Indirect *Ortho* Functionalization of Substituted Toluenes through *Ortho* Olefination of N,N-Dimethylbenzylamines Tuned by Acidity of Reaction Conditions

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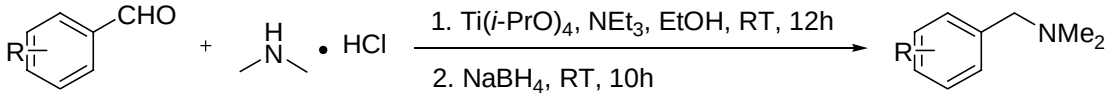
Preparation of N,N-dimethylbenzylamines by Reductive Amination.



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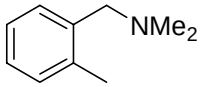
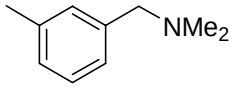


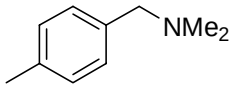
1g

N,N-dimethyl(o-tolyl)methanamine (1g): 1g was obtained as a light yellow oil (1.4 g, 65% yield). ^{1}H NMR ($CDCl_3$, 300MHz) δ7.26 (m, 1H), 7.22 (m, 3H), 3.39 (s, 2H), 2.39(s, 3H), 2.26 (s, 6H) ppm; ^{13}C NMR ($CDCl_3$, 75MHz) 137.2, 137.0, 130.2, 129.8, 126.9, 125.5, 62.0, 45.5, 19.0 ppm; IR ν 2942, 2855, 2762, 1459, 1021, 741 cm^{-1} MS: (m/z) (%): 149 (6) [M$^+$], 42 (100).



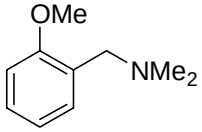
1h

N, N, 3-trimethylbenzylamine(1h): **1h** was obtained as red oil (2.2 g, 63% yield). ^{1}H NMR ($CDCl_3$, 300MHz) δ 7.08 (m, 4H), 3.33 (s, 2H),2.28 (s, 3H), 2.18 (s, 6H) ppm; ^{13}C NMR ($CDCl_3$, 75MHz) 138.7, 137.7, 129.7, 128.0, 127.7, 126.0, 64.3, 45.3, 21.2 ppm; IR ν 2941, 2814, 2769, 1456, 1032, 844, 779, 696 cm^{-1} MS: (m/z) (%): 149 (2) [M$^+$], 58 (100).



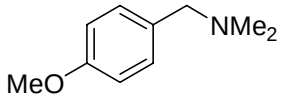
1i

N, N, 4-trimethylbenzylamine(1i): **1i** was obtained as a light yellow oil (1.2 g, 52% yield). ^{1}H NMR ($CDCl_3$, 300MHz) δ 7.19 (d, 2H, J=7.2), 7.12 (d, 2H, J=7.5), 3.37 (s, 2H), 2.32(s, 3H), 2.22 (s, 6H) ppm; ^{13}C NMR ($CDCl_3$, 75MHz) 136.5, 135.6, 129.0, 128.9, 64.0, 45.2, 21.0 ppm; IR ν 2943, 2858, 2766, 1456, 1031, 855, 800 cm^{-1} MS: (m/z) (%): 149 (5) [M$^+$], 42 (100).



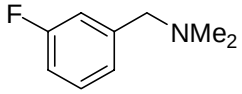
1j

N, N-dimethyl-2-methoxylbenzylamine(1j): **1j** was obtained as a light yellow oil (1.3 g, 53% yield). ^{1}H NMR ($CDCl_3$, 300MHz) δ 7.22 (m, 2H), 6.87 (m, 2H), 3.80 (s, 3H), 3.43(s, 2H), 2.24(s, 6H) ppm; ^{13}C NMR ($CDCl_3$, 75 MHz) 157.8, 130.7, 128.1, 126.7, 120.0, 110.3, 57.8, 55.3, 45.4 ppm; IR ν 2960, 2858, 1713, 1255, 1177,1020, 788 cm^{-1} MS: (m/z) (%): 165 (9) [M$^+$], 58 (100).



1k

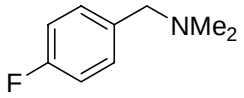
N, N-dimethyl-4-methoxylbenzylamine(1k): **1k** was obtained as a light yellow oil (0.9 g, 35% yield). ^{1}H NMR ($CDCl_3$, 300MHz) δ 7.18 (d, 2H, J=9), 6.82 (d, 2H, J=9), 3.76(s, 3H), 3.32 (s, 2H), 2.18(s, 6H) ppm; ^{13}C NMR ($CDCl_3$, 75MHz) 158.6, 130.8, 130.2, 113.5, 63.6, 55.1, 45.1 ppm; IR ν 2942, 2813, 2768, 1511, 1243, 1028, 811 cm^{-1} MS: (m/z) (%): 165 (2) [M$^+$], 58 (100).



1l

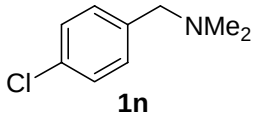
N, N-dimethyl-3-fluorobenzylamine(1l): **1l** was obtained as a light yellow oil (1.4 g, 61% yield).^{1}H NMR ($CDCl_3$, 300MHz) δ 7.24 (m, 1H), 7.03 (m, 2H), 6.88(m, 1H), 3.38 (s, 2H), 2.21(s, 6H) ppm; ^{13}C NMR ($CDCl_3$, 75MHz) 164.5, 161.2, 141.6, 141.5, 129.6, 129.5, 124.5, 124.4, 115.8, 115.5, 114.0, 113.7, 63.8, 63.7, 45.3

ppm; IR ν 2945, 2819, 2775, 1590, 1487, 1455, 1256, 783, 687 cm^{-1} MS: (m/z) (%): 153 (6) [M^+], 58 (100).



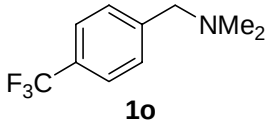
1m

N, N-dimethyl-4-fluorobenzylamine(1m): **1m** was obtained as a light yellow oil (1.5 g, 60% yield).^{1}H NMR ($CDCl_3$, 300MHz) δ 7.22 (m, 2H), 6.95 (m, 2H), 3.33 (s, 2H), 2.19(s, 6H) ppm; ^{13}C NMR ($CDCl_3$, 75MHz) 163.5, 160.3, 134.6, 134.5, 130.5, 130.4, 130.0, 115.0, 114.8, 112.4, 63.5, 45.1 ppm; IR ν 2925, 2854, 1614, 1525, 1361, 1168, 803.6 cm^{-1} MS: (m/z) (%): 153 (51) [M^+], 58 (100).



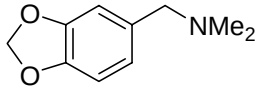
1n

N, N-dimethyl-3-fluorobenzylamine(1n): **1n** was obtained as a light yellow oil (1.8 g, 71% yield). ^{1}H NMR ($CDCl_3$, 300MHz) δ 7.26 (m, 4H), 3.37 (s, 2H), 2.21(s, 6H) ppm; ^{13}C NMR ($CDCl_3$, 75MHz) 137.4, 132.7, 130.3, 128.3, 63.5, 45.2 ppm; IR ν 2944, 2817, 2769, 1490, 1086, 1015, 857, 801 cm^{-1} MS: (m/z) (%): 169 (1) [M^+], 58 (100).



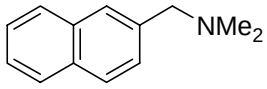
1o

N, N-dimethyl-3-fluorobenzylamine(1o): **1o** was obtained as a light yellow oil (1.8 g, 58% yield). ^{1}H NMR ($CDCl_3$, 300MHz) δ 7.55 (d, 2H, J=8.1), 7.40 (d, 2H, J=7.8), 3.44 (s, 2H), 2.21(s, 6H) ppm; ^{13}C NMR ($CDCl_3$, 75MHz) 142.9, 129.4, 125.14, 125.09, 125.04, 124.99, 63.7, 45.3 ppm; IR ν 1329, 1171, 1129, 1069, 1020, 870, 817 cm^{-1} MS: (m/z) (%): 203 (3) [M^+], 58 (100).



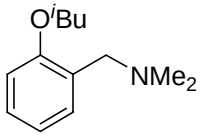
1p

N, N-dimethyl-piperonylamine(1p): **1p** was obtained as light yellow oil (2.0 g, 73% yield). ^{1}H NMR ($CDCl_3$, 300MHz) δ 6.79 (s, 1H), 6.70 (m, 2H), 5.89 (s, 2H), 3.27 (s, 2H), 2.17 (s, 6H) ppm; ^{13}C NMR ($CDCl_3$, 75MHz) 147.5, 146.5, 132.7, 122.0, 109.4, 107.7, 100.8, 64.0, 45.1 ppm; IR ν 2943, 2815, 2768, 1499, 1442, 1240, 1040, 930, 805 cm^{-1} MS: (m/z) (%): 179 (2) [M^+], 58 (100).



1q

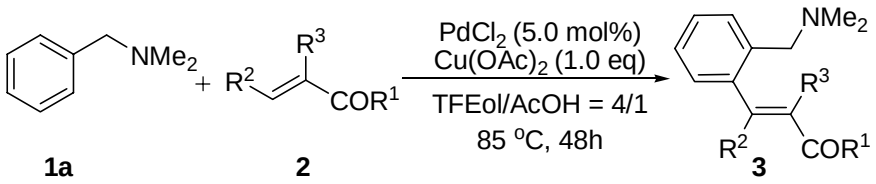
N, N-dimethyl-2-naphthalenemethanamine (1q): **1q** was obtained as a colorless oil (0.8 g, 30% yield). ^{1}H NMR ($CDCl_3$, 300MHz) δ 7.20 (m, 10H), 3.43 (s, 2H), 2.09(s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 75MHz) 138.3, 128.9, 128.2, 126.9, 61.8, 42.2 ppm; IR ν 3055,2941, 2854, 2768, 1455, 1366, 1261, 1031, 894, 814, 752 cm^{-1} MS: (m/z) (%): 185 (60) [M^+], 141 (100).



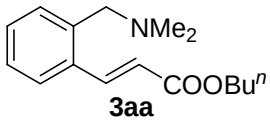
1r

(2-isobutoxyphenyl)-N,N-dimethylmethanamine (1r): **1r** was obtained as a colorless oil (3.5 g, 68% yield). ^{1}H NMR ($CDCl_3$, 300MHz) δ 7.29 (m, 1H), 7.20 (m, 1H), 6.90 (m, 1H), 6.82 (m, 1H), 3.71 (d, 2H, J=6.3), 3.48 (s, 2H), 2.27 (s, 6H), 2.09 (m, 1H), 1.04 (d, 6H, J=6.9) ppm; ^{13}C NMR ($CDCl_3$, 75MHz) 157.2, 130.5, 127.8, 127.0, 119.9, 111.1, 74.2, 57.3, 45.4, 28.3, 19.3 ppm; IR ν 2960, 2911, 2815, 2766, 1495, 1287, 1031, 753 cm^{-1} MS: (m/z) (%): 233 (5) [M^+], 58 (100), HRMS: Anal. Calcd. for $C_{13}H_{21}NO$ 207.16231, Found: 207.16237.

***Ortho*-Functionalization of N,N-Dimethylbenzylamine with Different Alkenes.**

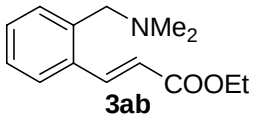


1a **2** **3**



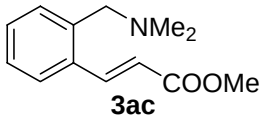
3aa

(E)-butyl 3-(2-((dimethylamino)methyl)phenyl)acrylate (3aa): Startinging from **1a** (75 μL, 0.5 mmol) with **2a** (145 μL, 1.0 mmol) to afford **3aa** (112 mg), yield 86%. ^{1}H NMR ($CDCl_3$, 300MHz) δ 8.21 (d, 1H, J=15.9), 7.61 (d, 1H, J=6.3), 7.33-7.27 (m, 3H), 6.39 (d, 1H, J=15.9), 4.23 (t, 2H, J=6.6), 3.51 (s, 2H), 2.26 (s, 6H),1.71 (m, 2H), 1.46 (m, 2H), 0.98 (t, 3H, J=7.2) ppm; ^{13}C NMR ($CDCl_3$, 75MHz) 167.3, 142.3, 138.3, 134.4, 130.9, 129.7, 127.7, 126.6, 119.3, 64.3, 61.7, 45.2, 30.7, 19.1, 13.7 ppm; IR ν 2959, 1713, 1308, 1170, 766 cm^{-1} ; MS: (m/z) (%): 261 (8) [M$^+$], 115 (100), HRMS: Anal. Calcd. for $C_{16}H_{23}NO_2$ 261.17310, Found: 261.17288.



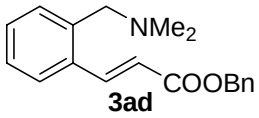
3ab

(E)-ethyl 3-(2-((dimethylamino)methyl)phenyl)acrylate (3ab): Startinging from **1a** (75 μL, 0.5 mmol) with **2b** (108 μL, 1.0 mmol) to afford **3ab** (99 mg), yield 85%. ^{1}H NMR ($CDCl_3$, 300MHz) δ 8.09 (d, 1H, J=15.6), 7.50 (d, 1H, J=6.3), 7.22-7.18 (m, 3H), 6.27 (d, 1H, J=15.0), 4.16 (q, 2H, J=6.6), 3.40 (s, 2H), 2.15 (s, 6H) ,1.24 (t, 3H,) ppm; ^{13}C NMR ($CDCl_3$, 75MHz) 167.0, 142.5, 138.1, 134.2, 130.7, 129.5, 127.6, 126.4, 119.1, 61.6, 60.3, 45.1, 14.22 ppm; IR ν 2978, 2768, 1712, 1174, 766 cm^{-1}; MS: (m/z) (%): 233 (10) [M$^+$], 43 (100), HRMS: Anal. Calcd. for $C_{14}H_{19}NO_2$ 233.14158, Found: 233.14123.



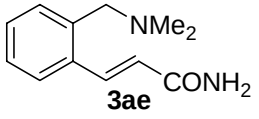
3ac

(E)-3-(2-((dimethylamino)methyl)phenyl)acrylamide (3ac): Starting from **1a** (75 μL, 0.5 mmol) with **2c** (71 mg, 1.0 mmol) to afford **3ac** (84 mg), yield 66%. ^{1}H NMR ($CDCl_3$, 300MHz) δ 8.03 (d, 1H, J=15.6), 7.53 (d, 1H, J=7.2), 7.29-7.24 (m, 3H), 6.39 (d, 1H, J=17.4), 5.9 (br, 2H), 3.50 (s, 2H), 2.22 (s, 6H) ppm; ^{13}C NMR ($CDCl_3$, 75MHz) 168.1, 139.6, 137.8, 134.4, 130.8, 129.3, 127.6, 126.4, 121.2, 61.5, 45.1 ppm; IR ν 3441, 3173, 2819, 1669, 1601, 1396, 741 cm^{-1}; MS: (m/z) (%): 204 (10) [M$^+$], 116 (100), HRMS: Anal. Calcd. for $C_{12}H_{16}N_2O$ 204.12626, Found: 204.12617.



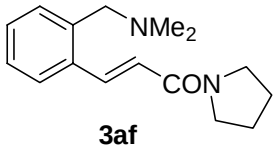
3ad

(E)-benzyl 3-(2-((dimethylamino)methyl)phenyl)acrylate (3ad): Starting from **1a** (75 μL, 0.5 mmol) with **2d** (162 mg, 1.0 mmol) to afford **3ad** (127 mg), yield 86%. ^{1}H NMR ($CDCl_3$, 300MHz) δ 8.26 (d, 1H, J=15.9), 7.59 (d, 1H, J=8.1), 7.44-7.24 (m, 9H), 6.42 (d, 1H, J=15.9), 5.25 (s, 2H), 3.48 (s, 2H), 2.19 (s, 6H) ppm; ^{13}C NMR ($CDCl_3$, 75MHz) 166.7, 142.9, 138.2, 136.0, 134.0, 130.7, 129.6, 128.4, 128.1, 127.6, 126.5, 118.6, 66.2, 61.7, 45.2 ppm; IR 2817, 1713, 1456, 1308, 1164, 766 cm^{-1}; MS: (m/z) (%): 295 (10) [M$^+$], 204 (100), HRMS: Anal. Calcd. for $C_{19}H_{22}NO_2$ 295.15723. Found: 295.15774.



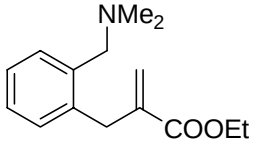
3ae

(E)-3-(2-((dimethylamino)methyl)phenyl)acrylamide (3ae): Start from **1a** (75 μL, 0.5 mmol) with **2e** (71 mg, 1.0 mmol) to afford **3ae** (84 mg), yield 82%. ^{1}H NMR ($CDCl_3$, 300MHz) δ 8.03 (d, 1H, J=15.6), 7.53 (d, 1H, J=7.2), 7.29-7.24 (m, 3H), 6.39 (d, 1H, J=17.4), 5.9 (br, 2H), 3.50 (s, 2H), 2.22 (s, 6H) ppm; ^{13}C NMR ($CDCl_3$, 75MHz) 168.1, 139.6, 137.8, 134.4, 130.8, 129.3, 127.6, 126.4, 121.2, 61.5, 45.1 ppm; IR 3441, 3173, 2819, 1669, 1601, 1396, 741 cm^{-1}; MS: (m/z) (%): 204 (110) [M$^+$], 116 (100), HRMS: Anal. Calcd. for $C_{12}H_{16}N_2O$ 204.12626, Found: 204.12617.



3af

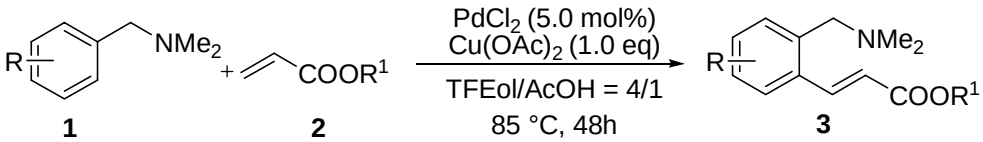
(E)-3-(2-((dimethylamino)methyl)phenyl)-1-(pyrrolidin-1-yl)prop-2-en-1-one (3af): Starting from **1a** (75 μL, 0.5 mmol) with **3f** (125 mg, 1.0 mmol) to afford **3af** (71 mg), yield 54%. ^{1}H NMR ($CDCl_3$, 300MHz) δ 8.13 (d, 1H, J=15.6), 7.57 (d, 1H, J=6.6), 7.33-7.26 (m, 3H), 6.68 (d, 1H, J=15.6), 3.61 (m, 4H), 3.52 (s, 2H), 2.25 (s, 6H), 2.03-1.88 (m, 4H) ppm; ^{13}C NMR ($CDCl_3$, 75MHz) 164.7, 139.3, 138.1, 135.0, 128.8, 127.2, 126.4, 120.2, 61.4, 45.4, 45.9, 45.3, 26.0, 24.2 ppm; IR ν 2972, 2872, 1652, 1609, 1426, 1167, 1014, 768 cm^{-1}; MS: (m/z) (%): 258 (30) [M$^+$], 70 (100), HRMS: Anal. Calcd. for $C_{16}H_{22}N_2O$ 258.17321, Found: 258.17318.



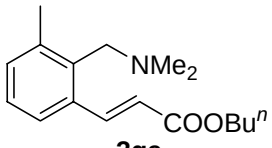
3ag

Ethyl 2-(2-((dimethylamino)methyl)benzyl)acrylate (3ag): Starting from **1a** (75 μL, 0.5 mmol) with **2g** (124 μL, 1.0 mmol) to afford 3**ag** (66 mg), yield 53%. ^{1}H NMR ($CDCl_3$, 300MHz) δ 7.27-7.10 (m, 4H), 6.17 (q, 1H, J=1.2), 5.16 (t, 1H), 4.19 (q, 2H, J=6.9), 3.73 (s, 2H), 3.32 (s 2H) 2.18 (s, 6H, 2.4), 1.26 (t, 3H) ppm; ^{13}C NMR ($CDCl_3$, 75MHz) 167.0, 140.1, 137.6, 137.3, 130.2, 130.1, 127.1, 126.3, 125.4, 61.6, 60.6, 45.4, 34.2, 14.1 ppm; IR ν 2941, 2765, 1717, 1134, 1024, 753 cm^{-1} ; MS: (m/z) (%): 247 (15) [M$^+$], 129 (100), HRMS: Anal. Calcd. for $C_{15}H_{21}NO_2$ 247.15709, Found: 247.15723.

***Ortho* Olefination of Different Substituted Benzyl Amines.**

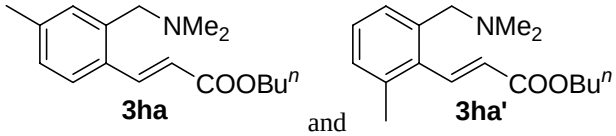


1 **2** **3**



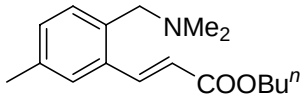
3ga

(E)-butyl 3-(2-((dimethylamino)methyl)-3-methylphenyl)acrylate (3ga): Start from **1g** (75 mg, 0.5 mmol) with **2a** (145 μL, 1.0 mmol) to afford **3ga** (103 mg), yield 75%. ^{1}H NMR ($CDCl_3$, 300MHz) δ 8.25 (d, 1H, J=15.9), 7.41 (m, 1H), 7.15 (m, 2H), 6.29 (d, 1H, J=15.9), 4.18 (t, 2H, J=6.6), 3.47 (s, 2H), 2.37 (s, 3H),2.21 (s, 6H), 1.66 (m, 2H), 1.41 (m, 2H), 0.93 (t, 3H, J=7.8) ppm; ^{13}C NMR ($CDCl_3$, 75MHz) 167.2, 143.6, 138.3, 136.5, 135.1, 131.9, 127.2, 124.4, 119.0, 64.2, 56.3, 45.0, 30.7, 20.0, 19.2, 13.7 ppm; IR 2960, 1714, 1311, 1164, 788 cm^{-1} ; MS: (m/z) (%): 275 (33) [M$^+$], 129 (100), HRMS: Anal. Calcd. for $C_{17}H_{25}NO_2$ 275.18853, Found: 275.18934.



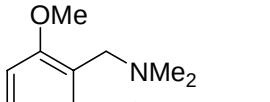
3ha and **3ha'**

(E)-butyl 3-(2-((dimethylamino)methyl)-3-methylphenyl)acrylate (3ha) and **(E)-butyl 3-(2-((dimethylamino)methyl)-6-methylphenyl)acrylate (3ha'):** Start from **1h** (75 mg, 0.5 mmol) with **2a** (145 μL, 1.0 mmol) to afford a mixture of **3ha** and **3ha'** (104 mg, **3ha**:**3ha'**=9:1), yield 75%. ^{1}H NMR ($CDCl_3$, 300MHz) δ 8.12 (d, 0.69H, J=16.2), 7.95 (d, 0.04H, J=16.2), 7.47 (d, 0.76H, J=7.8) 7.06 (m, 2.06H), 6.30 (d, 0.76H, J=15.9), 6.18 (d, 0.10H, J=16.5), 4.16 (t, 2.00H) , 3.41 (s, 1.77H), 3.32 (s, 0.25H), 2.30 (s, 3.16H), 2.20 (s, 6.73H), 1.65 (m, 2.21H), 1.40 (m, 2.13H), 0.92 (t, 3.12H) ppm; ^{13}C NMR ($CDCl_3$, 75MHz) 167.2, 143.0, 142.0, 139.7, 138.1, 137.4, 131.3, 131.2, 129.4, 128.2, 128.0, 127.8, 126.3, 124.0, 117.9, 64.0, 62.1, 61.6, 45.2, 45.0, 30.6, 21.0, 19.1, 13.6 ppm; IR ν2816, 1713, 1633, 1464, 1311, 1261, 1173, 1029, 842 cm^{-1} MS: (m/z) (%): 275 (28) [M$^+$], 58 (100), HRMS: Anal. Calcd. for $C_{17}H_{25}NO_2$ 275.18853, Found: 275.18849.



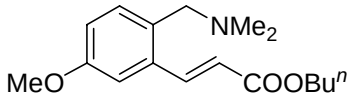
3ia

(E)-butyl 3-(2-((dimethylamino)methyl)-5-methylphenyl)acrylate (3ia): Start from **1i** (75 mg, 0.5 mmol) with **2a** (145 μL, 1.0 mmol) to afford **3ia** (97 mg), yield 70%. ^{1}H NMR ($CDCl_3$, 300MHz) δ 8.14 (d, 1H, J=15.9), 7.39 (s, 1H), 7.11 (m, 2H), 6.34 (d, 1H, J=15.9), 4.17 (t, 2H), 3.41 (s, 2H), 2.29 (s, 3H), 2.19(s, 6H), 1.64 (m, 2H), 1.42 (m, 2H), 0.93 (t, 3H, J=7.2) ppm; ^{13}C NMR ($CDCl_3$, 75MHz) 170.9, 146.1, 140.8, 139.1, 137.7, 134.5, 134.1, 132.8, 132.6, 130.8, 122.5, 67.9, 65.2, 48.9, 34.5, 24.7, 22.9, 17.4 ppm; IR ν 2959, 2816, 2766, 1713, 1306, 1171, 1024 cm^{-1} MS: (m/z) (%): 275 (30) [M$^+$], 218 (100), HRMS: Anal. Calcd. for $C_{17}H_{25}NO_2$ 275.18853, Found: 275.18823.



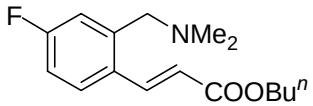
3ja

(E)-butyl 3-(2-((dimethylamino)methyl)-3-methoxyphenyl)acrylate (3ja): Start from **1j** (82 mg, 0.5 mmol) with **2a** (145 μL, 1.0 mmol) to afford **3ja** (110 mg), yield 75%. ^{1}H NMR ($CDCl_3$, 300MHz) δ 8.16(d, 1H, J=15.9), 7.21(m, 2H), 6.87 (m, 1H), 6.33 (d, 1H, J=15.9), 4.17 (t, 2H, J=6.6), 3.80 (s, 3H), 3.53 (s, 2H), 2.22 (s, 6H), 1.67 (m, 2H), 1.42 (m, 2H), 0.93 (t, 3H, J=7.5) ppm; ^{13}C NMR ($CDCl_3$, 75MHz) 167.1, 158.4, 142.7 136.1, 128.3, 126.6, 119.7, 118.7, 111.8, 64.3, 55.7, 52.4, 45.0, 30.7, 19.2, 13.7 ppm; IR ν 2959, 2815, 2766, 1713, 1171, 1022 cm^{-1} MS: (m/z) (%): 291(45) [M$^+$], 234 (100), HRMS: Anal. Calcd. for C_{17} $H_{25}NO_3$ 291.18344, Found: 291.18360.

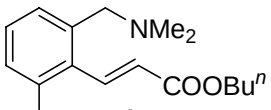


3ka

(E)-butyl 3-(2-((dimethylamino)methyl)-5-methoxyphenyl)acrylate (3ka): Start from **1k** (82 mg, 0.5 mmol) with **2a** (145 μL, 1.0 mmol) to afford **3ka** (111 mg), yield 76%. ^{1}H NMR ($CDCl_3$, 300MHz) δ 8.15 (d, 1H, J=15.9), 7.19 (d, 1H, J=8.4), 7.12 (d, 1H, 2.1), 6.88 (m, 1H), 6.37 (d, 1H, J=16.2), 4.21 (t, 2H, J=6.6), 3.85 (s, 3H), 3.43 (s, 2H), 2.22 (s, 6H), 1.70 (m, 2H), 1.47 (m, 2H), 0.97 (t, 3H, J=6.9) ppm; ^{13}C NMR ($CDCl_3$, 75MHz) 167.0, 158.8, 142.2, 135.2, 132.0, 130.7, 119.1, 115.3, 111.1, 64.2, 61.1, 55.1, 45.0, 30.6, 19.1, 13.6 ppm; IR ν 2960, 2815, 1713, 1173, 1022, 852, 805 cm^{-1} MS: (m/z) (%): 291 (40) [M$^+$], 234 (100), HRMS: Anal. Calcd. for C_{17} $H_{25}NO_3$ 291.18344, Found: 291.18281.

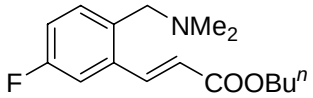


3la and



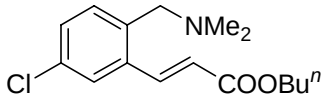
3la'

(E)-butyl 3-(2-((dimethylamino)methyl)-4-fluorophenyl)acrylate (3la) and **(E)-butyl 3-(2-((dimethylamino)methyl)-6-fluorophenyl)acrylate (3la'):** Start from **1l** (76 mg, 0.5 mmol) with **2a** (145 μL, 1.0 mmol) to afford a mixture of **3la** and **3la'** (122 mg, **3la**:**3la'**=5:3), yield 86%. ^{1}H NMR ($CDCl_3$, 300MHz) δ 8.11 (d, 0.69H, J=16.2), 7.95 (d, 0.04H, J=16.2), 7.46 (d, 0.76H, J=8.1), 7.05 (m, 2.06H), 6.30 (d, 0.76H, J=15.6), 6.18 (d, 0.10H, J=16.2), 4.16 (t, 2.00H, J=6.9), 4.41 (s, 1.77H), 4.32 (s, 0.25H), 2.31 (s, 3.16H), 2.20 (s, 6.73H), 1.64 (m, 2.21H), 1.39 (m, 2.13H), 0.92 (t, 3.12H) ppm; ^{13}C NMR ($CDCl_3$, 75MHz) 167.3, 163.6, 161.7, 160.3, 141.0, 140.9, 136.0, 130.1, 129.9, 129.7, 128.4, 128.3, 126.3, 126.2, 123.8, 123.6, 122.3, 122.2, 118.8, 117.2, 116.9, 115.3, 115.0, 114.6, 114.3, 64.2, 61.8, 61.3, 45.2, 45.1, 30.6, 19.1, 13.6 ppm; IR ν 2960, 2866, 2819, 2770, 1715, 1313, 1252, ,1173, 1029, 844 cm^{-1} MS: (m/z) (%): 279 (40) [M$^+$], 178 (100), HRMS: Anal. Calcd. for $C_{16}H_{22}NO_2F$ 279.16346, Found: 279.16296.



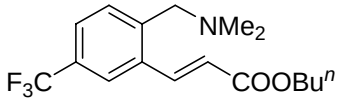
3ma

(E)-butyl 3-(2-((dimethylamino)methyl)-5-fluorophenyl)acrylate (3ma): Start from **1m** (76 mg, 0.5 mmol) with **2a** (145 μL, 1.0 mmol) to afford **3ma** (106 mg), yield 76%. ^{1}H NMR ($CDCl_3$, 300MHz) δ 8.13 (d, 1H, J=16.2), 7.28 (m, 2H), 7.00 (m, 1H), 6.34 (d, 1H, J=16.2), 4.21 (t, 2H, J=6.9), 3.45 (s, 2H), 2.22 (s, 6H), 1.67 (m, 2H), 1.43 (m, 2H), 0.96 (t, 3H, J=7.2) ppm; ^{13}C NMR ($CDCl_3$, 75MHz) 166.7, 163.7, 160.4, 141.1, 141.1, 136.2, 136.1, 134.12, 134.08, 132.4, 132.3, 120.2, 116.4, 116.1, 113.1, 112.8, 64.4, 61.1, 45.1, 30.7, 19.1, 13.7 ppm; IR ν 2961, 2818, 2769, 1717, 1363, 1273, 1173, 1024, 990, 863 cm^{-1} MS: (m/z) (%): 279 (20) [M$^+$], 222 (100), HRMS: Anal. Calcd. for $C_{16}H_{22}NO_2F$ 279.16346, Found: 279.16329.



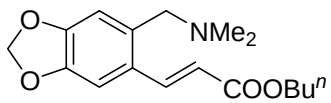
3na

(E)-butyl 3-(5-chloro-2-((dimethylamino)methyl)phenyl)acrylate (3na): Start from **1n** (85 mg, 0.5 mmol) with **2a** (145 μL, 1.0 mmol) to afford **3na** (127 mg), yield 85%. ^{1}H NMR ($CDCl_3$, 300MHz) δ 8.06 (d, 1H, J=15.9), 7.52 (s, 1H), 7.20 (m, 2H), 6.33 (d, 1H, J=15.9), 4.17 (t, 2H, J=6.6), 3.40 (s, 2H), 2.18 (s, 6H), 1.64 (m, 2H), 1.41 (m, 2H), 0.92 (t, 3H, J=7.8) ppm; ^{13}C NMR ($CDCl_3$, 75MHz) 166.7, 140.8, 136.7, 135.9, 133.4, 131.9, 129.2, 26.3, 120.3, 64.4, 61.1, 45.1, 30.6, 19.1, 13.7 ppm; IR ν2960, 2866, 2818, 2769, 1715, 1637, 1464, 1310, 1173, 1025, 863 cm^{-1} MS: (m/z) (%): 321 (8) [M$^+$], 238 (100), HRMS: Anal. Calcd. for $C_{16}H_{22}NO_2{}^{35}Cl$ 295.13391, Found: 295.13509.

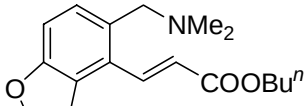


3oa

(E)-butyl 3-(2-((dimethylamino)methyl)-5-(trifluoromethyl)phenyl)acrylate (3oa): Start from **1o** (102 mg, 0.5 mmol) with **2a** (145 μL, 1.0 mmol) to afford **3oa** (123 mg), yield 74%. ^{1}H NMR ($CDCl_3$, 300MHz) δ 8.13 (d, 1H, J=16.2), 7.79 (s, 1H), 7.53 (d, 1H, J=7.8), 7.43 (d, 1H, J=7.8), 6.39 (d, 1H, J=15.9), 4.19 (t, 2H, J=6.9), 3.50 (s, 2H), 2.21 (s, 6H), 1.64 (m, 2H), 1.41 (m, 2H), 0.92 (t, 3H, J=7.2) ppm; ^{13}C NMR ($CDCl_3$, 75MHz) 166.7, 140.8, 136.7, 135.9, 133.4, 131.9, 129.2, 26.3, 120.3, 64.4, 61.1, 45.1, 30.6, 19.1, 13.7 ppm; IR ν 2962, 2822, 2771, 1717, 1335, 1266, 1166, 1137 cm^{-1} MS: (m/z) (%): 329 (40) [M$^+$], 272 (100), HRMS: Anal. Calcd. for $C_{17}H_{22}NO_2F_3$ 329.16026, Found: 329.16037.

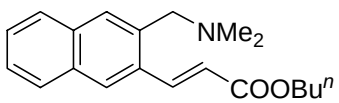


3pa and

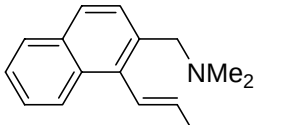


3pa'

(E)-butyl 3-(6-((dimethylamino)methyl)benzo[d][1,3]dioxol-5-yl)acrylate (3pa) and **(E)-butyl 3-(5-((dimethylamino)methyl)benzo[d][1,3]dioxol-4-yl)acrylate (3pa'):** Start from **1p** (90 mg, 0.5 mmol) with **2a** (145 μL, 1.0 mmol) to afford **3pa** and **3pa'** (122 mg, **3pa**:**3pa'**=12:1), yield 80%. ^{1}H NMR ($CDCl_3$, 300MHz) δ 8.05 (d, 0.08H, J=15.9), 7.92 (d, 1.00H, J=16.2), 6.98 (d, 0.17H, J=9.9), 6.70 (d, 1.10H, 17.1), 6.65 (s, 1.92H), 6.15 (d, 0.19H, 15.6), 5.97 (s, 2.29H), 5.90 (s, 0.38H), 4.13 (t, 2.85H, J=6.6), 3.49 (s, 0.24H), 3.31 (s, 2.47H), 2.20 (s, 1.19H), 5.15 (s, 7.31H), 1.56 (m, 2H), 1.38 (m, 2H), 0.89 (t, 3H, J=7.5) ppm; ^{13}C NMR ($CDCl_3$, 75MHz) 167.5, 167.3, 149.0, 147.2, 142.1, 141.4, 137.0, 133.6, 132.0, 128.9, 127.6, 123.6, 122.9, 121.9, 118.6, 117.7, 116.9, 110.5, 108.2, 106.4, 105.5, 101.3, 64.2, 64.0, 61.8, 61.1, 55.214, 44.8, 44.5, 30.6, 19.0, 13.6 ppm; IR ν 2960, 2766, 1458, 1239, 1174, 1070, 979 cm^{-1} MS: (m/z) (%): 305 (20) [M$^+$], 29 (100), HRMS: Anal. Calcd. for $C_{17}H_{23}NO_4$ 305.16271, Found: 305.16328.



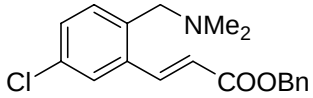
3qa and



3qa'

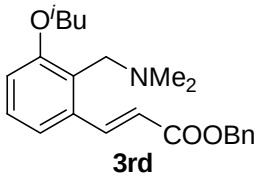
(E)-butyl 3-(3-((dimethylamino)methyl)naphthalen-2-yl)acrylate (3qa) and **(E)-butyl 3-(2-((dimethylamino)methyl)naphthalen-1-yl)acrylate (3qa'):** Starting from **1q** (92 mg, 0.5 mmol) with **2a** (145 μL, 1.0 mmol) to afford **3qa** and **3qa'** (133 mg, **3qa**:**3qa'**=11:1), yield 85%. ^{1}H NMR ($CDCl_3$, 300MHz) δ 8.31 (d, 1H, J=15.9), 8.07 (s, 1H), 7.75 (m, 2H), 7.67 (s, 1H), 7.44 (m, 2H), 6.52 (d, 1H, J=16.5) 4.23 (t, 2H), 3.56 (s, 2H), 2.26 (s, 6H), 1.69 (m, 2H), 1.45 (m, 2H), 0.92 (t, 3H) ppm; ^{13}C NMR ($CDCl_3$, 75MHz) 167.0, 142.8, 135.2, 133.6, 132.7, 132.4, 129.0, 128.0, 127.3, 126.8, 126.3, 126.1, 119.3, 64.2, 62.4,

45.2, 30.7, 19.1, 13.7 ppm; IR ν 2960, 2817, 2767,1712, 1638, 1304, 1171, 1025, 749 cm^{-1} MS: (m/z) (%): 311 (30) [M^+], 165 (100), HRMS: Anal. Calcd. for $C_{20}H_{25}NO_2$ 311.18853, Found: 311.18901.



3nd

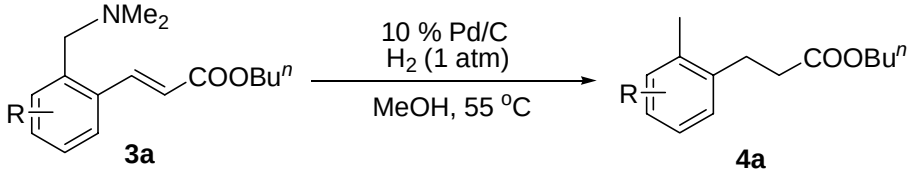
(E)-benzyl 3-(5-chloro-2-((dimethylamino)methyl)phenyl)acrylate (3nd): Starting from **1n** (85 mg, 0.5 mmol) with **2d** (162 mg, 1.0 mmol) to afford **3nd** (136 mg), yield 82%. ^{1}H NMR ($CDCl_3$, 300MHz) δ 8.13 (d, 1H, J=16.2), 7.54 (s, 1H), 7.40-7.22 (m, 7H), 6.38 (d, 1H, J=15.9), 5.24 (s, 2H), 3.42 (s, 2H), 2.20 (s, 6H) ppm; ^{13}C NMR ($CDCl_3$, 75MHz) 166.3, 141.4, 136.6, 135.8, 135.7, 133.3, 131.9, 129.3, 128.4, 128.3, 128.1, 128.0, 126.3, 119.8, 66.2, 61.0, 45.0 ppm; IR ν 2948, 2818, 2768, 1716, 1636, 1456, 1304, 1166, 1024, 863, 744, 697, cm^{-1} MS: (m/z) (%): 329 (1) [M^+], 238 (100), HRMS: Anal. Calcd. for $C_{19}H_{20}NO_2{}^{35}Cl$ 329.11826, Found: 329.11885.



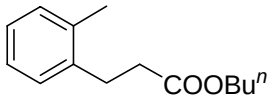
3rd

(E)-benzyl 3-(3-butoxy-2-((dimethylamino)methyl)phenyl)acrylate (**3rd**): Starting from **1r** (104 mg, 0.5 mmol) with **2d** (162 mg, 1.0 mmol) to afford **3rd** (148 mg), yield 81%. ^{1}H NMR ($CDCl_3$, 300MHz) δ 8.26 (d, 1H, J=15.9), 7.43-7.20 (m, 7H), 6.86 (m, 1H), 6.43 (d, 1H, J=16.2), 5.24 (s, 2H), 3.71 (d, 2H, J=6.6), 3.575 (s, 2H), 2.24 (s, 6H), 2.12 (m, 1H), 1.05 (d, 6H, J=6.6) ppm; ^{13}C NMR ($CDCl_3$, 75MHz) 166.8, 157.7, 143.5, 136.1, 135.9, 128.5, 128.4, 128.1, 128.1, 127.2, 118.8, 118.4, 112.5, 74.6, 52.5, 45.3, 28.4, 19.4 ppm; IR ν 2958, 2856, 2817, 2768, 1715, 1578, 1467, 1258, 1162, 1020 cm^{-1} MS: (m/z) (%): 367 (20) [M^+], 91 (100), HRMS: Anal. Calcd. for $C_{23}H_{29}NO_3N$ 367.21474, Found: 367.21367.

Transforamtion from Functionalized Tertiary Amines to Toluene Derivatives (Eq. 4).

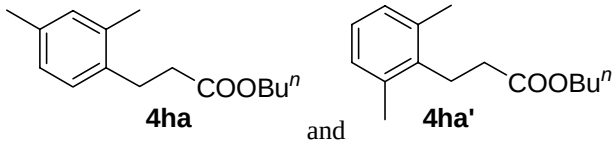


3a **4a**



4aa

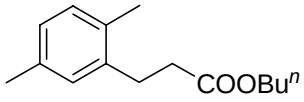
butyl 3-*o*-tolylpropanoate (4aa): 4aa (118 mg) was obtained from **3aa** (130 mg, 0.5 mmol) with a reaction time of 8h, yield 81%. ^{1}H NMR ($CDCl_3$, 300MHz) δ 7.14-7.12 (m, 4H), 4.09 (t, 2H, J=6.6), 2.95 (t, 2H, J= 7.5), 2.59 (t, 2H, J=7.5), 2.33 (s, 3H), 1.60 (m, 2H), 1.35 (m, 2H), 0.93 (t, 3H, J=6.9) ppm; ^{13}C NMR ($CDCl_3$, 75MHz) 173.1, 136.6, 135.9, 130.2, 130.2, 128.4, 126.3, 126.0, 64.3, 34.5, 30.6, 28.3, 19.2, 13.6 ppm; IR ν 2960, 1735, 1176, 750 cm^{-1} MS: (m/z) (%): 220 (40) [M^+], 105 (100).



4ha and **4ha'**

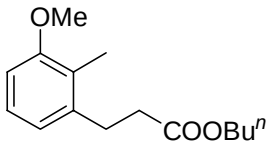
butyl 3-(2,4-dimethylphenyl)propanoate (4ha) and **butyl 3-(2,6-dimethylphenyl) propanoate (4ha'): 4ha** and **4ha'** (57 mg, **4ha**:**4ha'**=9:1) was obtained from **3ha** and **3ha'** (75 mg, 0.27 mmol, **3ha**:**3ha'**=9:1) with a reaction time of 8h, yield 90%. ^{1}H NMR ($CDCl_3$, 300MHz) δ 7.05-7.00 (m, 3H), 4.10 (t, 2H, J=6.6), 2.92 (t, 2H, J=7.5), 2.58 (t, 2H, J=7.5), 2.29 (s, s, 6H), 1.61 (m, 2H), 1.38 (m, 2H), 0.95 (t, 3H, J=7.4) ppm; ^{13}C NMR ($CDCl_3$, 75MHz) 173.1(h), 136.0, 135.64, 135.59, 135.5, 131.0(h), 128.3(h), 128.1, 126.6, 126.0, 64.3, 64.2(h), 34.7(h), 34.4, 33.3, 30.5(h), 27.9(h), 25.0, 20.7(h), 19.6, 19.0(h), 13.6(h) ppm; IR ν 2960, 1736, 1172, 819 cm^{-1}

MS: (m/z) (%): 234 (30) [M^+], 119 (100).



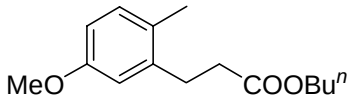
4ia

butyl 3-(2,5-dimethylphenyl)propanoate (4ia): 4ia (52 mg) was obtained from **3ia** (66 mg, 0.24 mmol) with a reaction time of 8h, yield 90%. ^{1}H NMR ($CDCl_3$, 300MHz) δ 7.02 (d, 1H, J=7.8), 6.94 (m, 2H), 4.09 (t, 2H, J=6.9), 2.90 (t, 2H, J=7.8), 2.57 (t, 2H, J=8.7), 2.28 (s, s, 6H), 1.60 (m, 2H), 1.35 (m, 2H), 0.92 (t, 3H, J=6.9) ppm; ^{13}C NMR ($CDCl_3$, 75MHz) 173.1, 138.4, 135.4, 132.6, 130.1, 138.2, 136.9, 64.3, 34.6, 30.6, 28.3, 20.9, 19.0, 18.7, 13.6 ppm; IR ν 2960, 1736, 1468, 1171, 810 cm^{-1} MS: (m/z) (%): 234 (50) [M^+], 119 (100), HRMS: Anal. Calcd. for $C_{15}H_{22}O_2$ 234.16198, Found: 234.16181.



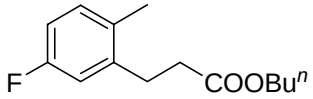
4ja

butyl 3-(3-methoxy-2-methylphenyl)propanoate (4ja): 4ja (48 mg) was obtained from **3ja** (63 mg, 0.22 mmol) with a reaction time of 20 h, yield 89%. ^{1}H NMR ($CDCl_3$, 300MHz) δ 7.02 (t, 1H, J=7.8), 6.69 (m, 2H), 4.01 (t, 2H, J=6.9), 3.74 (s, 3H), 2.89 (t, 2H, J=7.8), 2.49 (t, 2H, J=8.4), 2.12 (s, 3H), 1.53 (m, 2H), 1.29 (m, 2H), 0.86 (t, 3H, J=7.8) ppm; ^{13}C NMR ($CDCl_3$, 75MHz) 173.1, 157.7, 140.0, 131.0, 127.8, 114.3, 111.2, 64.3, 55.1, 34.5, 30.6, 28.5, 19.0, 18.2, 13.6 ppm; IR ν 2958, 1734, 1468, 1258, 1176, 1102, 780 cm^{-1} MS: (m/z) (%): 234 (50) [M^+], 119 (100).



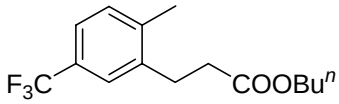
4ka

butyl 3-(5-methoxy-2-methylphenyl)propanoate(4ka): 4ka (57 mg) was obtained from **3ka** (81 mg, 0.28 mmol) with a reaction time of 8 h, yield 82%. ^{1}H NMR ($CDCl_3$, 300MHz) δ 7.02 (d, 1H, J=8.4), 6.67 (m, 2H), 4.07 (t, 2H, J=6.6), 3.75 (s, 3H), 2.89 (t, 2H, J=7.5), 2.55 (t, 2H, J=8.0), 2.23 (s, 3H), 1.58 (m, 2H), 1.33 (m, 2H), 0.91 (t, 3H, J=7.2) ppm; ^{13}C NMR ($CDCl_3$, 75MHz) 173.0, 157.8, 140.0, 126.1, 124.5, 121.1, 108.2, 64.3, 55.4, 34.9, 30.6, 28.7, 19.1, 13.7, 11.1 ppm; IR ν 2959, 1734, 1504, 1252, 1162, 1047, 812 cm^{-1} MS: (m/z) (%): 250 (100) [M^+].



4ma

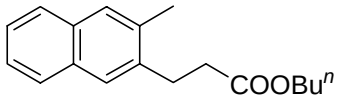
butyl 3-(5-fluoro-2-methylphenyl)propanoate (4ma): 4ma (40 mg) and **methyl 3-(5-fluoro-2-methylphenyl)propanoate (4mc)** (11 mg) was obtained from **3ma** (96 mg, 0.34 mmol) with a reaction time of 36 h, yield 67%. ^{1}H NMR ($CDCl_3$, 300MHz) δ 7.10 (m, 1H), 6.86-6.77 (m, 2H), 4.08 (t, 2H, J=6.9), 2.91 (t, 2H, J=7.2), 2.57 (t, 2H, J=8.4), 2.27 (s, 3H), 1.62 (m, 2H), 1.35 (m, 2H), 0.92 (t, 3H, J=6.9) ppm; ^{13}C NMR ($CDCl_3$, 75MHz) 172.8, 162.8, 159.6, 140.6 (d, J=6.4), 131.4, 131.2, 115.0 (d, J=21.4), 112.8 (d, J=20.2), 64.4, 34.1, 30.6, 28.3, 28.2, 19.1, 18.5, 13.6 ppm; IR ν 2961, 2935, 2874, 1735, 1499, 1458, 1248, 1178, 810 cm^{-1} MS: (m/z) (%): 238 (60) [M^+], 123 (100), HRMS: Anal. Calcd. for $C_{14}H_{19}O_2F$ 238.13691, Found: 238.13686



4oa

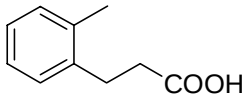
butyl 3-(2-methyl-5-(trifluoromethyl)phenyl)propanoate (4oa): 4oa (85 mg) was obtained from **3oa** (98 mg, 0.30 mmol) with a reaction time of 48 h, yield 47%. ^{1}H NMR ($CDCl_3$, 300MHz) δ 7.30 (d, 2H, J=8.4), 7.17 (d, 1H, J=7.5), 4.01 (t, 2H, J=6.6), 2.91 (t, 2H, J=7.2), 2.54 (t, 2H, J=7.8), 2.30 (s, 3H), 1.53 (m, 2H), 1.27 (m, 2H), 0.85 (t, 3H, J=7.2) ppm; ^{13}C NMR ($CDCl_3$, 75MHz) 172.6, 140.2, 139.4, 130.5, 125.2, 125.1, 125.0,

123.13, 123.09, 64.5, 34.2, 30.6, 28.1, 19.3, 19.0, 13.6 ppm; IR ν 2962, 1736, 1330, 1161, 1130, 826 cm^{-1} MS: (m/z) (%): 288 (30) [M^+], 173 (100), HRMS: Anal. Calcd. for $C_{15}H_{19}O_2F_3$ 288.13371, Found: 288.13329.



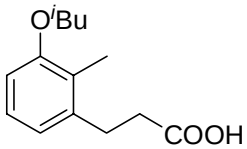
4qa

butyl 3-(3-methylnaphthalen-2-yl)propanoate (4qa): 4qa (55 mg) was obtained from **3qa** (64 mg, 0.20 mmol) with a reaction time of 48 h, yield 66 %. ^{1}H NMR ($CDCl_3$, 300MHz) δ 7.73 (m, 2H), 7.60 (m, 2H), 7.39 (m, 2H), 4.10 (t, 2H, J=6.6), 3.10 (t, 2H, J=7.5), 2.70 (t, 2H, J=7.8), 2.50 (s, 3H), 1.60 (m, 2H), 1.31 (m, 2H), 0.90 (t, 3H, J=7.5) ppm; ^{13}C NMR ($CDCl_3$, 75MHz) 173.1, 137.5, 134.6, 132.4, 132.2, 128.2, 128.1, 127.1, 126.8, 125.4, 125.3, 125.11, 125.08, 64.4, 34.5, 30.6, 28.4, 19.7, 19.1, 13.6 ppm; IR ν 2960, 1735, 1173, 747 cm^{-1} MS: (m/z) (%): 270 (55) [M^+], 155 (100), HRMS: Anal. Calcd. for $C_{18}H_{22}O_2$ 270.16198, Found: 270.16159.



4ad

3-o-tolylpropanoic acid (4ad): Follow the general procedure for reduction of functionalized amine to substituted toluene from the starting **3ad** (79 mg, 0.27 mmol) with a reaction time of 12h, after the evaporation of MeOH, the residue was dissolved in CH_2Cl_2 and washed with HCl (2N), the water phase was extracted by CH_2Cl_2 twice, the organic layer was combined, dried over Na_2SO_4, and evaporated to give **4ad** (37.7 mg) as a white needle crystal, yield 77%. m. p. 104-106 □; ^{1}H NMR ($CDCl_3$, 300MHz) δ 11.3 (br, 1H), 7.15 (m, 4H), 2.96 (t, 2H, J=7.8), 2.65 (t, 2H, J=8.0), 2.33 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 75MHz) 179.5, 138.2, 135.9, 130.3, 128.4, 126.5, 126.2, 34.3, 27.9, 19.2 ppm; IR ν 3394, 2927, 2470, 1718, 1461, 1261, 1159, 1024, 745 cm^{-1} MS: (m/z) (%): 162 (50) [M^+], 105 (100).

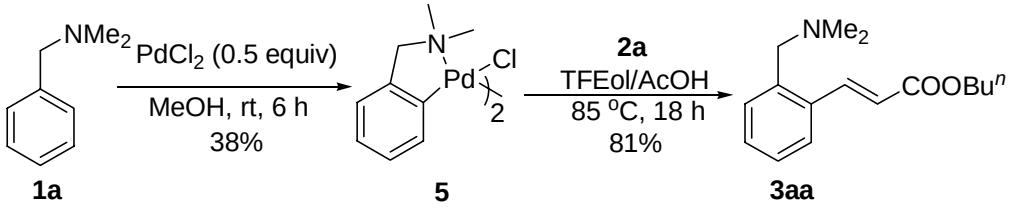


4rd

3-(3-isobutoxy-2-methylphenyl)propanoic acid (4rd): Follow the procedure of **4ad**, **4rd** (57.0 mg) was obtained as a white needle crystal from the starting **3rd** (110 mg, 0.3 mmol) in 2-methoxyethanol (3.0 mL) with a reaction time of 22h, yield 81%. m. p. 105-107 □; ^{1}H NMR ($CDCl_3$, 300MHz) δ 7.07 (t, 1H, J=8.1), 6.77-6.68 (m, 2H) 3.69 (d, 2H, J=6.3) 2.95 (t, 2H, J=7.8), 2.61 (t, 2H, J=8.7), 2.20 (s, 3H) 2.08 (m, 1H) 1.03 (d, 6H, J=6.9) ppm; ^{13}C NMR ($CDCl_3$, 75MHz) 178.8, 157.3, 139.5, 126.2, 124.8, 120.7, 109.2, 74.4, 34.5, 28.44, 28.40, 19.3, 11.2 ppm; IR ν 2957, 2926, 2873, 1740, 1462, 1260, 1173, 1096, 778 cm^{-1} MS: (m/z) (%): 236 (10) [M^+], 134 (100).

Mechanistic Investigation

***Ortho* Olefination of Palladacycle 5 (Eq. 5)**



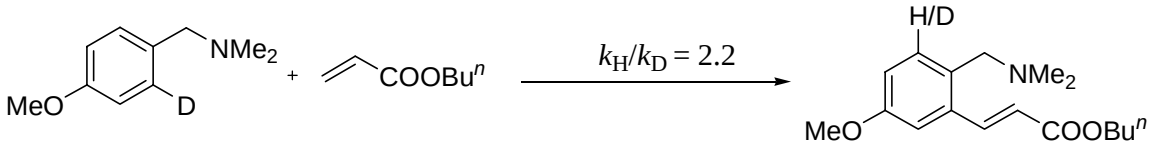
1a **5** **3aa**

Preparation of μ-(Dichloro)-bis(N, N-dimethylbenzylamine-C, N)dipalladium (5): The Pd-complex was prepared according to the literature[1] from **1a** (270 mg, 2 mmol), and palladium dichloride (177 mg, 1 mmol) in methanol at RT, recrystallization in benzene and hexane give **5** (106 mg, 38%). m. p. 184-186 □; ^{1}H NMR ($CDCl_3$, 300MHz) δ 6.85–7.24 (m, 4H), 3.91 (s, 2H), 2.83 (d, 6H, J=7.8) ppm; ^{13}C NMR ($CDCl_3$, 75MHz)

146.9, 143.0, 133.3, 132.8, 125.1, 124., 121.5, 73.2, 73.1, 52.8, 52.5 ppm; IR ν 3002, 2911, 1578, 1448, 1286, 1044, 1026, 983, 861, 734 cm^{-1} MS: (m/z) (%): 552 (6) [M^+], 134 (100).

Procedure from 5 to 3aa: 5 (55.2 mg, 0.1 mmol) was dissolved in CF_3CH_2OH (0.4 mL) in a Schlenck tube. Then **2a** (29 μL, 0.2 mmol) and HOAc (0.1 ml, 3.2 mmol) were added. The flask was stoppered and heated at 85 °C in an oil bath for 18 h. Work up was the same as the general procedure and afforded **3aa** (42.1 mg, 81%).

Determination of Kinetic Isotope Effect (k_H/k_D) (Eq. 6)



1k-d **2a** **3ka**

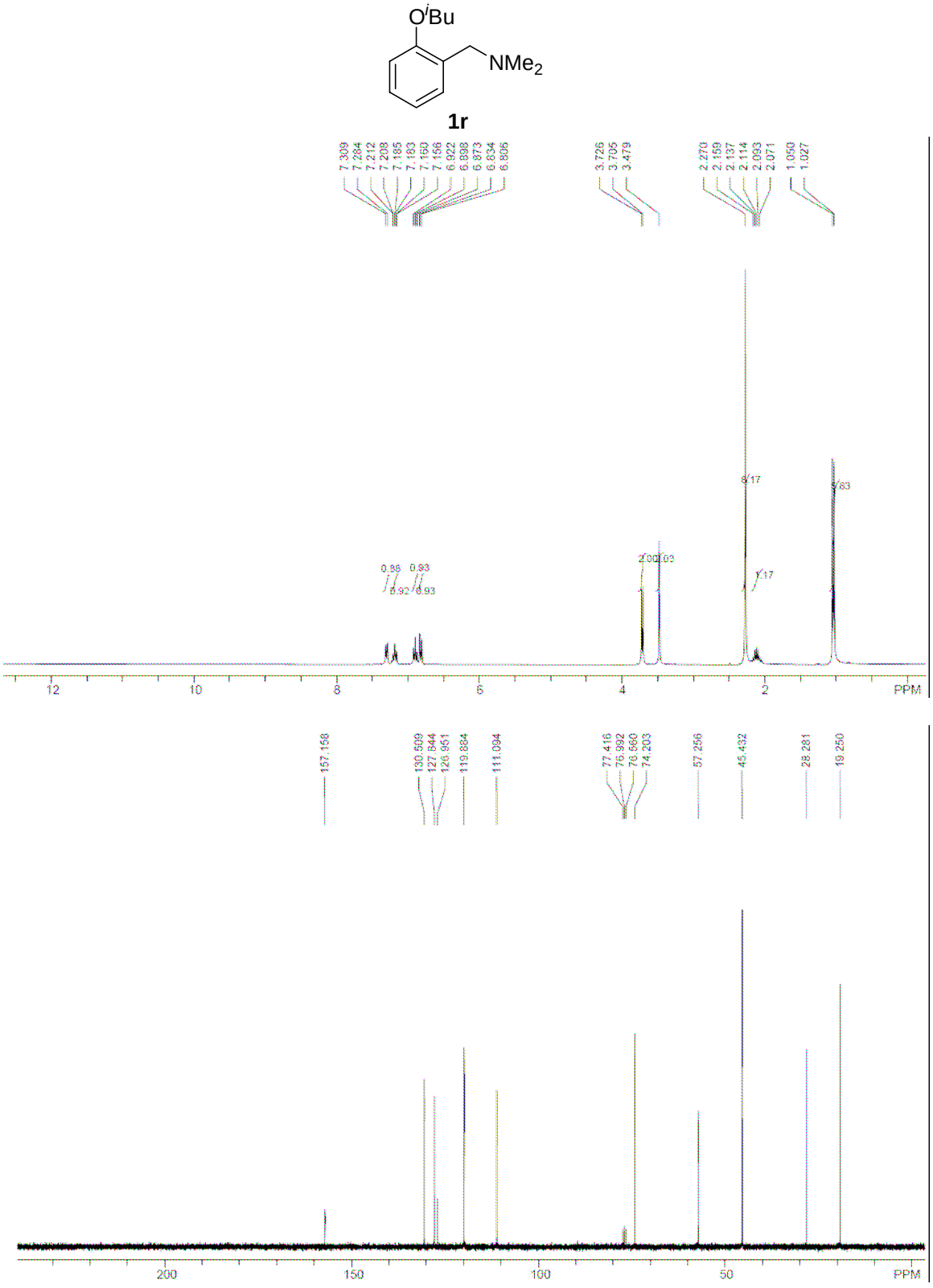
2-Deuterated N,N-dimethyl-4-methoxyl- benzylamine (1k-d**): 1k-**d was prepared from **1k** according to the literature.[2] In a dried Schlenck tube were combined **1k** (330 mg, 2 mmol), dried ether (3 mL) and *n*-BuLi (2.5 mL, 4 mmol), tightly soppered, and stirred at RT for 22 h. Then D_2O (0.5 mL, 2.2 mmol) was added with an ice bath. The mixture was stirred at RT for 1h. After that, the organic layer was filtered free of the damp solid which had separated, dried over $MgSO_4$, and evaporated the solvent to get **1k-**d quantitatively (deuterated rate 79%).

Procedure of determination of isotope effect: Olefination of **1k-**d (84mg, 0.5mmol) according to the general procedure afforded **3ka** (106 mg, yield 73%, deuterated rate 48%). The kinetic isotope effect (k_H/k_D) was determined to be 2.2.

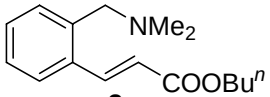
References:

1. Cope, A. C.; Friedrich, E. C. *J. Am. Chem. Soc*. **1968**, *90*, 909.
2. Jones, F. N.; Zinn, M. F.; Hauser, C. R. *J. Org. Chem.* **1963**, *28*, 663.

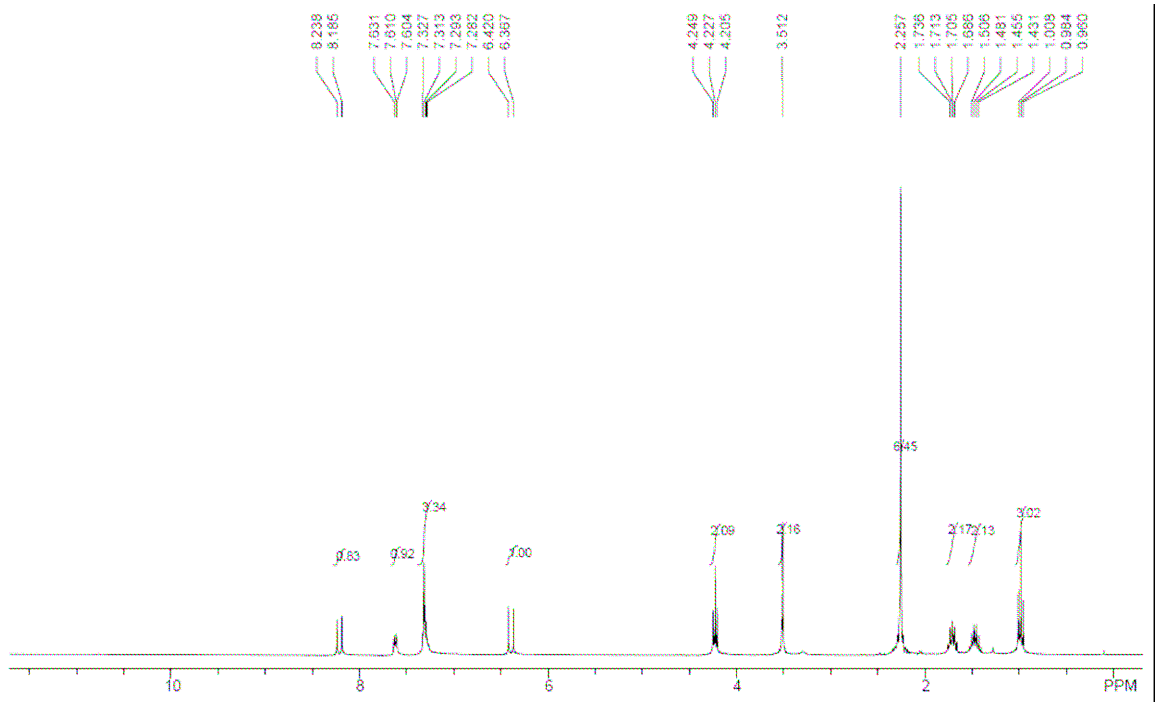
NMR spectrum of compounds **1r**

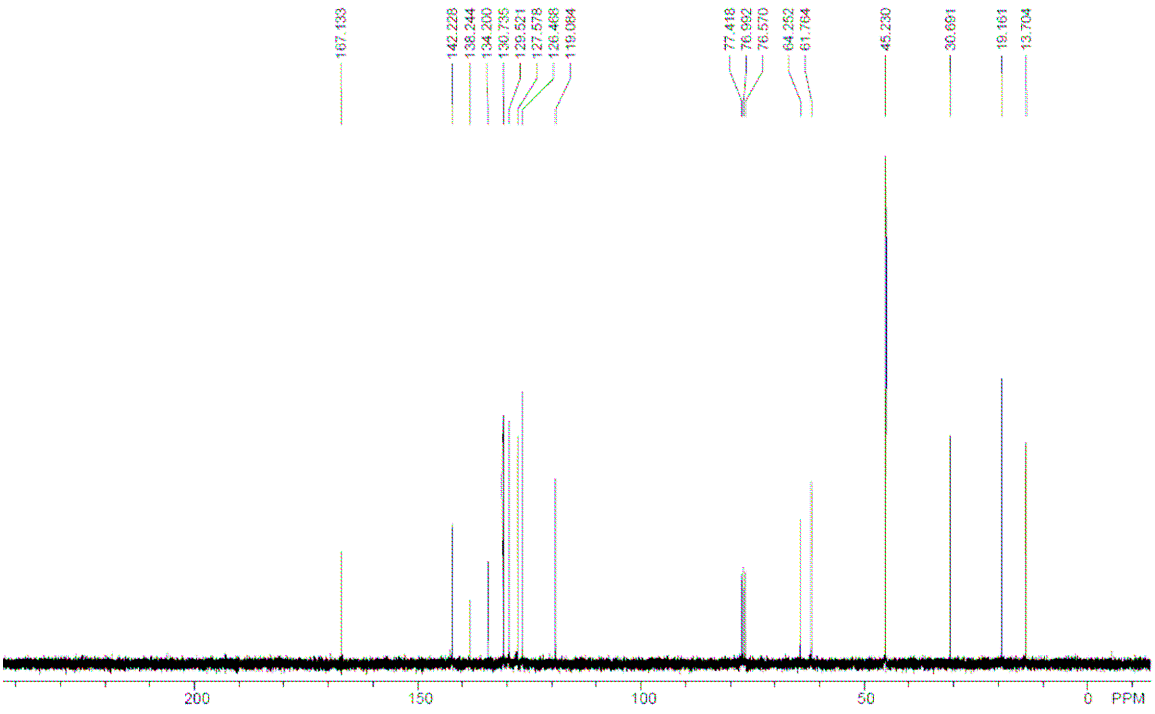


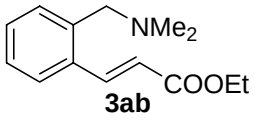
NMR spectrum of compounds **3aa-3rd**



3aa



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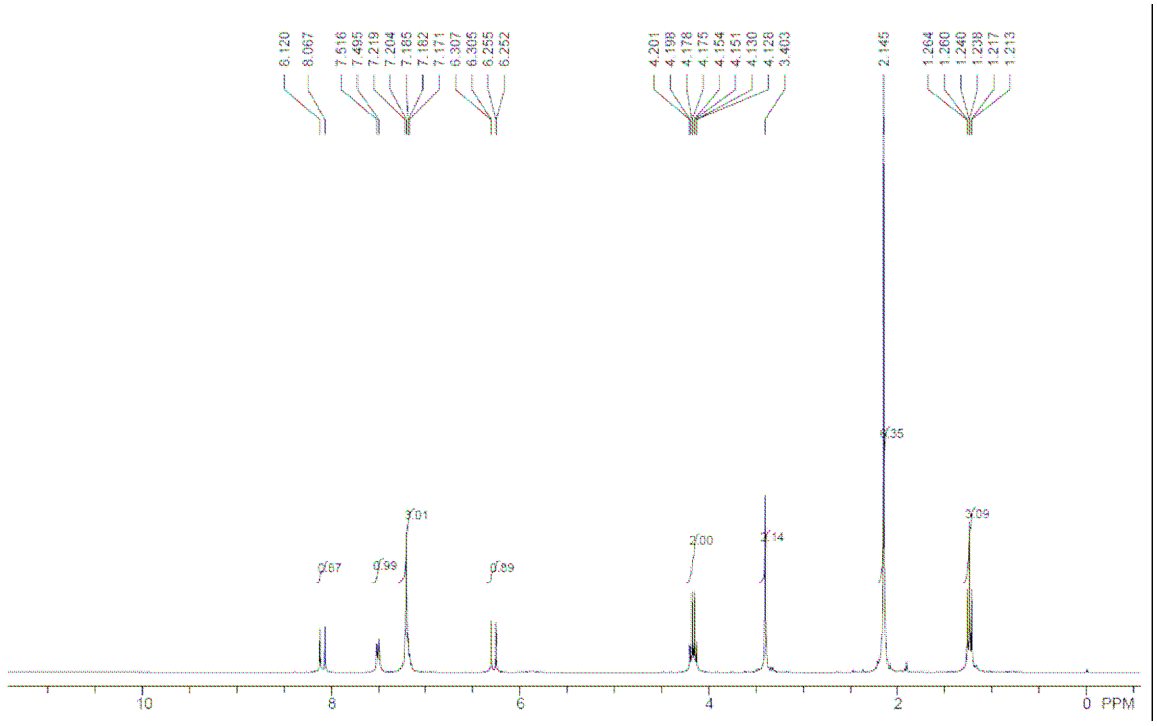
COOEt

3ab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1.240
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1.217
1.213
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3.01
0.89
2.00
2.14
6.35
3.09
10
8
6
4
2
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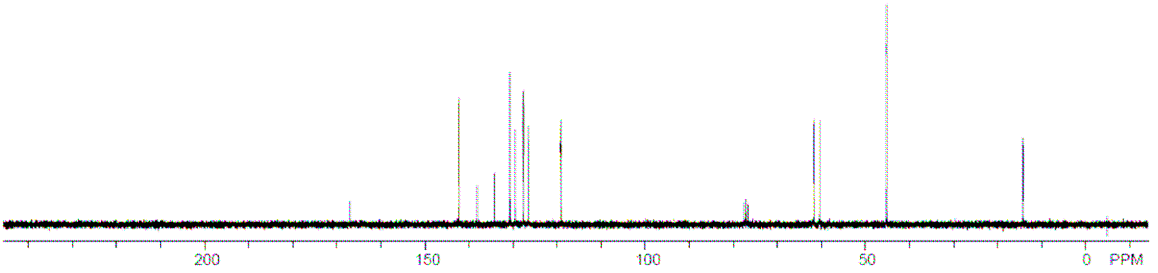
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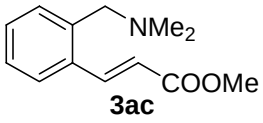
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COOMe

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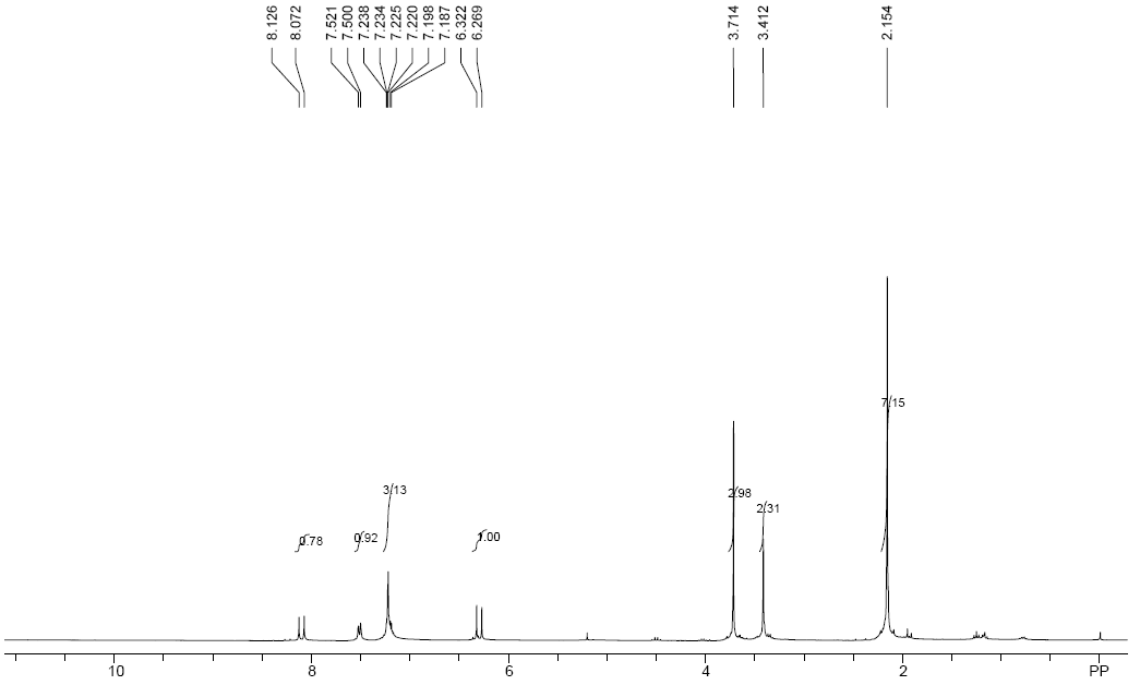
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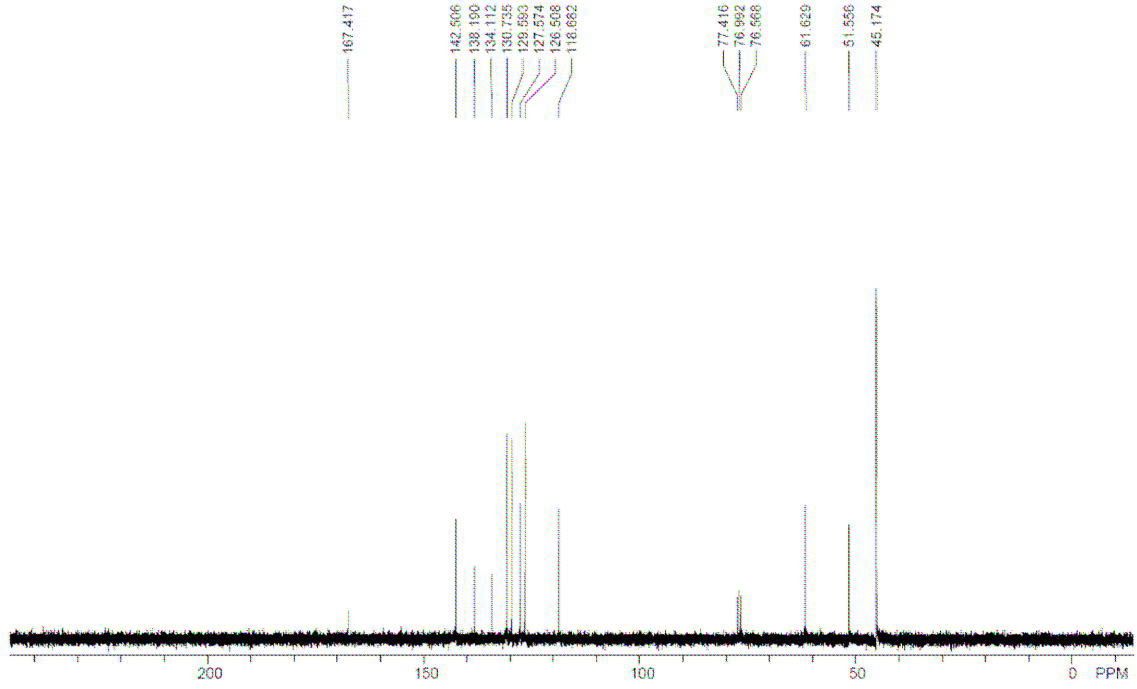
4
2
PP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45.174
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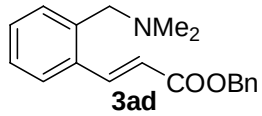
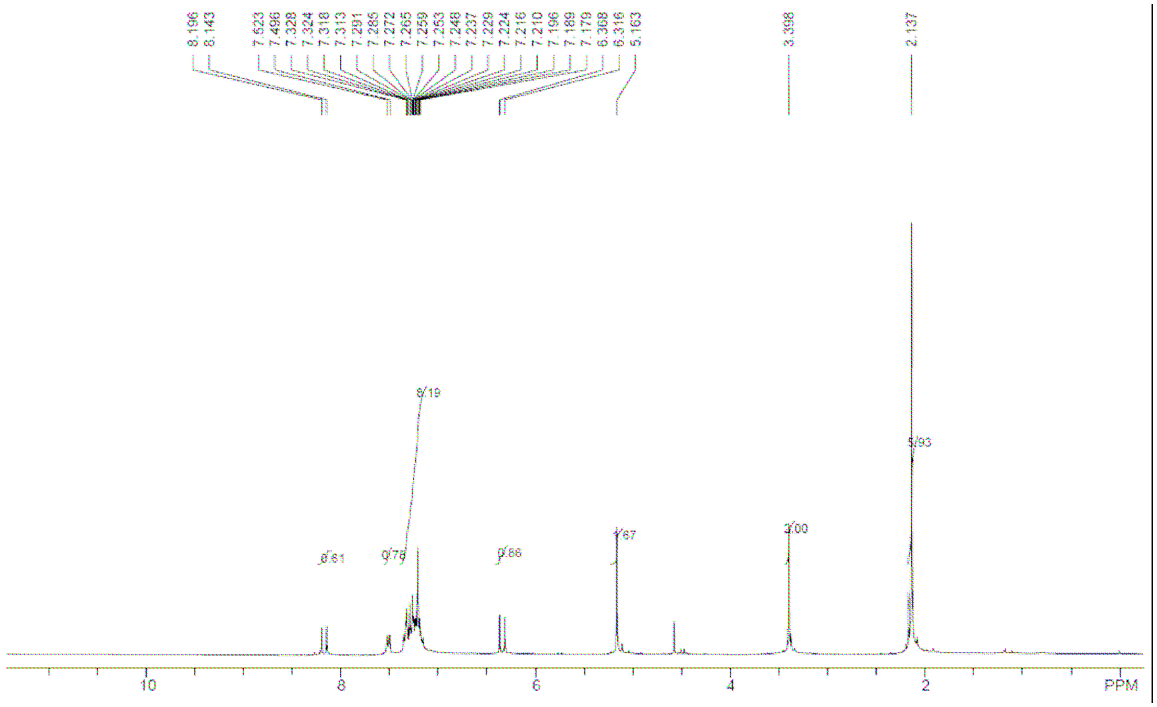
PPM


NMe2
COOBn

3ad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1.67
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0.79
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PPM


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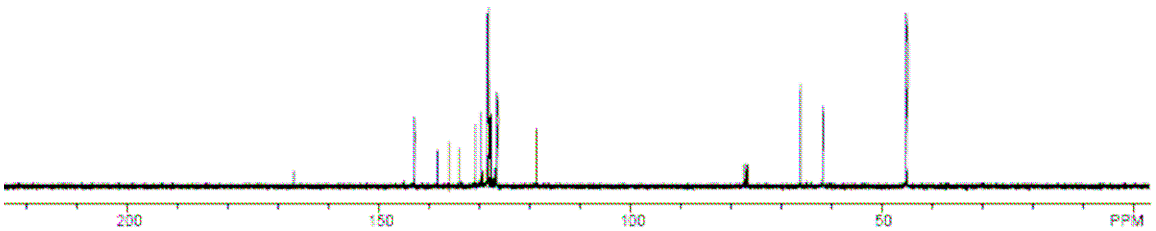
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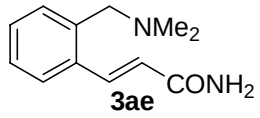
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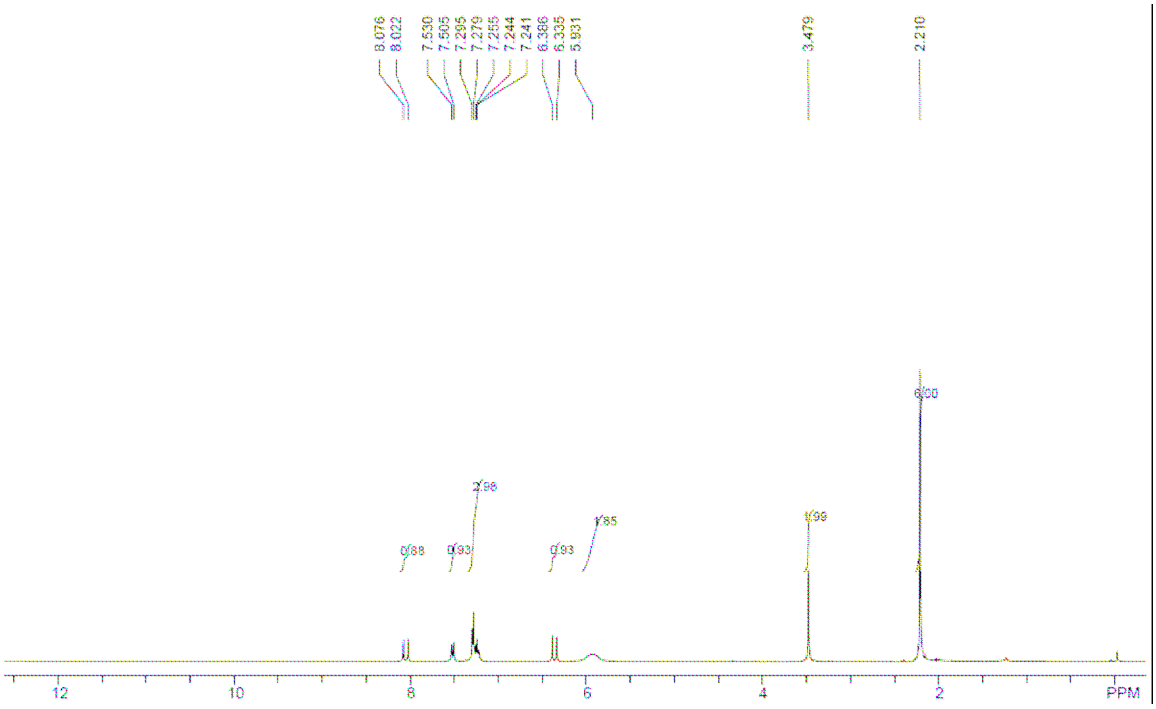
CONH2

3ae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7.244
7.241
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6.335
5.931
3.479
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0.93
0.85
1.99
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8
6
4
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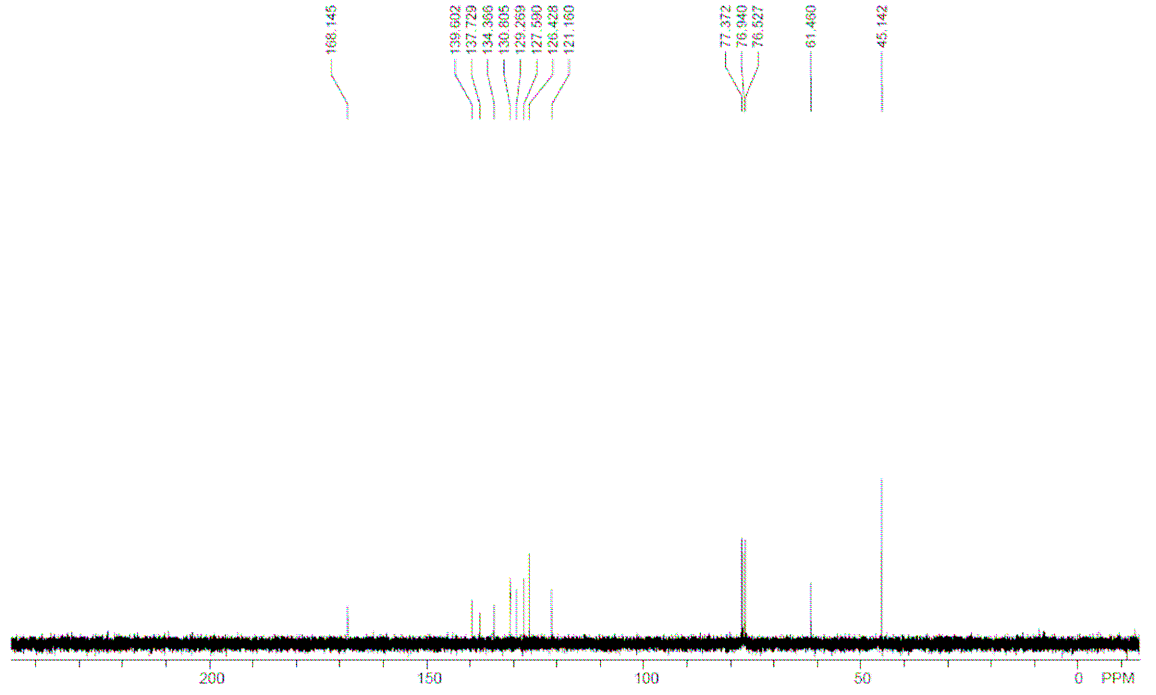
PPM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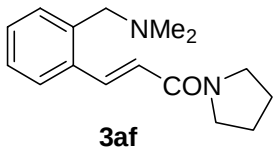
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CON

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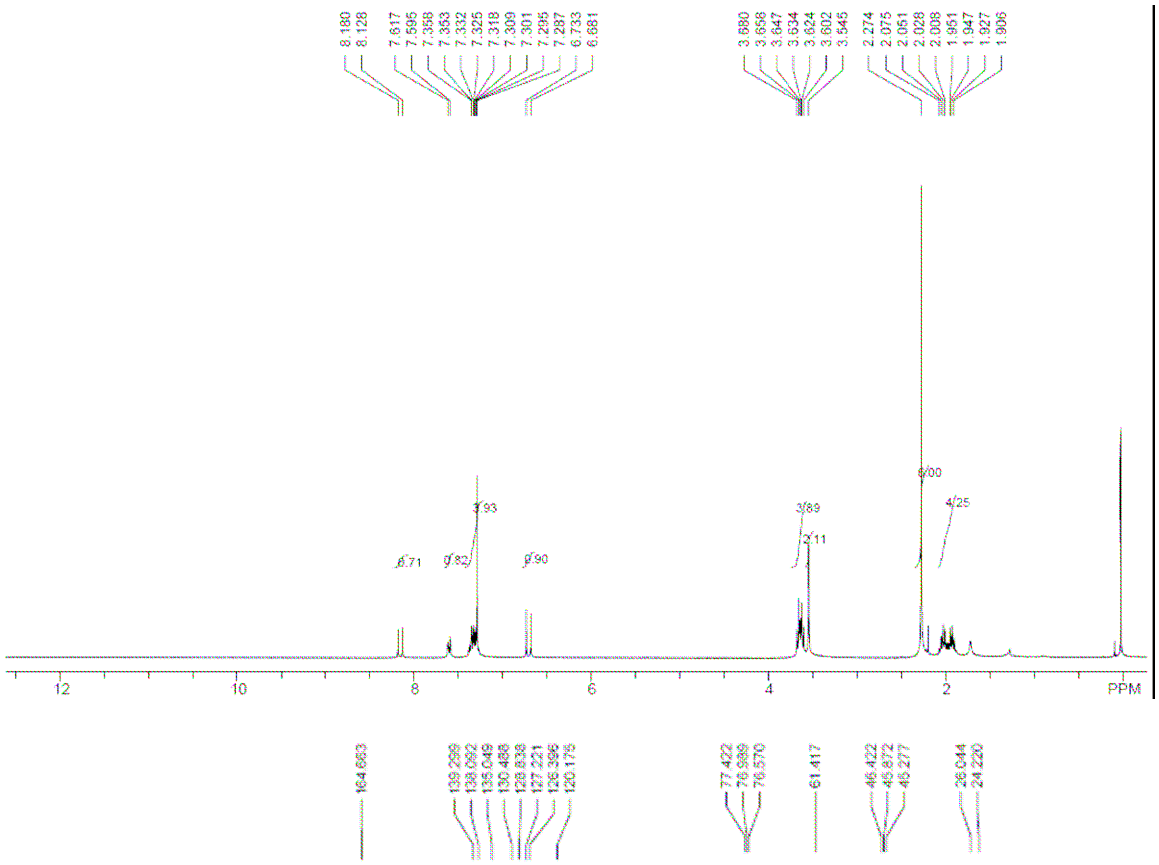
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7.325
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7.301
7.295
7.287
6.733
6.681
3.690
3.656
3.647
3.634
3.624
3.602
3.545
2.274
2.075
2.051
2.028
2.008
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1.906
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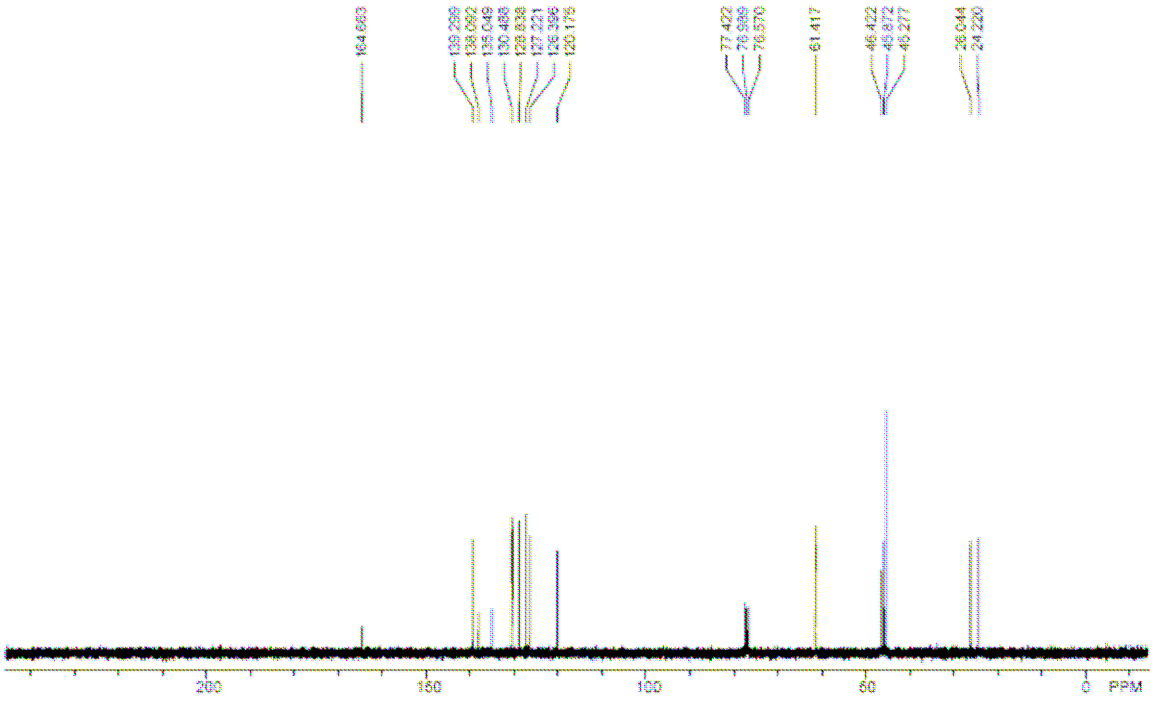
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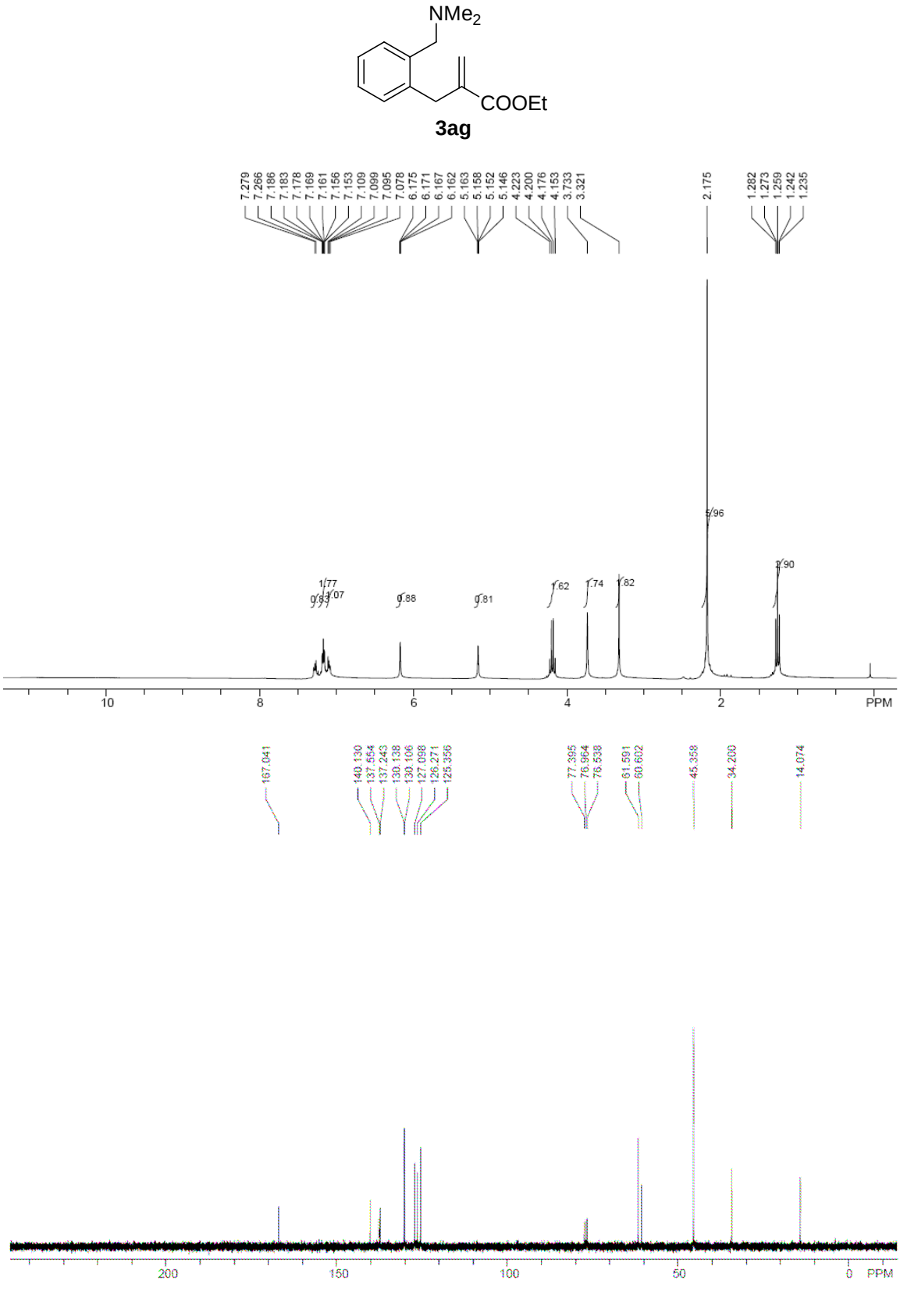
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COOEt
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7.095
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5.158
5.152
5.146
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4.176
4.153
3.733
3.321
2.175
1.282
1.273
1.259
1.242
1.235
6.96
2.90
1.77
1.07
0.88
0.81
1.62
1.74
1.82
10
8
6
4
2
PPM
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137.243
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130.106
127.098
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76.964
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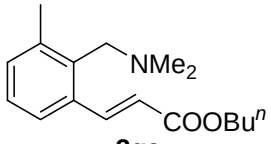
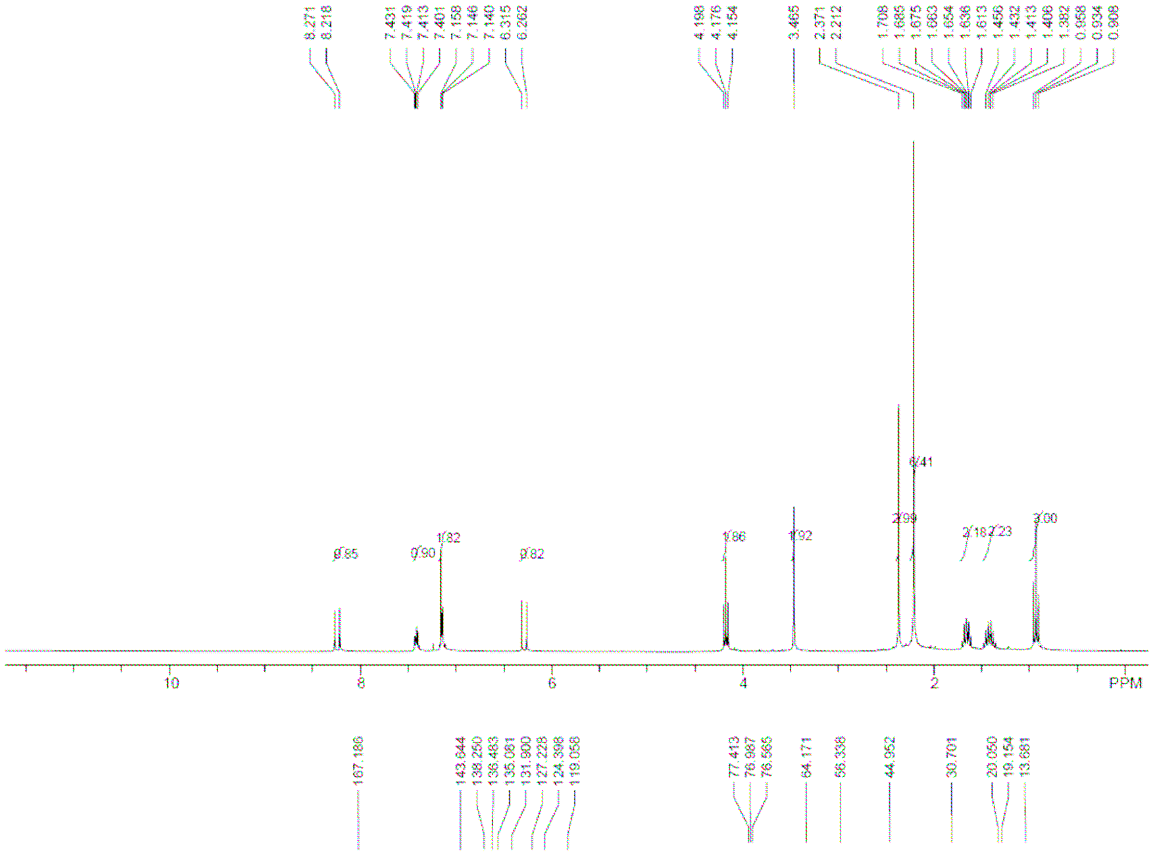
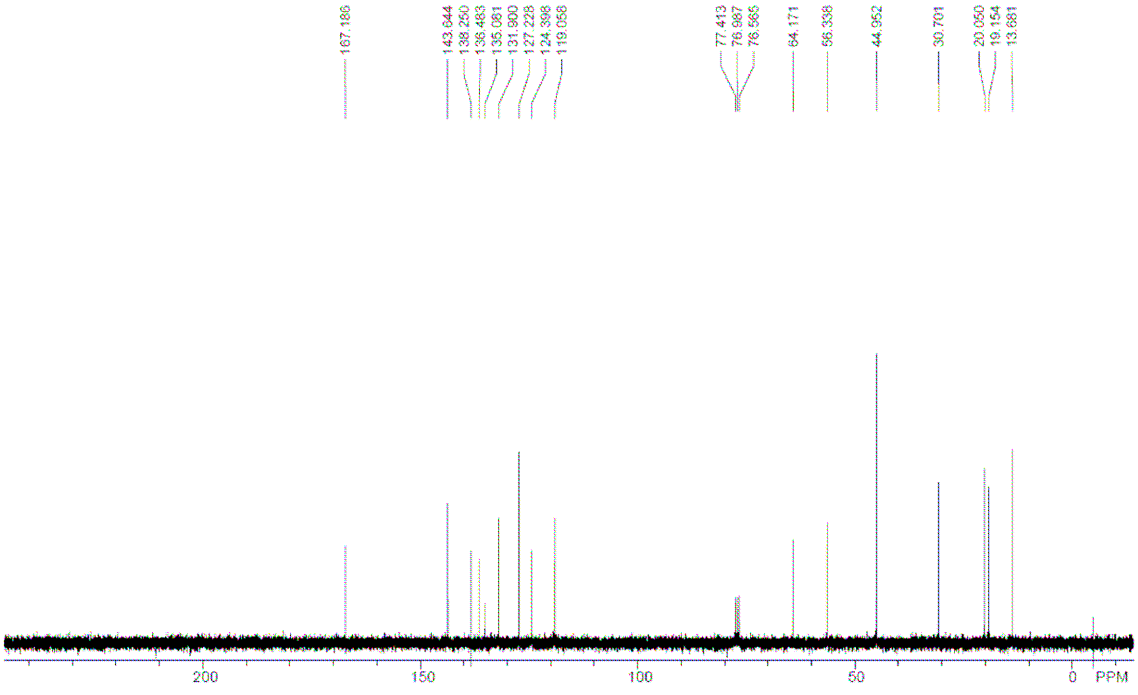
PPM

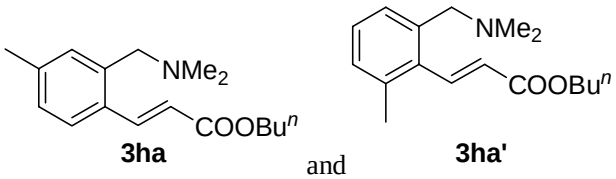
NMR spectrum of compounds **3ga-3rd**



3ga



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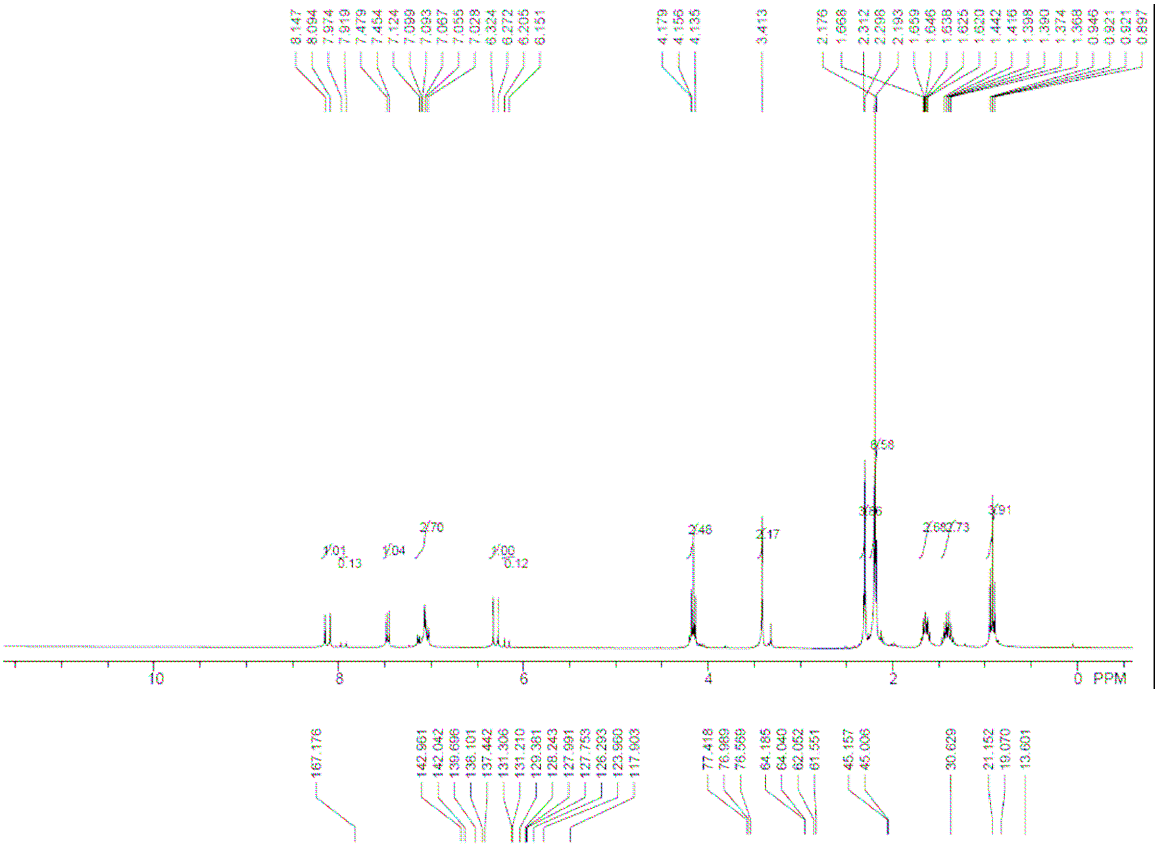
COOBu^n
NMe2
COOBu^n

3ha and **3ha'**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7.067
7.055
7.028
6.324
6.272
6.205
6.151
4.179
4.156
4.135
3.413
2.176
1.668
2.312
2.286
2.193
1.659
1.646
1.638
1.625
1.620
1.442
1.415
1.399
1.390
1.374
1.368
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0.921
0.921
0.897
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0.13
1.04
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1.00
0.12
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2.17
6.58
3.06
2.68
2.73
3.91
10
8
6
4
2
0 PPM

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138.101
137.442
131.306
131.210
129.361
128.243
127.991
127.753
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123.560
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77.418
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19.070
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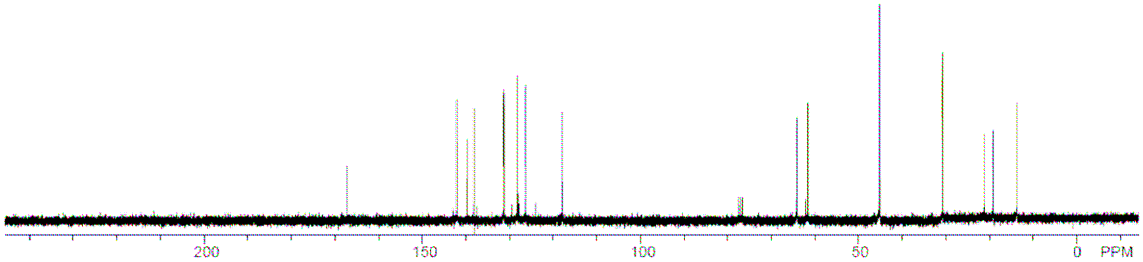
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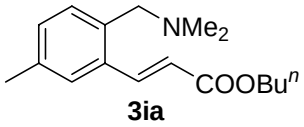
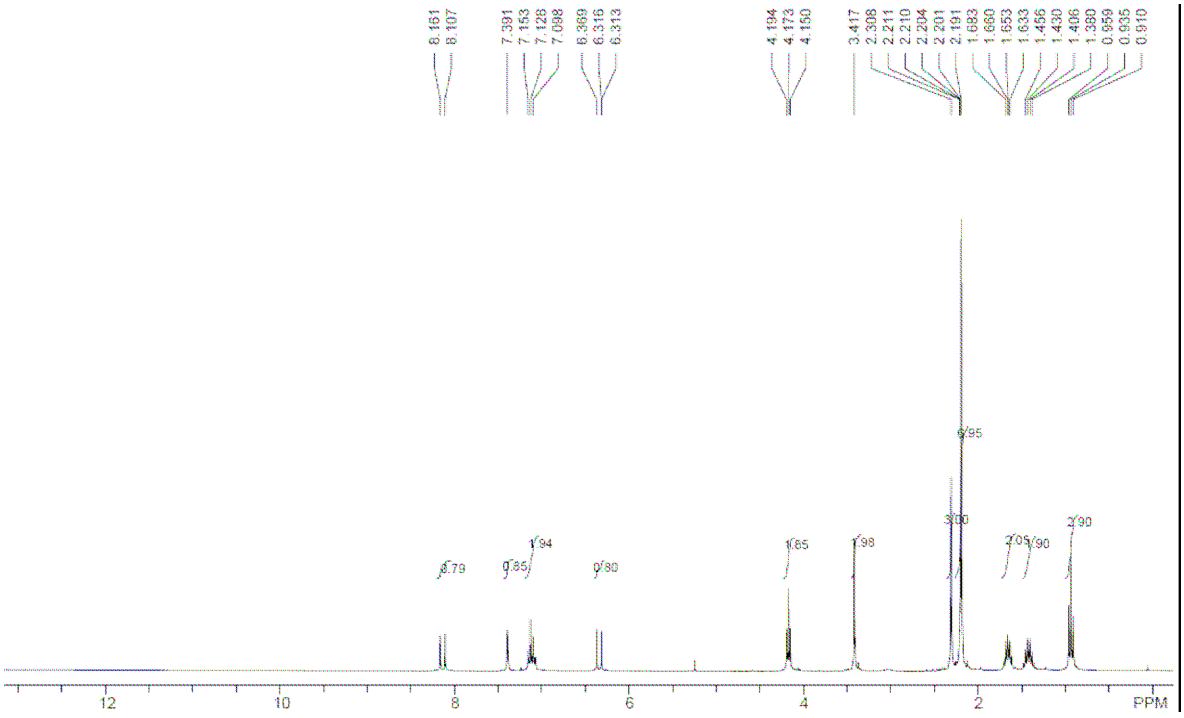

NMe2
COOBun

3ia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4.150
3.417
2.308
2.211
2.210
2.204
2.201
2.191
1.683
1.660
1.653
1.633
1.456
1.430
1.406
1.380
0.959
0.935
0.910
0.79
0.85
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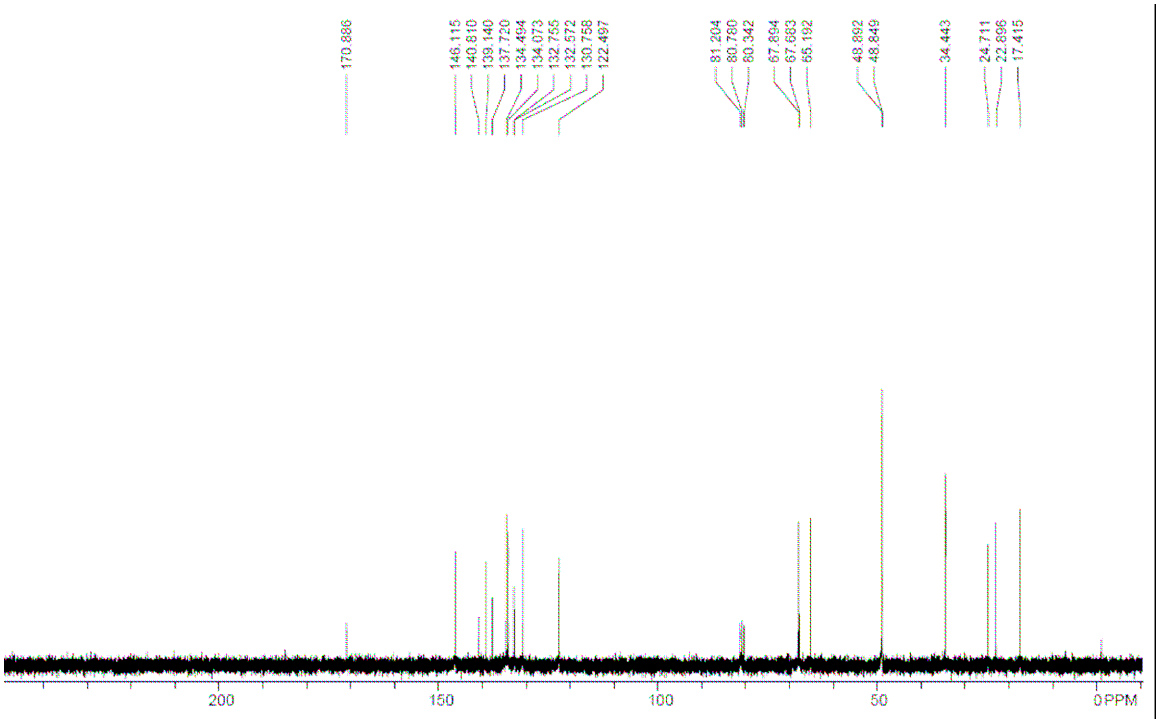
12
10
8
6
4
2
PPM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80.780
80.342
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17.415
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100
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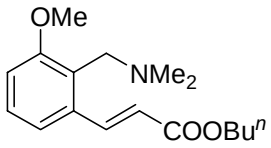
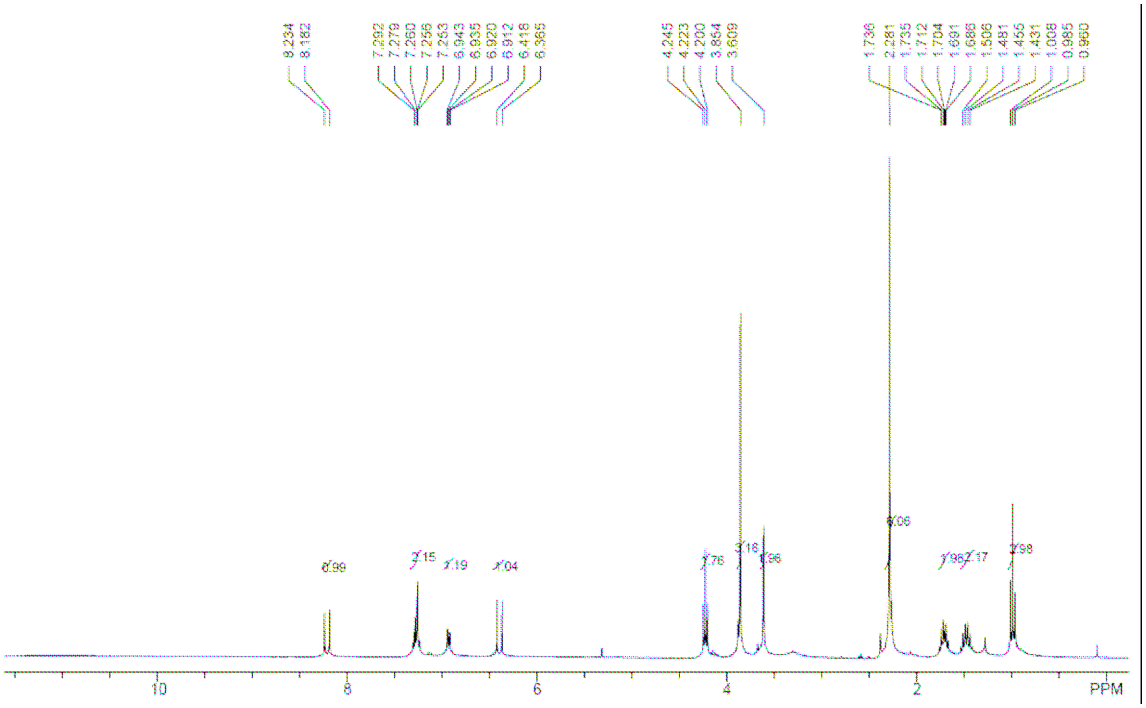
0 PPM


OMe
NMe2
COOBun

3ja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6.365
4.245
4.223
4.200
3.854
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1.704
1.691
1.688
1.506
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1.453
1.431
1.008
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0.960
0.99
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1.19
1.04
1.76
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6.06
1.96
2.17
1.98
10
8
6
4
2
PPM


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142.688
136.086
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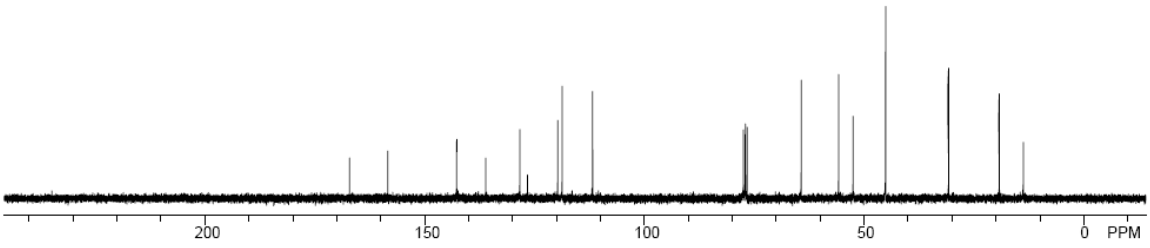
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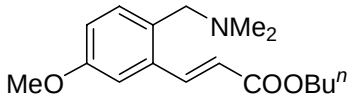
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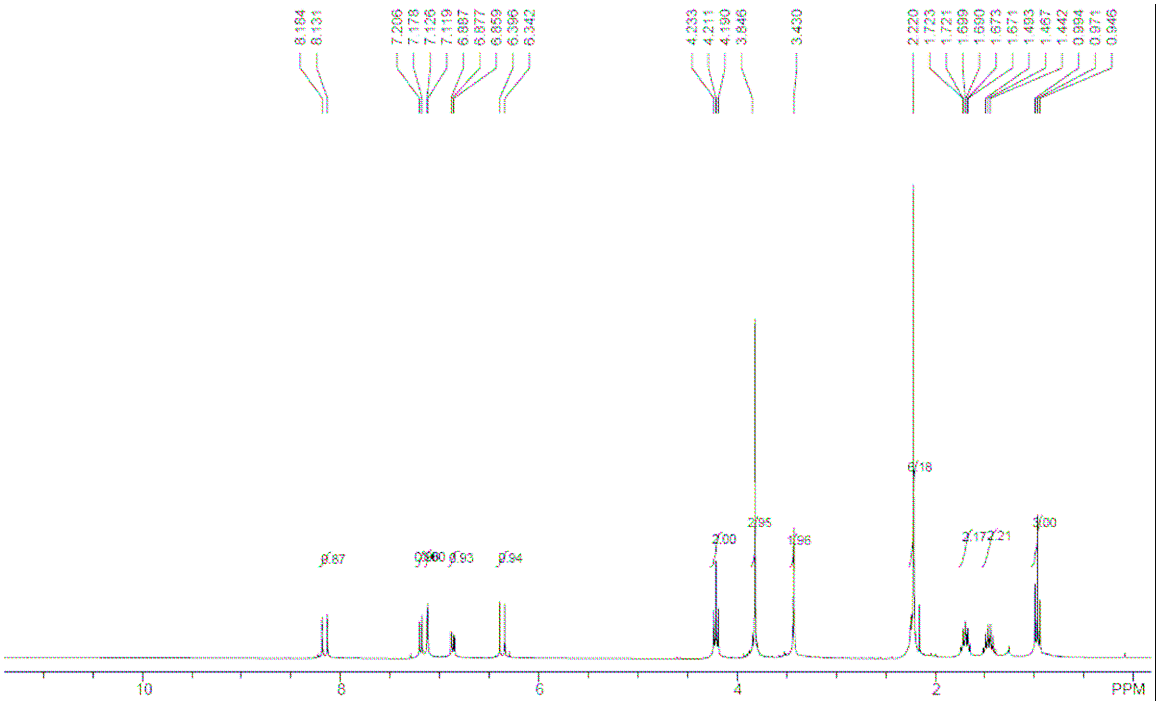
MeO
COOBu^n

3ka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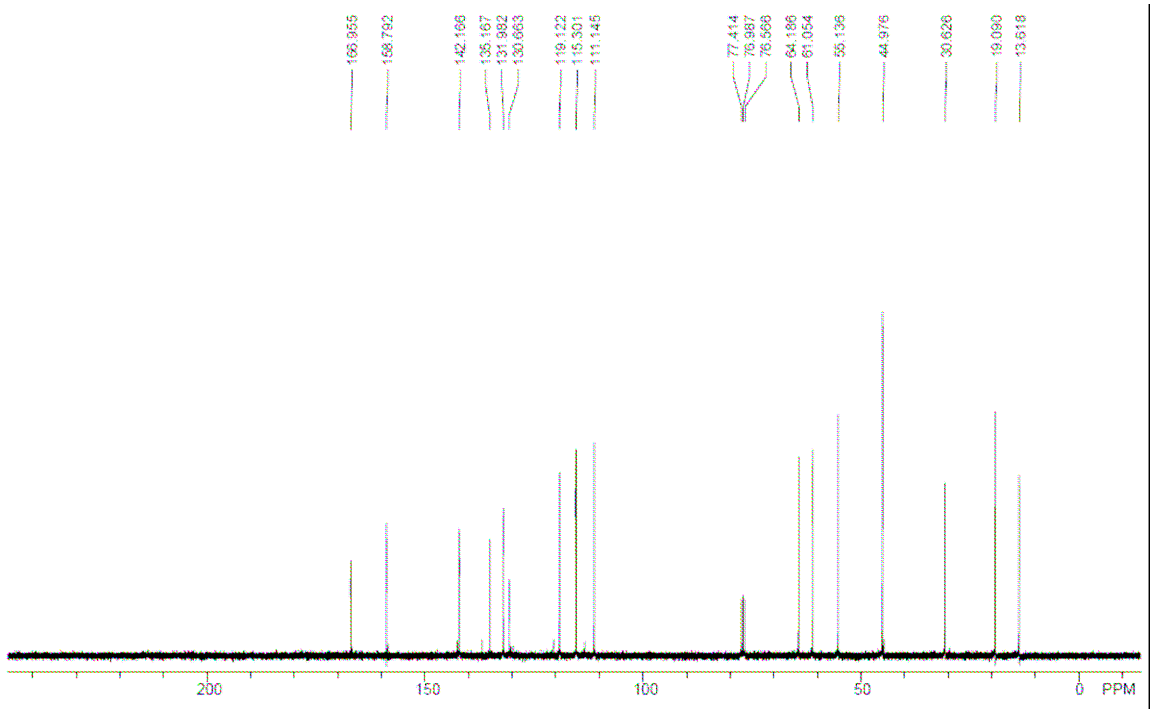
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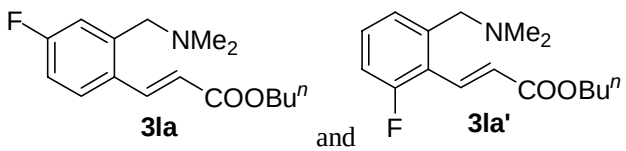
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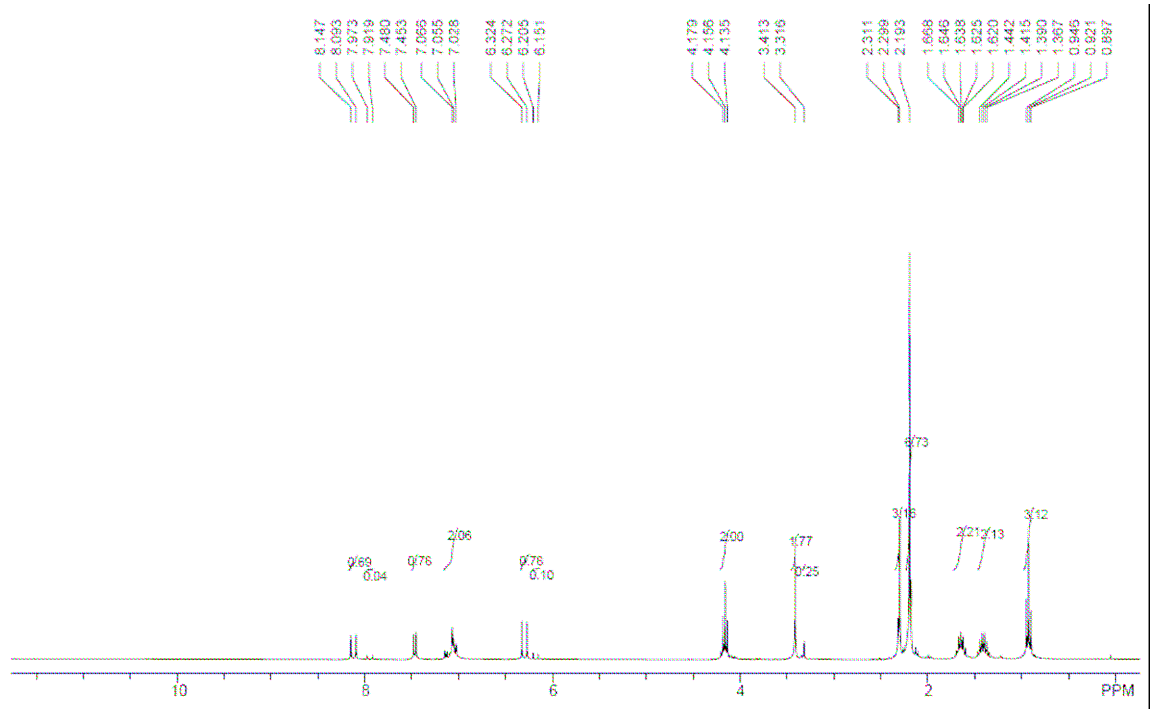
COOBun
3la
and
NMe2
COOBun
F
3la'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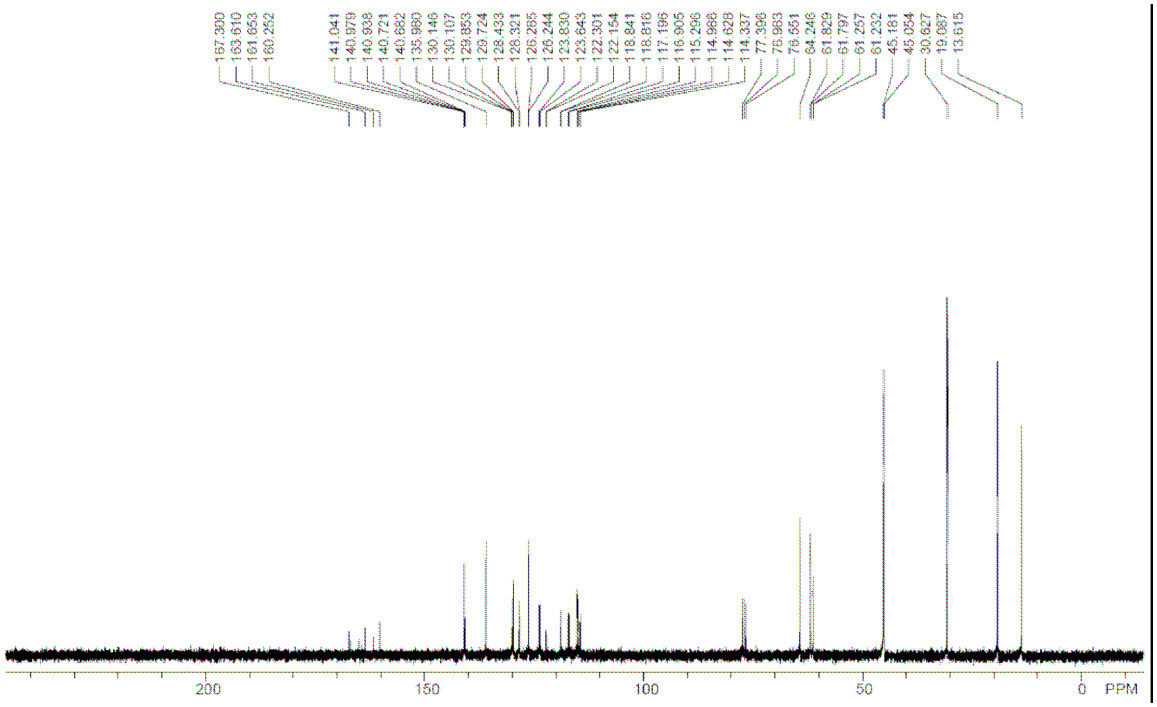
PPM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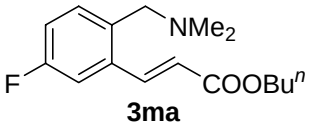
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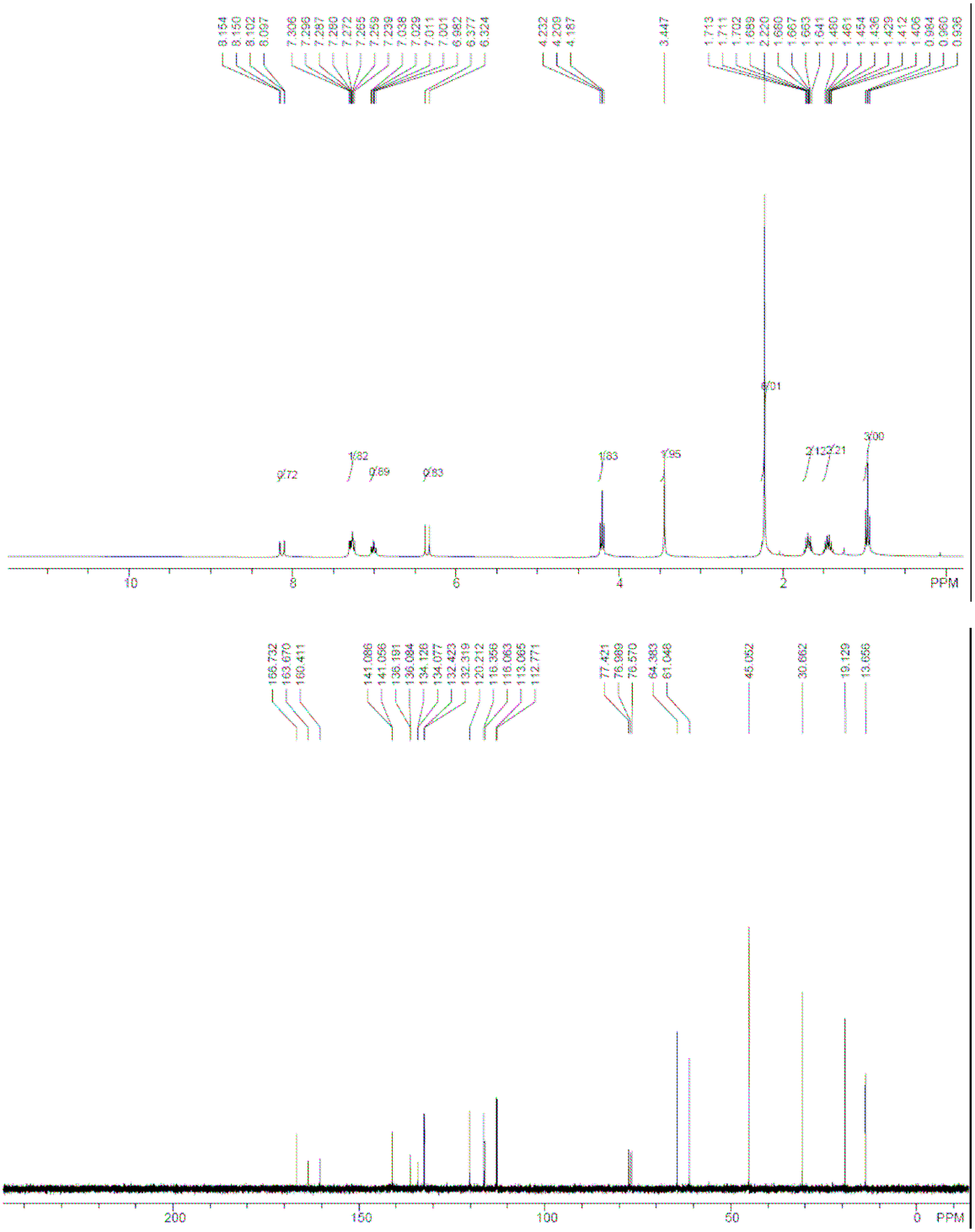
COOBu^n

3ma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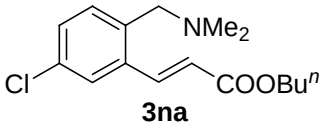
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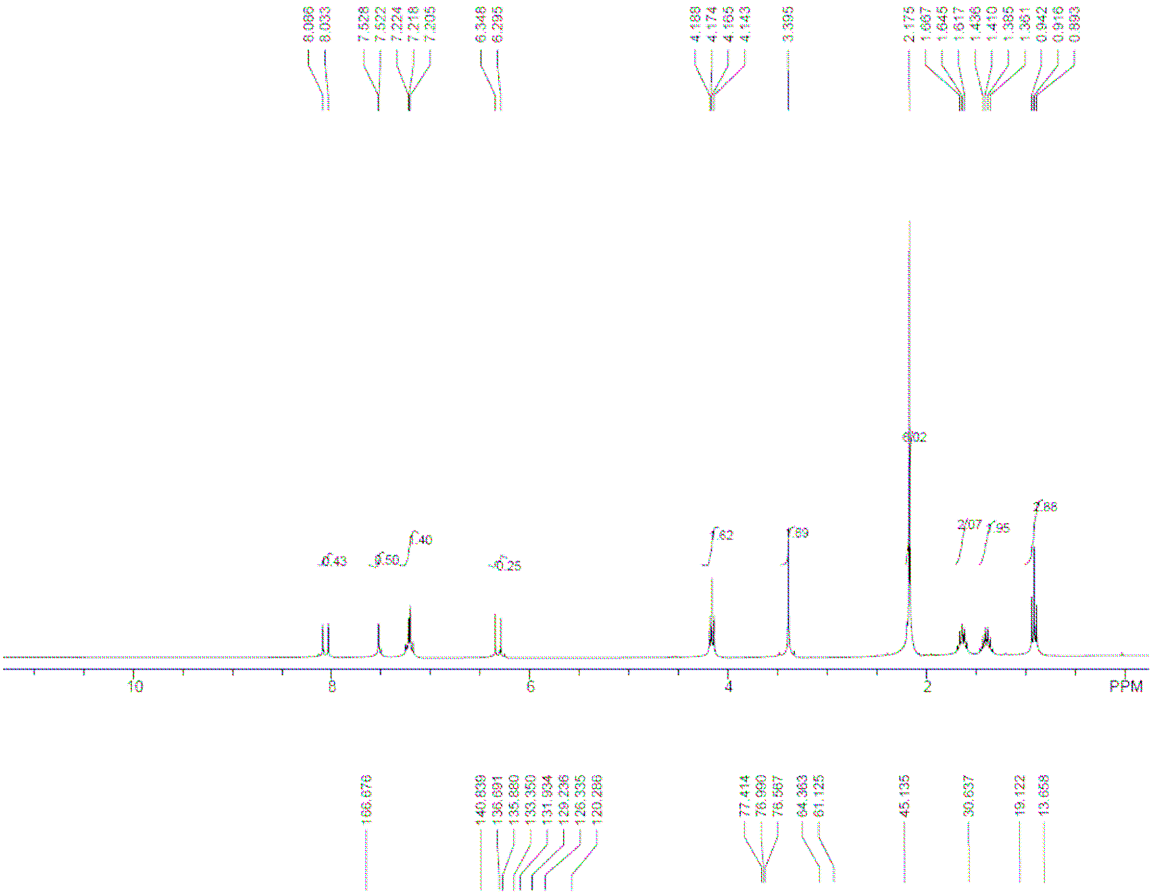
Cl
COOBu^n

3na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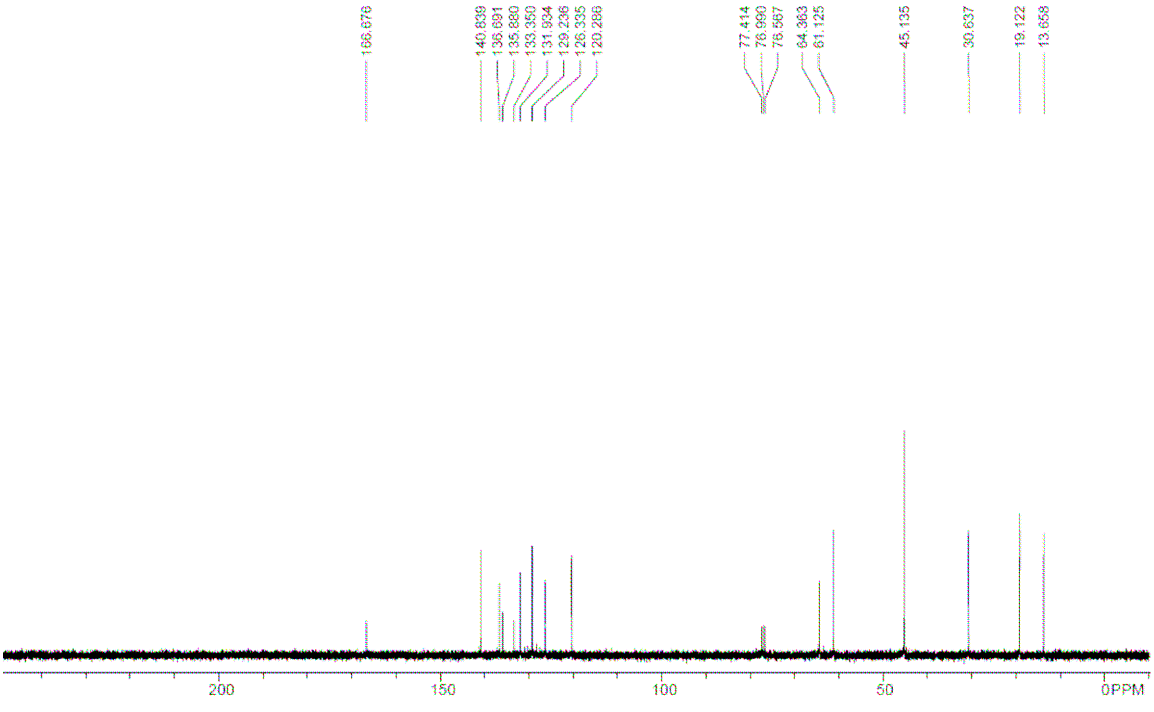
6
4
2
PPM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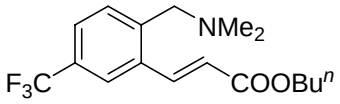
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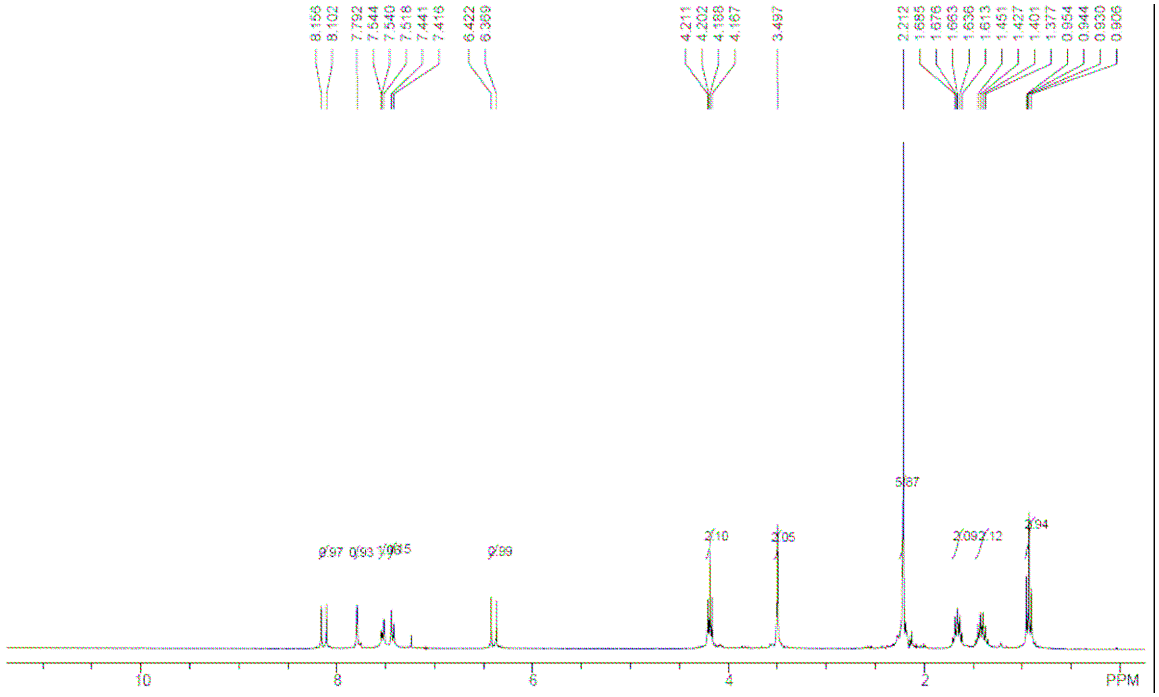
F3C
COOBun

3oa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7.416
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6.359
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4.202
4.188
4.167
3.497
2.212
1.685
1.676
1.663
1.636
1.613
1.451
1.427
1.401
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0.944
0.930
0.906
5.87
2.94
10
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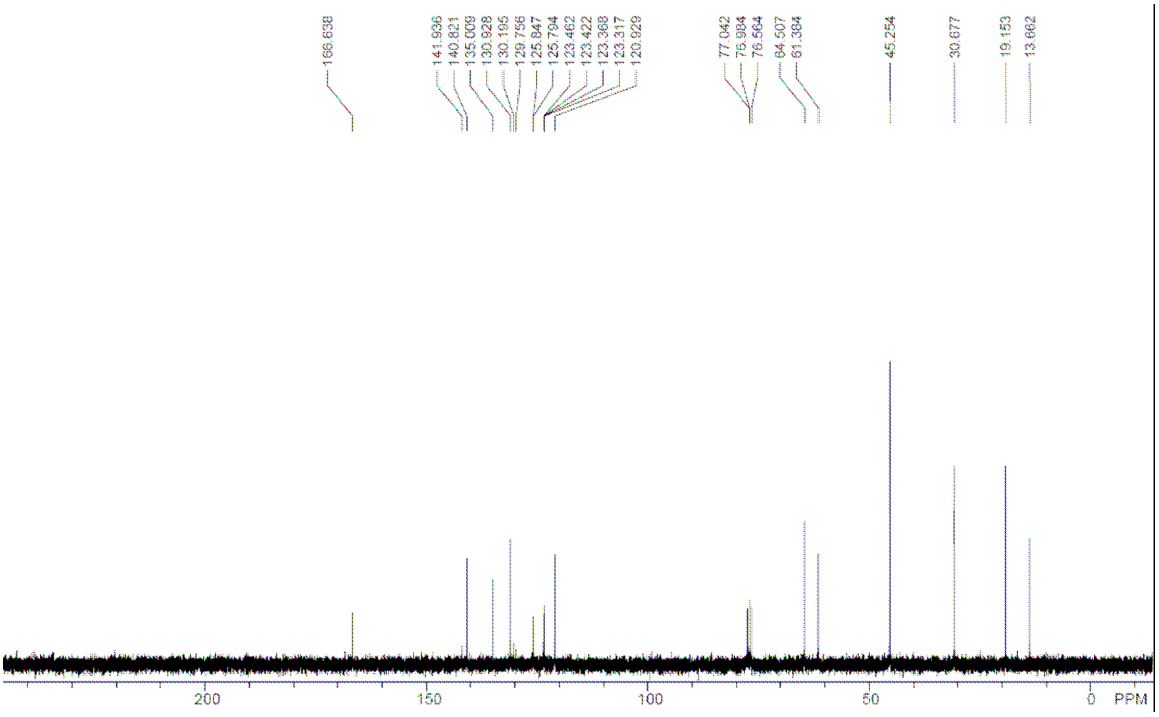
6
4
2
PPM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140.821
135.009
130.928
130.195
129.756
125.947
125.794
123.462
123.422
123.368
123.317
120.929
77.042
76.984
76.564
64.507
61.384
45.254
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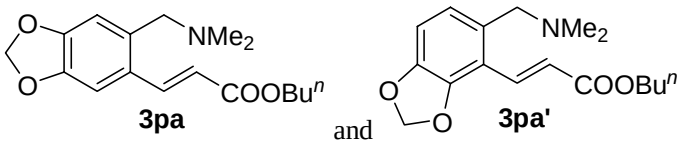
19.153
13.662
200
150
100
50
0
PPM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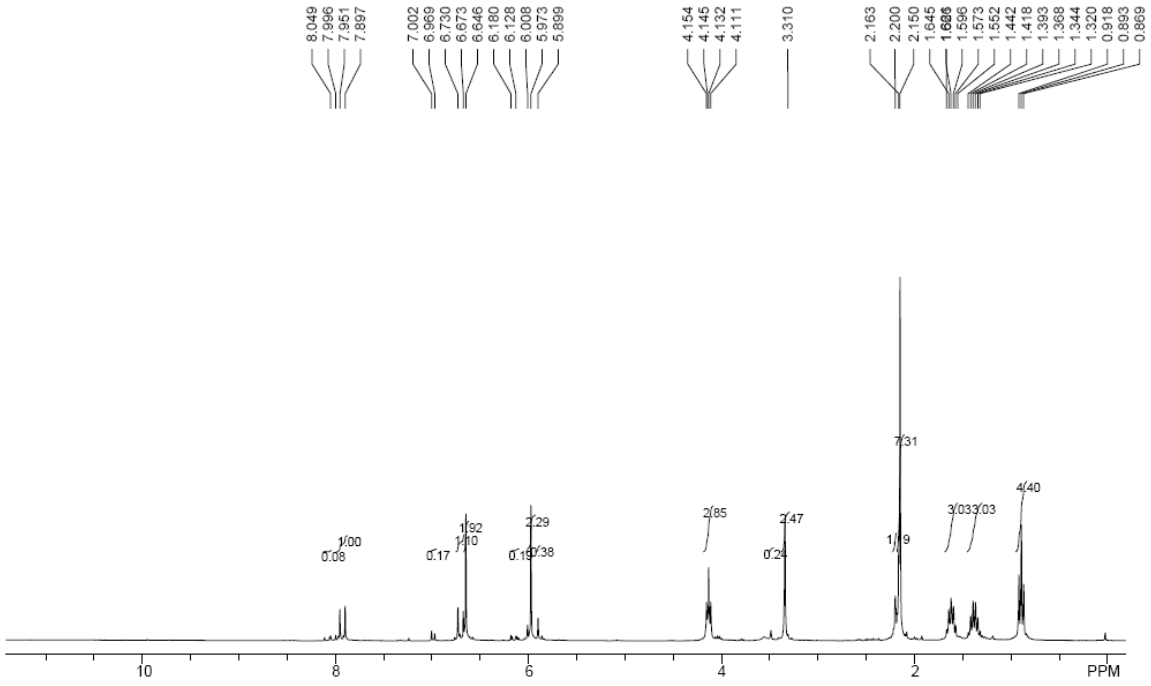
COOBu^n
3pa
and
NMe2
COOBu^n
3pa'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6.730
6.673
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6.180
6.128
6.008
5.973
5.899
4.154
4.145
4.132
4.111
3.310
2.163
2.200
2.150
1.645
1.596
1.573
1.552
1.442
1.418
1.393
1.368
1.344
1.320
0.918
0.893
0.869
1.00
0.08
0.17
1.92
1.10
2.29
0.38
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3.03
4.40
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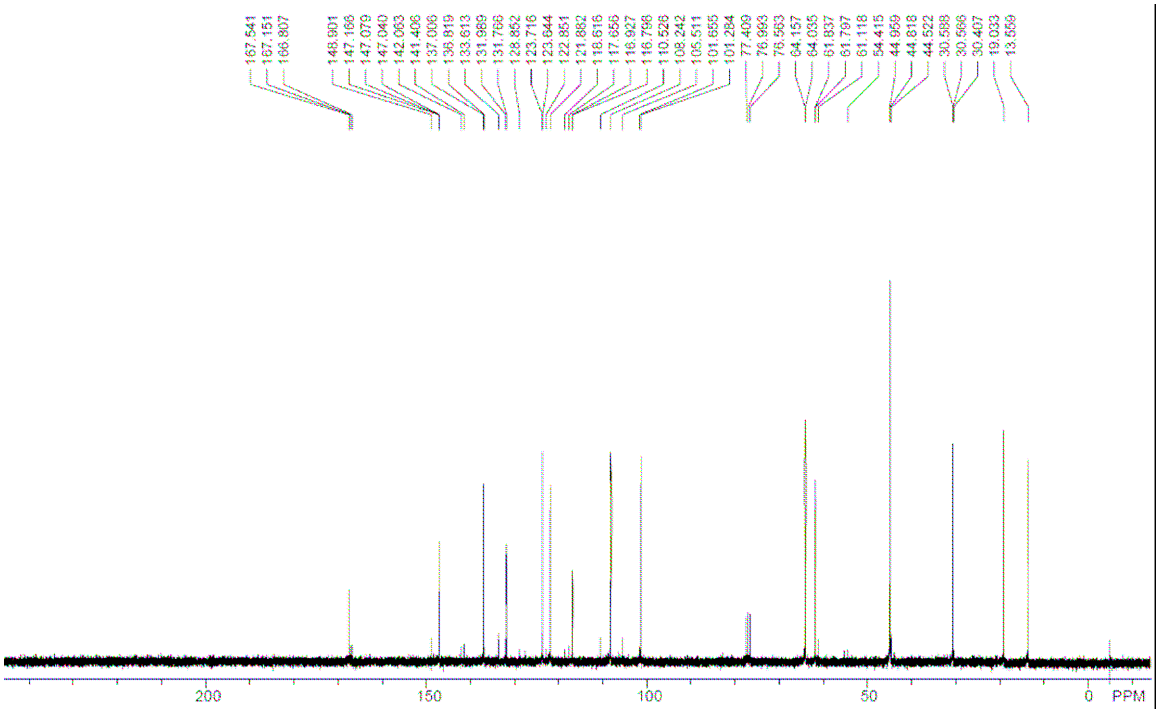
2
PPM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166.807
148.901
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147.079
147.040
142.063
141.406
137.006
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133.613
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131.766
128.852
123.716
123.644
122.951
121.862
118.616
117.856
116.927
116.758
110.526
108.242
105.511
101.655
101.284
77.409
76.993
76.583
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64.035
61.837
61.797
61.118
54.415
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30.566
30.407
19.033
13.559
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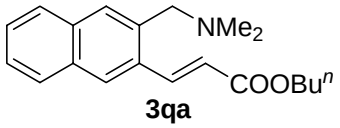
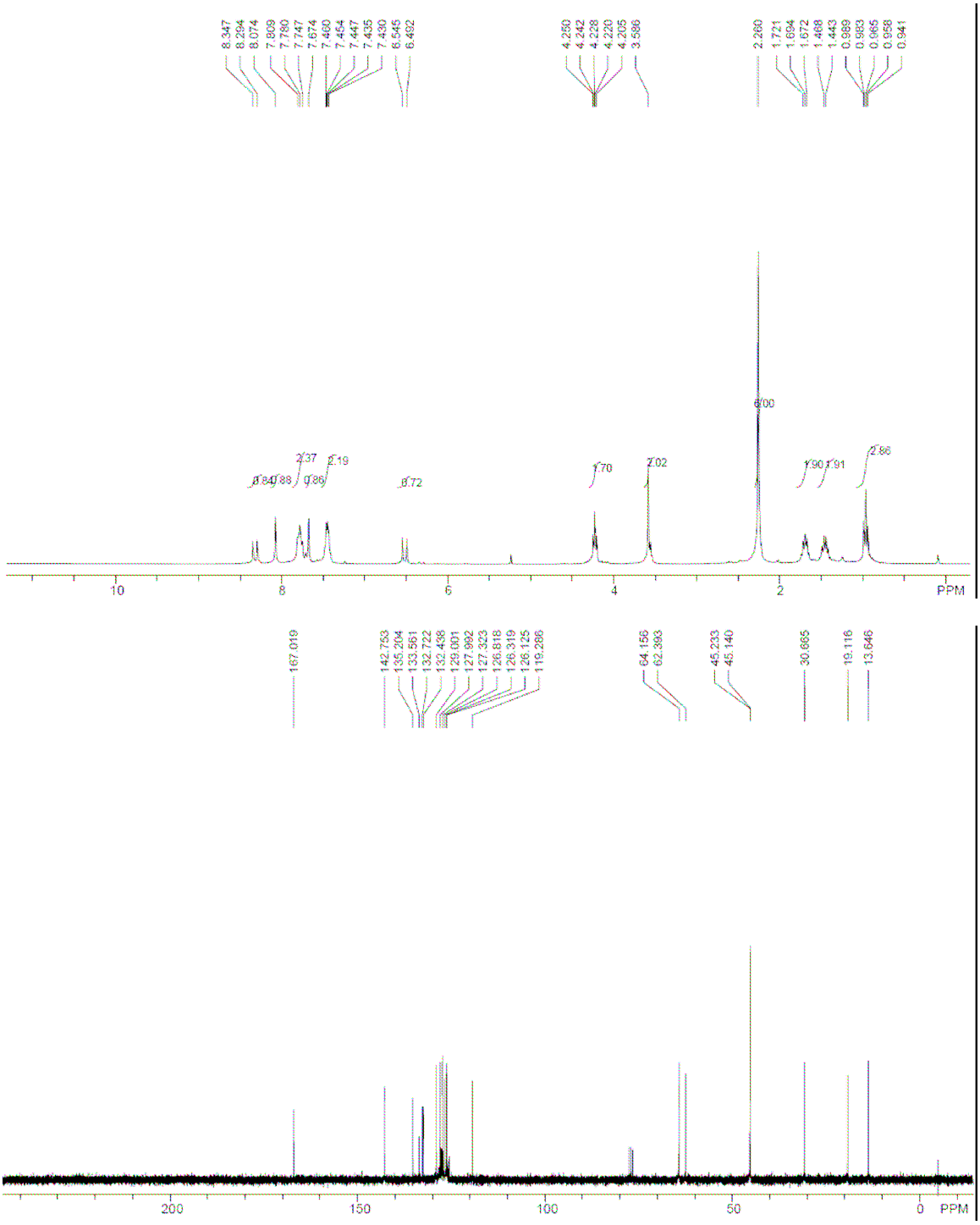
150
100
50
0
PPM


NMe2
COOBun

3qa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7.447
7.435
7.430
6.545
6.492
4.250
4.242
4.238
4.220
4.205
3.586
2.260
1.721
1.694
1.672
1.468
1.443
0.989
0.983
0.965
0.958
0.941
0.84
0.88
2.37
0.86
2.19
0.72
1.70
2.02
6.00
1.90
1.91
2.86
10
8
6
4
2
PPM
167.019
142.753
135.204
133.561
132.722
132.438
129.001
127.992
127.323
126.818
126.319
126.125
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13.646
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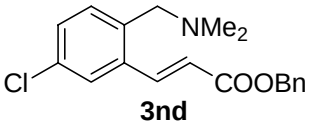
150
100
50
0
PPM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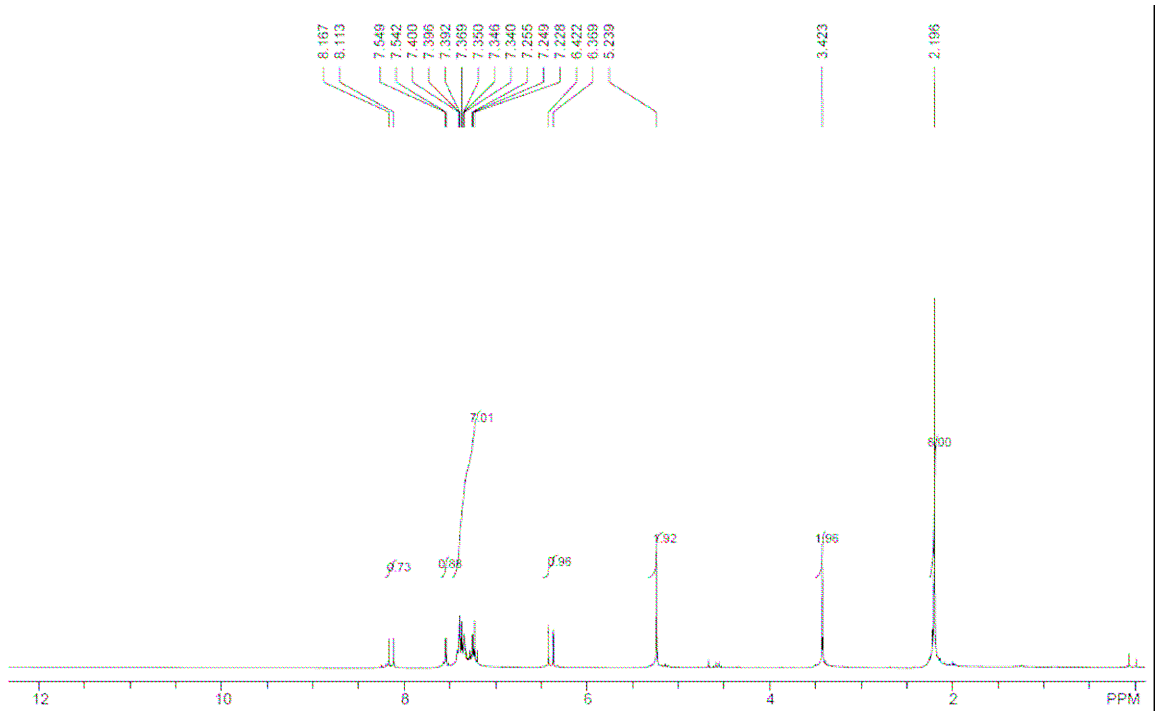
Cl
COOBn

3nd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7.392
7.369
7.350
7.346
7.340
7.255
7.249
7.228
6.422
6.369
5.239
3.423
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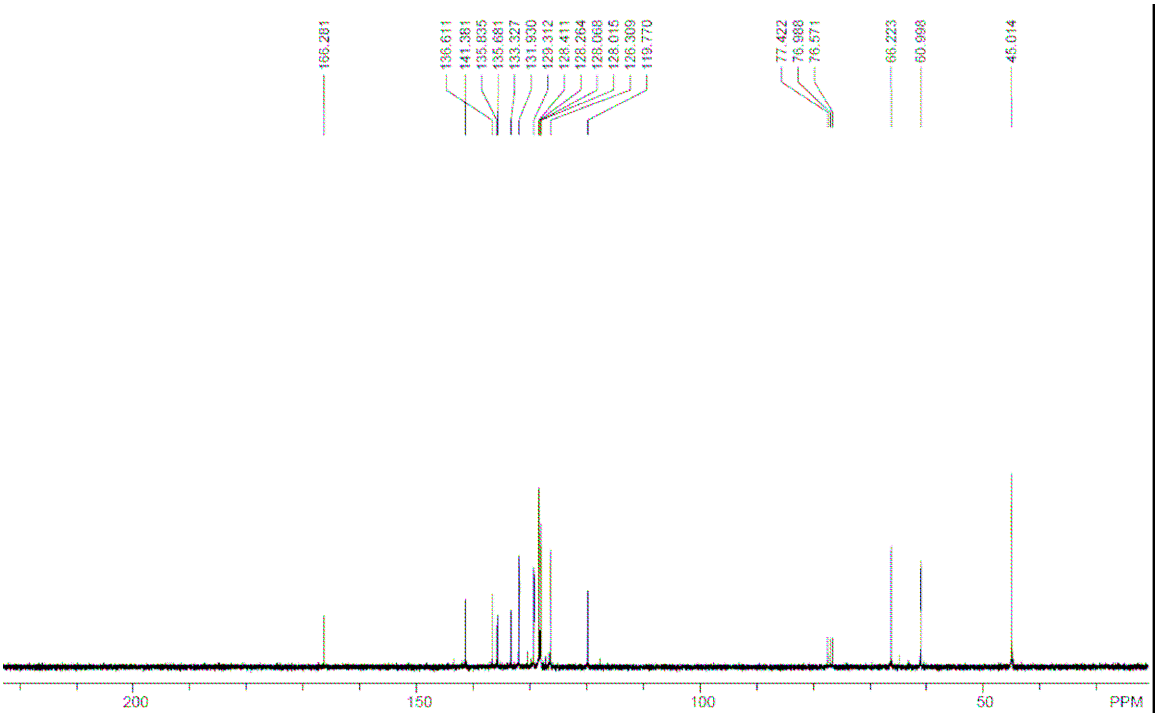
0.73
0.88
0.96
1.92
1.96
12
10
8
6
4
2
PPM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131.930
129.312
128.411
128.264
128.068
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126.309
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77.422
76.988
76.571
66.223
60.998
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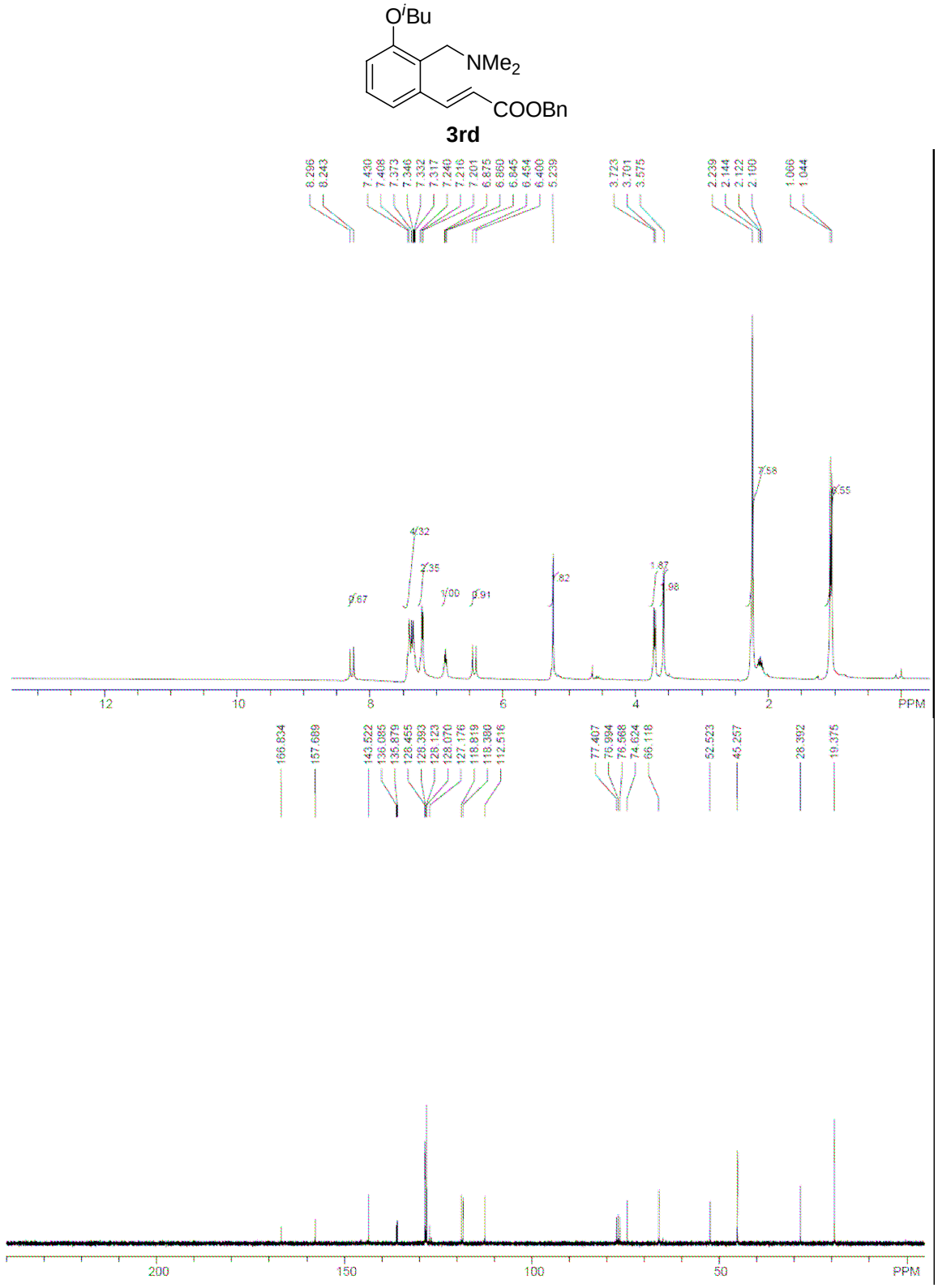
200
150
100
50
PPM


O^{i}Bu
NMe$_2$
COOBn
3rd
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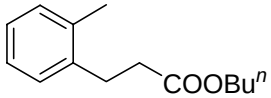
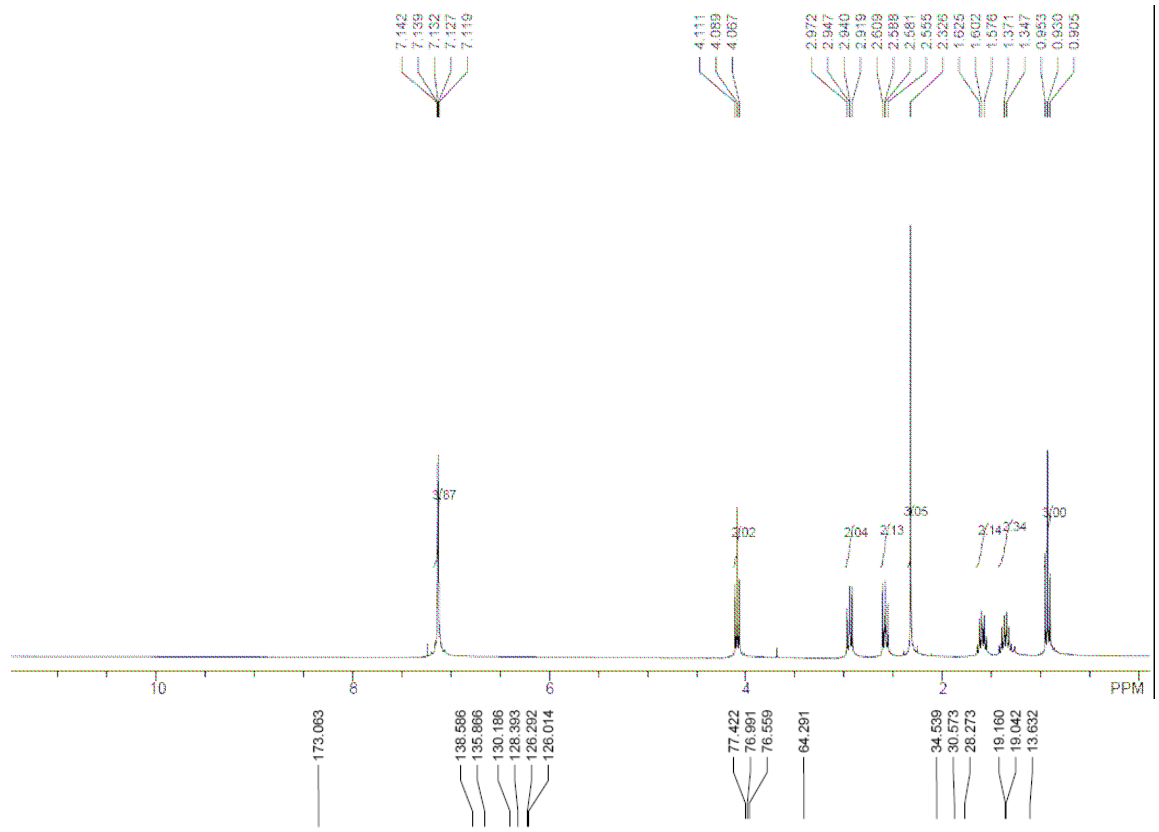
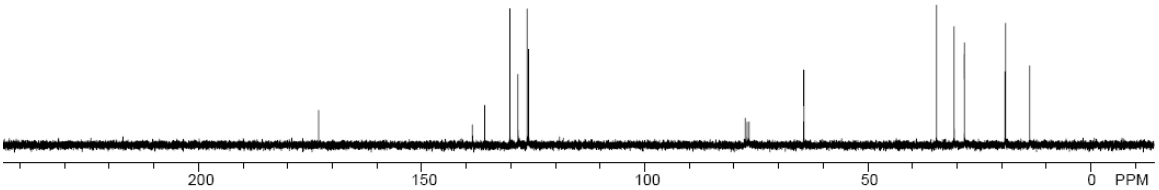
7.430
7.408
7.373
7.346
7.332
7.317
7.240
7.216
7.201
6.875
6.860
6.845
6.454
6.400
5.239
3.723
3.701
3.575
2.239
2.144
2.122
2.100
1.066
1.044
7.58
6.55
4.32
2.35
1.87
1.98
1.00
0.91
0.67
2.82
12
10
8
6
4
2
PPM
166.834
157.689
143.522
136.085
135.879
128.455
128.393
128.123
128.070
127.176
118.819
118.380
112.516
77.407
76.994
76.568
74.624
66.118
52.523
45.257
28.392
19.375
200
150
100
50
PPM

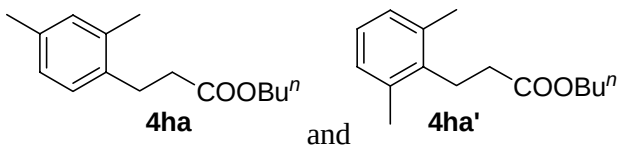
NMR spectrum of compounds **4aa-4rd**



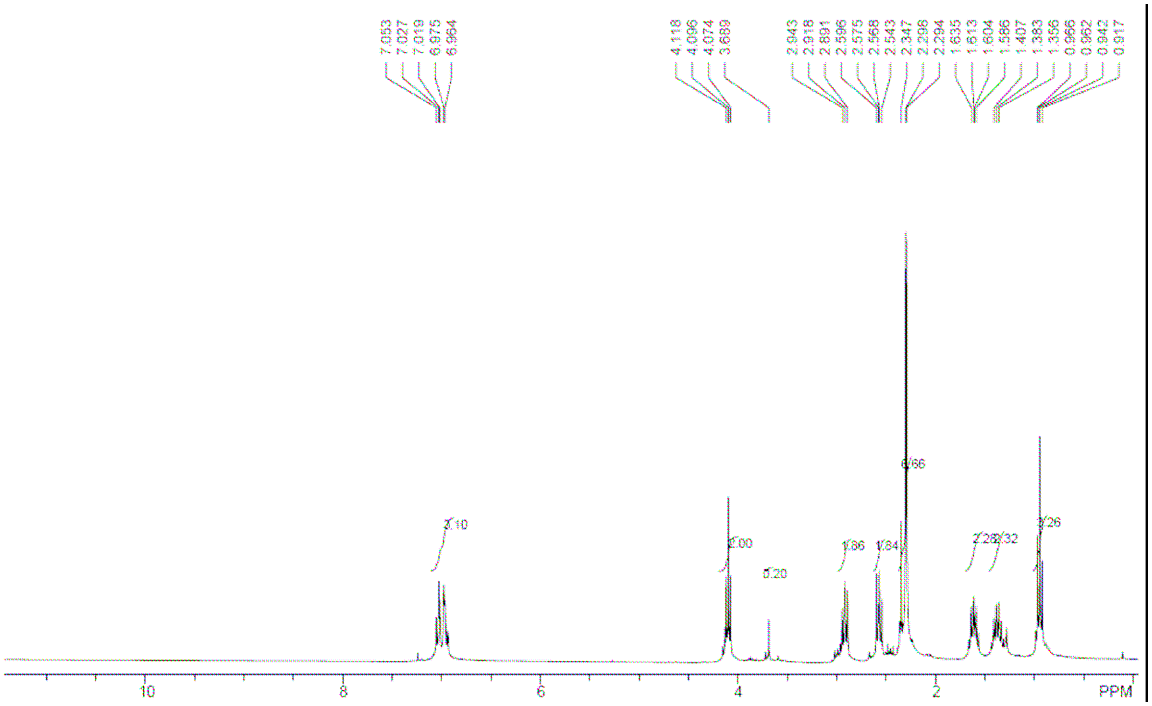
4aa






COOBu^n
COOBu^n

4ha and **4ha'**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4.074
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2.943
2.918
2.891
2.595
2.575
2.568
2.543
2.347
2.296
2.294
1.635
1.613
1.604
1.586
1.407
1.383
1.356
0.966
0.962
0.942
0.917
2.10
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1.84
6.66
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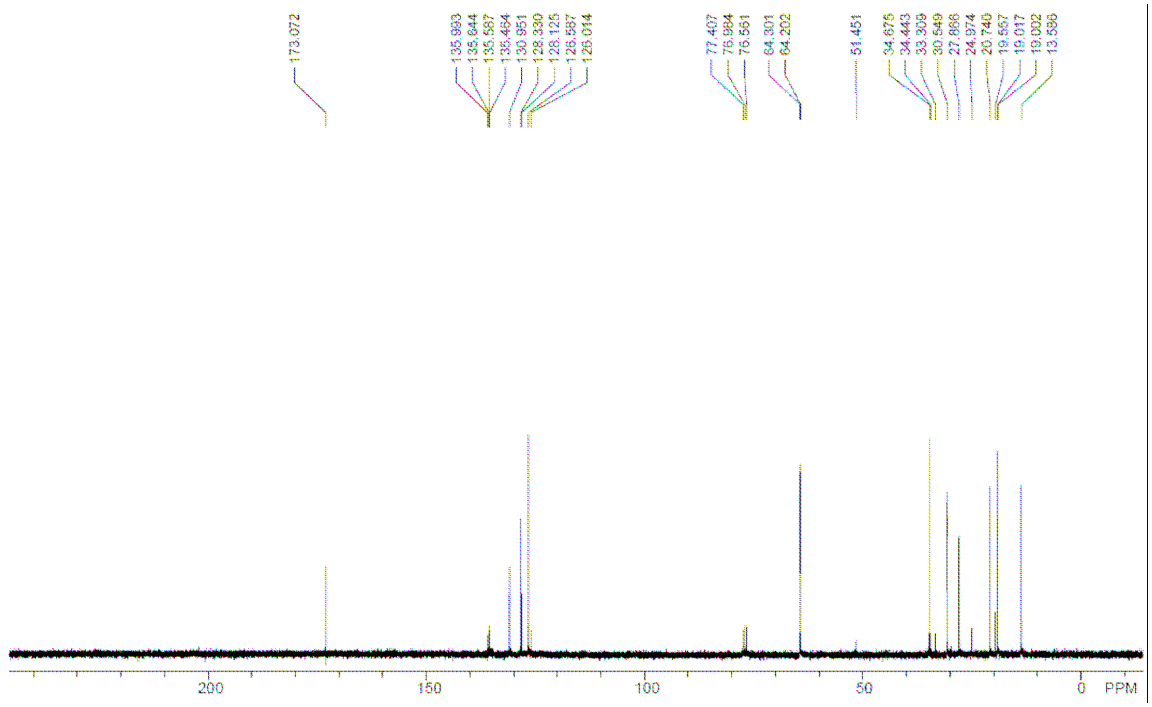
2.32
3.26
10
8
6
4
2
PPM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128.125
128.087
128.014
77.407
76.984
76.561
64.301
64.202
51.451
34.675
34.443
33.369
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19.002
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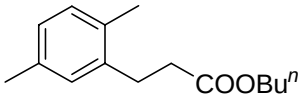
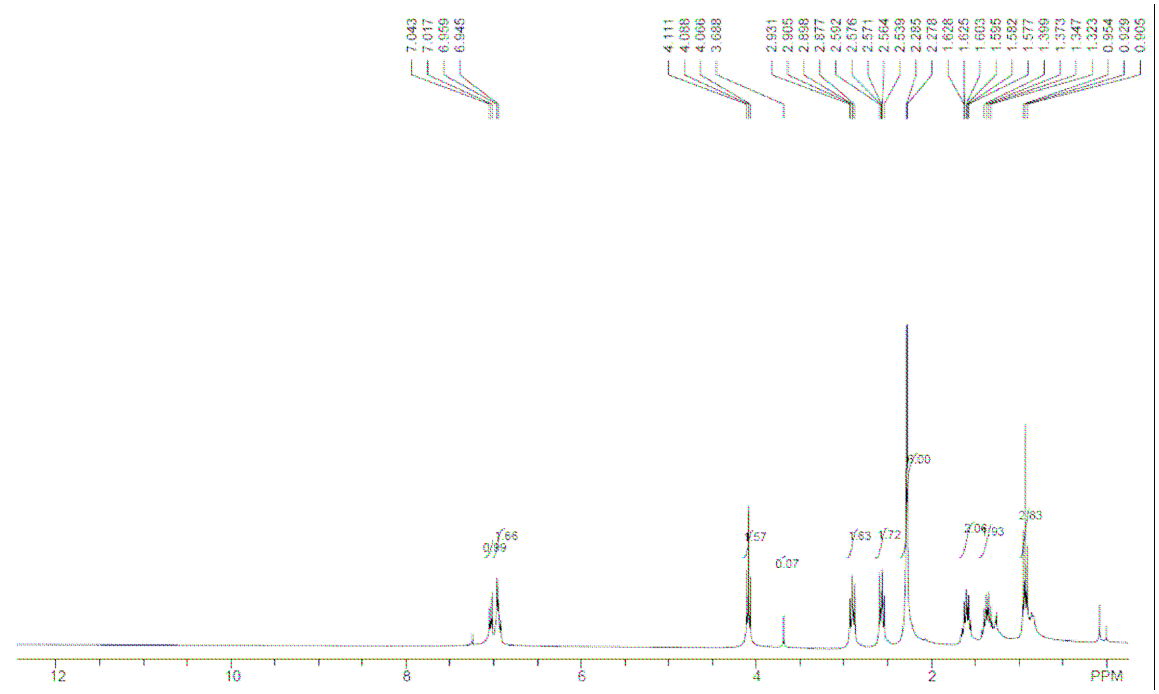
200
150
100
50
0
PPM


COOBu^n

4ia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4.066
3.688
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2.905
2.898
2.877
2.592
2.576
2.571
2.564
2.539
2.285
2.278
1.628
1.625
1.603
1.595
1.582
1.577
1.399
1.373
1.347
1.323
0.954
0.929
0.905
9.00
2.83
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1.57
1.66
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4
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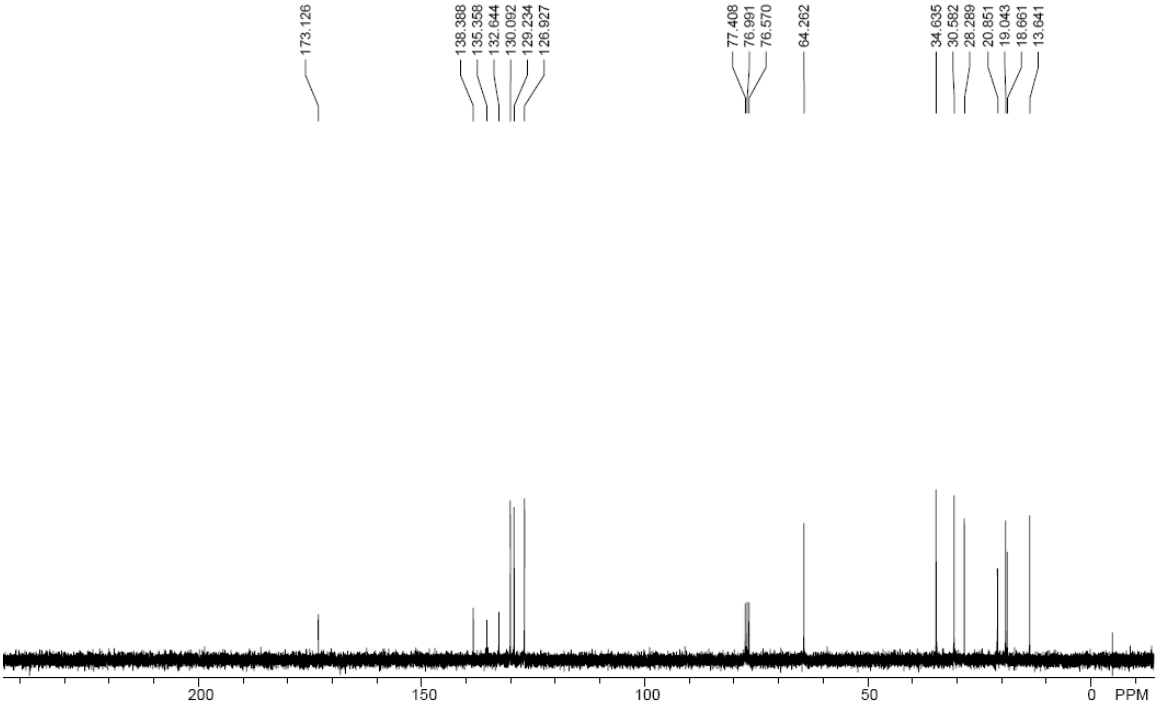
PPM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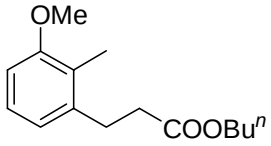
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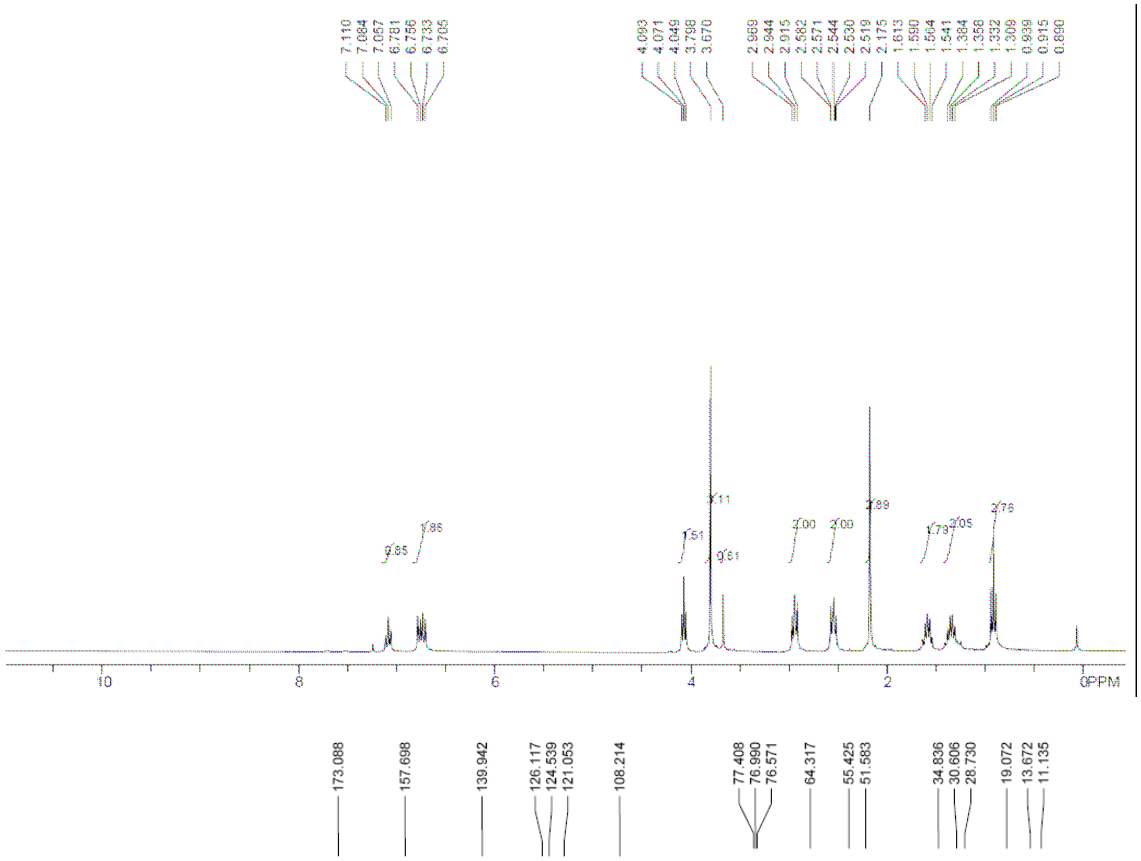
COOBu^n

4ja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6.705
4.093
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4.049
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2.969
2.944
2.915
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2.519
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1.590
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1.541
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1.332
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2.05
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4
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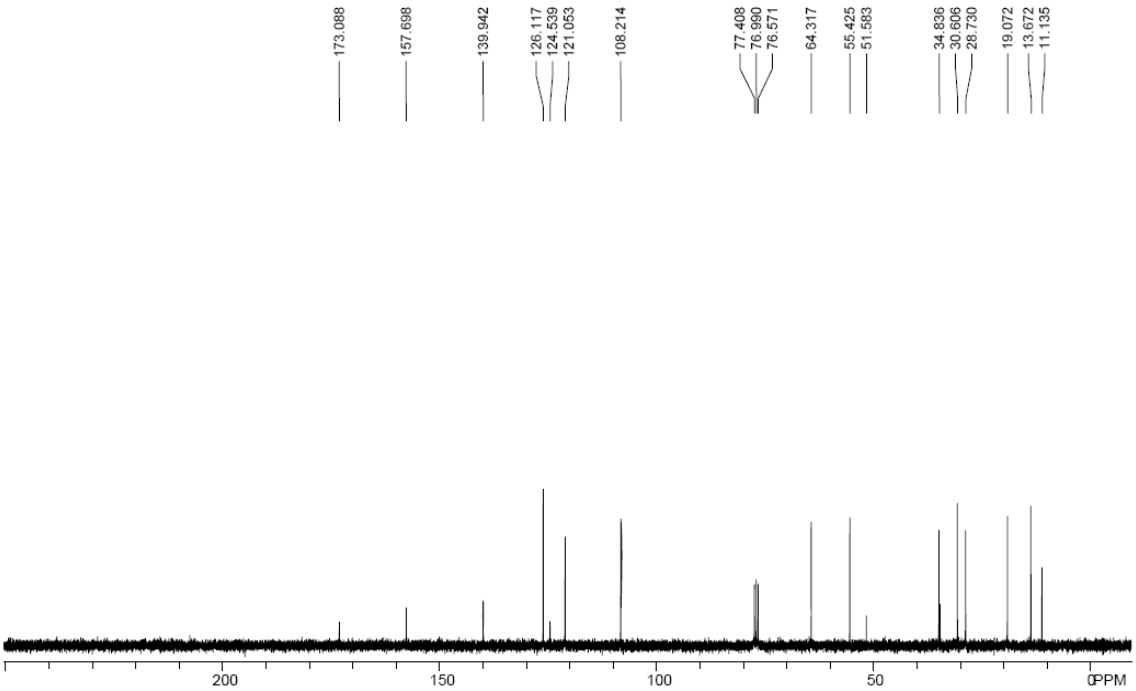
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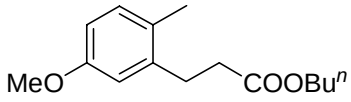
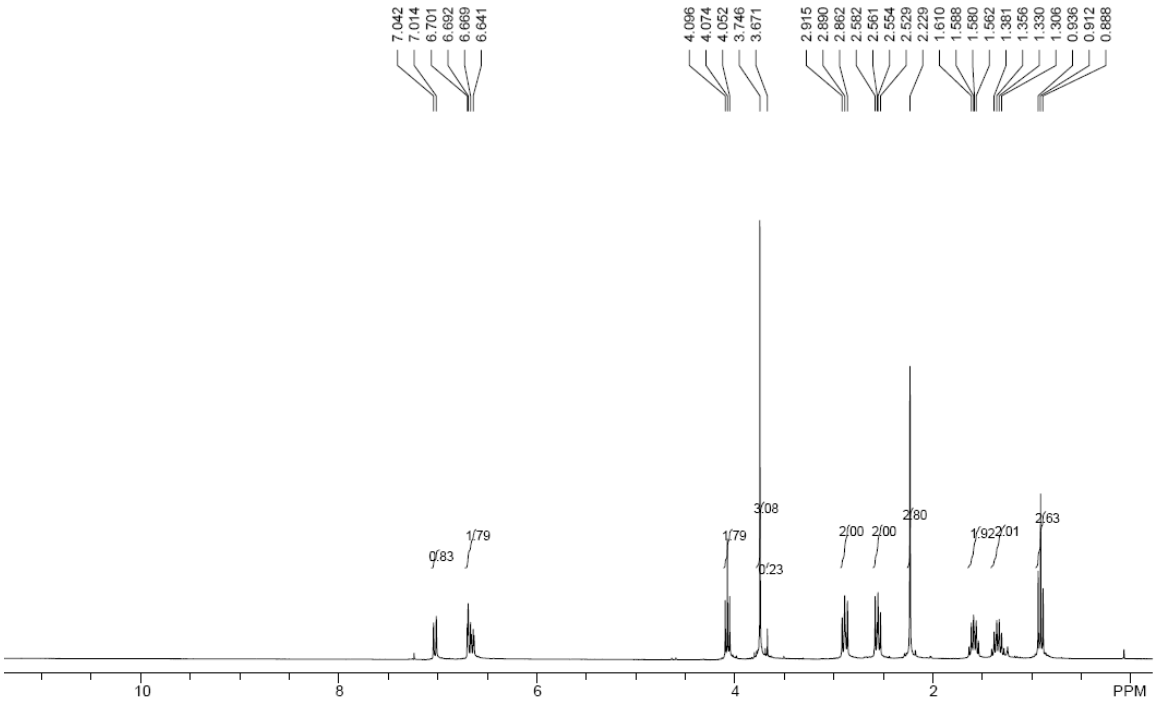
200
150
100
50
0PPM


MeO
COOBu^n

4ka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1.562
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1.330
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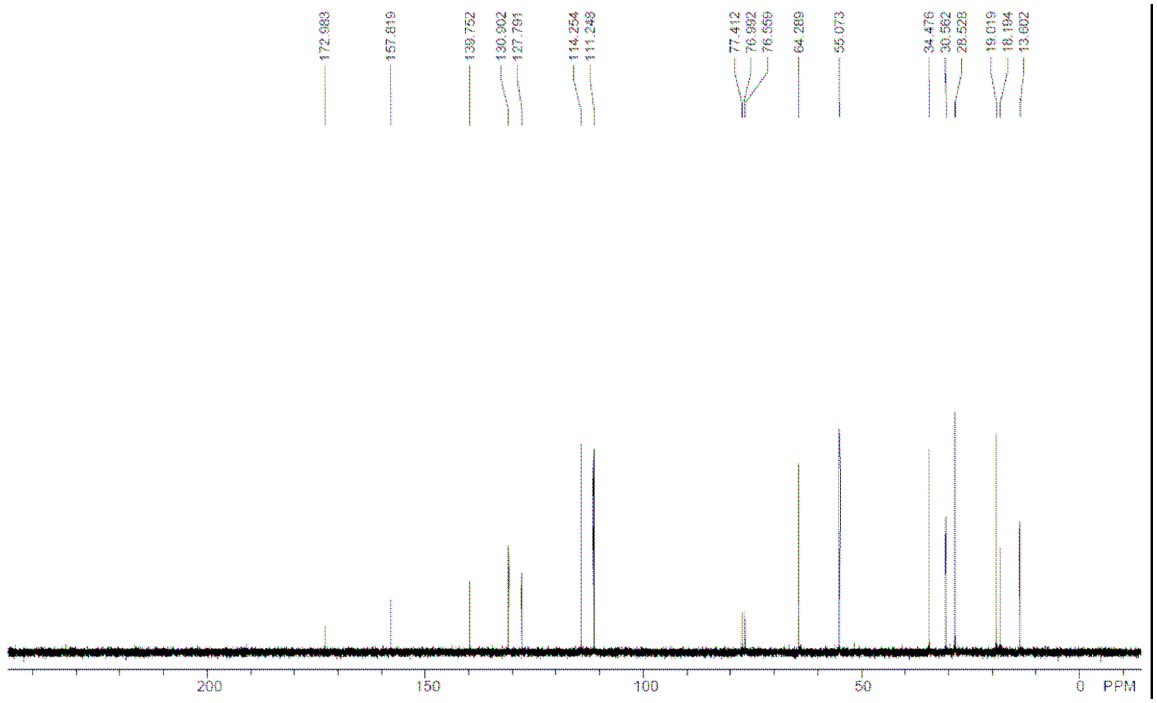
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13.602
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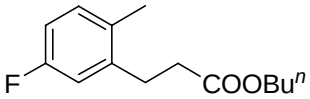
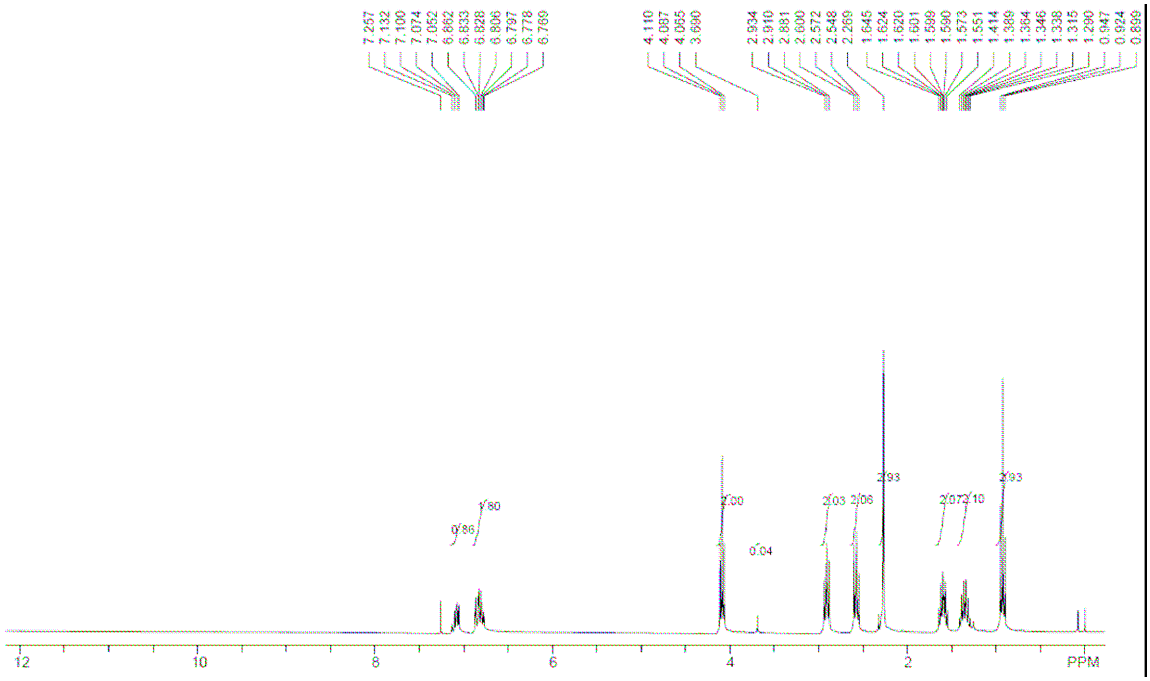

F
COOBu^n

4ma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4.110
4.097
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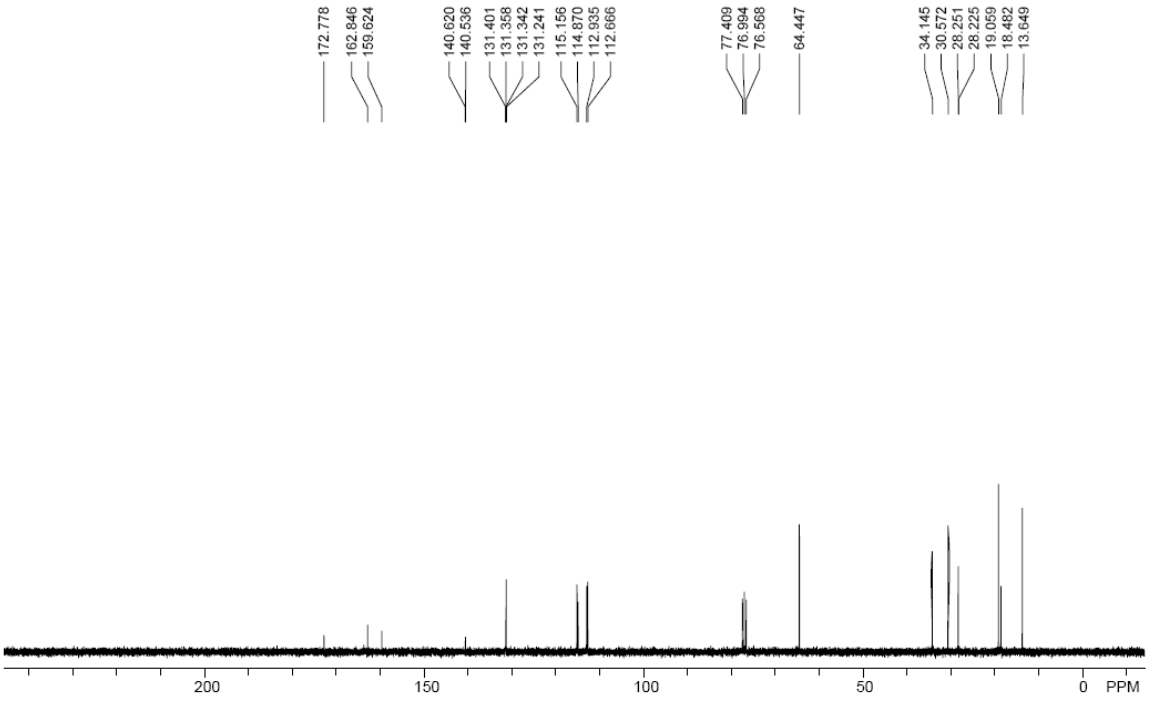
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114.870
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112.666
77.409
76.994
76.568
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28.225
19.059
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13.649
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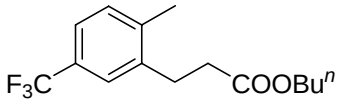
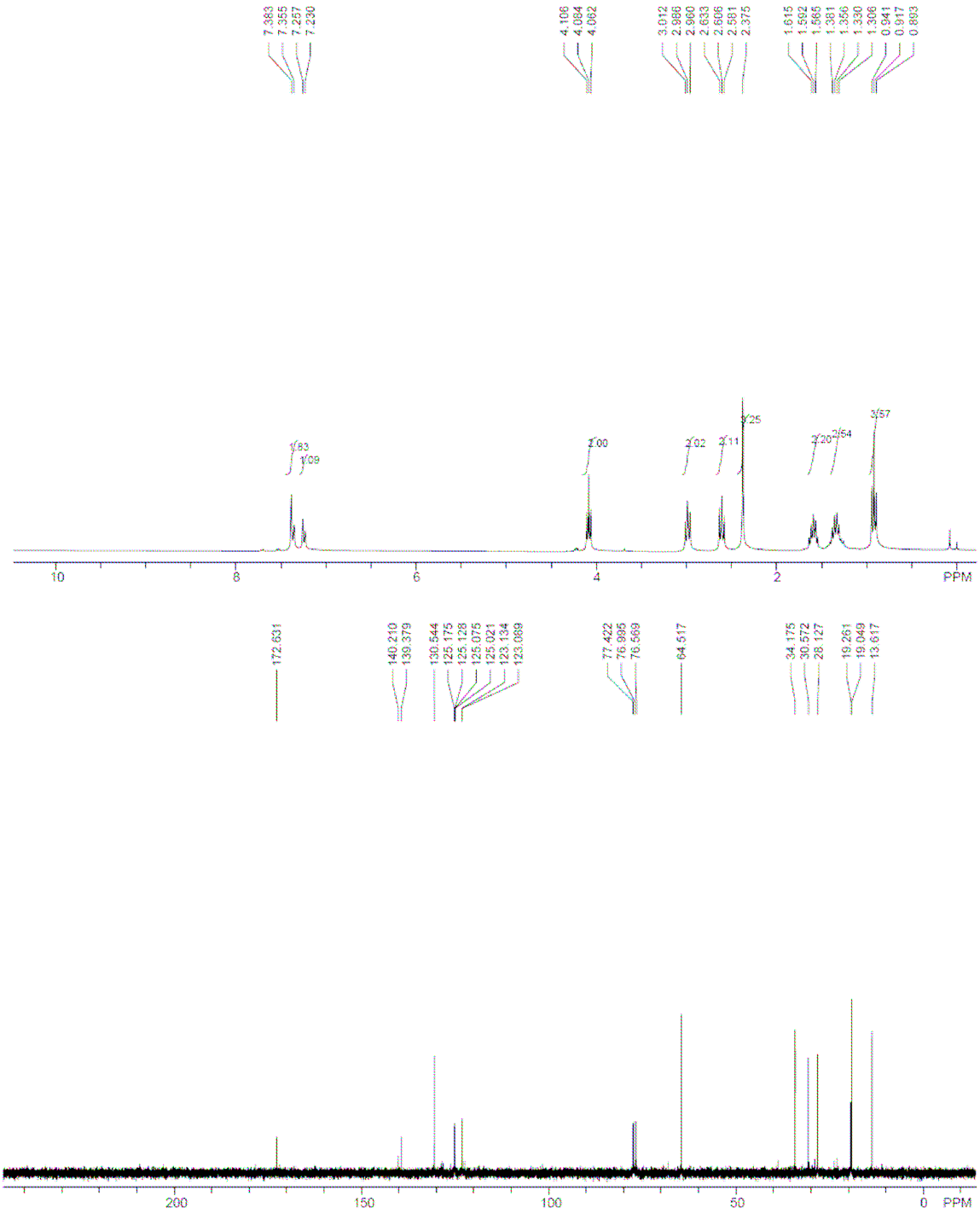
150
100
50
0
PPM


F3C
COOBun

4oa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2.375
1.615
1.592
1.565
1.381
1.356
1.330
1.306
0.941
0.917
0.893
1.83
1.09
1.00
2.02
2.11
3.25
3.20
2.54
3.57
10
8
6
4
2
PPM
172.631
140.210
139.379
130.544
125.175
125.128
125.075
125.021
123.134
123.089
77.422
76.995
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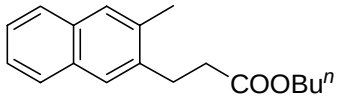
PPM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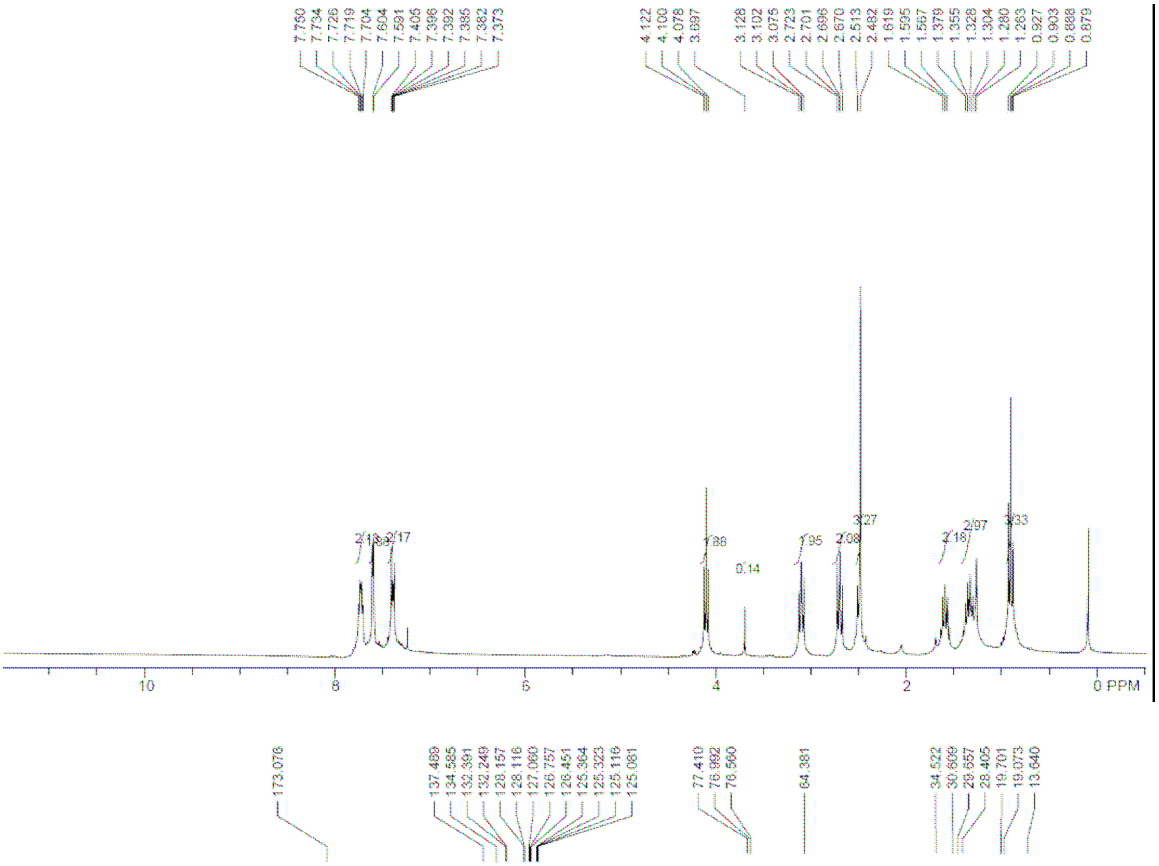
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7.373
4.122
4.100
4.078
3.697
3.128
3.102
3.075
2.723
2.701
2.696
2.670
2.513
2.492
1.619
1.595
1.567
1.379
1.355
1.328
1.304
1.280
1.263
0.927
0.903
0.888
0.879
2.18
2.18
2.17
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1.95
2.08
3.27
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2.97
3.33
10
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6
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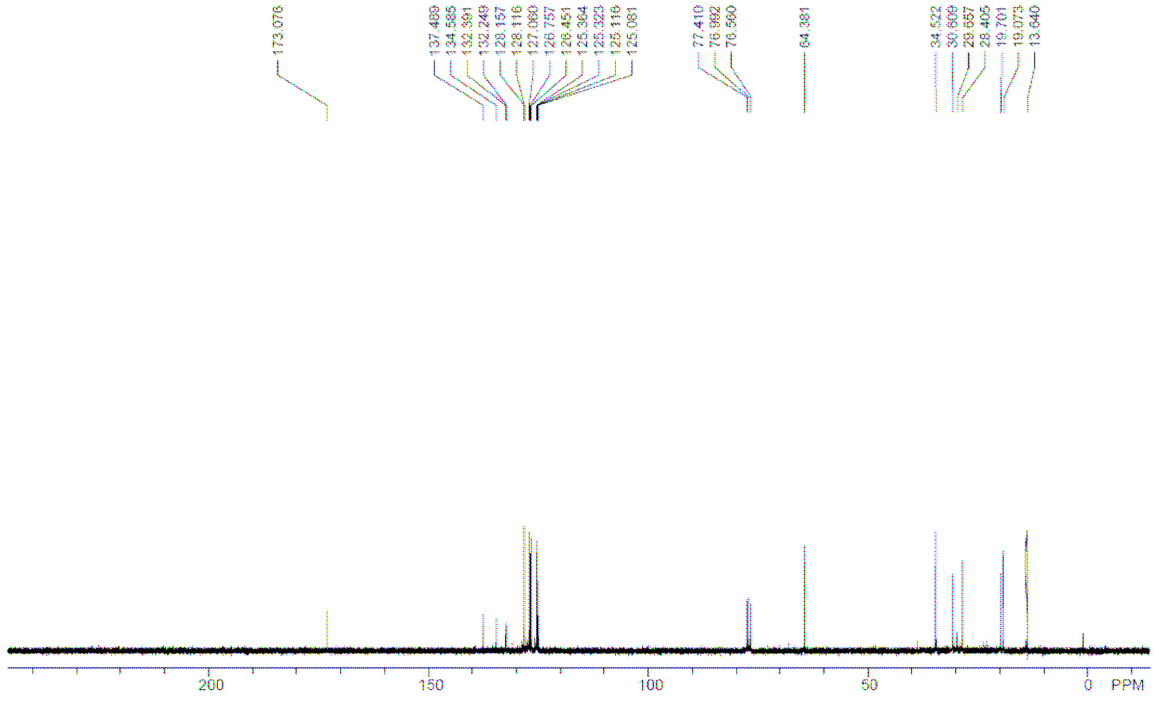
2
0 PPM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132.249
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128.116
127.060
126.757
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125.323
125.116
125.081
77.410
76.992
76.560
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30.609
29.657
28.405
19.701
19.073
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200
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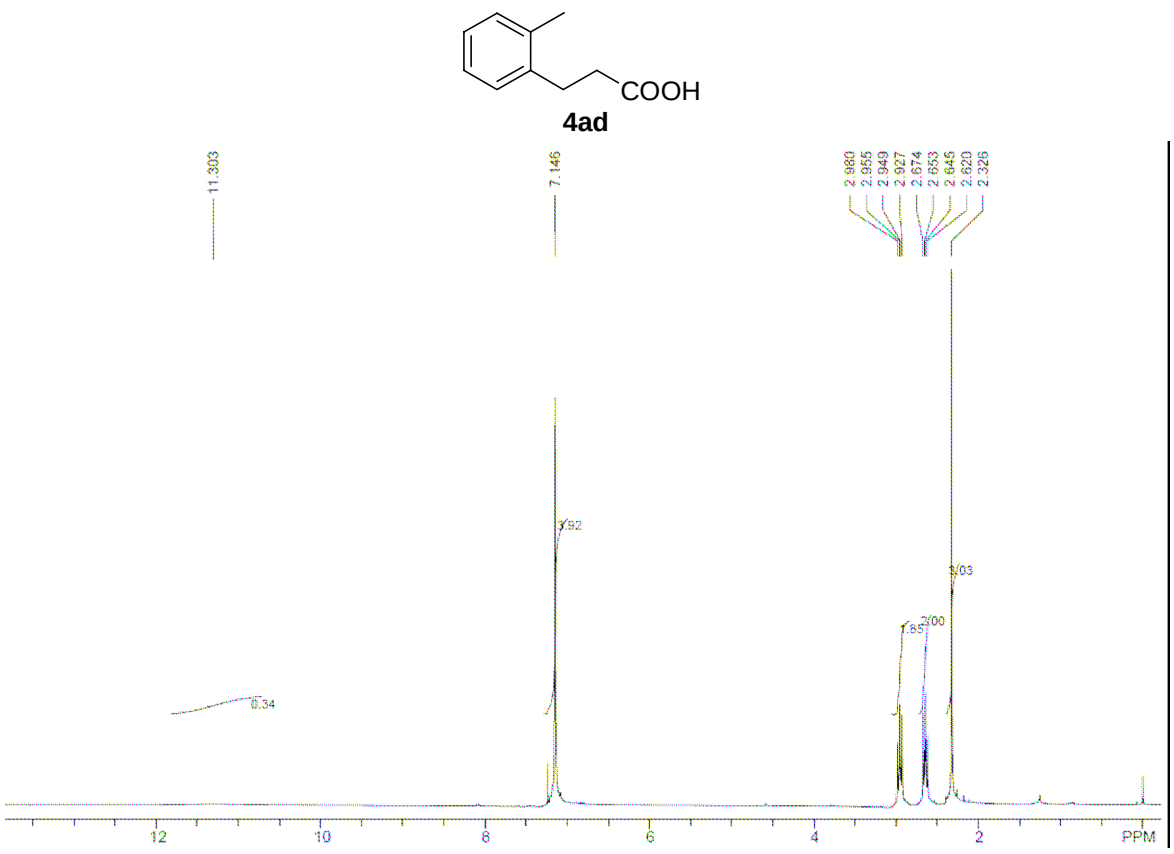
100
50
0 PPM


COOH
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2.949
2.927
2.674
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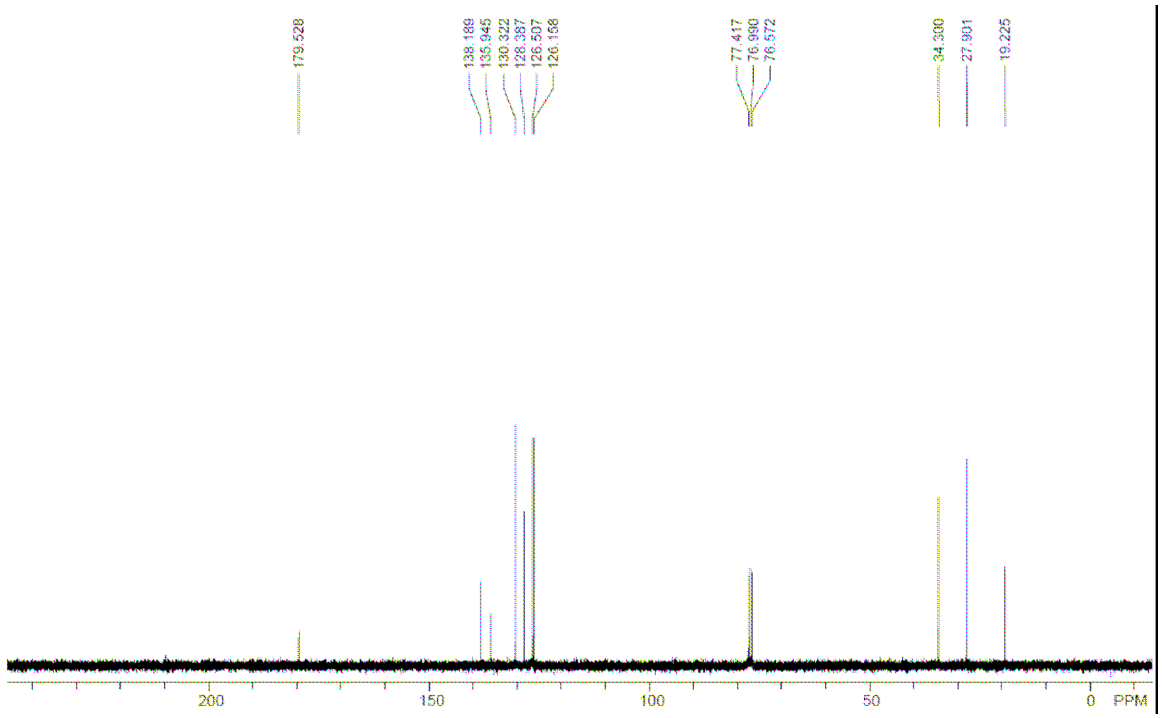
2.645
2.620
2.326
0.34
1.92
3.03
1.85
2.00
12
10
8
6
4
2
PPM

4ad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130.322
128.387
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77.417
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76.572
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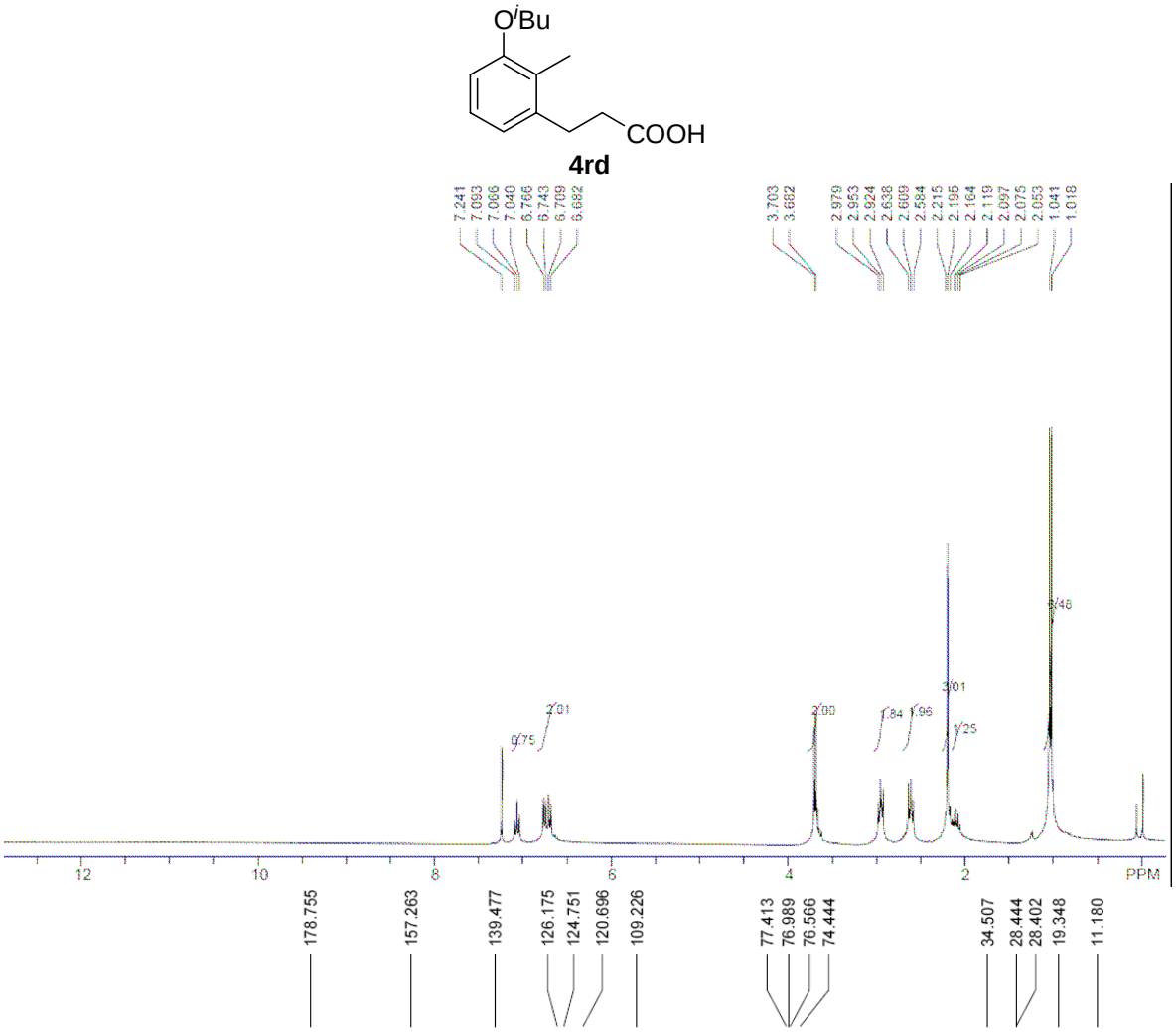
19.225
200
150
100
50
0
PPM


O^{i}Bu
COOH
4rd
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7.040
6.766
6.743
6.709
6.682
3.703
3.682
2.979
2.953
2.924
2.638
2.609
2.584
2.215
2.195
2.164
2.119
2.097
2.075
2.053
1.041
1.018
0.75
2.01
2.00
1.84
1.96
3.01
1.25
6.48
12
10
8
6
4
2
PPM
178.755
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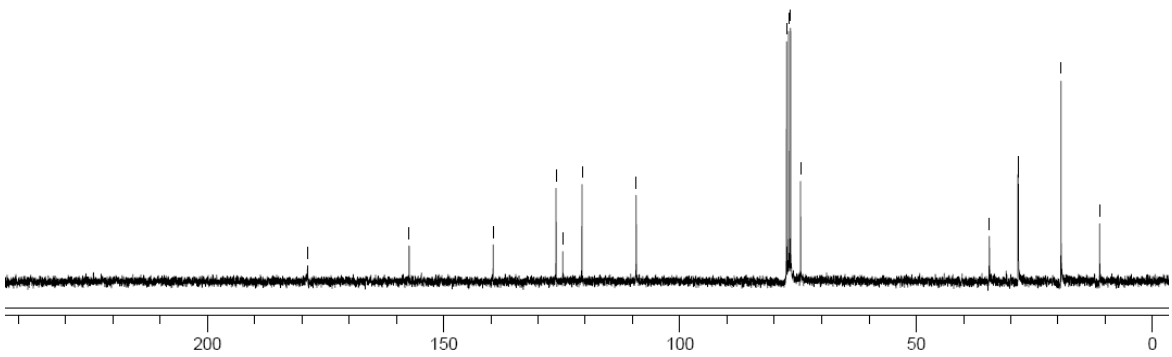
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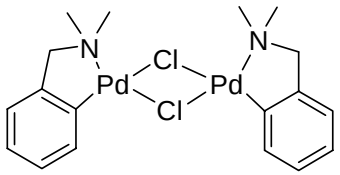
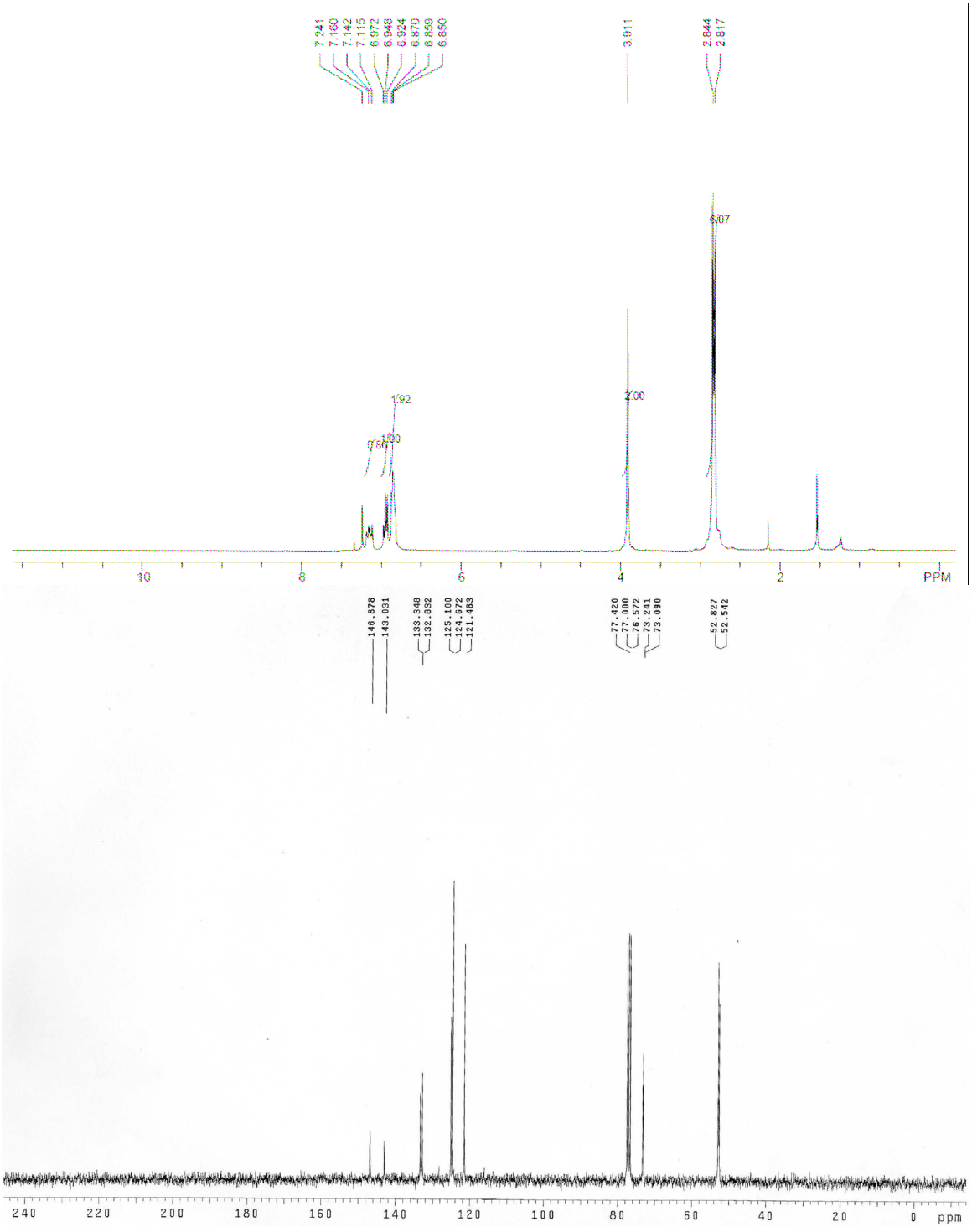
150
100
50
0


N
Pd
Cl
Cl
Pd
N

5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6.948
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6.870
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6.850
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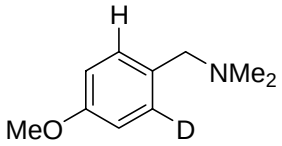
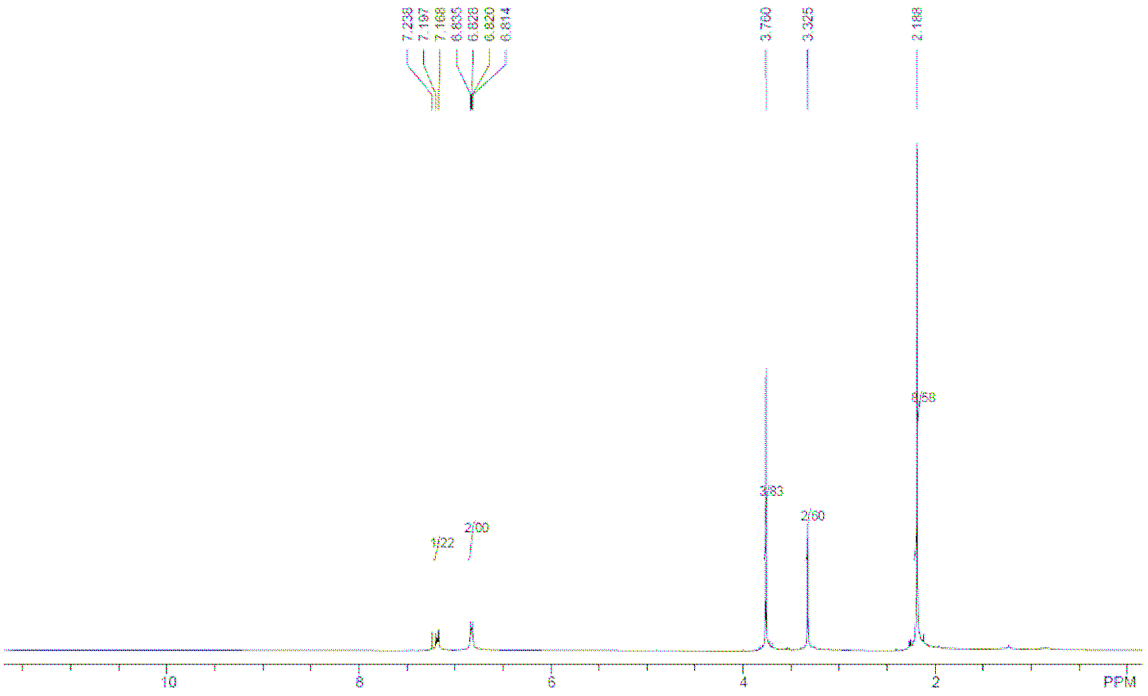
2.844
2.817
6.07
2.00
1.92
0.86
1.00
10
8
6
4
2
PPM
146.878
143.031
133.348
132.832
125.100
124.672
121.483
77.420
77.000
76.572
73.241
73.090
52.827
52.542
240
220
200
180
160
140
120
100
80
60
40
20
0
ppm


H
NMe2
MeO
D

1k-d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7.168
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6.828
6.820
6.814
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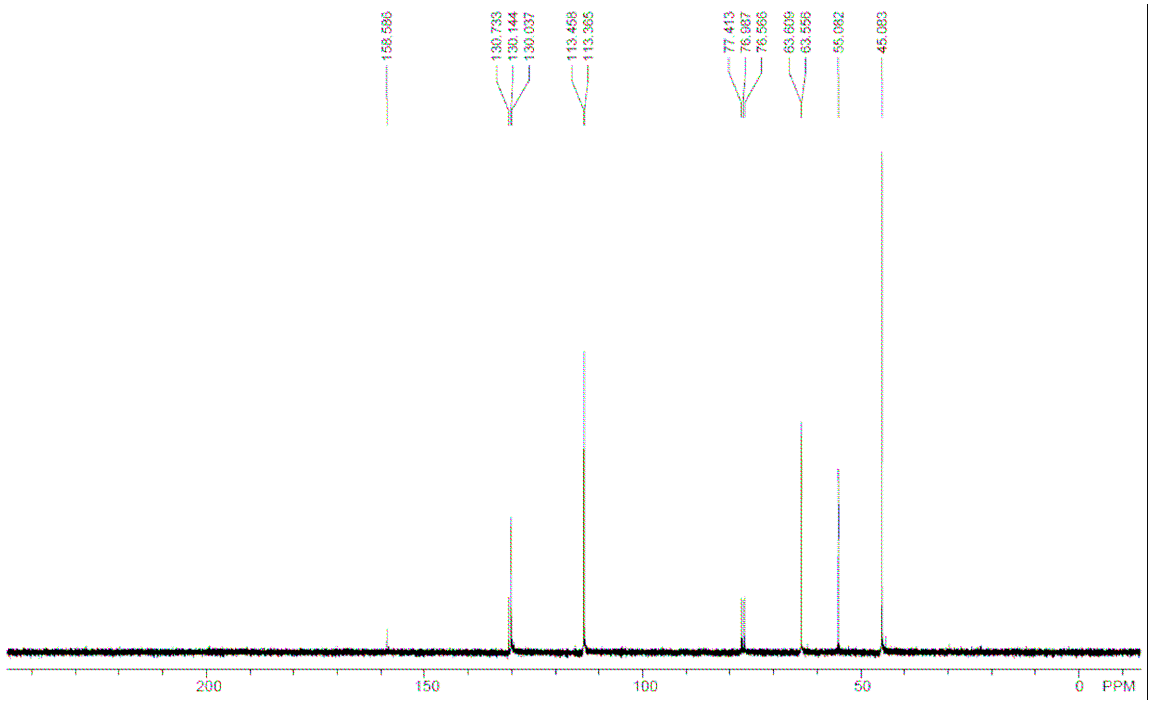
2.188
1.22
2.00
3.83
2.60
9.58
10
8
6
4
2
PPM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130.733
130.144
130.037
113.458
113.365
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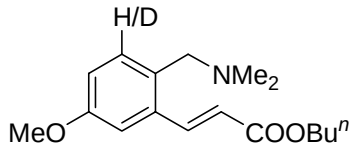
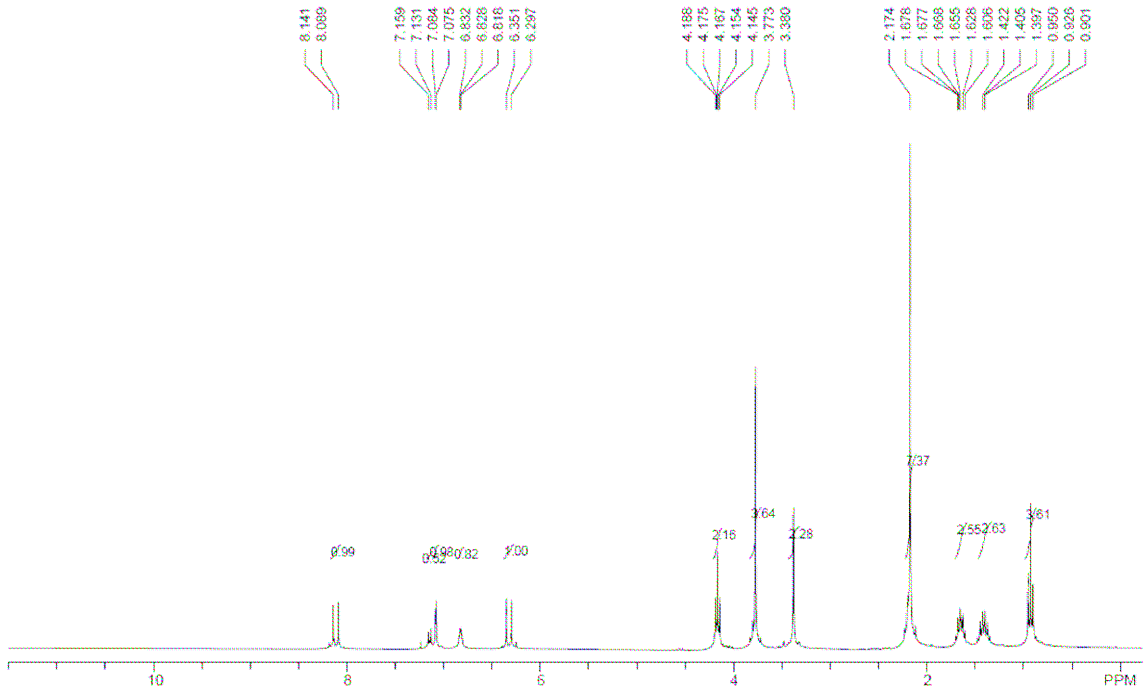
76.987
76.566
63.609
63.556
55.062
45.083
200
150
100
50
0
PPM


H/D
NMe2
MeO
COOBu^n

3ka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7.131
7.084
7.075
6.832
6.628
6.618
6.351
6.297
4.188
4.175
4.167
4.154
4.145
3.773
3.380
2.174
1.678
1.677
1.668
1.655
1.628
1.606
1.422
1.405
1.397
0.950
0.926
0.901
0.99
0.98
0.82
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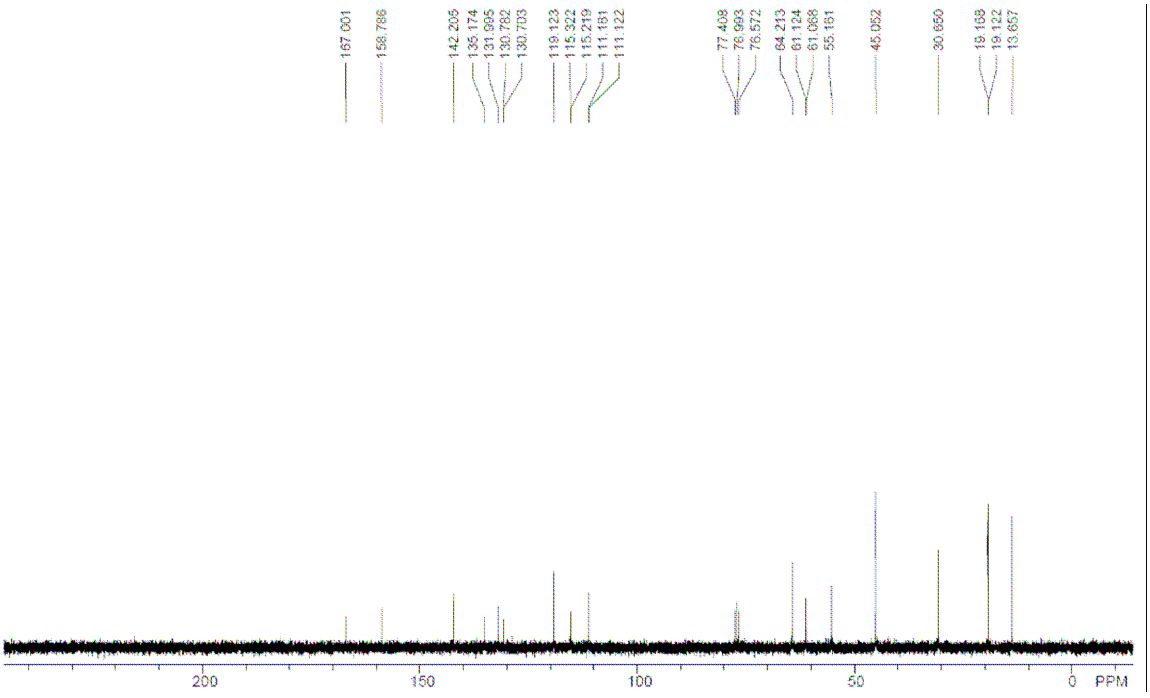
3.64
2.28
7.37
2.55
2.63
3.61
10
8
6
4
2
PPM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115.322
115.219
111.181
111.122
77.408
76.993
76.572
64.213
61.124
61.068
55.161
45.052
30.650
19.168
19.122
13.657
200
150
100
50
0
PPM