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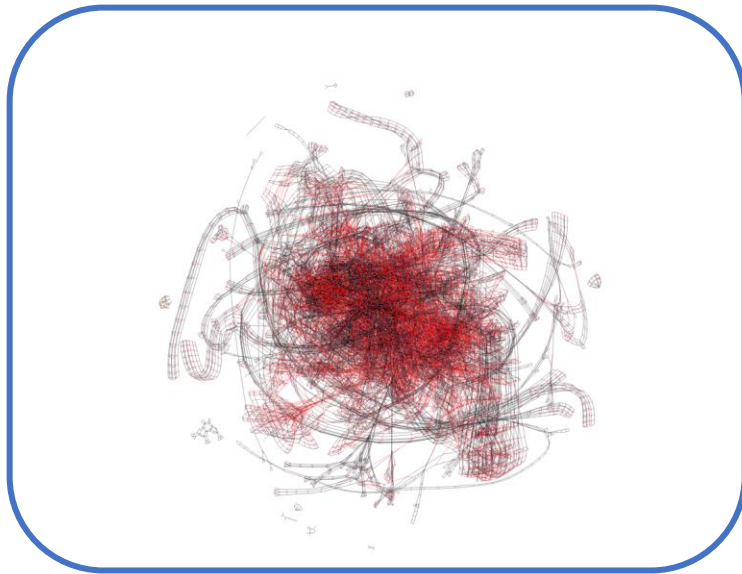
MATOMIC Mathematical Modelling for Microbial Community Induced
Metabolic Diseases

Converting KEGG RCLASS data into DPO graph rewriting rules

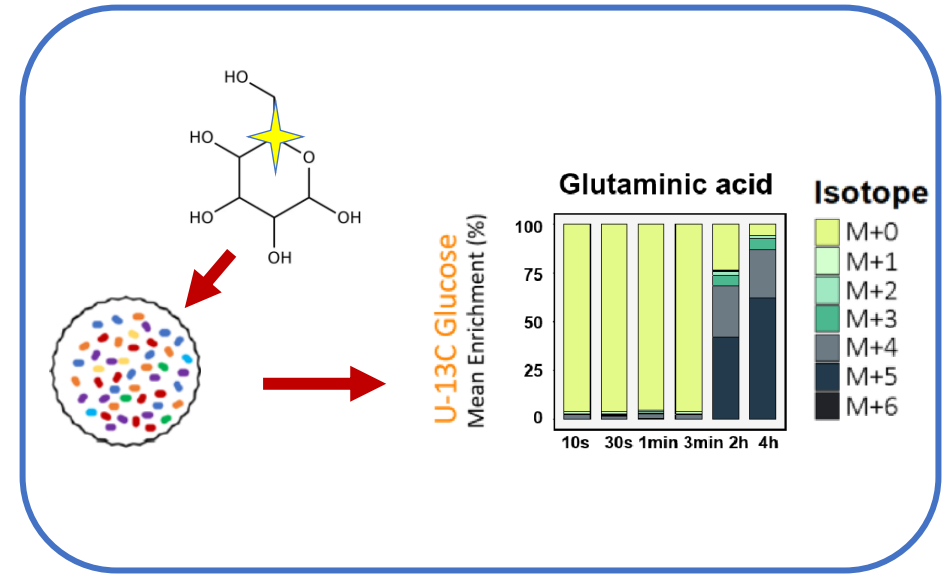
Nora Beier, 13.02.2024

Atom Tracing for Better Understanding of Metabolic Mechanism

Computational Metabolic Network Modelling

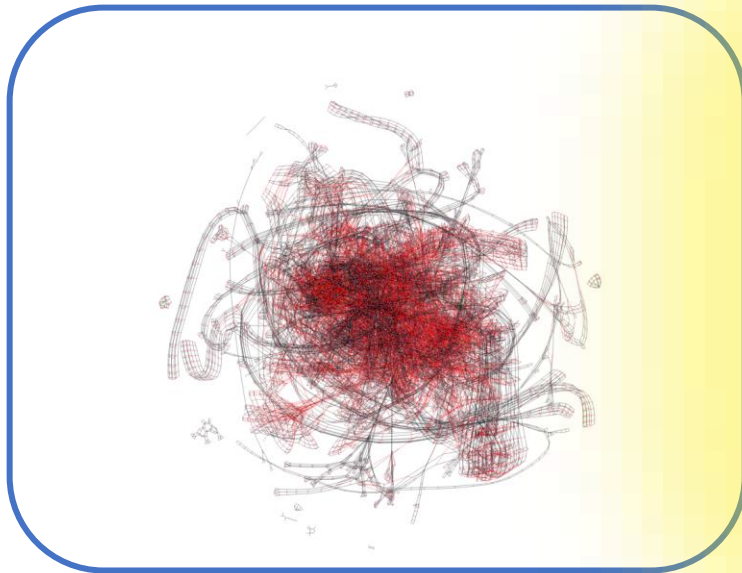


Isotopic Labelling Experiments



Atom Tracing for Better Understanding of Metabolic Mechanism

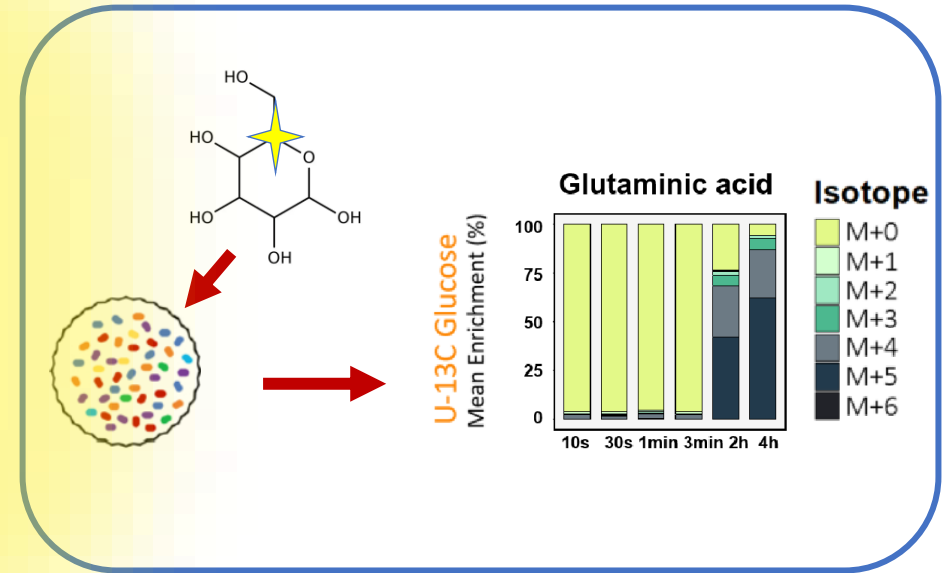
Computational Metabolic
Network Modelling



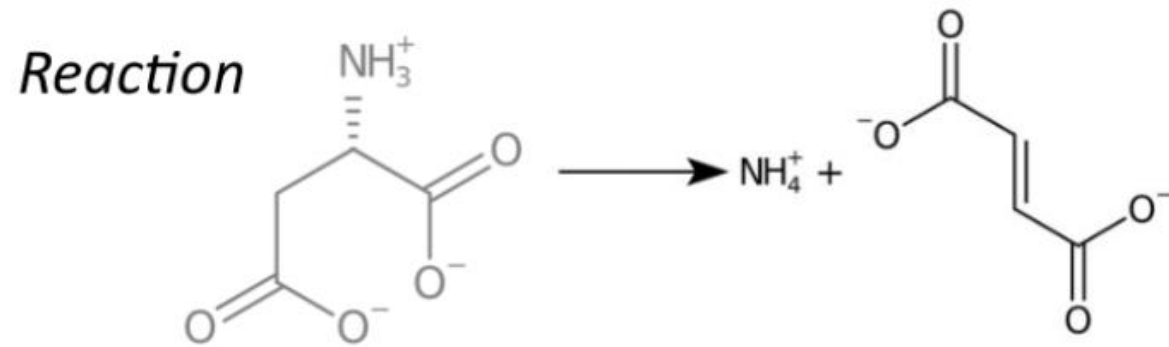
Correct Atom-to-Atom-
Maps



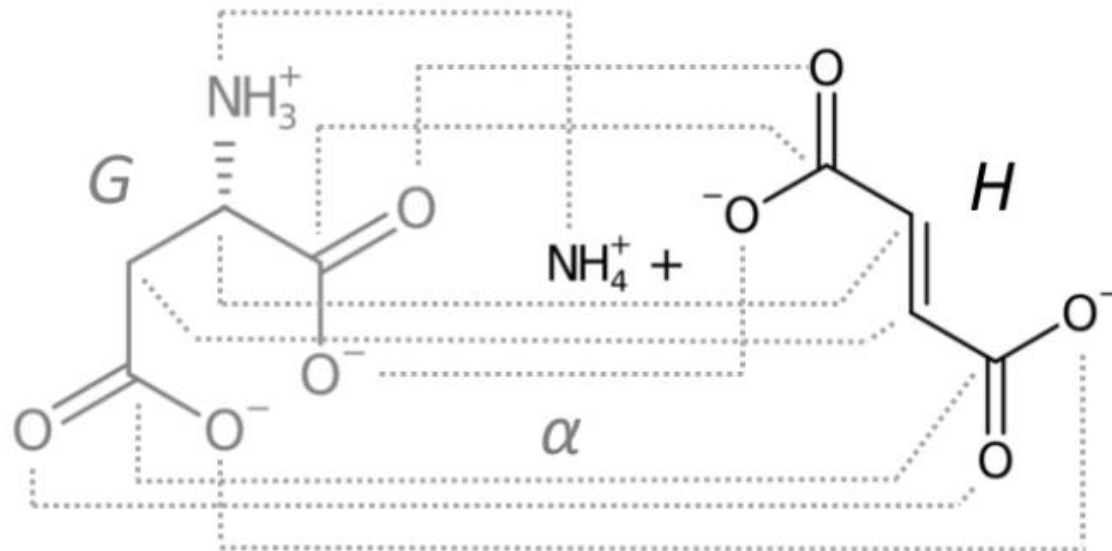
Isotopic Labelling
Experiments



Atoms-to-Atom-Maps



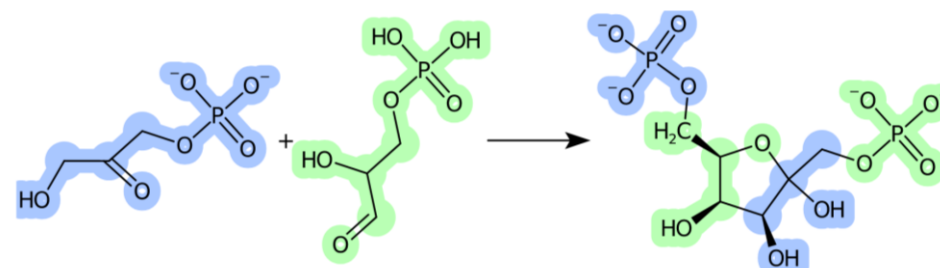
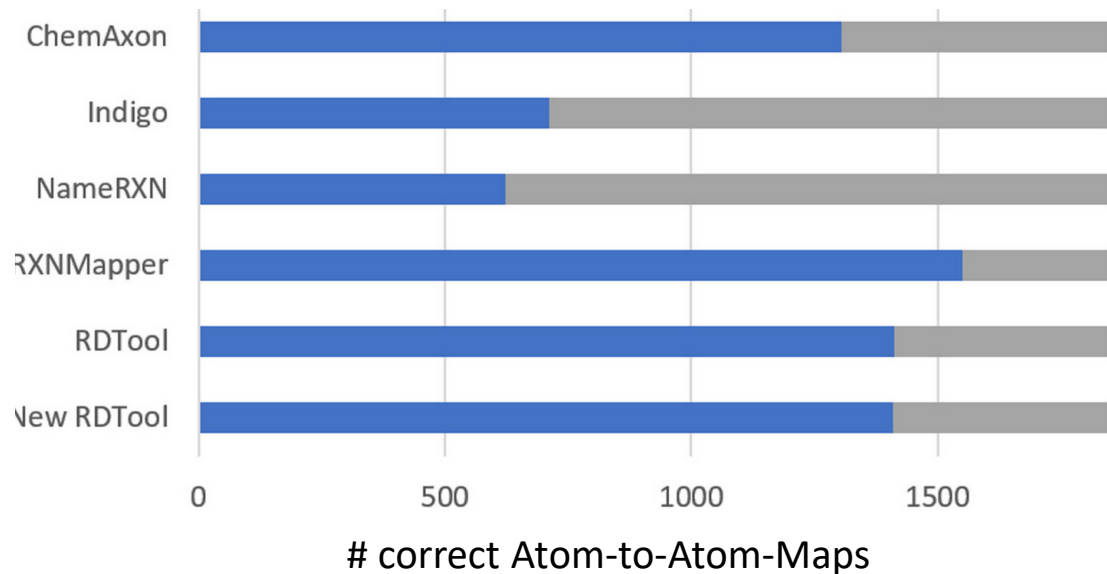
Atom map



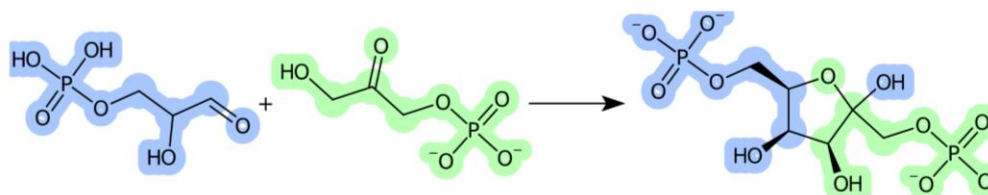


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The Problem with Atom-to-Atom Maps



RXNmapper

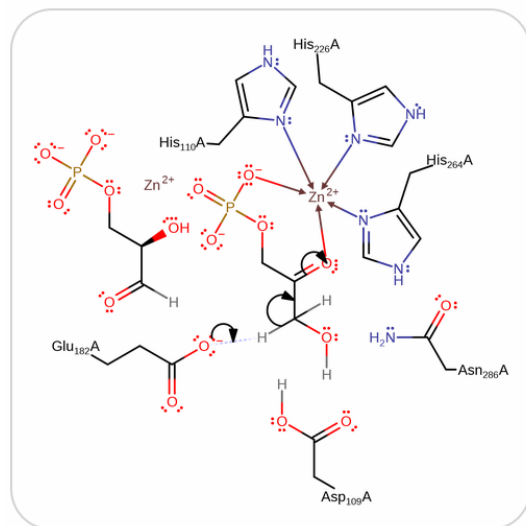
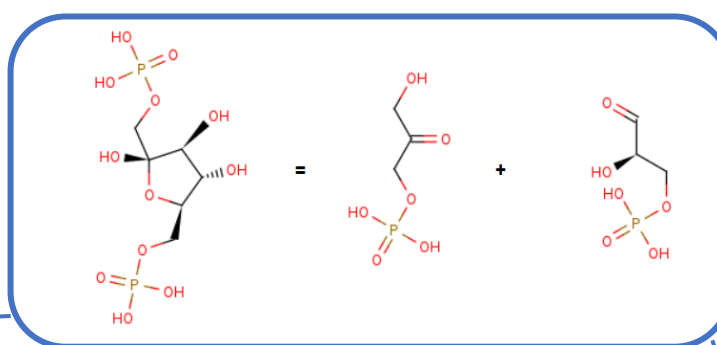


Graphormer

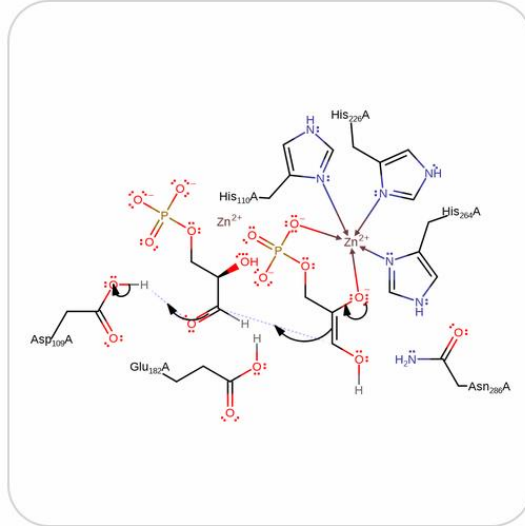
Source: Arkadii Lin et al. 2021 'Atom-to-atom Mapping: A Benchmarking Study of Popular Mapping Algorithms and Consensus Strategies', molecular informatics



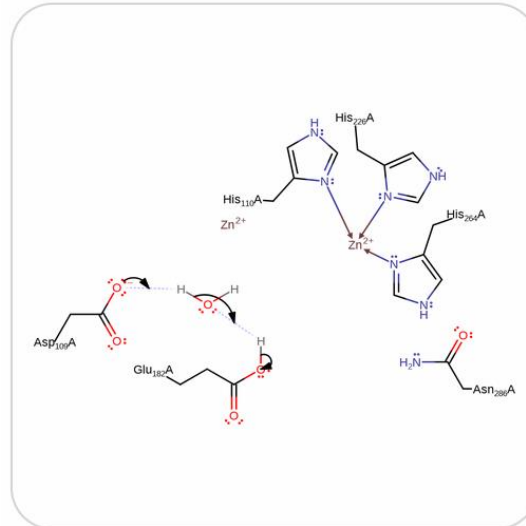
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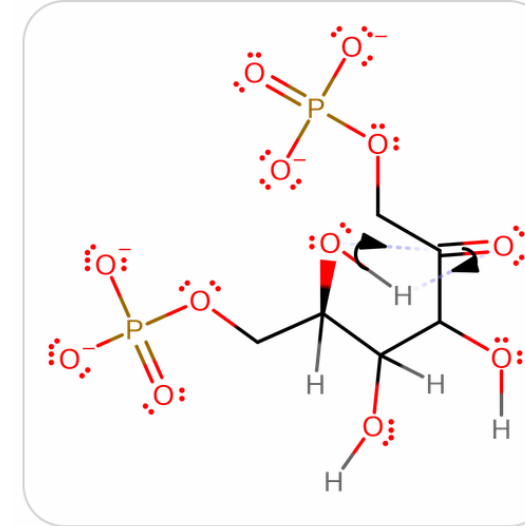
Step 1. Glu182 deprotonates the C1 carbon of the substrate, which initiates double bond rearrangement to form the enol-intermediate



Step 2. The oxyanion collapses, initiating nucleophilic addition of the intermediate to the glyceraldehyde-3-phosphate at the carbonyl carbon. The oxyanion formed deprotonates Asp109



Step 3. Asp109 deprotonates water which deprotonates Glu182 in an inferred step.

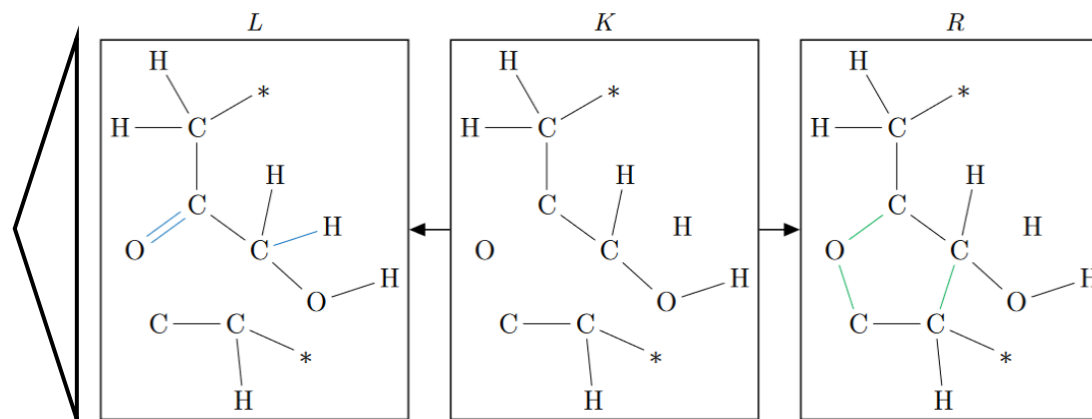
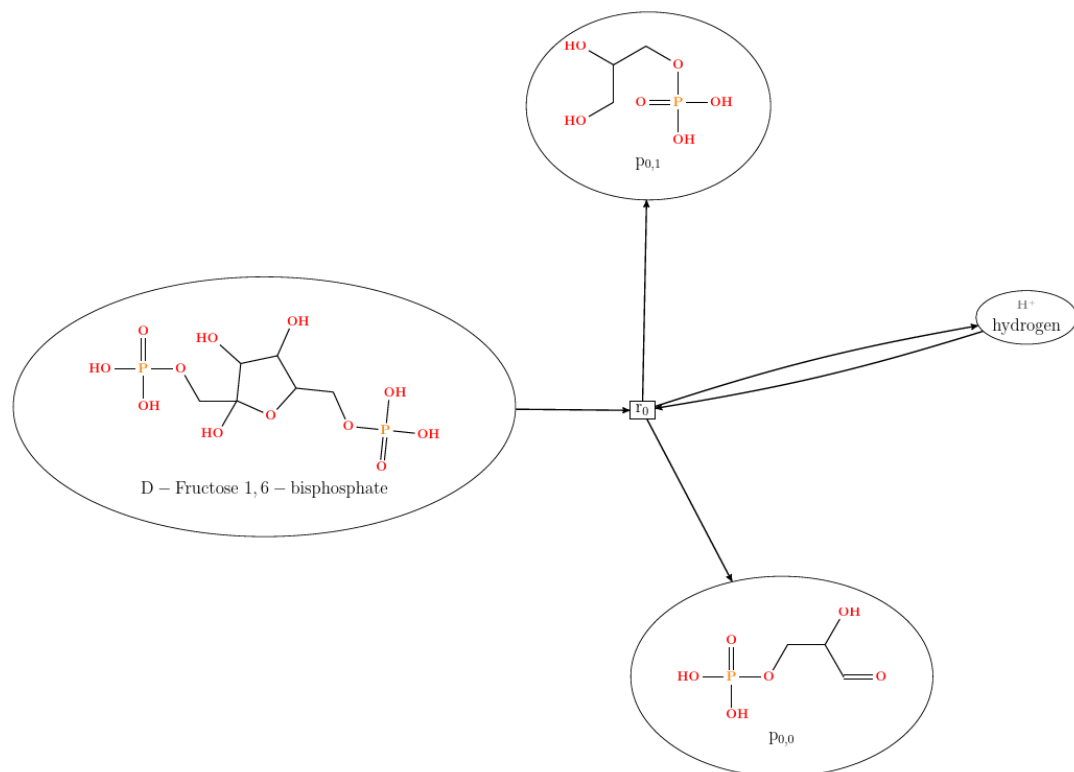


Step 4. The sugar cyclises outside the enzyme active site.



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Reactions as Graph Rewriting



Atom-Atom Maps



REACTION: R01070

Entry	R01070	Reaction
Name	beta-D-fructose-1,6-bisphosphate D-glyceraldehyde (glycerone-phosphate-forming)	
Definition	beta-D-Fructose 1,6-bisphosphate <=> Glycerone D-Glyceraldehyde 3-phosphate	
Equation	C05378 <=> C00111 + C00118	
Reaction class	RC00438	C00111_C05378
	RC00439	C00118_C05378
Enzyme	4.1.2.13	
Pathway	rn00010	Glycolysis / Gluconeogenesis
	rn00030	Pentose phosphate pathway



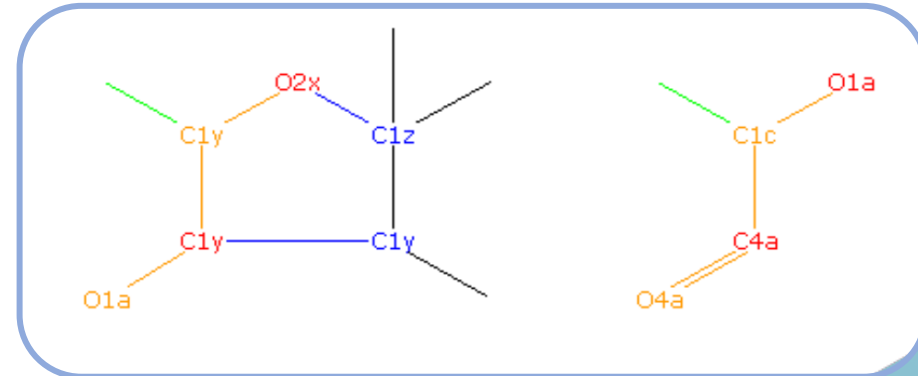
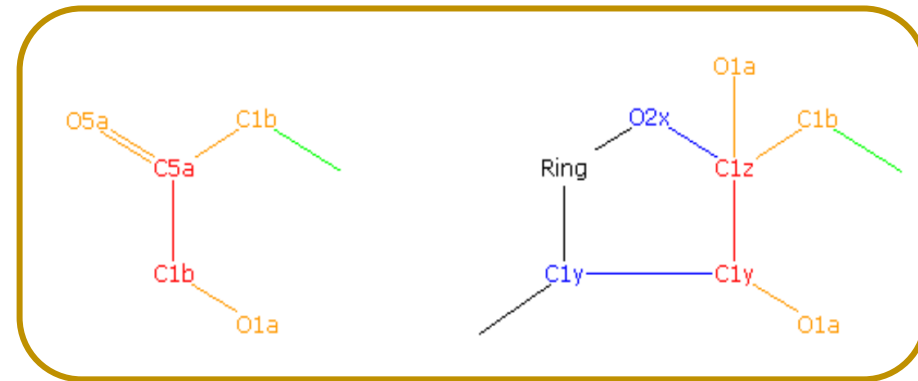
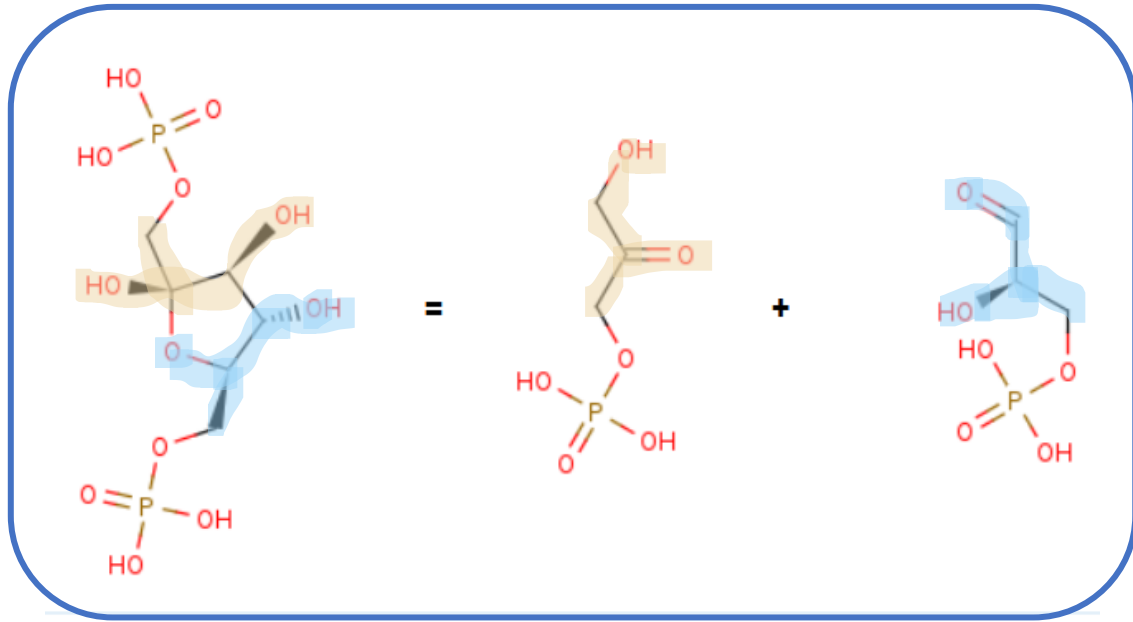
RCLASS: RC00438

Help

Entry	RC00438	RClass
Definition	C1b-C1y:*-C1y:C5a+O1a-C1z+O1a C5a-C1z:*-O2x:C1b+C1b+O5a-C1b+C1y+O1a	
Reactant pair	C00111_C00354 C00111_C05378	C00111_C01094 C00111_C06441
	C00111_C03785 C00111_C20831	



RCLASS as Graph Rewriting Rules

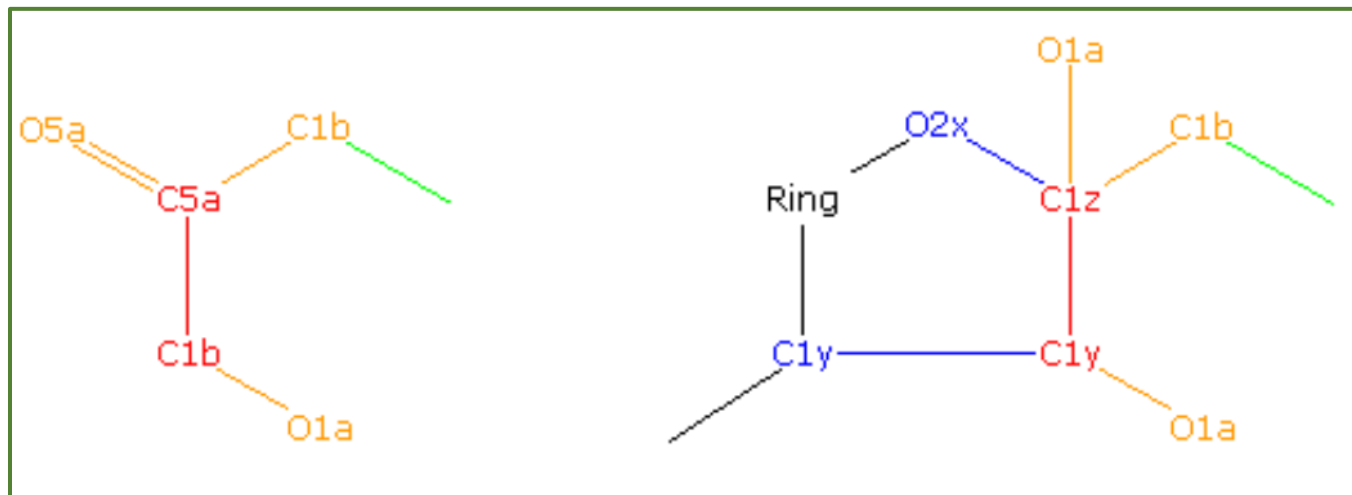




RCLASS: RC00438

Help

Entry	RC00438	RClass	
Definition	C1b-C1y:*-C1y:C5a+O1a-C1z+O1a C5a-C1z:*-O2x:C1b+C1b+O5a-C1b+C1y+O1a		
	<p>The diagram illustrates a graph rewriting rule. On the left, the reactant pair consists of two connected graphs. The first graph has a central node C5a (red) connected to O5a (orange) above and C1b (red) below. The second graph has a central node C1b (red) connected to C1b (orange) above and O1a (orange) below. On the right, the product pair consists of two connected graphs. The first graph has a central node Ring (black) connected to C1y (blue) below. The second graph has a central node C1z (red) connected to O2x (blue) above, C1b (orange) to the right, C1y (red) below, and O1a (orange) to the right. The connections between the two graphs in the product pair are C1y (blue) from the first graph to C1y (red) in the second graph, and C1z (red) from the second graph to C1y (blue) in the first graph.</p>		
Reactant pair	C00111_C00354 C00111_C05378	C00111_C01094 C00111_C06441	C00111_C03785 C00111_C20831



Reaction Atom I

Reaction Atom II

$C1b-C1y: *-C1y:C5a+O1a-C1z+O1a$

Left RXN side:

$C1b: *:C5a+O1a$

Right RXN side:

$C1y:C1y:C1z+O1a$

$C5a-C1z: *-O2x:C1b+C1b+O5a-C1b+C1y+O1a$

Left RXN side:

$C5a: *:C1b+C1b+O5a$

Right RXN side:

$C1z: O2x:C1b+C1y+O1a$

Definition formulas describe the environment of the reaction atom

Three Parts:

Red: (R-Atoms) how the environment of the R-atom changes

Blue: (D-Atoms) which atoms combine/split from the R atom

Yellow: (M-atoms) which atoms in the environment of the R-atom do not change



RCLASS - Reconstruction – Trees out of RDM Patterns

RDM Patterns

$C1b-C1y: * -C1y: C5a+O1a-C1z+O1a$
 $C5a-C1z: * -O2x: C1b+C1b+O5a-C1b+C1y+O1a$

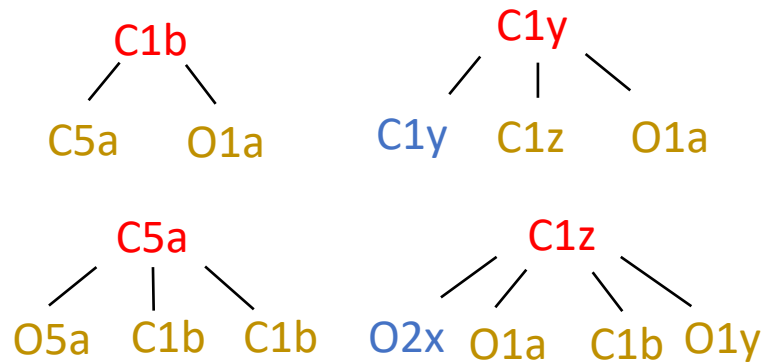
Left reaction side:

$C1b: C5a+O1a$
 $C5a: C1b+C1b+O5a$

Right reaction side:

$C1y: C1y: C1z+O1a$
 $C1z: O2x: C1b+C1y+O1a$

constructed tree structure



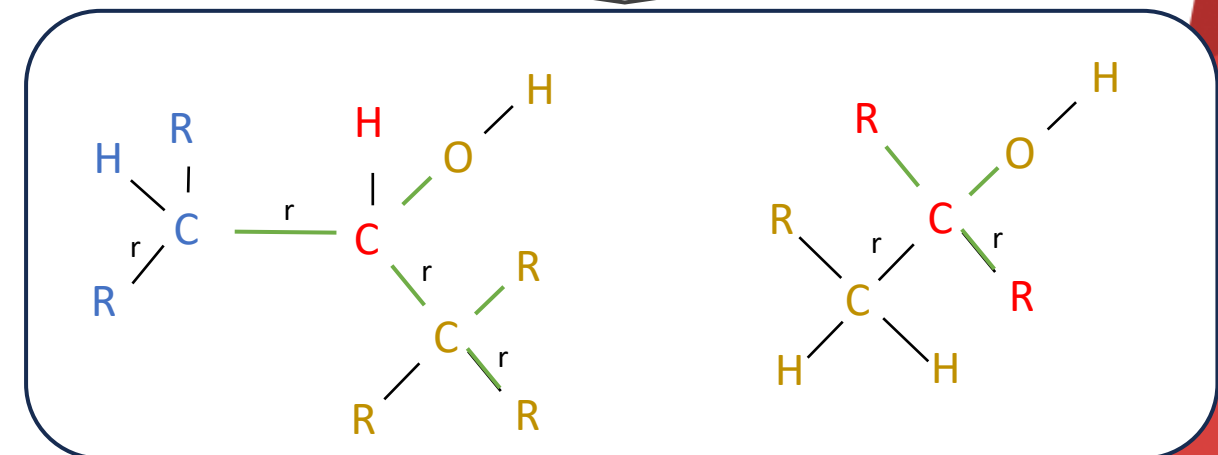
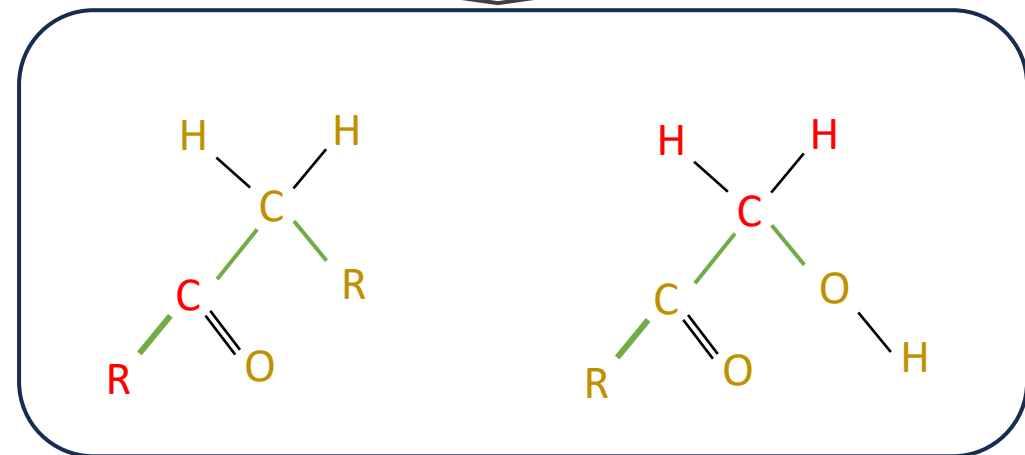
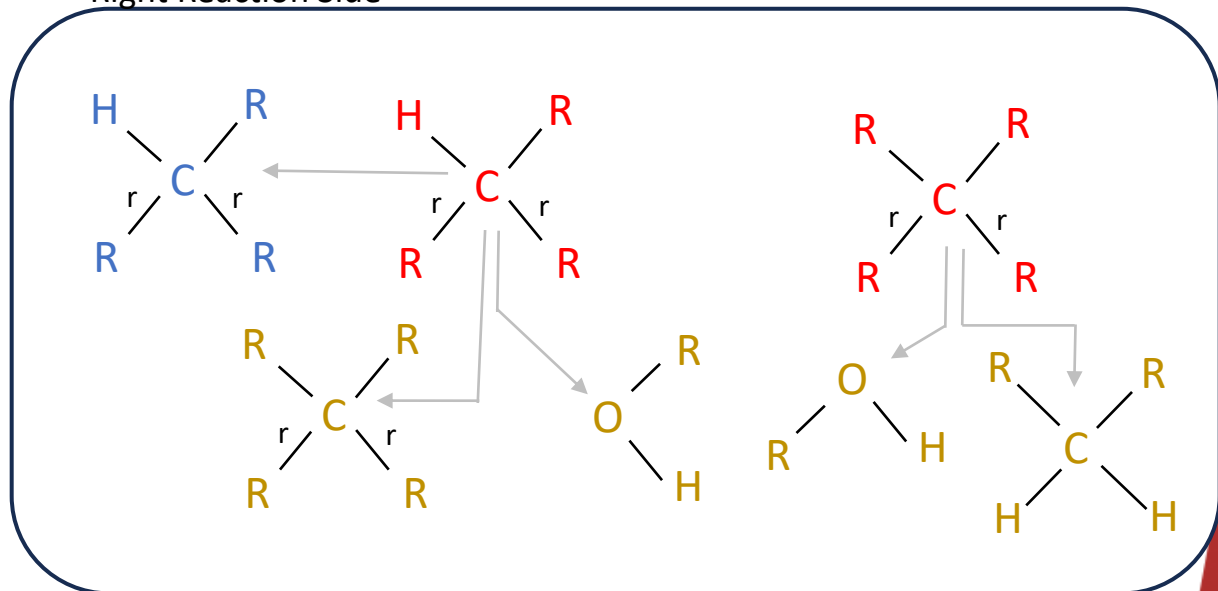
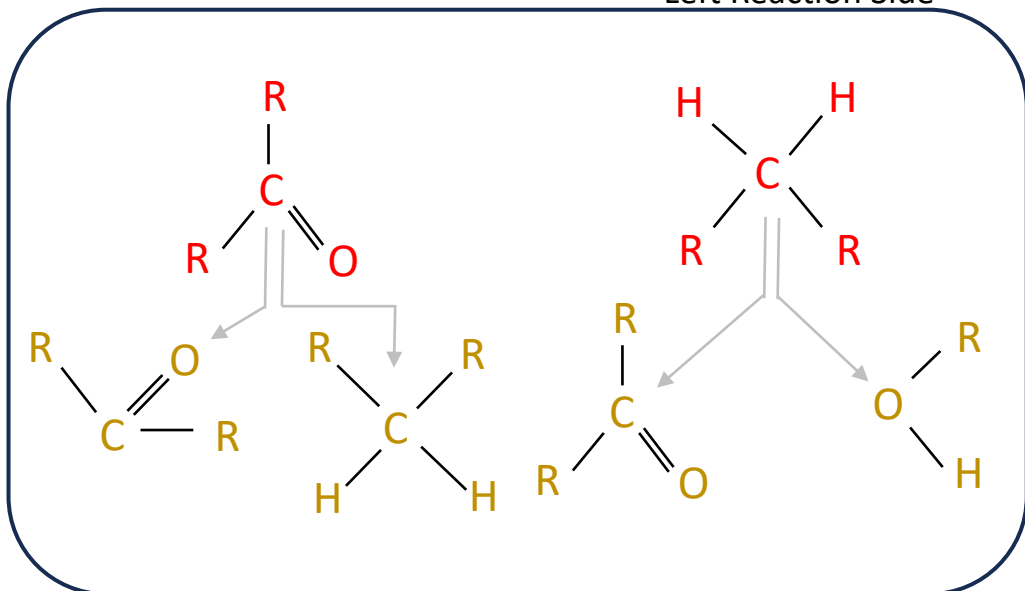


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RCLASS - Reconstruction Assemble to molecule Sub-structure

Left Reaction Side

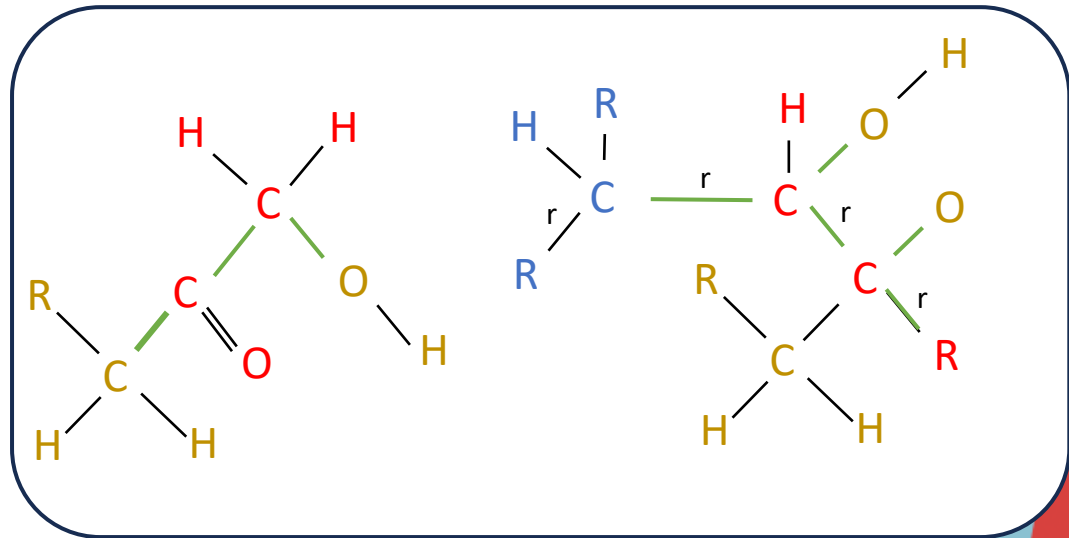
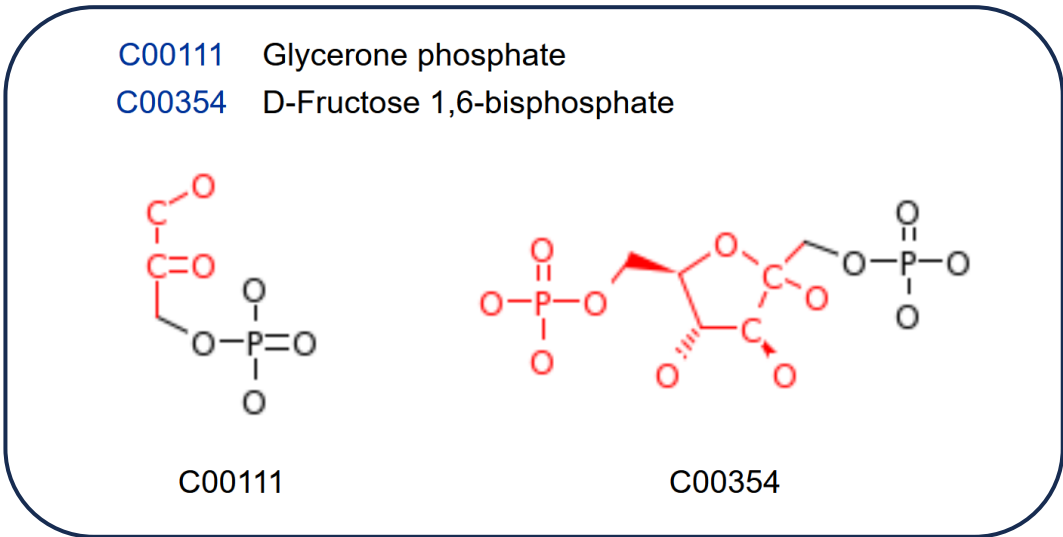
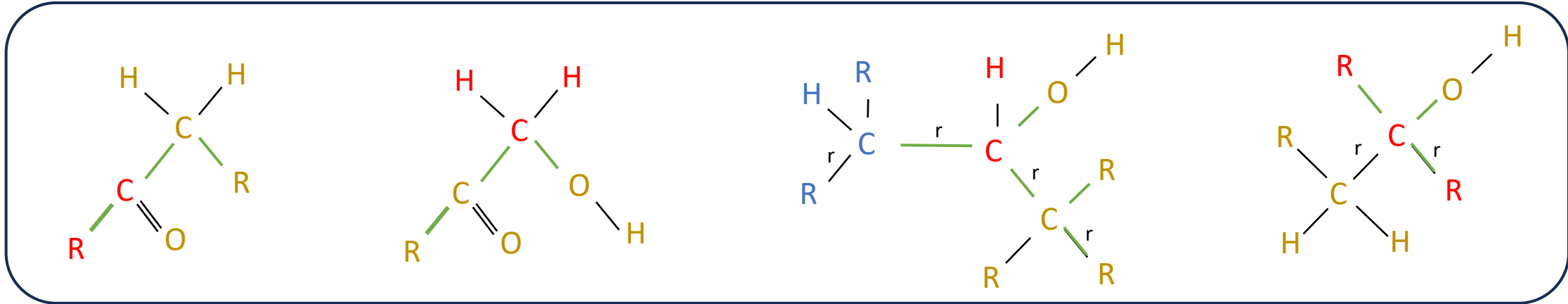
Right Reaction Side





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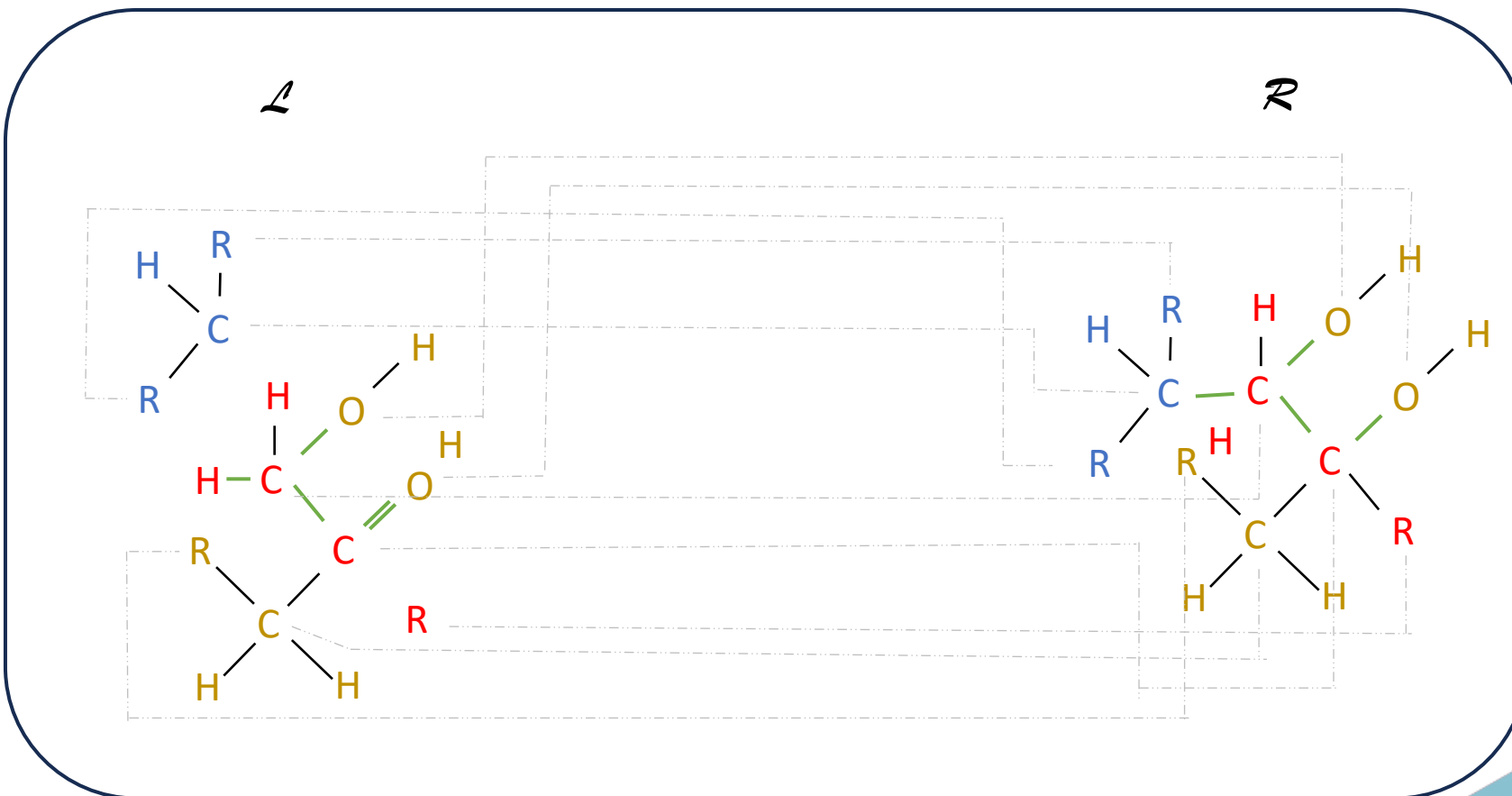
RCLASS - puzzling and control to rewriting rule





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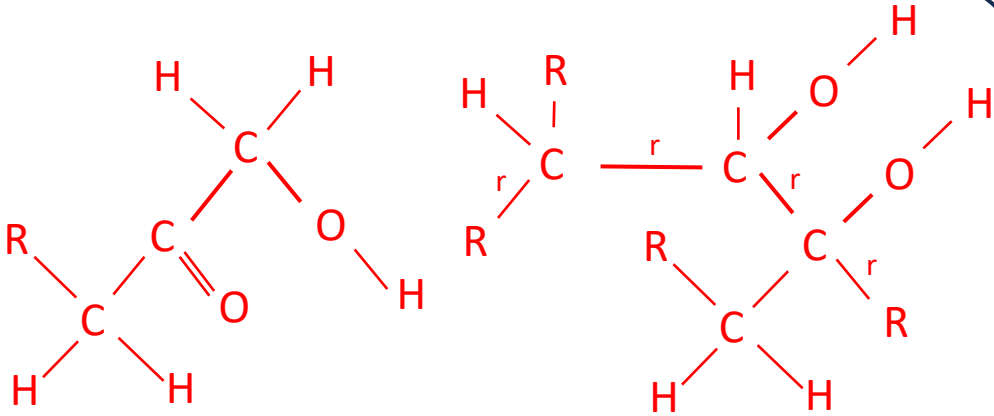
Atom-Atom-Mappings out of RCLASSES



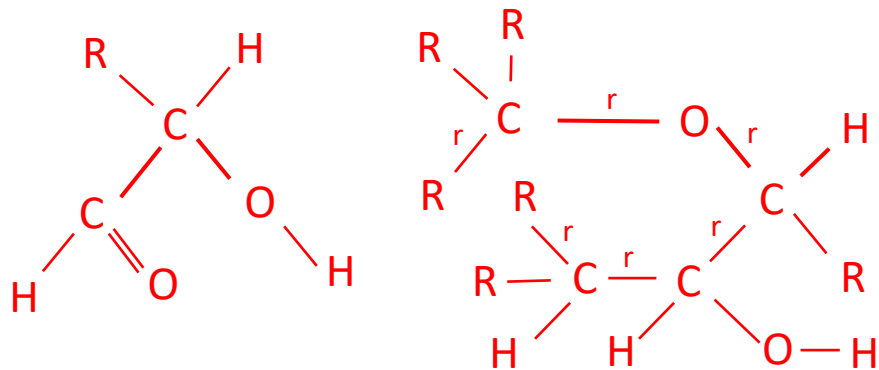


Atom-Atom-Mappings out of RCLASSEs

RC00438



RC00439



- C00118 D-Glyceraldehyde 3-phosphate
- C00111 Glycerone phosphate
- C00354 D-Fructose 1,6-bisphosphate

