Metal Free Amination of Congested and Functionalized Alkyl Bromide at Room Temperature

Arshad J. Ansari,[†a] Ayushi Yadav,[†a] Anirban Mukherjee,[b] Elagandhula Sathish,[a] Kommu Nagesh,[c] and Ritesh Singh[*a]

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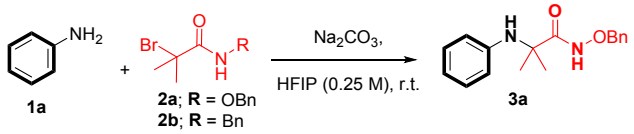
S1 General Considerations

All the reactions were carried out in flame or oven dried glassware using anhydrous solvents unless otherwise indicated. All the reagents and some solvents such as anhyd. methanol (MeOH), anhyd. isopropyl alcohol (IPA), 2, 2, 2-Trifluoroethanol and 1, 1, 1, 3, 3, 3-Hexafluoroisopropanol (HFIP) were commercially procured form Aldrich, TCI and Alfa Aesar and used without further purification. Other solvents like THF was freshly dried and distilled over Na/benzophenone and kept under an inert atmosphere and dichloroethane (DCE) (over CaH) was freshly distilled before use. ^{1}H and ^{13}C NMR spectra were recorded on Bruker's Ascend 500 MHz spectrophotometer operating at 500 MHz for ^{1}H and 101 MHz for ^{13}C experiments; Spectra were recorded at 295 K in $CDCl_3$. Chemical shifts were calibrated to the residual proton and carbon resonance of the solvent, $CDCl_3$ (^{1}H δ 7.269; ^{13}C δ 77.0). Spin multiplicities are described as s (singlet), bs (broad singlet), d (doublet), dd (double doublet), t (triplet), q (quartet), sept (septet) and m (multiplet). Peaks at 1.26 ppm and 1.56 ppm in ^{1}H NMR spectra correspond to grease and moisture respectively whereas peak at 29.67 ppm in ^{13}C NMR spectra corresponds to grease. Coupling constant (J) values are reported in hertz (Hz). Analytical TLC was performed using 2 x 4 cm plate coated with a 0.25 mm thickness of silica gel (60_F-254 Merck), and visualization was accomplished with UV light or staining the plates with ethanolic p-anisaldehyde solution/ phosphomolybdic acid solution/ ninhydrin solution and heating to 120 °C. The abbreviations used: singlet = s, doublet = d, triplet = t, quartet = q, double doublet = dd, multiplet = m, broad singlet = brs. Mass spectra were recorded on Water Q-ToF-Micro Micromass. α-bromohydroxamate precursors **2** were synthesized by following literature procedure.[1] Optically active amide **8** was synthesized as per

literature known procedure.[2] Chiral HPLC was performed on column (CHIRAL PAK IA 250x 4.6 mm 4u), with mobile phase (10% IPA/hexane for **8**; 40% IPA/hexane for **3an**/**3an′**) at flow rate of 1 ml/min for 15 min.

Table S1. Reaction optimization table[a]



entry	substrate (equiv.)	base (equiv.)	solvent	3a(%)[b]
1	**1a**:**2a**(1:1.3)	Na_2CO_3(2)	HFIP	82
2	**1a**:**2a**(1:1.3)	Na_2CO_3(2)	TFE	45
3	**1a**:**2a**(1:1.3)	Na_2CO_3(2)	THF	NR
4	**1a**:**2a**(1:1.3)	Na_2CO_3(2)	DCE	NR
5	1a:2a(1:1.3)	Na_2CO_3(2)	CH_3CN	NR
6	**1a**:**2a**(1:1.3)	K_2CO_3(2)	HFIP	74
7	**1a**:**2a**(1:1.3)	Et_3N(2)	HFIP	52
8	**1a**:**2a**(1:1.3)	DBU(2)	HFIP	38
9	**1a**:**2a**(1:1.3)	DIPEA(2)	HFIP	58
10	**1a**:**2a** (1:1.3)	Na_2CO_3(2)	HFIP (0.1 M)	90
11[c]	**1a**:**2a** (1:1.3)	Na_2CO_3(2)	HFIP (0.1 M)	91
12	**1a**:**2b** (1:1.3)	Na_2CO_3(2)	HFIP (0.1 M)	NR
13[d]	**1a**:**2a** (1:1.3)	Na_2CO_3(2)	HFIP (0.1 M)	87

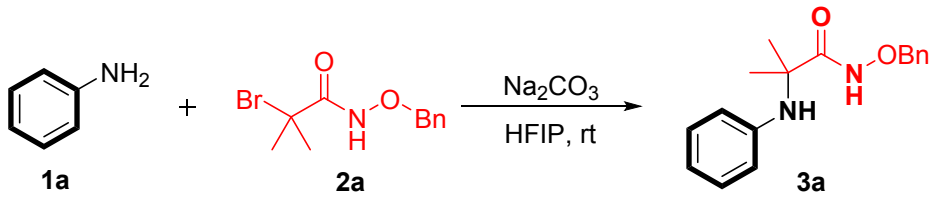
[a]Reactions were conducted in an open vessel at rt with **1a**, **2**, base, and solvent, 2-3 h (see SI for details). [b]Isolated yields. [c]Under inert atmosphere. [d]5.4 mmol scale. NR = No Reaction

Our initial efforts started with direct alkylation of aniline **1a** with α-bromoamide **2a** using Na_2CO_3 as base in 1,1,3,3,3-hexafluoro-2-propanol (HFIP, 0.25 M) at room temperature, which pleasingly furnished the desired title compound **3a** in decent yield within 2h (entry 1, Table S1). Moderate yield of **3a** was observed when reaction was conducted in 2,2,2-trifluoroethanol (TFE) as solvent (Table S1; entry 2). Further screening with non-fluorinated solvents (Dichloroethane (DCE), Tetrahydrofuran (THF), Acetonitrile (CH_3CN) under otherwise identical reaction conditions remained unfruitful (entries 3-5). Bases, other than Na_2CO_3 were found to be detrimental (entries 6-9). Dilution (0.1M) of the reaction medium helped in achieving best yield (90%) of **3a** (entry 10). Conducting the reaction under inert atmosphere led to similar outcome in yield (entry 11), thus indicating the excellent tolerance of air and moisture in current transformation. However, the reaction of N-Bn substituted bromoacetamide derivative **2b**, with aniline under similar reaction condition gave no corresponding product, thus confirming the involvement of alkoxy group in stabilizing the aza-oxyallyl cation in this reaction (entry 12). Scale up of the reaction under standard reaction condition did not affect the yield much (refer Table S1; entry 13).

S2. Experimental Procedures

S2.1 General Procedure 1; for the synthesis of 3

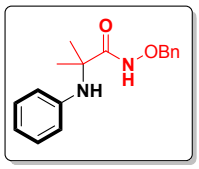
In a flame dried schlenk tube, anilines **1a** (100 mg, 1.06 mmol), was dissolved in HFIP (0.1 M) and haloamide **2a** (376.17 mg, 1.38 mmol) was added portion wise and Na_2CO_3 (222 mg, 2.12 mmol) was added simultaneously. Reaction mixture was then stirred at ambient temperature. After the consumption of starting material, reaction mixture was quenched with water followed by workup with ethyl acetate. Organics were washed with brine and dried over anhyd Na_2SO_4. Evaporation of organic solvent gave crude which was purified over flash column chromatography (EtOAc/Hexanes) to afford the desired product **3a** (90% yield).



1a 2a 3a

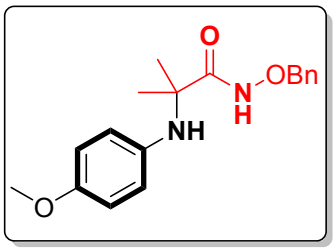
Analytical Data of compound 3

***N*-(benzyloxy)-2-methyl-2-(phenylamino)propanamide (3a)**



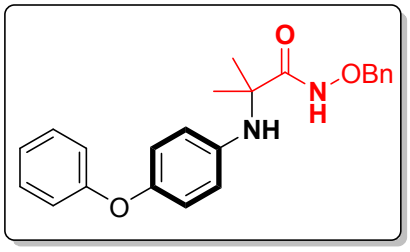
The general procedure was followed. White solid (0.255 g, 90%), R_f = 0.4 (30:70 EtOAc:hexanes, visualized by 254 nm UV light). ^{1}H NMR (δ ppm): (500 MHz, $CDCl_3$), ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.25 (s, 1H), 7.37 – 7.29 (m, 5H), 7.19 – 7.14 (m, 2H), 6.81 (t, *J* = 7.4 Hz, 1H), 6.55 (dd, *J* = 8.5, 0.9 Hz, 2H), 4.90 (s, 2H), 3.67 (s, 1H), 1.49 (s, 6H). ^{13}C{1H} NMR (δ ppm): 172.9, 144.3, 135.1, 129.4, 129.2, 128.7, 128.5, 119.3, 115.9, 78.1, 57.5, 26.1. HRMS (EI) calcd for $C_{17}H_{21}N_2O_2$ (M+H$^+$) 285.1598 found 285.1601.

N-(benzyloxy)-2-((4-methoxyphenyl)amino)-2-methylpropanamide (3b)



The general procedure was followed. White solid (0.285 g, 91%), R_f = 0.2 (15:85 EtOAc:hexanes, visualized by 254 nm UV light). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.39 (s, 1H), 7.45–7.32 (m, 5H), 6.76 (d, *J* = 8.8 Hz, 2H), 6.54 (d, *J* = 8.8 Hz, 2H), 4.96 (s, 2H), 3.77 (s, 3H), 3.41 (s, 1H), 1.47 (s, 6H). ^{13}C{1H} NMR (δ ppm): 173.2, 153.5, 138.0, 135.2, 129.3, 128.7, 128.5, 117.8, 114.6, 78.0, 57.9, 55.6, 26.0. HRMS (EI) calcd for $C_{18}H_{23}N_2O_3$ (M+H$^+$) 315.1703 found 315.1707.

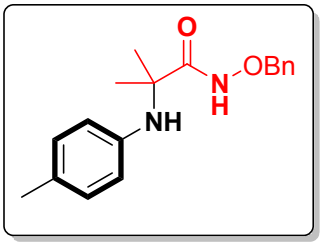
N-(benzyloxy)-2-methyl-2-((4-phenoxyphenyl)amino)propanamide (3c)



The general procedure was followed. White solid (0.335 g, 89%), R_f = 0.4 (40:60 EtOAc:hexanes, visualized by 254 nm UV light). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.34 (s, 1H), 7.41 – 7.30 (m, 7H), 7.07

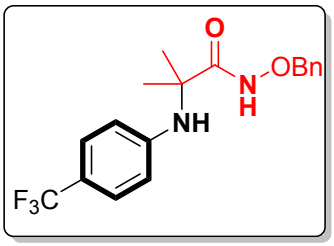
(dd, J = 10.6, 4.2 Hz, 1H), 6.97–6.93 (m, 2H), 6.90–6.86 (m, 2H), 6.57–6.52 (m, 2H), 4.95 (s, 2H), 1.51 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.9, 158.3, 149.5, 140.5, 135.1, 129.6, 129.3, 128.6, 122.4, 120.5, 117.6, 117.3, 78.0, 77.4, 77.0, 76.7, 57.8, 26.1. HRMS (EI) calcd for $C_{23}H_{25}N_2O_3$ ($M+H^+$) 377.1860 found 377.1862.

N-(benzyloxy)-2-methyl-2-(p-tolylamino)propanamide (3d)



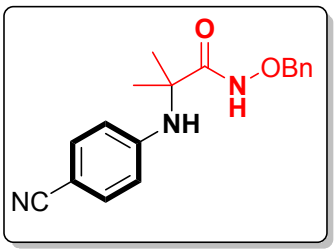
The general procedure was followed. White solid (0.253 g, 85%), R_f = 0.3 (25:75 EtOAc:hexanes, visualized by 254 nm UV light). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.32 (s, 1H), 7.35 (dd, J = 7.0, 3.5 Hz, 5H), 7.00 (d, J = 8.0 Hz, 2H), 6.50 (d, J = 8.3 Hz, 2H), 4.94 (s, 2H), 3.55 (s, 1H), 2.27 (s, 3H), 1.50 (d, J = 3.6 Hz, 6H). ^{13}C{1H} NMR (δ ppm): 173.1, 141.8, 135.2, 129.7, 129.3, 128.8, 128.7, 128.5, 116.2, 78.0, 57.1, 26.1, 20.4. HRMS (EI) calcd for C18$H_{23}N_2$O2 ($M+H^+$) 299.1754 found 299.1754.

N-(benzyloxy)-2-methyl-2-((4-(trifluoromethyl)phenyl)amino)propanamide (3e)



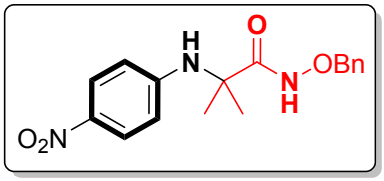
The general procedure was followed. White solid (0.296 g, 84%), R_f = 0.56 (30:70 EtOAc:hexanes, visualized by 254 nm UV light). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.05 (s, 1H), 7.42 (d, J = 8.5 Hz, 2H), 7.37 – 7.31 (m, 5H), 6.58 (d, J = 8.5 Hz, 2H), 4.93 (s, 2H), 4.00 (s, 1H), 1.55 (s, 6H). ^{13}C{1H} NMR (δ ppm): 172.1, 146.9, 134.4, 129.2, 128.8, 128.6, 126.5 (q, J = 3.7 Hz), 114.9, 78.1, 57.4, 26.0. HRMS (EI) calcd for $C_{18}H_{20}F_3N_2O_2$ ($M+H^+$) 353.1471 found 353.1472.

N-(benzyloxy)-2-((4-cyanophenyl)amino)-2-methylpropanamide (3f)



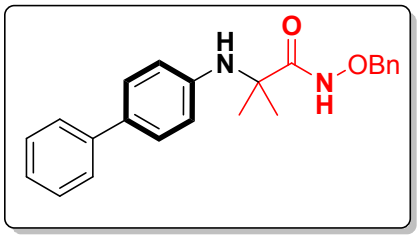
The general procedure was followed. White solid (0.244 g, 83%), R_f = 0.2 (30:70 EtOAc:hexanes, visualized by 254 nm UV light). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.98 (s, 1H), 7.43 (d, J = 8.8 Hz, 2H), 7.38 – 7.29 (m, 5H), 6.58 – 6.51 (m, 2H), 4.91 (s, 2H), 4.26 (s, 1H), 1.55 (s, 6H). ^{13}C{1H} NMR (δ ppm): 171.86, 147.9, 134.8, 133.5, 129.3, 129.2, 128.9, 128.6, 128.5, 119.6, 115.2, 101.2, 78.1, 57.4, 25.9. HRMS (EI) calcd for $C_{18}H_{20}F_3N_2O_2$ ($M+H^+$) 310.1550 found 310.1553.

N-(benzyloxy)-2-methyl-2-((4-nitrophenyl)amino)propanamide (3g)



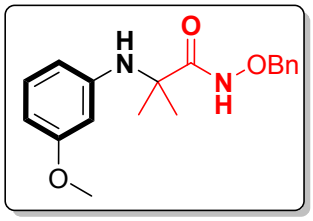
The general procedure was followed. yellow solid (0.205 g, 86%), R_f = 0.2 (70:30 EtOAc:hexanes, visualized by 254 nm UV light). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.89 (s, 1H), 8.18 – 7.97 (m, 2H), 7.39 – 7.29 (m, 5H), 6.59 – 6.46 (m, 2H), 4.93 (s, 2H), 4.46 (s, 1H), 1.58 (s, 6H). ^{13}C{1H} NMR (δ ppm): 171.4, 149.9, 139.6, 134.8, 129.2, 128.9, 128.6, 125.9, 114.1, 78.2, 57.6, 26.1. HRMS (EI) calcd for $C_{18}H_{20}F_3N_2O_2$ ($M+H^+$) 330.1448 found 330.1454.

2-([1,1'-biphenyl]-4-ylamino)-N-(benzyloxy)-2-methylpropanamide (3h)



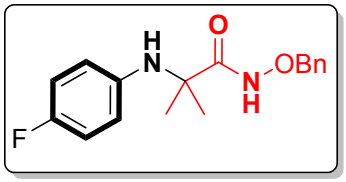
The general procedure was followed. Yellow solid (0.292, 81%), R_f = 0.2 (20:80 EtOAc:hexanes, visualized by 254 nm UV light). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.28 (s, 1H), 7.57 – 7.52 (m, 2H), 7.47 – 7.41 (m, 4H), 7.39 – 7.31 (m, 7H), 6.65 (d, J = 8.5 Hz, 2H), 4.95 (s, 2H), 1.55 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.8, 143.6, 140.7, 135.1, 132.3, 129.3, 128.9, 127.8, 126.4, 116.2, 78.0, 57.5, 26.1. HRMS (EI) calcd for: $C_{23}H_{25}N_2O_2$ ($M+H^+$) 361.1911 found 361.1913.

***N*-(benzyloxy)-2-((3-methoxyphenyl)amino)-2-methylpropanamide (3i)**



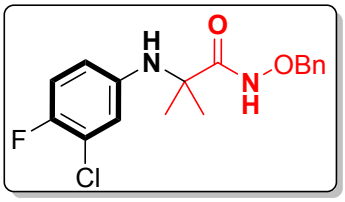
The general procedure was followed. White solid (0.276 g, 88%), R_f = 0.4 (30:70 EtOAc:hexanes, visualized by 254 nm UV light). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.24 (s, 1H), 7.42 – 7.30 (m, 5H), 7.10 (t, J = 8.1 Hz, 1H), 6.44 – 6.36 (m, 1H), 6.19 – 6.14 (m, 2H), 4.93 (s, 2H), 3.77 (d, J = 4.3 Hz, 3H), 3.67 (s, 1H), 1.52 (s, 6H). ^{13}C{1H} NMR (δ ppm): 172.9, 160.5, 145.8, 135.1, 129.9, 129.4, 128.7, 128.5, 108.6, 104.4, 102.3, 78.0, 57.4, 55.1, 26.13. HRMS (EI) calcd for $C_{18}H_{23}N_2O_3$ ($M+H^+$) 315.1703 found 315.1703.

N-(benzyloxy)-2-((4-fluorophenyl)amino)-2-methylpropanamide (3j)



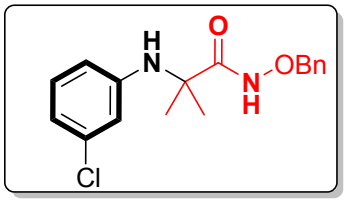
The general procedure was followed. White solid, (0.263 g, 87%), R_f = 0.40 (30:70 EtOAc:hexanes, visualized by 254 nm UV light).^{1}H NMR (500 MHz, $CDCl_3$) δ 9.30 (s, 1H), 7.36 (d, J = 7.3 Hz, 5H), 6.88 (t, J = 8.6 Hz, 2H), 6.57 – 6.43 (m, 2H), 4.94 (s, 2H), 3.57 (s, 1H), 1.48 (s, 6H). ^{13}C{1H} NMR (δ ppm): 172.9, 156.8 (d, J = 237.9 Hz), 155.6, 140.56 (d, J = 2.0 Hz), 135.1, 129.3, 128.7, 128.5, 117.2 (d, J = 7.5 Hz), 115.6 (d, J = 22.4 Hz), 78.0, 57.8, 25.9. HRMS (EI) calcd for $C_{17}H_{20}FN_2O_2$ ($M+H^+$) 303.1503 found 303.1504.

N-(benzyloxy)-2-((3-chloro-4-fluorophenyl)amino)-2-methylpropanamide (3k)



The general procedure was followed. White solid (0.275 g, 82%), R_f = 0.4 (30:70 EtOAc:hexanes, visualized by 254 nm UV light). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.20 (s, 1H), 7.40 – 7.32 (m, 5H), 6.94 (t, *J* = 8.8 Hz, 1H), 6.61 (dd, *J* = 6.0, 2.9 Hz, 1H), 6.43 – 6.33 (m, 1H), 4.94 (s, 2H), 3.64 (s, 1H), 1.49 (s, 6H). ^{13}C{1H} NMR (δ ppm): 172.5, 151.9 (d, *J* = 240.3 Hz), 141.4 (d, *J* = 2.4 Hz), 134.9, 129.2, 128.8, 128.6, 120.9(d, *J* = 18.6 Hz), 117.5, 116.7 (d, *J* = 21.9 Hz), 115.1(d, *J* = 6.3 Hz), 78.1, 57.6, 25.9. HRMS (EI) calcd for (M+H$^+$) 337.1114 found 337.1117.

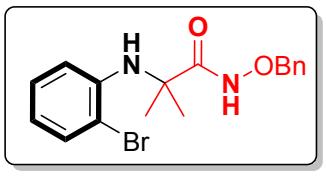
***N*-(benzyloxy)-2-((3-chlorophenyl)amino)-2-methylpropanamide (3l)**



The general procedure was followed. White solid (0.270 g, 85%), R_f = 0.4 (30:70 EtOAc:hexanes, visualized by 254 nm UV light).^{1}H NMR (500 MHz, $CDCl_3$) δ 9.18 (s, 1H), 7.34 (s, 5H), 7.09 (t, *J* = 8.1 Hz, 1H), 6.80 (dd, *J* = 7.9, 1.1 Hz, 1H), 6.59 (t, *J* = 2.0 Hz, 1H), 6.43 (dd, *J* = 8.1, 1.9 Hz, 1H), 4.92 (s, 2H), 3.79 (s, 1H), 1.51 (s, 6H). ^{13}C{1H} NMR (δ ppm): 172.3, 145.5, 134.9, 134.8, 130.1, 129.3, 128.7, 128.5, 119.2, 115.8, 113.8, 78.1, 57.4, 26.0. HRMS (EI) calcd for $C_{17}H_{20}ClN_2O_2$ (M+H$^+$) 319.1208 found. 319.1214.

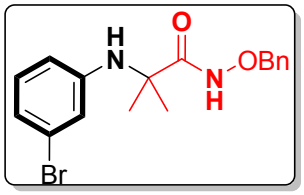
***N*-(benzyloxy)-2-((2-bromophenyl)amino)-2-methylpropanamide (3m)**

The general procedure was followed. White solid (0.324 g, 87%), R_f = 0.4 (30:70 EtOAc:hexanes, visualized by 254 nm UV light). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.16 (s, 1H), 7.47 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.35 (s, 5H), 7.20 – 7.11 (m, 1H), 6.70 (td, *J* = 7.9, 1.4 Hz, 1H), 6.60 (dd, *J* = 8.2, 1.4 Hz, 1H), 4.93 (s, 2H), 4.43 (s, 1H), 1.55 (s, 6H). ^{13}C{1H} NMR (δ ppm): 172.4, 141.4, 135.0, 129.3, 128.7, 128.5, 128.2, 120.0, 115.5, 111.7, 78.1, 57.9, 26.1. HRMS (EI) calcd for $C_{17}H_{20}BrN_2O_2$ (M+H$^+$) 363.0703 found 363.0703.



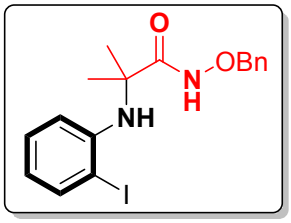
N-(benzyloxy)-2-((3-bromophenyl)amino)-2-methylpropanamide (3m′)

The general procedure was followed. White solid (0.316 g, 84%), R_f = 0.4 (30:70 EtOAc:hexanes, visualized by 254 nm UV light). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.15 (s, 1H), 7.42 – 7.30 (m, 5H), 7.03 (t, *J* = 8.0 Hz, 1H), 6.97 – 6.94 (m, 1H), 6.75 (t, *J* = 2.0 Hz, 1H), 6.47 (ddd, *J* = 8.1, 2.3, 0.8 Hz, 1H), 4.93 (s, 2H), 3.74 (s, 1H), 1.52 (s, 6H).^{13}C{1H} (101 MHz, $CDCl_3$) NMR (δ ppm): 172.21, 145.65,



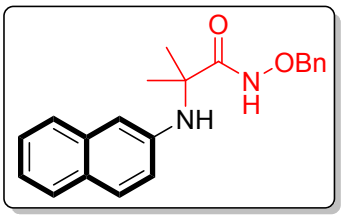
134.96, 130.46, 129.33, 128.77, 128.55, 122.97, 122.25, 118.77, 114.24, 78.16, 57.51, 26.03. HRMS (EI) calcd for $C_{17}H_{20}BrN_2O_2$ ($M+H^+$) 363.0703 found 363.0703.

N-(benzyloxy)-2-((2-iodophenyl)amino)-2-methylpropanamide (3n)



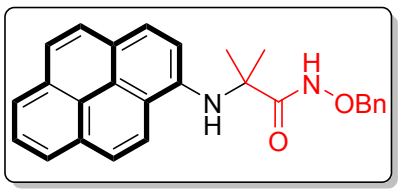
The general procedure was followed. White solid (0.324 g, 79%), R_f = 0.2 (20:80 EtOAc:hexanes, visualized by 254 nm UV light). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.18 (s, 1H), 7.71 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.44 – 7.32 (m, 5H), 7.24 – 7.12 (m, 1H), 6.61 – 6.48 (m, 2H), 4.92 (s, 2H), 4.28 (s, 1H), 1.56 (s, 6H). ^{13}C{1H} NMR (δ ppm): 172.5, 143.9, 139.4, 134.9, 129.3, 129.2, 128.8, 128.6, 120.9, 114.8, 88.0, 78.1, 57.9, 26.0. HRMS (EI) calcd for : $C_{17}H_{20}IN_2O_2$ ($M+H^+$) 411.0564 found 411.0572.

N-(benzyloxy)-2-methyl-2-(naphthalen-2-ylamino)propanamide (3o)



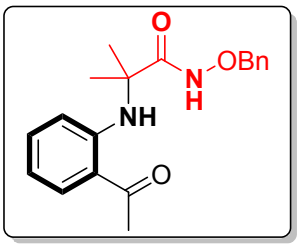
The general procedure was followed. White solid (0.347 g, 74%), R_f = 0.54 (30:70 EtOAc:hexanes, visualized by 254 nm UV light). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.22 (s, 1H), 7.86 (dd, *J* = 6.7, 2.7 Hz, 1H), 7.77 – 7.70 (m, 1H), 7.50 (pd, *J* = 6.8, 3.3 Hz, 2H), 7.33 (ddd, *J* = 8.5, 6.5, 5.0 Hz, 3H), 7.32 – 7.22 (m, 5H), 6.59 (dd, *J* = 7.2, 1.3 Hz, 1H), 4.90 (s, 2H), 4.47 (s, 1H), 1.66 (s, 6H). HRMS (EI) calcd for $C_{21}H_{23}N_2O_2$ ($M+H^+$) 335.1754 found 335.1756.

N-(benzyloxy)-2-methyl-2-(pyren-1-ylamino)propanamide (3p)



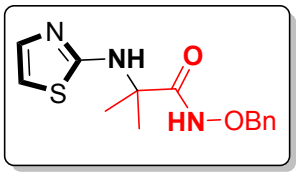
The general procedure was followed. Greenish black solid (0.228 g, 56%), R_f = 0.3 (20:80 EtOAc:hexanes, visualized by 254 nm UV light). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.36 (s, 1H), 8.00 (ddd, *J* = 61.7, 27.1, 17.6 Hz, 7H), 7.33 – 7.26 (m, 4H), 7.27 – 7.18 (m, 3H), 4.95 (s, 2H), 1.73 (s, 8H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.9, 138.1, 134.9, 129.2, 128.6, 128.5, 128.0, 126.1, 125.6, 124.4, 118.9, 113.1, 78.1, 58.0, 26.5. HRMS (EI) calcd for $C_{27}H_{25}N_2O_2$ ($M+H^+$) 409.1911 found 409.1917.

2-((2-acetylphenyl)amino)-N-(benzyloxy)-2-methylpropanamide (3q)



The general procedure was followed. White solid (0.267g, 82%), R_f = 0.3 (25:75 EtOAc:hexanes, visualized by 254 nm UV light). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.07 (d, *J* = 25.1 Hz, 1H), 7.81 (dd, *J* = 8.1, 1.4 Hz, 1H), 7.38 – 7.31 (m, 6H), 6.80 – 6.69 (m, 1H), 6.59 (d, *J* = 8.5 Hz, 1H), 4.89 (s, 2H), 2.58 (s, 3H), 1.59 (s, 6H). ^{13}C{1H} NMR (δ ppm): 201.5, 172.7, 148.0, 135.1, 134.7, 132.9, 129.4, 128.7, 128.4, 119.0, 116.0, 115.1, 78.0, 56.5, 27.7, 26.2. HRMS (EI) calcd for $C_{19}H_{23}N_2O_3$ ($M+H^+$) 327.1703 found 327.1704.

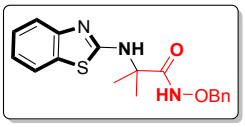
N-(benzyloxy)-2-methyl-2-(thiazol-2-ylamino)propanamide (3s)



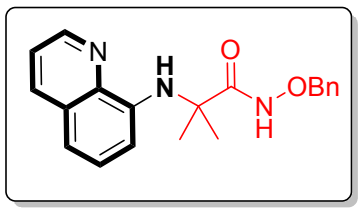
The general procedure was followed. White solid (0.213 g, 73%), R_f = 0.2 (60:40 EtOAc:hexanes, visualized by 254 nm UV light). ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.07 (s, 1H), 7.44 – 7.31 (m, 5H), 7.05 (d, *J* = 3.7 Hz, 1H), 6.56 (d, *J* = 3.7 Hz, 1H), 5.06 (s, 1H), 4.93 (s, 3H), 1.60 (s, 6H). HRMS (EI) calcd for: $C_{14}H_{18}N_3O_2S$ ($M+H^+$) 292.1114 found 292.1110.

2-(benzo[d]thiazol-2-ylamino)-N-(benzyloxy)-2-methylpropanamide (3t)

The general procedure was followed. White solid (0.266 g, 78%), R_f = 0.2 (60:40 EtOAc:hexanes, visualized by 254 nm UV light). ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.25 (s, 1H), 7.61 – 7.58 (m, 1H), 7.44 (d, *J* = 8.0 Hz, 1H), 7.35 – 7.31 (m, 3H), 7.22 (dd, *J* = 6.4, 3.6 Hz, 4H), 7.19 – 7.14 (m, 1H), 5.21 (s, 1H), 4.93 (s, 2H), 1.69 (s, 6H). ^{13}C{1H} NMR (δ ppm): 171.8, 163.9, 151.6, 135.4, 130.6, 129.2, 128.5, 128.4, 125.9, 122.6, 120.7, 119.8, 77.8, 59.4, 25.7. HRMS (EI) calcd for $C_{18}H_{20}N_3O_2S$ ($M+H^+$) 342.1271 found. 342.1273.

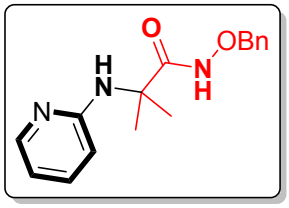


N-(benzyloxy)-2-methyl-2-(quinolin-8-ylamino)propanamide (3u)



The general procedure was followed. White solid (0.257 g, 79%), R_f = 0.56 (30:70 EtOAc:hexanes, visualized by 254 nm UV light). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.27 (s, 1H), 8.74 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.12 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.43 (dd, *J* = 8.2, 4.2 Hz, 1H), 7.37 (t, *J* = 7.9 Hz, 1H), 7.34 – 7.28 (m, 5H), 7.20 (d, *J* = 8.2 Hz, 1H), 6.67 (dd, *J* = 7.6, 0.8 Hz, 1H), 6.43 (s, 1H), 4.93 (s, 2H), 1.66 (s, 6H). ^{13}C{1H} NMR (δ ppm): 172.9, 147.3, 140.7, 138.8, 136.3, 135.1, 129.3, 128.7, 128.6, 128.4, 127.0, 121.6, 116.2, 109.7, 78.1, 57.1, 25.8. HRMS (EI) calcd for : $C_{20}H_{22}N_3O_2$ ($M+H^+$) 336.1707 found. 336.1708.

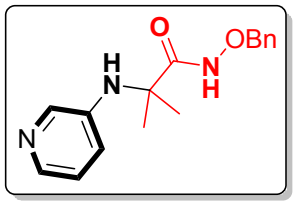
N-(benzyloxy)-2-methyl-2-(pyridin-2-ylamino)propanamide (3v)



The general procedure was followed. White solid (0.216 g, 76%), R_f = 0.56 (60:40 EtOAc:hexanes, visualized by 254 nm UV light). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.81 (s, 1H), 8.07 – 7.91 (m, 1H), 7.48 – 7.30 (m, 6H), 6.67 (dt, *J* = 11.7, 6.8 Hz, 1H), 6.41 (t, *J* = 9.4 Hz, 1H), 4.91 (s, 2H), 1.56 (s, 6H). ^{13}C{1H} NMR (δ ppm): 172.3, 155.0, 143.8, 139.8, 135.3, 129.3, 129.3, 128.6, 128.5, 128.5, 128.4, 113.7, 110.3, 77.9, 56.9, 25.8, HRMS (EI) calcd $C_{16}H_{20}N_3O_2$ ($M+H^+$) 286.1550 found 286.1551.

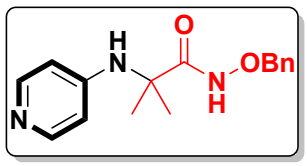
N-(benzyloxy)-2-methyl-2-(pyridin-3-ylamino)propanamide (3w)

The general procedure was followed. White solid (0.222g, 76%), R_f = 0.2 (60:40 EtOAc:hexanes, visualized by 254 nm UV light). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.32 (s, 1H), 8.06 (dd, *J* = 4.7, 1.2 Hz, 1H), 7.96 (d, *J* = 2.9 Hz, 1H), 7.35 (s, 5H), 7.09 (dd, *J* = 8.3, 4.5 Hz, 1H), 6.83 (ddd, *J* = 8.3, 2.9, 1.3 Hz, 1H), 4.94 (s, 2H), 3.78 (s, 1H), 1.53 (s, 6H). ^{13}C{1H} NMR (δ ppm): 172.2, 140.9, 139.4, 138.3, 135.1, 129.3, 128.7, 128.5, 123.5, 121.0, 77.9, 57.13, 25.9. HRMS (EI) calcd for $C_{16}H_{20}N_3O_2$ ($M+H^+$) 286.1550 found 286.1551.

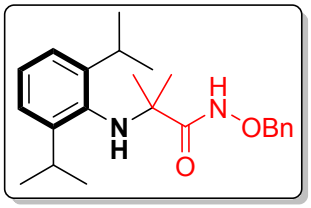


N-(benzyloxy)-2-methyl-2-(pyridin-4-ylamino)propanamide (3x)

The general procedure was followed. White solid (0.220 g, 76%), R_f = 0.56 (70:30 EtOAc:hexanes, visualized by 254 nm UV light). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 (m, 2H), 7.40 (dd, *J* = 6.3, 3.0 Hz, 2H), 7.36 – 7.33 (m, 3H), 6.59 (d, *J* = 6.3 Hz, 2H), 4.96 (s, 2H), 1.60 (s, 6H). HRMS (EI) calcd for $C_{16}H_{20}N_3O_2$ ($M+H^+$) 286.1550 found. 286.1551.



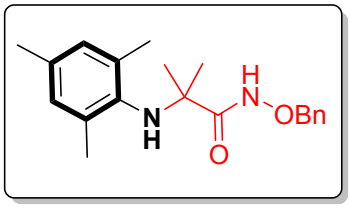
N-(benzyloxy)-2-((2,6-diisopropylphenyl)amino)-2-methylpropanamide (3y)



The general procedure was followed. White solid (0.279 g, 75%), R_f = 0.54 (30:70 EtOAc:hexanes, visualized by 254 nm UV light). ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.01 (s, 1H), 7.52 – 7.46 (m, 2H), 7.46 – 7.37 (m, 3H), 7.11 (s, 3H), 5.03 (s, 2H), 3.09 (dt, *J* = 13.6, 6.9 Hz, 3H), 1.34 (s, 6H), 1.19 (d, *J* = 6.8 Hz, 12H). ^{13}C{1H} NMR (δ ppm): 175.4, 144.2, 138.3, 135.6, 129.1, 128.7, 128.6, 125.1, 123.4, 77.9, 60.5, 28.5, 26.7, 23.7. HRMS (EI) calcd for : $C_{23}H_{33}N_2O_2$ ($M+H^+$) 369.2537 found 369.2541.

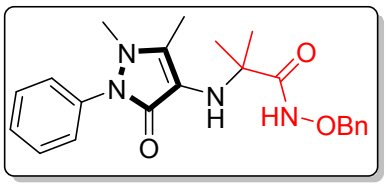
N-(benzyloxy)-2-(mesitylamino)-2-methylpropanamide (3z)

The general procedure was followed. White solid (0.238 g, 73%), R_f = 0.58 (30:70 EtOAc:hexanes, visualized by 254 nm UV light). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.98 (s, 1H), 7.49 – 7.46 (m, 2H), 7.45 – 7.37 (m, 3H), 6.81 (s, 2H), 5.01 (s, 2H), 2.98 (s, 1H), 2.24 (s, 3H), 2.16 (s, 6H), 1.34 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.6, 139.6, 135.6, 133.1, 132.4, 129.6, 129.0, 128.6, 77.8, 59.8, 27.0, 20.0. HRMS (EI) calcd for $C_{20}H_{27}N_2O_2$ ($M+H^+$) 327.2067 found 327.2067.



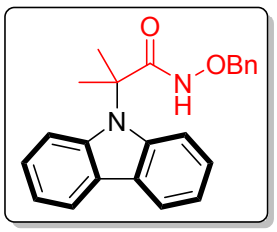
N-(benzyloxy)-2-((1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)amino)-2-methyl propanamide (3ab)

The general procedure was followed. Red solid (0.319g, 81%), R_f = 0.2 (70:30 EtOAc:hexanes, visualized by 254 nm UV light). ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.69 (s, 1H), 7.52 – 7.45 (m, 4H), 7.43 – 7.39 (m, 2H), 7.38 – 7.31 (m, 4H), 4.96 (s, 2H), 3.02 (s, 3H), 2.19 (s, 3H), 1.41 (s, 6H). ^{13}C{1H} NMR (δ ppm): 165.0, 149.9, 135.8, 134.6, 129.3, 129.2, 128.3, 126.9, 123.9, 115.3, 76.7, 60.6, 36.5, 26.9, 11.5. HRMS (EI) calcd for $C_{22}H_{27}N_4O_3$ ($M+H^+$) 395.2078 found 395.2080.



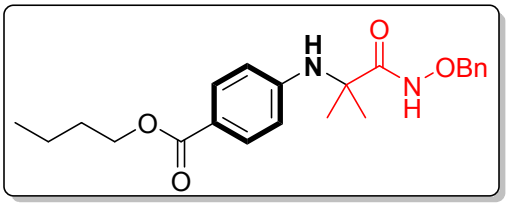
N-(benzyloxy)-2-(9H-carbazol-9-yl)-2-methylpropanamide (3ac)

The general procedure was followed. White solid (0.293g, 82%), R_f = 0.4 (25:75 EtOAc:hexanes, visualized by 254 nm UV light). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.38 (s, 1H), 8.12 (d, J = 7.7 Hz, 2H), 7.62 (d, J = 8.5 Hz, 2H), 7.42 (ddd, J = 8.5, 7.2, 1.3 Hz, 2H), 7.33 – 7.24 (m, 5H), 7.17 (d, J = 6.1 Hz, 2H), 4.83 (s, 2H), 2.09 (s, 6H). ^{13}C{1H} NMR (δ ppm): 172.9, 140.2, 134.7, 129.4, 128.8, 128.5, 126.1, 124.8, 120.2, 120.1, 112.6, 78.2, 64.2, 26.9. HRMS (EI) calcd for $C_{23}H_{22}N_2O_2$ ($M+H^+$) 359.1754 found 359.1754.

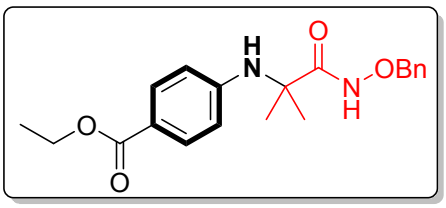


Butyl 4-((1-((benzyloxy)amino)-2-methyl-1-oxopropan-2-yl)amino)benzoate (3ad)

The general procedure was followed. White solid (0.299g, 78%), R_f = 0.2 (20:80 EtOAc:hexanes, visualized by 254 nm UV light). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.12 (s, 1H), 7.85 (d, J = 8.6 Hz, 2H), 7.31 (s, 5H), 6.53 (d, J = 8.8 Hz, 2H), 4.89 (s, 2H), 4.28 (t, J = 6.6 Hz, 2H), 4.19 (s, 1H), 1.76 – 1.70 (m, 4H), 1.53 (s, 6H), 1.47 (dd, J = 15.0, 7.5 Hz, 3H), 0.98 (t, J = 7.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.0, 166.5, 148.2, 134.9, 131.2, 129.3, 128.7, 128.5, 121.0, 114.6, 64.3, 57.4, 30.8, 26.1, 19.2, 13.7. HRMS (EI) calcd for $C_{22}H_{29}N_2O_4$ ($M+H^+$) 385.2122 found 385.2126.

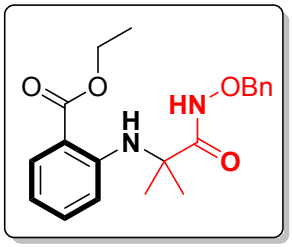


Ethyl 4-((1-((benzyloxy)amino)-2-methyl-1-oxopropan-2-yl)amino)benzoate (3ae)



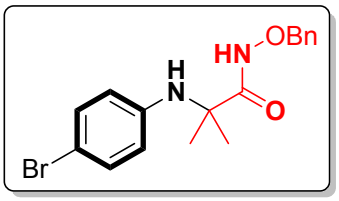
The general procedure was followed. Red solid (0.281g, 79%), R_f = 0.2 (20:80 EtOAc:hexanes, visualized by 254 nm UV light). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.08 (s, 1H), 7.92 – 7.81 (m, 2H), 7.34 – 7.30 (m, 5H), 6.58 – 6.48 (m, 2H), 4.91 (s, 2H), 4.35 (d, *J* = 7.1 Hz, 2H), 4.13 (s, 1H), 1.55 (s, 6H), 1.39 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.0, 166.4, 148.1, 134.9, 131.2, 129.3, 128.7, 128.5, 121.0, 114.6, 78.1, 60.4, 57.4, 26.1, 14.4. HRMS (EI) calcd for $C_{20}H_{25}N_2O_4$ ($M+H^+$) 357.1809 found 357.1813.

Ethyl 2-((1-((benzyloxy)amino)-2-methyl-1-oxopropan-2-yl)amino)benzoate (3af)



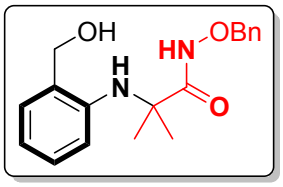
The general procedure was followed. White solid (0.270 g, 76%), R_f = 0.4 (30:50 EtOAc:hexanes, visualized by 254 nm UV light). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.12 (s, 1H), 8.04 (s, 1H), 7.98 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.33 – 7.31 (m, 5H), 6.75 – 6.70 (m, 1H), 6.57 (dd, *J* = 8.4, 0.5 Hz, 1H), 4.89 (s, 2H), 4.30 (q, *J* = 7.1 Hz, 2H), 1.58 (s, 6H), 1.39 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.9, 168.6, 148.0, 135.0, 134.0, 131.9, 129.3, 128.7, 128.4, 116.6, 114.9, 112.5, 78.0, 60.6, 56.7, 26.1, 14.2. HRMS (EI) calcd for $C_{20}H_{25}N_2O_4$ ($M+H^+$) 357.1809 found 357.1813.

N-(benzyloxy)-2-((4-bromophenyl)amino)-2-methylpropanamide (3ag)



The general procedure was followed. White solid (0.318g, 88%), R_f = 0.4 (30:70 EtOAc:hexanes, visualized by 254 nm UV light). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.18 (s, 1H), 7.35 (s, 5H), 7.28 – 7.25 (m, 2H), 6.50 – 6.34 (m, 2H), 4.92 (s, 2H), 3.71 (s, 1H), 1.50 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.4, 143.2, 135.0, 131.9, 129.2, 128.7, 128.5, 117.4, 111.4, 78.0, 57.5, 25.9. HRMS (EI) calcd for $C_{17}H_{20}BrN_2O_2$ ($M+H^+$) 363.0703 found 363.0713.

N-(benzyloxy)-2-((2-(hydroxymethyl)phenyl)amino)-2-methylpropanamide (3ah)

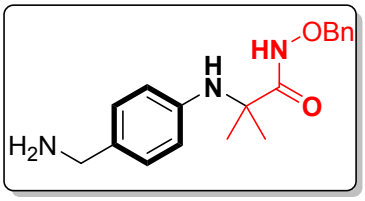


The general procedure was followed. White solid (0.261g, 83%), R_f = 0.2 (50:50 EtOAc:hexanes, visualized by 254 nm UV light). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.33 (s, 1H), 7.33 – 7.27 (m, 5H), 6.96 (d, *J* = 8.0 Hz, 1H), 6.71 (dd, *J* = 7.9, 1.8 Hz, 1H), 6.55 (d, *J* = 1.1 Hz, 1H), 5.19 (s, 1H), 4.85 (s, 2H), 4.55 (s, 2H), 2.58 (s, 1H), 1.52 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.4, 145.2, 134.8, 130.3, 129.3, 128.7,

128.5, 124.1, 117.9, 114.4, 78.2, 64.1, 57.0, 29.7, 26.2. HRMS (EI) calcd for $C_{18}H_{23}N_2O_3$ ($M+H^+$) 315.1703 found 315.1705.

2-((4-(aminomethyl)phenyl)amino)-N-(benzyloxy)-2-methylpropanamide (3ah′)

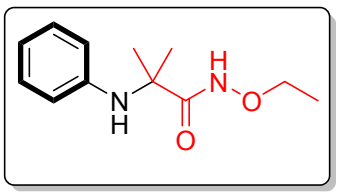
The general procedure was followed. Yellow oil (0.288 g, 87%), R_f = 0.25 (20:80 MeOH:EtOAc, visualized by 254 nm UV light). ^{1}H NMR (500 MHz, CD_3OD) δ 7.40-7.38 (m, 2H), 7.35-7.33 (m, 3H), 7.21 (d, J = 8.6 Hz, 1H), 6.62 (d, J = 8.6 Hz, 1H), 4.82 (s, 2H), 3.98 (s, 2H), 1.47 (s, 6H). ^{13}C NMR (101 MHz, CD_3OD) δ 174.0, 146.4, 135.3, 129.5, 129.1, 128.2, 128.0, 121.6, 118.3, 115.4, 115.0, 77.4, 56.2, 42.8, 24.7. HRMS (EI) calcd for $C_{18}H_{24}N_3O_2$ ($M+H^+$) 314.1863 found 314.1867.



Functional group tolerance

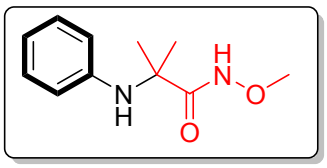
Further, functional group tolerance was demonstrated by alkylation of aniline **1a** in presence of additives like carboxylic acid (benzoic acid), alkyne (Phenyl acetylene), and alkene (styrene) which provided the desired product **3a** without hampering the yield, and the additives were recovered intact after the reaction, this underpins the sheer mildness of this reaction. (Reaction was conducted in a vessel with equimolar aniline and additives under standard reaction condition).

N-ethoxy-2-methyl-2-(phenylamino)propanamide (3ai)



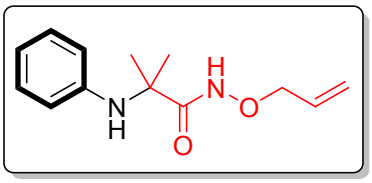
The general procedure was followed. White solid (0.197g, 90%), R_f = 0.2 (20:80 EtOAc:hexanes, visualized by 254 nm UV light). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.32 (s, 1H), 7.22 – 7.17 (m, 2H), 6.82 (t, J = 7.4 Hz, 1H), 6.60 (dd, J = 8.6, 1.0 Hz, 2H), 3.96 (q, J = 7.0 Hz, 2H), 1.53 (s, 6H), 1.25 – 1.22 (t, J = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.4, 148.1, 134.9, 131.2, 129.3, 128.7, 121.1, 114.6, 78.1, 60.4, 57.4, 29.7, 27.9, 26.1, 14.4. HRMS (EI) calcd for $C_{12}H_{19}N_2O_2$ ($M+H^+$) 223.1441 found 223.1442.

N-methoxy-2-methyl-2-(phenylamino)propanamide (3aj)



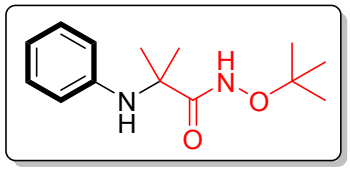
The general procedure was followed. whilte solid (0.187g, 90%), R_f = 0.2 (20:80 EtOAc:hexanes, visualized by 254 nm UV light). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.37 (s, 1H), 7.21 (dd, J = 8.5, 7.4 Hz, 2H), 6.85 (d, J = 7.4 Hz, 1H), 6.60 (dd, J = 8.6, 0.9 Hz, 2H), 3.77 (s, 3H), 1.54 (s, 6H). HRMS (EI) calcd for $C_{11}H_{17}N_2O_2$ ($M+H^+$) 209.1285 found 209.1291.

N-(allyloxy)-2-methyl-2-(phenylamino)propanamide (3ak)



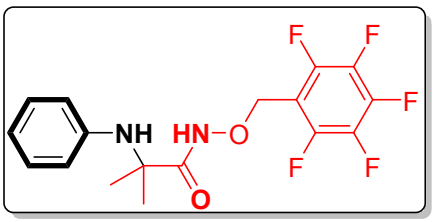
The general procedure was followed. white solid (0.180 g, 77%), R_f = 0.2 (20:80 EtOAc:hexanes, visualized by 254 nm UV light). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.41 (s, 1H), 7.18 (t, *J* = 7.6 Hz, 2H), 6.83 (d, *J* = 7.3 Hz, 1H), 6.61 (d, *J* = 7.9 Hz, 2H), 6.00 – 5.89 (m, 1H), 5.27 (d, *J* = 12.6 Hz, 2H), 4.38 (d, *J* = 6.3 Hz, 2H), 1.52 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.8, 144.2, 132.1, 129.1, 120.7, 119.4, 116.0, 57.5, 26.1, 26.1. HRMS (EI) calcd for $C_{13}H_{18}N_2O_2$ ($M+H^+$) 235.1441 found 235.1448.

N-(tert-butoxy)-2-methyl-2-(phenylamino)propanamide (3al)



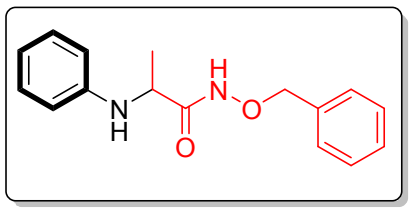
The general procedure was followed. White solid (0.195 g, 78%), R_f = 0.2 (20:80 EtOAc:hexanes, visualized by 254 nm UV light). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.99 (s, 1H), 7.21 (dd, *J* = 8.4, 7.5 Hz, 2H), 6.84 (t, *J* = 7.4 Hz, 1H), 6.64 (d, *J* = 7.7 Hz, 2H), 1.56 (s, 6H), 1.26 (s, 9H). HRMS (EI) calcd for$C_{14}H_{23}N_2O_2$ ($M+H^+$) 251.1754 found 251.1755.

2-methyl-N-(perfluorophenoxy)-2-(phenylamino)propanamide (3am)



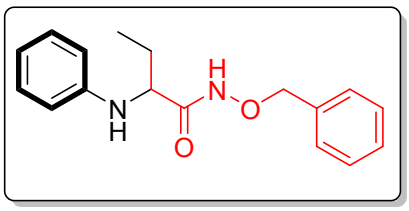
The general procedure was followed. Yellow Oil, (0.284 g, 79 %), R_f = 0.3 (30:70 EtOAc:hexanes, visualized by 254 nm UV light). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.36 (s, 1H), 7.20 (dd, *J* = 8.4, 7.5 Hz, 2H), 6.84 (t, *J* = 7.4 Hz, 1H), 6.56 (d, *J* = 7.7 Hz, 2H), 5.07 (s, 2H), 1.51 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.6, 144.0, 129.2, 119.6, 115.8, 64.3, 57.6, 26.0. HRMS (EI) calcd for $C_{16}H_{14}F_5N_2O_2$ ($M+H^+$) 375.1126 found 375.1127.

N-(benzyloxy)-2-(phenylamino)propanamide (3an)



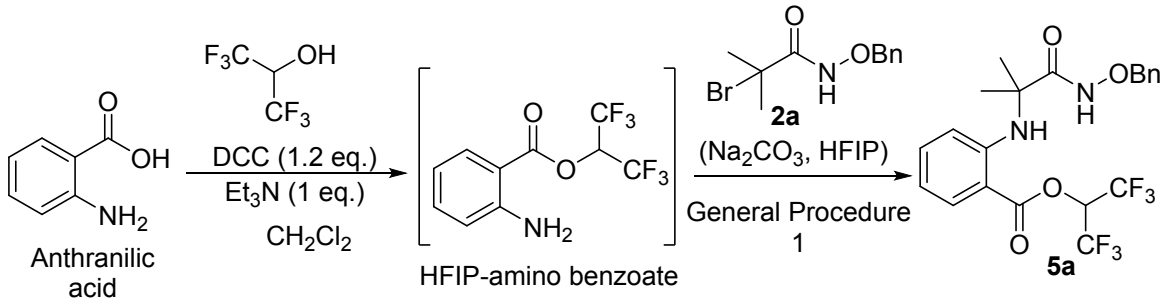
The general procedure was followed. White solid (0.205g, 76%), R_f = 0.2 (20:80 EtOAc:hexanes, visualized by 254 nm UV light). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.23 (s, 1H), 7.28 (dd, *J* = 7.6, 4.3 Hz, 6H), 7.18 (t, *J* = 7.8 Hz, 2H), 6.80 (t, *J* = 7.3 Hz, 1H), 6.57 (d, *J* = 8.0 Hz, 2H), 4.85 (dd, *J* = 33.9, 11.2 Hz, 2H), 1.48 (d, *J* = 6.8 Hz, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.9, 146.1, 134.8, 129.4, 128.7, 128.5, 119.4, 113.6, 78.2, 54.2, 19.6. HRMS (EI) calcd for $C_{16}H_{18}N_2O_2$ ($M+H^+$) 271.1441 found 271.1451.

N-(benzyloxy)-2-(phenylamino)butanamide (3ao)



The general procedure was followed. White solid (0.218g, 77%), R_f = 0.3 (30:70 EtOAc:hexanes, visualized by 254 nm UV light). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.25 (s, 1H), 7.36 – 7.25 (m, 5H), 7.22 (t, *J* = 7.9 Hz, 2H), 6.84 (t, *J* = 7.4 Hz, 1H), 6.67 – 6.56 (m, 2H), 4.86 (dd, *J* = 29.4, 11.2 Hz, 2H), 3.90 (s, 1H), 3.81 – 3.67 (m, 1H), 2.06 – 1.91 (m, 1H), 1.87 – 1.69 (m, 1H), 1.04 (t, *J* = 7.5 Hz, 3H).). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.5, 146.6, 134.9, 129.4, 128.7, 128.5, 119.1, 113.6, 78.3, 59.6, 26.6, 10.3. HRMS (EI) calcd for $C_{17}H_{21}N_2O_2$ ($M+H^+$) 285.1598 found 285.1602.

S2.2 Synthesis of 5a via Steglich Esterification

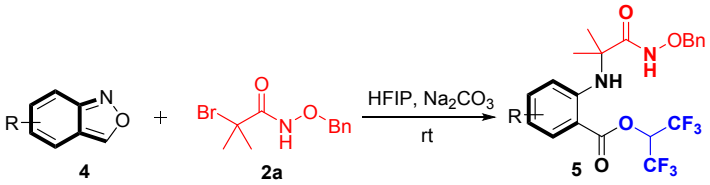


To a stirred solution of anthranilic acid (100 mg, 0.73 mmol) and hexafluoroisopropyl alcohol (HFIP) (147 mg, 0.87 mmol) in anhydrous CH_2Cl_2 (5 mL) at 0 °C, was added Et_3N (0.10 mL, 0.73 mmol), and 1,3-Dicyclohexylcarbodiimide (DCC) (62 mg, 0.95 mmol) and the solution was allowed to stir at 0 °C for 3 h. Resulting suspension was filtered over celite and the solvent reduced in vacuo. Purification by flash column chromatography (20% EtOAc/hexane) gave the desired HFIP amino benzoate ester (136 mg, 65% yield) as colorless semi solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 – 7.91 (m, 1H), 7.39 (ddd, J = 8.6, 7.2, 1.6 Hz, 1H), 6.78 – 6.67 (m, 2H), 6.03 (hept, J = 6.2 Hz, 1H), 5.77 (s, 2H). Obtained compound was then converted to the congested amine following the General procedure 1 as described for **3**, furnishing **5a** in 81% yield. However, procedure being non-greener and multistep, an alternative pathway was devised to synthesize the hindered amine **5a**, using anthranil as aminating reagent as described in General procedure 2, and was adapted for the synthesis of other HFIP esters **5b** and **5c.**

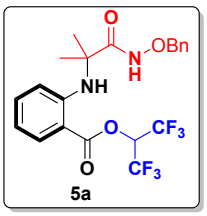
S2.3 General Procedure 2; for the synthesis of 5

In a flame dried round bottom flask, anthranil **4** (50 mg, 0.42 mmol) and haloamide **2a** (148 mg, 0.55 mmol) was dissolved in HFIP (0.1 M) at room temperature (rt) followed by addition of Na_2CO_3(89 mg, 0.84 mmol). Reaction mixture was then stirred at ambient temperature. After the consumption of starting material (typically 30 mins), reaction mixture was quenched with water followed by workup

with ethyl acetate. Organics were washed with brine and dried over anhyd. Na_2SO_4. Evaporation of organic solvent gave crude which was purified over flash column chromatography (10-15% EtOAc/Hexanes) to afford the desired product **5a** (89% yield).



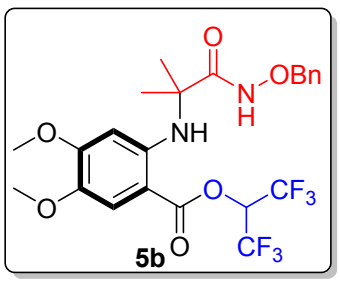
1,1,3,3,3-hexafluoropropan-2-yl2-((1-((benzyloxy)amino)-2-methyl-1-oxopropan-2-yl)amino)benzoate (5a)



The general procedure was followed. Whilte solid (0.179 g, 89 %), R_f = 0.4 (20:80 EtOAc:Hexanes, visualized by 254 nm UV light). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.93 (brs, 1H), 8.03 (dd, 1H, *J* = 1.3, 8.1 Hz), 7.63 (brs, 1H), 7.31-7.25 (m, 5H), 6.80 (t, 1H, *J* = 7.5 Hz), 6.31 (m, 1H), 5.95 (sept, 1H, *J* = 6.2 Hz), 4.86 (s, 2H), 1.58 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.4, 164.7, 149.3, 136.3, 134.9, 132.4, 129.5, 128.9, 128.6, 120.6 (q, *J* = 280.3 Hz), 117.4, 115.2, 108.8, 78.3, 66.5 (sept, *J* = 35.1 Hz), 57.1, 26.2. HRMS (ESI) calcd. for $C_{21}H_{21}F_6N_2O_4$ ($M+H^+$) 479.1400; found: 479.1413.

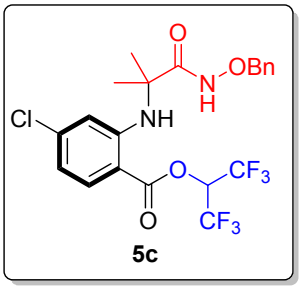
^{19}F NMR (376 MHz, $CDCl_3$) δ – 73.1(d, *J* = 10.4 Hz)

1,1,1,3,3,3-hexafluoropropan-2-yl 2-((1-((benzyloxy)amino)-2-methyl-1-oxopropan-2-yl)amino)-4,5-dimethoxybenzoate (5b)



The general procedure was followed. White solid (0.187 g, 83%), R_f = 0.38 (20:80 EtOAc:Hexanes, visualized by 254 nm UV light). ^{1}H NMR (500 MHz, $CDCl_3$) **δ** 8.29 (brs, 1H), 7.64 (s, 1H), 7.39 (brs, 1H), 7.35-7.32 (m, 5H), 6.10 (s, 1H), 5.98 (sept, 1H, *J* = 6.1 Hz), 4.90 (s, 2H), 3.89 (s, 3H), 3.87 (s, 3H), 1.60 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.8, 163.9, 156.7, 146.9, 141.1, 134.8, 129.2, 128.8, 128.5, 120.5 (q, *J* = 283.2 Hz), 113.2, 99.6, 97.8, 78.3, 66.3 (sept, *J* = 35.1 Hz), 57.0, 56.5, 56.1, 26.2. HRMS (ESI) calcd. for $C_{23}H_{25}F_6N_2O_6$ ($M+H^+$) 539.1611; found: 539.1621.

1,1,1,3,3,3-hexafluoropropan-2-yl 2-((1-((benzyloxy)amino)-2-methyl-1-oxopropan-2-yl)amino)-4-chlorobenzoate (5c)

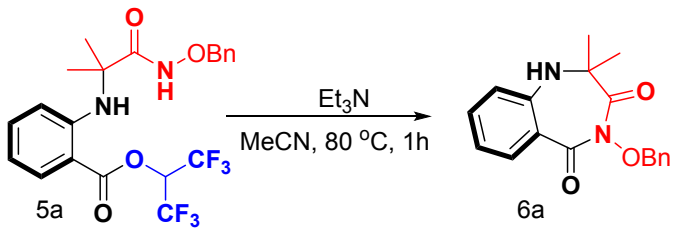


The general procedure was followed. White solid (0.176 g, 82%), R_f = 0.47 (20:80 EtOAc:Hexanes, visualized by 254 nm UV light). ^{1}H NMR (500 MHz, $CDCl_3$) **δ** 8.88 (brs, 1H), 7.90 (d, 1H, *J* = 2.5 Hz), 7.64 (brs, 1H), 7.37-7.29 (m, 6H), 6.56 (d, 1H, *J* = 9.1 Hz), 5.95 (sept, 1H, *J* = 6.1 Hz), 4.89 (s, 2H), 1.59

(s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.8, 163.8, 154.0, 147.7, 136.2, 134.8, 131.2, 129.2, 128.8, 128.5, 120.1 (q, J = 279.7 Hz), 116.3, 109.5, 78.2, 66.6 (sept, J = 35.1 Hz), 57.1, 26.1. **HRMS (ESI)** calcd. for $C_{21}H_{20}ClF_6N_2O_4$ ($M+H^+$) 513.8407; found: 513.8411.

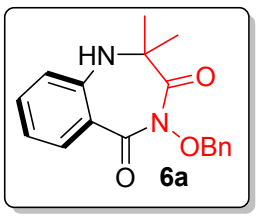
S2.4 General Procedure for the synthesis of 6

In a 10 mL reaction vial, **5a** (0.2 mmol) dissolved in acetonitrile and triethylamine (0.3 mmol) was added. Reaction mixture was then stirred at 80 °C and monitored through TLC. After the consumption of starting material (**5a**) (typically 1 h), reaction mixture was quenched with water followed by workup with ethyl acetate. Organics were washed with brine and dried over anhyd. Na_2SO_4. Evaporation of organic solvent gave crude which was purified over flash column chromatography (10-15% EtOAc/Hexanes) to afford the desired product **6a** (98% yield).

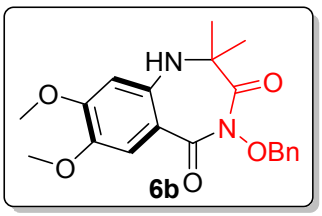


4-(benzyloxy)-2,2-dimethyl-1,2-dihydro-3H-benzo[e][1,4]diazepine-3,5(4H)-dione (6a)

The general procedure was followed. Creamy semi-solid (0.60 g, 98%), R_f = 0.4 (5:95 EtOAc:Hexanes, visualized by 254 nm UV light). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.24 (dd, 1H, J = 2.5, 13 Hz), 7.55-7.52 (m, 2H), 7.36-7.31 (m, 4H), 7.00 (dt, 1H, J = 1.8, 13 Hz), 6.77 (dd, 1H, J = 1.4, 13.5 Hz), 5.02 (s, 2H), 4.24 (brs, 1H), 1.42 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.8, 163.6, 144.9, 134.6, 134.5, 133.3, 129.9, 128.9, 128.4, 120.7, 119.9, 118.0, 57.6, 29.8, 24.8. HRMS (ESI) calcd. for $C_{18}H_{19}N_2O_3$ ($M+H^+$) 311.1390; found: 311.1392.

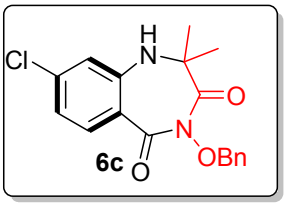


4-(benzyloxy)-7,8-dimethoxy-2,2-dimethyl-1,2-dihydro-3H-benzo[e][1,4]diazepine-3,5(4H)-dione



(6b) The general procedure was followed. Yellow solid (0.73 g, 99%), R_f = 0.48 (30:70 EtOAc:Hexanes, visualized by 254 nm UV light). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 (s, 1H), 7.59-7.58 (m, 2H), 7.59-7.35 (m, 3H), 6.19 (s, 1H), 5.04 (s, 2H), 3.93 (s, 3H), 3.93 (s, 3H), 1.46 (s, 6H). HRMS (ESI) calcd. for $C_{20}H_{23}N_2O_5$ ($M+H^+$) 371.1601; found: 371.16013.

4-(benzyloxy)-7-chloro-2,2-dimethyl-1,2-dihydro-3H-benzo[e][1,4]diazepine-3,5(4H)-dione (6c)

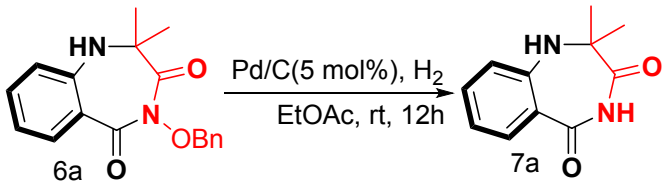


The general procedure was followed. Yellow solid (0.66 g, 97%), R_f = 0.62 (20:80 EtOAc:Hexanes, visualized by 254 nm UV light). ^{1}H NMR

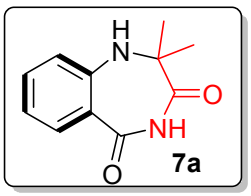
(500 MHz, $CDCl_3$) δ 8.22 (d, 1H, J = 2.5 Hz), 7.56-7.54 (m, 2H), 7.36-7.28 (m, 5H), 6.75 (d, 1H, J = 8.65 Hz), 5.04 (s, 2H), 4.29 (brs, 1H), 1.45 (s, 6H). HRMS (ESI) calcd. for $C_{18}H_{18}ClN_2O_3$ ($M+H^+$) 345.1000; found: 345.1002.

S2.5 General Procedure for the synthesis of 7a

In a 10 mL reaction vial, **6a** (0.1 mmol) dissolved in ethyl acetate under inert atmosphere, Pd/C was added (5 mol %). Reaction vessel was then evacuated/purged with hydrogen (3 times), before letting it stirred at room temperature under hydrogen atmosphere. After the consumption of starting material (**6a**), reaction mixture was filter through celite bed and washed with ethyl acetate. Organics were dried over anhyd. Na_2SO_4. Evaporation of organic solvent gave crude which was purified over flash column chromatography (10-15% EtOAc/Hexanes) to afford the desired product **7a** (94% yield).

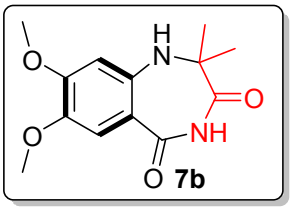


2,2-dimethyl-1,2-dihydro-3H-benzo[e][1,4]diazepine-3,5(4H)-dione (7a)



White solid (0.19 g, 94%), R_f = 0.5 (20:80 EtOAc:Hexanes, visualized by 254 nm UV light). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.25 (d, 1H, J = 8.1 Hz), 8.12 (brs, 1H), 7.43 (t, 1H, J = 8.2 Hz), 7.04 (t, 1H, 8.15), 6.79 (d, 1H, 8.1), 4.12 (brs, 1H), 1.48 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.8, 164.4, 145.7, 134.8, 133.2, 120.8, 120.3, 118.1, 57.6, 24.7. HRMS (ESI) calcd. for $C_{11}H_{12}N_2O_2$ ($M+H^+$) 205.0972; found: 205.0976.

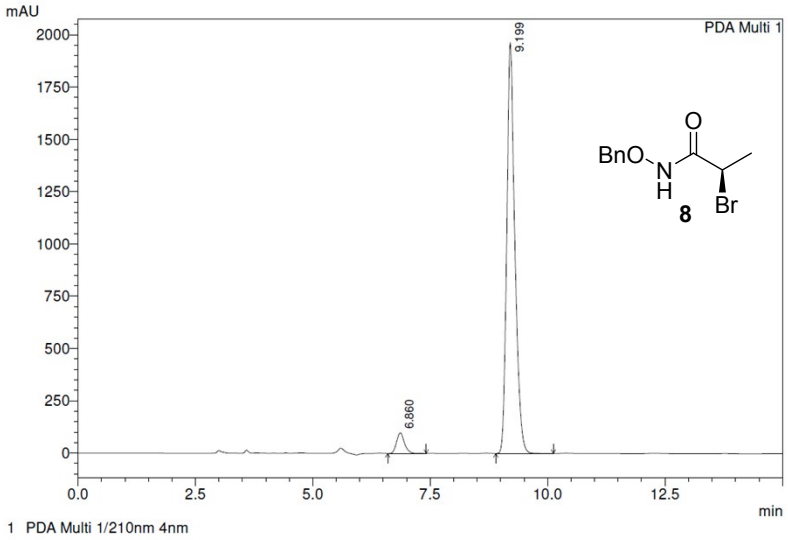
7,8-dimethoxy-2,2-dimethyl-1,2-dihydro-3H-benzo[e][1,4]diazepine-3,5(4H)-dione (7b)



White solid (0.24 g, 93%), R_f = 0.5 (20:80 EtOAc:Hexanes, visualized by 254 nm UV light). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09 (s, 1H), 7.62 (s, 1H), 6.21 (s, 1H), 3.97 (brs, 1H), 3.94 (s, 3H), 3.92 (s, 3H), 1.48 (s, 6H). HRMS (ESI) calcd. for $C_{13}H_{17}N_2O_4$ ($M+H^+$) 265.1183; found: 265.1184.

S2.6 Chromatograms for Experiment with Chiral amide 8

<Chromatogram>



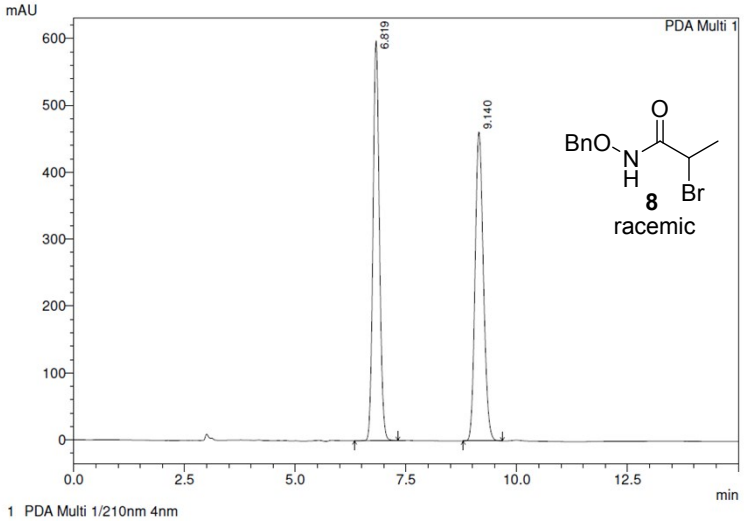
1 PDA Multi 1/210nm 4nm

PeakTable

PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.860	1139535	98356	4.625	4.766
2	9.199	23498691	1965359	95.375	95.234
Total		24638227	2063715	100.000	100.000

<Chromatogram>



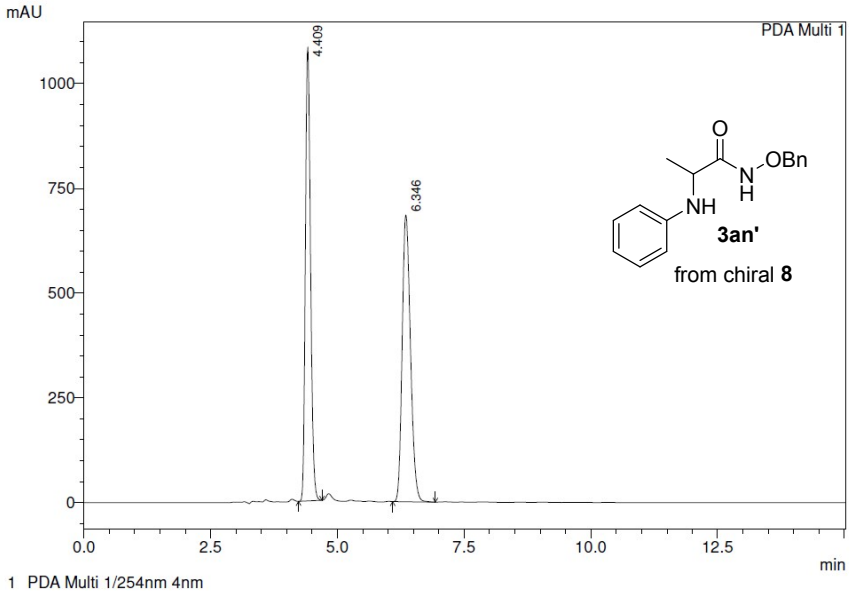
1 PDA Multi 1/210nm 4nm

PeakTable

PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.819	5983774	597944	49.830	56.423
2	9.140	6024707	461813	50.170	43.577
Total		12008481	1059758	100.000	100.000

<Chromatogram>



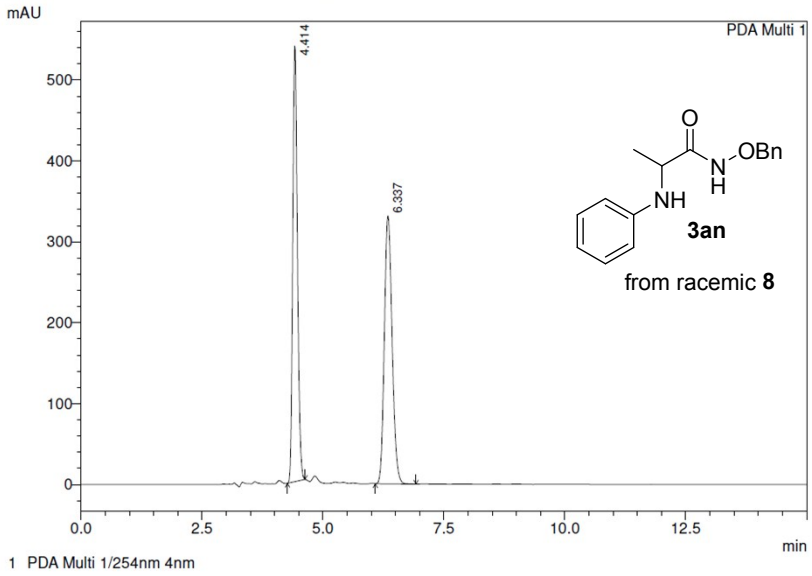
1 PDA Multi 1/254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	4.409	7625887	1083656	49.222	61.279
2	6.346	7867056	684755	50.778	38.721
Total		15492943	1768412	100.000	100.000

<Chromatogram>



1 PDA Multi 1/254nm 4nm

PeakTable

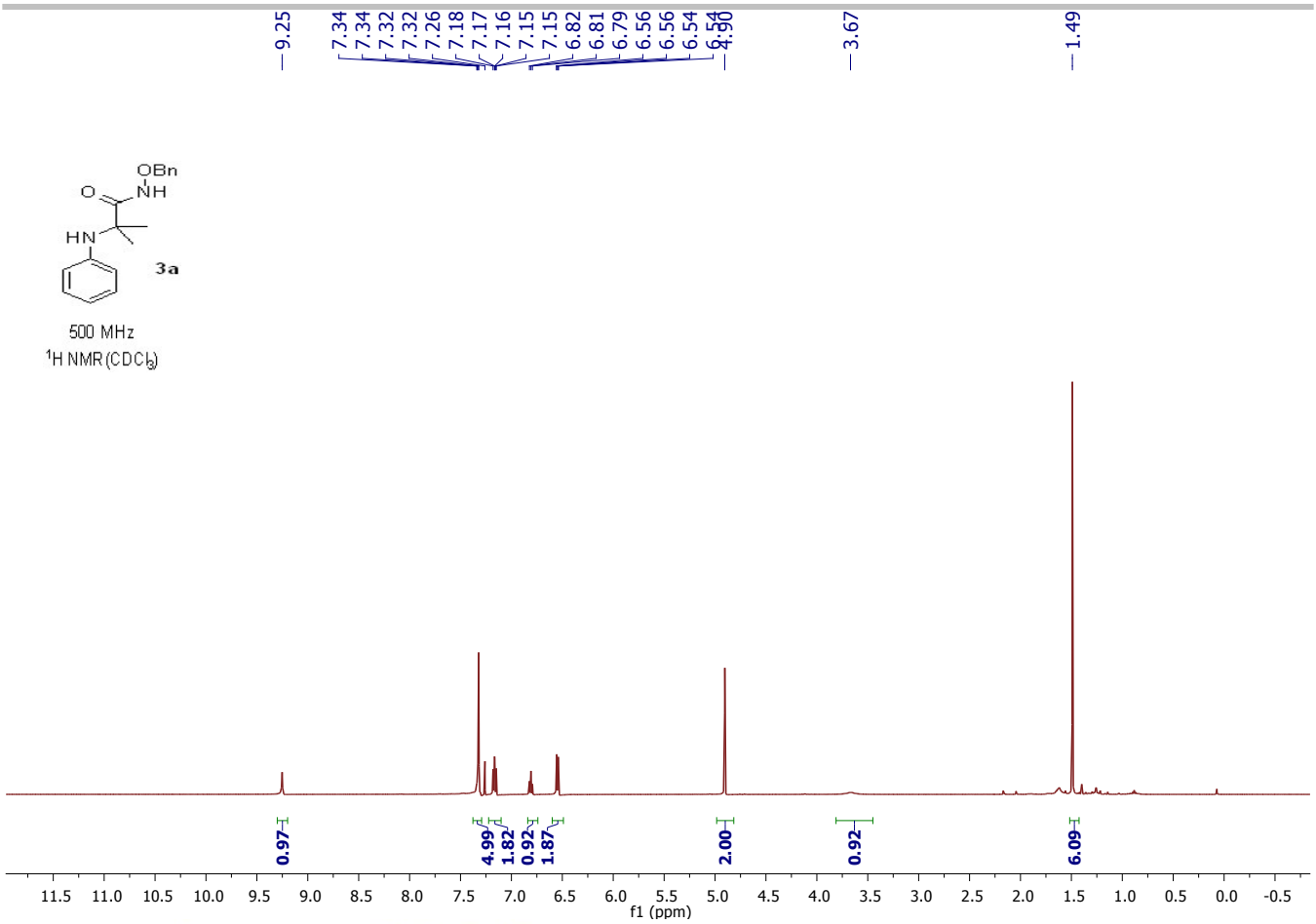
PDA Ch1 254nm 4nm

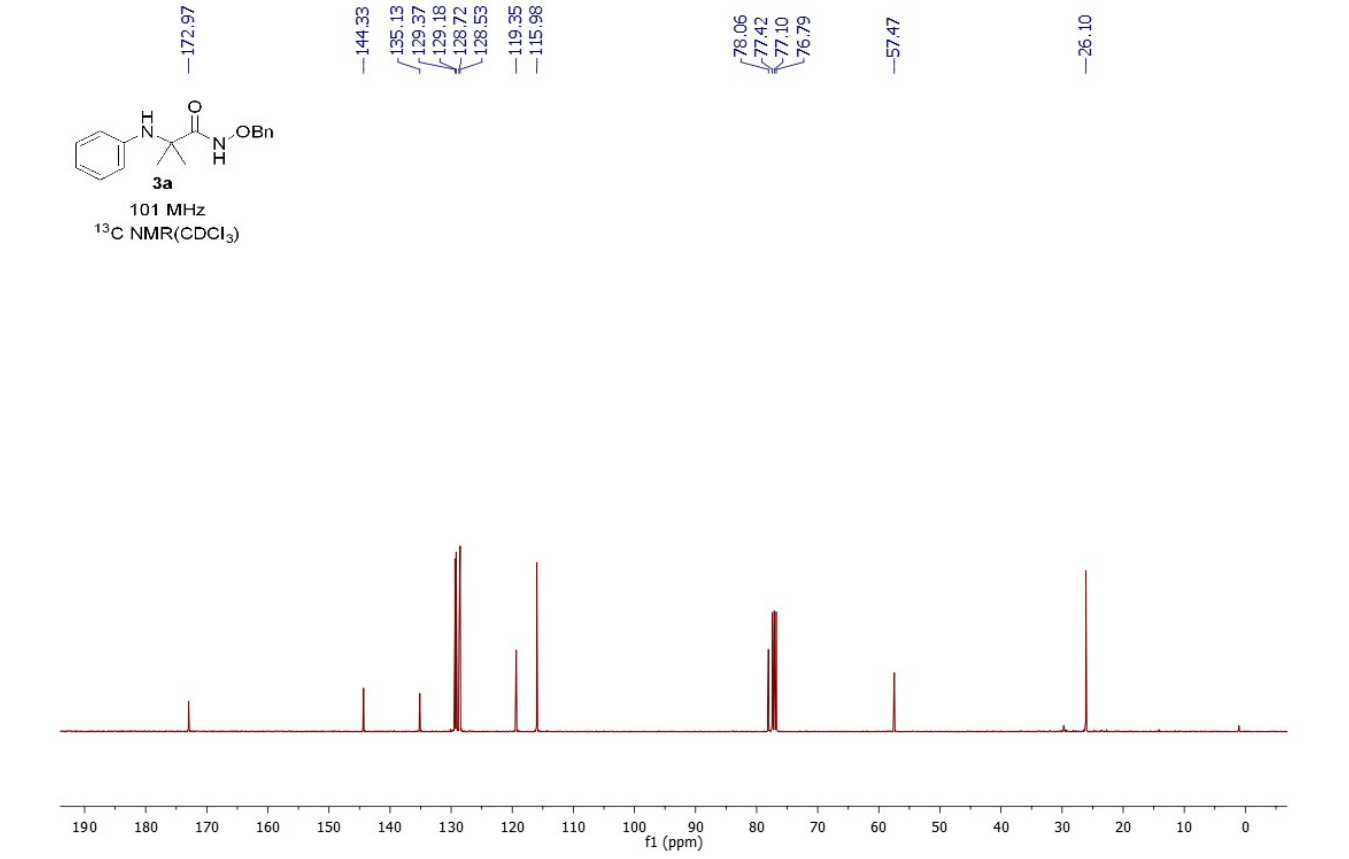
Peak#	Ret. Time	Area	Height	Area %	Height %
1	4.414	3629303	538872	49.596	61.925
2	6.337	3688363	331331	50.404	38.075
Total		7317666	870203	100.000	100.000

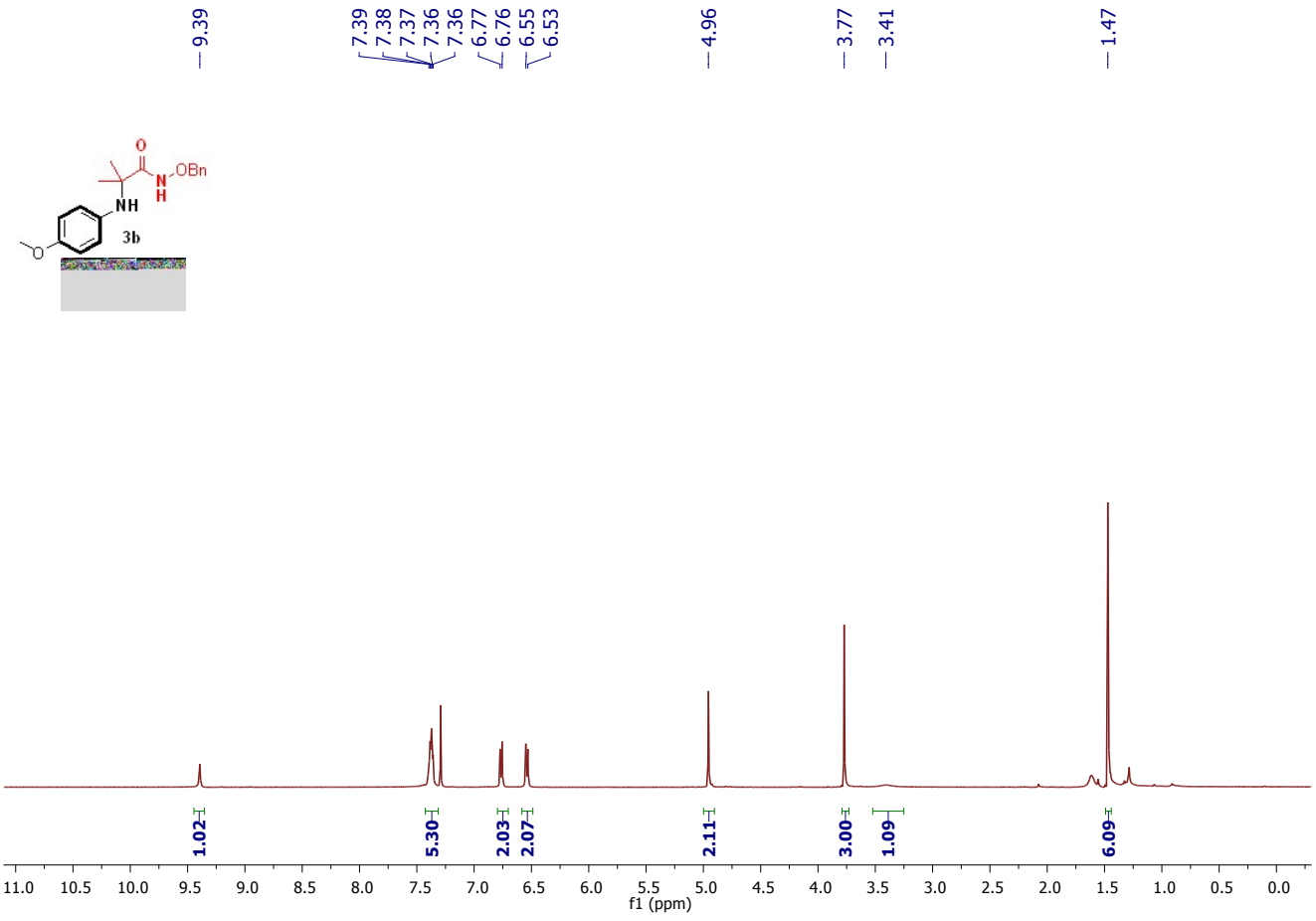
References:

1. C. S. Jeffrey, K. L. Barnes, J. A. Eickhoff and C. R. Carson, *J. Am. Chem. Soc.*, 2011, **133**, 7688-7691.
2. J. Zhou, H. Zhang, X.-L. Chen, Y.-L. Qu, Q. Zhu, C.-G. Feng and Y.-J. Chen, *J. Org. Chem.*, 2019, **84**, 9179-9187.

Copies of ^{1}H,^{13}C NMR Spectra and Representative HRMS


9.25
7.34
7.34
7.32
7.32
7.26
7.18
7.17
7.16
7.15
7.15
6.82
6.81
6.79
6.56
6.56
6.54
6.54
4.90
3.67
1.49
OBn
NH
O
HN
3a
500 MHz
1H NMR(CDCl3)
0.97
4.99
1.82
0.92
1.87
2.00
0.92
6.09
f1 (ppm)


172.97
144.33
135.13
129.37
129.18
128.72
128.53
119.35
115.98
78.06
77.42
77.10
76.79
57.47
26.10
OBn
3a
101 MHz
13C NMR(CDCl3)
f1 (ppm)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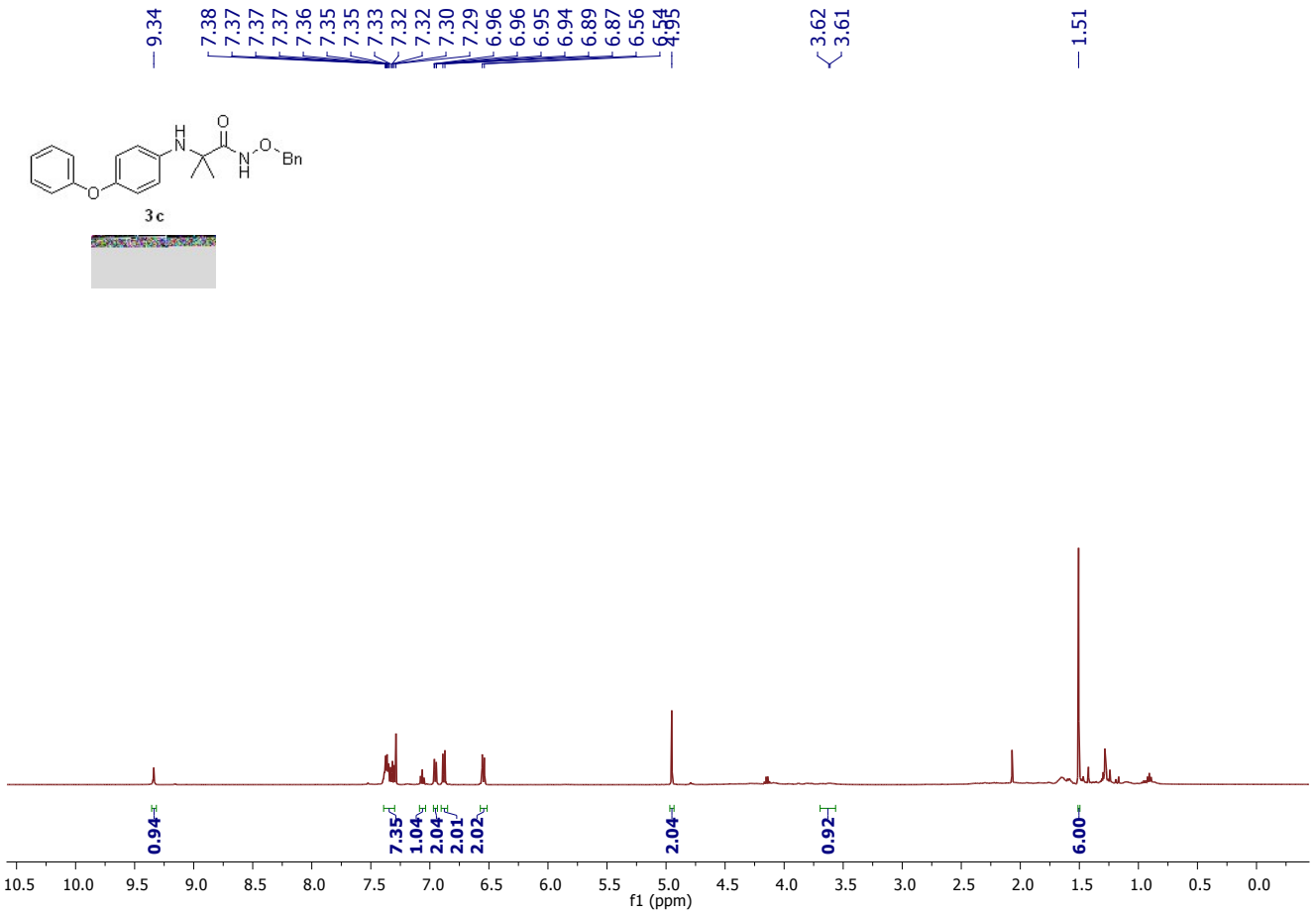
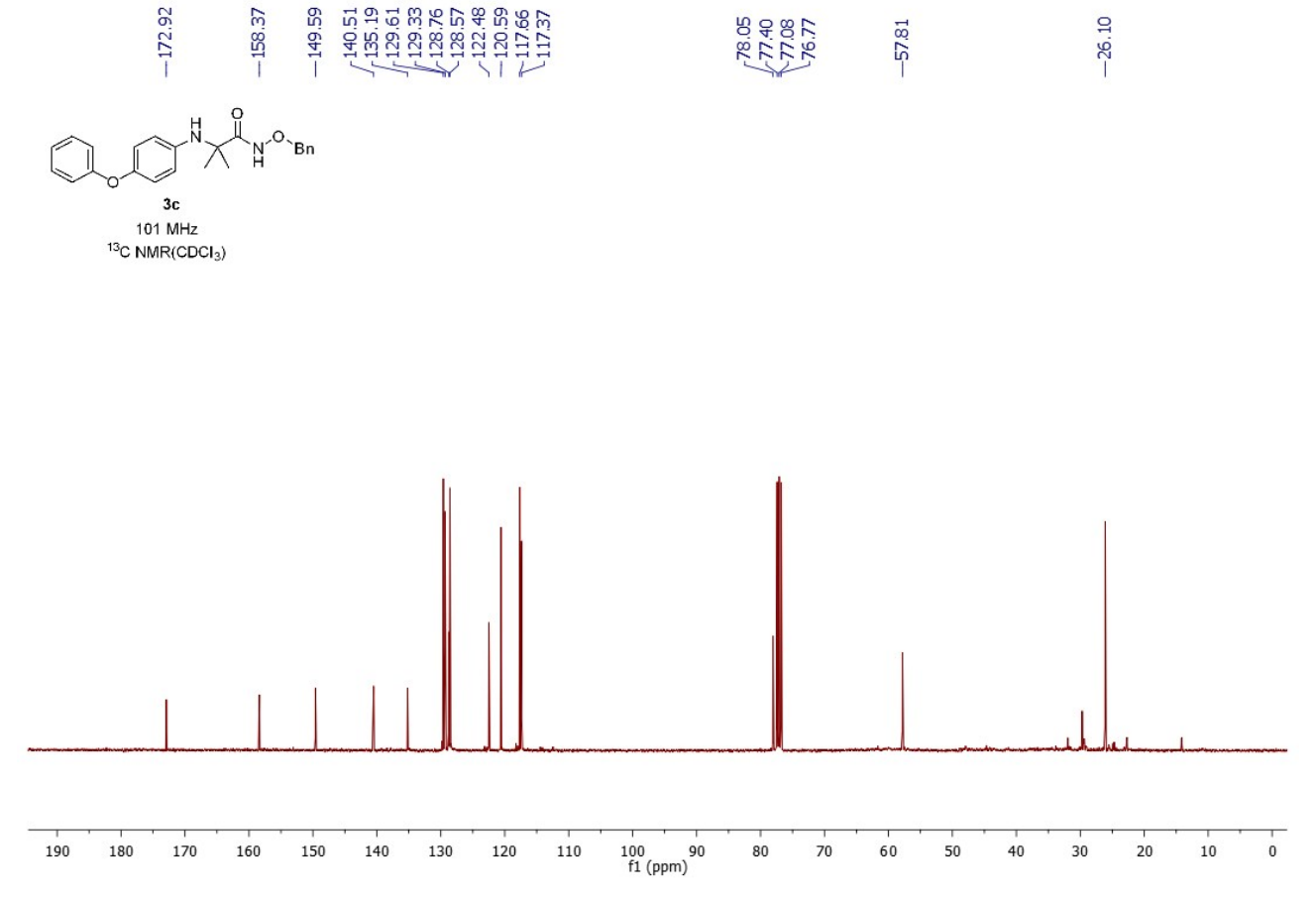
7.39
7.38
7.37
7.36
7.36
6.77
6.76
6.55
6.53
4.96
3.77
3.41
1.47
OBn
NH
3b
1.02
5.30
2.03
2.07
2.11
3.00
1.09
6.09
f1 (ppm)
173.23
153.48
138.00
135.21
129.31
128.70
128.53
117.83
114.61
78.01
77.38
77.06
76.74
57.98
55.64
26.08
3b
101 MHz
13C NMR(CDCl3)


9.34
7.38
7.37
7.37
7.37
7.36
7.35
7.35
7.33
7.32
7.32
7.30
7.29
6.96
6.96
6.95
6.94
6.89
6.87
6.56
6.54
4.95
3.62
3.61
1.51
Bn
3c
0.94
7.35
1.04
2.04
2.01
2.02
2.04
0.92
6.00
f1 (ppm)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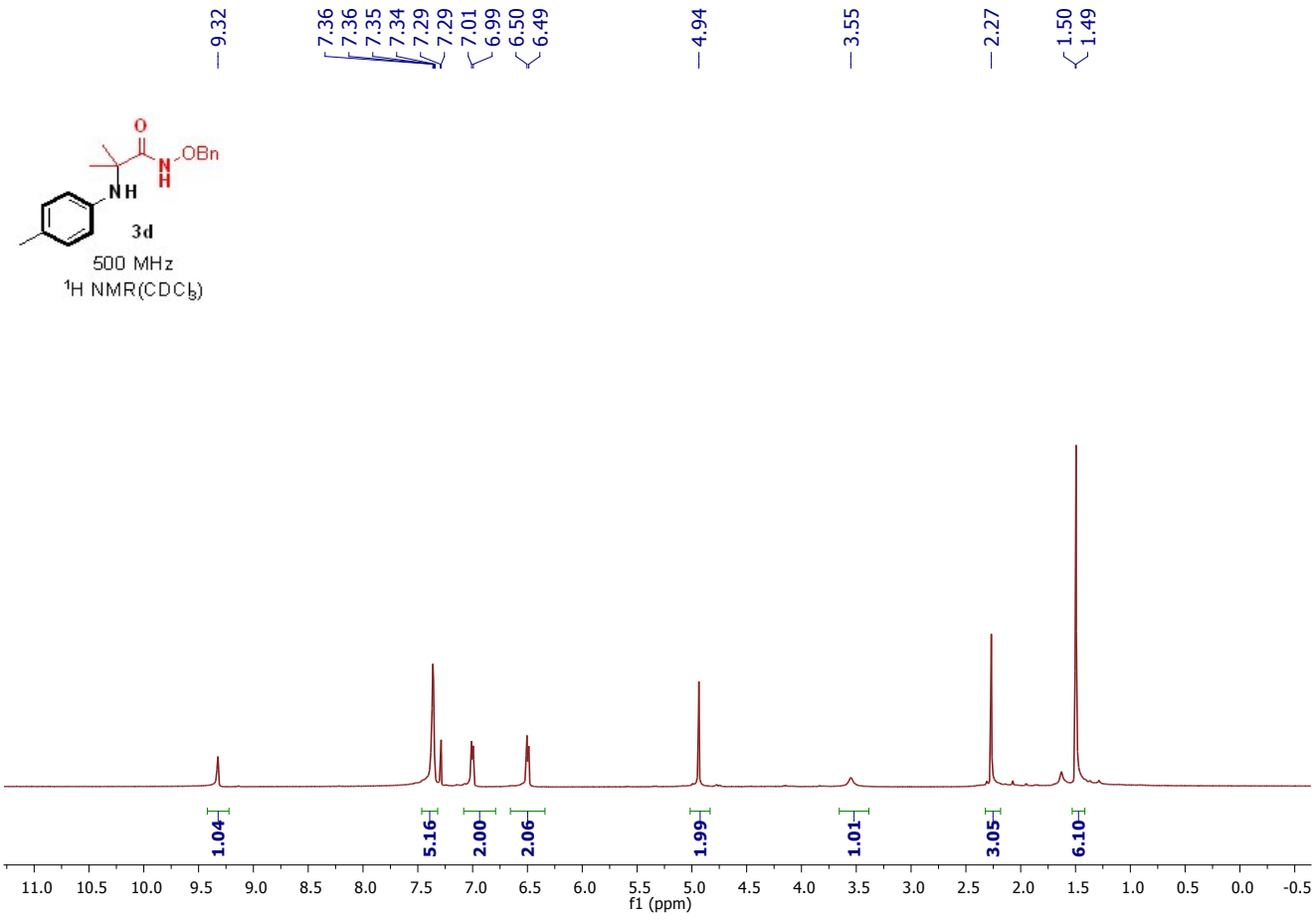
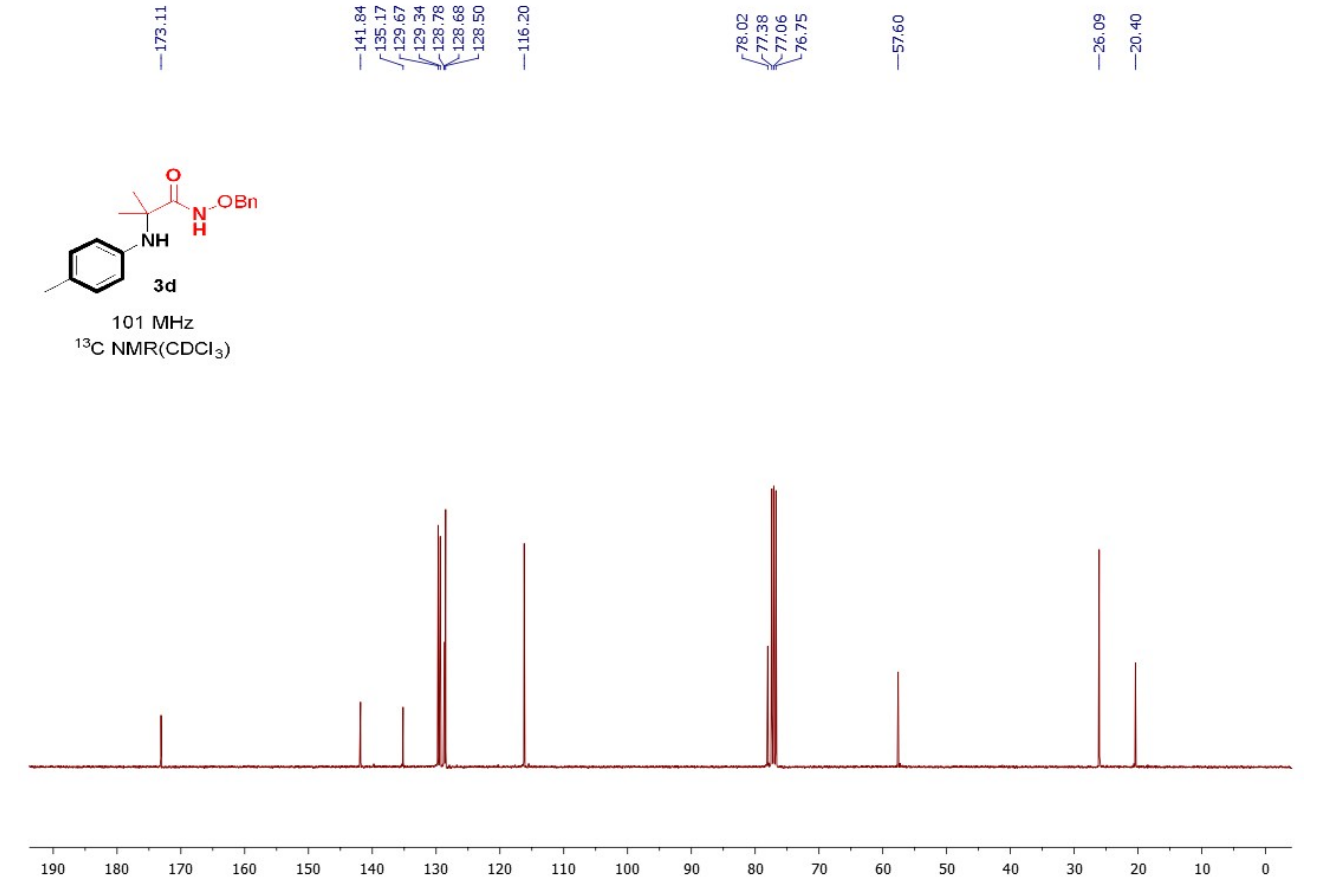
158.37
149.59
140.51
135.19
129.61
129.33
128.76
128.57
122.48
120.59
117.66
117.37
78.05
77.40
77.08
76.77
57.81
26.10
Bn
3c
101 MHz
13C NMR(CDCl3)
f1 (ppm)


9.32
7.36
7.36
7.35
7.34
7.29
7.29
7.01
6.99
6.50
6.49
4.94
3.55
2.27
1.50
1.49
OBn
NH
3d
500 MHz
1H NMR(CDCl3)
1.04
5.16
2.00
2.06
1.99
1.01
3.05
6.10
f1 (ppm)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129.34
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128.68
128.50
116.20
78.02
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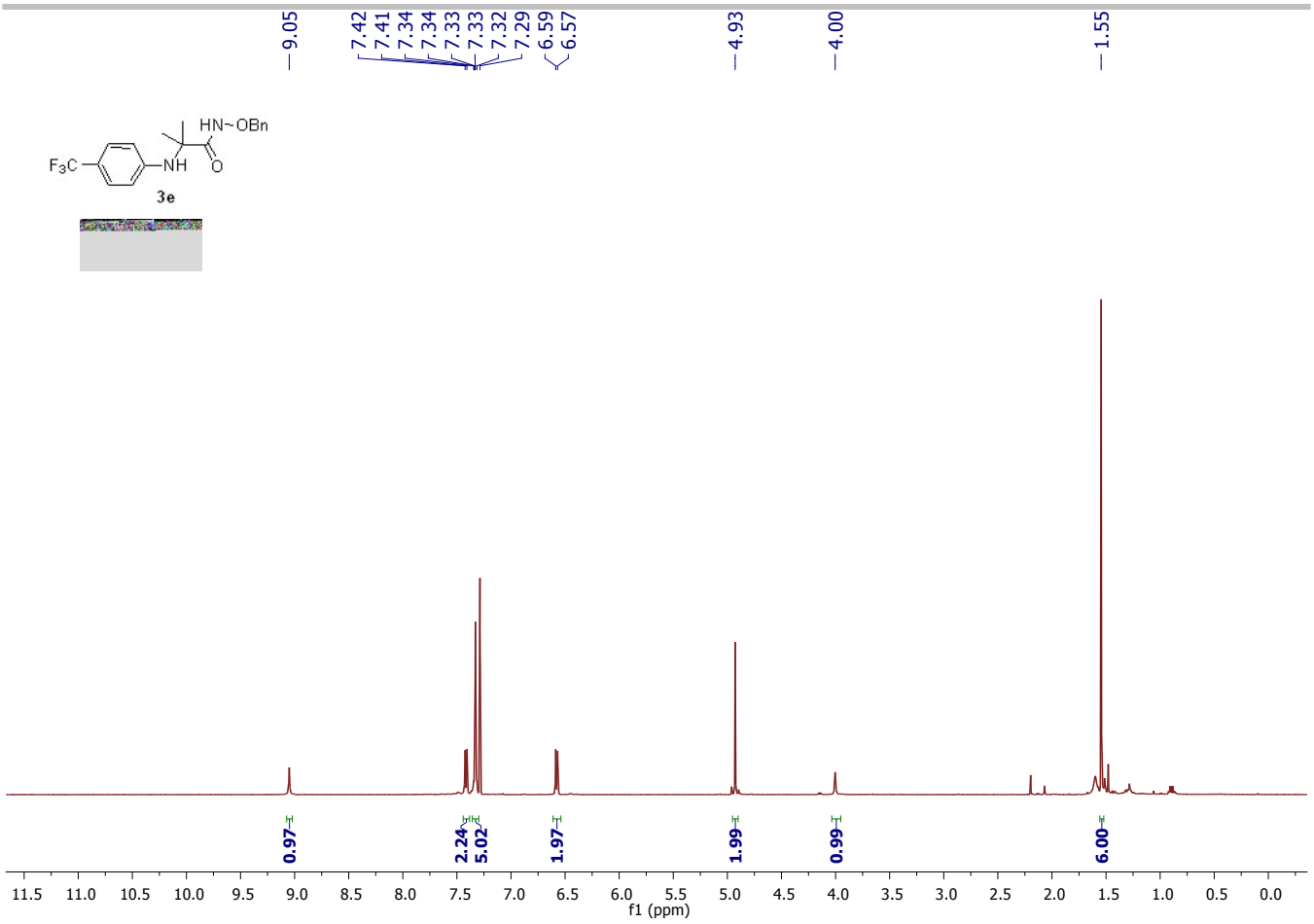
77.06
76.75
57.60
26.09
20.40
OBn
NH
3d
101 MHz
13C NMR(CDCl3)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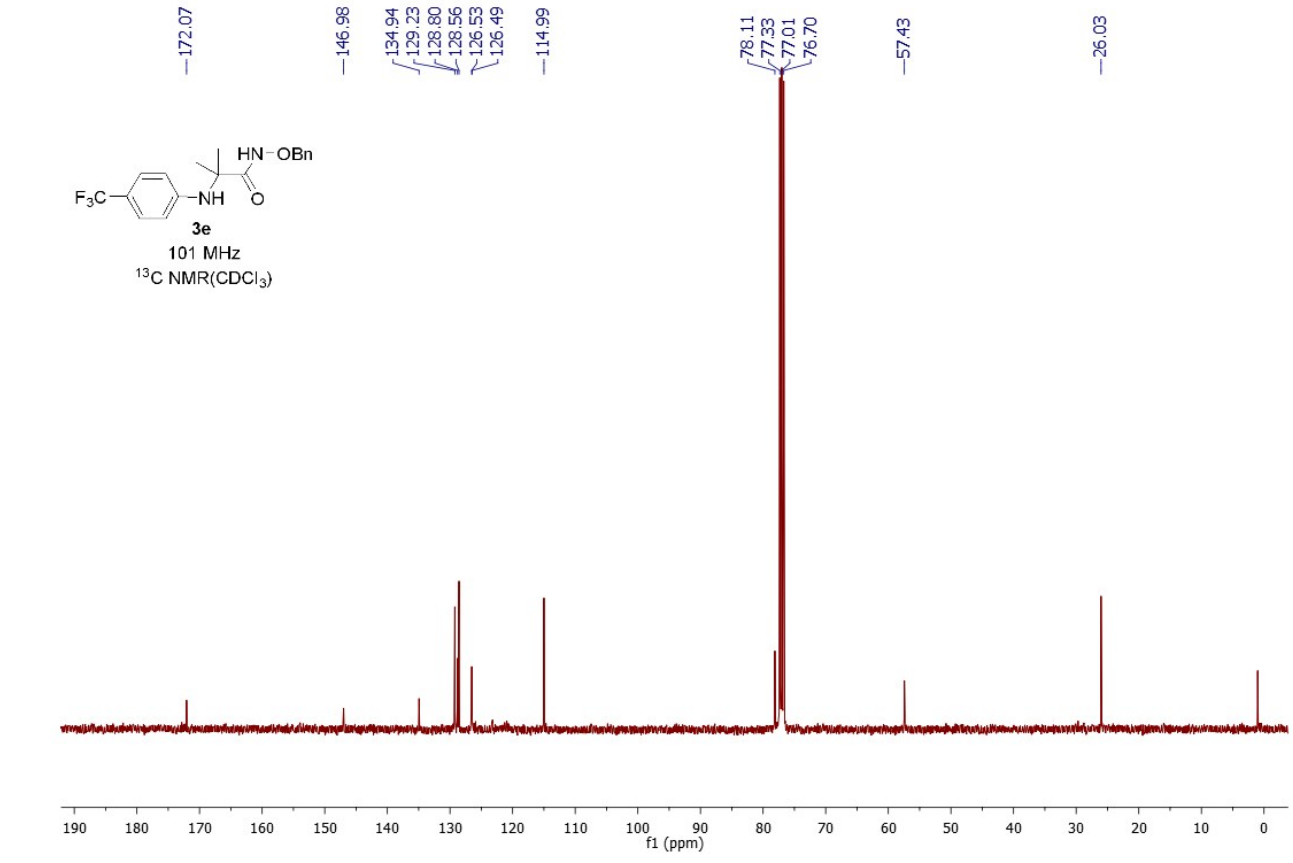
7.42
7.41
7.34
7.34
7.33
7.33
7.32
7.29
6.59
6.57
4.93
4.00
1.55
HN~OBn
F3C
NH
O
3e
0.97
2.24
5.02
1.97
1.99
0.99
6.00
f1 (ppm)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129.23
128.80
128.56
126.53
126.49
114.99
78.11
77.33
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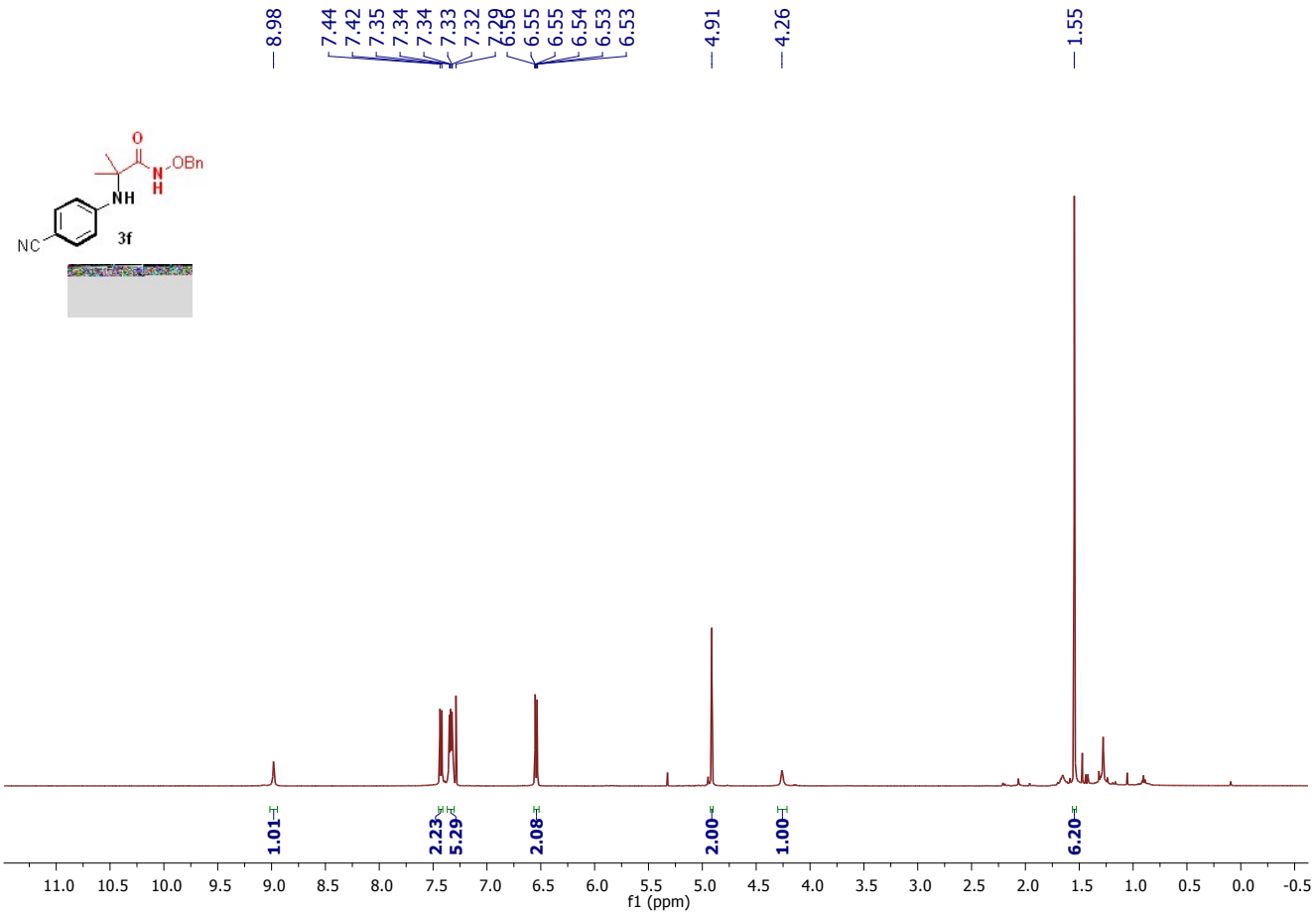
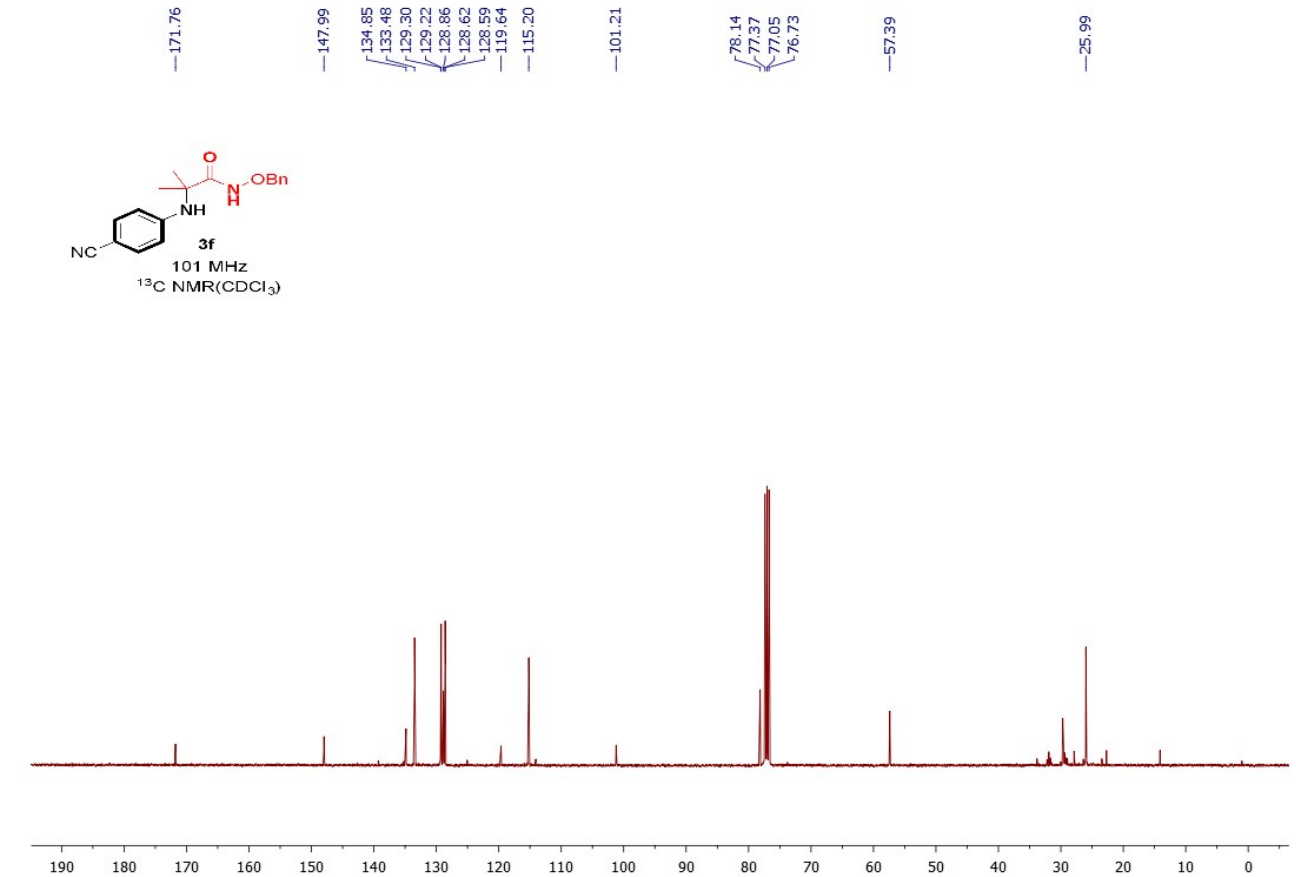
57.43
26.03
HN−OBn
F3C
NH
O
3e
101 MHz
13C NMR(CDCl3)
f1 (ppm)


8.98
7.44
7.42
7.35
7.34
7.34
7.33
7.32
6.56
6.55
6.55
6.54
6.53
6.53
4.91
4.26
1.55
3f
1.01
2.23
5.29
2.08
2.00
1.00
6.20
f1 (ppm)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119.64
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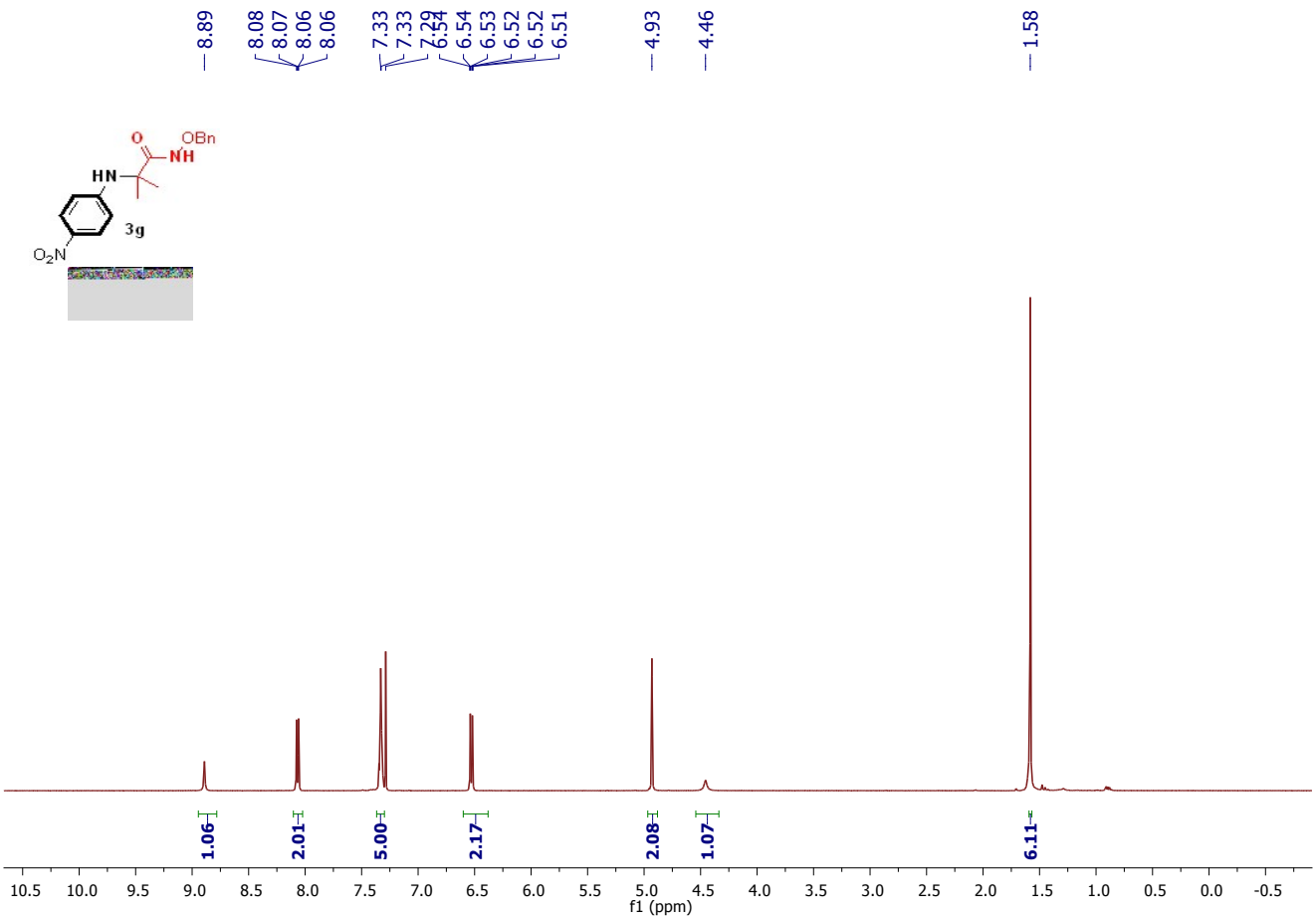
78.14
77.37
77.05
76.73
57.39
25.99
3f
101 MHz
13C NMR(CDCl3)


8.89
8.08
8.07
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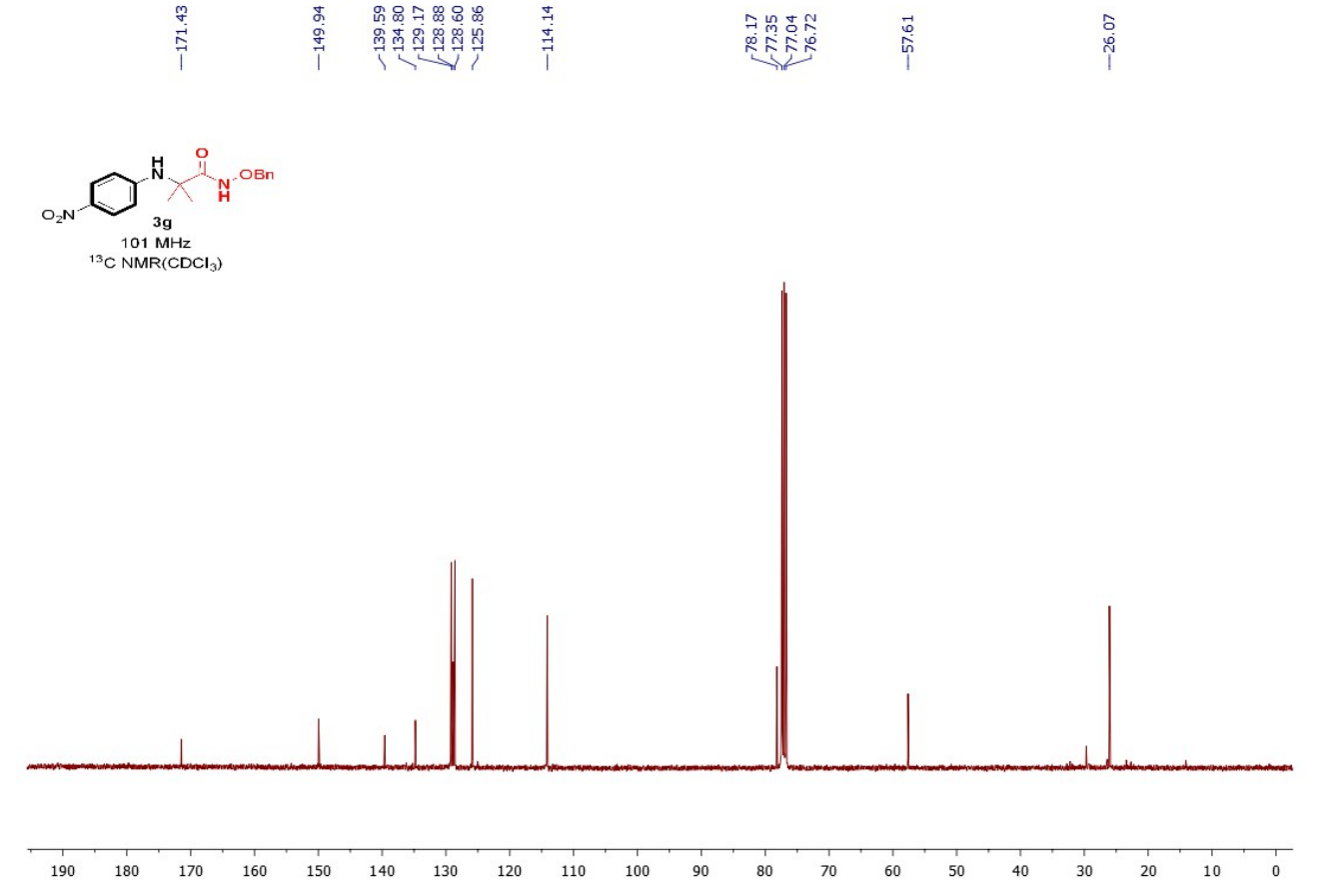
8.06
7.33
7.33
6.54
6.54
6.53
6.52
6.52
6.51
4.93
4.46
1.58
OBn
NH
HN
3g
O2N
1.06
2.01
5.00
2.17
2.08
1.07
6.11
f1 (ppm)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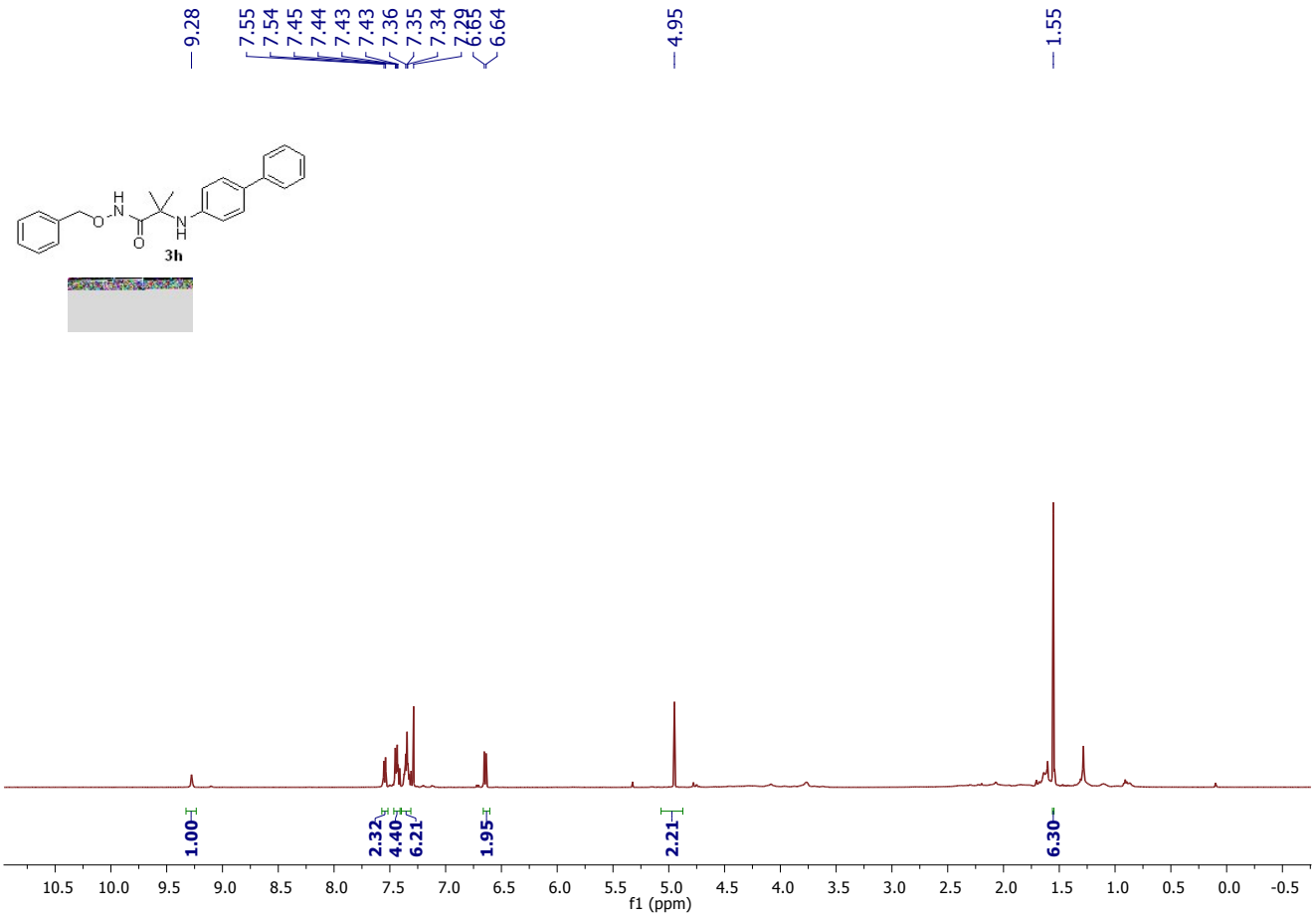
125.86
114.14
78.17
77.35
77.04
76.72
57.61
26.07
OBn
3g
101 MHz
13C NMR(CDCl3)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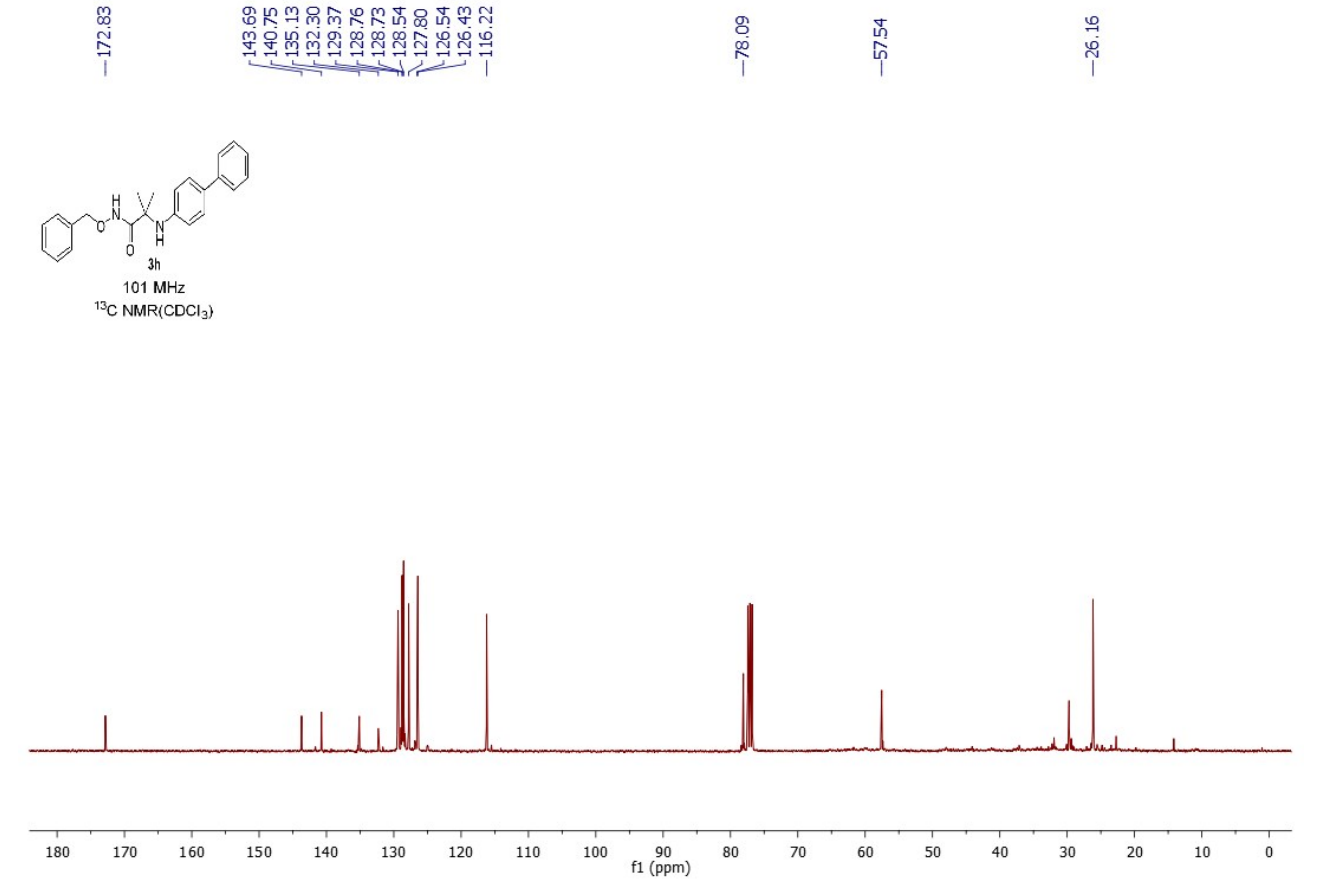
6.30
f1 (ppm)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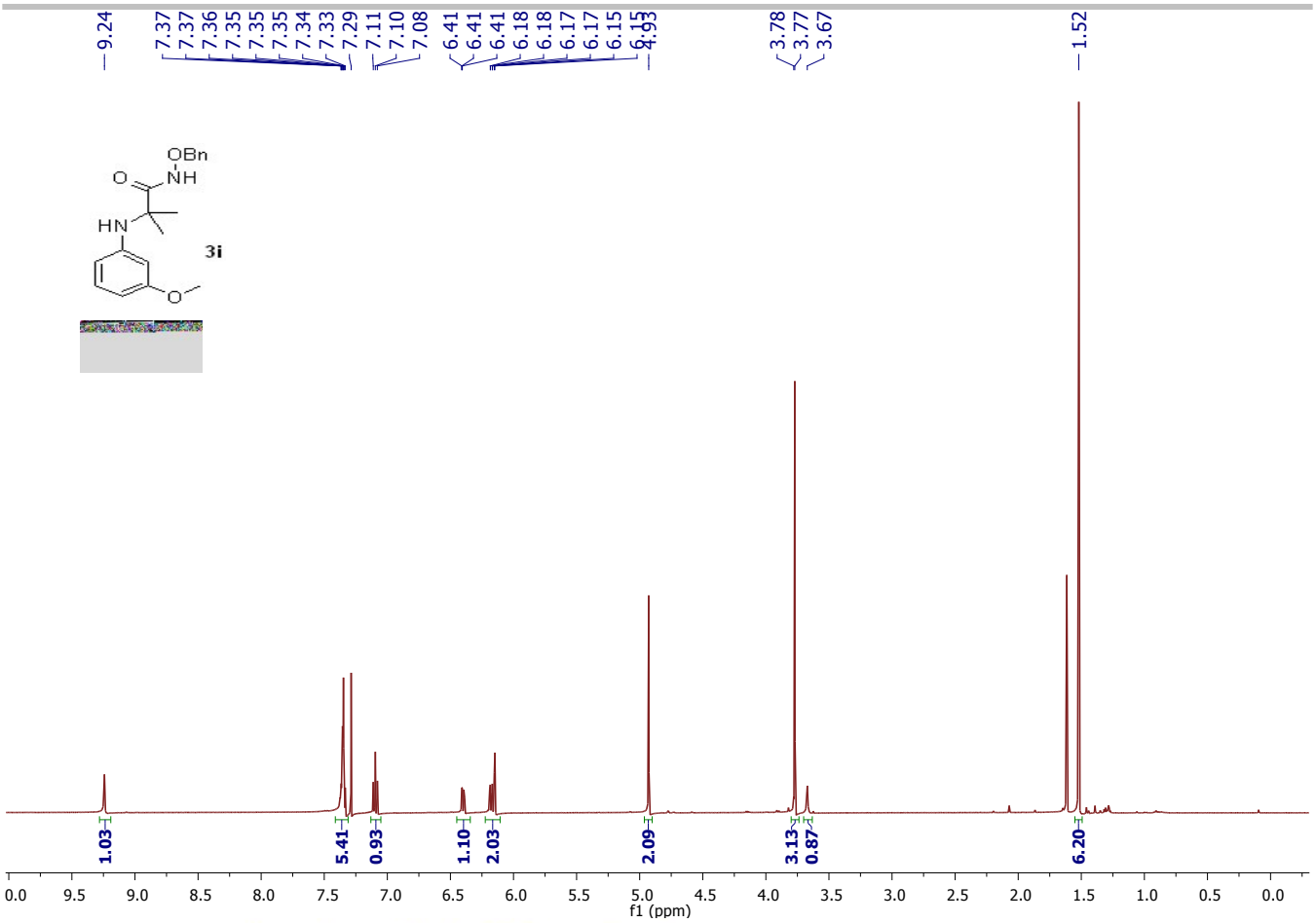
57.54
26.16
3h
101 MHz
13C NMR(CDCl3)
f1 (ppm)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7.36
7.35
7.35
7.35
7.34
7.33
7.29
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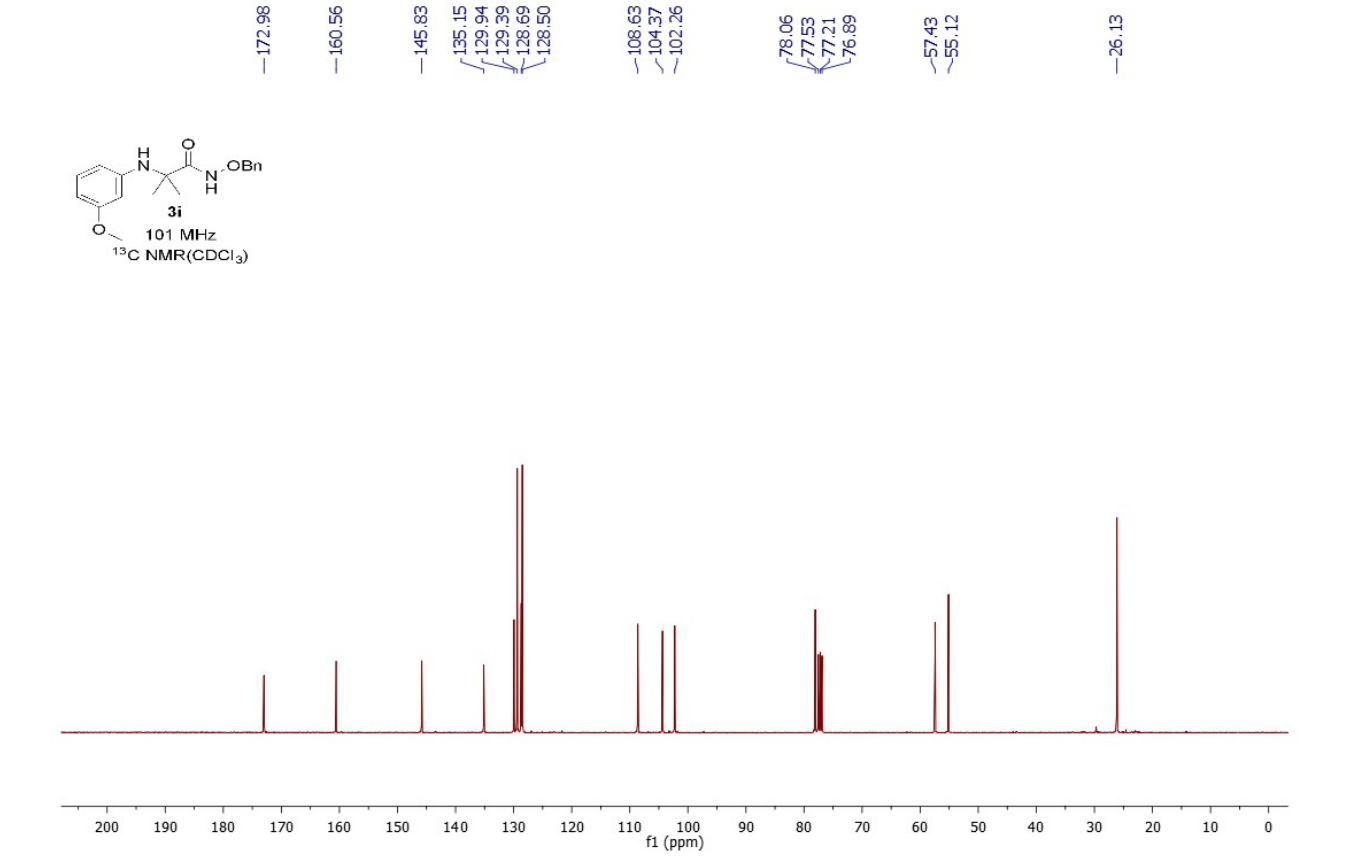
7.08
6.41
6.41
6.41
6.18
6.18
6.17
6.17
6.15
6.15
4.93
3.78
3.77
3.67
1.52
OBn
O
NH
HN
3i
1.03
5.41
0.93
1.10
2.03
2.09
3.13
0.87
6.20
f1 (ppm)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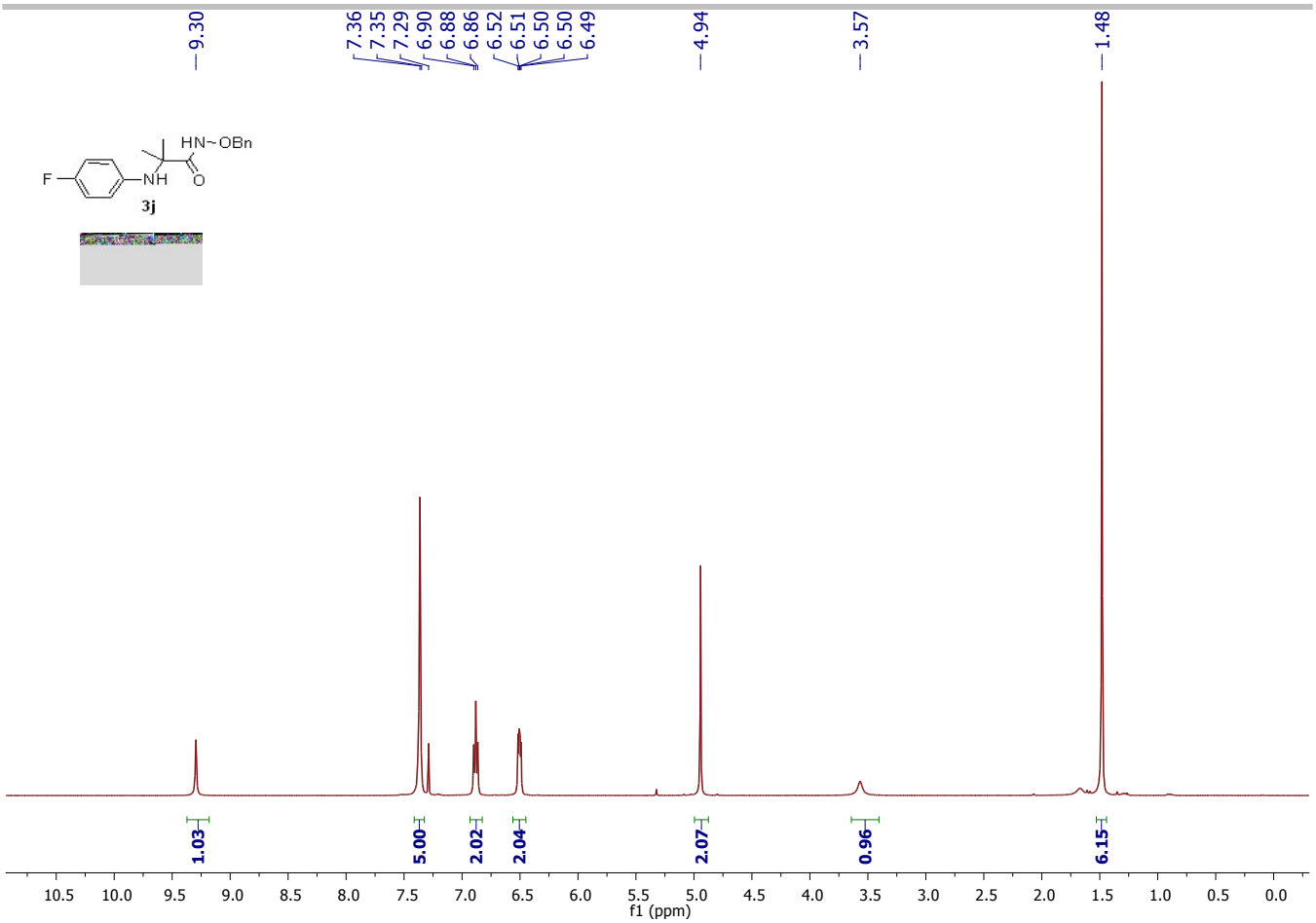
145.83
135.15
129.94
129.39
128.69
128.50
108.63
104.37
102.26
78.06
77.53
77.21
76.89
57.43
55.12
26.13
H
N
O
N
OBn
H
O
3i
101 MHz
13C NMR(CDCl3)
f1 (ppm)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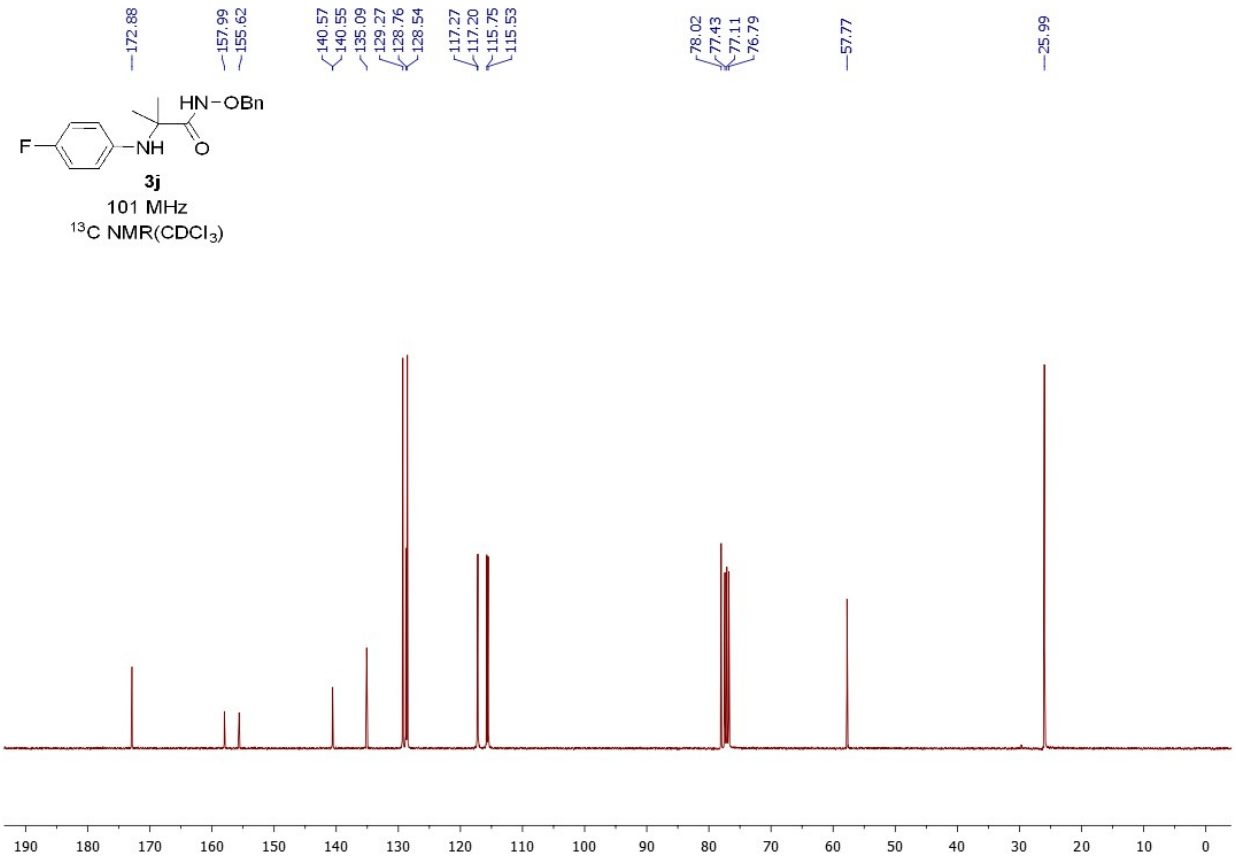
7.36
7.35
7.29
6.90
6.88
6.86
6.52
6.51
6.50
6.50
6.49
4.94
3.57
1.48
HN~OBn
F
NH
O
3j
1.03
5.00
2.02
2.04
2.07
0.96
6.15
f1 (ppm)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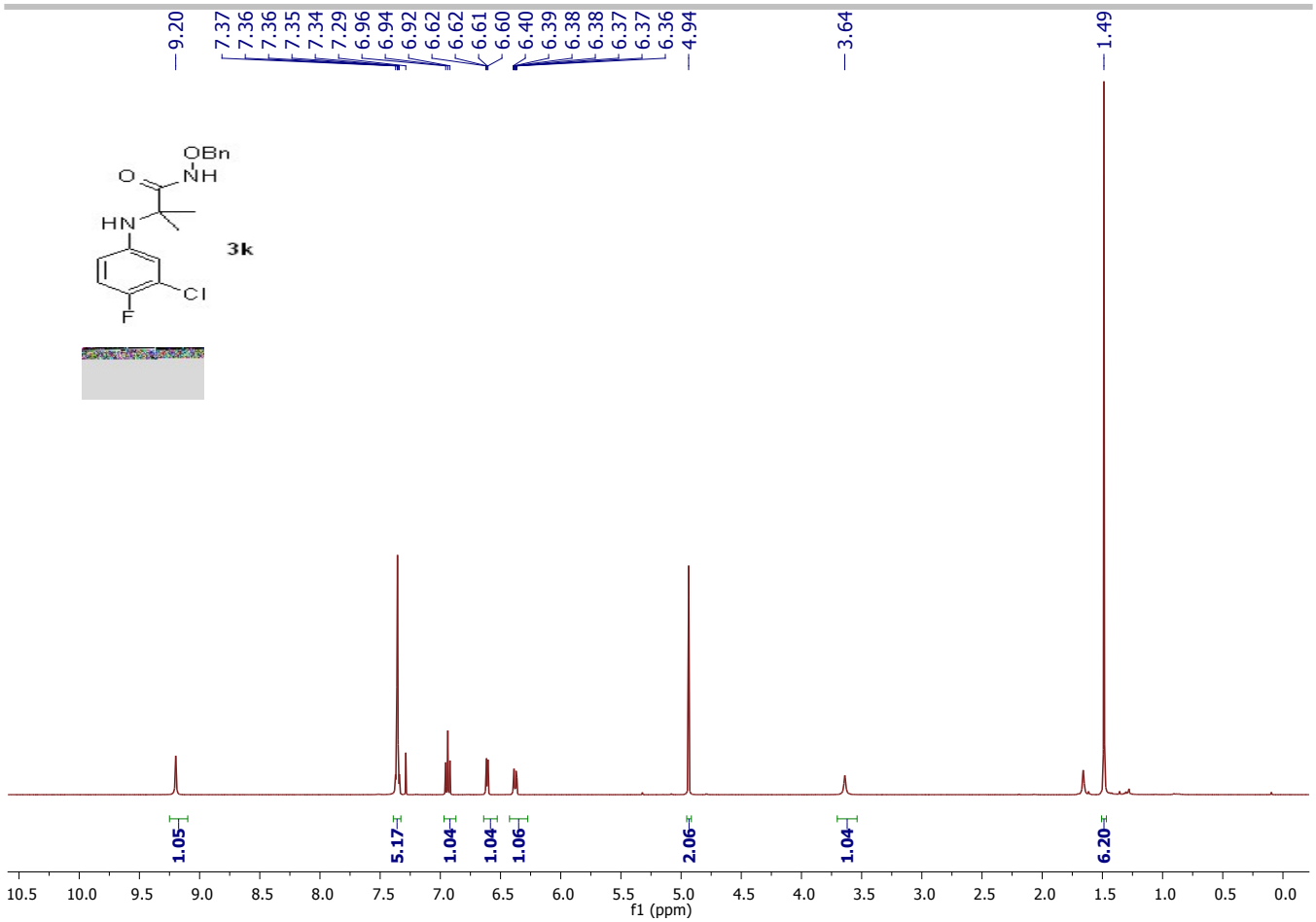
128.76
128.54
117.27
117.20
115.75
115.53
78.02
77.43
77.11
76.79
57.77
25.99
HN−OBn
F
NH
O
3j
101 MHz
13C NMR(CDCl3)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6.94
6.92
6.62
6.62
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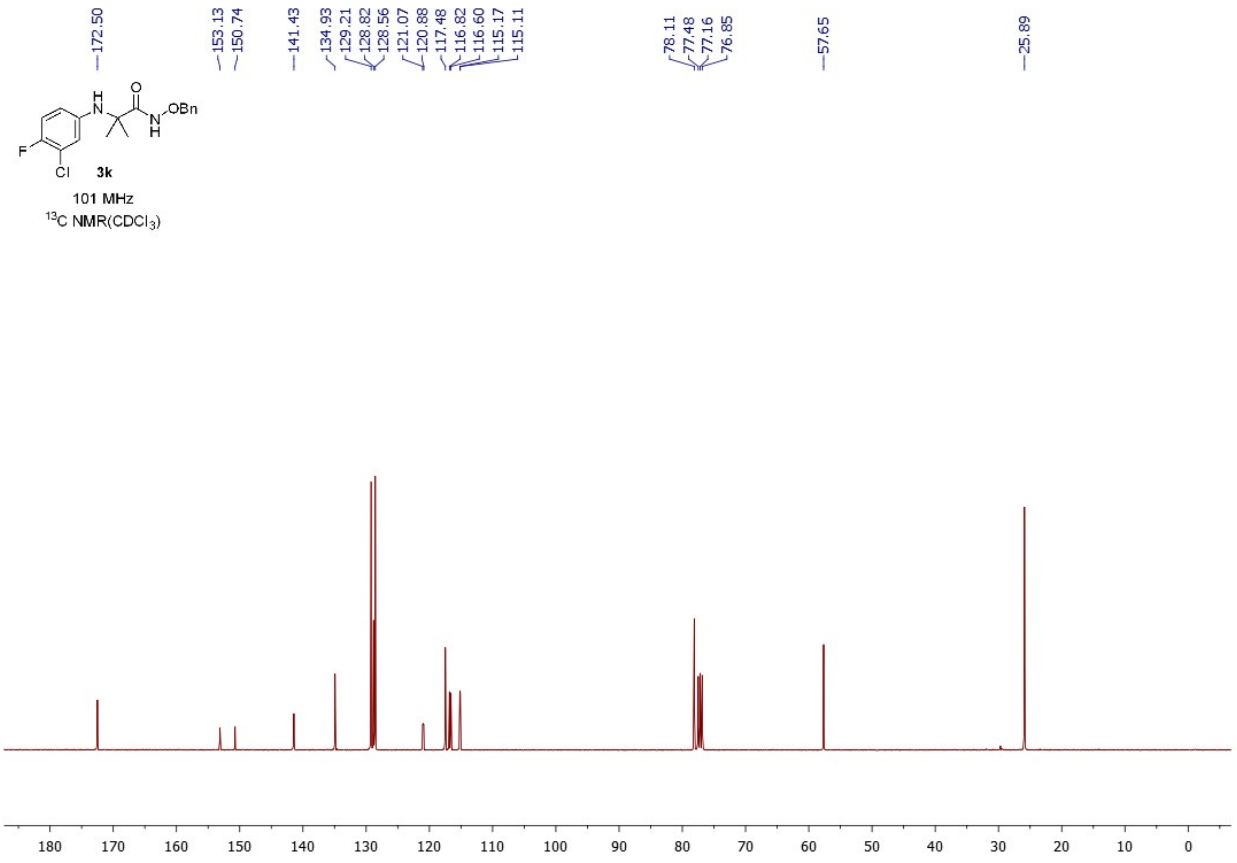
6.60
6.40
6.39
6.38
6.38
6.37
6.37
6.36
4.94
3.64
1.49
OBn
O
NH
HN
Cl
F
3k
1.05
5.17
1.04
1.04
1.06
2.06
1.04
6.20
f1 (ppm)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129.21
128.82
128.56
121.07
120.88
117.48
116.82
116.60
115.17
115.11
78.11
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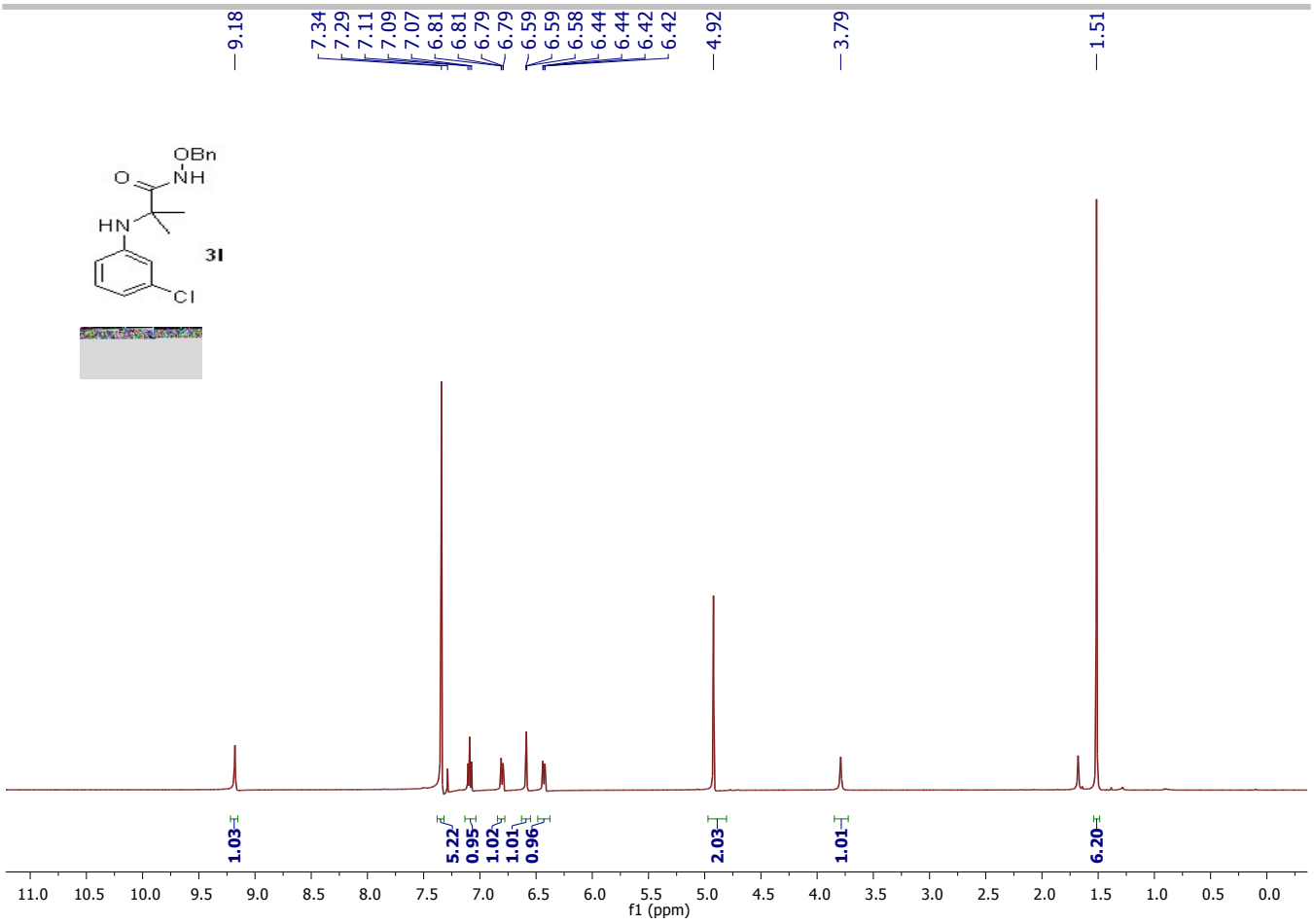
77.16
76.85
57.65
25.89
OBn
F
Cl
3k
101 MHz
13C NMR(CDCl3)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7.09
7.07
6.81
6.81
6.79
6.79
6.59
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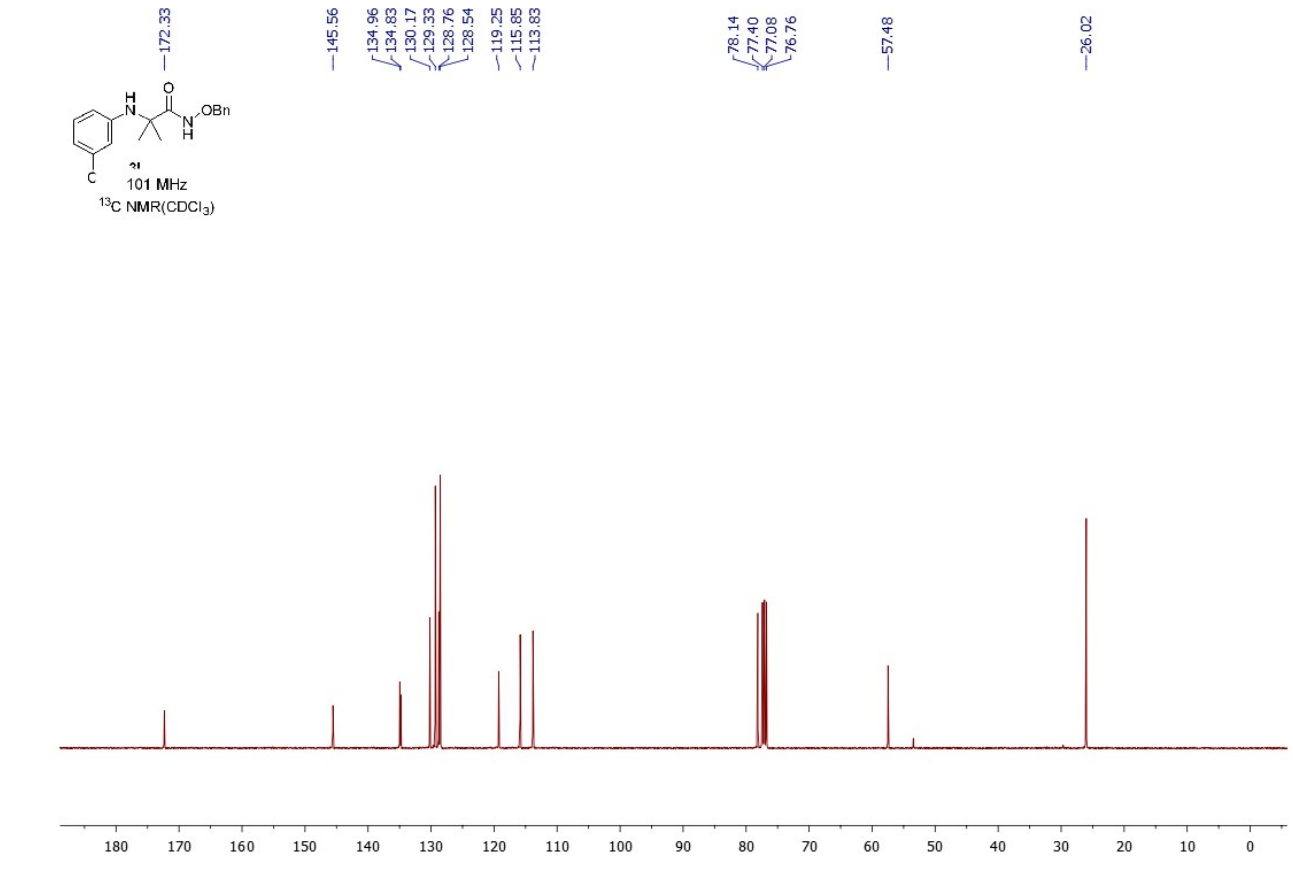
6.44
6.44
6.42
6.42
4.92
3.79
1.51
OBn
O
NH
HN
Cl
3l
1.03
5.22
0.95
1.02
1.01
0.96
2.03
1.01
6.20
f1 (ppm)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130.17
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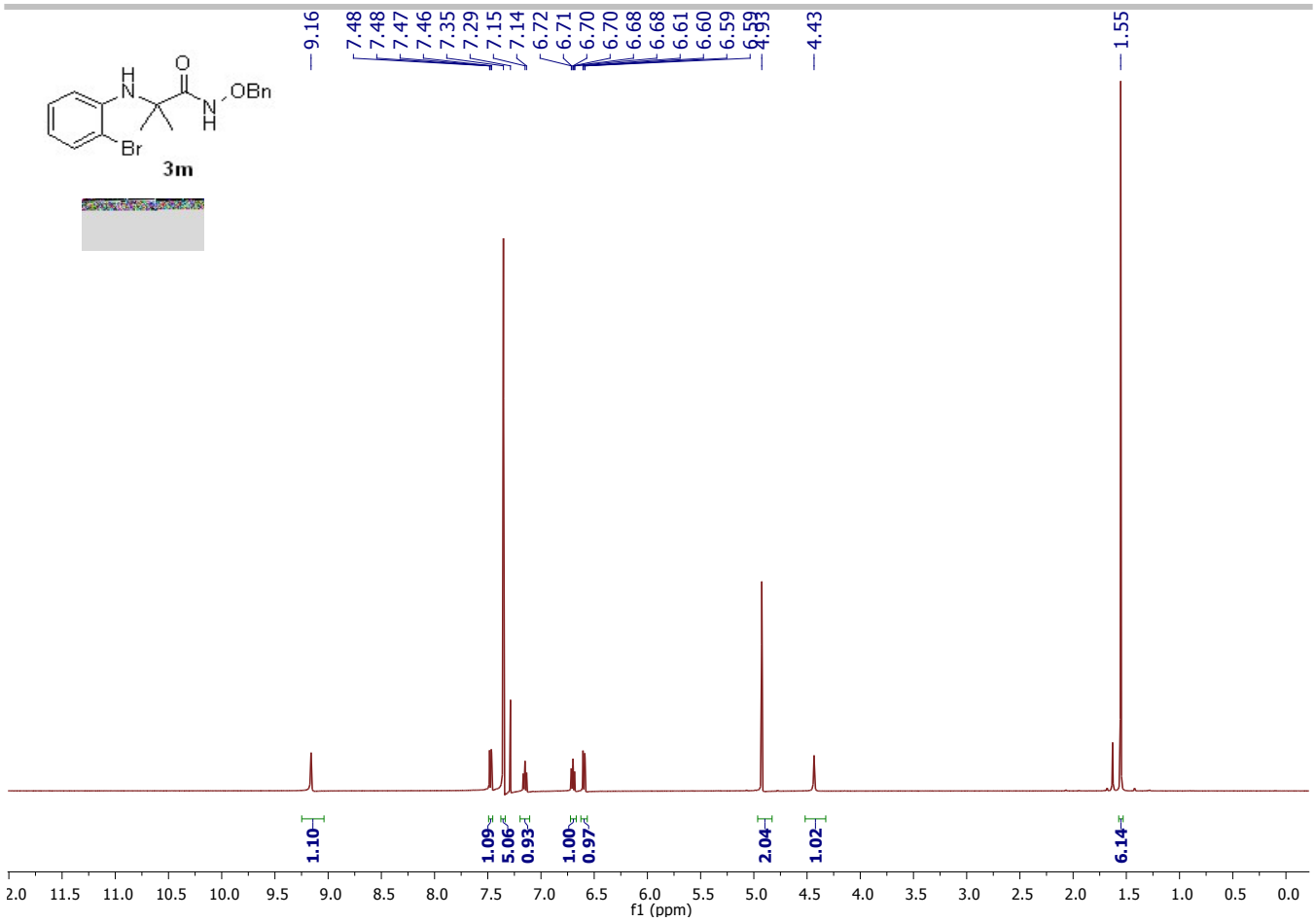
128.76
128.54
119.25
115.85
113.83
78.14
77.40
77.08
76.76
57.48
26.02
OBn
101 MHz
13C NMR(CDCl3)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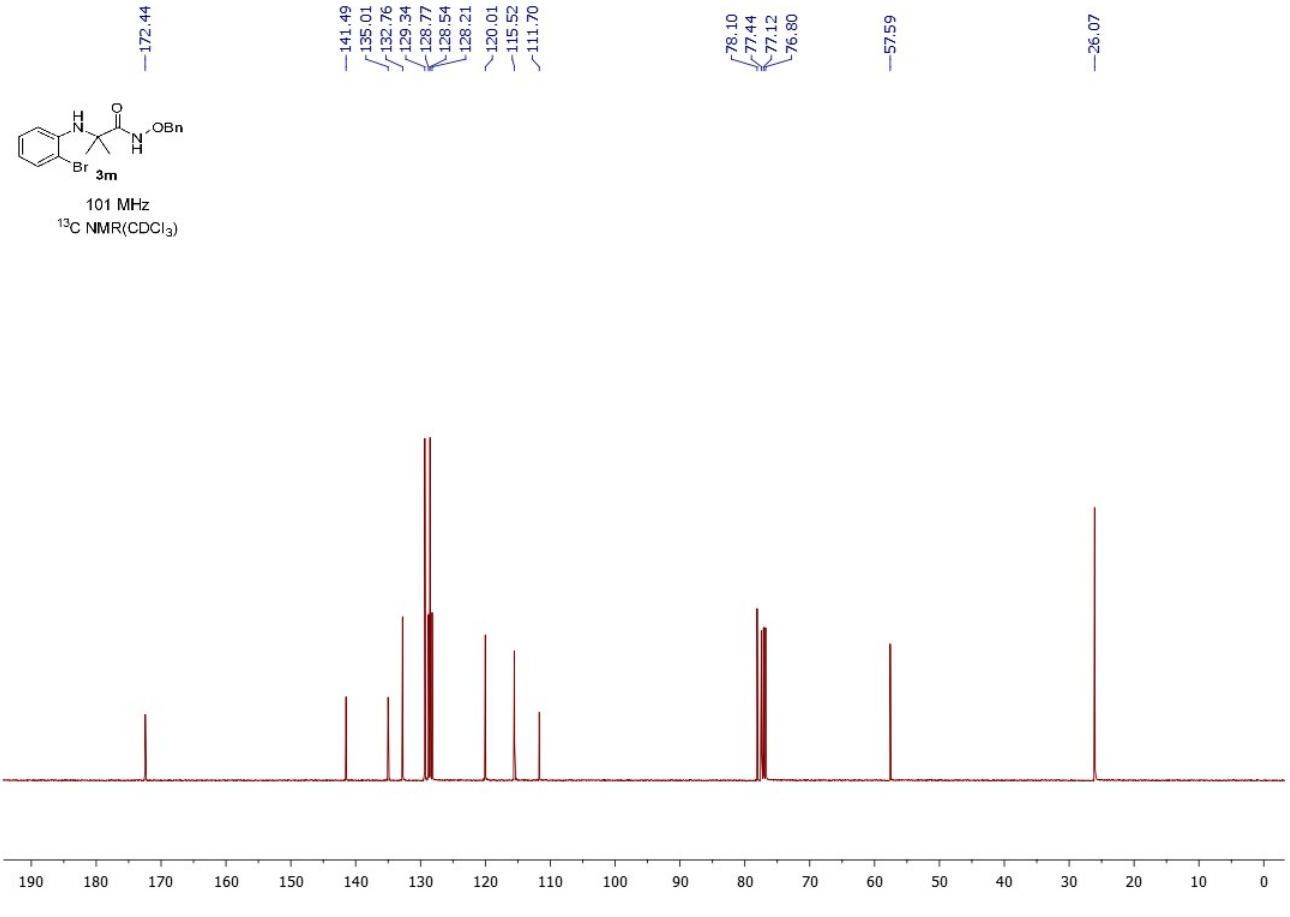
7.48
7.48
7.47
7.46
7.35
7.29
7.15
7.14
6.72
6.71
6.70
6.70
6.68
6.68
6.61
6.60
6.59
6.59
4.93
4.43
1.55
OBn
Br
3m
1.10
1.09
5.06
0.93
1.00
0.97
2.04
1.02
6.14
f1 (ppm)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132.76
129.34
128.77
128.54
128.21
120.01
115.52
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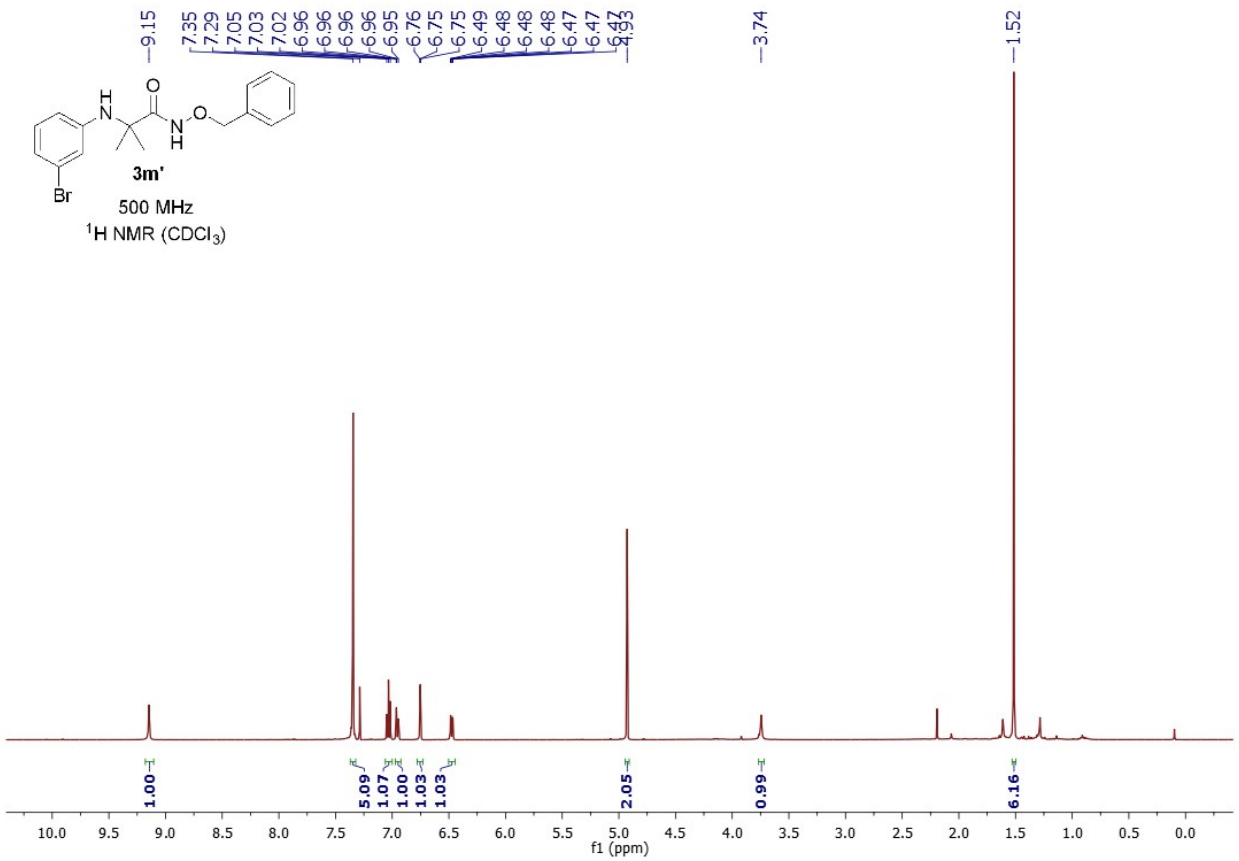
77.44
77.12
76.80
57.59
26.07
OBn
Br
3m
101 MHz
13C NMR(CDCl3)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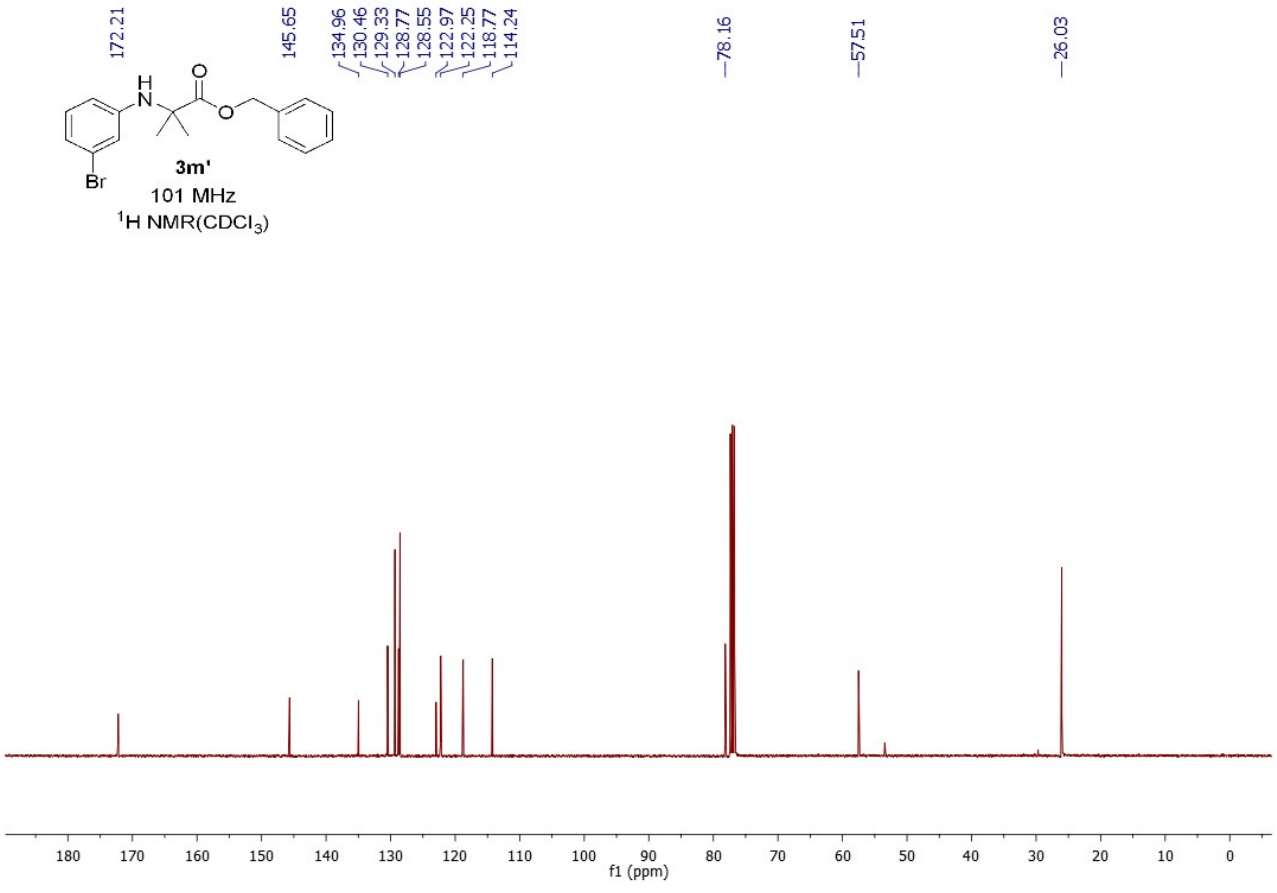
7.35
7.29
7.05
7.03
7.02
6.96
6.96
6.96
6.96
6.95
6.76
6.75
6.75
6.49
6.48
6.48
6.47
6.47
6.47
4.93
3.74
1.52
3m'
500 MHz
1H NMR (CDCl3)
1.00
5.09
1.07
1.00
1.03
1.03
2.05
0.99
6.16
f1 (ppm)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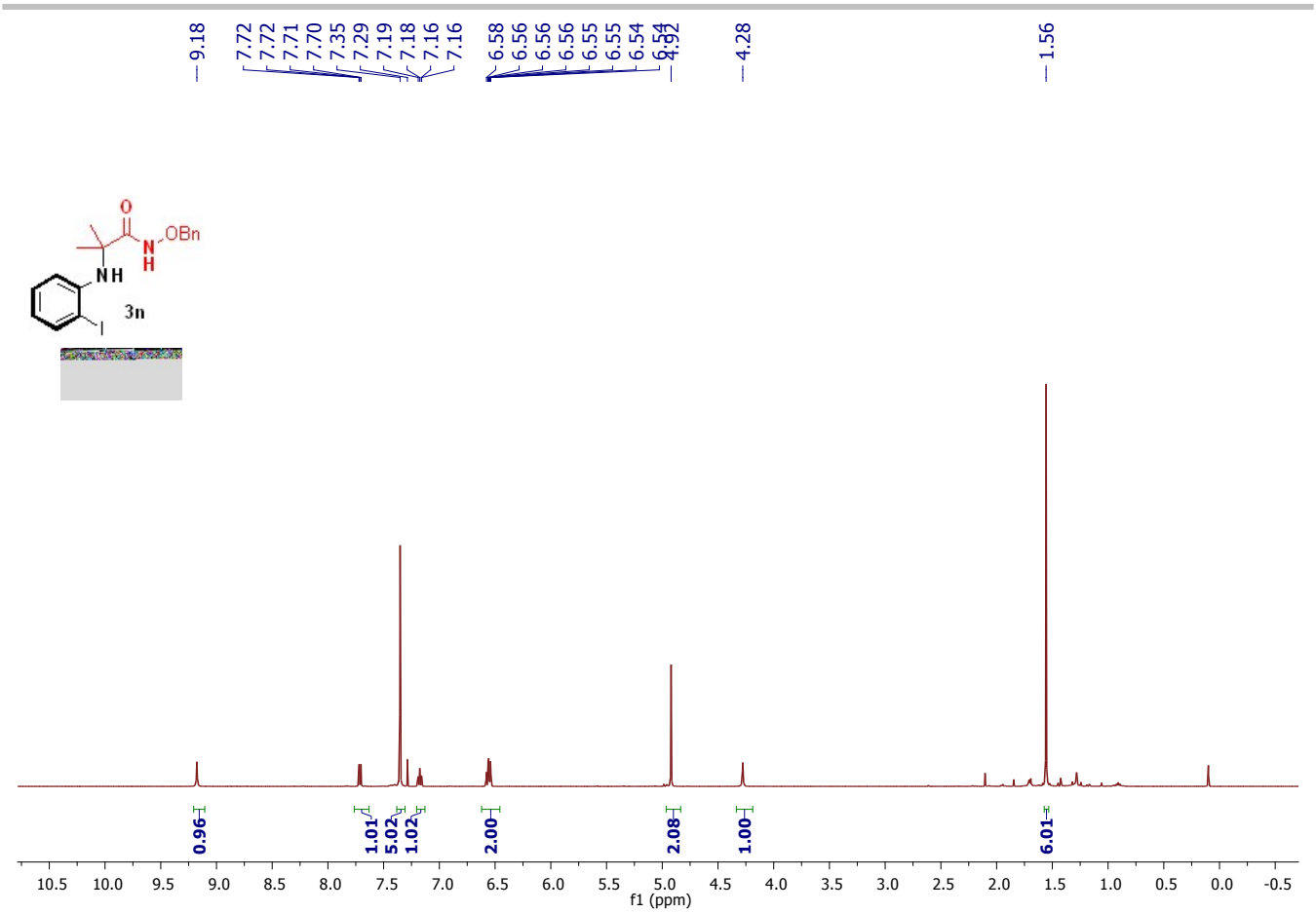
134.96
130.46
129.33
128.77
128.55
122.97
122.25
118.77
114.24
78.16
57.51
26.03
3m'
101 MHz
1H NMR(CDCl3)
f1 (ppm)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7.72
7.72
7.71
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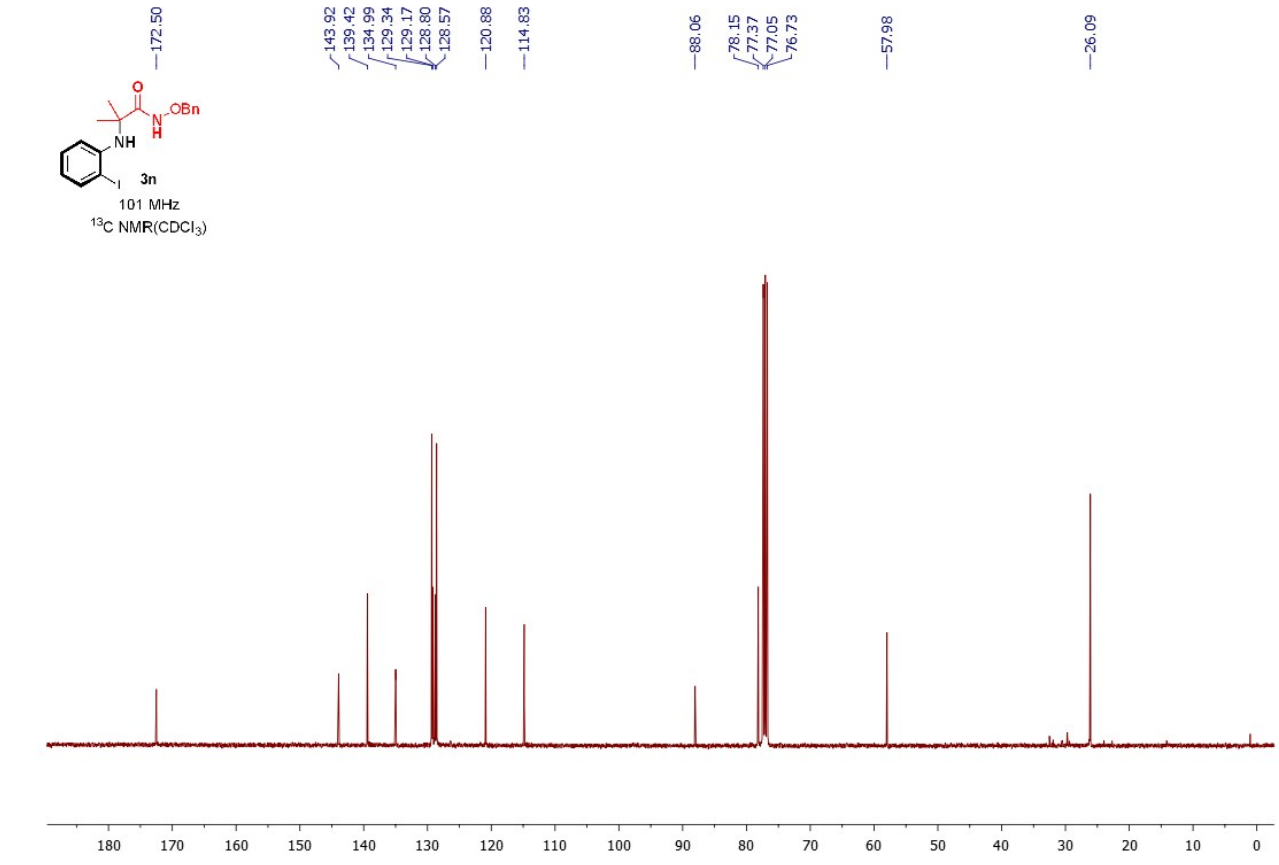
7.35
7.29
7.19
7.18
7.16
7.16
6.58
6.56
6.56
6.56
6.55
6.55
6.54
6.54
4.92
4.28
1.56
O
N
OBn
H
NH
3n
0.96
1.01
5.02
1.02
2.00
2.08
1.00
6.01
f1 (ppm)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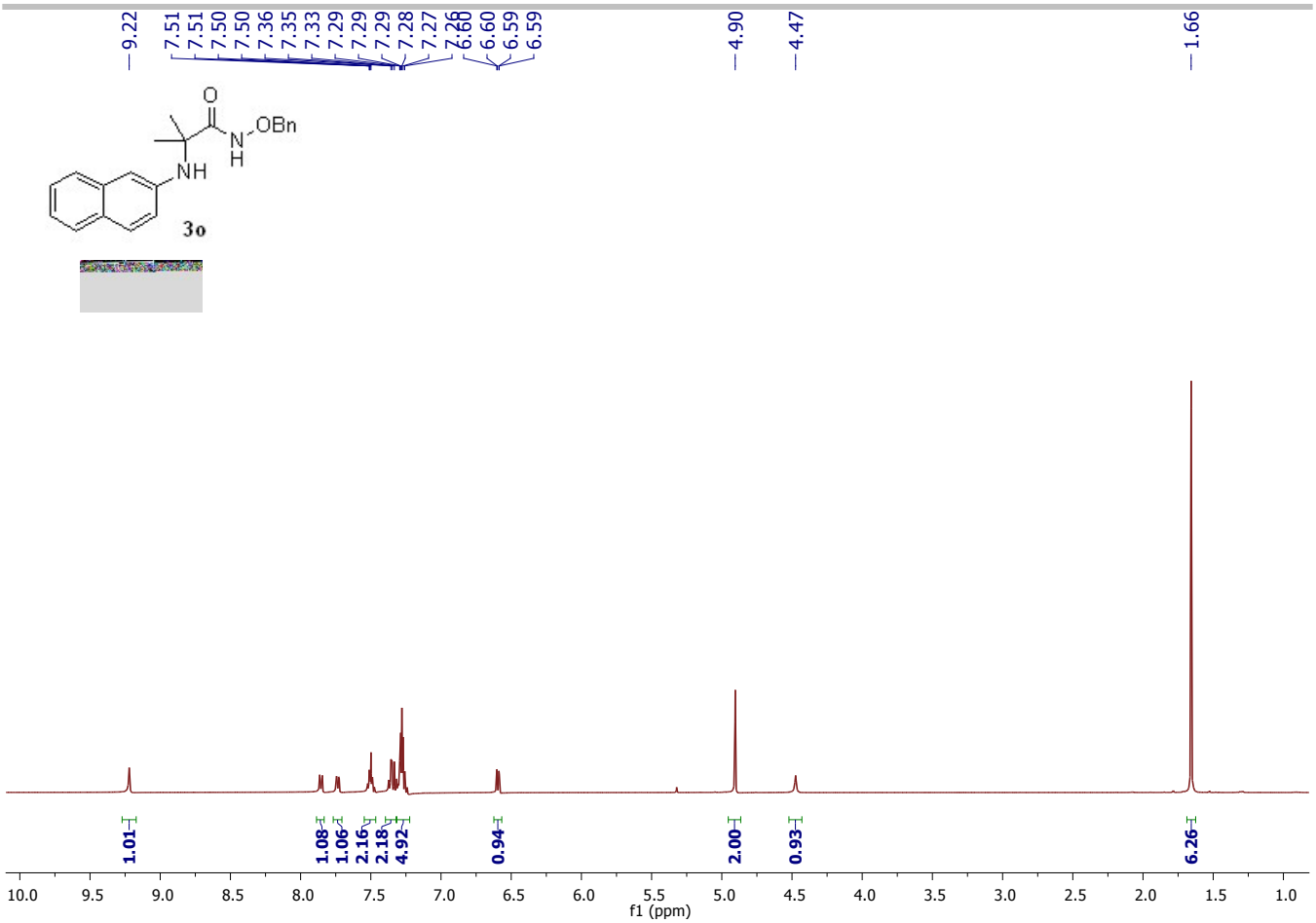
129.34
129.17
128.80
128.57
120.88
114.83
88.06
78.15
77.37
77.05
76.73
57.98
26.09
O
N
OBn
H
NH
3n
101 MHz
13C NMR(CDCl3)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7.33
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7.29
7.29
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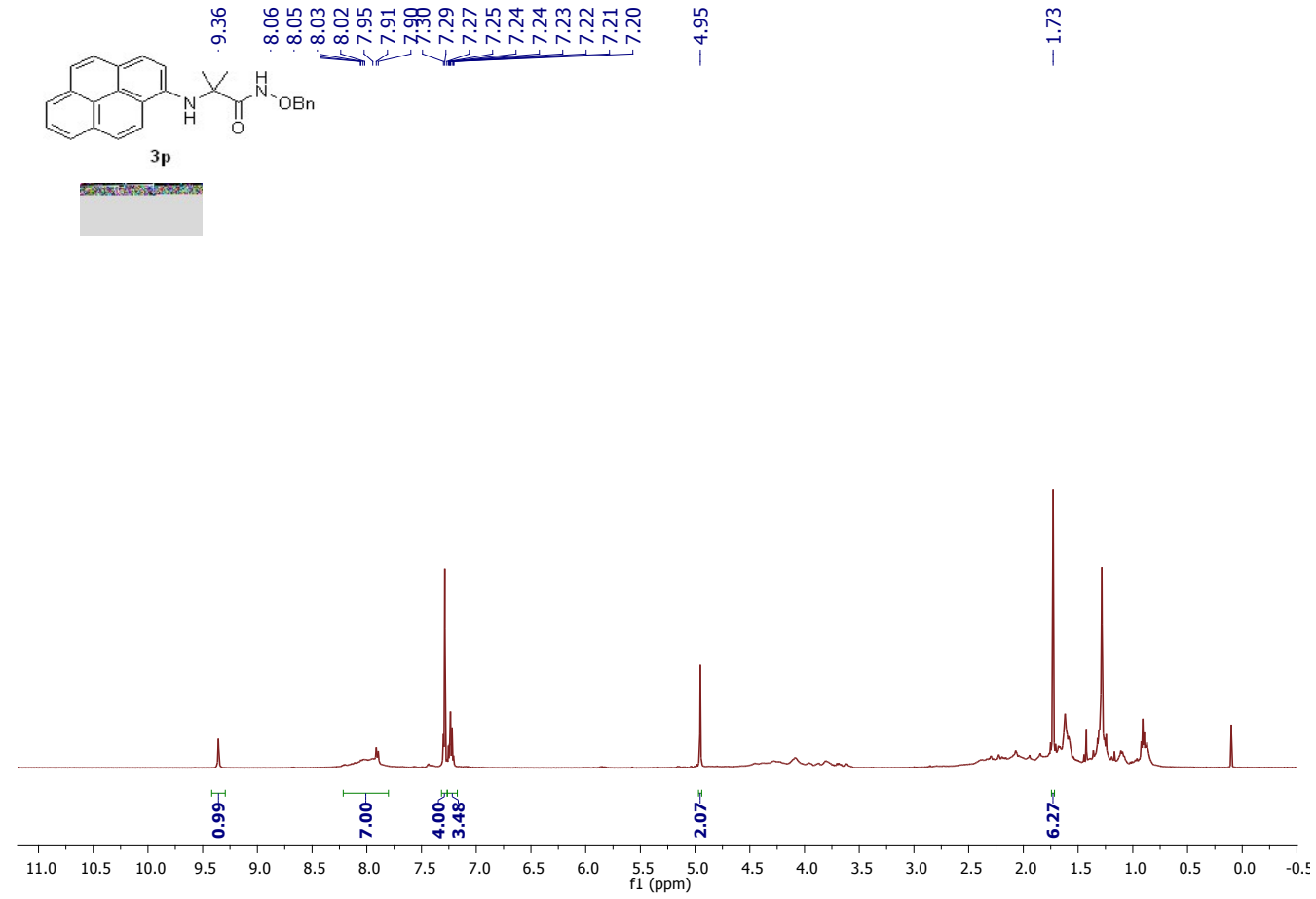
7.26
6.60
6.60
6.59
6.59
4.90
4.47
1.66
O
OBn
N
H
NH
3o
1.01
1.08
1.06
2.16
2.18
4.92
0.94
2.00
0.93
6.26
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)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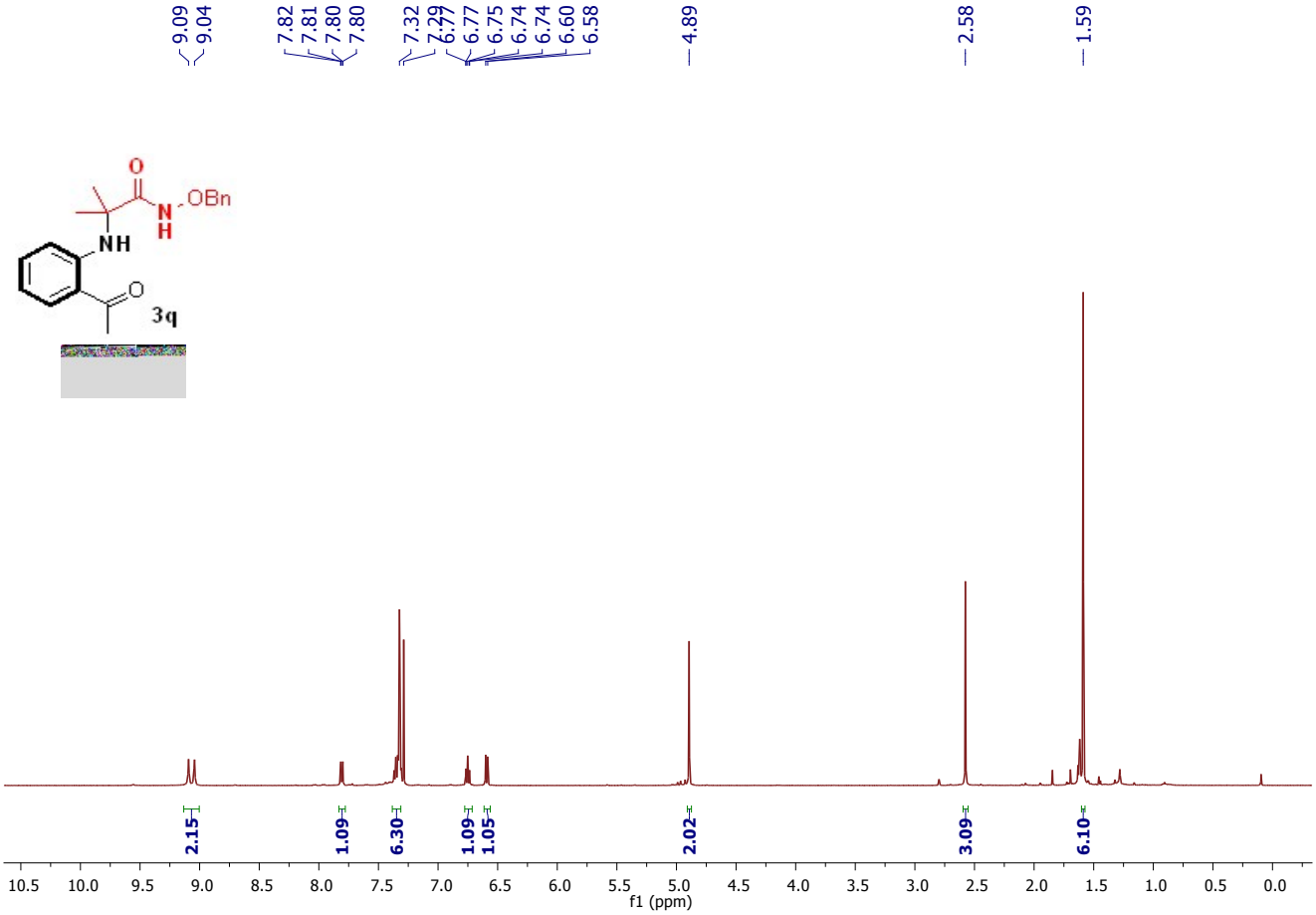
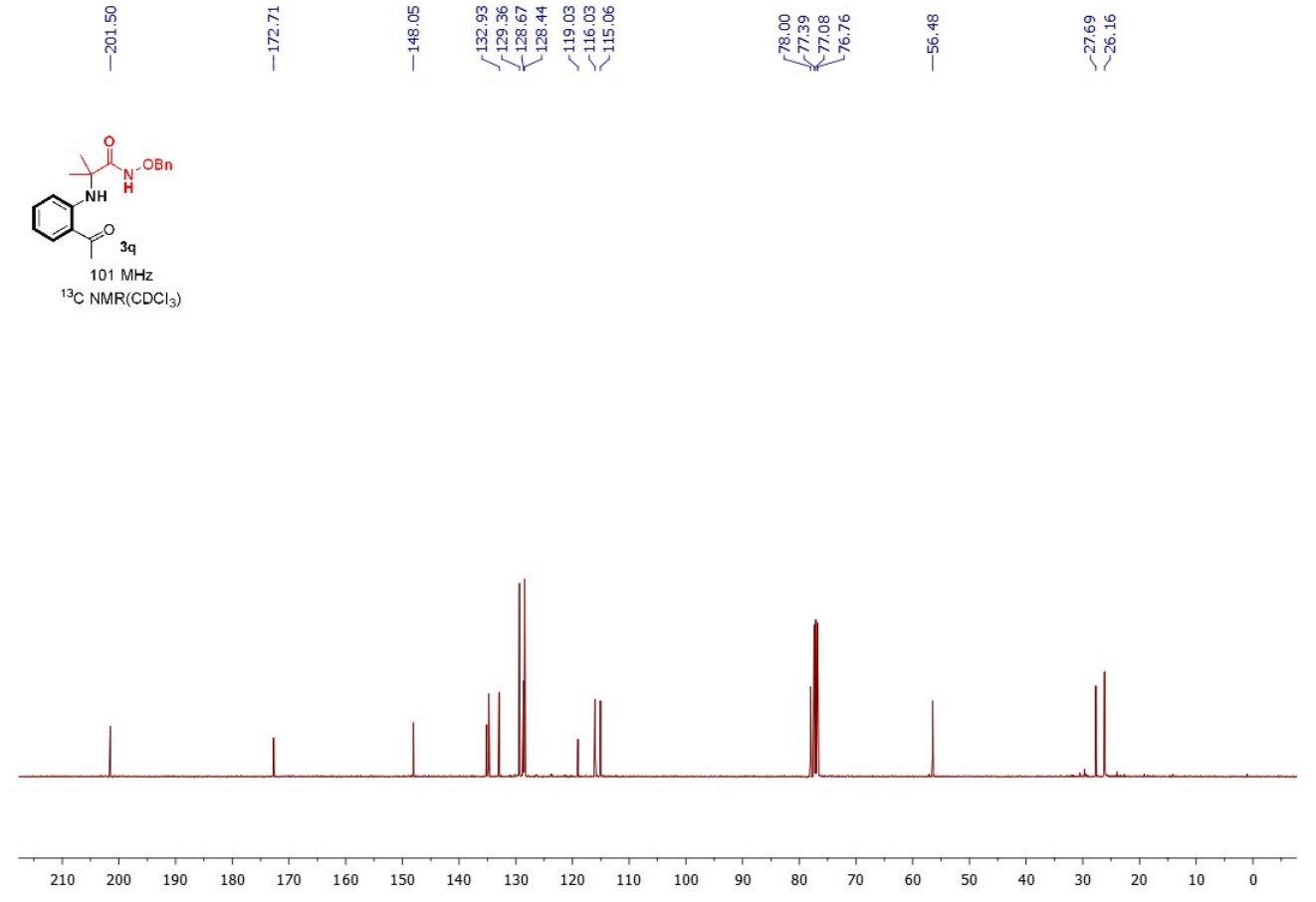
8.05
8.03
8.02
7.95
7.91
7.90
7.30
7.29
7.27
7.25
7.24
7.24
7.23
7.22
7.21
7.20
4.95
1.73
N
H
H
N
OBn
O
3p
0.99
7.00
4.00
3.48
2.07
6.27
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


9.09
9.04
7.82
7.81
7.80
7.80
7.32
7.29
7.27
6.77
6.75
6.74
6.74
6.60
6.58
4.89
2.58
1.59
O
N
OBn
H
NH
O
3q
2.15
1.09
6.30
1.09
1.05
2.02
3.09
6.10
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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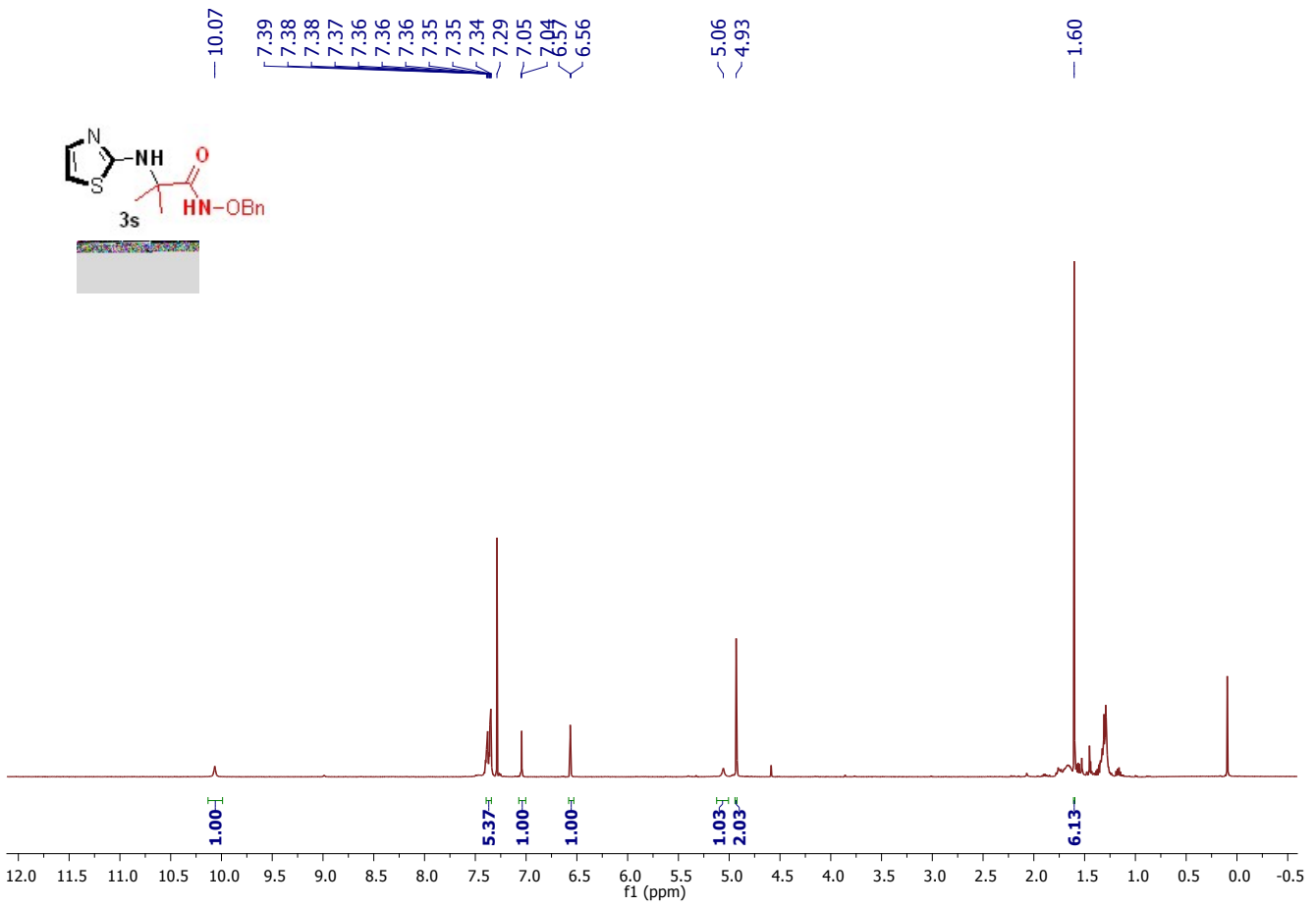
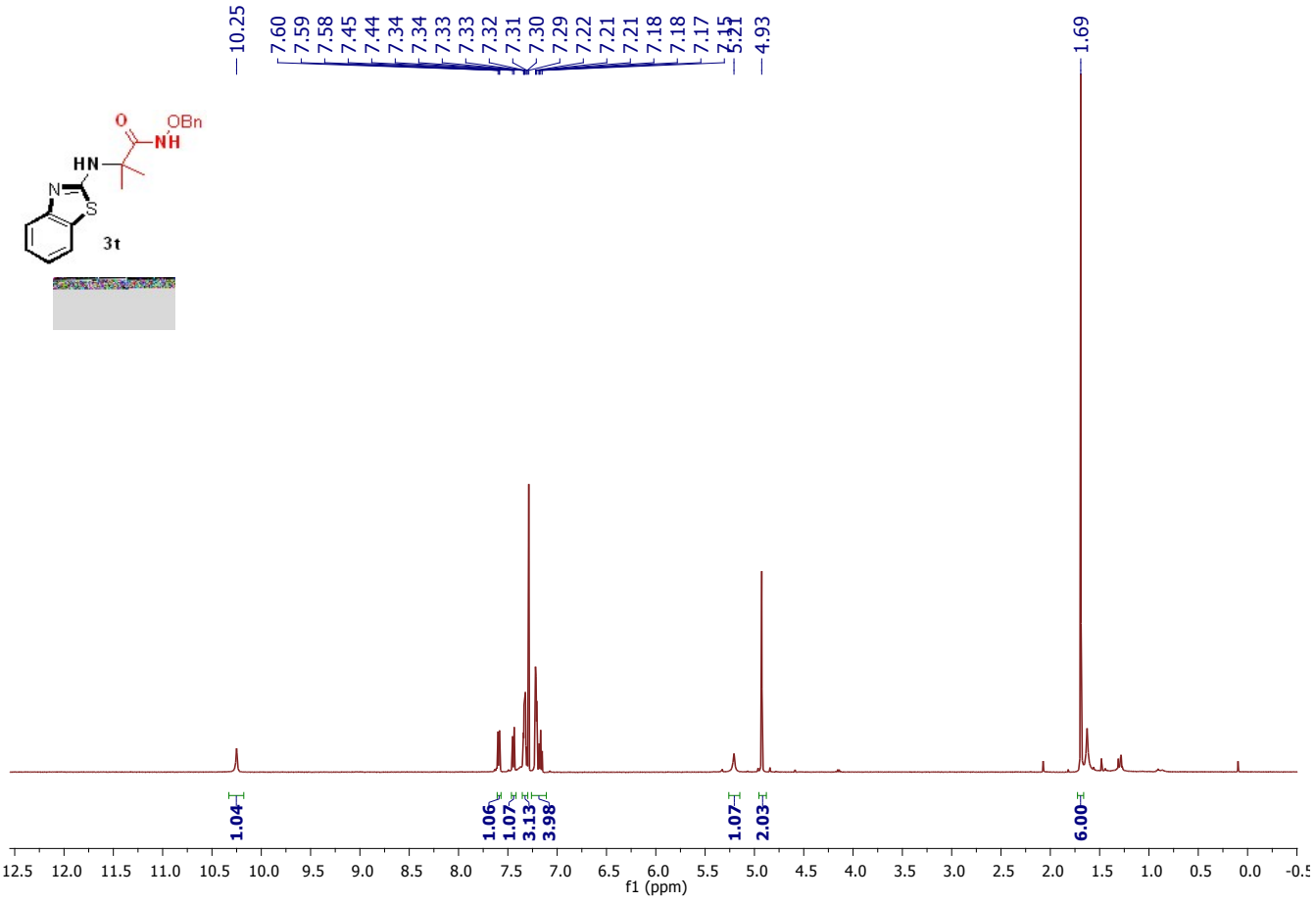
148.05
132.93
129.36
128.67
128.44
119.03
116.03
115.06
78.00
77.39
77.08
76.76
56.48
27.69
26.16
O
N
OBn
H
NH
O
3q
101 MHz
13C NMR(CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


10.07
7.39
7.38
7.38
7.37
7.36
7.36
7.36
7.35
7.35
7.34
7.29
7.05
7.04
6.57
6.56
5.06
4.93
1.60
NH
O
HN–OBn
3s
1.00
5.37
1.00
1.00
1.03
2.03
6.13
f1 (ppm)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7.58
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7.44
7.34
7.34
7.33
7.33
7.32
7.31
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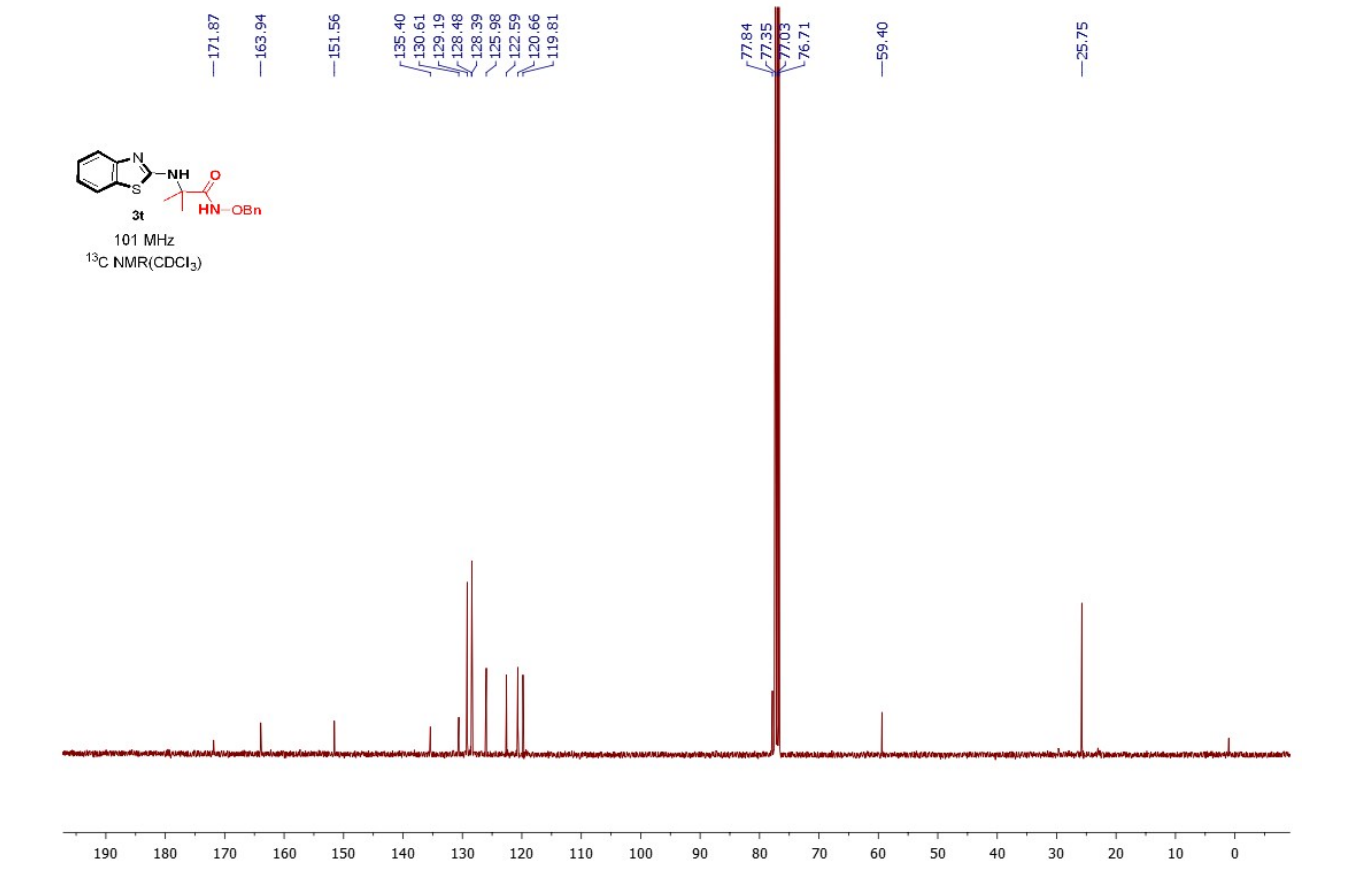
7.29
7.22
7.21
7.21
7.18
7.18
7.17
7.15
5.21
4.93
1.69
O
OBn
NH
HN
3t
1.04
1.06
1.07
3.13
3.98
1.07
2.03
6.00
f1 (ppm)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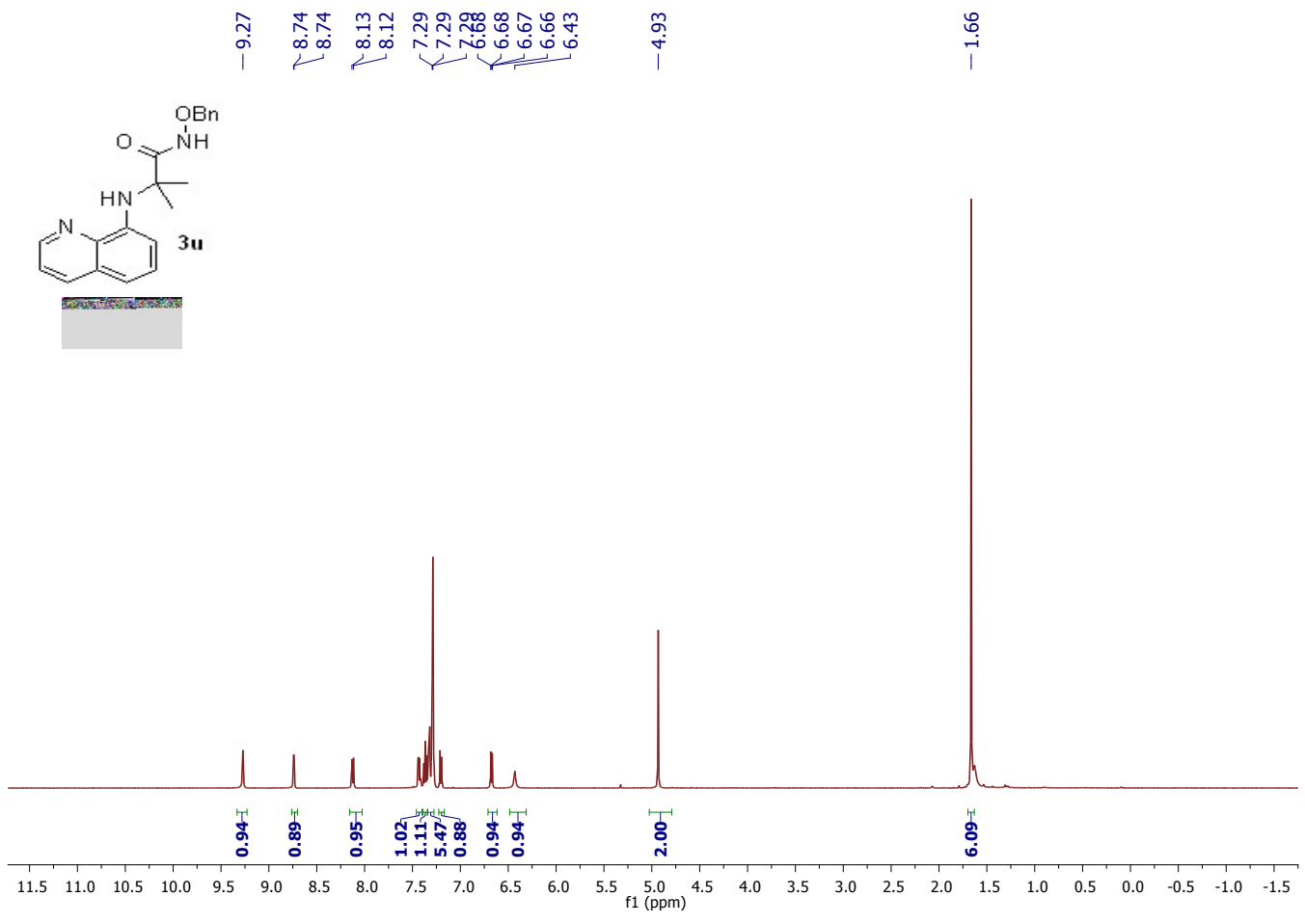
130.61
129.19
128.48
128.39
125.98
122.59
120.66
119.81
77.84
77.35
77.03
76.71
59.40
25.75
3t
101 MHz
13C NMR(CDCl3)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0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8.74
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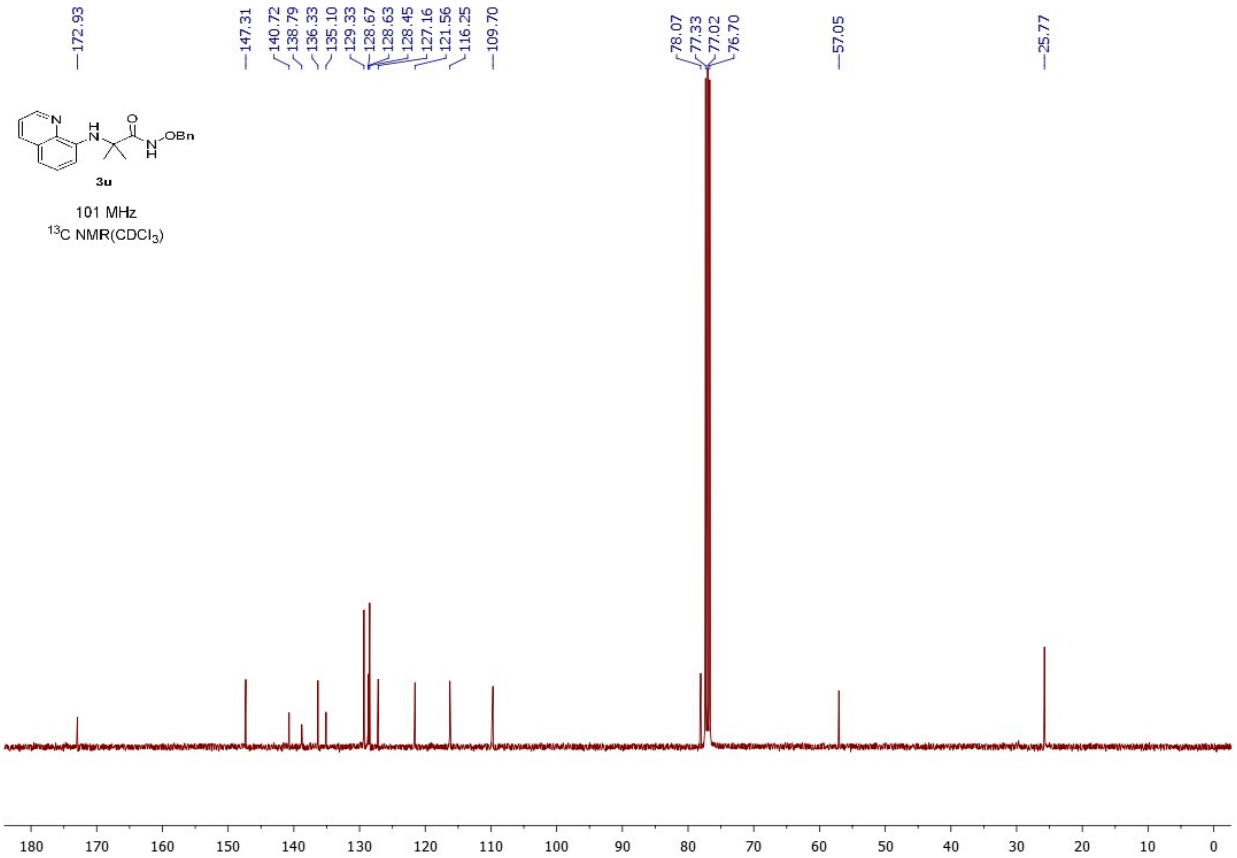
8.12
7.29
7.29
6.68
6.68
6.67
6.66
6.43
4.93
1.66
3u
0.94
0.89
0.95
1.02
1.11
5.47
0.88
0.94
0.94
2.00
6.09
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0 -1.5
f1 (ppm)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147.31
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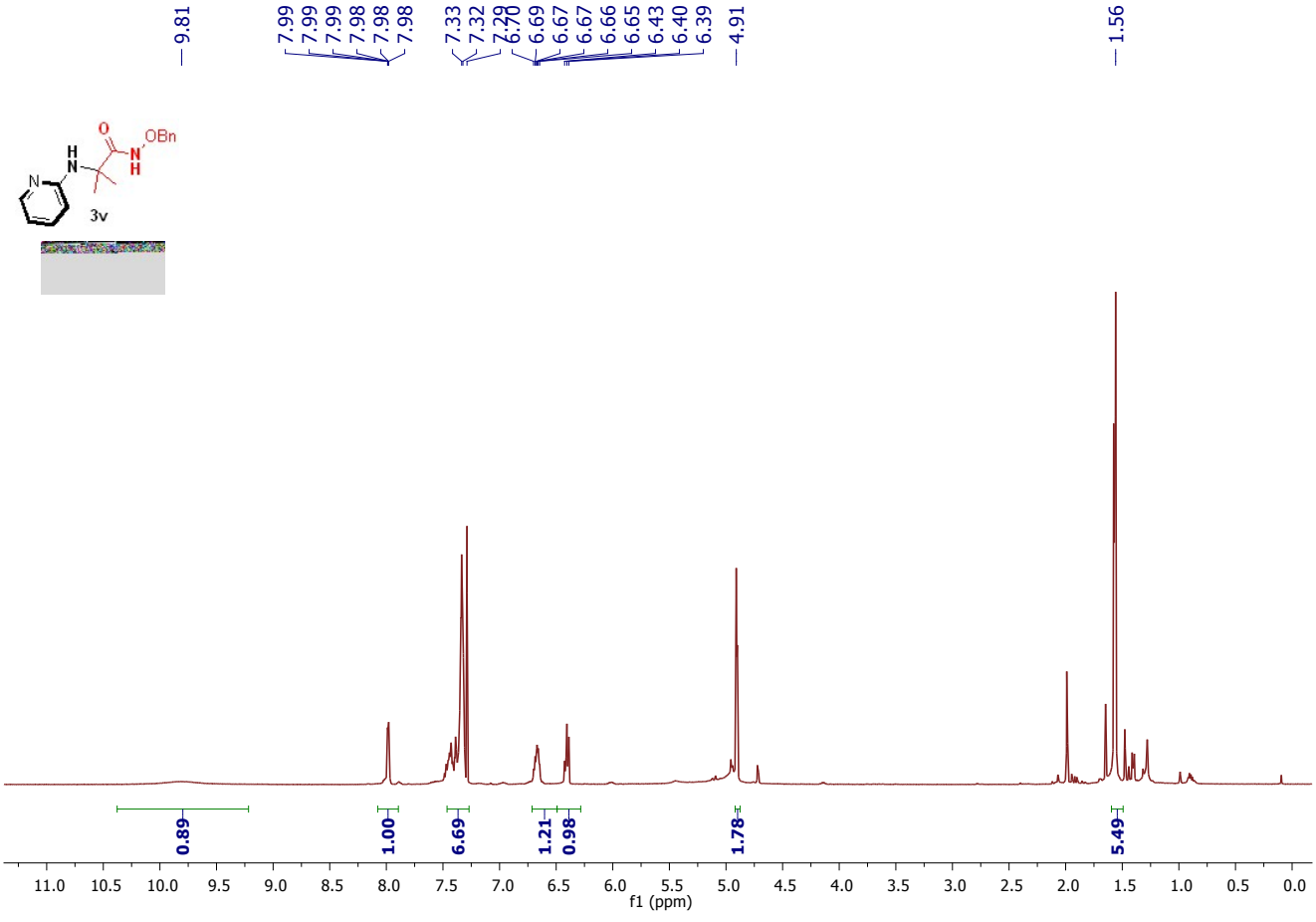
138.79
136.33
135.10
129.33
128.67
128.63
128.45
127.16
121.56
116.25
109.70
78.07
77.33
77.02
76.70
57.05
25.77
3u
101 MHz
13C NMR(CDCl3)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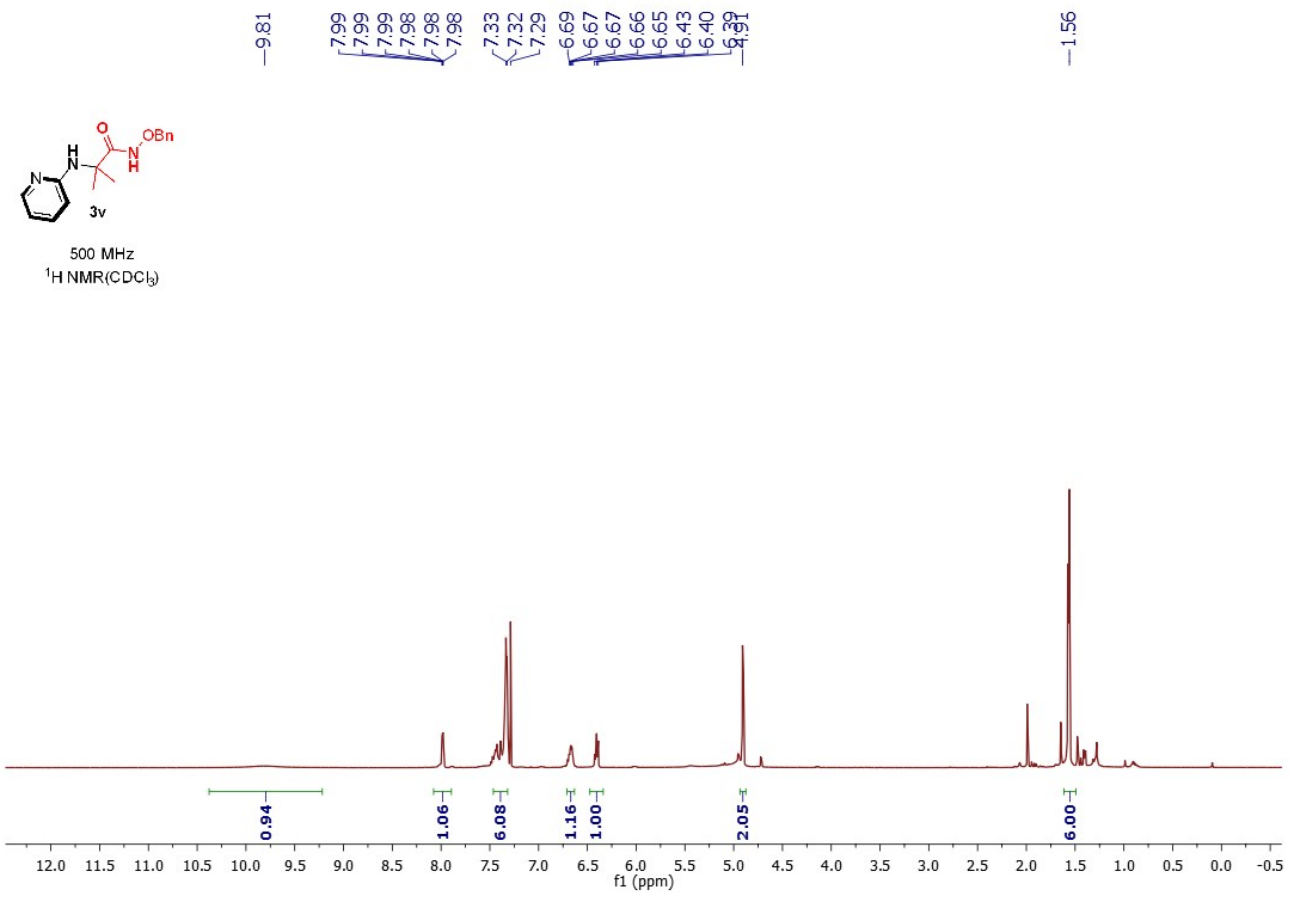
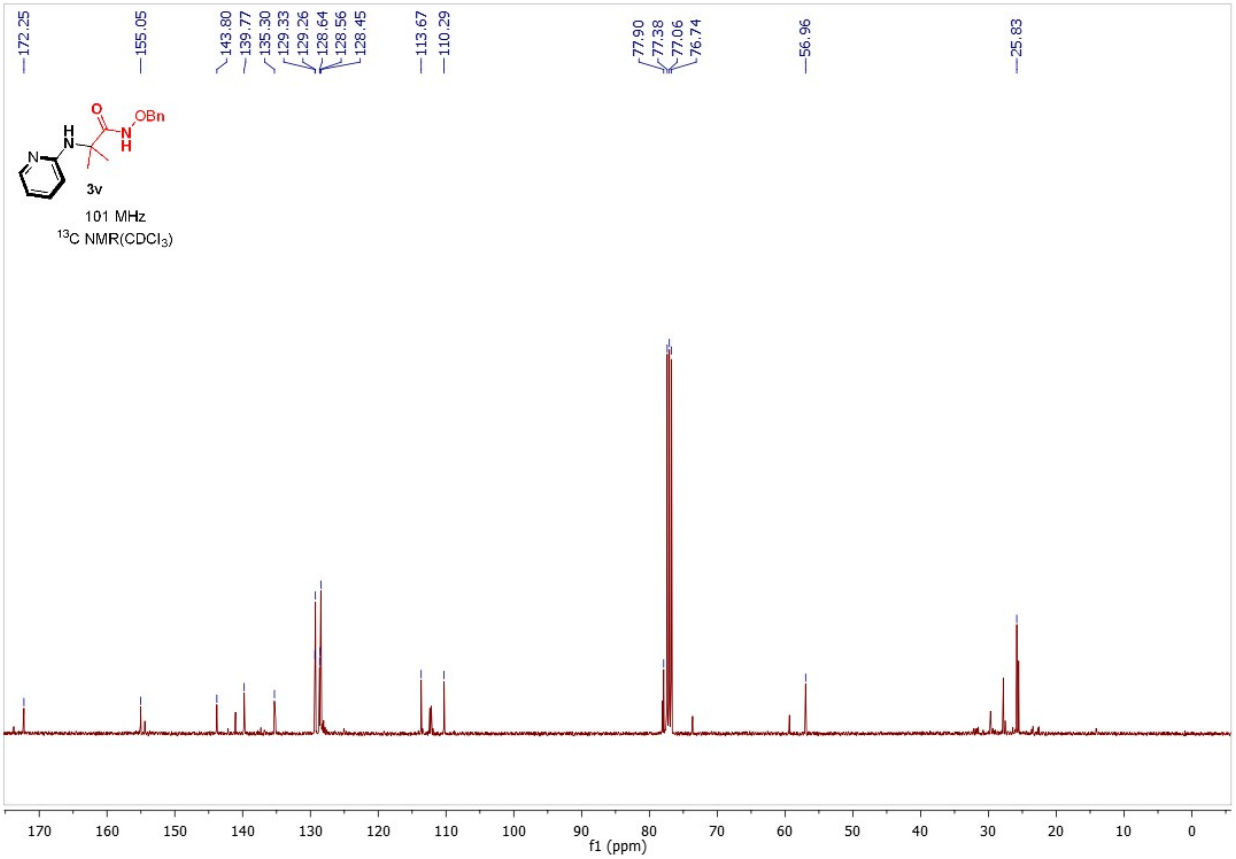
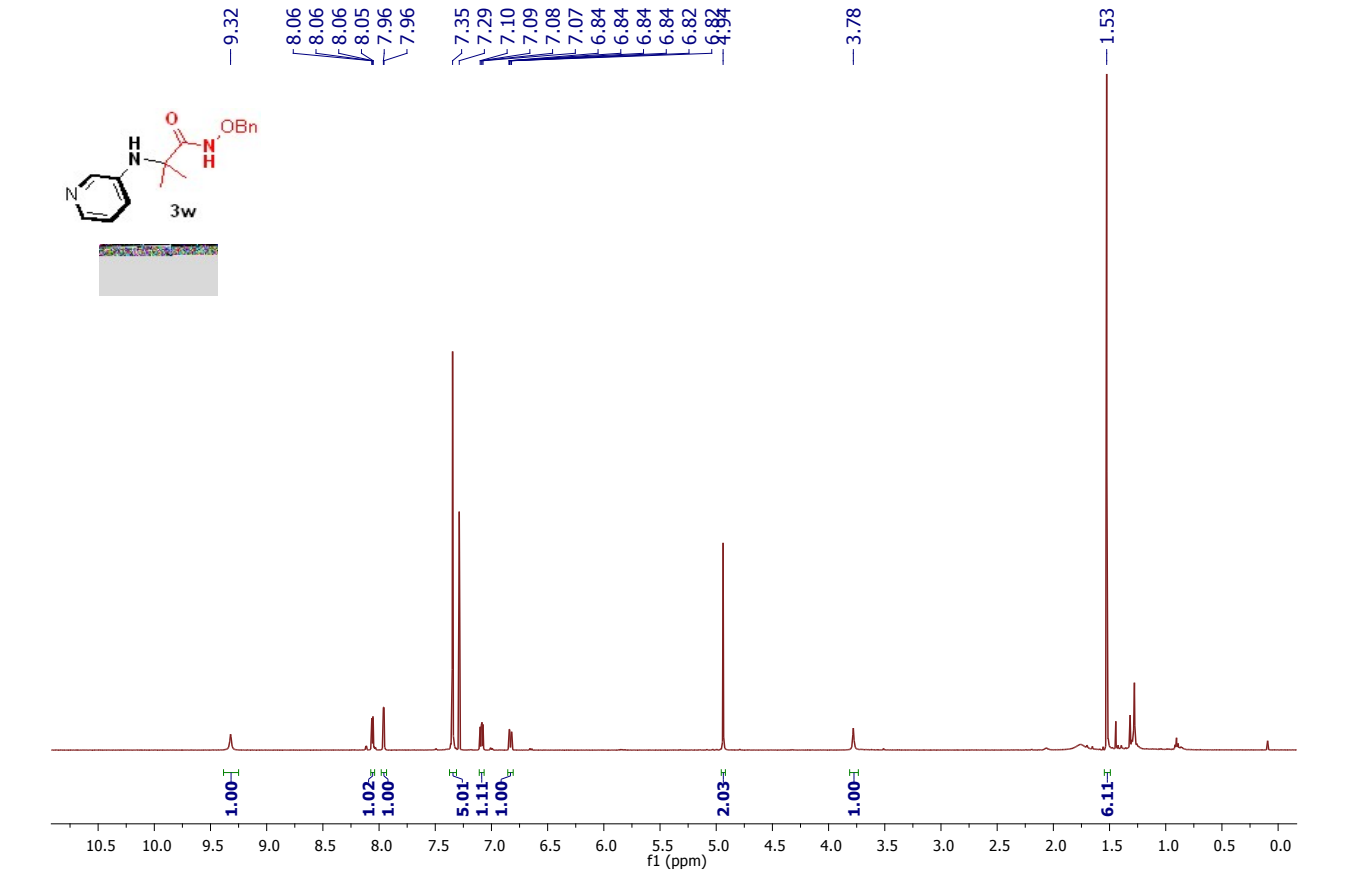
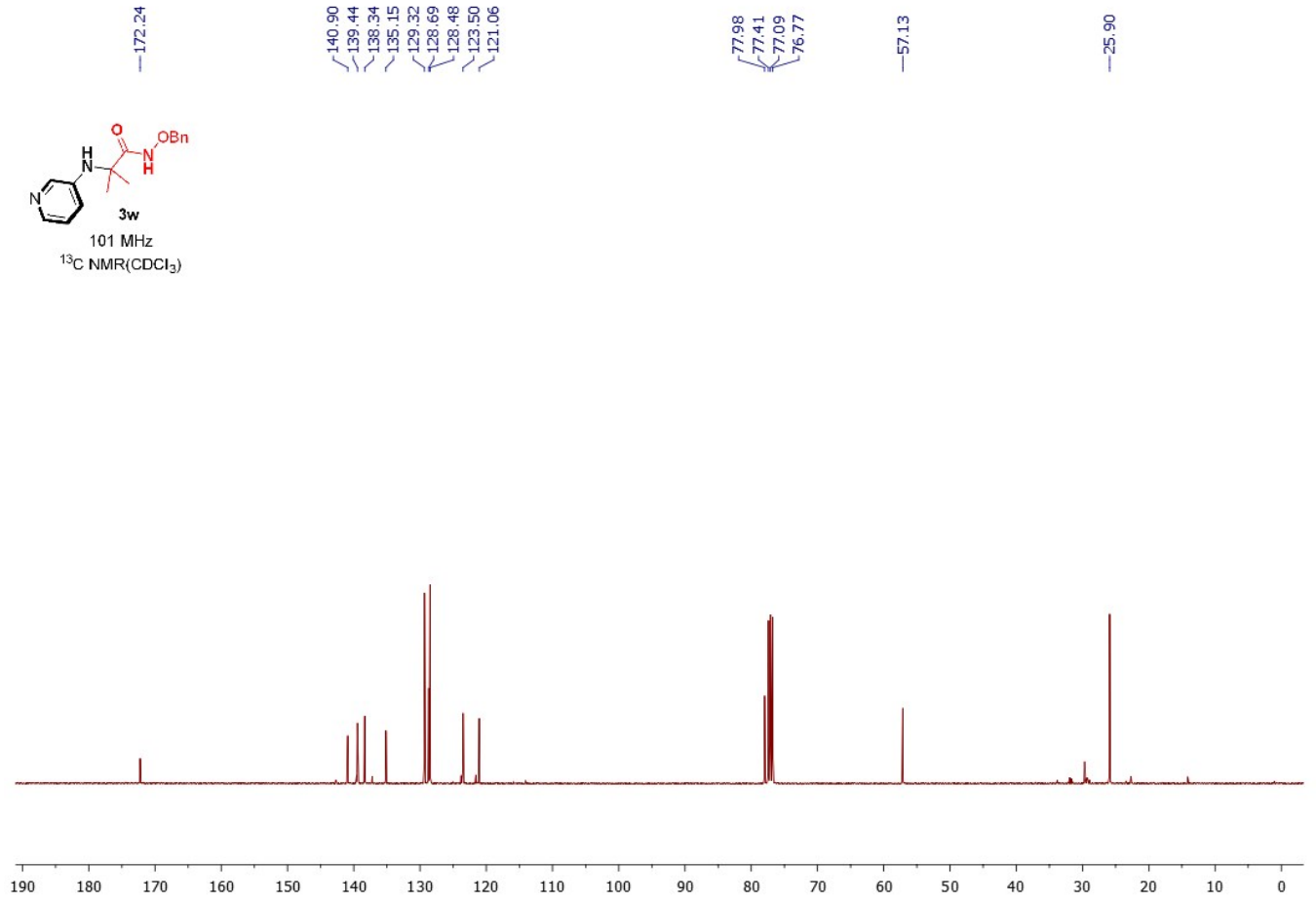
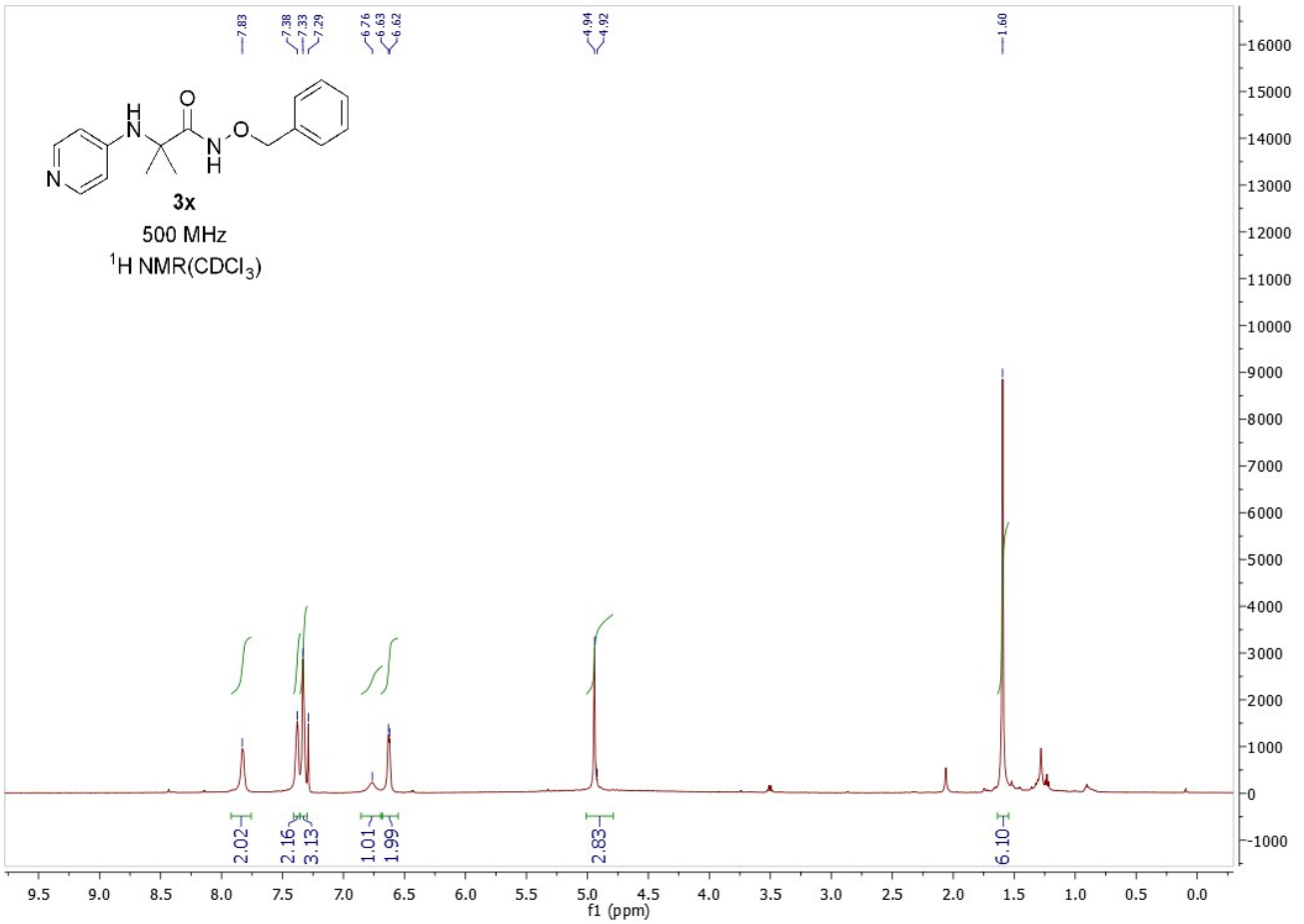
7.99
7.99
7.98
7.98
7.98
7.33
7.32
7.29
6.70
6.69
6.67
6.67
6.66
6.65
6.43
6.40
6.39
4.91
1.56
3v
0.89
1.00
6.69
1.21
0.98
1.78
5.49
f1 (ppm)

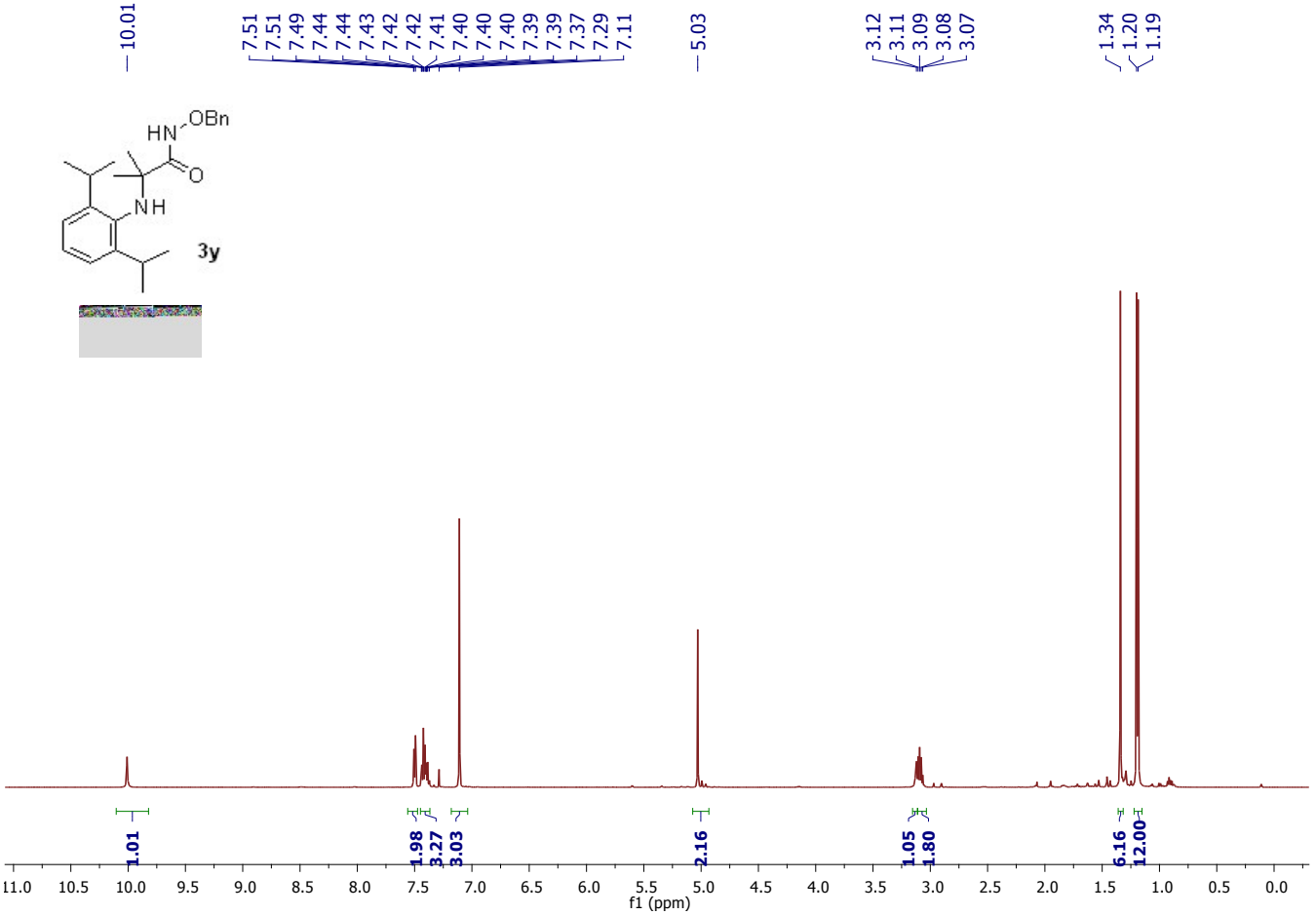

9.81
7.99
7.99
7.99
7.98
7.98
7.98
7.33
7.32
7.29
6.69
6.67
6.67
6.66
6.65
6.43
6.40
6.39
4.91
1.56
OBn
3v
500 MHz
^{1}H NMR(CDCl$_3$)
0.94
1.06
6.08
1.16
1.00
2.05
6.00
f1 (ppm)

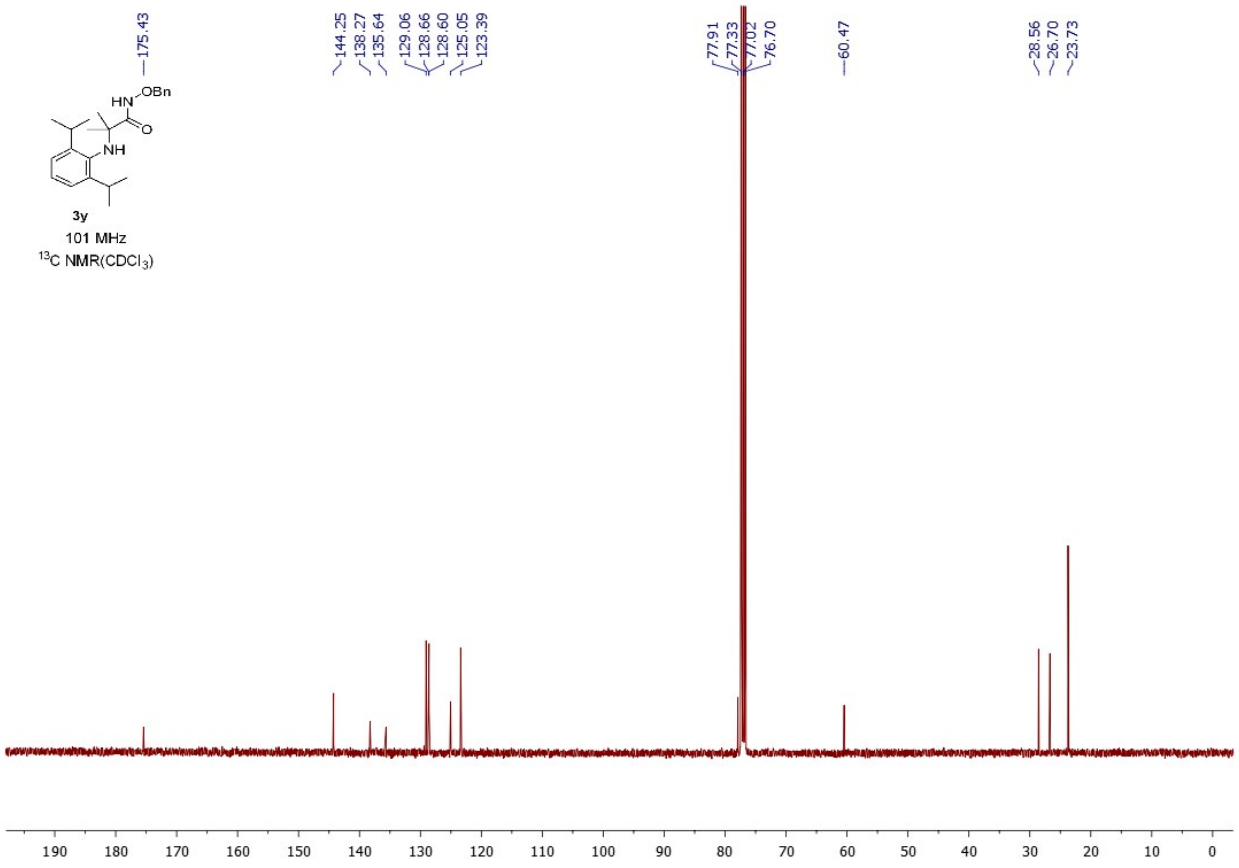

172.25
155.05
143.80
139.77
135.30
129.33
129.26
128.64
128.56
128.45
113.67
110.29
77.90
77.38
77.06
76.74
56.96
25.83
OBn
3v
101 MHz
^{13}C NMR(CDCl$_3$)
f1 (ppm)


9.32
8.06
8.06
8.06
8.05
7.96
7.96
7.35
7.29
7.10
7.09
7.08
7.07
6.84
6.84
6.84
6.84
6.82
6.82
4.94
3.78
1.53
OBn
3w
1.00
1.02
1.00
5.01
1.11
1.00
2.03
1.00
6.11
f1 (ppm)


172.24
140.90
139.44
138.34
135.15
129.32
128.69
128.48
123.50
121.06
77.98
77.41
77.09
76.77
57.13
25.90
OBn
3w
101 MHz
13C NMR(CDCl3)


3x
500 MHz
^{1}H NMR(CDCl$_3$)
f1 (ppm)


3y
f1 (ppm)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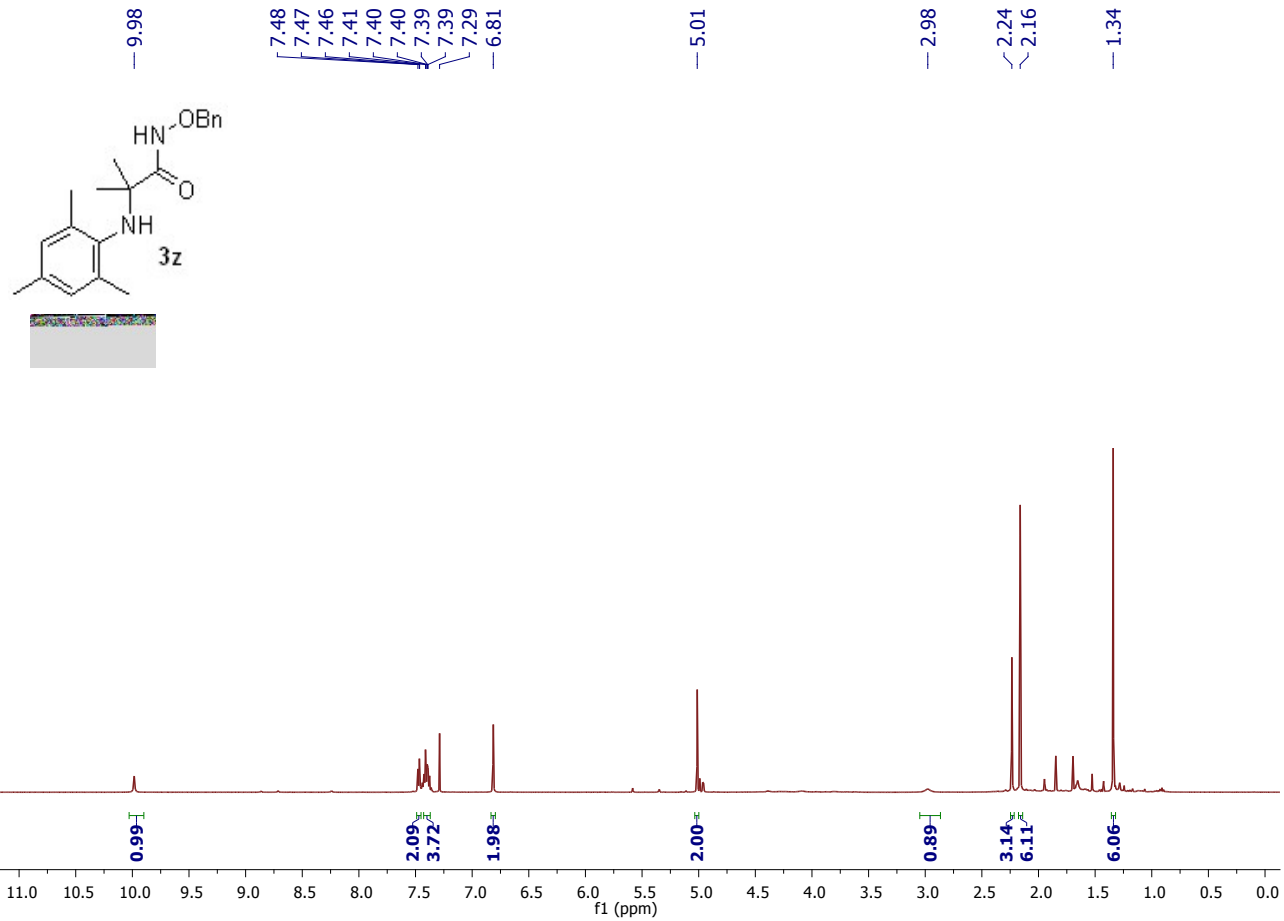
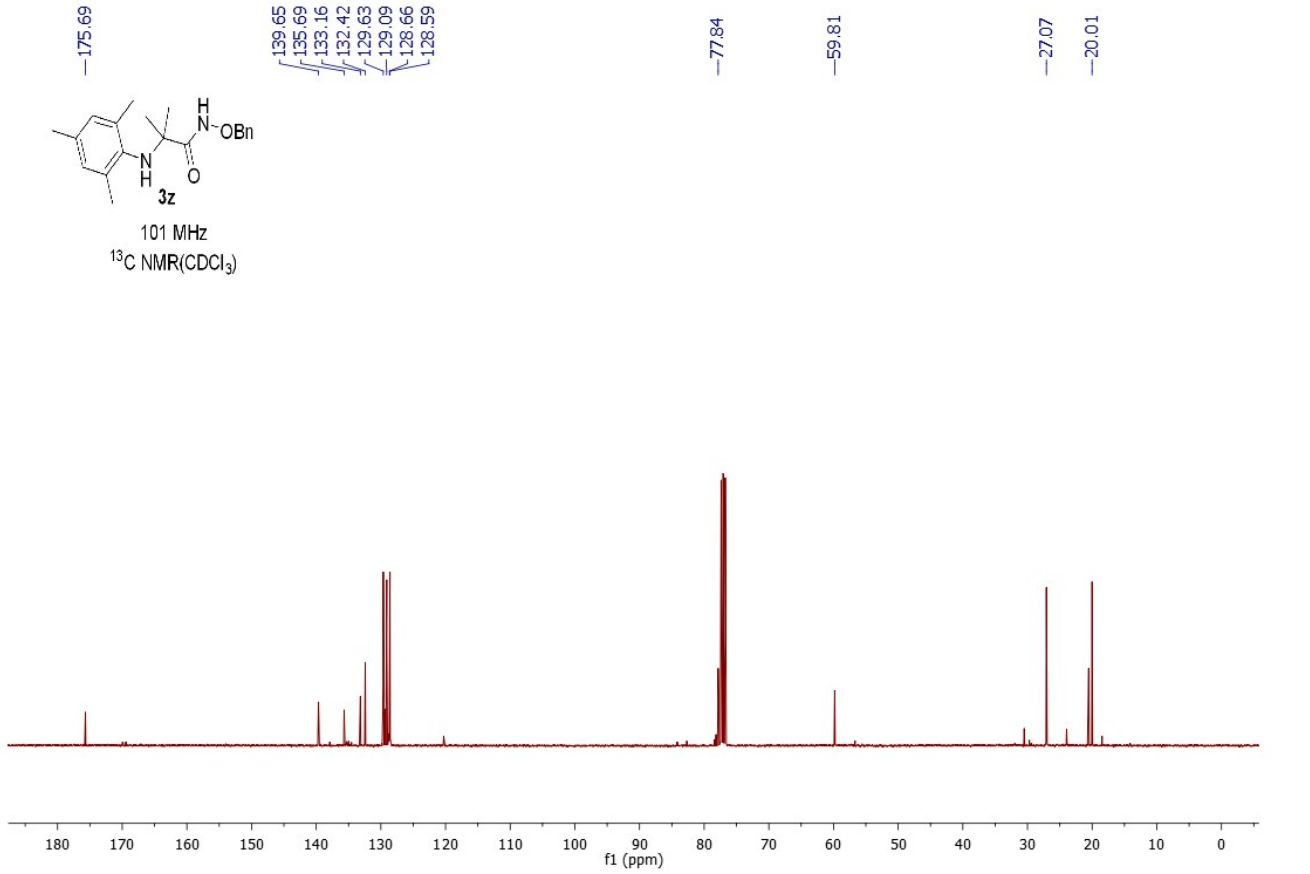
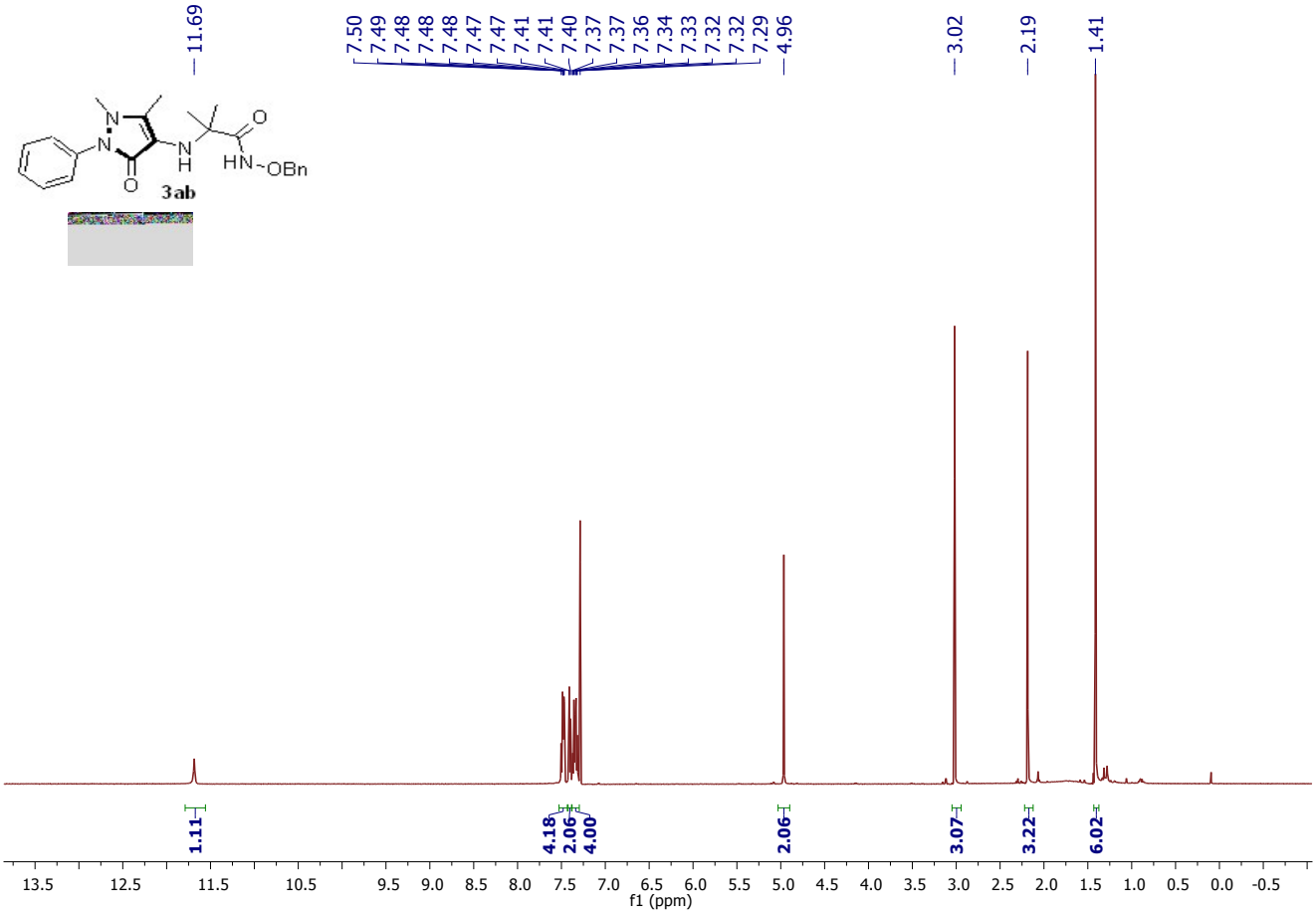
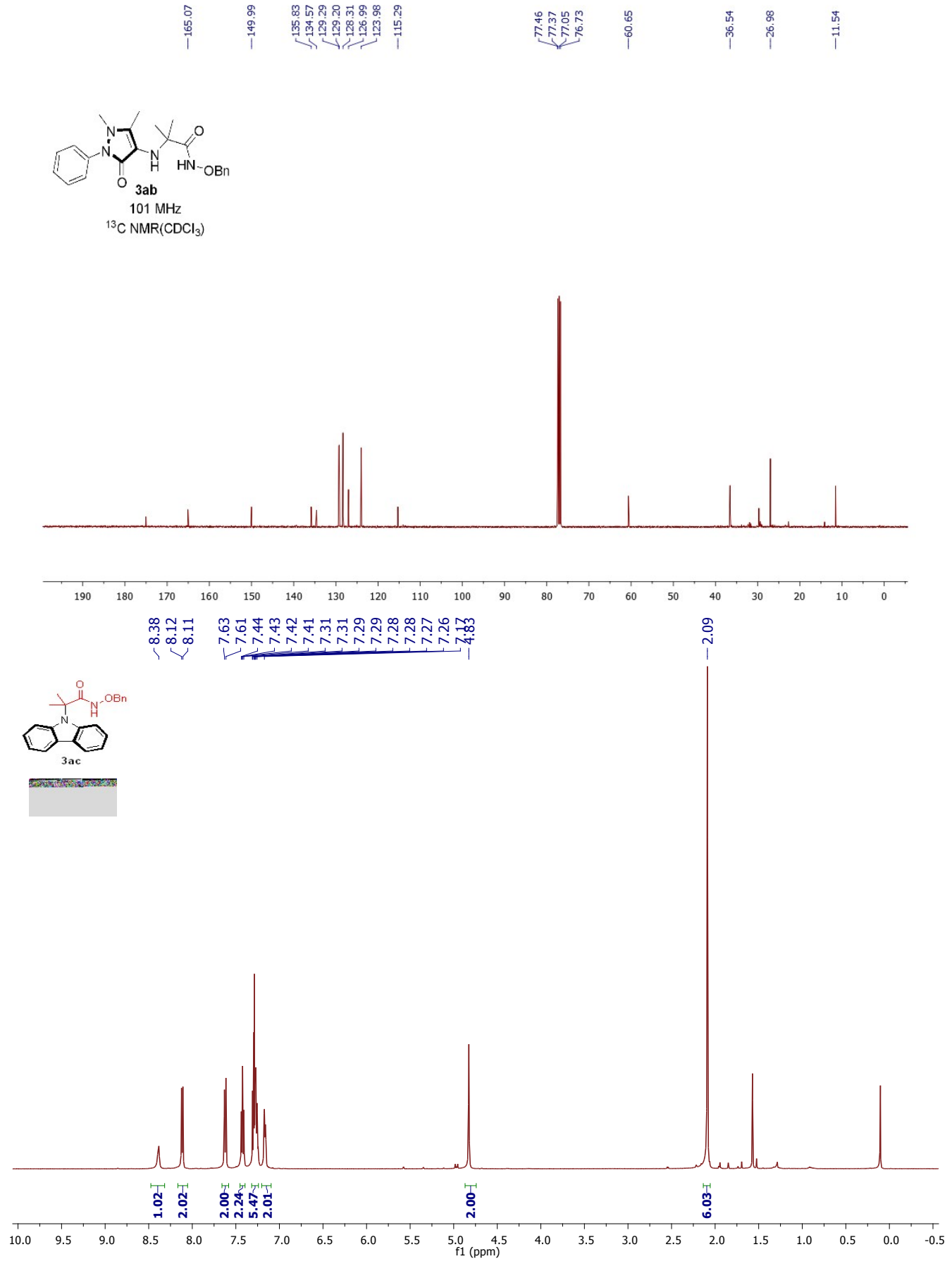
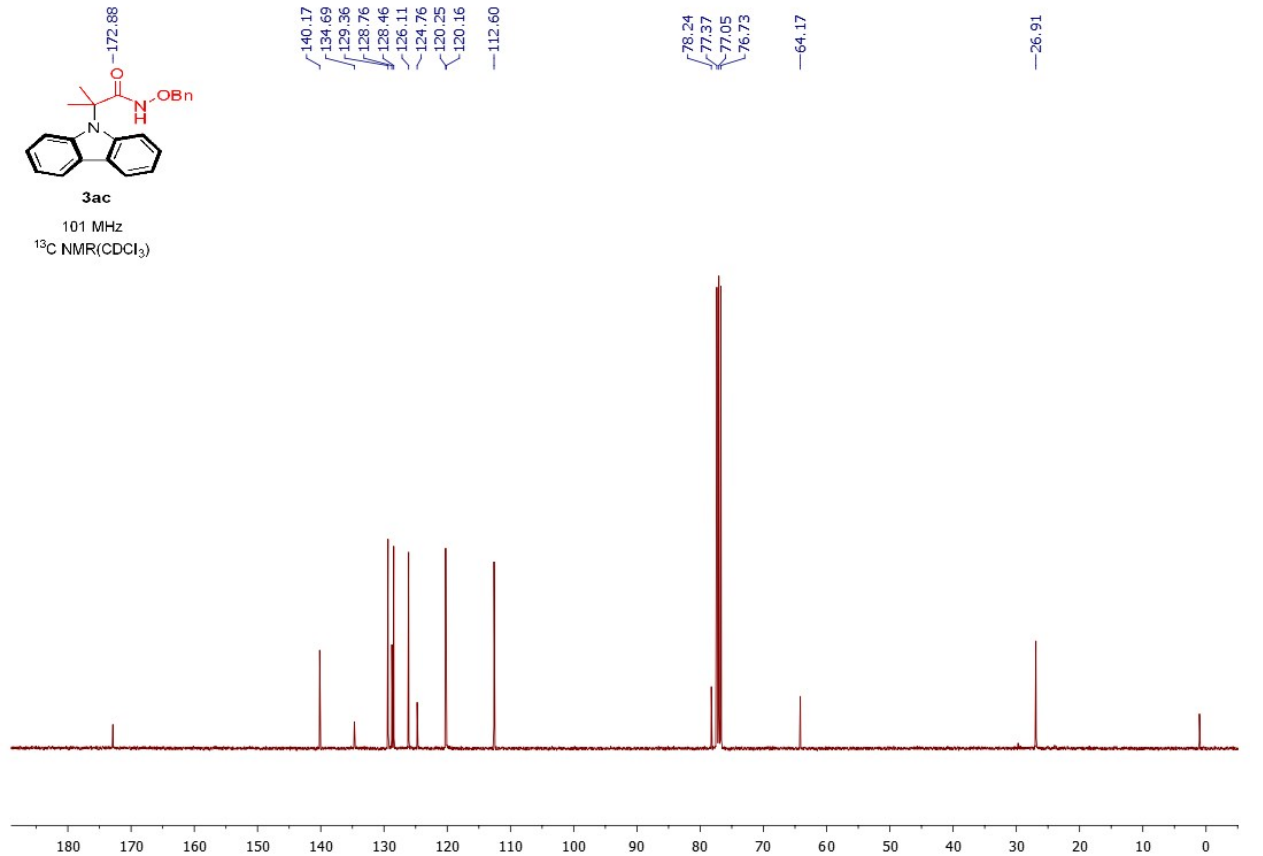
144.25
138.27
135.64
129.06
128.66
128.60
125.05
123.39
77.91
77.33
77.02
76.70
60.47
28.56
26.70
23.73
HN
OBn
O
NH
3y
101 MHz
13C NMR(CDCl3)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0


9.98
7.48
7.47
7.46
7.41
7.40
7.40
7.39
7.39
7.29
6.81
5.01
2.98
2.24
2.16
1.34
HN
OBn
O
NH
3z
0.99
2.09
3.72
1.98
2.00
0.89
3.14
6.11
6.06
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


175.69
139.65
135.69
133.16
132.42
129.63
129.09
128.66
128.59
77.84
59.81
27.07
20.01
3z
101 MHz
13C NMR(CDCl3)
f1 (ppm)


11.69
7.50
7.49
7.48
7.48
7.48
7.47
7.47
7.41
7.41
7.40
7.37
7.37
7.36
7.34
7.33
7.32
7.32
7.29
4.96
3.02
2.19
1.41
3ab
1.11
4.18
2.06
4.00
2.06
3.07
3.22
6.02
f1 (ppm)


165.07
149.99
135.83
134.57
129.29
129.20
128.31
126.99
123.98
115.29
77.46
77.37
77.05
76.73
60.65
36.54
26.98
11.54
3ab
101 MHz
13C NMR(CDCl3)
8.38
8.12
8.11
7.63
7.61
7.44
7.43
7.42
7.41
7.31
7.31
7.29
7.29
7.28
7.27
7.26
4.83
2.09
3ac
1.02
2.02
2.00
2.24
5.47
2.01
2.00
6.03
f1 (ppm)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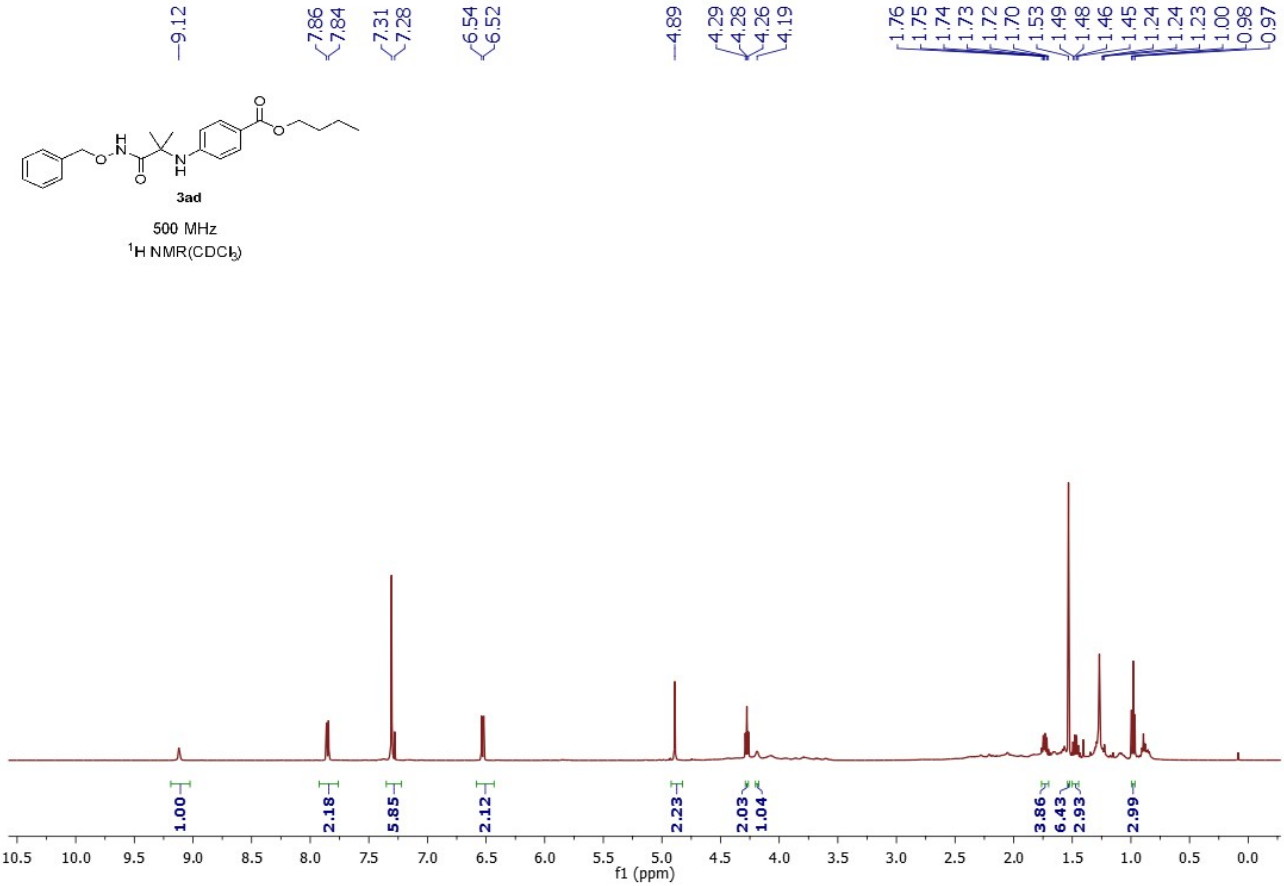
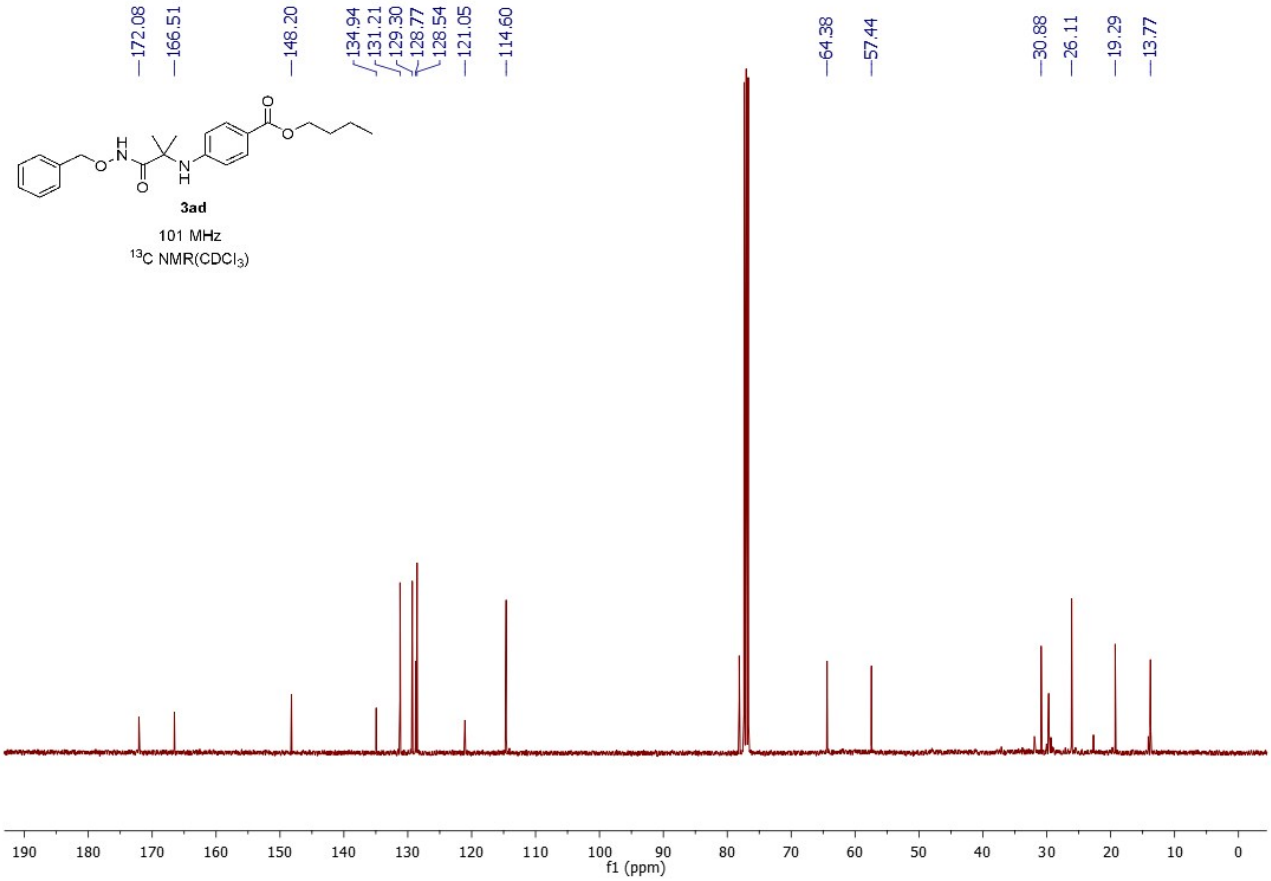
140.17
134.69
129.36
128.76
128.46
126.11
124.76
120.25
120.16
112.60
78.24
77.37
77.05
76.73
64.17
26.91
OBn
3ac
101 MHz
13C NMR(CDCl3)


9.12
7.86
7.84
7.31
7.28
6.54
6.52
4.89
4.29
4.28
4.26
4.19
1.76
1.75
1.74
1.73
1.72
1.70
1.53
1.49
1.48
1.46
1.45
1.24
1.24
1.23
1.00
0.98
0.97
3ad
500 MHz
1H NMR(CDCl3)
1.00
2.18
5.85
2.12
2.23
2.03
1.04
3.86
6.43
2.93
2.99
f1 (ppm)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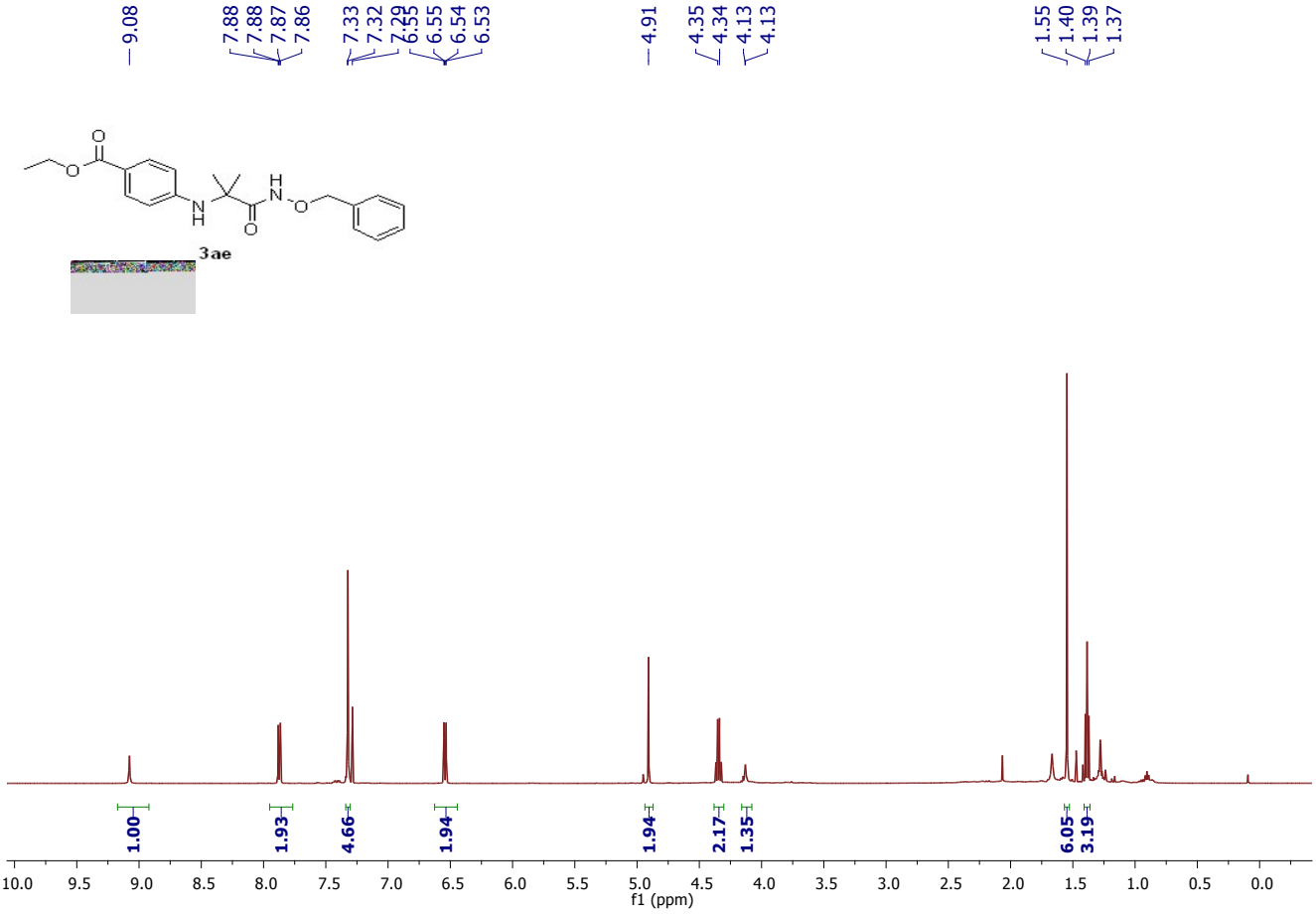
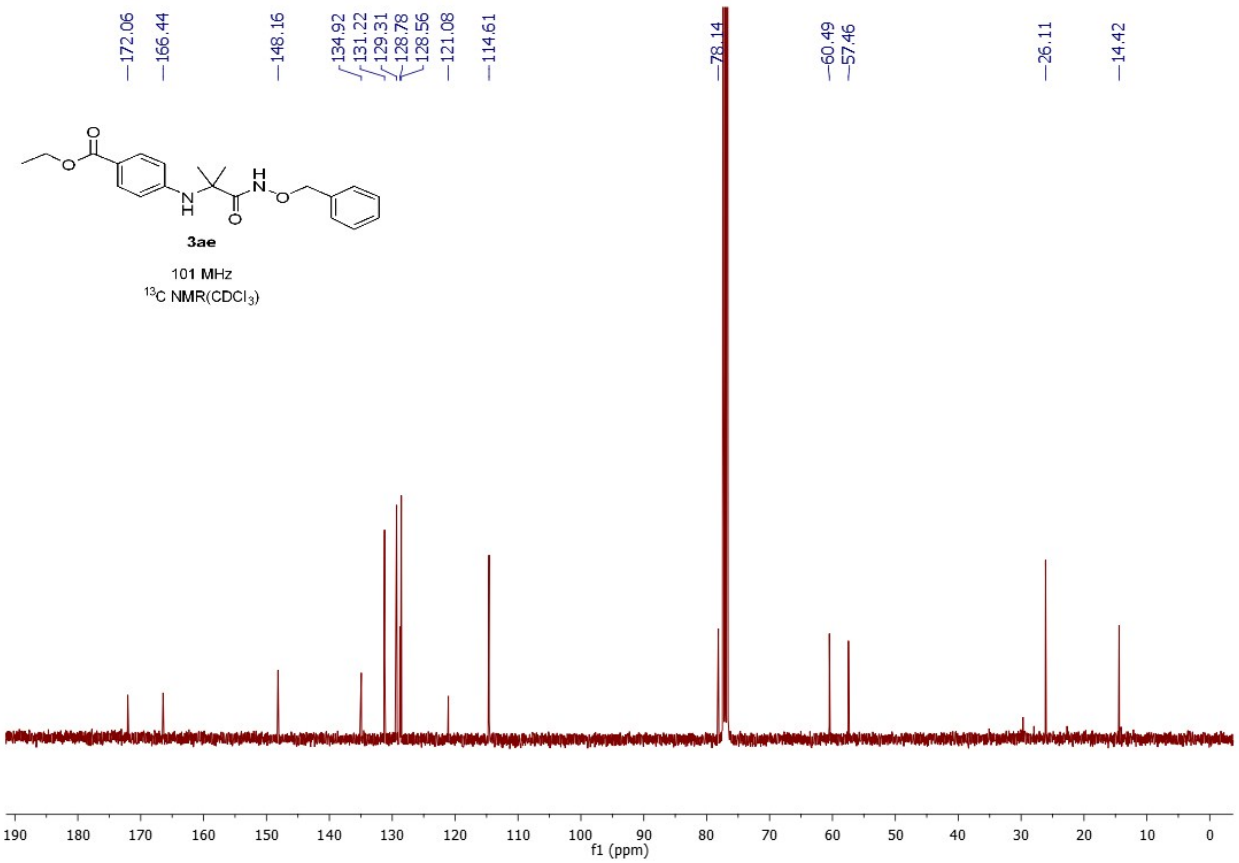
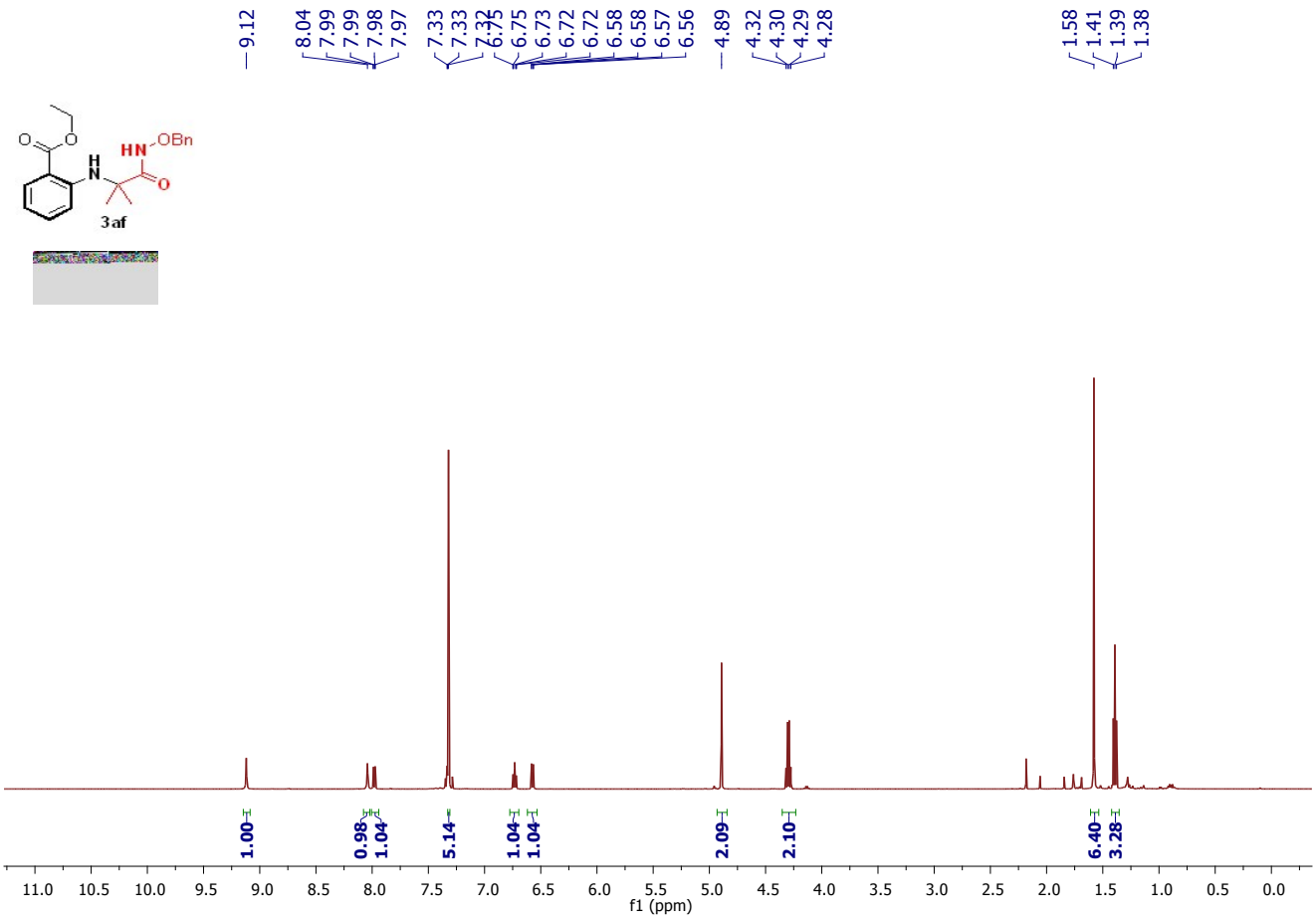
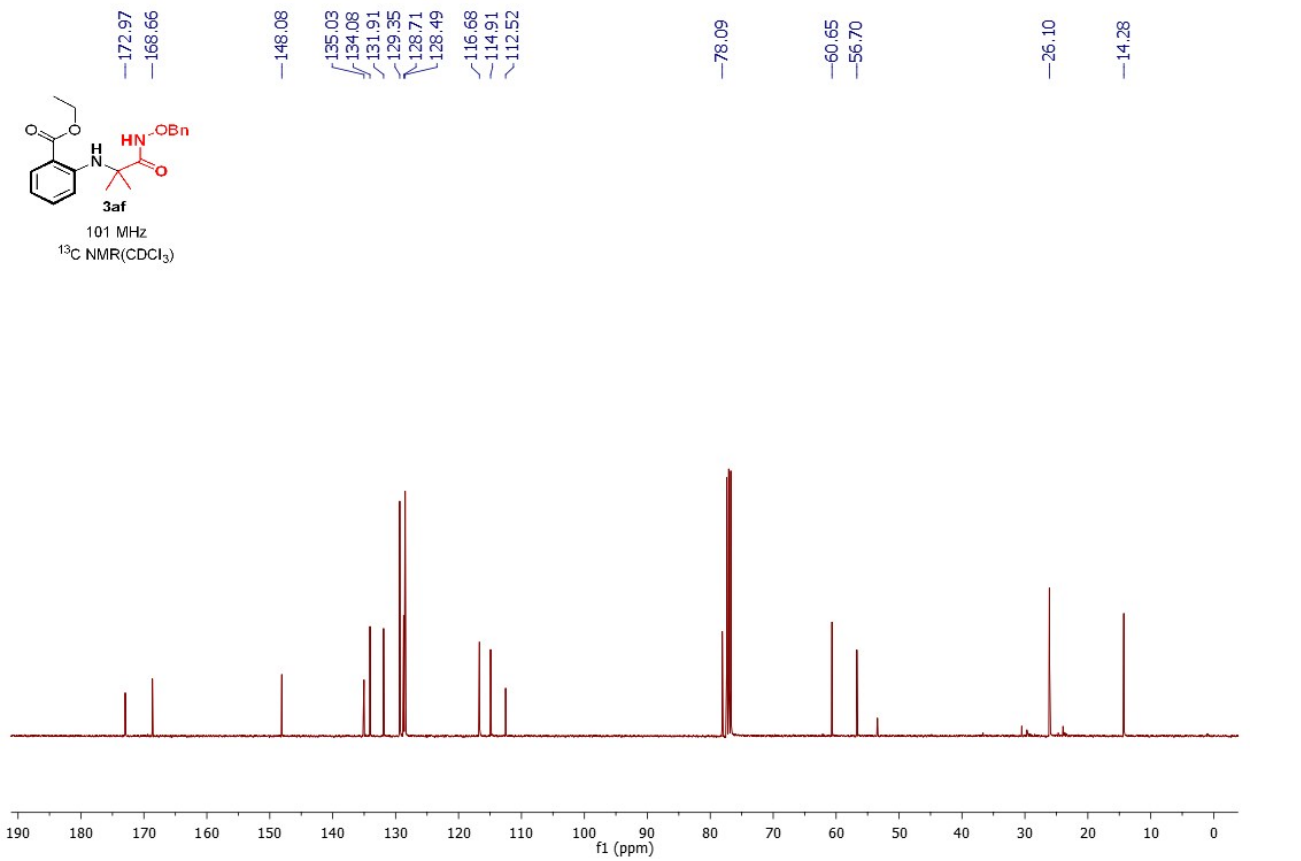
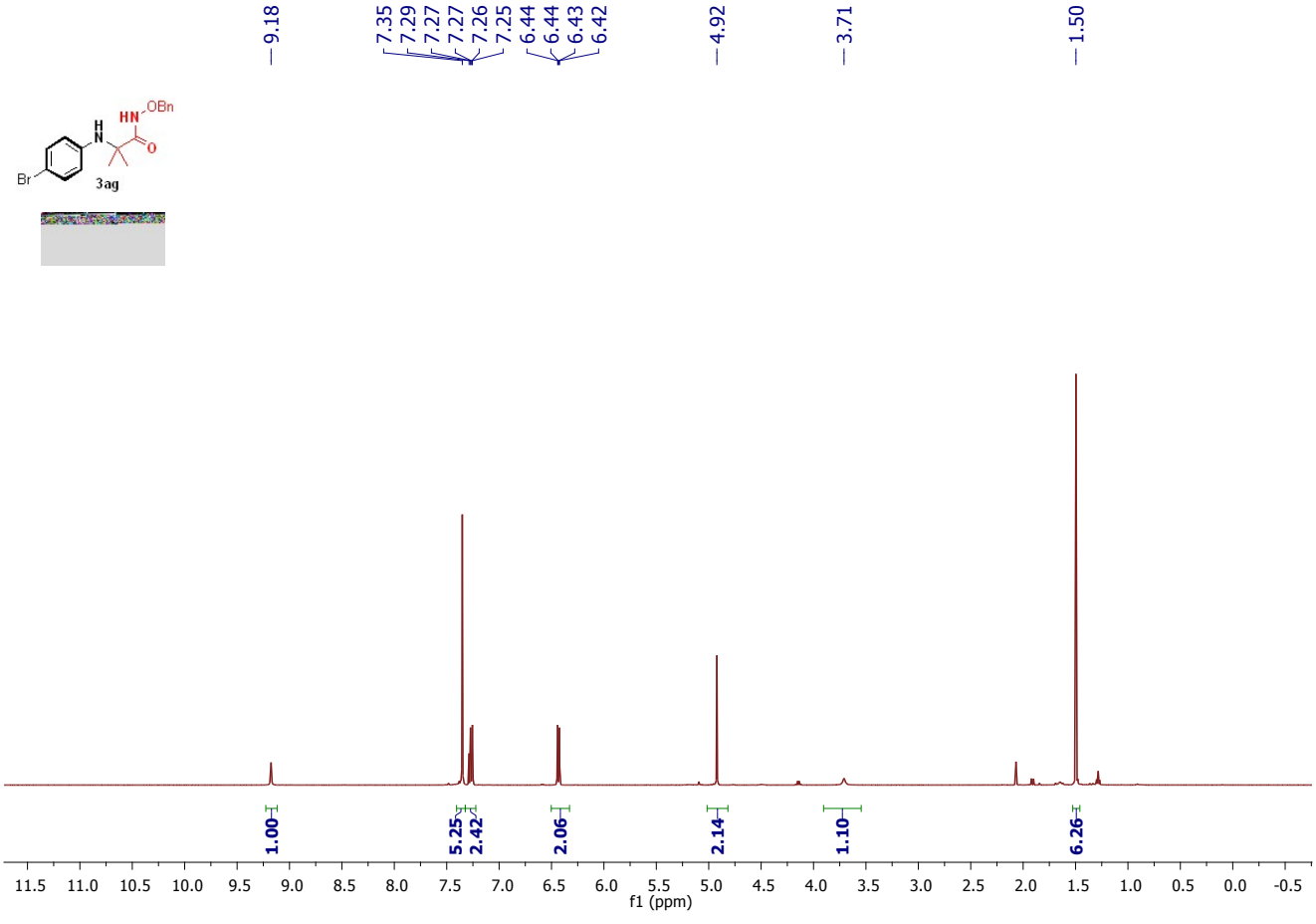
166.51
148.20
134.94
131.21
129.30
128.77
128.54
121.05
114.60
64.38
57.44
30.88
26.11
19.29
13.77
3ad
101 MHz
13C NMR(CDCl3)
f1 (ppm)

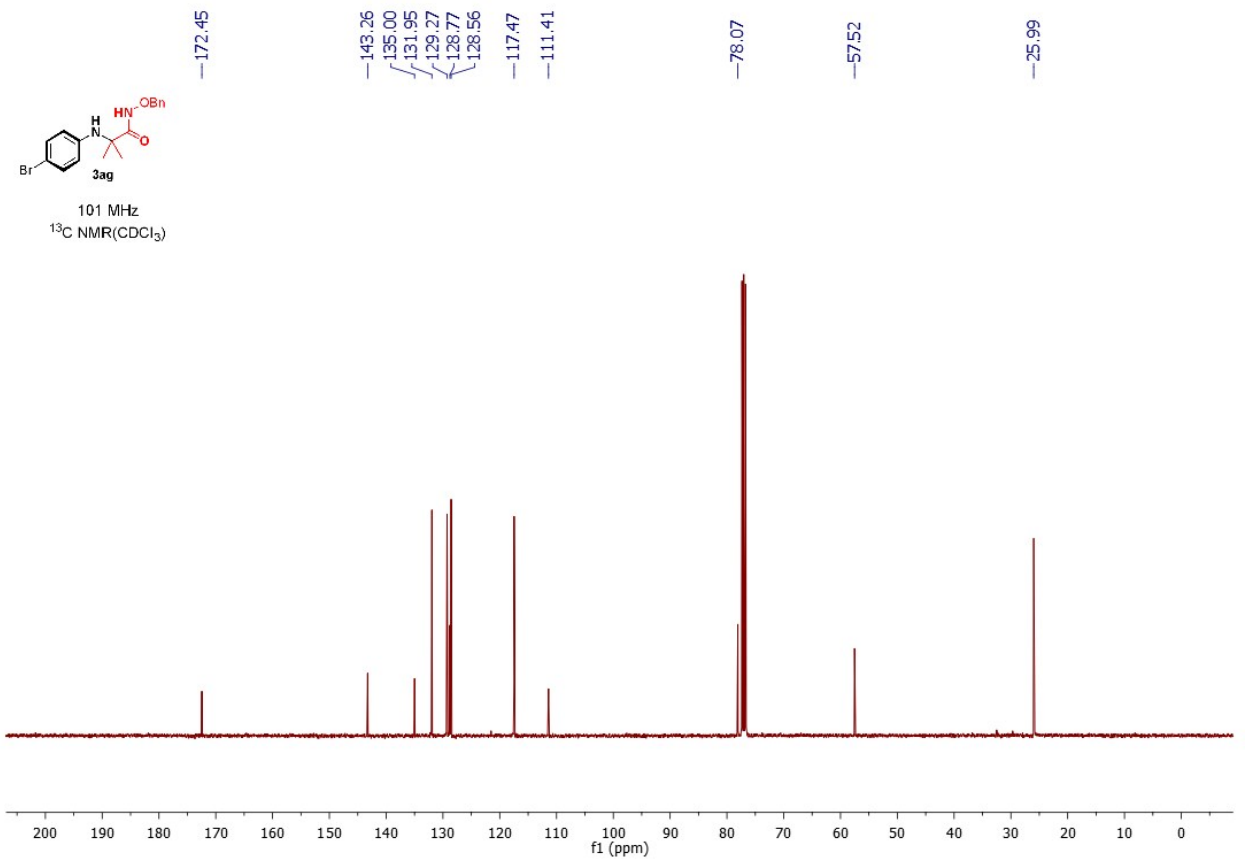

9.08
7.88
7.88
7.87
7.86
7.33
7.32
7.29
6.55
6.54
6.53
4.91
4.35
4.34
4.13
4.13
1.55
1.40
1.39
1.37
3ae
1.00
1.93
4.66
1.94
1.94
2.17
1.35
6.05
3.19
f1 (ppm)


172.06
166.44
148.16
134.92
131.22
129.31
128.78
128.56
121.08
114.61
78.14
60.49
57.46
26.11
14.42
3ae
101 MHz
13C NMR(CDCl3)
f1 (ppm)


9.12
8.04
7.99
7.99
7.98
7.97
7.33
7.33
6.75
6.75
6.73
6.72
6.72
6.58
6.58
6.57
6.56
4.89
4.32
4.30
4.29
4.28
1.58
1.41
1.39
1.38
HN
OBn
3af
1.00
0.98
1.04
5.14
1.04
1.04
2.09
2.10
6.40
3.28
f1 (ppm)


172.97
168.66
148.08
135.03
134.08
131.91
129.35
128.71
128.49
116.68
114.91
112.52
78.09
60.65
56.70
26.10
14.28
HN
OBn
O
H
N
O
3af
101 MHz
13C NMR(CDCl3)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


9.18
7.35
7.29
7.27
7.27
7.26
7.25
6.44
6.44
6.43
6.42
4.92
3.71
1.50
HN
OBn
H
N
O
Br
3ag
1.00
5.25
2.42
2.06
2.14
1.10
6.26
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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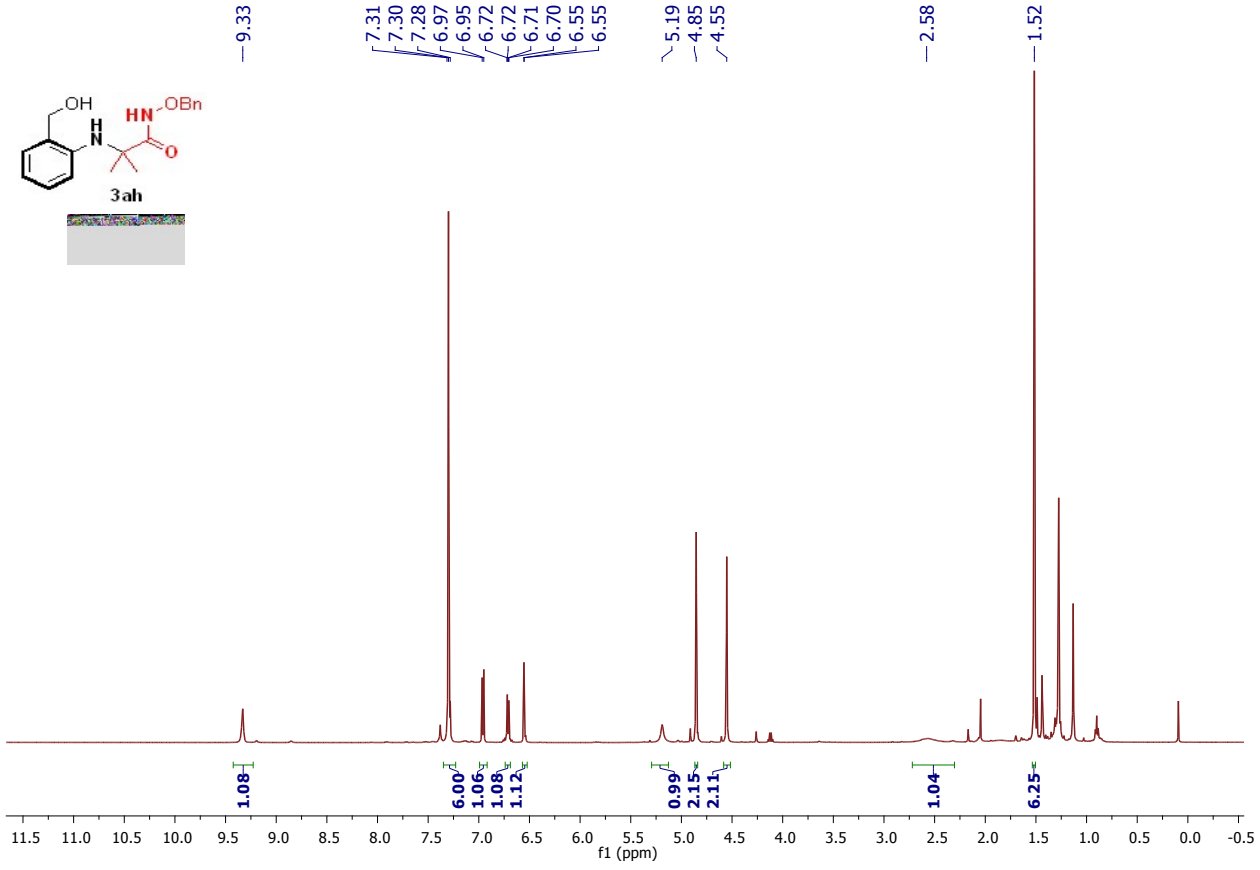
143.26
135.00
131.95
129.27
128.77
128.56
117.47
111.41
78.07
57.52
25.99
3ag
101 MHz
13C NMR(CDCl3)
f1 (ppm)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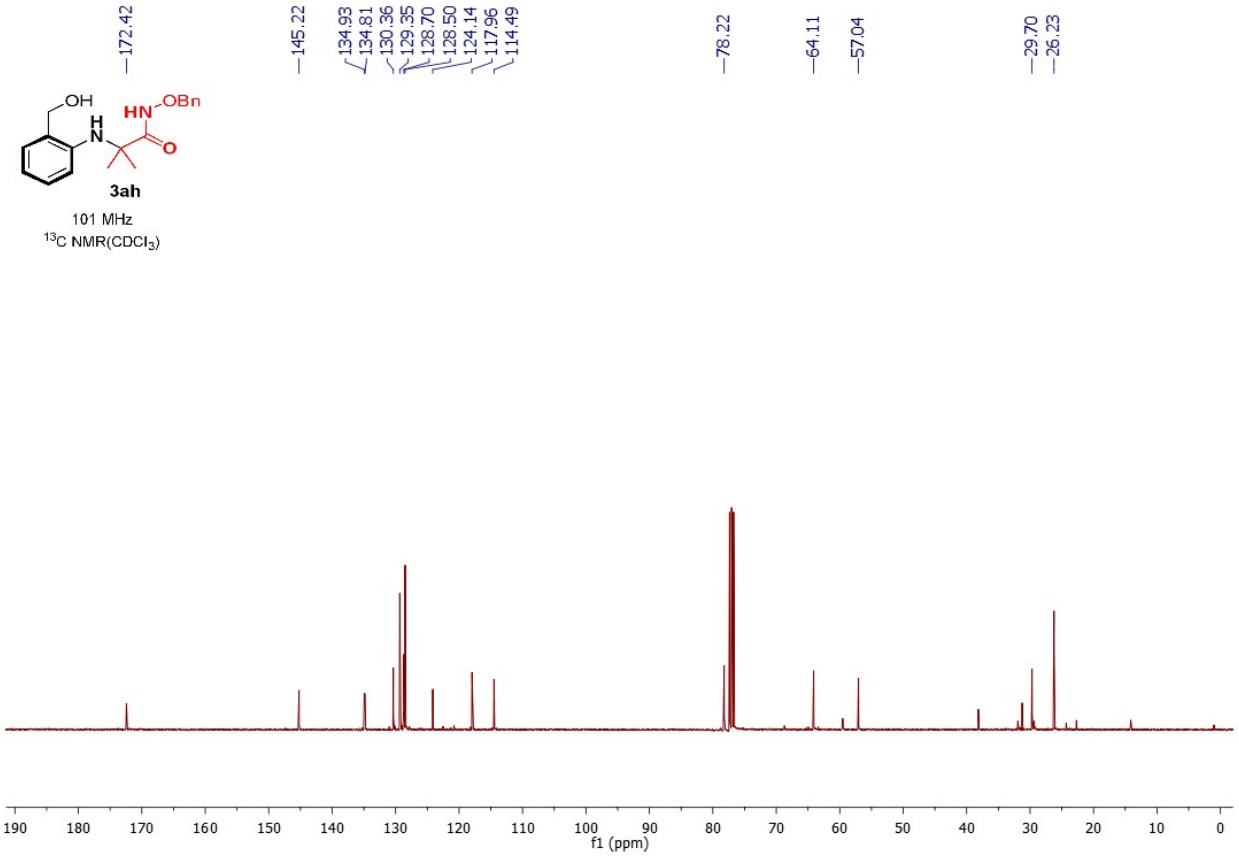
7.31
7.30
7.28
6.97
6.95
6.72
6.72
6.71
6.70
6.55
6.55
5.19
4.85
4.55
2.58
1.52
3ah
1.08
6.00
1.06
1.08
1.12
0.99
2.15
2.11
1.04
6.25
f1 (ppm)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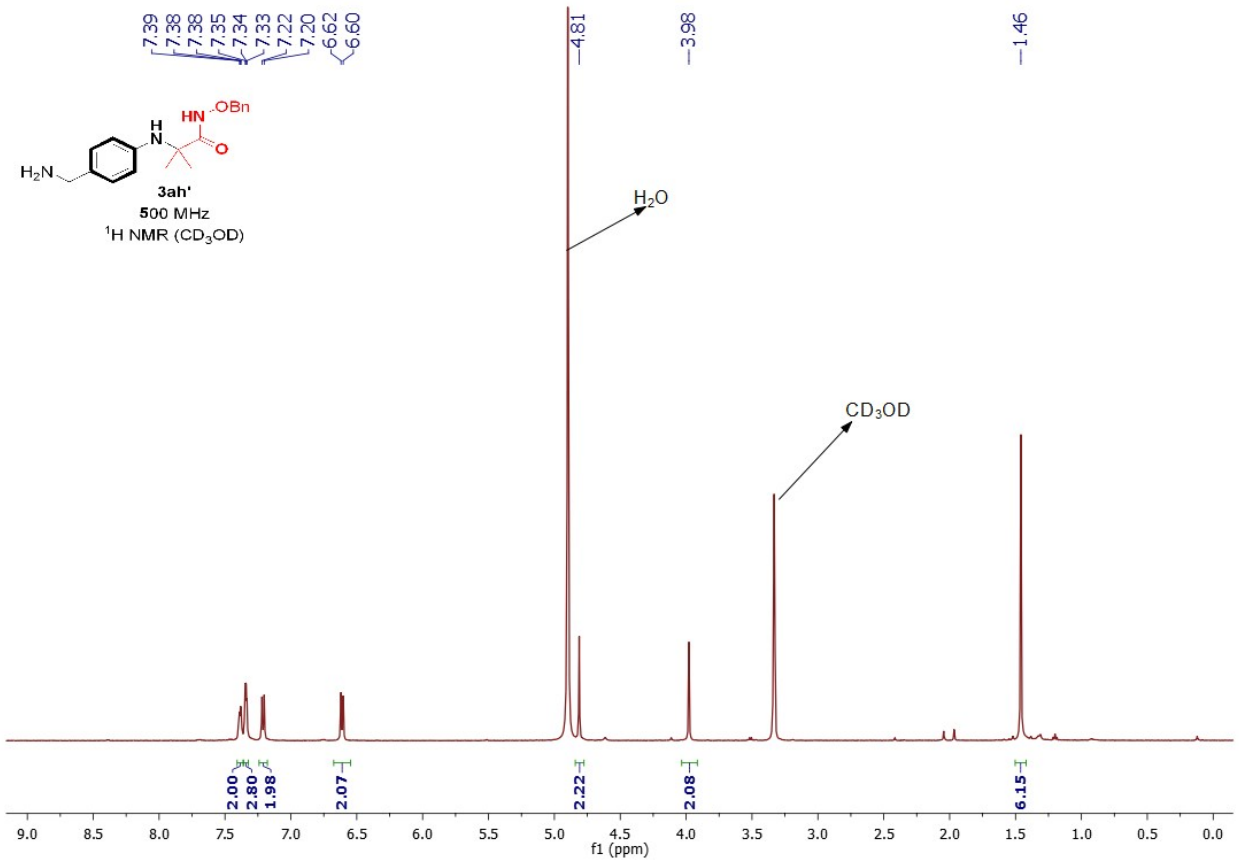
145.22
134.93
134.81
130.36
129.35
128.70
128.50
124.14
117.96
114.49
78.22
64.11
57.04
29.70
26.23
OH
HN
OBn
H
N
O
3ah
101 MHz
13C NMR(CDCl3)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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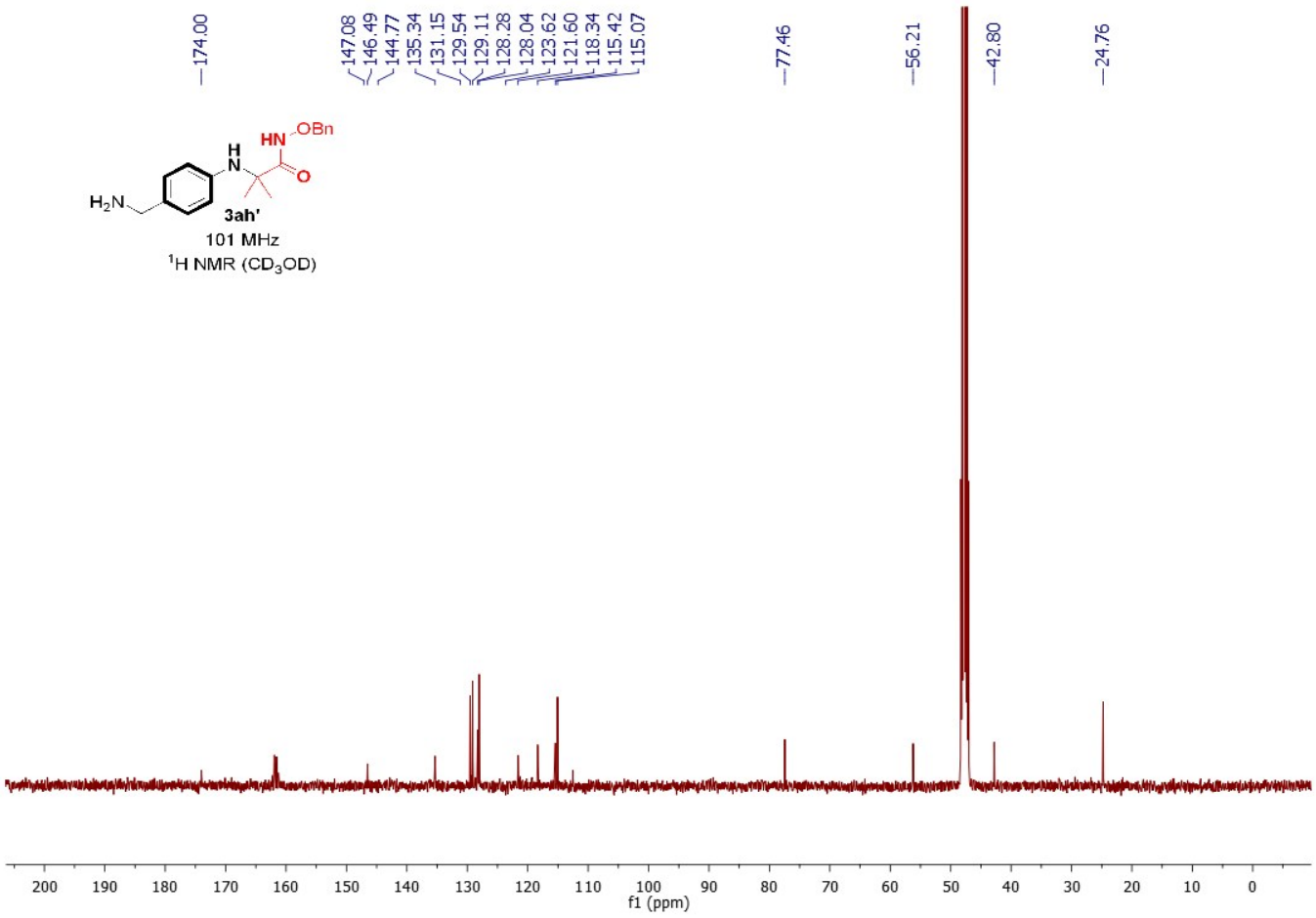
7.38
7.38
7.35
7.34
7.33
7.22
7.20
6.62
6.60
4.81
3.98
1.46
HN
OBn
H
N
O
H2N
3ah'
500 MHz
1H NMR (CD3OD)
H2O
CD3OD
2.00
2.80
1.98
2.07
2.22
2.08
6.15
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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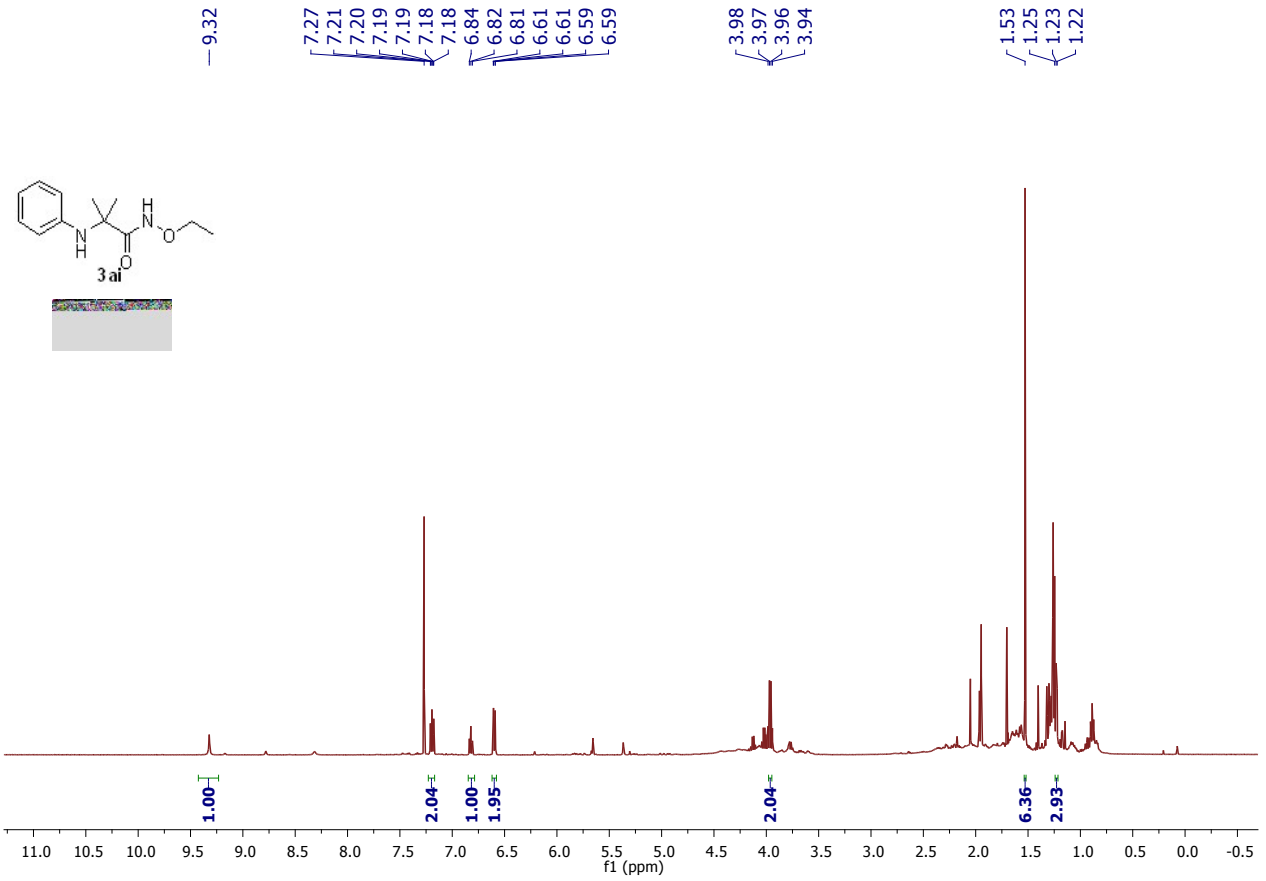
147.08
146.49
144.77
135.34
131.15
129.54
129.11
128.28
128.04
123.62
121.60
118.34
115.42
115.07
77.46
56.21
42.80
24.76
HN
OBn
H
N
O
H2N
3ah'
101 MHz
1H NMR (CD3OD)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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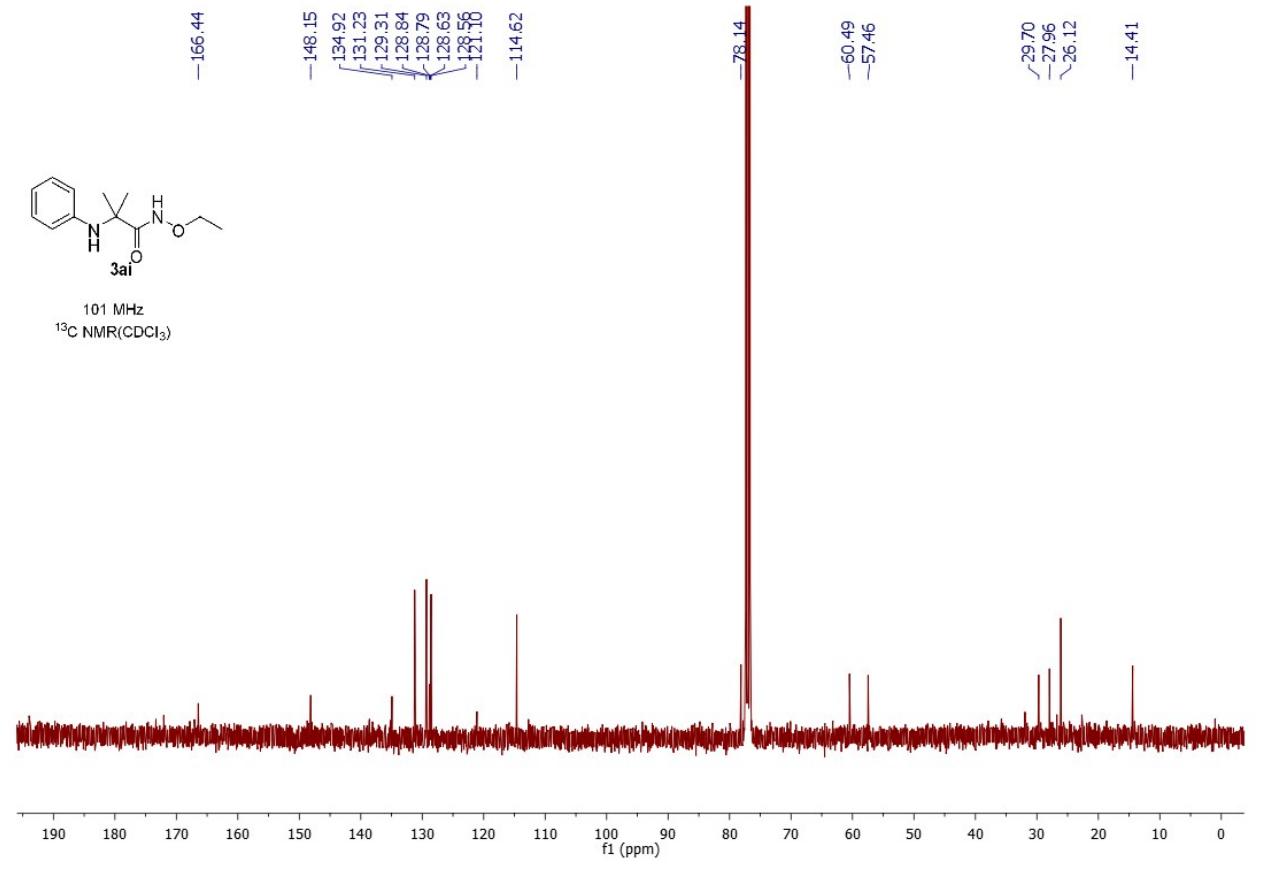
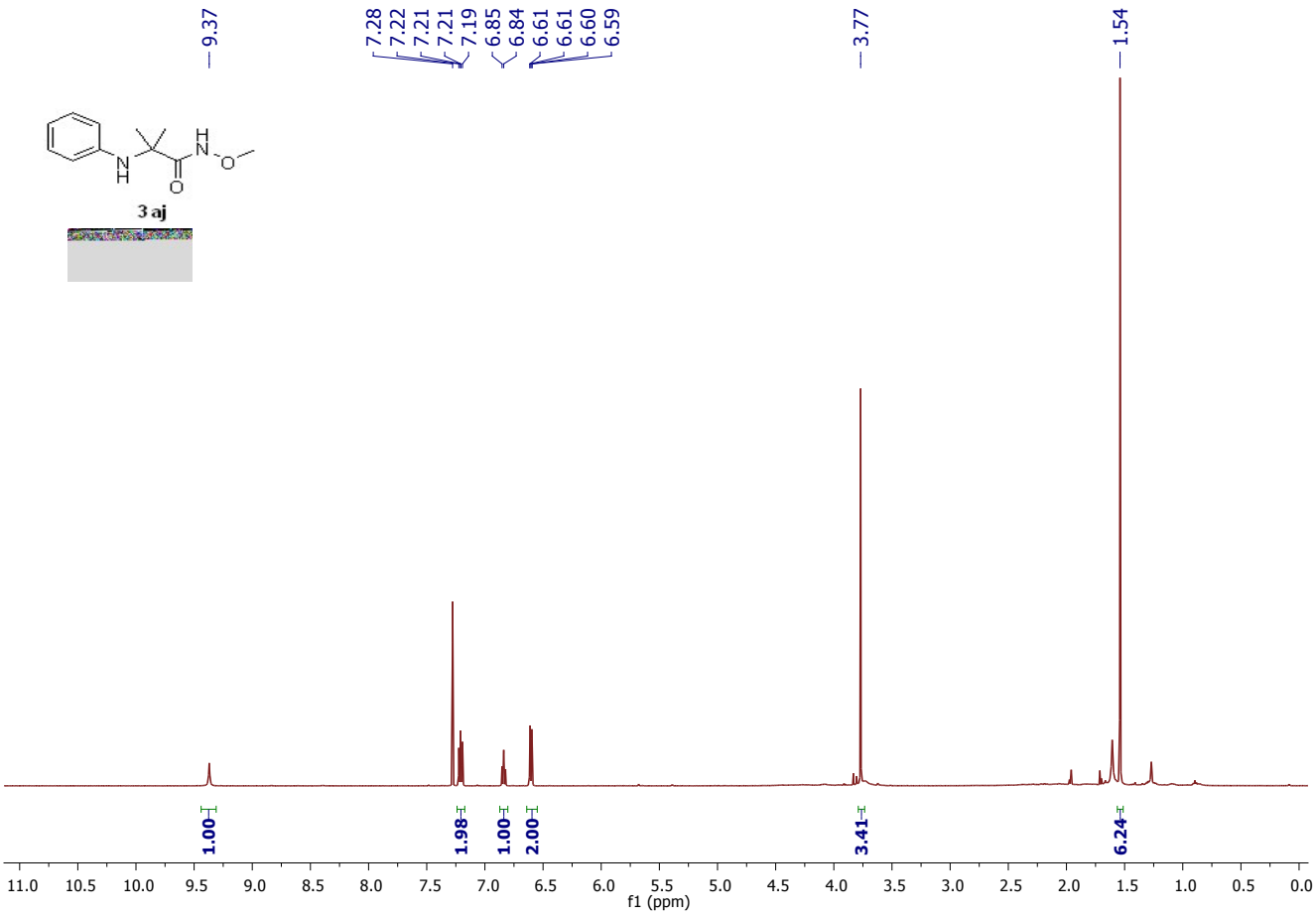
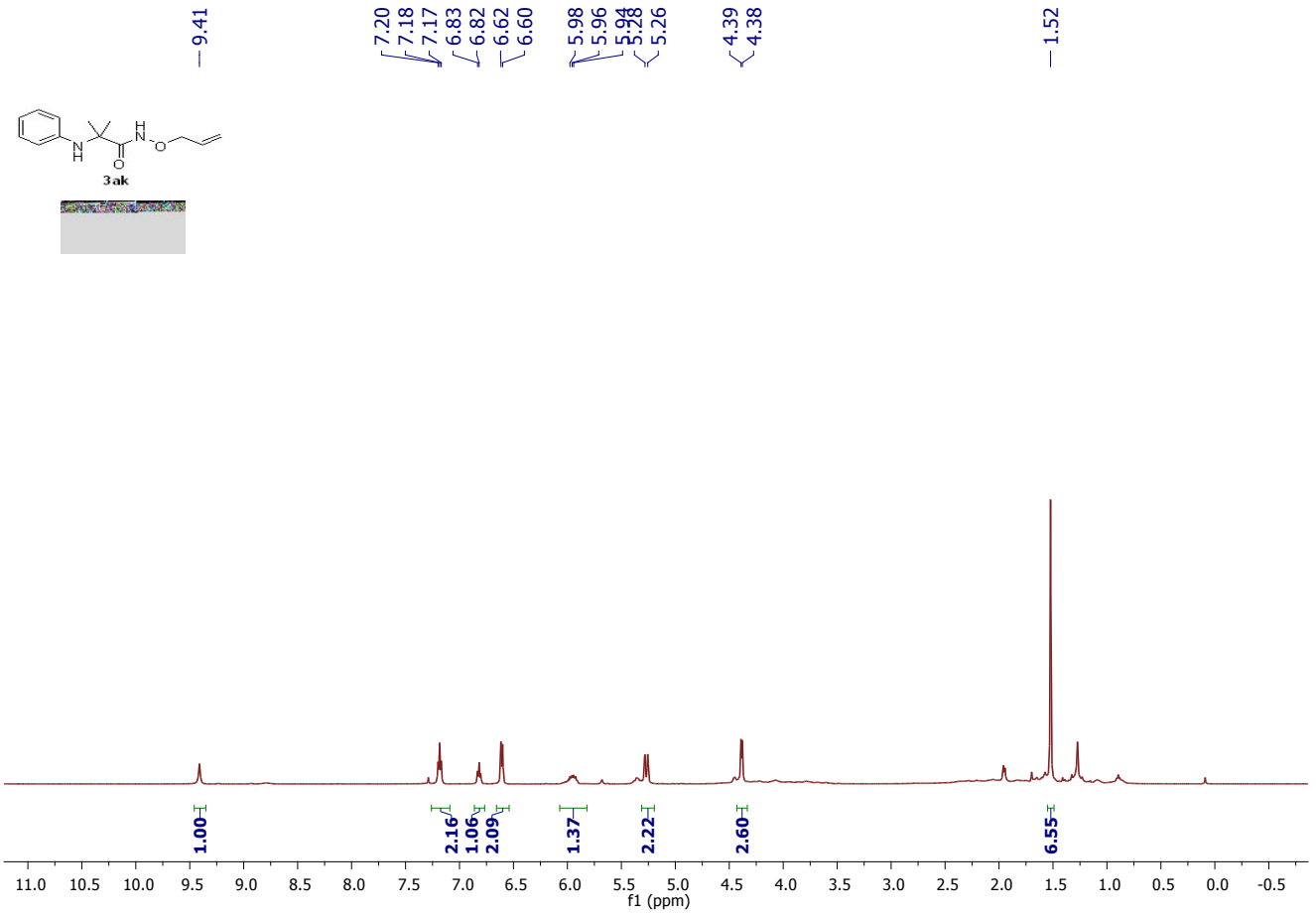
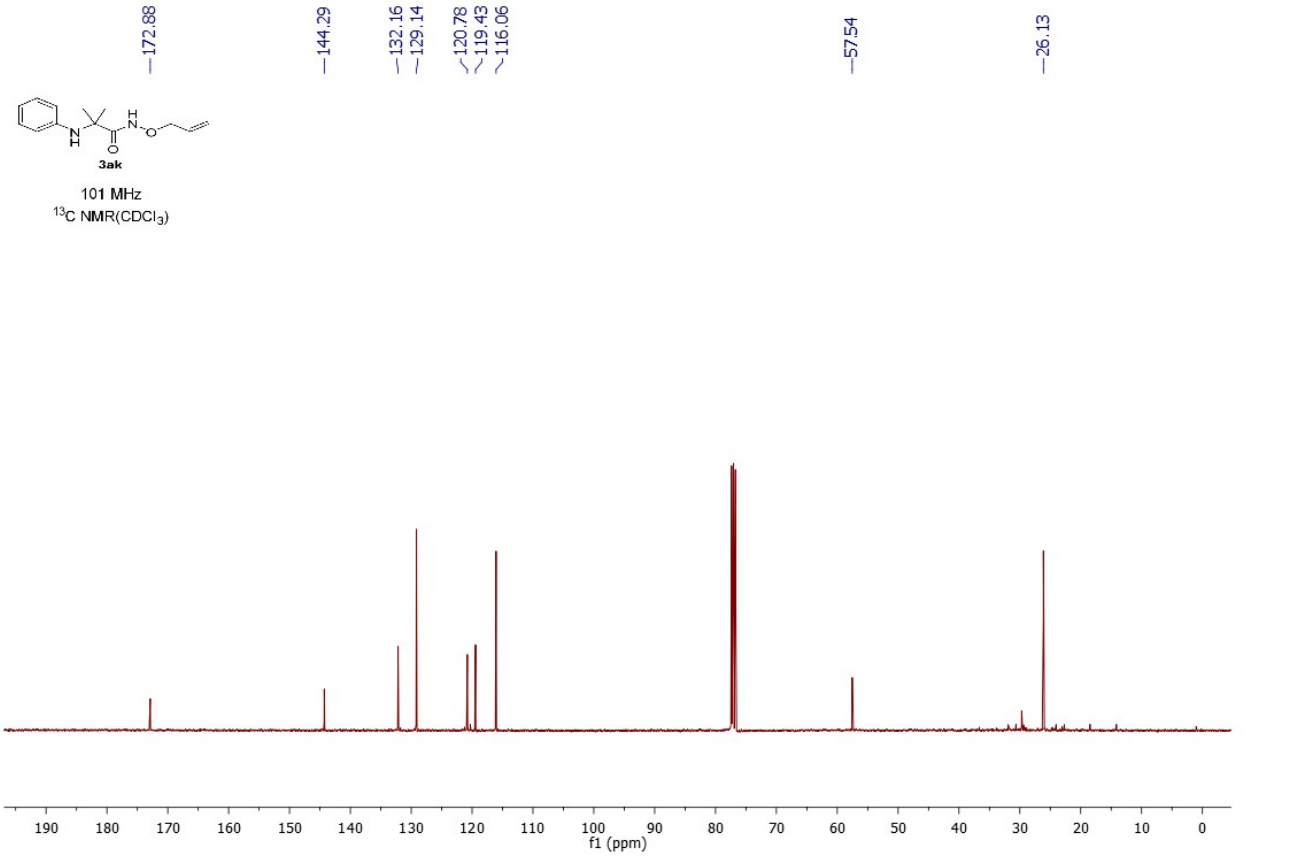
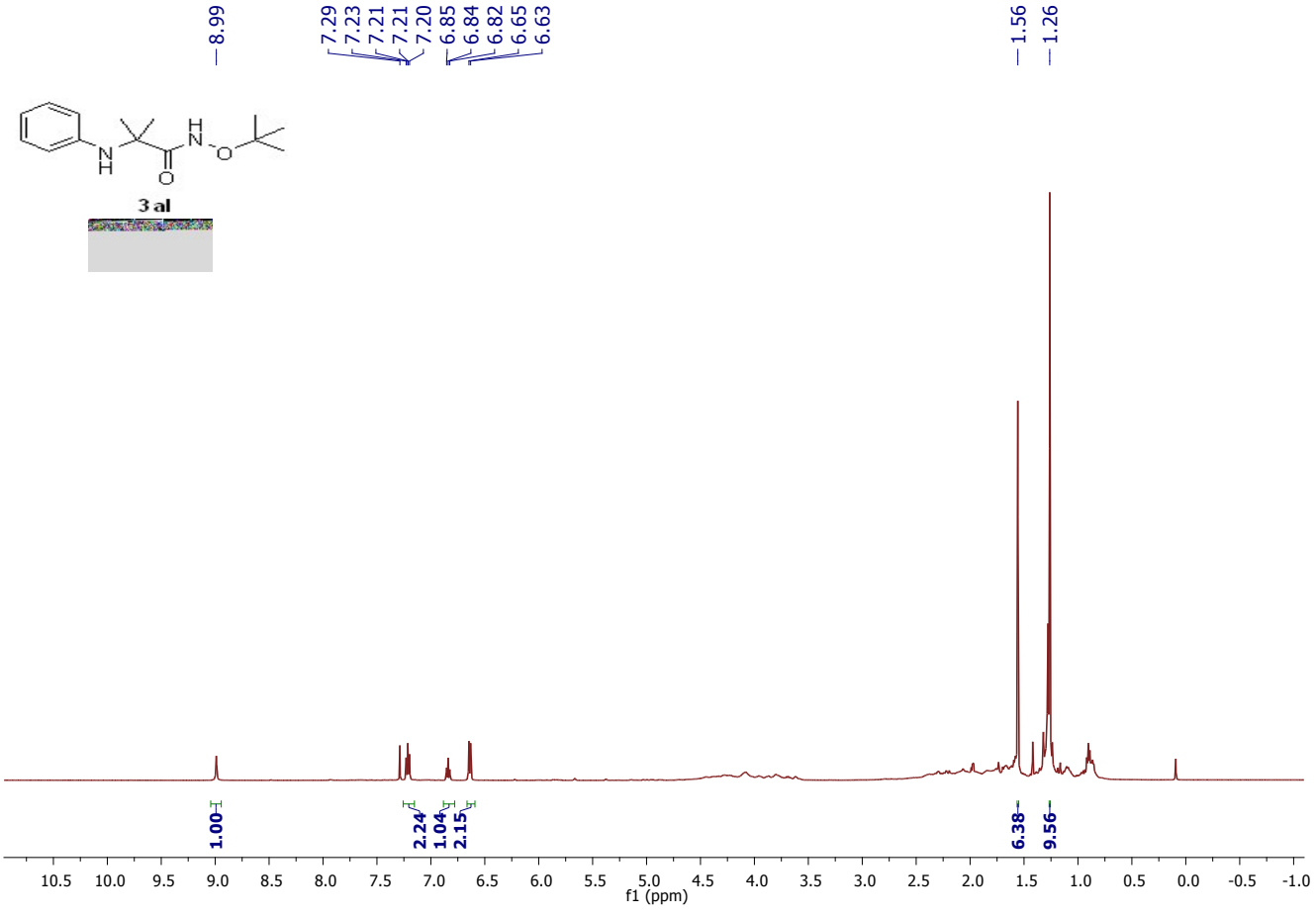
7.27
7.21
7.20
7.19
7.19
7.18
7.18
6.84
6.82
6.81
6.61
6.61
6.59
6.59
3.98
3.97
3.96
3.94
1.53
1.25
1.23
1.22
3 ai
1.00
2.04
1.00
1.95
2.04
6.36
2.93
f1 (ppm)


166.44
148.15
134.92
131.23
129.31
128.84
128.79
128.63
128.56
121.10
114.62
78.14
60.49
57.46
29.70
27.96
26.12
14.41
3ai
101 MHz
13C NMR(CDCl3)
f1 (ppm)


9.37
7.28
7.22
7.21
7.21
7.19
6.85
6.84
6.61
6.60
6.59
3.77
1.54
3aj
1.00
1.98
1.00
2.00
3.41
6.24
f1 (ppm)


9.41
7.20
7.18
7.17
6.83
6.82
6.62
6.60
5.98
5.96
5.94
5.28
5.26
4.39
4.38
1.52
3ak
1.00
2.16
1.06
2.09
1.37
2.22
2.60
6.55
f1 (ppm)


172.88
144.29
132.16
129.14
120.78
119.43
116.06
57.54
26.13
3ak
101 MHz
13C NMR(CDCl3)
f1 (ppm)


8.99
7.29
7.23
7.21
7.21
7.20
6.85
6.84
6.82
6.65
6.63
1.56
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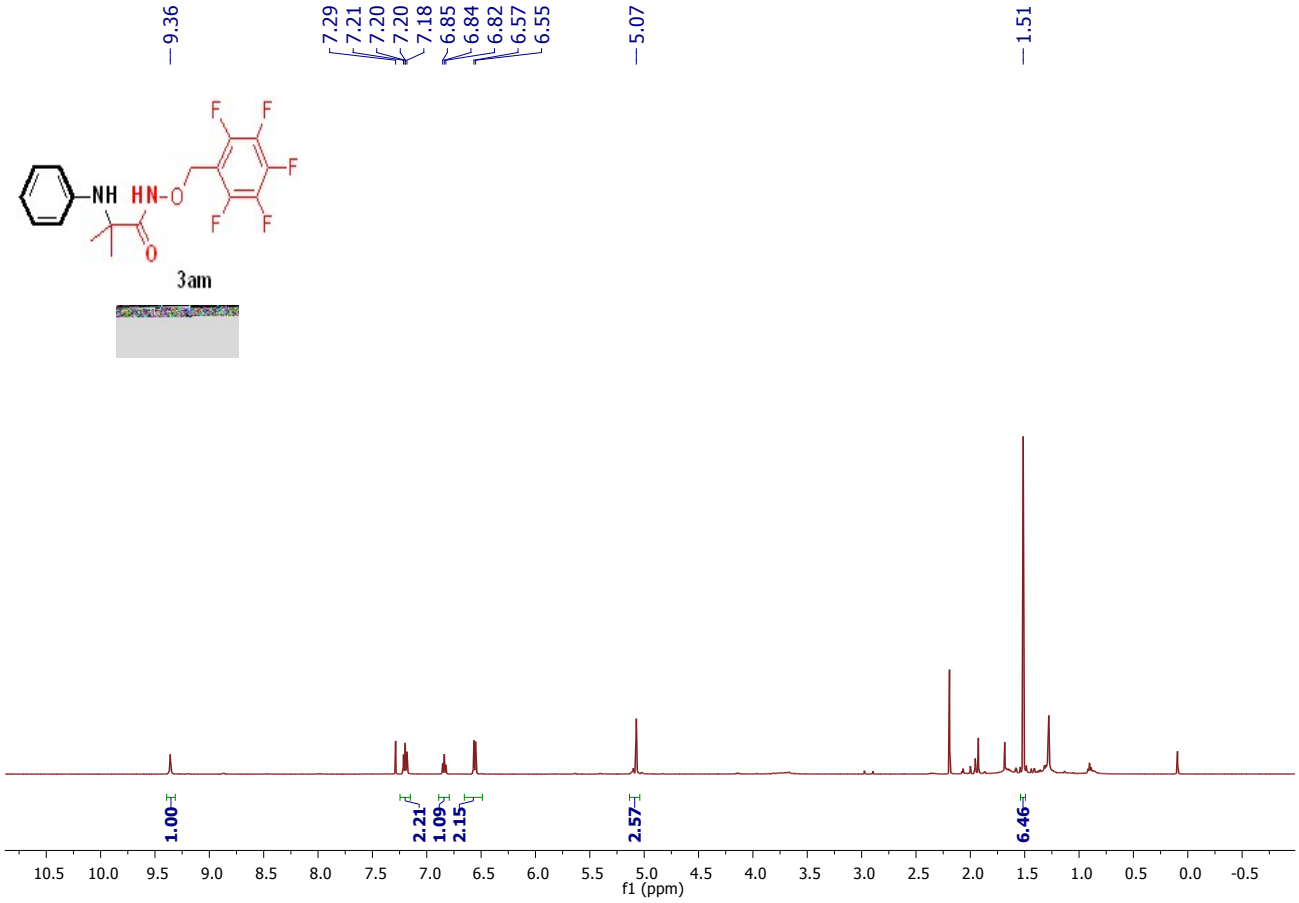
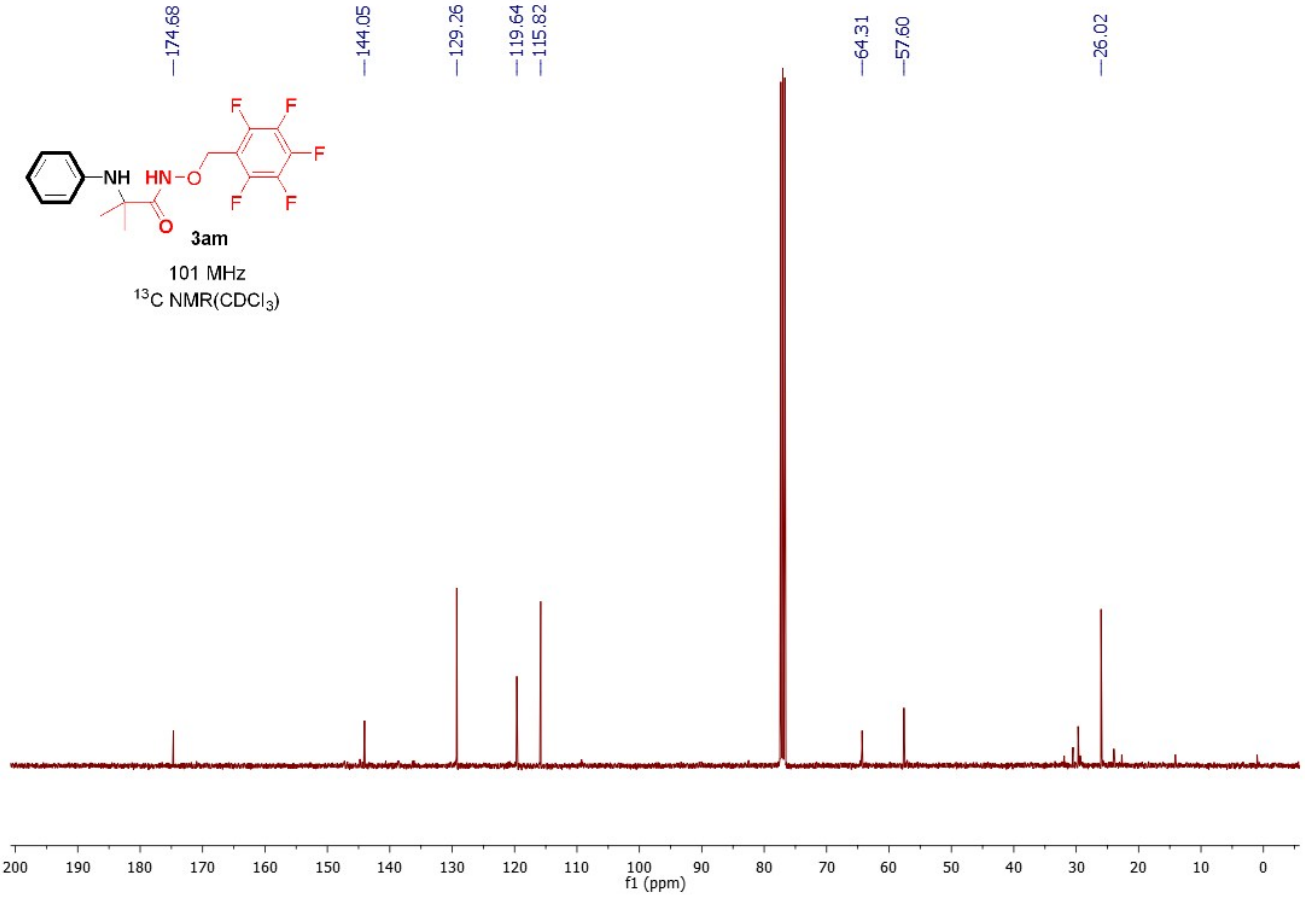
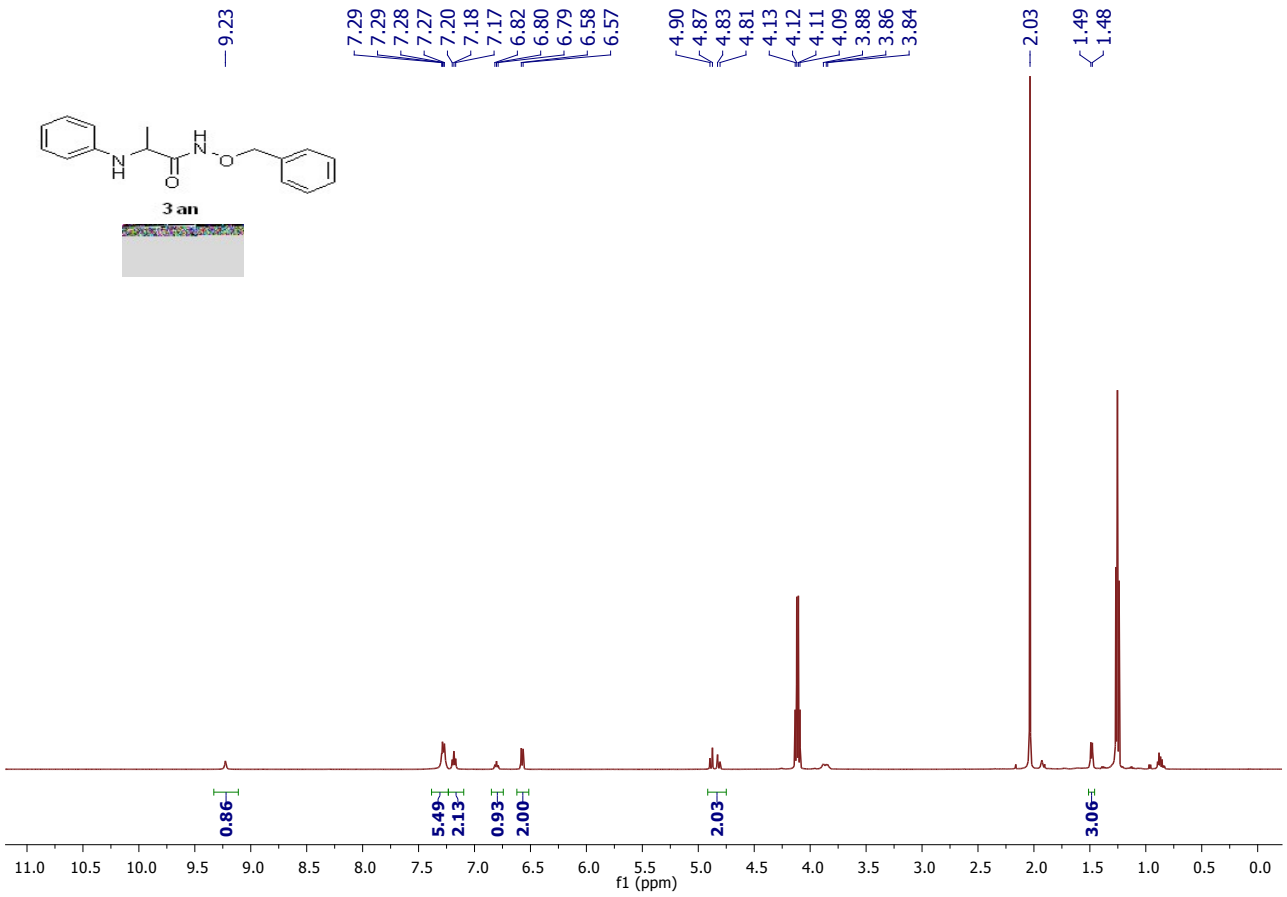
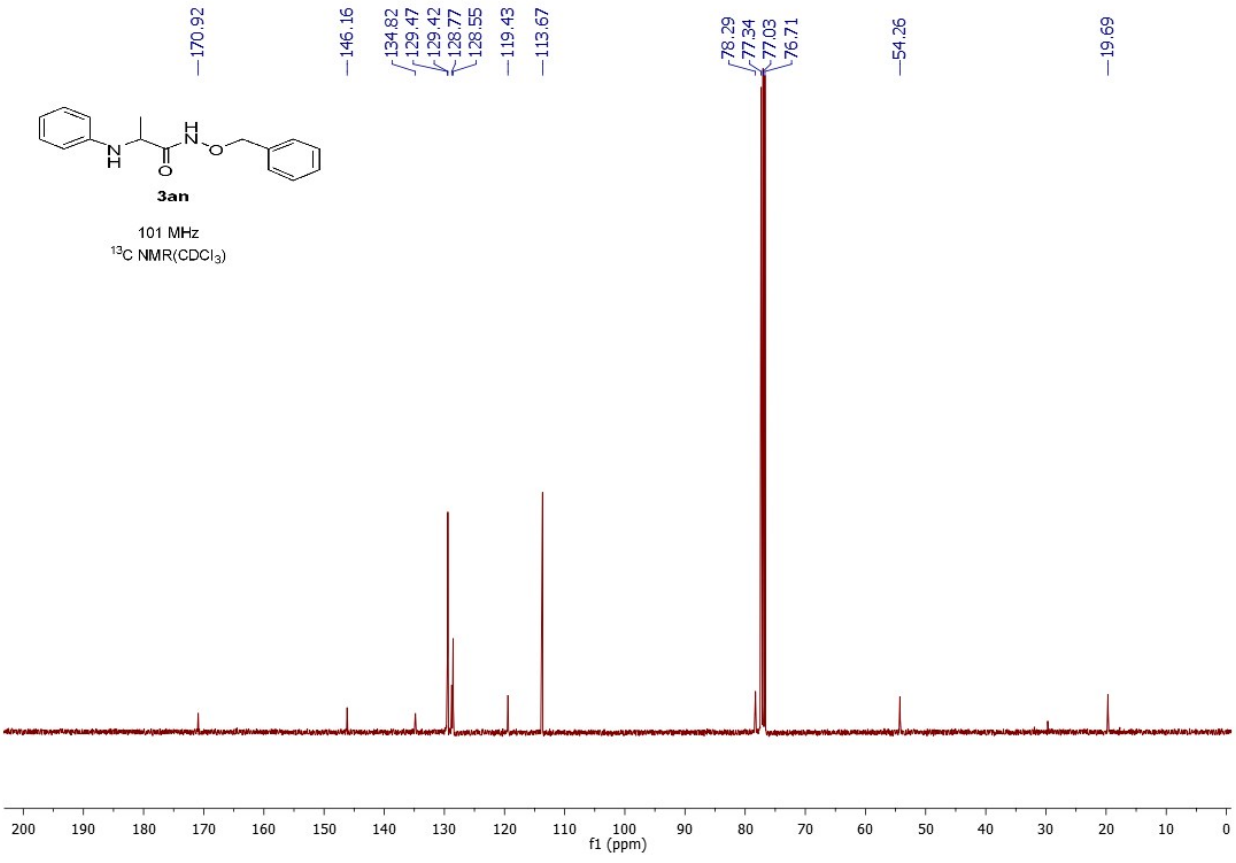
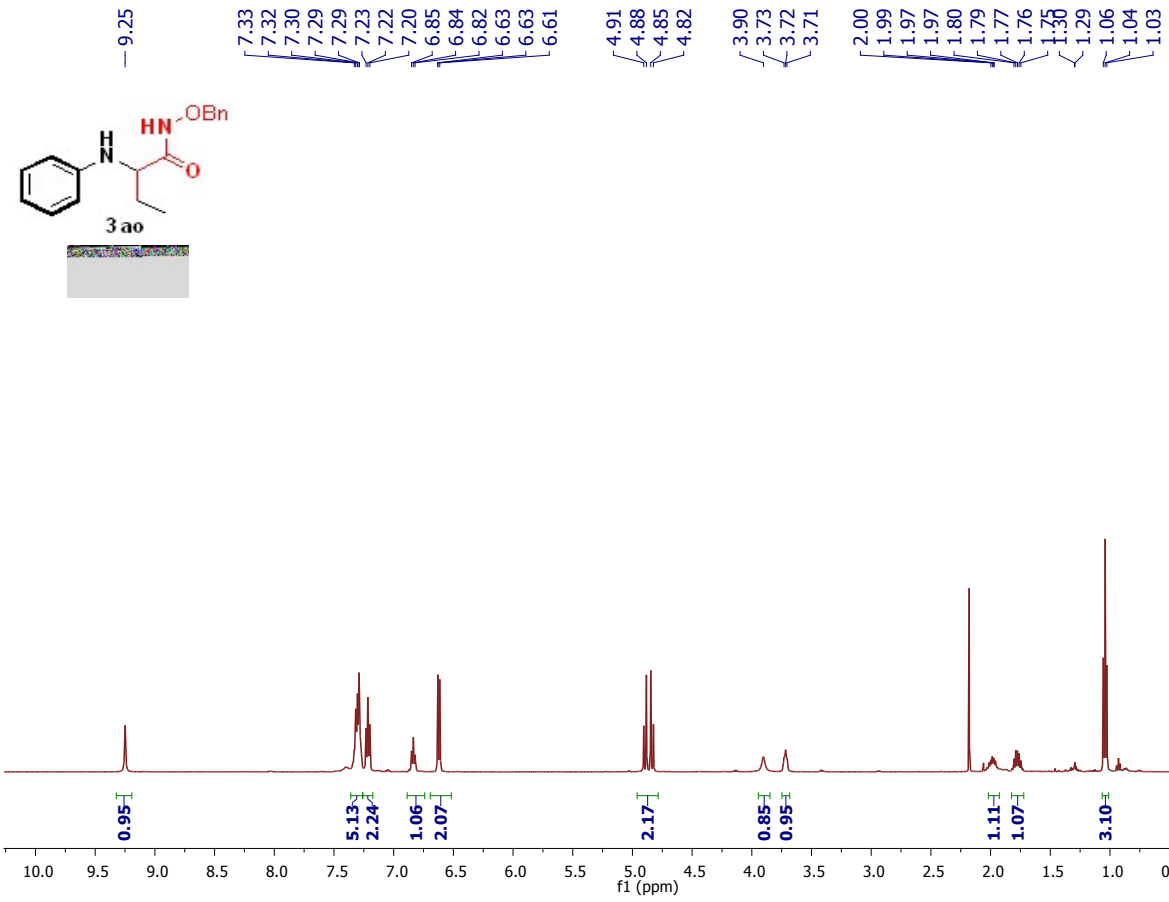
1.04
2.15
6.38
9.56
f1 (ppm)

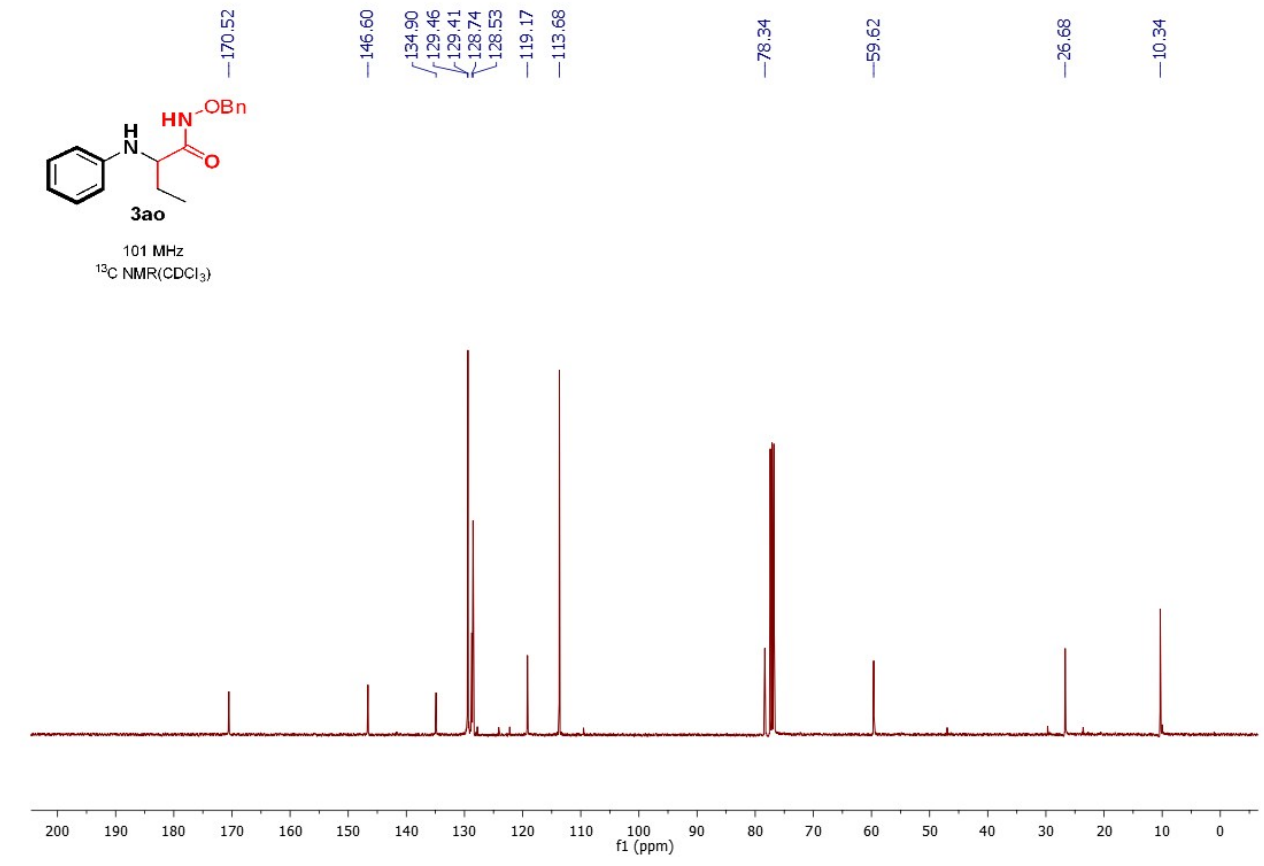

9.36
7.29
7.21
7.20
7.20
7.18
6.85
6.84
6.82
6.57
6.55
5.07
1.51
NH HN-O
F
F
F
F
F
O
3am
1.00
2.21
1.09
2.15
2.57
6.46
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

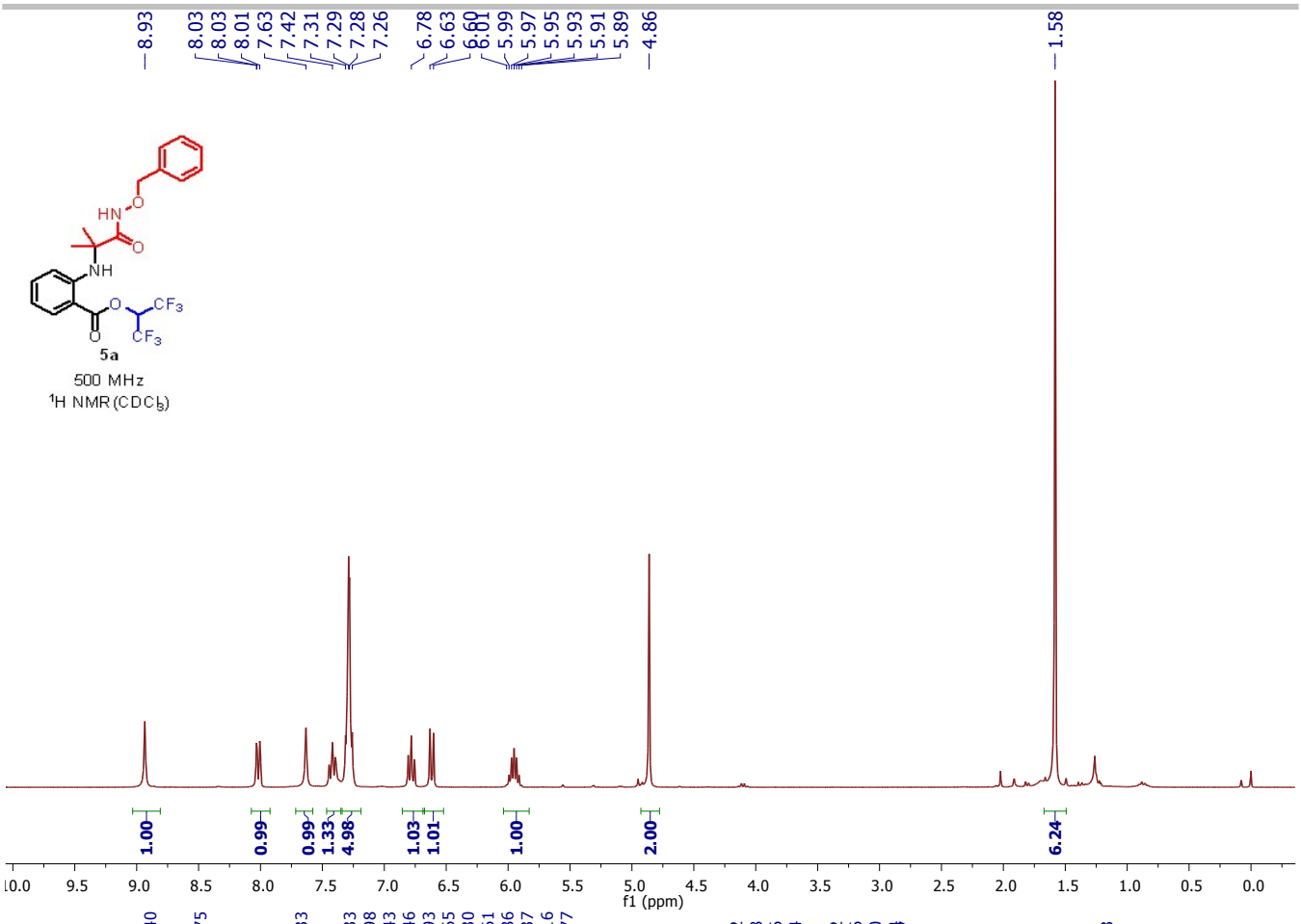

174.68
144.05
129.26
119.64
115.82
64.31
57.60
26.02
NH HN-O
F
F
F
F
F
O
3am
101 MHz
13C NMR(CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

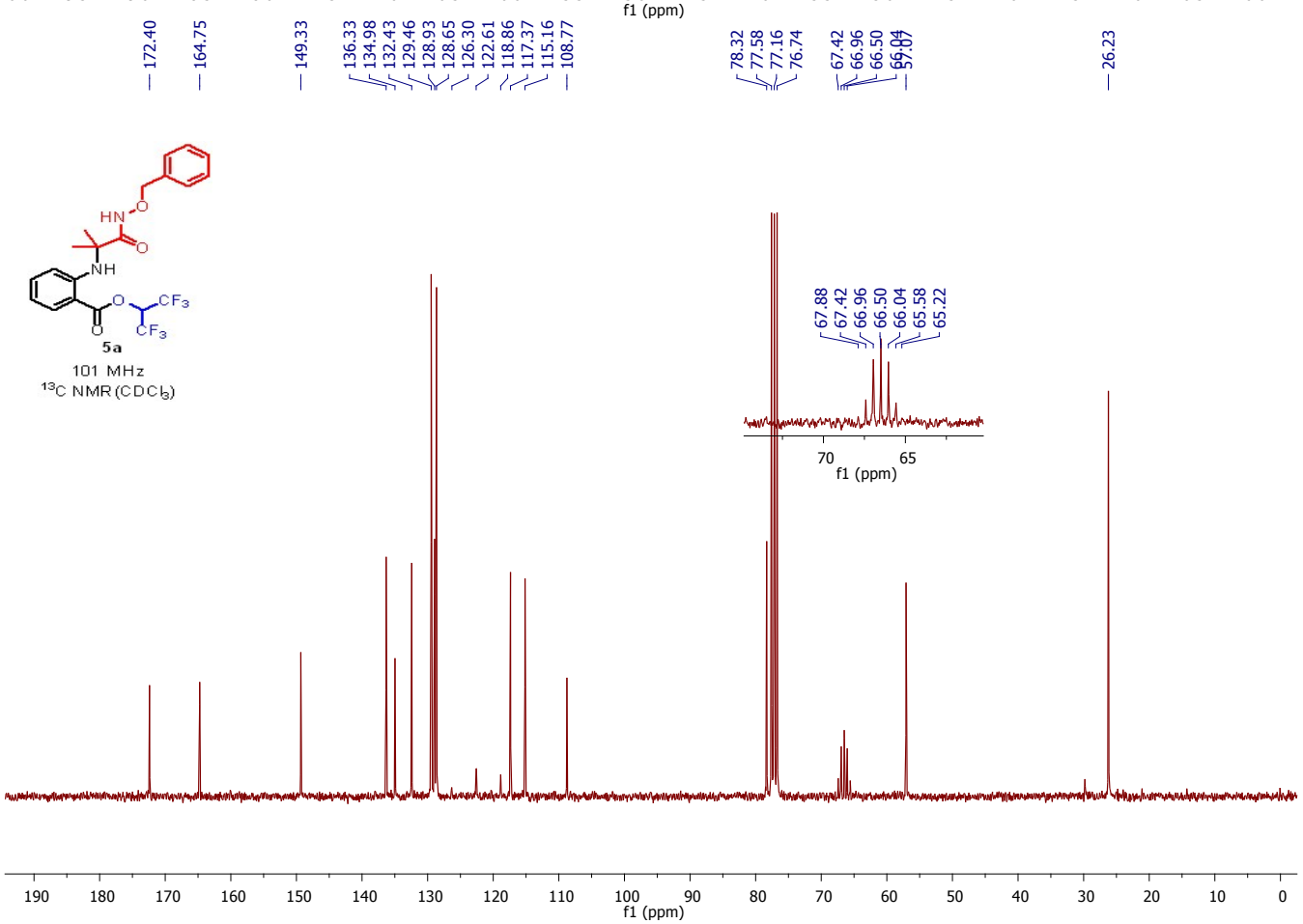

9.23
7.29
7.29
7.28
7.27
7.20
7.18
7.17
6.82
6.80
6.79
6.58
6.57
4.90
4.87
4.83
4.81
4.13
4.12
4.11
4.09
3.88
3.86
3.84
2.03
1.49
1.48
3 an
0.86
5.49
2.13
0.93
2.00
2.03
3.06
f1 (ppm)

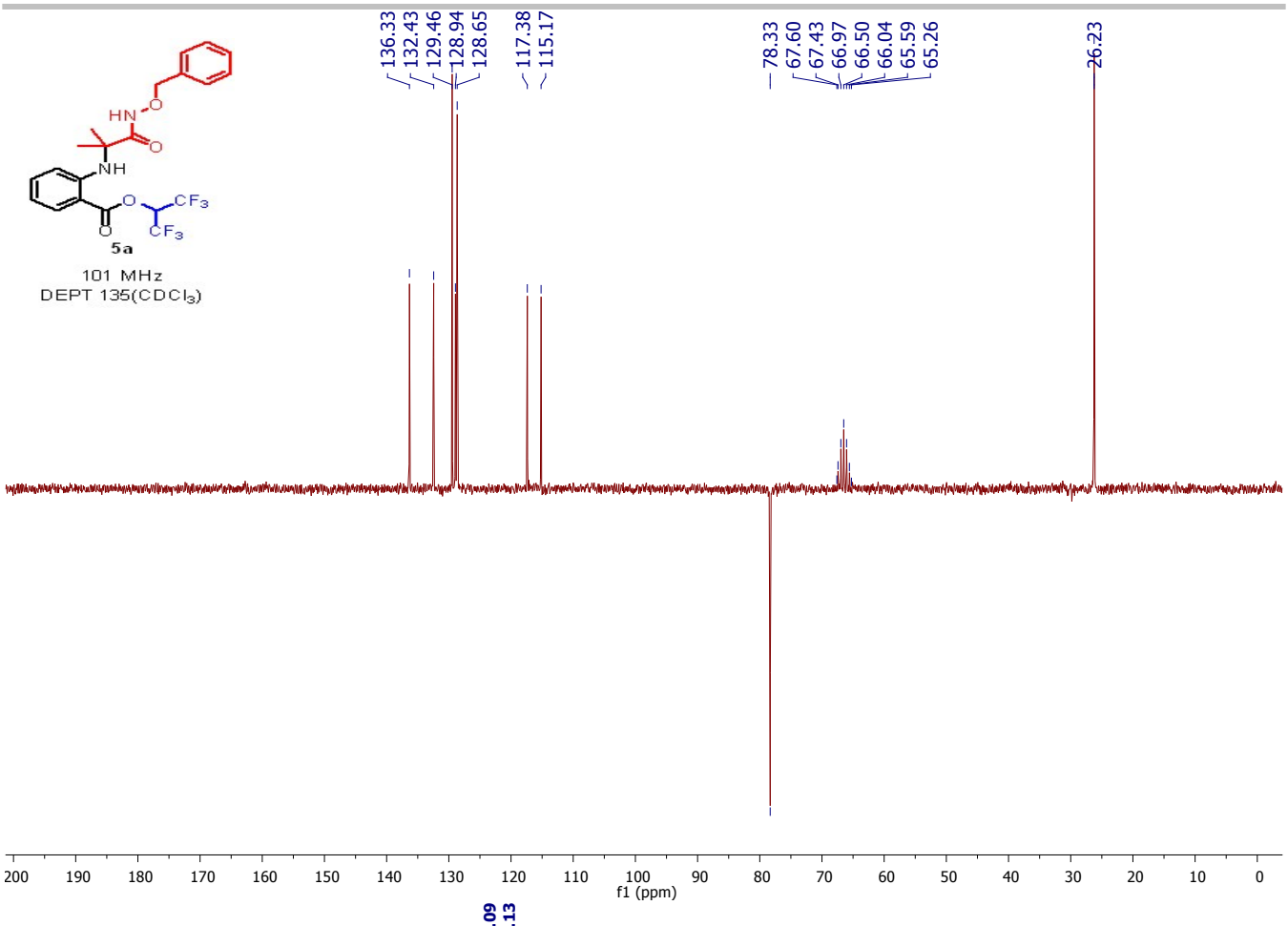

170.92
146.16
134.82
129.47
129.42
128.77
128.55
119.43
113.67
78.29
77.34
77.03
76.71
54.26
19.69
3an
101 MHz
13C NMR(CDCl3)
f1 (ppm)

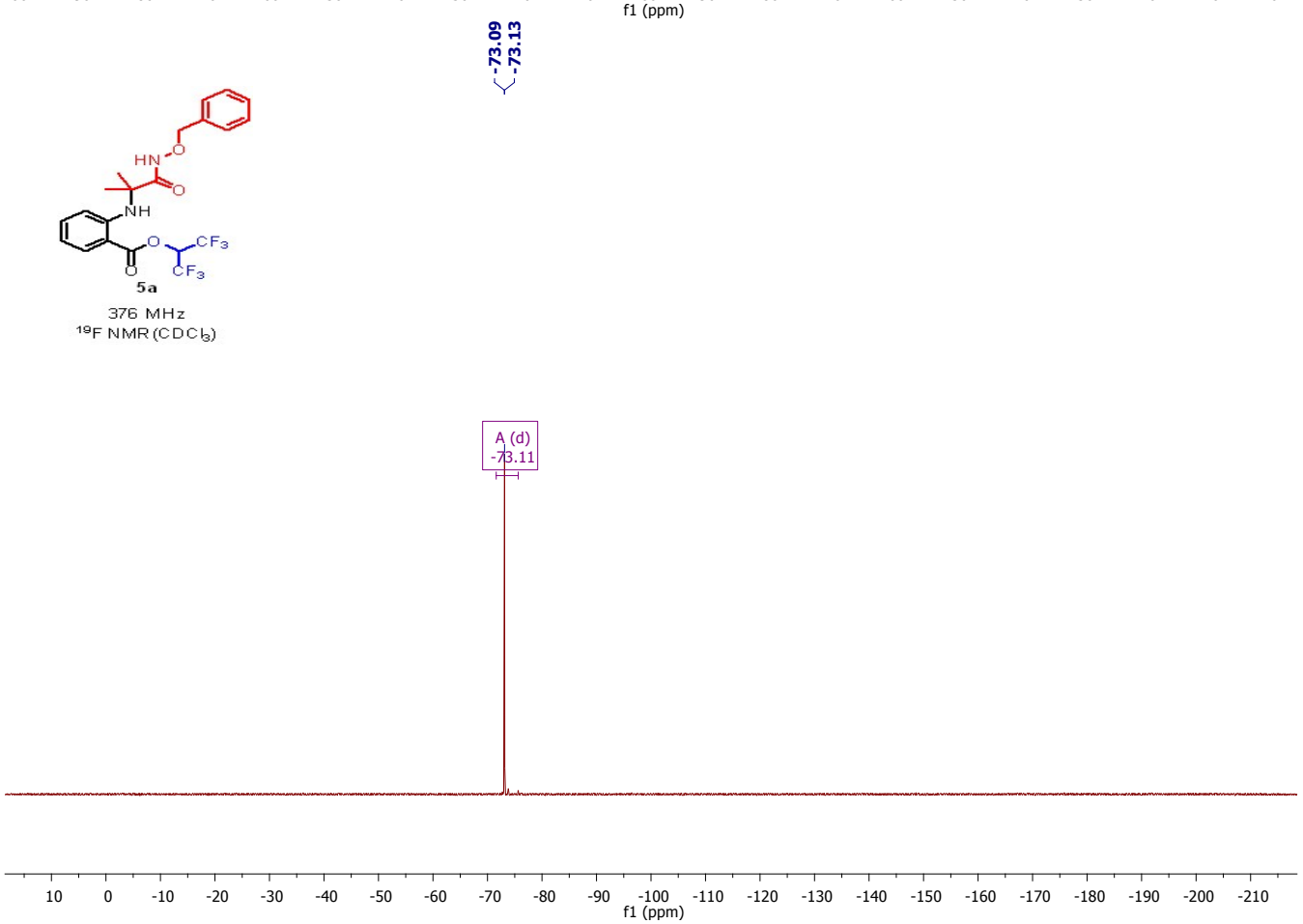

9.25
7.33
7.32
7.30
7.29
7.29
7.23
7.22
7.20
6.85
6.84
6.82
6.63
6.63
6.61
4.91
4.88
4.85
4.82
3.90
3.73
3.72
3.71
2.00
1.99
1.97
1.97
1.80
1.79
1.77
1.76
1.75
1.30
1.29
1.06
1.04
1.03
HN
OBn
O
3 ao
0.95
5.13
2.24
1.06
2.07
2.17
0.85
0.95
1.11
1.07
3.10
f1 (ppm)

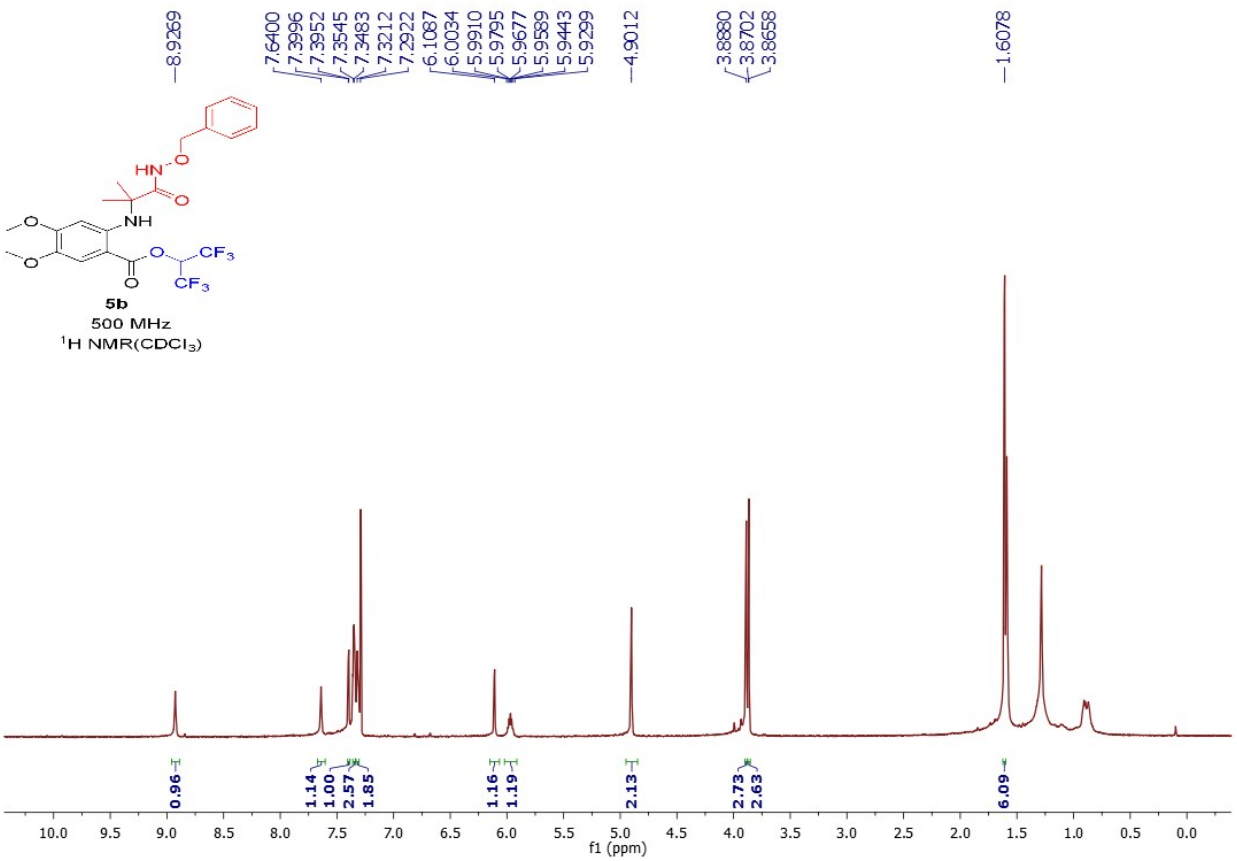

170.52
146.60
134.90
129.46
129.41
128.74
128.53
119.17
113.68
78.34
59.62
26.68
10.34
HN
OBn
O
3ao
101 MHz
13C NMR(CDCl3)
f1 (ppm)

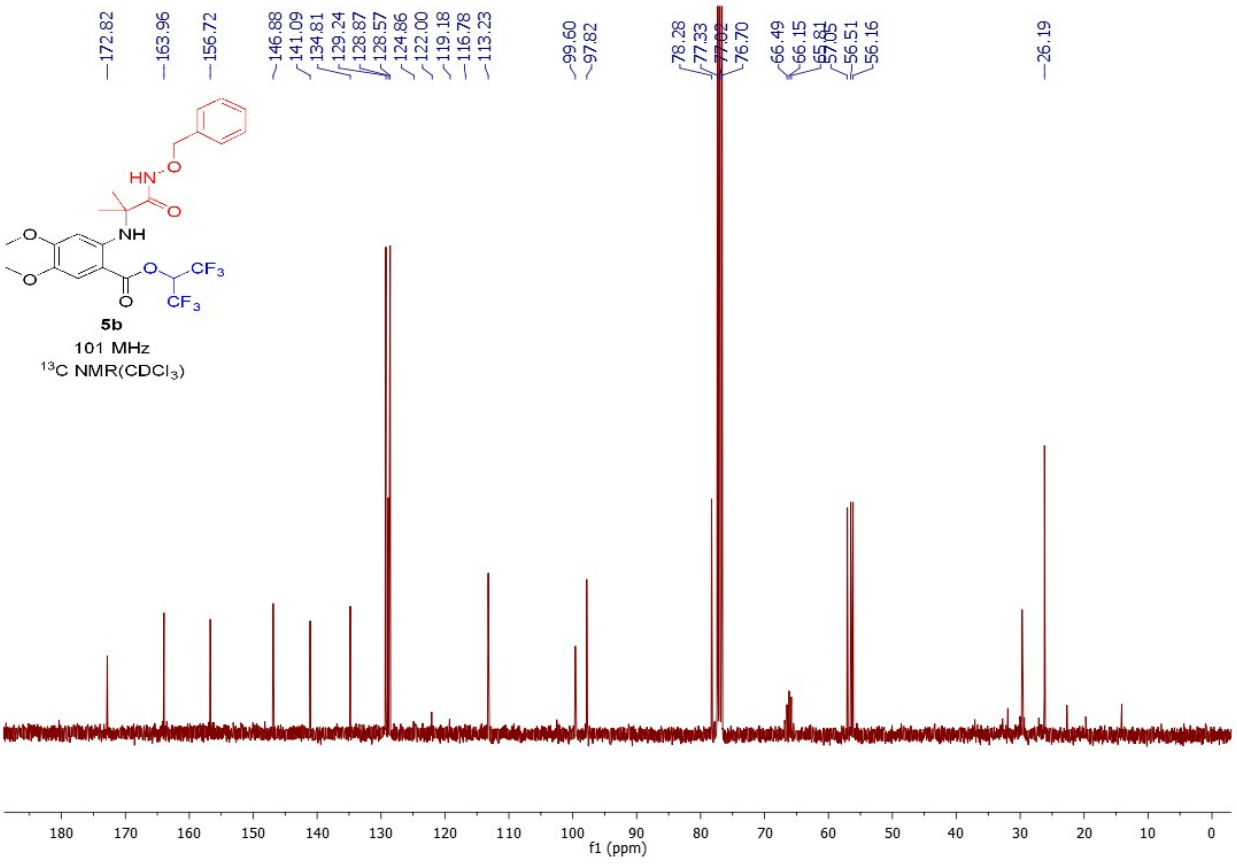

8.93
8.03
8.03
8.01
7.63
7.42
7.31
7.29
7.28
7.26
6.78
6.63
6.60
6.01
5.99
5.97
5.95
5.93
5.91
5.89
4.86
1.58
HN
O
O
NH
O
CF3
O
CF3
5a
500 MHz
1H NMR (CDCl3)
1.00
0.99
0.99
1.33
4.98
1.03
1.01
1.00
2.00
6.24
f1 (ppm)

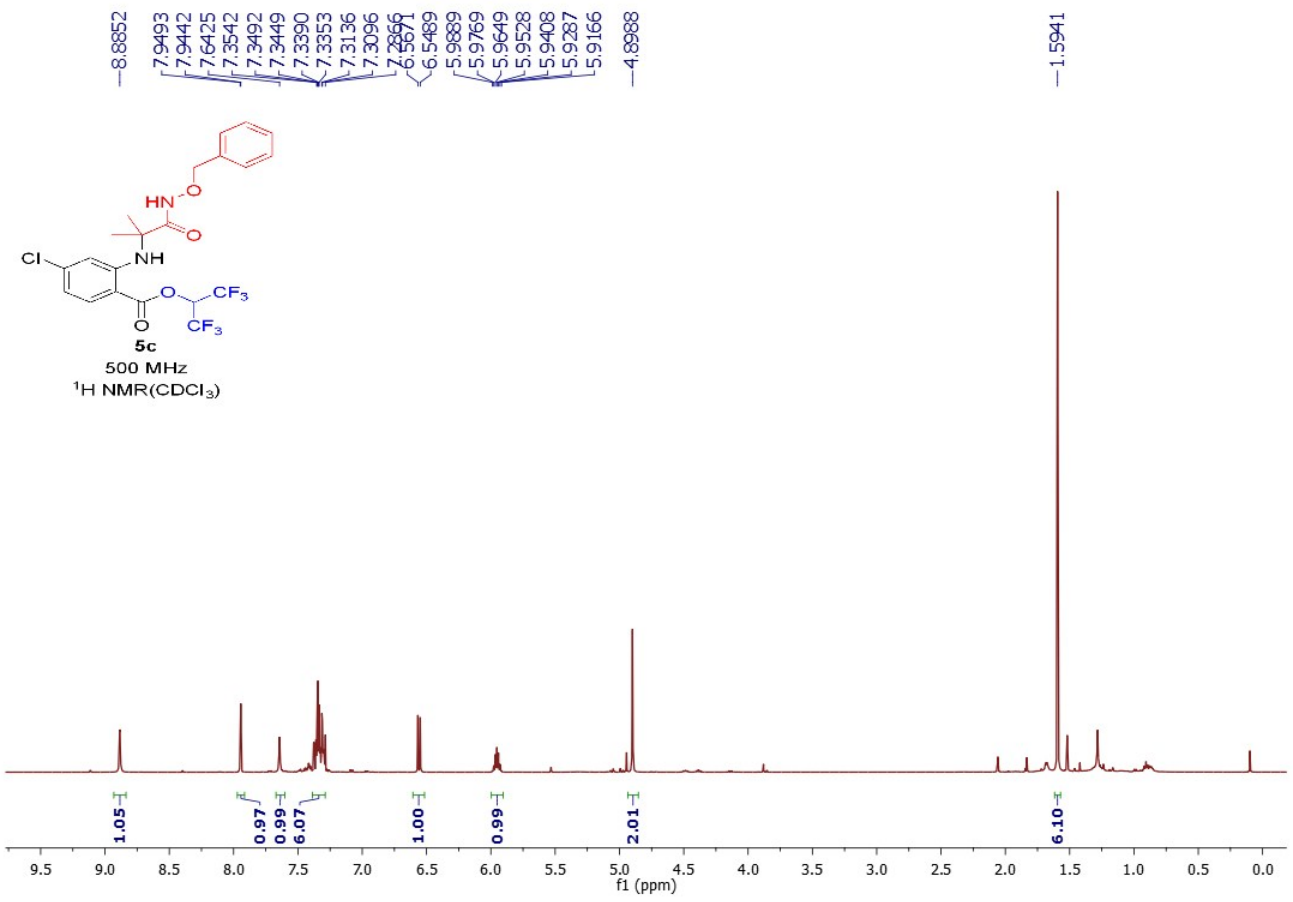

172.40
164.75
149.33
136.33
134.98
132.43
129.46
128.93
128.65
126.30
122.61
118.86
117.37
115.16
108.77
78.32
77.58
77.16
76.74
67.42
66.96
66.50
66.04
65.58
65.22
26.23
HN
O
O
NH
O
CF3
O
CF3
5a
101 MHz
13C NMR (CDCl3)
67.88
67.42
66.96
66.50
66.04
65.58
65.22
70
65
f1 (ppm)
f1 (ppm)

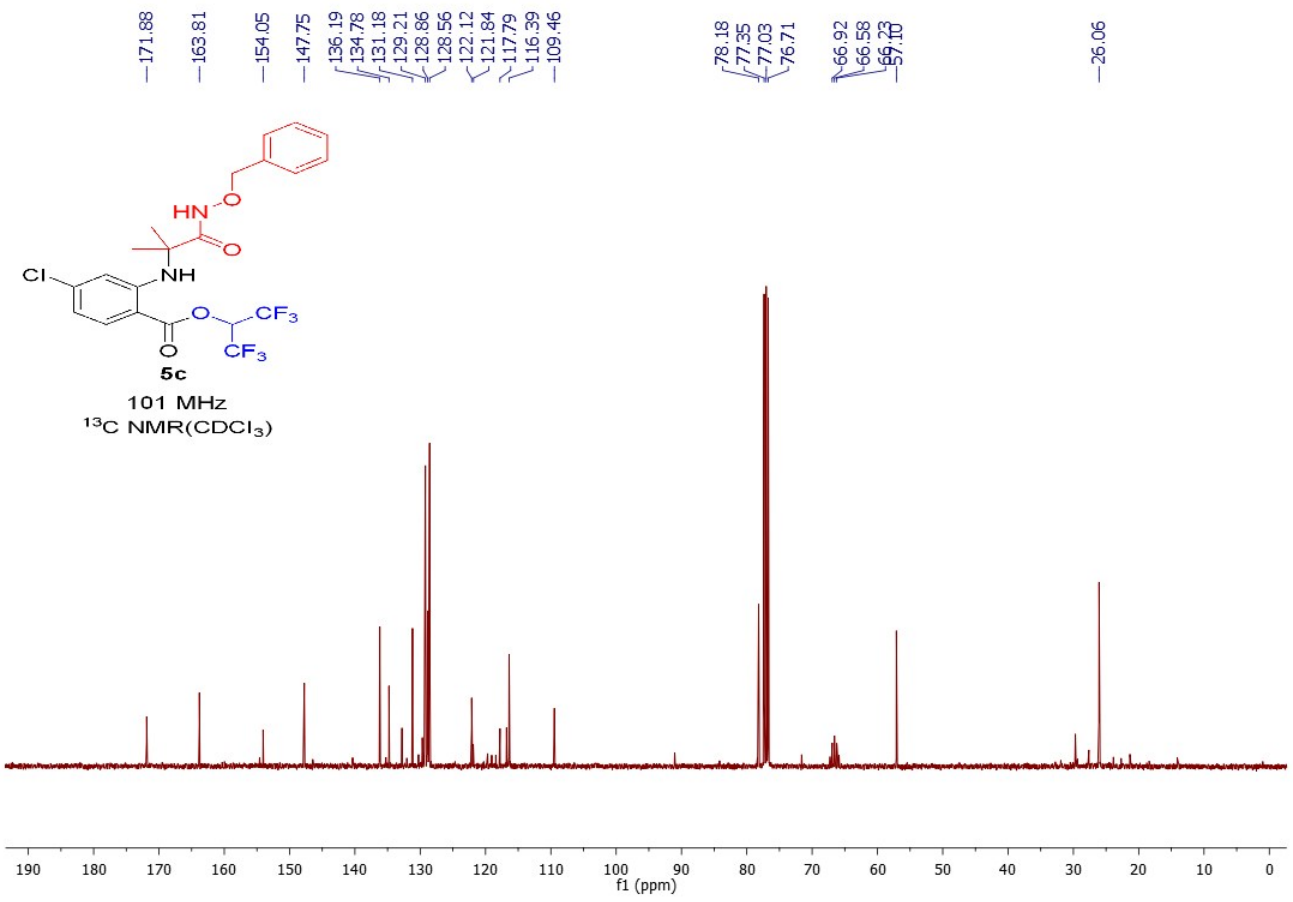

136.33
132.43
129.46
128.94
128.65
117.38
115.17
78.33
67.60
67.43
66.97
66.50
66.04
65.59
65.26
26.23
5a
101 MHz
DEPT 135(CDCl3)
f1 (ppm)

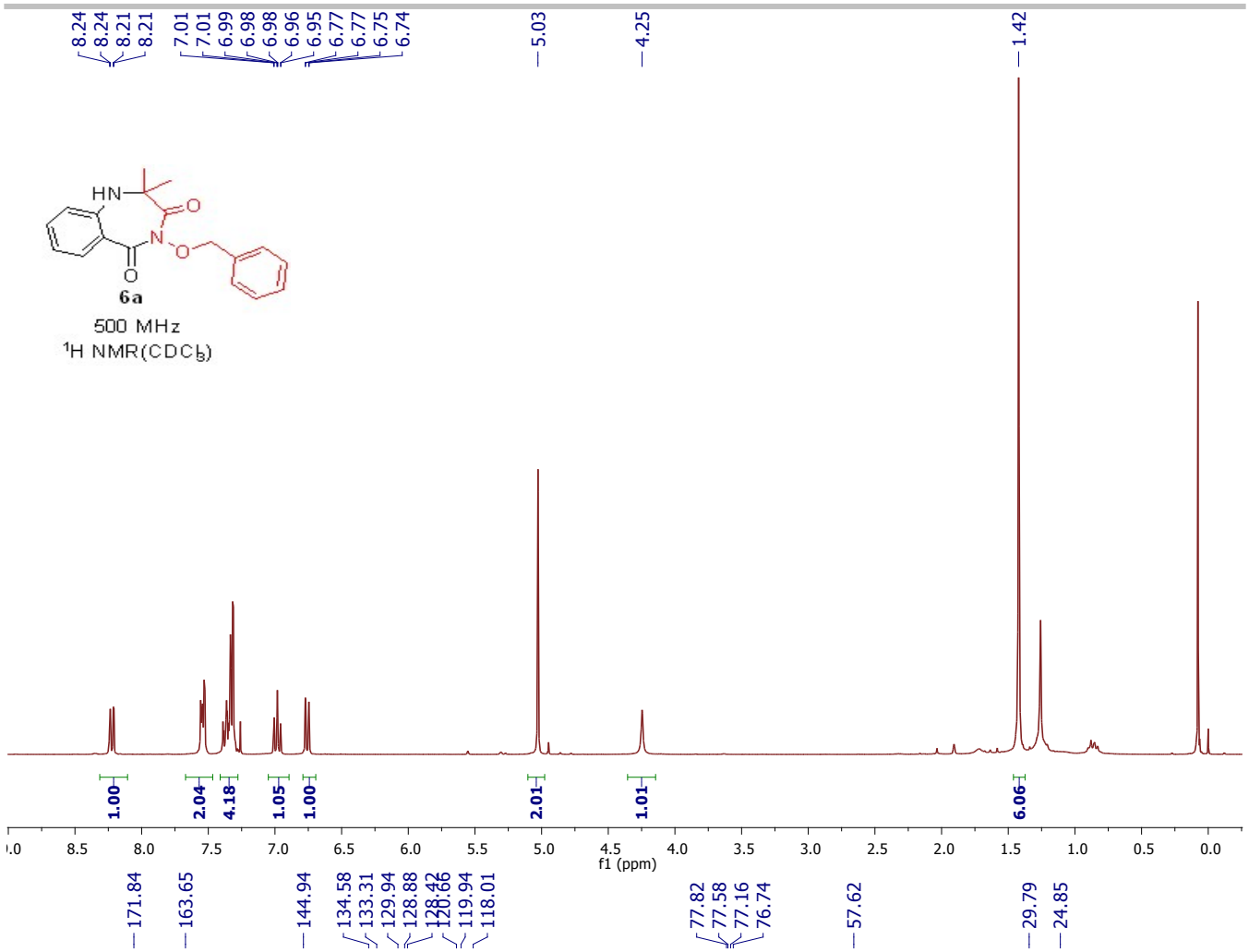

-73.09
-73.13
5a
376 MHz
19F NMR(CDCl3)
A (d)
-73.11
f1 (ppm)

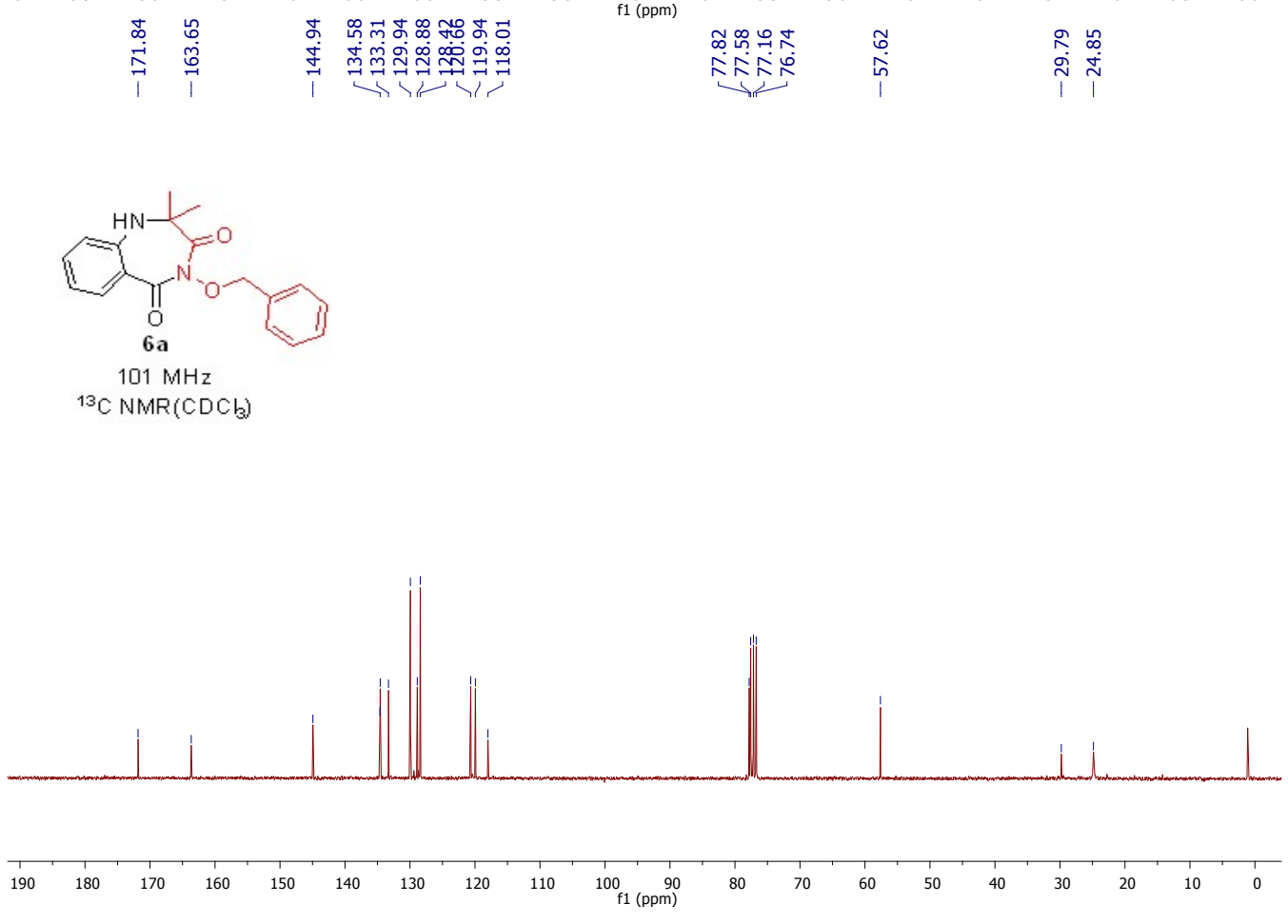

8.9269
7.6400
7.3996
7.3952
7.3545
7.3483
7.3212
7.2922
6.1087
6.0034
5.9910
5.9795
5.9677
5.9589
5.9443
5.9299
4.9012
3.8880
3.8702
3.8658
1.6078
HN
O
O
NH
O
O
O
CF3
CF3
O
5b
500 MHz
1H NMR(CDCl3)
0.96
1.14
1.00
2.57
1.85
1.16
1.19
2.13
2.73
2.63
6.09
f1 (ppm)

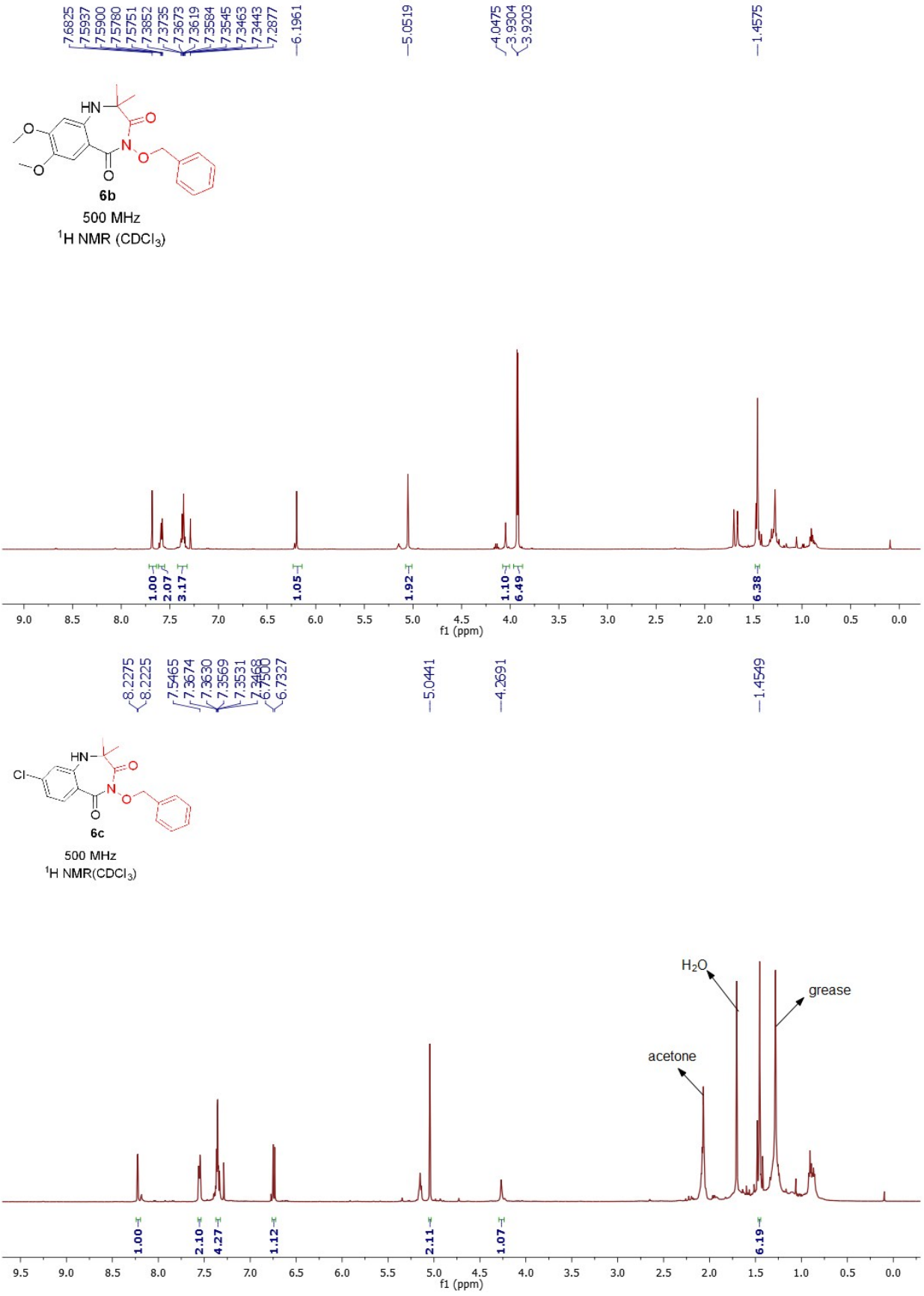

172.82
163.96
156.72
146.88
141.09
134.81
129.24
128.87
128.57
124.86
122.00
119.18
116.78
113.23
99.60
97.82
78.28
77.33
77.02
76.70
66.49
66.15
65.81
57.05
56.51
56.16
26.19
HN
O
O
NH
O
O
O
CF3
CF3
O
5b
101 MHz
13C NMR(CDCl3)
f1 (ppm)

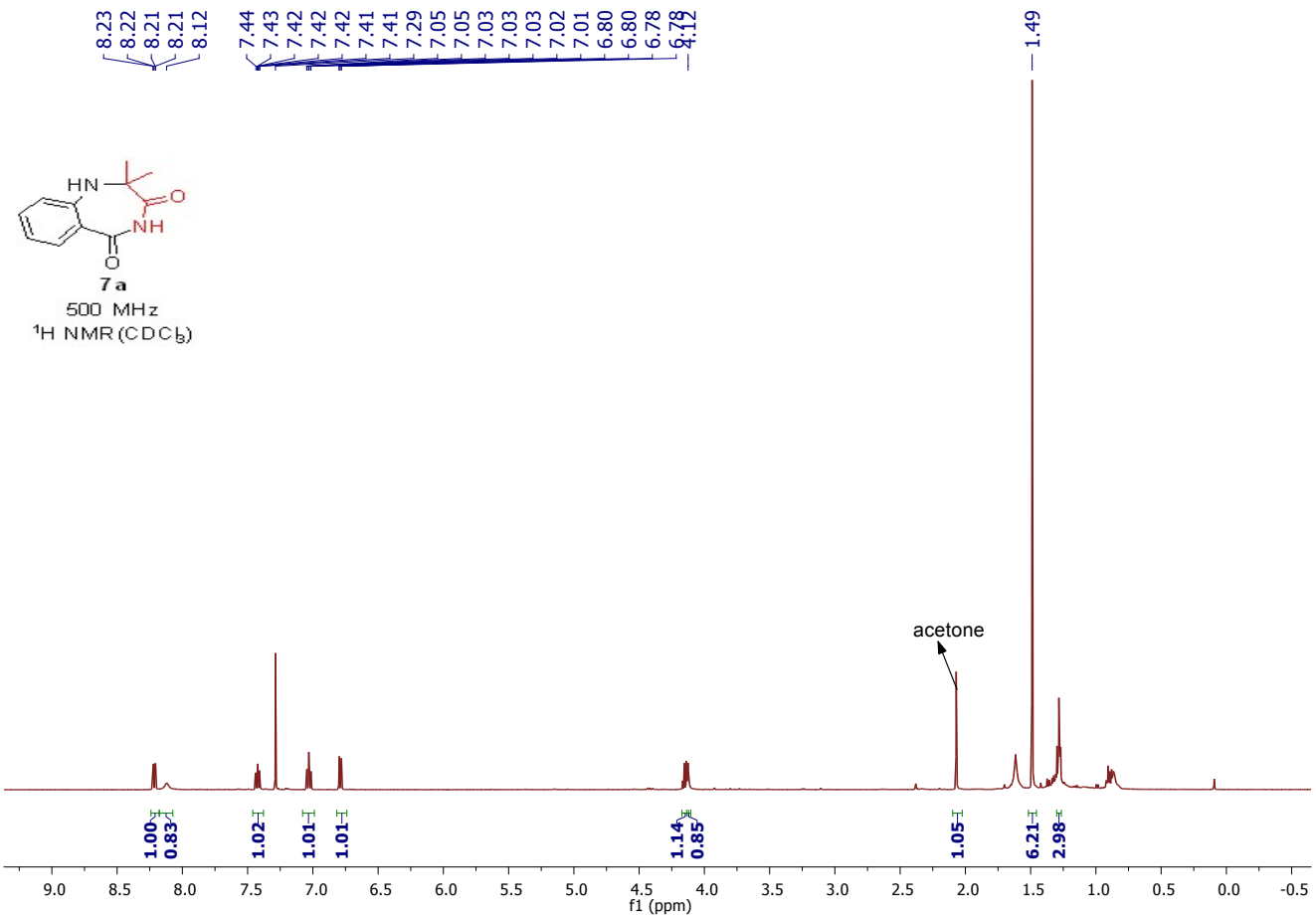

8.8852
7.9493
7.9442
7.6425
7.3542
7.3492
7.3449
7.3390
7.3353
7.3136
7.3096
6.5671
6.5489
5.9889
5.9769
5.9649
5.9528
5.9408
5.9287
5.9166
4.8988
1.5941
HN
O
O
NH
Cl
O
CF3
O
CF3
5c
500 MHz
1H NMR(CDCl3)
1.05
0.97
0.99
6.07
1.00
0.99
2.01
6.10
f1 (ppm)

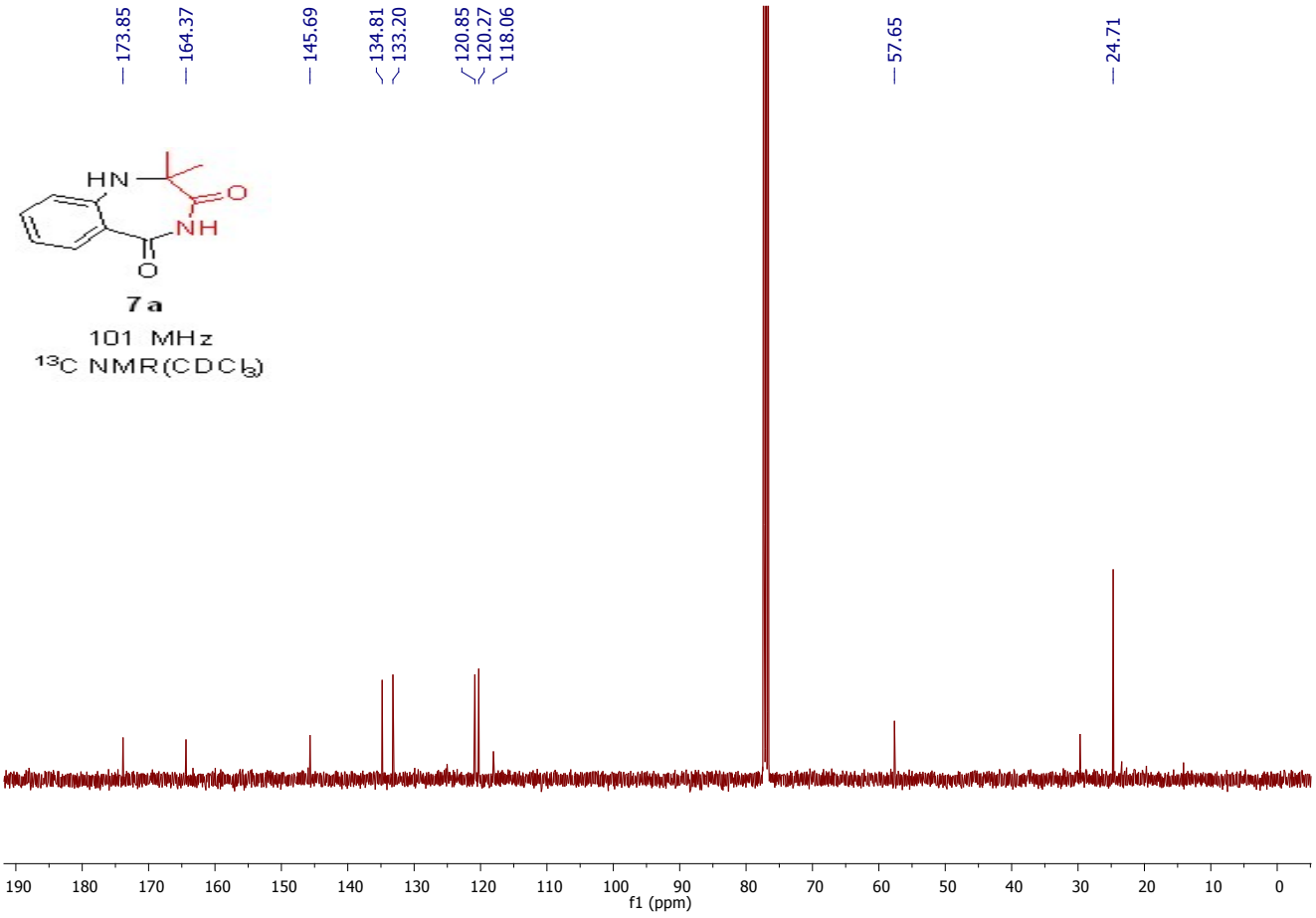

171.88
163.81
154.05
147.75
136.19
134.78
131.18
129.21
128.86
128.56
122.12
121.84
117.79
116.39
109.46
78.18
77.35
77.03
76.71
66.92
66.58
66.23
57.10
26.06
HN
O
O
NH
Cl
O
CF3
O
CF3
5c
101 MHz
13C NMR(CDCl3)
f1 (ppm)

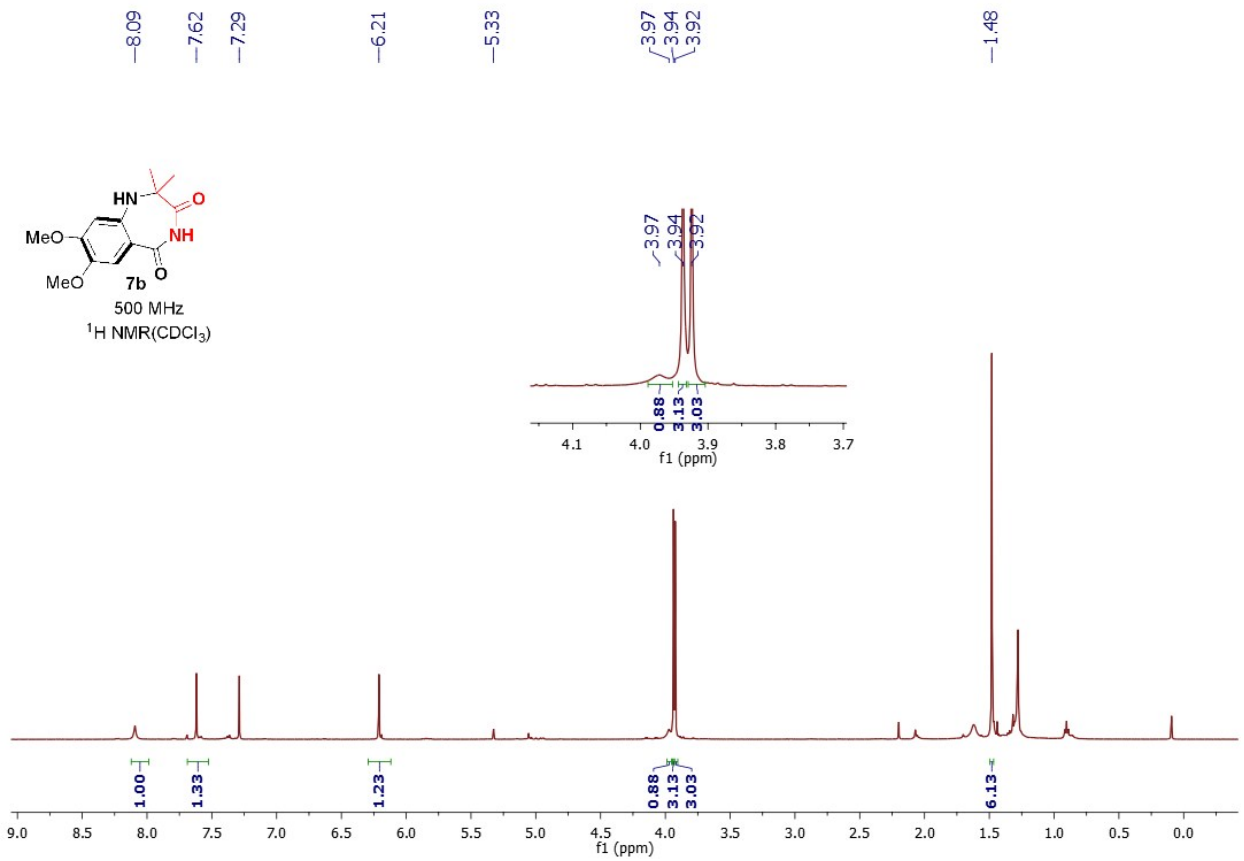

8.24
8.24
8.21
8.21
7.01
7.01
6.99
6.98
6.98
6.96
6.95
6.77
6.75
6.74
5.03
4.25
1.42
HN
O
N
O
O
6a
500 MHz
1H NMR(CDCl3)
1.00
2.04
4.18
1.05
1.00
2.01
1.01
6.06
f1 (ppm)


171.84
163.65
144.94
134.58
133.31
129.94
128.88
119.94
118.01
77.82
77.58
77.16
76.74
57.62
29.79
24.85
HN
O
N
O
O
6a
101 MHz
13C NMR(CDCl3)
f1 (ppm)


7.6825
7.5937
7.5900
7.5780
7.5751
7.3852
7.3735
7.3673
7.3619
7.3584
7.3545
7.3463
7.3443
7.2877
6.1961
5.0519
4.0475
3.9304
3.9203
1.4575
HN
O
O
O
N
O
O
6b
500 MHz
^{1}H NMR ($CDCl_3$)
1.00
2.07
3.17
1.05
1.92
1.10
6.49
6.38
f1 (ppm)
8.2275
8.2225
7.5465
7.3674
7.3630
7.3569
7.3531
7.3468
6.7500
6.7327
5.0441
4.2691
1.4549
HN
Cl
O
N
O
O
6c
500 MHz
^{1}H NMR($CDCl_3$)
H_2O
grease
acetone
1.00
2.10
4.27
1.12
2.11
1.07
6.19
f1 (ppm)


8.23
8.22
8.21
8.21
8.12
7.44
7.43
7.42
7.42
7.42
7.41
7.41
7.29
7.05
7.05
7.03
7.03
7.03
7.02
7.01
6.80
6.80
6.78
6.78
4.12
1.49
HN
NH
O
O
7a
500 MHz
1H NMR(CDCl3)
acetone
1.00
0.83
1.02
1.01
1.01
1.14
0.85
1.05
6.21
2.98
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

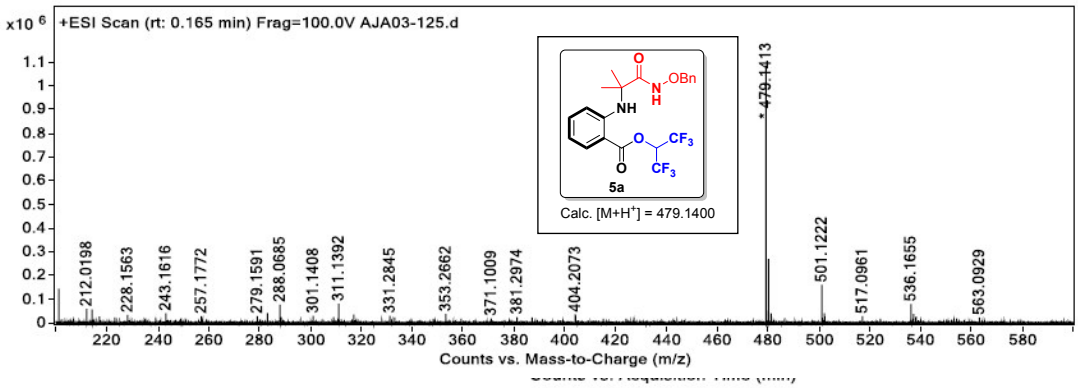

173.85
164.37
145.69
134.81
133.20
120.85
120.27
118.06
57.65
24.71
HN
NH
O
O
7a
101 MHz
13C NMR(CDCl3)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


8.09
7.62
7.29
6.21
5.33
3.97
3.94
3.92
1.48
HN
O
NH
O
MeO
MeO
7b
500 MHz
1H NMR(CDCl3)
0.88
3.13
3.03
f1 (ppm)
1.00
1.33
1.23
6.13

Representative HRMS

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
100	0	ESI



MS Zoomed Spectrum