



The N-Formamide as Carbonyl Precursor in the Catalytic Synthesis of Passerini Adducts under Aqua and Mechanochemical Conditions.



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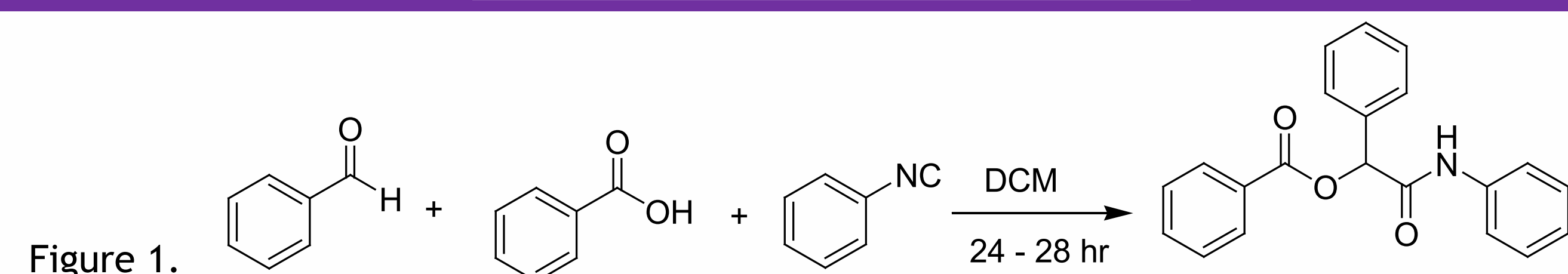
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INTRODUCTION

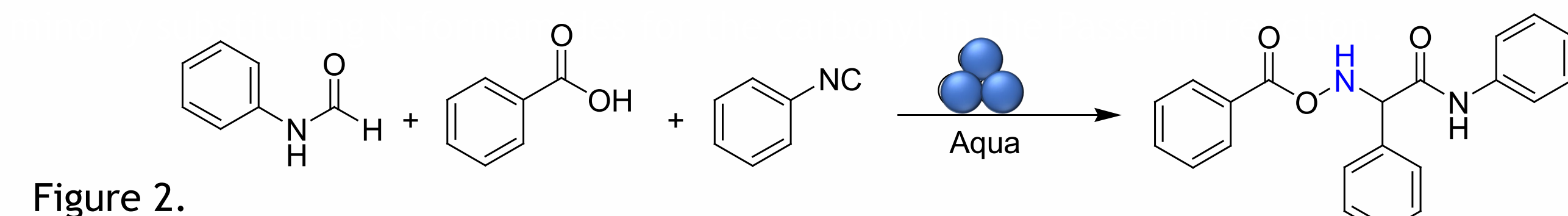
The Passerini three-component reaction (P-3CR) was developed after Passerini's discovery of the reaction between isocyanides, aldehydes, and carboxylic acids to produce α -acyloxy carboxamides in 1921 (see Figure 1).¹ It has since grown to be a potent tool in combinatorial chemistry and hetero cyclic chemistry for drug discovery as well as natural product synthesis.²

TYPICAL PASSERINI REACTION



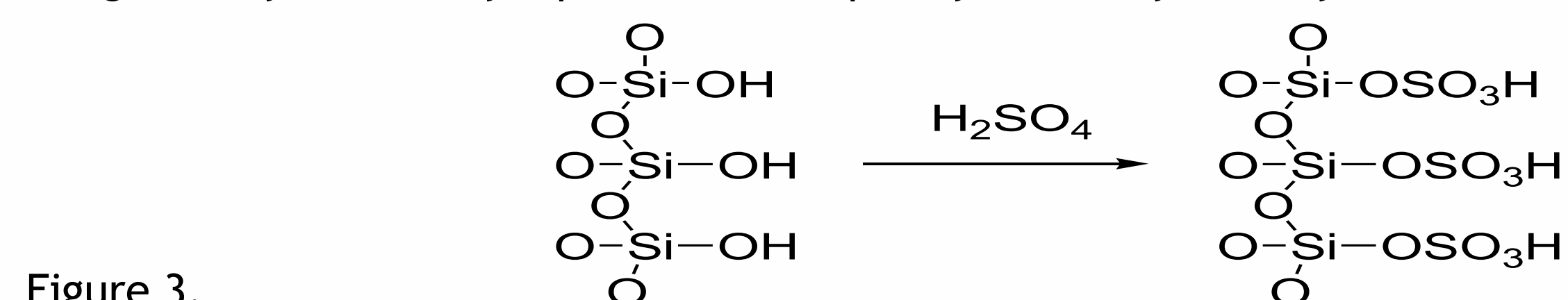
NEW SYNTHETIC ROUTE

Passerini reaction has been known for over 80 years, little or nothing is known about the scope of carbonyl-type electrophiles that undergo the reaction. On the other hand, the impact of including neighbouring reactive groups within the carbonyl component such as esters and formamides has not been investigated. We set out to replace the carbonyl component, keeping in mind the potential effects of even minor functional modifications, by simply substituting N-formamides for the carbonyl in the Passerini reaction (see Figure 2).³



THE IMMOBILIZED SULFURIC ACID ON SILICA GEL

In the last few years, $\text{SiO}_2\text{-H}_2\text{SO}_4$ (see Figure 3) has demonstrated significant promise as a cost-effective and easily retrievable solid catalyst for driving a variety of essential organic reactions in solvent-free environments $\text{SiO}_2\text{-H}_2\text{SO}_4$ is appealing for industrial usage because of its high catalytic activity, operational simplicity, and recyclability.

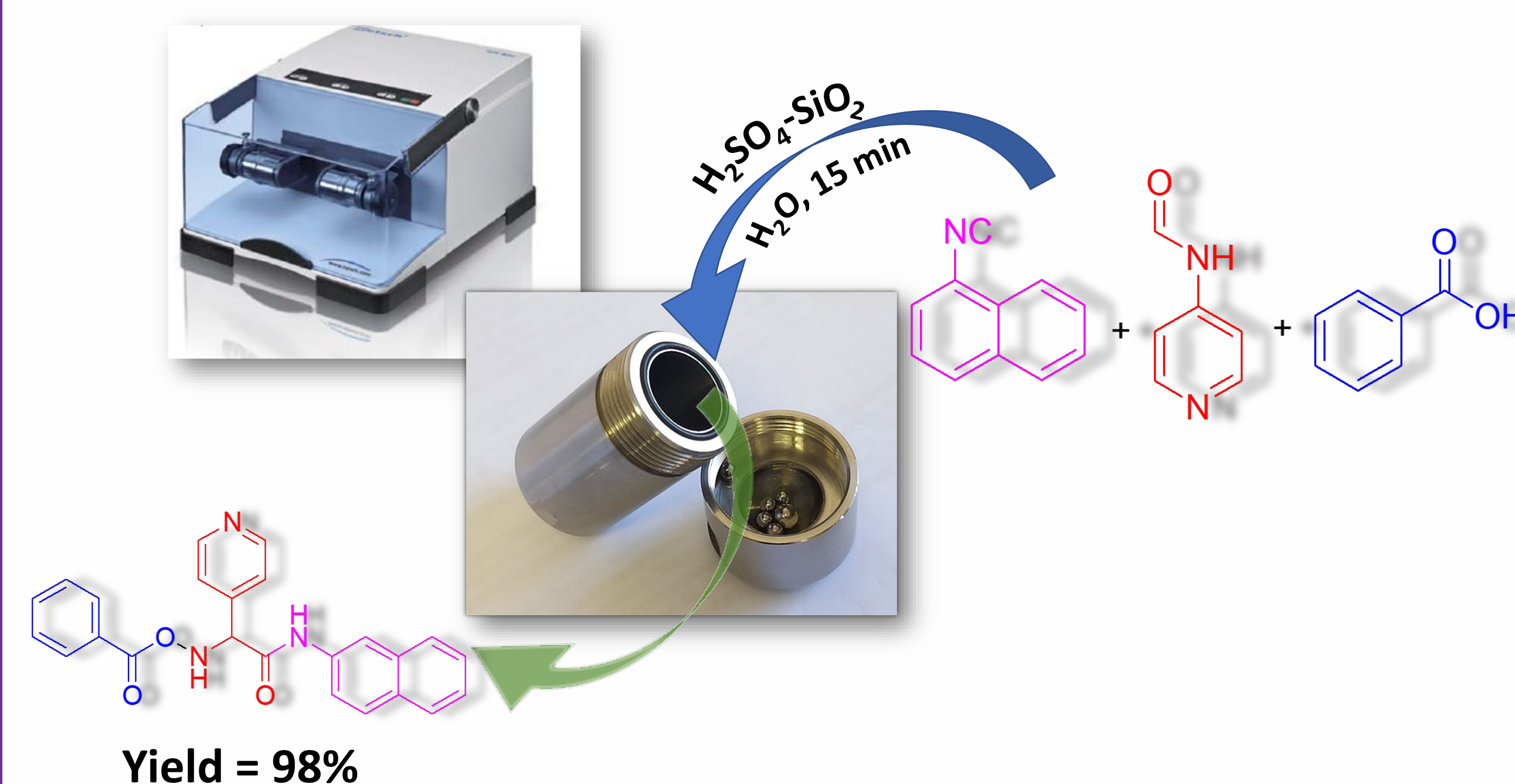


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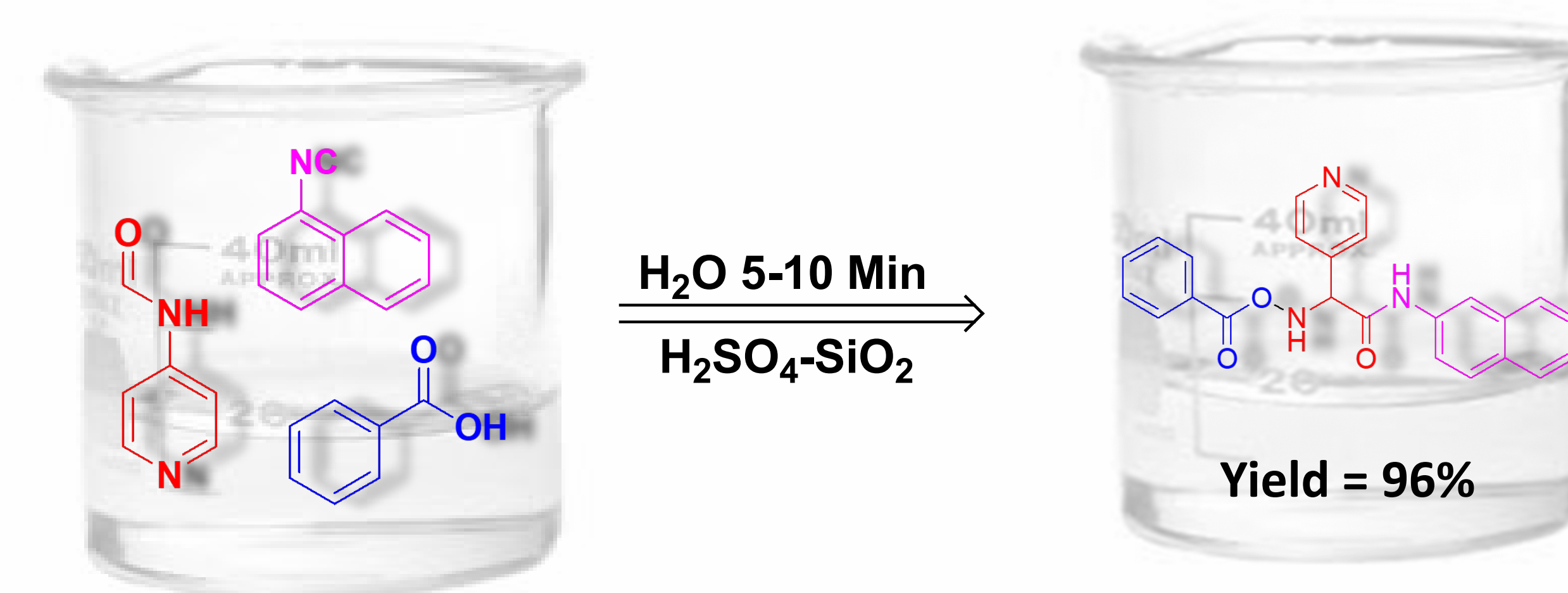
- 1 Ganem, B.; "Strategies for Innovation in Multicomponent Reaction Design," Acc. Chem. Res., 2009, 42, 463-472.
- 2 Cioc, R.C.; Ruijter, E.; and Orru, R.V.A. "Multicomponent reactions: Advanced tools for sustainable organic synthesis," Green Chem., 2014, 16, 2958-2975.
- 3 Zhang, O.B.; and Studer, A. "Recent advances in the synthesis of nitrogen heterocycles via radical cascade reactions using isonitriles as radical acceptors," Chem. Soc. Rev., 2015, 44, pp. 3505-3521.

MECHANO-CHEMICAL SYNTHESIS

This is an emerging technique according to IUPAC that would change the world, and they are on their way to becoming mainstream. Various investigations have shown that mechanochemical activation and methods have several advantages, such as shorter reaction milling times, greater yield, reduced waste formation, improved selectivity, and stoichiometry control.



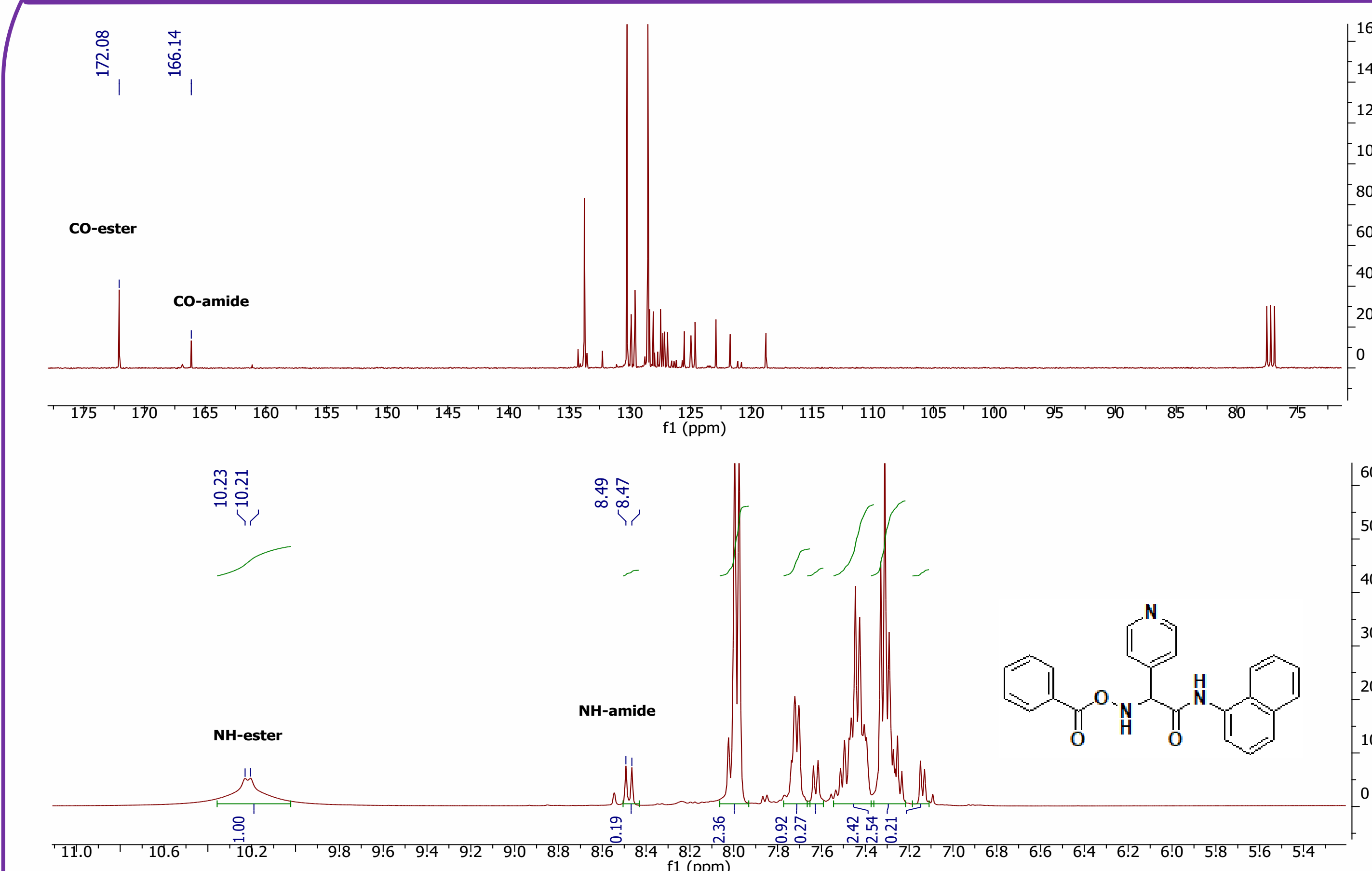
PASSERINI REACTION IN WATER UNDER CATALYTIC CONDITION.



WHY AQUEOUS MEDIA?



RESULTS



CONCLUSIONS

Summary

A practical synthesis of Passerini 3-CR adducts under aqua and mechanochemical (ball-milling) conditions were developed to demonstrate the usefulness of aqueous organic reaction and mechanochemical activation for isocyanide-based multicomponent reactions.

Conclusion.

We found that liquid assisted mechanochemical activation was very effective and useful in our work, which was superior to the reaction carried out under aqueous condition with respect to yields and experimental simplicity. Thus, we propose the application of aqua and mechanochemical methodologies as a biologically and environmentally safe techniques to provide an eco-friendly and economical procedure for the synthesis of biologically important molecules, which can be afforded in 10 to 15 min.

APPRECIATION

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