# An Open Standard for Automation of and Programming of Organic Synthesis

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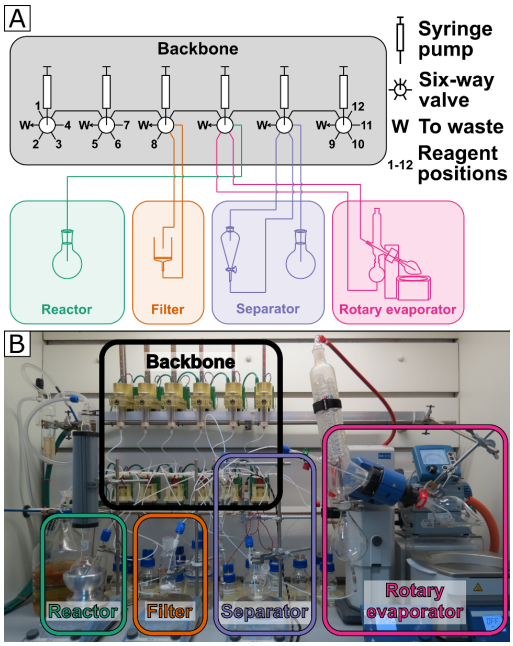
Much of chemical synthesis must be done manually as automation is limited to single classes of reactions, or work-flows. To address this, we developed an abstraction of organic synthesis which allows a universal connection between the conceptual steps and automation of the process[1-2]. These steps were implemented in a modular robotic platform, running a chemical programming language which formalizes and controls the assembly of the molecules, see Fig. 1. We validated and demonstrated the concept by making three pharmaceutical compounds and doing over ten different classes of reactions without any physical intervention. Execution was demonstrated by the fully autonomous synthesis of the pharmaceuticals, Nytol, Rufinamide, and Sildenafil, with yields and purities of products and intermediates comparable or better to those achieved manually. The syntheses are captured as digital code that can be transferred flexibly between platform instances with no modification, published and versioned, thereby greatly enhancing reproducibility and reliable access to complex molecules.




```
<Synthesis>
    <Hardware>
        <Reactor id="reactor1"
                 volume="500ml" />
    </Hardware>
    <Reagents>
        <Reagent id="magnesium_grit" cas="7439-95-4" />
        <Reagent id="diethyl_ether"  cas="60-29-7" />
        <Reagent id="bromobenzene" cas="108-86-1" />
    </Reagents>
    <Procedure>
        <Add reagent="magnesium_grit" mass="2.5047g"
             dest="reactor1" />
        <Add reagent="diethyl_ether" volume="40ml"
             dest="reactor1" />
        <Stir vessel="reactor1" temperature="34.6" />
        <Add reagent="bromobenzene" volume="1ml"
             dest="reactor1" />
        <Add reagent="bromobenzene" volume="10ml"
             dest="reactor1"
             time="0.5hr" />
        <Wait time="0.5hr" />
    </Procedure>
</Synthesis>
```

Figure 1. LEFT: Our Chemputer platform. RIGHT: Code to run a Grignard reaction.

## References

[1] J. Granda, L. Donina, V. Dragone, D. –L. Long, L. Cronin 'Controlling an organic synthesis robot with machine learning to search for new reactivity', *Nature*, **2018**, 559, 377-381.

[2] P. Kitson, G. Marie, J. –P. Francoia, S. Zalesskiy, R. Sigerson, J. S. Mathieson, L. Cronin 'Digitization of multistep organic synthesis in reactionware for on-demand pharmaceuticals', *Science*, **2018**, 359, 314-319.