Supporting Information

Palladium-Catalyzed Reductive Cross-Coupling between α-Bromo Carboxamide with Terminal Alkynes

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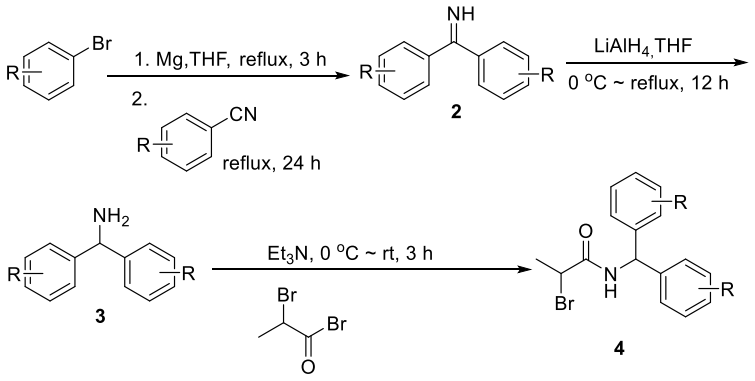
General Experimental Information

All reactions were carried out in oven dried glass wares. Nitrogen-flushed syringes were used to transfer air and moisture sensitive reagents. Unless otherwise noted, commercialized reagents were used without further purifications. Toluene and THF were purchased from Sigma-Aldrich Chemical Co. All other solvents were purified and dried according to standard methods prior to use. Reactions were carried out under nitrogen atmosphere and monitored by thin layer chromatography (TLC) using Merck Silica Gel F_{254} plates (5x20 cm) with detection by visualizing by UV irradiation (254 nm and 365 nm), staining with 5% (v/v) H_2SO_4 in ethanol or 5% solution of Phosphomolybdic acid, followed by charring with a heat gun. Flash chromatography was performed on silica gel (200-300 mesh, sorbent).

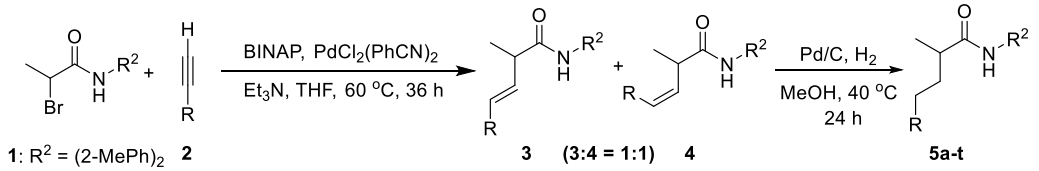
^{1}H NMR, ^{19}F NMR and ^{13}C NMR data were recorded on a Bruker-Ultrashield PLUS400 NMR or a 500 NMR Agilent spectrometer with $CDCl_3$ as the solvent. ^{1}H chemical shifts were referenced to $CDCl_3$ at 7.26 ppm. ^{13}C chemical shifts were referenced to $CDCl_3$ at 77.16 ppm and obtained with ^{1}H decoupling. Multiplicities are abbreviated as follows: singlet (s), doublet (d), triplet (t), quartet (q), doublet-doublet (dd), quintet (quint), sextet (sextet), septet (septet), multiplet (m), and broad (br). ^{1}H NMR data are reported as though they were first order. The errors between the coupling constants for two coupled protons were less than 0.5 Hz, and the average numbers were reported. MS was measured on Agilent 7890A/5975C Series GC/MSD mass spectrometer. High resolution mass spectra (HRMS) were performed with an ion cyclotron resonance analyzer by electrospray ionization.

General Procedure for the Synthesis of α-Bromo Amides

To Mg (1.2 equiv) under N_2 were added two scoops of iodine for initiation. This was followed by the addition of some amount of THF and aryl bromide. After initiation, (i.e. the disappearance of deep brown color to give a colorless solution) the remaining amount of aryl bromide (1.2 equiv) and THF were added. The resulting mixture was heated to reflux for 3 hours before being charged with aryl nitrile (1.0 equiv). The reaction was then refluxed for 24 hours and followed with the addition of $LiAlH_4$ (1.0 equiv) at 0 ^oC after the total consumption of the starting material. The reaction was allowed to warm to room temperature before it was heated to reflux for 15 hours. The reaction was quenched by (H_2O: NaOH: H_2O= 1:2:3) and the suspension formed was filtered over celite. The combined organic layers was concentrated and purified by silica gel chromatography (PE:EA=5:1) to afford the amine product **3**. To a solution of amine (1.1 equiv) in DCM was added Et_3N (1.0 equiv) at room temperature. The resulting mixture was cooled down to 0 ^oC and charged slowly with α-bromopropanoyl bromide (1.0 equiv). After three hours, the reaction was quenched with water and extracted with DCM. Combined organic layers were washed with brine, dried over Na_2SO_4 and purified by flash chromatography to afford the desired product.

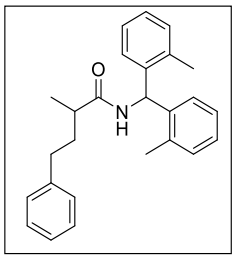


General Procedure for Palladium-Catalyzed Reductive Coupling of α-Bromo Carboxamides with Terminal Alkynes



An oven-dried schlenk tube was charged with a stir bar, α-bromo carboxamide (50 mg, 0.145 mmol, 1.0 equiv), aryl alkyne (if solid), (0.29 mmol, 2.0 equiv), BINAP (9mg, 0.0145 mmol, 10 mol %) and $PdCl_2(PhCN)_2$ (2.76 mg, 0.0072 mmol, 5 mol %). The tube was evacuated under vacuum and back filled with nitrogen (3 times). Et_3N (0.1 ml, 0.72 mmol, 5.0 equiv), aryl alkyne (if liquid) and THF (1.8mL) were finally added under nitrogen atmosphere. The reaction was stirred at 60 ^oC for 36 h before it was quenched with water. Organic layer was extracted by DCM, concentrated and purified by column chromatography (PE:DCM:ACETONE = 9:2:0.5) to afford the desired product. The combined isomer **3** and **4** was dissolved with methanol and charged with 10 % Pd/C. The resulting mixture was evacuated and back filled with H_2 (1 atm) before stirring vigorously at 40^{o}C (the reaction was conducted during winter, so room temperature was relatively low) for 24 h. The crude was subsequently filtered over celite and the filtrate purified by silica gel column chromatography to obtain the desired products.

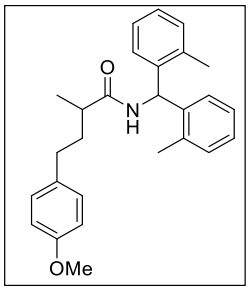
N-benzhydryl-2-methyl-4-phenylbutanamide (5a)



White solid, 78% yield, m.p. = 152-155 ^oC. ^1H NMR (500 MHz, $CDCl_3$) δ 7.30-7.23 (m, 2H), 7.24-7.15 (m, 6H), 7.17-7.11 (m, 3H), 7.05 (dd, *J* = 16.4, 7.6 Hz, 2H), 6.52 (d, *J* = 7.9 Hz, 1H), 5.85 (d, *J* = 7.9 Hz, 1H), 2.67 (m, 1H), 2.63-2.54 (m, 1H), 2.33-2.23 (m, 7H), 2.05 (m, 1H), 1.76-1.67 (m, 1H), 1.22 (d, *J* =6.8 Hz, 3H)); ^{13}C NMR (125 MHz, $CDCl_3$)

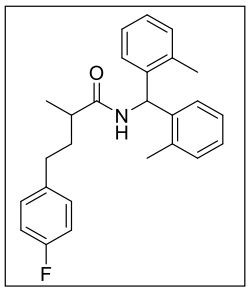
δ 174.8, 141.8, 139.2, 136.6, 136.5, 130.9, 128.5, 128.5, 127.6, 127.6, 126.5, 126.3, 126.2, 126.2, 126.0, 51.2, 40.9, 35.8, 33.7, 19.3, 19.2, 18.4. ESI-MS: m/z 372.35 $[M+H]^+$, 394.35 $[M+Na]^+$; HRMS (ESI) calculated for [M+H, $C_{26}H_{30}NO]^+$: 372.2320, found: 372.2322; [M+Na, $C_{26}H_{29}NNaO]^+$: 394.2144, found 394.2141.

***N*-(di-o-tolylmethyl)-4-(4-methoxyphenyl)-2-methylbutanamide (5b)**



White solid, 73% yield. m.p. = 136-138 ^oC. ^1H NMR (500 MHz, $CDCl_3$) δ 7.24-7.11 (m, 6H), 7.04 (m, 4H), 6.82-6.76 (m, 2H), 6.51 (d, *J* = 7.9 Hz, 1H), 5.82 (d, *J* = 8.0 Hz, 1H), 3.78 (s, 3H), 2.67-2.57 (m, 1H), 2.56-2.47 (m, 1H), 2.32-2.15 (m, 7H), 2.06-1.96 (m, 1H), 1.74-1.62 (m, 1H), 1.21 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.9, 157.9, 139.3, 139.2, 136.6, 136.5, 133.8, 130.9, 130.9, 130.8, 129.3, 129.3, 129.3, 129.2, 128.7, 127.6, 127.8, 126.5 126.3, 126.2 126.2, 125.9, 113.9, 55.4, 51.2, 40.9, 36.1, 32.8, 19.3, 19.2, 18.4 ESI-MS: m/z 402.45 $[M+H]^+$; HRMS (ESI) calculated for [M+H, $C_{27}H_{32}NO_2]^+$: 402.2427, found: 402.2428; [M+Na, $C_{27}H_{31}NNaO_2]^+$: 424.2249, found 424.2247.

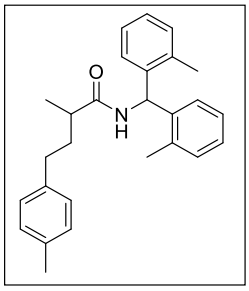
***N*-(di-o-tolylmethyl)-4-(4-fluorophenyl)-2-methylbutanamide (5c)**



White solid, 77 % yield, m.p. = 175-177 ^oC. ^1H NMR (500 MHz, $CDCl_3$) δ 7.24-7.11 (m, 6H), 7.09-7.00 (m, 4H), 6.93 (t, *J* = 8.6 Hz, 2H), 6.51 (d, *J* = 7.9 Hz, 1H), 5.84 (d, *J* = 7.9 Hz, 1H), 2.68-2.58 (m, 1H), 2.59-2.50 (m, 1H), 2.35-2.15 (m, 7H), 2.07-1.95 (m, 1H), 1.73-1.63 (m, 1H), 1.21 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.6, 161.2

(d, *J* = 243.5 Hz), 139.1(d, *J* = 9.4 Hz), 139.1, 137.3, 136.4 (d, *J* = 13.4 Hz), 130.8, 130.8, 129.7, 129.6, 127.6, 127.5, 126.4, 126.2, 126.1, 126.1, 115.2, 115.0, 51.1, 40.8, 35.8, 32.8, 19.2, 19.1, 18.4; ESI-MS: m/z 372.35 $[M+H]^+$, 394.35 $[M+Na]^+$; HRMS (ESI) calculated for [M+H, $C_{26}H_{30}NO]^+$: 372.2320, found: 372.2322; [M+Na, $C_{26}H_{29}NNaO]^+$: 394.2144, found 394.2141. FTIR (neat, cm-1): 3248 (s), 2960 (m), 2924 (m), 2854 (m), 1635 (s), 1540 (m), 1493 (m), 1455 (m), 1371 (m), 1235 (m), 870 (m), 757 (s), 743 (s), 725 (m), 698 (m), 449 (m).

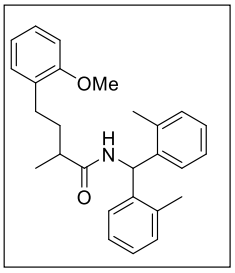
***N*-(di-o-tolylmethyl)-2-methyl-4-(p-tolyl)butanamide (5d)**



White solid, 72% yield, m.p. = 169-170 ^oC. ^1H NMR (500 MHz, $CDCl_3$) δ 7.24-7.11 (m, 6H), 7.09-6.99 (m, 6H), 6.51 (dd, *J* = 8.0, 2.8 Hz, 1H), 5.81-5.73 (m, 1H), 2.64 (m, 1H), 2.59-2.49 (m, 1H), 2.32-2.26 (m, 7H), 2.25 (3H), 2.08-1.98 (m, 1H), 1.74-1.65 (m, 1H), 1.21 (dd, *J* = 6.9, 2.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.9, 139.3, 139.3, 138.7, 136.6, 136.5, 135.5, 130.9, 129.2, 128.4, 127.6, 127.6, 126.5, 126.3, 126.2, 126.2, 51.2, 40.9, 35.9, 33.2, 21.1, 19.3, 19.2, 18.4; ESI-MS: m/z 386.40 $[M+H]^+$, 408.45 $[M+Na]^+$; HRMS (ESI) calculated for [M+H, $C_{27}H_{32}NO]^+$: 386.2473, found: 386.2478; [M+Na, $C_{27}H_{31}NNaO]^+$: 408.2299, found 408.2298. FTIR (neat, cm-1): 3258 (m), 3028 (w), 1638 (s, sh), 1532 (s), 1456 (m), 1236 (w), 808 (w), 755 (m).

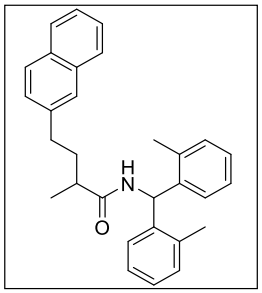
***N*-(di-o-tolylmethyl)-4-(2-methoxyphenyl)-2-methylbutanamide (5e)**

White solid, 72% yield, m.p. = 145-147 ^oC. ^1H NMR (500 MHz, $CDCl_3$) δ 7.21-7.11 (m, 7H), 7.07 (dd, *J* = 11.6, 7.3 Hz, 3H), 6.89-6.80 (m, 2H), 6.50 (d, *J* = 7.7 Hz, 1H), 5.97 (d, *J* = 7.8 Hz, 1H), 3.68 (s, 3H), 2.66 (td, *J* = 8.5, 8.1, 3.9 Hz, 2H), 2.27 (d, *J* = 16.9



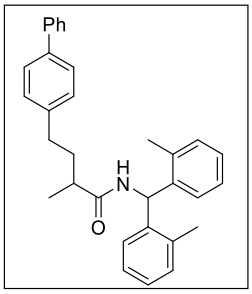
Hz, 7H), 2.06-1.96 (m, 1H), 1.68 (m, 1H), 1.21 (d, *J* = 6.8 Hz, 3H);^{13}C NMR (125 MHz, $CDCl_3$) δ 175.1, 157.5, 139.4, 139.4, 136.7, 130.9, 130.3, 130.1, 127.6, 127.6, 127.3, 126.6, 126.4, 126.2, 126.2, 120.7, 110.4, 55.2, 51.30, 41.1, 34.6, 28.3, 19.3, 19.2, 18.5; ESI-MS: m/z 402.50 $[M+H]^+$, 424.45 $[M+Na]^+$; HRMS (ESI) calculated for [M+Na, $C_{27}H_{31}NNaO_2]^+$: 424.2256, found:424.2247. FTIR (neat, cm-1): 3282 (m), 2968 (m), 2926 (m), 1643 (s), 1537 (s), 1495 (m), 1460 (m), 1244 (s), 1047 (m), 750 (m), 736 (m).

***N*-(di-o-tolylmethyl)-2-methyl-4-(naphthalen-2-yl)butanamide (5f)**



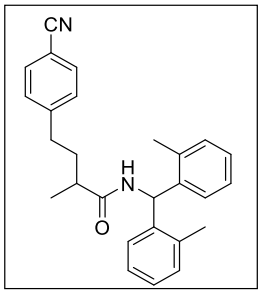
White solid, 66% yield, m.p = 173-175 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81-7.77 (m, 1H), 7.74 (d, *J* = 8.4 Hz, 1H), 7.69-7.64 (m, 1H), 7.51 (s, 1H), 7.46-7.38 (m, 2H), 7.28 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.23 (d, *J* = 2.5 Hz, 2H), 7.19 (d, *J* = 6.4 Hz, 3H), 7.13 (d, *J* = 2.3 Hz, 1H), 7.07-7.00 (m, 2H), 6.53 (d, *J* = 7.3 Hz, 1H), 5.78 (s, 1H), 2.84 (m, 1H), 2.74 (dt, *J* = 13.9, 8.2 Hz, 1H), 2.33-2.24 (m, 7H), 2.15 (m, 1H), 1.86-1.75 (m, 1H), 1.23 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.8, 139.3, 139.3, 139.3, 136.6, 133.7, 132.1, 130.9, 130.9, 128.2, 127.7, 127.6, 127.5, 127.2, 126.6, 126.3, 126.3, 126.2, 126.1, 125.4, 51.2, 40.9, 35.6, 33.8, 19.4, 19.3, 18.5; ESI-MS: m/z 444.50 $[M+Na]^+$; HRMS (ESI) calculated for [M+Na, $C_{30}H_{31}NNaO]^+$: 444.2303, found 444.2298. FTIR (neat, cm-1): 3266 (m), 2923 (m), 1643 (s), 1540 (s), 1239 (m), 851 (w), 758 (m), 472 (w).

4-([1,1'-biphenyl]-4-yl)-*N*-(di-o-tolylmethyl)-2-methylbutanamide (5g)



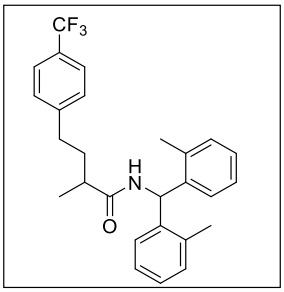
Yellow solid, 49% yield, m.p. = 185-187 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61-7.56 (m, 2H), 7.50 (d, *J* = 8.1 Hz,2H), 7.44 (s, 2H), 7.35 (d, *J* = 7.4 Hz, 1H), 7.24-7.13 (m, 8H), 7.06 (dd, *J* = 18.3, 7.6 Hz, 2H), 6.53 (d, *J* = 7.9 Hz, 1H) 5.85 (d, *J* = 8.0 Hz, 1H), 2.71 (dd, *J* = 9.5, 5.3 Hz, 1H), 2.63 (m, 1H), 2.38-2.21 (m, 7H), 2.16-2.02 (m, 1H), 1.81-1.74 (m, 1H), 1.24 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.8, 141.1, 140.9, 139.3, 139.2, 138.9, 136.6, 136.5, 130.9, 130.9, 128.9, 128.8, 127.7, 127.6, 127.3, 127.2, 127.1, 126.5, 126.3, 126.2, 126.2, 51.2, 40.9, 35.8, 33.3, 19.3, 19.2, 18.5; ESI-MS: m/z 448.50 $[M+H]^+$; HRMS (ESI) calculated for [M+H, $C_{32}H_{34}NO]^+$: 448.2635, found 448.2635, [M+Na, $C_{32}H_{33}NNaO]^+$: 470.2458, found 470.2454. FTIR (neat, cm-1): 3265 (m), 2923 (m), 1640 (s), 1537 (s), 1487 (s), 1459 (m), 1238 (w), 757 (s), 737 (s), 727 (m).

4-(4-cyanophenyl)-*N*-*(*di-o-tolylmethyl)-2-methylbutanamide (5h)



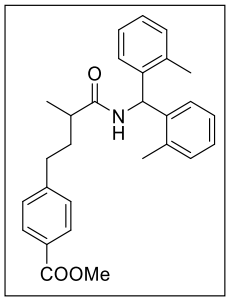
White solid, 61% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58-7.49 (m, 2H), 7.25-7.11 (m, 8H), 7.02 (dd, *J* = 14.0, 7.6 Hz, 2H), 6.49 (d, *J* = 7.9 Hz, 1H), 5.80 (s, 1H), 2.74-2.68 (m, 1H), 2.67-2.57 (m, 1H), 2.30-2.23 (m, 7H), 2.09-2.00 (m, 1H), 1.76-1.66 (m, 1H), 1.23 (d, *J* = 6.8 Hz, 3H);^{13}C NMR (125 MHz, $CDCl_3$) δ 174.3, 147.6, 139.2, 139.1, 136.6, 136.5, 132.6, 132.4, 130.8, 129.3, 127.7, 127.7, 126.4, 126.3, 126.2, 119.1, 110, 51.3, 41.0, 35.3, 33.90, 19.3, 19.2, 18.6; ESI-MS: 397.30 $[M+H]^+$, 419.30 $[M+Na]^+$; HRMS (ESI) calculated for [M+H, $C_{27}H_{29}N_2O]^+$: 397.2269, found 397.2274, [M+Na, $C_{27}H_{28}N_2NaO]^+$: 419.2095 found 419.2094.

***N*-(di-o-tolylmethyl)-2-methyl-4-(4-(trifluoromethyl)phenyl)butanamide (5i)**



White solid, 69% yield, m.p. = 197-198 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 (d, J = 8.0 Hz, 2H), 7.25-7.11 (m, 8H), 7.03 (dd, *J* = 15.3, 7.7 Hz, 2H), 6.50 (d, *J* = 7.9 Hz, 1H), 5.81 (d, *J* = 7.9 Hz, 1H), 2.70 (dd, *J* = 9.7, 5.3 Hz, 1H), 2.62 (m, 1H), 2.27 (d, *J* = 13.0 Hz, 7H), 2.10-2.01 (m, 1H), 1.78-1.66 (m, 1H), 1.22 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.4, 145.8, 139.0 (d, *J* = 12.8 Hz), 136.4 (d, *J* = 15.2 Hz), 130.8 (d, *J* = 2.0 Hz), 128.6, 127.6 (d, *J* = 3.8 Hz), 126.3, 126.2, 126.1 (d, J = 1.9 Hz), 125.30 (q, *J* = 3.8 Hz), 51.1, 40.8, 35.4, 33.4, 19.1 (d, *J* = 6.1 Hz), 18.4. ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.34 (s, 3F); ESI-MS: m/z 440.20 $[M+H]^+$, 462.25 $[M+Na]^+$; HRMS (ESI) calculated for [M+H, $C_{27}H_{29}F_3NO]^+$: 440.2197, found 440.2196, [M+Na, $C_{27}H_{28}F_3NNaO]^+$: 462.2014, found 460.2015. FTIR (neat, cm-1): 3262 (s), 2936 (w), 1693 (s, sh), 1537 (s), 1459 (m), 1338 (s), 1161 (s), 1112 (s), 1069 (s), 758 (m), 747 (m), 593 (w).

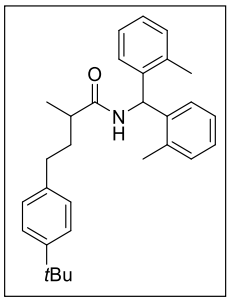
methyl 4-(4-((di-o-tolylmethyl)amino)-3-methyl-4-oxobutyl)benzoate (5j)



White solid, 61% yield, m.p. = 147-149 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.2 Hz, 2H), 7.23-7.09 (m, 8H), 7.02 (d, *J* = 9.1 Hz, 2H), 6.50 (d, *J* = 7.9 Hz, 1H), 5.87-5.78 (m, 1H), 3.89 (s, 3H), 2.69 (dd, *J* = 9.7, 5.3 Hz, 1H), 2.66-2.57 (m, 1H), 2.34-2.22 (m, 7H), 2.05 (d, *J* = 8.9 Hz, 1H), 1.75-1.67 (m, 1H), 1.21 (d, *J* = 6.9 Hz, 3H),^{13}C NMR (125 MHz, $CDCl_3$) δ 174.6, 167.2, 147.4, 139.2, 139.1, 136.6, 136.5, 130.9, 130.9, 130.9,

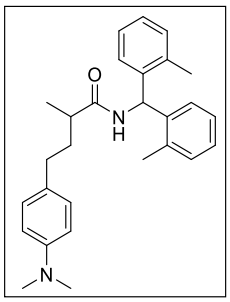
129.9, 128.5, 128.0, 127.7, 127.7, 127.6 126.4, 126.4, 126.3, 126.2, 126.2, 52.1, 51.2, 40.9, 35.4, 33.7, 19.3, 19.3, 19.2, 18.5; ESI-MS: m/z 430.50 $[M+H]^+$; HRMS (ESI) calculated for [M+H, $C_{28}H_{32}NO_3]^+$: 430.2379 found 430.2377, [M+Na, $C_{28}H_{31}NNaO_3]^+$: 452.2201, found 452.2196. FTIR (neat, cm-1): 3259 (m), 2949 (w), 1721 (s), 1640 (s, sh), 1537 (s), 1459 (m), 1281 (s), 1107 (m), 758 (s), 737 (m).

4-(4-(tert-butyl)phenyl)-*N*-(di-o-tolylmethyl)-2-methylbutanamide (5k)



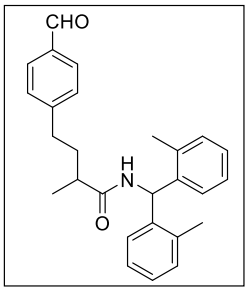
White solid, 84% yield, m.p. = 152-154 ^oC. ^1H NMR (500 MHz, $CDCl_3$) δ 7.30-7.27 (m, 2H), 7.22-7.17 (m, 4H), 7.17-7.11 (m, 2H), 7.09-7.04 (m, 3H), 7.03 (d, *J* = 8.3 Hz, 1H), 6.50 (dd, *J* = 7.9, 2.1 Hz, 1H), 5.82 (s, 1H), 2.69-2.60 (m, 1H), 2.59-2.52 (m, 1H), 2.28 (m, 7H), 2.09-1.98 (m, 1H), 1.75-1.67 (m, 1H), 1.31 (d, *J* = 2.0 Hz, 9H), 1.22 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.7, 148.7, 139.1, 138.6, 138.6, 138.6, 136.5, 136.5, 136.4, 136.4, 130.8, 128.0, 128, 127.5, 126.4, 126.4, 126.2, 126.2, 126.1, 126.1, 126.0, 125.3, 125.3, 51.1, 40.1, 35.7, 33.1, 31.4, 19.2, 19.1, 19.1, 19.1,18.3, 18.3; ESI-MS: m/z 450.40 $[M+Na]^+$; HRMS (ESI) calculated for [M+H, $C_{30}H_{38}NO]^+$: 428.2941 found 428.2948, [M+Na, $C_{30}H_{37}NNaO]^+$: 450.2769, found 450.2767. FTIR (neat, cm-1): 3253 (s), 2960 (s), 1637 (s, sh), 1459 (s), 1239 (m), 1166 (m), 848 (m), 757 (s), 747 (m), 563 (m).

***N*-(di-o-tolylmethyl)-4-(4-(dimethylamino)phenyl)-2-methylbutanamide (5l)**



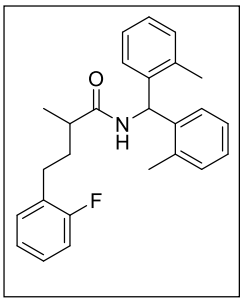
White solid, 60% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23-7.11 (m, 7H), 7.07-6.97 (m, 4H), 6.69 (d, *J* = 7.9 Hz, 1H), 6.49 (d, *J* = 7.9 Hz, 1H), 5.79 (t, *J* = 10.2 Hz, 1H), 2.91 (s, 6H), 2.59 (m,1H), 2.49 (m, H), 2.27 (d, *J* = 20.2 Hz, 6H), 2.00 (d, *J* = 8.5 Hz, 1H), 1.72-1.59 (m, 1H), 1.20 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.0, 175.0, 139.3, 136.6, 136.5, 130.9, 129.1, 127.6, 127.6, 126.6, 126.5, 126.3, 126.3, 126.2, 126.2, 113.2, 51.2, 41.1, 40.9, 36.2, 32.6, 19.3, 19.3, 18.4; ESI-MS: m/z 415.30 $[M+H]^+$; 437.35 $[M+Na]^+$; HRMS (ESI) calculated for [M+H, $C_{28}H_{35}N_2O]^+$: 415.2748 found 415.2744, [M+Na, $C_{28}H_{34}N_2NaO]^+$: 437.2565, found 437.2563.

***N*-(di-o-tolylmethyl)-4-(4-formylphenyl)-2-methylbutanamide (5m)**



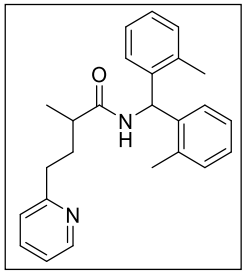
White solid, 56% yield, m.p = 153-157 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.92 (s,1H), 7.76 (dd, *J* = 7.9, 2.4 Hz, 2H), 7.30-7.26 (m, 2H), 7.22-7.10 (m, 6H), 7.07-6.99 (m, 2H), 6.51 (dd, *J* = 7.9, 2.3 Hz, 1H), 5.93 (d, *J* = 7.9 Hz, 1H), 2.78-2.69 (m, 1H), 2.70-2.60 (m, 1H), 2.35-2.21 (m, 7H), 2.13-2.02 (m, 1H), 1.80-1.66 (m, 1H), 1.23 (dd, *J* = 6.9, 2.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.1, 192.1, 174.5, 174.5, 149.4, 149.4, 139.2, 139.2, 139.1, 139.1, 136.6, 136.6, 136.5, 134.7, 131, 131, 131, 130, 130, 129.2, 129.2, 127.7, 127.7, 127.7, 126.5, 126.4, 126.3, 126.3, 126.2, 126.2, 126.2, 51.3, 51.2, 41.0, 41, 35.4, 35.3, 34.0, 34.0, 19.3, 19.3, 19.2, 19.2, 18.5, 18.5; ESI-MS: m/z 400.4 $[M+H]^+$, 422.35 $[M+Na]^+$; HRMS (ESI) calculated for [M+H, $C_{27}H_{30}NO_2]^+$ 400.2262 found 400.2271, [M+Na, $C_{27}H_{29}NNaO_2]^+$ 422.2093 found 422.2091. FTIR (neat, cm-1): 3258 (s), 2924 (m), 1705 (s), 1639 (s, sh), 1605 (s), 1534 (s), 1458 (m), 746 (m).

***N*-(di-o-tolylmethyl)-4-(2-fluorophenyl)-2-methylbutanamide (5n)**



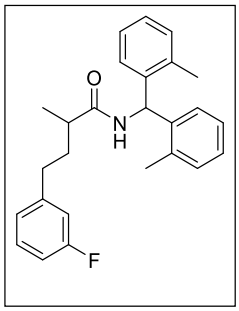
White solid, 71% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23-7.07 (m, 9H), 7.03 (m, 3H), 6.50 (d, *J* = 7.9 Hz, 1H), 5.89 (d, *J* = 7.9 Hz, 1H), 2.66 (t, *J* = 7.8 Hz, 2H), 2.33-2.23 (m, 7H), 2.03 (m, 1H), 1.70 (m, 1H), 1.22 (d, *J* = 6.9 Hz, 3H); δ 174.5, 161 (d, *J* = 244.7 Hz), 139, 136, 136.3, 130.7, 130.5, 128.5, 128.4, 127.6, 127.5, 127.4, 126.3, 126.2, 126, 126.0, 123.9 (d, *J* = 3.4 Hz), 115.1 (d, *J* = 22.0 Hz), 51.04, 40.9, 34.3, 26.8, 26.8, 19.0, 18.2. ^{19}F NMR (376 MHz, $CDCl_3$) δ -118.62 (dt, *J* = 13.6, 6.4 Hz); ESI-MS: m/z 390.30 $[M+H]^+$; 412.35 $[M+Na]^+$; HRMS (ESI) calculated for [M+H, $C_{26}H_{29}FNO]^+$: 390.2225 found 390.2228, [M+Na, $C_{26}H_{28}FNNaO]^+$: 412.2050, found 412.2047.

***N*-(di-o-tolylmethyl)-2-methyl-4-(pyridin-2-yl)butanamide (5o)**



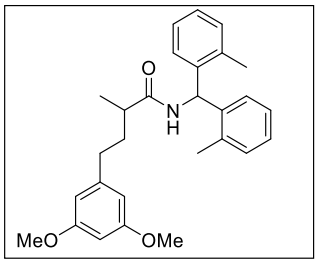
Yellow solid, 65% yield, m.p = 131-135 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.36 (d, *J* = 4.9, 0.9 Hz, 1H), 7.58 (td, *J* = 7.7, 1.9 Hz, 1H), 7.20-7.04 (m, 10H), 6.82 (d, *J* = 8.0 Hz, 1H), 6.52 (d, *J* = 8.0 Hz, 1H), 2.84-2.79 (m, 2H), 2.37 (m, 1H), 2.27 (d, *J* = 5.3 Hz, 6H), 2.12 (m, 1H), 1.79 (m, H), 1.18 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.9, 161.5, 148.9, 139.5, 139.5, 136.9, 136.7, 136.4, 130.8, 130.8, 127.5, 127.4, 126.7, 126.5, 126.1, 126.0, 123.4, 121.3, 51.2, 40.1, 35.5, 34.5, 19.3, 19.3, 18.2; ESI-MS: m/z 373.40 $[M+H]^+$; HRMS (ESI) calculated for [M+H, $C_{25}H_{29}N_2O]^+$: 373.2278, found 373.2274, [M+Na, $C_{25}H_{28}N_2NaO]^+$: 395.2088, found 395.2094. FTIR (neat, cm-1): 3260 (m), 2923 (m), 1640 (s, sh), 1541 (s), 1459 (m), 738 (s).

***N*-(di-o-tolylmethyl)-4-(3-fluorophenyl)-2-methylbutanamide (5p)**



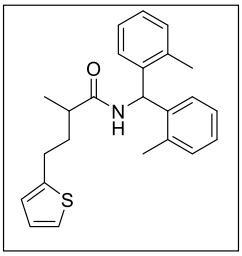
White solid, 70% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23-7.11 (m, 7H), 7.07-7.04 (m, 1H), 7.01 (d, *J* = 7.6 Hz, 1H), 6.91-6.81 (m, 3H), 6.50 (d, *J* = 7.9 Hz, 1H), 5.82 (d, *J* = 7.9 Hz, 1H), 2.71-2.61 (m, 1H), 2.60-2.51 (m, 1H), 2.30-2.21 (m, 7H), 2.10-1.99 (m, 1H), 1.74-1.63 (m, 1H), 1.21 (d, *J* = 6.8 Hz, 3H), ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.3, 162.8 (d, *J* = 245.5 Hz), 139.0, 138.9, 136.4, 136.2, 130.7, 130.7, 130.0, 129.6, 127.4, 127.4, 126.2, 126.1, 126.0, 125.9, 124.0, 123.9, 115.0 (d, *J* = 20.7 Hz), 112.7 (d, *J* = 21.0 Hz), 51.0, 40.6, 35.2, 33.2, 19.0 ^{19}F NMR (376 MHz, $CDCl_3$) δ -113.64 (td, *J* = 9.4, 5.9 Hz); ESI-MS: m/z 390.45 $[M+H]^+$; 412.45 $[M+Na]^+$; HRMS (ESI) calculated for [M+Na, $C_{26}H_{28}FNNaO]^+$: 412.2054, found 412.2047.

***N*-(di-o-tolylmethyl)-4-(3,5-dimethoxyphenyl)-2-methylbutanamide (5q)**



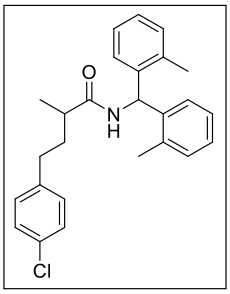
Yellow solid, 64% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23-7.12 (m, 7H), 7.10-6.99 (m, 2H), 6.50 (d, *J* = 7.9 Hz, 1H), 6.33-6.28 (m, 2H), 5.90 (d, *J* = 8.0 Hz, 1H), 3.74 (s, 6H), 2.67-2.57 (m, 1H), 2.55-2.48 (m, 1H), 2.33-2.23 (m, 7H), 2.10-2.00 (m, 1H), 1.74-1.64 (m, 1H), 1.21 (d, *J* = 6.8 Hz, 3H),^{13}C NMR (125 MHz, $CDCl_3$) δ 174.8, 160.9, 144.3, 139.2, 130.9, 127.6, 127.6, 126.5, 126.3, 126.2, 126.2, 106.5, 98.1, 55.3, 51.2, 40.9, 35.6, 34.1, 29.6, 19.2, 19.2, 18.5; ESI-MS: m/z 432.30 $[M+H]^+$; 454.25 $[M+Na]^+$; HRMS (ESI) calculated for [M+H, $C_{28}H_{34}NO_3]^+$: 432.2539 found 432.2533, [M+Na, $C_{28}H_{33}NNaO_3]^+$: 454.2360, found 454.2353.

***N*-(di-o-tolylmethyl)-2-methyl-4-(thiophen-2-yl)butanamide (5r)**



Yellow solid, 55% yield, m.p. = 140-142 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24-7.09 (m, 7H), 7.06 (d, *J* = 7.6 Hz, 1H), 7.00 (d, *J* = 7.7 Hz, 1H), 6.89 (t, *J* = 5.0, 3.5, 0.8 Hz, 1H), 6.72 (d, *J* = 3.5 Hz, 1H), 6.49 (d, *J* = 7.7 Hz, 1H), 5.81 (d, *J* = 7.8 Hz, 1H), 2.93-2.85 (m, 1H), 2.84-2.75 (m, 1H), 2.37-2.30 (m, 1H), 2.27 (d, *J* =9.3 Hz, 6H), 2.16-2.08 (m, 1H), 1.80-1.71 (m, 1H), 1.21 (d, *J* = 6.6 Hz, 3H), ^{13}C NMR (125 MHz, $CDCl_3$) ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.6, 144.6, 139.2, 139.1, 136.7, 136.5, 130.9, 130.9, 127.7, 127.7, 126.9, 126.5, 126.4, 126.2, 126.2, 124.5, 123.3, 51.3, 40.5, 36.1, 27.8, 19.3, 19.2, 18.4; ESI-MS: m/z 378.40 $[M+H]^+$; 400.40 $[M+Na]^+$; HRMS (ESI) calculated for [M+Na, $C_{24}H_{27}NNaOS]^+$: 400.1708, found 400.1706. FTIR (neat, cm-1):3252 (s), 2926 (m), 1636 (s, sh), 1533 (s), 1457 (s), 1238 (m), 1054 (m), 845 (w), 756 (s), 691 (s), 446 (w).

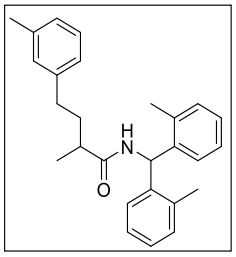
4-(4-chlorophenyl)-*N*-(di-o-tolylmethyl)-2-methylbutanamide (5s)



White solid, 60% yield, m.p. = 184-186 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24-7.11 (m,7H), 7.06-6.99 (m, 3H), 6.52-6.47 (m, 1H), 5.77 (d, *J* = 7.9 Hz, 1H), 2.69-2.58 (m, H), 2.58-2.50 (m, 1H), 2.27 (d, *J* = 15.8 Hz, 6H), 2.11-1.96 (m, 1H), 1.84 (s, 1H), 1.71-1.61 (m, 1H), 1.21 (d, *J* = 6.6 Hz, 3H), ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.6, 140.3, 139.3, 139.2, 136.6, 136.5, 131.8, 131, 131, 130, 128.6, 128.5, 128.5, 127.7, 127.7, 126.5, 126.3, 126.2, 126.2, 51.2, 40.9, 35.8, 35.7, 33.1, 19.3, 19.2, 18.5; ESI-MS: m/z 406.35 $[M+H]^+$; 428.35 $[M+Na]^+$; HRMS (ESI) calculated for [M+Na, $C_{26}H_{28}$ ClNNaO]$^+$: 428.1760,

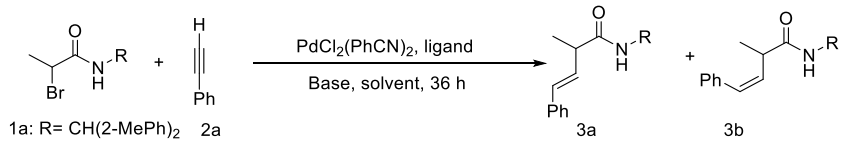
found 428.1752. FTIR (neat, cm-1): 3254 (m), 2926 (w), 1638 (s, sh), 1532 (s), 1491 (s), 1457 (m), 1237 (w), 1085 (w), 830 (m), 755 (m), 724 (m).

N-(di-o-tolylmethyl)-2-methyl-4-(m-tolyl)butanamide (5t)



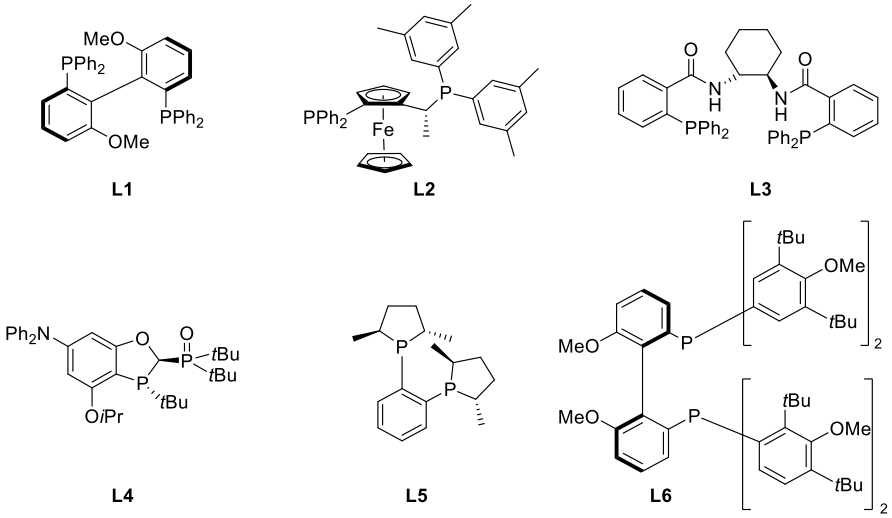
White solid, 72% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24-7.12 (m, 7H), 7.08-6.91 (m, 5H), 6.94 (t, *J* = 6.5 Hz, 2H), 6.54-6.48 (m, 1H), 5.82 (s, 1H), 2.70-2.62 (m, 1H), 2.55 (d, *J* = 6.8 Hz, 1H), 2.33-2.27 (m, 7H), 2.27-2.25 (m, 3H), 2.10-1.99 (m, 1H), 1.76-1.66 (m, 1H), 1.22 (dd, *J* = 6.8, 1.2 Hz, 3H), ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.8, 138.1, 136.6, 136.5, 130.9, 129.3, 128.4, 127.6, 127.6, 126.8, 126.5, 126.3, 126.2, 126.2, 125.5, 51.2, 41.0, 36.0, 33.7, 21.5, 19.3, 19.2, 18.5; ESI-MS: m/z 386.30 $[M+H]^+$; 408.25 $[M+Na]^+$; HRMS (ESI) calculated for [M+Na, $C_{27}H_{31}NNaO]^+$: 408.2304, found 4082298.

Parameters Screening



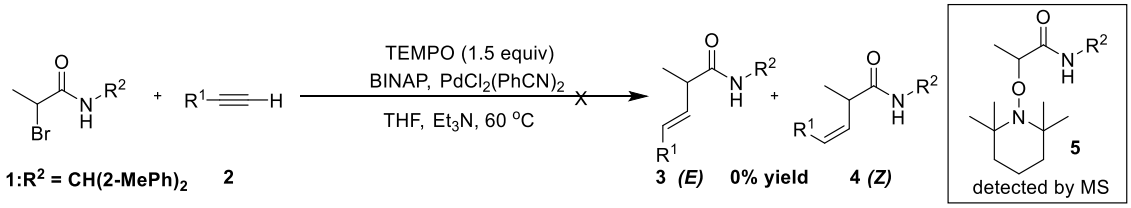
S/N	Ligand	Base	Solvent	Yield (%)
1	*(R,R)*-QuinoxP*	Et_3N	THF	0
2	(*R*)-(*S*)-JosiPhos	Et_3N	THF	0
3	*R,S*-DIPAMP	Et_3N	THF	0
4	L1	Et_3N	THF	0
5	L2	Et_3N	THF	45
6	L3	Et_3N	THF	47
7	L4	Et_3N	THF	10
8	L5	Et_3N	THF	0

9	L6	Et_3N	THF	0
10	XantPhos	Et_3N	THF	77
11	BINAP	Et_3N	THF	78



Mechanistic Studies

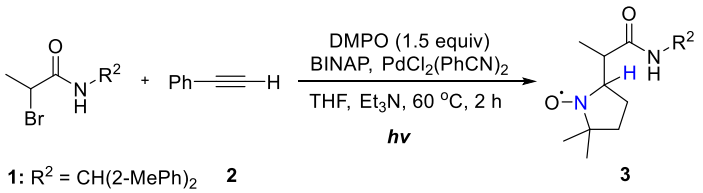
Radical Scavenger



An oven-dried schlenk tube was charged with stir bar, α-bromo carboxamide **1** (0.145 mmol, 1.0 equiv), **2** (0.29 mmol, 2.0 equiv), TEMPO (1.5 equiv), BINAP (20 mol %), $PdCl_2(PhCN)_2$ (20 mol %) and Et_3N (5 equiv) under N_2 atmosphere. The resulting

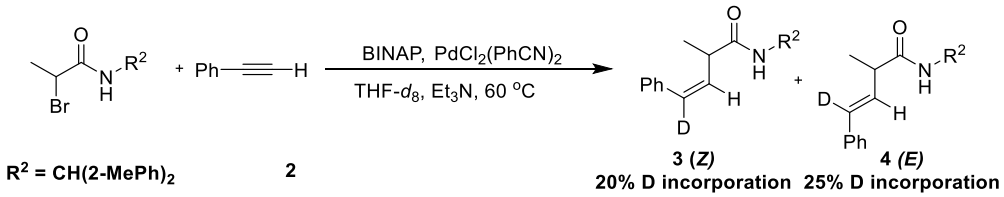
mixture was heated to 60 ^{o}C and stirred for 48 h. The hydroalkylation product (**3 &4**) was not formed but alkyl-TEMPO adduct was detected by ESI-MS.

EPR Study

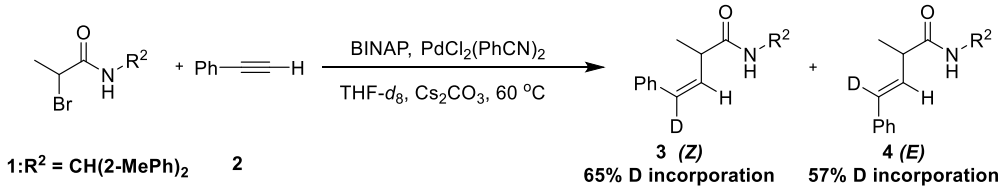


Deuterium Labelling Experiment

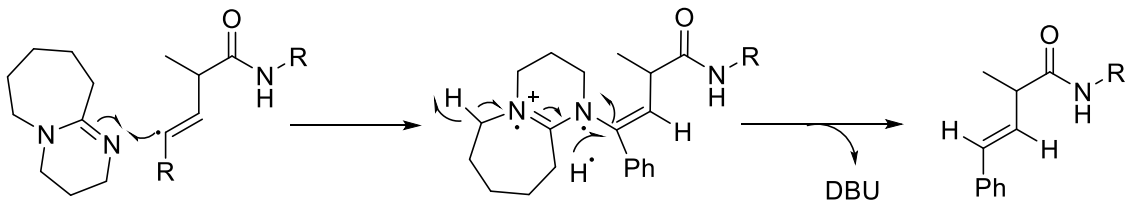
Reaction was carried out under N_2 atmosphere with α-bromo carboxamide **1** (0.145 mmol, 1.0 equiv), **2** (0.29 mmol, 2.0 equiv), BINAP (10 mol %), $PdCl_2(PhCN)_2$ (5 mol %) and Et_3N (5 equiv) at 60^{o}C for 48 h.



D-incorporation of products **3** and **4** was 20% and 25% respectively. Owing to the low deuteration recorded, we thought Et_3N might have undergone H-D exchange with THF-d_8, so the experiment was repeated with an inorganic base Cs_2CO_3 (5 equiv).

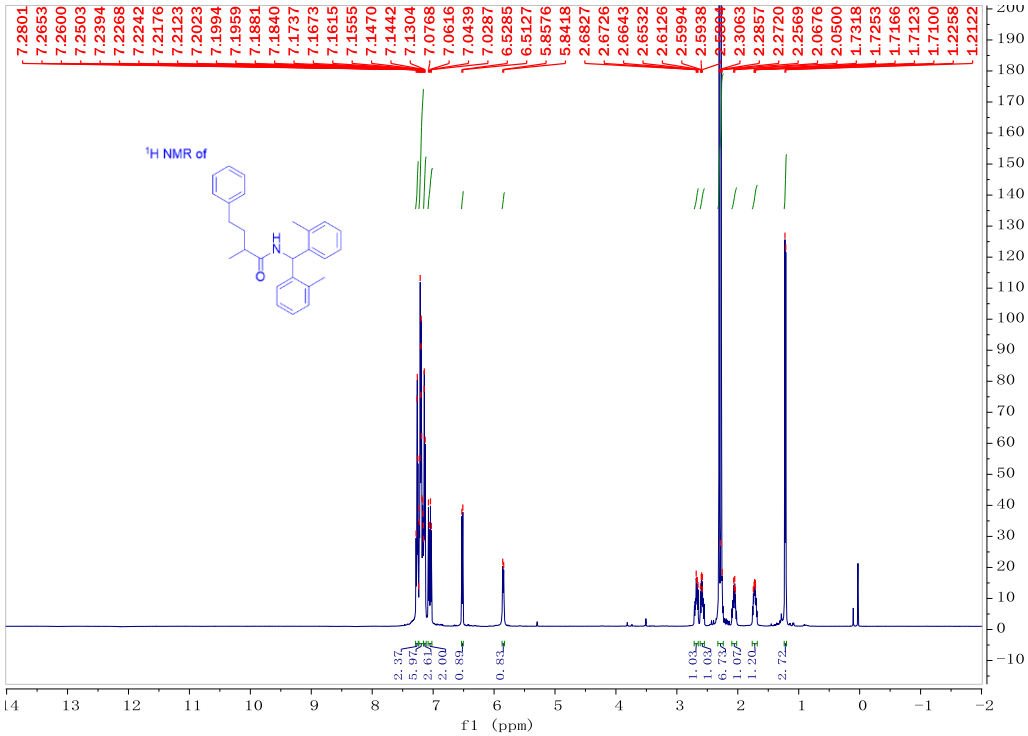


Role of DBU in Controlling Stereoselectivity

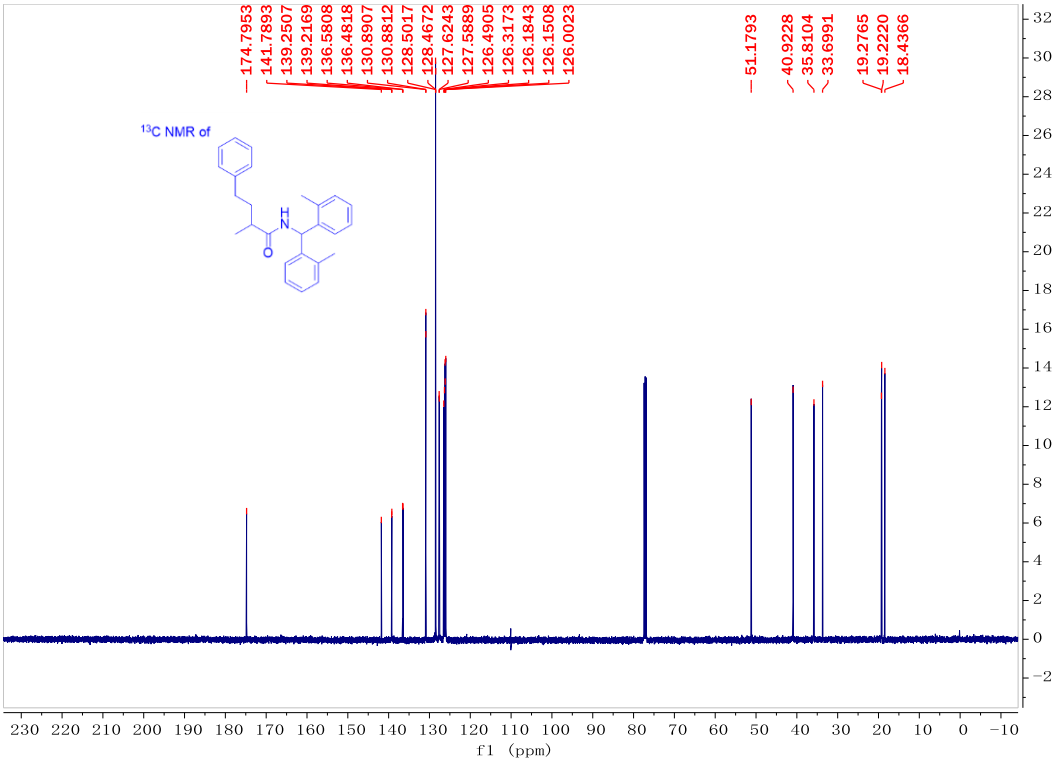


^{1}H, ^{13}C and ^{19}F NMR Spectra of Compounds

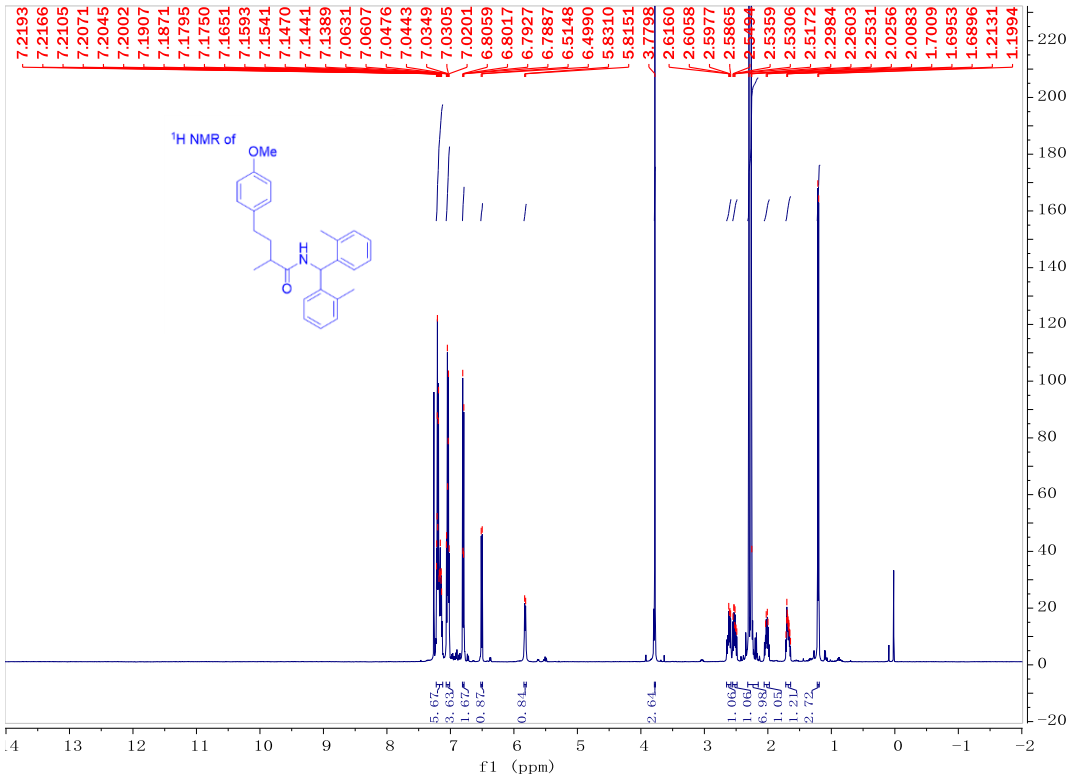
^{1}H NMR of 5a



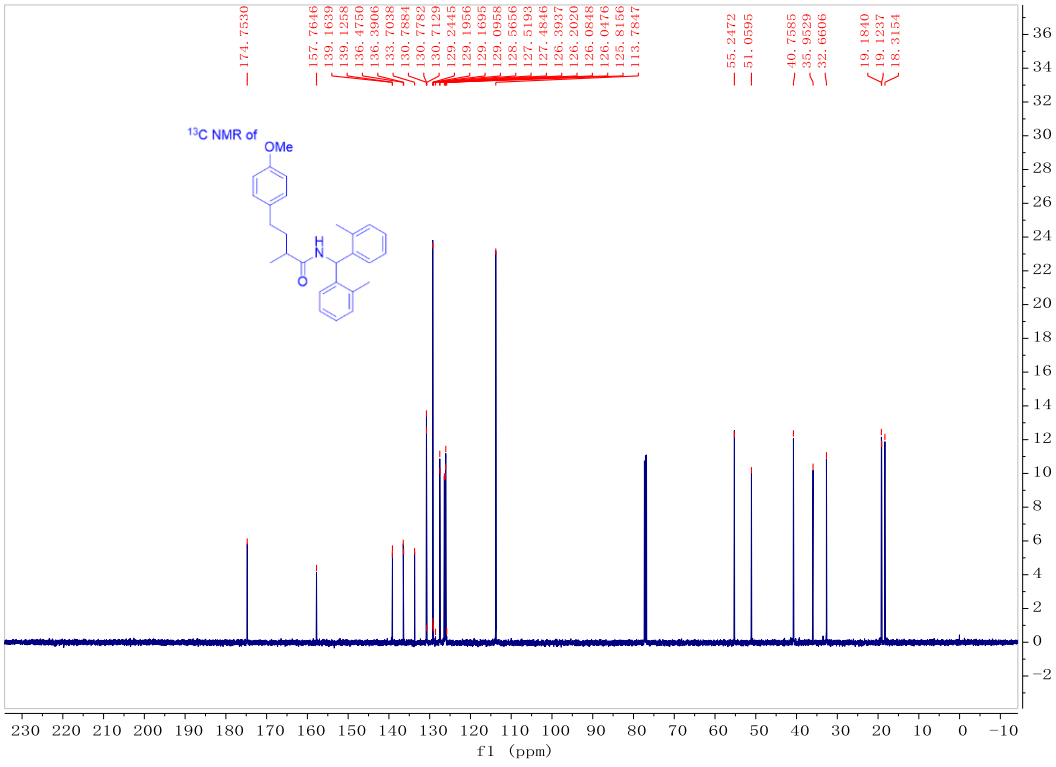
^{13}C NMR of 5a



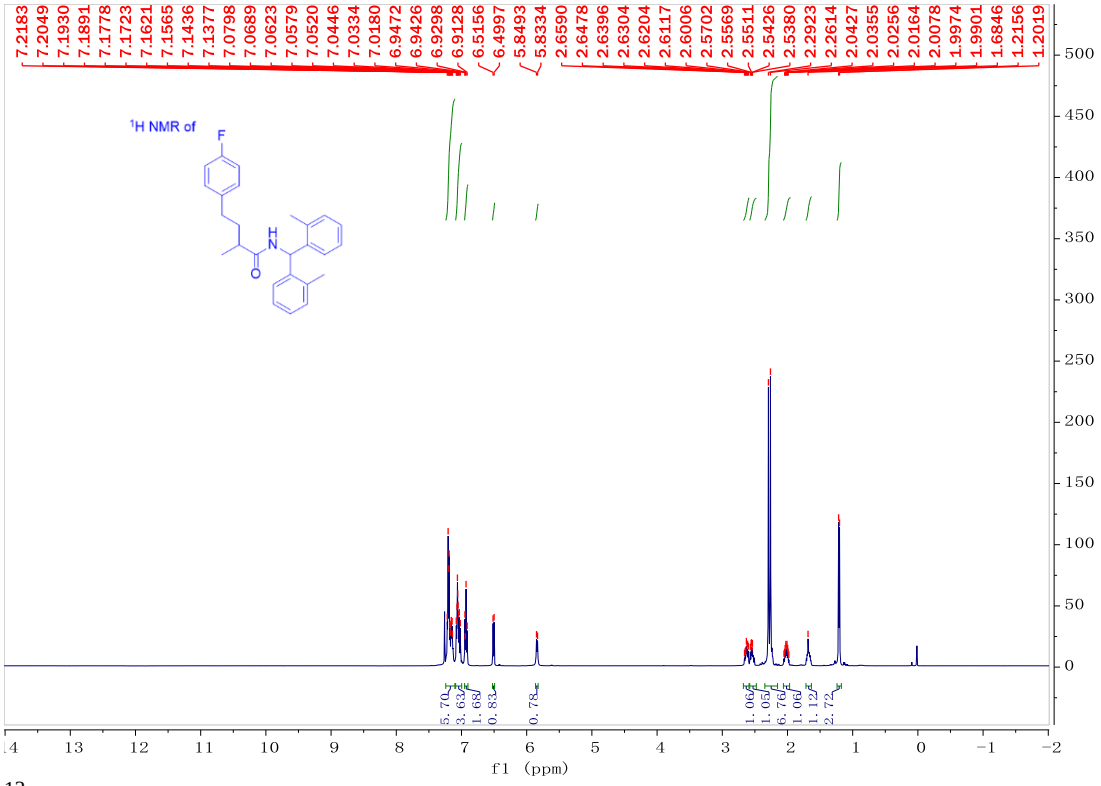
^{1}H NMR of 5b



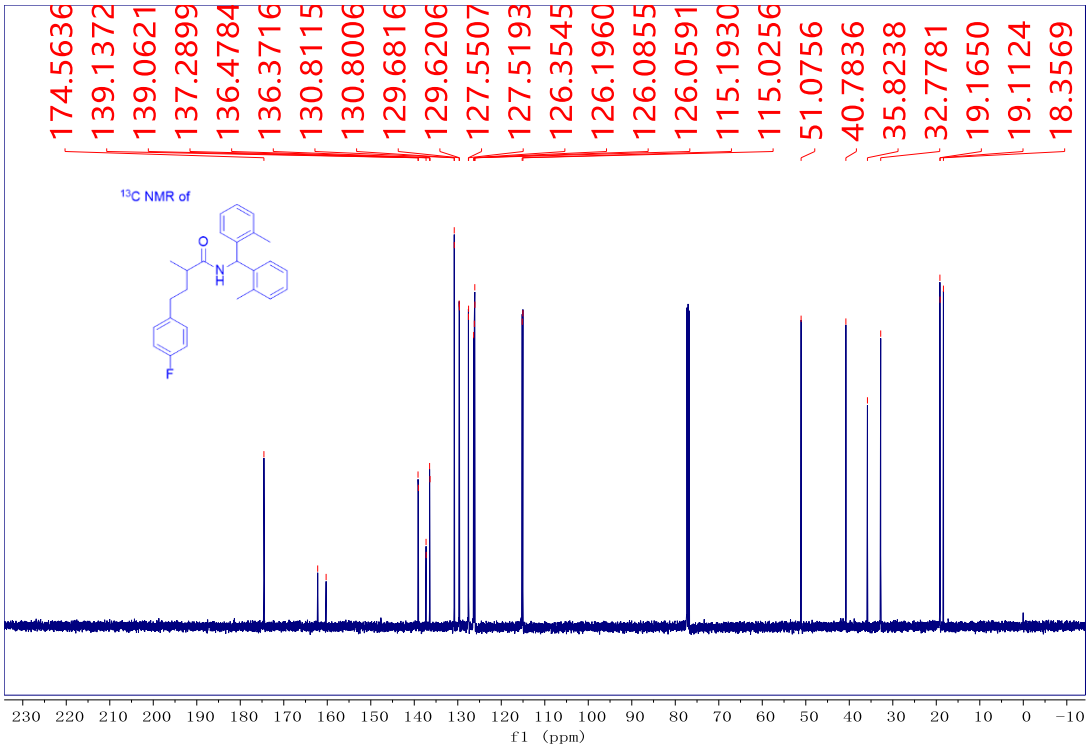
^{13}C NMR of 5b



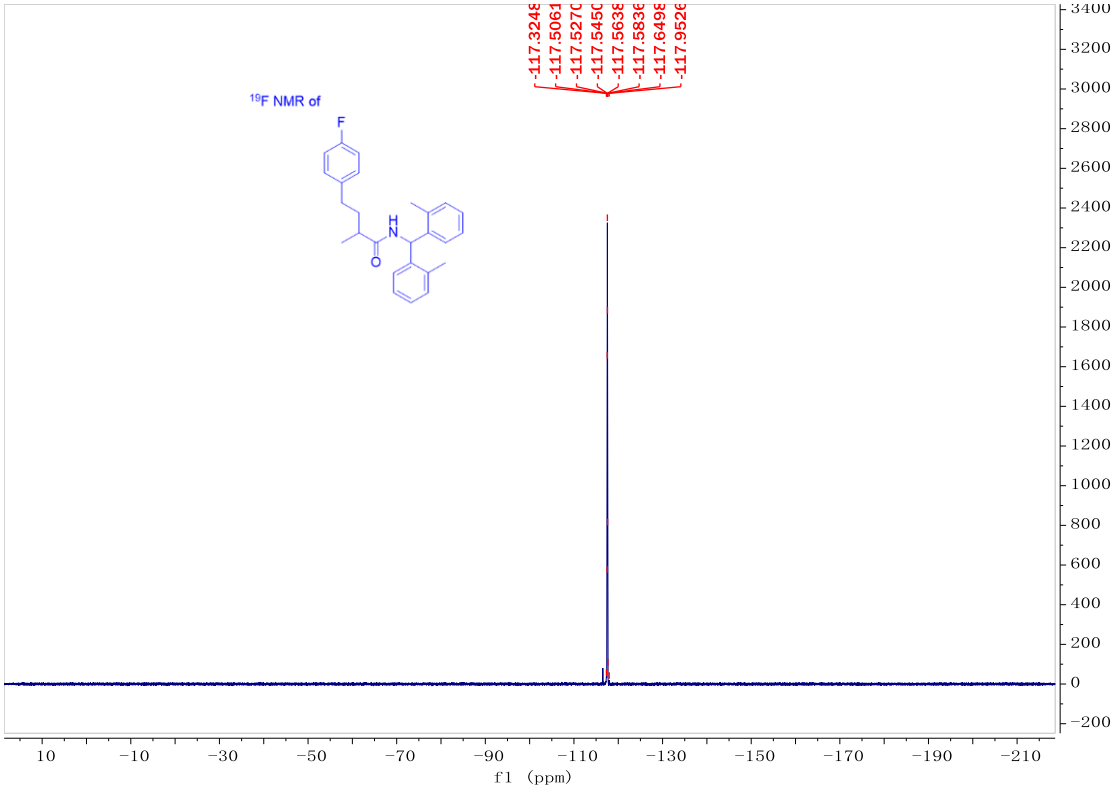
^{1}H NMR of 5c



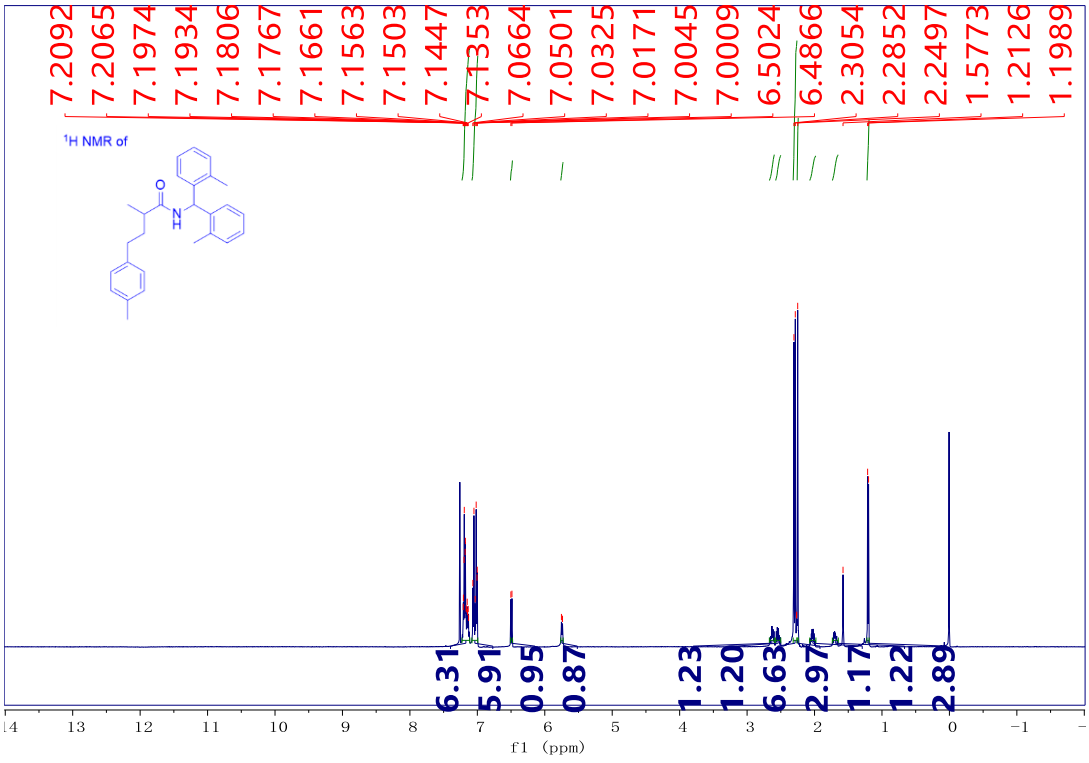
^{13}C NMR of 5c



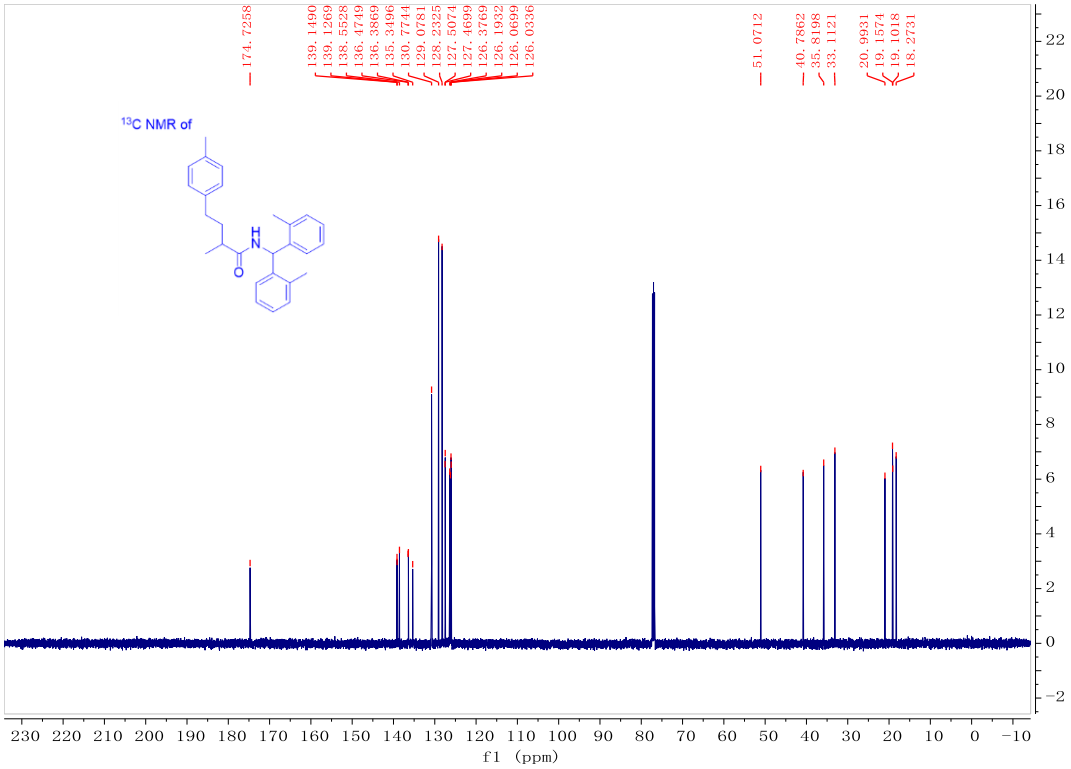
^{19}F NMR of 5c



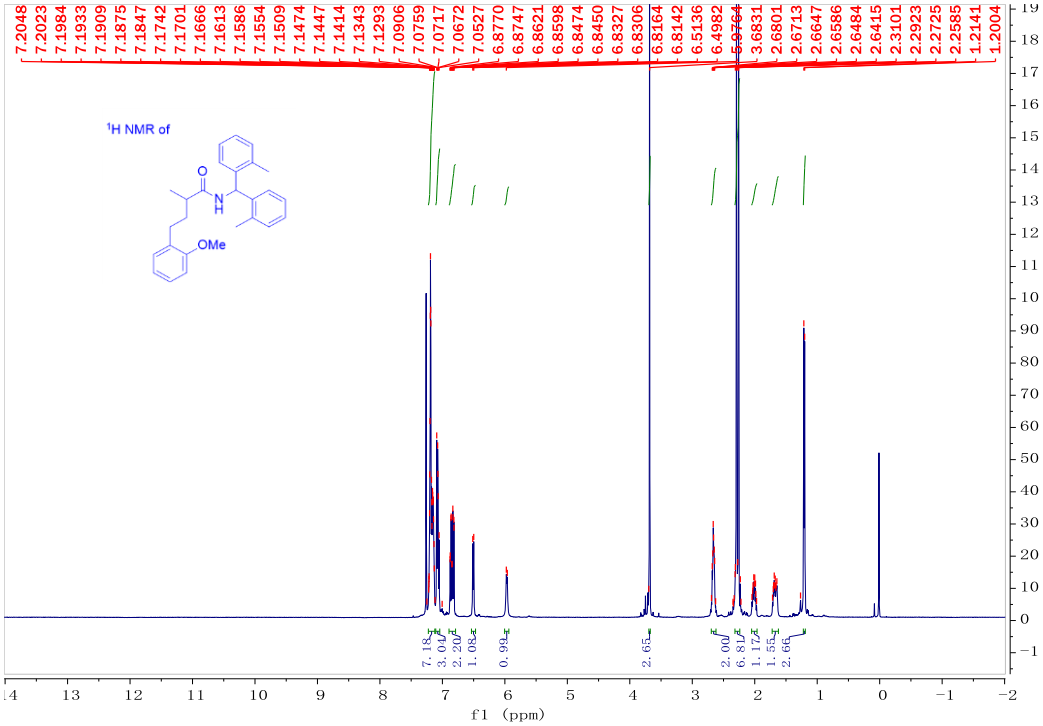
^{1}H NMR of 5d



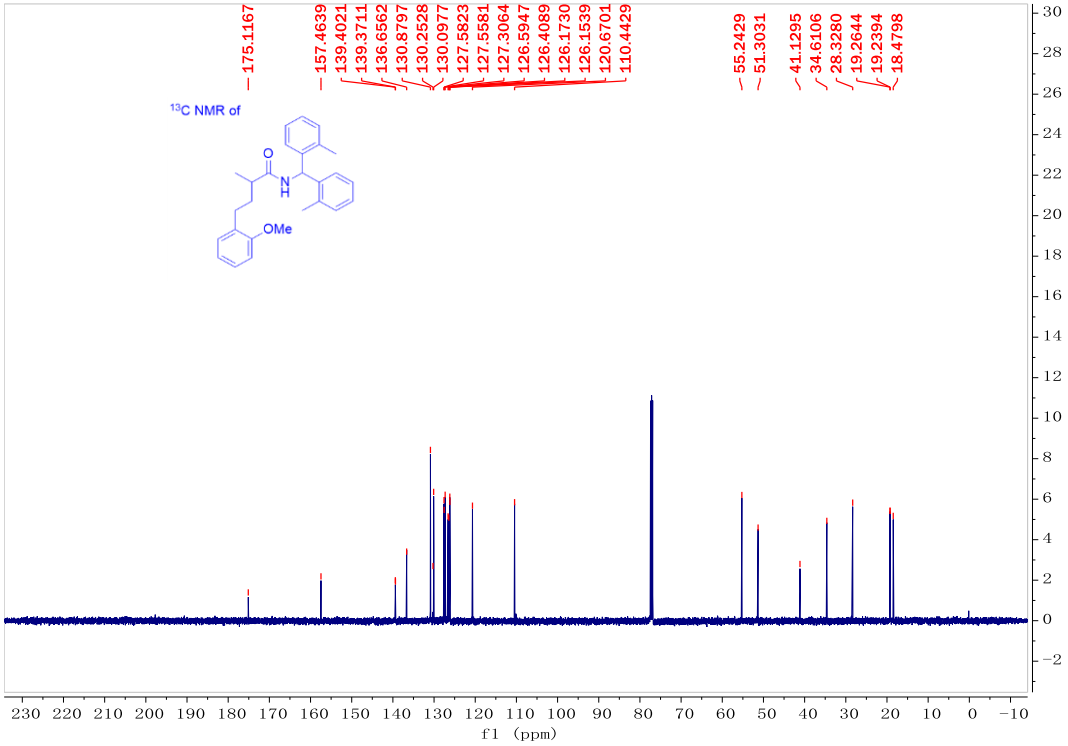
^{13}C NMR of 5d



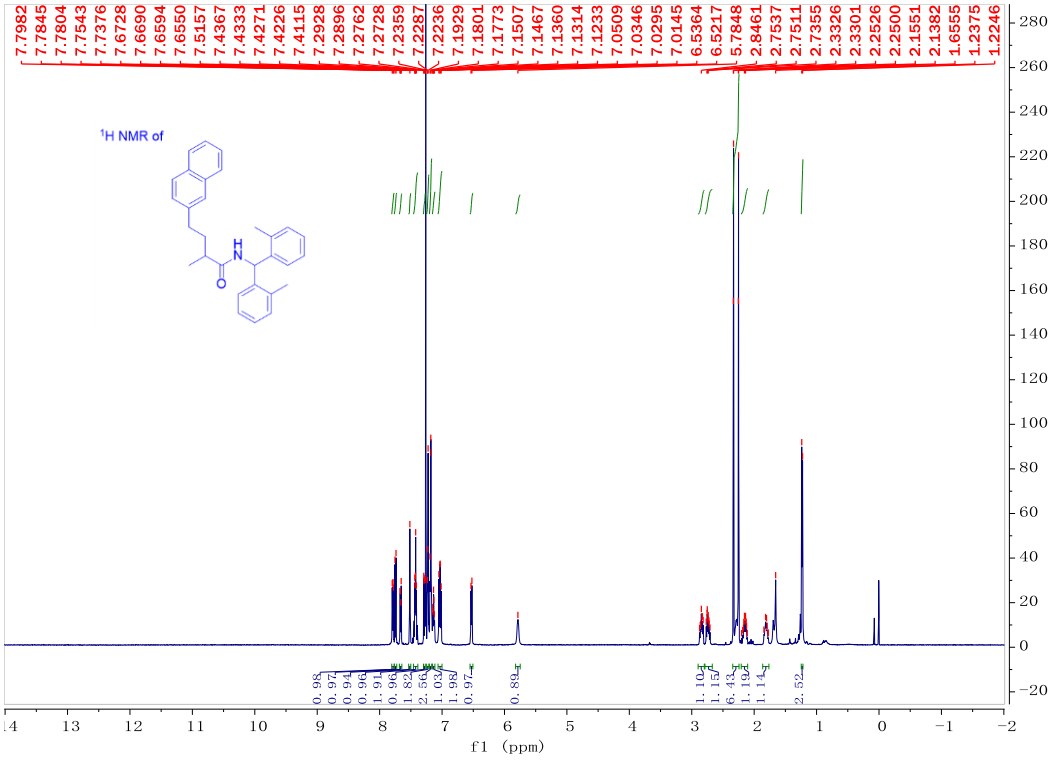
^{1}H NMR of 5e



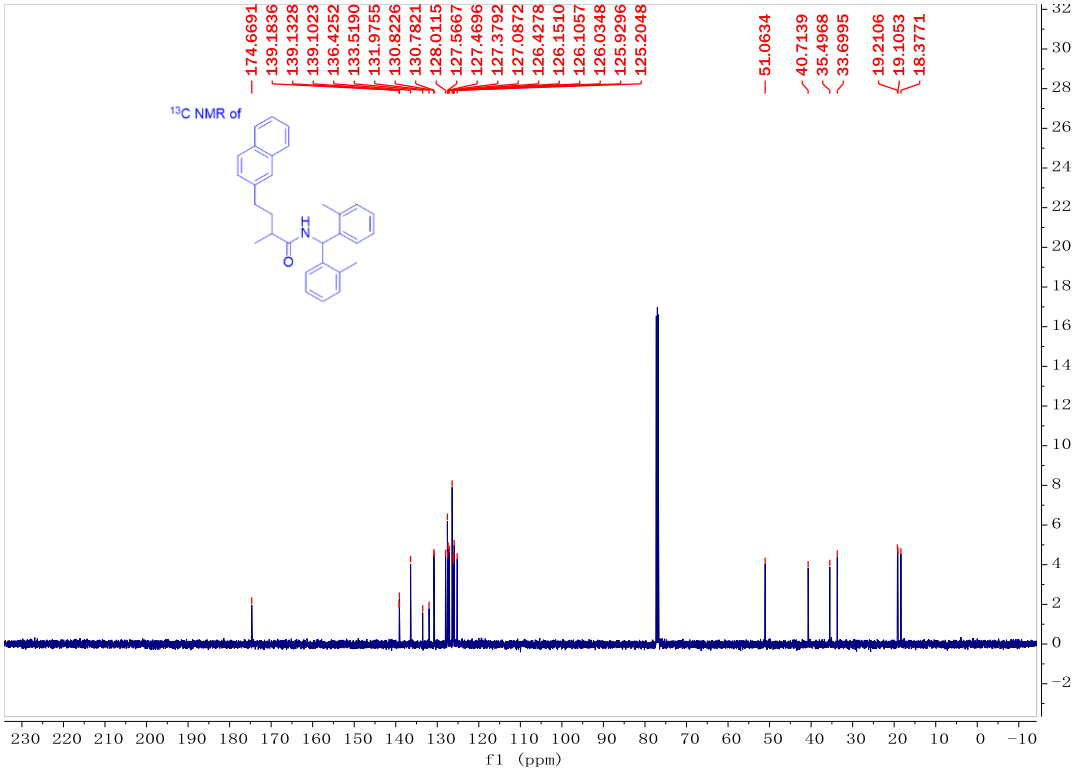
^{13}C NMR of 5e



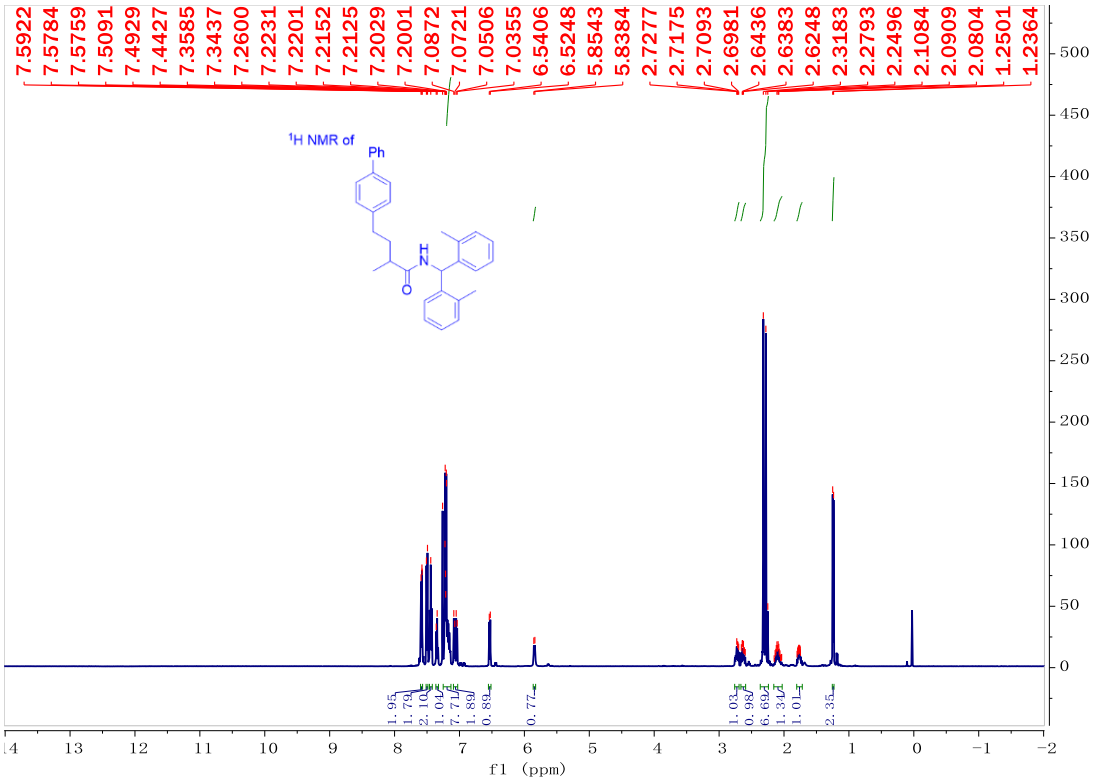
^{1}H NMR of 5f



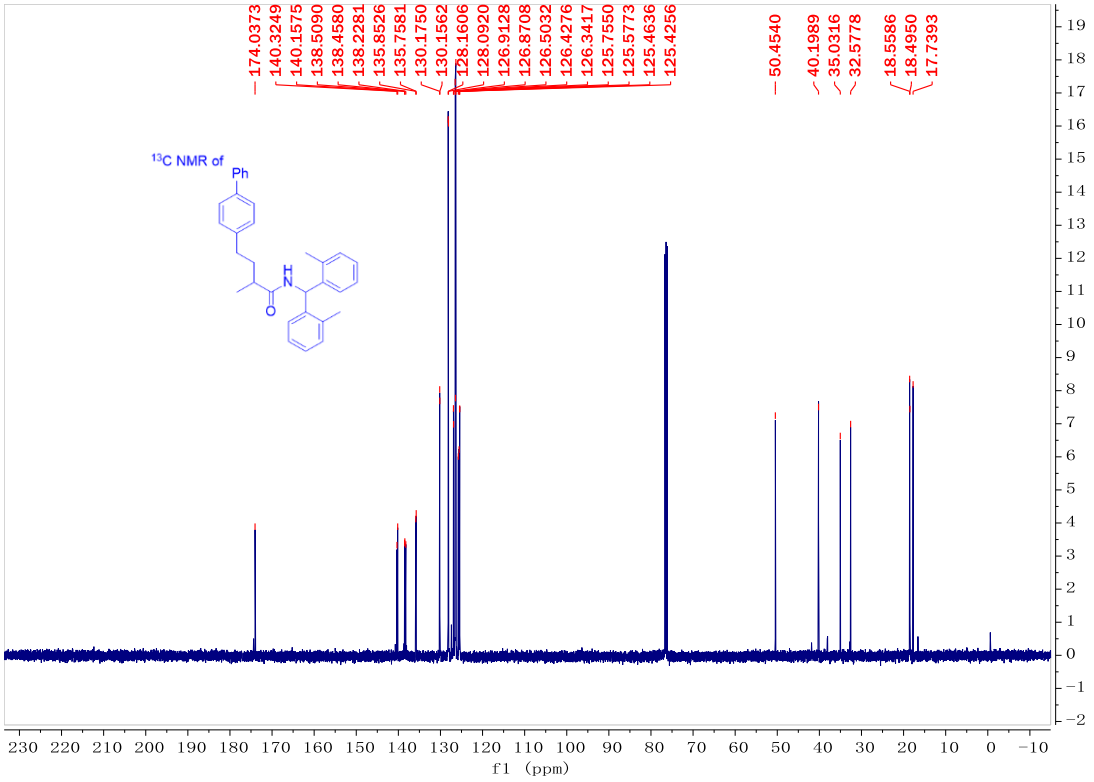
^{13}C NMR of 5f



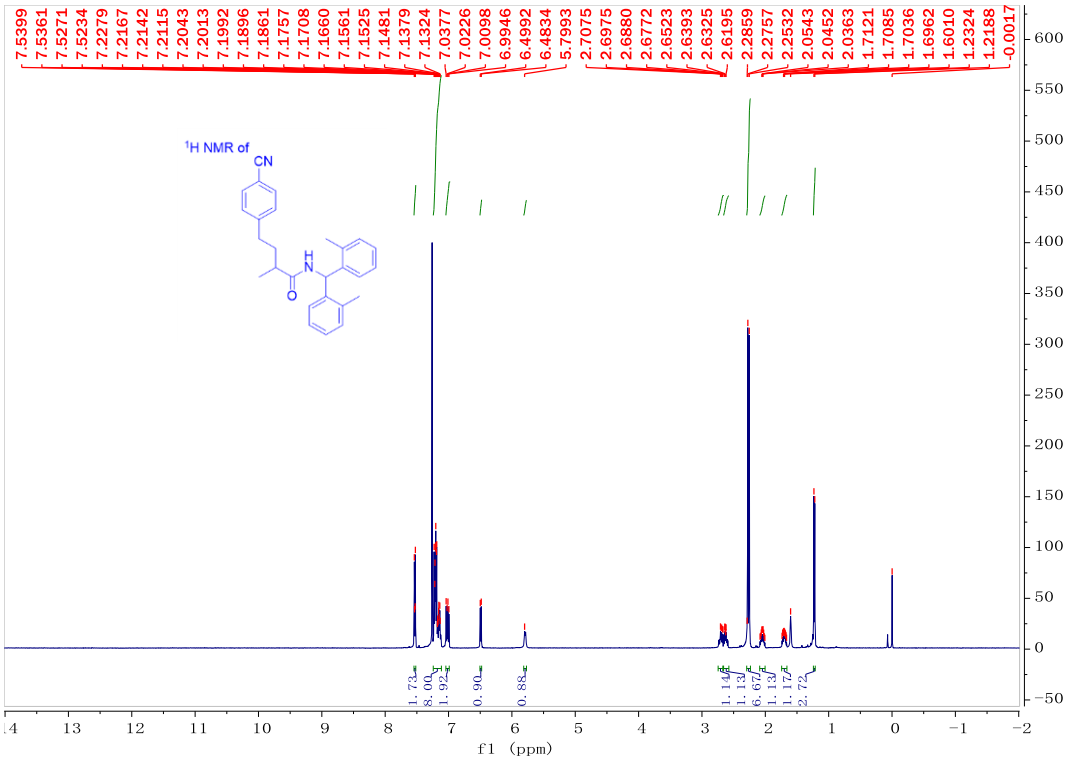
^{1}H NMR of 5g



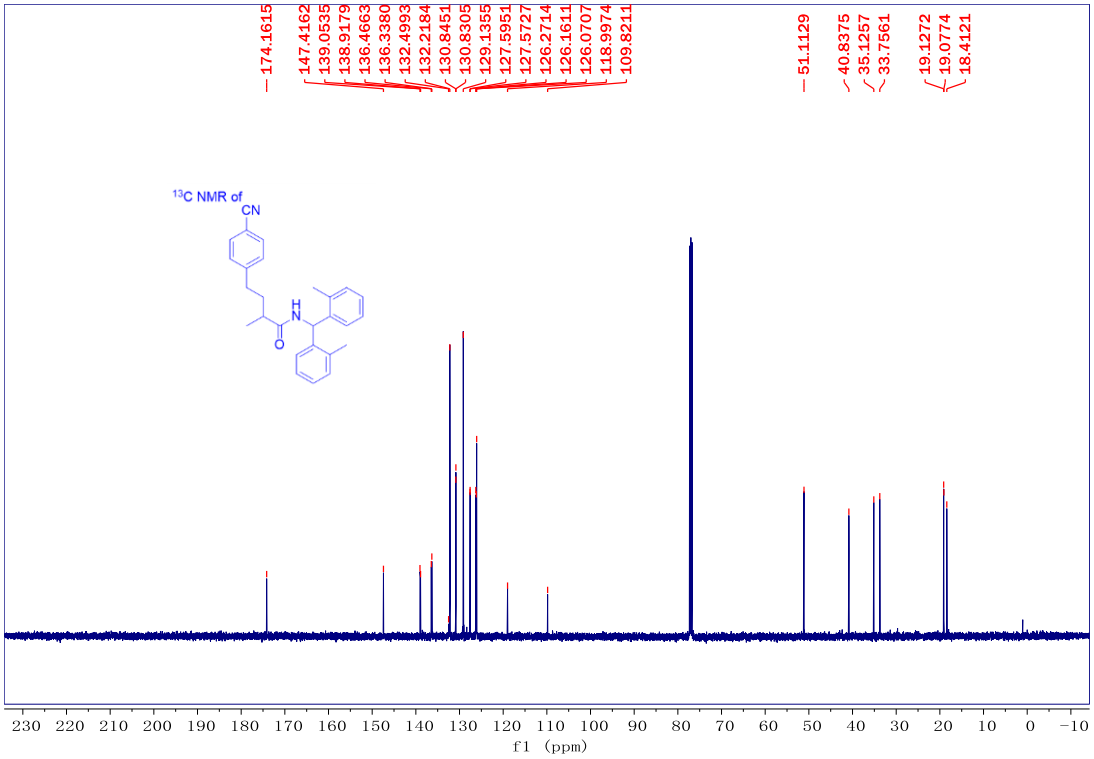
^{13}C NMR of 5g



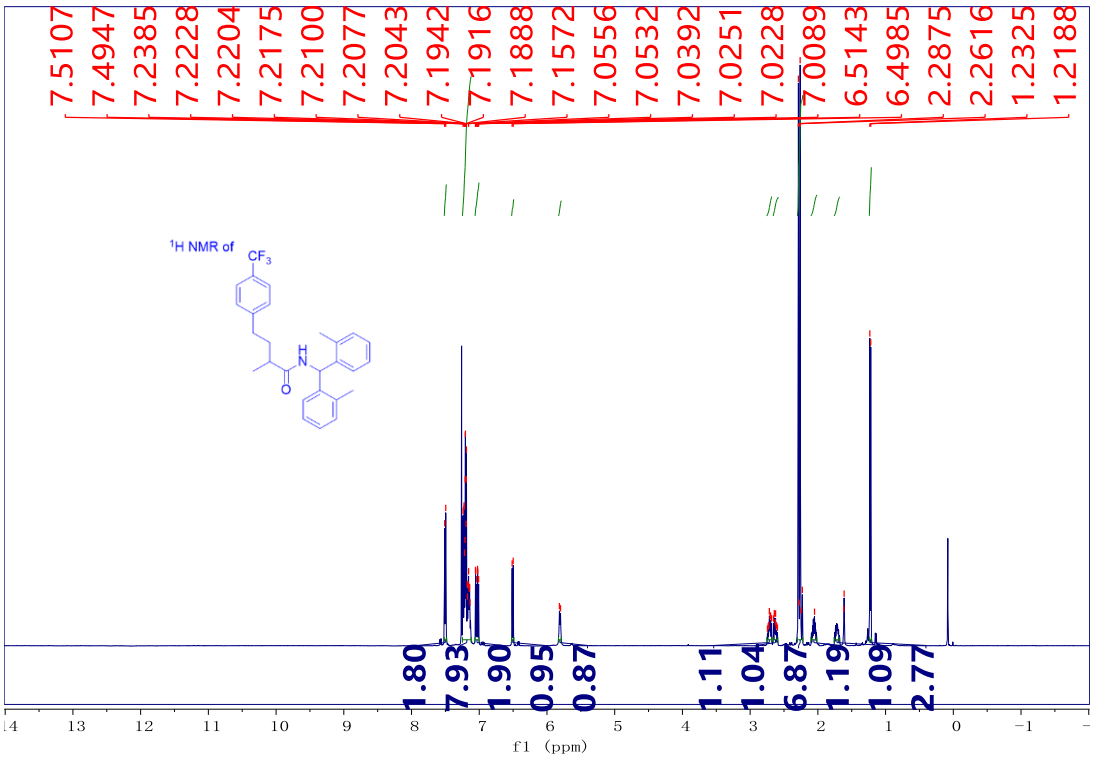
^{1}H NMR of 5h



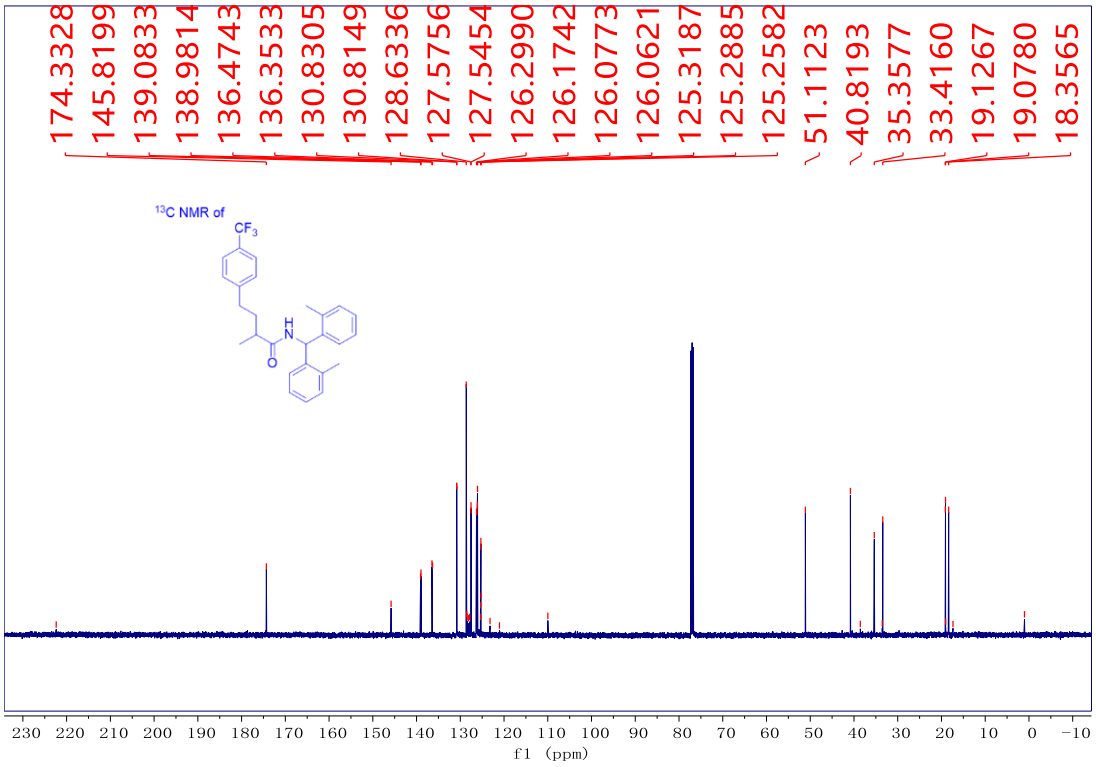
^{13}C NMR of 5h

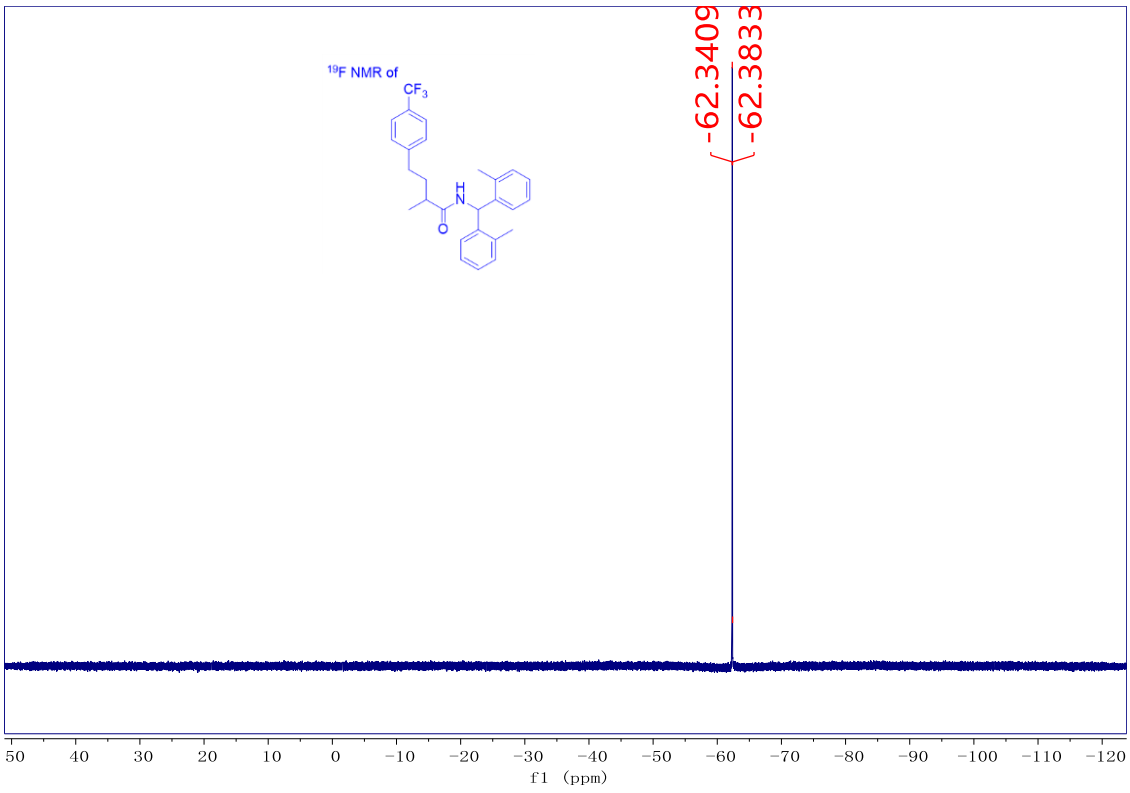


^{1}H NMR of 5i

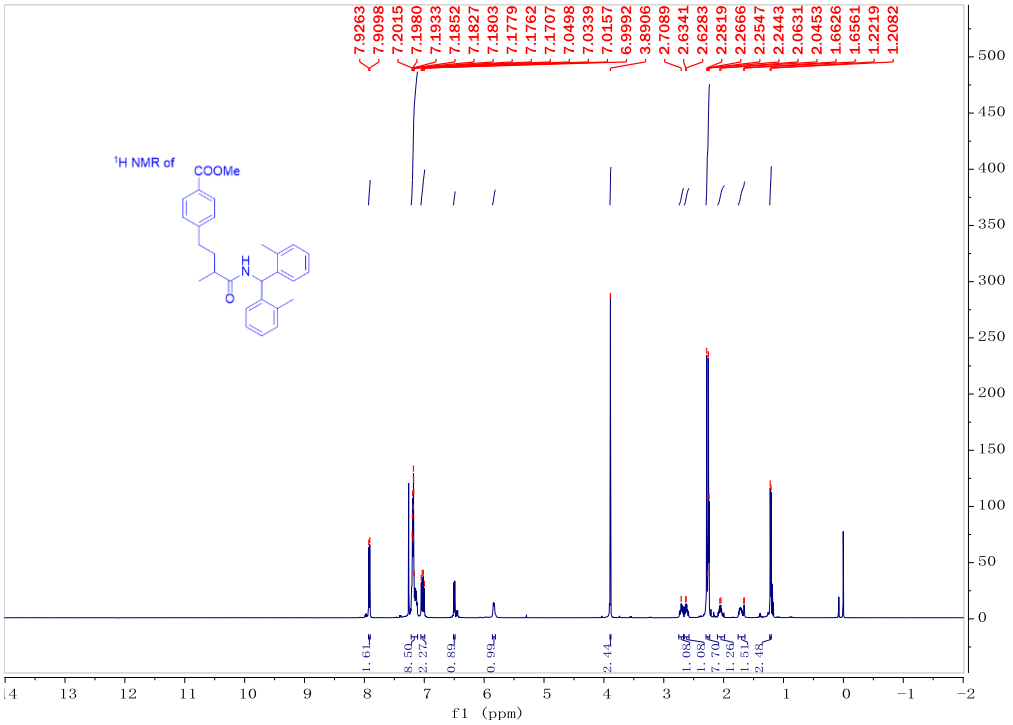


^{13}C NMR of 5i

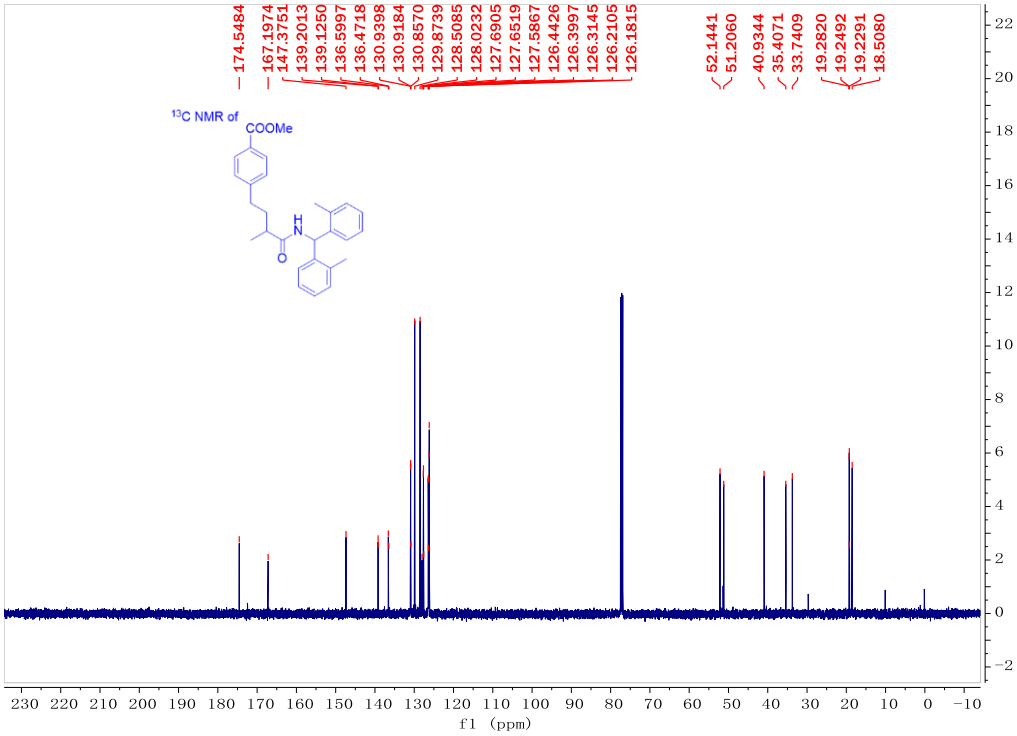




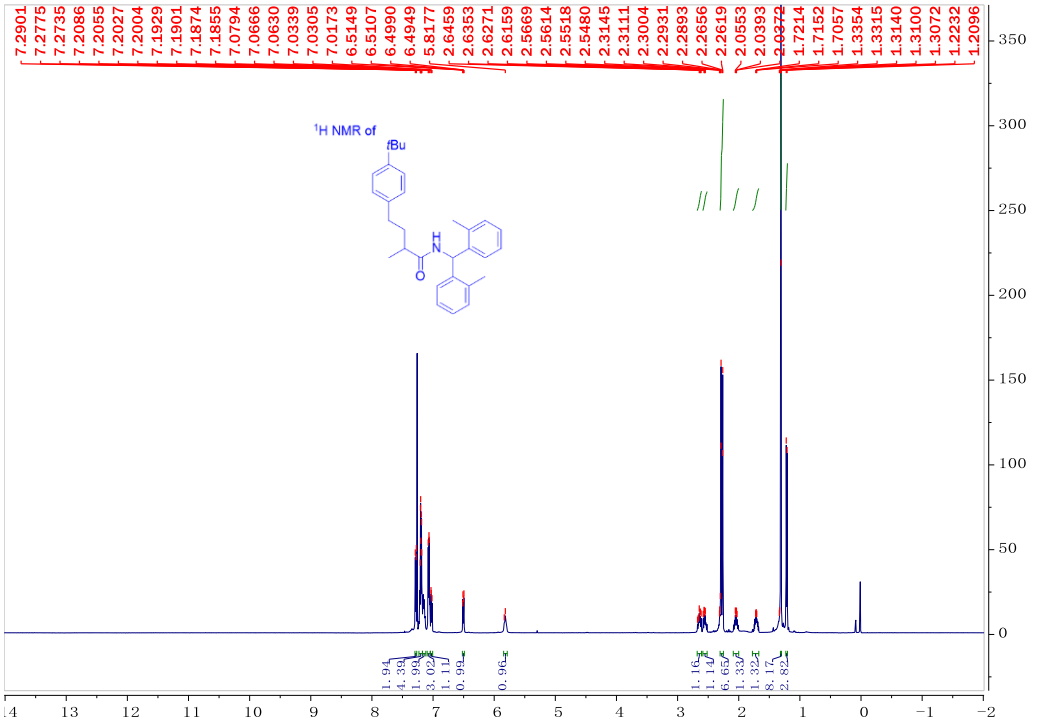
^{1}H NMR of 5j



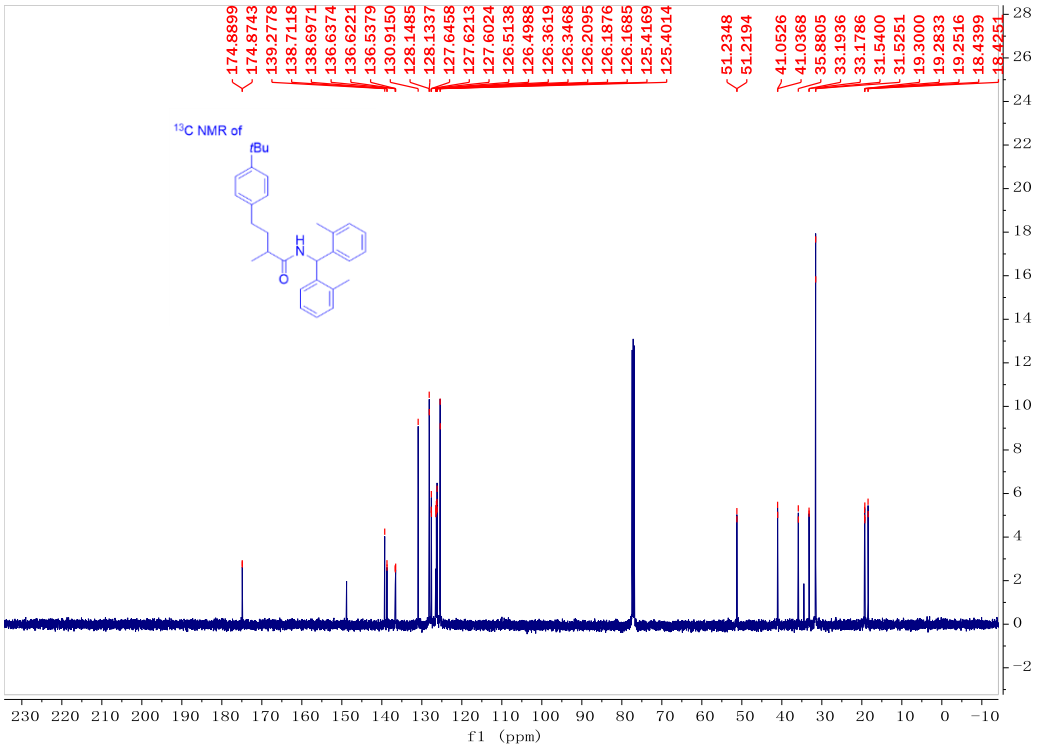
^{13}C NMR of 5j



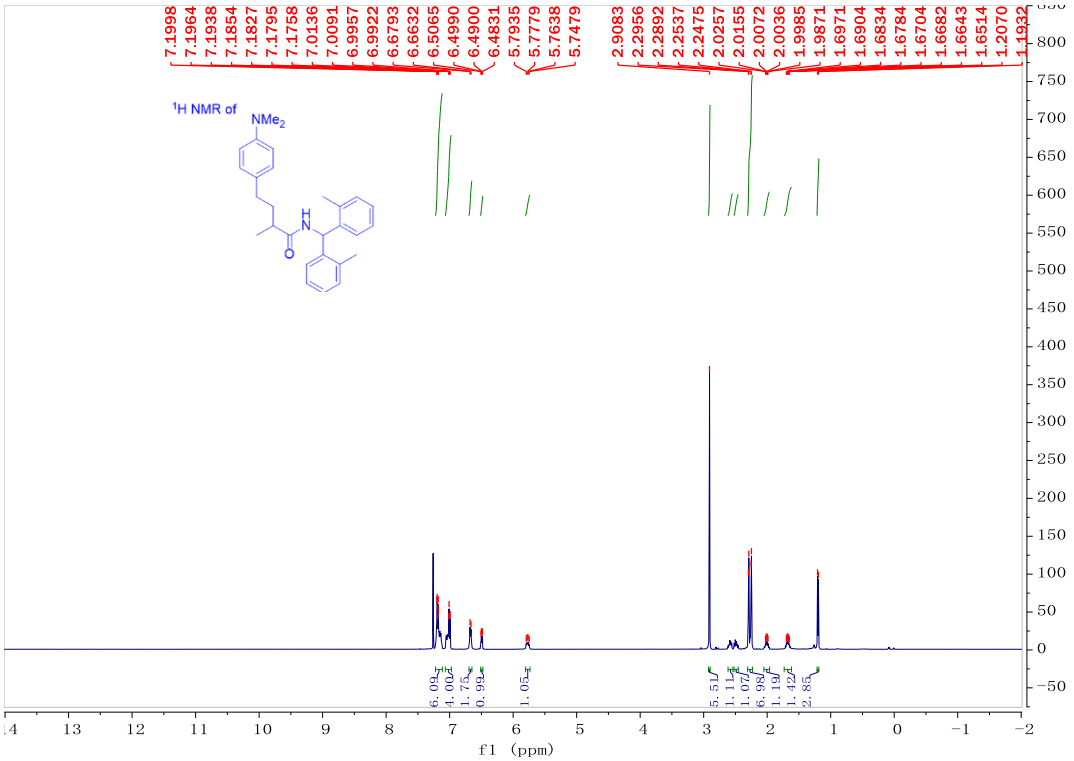
^{1}H NMR of 5k



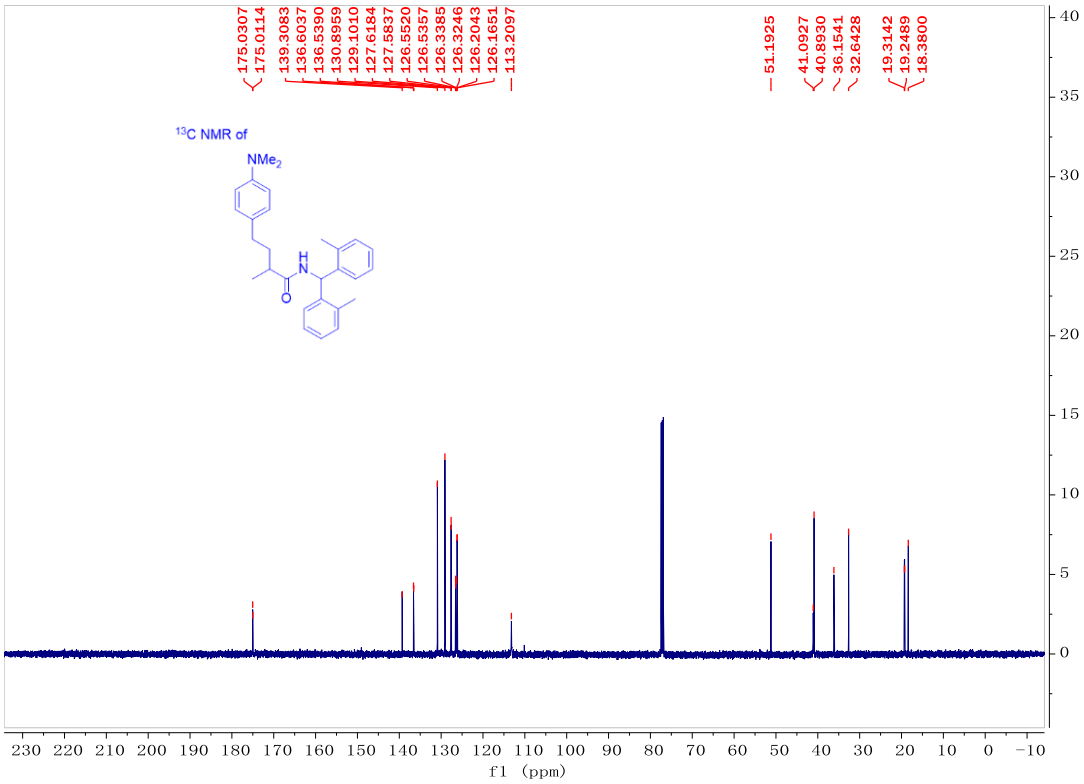
^{13}C NMR of 5k



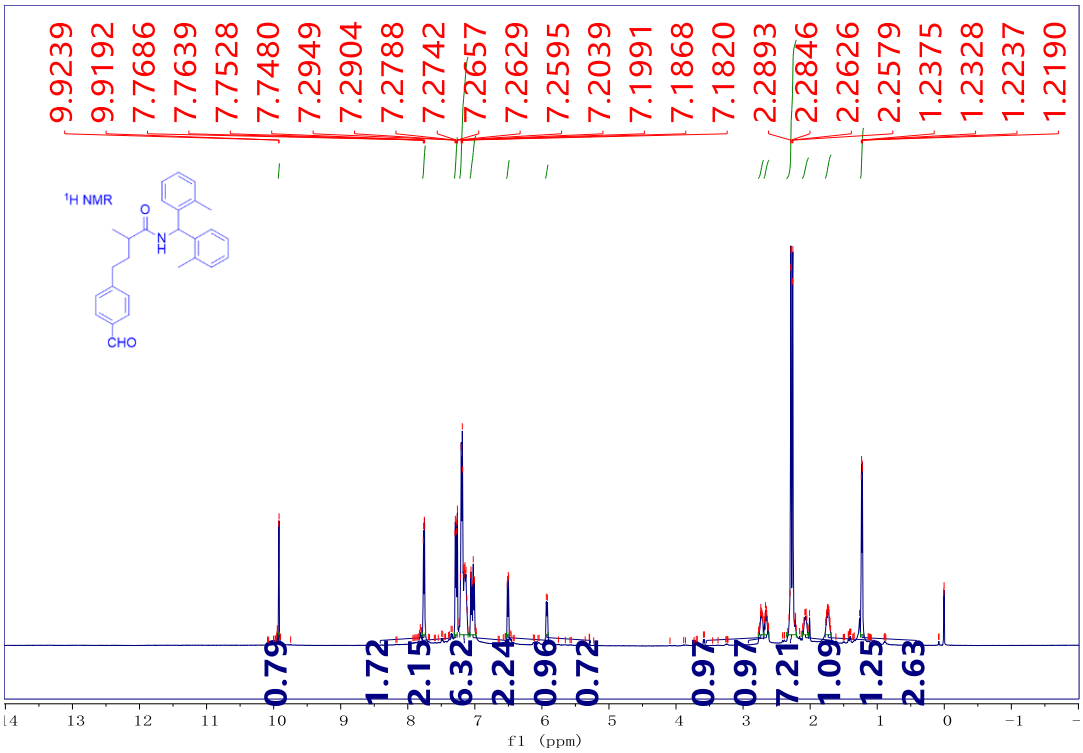
^{1}H NMR of 5l



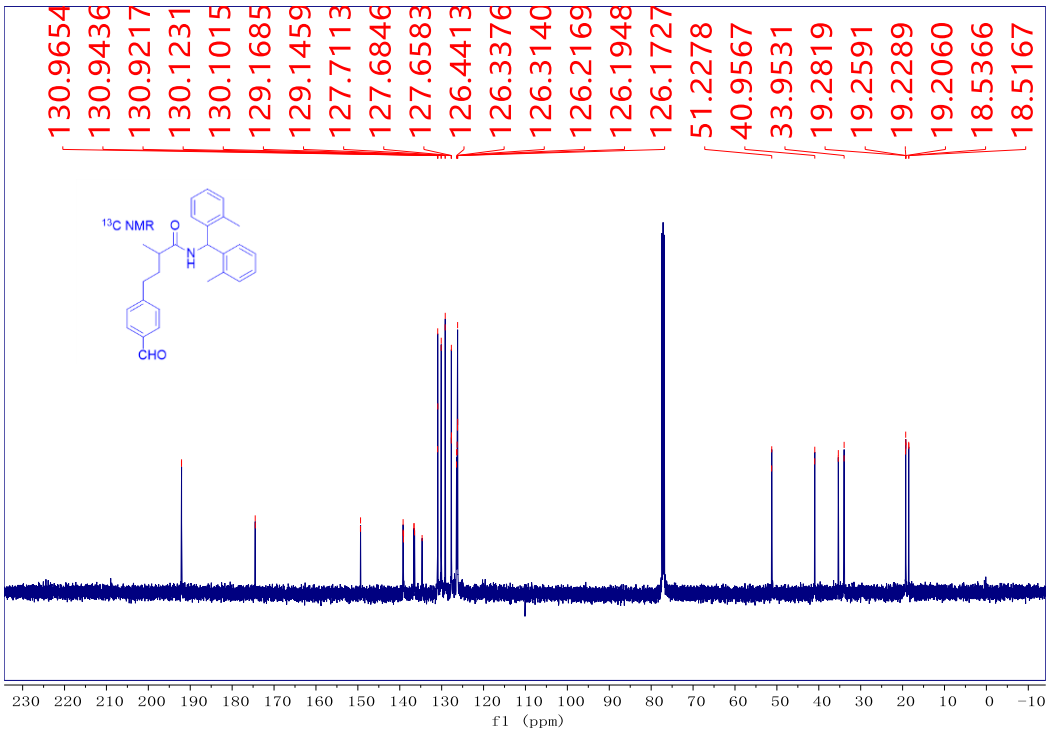
^{13}C NMR of 5l



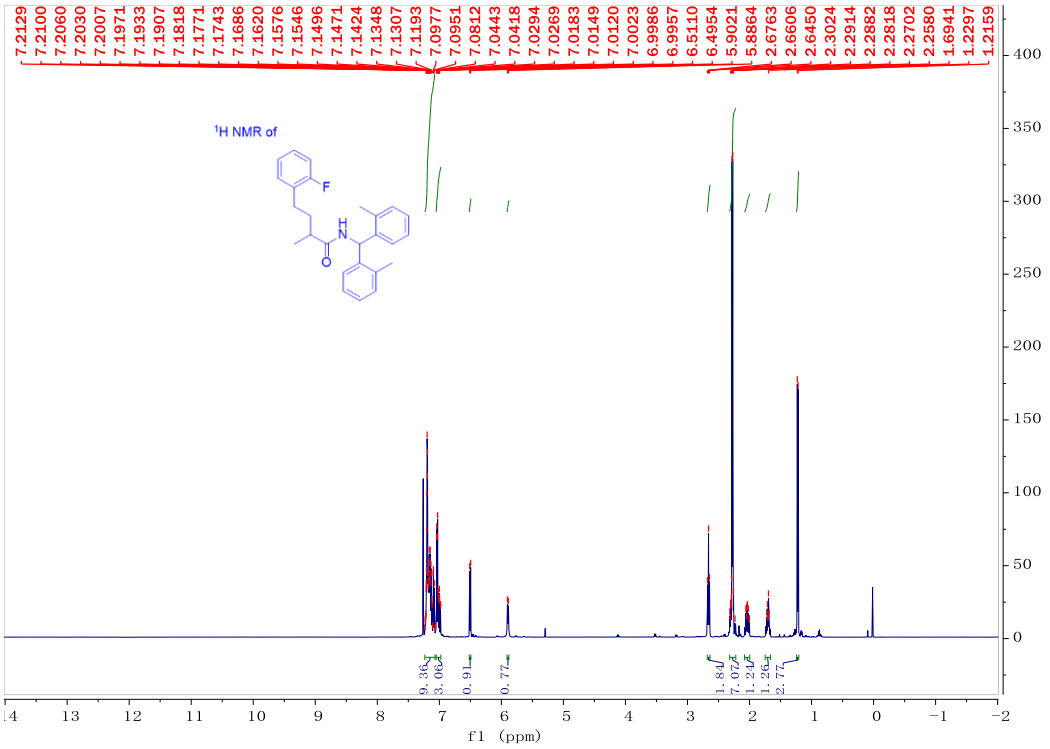
^{1}H NMR of 5m



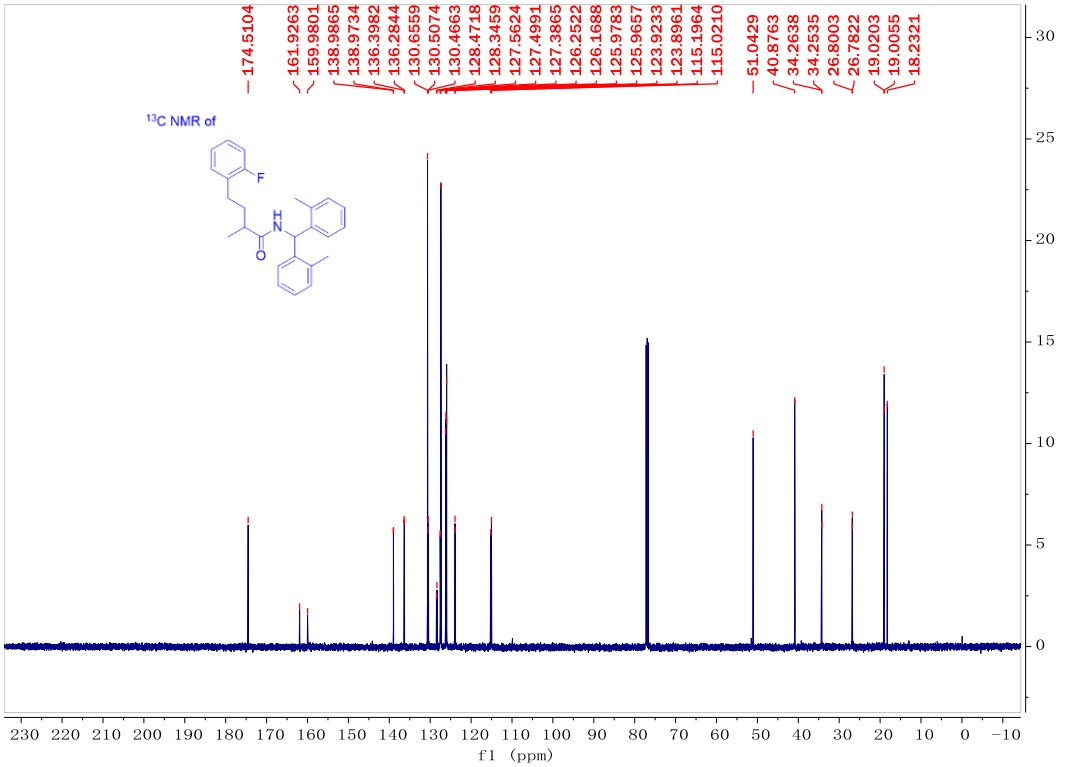
^{13}C NMR of 5m



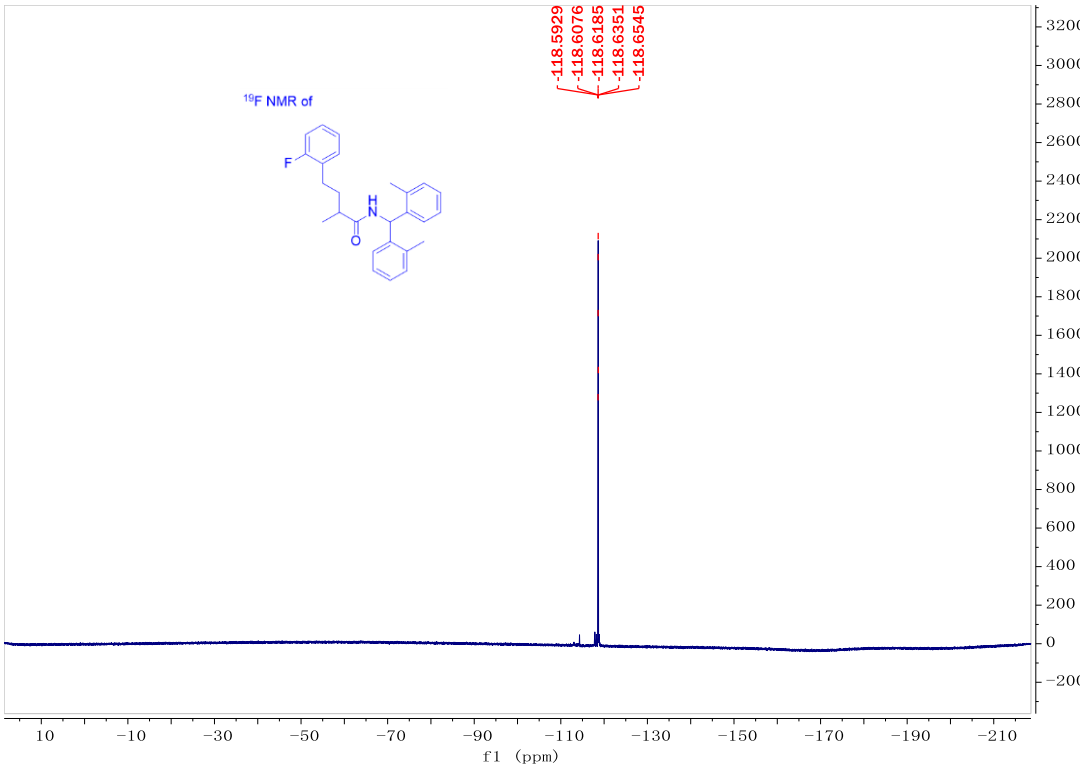
^{1}H NMR of 5n



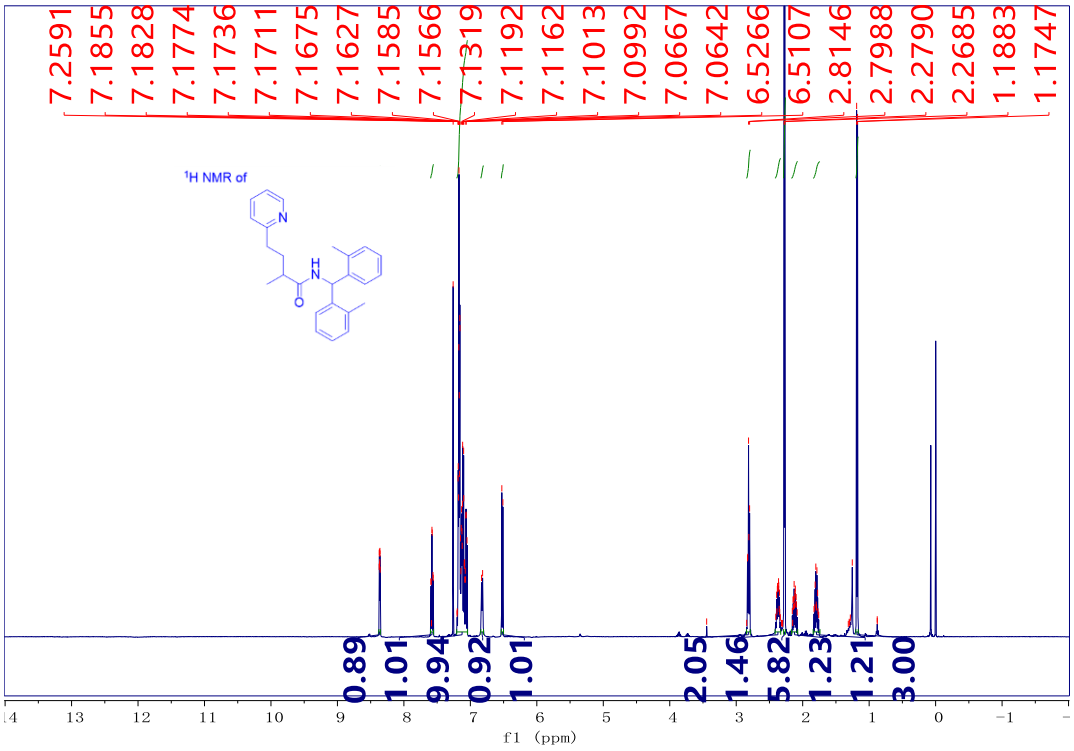
^{13}C NMR of 5n



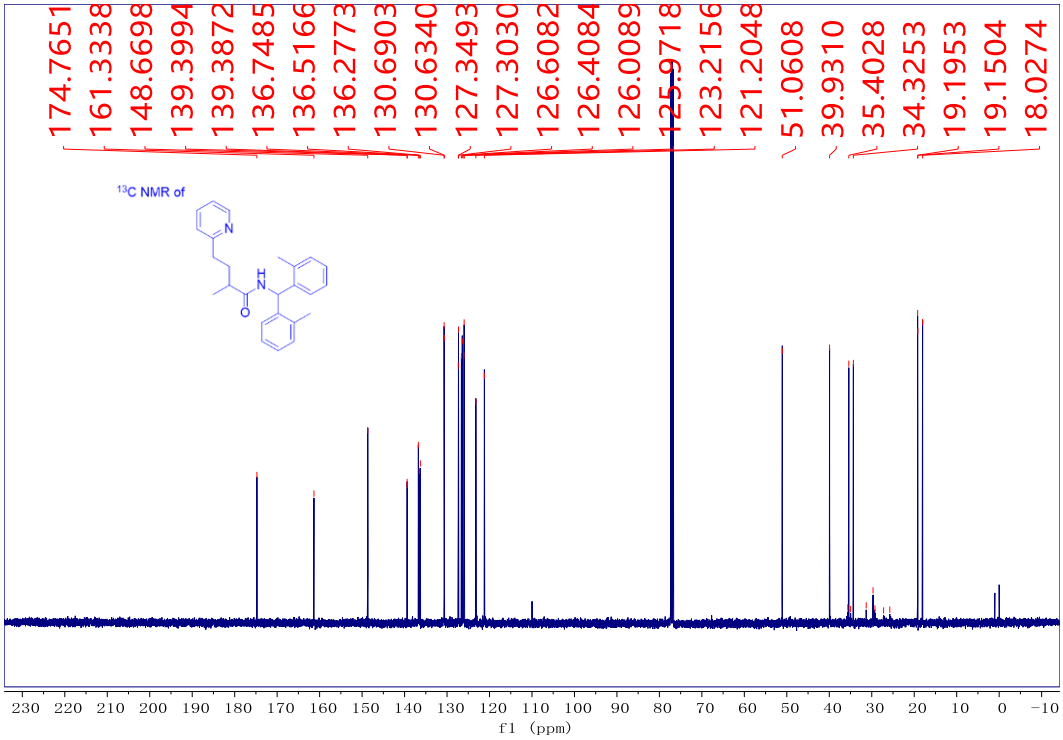
^{19}F NMR of 5n


-118.5929
-118.6076
-118.6185
-118.6351
-118.6545
19F NMR of
F
H
N
O
f1 (ppm)

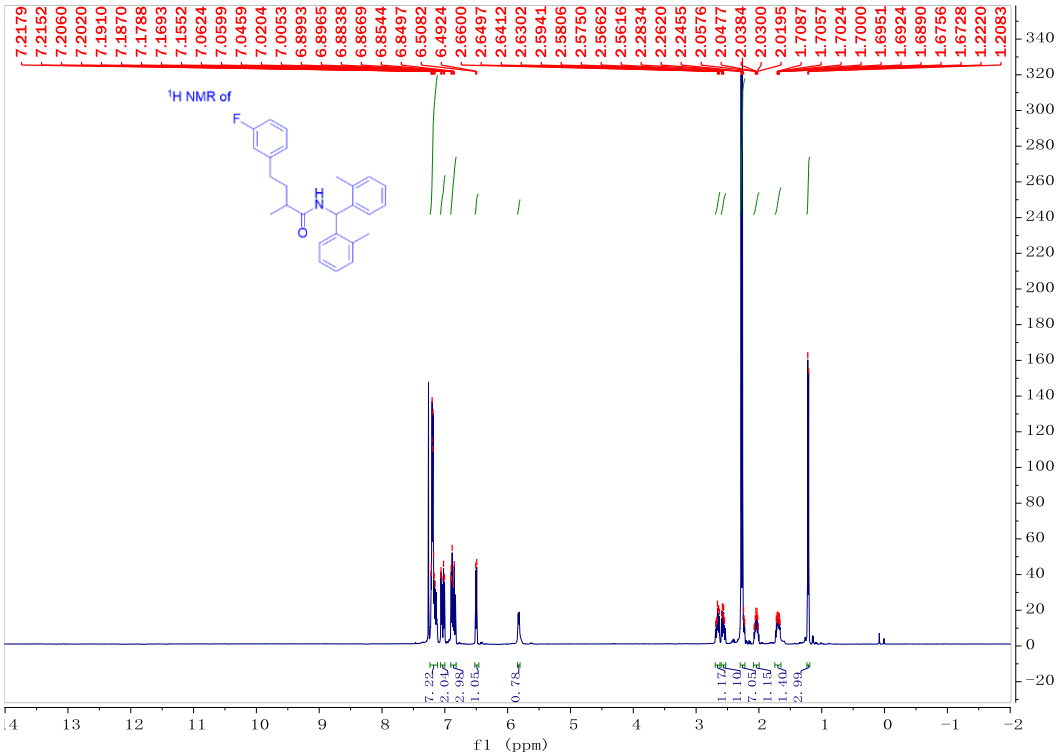
^{1}H NMR of 5o


7.2591
7.1855
7.1828
7.1774
7.1736
7.1711
7.1675
7.1627
7.1585
7.1566
7.1319
7.1192
7.1162
7.1013
7.0992
7.0667
7.0642
6.5266
6.5107
2.8146
2.7988
2.2790
2.2685
1.1883
1.1747
1H NMR of
N
H
N
O
0.89
1.01
9.94
0.92
1.01
2.05
1.46
5.82
1.23
1.21
3.00
f1 (ppm)

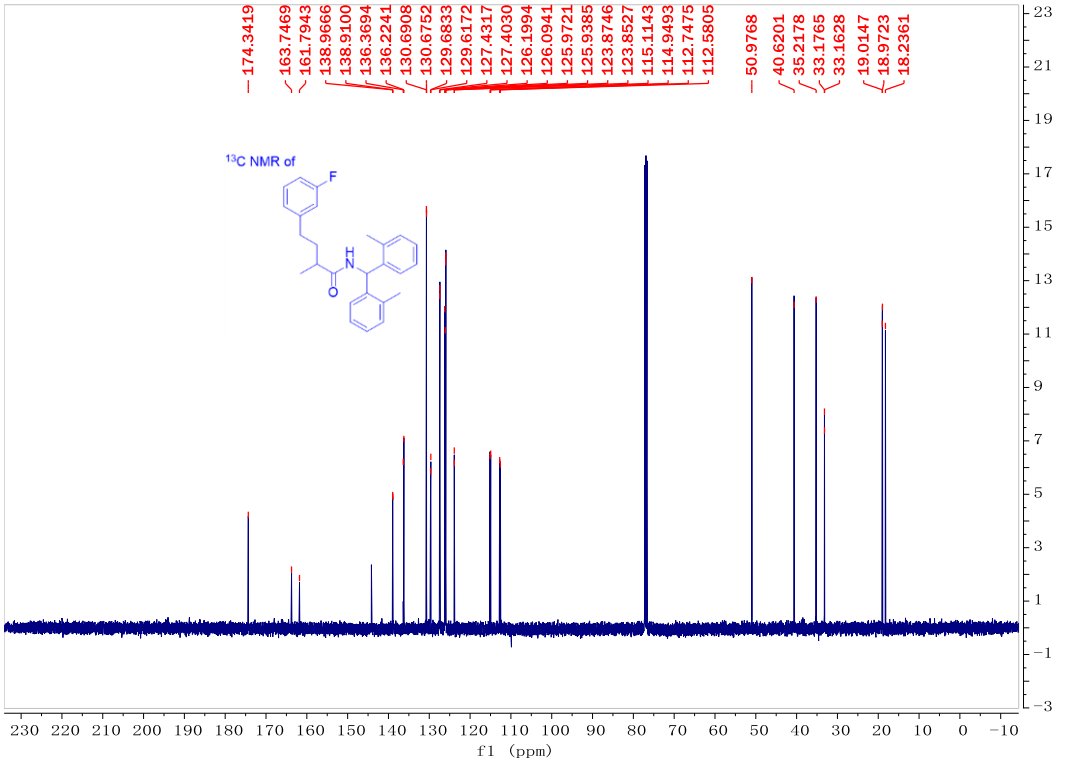
^{13}C NMR of 5o



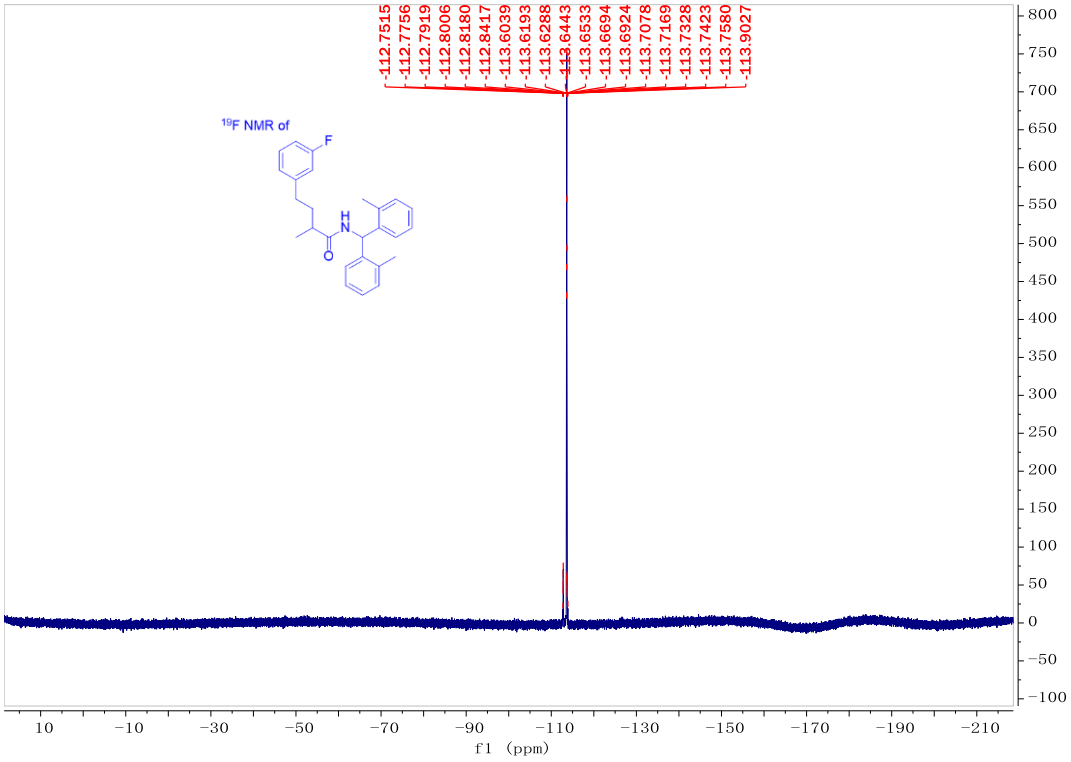
^{1}H NMR of 5p



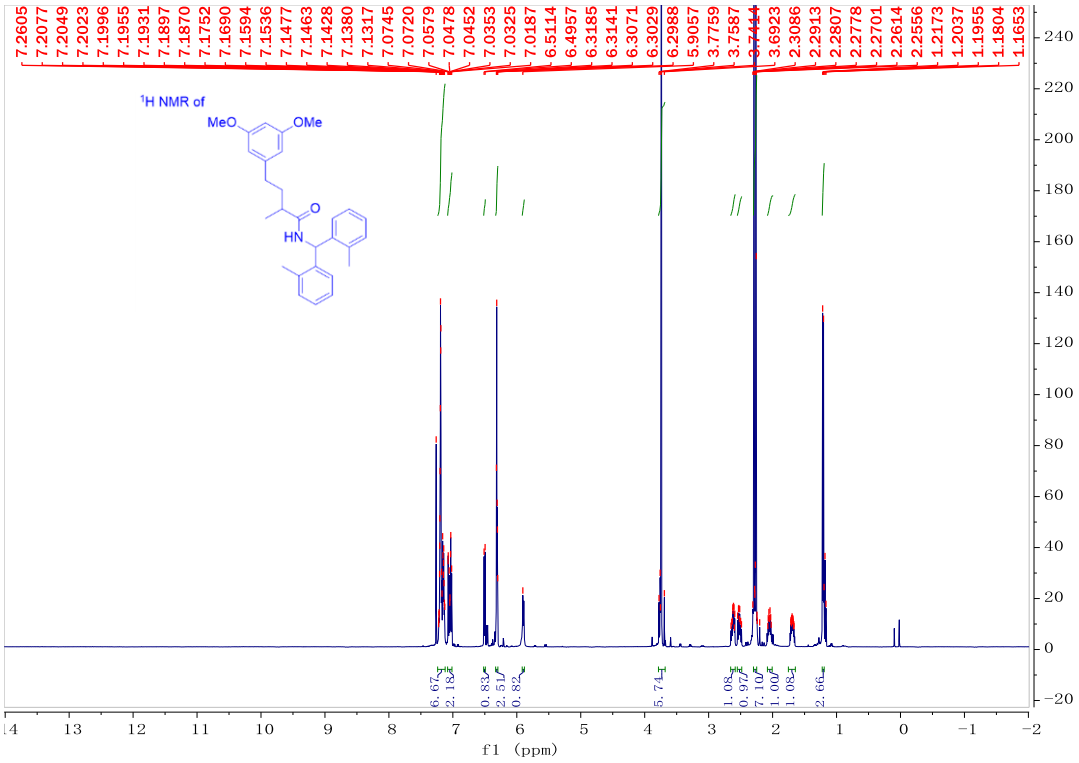
^{13}C NMR of 5p



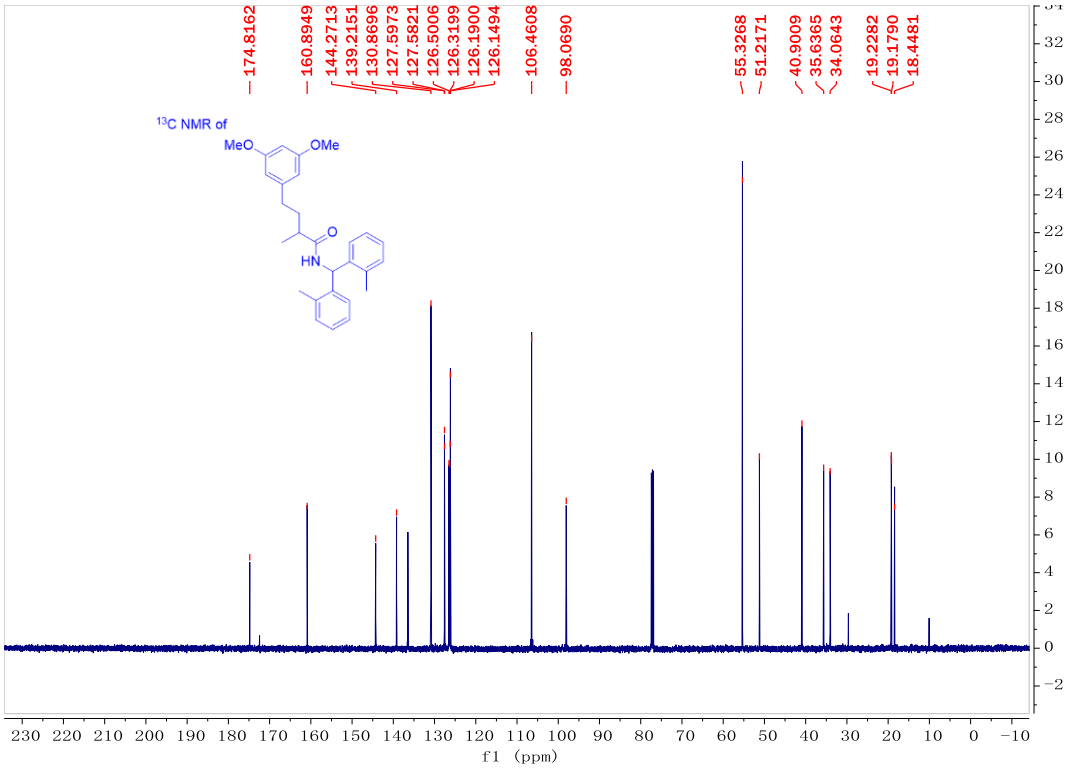
^{19}F NMR of 5p



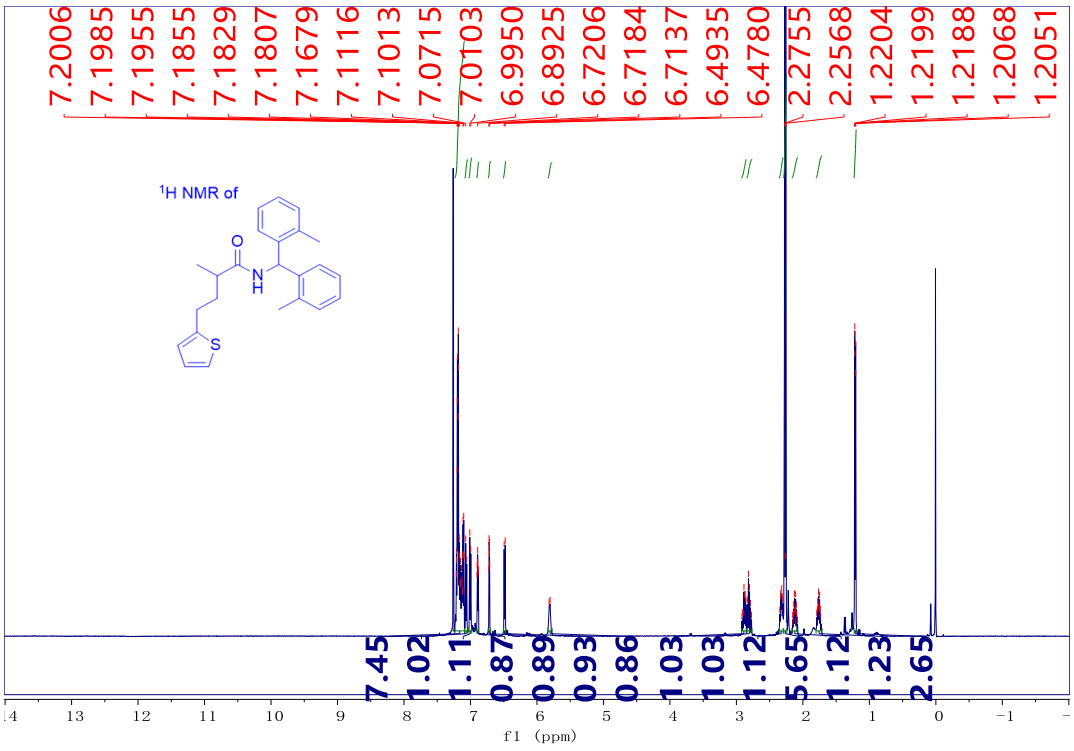
^{1}H NMR of 5q



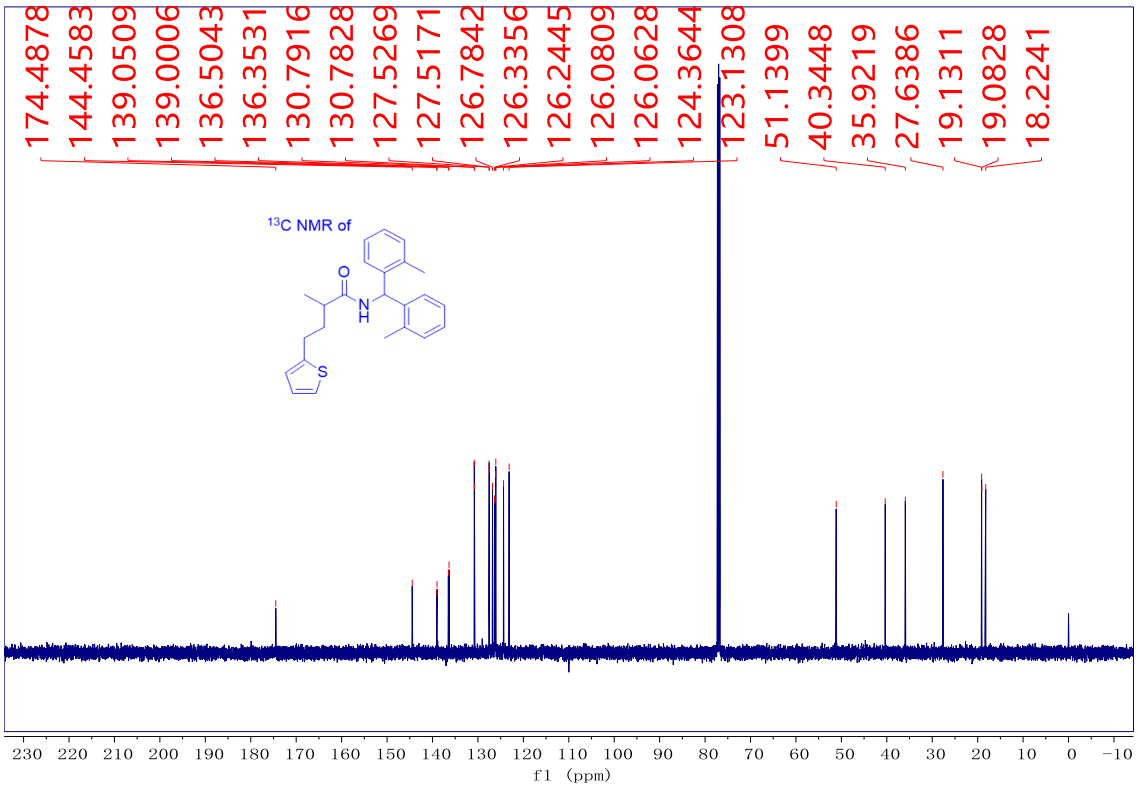
^{13}C NMR of 5q



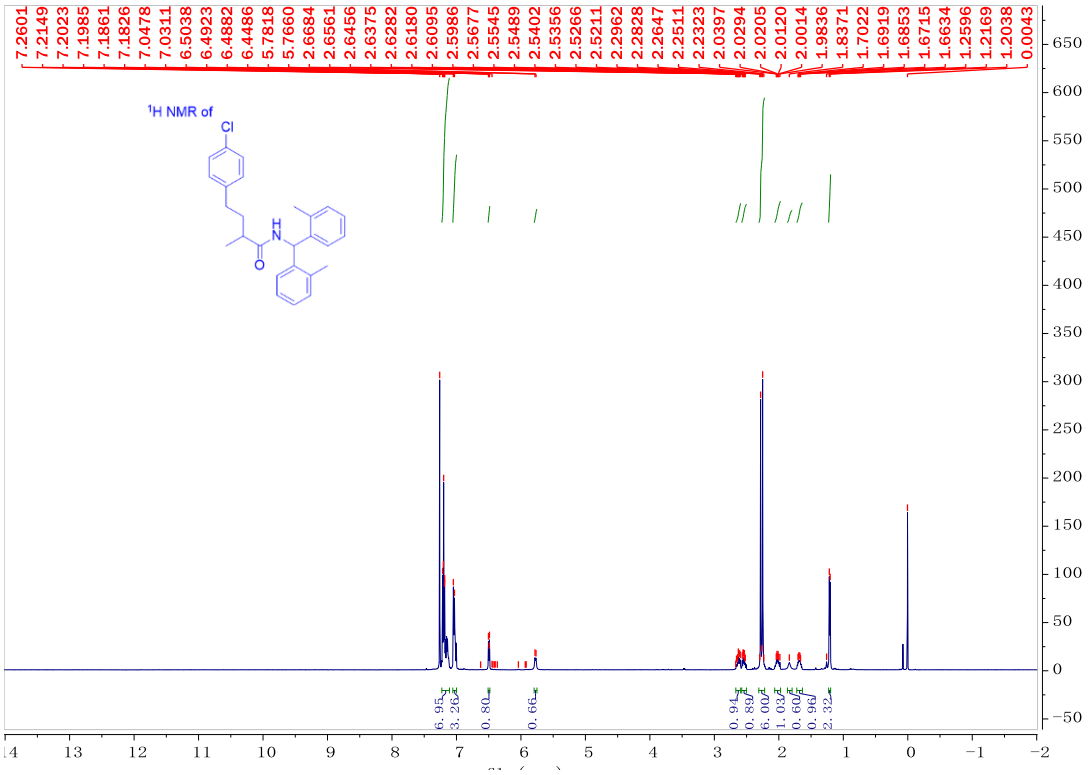
^{1}H NMR of 5r



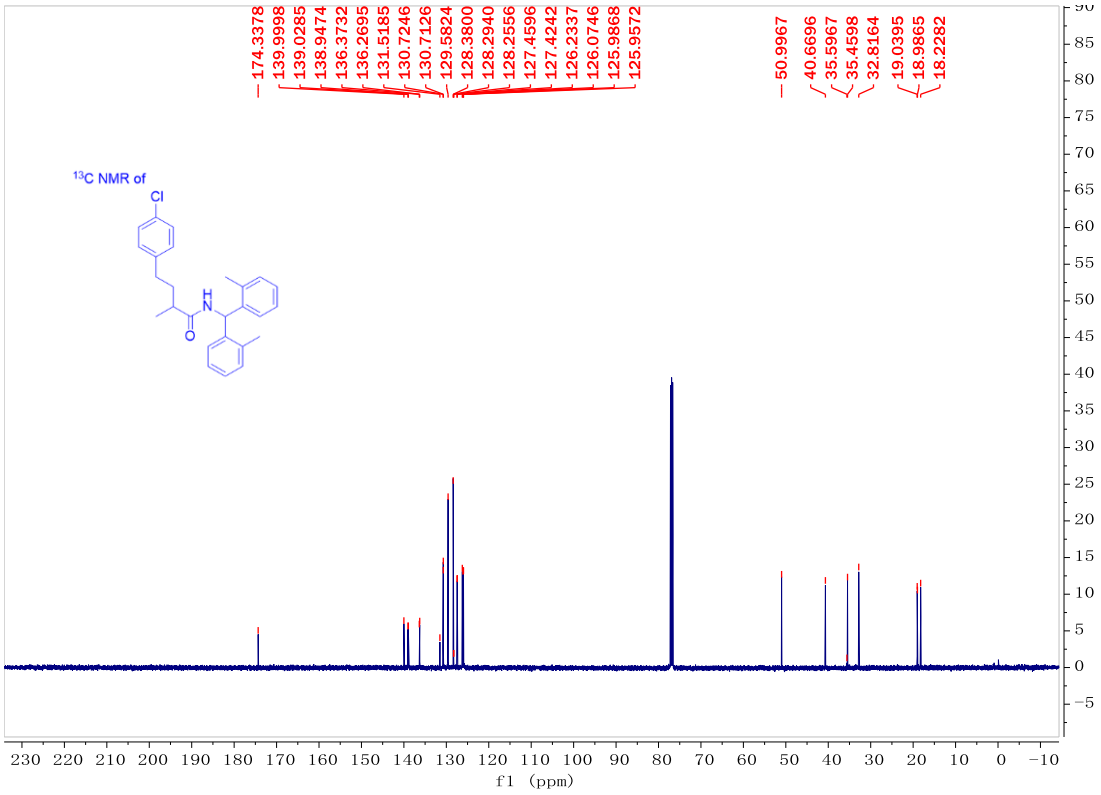
^{13}C NMR of 5r


174.4878
144.4583
139.0509
139.0006
136.5043
136.3531
130.7916
130.7828
127.5269
127.5171
126.7842
126.3356
126.2445
126.0809
126.0628
124.3644
123.1308
51.1399
40.3448
35.9219
27.6386
19.1311
19.0828
18.2241
13C NMR of
f1 (ppm)

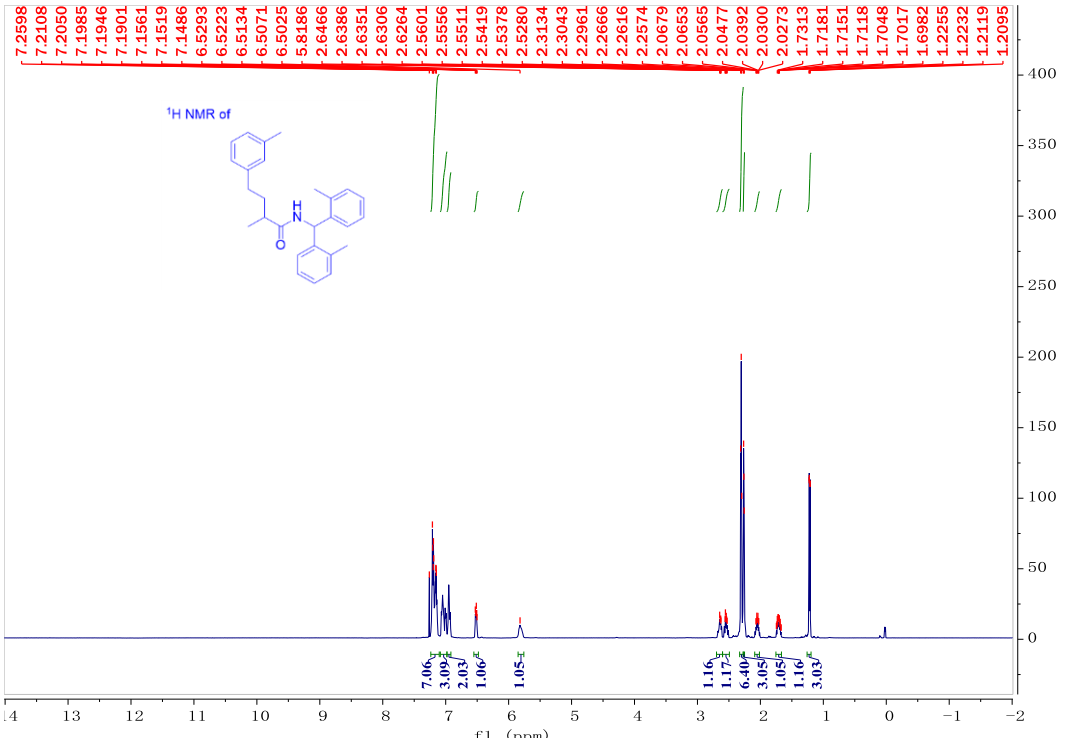
^{1}H NMR of 5s


1H NMR of
f1 (ppm)

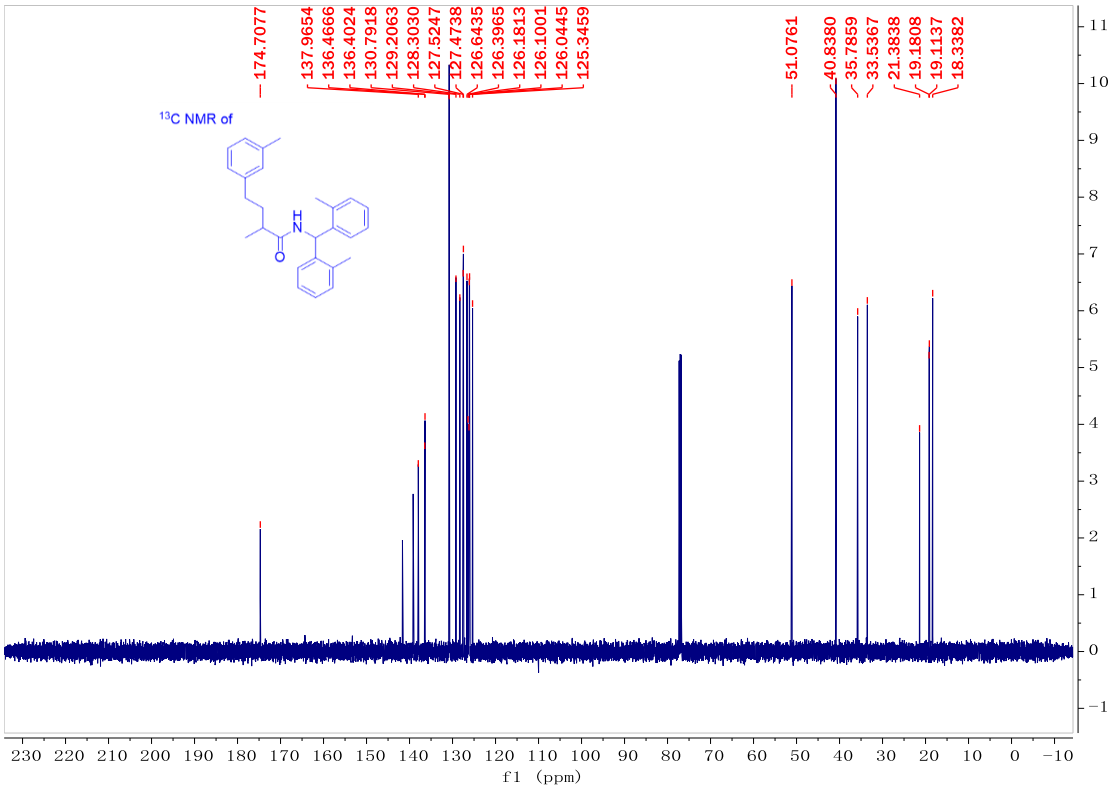
^{13}C NMR of 5s



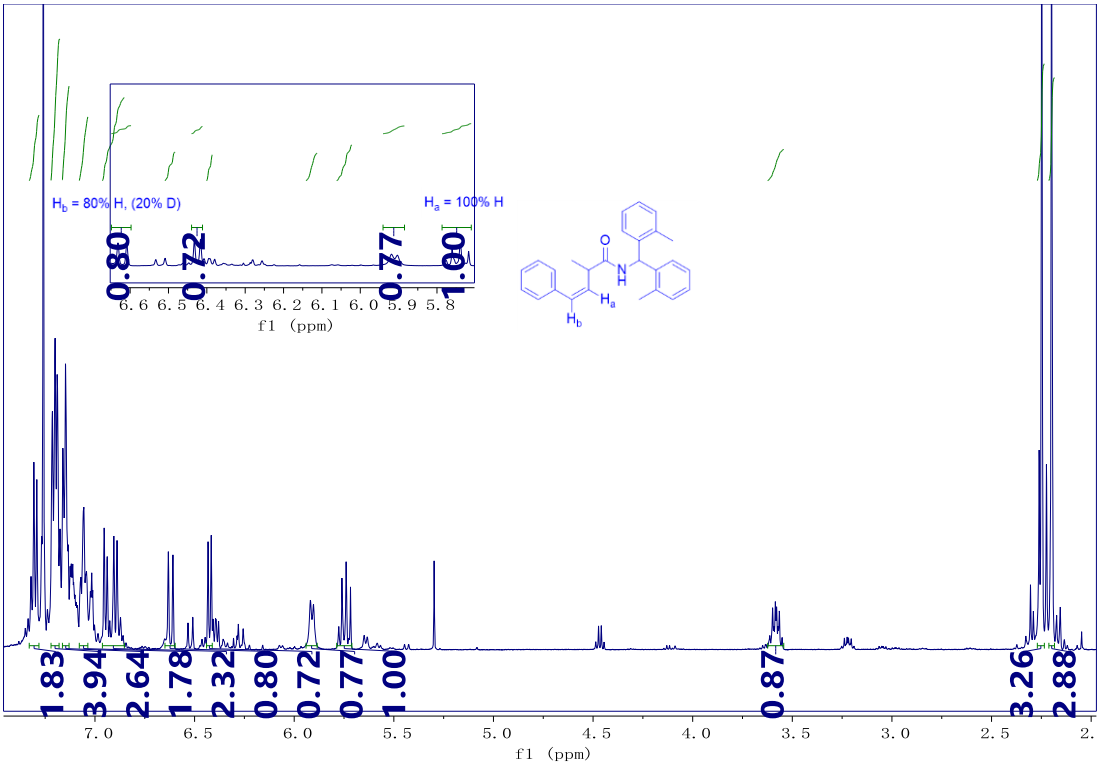
^{1}H NMR of 5t

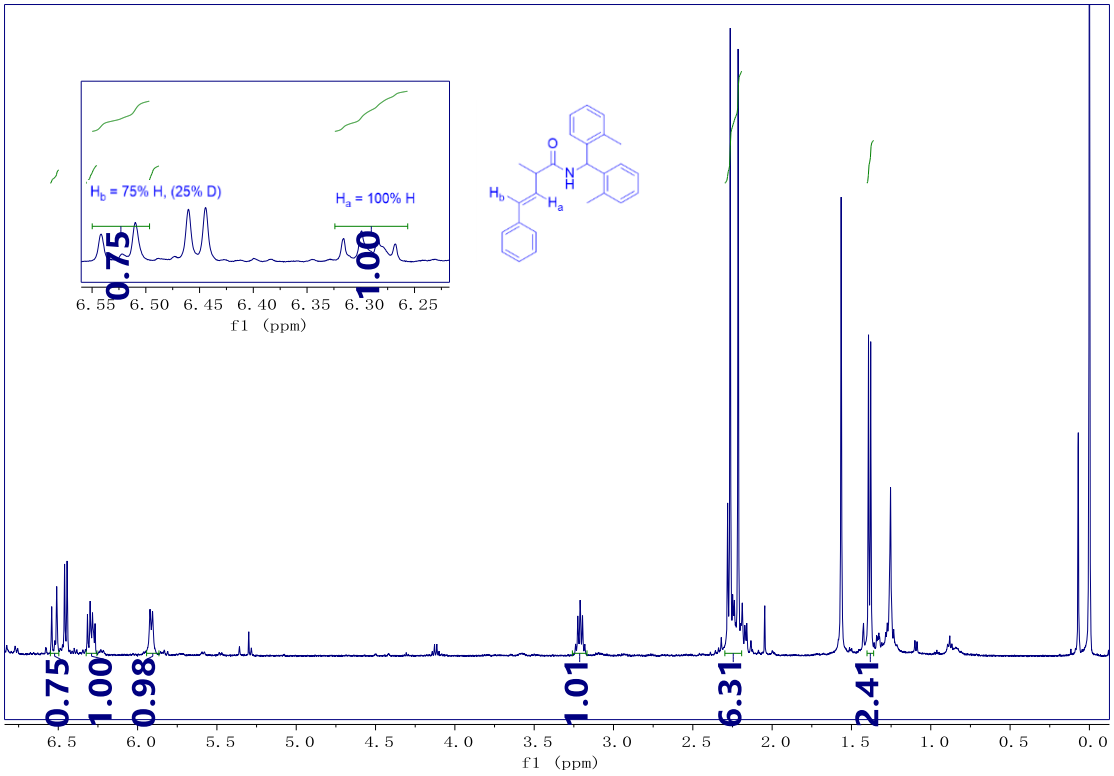

7.2598
7.2108
7.2050
7.1985
7.1946
7.1901
7.1561
7.1519
7.1486
6.5293
6.5223
6.5134
6.5071
6.5025
5.8186
2.6466
2.6386
2.6351
2.6306
2.6264
2.5601
2.5556
2.5511
2.5419
2.5378
2.5280
2.3134
2.3043
2.2961
2.2666
2.2616
2.2574
2.0679
2.0653
2.0565
2.0477
2.0392
2.0300
2.0273
1.7313
1.7181
1.7151
1.7118
1.7048
1.7017
1.6982
1.2255
1.2232
1.2119
1.2095
1H NMR of
7.06
3.09
2.03
1.06
1.05
1.16
1.17
6.40
3.05
1.05
1.16
3.03
f1 (ppm)

^{13}C NMR of 5t

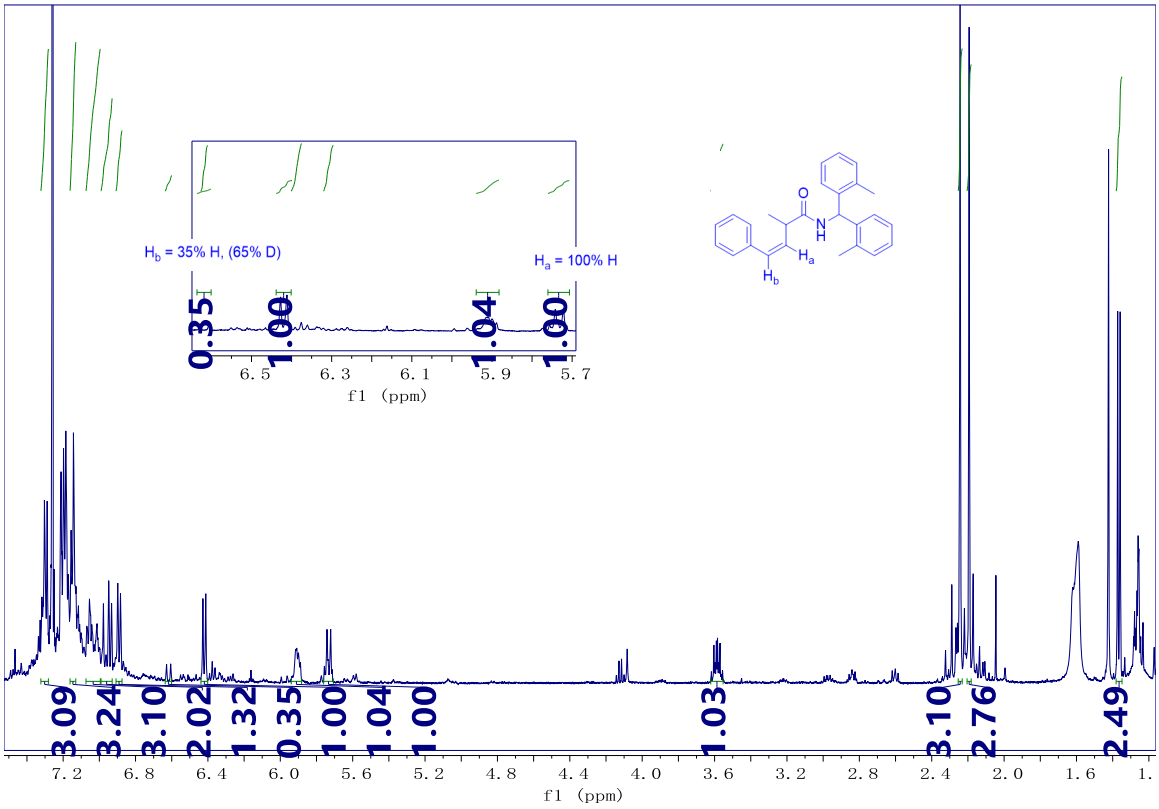

174.7077
137.9654
136.4666
136.4024
130.7918
129.2063
128.3030
127.5247
127.4738
126.6435
126.3965
126.1813
126.1001
126.0445
125.3459
51.0761
40.8380
35.7859
33.5367
21.3838
19.1808
19.1137
18.3382
13C NMR of
f1 (ppm)

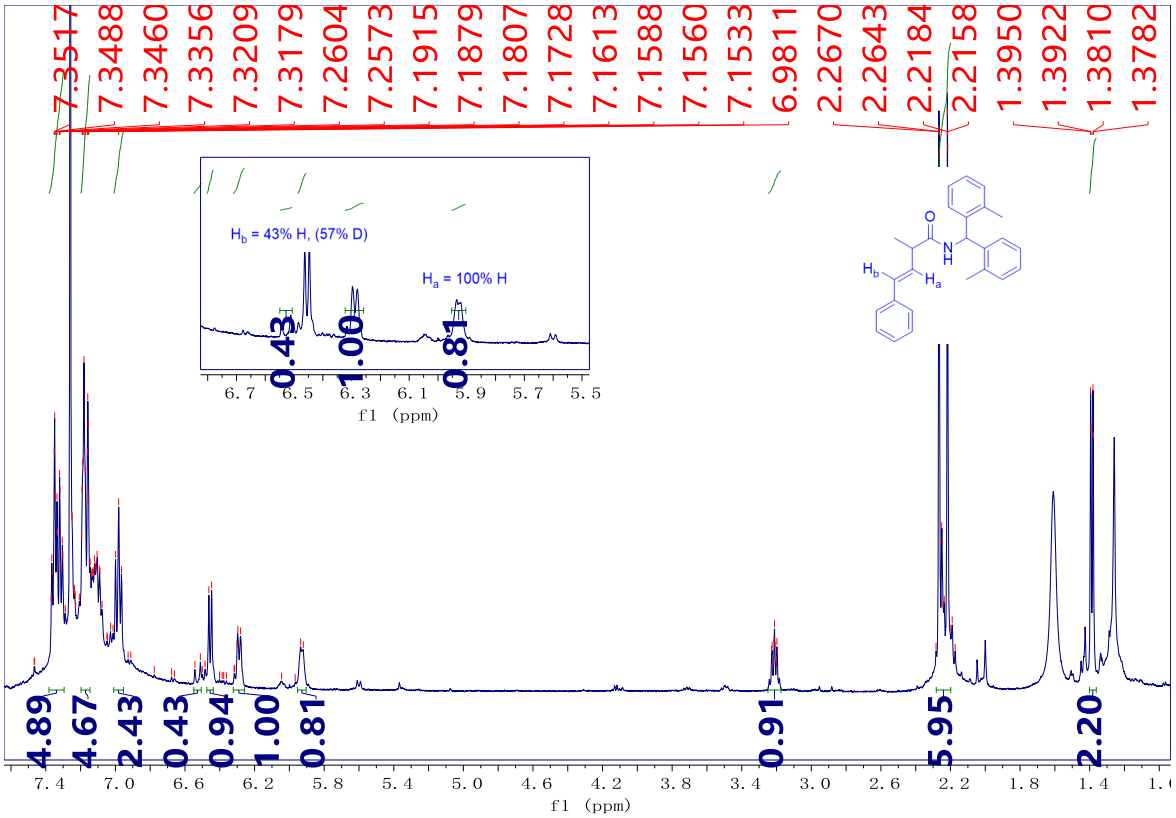
Reaction with Et_3N in THF-*d8*





Reaction with Cs_2CO_3 in THF-*d8*




7.3517
7.3488
7.3460
7.3356
7.3209
7.3179
7.2604
7.2573
7.1915
7.1879
7.1807
7.1728
7.1613
7.1588
7.1560
7.1533
6.9811
2.2670
2.2643
2.2184
2.2158
1.3950
1.3922
1.3810
1.3782
H_b = 43% H, (57% D)
H_a = 100% H
0.43
1.00
0.81
f1 (ppm)
4.89
4.67
2.43
0.43
0.94
1.00
0.81
0.91
5.95
2.20
f1 (ppm)