Continuous organocatalytic flow synthesis of 2-substituted oxazolidinones using carbon dioxide

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SUPPORTING INFORMATION:

82 pages, 6 figures, 4 tables

Contents:

1. General considerations

All commercial reagents were used as received and all reactions were carried out under air unless stated otherwise. ^{1}H-NMR and ^{13}C-NMR spectra were recorded at room temperature or at 398K using Bruker Advance 300 Ultrashield spectrometer operating at 300 and 75 MHz respectively, a Bruker Advance 400 Ultrashield spectrometer operating at 400 and 100 MHz respectively, or Bruker Advance 500 Ultrashield spectrometeroperating at 500 and 125 MHz respectively.

All ^{1}H NMR spectra were reported in parts per million (ppm) downfield of TMS and were measured relative to the signal for $CHCl_3$ (7.26 ppm) and DMSO (2.50 ppm). All ^{13}C NMR spectra were reported in parts per million (ppm) relative to residual $CHCl_3$ (77.16 ppm) and DMSO (39.52 ppm) and were obtained with ^{1}H decoupling. Coupling constants, J, are reported in hertz. The spectra were recorded using samples of 20-40 mg to facilitate sequential ^{1}H +^{13}C NMR analysis.[1] IR spectra were recorded on a Bruker Tensor 27 / Diamond ATR FT-IR spectrometer or a Thermo Scientific iS50 FT-IR spectrometer. Elemental analyses of the PS-Supported catalyst were performed on a LECO CHNS 932 micro-analyzer at the Universidad Complutense de Madrid, Spain and by MEDAC LTD, UK. Flash chromatography was performed using 60 mesh silica gel on a Combiflash RF TeledineISCO. Thin layer chromatography was carried out using Merck TLC Silica gel 60 F254 aluminum sheets. Components were visualized by UV light (λ = 254 nm) and/or by phosphomolybdic acid, p-anisaldehyde, ninhydrin solution or $KMNO_4$ solution.

[1] We used MestReNova v14.2.0-26256, architecture x86_64 released on 2020-09-25. The spectra were copied into a Word file and then printed as a PDF on a iOS based computer.

2. Experimental flow setup

The feed of starting material, the epoxy amine dissolved in a methylethyl ketone (MEK) and dimethyl sulfoxide (DMSO), was provided by a Thales nano micro HPLC pump. The feed was flowed through a Swagelok® check-valve (CV) (1/3 psi) and joined the gas stream in a static Tee-mixer. The gas stream was provided by a Bronkhorst EL-Flow Prestige mass flow controller (MFC) and passed through two Swagelok® CV (1/3 psi) before reaching the Tee. After the mixer the mixed stream entered the Packed Bed Reactor (stainless steel, ϕ 0.46 cm × 5 cm, 0.83 mL, closed by a thin layer of glass wool or cotton). The PBR was located inside of a vent oven heated by a heating plack, the temperature was double-checked by a digital thermometer. The system was closed by a back-pressure regulator (BPR) from IDEX. Finally, the gas liquid stream was directed into an homemade autocollector (containing Bruphny Micro Servo Motor SG90 9G) and controlled by a Raspberry pi 4b programmed in Python3. The collection was performed into glass vials (ϕ 5.0 cm, 10 mL) the outgassing was performed with a cut syringe Figure S1.g, or alternatively by a cotton thread located at the end of the tubing.

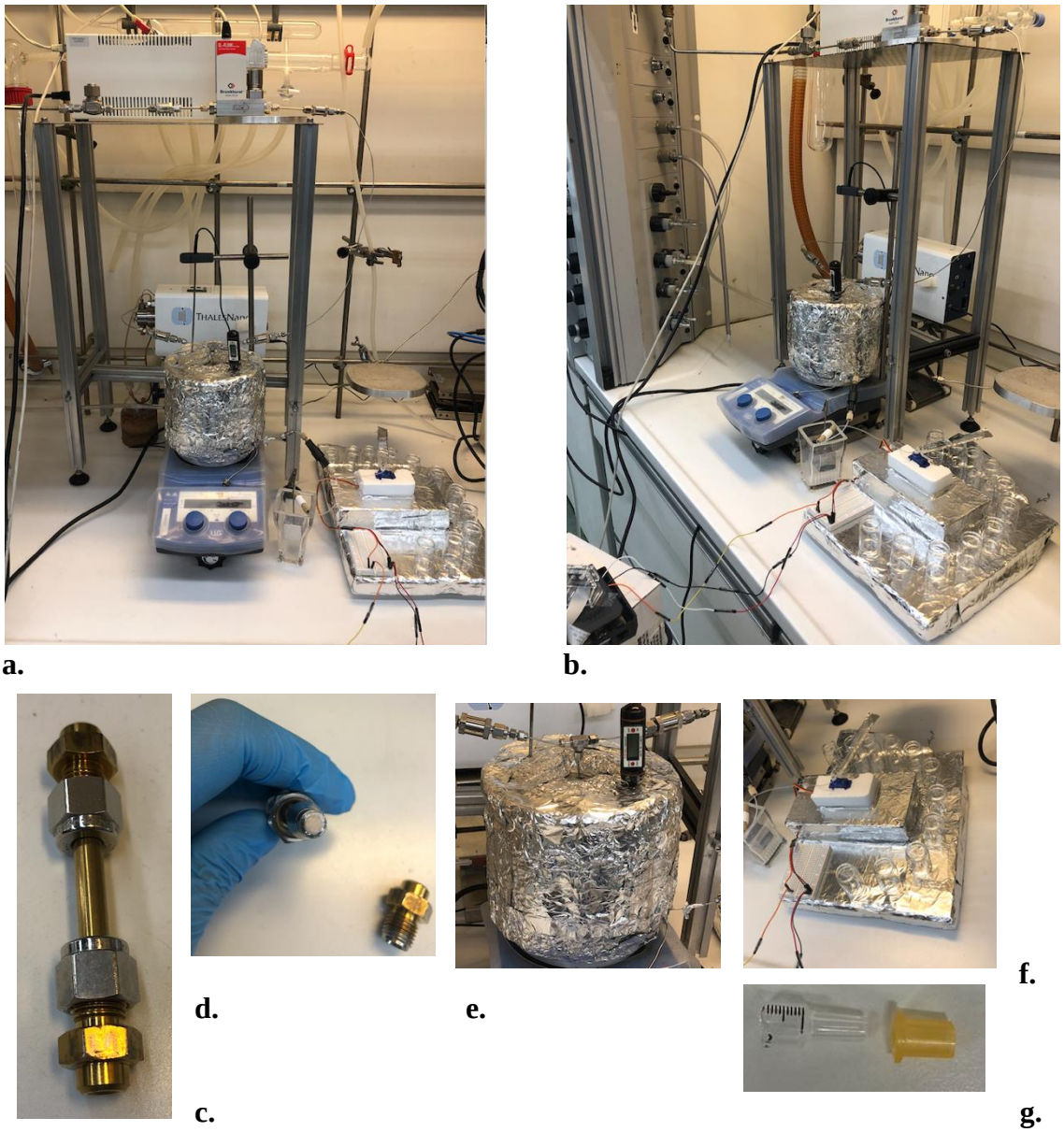


Figure S1. Pictures of the setup (a and b), PBR (c and d), the vented oven (e), auto-collector (f) and the degassing at the outlet of the system (g) in order to avoid spilling droplets.

3. Experimental flow protocol:

- MFC is turned on and connected to the PC
- The gas manometer is opened at the desired inlet pressure
- The gas flow is started
- A leak test is performed
- Calibration of the auto-collector is done
- HPLC pump is turned on and set at the desired flow rate (flows only solvent)
- Wait for system stabilization (usually 5 to 10 minutes)
- Solvent flask is exchanged for the reaction feed
- The heating plate is turned on
- The auto-collector is set to collect the desired fraction in the desired timeframe
- When the feed is about to end, the flask is rinsed with reaction solvent(s)
- Finally, the flask is exchanged for a clean one with reaction solvent and washed

4. System stability test

The flow setup described on page S4 was equipped with a Knauer Azura P4.1 pump with an integrated pressure sensor to determine the necessary pressure to efficiently flow the gas (5 to 24 hours long).

Selected Examples:

Flowing stream: MEK/DMSO 6.5% (0.1 mL/min) + CO_2 (5 mL/min)
BPR: 5.17 Bar
Knauer pressure read: 8 bar
Necessary gas inlet pressure to achieve a stable flow: 9 bar

Flowing stream: 0.1 M solution of Toloxatone based epoxy amine precursor in MEK/DMSO 6.5% (0.1 mL/min) + CO_2 (5 mL/min)
BPR: 5.17 Bar
Knauer pressure read: 9 bar
Necessary gas inlet pressure to achieve a stable flow: 10 bar

Considerations: The designed setup proved to be stable at several flow-rates if the inlet pressure was kept above 9 bar. During the reactions, we kept the inlet pressure at 10 bar to maintain a stable system and to avoid the influence of any possible variation of the pressure from the line. This was done mainly because the line is shared within the entire infrastructre and because the solution of different compounds could have properties that could influence the pressure in the reactor.

With regard to the PBR configuration, when the PBR was used in a horizontal position the output of the MFC was not stable, the same applies to the vertical up-flow configuration. The CO_2 flow rate can be changed in a range between 2 mL/min and 20 mL/min and the stability of the system is not affected. The system was operated in blank tests at temperatures between 25 and 110 ºC. Other kinds of supports were tested for the TBD derivative such as SBA15 and porous glass beads both with and without filler. The problem of these types of supports is that they lead to very high column pressure (>10 bar) under the reaction conditions and therefore the CO_2 could not flow well with the inlet pressure provided by the infrastructure.

Note about the mixing of the liquid and gas: we could not see and control the segments at the mixing junction since the tubing was stainless steel. However, the tubing before the BPR is made from PTFE and we could observe a pattern reminiscent to a segmented flow. It has to be noted that this does not mean that inside the reactor this pattern is necessarily followed, as the catalyst itself could act as a mixing unit. Furthermore, inside the reactor there surely are multiple phases: the solid catalyst phase, the interphase between catalyst and liquid, the interphase between liquid and gas and the gas itself.

5. First catalytic tests

Table S1. General reaction conditions: the feed, substrate 0.1 M in MEK was flowed at the indicated flow rate and with 20 mL/min of CO_2 (10 bar inlet pressure), the PBR was heated at 70 ºC, BPR 40 psi, catalyst amount was 270 mg. The crude was collected at intervals of 30 minutes and in the table is reported the conversion at the steady state (ss) and analyzed by ^{1}H-NMR spectroscopy.

Entry	substrate	mL/min	Conversion at ss
1	Glycidol	0.1	75
2	Glycidol	0.05	100
3	Toloxatone precursor	0.1	25
4	Toloxatone precursor	0.05	40

These experiments showed a preliminary difference in the reactivity between glycidol and epoxy amines, and thus more demanding conditions were needed to achieve high yields with epoxy amines.

6. Full optimization table

Table S2. General reaction conditions unless stated otherwise: pCO_2 (*inlet pressure*) 10 bar, MEK, 270 mg of catalyst, f_{exp} = 1.96 mmol/g (entry 6: f_{exp} = 2.04 mmol/g; entry 13: f_{exp} = 1.55 mmol/g), BPR 75 psi (= 5.17 bar), experiments were carried out for 3 h at the steady state (ss), then reactor was washed with the reaction solvent. Conv = conversion at the steady state with fresh catalyst, determined by ^{1}H NMR collecting fractions at the steady state. Unless stated otherwise, the selectivity was >99%; BPR = back pressure regulator, PBR = packed back reactor. NA = not assessed. The yield was calculated according to the fractions collected at the steady state. [a]Reaction without DMSO as co-solvent, the reactor clogged. [b]BPR 40 psi (2.76 bar).

Entry	Feed **1a** (mL/min)	CO_2 (mL_n/min)	T (ºC)	Conc. (mol/L)	Conv. (%)	Yield (%)	**TBD@PS** (mmol)	**2a** ($mmol \cdot h^{-1}$)	Productivity ($mmol \cdot h^{-1} \cdot mmol \cdot cat^{-1}$)
1	0.1	5	80	0.2	80	79	0.551	0.960	1.742
2[a]	0.1	5	80	0.2	NA	NA	0.551	NA	NA
3	0.1	2	80	0.2	52	NA	0.551	0.624	1.132
4	0.05	5	80	0.2	96	90	0.487	0.622	1.277
5	0.05	5	80	0.1	96	93	0.487	0.311	0.639
6	0.1	5	80	0.15	85	84	0.573	0.765	1.335
7	0.1	5	25	0.15	5	NA	0.551	0.045	0.082
8[a]	0.1	5	90	0.15	85	73	0.551	0.765	1.388
9	0.1	5	70	0.2	57	50	0.551	0.684	1.241
10	0.1	5	70	0.1	52	NA	0.551	0.312	0.566
11	0.1	20	70	0.1	20	NA	0.434	0.120	0.276
12	0.07	5	80	0.15	88	86	0.551	0.554	1.006
13	0.12	5	90	0.15	79	74	0.551	0.853	1.548
14	0.12	4	90	0.15	77	74	0.551	0.832	1.509
15	0.05	5	80	0.1	0	NA	0	NA	NA
16	0.1	10	70	0.2	48	NA	0.551	0.576	1.045
17[b]	0.1	10	70	0.1	30	NA	0.434	0.180	0.415
18[b]	0.1	10	80	0.1	26	NA	0.551	0.156	0.283
19[b]	0.1	5	70	0.1	27	NA	0.434	0.162	0.373
20[b]	0.1	20	70	0.1	45	NA	0.551	0.270	0.490

The “ss” did not depend on the gas flow rate but only on the feed flow rate, and was reached after 50 minutes at 0.1 mL/min and at 100 minutes at 0.05 mL/min, respectively. In the latter case we determined by volumetric measurements that the real flow rate at which the HLPC pump was working was 0.0557 mL/min and this value was considered in all the calculations. Both increasing the gas flow rate to 10 or 20 mL/min or decreasing it to 4 or 2 mL/min resulted in a reduced conversion when the epoxy amine precursor of Toloxatone was flowed at 0.1 mL/min.

During the optimisation we did not optimise the amount of gas that was employed, but surely it has to be present in excess. As indicated in the notes of Table 1 in the MS, we used 1.04 mmol/min of CO_2 in entry 5. This amount was calculated using the ideal law of gases (pV = nRT) to make an estimation. Considering that 0.00557 mmol of substrate are being "flowed in" every minute the amount of CO_2 that is consumed is clearly minimal.

The excess is probably needed to obtain a stable amount of gas in solution and is essentially caused by the limitation of pressure that we could use (max 10 bar). It might be possible that, without limitation of inlet pressure, it would be possible to increase the pressure (by a larger BPR) and thus decrease the flow-rate of the gas. Furthermore, as a future requisite for sustainable processing the recycling of the excess of CO_2 utilized will be important.

Further notes: Inside the PBR there is likely a triphasic mixture present and it appears that the liquid and the gas have different interactions with the catalyst. In fact, considering the total flow rate (gas + liquid) and the volume of the catalyst, the results would be consistent with a very low residence time. This was clearly not the case, in fact no starting material and/or product was detectable in this time frame. A steady state was achieved after 50 minutes when 0.1 mL/min was applied as feed, and after 100 minutes when 0.05 mL/min was used as flow-rate (see page S8). Regarding the reactor volume, this was filled with a weighed amount of catalyst but at the two termini, glass wool or cotton was used to seal the tube with a minor change of the reactor volume as these "stoppers" were <1 mm thick.

7. Example of crude mixture in a typical reaction under continuous flow

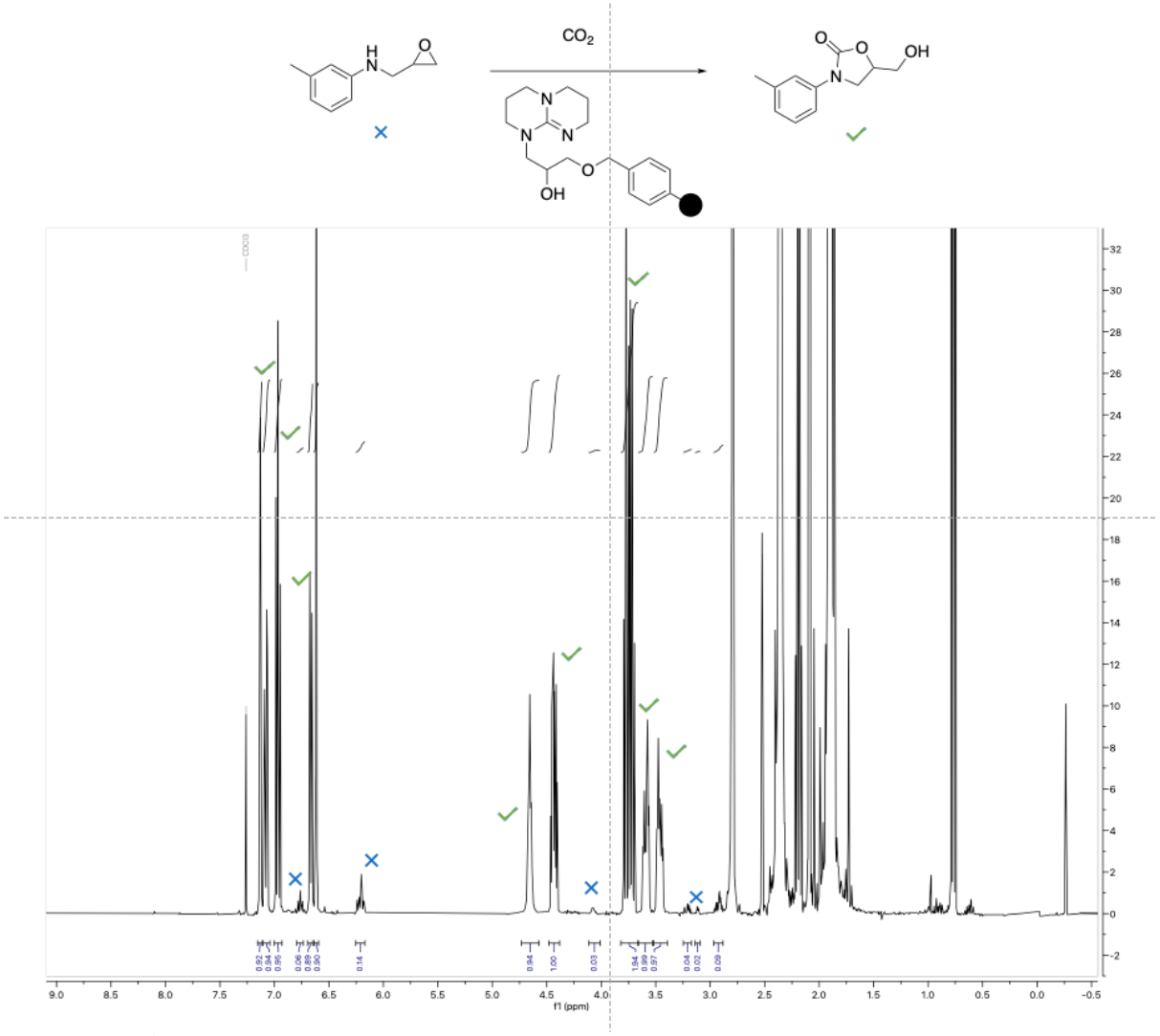


Figure S2: ^{1}H NMR spectrum ($CDCl_3$) containing durene as standard, product (toloxatone) and starting material and selected integration values.

8. Example of a crude mixture with cyclic carbonate byproduct

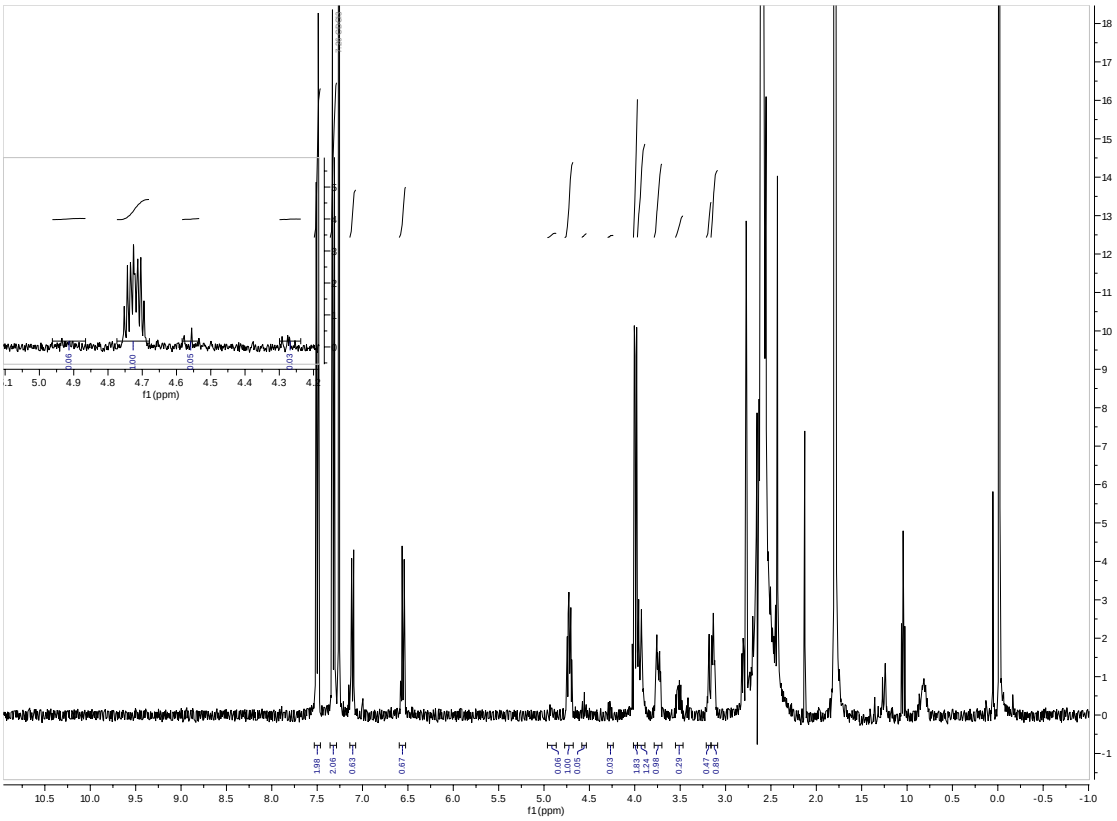


Figure S3: ^{1}H NMR spectrum ($CDCl_3$), it contains product (3-(4-chlorophenyl)-5-(hydroxymethyl)oxazolidin-2-one), starting material (4-chloro-N-(oxiran-2-ylmethyl)aniline) and carbonate byproduct (4-(((4-chlorophenyl)amino)methyl)-1,3-dioxolan-2-one). The latter was identified by comparison with reported spectra in literature.

The pattern and the displacement of the ^{1}H NMR signals of carbonates product are characteristic. Specially the multiplet, triplet, doublet of doublets which can be found between 4 ppm and 5 ppm.

9. Scope and additional experiments

Entry	Product identity	**C** (mL/min)	Conv. (%)	Yield (%)	**TBD@PS** (mmol)	product (mmol·h^{-1})	productivity (mmol·h^{-1}·mmol·cat^{-1})	T (h)	Yield (g)
1	**2d**	0.1	99	99	0.539	0.594	1.102	7.3	0.974
2	**2g**	0.1	90	88	0.539	0.81	1.500	2.7	0.465
3[a]	**2m**	0.1	42*	NA	0.539	0.252	0.468	–	NA
4[a]	**2m**	0.05	77*	65	0.539	0.386	0.716	6	0.378
5	**2h**	0.05	96	80	0.478	0.288	0.603	7.8	0.426
6	**2j**	0.1	18	NA	0.478	0.108	0.226	–	NA
7	**2j**	0.05	30	28	0.478	0.09	0.188	7.7	0.161
8	**2b**	0.05	80	79	0.478	0.24	0.502	4.3	0.280
9	**2e**	0.05	64	60	0.478	0.192	0.402	5.3	0.247
10	**2k**	0.05	84	79	0.478	0.252	0.527	6.8	0.330
11	**2i**	0.05	93	86	0.478	0.279	0.584	5.2	0.368
12	**2c**	0.1	80	NA	0.539	0.48	0.891	NA	NA
13	**2c**	0.05	99	91	0.478	0.297	0.621	6.4	0.387
14[*]	**2f**	0.05	65*	49	0.478	0.195	0.408	5.6	0.228
15	**2n**	0.02	93	NA	0.478	0.112	0.234	–	NA
16	**2n**	0.05	67	60	0.478	0.21	0.439	–	NA
17[b]	**2n**	0.08	70	66	0.539	0.336	0.623	6	0.524
18[b]	**2l**	0.08	60	47	0.539	0.288	0.534	8.8	0.496
19	**2o**	0.05	75	69	0.478	0.225	0.471	7	0.356
20	**2p**	0.05	74	74	0.478	0.222	0.464	7.3	0.356

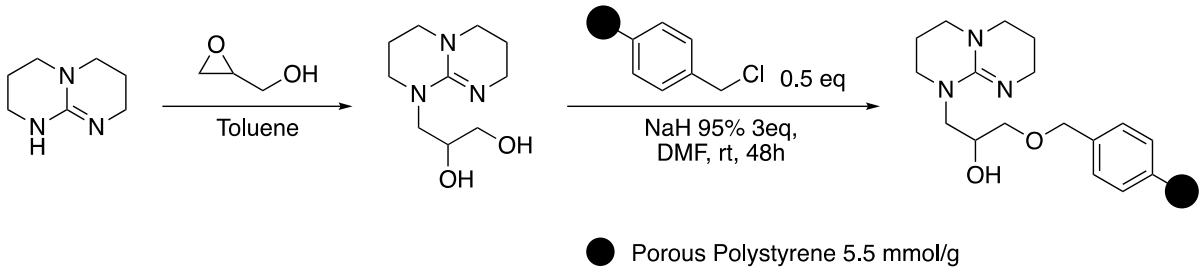
Table S3: General reaction conditions unless stated otherwise: pCO_2 (*inlet pressure*) 10 bar, CO_2 mL/min (= 5.1 – HPLC flowrate), solvent MEK/DMSO 6.5% 0.1 M (entry 2 0.15 M), PBR 270 mg catalyst, f_{exp} = 1.77 mmol/g (entry 1-4, 17-18: f_{exp} = 1.96 mmol/g), BPR 75 psi (= 5.17 bar). Conversion at the steady state (ss) with fresh catalyst as determined by ^{1}H NMR collecting fractions at the ss; unless stated otherwise the selectivity was >99%. For entry 3: 88%. For entry 4: 95%. For entry 14: 92%. T refers to how long the reaction was carried out. Yield (g) = overall yield in gram of the entire experiment. BPR = back pressure regulator, PBR = packed back reactor. [a] Solvent MEK. [b] Carried out at 75 ºC.

10. Sequential experiments

In a typical experiment, the feed of the desired epoxy amine (0.1 M) dissolved in MEK/DMSO (DMSO 6.5 volume %) was flowed at 0.05 mL/min and the CO_2 (10 bar inlet pressure) was flowed at 5 mL/min inside the PBR containing 270 mg of catalyst, and the system heated at 80 ^{o}C. The system was pressurized at 5 bar and fractions were collected every 20 minutes. Experiments were carried out for the desired time interval and under stable conditions. Then the reactor was washed with the reaction solvent. The collected products fractions were individually analyzed by ^{1}H NMR to determine the conversion, and the combined crude was also analyzed. After the system was washed adequately by the reaction solvent, the flask containing the feed was rinsed with the solvent mixture and finally exchanged for the solvent mixture in order to fully wash the system.

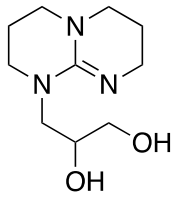
Comment on the washing: the reactor was extensively washed for 6 h to remove any possible trace of product in the reactor. The eluting phase was checked by TLC to ensure no product remained inside the reactor to avoid possible cross-contamination. An additional confirmation was obtained by comparing the FT-IR analysis of the fresh catalyst with the used one (see **Figure S4** on page S14).

11. Catalyst synthesis

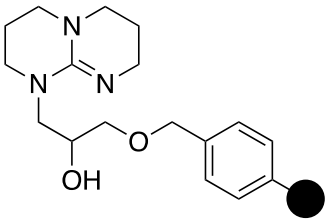


Freshly distilled oxiran-2-ylmethanol (37.55 mmol, 1 equiv) was added to a stirred solution of 1,3,4,6,7,8-hexahydro-2*H*-pyrimido[1,2-a] pyrimidine (37.55 mmol, 1 equiv) in toluene (100 mL) at 50 ºC. The reaction mixture was stirred at 50 ºC for 24 h and filtered through a PTFE filter (0.45 micron), and the solvent was removed under reduced pressure. Then NaH (95%, 3 equiv) was added portion-wise to a stirred solution of 3-(3,4,7,8-tetrahydro-2*H*-pyrimido[1,2-a]-pyrimidin-1(6*H*)-yl)propane-1,2-diol (1 equiv) at 0 ºC and under a N_2 atmosphere. The resultant suspension was stirred for 15 min and then added through a cannula to a closed flask containing the respective resin support (porous polystyrene 5.5% DVB, Aldrich, 16-50 Mesh, 5.5 mmol/g, 0.5 equiv) in DMF (100 mL) under N_2. Then, the reaction mixture was shaken for 2 days at rt. Hereafter, the catalyst was filtered and washed with water (200 mL), water:THF 1:4 (200 mL), MeOH (200 mL) and DCM (200 mL). The obtained heterogeneous catalyst was characterized by IR to assess the presence of C=N "stretching" absorptions. Elemental analysis was additionally performed to quantify the number of active sites (functionalization degree, *f*) on the support.

Precursor 8-tetrahydro-2*H*-pyrimido[1,2-a]pyrimidin-1(6*H*)-yl)propane-1,2-diol:



Prepared according a reported procedure[2], Yield: 99%. **^{1}H NMR**($CDCl_3$, 400 MHz): δ= 1.75 –1.81 (m, 2H), 1.89 –1.98 (m, 2H),3.07 –3.12 (m, 4H), 3.15 – 3.28 (m, 4H), 3.34 –3.45 (dd, 2H), 3.48 –3.49 (d, 1H), 3.67 –3.72 (m, 1H); **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ= 22.7, 22.8, 42.2, 47.9, 48.2, 48.4, 53.3, 63.7, 71.0, 152.7.



Synthesis of porous polystyrene supported catalyst: NaH 95% (3 equiv) was added portion-wise to a stirred solution of 3-(3,4,7,8-tetrahydro-2*H*-pyrimido[1,2-a]-pyrimidin-1(6*H*)-yl)propane-1,2-diol (1 equiv) at 0 ºC and under a N_2 atmosphere. The suspension was stirred for 15 min and then added through a cannula to a sealed flask containing (chloromethyl)polystyrene (porous polystyrene 5.5% DVB, Aldrich, 16-50 Mesh, 5.5 mmol/g, SKU 63868-10G, CAS 55844-94-5, 0.5 equiv) in DMF (200 mL) under N_2. The suspension was shaken for 5 days at r.t. **CHNO (%) Analyses**: C 69.62, H 7.43, N 7.47, O 3.02; f_{exp}: 1.77 mmol/g; **FT-IR** (neat, ν in cm^{-1}): 3350, 2922, 1597, 1510, 1321, 1085, 813.

[2] N. Zanda, A. Sobolewska, E. Alza, A. W. Kleij and M. A. Pericàs, *ACS Sustainable Chem. Eng*., 2021, **9**, 4391–4397.

12. Analyses of the catalyst

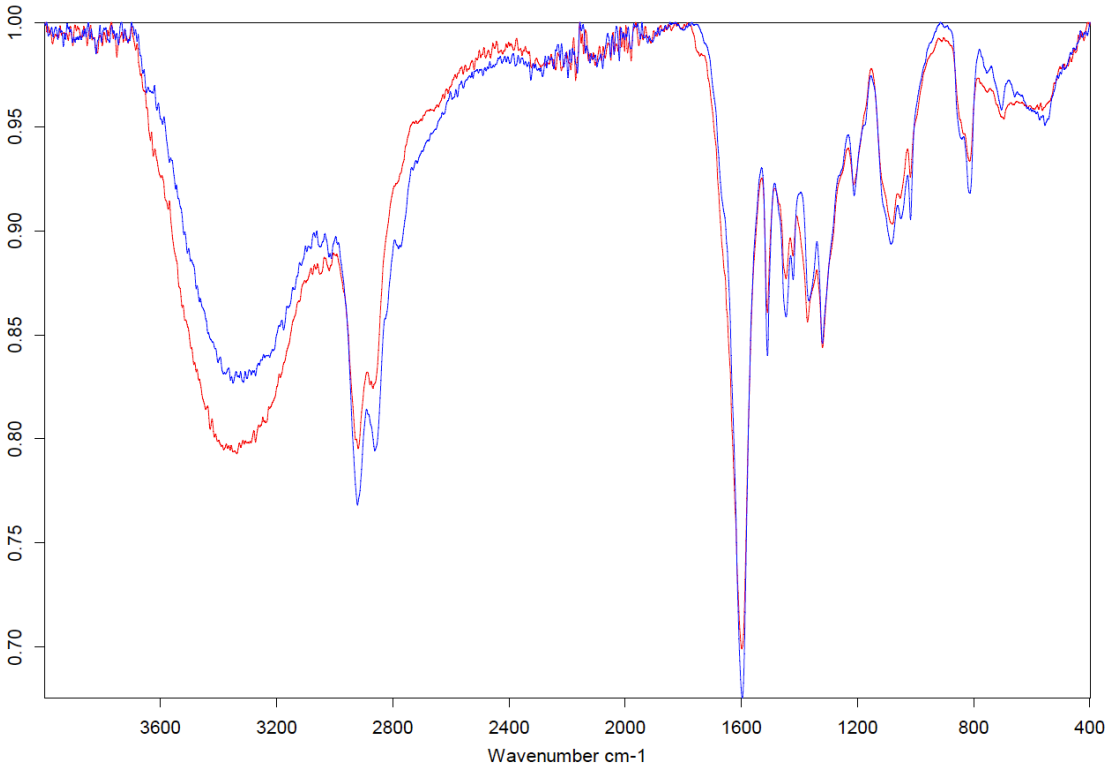


Figure S4: FT-IR spectroscopic analysis of the fresh catalyst (*blue color*) and the used one (*red color*). No significant difference was detected by comparison of the fresh and the used catalyst in the reaction. Thus, the product did not contaminate the catalyst in sequential runs.

Table S4: Elemental analysis of fresh and used catalyst.

Element→	C	H	N	Cl	N/C	Cl/C
Fresh catalyst	69.62	7.43	7.47	2.19	0.107	0.0315
Used catalyst	67.21	7.56	7.08	2.04	0.105	0.0303

NB. The N/C and Cl/C ratios do not show any significant difference.

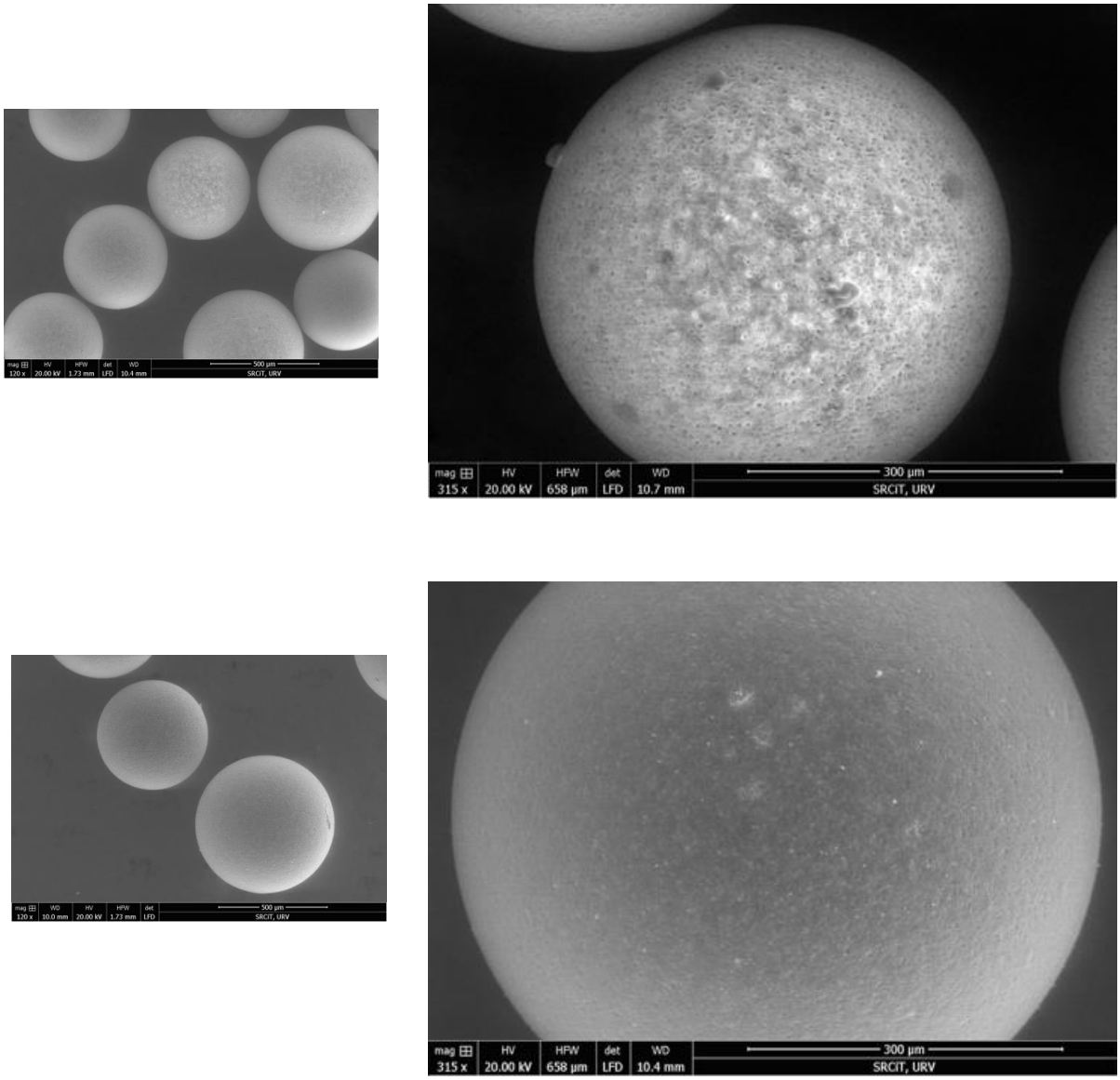
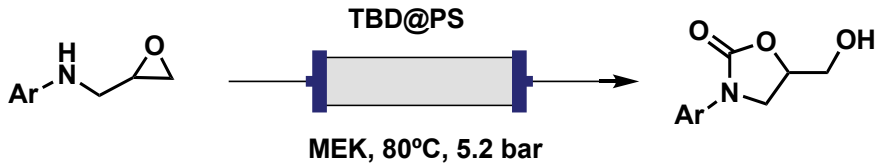


Figure S5. SEM pictures of polystyrene beads morphology of the Merrifield resin (5.5% DVB) with 120,315 au.

The presence of crystals of NaCl could justify the decreased selectivity towards the oxazolidinone when the substrate is not well-dried, and, over time due, to water accumulation inside the reactor. Traces of water present can locally dissolve NaCl thus releasing the halogen nucleophile that can ring open the epoxide and catalyze the formation of a cyclic carbonate rather than the target carbamate.

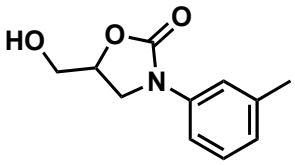
In general, the presence of water favors the formation of the carbonate (4% identified during the preparation of Toloxatone). This was determined by comparing known ^{1}H NMR spectra with the experimental one. It was not possible to fully remove the NaCl crystals by washing with water or water/organic solvent mixtures (water/dioxane and water/THF), with these crystals originating from the grafting of the TBD monomer. The intrinsic properties of the polymer made the removal of the salt difficult. However, this did not significantly affect the selectivity if the epoxy amine was well-dried.

13. Synthesis and characterization of oxazolidinones products



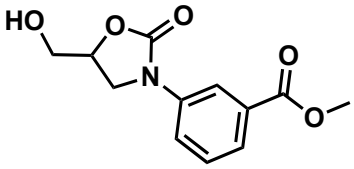
General procedure: In a typical experiment, the feed of the desired epoxy amine dissolved in MEK/DMSO (DMSO at 6.5 v%) was flowed at 0.05 mL/min and the CO_2 (10 bar inlet pressure) was flowed at 5 mL/min inside the PBR (containing 270 mg of catalyst) heated at 80 ºC. The system was pressurized at 75 psi. After the desired volume of substrate feed was flowed through the system, the flask containing the feed was rinsed with the solvent mixture and finally the feed was exchanged for the solvent mixture in order to fully wash the system. Then all the fractions were joined and the solvents removed. DMSO was then removed first by washing with water (3 times) and brine (1 time). The organic fractions were joined and the solvent removed under reduced pressure. Minor traces of DMSO were removed under vacuum and the crude purified by flash chromatography to get the desired oxazolidinone.

5-(hydroxymethyl)-3-(*m*-tolyl)oxazolidin-2-one (2a) (Toloxatone).[3] Synthesized according



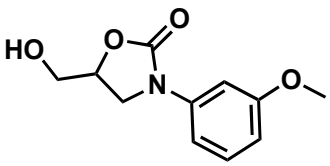
the general procedure (0.05 mL/min, 0.1 M, 5 mL/min CO_2) 1.560 g, White solid, 93% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.38 (s, 1H), 7.34 – 7.28 (m, 1H), 7.28 – 7.21 (m, 1H), 6.98 – 6.92 (m, 1H), 4.76 – 4.67 (m, 1H), 4.05 – 3.90 (m, 3H), 3.79 – 3.69 (m, 1H), 2.79 – 2.70 (m, 1H), 2.36 (s, 3H), 1.77 (bs, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ154.9, 139.0, 138.0, 128.9, 125.1, 119.1, 115.5, 72.9, 62.8, 46.5, 21.6. **FT-IR** (neat, *v* in cm^{-1}): 1724 (C=O).

Methyl 3-(5-(hydroxymethyl)-2-oxooxazolidin-3yl)benzoate (2b).[4] Synthesized according



the general procedure (0.05 mL/min, 0.1M, 5 mL/min CO_2) 0.280 g, white solid, 79% yield. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.29 (t, *J* = 8.2 Hz, 1H), 7.23 (t, *J* = 2.3 Hz, 1H), 7.10 (dd, *J* = 8.2, 0.9 Hz, 1H), 6.70 (ddd, *J* = 8.3, 2.5, 0.8 Hz, 1H), 5.21 (t, *J* = 5.6 Hz, 1H), 4.73 – 4.63 (m, 1H), 4.11 – 4.03 (m, 1H), 3.82 (dd, *J* = 8.9, 6.3 Hz, 1H), 3.75 (s, 3H), 3.71 – 3.63 (m, 1H), 3.61 – 3.50 (m, 1H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 166.0, 154.5, 139.0, 130.3, 129.4, 123.8, 122.1, 118.0, 73.4, 61.7, 52.3, 46.0. **FT-IR** (neat, *v* in cm^{-1}): 1711 (C=O) **ESI-MS** $[C_{12}H_{13}NNaO_5]^+$: calcd, 274.0686; found, 274.0686.

5-(hydroxymethyl)-3-(3-methoxyphenyl)oxazolidin-2-one (2c).[5] Synthesized according the



general procedure (0.05 mL/min, 0.1M, 5 mL/min CO_2) 0.387 g, white solid, 91% yield. **^{1}H NMR** (400 MHz, DMSO-d_6): δ 7.29 (t, *J* = 8.2 Hz, 1H), 7.23 (t, *J* = 2.3 Hz, 1H), 7.10 (dd, *J* = 8.2, 0.9 Hz, 1H), 6.70 (ddd, *J* = 8.3, 2.5, 0.8 Hz, 1H), 5.21 (t, *J* = 5.6 Hz, 1H), 4.73 – 4.63 (m, 1H), 4.11 – 4.03 (m, 1H), 3.82 (dd, *J* = 8.9, 6.3 Hz, 1H), 3.75 (s, 3H), 3.71 – 3.63 (m, 1H), 3.61 – 3.50 (m, 1H). **^{13}C NMR** (101 MHz, DMSO-d_6)

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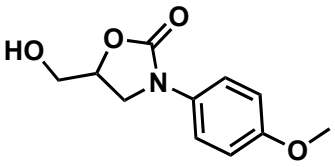
[3] J. Rintjema, R. Epping, G. Fiorani, E. Martin, E. C. Escudero-Adan and A. W. Kleij, *Angew. Chem. Int. Ed.*, 2016, **55**, 3972-3976.

[4] World Intellectual Property Organization, WO2018212534 A1 2018-11-22

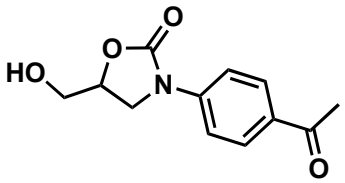
[5] A. Ali, K. K. Reddy, H. Cao, S. G. Anjum, M. N. L. Nalam, C. A. Schiffer and T. M. Rana, *J. Med. Chem.* 2006, **49**, 7342-7356.

δ 159.7, 154.4, 139.8, 129.7, 110.0, 108.7, 103.9, 73.1, 61.7, 55.1, 46.1, 40.2, 39.9, 39.7, 39.5, 39.3, 39.1, 38.9. **FT-IR** (neat, *v* in cm^{-1}): 1713 (C=O).

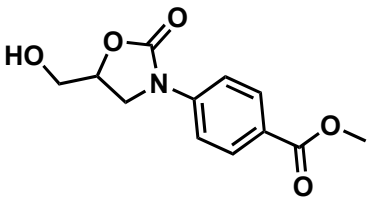
5-(hydroxymethyl)-3-(4-methoxyphenyl)oxazolidin-2-one (2d).[6] Synthetized according the general procedure (0.1 mL/min, 0.1M, 5 mL/min CO_2) 0.974 g, white solid, 99% yield. **^{1}H NMR** (400 MHz, DMSO-d_6) ^{1}H NMR (400 MHz, DMSO) δ 7.51 – 7.42 (m, 2H), 7.00 – 6.89 (m, 2H), 5.22 – 5.14 (m, 1H), 4.72 – 4.59 (m, 1H), 4.04 (t, *J* = 3.3 Hz, 1H), 3.79 (t, *J* = 3.3 Hz, 1H), 3.74 (s, 3H), 3.70 – 3.49 (m, 2H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 155.4, 154.6, 131.8, 119.7, 114.1, 73.0, 61.7, 55.2, 46.4, 39.5. **FT-IR** (neat, *v* in cm^{-1}): 1714 (C=O).



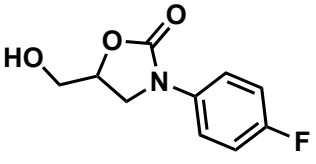
3-(4-acetylphenyl)-5-(hydroxymethyl)oxazolidin-2-one (2e).[7] Synthesized according the general procedure (0.05 mL/min, 0.1M, 5 mL/min CO_2) 0.247g, white solid, 60% yield. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.10 – 7.94 (m, 2H), 7.76 – 7.63 (m, 2H), 5.23 (t, *J* = 5.5 Hz, 1H), 4.81 – 4.72 (m, 1H), 4.20 – 4.10 (m, 1H), 3.92 – 3.85 (m, 1H), 3.75 – 3.66 (m, 1H), 3.65 – 3.51 (m, 1H), 2.55 (s, 3H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 196.6, 154.3, 142.6, 131.3, 129.4, 116.9, 73.4, 61.6, 45.9, 26.5. **FT-IR** (neat, *v* in cm^{-1}): 1738 (C=O), 1662.



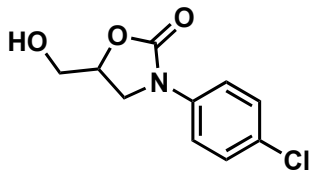
Methyl 4-(5-(hydroxymethyl)-2-oxooxazolidin-3yl)benzoate (2f). Synthesized according the general procedure (0.05 mL/min, 0.1M, 5 mL/min CO_2) 0.228 g, White solid, 47% yield. **^{1}H NMR** (400 MHz, DMSO-d_6): δ 7.97 (d, *J* = 8.8 Hz, 2H), 7.72 (d, *J* = 8.9 Hz, 2H), 5.30 – 5.19 (m, 1H), 4.79 – 4.66 (m, 1H), 4.20 – 4.06 (m, 1H), 3.88 (dd, *J* = 9.1, 6.2 Hz, 1H), 3.83 (s, 3H), 3.75 – 3.50 (m, 2H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 166.2, 154., 143.2, 130.7, 124.3, 117.5, 73.9, 62.1, 52.4, 46.4, 40.0. **FT-IR** (neat, *v* in cm^{-1}): 1739 (C=O), 1701 **ESI-MS** $[C_{12}H_{13}NNaO_5+H]^+$: calcd, 274.0686; found, 274.0695.



3-(4-fluorophenyl)-5-(hydroxymethyl)oxazolidin-2-one (2g).[8] Synthesized according the general procedure (0.1 mL/min, 0.15M, 5 mL/min CO_2) 0.465 g, White solid, 88% yield. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.64 – 7.54 (m, 2H), 7.28 – 7.18 (m, 2H), 5.20 (t, *J* = 5.6 Hz, 1H), 4.74 – 4.64 (m, 1H), 4.12 – 4.03 (m, 1H), 3.82 (dd, *J* = 8.7, 6.2 Hz, 1H), 3.72 – 3.61 (m, 1H), 3.61 – 3.51 (m, 1H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 157.0, 154.6, 135.0, 119.8, 119.7, 115.6, 115.4, 73.1, 61.6, 46.2. **FT-IR** (neat, *v* in cm^{-1}): 1724 (C=O).



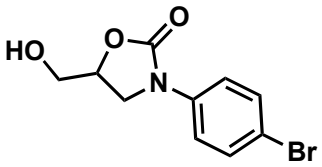
3-(4-chlorophenyl)-5-(hydroxymethyl)oxazolidin-2-one (2h).[7] Synthesized according the general procedure (0.05 mL/min, 0.1M, 5 mL/min CO_2) 0.426 g, White solid, 80% yield. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.64 – 7.54 (m, 2H), 7.48 – 7.38 (m, 2H), 5.27 – 5.16 (m, 1H), 4.76 – 4.64 (m, 1H), 4.07 (s, 1H), 3.82 (dd, *J* = 8.8, 6.2 Hz, 1H), 3.74 – 3.63



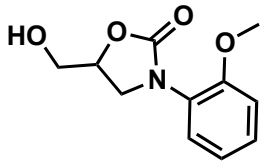
[6] R. Ilg, C. Burschka, D. Schepmann, B. Wünsch and R. Tacke, *Organometallics* 2006, **25**, 5396-5408.
[7] C. L. J. Wang, W. A. Gregory and M. A. Wuonola, *Tetrahedron*, 1989, **45**, 1323-1326.
[8] Y. Lee, J. Choi and H. Kim, *Org. Lett*., 2018, **20**, 5036-5039.

(m, 1H), 3.63 – 3.50 (m, 2H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 154.4, 137.5, 128.7, 127.1, 119.3, 73.2, 61.6, 45.9. **FT-IR** (neat, *v* in cm^{-1}): 1724 (C=O).

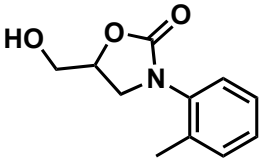
3-(4-bromophenyl)-5-(hydroxymethyl)oxazolidin-2-one (2i).[9] Synthesized according the general procedure (0.05 mL/min, 0.1M, 5 mL/min CO_2) 0.368 g, light yellow solid, 86% yield. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.65 – 7.50 (m, 4H), 5.27 – 5.13 (m, 1H), 4.77 – 4.63 (m, 1H), 4.07 (t, *J* = 9.0 Hz, 1H), 3.87 – 3.78 (m, 1H), 3.74 – 3.49 (m, 2H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 154.4, 138.0, 131.6, 119.7, 115.1, 73.2, 61.6, 45.9 **FT-IR** (neat, *v* in cm^{-1}): 1709 (C=O).



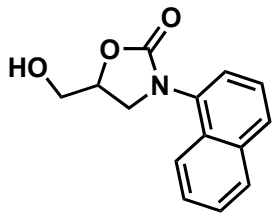
5-(hydroxymethyl)-3-(2-methoxyphenyl)oxazolidin-2-one (2j). Synthesized according the general procedure (0.05 mL/min, 0.1M, 5 mL/min CO_2) 0.161 g, white solid, 28% yield. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.34 – 7.24 (m, 2H), 7.15 – 7.06 (m, 1H), 7.01 – 6.91 (m, 1H), 5.19 (t, *J* = 5.7 Hz, 1H), 4.65 (m, 1H), 3.94 - 3.90 (m, 1H), 3.81 (s, 3H), 3.68 – 3.51 (m, 3H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 156.1, 154.7, 128.6, 128.2, 126.2, 120.5, 112.5, 74.0, 61.9, 55.7, 48.0. **FT-IR** (neat, *v* in cm^{-1}): 1709 (C=O) **ESI-MS** $[C_{11}H_{13}NNaO_4+H]^+$: calcd, 246.0737; found, 246.0736.



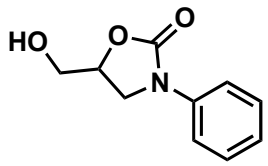
5-(hydroxymethyl)-3-(*o*-tolyl)oxazolidin-2-one (2k).[7] Synthesized according the general procedure (0.05 mL/min, 0.1M, 5 mL$_n$/min CO_2) 0.330 g, white solid, 79% yield. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.35 – 7.18 (m, 4H), 5.24 (t, *J* = 5.7 Hz, 1H), 4.75 – 4.65 (m, 1H), 4.01 – 3.91 (m, 1H), 3.74 – 3.64 (m, 2H), 3.61 – 3.52 (m, 1H), 2.22 (s, 3H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 155.6, 136.6, 135.7, 130.9, 127.6, 126.7, 126.7, 73.9, 61.8, 48.5, 17.4. **FT-IR** (neat, *v* in cm^{-1}): 1736 (C=O).



5-(hydroxymethyl)-3-(naphthalen-1-yl)oxazolidin-2-one (2l).[7] Synthesized according the general procedure (0.08 mL/min, 0.1 M, 5 mL/min CO_2) 75 ºC, 0.496 g, pink solid, 47% yield. **^{1}H NMR** (500 MHz, DMSO-d_6) δ 8.03 – 7.98 (m, 2H), 7.98 – 7.93 (m, 1H), 7.62 – 7.53 (m, 4H), 5.39 (t, *J* = 5.6 Hz, 1H), 4.88 – 4.81 (m, 1H), 4.15 – 4.07 (m, 1H), 3.88 (dd, *J* = 8.4, 5.8 Hz, 1H), 3.83 – 3.76 (m, 1H), 3.70 – 3.61 (m, 1H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 156.5, 134.5, 134.0, 129.8, 128.3, 128.1, 126.7, 126.5, 125.8, 124.9, 123.0, 74.2, 61.9, 49.6. **FT-IR** (neat, *v* in cm^{-1}): 1711 (C=O).



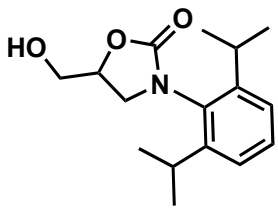
5-(hydroxymethyl)-3-phenyloxazolidin-2-one (2m).[10] Synthesized according the general procedure (0.05 mL/min, 0.1 M, 5 mL/min CO_2) 0.378 g, white solid, 65% yield. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.58 (m, 2H), 7.44 – 7.33 (m, 2H), 7.11 (m, 1H), 5.21 (t, *J* = 5.7, 1H), 4.70 (m, 1H), 4.08 (t, *J* = 9.0 Hz, 1H)), 3.84 (t, *J* = 9.0 Hz, 1H), 3.72 – 3.63 (m, 1H), 3.72 – 3.51 (m, 1H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 154.9, 138.6, 128.9, 123.2, 117.7, 73.1, 61.6, 46.0. FT-IR (neat, *v* in cm^{-1}): 1709 (C=O).



[9] S. M. Kelly, C. Han, L. Tung and F. Gosselin *Org. Lett.* 2017, **19**, 3021-3024.

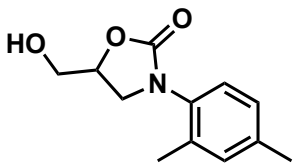
[10] E. J. Brnardic, M. E. Fraley, R. M. Garbaccio, M. E. Layton, J. M. Sanders, C. Culberson, M. A Jacobson, B. C. Magliaro, P. H. Hutson, J. A. O'Brien, S. L. Huszar, J. M. Uslaner, K. L. Fillgrove, C. Tang; Y. Kuo, S. M. Sur and G. D. Hartman, *Bioorg. Med. Chem. Lett.* 2010, **20**, 3129-3133.

3-(2,6-di-*iso*-propylphenyl)-5-(hydroxymethyl)oxazolidin-2-one (2n). Synthesized



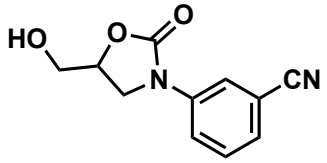
according the general procedure (0.08 mL/min, 0.1 M, 5 mL/min CO_2) 75 ºC, 0.524 g, White solid, 66% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.35 (t, *J* = 7.7 Hz, 1H), 7.23 – 7.18 (m, 2H), 4.86 – 4.76 (m, 1H), 4.06 – 3.96 (m, 1H), 3.85 – 3.66 (m, 3H), 3.13 – 2.93 (m, 2H), 2.65 – 2.55 (m, 1H), 1.35 – 1.15 (m, 12H). **^{13}C NMR** (101 MHz, DMSO-*d*$_6$) δ 156.6, 147.4, 147.2, 131.9, 129.0, 124.0, 123.9, 73.8, 61.5, 49.2, 30.7, 28.0, 27.6, 24.3, 24.2, 23.9, 23.7. **FT-IR** (neat, *v* in cm^{-1}): 1720 (C=O) **ESI-MS** $[C_{16}H_{24}NO_3+H]^+$: calcd, 278.1757; found, 278.1751.

3-(2,4-dimethylphenyl)-5-(hydroxymethyl)oxazolidin-2-one (2o). Synthesized according



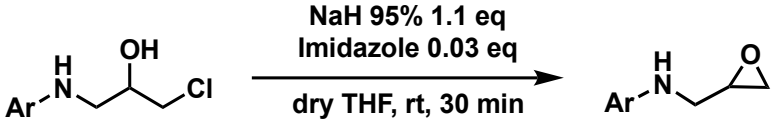
the general procedure (0.05 mL/min, 0.1 M, 5 mL/min CO_2) 0.356 g, White solid, 69% yield. **^{1}H NMR** (400 MHz, DMSO-*d*$_6$) δ 7.17 (d, *J* = 8.0 Hz, 1H), 7.10 (s, 1H), 7.04 (d, *J* = 2.1 Hz, 1H), 5.28 – 5.17 (m, 1H), 4.74 – 4.60 (m, 1H), 3.93 (s, 1H), 3.72 – 3.62 (m, 2H), 3.61 – 3.51 (m, 1H), 2.27 (s, 3H), 2.17 (s, 3H). **^{13}C NMR** (101 MHz, DMSO-*d*$_6$) δ 155.6, 137.0, 135.3, 134.0, 131.3, 127.2, 126.6, 73., 61.8, 48.6, 20.5, 17.3. **FT-IR** (neat, *v* in cm^{-1}): 1723 (C=O) **ESI-MS** $[C_{12}H_{15}NNaO_3+H]^+$: calcd, 244.0944; found, 244.0956.

3-(5-(hydroxymethyl)-2-oxooxazolidin-3-yl)benzonitrile (2p). Synthesized according the



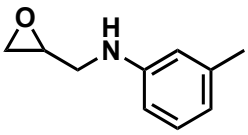
general procedure (0.05 mL/min, 0.1 M, 5 mL/min CO_2) 0.356 g, white solid, 74% yield. **^{1}H NMR** (400 MHz, DMSO-*d*$_6$) δ 8.00 (s, 1H), 7.95 – 7.88 (m, 1H), 7.64 – 7.51 (m, 2H), 5.29 – 5.17 (m, 1H), 4.81 – 4.67 (m, 1H), 4.18 – 4.07 (m, 1H), 3.87 (dd, *J* = 6.1, 1.1 Hz, 1H), 3.77 – 3.64 (m, 1H), 3.64 – 3.53 (m, 1H). **^{13}C NMR** (101 MHz, DMSO-*d*$_6$) δ 154.4, 139.4, 130.3, 126.6, 122.1, 120.5, 118.6, 111.8, 73.5, 61.6, 45.8. **FT-IR** (neat, *v* in cm^{-1}): 1708 (C=O) **ESI-MS** $[C_{11}H_{10}N_2NaO_3]^+$: calcd, 241.0584; found, 241.0584.

14. Synthesis and characterization of intermediate epoxy amines

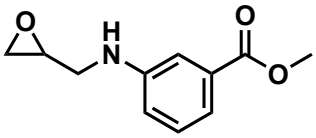


General Procedure:[11] NaH (95%, 1.1 equiv) was added at 0 ºC to a stirred solution of the desired starting material (1 equiv, 0.5 M) and imidazole (0.03 equiv) in dry THF. Then the suspension was warmed up to r.t. and stirred at the same temperature for 30 min. EtOAc was added to this mixture, after which it was washed with water (3 times). The organic fractions were joined and dried over Na_2SO4, then filtered and the solvents removed under vacuum. The sample was further dried overnight under vacuum to get the epoxy amine target.

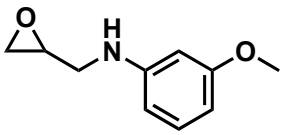
3-methyl-N-(oxiran-2-ylmethyl)aniline (1a).[2] Yellow oil, 1.320 g, 89% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.08 (t, *J* = 1.2 Hz, 1H), 6.56 (d, *J* = 0.9 Hz, 1H), 6.49 – 6.42 (m, 2H), 3.80 (bs, 1H), 3.56 – 3.46 (m, 1H), 3.29 – 3.14 (m, 2H), 2.85 – 2.76 (m, 1H), 2.73 – 2.65 (m, 1H), 2.28 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 148.0, 139.1, 129.3, 118.9, 113.9, 110.2, 51.1, 45.4, 45.1, 21.7.



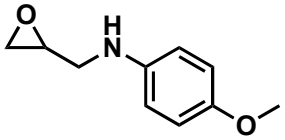
Methyl 3-((oxiran-2-ylmethyl)amino)benzoate (1b). Yellow oil, 0.273 g, 91% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.39 (dt, *J* = 7.7, 0.7 Hz, 1H), 7.31 – 7.28 (m, 1H), 7.23 (t, *J* = 7.9 Hz, 1H), 6.81 (ddd, *J* = 8.1, 2.6, 1.0 Hz, 1H), 4.06 – 3.99 (m, 1H), 3.89 (s, 3H), 3.63 – 3.55 (m, 1H), 3.29 – 3.18 (m, 2H), 2.84 – 2.80 (m, 1H), 2.70 – 2.66 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.5, 148.0, 131.3, 129.4, 119.2, 117.8, 113.4, 52.2, 50.9, 45.4, 45.0. **FT-IR** (neat, *v* in cm^{-1}): 3390, 2951, 1712, 1605, 1234, 751 **ESI-MS** $[C_{11}H_{13}NNaO_3]^+$: calcd, 230.0788; found, 230.0782.



3-Methoxy-N-(oxiran-2-ylmethyl)aniline (1c).[12] Brown oil, 0.820 g, 99% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.09 (t, *J* = 8.1 Hz, 1H), 6.30 (ddd, *J* = 8.2, 2.4, 0.9 Hz, 1H), 6.26 (ddd, *J* = 8.0, 2.2, 0.8 Hz, 1H), 6.20 (t, *J* = 2.3 Hz, 1H), 3.89 (bs, 1H), 3.77 (s, 3H), 3.58 – 3.49 (m, 1H), 3.29 – 3.17 (m, 2H), 2.84 – 2.78 (m, 1H), 2.73 – 2.65 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 160.9, 149.3, 130.1, 106.1, 103.0, 99.1, 55.1, 51.0, 45.4, 45.0.



4-Methoxy-N-(oxiran-2-ylmethyl)aniline (1d).[13] Brown oil, 0.794 g, 95% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.85 – 6.70 (m, 2H), 6.64 – 6.55 (m, 1H), 3.74 (s, 3H), 3.66 – 3.55 (bs, 1H), 3.54 – 3.45 (m, 1H), 3.23 – 3.10 (m, 2H), 2.83 – 2.77 (m, 1H), 2.72 – 2.66 (m, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 154.0, 140.2, 115.6, 113.8, 54.8, 51.9, 47.6, 45.6.



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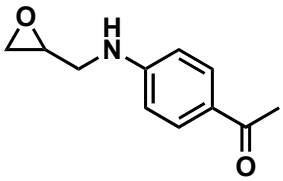
[11] N. Tsiakopoulos, C. Damianakos, G. Karigiannis, D. Vahliotis, D. Papaioannou and G. Sindona *Arkivoc,* 2002, **13**, 79-104.

[12] K. S. MacMillan, J. Naidoo, J. Liang, L. Melito, N. S. Williams, L. Morlock, P. J. Huntington, S. J. Estill, J. Longgood, G. L. Becker, S. L. McKnight, A. A. Pieper, J. K. Brabander and J. M. Ready, *J. Am. Chem. Soc.,* 2011, **133**, 1428-1437.

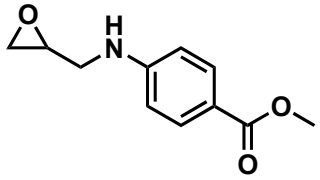
[13] D. Bradley and G. Williams, *J. Org. Chem.,* 2009, **24**, 9509–9512.

1-(4-((Oxiran-2-ylmethyl)amino)phenyl)ethan-1-one (1e).[8] White solid, 0.401 g 93% yield.

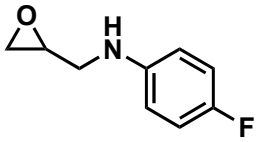


^{1}H NMR (300 MHz, $CDCl_3$) δ 7.95 – 7.79 (m, 2H), 6.73 – 6.57 (m, 2H), 4.41 (bs, 1H), 3.72 – 3.60 (m, 1H), 3.38 – 3.18 (m, 2H), 2.92 – 2.81 (m, 1H), 2.75 – 2.67 (m, 1H), 5.54 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 196.5, 151.9, 130.9, 127.4, 111.8, 50.7, 45.3, 44.3, 26.2.

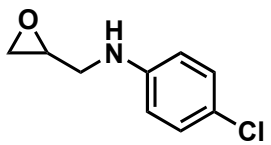
Methyl 4-((oxiran-2-ylmethyl)amino)benzoate (1f). White solid, 0.837 g, 98% yield. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.73 – 7.61 (m, 2H), 6.75 – 6.70 (m, 1H), 6.69 – 6.63 (m, 2H), 3.74 (d, J = 1.1 Hz, 3H), 3.49 – 3.40 (m, 1H), 3.18 – 3.06 (m, 2H), 2.78 – 2.70 (m, 1H), 2.60 – 2.54 (m, 1H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 204.0, 190.5, 168.6, 153.8, 148.8, 88.9, 88.2, 82.3, 81.8, 77.8, 77.6, 77.4, 77.2, 77.0, 76.7, 76.5. **FT-IR** (neat, v in cm^{-1}): 3362, 2946, 1679, 1600, 1278 **ESI-MS** $[C_{11}H_{13}NNaO_3]^+$: calcd, 230.0788; found, 230.0784.



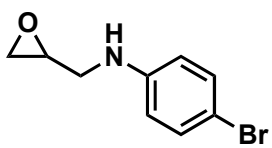
4-Fluoro-N-(oxiran-2-ylmethyl)aniline (1g).[8] Violet oil, 0.824, 99% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.93 – 6.84 (m, 2H), 6.62 – 6.54 (m, 2H), 3.75 (bs, 1H), 3.56 – 3.45 (m, 1H), 3.23 – 3.12 (m, 2H), 2.85 – 2.79 (m, 1H), 2.73 – 2.66 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 116.0, 115.8, 114.1, 114.0, 77.5, 77.2, 76.8, 51.1, 45.9, 45.5.



4-chloro-N-(oxiran-2-ylmethyl)aniline (1h).[13] Yellow oil, 0.257 g 68% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.15 – 7.09 (m, 2H), 6.59 – 6.52 (m, 2H), 3.88 (bs, 1H), 3.58 – 3.47 (m, 1H), 3.23 – 3.14 (m, 2H), 2.84 – 2.79 (m, 1H), 2.70 – 2.65 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 146.6, 129.3, 122.6, 114.2, 51.0, 45.0, 45.2.



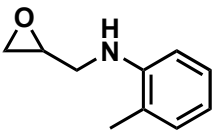
4-Bromo-N-(oxiran-2-ylmethyl)aniline (1i).[8] Yellow oil, 0.416 g, 90% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.35 – 7.18 (m, 2H), 6.59 – 6.45 (m, 2H), 3.90 (bs, 1H), 3.58 – 3.46 (m, 1H), 3.23 – 3.11 (m, 2H), 2.83 – 2.78 (m, 1H), 2.71 – 2.63 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 147.0, 132.1, 114.7, 109.6, 50.9, 45.4, 45.1.



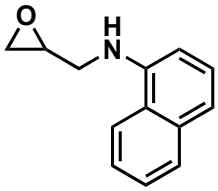
2-Methoxy-N-(oxiran-2-ylmethyl)aniline (1j).[14] Dark oil, 99% 0.850 g, 98% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.88 (td, J = 7.6, 1.5 Hz, 1H), 6.78 (dd, J = 7.9, 1.5 Hz, 1H), 6.73 – 6.63 (m, 2H), 4.46 (bs, 1H), 3.85 (s, 3H), 3.57 – 3.48 (m, 1H), 3.31 – 3.19 (m, 2H), 2.84 – 2.80 (m, 1H), 2.72 – 2.66 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 147.0, 137.8, 121.2, 117.1, 110.0, 109.6, 55.4, 51.1, 45.5, 45.1. **FT-IR** (neat, v in cm^{-1}): 3413, 2936, 1061, 1511, 1220. **ESI-MS** $[C_{10}H_{14}NO_2]^+$: calcd, 180.1019; found, 180.1019

[14] Patent, CN2021-10747869, CN113461629 A 2021-07-01, Preparation of the compound 5-hydroxymethyl-oxazolidin-2-one.

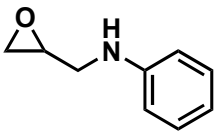
2-Methyl-N-(oxiran-2-ylmethyl)aniline (1k).[8] Violet oil, 0.494 g, 82% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.16 – 7.10 (m, 1H), 7.07 (d, *J* = 0.9 Hz, 1H), 6.72 – 6.67 (m, 1H), 6.67 – 6.62 (m, 1H), 3.73 (bs, 1H), 3.63 – 3.55 (m, 1H), 3.33 – 3.22 (m, 2H), 2.87 – 2.82 (m, 1H), 2.74 – 2.69 (m, 1H), 2.16 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 145.9, 130.1, 127.3, 122.50, 117.7, 110.0, 77.5 77.2, 76.8, 51.1, 45.6, 45.1, 17.6.



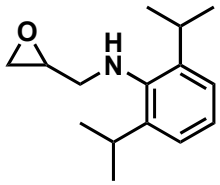
N-(oxiran-2-ylmethyl)naphthalen-1-amine (1l).[8] Brownish solid, 1.01 g, 94% yield. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.85 – 7.73 (m, 2H), 7.50 – 7.39 (m, 2H), 7.38 – 7.21 (m, 2H), 6.64 (d, *J* = 1.2 Hz, 1H), 4.56 (bs, 1H), 3.77 – 3.64 (m, 1H), 3.45 – 3.30 (m, 2H), 2.87 (dd, *J* = 3.9, 0.9 Hz, 1H), 2.79 – 2.74 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 143.2, 134.5, 128.8, 126.6, 126.0, 125.0, 123.7, 120.1, 118.2, 104.8, 51.0, 45.7, 45.2.



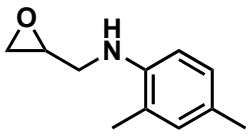
N-(oxiran-2-ylmethyl)aniline (1m).[8,13] Transparent oil, 0.777 g, 97% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.22 – 7.14 (m, 2H), 6.74 (tt, *J* = 7.4, 1.1 Hz, 1H), 6.68 – 6.62 (m, 2H), 3.87 (bs, 1H), 3.58 – 3.50 (m, 1H), 3.28 – 3.24 (m, 1H), 3.24 – 3.18 (m, 1H), 2.85 – 2.79 (m, 1H), 2.73 – 2.67 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 148.0, 129.5, 118.1, 113.1, 77.5, 77.2, 76.8, 51.1, 45.5, 45.1.



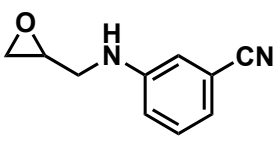
2,6-Di-*iso*-propyl-N-(oxiran-2-ylmethyl)aniline (1n). Orange oil, 0.373 g, 99% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.14 – 7.04 (m, 3H), 3.37 – 3.17 (m, 4H), 2.91 (dd, *J* = 12.8, 5.6 Hz, 1H), 2.85 (dd, *J* = 5.0, 3.9 Hz, 1H), 2.80 – 2.76 (m, 1H), 1.29 – 1.22 (m, 12H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 142.9, 142.4, 124.2, 123.8, 53.2, 51.7, 45.6, 27.7, 24.4, 24.4. **FT-IR** (neat, *v* in cm^{-1}): 2960, 1447, 1255, 752 **ESI-MS** $[C_{15}H_{24}NO+H]^+$: calcd, 234.1863; found, 234.1852.



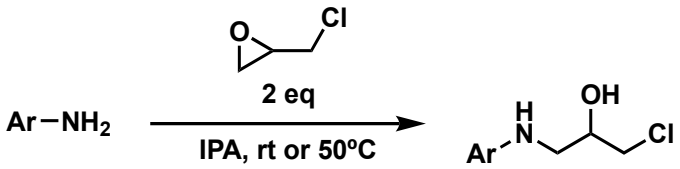
2,4-Dimethyl-N-(oxiran-2-ylmethyl)aniline (1o). Dark oil, 0.382 g, 90% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.98 – 6.88 (m, 2H), 6.57 (d, *J* = 8.1 Hz, 1H), 3.61 – 3.52 (m, 1H), 3.30 – 3.20 (m, 2H), 2.86 – 2.82 (m, 1H), 2.73 – 2.69 (m, 1H), 2.25 (s, 3H), 2.15 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 143.6, 131.3, 127.5, 126.8, 122.7, 110.3, 51.2, 45.6, 45.4, 20.4, 17.5. **FT-IR** (neat, *v* in cm^{-1}): 3409, 2917, 1618, 1513 **ESI-MS** $[C_{11}H_{16}NO]^+$: calcd,178.1226; found, 178.1218.



3-((Oxiran-2-ylmethyl)amino)benzonitrile (1p). Yellow oil, 0.310 g, 75% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.25 – 7.19 (m, 1H), 7.00 – 6.95 (m, 1H), 6.86 – 6.80 (m, 2H), 4.15 (bs, 1H), 3.63 – 3.52 (m, 1H), 3.24 – 3.15 (m, 2H), 2.84 (dd, *J* = 4.8, 3.8 Hz, 1H), 2.70 – 2.64 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 148.2, 130.1, 121.5, 119.5, 117.6, 115.2, 50.7, 45.3, 44.7. **FT-IR** (neat, *v* in cm^{-1}): 3380, 2919, 2226, 1601, 1491, 780 **ESI-MS** $[C_{10}H_{11}N_2O+H]^+$: calcd, 175.0866; found, 175.0874.

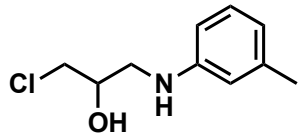


15. Synthesis and characterization of intermediate halohydrins

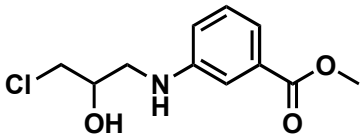


General procedure:[2] To a stirred solution of the respective aniline (25.0 mmol) in *iso*-propanol (6.4 mL, 2 M) at 0 ºC was slowly added epichlorohydrin (50.0 mmol) and then the reaction mixture was further stirred at r.t. for 16 h. The solvent was evaporated and the mixture was purified by column chromatography over silica to obtain the crude halohydrin product.

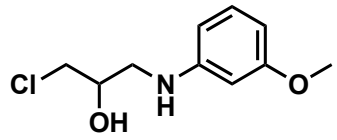
3-Methyl-N-(oxiran-2-ylmethyl)aniline (1'a).[2] Orange oil, 5.77 g , 57% yield. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.16 (m, 1H), 6.64 (m, 1H), 6.54 (m, 2H), 3.89 (bs, 1H), 3.61 –3.52 (m, 1H), 3.28 (m, 2H), 2.87 (m, 1H), 2.75 (m, 1H), 2.40 –2.33 (m, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 148.0, 139.1, 129.3, 118.9, 113.9, 110.2, 51.1, 45.4, 45.1, 21.7.



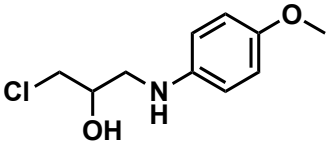
Methyl 3-((3-chloro-2-hydroxypropyl)amino)benzoate (1'b). Yellowish oil, 2.05 g, 51% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.43 (ddd, *J* = 7.6, 1.6, 1.0 Hz, 1H), 7.34 – 7.32 (m, 1H), 7.31 – 7.22 (m, 1H), 6.87 (ddd, *J* = 8.1, 2.6, 1.0 Hz, 1H), 4.10 (m, 1H), 3.91 (s, 3H), 3.75 – 3.62 (m, 2H), 3.44 (dd, *J* = 13.2, 4.3 Hz, 1H), 3.29 (dd, *J* = 13.2, 7.3 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.6, 147.90, 131.3, 129.5, 119.5, 118.1, 113.9, 77.5, 77.2, 76.8, 69.9, 52.3, 47.8, 47.2. **FT-IR** (neat, *v* in cm^{-1}): 3393, 1702, 1604, 1437, 1282. **ESI-MS** $[C_{15}H_{24}NO+H]^+$: calcd, 244.0735; found, 244.0731.



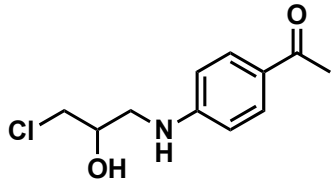
1-Chloro-3-((3-methoxyphenyl)amino)propan-2-ol (1'c).[15] Dark oil, 0.996 g, 26% Yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.10 (t, *J* = 8.1 Hz, 1H), 6.30 (dddd, *J* = 16.8, 8.0, 2.3, 0.9 Hz, 2H), 6.22 (t, *J* = 2.3 Hz, 1H), 4.15 – 4.03 (m, 1H), 3.73 – 3.61 (m, 2H), 3.38 (dd, *J* = 13.3, 4.5 Hz, 1H), 3.24 (dd, *J* = 13.4, 7.1 Hz, 1H), 2.44 (bs, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 130.1, 106.1, 103.2, 99.2, 69.6, 54.7, 47.6, 46.9.



1-Chloro-3-((4-methoxyphenyl)amino)propan-2-ol (1'd).[13] Dark oil, 2.63 g 50% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.82 – 6.77 (m, 2H), 6.67 – 6.61 (m, 2H), 4.11 – 4.01 (m, 1H), 3.75 (s, 3H), 3.71 – 3.61 (m, 2H), 3.34 (dd, *J* = 13.1, 4.3 Hz, 1H), 3.19 (dd, *J* = 13.1, 7.2 Hz, 1H), 3.07 – 2.33 (bs, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 152.9, 142.0, 115.1, 115.0, 70.00 55.9, 48.4, 47.8.



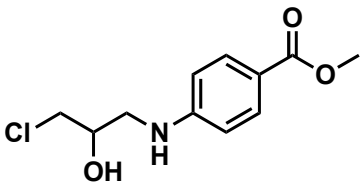
1-(4-((3-Chloro-2-hydroxypropyl)amino)phenyl)ethan-1-one (1'e). Transparent oil 2.05 g, purity 99%, 41% yield (50 ºC, 48 h) **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.86 – 7.79 (m, 2H), 6.67 – 6.57 (m, 2H), 4.60 (s, 1H), 4.16 – 4.06 (m, 1H), 3.74 – 3.59 (m, 2H), 3.52 – 3.42 (m, 1H), 3.35 – 3.26 (m, 1H), 2.68 (d, *J* = 5.2 Hz, 1H), 2.50 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 152.0, 131.0, 127.5, 112.0, 69.9, 47.6, 46.3,



[15] E. Raflee, S. Tangestaninejad, M. H. Habibi and V. Mirkhani, *Synth. Commun.*, 2004, **20**, 3673-3681.

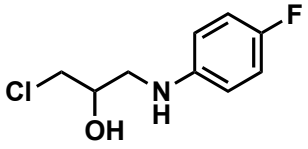
26.2. **FT-IR** (neat, *v* in cm^{-1}): 3300, 1644, 1587, 1279, 1174. **ESI-MS** $[C_{11}H_{15}ClNO_2]^+$: calcd, 228.0786; found, 228.0790.

Methyl 4-((3-chloro-2-hydroxypropyl)amino)benzoate (1'f). White solid. 2.05 g 45% Yield

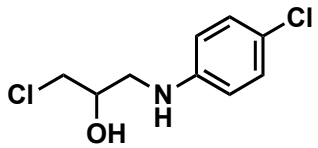


^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 – 7.78 (m, 2H), 6.70 – 6.55 (m, 2H), 4.56 – 4.48 (bs, 1H), 4.16 – 4.07 (m, 1H), 3.87 (s, 3H), 3.74 – 3.61 (m, 2H), 3.46 (ddd, *J* = 13.4, 6.7, 4.4 Hz, 1H), 3.31 (ddd, *J* = 13.4, 7.2, 5.4 Hz, 1H), 2.64 (d, *J* = 5.2 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.4, 151.8, 131.8, 119.2, 112., 69.9, 51.8, 47.6, 46.4. **FT-IR** (neat, *v* in cm^{-1}): 3354, 2947, 1678, 1607, 1280, 1107. **ESI-MS** $[C_{11}H_{14}ClNNaO_3]^+$: calcd, 266.0554; found, 266.0551.

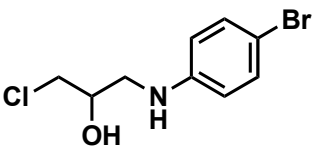
1-Chloro-3-((4-fluorophenyl)amino)propan-2-ol (1'g).[16] Violet oil, 2.62 g 51% Yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.95 – 6.87 (m, 2H), 6.70 – 6.64 (m, 2H), 4.13 – 4.07 (m, 1H), 3.88 – 3.70 (bs, 1H), 3.70 – 3.59 (m, 2H), 3.34 (dd, *J* = 13.0, 4.2 Hz, 1H), 3.20 (dd, *J* = 13.0, 7.4 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 155.8, 144.2, 116.2, 115.9, 115.2, 115.2, 69.7, 48.61, 47.7, 31.0.



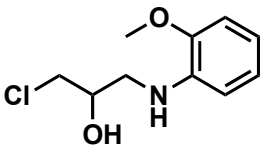
1-Chloro-3-((4-chlorophenyl)amino)propan-2-ol (1'h).[13] Yellow oil, 3.9 g, 45% Yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.19 – 7.09 (m, 2H), 6.62 – 6.54 (m, 2H), 4.11 – 4.03 (m, 1H), 3.72 – 3.58 (m, 2H), 3.35 (dd, *J* = 13.2, 4.3 Hz, 1H), 3.20 (dd, *J* = 13.2, 7.2 Hz, 1H), 2.46 (s, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 146.4, 129.3, 123.1, 114.6, 69.9, 47.8, 47.4.



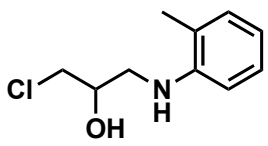
1-chloro-3-((4-bromophenyl)amino)propan-2-ol (1'i).[17] Yellow oil, 2.1 g, 54% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.31 – 7.21 (m, 2H), 6.56 – 6.48 (m, 2H), 4.09 – 4.00 (m, 1H), 3.71 – 3.57 (m, 2H), 3.33 (dd, *J* = 13.2, 4.3 Hz, 1H), 3.19 (dd, *J* = 13.2, 7.2 Hz, 1H), 3.06 – 2.21 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 146.9, 132.2, 115.0, 110.0, 69.9, 47.8, 47.2.



1-Chloro-3-((2-methoxyphenyl)amino)propan-2-ol (1'j).[18] Dark oil, 2.62 g, 49% Yield. **^{1}H NMR** ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.88 (td, *J* = 7.6, 1.5 Hz, 1H), 6.79 (dd, *J* = 8.0, 1.5 Hz, 1H), 6.75 – 6.69 (m, 1H), 6.67 (dd, *J* = 7.8, 1.5 Hz, 1H), 4.53 (bs, 1H), 4.15 – 4.05 (m, 1H), 3.86 (s, 3H), 3.75 – 3.61 (m, 2H), 3.45 – 3.34 (m, 1H), 3.33 – 3.24 (m, 1H), 2.48 (bs, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 121.4, 117.5, 110.4, 109.8, 70.1, 55.6, 47.9, 47.1.

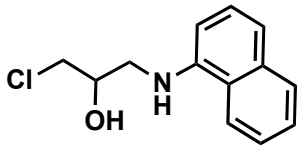


1-Chloro-3-(*o*-tolyl-amino)propan-2-ol (1'k).[19] Dark oil, 1.79 g, 19% Yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.16 – 7.10 (m, 1H), 7.10 – 7.06 (m, 1H), 6.74 – 6.68 (m, 1H), 6.68 – 6.63 (m, 1H), 4.18 – 4.10 (m, 1H), 3.87 (bs, 1H), 3.76 – 3.64 (m, 2H), 3.48 – 3.39 (m, 1H), 3.33 – 3.24 (m, 1H), 2.17 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 130.5, 127.3, 118.0, 109.8, 67.8, 48.0, 47.2, 17.6.

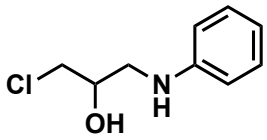


[16] A. Kamal, B. R. Prasad, A. M. Reddy and M. N. A. Khan *Catal. Comm.*, 2007, **8**, 1876–1880.
[17] V. Mirkhani, S.Tangestaninejad, B. Yadollahi and L. Alipanah, *Catal. Lett.*, 2005, **101**, 93-97.
[18] A.V. Nakhate, A.M. Doke and G. D. Yadav *Ind. Engin. Chem. Res.*, 2016, **41**, 10829-10838.
[19] L. Saikia, J.K. Satyarthi, D. Srinivas and K. Ratnasamy, *J. Catal.*, 2007, **252**, 148-160.

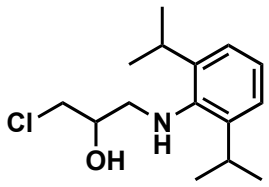
1-Chloro-3-(naphthalen-1-ylamino)propan-2-ol (1'l).[20] Violet oil, 1.26 g, 26% Yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.90 – 7.76 (m, 2H), 7.50 – 7.42 (m, 2H), 7.39 – 7.28 (m, 2H), 6.69 (d, *J* = 1.3 Hz, 1H), 4.32 – 4.20 (m, 1H), 3.82 – 3.67 (m, 2H), 3.64 – 3.53 (m, 1H), 3.48 – 3.37 (m, 1H), 2.61 (bs, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 129.2, 126.9, 126.4, 125.6, 120.4, 119.1, 105.8, 77.8, 77.5, 77.2, 70.2, 48.4, 47.9.



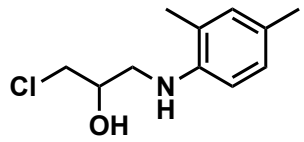
1-Chloro-3-(phenylamino)propan-2-ol (1'm).[21] Yellow oil, 2.36 g, 51% Yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.23 – 7.16 (m, 2H), 6.80 – 6.74 (m, 1H), 6.72 – 6.66 (m, 2H), 4.13 – 4.05 (m, 1H), 3.71 – 3.59 (m, 2H), 3.55 – 3.33 (m, 2H), 3.24 (dd, *J* = 13.3, 7.2 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 147.5, 129.6, 118.8, 113.8, 77.5, 77.2, 76.8, 69.9, 47.8, 47.6, 31.1.



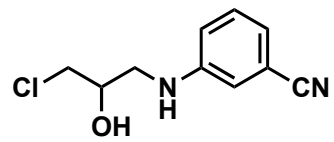
1-Chloro-3-((2,6-di-*iso*-propylphenyl)amino)propan-2-ol (1'n).[22] Reddish solid, 2.94 g, 44% Yield. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.15 – 7.03 (m, 3H), 4.10 – 4.03 (m, 1H), 3.75 – 3.65 (m, 2H), 3.38 – 3.22 (m, 2H), 3.11 – 3.03 (m, 1H), 3.03 – 2.95 (m, 1H), 2.82 (bs, 1H), 1.25 (d, *J* = 6.9 Hz, 12H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 143.0, 142.2, 124., 123.81, 70.9, 54.4, 47.9, 27.7, 24.4.



1-Chloro-3-((2,4-dimethylphenyl)amino)propan-2-ol (1'o).[23] Dark oil, 2.54 g, 37 % Yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.95 (d, *J* = 2.1 Hz, 1H), 6.92 (s, 1H), 6.59 (d, *J* = 8.0 Hz, 1H), 4.17 – 4.09 (m, 1H), 3.74 – 3.62 (m, 2H), 3.44 – 3.37 (m, 1H), 3.16 – 2.50 (bs, 1H), 2.24 (s, 3H), 2.16 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 143.3, 131.4, 127.6, 123.2, 110.9, 69.9, 48.0, 47.7, 20.5, 17.6.



3-((3-Chloro-2-hydroxypropyl)amino)benzonitrile (1'p). Yellow oil, 3.20 g, 36% Yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.29 – 7.19 (m, 1H), 6.99 (dt, *J* = 7.6, 1.2 Hz, 1H), 6.88 – 6.80 (m, 2H), 4.30 (bs, 1H), 4.15 – 4.03 (m, 1H), 3.74 – 3.60 (m, 2H), 3.44 – 3.32 (m, 1H), 3.28 – 3.17 (m, 1H), 2.57 (d, *J* = 5.1 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 148.3, 130.1, 121.4, 119.5, 117.8, 115.4, 112.9, 69.8, 47.4, 46.6. **FT-IR** (neat, *v* in cm^{-1}): 3387, 2228, 1724, 1601, 1268. **ESI-MS** $[C_{10}H_{11}ClN_2NaO]^+$: calcd, 233.0452; found, 233.0443.



[20] S. Bansal, Y. Kumar, P. Pippal, D. K. Das, P. Pramanik and P.P. *New J. Chem.*, 2017, **41**, 2668-2671.

[21] A. K. Chakraborti. S. Rudrawar and A. Kondaskar *Eur. J. Org. Chem*., 2004, 3597-3600

[22] Y. L. N. Murthy, B. S. Diwakar, B. Govindh, R. Venu and K. Nagalakshmi, *Chem. Sci. Trans.*, 2013, **3**, 805-812.

[23] Z. Du, W. Zhang, Y. Zhang and Z. Wei, *J. Chem. Res.*, 2011, **12**, 726-728.

16. Schematic illustration of the vent oven

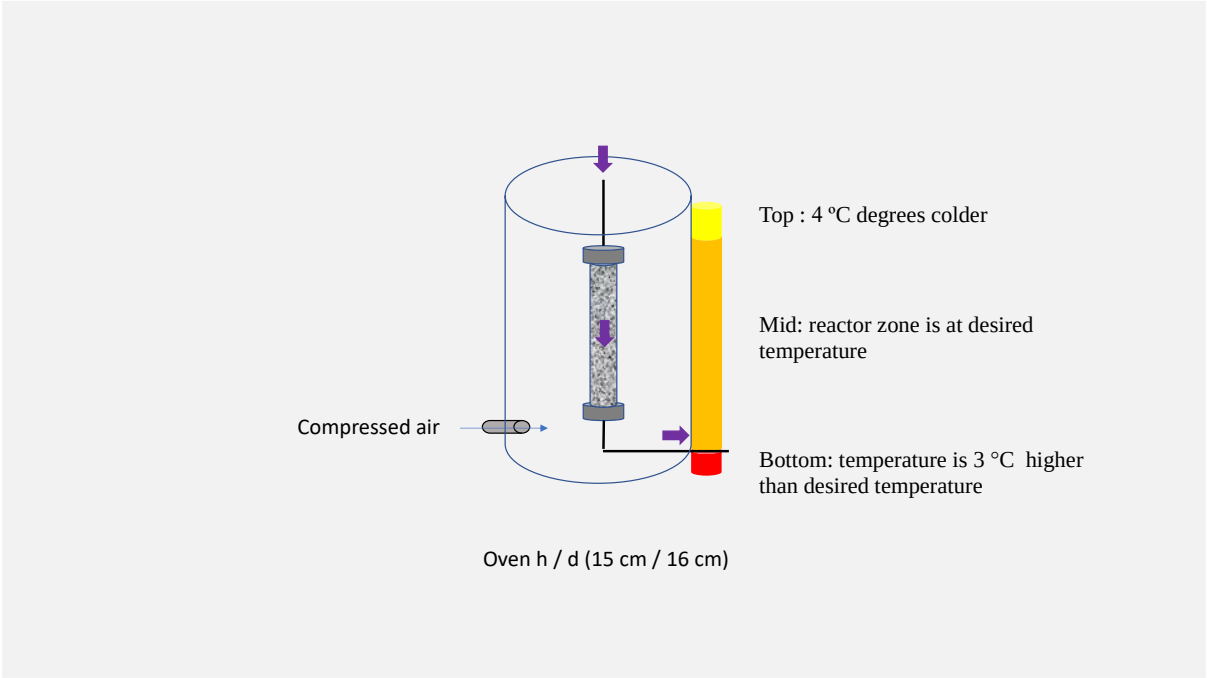


Figure S6. The figure shows the schematic set up of the ventilating oven. A digital thermometer was used to measure the temperature at different heights (h) in order to decide where to position the reactor. The oven was heated by an IKA heating plate, the oven was located on the top of the plate and the IKA sensor placed close to the reactor and inserted from a hole in the oven roof. To ensure a homogeneous temperature, compressed air was flowed from a channel located at the lower part of the oven and kept at a low flow during the experiments. d = diameter.

17. Auto-collector programming

A raspberry pi 4b was used as microcontroller, it was connected to a the Microservo SG90 (average price ~3€ at Amazon). The Servo was located in a polystyrene platform covered with Aluminum tape to protect it from any possible solvent leakage. The servo was controlled by a code written in Python using Mu a simple python editor. The code was modified from the one that can be found at the following link:
https://www.explainingcomputers.com/pi_servos_video.html

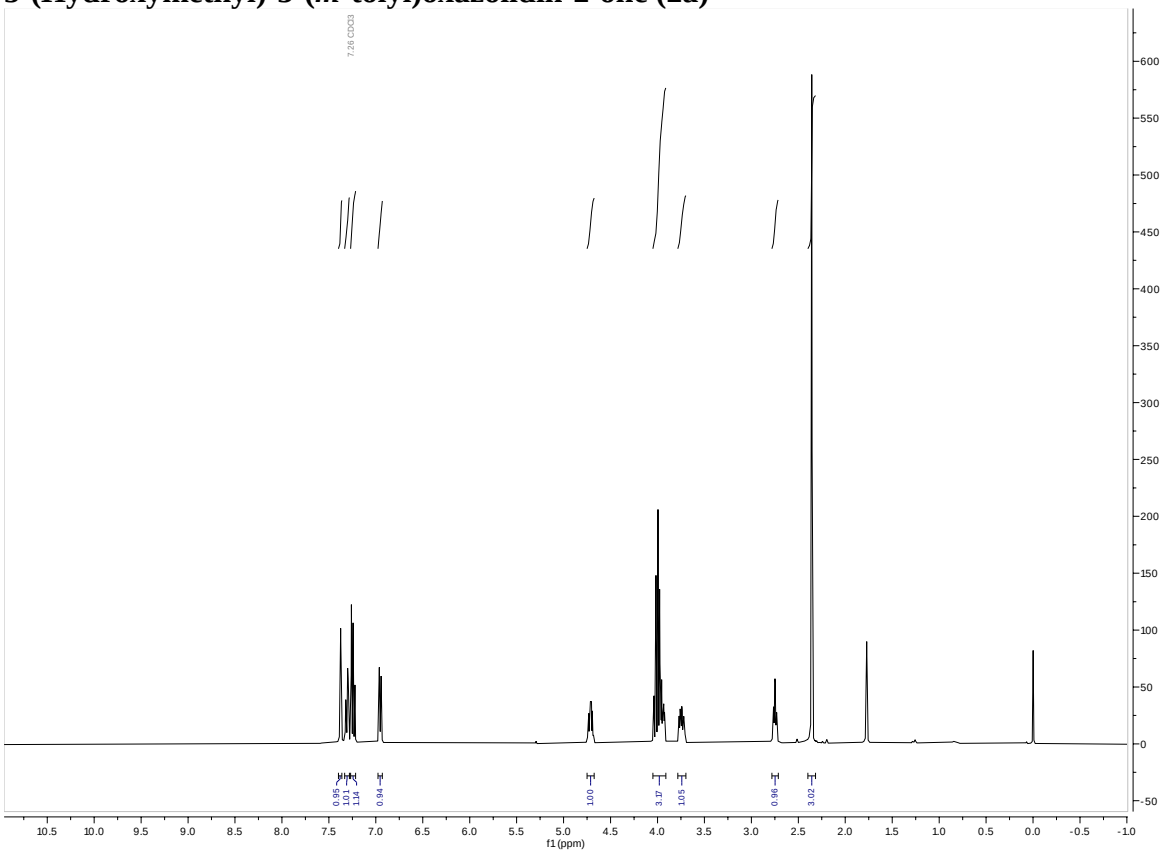
Python3 code for homemade auto-collector

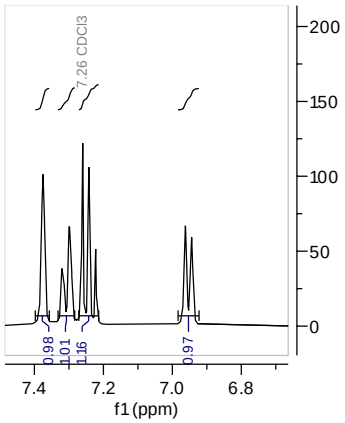
```
# Import libraries
import RPi.GPIO as GPIO
import time

# Set GPIO numbering mode
GPIO.setmode(GPIO.BOARD)
#  f number of fractions to be collected
f = int(input('how many fractions (values between 1 and 10)?'))
#  col number of seconds in which the collector stays still until next impulse
col = int(input('how many seconds do you want to collect?'))
# first fraction
f0 = int(input('how long do you want to collect f0 ?'))

#  Set pin 15 as an output, and set servo1 as pin 11 as PWM
GPIO.setup(15, GPIO.OUT)
# Note 15 is pin, 50 = 50Hz pulse
servo1 = GPIO.PWM(15, 50)

#  start PWM running, but with value of 0 (pulse off)
servo1.start(0)
f_str = str(f)
print('collecting ' + f_str + ' fractions')
col_str = str(col)
print(col_str + ' seconds collecting in every vial')
f0_str = str(f0)
print(f0_str + ' seconds collected in vial 0 ’)
time.sleep(f0)

#  Let's move the servo!
print('starting collection')

# Define variable duty
duty = 2

# Loop for duty values from 2 to 12 (0 to 180 degrees)
while duty <= 12:
    servo1.ChangeDutyCycle(duty)
    time.sleep(0.3)
```

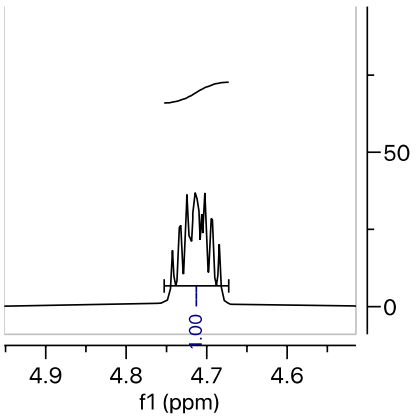
```
    servo1.ChangeDutyCycle(0)
    time.sleep(col)
    duty = duty + (10/f)

# Wait a couple of seconds
time.sleep(0.3)

# Turn back to 90 degrees
print('Turning back to initial position')
servo1.ChangeDutyCycle(2)
time.sleep(0.5)
servo1.ChangeDutyCycle(0)
time.sleep(1.5)

#  turn back to 0 degrees
print('Turning back to 0 degrees')
servo1.ChangeDutyCycle(2)
time.sleep(0.5)
servo1.ChangeDutyCycle(0)

#  Clean things up at the end
servo1.stop()
GPIO.cleanup()
print('Going back to position 0')
```

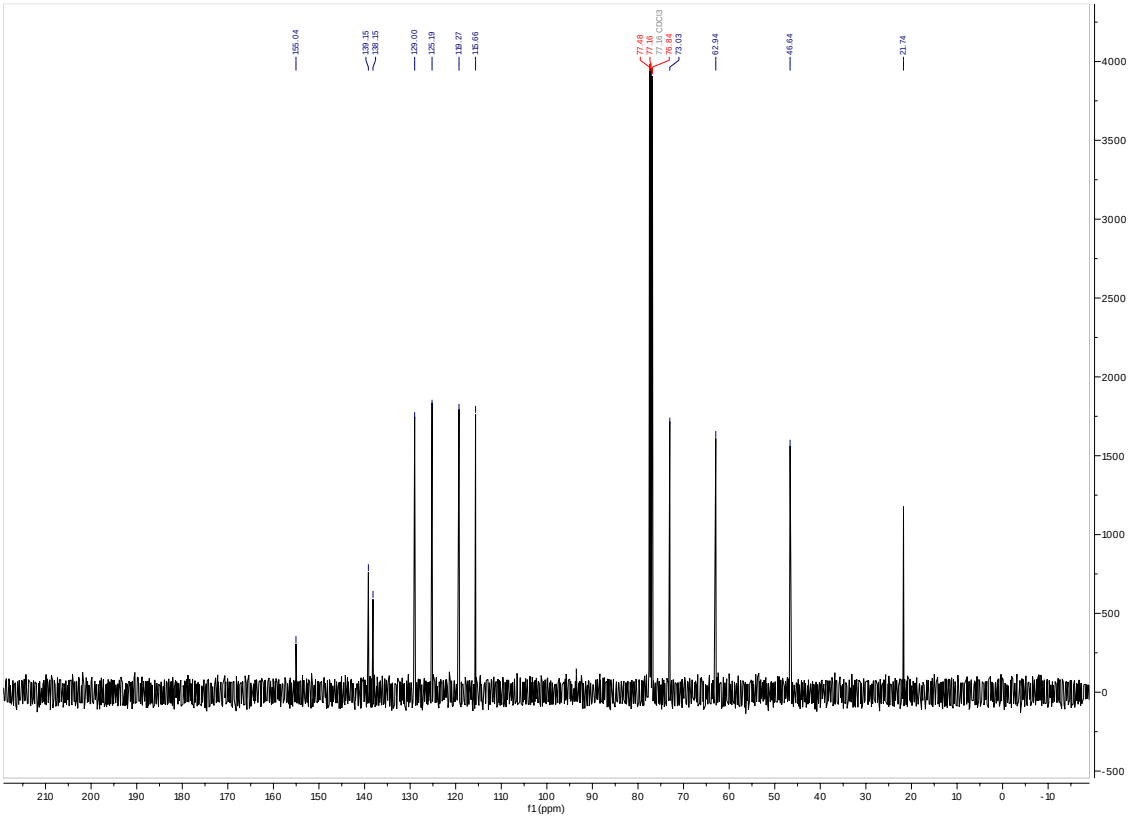
18. ^{1}H NMR, ^{13}C NMR, FT-IR spectra of the oxazolidinones products

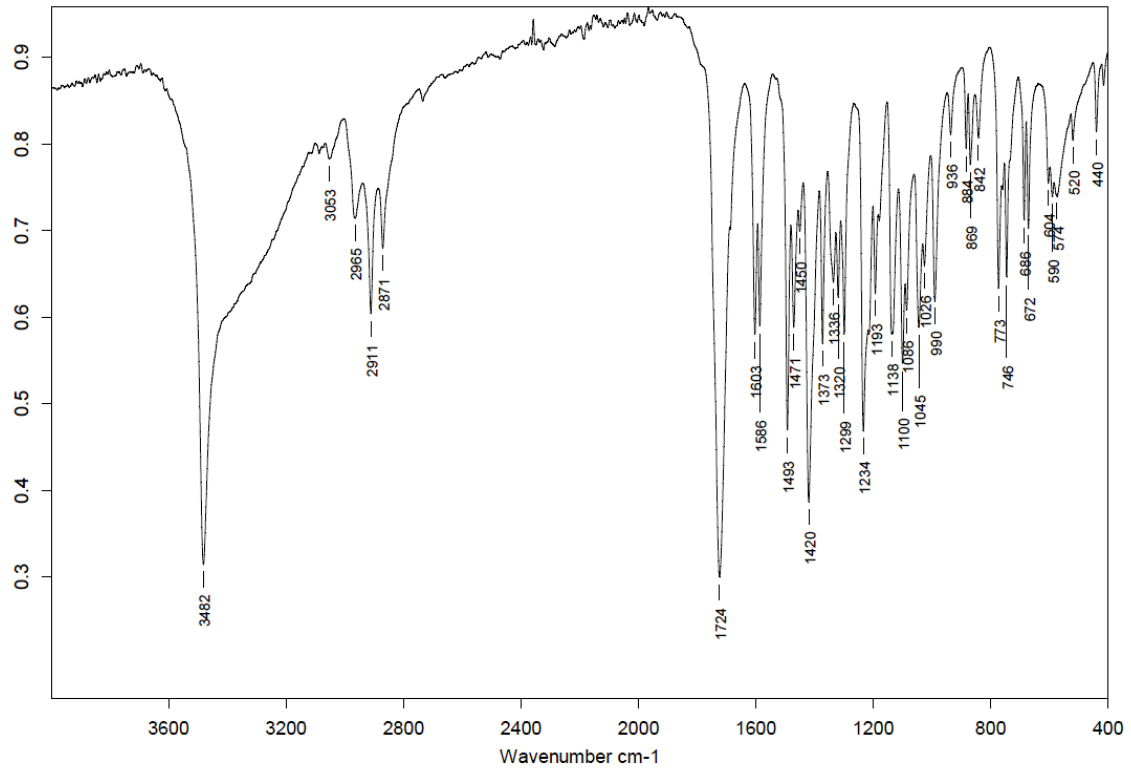
5-(Hydroxymethyl)-3-(*m*-tolyl)oxazolidin-2-one (2a)



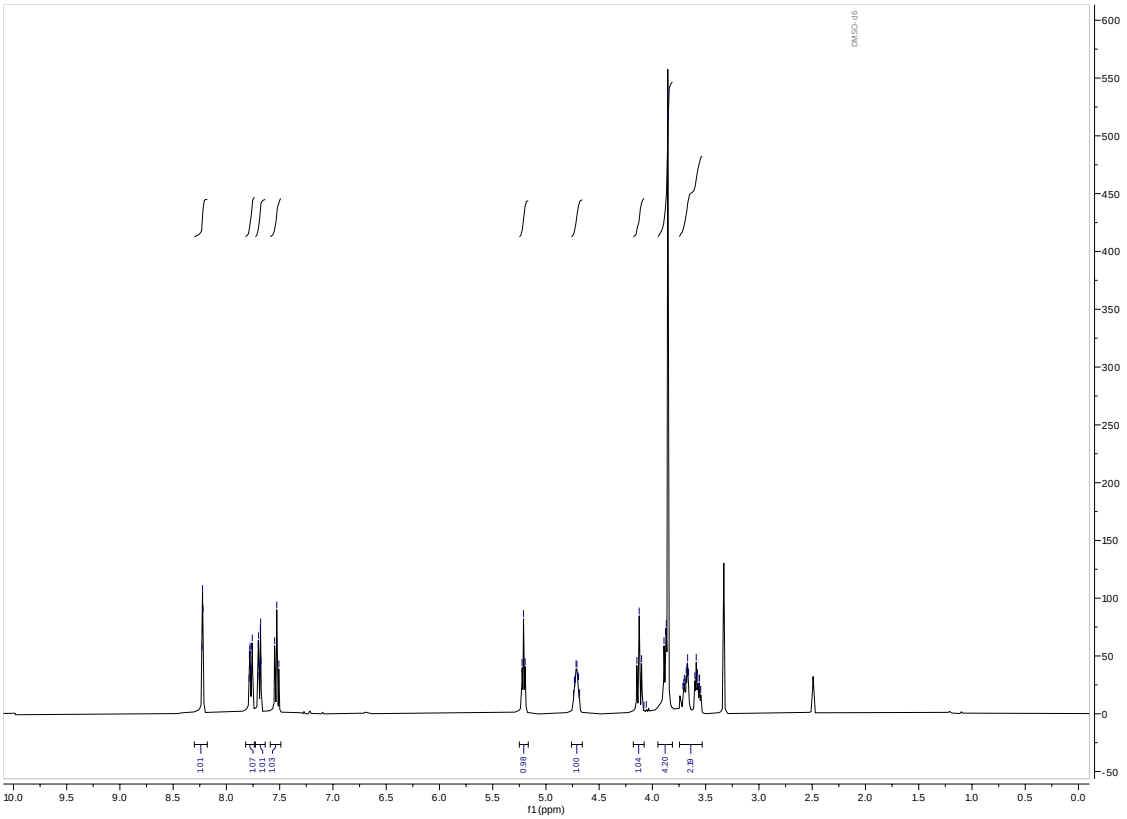


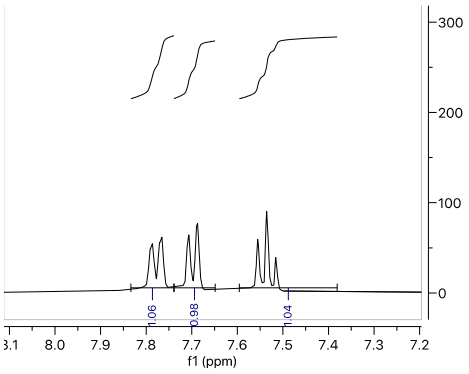


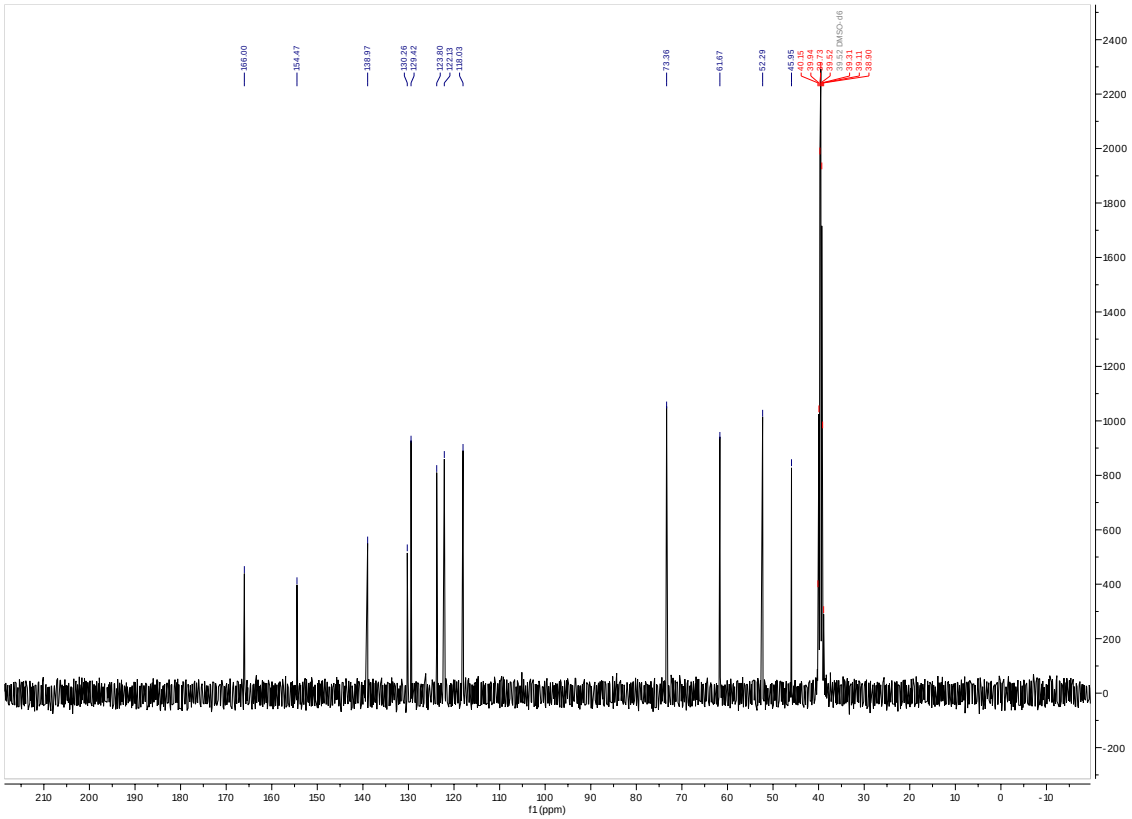

155.04
139.15
138.15
129.00
125.19
118.27
115.66
77.48
77.16
76.84
CDCl3
73.03
62.94
46.64
21.74
f1 (ppm)


3482
3053
2965
2911
2871
1724
1603
1586
1493
1471
1450
1420
1373
1336
1320
1299
1234
1193
1138
1100
1086
1045
1026
990
936
884
869
842
773
746
686
672
604
590
574
520
440
Wavenumber cm-1

Ethyl 3-(5-(hydroxymethyl)-2-oxooxazolidin-3yl)benzoate (2b)






166.00
154.47
138.97
130.26
129.42
123.80
123.33
118.03
73.36
61.67
52.29
45.95
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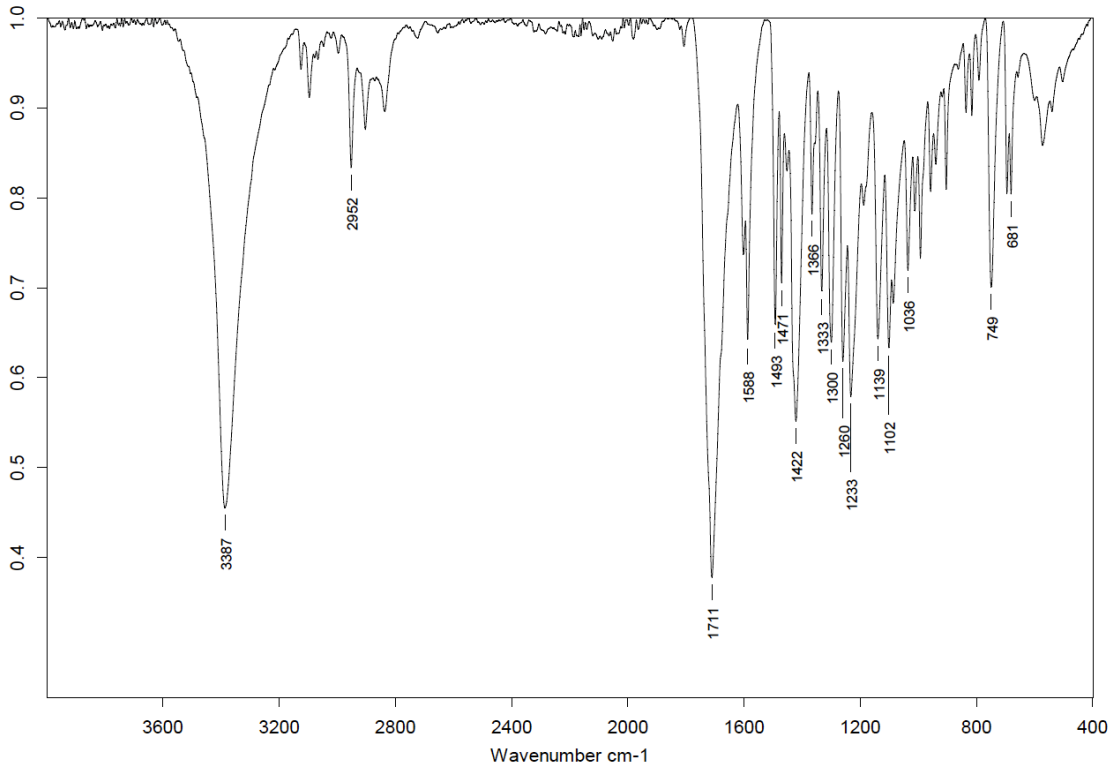
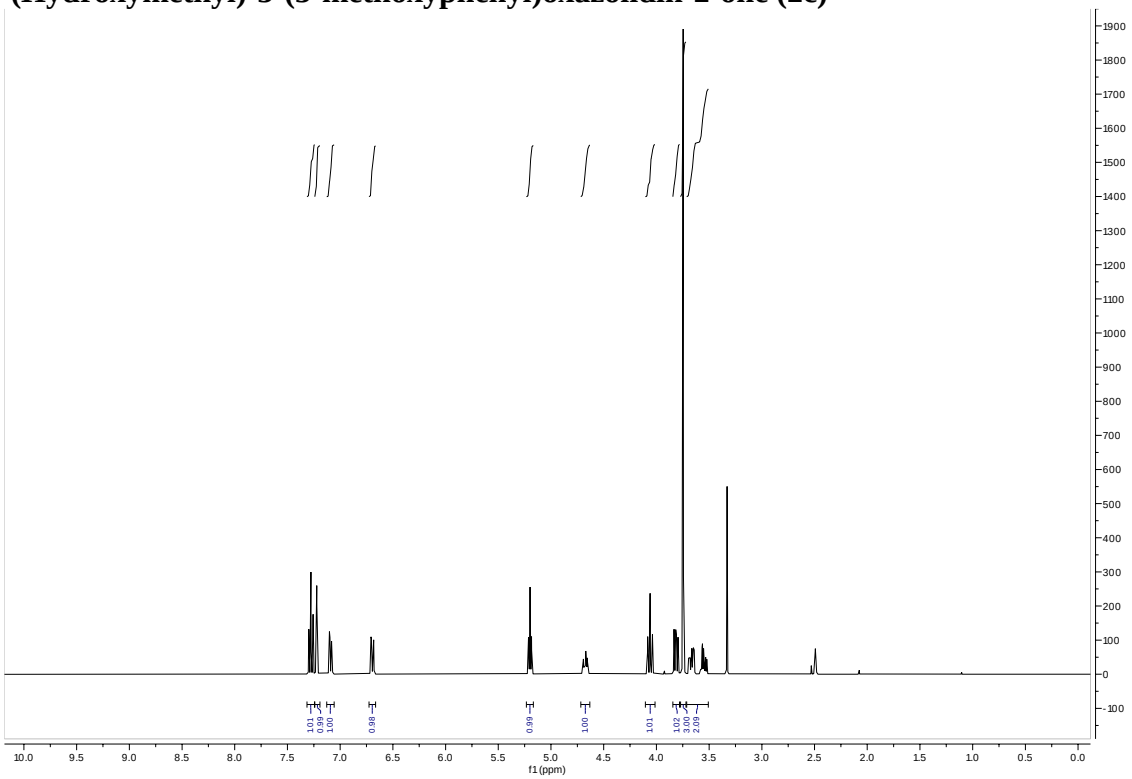
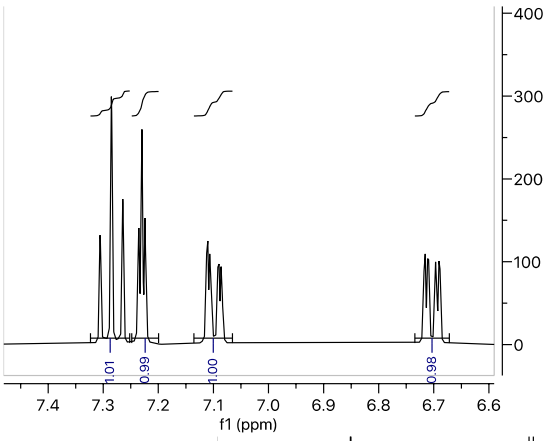
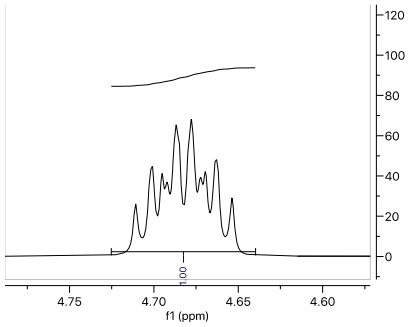
39.94
39.73
39.52
39.31
39.11
38.90
DMSO-d6
f1 (ppm)

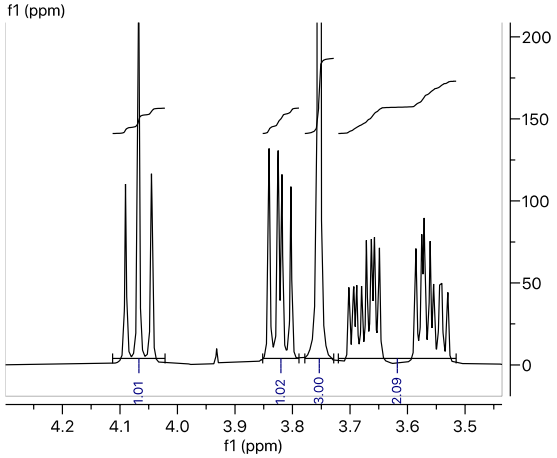

3387
2952
1711
1588
1493
1471
1422
1366
1333
1300
1260
1233
1139
1102
1036
749
681
Wavenumber cm-1

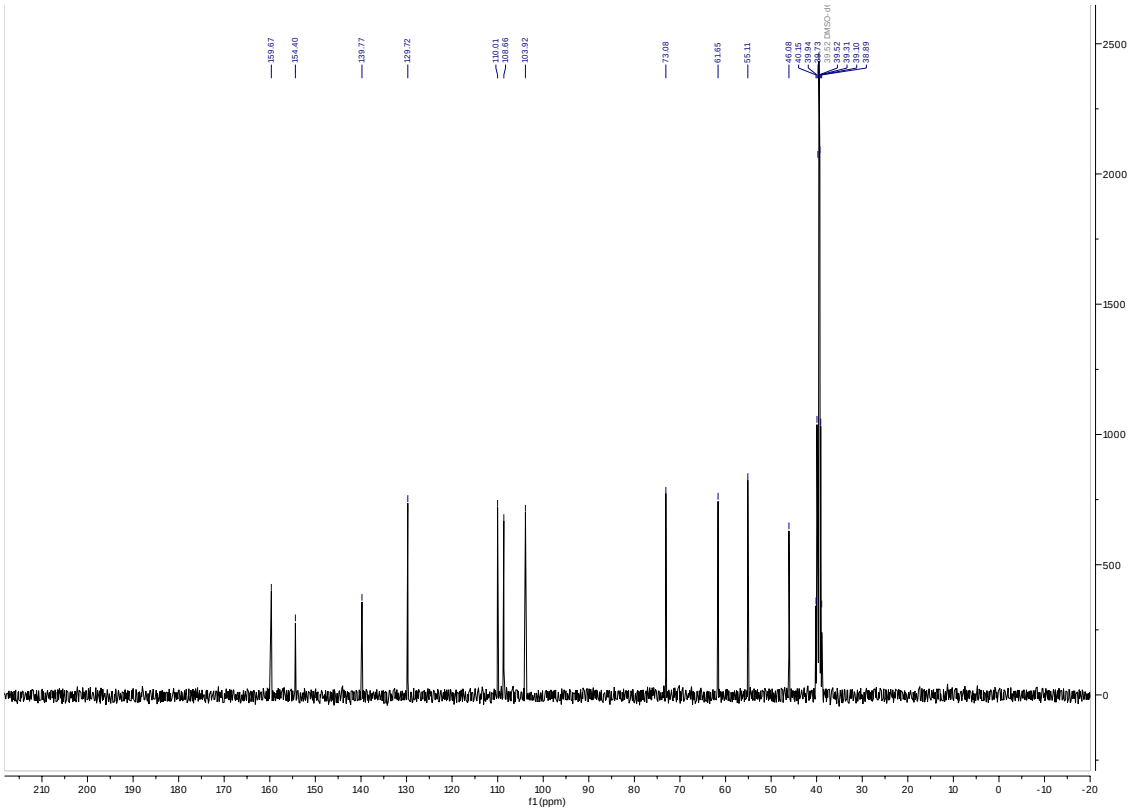
5-(Hydroxymethyl)-3-(3-methoxyphenyl)oxazolidin-2-one (2c)

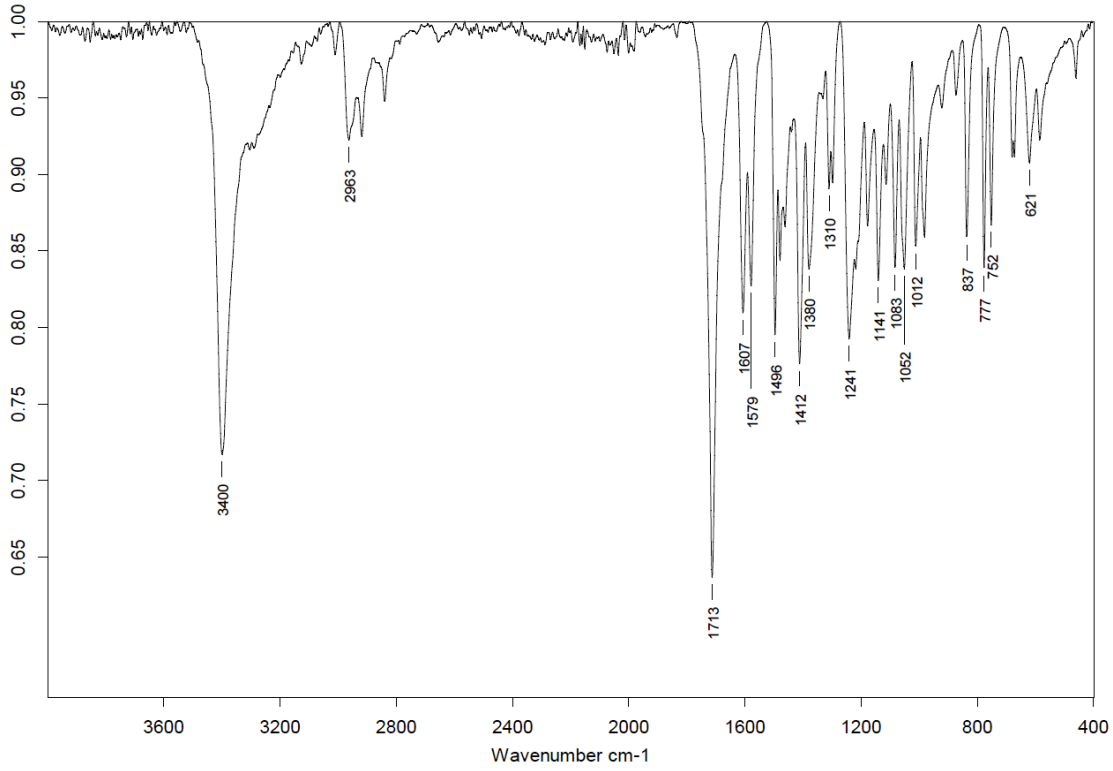




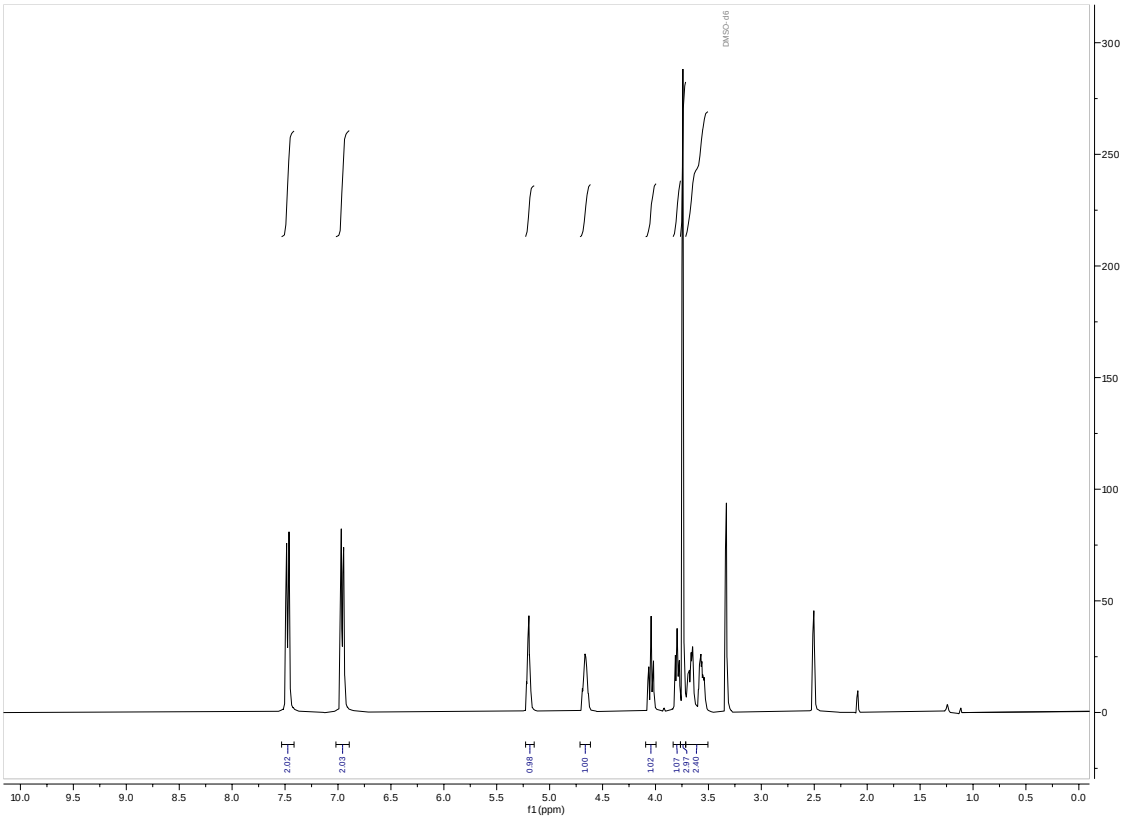


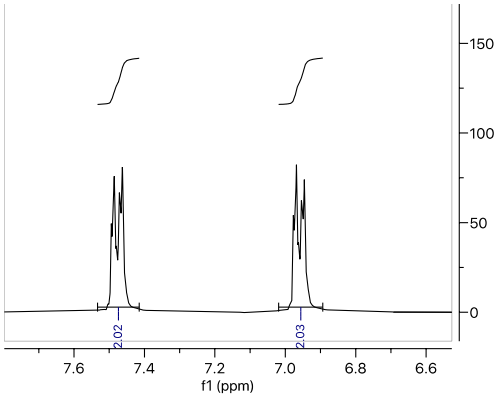


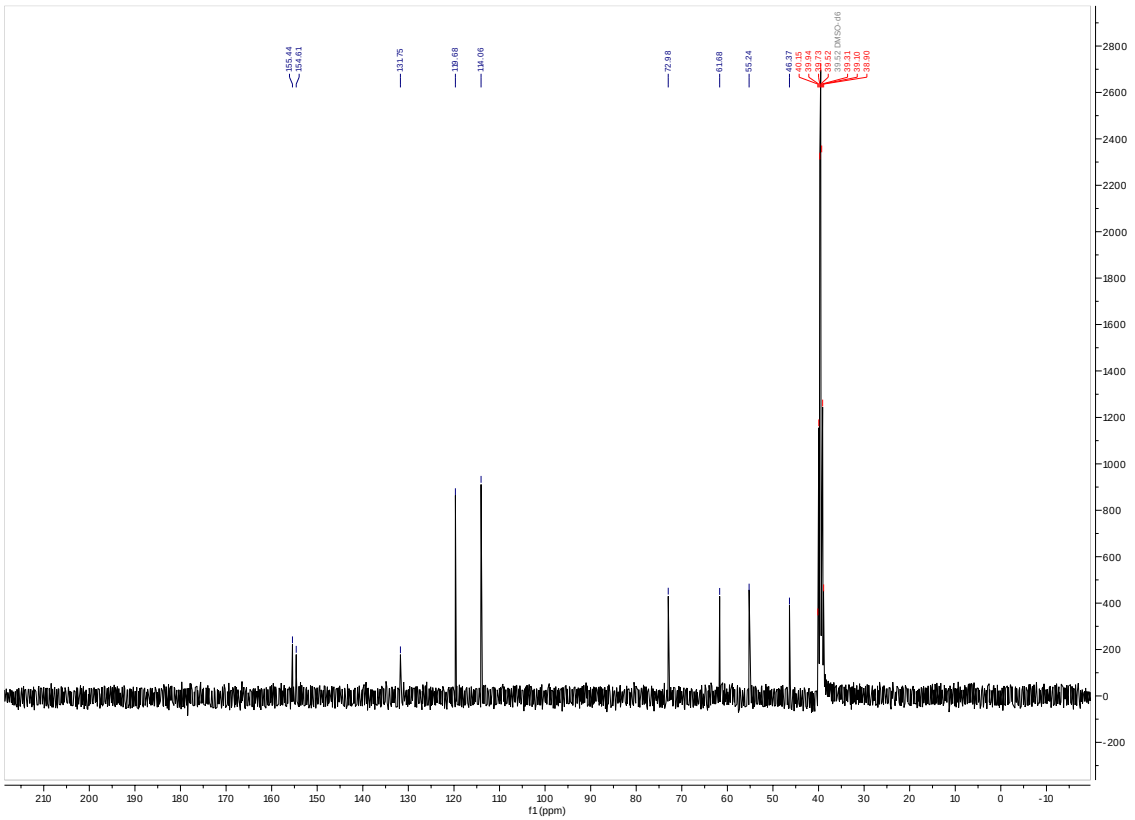

159.67
154.40
139.77
129.72
110.01
109.66
103.92
73.08
61.65
55.11
40.08
39.94
39.73
39.52
39.31
39.10
38.89
DMSO-d6
f1 (ppm)

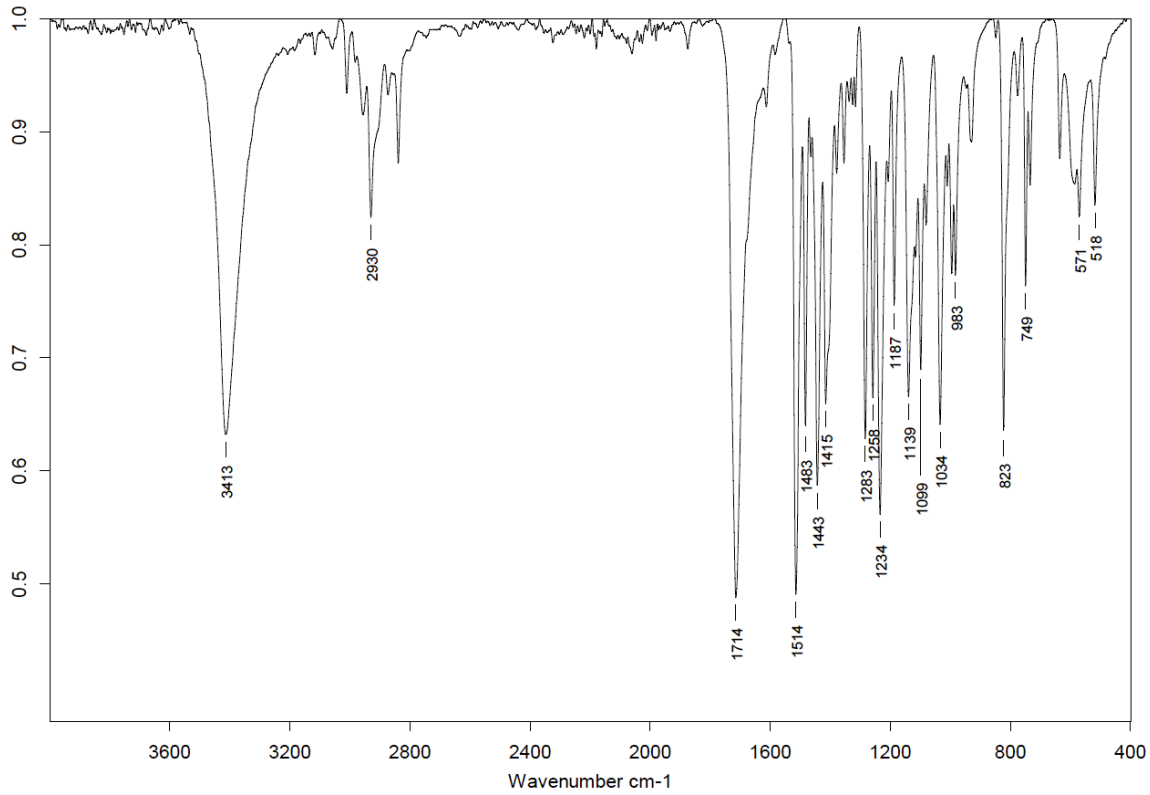

3400
2963
1713
1607
1579
1496
1412
1380
1310
1241
1141
1083
1052
1012
837
777
752
621
Wavenumber cm-1

5-(Hydroxymethyl)-3-(4-methoxyphenyl)oxazolidin-2-one (2d)

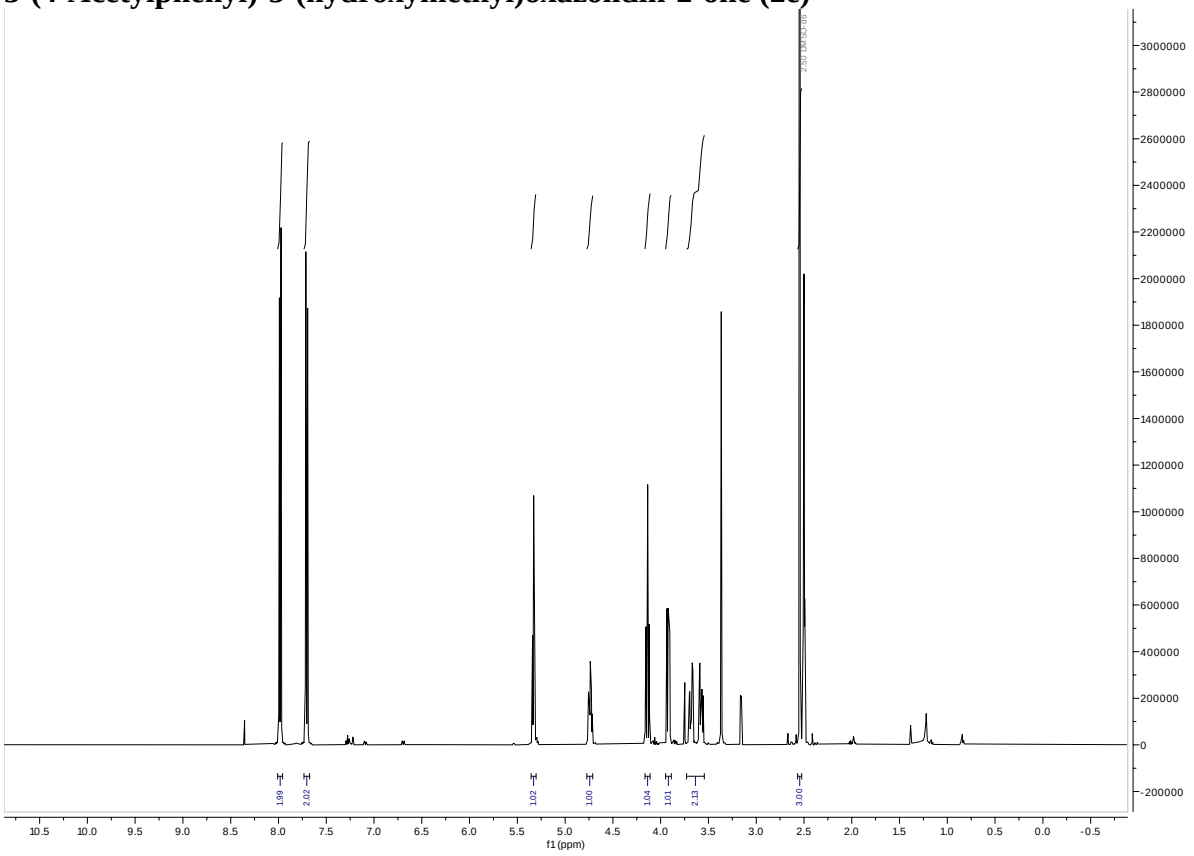


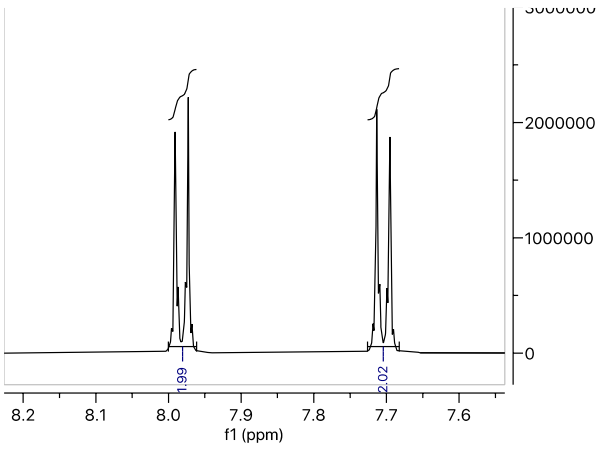


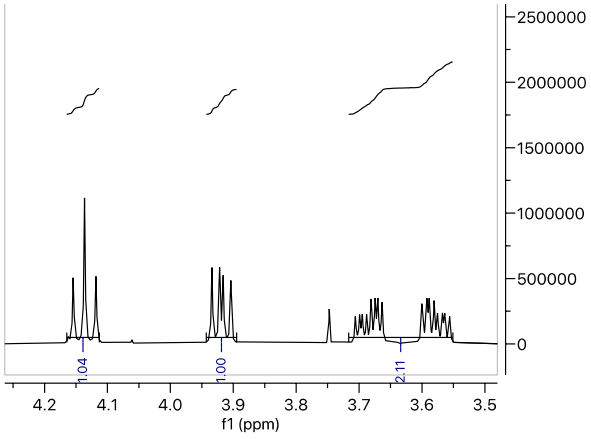

155.44
154.61
131.75
120.68
114.06
72.98
61.68
55.24
46.37
40.15
39.94
39.73
39.52
39.31
39.10
38.90
DMSO-d6
f1 (ppm)

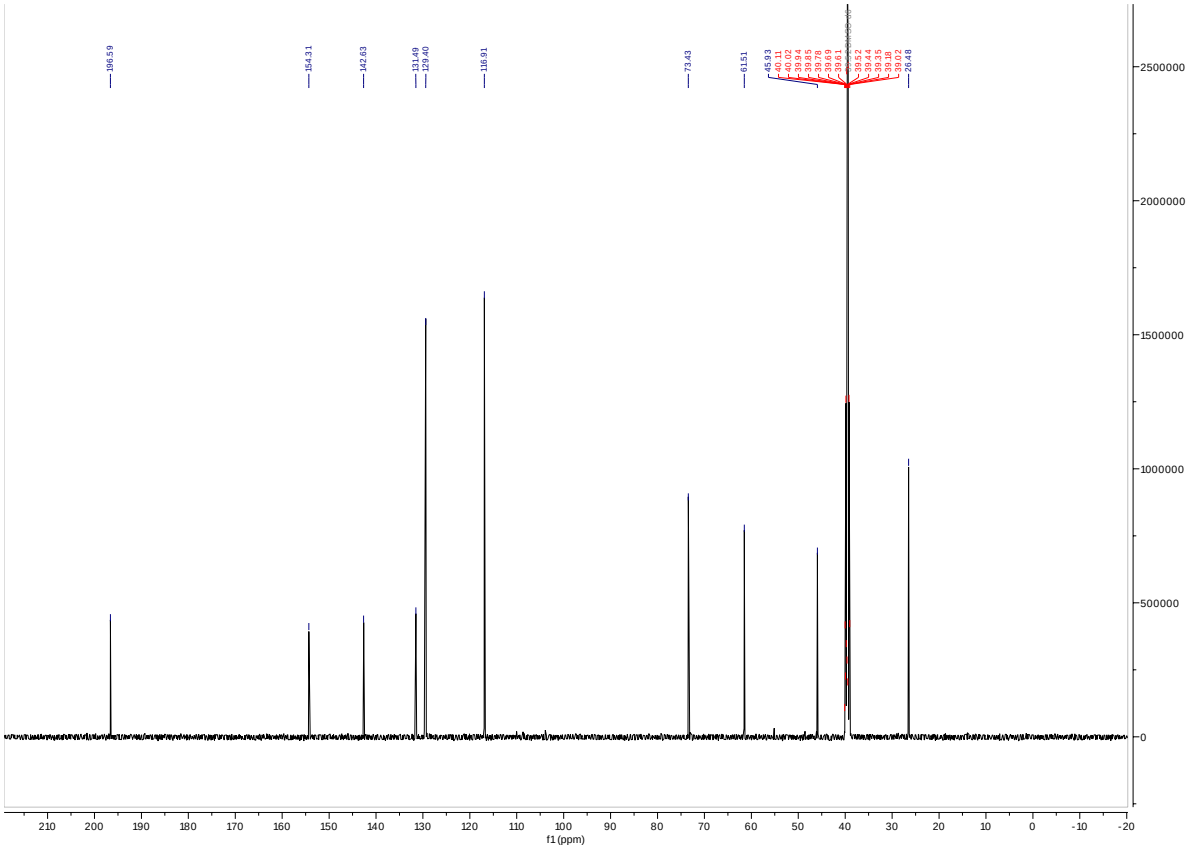

3413
2930
1714
1514
1483
1443
1415
1283
1258
1234
1187
1139
1099
1034
983
823
749
571
518
Wavenumber cm-1

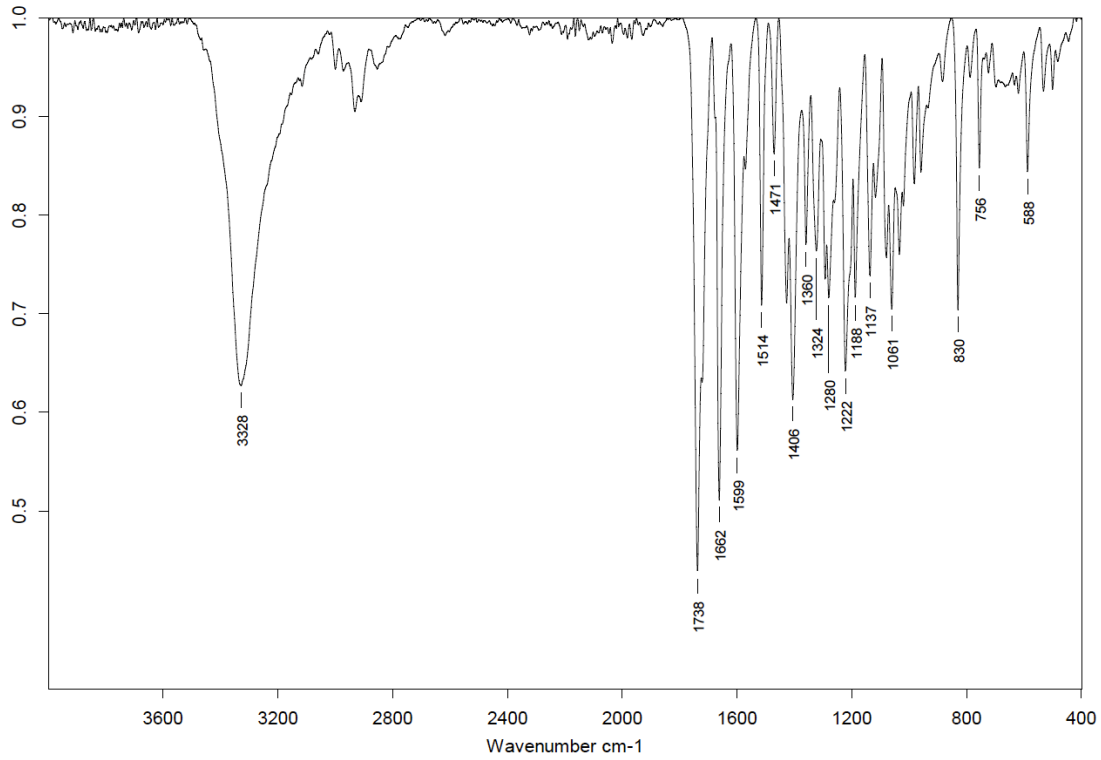
3-(4-Acetylphenyl)-5-(hydroxymethyl)oxazolidin-2-one (2e)



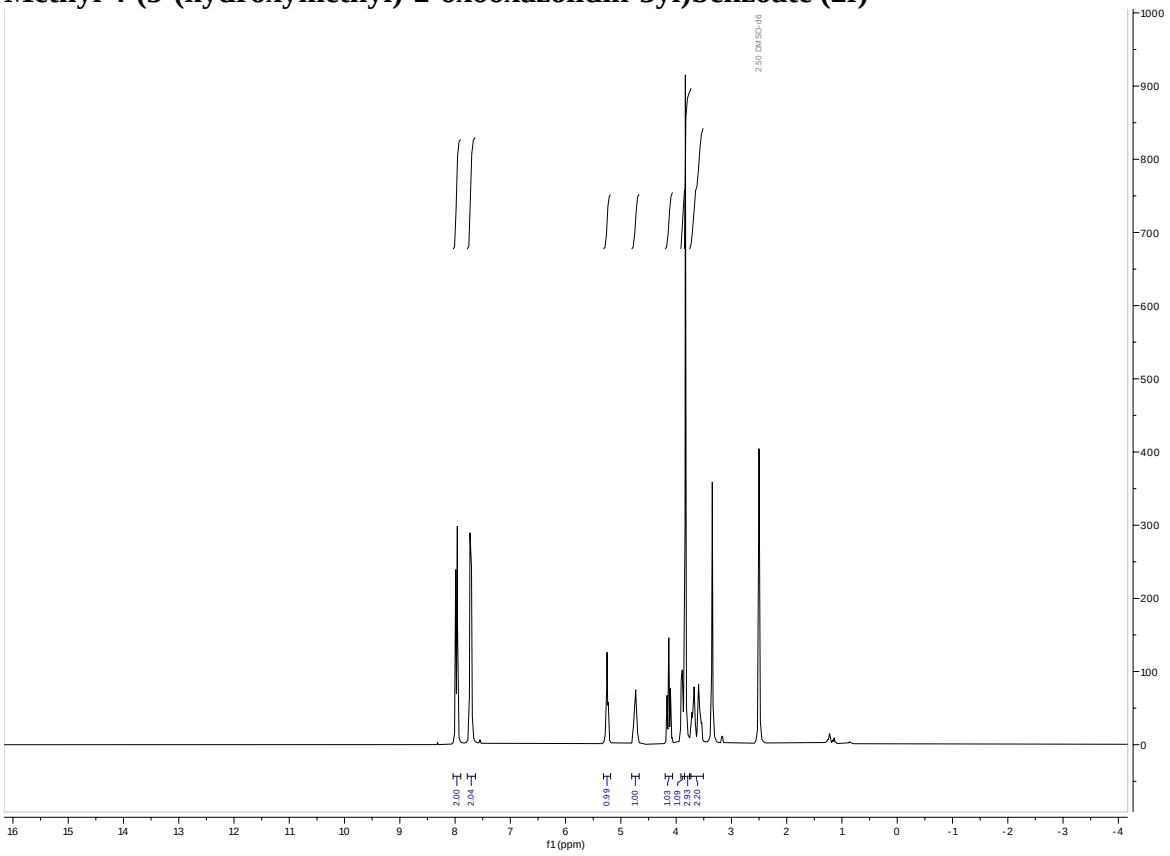


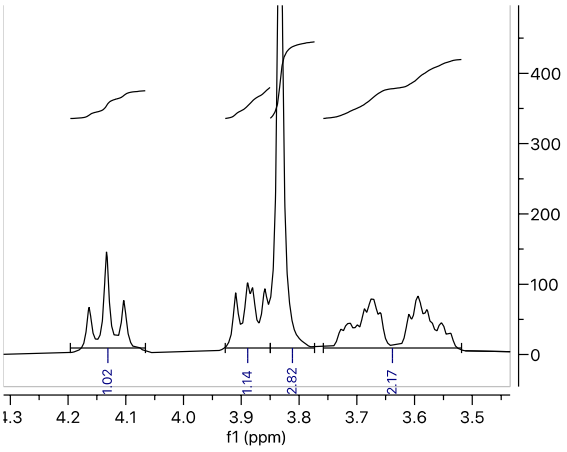


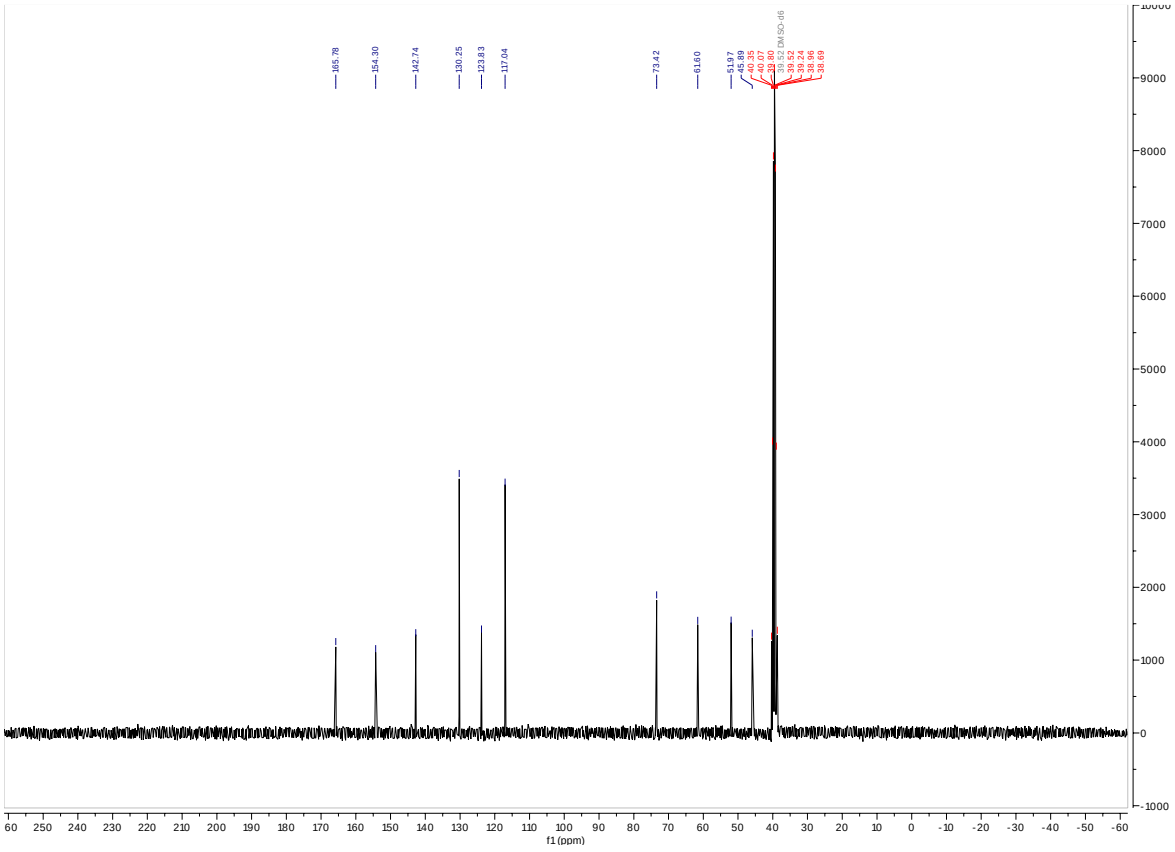

196.59
154.31
142.63
131.46
129.40
116.91
73.43
61.51
45.93
40.11
40.02
39.94
39.85
39.78
39.69
39.61
39.52
39.44
39.35
39.26
39.18
39.02
26.48
2500000
2000000
1500000
1000000
500000
0
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

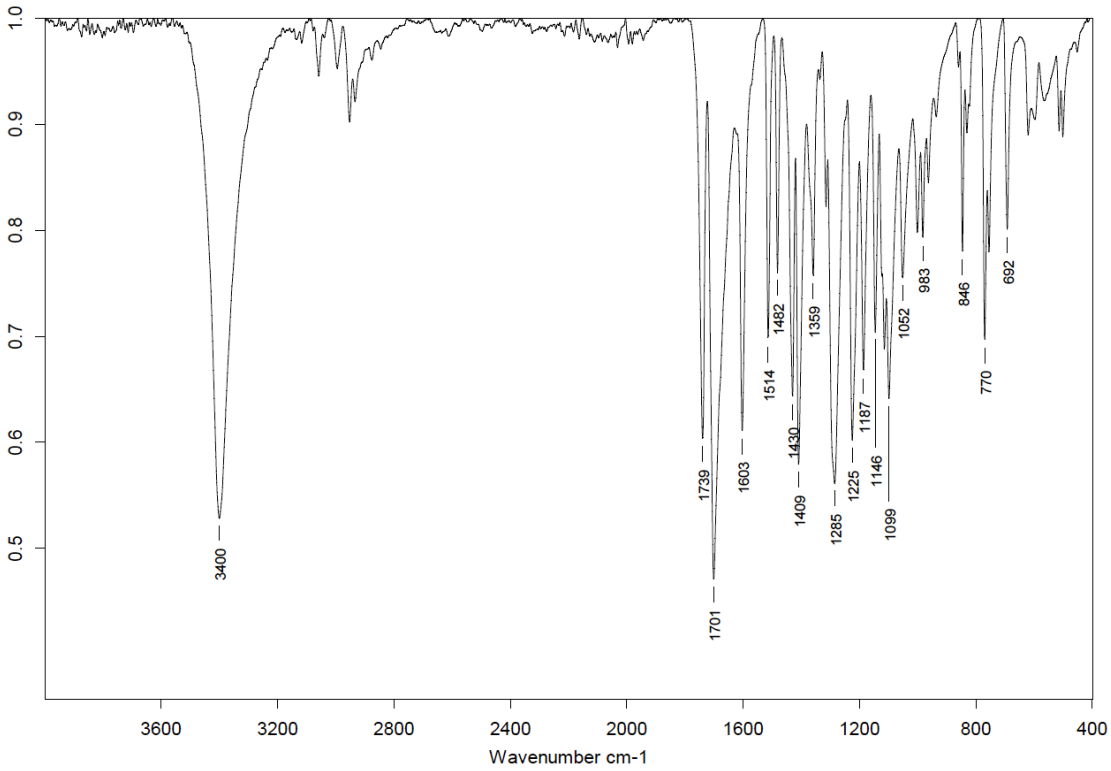

1.0
0.9
0.8
0.7
0.6
0.5
3328
1738
1662
1599
1514
1471
1406
1360
1324
1280
1222
1188
1137
1061
830
756
588
3600 3200 2800 2400 2000 1600 1200 800 400
Wavenumber cm-1

Methyl 4-(5-(hydroxymethyl)-2-oxooxazolidin-3yl)benzoate (2f)

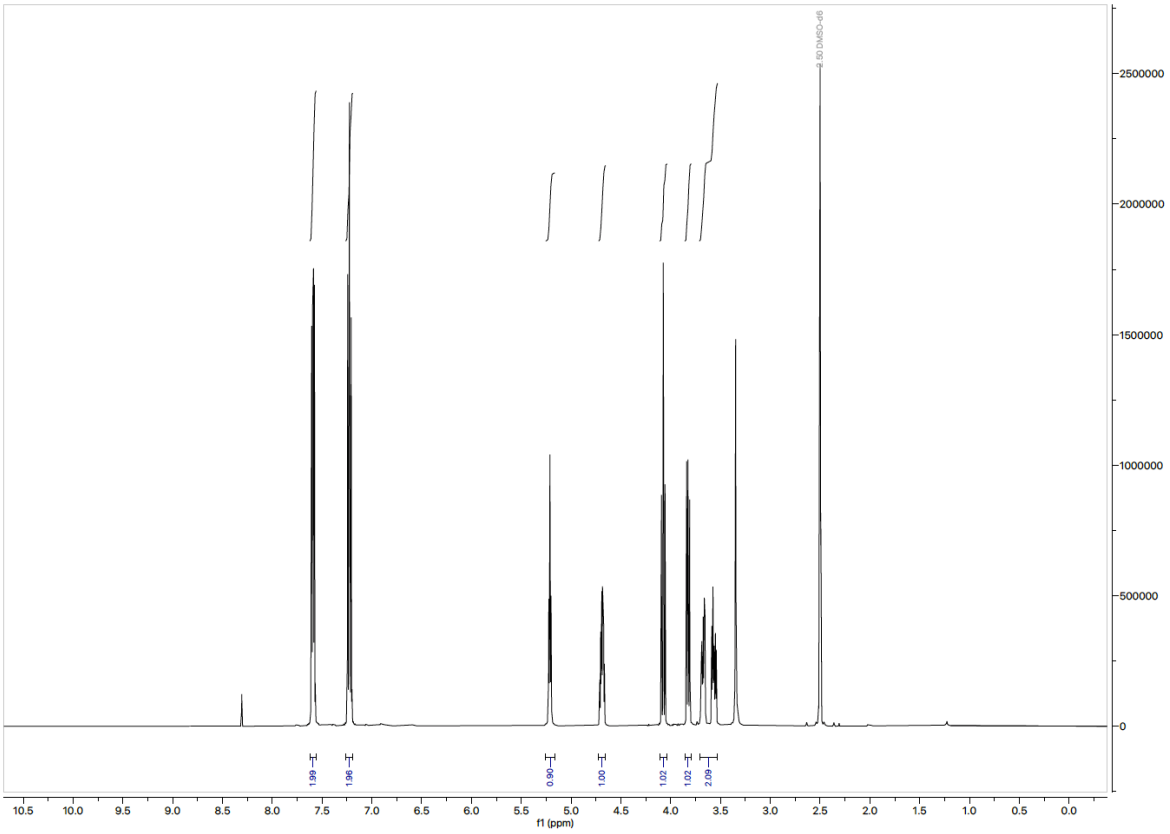


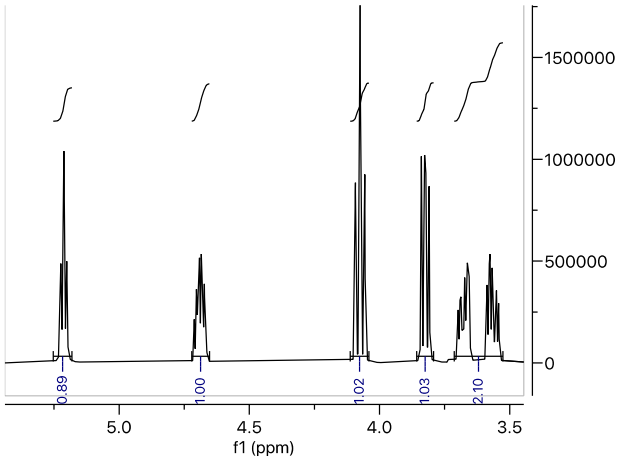


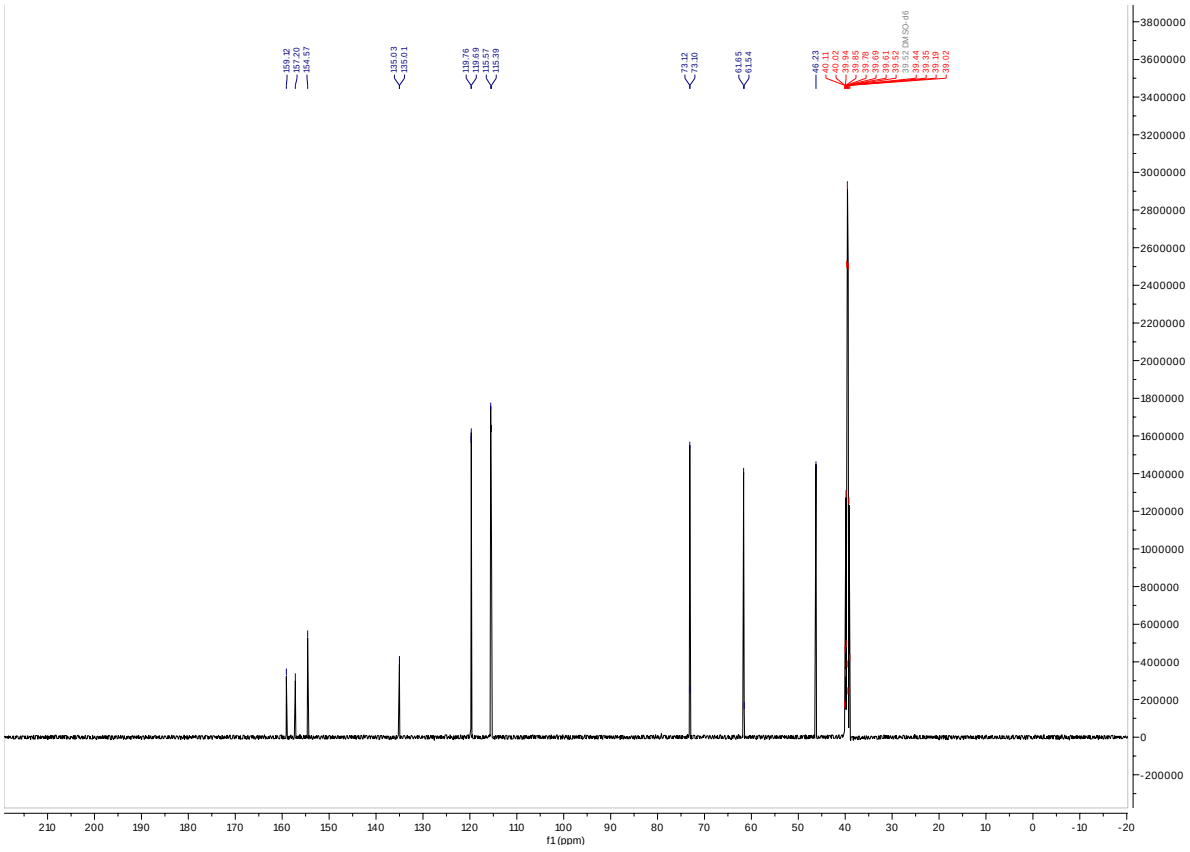

165.78
154.30
142.74
130.25
123.83
117.04
73.42
61.60
51.97
46.89
40.07
39.80
39.52 DMSO-d6
39.24
38.96
38.69
f1 (ppm)

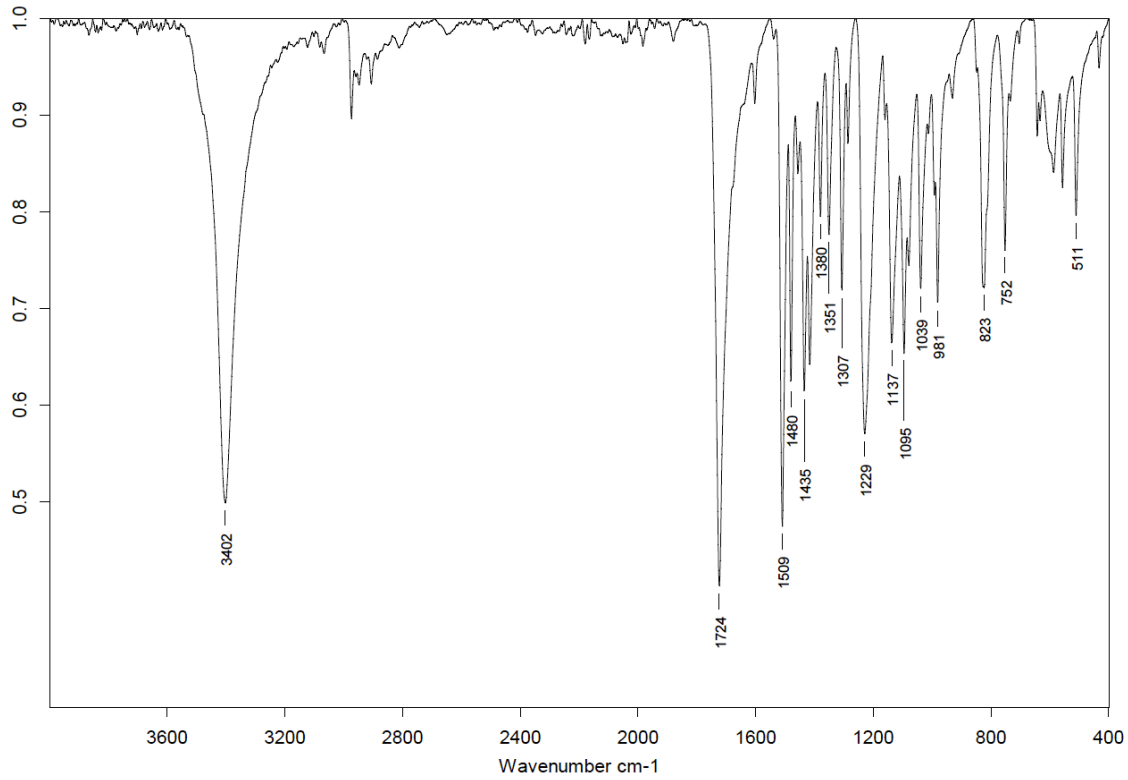

3400
1739
1701
1603
1514
1482
1430
1409
1359
1285
1225
1187
1146
1099
1052
983
846
770
692
Wavenumber cm-1

3-(4-Fluorophenyl)-5-(hydroxymethyl)oxazolidin-2-one (2g)

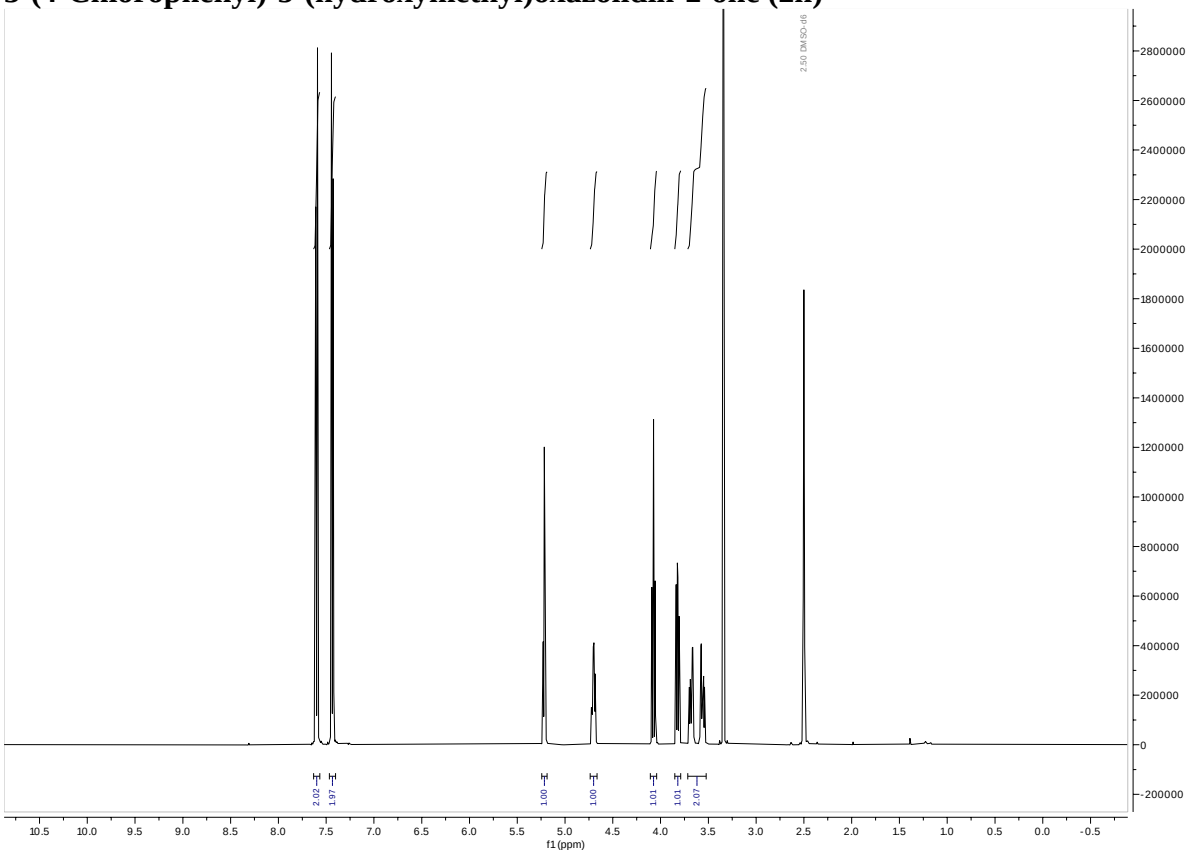


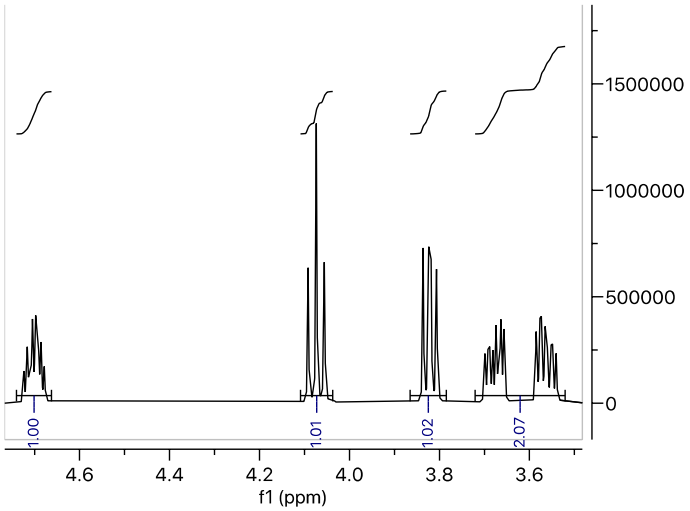


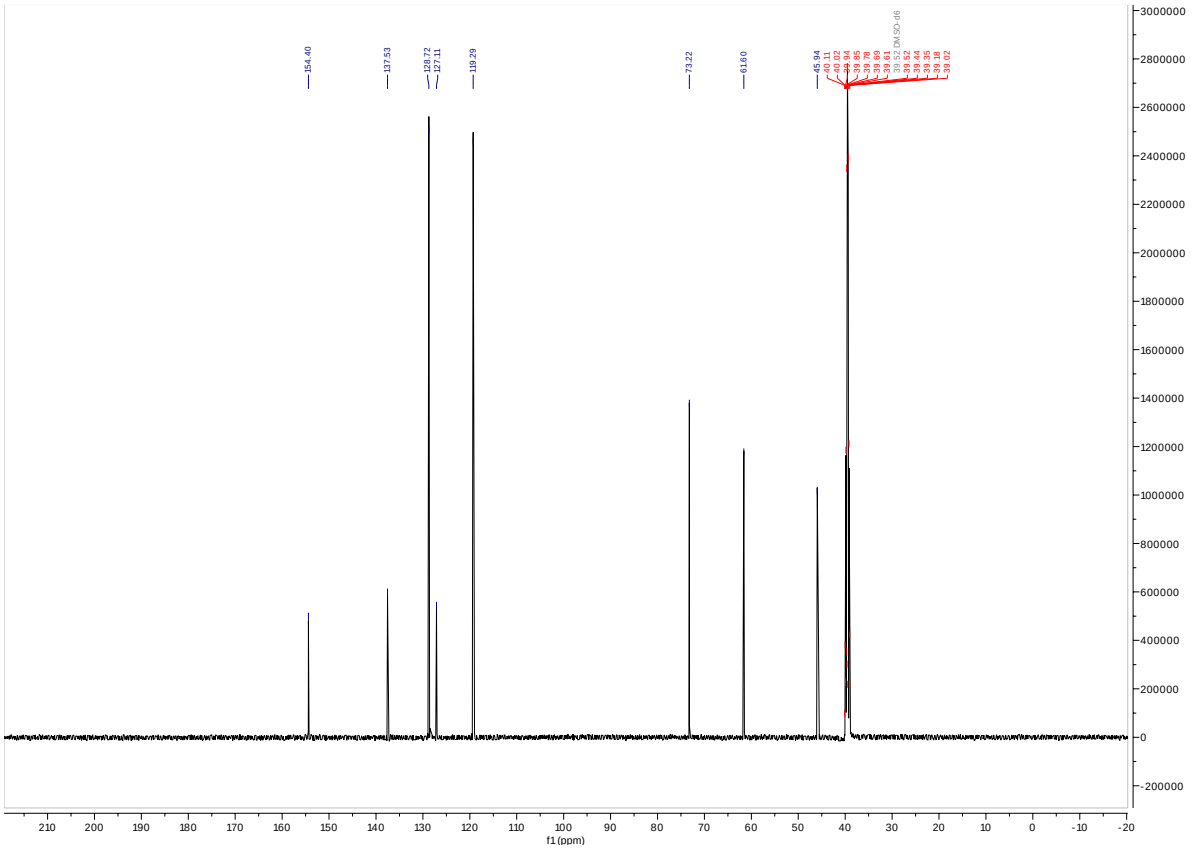

159.12
157.20
154.57
135.03
135.01
119.76
119.69
115.57
115.39
73.12
73.10
61.65
61.54
46.23
40.11
40.02
39.94
39.85
39.78
39.69
39.61
39.52
39.44
39.35
39.19
39.02
f1 (ppm)

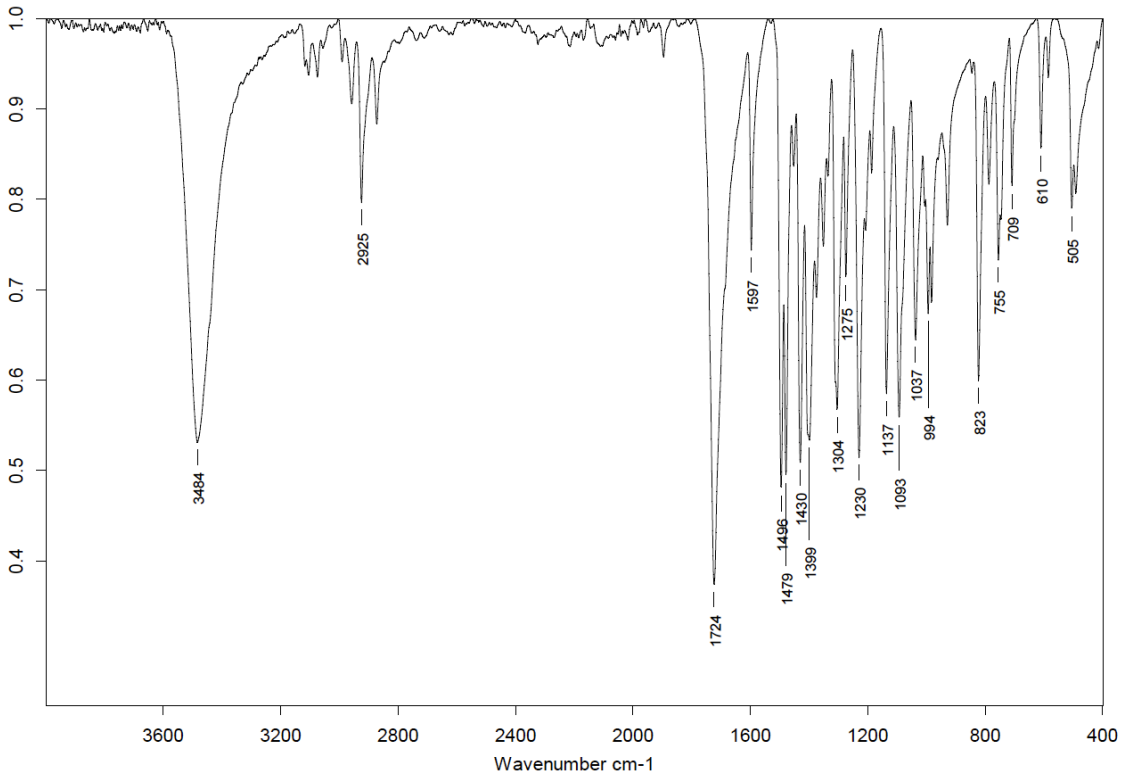

3402
1724
1509
1480
1435
1380
1351
1307
1229
1137
1095
1039
981
823
752
511
Wavenumber cm-1

3-(4-Chlorophenyl)-5-(hydroxymethyl)oxazolidin-2-one (2h)

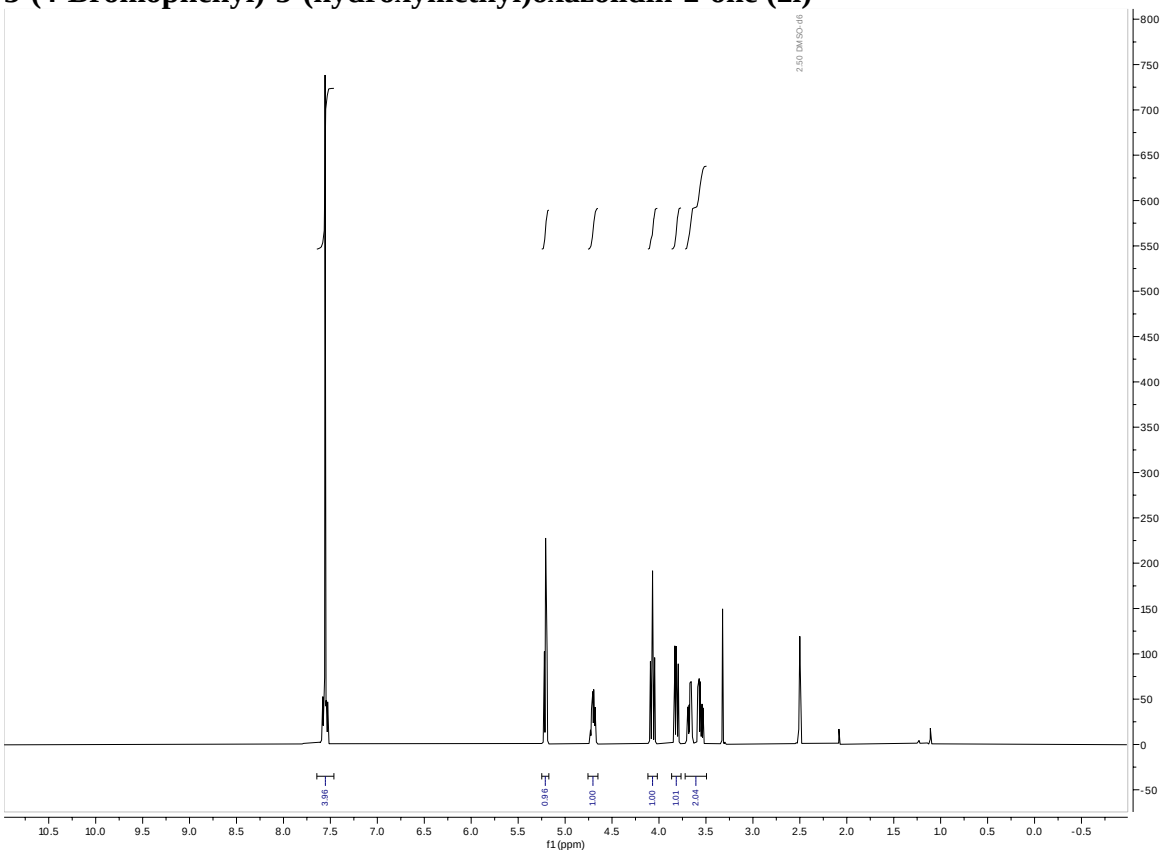


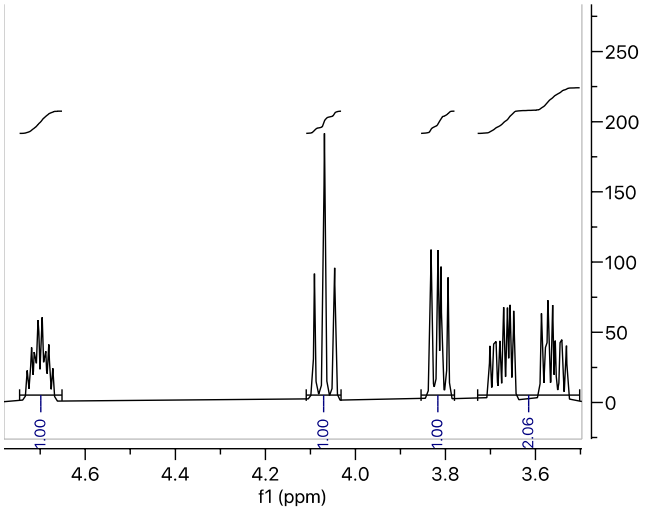


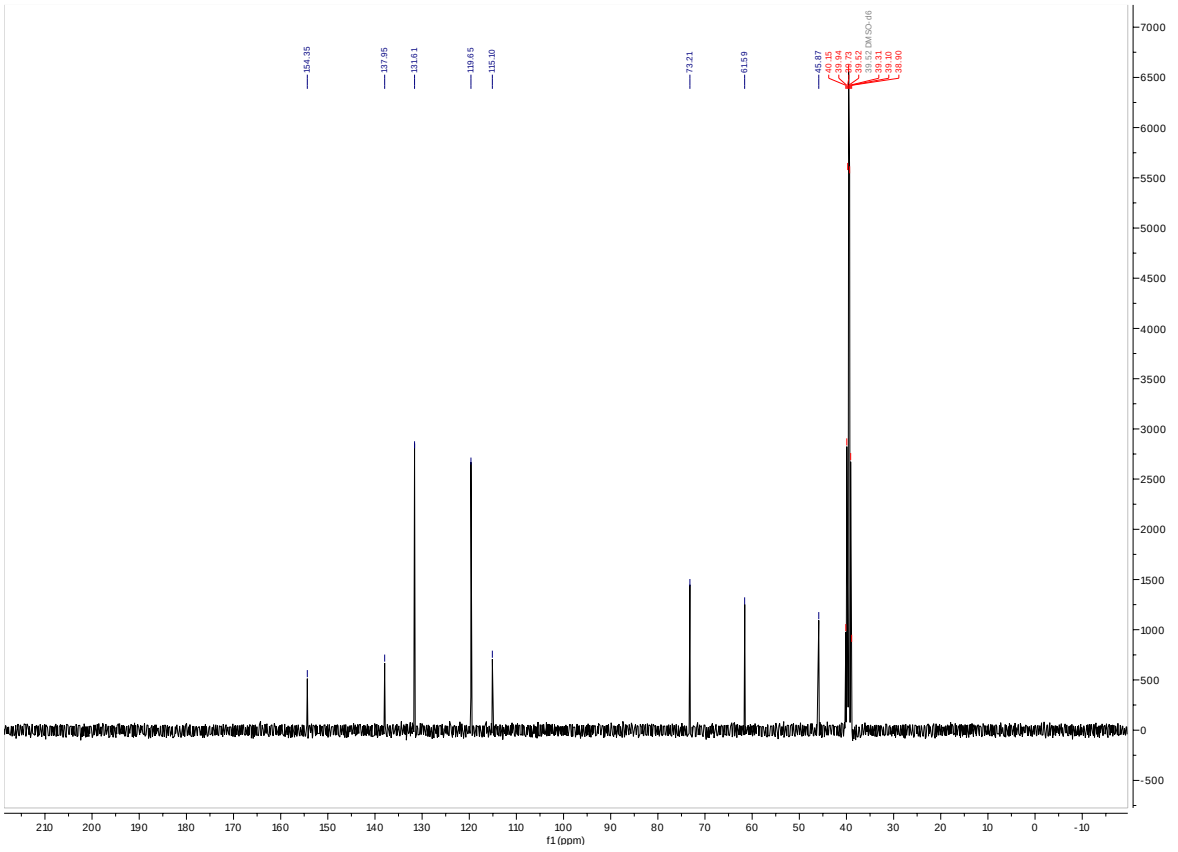

154.40
137.53
128.72
127.11
119.29
73.22
61.60
45.94
40.11
40.02
39.94
39.85
39.78
39.69
39.61
39.52 DMSO-d6
39.44
39.35
39.18
39.02
f1 (ppm)

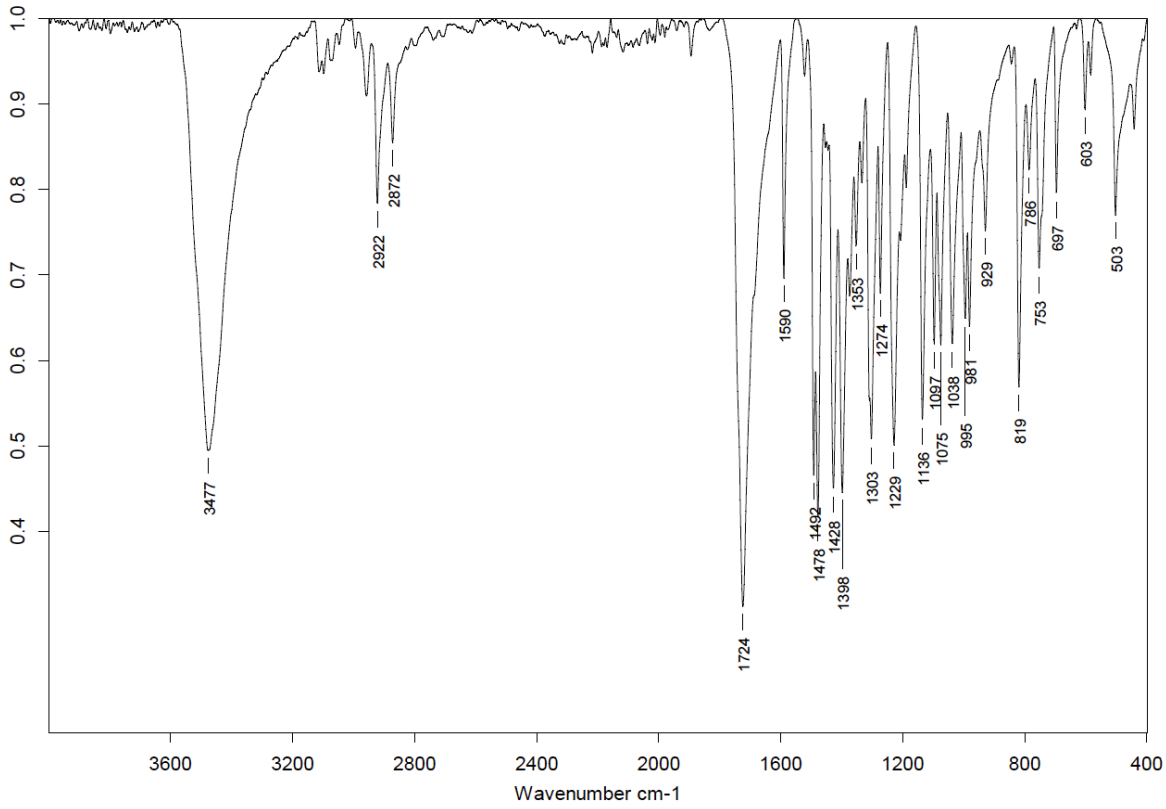

3484
2925
1724
1597
1496
1479
1430
1399
1304
1275
1230
1137
1093
1037
994
823
755
709
610
505
Wavenumber cm-1

3-(4-Bromophenyl)-5-(hydroxymethyl)oxazolidin-2-one (2i)

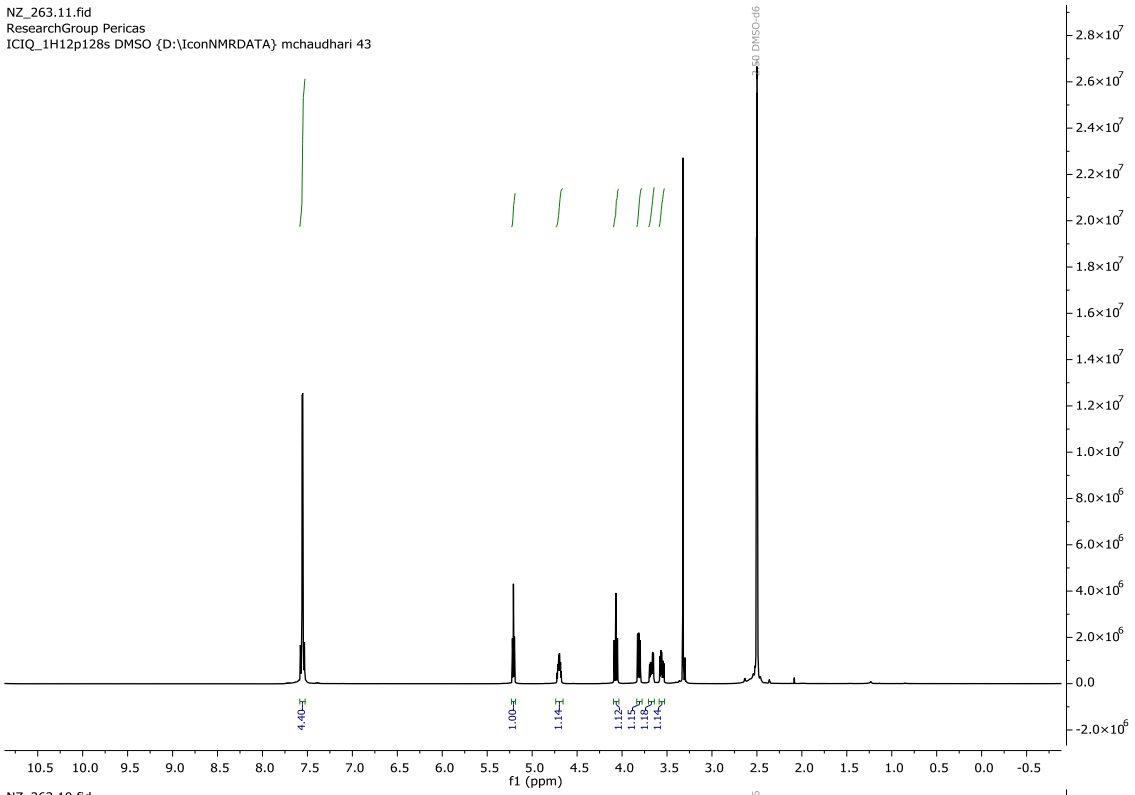


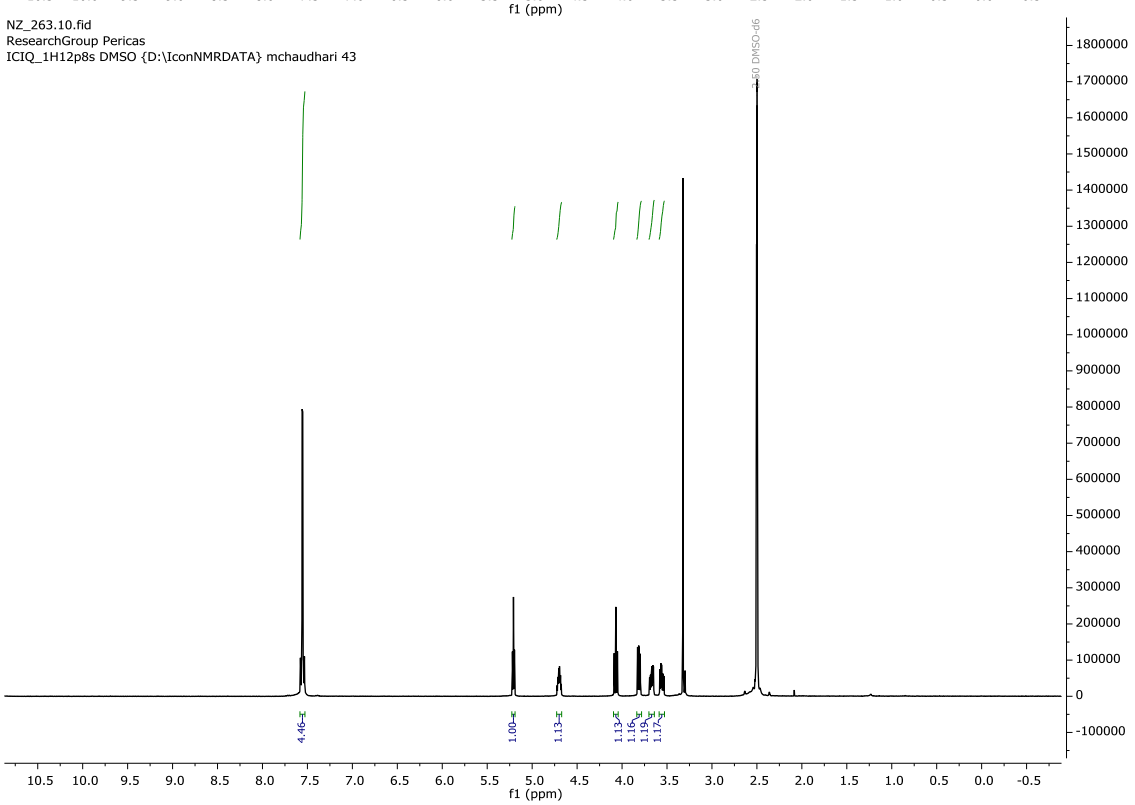



154.35
137.95
131.61
119.65
115.10
73.21
61.59
45.87
40.15
39.94
39.73
39.52 DMSO-d6
39.31
39.10
38.90
f1 (ppm)

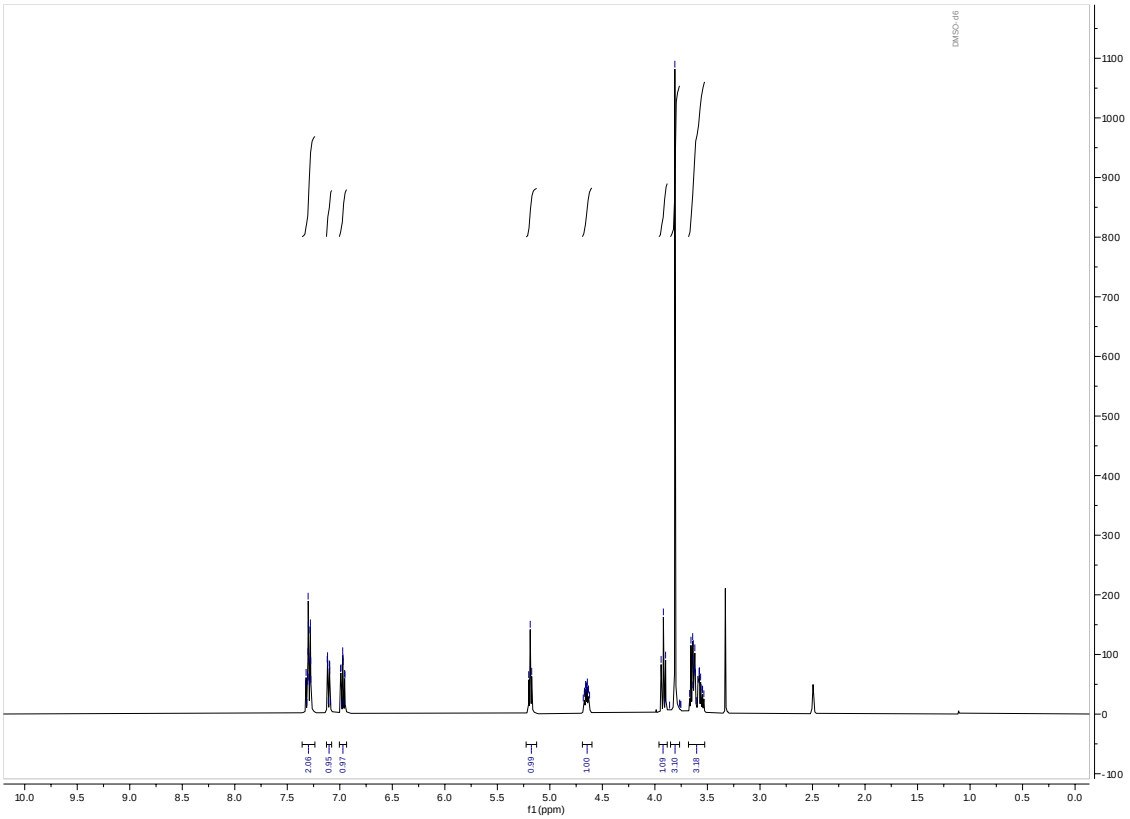

3477
2922
2872
1724
1590
1492
1478
1428
1398
1353
1303
1274
1229
1136
1097
1075
1038
995
981
929
819
786
753
697
603
503
Wavenumber cm-1

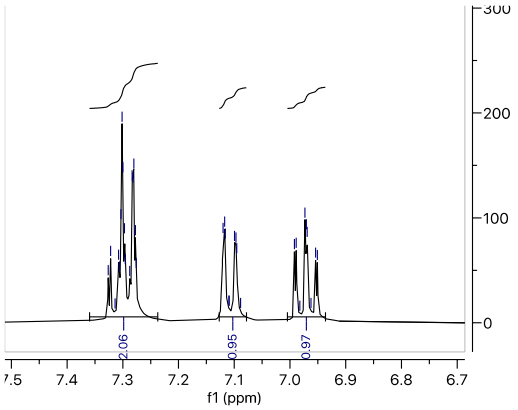
^{1}H NMR (DMSO-d_6) analysis of compound **2i** (5 mg) at lower concentration and using 8 and 128 scans respectively:

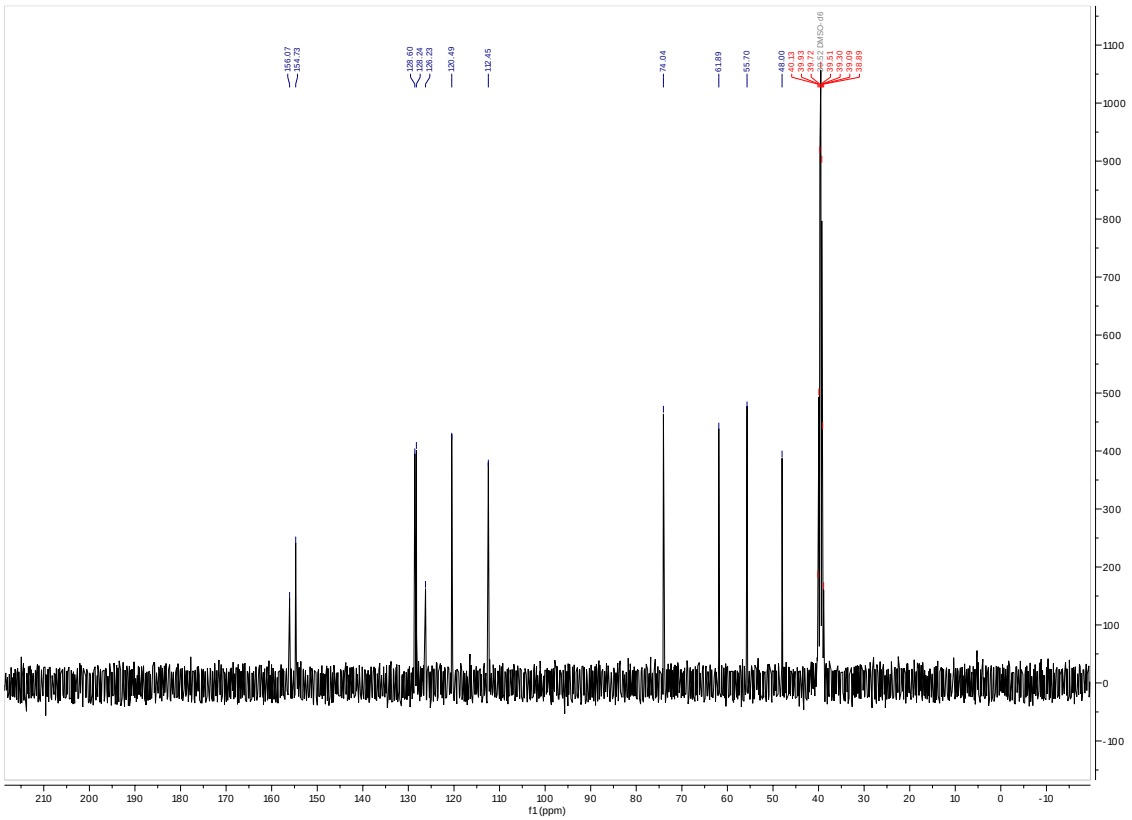


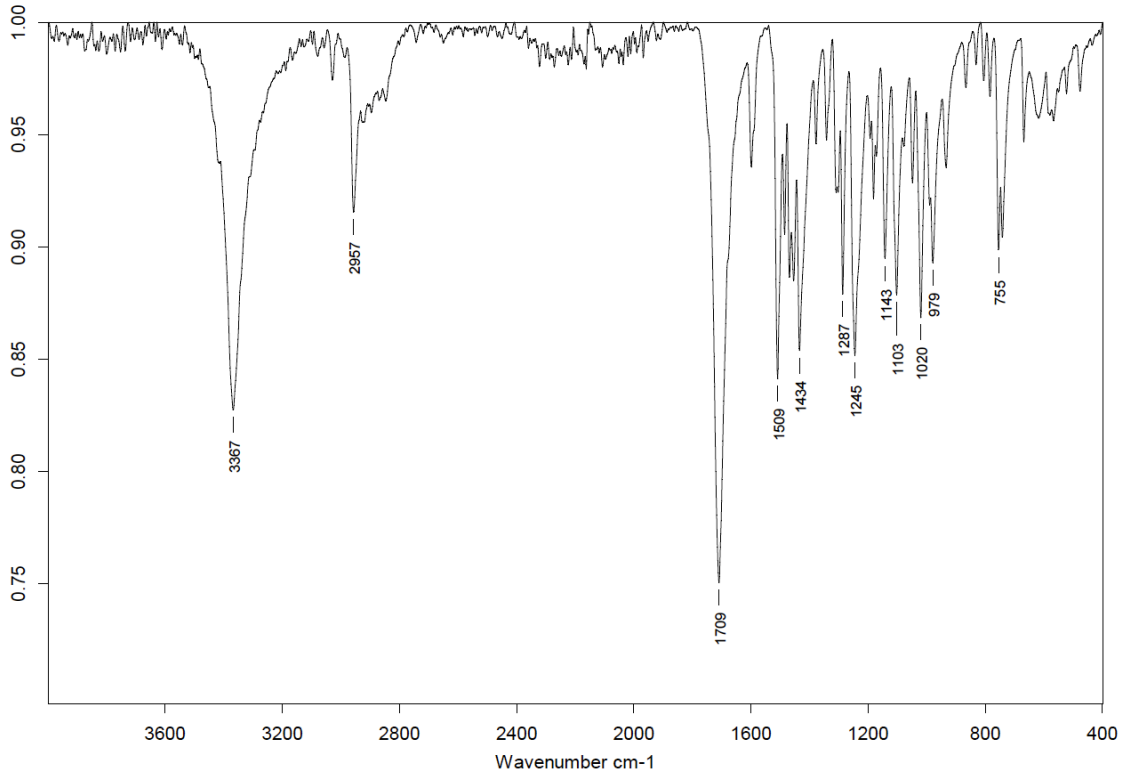


5-(Hydroxymethyl)-3-(2-methoxyphenyl)oxazolidin-2-one (2j)

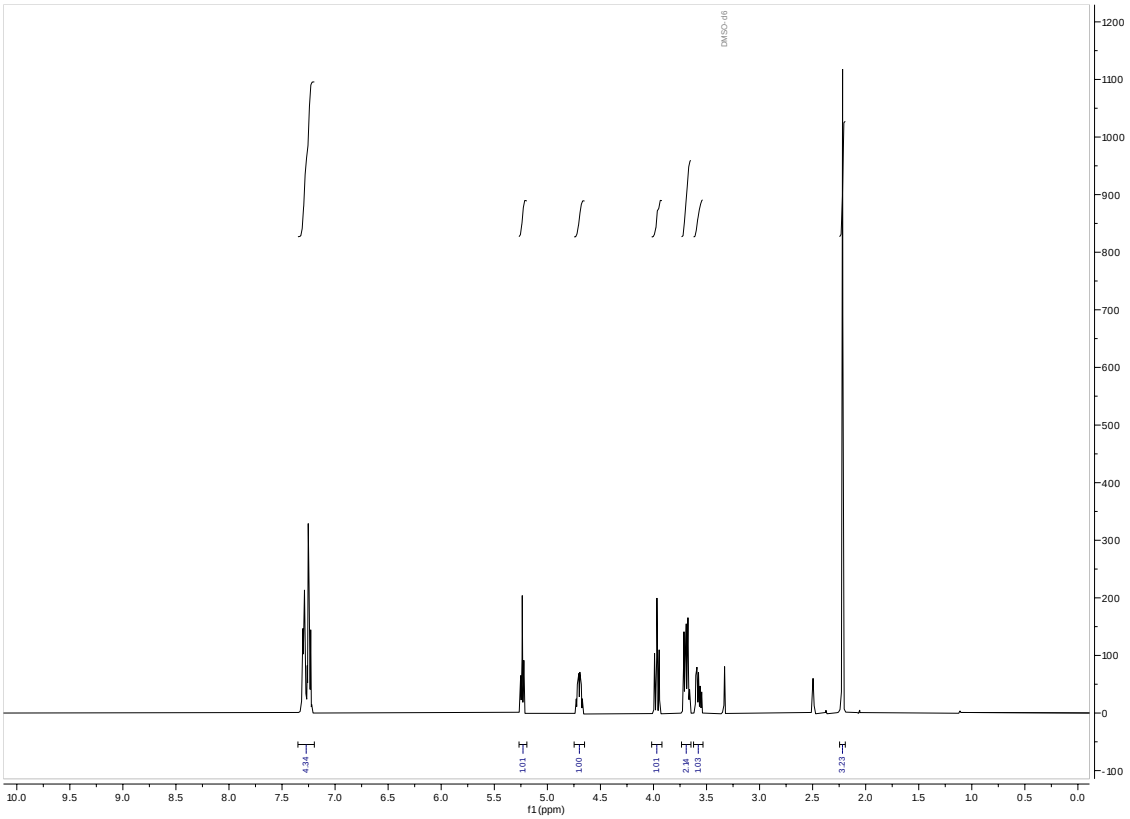


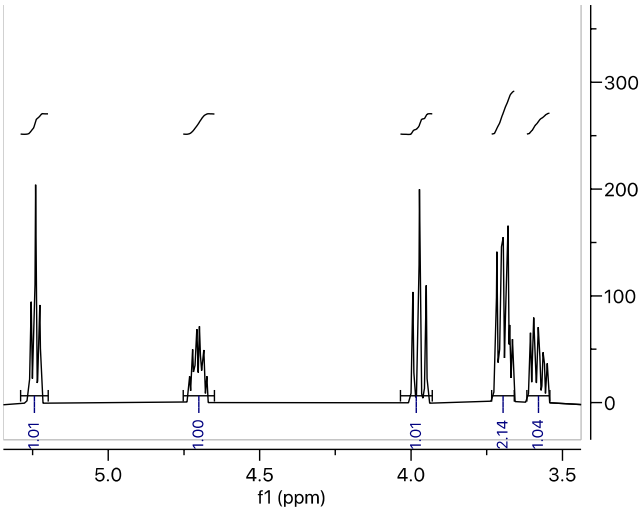


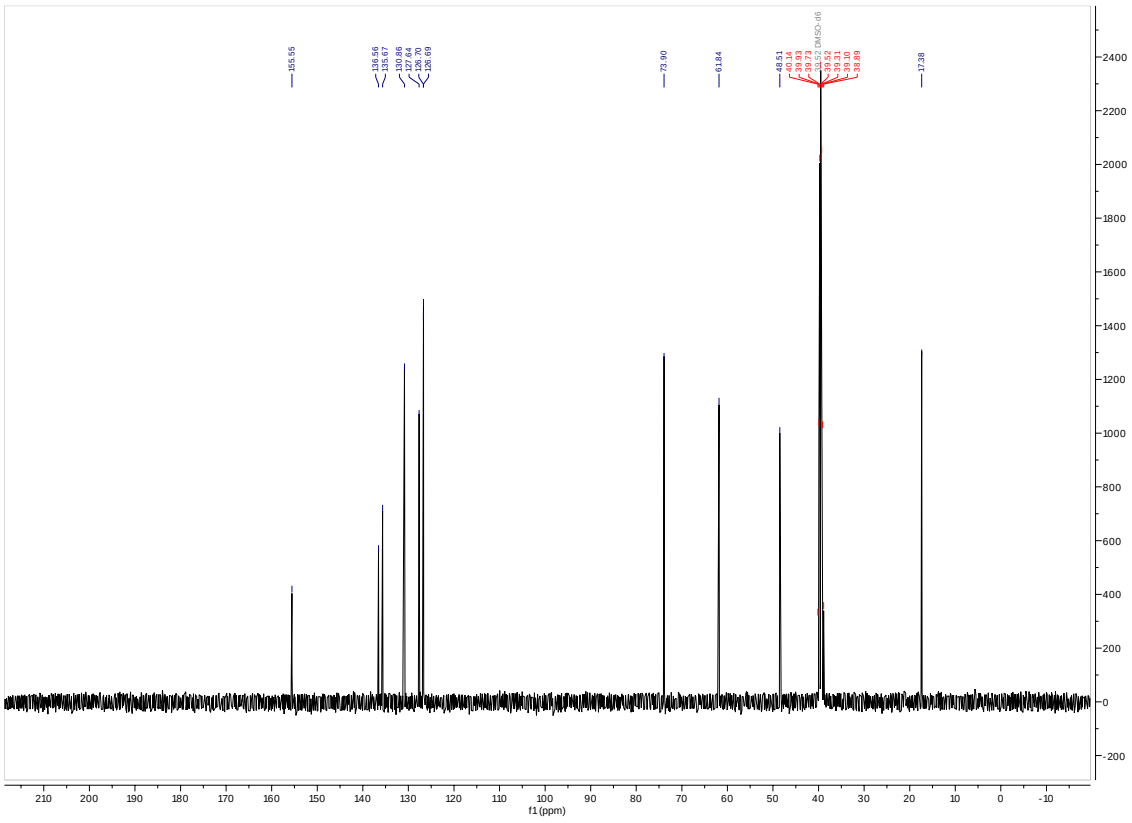

156.07
154.73
128.60
128.34
126.23
120.49
112.45
74.04
61.89
55.70
48.00
40.13
39.93
39.72
39.51
39.30
39.09
38.89
f1 (ppm)

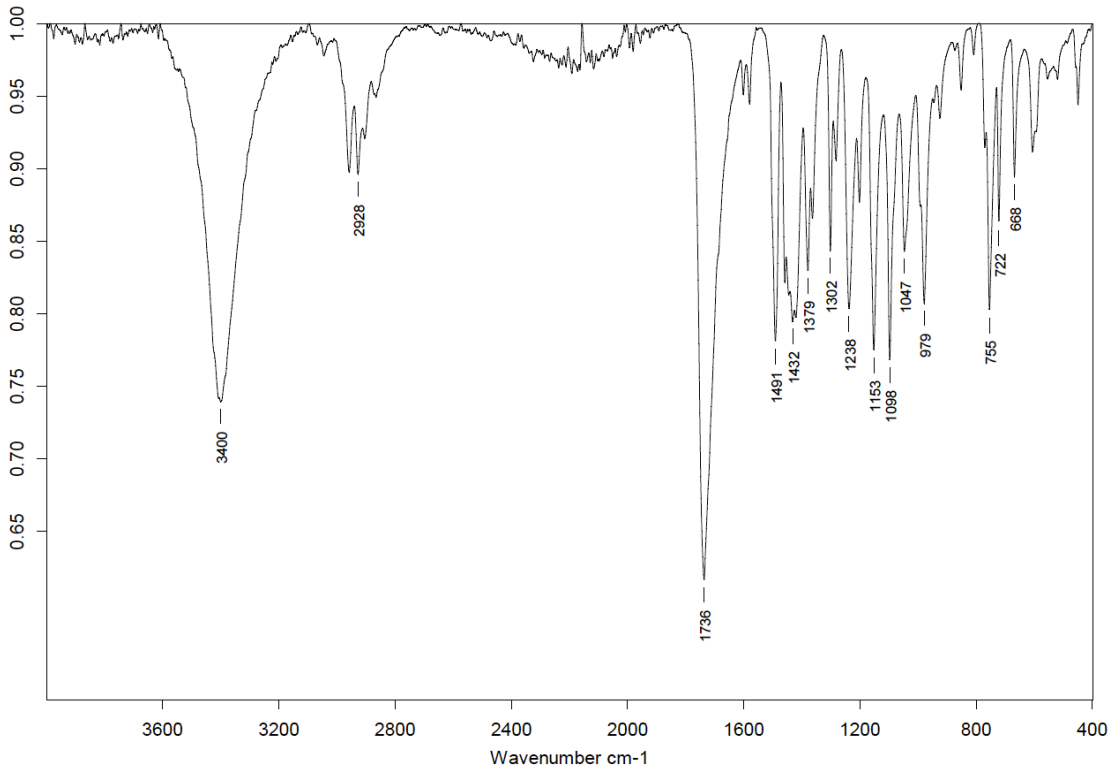

3367
2957
1709
1509
1434
1287
1245
1143
1103
1020
979
755
Wavenumber cm-1

5-(Hydroxymethyl)-3-(o-tolyl)oxazolidin-2-one (2k)

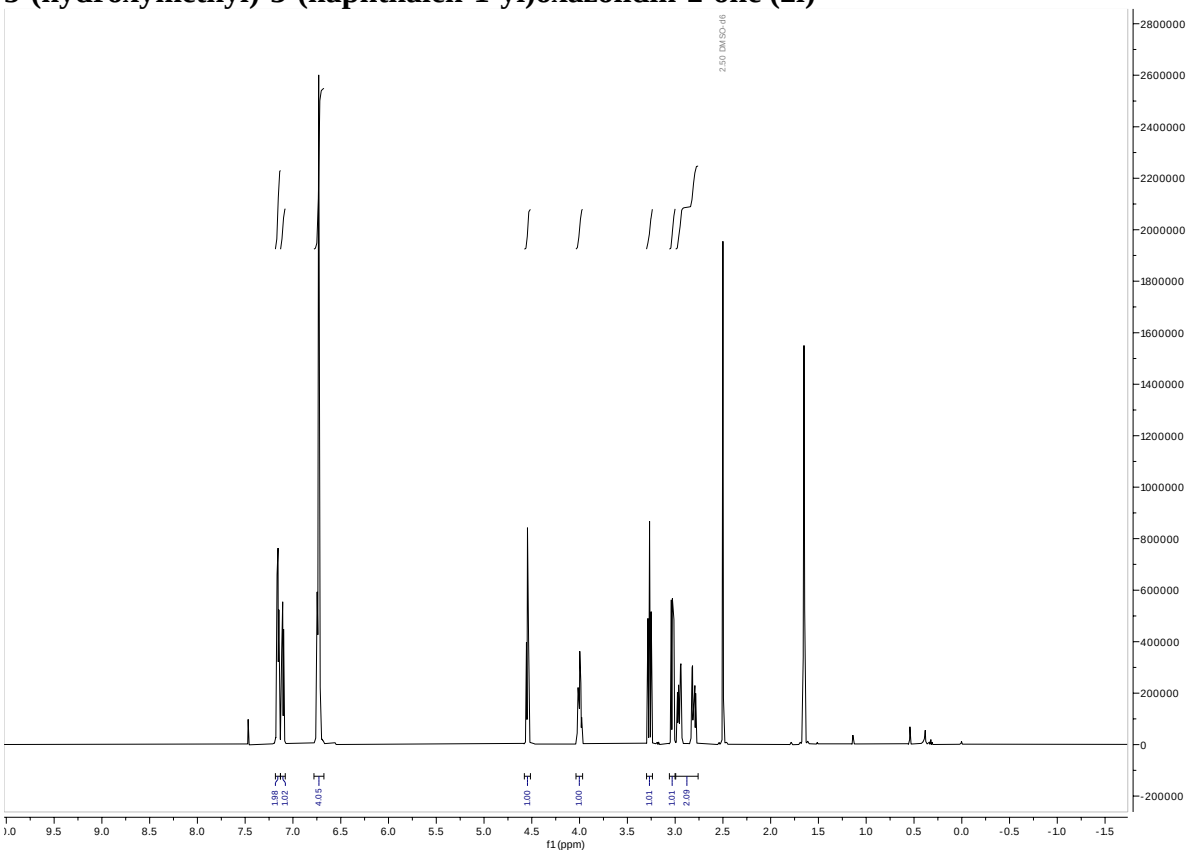


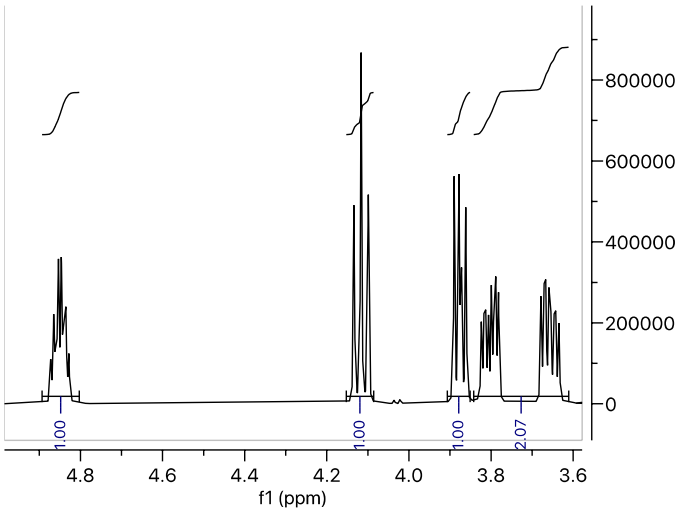


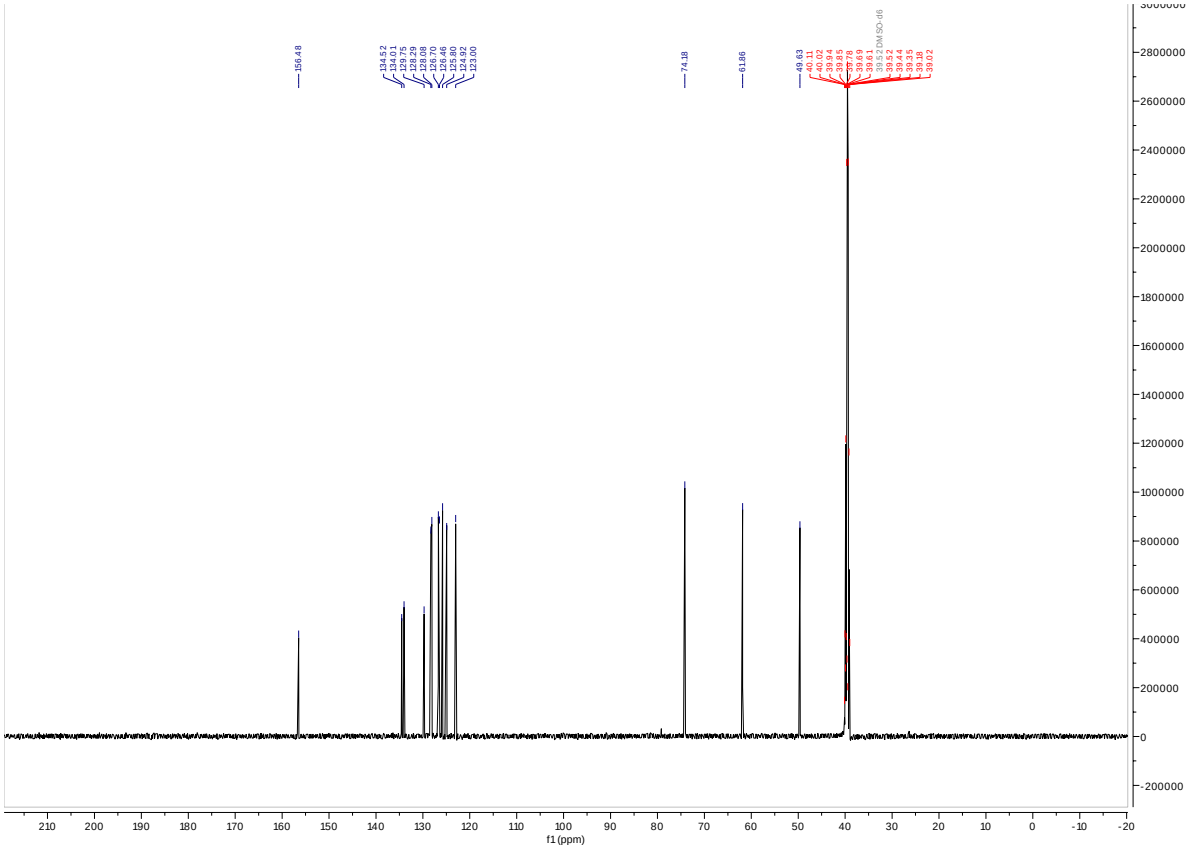

155.55
136.56
135.67
130.86
129.64
128.70
126.69
73.90
61.84
48.51
40.14
39.93
39.73
39.52 DMSO-d6
39.31
39.10
38.89
17.38
f1 (ppm)

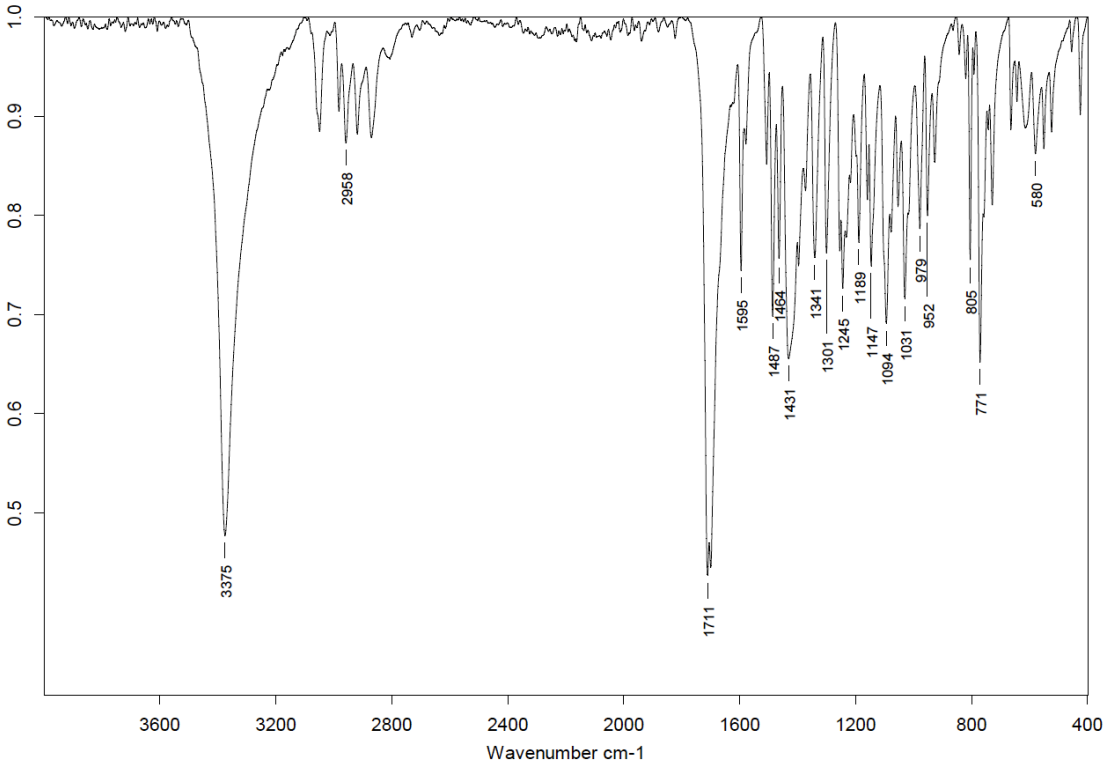

3400
2928
1736
1491
1432
1379
1302
1238
1153
1098
1047
979
755
722
668
Wavenumber cm-1

5-(hydroxymethyl)-3-(naphthalen-1-yl)oxazolidin-2-one (2l)

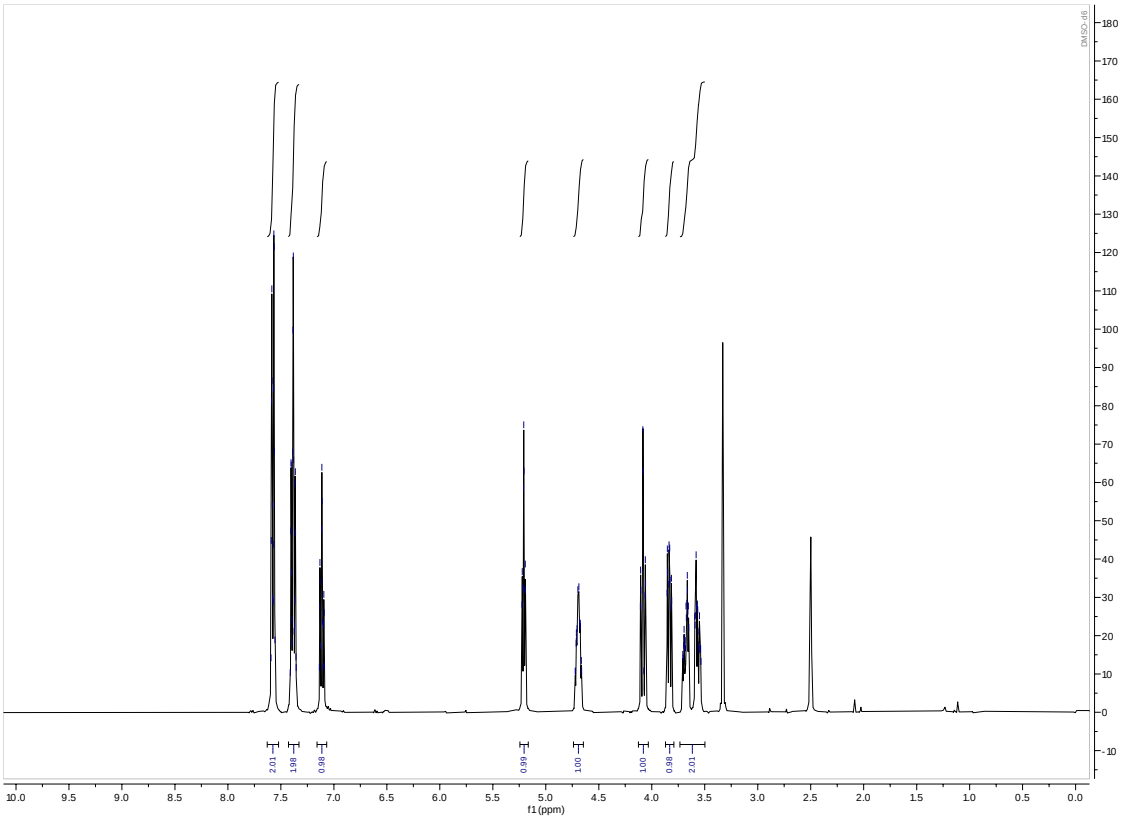


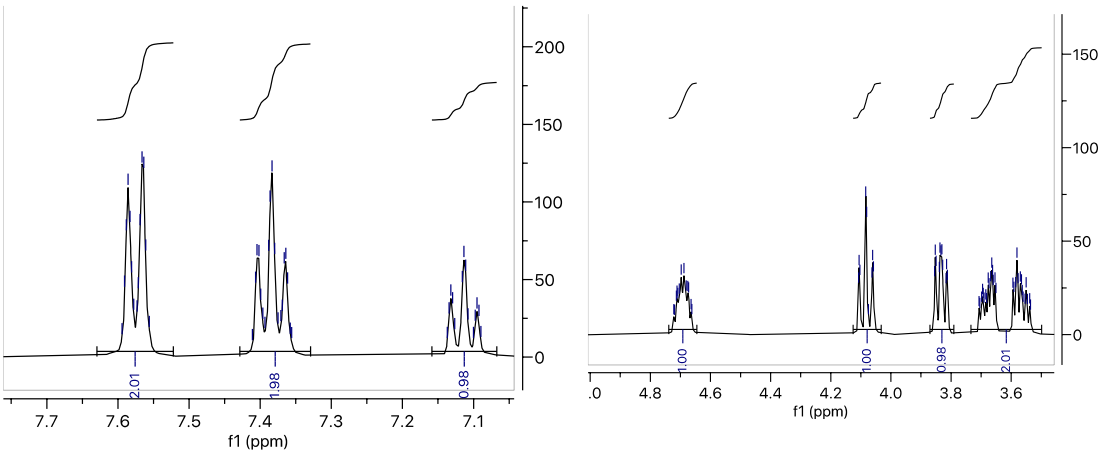


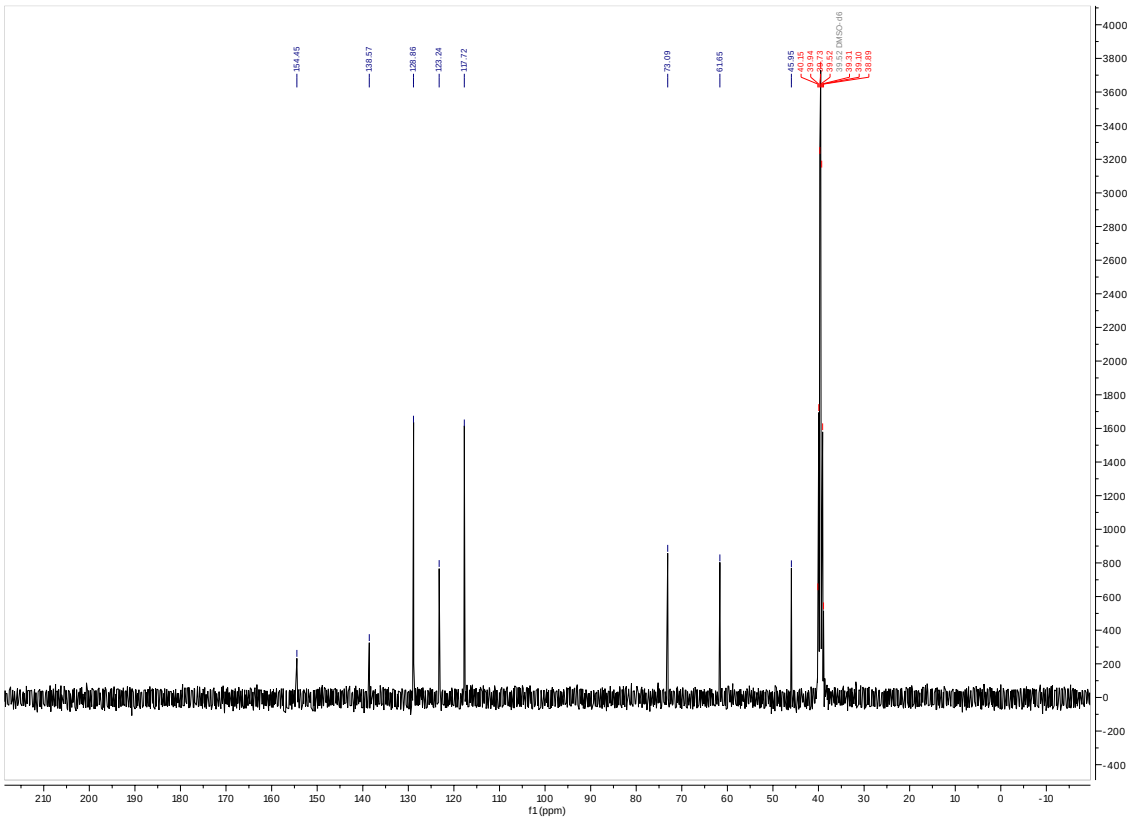

156.48
134.52
134.01
129.75
129.29
128.08
126.70
125.46
125.40
124.92
123.00
74.18
61.86
49.63
40.11
40.07
39.94
39.85
39.78
39.61
39.52 DMSO-d6
39.44
39.35
39.18
39.02
f1 (ppm)

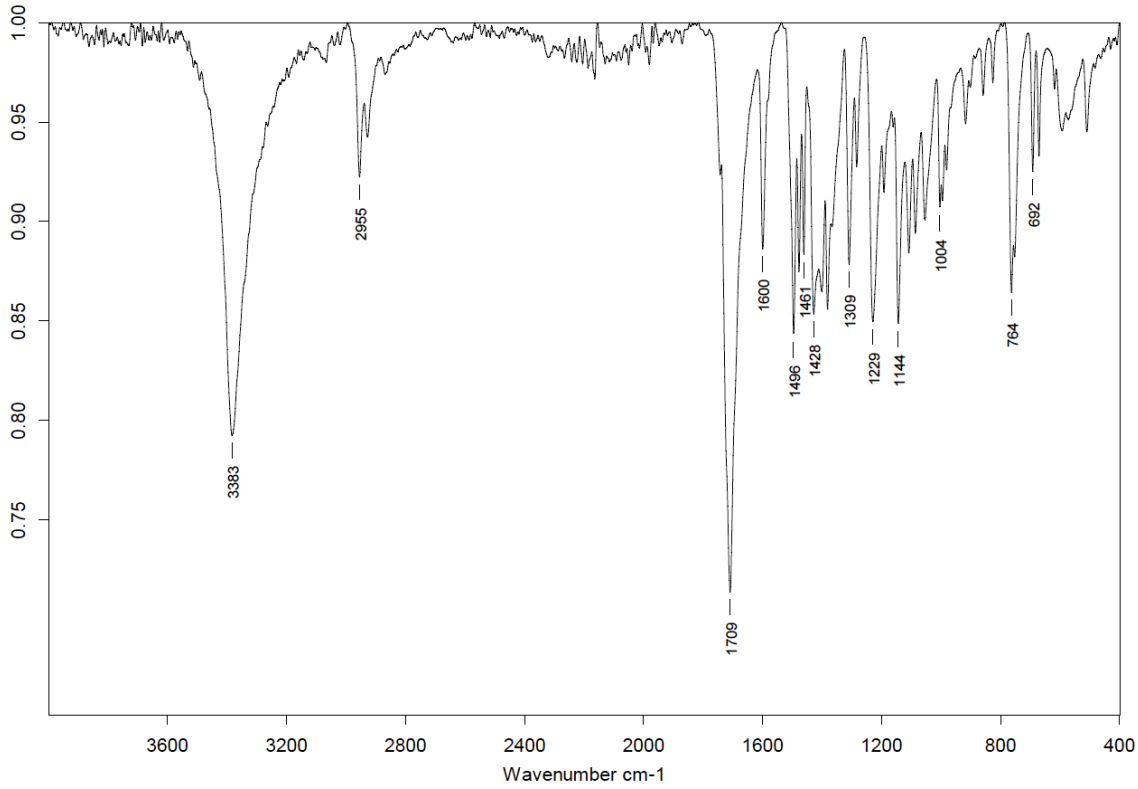

3375
2958
1711
1595
1487
1464
1431
1341
1301
1245
1189
1147
1094
1031
979
952
805
771
580
Wavenumber cm-1

5-(Hydroxymethyl)-3-phenyloxazolidin-2-one (2m)

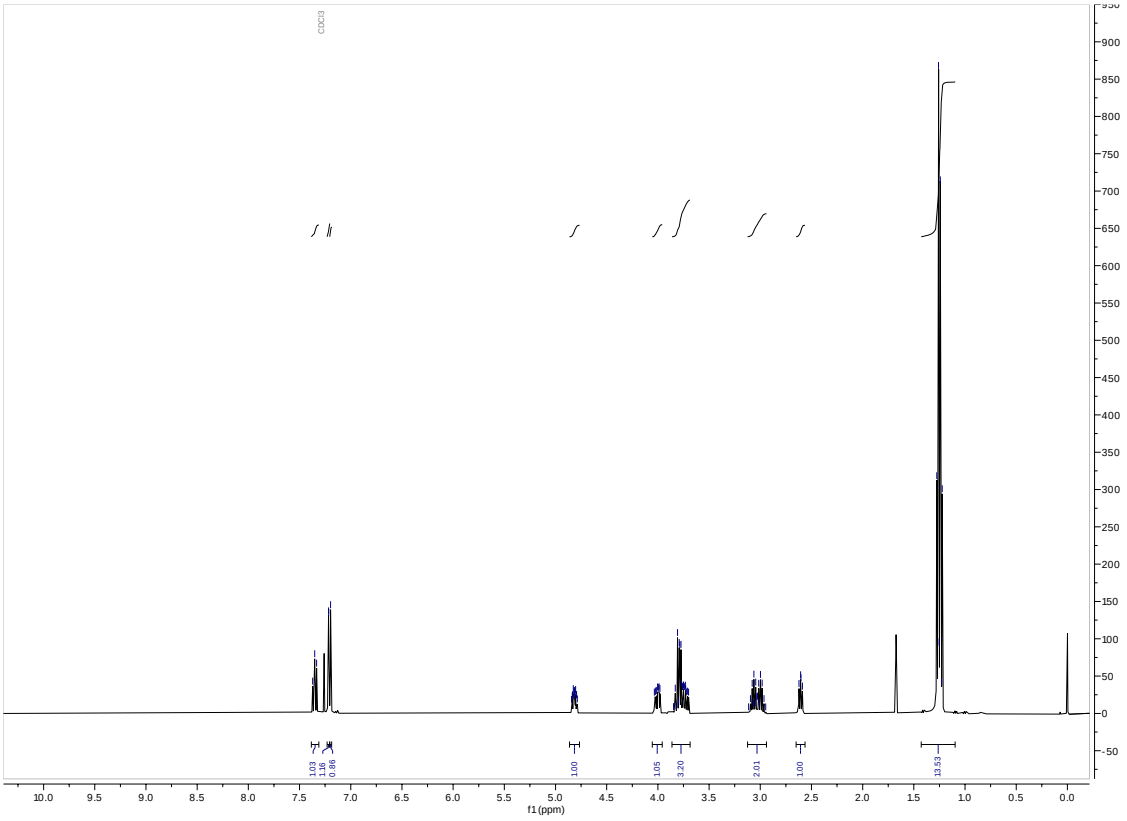


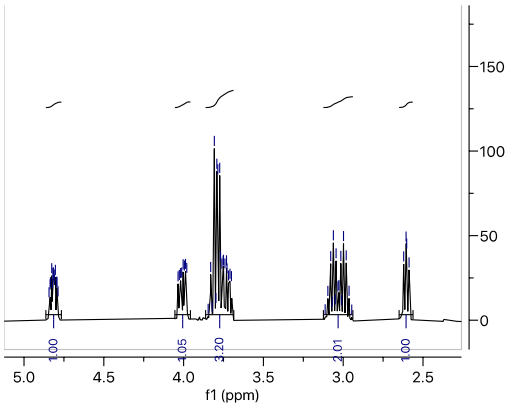


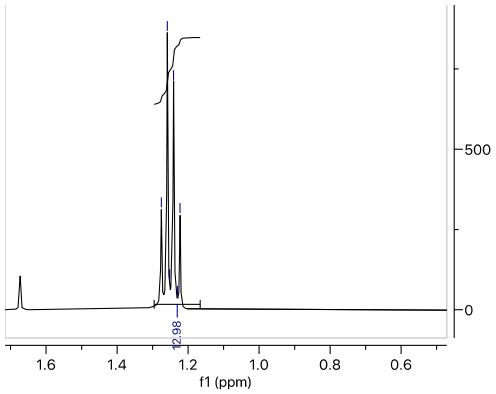

154.45
138.57
128.86
123.24
117.72
73.09
61.65
45.95
40.15
39.94
39.73
39.52
39.31
39.10
38.89
DMSO-d6
f1 (ppm)

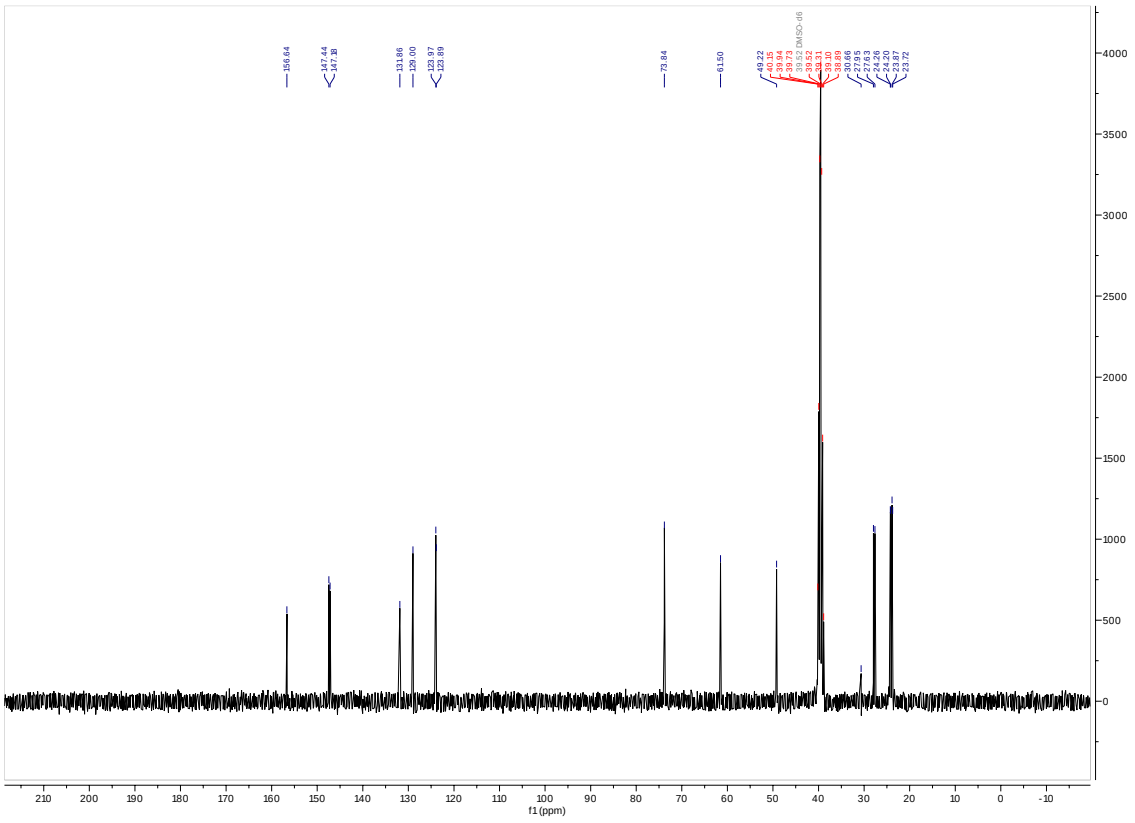

3383
2955
1709
1600
1496
1461
1428
1309
1229
1144
1004
764
692
Wavenumber cm-1

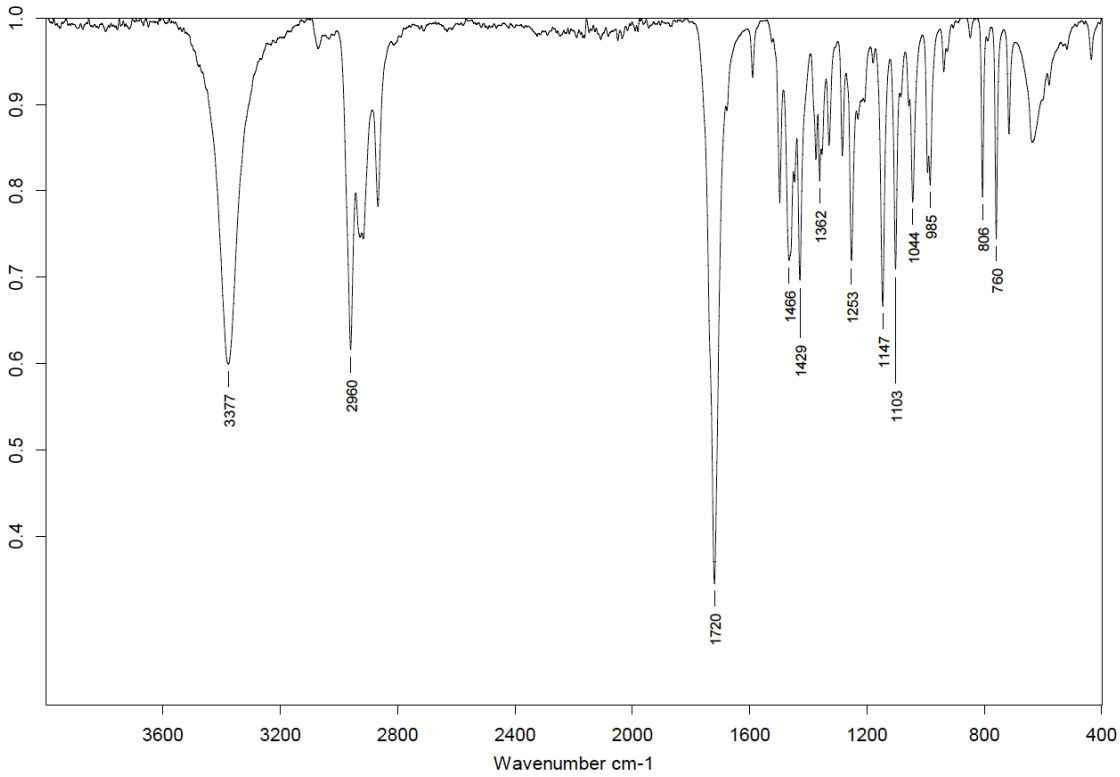
3-(2,6-diisopropylphenyl)-5-(hydroxymethyl)oxazolidin-2-one (2n)



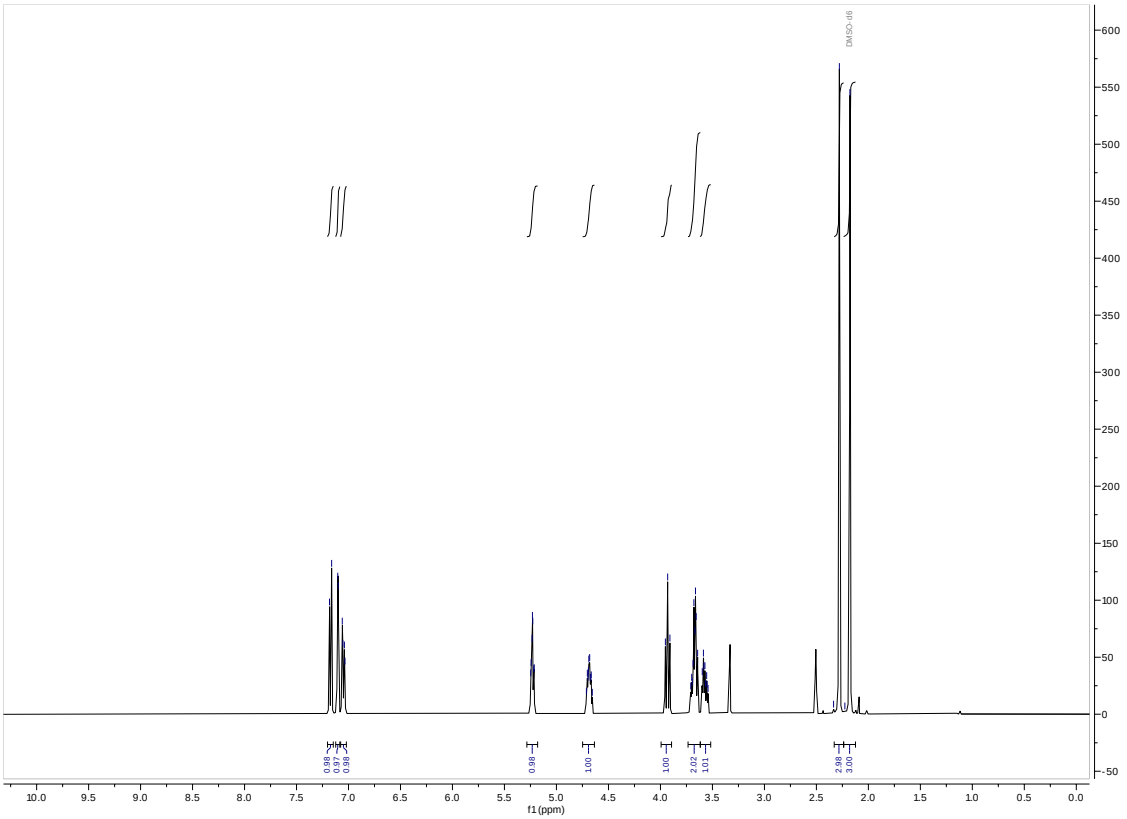


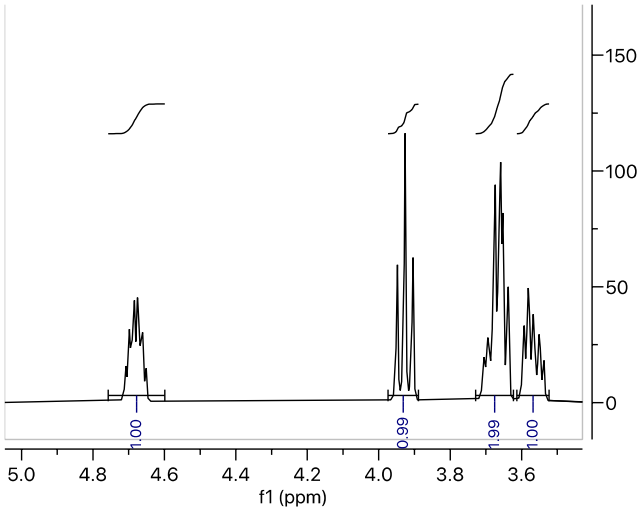


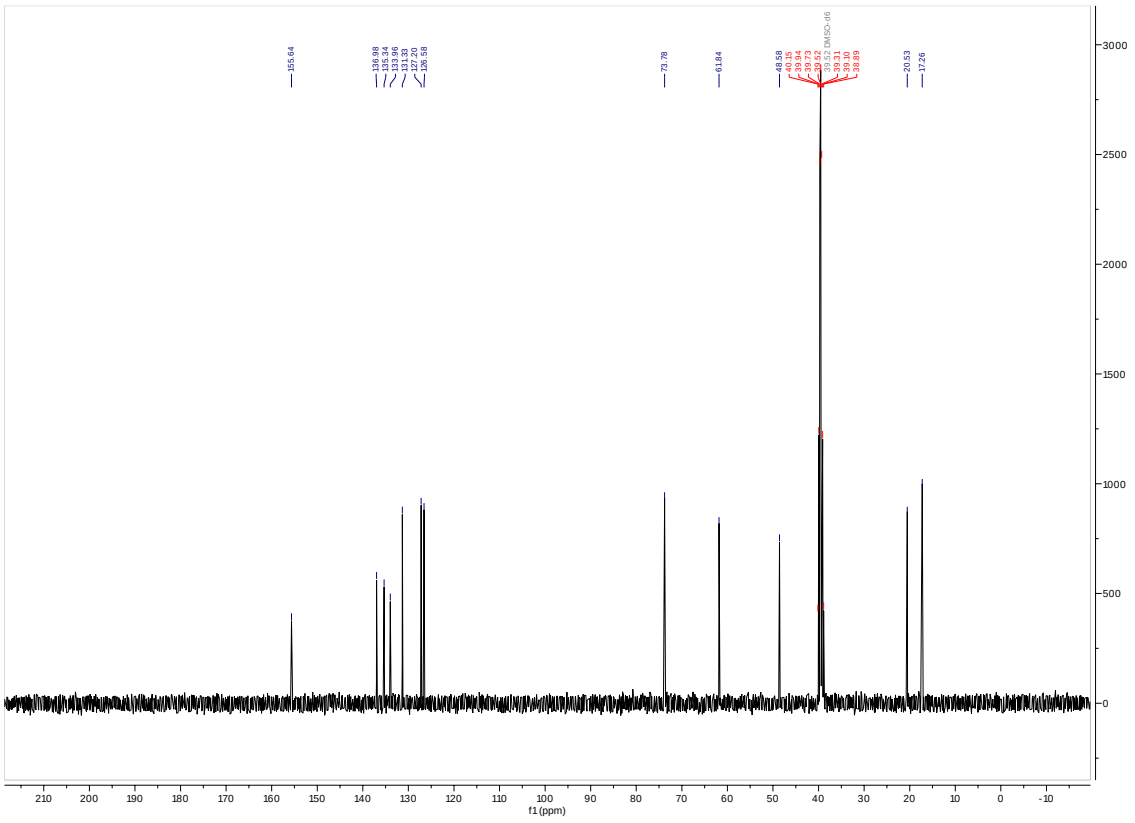

156.64
147.44
147.30
131.86
129.00
123.97
123.89
73.84
61.50
40.22
40.15
39.94
39.73
39.52
39.31
39.10
38.89
30.66
27.85
27.63
24.26
24.20
23.87
23.72
DMSO-d6
f1 (ppm)

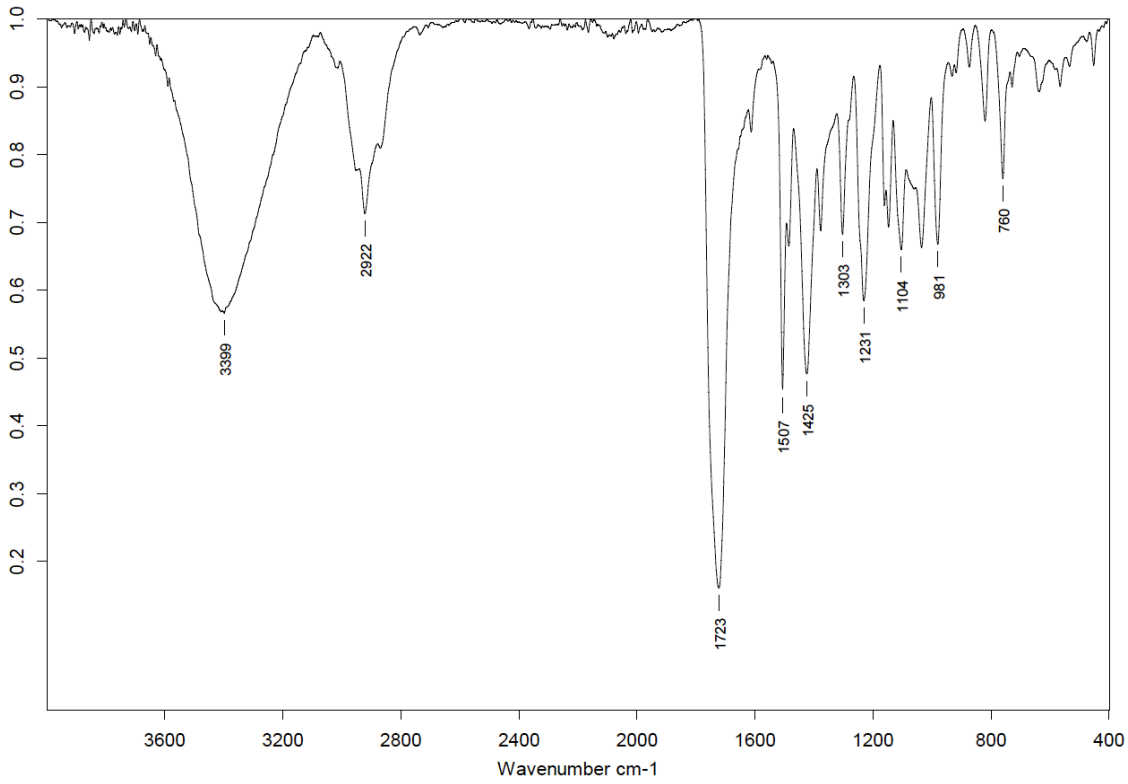

3377
2960
1720
1466
1429
1362
1253
1147
1103
1044
985
806
760
Wavenumber cm-1

3-(2,4-dimethylphenyl)-5-(hydroxymethyl)oxazolidin-2-one (2o)

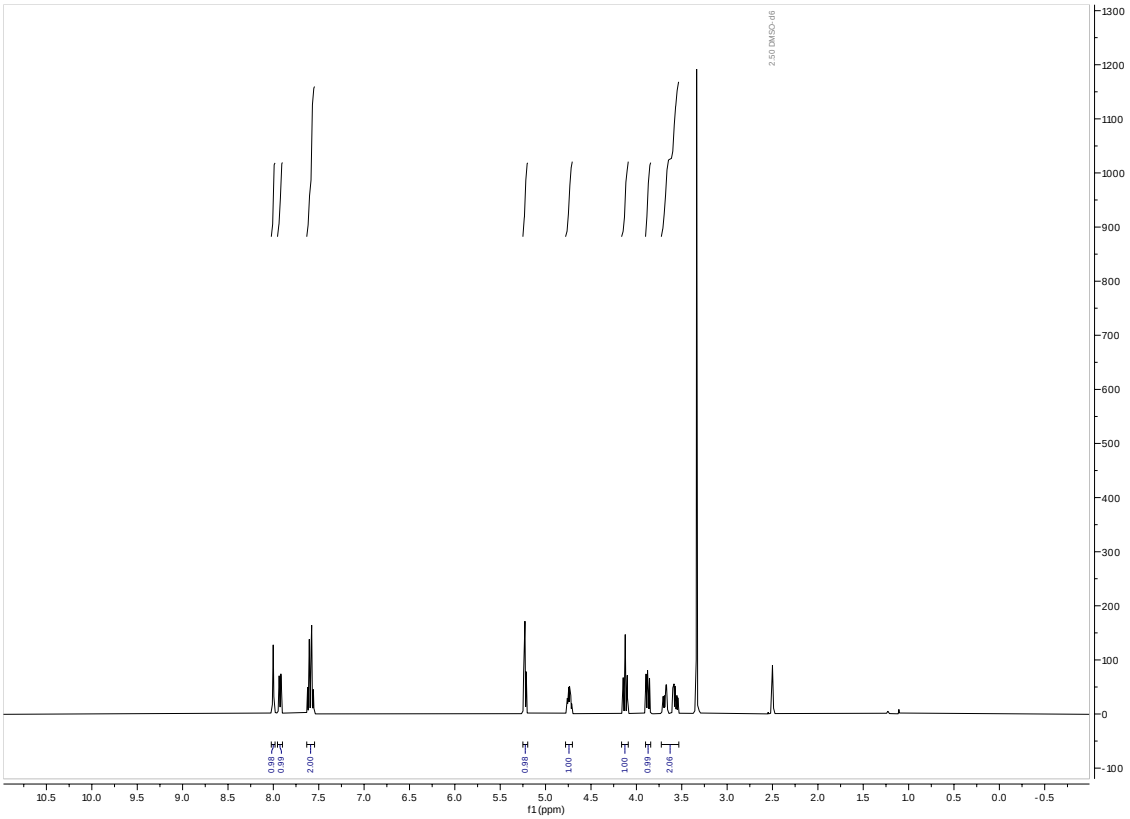


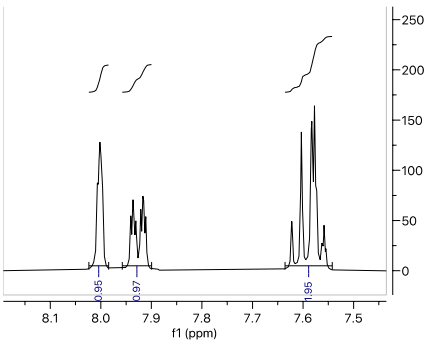


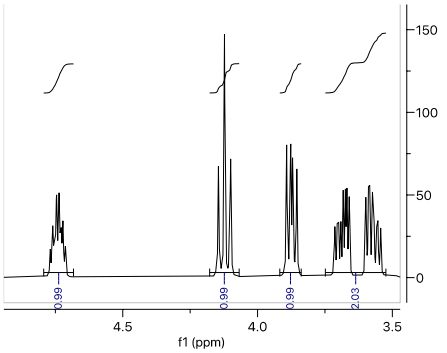

155.64
136.98
135.34
133.68
131.38
127.20
126.58
73.78
61.84
48.58
40.35
40.14
39.73
39.52
39.31
39.10
38.89
DMSO-d6
20.53
17.26
f1 (ppm)

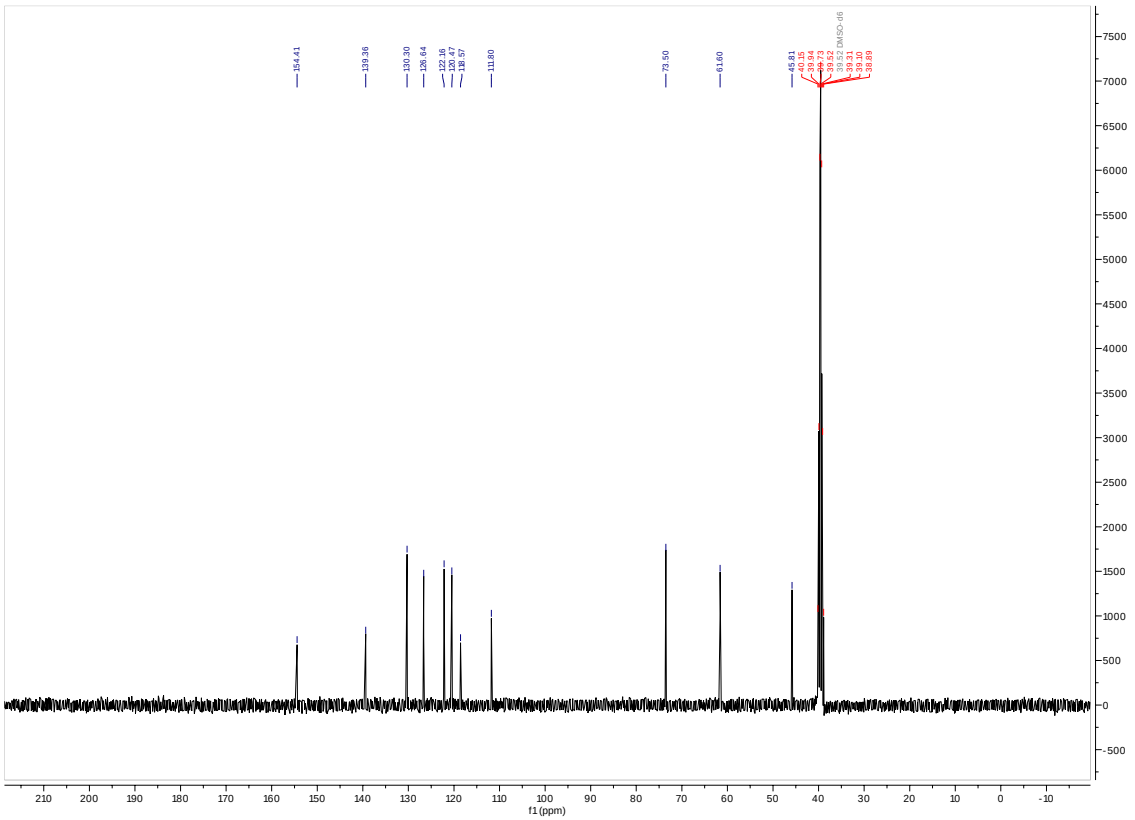

3399
2922
1723
1507
1425
1303
1231
1104
981
760
Wavenumber cm-1

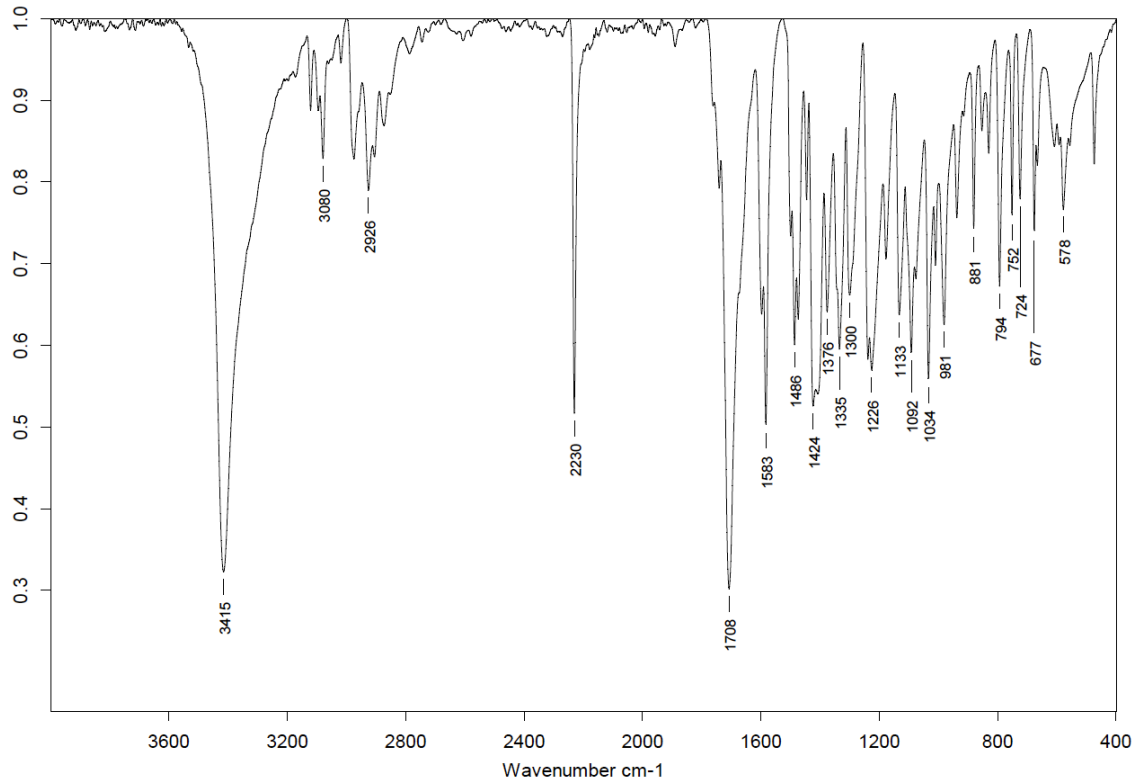
3-(5-(Hydroxymethyl)-2-oxooxazolidin-3-yl)benzonitrile (2p)





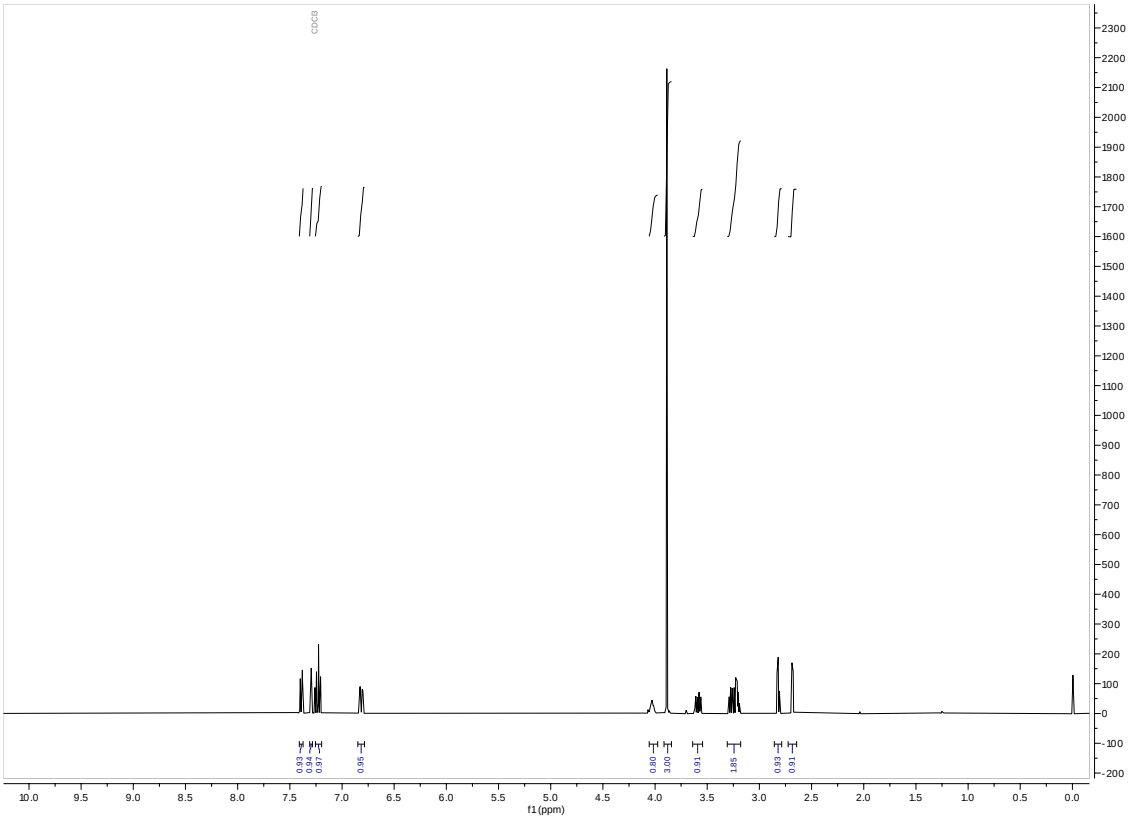


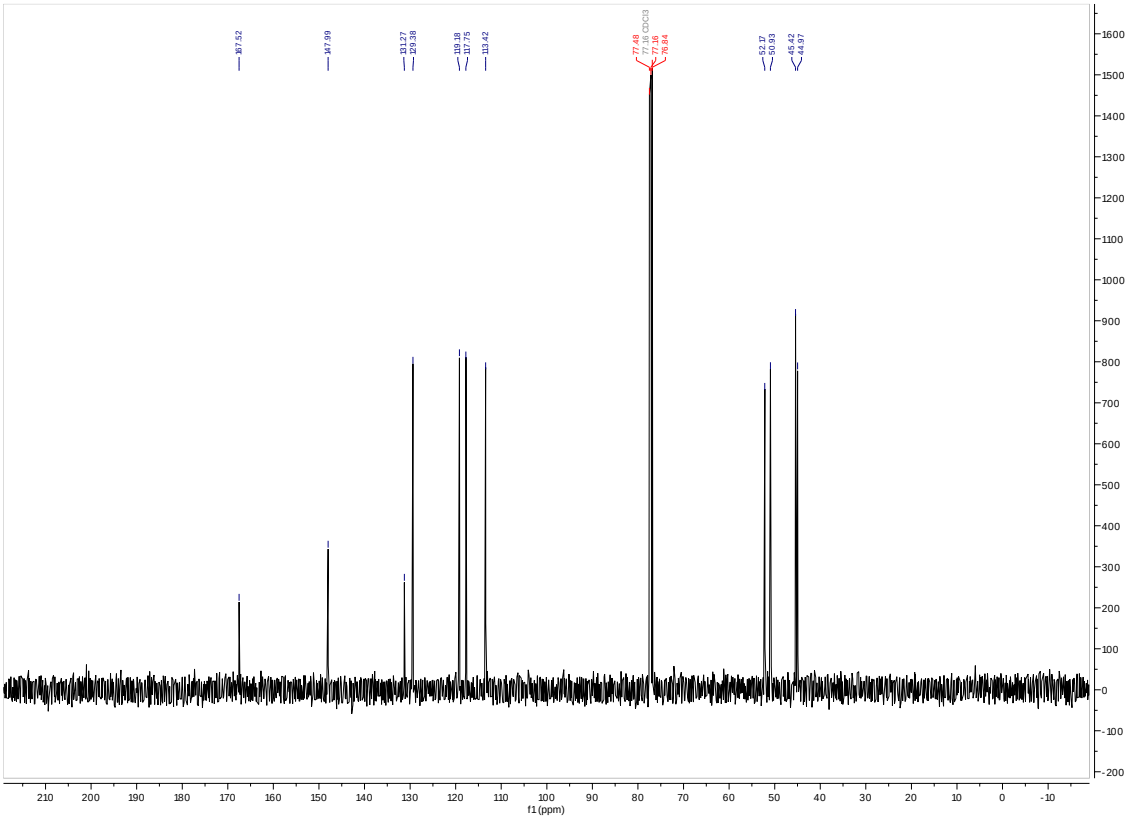

154.41
139.36
130.30
126.64
122.16
120.47
118.57
111.80
73.50
61.60
45.81
40.45
40.04
39.73
39.52
39.31
39.10
38.89
DMSO-d6
f1 (ppm)

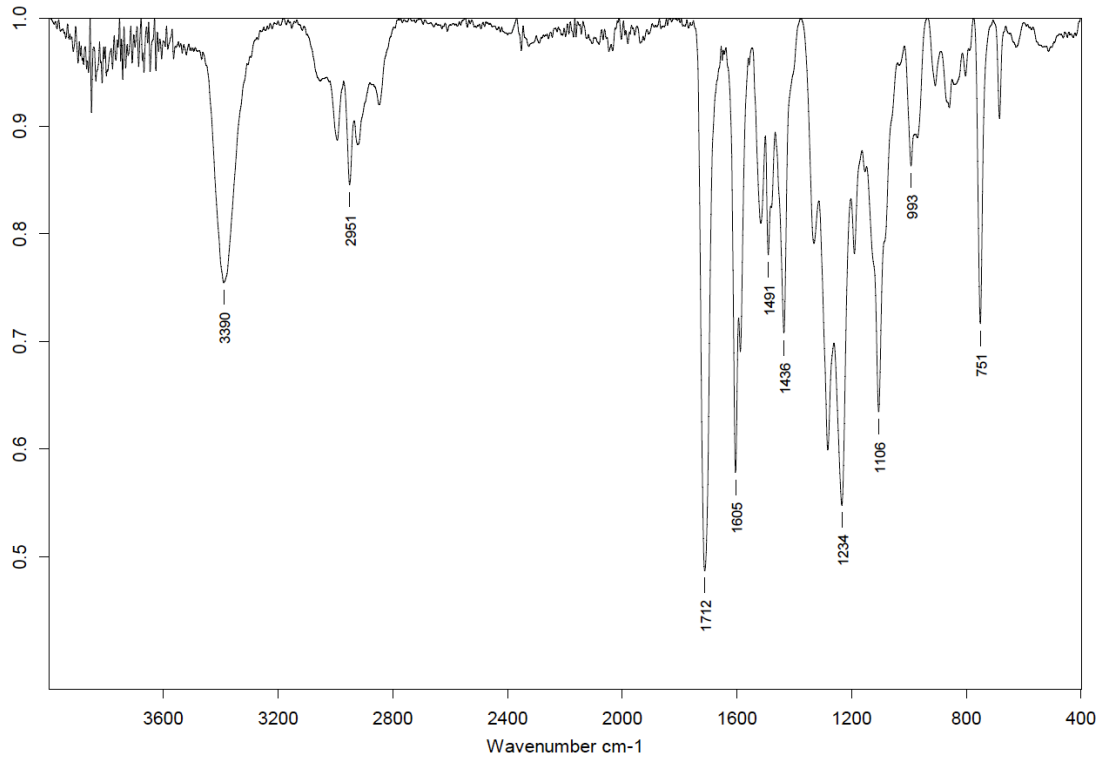

3415
3080
2926
2230
1708
1583
1486
1424
1376
1335
1300
1226
1133
1092
1034
981
881
794
752
724
677
578
Wavenumber cm-1

19. ^{1}H NMR, ^{13}C NMR, FT-IR spectra of intermediate epoxy amines

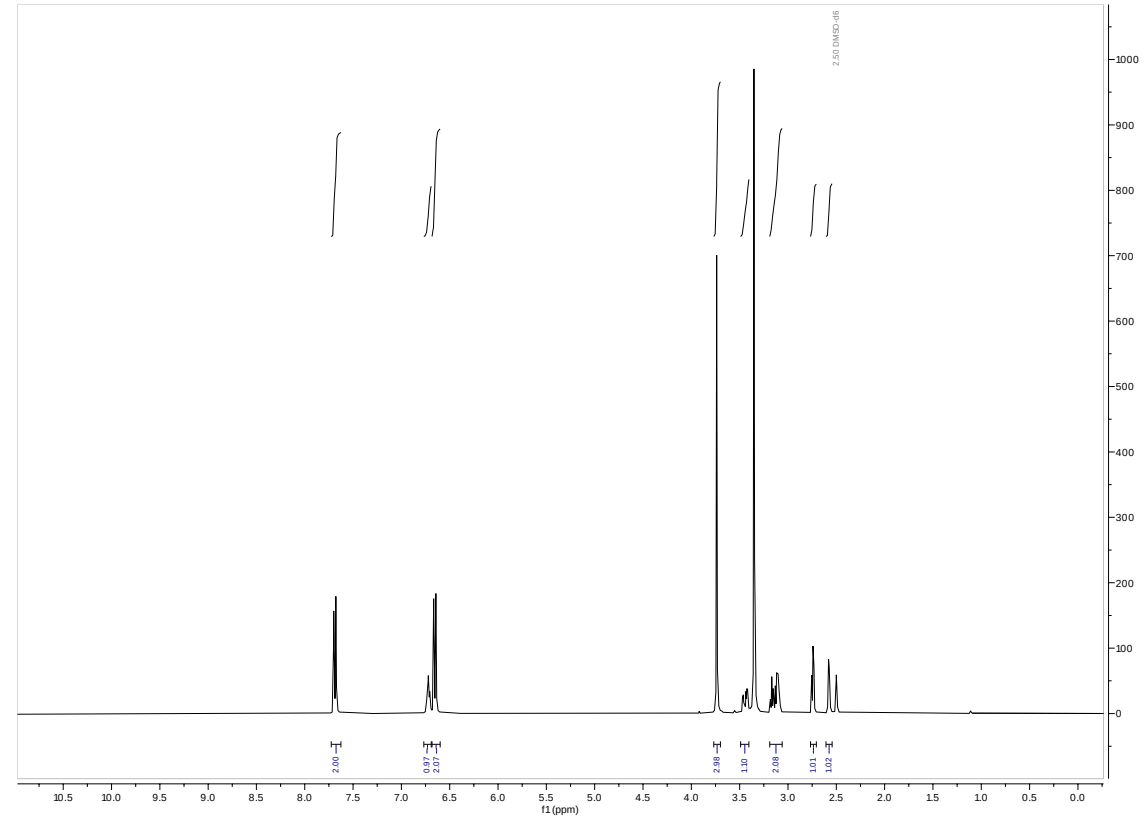
Methyl 3-((oxiran-2-ylmethyl)amino)benzoate (1b)

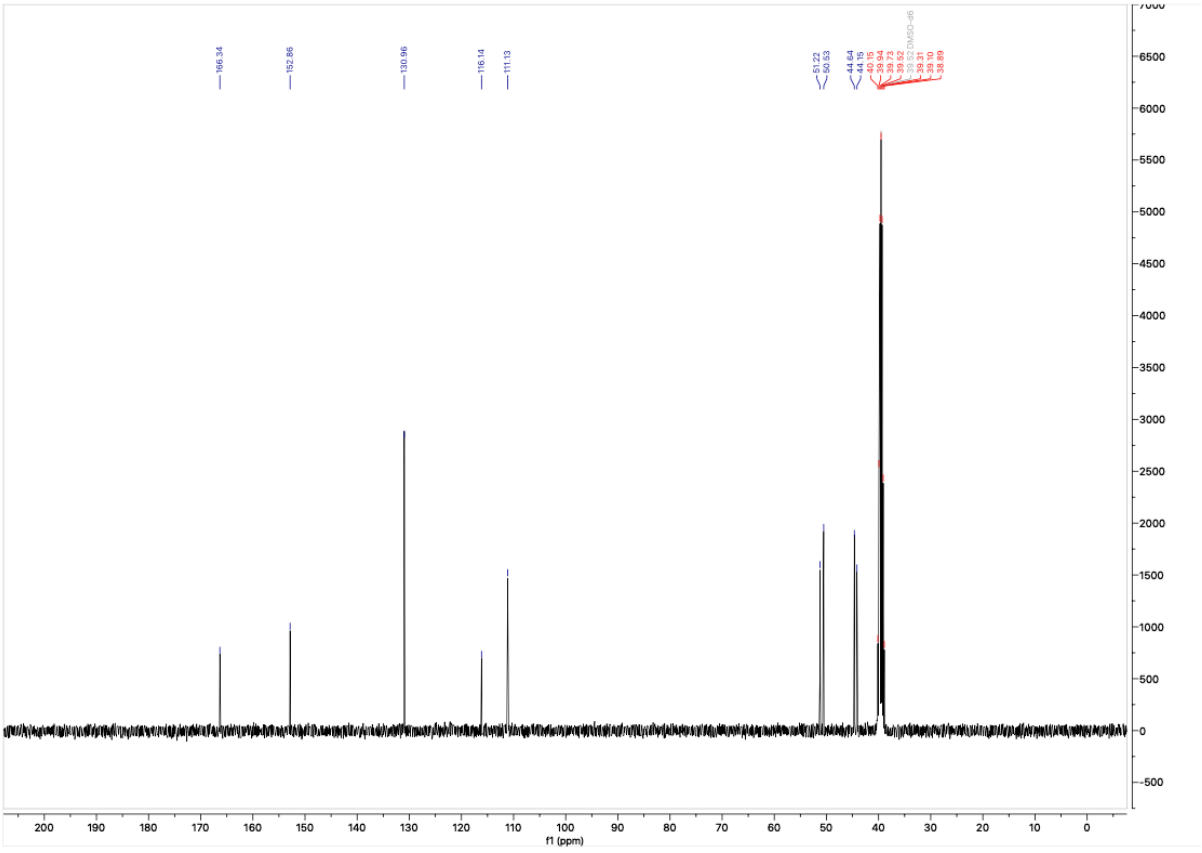


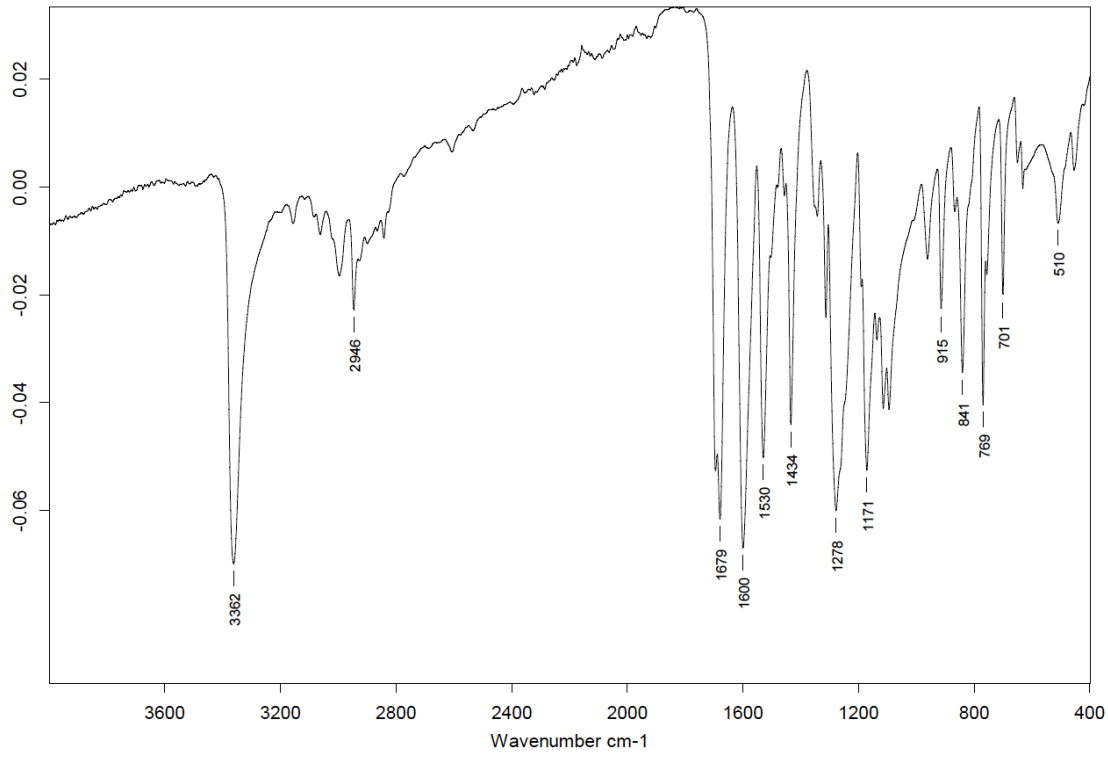



1.0
0.9
0.8
0.7
0.6
0.5
3390
2951
1712
1605
1491
1436
1234
1106
993
751
3600
3200
2800
2400
2000
1600
1200
800
400
Wavenumber cm-1

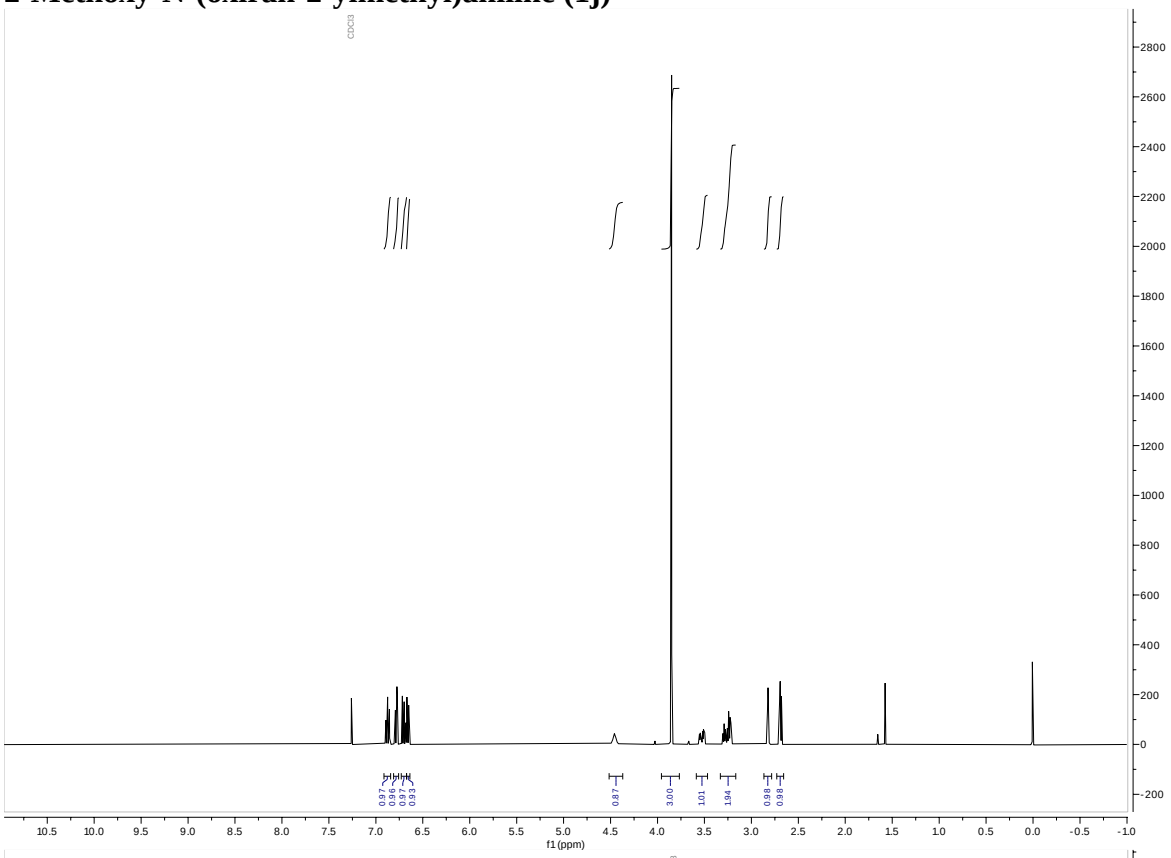
Methyl 4-((oxiran-2-ylmethyl)amino)benzoate (1f)

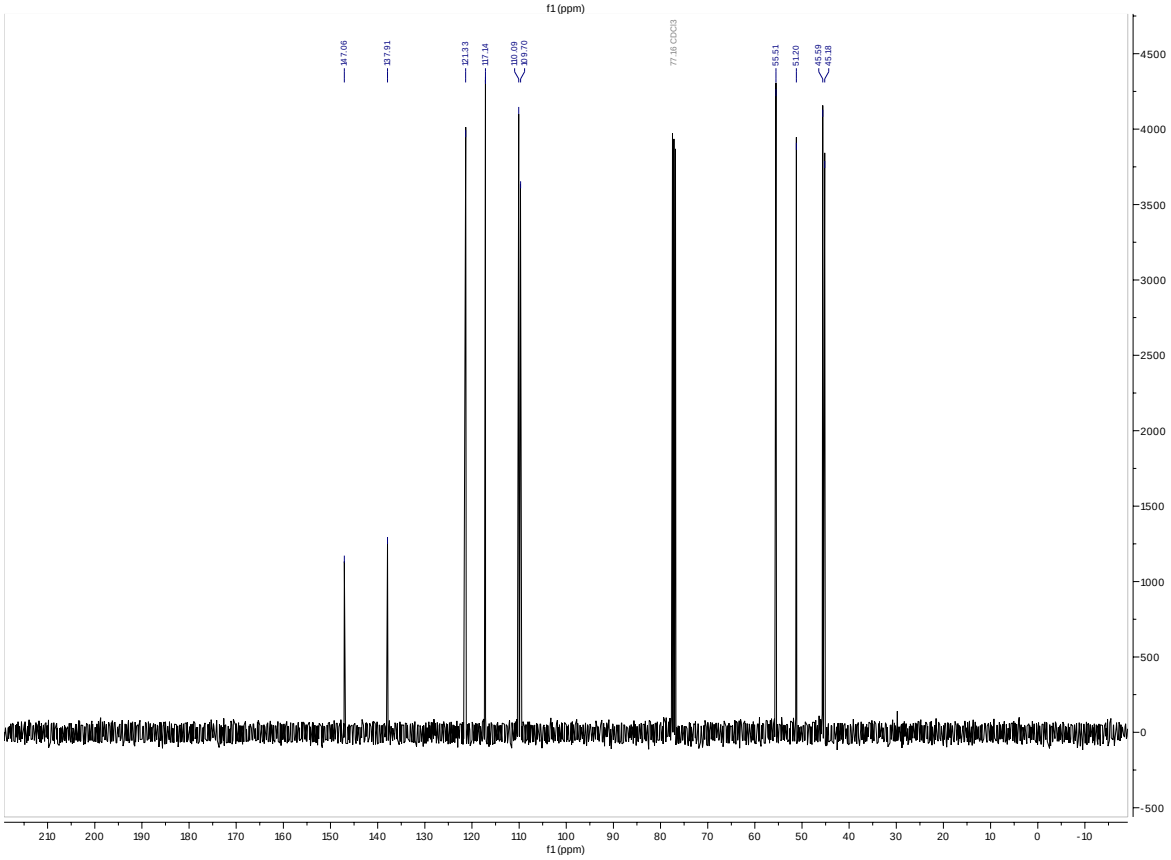


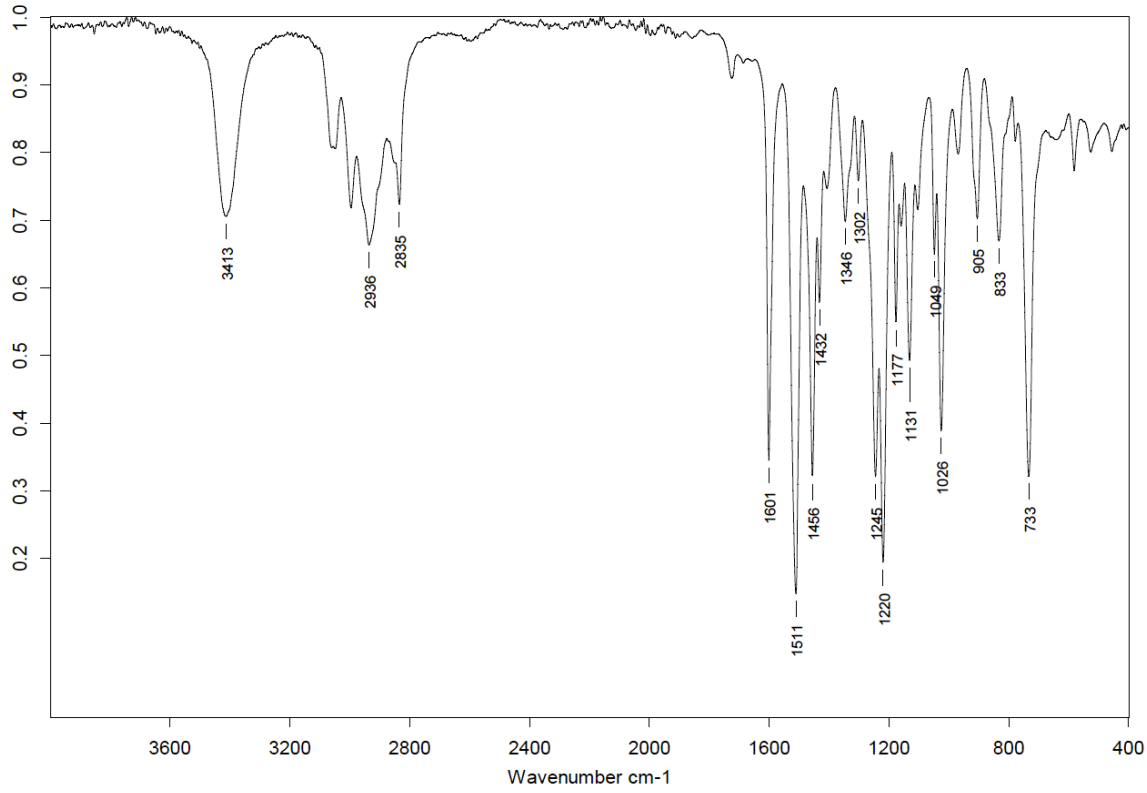



0.02
0.00
-0.02
-0.04
-0.06
3362
2946
1679
1600
1530
1434
1278
1171
915
841
769
701
510
3600
3200
2800
2400
2000
1600
1200
800
400
Wavenumber cm-1

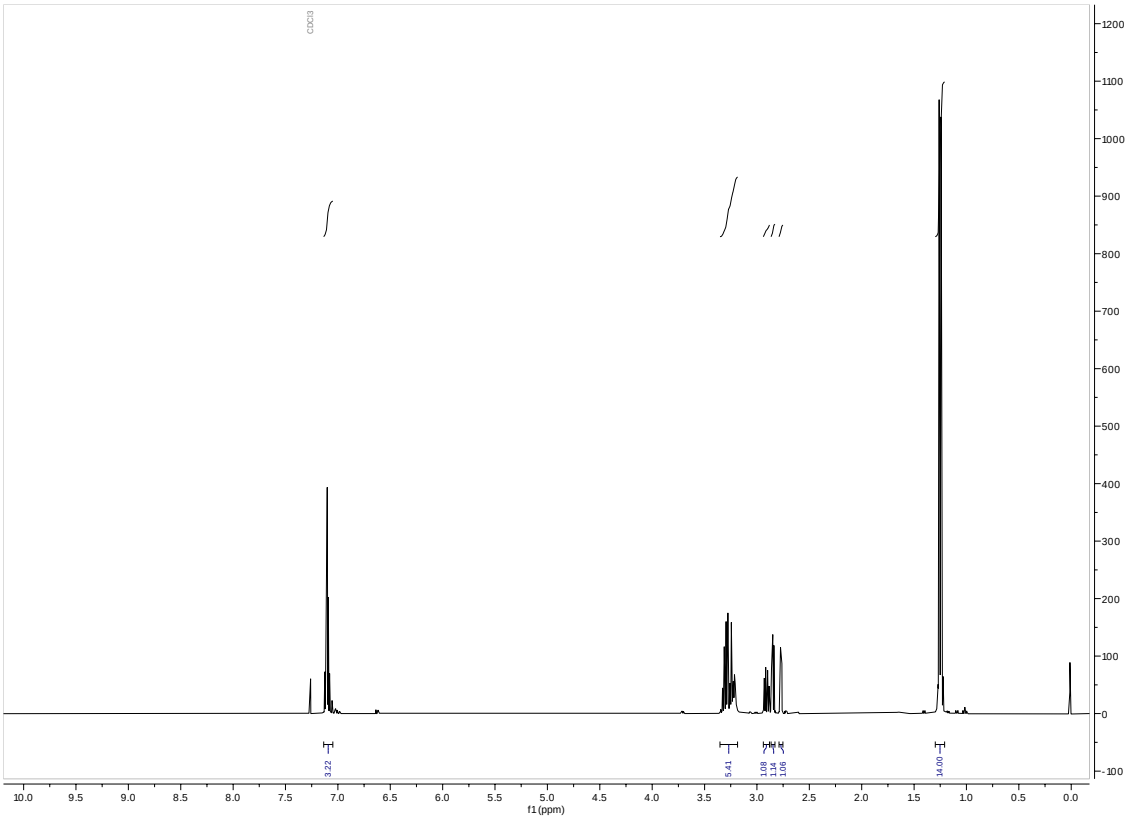
2-Methoxy-N-(oxiran-2-ylmethyl)aniline (1j)

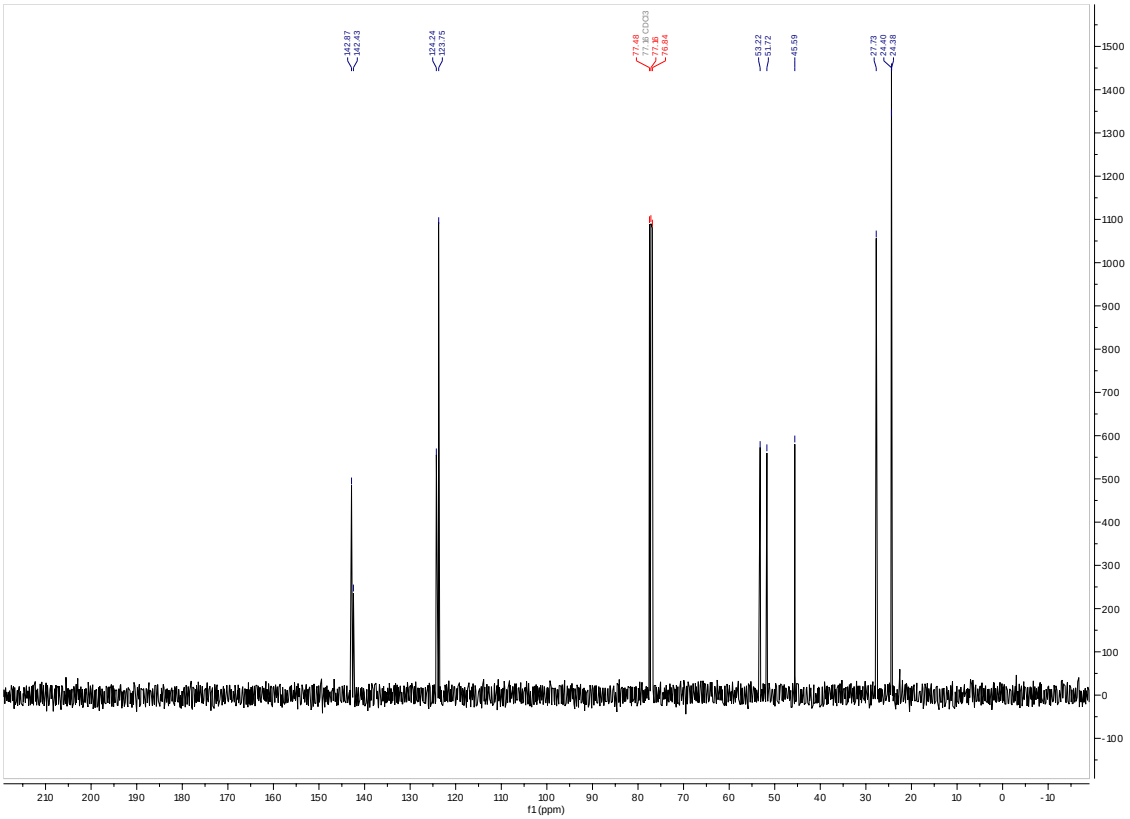


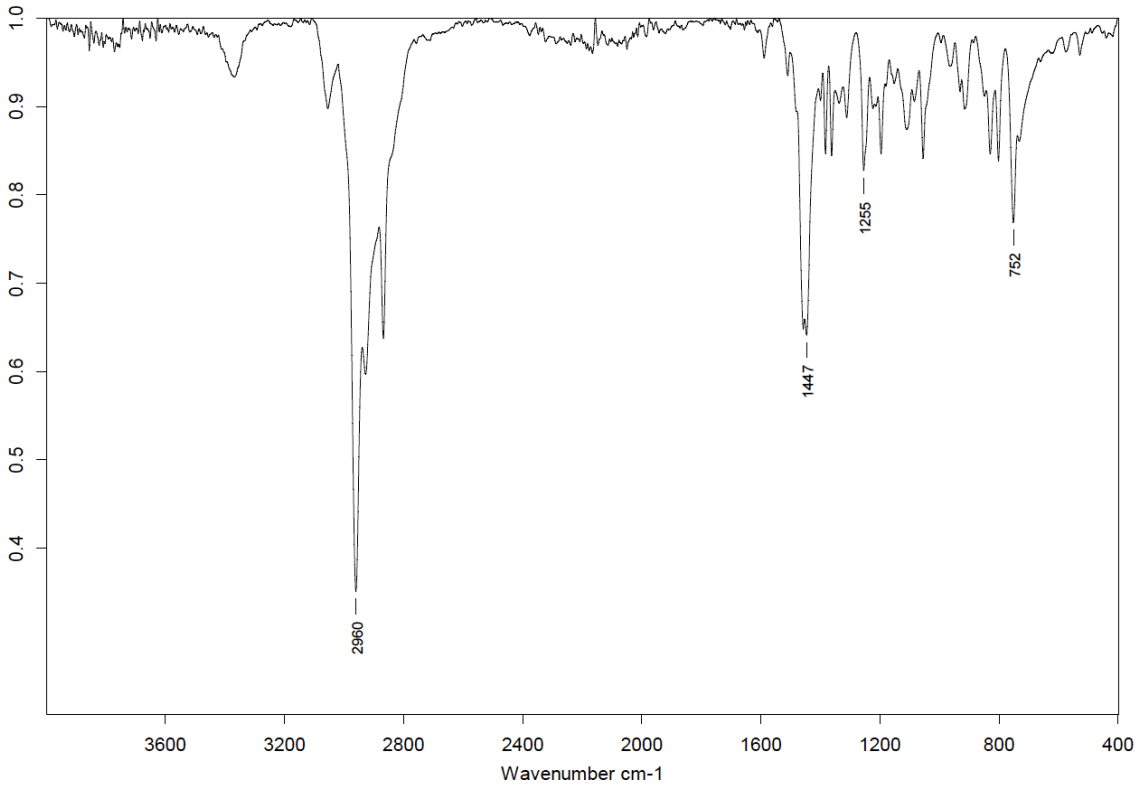



1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
3413
2936
2835
1601
1511
1456
1432
1346
1302
1245
1220
1177
1131
1049
1026
905
833
733
3600
3200
2800
2400
2000
1600
1200
800
400
Wavenumber cm-1

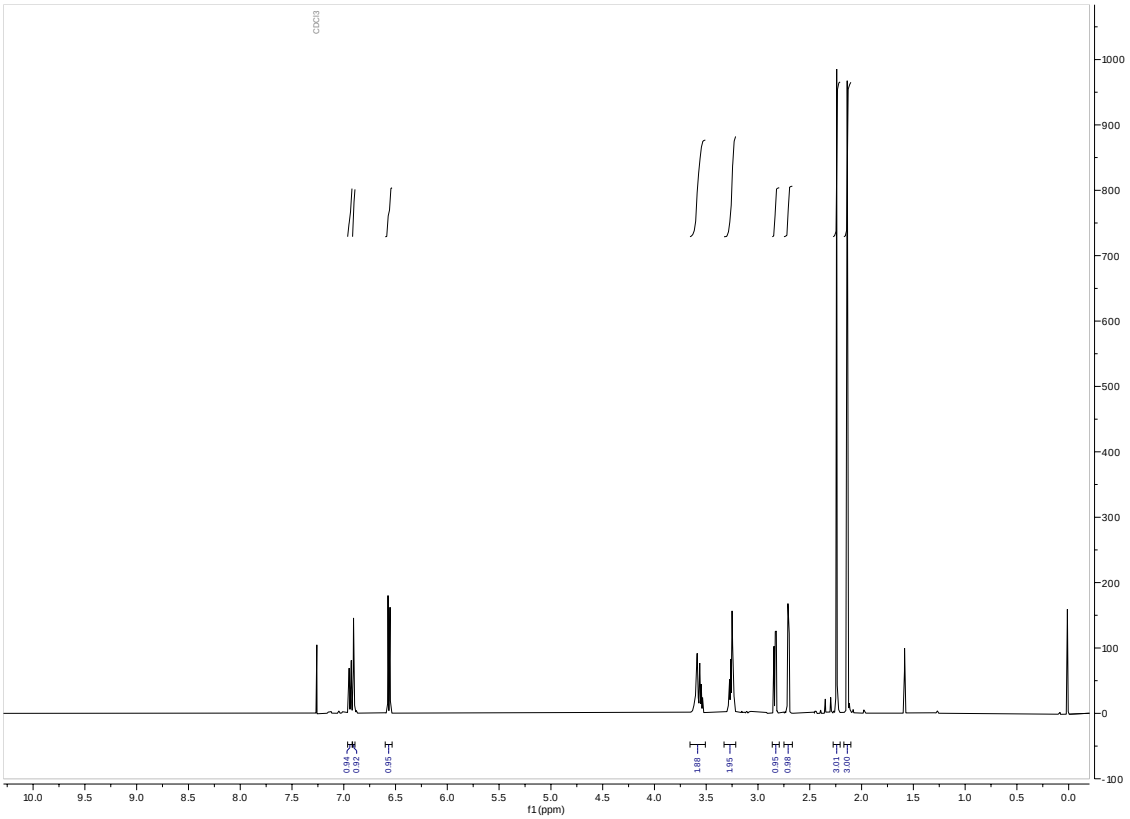
2,6-Di-*iso*-propyl-N-(oxiran-2-ylmethyl)aniline (1n)

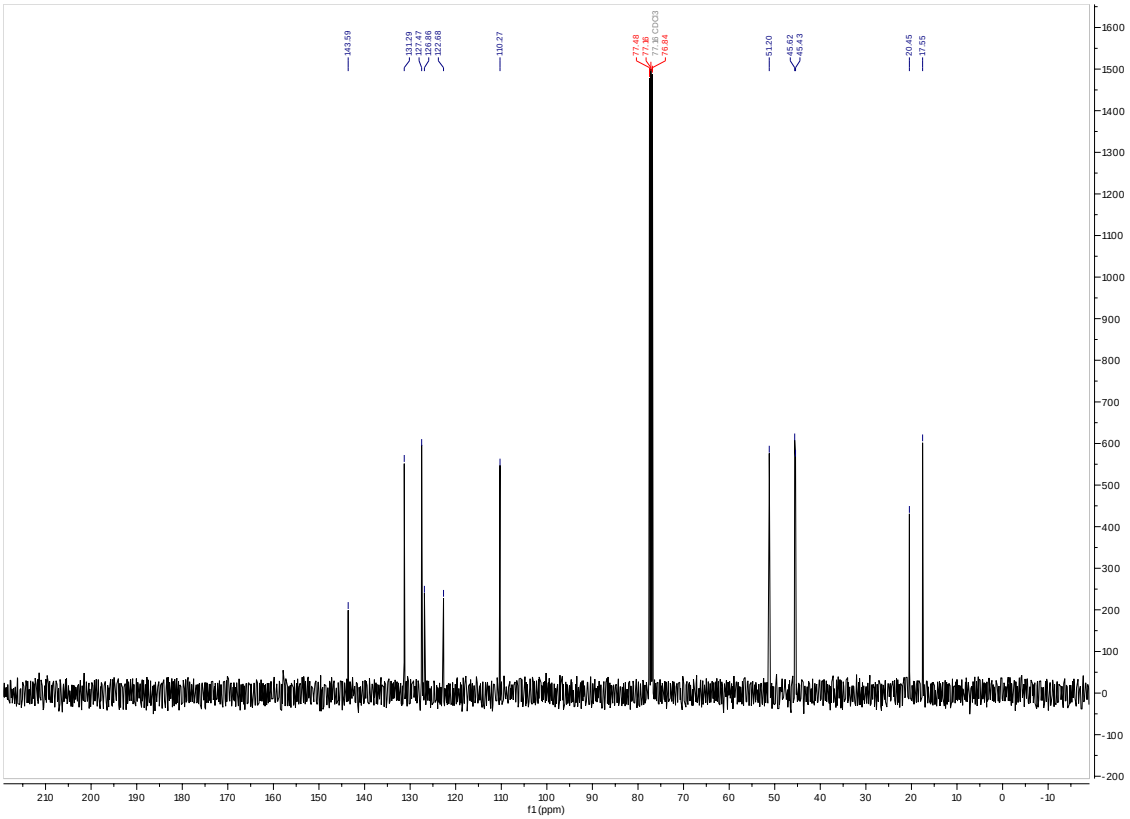


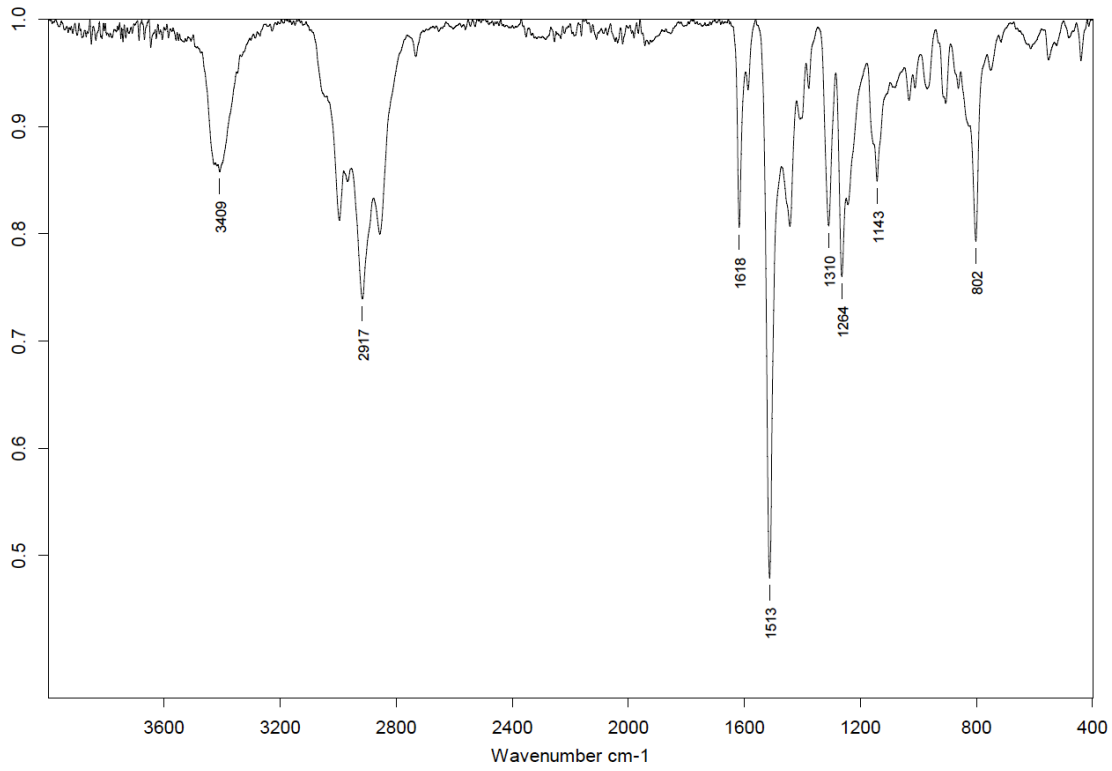



1.0
0.9
0.8
0.7
0.6
0.5
0.4
2960
1447
1255
752
3600
3200
2800
2400
2000
1600
1200
800
400
Wavenumber cm-1

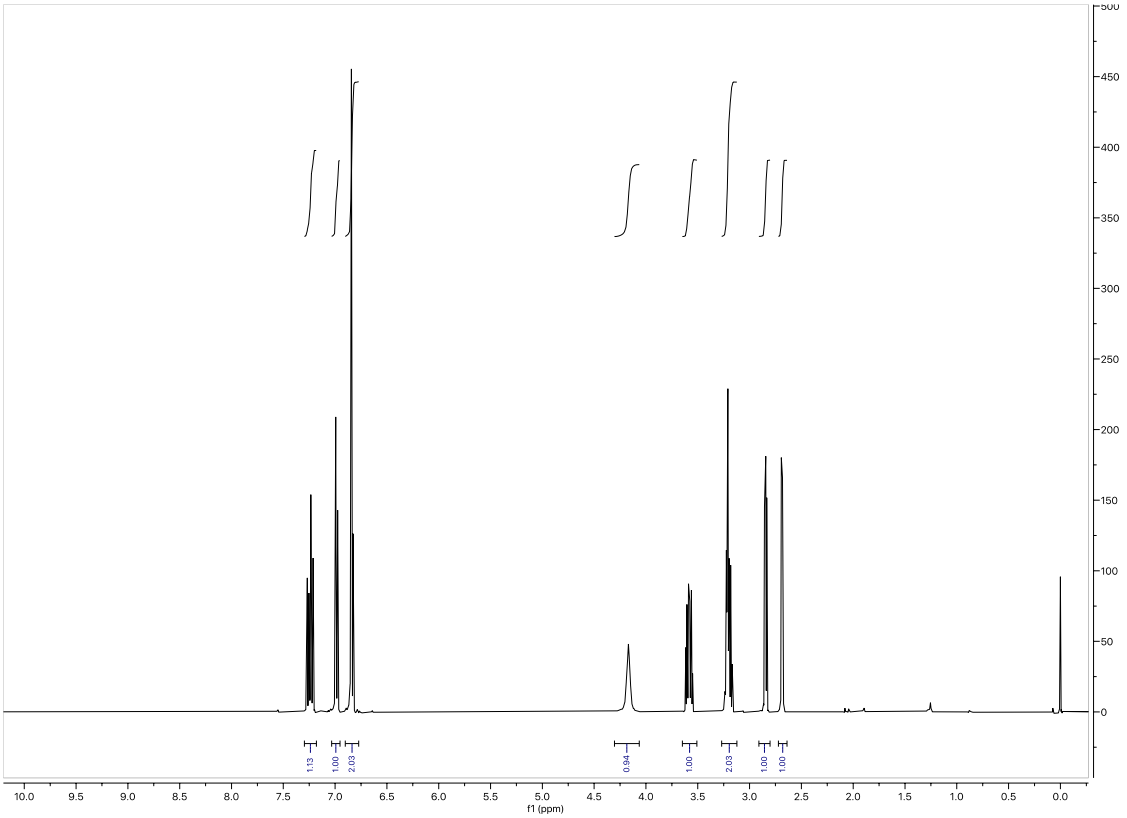
2,4-Dimethyl-N-(oxiran-2-ylmethyl)aniline (1o)

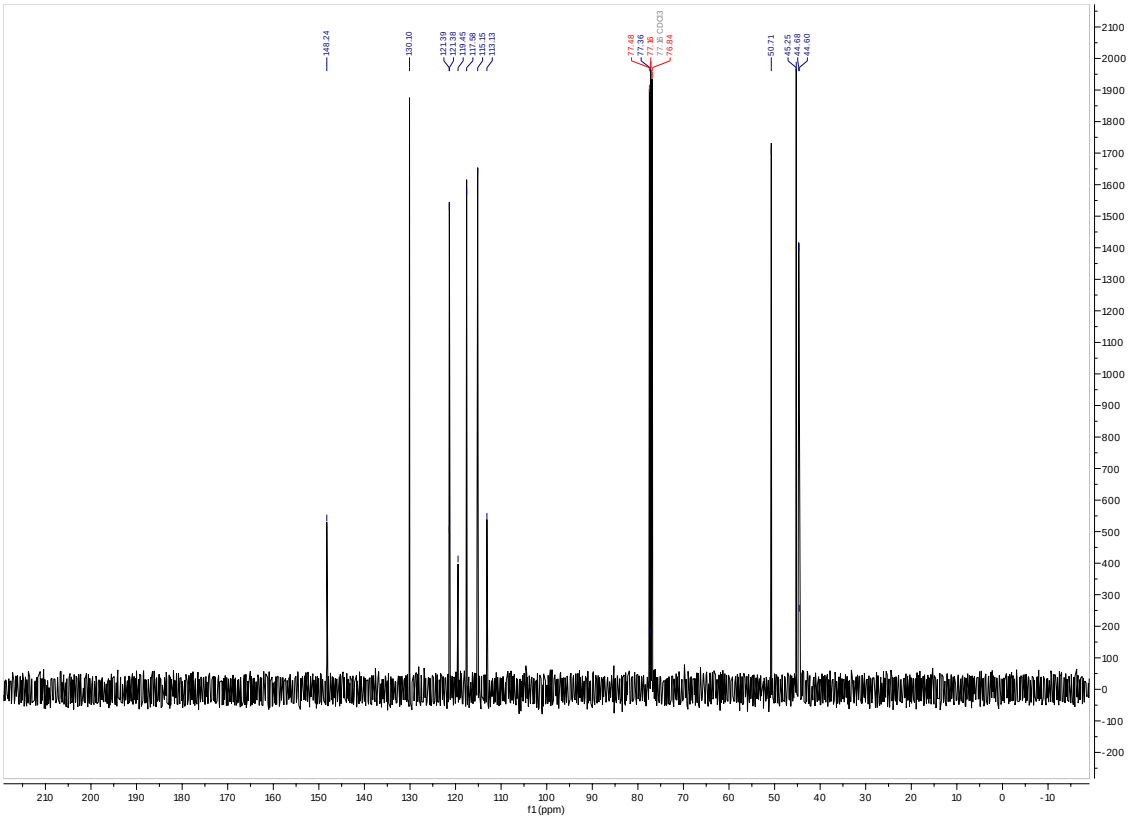


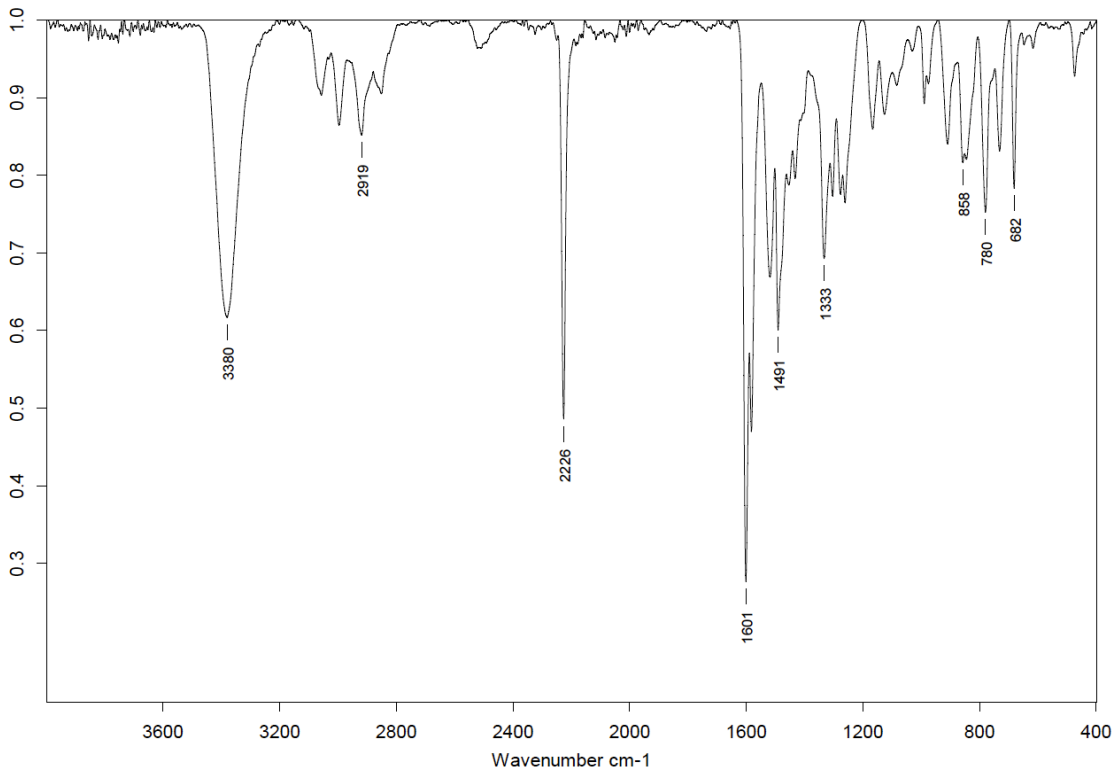



1.0
0.9
0.8
0.7
0.6
0.5
3409
2917
1618
1513
1310
1264
1143
802
3600
3200
2800
2400
2000
1600
1200
800
400
Wavenumber cm-1

3-((Oxiran-2-ylmethyl)amino)benzonitrile (1p)

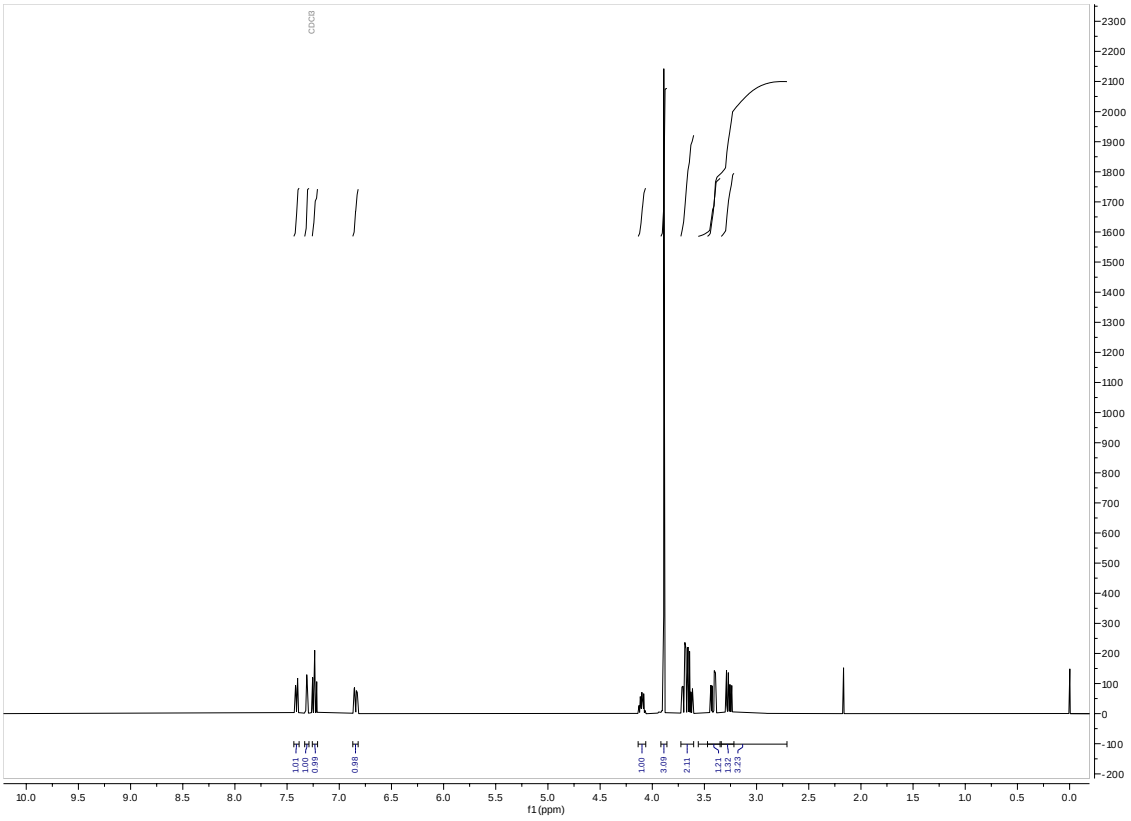


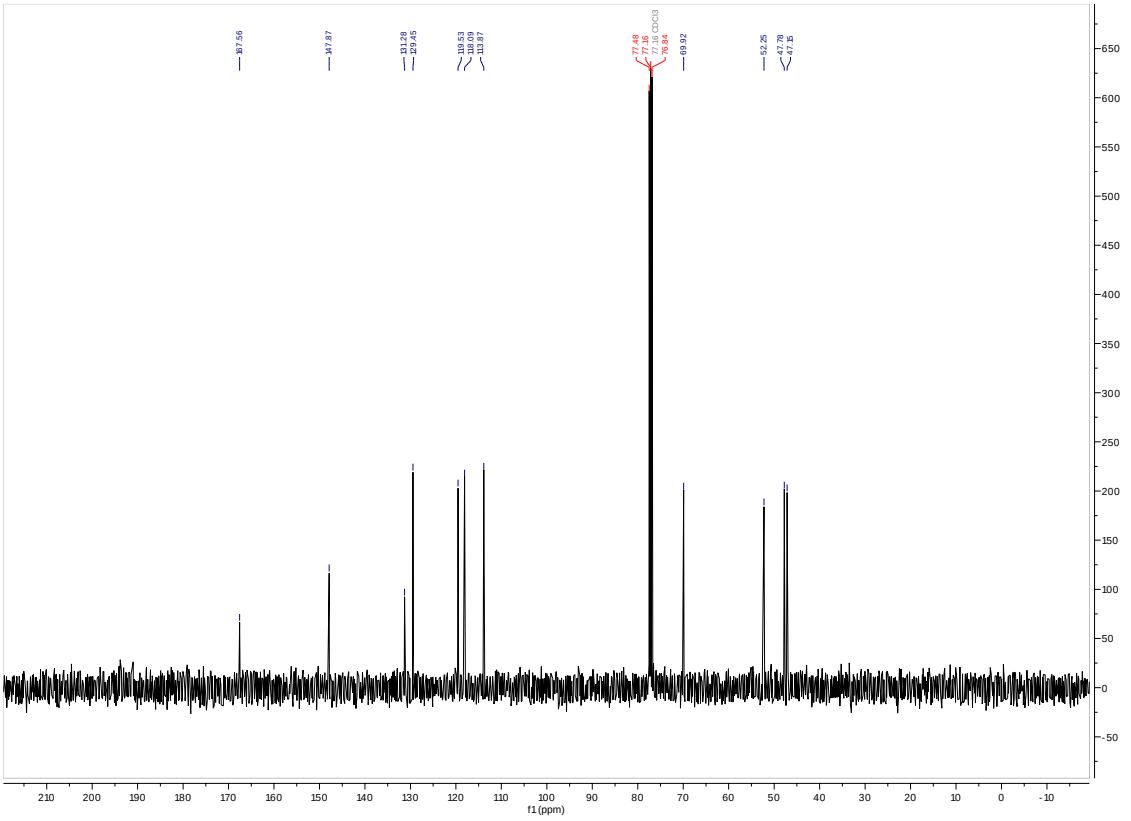


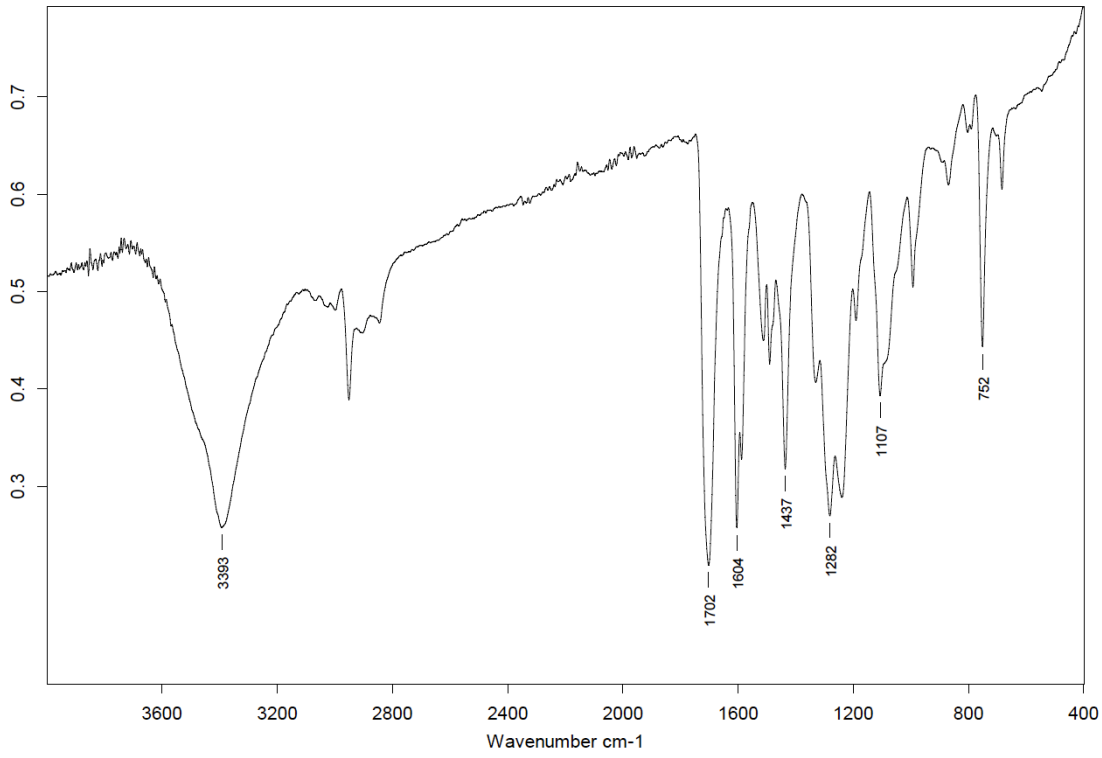

1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
3380
2919
2226
1601
1491
1333
858
780
682
3600
3200
2800
2400
2000
1600
1200
800
400
Wavenumber cm-1

20. ^{1}H NMR, ^{13}C NMR, FT-IR spectra of intermediate halohydrins

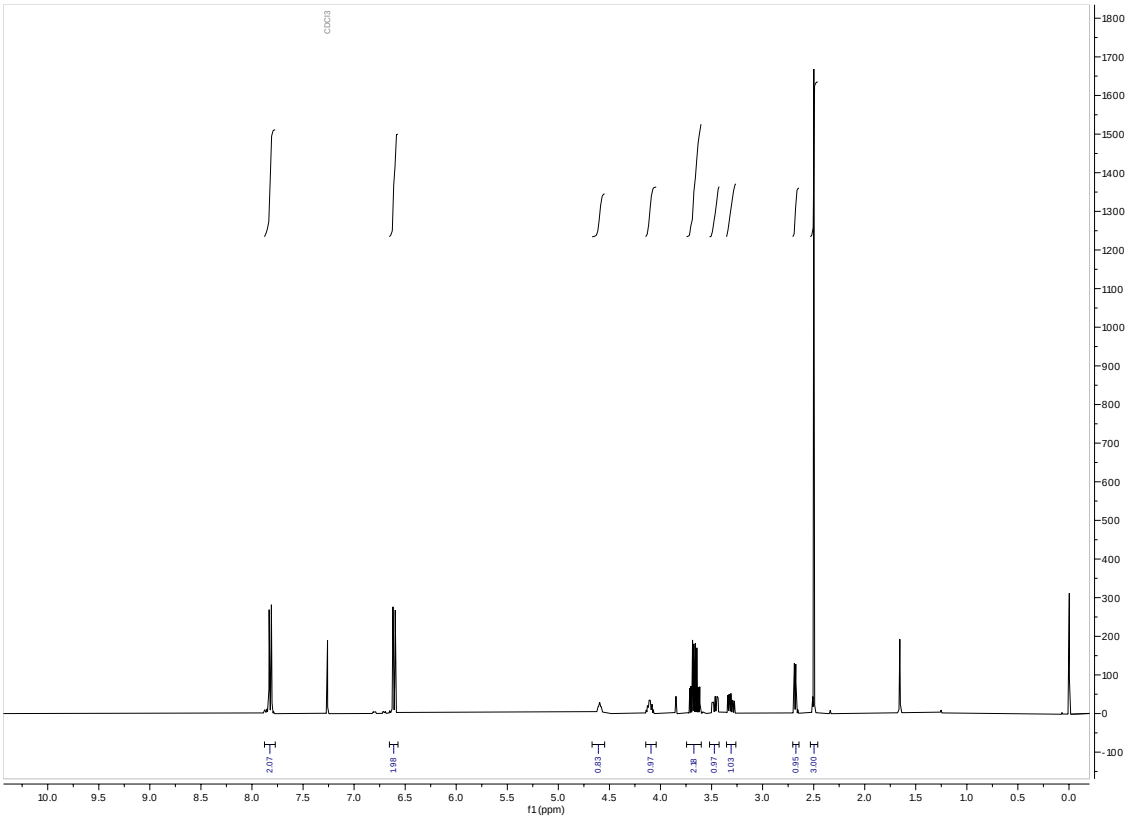
Methyl 3-((3-chloro-2-hydroxypropyl)amino)benzoate (1'b)

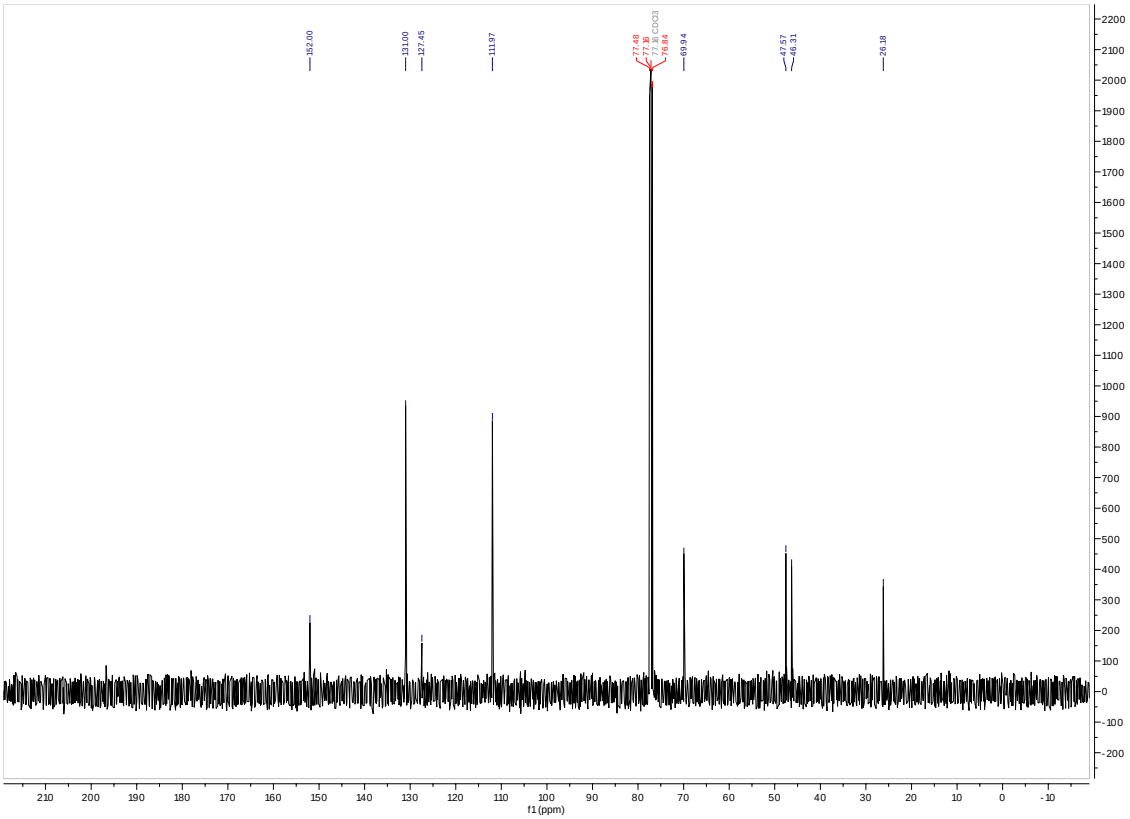


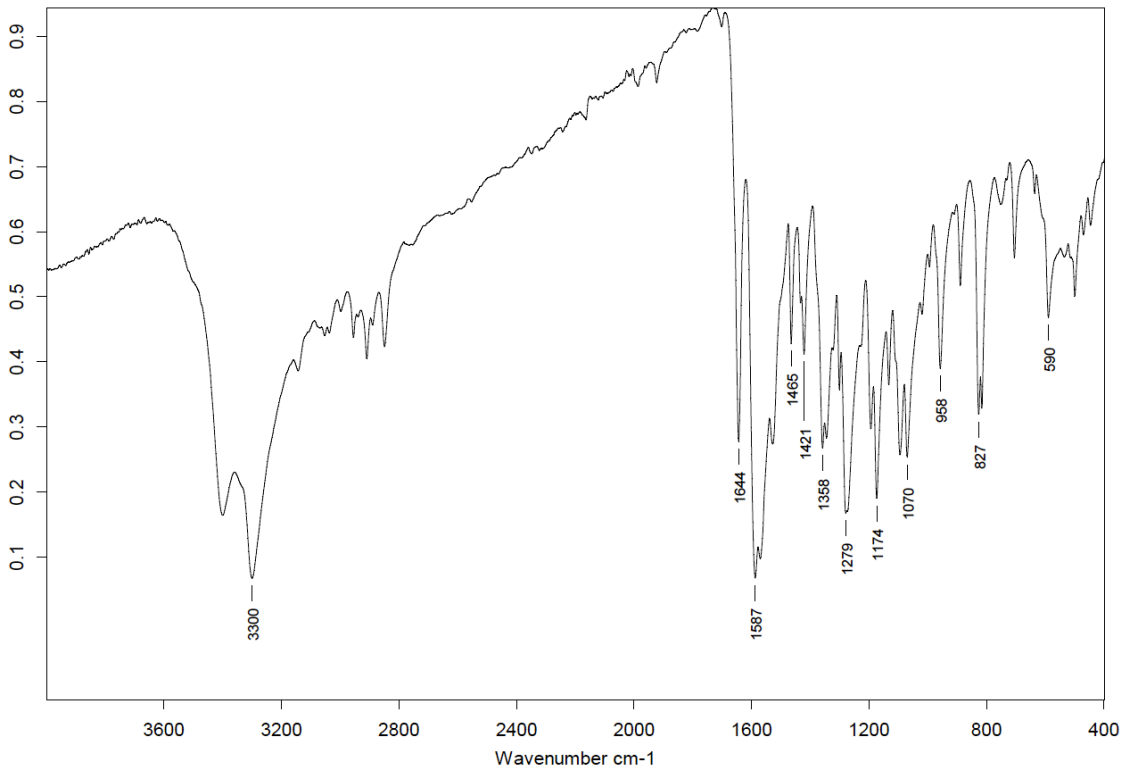



0.7
0.6
0.5
0.4
0.3
3393
1702
1604
1437
1282
1107
752
3600
3200
2800
2400
2000
1600
1200
800
400
Wavenumber cm-1

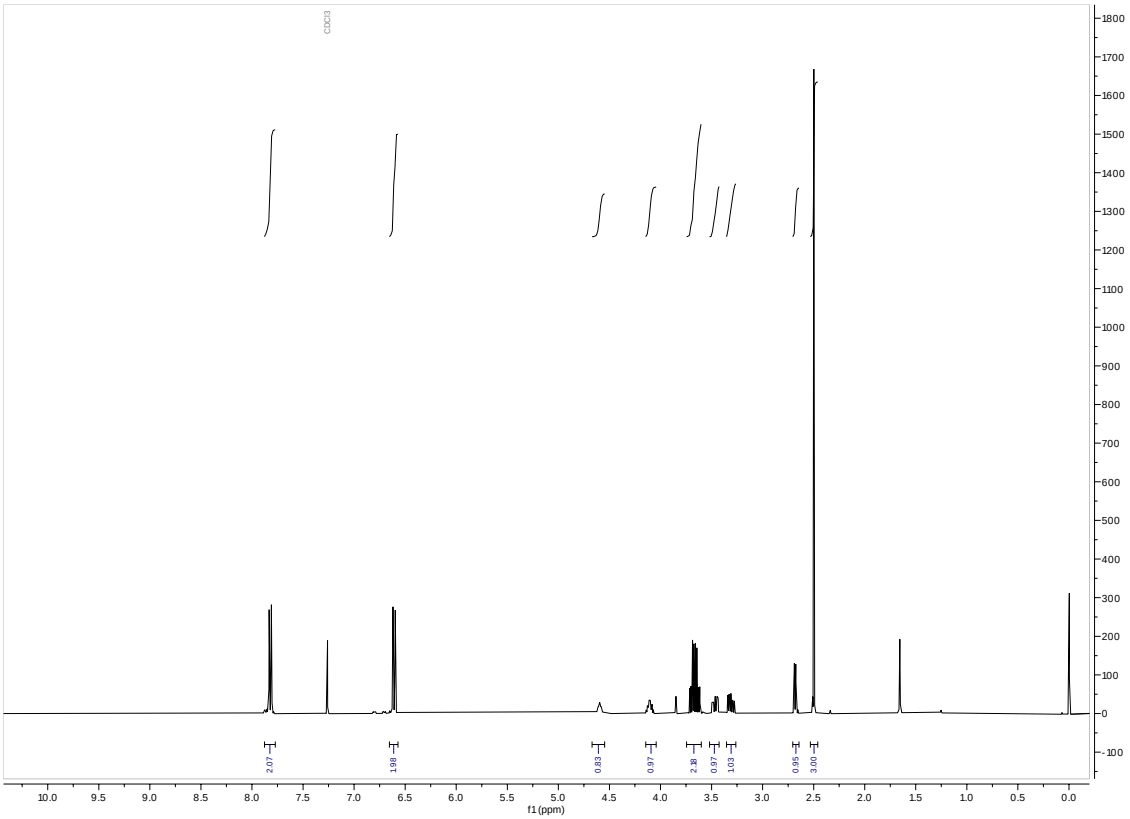
1-(4-((3-Chloro-2-hydroxypropyl)amino)phenyl)ethan-1-one (1’e)

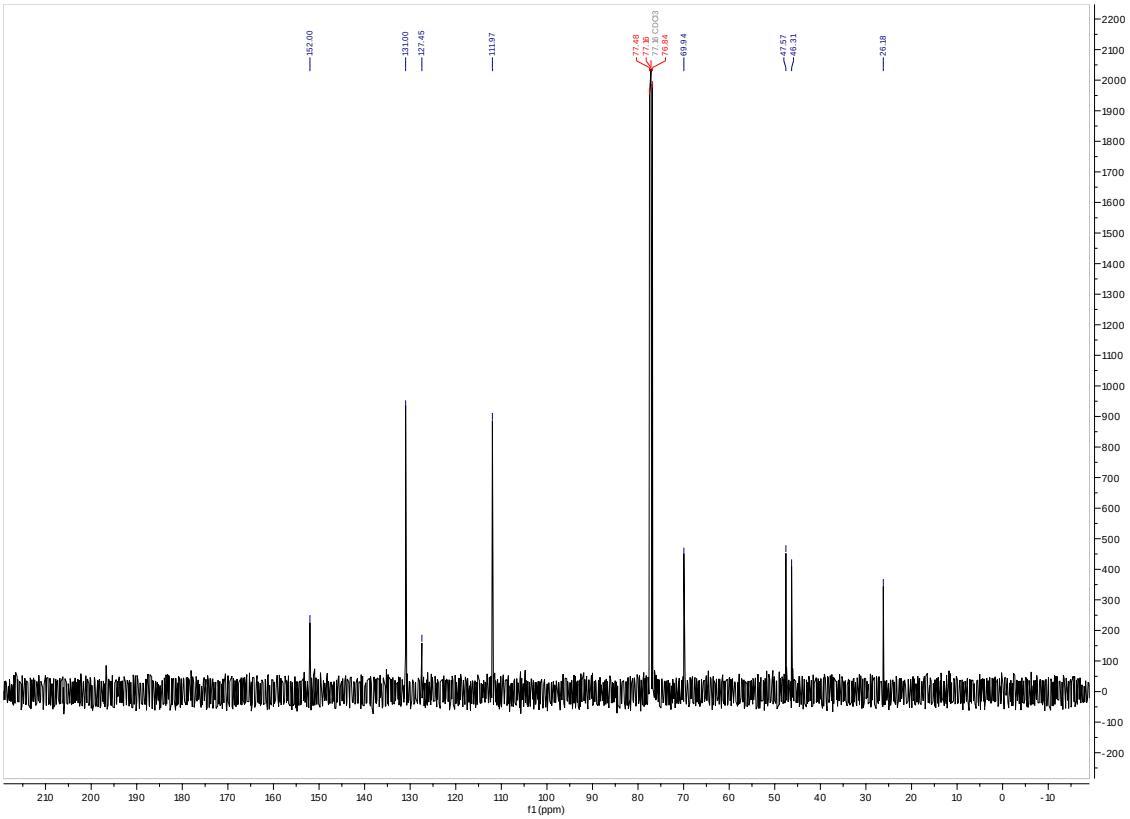


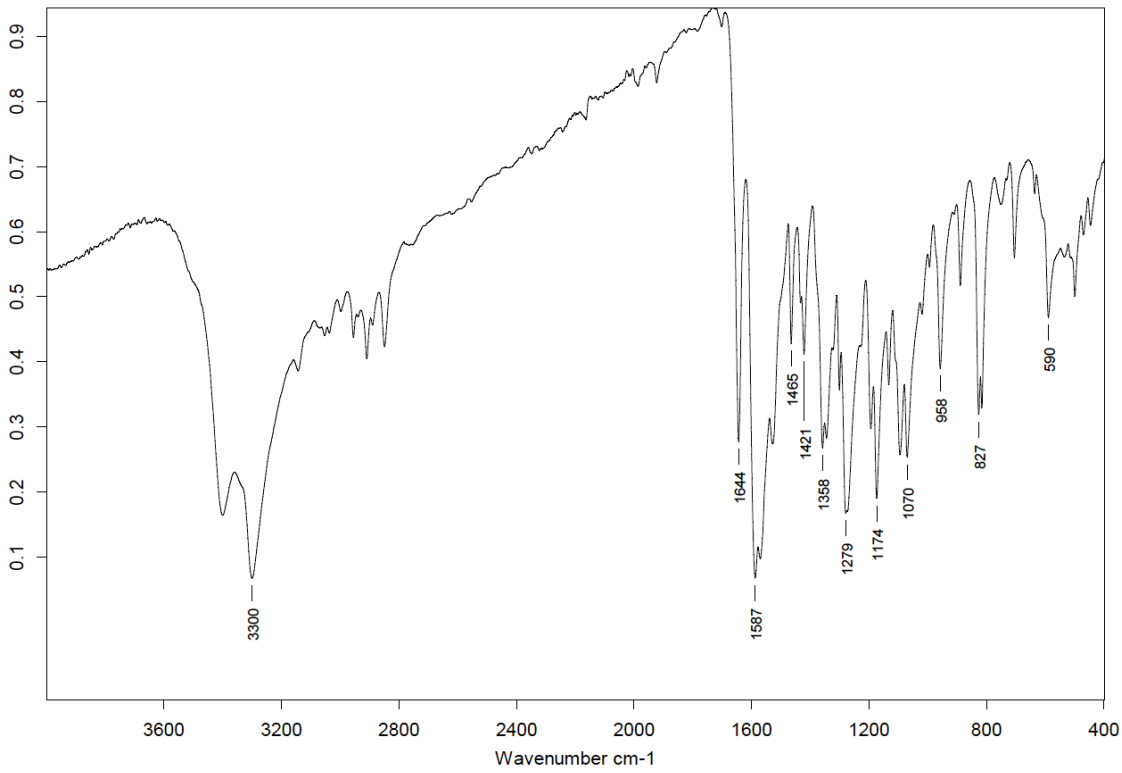



0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
3600
3200
2800
2400
2000
1600
1200
800
400
Wavenumber cm-1
3300
1644
1587
1465
1421
1358
1279
1174
1070
958
827
590

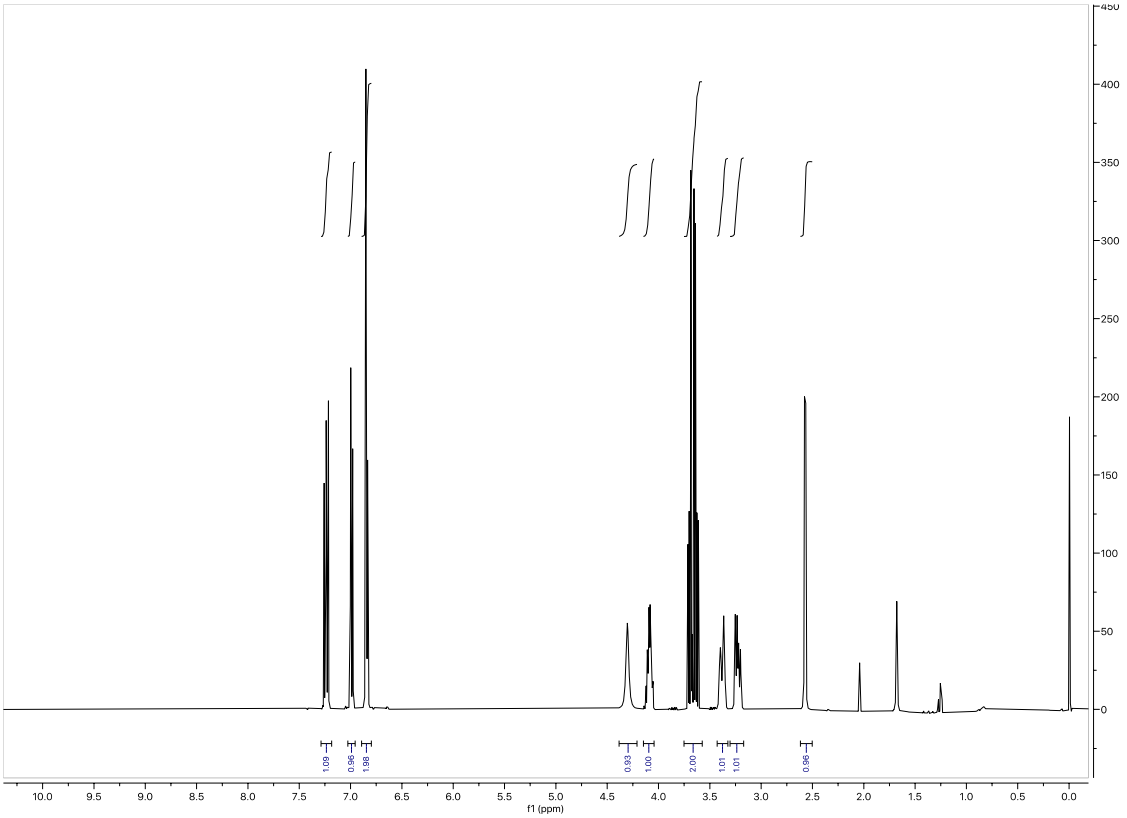
Methyl 4-((3-chloro-2-hydroxypropyl)amino)benzoate (1’f)

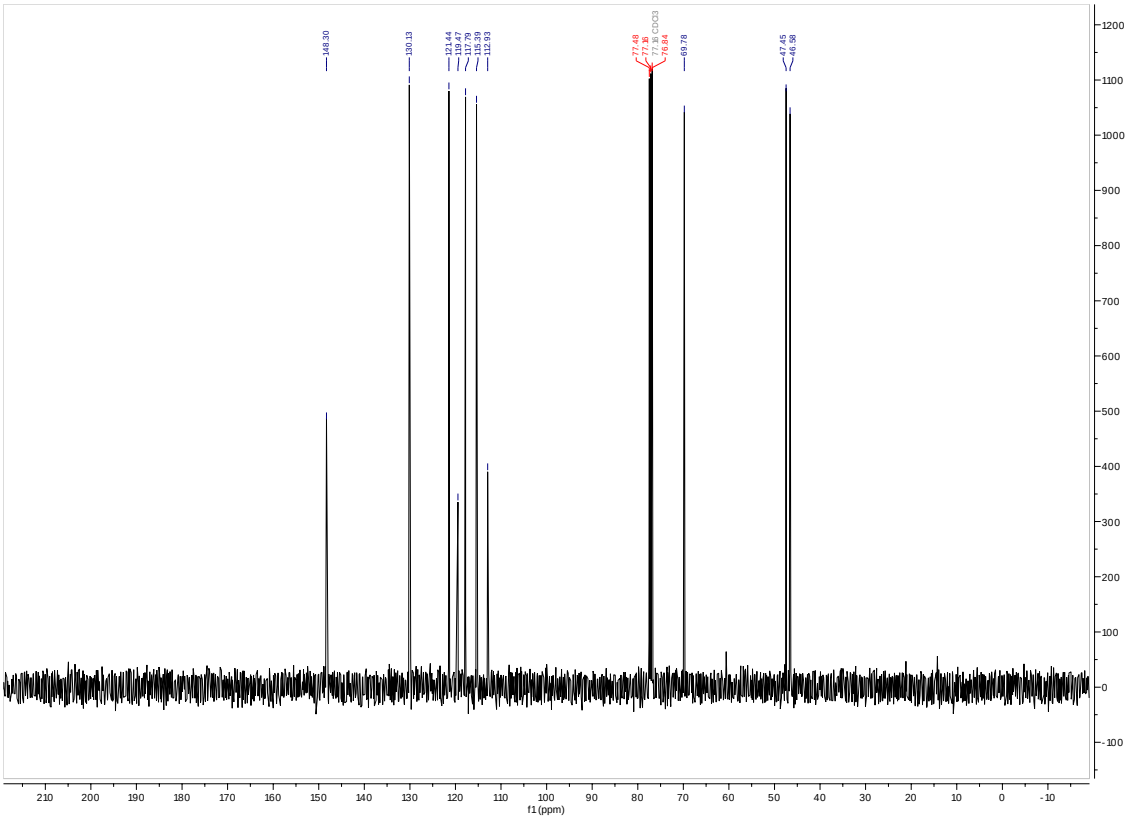


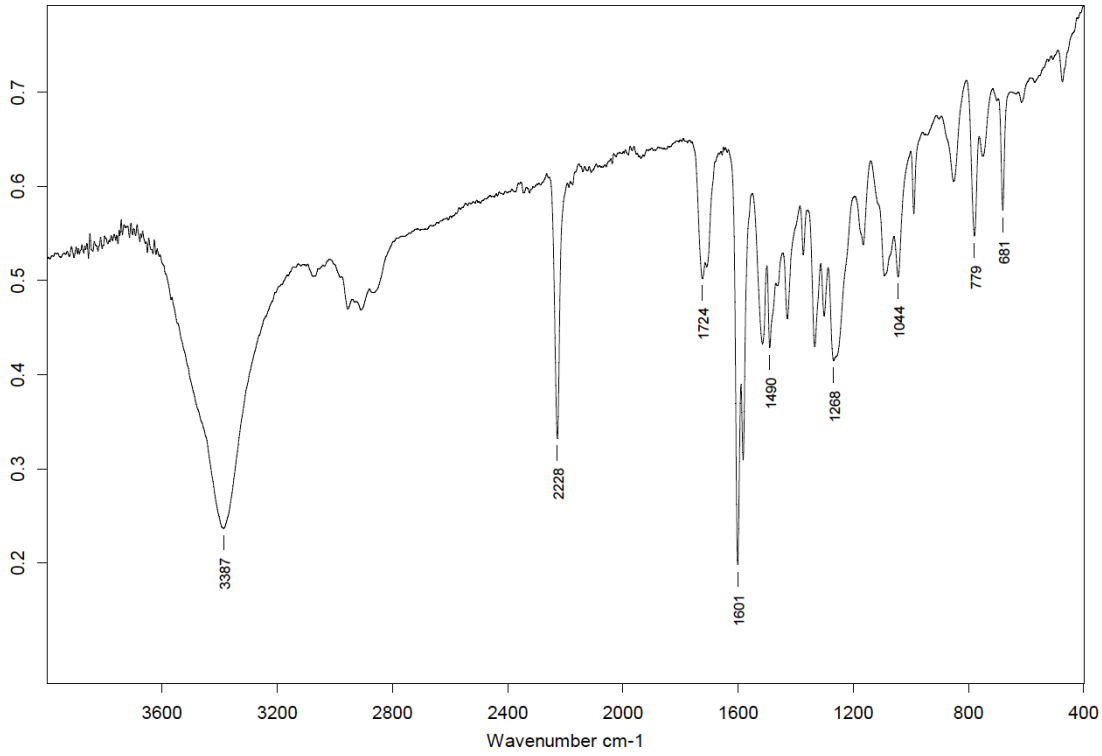



0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
3600
3200
2800
2400
2000
1600
1200
800
400
Wavenumber cm-1
3300
1644
1587
1465
1421
1358
1279
1174
1070
958
827
590

3-((3-Chloro-2-hydroxypropyl)amino)benzonitrile (1’p)






0.2
0.3
0.4
0.5
0.6
0.7
3387
2228
1724
1601
1490
1268
1044
779
681
3600
3200
2800
2400
2000
1600
1200
800
400
Wavenumber cm-1