

Rhea

Annotated reactions database



# Motivation for decomposed reactions

- The reactions provided by the NC-IUBMB are free-text...
- Can result in duplicate reactions for example....
  - acetic acid + ATP + CoA <?> acetyl-CoA + AMP

is the same as



- acetic acid + CoA + ATP <?> acetyl-CoA + AMP

But unless you tell a computer that it will just interpret two different strings....

# What is Rhea

- A manually annotated database of reactions.
- Initially populated with reactions from the EC nomenclature (IntEnz/ENZYME databases).
- Also contains non-enzymatic (spontaneous) reactions of biological interest.

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## Rhea - Home

Rhea is a freely available, manually annotated database of chemical reactions created in collaboration with the [Swiss Institute of Bioinformatics \(SIB\)](#).  
**All data in Rhea is freely accessible and available for anyone to use.**  
Last release: 28 (2012-01-19)  
[Read more about Rhea.](#)



[Advanced search](#)

Search by compound name, ChEBI ID, reaction ID, cross reference (e.g. EC number) or citation (author name, title, abstract text, publication ID). You can use double quotes - to match an exact phrase - and the following wildcards: ? (question mark = one character), \* (asterisk = several characters).


**Examples:**

- Searching for *caffe\** will find reactions with participants such as *caffeine*, *trans-caffeic acid* or *caffeoyl-CoA*.
- Searching for *a?e?o\** will find reactions with participants such as *acetoin*, *acetone* or *adenosine*.

**News**

2012-01-20  
[Rhea release 28](#)  
A new Rhea release is available (<http://www.ebi.ac.uk/rhea>) with 188 new accepted reaction identifiers. Now you can cite Rhea and download its compounds in MOL and SDF formats.  
[More news...](#)

**Partners**



Rhea is a collaborative effort between the [Swiss-Prot Group](#) at the Swiss Institute of Bioinformatics (SIB) and the [Panda Chemoinformatics and Metabolism Group](#) at the EBI.

# What does Rhea provide

- Stable reaction identifiers and directionality (or lack of it).
- Reaction participants linked to ChEBI

EBI > Databases > Reactions & Pathways > Rhea

**RHEA:20736**

Last modified: 2011-04-20

Qualifiers: Chemically balanced

Show  names

acetyl-CoA

[CHEBI:57288](#)

+

glycine

[CHEBI:57305](#)

<?>

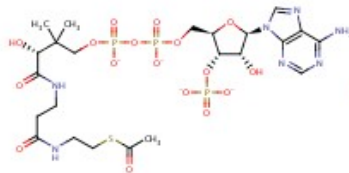
L-2-amino-3-oxobutanoate

[CHEBI:16944](#)

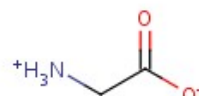
+

CoA

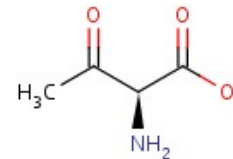
[CHEBI:57287](#)



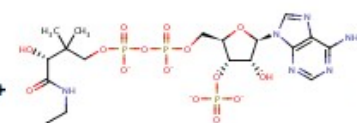
+



<?>



+



## Same participants, different directions

- [RHEA:20737](#) acetyl-CoA + glycine => L-2-amino-3-oxobutanoate + CoA + H<sup>+</sup>
- [RHEA:20738](#) L-2-amino-3-oxobutanoate + CoA + H<sup>+</sup> => acetyl-CoA + glycine
- [RHEA:20739](#) acetyl-CoA + glycine <=> L-2-amino-3-oxobutanoate + CoA + H<sup>+</sup>

# What does Rhea provide (continued)

- Validation of stoichiometry (mass and charge balance)
- Families of reactions

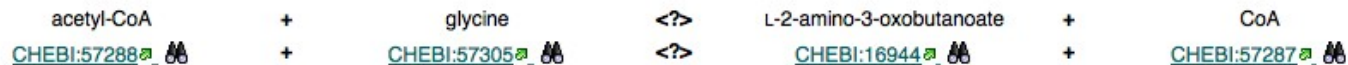
EBI > Databases > Reactions & Pathways > Rhea

**RHEA:20736**

Last modified: 2011-04-20

Qualifiers: Chemically balanced

Show  names

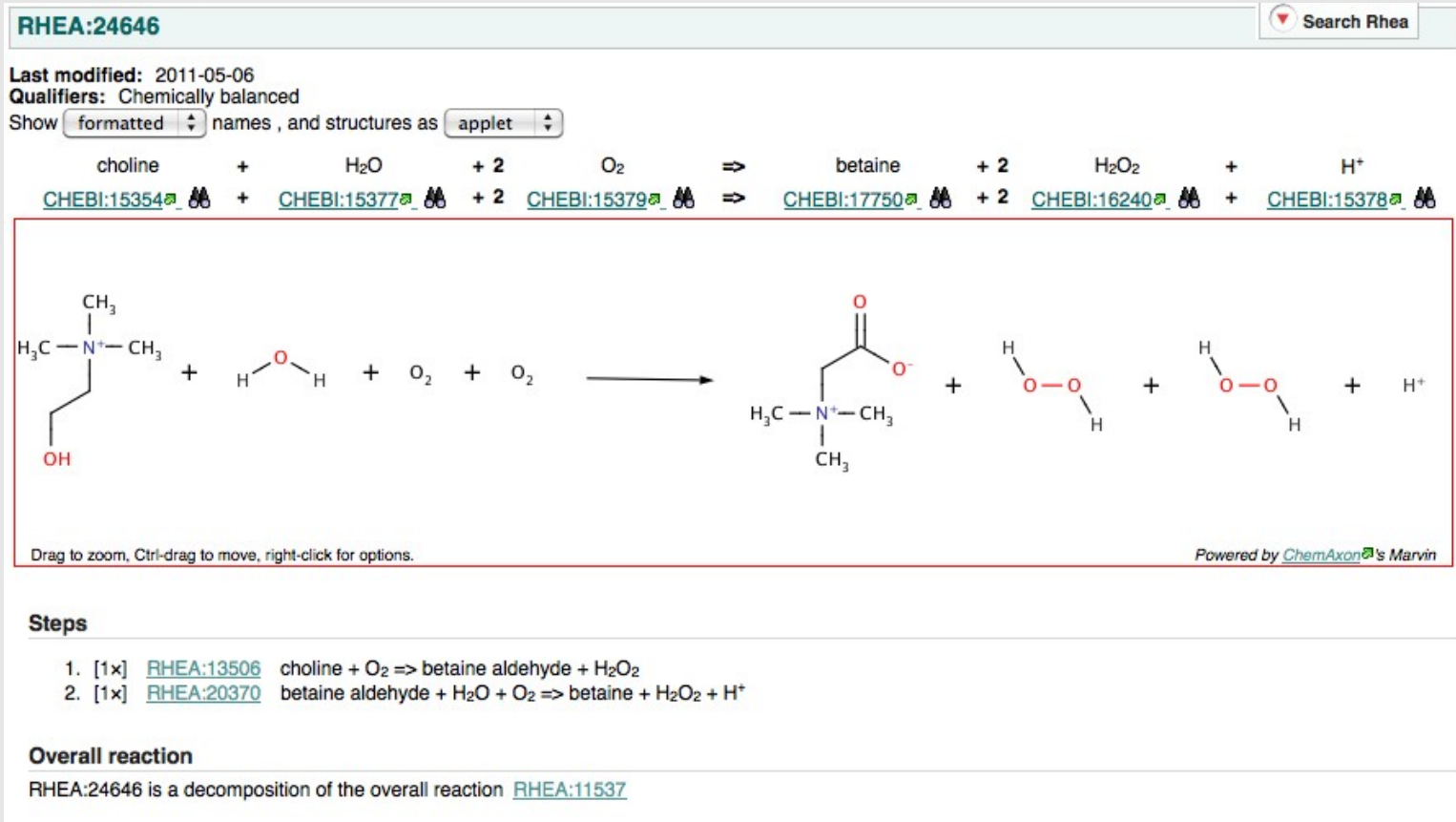


### Same participants, different directions

- [RHEA:20737](#) acetyl-CoA + glycine => L-2-amino-3-oxobutanoate + CoA + H<sup>+</sup>
- [RHEA:20738](#) L-2-amino-3-oxobutanoate + CoA + H<sup>+</sup> => acetyl-CoA + glycine
- [RHEA:20739](#) acetyl-CoA + glycine <=> L-2-amino-3-oxobutanoate + CoA + H<sup>+</sup>

# What does Rhea provide (continued)

- Decompositions of reactions in elementary processes ordered in time (steps) or not (coupled).



# What does Rhea provide (continued)

- Cross references.
- Bibliographic citations.

## Cross references

### Reactions and Pathways (4)

**UniPathway**: Database of manually curated metabolic pathways, whose primary goal is to describe the metabolic data of UniProtKB/Swiss-Prot Database entries.

[UER00169](#) ↔ , [UCR04993](#) ↔

**KEGG reaction**: Knowledge base for biochemical reactions by the Kyoto Encyclopedia of Genes and Genomes.

[R04993](#) ↔

**MetaCyc**: Database of nonredundant, experimentally elucidated metabolic pathways.

[RXN-11046](#) ↔

### Enzymes (1)

**IntEnz**: (Integrated relational Enzyme database) A freely available resource focused on enzyme nomenclature.

[EC 2.1.1.163](#) ↔

### Proteins (393)

**UniProt**: The Universal Protein Resource (UniProt) is a comprehensive resource for protein sequence and annotation data.

[UBIE\\_LISW6](#) ↔ , [UBIE\\_BURCH](#) ↔ , [UBIE\\_SHESA](#) ↔ , [UBIE\\_MYCUA](#) ↔ , [UBIE\\_FRATN](#) ↔ , [UBIE\\_MYCS2](#) ↔ , [UBIE\\_ECOK1](#) ↔ , [UBIE\\_PARDP](#) ↔ ,  
[UBIE\\_YERE8](#) ↔ , [UBIE\\_MYCBP](#) ↔ , [UBIE\\_NEIMF](#) ↔ , [UBIE\\_ARTAT](#) ↔ , [UBIE\\_SHESW](#) ↔ , [UBIE\\_SHEAM](#) ↔ , [UBIE\\_NOCSJ](#) ↔ , [UBIE\\_PSYIN](#) ↔ ,  
[UBIE\\_MYCVP](#) ↔ , [UBIE\\_MYCSK](#) ↔ , [UBIE\\_BARBK](#) ↔ , [UBIE\\_BURMS](#) ↔ , [UBIE\\_CAMJJ](#) ↔ , [UBIE\\_BURM9](#) ↔ , [UBIE\\_SHEB5](#) ↔ , [UBIE\\_BURM7](#) ↔ ,

→Show 368 more

## Citations

1. Wissenbach U, Ternes D, Unden G (1992)  
**An Escherichia coli mutant containing only demethylmenaquinone, but no menaquinone: effects on fumarate, dimethylsulfoxide, trimethylamine N-oxide and nitrate respiration.**  
*Archives of microbiology* **158**, 68-73 [PMID:1444716]  
→Abstract
2. Lee PT, Hsu AY, Ha HT, Clarke CF (1997)  
**A C-methyltransferase involved in both ubiquinone and menaquinone biosynthesis: isolation and identification of the Escherichia coli ubiE gene.**  
*Journal of bacteriology* **179**, 1748-54 [PMID:9045837]  
→Abstract



# Rhea compared to similar reaction DBs

- Consistency in the use of compounds and their nomenclature.
- Directionality.
- Stoichiometry check.
- Independence from spatial location.

# Compounds in Rhea

- Unique name (SOURCE='UniProt' in ChEBI)  
→ 'CoA'/'CoA-SH'/'Coenzyme A' problem solved.
- Normalized to pH 7.3.
- Updated with any changes in ChEBI (name, formula, merging of ChEBI ID).

# Simple search

- By compound name:
  - urea
  - Caffe\*
  - a?e?o\*
- By compound identifier:
  - CHEBI:17015



# Advanced Search - Text

## Rhea - Advanced search

### Reaction search

#### Text search

Wildcard characters: ? (one character), \* (one or more characters).

All of these words  :

Excluding words:

In field:

all

Select category

#### Reaction attribute search

Polymerization:

any

Transport:

any

Class of reactions:

any

Decomposition:

any

#### Cross-referenced database search

With cross-references to

Filter by cross-referenced database

Filter by attribute

Search

Menu

# Advanced Search - Chemical

Search type

Search on formula and range searches

Rhea selected

File Edit View Atom Bond Tools Templates Help

Chemical Structure Search?

Substructure  
Similarity  
Identity [Help](#)

Results per page: 15  
Total results: 200

Search Reset

Applet powered by [JChemPaint](#).

Structure Search powered by [OrChem](#).

C H O N P S F Cl Br I +1 -1

**Text Queries:** (Example: water)  
AND in Category All

**Formula:** (Example: NaHCO<sub>3</sub>) \*Case sensitive.  
AND Formula: + -

**Mass range:** (Example: 0 to 30.5)  
AND range from to + -

**Charge range:** (Example: -1 to 1)  
AND range from None to None + -

**Filter by Ontology Term:** (Example "is a CHEBI:15377" or "is a water")  
AND Select relationship + -

**Filter by Database:**  
AND contains a database cross-reference in Rhea + -

**Filter by Stars:**  
Results for: All Stars

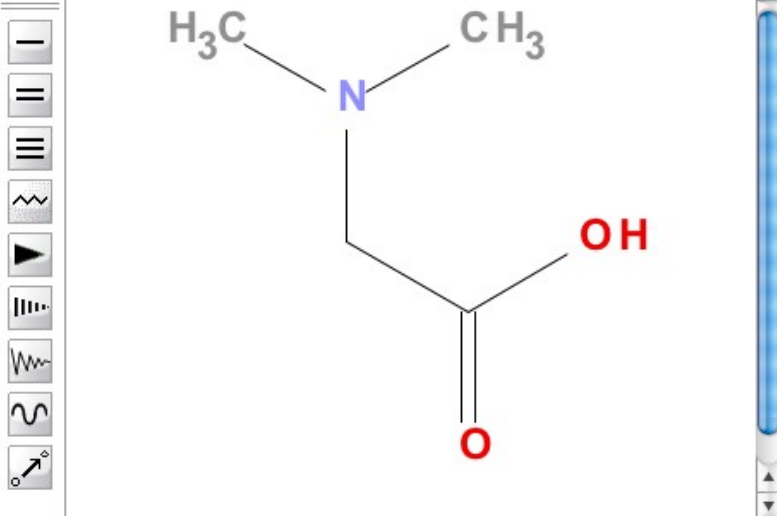
**Filter by Chemical Structure:**  
Results only with chemical structures? Yes:  No:

# Advanced Search Example

## Chemical structure search

Powered by [ChEBI](#)

File Edit View Atom Bond Tools R-groups Templates Help



C H O N P S F Cl Br I +1 -1

Chemical Structure Search?

- Find compounds which contain this structure
- Find compounds which resemble this structure
- Find this entity

[Help](#) ?

Strictly Stereo:  Yes

Results per page: 15

Total results: 1000

Search for only

Applet powered by [JChemPaint](#).

Structure Search powered by [OrChem](#).

# Advanced Search Example (continued)

You searched for

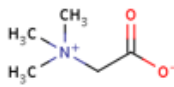
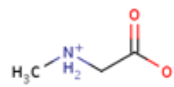
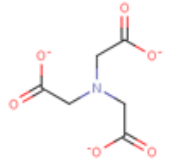
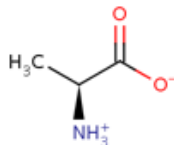
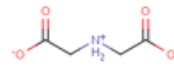
**Rhea in Cross Reference Sources, and 3 in Stars, and structures similar to**

Edit Query

Download your search results: [Tab-delimited](#), [XML](#), [SDF](#)

5 entries found, displaying 1 to 5.

<< < 1 > >>

 <p><a href="#">CHEBI:17750</a> glycine betaine</p> <p>Stars: ★★★★★</p> <p><a href="#">Rhea reactions</a></p>	 <p><a href="#">CHEBI:57433</a> sarcosine zwitterion</p> <p>Stars: ★★★★★</p> <p><a href="#">Rhea reactions</a></p>	 <p><a href="#">CHEBI:25548</a> nitrilotriacetate(3-)</p> <p>Stars: ★★★★★</p> <p><a href="#">Rhea reactions</a></p>
 <p><a href="#">CHEBI:57972</a> L-alanine zwitterion</p> <p>Stars: ★★★★★</p> <p><a href="#">Rhea reactions</a></p>	 <p><a href="#">CHEBI:62745</a> ammoniodiacetate</p> <p>Stars: ★★★★★</p> <p><a href="#">Rhea reactions</a></p>	

5 entries found, displaying 1 to 5.

<< < 1 > >>

# Downloads

- BioPAX format (<http://www.biopax.org>).
- RXN format (<http://www.mdl.com>).
- RD format (<http://www.mdl.com>).
- Compounds: RD, SDF formats (<http://www.mdl.com> ).



# Web services

- <http://www.ebi.ac.uk/rhea/rest/1.0/>
- Simple text search
- RXN format (<http://www.mdl.com>).
- BioPAX level 2 format (<http://www.biopax.org>).
- CMLReact format.

# Rhea team and resources

Rafael Alcántara (Developer, EBI)

Kristian Axelsen (Curator, SIB)

Anne Morgat (Curator, SIB)

Mohamed Zerara (Developer, SIB)

Alan Bridge (Coordinator, SIB)

Paula de Matos (Coordinator, EBI)

Christoph Steinbeck (Team leader, EBI)

<http://www.ebi.ac.uk/rhea>

<ftp://ftp.ebi.ac.uk/pub/databases/rhea>

<http://sourceforge.net/projects/rhea-ebi>

[rhea-ebi-help@lists.sourceforge.net](mailto:rhea-ebi-help@lists.sourceforge.net)

# Exercises!



<http://www.ebi.ac.uk/rhea>