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# Advancing Organic Chemistry with Computer-Aided Synthesis Planning

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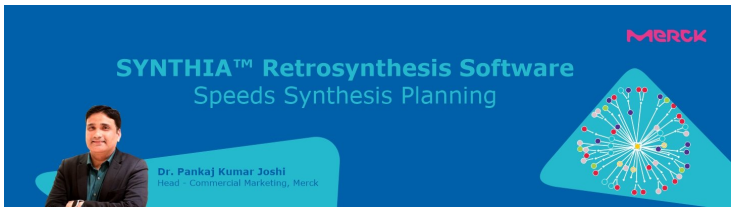
**SYNTHIA™ Retrosynthesis Software Speeds Synthesis Planning**




Synthesis planning can be a daunting task especially when one is working to meet demanding project goals within compressed timelines. Fortunately, there are commercially available software tools that can help to accelerate this process.

**Reduce Risk & Improve Synthesis Outcomes**

Developed over 15 years and powered by advanced algorithms that are coded with the organic chemistry rules that we all know, Synthia™ Retrosynthesis Software helps organic chemists to think beyond the published literature. Developing novel, yet robust routes to complex molecular targets requires a synergistic human-computer interface that, by design, encourages the end user to go further. SYNTHIA™ meets this objective by proposing computer-vetted routes that can be easily modified and expanded based on the preferences of the end-user. Expert-coded chemistry rules that know what reactions work and what reactions won't work in the context of a synthetic route are what differentiate this software from other retrosynthesis platforms on the market today.

**SYNTHIA™…Problem Solved**

Synthia™ Retrosynthesis Software is a decision support platform that assists both discovery and process chemists to design synthesis routes to structurally diverse chemical targets. Since the software is not reliant upon the published scientific literature alone, synthesis routes to new and previously unreported molecules can be planned with confidence.

In one of the recent editions of "Small Molecules of the Month", Drughunter.com presented an oral plasma kallikrein inhibitor, berotralstat, which was recently approved as the first non-steroidal treatment of hereditary angioedema (HAE).

SYNTHIA™ designed an efficient, convergent, chiral synthesis starting with moderately priced commercial compounds using the default automatic retrosynthesis settings.

Computer-assisted synthesis planning can also speed the development of new routes to existing drugs. As detailed in their 2020 publication in *Chemical Science, Szymuc1 et al.* detailed how her team was able to quickly identify multiple viable routes to two potential yet unproven COVID-19 therapeutics. SYNTHIA™ was tasked with identifying alternative routes to both remdesivir and hydroxychloroquine given the global supply chain disruptions at the time and the potential need to source more widely available starting materials.

A similar strategy to address global chemical supply chain disruptions was taken by *Lin2 et al.* in the 2021 *Nature Communications* publication detailing the syntheses of eleven 3 of 3 potential COVID-19 therapeutics including the known anti-viral Umefenovir which is primarily used to treat Influenza A and Influenza B viral infections.

In both examples, laboratory validation of synthetic routes suggested by SYNTHIA™ was performed and demonstrates the utility and speed of the software to assist in the synthesis planning. As commercial and academic organic chemists become more accustomed to using computer-assisted synthesis planning software such as SYNTHIA™, we anticipate reading more about the efficient and innovative approaches used to produce commercially available high-value and structurally complex organic compounds that benefit humanity.

**Speeding up drug discovery**

Many therapeutic candidates can now be designed computationally, before being synthesized and experimentally validated. Identifying which of these compounds can be easily and rapidly synthesized is crucial to accelerating the drug discovery pipeline. Narrowing down lists of potential drug candidates is particularly helpful for medicinal chemists who runs a synthetic organic chemistry laboratory focused on drug discovery and preclinical development. It would be time consuming to manually evaluate the potential synthesis pathways for each unique proposed compound. Every compound that comes through such computational drug discovery project if goes through Synthia™, it quickly becomes clear which compounds may be the easiest to make. Automated retrosynthesis planning through Software such as Synthia™ gives researchers the ability to test and validate compounds faster. The acceleration helps scientists better respond to public health crises that demand novel therapeutics.

1 Szymku?, S., et. al. Computer-generated “synthetic contingency” plans at times of logistics and supply problems: scenarios for hydroxychloroquine and remdesivir. *Chem. Sci.* [Online], **2020**, *11*, 6736-6744. https://doi.org/10.1039/D0SC01799J

2 Lin, Y., Zhang, Z., Mahjour, B.*et al.*Reinforcing the supply chain of umifenovir and other antiviral drugs with retrosynthetic software. *Nat Commun* **12**, 7327 (2021). https://doi.org/10.1038/s41467-021-27547-3