Supplementary Information

Automatic Generation of 3D Printed Reactionware for Chemical Synthesis Digitization using ChemSCAD

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1 Supplementary Methods

Solvents and reagents were used as received from commercial suppliers unless otherwise stated and no unexpected or unusually high safety hazards were encountered. All reactors used in this study were designed using ChemSCAD and printed on Ultimaker 2+ 3D printers (https://ultimaker.com/), with 0.6 mm nozzles using polypropylene from purchased from Barnes Plastic Welding Equipment Ltd as natural polypropylene (3 mm plastic welding rod). The designs for the synthesis cartridges were exported as stereolithography (.stl) files and the models were sliced and translated into .gcode instruction files using Cura (https://ultimaker.com/en/products/cura-software), a freely available slicer software package developed by Ultimaker. These instruction files were then transferred to the 3D printer for fabrication. Devices were printed at 260 °C on 12 mm thick polypropylene plates with 3-layer raft extending 12 mm outside the model footprint to avoid warping. To allow the introduction of necessary reagents, starting materials, or non-printed components the printing process was modified to pause at pre-programmed intervals during the fabrication to allow their placement. ^{1}H, ^{13}C NMR spectra were recorded on a Bruker Avance III HD 600 MHz and Bruker Avance II 400 MHz spectrometers. Chemical shifts are reported in ppm relative to residual solvent (multiplicities are given as s: singlet, d: doublet, t: triplet, q: quartet, m: multiplet, with coupling constants reported in Hz).

Mass spectra were recorded on a Bruker (Daltonics) Maxis Impact time-of-flight mass spectrometer instrument equipped with an electrospray (ESI) source. The spectrometer was calibrated using ESI-L Low Concentration Tuning Mix supplied by Agilent Technologies. Analysis was carried out in positive mode. Parameters used were End plate offset – 500 V, Capillary voltage– 4800 V, Nebuliser pressure – 1.6 Bar, Dry gas flow rate – 8.0 l/min, Dry gas temperature – 200 °C, Funnel 1 RF – 400 Vpp, Funnel 2 RF – 400 Vpp, Hexapole RF – 100 Vpp, isCID – 0 eV, Ion Energy – 5 eV, Low mass – 50 *m/z*, Collision Energy – 5 ev, Collision Cell RF – 200 Vpp, Transfer Time – 100 µs, PrePulse Storage time – 1 µs.

Percentage purity assessment for **Modafinil** and **Ribavirin**:

Percentage purity was assessed on a Thermo Dionex 3000 Ultimate HPLC system comprising of an LPG-3400RS pump, WPS-3000 autosampler, TCC-3000 column compartment, DAD-3000 detector. The flow rate used was 1 mL/min and the column oven was set to 30 °C. The eluents used were water with 0.1% formic acid (channel A) and acetonitrile with 0.1% formic acid (channel B) and the method used, along with an Agilent Poroshell 120 EC18 (150 mm x 4.6mm x 2.7 µm) column, is as follows:

Time (min)	A (%)	B (%)

0	0	0
4	90	10
16	30	70
19	0	100
23	0	0
26	0	0

The detector was set to record at the wavelength of 254 nm, 220 nm and 214 nm.

Percentage purity assessment for **Lomustine**:

Percentage purity was assessed on a Thermo Dionex 3000 Ultimate HPLC system comprising of an LPG-3400RS pump, WPS-3000 autosampler, TCC-3000 column compartment, DAD-3000 detector. The flow rate used was 1 mL/min and the column oven was set to 30 °C. An isocratic gradient with an Agilent Poroshell 120 EC18 (150 mm x 4.6mm x 2.7 µm) column was used with a 50:50 water with 0.1% formic acid (channel A) and acetonitrile with 0.1% formic acid (channel B) eluent mixture.

The detector was set to record at the wavelength of 254 nm, 230 nm and 214 nm.

2 Background

Chemical **S**ynthesis by **C**omputer **A**ided **D**esign (**ChemSCAD**) is a graphical user interface (GUI) software program built in Python for the simplified design and prototyping of 3D printed **Reactionware** batch and flow synthesis devices. The program can be installed on all three major operating systems – Windows, MacOS and Linux. Specific installation instructions for each operating system are provided in **Section 2.1.2** below.

In ChemSCAD, there are three key components which allow it to operate for producing **Reactionware**.

These are:

1. ***ChemSCAD***: the GUI for producing **Reactionware** as 3D objects to the user to view
2. ***ccad:*** the API for ChemSCAD, containing all the reactor types as individual classes, including the various topological parameters required
3. ***OpenSCAD:*** the rendering engine used to produce the 3D objects as code and output these to ChemSCAD as 3D viewable constructs

An application program interface (API) is a set of routines, protocols, and tools for building software applications. The API specifies how software components should interact, namely ccad as the Python API here. In addition, the API in this instance is used for programming graphical user interface (GUI) components of ChemSCAD.

Therefore, the software can be thought as a hierarchy, with OpenSCAD at the base, as the engine to produce the code and render the objects *in silico*, ccad as middle-layer API for providing the detailed parameter information required to build each object and ChemSCAD the top-level interface which the user interacts with to build the **Reactionware** objects in a graphical user interface, which directly calls the ccad API and simplifies the software workflow for building **Reactionware**.

2.1 Software overview

The ***ChemSCAD*** software is built on the open-source OpenSCAD platform (https://www.openscad.org/) for the back-end rendering of the 3D models and PyQt5 (https://www.riverbankcomputing.com/software/pyqt/) [1] for the graphical user interface on the front-end, which the user will interact to design their monoliths. Additional packages including numpy, scipy and vispy are necessary for calculating dimensions of reactors and viewing the 3D meshes respectively. ***Numpy*** [2] is used for the mathematical calculations carried out in ChemSCAD, such as: calculating reactor radius automatically based on volume, adjusting volumes of chambers for filter/floating filter reactors. ***Scipy*** [3] is a scientific mathematical geometry package which is used for spatial orientation of aspects of the reactionware design in ChemSCAD. For example, ***scipy*** uses Cartesian coordinates to orientate the default output of a reactor to connect to a second reactor input by minimising the distance between them. Other uses for ***scipy*** include correct alignment of filters when multiple filters are used in a monolith design which aids 3D printing where pauses are required to insert the filters. ***Vispy*** is responsible for the visualisation of the 2D and 3D views shown in ChemSCAD, and, in addition, controls the colours of the different reactionware objects which helps the user distinguish between individual structural elements easily.

Further details of all the packages used and their licenses are available in Section 4 of the Supporting Information.

2.1.1 Use of OpenSCAD and ccad

As previously outlined, ChemSCAD is a GUI wrapper for the ccad Python API which uses OpenSCAD for the rendering the 3D reactionware and flow device objects. Thus, ccad as the Python API, is the lowest level of code within ChemSCAD and includes classes for each of the reactor and flow reactor types with the associated parameters values including I/O and volume information. This API communicates directly with ChemSCAD when the user inputs their desired requirements for the reactionware/flow reactor, and ccad builds the OpenSCAD code for these in the background and

passes into OpenSCAD to perform the object rendering asynchronously, before passing the finished 3D render back into ChemSCAD for the user to modify and view in the STL viewer on the right-hand side panel.

As the Python API for ChemSCAD, ccad is comprised of multiple sub-classes within a base class called ObjectCAD. This base class will interact with ChemSCAD (the wrapper around ccad) to create the reactionware objects, and asynchronously pass this generated code into OpenSCAD to be rendered. Below in Figure S1 is an overview of the classes involved in ccad, abstracted to give a basic overview of how each of the sub-classes is related.

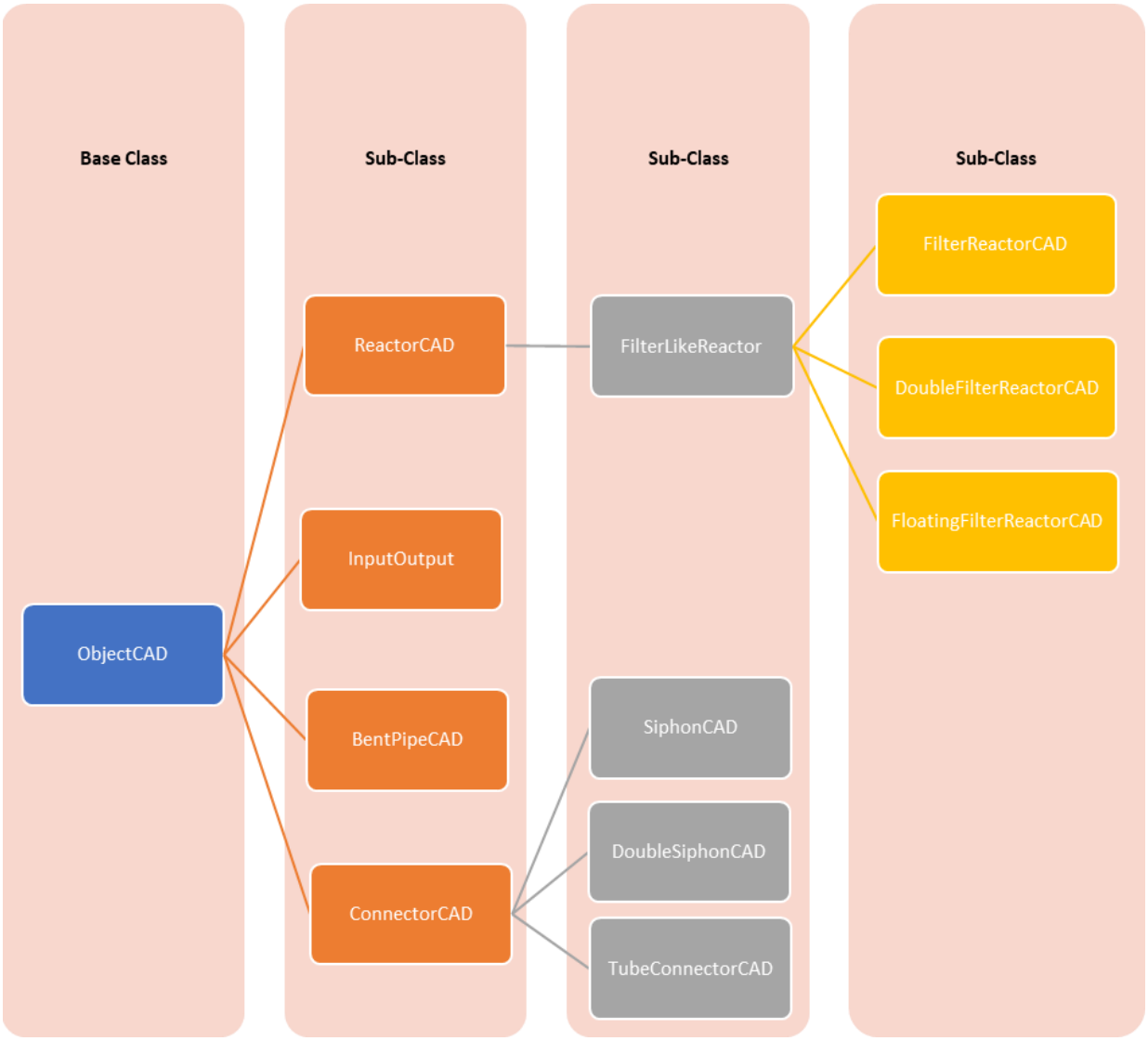


Figure S1: Software workflow.

The following figure describes the workflow in ChemSCAD. The GUI is the highest-level, which the user interacts with, OpenSCAD is primarily the rendering engine and ccad is low-level Python API which communicates directly with OpenSCAD and asynchronously generates the code for rendering of the 3D objects, and with ChemSCAD for displaying these to the user.

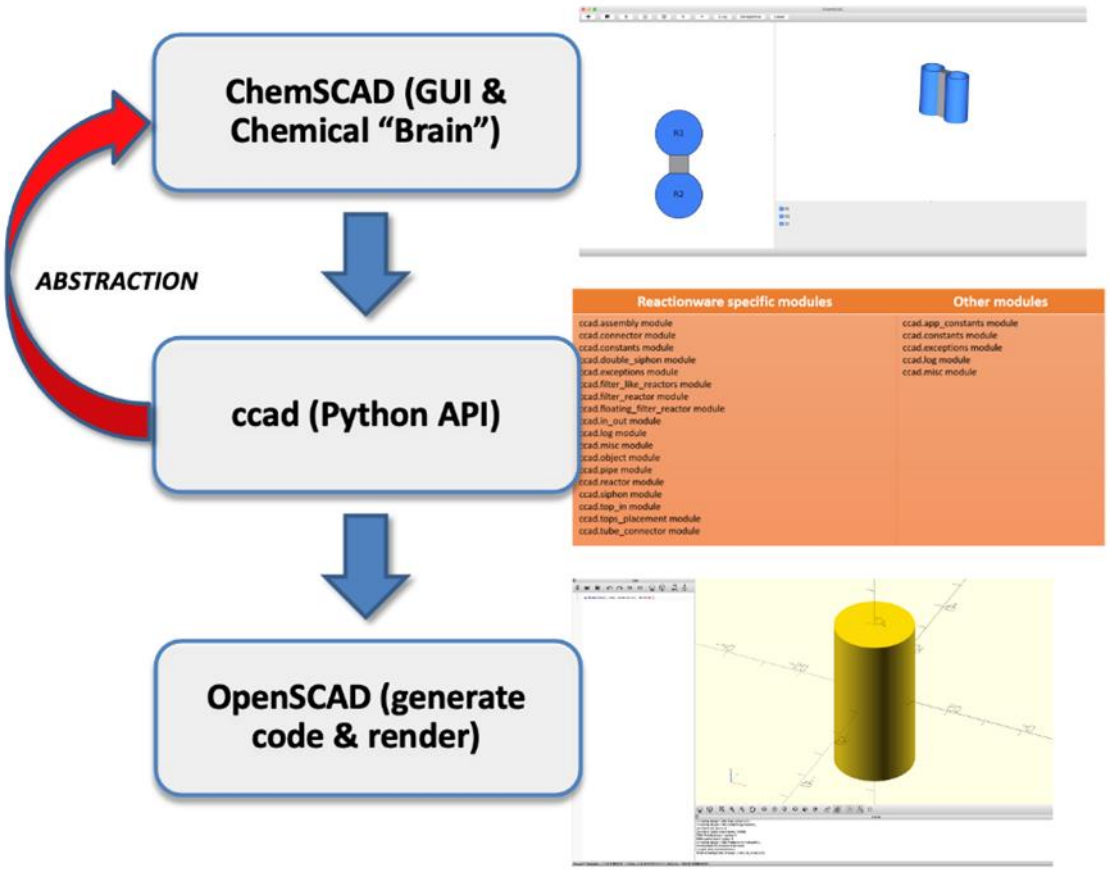


Figure S2: ChemSCAD structural architecture workflow.

2.1.2 Installation instructions

Please note the following instructions are taken directly from PyPi and for future reference can be found at: https://pypi.org/project/chemscad/

ChemSCAD requires Python **3.6** or above. Tested and working with latest Python release (3.8).

2.1.2.1 OpenSCAD installation:

ChemSCAD was tested with OpenSCAD 2019-05 (most up-to-date version as of March 2020)

For Windows:

All OpenSCAD dependencies including the binaries are included in the setup.py for ChemSCAD, so will be installed automatically when installing the requirements.txt file.

Therefore, please proceed to the ChemSCAD installations instructions below.

For Mac:

OpenSCAD can be installed using the .dmg installable from the following link: https://files.openscad.org/OpenSCAD-2019.05.dmg

Install this .dmg file, making sure to accept all permissions in Security & Privacy from within System Preferences.

For Ubuntu:

```
sudo add-apt-repository ppa:openscad/releases

sudo apt-get update

sudo apt-get install openscad

sudo apt-get install python-dev graphviz libgraphviz-dev pkg-config mesa-common-dev
libglu1-mesa-dev -y
```

2.1.2.2 **ChemSCAD installation:**

A video detailing the installation of ChemSCAD on Windows is provided within the Supporting Information entitled ‘ChemSCAD_installation_updated.mp4’. A text outline of these instructions is provided below.

For Windows:

```
python -m venv chemscad-env

cd chemscad-env/Scripts

source activate

pip install chemscad

chemscad
```

For Mac & Linux/Ubuntu:

```
python3 -m venv chemscad-env
```

```
cd chemscad-env/bin

activate

sudo pip3 install chemscad

sudo chemscad
```

2.1.2.3 Updating ChemSCAD

When bug fixes and new features are released for ChemSCAD, you may wish to update to the latest version available on PyPi. To do so please follow these steps for your operating system.

For Windows: from inside venv as above

```
pip install –-upgrade chemscad
```

For Mac & Linux/Ubuntu: from inside venv as above

```
sudo pip3 install –-upgrade chemscad
```

2.1.2.4 Instructions for developers: bug fixes and new features

Due to the need for implementing new features and bug fixes in ChemSCAD, we have outlined the following instructions for developers to follow. If you wish to work on fixing a bug or implementing a new feature in ChemSCAD you may do so by creating a **Feature** branch from the **dev** branch as follows:

N.B: the following instructions assume you are currently on the **master** branch and have performed ***git add*** and ***git commit*** commands to clean the working tree prior to moving branches.

```
git checkout -b dev # moves current branch from master to dev

git checkout -b [new-branch] # switches from new branch from dev & creates new branch from dev for new feature/bug fix

git push -u origin [new-branch] # sets new branch to track local changes on the remote origin host
```

Once a new feature/bug fix is added and tested as working, create a merge request to merge new-branch into dev and eventually merge dev into master to release the new stable build of ChemSCAD with new features and bug fixes implemented.

2.1.3 Software layout

ChemSCAD uses a simple graphical user interface (GUI) with two clearly defined panes: a 2D representative view (left) and a 3D view (right), shown in **Figure S3** below.

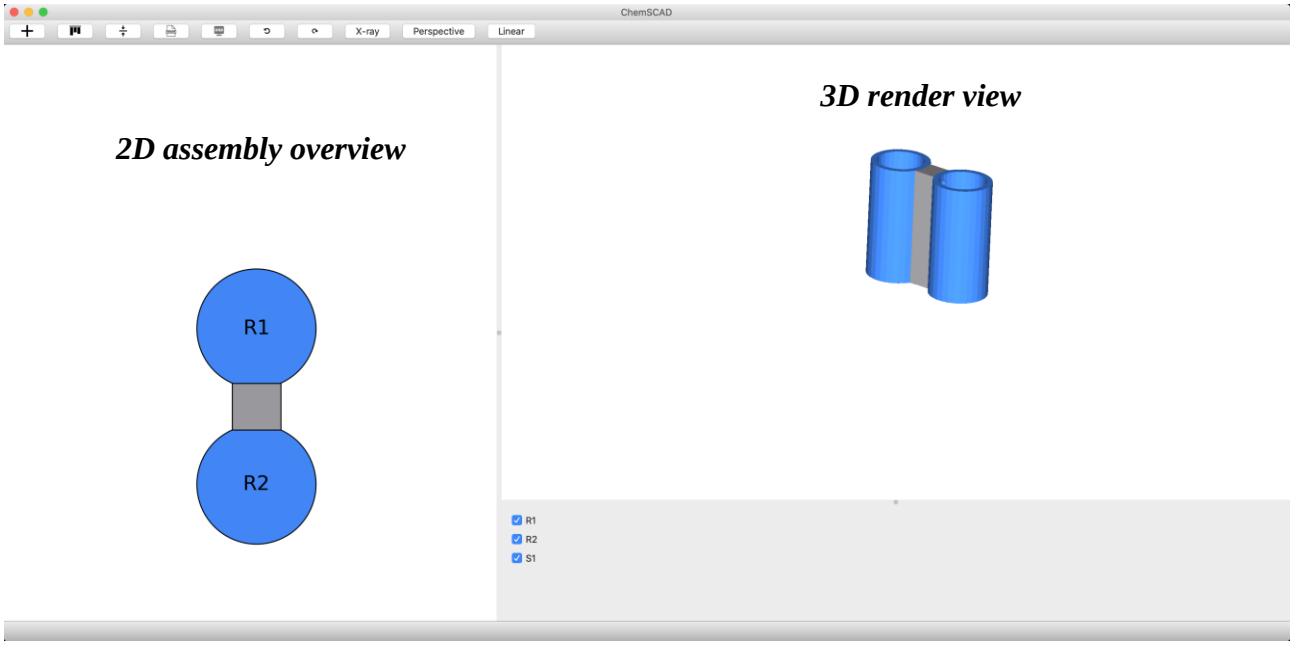


Figure S3: Main dashboard layout of ChemSCAD.

The implementation of a toolbar above the 2D view panel allows for intuitive use of the software, guiding the user towards the various functions including adding a new module, aligning tops of reactors and aligning filters. Other buttons include those to render the finalized monolith from the proprietary .ccad to .stl format for 3D printing via conversion to .gcode using Ultimaker Cura slicing software (freely available, open-source). Additional toggles for both x-ray and perspective views are included with the former giving a transparent view of the assembly, allowing the user to check all the connections between, and arrangement of, modules, and the latter giving the user a more realistic three-dimensional view of the complete assembly in space.

Figure S4: Main toolbar in ChemSCAD: from left to right – i) add new module, ii) align reactor tops, iii) align filters iv) export STL for printing, iv) export STL for publication, v) undo action, vi) redo action, vii) toggle x-ray view, viii) toggle 3D perspective view, ix) toggle linear assembly.

2.1.3.1 **Menu options**

The menu options in ChemSCAD are very simple and therefore easy to navigate for the user with two sub-menus for 'File' and 'Edit'. As shown below in Figure S5 below, the 'File' drop-down menu contains options to create a new project, save an existing project and export the existing project as an STL file to 3D print the Reactionware object. Each of these options is accompanied by a keyboard shortcut which seeks to make the users' experience and workflow when building Reactionware more efficient. The 'Edit' menu contains options to undo or redo actions such as adding a new module or aligning tops, with the corresponding keyboard shortcuts shown to speed up these processes for the user.

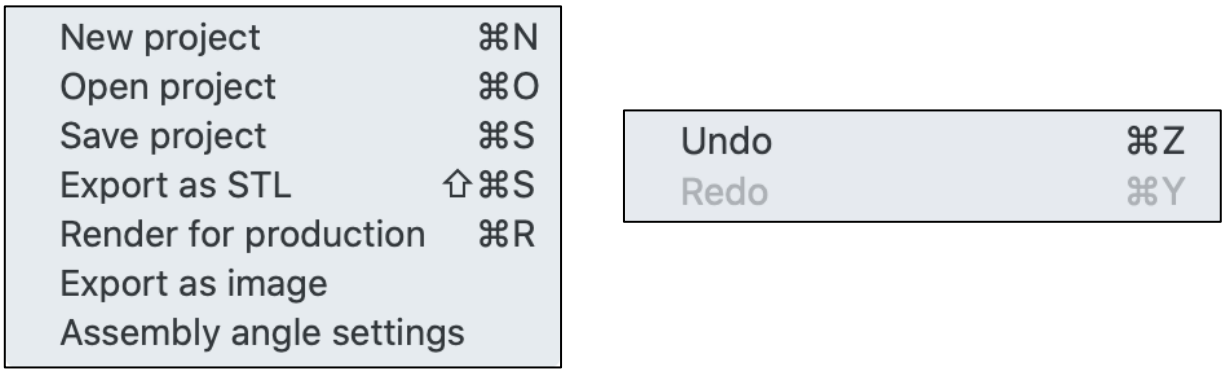


Figure S5: Menu options in ChemSCAD: 'File' sub-menu (left) and 'Edit' sub-menu (right).

2.1.3.2 **Reactor types**

Using the custom-built Python API, ccad, which contains all the code information required to build the desired reactionware object, ChemSCAD simplifies this by presenting the user with a drop-down menu to select which module they wish to add.

The main three reactor modules available in ChemSCAD are shown below in **Figure S6**.

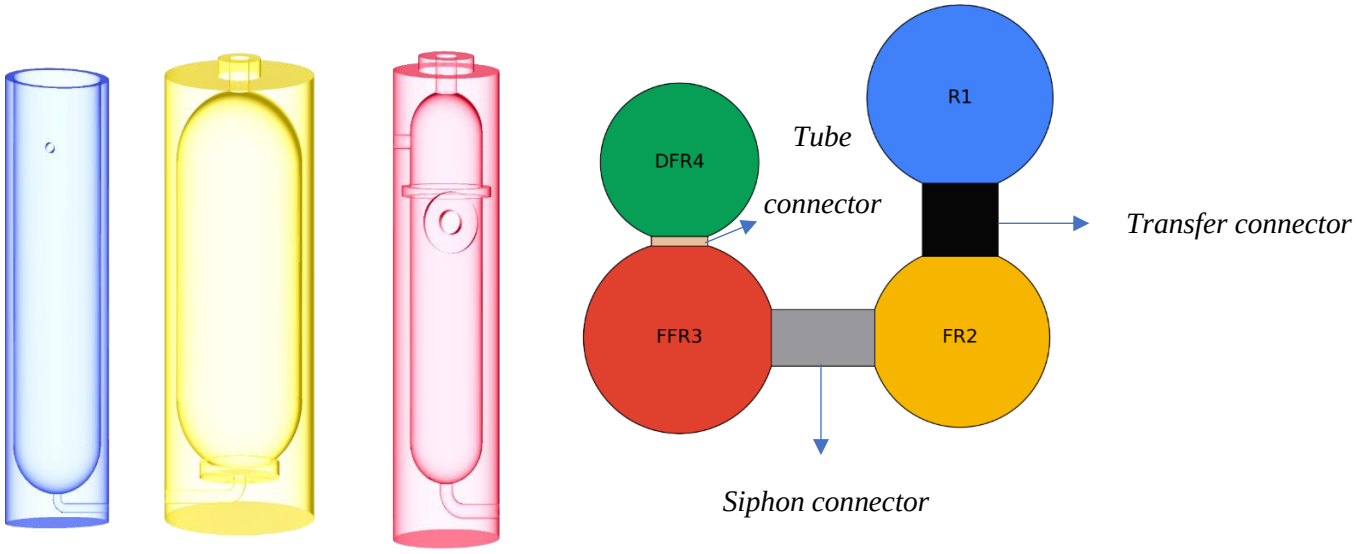


Figure S6: Three main reactor types in ChemSCAD, from left to right: i) reactor, ii) filter reactor, iii) floating filter reactor. Not shown: iv) double filter reactor.

2.1.3.3 **Connector types**

In ChemSCAD, there are three main connector types for the user to select from that allow individual modules to be joined to create a monolith.

The first type is a '***Transfer (S) Connector***', which as the name suggests is used to connect two modules where a solution transfer is taking place, for example moving a reaction mixture from a reactor module into a filter module to evacuate the solvent. This is the most commonly used connector type and has options to add a drill mark (to add a screw to prevent back transfer of liquid) and a reverse connector (to create a Soxhlet type chamber), where on a single reactor module, liquid can flow directly back into the same chamber through reversing the direction of the bottom half of the connector.

The second type is a '**Siphon connector**', which connects outputs with inputs but in between the siphon tube rises to the height of a specified chamber to ensure no back transfer of material through the cartridge upon addition of more material to the latter chamber.

The third type is a '***Tube Connector***', which allows a horizontal connection to be printed between two modules which is useful when connecting two modules which will not involve a transfer step, as is the case in the above two connector types.

2.1.3.4 **Alignment options**

A key feature in ChemSCAD is the ability to align the tops of two or more reactor type modules. Doing this not only reducing printing time since multiple pauses can take place at the same time, but also ensures efficient transfers since the cannula is horizontally aligned with both reactors.

The alignment options are shown below (Figure S7) for the reactor module. The two options are: i) lift reactor and ii) expand body. The former will add an excess amount of polypropylene to the base of the reactor to align the top of R1 to the top of R2 as shown in this example. This is compared with the latter which changes the radius of R1 in order to align the top with R2. In my cases the former option is preferred since volumes are relatively small in Reactionware, however when reactors have larger volumes (>100 mL) then the latter option of 'expand body' may be preferred.

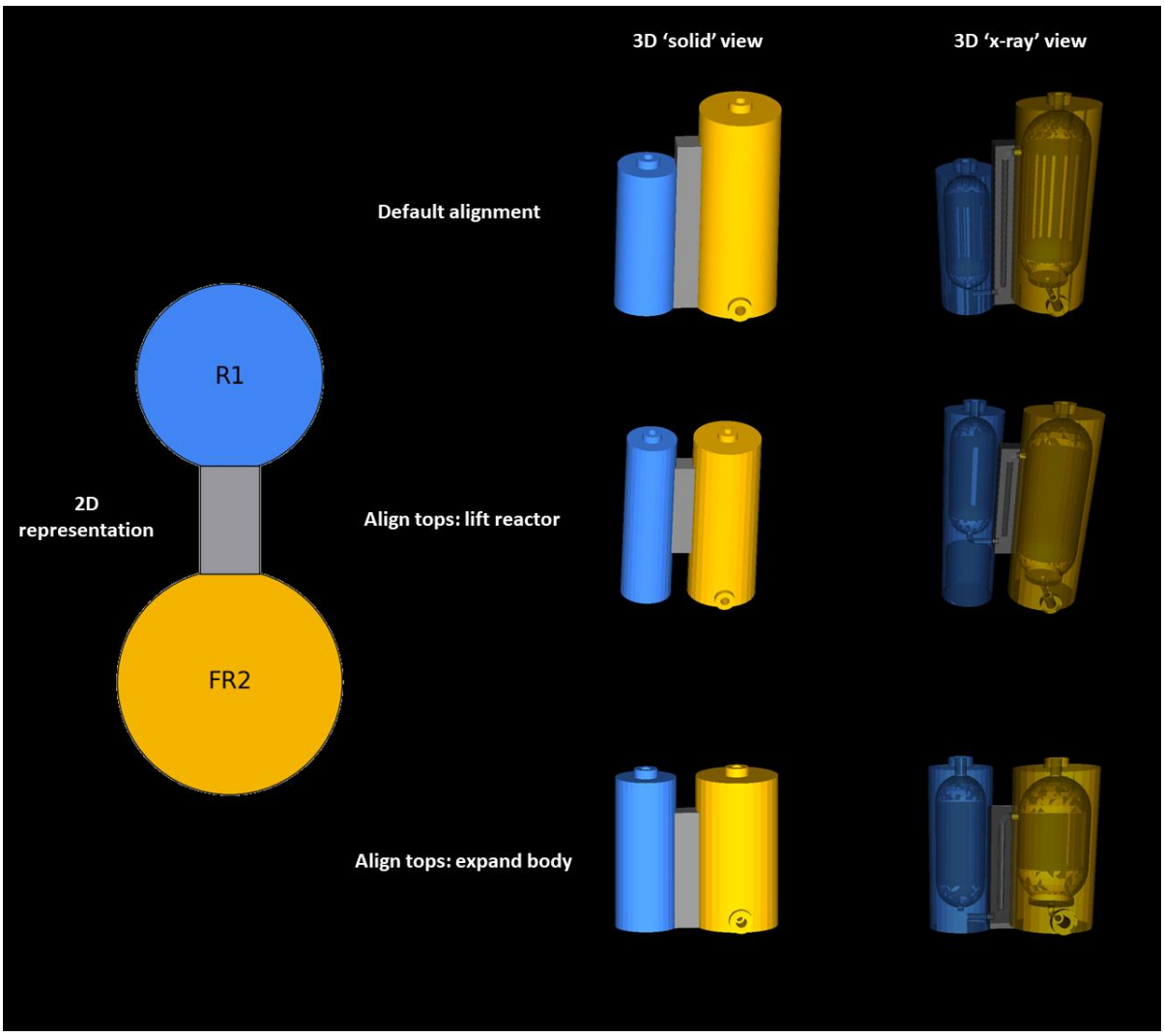


Figure S7: Alignment options in ChemSCAD for a two-module assembly: R = Reactor, FR = Filter Reactor. Far left: 2D representative view of assembly, Top to Bottom: i) default alignment of assembly, ii) lift reactor alignment, adding excess material to R1 to align the top to FR2, iii) expand body alignment, expanding the radius of FR2 to align to the top of R1. – N.**B: alignment option is an experimental feature so may not always work as expected.**

2.1.3.5 **Flow reactor options**

To demonstrate the versatility of 3D printed reactionware, we have implemented flow reactors into ChemSCAD which allows the user to produce bespoke flow reactors for performing flow chemistry, such is the case here to produce Lomustine in flow.

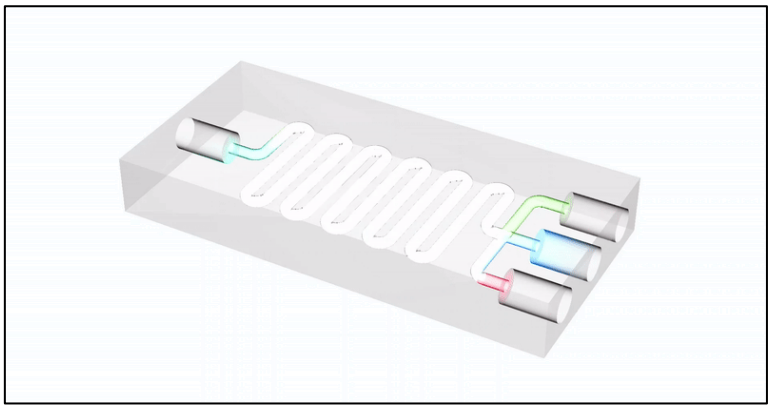


Figure S8: Example flow reactor designed and built in ChemSCAD.

To build a flow reactor in ChemSCAD the user first clicks the '+' icon to add a new module and selects 'flow reactor' from the drop-down menu.

Next, a series of tabs will appear allowing user to select an existing template flow reactor from the 'Templates' tab or design their own by inputting all the parameters in the 'Advanced' tab. The templates simplify the design of the flow reactor to the click of a button, with user simply choosing which number of inputs and volume closely matches their requirements. Once built the user may click the flow reactor in the left-hand side 2D viewer and navigate to the 'Advanced' tab to further modify the device parameters to suit their specific needs. Clicking 'OK' will generate the flow reactor with the specific device parameters. The user can then click the x-ray toggle to view the internals of the device and make changes if needed before exporting as an STL to 3D print and use. See **Figure S9** below for an overview of this process:

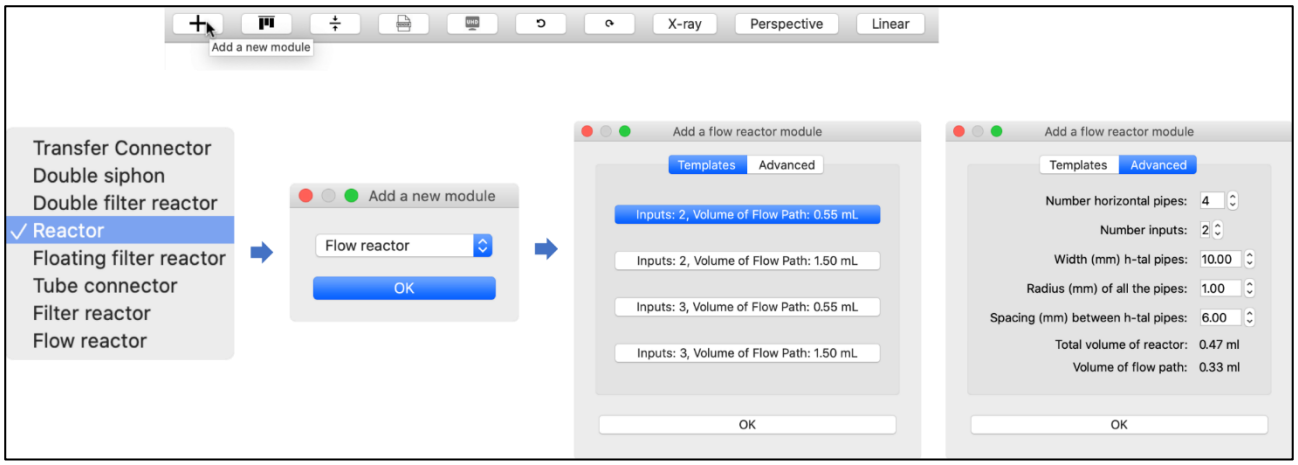


Figure S9: Process to build a flow reactor in ChemSCAD: shows the windows involved for generating a flow reactor in ChemSCAD. At top: '+' button to add a new module. At bottom (left to right): a) list of available modules, b) flow reactor selected, c) templates tab selected to choose from pre-defined flow reactor topologies, d) advanced tab for the user to define flow reactor parameters.

2.1.3.6 **Rendering options**

The rendering options in ChemSCAD for converting the .ccad file into a .stl file have been chosen to allow the user to decide whether to export the STL for 3D printing or for further manipulation, for example to be used in a publication figure. Knowing this, the facet number ($fn), which is the number of individual triangles which comprises the 3D mesh and directly correlates to the object resolution, is set differently for the different export options:

i) *Export as STL (for printing):* $ fn = 75 (standard 'resolution')

ii) *Export as STL (for publication):* $ fn = 200 (4K 'resolution')

The 'export for publication' options displays a warning to the user prior to proceeding since rendering the object at this higher resolution requires more computing power and therefore on most PCs will take up to 10x longer compared with the standard 'export for printing' option. In practice, this means a two-module reactor monolith with a connector will take approximately 2 min 30s to export for

printing but will take 9 mins to export for publication. Please note, these are approximate timings so your results may vary.

2.1.3.7 **File extensions**

ChemSCAD uses a proprietary file extension for saving its projects based on the base level Python API: ***.ccad***. Therefore if the user wishes to edit a **Reactionware** object/assembly, they must first open the .ccad file in ChemSCAD and when the desired changes have been made, this made can be saved again as a .ccad file or alternatively exported as an ***.stl*** file, which allows for 3D printing of the designed **Reactionware** by importing this file into the chosen slicing software such as Ultimaker Cura and then converted into ***.gcode*** format for 3D printing of the **Reactionware**.

2.1.3.8 **Keyboard shortcuts in ChemSCAD**

In ChemSCAD, we have mapped important, commonly used, functions to keyboard shortcuts to allows the user to make their use of the program more efficient. The following table outlines these shortcuts for Windows, MacOS and Linux.

Table S1: Table of available keyboard shortcuts for the various features within ChemSCAD.

Shortcut name	Shortcut keys (Windows)	Shortcut keys (MacOS/Linux)
New Project	**CTRL + N**	**⌘ + N**
Open Project	**CTRL + O**	**⌘ + O**
Save Project	**CTRL + S**	**⌘ + S**
Export as STL	**CTRL + SHIFT + S**	**⌘ + SHIFT + S**
Render for production	**CTRL + R**	**⌘ + R**
Undo	**CTRL + Z**	**⌘ + Z**
Redo	**CTRL + Y**	**⌘ + Y**
Go to database	**CTRL + D**	**⌘ + D**
Go to documentation	**CTRL + H**	**⌘ + H**

2.1.4 ChemSCAD Database

In order to enhance the digital domain of the reactionware generated using ChemSCAD, we have integrated a digital database which allows the user to create a history of their synthesis including the three key aspects of the iterative process: i) Reactionware Procedure, ii) Design Files, iii) Analytical Data. In this way, we hope to foster an open-access culture for digitally designing, and, importantly critically assessing Reactionware, allowing others to share their syntheses and designs globally, thus creating a network of academics and industry professionals who can use ChemSCAD and the integrated digital database to iterate the process of Reactionware design for their specific purposes.

As shown in Figure S10 below, each of these high-level folders contains sub-folders/files which pertain to the synthesis in question. Each molecule is assigned to an individual branch on GitLab, which is formatted according to the template created on the master branch, which the structure shown below. The user must clone the repository to their local machine, create a new branch from master, duplicate the 'Version_#' folder (where # is the associated version number i.e. 1, 2, 3, final etc) for a given design. They can then follow the folder structure adding the necessary files and then commit these changes and push them to GitLab, allowing for clear version control when developing a synthesis for a given molecule in Reactionware. The instructions on how to do this are provided below.

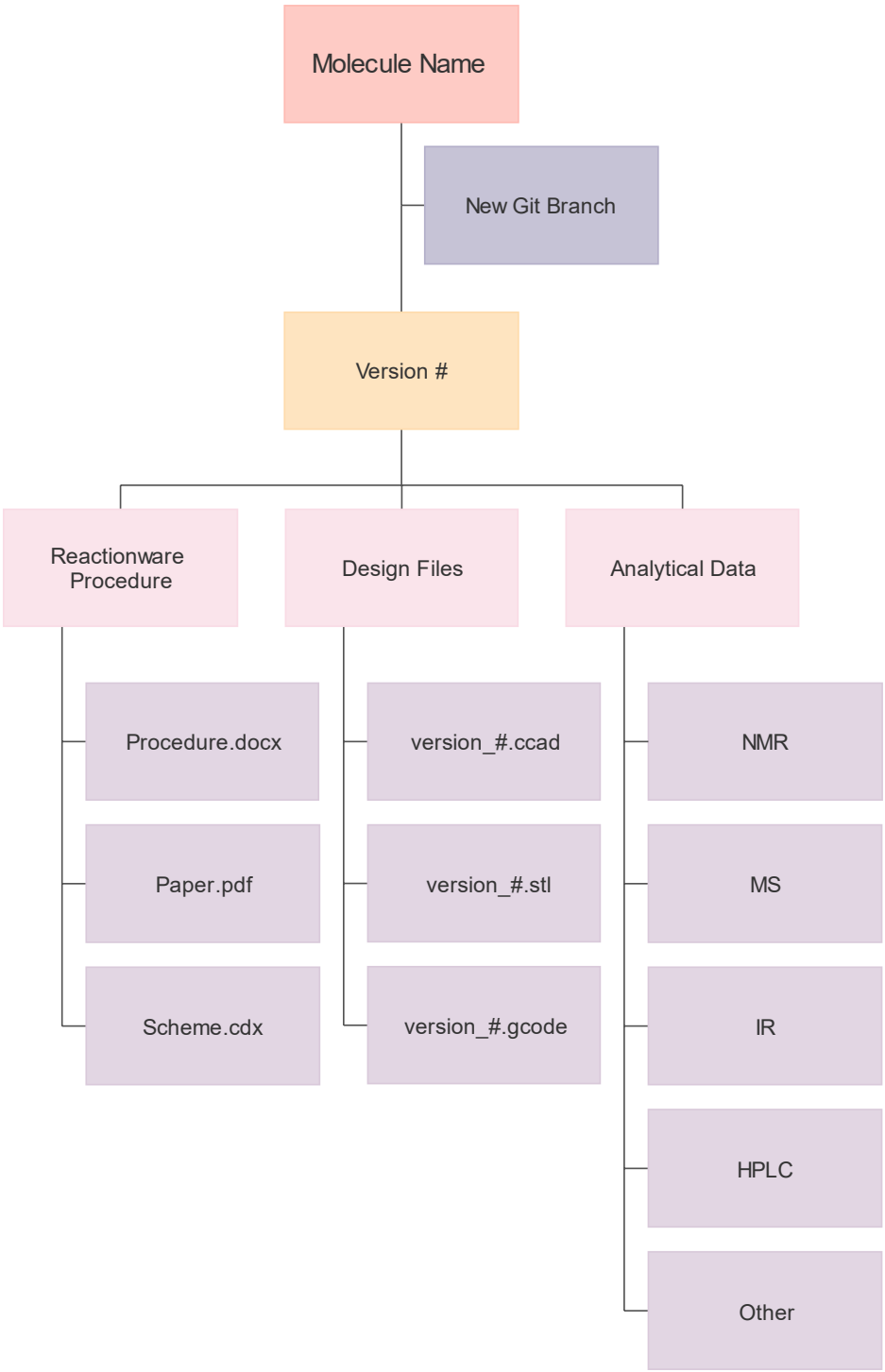


Figure S10: Flow diagram for the ChemSCAD digital database workflow

On the template (master) branch, there is a CHANGELOG.txt file that allows for a chronological history of **key** changes made to a Reactionware design, synthesis or analysis method when developing a new version. The format for this is as follows: at the top of the file is [VERSION_#], corresponding to the latest version being worked on, the user will provide a date and time for when the change(s)

was made, along with a unique identifier (i.e. their name/initials) and a short description of the change(s) made. They can also provide ‘tags’ if they wish in square brackets at the start of these comments, for example [DESIGN] as this allows another user to quickly use the ‘Find’ functionality to quickly identify and filter particular changes of a certain type.

To access the database please either go to: < insert GitHub link here > or use the keyboard shortcut from within ChemSCAD (see above)

2.1.4.1 **How to use the ChemSCAD Database**

First, you need to clone the repository to your local computer:

```
git clone https://gitlab.com/croningroup/reactionware/reactionware_files.git
cd reactionware_files
```

Then, create a new branch for the molecule you have/are interested in synthesising in Reactionware:

```
git checkout -b <molecule_name>
```

This will create a new branch with the name of the molecule and will contain the template folder structure for:

Version_# - the version number (#) should be changed for each new version and the template folder duplicated to allow ease of version control

1. **Reactionware Procedure** (procedure document, paper, chemdraw scheme)*
2. **Design Files** (files for this version, with .ccad, .stl and .gcode extensions)
3. **Analytical Data** (sub-folders for different analyses: NMR, MS, IR, HPLC and other)

*** -** *this folder can also contain glassware procedures for future reference/comparison with Reactionware procedures*

Once all the relevant files have been saved into the correct sub-folders, the changes must be pushed to Git using the following commands:

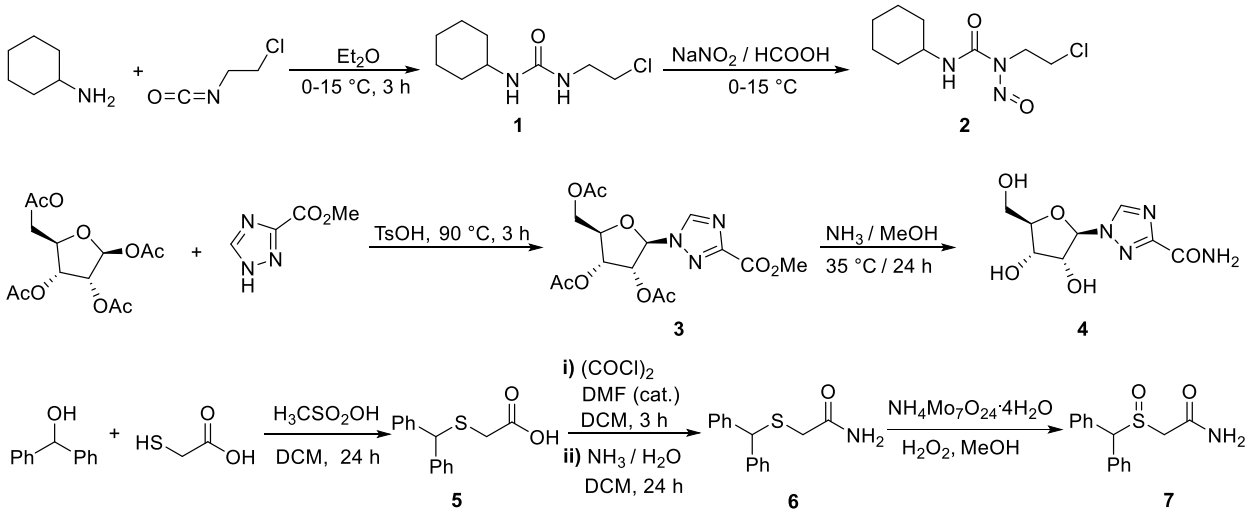
```
git add . # adds all new files to the commit
git commit -m "Add your commit message here...for example new files added"
```

```
git push origin <branch_name>
```

Doing the above will upload all the files to the Git repository, on the correct branch.

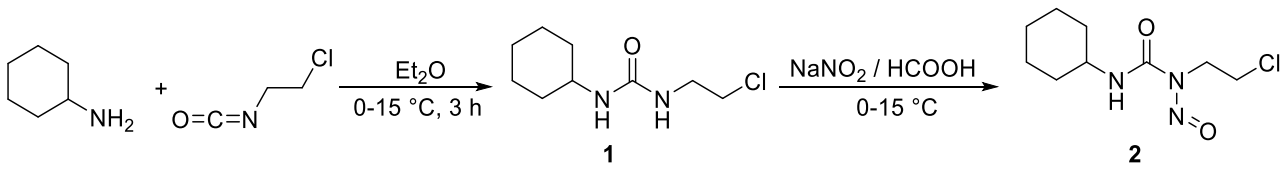
For each new version of a synthesis, the root 'Version_#' folder can be copied and pasted on your local computer and the version number changed, the new files added to the respective sub-folders and the same procedure followed for uploading the changes to Git. For example, there may be **Version_1** and **Version_final** folders for the same molecule on a given branch.

3 Traditional / Reactionware Synthesis of Drug Molecules

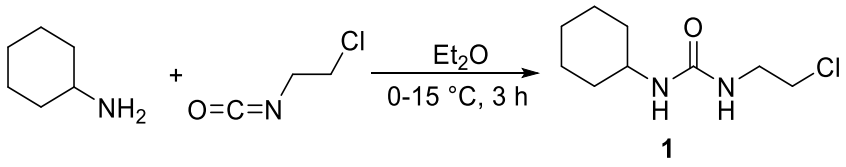


3.1 Lomustine Synthesis in Glassware

The synthetic procedure for the glassware synthesis of *N*-(2-Chloroethyl)-*N'*-cyclohexyl-*N*-nitrosourea - (Lomustine) was adapted from a literature procedure. [4]



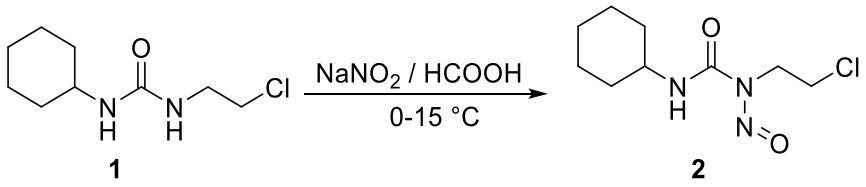
3.1.1 Compound **1**: 1-(2-Chloroethyl)-3-cyclohexylurea



2-Chloroethyl isocyanate (1.05 g, 10.0 mmol) and Et_2O (20 mL) were added to 100 mL round bottom flask. The reaction vessel was placed in a cooling bath at 0-5 °C. Cyclohexanamine (1.0 g, 10.0 mmol) in Et_2O (20 mL) was added dropwise to the 100mL round bottom flask with stirring. The mixture was

stirred for 3 h at 0-15 °C. A solid separated and was collected and washed with ether to give the urea product (1.8 g, 9.0 mmol, 90%) as a white solid.

3.1.2 Compound **2** (Lomustine): N-(2-Chloroethyl)-N'-cyclohexyl-N-nitrosourea



1 **2**

1-(2-Chloroethyl)-3-cyclohexylurea (1.8 g, 9.0 mmol) and HCOOH (32 mL) was added to round bottom flask. The reaction vessel was placed in a cooling bath at 0-5 °C. $NaNO_2$ (1.6 g, 23.0 mmol) was added in portions to the solution with stirring. The mixture was stirred for 2 h at 0-15 °C. After the stirring for 2 h water (60 mL) was added. A solid crashed out which was collected and washed with water to give Lomustine (1.6 g, 6.8 mmol, 76 %) as a pale yellow solid.

Overall yield (Based on Cyclohexanamine): 68 %.

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.73 (d, *J* = 6.0 Hz, 1H), 4.10 (t, *J* = 6.8 Hz, 2H), 3.87 – 3.72 (m, 1H), 3.43 (t, *J* = 6.8 Hz, 2H), 2.07 – 1.83 (m, 2H), 1.78 – 1.64 (m, 2H), 1.63 – 1.48 (m, 1H), 1.43 – 1.05 (m, 5H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 151.8, 50.0, 40.0, 38.9, 33.1, 25.4, 24.7.

3.1.3 ^{1}H and ^{13}C NMR Spectra of Lomustine in Glassware

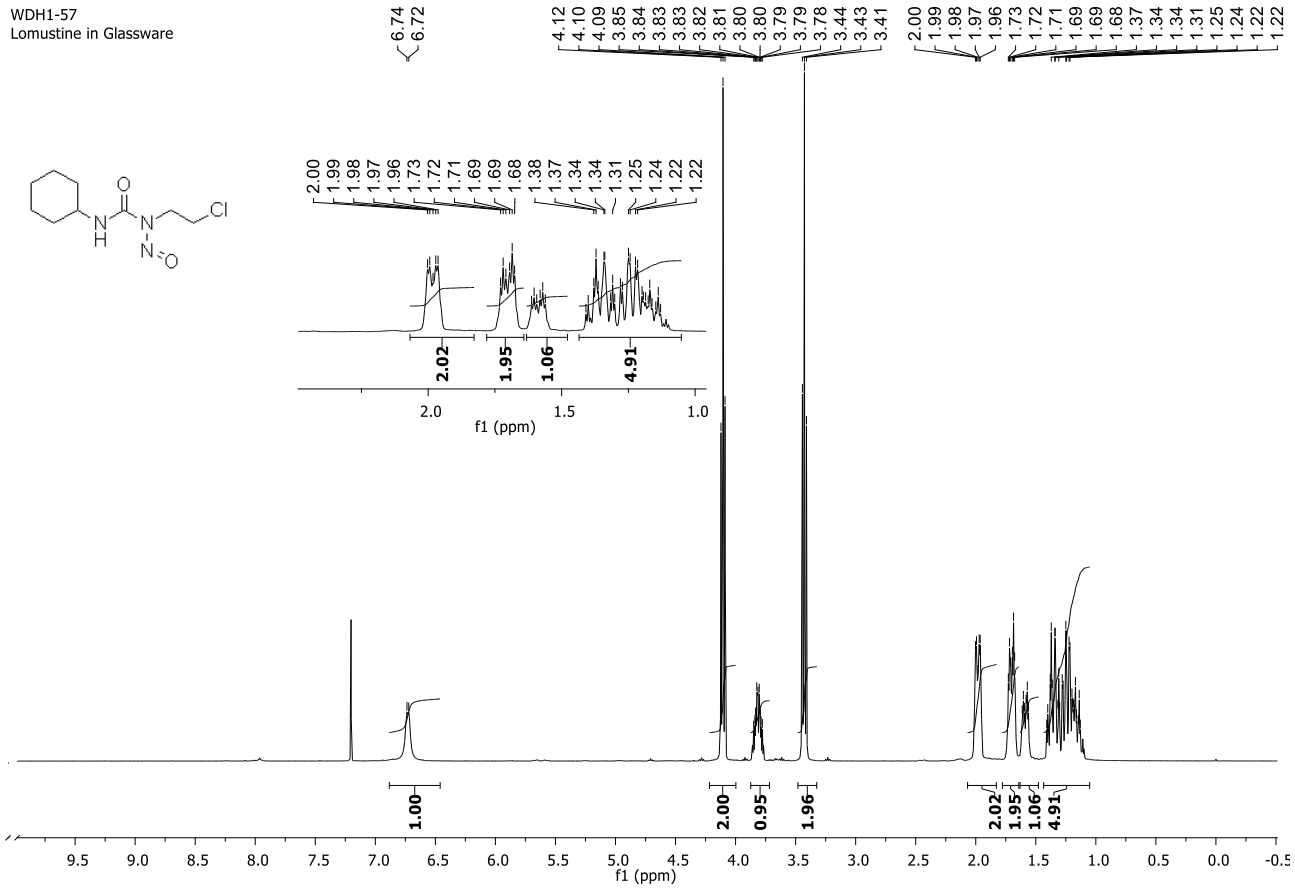


Figure S11: The ^{1}H NMR of Lomustine in Glassware.

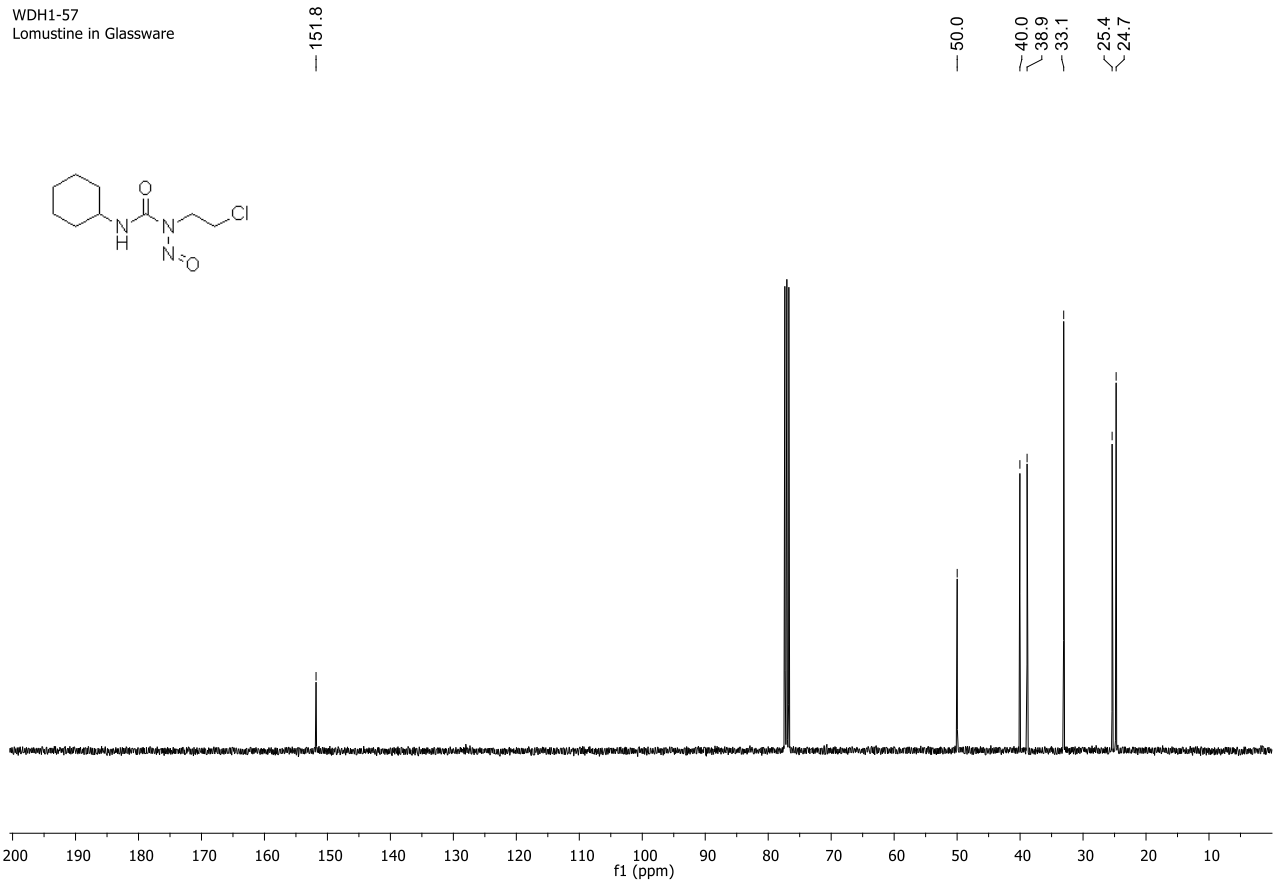
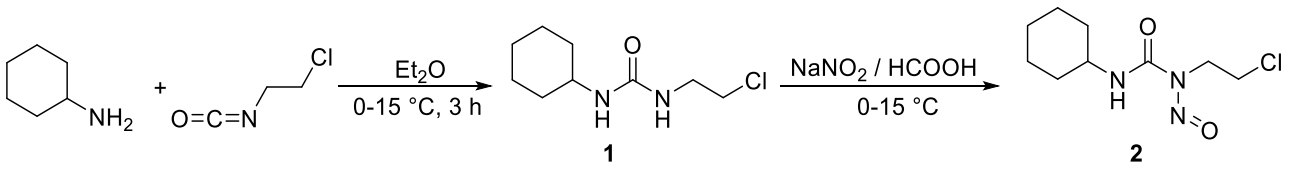


Figure S12: The ^{13}C NMR of Lomustine in Glassware.

3.2 Lomustine Synthesis in Reactionware



For following reference modules will be referred to as **M**#, i.e. module 1 is **M1**.

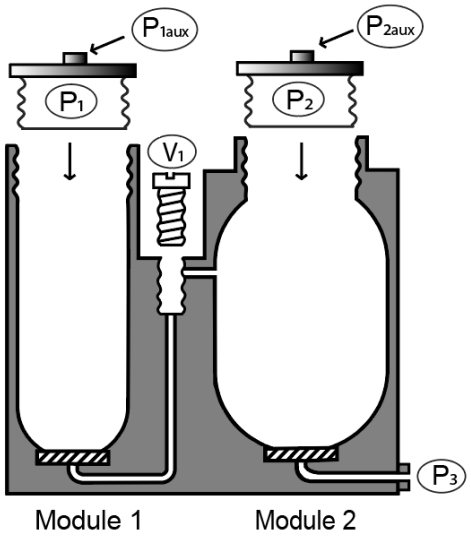


Figure S13: **2D representation of the reactionware monolith used in the synthesis of Lomustine.**

3.2.1 Experimental

2-Chloroethyl isocyanate (1.05 g, 10.0 mmol) and Et_2O (20 mL) was added into **M1**. The monolith was then placed in a cooling bath at 0-5 °C. Cyclohexanamine (1.0 g, 10.0 mmol) in Et_2O (20 mL) was added dropwise to **M1** with stirring. The mixture was stirred for 3 h at 0-15 °C. Then filtered, washed with Et_2O (5 mL) and dried under vacuum for 0.5-1 h at 20-25 °C. HCOOH (32 mL) was added to **M1** and the mixture was stirred until dissolved. The solution was transfered to **M2**. The monolith was placed in a cooling bath at 0-5 °C. $NaNO_2$ (1.6 g, 23.0 mmol) was added in portions to the solution with stirring. The mixture was stirred for 2 h at 0-15 °C. Then water (60 mL) was added to it. A solid separated and was collected and washed with water. The wet product was dried on vacuum for 10-12 h at 20-25 °C to give 1.6 g of Lomustine with the yield of 68 % and purity of 98 %.

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.72 (d, *J* = 5.8 Hz, 1H), 4.11 (t, *J* = 6.8 Hz, 2H), 3.91 – 3.74 (m, 1H), 3.43 (t, *J* = 6.8 Hz, 2H), 2.06 – 1.90 (m, 2H), 1.77 – 1.65 (m, 2H), 1.64 – 1.54 (m, 1H), 1.43 – 1.08 (m, 5H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 151.8, 50.0, 40.0, 38.9, 33.1, 25.4, 24.7.

HRMS (ESI) calculated for $C_9H_{16}ClN_3O_2Na$ $[M + Na]^+$ 256.0829, found 256.0843, $\Delta = 5.47$ ppm.

3.2.2 Operations Table

Each synthetic procedure in reactionware described here includes an 'Operations Table' which details each of the individual actions (with timestamps) required to be taken in order to afford the target molecule.

Here is a key of symbols provided in each table:

Symbol	Meaning
O	Open (port)
C	Close (port)
P # aux	Auxiliary cavity in port #, where # is a number
Remove	Remove contents from vessel
Vacuum	Pull vacuum on port (to dry)
M#	Module, where # is a number
N2 gas / compressed air	Pressure applied by either nitrogen gass or compressed air to respective port
Condenser	Mount 3D-printed polypropylene condenser to respective port

The columns consist of: a timestamp defining how much time passed since the start of the synthesis, action column describing the individual step of the synthesis, followed by a series of columns respective to ports and valves that are depicted in 2D representations of reactionware monoliths before each operation table.

Compound **1**					
Time d/hh:mm	Action	P_1	V_1	P_2	P_3
0/00:00	Add Et_2O (20 mL) through port P_{1aux}	O aux	C	C	C

0/00:01	Add 2-Chloroethyl isocyanate (1.05 g, 10.0 mmol) through port P_{1aux}	O aux	C	C	C
0/00:02	Place the Reactionware into an ice bath	O aux	C	C	C
0/00:03-0/00:19	Stir at 400 rpm	O aux	C	C	C
0/00:20-0/00:29	Add Cyclohexanamine (1.00 g,10.0 mmol) in Et_2O (20 mL) through port P_{1aux}	O aux	C	C	C
0/00:30-0/03:30	Stir for 3 h	O aux	C	C	C
0/03:31	Remove the ice bath and the valve V_1	O aux	Remove	C	C
0/03:32-0/03:34	Withdraw the liquid from the reaction module **M1** by applying vacuum to V_1	O aux	Remove	C	C
0/03:35	Add 5 mL of Et_2O to the reaction module **M1**	O aux	Remove	C	C
0/03:36	Withdraw the liquid from the module **M1** by applying vacuum to V_1	O aux	Remove	C	C
0/03:37-0/04:37	Close P_{1aux} and dry the product by applying vacuum to V_1 at rt.	C	Remove	C	C
Compound **2** - Lomustine					
Time d/hh:mm	Action	P_1	V_1	P_2	P_3
0/04:38	Open the Port P_{1aux} and Close the V_1	O aux	C	C	C
0/04:39	HCOOH (27 mL) was added to the M1 through port P_{1aux}	O aux	C	C	C
0/04:40-0/04:45	Stir and dissolve the solid	O aux	C	C	C
0/04:46	Open V_1 and P_{2aux}	O aux	O	O aux	C
0/04:47-0/04:49	Withdraw the liquid from the **M1** to **M2** by applying vacuum to P_{2aux}	O aux	O	O aux	C
0/04:50	HCOOH (5 mL) was added to the **M1** through port P_{1aux}	O aux	O	O aux	C
0/04:51-0/04:52	Withdraw the liquid from the **M1** to **M2** by applying vacuum to port P_{2aux}	O aux	O	O aux	C
0/04:53	Close P_{1aux} and V_1	C	C	O aux	C
0/04:54	Stir at 400 rpm	C	C	O aux	C
0/04:55-0/05:05	Cool to 0-15 °C	C	C	O aux	C
0/05:06	Open P_2	C	C	O	C
0/05:07-0/05:17	$NaNO_2$ (1.60 g, 23.0 mmol) was added in portions to the solution of **M2**	C	C	O	C

0/05:18	Close P_2 and open P_{2aux}	C	C	O aux	C
0/05:19-0/06:19	Stir 0-15 °C for 1 h	C	C	O aux	C
0/06:20-0/06:29	Add cold water (0-15 °C , 60 mL) to **M2** though port P_{2aux}	C	C	O aux	C
0/06:30-0/07:00	Stir at 0-15 °C for 0.5 h	C	C	O aux	C
0/07:01-0/07:02	Open port P_2 and P_3	C	C	O	O
0/07:03-0/07:05	Connect vacuum to port P_3 and withdraw liquid from the **M2**	C	C	O	O
0/07:06	Add cold water (0-15 °C, 5mL) to **M2** through port P_2	C	C	O	O
0/07:07	Withdraw the liquid from the M2 by applying vacuum to port P_3	C	C	O	O
0/07:08-0/18:00	Close P_2 and P_{2aux} and dry the product by applying vacuum to P_3	C	C	C	O
Complete					

3.2.3 ^{1}H and ^{13}C NMR Spectra of Lomustine in Reactionware

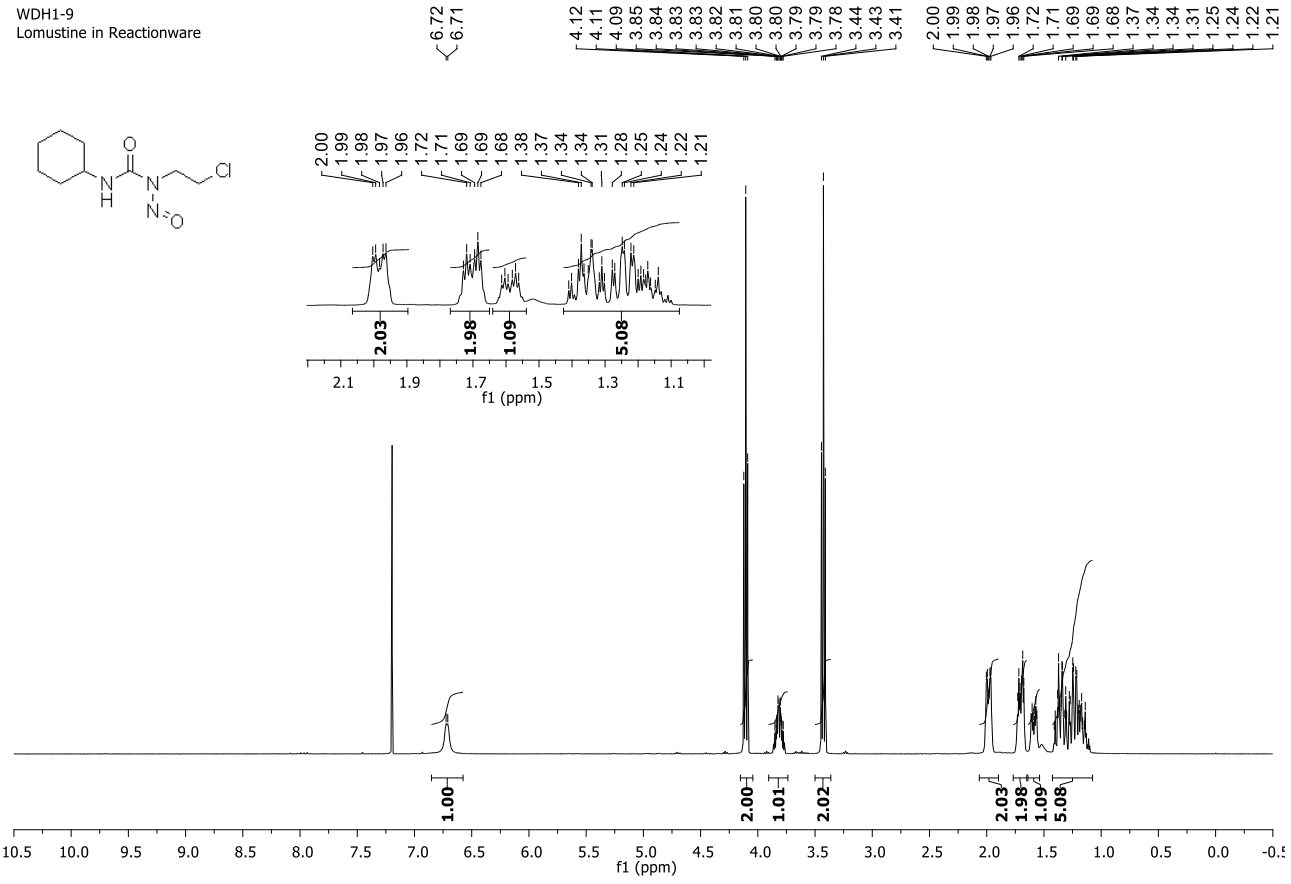


Figure S14: ^{1}H NMR of Lomustine in Reactionware.

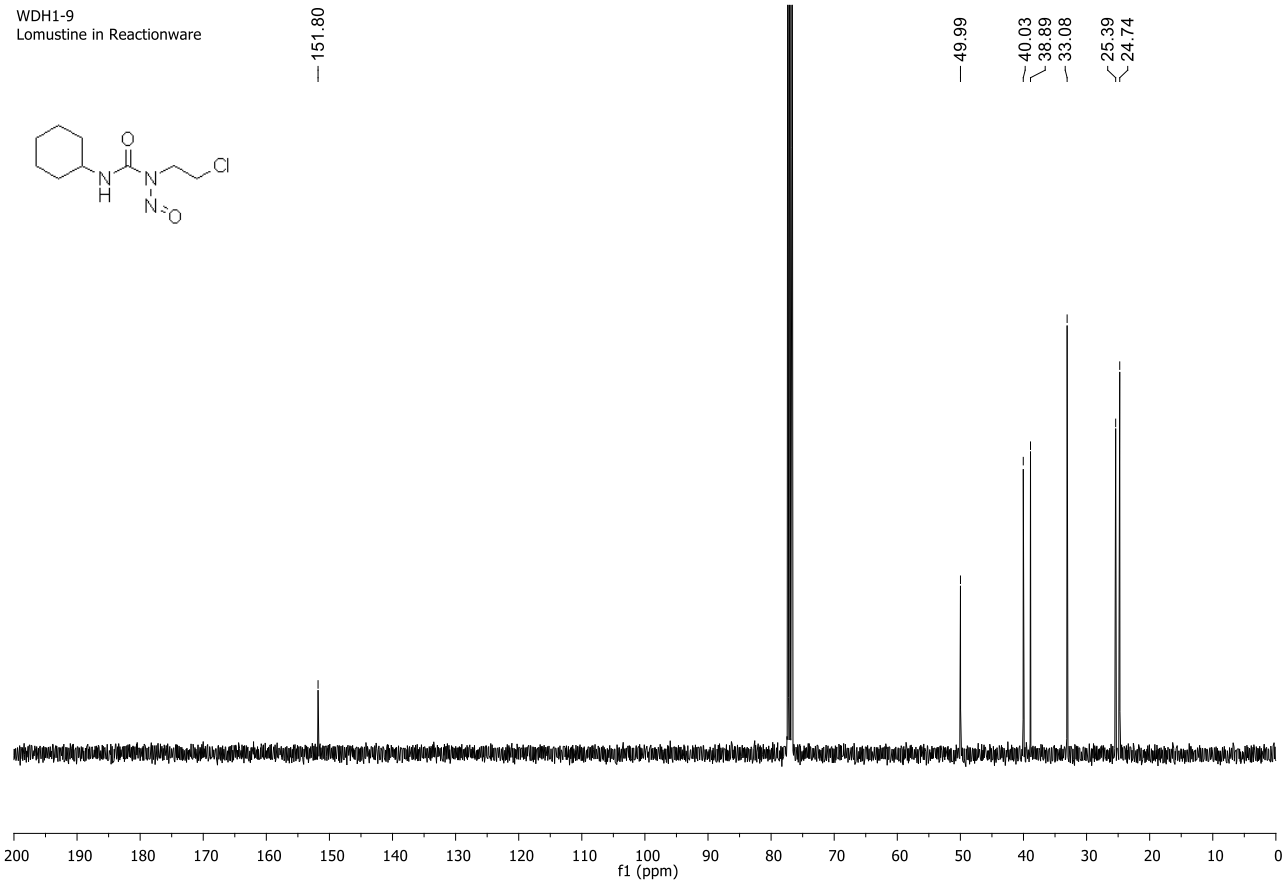
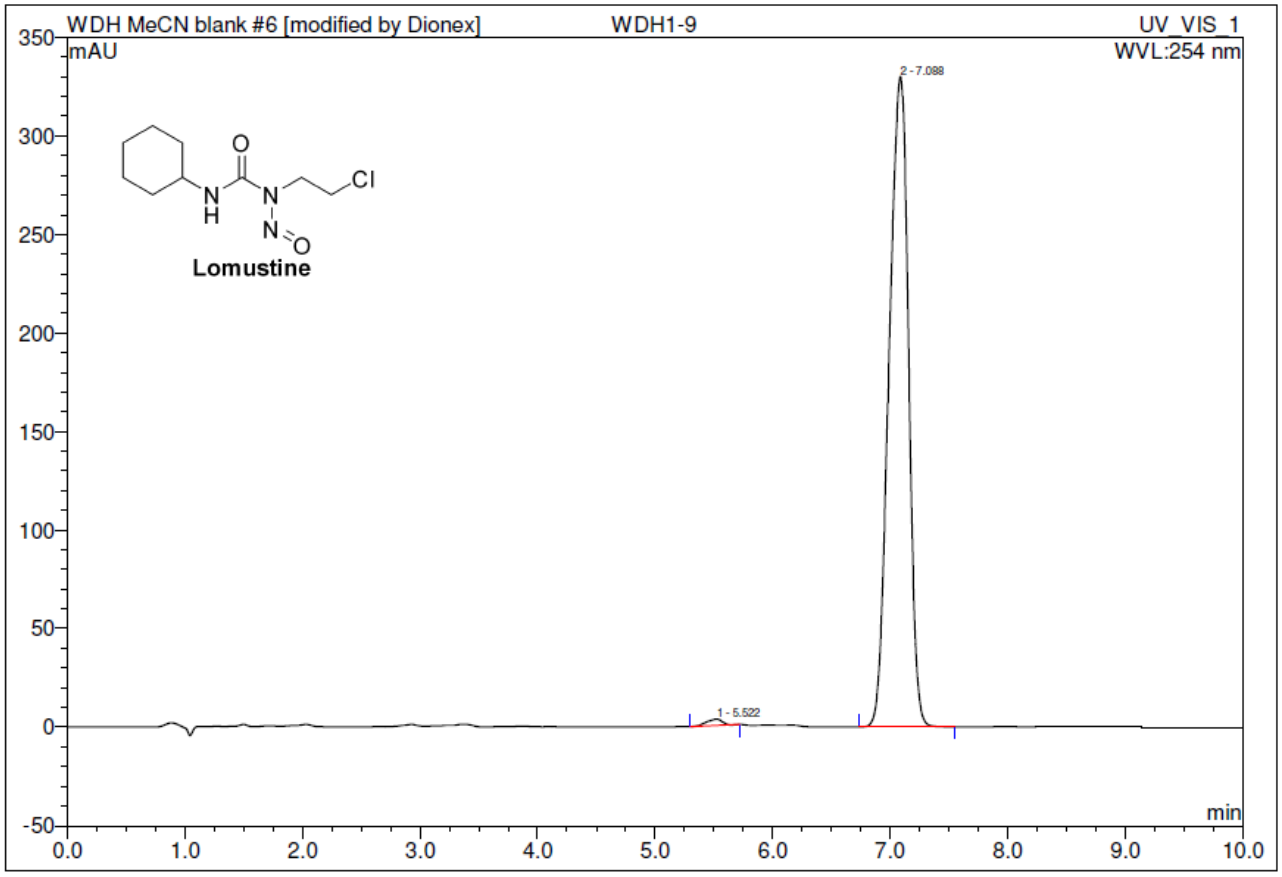


Figure S15: ^{13}C NMR of Lomustine in Reactionware.

3.2.4 HPLC Spectra of Lomustine in Reactionware

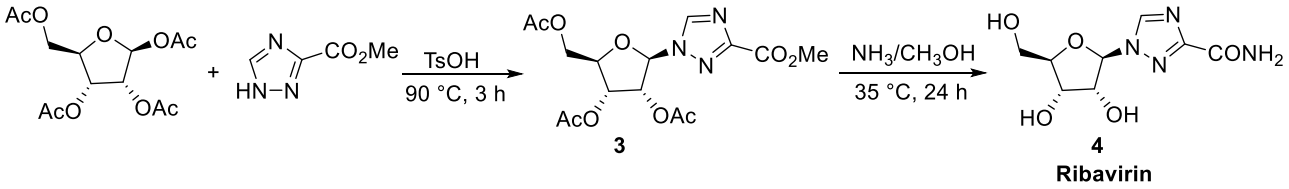


No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	5.52	n.a.	3.228	0.494	0.78	n.a.	BMB*
2	7.09	n.a.	330.038	63.060	99.22	n.a.	BMB
Total:			333.267	63.553	100.00	0.000	

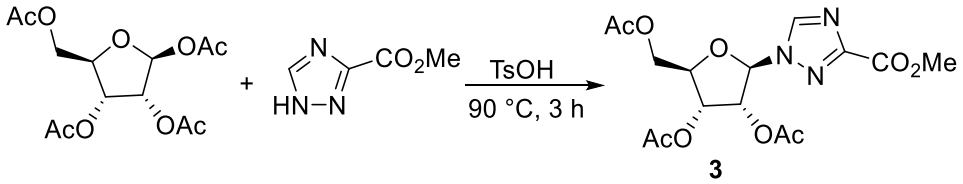
Figure S16. Integrated HPLC trace for sample obtained from the Reactionware on Lomustine. Peak 2 (retention time 7.09 minutes) represents Lomustine and has a peak area equivalent to 99.22% of the total area of the trace.

3.3 Ribavirin Synthesis in Glassware

The synthetic procedure for the glassware synthesis of Ribavirin was adapted from a literature procedure. [5]

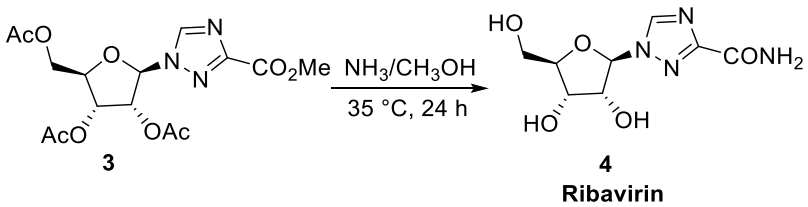


3.3.1 Compound 3: (2R,3R,4R,5R)-2-(acetoxymethyl)-5-(3-(methoxycarbonyl)-1H-1,2,4-triazol-1-yl)tetrahydrofuran-3,4-diyl diacetate



β-D-ribofuranosyl-1,2,3,5-tetraacetate (6.0 g, 18.9 mmol) and Methyl 1,2,4-triazole-3-carboxylate (2.72 g, 21.4 mmol) were added to round bottom flask and heat to 90 °C until the solid was melted. Then *p*-Toluenesulfonic acid (110 mg) was added to the molten mixture. The reaction mixture was reacted for 3 h, while maintaining the temperature of the reaction mixture at 90 °C. Then the mixture was cooled to 80 °C and 40 mL of ethanol was added to it. After stirring for 15 min, then cooled to rt. And stirring at rt for 0.5 h. A solid was separated and collected and washed with EtOH (4 mL) to give 5.7 g (Yield: 78%) of **3** ((2R,3R,4R,5R)-2-(acetoxymethyl)-5-(3-(methoxycarbonyl)-1H-1,2,4-triazol-1-yl)tetrahydrofuran-3,4-diyl diacetate).

3.3.2 Compound 4 (Ribavirin): (1-[(2R,3R,4S,5R)-3,4-Dihydroxy-5-(hydroxymethyl)oxolan-2-yl]-1H-1,2,4-triazole-3-carboxamide)



3 **4**
Ribavirin

3 (5.7 g) and 7M Ammonia in Methanol (30 mL) was added to round bottom flask. The mixture was stirring at 35 °C for 24 h. A solid separated and was collected and washed with cold EtOH to give white solid 2.9 g of crude Ribavirin. Then solid was recrystallized by 80% EtOH to give product 2.1 g (Yield: 58%).

Overall yield (Based on β-D-ribofuranosyl-1,2,3,5-tetraacetate): 45%

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.87 (s, 1H), 7.82 (s, 1H), 7.61 (s, 1H), 5.82 (d, *J* = 3.9 Hz, 1H), 5.57 (d, *J* = 5.5 Hz, 1H), 5.19 (d, *J* = 5.5 Hz, 1H), 4.91 (t, *J* = 5.5 Hz, 1H), 4.35 (dd, *J* = 9.1, 4.7 Hz, 1H), 4.14 (dd, *J* = 10.1, 5.0 Hz, 1H), 3.95 (dd, *J* = 9.2, 4.7 Hz, 1H), 3.66 -3.61 (m, 1H), 3.55 – 3.39 (m, 1H).

^{13}C NMR (400 MHz, DMSO-d_6) δ 160.9, 157.8, 145.4, 92.3, 86.0, 75.0, 70.5, 61.8.

3.3.3 ^{1}H and ^{13}C NMR Spectra of Ribavirin in Glassware

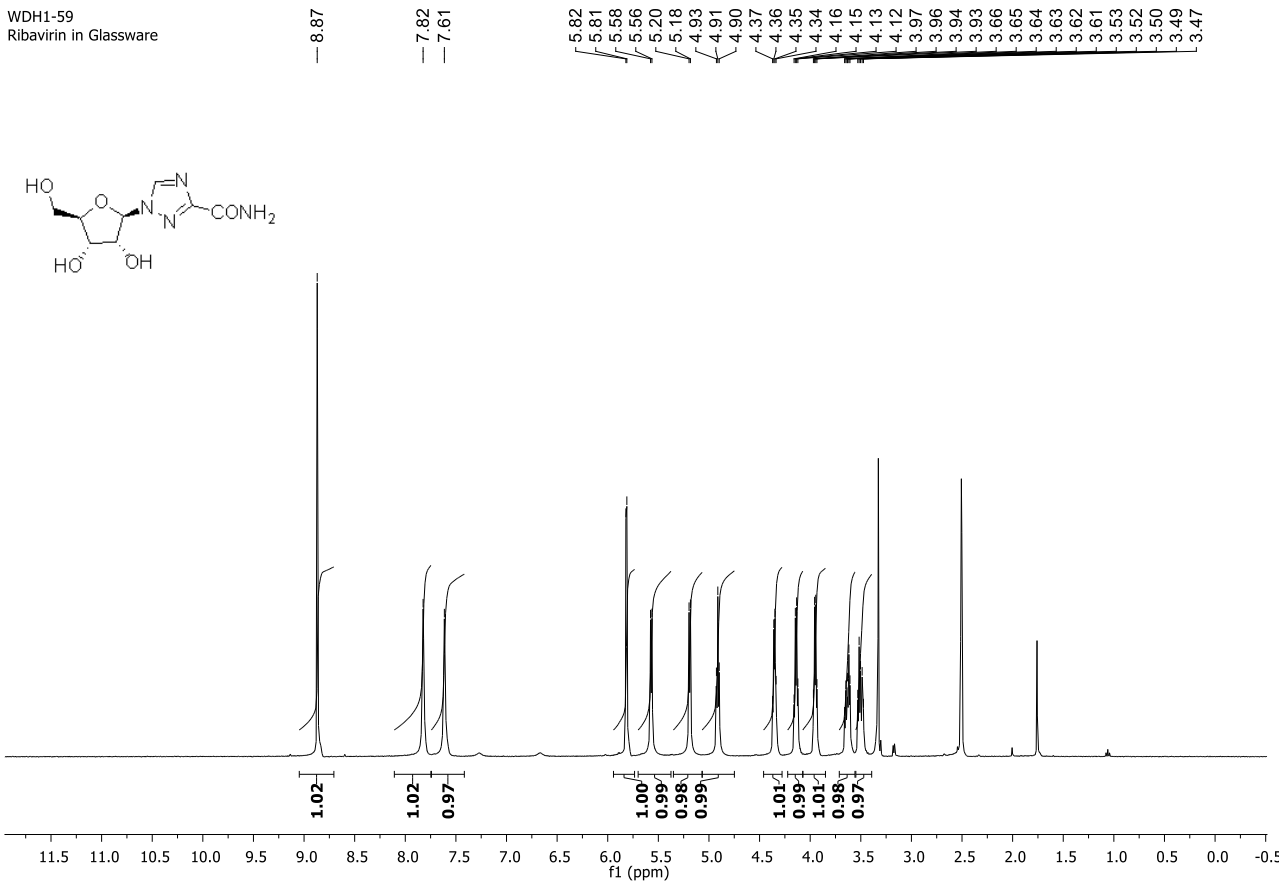


Figure S17: ^{1}H NMR of Ribavirin in Glassware.

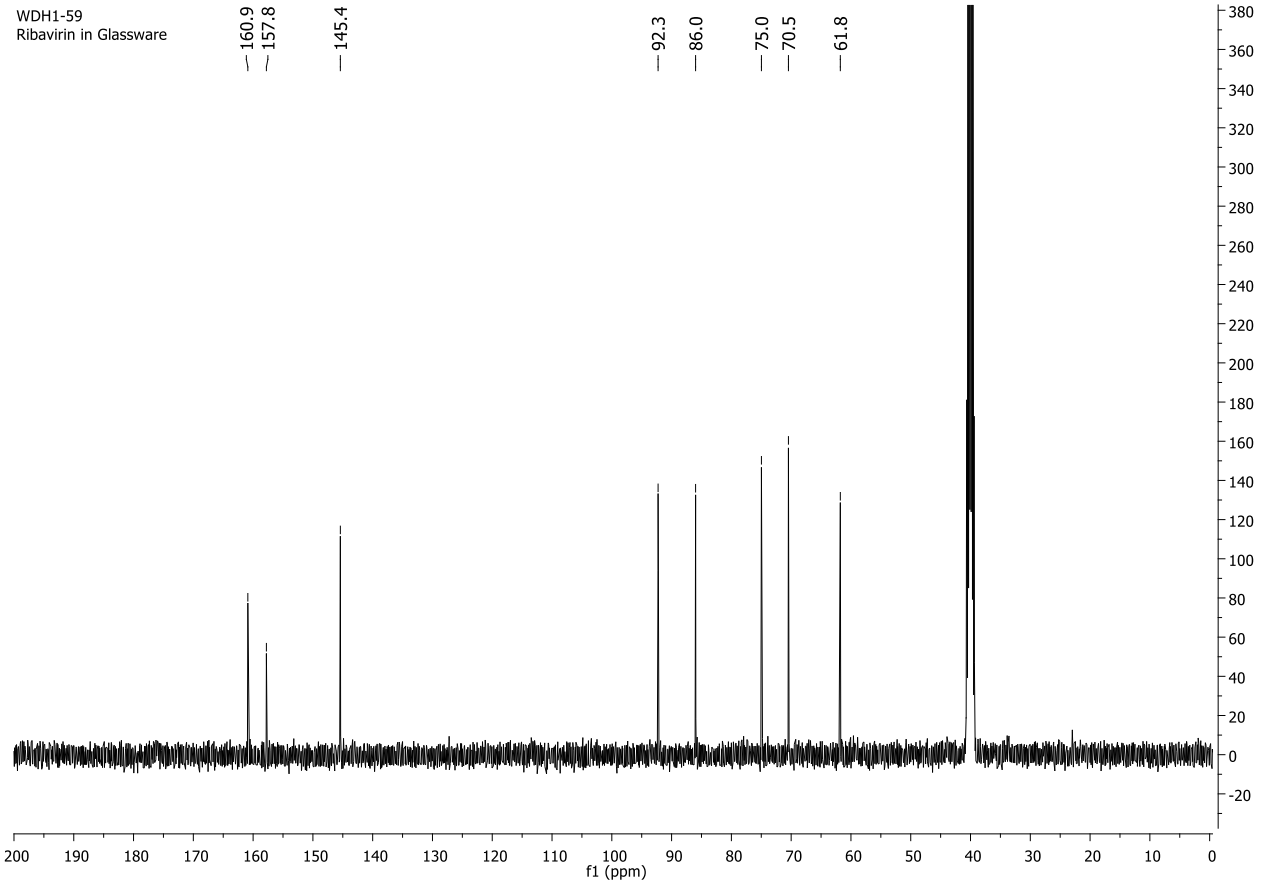
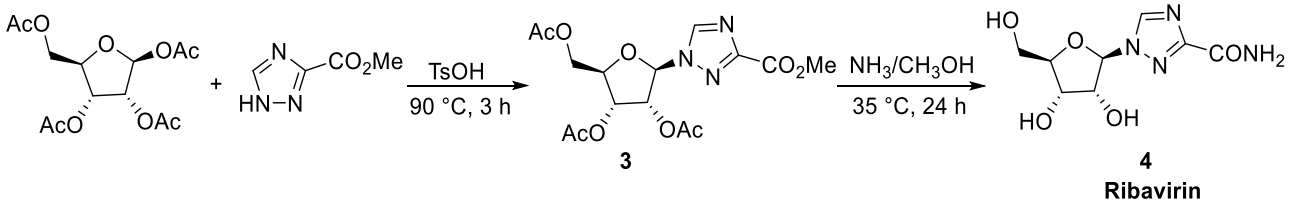


Figure S18: ^{13}C NMR of Ribavirin in Glassware.

3.4 Ribavirin Synthesis in Reactionware



For following reference modules will be referred to as **M**#, i.e. module 1 is **M1**.

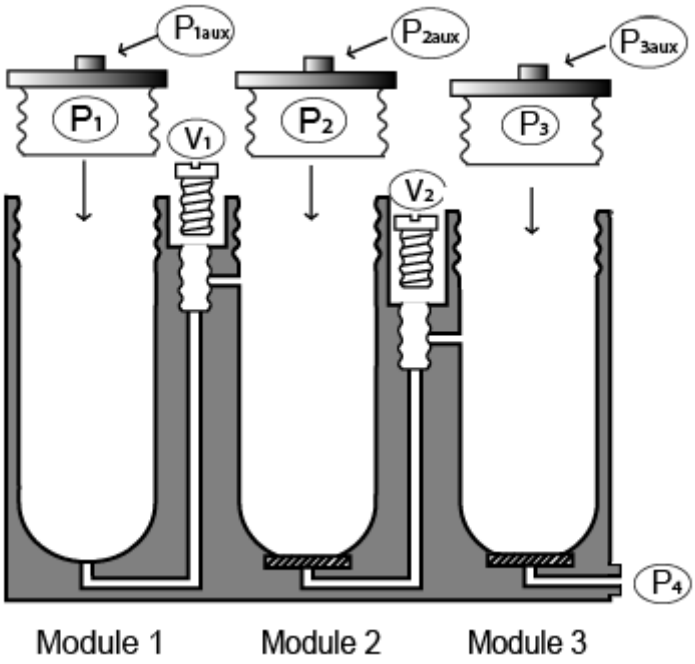


Figure S19: 2D representation of the reactionware monolith used in the synthesis of Ribavirin.

3.4.1 Experimental

Methyl 1,2,4-triazole-3-carboxylate (2.72 g) and β-D-ribofuranosyl-1,2,3,5-tetraacetate (6.0 g) were added to **M1** and heated to 110 °C until the solid melted. Then *p*-toluenesulfonic acid (110 mg) was added to the molten mixture. The reaction mixture was reacted for 3 h, while maintaining the temperature of the reaction mixture at 110 °C (Oil bath temp.). Then oil bath temp. was cooled to 80 °C and 35 mL of ethanol was added to it. After stirring for 15 min, then transfer the solution to **M2**. 5 mL of ethanol was added to **M1**, then transfer the solution to **M2**. Cool to rt, and stirring at rt for 0.5 h. Filtration and solid was washed by ethanol (4 mL). Then 7M ammonia in Methanol (30 mL) was added to **M2**. The mixture was stirring at 35 °C for 24 h. Filtration and solid was washed by ethanol (4 mL). Then 35 mL of 80% EtOH solution was added to **M2**. Heat to 95 °C (Inner: 70 °C) until dissolved. Transfer the solution to **M3**. 5 mL of 80% EtOH solution was added to **M2**, then transfer the solution to **M3**. Cool to 0 °C and stirring at 0 °C for 0.5 h. Filtration and drying, then 2.0 g (Yield: 43%) of Ribavirin was obtained with purity of 98%.

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.93 (s, 1H), 7.87 (s, 1H), 7.67 (s, 1H), 5.87 (d, *J* = 3.9 Hz, 1H), 5.62 (d, *J* = 5.6 Hz, 1H), 5.24 (d, *J* = 5.6 Hz, 1H), 4.96 (t, *J* = 5.5 Hz, 1H), 4.41 (dd, *J* = 9.4, 4.9 Hz, 1H), 4.20 (dd, *J* = 10.4, 5.2 Hz, 1H), 4.01 (dd, *J* = 9.3, 4.8 Hz, 1H), 3.79 – 3.64 (m, 1H), 3.61 – 3.45 (m, 1H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 160.9, 157.7, 145.4, 92.2, 86.0, 75.0, 70.5, 61.8.

HRMS (ESI) calculated for $C_8H_{13}N_4O_5$ $[M + H]^+$ 245.0886, found 245.0961, Δ = 30.60 ppm.

3.4.2 Operations Table

Compound **3**							
Time d/hh:mm	Action	P_1	V_1	P_2	V_2	P_3	P_4
0/00:00	Flush the module with Argon gas from P_{1aux} for 5min	O aux	O	C	O	C	O
0/00:05	Close V_1, V_2 and P_4	O aux	C	C	C	C	C
0/00:06	Place the cartridge into an oil bath	O aux	C	C	C	C	C
0/00:07-0/00:32	Heat to 110 °C	O aux	C	C	C	C	C
0/00:33	Remove P_1	O	C	C	C	C	C
0/00:34	Add Methyl 1,2,4-triazole-3-carboxylate (2.72 g) and β-D-ribofuranosyl-1,2,3,5-tetraacetate (6.0 g) to Module 1 through port P_1	O	C	C	C	C	C
0/00:35	Open stir	O	C	C	C	C	C
0/00:36	Add *p*-toluenesulfonic acid after the mixture was melted	O	C	C	C	C	C
0/00:37	Put on P_1 and Connect an empty balloon to P_{1aux}	O aux	C	C	C	C	C
0/00:38-0/03:38	Stir at 110 °C (Inner: 90 °C) for 3 h	O aux	C	C	C	C	C
0/03:39-0/03:53	Cool to 80 °C	O aux	C	C	C	C	C
0/03:54	Remove P_1 and add 35 mL of ethanol to **M1** through port P_1	O	C	C	C	C	C

0/03:55-0/04:09	Stir at 80 °C for 15 min	O	C	C	C	C	C
0/04:10-0/04:11	Put on P_1, and open V_1 and P_2	O aux	O	O	C	C	C
0/04:12-0/04:13	Transfer the solution to **M2** by N_2 from P_{1aux}	O aux	O	O	C	C	C
0/04:14	Add 5 mL of ethanol to **M1** from P_{1aux}	O aux	O	O	C	C	C
0/04:15-0/04:19	Stir at 80 °C for 5 min	O aux	O	O	C	C	C
0/04:20	Transfer the solution to **M2** by N_2 from P_{1aux}	O aux	O	O	C	C	C
0/04:21	Close P_{1aux} and V_1, and put on P_2 with an empty balloon on P_{2aux}	C	C	O aux	C	C	C
0/04:22-0/04:41	Cool to rt	C	C	O aux	C	C	C
0/04:42-0/05:12	Stir at rt for 30 min	C	C	O aux	C	C	C
0/05:13	Remove V_2 and the empty balloon on P_{2aux}	C	C	O aux	Remove	C	C
0/05:14-0/05:18	Withdraw the liquid from the module by applying vacuum to V_2	C	C	O aux	Remove Vacuum on	C	C
0/05:19	Add 4 mL Ethanol to **M2**	C	C	O aux	Remove Vacuum off	C	C
0/05:20	Withdraw the liquid from the module by applying vacuum to V_1	C	C	O aux	Remove Vacuum on	C	C
0/05:25	Close P_{2aux}	C	C	C	Remove Vacuum on	C	C
0/05:26-0/22:26	Dry the product by applying vacuum to V_2 for 17 h	C	C	C	Remove Vacuum on	C	C
Compound **4** - Ribavirin							
Time d/hh:mm	Action	P_1	V_1	P_2	V_2	P_3	C
0/22:07	Open the P_{2aux} and close V_2	C	C	O aux	C	C	C
0/22:08	Add 30 mL of NH_3/Methanol (7M) through P_{2aux}	C	C	O aux	C	C	C
0/22:09	Connect an empty balloon to P_{2aux}	C	C	O aux	C	C	C
0/22:10	Open stir and heat to 35 °C	C	C	O aux	C	C	C
0/22:11-1/22:11	Stir at 35 °C for 24 h	C	C	O aux	C	C	C
1/22:12-1/22:42	Cool to rt	C	C	O aux	C	C	C
1/22:42-1/23:12	Stir at rt for 30 min	C	C	O aux	C	C	C

1/23:13-1/23:23	Remove valve V_2 completely and the empty balloon on P_{2aux}, use vacuum suction to pull liquid waste from the **M2**	C	C	O aux	Remove Vacuum on	C	C
1/23:24	Close the vacuum, And add 4 mL of ethanol	C	C	O aux	Remove Vacuum off	C	C
1/23:24-1/23:26	Stir	C	C	O aux	Remove Vacuum off	C	C
1/23:27-1/23:30	Use vacuum suction to pull liquid waste from the **M2**	C	C	O aux	Remove Vacuum on	C	C
1/23:31	Close V_2	C	C	O aux	C	C	C
1/23:32	Open the P_2, and add 35 mL of 80% ethanol solution to **M2**	C	C	O	C	C	C
1/23:33-2/00:03	Open the stir and heat to 95 °C (Inner: 70 °C)	C	C	O	C	C	C
2/00:03-2/00:33	Stir at 95 °C for 30 min until the solid was dissolved	C	C	O	C	C	C
2/00:34	Close P_2, Open V_2 and P_3	C	C	O aux	O	O	C
2/00:35-2/00:45	Flush by N_2 from P_{2aux} to transfer the solution to **M3**	C	C	O aux	O	O	C
2/00:46	Add 5 mL of 80% ethanol solution to **M2** from P_{2aux}	C	C	O aux	O	O	C
2/00:47-2/00:52	Stir 5 min	C	C	O aux	O	O	C
2/00:53-2/00:55	Flush by N_2 from P_{2aux} to transfer the solution to **M3**	C	C	O aux	O	O	C
2/00:56	Close P_{2aux} and V_2	C	C	C	C	O	C
2/00:57-2/01:34	Cool to 0 °C	C	C	C	C	O	C
2/01:35-2/02:35	Stir at 0 °C for 1h	C	C	C	C	O	C
2/02:36	Open P_4	C	C	C	C	O	O
2/02:37-2/02:41	Use vacuum suction from P_4 to pull liquid waste from **M3**	C	C	C	C	O	O
2/02:42	Close P_3 and P_4	C	C	C	C	O aux	C
2/02:43-2/19:43	Dry the product by applying vacuum to P_{3aux} to dry the product for 17 h	C	C	C	C	O aux	C
Complete							

3.4.3 ^{1}H and ^{13}C Spectra of Ribavirin in Reactionware

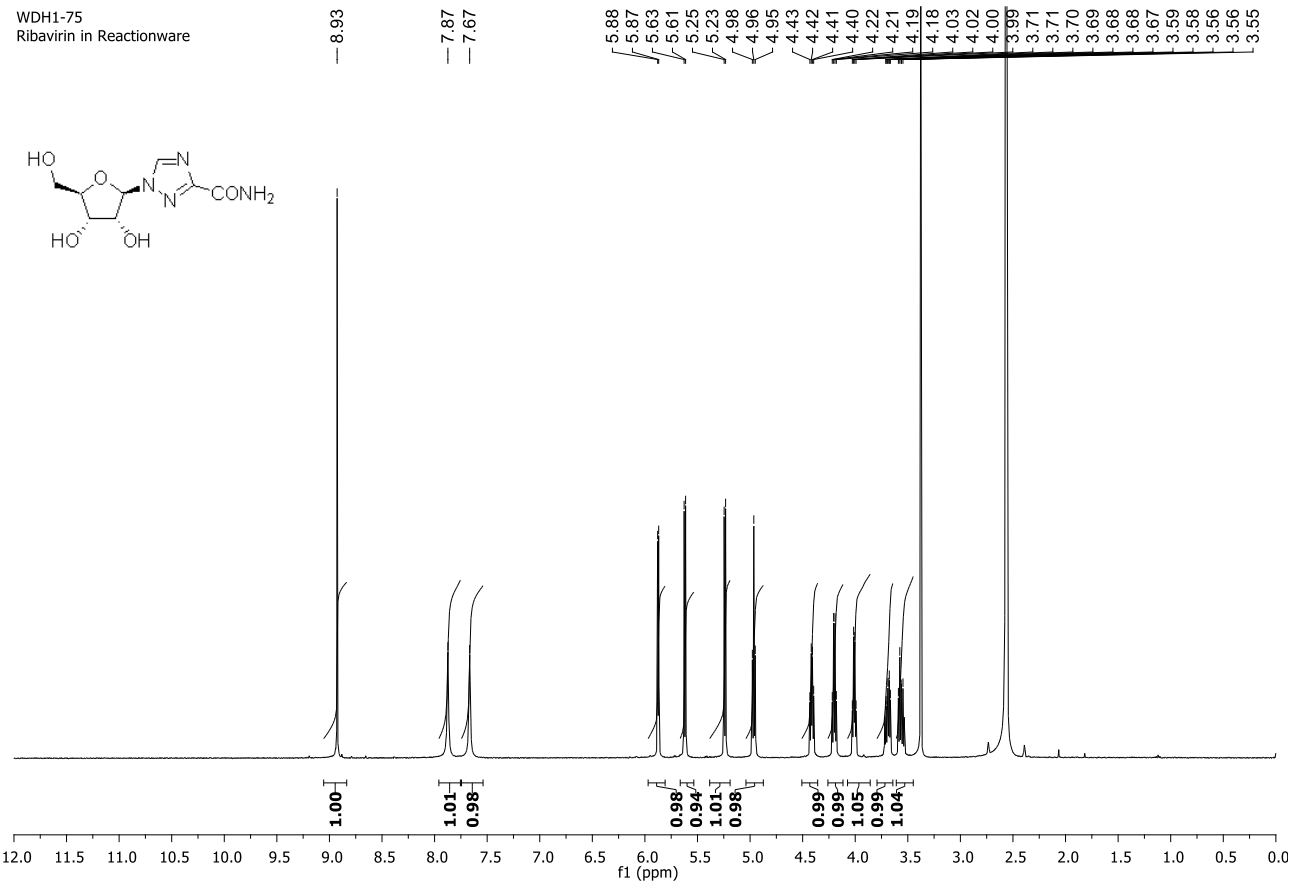


Figure S20: ^{1}H NMR of Ribavirin in Reactionware.

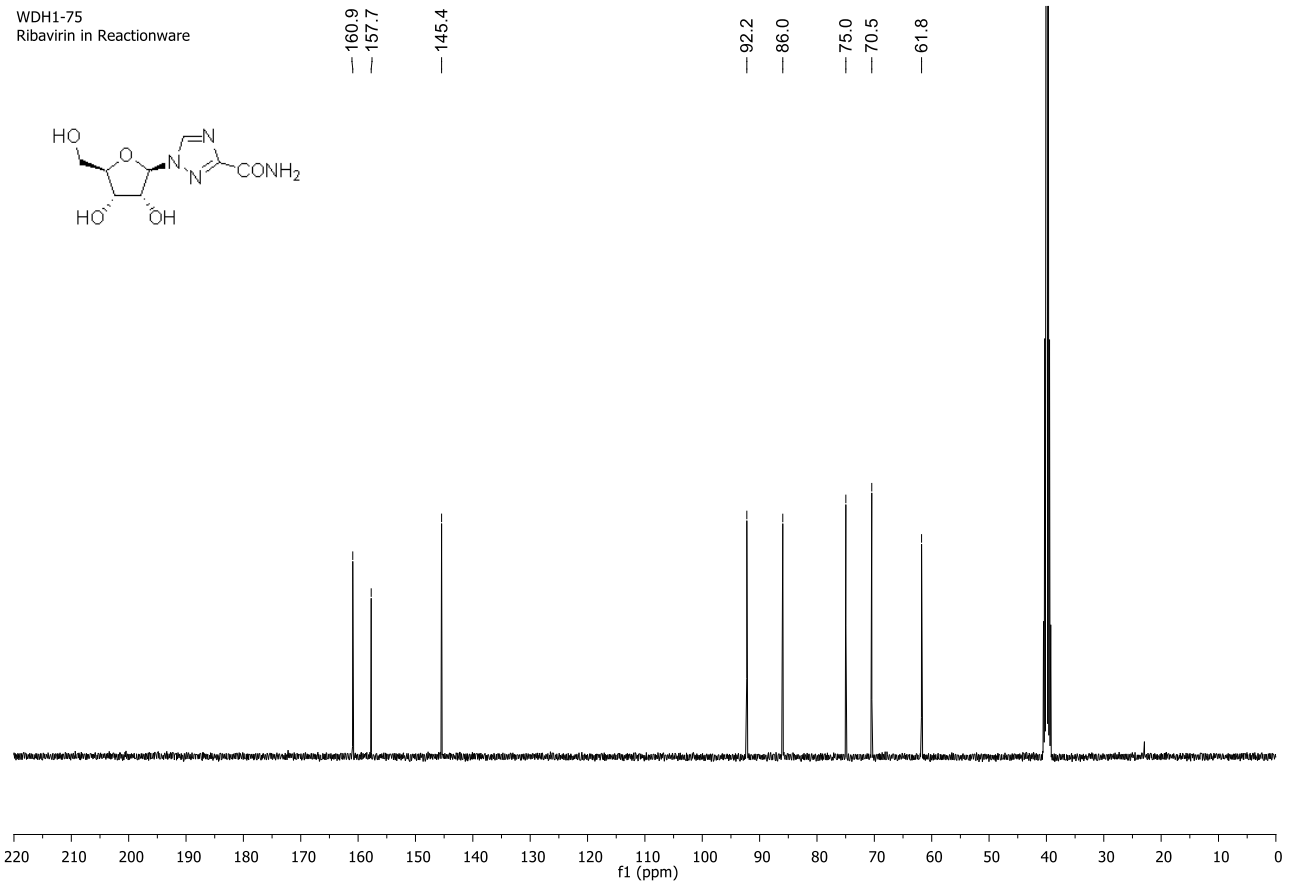
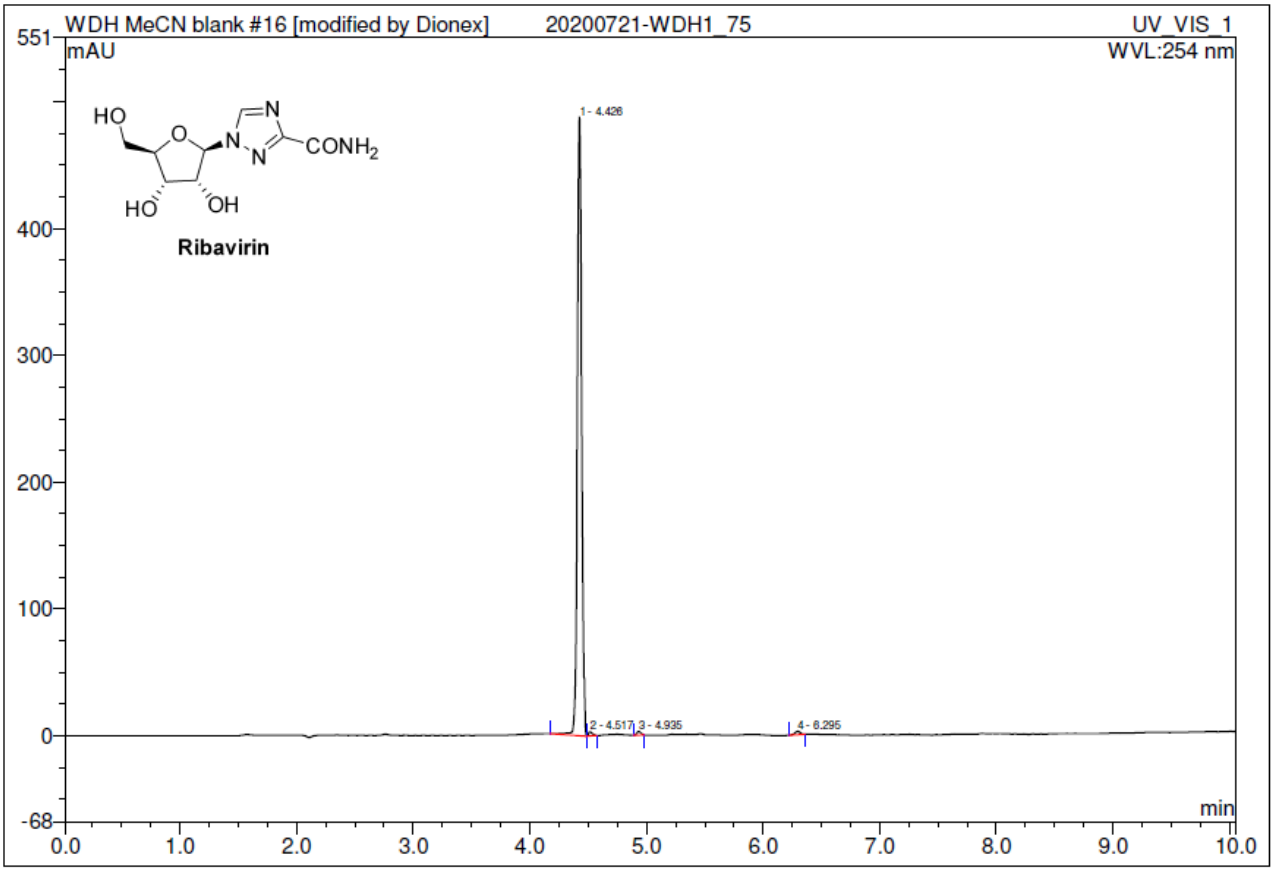


Figure S21: ^{13}C NMR of Ribavirin in Reactionware.

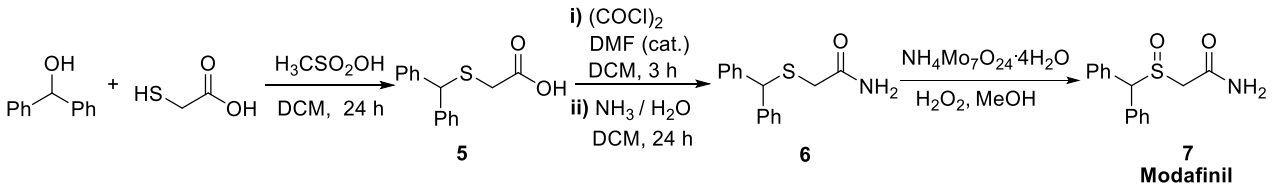
3.4.4 HPLC Spectra of Ribavirin in Reactionware



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	4.43	n.a.	487.805	21.088	98.18	n.a.	BMB*
2	4.52	n.a.	3.216	0.129	0.60	n.a.	BMB*
3	4.94	n.a.	2.884	0.118	0.55	n.a.	BMB*
4	6.30	n.a.	2.646	0.144	0.67	n.a.	BMB*
Total:			496.550	21.479	100.00	0.000	

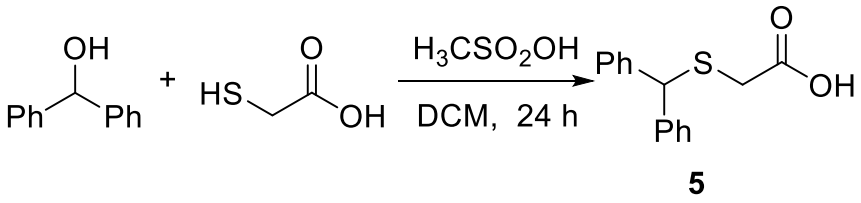
Figure S22: **Integrated HPLC trace for sample obtained from the Reactionware on Ribavirin. Peak 1 (retention time 4.43 minutes) represents Ribavirin and has a peak area equivalent to 98.18% of the total area of the trace**.

3.5 Modafinil Synthesis in Glassware



3.5.1 Compound 5: (benzhydrylthio)acetic acid

The synthetic procedure for the glassware synthesis of (benzhydrylthio)acetic acid was adapted from a literature procedure. [6]



Benzhydrol (1.82 g, 10.0 mmol) and DCM (40 mL) was added to a 100 mL round bottom flask under stirring. Thioglycolic acid (0.76 mL, 10.8 mmol) and methane sulfonic acid (24 µL, 0.36 mmol) was added to the reaction mixture. The round bottom flask was heated up in a silicon oil bath to reflux and the reaction was left to stir for 24 h. At the 24 h mark, the reaction mixture was let to cool to room temperature slowly. The solvent was evaporated using a rotary evaporator affording a white powder. The white powder was collected and suspended in 50 mL of H_2O. The pH of the suspension was raised to ~13.5 using 6M $NaOH_{(aq.)}$ (8 mL) and after some stirring turned into a clear solution. 4M HCl (9 mL) was used to lower the pH to ~1.5. A white powder precipitated out and was vacuum-dried overnight to afford 2.4 g of product. (Yield 95%, purity of 95% by LCMS).

^{1}H NMR (400 MHz, CDCl3) δ 7.49-7.47 (d, 2H), 7.38-7.34 (t, 4H), 7.30 – 7.26 (t, 2H), 5.46 (s, 1H), 3.14 (s, 2H).

^{13}C NMR (400 MHz, CDCl3) δ 174.9, 140.0, 128.7, 128.5, 127.6, 54.12, 33.3

HRMS (ESI) calculated for $C_{15}H_{13}O_2S$ $[M]^-$ 257.0636, found 257.0687, Δ = 19.839448 ppm.

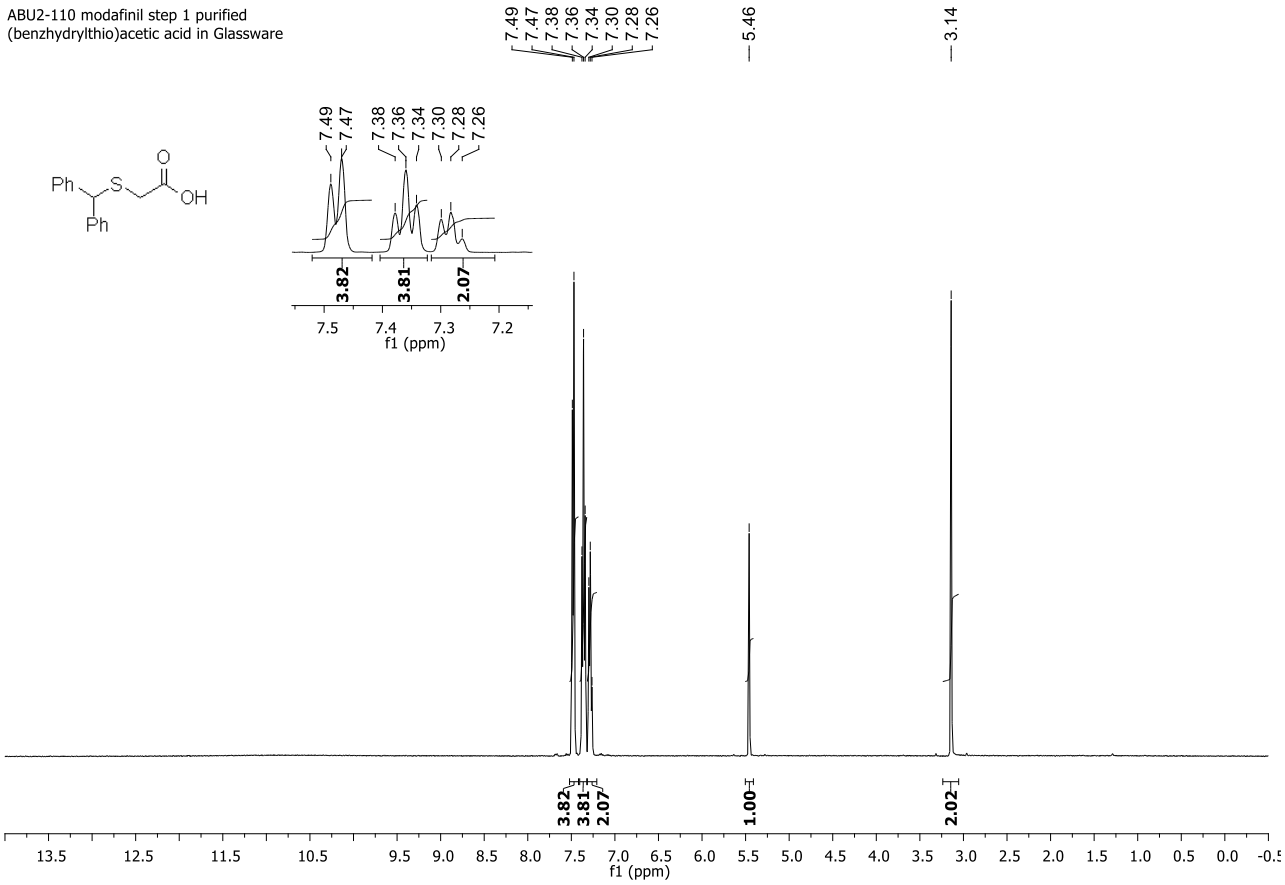


Figure S23: ^{1}H NMR of (benzhydrylthio)acetic acid in Glassware.

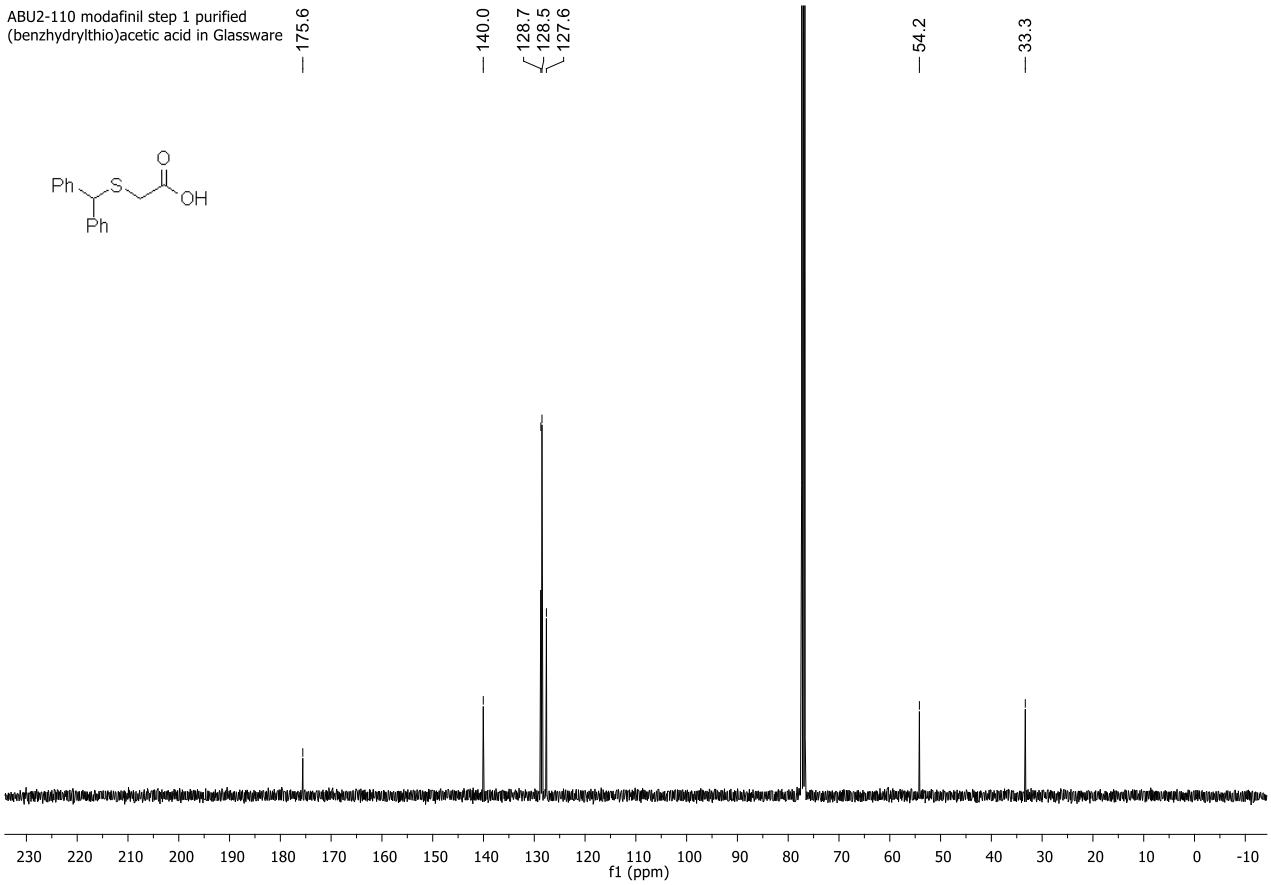
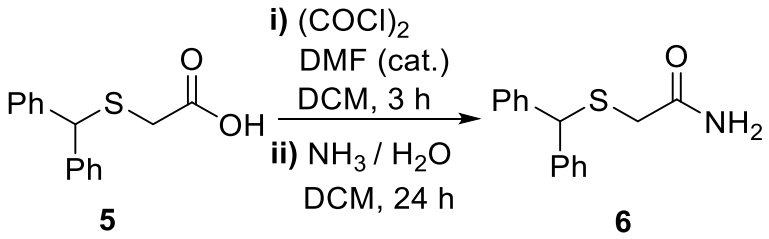


Figure S24: ^{13}C NMR of (benzhydrylthio)acetic acid in Glassware.

3.5.2 Compound 6: 2-(diphenylmethylthio)acetamide



(Benzhydrylthio)acetic acid (1.468 g, 5.7 mmol) was added to 58 mL of DCM under stirring in a round bottom flask suspended in an ice bath. A catalytic amount of DMF was introduced (1 drop). Oxalyl chloride was taken out of the refrigerator and allowed to warm up to room temperature. After reaching RT, oxalyl chloride (0.975 mL, 11.4 mmol) was added to the reaction flask and the mixture

was stirred for 30 minutes. After 30 min, the mixture was taken out of the ice bath and further stirred for another 2.5 h. The flask was immersed in an ice bath and allowed to cool. Once cooled, cold 25% NH_3/H_2O (6.59 mL, 87.1 mmol) was added dropwise (HCl fumes develop during addition). The flask was taken out of the ice bath and stirred for 24 hours. The reaction mixture was filtered, and the filtrate concentrated. Target acetamide was afforded as a pale yellow solid (1.056 g, 4.1 mmol, **72%**) which was dried overnight under vacuum.

^{1}H NMR (400 MHz, CDCl3) δ 7.43-7.23 (m, 10H), 6.51 (s, 1H), 5.85 (s, 1H), 5.19 (s, 1H), 3.08 (s, 2H).

HRMS (ESI) calculated for $C_{15}H_{13}O_2S$ $[M + H]^+$ 258.0953, found 258.0775, Δ = -68.966773 ppm.

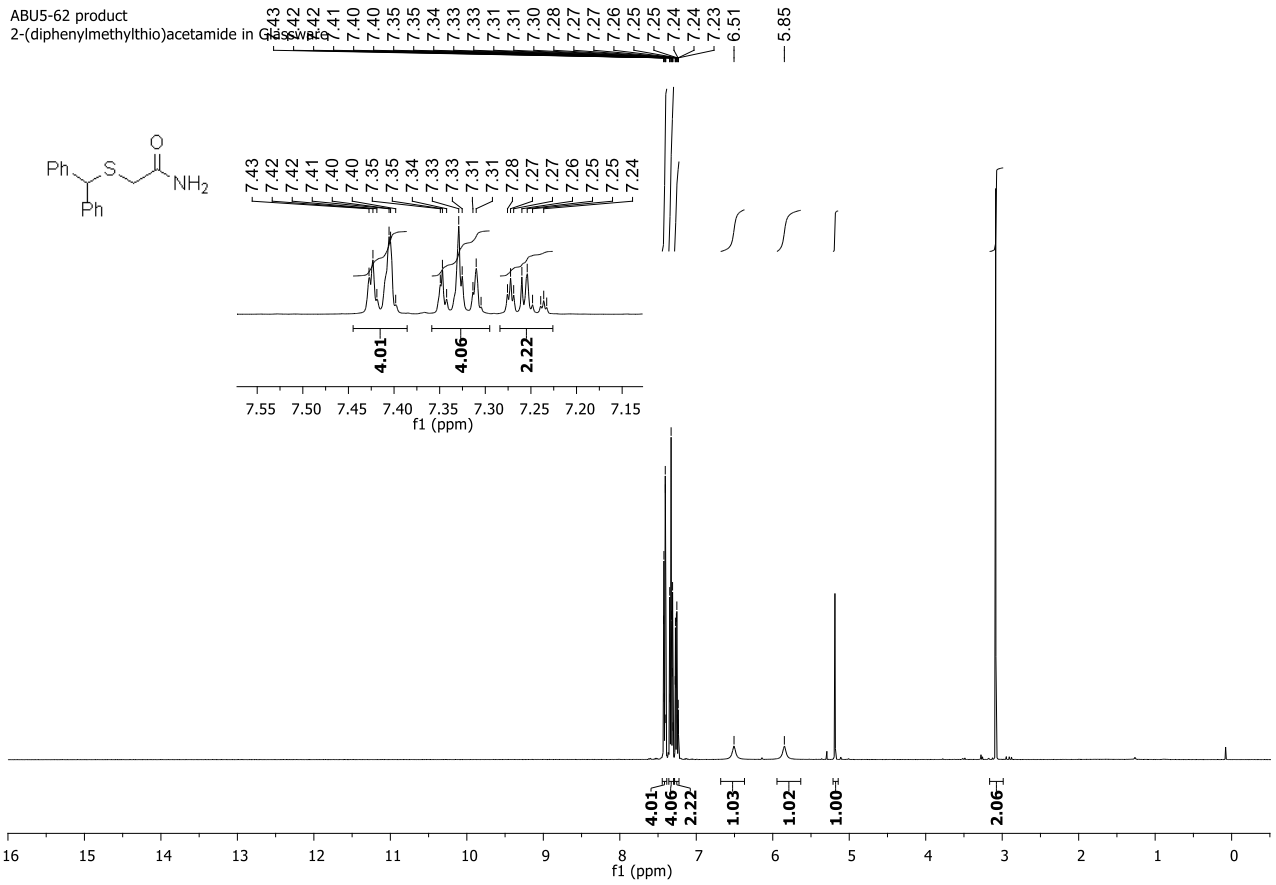
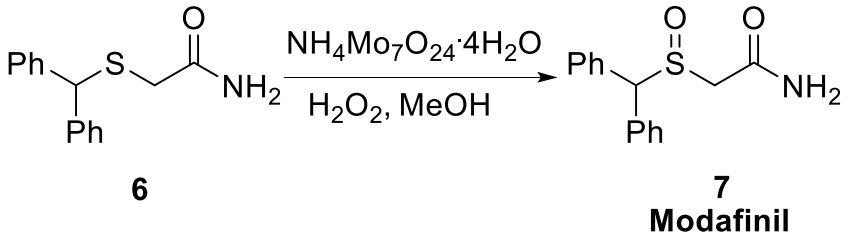


Figure S25: ^{1}H NMR of 2-(diphenylmethylthio)acetamide in Glassware.

3.5.3 Compound 7 (Modafinil): diphenylmethylsulfinylacetamide



6 **7**
Modafinil

Overnight drying under vacuum of 2-(diphenylmethylthio)acetamide is important for the formation of Modafinil. Solutions of aqueous ammonium molybdate and sodium thiosulfate were prepared prior to synthesis:

$NH_4Mo_7O_{24}{\cdot}4H_2O_{(aq.)}$: 1 g of was dissolved in 5 mL of deionised H_2O.

$Na_2S_2O_{3\,(aq.)}$: 2 g of was dissolved in 5 mL of deionised H_2O.

2-(diphenylmethylthio)acetamide (1.00 g, 3.89 mmol, 1 eq.) was dissolved using MeOH (30 mL) in a 25 mL round bottom flask. Na_2CO_3 (25 mg, 232 µmol) was added. Aqueous ammonium molybdate tetrahydrate solution (55 µL, 9.9 µmol) was added to the flask *via* a micropipette. The flask was suspended in an ice bath and allowed to equilibrate. 50% H_2O_2 (aq.) (0.44 mL, 7.74 mmol, 2 eq.) was added to the reaction mixture dropwise under stirring. After addition, the round bottom flask was taken out of the ice bath and allowed to warm up to RT, and then was suspended in a 50 °C silicone oil bath and left to stir for 24 h. Reaction was monitored by TLC until full starting material conversion of 2-(diphenylmethylthio)acetamide. The flask was taken out of the oil bath and left to cool to RT. Once cooled, $Na_2S_2O_{3\,(aq.)}$ (39 µL, 97.84 µmol) was added to the reaction flask using a micropipette. Reaction mixture was transferred to a 100 mL beaker and deionised water (50 mL) was added. The mixture was left to stir for 2 h. Precipitate formed which was then filtered and isolated. Modafinil was afforded as a white powder (636 mg, 2.33 mmol, **60%**). 97% purity assessed by LCMS at 220 nm. Modafinil spot R_f (1:4 MeOH:$CHCl_3$): 0.73. 2-(diphenylmethylthio)acetamide R_f: 0.78

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.65 (s, 1H), 7.52-7.49 (dt, 4H), 7.43-7.32 (m, 6H), 7.29 (s, 1H), 5.33 (s, 1H), 3.38-3.35 (s, 1H), 3.23-3.20 (s, 1H).

^{13}C NMR (400 MHz, $CDCl_3$) δ 166.3, 137.2, 129.7, 129.0, 128.5 (d), 127.9 (d), 68.8, 56.1.

HRMS (ESI) calculated for $C_{15}H_{15}O_2SNH_3$ $[M]^+$ 274.0918, found 274.08939, Δ = 2.88 ppm.

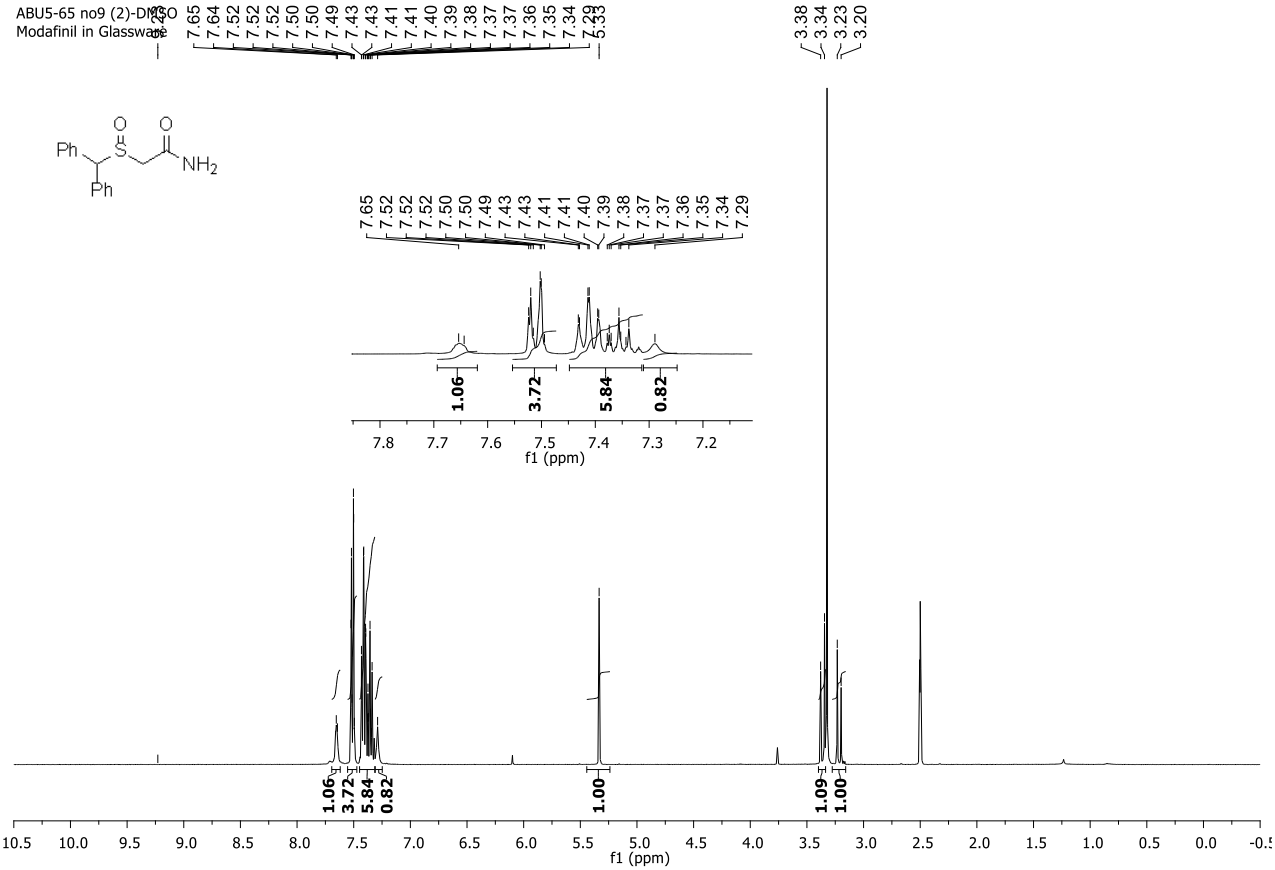


Figure S26: ^{1}H NMR of Modafinil in Glassware.

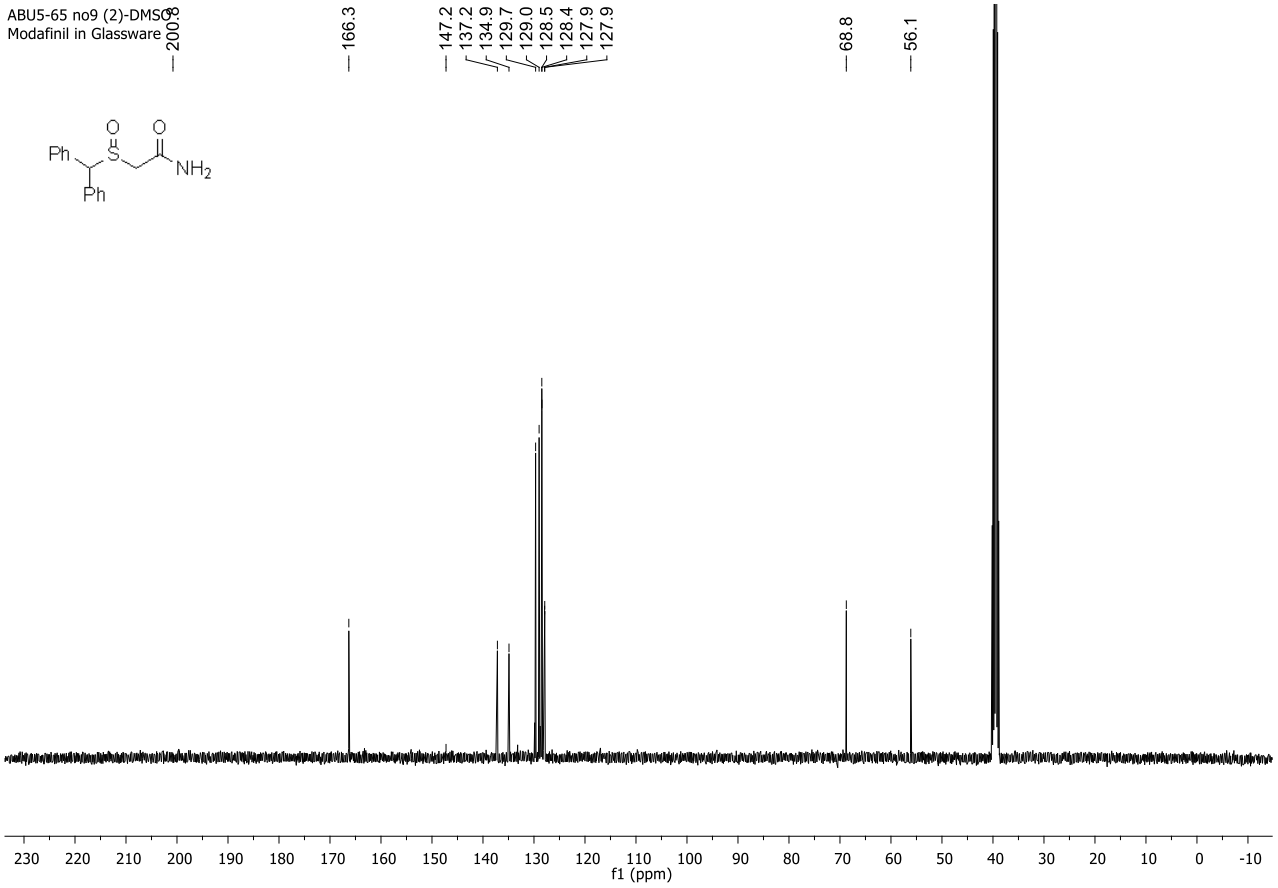
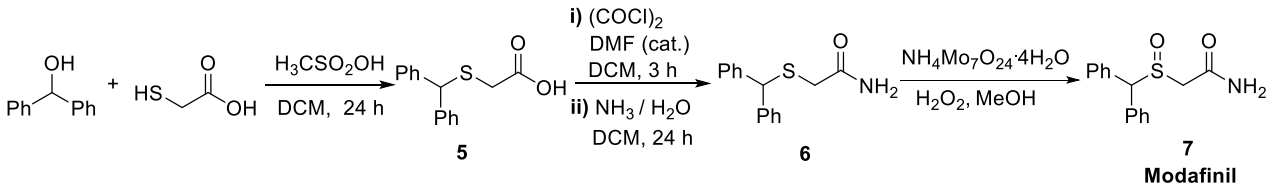


Figure S27: ^{13}C NMR of Modafinil in Glassware.

3.6 Modafinil Synthesis in Reactionware



For following reference modules will be referred to as **M**#, i.e. module 1 is **M1**.

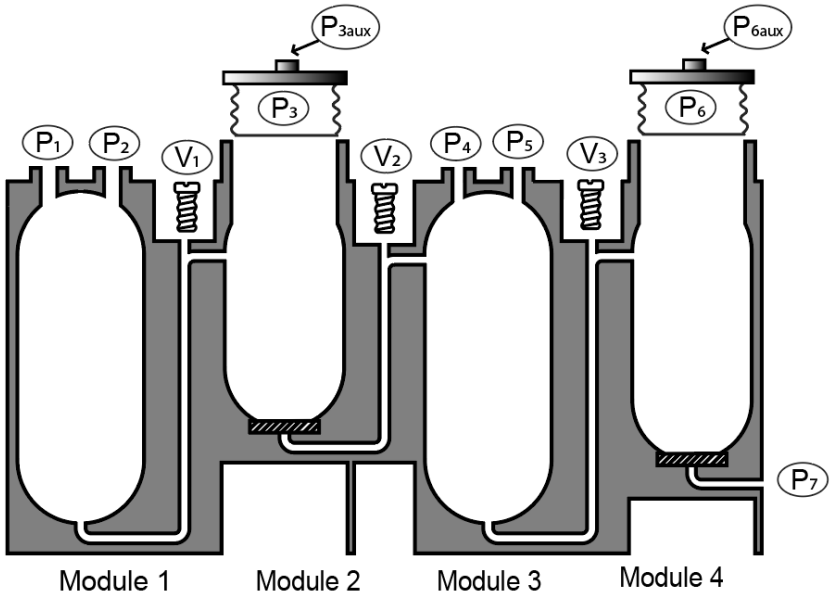


Figure S28: 2D representation of the reactionware monolith used in the synthesis of Modafinil.

3.6.1 Experimental

3.6.1.1 Compound 5: (benzhydrylthio)acetic acid

Reactor modules **M1** and **M3** were each equipped with PTFE coated magnetic stir bars (25x8 mm) during the 3D printing process.

Syringe R_1 preparation: Diphenylmethanol (0.92 g, 5 mmol), cold thioglycolic acid (0.38 mL, 5.4 mmol) and methane sulfonic acid (12 µL, 0.18 mmol) was dissolved in DCM (20 mL).

Syringe R_1 containing starting materials was prepared and added to **M1**. **M1** was equipped with a 3D printed polypropylene high surface condenser. The monolith was lowered into a preheated silicone oil bath (50 °C). Reaction mixture was left to stir for 24 hours at 400 RPM. The monolith was taken out of the oil bath and let to cool to RT. Once at RT, the condenser was unmounted, and a vacuum was applied to **M1** under stirring to remove DCM (400 mbar for 3 hours, afterwards 200 mbar for 30 minutes). H_2O (25 mL) was added to **M1**. 6M $NaOH_{(aq.)}$ (4 mL) was added to **M1**. The mixture was stirred until full dissolution. **M1 was** equipped with a $N_{2(g.)}$ line to apply pressure for solution transfer.

$N_{2(g.)}$ was line was turned on reaction liquid transferred from **M1** to **M2**. **M2** was equipped with a PTFE stir bar (25x8 mm). 4M $HCl_{(aq.)}$ (4.5 mL) was added to **M2** at which point a white precipitate started forming. Vacuum applied to port V_2 and the mixture filtered. White precipitate formed in **M2** was isolated. Reaction mixture was dried under vacuum overnight.

3.6.1.2 **Compound 6: 2-(diphenylmethylthio)acetamide**

90% yield assumed from first step, mass of **compound 5** ≈ 1.2 g, 4.6 mmol.

Oxalyl chloride was taken out of the refrigerator to warm up to RT for 30 minutes. Anhydrous DCM (46 mL), 1 drop of DMF was added to **M2**. The mixture stirred until the white powder dissolved. Reactionware monolith was lowered into an ice-bath. Once the temperature reached equilibrium, oxalyl chloride (0.797 mL, 9.3 mmol) was added to **M2** dropwise while stirring. The reaction was left to stir for 30 minutes, then the reactionware monolith was raised from the ice bath and left to stir for another 2.5 h. Reactionware was submerged in an ice bath once more. Once the temperature reached equilibrium 25% NH_3/H_2O (5.5 mL, 72.6 mmol) was added to **M2** dropwise and the monolith was taken out of the ice bath and left to stir for 24 h. The reaction mixture was filtered by transferring the filtrate from **M2** to **M3**. **M3** was attached to a vacuum line (250 mbar for 2 hours) until all of the DCM was evaporated. To ensure full removal of DCM, MeOH (30 mL) was added to **M3** and the mixture stirred until dissolved. Reactionware monolith was lowered into a preheated 30 °C water bath, **M3** was attached to a vacuum line and MeOH was evaporated under stirring (200 mbar) until full evaporation. Reactionware monolith was taken out of the water bath. MeOH (30 mL) was added to **M3** and the mixture stirred until full dissolution. **M3** was equipped with a vacuum line and MeOH was evaporated (150 mbar, overnight). Product acetamide formed as a pale yellow solid.

3.6.1.3 **Compound 7 (Modafinil): diphenylmethylsulfinylacetamide**

90% yield assumed from first step, mass of **compound 6** ≈ 1.07 g, 4.2 mmol. See molybdate and thiosulfate solution preparation in section 2.3.

Syringe R_2 preparation: aqueous ammonium molybdate tetrahydrate solution (48 µL, 8.7 µmol), Na_2CO_3 (22 mg, 203 µmol) in MeOH (30 mL).

Syringe R_2 containing starting materials was prepared and added to **M3** to dissolve 2-(diphenylmethylthio) acetamide (1.07 g, 4.2 mmol, 1 eq.). The reactionware monolith was suspended in an ice bath and left for the temperature inside the reactor to equilibrate. Once a constant temperature was reached, 50% H_2O_2 (aq.) (0.24 mL, 4.1 mmol, 1 eq.) was added in portions to **M3** under stirring. Following the addition, the reactionware monolith was taken out of the ice bath and put in a preheated to 70 °C oil bath. The reaction was allowed to stir for 6 hours. During these six hours the reaction mixture changed in colour by developing a slightly darker yellow hue. After the 6-hour mark, compound **2** (R_f = 0.78) was still visible on TLC (1:4 MeOH: $CHCl_3$) along with product compound **3** (R_f = 0.73). Thus, another equivalent of 50% H_2O_2 (aq.) (0.24 mL, 4.1 mmol, 1 eq.) was added to **M3**. Reaction was allowed to stir for another 2 hours at which point TLC indicated that no starting material left. Material was transferred from **M3** to **M4**. H_2O (54 mL) was added to **M4** and the reaction mixture was left to stir for 1 hour during which period a white precipitate started to form. The mixture was filtered and compound **3** was afforded as a pale-yellow powder (0.82 g, 3.0 mmol, **60%** based on diphenylmethanol starting material) which was dried under vacuum overnight. 94.7% purity assessed by LCMS at 220 nm and 96.0 % purity by HPLC at 220 nm. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.65 (s, 1H), 7.52-7.49 (m, 4H), 7.44-7.32 (m, 6H), 7.29 (s, 1H), 5.33 (s, 1H), 3.38-3.34 (d, 1H), 3.23-3.20 (d, 1H). **^{13}C NMR** (400 MHz, $CDCl_3$) δ 166.30, 137.17, 134.90, 129.68, 128.99, 128.46, 128.44, 127.91, 127.88, 68.75, 56.11 **HRMS** (ESI) calculated for $C_{15}H_{15}O_2SNH_3$ $[M]^+$ 274.0918, found 274.08948, Δ = 2.55 ppm.

3.6.2 Operations Table

Compound **5**							
Time d/hh:mm	Action	P_1	P_2	V_1	P_3	$P_{3\ aux}$	V_2
0/00:00	Add R_1 to port P_1	O	O	C	C	C	C
0/00:01	Equip P_1 with a PP condenser	C	O	C	C	C	C
0/00:02	Close P_2	C	C	C	C	C	C
0/00:03	Lower reactionware monolith into oil bath	C	C	C	C	C	C
0/00:03	Stir at 400 RPM	C	C	C	C	C	C
0/00:05-1/00:05	Raise reactionware monolith from oil bath	C	C	C	C	C	C
1/00:35	Let monolith warm up to RT	C	C	C	C	C	C
1/00:36	Unmount PP condenser	O	C	C	C	C	C
1/00:36	Attach vacuum line to P_1	Vacuum	C	C	C	C	C
1/00:37	Vacuum at 400 mbar	Vacuum	C	C	C	C	C
1/03:37	Vacuum at 200 mbar	Vacuum	C	C	C	C	C
1/04:07	Detach vacuum line	O	C	C	C	C	C
1/04:08	Open P_2	O	O	C	C	C	C
1/04:08	Add water to P_1	O	O	C	C	C	C
1/04:08	Stir at 400 RPM	O	O	C	C	C	C
Continue to follow instructions on the following page							

Compound **5** continued							
Time d/hh:mm	Action	P_1	P_2	V_1	P_3	$P_{3\ aux}$	V_2
1/04:18	Add 6M NaOH to P_1	O	O	C	C	C	C
1/04:18	Stir until dissolution	O	O	C	C	C	C
1/04:23	Close P_2, open V_1 and P_3	O	C	O	O	C	C
1/04:24	Apply $N_{2(g.)}$ to P_1	O	C	O	O	C	C

1/04:24	Close P_1 and V_1	C	C	C	O	C	C
1/04:25	Equip **M2** with stir bar	C	C	C	O	C	C
1/04:25	Add 4M HCl to P_3	C	C	C	O	C	C
1/04:25	Stir at 400 RPM	C	C	C	O	C	C
1/04:35	Open V_2	C	C	C	O	C	O
1/04:35	Pull solvent from V_2	C	C	C	O	C	Vacuum
1/04:40	Close P_3 and V_2, open $P_{3\ aux}$	C	C	C	C	O	C
1/16:40	Pull vacuum overnight from $P_{3\ aux}$	C	C	C	C	Vacuum	C
End							

Compound **6**						
Time d/hh:mm	Action	P_3	$P_{3\ aux}$	V_2	P_4	P_5
0/00:00	Open P_3	O	C	C	C	C
0/00:01	Add DCM to P_3	O	C	C	C	C
0/00:01	Add DMF to P_3	O	C	C	C	C
0/00:01-0/00:06	Stir at 400 RPM	O	C	C	C	C
0/00:07	Lower monolith into ice bath	O	C	C	C	C
0/00:37	Stir at 400 RPM	O	C	C	C	C
0/00:38	Add $(COCl)_2$ dropwise	O	C	C	C	C
0/00:38-0/01:38	Stir at 400 RPM	O	C	C	C	C
0/01:38	Take monolith out of ice bath	O	C	C	C	C
0/04:08	Stir at 400 RPM	O	C	C	C	C
0/04:09	Lower monolith into ice bath	O	C	C	C	C
0/04:09-0/04:39	Stir at 400 RPM	O	C	C	C	C
0/04:39	Add NH_3/H_2O to P_3	O	C	C	C	C
0/04:40	Take monolith out of ice bath	O	C	C	C	C
0/04:40	Close P_3	C	C	C	C	C

0/04:40-1/04:40	Stir at 400 RPM	C	C	C	C	C
1/04:41	Open $P_{3\ aux}$, V_2, P_4	C	O	O	O	C
1/04:42	Apply $N_{2(g.)}$ to $P_{3\ aux}$	C	N_2 gas	O	O	C
1/04:47	Close $P_{3\ aux}$, V_2	C	C	C	O	C
1/04:47-1/06:47	Attach vacuum line (250 mbar) to P_4	C	C	C	Vacuum	C
Continue to follow instructions on the following page						

Compound **6** continued						
Time d/hh:mm	Action	P_3	$P_{3\ aux}$	V_2	P_4	P_5
1/06:47	Open P_5	C	C	C	O	O
1/06:48	Add MeOH to P_4	C	C	C	O	O
1/06:48-1/06:53	Stir at 400 RPM	C	C	C	O	O
1/06:54	Put reactionware monolith in a 30 °C H_2O bath	C	C	C	O	O
1/06:55	Close P_5	C	C	C	O	C
1/06:55	Attach vacuum line (250 mbar) to P_4	C	C	C	Vacuum	C
1/06:55-1/11:55	Stir at 400 RPM	C	C	C	Vacuum	C
1/11:55	Take reactionware monolith out of bath	C	C	C	O	C
1/11:55	Open P_5	C	C	C	O	O
1/11:56	Add MeOH to P_4	C	C	C	O	C
1/11:56-1/12:01	Stir at 400 RPM	C	C	C	O	C
1/12:01	Close P_5	C	C	C	O	C
1/12:02	Attach vacuum line (150 mbar) to P_4	C	C	C	Vacuum	C
1/12:02-2/04:02	Stir at 400 RPM	C	C	C	Vacuum	C
End						

Compound **7** - Modafinil							
Time d/hh:mm	Action	P_4	P_5	V_3	P_6	$P_{6\ aux}$	P_7
0/00:00	Detach vacuum from P_4	O	C	C	C	C	C
0/00:01	Open P_5	O	O	C	C	C	C
0/00:01	Add R_2 to P_4	O	O	C	C	C	C
0/00:01-0/00:06	Start to stir at 400 RPM	O	O	C	C	C	C
0/00:07	Lower reactionware monolith into ice-bath	O	O	C	C	C	C
0/00:07-0/00:27	Stir at 400 RPM	O	O	C	C	C	C
0/00:28	Add 50% H_2O_2 to P_4	O	O	C	C	C	C
0/00:28-0/00:29	Stir at 400 RPM	O	O	C	C	C	C
0/00:29	Raise monolith out of ice-bath	O	O	C	C	C	C
0/00:31	Lower monolith into oil bath	O	O	C	C	C	C
0/00:31	Attach PP reflux condenser to P_4	Condenser	O	C	C	C	C
0/00:32	Close P_5	Condenser	C	C	C	C	C
0/00:32-0/06:32	Stir at 400 RPM	Condenser	C	C	C	C	C
0/06:32	Add 50% H_2O_2 to P_4	Condenser	C	C	C	C	C
0/06:32-0/08:32	Stir at 400 RPM	Condenser	C	C	C	C	C
0/08:33	Raise monolith from oil bath	Condenser	C	C	C	C	C
0/08:33-0/09:03	Allow monolith to cool to RT	Condenser	C	C	C	C	C
Continue to follow instructions on the following page							

Compound **7** - Modafinil continued							
Time d/hh:mm	Action	P_4	P_5	V_3	P_6	$P_{6\ aux}$	P_7
0/09:03	Take off condenser	O	C	C	C	C	C

0/09:04	Open V_3 and P_6	O	C	O	O	C	C
0/09:05-0/09:10	Apply $N_{2\,(g.)}$ to P_4	N_2 gas	C	O	O	C	C
0/09:10	Close P_4 and V_3	C	C	C	O	C	C
0/09:11	Add stir bar to P_6	C	C	C	O	C	C
0/09:11	Add H_2O to P_6	C	C	C	O	C	C
0/09:11-0/10:11	Stir at 400 RPM	C	C	C	O	C	C
0/10:12	Close P_6, open $P_{6\,aux}$ and P_7	C	C	C	C	O	O
0/10:12-0/10:17	Apply $N_{2\,(g.)}$ to $P_{6\,aux}$	C	C	C	C	N_2 gas	O
0/10:18	Detach $N_{2\,(g.)}$	C	C	C	C	O	O
0/10:18	Close P_7	C	C	C	C	O	C
1/02:18	Attach vacuum (150 mbar)	C	C	C	C	O	C
End, unless purification is performed. See operation table on next page.							

Compound **7**- Modafinil purification				
Time d/hh:mm	Action	P_6	$P_{6\,aux}$	P_7
0/00:00	Open P_6	O	C	C
0/00:01	Add DMC to P_6	O	C	C
0/00:01	Add stir bar to P_6	O	C	C
0/00:01	Close P_6	C	C	C
0/00:01	Open $P_{6\,aux}$	C	O	C
0/00:02	Attach PP reflux condenser to $P_{6\,aux}$	C	Condenser	C
0/00:02	Lower monolith to oil bath	C	Condenser	C
0/00:03-0/01:03	Stir at 400 RPM	C	Condenser	C
0/01:03	Raise monolith from oil bath	C	Condenser	C
0/01:03-0/02:03	Allow to cool to RT	C	Condenser	C
0/02:03	Take condenser off from $P_{6\,aux}$	C	O	C
0/02:03-0/18:03	Leave to crystallise	C	O	C
0/18:04	Open P_7	C	O	C
0/18:04-0/18:09	Apply $N_{2(g.)}$ to P_{6aux}	C	$N_{2(g.)}$	C
0/18:10	Detach $N_{2(g.)}$	C	O	C
0/18:10-1/08:10	Attach vacuum to $P_{6\,aux}$ (150 mbar)	C	Vacuum	C
End				

3.6.3 ^{1}H and ^{13}C NMR spectra for Modafinil

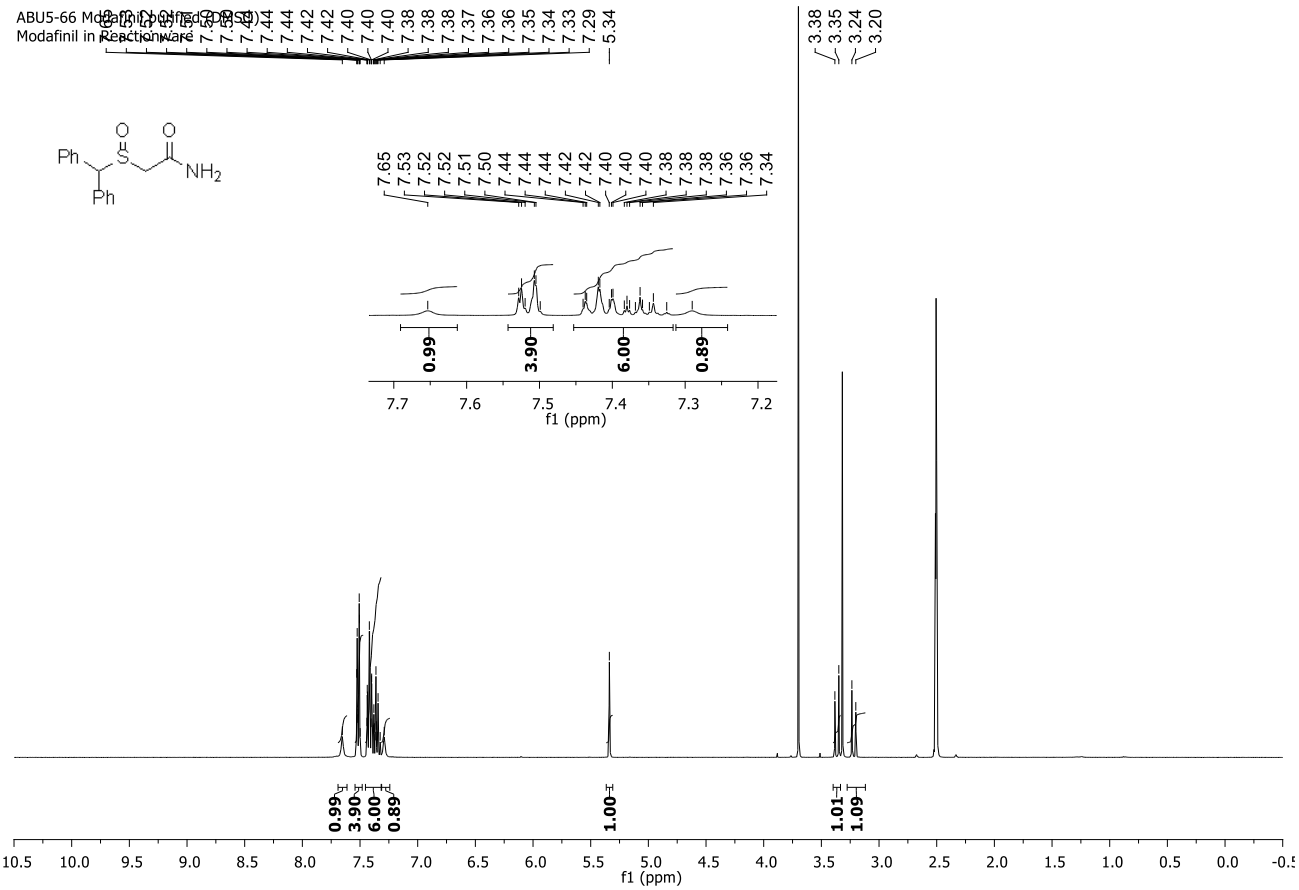


Figure S29: ^{1}H NMR of Modafinil in Reactionware.

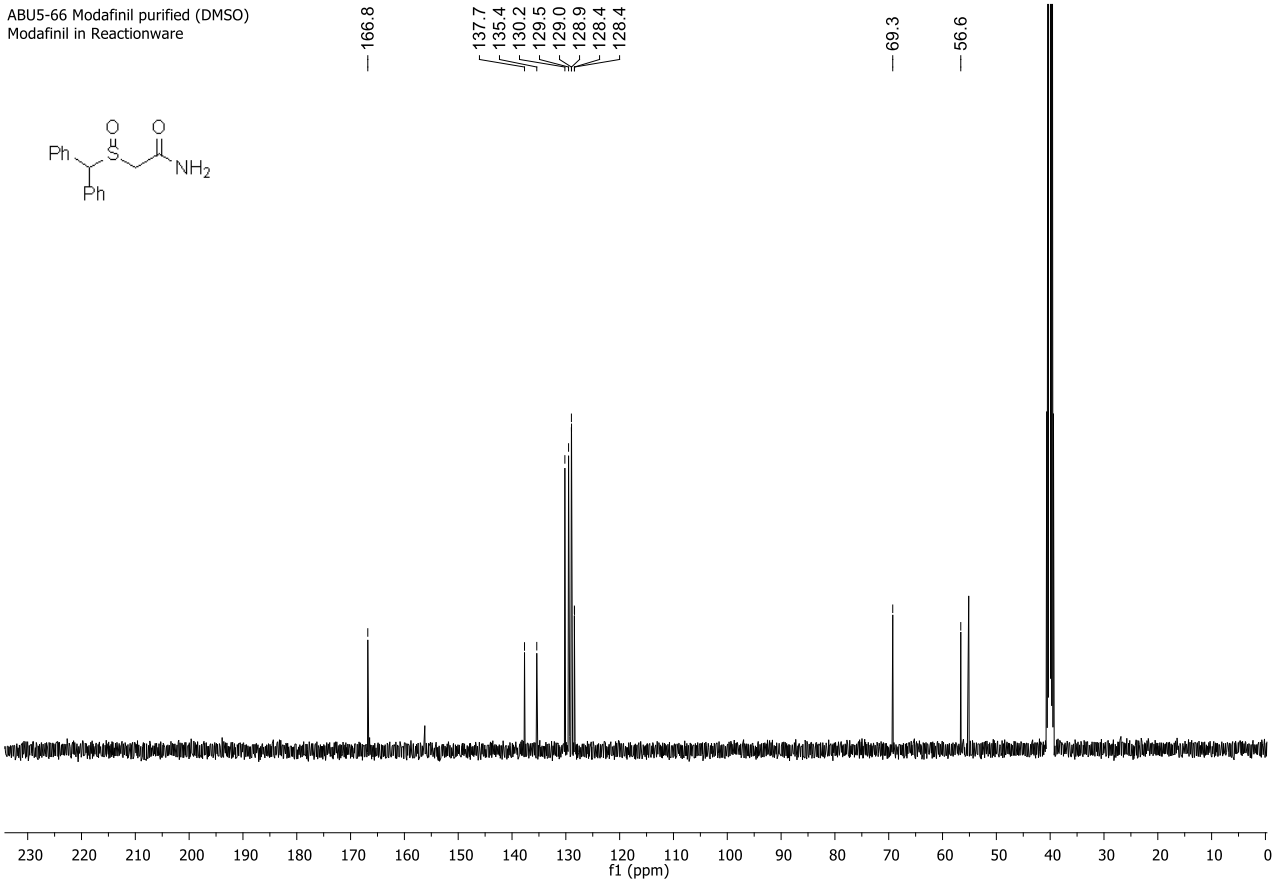
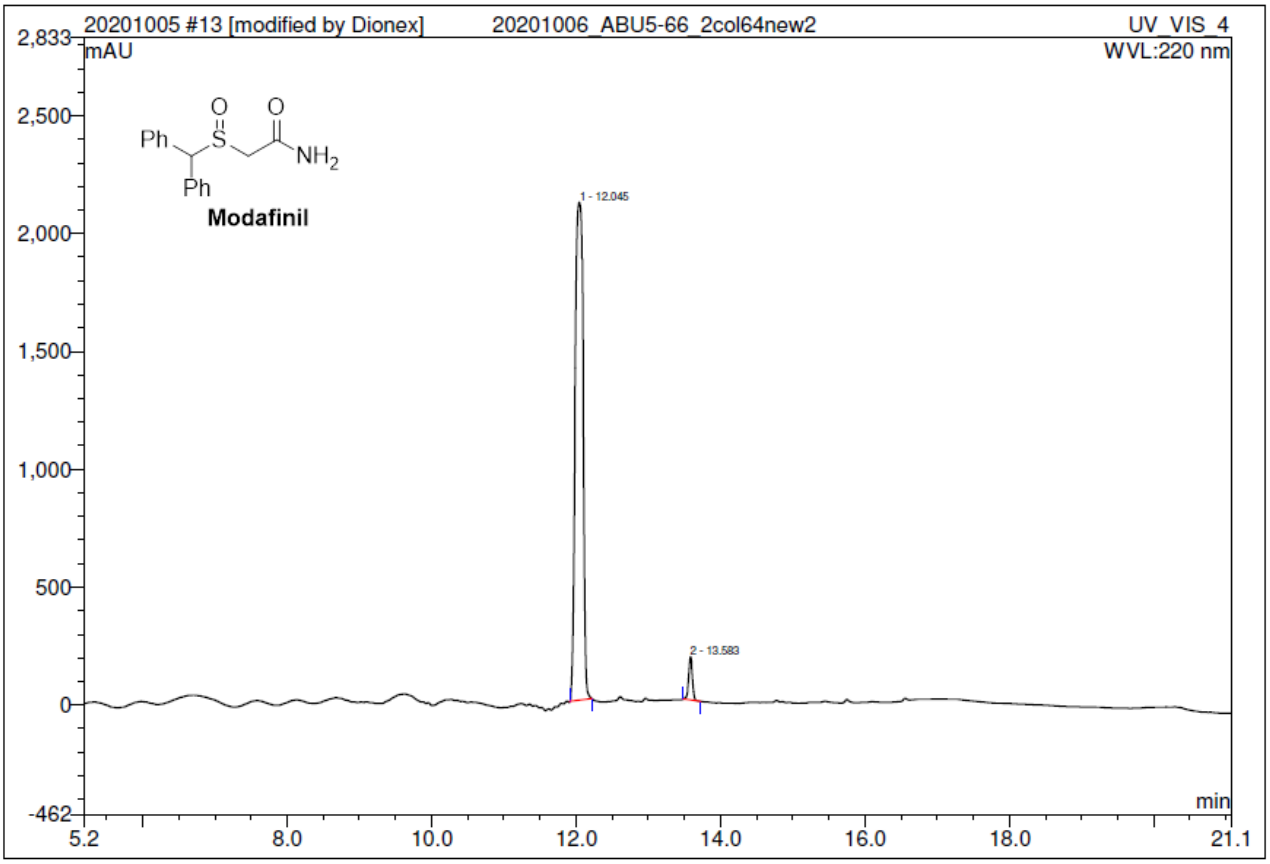


Figure S30: ^{13}C NMR of Modafinil in Reactionware.

3.6.4 HPLC spectra of Modafinil in Reactionware



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	12.05	n.a.	2111.389	262.823	95.95	n.a.	BMB*
2	13.58	n.a.	183.643	11.087	4.05	n.a.	BMB*
Total:			2295.031	273.911	100.00	0.000	

Figure S31. Integrated HPLC trace for sample obtained from the Reactionware on Modafinil. Peak 1 (retention time 12.05 minutes) represents Modafinil and has a peak area equivalent to 96.0 % of the total area of the trace.

3.7 Lomustine Synthesis in Reactionware under Continuous Flow

3.7.1 Flow Chemistry Setup

All polypropylene flow reactors were designed using ChemSCAD and 3D-printed using a Ultimaker 2+ printer on a polypropylene sheet as a bed. The reactor inputs were manually tapped using a ¼-28 UNF straight flute tap and cleaned from residual polypropylene after tapping. The inputs were mounted with female Luer to threaded 1/4-28 UNF Masterflex polypropylene fittings. These were equipped with 1/4-28 female to male Luer Assy polypropylene adapters which in turn were connected to 1/4-28 flat-bottom flangeless short natural PEEK fittings with a 3.2 mm (1/8") outer diameter. The tubing used in the set-up was purchased as 3.2 mm (1/8") outer diameter x 1.5 mm inner diameter PTFE tubing. Syringes **A** and **B** were mounted onto a KDS230 Multi Syringe Infusion Pump, whereas syringe **C** was mounted onto a Harvard PHD 22/2000 syringe pump (see **Figure S32**).

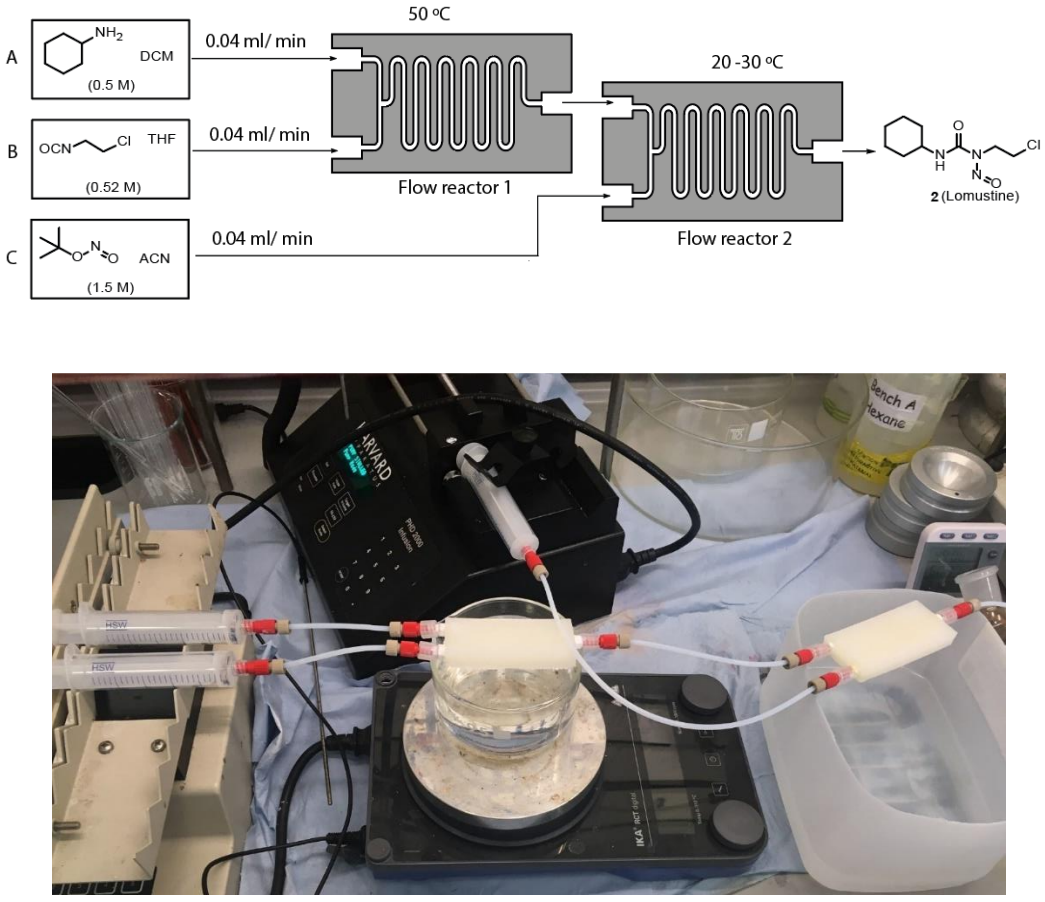


Figure S32: Flow setup scheme (top) and the assembled setup in real life (bottom).

3.7.2 Determination of Reaction Conditions

The reactant equivalents, residence times, temperatures were adapted from a literature procedure [7] and monitoring reaction intermediate and product formation using thin layer chromatography (petroleum ether: ethyl acetate, 2:1) and ^{1}H NMR.

3.7.2.1 Experimental

All solutions were prepared in volumetric flasks and then loaded to 20 mL Norm-Ject plastic syringes. 1-chloro-2-isocyanoethane in THF syringe was covered in aluminium foil to protect the reactant from light.

A stream of cyclohexylamine (0.04 ml/min, 0.5 M, 1 eq., DCM) and a solution of 1-chloro-2-isocyanatoethane (0.04 ml/min, 0.52 M, 1.05 eq., THF) were combined in a 3D-printed 0.56 mL polypropylene flow reactor 1 (see **Figure S32**) reactor at 50 °C. A third solution of tert-butyl nitrite (0.04 ml/min, 1.50 M, 3 eq., ACN) was pumped into 0.56 mL polypropylene flow reactor 2 which was kept ambient temperature and had an output to a collection flask. The flow was continuously ran for 20 minutes before the collection flask was switched for a new one. The product solution was collected for 1 h. 2 mL of deionized water and 5 mL of diethyl ether were added to the collection flask with stirring. The contents were transferred to a separation funnel. The layers were separated and the water phase was washed by 5 mL of diethyl ether. The organic phases were combined and dried. The solution was concentrated under vacuum to give Lomustine (0.274 g, 1.2 mmol, **98%**).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.72 (s, 1H), 4.11 (t, J = 6.8 Hz, 2H), 3.93 – 3.71 (m, 1H), 3.43 (t, J = 6.8 Hz, 2H), 2.12 – 1.90 (m, 2H), 1.77 – 1.64 (m, 2H), 1.62 – 1.46 (m, 1H), 1.42 – 1.06 (m, 5H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 151.8, 50.0, 40.0, 38.9, 33.1, 25.4, 24.7.

3.7.3 ^{1}H and ^{13}C NMR Spectra of Lomustine Synthesized under Flow

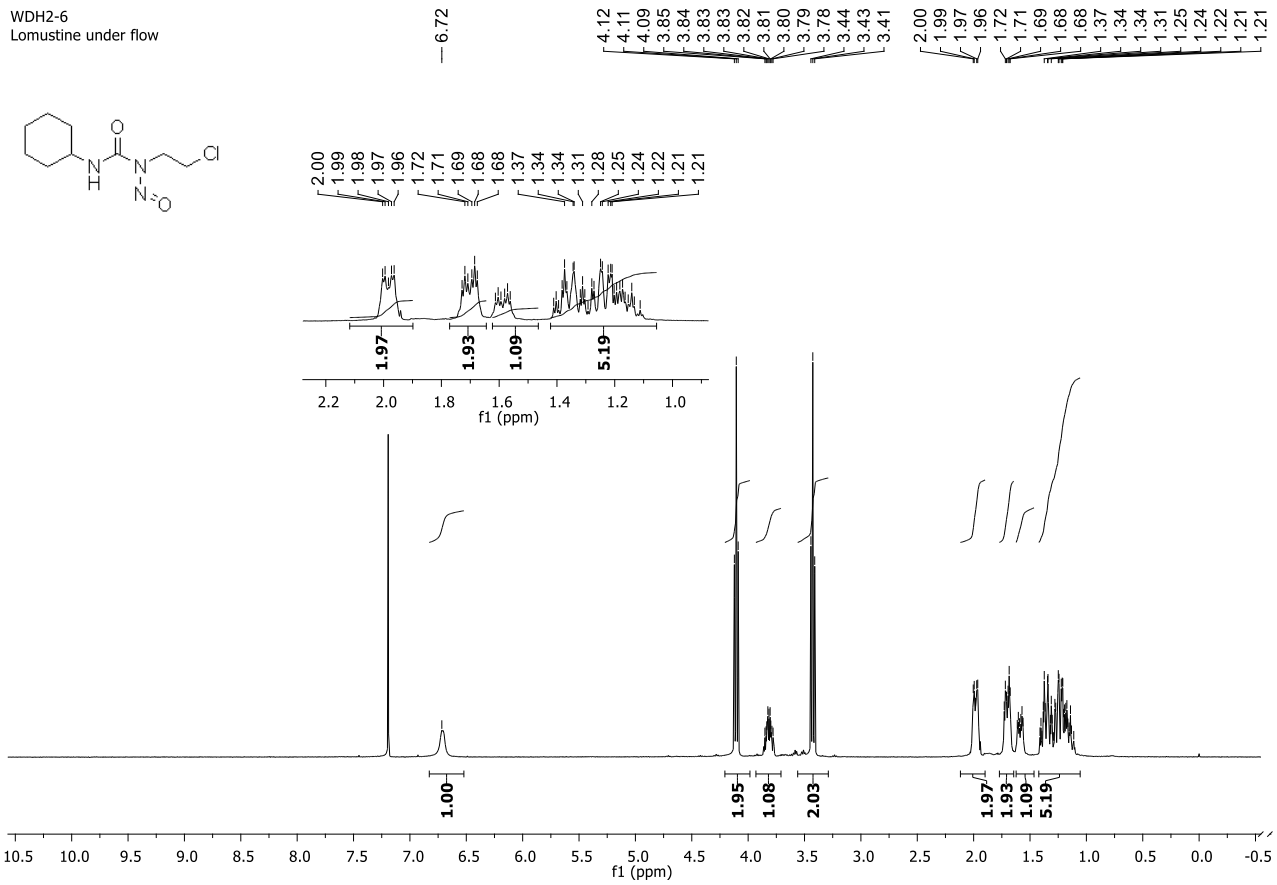


Figure S33: ^{1}H NMR of Lomustine synthesized under flow.

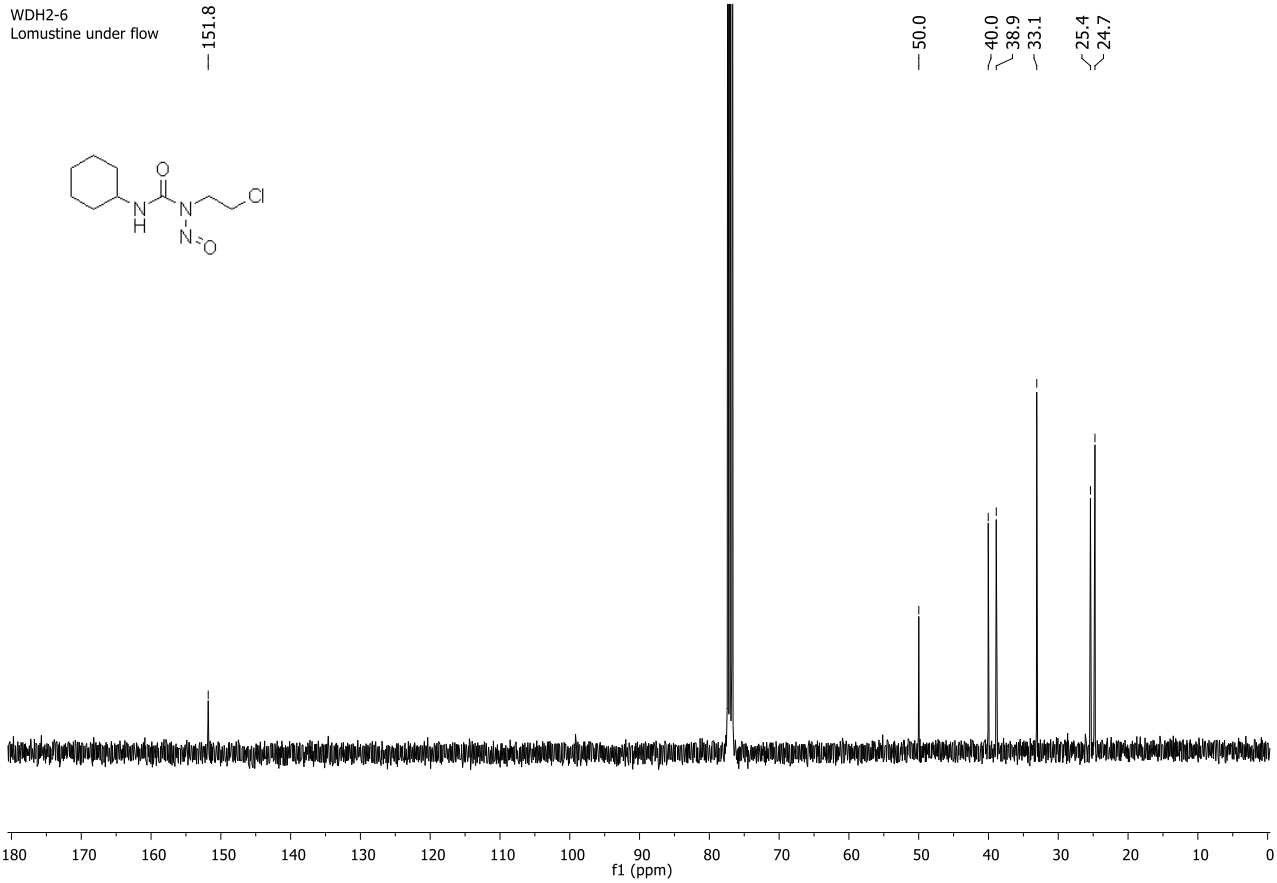


Figure S34: ^{13}C NMR of Lomustine synthesized under flow.

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Table S2: Table of licenses for the pip-installed packages required for ChemSCAD

Name	Version	License	URL
Pillow	7.0.0	Historical Permission Notice and Disclaimer (HPND)	https://python-pillow.org
PyQt5	5.14.0	GPL v3	https://www.riverbankcomputing.com/software/pyqt/
PyQt5-sip	12.7.0	SIP	https://www.riverbankcomputing.com/software/sip/
PyYAML	5.3	MIT License	https://github.com/yaml/pyyaml
aspy.yaml	1.3.0	MIT License	https://github.com/asottile/aspy.yaml
atomicwrites	1.3.0	MIT License	https://github.com/untitaker/python-atomicwrites
attrs	19.3.0	MIT License	https://www.attrs.org/
business-rules	1.0.1	UNKNOWN	UNKNOWN

cached-property	1.5.1	BSD License	https://github.com/pydanny/cached-property
ccad	1	UNKNOWN	https://github.com/SolidCode/SolidPython
cfgv	2.0.1	MIT License	https://github.com/asottile/cfgv
colorama	0.4.3	BSD License	https://github.com/tartley/colorama
cycler	0.10.0	BSD	http://github.com/matplotlib/cycler
decorator	4.4.1	BSD License	https://github.com/micheles/decorator
euclid3	0.1	UNKNOWN	http://partiallydisassembled.net/euclid.html
freetype-py	2.1.0.post1	BSD License	https://github.com/rougier/freetype-py
future	0.18.2	MIT License	https://python-future.org
graphviz	0.13.2	MIT License	https://github.com/xflr6/graphviz
identify	1.4.9	MIT License	https://github.com/chriskuehl/identify
importlib-metadata	1.4.0	Apache Software License	http://importlib-metadata.readthedocs.io/
jedi	0.15.2	MIT License	https://github.com/davidhalter/jedi

kiwisolver	1.1.0	BSD	https://github.com/nucleic/kiwi
licenses	0.6.1	UNKNOWN	UNKNOWN
lxml	4.4.2	BSD License	http://lxml.de/
matplotlib	3.1.2	Python Software Foundation License	https://matplotlib.org
more-itertools	8.1.0	MIT License	https://github.com/erikrose/more-itertools
mypy	0.761	MIT License	http://www.mypy-lang.org/
mypy-extensions	0.4.3	MIT License	https://github.com/python/mypy_extensions
networkx	2.4	BSD License	http://networkx.github.io/
nodeenv	1.3.4	BSD License	https://github.com/ekalinin/nodeenv
numpy	1.18.1	BSD	https://www.numpy.org
packaging	20	Apache Software License, BSD License	https://github.com/pypa/packaging
parso	0.5.2	MIT License	https://github.com/davidhalter/parso
pluggy	0.13.1	MIT License	https://github.com/pytest-dev/pluggy
pre-commit	1.21.0	MIT License	https://github.com/pre-commit/pre-commit

prettytable	0.7.2	BSD License	http://code.google.com/p/prettytable
py	1.8.1	MIT License	http://py.readthedocs.io/
pyglet	1.4.9	BSD License	http://pyglet.readthedocs.org/en/latest/
pyparsing	2.4.6	MIT License	https://github.com/pyparsing/pyparsing/
pypng	0.0.19	MIT License	https://github.com/drj11/pypng
pytest	5.3.2	MIT License	https://docs.pytest.org/en/latest/
python-dateutil	2.8.1	BSD License, Apache Software License	https://dateutil.readthedocs.io
pytz	2019.3	MIT License	http://pythonhosted.org/pytz
regex	2019.12.20	Python Software Foundation License	https://bitbucket.org/mrabarnett/mrab-regex
scipy	1.4.1	BSD License	https://www.scipy.org
sip	5.1.0	SIP	https://www.riverbankcomputing.com/software/sip/
six	1.13.0	MIT License	https://github.com/benjaminp/six
solidpython	0.4.6	GNU Lesser General Public License v2 or later (LGPLv2+)	https://github.com/SolidCode/SolidPython

toml	0.10.0	MIT License	https://github.com/uiri/toml
trimesh	3.5.14	MIT License	https://github.com/mikedh/trimesh
typed-ast	1.4.1	Apache License 2.0	https://github.com/python/typed_ast
typing-extensions	3.7.4.1	Python Software Foundation License	https://github.com/python/typing/blob/master/typing_extensions/README.rst
virtualenv	16.7.9	MIT License	https://virtualenv.pypa.io/
vispy	0.6.1	BSD License	http://vispy.org
wcwidth	0.1.8	MIT License	https://github.com/jquast/wcwidth
zipp	1.0.0	MIT License	https://github.com/jaraco/zipp

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