Retrosynthetic Route Planning Based on Molecular Similarity

INQUIRY

The goal of creating a retrosynthetic route is to design a synthetic route from a given ideal molecule to commercially available materials. Early retrosynthesis systems rely heavily on hand-coded reaction rules or algorithms obtained from a diversity of databases. The applicability of a feasible reaction rule to the target product is evaluated based on the existence of the local structure or atomic features around the candidate reaction site in the rule set. This type of method is a purely data-driven reverse synthesis methodology in which scientists use many known reactions to build the model. Alfa Chemistry select and use reaction templates to generate ideal precursor molecules in the similarity-based method. We do not perform any adjustment or training of any model parameters and apply this technique to directly act on the data.

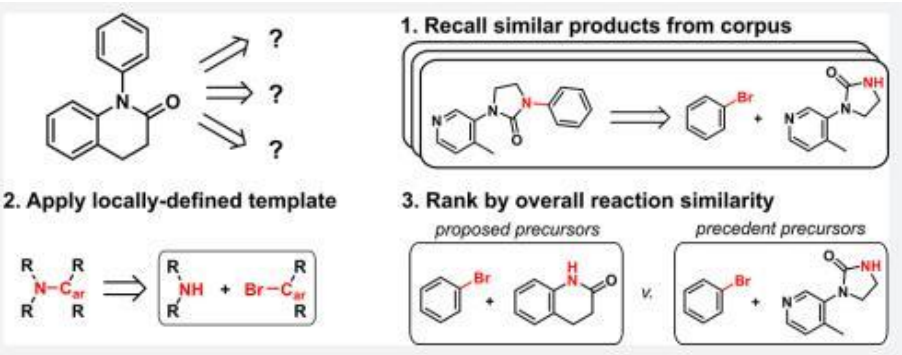

Figure 1. Design a molecular similarity based retrosynthetic route with the assistance of computer. (Coley, C. W.; *et al*. 2017)

Our Workflow

- First, reaction precedents can be developed based on product similarity. We determine how molecules with similar functions are produced in this step.
- Second, we obtain a local transform and apply them to the target compound.
- Third, based on the similarity between the candidate molecule and the precedent reactant, our teams perform scoring operation.

Similarity Calculation

We study the molecular similarity by observing the degree of overlap of atoms in a molecule. Our experts select the optimal reaction precedents and rank the candidate precursors by calculating the molecular similarity. Alfa Chemistry mainly applies 2D structure based method to quantify molecular similarity.

Evaluation Procedure

The goal of evaluation procedure is to propose a rational reaction route that have a high likelihood of success in the forward direction and fit into a broader synthesis plan with an acceptably high overall yield. We use a set of reaction data for accurate retrosynthesis prediction. In addition, our experts have prepared an additional program for handling of stereochemistry when handling simulating reactions.

Reference

1. Coley, C. W.; *et al*. Computer-Assisted Retrosynthesis Based on Molecular Similarity. *ACS Central Science*. 2017, 3(12): 1237-1245.