Cu-Catalyzed Redox-Neutral Ring Cleavage of Cycloketone O-Acyl Oximes: Chemodivergent Access to Distal Oxygenated Nitriles

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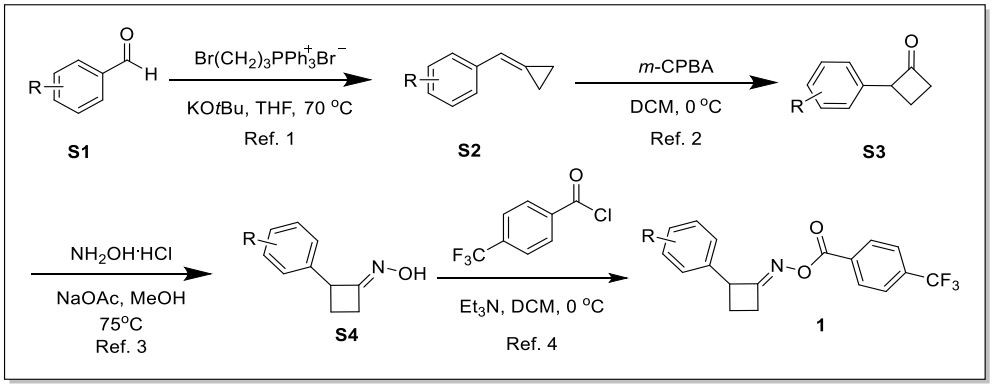
1. General Considerations

Unless otherwise noted, all experiments were carried out under Ar atmosphere. Most solvents were dried over solvent purification system (Innovative Technology PS-MD-5) and alcohol solvents were dried over magnesium and iodine. Deuterated solvents were purchased from Cambridge Isotope Laboratories. The other regular chemicals were obtained from commercial suppliers with purity over 95% and used without further purification. Nuclear magnetic resonance spectra (^{1}H NMR and ^{13}C NMR) were recorded using a Bruker 400 MHz spectrometer. The chemical shifts were reported in ppm referenced to the deuterated solvents. High resolution exact mass measurements (HRMS) were obtained on a Thermo SCIENTIFIC Q EXACTIVE instrument.

2. Typical procedure for the synthesis of oximes 1

Scheme S1. Synthetic route of cyclobutanone *O*-(4-(trifluoromethyl)benzoyl) oximes



Cyclobutanone *O*-(4-(trifluoromethyl)benzoyl) oximes were prepared from the correspounding cyclobutanones **S3**, which were produced by the oxidation of (phenylmethylene)cyclopropanes **S2** synthesized from the corresponding benzaldehydes **S1** through a Wittig reaction[1].

General procedure for the synthesis of cyclobutanone oximes 1a

A solution of KO*t*Bu (6.74 g, 60 mmol, 3.0 equiv) in THF (46 mL, 1.3 M) was slowly added to a solution of (3-bromopropyl)triphenylphosphonium bromide (13.92 g, 30 mmol, 1.5 equiv) in dry THF (60 mL, 0.5 M) and stirred at 70 °C for 1 h. Then a THF solution of benzaldehyde **S1a** (2.04 mL, 20 mmol, 2.0 M in THF, 1.0 equiv) was added dropwise and the mixture was refluxed for 3 h. After cooling, the suspension was filtered and the solvent of the filtrate was removed under vacuum, the products were purified by column chromatography on silica gel, eluting with petroleum to afford (phenylmethylene)cyclopropanes **S2a** (2.47 g, 95%).

To the solution of (phenylmethylene)cyclopropanes **S2a** (2.47 g, 19 mmol, 1.0 equiv) in DCM (127 mL, 0.15 M) was added a solution of *m*-CPBA (4.37 g, 19 mmol, 1.0 equiv) in DCM (50 mL, 0.38 M) dropwise at 0 °C and stirred for 1 h. Then, the solution was diluted with a saturated solution of aqueous Na_2SO_3 (30 mL) and extracted with DCM (3*20 mL). The organic phase was washed successively with a saturated solution of aqueous $NaHCO_3$ (3*30 mL), and brine (30 mL), then dried over Na_2SO_4 and concentrated in vacuum. The crude material was then purified by column chromatography on silica gel with a mixture of petroleum ether and ethyl acetate (20:1) to give various cyclobutanones **S3a** (2.47 g, 89 %)[2].

To a mixture of hydroxylamine hydrochloride (1.41 g, 20.3 mmol, 1.2 equiv), sodium acetate (2.08 g, 25.4 mmol, 1.5 equiv), methanol (30 mL, 0.56 M) in a 100-mL two-necked flask was added cyclobutanone **S3a** (2.47 g, 16.9 mmol, 1.0 equiv) and the mixture was stirred at 75 °C for 12 h. The reaction mixture was cooled to room temperature and then methanol was removed under vacuum and the resulting mixture was extracted with diethyl ether. The organic layer was washed with water and dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude material was subjected to column chromatography to afford cyclobutanone oximes **S4a** (2.23 g, 82%)[3].

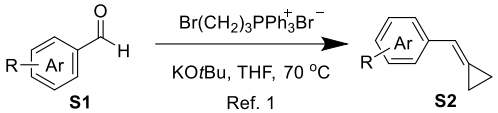
To a mixture of cyclobutanone oxime **S4a** (865.8 mg, 5.37 mmol, 1.0 equiv), triethylamine (1.12 mL, 8.06 mmol, 1.5 equiv) and DCM (10.7 mL, 0.5 M) in a 30-mL two-necked flask was added 4-(trifluoromethyl)benzoyl chlorides (0.88 mL, 5,91 mmol, 1.1 equiv) at 0 °C. After 1 h, a saturated solution of aqueous $NaHCO_3$ (30 mL) was added to the above solution, and the mixture was diluted with DCM. The organic layer was washed with brine (30 mL) and dried over $MgSO_4$. The solvent was removed under vacuum and the residue was subjected to column chromatography on silica gel with EtOAc–petroleum ether (1/20) as an eluent to give cyclobutanone *O*-(4-(trifluoromethyl)benzoyl) oximes **1a** (1.3 g, 73 %)[4].

General procedure for the synthesis of (phenylmethylene)cyclopropanes S2

The following experimental procedure is typical: a solution of KO*t*Bu (3.0 equiv) in THF (1.3 M) was slowly added to a solution of (3-bromopropyl)triphenylphosphonium bromide (1.5 equiv) in dry THF (0.5 M) and stirred at 70 °C for 1 h. Then a THF solution of benzaldehyde **S1** (2.0 M, 1.0 equiv) was added dropwise and the mixture was refluxed for 3~6 h. After cooling, the suspension was filtered and the solvent of the filtrate was removed under vacuum, the products were purified by column

chromatography on silica gel, eluting with petroleum to afford various (phenylmethylene)cyclopropanes **S2**.

Table S1. Preparation of (phenylmethylene)cyclopropanes

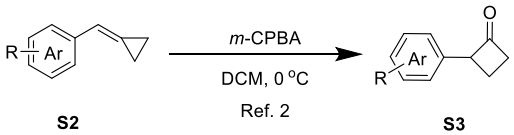


S2a, R = H, 95 %	**S2e**, R = 4-Br, 95 %
S2b, R = 4-Me, 97 %	**S2f**, R = I, 90 %
S2c, R = 4-OMe, 88 %	**S2g**, R = 3-F, 87 %
S2d, R = 2-Me, 90 %	**S2h**, Ar = 2-Nap, 92 %

General procedure for the synthesis of cyclobutanones S3

To the solution of (phenylmethylene)cyclopropanes (1.0 equiv) in DCM (0.15 M) was added a solution of *m*-CPBA (1.0 equiv) in DCM (0.38 M) dropwise at 0 °C and stirred for 1 h. Then, the solution was diluted with a saturated solution of aqueous Na_2SO_3 (30 mL) and extracted with DCM (3*20 mL). The organic phase was washed successively with a saturated solution of aqueous $NaHCO_3$ (3*30 mL), and brine (30 mL), then dried over Na_2SO_4 and concentrated in vacuum. The crude material was then purified by column chromatography on silica gel with a mixture of petroleum ether and ethyl acetate to give various cyclobutanones **S3**[2].

Table S2. Preparation of cyclobutanones



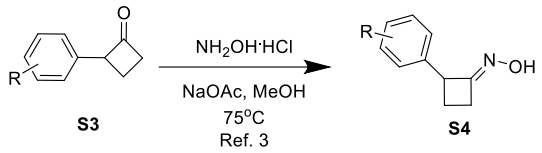
S3a, R = H, 89 %	**S3e**, R = 4-Br, 89 %
S3b, R = 4-Me, 95 %	**S3f**, R = I, 76 %
S3c, R = 4-OMe, 93 %	**S3g**, R = 3-F, 55 %
S3d, R = 2-Me, 90 %	**S3h**, Ar = 2-Nap, 72 %

General procedure for the synthesis of cyclobutanone oximes S4

To a mixture of hydroxylamine hydrochloride (1.2 equiv), sodium acetate (1.5 equiv), methanol (0.56 M) in a 100-mL two-necked flask was added cyclobutanone (1.0 equiv) and the mixture was stirred at

75 °C for 12 h. The reaction mixture was cooled to room temperature and then methanol was removed under vacuum and the resulting mixture was extracted with diethyl ether. The organic layer was washed with water and dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude material was subjected to column chromatography to afford cyclobutanone oximes.

Table S3. Preparation of cyclobutanone oximes



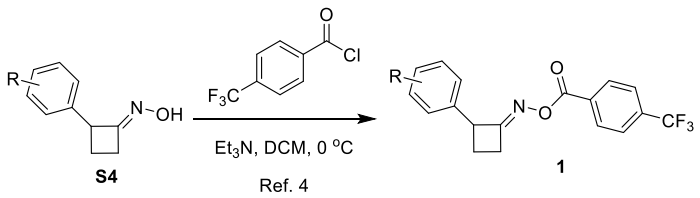
S3 **S4**

S4a, R = H, 82 %	**S4e**, R = 4-Br, 98 %
S4b, R = 4-Me, 95 %	**S4f**, R = I, 83 %
S4c, R = 4-OMe, 92 %	**S4g**, R = 3-F, 76 %
S4d, R = 2-Me, 80 %	**S4h**, Ar = 2-Nap, 95 %

General procedure for the synthesis of cyclobutanone *O*-(4-(trifluoromethyl)benzoyl) oximes 1

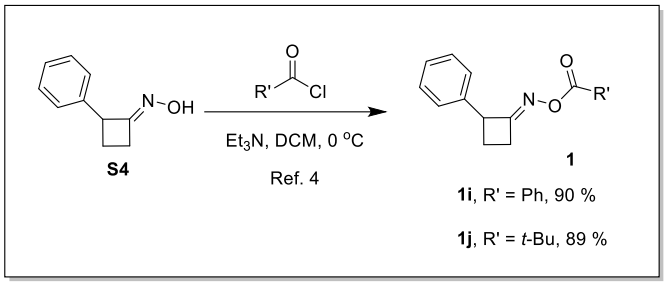
To a mixture of cyclobutanone oxime (1.0 equiv), triethylamine (1.5 equiv) and DCM (0.5 M) in a 30-mL two-necked flask was added 4-(trifluoromethyl)benzoyl chlorides (1.1 equiv) at 0 °C. After 1 h, a saturated solution of aqueous $NaHCO_3$ (30 mL) was added to the above solution, and the mixture was diluted with DCM. The organic layer was washed with brine (30 mL) and dried over $MgSO_4$. The solvent was removed under vacuum and the residue was subjected to column chromatography on silica gel with EtOAc–petroleum ether (1/20) as an eluent to give cyclobutanone *O*-(4-(trifluoromethyl)benzoyl) oximes (**1**)[4].

Table S4. Preparation of cyclobutanone *O*-(4-(trifluoromethyl)benzoyl) oximes



1a, R = H, 73 %	**1e**, R = 4-Br, 81 %
1b, R = 4-Me, 50 %	**1f**, R = I, 61 %
1c, R = 4-OMe, 32 %	**1g**, R = 3-F, 43 %
1d, R = 2-Me, 60 %	**1h**, Ar = 2-Nap, 81 %

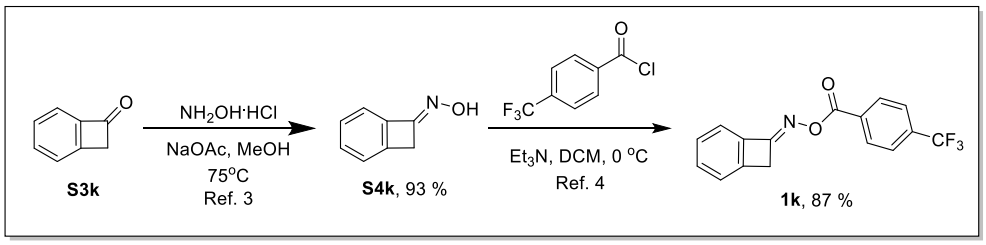
Scheme S2. Synthetic route to different acyl substituted 2-phenylcyclobutan-1-one oximes



General procedure for the synthesis of 1i and 1j

To a mixture of 2-phenylcyclobutan-1-one oxime (1.0 equiv), triethylamine (1.5 equiv) and DCM (0.5 M) in a 30-mL two-necked flask was added benzoyl chloride or pivaloyl chloride (1.1 equiv) at 0 ℃. After 1 h, a saturated solution of aqueous $NaHCO_3$ (30 mL) was added to the above solution, and the mixture was diluted with DCM. The organic layer was washed with brine (30 mL) and dried over $MgSO_4$. The solvent was removed under vacuum and the residue was subjected to column chromatography on silica gel with EtOAc–petroleum ether (1/20) as an eluent to give 2-phenylcyclobutan-1-one *O*-benzoyl oxime or 2-phenylcyclobutan-1-one *O*-pivaloyl oxime (**1i** or **1j**)[4].

Scheme S3. Synthetic route to benzocyclobutenone oxime

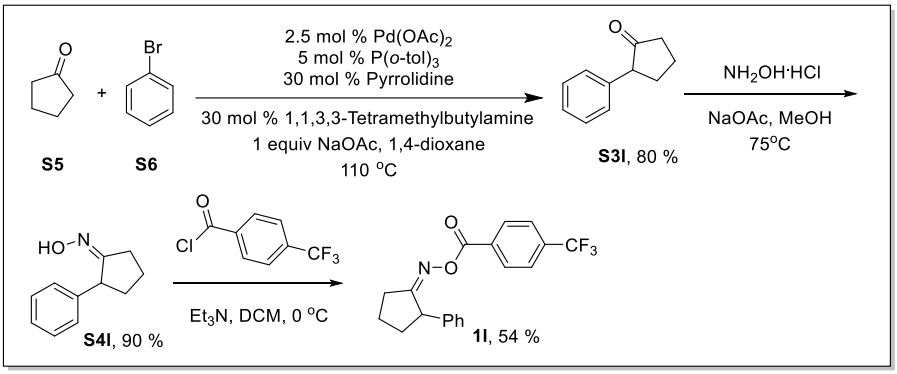


General procedure for the synthesis of 1k

To a mixture of hydroxylamine hydrochloride (1.2 equiv), sodium acetate (1.5 equiv), methanol (30 mL) in a 100-mL two-necked flask was added bicyclo[4.2.0]octa-1(6),2,4-trien-7-one (1.0 equiv) and the mixture was stirred at 75 °C for 12 h. The reaction mixture was cooled to room temperature and then methanol was removed under vacuum and the resulting mixture was extracted with diethyl ether. The organic layer was washed with water and dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude material was subjected to column chromatography to afford bicyclo[4.2.0]octa-1(6),2,4-trien-7-one oxime in 93 % yield[3].

To a mixture of bicyclo[4.2.0]octa-1(6),2,4-trien-7-one oxime (1.0 equiv), triethylamine (1.5 equiv) and DCM (0.5 M) in a 30-mL two-necked flask was added 4-(trifluoromethyl)benzoyl chlorides (1.1 equiv) at 0 °C. After 1 h, a saturated solution of aqueous $NaHCO_3$ (30 mL) was added to the above solution, and the mixture was diluted with DCM. The organic layer was washed with brine (30 mL) and dried over $MgSO_4$. The solvent was removed under vacuum and the residue was subjected to column chromatography on silica gel with EtOAc–petroleum ether as an eluent to give bicyclo[4.2.0]octa-1(6),2,4-trien-7-one *O*-(4-(trifluoromethyl)benzoyl) oxime (**1k**) in 87 % yield[4].

Scheme S4. Synthetic route to 2-phenylcyclopentan-1-one *O*-(4-(trifluoromethyl)benzoyl) oxime



General procedure for the synthesis of 1l

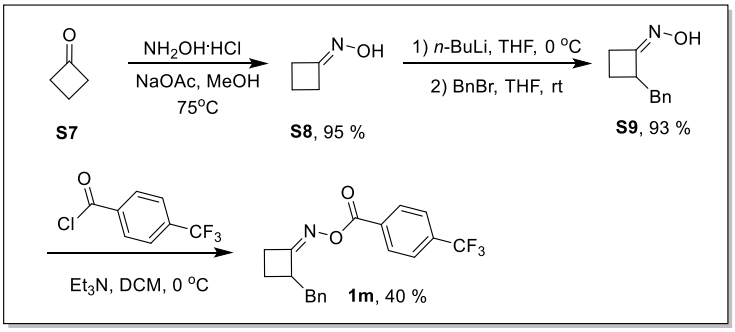
A 100 mL vial was charged with $Pd(OAc)_2$ (0.025 equiv), P(*o*-tol)$_3$ (0.05 equiv), NaOAc (1.0 equiv), cyclopentanones (1.0 equiv), bromobenzene (1.3 equiv), pyrrolidine (0.3 equiv), 1,1,3,3-tetramethylbutylamine (0.3 equiv) and 1,4-dioxane (0.2 M). The vial was sealed with a PTFE lined cap and transferred into a glove box. After opened and purged under N_2 atmosphere for 5 min, the vial was

then sealed again and heated in a pie-block at 110 °C for 12 hours, before cooled to room temperature. The mixture was filtered through a small plug of silica gel and eluted with ethyl acetate. The filtrate was then concentrated under vacuo and further purified by flash column chromatography (petroleum ether/ethyl acetate) to give the 2-phenylcyclopentan-1-one in 80 % yield[5].

To a mixture of hydroxylamine hydrochloride (1.2 equiv), sodium acetate (1.5 equiv), methanol (30 mL) in a 100-mL two-necked flask was added 2-phenylcyclopentan-1-one (1.0 equiv) and the mixture was stirred at 75 °C for 12 h. The reaction mixture was cooled to room temperature and then methanol was removed under vacuum and the resulting mixture was extracted with diethyl ether. The organic layer was washed with water and dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude material was subjected to column chromatography to afford 2-phenylcyclopentan-1-one oxime in 90 % yield[3].

To a mixture of 2-phenylcyclopentan-1-one oxime (1.0 equiv), triethylamine (1.5 equiv) and DCM (0.5 M) in a 30-mL two-necked flask was added 4-(trifluoromethyl)benzoyl chlorides (1.1 equiv) at 0 °C. After 1 h, a saturated solution of aqueous $NaHCO_3$ (30 mL) was added to the above solution, and the mixture was diluted with DCM. The organic layer was washed with brine (30 mL) and dried over $MgSO_4$. The solvent was removed under vacuum and the residue was subjected to column chromatography on silica gel with EtOAc–petroleum ether as an eluent to give 2-phenylcyclopentan-1-one *O*-(4-(trifluoromethyl)benzoyl) oxime (**1l**) in 54 % yield[4].

Scheme S5. Synthetic route to 2-benzylcyclobutan-1-one *O*-(4-(trifluoromethyl)benzoyl) oxime (1m)



General procedure for the synthesis of 1m

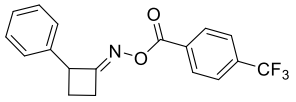
To a mixture of hydroxylamine hydrochloride (1.2 equiv), sodium acetate (1.5 equiv), methanol (30

mL) in a 100-mL two-necked flask was added cyclobutanone (1.0 equiv) and the mixture was stirred at 75 °C for 12 h. The reaction mixture was cooled to room temperature and then methanol was removed under vacuum and the resulting mixture was extracted with diethyl ether. The organic layer was washed with water and dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude material was subjected to column chromatography to afford cyclobutanone oxime in 95 % yield[3].

To the solution of cyclobutanone oxime (548 mg, 6.4 mmol, 1.0 equiv) in THF (0.5 M) was added *n*BuLi (5.2 mL, 13.0 mmol, 2.0 equiv) slowly at 0 °C, then the mixture was continue to stirring for another 15 min at this temperature for the formation of syn dianion. After that, BnBr (766.6 μL, 6.4 mmol, 1.0 equiv) was added dropwise at this temperature, then the mixture was warmed to RT for 2 h. Subsequently, cold water was added to the solution, and the mixture was diluted with EA. The organic layer was washed with water, then dried over Na_2SO_4 and concentrated in vacuum. The residue was purified by column chromatography (EtOAc/petroleum ether) to give 2-benzylcyclobutan-1-one oxime in 93 % yield[6].

To a mixture of 2-phenylcyclopentan-1-one oxime (1.0 equiv), triethylamine (1.5 equiv) and DCM (0.5 M) in a 30-mL two-necked flask was added 4-(trifluoromethyl)benzoyl chlorides (1.1 equiv) at 0 °C. After 1 h, a saturated solution of aqueous $NaHCO_3$ (30 mL) was added to the above solution, and the mixture was diluted with DCM. The organic layer was washed with brine (30 mL) and dried over $MgSO_4$. The solvent was removed under vacuum and the residue was subjected to column chromatography on silica gel with EtOAc–petroleum ether as an eluent to give 2-benzylcyclobutan-1-one *O*-(4-(trifluoromethyl)benzoyl) oxime (**1m**) in 40 % yield[4].

3. Characterization data of oximes 1

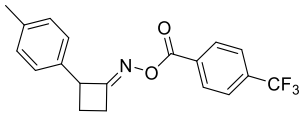


1a

2-phenylcyclobutan-1-one *O*-(4-(trifluoromethyl)benzoyl) oxime (1a)

According to the general procedure, **1a** was prepared from the commercially available benzaldehyde as a white solid: **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.17 (d, *J* = 8.1 Hz, 2H), 7.74 (d, *J* = 8.2 Hz, 2H), 7.44–7.26 (m, 5H), 4.70 (ddd, *J* = 10.0, 7.1, 2.8 Hz, 1H), 3.31–3.07 (m, 2H), 2.65 (dtd, *J* = 11.3, 9.6, 6.1 Hz, 1H), 2.31 (ddt, *J* = 11.2, 9.9, 7.3 Hz, 1H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 171.6, 162.7, 138.5, 134.7 (q,

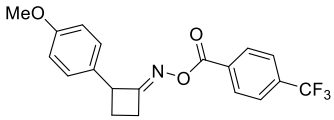
J = 33.3 Hz), 132.4, 130.0, 128.7, 127.2, 127.1, 125.5 (q, *J* = 4.0 Hz), 123.5 (q, *J* = 274.7 Hz), 49.7, 29.6, 23.2. **HRMS m/z (ESI)** calcd for $C_{18}H_{14}F_3NNaO_2$ $(M + Na)^+$ 356.0869, found 356.0859. **M.P.** 113~115 ℃. **TLC:** Rf = 0.32 (petroleum ether / ethyl acetate = 9:1).



1b

2-(p-tolyl)cyclobutan-1-one O-(4-(trifluoromethyl)benzoyl) oxime (1b)

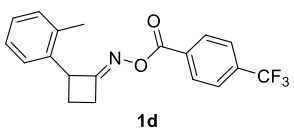
According to the general procedure, **1b** was prepared from the commercially available 4-methylbenzaldehyde as a yellow oil: **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.21–8.13 (m, 2H), 7.73 (d, *J* = 8.2 Hz, 2H), 7.29 (d, *J* = 7.8 Hz, 2H), 7.17 (d, *J* = 7.9 Hz, 2H), 4.66 (ddd, *J* = 10.0, 6.9, 2.9 Hz, 1H), 3.34–3.04 (m, 2H), 2.62 (dtd, *J* = 11.3, 9.7, 6.1 Hz, 1H), 2.34 (s, 3H), 2.33–2.22 (m, 1H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 171.8, 162.7, 136.8, 135.5, 134.7 (q, *J* = 32.3 Hz), 132.4, 130.0, 129.3, 127.0, 125.5 (q, *J* = 4.0 Hz), 123.5 (q, *J* = 273.7 Hz), 49.4, 29.5, 23.2, 21.1. **HRMS m/z (ESI)** calcd for $C_{19}H_{15}F_3NO_2$ $(M - H)^-$ 346.1060, found 346.1056. **TLC:** Rf = 0.26 (petroleum ether / ethyl acetate = 9:1).



1c

2-(4-methoxyphenyl)cyclobutan-1-one O-(4-(trifluoromethyl)benzoyl) oxime (1c)

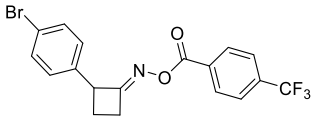
According to the general procedure, **1c** was prepared from the commercially available 4-methoxybenzaldehyde as a yellow oil: **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.63–7.40 (m, 4H), 7.22 (d, *J* = 8.7 Hz, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 4.50 (ddd, *J* = 10.2, 7.4, 2.8 Hz, 1H), 3.77 (s, 3H), 3.28–3.08 (m, 2H), 2.65–2.49 (m, 1H), 2.23–2.08 (m, 1H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 170.5, 162.5, 158.8, 134.3 (q, *J* = 32.3 Hz), 131.9, 131.0, 129.8, 128.4, 125.1 (q, *J* = 3.0 Hz), 123.4 (q, *J* = 273.7 Hz), 114.1, 55.2, 50.8, 29.1, 24.3. **HRMS m/z (ESI)** calcd for $C_{19}H_{15}F_3NO_3$ $(M - H)^-$ 362.1010, found 362.1015. **TLC:** Rf = 0.17 (petroleum ether / ethyl acetate = 9:1).



1d

2-(*o*-tolyl)cyclobutan-1-one *O*-(4-(trifluoromethyl)benzoyl) oxime (1d)

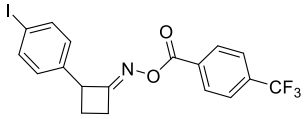
According to the general procedure, **1d** was prepared from the commercially available 2-methylbenzaldehyde as a yellow oil: **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.19 (d, *J* = 8.1 Hz, 2H), 7.74 (d, *J* = 8.2 Hz, 2H), 7.60–7.53 (m, 1H), 7.27–7.13 (m, 3H), 4.80 (ddd, *J* = 10.0, 7.1, 3.0 Hz, 1H), 3.33–3.03 (m, 2H), 2.65 (dtd, *J* = 11.2, 9.6, 6.1 Hz, 1H), 2.33 (s, 3H), 2.22–2.05 (m, 1H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 171.6, 162.7, 136.9, 135.5, 134.7 (q, *J* = 33.3 Hz), 132.4, 130.4, 130.0, 127.2, 126.2, 126.1, 125.5 (q, *J* = 4.0 Hz), 123.5 (q, *J* = 243.4 Hz), 47.9, 29.3, 23.4, 19.5. **HRMS m/z (ESI)** calcd for $C_{19}H_{16}F_3NNaO_2$ $(M + Na)^+$ 370.1025, found 370.1015. **TLC:** Rf = 0.39 (petroleum ether / ethyl acetate = 9:1).



1e

2-(4-bromophenyl)cyclobutan-1-one O-(4-(trifluoromethyl)benzoyl) oxime (1e)

According to the general procedure, **1e** was prepared from the commercially available 4-bromobenzaldehyde as a yellow solid: **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.16 (d, *J* = 8.1 Hz, 2H), 7.73 (d, *J* = 8.3 Hz, 2H), 7.47 (d, *J* = 8.4 Hz, 2H), 7.29 (d, *J* = 8.2 Hz, 2H), 4.64 (ddd, *J* = 10.1, 7.1, 2.9 Hz, 1H), 3.37–3.06 (m, 2H), 2.64 (dtd, *J* = 11.4, 9.6, 6.1 Hz, 1H), 2.38–2.17 (m, 1H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 170.9, 162.6, 137.4, 134.7 (q, *J* = 33.3 Hz), 132.3, 131.8, 130.0, 128.8, 125.5 (q, *J* = 3.0 Hz), 123.5 (q, *J* = 274.7 Hz), 121.1, 49.0, 29.5, 23.2. **HRMS m/z (ESI)** calcd for $C_{18}H_{13}BrF_3NNaO_2$ $(M + Na)^+$ 433.9974, 435.9954, found 433.9962, 435.9941. **M.P.** 112~115 ℃. **TLC:** Rf = 0.22 (petroleum ether / ethyl acetate = 9:1).

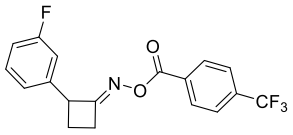


1f

2-(4-iodophenyl)cyclobutan-1-one O-(4-(trifluoromethyl)benzoyl) oxime (1f)

According to the general procedure, **1f** was prepared from the commercially available 4-iodobenzaldehyde as a yellow solid: **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.16 (d, J = 8.1 Hz, 2H), 7.73 (d, *J* = 8.2 Hz, 2H), 7.68 (d, *J* = 8.4 Hz, 2H), 7.16 (d, *J* = 8.0 Hz, 2H), 4.63 (ddd, *J* = 10.0, 7.1, 2.8 Hz, 1H), 3.31–3.05 (m, 2H), 2.64 (dtd, *J* = 11.4, 9.6, 6.1 Hz, 1H), 2.25 (ddt, *J* = 11.4, 10.0, 7.4 Hz, 1H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 170.9, 162.6, 138.1, 137.8, 134.8 (q, *J* = 32.3 Hz), 132.3, 130.0, 129.1, 125.6 (q, *J* = 4.0 Hz), 123.5 (q, *J* = 273.7 Hz), 92.6, 49.1, 29.6, 23.1. **HRMS m/z (ESI)** calcd for $C_{18}H_{13}F_3INNaO_2$

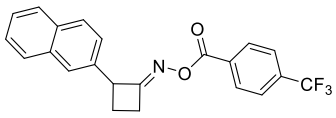
$(M + Na)^+$ 481.9835, found 481.9826. **M.P.** 109~111 ℃. **TLC:** Rf = 0.11 (petroleum ether / ethyl acetate = 9:1).



1g

2-(3-fluorophenyl)cyclobutan-1-one O-(4-(trifluoromethyl)benzoyl) oxime (1g)

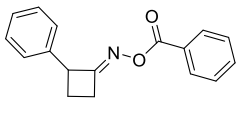
According to the general procedure, **1g** was prepared from the commercially available 3-fluorobenzaldehyde as a white solid: **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.62–7.51 (m, 4H), 7.33 (td, *J* = 7.9, 6.0 Hz, 1H), 7.10 (d, *J* = 7.7 Hz, 1H), 7.06–6.94 (m, 2H), 4.56 (ddd, *J* = 10.2, 7.2, 2.8 Hz, 1H), 3.34–3.13 (m, 2H), 2.64 (dtd, *J* = 11.5, 9.7, 6.2 Hz, 1H), 2.21 (ddt, *J* = 11.5, 9.9, 7.6 Hz, 1H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 169.1, 163.1 (d, *J* = 247.4 Hz), 162.4, 141.3 (d, *J* = 7.1 Hz), 134.6 (d, *J* = 33.3 Hz), 131.8, 130.4 (d, *J* = 9.1 Hz), 129.8, 125.3 (q, *J* = 4.0 Hz), 123.5 (q, *J* = 273.7 Hz), 123.0 (d, *J* = 3.0 Hz), 114.5 (d, *J* = 18.2 Hz), 114.3 (d, *J* = 18.2 Hz), 50.9 (d, *J* = 2.0 Hz), 29.4, 24.2. **HRMS m/z (ESI)** calcd for $C_{18}H_{13}F_4NNaO_2$ $(M + Na)^+$ 374.0775, found 374.0767. **M.P.** 108~110 ℃. **TLC:** Rf = 0.26 (petroleum ether / ethyl acetate = 9:1).



1h

2-(naphthalen-2-yl)cyclobutan-1-one *O*-(4-(trifluoromethyl)benzoyl) oxime (1h)

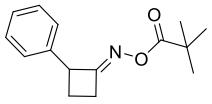
According to the general procedure, **1h** was prepared from the commercially available 2-naphthaldehyde as a white solid: **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.19 (d, *J* = 8.1 Hz, 2H), 7.84 (ddd, *J* = 12.3, 8.4, 3.6 Hz, 4H), 7.74 (d, *J* = 8.2 Hz, 2H), 7.59–7.38 (m, 3H), 4.86 (ddd, *J* = 10.0, 6.8, 2.9 Hz, 1H), 3.41–3.13 (m, 2H), 2.71 (dtd, *J* = 11.3, 9.7, 6.1 Hz, 1H), 2.40 (ddt, *J* = 11.2, 9.9, 7.1 Hz, 1H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 171.4, 162.7, 135.8, 134.7 (q, *J* = 32.3 Hz), 133.3, 132.6, 132.4, 130.0, 128.6, 127.9, 127.6, 126.3, 125.9, 125.6 (q, *J* = 3.0 Hz), 125.3, 123.5 (d, *J* = 273.7 Hz), 49.8, 29.6, 23.2. **HRMS m/z (ESI)** calcd for $C_{22}H_{16}F_3NNaO_2$ $(M + Na)^+$ 406.1025, found 406.1024. **M.P.** 132~134 ℃. **TLC:** Rf = 0.29 (petroleum ether / ethyl acetate = 9:1).



1i

2-phenylcyclobutan-1-one *O*-benzoyl oxime (1i)

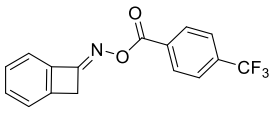
According to the general procedure, **1i** was prepared from 2-phenylcyclobutan-1-one oxime and benzoyl chloride as a yellow oil: **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.14–8.01 (m, 2H), 7.62–7.56 (m, 1H), 7.51–7.44 (m, 2H), 7.44–7.40 (m, 2H), 7.39–7.33 (m, 2H), 7.28–7.24 (m, 1H), 4.69 (ddd, *J* = 10.0, 7.0, 3.0 Hz, 1H), 3.34–3.07 (m, 2H), 2.63 (ddd, *J* = 9.6, 6.2, 1.6 Hz, 1H), 2.38–2.20 (m, 1H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 170.8, 163.9, 138.7, 133.2, 129.6, 129.1, 128.7, 128.5, 127.1, 127.1, 49.6, 29.6, 23.3. **HRMS m/z (ESI)** calcd for $C_{17}H_{15}NNaO_2$ $(M + Na)^+$ 288.0995, found 288.0990. **TLC:** Rf = 0.29 (petroleum ether / ethyl acetate = 9:1).



1j

2-phenylcyclobutan-1-one O-pivaloyl oxime (1j)

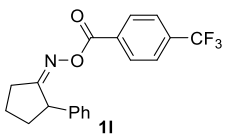
According to the general procedure, **1j** was prepared 2-phenylcyclobutan-1-one oxime and pivaloyl chloride as a yellow oil: **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.42–7.30 (m, 4H), 7.26–7.20 (m, 1H), 4.61 (ddd, *J* = 10.0, 7.0, 2.7 Hz, 1H), 3.18–2.94 (m, 2H), 2.67–2.49 (m, 1H), 2.23 (ddt, *J* = 11.3, 10.0, 7.4 Hz, 1H), 1.28 (s, 9H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 175.2, 170.4, 138.7, 128.6, 127.1, 127.0, 49.6, 38.8, 29.3, 27.3, 23.1. **HRMS m/z (ESI)** calcd for $C_{15}H_{19}NNaO_2$ $(M + Na)^+$ 268.1308, found 268.1299. **TLC:** Rf = 0.16 (petroleum ether / ethyl acetate = 9:1).



1k

bicyclo[4.2.0]octa-1(6),2,4-trien-7-one O-(4-(trifluoromethyl)benzoyl) oxime (1k)

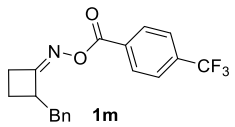
According to the general procedure, **1k** was prepared from the commercially available compound bicyclo[4.2.0]octa-1(6),2,4-trien-7-one as a white solid: **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.27 (d, *J* = 8.1 Hz, 2H), 7.79 (d, *J* = 8.1 Hz, 2H), 7.62–7.49 (m, 2H), 7.42 (dd, *J* = 9.8, 7.3 Hz, 2H), 4.07 (s, 2H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 162.9, 158.7, 146.1, 138.1, 134.8 (q, *J* = 33.3 Hz), 133.9, 132.2, 130.0, 128.8, 125.7 (q, *J* = 4.0 Hz), 123.6, 123.5 (q, *J* = 273.7 Hz), 123.4, 39.8. **HRMS m/z (ESI)** calcd for $C_{16}H_{10}F_3NNaO_2$ $(M + Na)^+$ 328.0556, found 328.0547. **M.P.** 136~140 ℃. **TLC:** Rf = 0.25 (petroleum ether / ethyl acetate = 9:1).



1l

2-phenylcyclopentan-1-one O-(4-(trifluoromethyl)benzoyl) oxime (1l)

According to the synthestic procedure, **1l** was prepared from 2-phenylcyclopentan-1-one as a white solid: **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.17 (d, *J* = 8.1 Hz, 2H), 7.73 (d, *J* = 8.2 Hz, 2H), 7.39–7.29 (m, 4H), 7.25 (dt, *J* = 9.2, 2.9 Hz, 1H), 4.07 (td, *J* = 7.6, 1.6 Hz, 1H), 3.04–2.89 (m, 1H), 2.89–2.73 (m, 1H), 2.41–2.24 (m, 1H), 2.04 (dddd, *J* = 16.5, 14.6, 8.1, 3.7 Hz, 2H), 1.96–1.80 (m, 1H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 178.2, 162.6, 140.1, 134.6 (q, *J* = 32.3 Hz), 132.5, 129.9, 128.6, 127.8, 126.9, 125.5 (q, *J* = 4.0 Hz), 123.5 (q, *J* = 273.7 Hz), 49.2, 34.7, 30.0, 22.5. **HRMS m/z (ESI)** calcd for $C_{19}H_{16}F_3NNaO_2$ $(M + Na)^+$ 370.1025, found 370.1016. **M.P.** 96~99 ℃. **TLC:** Rf = 0.38 (petroleum ether / ethyl acetate = 9:1).



1m

2-benzylcyclobutan-1-one O-(4-(trifluoromethyl)benzoyl) oxime (1m)

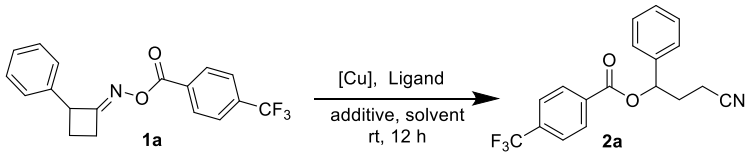
According to the synthestic procedure, **1m** was prepared from 2-benzylcyclobutan-1-one oxime as a white solid: **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.16 (d, *J* = 8.1 Hz, 2H), 7.73 (d, *J* = 8.2 Hz, 2H), 7.35–7.29 (m, 2H), 7.26–7.21 (m, 3H), 3.72 (ddq, *J* = 9.3, 4.5, 2.2 Hz, 1H), 3.28 (dd, *J* = 14.1, 4.9 Hz, 1H), 3.12–2.88 (m, 3H), 2.24–2.10 (m, 1H), 1.90 (ddt, *J* = 11.4, 9.6, 7.1 Hz, 1H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 172.3, 162.7, 138.3, 134.5 (q, *J* = 32.3 Hz), 132.3, 129.9, 128.7, 128.4, 126.4, 125.4 (q, *J* = 3.0 Hz), 123.4 (q, *J* = 273.7 Hz), 46.3, 37.7, 28.9, 20.4. **HRMS m/z (ESI)** calcd for $C_{19}H_{15}F_3NO_2$ $(M - H)^-$ 346.1060, found 346.1060. **M.P.** 123~126 ℃. **TLC:** Rf = 0.32 (petroleum ether / ethyl acetate = 9:1).

4. Optimization of reaction conditions

General procedure for the C-cyanoacyloxylation of cyclobutanone oximes monitored by ^{1}H NMR

To a 25 mL Schlenk tube under argon were added CuBr (0.9 mg, 0.006 mmol, 10 mol %), TBAB (3.9 mg, 0.012 mmol, 20 mol %), **1a** (20.0 mg, 0.06 mmol, 1.0 equiv), PMDTA (1.3 μL, 0.006 mmol, 10 mol %) and DMF (1.0 mL). Then the mixture was stirred 12 h at room tempreture. The solvent was removed under vacuum and the final product **2a** was monitored by ^{1}H NMR spectroscopy using benzaldehyde as the internal standard.

Table S5. Optimization of reaction conditions for the copper-catalyzed C-cyanoacyloxylation of **1a**.[a]



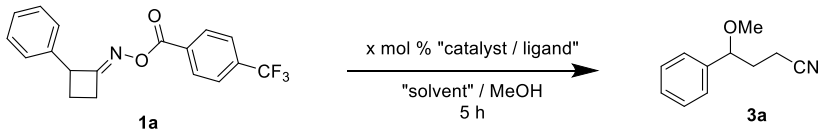
entry	solvent	additive	ligand	[Cu]	yield[d]
1	Tol	none	PMDTA	CuI	42 %
2	Tol	none	DMEDA	CuI	13 %
3	Tol	none	TMEDA	CuI	3 %
4	Tol	none	none	CuI	none
5	DCM	none	PMDTA	CuI	25 %
6	THF	none	PMDTA	CuI	25 %
7	DMF	none	PMDTA	CuI	46 %
8	DMF	TBAI	PMDTA	CuI	53 %
9	DMF	TBAC	PMDTA	CuI	46 %
10	DMF	TBAB	PMDTA	CuI	69 %
11	DMF	TBAB	PMDTA	CuCl	59 %
12	DMF	TBAB	PMDTA	CuOAc	33 %
13	DMF	TBAB	PMDTA	$CuCl_2·H_2O$	61 %
14[b]	DMF	TBAB	PMDTA	CuBr	78 % (75 %)
15[c]	DMF	TBAB	PMDTA	CuBr	59 %

[a] Conditions: **1a** (0.06 mmol), [Cu] (20 mol %), ligand (20 mol %), additive (20 mol %), solvent (1.0 mL), room temperature, 12 h, under Ar. [b] Conditions: **1a** (0.06 mmol), CuBr (10 mol %), PMDTA (10 mol %), TBAB (20 mol %), solvent (1.0 mL), room temperature, 12 h, under Ar. [c] Conditions: **1a** (0.06 mmol), CuBr (5 mol %), PMDTA (5 mol %), TBAB (20 mol %), solvent (1.0 mL), room temperature, 12 h, under Ar. [d] Yields determined by ^{1}H NMR with benzaldehyde as the internal standard and isolated yields in parenthesis.

General procedure for the C-cyanoalkoxylation of cyclobutanone oximes detected by ^{1}H NMR

To a 25 mL Schlenk tube under argon were added $Cu(MeCN)_4PF_6$ (1.1 mg, 0.003 mmol, 5 mol %), *t*-BuXPhos (1.3 mg, 0.003 mmol, 5 mol %), and MeOH (0.5 mL). The suspension was stirred 15 min at room tempreture. To this was added a solution of **1a** (20 mg, 0.06 mmol, 1.0 equiv) in MeOH (0.5 mL). Then the mixture was stirred 5 h at 60 °C. The solvent was removed under vacuum and the final product **3a** was detected by ^{1}H NMR spectroscopy using benzaldehyde as the internal standard.

Table S6. Optimization of reaction conditions for the copper-catalyzed C-cyanoalkoxylation of **1a**.[a]



1a **3a**

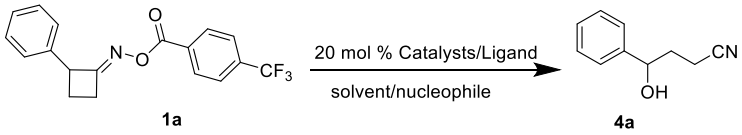
entry	catalyst	ligand	temperature	solvent	yield	conversion
1	CuBr	none	r.t.	DMF/MeOH (9/1)	0 %	0 %
2	CuOAc	none	r.t.	DMF/MeOH (9/1)	0 %	0 %
3	$Cu(MeCN)_4PF_6$	none	r.t.	DMF/MeOH (9/1)	0 %	0 %
4	$Cu(MeCN)_4PF_6$	none	60 °C	DMF/MeOH (9/1)	0 %	100 %
5	$Cu(MeCN)_4PF_6$	Xantphos	60 °C	DMF/MeOH (9/1)	11 %	100 %
6	$Cu(MeCN)_4PF_6$	Brettphos	60 °C	DMF/MeOH (9/1)	15 %	100 %
7	$Cu(MeCN)_4PF_6$	*t*-BuXphos	60 °C	DMF/MeOH (9/1)	18 %	100 %
8	$Cu(MeCN)_4PF_6$	*t*-BuXphos	60 °C	MeOH	92 %	100 %
9[b]	$Cu(MeCN)_4PF_6$	*t*-BuXphos	60 °C	MeOH	92 %	100 %
10[c]	$Cu(MeCN)_4PF_6$	*t*-BuXphos	60 °C	MeOH	95 % (92 %)	100 %

[a] Conditions: **1a** (0.06 mmol), [Cu] (20 mol %), ligand (20 mol %), DMF/MeOH (1.0 mL/0.11 mL), under Ar. [b] Conditions: **1a** (0.06 mmol), $Cu(MeCN)_4PF_6$ (10 mol %), *t*-BuXphos (10 mol %), MeOH (1.0 mL), 60 °C, under Ar. [c] Conditions: **1a** (0.06 mmol), $Cu(MeCN)_4PF_6$ (5 mol %), *t*-BuXphos (5 mol %), MeOH (1.0 mL), 60 °C, under Ar. [d] Yields determined by ^{1}H NMR with benzaldehyde as the internal standard and isolated yields in parenthesis.

General procedure for the C-cyanohydroxylation of cyclobutanone oximes detected by ^{1}H NMR

To a 25 mL Schlenk tube under argon were added $Cu(MeCN)_4PF_6$ (4.5 mg, 0.012 mmol, 20 mol %), *t*-BuXPhos (10.2 mg, 0.024 mmol , 40 mol %), and DMF (0.5 mL). The suspension was stirred 15 min at room tempreture. To this was added a solution of **1a** (20 mg, 0.06 mmol, 1.0 equiv) in DMF (0.5 mL) and MeOH (0.11 mL). Then the mixture was stirred 6 h at 60 °C. The solvent was removed under vacuum and the final product **4a** was detected by ^{1}H NMR spectroscopy using benzaldehyde as the internal standard.

Table S7. Optimization of reaction conditions for the copper-catalyzed C-cyanohydroxylation of **1a**.[a]

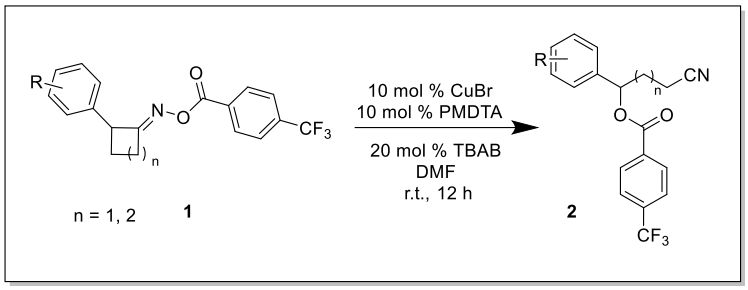


1a **4a**

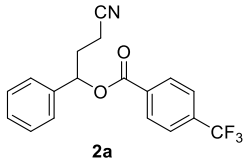
entry	Catalysts/Ligand	solvent/nucleophile	temperature	time	yield[f]
1	$Cu(MeCN)_4PF_6$/ Xantphos	DMF/MeOH (9/1)	60 °C	6 h	46 %
2	$Cu(MeCN)_4PF_6$/ Brettphos	DMF/MeOH (9/1)	60 °C	6 h	54 %
3	$Cu(MeCN)_4PF_6$/ *t*-BuXphos	DMF/MeOH (9/1)	60 °C.	6 h	62 %
4	$Cu(MeCN)_4PF_6$/ Ruphos	DMF/MeOH (9/1)	60 °C	6 h	42 %
5	$Cu(MeCN)_4PF_6$/ Dpephos	DMF/MeOH (9/1)	60 °C	6 h	59 %
6[b]	$Cu(MeCN)_4PF_6$/ *t*-BuXphos	DMF/MeOH (9/1)	60 °C	6 h	68 % (66 %)
7[c]	$Cu(MeCN)_4PF_6$/ *t*-BuXphos	DMF/MeOH (9/1)	60 °C	6 h	44 %
8[b]	$Cu(MeCN)_4PF_6$/ *t*-BuXphos	DMF/EtOH (9/1)	60 °C	6 h	55 %
9[b]	$Cu(MeCN)_4PF_6$/ *t*-BuXphos	DMF/*i*-PrOH (9/1)	60 °C	6 h	36 %
10[b]	$Cu(MeCN)_4PF_6$/ *t*-BuXphos	DMF/$BnNH_2$ (9/1)	60 °C	6 h	26 %
11[b]	$Cu(MeCN)_4PF_6$/ *t*-BuXphos	MeCN/MeOH (9/1)	60 °C	12 h	0 %
12[b]	$Cu(MeCN)_4PF_6$/ *t*-BuXphos	THF/MeOH (9/1)	60 °C	12 h	0 %
13[b]	$Cu(MeCN)_4PF_6$/ *t*-BuXphos	Tol/MeOH (9/1)	60 °C	12 h	0 %
14[b]	$Cu(MeCN)_4PF_6$/ *t*-BuXphos	DMA/MeOH (9/1)	60 °C	6 h	54 %
15[b]	$Cu(MeCN)_4PF_6$/ *t*-BuXphos	DMSO/MeOH (9/1)	60 °C	6 h	53 %
16[b]	$Cu(MeCN)_4PF_6$/ *t*-BuXphos	DMF/MeOH (4.5/1)	60 °C	6 h	42 %
17[b]	$Cu(MeCN)_4PF_6$/ *t*-BuXphos	DMF/MeOH (18/1)	60 °C	6 h	46 %
18[d]	$Ir(ppy)_3$	DMF/MeOH (9/1)	r.t.	2 h	75 % (72 %)
19[e]	$[Ir(1,5\text{-cod})Cl]_2$	DMF/MeOH (9/1)	r.t.	2 h	45 %

[a] Conditions: **1a** (0.06 mmol), [Cu] (20 mol %), ligand (20 mol %), DMF/MeOH (1.0 mL/0.11 mL), room temperature, under Ar. [b] Conditions: **1a** (0.06 mmol), $Cu(MeCN)_4PF_6$ (20 mol %), *t*-BuXphos (40 mol %), DMF/MeOH (1.0 mL/0.11 mL), 60 °C, 6 h, under Ar. [c] Conditions: **1a** (0.06 mmol), $Cu(MeCN)_4PF_6$ (10 mol %), *t*-BuXphos (20 mol %), DMF/MeOH (1.0 mL/0.11 mL), 60 °C, 6 h, under Ar. [d] Conditions: **1a** (0.06 mmol), $Ir(ppy)_3$ (2 mol %), DMF/MeOH (1.0 mL/0.11 mL), room temperature, 2 h, under Ar. [e] Conditions: **1a** (0.06 mmol), $[Ir(1,5\text{-cod})Cl]_2$ (2 mol %), DMF/MeOH (1.0 mL/0.11 mL), room temperature, 2 h, under Ar. [f] Yields determined by ^1H NMR with benzaldehyde as the internal standard and isolated yields in parenthesis.

5. General procedures and characterization of γ-carboxylated alkyl nitriles



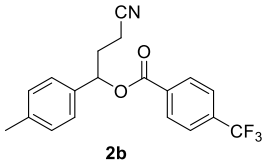
General procedure A: To a 25 mL Schlenk tube under argon were added CuBr (4.3 mg, 0.03 mmol, 10 mol %), TBAB (19.3 mg, 0.06 mmol, 20 mol %), cyclobutanone oxime derivatives **1** (0.3 mmol, 1.0 equiv), PMDTA (6.3 μL, 0.03 mmol, 10 mol %) and DMF (5.0 mL). Then the mixture was stirred 12 h at room tempreture. The solvent was removed under vacuum and the residue was purified by column chromatography (petroleum ether/ethyl acetate = 20/1) to give ester **2**.



2a

3-cyano-1-phenylpropyl 4-(trifluoromethyl)benzoate (2a)

According to the general procedure, **2a** was prepared from **1a** as a white solid (74.9 mg, 75 %): **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.21 (d, *J* = 8.1 Hz, 2H), 7.73 (d, *J* = 8.2 Hz, 2H), 7.49–7.30 (m, 5H), 6.17–6.07 (m, 1H), 2.56–2.19 (m, 4H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 164.4, 138.2, 134.8 (q, *J* = 32.3 Hz), 132.9, 130.2, 129.0, 128.9, 126.2, 125.5 (q, *J* = 3.0 Hz), 123.5 (q, *J* = 273.7 Hz), 118.7, 75.4, 32.0, 13.7. **HRMS m/z (ESI)** calcd for $C_{18}H_{14}F_3NNaO_2$ $(M + Na)^+$ 356.0869, found 356.0857. **M.P.** 91~93 ℃. **TLC:** Rf = 0.32 (petroleum ether / ethyl acetate = 9:1).

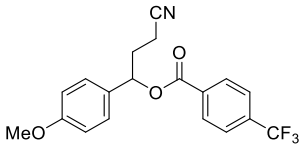


2b

3-cyano-1-(*p*-tolyl)propyl 4-(trifluoromethyl)benzoate (2b)

According to the general procedure, **2b** was prepared from **1b** as a white solid (71.0 mg, 68 %): **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.20 (d, *J* = 8.1 Hz, 2H), 7.72 (d, *J* = 8.2 Hz, 2H), 7.30 (d, *J* = 8.1 Hz, 2H), 7.20 (d, *J* = 7.9 Hz, 2H), 6.15–6.01 (m, 1H), 2.52–2.22 (m, 7H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 164.4, 138.8, 135.2, 134.8 (q, *J* = 33.3 Hz), 133.0, 130.1, 129.7, 126.2, 125.5 (q, *J* = 3.0 Hz), 123.5 (q, *J* =273.7

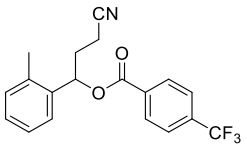
Hz), 118.8, 75.4, 31.9, 21.2, 13.8. **HRMS m/z (ESI)** calcd for $C_{19}H_{16}F_3NNaO_2$ $(M + Na)^+$ 370.1025, found 370.1020. **M.P.** 99~101 ℃. **TLC:** Rf = 0.26 (petroleum ether / ethyl acetate = 9:1).



2c

3-cyano-1-(*p*-tolyl)propyl 4-(trifluoromethyl)benzoate (2c)

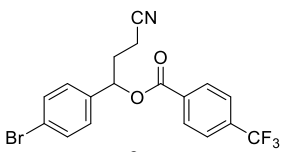
According to the general procedure, **2c** was prepared from **1c** as a white solid (68.6 mg, 63 %): **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.19 (d, *J* = 8.2 Hz, 2H), 7.71 (d, *J* = 8.2 Hz, 2H), 7.35 (d, *J* = 8.7 Hz, 2H), 6.92 (d, *J* = 8.7 Hz, 2H), 6.13–5.98 (m, 1H), 3.80 (s, 3H), 2.53–2.18 (m, 4H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 164.4, 159.9, 134.7 (q, *J* = 33.3 Hz), 133.0, 130.1, 130.1, 127.7, 125.5 (q, *J* = 3.0 Hz), 123.5 (q, *J* = 273.7 Hz), 118.8, 114.3, 75.2, 55.3, 31.8, 13.8. **HRMS m/z (ESI)** calcd for $C_{19}H_{16}F_3NNaO_3$ $(M + Na)^+$ 386.0974, found 386.0966. **M.P.** 69~72 ℃. **TLC:** Rf = 0.17 (petroleum ether / ethyl acetate = 9:1).



2d

3-cyano-1-(*o*-tolyl)propyl 4-(trifluoromethyl)benzoate (2d)

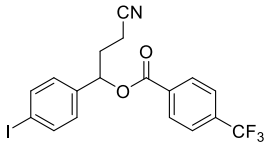
According to the general procedure, **2d** was prepared from **1d** as a yellow oil (82.5 mg, 79 %): **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.21 (d, *J* = 8.1 Hz, 2H), 7.72 (d, *J* = 8.2 Hz, 2H), 7.39 (dd, *J* = 6.1, 2.9 Hz, 1H), 7.31–7.14 (m, 3H), 6.31 (dd, *J* = 8.1, 4.7 Hz, 1H), 2.55–2.44 (m, 5H), 2.44–2.34 (m, 1H), 2.32–2.21 (m, 1H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 164.4, 136.8, 135.0, 134.7 (q, *J* = 33.3 Hz), 132.9, 130.9, 130.1, 128.5, 126.6, 125.5 (q, *J* = 4.0 Hz), 125.3, 123.5 (q, *J* = 274.7 Hz), 118.8, 72.4, 31.3, 19.1, 13.9. **HRMS m/z (ESI)** calcd for $C_{19}H_{16}F_3NNaO_2$ $(M + Na)^+$ 370.1025, found 370.1017. **TLC:** Rf = 0.27 (petroleum ether / ethyl acetate = 9:1).



2e

1-(4-bromophenyl)-3-cyanopropyl 4-(trifluoromethyl)benzoate (2e)

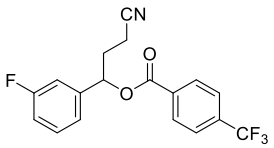
According to the general procedure, **2e** was prepared from **1e** as a white solid (68.0 mg, 55 %): **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.19 (d, *J* = 8.1 Hz, 2H), 7.73 (d, *J* = 8.2 Hz, 2H), 7.57–7.47 (m, 2H), 7.35–7.27 (m, 2H), 6.05 (dd, *J* = 7.7, 5.0 Hz, 1H), 2.61–2.13 (m, 4H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 164.3, 137.3, 134.9 (q, *J* = 32.3 Hz), 132.6, 132.2, 130.1, 127.9, 125.6 (q, J = 4.0 Hz), 123.5 (d, J = 273.7 Hz), 122.9, 118.5, 74.7, 31.8, 13.8. **HRMS m/z (ESI)** calcd for $C_{18}H_{13}BrF_3NNaO_2$ $(M + Na)^+$ 433.9974, 435.9954, found 433.9973, 435.9951. **M.P.** 92~95 ℃. **TLC:** Rf = 0.14 (petroleum ether / ethyl acetate = 9:1).



2f

3-cyano-1-(4-iodophenyl)propyl 4-(trifluoromethyl)benzoate (2f)

According to the general procedure, **2f** was prepared from **1f** as a white solid (70.2 mg, 51 %): **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.19 (d, *J* = 8.1 Hz, 2H), 7.85–7.67 (m, 4H), 7.16 (d, *J* = 8.3 Hz, 2H), 6.04 (dd, *J* = 7.7, 5.0 Hz, 1H), 2.63–2.13 (m, 4H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 164.3, 138.1, 137.9, 134.9 (q, *J* = 32.3 Hz), 132.6, 130.2, 128.0, 125.6 (q, *J* = 4.0 Hz), 123.5 (d, *J* = 273.7 Hz), 118.5, 94.6, 74.8, 31.8, 13.8. **HRMS m/z (ESI)** calcd for $C_{18}H_{13}F_3INNaO_2$ $(M + Na)^+$ 481.9835, found 481.9831. **M.P.** 107~110 ℃. **TLC:** Rf = 0.11 (petroleum ether / ethyl acetate = 9:1).

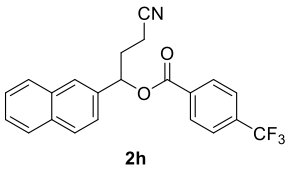


2g

3-cyano-1-(3-fluorophenyl)propyl 4-(trifluoromethyl)benzoate (2g)

According to the general procedure, **2g** was prepared from **1g** as a white solid (56.9 mg, 54 %): **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.21 (dt, *J* = 7.7, 0.9 Hz, 2H), 7.74 (d, *J* = 8.3 Hz, 2H), 7.38 (td, *J* = 8.0, 5.7 Hz, 1H), 7.20 (dt, *J* = 7.9, 1.3 Hz, 1H), 7.12 (dt, *J* = 9.4, 2.1 Hz, 1H), 7.05 (tdd, *J* = 8.4, 2.6, 1.0 Hz, 1H), 6.10 (td, *J* = 5.0, 2.8 Hz, 1H), 2.60–2.21 (m, 4H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 164.3, 161.8, 140.7 (d, *J* = 7.1 Hz), 135.0 (q, *J* = 32.3 Hz), 132.6, 130.7 (d, *J* = 8.1 Hz), 130.2, 125.6 (q, *J* = 4.0 Hz), 123.5 (q, *J* = 273.7 Hz), 121.8 (d, *J* = 3.0 Hz), 118.5, 115.9 (d, *J* = 21.2 Hz), 113.1 (d, *J* = 23.2 Hz), 74.6 (d, *J*

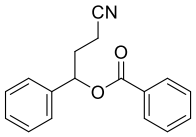
= 2.0 Hz), 32.0, 13.7. **HRMS m/z (ESI)** calcd for $C_{18}H_{13}F_4NNaO_2$ $(M + Na)^+$ 374.0775, found 374.0769. **M.P.** 60~62 ℃. **TLC:** Rf = 0.19 (petroleum ether / ethyl acetate = 9:1).



2h

3-cyano-1-(naphthalen-2-yl)propyl 4-(trifluoromethyl)benzoate (2h)

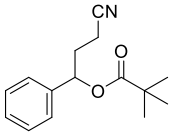
According to the general procedure, **2h** was prepared from **1h** as a white solid (57.5 mg, 50 %): **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.24 (d, *J* = 8.2 Hz, 2H), 7.96–7.82 (m, 4H), 7.74 (d, *J* = 8.2 Hz, 2H), 7.57–7.47 (m, 3H), 6.28 (dd, *J* = 7.2, 4.9 Hz, 1H), 2.63–2.31 (m, 4H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 164.4, 135.4, 134.8 (q, *J* = 32.3 Hz), 133.4, 133.1, 132.9, 130.2, 129.1, 128.1, 127.7, 126.7, 126.7, 125.8, 125.6 (q, J = 3.0 Hz), 123.5 (q, J = 273.7 Hz), 123.3, 118.7, 75.6, 31.9, 13.8. **HRMS m/z (ESI)** calcd for $C_{22}H_{16}F_3NNaO_2$ $(M + Na)^+$ 406.1025, found 406.1023. **M.P.** 104~108 ℃. **TLC:** Rf = 0.22 (petroleum ether / ethyl acetate = 9:1).



2i

3-cyano-1-phenylpropyl benzoate (2i)

According to the general procedure, **2i** was prepared from **1i** as a yellow solid (47.7 mg, 60 %): **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.10 (d, *J* = 7.6 Hz, 2H), 7.59 (t, *J* = 7.4 Hz, 1H), 7.53–7.29 (m, 7H), 6.09 (t, *J* = 6.1 Hz, 1H), 2.56–2.17 (m, 4H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 165.5, 138.6, 133.3, 129.7, 129.7, 128.9, 128.6, 128.5, 126.1, 118.8, 74.5, 32.2, 13.7. **HRMS m/z (ESI)** calcd for $C_{17}H_{15}NNaO_2$ $(M + Na)^+$ 288.0995, found 288.0990. **M.P.** 70~72 ℃. **TLC:** Rf = 0.21 (petroleum ether / ethyl acetate = 9:1).

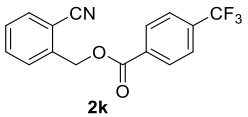


2j

3-cyano-1-phenylpropyl pivalate (2j)

According to the general procedure, **2j** was prepared from **1j** as a white solid (24.3 mg, 33 %): **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.42–7.27 (m, 5H), 5.79 (dd, *J* = 7.7, 5.2 Hz, 1H), 2.45–2.08 (m, 4H), 1.23 (s, 9H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 177.2, 139.0, 128.8, 128.4, 125.9, 118.8, 73.70, 38.9, 32.2, 27.1,

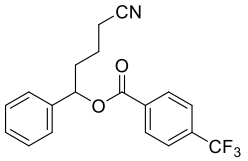
13.5. **HRMS m/z (ESI)** calcd for $C_{15}H_{19}NNaO_2$ $(M + Na)^+$ 268.1308, found 268.1301. **TLC:** Rf = 0.16 (petroleum ether / ethyl acetate = 9:1).



2k

2-cyanobenzyl 4-(trifluoromethyl)benzoate (2k)

According to the general procedure, **2k** was prepared from **1k** as a white solid (68.6 mg, 75 %): **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.26–8.16 (m, 2H), 7.77–7.67 (m, 3H), 7.68–7.57 (m, 2H), 7.48 (ddd, *J* = 7.6, 6.4, 2.4 Hz, 1H), 5.57 (s, 2H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 164.8, 138.9, 134.7 (q, *J* = 33.3 Hz), 133.2, 133.0, 132.7, 130.2, 129.7, 129.1, 125.5 (q, *J* = 4.0 Hz), 123.5 (q, *J* = 273.7 Hz), 117.0, 112.4, 64.7. **HRMS m/z (ESI)** calcd for $C_{16}H_{10}F_3NNaO_2$ $(M + Na)^+$ 328.0556, found 328.0551. **M.P.** 135~139 ℃. **TLC:** Rf = 0.19 (petroleum ether / ethyl acetate = 9:1).

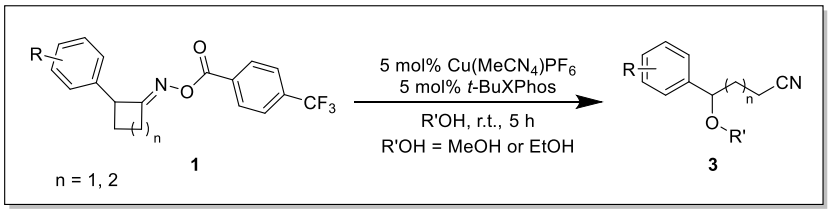


2l

4-cyano-1-phenylbutyl 4-(trifluoromethyl)benzoate (2l)

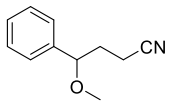
According to the general procedure, **2l** was prepared from **1l** as a white solid (74.0 mg, 71 %): **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.19 (d, *J* = 8.2 Hz, 2H), 7.72 (d, *J* = 8.1 Hz, 2H), 7.50–7.29 (m, 5H), 6.04 (dd, *J* = 7.7, 5.7 Hz, 1H), 2.40 (t, *J* = 7.1 Hz, 2H), 2.25 (ddd, *J* = 10.4, 5.2, 2.3 Hz, 1H), 2.11 (ddd, *J* = 10.3, 7.9, 5.2 Hz, 1H), 1.91–1.62 (m, 2H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 164.5, 139.3, 134.6 (q, *J* = 32.3 Hz), 133.2, 130.0, 128.8, 128.5, 126.3, 125.5 (q, *J* = 3.0 Hz), 123.5 (q, *J* = 273.7 Hz), 119.0, 76.2, 35.2, 21.6, 17.0. **HRMS m/z (ESI)** calcd for $C_{19}H_{16}F_3NNaO_2$ $(M + Na)^+$ 370.1025, found 370.1018. **M.P.** 96~98 ℃. **TLC:** Rf = 0.38 (petroleum ether / ethyl acetate = 9:1).

6. General procedures and characterization of methoxy ether products



General procedure B: To a 25 mL Schlenk tube under argon were added $Cu(MeCN)_4PF_6$ (5.6 mg,

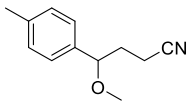
0.015 mmol, 5 mol %), *t*-BuXPhos (6.4 mg, 0.015 mmol, 5 mol %), and R'OH (1.0 mL). The suspension was stirred 15 min at room tempreture. To this was added a solution of cyclobutanone oxime derivatives (0.3 mmol, 1.0 equiv) in R'OH (4.0 mL). Then the mixture was stirred 5 h at 60 °C. The solvent was removed under vacuum and the residue was purified by column chromatography (petroleum ether/ethyl acetate = 20/1) to give methoxy ether **3**.



3a

4-methoxy-4-phenylbutanenitrile (3a)[7]

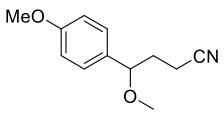
According to the general procedure, **3a** was prepared from **1a** as a yellow oil (48.3 mg, 92 %): **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.41–7.27 (m, 5H), 4.25 (dd, *J* = 8.7, 4.7 Hz, 1H), 3.24 (s, 3H), 2.54 (ddd, *J* = 16.9, 8.2, 7.3 Hz, 1H), 2.37 (ddd, *J* = 16.9, 7.3, 5.7 Hz, 1H), 2.12–1.87 (m, 2H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 140.4, 128.7, 128.2, 126.5, 119.5, 81.5, 56.8, 33.6, 13.8. **HRMS m/z (ESI)** calcd for $C_{11}H_{13}NNaO$ $(M + Na)^+$ 198.0889, found 198.0888. **TLC:** Rf = 0.32 (petroleum ether / ethyl acetate = 9:1).



3b

4-methoxy-4-(*p*-tolyl)butanenitrile (3b)[7a]

According to the general procedure, **3b** was prepared from **1b** as a yellow oil (52.2 mg, 92 %): **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.18 (s, 4H), 4.22 (dd, *J* = 8.7, 4.7 Hz, 1H), 3.22 (s, 3H), 2.52 (dt, *J* = 16.9, 7.7 Hz, 1H), 2.42–2.28 (m, 4H), 2.11–1.87 (m, 2H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 137.9, 137.3, 129.4, 126.4, 119.6, 81.3, 56.7, 33.6, 21.1, 13.8. **HRMS m/z (ESI)** calcd for $C_{12}H_{15}NNaO$ $(M + Na)^+$ 212.1046, found 212.1043. **TLC:** Rf = 0.30 (petroleum ether / ethyl acetate = 9:1).

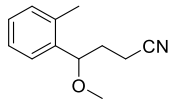


3c

4-methoxy-4-(4-methoxyphenyl)butanenitrile (3c)

According to the general procedure, **3c** was prepared from **1c** as a yellow oil (57.2 mg, 93 %): **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.25–7.15 (m, 2H), 6.95–6.86 (m, 2H), 4.19 (dd, *J* = 8.6, 4.9 Hz, 1H), 3.81

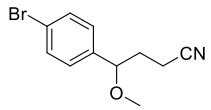
(s, 3H), 3.20 (s, 3H), 2.50 (dt, *J* = 16.9, 7.7 Hz, 1H), 2.35 (ddd, *J* = 16.9, 7.3, 5.9 Hz, 1H), 2.13–1.99 (m, 1H), 1.99–1.85 (m, 1H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 159.5, 132.3, 127.7, 119.5, 114.1, 81.0, 56.5, 55.3, 33.5, 13.8. **HRMS m/z (ESI)** calcd for $C_{12}H_{15}NNaO_2$ $(M + Na)^+$ 228.0995, found 228.0998. **TLC:** Rf = 0.44 (petroleum ether / ethyl acetate = 4:1).



3d

4-methoxy-4-(*o*-tolyl)butanenitrile (3d)[7]

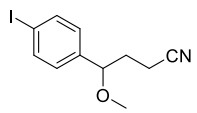
According to the general procedure, **3d** was prepared from **1d** as a yellow oil (31.8 mg, 56 %): **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.42 (dd, *J* = 7.3, 1.8 Hz, 1H), 7.38–7.20 (m, 3H), 4.62 (t, *J* = 6.4 Hz, 1H), 3.33 (s, 3H), 2.71 (dd, *J* = 16.6, 8.2 Hz, 1H), 2.53 (dt, *J* = 16.9, 6.1 Hz, 1H), 2.44 (s, 3H), 2.03 (dt, *J* = 7.8, 6.2 Hz, 2H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 138.3, 135.3, 130.7, 127.6, 126.4, 125.5, 119.6, 78.0, 56.8, 32.5, 18.8, 13.9. **HRMS m/z (ESI)** calcd for $C_{12}H_{15}NNaO$ $(M + Na)^+$ 212.1046, found 212.1043. **TLC:** Rf = 0.62 (petroleum ether / ethyl acetate = 4:1).



3e

4-(4-bromophenyl)-4-methoxybutanenitrile (3e)[7]

According to the general procedure, **3e** was prepared from **1e** as a yellow oil (55.4 mg, 73 %): **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.50 (d, *J* = 8.4 Hz, 2H), 7.17 (d, *J* = 8.4 Hz, 2H), 4.22 (dd, *J* = 8.8, 4.5 Hz, 1H), 3.23 (s, 3H), 2.54 (ddd, *J* = 16.9, 8.4, 7.2 Hz, 1H), 2.37 (ddd, *J* = 16.9, 7.1, 5.7 Hz, 1H), 2.10–1.83 (m, 2H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 139.5, 131.9, 128.1, 122.0, 119.3, 80.8, 56.9, 33.5, 13.8. **HRMS m/z (ESI)** calcd for $C_{11}H_{12}BrNNaO$ $(M + Na)^+$ 275.9994, 277.9974, found 275.9990, 277.9969. **TLC:** Rf = 0.54 (petroleum ether / ethyl acetate = 4:1).

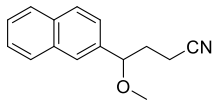


3f

4-(4-iodophenyl)-4-methoxybutanenitrile (3f)

According to the general procedure, **3f** was prepared from **1f** as a yellow oil (83.0 mg, 92 %): **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.71 (d, *J* = 8.3 Hz, 2H), 7.05 (d, *J* = 8.2 Hz, 2H), 4.20 (dd, *J* = 8.8, 4.5 Hz, 1H), 3.23 (s, 3H), 2.54 (ddd, *J* = 17.0, 8.3, 7.2 Hz, 1H), 2.37 (ddd, *J* = 16.9, 7.1, 5.7 Hz, 1H), 2.13–1.79

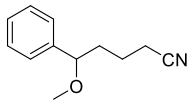
(m, 2H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 140.2, 137.9, 128.4, 119.3, 93.6, 80.9, 56.9, 33.5, 13.8. **HRMS m/z (ESI)** calcd for $C_{11}H_{12}INNaO$ $(M + Na)^+$ 323.9856, found 323.9848. **TLC:** Rf = 0.30 (petroleum ether / ethyl acetate = 9:1).



3h

4-methoxy-4-(naphthalen-2-yl)butanenitrile (3h)

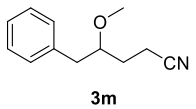
According to the general procedure, **3h** was prepared from **1h** as a yellow oil (59.5 mg, 88 %): **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.92–7.79 (m, 3H), 7.76 (d, *J* = 1.6 Hz, 1H), 7.62–7.48 (m, 2H), 7.43 (dd, *J* = 8.5, 1.7 Hz, 1H), 4.43 (dd, *J* = 8.7, 4.8 Hz, 1H), 3.29 (s, 3H), 2.58 (ddd, *J* = 16.9, 8.1, 7.2 Hz, 1H), 2.40 (ddd, *J* = 16.9, 7.2, 5.8 Hz, 1H), 2.16 (dddd, *J* = 14.4, 8.7, 7.2, 5.9 Hz, 1H), 2.10–1.96 (m, 1H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 137.7, 133.3, 133.2, 128.8, 127.8, 127.7, 126.4, 126.2, 125.9, 123.8, 119.5, 81.6, 56.9, 33.4, 13.9. **HRMS m/z (ESI)** calcd for $C_{15}H_{15}NNaO$ $(M + Na)^+$ 248.1046, found 248.1055. **TLC:** Rf = 0.32 (petroleum ether / ethyl acetate = 9:1).



3l

5-methoxy-5-phenylpentanenitrile (3l)[8]

According to the general procedure, **3l** was prepared from **1l** as a yellow oil (43.7 mg, 77 %): **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.46–7.20 (m, 5H), 4.14 (dd, *J* = 7.8, 4.4 Hz, 1H), 3.21 (s, 3H), 2.50–2.17 (m, 2H), 1.98 – 1.55 (m, 4H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 141.4, 128.5, 127.8, 126.5, 119.6, 83.0, 56.7, 36.9, 21.9, 17.1. **HRMS m/z (ESI)** calcd for $C_{12}H_{15}NNaO$ $(M + Na)^+$ 212.1046, found 212.1041. **TLC:** Rf = 0.32 (petroleum ether / ethyl acetate = 9:1).

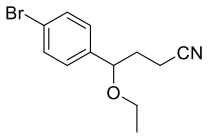


3m

4-methoxy-5-phenylpentanenitrile (3m)

According to the general procedure, **3m** was prepared from **1m** as a yellow oil (48.2 mg, 85 %): **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.35–7.16 (m, 5H), 3.49 (dtd, *J* = 9.2, 5.5, 4.7, 2.0 Hz, 1H), 3.39 (s, 3H), 2.96 (dd, *J* = 13.7, 5.3 Hz, 1H), 2.68 (dd, *J* = 13.7, 7.1 Hz, 1H), 2.42 (ddd, *J* = 8.1, 6.5, 1.9 Hz, 2H), 1.88 –1.73 (m, 1H), 1.73–1.60 (m, 1H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 137.4, 129.4, 128.5, 126.5, 119.7,

80.0, 57.4, 39.4, 29.5, 13.4. **HRMS m/z (ESI)** calcd for $C_{12}H_{15}NNaO$ $(M + Na)^+$ 212.1046, found 212.1042. **TLC:** Rf = 0. 27 (petroleum ether / ethyl acetate = 9:1).

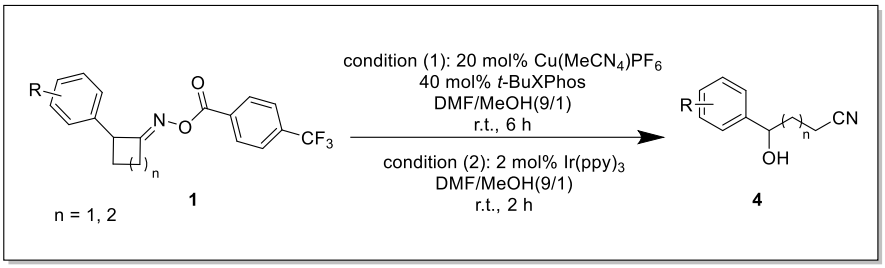


3n

4-(4-bromophenyl)-4-ethoxybutanenitrile (3n)

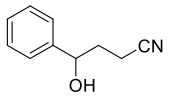
According to the general procedure, **3n** was prepared from **1e** and ethanol as a yellow oil (60.1 mg, 75 %): **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.49 (d, *J* = 8.3 Hz, 2H), 7.18 (d, *J* = 8.4 Hz, 2H), 4.33 (dd, *J* = 9.0, 4.4 Hz, 1H), 3.47–3.26 (m, 2H), 2.57 (ddd, *J* = 16.9, 8.4, 7.1 Hz, 1H), 2.39 (ddd, *J* = 16.9, 7.0, 5.6 Hz, 1H), 2.07–1.82 (m, 2H), 1.18 (t, *J* = 7.0 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 140.3, 131.8, 128.0, 121.8, 119.4, 78.9, 64.6, 33.7, 15.1, 13.8. **HRMS m/z (ESI)** calcd for $C_{12}H_{14}BrNNaO$ $(M + Na)^+$ 290.0151, found 290.0150. **TLC:** Rf = 0.32 (petroleum ether / ethyl acetate = 9:1).

7. General procedures and characterization of *γ*-hydroxyl alkyl nitriles



General condition C: condition (1): To a 25 mL Schlenk tube under argon were added $Cu(MeCN)_4PF_6$ (22.4 mg, 0.06 mmol, 20 mol %), *t*-BuXPhos (51.0 mg, 0.12 mmol , 40 mol %), and DMF (0.5 mL). The suspension was stirred at room tempreture for 15 min. To this was added a solution of cyclobutanone oxime derivatives (0.3 mmol, 1.0 equiv) in DMF (4.5 mL) and MeOH (0.55 mL). Then the mixture was stirred 6 h at 60 ºC. The solvent was removed under vacuum and the residue was purified by column chromatography (petroleum ether/ethyl acetate = 10/1) to give alcohol **4**.

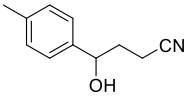
General condition D: condition (2): To a 25 mL Schlenk tube under argon were added $Ir(ppy)_3$ (3.9 mg, 0.006 mmol, 2 mol %), cyclobutanone oxime derivatives (0.3 mmol, 1.0 equiv), and DMF/MeOH (5.0 mL/0.55 mL). The suspension was stirred at room tempreture for 2 h. The solvent was removed under vacuum and the residue was purified by column chromatography (petroleum ether/ethyl acetate = 10/1) to give alcohol **4**.



4a

4-hydroxy-4-phenylbutanenitrile (4a)[7a,9]

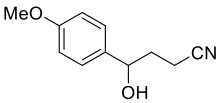
According to the general procedure, **4a** was prepared from **1a** as a yellow oil (condition (1): 31.9 mg, 66 %; condition (2): 35.3 mg, 72 %): **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.46–7.29 (m, 5H), 4.84 (dd, *J* = 8.3, 4.9 Hz, 1H), 2.55 (dt, *J* = 17.0, 7.7 Hz, 1H), 2.40 (ddd, *J* = 17.0, 7.4, 5.9 Hz, 1H), 2.05 (dtd, *J* = 10.0, 7.8, 5.3 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 142.9, 128.8, 128.2, 125.6, 119.6, 72.4, 34.2, 13.8. **TLC:** Rf = 0.23 (petroleum ether / ethyl acetate = 4:1).



4b

4-hydroxy-4-(p-tolyl)butanenitrile (4b)[10]

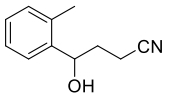
According to the general procedure, **4b** was prepared from **1b** as a yellow oil (condition (1): 27.3 mg, 52 %; condition (2): 41.0 mg, 78 %): **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.31–7.11 (m, 4H), 4.79 (dd, *J* = 8.3, 4.9 Hz, 1H), 2.61–2.46 (m, 1H), 2.45–2.26 (m, 4H), 2.02 (dddd, *J* = 18.6, 13.9, 9.4, 5.9 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 139.9, 138.0, 129.4, 125.6, 119.6, 72.3, 34.2, 21.1, 13.8. **HRMS m/z (ESI)** calcd for $C_{11}H_{13}NNaO$ $(M + Na)^+$ 198.0889, found 198.0887. **TLC:** Rf = 0.26 (petroleum ether / ethyl acetate = 4:1).



4c

4-hydroxy-4-(4-methoxyphenyl)butanenitrile (4c)[9-10]

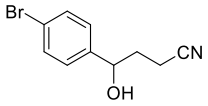
According to the general procedure, **4c** was prepared from **1c** as a yellow oil (condition (1): 13.2 mg, 23 %; condition (2): 24.7 mg, 43 %): **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.33–7.21 (m, 2H), 6.97–6.85 (m, 2H), 4.77 (ddd, *J* = 8.3, 4.8, 1.5 Hz, 1H), 3.81 (d, *J* = 1.7 Hz, 3H), 2.59–2.29 (m, 2H), 2.17–1.87 (m, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 159.5, 135.0, 126.9, 119.6, 114.1, 72.0, 55.3, 34.1, 13.8. **TLC:** Rf = 0.15 (petroleum ether / ethyl acetate = 4:1).



4d

4-hydroxy-4-(o-tolyl)butanenitrile (4d)

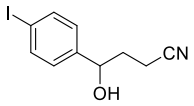
According to the general procedure, **4d** was prepared from **1d** as a yellow oil (condition (1): 26.2 mg, 50 %; condition (2): 42.0 mg, 80 %): **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.53–7.39 (m, 1H), 7.20 (ddd, *J* = 24.2, 15.0, 6.2 Hz, 3H), 5.07 (dd, *J* = 7.8, 4.9 Hz, 1H), 2.75–2.55 (m, 1H), 2.47 (dt, *J* = 16.9, 6.3 Hz, 1H), 2.35 (s, 3H), 2.12–1.86 (m, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 141.1, 134.3, 130.7, 127.8, 126.5, 124.9, 119.7, 68.7, 33.0, 18.8, 13.9. **HRMS m/z (ESI)** calcd for $C_{11}H_{13}NNaO$ $(M + Na)^+$ 198.0889, found 198.0888. **TLC:** Rf = 0.31 (petroleum ether / ethyl acetate = 4:1).



4e

4-(4-bromophenyl)-4-hydroxybutanenitrile (4e)

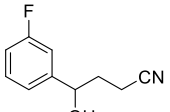
According to the general procedure, **4e** was prepared from **1e** as a yellow oil (condition (1): 22.9 mg, 32 %; condition (2): 37.3 mg, 52 %): **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.61–7.39 (m, 2H), 7.24 (dd, *J* = 8.1, 6.3 Hz, 2H), 4.82 (ddd, *J* = 7.8, 4.8, 2.2 Hz, 1H), 2.57 (dt, *J* = 17.0, 7.7 Hz, 1H), 2.40 (ddd, *J* = 17.0, 7.1, 5.9 Hz, 1H), 2.15 (d, *J* = 3.3 Hz, 1H), 2.09–1.87 (m, 2H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 142.0, 131.9, 127.3, 122.0, 119.4, 71.7, 34.2, 13.7. **HRMS m/z (ESI)** calcd for $C_{10}H_{10}BrNNaO$ $(M + Na)^+$ 261.9838, found 261.9836. **TLC:** Rf = 0.21 (petroleum ether / ethyl acetate = 4:1).



4f

4-hydroxy-4-(4-iodophenyl)butanenitrile (4f)

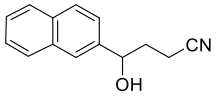
According to the general procedure, **4f** was prepared from **1f** as a yellow oil (condition (1): 26.7 mg, 31 %; condition (2): 26.7 mg, 31 %): **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.79–7.62 (m, 2H), 7.10 (d, *J* = 8.3 Hz, 2H), 4.79 (dd, *J* = 8.0, 5.1 Hz, 1H), 2.66–2.49 (m, 1H), 2.39 (ddd, *J* = 16.9, 7.1, 5.9 Hz, 1H), 2.22 (s, 1H), 1.99 (tt, *J* = 7.8, 5.5 Hz, 2H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 142.7, 137.8, 127.6, 119.4, 93.6, 71.7, 34.1, 13.7. **HRMS m/z (ESI)** calcd for $C_{10}H_{10}INNaO$ $(M + Na)^+$ 309.9699, found 309.9693. **TLC:** Rf = 0.23 (petroleum ether / ethyl acetate = 4:1).



4g

4-(3-fluorophenyl)-4-hydroxybutanenitrile (4g)

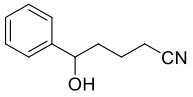
According to the general procedure, **4g** was prepared from **1g** as a yellow oil (condition (1): 15.1 mg, 28 %; condition (2): 34.9 mg, 65 %): **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.33 (td, *J* = 7.9, 5.8 Hz, 1H), 7.14–7.05 (m, 2H), 7.00 (tdd, *J* = 8.4, 2.6, 1.0 Hz, 1H), 4.84 (t, *J* = 6.5 Hz, 1H), 2.57 (dt, *J* = 17.0, 7.8 Hz, 1H), 2.40 (dt, *J* = 17.0, 6.5 Hz, 1H), 2.31 (s, 1H), 2.02 (tdd, *J* = 7.2, 5.7, 1.2 Hz, 2H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 163.0 (d, *J* = 248.5 Hz), 145.7 (d, *J* = 7.1 Hz), 130.3 (d, *J* = 8.1 Hz), 121.2 (d, *J* = 2.0 Hz), 119.4, 115.0 (d, *J* = 21.2 Hz), 112.6 (d, *J* = 22.2 Hz), 71.6 (d, *J* = 2.0 Hz), 34.2, 13.7. **HRMS m/z (ESI)** calcd for $C_{10}H_{10}FNNaO$ $(M + Na)^+$ 202.0639, found 202.0637. **TLC:** Rf = 0.26 (petroleum ether / ethyl acetate = 4:1).



4h

4-hydroxy-4-(naphthalen-2-yl)butanenitrile (4h)

According to the general procedure, **4h** was prepared from **1h** as a yellow oil (condition (1): 35.5 mg, 56 %; condition (2): 43.1 mg, 68 %): **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.88–7.78 (m, 4H), 7.55–7.39 (m, 3H), 4.97 (dd, *J* = 8.1, 4.9 Hz, 1H), 2.56 (dt, *J* = 17.0, 7.7 Hz, 1H), 2.39 (ddd, *J* = 16.9, 7.4, 5.9 Hz, 2H), 2.11 (dtd, *J* = 9.5, 7.7, 5.4 Hz, 2H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 140.2, 133.2, 133.2, 128.7, 127.9, 127.7, 126.5, 126.2, 124.6, 123.4, 119.6, 72.4, 34.1, 13.8. **HRMS m/z (ESI)** calcd for $C_{14}H_{13}NNaO$ $(M + Na)^+$ 234.0889, found 234.0895. **TLC:** Rf = 0.18 (petroleum ether / ethyl acetate = 4:1).



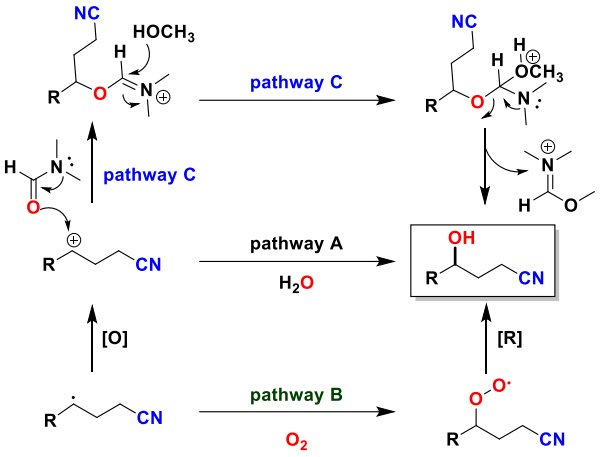
4l

5-hydroxy-5-phenylpentanenitrile (4l)

According to the general procedure, **4l** was prepared from **1l** as a yellow oil (condition (1): 15.8 mg, 30 %; condition (2): 38.9 mg, 74 %): **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.34–7.12 (m, 5H), 4.63 (dq, *J* = 4.8, 3.0 Hz, 1H), 2.37–2.23 (m, 2H), 2.16–1.88 (m, 1H), 1.90–1.67 (m, 3H), 1.62 (dtd, *J* = 9.8, 7.2, 2.4 Hz, 1H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 143.9, 128.6, 127.8, 125.7, 119.6, 73.6, 37.6, 21.8, 17.0. **HRMS m/z (ESI)** calcd for $C_{11}H_{13}NNaO$ $(M + Na)^+$ 198.0889, found 198.0888. **TLC:** Rf = 0.18 (petroleum ether / ethyl acetate = 4:1).

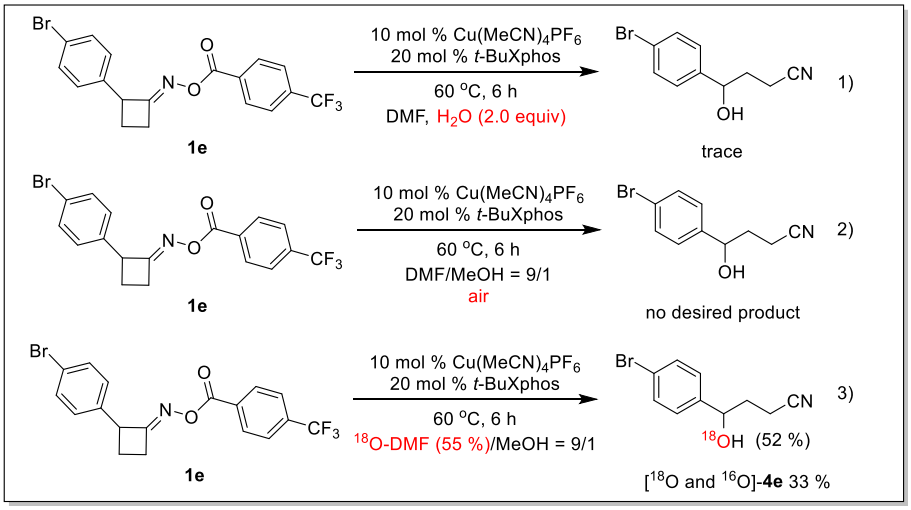
8. Mechanistic studies.

Scheme S6. Possible mechanistic pathways for the formation of γ-hydroxyl alkyl nitriles.



Regarding the source of the hydroxyl group, three reaction pathways might be possible (Scheme S6): (1) the trace amount of water in solvent may provide the hydroxide for the nucleophilic substitution (pathway A); (2) the trace molecular oxygen remaining in the reaction system may provide the hydroxyl group via a peroxide intermediate (pathway B); (3) similar to Vilsmeier-Haack formylation, the observed alcohols might be generated from DMF as the nucleophile (pathway C). To elucidate the mechanism, control experiments were conducted (Scheme S7).

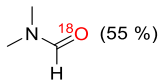
Scheme S7. Control experiments.



Preparation of ^{18}O-dimethylformamide[11]

Dry dimethylformamide (2.84 ml, 36.6 mmol) and dry benzoyl chloride (4.22 mL, 36.6 mmol) were added to a three necked flask equipped with a calcium chloride drying tube. The flask was then cooled to 0 °C and ^{18}O labelled water (90 % mole of ^{18}O isotope, 0.66 g, 36.6 mmol) was introduced slowly into the reaction flask. The contents solidified instantaneously due to the formation of benzoic acid Mass spectrometry of the crude reaction mixture indicated the presence of ^{18}O labelled dimethylformamide.

Petroleum ether (40 - 60 °C, 10 ml) was added to the reaction flask and stirred for 10 min and sodium bicarbonate (excess) was added to the reaction flask. When the evolution of carbon dioxide ceased, the contents were extracted with ethyl acetate (3 x 20 ml). The combined ethyl acetate layers were dried over anhydrous potassium carbonate and filtered, and the resulting solution was concentrated under vacuum. The crude product was purified by distillation (90 °C @30 mm Hg) and provided ^{18}O-labelled dimethylformamide (55% mole of ^{18}O isotope, 1.22 g, 43 %).



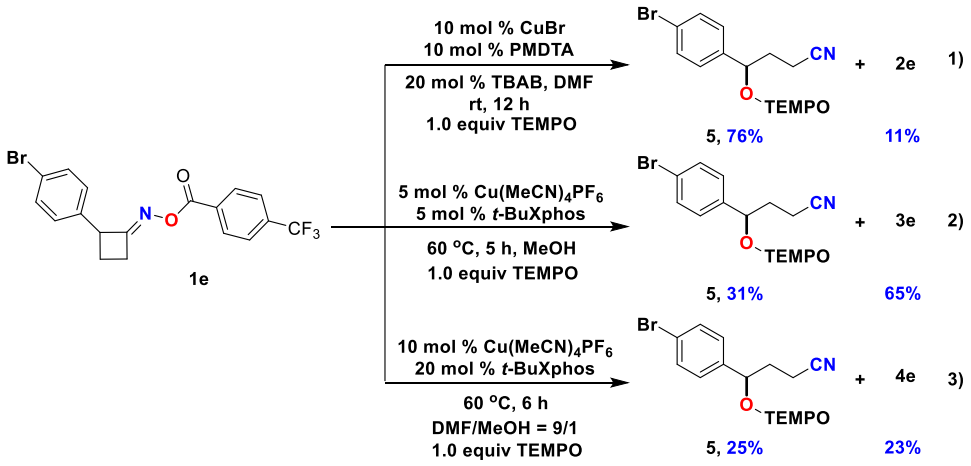
N,N-dimethylformamide-^{18}O

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.99 (s, 1H), 2.94 (s, 3H), 2.86 (s, 3H). **^{13}C NMR (101 MHz, CDCl$_3$)** δ 162.4, 36.4, 31.3. **HRMS m/z (ESI)** calcd for C_3H_8NO $(M + H)^+$ 76.0643, found 76.0649.

Reaction with substrate 1e

To a 25 mL Schlenk tube under argon were added $Cu(MeCN)_4PF_6$ (4.2 mg, 0.01129 mmol), *t*-BuXPhos (9.6 mg, 0.02258 mmol), and ^{18}O-dimethylformamide (0.5 mL). The suspension was stirred 15 min at room tempreture. To this was added a solution of cyclobutanone oxime **1e** (0.05645 mmol, 1.0 equiv) in DMF (0.8 mL) and MeOH (0.14 mL). Then the mixture was stirred 6 h at 60 °C. The solvent was removed under vacuum and the residue was purified by column chromatography (petroleum ether/ethyl acetate = 10/1) to give alcohol [^{18}O and ^{16}O]-**4e** (52% mole of ^{18}O isotope, 4.5 mg, 33 %). Mass spectroscopy showed that ^{18}O and ^{16}O products were detected in the ratio 1.08:1 when ^{18}O-DMF was used as solvent and the data were given in the supporting information. These results demonstrate that the oxygen atom of hydroxyl in the product is mainly originated from solvent DMF.

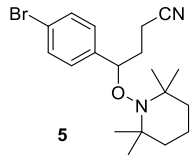
Scheme S8. The reaction of 1e with radical acceptor TEMPO.



1) To a 25 mL Schlenk tube under argon were added CuBr (4.3 mg, 0.03 mmol, 10 mol %), TBAB (19.3 mg, 0.06 mmol, 20 mol %), **1e** (123.3 mg, 0.3 mmol, 1.0 equiv), PMDTA (5.2 mg, 6.3 μL, 0.03 mmol, 10 mol %), TEMPO (46.9 mg, 0.3 mmol, 1.0 equiv) and DMF (5 mL). Then the mixture was stirred at room tempreture for 12 h. The solvent was removed under vacuum and the residue was purified by column chromatography (petroleum ether/ethyl acetate = 20/1) to give 13.5 mg (11 %) of **2e** and 86.2 mg (76 %) of **5** as a colorless oil.

2) To a 25 mL Schlenk tube under argon were added $Cu(MeCN)_4PF_6$ (5.6 mg, 0.015 mmol, 5 mol %), *t*-BuXPhos (6.4 mg, 0.015 mmol, 5 mol %), and MeOH (1.0 mL). The suspension was stirred 15 min at room tempreture. To this was added a solution of **1e** (123.3 mg, 0.3 mmol, 1.0 equiv) and TEMPO (46.9 mg, 0.3 mmol, 1.0 equiv) in MeOH (4.0 mL). Then the mixture was stirred at 60 °C for 5 h. The solvent was removed under vacuum and the residue was purified by column chromatography (petroleum ether/ethyl acetate = 20/1) to give 49.3 mg (65 %) of **3e** and 35.2 mg (31 %) of **5** as a colorless oil.

3) To a 25 mL Schlenk tube under argon were added $Cu(MeCN)_4PF_6$ (22.4 mg, 0.06 mmol, 20 mol %), *t*-BuXPhos (50.9 mg, 0.12 mmol, 40 mol %), and DMF (0.5 mL). The suspension was stirred at room tempreture for 15 min. To this was added a solution of **1e** (123.3 mg, 0.3 mmol, 1.0 equiv) and TEMPO (46.9 mg, 0.3 mmol, 1.0 equiv) in DMF (4.5 mL) and MeOH (0.55 mL). Then the mixture was stirred at 60 °C for 6 h. The solvent was removed under vacuum and the residue was purified by column chromatography (petroleum ether/ethyl acetate = 20/1 to 10/1) to give 16.5 mg (23 %) of **4e** and 28.3 mg (25 %) of **5** as a colorless oil.

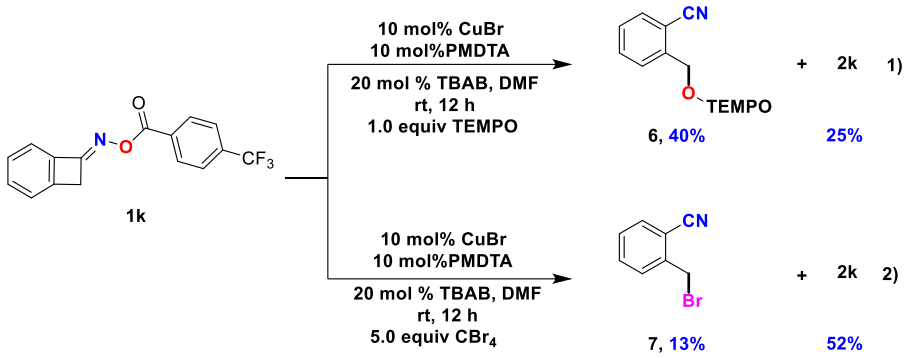


5

4-(4-bromophenyl)-4-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)butanenitrile (5)

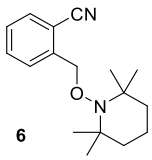
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, *J* = 8.4 Hz, 2H), 7.17 (d, *J* = 8.4 Hz, 2H), 4.76 (dd, *J* = 8.9, 4.1 Hz, 1H), 2.41 (ddd, *J* = 12.7, 8.5, 4.2 Hz, 1H), 2.24 (ddd, *J* = 16.5, 8.4, 4.7 Hz, 1H), 2.12 (dtd, *J* = 13.4, 8.7, 4.8 Hz, 1H), 1.95 (dt, *J* = 16.5, 8.3 Hz, 1H), 1.49 (s, 3H), 1.42 – 1.22 (m, 6H), 1.16 (s, 3H), 1.00 (s, 3H), 0.62 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 140.2, 131.6, 129.0, 121.7, 119.2, 84.4, 60.0, 40.4, 34.5, 34.1, 31.3, 20.4, 17.1, 13.2. **HRMS m/z (ESI)** calcd for $C_{19}H_{28}BrN_2O$ $(M + H)^+$ 379.1380, found 379.1376. **TLC:** Rf = 0.35 (petroleum ether / ethyl acetate = 9:1).

Scheme S9. The reaction of 1k with radical acceptors TEMPO and CBr_4.



4) To a 25 mL Schlenk tube under argon were added CuBr (4.3 mg, 0.03 mmol, 10 mol %), TBAB (19.3 mg, 0.06 mmol, 20 mol %), **1k** (91.5 mg, 0.3 mmol, 1.0 equiv), PMDTA (5.2 mg, 6.3 μL, 0.03 mmol, 10 mol %), TEMPO (46.9 mg, 0.3 mmol, 1.0 equiv) and DMF (5 mL). Then the mixture was stirred at room tempreture for 12 h. The solvent was removed under vacuum and the residue was purified by column chromatography (petroleum ether/ethyl acetate = 20/1) to give 22.9 mg (25 %) of **2k** and 27.8 mg (40 %) of **6** as a colorless oil.

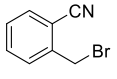
5) To a 25 mL Schlenk tube under argon were added CuBr (4.3 mg, 0.03 mmol, 10 mol %), TBAB (19.3 mg, 0.06 mmol, 20 mol %), **1k** (91.5 mg, 0.3 mmol, 1.0 equiv), PMDTA (5.2 mg, 6.3 μL, 0.03 mmol, 10 mol %), CBr_4 (497.4 mg, 1.5 mmol, 5.0 equiv) and DMF (5 mL). Then the mixture was stirred at room tempreture for 12 h. The solvent was removed under vacuum and the residue was purified by column chromatography (petroleum ether/ethyl acetate = 20/1) to give 47.6 mg (52 %) of **2k** and 12.6 mg (13 %) of **7** as a white solid.



6

2-(((2,2,6,6-tetramethylpiperidin-1-yl)oxy)methyl)benzonitrile (6)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 – 7.53 (m, 3H), 7.46 – 7.30 (m, 1H), 5.03 (s, 2H), 1.71 – 1.43 (m, 5H), 1.43 – 1.33 (m, 1H), 1.26 (s, 6H), 1.16 (s, 6H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 142.0, 132.7, 132.6, 128.4, 127.6, 117.5, 110.9, 76.2, 60.1, 39.7, 33.0, 20.3, 17.1. **HRMS m/z (ESI)** calcd for $C_{17}H_{25}N_2O^+$ $(M + H)^+$ 273.1961, found 273.1956. **TLC:** Rf = 0.33 (petroleum ether / ethyl acetate = 9:1).

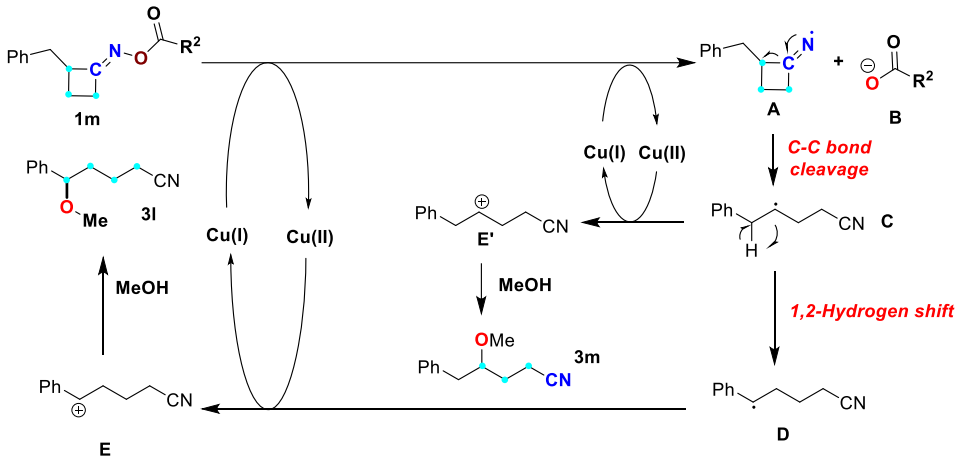


7

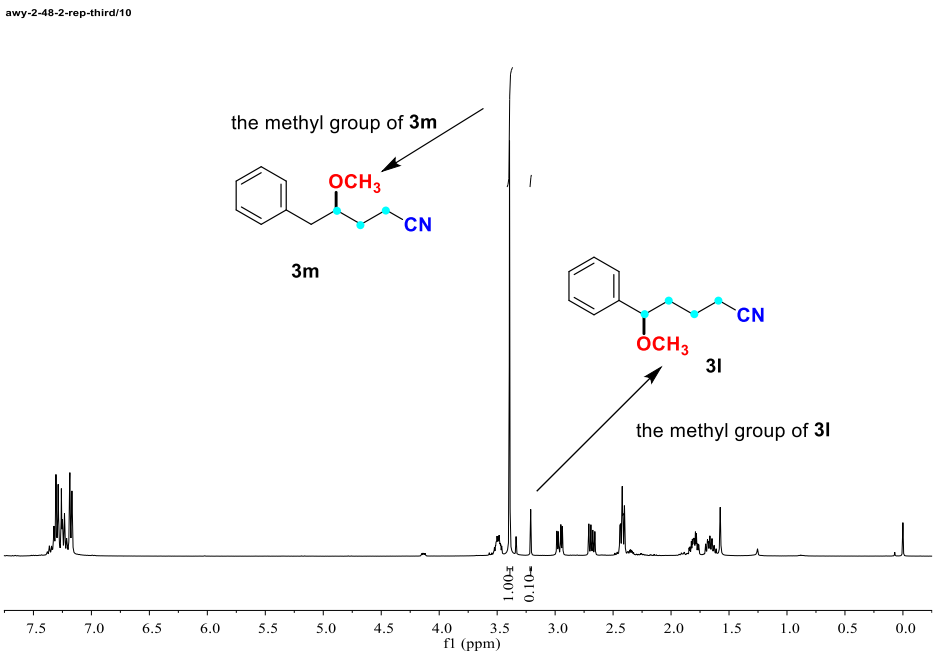
2-(bromomethyl)benzonitrile (7)[12]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 – 7.52 (m, 3H), 7.42 (td, *J* = 7.4, 1.6 Hz, 1H), 4.64 (s, 2H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 141.1, 133.2, 133.2, 130.5, 128.9, 116.7, 112.5, 29.3, 29.3. **TLC:** Rf = 0.35 (petroleum ether / ethyl acetate = 9:1).

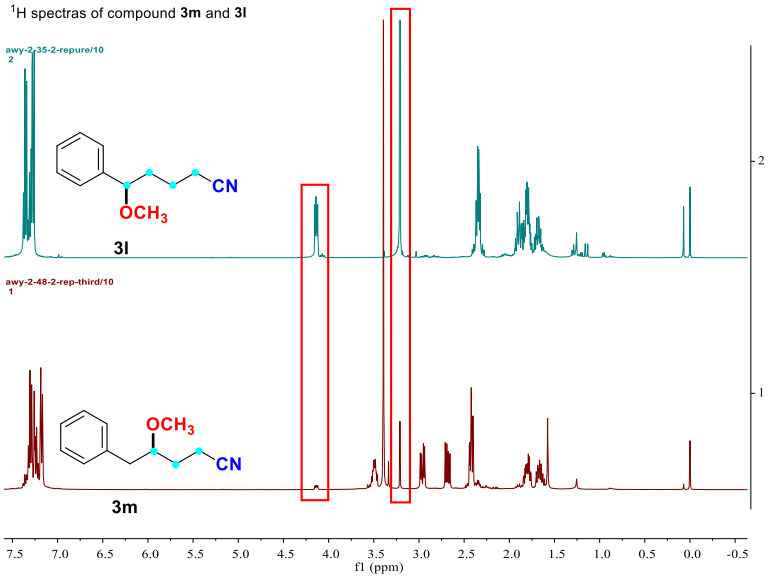
Scheme S10. The 1,2-hydrogen shif process in the γ-methoxylation reaction of 2-benzylcyclobutan-1-one *O*-(4-(trifluoromethyl)benzoyl) oxime (1m).



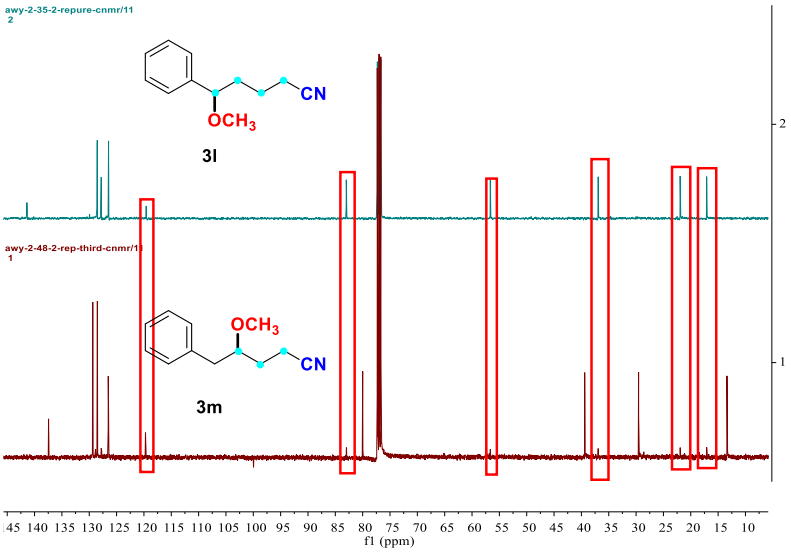
The ^{1}H and ^{13}C spectra of compound **3m** indicated the impurity is regioisomer **3l**. From the ^{1}H spectra, we could find that the crude ratio of regioselectivity is about 10:1 (**3l** : **3m**).



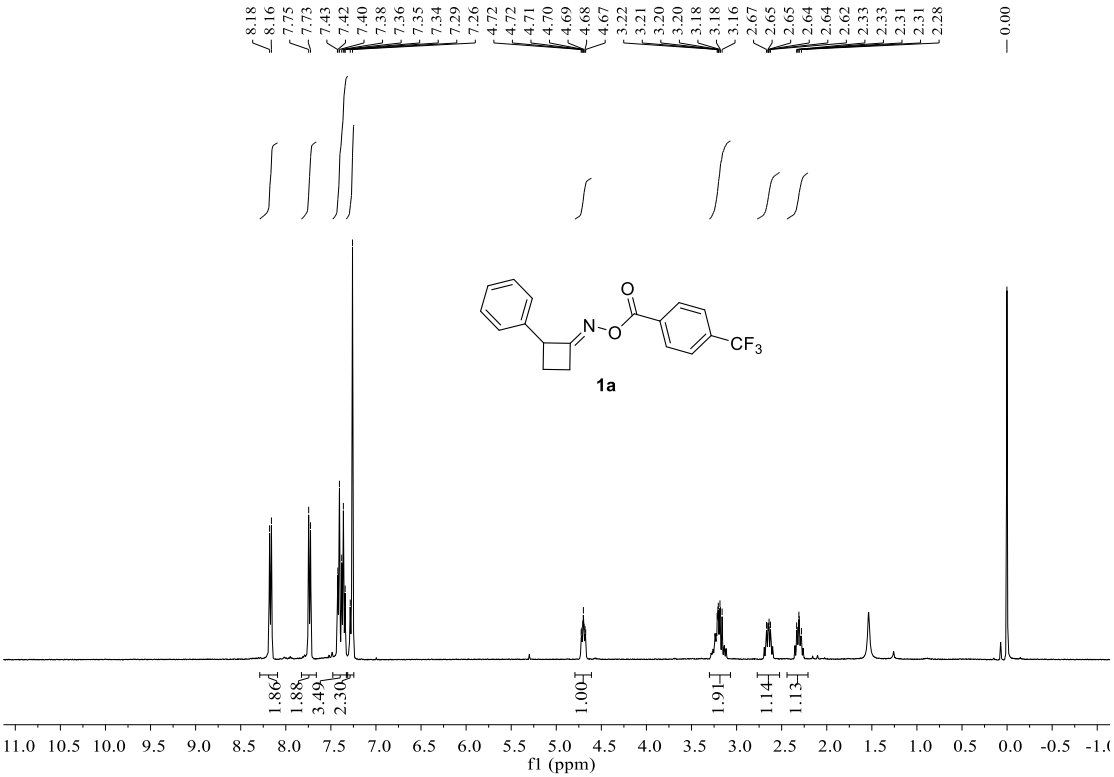
^{1}H spectras of compound **3m** and **3l**

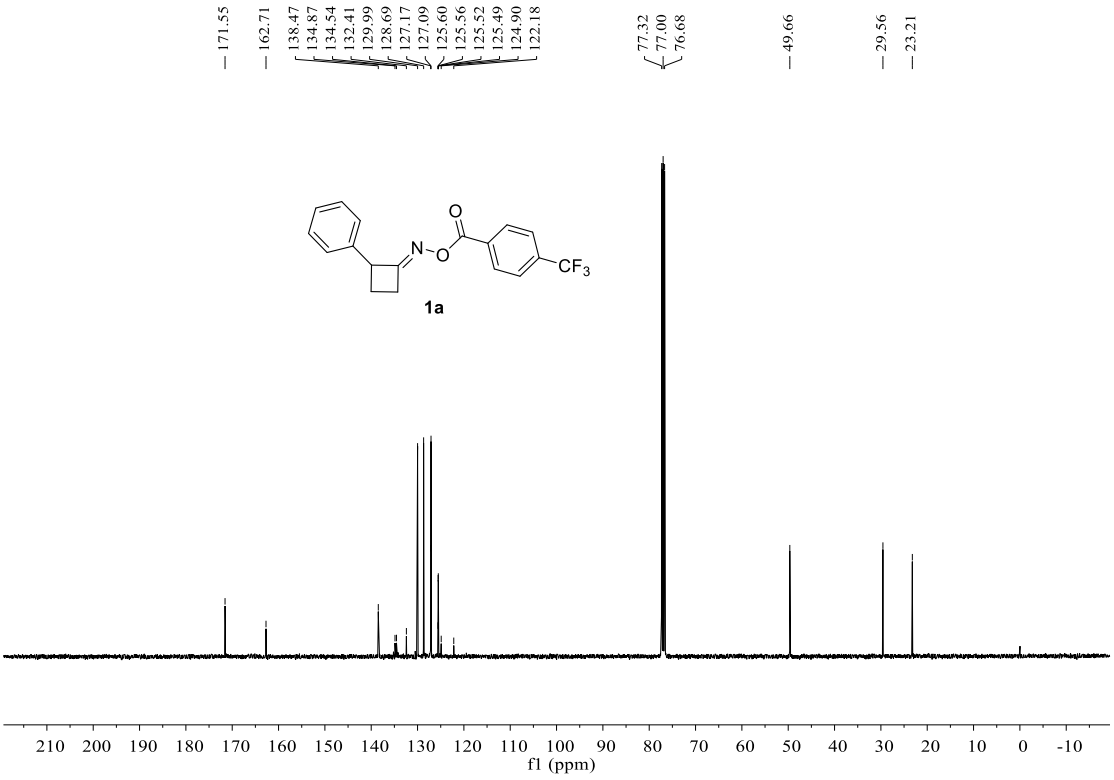


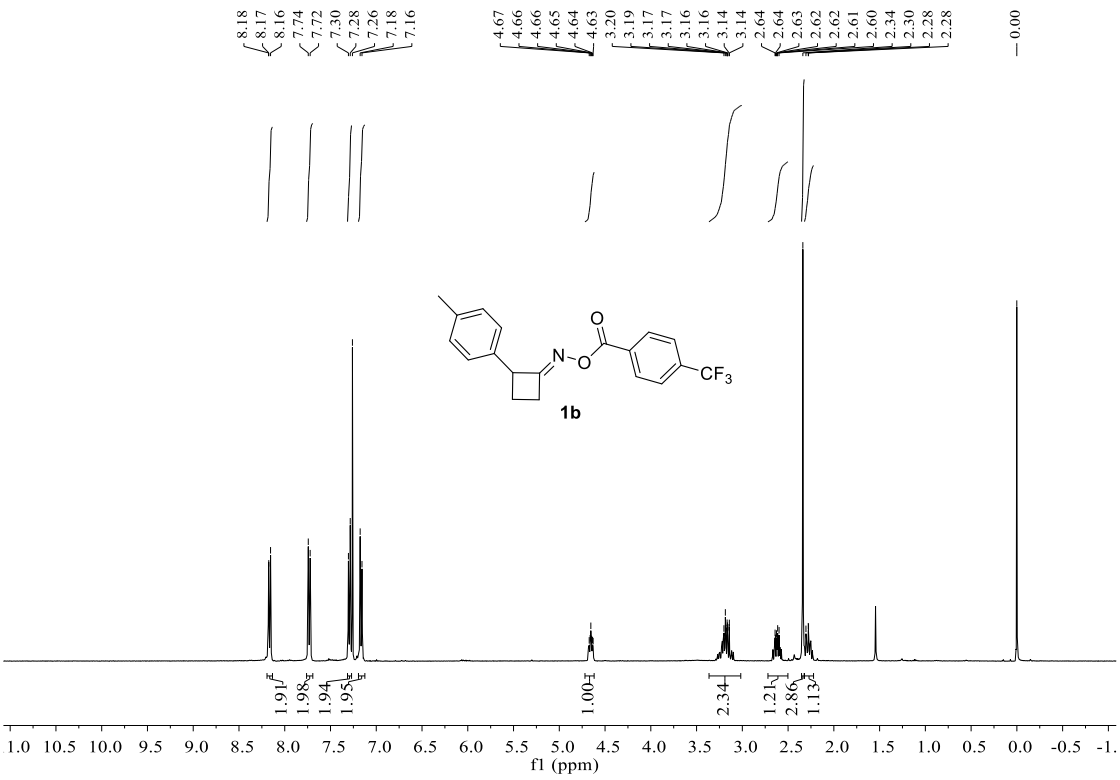
^{13}C spectra of compound **3m** and **3l**



9. Copies of NMR Spectra



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7.30
7.28
7.26
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7.16
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4.66
4.65
4.64
4.63
3.20
3.19
3.17
3.17
3.16
3.16
3.14
3.14
2.64
2.64
2.63
2.62
2.62
2.61
2.60
2.34
2.30
2.28
2.28
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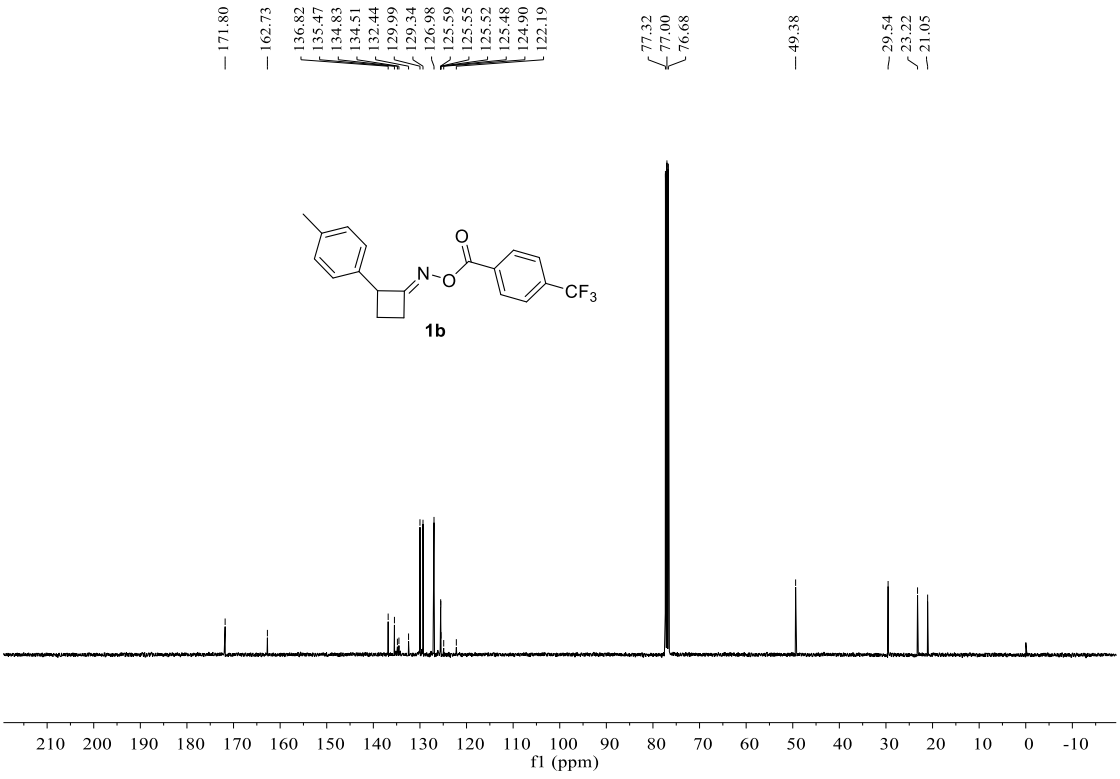
1.98
1.94
1.93
1.00
2.34
1.21
2.86
1.13
1b
f1 (ppm)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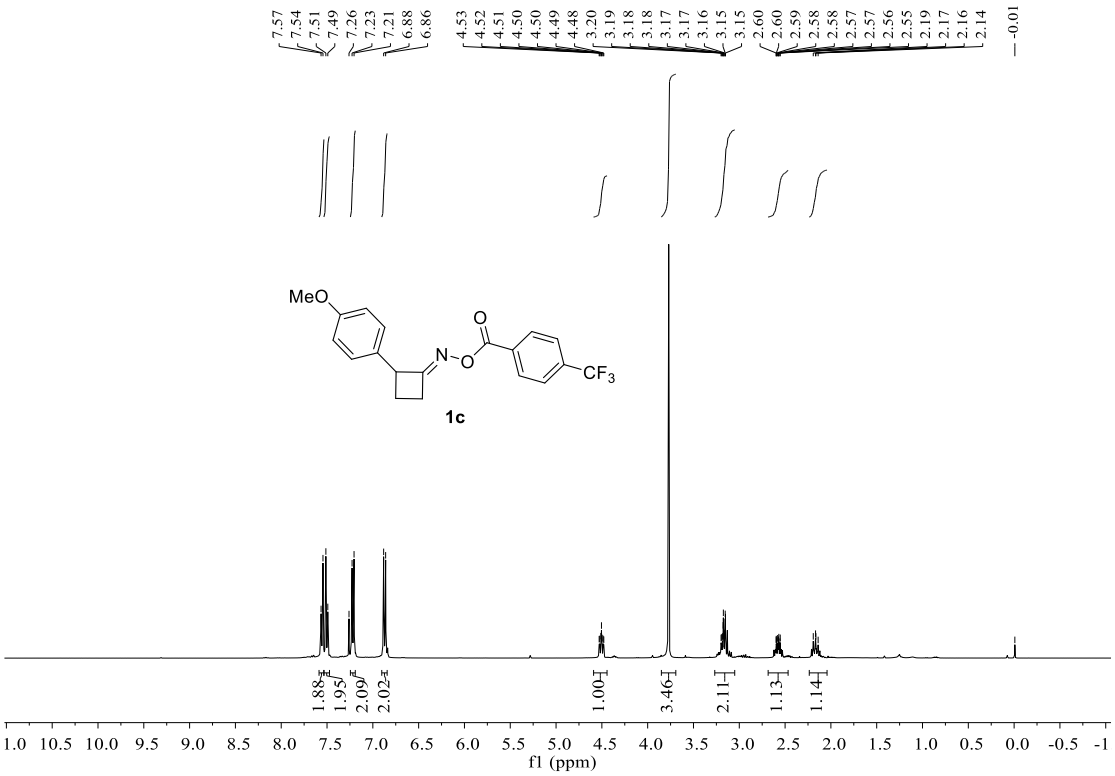
136.82
135.47
134.83
134.51
132.44
129.99
129.34
126.98
125.59
125.55
125.52
125.48
124.90
122.19
77.32
77.00
76.68
49.38
29.54
23.22
21.05
1b
f1 (ppm)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7.23
7.21
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6.86
4.53
4.52
4.51
4.50
4.50
4.49
4.48
3.20
3.19
3.18
3.18
3.17
3.17
3.16
3.15
3.15
2.60
2.60
2.59
2.58
2.58
2.57
2.57
2.56
2.55
2.19
2.17
2.16
2.14
-0.01
MeO
O
N
O
CF3
1c
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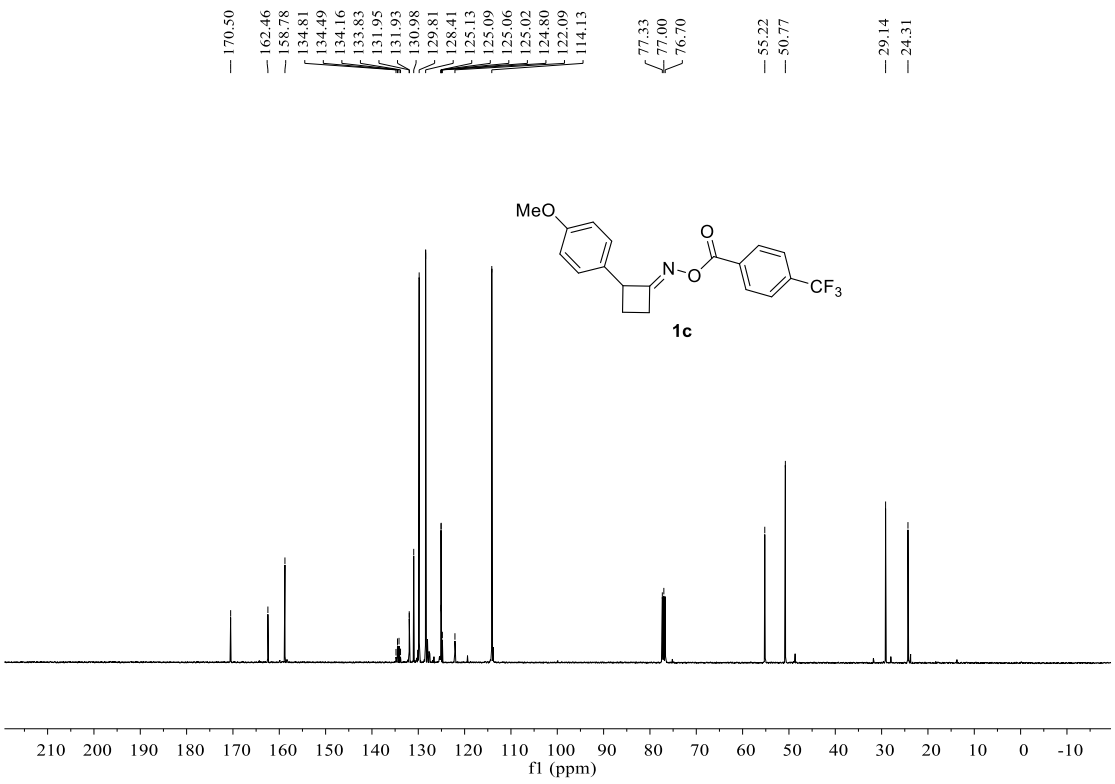
1.95
2.09
2.02
1.00
3.46
2.11
1.13
1.14
f1 (ppm)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158.78
134.81
134.49
134.16
133.83
131.95
131.93
130.98
129.81
128.41
125.13
125.09
125.06
125.02
124.80
122.09
114.13
77.33
77.00
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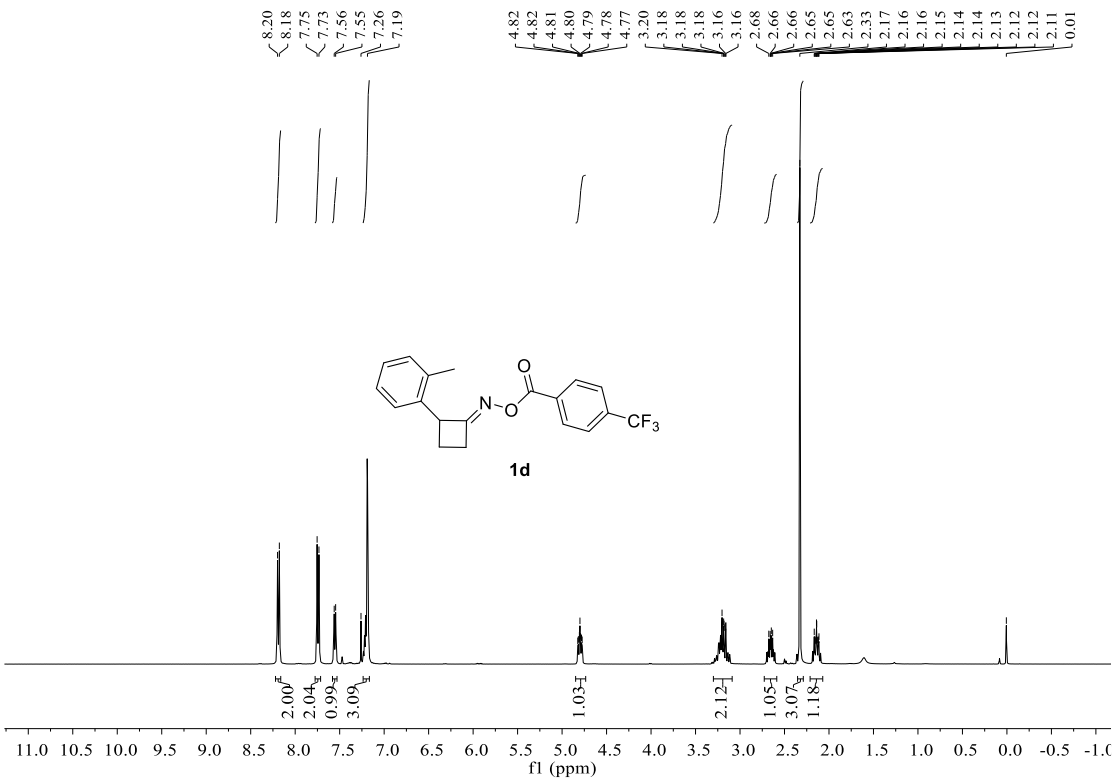
55.22
50.77
29.14
24.31
MeO
O
N
O
CF3
1c
f1 (ppm)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7.55
7.26
7.19
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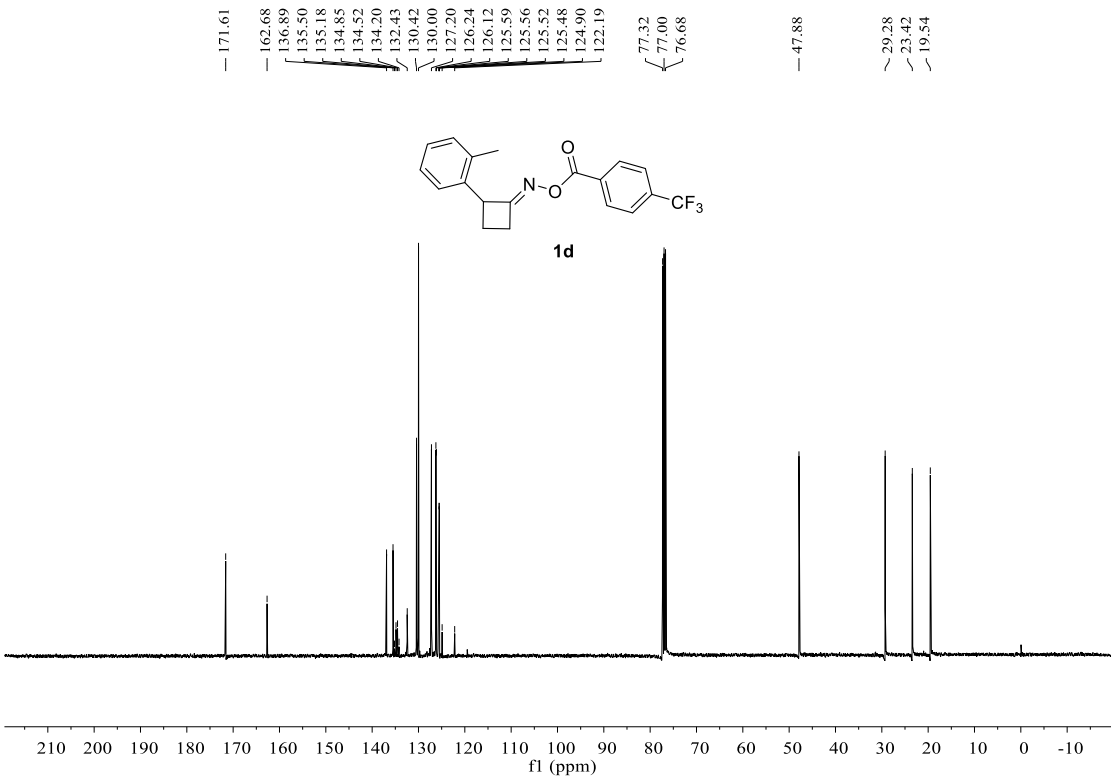
4.82
4.81
4.80
4.79
4.78
4.77
3.20
3.18
3.18
3.16
3.16
2.68
2.66
2.66
2.65
2.65
2.63
2.33
2.17
2.16
2.16
2.15
2.14
2.14
2.13
2.12
2.12
2.11
0.01
O
N
O
CF3
1d
2.00
2.04
0.99
3.09
1.03
2.12
1.05
3.07
1.18
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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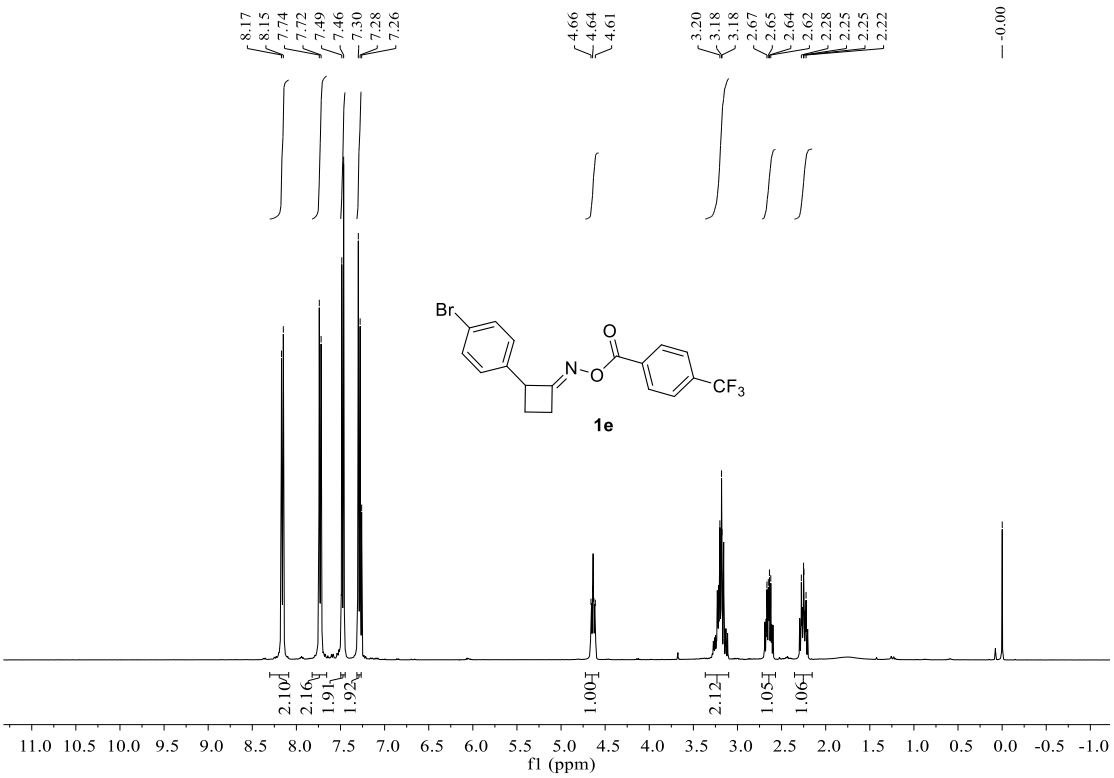
162.68
136.89
135.50
135.18
134.85
134.52
134.20
132.43
130.42
130.00
127.20
126.24
126.12
125.59
125.56
125.52
125.48
124.90
122.19
77.32
77.00
76.68
47.88
29.28
23.42
19.54
O
N
O
CF3
1d
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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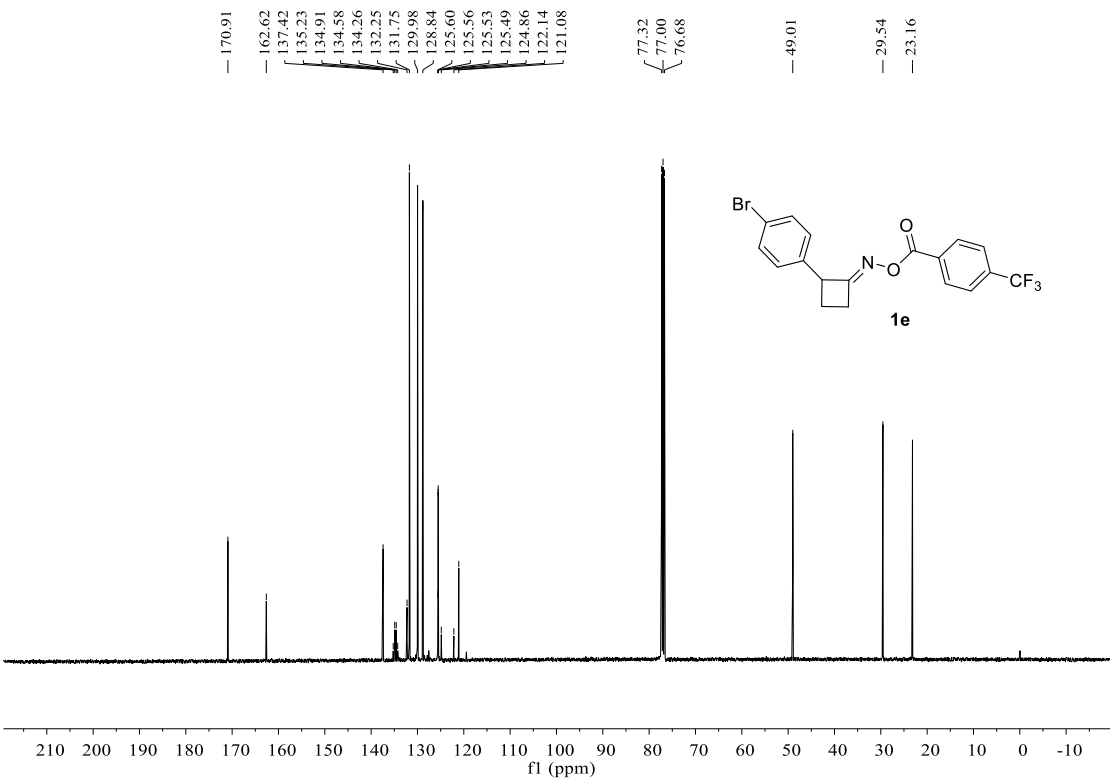
7.72
7.49
7.46
7.30
7.28
7.26
4.66
4.64
4.61
3.20
3.18
3.18
2.67
2.65
2.64
2.62
2.28
2.25
2.25
2.22
-0.00
Br
O
N
O
CF3
1e
2.10
2.16
1.91
1.92
1.00
2.12
1.05
1.06
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)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134.91
134.58
134.26
132.25
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125.53
125.49
124.86
122.14
121.08
77.32
77.00
76.68
49.01
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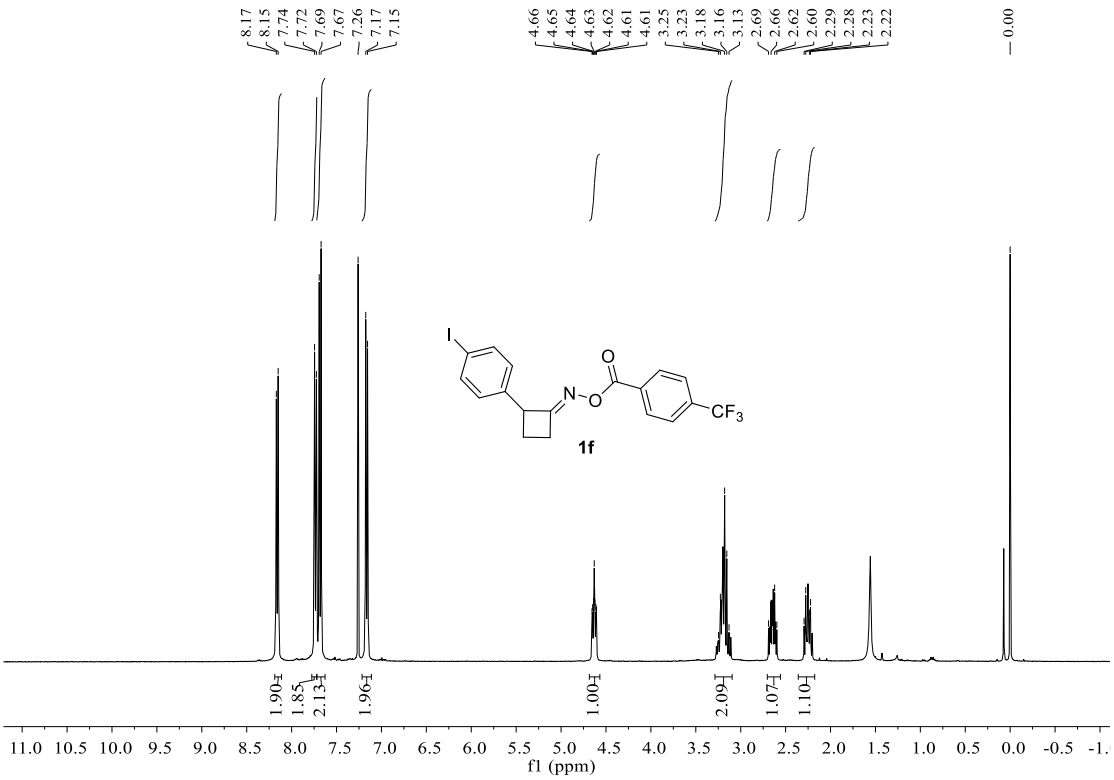
O
N
O
CF3
1e
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


8.17
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3.23
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2.23
2.22
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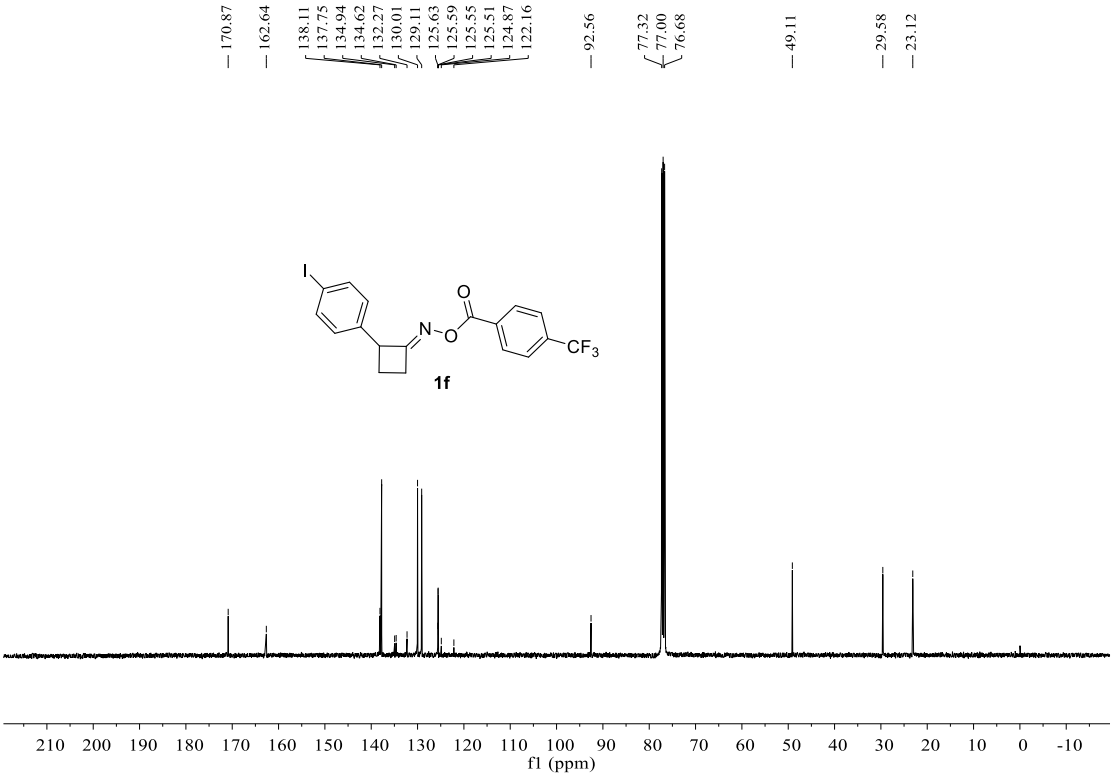
O
N
O
CF3
1f
1.90
1.85
2.13
1.96
1.00
2.09
1.07
1.10
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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125.51
124.87
122.16
92.56
77.32
77.00
76.68
49.11
29.58
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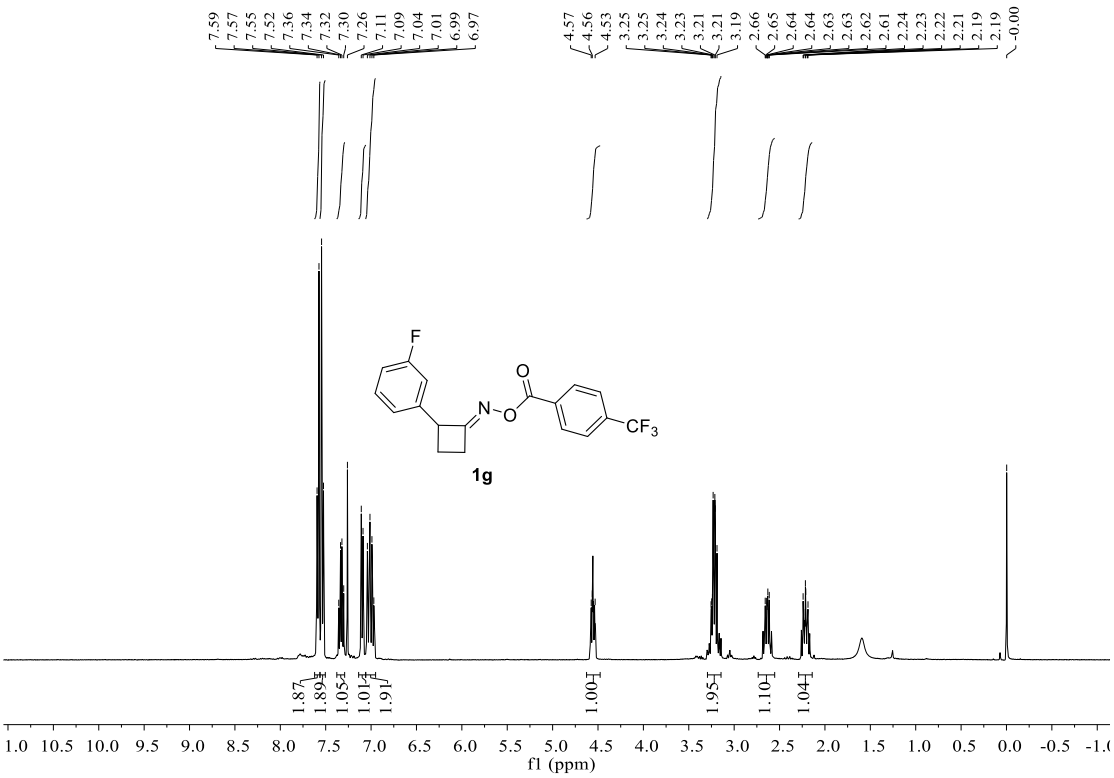
O
N
O
CF3
1f
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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7.04
7.01
6.99
6.97
4.57
4.56
4.53
3.25
3.25
3.24
3.23
3.21
3.21
3.19
2.66
2.65
2.64
2.64
2.63
2.63
2.62
2.61
2.24
2.23
2.22
2.21
2.19
2.19
-0.00
F
O
N
O
CF3
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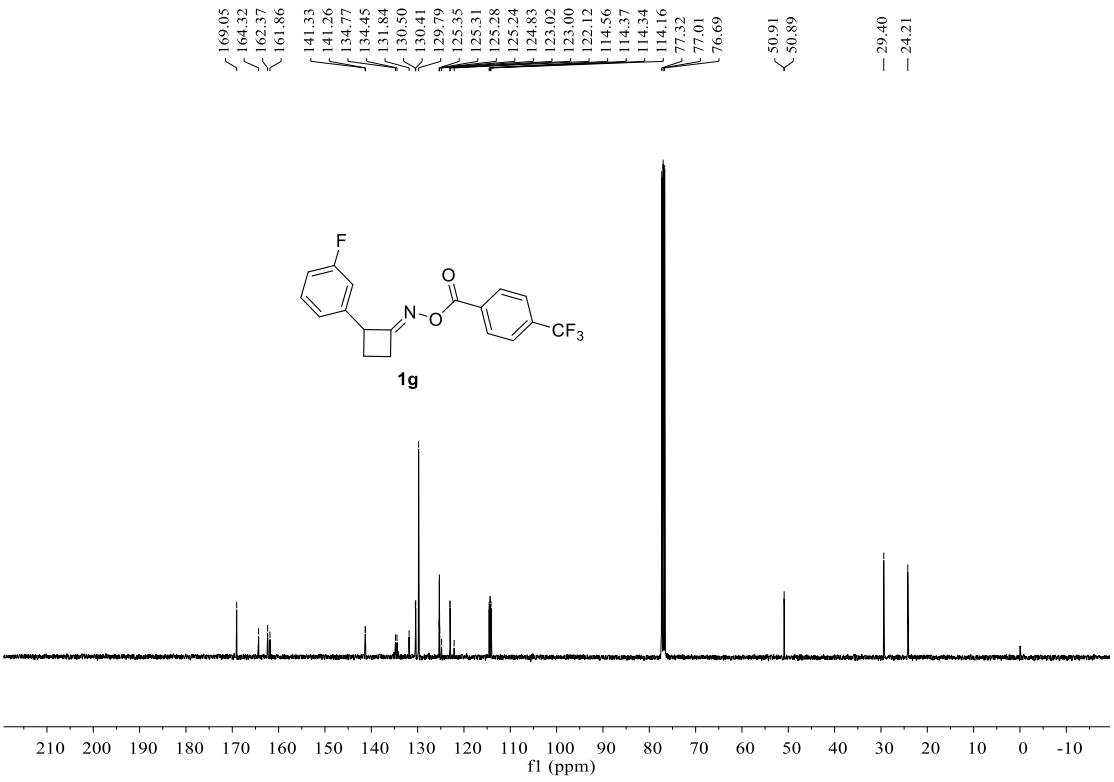
1.89
1.05
1.01
1.91
1.00
1.95
1.10
1.04
f1 (ppm)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134.45
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130.41
129.79
125.35
125.31
125.28
125.24
124.83
123.02
123.00
122.12
114.56
114.37
114.34
114.16
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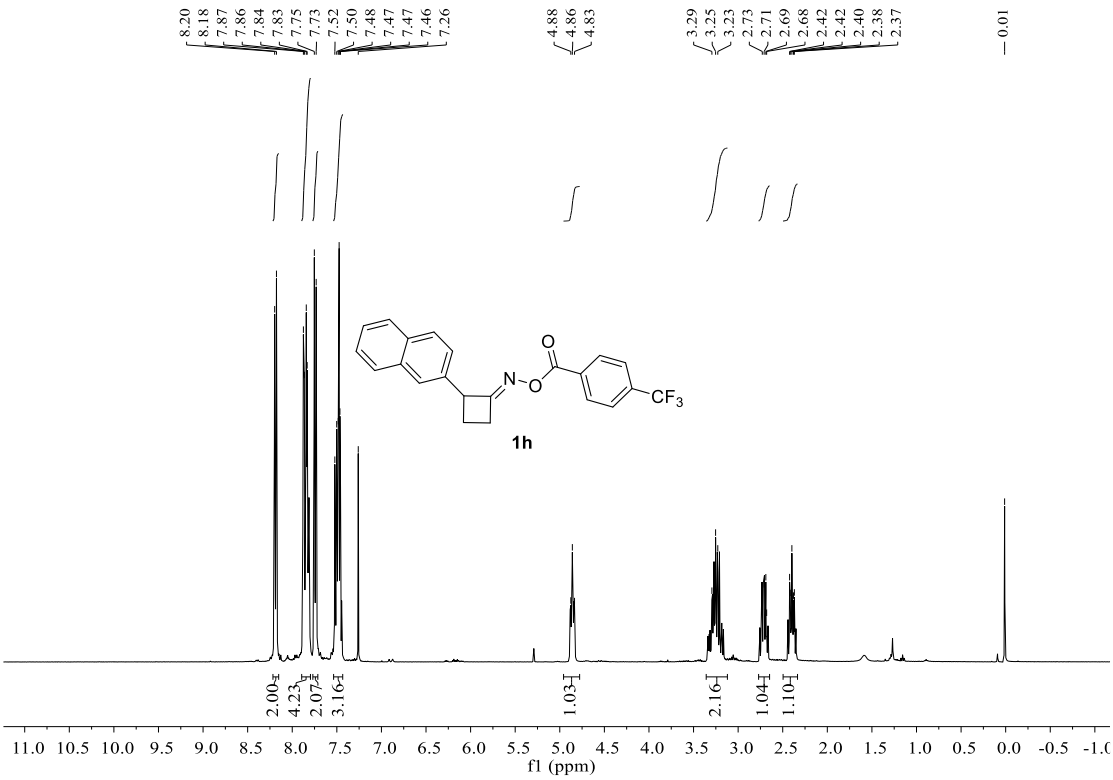
50.91
50.89
29.40
24.21
F
O
N
O
CF3
1g
f1 (ppm)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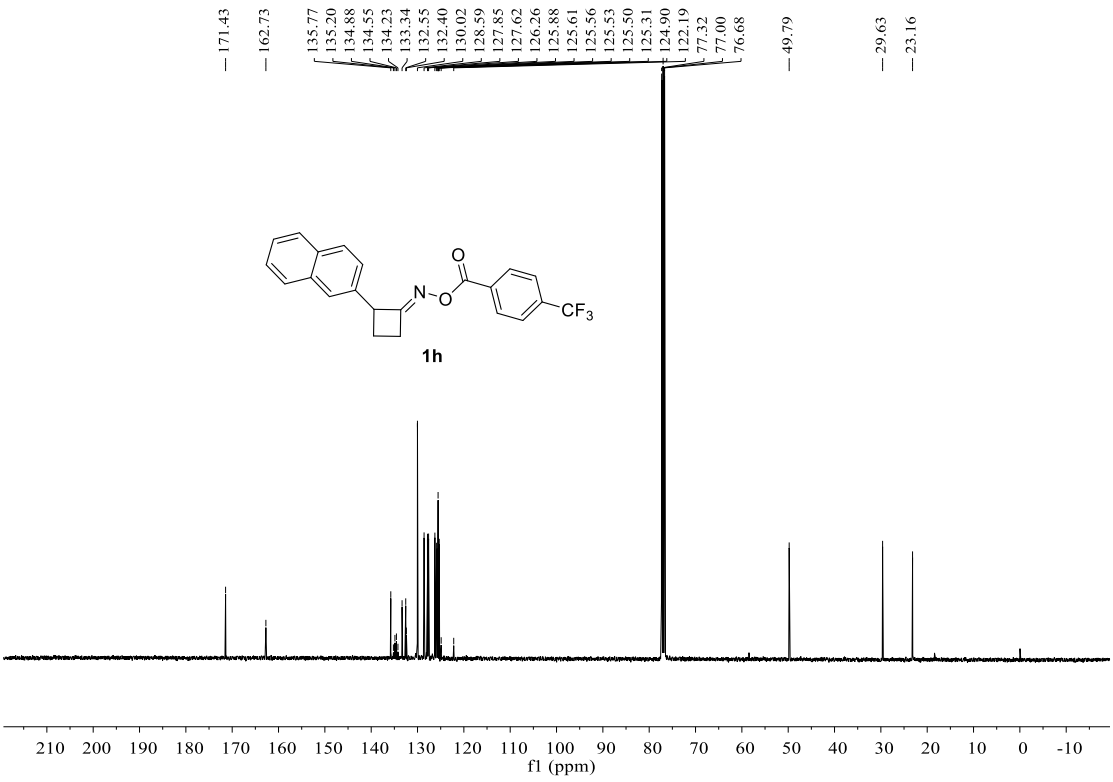
7.47
7.47
7.46
7.26
4.88
4.86
4.83
3.29
3.25
3.23
2.73
2.71
2.69
2.68
2.42
2.42
2.40
2.38
2.37
0.01
O
N
O
CF3
1h
2.00
4.23
2.07
3.16
1.03
2.16
1.04
1.10
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)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133.34
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127.85
127.62
126.26
125.88
125.61
125.56
125.53
125.50
125.31
124.90
122.19
77.32
77.00
76.68
49.79
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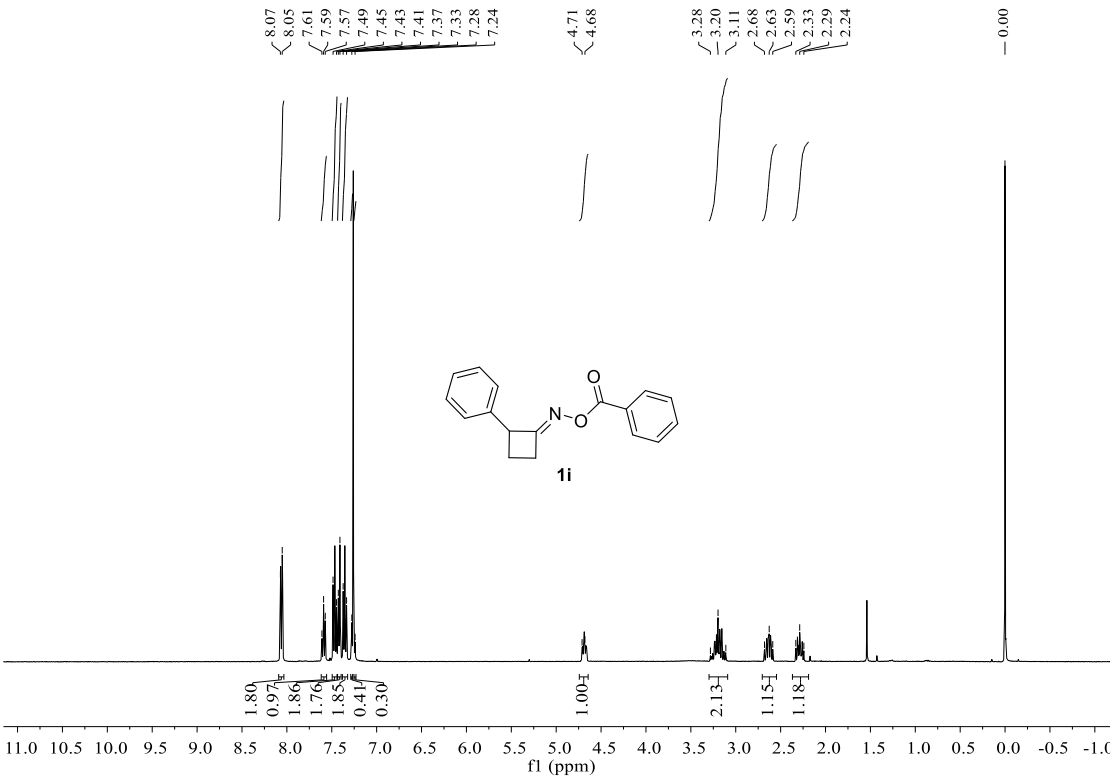
O
N
O
CF3
1h
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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7.37
7.33
7.28
7.24
4.71
4.68
3.28
3.20
3.11
2.68
2.63
2.59
2.33
2.29
2.24
0.00
1.80
0.97
1.86
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1.85
0.41
0.30
1.00
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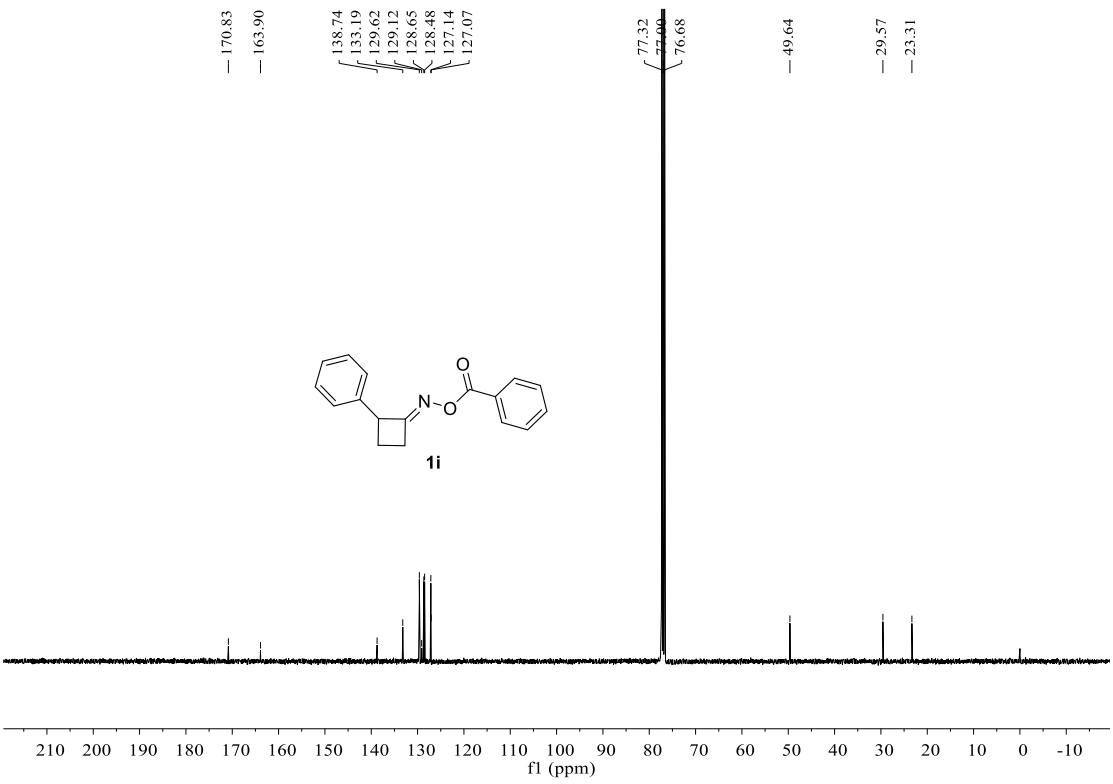
1.15
1.18
f1 (ppm)

1i


170.83
163.90
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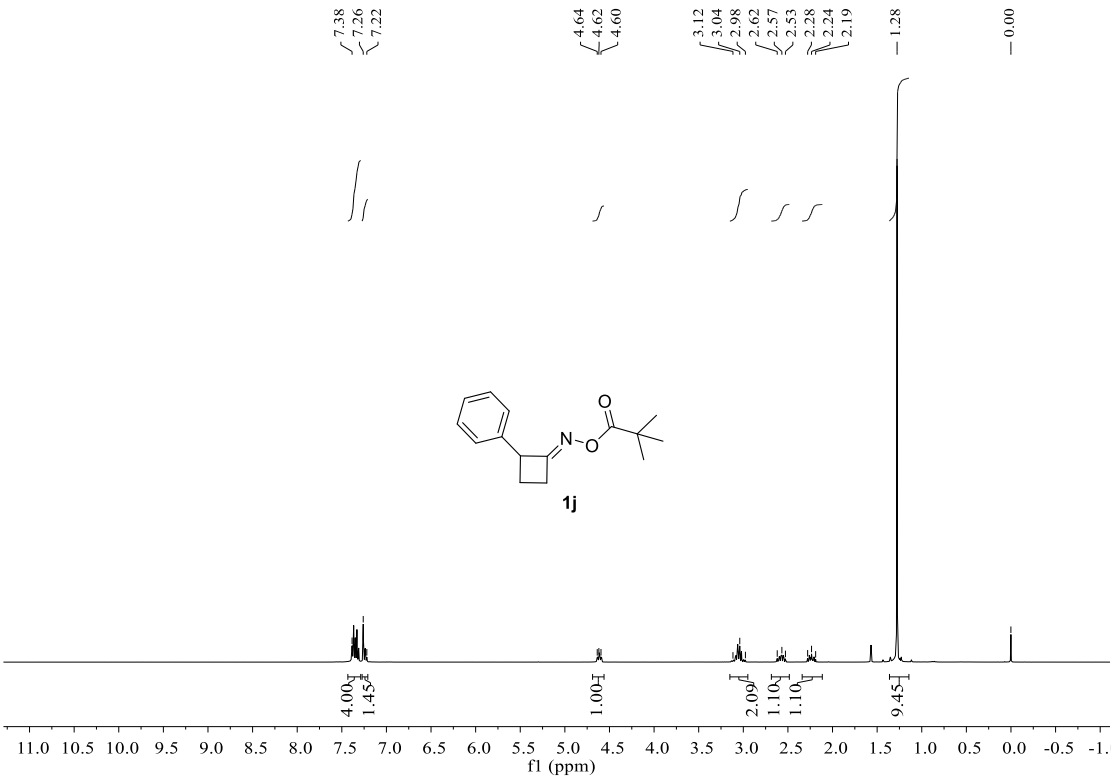
133.19
129.62
129.12
128.65
128.48
127.14
127.07
77.32
77.00
76.68
49.64
29.57
23.31
f1 (ppm)

1i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7.26
7.22
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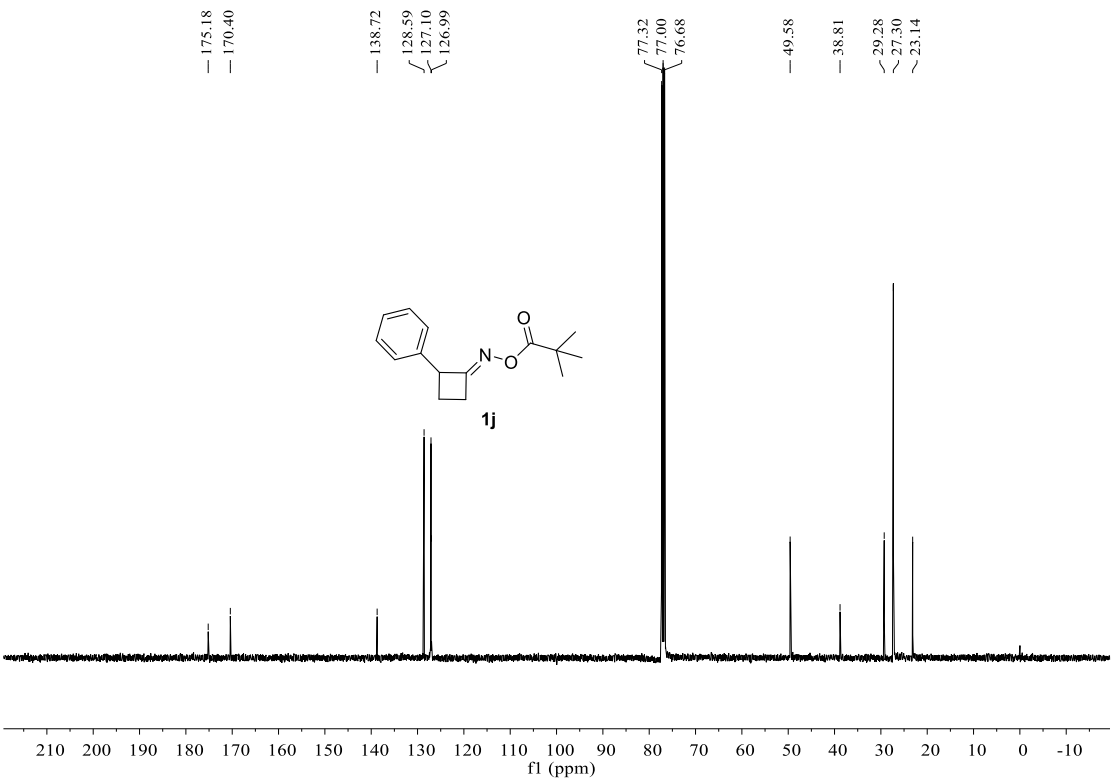
4.62
4.60
3.12
3.04
2.98
2.62
2.57
2.53
2.28
2.24
2.19
1.28
0.00
4.00
1.45
1.00
2.09
1.10
1.10
9.45
f1 (ppm)

1j


175.18
170.40
138.72
128.59
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126.99
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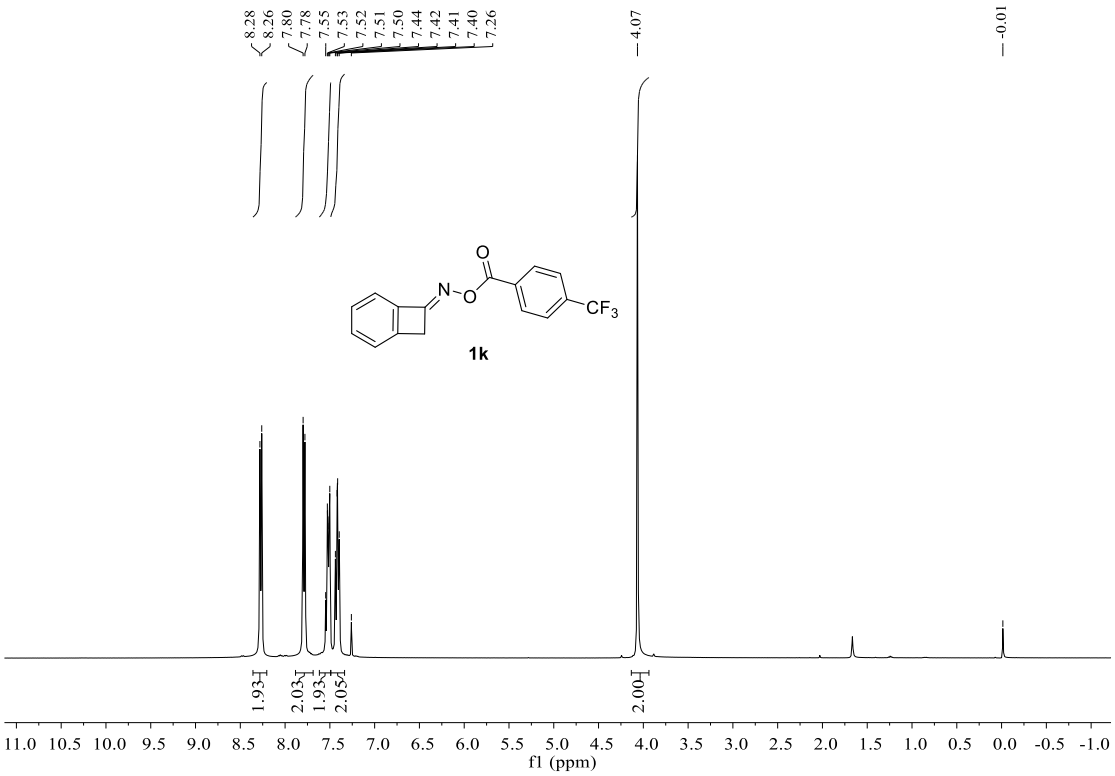
77.00
76.68
49.58
38.81
29.28
27.30
23.14
f1 (ppm)

1j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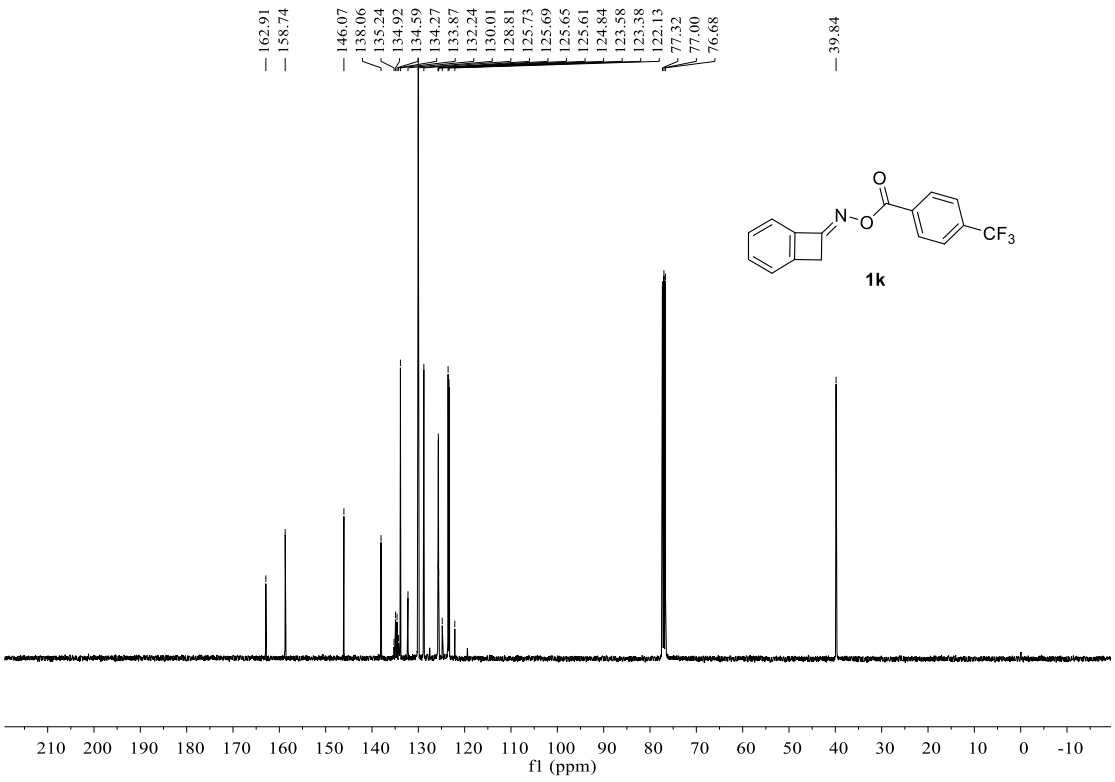
7.78
7.55
7.53
7.52
7.51
7.50
7.44
7.42
7.41
7.40
7.26
4.07
-0.01
O
N
O
CF3
1k
1.93
2.03
1.93
2.05
2.00
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)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134.27
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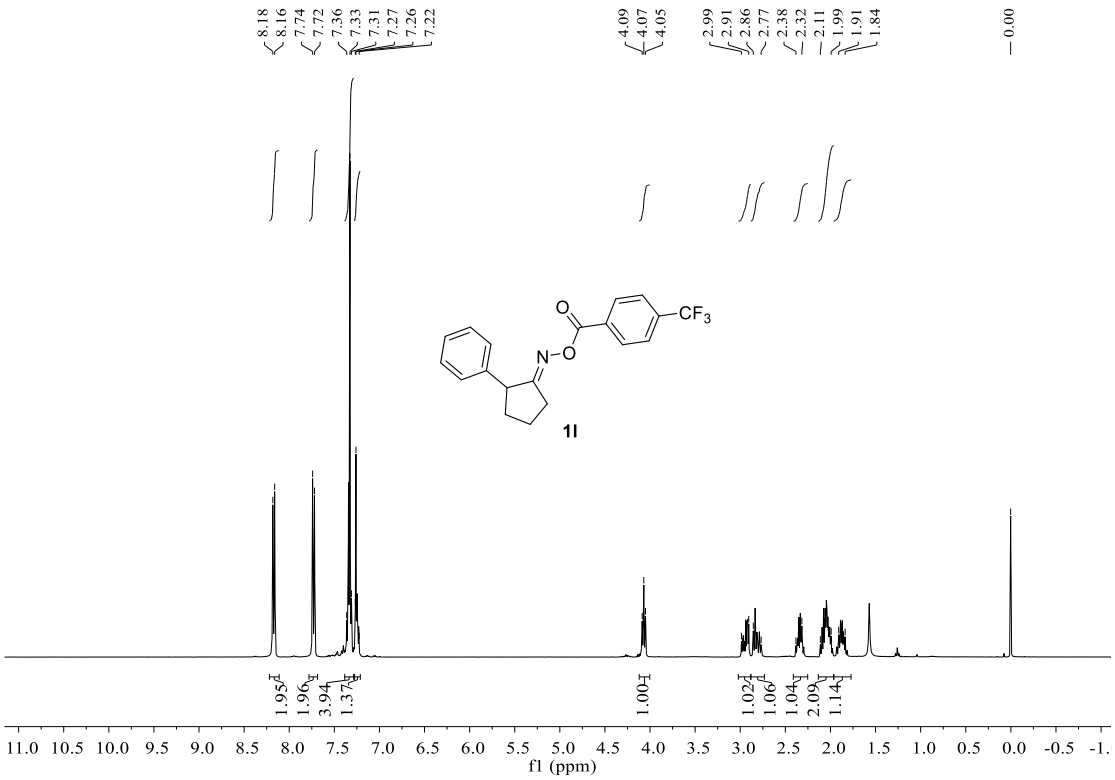
132.24
130.01
128.81
125.73
125.69
125.65
125.61
124.84
123.58
123.38
122.13
77.32
77.00
76.68
39.84
O
N
O
CF3
1k
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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7.72
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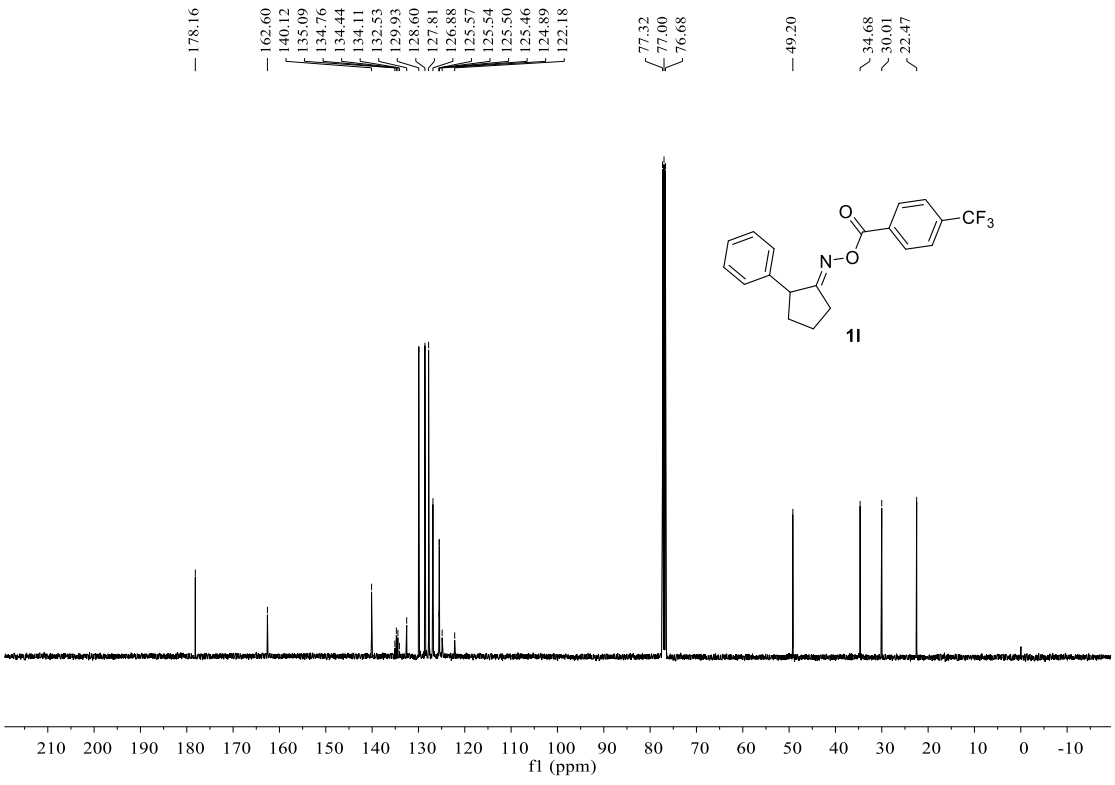
7.31
7.27
7.26
7.22
4.09
4.07
4.05
2.99
2.91
2.86
2.77
2.38
2.32
2.11
1.99
1.91
1.84
0.00
O
CF3
N
O
1l
1.95
1.96
3.94
1.37
1.00
1.02
1.06
1.04
2.09
1.14
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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128.60
127.81
126.88
125.57
125.54
125.50
125.46
124.89
122.18
77.32
77.00
76.68
49.20
34.68
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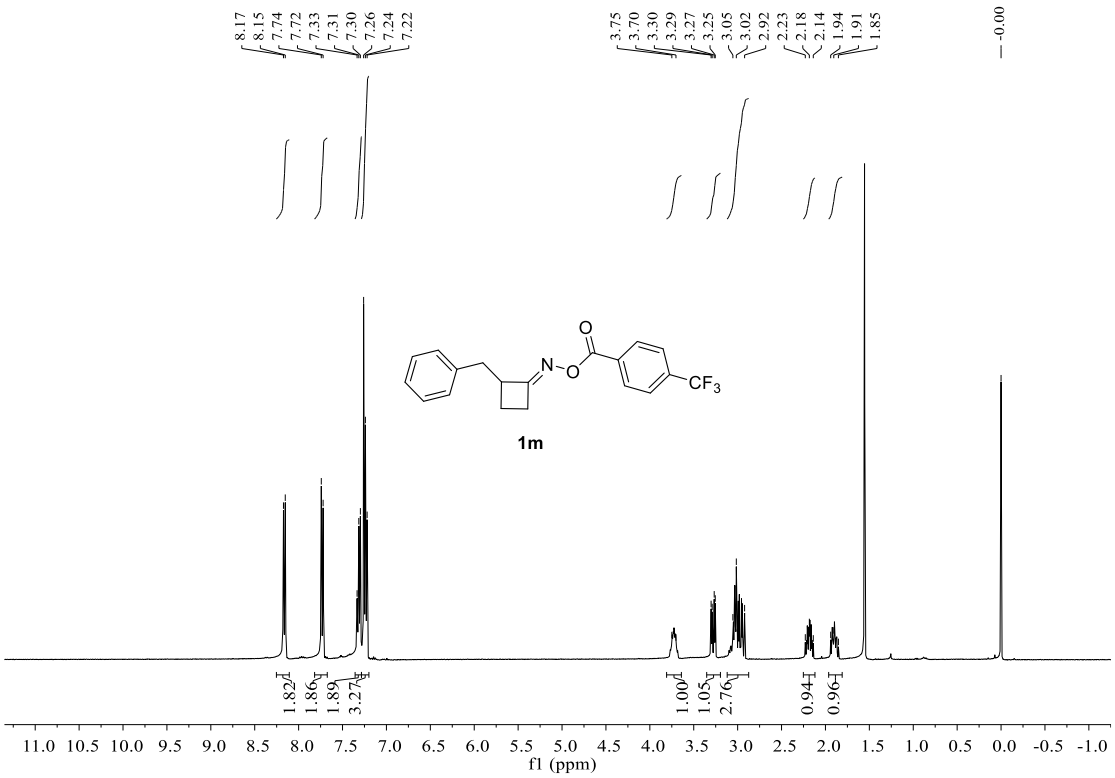
O
CF3
N
O
1l
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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7.72
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7.31
7.30
7.26
7.24
7.22
3.75
3.70
3.30
3.29
3.27
3.25
3.05
3.02
2.92
2.23
2.18
2.14
1.94
1.91
1.85
-0.00
1.82
1.86
1.89
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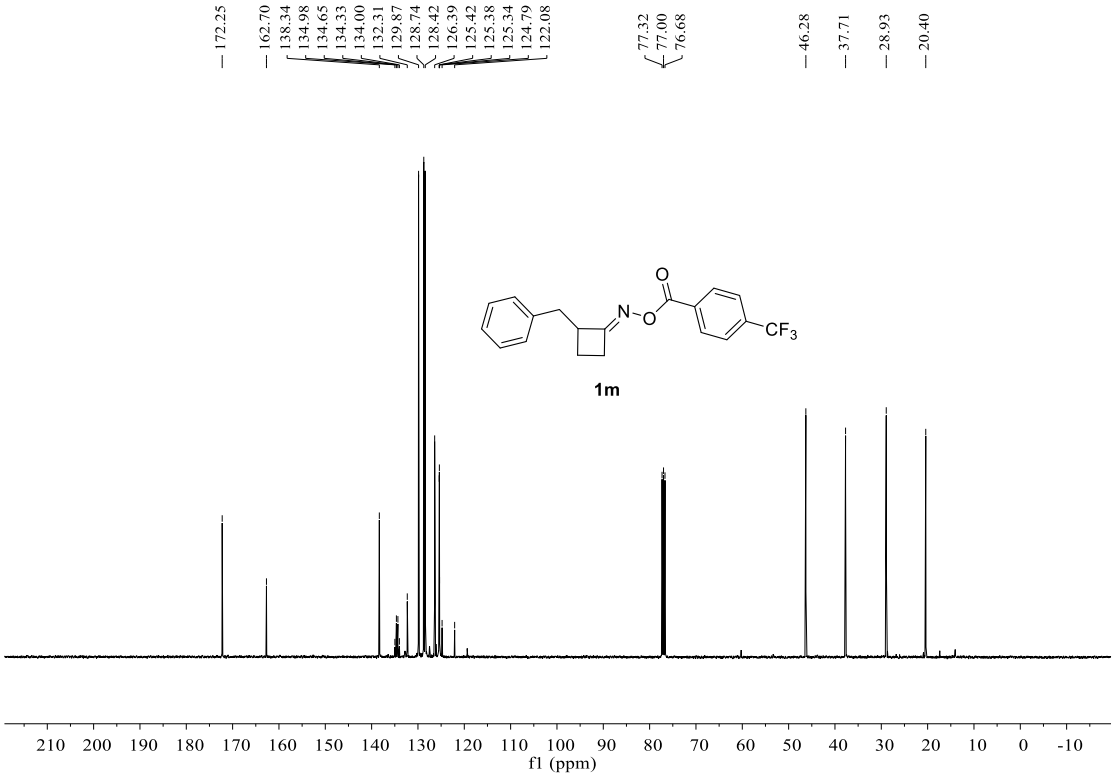
1.00
1.05
2.76
0.94
0.96
f1 (ppm)

O
N
O
CF3

1m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128.42
126.39
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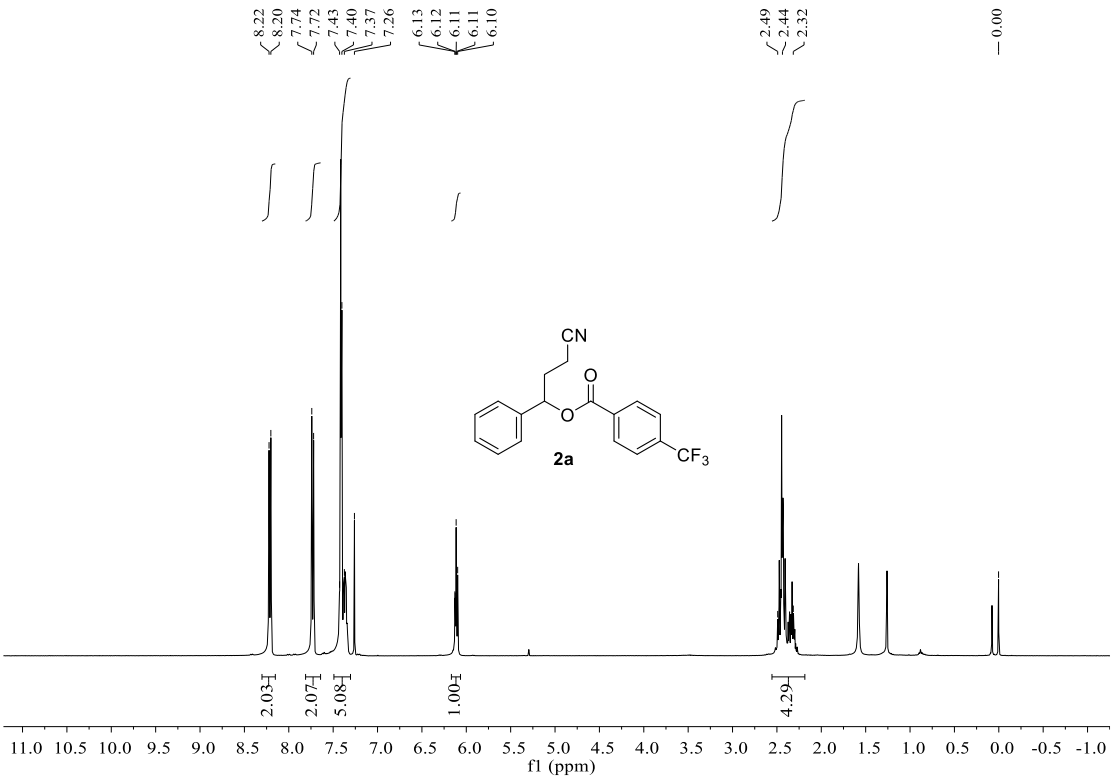
125.38
125.34
124.79
122.08
77.32
77.00
76.68
46.28
37.71
28.93
20.40
f1 (ppm)

O
N
O
CF3

1m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7.26
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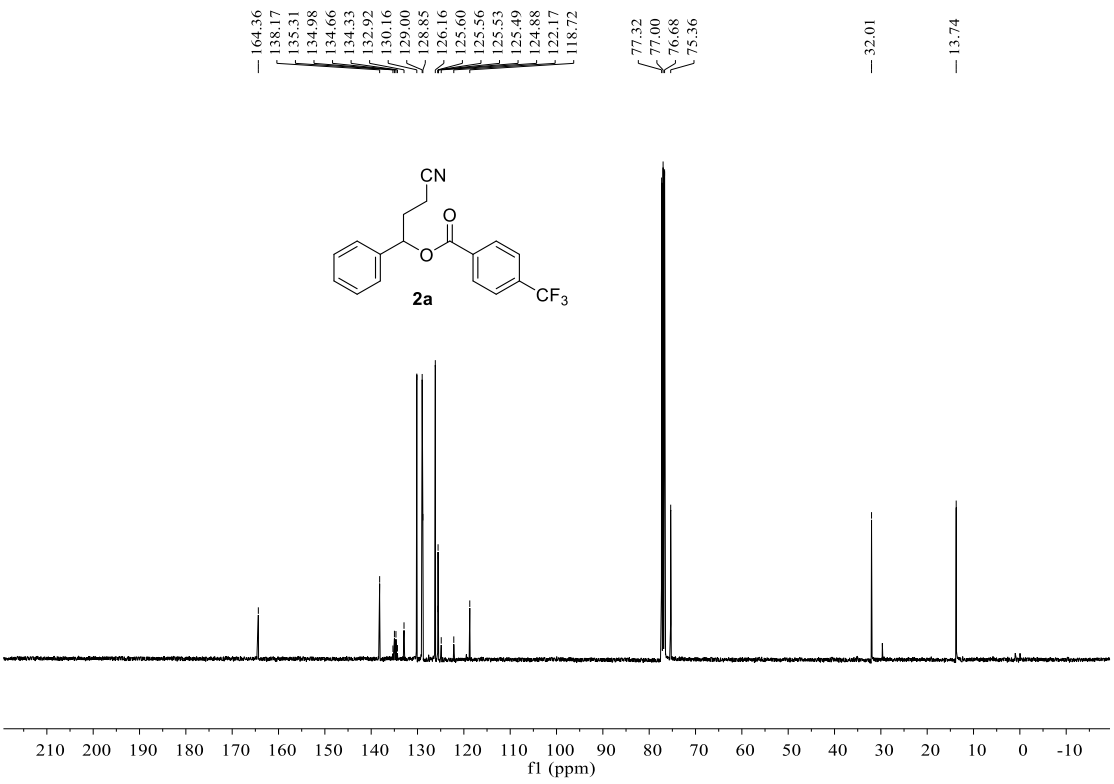
6.12
6.11
6.11
6.10
2.49
2.44
2.32
0.00
CN
O
O
CF3
2a
2.03
2.07
5.08
1.00
4.29
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)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126.16
125.60
125.56
125.53
125.49
124.88
122.17
118.72
77.32
77.00
76.68
75.36
32.01
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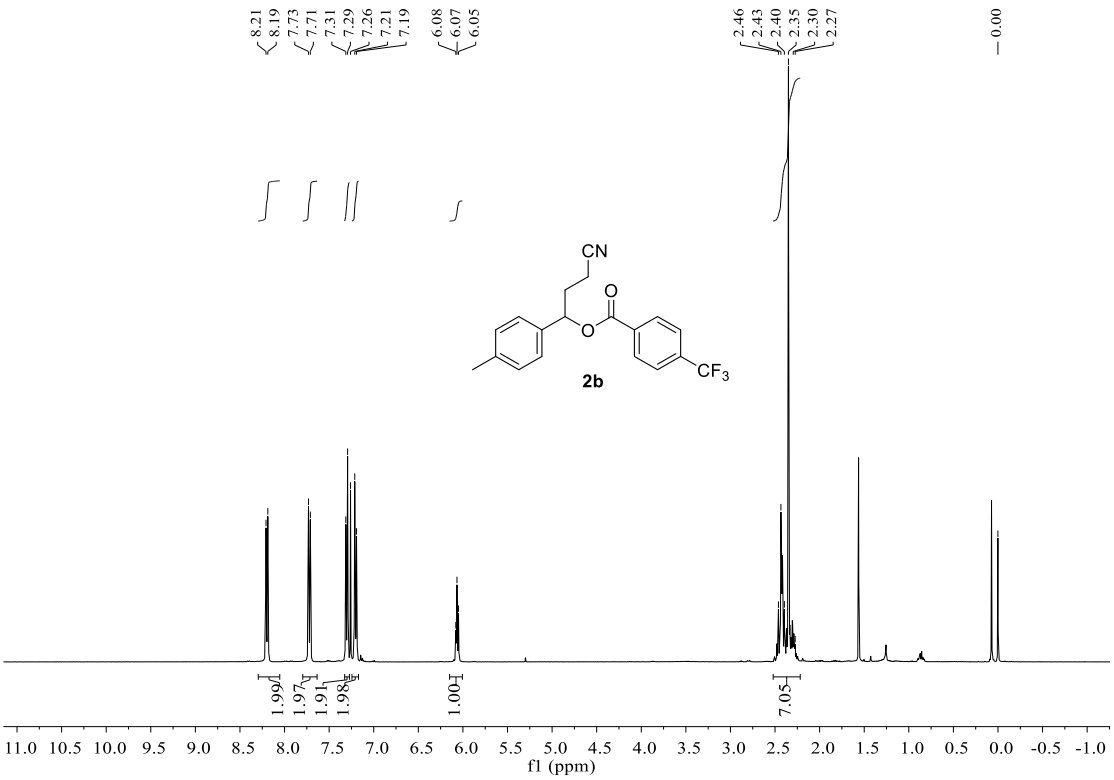
CN
O
O
CF3
2a
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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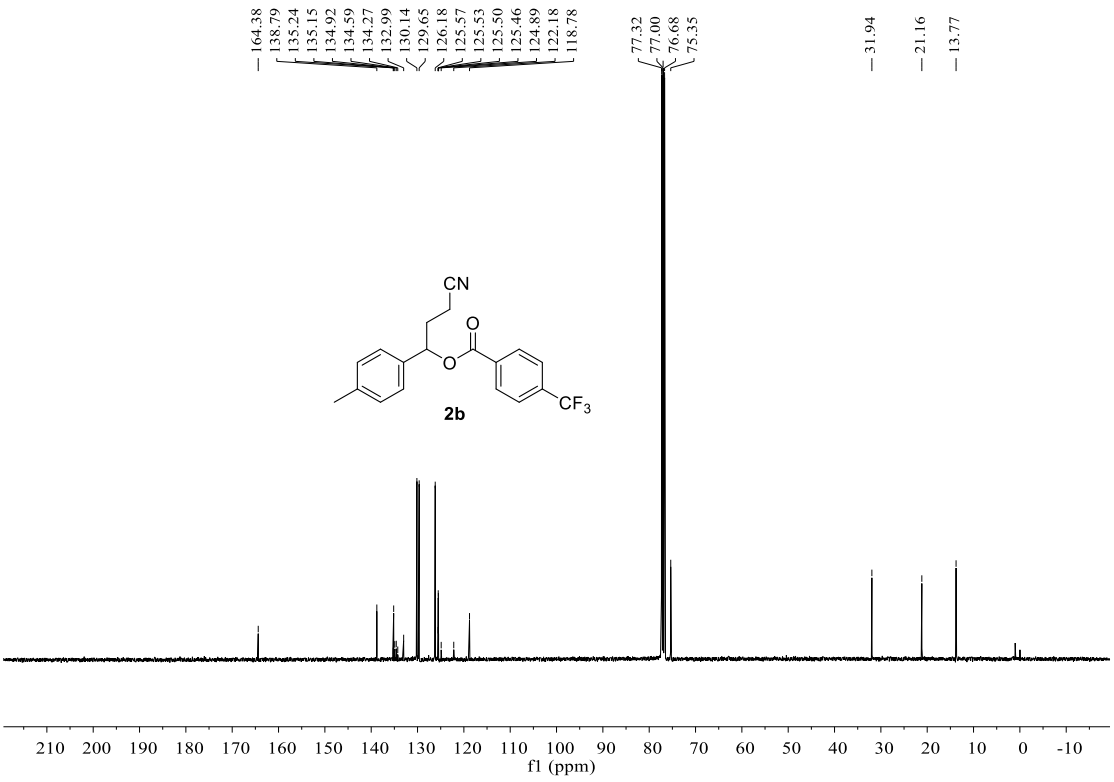
7.26
7.21
7.19
6.08
6.07
6.05
2.46
2.43
2.40
2.35
2.30
2.27
0.00
CN
O
O
CF3
2b
1.99
1.97
1.91
1.98
1.00
7.05
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)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126.18
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125.53
125.50
125.46
124.89
122.18
118.78
77.32
77.00
76.68
75.35
31.94
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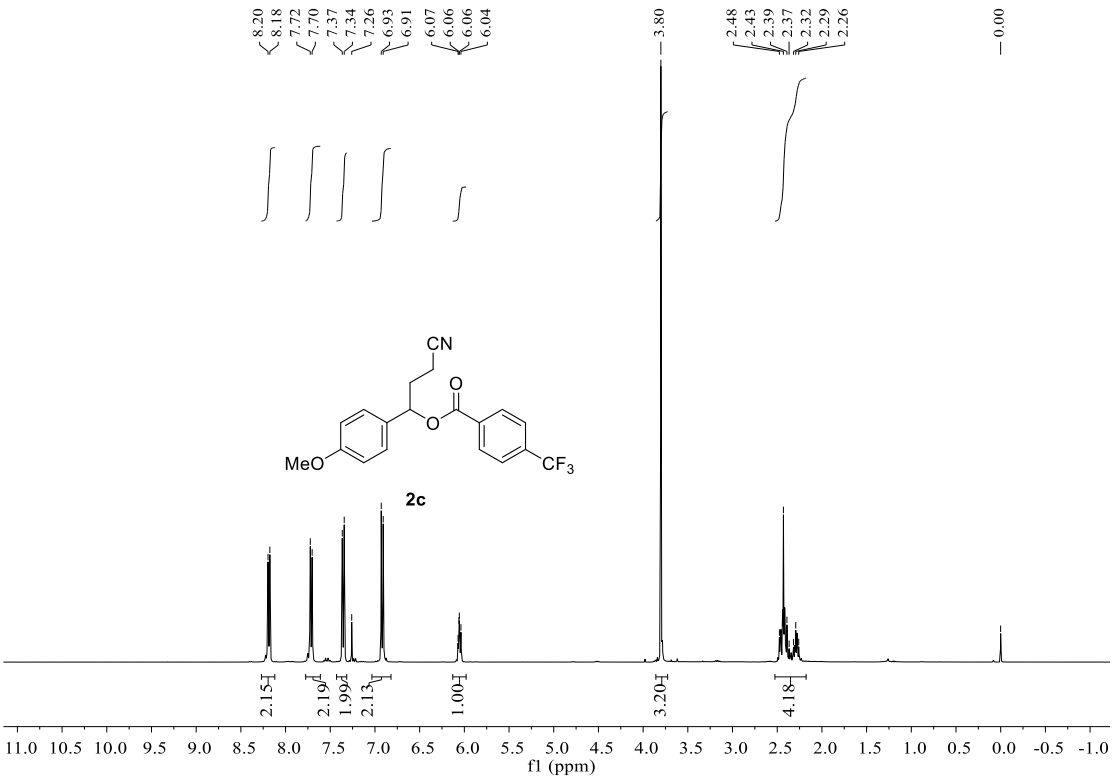
CN
O
O
CF3
2b
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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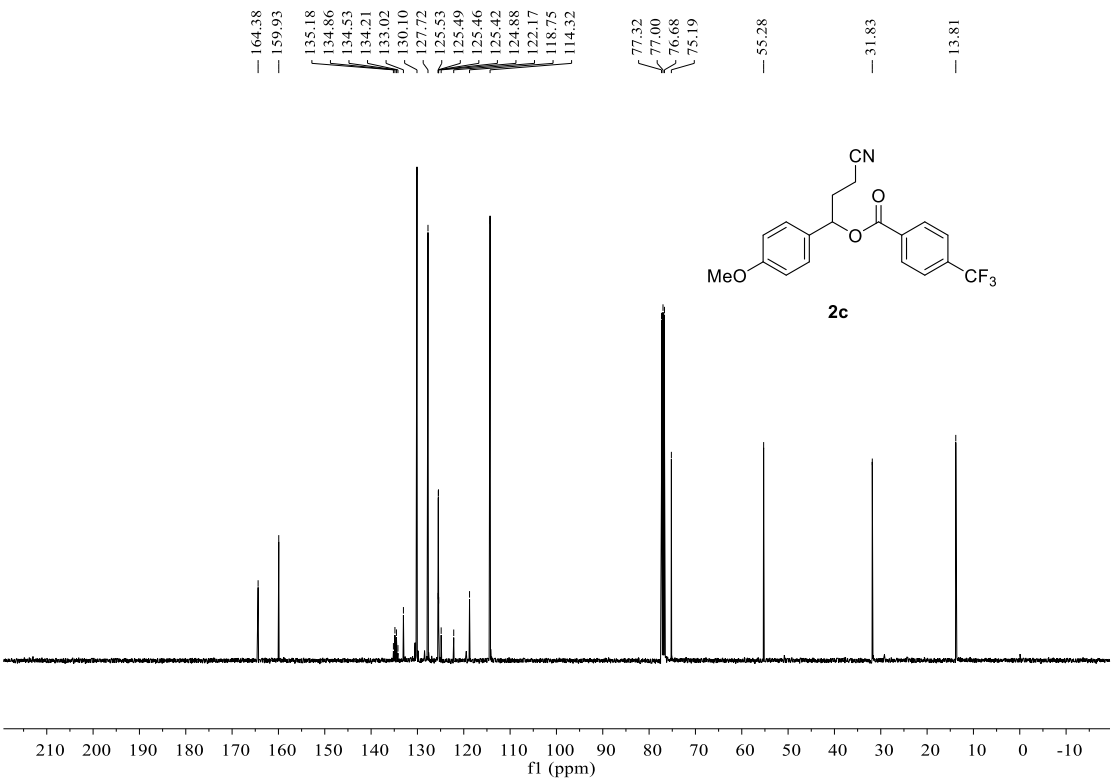
6.07
6.06
6.06
6.04
3.80
2.48
2.43
2.39
2.37
2.32
2.29
2.26
0.00
CN
O
O
MeO
CF3
2c
2.15
2.19
1.99
2.13
1.00
3.20
4.18
f1 (ppm)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125.49
125.46
125.42
124.88
122.17
118.75
114.32
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75.19
55.28
31.83
13.81
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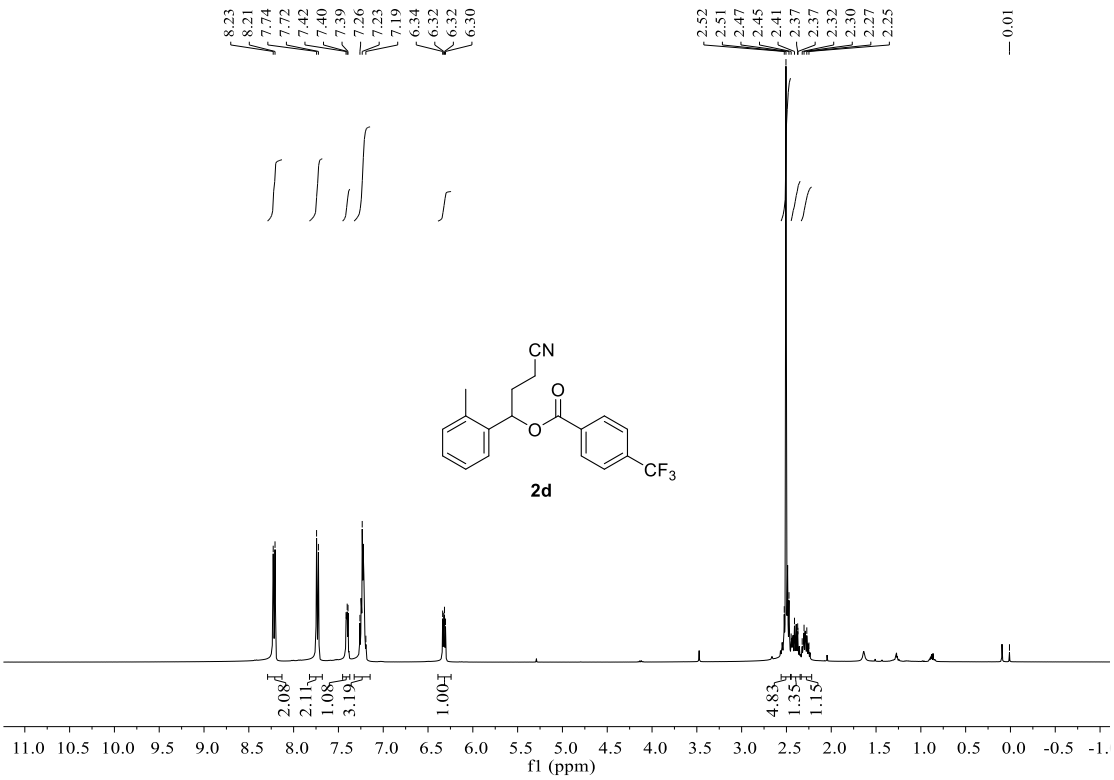
O
O
MeO
CF3
2c
f1 (ppm)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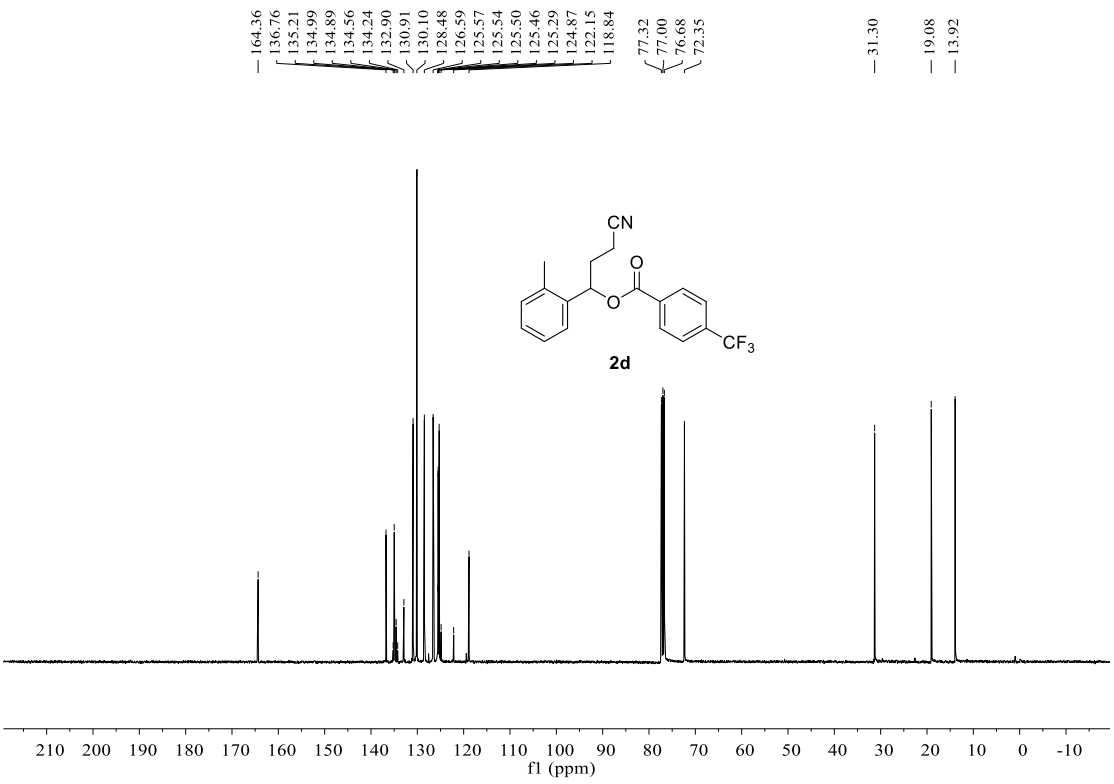
7.23
7.19
6.34
6.32
6.32
6.30
2.52
2.51
2.47
2.45
2.41
2.37
2.37
2.32
2.30
2.27
2.25
0.01
CN
O
O
CF3
2d
2.08
2.11
1.08
3.19
1.00
4.83
1.35
1.15
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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128.48
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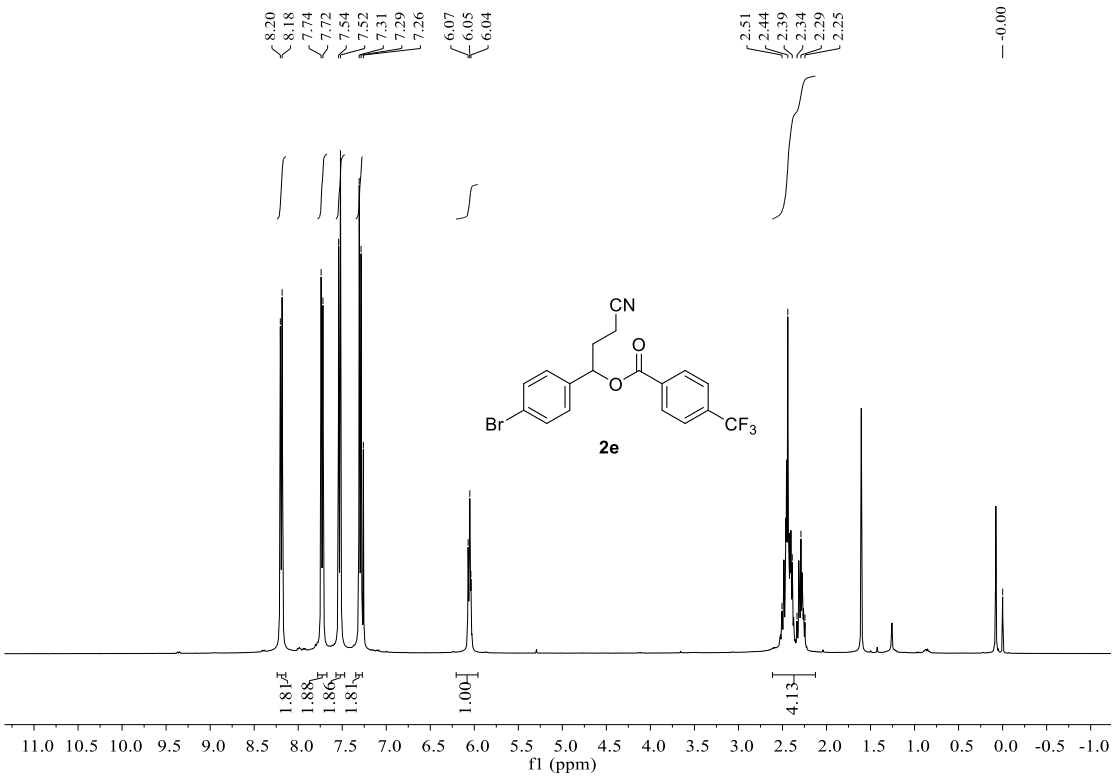
125.57
125.54
125.50
125.46
125.29
124.87
122.15
118.84
77.32
77.00
76.68
72.35
31.30
19.08
13.92
CN
O
O
CF3
2d
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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7.72
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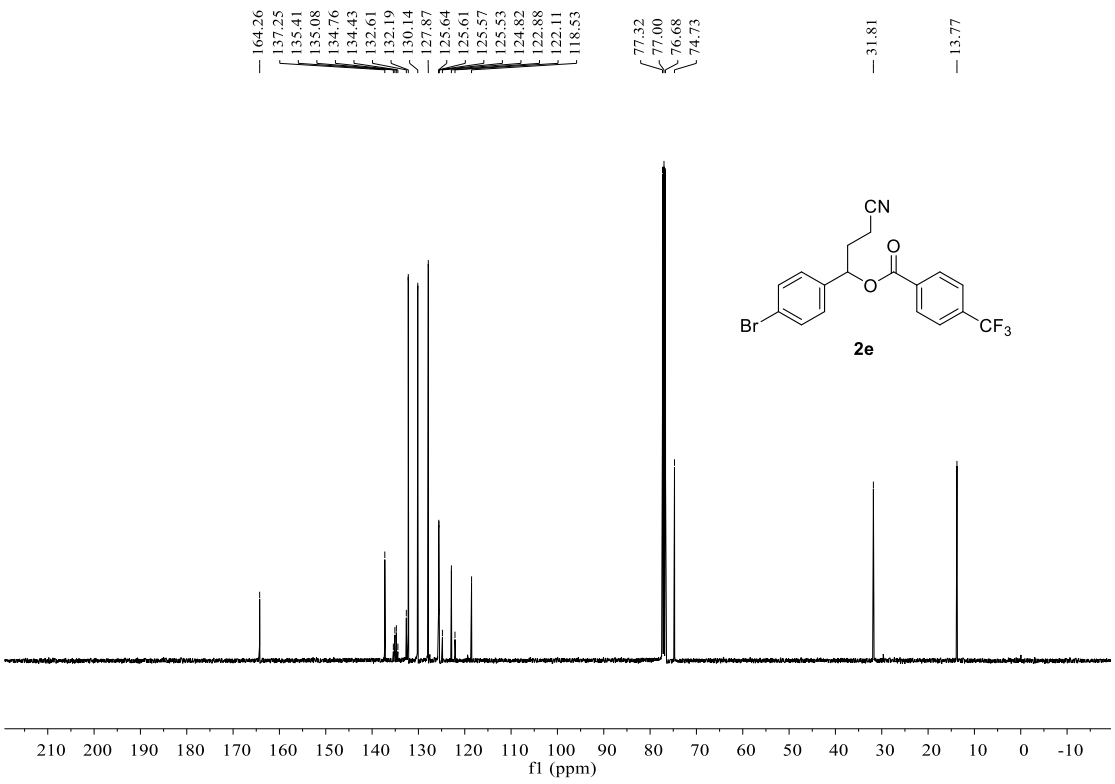
7.52
7.31
7.29
7.26
6.07
6.05
6.04
2.51
2.44
2.39
2.34
2.29
2.25
-0.00
CN
O
O
Br
CF3
2e
1.81
1.88
1.86
1.81
1.00
4.13
f1 (ppm)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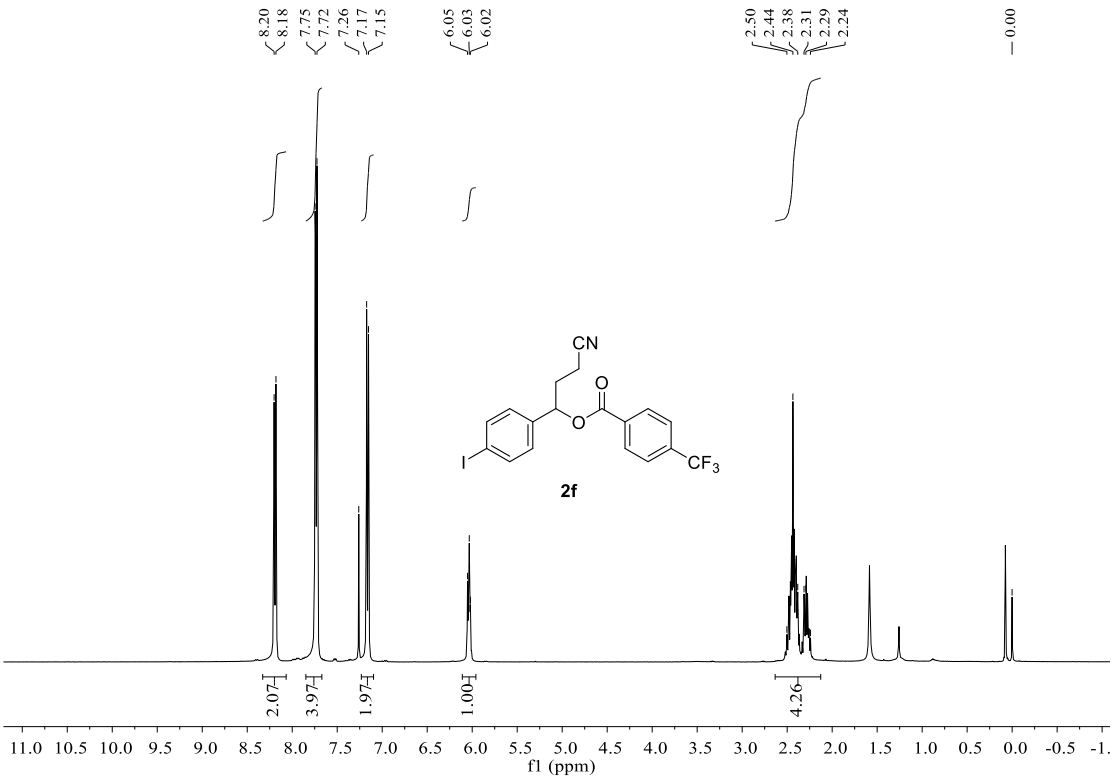
127.87
125.64
125.61
125.57
125.53
124.82
122.88
122.11
118.53
77.32
77.00
76.68
74.73
31.81
13.77
CN
O
O
Br
CF3
2e
f1 (ppm)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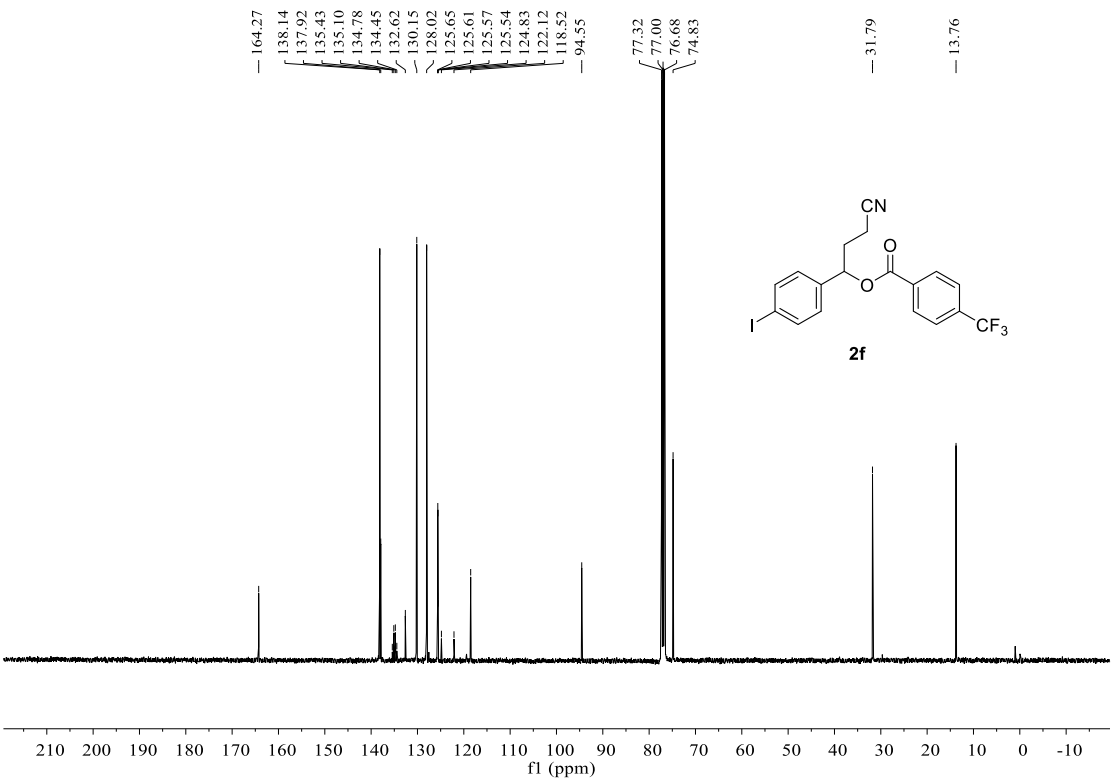
7.72
7.26
7.17
7.15
6.05
6.03
6.02
2.50
2.44
2.38
2.31
2.29
2.24
0.00
CN
O
O
I
CF3
2f
2.07
3.97
1.97
1.00
4.26
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)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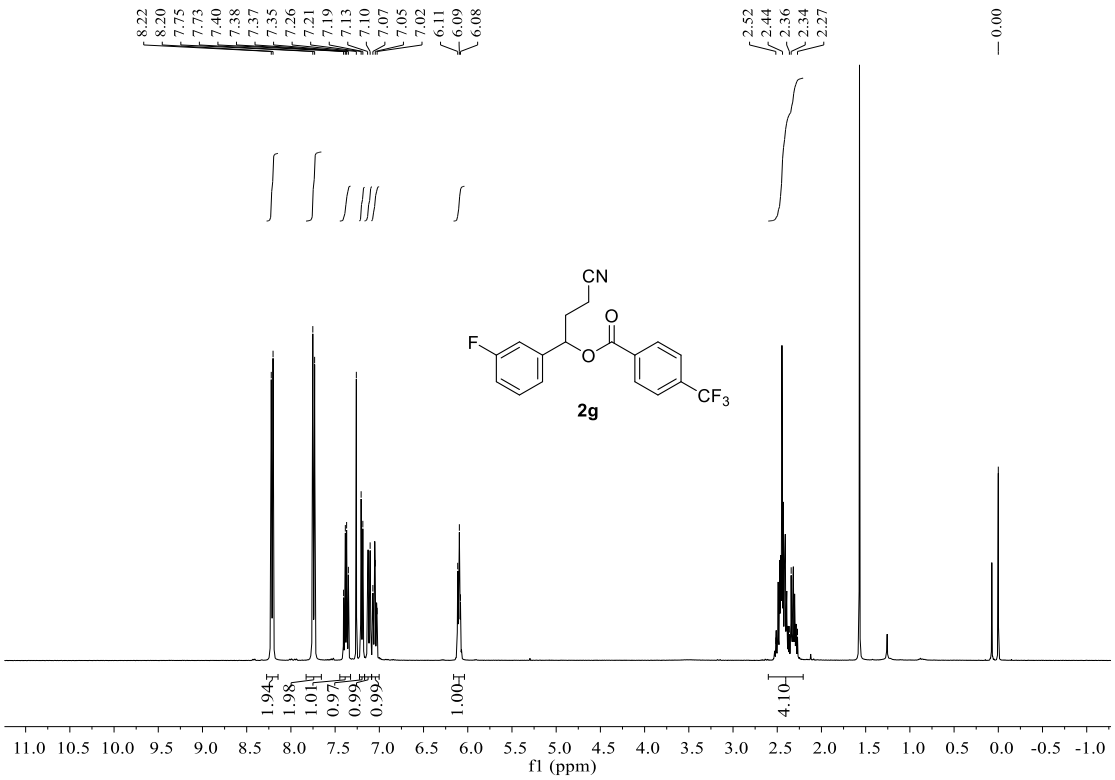
134.45
132.62
130.15
128.02
125.65
125.61
125.57
125.54
124.83
122.12
118.52
94.55
77.32
77.00
76.68
74.83
31.79
13.76
CN
O
O
I
CF3
2f
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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7.35
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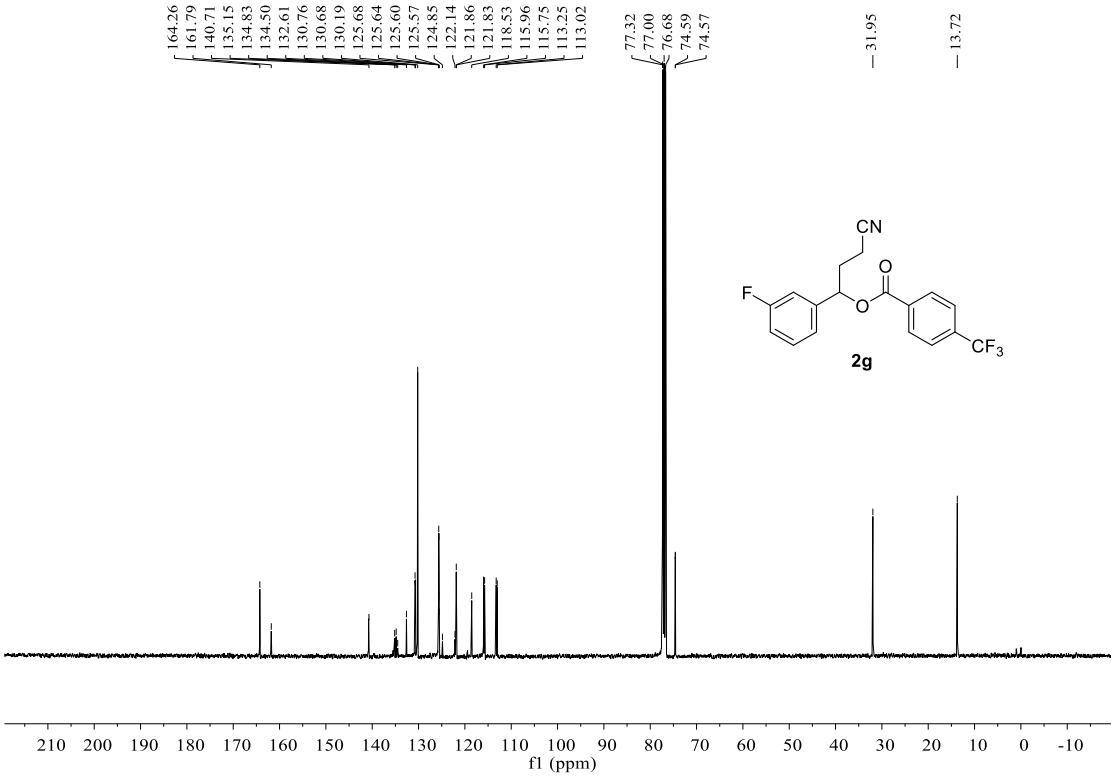
7.21
7.19
7.13
7.10
7.07
7.05
7.02
6.11
6.09
6.08
2.52
2.44
2.36
2.34
2.27
0.00
CN
O
F
O
CF3
2g
1.94
1.98
1.01
0.97
0.99
0.99
1.00
4.10
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)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125.60
125.57
124.85
122.14
121.86
121.83
118.53
115.96
115.75
113.25
113.02
77.32
77.00
76.68
74.59
74.57
31.95
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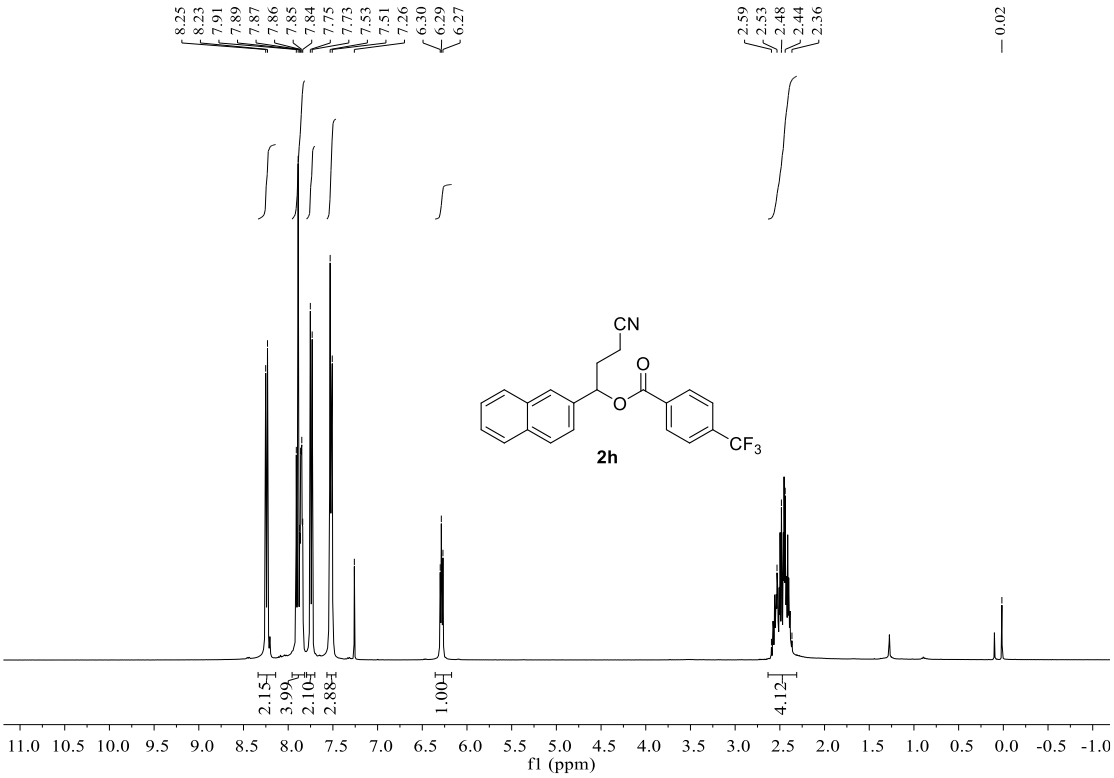
O
F
O
CF3
2g
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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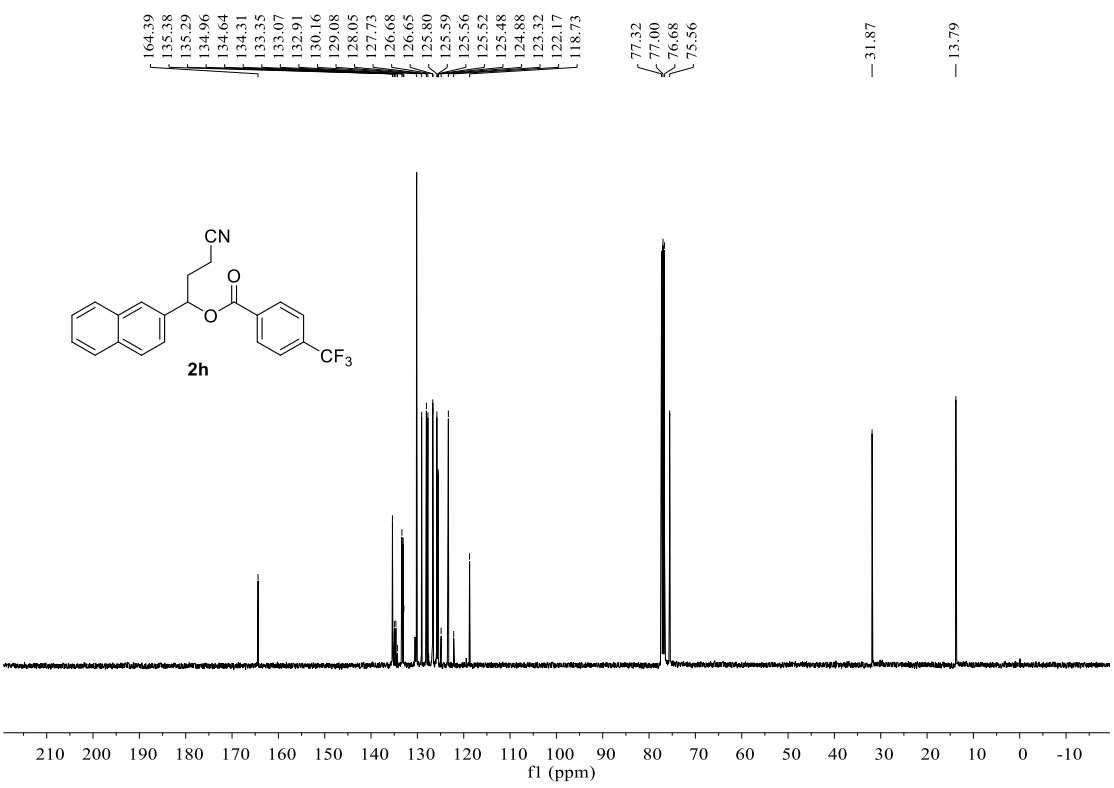
7.84
7.75
7.73
7.53
7.51
7.26
6.30
6.29
6.27
2.59
2.53
2.48
2.44
2.36
0.02
CN
O
O
CF3
2h
2.15
3.99
2.10
2.88
1.00
4.12
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)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130.16
129.08
128.05
127.73
126.68
126.65
125.80
125.59
125.56
125.52
125.48
124.88
123.32
122.17
118.73
77.32
77.00
76.68
75.56
31.87
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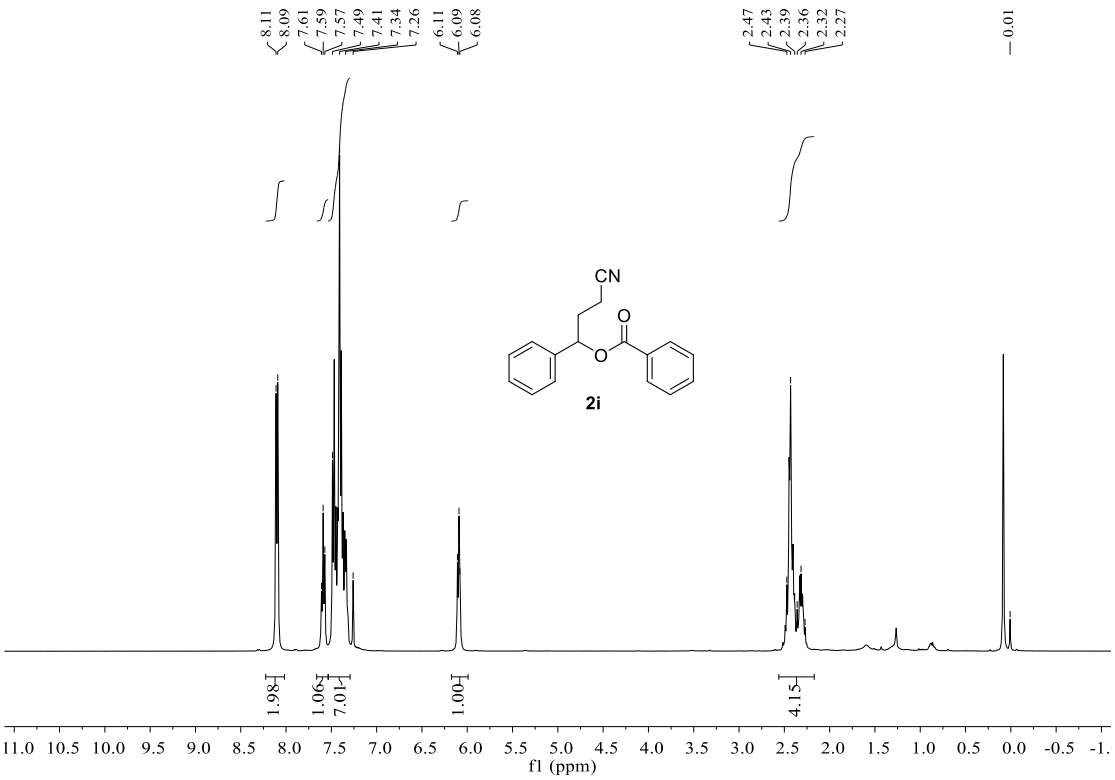
CN
O
O
CF3
2h
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


8.11
8.09
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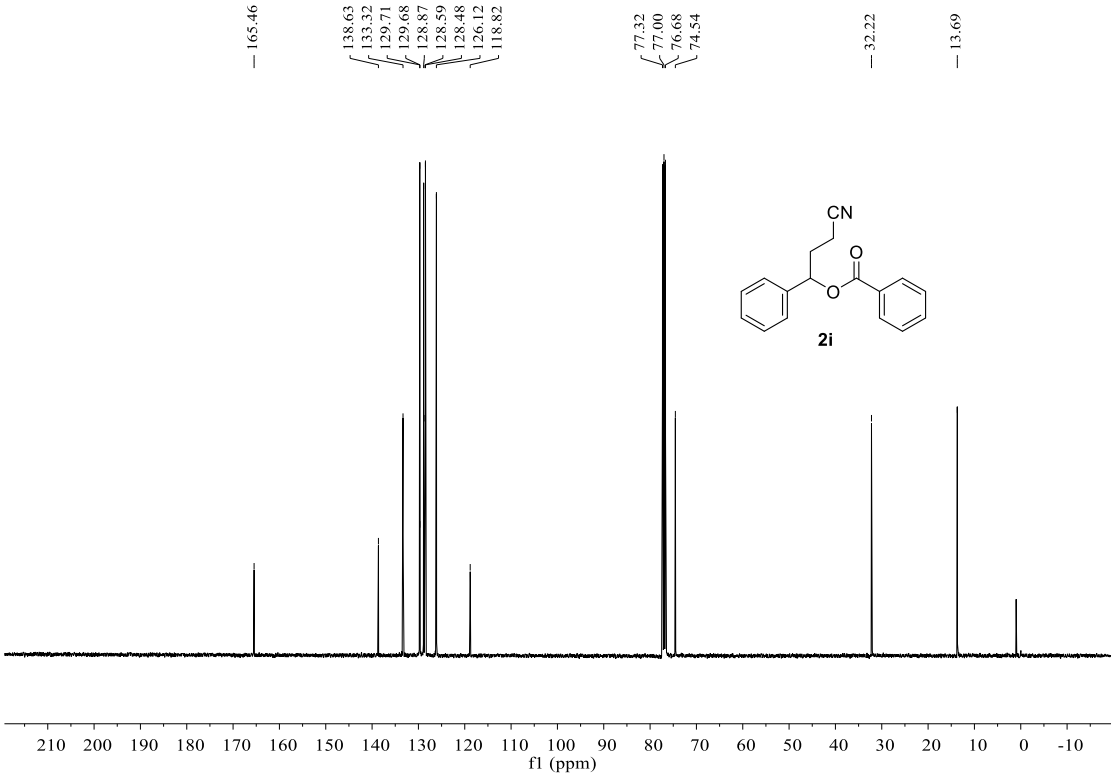
7.57
7.49
7.41
7.34
7.26
6.11
6.09
6.08
2.47
2.43
2.39
2.36
2.32
2.27
0.01
CN
O
O
2i
1.98
1.06
7.01
1.00
4.15
f1 (ppm)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128.87
128.59
128.48
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77.00
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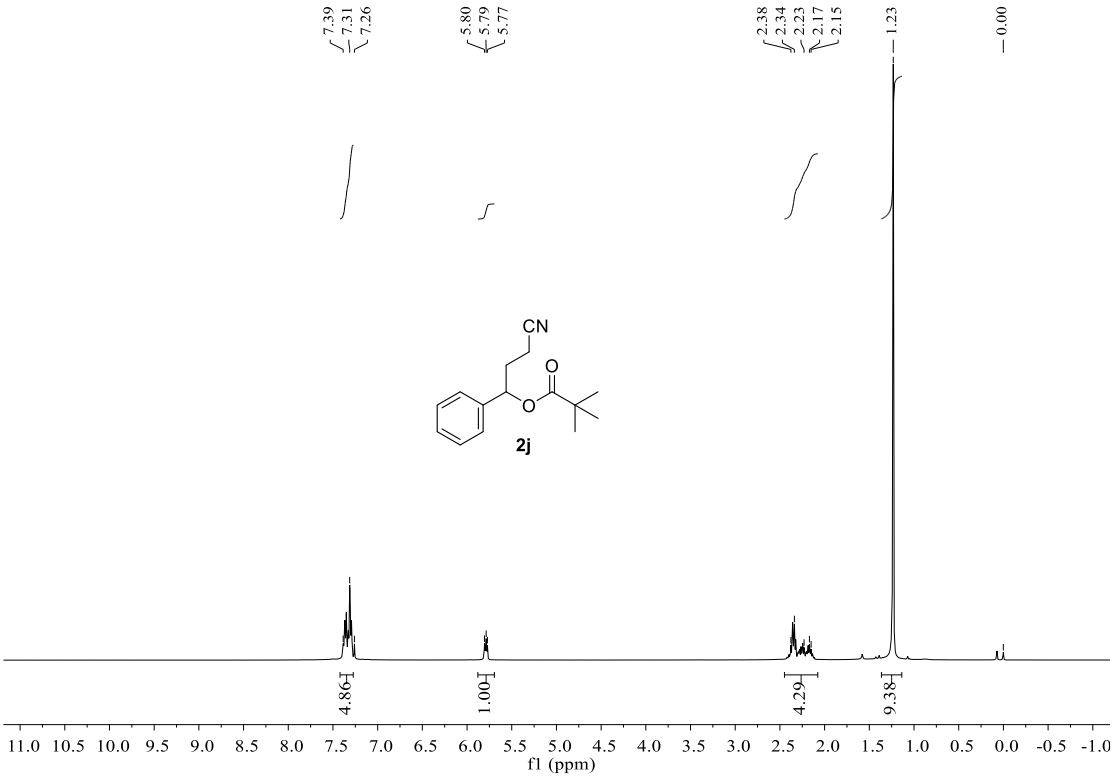
32.22
13.69
CN
O
O
2i
f1 (ppm)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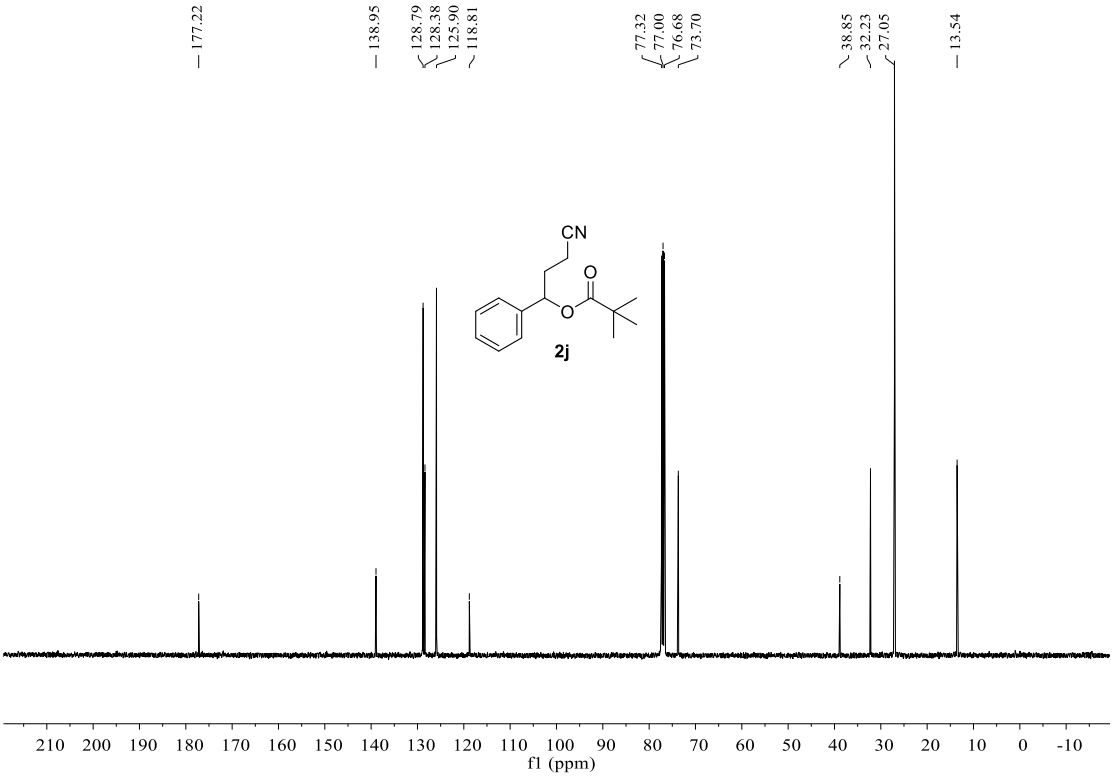
7.31
7.26
5.80
5.79
5.77
2.38
2.34
2.23
2.17
2.15
1.23
0.00
CN
O
O
2j
4.86
1.00
4.29
9.38
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)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77.00
76.68
73.70
38.85
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27.05
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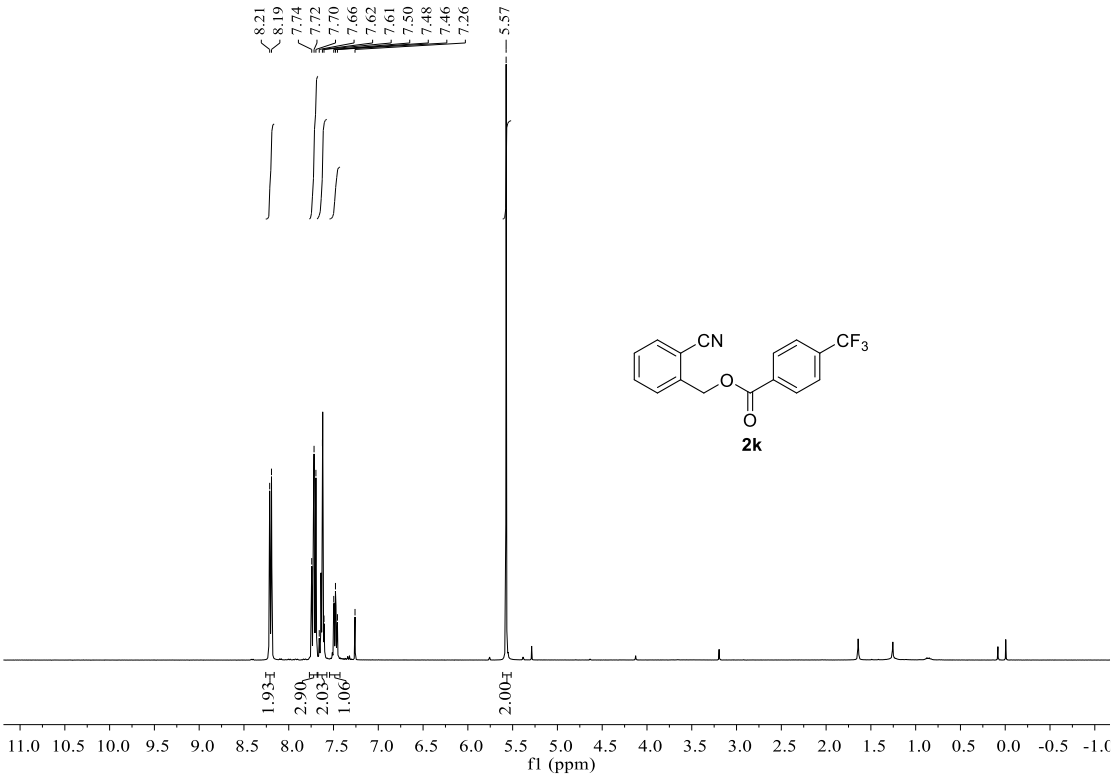
CN
O
O
2j
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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8.19
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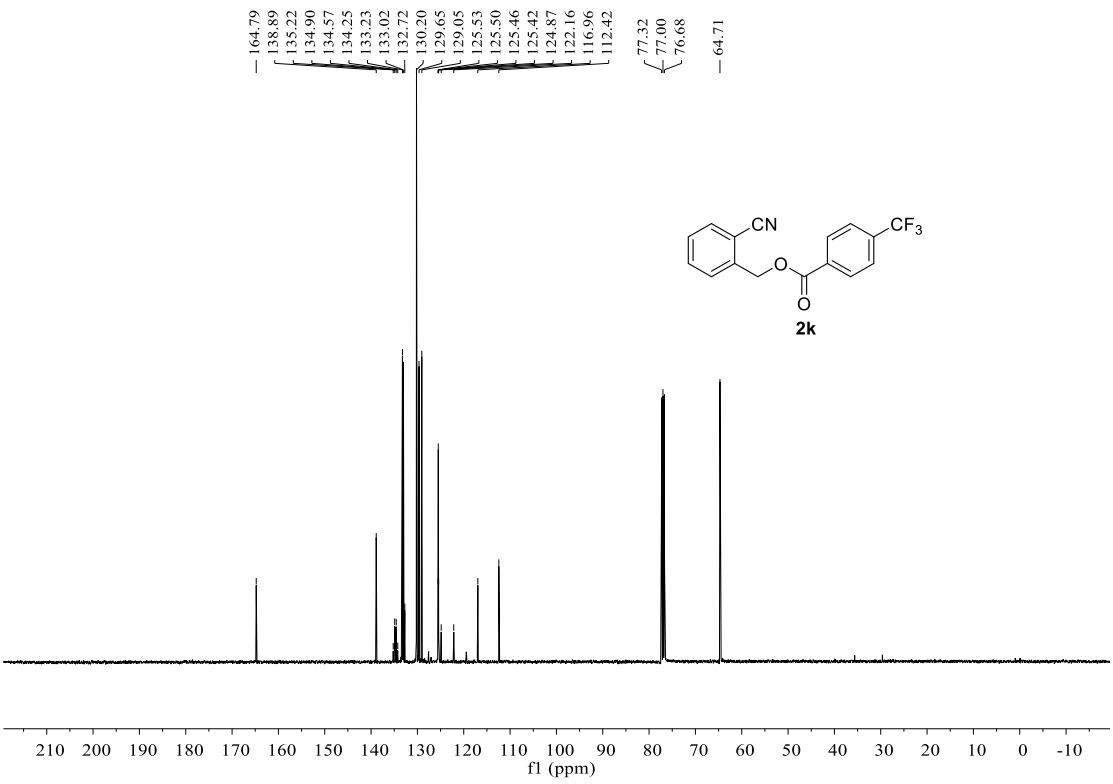
7.66
7.62
7.61
7.50
7.48
7.46
7.26
5.57
CN
CF3
O
O
2k
1.93
2.90
2.03
1.06
2.00
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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133.02
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130.20
129.65
129.05
125.53
125.50
125.46
125.42
124.87
122.16
116.96
112.42
77.32
77.00
76.68
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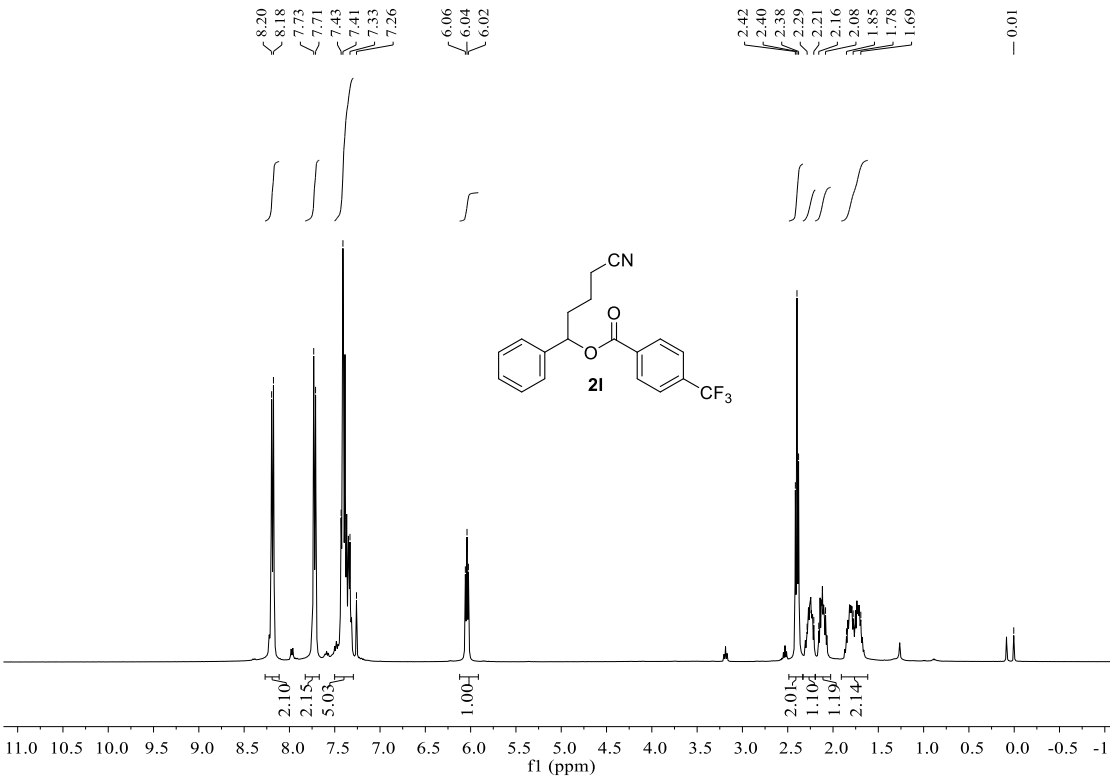
CN
CF3
O
O
2k
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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7.43
7.41
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7.26
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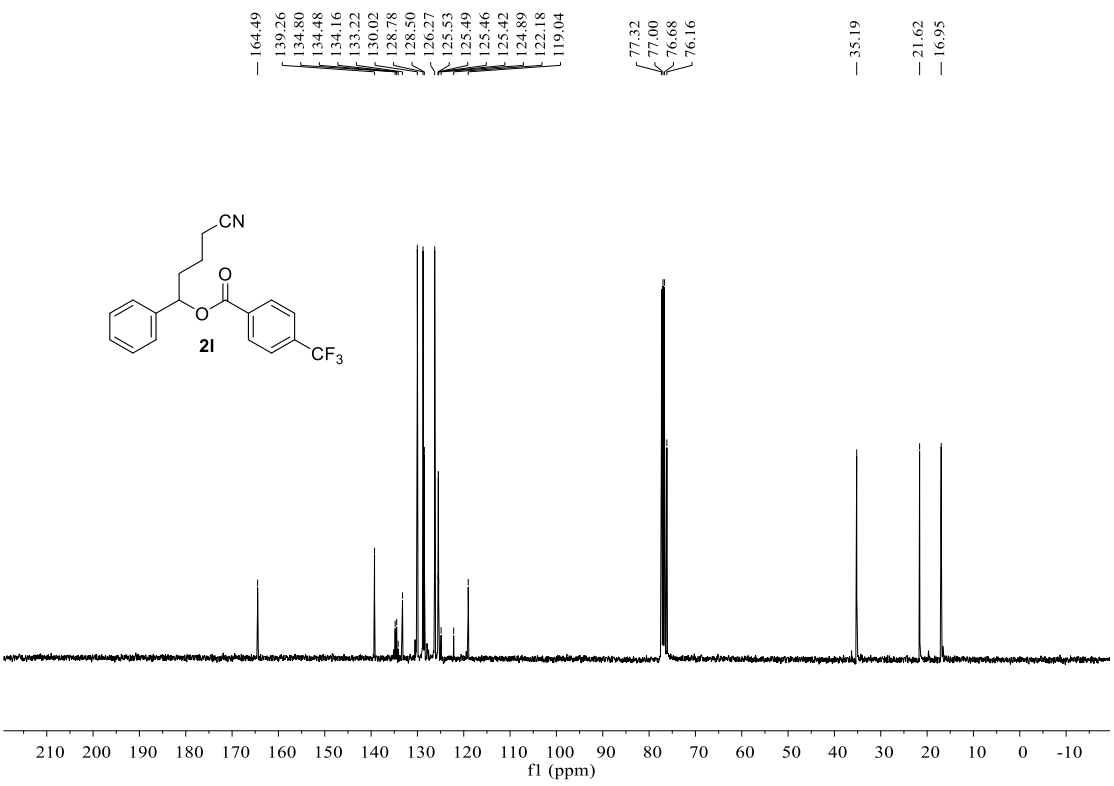
6.04
6.02
2.42
2.40
2.38
2.29
2.21
2.16
2.08
1.85
1.78
1.69
0.01
CN
O
O
2l
CF3
2.10
2.15
5.03
1.00
2.01
1.10
1.19
2.14
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)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128.50
126.27
125.53
125.49
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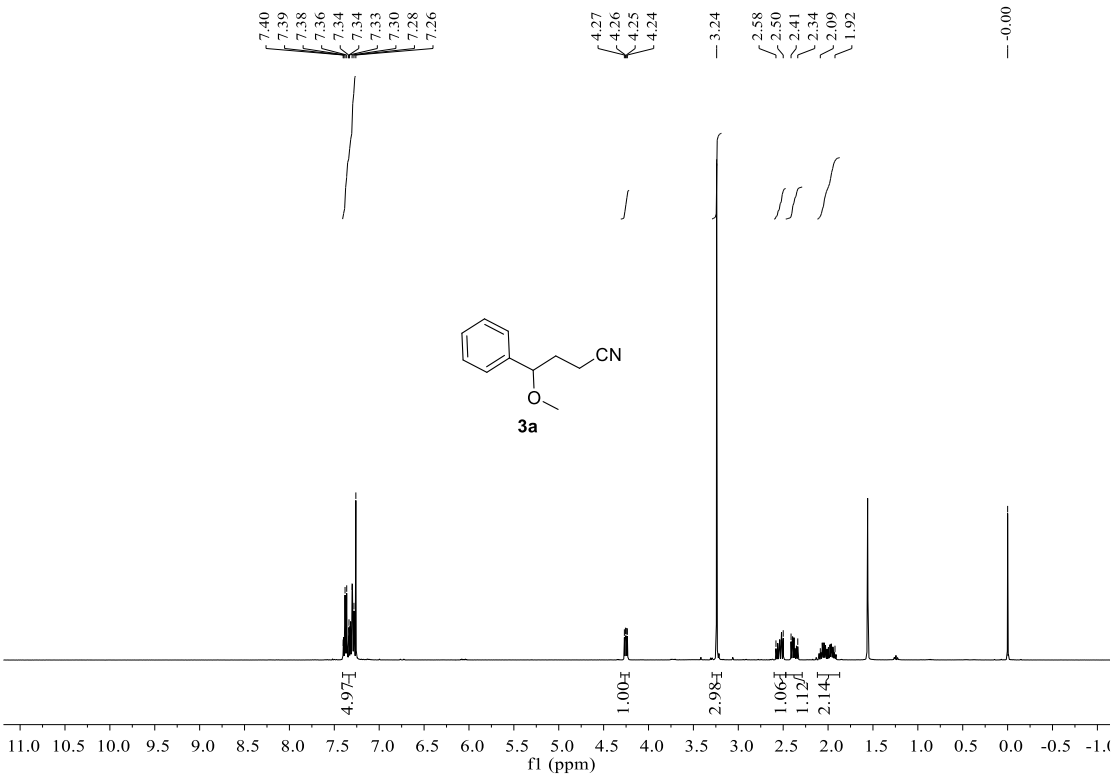
125.42
124.89
122.18
119.04
77.32
77.00
76.68
76.16
35.19
21.62
16.95
CN
O
O
2l
CF3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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7.33
7.30
7.28
7.26
4.27
4.26
4.25
4.24
3.24
2.58
2.50
2.41
2.34
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CN
O
3a
4.97
1.00
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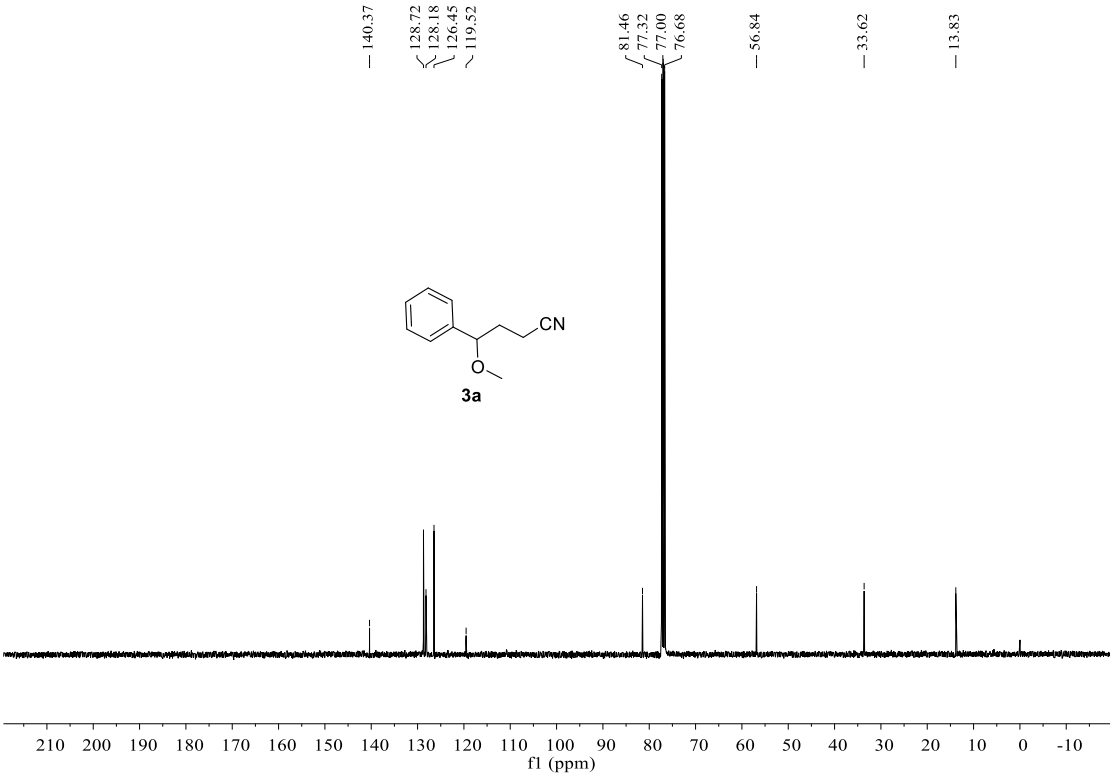
1.06
1.12
2.14
f1 (ppm)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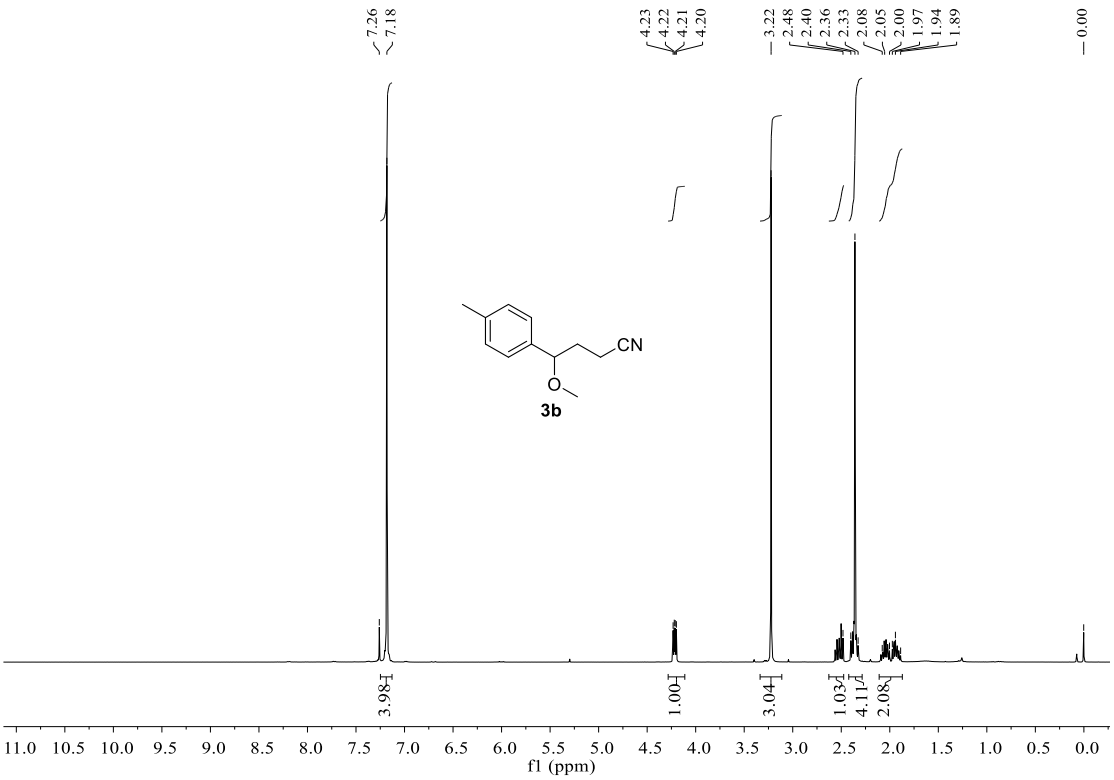
77.00
76.68
56.84
33.62
13.83
CN
O
3a
f1 (ppm)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7.18
4.23
4.22
4.21
4.20
3.22
2.48
2.40
2.36
2.33
2.08
2.05
2.00
1.97
1.94
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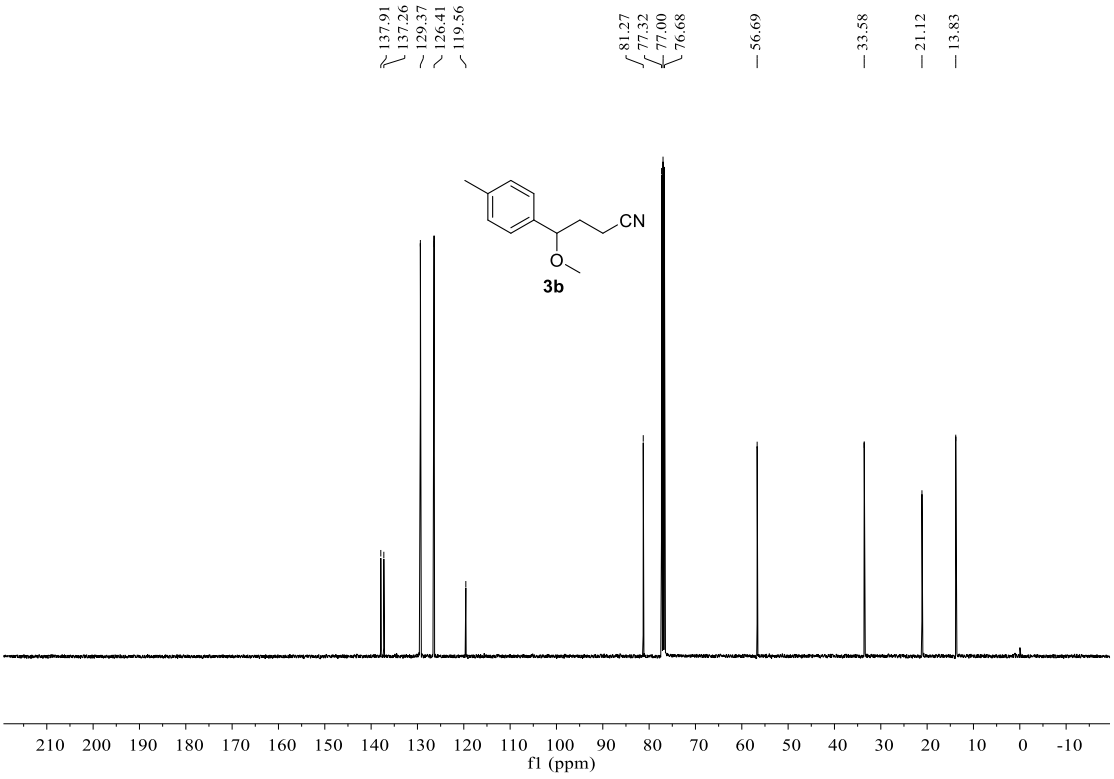
CN
O
3b
3.98
1.00
3.04
1.03
4.11
2.08
f1 (ppm)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77.00
76.68
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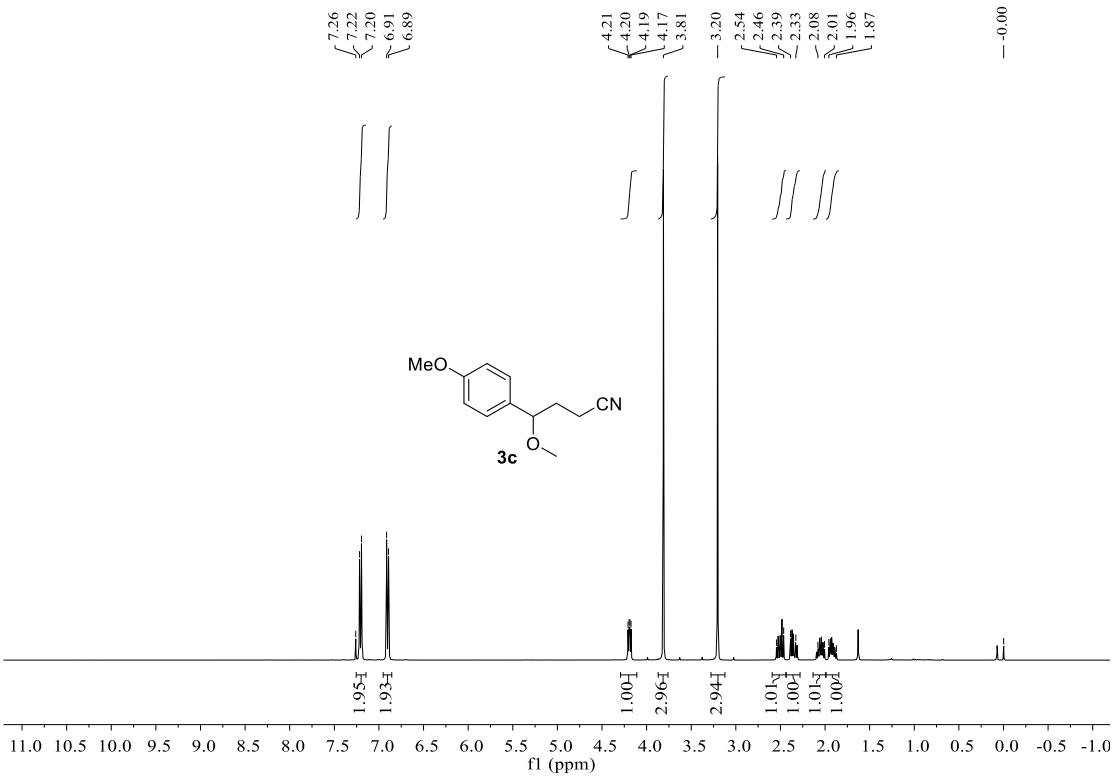
33.58
21.12
13.83
CN
O
3b
f1 (ppm)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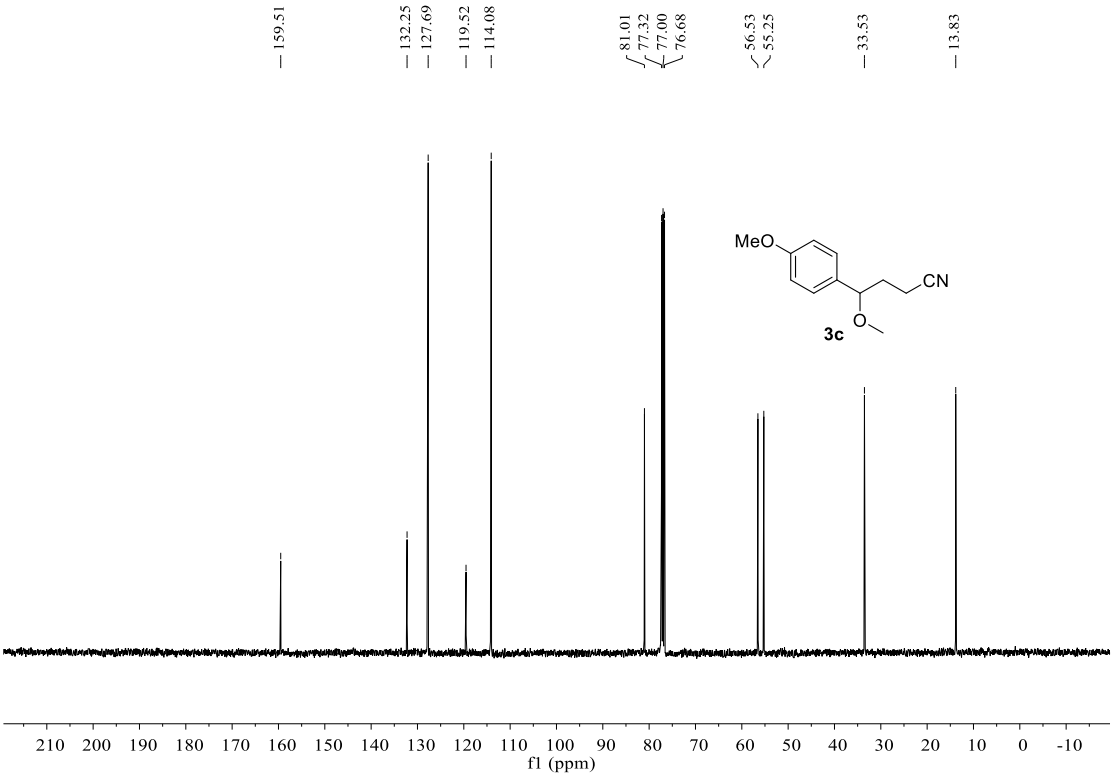
7.20
6.91
6.89
4.21
4.20
4.19
4.17
3.81
3.20
2.54
2.46
2.39
2.33
2.08
2.01
1.96
1.87
-0.00
MeO
CN
O
3c
1.95
1.93
1.00
2.96
2.94
1.01
1.00
1.01
1.00
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)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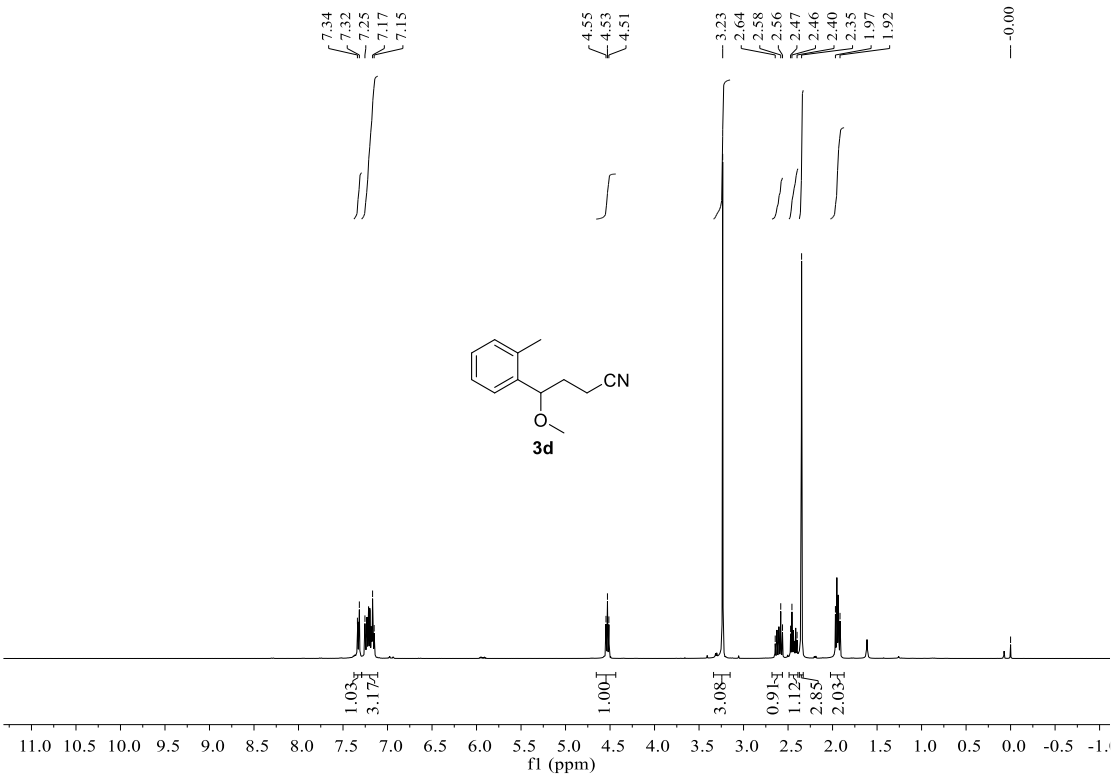
81.01
77.32
77.00
76.68
56.53
55.25
33.53
13.83
MeO
CN
O
3c
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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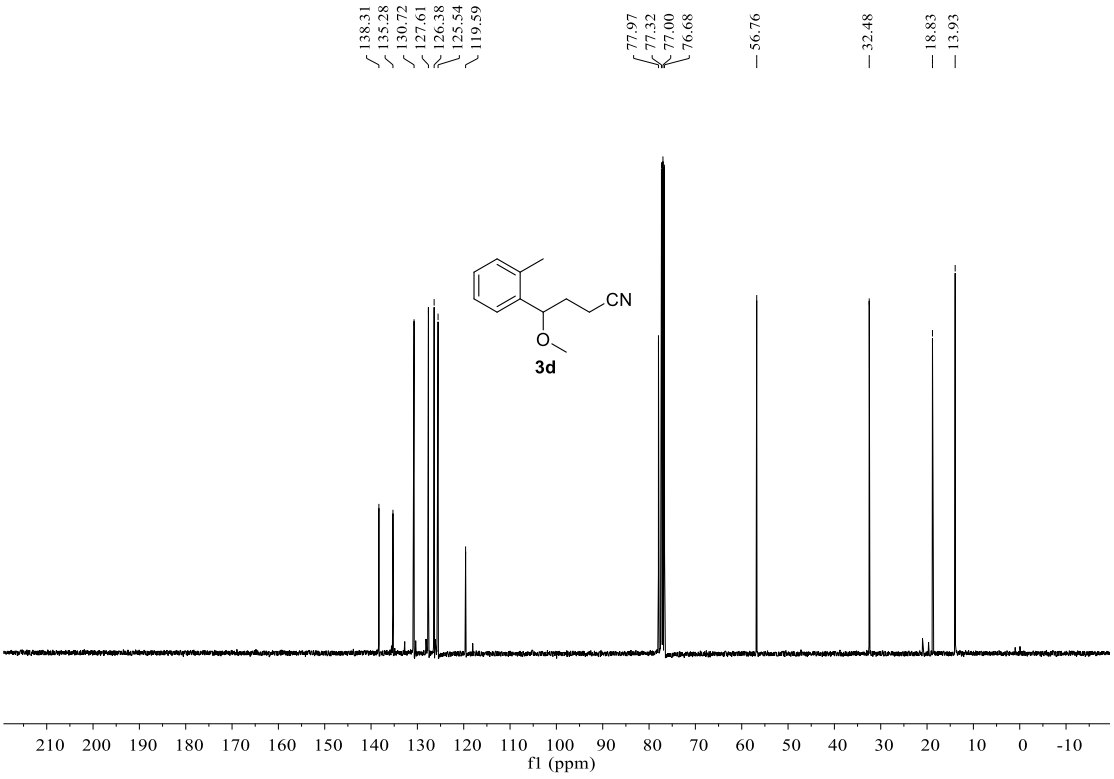
4.53
4.51
3.23
2.64
2.58
2.56
2.47
2.46
2.40
2.35
1.97
1.92
-0.00
CN
O
3d
1.03
3.17
1.00
3.08
0.91
1.12
2.85
2.03
f1 (ppm)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125.54
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77.00
76.68
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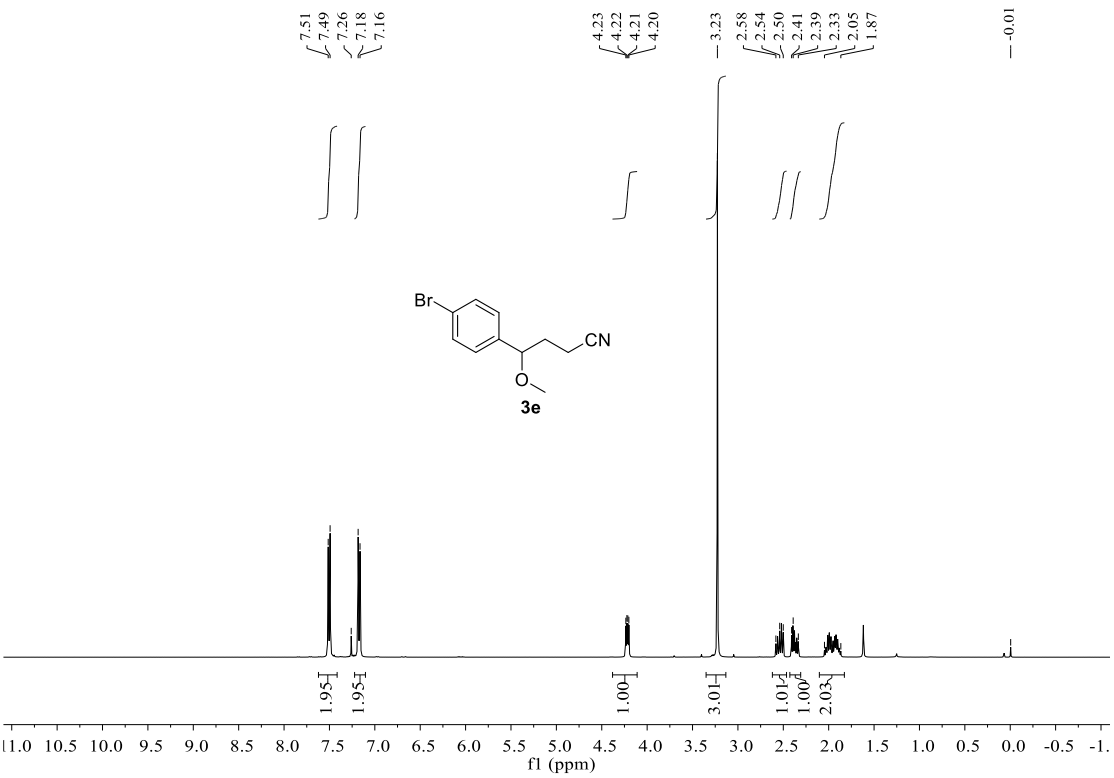
32.48
18.83
13.93
CN
O
3d
f1 (ppm)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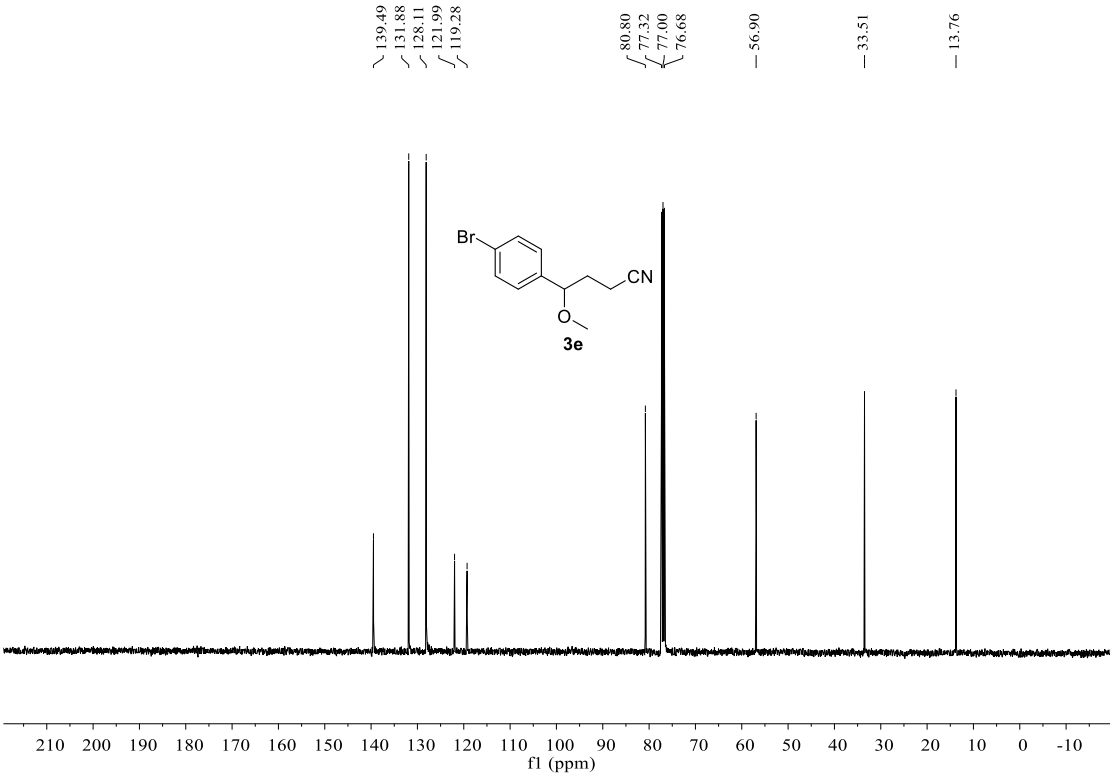
4.21
4.20
3.23
2.58
2.54
2.50
2.41
2.39
2.33
2.05
1.87
-0.01
Br
CN
O
3e
1.95
1.95
1.00
3.01
1.01
1.00
2.03
f1 (ppm)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121.99
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80.80
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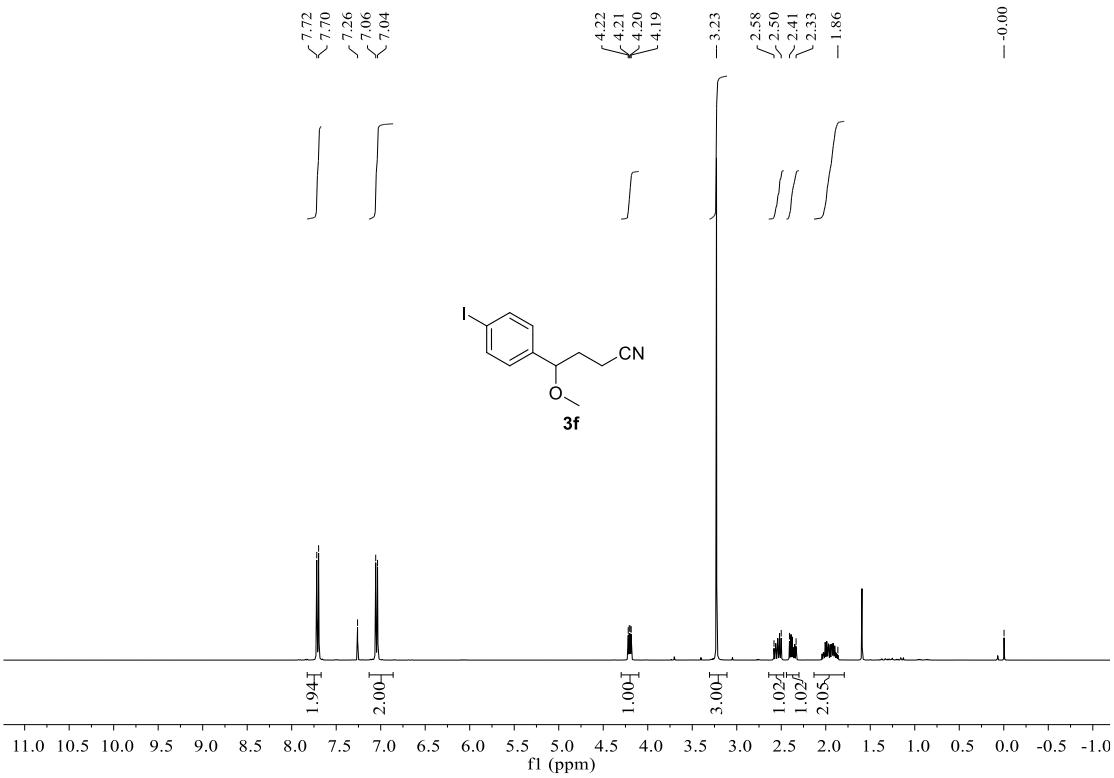
77.00
76.68
56.90
33.51
13.76
Br
CN
O
3e
f1 (ppm)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7.04
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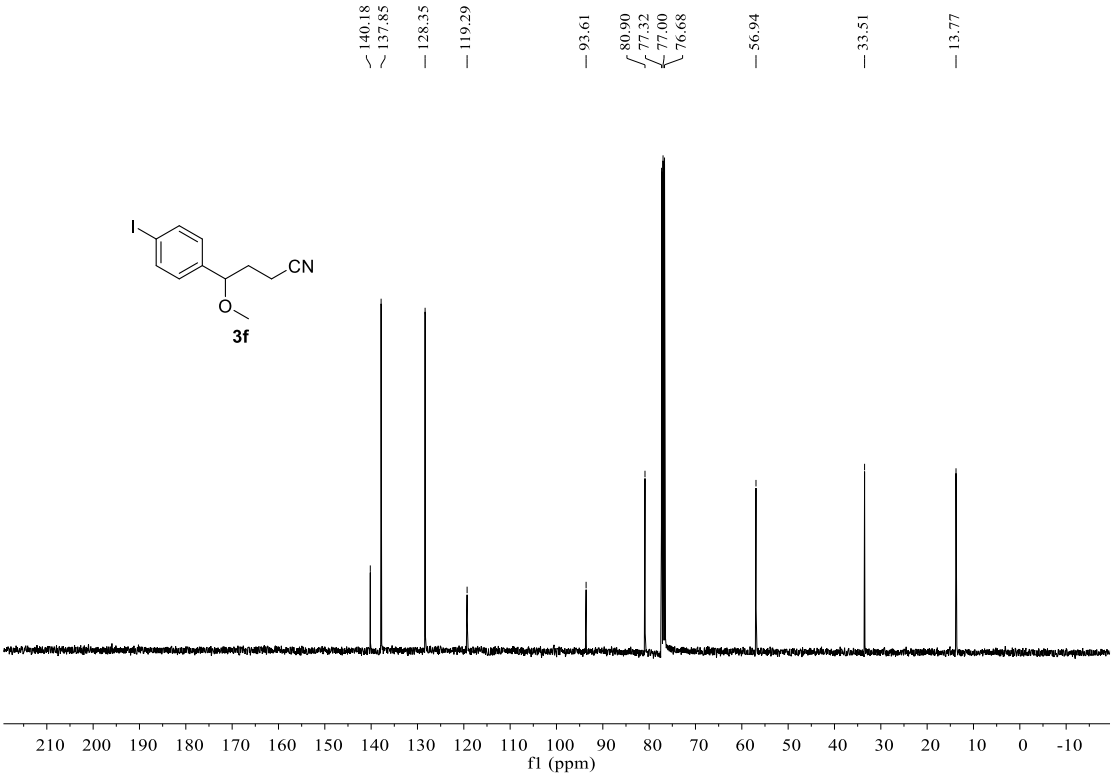
4.21
4.20
4.19
3.23
2.58
2.50
2.41
2.33
1.86
-0.00
I
CN
O
3f
1.94
2.00
1.00
3.00
1.02
1.02
2.05
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)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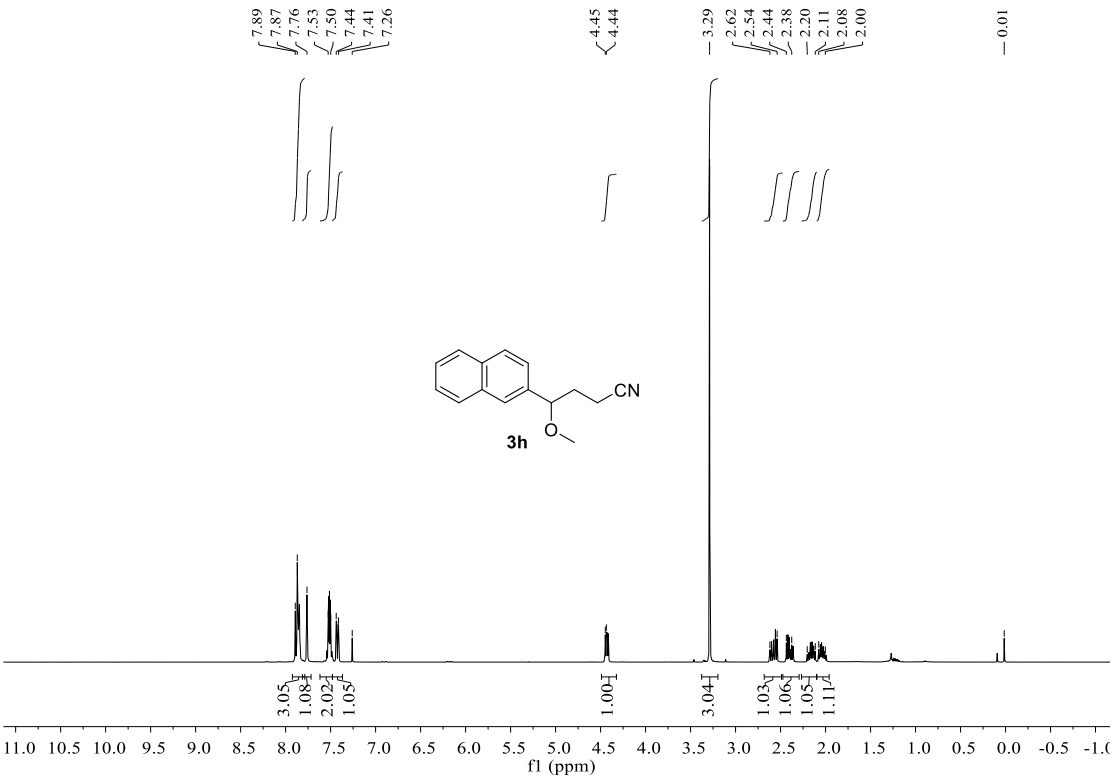
137.85
128.35
119.29
93.61
80.90
77.32
77.00
76.68
56.94
33.51
13.77
I
CN
O
3f
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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4.44
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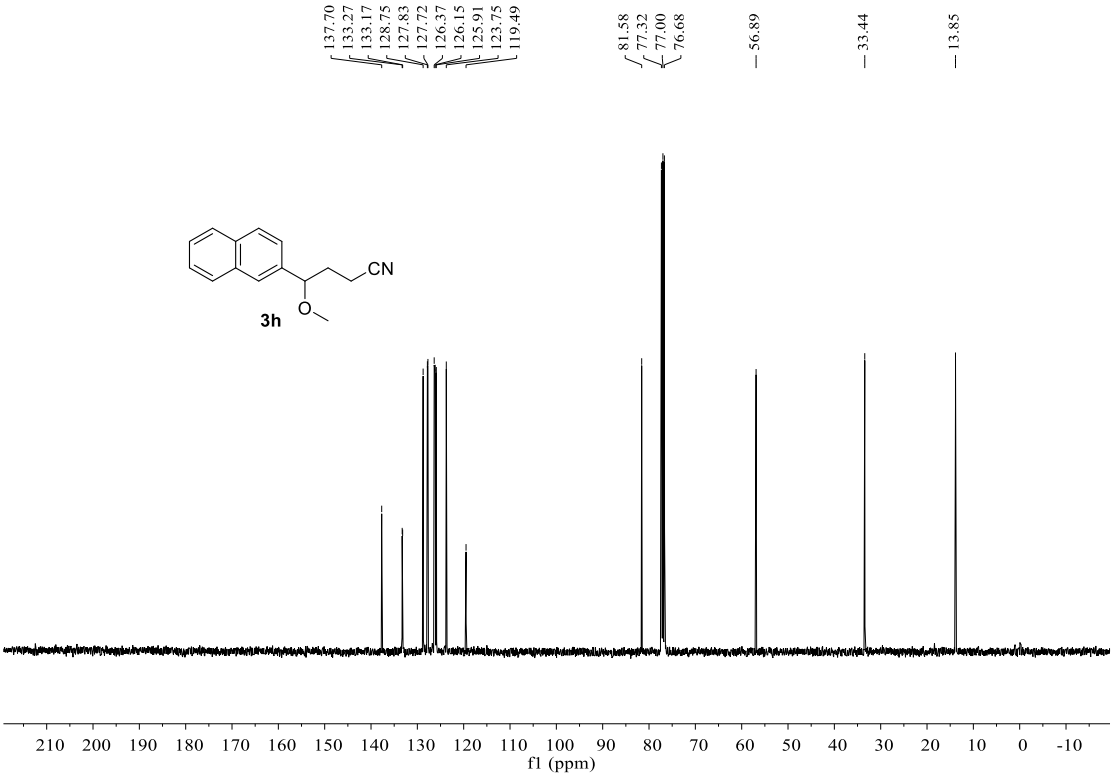
2.62
2.54
2.44
2.38
2.20
2.11
2.08
2.00
0.01
CN
O
3h
3.05
1.08
2.02
1.05
1.00
3.04
1.03
1.06
1.05
1.11
f1 (ppm)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76.68
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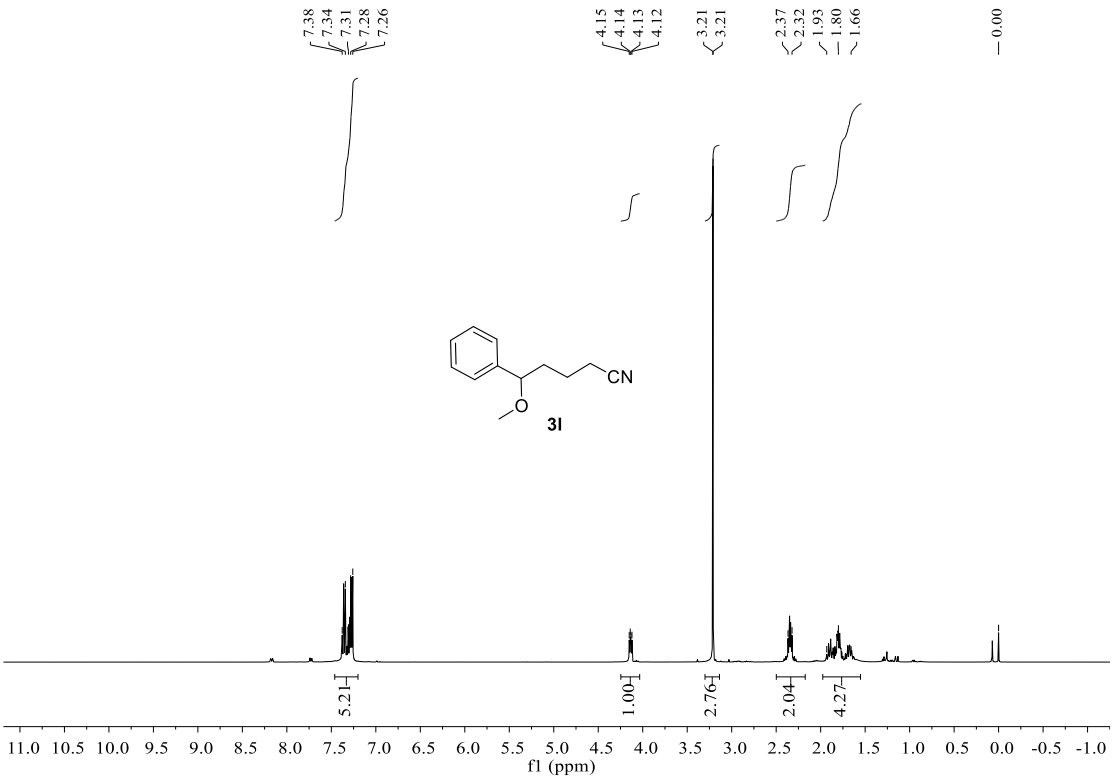
13.85
CN
O
3h
f1 (ppm)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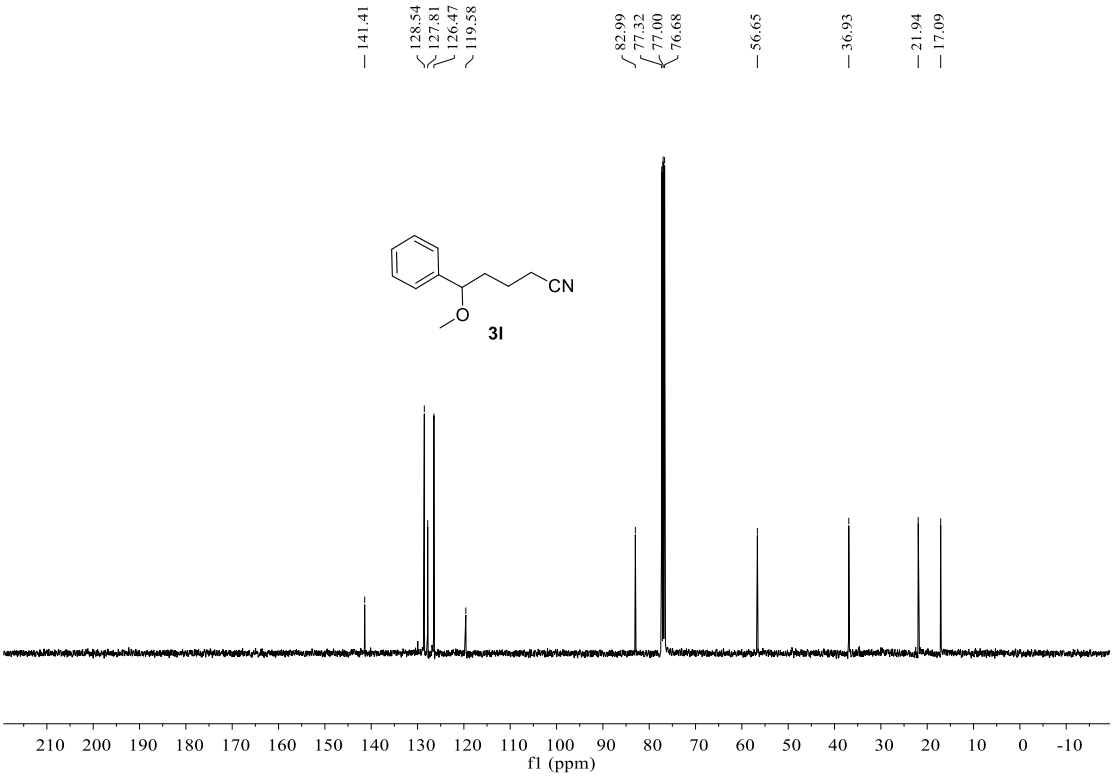
4.15
4.14
4.13
4.12
3.21
3.21
2.37
2.32
1.93
1.80
1.66
0.00
CN
O
3l
5.21
1.00
2.76
2.04
4.27
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)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119.58
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77.32
77.00
76.68
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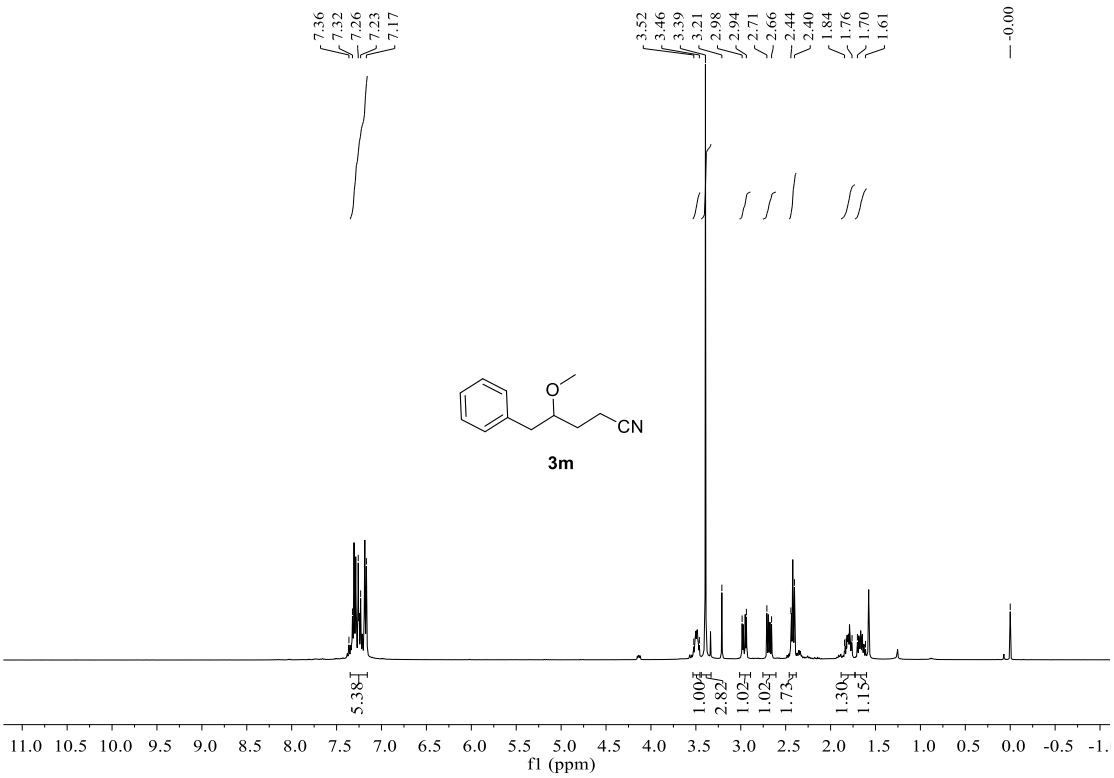
17.09
CN
O
3l
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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3.39
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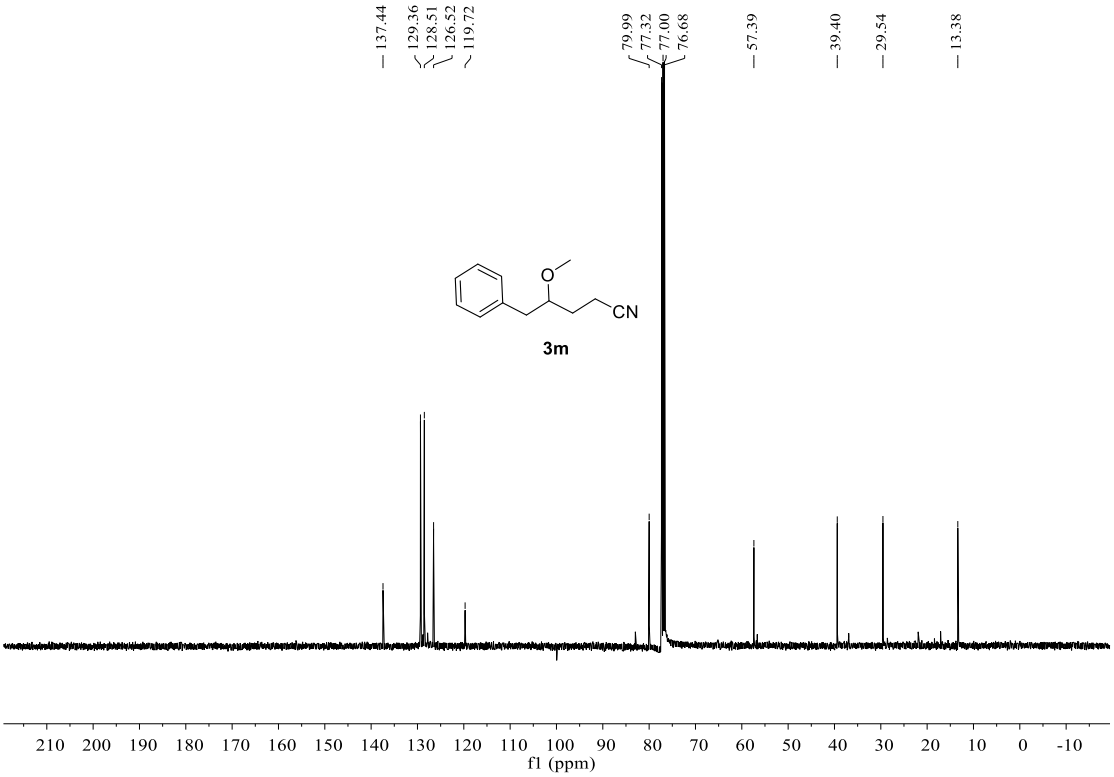
2.98
2.94
2.71
2.66
2.44
2.40
1.84
1.76
1.70
1.61
-0.00
O
CN
3m
5.38
1.00
2.82
1.02
1.02
1.73
1.30
1.15
f1 (ppm)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77.00
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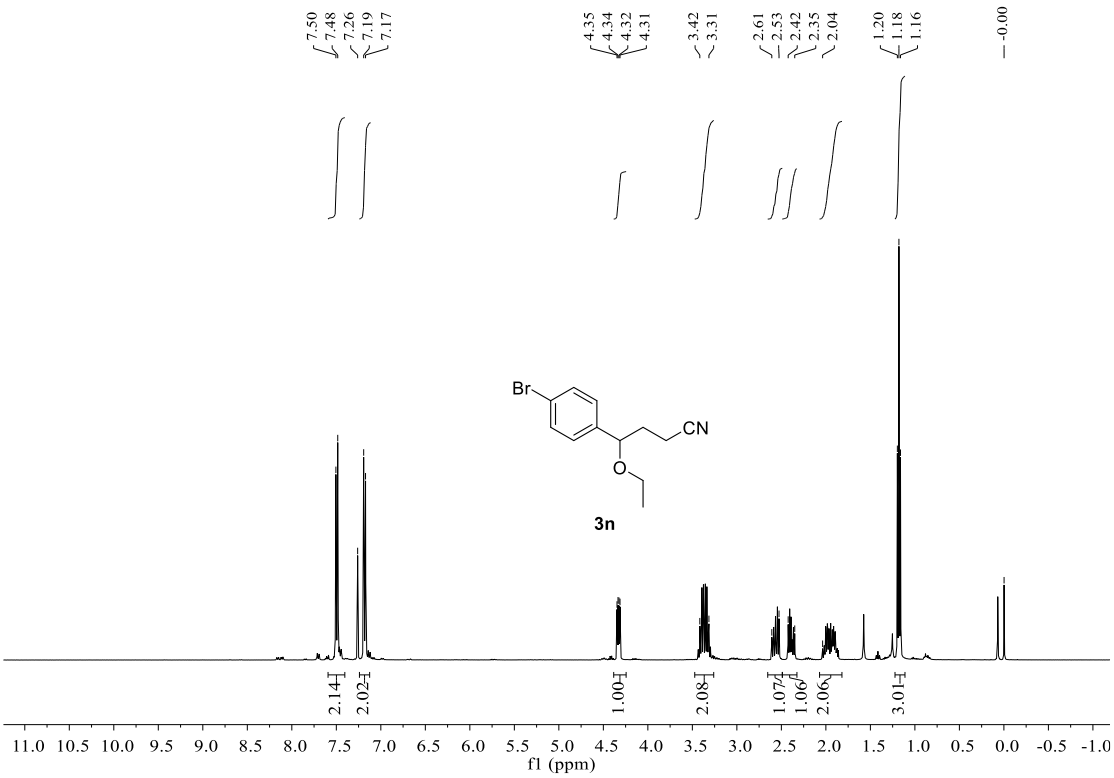
39.40
29.54
13.38
O
CN
3m
f1 (ppm)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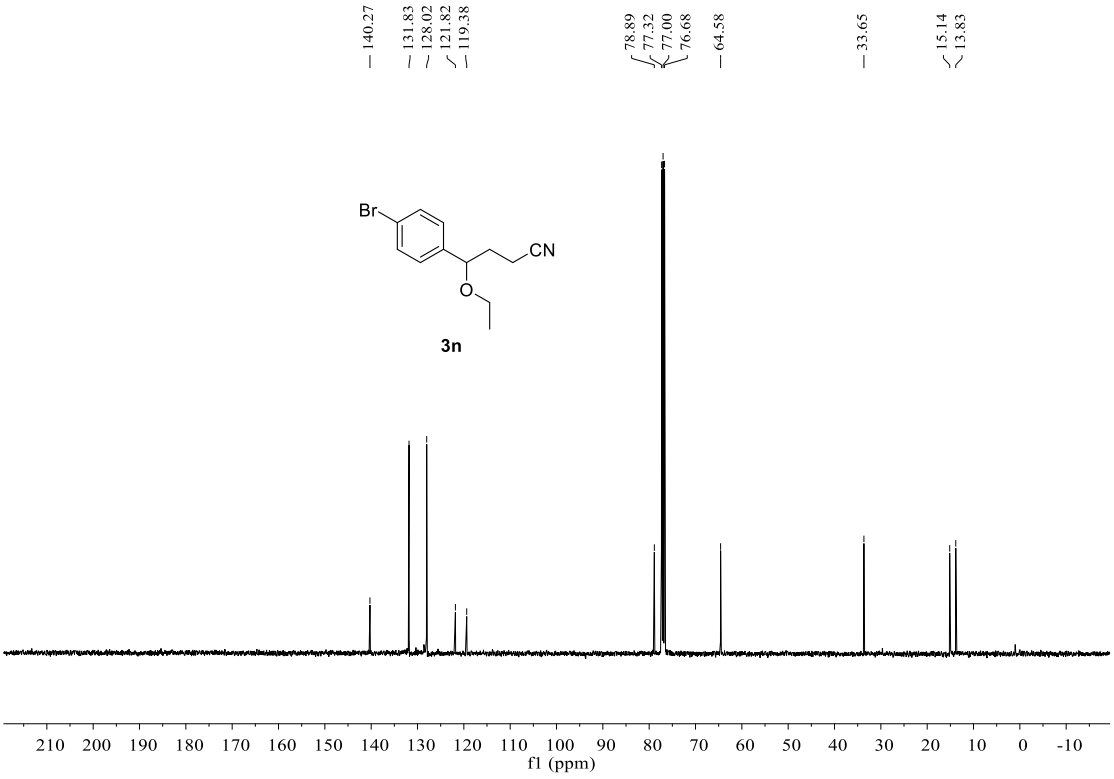
4.34
4.32
4.31
3.42
3.31
2.61
2.53
2.42
2.35
2.04
1.20
1.18
1.16
-0.00
Br
CN
O
3n
2.14
2.02
1.00
2.08
1.07
1.06
2.06
3.01
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)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77.32
77.00
76.68
64.58
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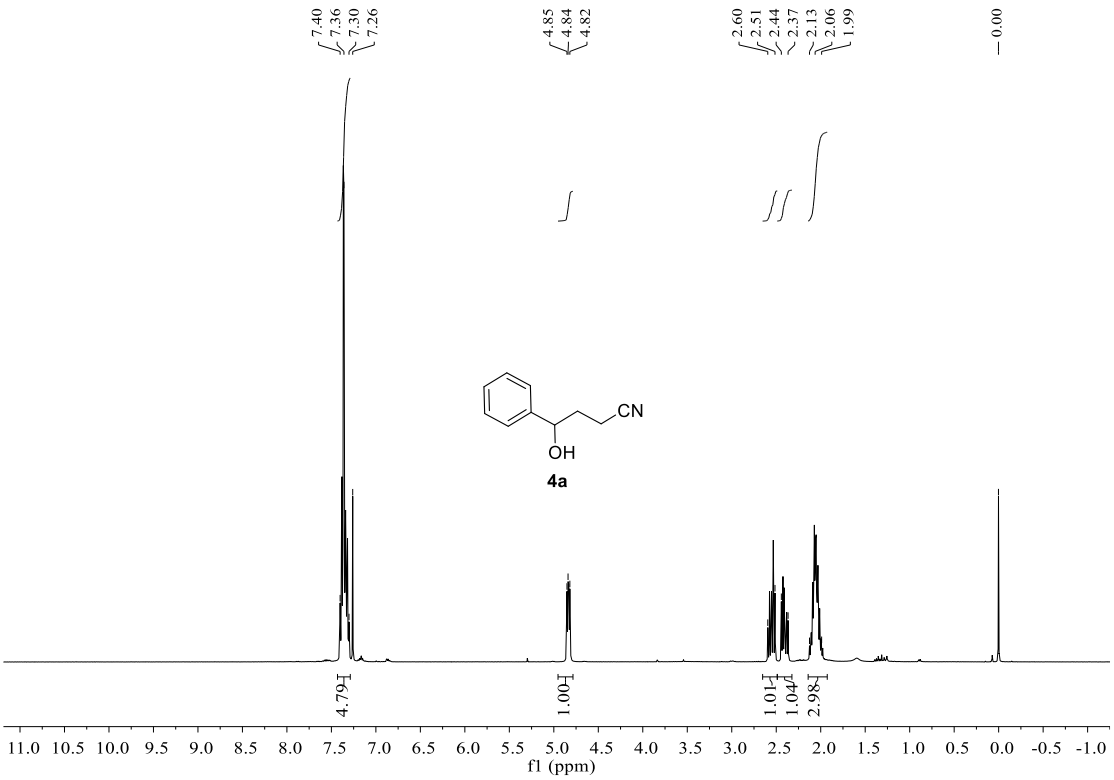
Br
CN
O
3n
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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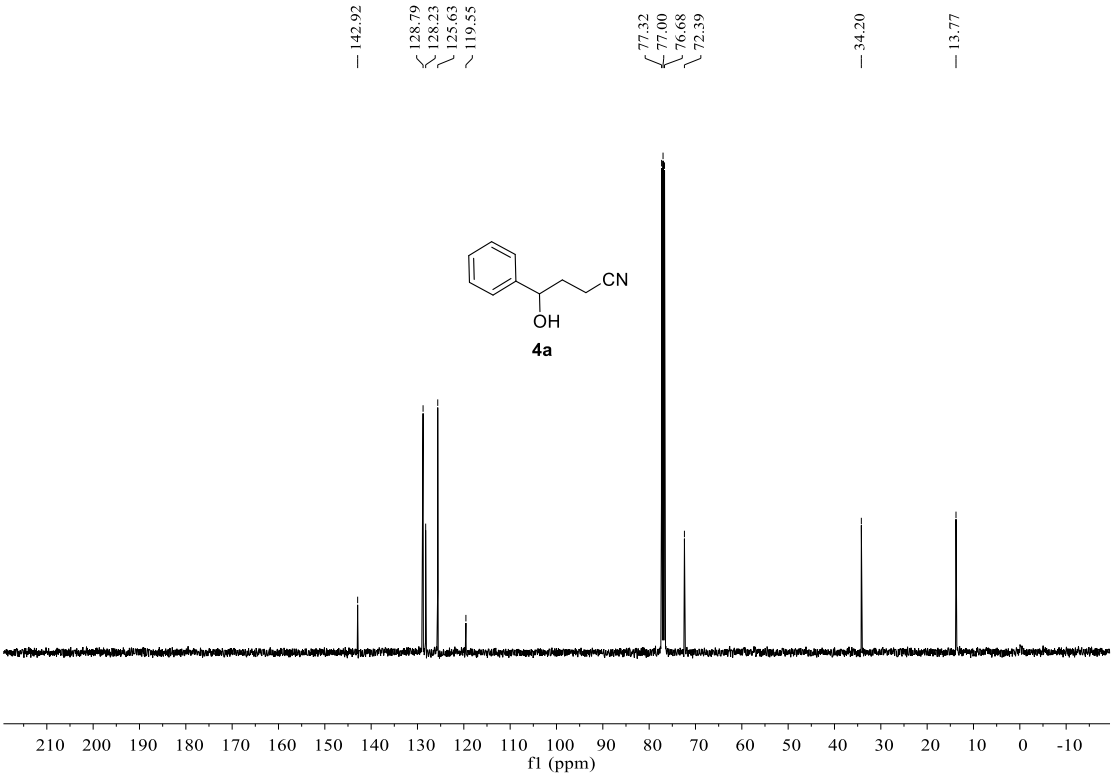
4.85
4.84
4.82
2.60
2.51
2.44
2.37
2.13
2.06
1.99
0.00
CN
OH
4a
4.79
1.00
1.01
1.04
2.98
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)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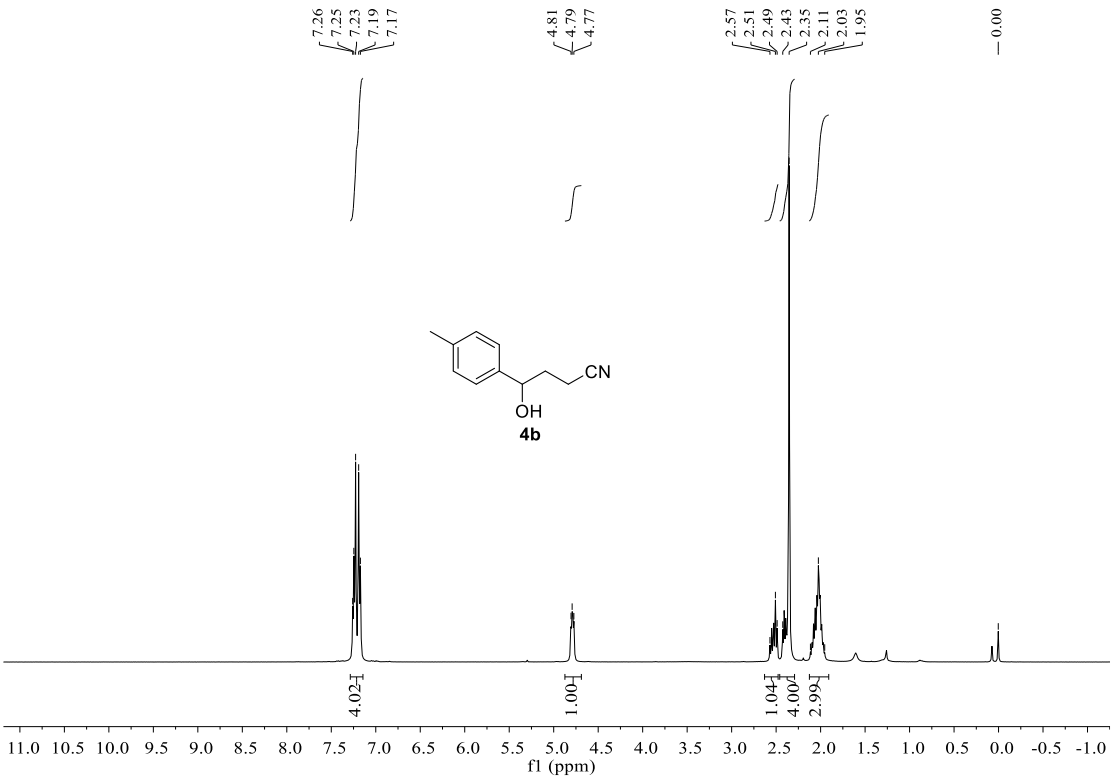
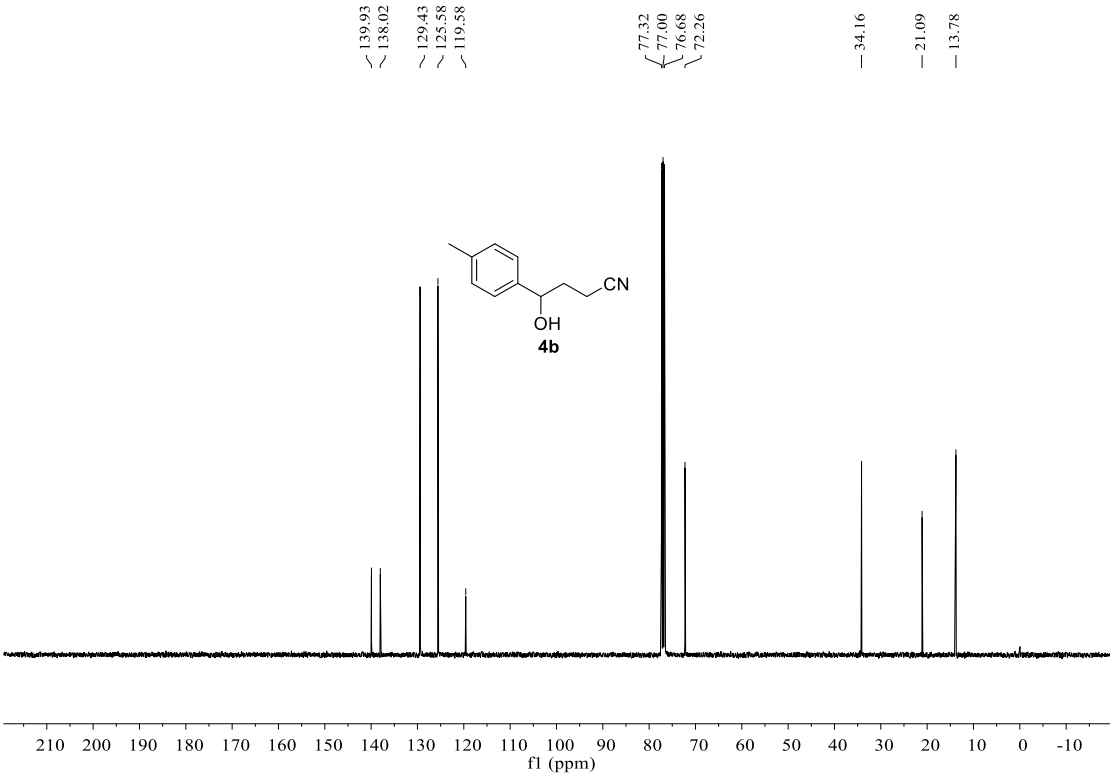
125.63
119.55
77.32
77.00
76.68
72.39
34.20
13.77
CN
OH
4a
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


7.26
7.25
7.23
7.19
7.17
4.81
4.79
4.77
2.57
2.51
2.49
2.43
2.35
2.11
2.03
1.95
0.00
CN
OH
4b
4.02
1.00
1.04
4.00
2.99
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)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138.02
129.43
125.58
119.58
77.32
77.00
76.68
72.26
34.16
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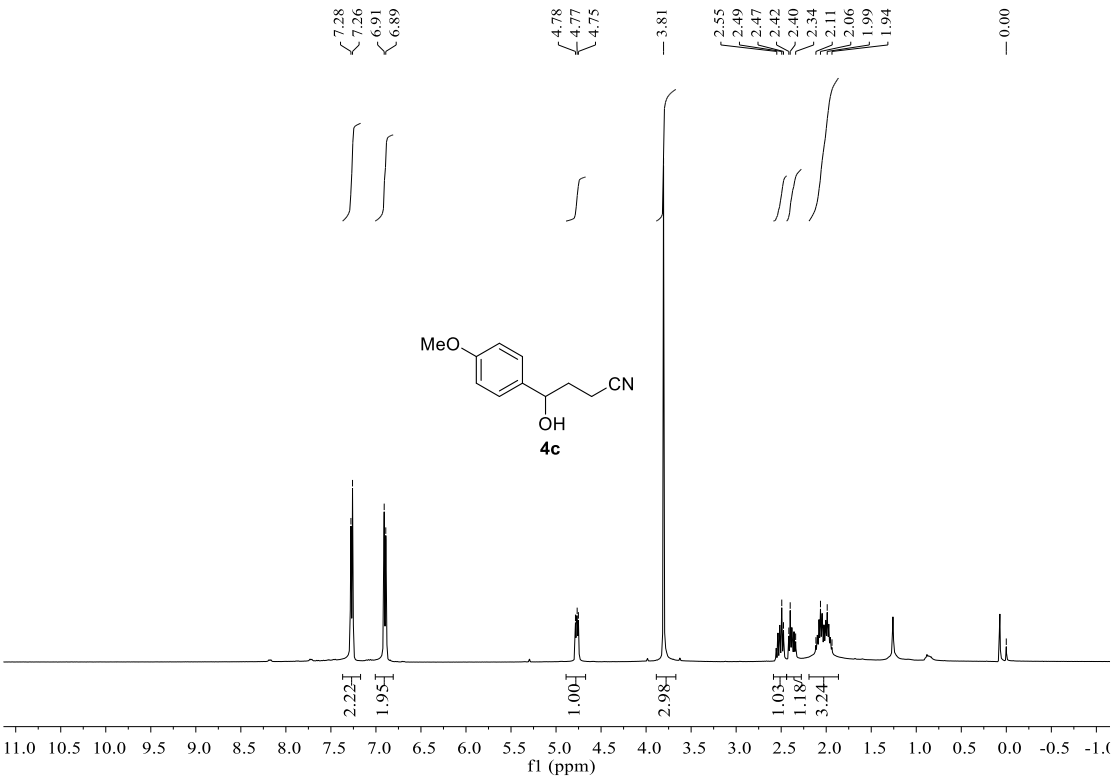
13.78
CN
OH
4b
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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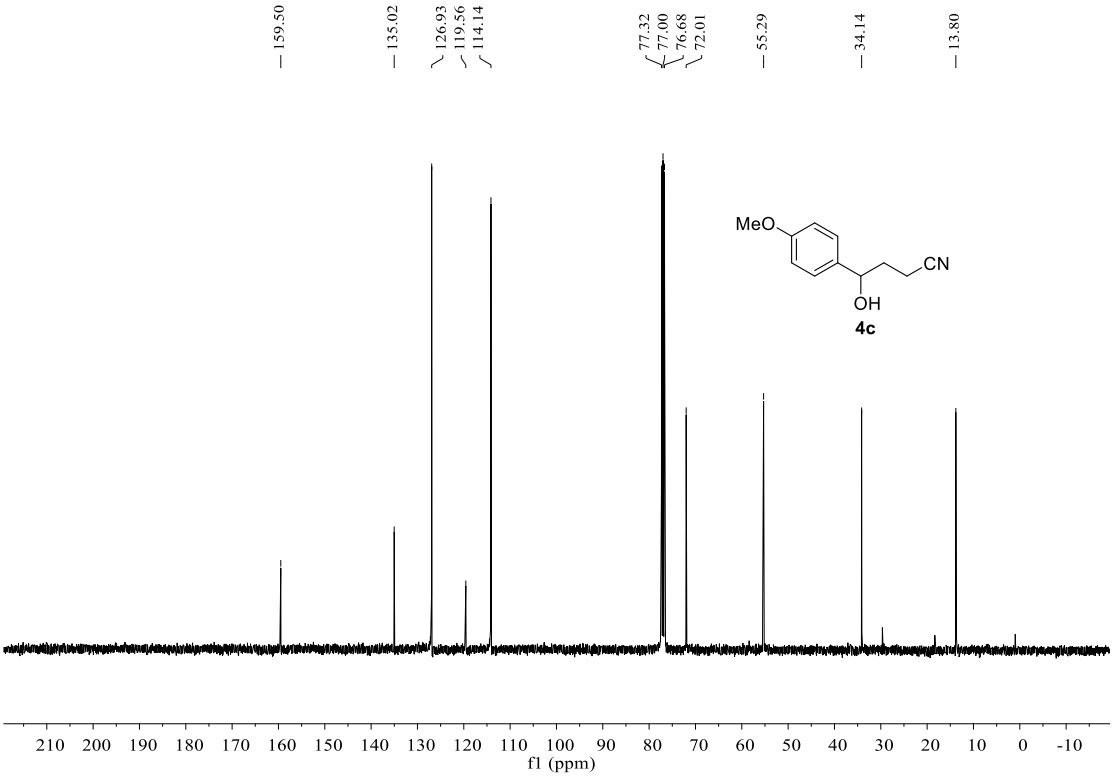
7.26
6.91
6.89
4.78
4.77
4.75
3.81
2.55
2.49
2.47
2.42
2.40
2.34
2.11
2.06
1.99
1.94
0.00
MeO
CN
OH
4c
2.22
1.95
1.00
2.98
1.03
1.18
3.24
f1 (ppm)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135.02
126.93
119.56
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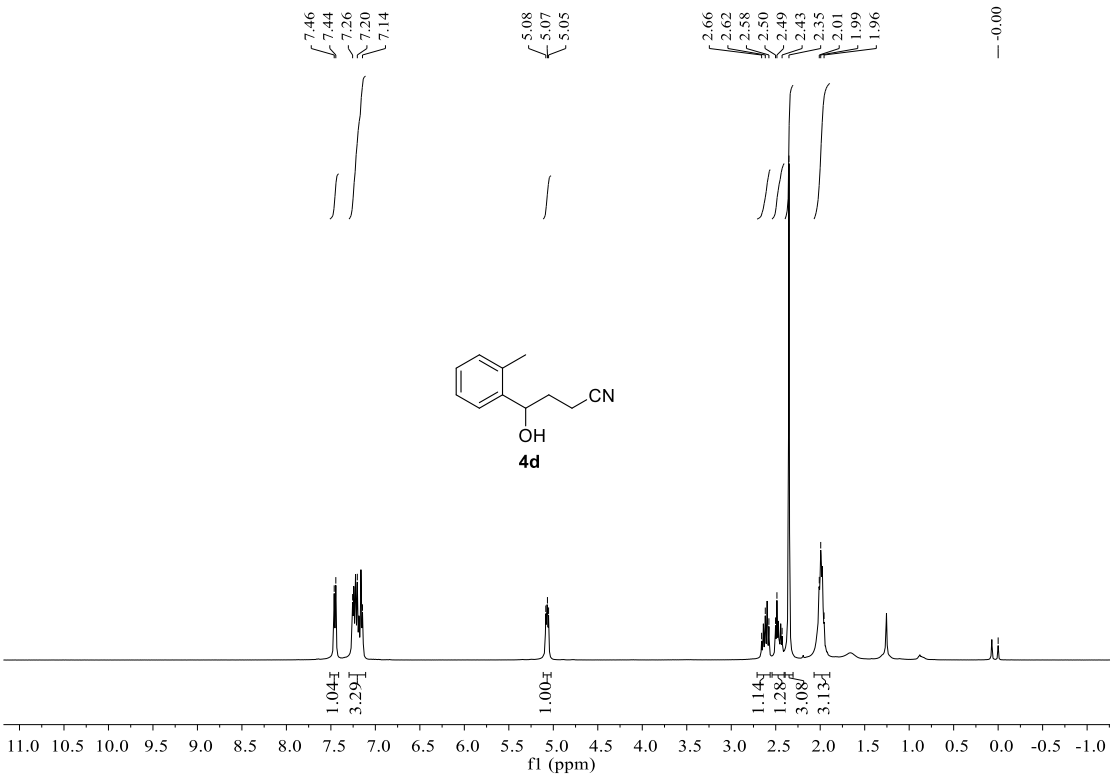
76.68
72.01
55.29
34.14
13.80
MeO
CN
OH
4c
f1 (ppm)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7.44
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7.20
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5.08
5.07
5.05
2.66
2.62
2.58
2.50
2.49
2.43
2.35
2.01
1.99
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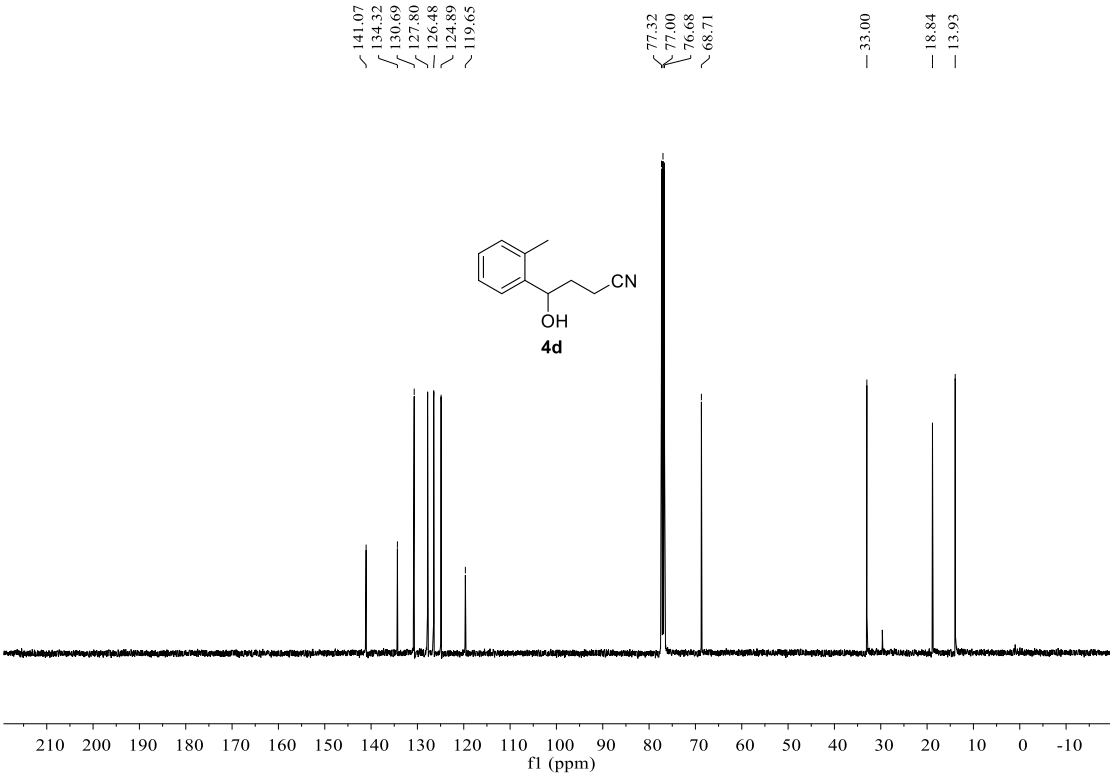
OH
4d
1.04
3.29
1.00
1.14
1.28
3.08
3.13
f1 (ppm)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76.68
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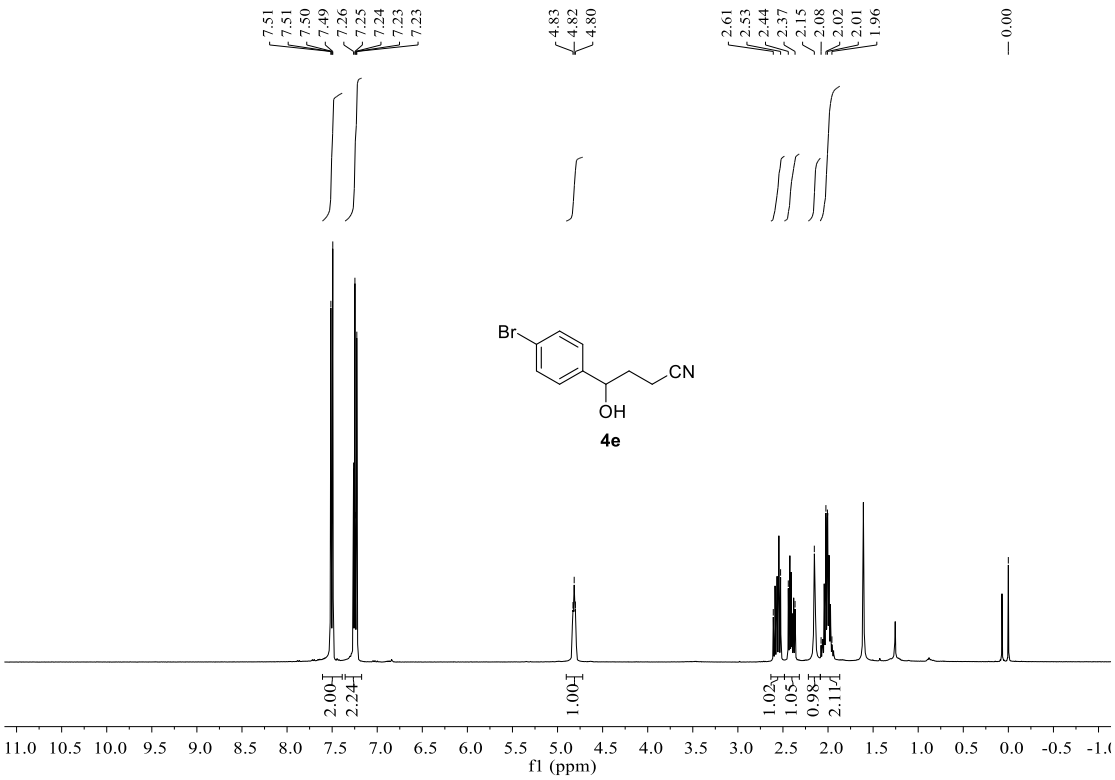
13.93
CN
OH
4d
f1 (ppm)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7.26
7.25
7.24
7.23
7.23
4.83
4.82
4.80
2.61
2.53
2.44
2.37
2.15
2.08
2.02
2.01
1.96
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CN
OH
4e
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2.24
1.00
1.02
1.05
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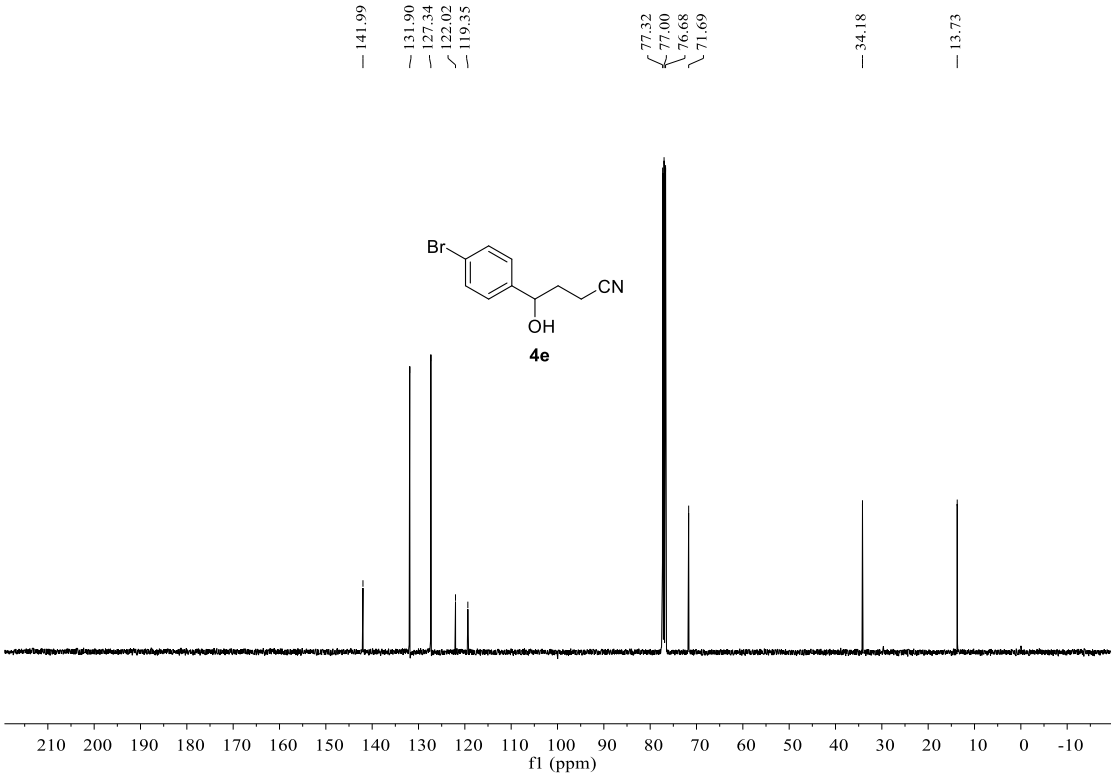
2.11
f1 (ppm)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122.02
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77.00
76.68
71.69
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13.73
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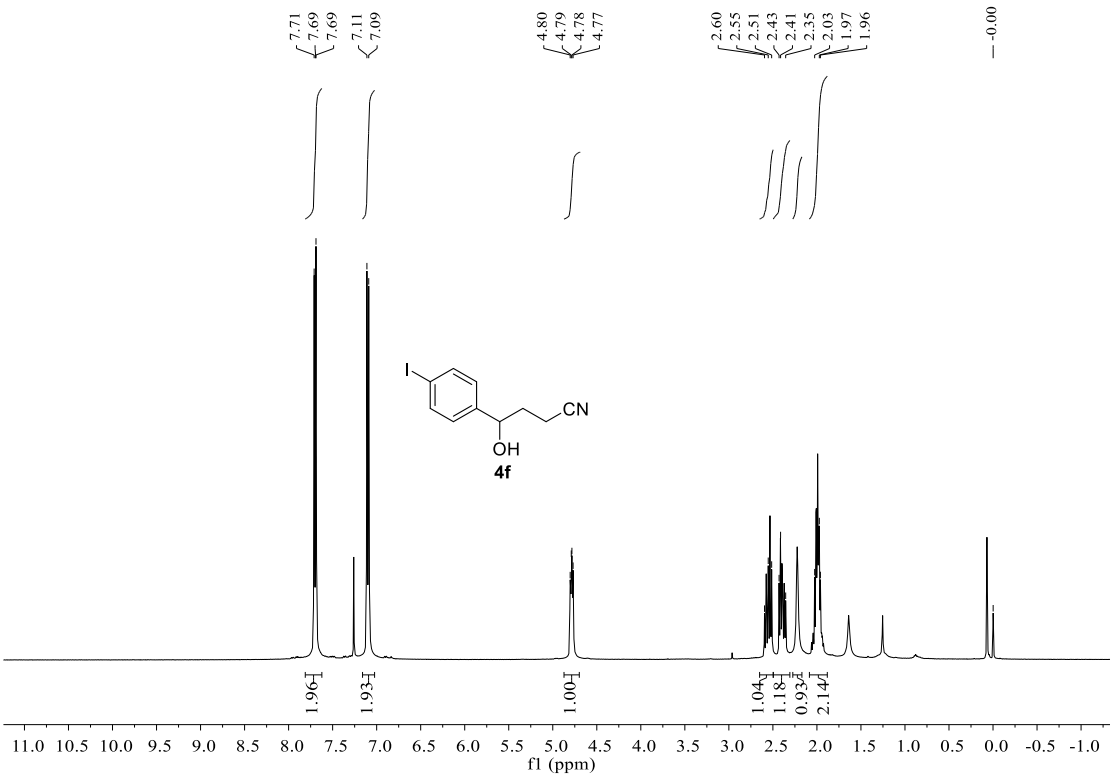
CN
OH
4e
f1 (ppm)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7.69
7.11
7.09
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4.79
4.78
4.77
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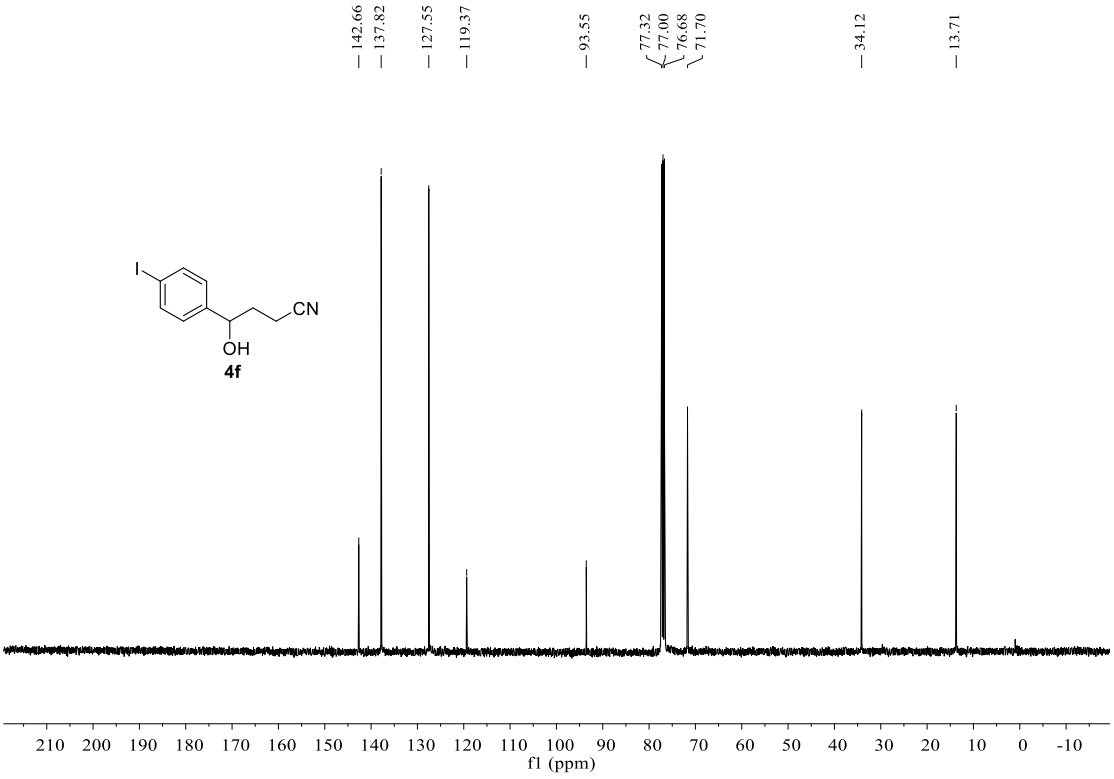
2.55
2.51
2.43
2.41
2.35
2.03
1.97
1.96
-0.00
I
CN
OH
4f
1.96
1.93
1.00
1.04
1.18
0.93
2.14
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)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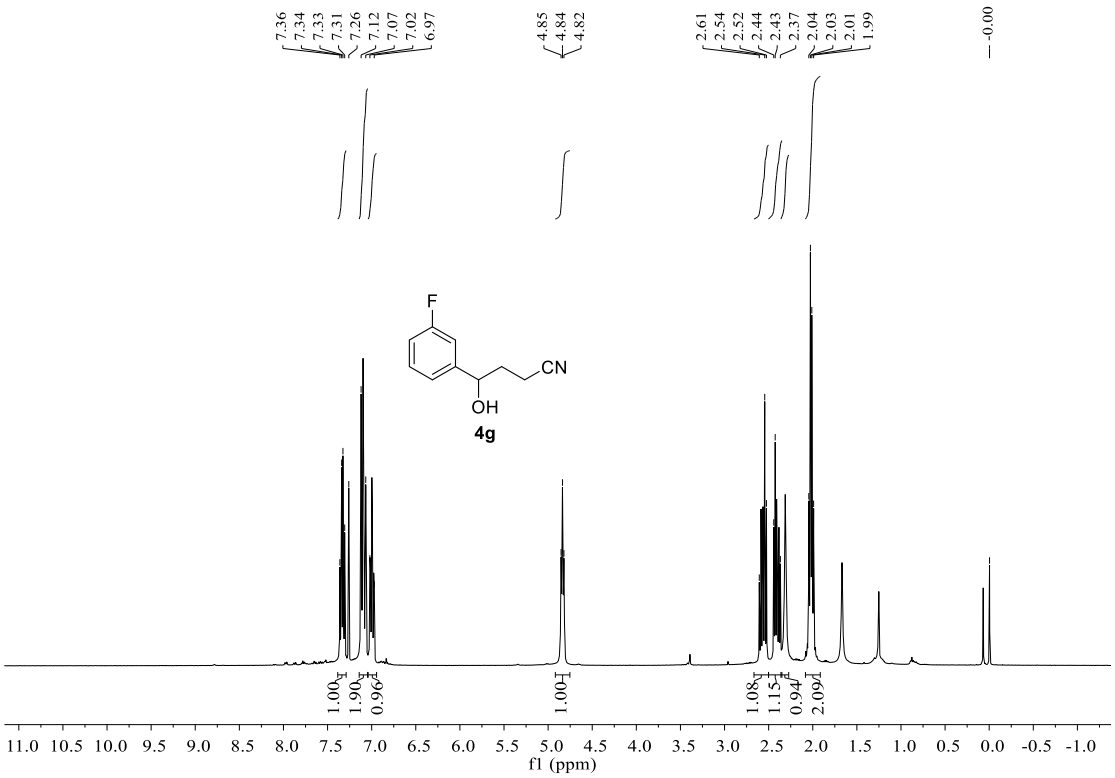
93.55
77.32
77.00
76.68
71.70
34.12
13.71
I
CN
OH
4f
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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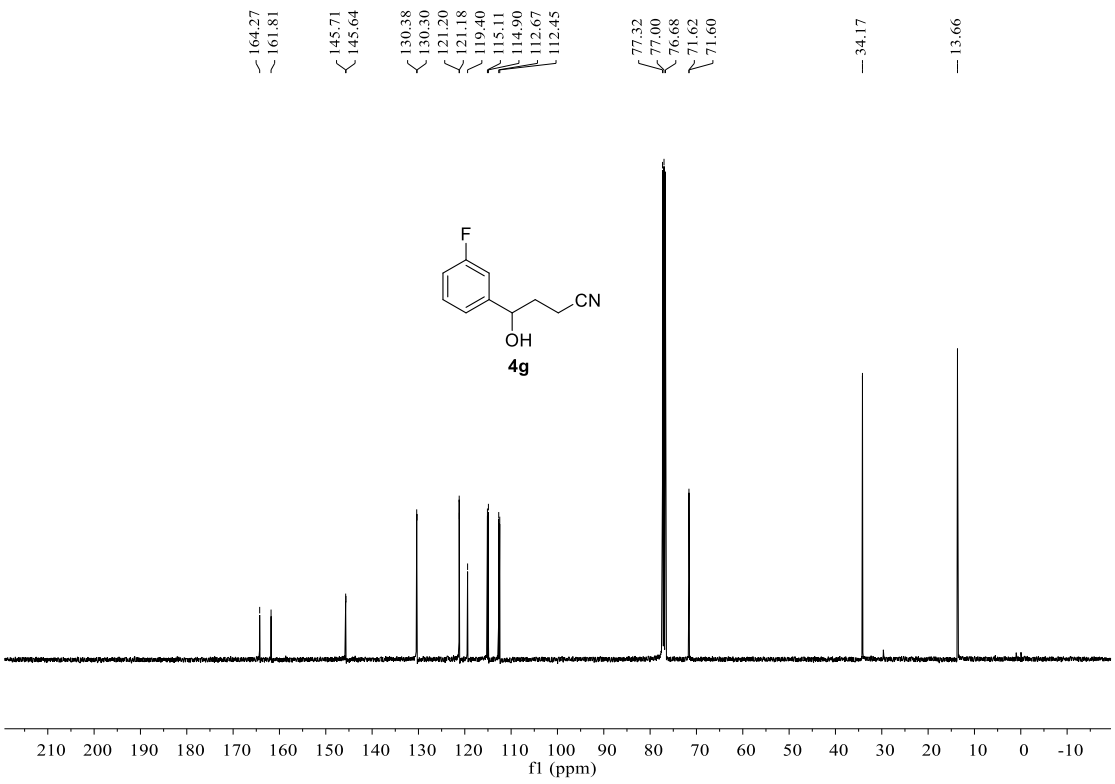
4.84
4.82
2.61
2.54
2.52
2.44
2.43
2.37
2.04
2.03
2.01
1.99
-0.00
F
CN
OH
4g
1.00
1.90
0.96
1.00
1.08
1.15
0.94
2.09
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)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121.18
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115.11
114.90
112.67
112.45
77.32
77.00
76.68
71.62
71.60
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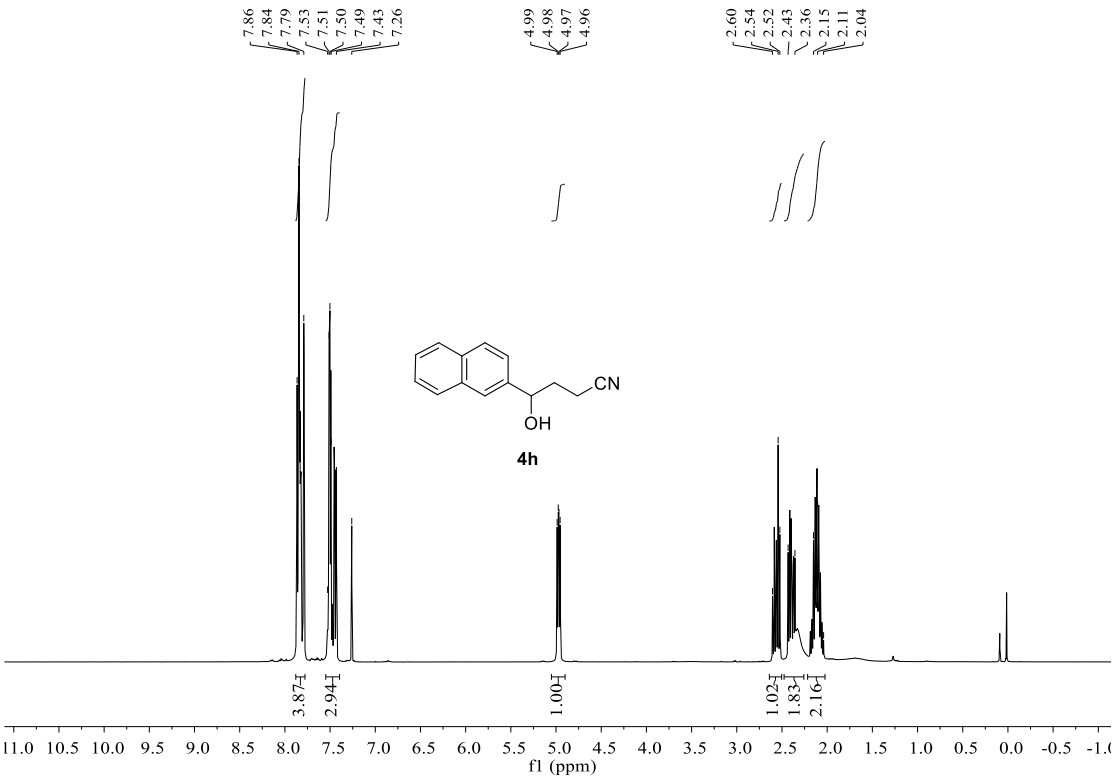
13.66
F
CN
OH
4g
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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7.43
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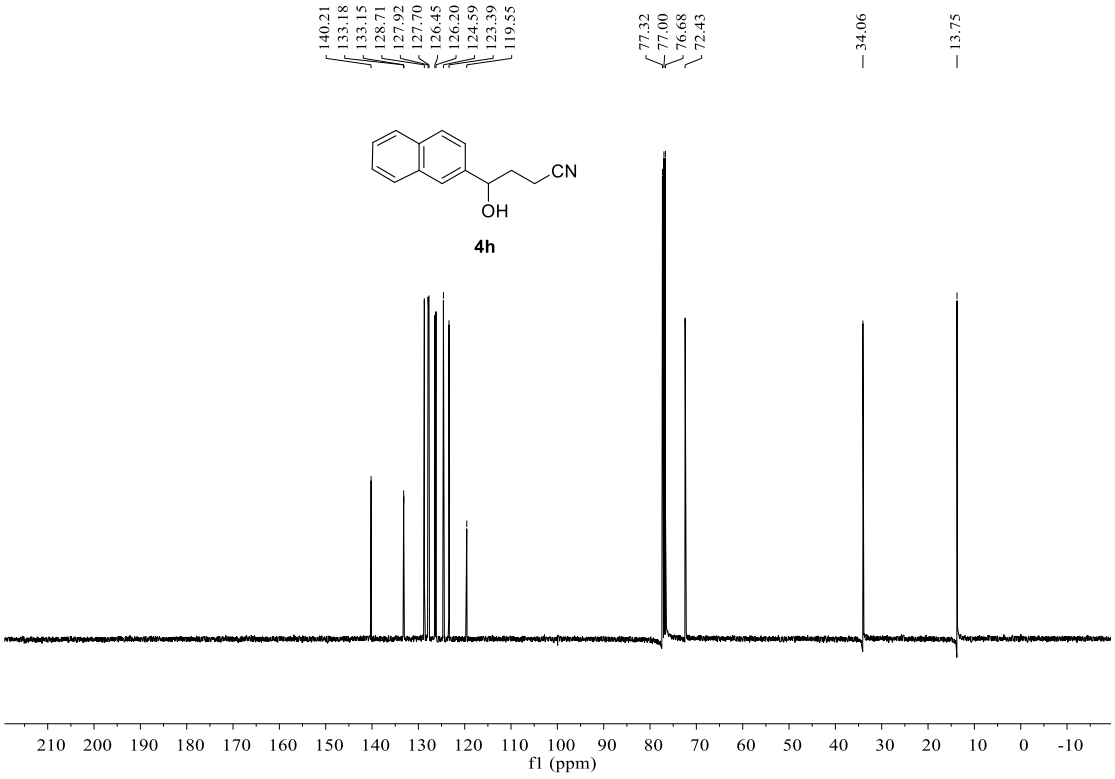
4.99
4.98
4.97
4.96
2.60
2.54
2.52
2.43
2.36
2.15
2.11
2.04
CN
OH
4h
3.87
2.94
1.00
1.02
1.83
2.16
f1 (ppm)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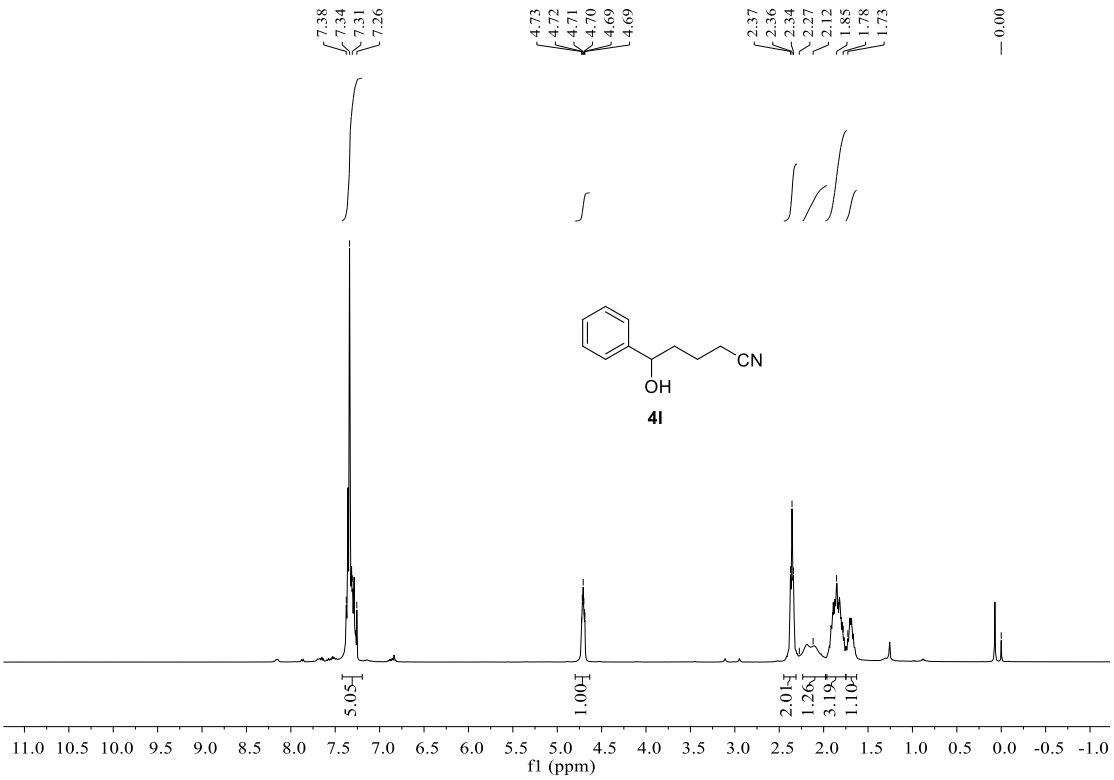
76.68
72.43
34.06
13.75
CN
OH
4h
f1 (ppm)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4.69
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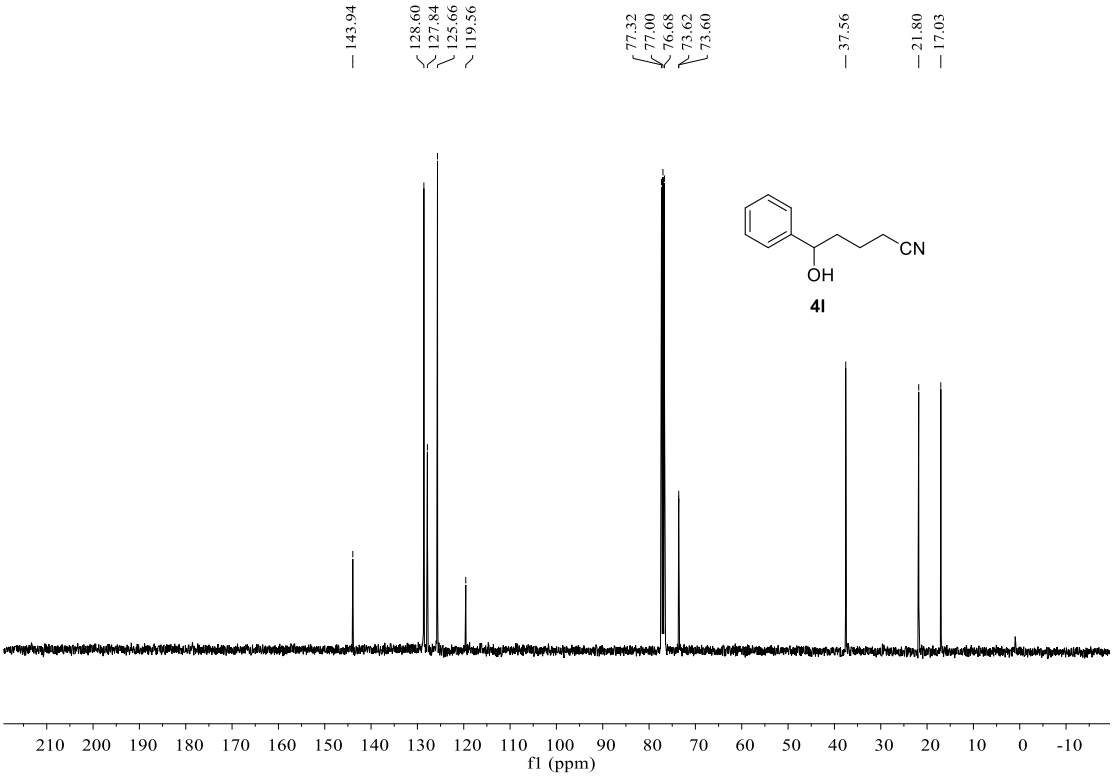
2.34
2.27
2.12
1.85
1.78
1.73
0.00
CN
OH
4l
5.05
1.00
2.01
1.26
3.19
1.10
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)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76.68
73.62
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17.03
CN
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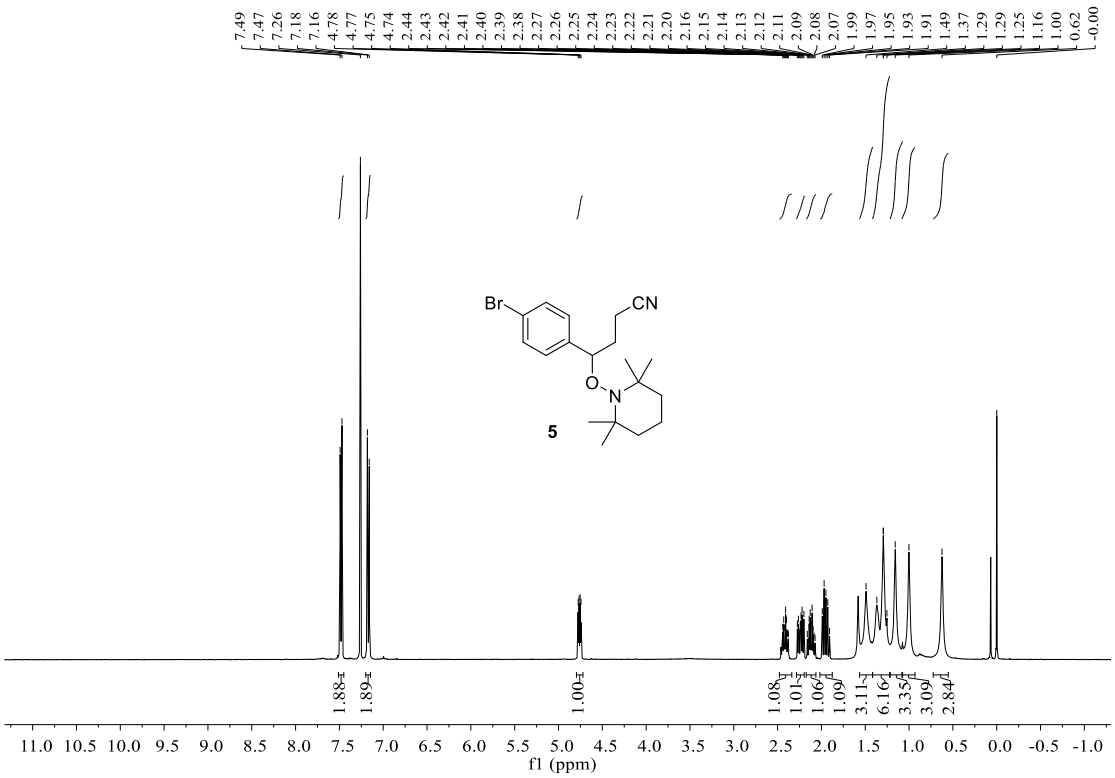
4l
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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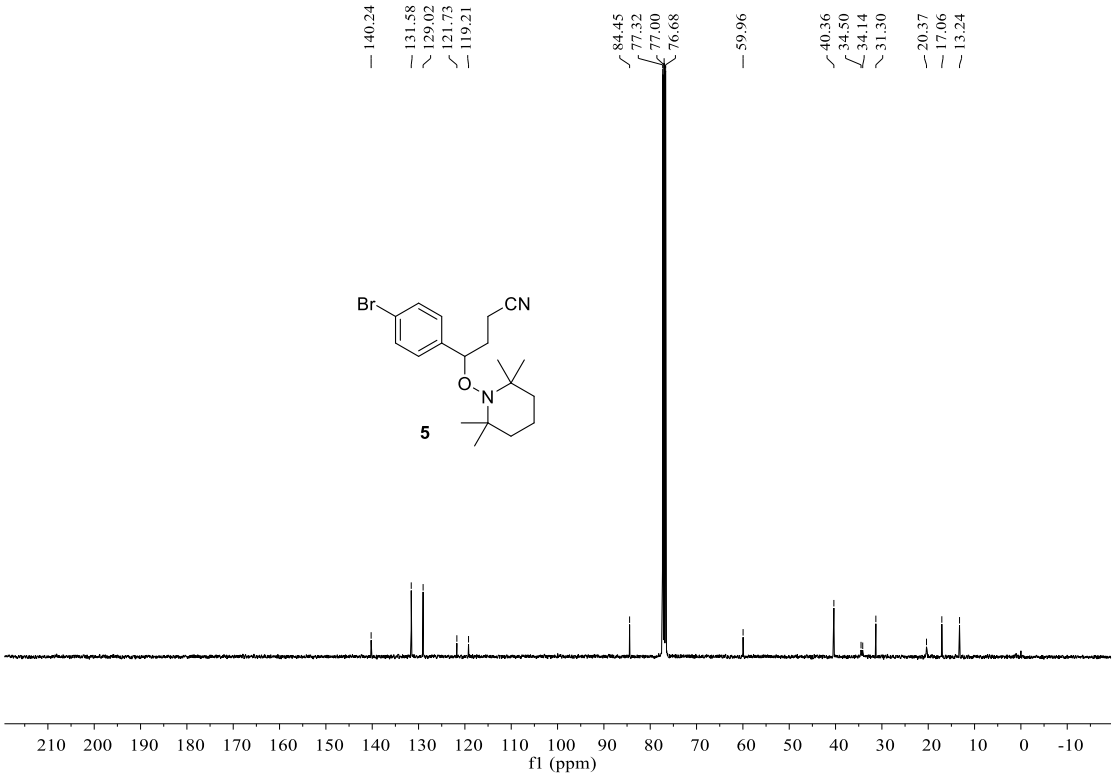
Br
CN
O
N
5
1.88 1.89 1.00 1.08 1.01 1.06 1.09 3.11 6.16 3.35 3.09 2.84
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)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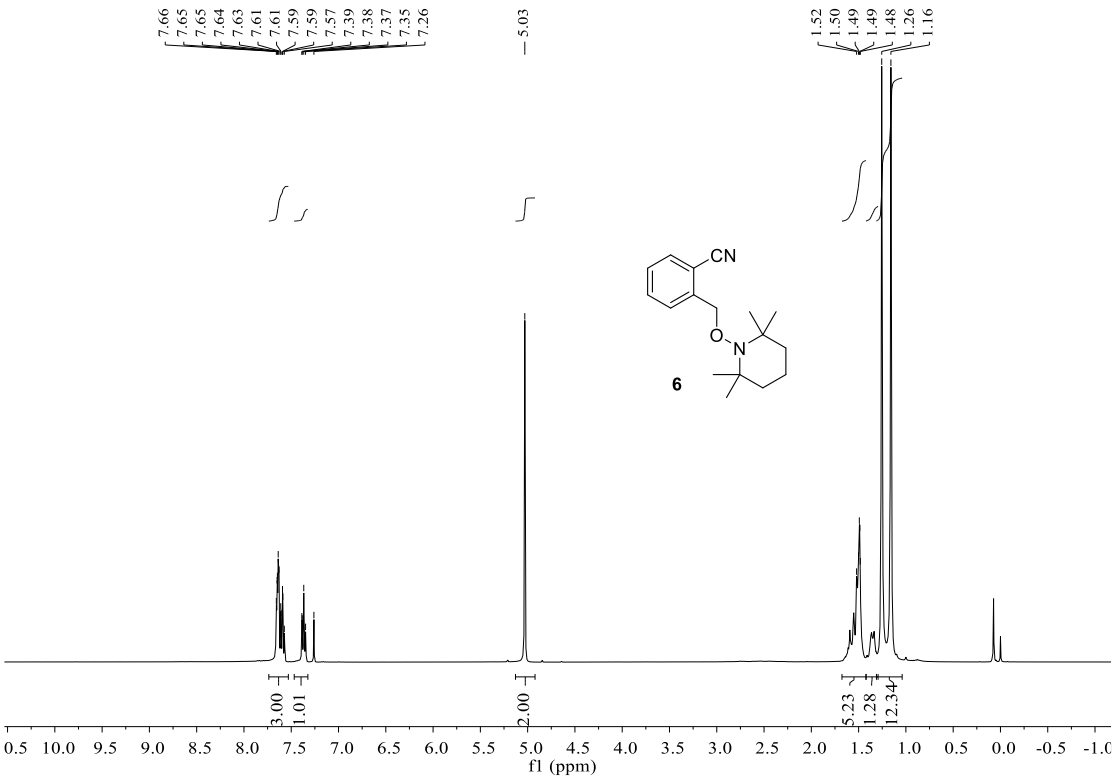
Br
CN
O
N
5
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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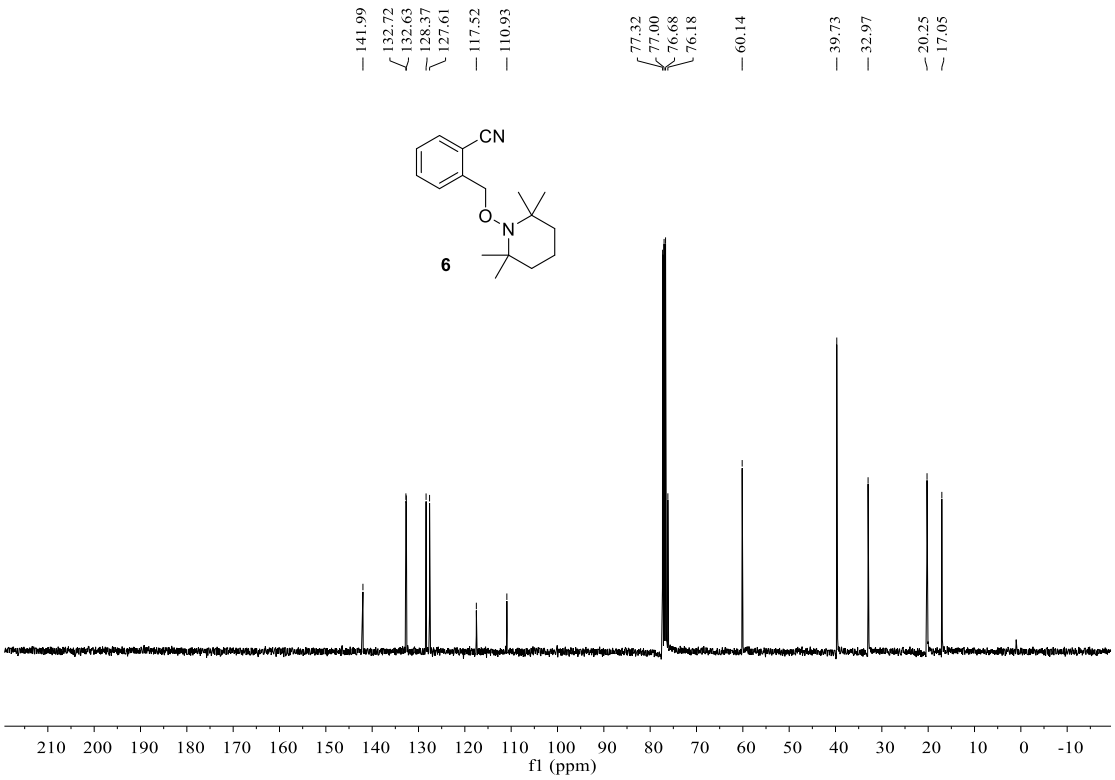
7.37
7.35
7.26
5.03
1.52
1.50
1.49
1.49
1.48
1.26
1.16
CN
O
N
6
3.00
1.01
2.00
5.23
1.28
12.34
f1 (ppm)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76.18
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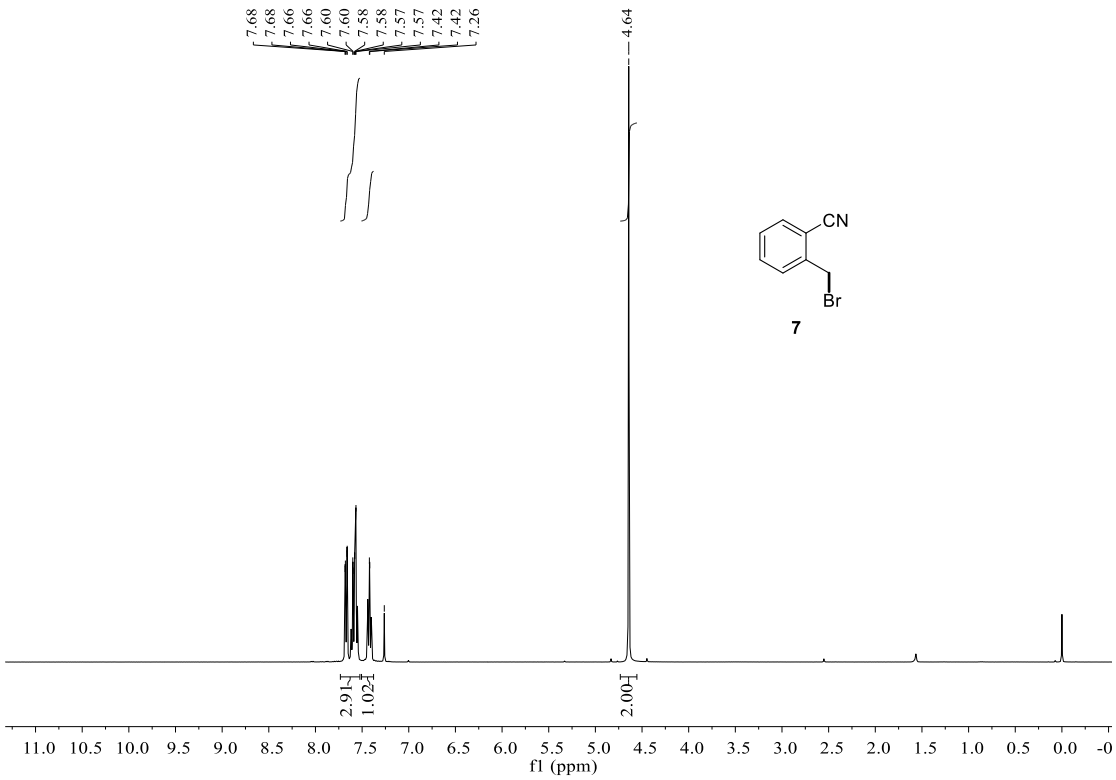
39.73
32.97
20.25
17.05
CN
O
N
6
f1 (ppm)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7.42
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4.64
CN
Br
7
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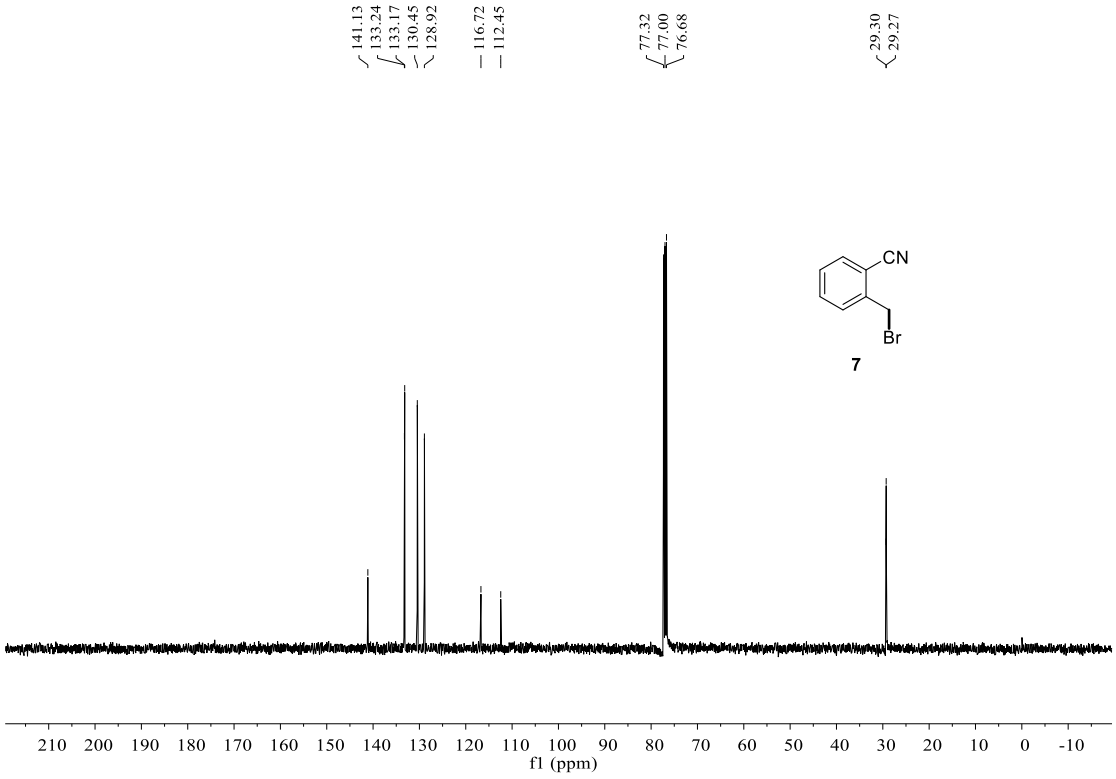
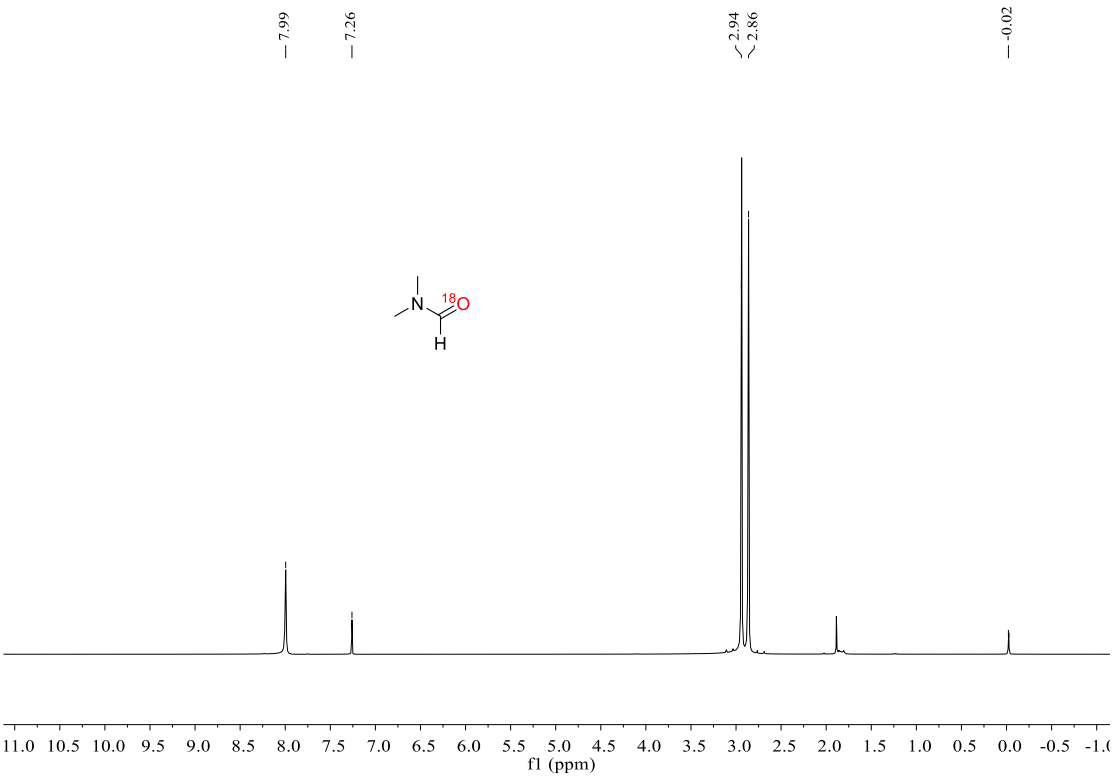
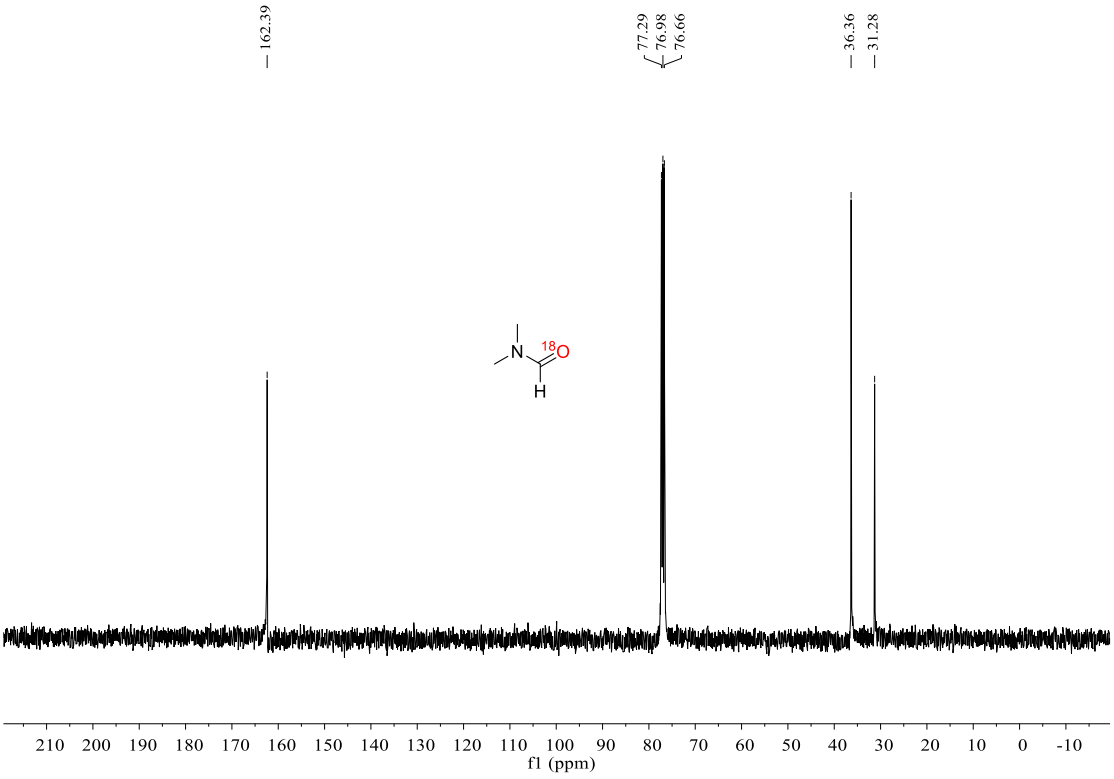
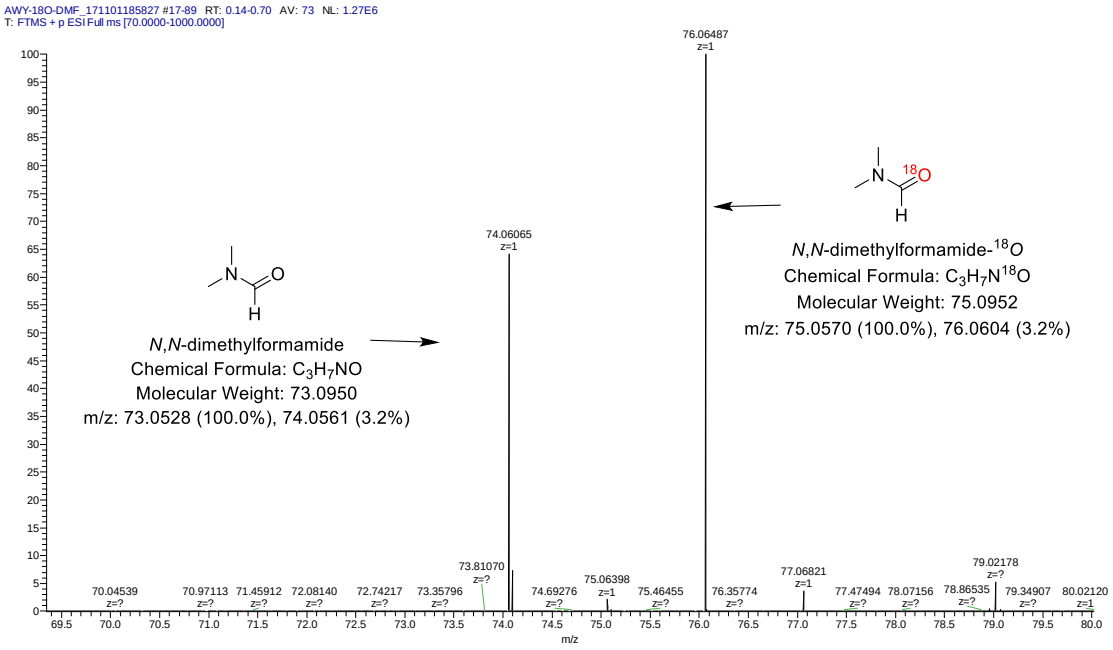
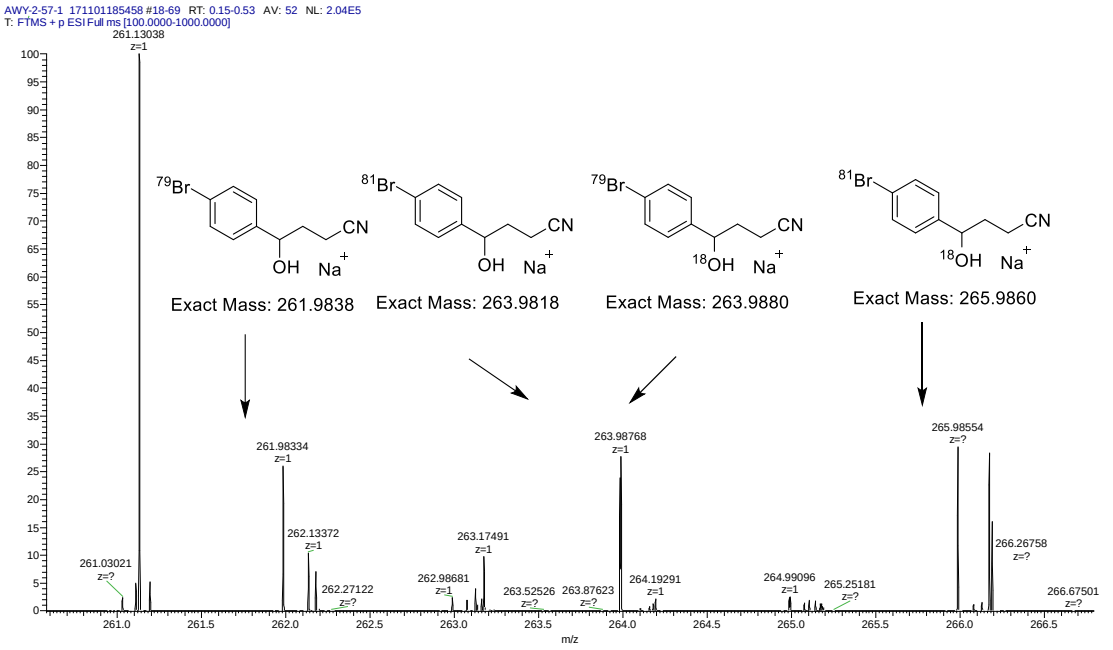
1.02
2.00
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0
f1 (ppm)


141.13
133.24
133.17
130.45
128.92
116.72
112.45
77.32
77.00
76.68
29.30
29.27
CN
Br
7
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


7.99
7.26
2.94
2.86
-0.02
N
18O
H
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


162.39
77.29
76.98
76.66
36.36
31.28
N
18O
H
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


AWY-18O-DMF_171101185827 #17-89 RT: 0.14-0.70 AV: 73 NL: 1.27E6
T: FTMS + p ESI Full ms [70.0000-1000.0000]
76.06487
z=1
74.06065
z=1
73.81070
z=?
77.06821
z=1
79.02178
z=?
N,N-dimethylformamide
Chemical Formula: C3H7NO
Molecular Weight: 73.0950
m/z: 73.0528 (100.0%), 74.0561 (3.2%)
N,N-dimethylformamide-18O
Chemical Formula: C3H7N18O
Molecular Weight: 75.0952
m/z: 75.0570 (100.0%), 76.0604 (3.2%)
m/z


AWY-2-57-1 171101185458 #18-69 RT: 0.15-0.53 AV: 52 NL: 2.04E5
T: FTMS + p ESI Full ms [100.0000-1000.0000]
261.13038
z=1
Exact Mass: 261.9838
Exact Mass: 263.9818
Exact Mass: 263.9880
Exact Mass: 265.9860
261.98334
z=1
263.98768
z=1
265.98554
z=?
262.13372
z=1
263.17491
z=1
266.26758
z=?
261.03021
z=?
262.27122
z=?
262.98681
z=1
263.52526
z=?
263.87623
z=?
264.19291
z=1
264.99096
z=1
265.25181
z=?
266.67501
z=?
m/z

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