SDU
University of Southern Denmark

TACsy

Training Alliance for Computational systems chemistry

UNIVERSITÄT LEIPZIG

SynCat: A light-weight model for reaction classification

Winterseminar-Bled

Presenter: Tieu-Long Phan

Date: 10.02.2025

MARIE CURIE ACTIONS

Founded by the European Union

This project has received funding from the European Unions Horizon 2021 research and innovation programme under the Marie-Skłodowska-Curie grant agreement No 101072930

OUTLINE

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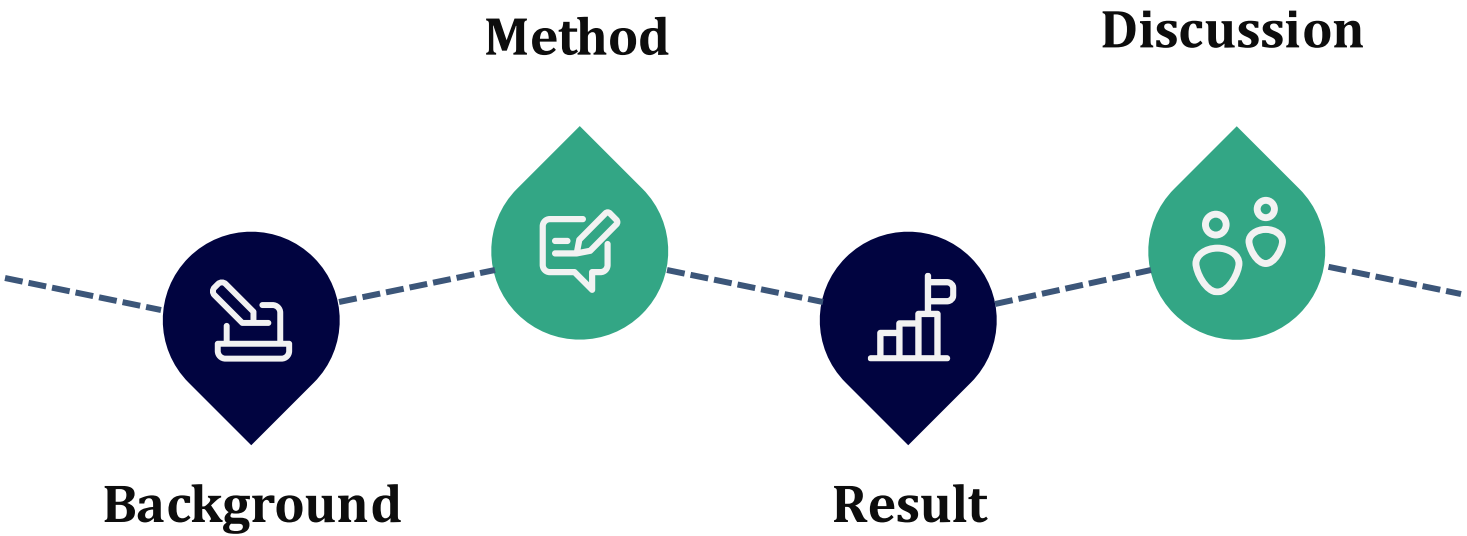

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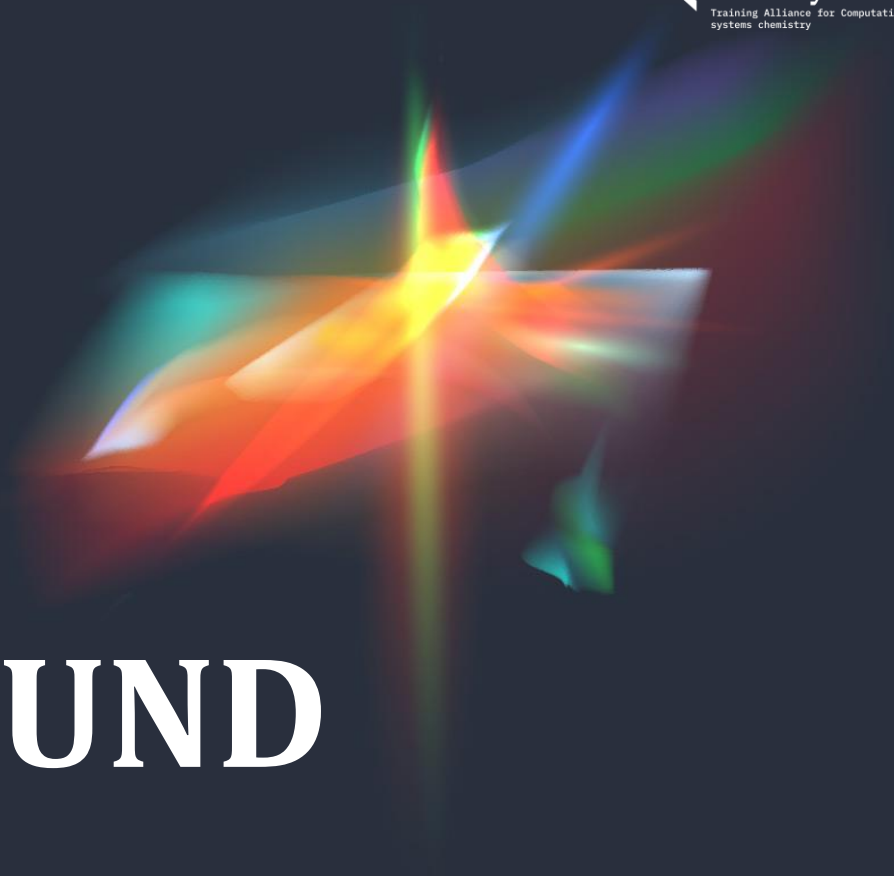
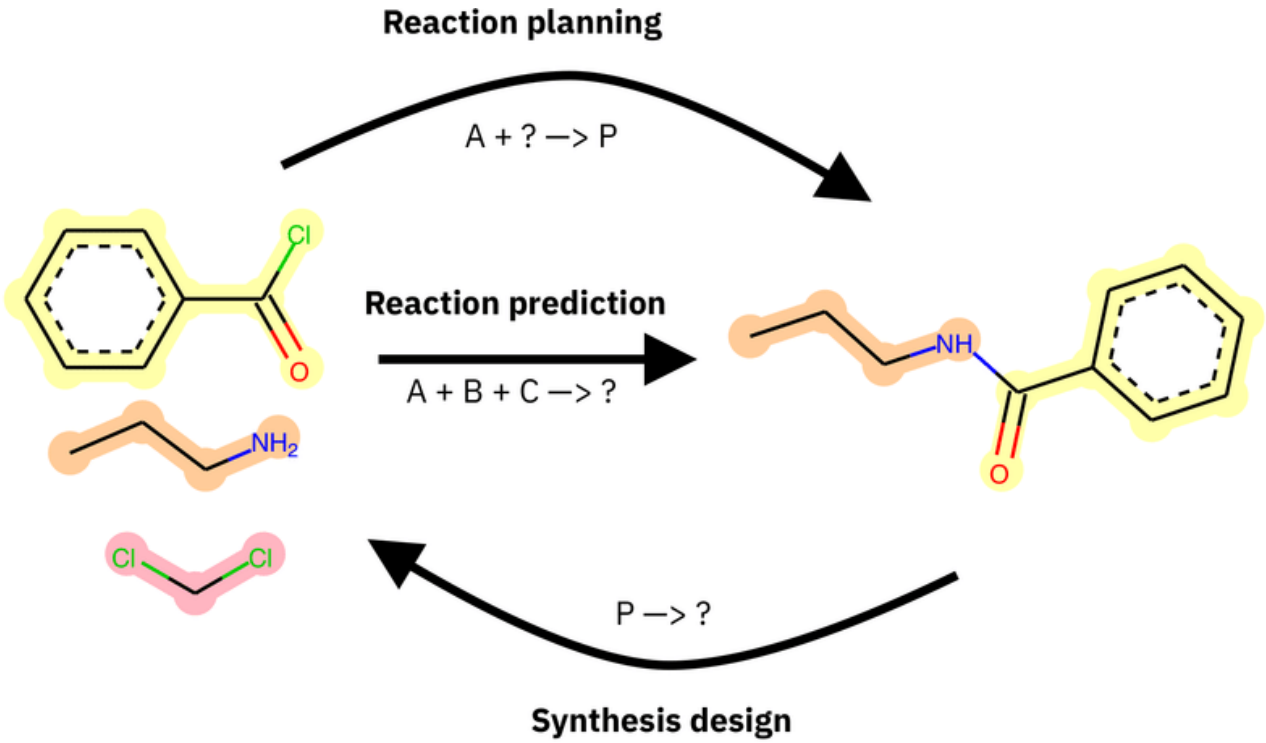


01

BACKGROUND

BACKGROUND

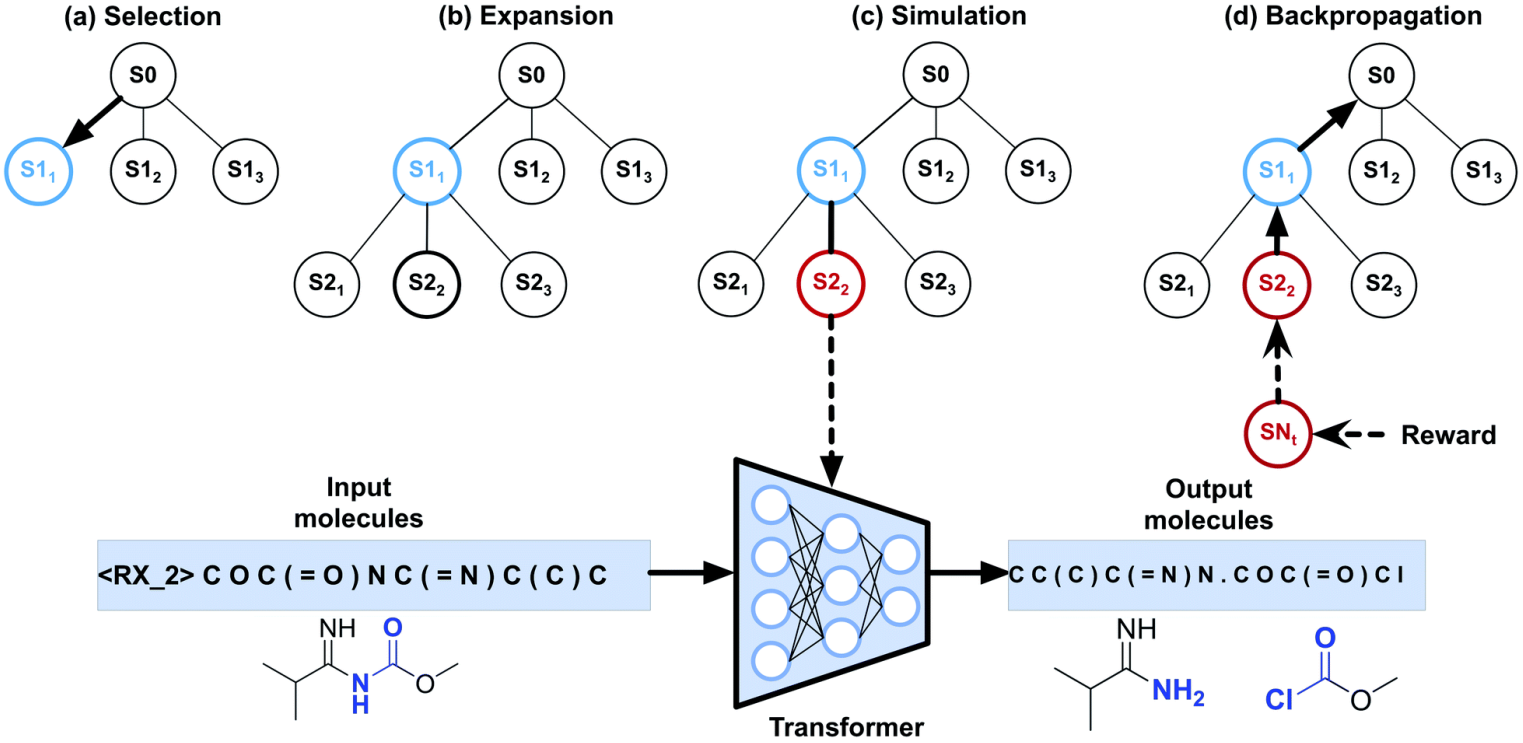
Synthesis Planning



Griffiths, R. R., et al. (2021). Dataset bias in the natural sciences: a case study in chemical reaction prediction and synthesis design. arXiv preprint arXiv:2105.02637.

BACKGROUND

Template-free synthesis planning



Lin, K., Xu, Y., Pei, J., & Lai, L. (2020). Automatic retrosynthetic route planning using template-free models. Chemical science, 11(12), 3355-3364.

BACKGROUND

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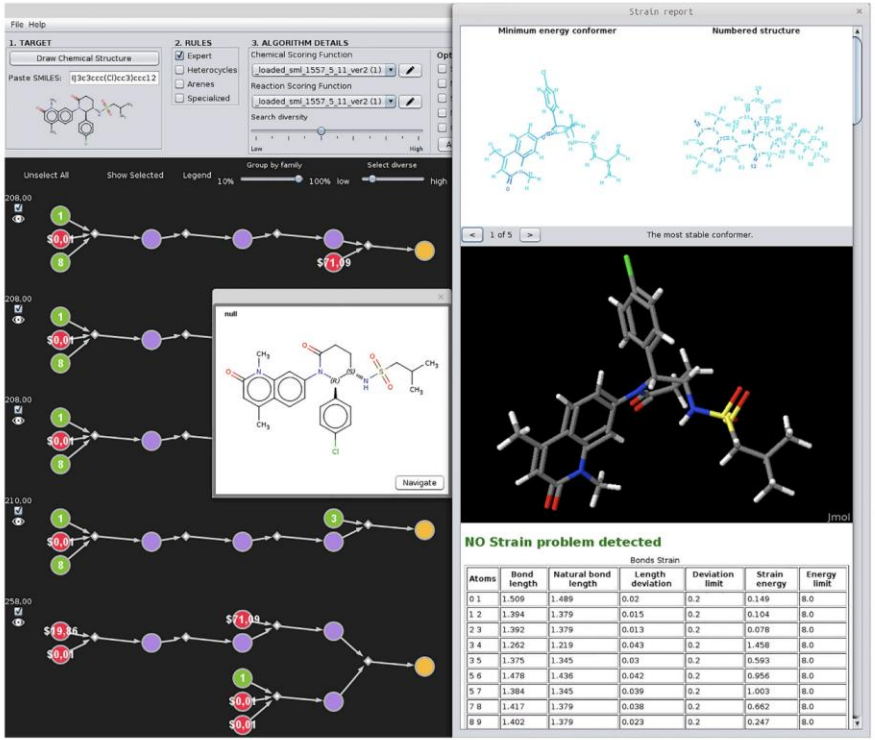
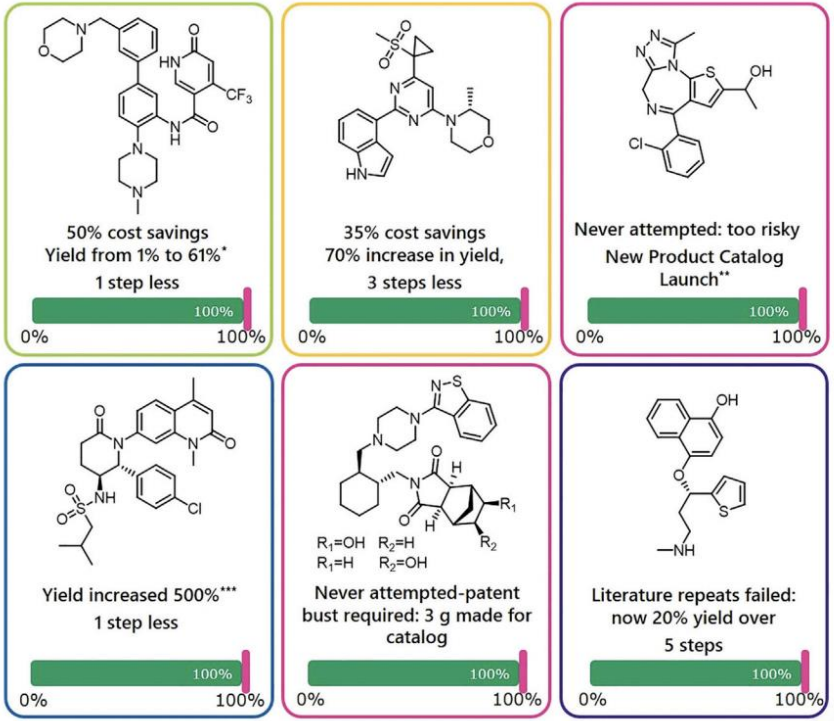
Template-based synthesis planning

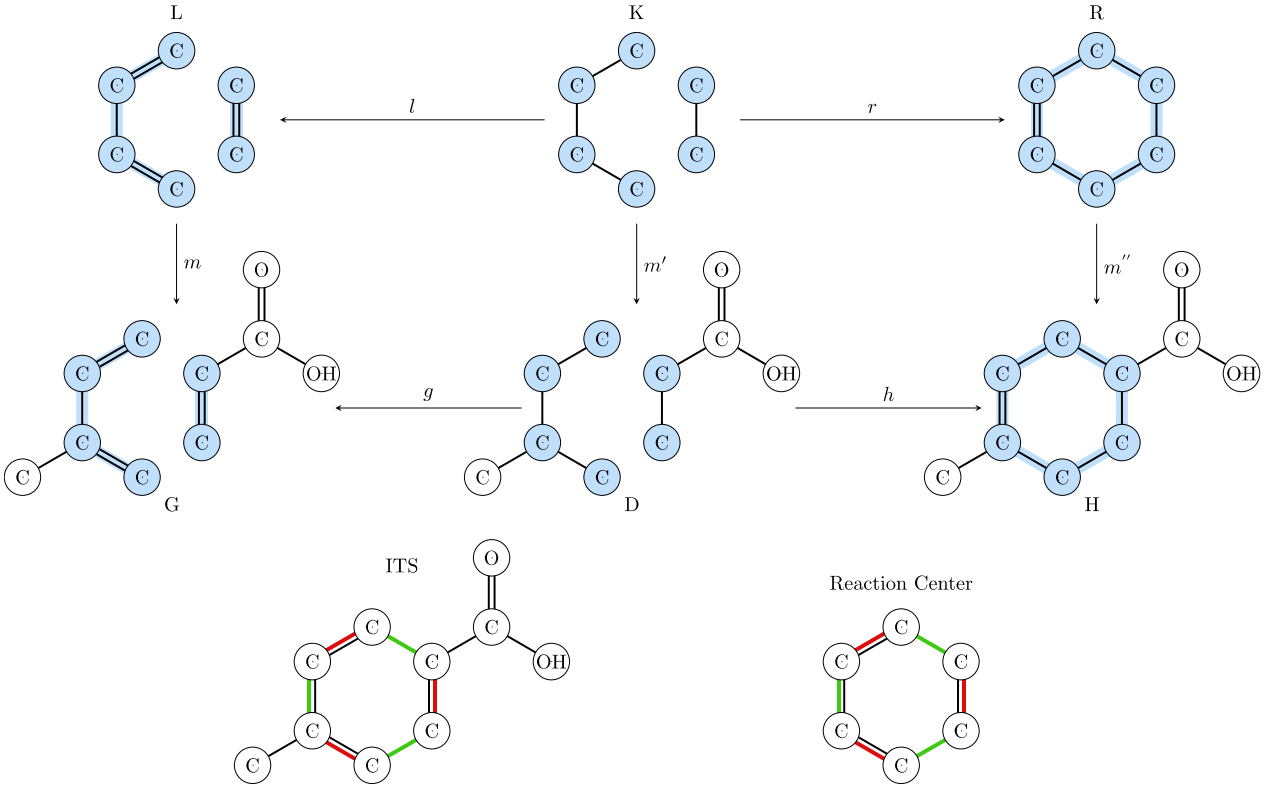




Grzybowski, B. A., Szymkuć, S., Gajewska, E. P., Molga, K., Dittwald, P., Wołos, A., & Klucznik, T. (2018). Chematica: a story of computer code that started to think like a chemist. Chem, 4(3), 390-398.

BACKGROUND

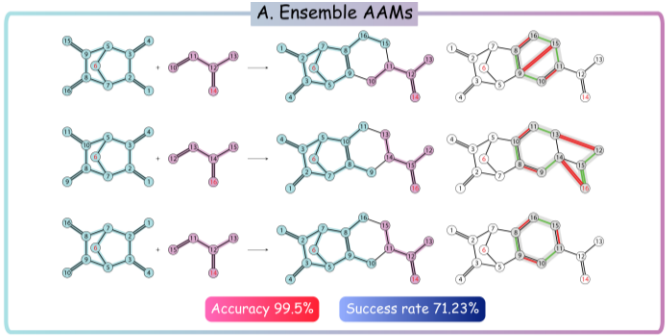
Double Pushout Rules

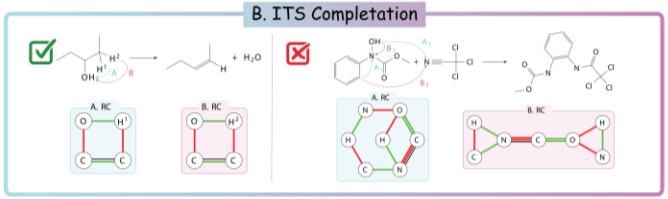


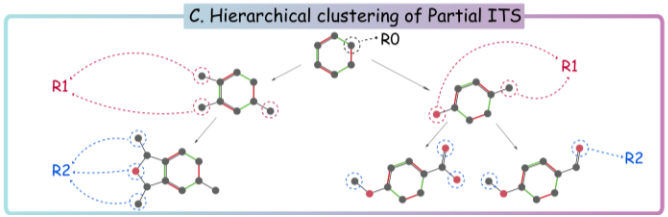
Phan, T. L., Weinbauer, K., Laffitte, M. E. G.,...,& Stadler, P. F. (2024). SynTemp: Efficient Extraction of Graph-Based Reaction Rules from Large-Scale Reaction Databases.

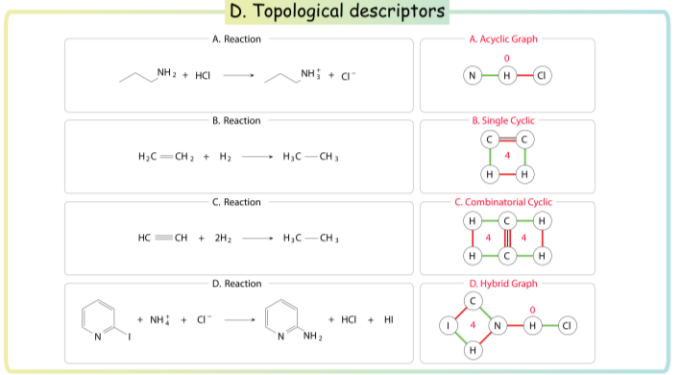
BACKGROUND

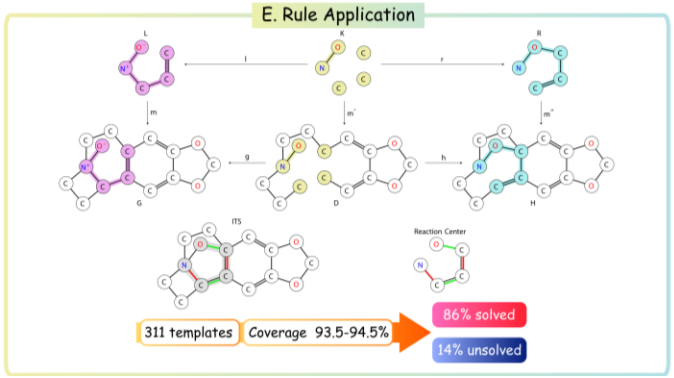
SynTemp











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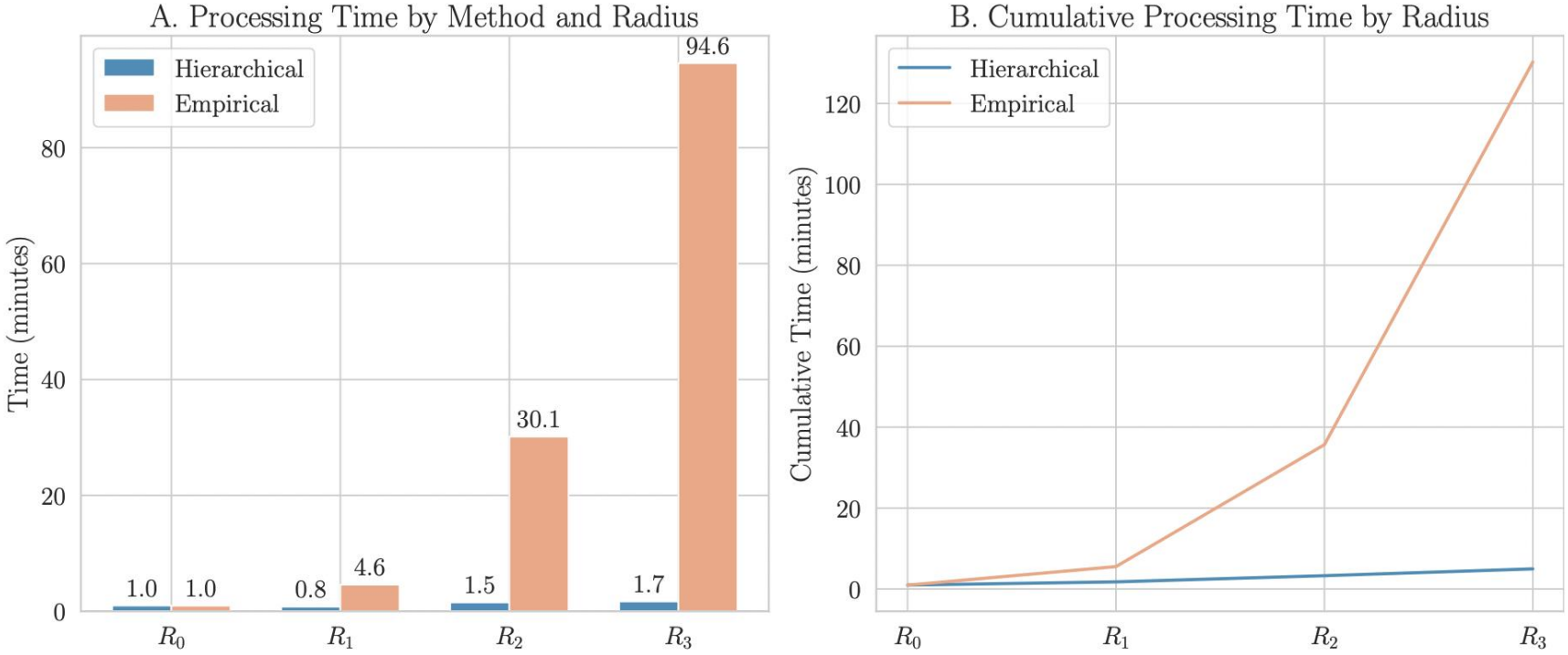
SynTemp - Challenge



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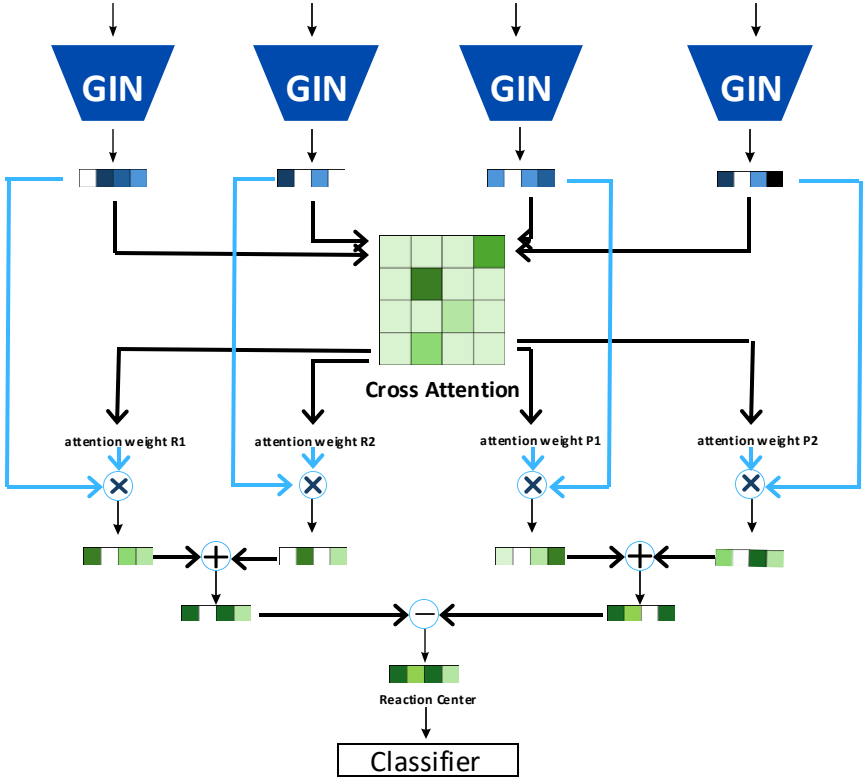
BACKGROUND

SynCat



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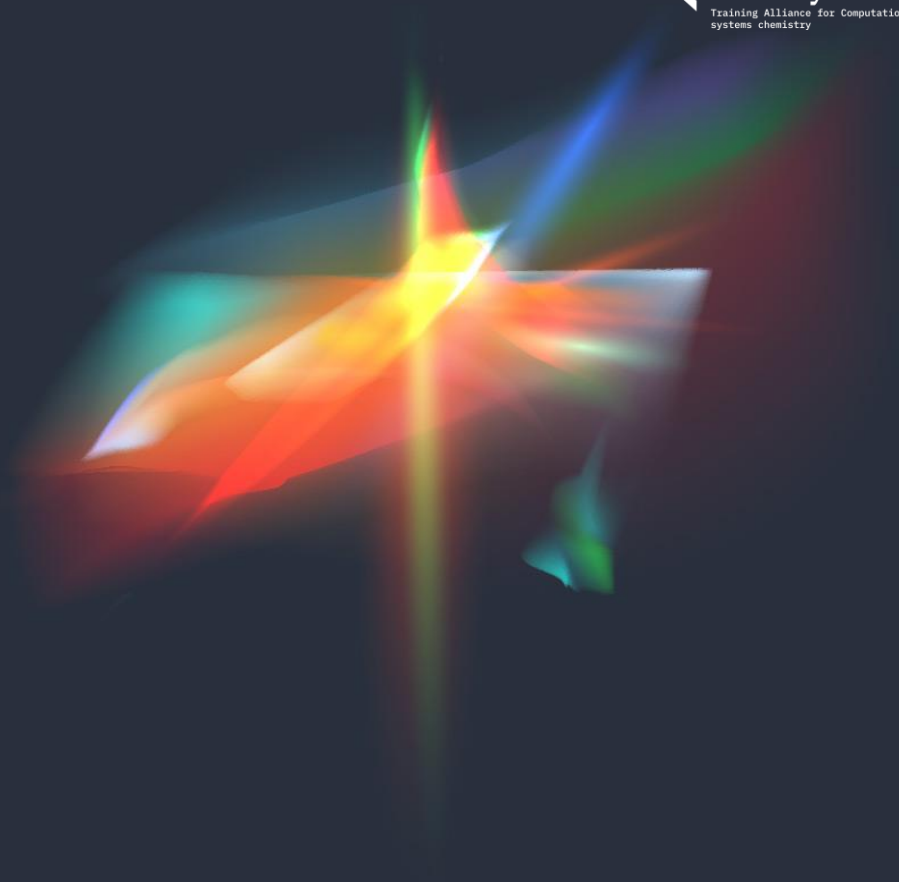

02

METHOD

METHOD

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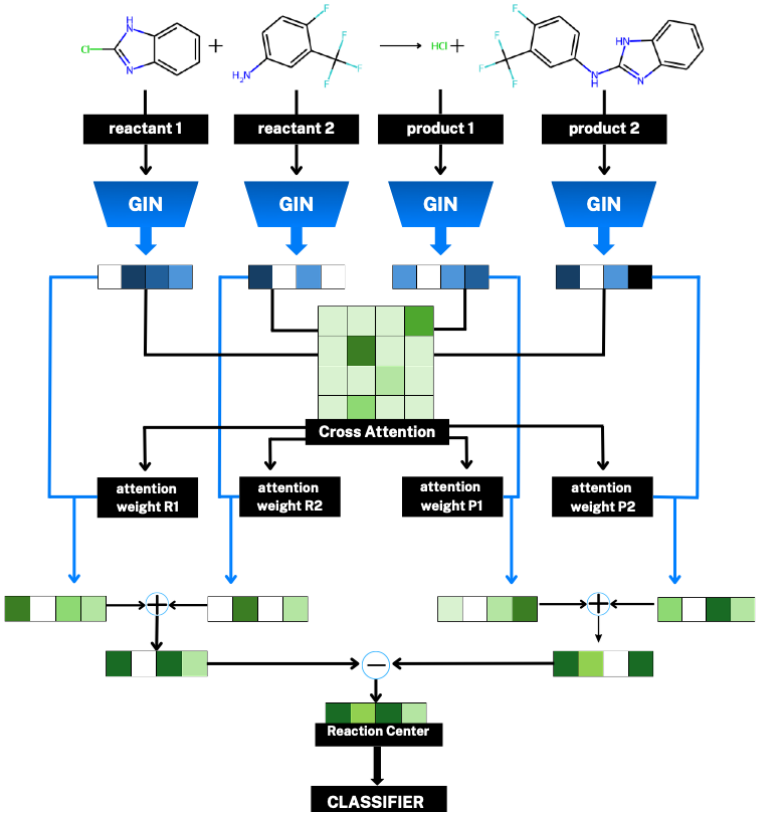
MODEL ARCHITECTURE



METHOD

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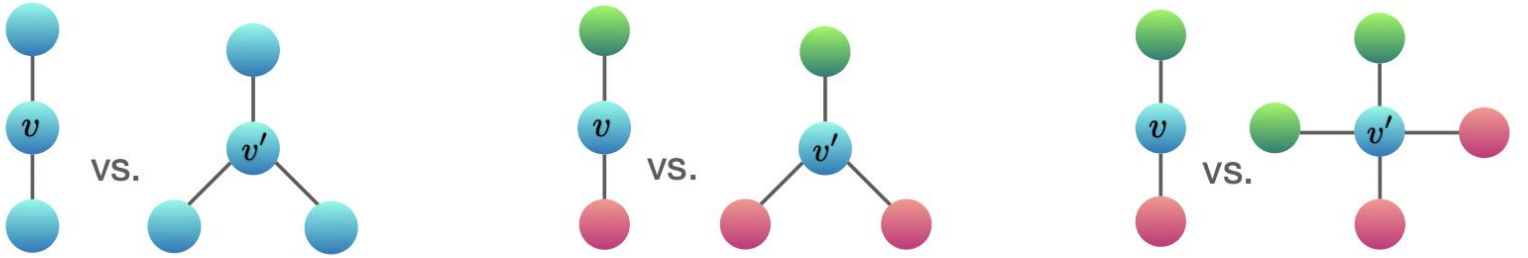
Graph isomorphism network



(a) Mean and Max both fail (b) Max fails (c) Mean and Max both fail

We utilize the Graph Isomorphism Network (GIN) to enhance graph representation accuracy, employing learnable transformations:

$$\mathbf{h}_v^{(0)} = \phi_n(\mathbf{v}), \quad \mathbf{h}_e^{(k)} = \phi_e(\mathbf{e}^{(k)}), \tag{1}$$

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Graph isomorphism network

Vertex embeddings update through layers, integrating local and neighboring data:

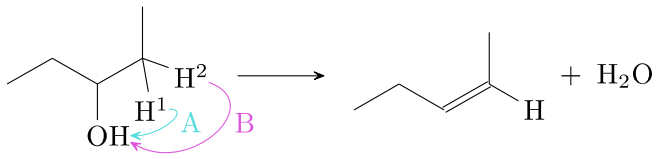
$$\mathbf{h}_v^{j,(l)} = \psi^{(l)} \left(\mathbf{h}_v^{j,(l-1)} + \sum_{k|\mathbf{e}^{j,k} \in E} \mathrm{ReLU}(\mathbf{h}_v^{j,(l-1)} + \mathbf{h}_e^{j,k}) \right), \qquad (2)$$

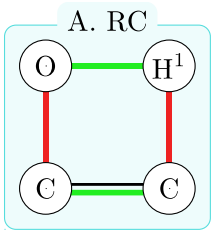
culminating in a comprehensive graph embedding:

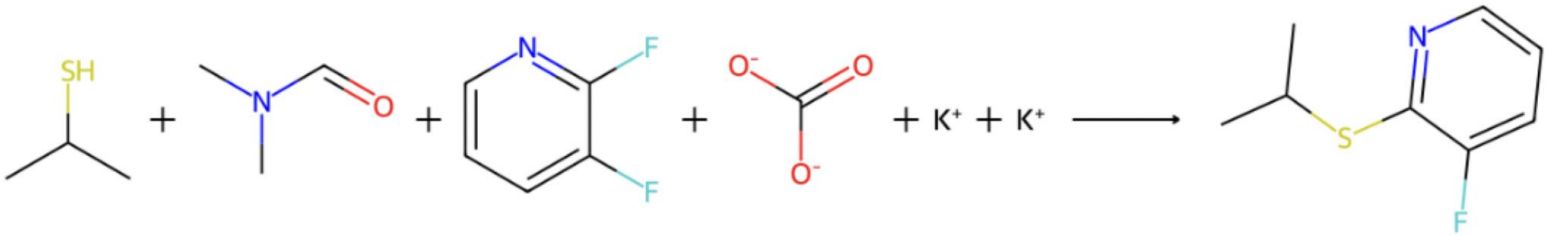
$$\mathbf{h}_g = \sum_{j|\mathbf{v}^j \in V} \mathbf{h}_v^{j,(L)}. \qquad (3)$$

METHOD

Cross-attention







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Cross-attention

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The reaction center, Γ, is calculated by subtracting the aggregated product embeddings from the reactant embeddings:

$$\Gamma = \mathcal{R} - \mathcal{P}$$

where $\mathcal{R}$ and $\mathcal{P}$ denote the embeddings of reactants and products, respectively. This difference highlights the differential characteristics crucial for reaction classification.

METHOD

Cross-attention

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To address noise from redundant substances, we implement cross-attention mechanisms that assign significance to compounds based on their contribution to the reaction center. The matrices $\mathcal{R}_{\text{org}}$ and $\mathcal{P}_{\text{org}}$ represent original reactant and product embeddings, from which we derive:

$$\mathcal{R}_{\text{updated}} = \begin{bmatrix} \mathcal{R}_{\text{org}} \\ S_{\mathcal{R}_{i,j}} \end{bmatrix}, \quad \mathcal{P}_{\text{updated}} = \begin{bmatrix} \mathcal{P}_{\text{org}} \\ S_{\mathcal{P}_{i,j}} \end{bmatrix}$$

Pairwise sums are integrated to enhance embeddings.

METHOD

Cross-attention

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Pairwise sums are integrated to enhance embeddings.

METHOD

Cross-attention

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Updated embeddings are processed to generate query and key vectors for attention calculations:

$$Q_{\mathcal{R}} = \mathcal{R}_{\text{updated}} \cdot W_q, \quad K_{\mathcal{R}} = \mathcal{R}_{\text{updated}} \cdot W_k$$

$$Q_{\mathcal{P}} = \mathcal{P}_{\text{updated}} \cdot W'_q, \quad K_{\mathcal{P}} = \mathcal{P}_{\text{updated}} \cdot W'_k$$

Attention weights are computed to emphasize the contributions of specific compounds.

METHOD

Cross-attention

The final embeddings for reactants and products are derived by applying attention weights:

$$\mathcal{R} = \sum_{i=0}^{n_r-1} \mathcal{R}_{\text{updated}}[i,:] \cdot A_{\mathcal{R}_{\text{avg}}}[i], \quad \mathcal{P} = \sum_{i=0}^{n_p-1} \mathcal{P}_{\text{updated}}[i,:] \cdot A_{\mathcal{P}_{\text{avg}}}[i]$$

The reaction center Γ is then used in a neural network with softmax activation for classification, optimizing using cross-entropy loss:

$$\mathcal{L} = -\sum_{i=1}^{N}\sum_{c=1}^{C} y_{i,c} \log(p_{i,c})$$

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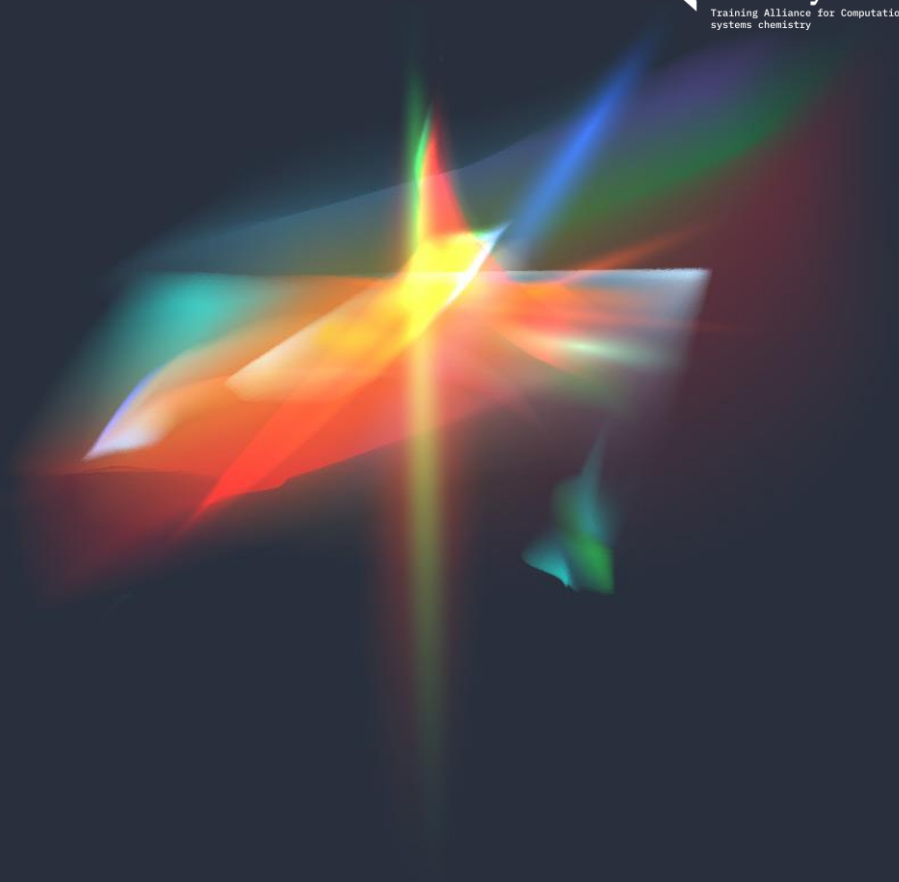

03

RESULT

RESULT

Benchmarking

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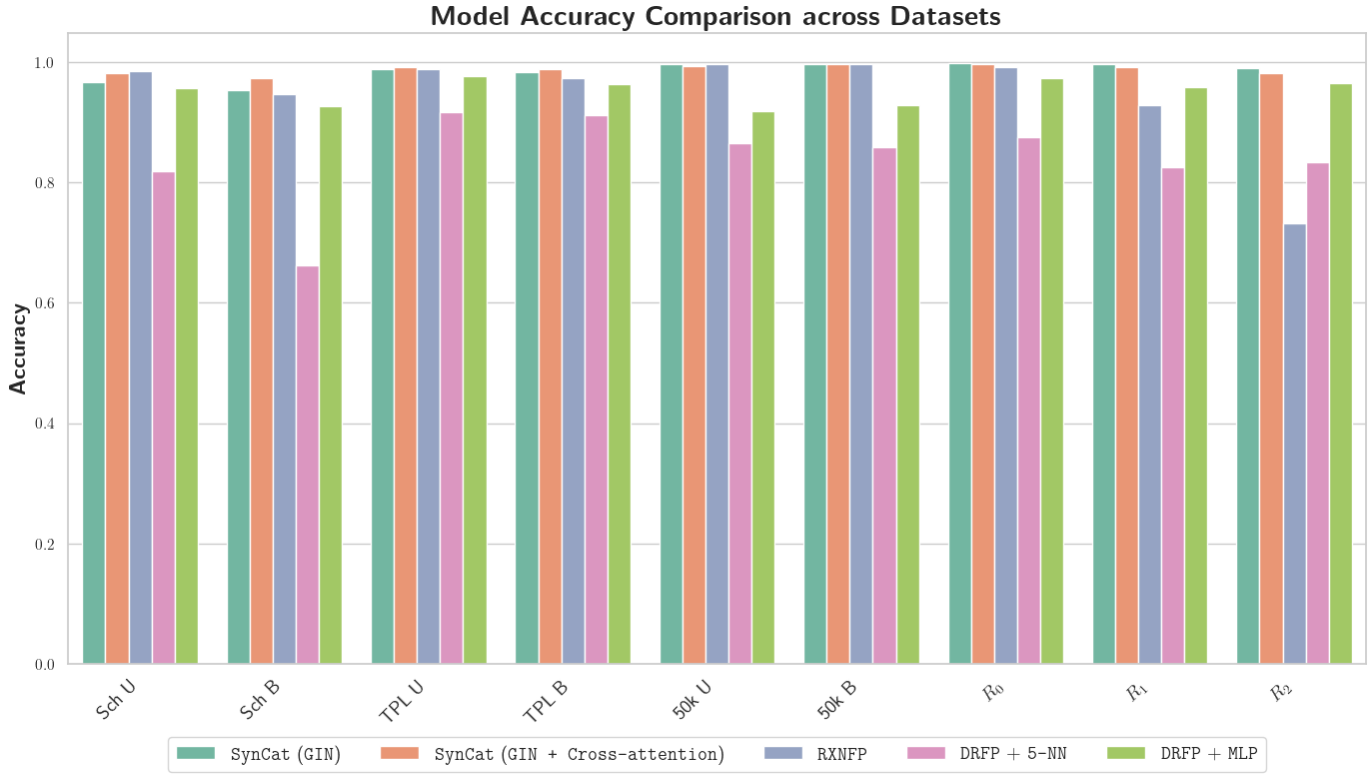
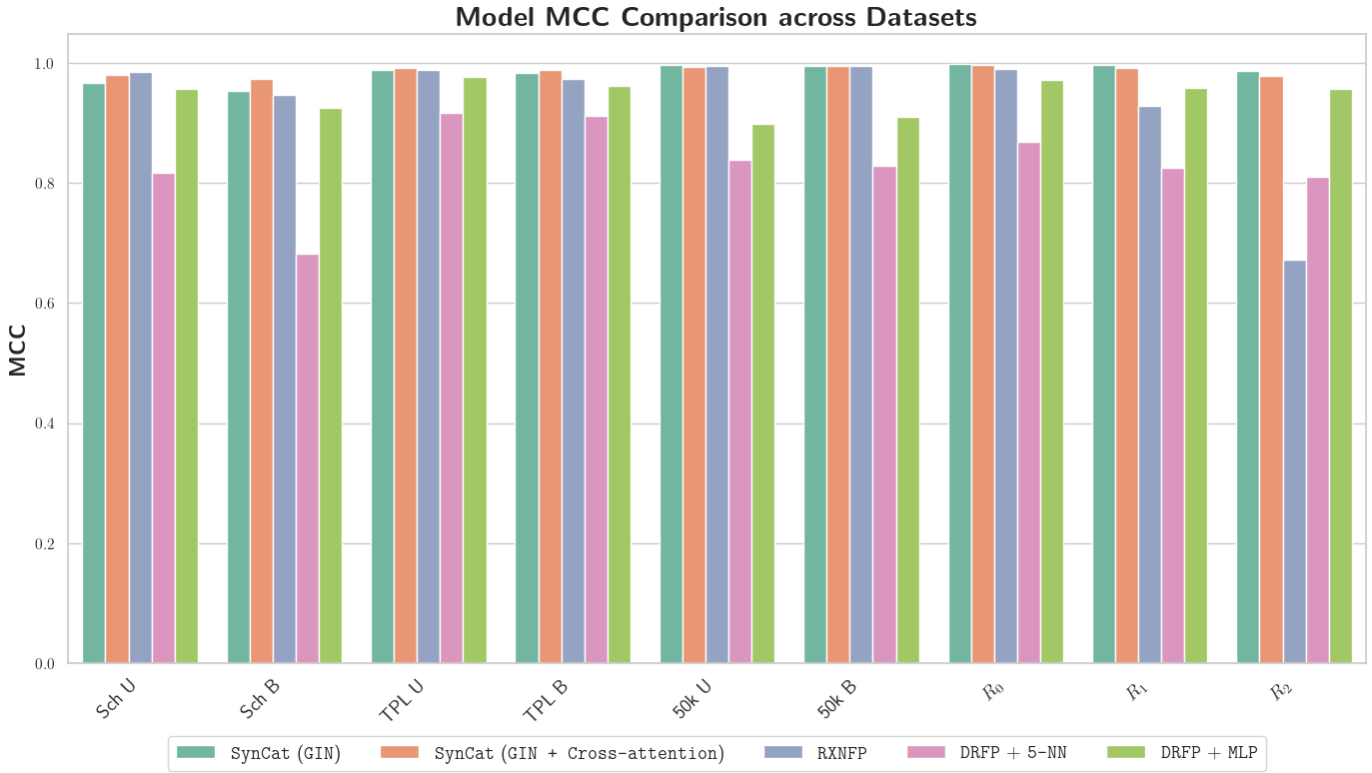


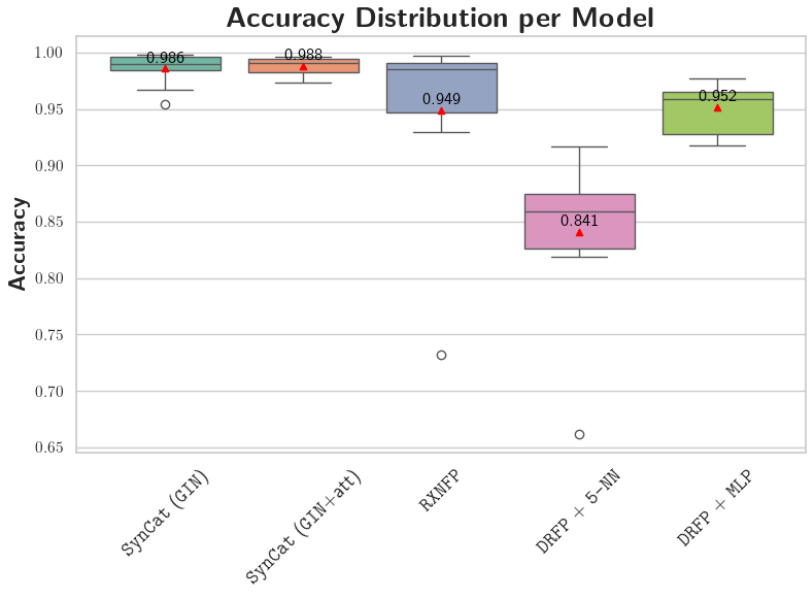
RESULT

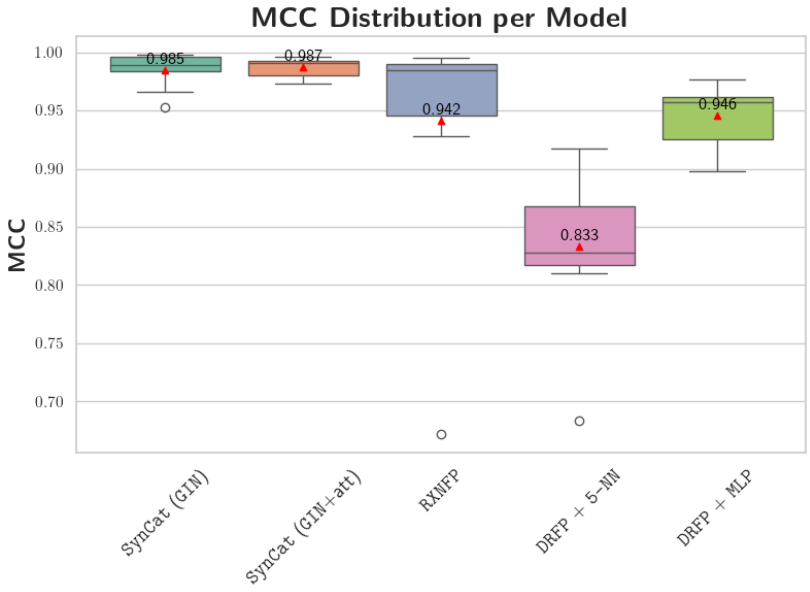
Benchmarking



RESULT

Benchmarking





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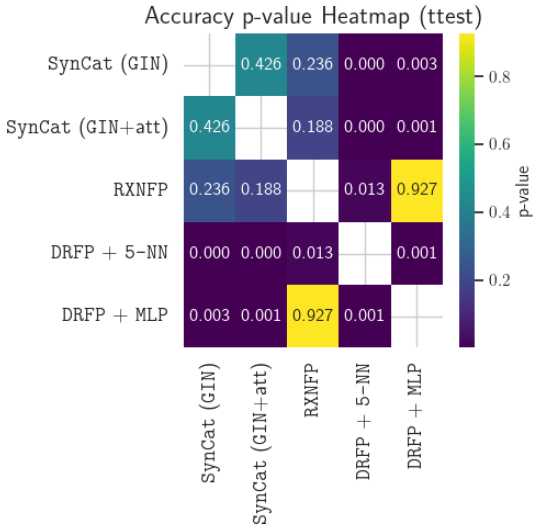
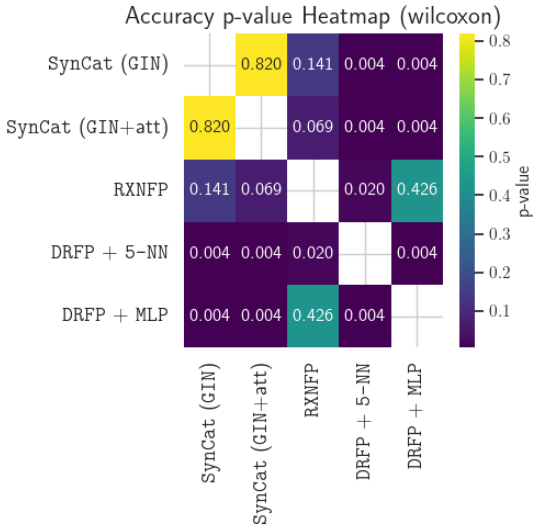
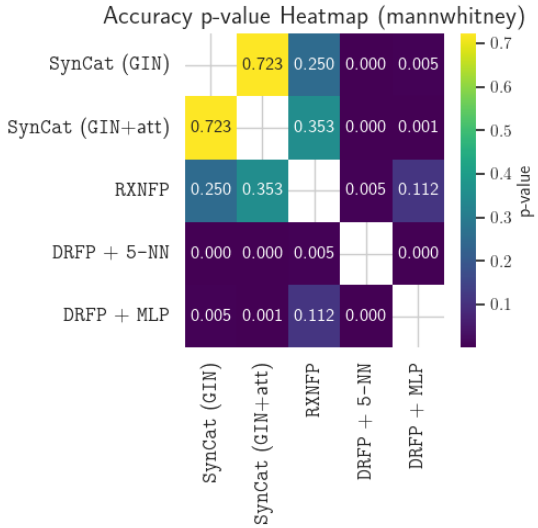
Benchmarking







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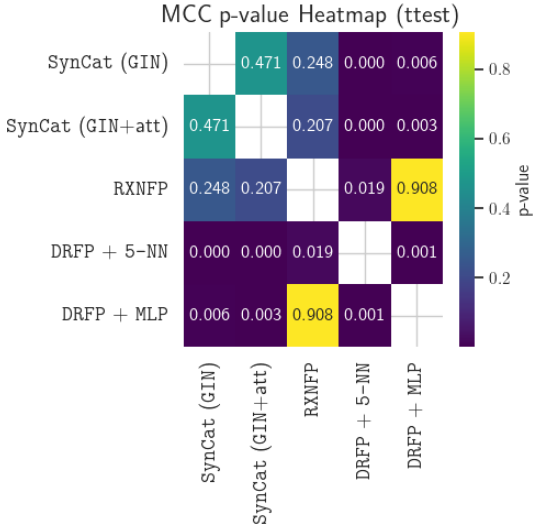

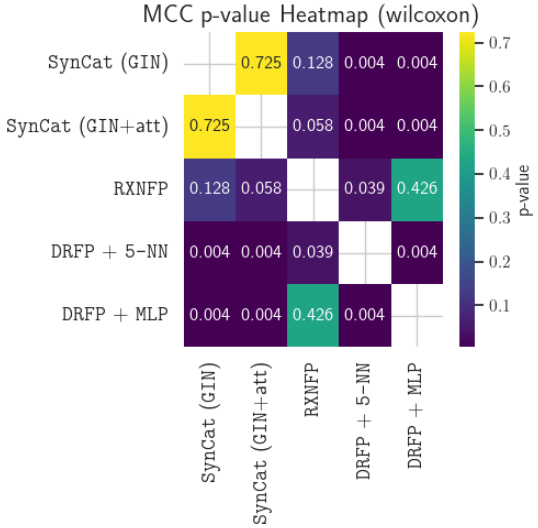

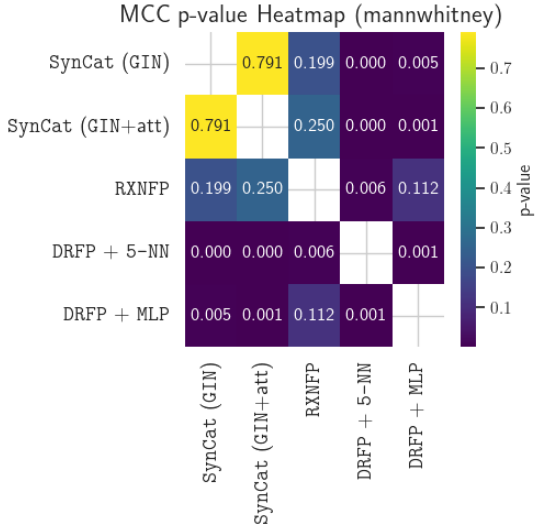

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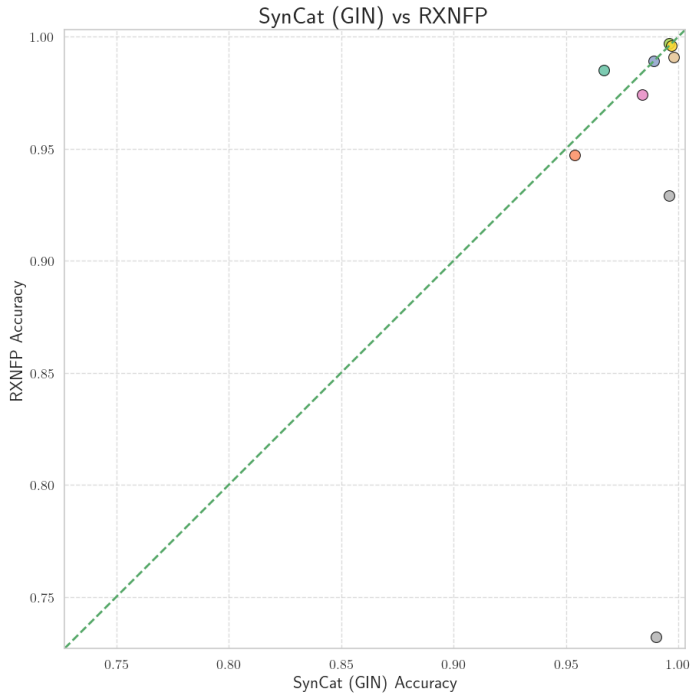

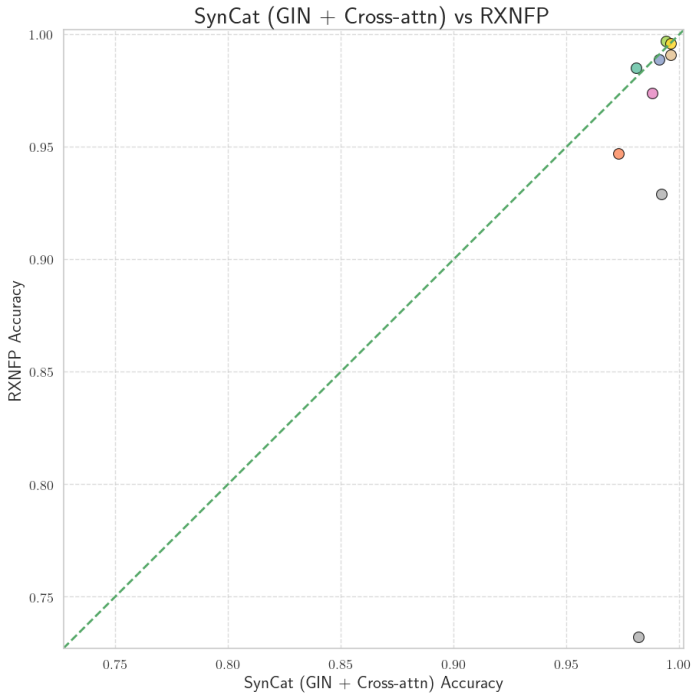

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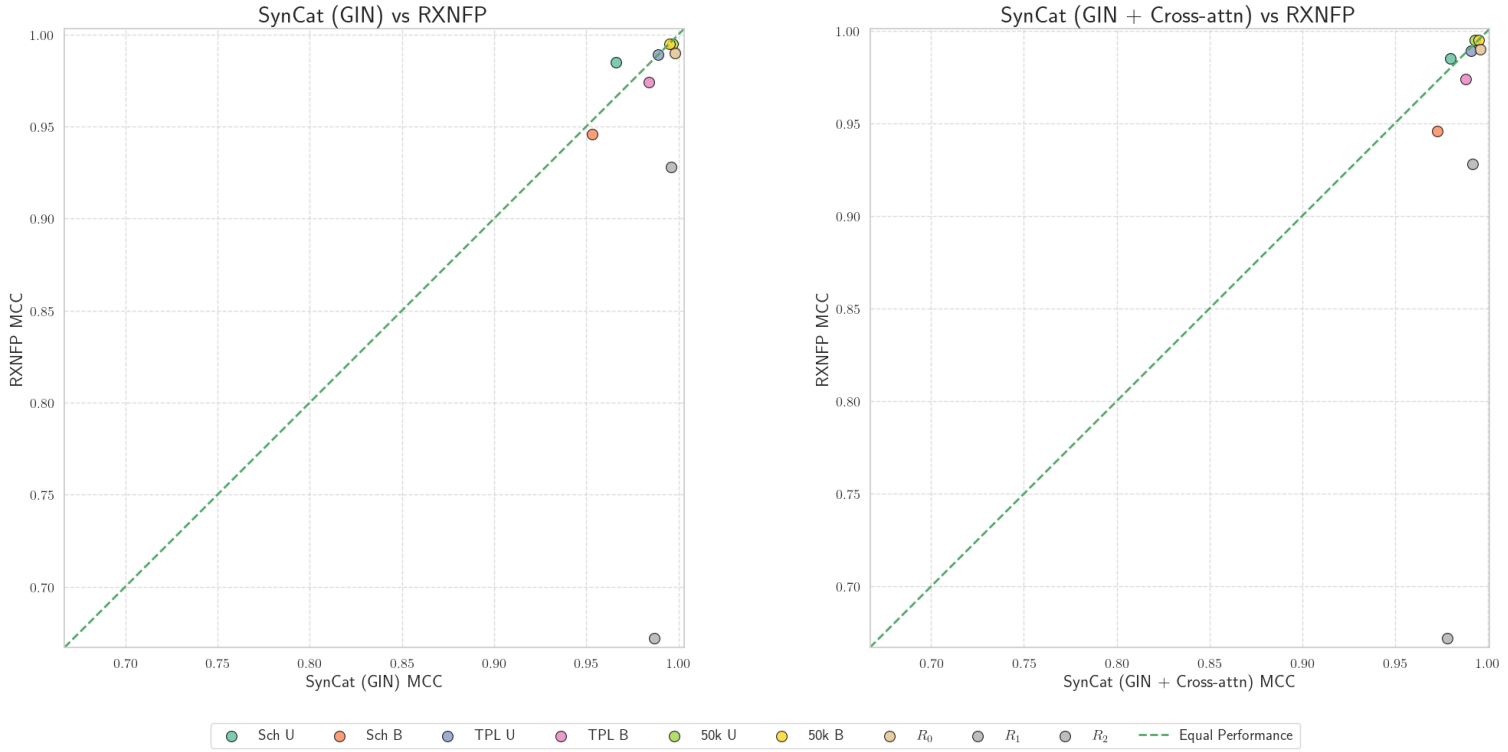

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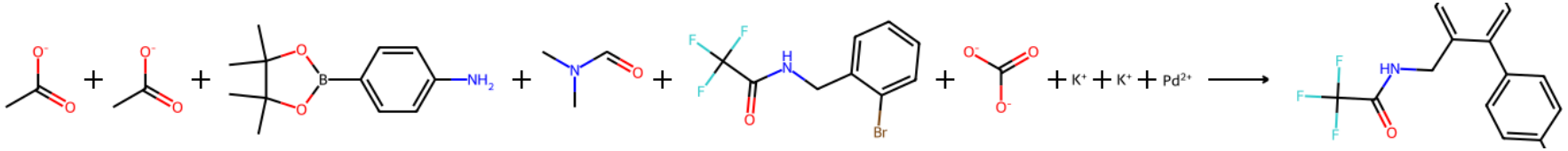
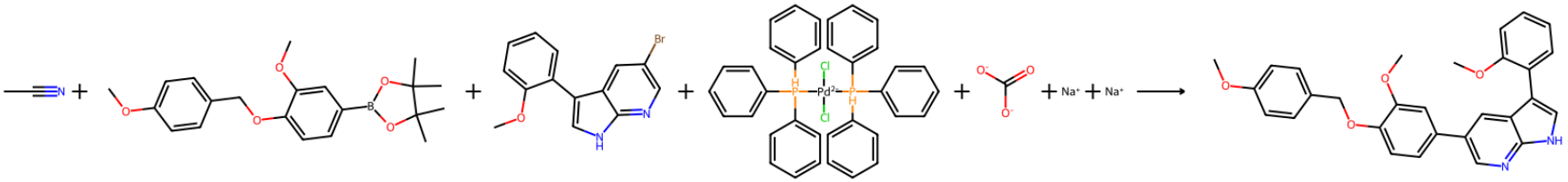


Dataset: Schneider
Label: Bromo Suzuki Coupling
Predict: Bromo Suzuki-type Coupling



Dataset: Schneider
Label: Bromo Suzuki Coupling
Predict: Bromo Suzuki-type Coupling

RESULT

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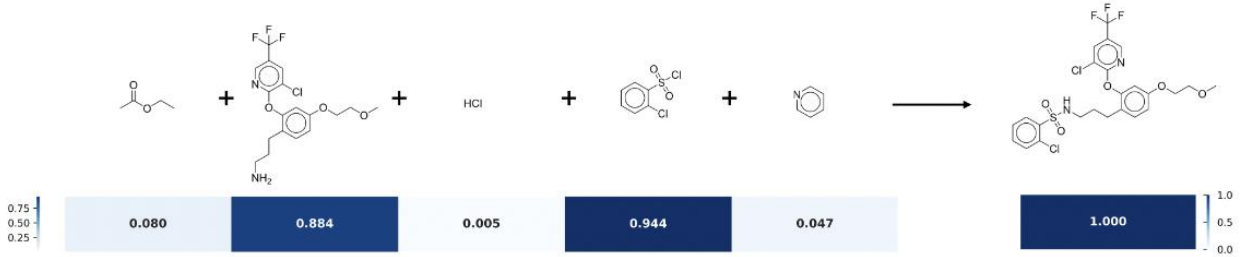
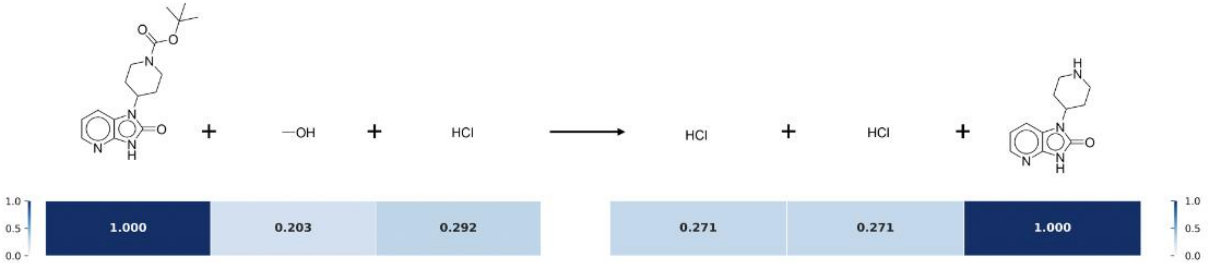
Reagent detection

Dataset: USPTO TPL
TPL label 43: [C:4][S:1](=[O:2])(=[O:3])Cl.[C:5][N:6]>>[C:5][N:6][S:1](=[O:2])(=[O:3])



Dataset: Schneider
Label: N-Boc deprotection



RESULT

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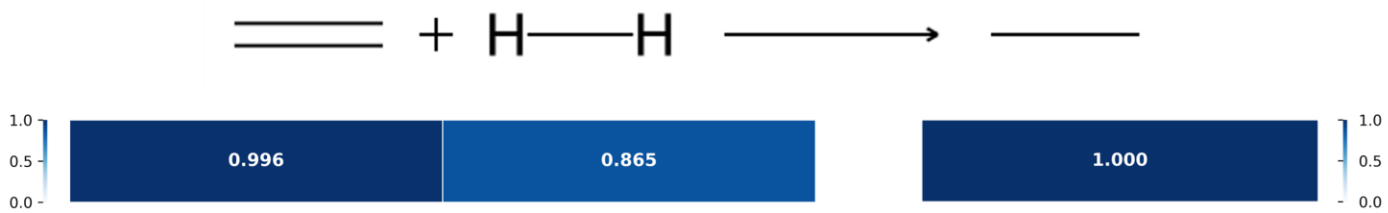
Reagent detection



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04

DISCUSSION

DISCUSSION

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Database Organization

SynCat + SynTemp

DISCUSSION

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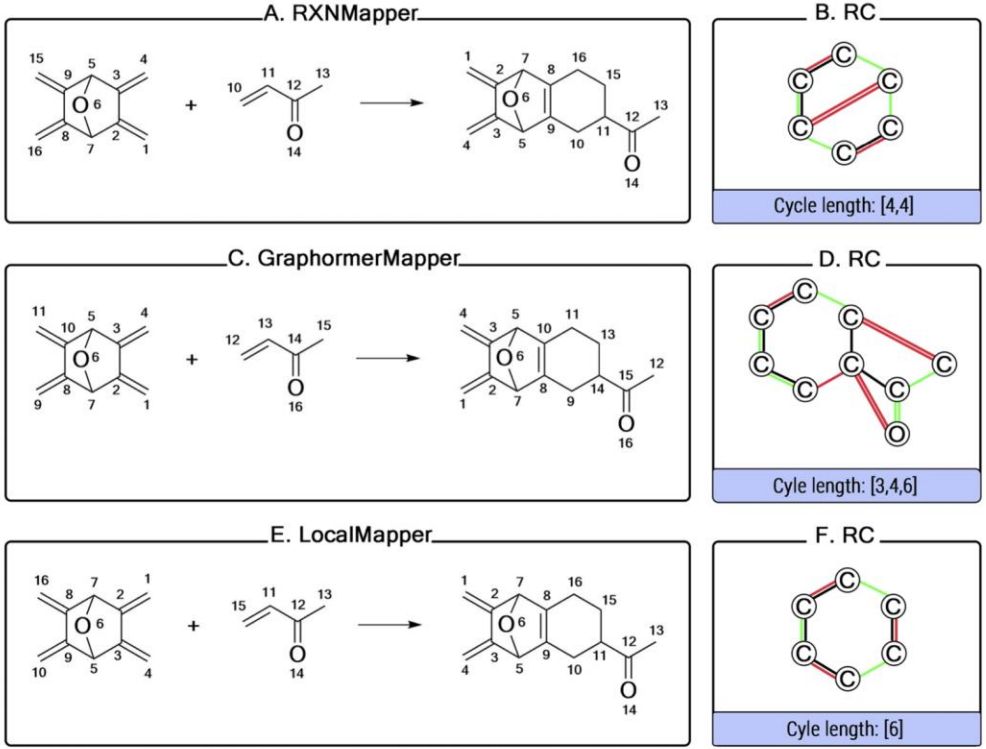
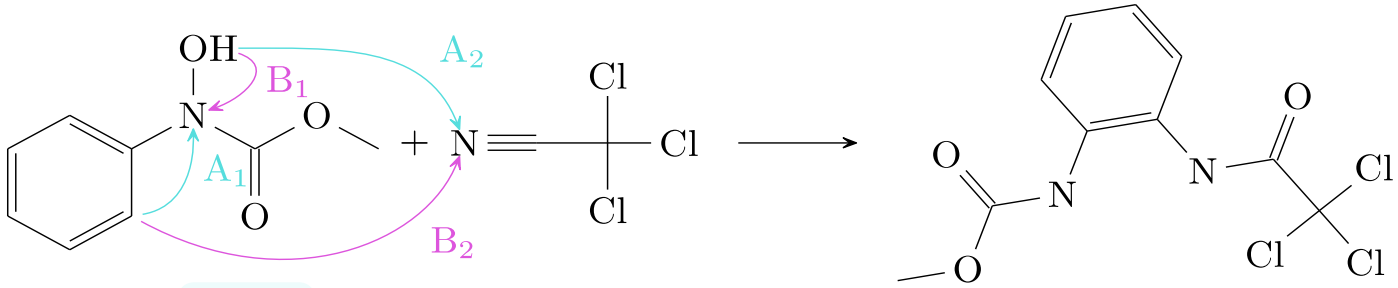
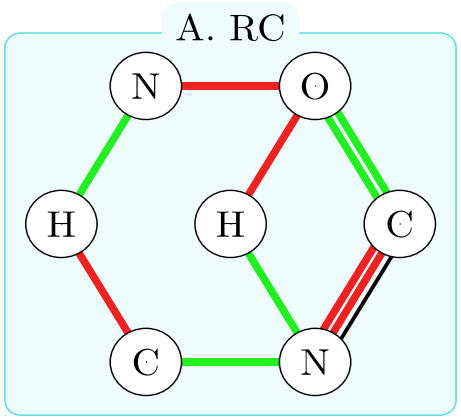
Inequivalent AAMs

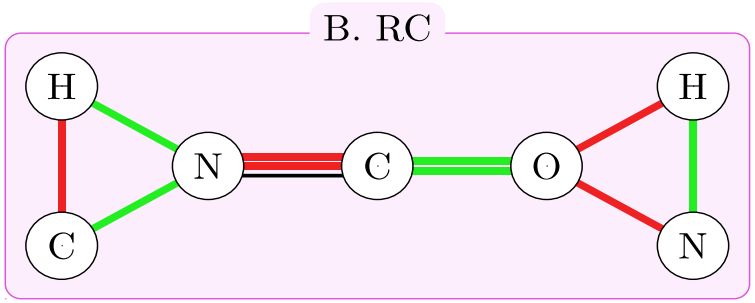


DISCUSSION

Ambiguous Hydrogen







Our team

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Uppsala University

Tieu-Long Phan
Leipzig University

Peter F. Stadler
Leipzig University

SDU University of Southern Denmark

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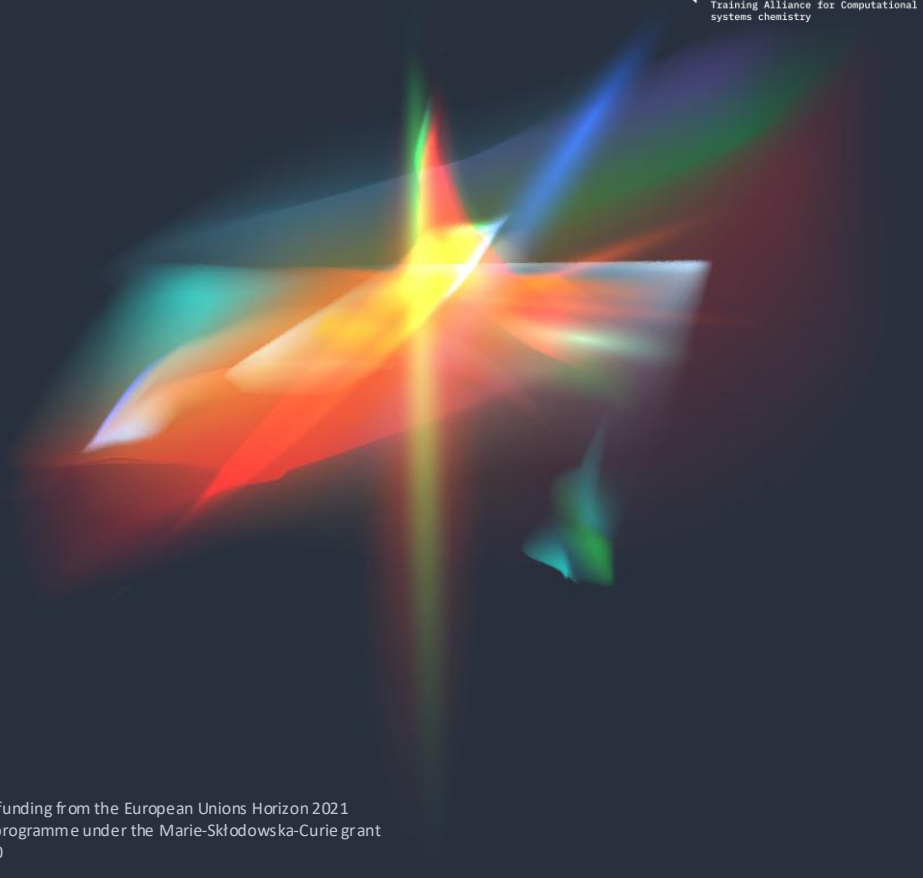
Thank you for your attendance



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