

Graph-based Self-Learning Retrosynthesis Planner

Dmitrii Zankov, Hokkaido University

Retrosynthetic analysis is a problem-solving technique in chemical synthesis, that involves a “molecular deconstruction” process converting a synthetic target molecule into simpler precursor structures (retrons) or pseudomolecular structures (synthons) through a retrosynthetic transformation (retro reaction rule). At the same time, retrosynthesis analysis can be performed with computer software, which accelerates its application for the synthesis of desired compounds. In this study, we introduce a novel tool for retrosynthetic planning, which combines Monte-Carlo Tree Search (MCTS) with graph neural networks for the prediction of reaction rules and synthesisability of intermediate products. We applied a self-learning approach, which allows the neural network to learn the synthesisability of intermediate products from the previous experience of retrosynthesis planning sessions. In this manner, the time-consuming rollout evaluation of synthesisability in classic MCTS can be replaced by instant predictions of neural networks. This approach not only significantly speeds up retrosynthetic analysis but increases the amount of successfully analyzed target molecules. The performance of this tool was evaluated through comparison with other retrosynthesis approaches and state-of-the-art tools, using both simple and complex compounds for synthesis.