Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supplementary Information

Functionalisation of esters via 1,3-chelation using NaO*t*Bu: mechanistic investigations and synthetic applications

Hye Sung Yang,[a] Lingamurthy Macha,[b] Hyun-Joon Ha*[b] and Jung Woon Yang*[a]

[a] Department of Energy Science, Sungkyunkwan University, Suwon 16419, Republic of Korea
[b] Department of Chemistry, Hankuk University of Foreign Studies, Yongin 17035, Republic of Korea

E-mail: hjha@hufs.ac.kr (H.-J. Ha); jwyang@skku.edu (J. W. Yang)

Contents

General information

Thin-layer chromatography (TLC) was performed on Merck silica gel 60 F254. ^{1}H NMR spectra were recorded on a Varian at 500 MHz in $CDCl_3$ (δ 7.26 ppm) or DMSO-d_6 (δ 2.50 ppm), ^{13}C NMR spectral measurements were performed at 126 MHz using $CDCl_3$ (δ 77.16 ppm) or DMSO-d_6 (δ 39.52 ppm) or Toluene-d_8 (δ 137.86 ppm). High-resolution mass spectra (HRMS) were obtained on an Agilent 6890 Series and a Bruker Compact mass spectrometer. Infrared (IR) spectra were recorded on a VERTEX 70 (Bruker) IR spectrometer in the range of 1000-4000 cm^{-1}. HPLC analyses for the enantiomeric excess (*ee*) were performed on YL 9100 HPLC systemusing the indicated chiral column (4.6 mm x 0.25 mm) column. Melting Point were checked with a M-560 (BUCHI). ReactIR monitoring was performed with Mettler Toledo ReactIR™ 45m equipped with DS AgX DiComp™ probe. Optical rotation were recorded on JASCO P-2000 polarimeter.

Experimental Procedures

General procedure for the synthesis of *t*-butyl ester 2 [Condition A]

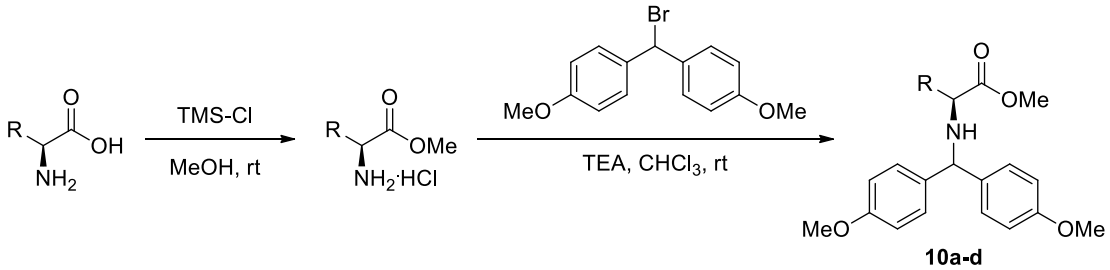
To a stirred suspension of NaO*t*Bu (1.25 mmol, 2.5 equiv.) in toluene (2.5 mL), ester **1** (0.5 mmol) was added. The mixture was stirred at room temperature for 3-4 h. The reaction mixture was quenched with 5% HCl solution and extracted with diethyl ether (2 × 10 mL). The combined organic extracts were dried over Na_2SO_4, concentrated under reduced pressure, and purified by column chromatography on silica gel (hexanes/EtOAc) to give the corresponding *t*-butyl ester **2**.

General procedure for the synthesis of carboxylic acid 3 [Condition B]

To a stirred solution of NaO*t*Bu (1.25 mmol, 2.5 equiv.) in THF (2.5 mL), ester **1** (0.5 mmol) was added. The mixture was stirred at room temperature for 24 h. The reaction mixture was quenched with water and extracted with diethyl ether (2 × 10 mL). The aqueous solution was treated with 5% HCl solution and extracted with diethyl ether (2 × 10 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated under reduced pressure to give the corresponding carboxylic acid **3**.

General procedure for the synthesis of *N*-protected amino acid methyl ester [Condition C]

This general procedure is a slight modification of the procedures available in literature.[1-3]



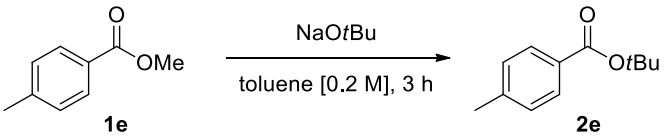
To a stirred solution of L-amino acid (3.0 mmol, 1.0 equiv.) in methanol (3.0 mL), trimethylsilyl chloride (6.0 mmol, 2.0 equiv.) was added at 0 °C and stirred overnight at room temperature. After the reaction reached completion, the volatiles were removed under reduced pressure, and the crude product was used without any further purification. A suspension of L-amino acid methyl ester hydrochloride (3.0 mmol, 1.0 equiv.) in $CHCl_3$ (4.5 mL) was treated with triethylamine (6.0 mmol, 2.0 equiv.) at 0 °C. After 5 min, 4,4'-(bromomethylene)bis(methoxybenzene) (3.0 mmol, 1.0 equiv.) was added to the

mixture and stirred overnight at room temperature. $CHCl_3$ (4.5 mL) was added to the mixture, and the resulting solution was washed with water (2 × 4.5 mL), dried over Na_2SO_4, and concentrated under reduced pressure, and purified by column chromatography on silica gel (hexanes / EtOAc) to afford *N*-protected amino acid methyl ester **10**.

General procedure for the synthesis of *N*-protected amino acid *t*-butyl ester [Condition D]

To a stirred solution of *N*-protected amino acid methyl ester **10** (0.5 mmol, 1.0 equiv.) in CH_2Cl_2 (2.5 mL), NaO*t*Bu solution dissolved in THF (1.35 mmol, 2.7 equiv.) was added slowly at 0 ºC. The mixture was stirred, and the reaction was monitored by TLC. After the reaction reached completion, the mixture was quenched with saturated NH_4Cl solution and CH_2Cl_2 (2 × 10 mL). The combined organic extracts were dried over Na_2SO_4, and concentrated under reduced pressure, and purified by column chromatography on silica gel (hexanes/EtOAc) to afford *N*-protected amino acid *t*-butyl ester **11**.

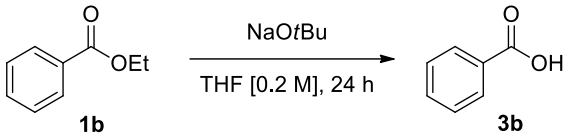
Table S1. Equivalent screening for transesterification.



Entry	Equivalent of NaO*t*Bu	Yield (%)[a]
1	2.0	70
2	2.5	88
3	3.0	89

[a]All yields are those of isolated products.

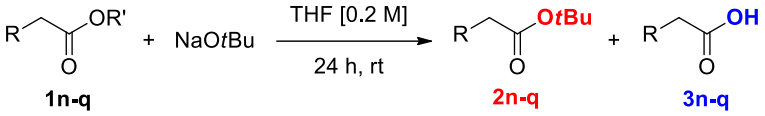
Table S2. Equivalent screening for deesterification.

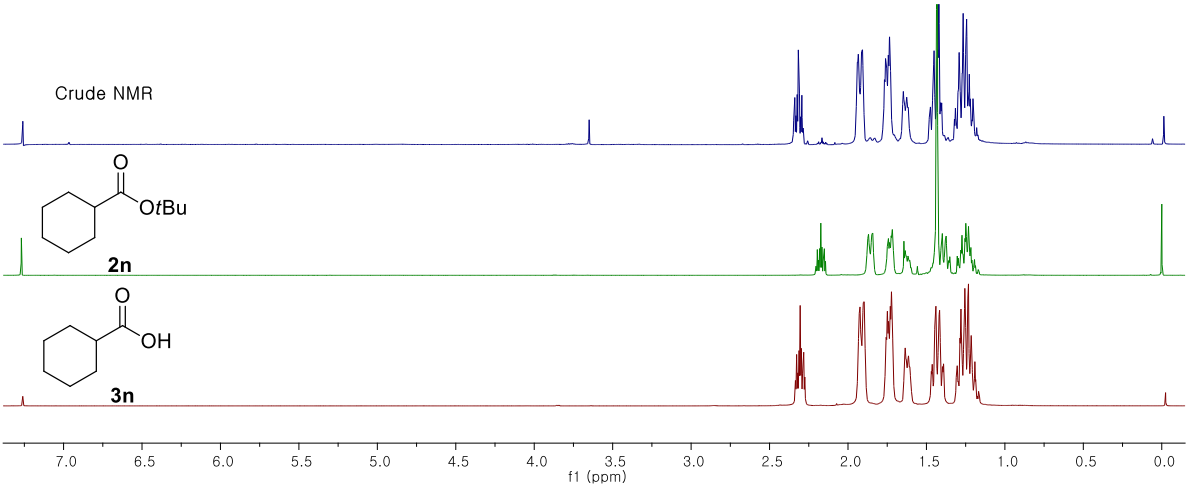


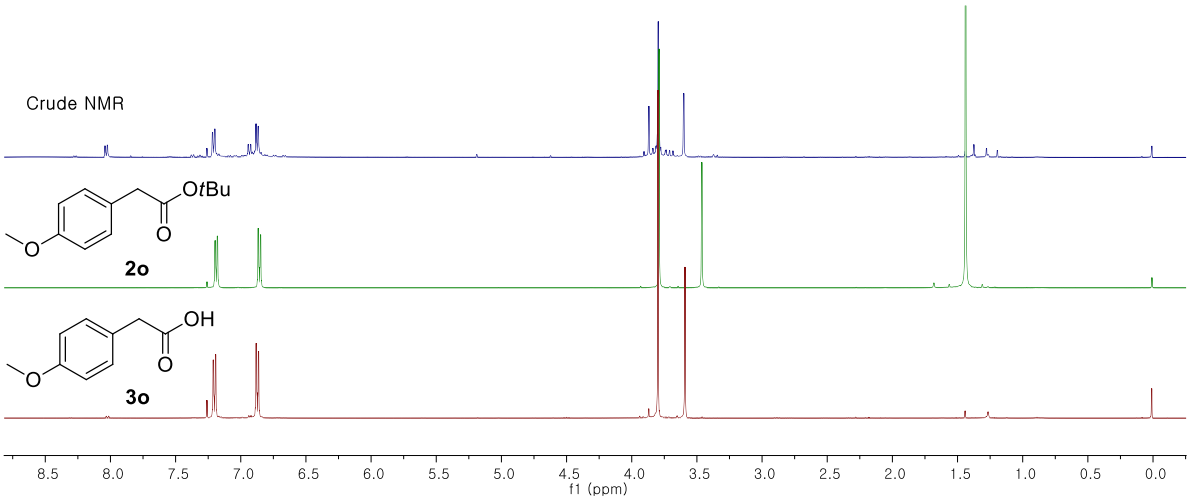
Entry	Equivalent of NaO*t*Bu	Yield (%)[a]
1	2.0	53
2	2.5	60
3	3.0	36

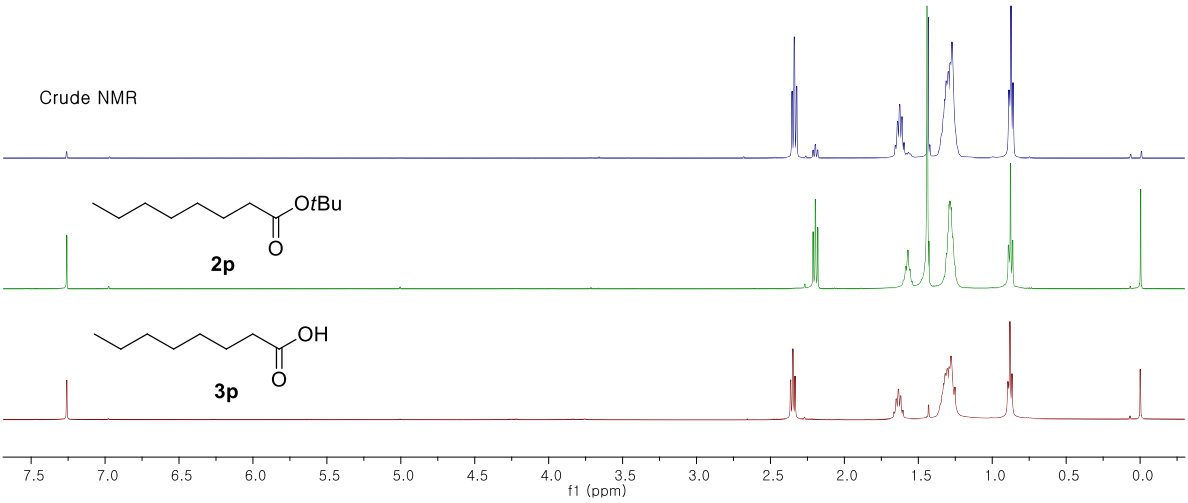
[a]All yields are those of isolated products.

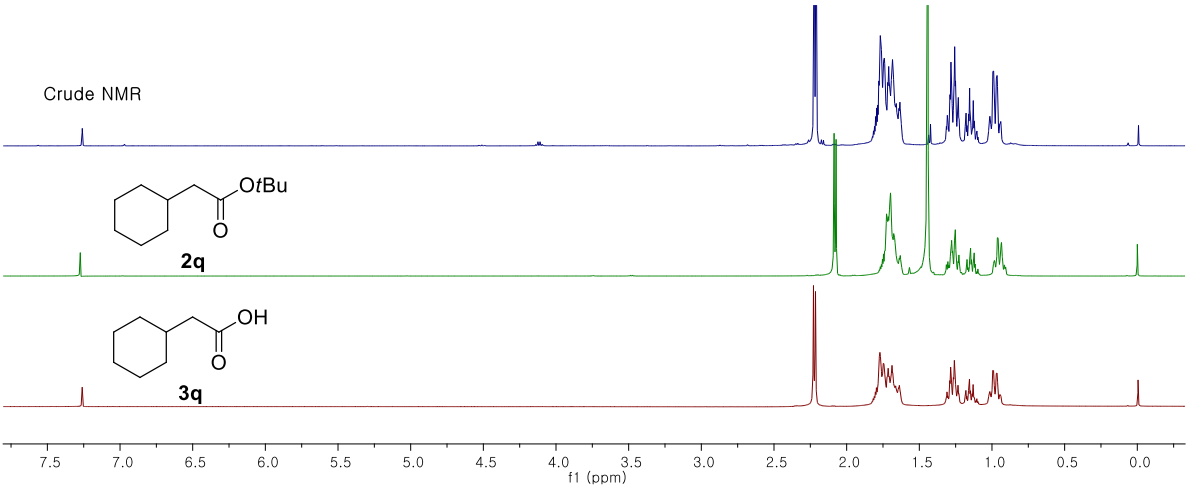
Confirmation of side reaction with enolisable esters



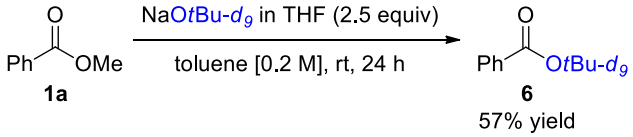







Crude NMR
OtBu
O
2q
OH
O
3q
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

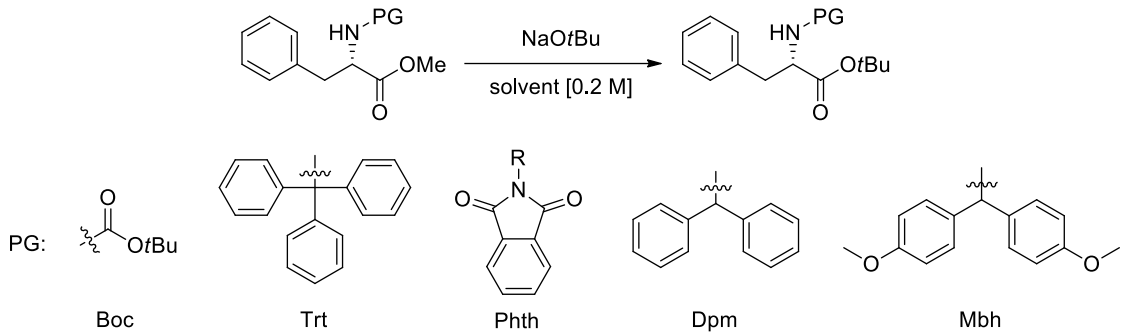
Deuterium-labeling experiment



NaH (60% in mineral oil, 1.25 mmol, 2.5 equiv.) was washed with pentane (3 × 2 mL) in a 10 mL round bottom flask. Dry THF (0.625 mL) was added with argon and *t*BuOH-d_{10} was slowly added to the mixture. After 5 h at room temperature, toluene (2.5 mL) and methyl benzoate (0.5 mmol) were added, and the reaction mixture was stirred for 24 h. The reaction was quenched with 5% HCl solution and extracted with diethyl ether (2 × 10 mL). The combined organic extracts were dried over Na_2SO_4, and concentrated under reduced pressure, and purified by column chromatography on silica gel (hexanes/diethyl ether 25:1) to afford the deuterium-incorporated *t*-butyl ester **6** as colorless liquid (57% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (d, J = 7.9 Hz, 2H), 7.54–7.50 (m, 1H), 7.41 (t, J = 7.7 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.9, 132.5, 132.2, 129.5, 128.3, 80.7, 27.3 (dt, J = 38.3, 19.3 Hz) ppm; HRMS (EI) *m/z* $[M]^+$ calcd. for $C_{11}H_5D_9O_2$ 187.1559, found 187.1534

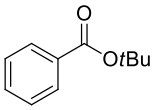
Table S4. Optimisation of the reaction conditions for *N*-protected amino *tert*-butyl esters



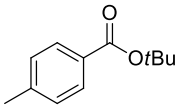
Entry	PG	Equiv. of NaO*t*Bu	Solvent	Temp. (°C)	Yield (%)[a]	*ee* (%)[b]
1	Boc	1.0	toluene	rt	7	0
2	Boc	1.0	toluene	-15	5	9
3	Trt	2.5	toluene	rt-50	n.d	n.d
4	Phth	2.0	toluene	rt	43	0
5	Dpm	2.0	toluene	rt	13	77
6	Mbh	2.0	toluene	rt	33	84
7	Mbh	2.0	THF	rt	28	0
8	Mbh	2.5	*p*-xylene	rt	42	74
9	Mbh	2.5	cyclohexane	rt	60	41
10	Mbh	2.5	benzene	rt	55	70
11	Mbh	2.5	diethyl ether	rt	41	21
12	Mbh	2.5	DCM	rt	27	92
13	Mbh	2.5	DCM	40	70	73
14	Mbh	2.5 (2 M in THF)	DCM	rt	91	80
15	Mbh	2.0 (2 M in THF)	DCM	rt	71	87
16	Mbh	2.5 (2 M in THF)	DCM	0	84	92
17	**Mbh**	**2.7 (2 M in THF)**	**DCM**	**0**	**86**	**94**

[a]All yields are those of isolated products. [b]The enantiomeric excess (*ee*) was determined by HPLC analysis.

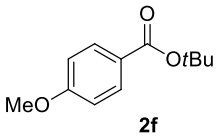
Analytical data of products



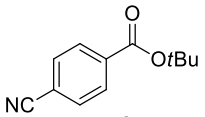
2a-2d ***tert*-Butyl benzoate (2a-2d)**, The title compound was synthesized according to general procedure A. Colorless liquid; Yield = 37-99%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (dd, J = 8.3, 1.3 Hz, 2H), 7.56–7.49 (m, 1H), 7.45–7.38 (m, 2H), 1.60 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.9, 132.5, 132.2, 129.5, 128.3, 81.1, 28.3 ppm. These data were consistent with those reported in the literature.[4]



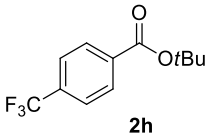
2e ***tert*-Butyl 4-methylbenzoate (2e)**, The title compound was synthesized according to general procedure A. Colorless liquid; Yield = 88%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89 (d, J = 8.2 Hz, 2H), 7.20 (d, J = 8.0 Hz, 2H), 2.39 (s, 3H), 1.59 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.9, 143.0, 129.5, 129.4, 128.9, 80.7, 28.3, 21.7 ppm. These data were consistent with those reported in the literature.[4]



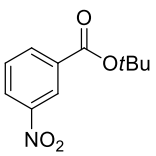
2f ***tert*-Butyl 4-methoxybenzoate (2f)**, The title compound was synthesized according to general procedure A. Colorless liquid; Yield = 88%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01–7.89 (m, 2H), 6.95–6.84 (m, 2H), 3.84 (s, 3H), 1.58 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.7, 163.1, 131.5, 124.6, 113.5, 80.6, 55.5, 28.4 ppm. These data were consistent with those reported in the literature.[4]



2g ***tert*-Butyl 4-cyanobenzoate (2g)**, The title compound was synthesized according to general procedure A. Colorless liquid; Yield = 99%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.17–7.91 (m, 2H), 7.84–7.57 (m, 2H), 1.58 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.0, 135.9, 132.1, 129.9, 118.2, 115.9, 82.4, 28.0 ppm. These data were consistent with those reported in the literature.[5]

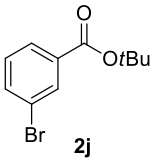


2h ***tert*-Butyl 4-(trifluoromethyl)benzoate (2h)**, The title compound was synthesized according to general procedure A. Colorless liquid; Yield = 98%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09 (d, J = 8.2 Hz, 2H), 7.67 (d, J = 8.2 Hz, 2H), 1.61 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.6, 135.4, 134.1 (q, $J_{C\text{-}F}$ = 32.5 Hz), 129.9, 125.3 (q, $J_{C\text{-}F}$ = 3.7 Hz), 123.9 (d, $J_{C\text{-}F}$ = 272.6 Hz); ^{19}F NMR (471 MHz, $CDCl_3$) δ -63.1 ppm. These data were consistent with those reported in the literature.[6]

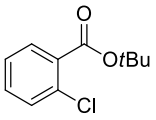


2i ***tert*-Butyl 3-nitrobenzoate (2i)**, The title compound was synthesized according to general procedure A. Yellow solid; Yield = 62%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.81–8.73 (m, 1H), 8.36 (ddd,

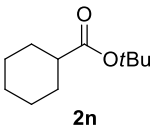
J = 8.2, 2.2, 1.0 Hz, 1H), 8.30 (dt, J = 7.7, 1.2 Hz, 1H), 7.61 (t, J = 8.0 Hz, 1H), 1.62 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.6, 148.3, 135.3, 133.9, 129.5, 127.0, 124.5, 82.7, 28.2 ppm. These data were consistent with those reported in the literature.[7]



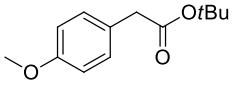
2j ***tert*-Butyl 3-bromobenzoate (2j)**, The title compound was synthesized according to general procedure A. Colorless liquid; Yield = 97%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.11 (t, J = 1.7 Hz, 1H), 8.01 – 7.83 (m, 1H), 7.63 (ddd, J = 8.0, 2.0, 1.0 Hz, 1H), 7.28 (t, J = 7.9 Hz, 1H), 1.59 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.4, 135.4, 134.1, 132.5, 129.8, 128.1, 122.4, 81.8, 28.2 ppm. These data were consistent with those reported in the literature.[4]



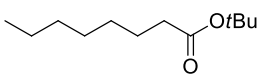
2k ***tert*-Butyl 2-chlorobenzoate (2k)**, The title compound was synthesized according to general procedure A. Colorless liquid; Yield = 95%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (dd, J = 7.7, 1.5 Hz, 1H), 7.38 (dtd, J = 9.5, 8.0, 1.3 Hz, 2H), 7.28 (dd, J = 10.6, 4.2 Hz, 1H), 1.61 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.3, 133.1, 132.3, 131.9, 131.0, 130.9, 126.6, 82.5, 28.3 ppm. These data were consistent with those reported in the literature.[8]



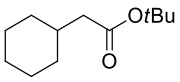
2n ***tert*-Butyl cyclohexanecarboxylate (2n)**, The title compound was synthesized according to general procedure A. Colorless liquid; Yield = 92%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.16 (tt, J = 11.2, 3.6 Hz, 1H), 1.91–1.80 (m, 2H), 1.77–1.68 (m, 2H), 1.66–1.57 (m, 1H), 1.44 (s, 9H), 1.42–1.32 (m, 2H), 1.31–1.14 (m, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.8, 79.7, 44.3, 29.2, 28.2, 26.0, 25.6 ppm. These data were consistent with those reported in the literature.[4]



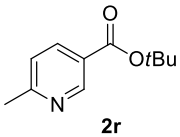
2o ***tert*-Butyl 2-(4-methoxyphenyl)acetate (2o)**, The title compound was synthesized according to general procedure A. Colorless liquid; Yield = 61%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.19 (d, J = 8.5 Hz, 2H), 6.86 (d, J = 8.6 Hz, 2H), 3.79 (s, 3H), 3.46 (s, 2H), 1.44 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.4, 158.7, 130.3, 127.0, 114.0, 80.8, 55.3, 41.8, 28.2 ppm. These data were consistent with those reported in the literature.[9]



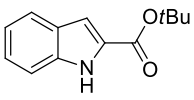
2p ***tert*-Butyl octanoate (2p)**, The title compound was synthesized according to general procedure A. Yellow liquid; Yield = 99%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.20 (t, J = 7.5 Hz, 2H), 1.61–1.53 (m, 2H), 1.44 (s, 9H), 1.34–1.23 (m, 8H), 0.88 (t, J = 7.0 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.5, 80.0, 35.8, 31.8, 29.2, 29.1, 28.3, 25.3, 22.8, 14.2 ppm. These data were consistent with those reported in the literature.[10]



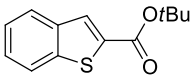
2q ***tert*-Butyl 2-cyclohexylacetate (2q)**, The title compound was synthesized according to general procedure A. Colorless liquid; Yield = 95%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.07 (d, J = 6.9 Hz, 2H), 1.79–1.60 (m, 6H), 1.43 (s, 9H), 1.32–1.07 (m, 3H), 1.02–0.87 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.8, 80.0, 43.6, 35.2, 33.1, 28.3, 26.4, 26.2 ppm; HRMS (FAB) *m/z* $[M+H]^+$ calcd. for $C_{12}H_{23}O_2$ 199.1698, found 199.1698



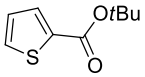
2r ***tert*-Butyl 6-methylnicotinate (2r)**, The title compound was synthesized according to general procedure A. Yellow liquid; Yield = 88%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.02 (d, J = 2.0 Hz, 1H), 8.08 (dd, J = 8.1, 2.2 Hz, 1H), 7.17 (d, J = 8.1 Hz, 1H), 2.58 (s, 3H), 1.57 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.7, 162.6, 150.5, 137.2, 125.1, 122.8, 81.8, 28.3, 24.8 ppm; HRMS (FAB) *m/z* $[M+H]^+$ calcd. for $C_{11}H_{16}NO_2$ 194.1181, found 194.1183



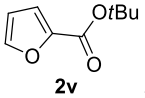
2s ***tert*-Butyl 1*H*-indole-2-carboxylate (2s)**, The title compound was synthesized according to general procedure A. White solid; Yield = 45%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.89 (s, 1H), 7.68 (dd, J = 8.0, 0.4 Hz, 1H), 7.42 (dd, J = 8.3, 0.6 Hz, 1H), 7.34–7.28 (m, 1H), 7.19–7.10 (m, 2H), 1.63 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.6, 136.8, 129.1, 127.7, 125.2, 122.6, 120.7, 112.0, 108.3, 81.9, 28.5 ppm. These data were consistent with those reported in the literature.[11]



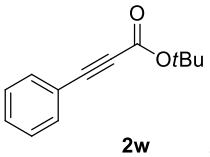
2t ***tert*-Butyl benzo[*b*]thiophene-2-carboxylate (2t)**, The title compound was synthesized according to general procedure A. Colorless liquid; Yield = 98%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 (s, 1H), 7.90–7.80 (m, 2H), 7.47–7.34 (m, 2H), 1.63 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.1, 142.2, 138.9, 135.9, 129.8, 126.7, 125.4, 124.8, 122.8, 82.4, 28.3 ppm. These data were consistent with those reported in the literature.[12]



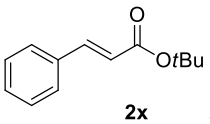
2u ***tert*-Butyl thiophene-2-carboxylate (2u)**, The title compound was synthesized according to general procedure A. Colorless liquid; Yield = 95%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 (dd, J = 3.7, 1.3 Hz, 1H), 7.48 (dd, J = 5.0, 1.3 Hz, 1H), 7.05 (dd, J = 5.0, 3.7 Hz, 1H), 1.57 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.6, 136.1, 132.8, 131.7, 127.6, 81.8, 28.3 ppm. These data were consistent with those reported in the literature.[5]



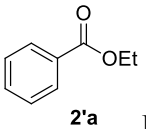
2v ***tert*-Butyl furan-2-carboxylate (2v)**, The title compound was synthesized according to general procedure A. Colorless liquid; Yield = 98%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56–7.48 (m, 1H), 7.05 (d, J = 3.5 Hz, 1H), 6.45 (dd, J = 3.4, 1.7 Hz, 1H), 1.56 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.2, 146.0, 145.8, 117.0, 111.7, 82.0, 28.3 ppm. These data were consistent with those reported in the literature.[4]



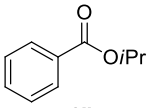
2w ***tert*-Butyl 3-phenylpropiolate (2w)**, The title compound was synthesized according to general procedure A. Pale yellow liquid; Yield = 92%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60–7.53 (m, 2H), 7.45–7.39 (m, 1H), 7.38–7.32 (m, 2H), 1.54 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.2, 133.0, 130.4, 128.6, 120.1, 83.8, 83.6, 82.2, 28.2 ppm. These data were consistent with those reported in the literature.[4]



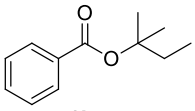
2x ***tert*-Butyl *trans*-cinnamate (2x)**, The title compound was synthesized according to general procedure A. Colorless liquid; Yield = 95%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 (d, J = 16.0 Hz, 1H), 7.55–7.46 (m, 2H), 7.42–7.31 (m, 3H), 6.38 (d, J = 16.0 Hz, 1H), 1.54 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.4, 143.6, 134.8, 130.0, 128.9, 128.0, 120.3, 80.5, 28.3 ppm. These data were consistent with those reported in the literature.[4]



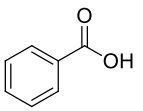
2'a **Ethyl benzoate (2'a)**, The title compound was synthesized according to general procedure A. Colorless liquid; Yield = 68%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (d, J = 7.2 Hz, 2H), 7.53 (t, J = 7.4 Hz, 1H), 7.42 (t, J = 7.6 Hz, 2H), 4.37 (q, J = 7.1 Hz, 2H), 1.39 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.7, 132.8, 130.6, 129.6, 128.4, 61.0, 14.4 ppm. These data were consistent with those reported in the literature.[13]



2'b **Isopropyl benzoate (2'b)**, The title compound was synthesized according to general procedure A. Colorless liquid; Yield = 78%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (d, J = 8.1 Hz, 2H), 7.54 (t, J = 7.4 Hz, 1H), 7.43 (t, J = 7.7 Hz, 2H), 5.33 – 5.18 (m, 1H), 1.37 (d, J = 6.4 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.3, 132.8, 131.1, 129.6, 128.4, 68.5, 22.1 ppm. These data were consistent with those reported in the literature.[14]

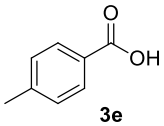


2'c ***tert*-Pentyl benzoate (2'c)**, The title compound was synthesized according to general procedure A. Colorless liquid; Yield = 99%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (d, J = 7.4 Hz, 2H), 7.52 (t, J = 7.4 Hz, 1H), 7.41 (t, J = 7.7 Hz, 2H), 1.93 (q, J = 7.5 Hz, 2H), 1.57 (s, 6H), 0.98 (t, J = 7.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.8, 132.5, 132.2, 129.5, 128.3, 83.5, 33.9, 25.8, 8.4 ppm. These data were consistent with those reported in the literature.[15]

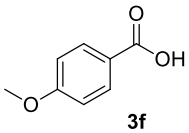


3a-3d **Benzoic acid (3a-3d)**, The title compound was synthesized according to general procedure B. White solid; Yield = 60-99%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.76 (s, 1H), 8.20–8.08 (m, 2H), 7.68–7.59 (m, 1H), 7.49 (dd, J = 10.8, 4.9 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.7, 134.0, 130.4, 129.5,

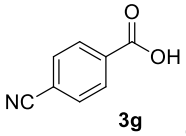
128.6 ppm. These data were consistent with those reported in the literature.[16]



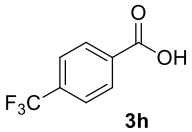
3e **4-Methylbenzoic acid (3e)**, The title compound was synthesized according to general procedure B. White solid; Yield = 80%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (d, J = 8.2 Hz, 2H), 7.28 (d, J = 8.0 Hz, 2H), 2.44 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.4, 144.8, 130.4, 129.4, 126.7, 21.9 ppm. These data were consistent with those reported in the literature.[17]



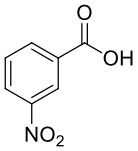
3f **4-Methoxybenzoic acid (3f)**, The title compound was synthesized according to general procedure B. White solid; Yield = 62%; ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.61 (s, 1H), 7.89 (d, J = 8.8 Hz, 2H), 7.01 (d, J = 8.7 Hz, 2H), 3.82 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 167.0, 162.8, 131.3, 123.0, 113.8, 55.4 ppm. These data were consistent with those reported in the literature.[17]



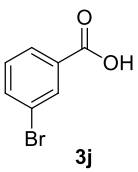
3g **4-Cyanobenzoic acid (3g)**, The title compound was synthesized according to general procedure B. White solid; Yield = 80%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 13.54 (s, 1H), 8.06 (d, J = 8.3 Hz, 2H), 7.94 (d, J = 8.3 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.1, 134.9, 132.7, 130.0, 118.2, 115.1 ppm. These data were consistent with those reported in the literature.[18]



3h **4-(Trifluoromethyl)benzoic acid (3h)**, The title compound was synthesized according to general procedure B. White solid; Yield = 88%; ^{1}H NMR (500 MHz, Acetone-d_6) δ 11.71 (s, 1H), 8.24 (d, J = 8.0 Hz, 2H), 7.88 (d, J = 8.3 Hz, 2H); ^{13}C NMR (126 MHz, Acetone-d_6) δ 166.5, 135.2, 134.5 (q, $J_{C\text{-}F}$= 32.3 Hz), 131.2, 126.4 (q, $J_{C\text{-}F}$ = 3.8 Hz), 124.9 (d, $J_{C\text{-}F}$ = 271.9 Hz); ^{19}F NMR (471 MHz, Acetone-d_6) δ -63.6 ppm. These data were consistent with those reported in the literature.[19]

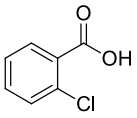


3i **3-Nitrobenzoic acid (3i)**, The title compound was synthesized according to general procedure B. White solid; Yield = 86%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.02–8.92 (m, 1H), 8.56–8.42 (m, 2H), 7.73 (t, J = 8.0 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.0, 148.5, 136.0, 131.0, 130.1, 128.5, 125.4 ppm. These data were consistent with those reported in the literature.[20]

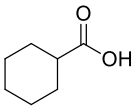


3j **3-Bromobenzoic acid (3j)**, The title compound was synthesized according to general procedure B. White solid; Yield = 72%; ^{1}H NMR (500 MHz, Acetone-d_6) δ 11.52 (s, 1H), 8.15 (t, J = 1.8 Hz, 1H), 8.09 – 7.97 (m, 1H), 7.81 (ddd, J = 8.0, 2.0, 1.0 Hz, 1H), 7.49 (t, J = 7.9 Hz, 1H); ^{13}C

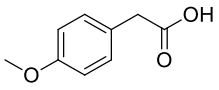
NMR (126 MHz, Acetone-d_6) δ 166.2, 136.6, 133.7, 133.1, 131.5, 129.3, 122.8 ppm. These data were consistent with those reported in the literature.[21]



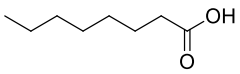
3k **2-Chlorobenzoic acid (3k)**, The title compound was synthesized according to general procedure B. White solid; Yield = 63%; ^{1}H NMR (500 MHz, Acetone-d_6) δ 11.60 (s, 1H), 7.96 – 7.84 (m, 1H), 7.59 – 7.50 (m, 2H), 7.48 – 7.38 (m, 1H); ^{13}C NMR (126 MHz, Acetone-d_6) δ 166.8, 133.7, 133.6, 132.2, 131.7, 131.7, 127.8 ppm. These data were consistent with those reported in the literature.[22]



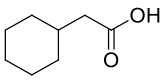
3n **Cyclohexanecarboxylic acid (3n)**, The title compound was synthesized according to general procedure B. White solid; Yield = 82%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.01 (s, 1H), 2.30 (tt, J = 11.2, 3.6 Hz, 1H), 1.91 (dd, J = 13.2, 2.7 Hz, 2H), 1.80–1.69 (m, 2H), 1.67–1.57 (m, 1H), 1.51–1.37 (m, 2H), 1.34–1.12 (m, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 183.2, 43.1, 28.8, 25.8, 25.4 ppm. These data were consistent with those reported in the literature.[23]



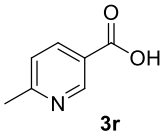
3o **2-(4-Methoxyphenyl)acetic acid (3o)**, The title compound was synthesized according to general procedure B. Brown solid; Yield = 89%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24–7.15 (m, 2H), 6.91–6.84 (m, 2H), 3.80 (s, 3H), 3.59 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 178.3, 159.0, 130.6, 125.5, 114.2, 55.4, 40.3 ppm. These data were consistent with those reported in the literature.[24]



3p **Octanoic acid (3p)**, The title compound was synthesized according to general procedure B. Colorless liquid; Yield = 87%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.35 (t, J = 7.5 Hz, 2H), 1.63 (dt, J = 14.9, 7.5 Hz, 2H), 1.39–1.22 (m, 8H), 0.88 (t, J = 6.9 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 180.0, 34.1, 31.8, 29.2, 29.0, 24.8, 22.7, 14.2 ppm. These data were consistent with those reported in the literature.[25]

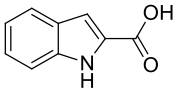


3q **2-Cyclohexylacetic acid (3q)**, The title compound was synthesized according to general procedure B. Yellow liquid; Yield = 90%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.88 (s, 1H), 2.22 (d, J = 6.8 Hz, 2H), 1.84–1.61 (m, 6H), 1.34–1.22 (m, 2H), 1.14 (ddt, J = 12.7, 7.0, 3.1 Hz, 1H), 1.06–0.90 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 180.0, 42.1, 34.8, 33.1, 26.2, 26.1 ppm. These data were consistent with those reported in the literature.[26]

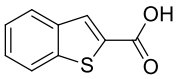


3r **6-Methylnicotinic acid (3r)**, The title compound was synthesized according to general procedure B. Yellow solid; Yield = 99%; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.97 (d, J = 1.5 Hz, 1H), 8.61 (d, J = 8.2 Hz, 1H), 7.84 (d, J = 8.2 Hz, 1H), 2.75 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 164.1, 158.5, 143.5, 143.3, 127.0, 126.8, 20.5 ppm. These data were consistent with those reported in the

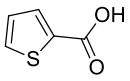
literature.[27]



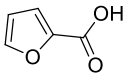
3s **1*H*-Indole-2-carboxylic acid (3s)**, The title compound was synthesized according to general procedure B. Brown solid; Yield = 50%; ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.92 (s, 1H), 11.74 (s, 1H), 7.64 (d, J = 8.0 Hz, 1H), 7.44 (d, J = 8.3 Hz, 1H), 7.29–7.18 (m, 1H), 7.14–7.01 (m, 2H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 162.8, 137.2, 128.4, 126.9, 124.3, 121.9, 120.0, 112.5, 107.3 ppm. These data were consistent with those reported in the literature.[28]



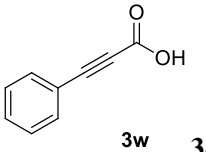
3t **Benzo[*b*]thiophene-2-carboxylic acid (3t)**, The title compound was synthesized according to general procedure B. Pale yellow solid; Yield = 71%; ^{1}H NMR (500 MHz, DMSO-d_6) δ 13.48 (s, 1H), 8.11 (s, 1H), 8.07–7.93 (m, 2H), 7.59–7.36 (m, 2H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 163.6, 141.4, 138.8, 134.8, 130.3, 127.0, 125.7, 125.1, 123.0 ppm. These data were consistent with those reported in the literature.[29]



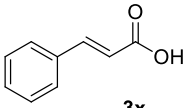
3u **Thiophene-2-carboxylic acid (3u)**, The title compound was synthesized according to general procedure B. White solid; Yield = 56%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.78 (s, 1H), 7.91 (dd, J = 3.8, 1.2 Hz, 1H), 7.66 (dd, J = 5.0, 1.2 Hz, 1H), 7.15 (dd, J = 4.9, 3.8 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.7, 135.2, 134.2, 133.0, 128.2 ppm. These data were consistent with those reported in the literature.[17]



3v **Furan-2-carboxylic acid (3v)**, The title compound was synthesized according to general procedure B. Beige solid; Yield = 62%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.60 (s, 1H), 7.65 (d, J = 0.6 Hz, 1H), 7.35 (d, J = 3.5 Hz, 1H), 6.57 (dd, J = 3.5, 1.6 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.7, 147.6, 143.9, 120.4, 112.5 ppm. These data were consistent with those reported in the literature.[29]

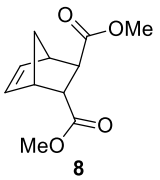


3w **3-Phenylpropiolic acid (3w)**, The title compound was synthesized according to general procedure B. Beige solid; Yield = 24%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 13.81 (s, 1H), 7.63 (d, J = 7.9 Hz, 2H), 7.55 (dd, J = 11.0, 3.9 Hz, 1H), 7.48 (t, J = 7.7 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.3, 132.6, 130.9, 129.0, 119.0, 84.4, 81.7 ppm. These data were consistent with those reported in the literature.[30]



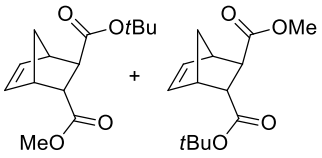
3x ***trans*-Cinnamic acid (3x)**, The title compound was synthesized according to general procedure B. White solid; Yield = 54%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.22 (s, 1H), 7.81 (d, J = 16.0 Hz, 1H), 7.57 (dd, J = 6.8, 2.8 Hz, 2H), 7.48–7.36 (m, 3H), 6.47 (d, J = 16.0 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.7, 147.3, 134.2, 130.9, 129.1, 128.5, 117.5 ppm. These data were consistent with

those reported in the literature.[31]



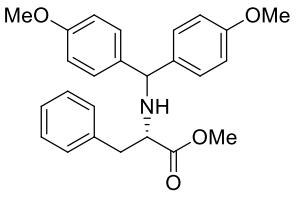
8

(1R,2R,3R,4S)-Dimethyl bicyclo[2.2.1]hept-5-ene-2,3-dicarboxylate (8), The title compound was synthesized according to reference. Colorless liquid; Yield = 99%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.27 (dd, J = 5.5, 3.2 Hz, 1H), 6.07 (dd, J = 5.6, 2.8 Hz, 1H), 3.71 (s, 3H), 3.64 (s, 3H), 3.37 (t, J = 4.1 Hz, 1H), 3.26 (s, 1H), 3.12 (s, 1H), 2.68 (dd, J = 4.5, 1.5 Hz, 1H), 1.61 (d, J = 8.9 Hz, 1H), 1.46 (dd, J = 8.8, 1.6 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.0, 173.9, 137.7, 135.3, 52.2, 52.0, 48.0, 47.8, 47.5, 47.2, 45.8 ppm. These data were consistent with those reported in the literature.[32]



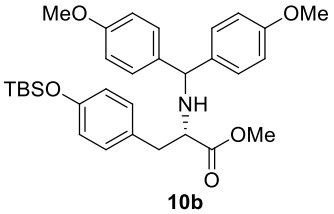
9 (major) **9'** (minor)

(1S,2R,3R,4R)-2-*tert*-Butyl 3-methyl bicyclo[2.2.1]hept-5-ene-2,3-dicarboxylate (9), The title compound was synthesized according to general procedure A. Colorless liquid; Yield = 60%; No attempt was made to separate the isomer mixture; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.26 (dd, J = 5.5, 3.1 Hz, 1H both isomers), 6.07–6.01 (m, 1H both isomers), 3.21 (s, 1H both isomers), 1.57 (d, J = 8.8 Hz, 1H both isomers); **Major** δ 3.62 (s, 3H), 3.33 (t, J = 4.1 Hz, 1H), 3.06 (m, 1H), 2.57 (dd, J = 4.4, 1.6 Hz, 1H), 1.44 (s, 9H), 1.42 (d, J = 1.7 Hz, 1H); **Minor** δ 3.69 (s, 3H), 3.27 (t, J = 4.1 Hz, 1H), 3.08 (m, 1H), 2.63 (dd, J = 4.4, 1.6 Hz, 1H), 1.41–1.40 (m, 1H), 1.40 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) **Major** δ 174.1, 173.7, 137.8, 135.2, 80.7, 51.8, 48.4, 47.9, 47.7, 47.3, 45.8, 28.2; **Minor** δ 175.3, 172.5, 137.6, 135.0, 80.5, 52.1, 49.0, 47.8, 47.5, 46.8, 46.0, 28.2 ppm. These data were consistent with those reported in the literature.[33]



10a

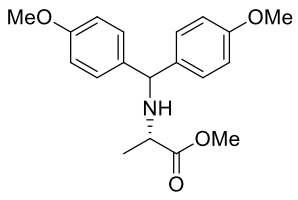
(*S*)-Methyl 2-((bis(4-methoxyphenyl)methyl)amino)-3-phenylpropanoate (10a), The title compound was synthesized according to general procedure C. White solid; $[\alpha]_D^{20}$ = -15.2 (*c* 0.1, MeOH); Yield = 89%; m.p. = 71-72 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30–7.17 (m, 5H), 7.17–7.12 (m, 2H), 7.07 (d, J = 8.6 Hz, 2H), 6.78 (d, J = 8.7 Hz, 2H), 6.72 (d, J = 8.7 Hz, 2H), 4.68 (s, 1H), 3.72 (d, J = 5.0 Hz, 6H), 3.64 (s, 3H), 3.43 (dd, J = 7.7, 5.9 Hz, 1H), 2.96 (dd, J = 13.4, 5.9 Hz, 1H), 2.88 (dd, J = 13.4, 7.8 Hz, 1H), 2.06 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.5, 158.7, 158.6, 137.7, 137.0, 135.1, 129.6, 128.5, 128.3, 128.3, 126.6, 113.9, 113.8, 64.2, 60.7, 55.3, 55.3, 51.7, 40.2 ppm; HRMS (EI) *m/z* $[M]^+$ calcd. for $C_{25}H_{27}NO_4$ 405.1940, found 405.1962



10b

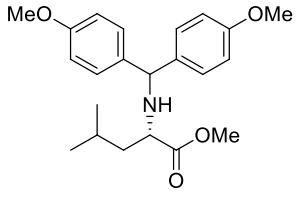
(*S*)-Methyl2-((bis(4-methoxyphenyl)methyl)amino)-3-(4-((tert-butyldimethylsilyl)oxy)phenyl) propanoate (10b), The title compound was synthesized according to general procedure C. Colorless oil; $[\alpha]_D^{20}$ = -0.2 (*c* 0.1, MeOH); Yield = 83%; ^{1}H NMR (500 MHz,

$CDCl_3$) δ 7.22 (d, J = 8.6 Hz, 2H), 7.11 (d, J = 8.6 Hz, 2H), 7.03 (d, J = 8.4 Hz, 2H), 6.81–6.76 (m, 6H), 4.69 (s, 1H), 3.76 (d, J = 4.7 Hz, 6H), 3.65 (s, 3H), 3.41 (dd, J = 7.6, 6.2 Hz, 1H), 2.87 (ddd, J = 21.3, 13.5, 6.9 Hz, 2H), 2.06 (s, 1H), 1.01 (s, 9H), 0.22 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.6, 158.7, 158.7, 154.5, 137.0, 135.1, 130.5, 130.5, 128.5, 128.4, 120.0, 113.9, 113.9, 64.2, 60.8, 55.3, 55.3, 51.7, 39.5, 25.8, 18.4, -4.3 ppm; HRMS (EI) *m/z* $[M]^+$ calcd. for $C_{31}H_{41}NO_5Si$ 535.2754, found 535.2775



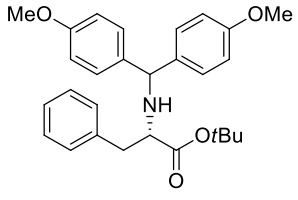
10c

(*S*)-Methyl 2-((bis(4-methoxyphenyl)methyl)amino)propanoate (10c), The title compound was synthesized according to general procedure C. Colorless oil; $[\alpha]_D^{20}$ = -32.8 (*c* 0.1, MeOH); Yield = 97%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35–7.33 (m, 2H) 7.28–7.26 (m, 2H), 6.87–6.82 (m, 4H), 4.76 (s, 1H), 3.77 (d, J = 10.7 Hz, 6H), 3.72 (s, 3H), 3.31 (q, J = 7.1 Hz, 1H), 2.10 (s, 1H), 1.32 (d, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.7, 158.7, 158.7, 136.9, 135.3, 128.5, 128.4, 113.9, 113.9, 64.1, 55.3, 55.3, 54.4, 51.8, 19.6 ppm; HRMS (EI) *m/z* $[M]^+$ calcd. for $C_{19}H_{23}NO_4$ 329.1627, found 329.1630



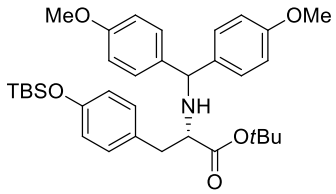
10d

(*S*)-Methyl 2-((bis(4-methoxyphenyl)methyl)amino)-4-methylpentanoate (10d), The title compound was synthesized according to general procedure C. Colorless oil; $[\alpha]_D^{20}$ = -46.6 (*c* 0.1, MeOH); Yield = 90%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 (d, J = 8.7 Hz, 2H), 7.31 (d, J = 8.7 Hz, 2H), 6.86 (dd, J = 18.9, 8.7 Hz, 4H), 4.73 (s, 1H), 3.78–3.73 (m, 9H), 3.26 (dd, J = 8.9, 5.5 Hz, 1H), 2.00–1.93 (m, 2H), 1.57–1.43 (m, 2H), 0.94 (d, J = 6.7 Hz, 3H), 0.85 (d, J = 6.6 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.8, 158.7, 158.6, 137.2, 135.2, 128.6, 128.2, 113.8, 64.3, 57.6, 55.2, 55.2, 51.6, 43.4, 24.8, 23.2, 22.02 ppm; HRMS (EI) *m/z* $[M]^+$ calcd. for $C_{22}H_{29}NO_4$ 371.2097, found 371.2092



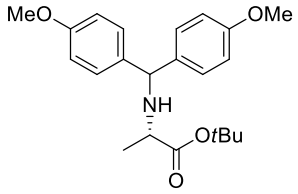
11a

(*S*)-*tert*-Butyl 2-((bis(4-methoxyphenyl)methyl)amino)-3-phenylpropanoate (11a), The title compound was synthesized according to general procedure D. Colorless oil; $[\alpha]_D^{20}$ = -12.9 (*c* 0.1, MeOH); Yield = 86%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27–7.16 (m, 7H), 7.12–7.09 (m, 2H), 6.79–6.73 (m, 4H), 4.70 (s, 1H), 3.73 (d, J = 10.0 Hz, 6H), 3.29 (t, J = 7.0 Hz, 1H), 2.92–2.84 (m, 2H), 2.05 (s, 1H), 1.38 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.3, 158.6, 158.6, 138.0, 137.2, 135.2, 129.7, 128.5, 128.4, 128.2, 126.5, 113.9, 113.8, 81.1, 64.2, 61.2, 55.3, 55.3, 40.3, 28.2 ppm; HRMS (EI) *m/z* $[M]^+$ calcd. for $C_{28}H_{33}NO_4$ 447.2410, found 447.2407; HPLC analysis: Chiralpak OD-H (hexane/isopropyl = 99:1, wavelength = 210 nm, flow rate = 0.7 mL/min), t_R = 10.6 min (major), 12.5 min (minor)



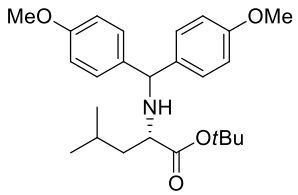
11b

(*S*)-*tert*-Butyl 2-((bis(4-methoxyphenyl)methyl)amino)-3-(4-((tert-butyldimethylsilyl)oxy)phenyl) propanoate (11b), The title compound was synthesized according to general procedure D. Colorless oil; $[\alpha]_D^{20}$ = -2.4 (*c* 0.1, MeOH); Yield = 56%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24 (d, *J* = 8.6 Hz, 2H), 7.17 (d, *J* = 8.6 Hz, 2H), 7.07 (d, *J* = 8.4 Hz, 2H), 6.80 (dd, *J* = 18.2, 8.8 Hz, 6H), 4.74 (s, 1H), 3.78 (d, *J* = 10.5 Hz, 6H), 3.29 (t, *J* = 7.0 Hz, 1H), 2.90–2.82 (m, 2H), 2.06 (s, 1H), 1.42 (s, 9H), 1.02 (s, 9H), 0.23 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.4, 158.6, 158.6, 154.3, 137.3, 135.3, 130.8, 130.7, 128.6, 128.4, 119.8, 113.9, 113.8, 81.0, 64.2, 61.3, 55.3, 55.3, 39.5, 28.2, 25.9, 18.4, -4.3 ppm; HRMS (EI) *m/z* $[M]^+$ calcd. for $C_{34}H_{47}NO_5Si$ 577.3224, found 577.3224; HPLC analysis: Chiralpak AD-H (hexane/isopropyl = 99:1, wavelength = 254 nm, flow rate = 0.4 mL/min), t_R = 10.9 min (major), 12.7 min (minor)



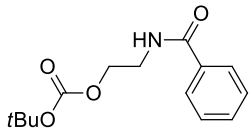
11c

(*S*)-*tert*-Butyl 2-((bis(4-methoxyphenyl)methyl)amino)propanoate (11c), The title compound was synthesized according to general procedure D. Colorless oil; $[\alpha]_D^{20}$ = -21.9 (*c* 0.1, MeOH); Yield = 82%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (d, *J* = 8.6 Hz, 2H), 7.24 (d, *J* = 8.7 Hz, 2H), 6.84 (d, *J* = 8.7 Hz, 2H), 6.80 (d, *J* = 8.7 Hz, 2H), 4.75 (s, 1H), 3.76 (d, *J* = 14.0 Hz, 6H), 3.14 (q, *J* = 7.0 Hz, 1H), 2.04 (s, 1H), 1.47 (s, 9H), 1.25 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.6, 158.7, 158.7, 137.2, 135.4, 128.6, 128.4, 113.9, 113.9, 80.9, 64.1, 55.3, 55.2, 28.3, 19.7 ppm; HRMS (EI) *m/z* $[M]^+$ calcd. for $C_{22}H_{29}NO_4$ 371.2097, found 371.2071; HPLC analysis: Chiralpak AD-H (hexane/isopropyl = 99:1, wavelength = 210 nm, flow rate = 0.7 mL/min), t_R = 11.7 min (major), 16.3 min (minor)



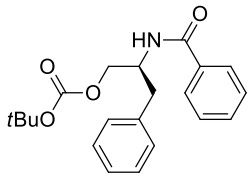
11d

(*S*)-*tert*-Butyl 2-((bis(4-methoxyphenyl)methyl)amino)-4-methylpentanoate (11d), The title compound was synthesized according to general procedure D. Colorless oil; $[\alpha]_D^{20}$ = -39.1 (*c* 0.1, MeOH); Yield = 71%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 (d, *J* = 8.6 Hz, 2H), 7.25 (d, *J* = 8.7 Hz, 2H), 6.82 (dd, *J* = 23.9, 8.7 Hz, 4H), 4.71 (s, 1H), 3.74 (d, *J* = 17.0 Hz, 6H), 3.05 (dd, *J* = 8.5, 5.9 Hz, 1H), 1.95–1.87 (m, 2H), 1.47 (s, 9H), 1.45–1.34 (m, 2H), 0.89 (d, *J* = 6.7 Hz, 3H), 0.81 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.8, 158.7, 158.6, 137.5, 135.4, 128.7, 128.3, 113.9, 113.8, 80.7, 64.2, 58.3, 55.3, 55.3, 43.4, 28.3, 24.9, 23.2, 22.3 ppm; HRMS (EI) *m/z* $[M]^+$ calcd. for $C_{25}H_{35}NO_4$ 413.2566, found 413.2570; HPLC analysis: Chiralpak IA (hexane/isopropyl = 97:3, wavelength = 260 nm, flow rate = 0.6 mL/min), t_R = 8.4 min (major), 13.5 min (minor)



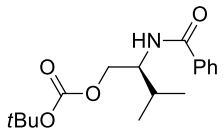
13a

2-Benzamidoethyl *tert*-butyl carbonate (13a), The title compound was synthesized according to general procedure A. White solid; Yield = 78%; m.p. = 92-93 ℃; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 (d, J = 7.5 Hz, 2H), 7.48 (t, J = 7.4 Hz, 1H), 7.40 (t, J = 7.6 Hz, 2H), 6.71 (s, 1H), 4.26–4.24 (m, 2H), 3.72 (dd, J = 10.4, 5.4 Hz, 2H), 1.47 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.7, 153.7, 134.3, 131.7, 128.6, 127.1, 82.8, 65.9, 39.5, 27.8 ppm; HRMS (EI) *m/z* $[M]^+$ calcd. for $C_{14}H_{19}NO_4$ 265.1314, found 265.1327



13b

(*S*)-2-Benzamido-3-phenylpropyl *tert*-butyl carbonate (13b), The title compound was synthesized according to general procedure A. White solid; $[\alpha]_D^{20}$ = -46.9 (*c* 0.1, MeOH); Yield = 88%; m.p. = 95-96 ℃; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (d, J = 7.4 Hz, 2H), 7.49 (t, J = 7.4 Hz, 1H), 7.42 (t, J = 7.6 Hz, 2H), 7.35–7.28 (m, 2H), 7.28–7.20 (m, 3H), 6.46 (d, J = 8.0 Hz, 1H), 4.70–4.52 (m, 1H), 4.17 (ddd, J = 15.2, 11.3, 4.4 Hz, 2H), 3.07 (dd, J = 13.7, 6.2 Hz, 1H), 2.95 (dd, J = 13.7, 8.0 Hz, 1H), 1.48 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.1, 153.9, 137.2, 134.5, 131.7, 129.5, 128.8, 128.7, 127.1, 127.0, 82.9, 67.1, 50.6, 37.4, 27.9 ppm; HRMS (FAB) *m/z* $[M+H]^+$ calcd. for $C_{21}H_{26}NO_4$ 356.1862, found 356.1868



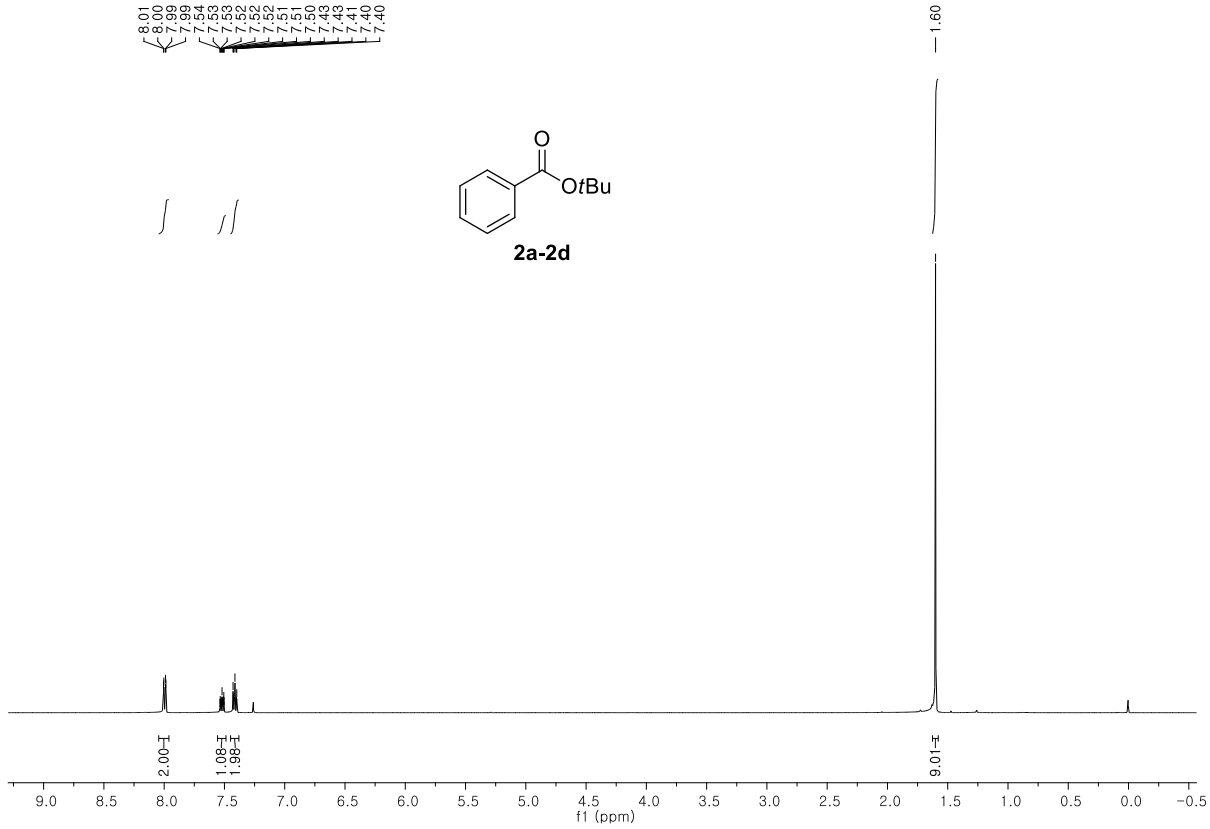
13c

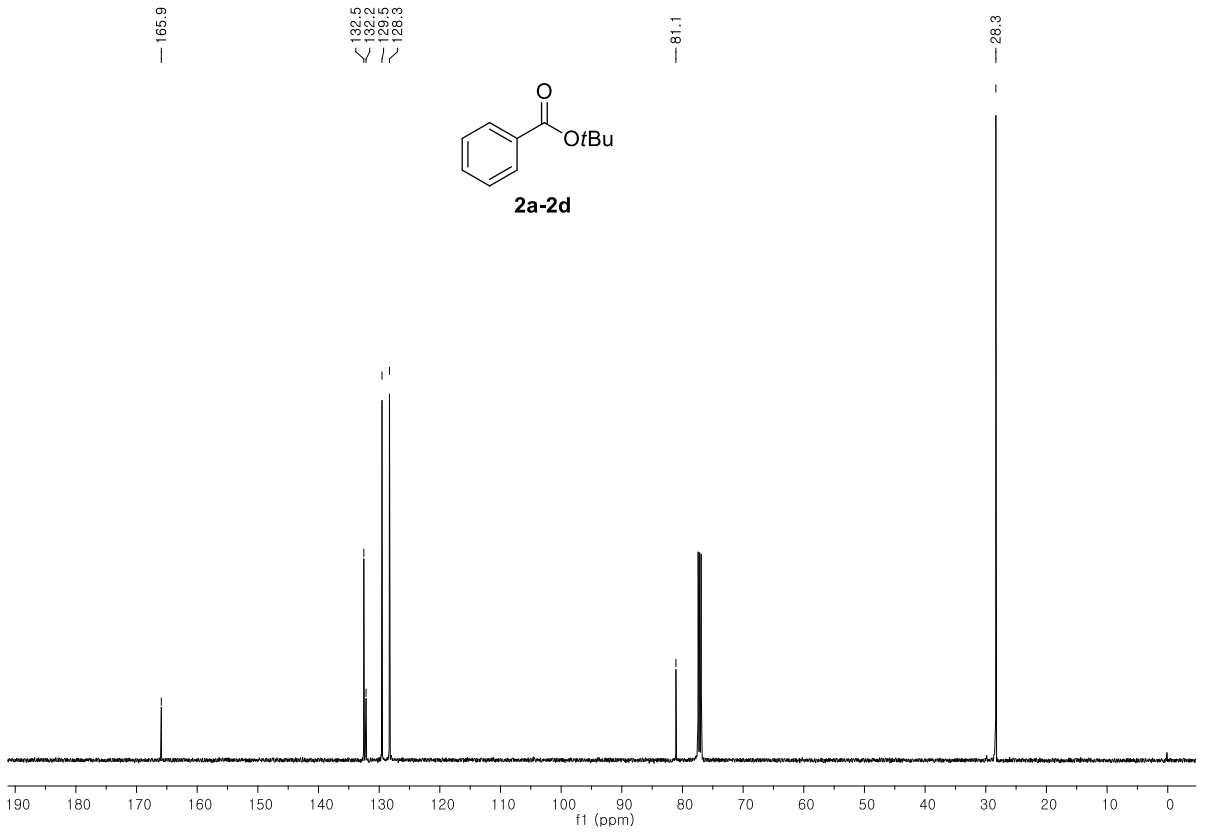
(*S*)-2-Benzamido-3-methylbutyl *tert*-butyl carbonate (13c), The title compound was synthesized according to general procedure A. White solid; $[\alpha]_D^{20}$ = -5.6 (*c* 0.1, MeOH); Yield = 72%; m.p. = 92-93 ℃; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 (d, J = 7.3 Hz, 2H), 7.50 (t, J = 7.3 Hz, 1H), 7.44 (t, J = 7.5 Hz, 2H), 6.32 (d, J = 8.9 Hz, 1H), 4.37 (dd, J = 11.3, 5.4 Hz, 1H), 4.23–4.10 (m, 2H), 2.04–1.95 (m, 1H), 1.45 (s, 9H), 1.02 (t, J = 6.5 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.3, 154.0, 134.7, 131.6, 128.6, 127.1, 82.6, 66.9, 54.3, 29.6, 27.8, 19.5, 19.0 ppm; HRMS (EI) *m/z* $[M]^+$ calcd. for $C_{17}H_{25}NO_4$ 307.1784, found 307.1770

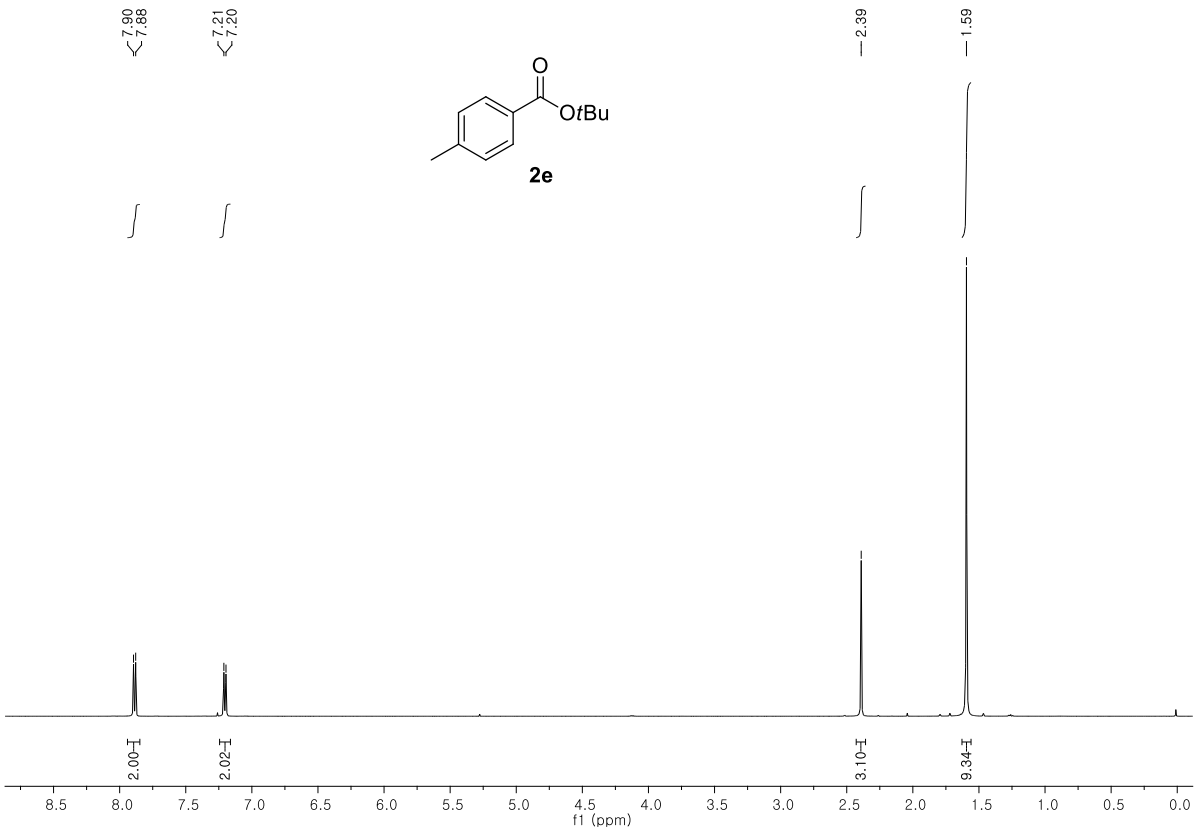
References

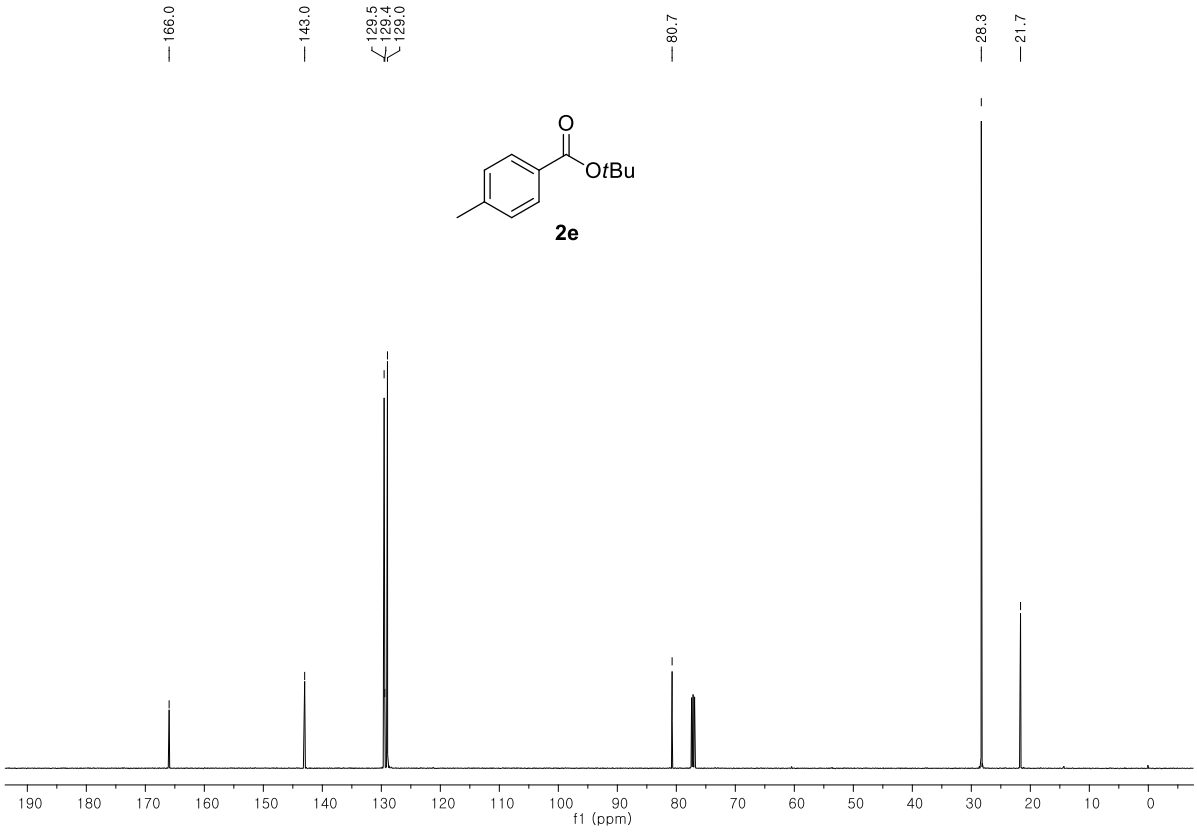
1 C.-P. Yu, Y. Tang, L. Cha, S. Milikisiyants, T. I. Smirnova, A. I. Smirnov, Y. Guo and W.-c. Chang, *J. Am. Chem. Soc.*, 2018, **140**, 15190-15193.
2 K. Tóth, G. Höfner and K. T. Wanner, *Bioorg. Med. Chem.*, 2018, **26**, 3668-3687.
3 R. W. Hanson and H. D. Law, *J. Chem. Soc.*, 1965, 7285-7296.
4 M. T. La and H.-K. Kim, *Tetrahedron*, 2018, **74**, 3748-3754.
5 K. Ghosh, R. A. Molla, M. A. Iqubal and S. M. Islam, *Green Chem.*, 2015, **17**, 3540-3551.
6 Z. Xin, T. M. Gøgsig, A. T. Lindhardt and T. Skrydstrup, *Org. Lett.*, 2012, **14**, 284-287.
7 W. C. Drewe, R. Nanjunda, M. Gunaratnam, M. Beltran, G. N. Parkinson, A. P. Reszka, W. D. Wilson and S. Neidle, *J. Med. Chem.*, 2008, **51**, 7751-7767.
8 Y. Nishimoto, S. A. Babu, M. Yasuda and A. Baba, *J. Org. Chem.*, 2008, **73**, 9465-9468.
9 I. Abdiaj, L. Huck, J. M. Mateo, A. de la Hoz, M. V. Gomez, A. Díaz-Ortiz and J. Alcázar, *Angew. Chem., Int. Ed.*, 2018, **57**, 13231-13236.
10 Y. Iuchi, Y. Obora and Y. Ishii, *J. Am. Chem. Soc.*, 2010, **132**, 2536-2537.
11 D. H. Kim, C. J. Guinosso, G. C. Buzby, Jr., D. R. Herbst, R. J. McCaully, T. C. Wicks and R. L. Wendt, *J. Med. Chem.*, 1983, **26**, 394-403.
12 B. Anxionnat, D. Gomez Pardo, G. Ricci, K. Rossen and J. Cossy, *Org. Lett.*, 2013, **15**, 3876-3879.
13 B. Teng, J. Shi and C. Yao, *Green Chem.*, 2018, **20**, 2465-2471.
14 C. C. D. Wybon, C. Mensch, K. Hollanders, C. Gadais, W. A. Herrebout, S. Ballet and B. U. W. Maes, *ACS Catal.*, 2018, **8**, 203-218.
15 X. Sang, X. Hu, R. Tao, Y. Zhang, H. Zhu and D. Wang, *ChemPlusChem*, 2020, **85**, 123-129.
16 T. Zweifel, J.-V. Naubron and H. Grützmacher, *Angew. Chem., Int. Ed.*, 2009, **48**, 559-563.
17 D. Yang, H. Yang and H. Fu, *Chem. Commun.*, 2011, **47**, 2348-2350.
18 S. Luliński and K. Zajac, *J. Org. Chem.*, 2008, **73**, 7785-7788.
19 T. Ohishi, M. Nishiura and Z. Hou, *Angew. Chem., Int. Ed.*, 2008, **47**, 5792-5795.
20 A. Chacko and B. Mathew, *J. Appl. Polym. Sci.*, 2003, **90**, 3708-3717.
21 C. Mukhopadhyay and A. Datta, *Catal. Commun.*, 2008, **9**, 2588-2592.
22 F. C. Lopez, A. Shankar, M. Thompson, B. Shealy, D. Locklear, T. Rawalpally, T. Cleary and C. Gagliardi, *Org. Process Res. Dev.*, 2005, **9**, 1003-1008.
23 W. Ren, J. Chu, F. Sun and Y. Shi, *Org. Lett.*, 2019, **21**, 5967-5970.
24 L. Shen, X. Yang, B. Yang, Q. He and Y. Hu, *Eur. J. Med. Chem.*, 2010, **45**, 11-18.
25 M. Liu and C.-J. Li, *Angew. Chem., Int. Ed.*, 2016, **55**, 10806-10810.
26 T. Nakashima, *Yakugaku Zasshi*, 1955, **75**, 1012-1013.
27 M. Sechi, L. Sannia, F. Carta, M. Palomba, R. Dallocchio, A. Dessì, M. Derudas, Z. Zawahir and N. Neamati, *Antivir. Chem. Chemother.*, 2005, **16**, 41-61.
28 T. Higa and A. J. Krubsack, *J. Org. Chem.*, 1976, **41**, 3399-3403.
29 E. Dalcanale and F. Montanari, *J. Org. Chem.*, 1986, **51**, 567-569.
30 L. J. Gooßen, N. Rodríguez, F. Manjolinho and P. P. Lange, *Adv. Synth. Catal.*, 2010, **352**, 2913-2917.
31 T. Fukuyama, M. Arai, H. Matsubara and I. Ryu, *J. Org. Chem.*, 2004, **69**, 8105-8107.
32 A. B. Chang, T.-P. Lin, N. B. Thompson, S.-X. Luo, A. L. Liberman-Martin, H.-Y. Chen, B. Lee and R. H. Grubbs, *J. Am. Chem. Soc.*, 2017, **139**, 17683-17693.
33 D. E. Rajsfus, P. Gilinsky-Sharon and A. A. Frimer, *J. Fluorine Chem.*, 2013, **148**, 59-66.

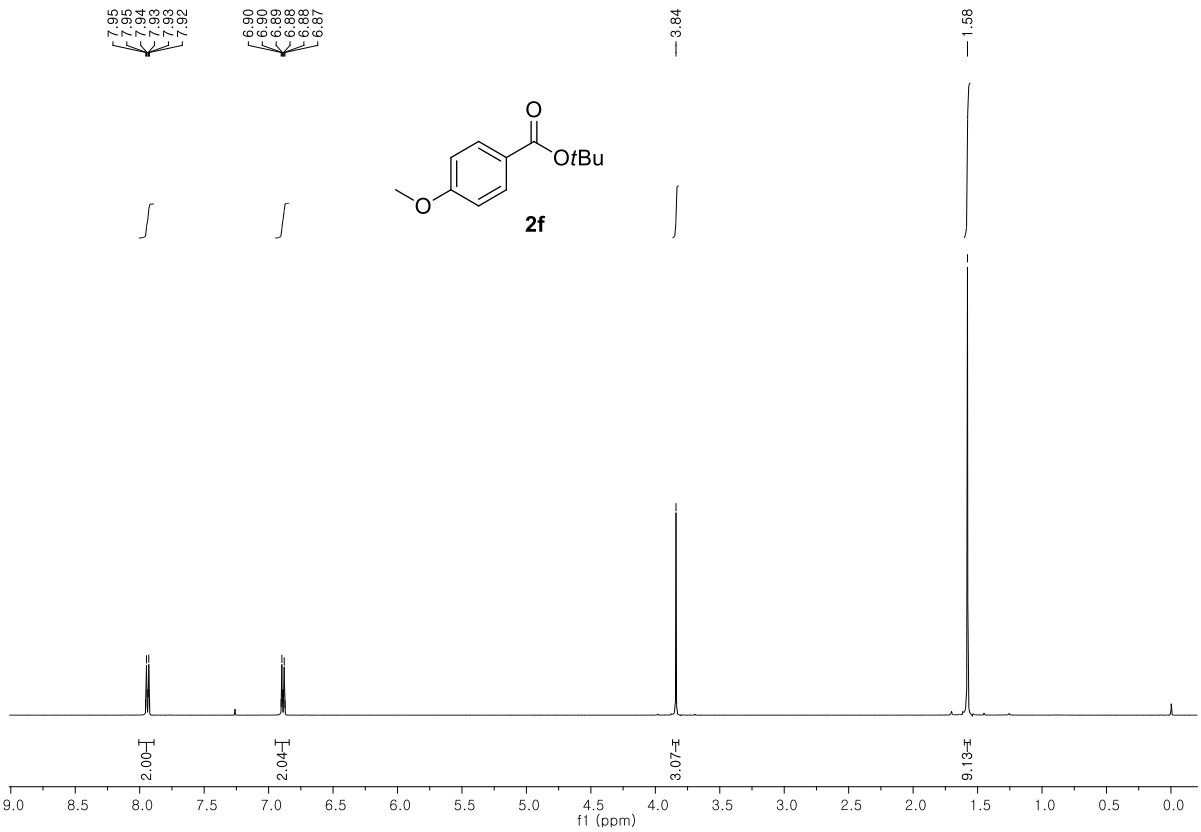
^{1}H NMR and ^{13}C NMR spectra of the products

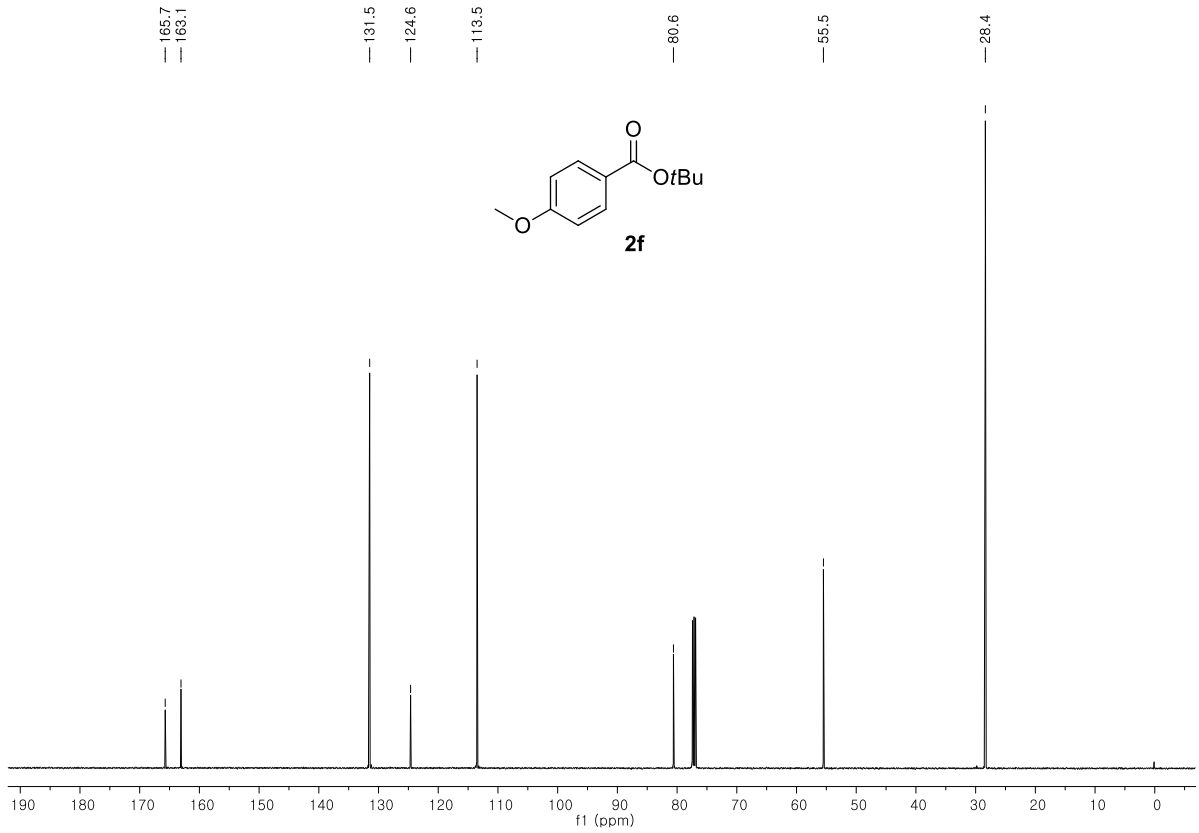


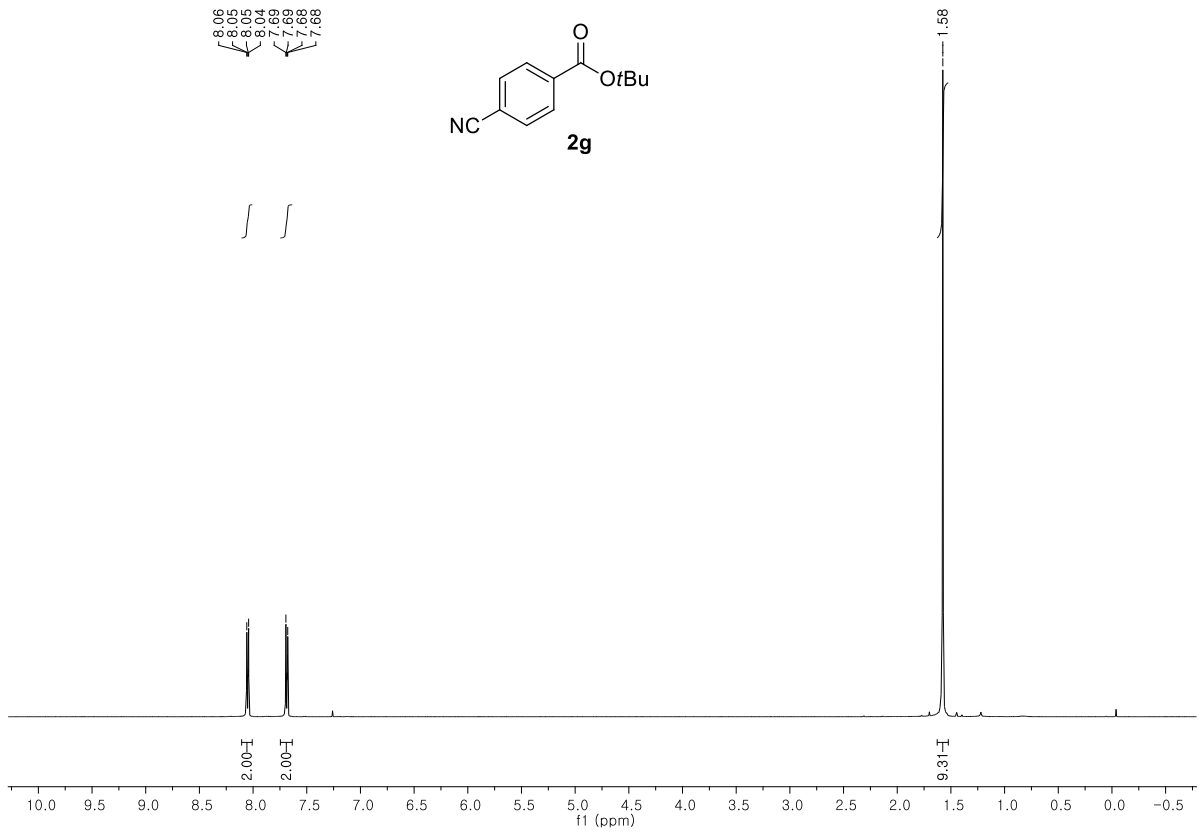


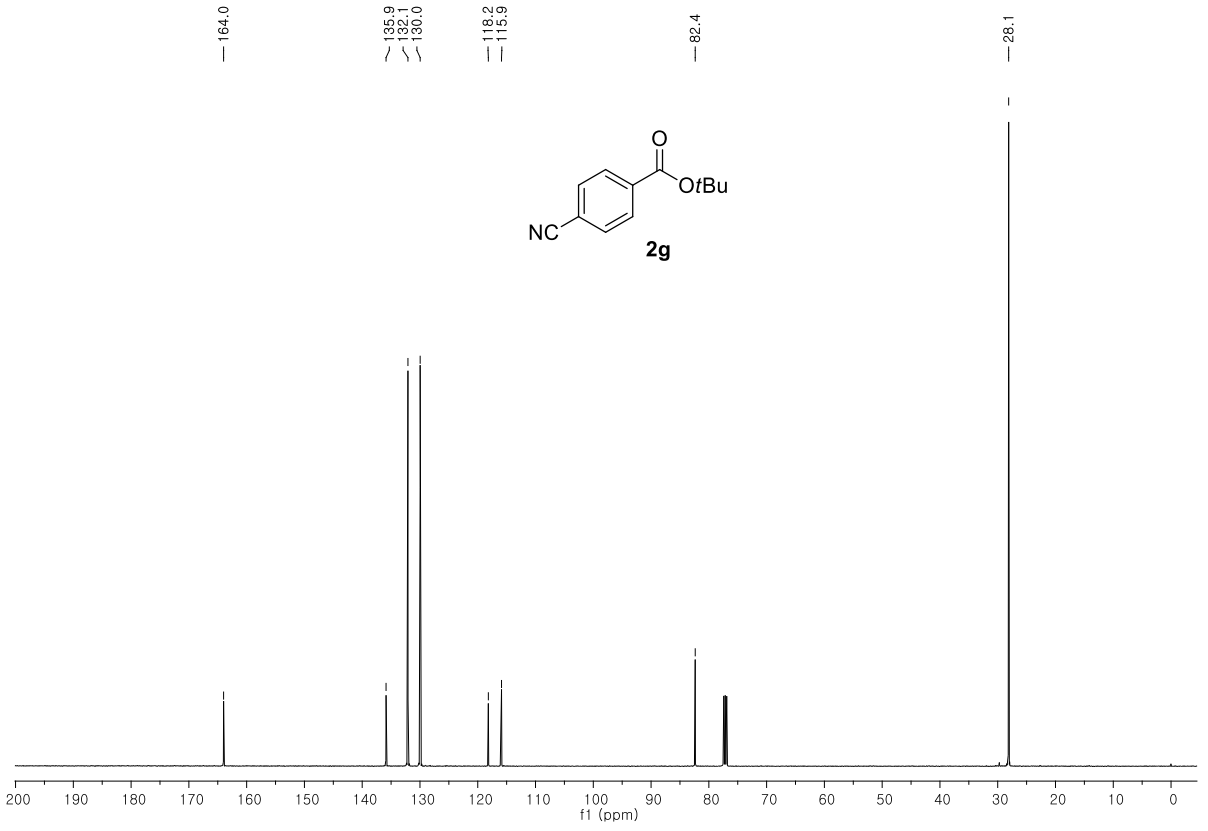

7.90
7.88
7.21
7.20
2.39
1.59
O
OtBu
2e
2.00
2.02
3.10
9.34
f1 (ppm)

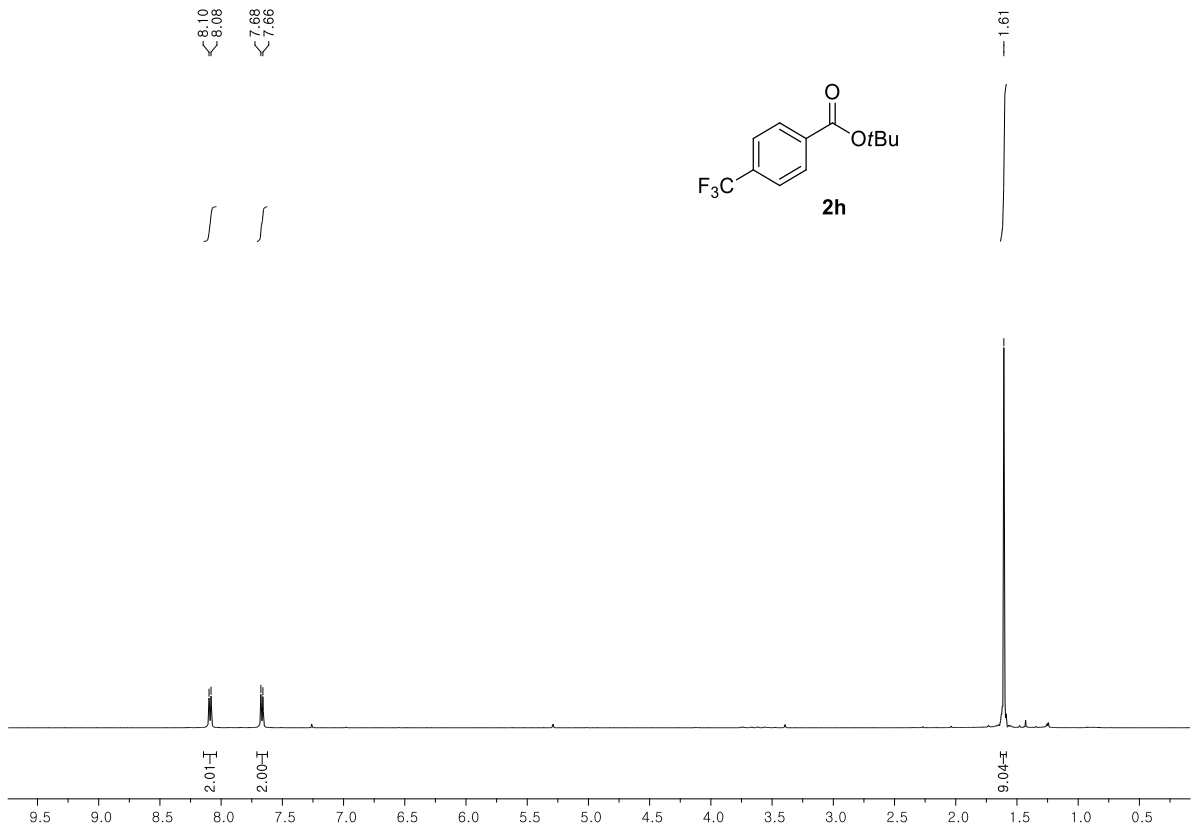

166.0
143.0
129.5
129.4
129.0
80.7
28.3
21.7
O
OtBu
2e
f1 (ppm)

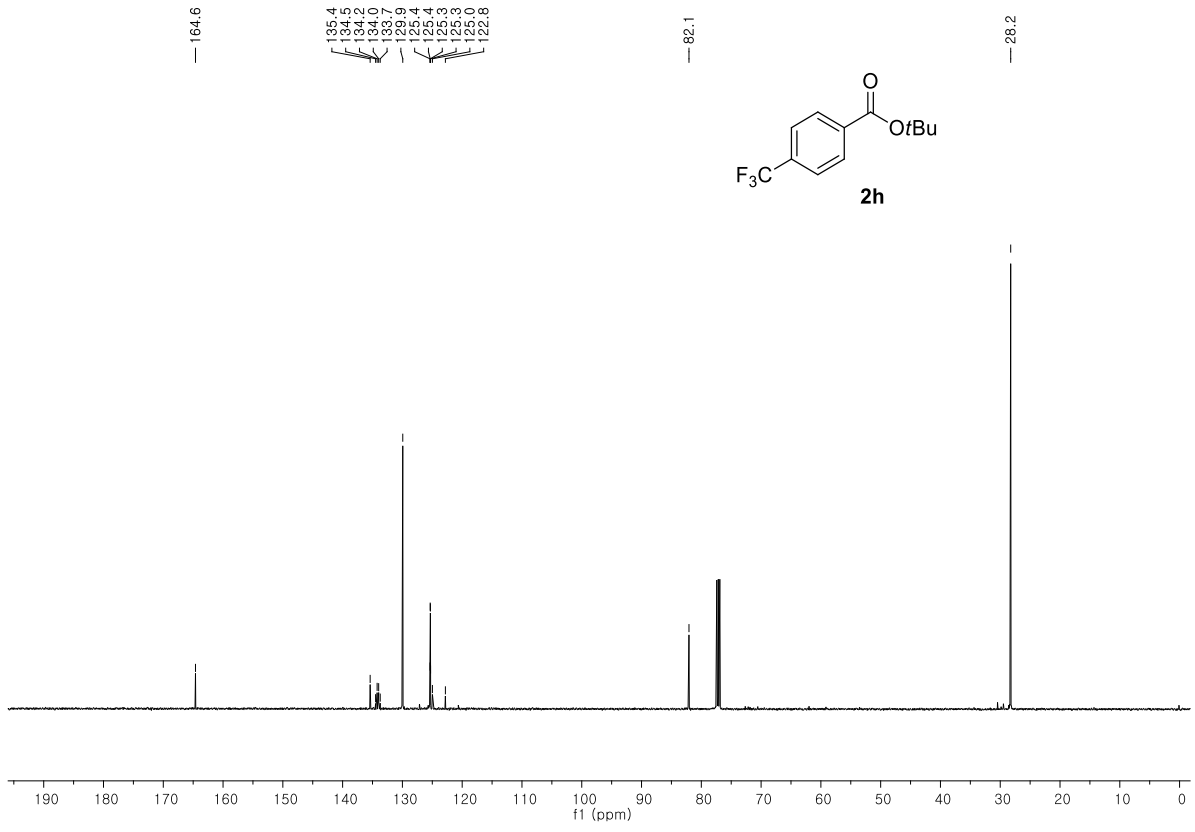

7.95
7.95
7.94
7.93
7.93
7.92
6.90
6.90
6.89
6.88
6.88
6.87
3.84
1.58
OtBu
2f
2.00
2.04
3.07
9.13
f1 (ppm)

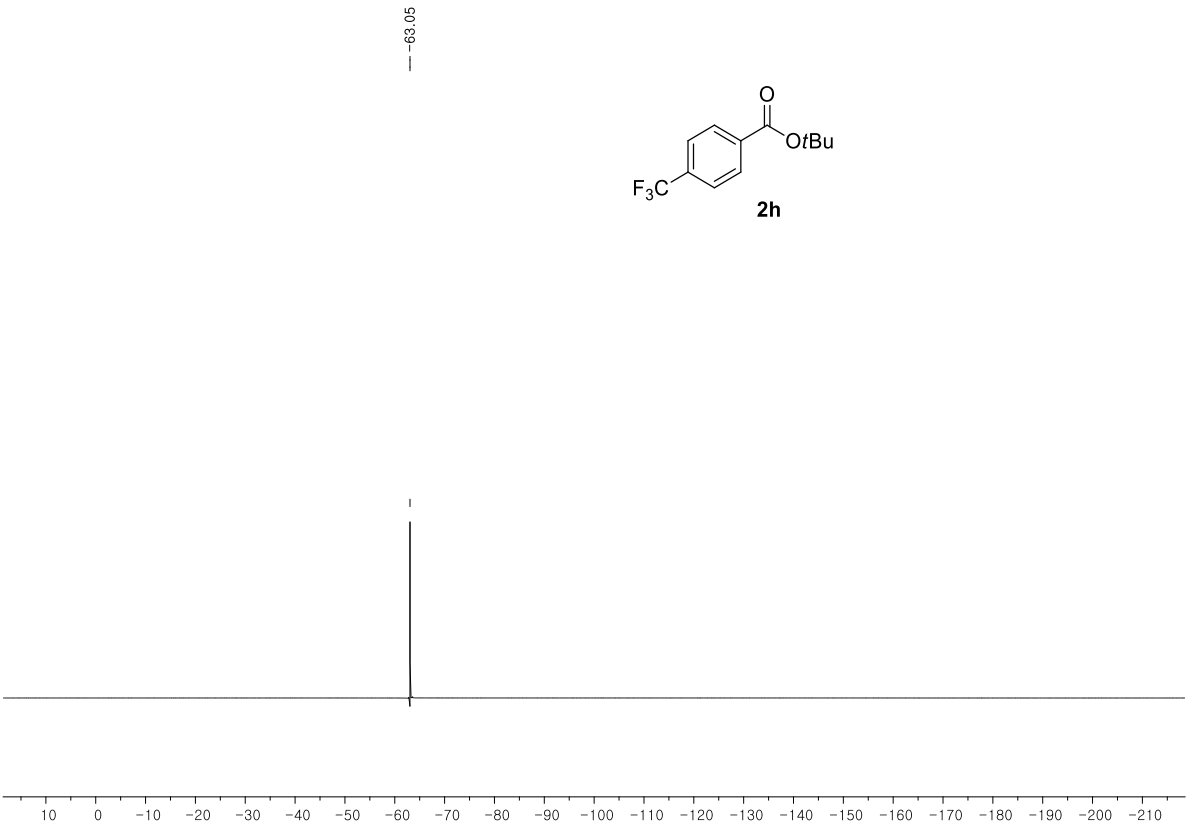

165.7
163.1
131.5
124.6
113.5
80.6
55.5
28.4
OtBu
2f
f1 (ppm)

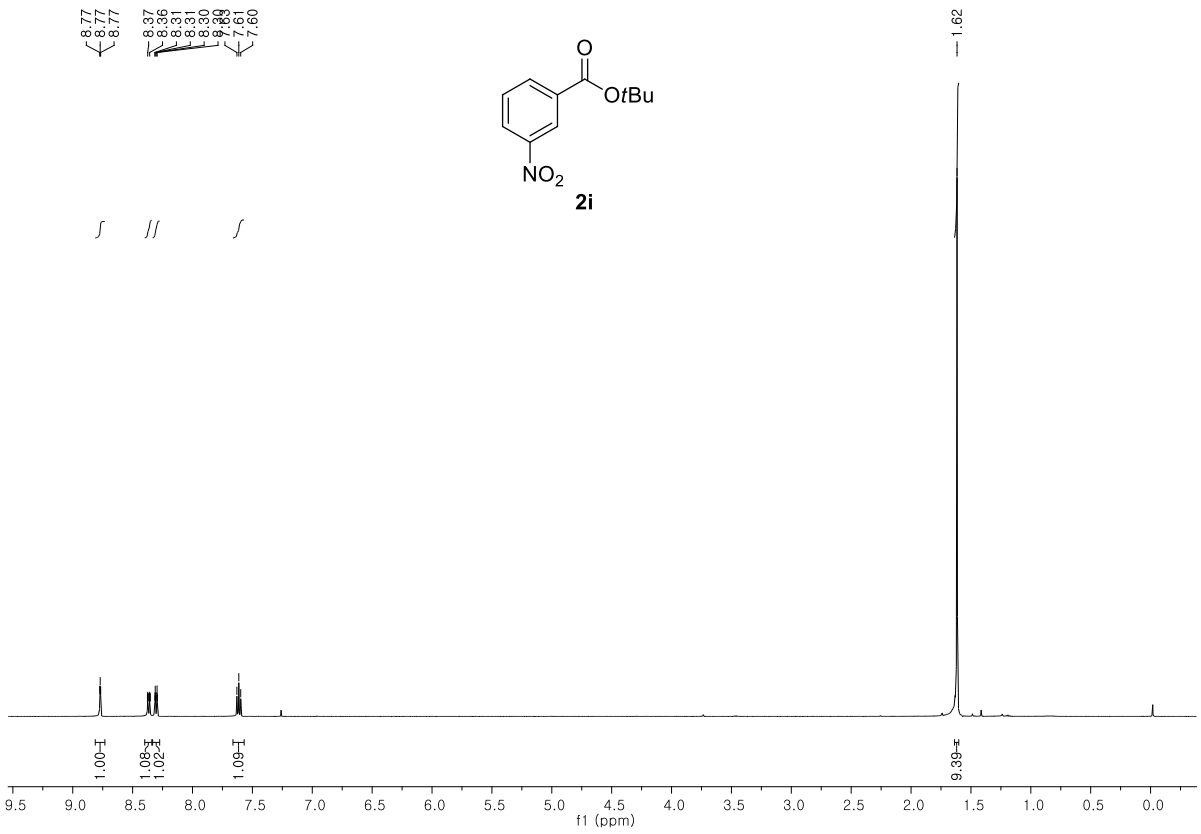

8.06
8.05
8.05
8.04
7.69
7.69
7.68
7.68
1.58
O
OtBu
NC
2g
2.00
2.00
9.31
f1 (ppm)

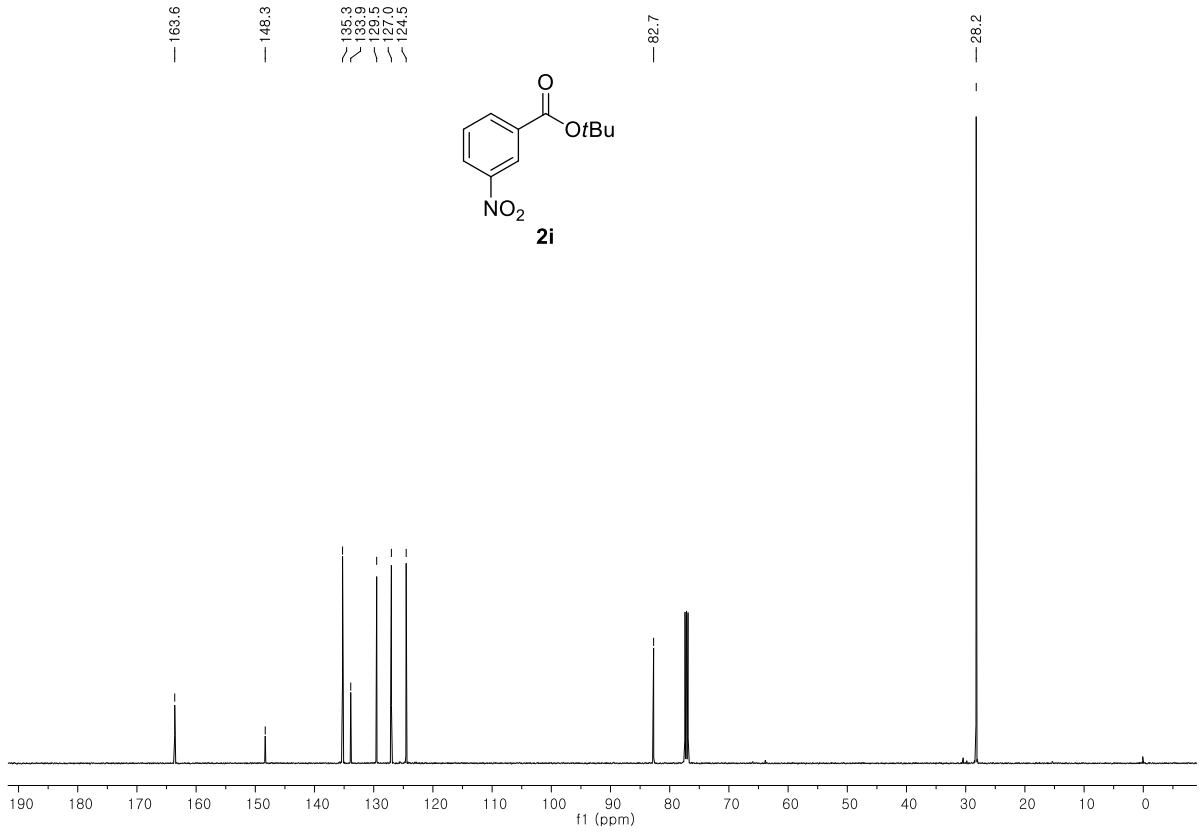

164.0
135.9
132.1
130.0
118.2
115.9
82.4
28.1
O
OtBu
NC
2g
f1 (ppm)

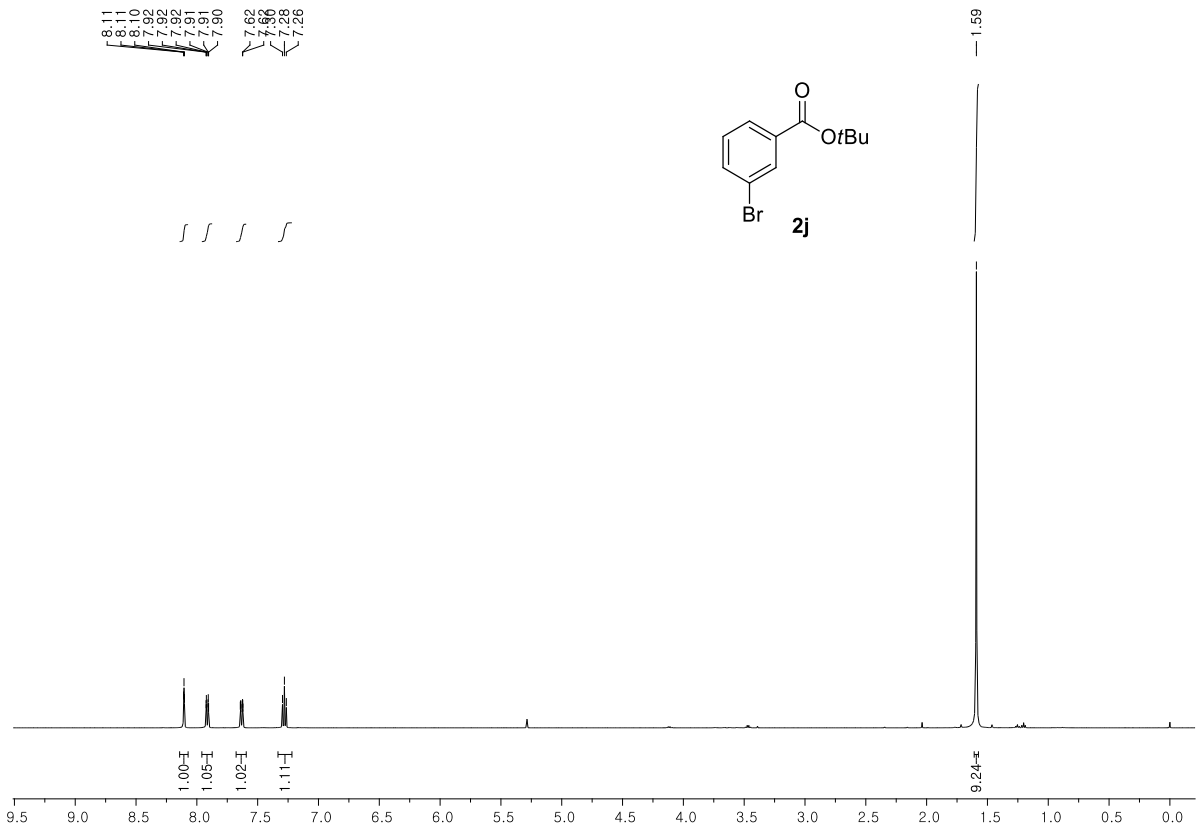

8.10
8.08
7.68
7.66
1.61
O
OtBu
F3C
2h
2.01
2.00
9.04
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5

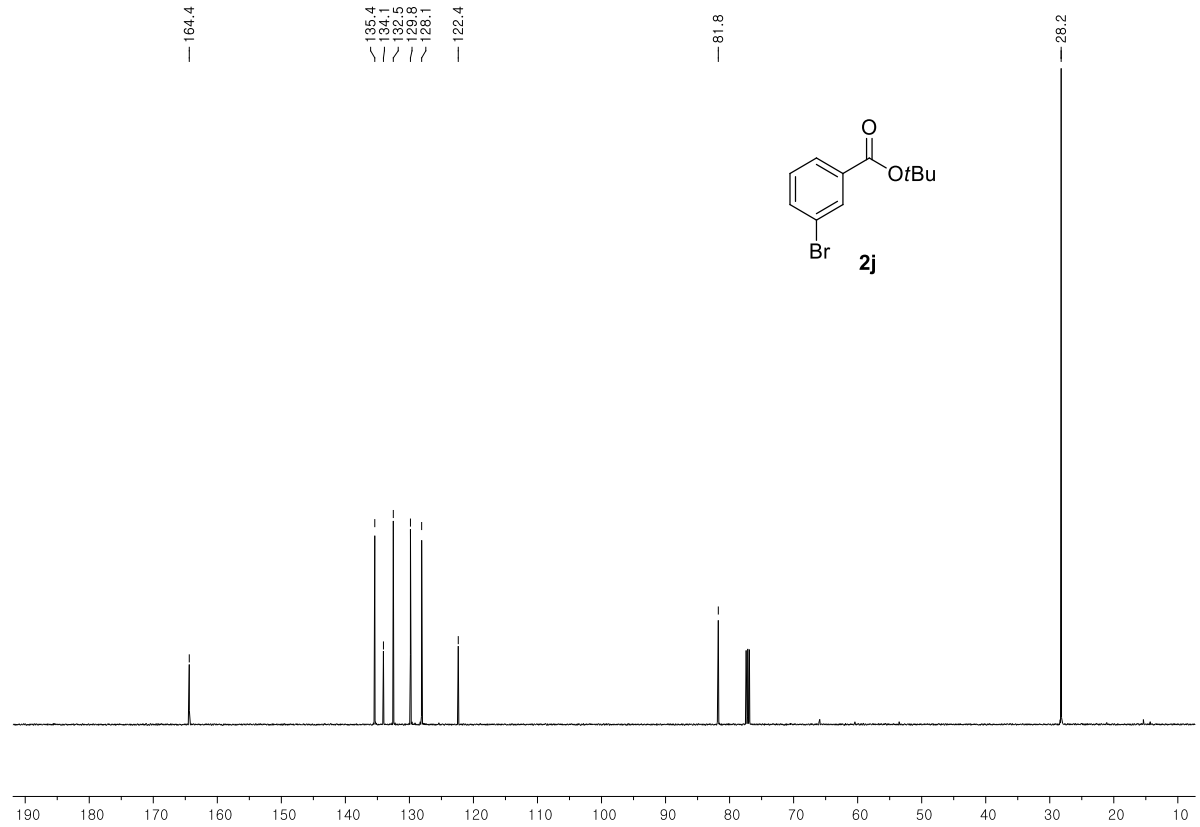

164.6
135.4
134.5
134.2
134.0
133.7
129.9
125.4
125.4
125.3
125.3
125.0
122.8
82.1
28.2
O
OtBu
F3C
2h
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

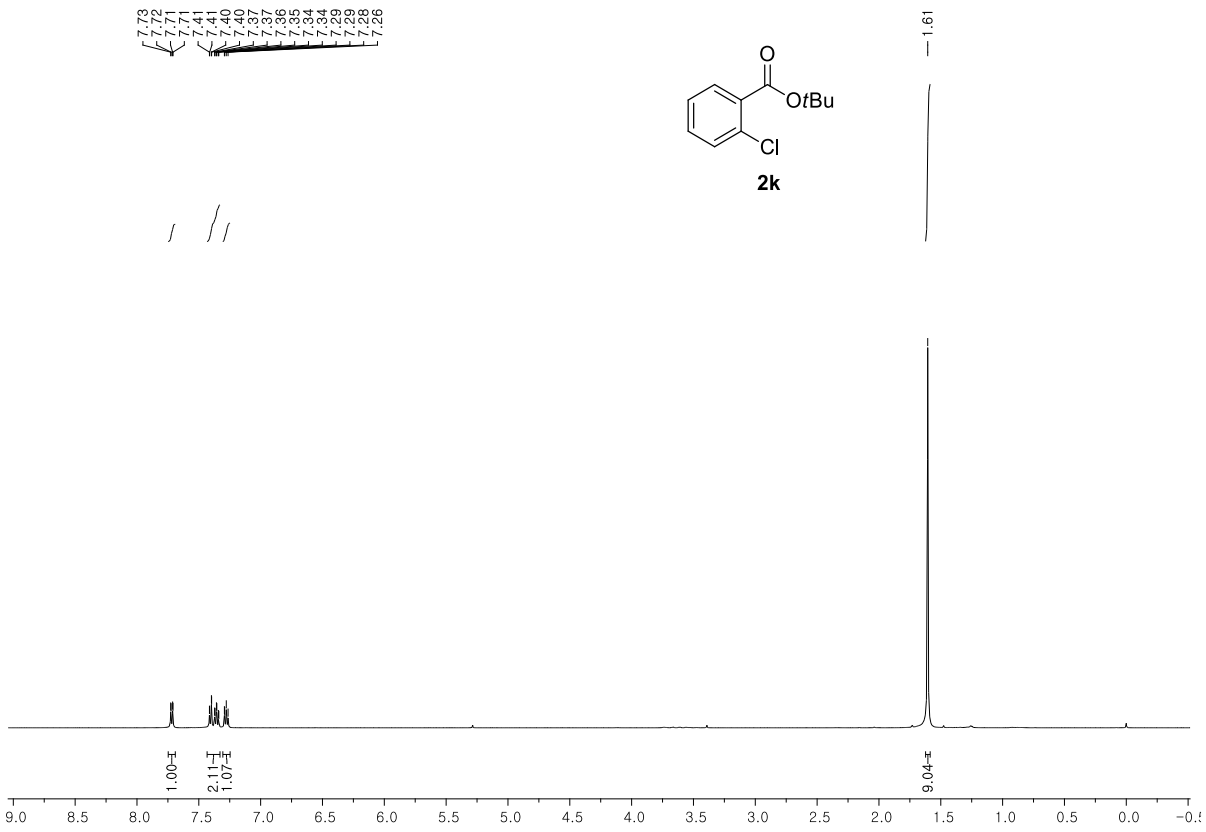

-63.05
O
OtBu
F3C
2h
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210

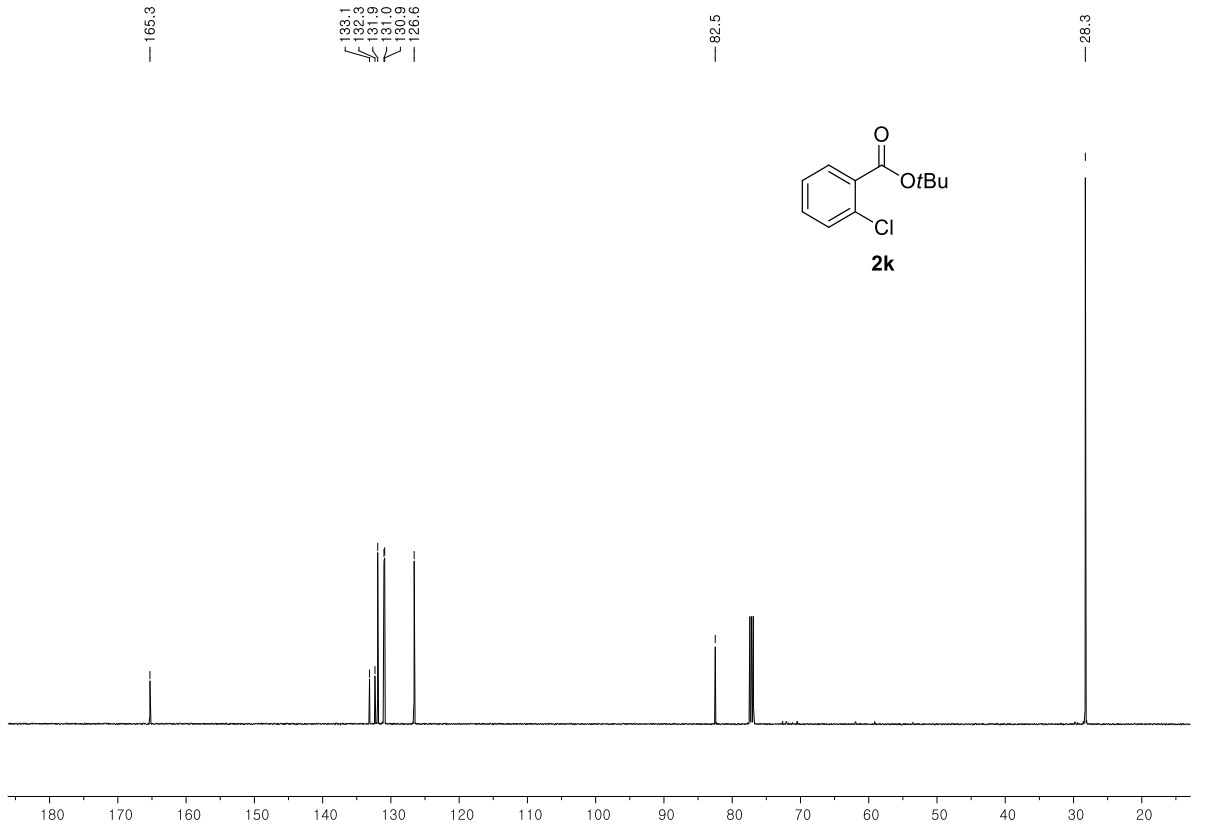

8.77
8.77
8.77
8.37
8.36
8.31
8.31
8.30
7.61
7.60
1.62
O
OtBu
NO2
2i
1.00
1.08
1.02
1.09
9.39
f1 (ppm)

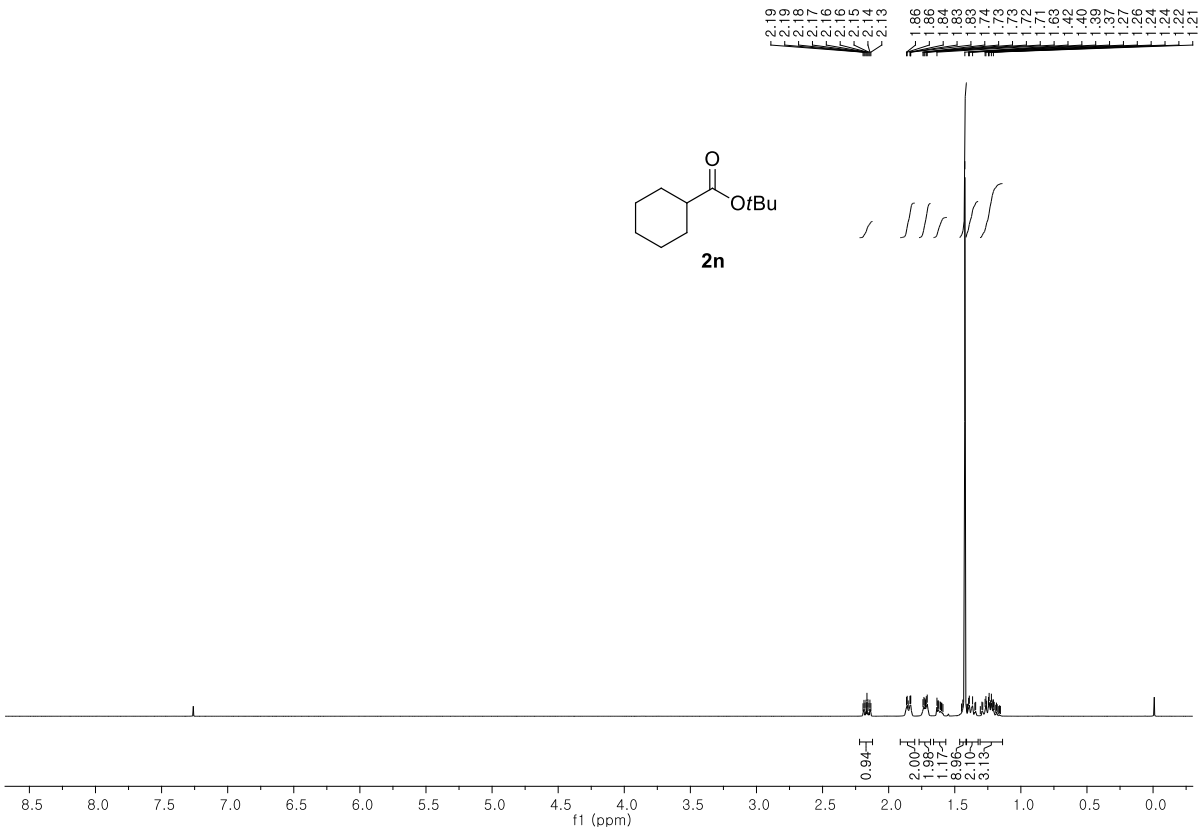

163.6
148.3
135.3
133.9
129.5
127.0
124.5
82.7
28.2
O
OtBu
NO2
2i
f1 (ppm)

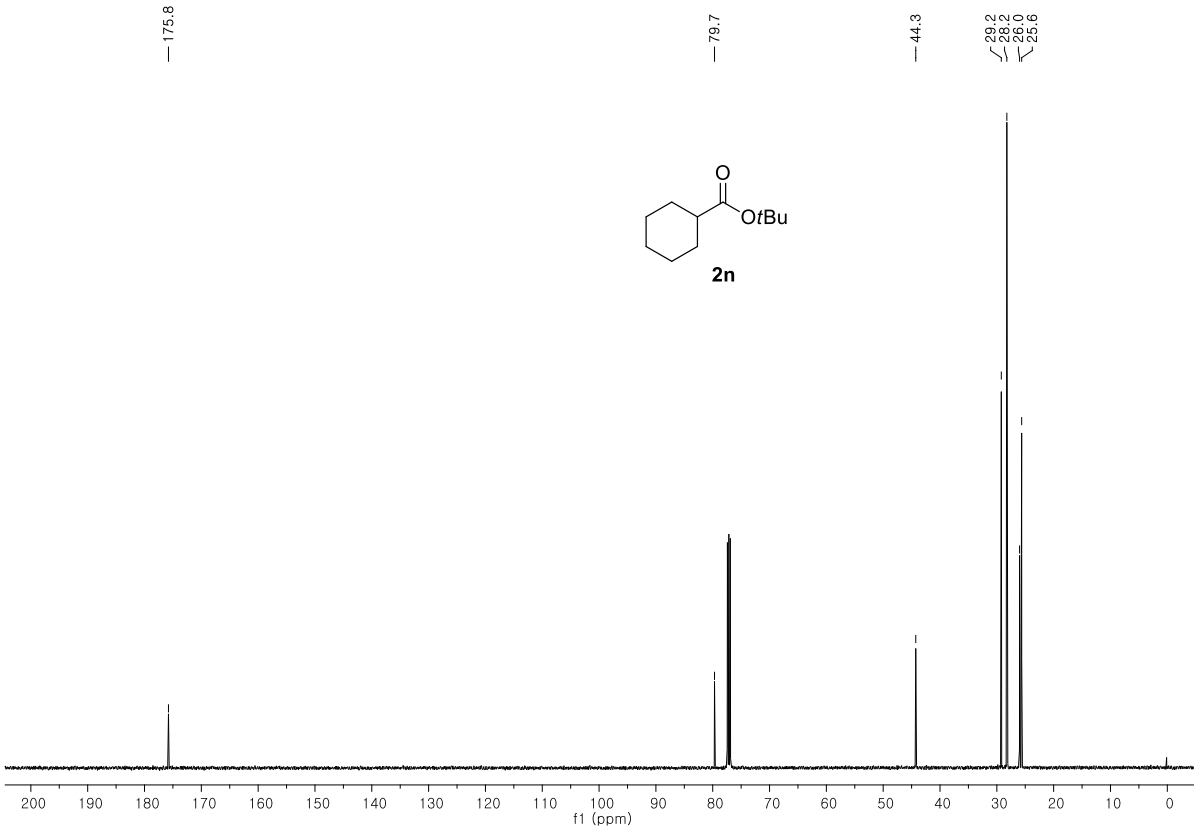

8.11
8.11
8.10
7.92
7.92
7.92
7.91
7.91
7.90
7.62
7.62
7.60
7.28
7.26
1.59
O
OtBu
Br
2j
1.00
1.05
1.02
1.11
9.24
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

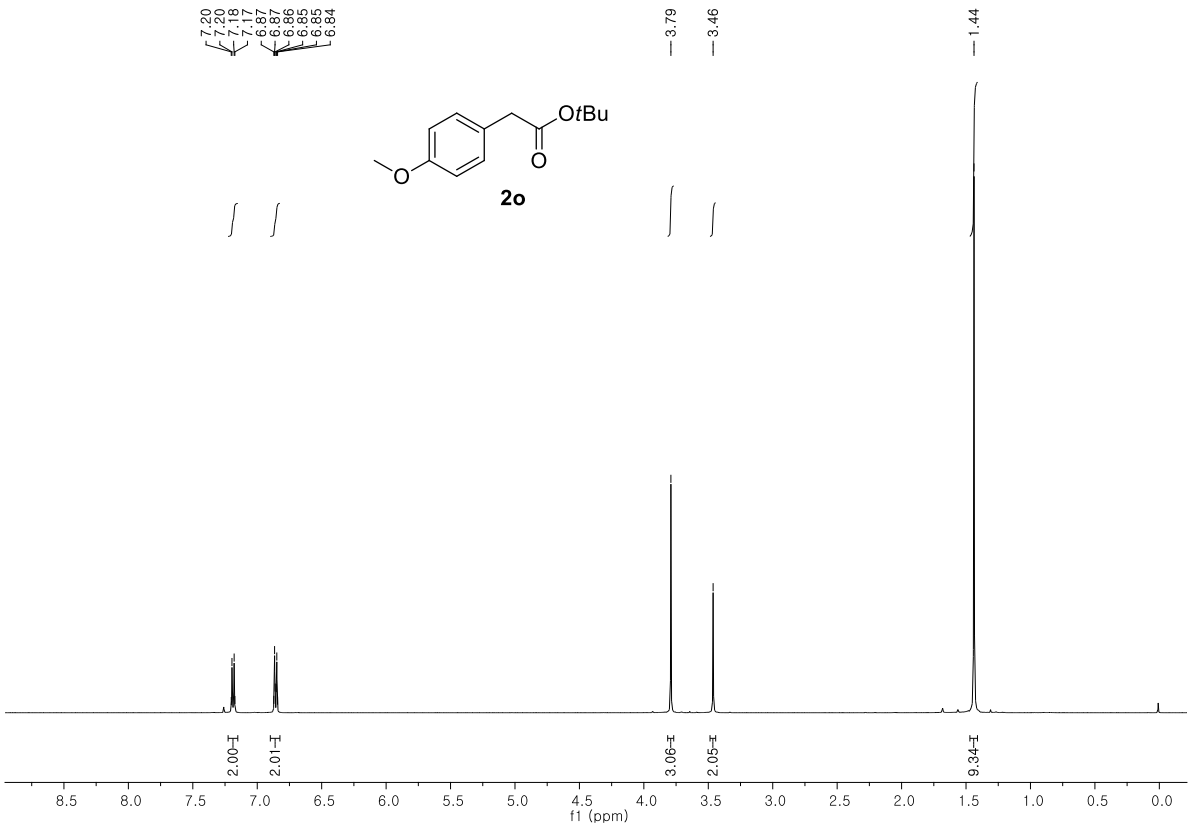

164.4
135.4
134.1
132.5
129.8
128.1
122.4
81.8
28.2
O
OtBu
Br
2j
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10

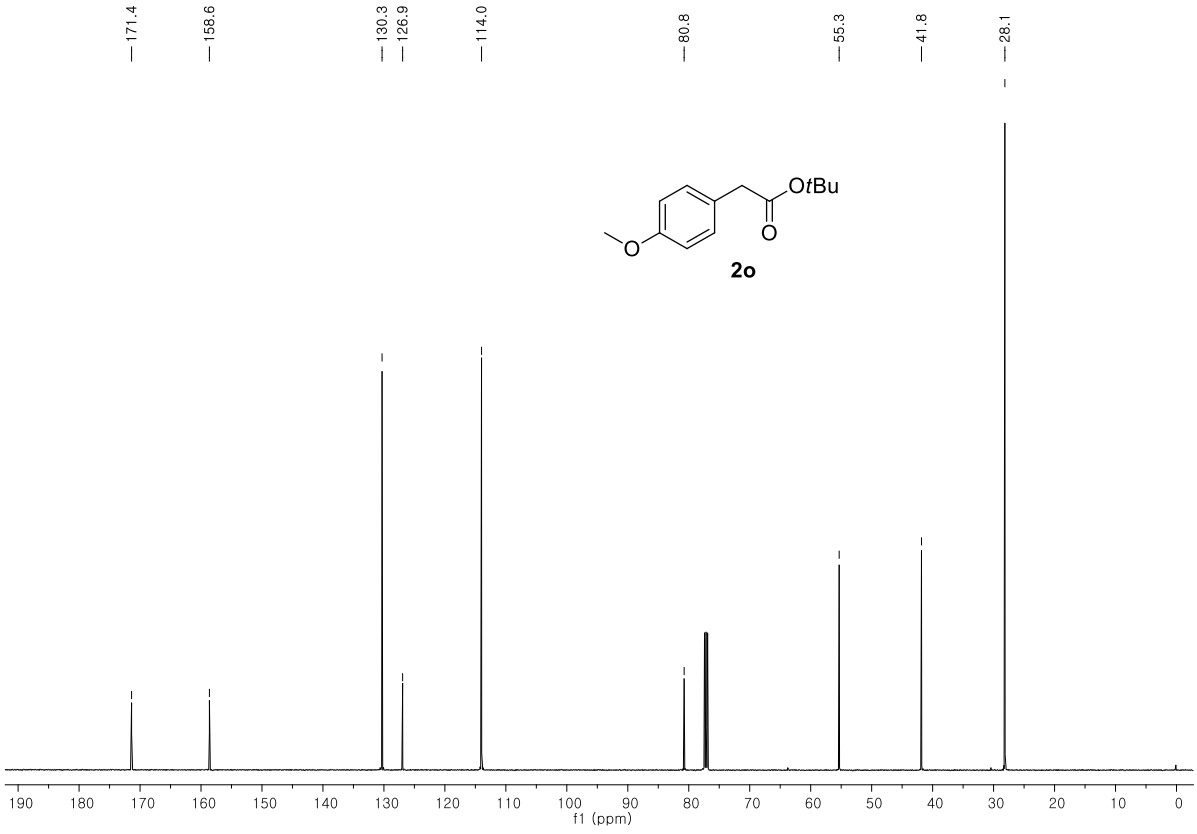

7.73
7.72
7.71
7.71
7.41
7.41
7.40
7.40
7.37
7.37
7.36
7.35
7.34
7.29
7.28
7.26
1.61
O
OtBu
Cl
2k
1.00
2.11
1.07
9.04
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

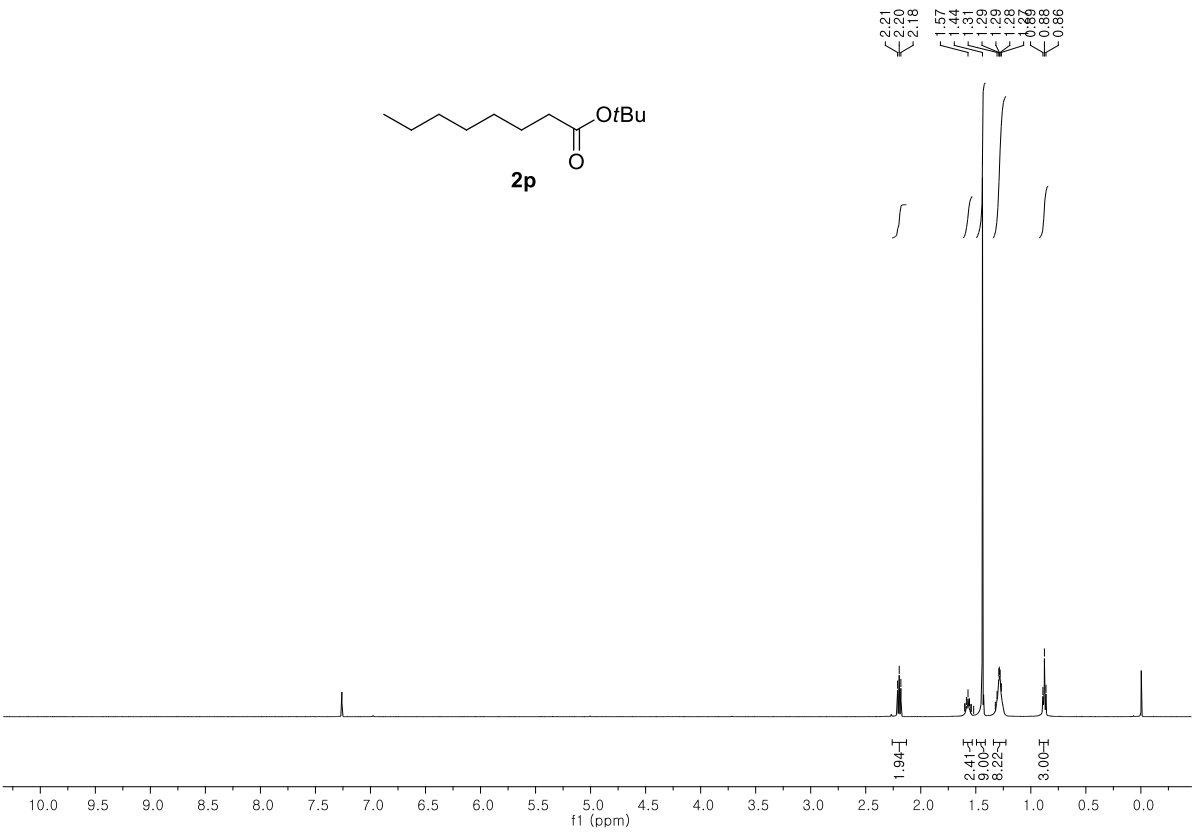

165.3
133.1
132.3
131.9
131.0
130.9
126.6
82.5
28.3
O
OtBu
Cl
2k
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20

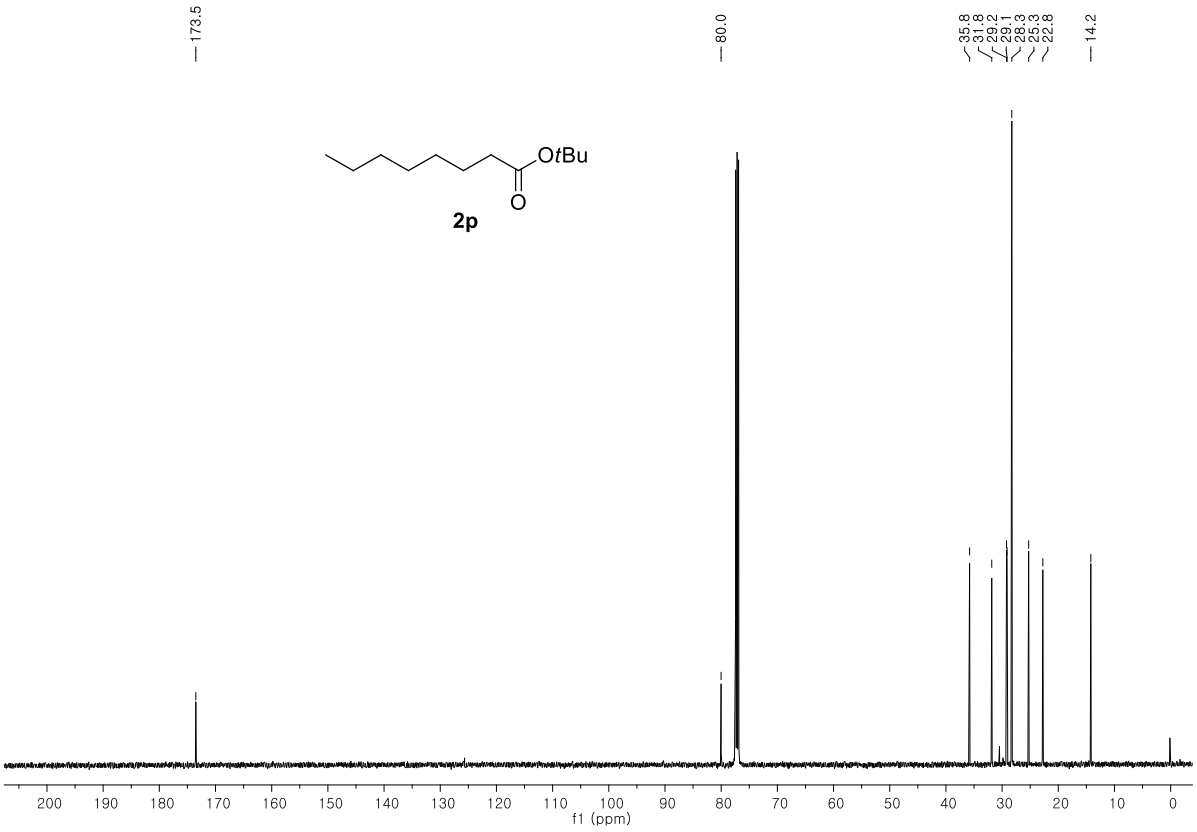

2.19
2.19
2.18
2.17
2.16
2.15
2.14
2.13
1.86
1.86
1.84
1.83
1.83
1.74
1.73
1.73
1.72
1.71
1.63
1.42
1.40
1.39
1.37
1.27
1.26
1.24
1.24
1.22
1.21
O
OtBu
2n
0.94
2.00
1.98
1.17
8.96
2.10
3.13
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

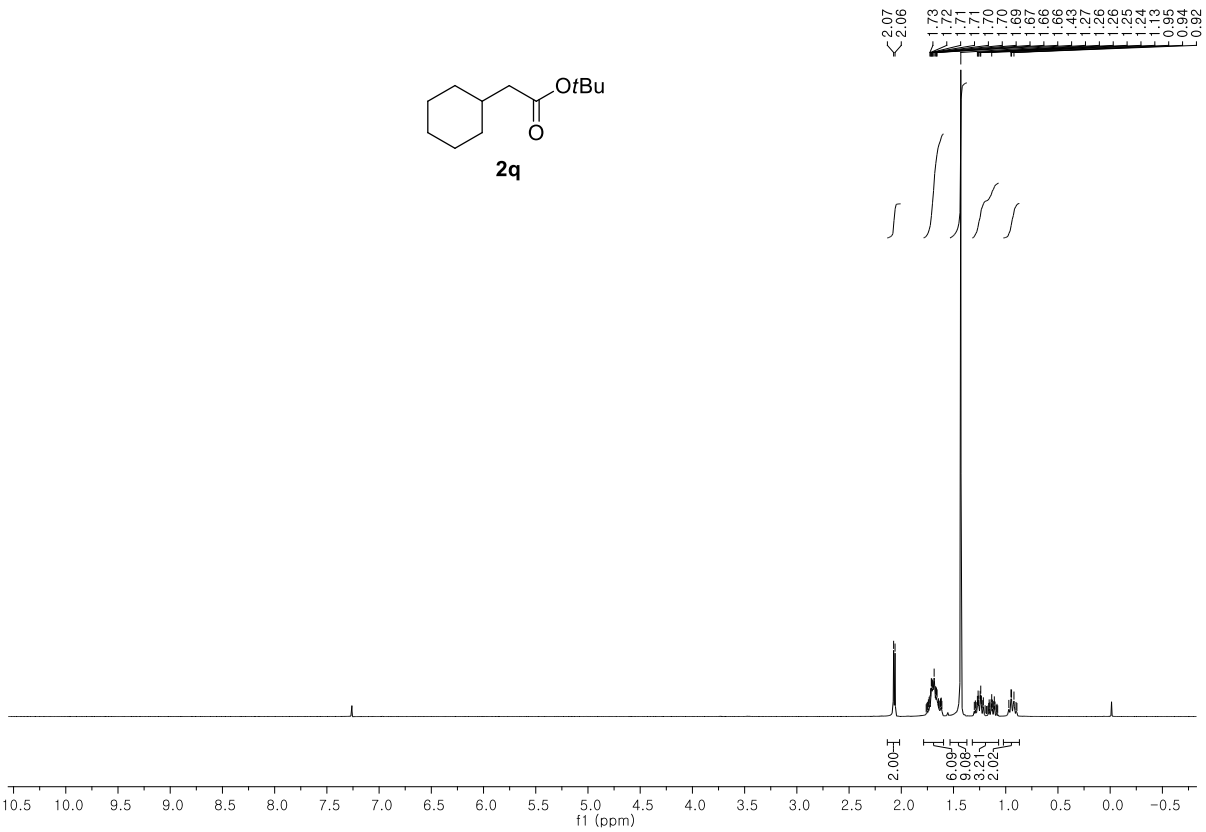

175.8
79.7
44.3
29.2
28.2
26.0
25.6
O
OtBu
2n
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

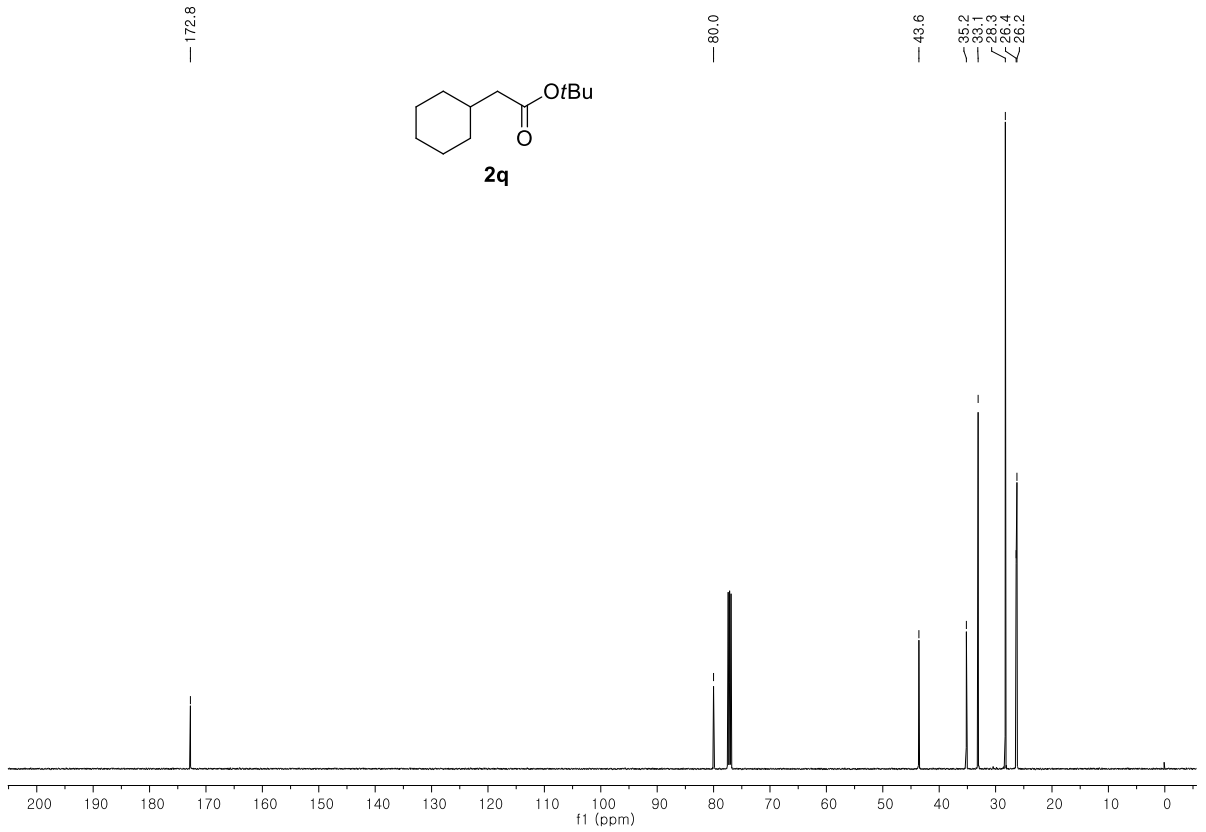

7.20
7.20
7.18
7.17
6.87
6.87
6.86
6.85
6.85
6.84
3.79
3.46
1.44
OtBu
O
O
2o
2.00
2.01
3.06
2.05
9.34
f1 (ppm)

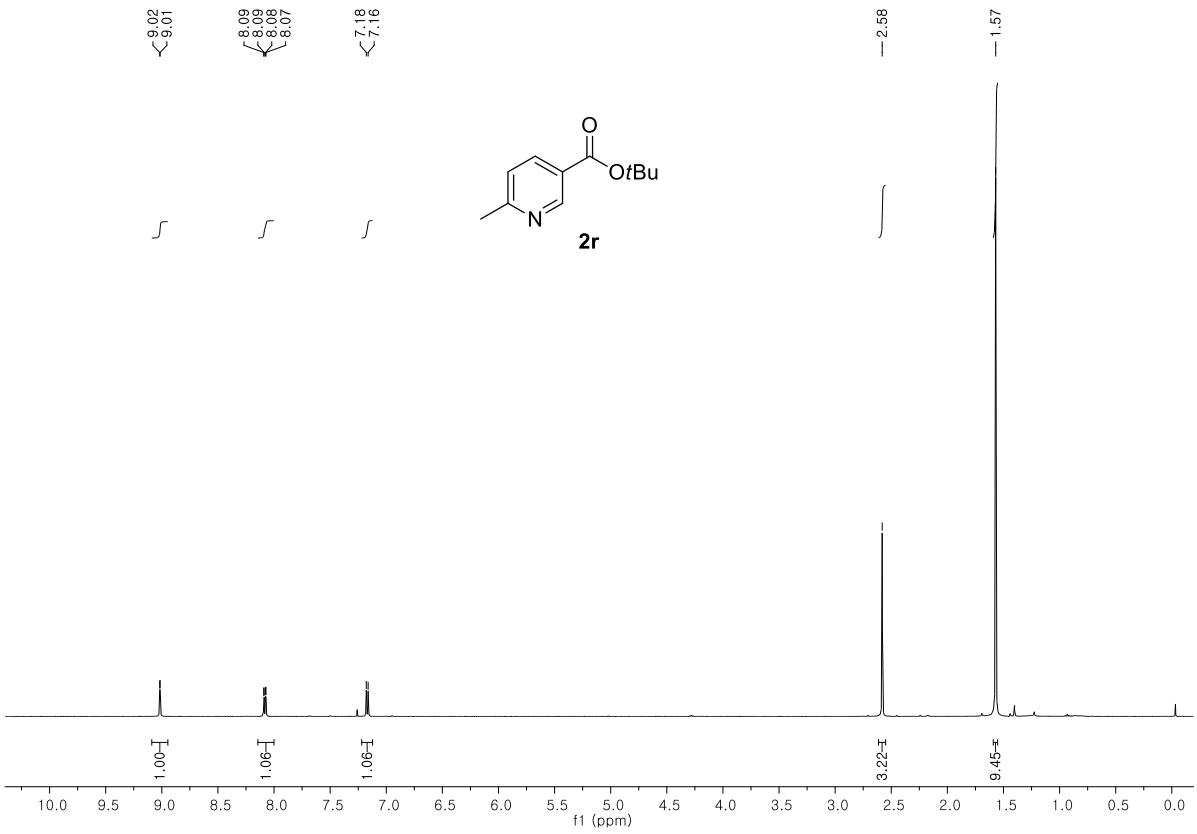

171.4
158.6
130.3
126.9
114.0
80.8
55.3
41.8
28.1
OtBu
O
O
2o
f1 (ppm)

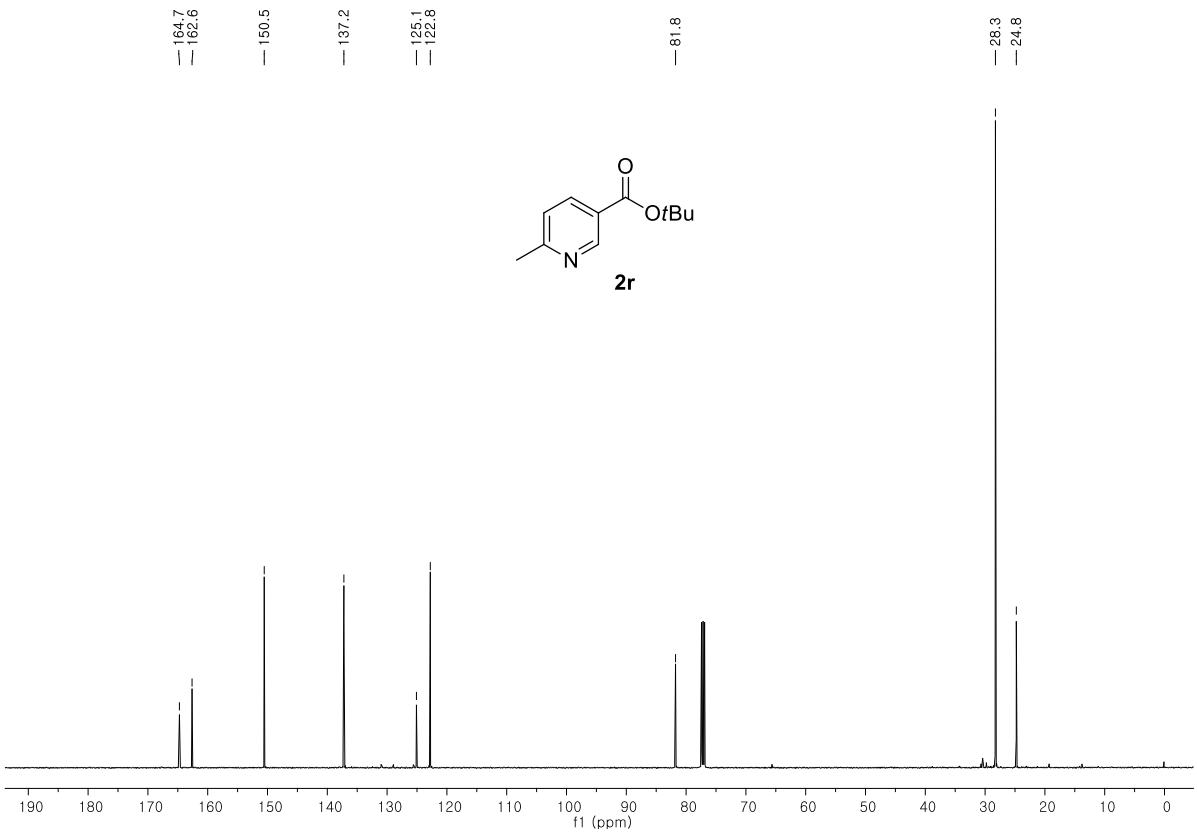

2.21
2.20
2.18
1.57
1.44
1.31
1.29
1.29
1.28
0.88
0.86
OtBu
O
2p
1.94
2.41
9.00
8.22
3.00
f1 (ppm)

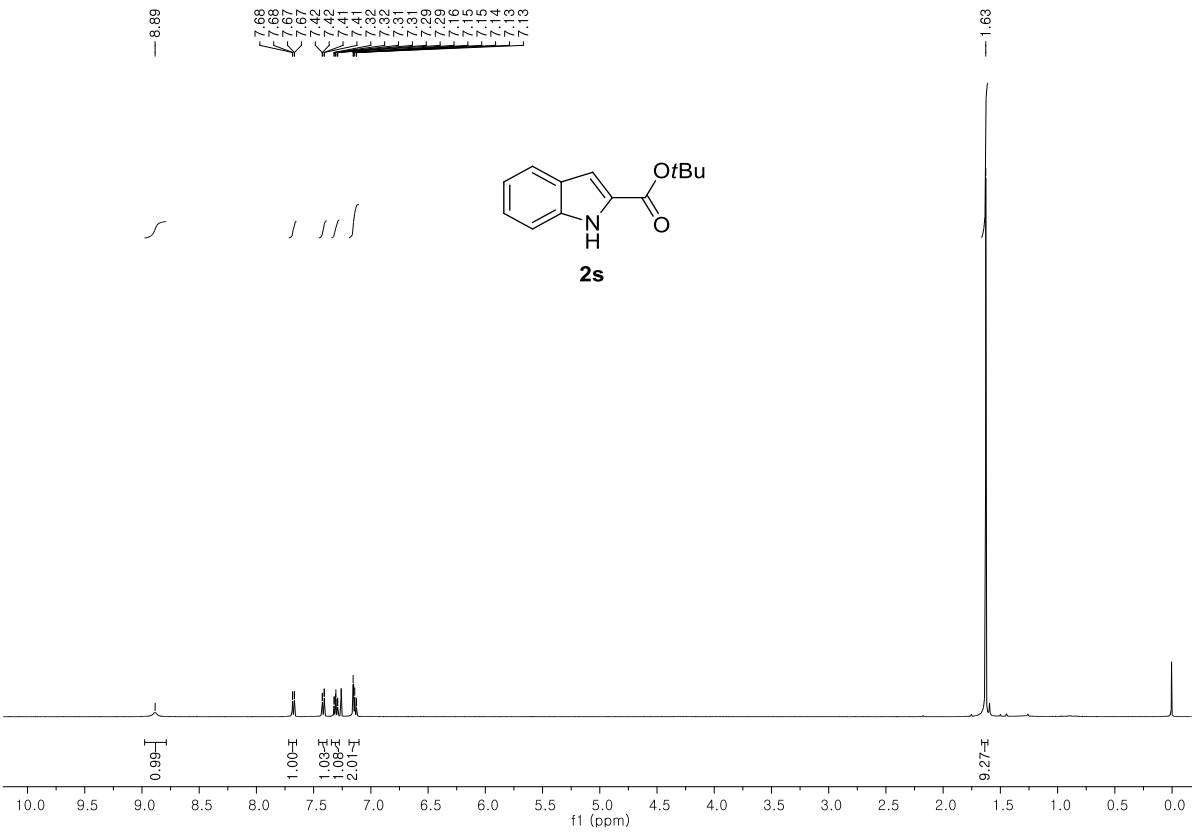

173.5
80.0
35.8
31.8
29.2
29.1
28.3
25.3
22.8
14.2
OtBu
O
2p
f1 (ppm)

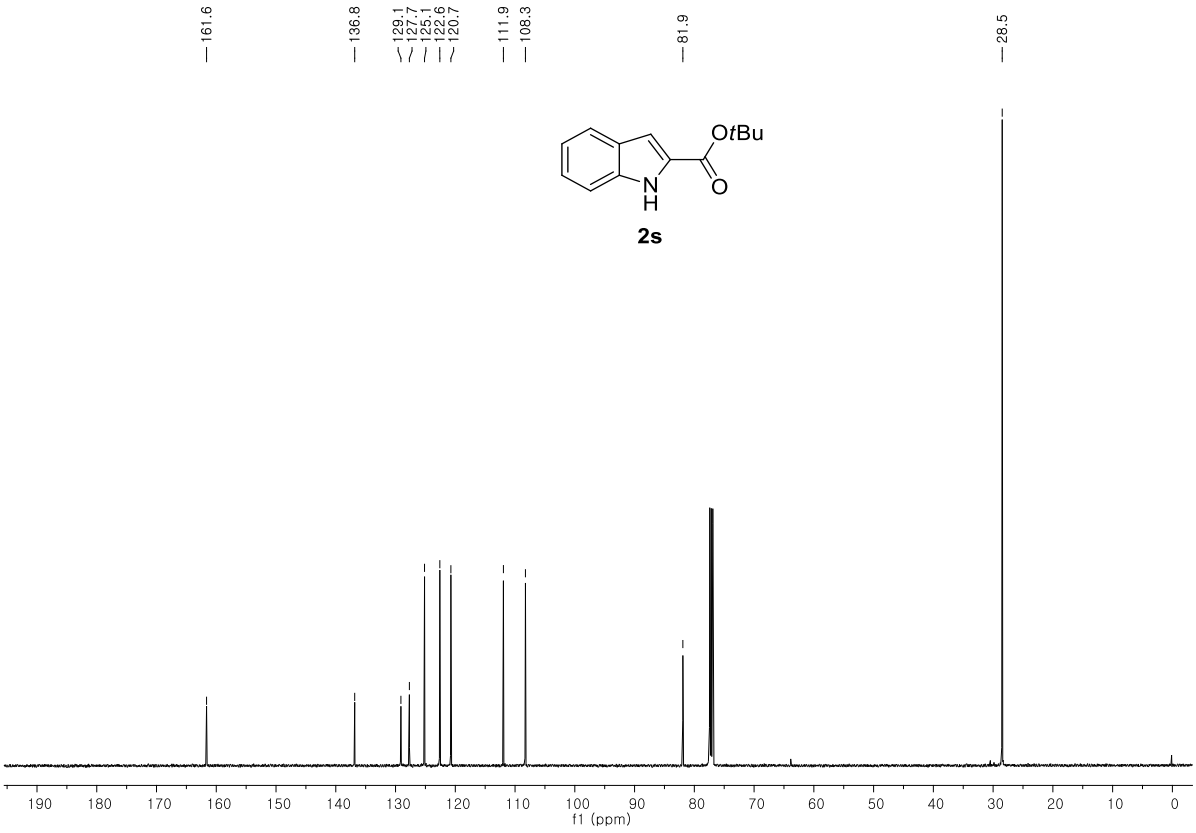

OtBu
O
2q
2.07
2.06
1.73
1.72
1.71
1.71
1.70
1.70
1.69
1.67
1.66
1.66
1.43
1.27
1.26
1.26
1.25
1.24
1.13
0.95
0.94
0.92
2.00
6.09
9.08
3.21
2.02
f1 (ppm)

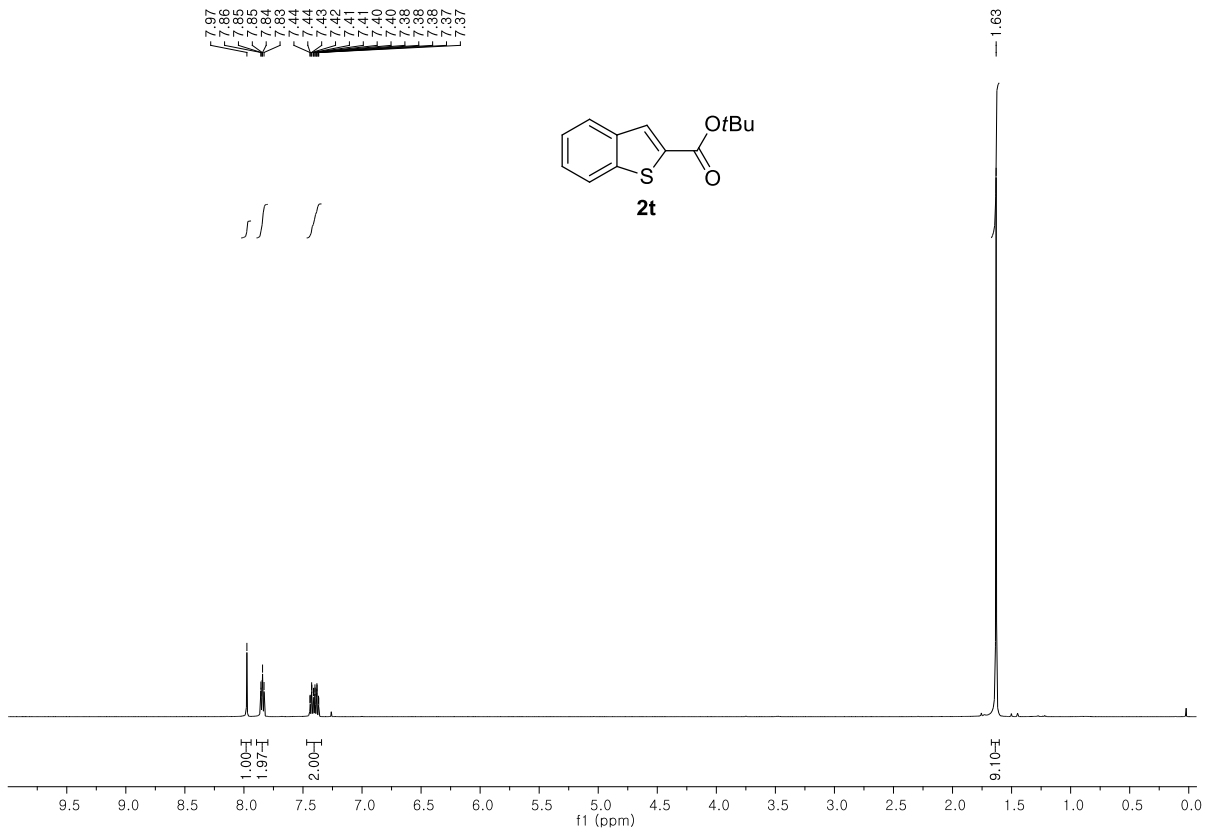

172.8
80.0
43.6
35.2
33.1
28.3
26.4
26.2
OtBu
O
2q
f1 (ppm)

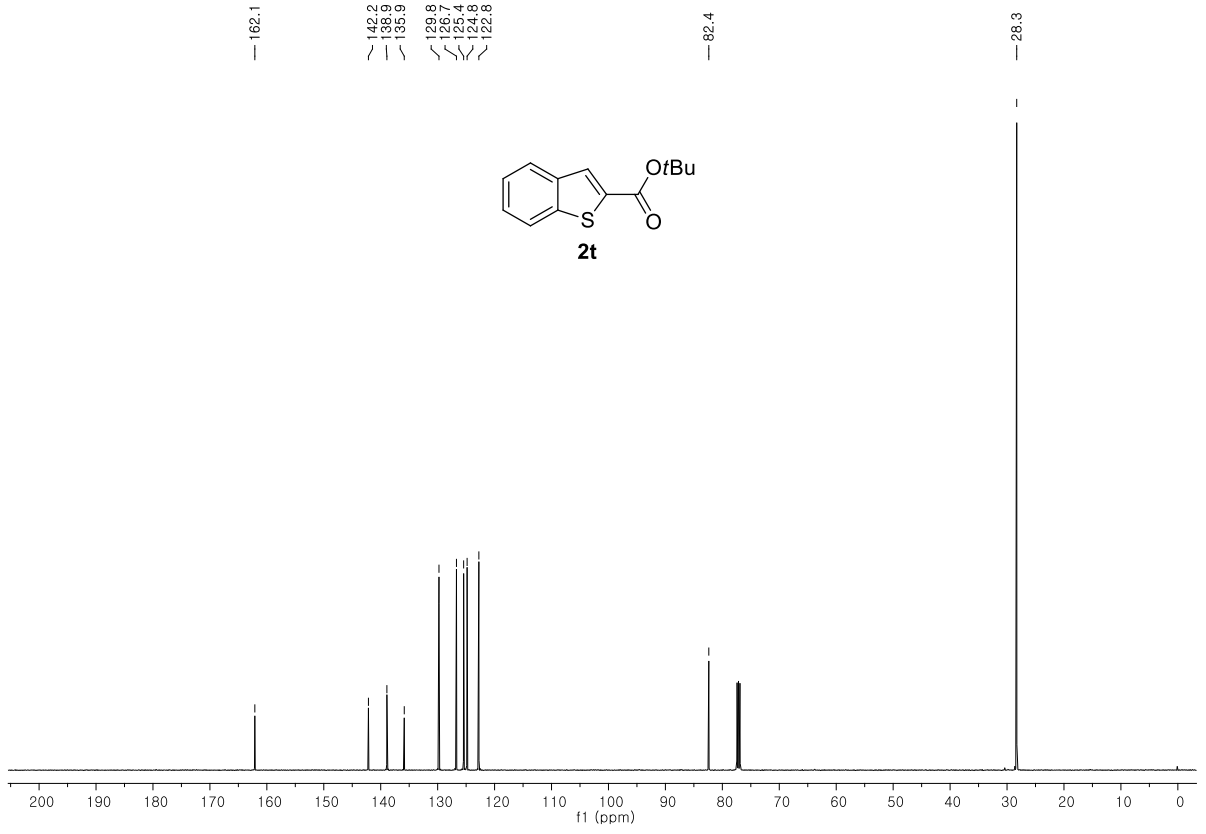

9.02
9.01
8.09
8.09
8.08
8.07
7.18
7.16
2.58
1.57
O
OtBu
N
2r
1.00
1.06
1.06
3.22
9.45
f1 (ppm)

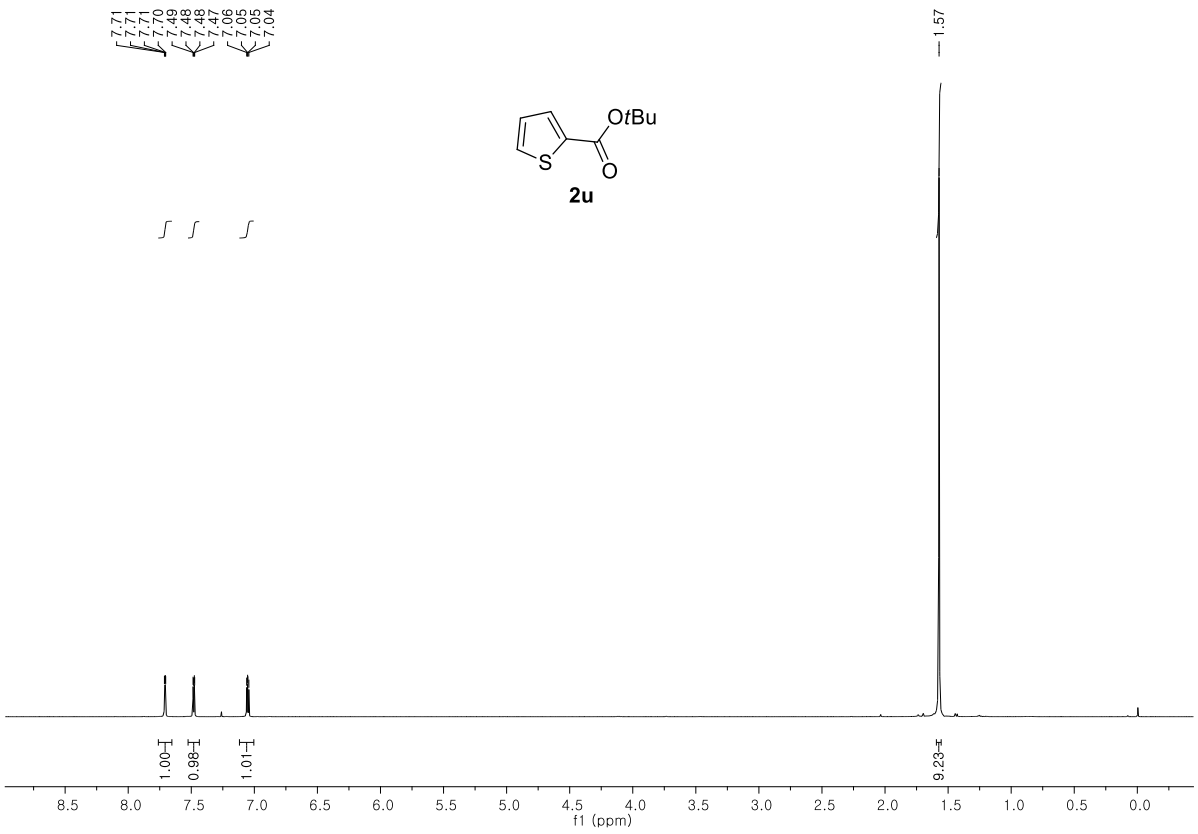

164.7
162.6
150.5
137.2
125.1
122.8
81.8
28.3
24.8
O
OtBu
N
2r
f1 (ppm)

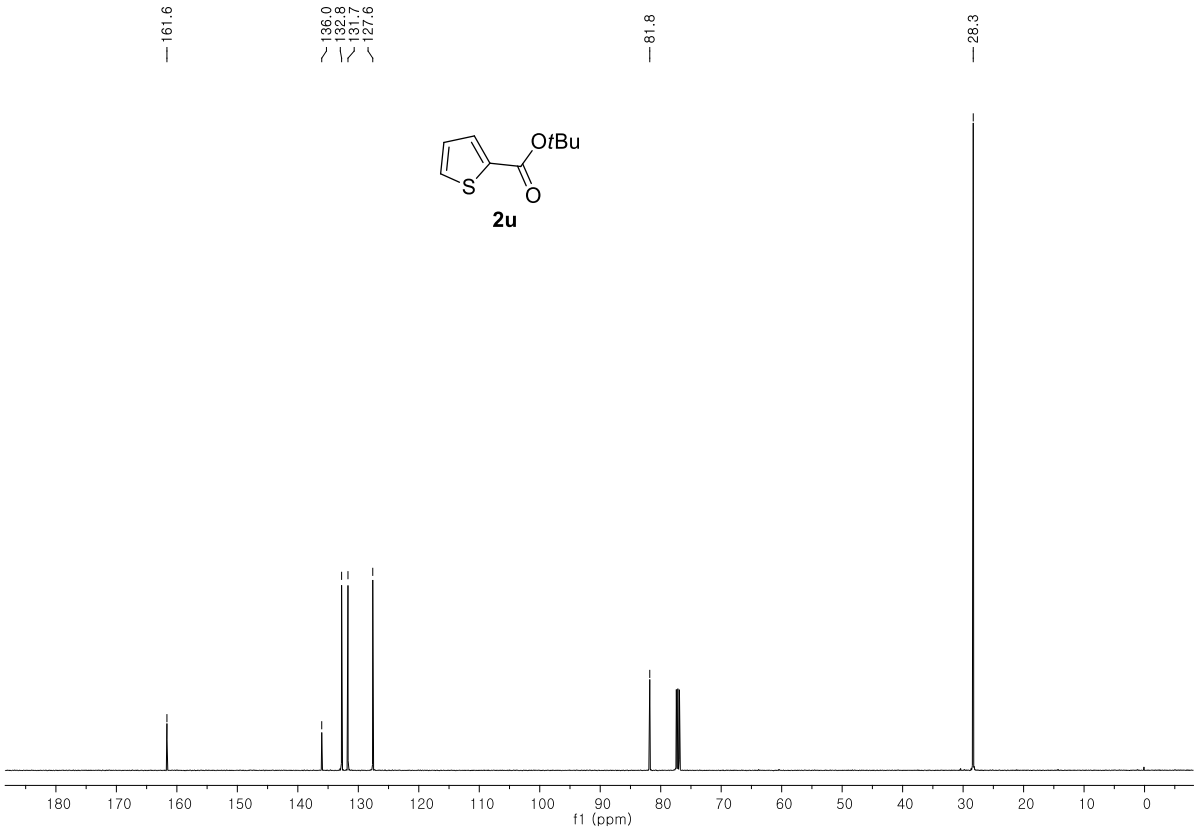

8.89
7.68
7.68
7.67
7.67
7.42
7.42
7.41
7.41
7.32
7.32
7.31
7.31
7.29
7.29
7.16
7.15
7.15
7.14
7.13
7.13
1.63
OtBu
N
H
O
2s
0.99
1.00
1.03
1.08
2.01
9.27
f1 (ppm)

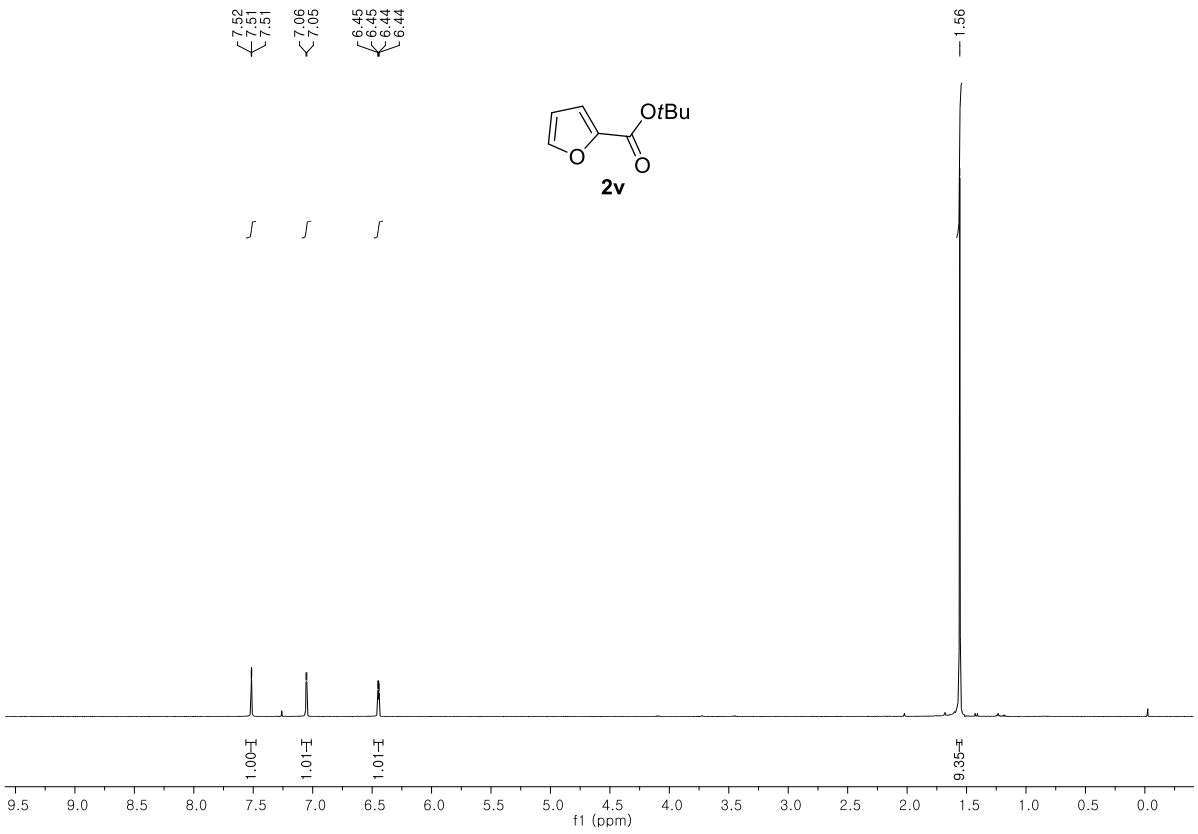

161.6
136.8
129.1
127.7
125.1
122.6
120.7
111.9
108.3
81.9
28.5
OtBu
N
H
O
2s
f1 (ppm)

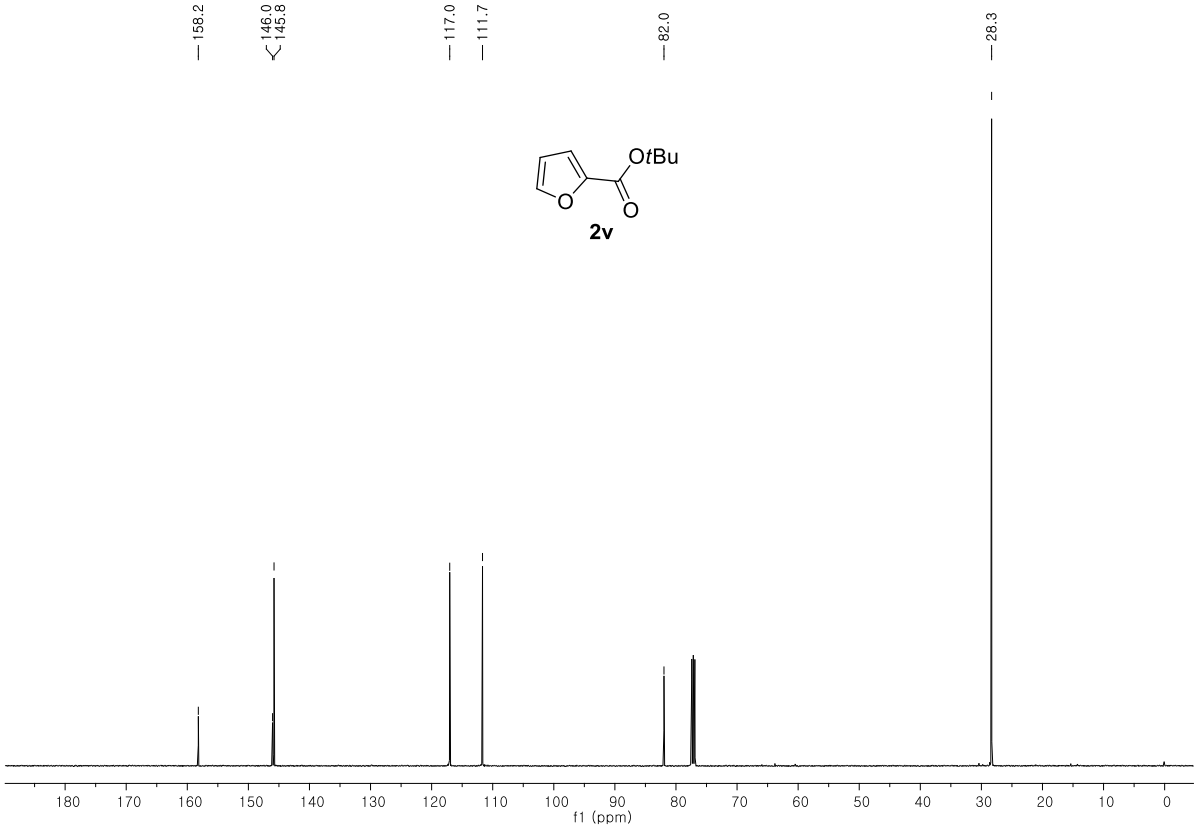

7.97
7.86
7.85
7.85
7.84
7.83
7.44
7.43
7.42
7.41
7.41
7.40
7.40
7.38
7.38
7.37
7.37
1.63
OtBu
S
O
2t
1.00
1.97
2.00
9.10
f1 (ppm)

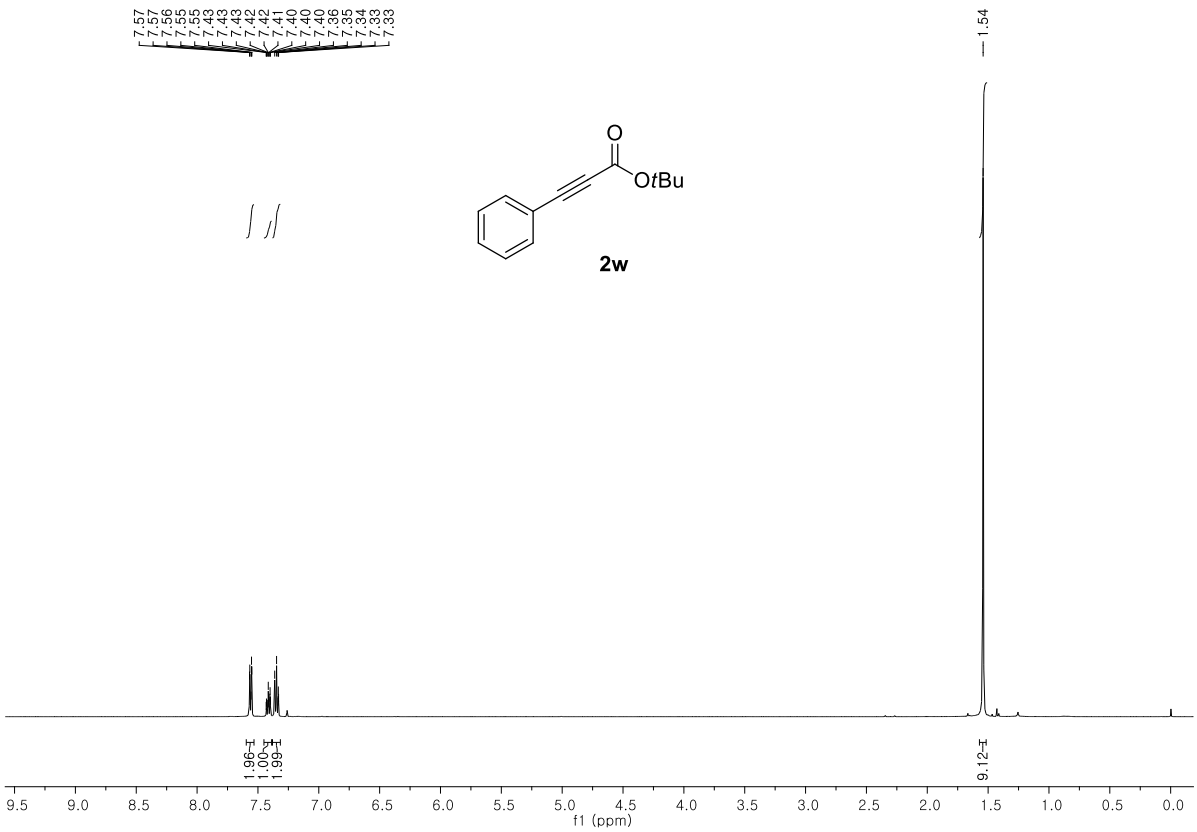

162.1
142.2
138.9
135.9
129.8
126.7
125.4
124.8
122.8
82.4
28.3
OtBu
S
O
2t
f1 (ppm)

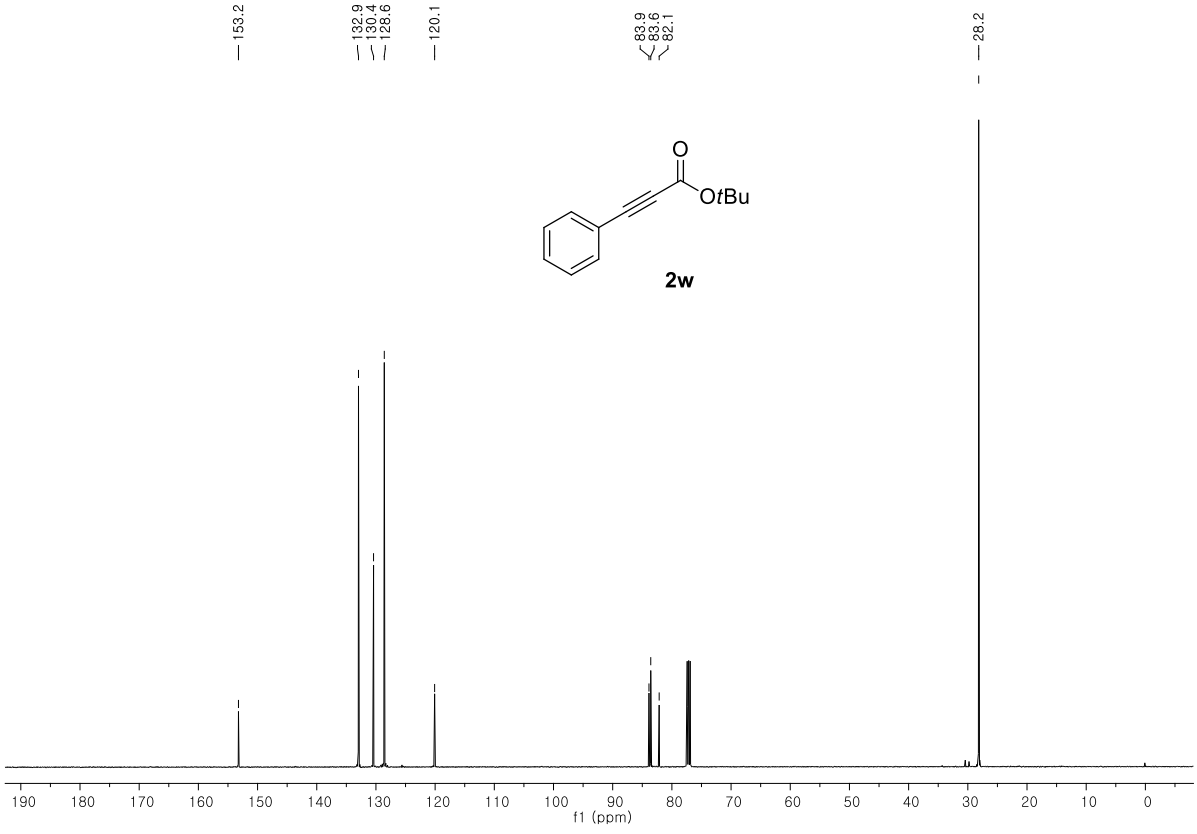

7.71
7.71
7.71
7.70
7.49
7.48
7.48
7.47
7.06
7.05
7.05
7.04
1.57
OtBu
S
O
2u
1.00
0.98
1.01
9.23
f1 (ppm)

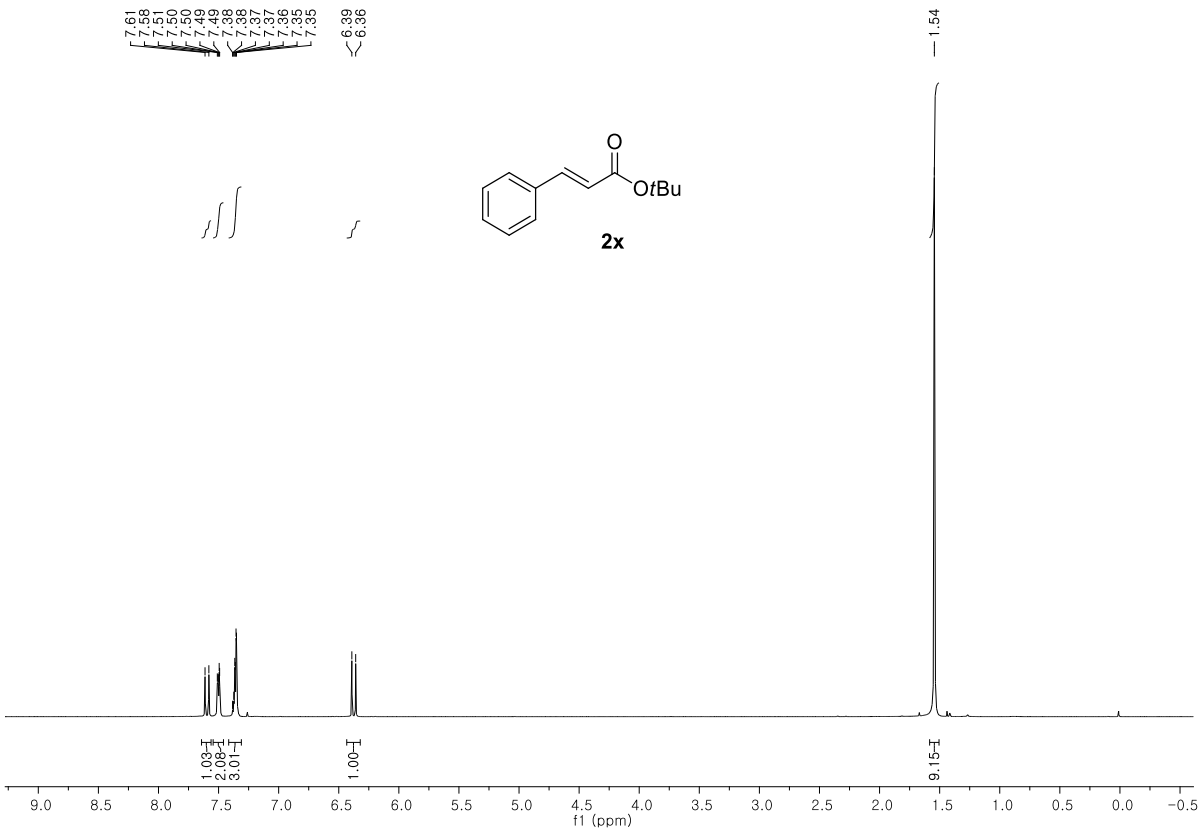

161.6
136.0
132.8
131.7
127.6
81.8
28.3
OtBu
S
O
2u
f1 (ppm)

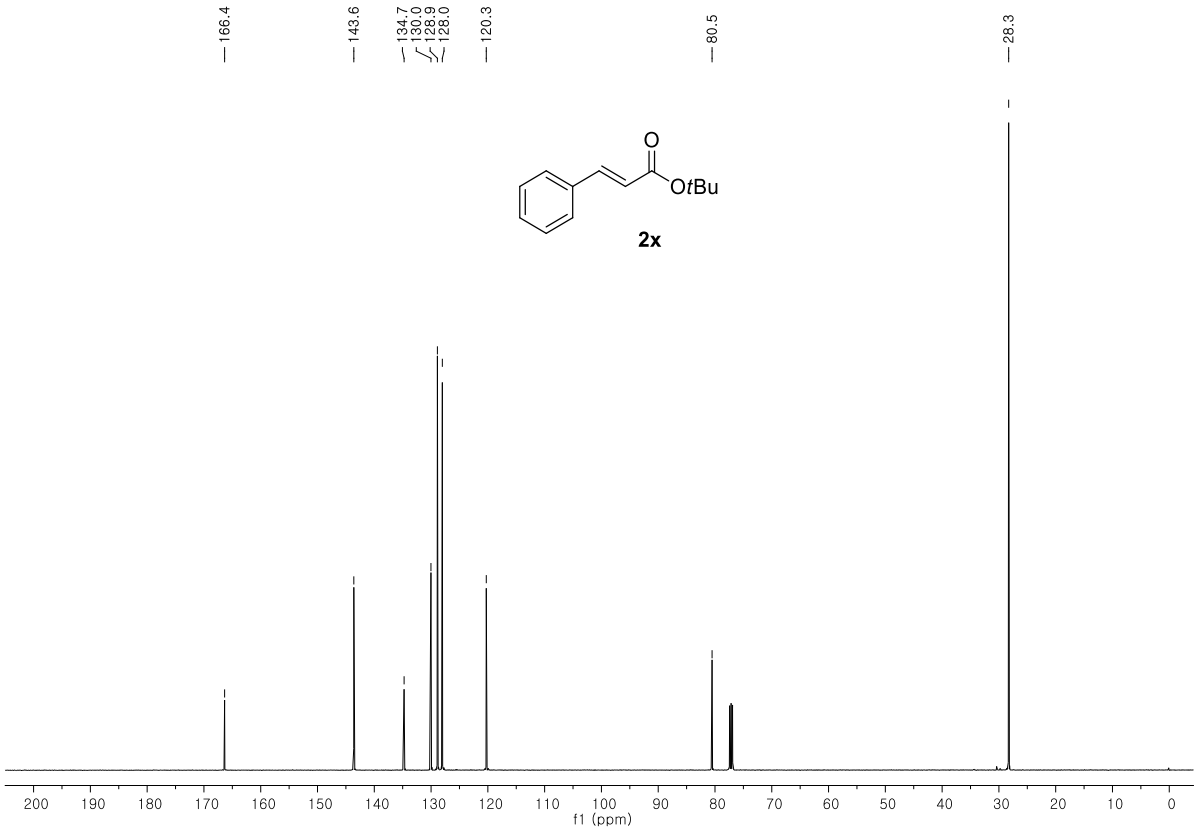

7.52
7.51
7.51
7.06
7.05
6.45
6.45
6.44
6.44
1.56
OtBu
O
O
2v
1.00
1.01
1.01
9.35
f1 (ppm)

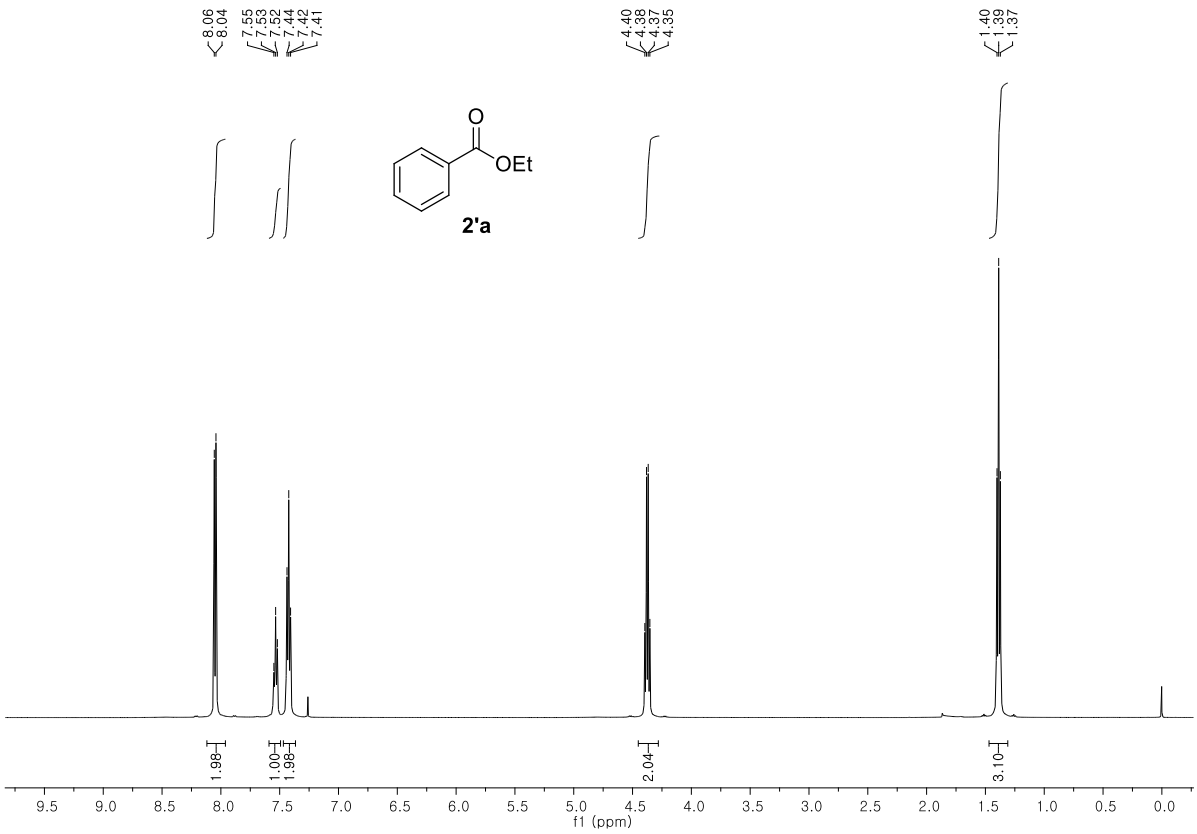

158.2
146.0
145.8
117.0
111.7
82.0
28.3
OtBu
O
O
2v
f1 (ppm)

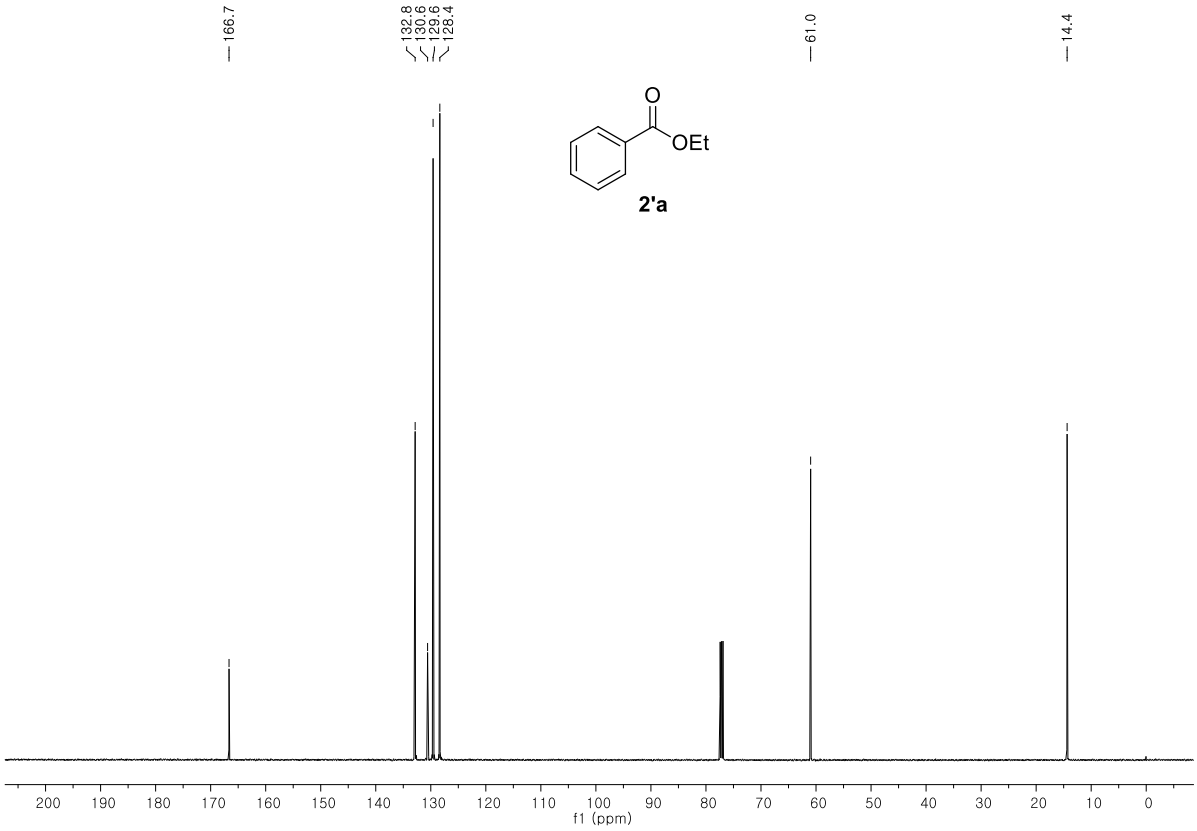

7.57
7.57
7.56
7.55
7.55
7.43
7.43
7.42
7.42
7.41
7.40
7.40
7.40
7.36
7.35
7.34
7.33
7.33
1.54
O
OtBu
2w
1.96
1.00
1.99
9.12
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

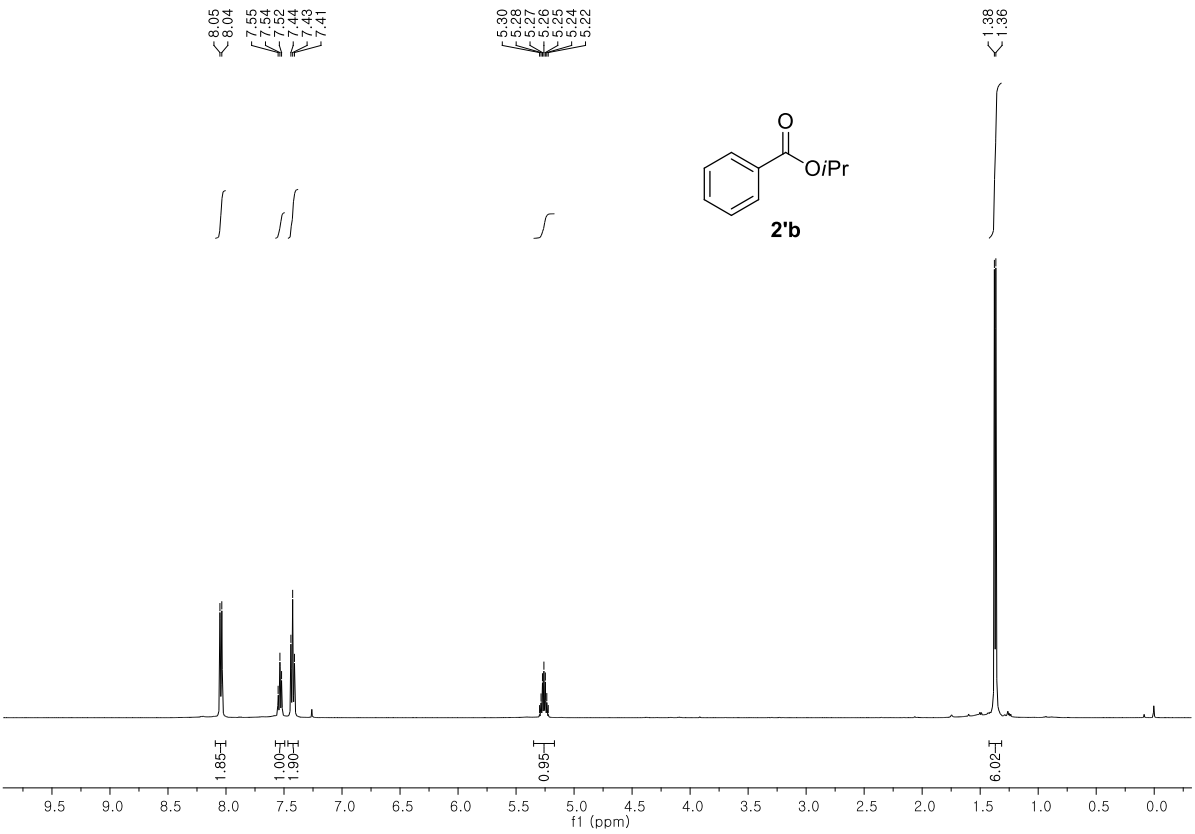

153.2
132.9
130.4
128.6
120.1
83.9
83.6
82.1
28.2
O
OtBu
2w
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

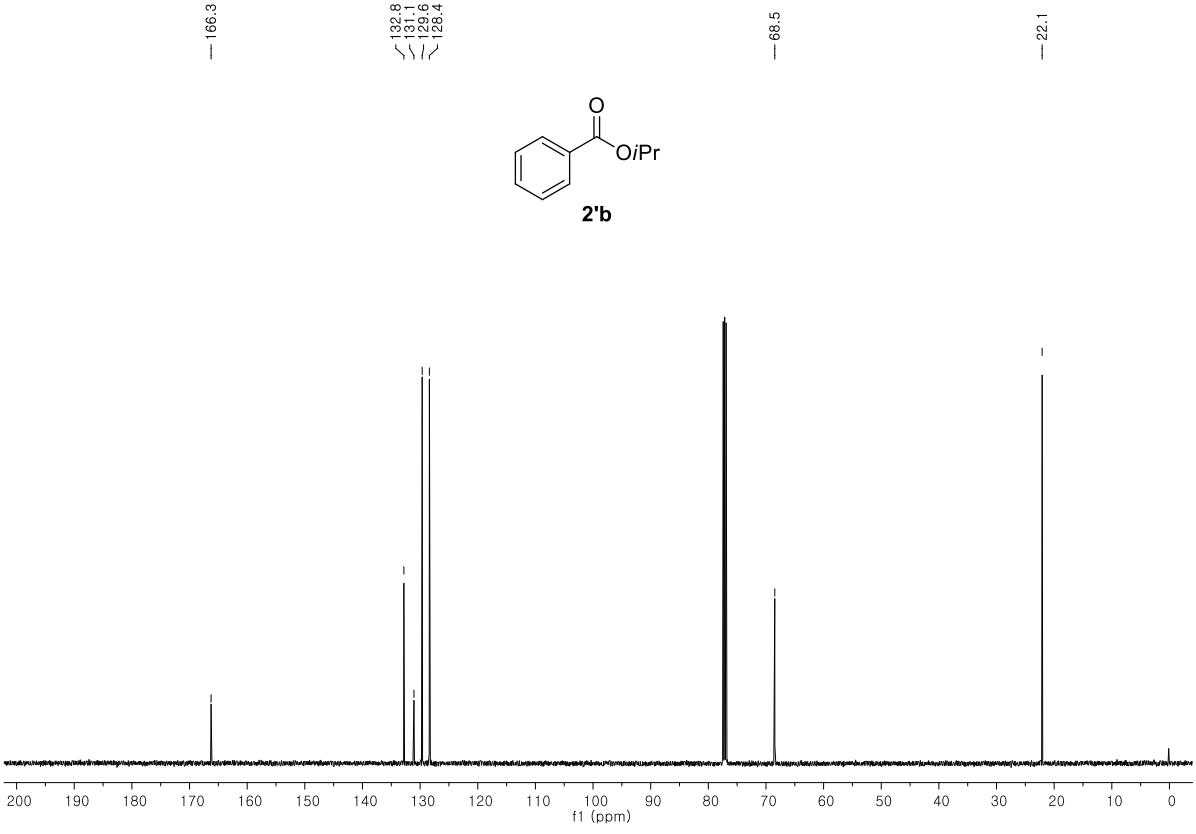

7.61
7.58
7.51
7.50
7.50
7.49
7.49
7.38
7.38
7.37
7.37
7.36
7.35
7.35
6.39
6.36
1.54
O
OtBu
2x
1.03
2.08
3.01
1.00
9.15
f1 (ppm)

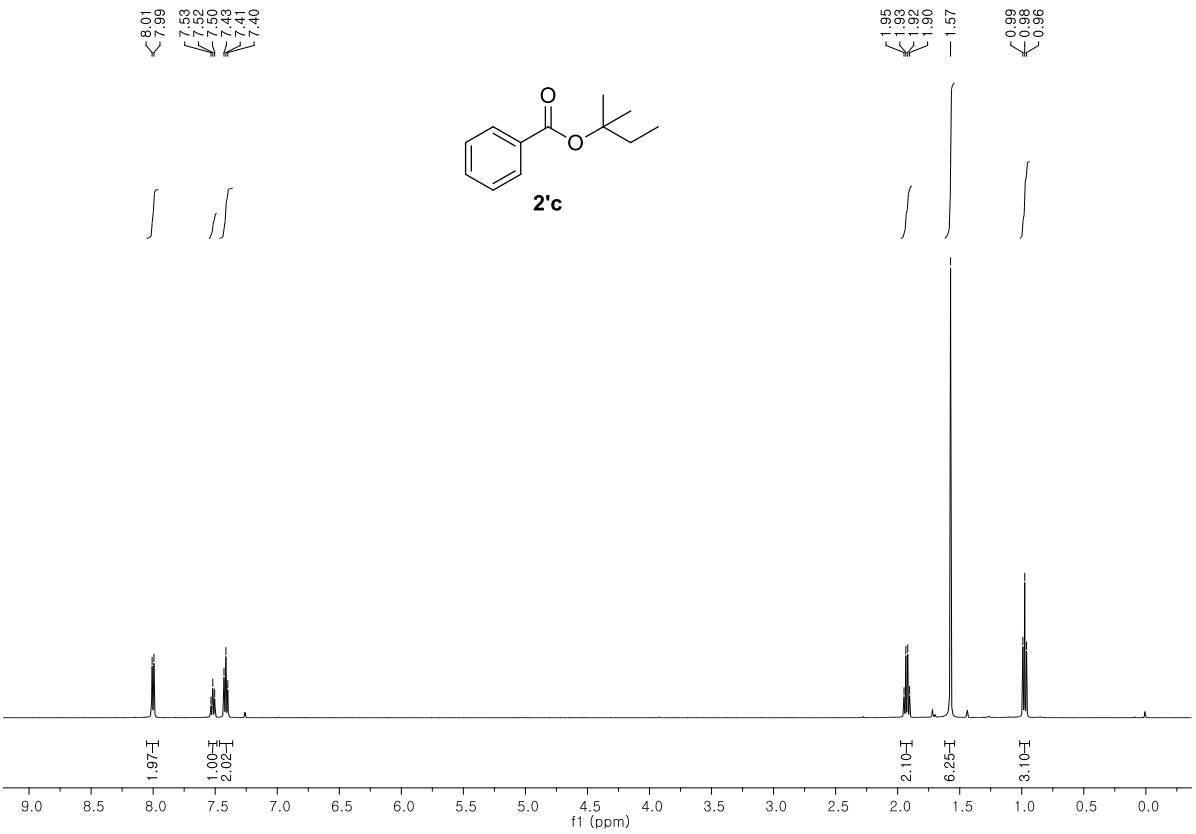

166.4
143.6
134.7
130.0
128.9
128.0
120.3
80.5
28.3
O
OtBu
2x
f1 (ppm)

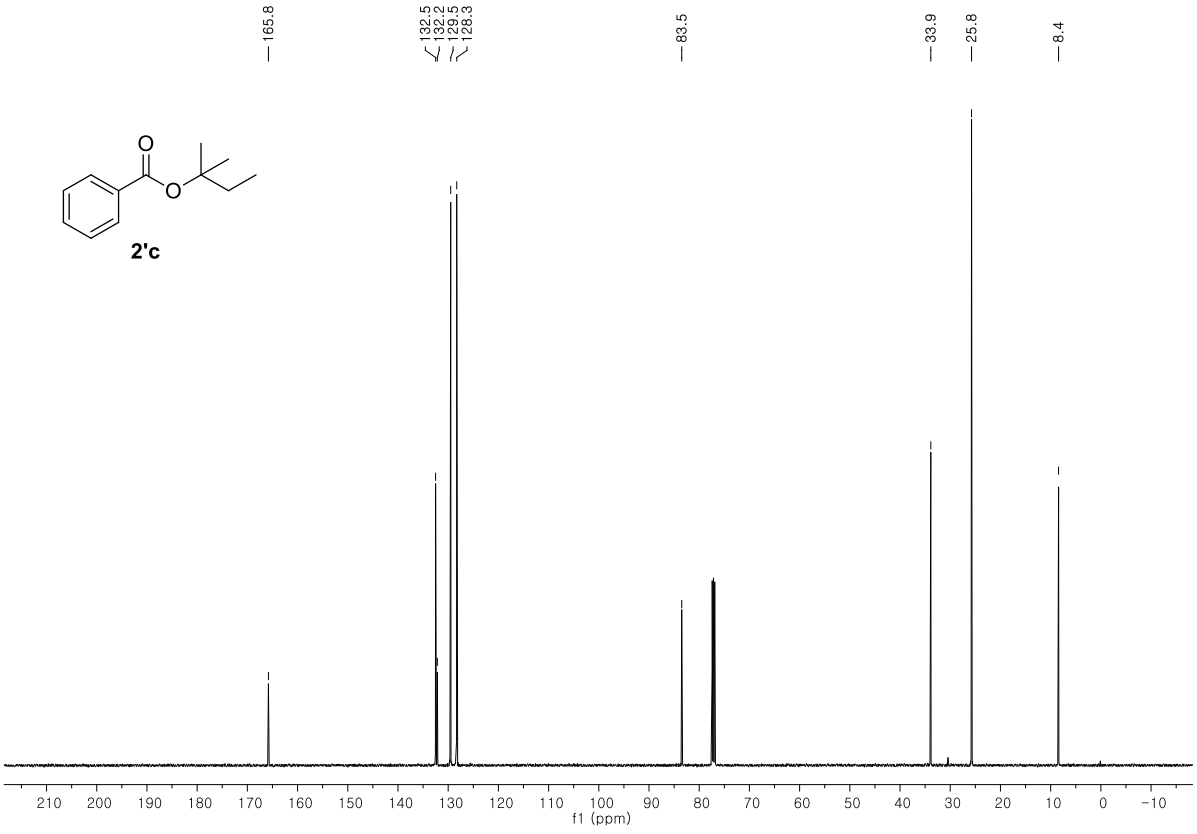

8.06
8.04
7.55
7.53
7.52
7.44
7.42
7.41
4.40
4.38
4.37
4.35
1.40
1.39
1.37
O
OEt
2'a
1.98
1.00
1.98
2.04
3.10
f1 (ppm)

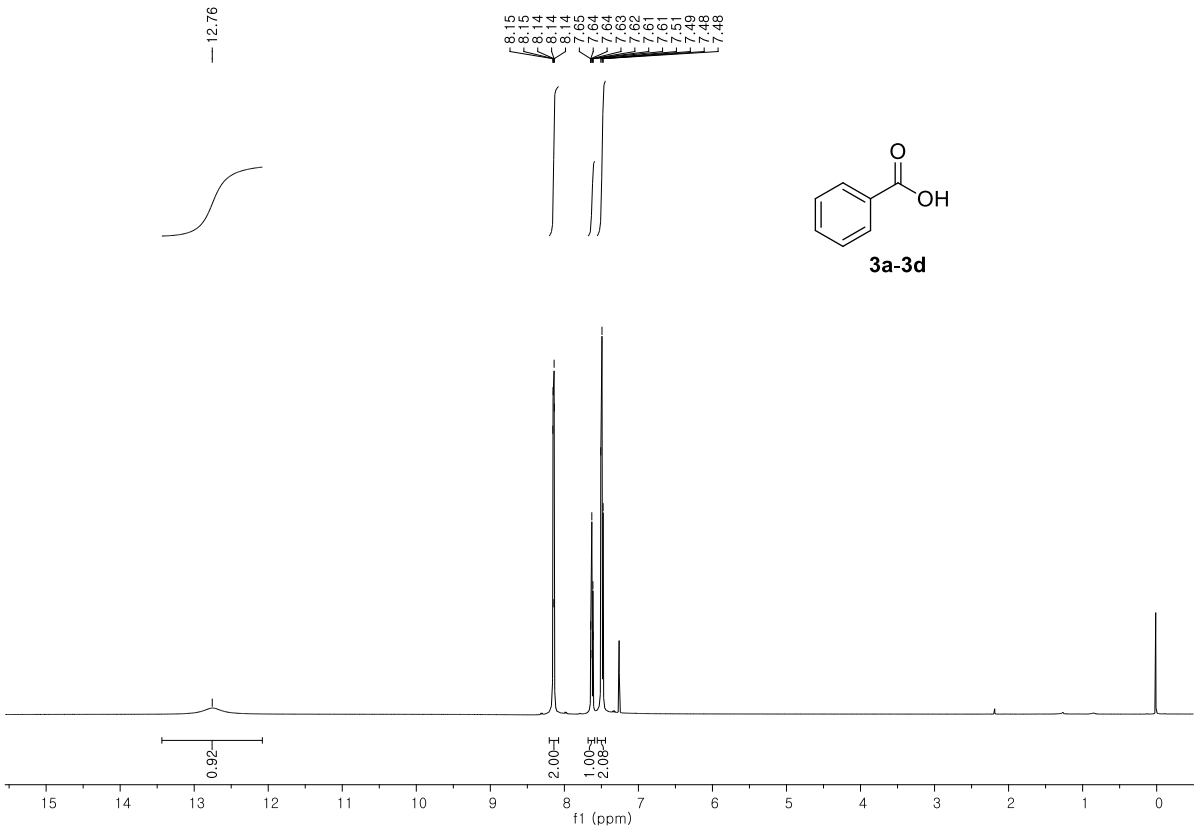

166.7
132.8
130.6
129.6
128.4
61.0
14.4
O
OEt
2'a
f1 (ppm)

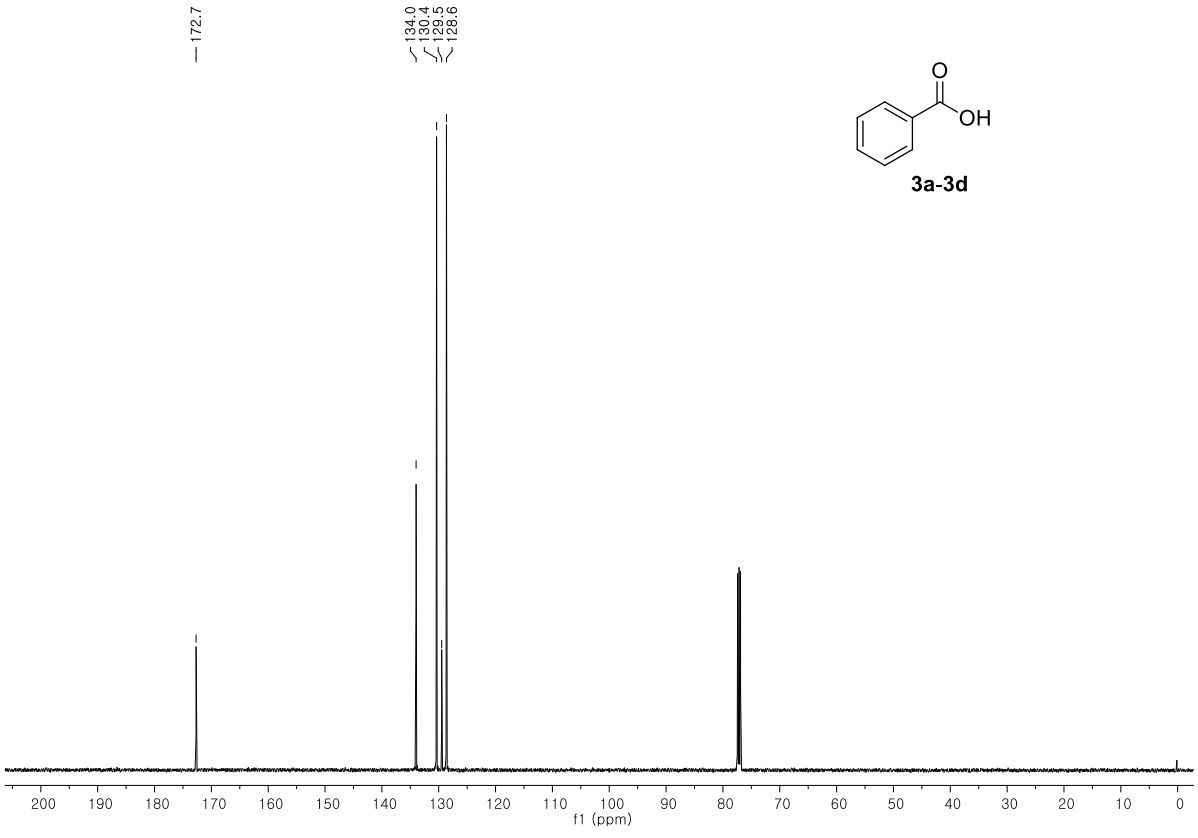

8.05
8.04
7.55
7.54
7.52
7.44
7.43
7.41
5.30
5.28
5.27
5.26
5.25
5.24
5.22
1.38
1.36
O
OiPr
2'b
1.85
1.00
1.90
0.95
6.02
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

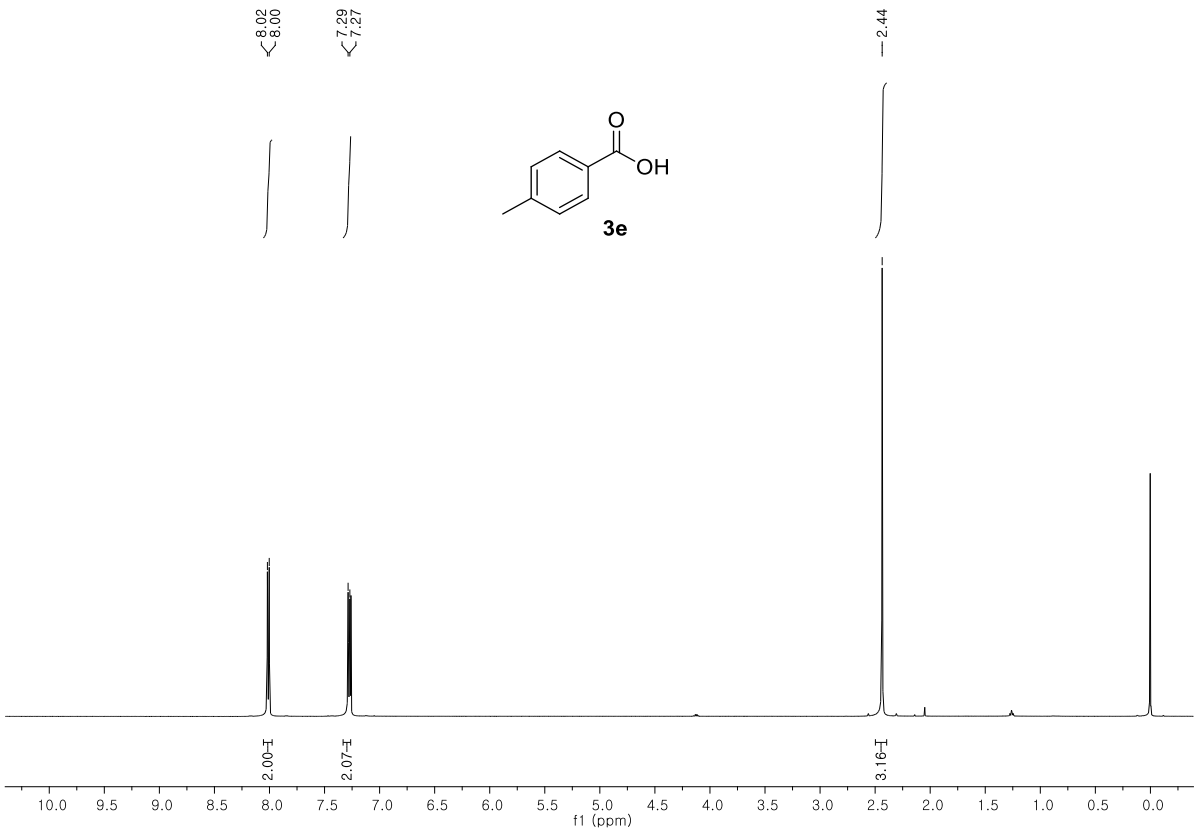

166.3
132.8
131.1
129.6
128.4
68.5
22.1
O
OiPr
2'b
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

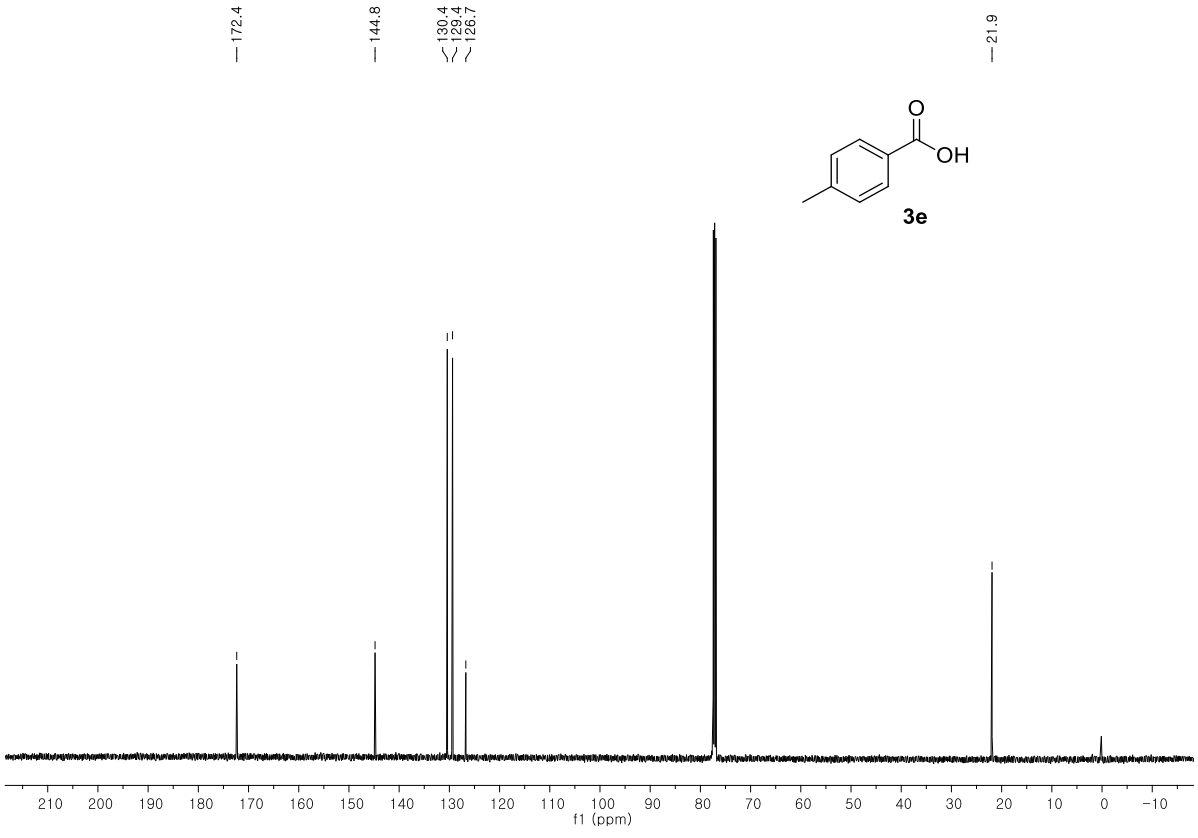

8.01
7.99
7.53
7.52
7.50
7.43
7.41
7.40
1.95
1.93
1.92
1.90
1.57
0.99
0.98
0.96
2'c
1.97
1.00
2.02
2.10
6.25
3.10
f1 (ppm)

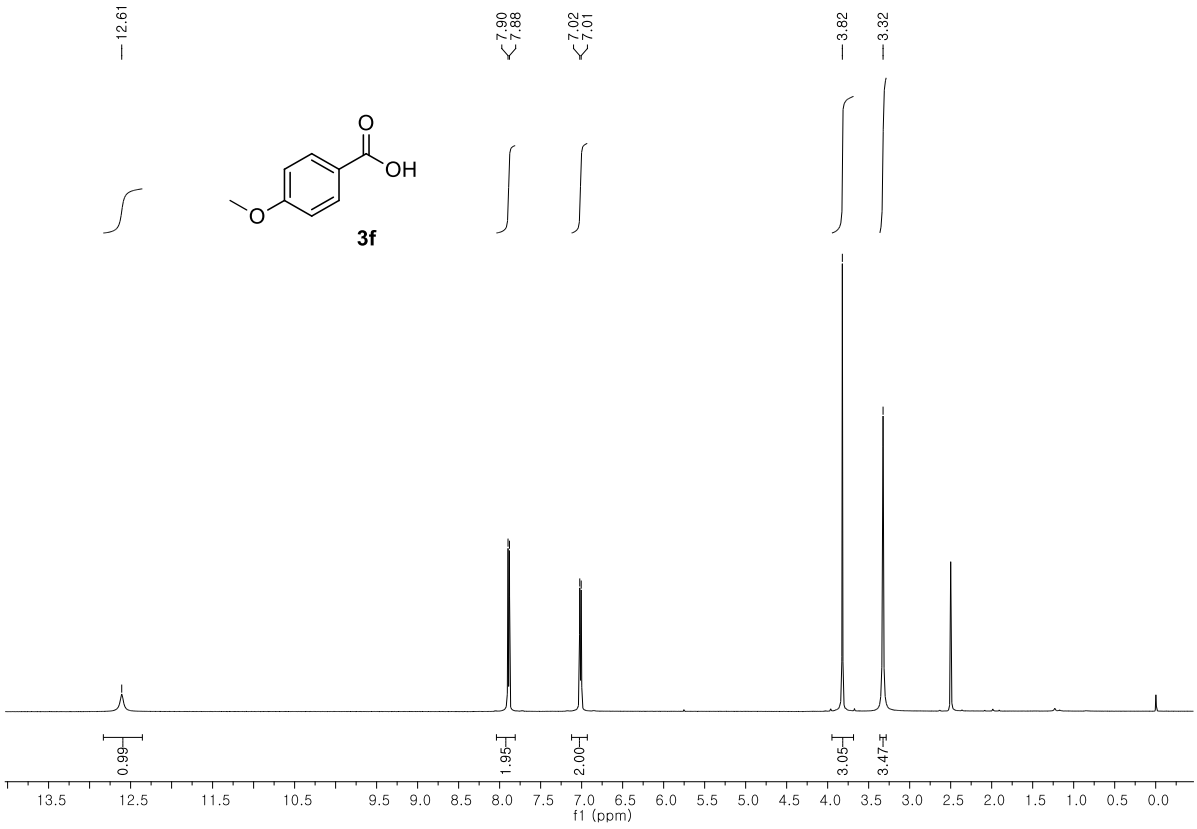

165.8
132.5
132.2
129.5
128.3
83.5
33.9
25.8
8.4
2'c
f1 (ppm)

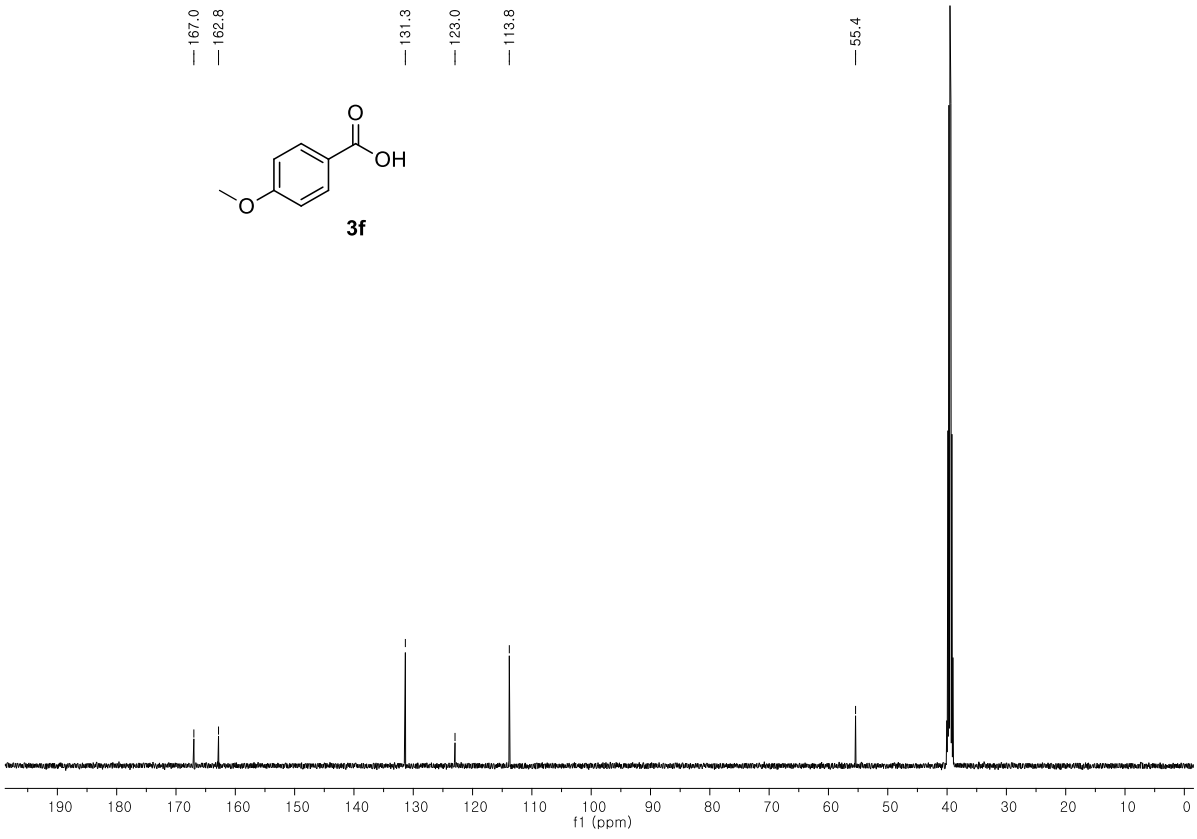

12.76
8.15
8.15
8.14
8.14
8.14
7.65
7.64
7.64
7.63
7.62
7.61
7.61
7.51
7.49
7.48
7.48
O
OH
3a-3d
0.92
2.00
1.00
2.08
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0
f1 (ppm)

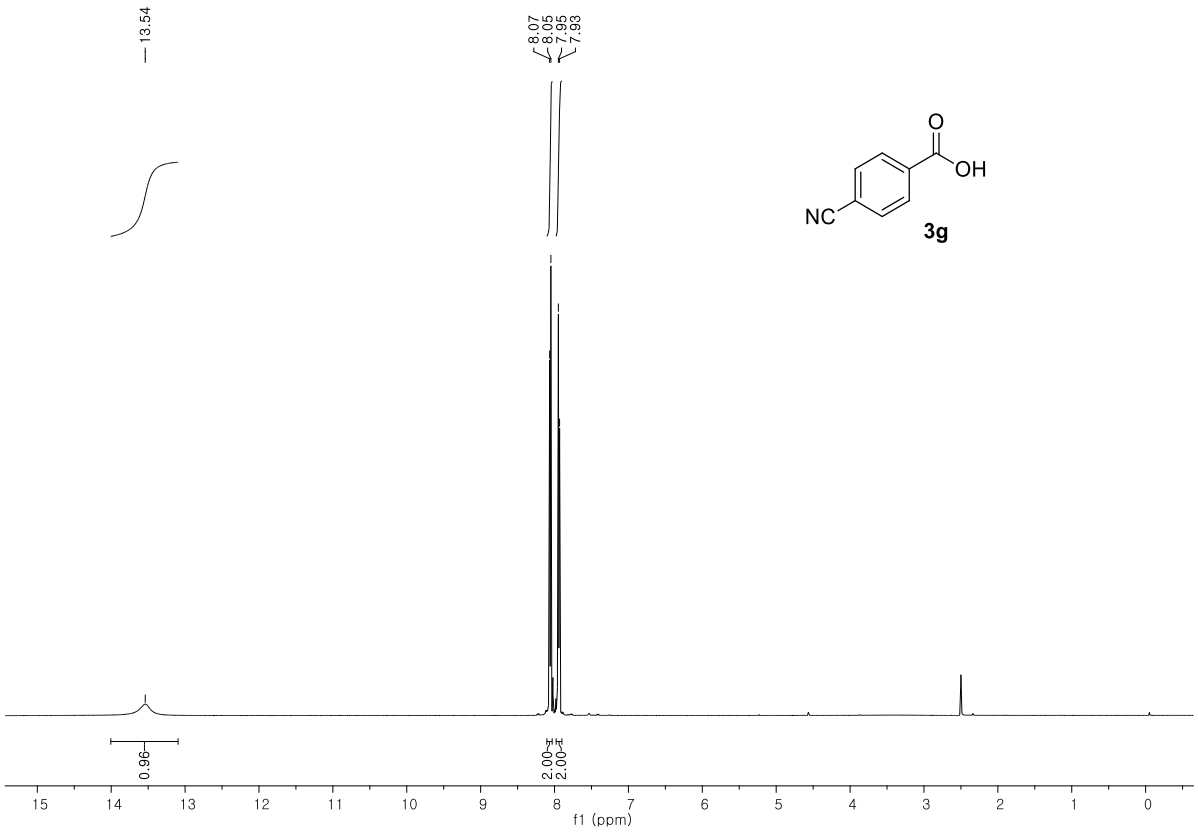

172.7
134.0
130.4
129.5
128.6
O
OH
3a-3d
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

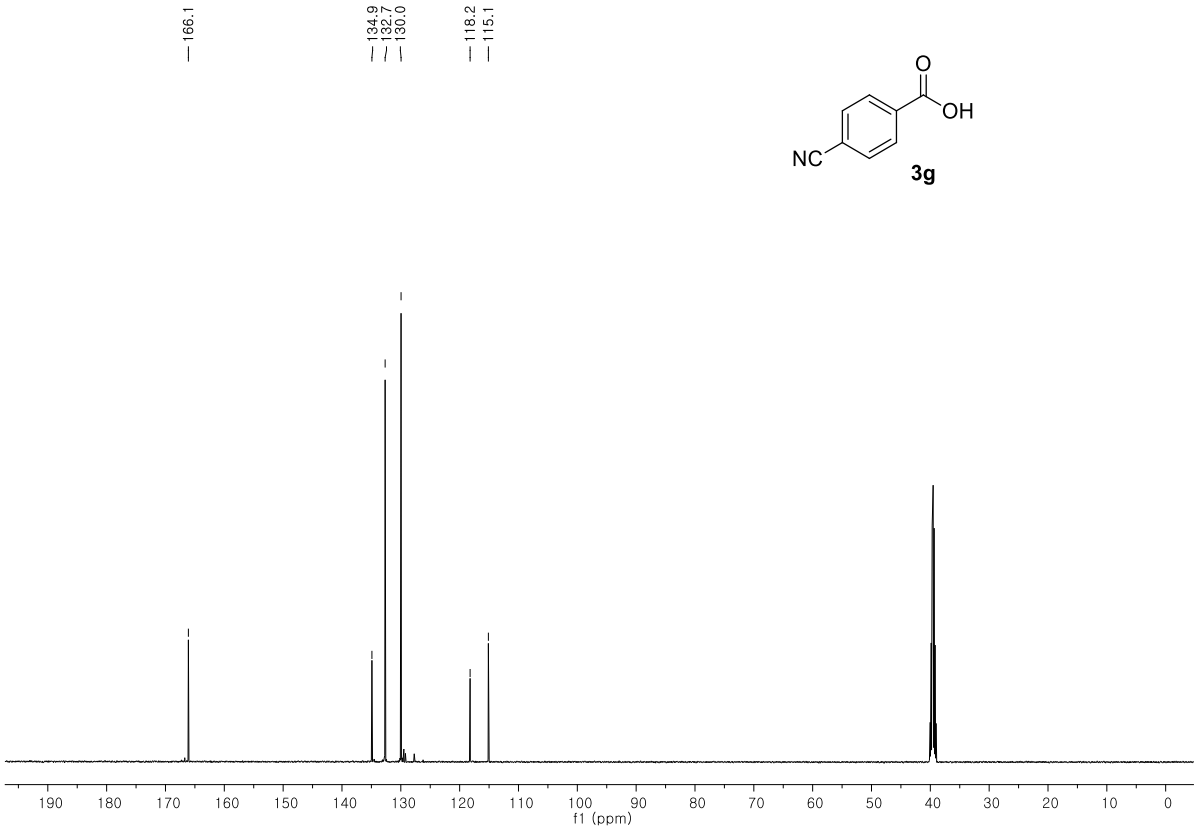

8.02
8.00
7.29
7.27
2.44
O
OH
3e
2.00
2.07
3.16
f1 (ppm)

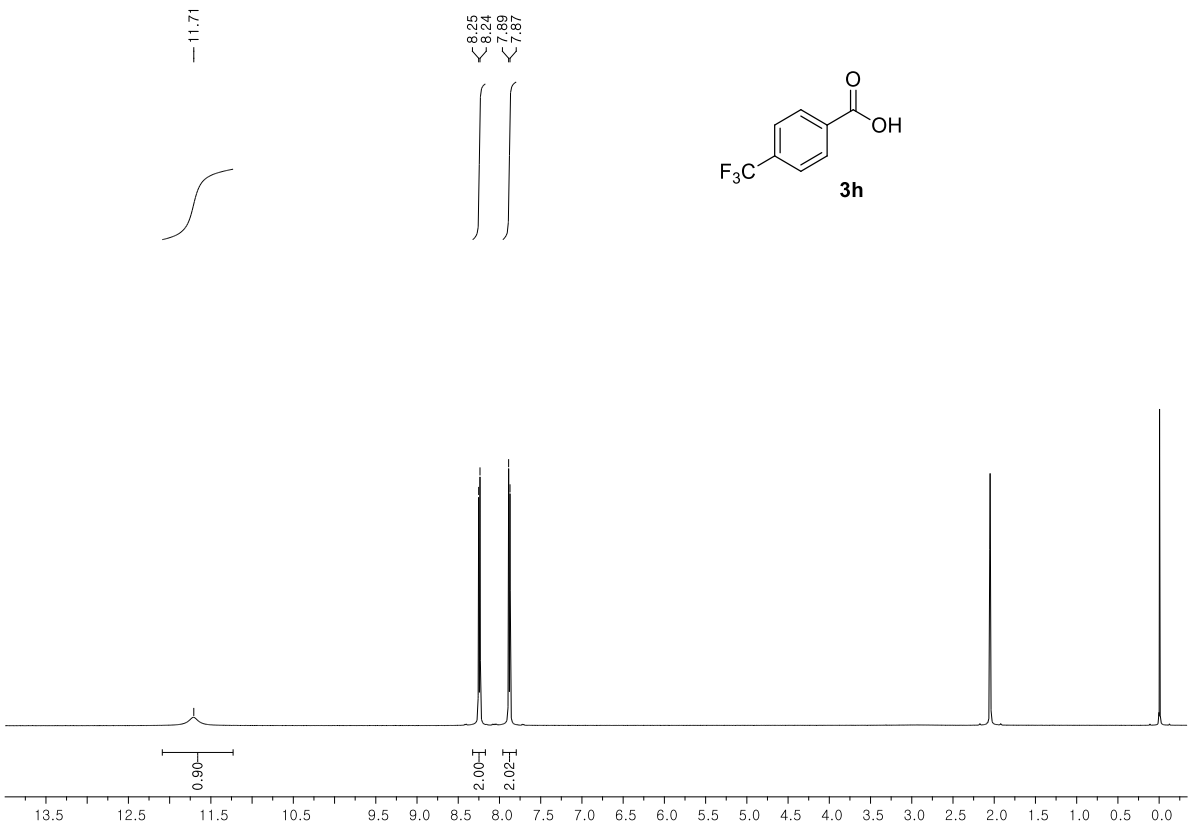

172.4
144.8
130.4
129.4
126.7
21.9
O
OH
3e
f1 (ppm)

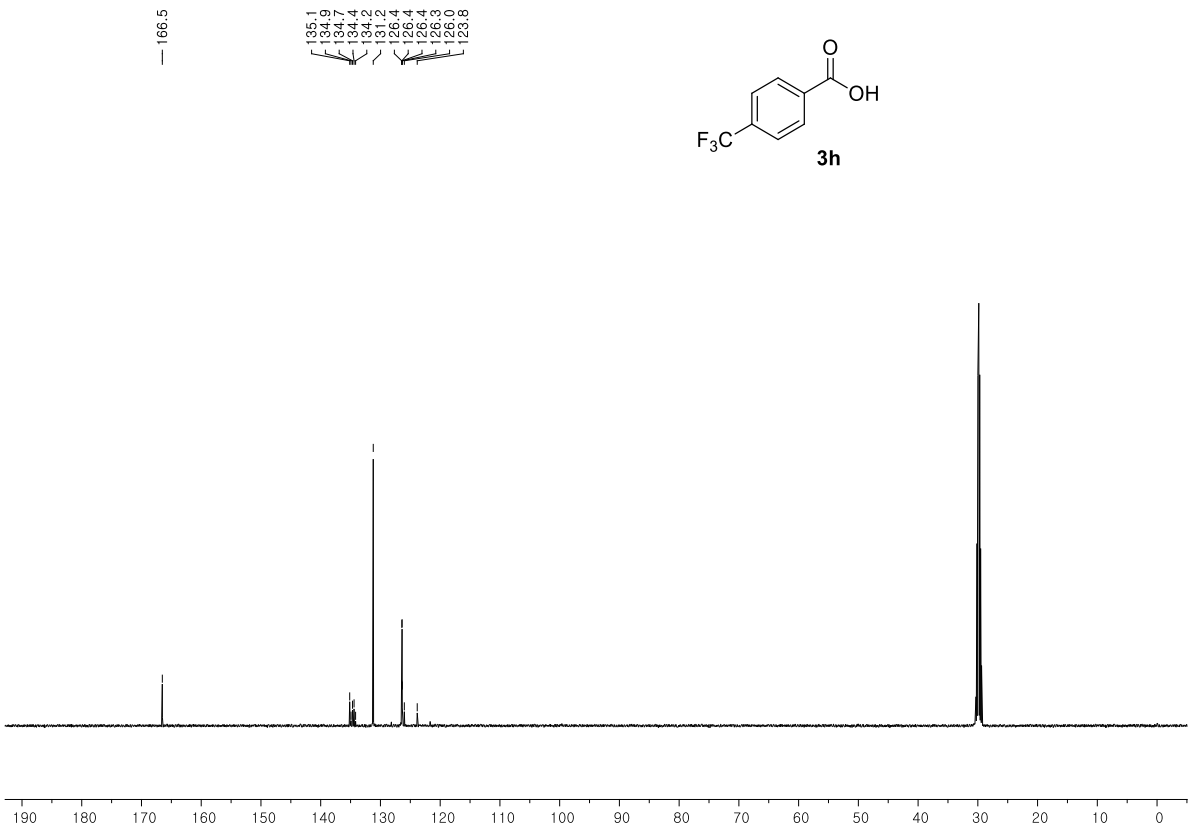

12.61
7.90
7.88
7.02
7.01
3.82
3.32
O
OH
O
3f
0.99
1.95
2.00
3.05
3.47
13.5 12.5 11.5 10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

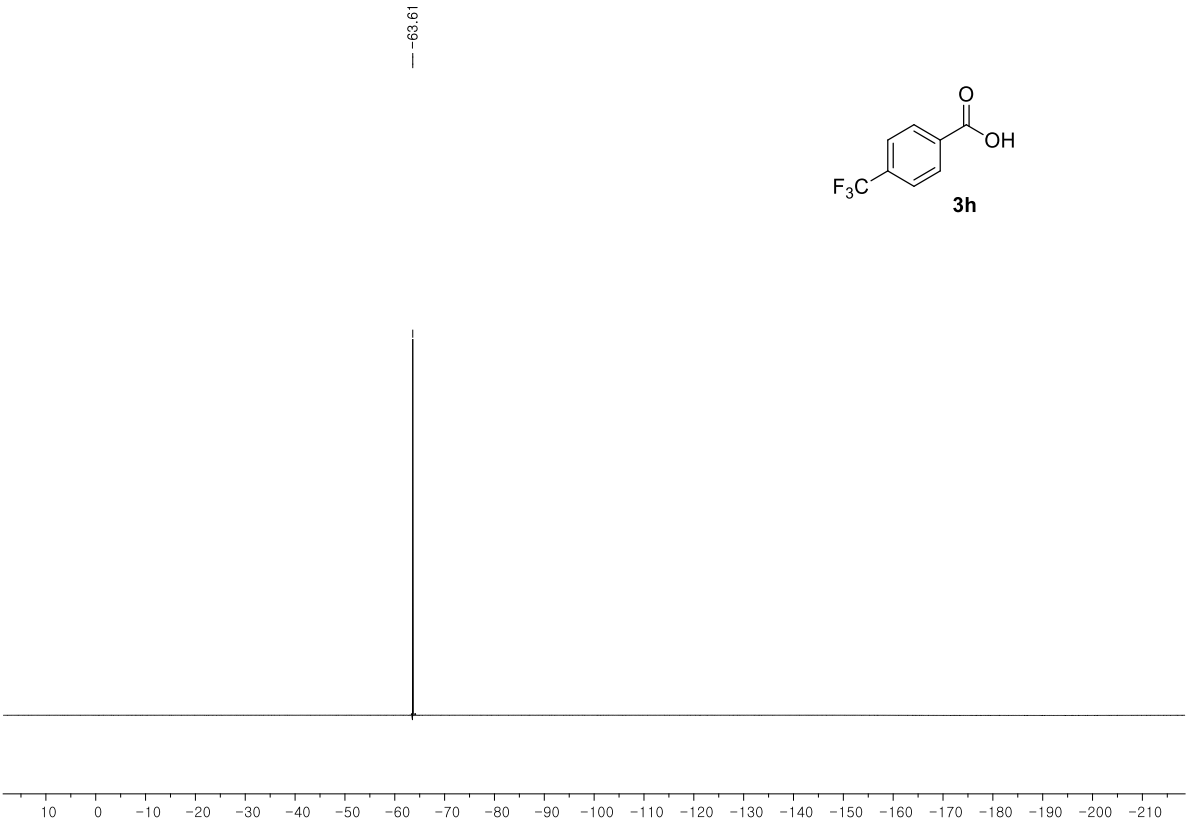

167.0
162.8
131.3
123.0
113.8
55.4
O
OH
O
3f
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

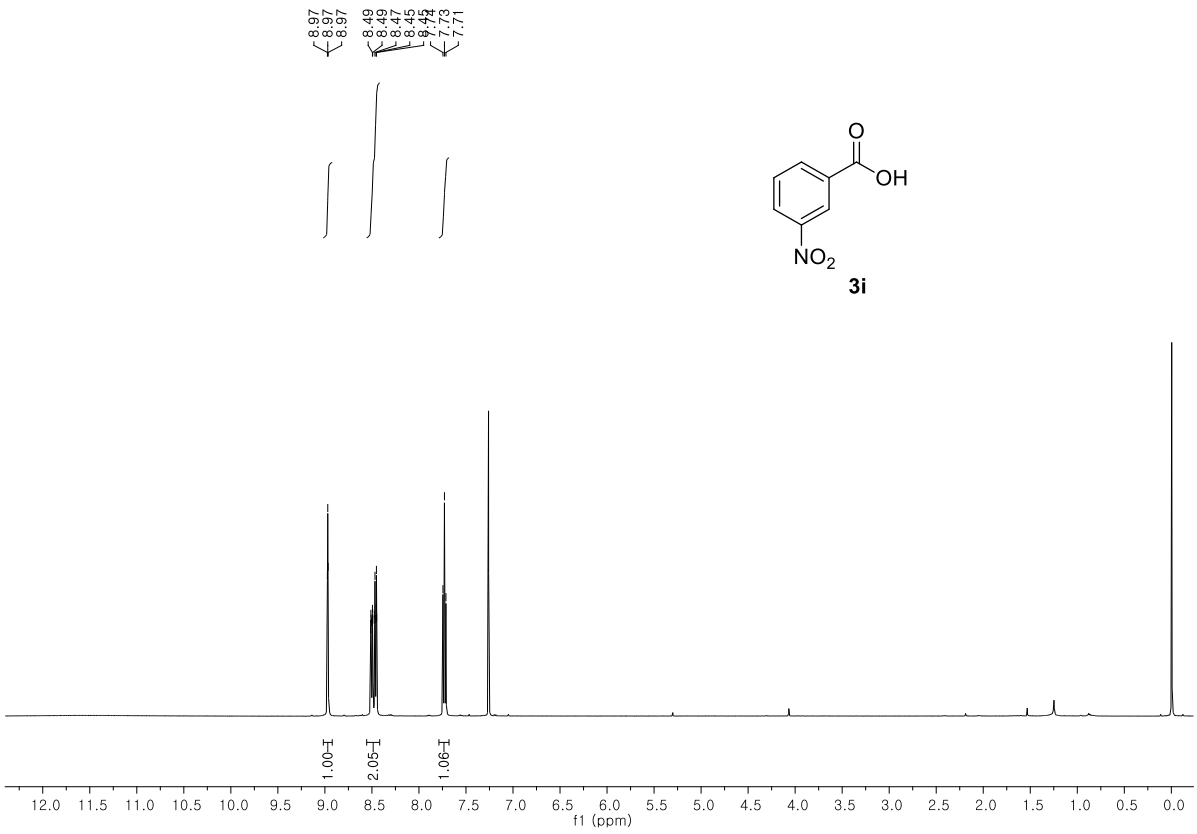

13.54
8.07
8.05
7.95
7.93
O
OH
NC
3g
0.96
2.00
2.00
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0
f1 (ppm)

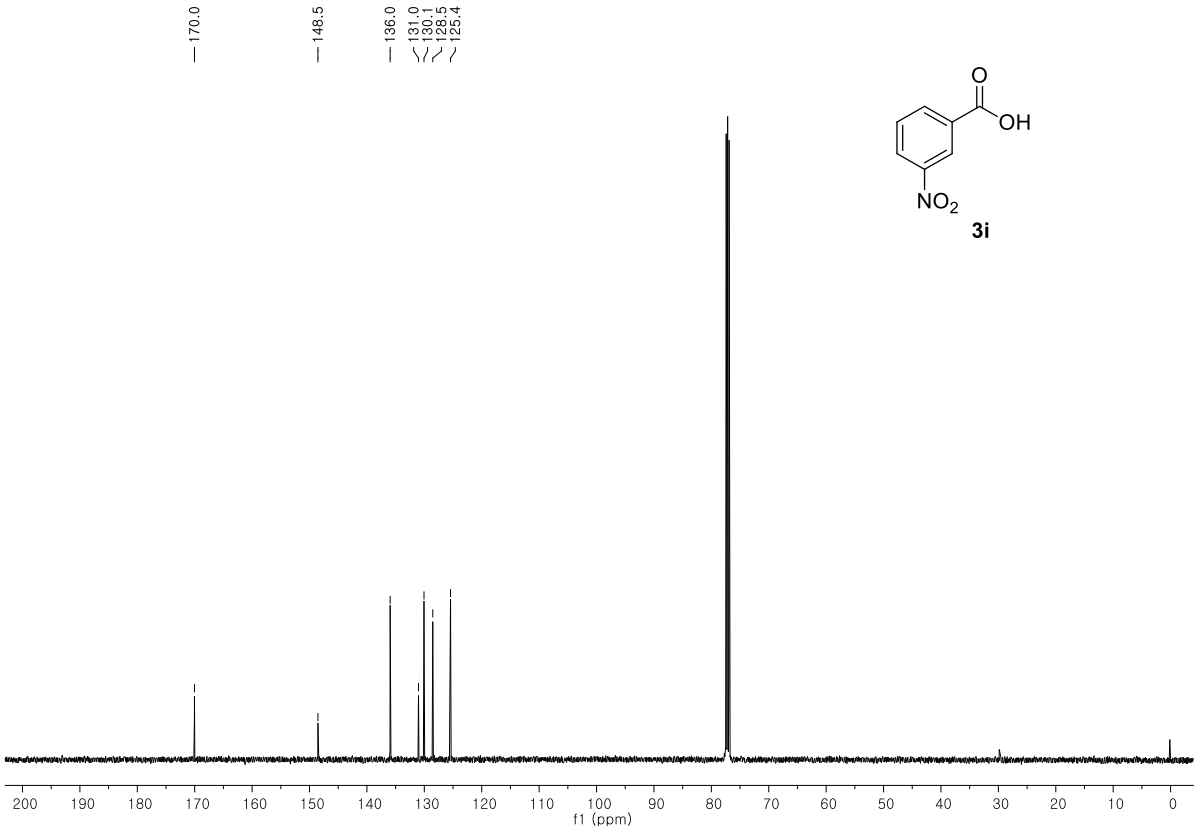

166.1
134.9
132.7
130.0
118.2
115.1
O
OH
NC
3g
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

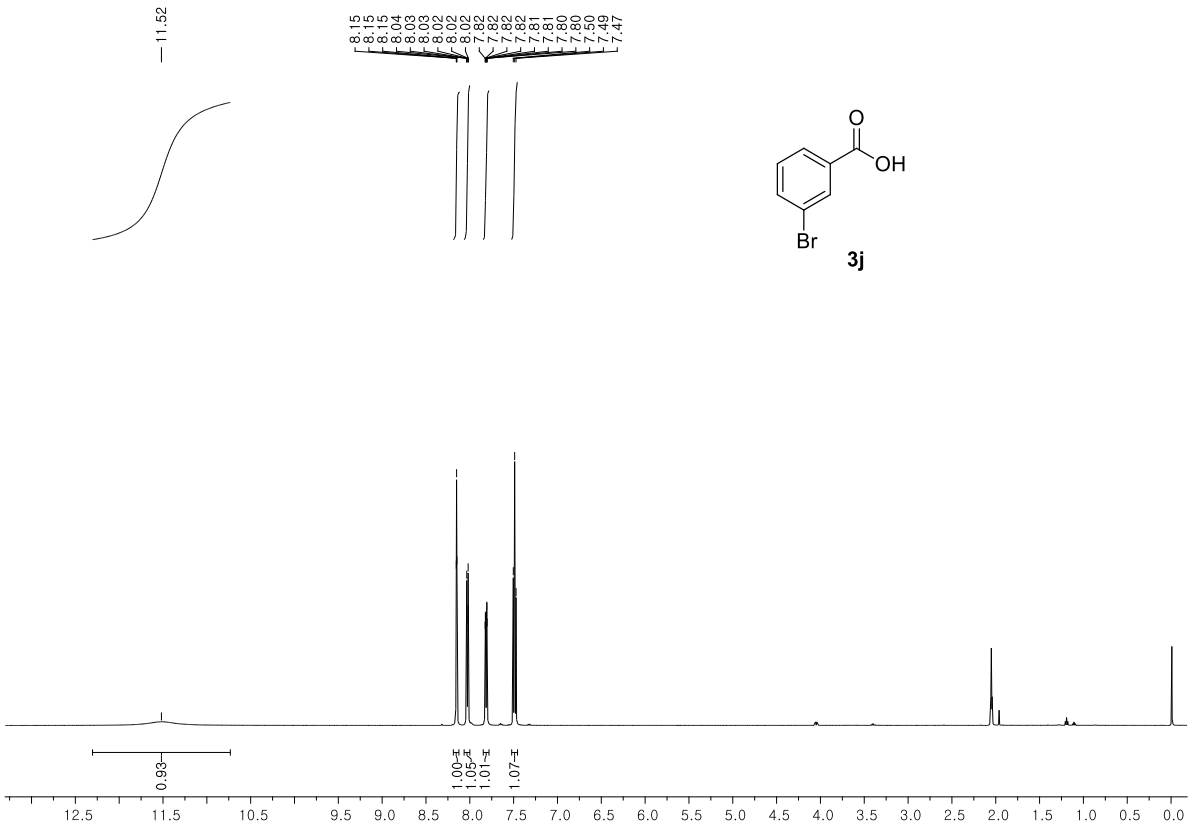

11.71
8.25
8.24
7.89
7.87
O
OH
F3C
3h
0.90
2.00
2.02
13.5
12.5
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

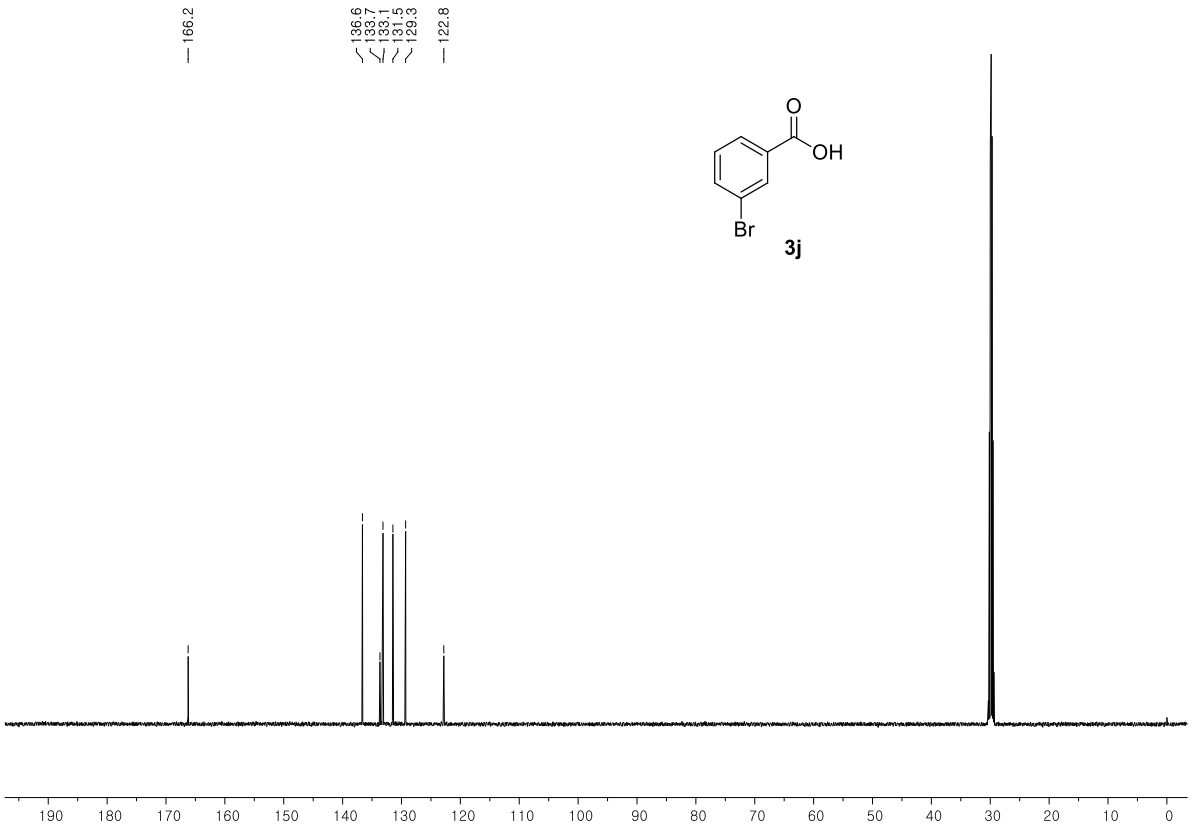

166.5
135.1
134.9
134.7
134.4
134.2
131.2
126.4
126.4
126.4
126.3
126.0
123.8
O
OH
F3C
3h
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

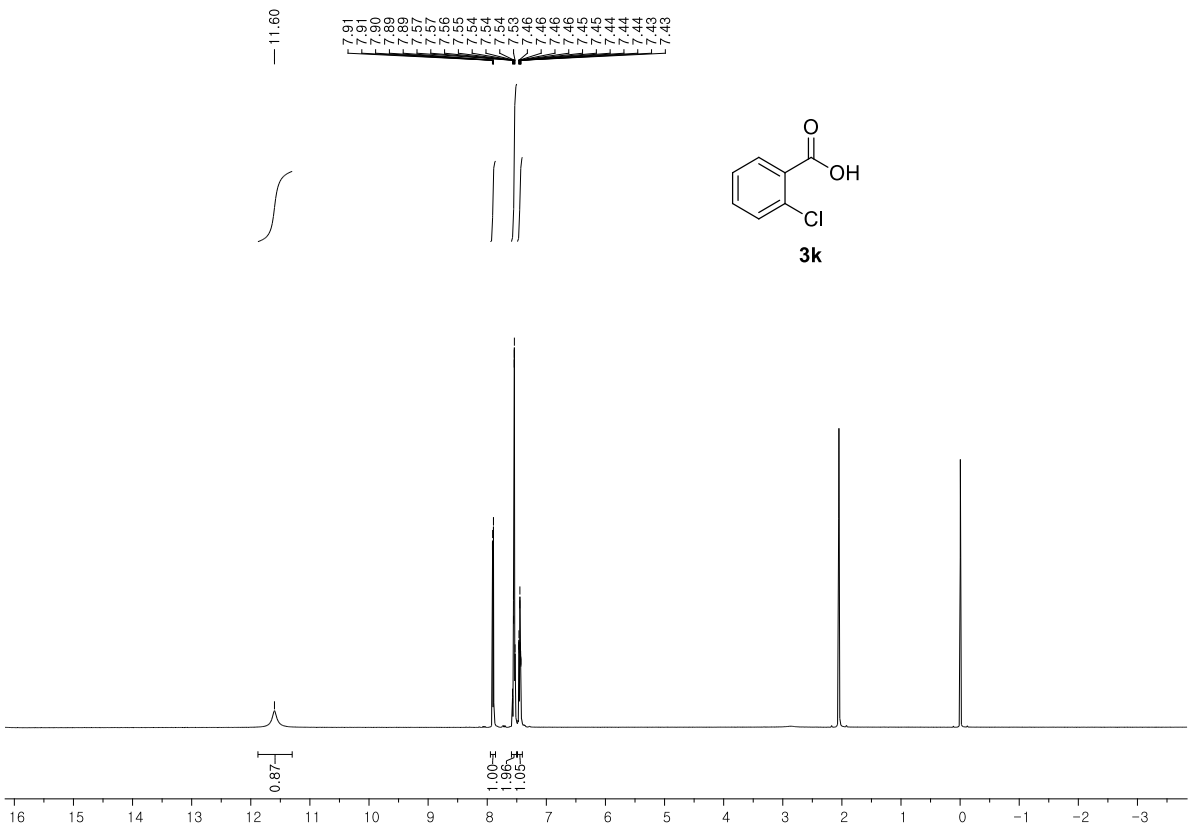

-63.61
O
OH
F3C
3h
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210

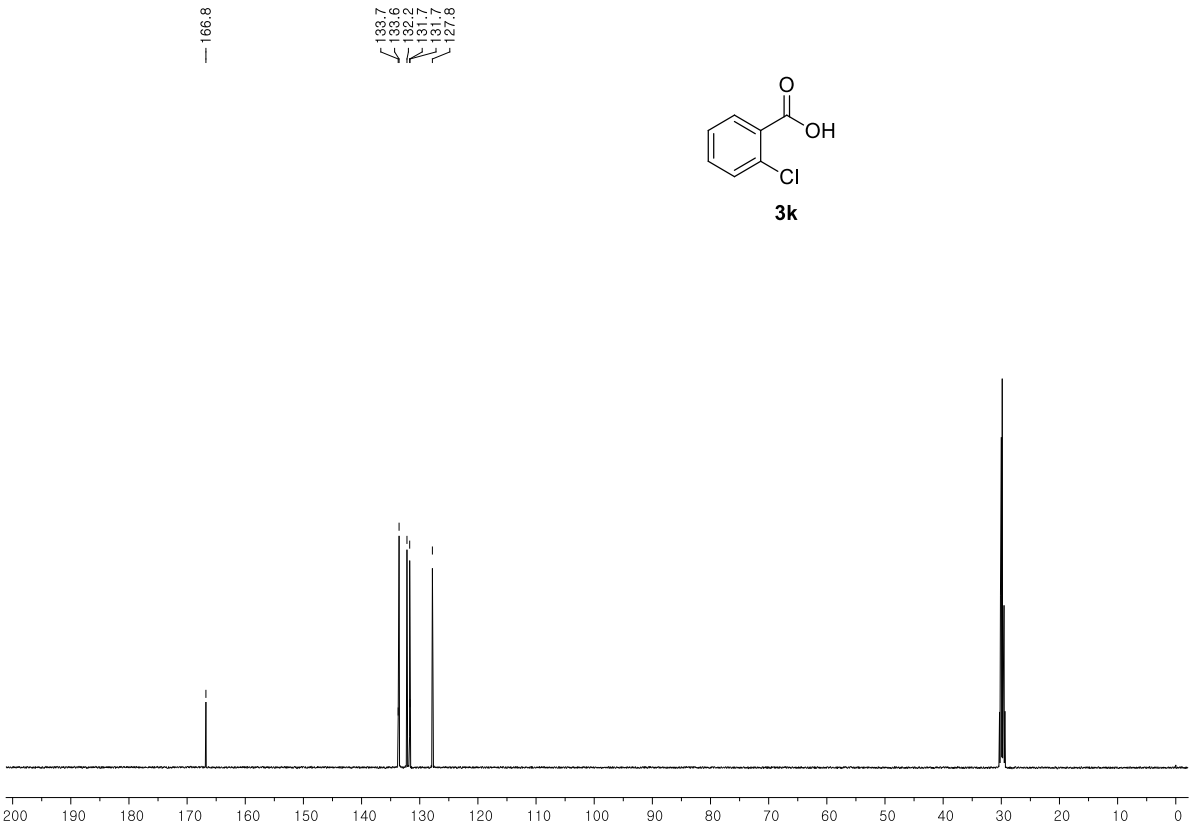

8.97
8.97
8.97
8.49
8.49
8.47
8.45
7.73
7.71
O
OH
NO2
3i
1.00
2.05
1.06
f1 (ppm)

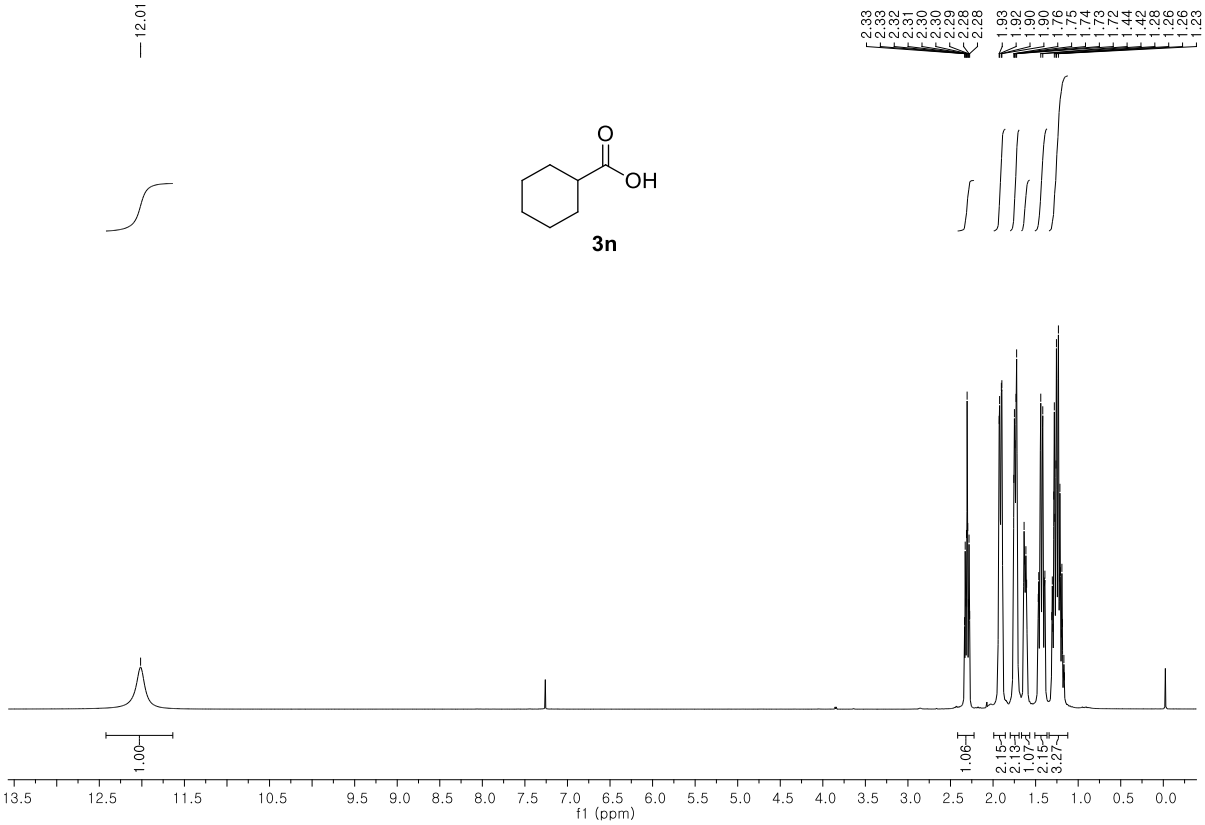

170.0
148.5
136.0
131.0
130.1
128.5
125.4
O
OH
NO2
3i
f1 (ppm)

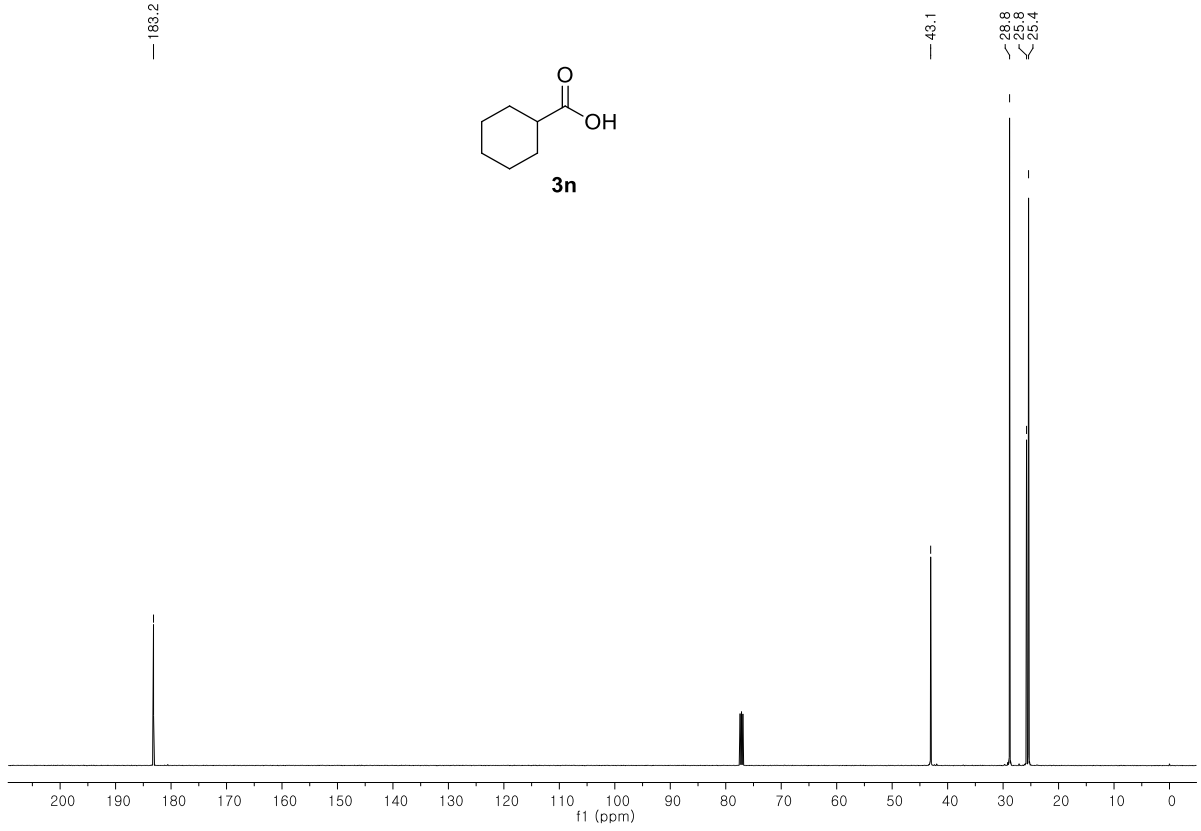

11.52
8.15
8.15
8.15
8.04
8.03
8.03
8.02
8.02
8.02
7.82
7.82
7.82
7.82
7.81
7.81
7.80
7.80
7.50
7.49
7.47
O
OH
Br
3j
0.93
1.00
1.05
1.01
1.07
12.5
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

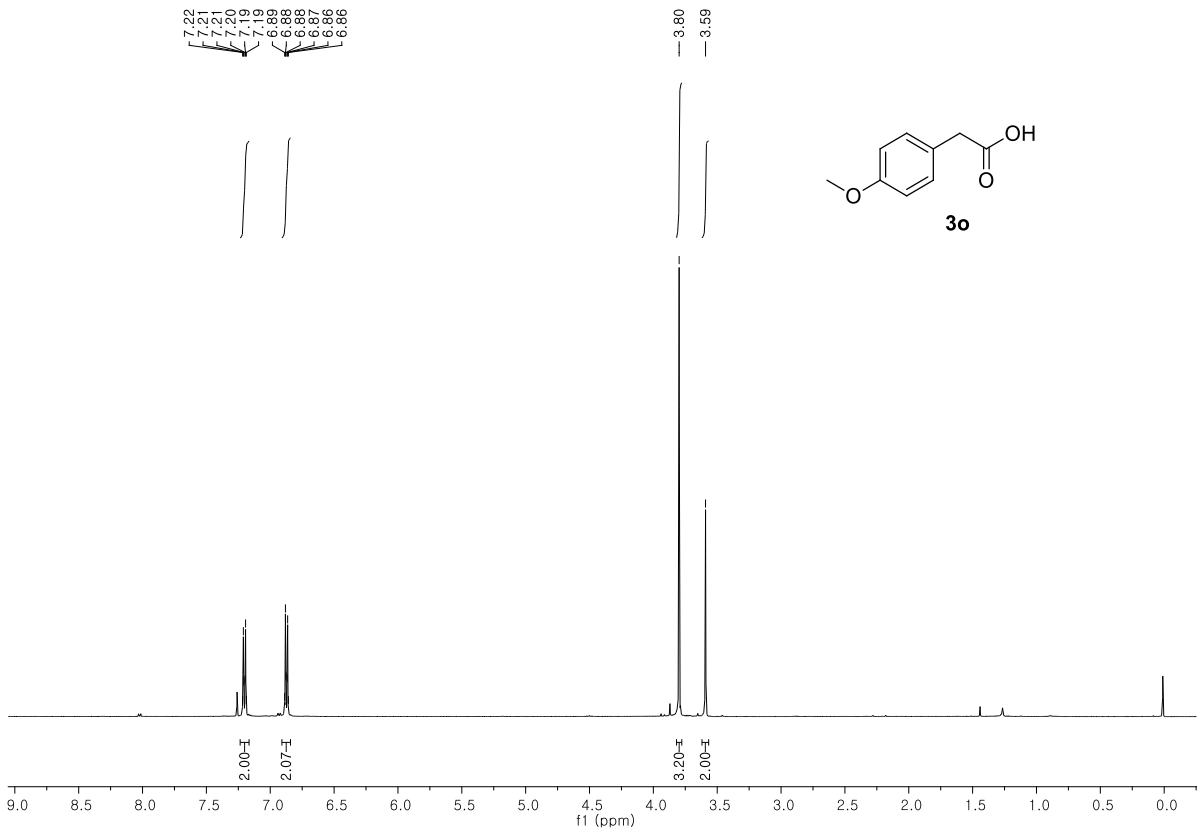

166.2
136.6
133.7
133.1
131.5
129.3
122.8
O
OH
Br
3j
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

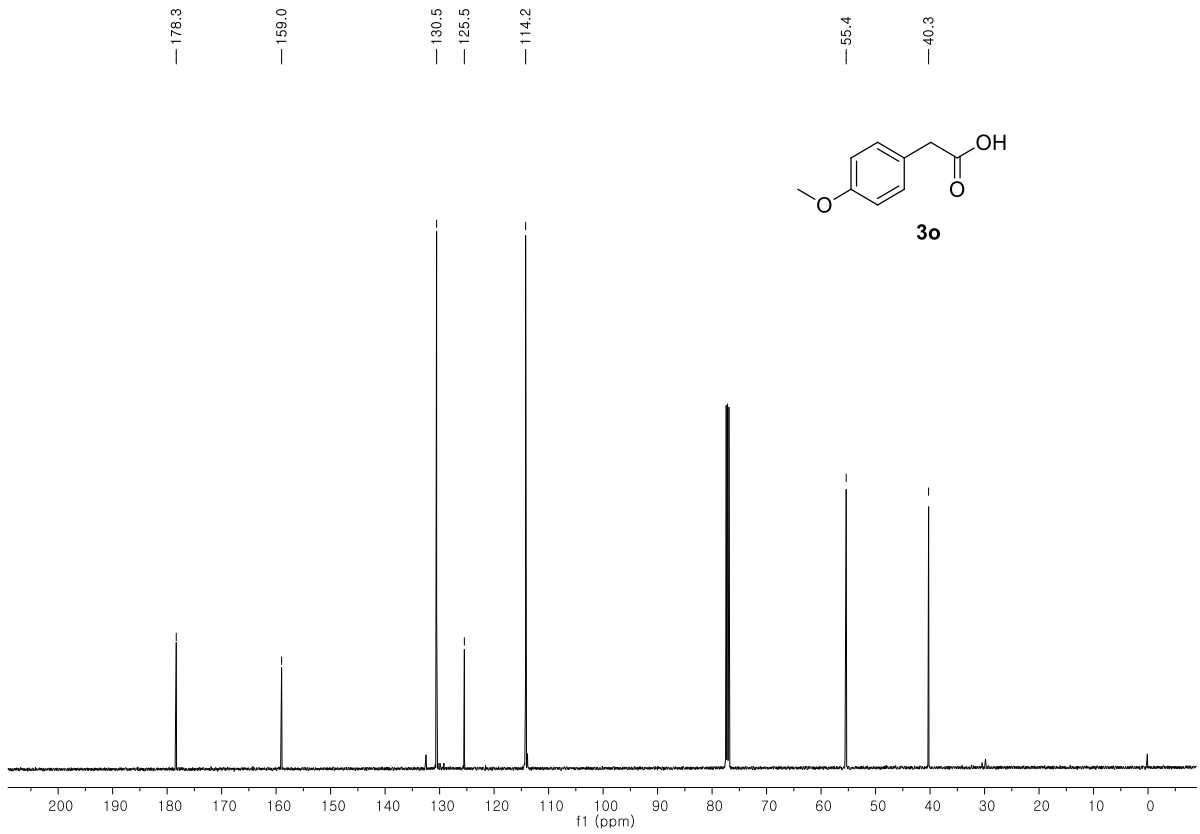

11.60
7.91
7.91
7.90
7.89
7.89
7.57
7.57
7.56
7.55
7.54
7.54
7.54
7.54
7.53
7.46
7.46
7.46
7.45
7.45
7.44
7.44
7.44
7.43
7.43
O
OH
Cl
3k
0.87
1.00
1.96
1.05
16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3

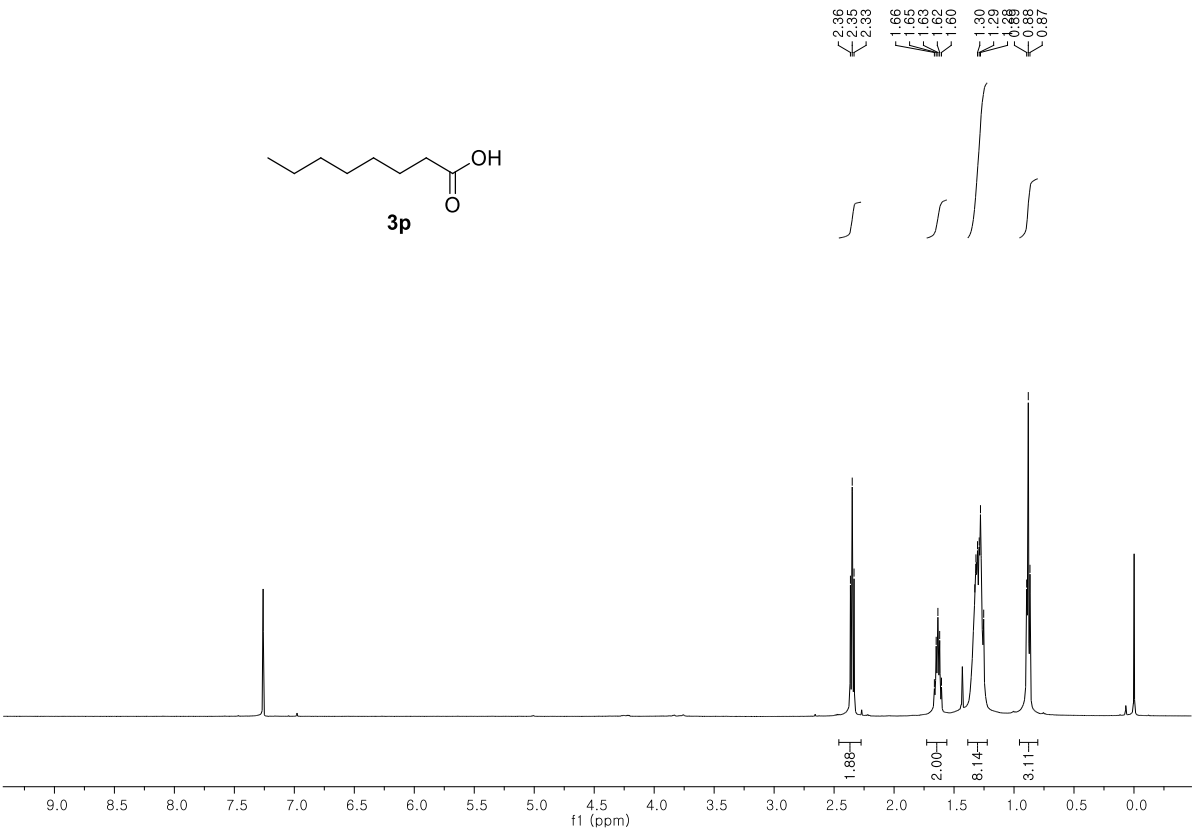

166.8
133.7
133.6
132.2
131.7
131.7
127.8
O
OH
Cl
3k
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

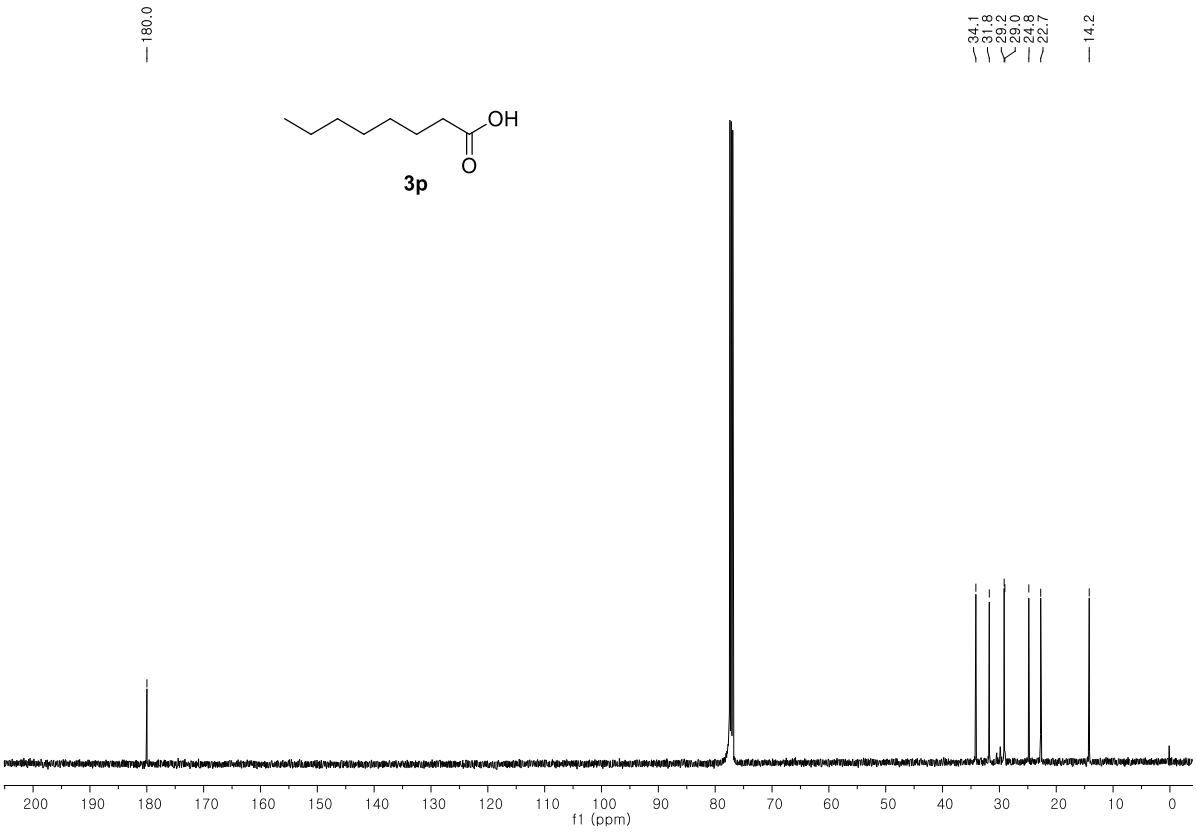

12.01
2.33
2.33
2.32
2.31
2.30
2.30
2.29
2.28
2.28
1.93
1.92
1.90
1.90
1.76
1.75
1.74
1.73
1.72
1.44
1.42
1.28
1.26
1.23
O
OH
3n
1.00
1.06
2.15
2.13
1.07
2.15
3.27
13.5
12.5
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

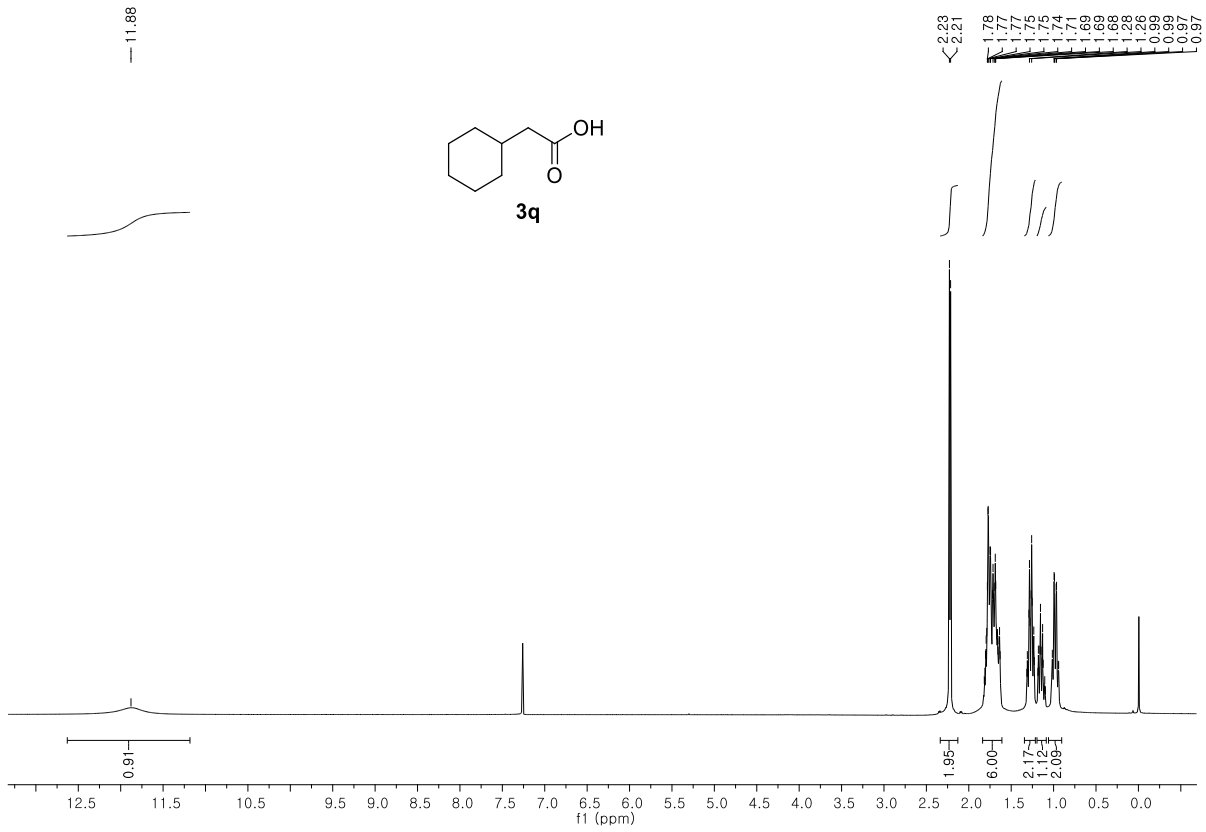

183.2
43.1
28.8
25.8
25.4
O
OH
3n
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

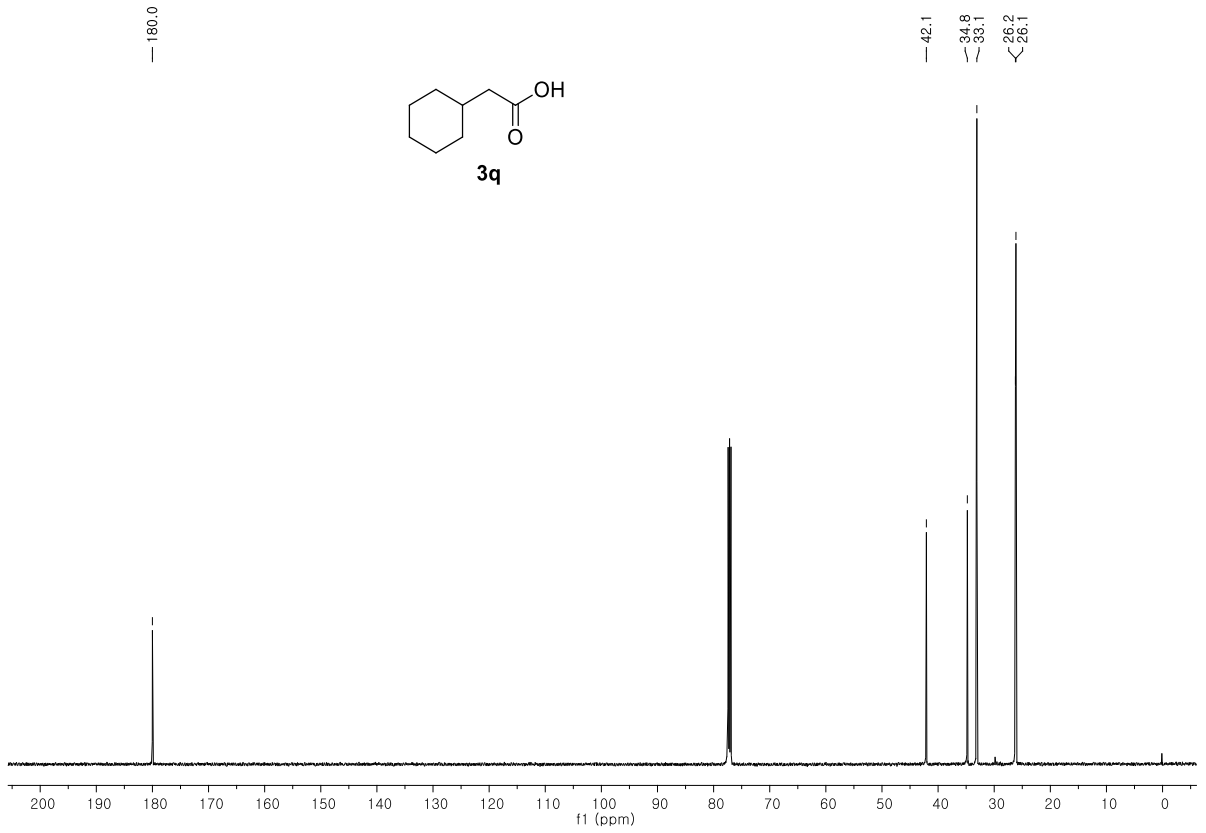

7.22
7.21
7.21
7.20
7.19
7.19
6.89
6.88
6.88
6.87
6.86
6.86
3.80
3.59
OH
O
O
3o
2.00
2.07
3.20
2.00
f1 (ppm)

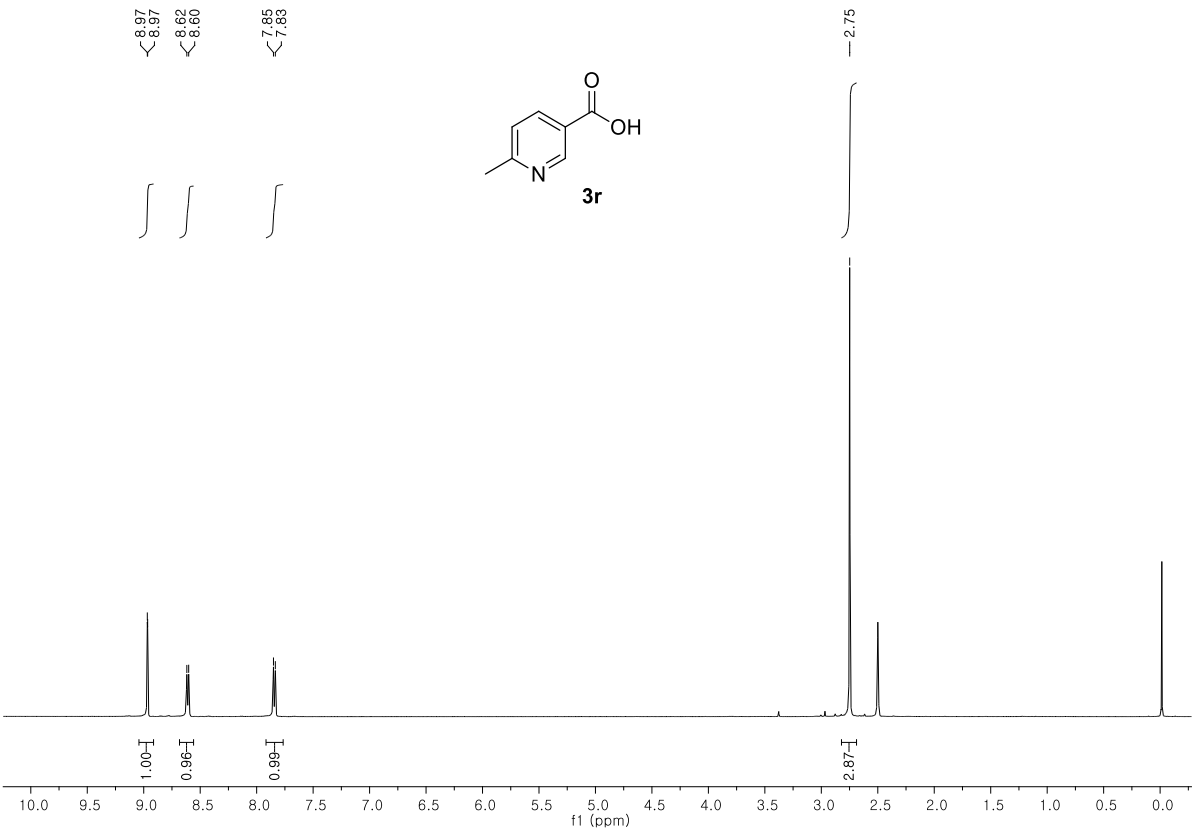

178.3
159.0
130.5
125.5
114.2
55.4
40.3
OH
O
O
3o
f1 (ppm)

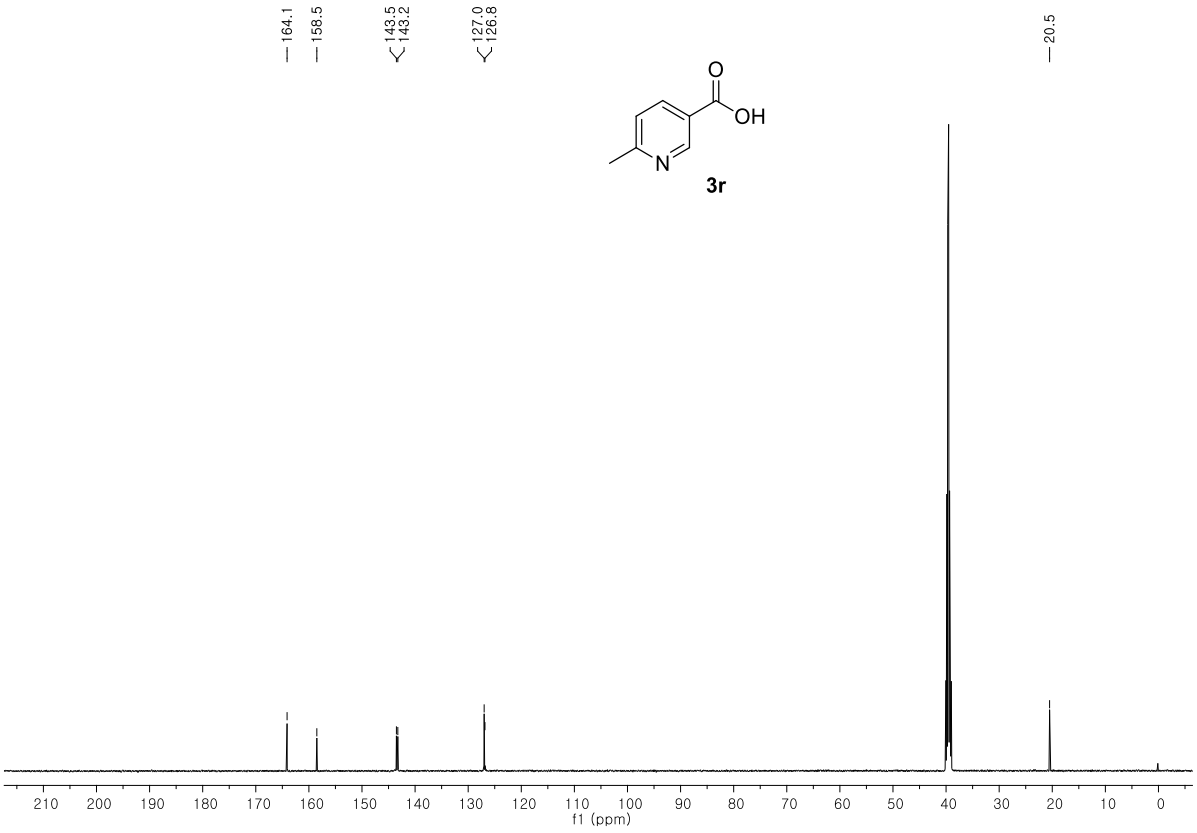

2.36
2.35
2.33
1.66
1.65
1.63
1.62
1.60
1.30
1.29
0.88
0.87
OH
O
3p
1.88
2.00
8.14
3.11
f1 (ppm)

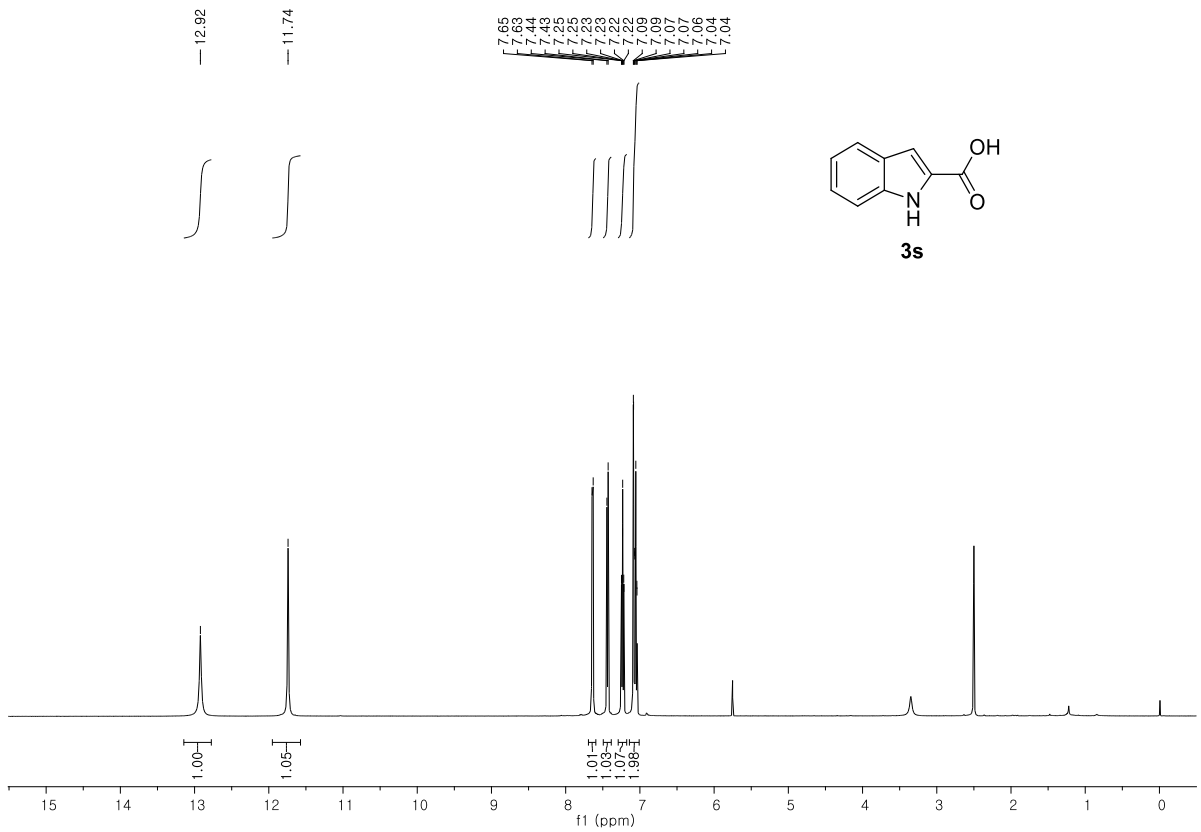

180.0
34.1
31.8
29.2
29.0
24.8
22.7
14.2
OH
O
3p
f1 (ppm)

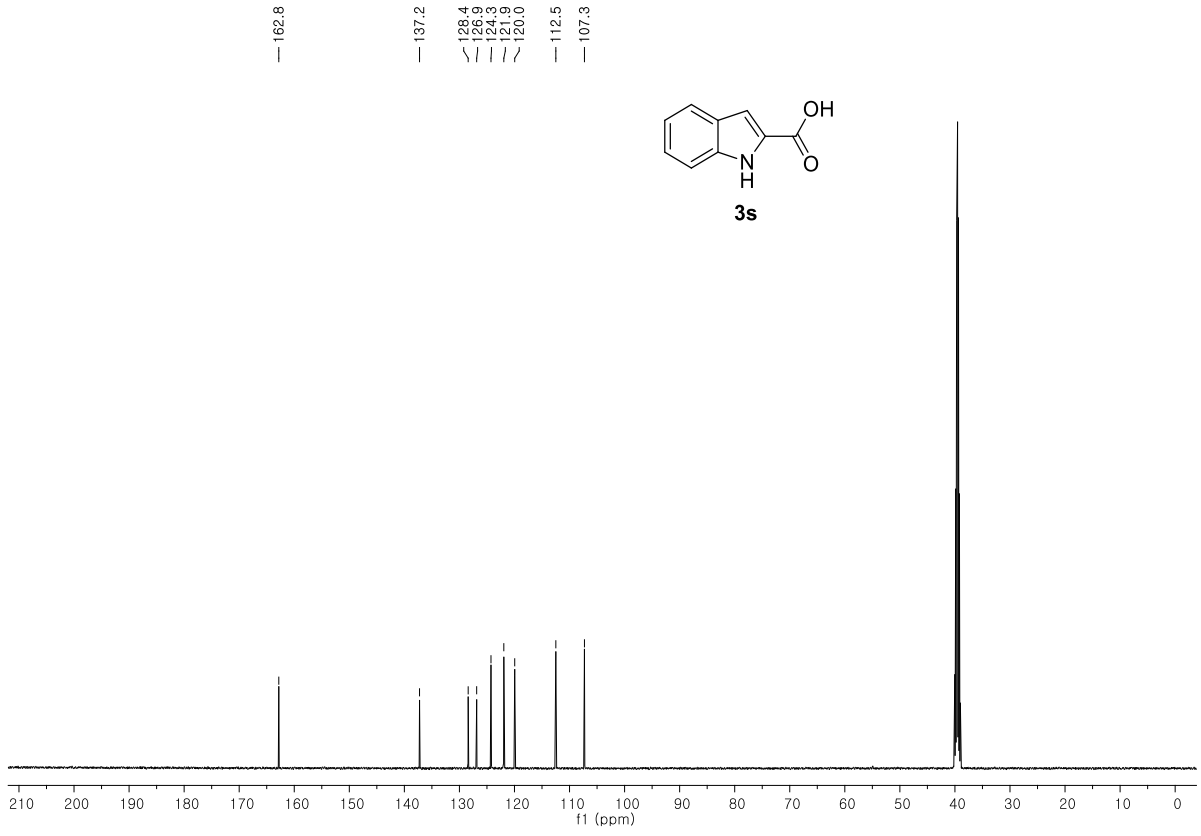

11.88
2.23
2.21
1.78
1.77
1.77
1.77
1.75
1.75
1.74
1.71
1.69
1.69
1.68
1.28
1.26
0.99
0.99
0.97
0.97
OH
O
3q
0.91
1.95
6.00
2.17
1.12
2.09
12.5
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

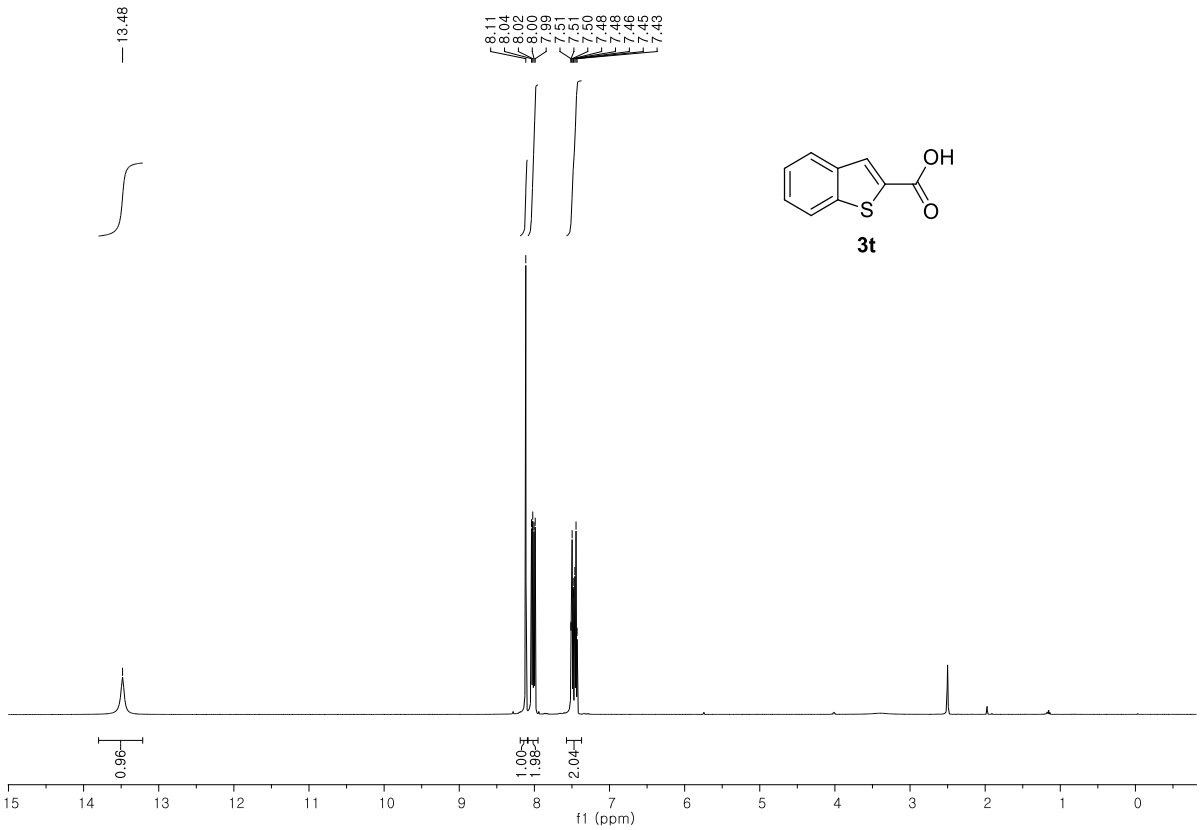

180.0
42.1
34.8
33.1
26.2
26.1
OH
O
3q
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

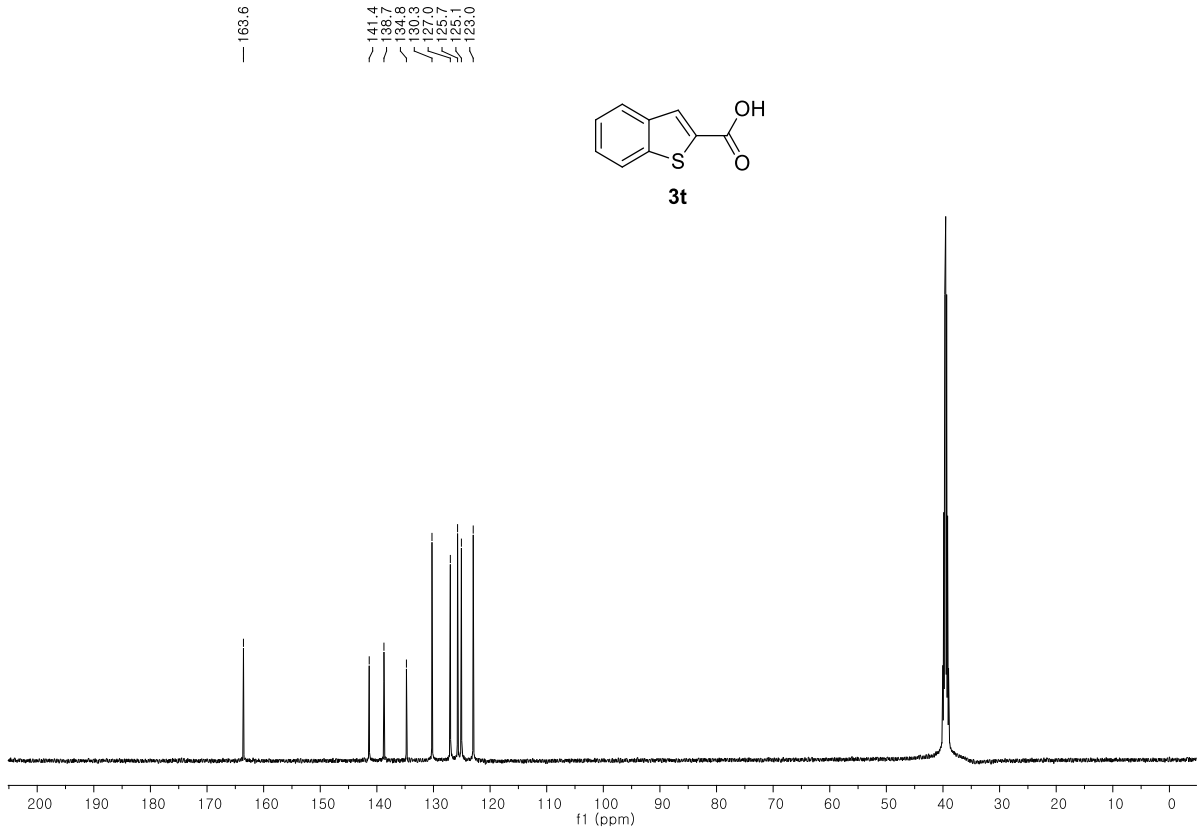

8.97
8.97
8.62
8.60
7.85
7.83
2.75
O
OH
N
3r
1.00
0.96
0.99
2.87
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

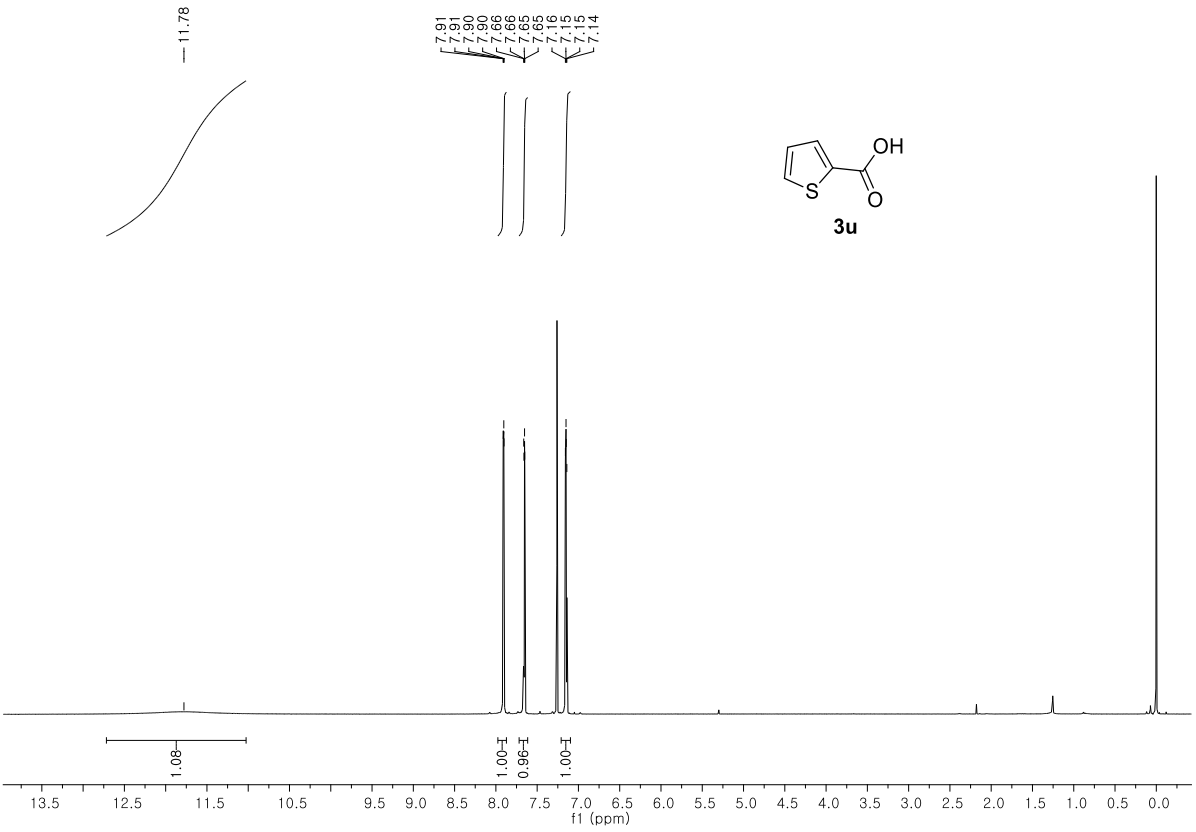

164.1
158.5
143.5
143.2
127.0
126.8
20.5
O
OH
N
3r
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

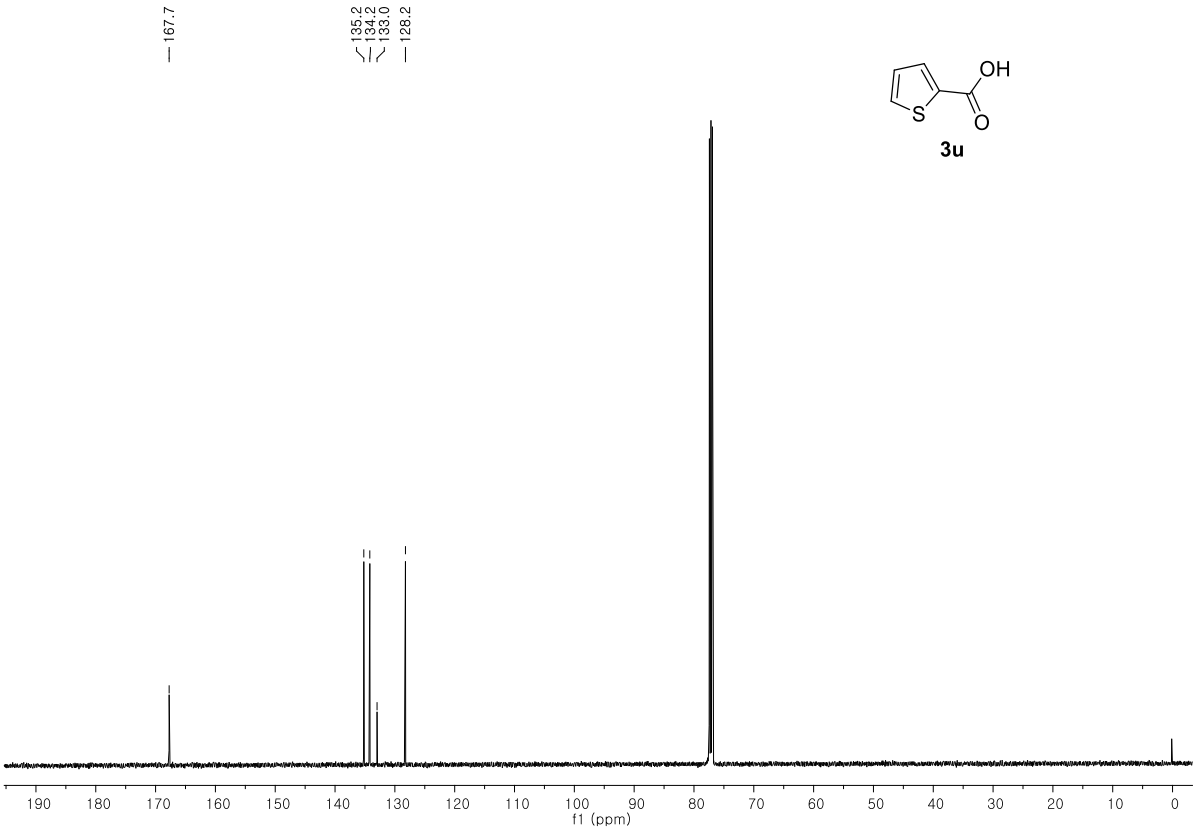

12.92
11.74
7.65
7.63
7.44
7.43
7.25
7.23
7.23
7.23
7.22
7.09
7.09
7.07
7.07
7.06
7.04
7.04
OH
N
H
O
3s
1.00
1.05
1.01
1.03
1.07
1.98
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0
f1 (ppm)

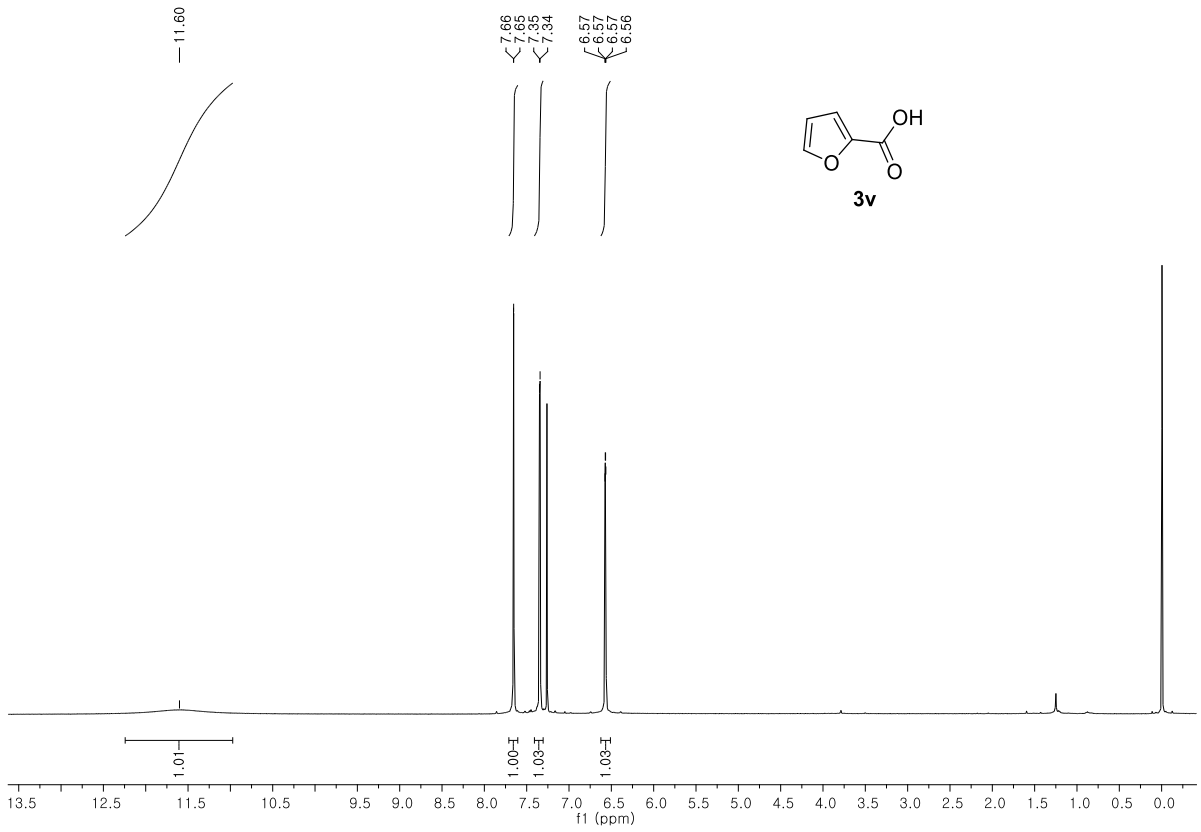

162.8
137.2
128.4
126.9
124.3
121.9
120.0
112.5
107.3
OH
N
H
O
3s
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

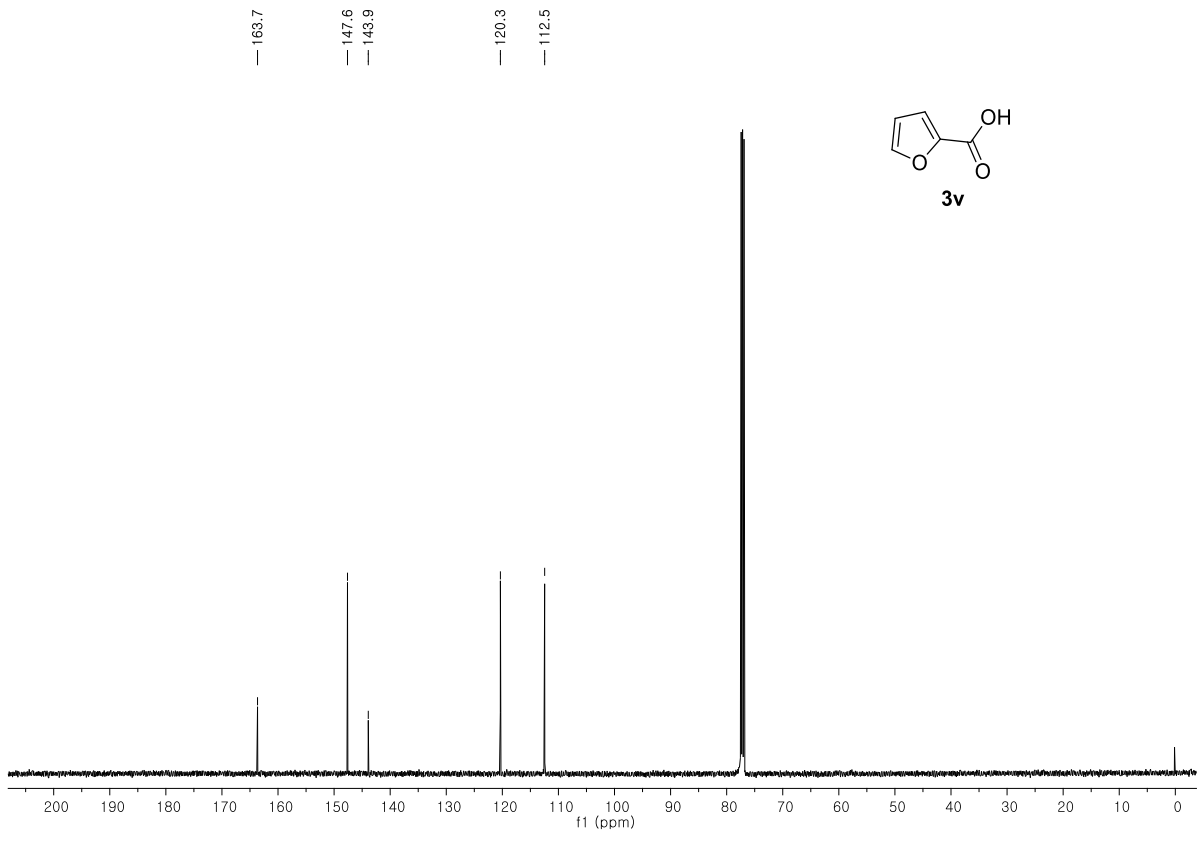

13.48
8.11
8.04
8.02
8.00
7.99
7.51
7.50
7.48
7.46
7.45
7.43
OH
O
S
3t
0.96
1.00
1.98
2.04
f1 (ppm)

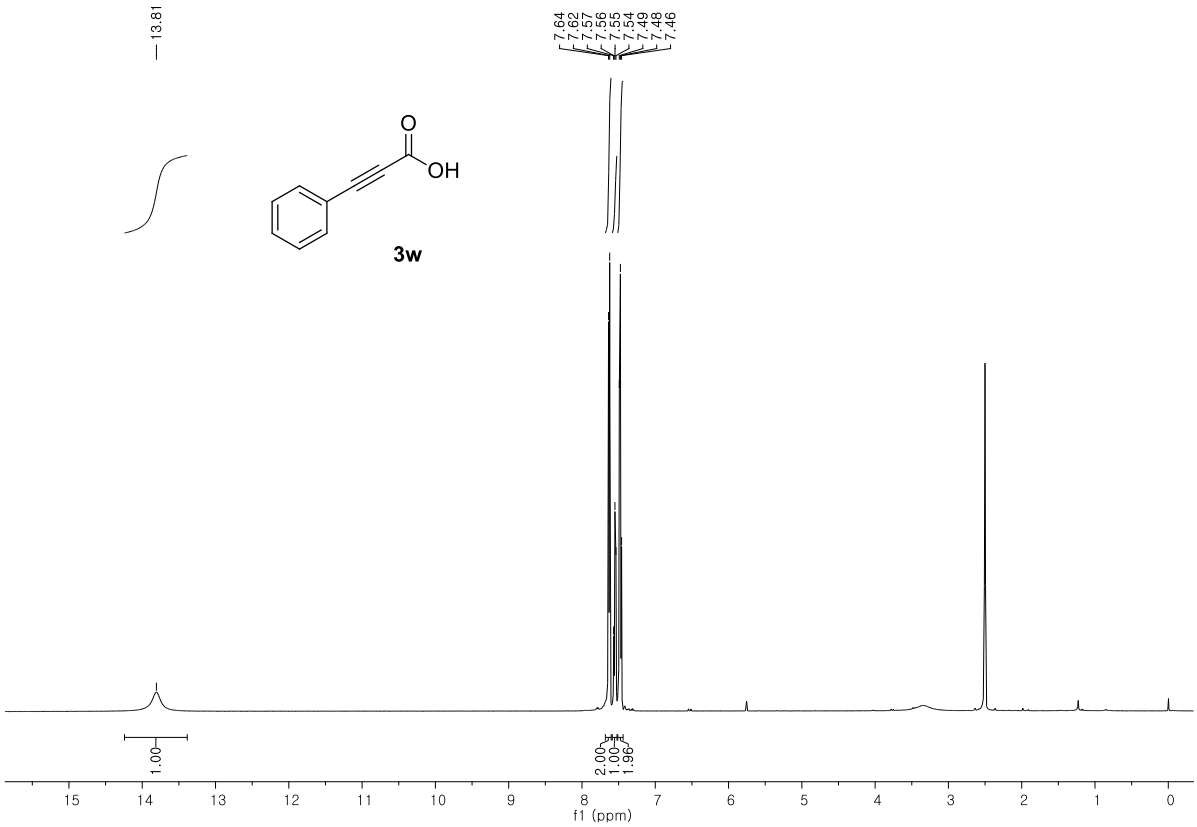

163.6
141.4
138.7
134.8
130.3
127.0
125.7
125.1
123.0
OH
O
S
3t
f1 (ppm)

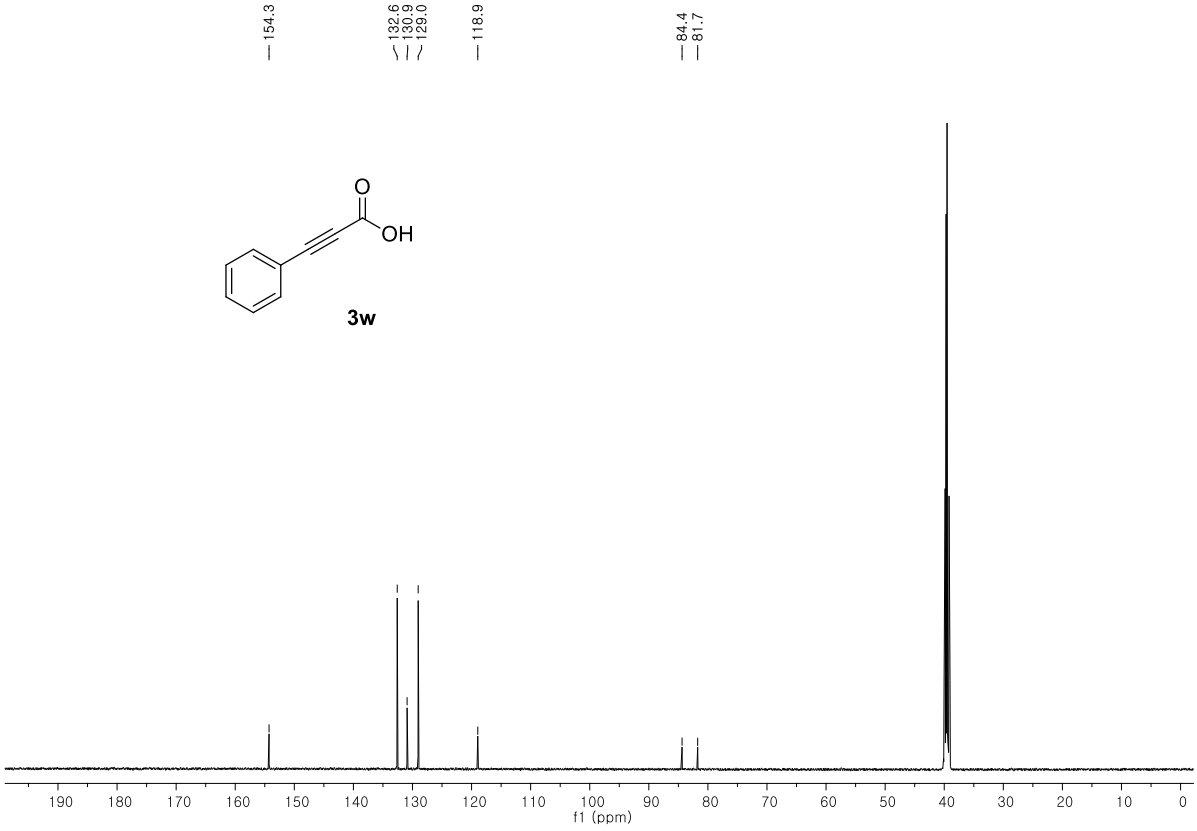

11.78
7.91
7.91
7.90
7.90
7.66
7.66
7.65
7.65
7.16
7.15
7.15
7.14
OH
S
O
3u
1.08
1.00
0.96
1.00
13.5 12.5 11.5 10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

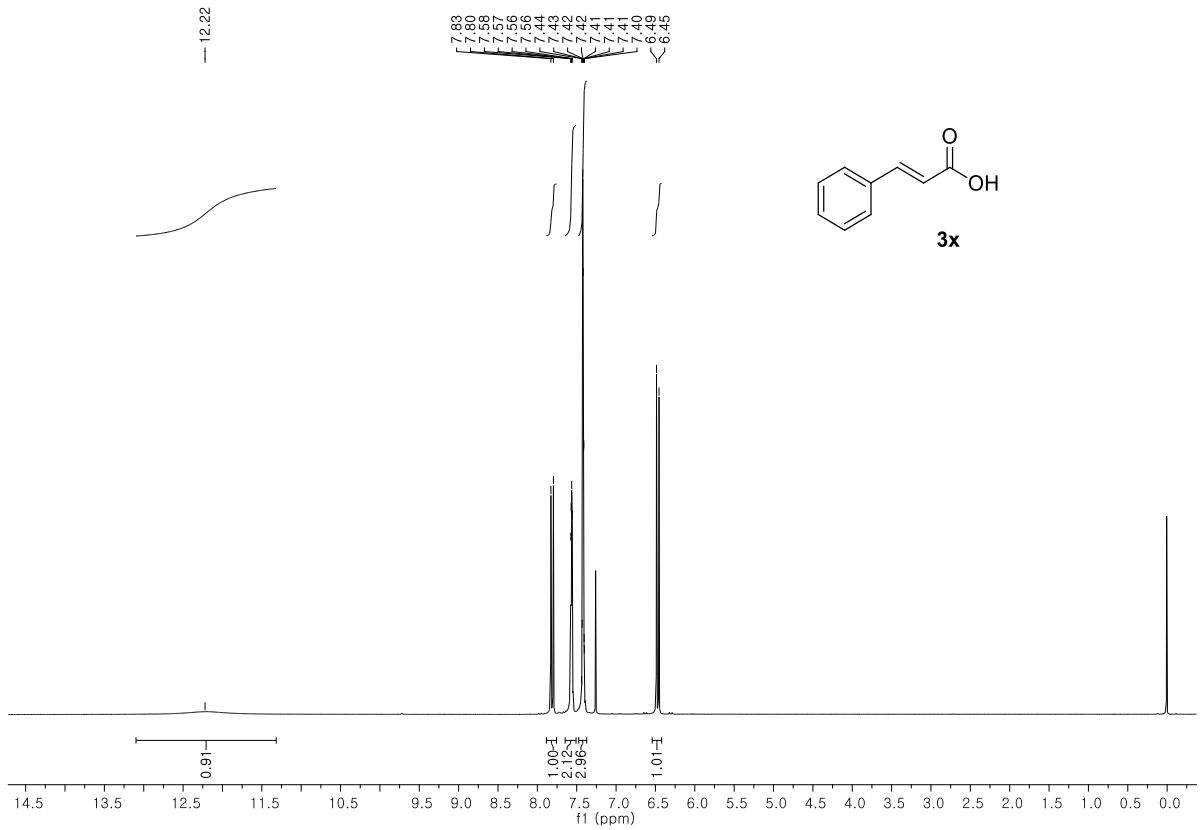

167.7
135.2
134.2
133.0
128.2
OH
S
O
3u
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

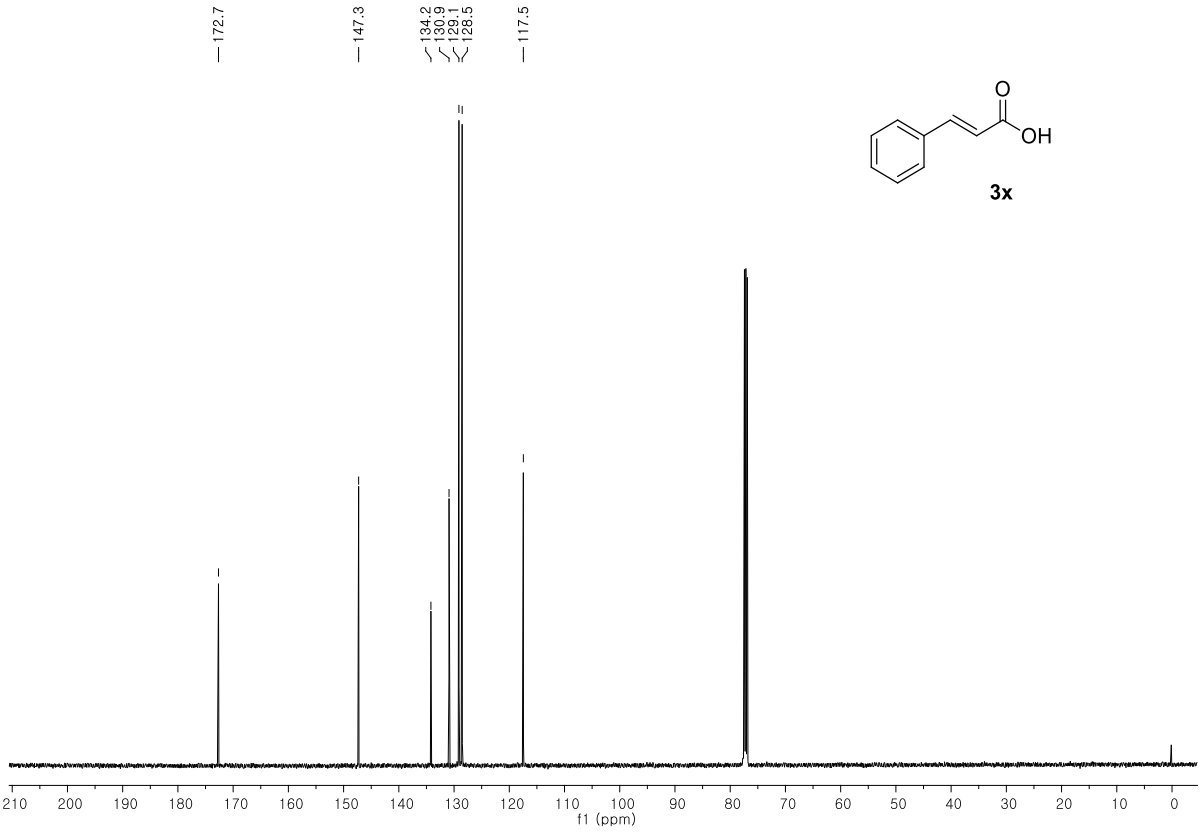

11.60
7.66
7.65
7.35
7.34
6.57
6.57
6.57
6.56
OH
O
O
3v
1.01
1.00
1.03
1.03
13.5 12.5 11.5 10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

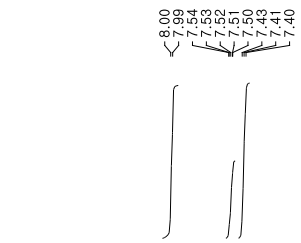

163.7
147.6
143.9
120.3
112.5
OH
O
O
3v
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

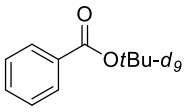

13.81
7.64
7.62
7.57
7.56
7.55
7.54
7.49
7.48
7.46
O
OH
3w
1.00
2.00
1.00
1.96
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0
f1 (ppm)


154.3
132.6
130.9
129.0
118.9
84.4
81.7
O
OH
3w
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

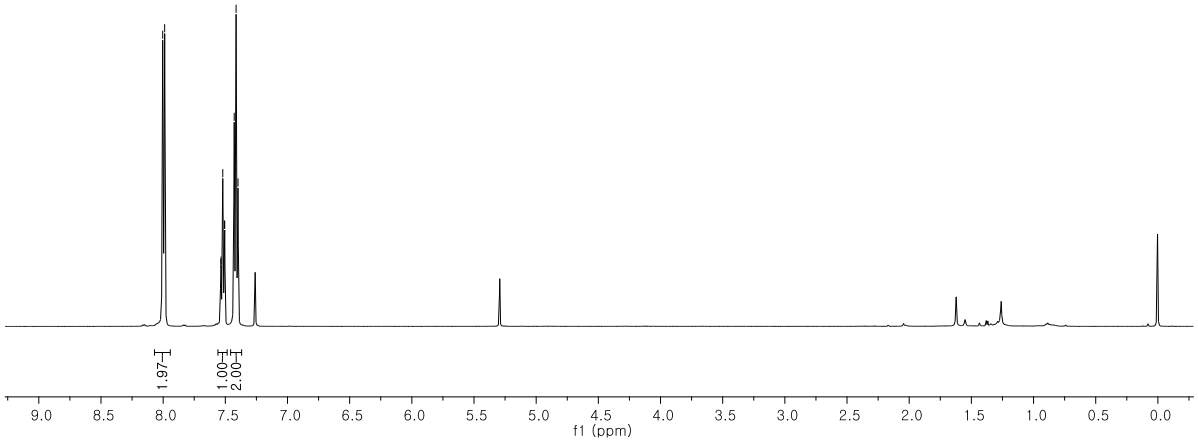

12.22
7.83
7.80
7.58
7.57
7.56
7.56
7.44
7.43
7.42
7.42
7.41
7.41
7.41
7.40
6.49
6.45
O
OH
3x
0.91
1.00
2.12
2.96
1.01
f1 (ppm)


172.7
147.3
134.2
130.9
129.1
128.5
117.5
O
OH
3x
f1 (ppm)

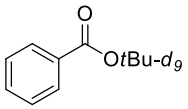

8.00
7.99
7.54
7.53
7.52
7.51
7.50
7.43
7.41
7.40


O
OtBu-d9

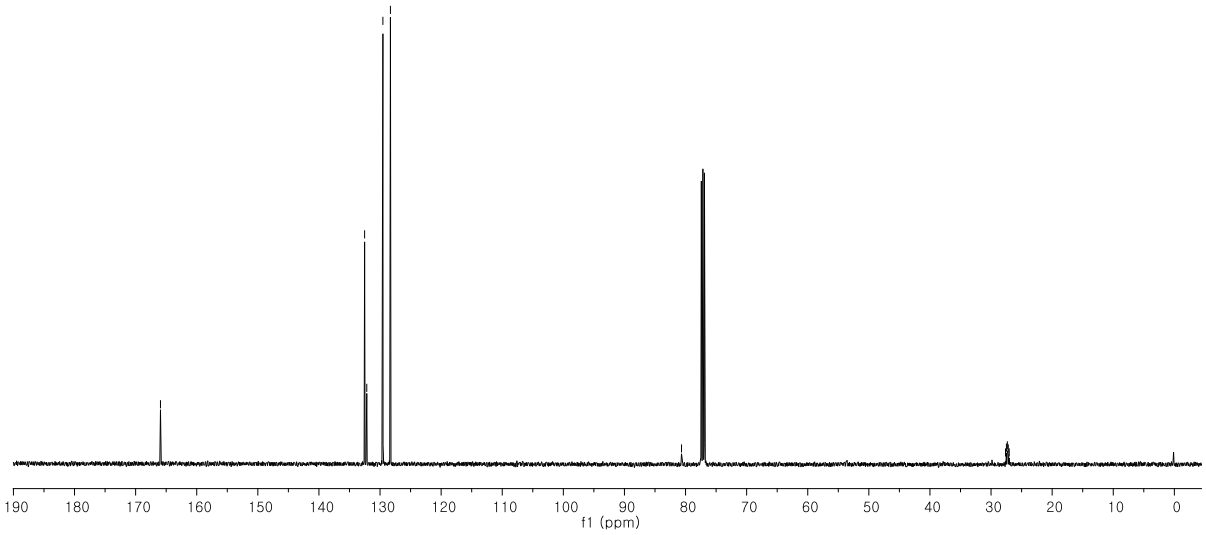
6

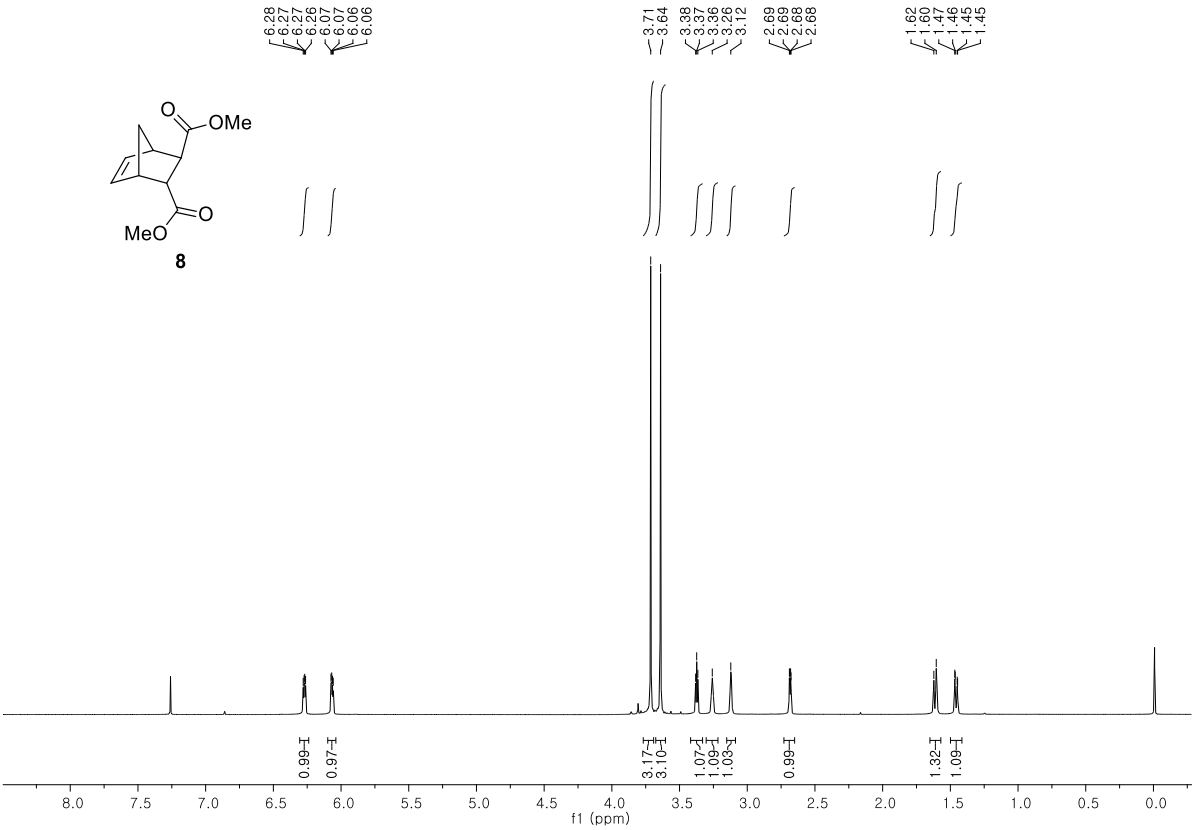

1.97
1.00
2.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


165.9
132.5
132.2
129.5
128.3
80.7
27.6
27.5
27.3
27.2
27.0

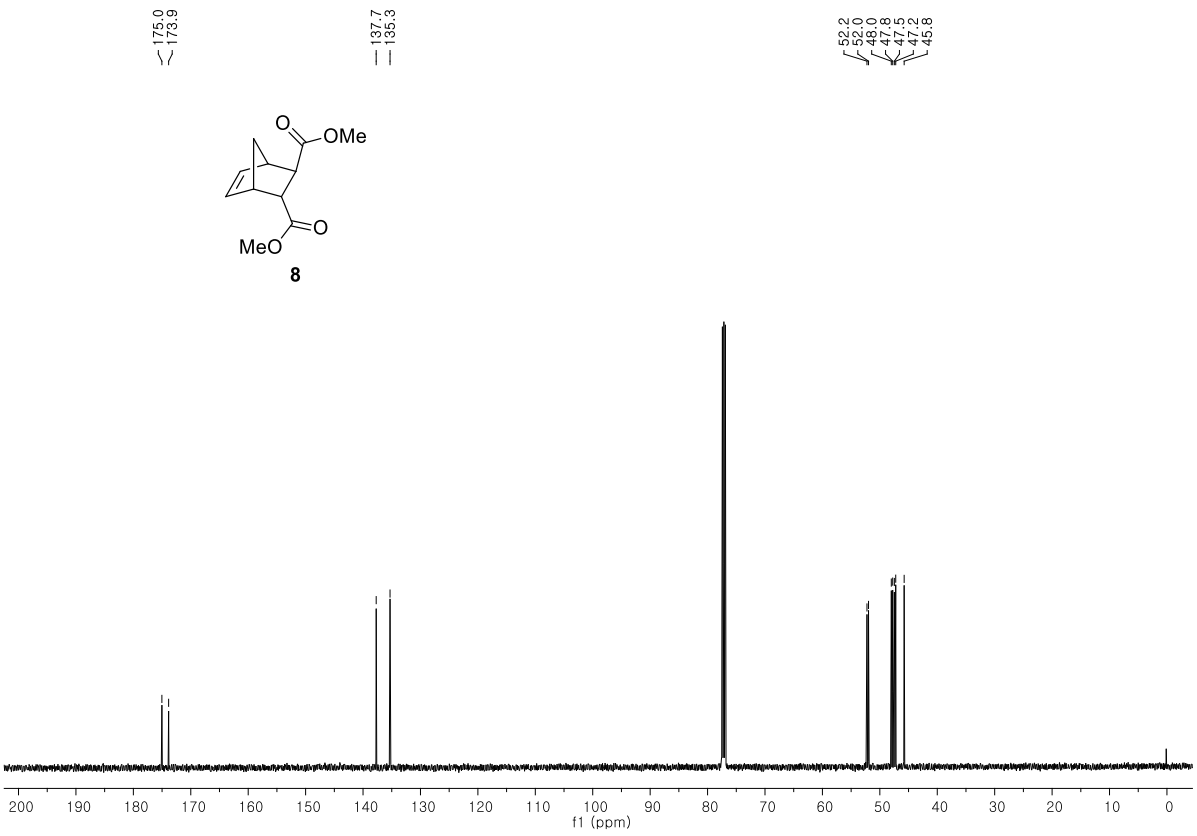

O
OtBu-d9

6


190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

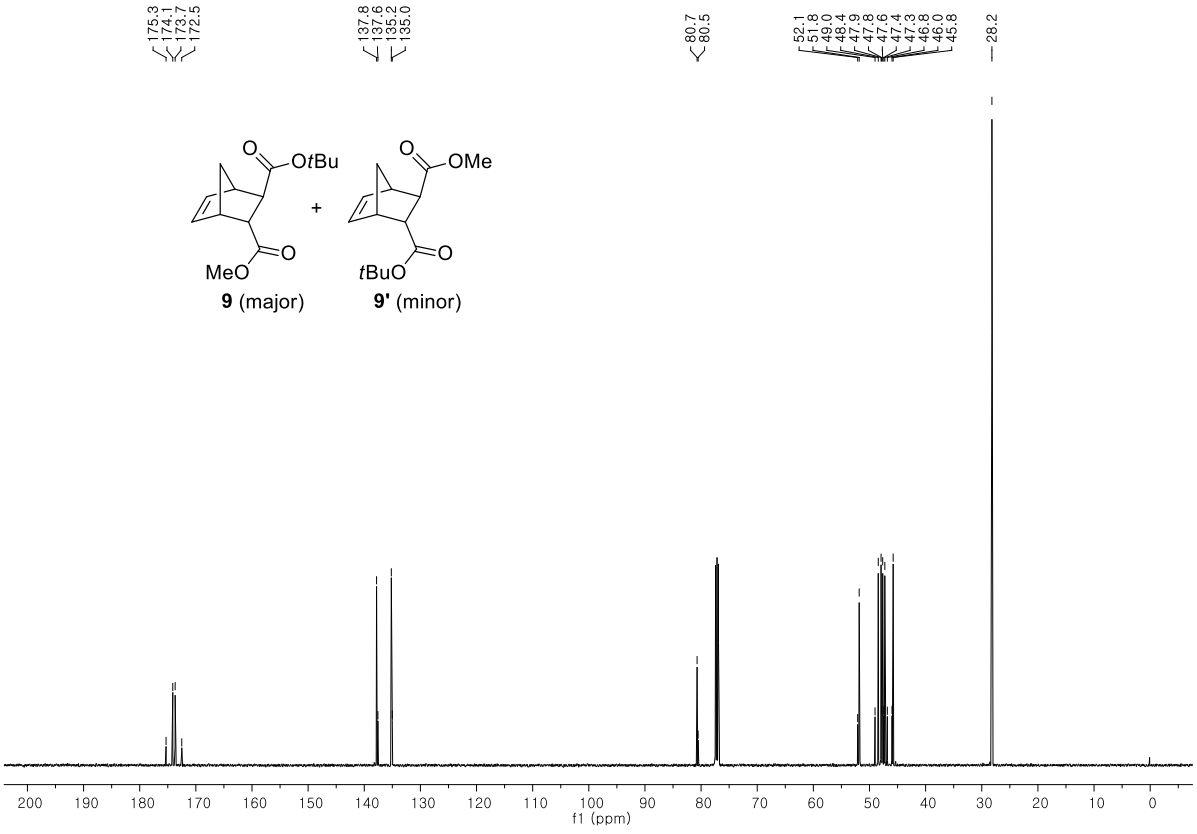

6.28
6.27
6.27
6.26
6.07
6.06
6.06
3.71
3.64
3.38
3.37
3.36
3.26
3.12
2.69
2.69
2.68
2.68
1.62
1.60
1.47
1.46
1.45
1.45
O
OMe
O
MeO
0.99
0.97
3.17
3.10
1.07
1.09
1.03
0.99
1.32
1.09
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

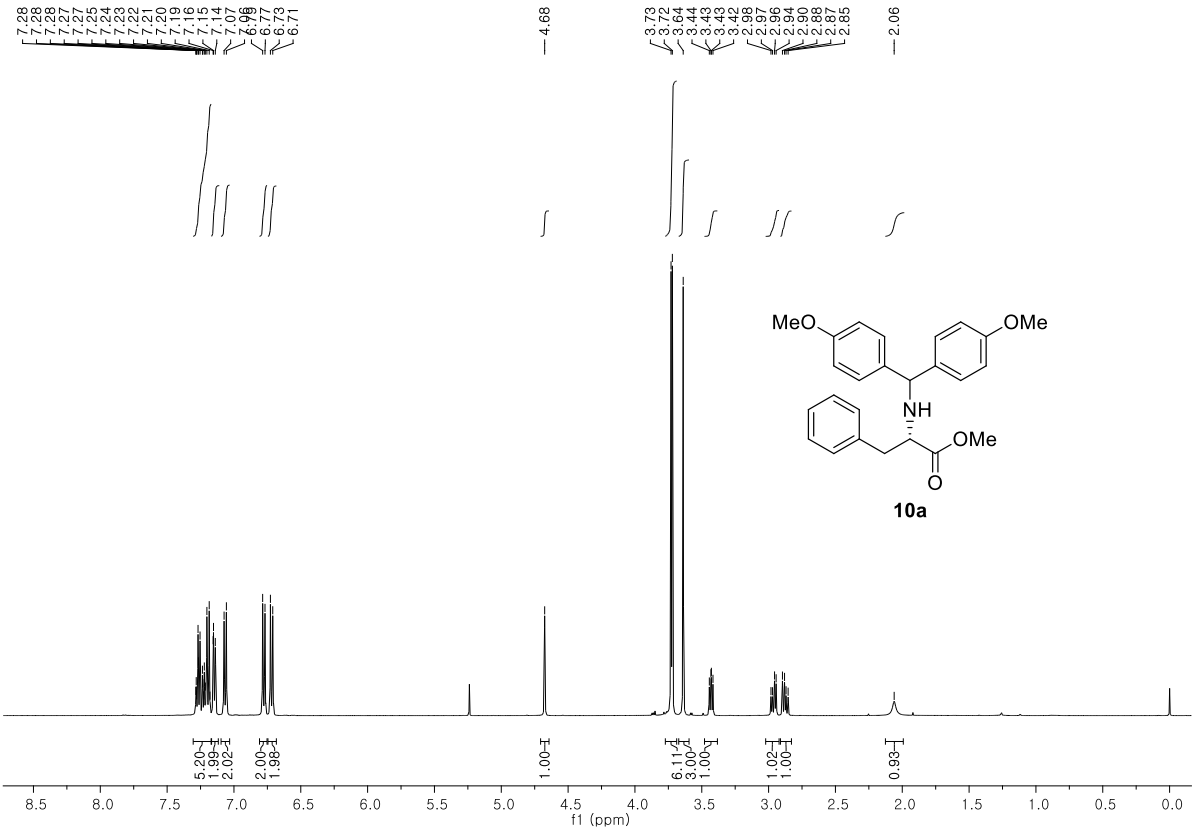
8

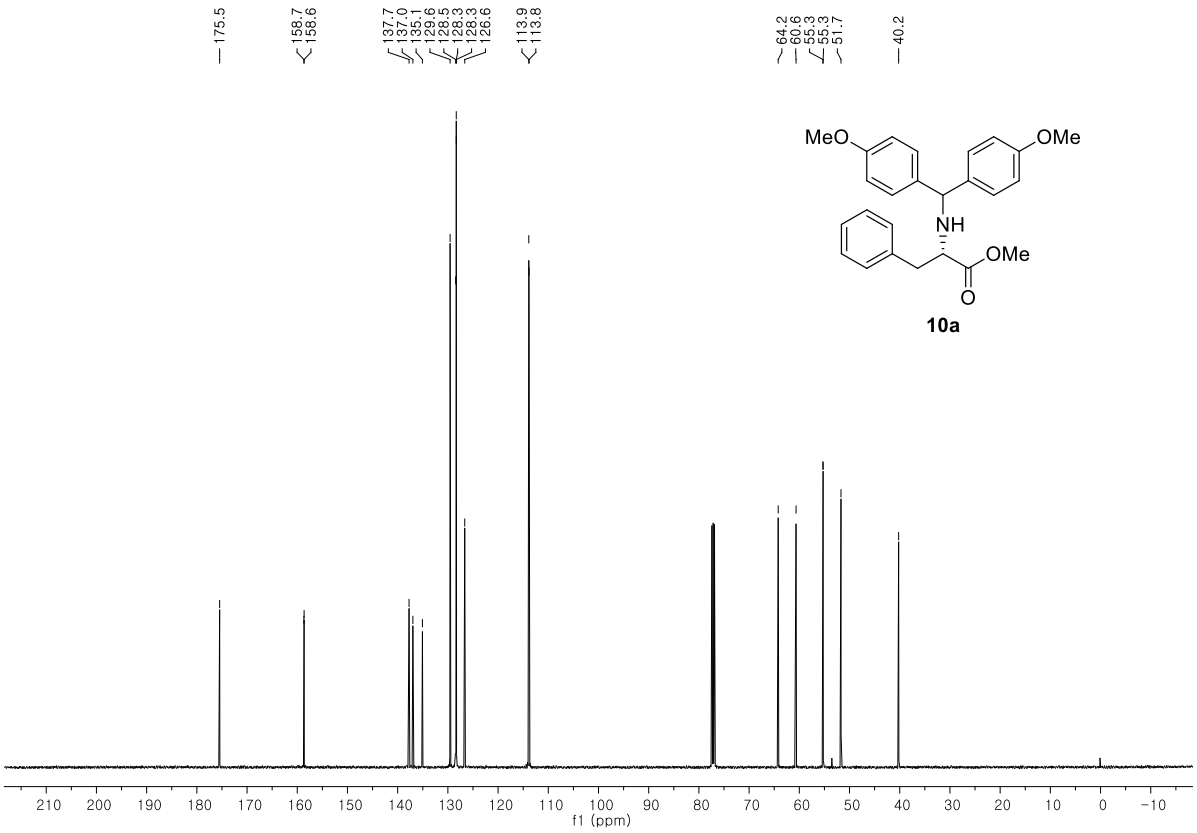

175.0
173.9
137.7
135.3
52.2
52.0
48.0
47.8
47.5
47.2
45.8
O
OMe
O
MeO
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

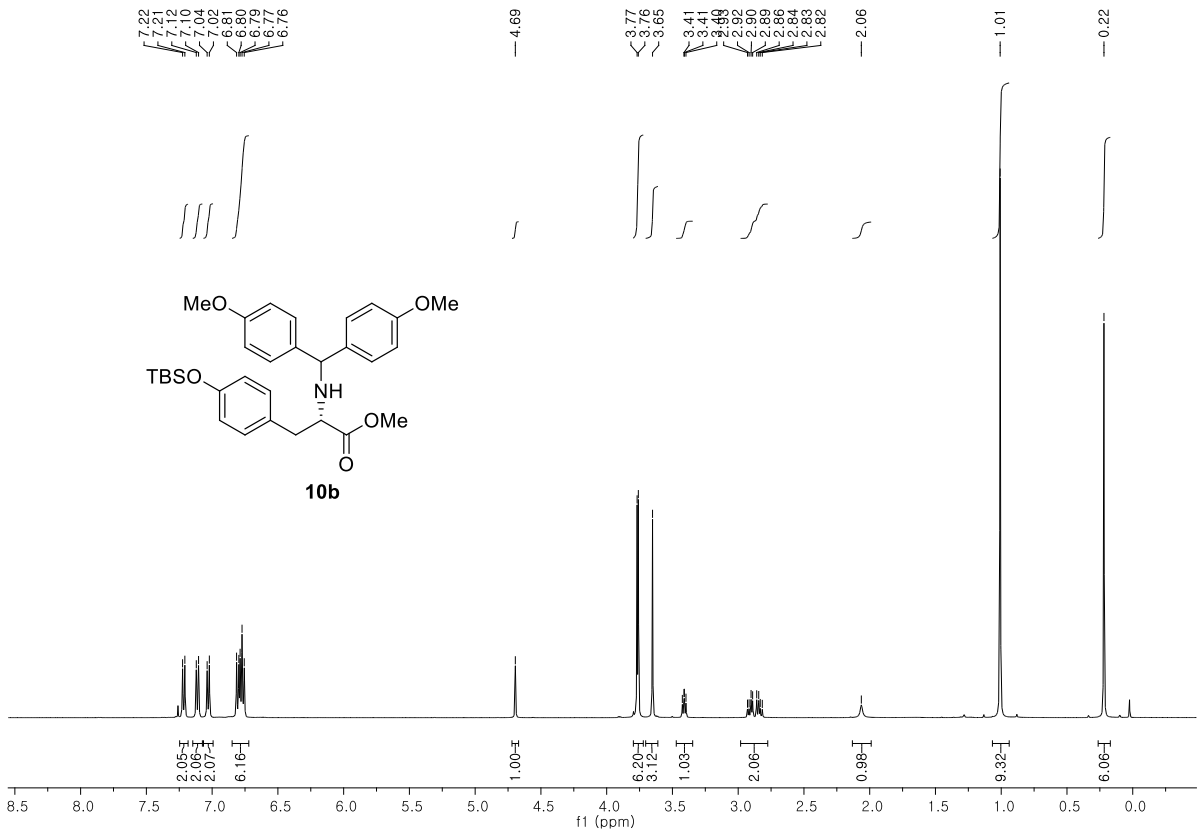
8

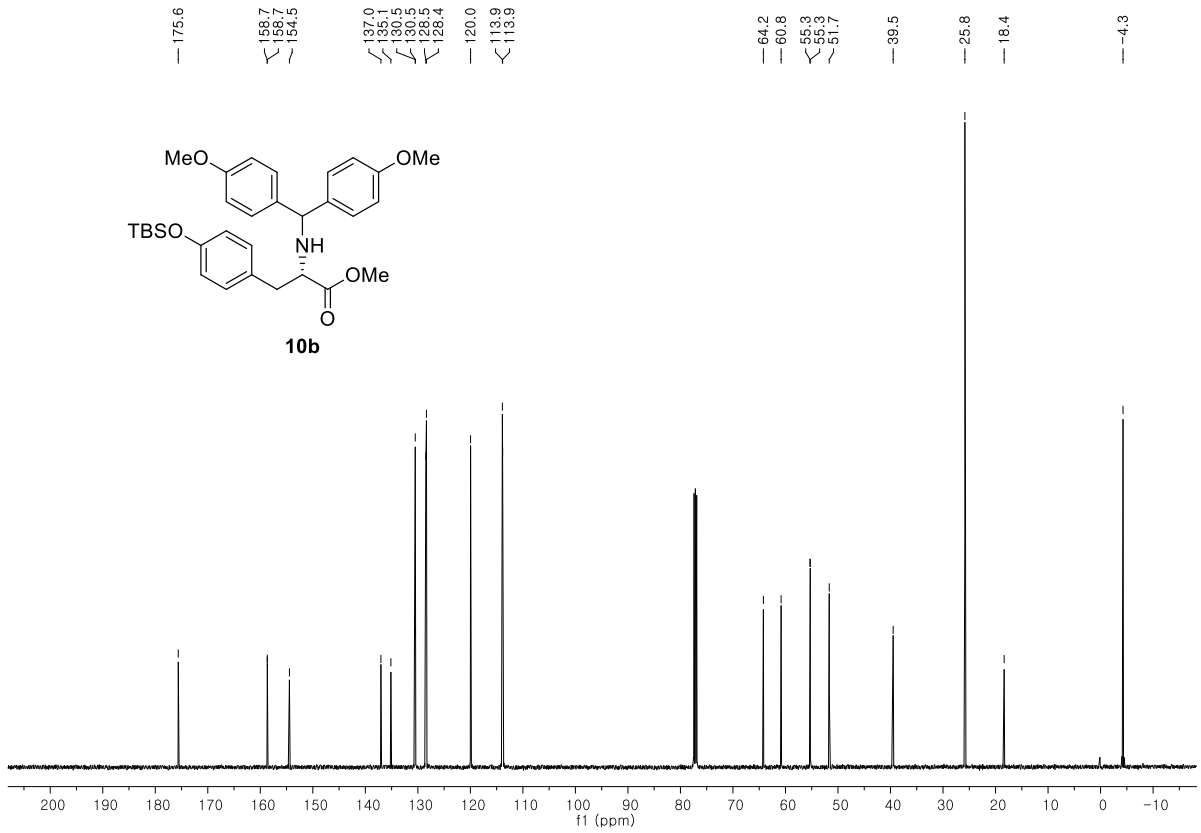

6.27
6.26
6.26
6.25
6.06
6.05
6.04
6.04
6.03
6.03
3.69
3.62
3.33
3.33
3.32
3.21
3.06
3.06
2.64
2.64
2.63
2.58
2.57
2.56
1.58
1.56
1.44
1.40
OtBu
MeO
O
O
+
OMe
tBuO
O
O
9 (major)
9' (minor)
1.24
1.22
0.72
3.00
0.99
0.25
1.26
1.28
0.23
0.96
1.26
9.19
3.97
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

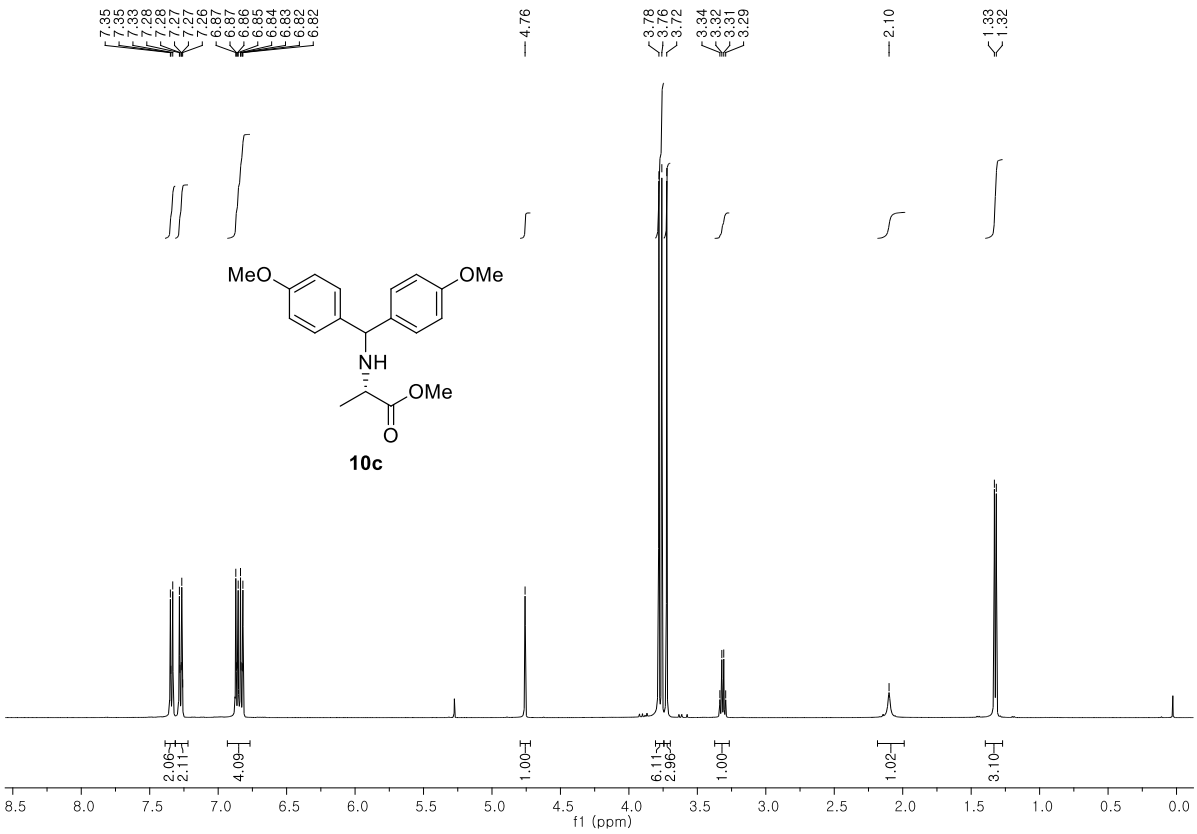

175.3
174.1
173.7
172.5
137.8
137.6
135.2
135.0
80.7
80.5
52.1
51.8
49.0
48.4
47.9
47.8
47.6
47.4
47.3
46.8
46.0
45.8
28.2
OtBu
MeO
O
O
+
OMe
tBuO
O
O
9 (major)
9' (minor)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

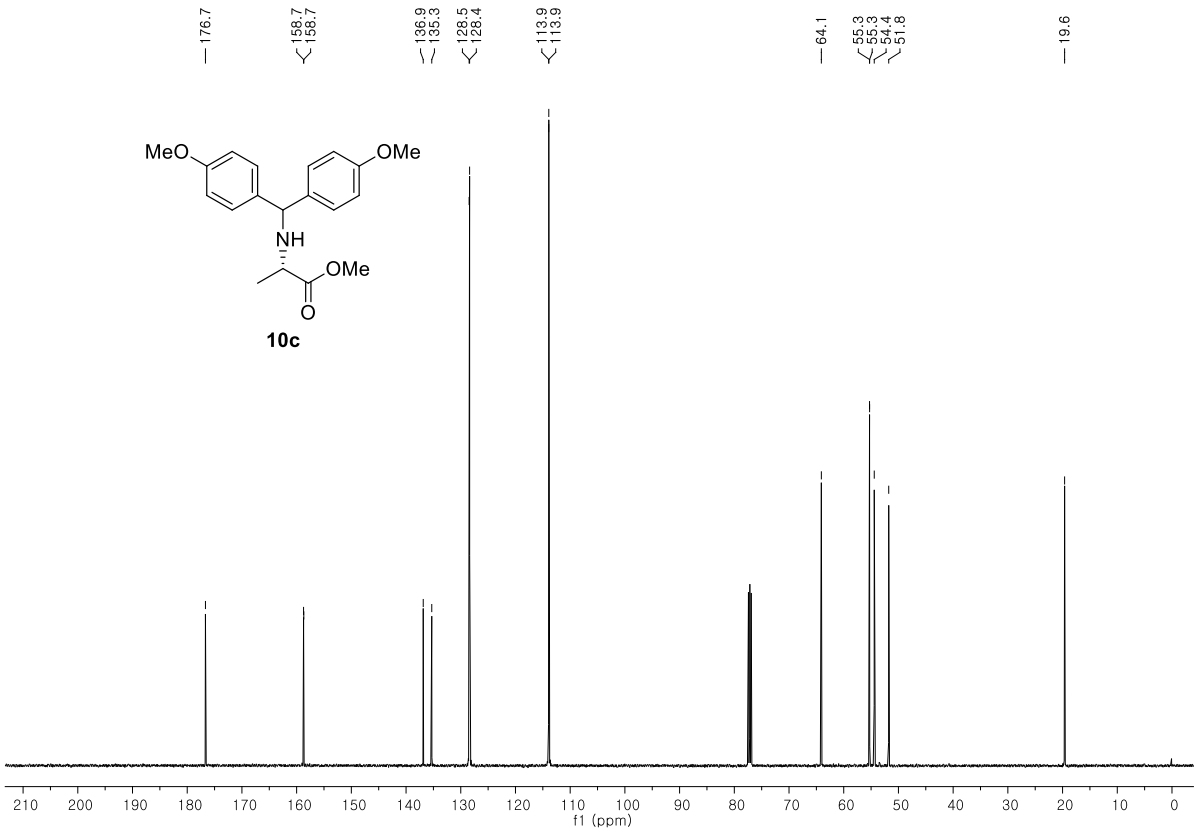

7.28
7.28
7.28
7.27
7.27
7.25
7.24
7.23
7.22
7.21
7.20
7.19
7.16
7.15
7.14
7.07
6.79
6.77
6.73
6.71
4.68
3.73
3.72
3.64
3.44
3.43
3.43
3.42
2.98
2.97
2.96
2.94
2.90
2.88
2.87
2.85
2.06
MeO
OMe
NH
OMe
O
10a
5.20
1.99
2.02
2.00
1.98
1.00
6.11
3.00
1.00
1.02
1.00
0.93
f1 (ppm)

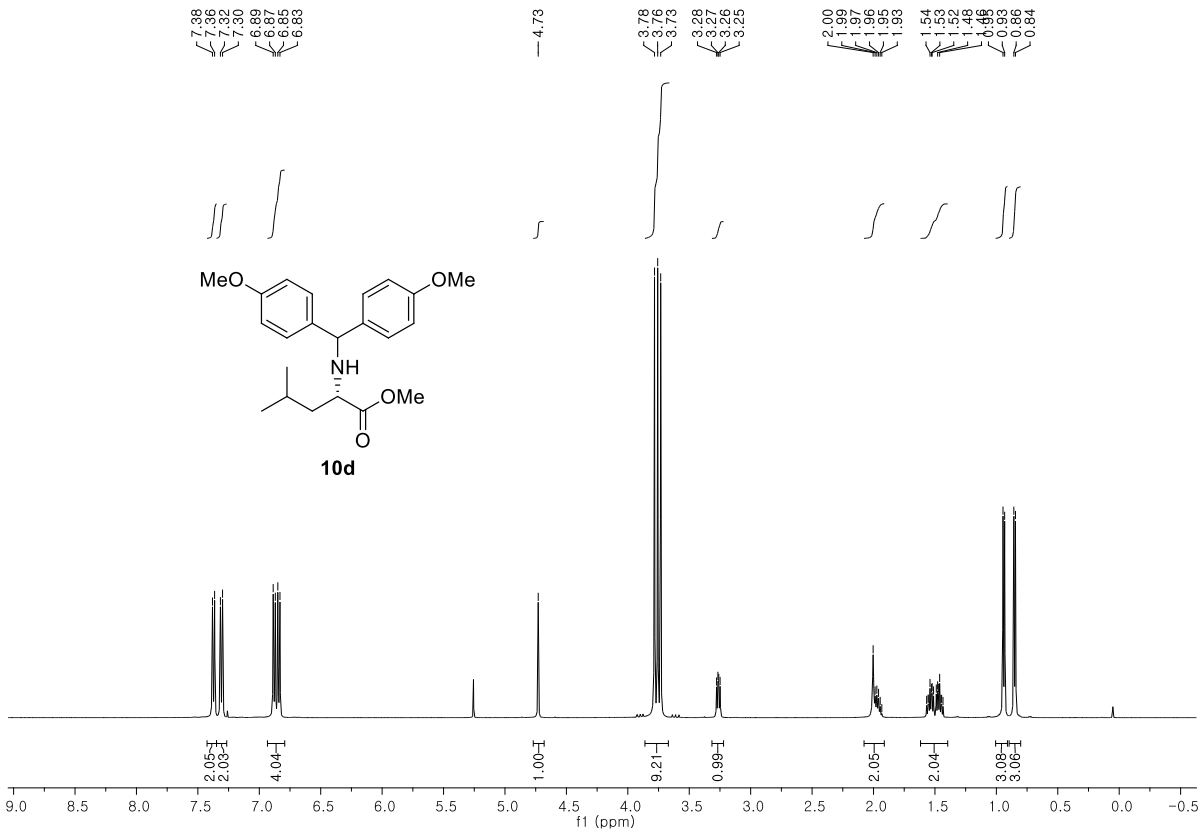

175.5
158.7
158.6
137.7
137.0
135.1
129.6
128.5
128.3
128.3
126.6
113.9
113.8
64.2
60.6
55.3
55.3
51.7
40.2
MeO
OMe
NH
OMe
O
10a
f1 (ppm)

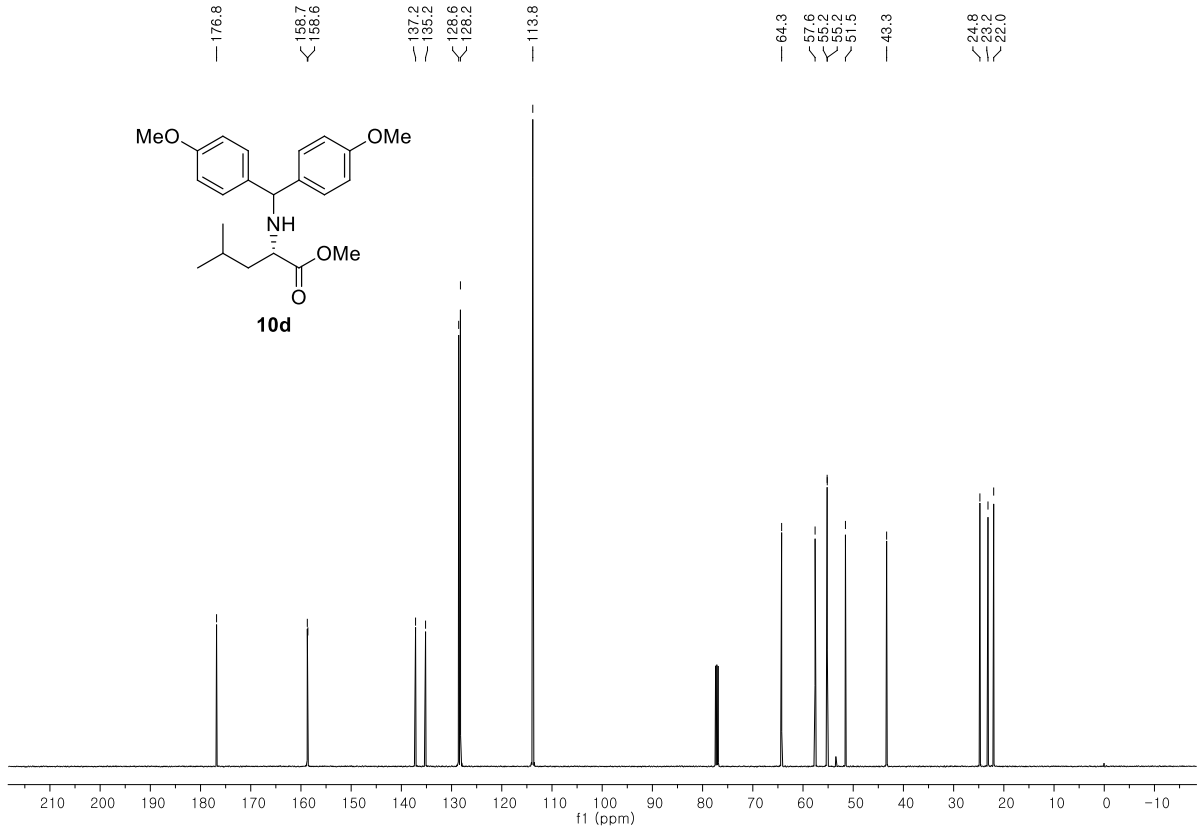

7.22
7.21
7.12
7.10
7.04
7.02
6.81
6.80
6.79
6.77
6.76
4.69
3.77
3.76
3.65
3.41
3.41
2.92
2.90
2.89
2.86
2.84
2.83
2.82
2.06
1.01
0.22
MeO
OMe
TBSO
NH
OMe
O
10b
2.05
2.06
2.07
6.16
1.00
6.20
3.12
1.03
2.06
0.98
9.32
6.06
f1 (ppm)

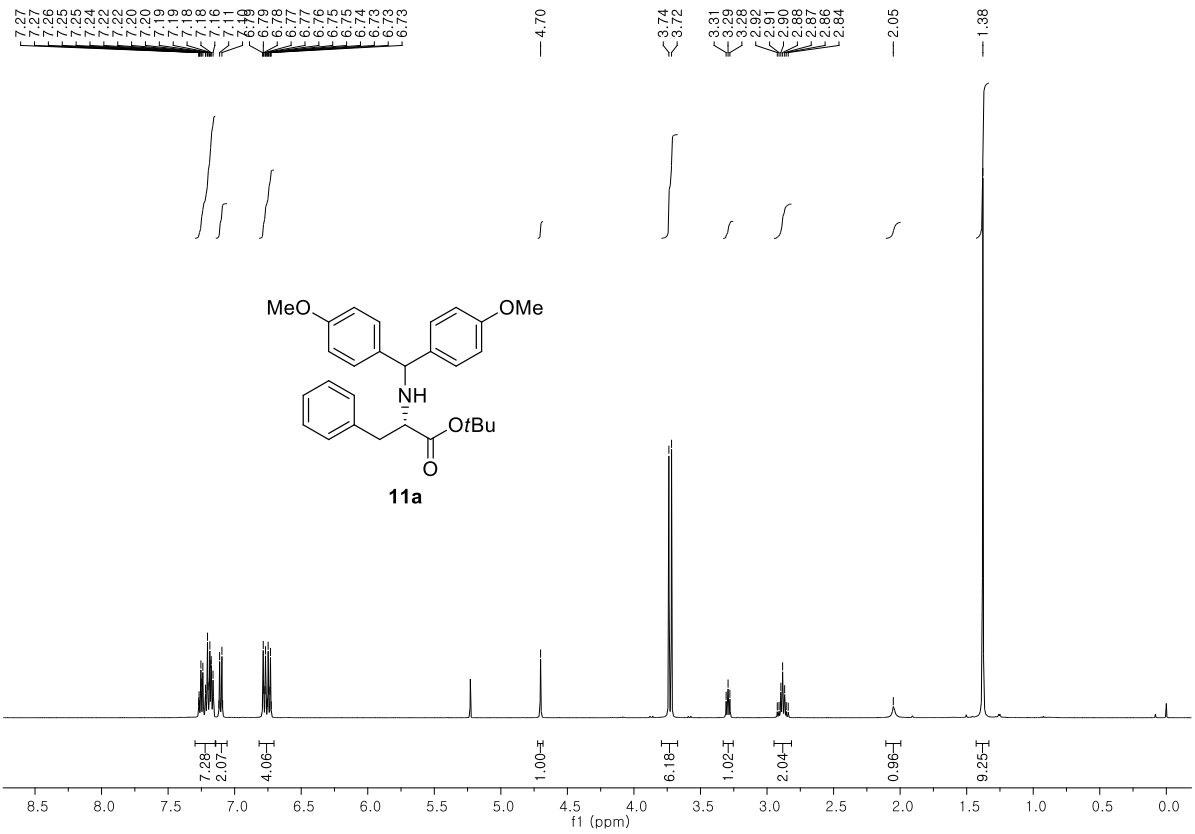

175.6
158.7
158.7
154.5
137.0
135.1
130.5
130.5
128.5
128.4
120.0
113.9
113.9
64.2
60.8
55.3
55.3
51.7
39.5
25.8
18.4
-4.3
MeO
OMe
TBSO
NH
OMe
O
10b
f1 (ppm)

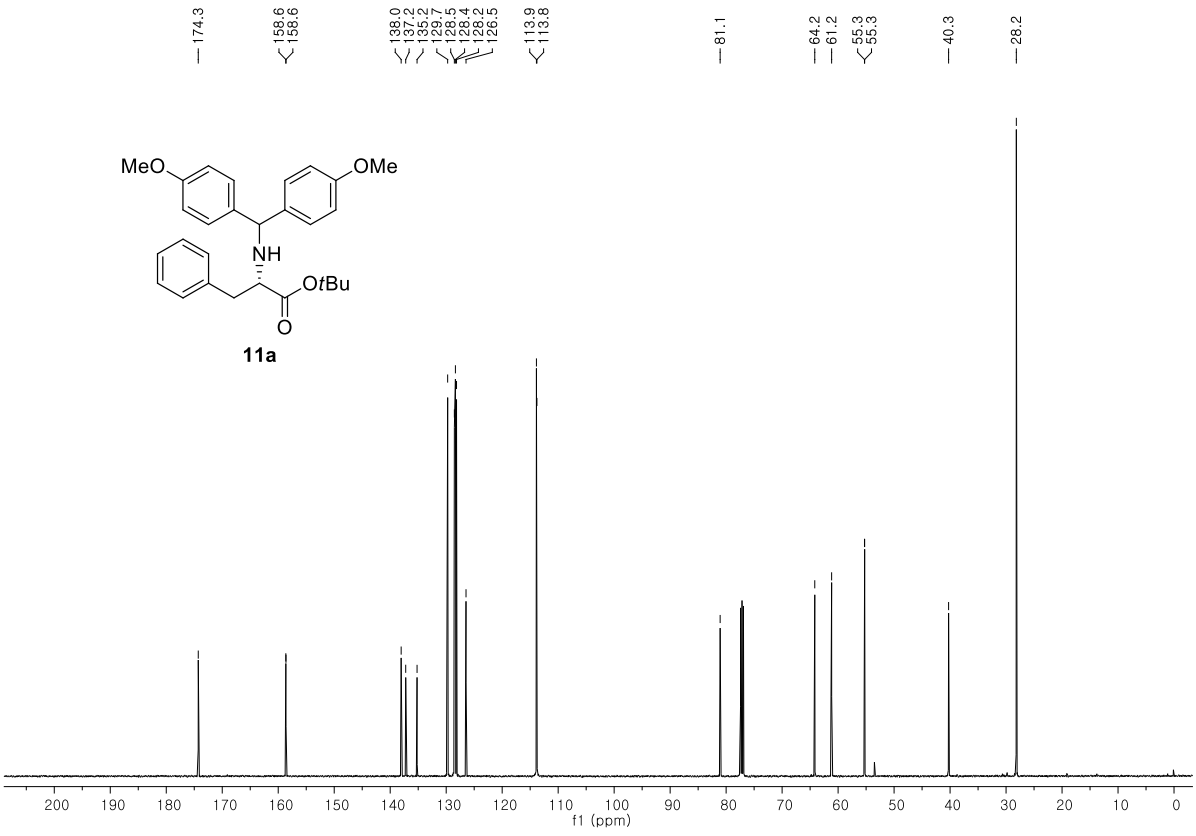

7.35
7.35
7.33
7.28
7.28
7.27
7.27
7.26
6.87
6.86
6.85
6.84
6.83
6.82
6.82
4.76
3.78
3.76
3.72
3.34
3.32
3.31
3.29
2.10
1.33
1.32
MeO
OMe
NH
OMe
O
10c
2.06
2.11
4.09
1.00
6.11
2.96
1.00
1.02
3.10
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

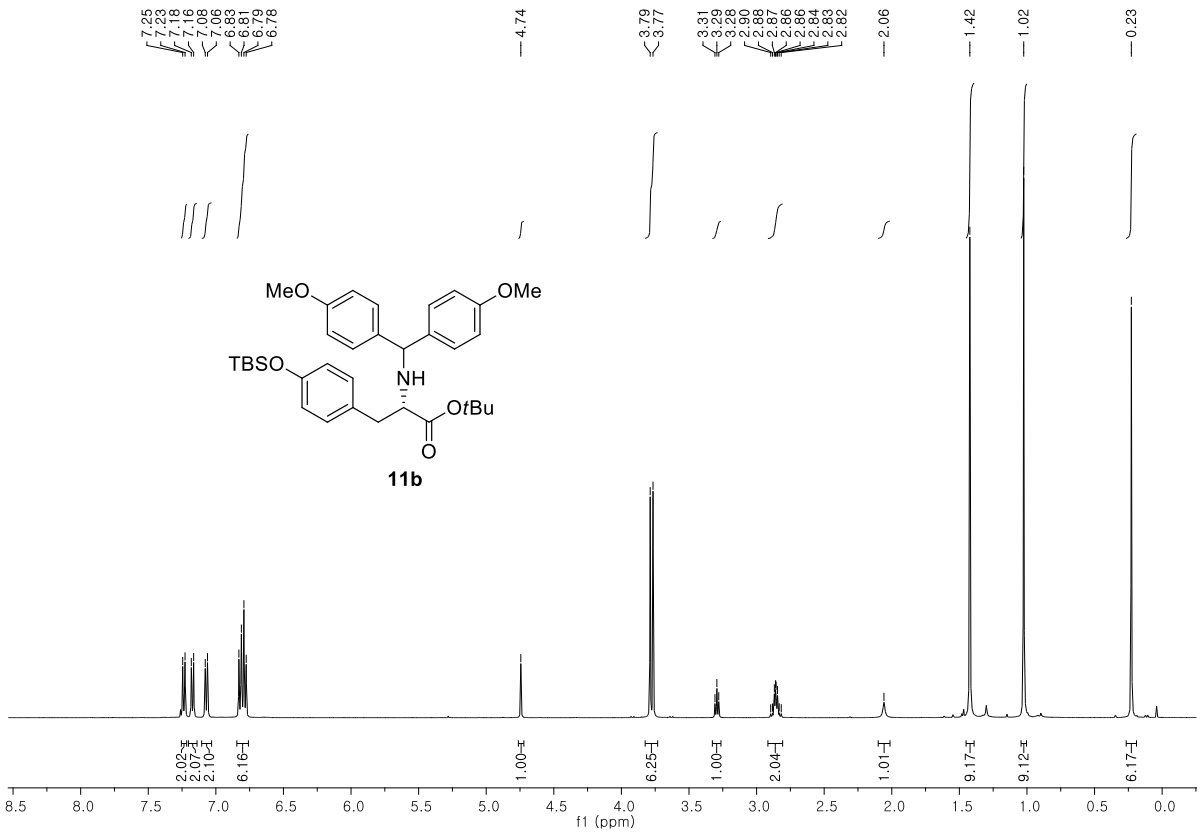

176.7
158.7
158.7
136.9
135.3
128.5
128.4
113.9
113.9
64.1
55.3
55.3
54.4
51.8
19.6
MeO
OMe
NH
OMe
O
10c
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

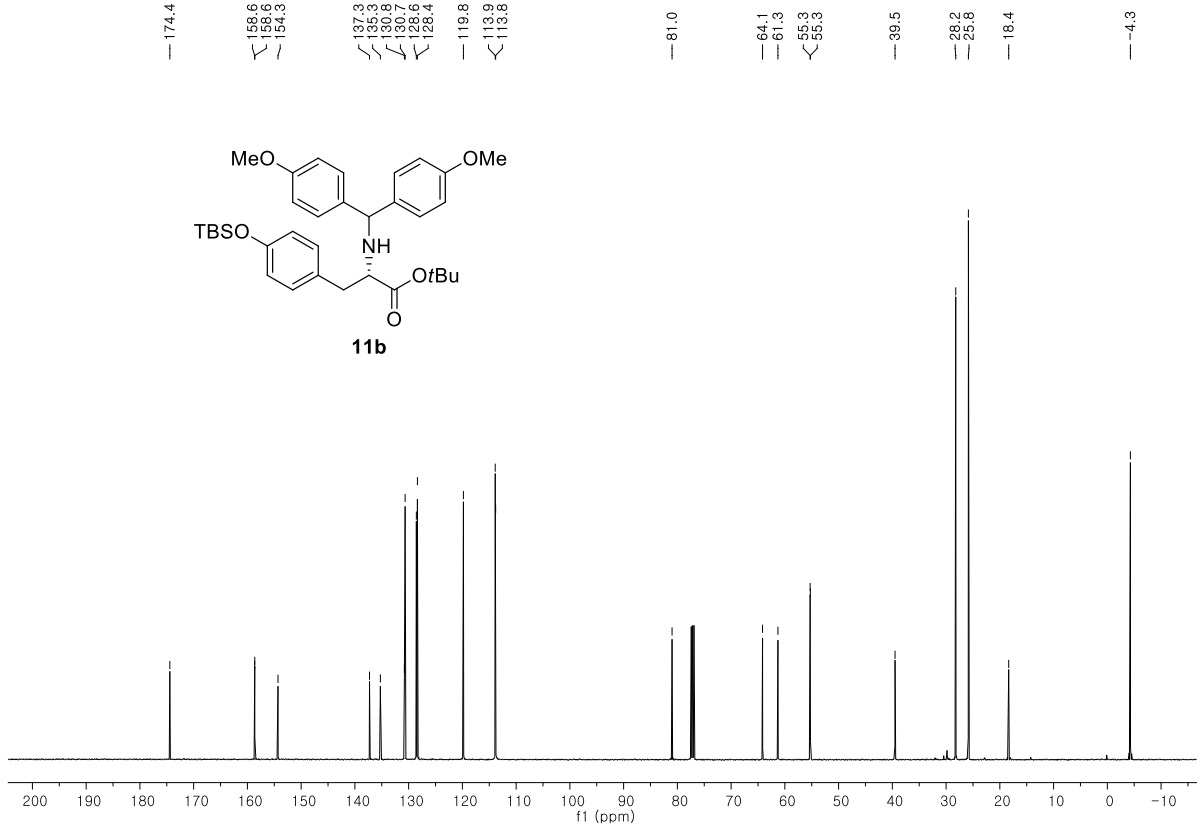

7.38
7.36
7.32
7.30
6.89
6.87
6.85
6.83
4.73
3.78
3.76
3.73
3.28
3.27
3.26
3.25
2.00
1.99
1.97
1.96
1.95
1.93
1.54
1.53
1.52
1.48
0.93
0.86
0.84
MeO
OMe
NH
OMe
O
10d
2.05
2.03
4.04
1.00
9.21
0.99
2.05
2.04
3.08
3.06
f1 (ppm)

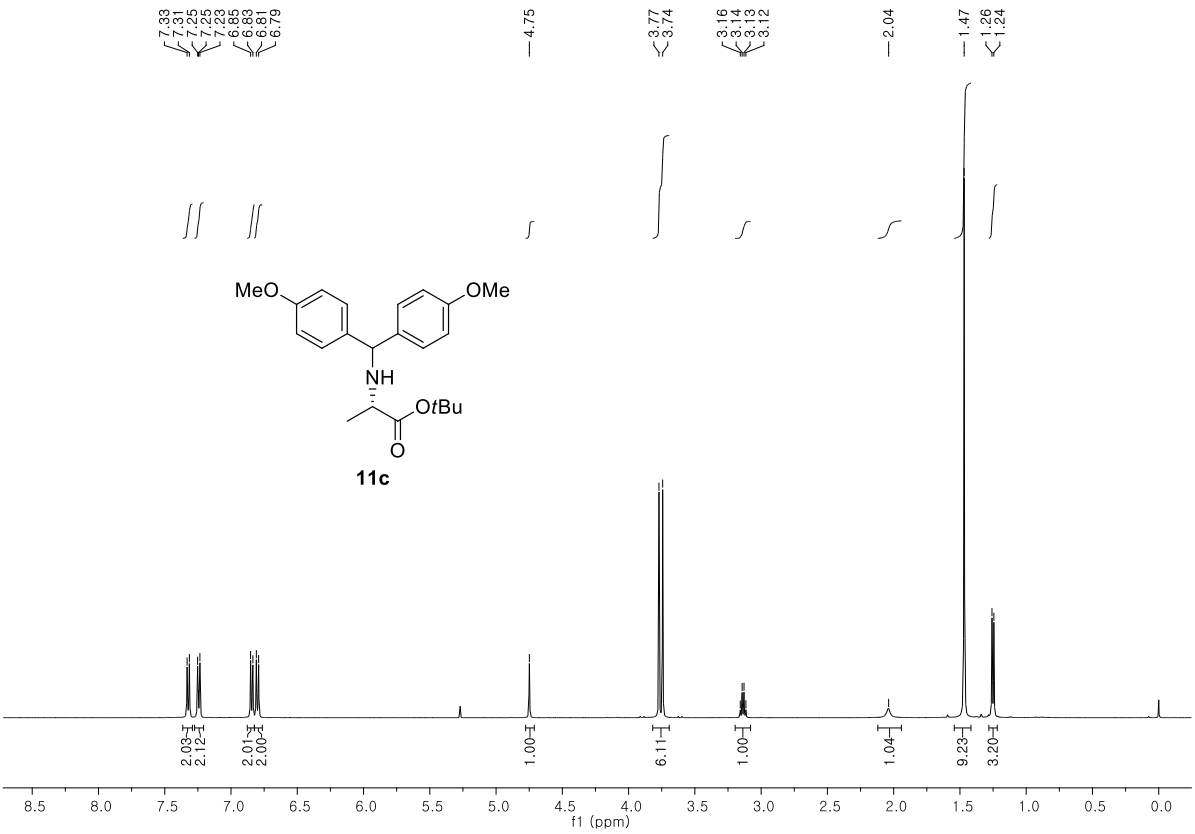

176.8
158.7
158.6
137.2
135.2
128.6
128.2
113.8
64.3
57.6
55.2
55.2
51.5
43.3
24.8
23.2
22.0
MeO
OMe
NH
OMe
O
10d
f1 (ppm)

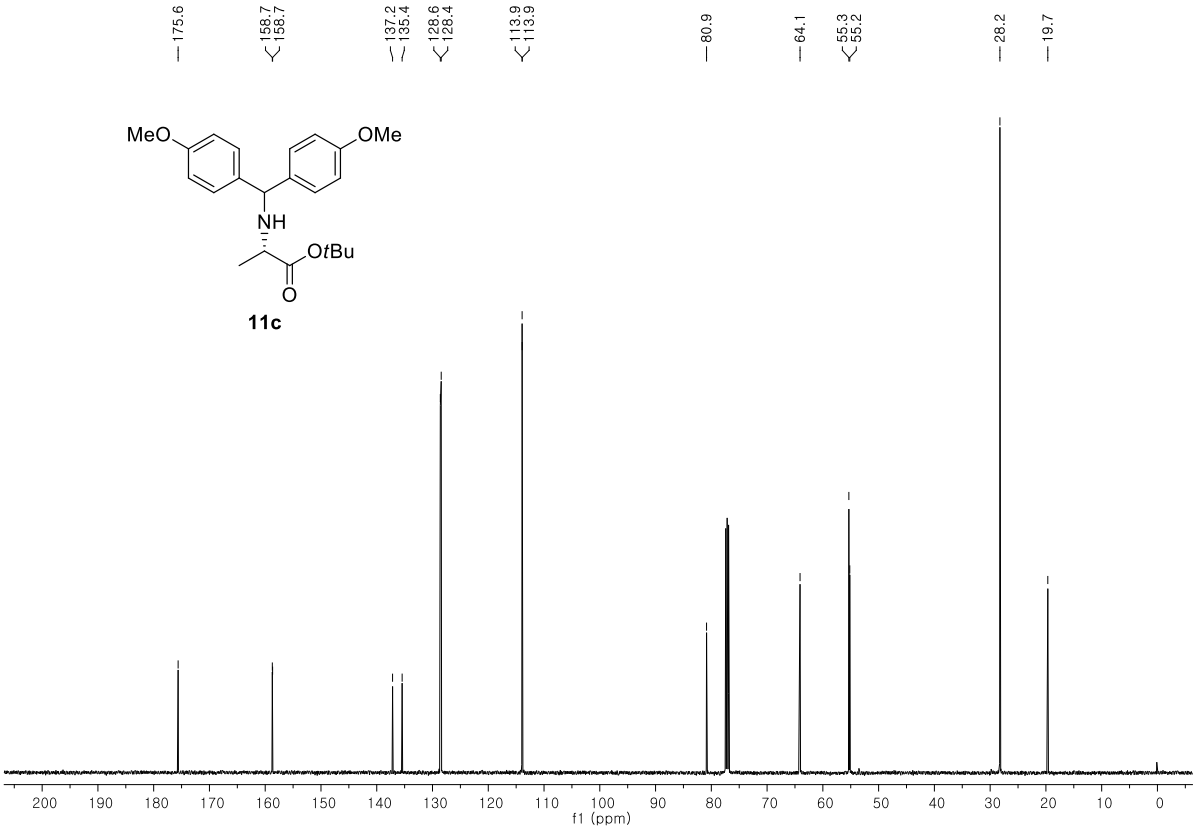

MeO
OMe
NH
OtBu
O
11a
f1 (ppm)

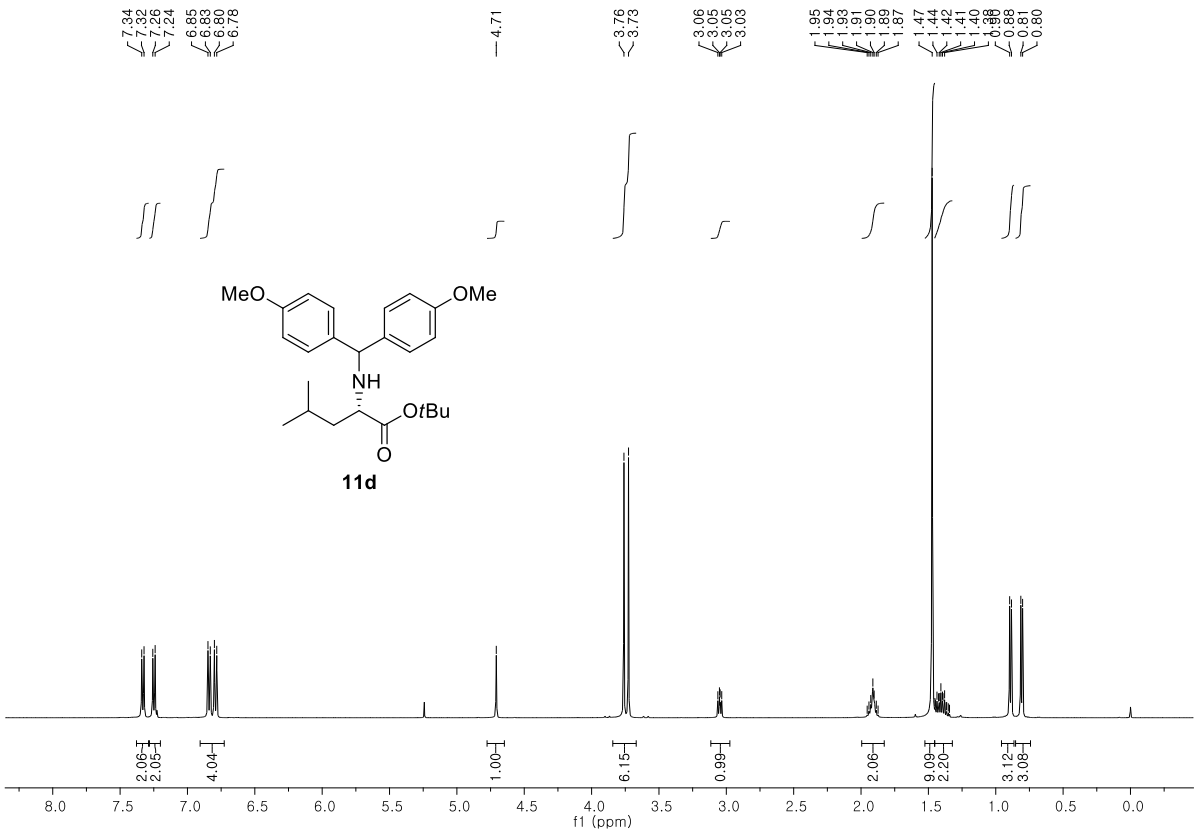

MeO
OMe
NH
OtBu
O
11a
f1 (ppm)

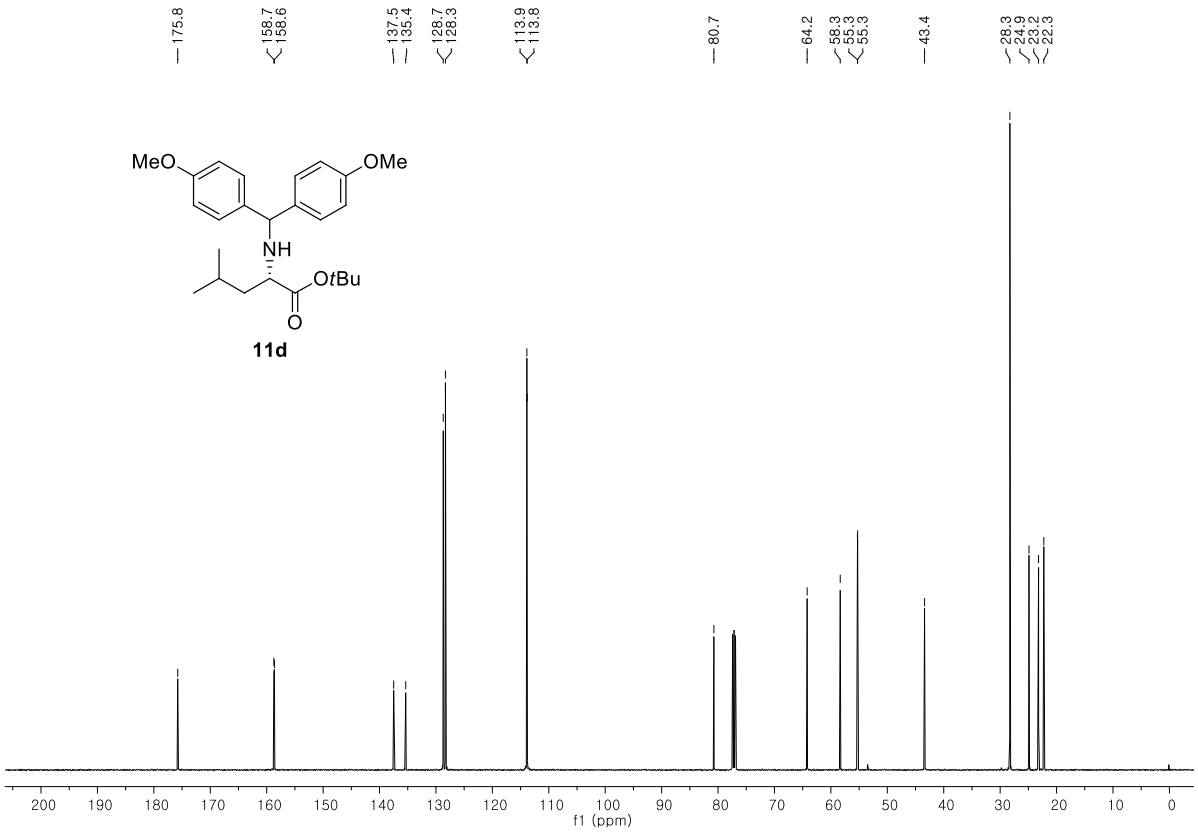

7.25
7.23
7.18
7.16
7.08
7.06
6.83
6.81
6.79
6.78
4.74
3.79
3.77
3.31
3.29
3.28
2.90
2.88
2.87
2.86
2.86
2.84
2.83
2.82
2.06
1.42
1.02
0.23
MeO
OMe
TBSO
NH
OtBu
O
11b
2.02
2.07
2.10
6.16
1.00
6.25
1.00
2.04
1.01
9.17
9.12
6.17
f1 (ppm)

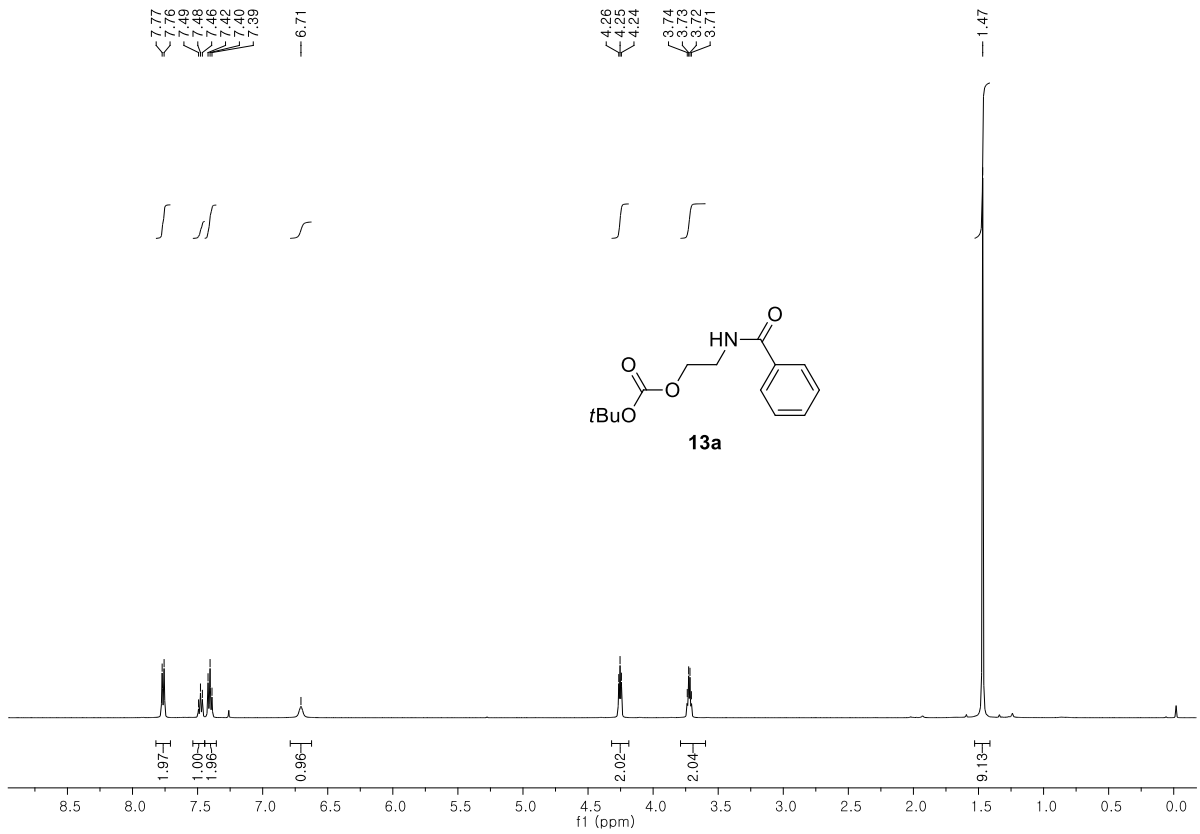

174.4
158.6
158.6
154.3
137.3
135.3
130.8
130.7
128.6
128.4
119.8
113.9
113.8
81.0
64.1
61.3
55.3
55.3
39.5
28.2
25.8
18.4
-4.3
MeO
OMe
TBSO
NH
OtBu
O
11b
f1 (ppm)

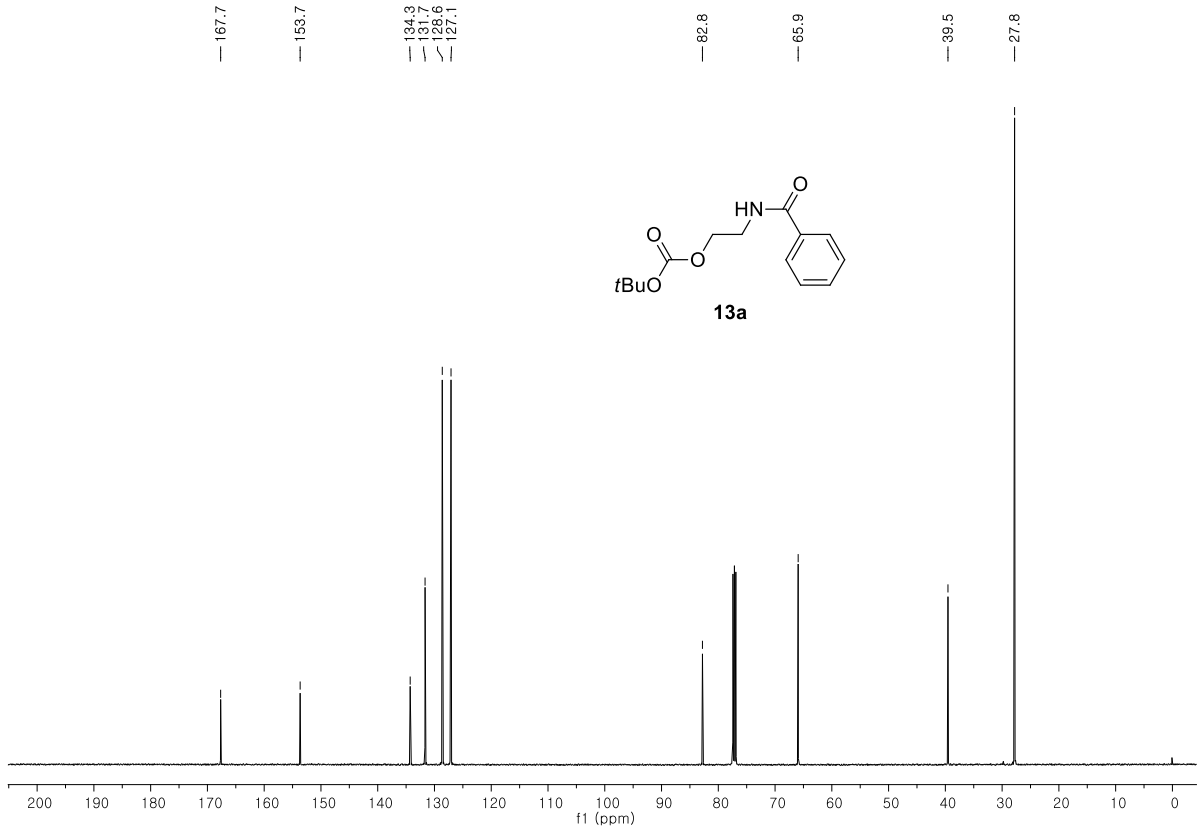

7.33
7.31
7.25
7.25
7.23
6.85
6.83
6.81
6.79
4.75
3.77
3.74
3.16
3.14
3.13
3.12
2.04
1.47
1.26
1.24
MeO
OMe
NH
OtBu
O
11c
2.03
2.12
2.01
2.00
1.00
6.11
1.00
1.04
9.23
3.20
f1 (ppm)

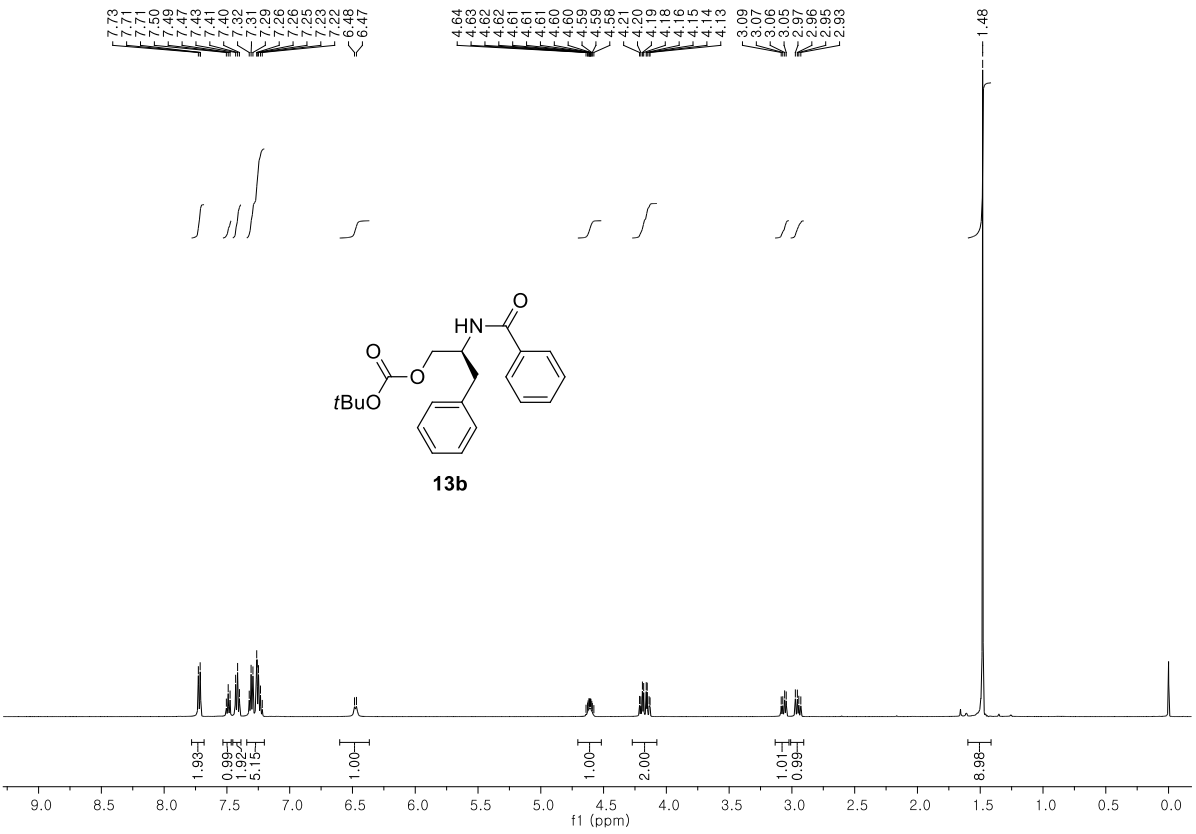

175.6
158.7
158.7
137.2
135.4
128.6
128.4
113.9
113.9
80.9
64.1
55.3
55.2
28.2
19.7
MeO
OMe
NH
OtBu
O
11c
f1 (ppm)


7.34
7.32
7.26
7.24
6.85
6.83
6.80
6.78
4.71
3.76
3.73
3.06
3.05
3.05
3.03
1.95
1.94
1.93
1.91
1.90
1.89
1.87
1.47
1.44
1.42
1.41
1.40
0.88
0.81
0.80
MeO
OMe
NH
OtBu
O
11d
2.06
2.05
4.04
1.00
6.15
0.99
2.06
9.09
2.20
3.12
3.08
f1 (ppm)

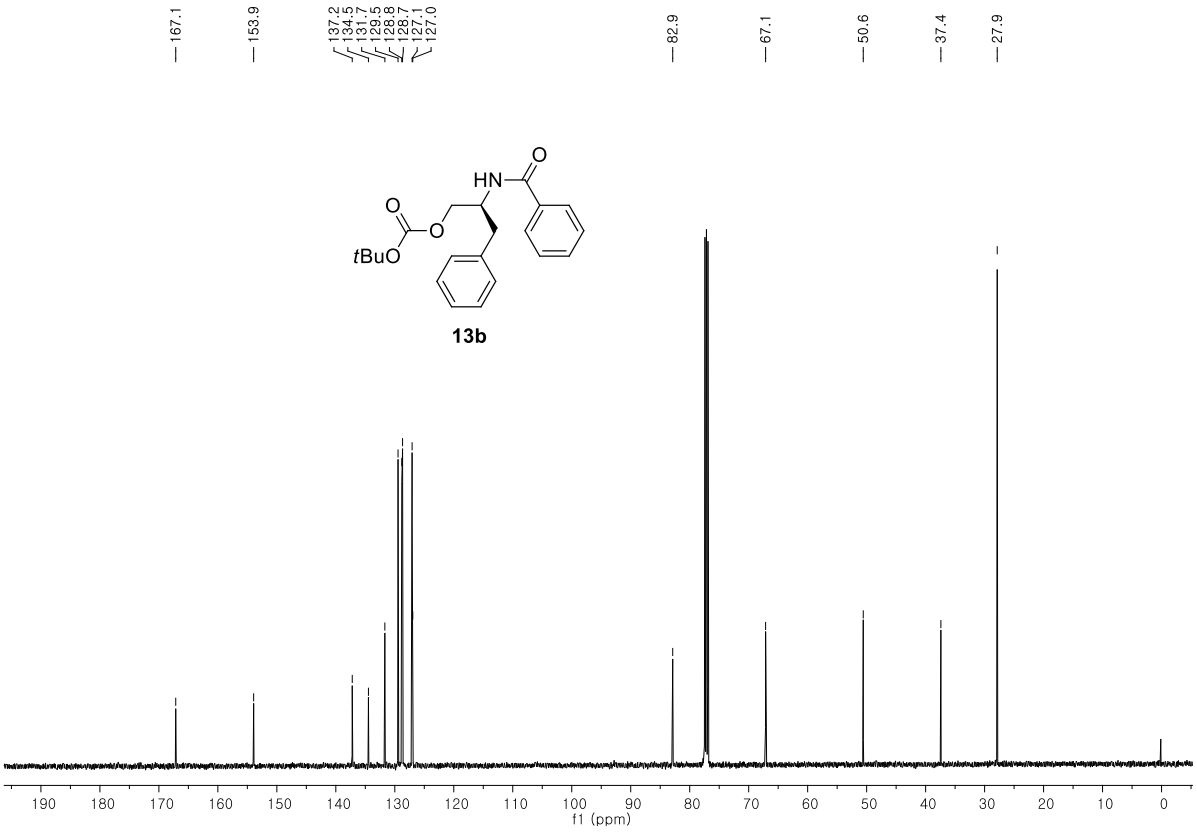

175.8
158.7
158.6
137.5
135.4
128.7
128.3
113.9
113.8
80.7
64.2
58.3
55.3
55.3
43.4
28.3
24.9
23.2
22.3
MeO
OMe
NH
OtBu
O
11d
f1 (ppm)


7.77
7.76
7.49
7.48
7.46
7.42
7.40
7.39
6.71
4.26
4.25
4.24
3.74
3.73
3.72
3.71
1.47
HN
O
O
O
tBuO
13a
1.97
1.00
1.96
0.96
2.02
2.04
9.13
f1 (ppm)

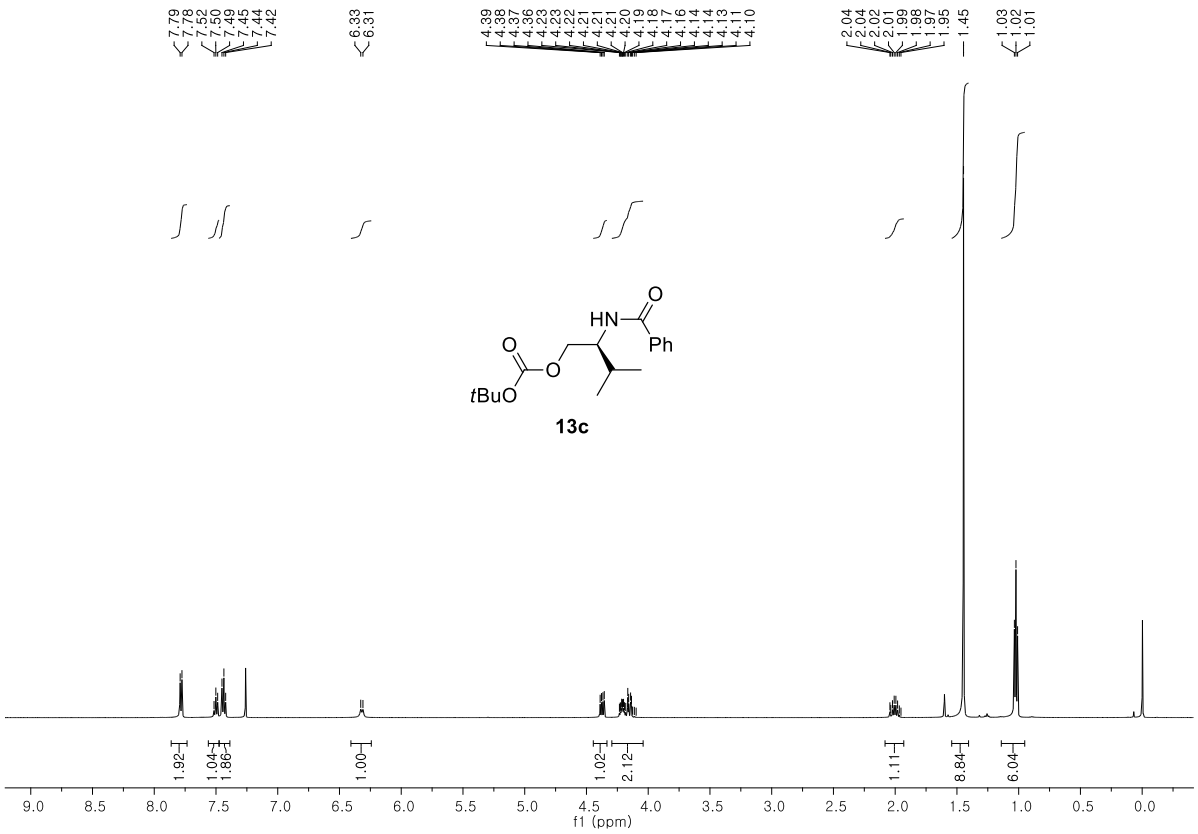

167.7
153.7
134.3
131.7
128.6
127.1
82.8
65.9
39.5
27.8
HN
O
O
O
tBuO
13a
f1 (ppm)

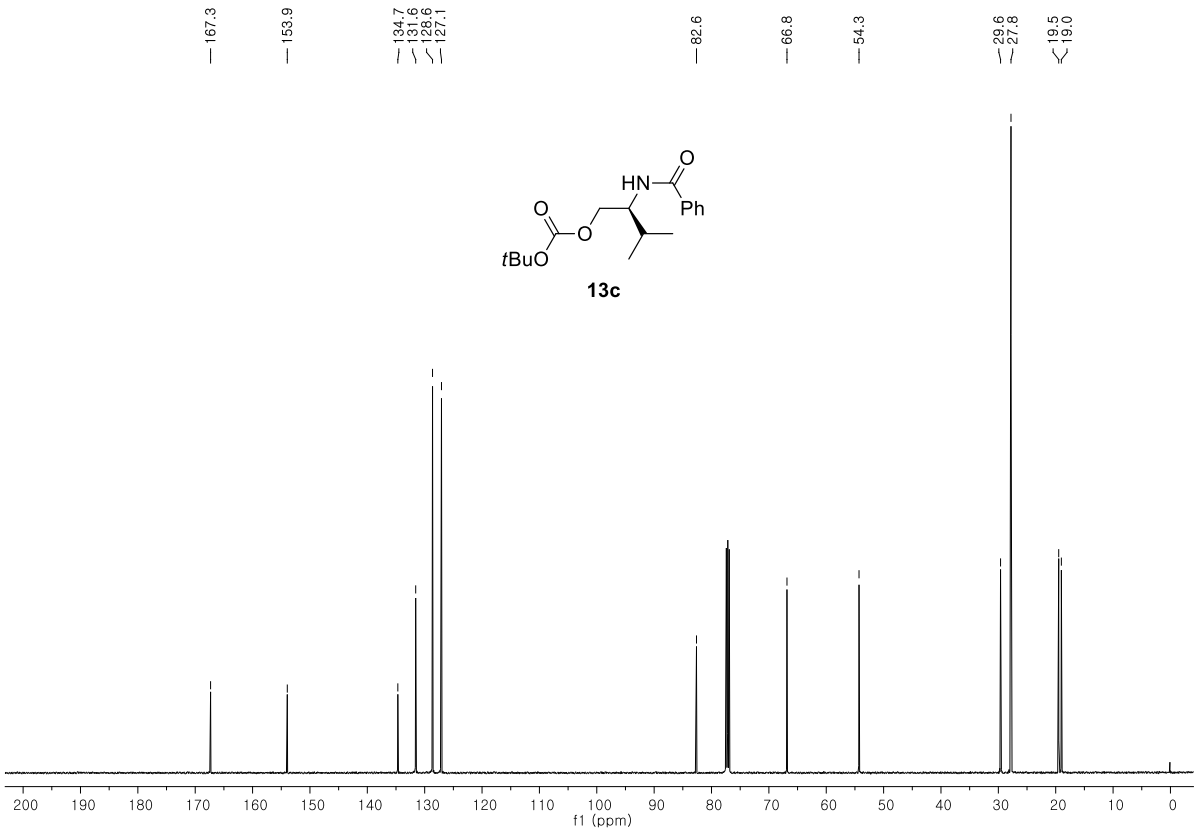

7.73
7.71
7.71
7.50
7.49
7.47
7.43
7.41
7.40
7.32
7.31
7.29
7.26
7.26
7.25
7.23
7.22
6.48
6.47
4.64
4.63
4.62
4.62
4.61
4.61
4.60
4.60
4.59
4.59
4.58
4.21
4.20
4.19
4.18
4.16
4.15
4.14
4.13
3.09
3.07
3.06
3.05
2.97
2.96
2.95
2.93
1.48
HN
O
O
O
tBuO
1.93
0.99
1.92
5.15
1.00
1.00
2.00
1.01
0.99
8.98
f1 (ppm)

13b

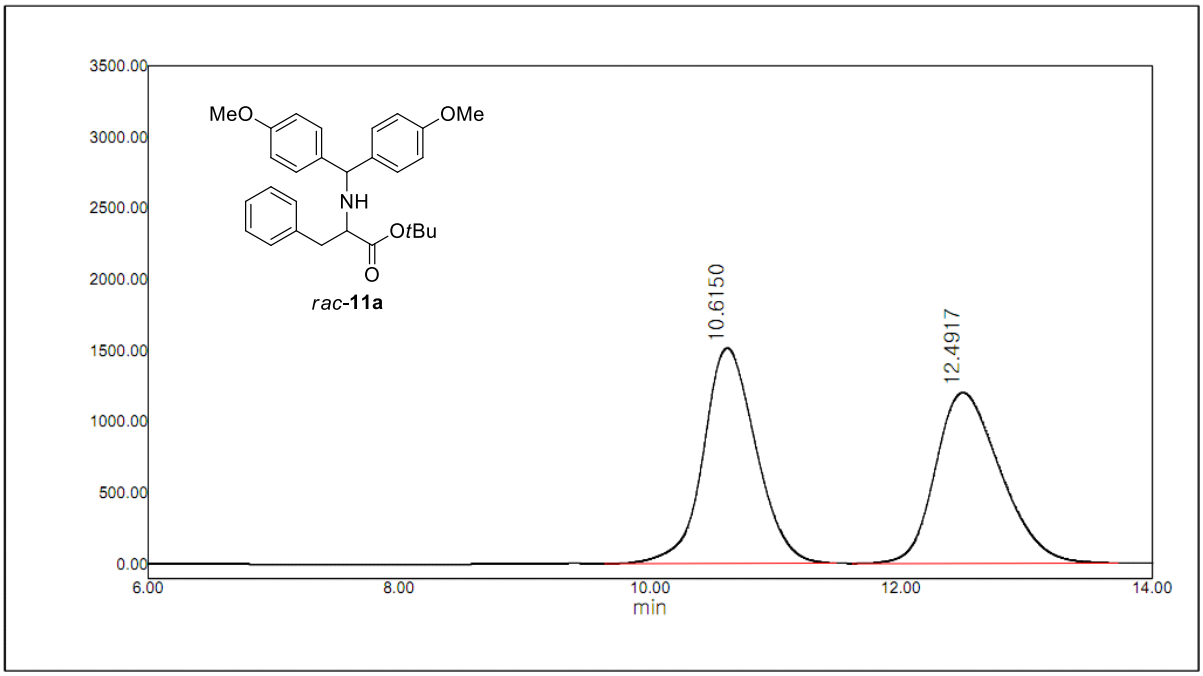

167.1
153.9
137.2
134.5
131.7
129.5
128.8
128.7
127.1
127.0
82.9
67.1
50.6
37.4
27.9
HN
O
O
O
tBuO
f1 (ppm)

13b

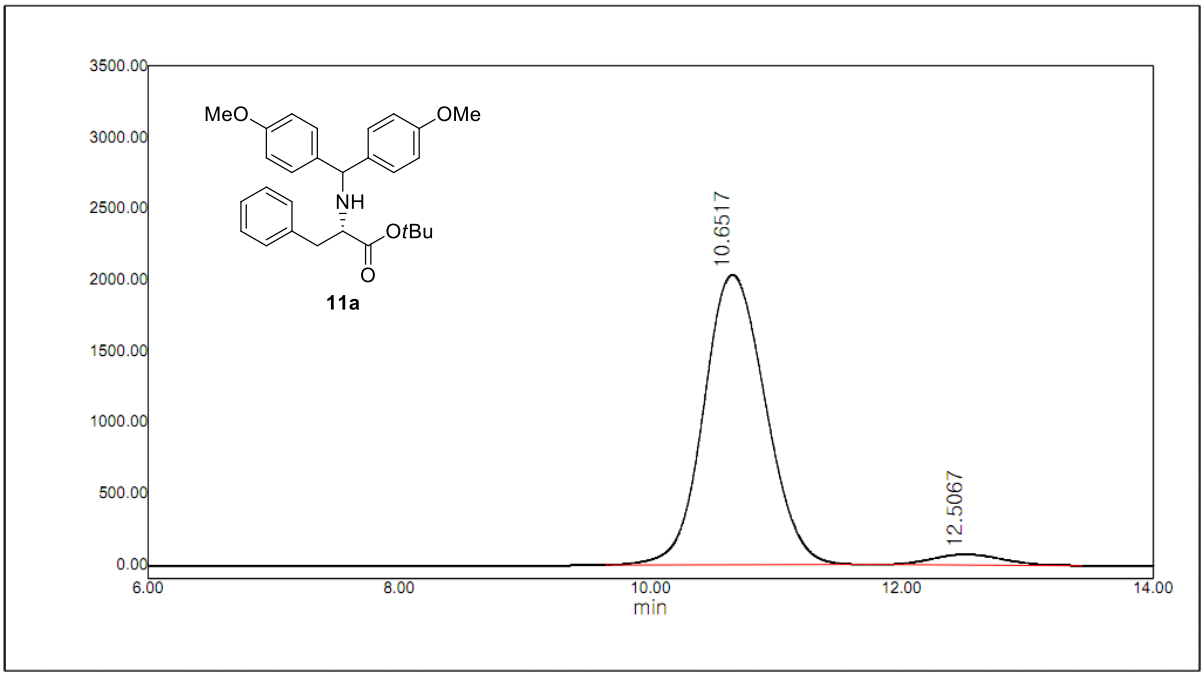

7.79
7.78
7.52
7.50
7.49
7.45
7.44
7.42
6.33
6.31
4.39
4.38
4.37
4.36
4.23
4.22
4.21
4.21
4.20
4.19
4.18
4.17
4.16
4.14
4.13
4.11
4.10
2.04
2.04
2.02
2.01
1.99
1.98
1.97
1.95
1.45
1.03
1.02
1.01
HN
O
Ph
O
O
tBuO
13c
1.92
1.04
1.86
1.00
1.02
2.12
1.11
8.84
6.04
f1 (ppm)


167.3
153.9
134.7
131.6
128.6
127.1
82.6
66.8
54.3
29.6
27.8
19.5
19.0
HN
O
Ph
O
O
tBuO
13c
f1 (ppm)

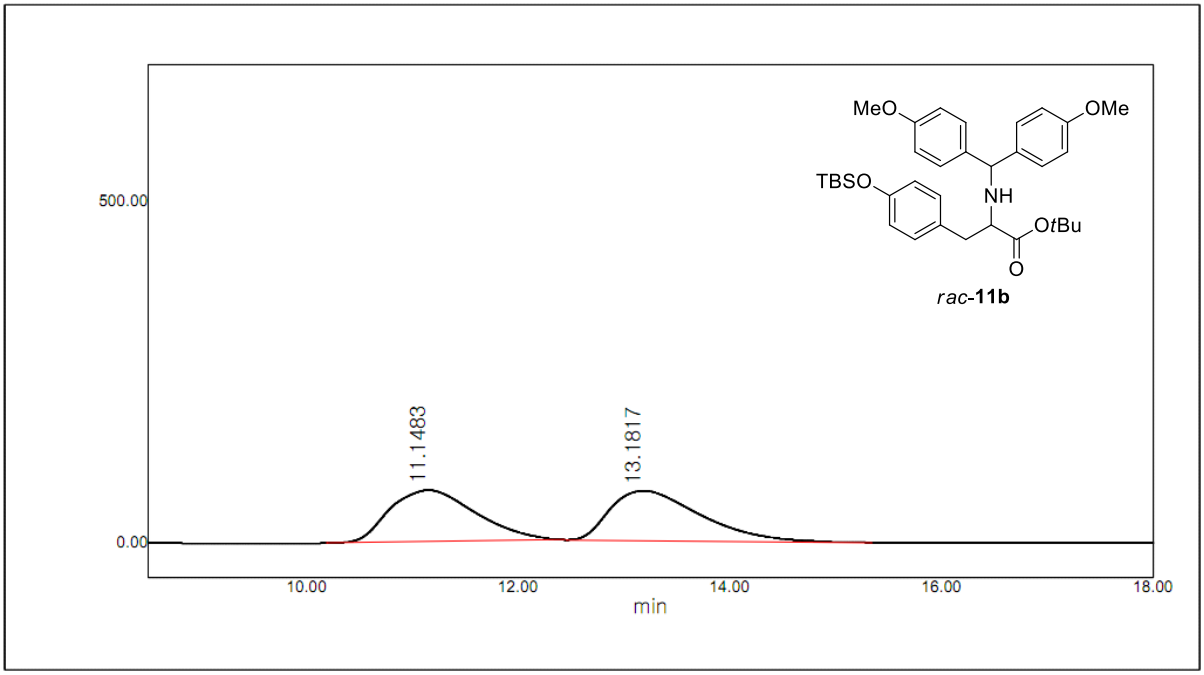
HPLC spectra of *N*-protected amino acid *t*-butyl esters



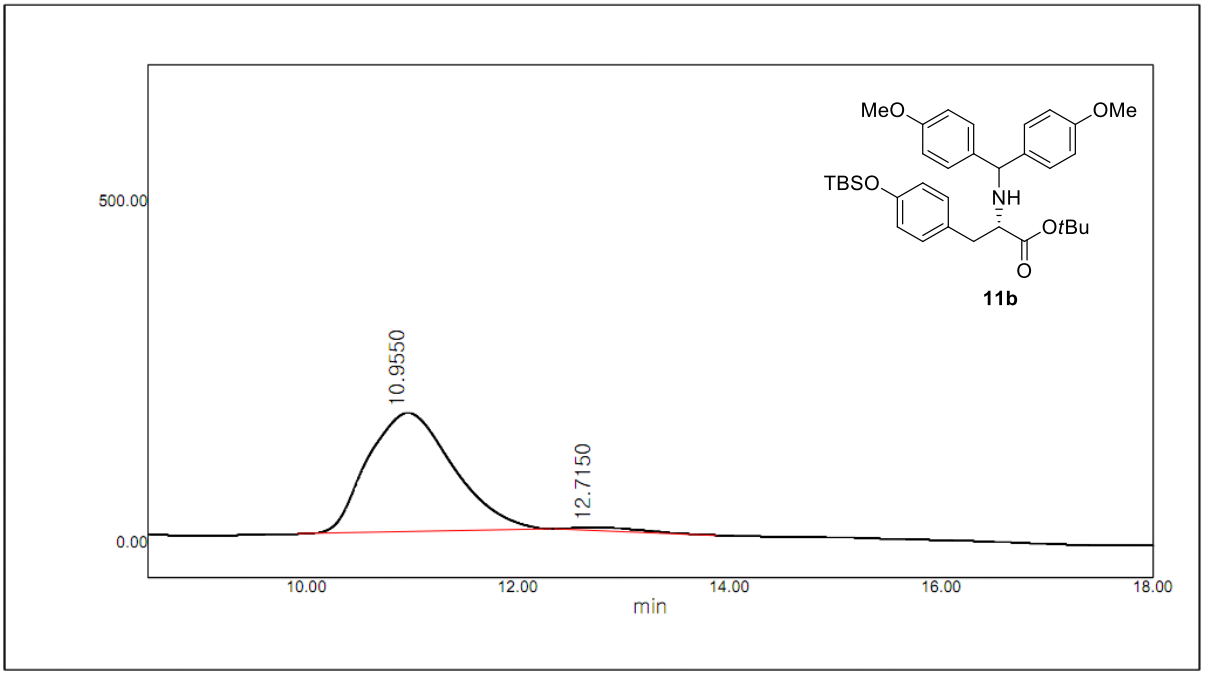
Peak #	Time(min.)	Area(%)
1	10.6150	50.57
2	12.4917	49.43



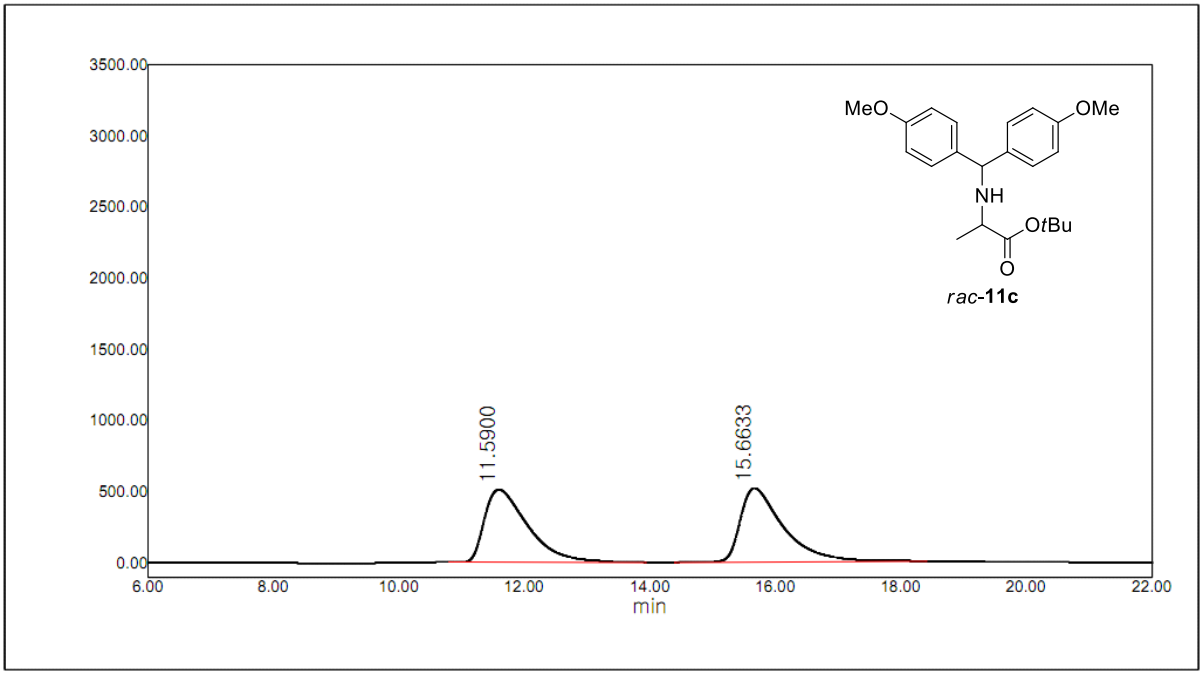
Peak #	Time(min.)	Area(%)
1	10.6517	96.01
2	12.5067	3.99



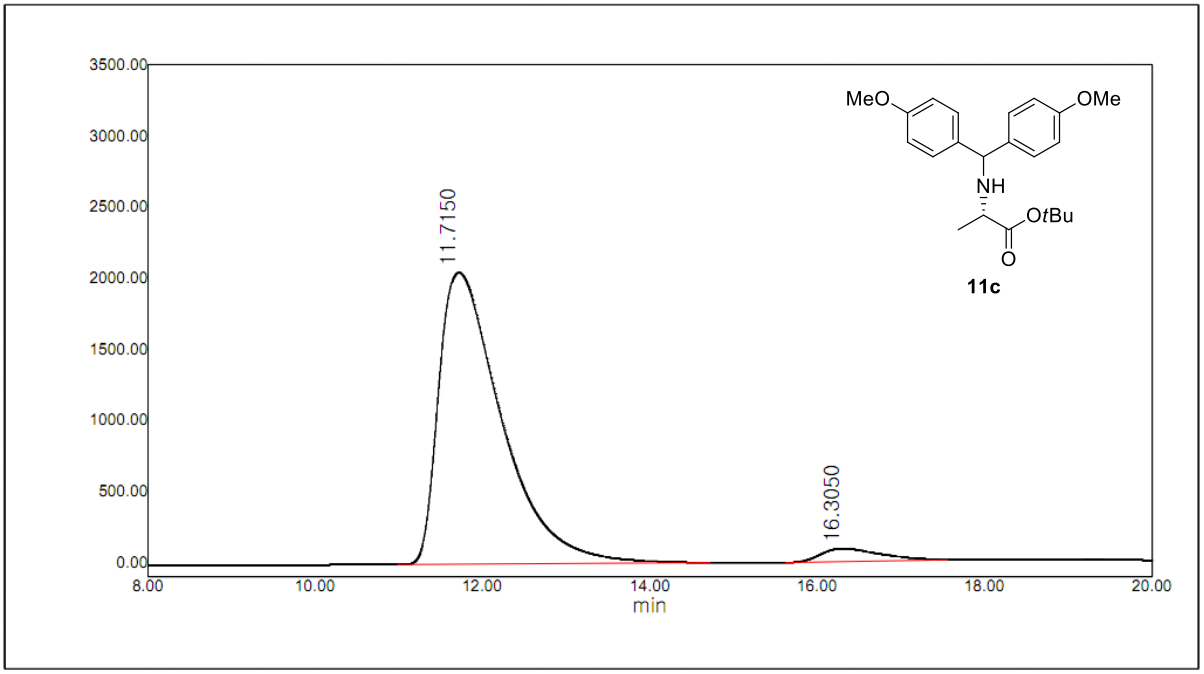
Peak #	Time(min.)	Area(%)
1	11.1483	49.73
2	13.1817	50.27



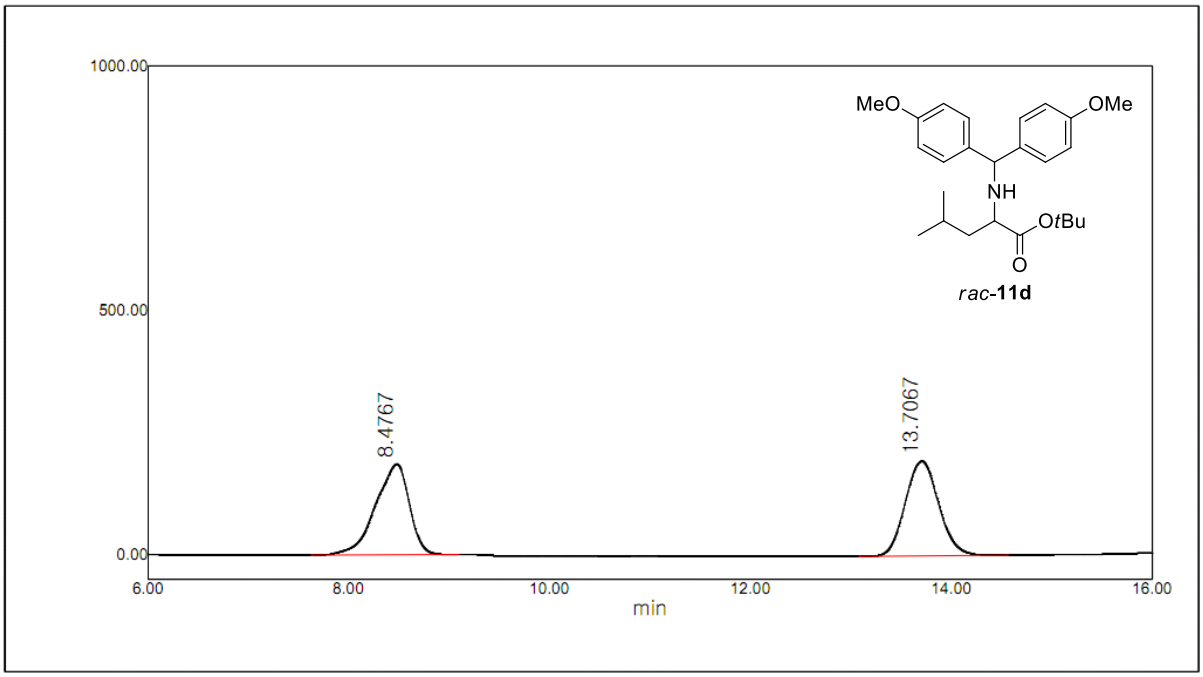
Peak #	Time(min.)	Area(%)
1	10.9550	97.82
2	12.7150	2.18



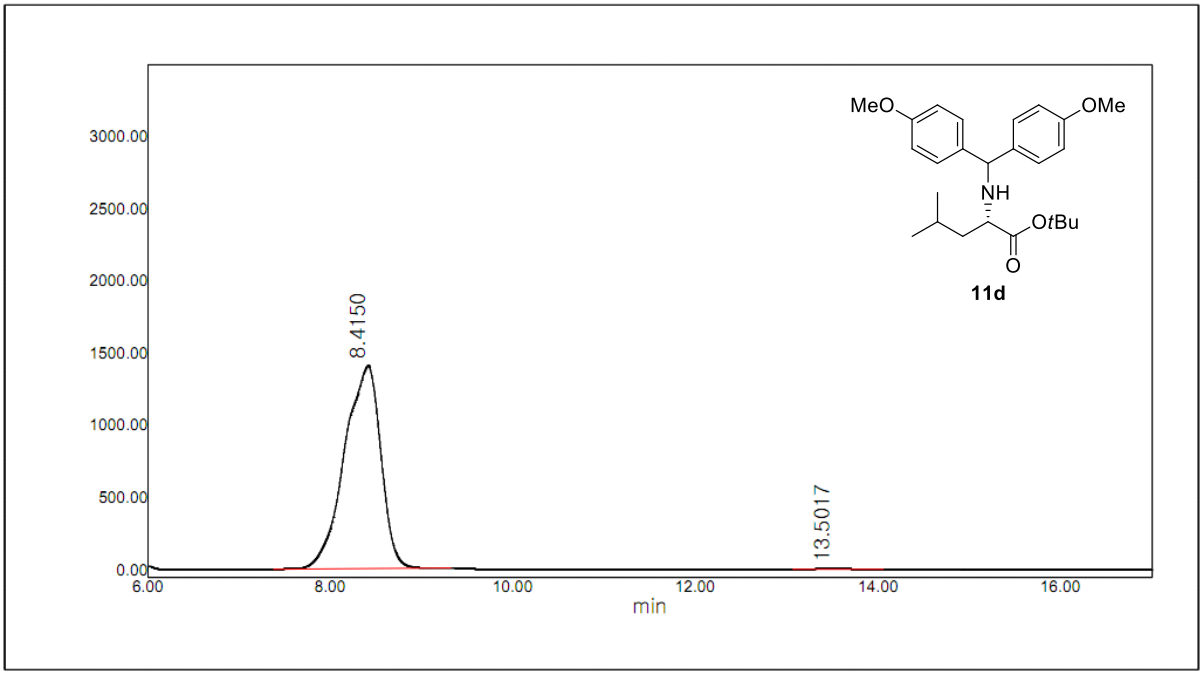
Peak #	Time(min.)	Area(%)
1	11.5900	49.80
2	15.6633	50.20



Peak #	Time(min.)	Area(%)
1	11.7150	95.97
2	16.3050	4.03



Peak #	Time(min.)	Area(%)
1	8.4767	49.28
2	13.7067	50.72



Peak #	Time(min.)	Area(%)
1	8.4150	99.61
2	13.5017	0.39