Arene Reduction by Rh/Pd or Rh/Pt under 1 atm Hydrogen Gas and Room Temperature

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I. General Information

All reactions were carried out in oven-dried glassware sealed with rubber septa under balloon-pressure H_2. "Room temperature" refers to a range of 20 ~ 28 °C, and a thermostat-controlled water bath was applied when the real room temperature was below 20 °C. Reactions were stirred using Teflon-coated magnetic stirring bars, which had been washed with aqua regia to rule out the influence of metallic residue. Organic solutions were concentrated using a Büchi rotary evaporator with a desktop vacuum pump. Analytical TLC was performed with 0.25 mm silica gel G plates with a 254 nm fluorescent indicator. The TLC plates were visualized by ultraviolet light and treatment with I_2 or with phosphomolybdic acid stain followed by gentle heating.

NMR spectra were measured on Bruker ARX 400 (^{1}H at 400 MHz, ^{13}C at 101 MHz) and Bruker AVANCE III (^{1}H at 500 MHz, ^{13}C at 126 MHz, ^{19}F at 471 MHz) nuclear magnetic resonance spectrometers. Data for ^{1}H NMR spectra were reported as follows: chemical shift (ppm, referenced to residual solvent peak ($CDCl_3$ = δ 7.26 ppm, CD_2Cl_2 = δ 5.32 ppm, $(CD_3)_2SO$ = δ 2.50 ppm; s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, dd = doublet of doublets, dt = doublet of triplets, ddd = doublet of doublet of doublets, ddt = doublet of doublet of triplets, tt = triplet of triplets, tq = triplet of quartets, m = multiplet, br = broad), coupling constant (Hz), and integration. Data for ^{13}C NMR were reported in terms of chemical shift (ppm) relative to residual solvent peak ($CDCl_3$ = δ 77.16 ppm, CD_2Cl_2 = δ 53.84 ppm, $(CD_3)_2SO$ = δ 39.52 ppm).

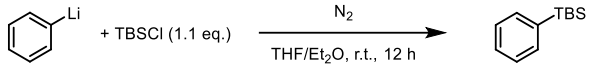
Abbreviations:
Bpin = boronic acid pinacol ester
cod = 1,5-cyclooctadiene
DCM = dichloromethane
EA = ethyl acetate
nbd = norbornadiene
PE = petroleum ether
r.t. = room temperature
TBS = *tert*-butyldimethylsilyl
THF = tetrahydrofuran
TLC = thin layer chromatography
Ts = *p*-toluenesulfonyl

II. Materials

Solvents (A. R.) were used without purification. Rh catalysts were purchased from TCI, J&K, and MREDA. Pd/C (dry, 10 %) was purchased from Alfa, Innochem and J&K. PtO_2 was purchased from BidePharm. Catalysts from different suppliers showed negligible difference in reactivity.

All substrates in this work except **1b** were commercially available. These compounds were purchased from Adamas, BidePharm, D&B, and Heowns, and were used without purification.

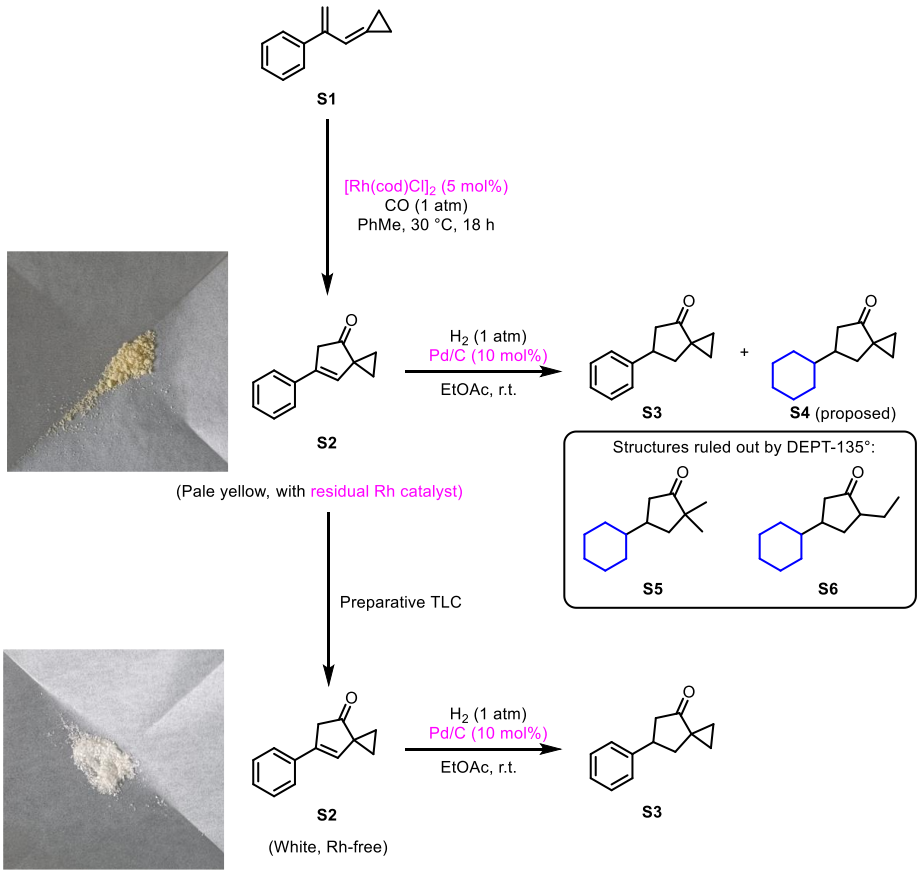
Compound **1b** was synthesized according to a reported procedure:[1]



1b

Under N_2 protection, TBSCl (0.81 g, 5.4 mmol) was dissolved in dry THF (11 mL). The resulting colorless solution was cooled to 0 °C. Under stirring, a solution of PhLi in Et_2O (1.0 mol/L, 5.0 mL, 5.0 mmol) was added dropwise. The reaction mixture was stirred at room temperature for 12 h, quenched with water (10 mL), and extracted with Et_2O (3×10 mL). The combined organic phase was washed with brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, PE as eluent) to give **1b** (0.62 g, 64% yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 – 7.49 (m, 2H), 7.38 – 7.32 (m, 3H), 0.88 (s, 9H), 0.27 (s, 6H). Consistent with previous report.[1]

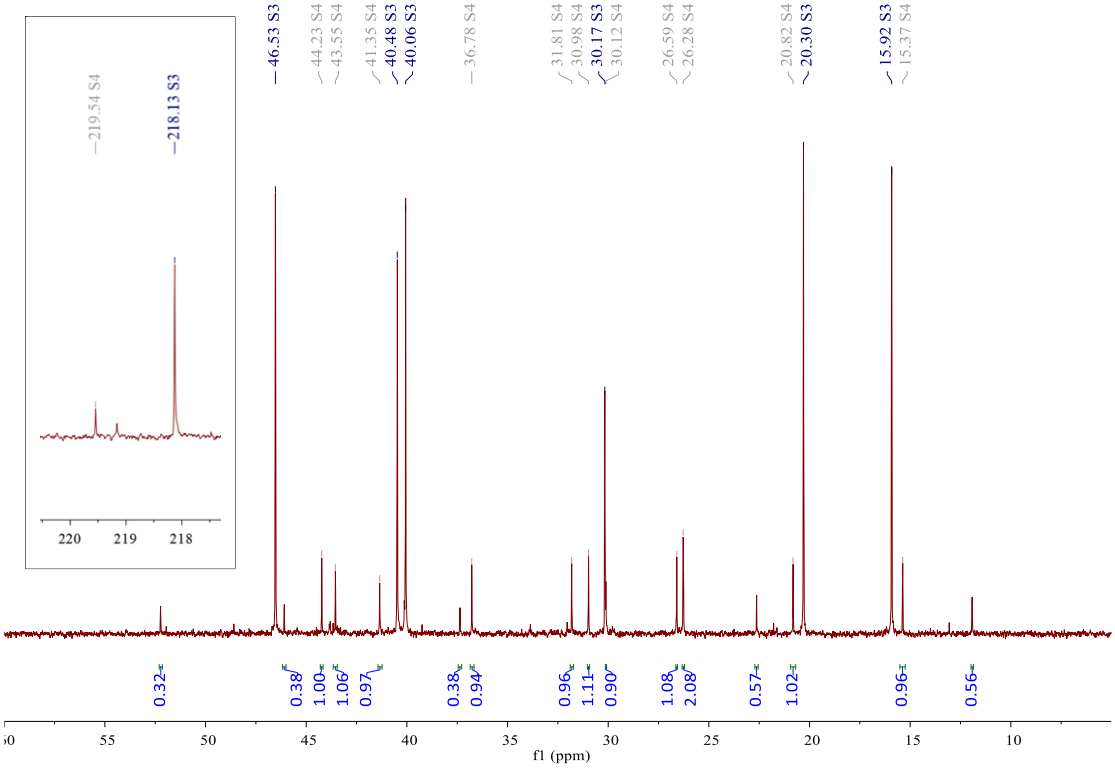
III. Serendipitous Discovery of Rh/Pd-Catalyzed Arene Hydrogenation



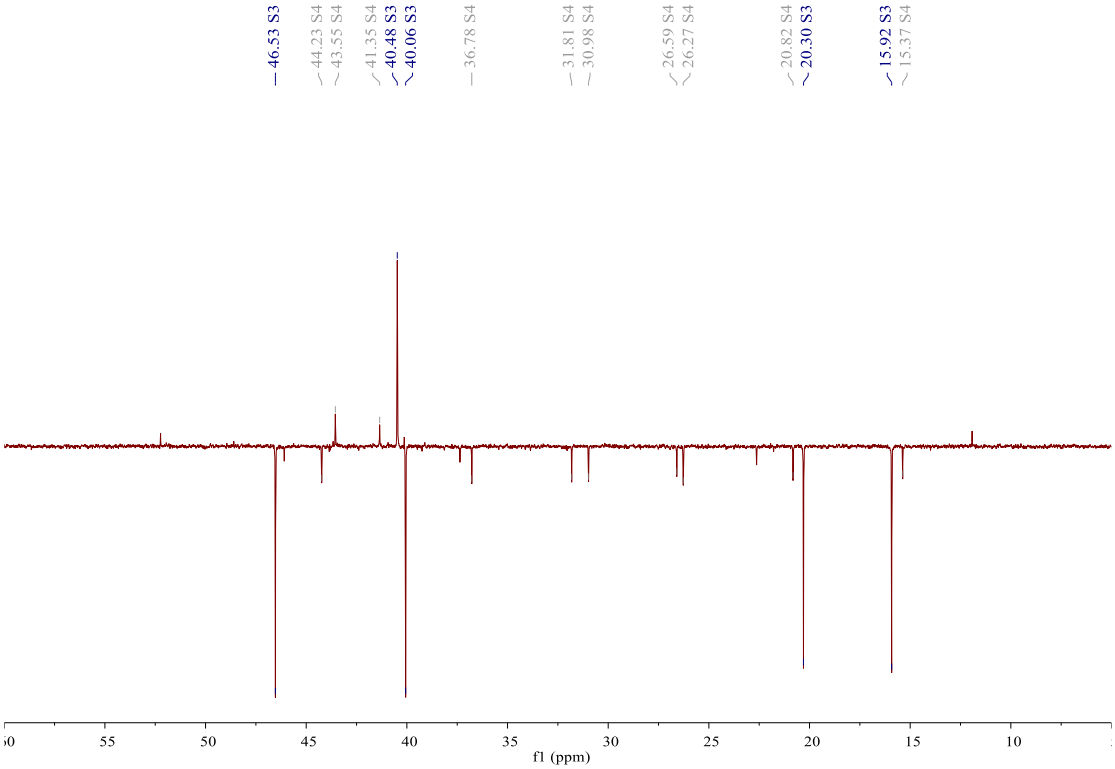
The [4+1] cycloadduct **S2**, which was pale yellow after column chromatography, gave the normal alkene reduction product **S3** (characterized in *J. Am. Chem. Soc.* **2023**, *145*, 17087.) and some unknown by-products when treated with 10% Pd/C and 1 atm H_2 in EtOAc. These by-products have similar R_f values in TLC and cannot be separated. The most abundant by-product, as judged by ^{13}C NMR, contained only aliphatic carbons except for a carbonyl carbon, and no alkene/arene carbons were detected. From the approximate integrals 11 aliphatic carbon peaks (marked in grey below) could be assigned to this compound and we proposed its structure as **S4**. Note that the two *ortho* carbon atoms in the cyclohexyl group were actually different due to proximity to the chiral center. However, the two *meta* carbon atoms were too far from the chiral center to be distinguishable (see the degenerate peak at 26.28 ppm). The potential ring-opening products **S5** and **S6** could be ruled out as they both contained 4 CH/CH_3 carbon atoms, which clearly contradicted with the DEPT-135° spectrum of the reaction mixture. These results prompted us to speculate that residual Rh in **S2** together with Pd/C could have the power to reduce aromatic rings. However, as it was difficult to obtain pure **S4**, we did not further investigate this particular reaction. Instead, we concentrated on establishing a protocol for arene hydrogenation under room temperature and 1 atm hydrogen gas, which is presented in the main text of this paper.

The ^{13}C NMR spectrum and DEPT-135° spectrum of the reaction mixture containing **S3** and **S4** are given below:

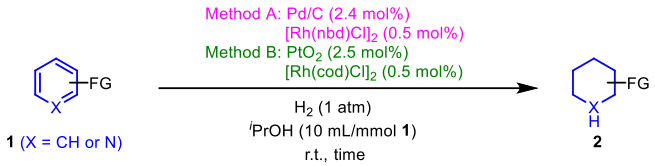
^{13}C NMR spectrum ($CDCl_3$, 101 MHz, only aliphatic region and carbonyl region shown):



DEPT-135° spectrum ($CDCl_3$, 101 MHz, only aliphatic region shown):



IV. General Procedure and Experimental Details of Rh/Pd- and Rh/Pt-Catalyzed Arene Hydrogenation



General procedure:

Method A ([Rh(nbd)Cl]$_2$ + Pd/C): A reaction vessel was charged with substrate **1** (0.50 mmol, 1.0 eq.) and 10% dry Pd/C (12.6 mg, containing 11.8 μmol of Pd, 2.4 mol%). The reaction vessel was then moved into a glove box. [Rh(nbd)Cl]$_2$ (1.2 mg, 2.6 μmol, 0.5 mol%) was added, and the reaction vessel was sealed with a rubber septum before being moved out of the glove box. Isopropanol (5 mL) was added via syringe to dissolve the Rh catalyst. A H_2 balloon (~1 L) was attached to the reaction vessel, which was then evacuated and refilled with H_2 for three times. The H_2 balloon was kept, and the reaction mixture was stirred at room temperature for the time indicated below. Upon completion, the reaction mixture was filtered through a thin pad of silica gel and eluted with EA. The filtrate was concentrated *in vacuo* to afford product **2**.

Method B ([Rh(cod)Cl]$_2$ + PtO$_2$): A reaction vessel was charged with substrate **1** (0.50 mmol, 1.0 eq.), PtO_2 (2.8 mg, 12.3 μmol, 2.5 mol%) and [Rh(cod)Cl]$_2$ (1.3 mg, 2.6 μmol, 0.5 mol%). Isopropanol (5 mL) was added to dissolve the Rh catalyst, and the vessel was sealed with a rubber septum. A H_2 balloon (~1 L) was attached to the reaction vessel, which was then evacuated and refilled with H_2 for three times. The H_2 balloon was kept, and the reaction mixture was stirred at room temperature for the time indicated below. Upon completion, the reaction mixture was filtered through a thin pad of silica gel and eluted with EA. The filtrate was concentrated *in vacuo* to afford product **2**.

Unless otherwise stated, the products obtained in these ways were pure enough for NMR characterization.

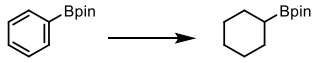
An illustration of the reaction setup is given below (Figure S1). This photograph was taken for Method B, substrate **1s**. Note the reaction mixture was initially pale yellow due to existence of [Rh(cod)Cl]$_2$ (Figure S2, left). However, the yellowish color soon (0.5~1 h after the beginning of the reaction) faded and black particles were formed (Figure S2, right). For some substrates, the black particles may aggregate after the reaction had completed, revealing a colorless supernatant.

For Method A, the yellowish color of [Rh(nbd)Cl]$_2$ was obscured by the black color of Pd/C, and it was difficult to observe the change in color. However, if the mixture was left to stand after the reaction had completed, the catalyst would precipitate, and one would also observe a colorless supernatant.

Figure S1. Setup for 0.5 mmol scale reaction (Method B, substrate **1s**)

Figure S2. Reaction mixture (Method B, substrate **1s**) at 0 h (left) and 12 h (right)

Experimental details and characterization data:



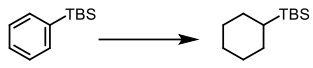
1a **2a**

Method A: Run 1: 101.9 mg (0.499 mmol) of **1a** gave 90.6 mg of **2a** after 24 h, 86% yield.
Run 2: 101.7 mg (0.498 mmol) of **1a** gave 93.4 mg of **2a** after 24 h, 89% yield.
Average yield: 88%

Method B: Run 1: 102.0 mg (0.500 mmol) of **1a** gave 86.3 mg of **2a** after 18 h, 82% yield.
Run 2: 102.1 mg (0.500 mmol) of **1a** gave 89.1 mg of **2a** after 18 h, 85% yield.
Average yield: 84%

2a: Colorless oil, TLC R_f = 0.6 (PE/EA = 20:1), a known compound.[2]

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.70 – 1.53 (m, 5H), 1.39 – 1.24 (m, 5H), 1.23 (s, 12H), 1.02 – 0.92 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 82.9, 28.1, 27.3, 26.9, 24.9.



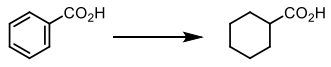
1b **2b**

Method A: Run 1: 96.2 mg (0.500 mmol) of **1b** gave 89.2 mg of **2b** after 18 h, 90% yield.
Run 2: 96.3 mg (0.501 mmol) of **1b** gave 88.7 mg of **2b** after 18 h, 89% yield.
Average yield: 90%

Method B: Run 1: 96.2 mg (0.500 mmol) of **1b** gave 86.7 mg of **2b** after 18 h, 87% yield.
Run 2: 96.2 mg (0.500 mmol) of **1b** gave 86.9 mg of **2b** after 18 h, 88% yield.
Average yield: 88%

2b: Colorless oil, TLC R_f = 0.9 (100% PE), a known compound.[3] This compound is potentially volatile and prolonged evacuation may lead to reduced yields.

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.76 – 1.67 (m, 5H), 1.28 – 1.08 (m, 5H), 0.89 (s, 9H), 0.78 – 0.68 (m, 1H), -0.12 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 28.9, 28.5, 27.5, 27.1, 24.2, 17.5, -7.4.



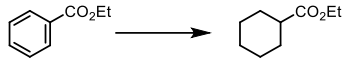
1c **2c**

Method A: Run 1: 61.1 mg (0.500 mmol) of **1c** gave 63.7 mg of **2c** after 12 h, 99% yield.
Run 2: 61.0 mg (0.500 mmol) of **1c** gave 63.8 mg of **2c** after 12 h, 100% yield.
Average yield: 100%

Method B: Run 1: 61.2 mg (0.501 mmol) of **1c** gave 64.1 mg of **2c** after 18 h, 100% yield.
Run 2: 61.1 mg (0.500 mmol) of **1c** gave 63.7 mg of **2c** after 18 h, 99% yield.
Average yield: 100%

2c: Colorless crystal, TLC R_f = 0.5 (6 mL PE + 2 mL EA + 3 drops of HOAc), a known compound.[4]

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.34 (br s, 1H), 2.40 – 2.27 (m, 1H), 1.99 – 1.88 (m, 2H), 1.81 – 1.72 (m, 2H), 1.68 – 1.61 (m, 1H), 1.52 – 1.40 (m, 2H), 1.36 – 1.19 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 182.8, 43.1, 28.9, 25.8, 25.5.



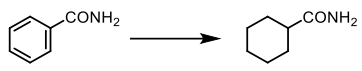
1d **2d**

Method A: Run 1: 75.5 mg (0.503 mmol) of **1d** gave 64.4 mg of **2d** after 12 h, 82% yield.
Run 2: 75.2 mg (0.501 mmol) of **1d** gave 67.2 mg of **2d** after 12 h, 86% yield.
Average yield: 84%

Method B: Run 1: 75.2 mg (0.501 mmol) of **1d** gave 63.8 mg of **2d** after 12 h, 82% yield.
Run 2: 75.2 mg (0.501 mmol) of **1d** gave 64.7 mg of **2d** after 12 h, 83% yield.
Average yield: 82%

2d: Colorless oil, TLC R_f = 0.4 (PE/EA = 20:1), a known compound.[4] This compound is volatile and prolonged evacuation will lead to reduced yields.

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.10 (q, J = 7.1 Hz, 2H), 2.27 (tt, J = 11.3, 3.7 Hz, 1H), 1.93 – 1.84 (m, 2H), 1.78 – 1.70 (m, 2H), 1.66 – 1.59 (m, 1H), 1.49 – 1.37 (m, 2H), 1.33 – 1.18 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.3, 60.2, 43.4, 29.2, 25.9, 25.6, 14.4.



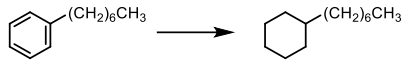
1e 2e

Method A: Run 1: 60.8 mg (0.502 mmol) of **1e** gave 63.8 mg of **2e** after 24 h, 100% yield.
Run 2: 60.6 mg (0.500 mmol) of **1e** gave 63.7 mg of **2e** after 24 h, 100% yield.
Average yield: 100%

Method B: Run 1: 60.6 mg (0.500 mmol) of **1e** gave 63.8 mg of **2e** after 36 h, 100% yield.
Run 2: 60.8 mg (0.502 mmol) of **1e** gave 63.6 mg of **2e** after 36 h, 100% yield.
Average yield: 100%

2e: White solid, TLC R_f = 0.2 (PE/EA = 1:1), a known compound.[5]

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.65 (br s, 1H), 5.51 (br s, 1H), 2.14 (tt, *J* = 11.7, 3.5 Hz, 1H), 1.95 – 1.84 (m, 2H), 1.84 – 1.74 (m, 2H), 1.72 – 1.61 (m, 1H), 1.49 – 1.34 (m, 2H), 1.35 – 1.13 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 178.9, 44.9, 29.8, 25.9, 25.8.



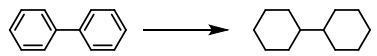
1f 2f

Method A: Run 1: 88.2 mg (0.500 mmol) of **1f** gave 87.8 mg of **2f** after 12 h, 96% yield.
Run 2: 88.1 mg (0.500 mmol) of **1f** gave 88.3 mg of **2f** after 12 h, 97% yield.
Average yield: 96%

Method B: Run 1: 88.3 mg (0.501 mmol) of **1f** gave 88.6mg of **2f** after 12 h, 97% yield.
Run 2: 88.2 mg (0.500 mmol) of **1f** gave 86.7 mg of **2f** after 12 h, 95% yield.
Average yield: 96%

2f: Colorless oil, TLC R_f = 0.9 (100% PE), a known compound.[6] This compound is potentially volatile and prolonged evacuation may lead to reduced yields.

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.75 – 1.55 (m, 5H), 1.35 – 1.09 (m, 16H), 0.93 – 0.78 (m, 5H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 37.9, 37.7, 33.6, 32.1, 30.1, 29.6, 27.1, 27.0, 26.6, 22.9, 14.3.



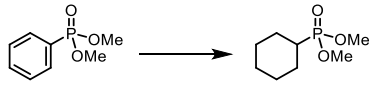
1g 2g

Method A: Run 1: 77.0 mg (0.499 mmol) of **1g** gave 74.8 mg of **2g** after 36 h, 90% yield.
Run 2: 77.2 mg (0.501 mmol) of **1g** gave 75.7 mg of **2g** after 36 h, 91% yield.
Average yield: 90%

Method B: Run 1: 77.6 mg (0.503 mmol) of **1g** gave 70.9 mg of **2g** after 48 h, 85% yield.
Run 2: 77.2 mg (0.501 mmol) of **1g** gave 74.5 mg of **2g** after 48 h, 89% yield.
Average yield: 87%

2g: Colorless oil, TLC R_f = 0.9 (100% PE), a known compound.[7] This compound is volatile and prolonged evacuation will lead to reduced yields.

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.75 – 1.59 (m, 10H), 1.26 – 0.89 (m, 12H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 43.6, 30.3, 27.07, 27.06.



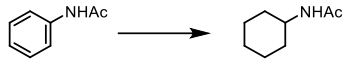
1h 2h

Method A: Run 1: 92.8 mg (0.498 mmol) of **1h** gave 92.8 mg of **2h** after 24 h, 97 % yield.
Run 2: 93.1 mg (0.500 mmol) of **1h** gave 88.2 mg of **2h** after 24 h, 92 % yield.
Average yield: 94%

Method B: Run 1: 92.9 mg (0.499 mmol) of **1h** gave 96.5 mg of **2h** after 18 h, 100% yield.
Run 2: 93.2 mg (0.501 mmol) of **1h** gave 91.7 mg of **2h** after 18 h, 95% yield.
Average yield: 98%

2h: Colorless oil, TLC R_f = 0.2 (PE/EA = 1:1), a known compound.[8,9]

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.72 (d, *J* = 10.4 Hz, 6H), 1.98 – 1.88 (m, 2H), 1.83 – 1.65 (m, 4H), 1.44 – 1.31 (m, 2H), 1.28 – 1.17 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 52.5 (d, *J* = 6.7 Hz), 35.4 (d, *J* = 142.0 Hz), 26.2 (d, *J* = 16.2 Hz), 25.9, 25.8.



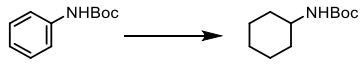
1i **2i**

Method A: Run 1: 67.8 mg (0.502 mmol) of **1i** gave 71.1 mg of **2i** after 12 h, 100% yield.
Run 2: 67.7 mg (0.501 mmol) of **1i** gave 70.9 mg of **2i** after 12 h, 100% yield.
Average yield: 100%

Method B: Run 1: 67.7 mg (0.501 mmol) of **1i** gave 69.4 mg of **2i** after 18 h, 98% yield.
Run 2: 67.6 mg (0.500 mmol) of **1i** gave 68.1 mg of **2i** after 18 h, 96% yield.
Average yield: 97%

2i: White solid, TLC R_f = 0.2 (PE/EA = 1:1), a known compound.[7]

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.65 (br s, 1H), 3.77 – 3.65 (m, 1H), 1.92 (s, 3H), 1.90 – 1.83 (m, 2H), 1.71 – 1.63 (m, 2H), 1.61 – 1.54 (m, 1H), 1.38 – 1.25 (m, 2H), 1.17 – 1.02 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.2, 48.3, 33.3, 25.6, 25.0, 23.6.



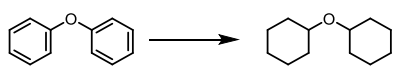
1j **2j**

Method A: Run 1: 96.4 mg (0.499 mmol) of **1j** gave 99.7 mg of **2j** after 12 h, 100% yield.
Run 2: 96.8 mg (0.501 mmol) of **1j** gave 99.6 mg of **2j** after 12 h, 100% yield.
Average yield: 100%

Method B: This reaction condition resulted in partial defunctionalization and $BocNH_2$ was formed as a by-product. To remove $BocNH_2$, the reaction mixture was concentrated *in vacuo* and the residue was purified by column chromatography (silica gel, PE/EA = 20:1).
Run 1: 96.7 mg (0.500 mmol) of **1j** gave 79.4 mg of **2j** after 18 h, 80% yield.
Run 2: 96.6 mg (0.500 mmol) of **1j** gave 83.4 mg of **2j** after 18 h, 84% yield.
Average yield: 82%

2j: Colorless crystal, TLC R_f = 0.6 (PE/EA = 5:1), a known compound.[10]

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.41 (br s, 1H), 3.41 (br s, 1H), 1.96 – 1.87 (m, 2H), 1.73 – 1.65 (m, 2H), 1.62 – 1.54 (m, 1H), 1.44 (s, 9H), 1.38 – 1.26 (m, 2H), 1.20 – 1.03 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.3, 79.1, 49.6, 33.7, 28.6, 25.7, 25.0.



1k **2k**

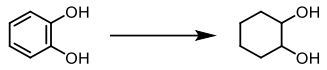
Method A: Run 1: 85.2 mg (0.501 mmol) of **1k** gave 79.6 mg of **2k** after 48 h, 87% yield.
Run 2: 85.1 mg (0.500 mmol) of **1k** gave 79.1 mg of **2k** after 48 h, 87% yield.
Average yield: 87%

Method B: Run 1: 85.1 mg (0.500 mmol) of **1k** gave 41.1 mg of **2k** after 48 h, 45% yield.
Run 2: 85.2 mg (0.501 mmol) of **1k** gave 39.1 mg of **2k** after 48 h, 43% yield.
Average yield: 44%

Note: In both methods, cyclohexanol was formed as a by-product, but could be removed simply by rotary evaporation.

2k: Colorless oil, TLC R_f = 0.2 (PE/EA = 50:1), a known compound.[4]

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.31 (tt, *J* = 9.2, 4.2 Hz, 2H), 1.93 – 1.81 (m, 4H), 1.78 – 1.67 (m, 4H), 1.58 – 1.49 (m, 2H), 1.30 – 1.10 (m, 10H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 74.8, 33.5, 26.0, 24.7.



1l **2l**

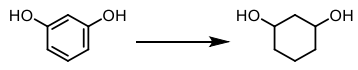
Note: Standard procedure resulted in red impurities in the product, which could be observed by ^{1}H NMR. For purification, the crude product was placed in a flask and dissolved in boiling hexane (2 mL). The red impurities were insoluble and clung to the flask during this process. The colorless supernatant was carefully transferred to a second flask using a glass pipette. This process was repeated for 3 times, and the combined solution was concentrated *in vacuo* to give **2l**.

Method A: Run 1: 55.0 mg (0.500 mmol) of **1l** gave 50.6 mg of **2l** after 24 h, 87% yield.
Run 2: 55.1 mg (0.500 mmol) of **1l** gave 48.9 mg of **2l** after 24 h, 84% yield.
Average yield: 86%, *cis*/*trans* = 3.4:1

Method B: Run 1: 55.1 mg (0.500 mmol) of **1l** gave 26.2 mg of **2l** after 24 h, 45% yield.
Run 2: 55.1 mg (0.500 mmol) of **1l** gave 25.9 mg of **2l** after 24 h, 45% yield.
Average yield: 45%, *cis*/*trans* = 4.9:1

2l: White solid, TLC R_f = 0.2 (PE/EA = 1:1). Both diastereomers are known compounds.[11]

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.80 – 3.74 (m, *cis* 2H), 3.38 – 3.31 (m, *trans* 2H), 2.53 (br s, *cis* 2H + *trans* 2H), 2.00 – 1.93 (m, *trans* 2H), 1.80 – 1.67 (m, *cis* 2H + *trans* 2H), 1.65 – 1.50 (m, *cis* 4H), 1.35 – 1.22 (m, *cis* 2H + *trans* 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 76.0 (*trans*), 70.8 (*cis*), 33.0 (*trans*), 30.0 (*cis*), 24.5 (*trans*), 21.6 (*cis*).



1m **2m**

Method A: Run 1: 55.1 mg (0.500 mmol) of **1m** gave 48.7 mg of **2m** after 18 h, 84% yield.
Run 2: 55.0 mg (0.500 mmol) of **1m** gave 47.4 mg of **2m** after 18 h, 82% yield.
Average yield: 83%, *cis*/*trans* = 1.9:1

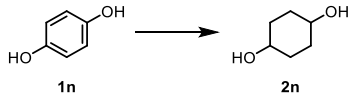
Method B: Run 1: 55.1 mg (0.500 mmol) of **1m** gave 28.1 mg of **2m** after 18 h, 48% yield.
Run 2: 55.0 mg (0.500 mmol) of **1m** gave 27.2 mg of **2m** after 18 h, 47% yield.
Average yield: 48%, *cis*/*trans* = 1.2:1

Note: In both methods, cyclohexanol was formed as a by-product, but could be removed simply by rotary evaporation.

2m: Colorless viscous oil, TLC R_f = 0.05 (PE/EA = 1:1). Both diastereomers are known compounds.[12,13]

cis isomer: ^{1}H NMR (400 MHz, DMSO-d_6) δ 4.53 (d, J = 4.7 Hz, 2H), 3.37 – 3.28 (m, 2H), 2.04 – 1.97 (m, 1H), 1.74 – 1.67 (m, 2H), 1.63 – 1.55 (m, 1H), 1.16 – 1.06 (m, 1H), 1.05 – 0.89 (m, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 67.5, 45.5, 34.9, 20.6.

trans isomer: ^{1}H NMR (400 MHz, DMSO-d_6) δ 4.30 (d, J = 4.0 Hz, 2H), 3.87 – 3.77 (m, 2H), 1.53 – 1.44 (m, 6H), 1.32 – 1.23 (m, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 65.0, 42.4, 33.9, 18.9.



1n 2n

Method A: Run 1: 55.2 mg (0.501 mmol) of **1n** gave 44.3 mg of **2n** after 18 h, 76% yield.
Run 2: 55.2 mg (0.501 mmol) of **1n** gave 44.9 mg of **2n** after 18 h, 77% yield.
Average yield: 76%, *cis*/*trans* = 1.4:1

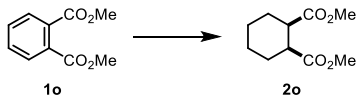
Method B: Run 1: 55.1 mg (0.500 mmol) of **1n** gave 19.5 mg of **2n** after 18 h, 34% yield.
Run 2: 54.9 mg (0.499 mmol) of **1n** gave 19.7 mg of **2n** after 18 h, 34% yield.
Average yield: 34%, *cis*/*trans* = 4.3:1

Note: In both methods, cyclohexanol was formed as a by-product, but could be removed simply by rotary evaporation.

2n: White solid, TLC R_f = 0.1 (PE/EA = 1:1). Both diastereomers are known compounds.[14]

cis isomer: ^{1}H NMR (400 MHz, DMSO-d_6) δ 4.29 (d, J = 3.8 Hz, 2H), 3.55 – 3.47 (m, 2H), 1.60 – 1.49 (m, 4H), 1.46 – 1.36 (m, 4H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 65.9, 30.4.

trans isomer: ^{1}H NMR (400 MHz, DMSO-d_6) δ 4.43 (d, J = 4.3 Hz, 2H), 3.40 – 3.33 (m, 2H), 1.80 – 1.68 (m, 4H), 1.19 – 1.08 (m, 4H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 68.2, 33.0.



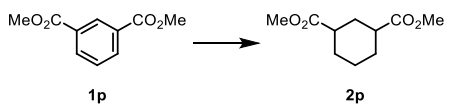
1o 2o

Method A: Run 1: 97.0 mg (0.500 mmol) of **1o** gave 98.6 mg of **2o** after 18 h, 98% yield.
Run 2: 97.2 mg (0.501 mmol) of **1o** gave 99.7 mg of **2o** after 18 h, 99% yield.
Average yield: 98%, *cis*/*trans* > 20:1

Method B: Run 1: 97.2 mg (0.501 mmol) of **1o** gave 98.5 mg of **2o** after 18 h, 98% yield.
Run 2: 97.1 mg (0.500 mmol) of **1o** gave 97.3 mg of **2o** after 18 h, 97% yield.
Average yield: 98%, *cis*/*trans* > 20:1

2o: Colorless oil, TLC R_f = 0.4 (PE/EA = 5:1), a known compound.[15]

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.67 (s, 6H), 2.89 – 2.77 (m, 2H), 2.05 – 1.94 (m, 2H), 1.82 – 1.71 (m, 2H), 1.57 – 1.46 (m, 2H), 1.45 – 1.34 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.3, 51.8, 42.8, 26.4, 23.9.



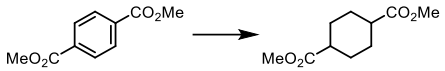
1p 2p

Method A: Run 1: 97.3 mg (0.501 mmol) of **1p** gave 99.6 mg of **2p** after 36 h, 99% yield.

Run 2: 97.3 mg (0.501 mmol) of **1p** gave 99.9 mg of **2p** after 36 h, 100% yield.
Average yield: 100%, *cis*/*trans* = 3.8:1

Method B: Run 1: 97.3 mg (0.501 mmol) of **1p** gave 98.5 mg of **2p** after 28 h, 98% yield.
Run 2: 97.3 mg (0.501 mmol) of **1p** gave 99.1 mg of **2p** after 28 h, 99% yield.
Average yield: 98%, *cis*/*trans* = 4.2:1

2p: Colorless oil, TLC R_f = 0.4 (PE/EA = 5:1). Both diastereomers are known compounds.[16,17] ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.68 (s, *trans* 6H), 3.67 (s, *cis* 6H), 2.68 (apparent p, *J* = 6.0 Hz, *trans* 2H), 2.32 (apparent tt, *J* = 11.9, 3.5 Hz, *cis* 2H), 2.22 (dtt, *J* = 13.1, 3.6, 1.9 Hz, *cis* 1H), 2.01 – 1.94 (m, *cis* 2H + *trans* 2H), 1.92 – 1.85 (m, *cis* 1H), 1.76 – 1.68 (m, *trans* 4H), 1.58 – 1.49 (m, *cis* 1H + *trans* 2H), 1.42 – 1.24 (m, *cis* 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.8 (*trans*), 175.7 (*cis*), 51.82 (*cis*), 51.76 (*trans*), 42.7 (*cis*), 39.1 (*trans*), 31.2 (*cis*), 29.4 (*trans*), 28.4 (*cis*), 28.0 (*trans*), 24.9 (*cis*), 22.2 (*trans*).

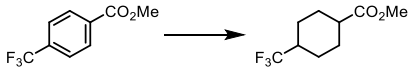


1q **2q**

Method A: Run 1: 97.1 mg (0.500 mmol) of **1q** gave 99.3 mg of **2q** after 24 h, 99% yield.
Run 2: 97.3 mg (0.501 mmol) of **1q** gave 99.8 mg of **2q** after 24 h, 99% yield.
Average yield: 99%, *cis*/*trans* = 4.1:1

Method B: Run 1: 97.1 mg (0.500 mmol) of **1q** gave 96.4 mg of **2q** after 24 h, 96% yield.
Run 2: 97.2 mg (0.501 mmol) of **1q** gave 97.3 mg of **2q** after 24 h, 97% yield.
Average yield: 96%, *cis*/*trans* = 4.1:1

2q: Colorless oil, TLC R_f = 0.4 (PE/EA = 5:1). Both diastereomers are known compounds.[18,19]
cis isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.67 (s, 6H), 2.51 – 2.43 (m, 2H), 1.94 – 1.84 (m, 4H), 1.72 – 1.63 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.6, 51.73, 40.8, 26.1.
trans isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.66 (s, 6H), 2.33 – 2.23 (m, 2H), 2.10 – 1.99 (m, 4H), 1.50 – 1.39 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.0, 51.75, 42.5, 28.1.



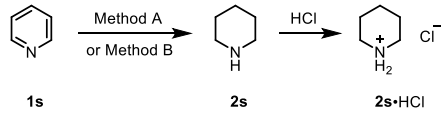
1r **2r**

Method A: Run 1: 102.2 mg (0.501 mmol) of **1r** gave 96.6 mg of **2r** after 18 h, 92% yield.
Run 2: 102.1 mg (0.500 mmol) of **1r** gave 94.4 mg of **2r** after 18 h, 90% yield.
Average yield: 91%, *cis*/*trans* = 7.8:1

Method B: Run 1: 102.1 mg (0.500 mmol) of **1r** gave 93.4 mg of **2r** after 36 h, 89% yield.
Run 2: 102.0 mg (0.500 mmol) of **1r** gave 94.2 mg of **2r** after 36 h, 90% yield.
Average yield: 90%, *cis*/*trans* = 12:1

2r: Colorless oil, TLC R_f = 0.4 (PE/EA = 10:1). Both diastereomers are known compounds.[20,21] ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.71 (s, *cis* 3H), 3.68 (s, *trans* 3H), 2.68 – 2.63 (m, *cis* 1H), 2.26 – 2.19 (m, *cis* 2H + *trans* 1H), 2.13 – 1.98 (m, *cis* 1H + *trans* 4H), 1.86 – 1.72 (m, *cis* 2H + *trans* 1H), 1.58 – 1.45 (m, *cis* 4H + *trans* 4H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 175.5 (*trans*), 174.8 (*cis*), 127.7 (q, *J* = 278.7 Hz, *cis*) 127.6 (q, *J* = 278.5 Hz, *trans*), 51.6 (*cis* + *trans*), 42.3 (*trans*), 41.3 (q, *J* = 26.7 Hz, *trans*), 41.1 (q, *J* = 26.6 Hz, *cis*), 38.6 (*cis*), 27.4 (*trans*), 25.7 (*cis*), 24.2 (q, *J* = 2.7 Hz, *trans*), 21.7 (q, *J* = 2.7 Hz, *cis*).

^{19}F NMR (471 MHz, $CDCl_3$) δ -73.26 (*cis*), -73.93 (*trans*).



1s **2s** **2s**•HCl

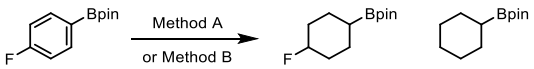
Note: Piperidine (**2s**) is volatile and strongly adsorbed by silica gel. Therefore, the product was isolated using a different procedure: After TLC had indicated complete conversion of pyridine (**1s**), the reaction mixture was filtered through a nylon filter membrane. The filter residue was washed with MeOH (4×2 mL). To the combined filtrate was added 1M HCl (1.0 mL, 1.0 mmol, 2 eq. to **2s**), and the resulting mixture was concentrated *in vacuo*. The residue was repeatedly dissolved in MeOH and evaporated to remove H_2O. Finally, the residue was dissolved in DCM and then evaporated to give the product as its hydrochloride salt.

Method A: Run 1: 39.8 mg (0.503 mmol) of **1s** gave 60.5 mg of **2s**•HCl after 12 h, 99% yield.
Run 2: 39.6 mg (0.501 mmol) of **1s** gave 59.6 mg of **2s**•HCl after 12 h, 98% yield.
Average yield: 98%

Method B: Run 1: 39.9 mg (0.504 mmol) of **1s** gave 60.4 mg of **2s**•HCl after 12 h, 99% yield.
Run 2: 39.5 mg (0.499 mmol) of **1s** gave 58.9 mg of **2s**•HCl after 12 h, 97% yield.
Average yield: 98%

2s•HCl: White solid, a known compound.[22]

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.99 (br s, 2H), 3.00 – 2.91 (m, 4H), 1.71 – 1.62 (m, 4H), 1.58 – 1.50 (m, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 43.4, 22.0, 21.7.



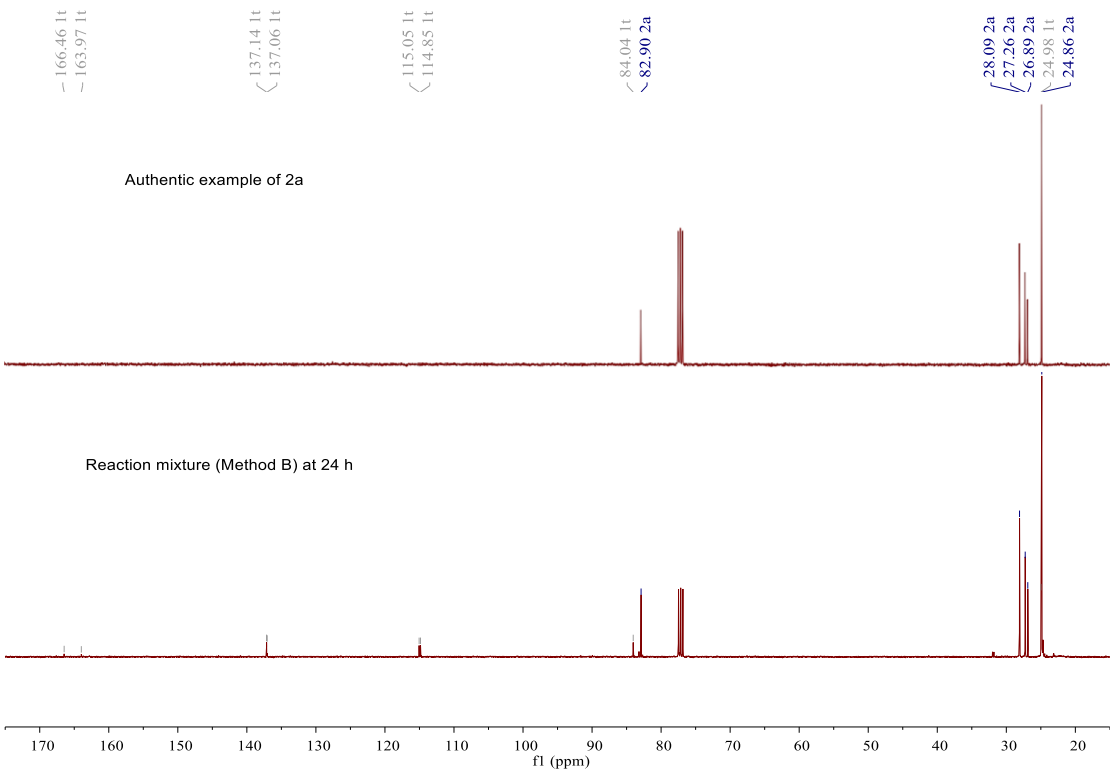
1t **2t** (N. D.) **2a** (Detected by NMR)

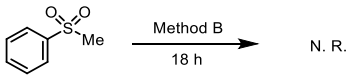
Method A: The reaction was performed with 111.1 mg (0.500 mmol) of **1t**. After 18 h, ^{1}H and ^{13}C NMR indicated that a small fraction of **1t** underwent hydrodefluorination to give **2a** (**1t**:**2a** = 15:1). The desired product **2t** was not detected.

Method B: The reaction was performed with 110.4 mg (0.497 mmol) of **1t**. After 24 h, ^{1}H and ^{13}C NMR indicated that a large proportion of **1t** underwent hydrodefluorination to give **2a** (**1t**:**2a** = 1:5.0). The desired product **2t** was not detected.

Because this reaction gave the undesired product and was also very slow by using both methods, we don't recommend to use this substrate for the present reaction. Therefore, we did not carry out this reaction to full conversion and no reaction yields are reported here.

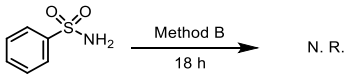
The ^{13}C spectra for **2a** and the reaction mixture (Method B, 24 h) are given below for comparison:





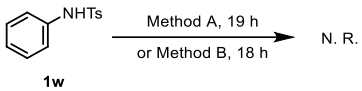
1u

Following Method B, 78.2 mg (0.501 mmol) of **1u** was used. After 18 h, ^{1}H NMR indicated that the starting material was left untouched.



1v

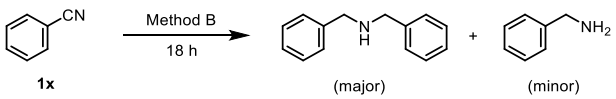
Following Method B, 78.0 mg (0.496 mmol) of **1v** was used. After 18 h, ^{1}H NMR indicated that the starting material was left untouched.



1w

Following Method A, 123.7 mg (0.500 mmol) of **1w** was used. After 19 h, ^{1}H NMR indicated that the starting material was left untouched.

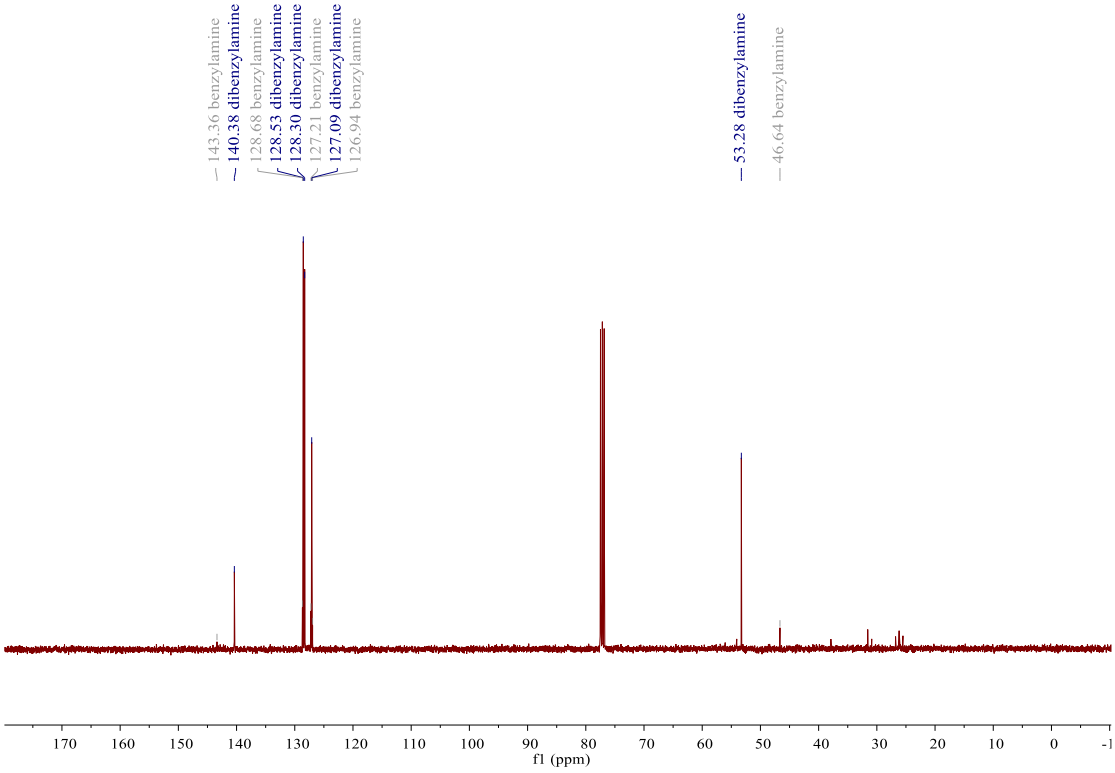
Following Method B, 123.7 mg (0.500 mmol) of **1w** was used. After 18 h, ^{1}H NMR indicated that the starting material was left untouched.



1x (major) (minor)

Following Method B, 51.5 mg (0.499 mmol) of **1x** was used. After 18 h, ^{1}H and ^{13}C NMR indicated

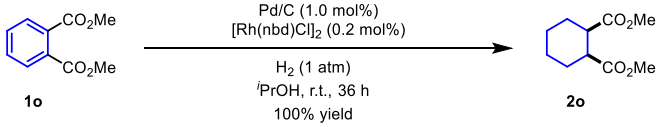
that the major product was dibenzylamine[23]. A tiny amount of benzylamine[24] could also be identified in the ^{13}C NMR spectrum:



V. Gram-Scale Reactions

To investigate whether the reaction can be performed with a lower catalyst loading, we carried out the hydrogenation of **1o** on gram scale with the catalyst loading reduced by a factor of 2.5. The hydrogenation product **2o** could still be obtained quantitatively, although prolonged stirring was required for complete conversion.

Method A:

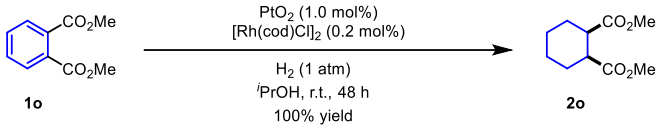


A 100-mL round-bottomed flask was charged with **1o** (1.17 g, 6.03 mmol, 1.0 eq.) and 10% Pd/C (63.7 mg, containing 59.9 μmol of Pd, 1.0 mol%). The flask was moved into a glove box. $[Rh(nbd)Cl]_2$ (5.5 mg, 12 μmol, 0.2 mol%) was added, and the flask was sealed with a rubber septum before being moved out of the glove box. ^{i}PrOH (24 mL) was added via syringe to dissolve the Rh catalyst. A H_2 balloon (~2 L) was attached to the flask, which was then evacuated and refilled with H_2 for three times. The H_2 balloon was kept, and the reaction mixture was stirred at room temperature. After 36 h, TLC indicated full conversion of **1o**. The reaction mixture was then filtered through a thin pad of silica gel and eluted with EA. The filtrate was concentrated *in vacuo* to give **2o** (1.21 g, 100% yield) as a colorless oil. The completeness of the reaction and the relative configuration of **2o** (*cis*/*trans* > 20:1) were confirmed by ^{1}H NMR.

An illustration of the reaction setup is given below (Figure S3).

Figure S3. Setup for gram-scale reaction

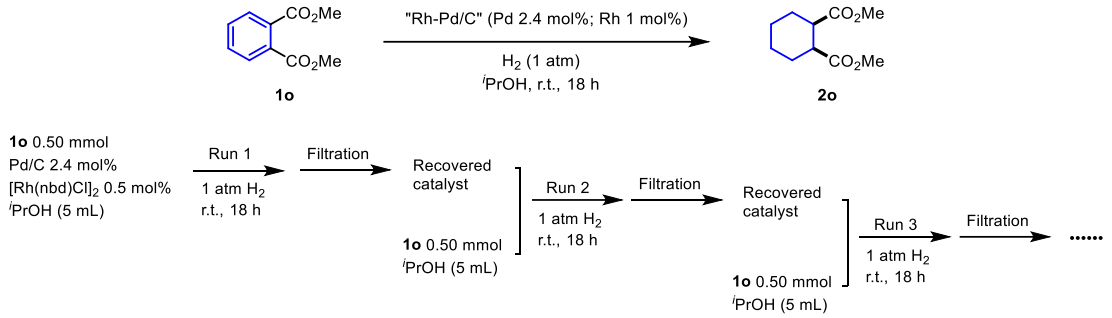
Method B:



To a 100-mL round-bottomed flask was added **1o** (1.16 g, 5.97 mmol, 1.0 eq.), PtO_2 (13.6 mg, 59.9 μmol, 1.0 mol%), $[Rh(cod)Cl]_2$ (5.9 mg, 12 μmol, 0.2 mol%), and ^{i}PrOH (24 mL). The flask was sealed with a rubber septum. A H_2 balloon (~2 L) was attached to the flask, which was then evacuated and refilled with H_2 for three times. The H_2 balloon was kept, and the reaction mixture was stirred at room temperature. After 18 h/36 h, TLC indicated partial conversion of **1o**, but at 48 h TLC showed no **1o** left. The reaction mixture was then filtered through a thin pad of silica gel and eluted with EA. The filtrate was concentrated *in vacuo* to give **2o** (1.20 g, 100% yield) as a colorless oil. The completeness of the reaction and the relative configuration of **2o** (*cis*/*trans* > 20:1) were confirmed by ^{1}H NMR.

VI. Catalyst Recycling

The recyclability of "Rh-Pd/C" formed in Method A was examined using **1o** as the substrate (Scheme S1).



Scheme S1. Procedure for catalyst recycling

Run 1: A reaction vessel was charged with **1o** (97.1 mg, 0.50 mmol, 1.0 eq.) and 10% dry Pd/C (12.6 mg, containing 11.8 μmol of Pd, 2.4 mol%). The reaction vessel was then moved into a glove box. $[Rh(nbd)Cl]_2$ (1.2 mg, 2.6 μmol, 0.5 mol%) was added, and the reaction vessel was sealed with a rubber septum before being moved out of the glove box. Isopropanol (5 mL) was added via syringe to dissolve the Rh catalyst. A H_2 balloon (~1 L) was attached to the reaction vessel, which was then evacuated and refilled with H_2 for three times. The H_2 balloon was kept, and the reaction mixture was stirred at room temperature for 18 h. The reaction mixture was then filtered through a nylon filter membrane. The filter residue was washed with MeOH (4×2 mL). The combined filtrate was concentrated *in vacuo* to afford **2o** as a colorless oil.

Runs 2~5: A reaction vessel was charged with **1o** (0.50 mmol). The filter residue of the previous step was washed with ^{i}PrOH (4 mL), and then flushed into the reaction vessel using 5 mL of ^{i}PrOH. The reaction vessel was sealed with a rubber septum. A H_2 balloon (~1 L) was attached to the reaction vessel, which was then evacuated and refilled with H_2 for three times. The H_2 balloon was kept, and the reaction mixture was stirred at room temperature for 18 h. The reaction mixture was then filtered through a nylon filter membrane. The filter residue was washed with MeOH (4×2 mL). The combined filtrate was concentrated *in vacuo* to afford **2o** as a colorless oil. The completeness of the reaction and the relative configuration of **2o** (*cis*/*trans* > 20:1) were confirmed by ^{1}H NMR.

The detailed results for each round are shown in Table S1. It can be concluded that the *in situ* generated "Rh-Pd/C" catalyst in Method A can be recycled and reused for several rounds without significant loss of catalytic activity.

Table S1. Results for catalyst recycling

Run	**1o** (mg)	Time (h)	**2o** (mg)	Conversion	Yield
1	97.1	18	99.3	100%	99%
2	97.1	18	100.1	100%	100%
3	97.2	18	99.2	100%	99%
4	97.3	18	99.8	100%	99%
5	97.2	18	98.1	100%	98%

We did not test the recyclability of “Rh-Pt” in Method B because the amount of the catalyst was too small, not only in terms of mass but also in terms of volume. As a result, it was practically difficult to recycle the catalyst: A large proportion of the catalyst stayed clinging to the filter membrane when we tried to recover it.

VII. References

(1) Ninomiya, R.; Arai, K.; Chen, G.; Morisaki, K.; Kawabata, T.; Ueda, Y. β-Silicon-Effect-Promoted Intermolecular Site-Selective C(Sp^3)–H Amination with Dirhodium Nitrenes. *Chem. Commun.* **2020**, *56*, 5759–5762.

(2) Fang, W.; Wang, H.-Q.; Zhou, W.; Luo, Z.-W.; Dai, J.-J. Photoinduced C(Sp^3)–H Borylation of Alkanes Mediated by Copper(II) Chloride. *Chem. Commun.* **2023**, *59*, 7108–7111.

(3) Amrein, S.; Timmermann, A.; Studer, A. Radical Transfer Hydrosilylation/Cyclization Using Silylated Cyclohexadienes. *Org. Lett.* **2001**, *3*, 2357–2360.

(4) Miyamura, H.; Suzuki, A.; Yasukawa, T.; Kobayashi, S. Polysilane-Immobilized Rh–Pt Bimetallic Nanoparticles as Powerful Arene Hydrogenation Catalysts: Synthesis, Reactions under Batch and Flow Conditions and Reaction Mechanism. *J. Am. Chem. Soc.* **2018**, *140*, 11325–11334.

(5) Kumar, P.; Qi, L.; Williams, S.; Dop, R. A.; Liu, Y.; Zhang, T.; Li, C.; Xiao, J. Selective Hydrogenation of Lignin-Derived Aromatics to Give Cyclohexanes with a Rhodium-Pincer Precatalyst. *J. Organomet. Chem.* **2023**, *997*, 122795.

(6) Maegawa, T.; Akashi, A.; Yaguchi, K.; Iwasaki, Y.; Shigetsura, M.; Monguchi, Y.; Sajiki, H. Efficient and Practical Arene Hydrogenation by Heterogeneous Catalysts under Mild Conditions. *Chem. - Eur. J.* **2009**, *15*, 6953–6963.

(7) Hattori, T.; Ida, T.; Tsubone, A.; Sawama, Y.; Monguchi, Y.; Sajiki, H. Facile Arene Hydrogenation under Flow Conditions Catalyzed by Rhodium or Ruthenium on Carbon. *Eur. J. Org. Chem.* **2015**, *2015*, 2492–2497.

(8) Geant, P.-Y.; Mohamed, B. S.; Périgaud, C.; Peyrottes, S.; Uttaro, J.-P.; Mathé, C. Probing the Reactivity of H-Phosphonate Derivatives for the Hydrophosphonylation of Various Alkenes and Alkynes under Free-Radical Conditions. *New J. Chem.* **2016**, *40*, 5318–5324.

(9) Wang, Y.; Chang, Z.; Hu, Y.; Lin, X.; Dou, X. Mild and Selective Rhodium-Catalyzed Transfer Hydrogenation of Functionalized Arenes. *Org. Lett.* **2021**, *23*, 1910–1914.

(10) Li, P.; Ma, N.; Wang, Z.; Dai, Q.; Hu, C. Base-Mediated Intramolecular Decarboxylative Synthesis of Alkylamines from Alkanoyloxycarbamates. *J. Org. Chem.* **2018**, *83*, 8233–8240.

(11) Hampton, C.; Simonetti, M.; Leonori, D. Olefin Dihydroxylation Using Nitroarenes as Photoresponsive Oxidants. *Angew. Chem. Int. Ed.* **2023**, *62*, e202214508.

(12) Abraham, R. J.; Chambers, E. J.; Thomas, W. A. Conformational Analysis. Part 21. Conformational Isomerism in Cis-Cyclohexane-1,3-Diol. *J. Chem. Soc. Perkin Trans. 2* **1993**, No. 6, 1061–1066.

(13) Slagmaat, C. A. M. R. van; Faber, T.; Chou, K. C.; Freire, A. J. S.; Hadavi, D.; Han, P.; Quaedflieg, P. J. L. M.; Verzijl, G. K. M.; Alsters, P. L.; Wildeman, S. M. A. D. Chemoselective Formation of Cyclo-Aliphatic and Cyclo-Olefinic 1,3-Diols via Pressure Hydrogenation of Potentially Biobased Platform Molecules Using Knölker-Type Catalysts. *Dalton Trans.* **2021**, *50*, 10102–10112.

(14) Abraham, R. J.; Byrne, J. J.; Griffiths, L.; Koniotou, R. ^{1}H Chemical Shifts in NMR: Part 22—Prediction of the ^{1}H Chemical Shifts of Alcohols, Diols and Inositols in Solution, a Conformational and Solvation Investigation. *Magn. Reson. Chem.* **2005**, *43*, 611–624.

(15) Bourriquen, F.; Hervochon, J.; Qu, R.; Bartling, S.; Rockstroh, N.; Junge, K.; Fischmeister, C.; Beller, M. Diastereoselective Hydrogenation of Arenes and Pyridines Using Supported Ruthenium Nanoparticles under Mild Conditions. *Chem. Commun.* **2022**, *58*, 8842–8845.

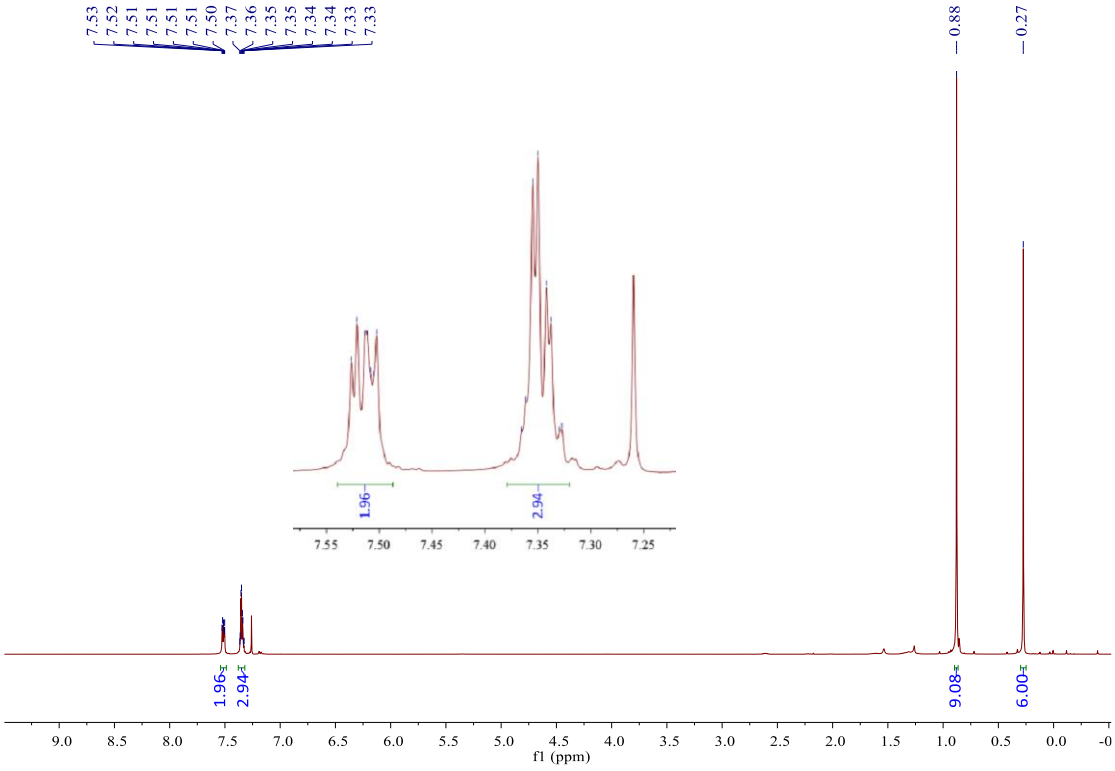
(16) Iida, T.; Kanazawa, J.; Matsunaga, T.; Miyamoto, K.; Hirano, K.; Uchiyama, M. Practical and

Facile Access to Bicyclo[3.1.1]Heptanes: Potent Bioisosteres of Meta-Substituted Benzenes. *J. Am. Chem. Soc.* **2022**, *144*, 21848–21852.
(17) Senda, Y.; Ishiyama, J.; Imaizumi, S. ^{13}C NMR Spectra of Some Methyl Cyclohexanecarboxylates. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 1359–1362.
(18) Tortajada, A.; Ninokata, R.; Martin, R. Ni-Catalyzed Site-Selective Dicarboxylation of 1,3-Dienes with CO_2. *J. Am. Chem. Soc.* **2018**, *140*, 2050–2053.
(19) Mao, C.; Zheng, J.; Matsagar, B. M.; Kankala, R. K.; Ahamad, T.; Yang, Y.; Wu, K. C.-W.; Zhang, X. Highly-Efficient Ru/Al–SBA-15 Catalysts with Strong Lewis Acid Sites for the Water-Assisted Hydrogenation of p-Phthalic Acid. *Catal. Sci. Technol.* **2020**, *10*, 2443–2451.
(20) Zhang, X.; Ling, L.; Luo, M.; Zeng, X. Accessing Difluoromethylated and Trifluoromethylated Cis-Cycloalkanes and Saturated Heterocycles: Preferential Hydrogen Addition to the Substitution Sites for Dearomatization. *Angew. Chem. Int. Ed.* **2019**, *58*, 16785–16789.
(21) Oohira, D.; Otaka, K. Nitrile Compound and Its Use in Pest Control. WO2005063694A1, July 14, 2005.
(22) Fan, G.-G.; Jiang, B.-W.; Sang, W.; Cheng, H.; Zhang, R.; Yu, B.-Y.; Yuan, Y.; Chen, C.; Verpoort, F. Metal-Free Synthesis of Heteroaryl Amines or Their Hydrochlorides via an External-Base-Free and Solvent-Free C–N Coupling Protocol. *J. Org. Chem.* **2021**, *86*, 14627–14639.
(23) Das, S.; Join, B.; Junge, K.; Beller, M. A General and Selective Copper-Catalyzed Reduction of Secondary Amides. *Chem. Commun.* **2012**, *48*, 2683–2685.
(24) Saavedra, J. Z.; Resendez, A.; Rovira, A.; Eagon, S.; Haddenham, D.; Singaram, B. Reaction of $InCl_3$ with Various Reducing Agents: $InCl_3$–$NaBH_4$-Mediated Reduction of Aromatic and Aliphatic Nitriles to Primary Amines. *J. Org. Chem.* **2012**, *77*, 221–228.

VIII. NMR Spectra

1b

^{1}H NMR spectrum ($CDCl_3$, 400 MHz):



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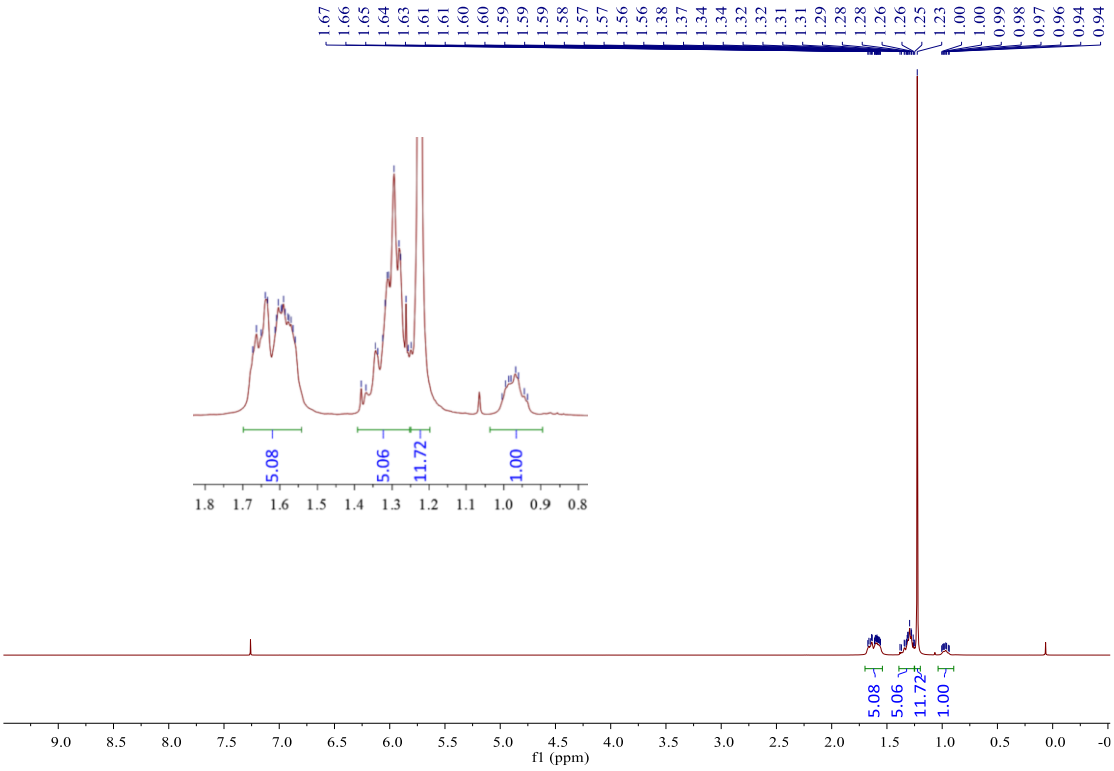
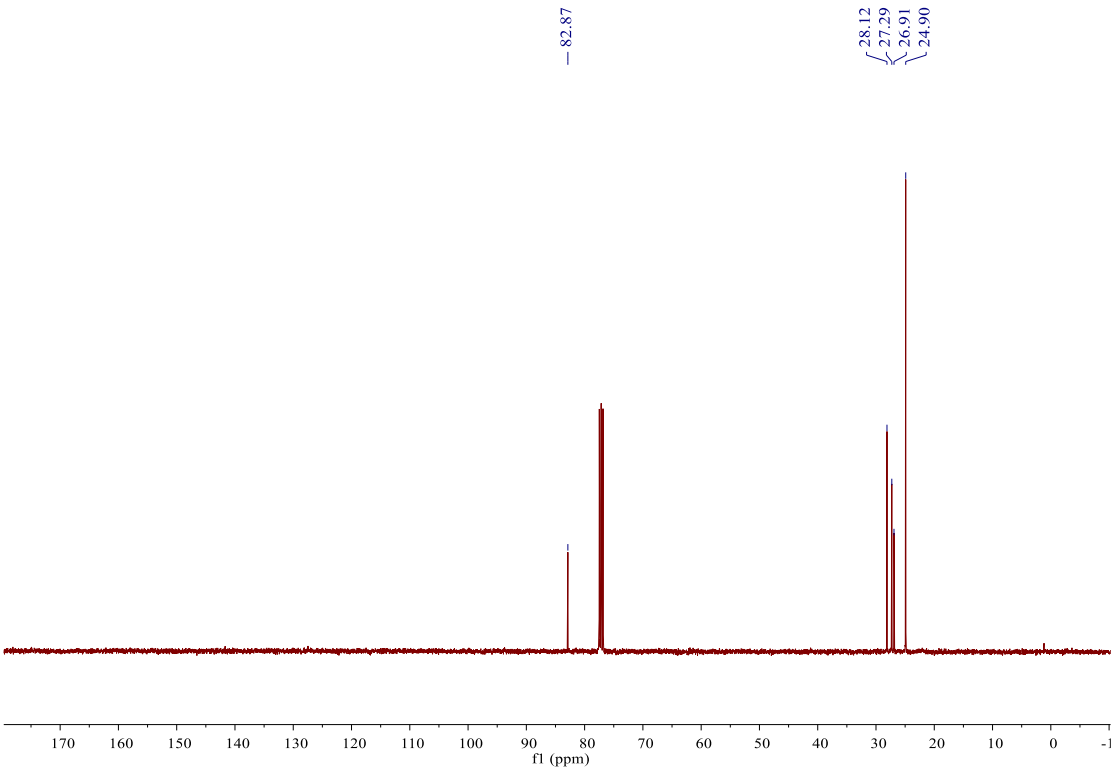


^{13}C NMR spectrum ($CDCl_3$, 101 MHz):



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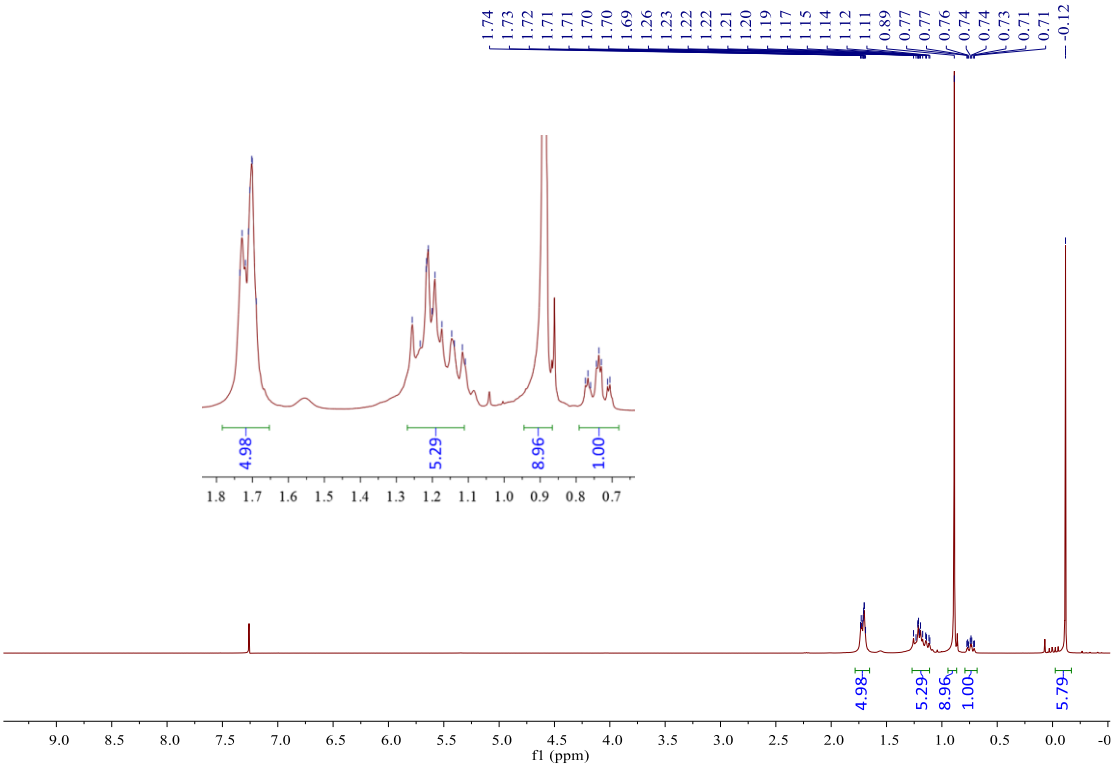

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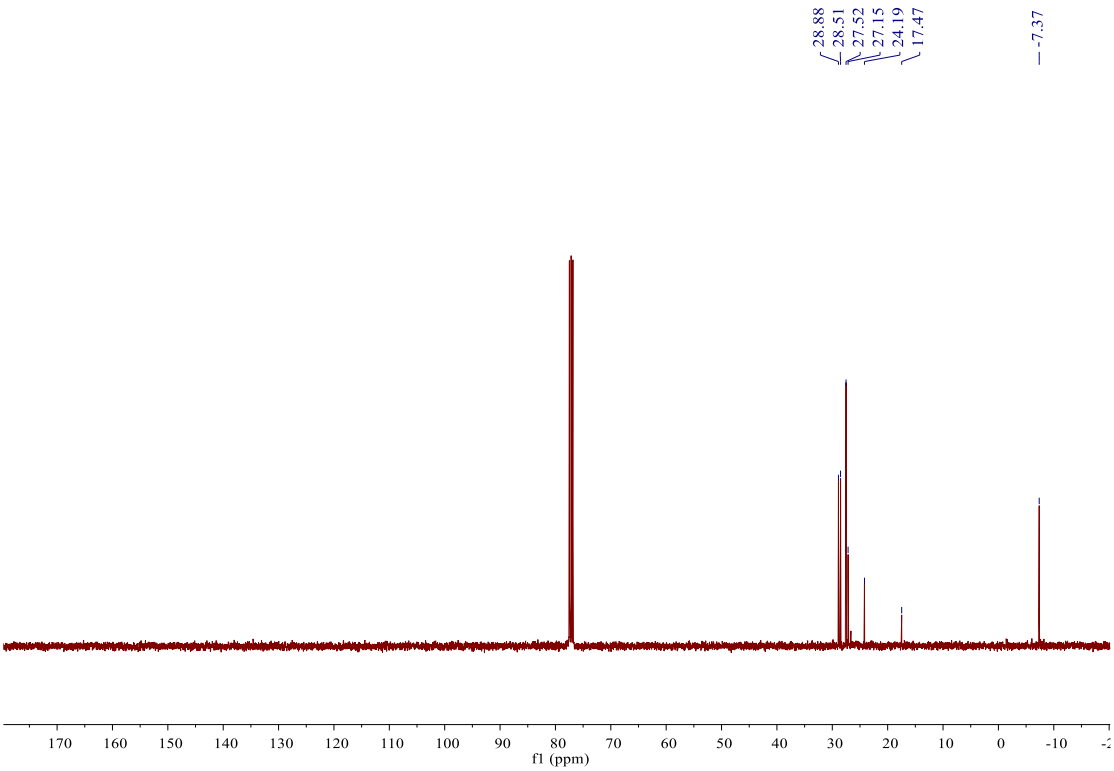

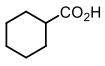

2c

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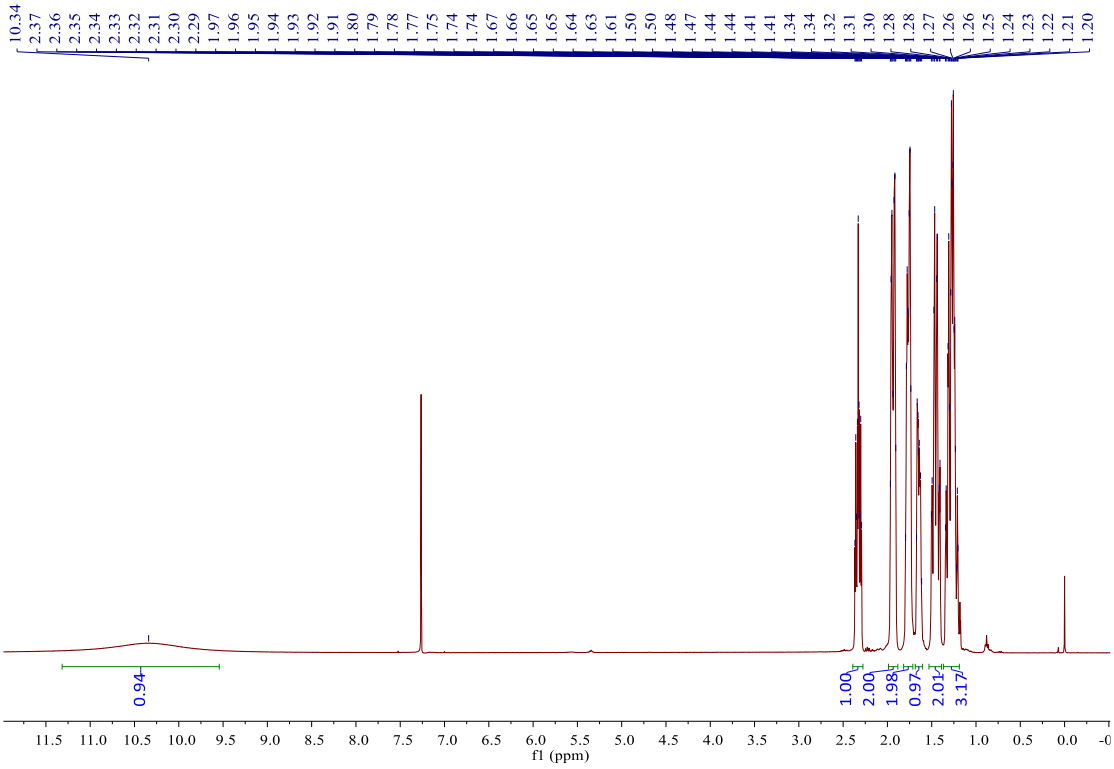

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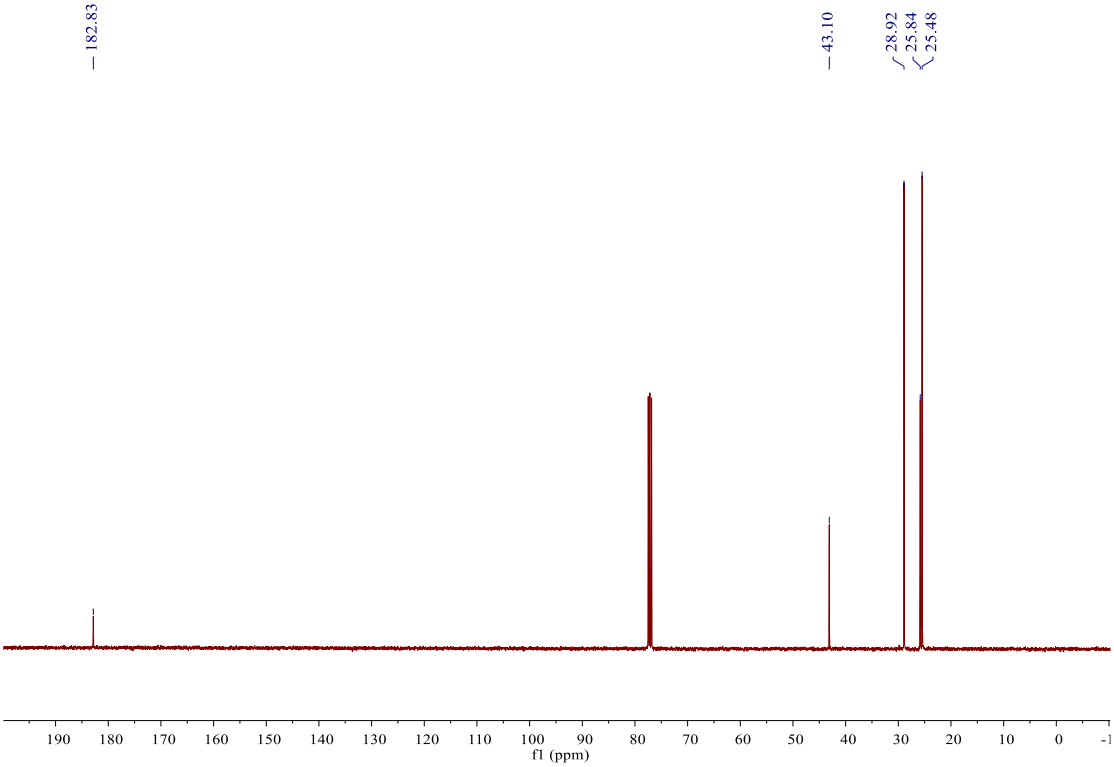

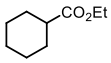

2d

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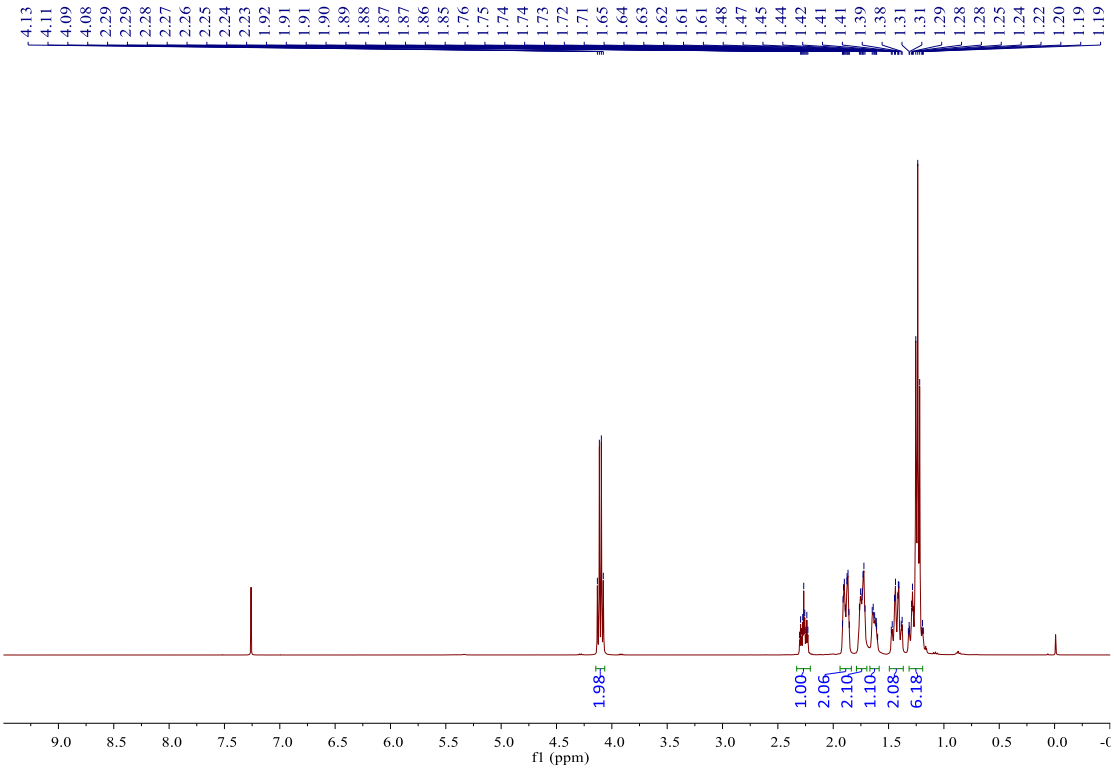

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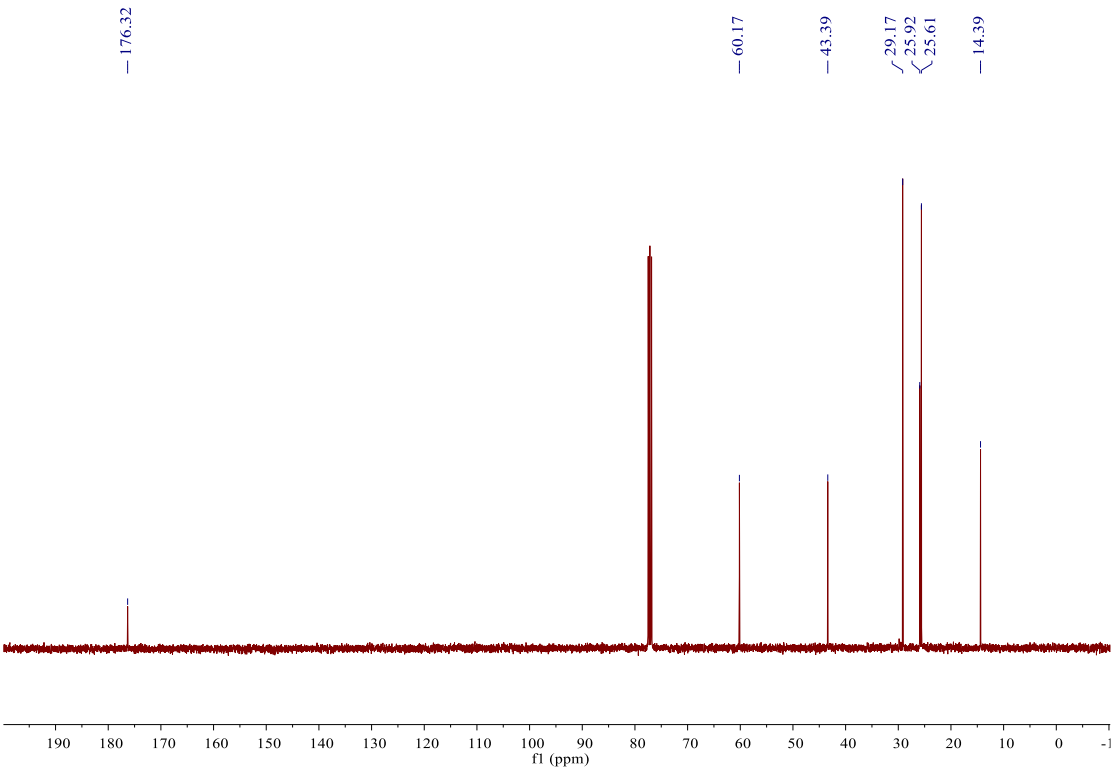

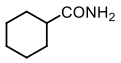

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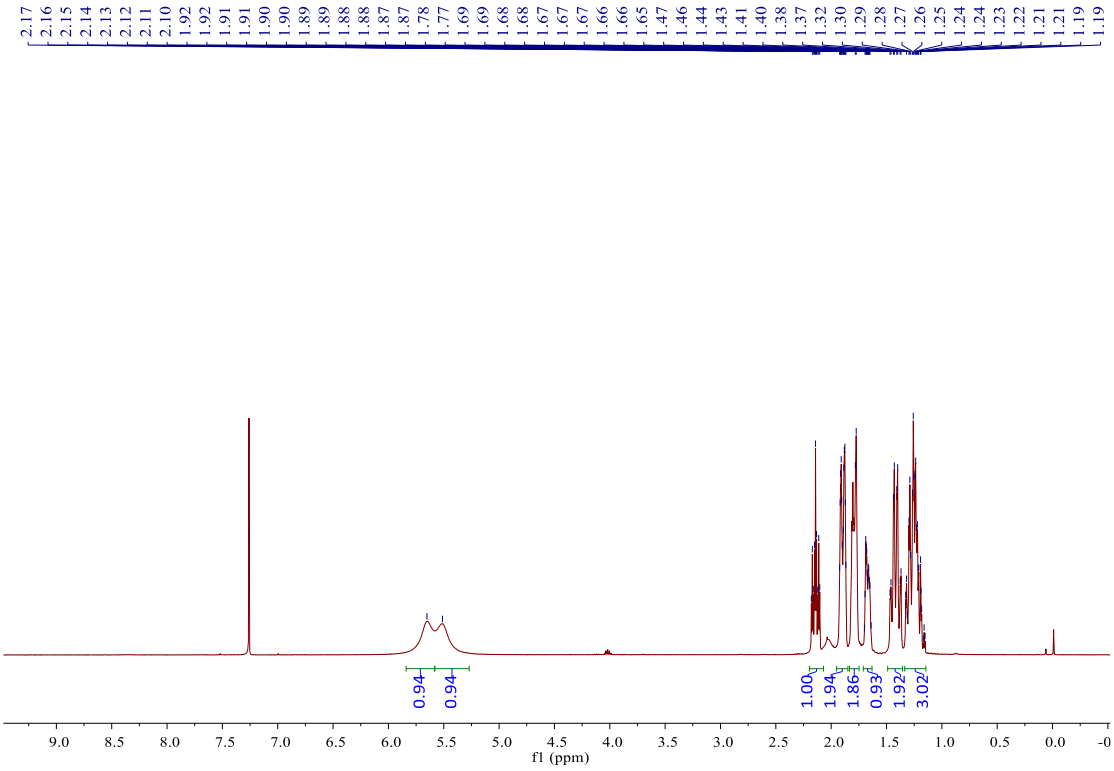

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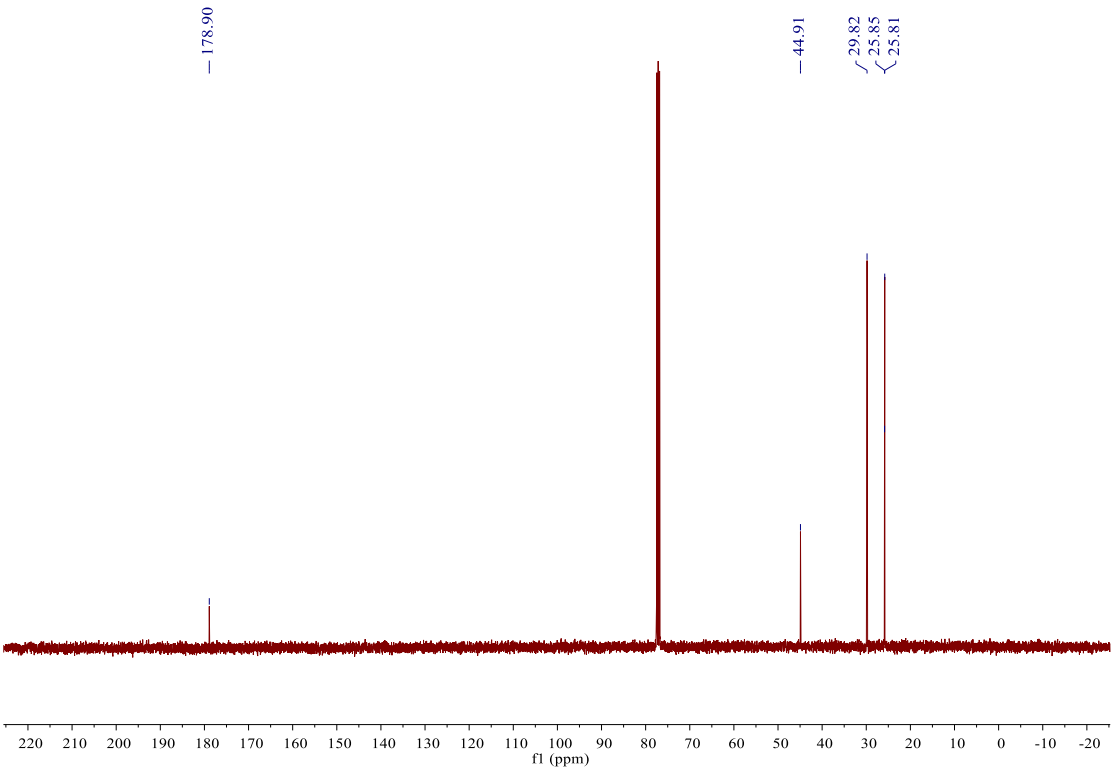

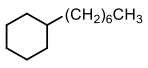

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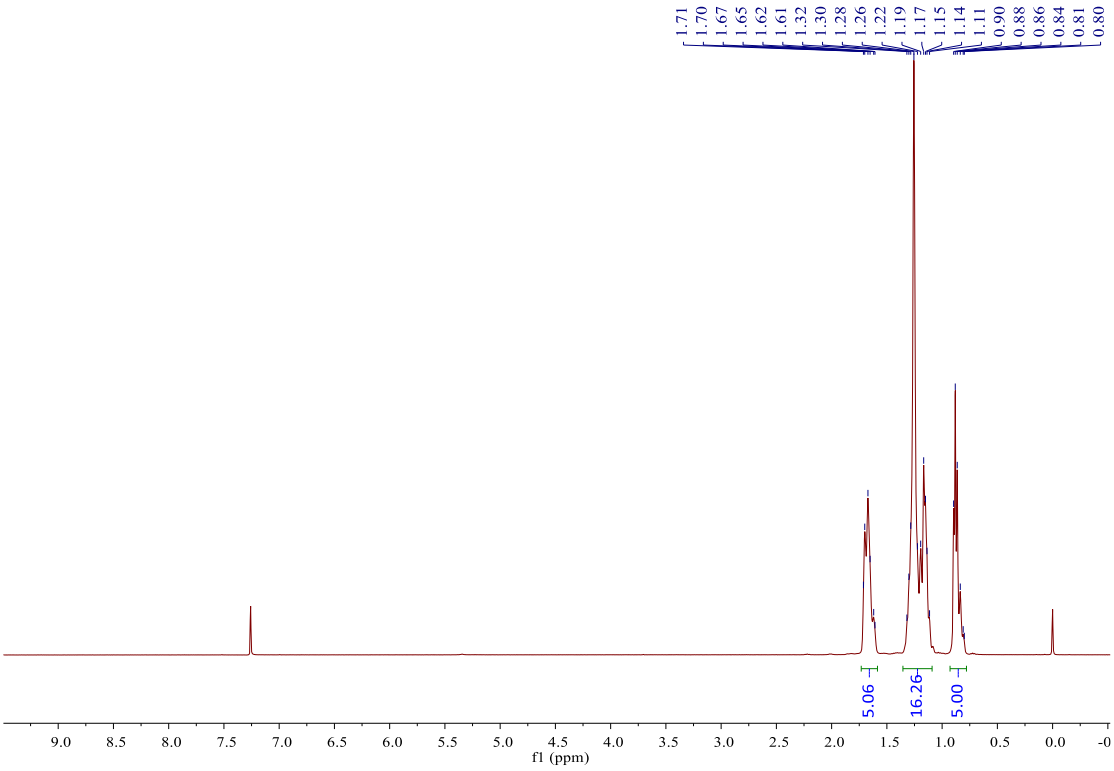

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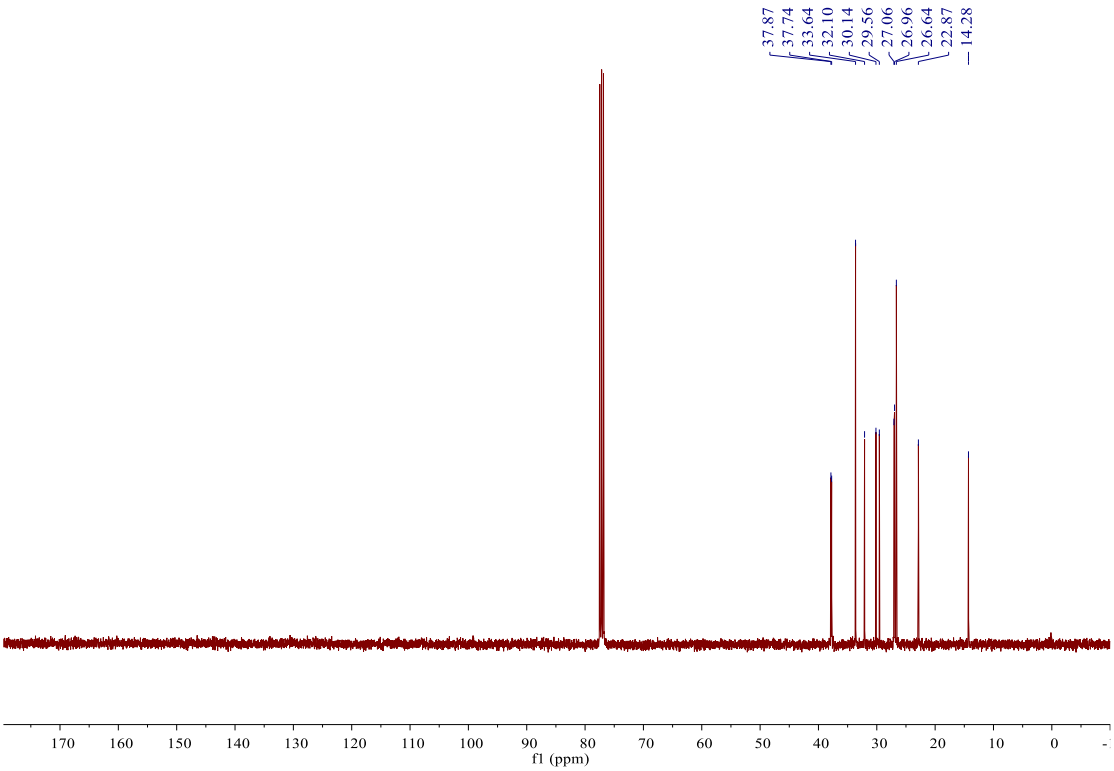

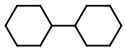

2g

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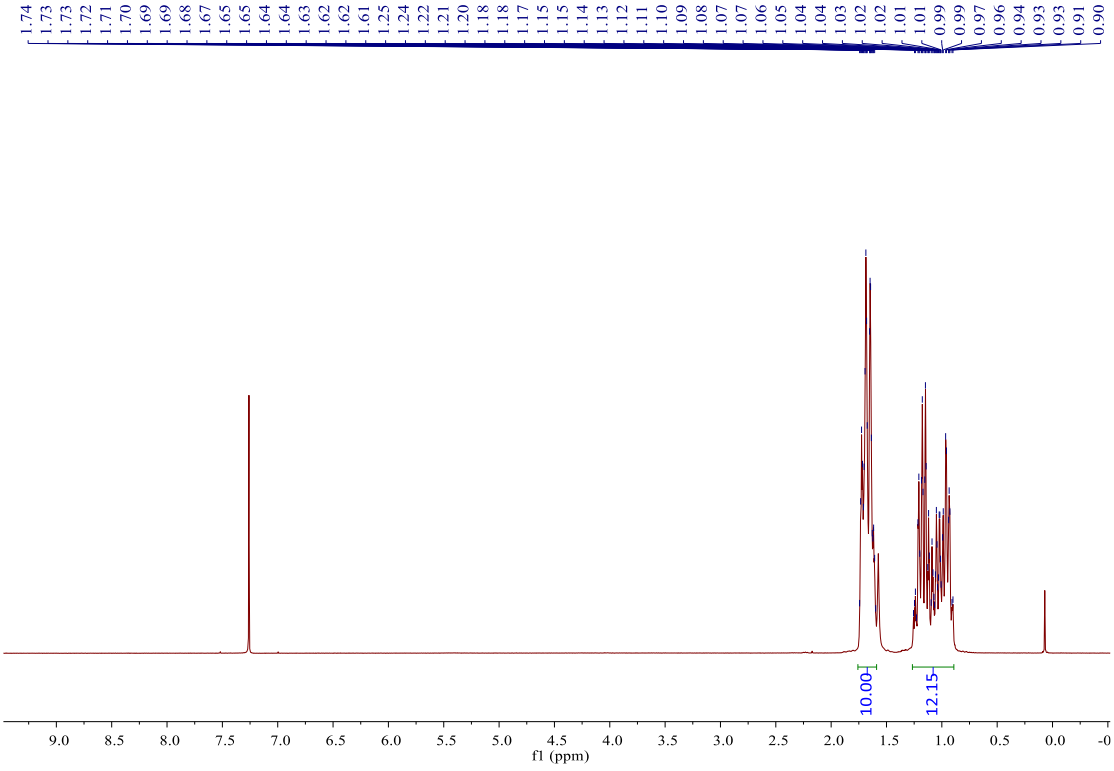

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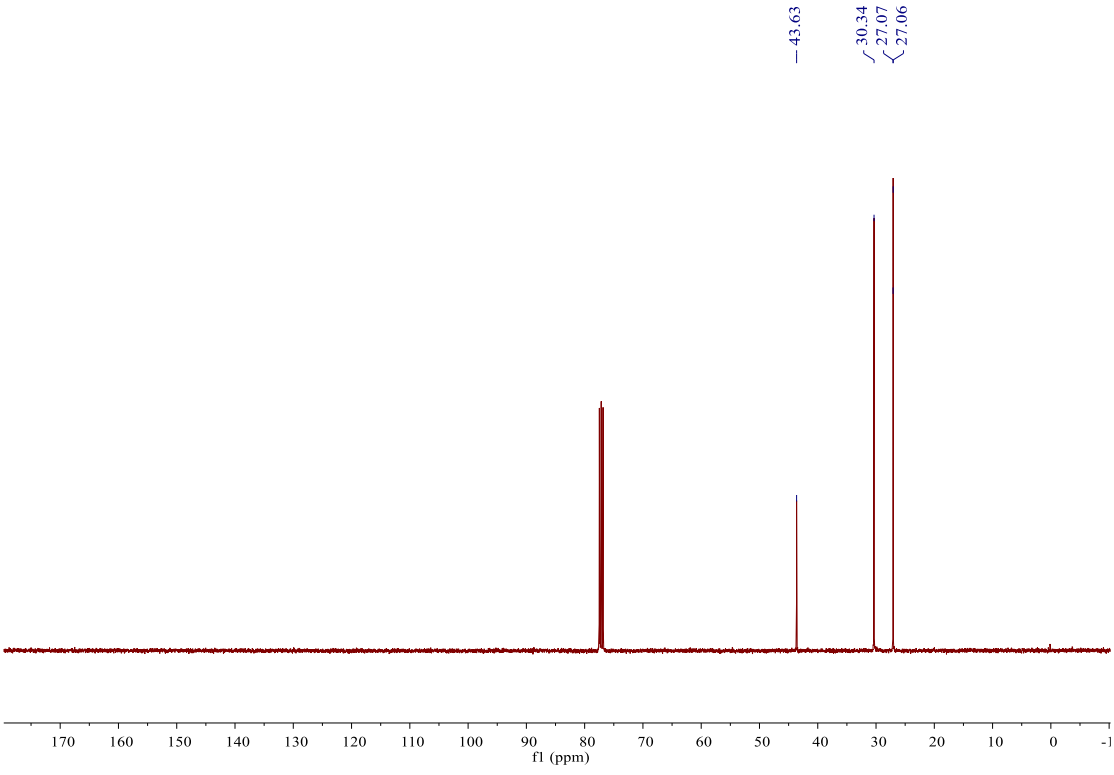

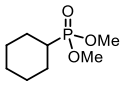

2h

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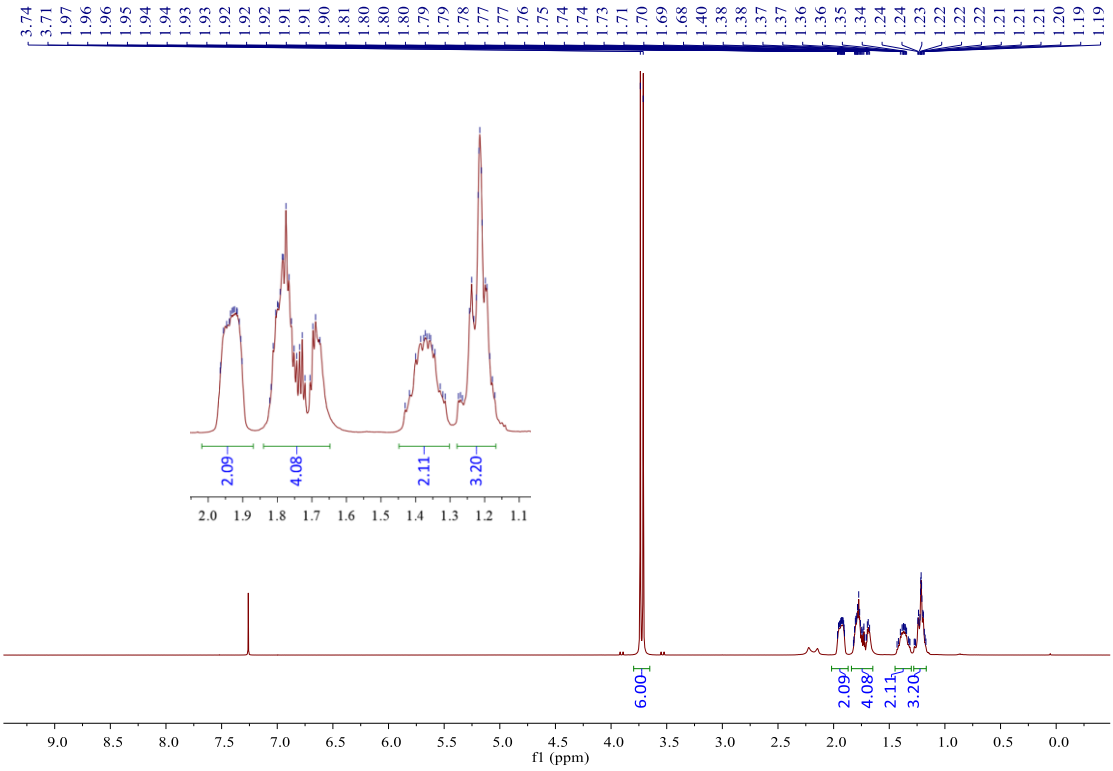
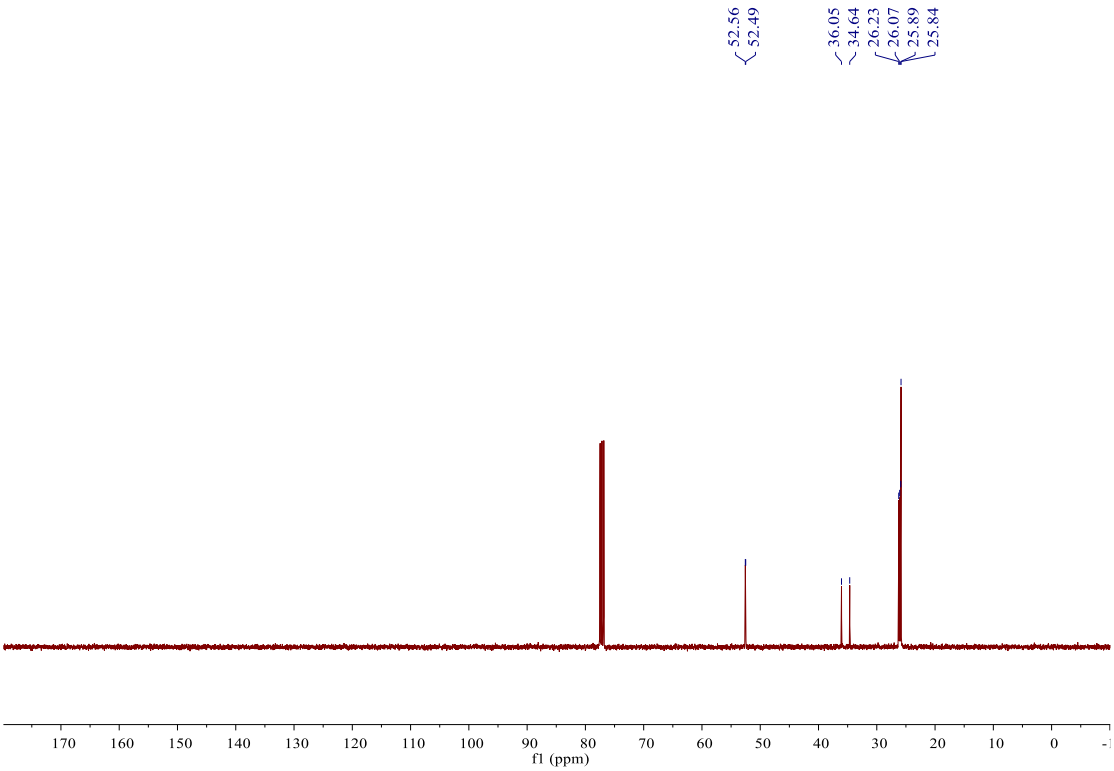
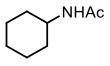


^{13}C NMR spectrum ($CDCl_3$, 101 MHz):





2i

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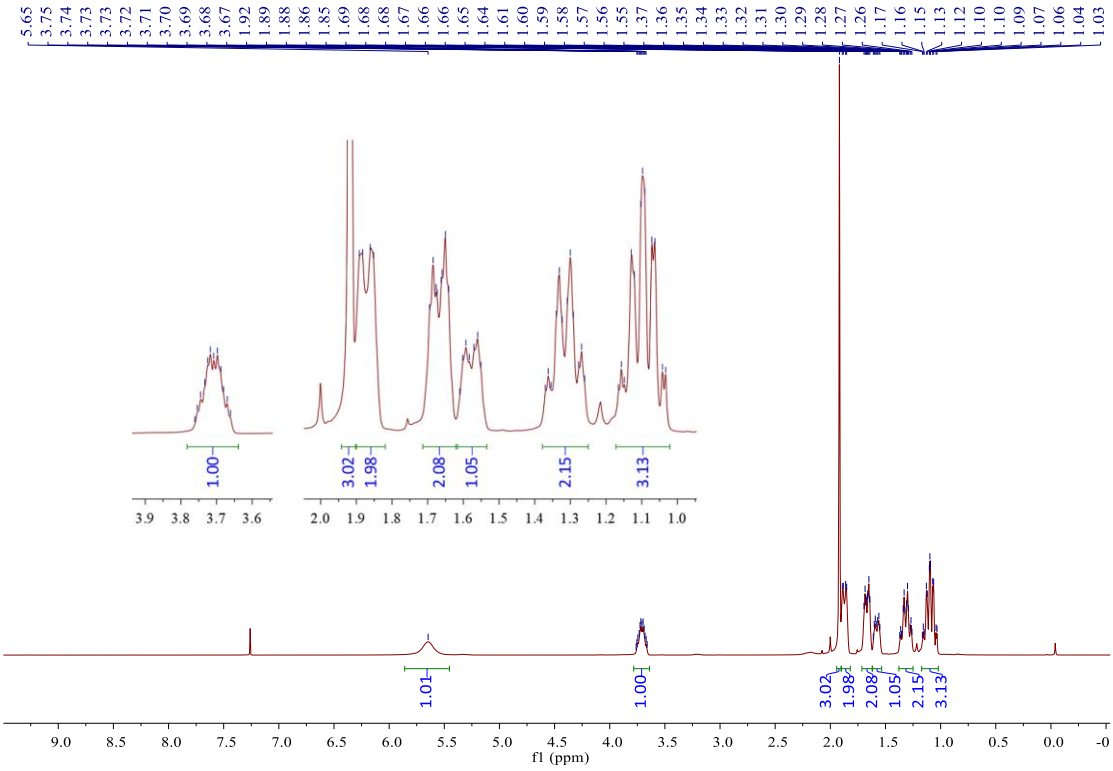

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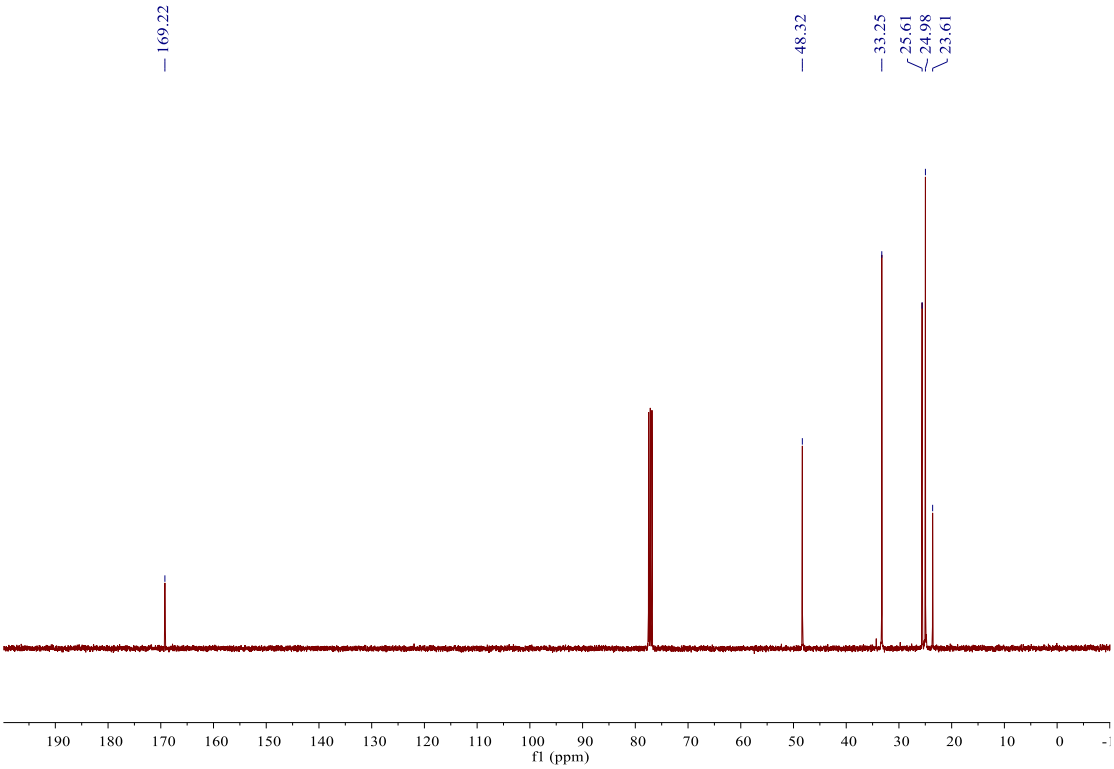

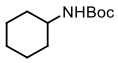

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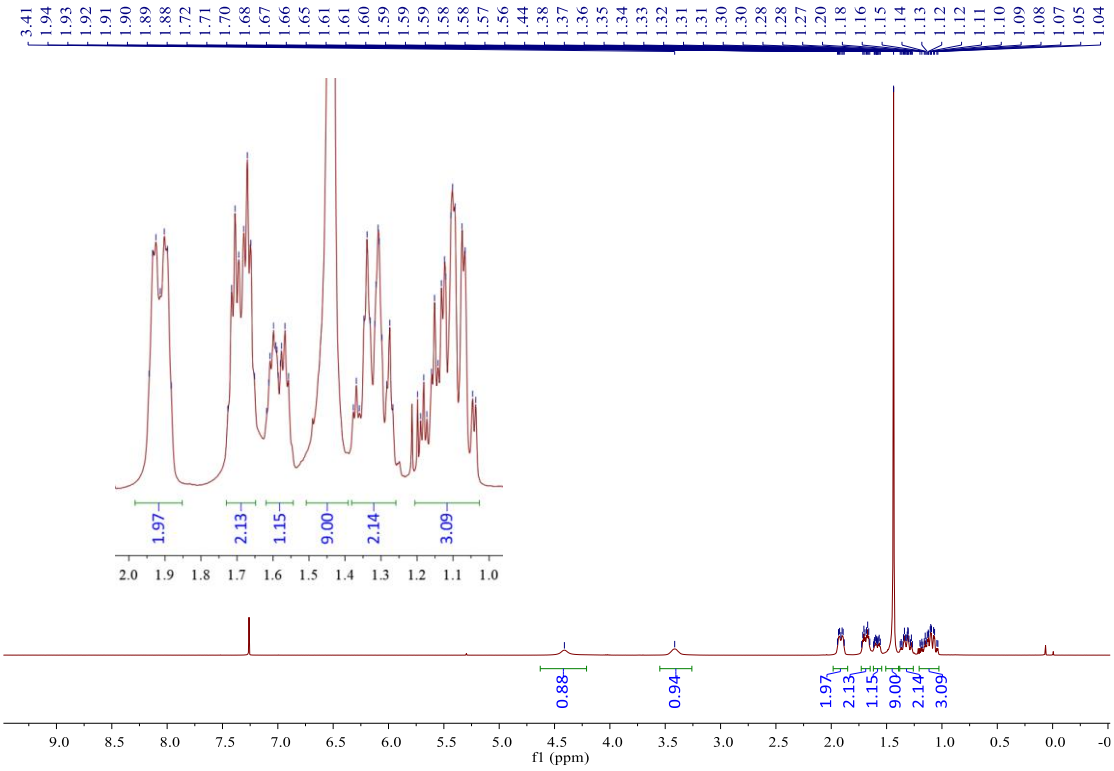

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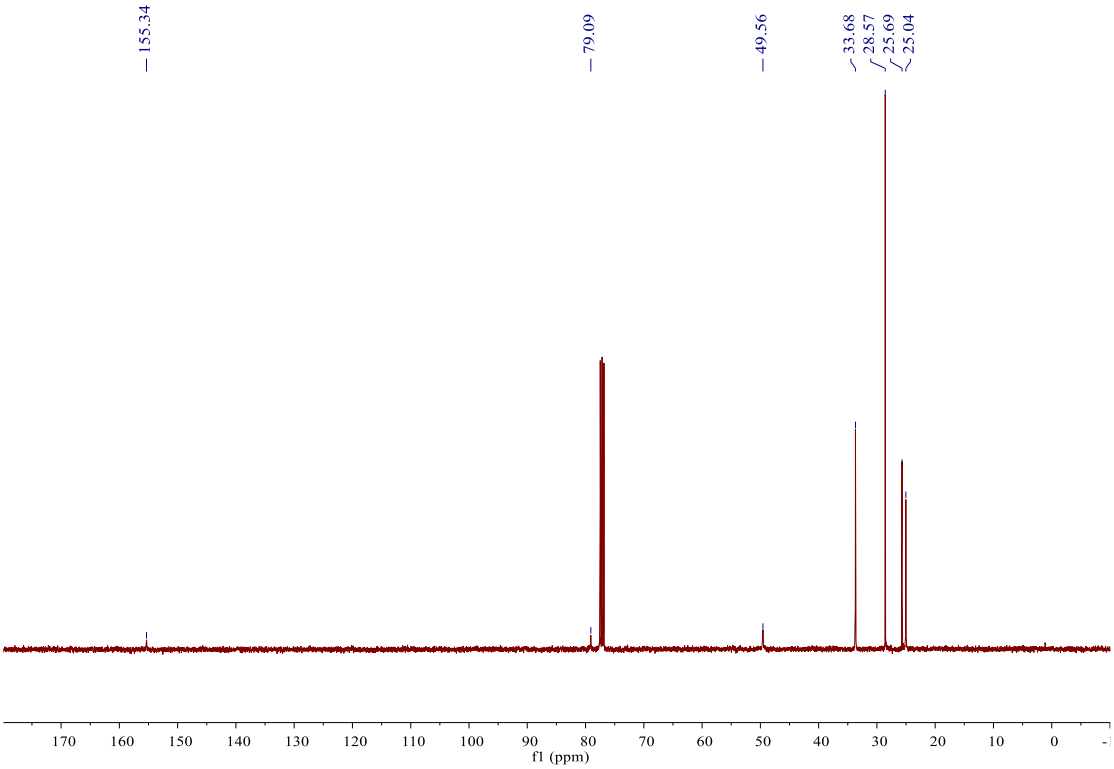

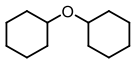

2k

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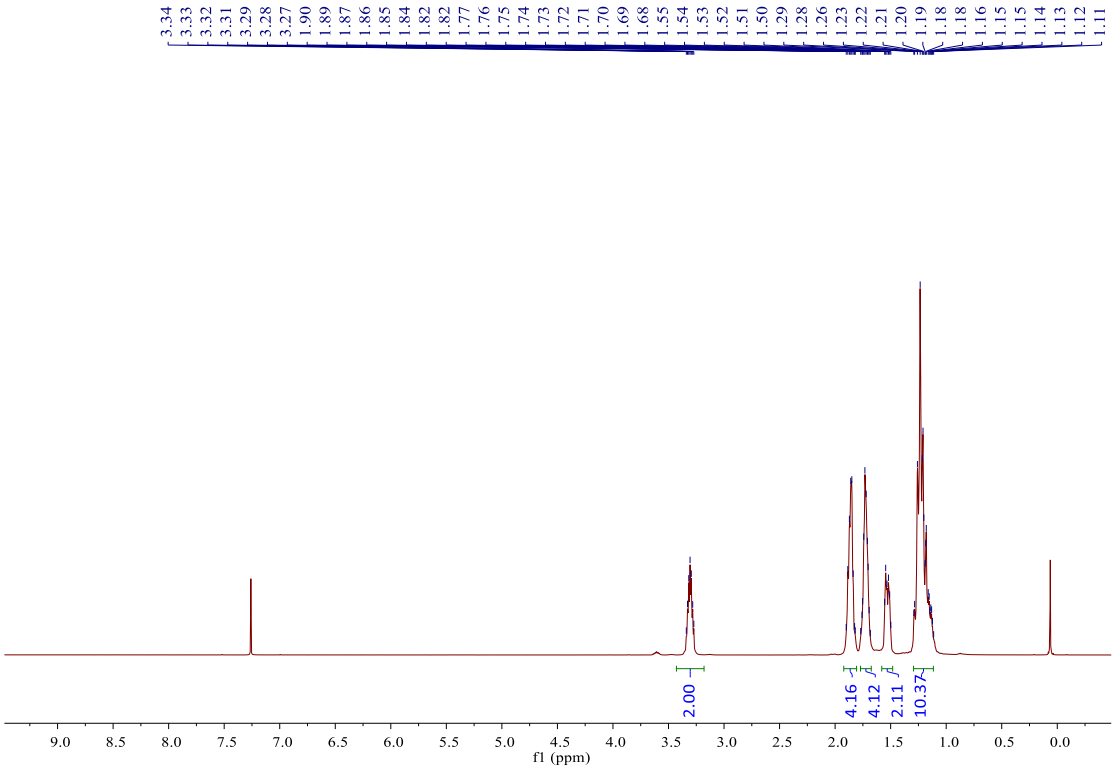

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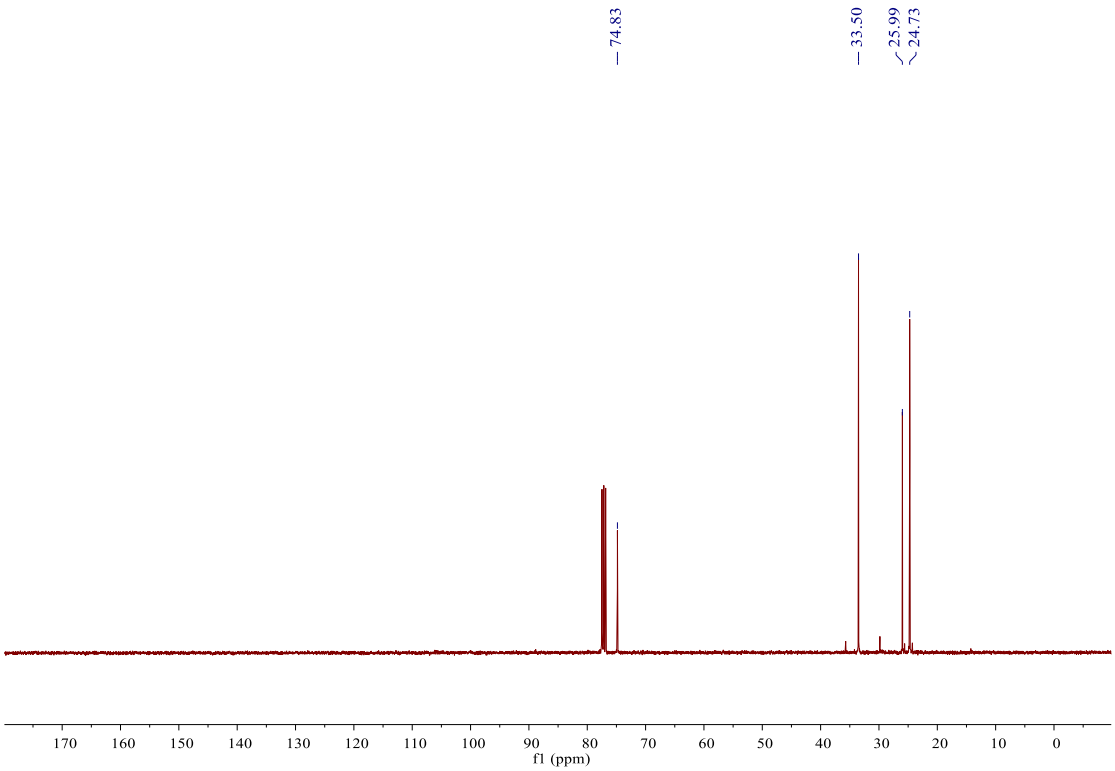

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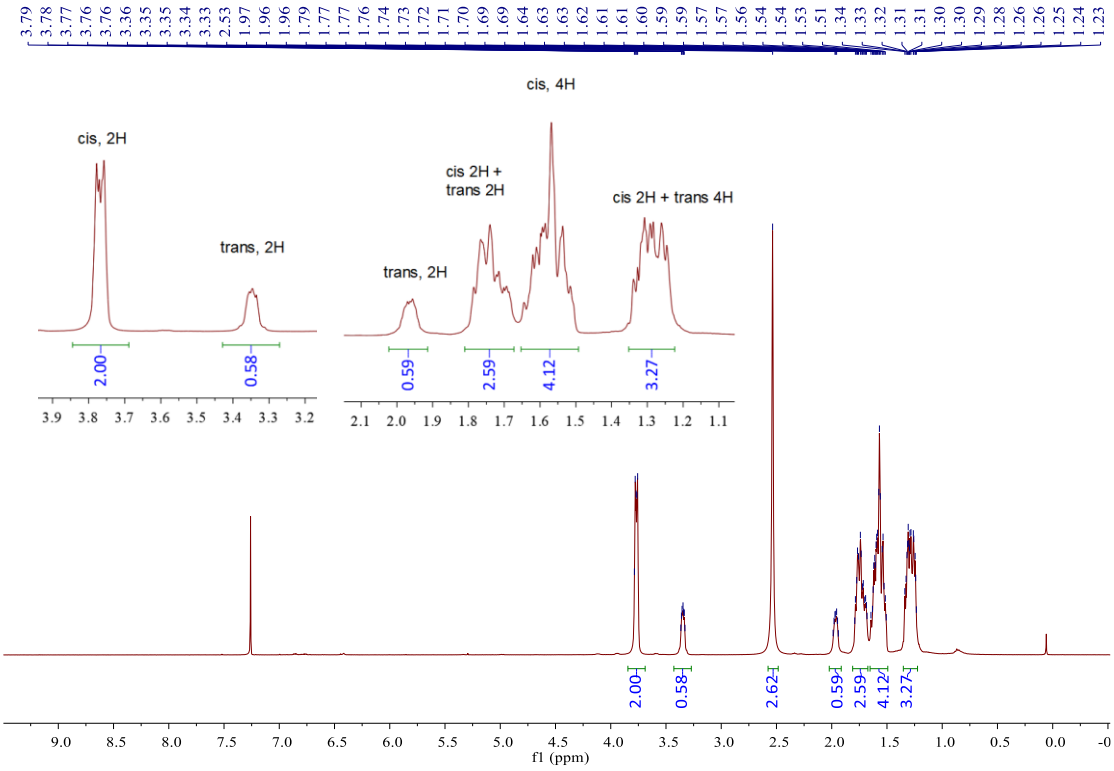

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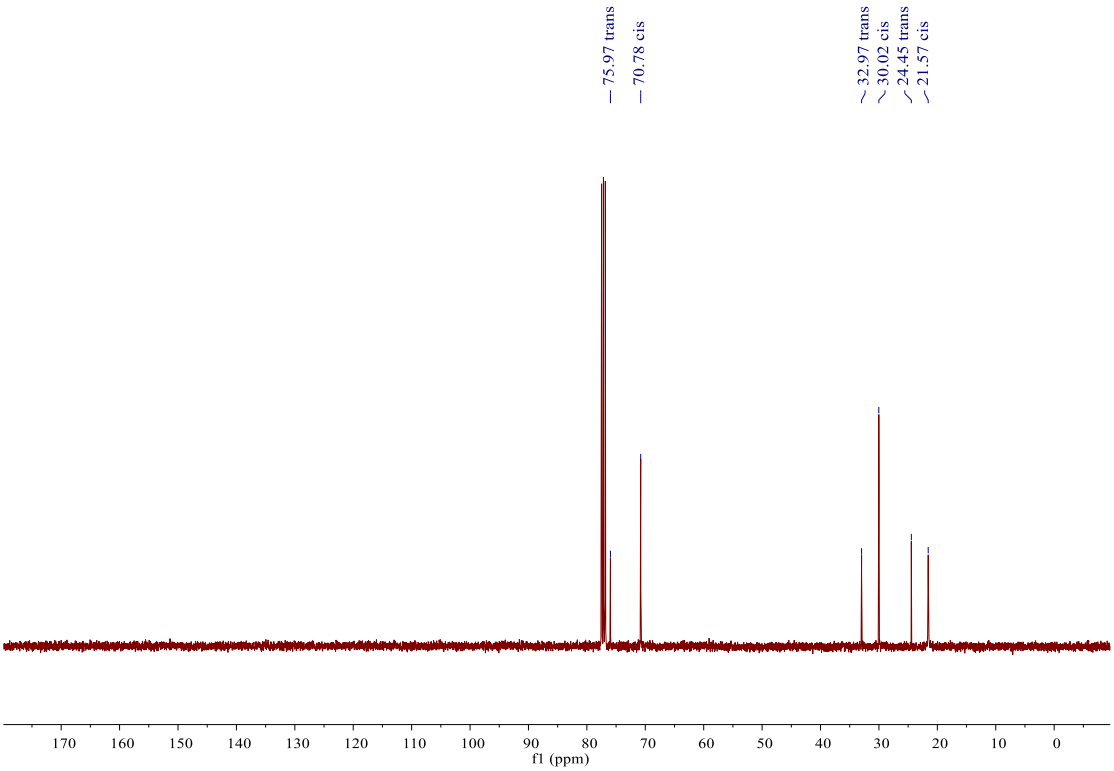

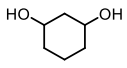

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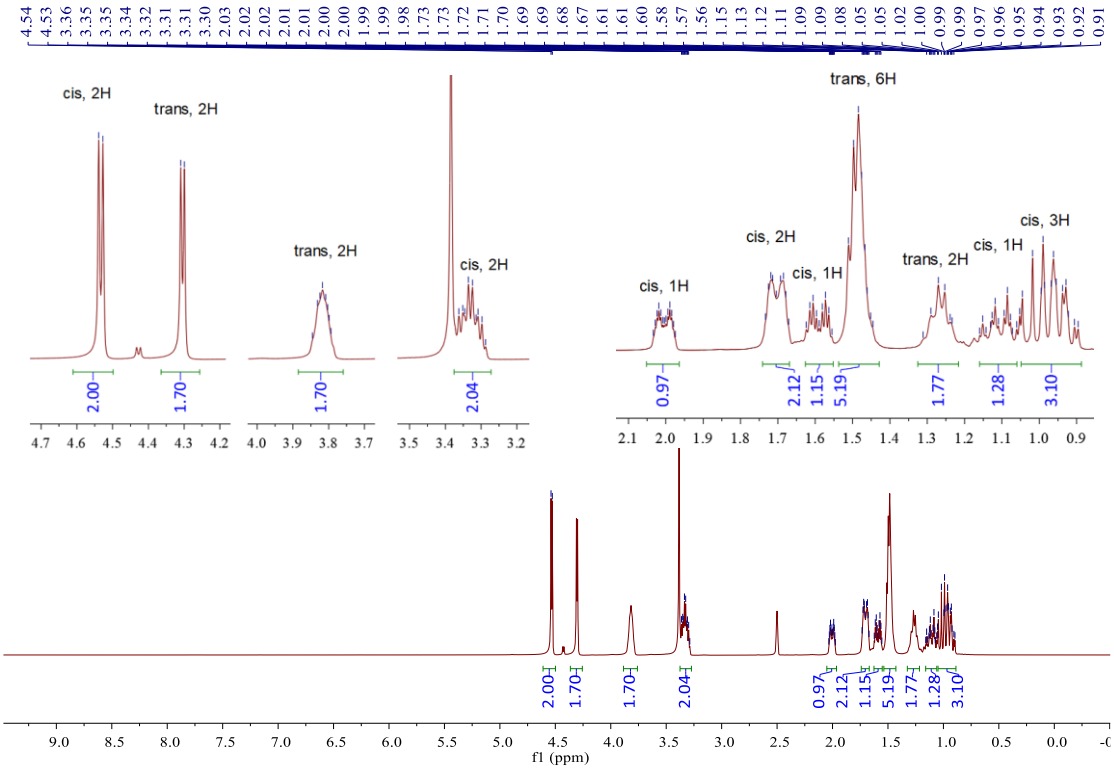
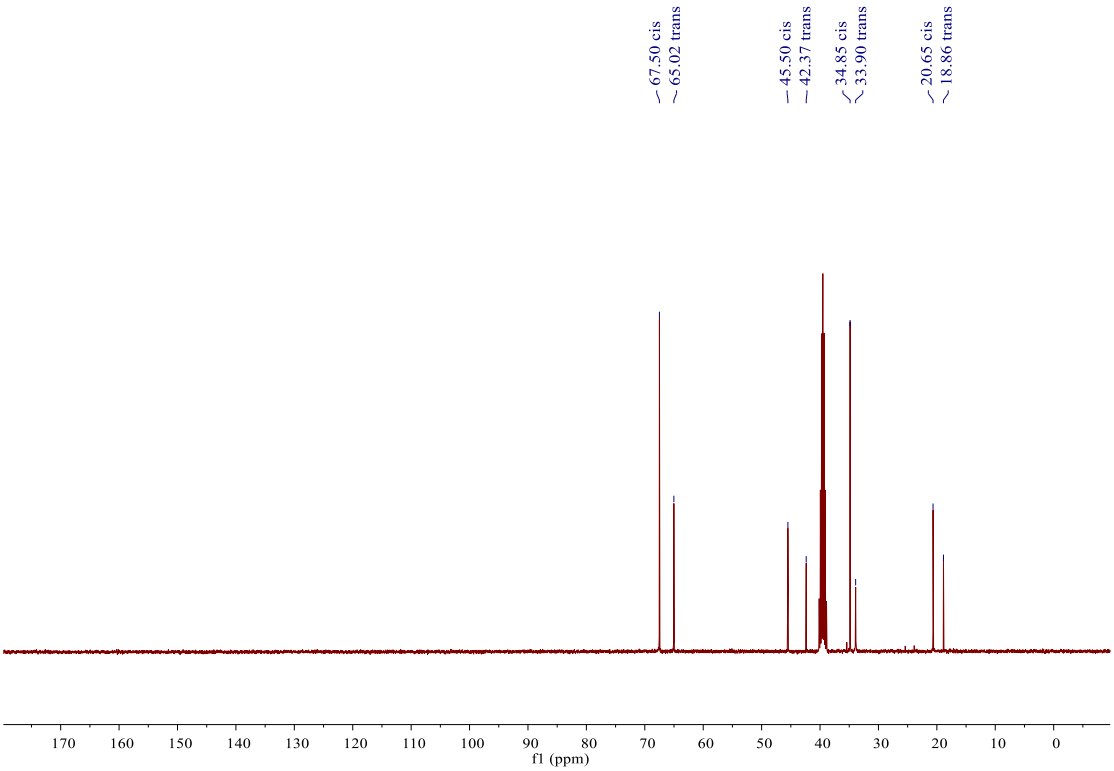
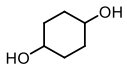


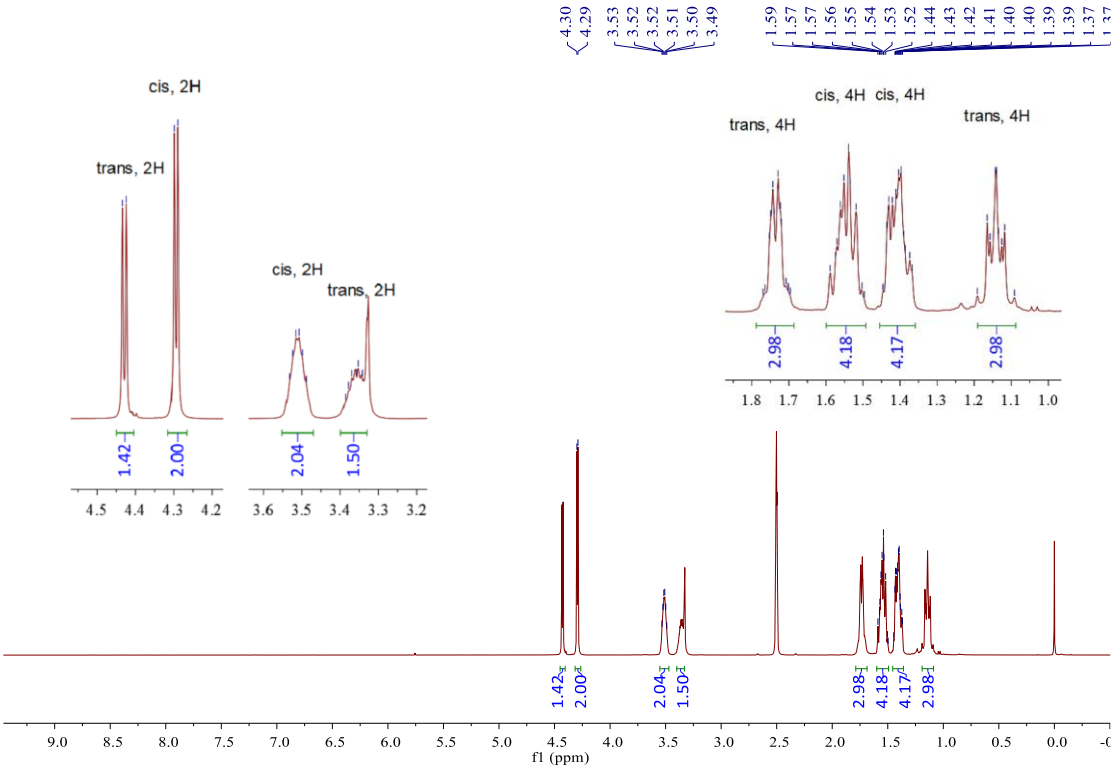
^{13}C NMR spectrum (DMSO-d_6, 101 MHz):



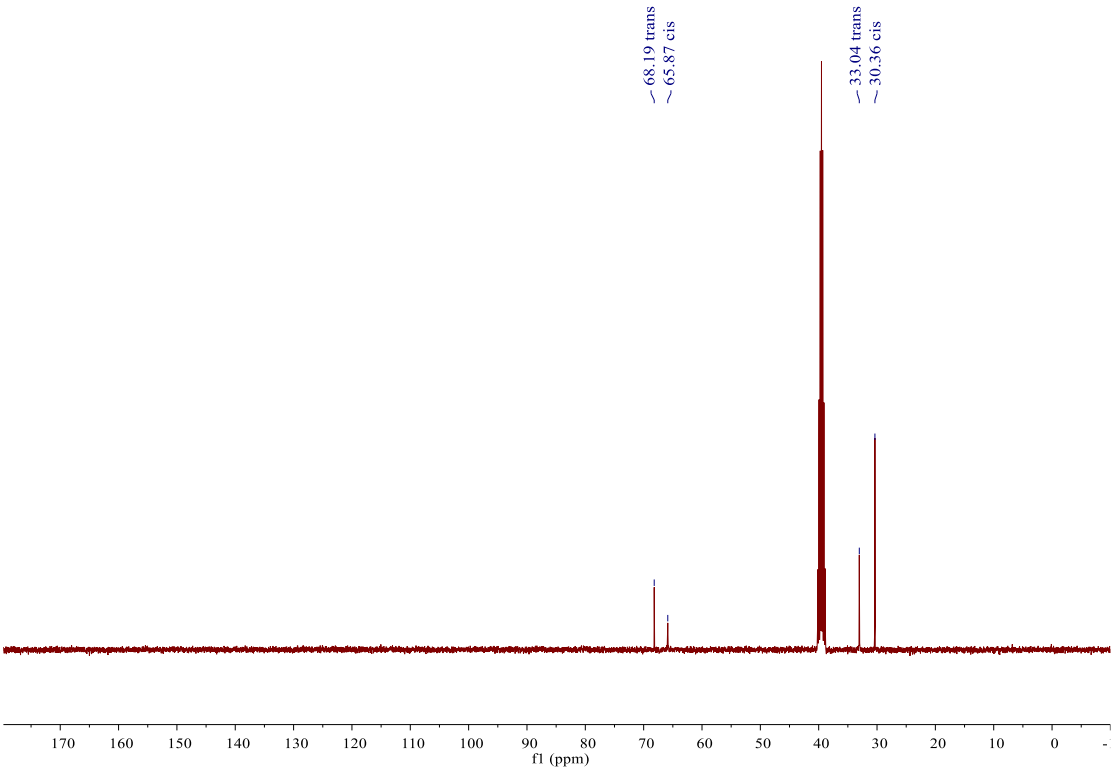


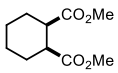
2n

^{1}H NMR spectrum (DMSO-d_6, 400 MHz, *cis*/*trans* = 1.4:1):



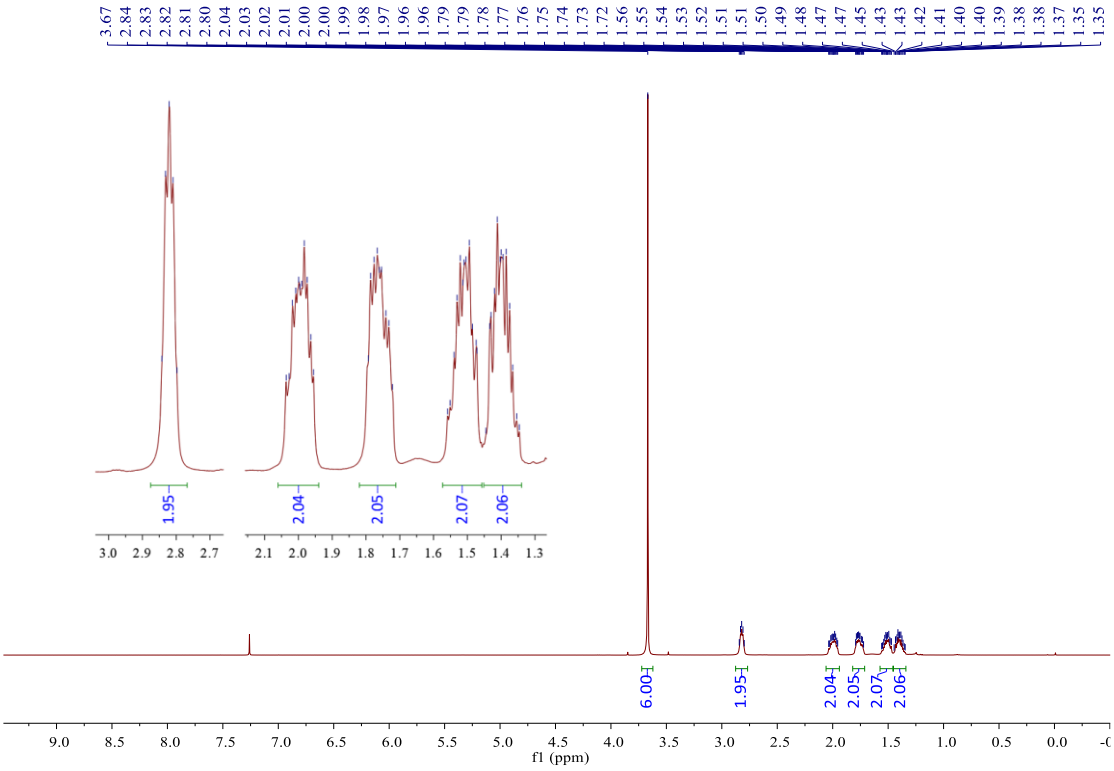
^{13}C NMR spectrum (DMSO-d_6, 101 MHz):



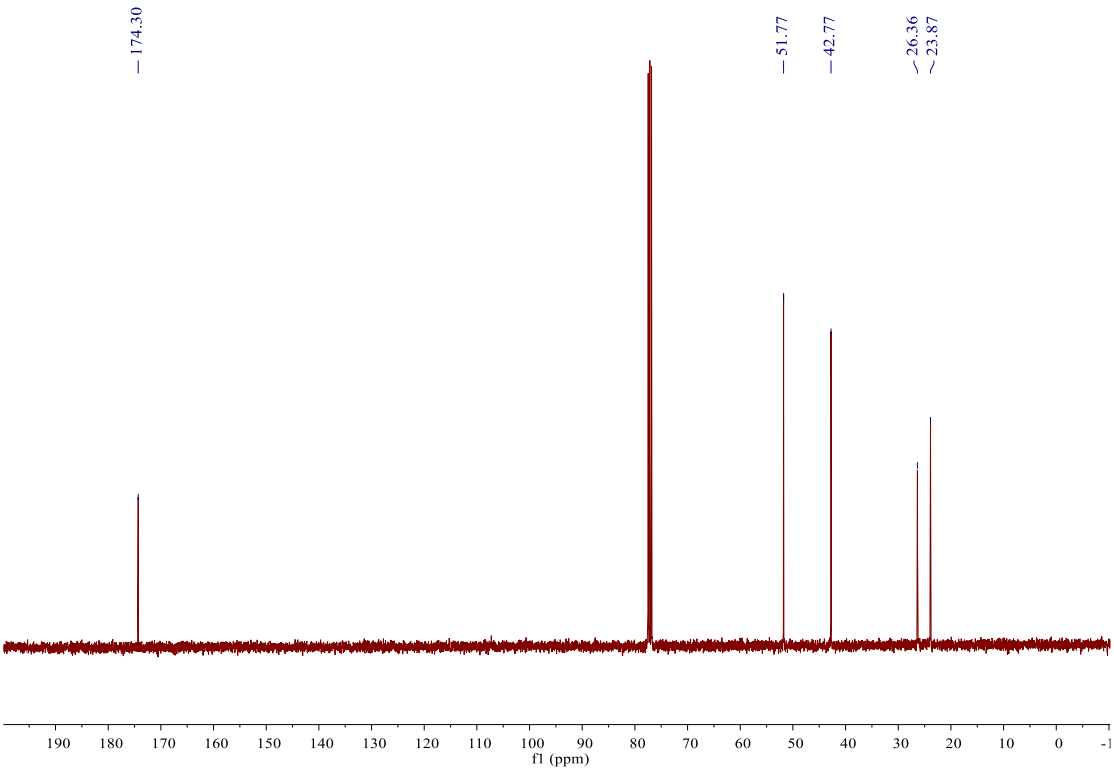


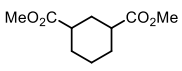
2o

^{1}H NMR spectrum ($CDCl_3$, 400 MHz):



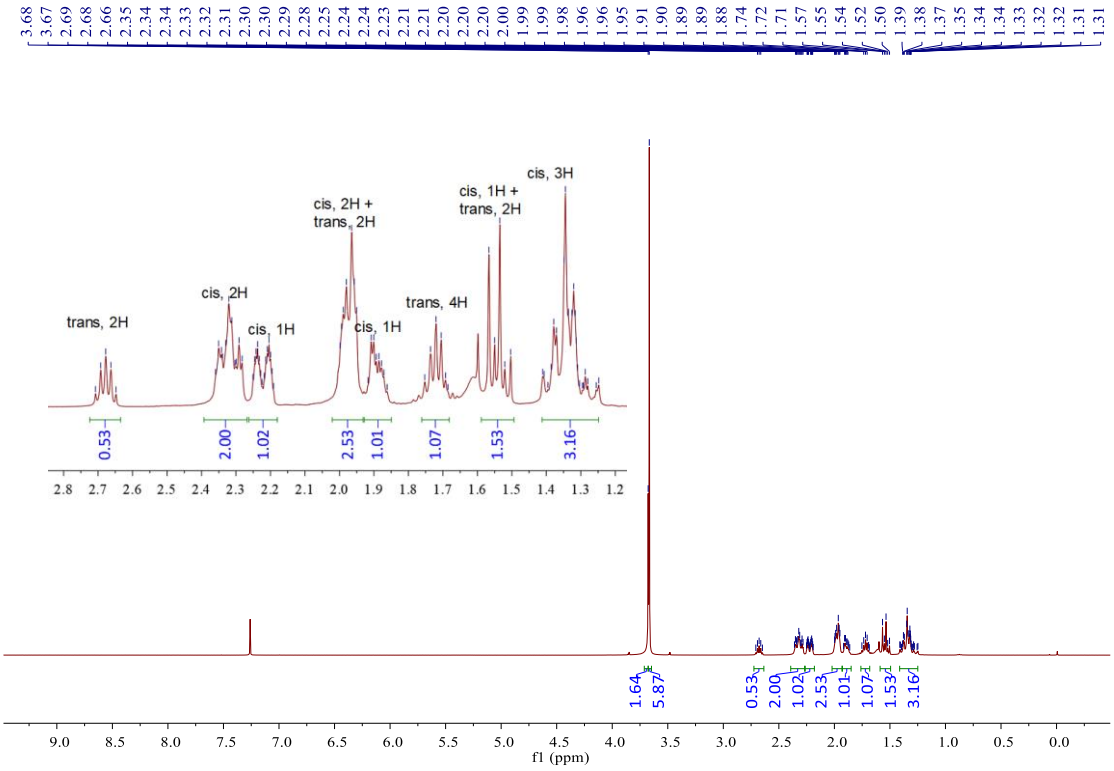
^{13}C NMR spectrum ($CDCl_3$, 101 MHz):



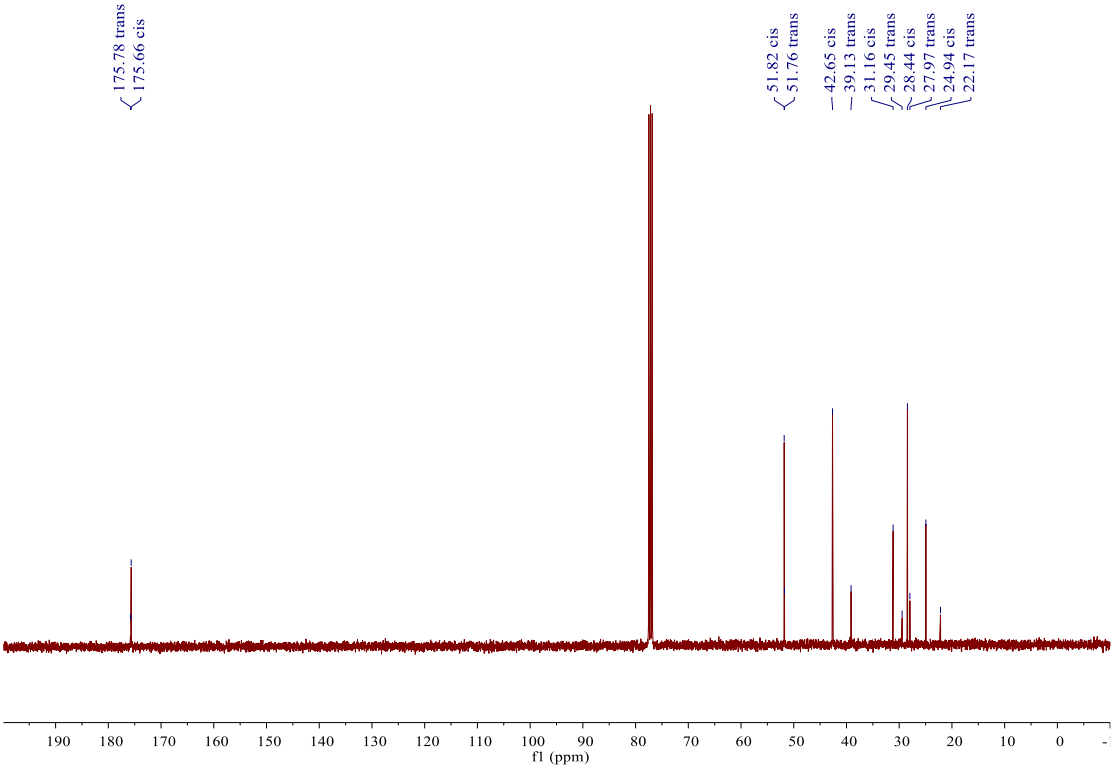


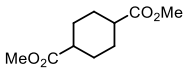
2p

^{1}H NMR spectrum ($CDCl_3$, 400 MHz, *cis*/*trans* = 3.8:1):



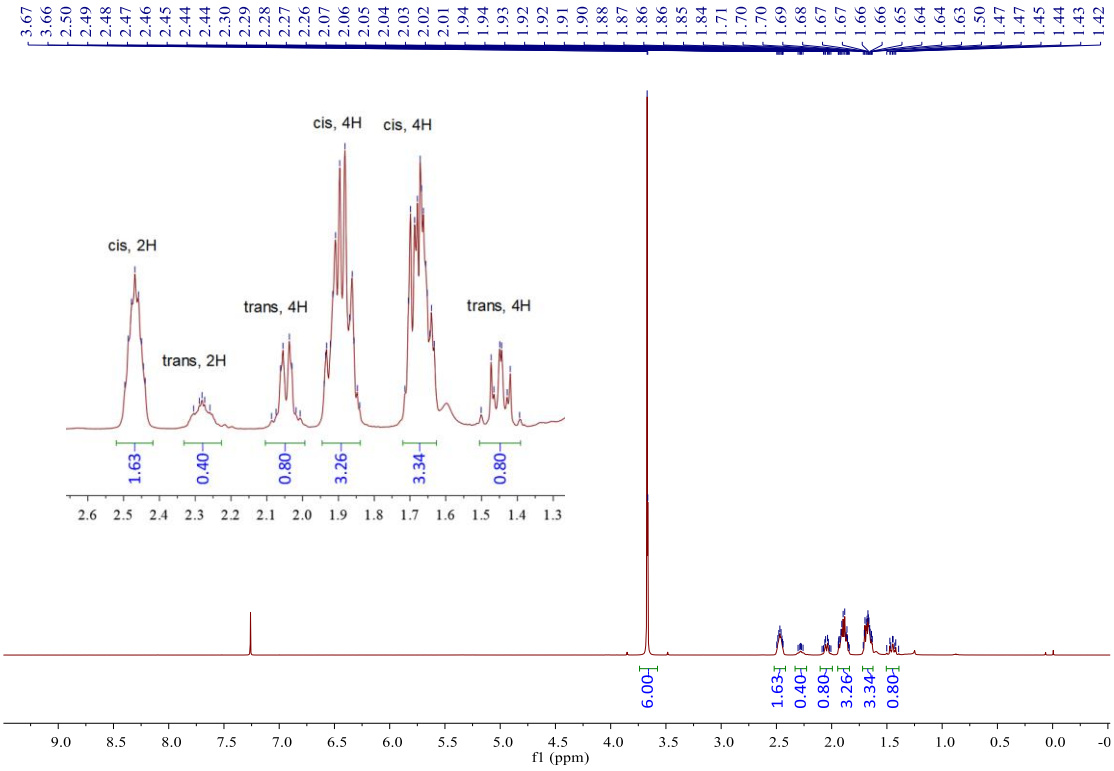
^{13}C NMR spectrum ($CDCl_3$, 101 MHz):



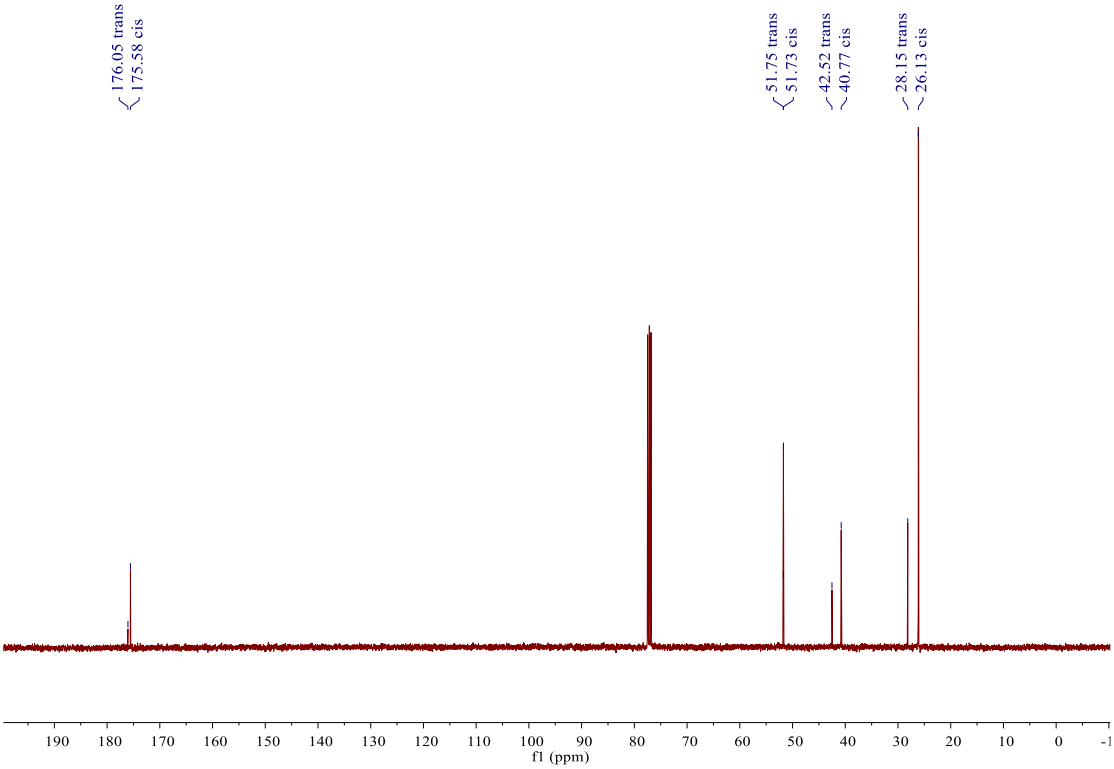


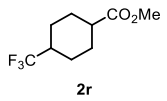
2q

^{1}H NMR spectrum ($CDCl_3$, 400 MHz, *cis*/*trans* = 4.1:1):



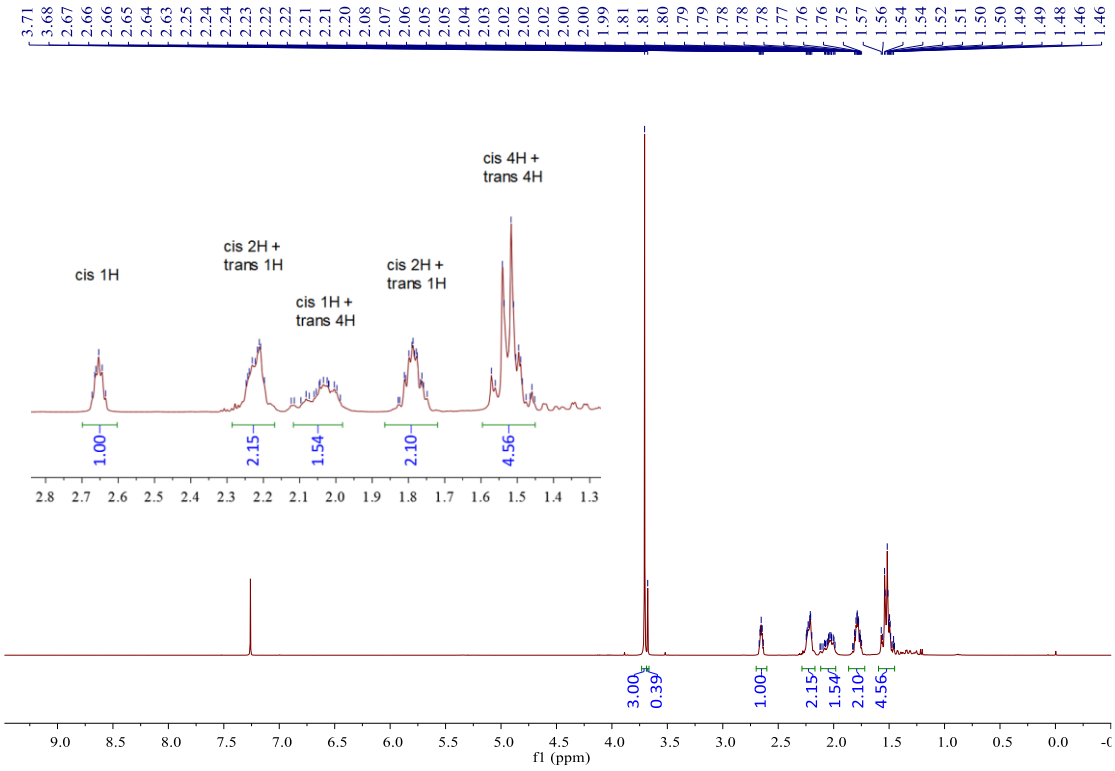
^{13}C NMR spectrum ($CDCl_3$, 101 MHz):



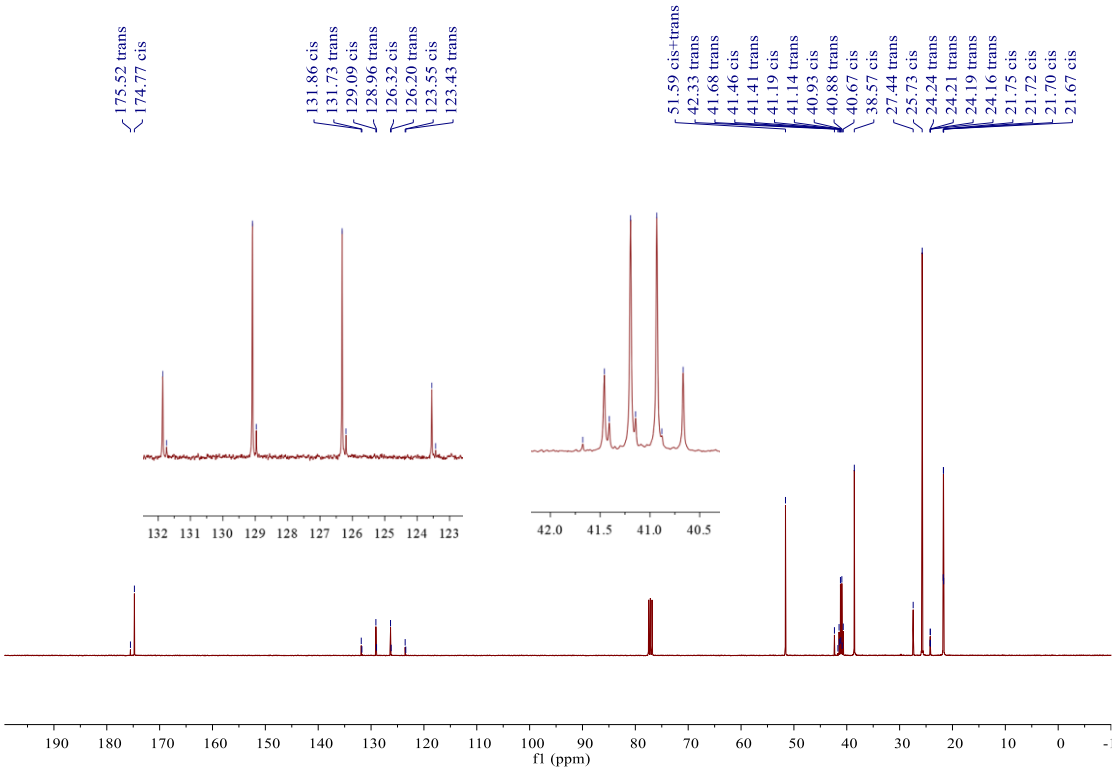


2r

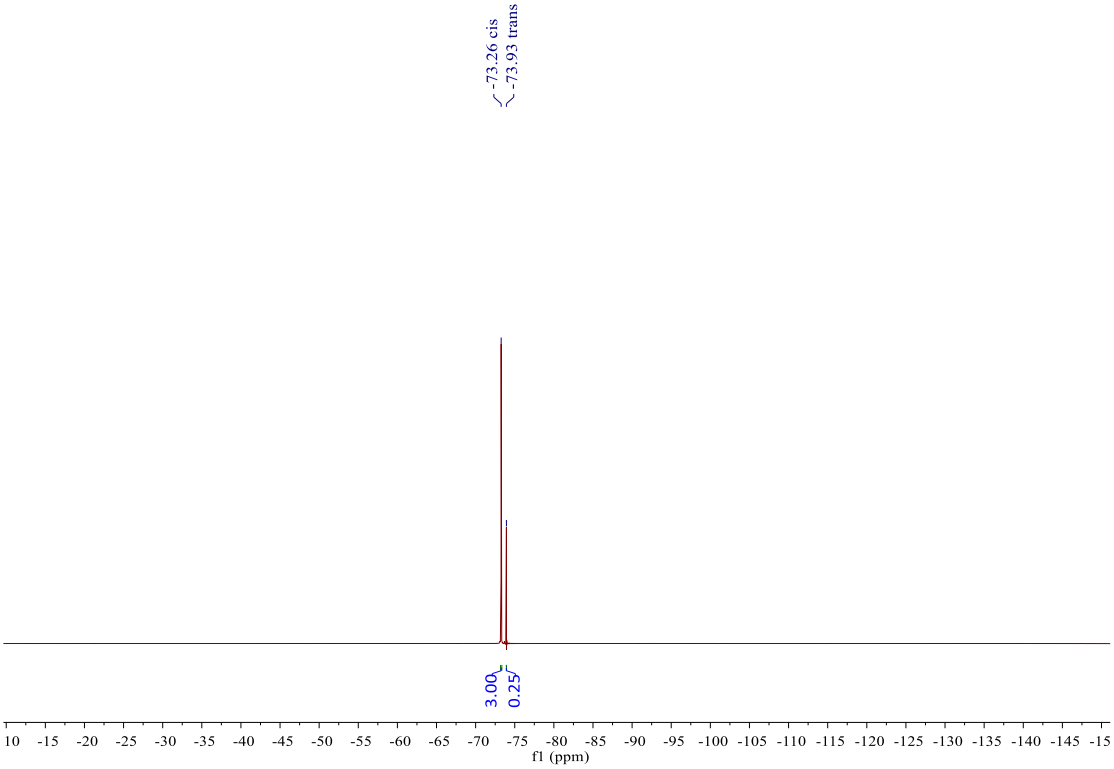
^{1}H NMR spectrum ($CDCl_3$, 400 MHz, *cis*/*trans* = 7.8:1):



^{13}C NMR spectrum ($CDCl_3$, 101 MHz):

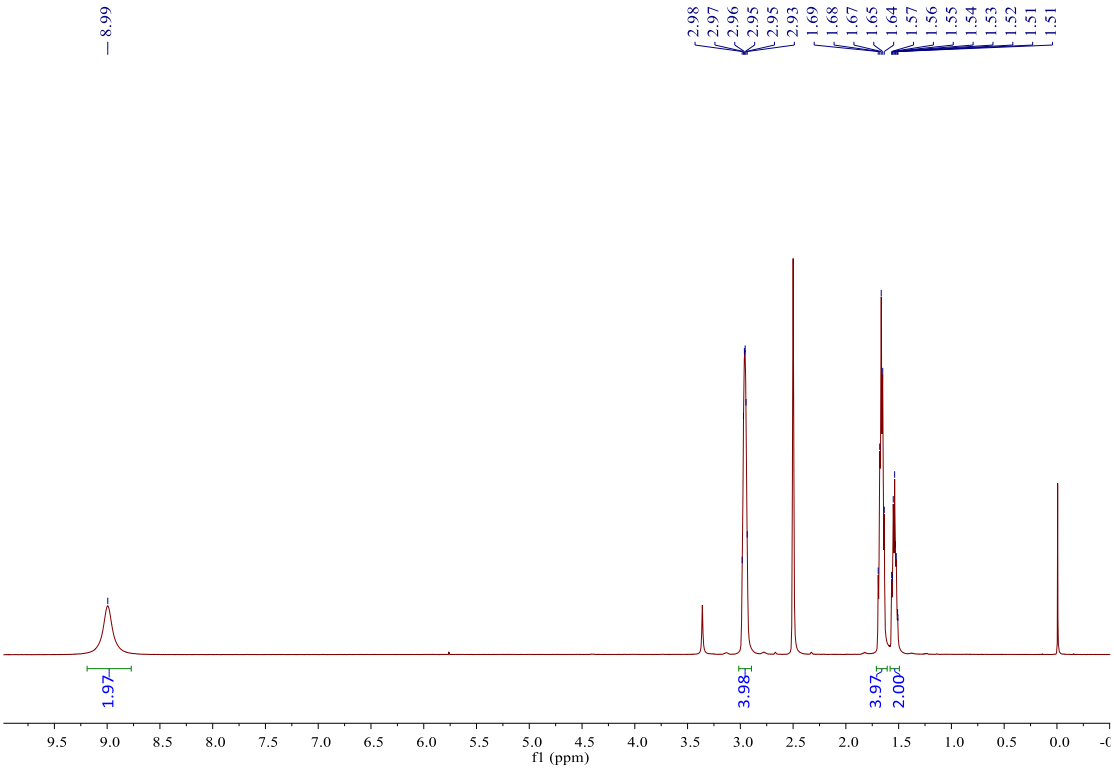


^{19}F NMR spectrum ($CDCl_3$, 471 MHz, *cis*/*trans* = 12:1)



2s•HCl

^{1}H NMR spectrum (DMSO-d_6, 400 MHz):



^{13}C NMR spectrum (DMSO-d_6, 101 MHz):