

Release notes for September 2021

Retrosynthesis release notes

Improved Synthesis Planning in Reaxys

Feedback from Reaxys users and the broader research community is important to our development plans. Synthesis planning is a major area of interest to our users, especially those interested in synthetic organic chemistry.

Therefore, throughout 2021, we are exponentially improving the synthesis planning capability in Reaxys. Earlier in the year we announced the release our Predictive Retrosynthesis module and now we are happy to announce that we have made significant steps forward in better supporting retrosynthesis from published literature for all our customers.

This release includes a complete redesign of our synthesis planning environment. The new Retrosynthesis feature allows chemists to start their retrosynthesis projects by drawing the desired compound, provides in one view all the information needed to decide which route to take to the lab and enables project management and options for easier collaboration.

Users can now:

- Easily search for relevant synthesis route for a known substance (published retrosynthesis)
- Users can organize their retrosynthesis projects in the central projects space and easily access:
 - Literature references for each reaction step
 - Reaction condition and experimental procedure
 - Commercial availability of starting materials
 - Export retrosynthesis route data in multiple formats

What is included in the current release:

- Redesign of Synthesis Planner to Retrosynthesis enabling users to launch a retrosynthesis search from ChemDraw JS or Marvin JS drawing tool
- Intuitive visualisation options with relevant literature references easily accessible to enable informed decision making
- Option to seamlessly integrate Reaxys predictive retrosynthesis module (additional subscription required).

What's next

- Further development to enable users to extend / edit the synthesis route giving them the ability to add new steps at any stage of the synthesis tree and to also remove single steps or complete branches

- Further development to enable users to define 'bonds to be broken' and 'bonds to be protected' in the target molecule when starting the retrosynthesis search
- Predictive retrosynthesis model update with the latest Reaxys reactions dataset

Users can now draw the desired compound by selecting the Retrosynthesis feature on the top bar and define the parameters for the project from the options on the left side menu:

The screenshot displays the Reaxys Retrosynthesis interface. At the top, the navigation bar includes 'Quick search', 'Query builder', 'Results', 'Retrosynthesis' (highlighted), 'History', and 'Alerts'. The main workspace is divided into three sections:

- Left Panel:** A vertical toolbar with icons for drawing and editing. The 'Draw' button is highlighted in purple. Below the toolbar, the text 'Structure editor selected: Marvins ChemDrawJS ' is visible.
- Center Panel:** A large canvas showing a chemical structure of a complex molecule. The structure consists of a piperazine ring with a methyl group, connected via a methylene bridge to a benzene ring. This benzene ring is further connected to an amide group, which is linked to another benzene ring with a methyl group. A pyridine ring is also attached to the second benzene ring.
- Right Panel:** A 'Parameters' panel with a 'Published' status indicator. It includes several settings:
 - 'Create upto' set to 5 synthesis plans.
 - 'Branches per step' set to 5.
 - 'Max. number of steps' set to 5.
 - 'Stop searching if starting material is commercially available' with 'Yes' selected.
 - 'Assumed yield for reactions without a given yield' with a slider set to approximately 50% between 0% and 100%.

At the bottom of the interface, there are buttons for 'Clear', 'Cancel', and 'Synthesize'.

Review, edit or delete Retrosynthesis projects:

No.	Date/Time	Project name	Draw new structure	No. of routes
5197	28 Sep 2021 08:58	Project #5197 Delete		Published View
5196	28 Sep 2021 08:57	Project #5196 Delete		Published 5 View
5195	28 Sep 2021 08:57	Project #5195 Delete		Published View
5193	28 Sep 2021 08:57	Project #5193 Delete		Published 5 View

Analyse results by reviewing experimental conditions, procedures, and literature reference for each reaction step:

Published route #5

Export Legend

Rotate

Published route #5

Step 1 Step 2

Conditions	Yield	Reference
Stage #1: 4-(4-N-methylpiperazine-1-yl)methyl benzoic acid dihydrochloride With N-ethyl-N,N-diisopropylamine In dichloromethane at 10 - 20°C; for 0.5h; Stage #2: With tetrabutyl ammonium fluoride; 1,1'-carbonyldiimidazole In dichloromethane at 20°C; for 3h; Stage #3: C ₂₂ H ₃₁ N ₅ Si ₂ In dichloromethane at 0 - 20°C; for 3h; Solvent; Reagent/catalyst;	91.3%	Anhui Haikang Pharmaceutical Co., Ltd.; Zhang Xiaoshun CN108752314, 2018, A Location in patent: Paragraph 0015; 0016; 0028; 0033; 0036; 0037 Full Text Details Abstract

1; 2 Synthesis of Compound (I)

In the second step, 4-[(4-methyl-1-piperazine)methyl]benzoic acid dihydrochloride 33.1 g (107.8 mmol, 1.1 eq) and 100 g of tetrahydrofuran were placed in a reaction flask at a temperature of 10-20 °C. After adding 21.8 g (215.6 mmol, 2.2 eq) of triethylamine under stirring for 30 minutes, 0.26 g (0.98 mmol, 1% eq) of tetrabutylammonium fluoride was added, and N,N'-carbonyldiimidazole 17.5 g was added in portions. (107.8 mmol, 1.1 eq) was stirred at room temperature for 3 hours, and 41.3 g of the compound (IV) (98.1 mmol, 1.0 eq) obtained in the above step was added dropwise to a solution of 60 g of tetrahydrofuran at 0-10 °C, and the mixture was stirred at room temperature for 2 hours. The TLC controlled raw material was completely reacted, the solvent was distilled off under reduced pressure, 150 g of a 10% aqueous hydrochloric acid solution was added, stirred for 2 hours, extracted with dichloromethane (90 g×2), and the aqueous layer was adjusted to adjust the pH with 10% sodium hydroxide. 8-9, filtration, solid recrystallized from isopropanol to give a white solid imatinib 43.8 g, yield 90.6%.

Reaxys is a trademark of Elsevier Limited.
Copyright © 2020, Elsevier.