cycle. AcnB was purified as 2-methylaconitate hydratase from E. coli cells grown on propionate and identified by its N-terminus. The enzyme has an apparent Km of 210 micro m for (2R,3S)-2-methylisocitrate but shows no activity with (2S,3S)-methylcitrate. On the other hand, PrpD is specific for (2S,3S)-methylcitrate (Km = 440 micro m) and catalyses in addition only the hydration of cis-aconitate at a rate that is five times lower. The product of the dehydration of enzymatically synthesized (2S,3S)-methylcitrate was designated cis-2-methylaconitate because of its ability to form a cyclic anhydride at low pH. Hence, PrpD catalyses an unusual syn elimination, whereas the addition of water to cis-2-methylaconitate occurs in the usual anti manner. The different stereochemistries of the elimination and addition of water may be the reason for the requirement for the novel methylcitrate dehydratase (PrpD), the sequence of which seems not to be related to any other enzyme of known function. Northern-blot experiments showed expression of acnB under all conditions tested, whereas the RNA of enzymes of the prp operon (PrpE, a propionyl-CoA synthetase, and PrpD) was exclusively present during growth on propionate. 2D gel electrophoresis showed the production of all proteins encoded by the prp operon during growth on propionate as sole carbon and energy source, except PrpE, which seems to be replaced by acetyl-CoA synthetase. This is in good agreement with investigations on Salmonella enterica LT2, in which disruption of the prpE gene showed no visible phenotype. << Less

  Eur. J. Biochem. 269:6184-6194(2002) [PubMed] [EuropePMC]

  This publication is cited by 2 other entries.

- **Salmonella typhimurium LT2 catabolizes propionate via the 2-methylcitric acid cycle.**

Horswill A.R., Escalante-Semerena J.C.

We previously identified the prpBCDE operon, which encodes catabolic functions required for propionate catabolism in Salmonella typhimurium. Results from (13)C-labeling experiments have identified the route of propionate breakdown and determined the biochemical role of each Prp enzyme in this path ... >> More

We previously identified the prpBCDE operon, which encodes catabolic functions required for propionate catabolism in Salmonella typhimurium. Results from (13)C-labeling experiments have identified the route of propionate breakdown and determined the biochemical role of each Prp enzyme in this pathway. The identification of catabolites accumulating in wild-type and mutant strains was consistent with propionate breakdown through the 2-methylcitric acid cycle. Our experiments demonstrate that the alpha-carbon of propionate is oxidized to yield pyruvate. The reactions are catalyzed by propionyl coenzyme A (propionyl-CoA) synthetase (PrpE), 2-methylcitrate synthase (PrpC), 2-methylcitrate dehydratase (probably PrpD), 2-methylisocitrate hydratase (probably PrpD), and 2-methylisocitrate lyase (PrpB). In support of this conclusion, the PrpC enzyme was purified to homogeneity and shown to have 2-methylcitrate synthase activity in vitro. (1)H nuclear magnetic resonance spectroscopy and negative-ion electrospray ionization mass spectrometry identified 2-methylcitrate as the product of the PrpC reaction. Although PrpC could use acetyl-CoA as a substrate to synthesize citrate, kinetic analysis demonstrated that propionyl-CoA is the preferred substrate. << Less

J. Bacteriol. 181:5615-5623(1999) [PubMed] [EuropePMC]