Derivatization of Secondary Aliphatic Alcohols to Picolinates – A New Option for HPLC Analysis with Chiral Stationary Phase

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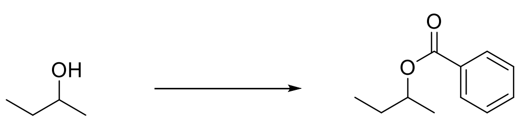
Experimental

General Remarks

Shimadzu chromatographs, SCL-10Avp, equipped with UV detectors (SPD-M10Avp and SPD-M20A) were used. Following chiral columns (250 mm H × 4.6 mm D) were purchased from Daicel, Japan. Immobilized types to silica gel: **B** (cellulose tris(3,5-dimethylphenylcarbamate), Chiralpak IB), **C** (cellulose tris(3,5-dichlorophenylcarbamate), Chiralpak IC), and **G** (amylose tris(3,5-dimethylphenylcarbamate), Chiralpak IA). Coated types on silica gel: **A** (cellulose tris(3,5-dimethylphenylcarbamate), Chiralcel OD-H), **D** (cellulose tribenzoate, Chiralcel OB-H), **E** (cellulose tris(4-methylbenzoate), Chiralcel OJ-H), **F** (amylose tris(3,5-dimethylphenylcarbamate), Chiralpak AD-H), and **H** (amylose tris[(*S*)-α-methylbenzylcarbamate], Chiralpak AS-H). The ^{1}H NMR (300 MHz), ^{13}C NMR (75 MHz), and ^{13}C–APT (attached proton test) spectra were measured in $CDCl_3$. Chemical shifts of carbons are accompanied by minus and plus signs of APT experiments, indicating *C*/*C*H_2 and *C*H/*C*H_3, respectively. CH_2Cl_2 was distilled from CaH_2 before use. Pyridine was dried over CaH_2.

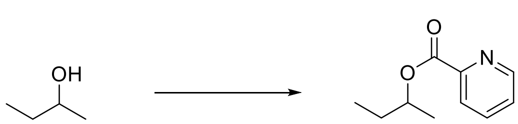
Butan-2-yl benzoate (1a)



1a

To an ice-cold solution of butan-2-ol (772 mg, 10.4 mmol) in pyridine (3.1 mL, 38.5 mmol) was added PhCOCl (1.0 mL, 8.61 mmol). The mixture was stirred at rt for 2.5 h and diluted with brine. The resulting mixture was extracted with EtOAc three times. The combined extracts were washed with 1 N HCl, saturated $NaHCO_3$, and brine, dried over $MgSO_4$, and concentrated. The residue was purified by chromatography on silica gel (hexane/EtOAc) to afford **1a** (1.34 g, 87% based on PhCOCl): liquid; R_f 0.63 (hexane/EtOAc 4:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.97 (t, *J* = 7.5 Hz, 3 H), 1.37 (d, *J* = 6.3 Hz, 3 H), 1.61–1.83 (m, 2 H), 5.10 (sext., *J* = 6.3 Hz, 1 H), 7.44 (t, *J* = 7.2 Hz, 2 H), 7.55 (tt, *J* = 7.2, 1.2 Hz, 1 H), 8.05 (d, *J* = 7.2 Hz, 2 H); ^{13}C–APT NMR (75 MHz, $CDCl_3$) δ 9.8 (+), 19.6 (+), 29.0 (–), 72.8 (+), 128.3 (+), 129.5 (+), 130.9 (–), 132.7 (+), 166.3 (–). The ^{1}H and ^{13}C NMR spectra were consistent with those reported.[S1]

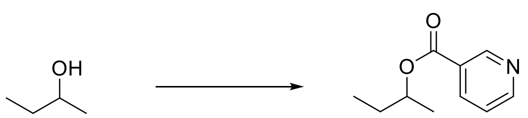
Butan-2-yl picolinate (1b)



1b

To an ice-cold solution of butan-2-ol (724 mg, 9.77 mmol) in CH_2Cl_2 (16 mL) were added picolinic acid (1.01 g, 8.18 mmol), 2-chloro-1-methylpridinium iodide (3.13 g, 12.3 mmol), DMAP (1.49 g, 12.2 mmol), and Et_3N (2.70 mL, 19.4 mmol). The mixture was stirred at rt for 4 h and diluted with saturated $NaHCO_3$. The resulting mixture was extracted with EtOAc three times. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated. The residue was purified by chromatography on silica gel (hexane/EtOAc) to afford **1b** (1.05 g, 72% based on picolinic acid): liquid; R_f 0.43 (hexane/EtOAc 1:1); IR (neat) 1714, 1309, 1142, 749 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.98 (t, J = 7.5 Hz, 3 H), 1.39 (d, J = 6.3 Hz, 3 H), 1.63–1.91 (m, 2 H), 5.19 (sext., J = 6.3 Hz, 1 H), 7.46 (ddd, J = 7.5, 4.8, 1.2 Hz, 1 H), 7.83 (dt, J = 1.8, 7.5 Hz, 1 H), 8.12 (d, J = 7.5 Hz, 1 H), 8.78 (dm, J = 4.8 Hz, 1 H); ^{13}C–APT NMR (75 MHz, $CDCl_3$) δ 9.8 (+), 19.5 (+), 28.8 (–), 74.0 (+), 125.0 (+), 126.6 (+), 136.8 (+), 148.6 (–), 149.9 (+), 164.8 (–); HRMS (EI^+) calcd for $C_{10}H_{13}NO_2$ [M^+] 179.0946, found 174.0946.

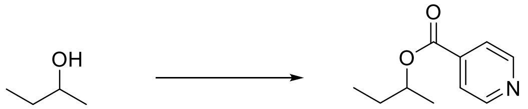
Butan-2-yl nicotinate (1c)



1c

According to the procedure for the synthesis of **1b**, nicotinic acid (201 mg, 1.63 mmol), 2-chloro-1-methylpridinium iodide (625 mg, 2.45 mmol), DMAP (311 mg, 2.54 mmol), and Et_3N (0.53 mL, 3.80 mmol) were added to an ice-cold solution of butan-2-ol (151 mg, 2.03 mmol) in CH_2Cl_2 (3.2 mL) and the mixture was stirred at rt for 7 h to afford **1c** (257 mg, 88% based on nicotinic acid): liquid; R_f 0.67 (hexane/EtOAc 2:3); IR (neat) 1721, 1285, 1109, 743 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.97 (t, J = 7.5 Hz, 3 H), 1.35 (d, J = 6.3 Hz, 3 H), 1.60–1.85 (m, 2 H), 5.12 (sext., J = 6.3 Hz, 1 H), 7.38 (dd, J = 8.1, 4.8 Hz, 1 H), 8.29 (dt, J = 8.1, 1.8 Hz, 1 H), 8.76 (dd, J = 4.8, 1.8 Hz, 1 H), 9.22 (d, J = 1.8 Hz, 1 H); ^{13}C–APT NMR (75 MHz, $CDCl_3$) δ 9.7 (+), 19.5 (+), 28.9 (–), 73.6 (+), 123.3 (+), 126.7 (–), 137.0 (+), 150.9 (+), 153.2 (+), 164.9 (–).

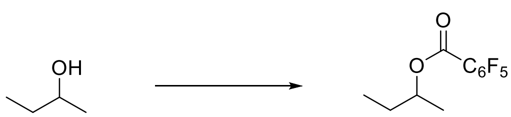
Butan-2-yl isonicotinate (1d)



1d

According to the procedure for the synthesis of **1b**, isonicotinic acid (202 mg, 1.64 mmol), 2-chloro-1-methylpridinium iodide (627 mg, 2.45 mmol), DMAP (295 mg, 2.41 mmol), and Et_3N (0.54 mL, 3.87 mmol) were added to an ice-cold solution of butan-2-ol (149 mg, 2.01 mmol) in CH_2Cl_2 (3.2 mL) and the mixture was stirred at rt for 3.5 h to afford **1d** (216 mg, 73% based on isonicotinic acid): liquid; R_f 0.47 (hexane/EtOAc 2:1); IR (neat) 1726, 1283, 1127, 759 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.98 (t, *J* = 7.5 Hz, 3 H), 1.35 (d, *J* = 6.3 Hz, 3 H), 1.60–1.84 (m, 2 H), 5.12 (sext., *J* = 6.3 Hz, 1 H), 7.85 (d, *J* = 4.5 Hz, 2 H), 8.77 (d, *J* = 4.5 Hz, 2 H); ^{13}C–APT NMR (75 MHz, $CDCl_3$) δ 9.7 (+), 19.4 (+), 28.8 (–), 74.0 (+), 122.8 (+), 138.0 (–), 150.5 (+), 164.7 (–); HRMS (EI^+) calcd for $C_{10}H_{13}NO_2$ [M^+] 179.0946, found 174.0945.

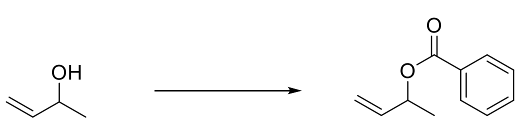
Butan-2-yl 2,3,4,5,6-pentafluorobenzoate (1e)



1e

According to the procedure for the synthesis of **1b**, pentafluorobenzoic acid (426 mg, 2.01 mmol), 2-chloro-1-methylpridinium iodide (519 mg, 2.03 mmol), DMAP (246 mg, 2.01 mmol), and Et_3N (0.277 mL, 1.99 mmol) were added to an ice-cold solution of butan-2-ol (0.092 mL, 1.00 mmol) in CH_2Cl_2 (10 mL) and the mixture was stirred at rt for 3 h to afford **1e** (241 mg, 90%): liquid; R_f 0.23 (hexane only); IR (neat) 1738, 1327, 1239, 1115, 998 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.98 (t, *J* = 7.2 Hz, 3 H), 1.36 (d, *J* = 6.3 Hz, 3 H), 1.63–1.79 (m, 2 H), 5.15 (sext., *J* = 6.3 Hz, 1 H); ^{13}C–APT NMR (75 MHz, $CDCl_3$) δ 9.5 (+), 19.3 (+), 28.7 (–), 75.9 (+), 109.2 (dt, *J* = 3.5, 17.2 Hz) (–), 137.8 (dm, *J* = 251.8 Hz) (–), 143.0 (dm, *J* = 257.5 Hz) (–), 145.3 (dm, *J* = 255.2 Hz) (–), 158.7 (–); HRMS (EI^+) calcd for $C_{11}H_9F_5O_2$ [M^+] 268.0523, found 268.0523.

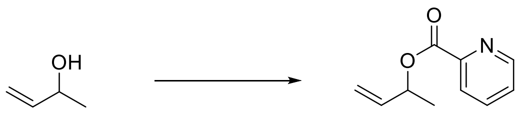
But-3-en-2-yl benzoate (2a)



2a

According to the procedure for the synthesis of **1a**, PhCOCl (0.036 mL, 3.10 mmol) was added to an ice-cold solution of but-3-en-2-ol (0.087 mL, 1.00 mmol) in pyridine (0.81 mL, 10.0 mmol). After 45 min at 0 °C, *N*,*N*-dimethyl-1,3-propanediamine (1.25 mL, 10.0 mmol) was added and the solution was stirred at 0 °C for 15 min to afford **2a** (167 mg, 95%): liquid; R_f 0.68 (hexane/EtOAc 4:1); ^1H NMR (300 MHz, $CDCl_3$) δ 1.45 (d, *J* = 6.6 Hz, 3 H), 5.19 (dt, *J* = 10.5, 1.2 Hz, 1 H), 5.34 (dt, *J* = 17.1, 1.2 Hz, 1 H), 5.55–5.66 (m, 1 H), 5.97 (ddd, *J* = 17.1, 10.5, 6.0 Hz, 1 H), 7.44 (t, *J* = 7.5 Hz, 2 H), 7.56 (tt, *J* = 7.5, 1.2 Hz, 1 H), 8.06 (d, *J* = 7.5 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.1, 71.6, 115.9, 128.4, 129.6, 130.6, 132.9, 137.8, 165.8. The ^1H and ^{13}C NMR spectra were consistent with those reported.[S2]

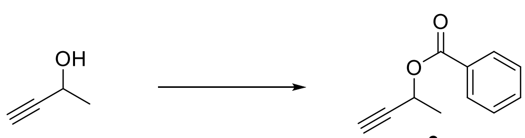
But-3-en-2-yl picolinate (2b)



2b

According to the procedure for the synthesis of **1b**, picolinic acid (247 mg, 2.01 mmol), 2-chloro-1-methylpridinium iodide (514 mg, 2.01 mmol), DMAP (245 mg, 2.01 mmol), and Et_3N (0.277 mL, 1.99 mmol) were added to an ice-cold solution of but-3-en-2-ol (0.087 mL, 1.00 mmol) in CH_2Cl_2 (2 mL) and the mixture was stirred at rt for 1 h to afford **2b** (161 mg, 91%): liquid; R_f 0.53 (hexane/EtOAc 1:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.51 (d, *J* = 6.3 Hz, 3 H), 5.21 (d, *J* = 10.5 Hz, 1 H), 5.37 (d, *J* = 17.1 Hz, 1 H), 5.69 (quint., *J* = 6.3 Hz, 1 H), 6.02 (ddd, *J* = 17.1, 10.5, 6.3 Hz, 1 H), 7.47 (dd, *J* = 7.8, 4.8 Hz, 1 H), 7.84 (dt, *J* = 1.8, 7.8 Hz, 1 H), 8.13 (d, *J* = 7.8 Hz, 1 H), 8.78 (dm, *J* = 4.8 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.9, 72.8, 116.6, 125.1, 126.8, 136.9, 137.2, 148.4, 149.9, 164.4. The ^{1}H and ^{13}C NMR spectra were consistent with those reported.[S3]

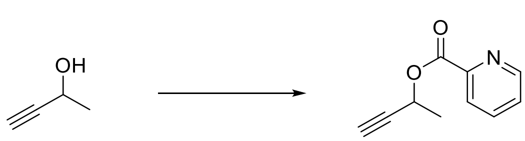
But-3-yn-2-yl benzoate (3a)



3a

According to the procedure for the synthesis of **1a**, PhCOCl (1.00 mL, 8.61 mmol) was added to an ice-cold solution of but-3-yn-2-ol (0.22 mL, 2.80 mmol) in pyridine (1.0 mL, 12.4 mmol). After 1.5 h at 0 °C, *N*,*N*-dimethyl-1,3-propanediamine (1.24 mL, 9.95 mmol) was added and the solution was stirred at 0 °C for 15 min to afford **3a** (434 mg, 89%): solid; mp 44–45 °C; R_f 0.77 (hexane/EtOAc 5:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.65 (d, *J* = 6.6 Hz, 3 H), 2.49 (d, *J* = 2.1 Hz, 1 H), 5.69 (dq, *J* = 2.1, 6.6 Hz, 1 H), 7.45 (t, *J* = 7.5 Hz, 2 H), 7.57 (tt, *J* = 7.5, 0.9 Hz, 1 H), 8.08 (d, *J* = 7.5 Hz, 2 H); ^{13}C–APT NMR (75 MHz, $CDCl_3$) δ 21.3 (+), 60.6 (+), 73.1 (–), 82.2 (–), 128.4 (+), 129.7 (+), 133.2 (+), 165.3 (–); HRMS (EI^+) calcd for $C_{11}H_{10}O_2$ [M^+] 174.0681, found 174.0679. The ^{1}H and ^{13}C NMR spectra were consistent with those reported.[S4,S5]

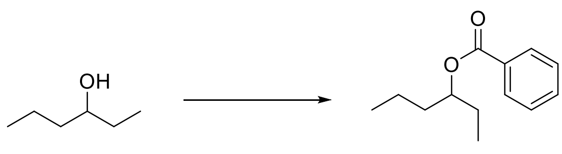
But-3-yn-2-yl picolinate (3b)



3b

According to the procedure for the synthesis of **1b**, picolinic acid (212 mg, 1.72 mmol), 2-chloro-1-methylpridinium iodide (551 mg, 2.16 mmol), DMAP (265 mg, 2.17 mmol), and Et_3N (0.47 mL, 3.37 mmol) were added to an ice-cold solution of but-3-yn-2-ol (103 mg, 1.47 mmol) in CH_2Cl_2 (3 mL) and the mixture was stirred at rt for 2.5 h to afford **3b** (188 mg, 73%): solid; mp 59–60 °C; R_f 0.17 (hexane/EtOAc 2:1); IR (CH_2Cl_2) 3302, 1726 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.70 (d, J = 6.6 Hz, 3 H), 2.51 (d, J = 2.4 Hz, 1 H), 5.76 (dq, J = 2.4, 6.6 Hz, 1 H), 7.49 (ddd, J = 7.5, 4.8, 1.2 Hz, 1 H), 7.85 (dt, J = 1.5, 7.5 Hz, 1 H), 8.16 (d, J = 7.5 Hz, 1 H), 8.79 (dm, J = 4.8 Hz, 1 H); ^{13}C–APT NMR (75 MHz, $CDCl_3$) δ 21.2 (+), 61.5 (+), 73.6 (–), 81.6 (–), 125.3 (+), 127.0 (+), 137.0 (+), 147.7 (–), 150.0 (+), 164.0 (–); HRMS (EI$^+$) calcd for $C_{10}H_9NO_2$ [M$^+$] 175.0633, found 175.06732.

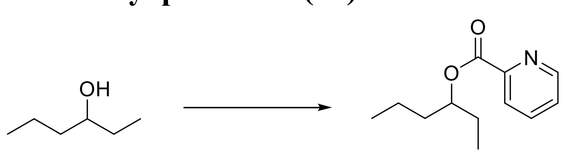
Hexan-3-yl benzoate (4a)



4a

According to the procedure for the synthesis of **1a**, PhCOCl (0.28 mL, 2.41 mmol) was added to an ice-cold solution of hexan-3-ol (200 mg, 1.95 mmol) in pyridine (0.70 mL, 8.7 mmol). After 1.5 h at rt, *N*,*N*-dimethyl-1,3-propanediamine (0.37 mL, 2.94 mmol) was added and the solution was stirred at rt for 30 min to afford **4a** (381 mg, 95%): liquid; R_f 0.81 (hexane/EtOAc 4:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.93 (t, J = 7.2 Hz, 3 H), 0.95 (t, J = 7.2 Hz, 3 H), 1.32–1.48 (m, 2 H), 1.58–1.77 (m, 4 H), 5.04–5.15 (m, 1 H), 7.44 (t, J = 7.2 Hz, 2 H), 7.55 (tt, J = 7.2, 1.2 Hz, 1 H), 8.06 (d, J = 7.2 Hz, 2 H); ^{13}C–APT NMR (75 MHz, $CDCl_3$) δ 9.7 (+), 14.1 (+), 18.7 (–), 27.2 (–), 35.9 (–), 76.0 (+), 128.3 (+), 129.6 (+), 130.9 (–), 132.7 (+), 166.5 (–). The ^{1}H and ^{13}C NMR spectra were consistent with those reported.[S2]

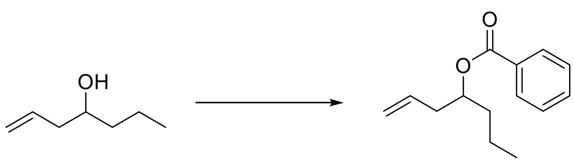
Hexan-3-yl picolinate (4b)



4b

According to the procedure for the synthesis of **1b**, picolinic acid (273 mg, 2.22 mmol), 2-chloro-1-methylpridinium iodide (707 mg, 2.77 mmol), DMAP (337 mg, 2.76 mmol), and Et_3N (0.60 mL, 4.31 mmol) were added to an ice-cold solution of hexan-3-ol (190 mg, 1.86 mmol) in CH_2Cl_2 (3.6 mL) and the mixture was stirred at rt for 1.5 h to afford **4b** (324 mg, 84%): liquid; R_f 0.58 (hexane/EtOAc 1:1); IR (neat) 1714, 1305, 1141, 748 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.93 (t, J = 7.2 Hz, 3 H), 0.96 (t, J = 7.5 Hz, 3 H), 1.32–1.49 (m, 2 H), 1.58–1.84 (m, 4 H), 5.19 (tt, J = 7.2, 5.7 Hz, 1 H), 7.46 (ddd, J = 7.5, 4.8, 1.2 Hz, 1 H), 7.83 (dt, J = 1.8, 7.5 Hz, 1 H), 8.12 (d, J = 7.5 Hz, 1 H), 8.78 (dm, J = 4.8 Hz, 1 H); ^{13}C–APT NMR (75 MHz, $CDCl_3$) δ 9.7 (+), 13.9 (+), 18.7 (–), 27.1 (–), 35.8 (–), 77.1 (+), 125.0 (+), 126.6 (+), 136.8 (+), 148.5 (–), 149.9 (+), 165.0 (–); HRMS (EI$^+$) calcd for $C_{12}H_{17}NO_2$ [M$^+$] 207.1259, found 207.1256.

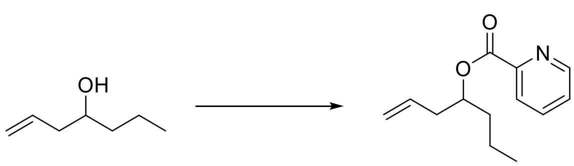
Hept-1-en-4-yl benzoate (5a)



5a

According to the procedure for the synthesis of **1a**, PhCOCl (0.035 mL, 0.30 mmol) was added to an ice-cold solution of hept-1-en-4-ol (11 mg, 0.097 mmol) in pyridine (0.5 mL, 6.2 mmol). After 1 h at 0 °C, *N*,*N*-dimethyl-1,3-propanediamine (0.12 mL, 0.96 mmol) was added and the solution was stirred at 0 °C for 15 min to afford **5a** (12 mg, 57%): liquid; R_f 0.83 (hexane/EtOAc 4:1); IR (neat) 1720, 1263, 1111, 804 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.93 (t, *J* = 7.2 Hz, 3 H), 1.30–1.51 (m, 2 H), 1.57–1.78 (m, 2 H), 2.45 (dd, *J* = 7.2, 6.0 Hz, 2 H), 5.06 (d, *J* = 10.2 Hz, 1 H), 5.11 (d, *J* = 17.1 Hz, 1 H), 5.13–5.24 (m, 1 H), 5.83 (ddt, *J* = 17.1, 10.2, 7.2 Hz, 1 H), 7.44 (t, *J* = 7.5 Hz, 2 H), 7.55 (tt, *J* = 7.5, 1.2 Hz, 1 H), 8.04 (d, *J* = 7.5 Hz, 1 H); ^{13}C–APT NMR (75 MHz, $CDCl_3$) δ 14.1 (+), 18.7 (–), 35.9 (–), 38.8 (–), 73.9 (+), 117.8 (–), 128.4 (+), 129.6 (+), 130.8 (–), 132.8 (+), 133.8 (+), 166.3 (–); HRMS (EI$^+$) calcd for $C_{14}H_{18}O_2$ [M$^+$] 218.1307, found 218.1307.

Hept-1-en-4-yl picolinate (5b)



5b

According to the procedure for the synthesis of **1b**, picolinic acid (47 mg, 0.38 mmol), 2-chloro-1-methylpridinium iodide (105 mg, 0.41 mmol), DMAP (50 mg, 0.41 mmol), and Et_3N (0.055 mL, 0.40 mmol) were added to an ice-cold solution of hept-1-en-4-ol (9 mg, 0.079 mmol) in CH_2Cl_2 (0.5 mL) and the mixture was stirred at rt for 1 h to afford **5b** (8.5 mg, 49%): liquid; R_f 0.26 (hexane/EtOAc 4:1); IR (neat) 1739, 1715, 1306, 1127, 748 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.93 (t, *J* = 7.2 Hz, 3 H), 1.31–1.53 (m, 2 H), 1.59–1.86 (m, 2 H), 2.49 (t, *J* = 6.9 Hz, 2 H), 5.06 (d, *J* = 9.9 Hz, 1 H), 5.11 (d, *J* = 17.1 Hz, 1 H), 5.23–5.34 (m, 1 H), 5.83 (ddt, *J* = 17.1, 9.9, 6.9 Hz, 1 H), 7.46 (ddd, *J* = 7.8, 4.8, 1.2 Hz, 1 H), 7.83 (dt, *J* = 1.5, 7.8 Hz, 1 H), 8.10 (d, *J* = 7.8 Hz, 1 H), 8.78 (dm, *J* = 4.8 Hz, 1 H); ^{13}C–APT NMR (75 MHz, $CDCl_3$) δ 14.0 (+), 18.8 (–), 35.9 (–), 38.8 (–), 75.0 (+), 118.0 (–), 125.1 (+), 126.8 (+), 133.7 (+), 137.0 (+), 148.5 (–), 150.1 (+), 164.9 (–); HRMS (FAB$^+$) calcd for $C_{13}H_{18}NO_2$ [(M+H)$^+$] 220.1338, found 220.1333.

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S5 L. C. Wilkins, J. R. Lawson, P. Wieneke, F. Rominger, A. S. K. Hashmi, M. M. Hansmann, and R. L. Melen, *Chem. Eur. J.*, 2016, **22**, 14618.

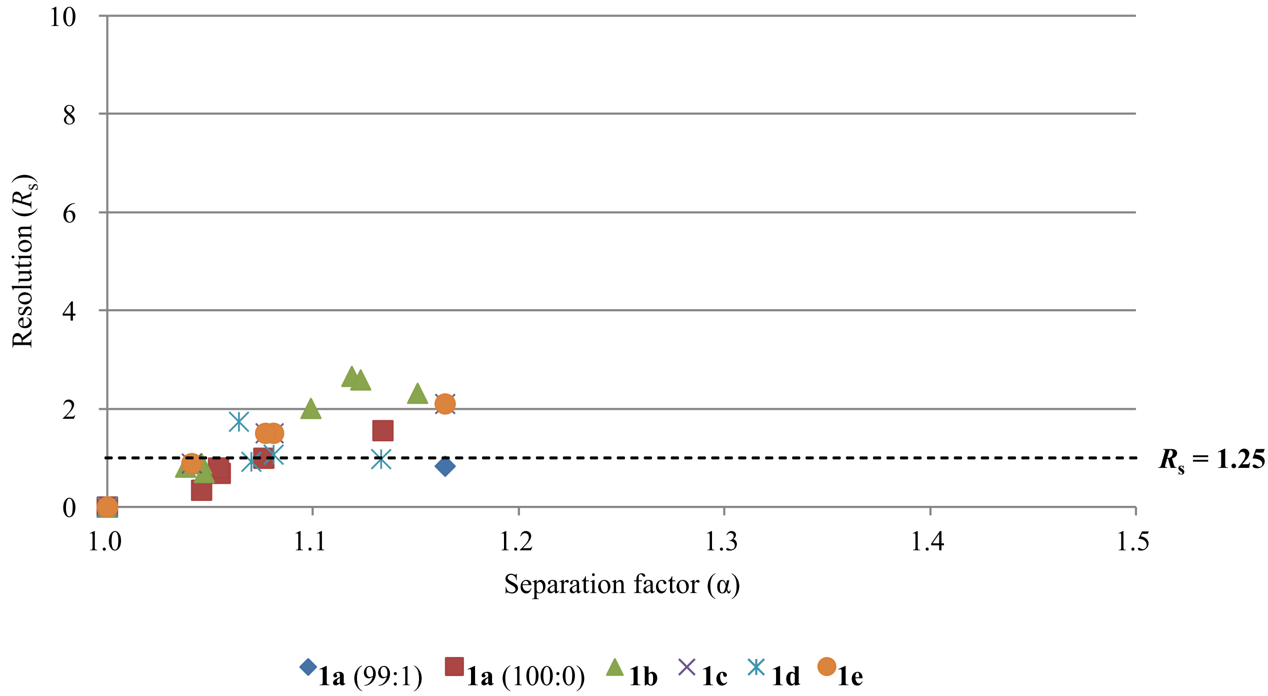


Fig. S1-1. A relation of between resolution (R_s) and separation factor (α) about **1a–e**.[a]

[a] Hexane:*i*-PrOH (99:1 and 100:0) was used as eluents for **1a**, whereas 99:1 was used for **1b-e**.

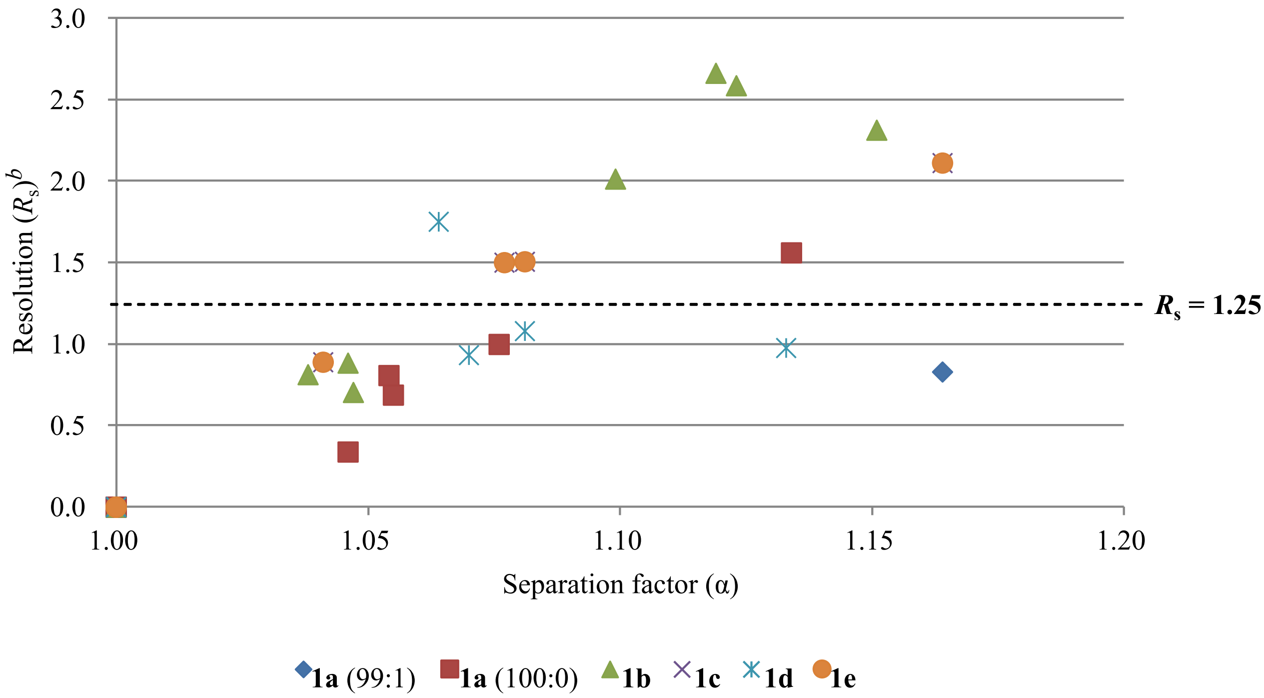


Fig. S1-2. Expansion of Fig. S1-1.[a]

[a] Ratios of hexane:*i*-PrOH are given in parenthesis.

[b] Bars beyond R_s = 1.25 indicate good to excellent separation.

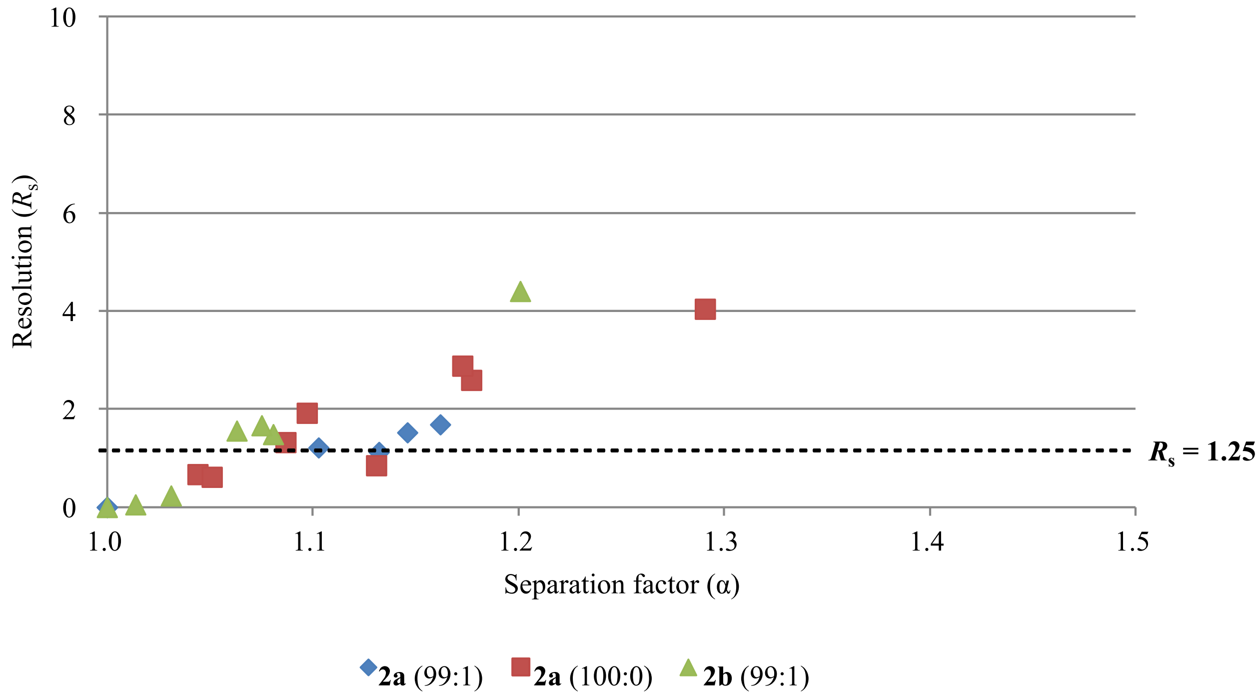


Fig. S2-1. A relation of between resolution (R_s) and separation factor (α) about **2a** and **2b**.[a]
[a] Ratios of hexane:*i*-PrOH are given in parenthesis.

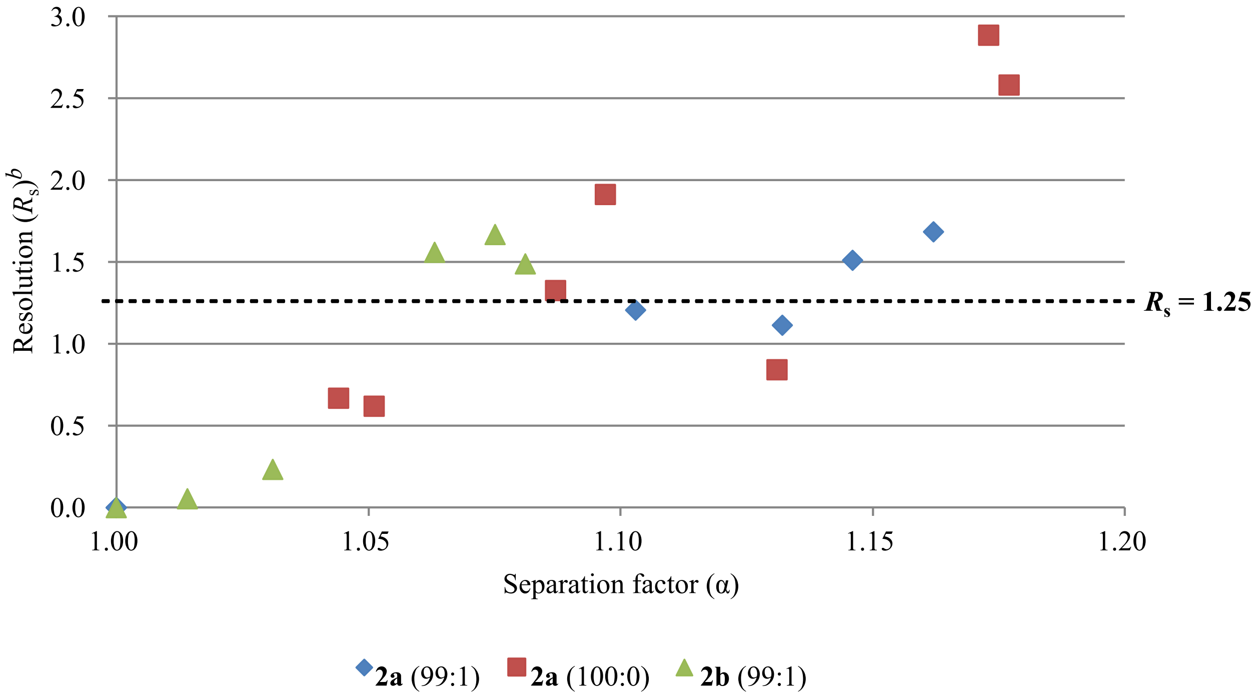


Fig. S2-2. Expansion of Fig. S2-1.[a]
[a] Ratios of hexane:*i*-PrOH are given in parenthesis.
[b] Bars beyond R_s = 1.25 indicate good to excellent separation.

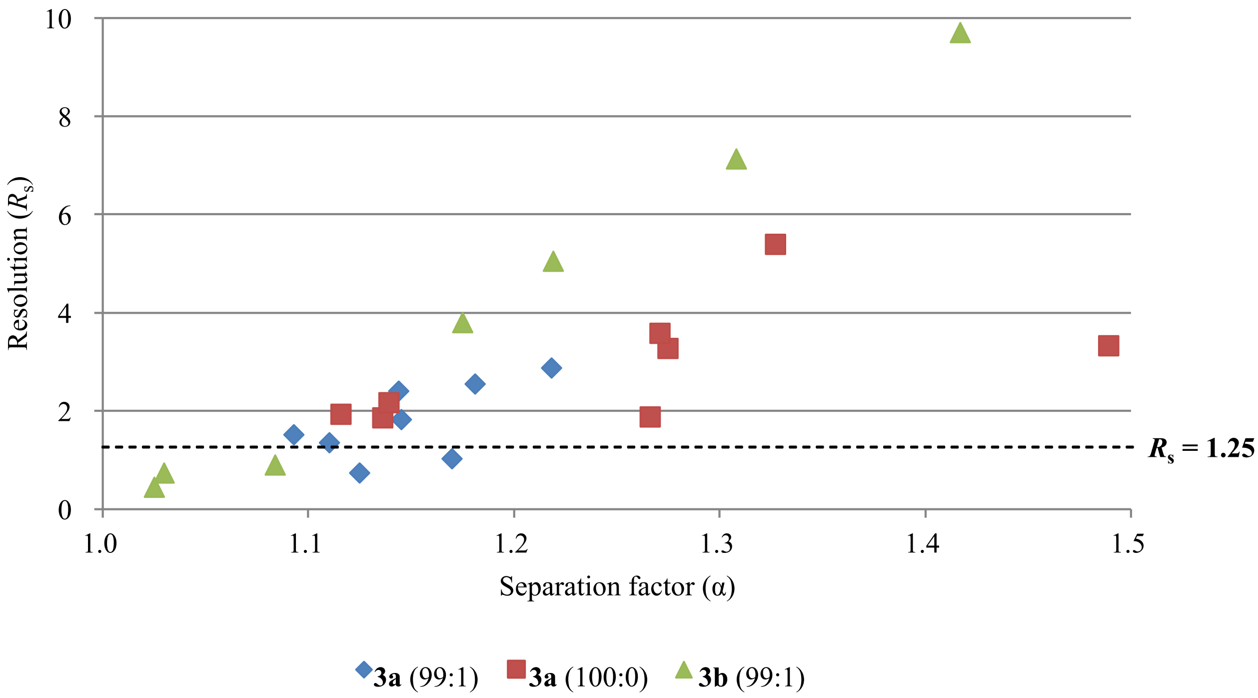


Fig. S3-1. A relation of between resolution (R_s) and separation factor (α) about **3a** and **3b**.[a]

[a] Ratios of hexane:*i*-PrOH are given in parenthesis.

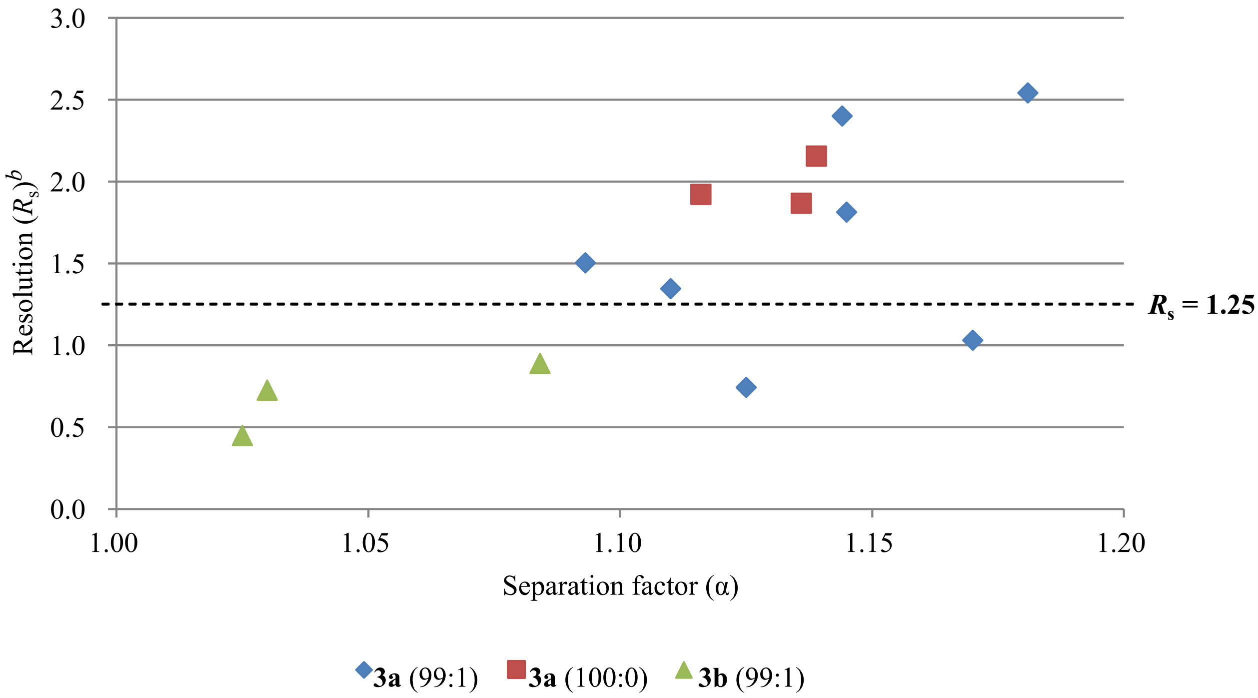


Fig. S3-2. Expansion of Fig. S3-1.[a]

[a] Ratios of hexane:*i*-PrOH are given in parenthesis.

[b] Bars beyond R_s = 1.25 indicate good to excellent separation.

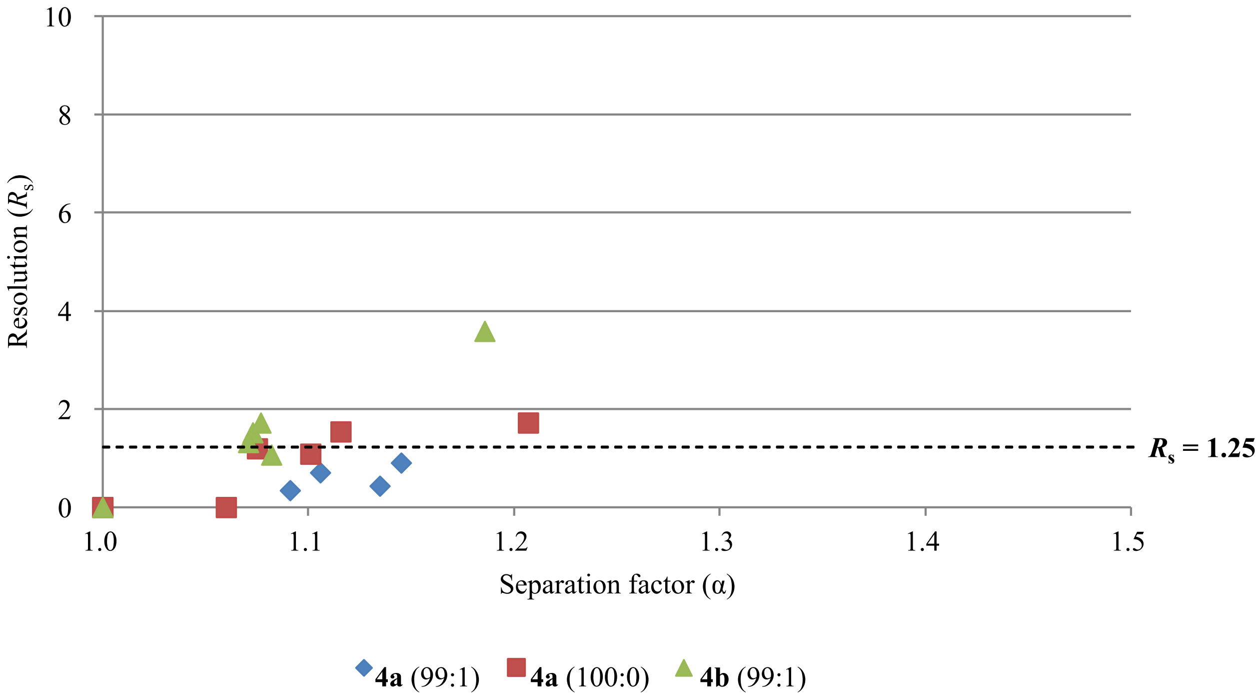


Fig. S4-1. A relation of between resolution (R_s) and separation factor (α) about **4a** and **4b**.[a]
[a] Ratios of hexane:*i*-PrOH are given in parenthesis.

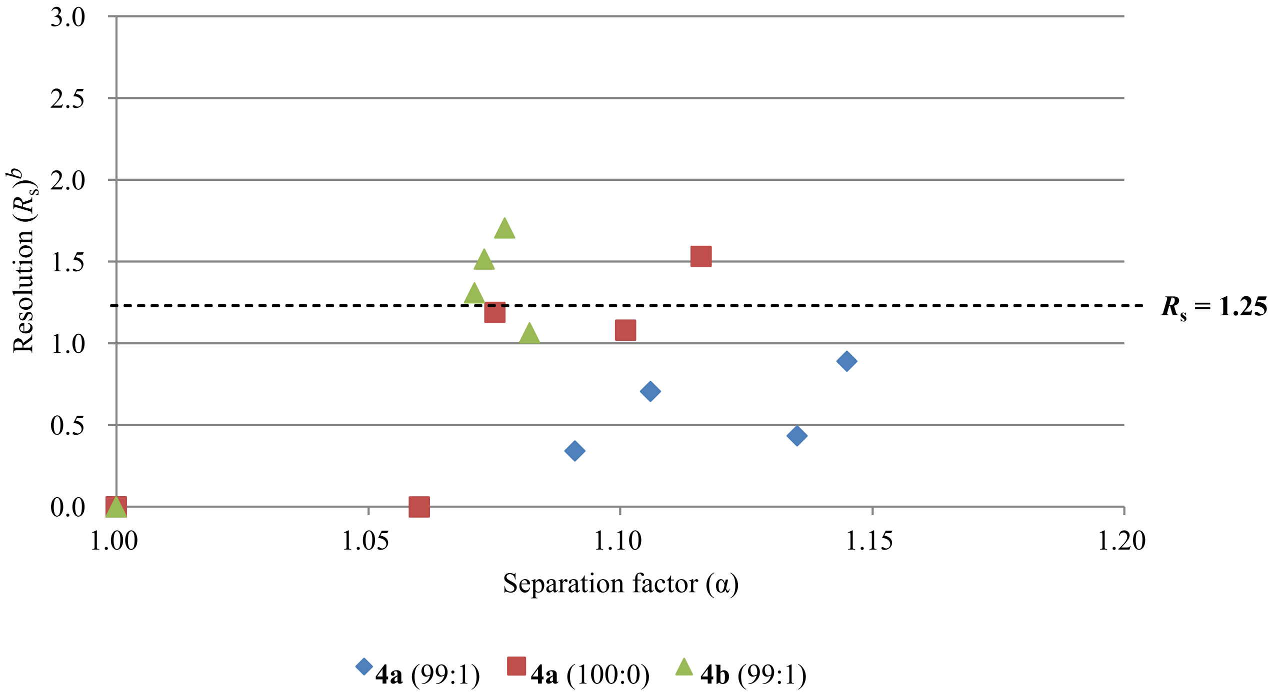


Fig. S4-2. Expansion of Fig. S4-1.[a]
[a] Ratios of hexane:*i*-PrOH are given in parenthesis.
[b] Bars beyond R_s = 1.25 indicate good to excellent separation.

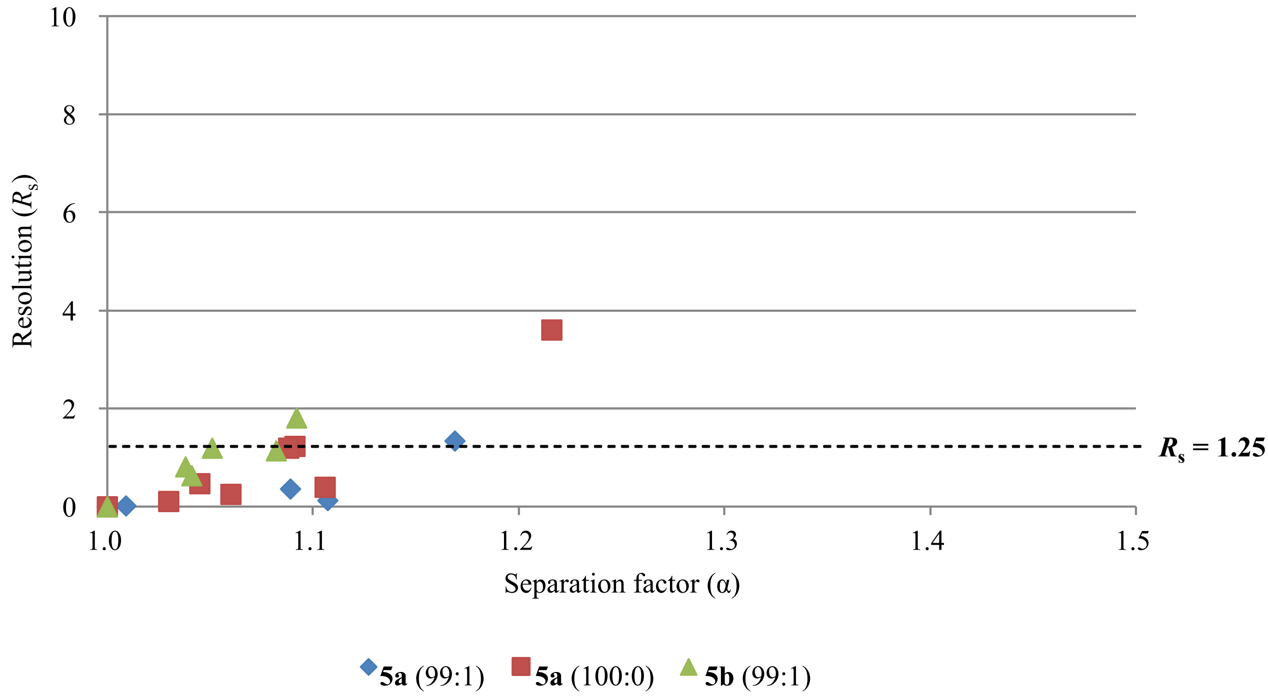


Fig. S5-1. A relation of between resolution (R_s) and separation factor (α) about **5a** and **5b**.[a]
[a] Ratios of hexane:*i*-PrOH are given in parenthesis.

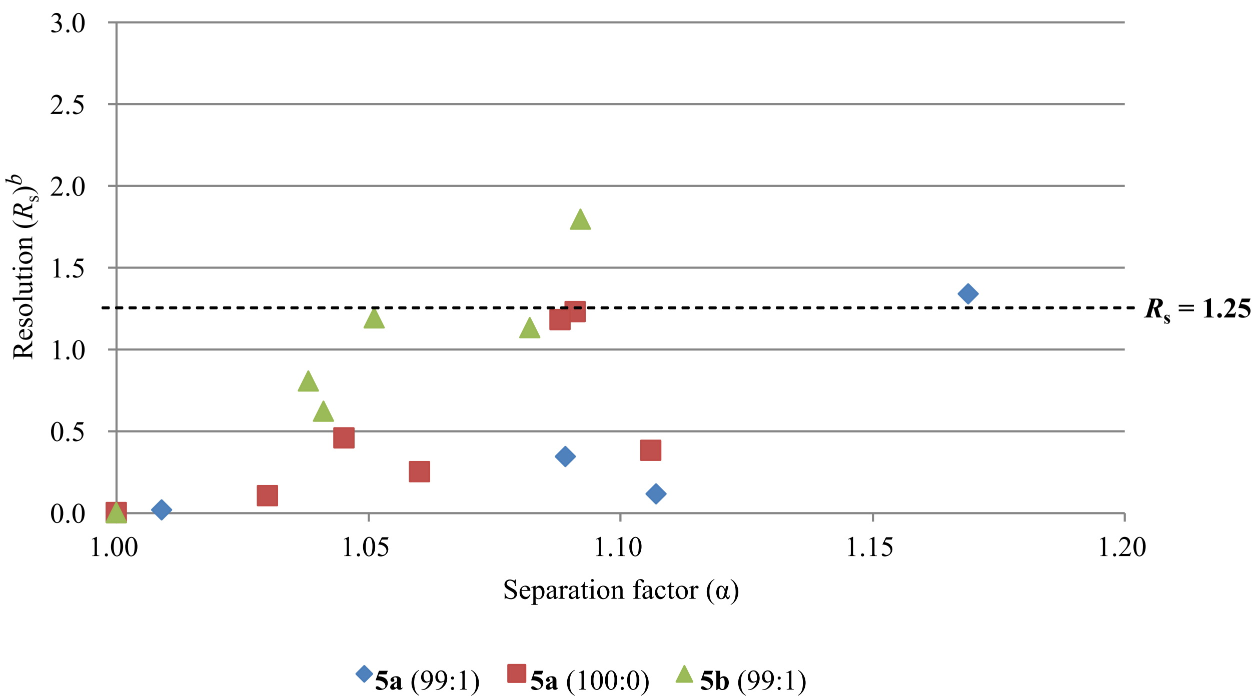
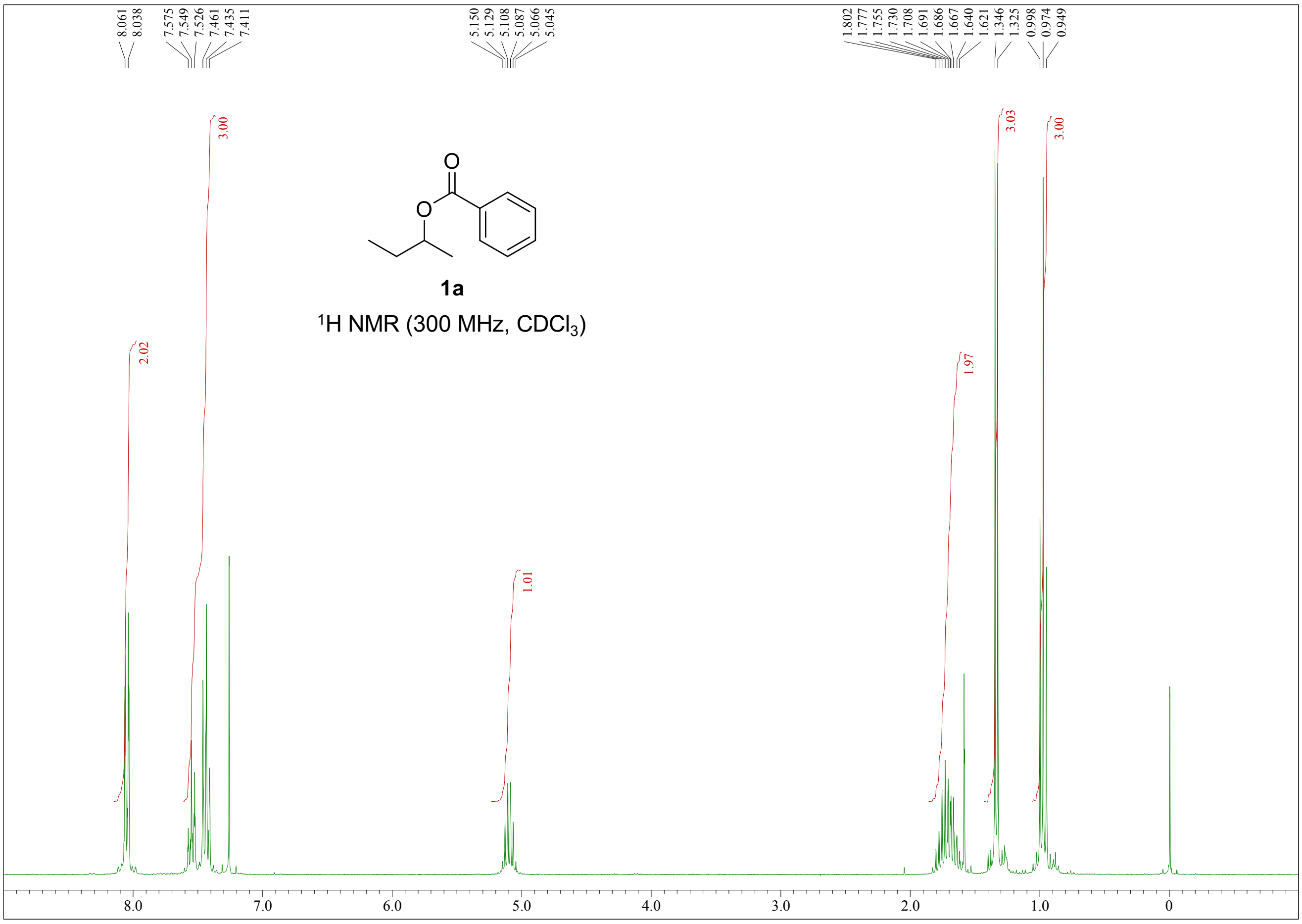


Fig. S5-2. Expansion of Figure S5-1.[a]
[a] Ratios of hexane:*i*-PrOH are given in parenthesis.
[b] Bars beyond R_s = 1.25 indicate good to excellent separation.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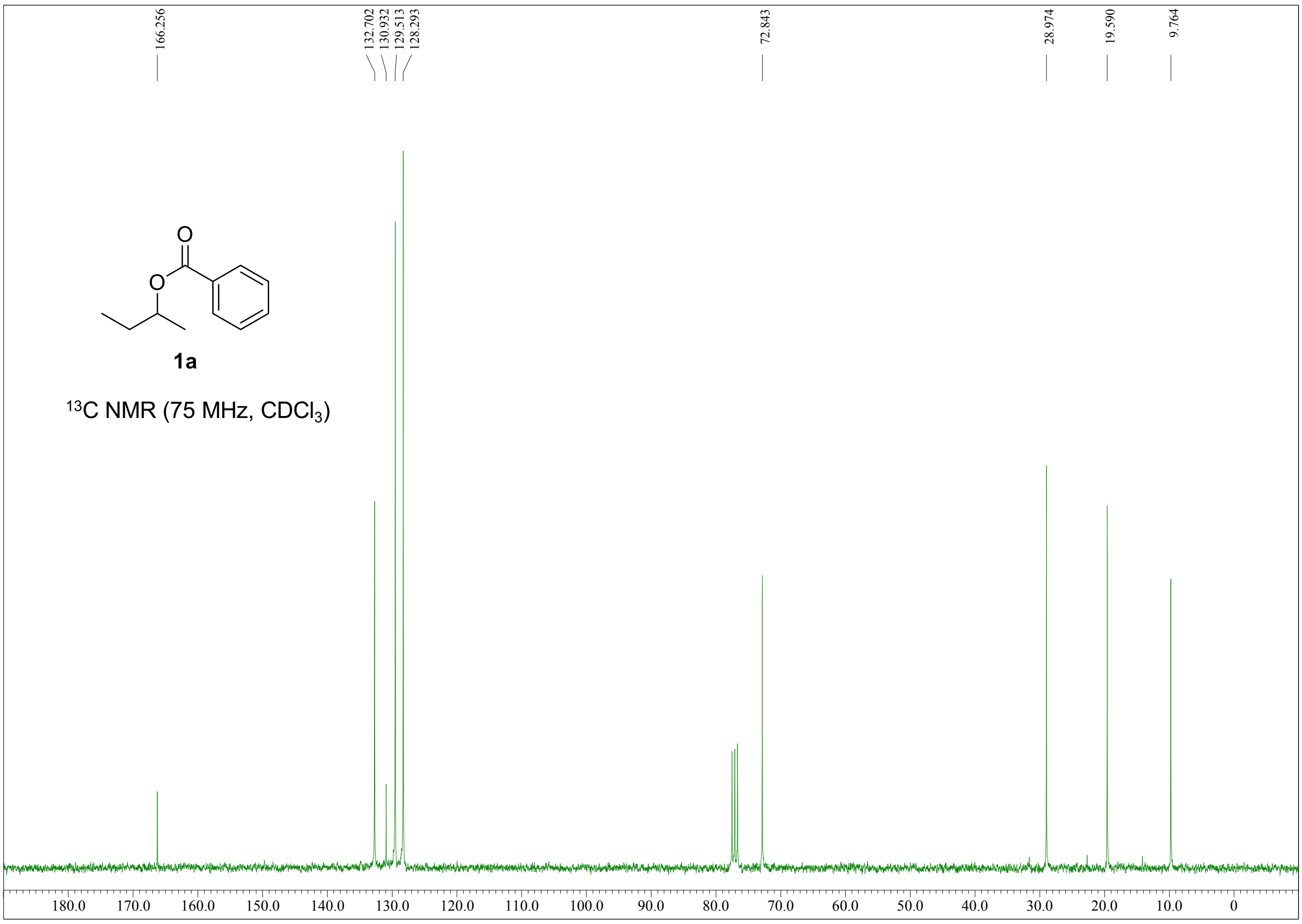
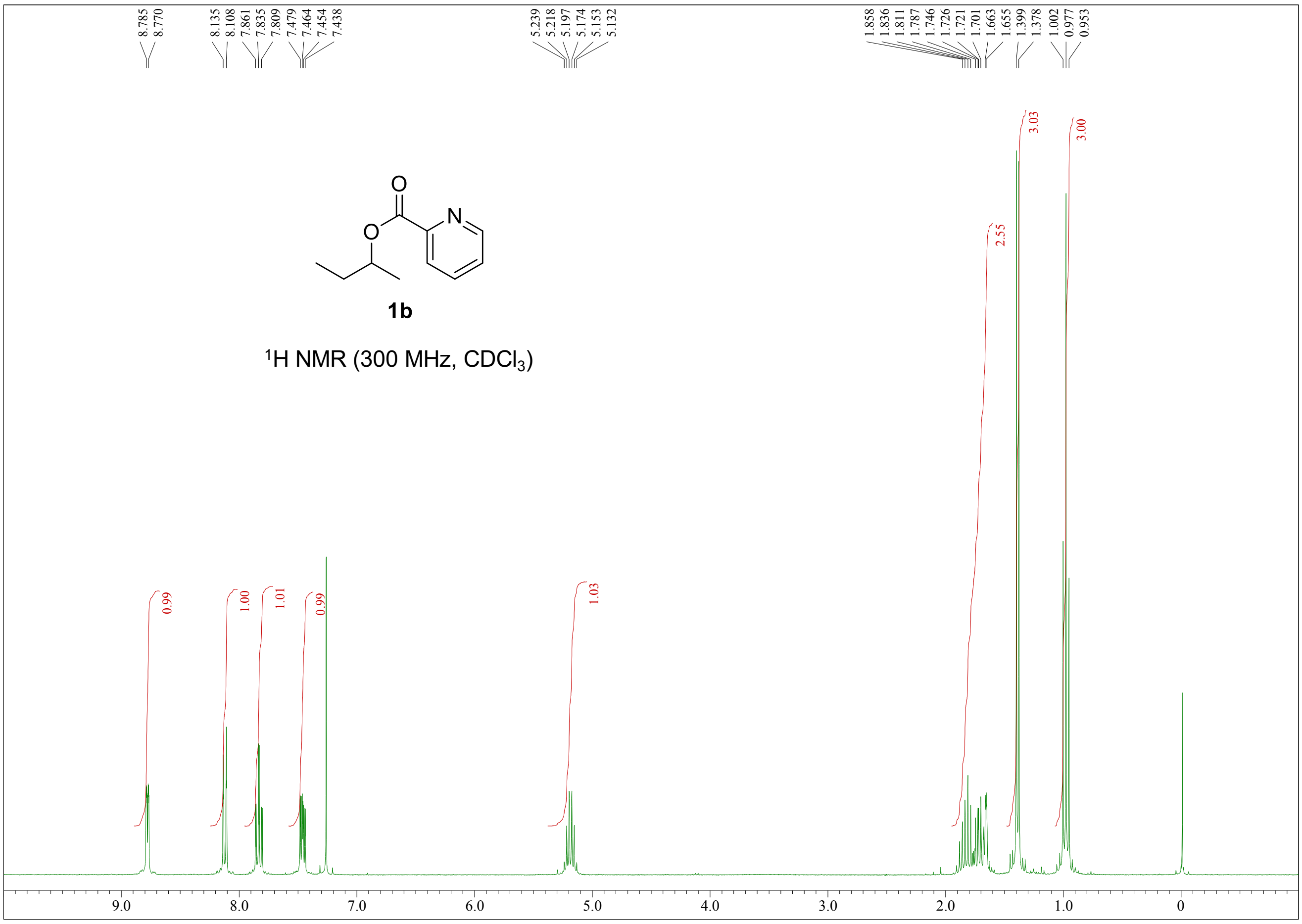
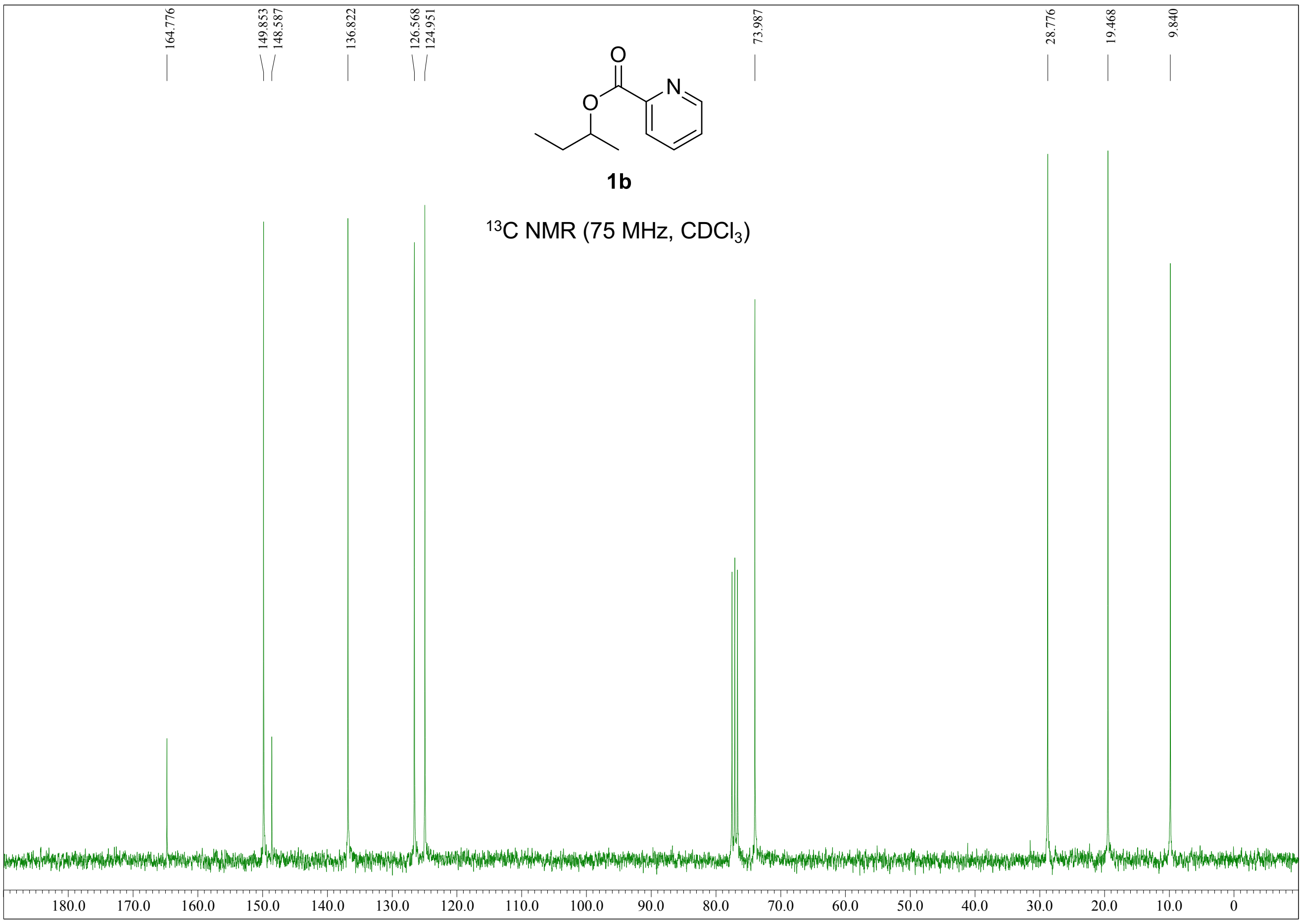
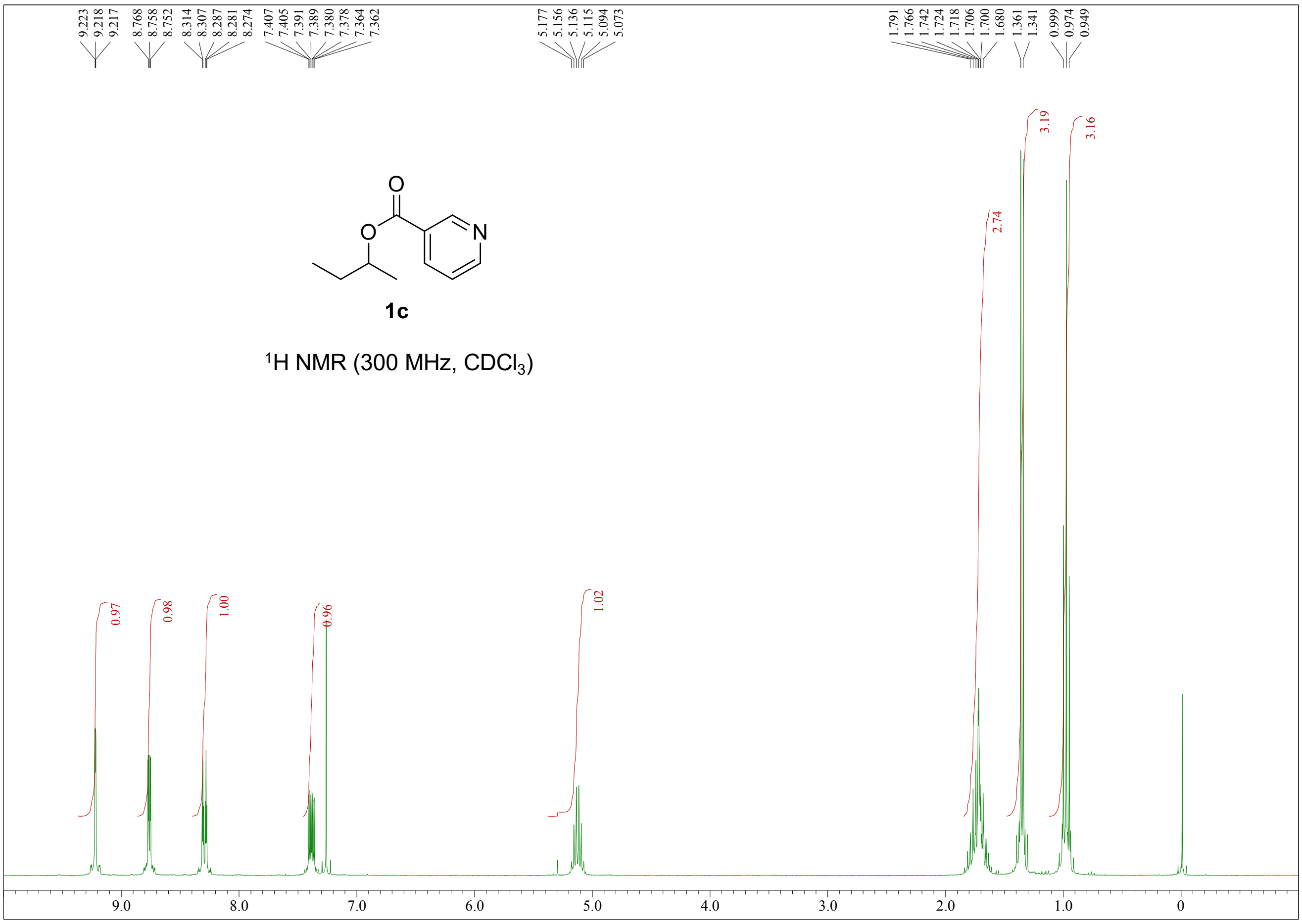
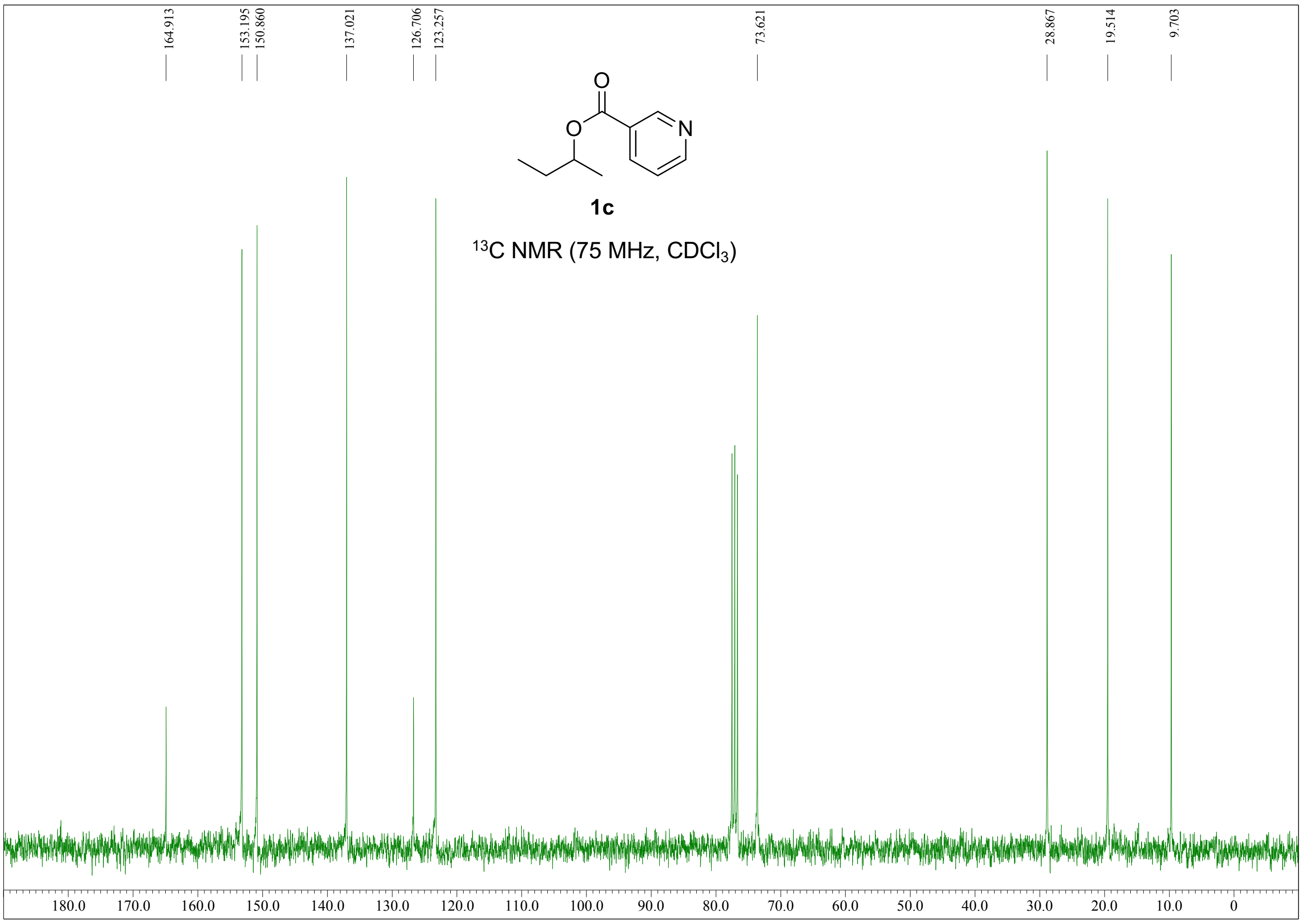
8.038
7.575
7.549
7.526
7.461
7.435
7.411
5.150
5.129
5.108
5.087
5.066
5.045
1.802
1.777
1.755
1.730
1.708
1.691
1.686
1.667
1.640
1.621
1.346
1.325
0.998
0.974
0.949
2.02
3.00
1.01
1.97
3.03
3.00
1a
¹H NMR (300 MHz, CDCl3)
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0


166.256
132.702
130.932
129.513
128.293
72.843
28.974
19.590
9.764
1a
¹³C NMR (75 MHz, CDCl3)
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0


8.785
8.770
8.135
8.108
7.861
7.835
7.809
7.479
7.464
7.454
7.438
5.239
5.218
5.197
5.174
5.153
5.132
1.858
1.836
1.811
1.787
1.746
1.726
1.721
1.701
1.663
1.655
1.399
1.378
1.002
0.977
0.953
0.99
1.00
1.01
0.99
1.03
2.55
3.03
3.00
1b
1H NMR (300 MHz, CDCl3)
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0


164.776
149.853
148.587
136.822
126.568
124.951
73.987
28.776
19.468
9.840
1b
13C NMR (75 MHz, CDCl3)
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0


9.223
9.218
9.217
8.768
8.758
8.752
8.314
8.307
8.287
8.281
8.274
7.407
7.405
7.391
7.389
7.380
7.378
7.364
7.362
5.177
5.156
5.136
5.115
5.094
5.073
1.791
1.766
1.742
1.724
1.718
1.706
1.700
1.680
1.361
1.341
0.999
0.974
0.949
O
O
N
1c
^{1}H NMR (300 MHz, CDCl$_3$)
0.97
0.98
1.00
0.96
1.02
2.74
3.19
3.16
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0


164.913
153.195
150.860
137.021
126.706
123.257
73.621
28.867
19.514
9.703
O
O
N
1c
^{13}C NMR (75 MHz, CDCl$_3$)
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
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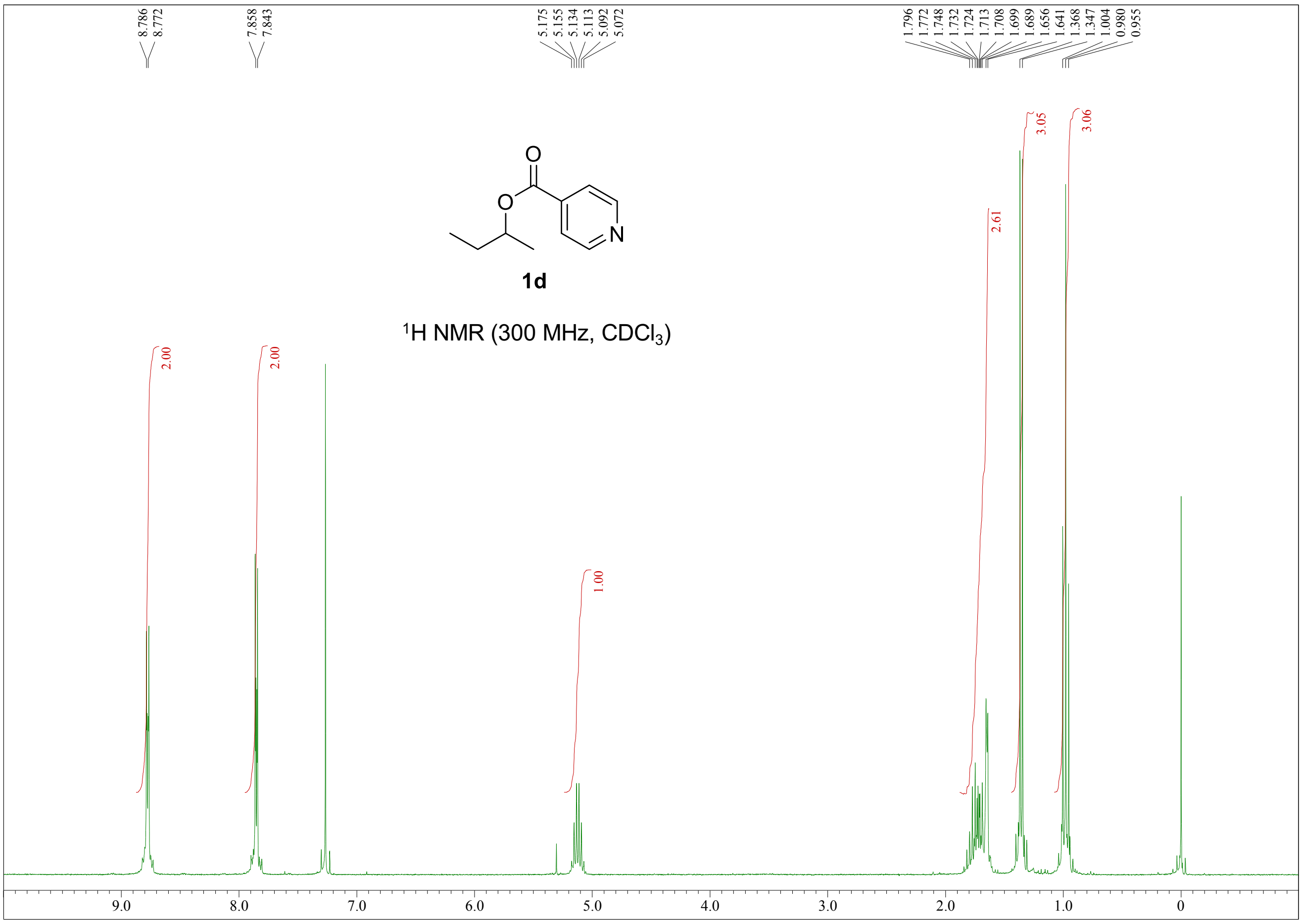
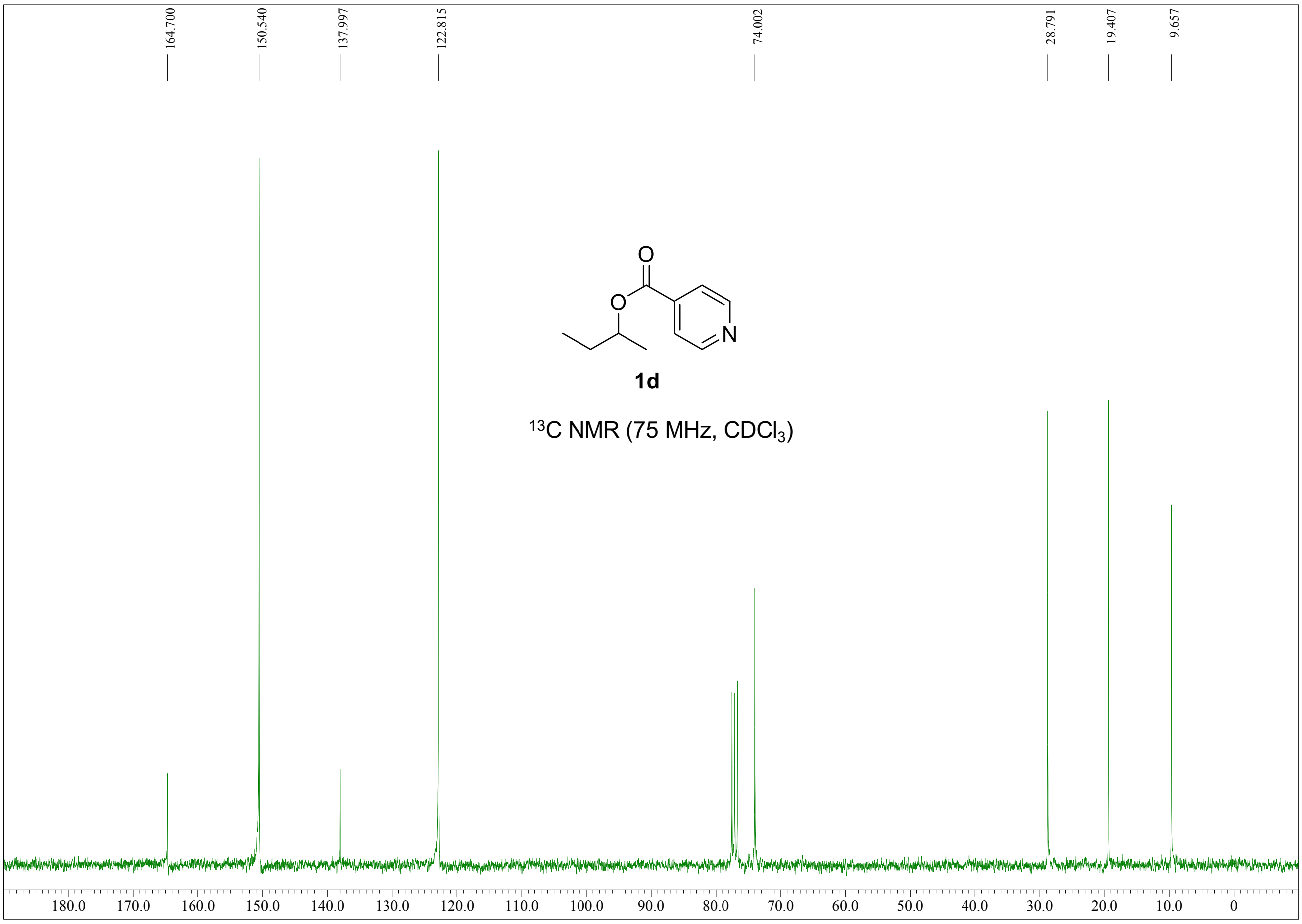
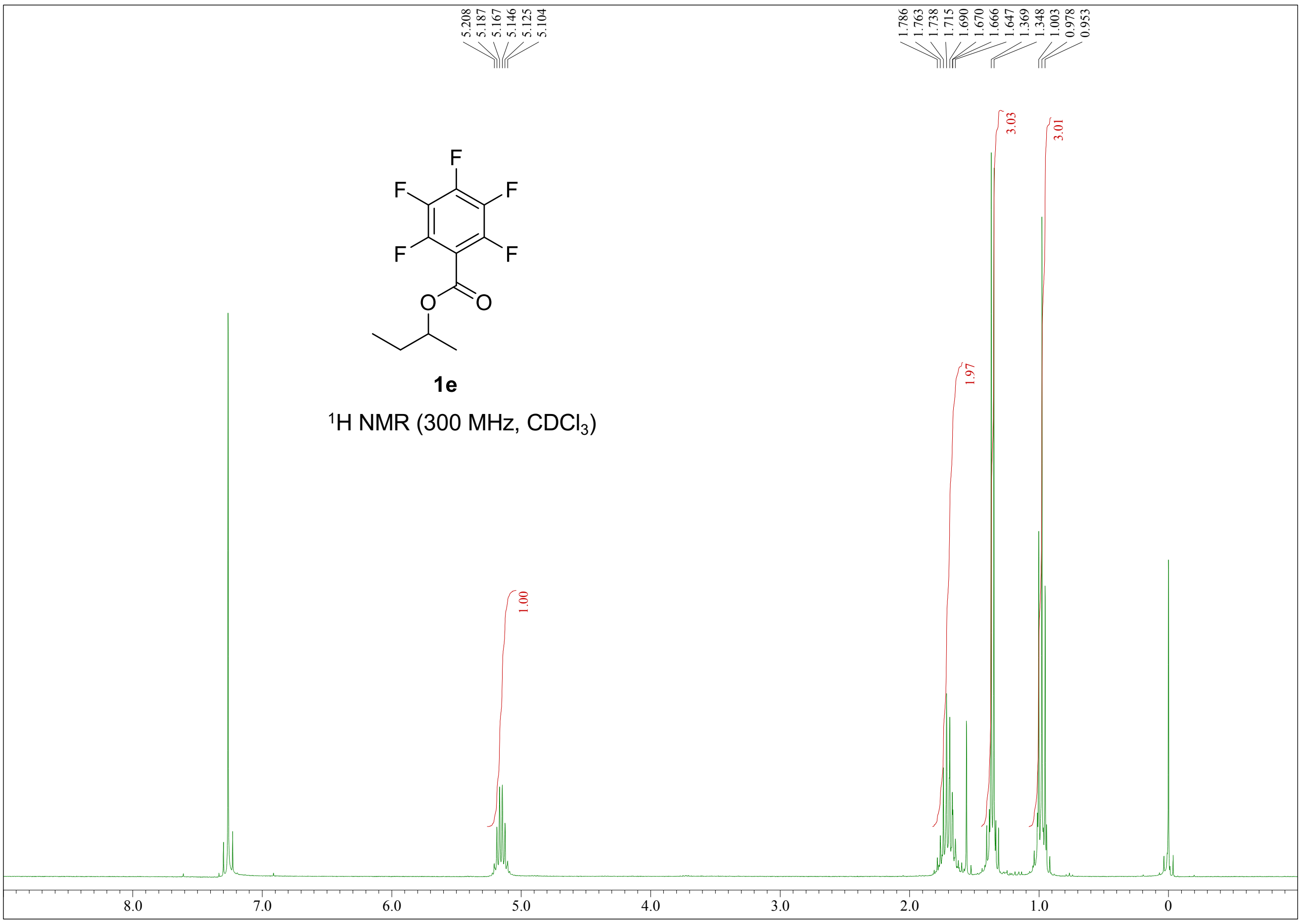
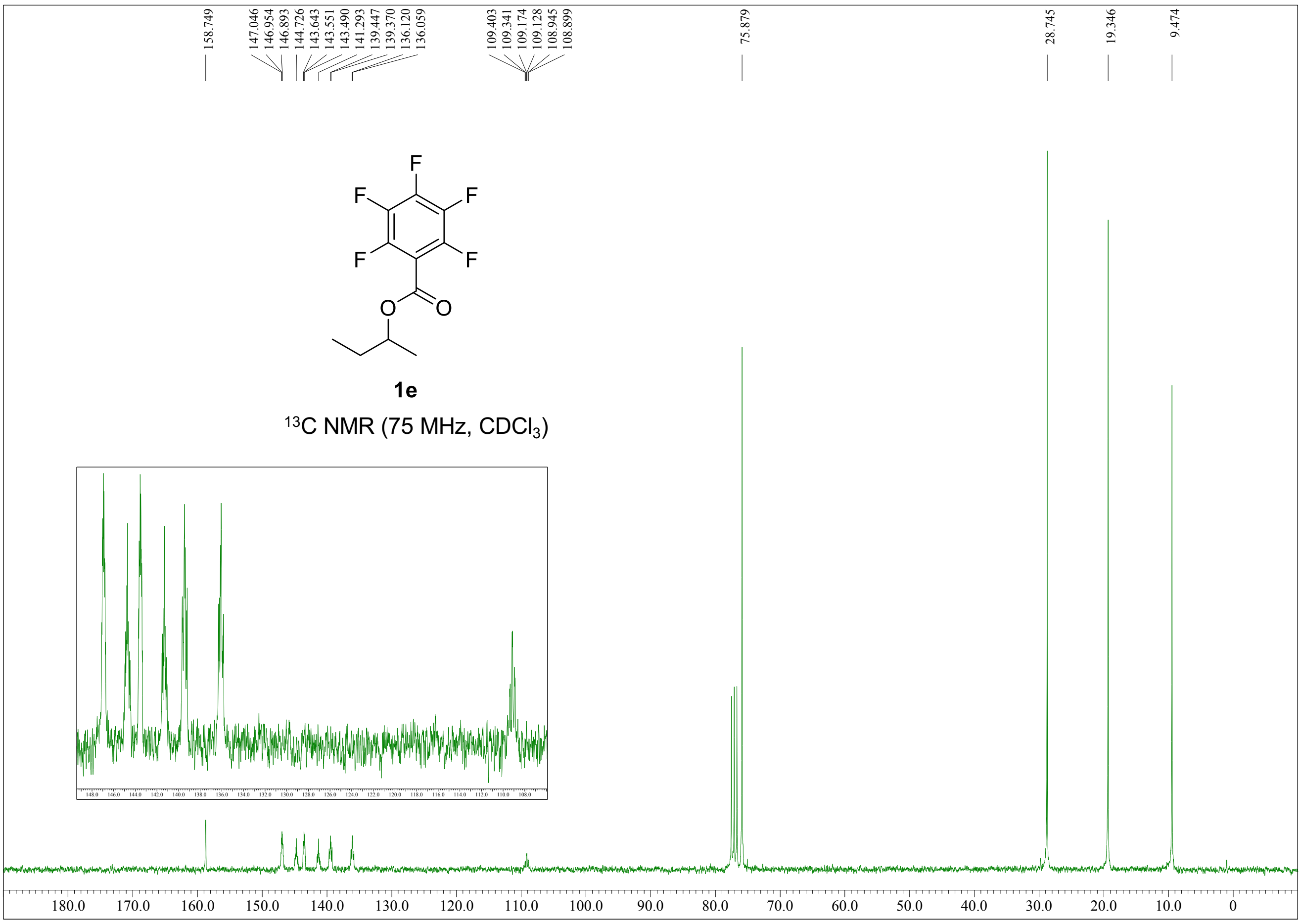
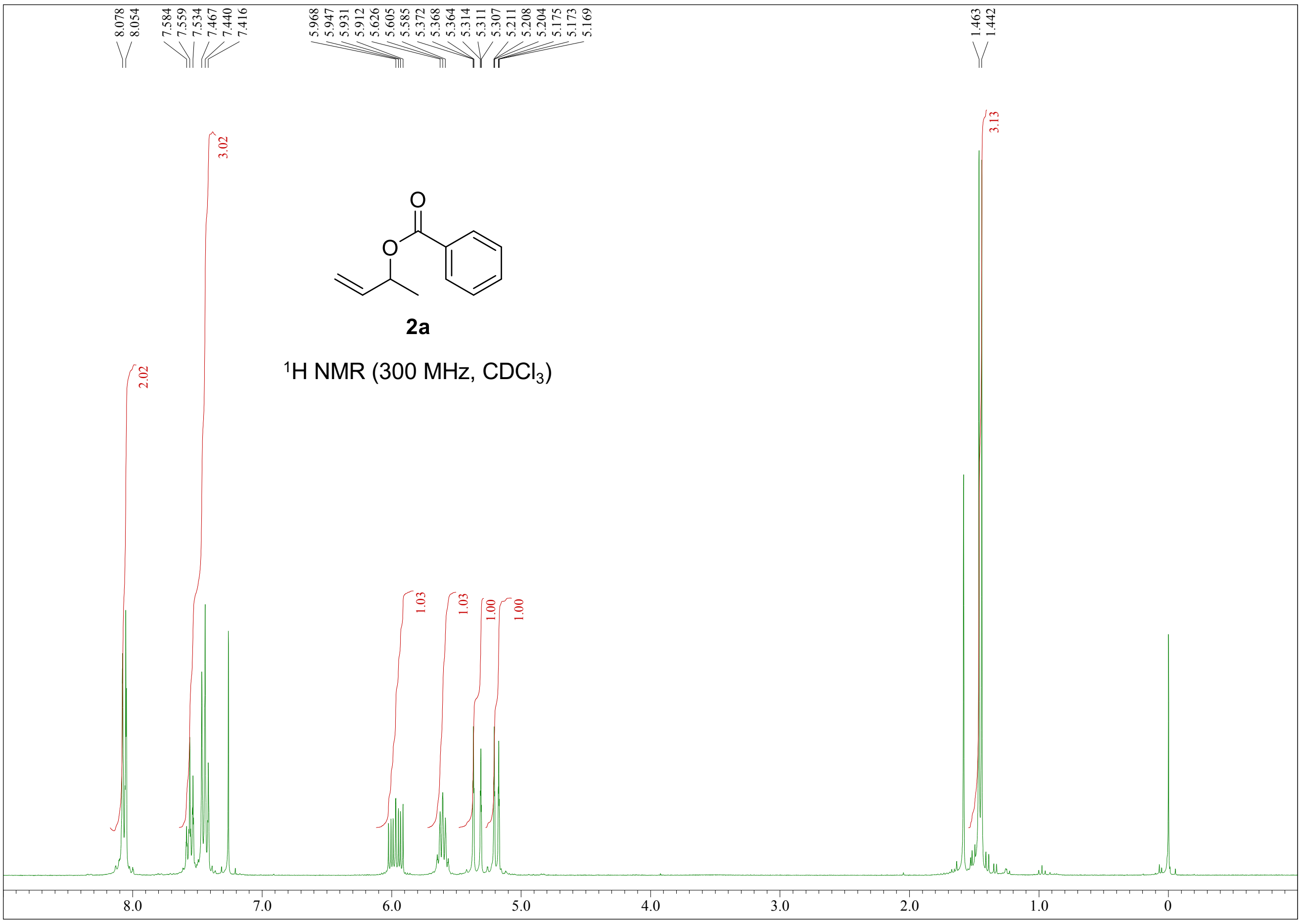
40.0
30.0
20.0
10.0
0

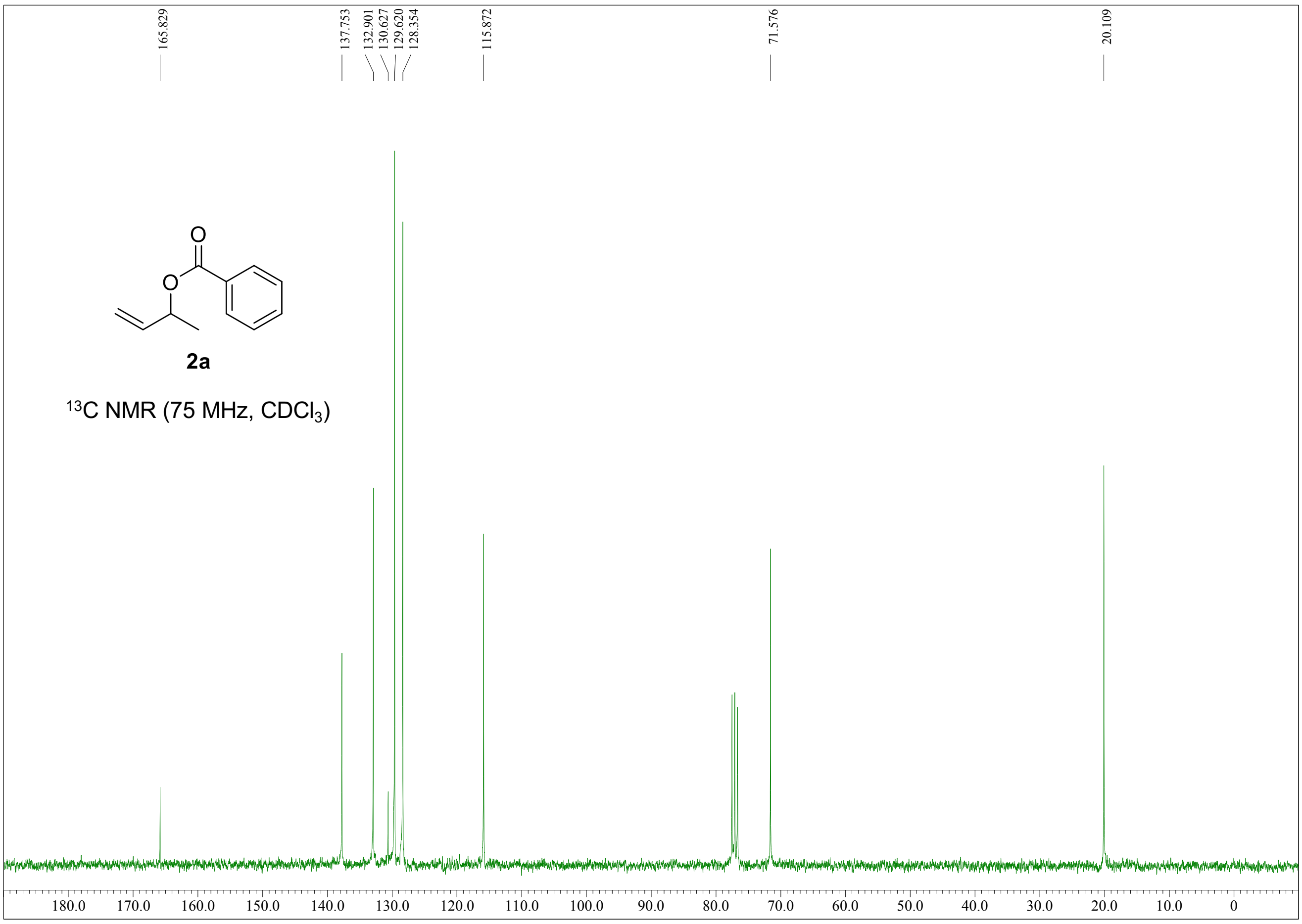

8.786
8.772
7.858
7.843
5.175
5.155
5.134
5.113
5.092
5.072
1.796
1.772
1.748
1.732
1.724
1.713
1.708
1.699
1.689
1.656
1.641
1.368
1.347
1.004
0.980
0.955
O
O
N
1d
1H NMR (300 MHz, CDCl3)
2.00
2.00
1.00
2.61
3.05
3.06
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0


164.700
150.540
137.997
122.815
74.002
28.791
19.407
9.657
O
O
N
1d
13C NMR (75 MHz, CDCl3)
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0


5.208 5.187 5.167 5.146 5.125 5.104
1.786 1.763 1.738 1.715 1.690 1.670 1.666 1.647 1.369 1.348 1.003 0.978 0.953
3.03
3.01
1.97
1.00
1e
1H NMR (300 MHz, CDCl3)
8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0


158.749
147.046 146.954 146.893 144.726 143.643 143.551 143.490 141.293 139.447 139.370 136.120 136.059
109.403 109.341 109.174 109.128 108.945 108.899
75.879
28.745
19.346
9.474
1e
13C NMR (75 MHz, CDCl3)
180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0


8.078
8.054
7.584
7.559
7.534
7.467
7.440
7.416
5.968
5.947
5.931
5.912
5.626
5.605
5.585
5.372
5.368
5.364
5.314
5.311
5.307
5.211
5.208
5.204
5.175
5.173
5.169
1.463
1.442
2.02
3.02
1.03
1.03
1.00
1.00
3.13
O
O
2a
^{1}H NMR (300 MHz, CDCl$_3$)
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0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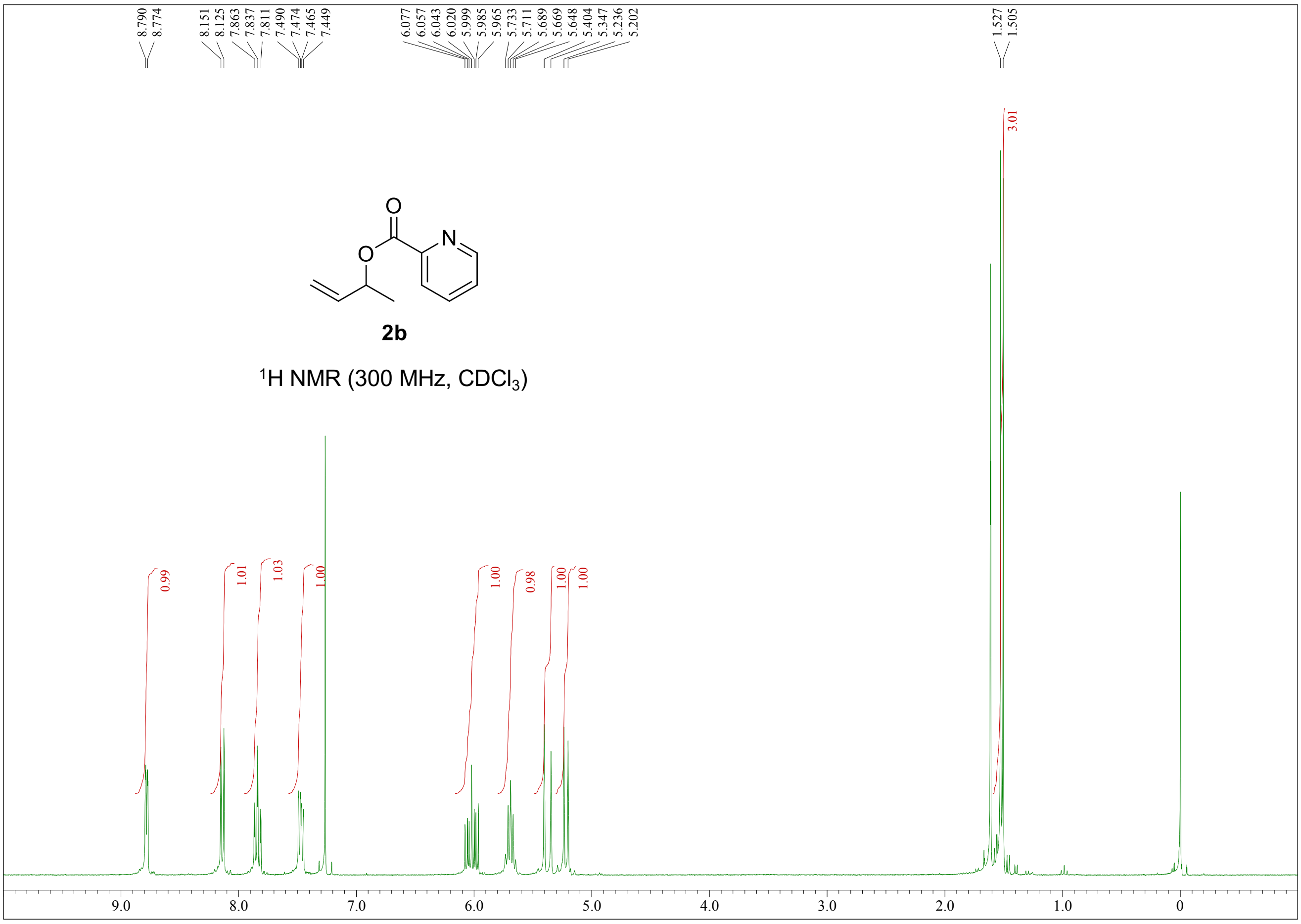
137.753
132.901
130.627
129.620
128.354
115.872
71.576
20.109
O
O
2a
^{13}C NMR (75 MHz, CDCl$_3$)
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0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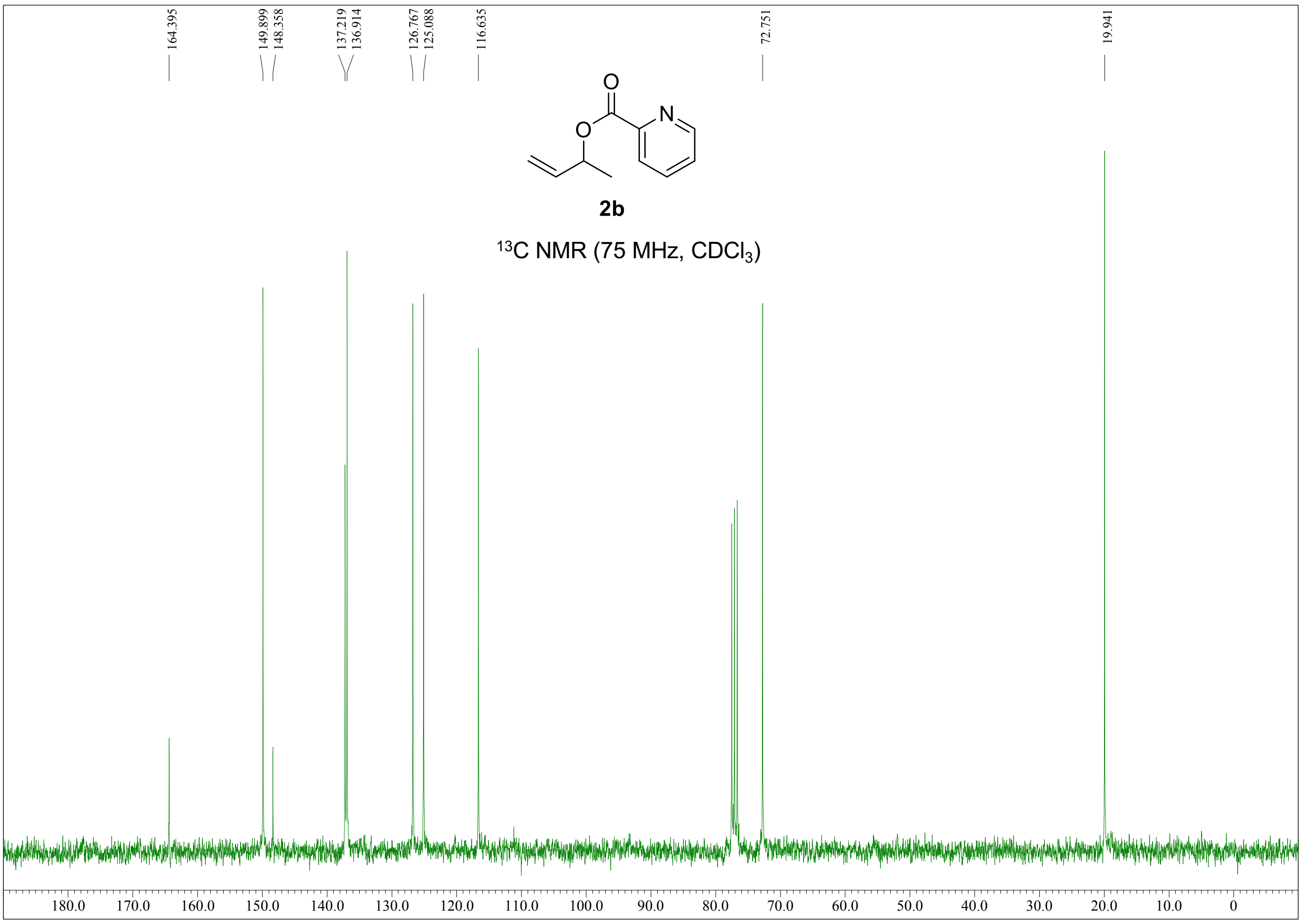
8.774
8.151
8.125
7.863
7.837
7.811
7.490
7.474
7.465
7.449
6.077
6.057
6.043
6.020
5.999
5.985
5.965
5.733
5.711
5.689
5.669
5.648
5.404
5.347
5.236
5.202
1.527
1.505
2b
1H NMR (300 MHz, CDCl3)
0.99
1.01
1.03
1.00
1.00
0.98
1.00
1.00
3.01
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0


164.395
149.899
148.358
137.219
136.914
126.767
125.088
116.635
72.751
19.941
2b
13C NMR (75 MHz, CDCl3)
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
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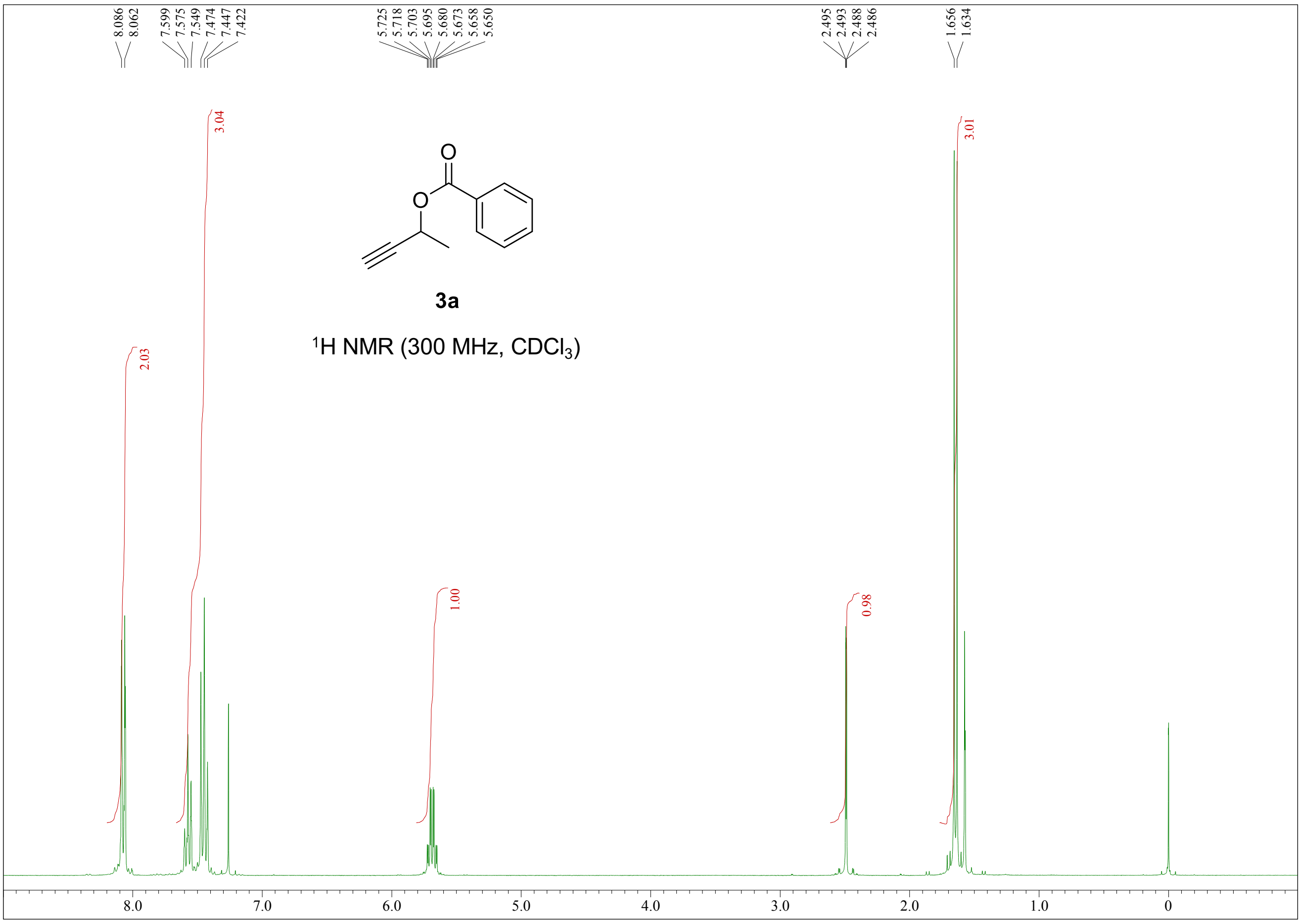
20.0
10.0
0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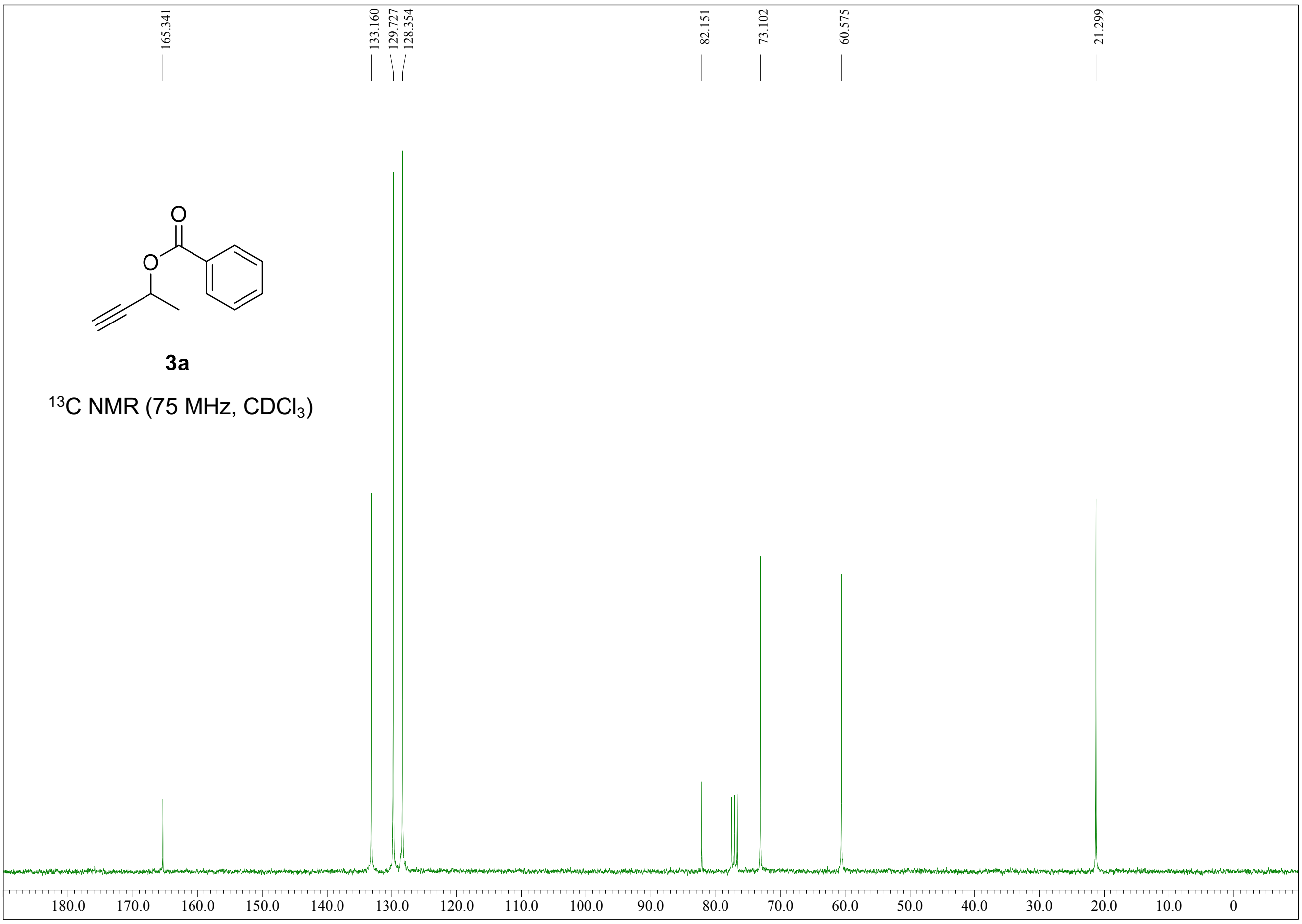
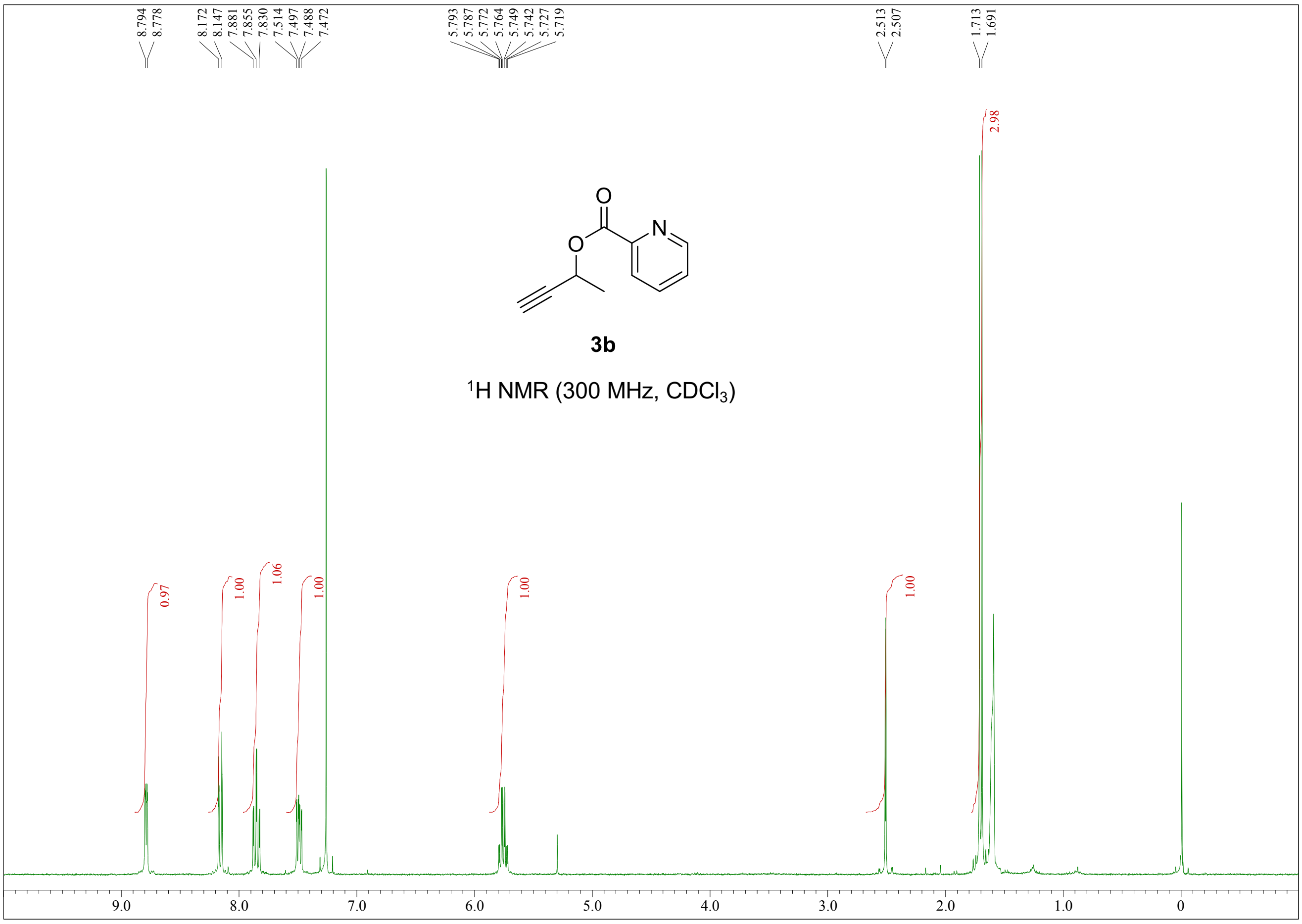
8.062
7.599
7.575
7.549
7.474
7.447
7.422
5.725
5.718
5.703
5.695
5.680
5.673
5.658
5.650
2.495
2.493
2.488
2.486
1.656
1.634
2.03
3.04
1.00
0.98
3.01
O
O
3a
1H NMR (300 MHz, CDCl3)
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0


165.341
133.160
129.727
128.354
82.151
73.102
60.575
21.299
O
O
3a
13C NMR (75 MHz, CDCl3)
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0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8.147
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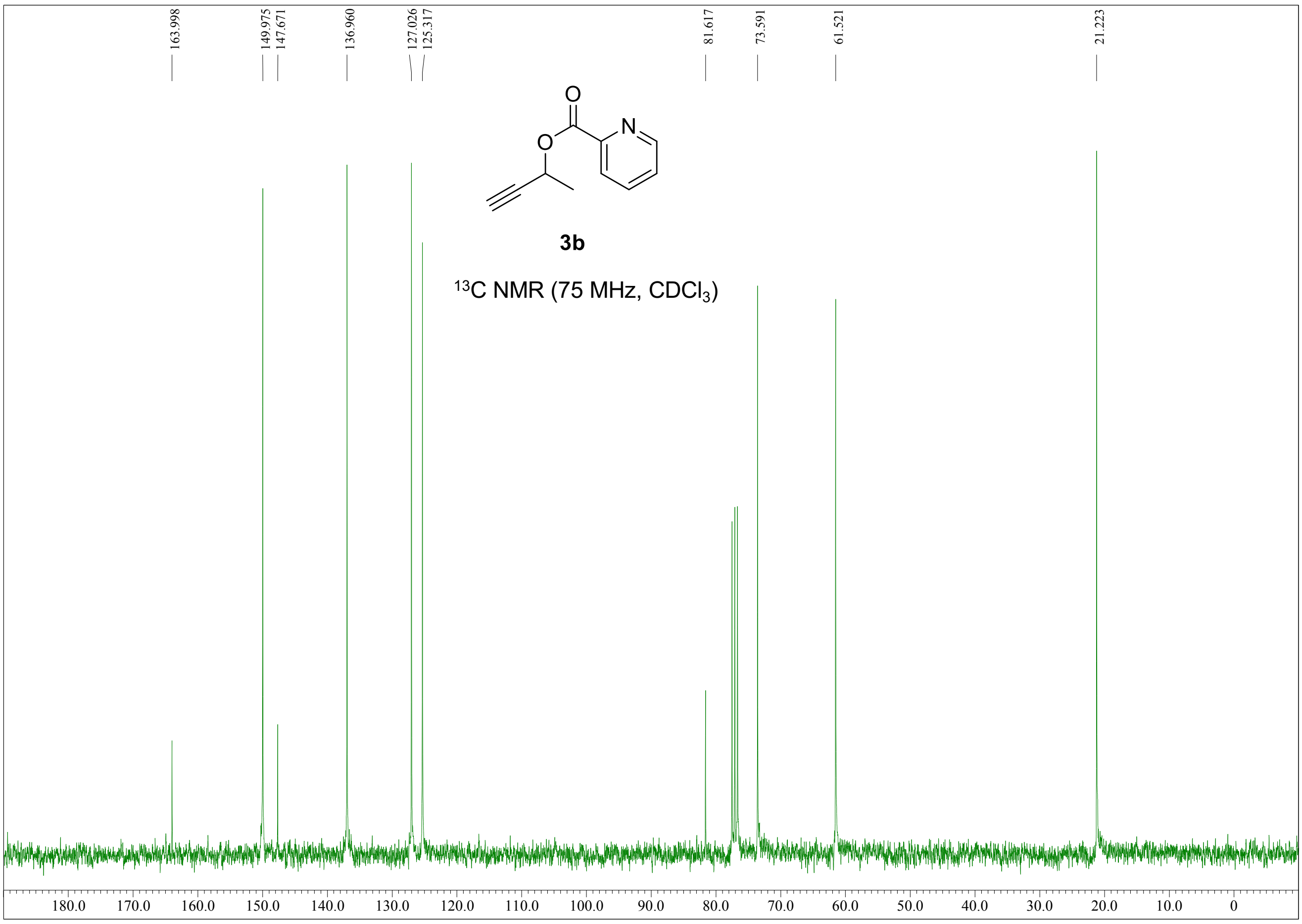
7.855
7.830
7.514
7.497
7.488
7.472
5.793
5.787
5.772
5.764
5.749
5.742
5.727
5.719
2.513
2.507
1.713
1.691
0.97
1.00
1.06
1.00
1.00
1.00
2.98
O
N
O
3b
1H NMR (300 MHz, CDCl3)
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0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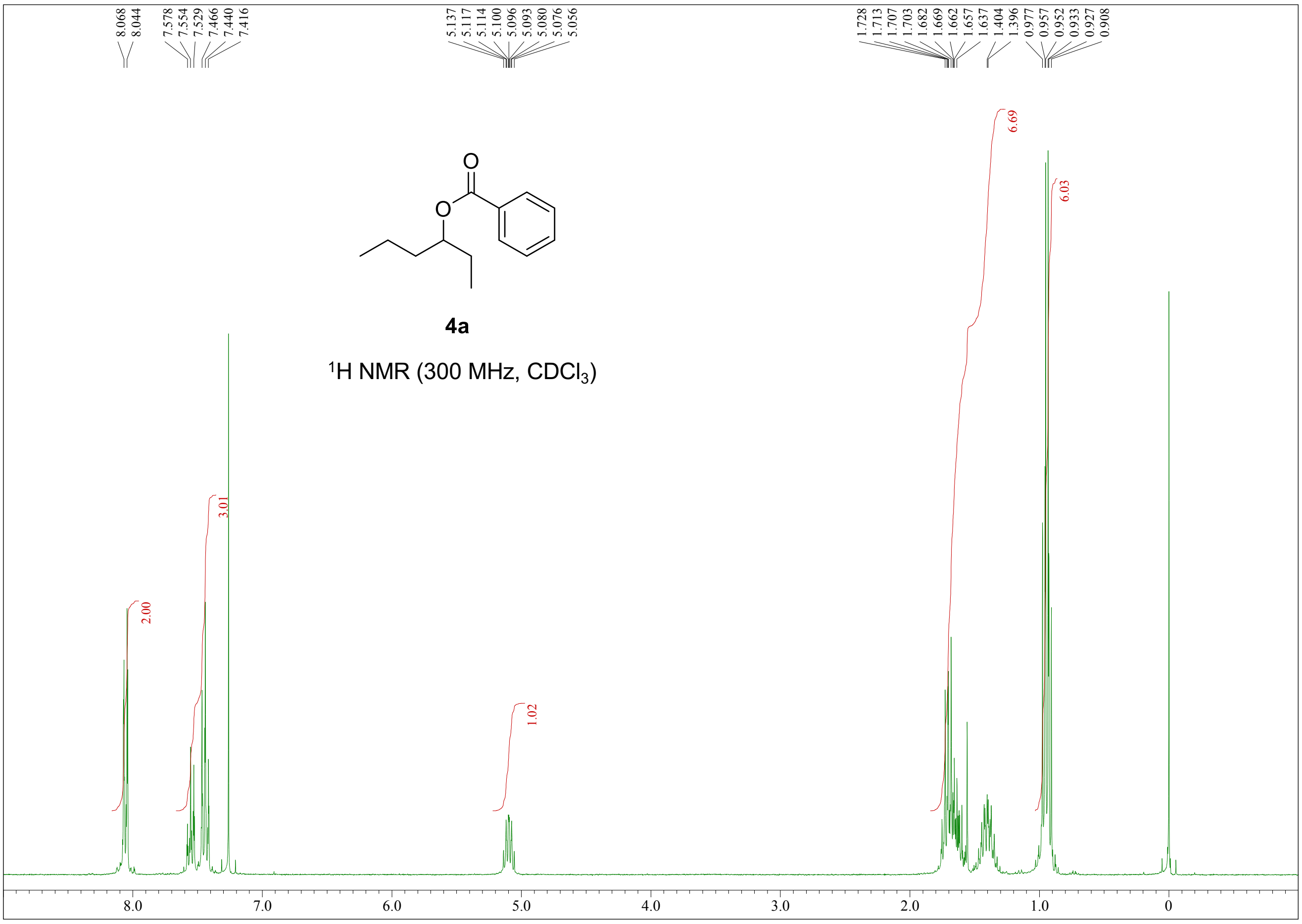
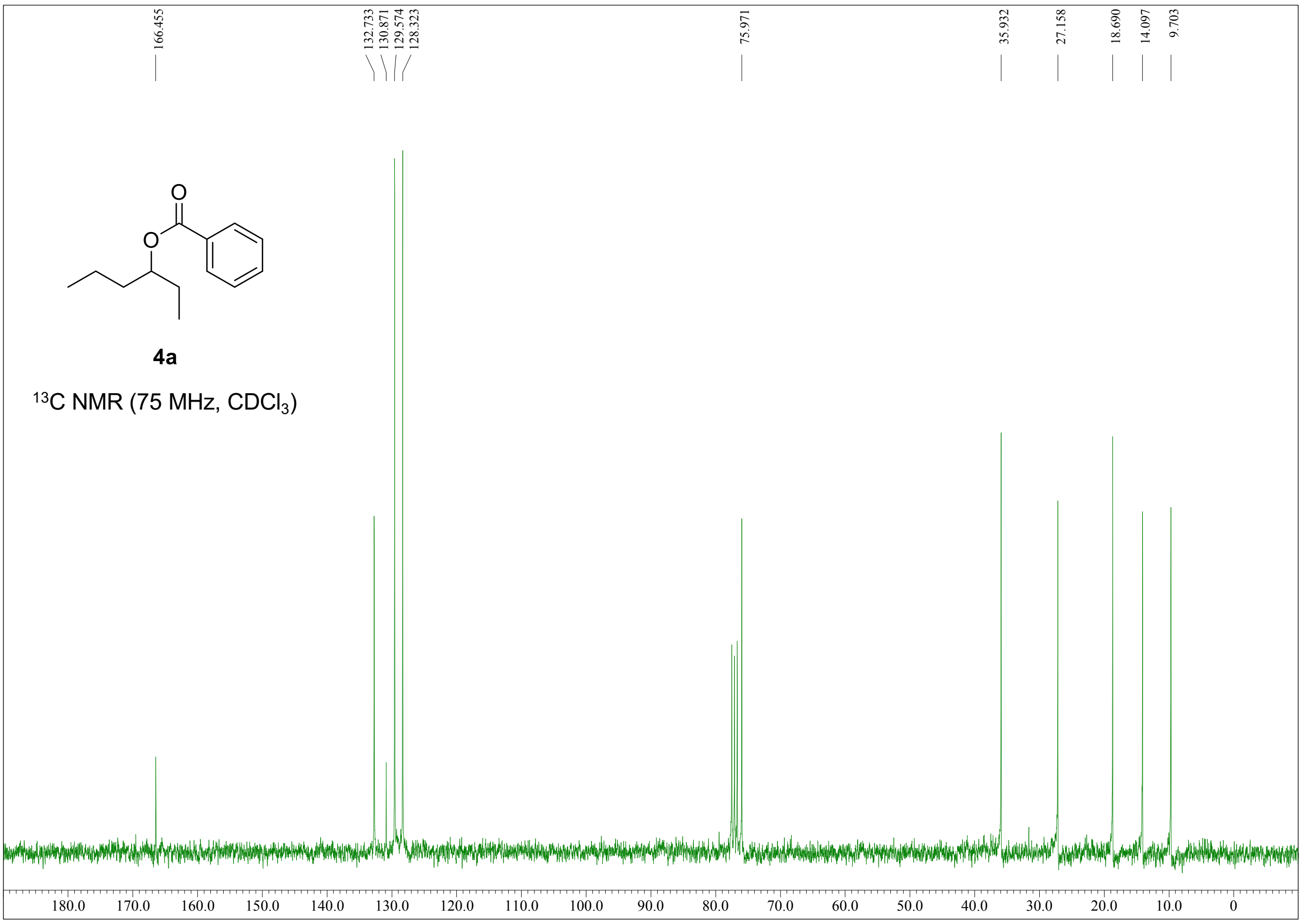
149.975
147.671
136.960
127.026
125.317
81.617
73.591
61.521
21.223
O
N
O
3b
13C NMR (75 MHz, CDCl3)
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0


8.068
8.044
7.578
7.554
7.529
7.466
7.440
7.416
5.137
5.117
5.114
5.100
5.096
5.093
5.080
5.076
5.056
1.728
1.713
1.707
1.703
1.682
1.669
1.662
1.657
1.637
1.404
1.396
0.977
0.957
0.952
0.933
0.927
0.908
O
O
4a
^{1}H NMR (300 MHz, CDCl$_3$)
2.00
3.01
1.02
6.69
6.03
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0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132.733
130.871
129.574
128.323
75.971
35.932
27.158
18.690
14.097
9.703
O
O
4a
^{13}C NMR (75 MHz, CDCl$_3$)
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
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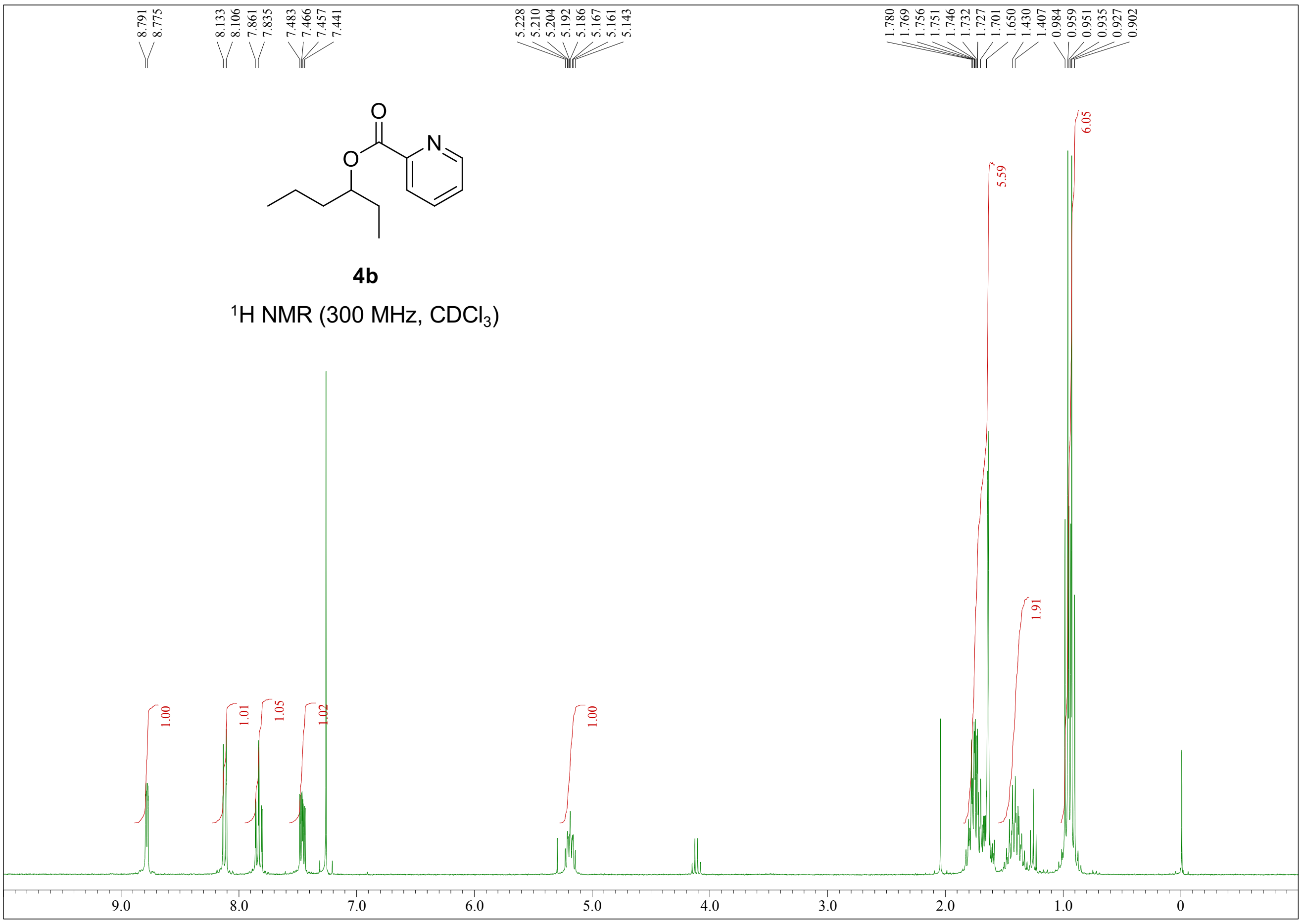
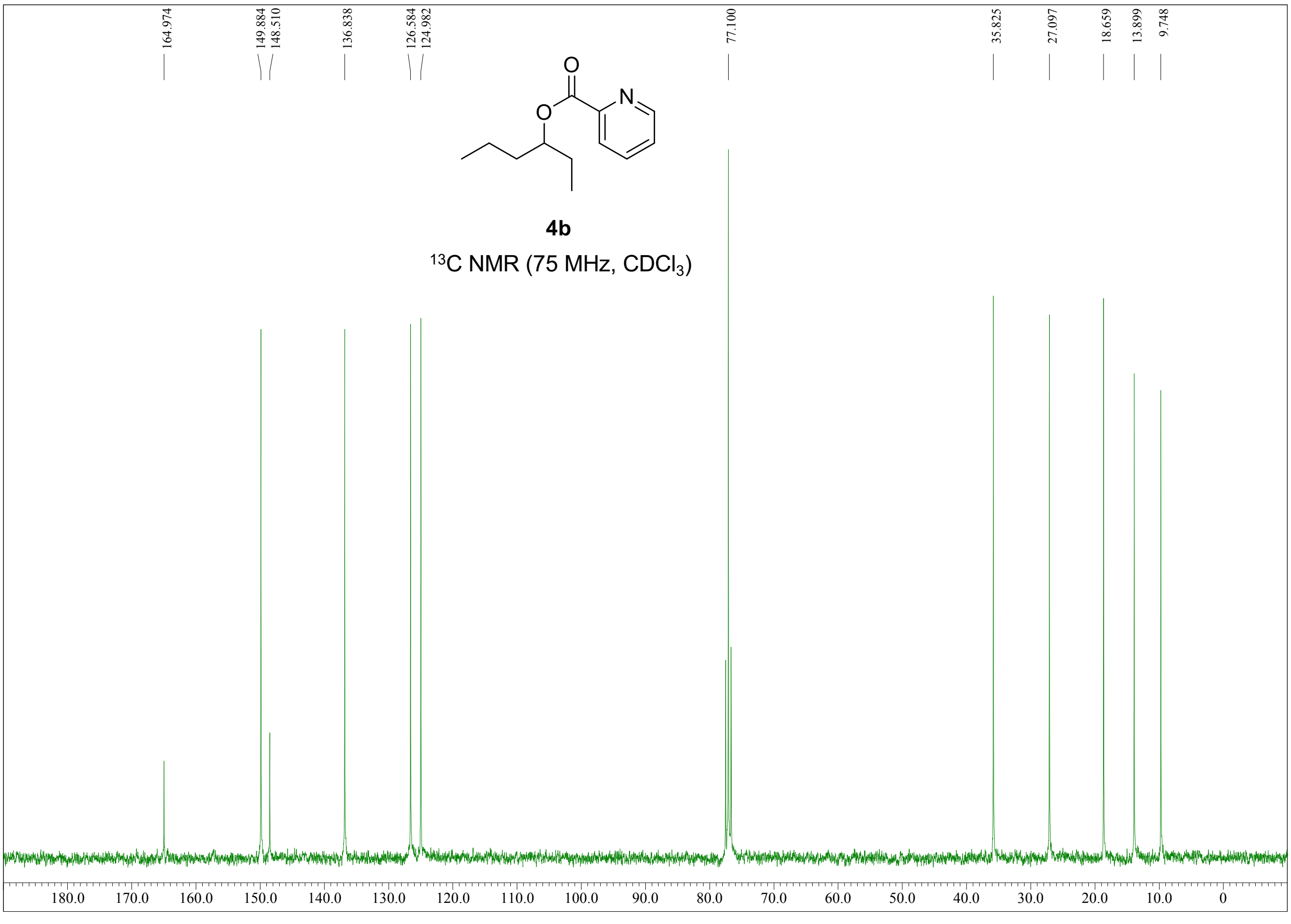
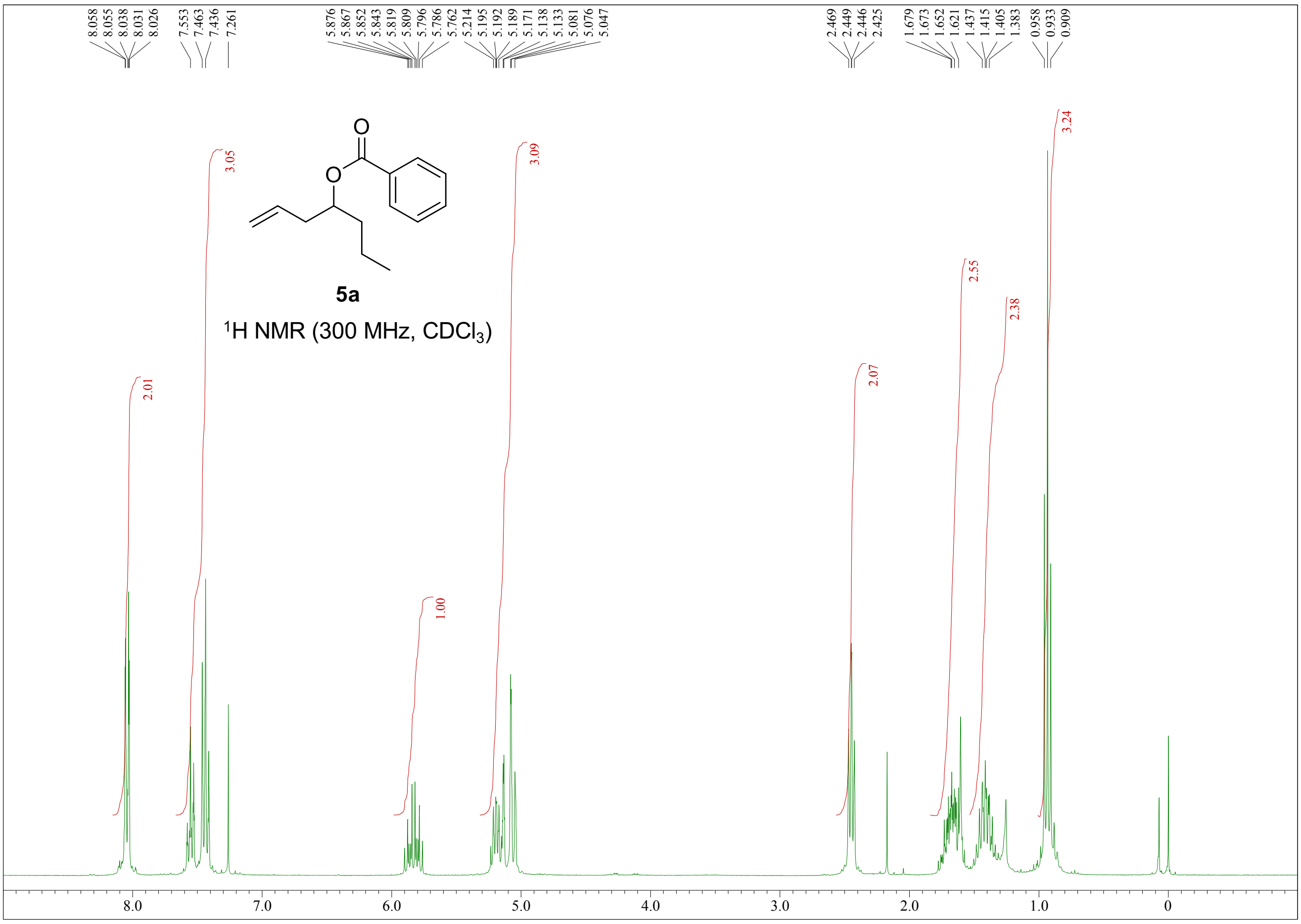
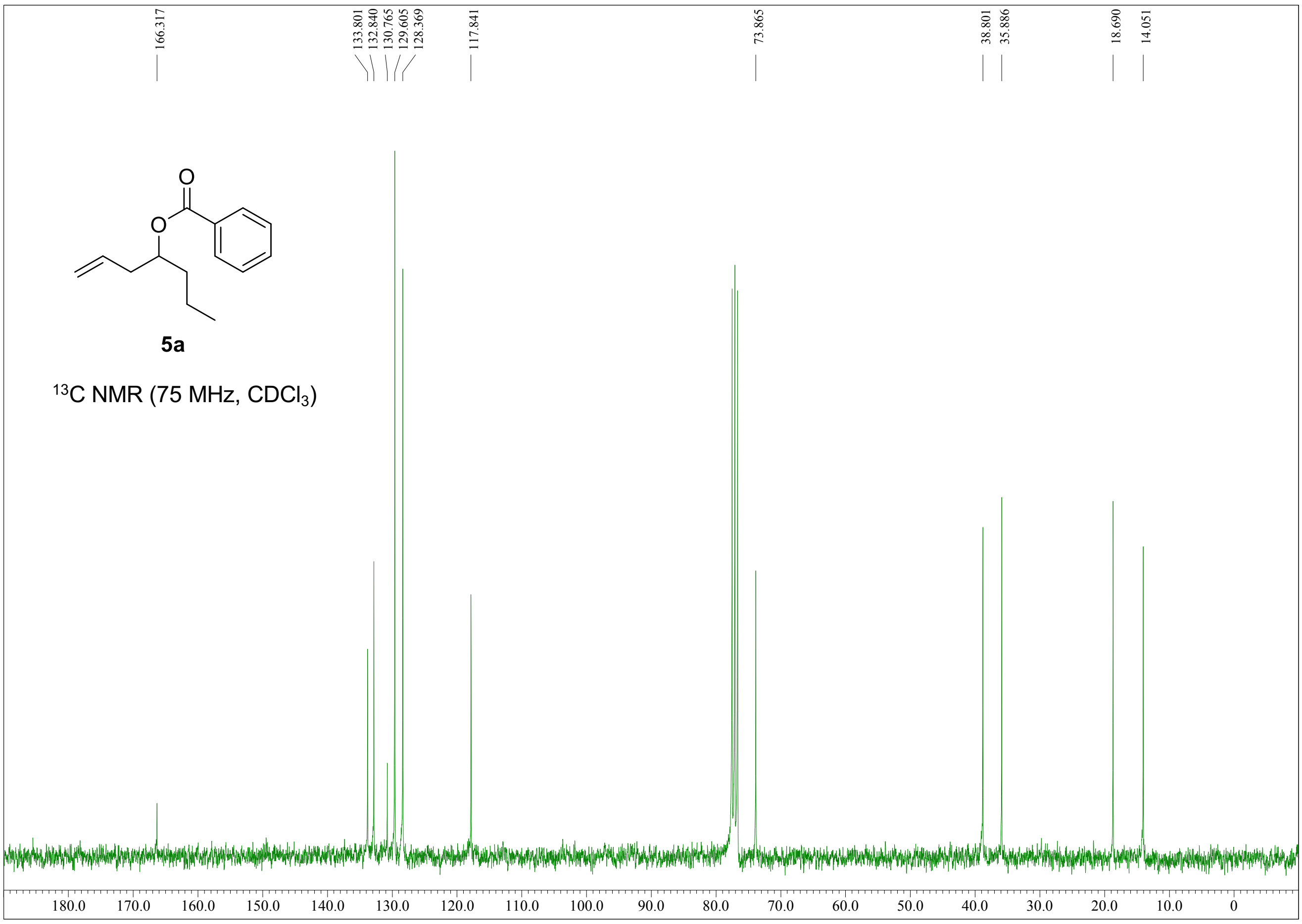
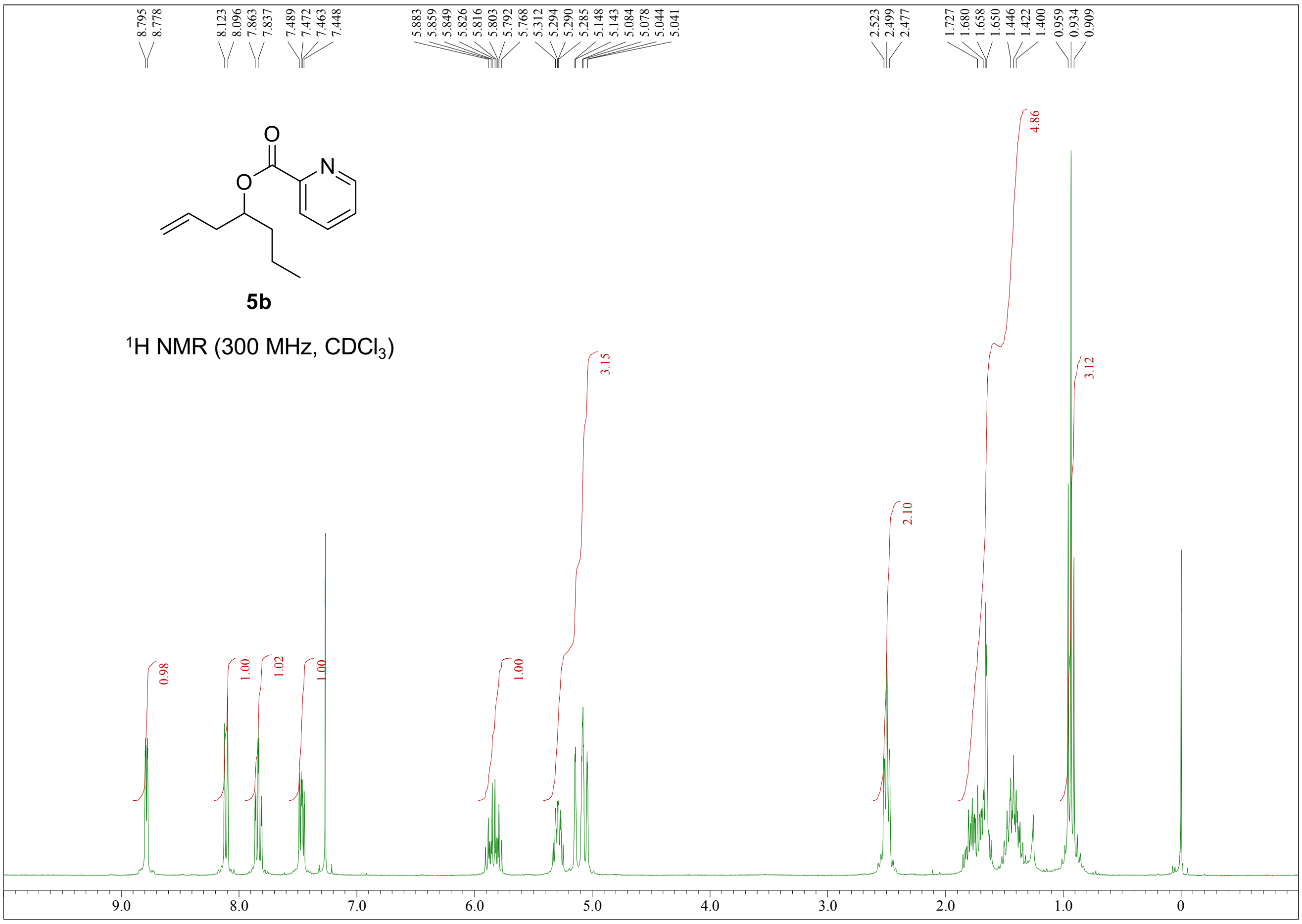
20.0
10.0
0


8.791
8.775
8.133
8.106
7.861
7.835
7.483
7.466
7.457
7.441
5.228
5.210
5.204
5.192
5.186
5.167
5.161
5.143
1.780
1.769
1.756
1.751
1.746
1.732
1.727
1.701
1.650
1.430
1.407
0.984
0.959
0.951
0.935
0.927
0.902
4b
^{1}H NMR (300 MHz, $CDCl_3$)
1.00
1.01
1.05
1.02
1.00
5.59
1.91
6.05
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0

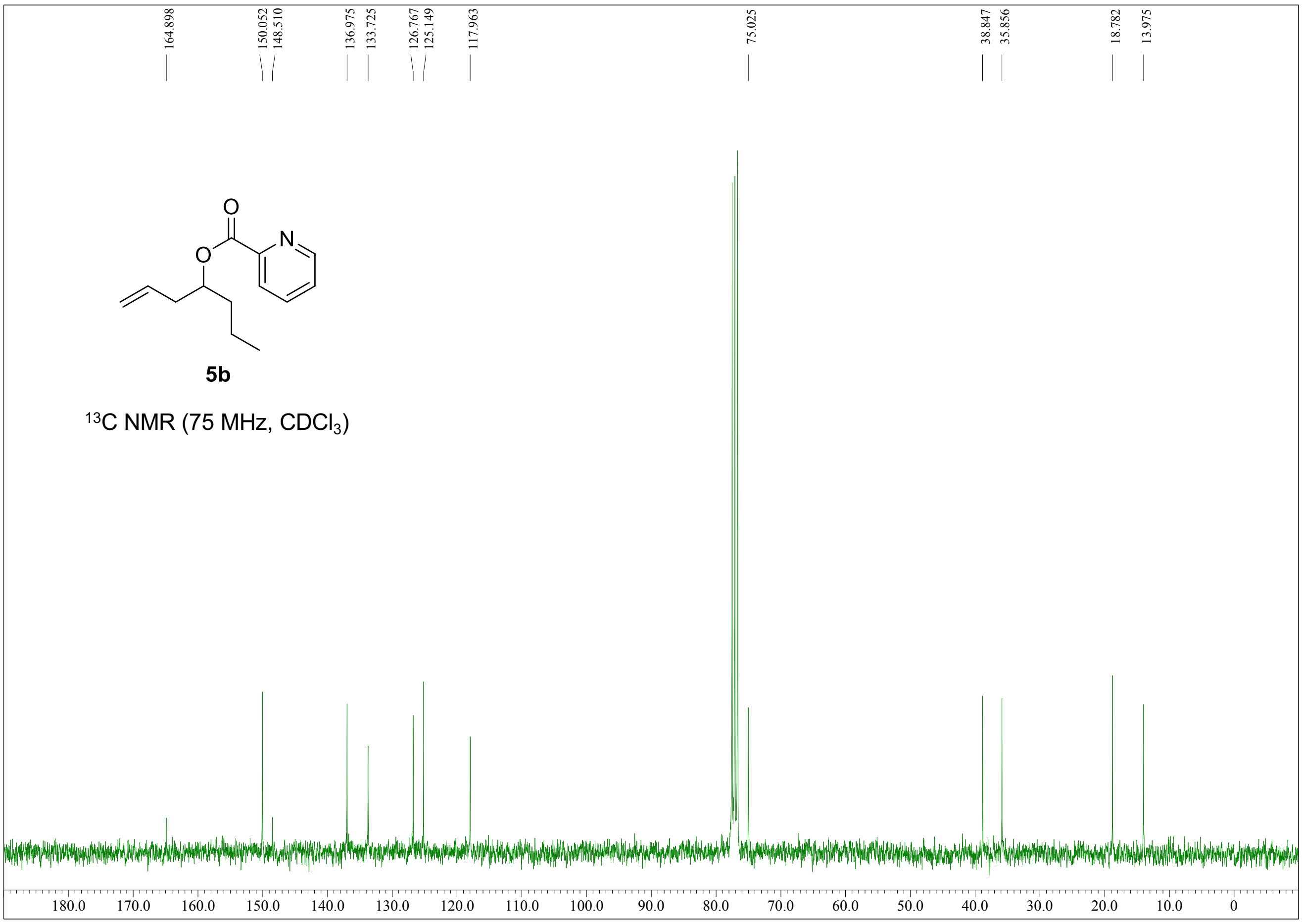

164.974
149.884
148.510
136.838
126.584
124.982
77.100
35.825
27.097
18.659
13.899
9.748
4b
^{13}C NMR (75 MHz, $CDCl_3$)
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0


8.058 8.055 8.038 8.031 8.026 7.553 7.463 7.436 7.261
5.876 5.867 5.852 5.843 5.819 5.809 5.796 5.786 5.762 5.214 5.195 5.192 5.189 5.171 5.138 5.133 5.081 5.076 5.047
2.469 2.449 2.446 2.425 1.679 1.673 1.652 1.621 1.437 1.415 1.405 1.383 0.958 0.933 0.909
2.01
3.05
1.00
3.09
2.07
2.55
2.38
3.24
O
O
5a
1H NMR (300 MHz, CDCl3)
8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0


166.317
133.801 132.840 130.765 129.605 128.369
117.841
73.865
38.801 35.886
18.690 14.051
O
O
5a
13C NMR (75 MHz, CDCl3)
180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0



8.795
8.778
8.123
8.096
7.863
7.837
7.489
7.472
7.463
7.448
5.883
5.859
5.849
5.826
5.816
5.803
5.792
5.768
5.312
5.294
5.290
5.285
5.148
5.143
5.084
5.078
5.044
5.041
2.523
2.499
2.477
1.727
1.680
1.658
1.650
1.446
1.422
1.400
0.959
0.934
0.909
O
N
O
5b
^{1}H NMR (300 MHz, $CDCl_3$)
4.86
3.15
3.12
2.10
0.98
1.00
1.02
1.00
1.00
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0



164.898
150.052
148.510
136.975
133.725
126.767
125.149
117.963
75.025
38.847
35.856
18.782
13.975
O
N
O
5b
^{13}C NMR (75 MHz, $CDCl_3$)
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0