Supplementary Material (ESI) for Green Chemistry

Supplementary Information

Catalyst-free and catalytic Friedel-Crafts alkylations of indoles in Solkane® 365mfc, an environmentally benign alternative solvent

*Xiu-Hua Xu, Akihiro Kusuda, Etsuko Tokunaga, and Norio Shibata**

Department of Applied Chemistry, Graduate School of Engineering, Nagoya Institute of Technology,

Gokiso, Showa-ku, Nagoya 466-8555, Japan

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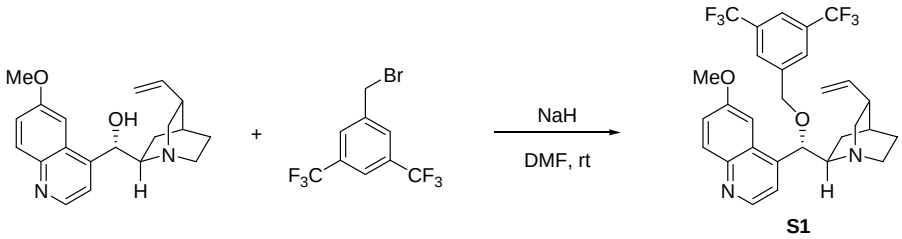
1. General Methods:

All reactions were performed in oven-dried glassware under a positive pressure of nitrogen. Solvents were transferred *via* syringe and were introduced into the reaction vessles though a rubber septum. All of the reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm Merck silica-gel (60-F254). The TLC plates were visualized with UV light and 7% phosphomolybdic acid or $KMnO_4$ in water/heat. Column chromatography was carried out on a column packed with silica-gel 60N spherical neutral size 63-210 μm. The ^{1}H-NMR (300 MHz), ^{1}H-NMR (200 MHz), ^{19}F-NMR (282.3 MHz), ^{19}F-NMR (188.2 MHz) and ^{13}C-NMR (150.9 MHz) spectra for solution in $CDCl_3$ or CD_3OD were recorded on a Buruker Avance 600 and Varian Mercury 200 or 300. Chemical shifts (δ) are expressed in ppm downfield from internal TMS or $CHCl_3$. HPLC analyses were performed on a JASCO U-2080 Plus using 4.6 x 250 mm CHIRALPAK AS-H or CHIRALCEL OD-H column. Mass spectra were recorded on a SHIMADZU LCMS-2050EV or SHIMADZU GCMS-QP5050A. Optical rotations were measured on a HORIBA SEPA-300. Infrared spectra were recorded on a JASCO FT/ IR-4100 spectrometer.

2. Preparation of catalyst 4a, 4d-4e and 4e':

Quinidine 9-*O*-[3,5-bis(trifluoromethyl)benzyl] ether (S1):

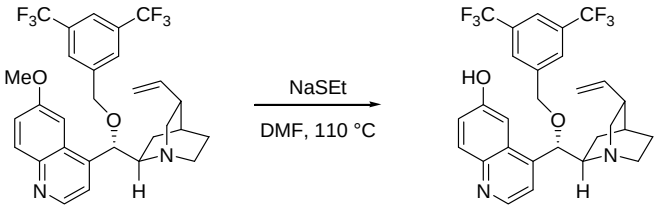


S1

To a stirred solution of Quinidine (100.0 mg, 0.31 mmol) in dry DMF (1.5 mL), NaH (30.9 mg, 60% suspension in mineral oil, 0.77 mmol) was added at room temperature under nitrogen atmosphere. The resulting mixture was stirred at room temperature for 2 h. Then 3,5-Bis(trifluoromethyl)benzyl bromide (62.3 μL, 0.34 mmol) was added slowly and it was stirred at room temperature for 4 h. After dilutiion with sat. NH_4Cl aq, aqueous layer was extracted with Et_2O, and the combined organic layer was washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (ethyl acetate/MeOH/Et_3N = 90/10/0.1) to give S1 as a white solid (129.0 mg, 76% yield).

^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.34 (m, 1H), 1.52-1.55 (m, 1H), 1.77-1.82 (m, 2H), 2.11 (dd, *J* = 13.2, 9.3 Hz, 1H), 2.26 (q, *J* = 8.4 Hz, 1H), 2.71-2.87 (m, 2H), 2.92-3.00 (m, 1H), 3.12-3.25 (m, 2H), 3.92 (s, 3H), 4.56 (s, 2H), 5.00 (s, 1H), 5.03-5.07 (m, 1H), 5.31 (brs, 1H), 5.93-6.04 (m, 1H), 7.31 (s, 1H), 7.39 (d, *J* = 2.4 Hz, 1H), 7.42 (d, *J* = 3.0 Hz, 1H), 7.80 (s, 2H), 7.82 (s, 1H), 8.07 (d, *J* = 9.3 Hz, 1H), 8.77 (d, *J* = 4.5 Hz, 1H) ; ^{19}F NMR ($CDCl_3$, 282.3 MHz) δ -63.4 (s, 6F) ; ^{13}C NMR ($CDCl_3$, 150.9 MHz) δ 22.1, 26.4, 27.8, 39.7, 49.8, 50.1, 55.5, 59.8, 69.8, 82.1, 100.9, 114.5, 118.7, 121.5, 121.8, 123.2 (q, *J* = 273.1 Mz), 127.1, 127.2, 131.7 (q, *J* = 34.7 Hz), 132.0, 140.1, 140.56, 143.61, 144.8, 147.5, 157.9 ; IR (KBr) 2939, 1620, 1506, 1473, 1357, 1280, 1185, 1134, 890, 858 cm^{-1} ; mp = 143-146 ºC ; MS (EI, *m/z*) 550 (M^+) ; HRMS calcd. for $C_{29}H_{28}F_6N_2O_2^+$: 550.2055 Found : 550.2051 ; $[\alpha]_D^{25}$ = +99.9 (c = 1.94, $CHCl_3$)

Cupreidine 9-*O*-[3,5-bis(trifluoromethyl)benzyl] ether (4d):

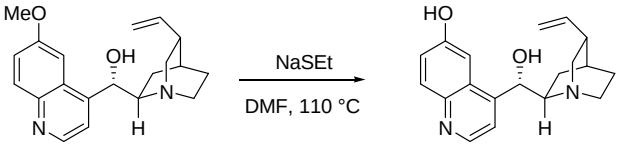


S1 **4d**

Cinchona alkaloid derivative S1 (555.0 mg, 1.01 mmol) and NaSEt (340.0 mg, 4.04 mmol) were dissolved in dry DMF (6.2 mL) at room temperature under nitrogen atmosphere. The resulting mixture was stirred at 110 °C for 18 h. The reaction mixture was cooled down to room temperature, diluted with sat. NH_4Cl aq. Then aqueous layer was extracted with ethyl acetate, and the combined organic layer was washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (ethyl acetate/MeOH/Et_3N = 90/10/0.1) to give 4d as a light brown solid (303.4 mg, 56% yield).

^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.26 (br, 1H), 1.51-1.1.61 (m, 1H), 1.69 (m, 1H), 1.92 (br, 1H), 2.37-2.43 (m, 2H), 2.89-2.99 (m, 1H), 3.13-3.26 (m, 3H), 3.65 (br, 1H), 4.52 (d, *J* = 12.3 Hz, 1H), 4.64 (d, *J* = 12.3 Hz, 1H), 5.01-5.11 (m, 2H), 5.89-6.01 (m, 2H), 7.36 (dd, *J* = 9.2, 2.4 Hz, 1H), 7.41 (d, *J* = 4.2 Hz, 1H), 7.83-7.87 (m, 4H), 8.03 (d, *J* = 9.0 Hz, 1H), 8.73-8.72 (m, 2H) ; ^{19}F NMR ($CDCl_3$, 282.3 MHz) δ -63.3 (s, 6F) ; ^{13}C NMR ($CDCl_3$, 150.9 MHz) δ 19.7, 25.6, 27.6, 39.2, 49.6, 49.7, 59.0, 69.8, 79.6, 105.2, 115.3, 117.4, 121.6, 123.1, 123.2 (q, *J* = 273.1 Hz), 127.0, 127.5, 131.66, 131.73 (q, *J* = 33.2 Hz), 139.0, 140.3, 142.4, 143.6, 146.5, 157.0 ; IR (KBr) 2940, 2875, 1619, 1509, 1468, 1280, 1176, 1134, 919, 884, 683 cm^{-1} ; mp = 99-102 ºC ; MS (EI, *m/z*) 536 (M^+), HRMS calcd. for $C_{28}H_{26}F_6N_2O_2^+$: 536.1898 Found : 536.1883 ; $[\alpha]_D^{25}$ = +94.0 (c = 1.77, $CHCl_3$)

Cupreidine (4a)[1]:

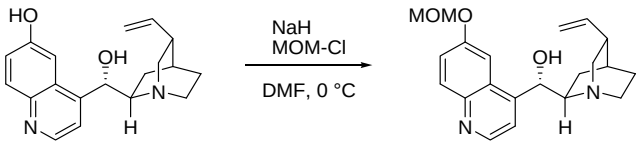


Quinidine **4a**

Quinidine (2.0 g, 6.16 mmol) and NaSEt (2.0 g, 24.6 mmol) were dissolved in dry DMF (20.0 mL) at room temperature under nitrogen atmosphere. The resulting mixture was stirred at 110 °C for 2.5 h. The reaction mixture was cooled down to room temperature, diluted with sat. NH_4Cl aq. Then aqueous layer was extracted with ethyl acetate, and the combined organic layer was washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (ethyl acetate/MeOH/Et_3N = 90/10/0.1) to give 4a as a yellowish solid (1.44 g, 75% yield).

^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.89-0.92 (m, 1H), 1.26-1.32 (m, 2H), 1.68 (br, 1H), 2.11 (d, *J* = 7.5 Hz, 1H), 2.26-2.33 (m, 2H), 2.58 (br, 1H), 2.85 (t, *J* = 11.4 Hz, 1H), 3.02 (t, *J* = 9.0 Hz, 1H), 3.82 (dd, *J* = 11.6, 8.3, 1H), 4.97-5.00 (m, 1H), 5.05 (s, 1H), 6.01-6.12 (m, 2H), 6.80 (br, 2H), 7.30 (s, 1H), 7.41 (s, 1H), 7.58 (d, *J* = 4.5 Hz, 1H), 7.91 (d, *J* = 9.0 Hz, 1H), 8.63 (d, *J* = 4.5 Hz, 1H) ; IR (KBr) 2939, 1618, 1469, 1407, 1242, 1103, 1047, 998, 932, 860, 832 cm^{-1} ; MS (ESI, *m/z*) 311.3 $[M+H]^+$; $[\alpha]_D^{25}$ = +355.2 (c = 2.13, $CHCl_3$)

6'-(Methoxymethyl) cupreidine (S2):

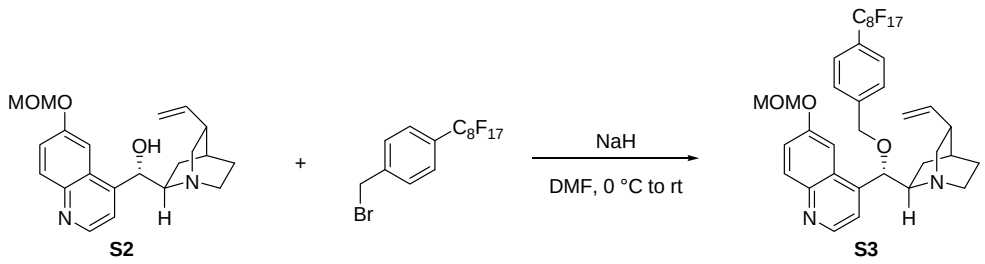


4a **S2**

To a stirred solution of 4a (200.0 mg, 0.64 mmol) in dry DMF (3.0 mL), NaH (33.5 mg, 60% suspension in mineral oil, 0.84 mmol) was added at room temperature under nitrogen atmosphere. The resulting mixture was stirred at 0 °C for 1 h. Then MOM chloride (53.8 μL, 0.71 mmol) was added slowly and it was stirred at room temperature for 3 h. After dilution with water, aqueous layer was extracted with Et_2O, and the combined organic layer was washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (ethyl acetate/MeOH/Et_3N = 90/10/0.1) to give S2 as a white solid (135.1 mg, 59% yield).

^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.20-1.29 (m, 1H), 1.50-1.55 (m, 2H), 1.76 (br, 1H), 1.95 (dd, *J* = 13.2, 9.6 Hz, 1H), 2.18-2.26 (m, 1H), 2.34 (brs, 1H), 2.69-2.79 (m, 1H), 2.84-2.92 (m, 2H), 3.10 (dt, *J* = 9.3 Hz, 4.8 Hz, 1H), 3.21 (ddd, *J* = 13.7, 8.0, 2.1 Hz, 1H), 3.47 (s, 3H), 4.99-5.01 (m, 1H), 5.04 (d, *J* = 0.9 Hz, 1H), 5.21 (d, *J* = 15.6 Hz, 1H), 5.24 (d, *J* = 15.9 Hz, 1H), 5.58 (d, *J* = 5.1 Hz, 1H), 5.91-6.02 (m, 1H), 7.40 (dd, *J* = 9.3, 2.7 Hz, 1 H), 7.49 (d, *J* = 2.4 Hz, 1H), 7.56 (d, *J* = 4.2 Hz, 1H), 8.02 (d, *J* = 9.3 Hz, 1H), 8.74 (d, *J* = 4.5 Hz, 1H) ;^{13}C NMR ($CDCl_3$, 150.9 MHz) δ 21.3, 26.4, 28.2, 40.0, 49.4, 50.1, 56.1, 59.9, 71.7, 94.5, 105.3, 114.5, 118.5, 121.9, 126.5, 131.7, 140.5, 144.5, 148.0, 148.2, 155.0 ; IR (KBr) 2932, 2698, 1625, 1509, 1237, 1178, 1152, 1068, 1016, 910, 867, 823 cm^{-1} ; mp = 160-163 ºC ; MS (EI, *m/z*) 354 (M^+), HRMS calcd. for $C_{21}H_{26}N_2O_3^+$: 354.1943 Found : 354.1936 ; $[\alpha]_D^{25}$ = +173.8 (c = 0.13, $CHCl_3$)

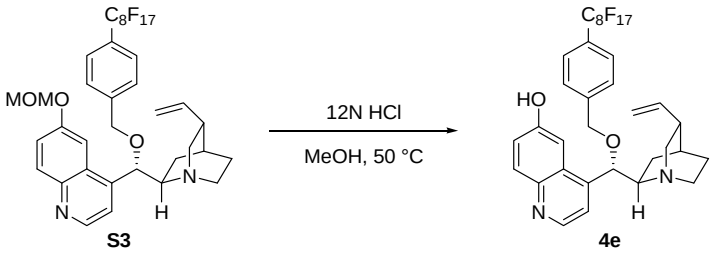
6'-(Methoxymethyl)-cupreidine 9-*O*-(4-*n*-Perfluorooctyl)benzyl ether (S3)[2, 3]:



To a stirred solution of S2 (660.0 mg, 1.86 mmol) in dry DMF (10 mL), NaH (186.4 mg, 60% suspension in mineral oil, 4.65 mmol) was added at room temperature under nitrogen atmosphere. The resulting mixture was stirred at 0 °C for 2 h. Then 4-*n*-Perfluorooctylbenzylbromide (1.01 g, 1.86 mmol) was added and it was stirred at room temperature for 3 h. After dilution with sat. NH_4Cl aq, aqueous layer was extracted with ethyl acetate, and the combined organic layer was washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (ethyl acetate/MeOH = 9/1) to give S3 as a colorless oil (1.42 g 89% yield).

^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.37 (m, 1H), 1.49-1.54 (m, 2H), 1.78 (br, 1H), 2.00-2.08 (m, 1H), 2.20-2.27 (m, 1H), 2.67-2.84 (m, 2H), 2.86-2.94 (m, 1H), 3.08-3.27 (m, 2H), 3.51 (s, 3H), 4.46 (d, *J* = 12.0 Hz, 1H), 4.53 (d, *J* = 12.3 Hz, 1H), 4.98 (s, 1H), 5.02-5.03 (m, 1H), 5.24-5.27 (m, 2H), 5.34 (d, *J* = 6.6 Hz, 1H), 5.89-6.00 (m, 1H), 7.45-7.65 (m, 7H), 8.08 (d, *J* = 9.3 Hz, 1H), 8.79 (d, *J* = 4.2 Hz, 1H) ; ^{19}F NMR ($CDCl_3$, 282.3 MHz) δ -81.2 (t, *J* = 10.2 Hz, 3F), -111.1 (t, *J* = 15.0 Hz, 2F), -121.7 (s, 2F), -122.3 (s, 6F), -123.2 (s, 2F), -126.6 (s, 2F) ; ^{13}C NMR ($CDCl_3$, 150.9 MHz) δ 22.4, 26.3, 28.0, 39.8, 49.3, 50.0, 56.1, 60.3, 70.4, 80.8, 94.6, 105.4, 108-120 (m, C_8F_{17}), 114.4, 118.8, 122.1, 126.9 (t, *J* = 7.5 Hz), 127.4, 127.6, 128.2 (t, *J* = 24.1 Hz), 131.9, 140.3, 142.2, 144.8, 145.0, 148.1, 155.3 ; IR (neat) 2935, 1619, 1508, 1241, 1213, 1152, 1000, 828, 803, 658 cm^{-1} ; MS (ESI, *m/z*) 863.3 $[M+H]^+$; HRMS calcd. for $[C_{36}H_{31}F_{17}N_2O_3+H]^+$: 863.2141 Found : 863.2134 ; $[\alpha]_D^{25}$ = +55.2 (c = 1.28, $CHCl_3$)

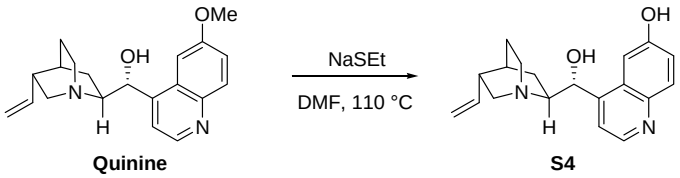
Cupreidine 9-*O*-(4-*n*-Perfluorooctyl)benzyl ether (4e):



To a stirred solution of S3 (1.25 g, 1.45 mmol) in dry MeOH (15.0 mL), 12N HCl (~10 drops) was added. The resulting mixture was stirred at 50 °C for 3 h. After dilution with water, aqueous layer was extracted with CH_2Cl_2, and the combined organic layer was washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (ethyl acetate/MeOH/Et_3N = 95/5/0.1) to give 4e as a yellowish solid (971.4 mg, 82% yield).

^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.18-1.26 (m, 1H), 1.40-1.51 (m, 1H), 1.59 (br, 1H), 1.82 (br, 1H), 2.78-2.33 (m, 2H), 2.82-2.94 (m, 2H), 3.09-3.13 (m, 2H), 3.55 (br, 1H), 4.34 (d, *J* = 11.7 Hz, 1H), 4.40 (d, *J* = 12.0 Hz, 1H), 4.96 (s, 1H), 5.01 (d, *J* = 4.2 Hz, 1H), 5.33 (brs, 1H), 5.59 (brs, 1H), 5.88-6.00 (m, 1H), 7.36 (dd, *J* = 9.0, 2.4 Hz, 1H), 7.43-7.58 (m, 5H), 7.82 (s, 1H), 8.03 (d, *J* = 9.0 Hz, 1H), 8.70 (d, *J* = 4.2 Hz, 1H) ; ^{19}F NMR ($CDCl_3$, 282.3 MHz) δ -81.3 (t, *J* = 9.9 Hz, 3F), -111.1 (t, *J* = 13.8 Hz, 2F), -121.7 (s, 2F), -122.3 (s, 6F), -123.2 (s, 2F), -126.6 (s, 2F) ; ^{13}C NMR ($CDCl_3$, 150.9 MHz) δ 19.6, 25.7, 27.8, 39.3, 49.3, 49.7, 59.0, 70.5, 79.3, 105.5, 108-120 (m, C_8F_{17}), 115.1, 117.5, 123.2, 126.9 (t, *J* = 7.5 Hz), 127.5, 127.6, 128.3 (t, *J* = 24.1), 131.7, 139.4, 141.9, 142.7, 143.7, 146.6, 157.1 ; IR (KBr) 2941, 1619, 1510, 1469, 1212, 1150, 830, 735, 723, 659 cm^{-1} ; mp = 100-103 ºC ; MS (ESI, *m/z*) 819.3 $[M+H]^+$; HRMS calcd. for $[C_{34}H_{27}F_{17}N_2O_2+H]^+$: 819.1879 Found : 819.1876 ; $[\alpha]_D^{25}$ = +73.4 (c = 2.32, $CHCl_3$)

Cupreine (S4)[4]:

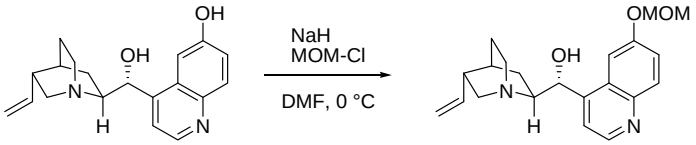


Quinine (2.60 g, 8.0 mmol) and NaSEt (2.69 g, 32.0 mmol) were dissolved in dry DMF (24.0 mL) at room temperature under nitrogen atmosphere. The resulting mixture was stirred overnight at 110 °C. The reaction mixture was cooled down to room temperature, diluted with sat. NH_4Cl aq. Then aqueous layer was extracted with ethyl acetate, and the combined organic layer was washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (ethyl acetate/MeOH/Et_3N = 90/10/0.1) to give S4 as a yellowish solid (1.37 g, 55% yield).

^{1}H NMR (CD_3OD, 300 MHz) δ 1.39-1.47 (m, 1H), 1.58-1.61 (m, 1H), 1.79 (br, 1H), 1.84-1.90 (m, 2H), 2.35 (br, 1H), 2.64-2.76 (m, 2H), 3.06-3.14 (m, 2H), 3.70-3.73 (m, 1H), 4.93 (br, 1H), 4.99 (br, 1H), 5.53 (d, *J* = 3.0 Hz, 1H), 5.68-5.79 (m, 1H), 7.30-7.35 (m, 2H), 7.61 (d, *J* = 4.5 Hz, 1H), 7.90 (d, *J* = 9.0 Hz, 1H), 8.58 (d, *J* = 4.8 Hz, 1H) ; IR (KBr) 3165, 2937, 1617, 1471, 1420, 1241, 1231, 1095, 856, 826 cm^{-1} ; MS (ESI, *m/z*) 311.3 $[M+H]^+$;

$[\alpha]_D^{25}$ = -173.8 (c = 0.68, MeOH)

6'-(Methoxymethyl) cupreine (S5):

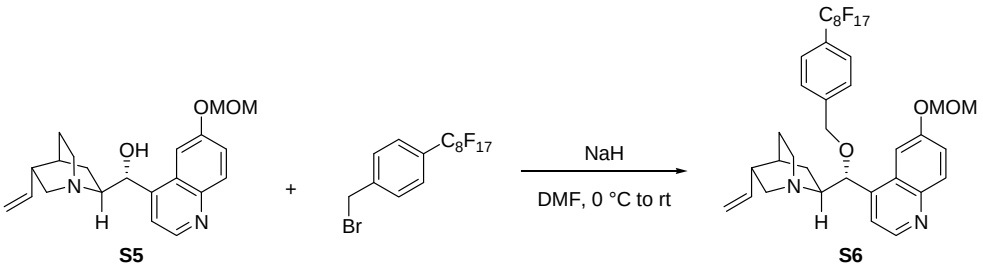


S4 **S5**

To a stirred solution of S4 (988.0 mg, 3.18 mmol) in dry DMF (12.0 mL), NaH (170.0 mg, 60% suspension in mineral oil, 4.24 mmol) was added at room temperature under nitrogen atmosphere. The resulting mixture was stirred at 0 °C for 1 h. Then MOM chloride (0.27 mL, 3.50 mmol) was added slowly and it was stirred overnight at room temperature. After dilution with water, aqueous layer was extracted with Et_2O, and the combined organic layer was washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (ethyl acetate/MeOH/Et_3N = 90/10/0.1) to give S5 as a white solid (135.1 mg, 59% yield).

^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.48-1.52 (m, 1H), 1.56-1.61 (m, 1H), 1.67-1.74 (m, 1H), 1.80 (br, 1H), 2.25 (br, 1H), 2.57-2.71 (m, 3H), 3.00-3.05 (m, 1H), 3.08-3.17 (m, 1H), 3.37-3.42 (m, 1H), 3.46 (s, 3H), 3.93 (brs, 1H), 4.89-4.98 (m, 2H), 5.19 (d, *J* = 9.3 Hz, 1H), 5.21 (d, *J* = 8.7 Hz, 1H), 5.51 (d, *J* = 4.2 Hz, 1H), 5.70-5.81 (m, 1H), 7.38 (dd, *J* = 9.2, 2.1 Hz, 1H), 7.49 (d, *J* = 2.1 Hz, 1H), 7.52 (d, *J* = 4.5 Hz, 1 H), 7.99 (d, *J* = 9.3 Hz, 1H), 8.68 (d, *J* = 4.5 Hz, 1H) ; ^{13}C NMR ($CDCl_3$, 150.9 MHz) δ 21.6, 27.5, 27.8, 39.9, 43.0, 56.0, 56.8, 60.0, 71.5, 94.2, 105.3, 114.2, 118.6, 121.6, 126.4, 131.3, 141.9, 144.2, 147.9, 148.7, 154.8 ; IR (KBr) 2933, 1621, 1590, 1509, 1458, 1239, 1184, 1152, 1072, 998, 922, 827 cm^{-1} ; mp = 141-144 ºC ; MS (ESI, *m/z*) 355.3 $[M+H]^+$; HRMS calcd. for $[C_{21}H_{26}N_2O_3+H]^+$: 355.2022 Found : 355.2037 ; $[\alpha]_D^{25}$ = -77.4 (c = 1.49, $CHCl_3$)

6'-(Methoxymethyl) cupreine 9-*O*-(4-*n*-Perfluorooctyl)benzyl ether (S6)[2, 3]:

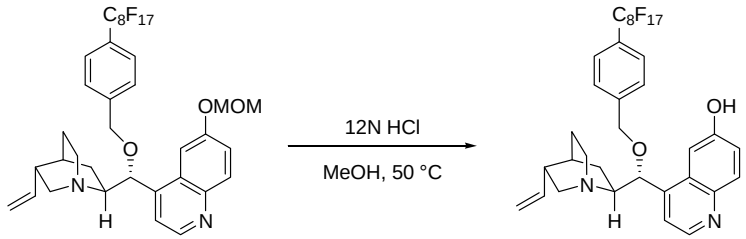


S5 **S6**

To a stirred solution of S5 (566.0 mg, 1.60 mmol) in dry DMF (8 mL), NaH (160.0 mg, 60% suspension in mineral oil, 4.0 mmol) was added at room temperature under nitrogen atmosphere. The resulting mixture was stirred at 0 °C for 2 h. Then 4-*n*-Perfluorooctylbenzylbromide (941.0 mg, 1.60 mmol) was added and it was stirred at room temperature for 2 h. After dilution with sat. NH_4Cl aq, aqueous layer was extracted with ethyl acetate, and the combined organic layer was washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (ethyl acetate/MeOH = 90/10) to give S6 as a colorless oil (1.14g 83% yield).

^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.53 (br, 1H), 1.68-1.77 (m, 2H), 1.82-1.83 (m, 1H), 1.92 (s, 1H), 2.27 (br, 1H), 2.58-2.73 (m, 2H), 3.06 (dd, *J* = 13.5, 10.2 Hz, 1H), 3.22-3.26 (m, 1H), 3.33-3.40 (m, 1H), 3.50 (s, 3H), 4.48 (s, 2H), 4.91-4.94 (m, 1H), 5.00 (s, 1H), 5.17 (brs, 1H), 5.29 (d, *J* = 18.3 Hz, 1H), 5.31 (d, *J* = 18.3 Hz, 1H), 5.72-5.84 (m, 1H), 7.44-7.59 (m, 6H), 7.67 (brs, 1H), 8.09 (d, *J* = 9.3 Hz, 1H), 8.78 (d, *J* = 4.5 Hz, 1H) ; ^{19}F NMR ($CDCl_3$, 282.3 MHz) δ -81.2 (t, *J* = 9.9 Hz, 3F), -111.0 (t, *J* = 14.1 Hz, 2F), -121.7 (s, 2F), -122.3 (s, 6F), -123.2 (s, 2F), -126.6 (s, 2F) ; ^{13}C NMR ($CDCl_3$, 150.9 MHz) δ 23.3, 27.85, 27.88, 40.0, 43.0, 56.1, 57.0, 60.4, 70.3, 81.7, 94.5, 105.6, 106-120 (m, C_8F_{17}), 114.2, 119.0, 122.0, 126.9, 127.2, 127.3 128.1 (t, *J* = 24.1 Hz), 132.0, 142.0, 142.3, 144.8, 145.1, 148.1, 155.2 ; IR (neat) 3420, 2944, 1620, 1508, 1463, 1371, 1200, 1149, 1011, 854, 661 cm^{-1} ; mp = 75-78 ºC ; MS (ESI, *m/z*) 863.4 $[M+H]^+$; HRMS calcd. for $[C_{36}H_{31}F_{17}N_2O_3+H]^+$: 863.2141 Found : 863.2150 ; $[\alpha]_D^{25}$ = -5.85 (c = 1.58, $CHCl_3$)

Cupreine 9-*O*-(4-*n*-Perfluorooctyl)benzyl ether (4e'):

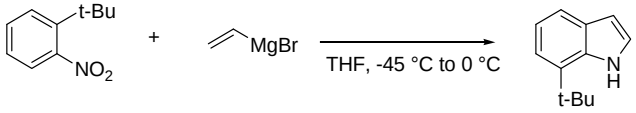


S6 **4e'**

To a stirred solution of S6 (1.04 g, 1.21 mmol) in dry MeOH (12.0 mL), 12N HCl (~10 drops) was added. The resulting mixture was stirred at 50 °C for 40 min. After dilution with water, aqueous layer was extracted with CH_2Cl_2, and the combined organic layer was washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (ethyl acetate/MeOH/Et_3N = 95/5/0.1) to give 4e' as a yellowish solid (886.0 mg, 90% yield).

^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.54-1.61 (m, 2H), 1.88 (br, 2H), 2.09 (br, 1H), 2.37 (br, 1H), 2.60-2.64 (m, 1H), 2.87-2.89 (m, 1H), 3.09 (br, 1H), 3.16-3.24 (m, 1H), 3.61 (br, 1H), 4.45 (s, 2H), 4.86-4.89 (m, 1H), 4.95 (s, 1H), 5.40 (brs, 1H), 5.56-5.68 (m, 2H), 7.32 (d, *J* = 9.0 Hz, 1H), 7.44-7.60 (m, 5H), 8.04 (d, *J* = 9.0 Hz, 1H), 8.09 (s, 1H), 8.70 (d, *J* = 4.2 Hz, 1H) ; ^{19}F NMR ($CDCl_3$, 282.3 MHz) δ -81.3 (t, *J* = 10.2 Hz, 3F), -111.1 (t, *J* = 15.0 Hz, 2F), -121.7 (s, 2F), -122.3 (s, 6F), -123.2 (s, 2F), -126.6 (s, 2F) ; ^{13}C NMR ($CDCl_3$, 150.9 MHz) δ 20.0, 27.0, 27.7, 39.3, 43.4, 56.4, 59.5, 70.2, 79.0, 105.7, 106-120 (m, C_8F_{17}), 115.0, 117.5, 123.2, 126.97, 127.01, 127.8, 128.2 (t, *J* = 25.7 Hz), 131.5, 140.6, 142.1, 143.2, 143.6, 146.5, 157.2 ; IR (KBr) 2942, 1618, 1509, 1470, 1419, 1213, 1150, 1114, 855, 822, 659 cm^{-1} ; mp = 95-98 ºC ; MS (ESI, *m/z*) 819.3 $[M+H]^+$; HRMS calcd. for $[C_{34}H_{27}F_{17}N_2O_2+H]^+$: 819.1879 Found : 819.1886 ; $[\alpha]_D^{25}$ = -13.0 (c = 4.62, $CHCl_3$)

3. Preparation of 7-*tert*-Butyl-1*H* indole (1n)[5]:

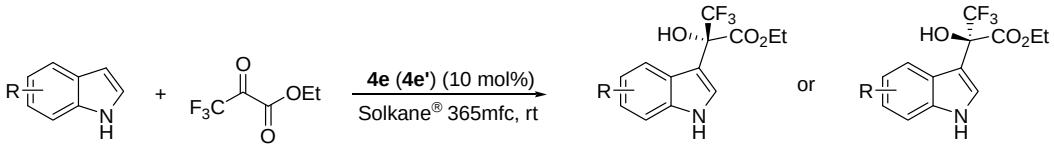


1n

2-*tert*-Butylnitrobenzene (310mg, 1.73 mmol) was dissolved in dry THF (10.0 mL). The resulting solution was cooled to -45 °C. Then a 1.0 M THF solution of vinylmagnesium bromide (5.2 mL, 5.19 mmol) was added at -45 °C under nitrogen atmosphere over 10 minitues. After the addion was complete, the raction mixture was stirred at -45 °C for 1 h and then it warmed to 0 °C and stirred at 0 °C for 2 h. After dilution with sat. NH_4Cl aq, aqueous layer was extracted with Et_2O, and the combined organic layer was washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (*n*-hexane = 100) to give 1n as a brown solid (127.4 mg, 43% yield).

^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.52 (s, 9H), 6.57 (t, *J* = 2.4 Hz, 1H), 7.05-7.15 (m, 2H), 7.22 (t, *J* = 3.0 Hz, 1H), 7.53 (d, *J* = 7.5 Hz, 1H), 8.30 (brs, 1H) ; ^{13}C NMR ($CDCl_3$, 150.9 MHz) δ 30.4, 34.5, 102.6, 118.6, 119.0, 119.8, 123.3, 128.8, 133.3, 133.5 ;IR (KBr) 3425, 2970, 2953, 1491, 1418, 1365, 1340, 1099, 1068, 1024, 797, 742 cm^{-1} ; mp = 63-66 ºC ; MS (EI, *m/z*) 173 (M^+), HRMS calcd. for $C_{12}H_{15}N^+$: 173.1204 Found : 173.1214

4. General experimental procedure for the F-C alkylation of indoles with ethyl trifluoropyruvate in Solkane® 365mfc:



1 (1.1 equiv) **(*S*)-2** **(*R*)-2**

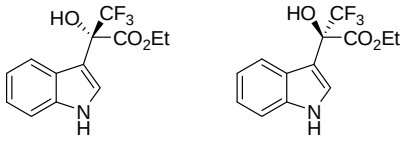
Catalyst free F-C alkylation (Racemic synthesis):

To a stirred solution of 1 (0.20 mmol) in Solkane® 365mfc (0.5 mL), ethyl trifluoropyruvate (29.2 μL, 0.22 mmol) was added at room temperature under nitrogen atmosphere. The mixture was stirred at room temperature for 0.5 - 2.0 h. Then the solvent was removed in vacuo, and the residue was purified by column chromatography (*n*-hexane/ethyl acetate = 80/20) to give 2 as a solid or liquid.

Catalytic enantioselective F-C alkylation (Asymmetric synthesis):

To a stirred solution of 1 (0.10 mmol) and catalyst 4e or 4e' (8.2 mg, 10 mol%) in Solkane® 365mfc (0.3 mL), ethyl trifluoropyruvate (14.6 μL, 0.11 mmol) in 0.2 mL Solkane® 365mfc was added at room temperature under nitrogen atmosphere. The mixture was stirred at room temperature for 1 h. Then the solvent was removed in vacuo, and the residue was purified by column chromatography (*n*-hexane/ethyl acetate = 80/20) give (*S*)-2 or (*R*)-2 as a solid or liquid.

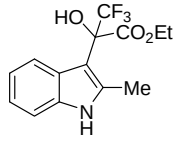
3,3,3-Trifluoro-2-hydroxy-2-(1H-indol-3-yl)-propionic acid ethyl ester (2a)[6]:



(*S*)-2a **(*R*)-2a**

Racemic synthesis: (52.9 mg, 92%) ; Asymmetric synthesis: (*S*)-2a (26.6 mg, 93%, 72% ee), (*R*)-2a (28.0 mg, 98 %, 71% ee) ; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.33 (t, *J* = 7.2 Hz, 3H), 4.25-4.53 (m, 2H), 4.40 (s, 1H), 7.09-7.25 (m, 2H), 7.31-7.35 (m, 1H), 7.41 (d, *J* = 2.8 Hz, 1H), 7.88 (d, *J* = 8.0 Hz, 1H), 8.24 (brs, 1H) ; ^{19}F NMR ($CDCl_3$, 188.2 MHz) δ -76.5 (s, 3F) ; IR (KBr) 3417, 3314, 1739, 1461, 1308, 1258, 1228, 1176, 1097, 1008, 756 cm^{-1} ; MS (ESI, *m/z*) 310.2 $[M+Na]^+$; The ee of the product was determined by HPLC using an OD-H column (*n*-hexane/*i*-PrOH = 95/5, flow rate 0.5 mL/min, λ = 254 nm, τ_{maj} = 55.4 min, τ_{min} = 67.6 min) ; (*S*)-2a $[\alpha]_D^{25}$ = +11.7 (c = 0.31, $CHCl_3$, 72% ee) ; (*R*)-2a $[\alpha]_D^{25}$ = -12.7 (c = 0.44, $CHCl_3$, 71% ee)

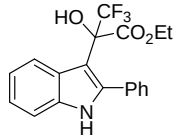
3,3,3-Trifluoro-2-hydroxy-2-(2-methyl-1*H*-indol-3-yl)-propionic acid ethyl ester (2b)[7]:



2b

Racemic synthesis: (54.9 mg, 91%) ; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.32 (t, *J* = 7.2 Hz, 3H), 2.48 (s, 3H), 3.98 (s, 1H), 4.24-4.50 (m, 2H), 7.06-7.24 (m, 3H), 7.78 (d, *J* = 8.6 Hz, 1H), 7.96 (brs, 1H) ; ^{19}F NMR ($CDCl_3$, 188.2 MHz) δ -76.3 (s, 3F) ; IR (KBr) 3374, 2967, 1722, 1460, 1432, 1298, 1161, 1087, 944, 903, 741 cm^{-1} ; MS (ESI, *m/z*) 324.2 $[M+Na]^+$

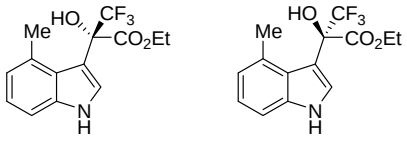
3,3,3-Trifluoro-2-hydroxy-2-(2-phenyl-1*H*-indol-3-yl)-propionic acid ethyl ester (2c)[8]:



2c

Racemic synthesis: (60.7 mg, 84%) ; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.10 (t, *J* = 7.2 Hz, 3H), 3.54 (dq, *J* = 10.8, 7.2 Hz, 1H), 3.73 (s, 1H), 3.89 (dq, *J* = 10.7, 7.5 Hz, 1H), 7.17-7.28 (m, 2H), 7.33-7.36 (m, 1H), 7.40-7.47 (m, 5H), 8.05 (d, *J* = 8.1 Hz, 1H), 8.16 (brs, 1H) ; ^{19}F NMR ($CDCl_3$, 188.2 MHz) δ -75.1 (s, 3F) ; IR (KBr) 3374, 3328, 1729, 1455, 1373, 1303, 1168, 1097, 1016, 995, 920, 746, 714, 702 cm^{-1} ; MS (ESI, *m/z*) 386.1 $[M+Na]^+$

3,3,3-Trifluoro-2-hydroxy-2-(4-methyl-1*H*-indol-3-yl)-propionic acid ethyl ester (2d):

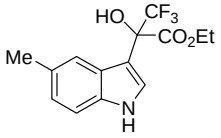


(*S*)-2d **(*R*)-2d**

Racemic synthesis: (49.9 mg, 83%) ; Asymmetric synthesis: (*S*)-2d (25.2 mg, 84%, 48% ee), (*R*)-2d (23.5 mg, 78 %, 43% ee) ; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.20 (t, *J* = 7.2 Hz, 3H), 2.53 (s, 3H), 4.20 (dq, *J* = 10.6, 7.2 Hz,

1H), 4.38 (s, 1H), 4.39 (dq, *J* = 10.6, 7.2 Hz, 1H), 6.88-6.92 (m, 1H), 7.07-7.10 (m, 2H), 7.25-7.27 (m, 1H), 8.16 (brs, 1H) ; ^{19}F NMR ($CDCl_3$, 188.2 MHz) δ -74.7 (s, 3F) ; ^{13}C NMR ($CDCl_3$, 150.9 MHz) δ 14.2, 22.4, 64.5, 77.5 (q, *J* = 30.2 Hz), 108.6, 109.7, 123.3, 123.4, 124.3 (q, *J* = 288.2 Hz), 125.4, 125.4, 130.8, 137.2, 171.1 ; IR (KBr) 3439, 3331, 1724, 1464, 1442, 1231, 1186, 1109, 1007, 907, 756, 747 cm^{-1} ; mp = 137-140 ºC ; MS (EI, *m/z*) 301 (M^+) ; HRMS calcd. for $C_{14}H_{14}F_3NO_3^+$: 301.0926 Found : 301.0922 ; The ee of the product was determined by HPLC using an OD-H column (*n*-hexane/*i*-PrOH = 95/5, flow rate 0.5 mL/min, λ = 254 nm, τ_{maj} = 54.0 min, τ_{min} = 59.5 min) ; (*S*)-2d $[\alpha]_D^{25}$ = +24.6 (c = 0.58, $CHCl_3$, 48% ee) ; (*R*)-2d $[\alpha]_D^{25}$ = -10.9 (c = 0.62, $CHCl_3$, 43% ee)

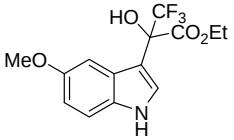
3,3,3-Trifluoro-2-hydroxy-2-(5-methyl-1*H*-indol-3-yl)-propionic acid ethyl ester (2e)[6]:



2e

Racemic synthesis: (58.0 mg, 96%) ; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.34 (t, *J* = 7.2 Hz, 3H), 2.44 (s, 3H), 4.25-4.53 (m, 2H), 4.37 (s, 1H), 7.03 (dd, *J* = 8.4, 1.4 Hz, 1H), 7.22 (d, *J* = 8.2 Hz, 1H), 7.37 (d, *J* = 2.4 Hz, 1H), 7.66 (s, 1H), 8.14 (brs, 1H) ; ^{19}F NMR ($CDCl_3$, 188.2 MHz) δ -76.5 (s, 3F) ; IR (KBr) 3397, 3333, 2988, 2919, 1729, 1302, 1262, 1228, 1173, 1102, 1008, 798 cm^{-1} ; MS (ESI, *m/z*) 324.2 $[M+Na]^+$

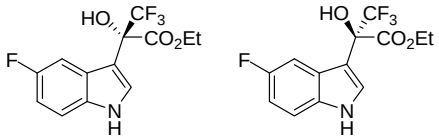
3,3,3-Trifluoro-2-hydroxy-2-(5-methoxy-1*H*-indol-3-yl)-propionic acid ethyl ester (2f)[6]:



2f

Racemic synthesis: (60.8 mg, 96%) ; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.34 (t, *J* = 7.2 Hz, 3H), 3.83, (s, 3H), 4.26-4.53 (m, 2H), 4.39 (s, 1H), 6.87 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.19-7.23 (m, 1H), 7.35 (d, *J* = 2.2 Hz, 1H), 7.37 (d, *J* =2.8 Hz, 1H), 8.21 (brs, 1H) ; ^{19}F NMR ($CDCl_3$, 188.2 MHz) δ -76.6 (s, 3F) ; IR (KBr) 3418, 3348, 2986, 2938, 2832, 1732, 1493, 1441, 1300, 1219, 1174, 1108, 838, 805 cm^{-1} ; MS (ESI, *m/z*) 340.2 $[M+Na]^+$

3,3,3-Trifluoro-2-hydroxy-2-(5-fluoro-1*H*-indol-3-yl)-propionic acid ethyl ester (2g)[6]:

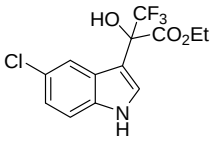


(*S*)-2g **(*R*)-2g**

Racemic synthesis: (54.7 mg, 90%) ; Asymmetric synthesis: (*S*)-2g (29.9 mg, 98%, 70% ee), (*R*)-2g (30.2 mg, 99 %, 56% ee) ; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.35 (t, *J* = 7.2 Hz, 3H), 4.28-4.54 (m, 2H), 4.41 (s, 1H), 6.95 (dt, *J* = 9.0, 2.6 Hz, 1H), 7.25 (dd, *J* = 8.6, 5.0 Hz, 1H), 7.47 (d, *J* = 2.4 Hz, 1H), 7.57 (dd, *J* = 10.5, 2.4 Hz, 1H), 8.31 (brs, 1H) ; ^{19}F NMR ($CDCl_3$, 188.2 MHz) δ -76.8 (s, 3F), -122.6 (dt, *J* = 10.5, 4.0 Hz, 1F) ; IR (KBr) 3389, 2984, 2908, 1731, 1280, 1179, 1096, 1021, 908, 805, 682 cm^{-1} ; MS (ESI, *m/z*) 328.2 $[M+Na]^+$; The ee of the product was determined by HPLC using an OD-H column (*n*-hexane/*i*-PrOH = 95/5, flow rate 0.5 mL/min, λ = 254 nm, τ_{maj} = 44.6 min, τ_{min} = 51.9 min) ; (*S*)-2g $[\alpha]_D^{25}$ = +10.6 (c = 0.24, $CHCl_3$, 70% ee) ; (*R*)-2g $[\alpha]_D^{25}$ = -16.5 (c = 0.40,

$CHCl_3$, 56% ee)

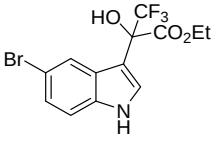
3,3,3-Trifluoro-2-hydroxy-2-(5-chloro-1*H*-indol-3-yl)-propionic acid ethyl ester (2h)[6]:



2h

Racemic synthesis: (58.2 mg, 91%) ; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.36 (t, *J* = 7.2 Hz, 3H), 4.28-4.54 (m, 2H), 4.43 (s, 1H), 7.15 (dd, *J* = 8.7, 2.0 Hz, 1H), 7.24 (d, *J* = 8.6 Hz, 1H), 7.44 (d, *J* = 2.6 Hz, 1H), 7.90 (d, *J* = 1.2 Hz, 1H), 8.34 (brs, 1H) ; ^{19}F NMR ($CDCl_3$, 188.2 MHz) δ -76.9 (s, 3F) ; IR (KBr) 3331, 2984, 1732, 1469, 1300, 1256, 1172, 1106, 1094, 1024, 914 ; 804 cm^{-1} ; MS (ESI, *m/z*) 344.1, 346.1 $[M+Na]^+$

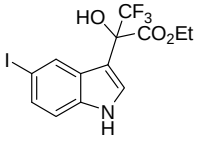
3,3,3-Trifluoro-2-hydroxy-2-(5-bromo-1*H*-indol-3-yl)-propionic acid ethyl ester (2i)[6]:



2i

Racemic synthesis : (64.9 mg, 89%) ; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.36 (t, *J* = 7.2 Hz, 3H), 4.28-4.53 (m, 2H), 4.44 (s, 1H), 7.18 (d, *J* = 8.8 Hz, 1H), 7.28 (dd, *J* = 8.8, 1.8 Hz, 1H), 7.42 (d, *J* = 2.6 Hz, 1H), 8.06 (d, *J* = 1.0 Hz, 1H), 8.36 (brs, 1H) ; ^{19}F NMR ($CDCl_3$, 188.2 MHz) δ -76.9 (s, 3F) ; IR (KBr) 3334, 2982, 1732, 1463, 1389, 1371, 1302, 1256, 1172, 1100, 1024, 803 cm^{-1} ; MS (ESI, *m/z*) 388.1, 390.1 $[M+Na]^+$

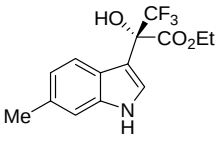
3,3,3-Trifluoro-2-hydroxy-2-(5-iodo-1*H*-indol-3-yl)-propionic acid ethyl ester (2j)[6]:



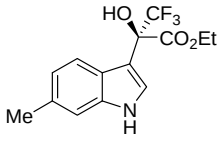
2j

Racemic synthesis : (78.3 mg, 95%) ; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.38 (t, *J* = 7.2 Hz, 3H), 4.33-4.52 (m, 3H), 7.14 (d, *J* = 8.4 Hz, 1H), 7.44 (d, *J* = 2.7 Hz, 1H), 7.47 (dd, *J* = 8.7, 1.8 Hz, 1H), 8.29 (s, 1H), 8.34 (brs, 1H) ; ^{19}F NMR ($CDCl_3$, 188.2 MHz) δ -76.9 (s, 3F) ; IR (KBr) 3334, 1731, 1456, 1388, 1301, 1256, 1171, 1085, 1024, 910, 881, 804 cm^{-1} ; MS (ESI, *m/z*) 436.1 $[M+Na]^+$

3,3,3-Trifluoro-2-hydroxy-2-(6-methyl-1*H*-indol-3-yl)-propionic acid ethyl ester (2k):



(*S*)-2k

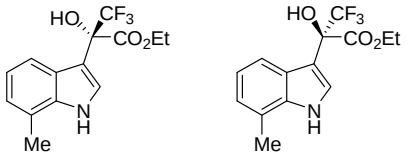


(*R*)-2k

Racemic synthesis : (59.7 mg, 99%) ; Asymmetric synthesis : (*S*)-2k (26.5 mg, 88%, 55% ee), (*R*)-2k (27.4 mg, 91 %, 63% ee) ; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.32 (t, *J* = 7.2 Hz, 3H), 2.43 (s, 3H), 4.23-4.52 (m, 2H), 4.37 (s, 1H), 6.95-6.99 (m, 1H), 7.08 (s, 1H), 7.31 (br, 1H), 7.74 (d, *J* = 8.2 Hz, 1H), 8.07 (brs, 1H) ; ^{19}F NMR ($CDCl_3$,

188.2 MHz) δ -77.2 (s, 3F) ; ^{13}C NMR ($CDCl_3$, 150.9 MHz) δ 13.8, 21.5, 64.2, 76.7 (q, *J* = 31.7 Hz), 108.2, 111.3, 120.5, 122.3, 122.7, 123.5 (q, *J* = 286.7 Hz), 123.8, 132.5, 136.7, 169.4 ; IR (KBr) 3417, 3343, 2988, 2925, 1742, 1455, 1370, 1034, 1255, 1101, 1010, 909, 861, 810 cm^{-1} ; mp = 98-101 ºC ; MS (EI, *m/z*) 301 (M^+) ; HRMS calcd. for $C_{14}H_{14}F_3NO_3^+$: 301.0926 Found : 301.0953 ; The ee of the product was determined by HPLC using an AS-H column (*n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm, τ_{maj} = 10.8 min, τ_{min} = 9.2 min) ; (*S*)-2k $[\alpha]_D^{25}$ = +7.3 (c = 0.35, $CHCl_3$, 55% ee) ; (*R*)-2k $[\alpha]_D^{25}$ = -12.4 (c = 0.25, $CHCl_3$, 63% ee)

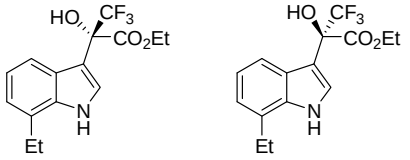
3,3,3-Trifluoro-2-hydroxy-2-(7-methyl-1*H*-indol-3-yl)-propionic acid ethyl ester (2l):



(*S*)-2l **(*R*)-2l**

Racemic synthesis : (60.5 mg, 99%) ; Asymmetric synthesis : (*S*)-2l (27.7 mg, 92%, 85% ee), (*R*)-2l (29.8 mg, 99 %, 77% ee) ; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.34 (t, *J* = 7.5 Hz, 3H), 2.48 (s, 3H), 4.29-4.51 (m, 2H), 4.39 (s, 1H), 7.02-7.11 (m, 2H), 7.48 (d, *J* = 2.7 Hz, 1H), 7.74 (d, *J* = 7.5 Hz, 1H), 8.22 (brs, 1H) ; ^{19}F NMR ($CDCl_3$, 188.2 MHz) δ -77.2 (s, 3F) ; ^{13}C NMR ($CDCl_3$, 150.9 MHz) δ 13.9, 16.4, 64.2, 76.7 (q, *J* = 31.7 Hz), 109.1, 118.8, 120.5, 120.7, 123.1, 123.5 (q, *J* = 286.7 Hz), 124.1, 124.6, 135.9, 169.4 ; IR (KBr) 3437, 3324, 1737, 1306, 1227, 1171, 1113, 1083, 787, 748, 692 cm^{-1} ; mp = 84-87 ºC ; MS (EI, *m/z*) 301 (M^+) ; HRMS calcd. for $C_{14}H_{14}F_3NO_3^+$: 301.0926 Found : 301.0951 ; The ee of the product was determined by HPLC using an OD-H column (*n*-hexane/*i*-PrOH = 95/5, flow rate 1.0 mL/min, λ = 254 nm, τ_{maj} = 24.1 min, τ_{min} = 35.2 min) ; (*S*)-2l $[\alpha]_D^{25}$ = +16.2 (c = 0.32, $CHCl_3$, 85% ee) ; (*R*)-2l $[\alpha]_D^{25}$ = -22.0 (c = 0.28, $CHCl_3$, 77% ee)

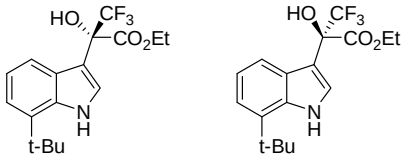
3,3,3-Trifluoro-2-hydroxy-2-(7-ethyl-1*H*-indol-3-yl)-propionic acid ethyl ester (2m):



(*S*)-2m **(*R*)-2m**

Racemic synthesis : (60.9 mg, 97%) ; Asymmetric synthesis : (*S*)-2m (30.7 mg, 97%, 81% ee), (*R*)-2m (28.9 mg, 92 %, 82% ee) ; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.29-1.35 (m, 6H), 2.80 (q, *J* = 7.8 Hz, 2H), 4.26-4.49 (m, 2H), 4.41 (s, 1H), 7.05 (d, *J* = 6.9 Hz, 1 H), 7.11 (t, *J* = 7.8 Hz, 1H), 7.40 (d, *J* = 2.4 Hz, 1H), 7.73 (d, *J* = 7.8 Hz, 1H), 8.25 (brs, 1H) ; ^{19}F NMR ($CDCl_3$, 282.3 MHz) δ -77.1 (s, 3F) ; IR (KBr) 3437, 3349, 1724, 1439, 1301, 1255, 1229, 1191, 1097, 1008, 748, 693 cm^{-1} ; MS (ESI, *m/z*) 338.2 $[M+Na]^+$; The ee of the product was determined by HPLC using an OD-H column (*n*-hexane/*i*-PrOH = 95/5, flow rate 1.0 mL/min, λ = 254 nm, τ_{maj} = 20.7 min, τ_{min} = 35.1 min) ; (*S*)-2m $[\alpha]_D^{25}$ = +8.9 (c = 0.23, $CHCl_3$, 81% ee) ; (*R*)-2m $[\alpha]_D^{25}$ = -20.8 (c = 0.29, $CHCl_3$, 82% ee)

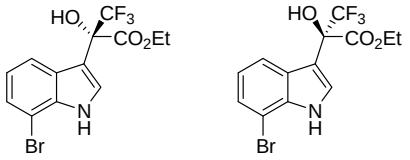
3,3,3-Trifluoro-2-hydroxy-2-(7-tert-butyl-1*H*-indol-3-yl)-propionic acid ethyl ester (2n):



(*S*)-2n **(*R*)-2n**

Racemic synthesis (Half scale of general procedure) : (32.1 mg, 94%) ; Asymmetric synthesis : (*S*)-2n (27.7 mg, 81%, 79% ee), (*R*)-2n (29.4 mg, 86 %, 80% ee) ; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.34 (t, *J* = 7.2 Hz, 3H), 1.50 (s, 9H), 4.29-4.52 (m, 2H), 4.38 (s, 1H), 7.10 (t, *J* = 7.8 Hz, 1H), 7.16 (dd, *J* = 7.5, 0.9 Hz, 1H), 7.47 (d, *J* = 2.7 Hz, 1H), 7.77 (d, *J* = 7.8 H, 1H), 8.42 (brs, 1H) ; ^{19}F NMR ($CDCl_3$, 282.3 MHz) δ -77.0 (s, 3F) ; ^{13}C NMR ($CDCl_3$, 150.9 MHz) δ 13.9, 30.4, 34.5, 64.2, 76.7 (q, *J* = 31.7 Hz), 108.5, 119.2, 119.4, 120.5, 123.5, 123.6 (q, *J* = 286.7 Hz), 126.1, 133.5, 134.1, 169.5 ; IR (neat) 3459, 2969, 1733, 1423, 1368, 1222, 1175, 1112, 1014, 900, 748, 690 cm^{-1} ; MS (EI, *m/z*) 343 (M^+), HRMS calcd. for $C_{17}H_{20}F_3NO_3^+$: 343.1395 Found : 343.1387 ; The ee of the product was determined by HPLC using an AS-H column (*n*-hexane/*i*-PrOH = 95/5, flow rate 0.5 mL/min, λ = 254 nm, τ_{maj} = 25.9 min, τ_{min} = 23.4 min) ; (*S*)-2n $[\alpha]_D^{25}$ = +7.5 (c = 0.34, $CHCl_3$, 79% ee) ; (*R*)-2n $[\alpha]_D^{25}$ = -9.5 (c = 0.41, $CHCl_3$, 80% ee)

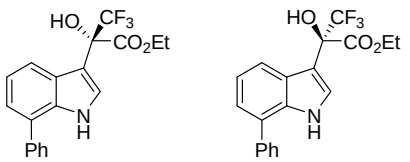
3,3,3-Trifluoro-2-hydroxy-2-(7-bromo-1*H*-indol-3-yl)-propionic acid ethyl ester (2o):



(*S*)-2o **(*R*)-2o**

Racemic synthesis : (62.0 mg, 85%) ; Asymmetric synthesis : (*S*)-2o (29.4 mg, 80%, 79% ee), (*R*)-2o (28.8 mg, 79 %, 58% ee) ; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.35 (t, *J* = 7.2 Hz, 3H), 4.32-4.52 (m, 2H), 4.43 (s, 1H), 7.05 (t, *J* = 8.1 Hz, 1H), 7.39 (d, *J* = 7.5 Hz, 1H), 7.56 (s, 1H), 7.88 (d, *J* = 8.1 Hz, 1H), 8.50 (brs, 1H) ; ^{19}F NMR ($CDCl_3$, 282.3 MHz) δ -77.5 (s, 3F) ; ^{13}C NMR ($CDCl_3$, 150.9 MHz) δ 13.9, 64.4, 76.6 (q, *J* = 33.2 Hz), 104.8, 110.0, 120.7, 121.7, 123.3 (q, *J* = 286.7 Hz), 124.9, 125.0, 126.3, 135.0, 169.1 ; IR (neat) 3428, 2984, 1738, 1434, 1286, 1227, 1207, 1179, 1109, 1013, 782, 739, 689 cm^{-1} ; MS (EI, *m/z*) 365, 367 (M^+), HRMS calcd. for $C_{13}H_{11}BrF_3NO_3^+$: 364.9874 Found : 364.9868 ; The ee of the product was determined by HPLC using an AS-H column (*n*-hexane/*i*-PrOH = 95/5, flow rate 1.0 mL/min, λ = 254 nm, τ_{maj} = 20.5 min, τ_{min} = 17.4 min) ; (*S*)-2o $[\alpha]_D^{25}$ = +13.6 (c = 0.30, $CHCl_3$, 79% ee) ; (*R*)-2o $[\alpha]_D^{25}$ = -23.4 (c = 0.42, $CHCl_3$, 58% ee)

3,3,3-Trifluoro-2-hydroxy-2-(7-phenyl-1*H*-indol-3-yl)-propionic acid ethyl ester (2p):

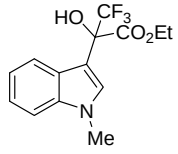


(*S*)-2p **(*R*)-2p**

Racemic synthesis : (69.8 mg, 96%) ; Asymmetric synthesis : (*S*)-2p (34.4 mg, 95%, 75% ee), (*R*)-2p (33.6 mg,

93 %, 74% ee) ;^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.36 (t, *J* = 7.2 Hz, 3H), 4.34-4.51 (m, 2H), 4.42 (s, 1H), 7.22-7.25 (m, 2H), 7.38-7.44 (m, 1H), 7.48-7.53 (m, 3H), 7.58-7.61 (m, 2H), 7.88-7.94 (m, 1H), 8.52 (brs, 1H) ; ^{19}F NMR ($CDCl_3$, 282.3 MHz) δ -77.2 (s, 3F) ; ^{13}C NMR ($CDCl_3$, 150.9 MHz) δ 13.9, 64.2, 76.7 (q, *J* = 31.7 Hz), 109.1, 120.4, 121.0, 122.6, 123.5 (q, *J* = 285.2 Hz), 124.6, 125.5, 125.9, 127.6, 128.2, 129.2, 134.3, 138.6, 169.3 ; IR (neat) 3439, 1736, 1428, 1306, 1253, 1226, 1177, 1013, 761, 703 cm^{-1} ; MS (EI, *m/z*) 363 (M^+), HRMS calcd. for $C_{19}H_{16}F_3NO_3^+$: 363.1082 Found : 363.1086 ; The ee of the product was determined by HPLC using an OD-H column (*n*-hexane/*i*-PrOH = 95/5, flow rate 1.0 mL/min, λ = 254 nm, τ_{maj} = 21.5 min, τ_{min} = 25.1 min) ; (*S*)-2p $[\alpha]_D^{25}$ = +21.0 (c = 0.33, $CHCl_3$, 75% ee) ; (*R*)-2p $[\alpha]_D^{25}$ = -23.0 (c = 0.24, $CHCl_3$, 74% ee)

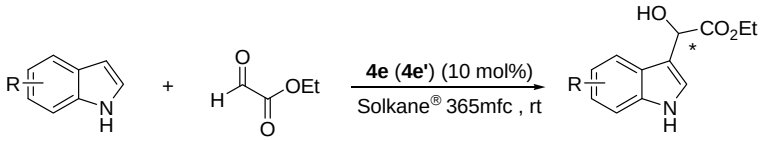
3,3,3-Trifluoro-2-hydroxy-2-(1-methyl-indol-3-yl)-propionic acid ethyl ester (2q)[8]:



2q

Racemic synthesis : (55.0 mg, 91%) ; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.36 (t, *J* = 7.2 Hz, 3H), 3.77 (s, 3H), 4.25-4.53 (m, 2H), 4.35 (s, 1H), 7.09-7.31 (m, 4H), 7.86 (d, *J* = 8.0 Hz, 1H) ; ^{19}F NMR ($CDCl_3$, 188.2 MHz) δ -76.6 (s, 3F) ; IR (KBr) 3474, 1731, 1541, 1474, 1369, 1307, 1231, 1184, 1009, 986, 746 cm^{-1} ; MS (ESI, *m/z*) 324.2 $[M+Na]^+$

5. General experimental procedure for the F-C alkylation of indoles with ethyl glyoxylate in Solkane® 365mfc:



1
(2.0 equiv)

(+)-3 or (-)-3

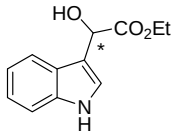
Catalyst free Friedel-Crafts alkylation of indoles (Racemic synthesis):

To a stirred solution of 1 (0.40 mmol) in Solkane® 365mfc (0.5 mL), ethyl glyoxylate (39.6 μL, 0.20 mmol) was added at room temperature under nitrogen atmosphere. The mixture was stirred at room temperature for 1.0 - 24.0 h. Then the solvent was removed in vacuo, and the residue was purified by column chromatography (*n*-hexane/ethyl acetate = 70/30) give 3 as a solid or liquid.

Catalytic enantioselective Friedel-Crafts alkylation of indoles (Asymmetric synthesis):

To a stirred solution of 1 (0.20 mmol) and catalyst 4e or 4e' (8.2 mg, 10 mol%) in Solkane® 365mfc (0.5 mL), ethyl glyoxylate (19.8 μL, 0.10 mmol) was added at room temperature under nitrogen atmosphere. The mixture was stirred at room temperature for 1.0 – 3.0 h. Then the solvent was removed in vacuo, and the residue was purified by column chromatography (*n*-hexane/ethyl acetate = 70/30) give (+)-3 or (-)-3 as a solid or liquid.

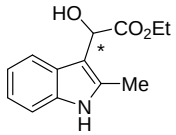
Hydroxy-(1*H*-indol-3-yl)-acetic acid ethyl ester (3a)[9]:



3a

Racemic synthesis : (31.8 mg, 73%) ; Asymmetric synthesis : (+)-3a (17.6 mg, 80%, 90% ee), (-)-3a (20.2 mg, 92 %, 92% ee) ; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.22 (t, *J* = 7.2 Hz, 3H), 3.28 (d, *J* = 6.0 Hz, 1H), 4.13-4.36 (m, 2H), 5.47 (d, *J* = 5.7 Hz, 1H), 7.12-7.25 (m, 3H), 7.37 (d, *J* = 8.1 Hz, 1H), 7.72 (d, *J* = 7.8 Hz, 1H), 8.16 (brs, 1H) ; IR (KBr) 3397, 2981, 1723, 1458, 1424, 1339, 1227, 1303, 1053, 744 cm^{-1} ; MS (ESI, *m/z*) 242.2 $[M+Na]^+$; The ee of the product was determined by HPLC using an AS-H column (*n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm, τ_{maj} = 21.6 min, τ_{min} = 30.0 min) ; (+)-3a $[\alpha]_D^{25}$ = +86.8 (c = 0.37, $CHCl_3$, 90 % ee) ; (-)-3a $[\alpha]_D^{25}$ = -87.0 (c = 0.50, $CHCl_3$, 92 % ee)

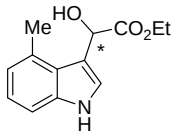
Hydroxy-(2-methyl-1*H*-indol-3-yl)-acetic acid ethyl ester (3b):



3b

Racemic synthesis : (41.7 mg, 89%) ; Asymmetric synthesis : (+)-3b (23.3 mg, 99%, 85% ee), (-)-3b (23.3 mg, 99%, 85% ee) ; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.18 (t, *J* = 7.5 Hz, 3H), 2.44 (s, 3H), 3.33 (brs, 1H), 4.09-4.33 (m, 2H), 5.41 (s, 1H), 7.04-7.15 (m, 2H), 7.23 (s, 1H), 7.56 (d, *J* = 7.5Hz, 1H), 7.96 (brs, 1H) ; ^{13}C NMR ($CDCl_3$, 150.9 MHz) δ 11.8, 14.1, 62.0, 66.4, 109.0, 110.4, 118.4, 120.0, 121.5, 126.4, 133.9, 135.1, 174.4 ; IR (neat) 3396, 2981, 2925, 1731, 1462, 1259, 1213, 1057, 1019, 745 cm^{-1} ; MS (EI, *m/z*) 233 (M^+), HRMS calcd. for $C_{13}H_{15}NO_3^+$: 233.1052 Found : 233.1072 ; The ee of the product was determined by HPLC using an AS-H column (*n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm, τ_{maj} = 17.6 min, τ_{min} = 22.4 min) ; (+)-3b $[\alpha]_D^{25}$ = +68.7 (c = 0.39, $CHCl_3$, 85 % ee) ; (-)-3b $[\alpha]_D^{25}$ = -22.8 (c = 0.70, $CHCl_3$, 85 % ee)

Hydroxy-(4-methyl-1*H*-indol-3-yl)-acetic acid ethyl ester (3d):

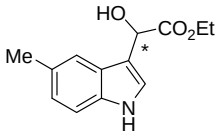


3d

Racemic synthesis : (25.9 mg, 56%) ; Asymmetric synthesis : (+)-3d (18.0 mg, 77%, 89% ee), (-)-3d (19.5 mg, 84%, 92% ee) ; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.27 (t, *J* = 7.2 Hz, 3H), 2.74 (s, 3H), 3.06 (d, *J* = 6.6 Hz, 1H), 4.17-4.38 (m, 2H), 5.68 (d, *J* = 6.6 Hz, 1H), 6.92 (d, *J* = 7.2 Hz, 1H), 7.11 (t, *J* = 8.1 Hz, 1H), 7.15 (s, 1H), 7.22 (d, *J* = 8.1 Hz, 1H), 8.19 (brs,1H) ; ^{13}C NMR ($CDCl_3$, 150.9 MHz) δ 14.1, 20.3, 61.8, 67.3, 109.2, 114.9, 121.9, 122.7, 123.1, 124.8, 130.6, 136.6, 174.4 ; IR (KBr) 3480, 3301, 2979, 1733, 1375, 1349, 1211, 1055, 1019, 750 cm^{-1} ; mp = 123-126 ºC ; MS (EI, *m/z*) 233 (M^+), HRMS calcd. for $C_{13}H_{15}NO_3^+$: 233.1052 Found : 233.1075 ; The ee of the product was determined by HPLC using an AS-H column (*n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm, τ_{maj} = 19.3 min, τ_{min} = 30.7 min) ; (+)-3d $[\alpha]_D^{25}$ = +85.2 (c = 0.40, $CHCl_3$, 89 % ee) ; (-)-3d $[\alpha]_D^{25}$ =

-86.6 (c = 0.49, $CHCl_3$, 92 % ee)

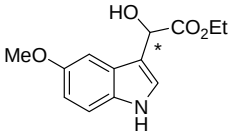
Hydroxy-(5-methyl-1*H*-indol-3-yl)-acetic acid ethyl ester (3e)[9]:



3e

Racemic synthesis : (30.9 mg, 66%) ; Asymmetric synthesis : (+)-3e (23.3 mg, 99%, 87% ee), (-)-3e (21.2 mg, 91%, 91% ee) ; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.23 (t, *J* = 7.2 Hz, 3H), 2.44 (s, 3H), 3.22 (d, *J* = 6.0 Hz, 1H), 4.09-4.38 (m, 2H), 5.43 (d, *J* = 5.6 Hz, 1H), 7.03 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.18-7.26 (m, 2H), 7.486-7.493 (m, 1H), 8.04 (brs, 1H) ; IR (KBr) 3536, 3407, 1729, 1305, 1281, 1259, 1201, 1078, 1045, 602 cm^{-1} ; MS (ESI, *m/z*) 256.0 $[M+Na]^+$; The ee of the product was determined by HPLC using an AS-H column (*n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm, τ_{maj} = 18.7 min, τ_{min} = 24.0 min) ; (+)-3e $[\alpha]_D^{25}$ = +76.9 (c = 0.50, $CHCl_3$, 90 % ee) ; (-)-3e $[\alpha]_D^{25}$ = -78.9 (c = 0.66, $CHCl_3$, 91 % ee)

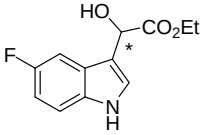
Hydroxy-(5-methoxy-1*H*-indol-3-yl)-acetic acid ethyl ester (3f)[9]:



3f

Racemic synthesis : (39.4 mg, 79%) ; Asymmetric synthesis : (+)-3f (24.0 mg, 96%, 83% ee), (-)-3f (22.9 mg, 92%, 88% ee) ; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.24 (t, *J* = 7.2 Hz, 3H), 3.23 (d, *J* = 6.0 Hz, 1H), 3.85 (s, 3H), 4.10-4.38 (m, 2H), 5.43 (d, *J* = 5.6 Hz, 1H), 6.86 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.14-7.26 (m, 3H), 8.06 (brs, 1H) ; IR (neat) 3403, 2982, 2939, 1731, 1487, 1456, 1442, 1213, 1069, 801 cm^{-1} ; MS (ESI, *m/z*) 272.2 $[M+Na]^+$; The ee of the product was determined by HPLC using an AS-H column (*n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm, τ_{maj} = 31.4 min, τ_{min} = 37.5 min) ; (+)-3f $[\alpha]_D^{25}$ = +73.9 (c = 0.61, $CHCl_3$, 83 % ee) ; (-)-3f $[\alpha]_D^{25}$ = -83.6 (c = 0.62, $CHCl_3$, 88 % ee)

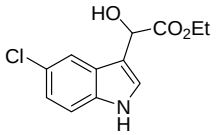
Hydroxy-(5-fluoro-1*H*-indol-3-yl)-acetic acid ethyl ester (3g)[9]:



3g

Racemic synthesis : (26.6 mg, 56%) ; Asymmetric synthesis : (+)-3g (17.6 mg, 74%, 89% ee), (-)-3g (21.3 mg, 90%, 92% ee) ; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.24 (t, *J* = 7.2 Hz, 3H), 3.30 (d, *J* = 5.2 Hz, 1H), 4.11-4.39 (m, 2H), 5.41 (d, *J* = 5.2 Hz, 1H), 6.95 (dt, *J* = 9.2, 2.6 Hz, 1H), 7.24-7.39 (m, 3H), 8.16 (brs, 1H) ; ^{19}F NMR ($CDCl_3$, 188.2 MHz) δ -123.1 (dt, *J* = 9.2, 4.2 Hz, 1F) ; IR (KBr) 3502, 3334, 1718, 1586, 1487, 1459, 1427, 1276, 1174, 1062, 1017, 810 cm^{-1} ; MS (ESI, *m/z*) 260.0 $[M+Na]^+$; The ee of the product was determined by HPLC using an AS-H column (*n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm, τ_{maj} = 19.7 min, τ_{min} = 27.6 min) ; (+)-3g $[\alpha]_D^{25}$ = +94.4 (c = 0.42, $CHCl_3$, 89 % ee) ; (-)-3g $[\alpha]_D^{25}$ = -88.4 (c = 0.48, $CHCl_3$, 92 % ee)

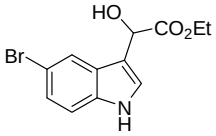
Hydroxy-(5-chloro-1*H*-indol-3-yl)-acetic acid ethyl ester (3h)[9]:



3h

Racemic synthesis : (27.5 mg, 54%) ; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.24 (t, *J* = 7.2 Hz, 3H), 3.32 (d, *J* = 5.6 Hz, 1H), 4.11-4.39 (m, 2H), 5.41 (d, *J* = 5.4Hz, 1H), 7.15 (dd, *J* = 8.7, 2.0 Hz, 1H), 7.25-7.30 (m, 2H), 7.69 (d, *J* = 1.8 Hz, 1H), 8.19 (brs, 1H) ; IR (KBr) 3505, 3283, 2988, 1737, 1456, 1214, 1110, 804, 756, 699 cm^{-1} ; MS (ESI, *m/z*) 276.0, 278.0 $[M+Na]^+$

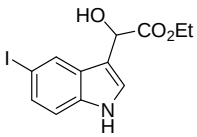
Hydroxy-(5-bromo-1*H*-indol-3-yl)-acetic acid ethyl ester (3i)[9]:



3i

Racemic synthesis : (48.6 mg, 82%) ; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.25 (t, *J* = 7.0 Hz, 3H), 3.31 (d, *J* = 5.6 Hz, 1H), 4.11-4.39 (m, 2H), 5.41 (d, *J* = 5.4 Hz, 1H), 7.20-7.32 (m, 3H), 7.85-7.86 (m, 1H), 8.17 (brs, 1H) ; IR (KBr) 3503, 3279, 2984, 2904, 1736, 1455, 1214, 1106, 869, 801, 755, 685, 607 cm^{-1} ; MS (ESI, *m/z*) 320.1, 322.1 $[M+Na]^+$

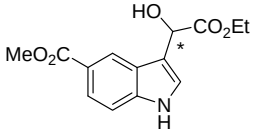
Hydroxy-(5-iodo-1*H*-indol-3-yl)-acetic acid ethyl ester (3j)[10]:



3j

Racemic synthesis : (58.0 mg, 84%) ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.26 (t, *J* = 7.2 Hz, 3H), 3.30 (d, *J* = 5.6 Hz, 1H), 4.11-4.39 (m, 2H), 5.41 (d, *J* = 5.2 Hz, 1H), 7.14 (d, *J* = 8.6 Hz, 1H), 7.21 (d, *J* = 2.4 Hz, 1H), 7.46 (dd, *J* = 8.6, 1.6 Hz, 1H), 8.06 (d, *J* = 1.0 Hz, 1H), 8.17 (brs, 1H) ; IR (KBr) 3502, 3278, 2979, 1735, 1456, 1241, 1214, 1104, 871, 799, 604 cm^{-1} ; MS (ESI, *m/z*) 368.1 $[M+Na]^+$;

Hydroxy-(5-methyl-1*H*-indol-carboxylate-3-yl)-acetic acid ethyl ester (3r):

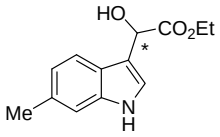


3r

Racemic synthesis : (15.9 mg, 29%) ; Asymmetric synthesis ((+)-3r is twice scale of general procedure) : (+)-3r (4.5 mg, 8%, 81% ee), (-)-3r (6.8 mg, 25%, 90% ee) ; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.25 (t, *J* = 7.2 Hz, 3H), 3.37 (d, *J* = 5.4 Hz, 1H), 3.94 (s, 3H), 4.15-4.37 (m, 2H), 5.52 (d, *J* = 5.4 Hz, 1H), 7.34 (d, *J* = 2.4 Hz, 1H), 7.39 (d, *J* = 8.7 Hz, 1H), 7.94 (dd, *J* = 8.4, 1.5 Hz, 1H), 8.37 (brs, 1H), 8.51 (d, *J* = 0.6 Hz, 1H) ; ^{13}C NMR ($CDCl_3$, 150.9 MHz) δ 14.1, 51.9, 62.3, 67.1, 111.0, 115.6, 122.3, 122.7, 124.0, 124.2, 125.0, 139.0, 168.0, 173.7 ; IR (KBr)

3421, 3302, 1742, 1679, 1358, 1293, 1259, 1123, 978, 756 cm^{-1} ; mp = 144-147 ºC ; MS (EI, *m/z*) 277 (M^+), HRMS calcd. for $C_{14}H_{15}NO_5^+$: 277.0950 Found : 277.0958 ; The ee of the product was determined by HPLC using an AS-H column (*n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm, τ_{maj} = 29.4 min, τ_{min} = 40.6 min) ; (+)-3r $[\alpha]_D^{25}$ = +65.7 (c = 0.15, $CHCl_3$, 81 % ee) ; (-)-3k $[\alpha]_D^{25}$ = -64.3 (c = 0.12, $CHCl_3$, 90 % ee)

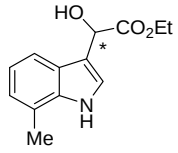
Hydroxy-(6-methyl-1*H*-indol-3-yl)-acetic acid ethyl ester (3k):



3k

Racemic synthesis (Half scale of general procedure) : (17.5 mg, 75%) ; Asymmetric synthesis (Half scale of general procedure) : (+)-3k (9.2 mg, 79%, 89% ee), (-)-3k (11.7 mg, 99%, 92% ee) ; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.22 (t, *J* = 7.5 Hz, 3H), 2.45 (s, 3H), 3.26 (d, *J* = 5.7 Hz, 1H), 4.11-4.35 (m, 2H), 5.44 (d, *J* = 5.7 Hz, 1H), 6.98 (d, *J* = 8.1 Hz, 1H), 7.14-7.16 (m, 2H), 7.59 (d, *J* = 8.1 Hz, 1H), 8.04 (brs, 1H) ; ^{13}C NMR ($CDCl_3$, 150.9 MHz) δ 14.1, 21.6, 62.0, 67.3, 111.3, 113.7, 119.0, 121.9, 122.6, 123.1, 132.3, 136.9, 174.1 ; IR (neat) 3403, 1732, 1628, 1547, 1455, 1230, 1200, 1095, 1077, 1043, 803 cm^{-1} ; MS (EI, *m/z*) 233 (M^+), HRMS calcd. for $C_{13}H_{15}NO_3^+$: 233.1052 Found : 233.1058 ; The ee of the product was determined by HPLC using an AS-H column (*n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm, τ_{maj} = 19.1 min, τ_{min} = 25.0 min) ; (+)-3k $[\alpha]_D^{25}$ = +82.0 (c = 0.23, $CHCl_3$, 89 % ee) ; (-)-3k $[\alpha]_D^{25}$ = -61.4 (c = 0.45, $CHCl_3$, 92 % ee)

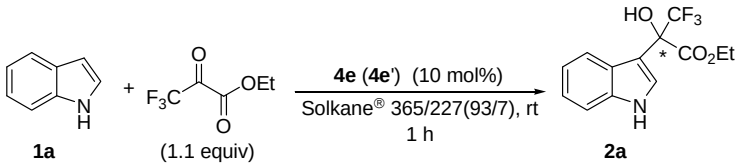
Hydroxy-(7-methyl-1*H*-indol-3-yl)-acetic acid ethyl ester (3l):



3l

Racemic synthesis : (33.9 mg, 73%) ; Asymmetric synthesis : (+)-3l (23.4 mg, 99%, 94% ee), (-)-3l (23.4 mg, 99%, 96% ee) ;^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.23 (t, *J* = 7.2 Hz, 3H), 2.49 (s, 3H), 3.27 (d, *J* = 5.7 Hz, 1H), 4.12-4.36 (m, 2H), 5.46 (d, *J* = 5.7 Hz, 1H), 7.01-7.10 (m, 2H), 7.27 (d, *J* = 2.7 Hz, 1H), 7.57 (d, *J* = 7.5 Hz, 1H), 8.11 (brs, 1H), ^{13}C NMR ($CDCl_3$, 150.9 MHz) δ 14.1, 16.5, 62.0, 67.4, 114.3, 117.1, 120.3, 120.5, 122.9, 123.0, 124.9, 136.0, 174.0 ; IR (KBr) 3348, 1732, 1440, 1228, 1197, 1107, 1062, 785, 751, 670 cm^{-1} ; mp = 124-127 ºC ; MS (EI, *m/z*) 233 (M^+), HRMS calcd. for $C_{13}H_{15}NO_3^+$: 233.1052 Found : 233.1060 ; The ee of the product was determined by HPLC using an AS-H column (*n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm, τ_{maj} = 19.3 min, τ_{min} = 27.6 min) ; (+)-3l $[\alpha]_D^{25}$ = +93.1 (c = 0.58, $CHCl_3$, 94 % ee) ; (-)-3l $[\alpha]_D^{25}$ = -100.1 (c = 0.57, $CHCl_3$, 96 % ee)

6. Catalyst-free and catalytic enantioselective F-C alkylation of 1a with ethyl trifluoropyruvate in Solkane® 365/227:



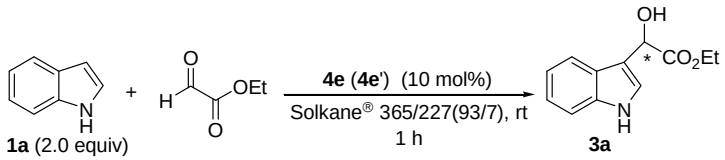
Catalyst-free F-C alkylaion:

To a stirred solution of 1a (23.4 mg, 0.20 mmol) in Solkane® 365/227 blend solvent (365/227 = 93/7) (0.5 mL), ethyl trifluoropyruvate (29.2 μL, 0.22 mmol) was added at room temperature under nitrogen atmosphere. The mixture was stirred at room temperature for 1.0 h. Then the solvent was removed in vacuo, and the residue was purified by column chromatography (*n*-hexane/ethyl acetate = 80/20) to give 2a as a white solid (55.6 mg, 97%). ^{1}H NMR spectrum is completely much with catalyst-free F-C alkylation of 1a with ethyl trifluoropyruvate in Solkane® 365mfc.

Catalytic enantioselective F-C alkylation:

To a stirred solution of 1a (23.4 mg, 0.10 mmol) and catalyst 4e or 4e' (8.2 mg, 10 mol%) in Solkane® 365/227 blend solvent (365/227 = 93/7) (0.3 mL), ethyl trifluoropyruvate (14.6 μL, 0.11 mmol) in 0.2 mL Solkane® 365/227 blend solvent (365/227 = 93/7) was added at room temperature under nitrogen atmosphere. The mixture was stirred at room temperature for 1 h. Then the solvent was removed in vacuo, and the residue was purified by column chromatography (*n*-hexane/ethyl acetate = 80/20) to give (*S*)-2a (26.2 mg, 91%, 73% ee) and (*R*)-2a (25.6 mg, 89%, 72% ee) as a white solid. ^{1}H NMR spectrum is completely much with catalytic enantioselective F-C alkylation of 1a with ethyl trifluoropyruvate in Solkane® 365mfc. The ee of the product was determined by HPLC using an OD-H column (*n*-hexane/*i*-PrOH = 95/5, flow rate 0.5 mL/min, λ = 254 nm, τ_{maj} = 55.4 min, τ_{min} = 65.5 min).

7. Catalyst-free and catalytic enantioselective F-C alkylation of 1a with ethyl glyoxylate in Solkane® 365/227:



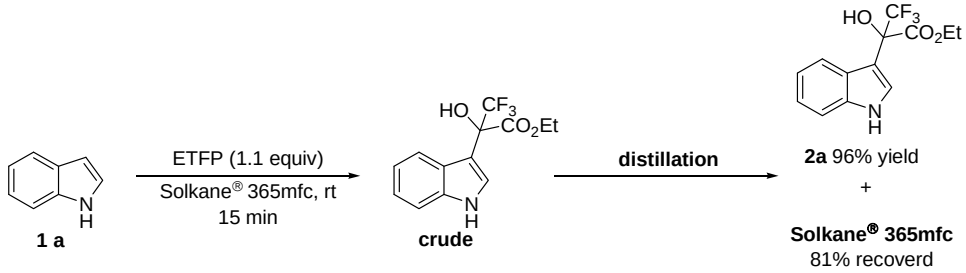
Catalyst-free F-C alkylaion:

To a stirred solution of **1a** (46.9 mg, 0.40 mmol) in Solkane® 365/227 blend solvent (365/227 = 93/7) (0.5 mL), ethyl glyoxylate (39.6 μL, 0.20 mmol) was added at room temperature under nitrogen atmosphere. The mixture was stirred at room temperature for 1.0 h. Then the solvent was removed in vacuo, and the residue was purified by column chromatography (*n*-hexane/ethyl acetate = 70/30) to give **2a** as a white solid (31.3mg, 71%).

Catalytic enantioselective F-C alkylation:

To a stirred solution of **1a** (23.4 mg, 0.20 mmol) and catalyst **4e** or **4e'** (8.2 mg, 10 mol%) in Solkane® 365/227 blend solvent (365/227 = 93/7) (0.5 mL), ethyl glyoxylate (19.8 μL, 0.10 mmol) was added at room temperature under nitrogen atmosphere. The mixture was stirred at room temperature for 1.0 h. Then the solvent was removed in vacuo, and the residue was purified by column chromatography (*n*-hexane/ethyl acetate = 70/30) to give (+)-**3a** (20.1 mg, 92%, 90% ee) and (-)-**3a** (21.0 mg, 96%, 91% ee) as a white solid. The ee of the product was determined by HPLC using an AS-H column (*n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm, τ_{maj} = 20.3 min, τ_{min} = 29.9 min).

8. Experimental procedure for the F-C alkylation of indole 1a with ethyl trifluoropyruvate, isolation of 2a with recovering Solkane® 365mfc:



To a stirred solution of **1a** (468.6 mg, 4.00 mmol) in Solkane® 365mfc (10 mL), ethyl trifluoropyruvate (0.58 mL, 4.40 mmol) was added at room temperature under nitrogen atmosphere. The mixture was stirred at room temperature for 15 min. Then distillation of the reaction mixture gave 8.1 mL (81%) of recovered Solkane® 365mfc, and 1.10g (96%) of product **2a** was left. The proton NMR spectrum indicated a pure **2a** compatible with the assigned structure.

9. References:

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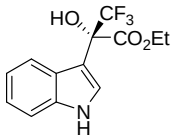
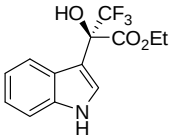
10. HPLC chart:

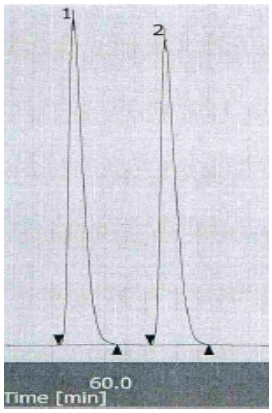


(*S*)-2a

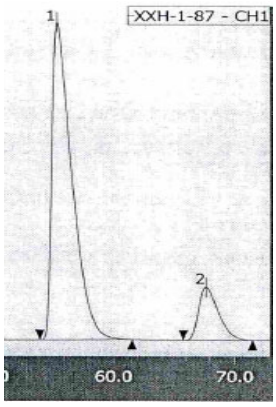


(*R*)-2a

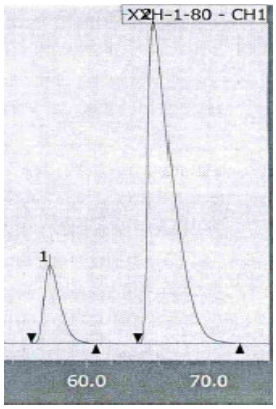
HPLC using an OD-H column (*n*-hexane/*i*-PrOH = 95/5, flow rate 0.5 mL/min, λ = 254 nm)



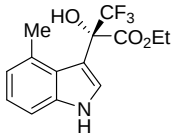
No.	tR (min)	Area (%)	High (%)
1	56.375	49.962	51.493
2	65.400	50.038	48.507



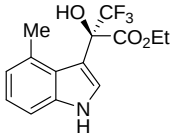
No.	tR (min)	Area (%)	High (%)
1	55.392	85.836	85.698
2	67.617	14.164	14.302



No.	tR (min)	Area (%)	High (%)
1	56.992	14.284	19.583
2	65.550	85.716	80.417

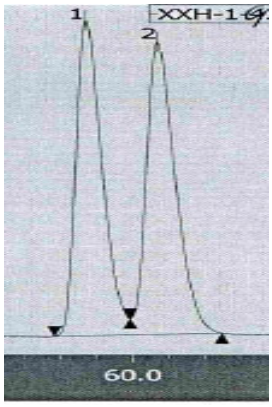


(*S*)-2d

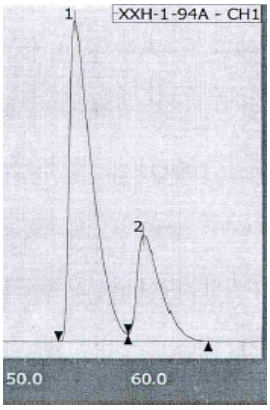


(*R*)-2d

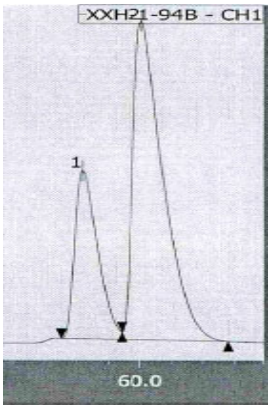
HPLC using an OD-H column(*n*-hexane/*i*-PrOH = 95/5, flow rate 0.5 mL/min, λ = 254 nm)



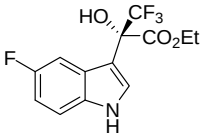
No.	tR (min)	Area (%)	High (%)
1	57.450	49.335	51.902
2	61.383	50.665	48.098



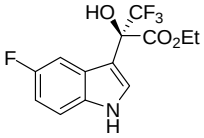
No.	tR (min)	Area (%)	High (%)
1	54.017	74.168	75.168
2	59.533	25.832	24.832



No.	tR (min)	Area (%)	High (%)
1	56.383	28.353	34.566
2	60.050	71.647	65.434

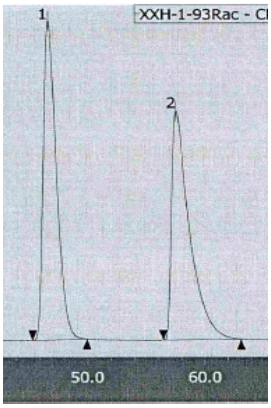


(*S*)-2g

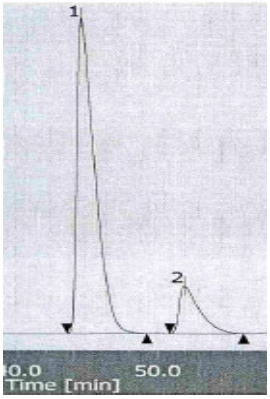


(*R*)-2g

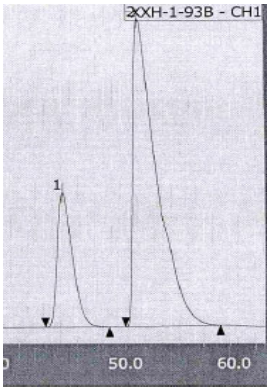
HPLC using an OD-H column (*n*-hexane/*i*-PrOH = 95/5, flow rate 0.5 mL/min, λ = 254 nm)



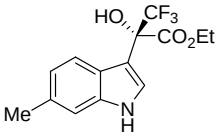
No.	tR (min)	Area (%)	High (%)
1	46.733	49.840	58.307
2	57.567	50.160	41.693



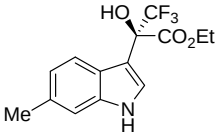
No.	tR (min)	Area (%)	High (%)
1	44.575	85.047	88.875
2	51.933	14.953	13.125



No.	tR (min)	Area (%)	High (%)
1	45.308	21.798	30.404
2	51.000	78.202	69.596

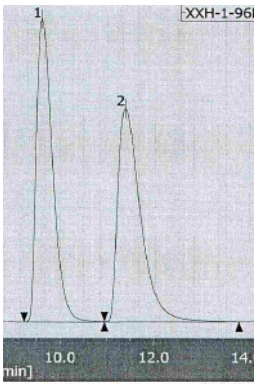


(*S*)-2k

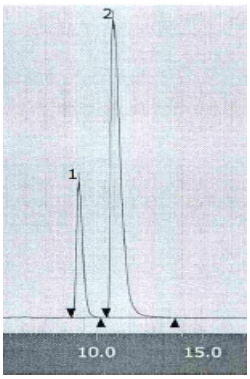


(*R*)-2k

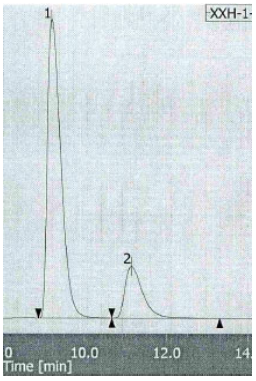
HPLC using an AS-H column (*n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm)



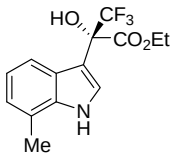
No.	tR (min)	Area (%)	High (%)
1	9.633	50.231	58.755
2	11.408	49.769	41.245



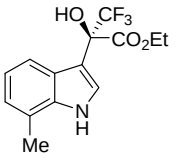
No.	tR (min)	Area (%)	High (%)
1	9.183	22.547	31.365
2	10.833	77.453	68.635



No.	tR (min)	Area (%)	High (%)
1	9.217	81.340	85.137
2	11.142	18.660	14.863

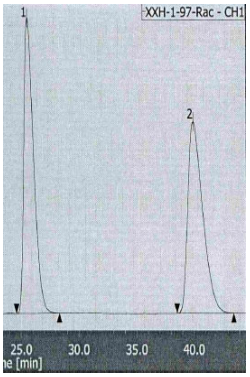


(*S*)-2l

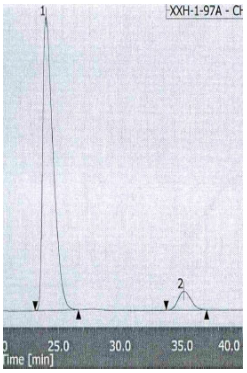


(*R*)-2l

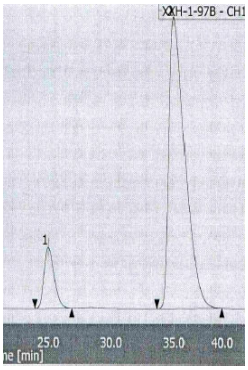
HPLC using an OD-H column (*n*-hexane/*i*-PrOH = 95/5, flow rate 1.0 mL/min, λ = 254 nm)



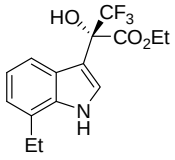
No.	tR (min)	Area (%)	High (%)
1	25.542	49.902	60.743
2	39.908	50.098	39.257



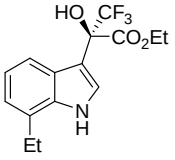
No.	tR (min)	Area (%)	High (%)
1	24.075	92.512	93.941
2	35.150	7.488	6.059



No.	tR (min)	Area (%)	High (%)
1	24.992	11.740	17.382
2	34.983	88.260	82.618

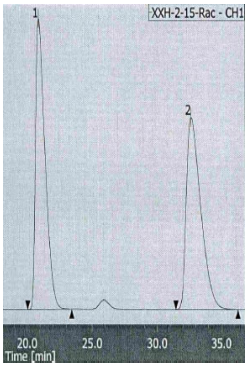


(*S*)-2m

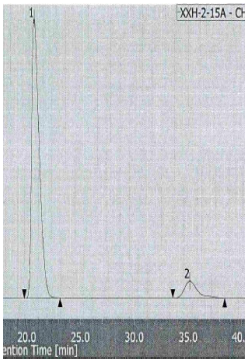


(*R*)-2m

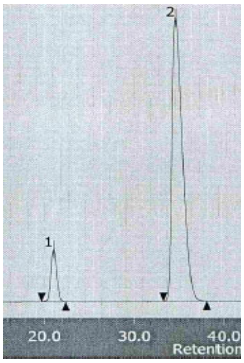
HPLC using an OD-H column (*n*-hexane/*i*-PrOH = 95/5, flow rate 1.0 mL/min, λ = 254 nm)



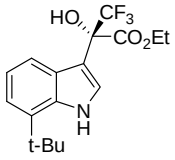
No.	tR (min)	Area (%)	High (%)
1	20.892	49.748	60.294
2	32.658	50.252	39.706



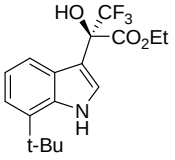
No.	tR (min)	Area (%)	High (%)
1	20.733	90.344	94.178
2	35.142	9.656	5.822



No.	tR (min)	Area (%)	High (%)
1	21.008	9.269	15.739
2	34.700	90.731	84.261

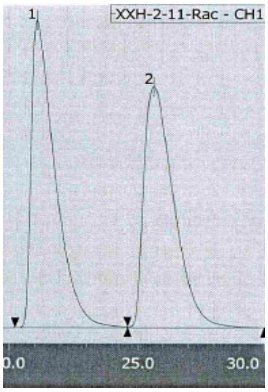


(*S*)-2n

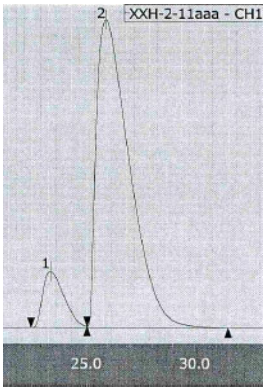


(*R*)-2n

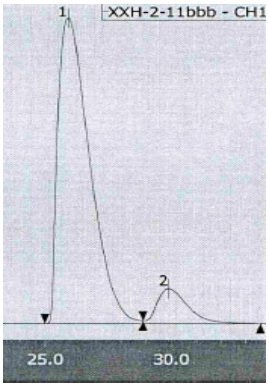
HPLC using an AS-H column (*n*-hexane/*i*-PrOH = 95/5, flow rate 0.5 mL/min, λ = 254 nm)



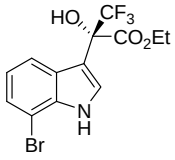
No.	tR (min)	Area (%)	High (%)
1	21.108	49.807	56.079
2	25.642	50.193	43.921



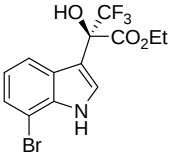
No.	tR (min)	Area (%)	High (%)
1	23.375	10.372	15.394
2	25.917	89.628	84.606



No.	tR (min)	Area (%)	High (%)
1	25.925	89.832	89.813
2	29.892	10.168	10.187

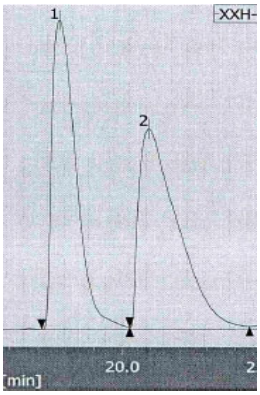


(*S*)-2o

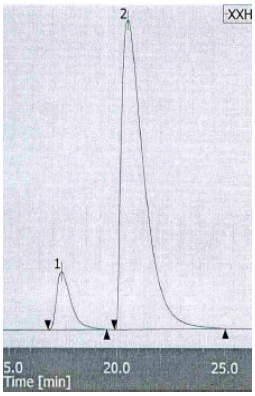


(*R*)-2o

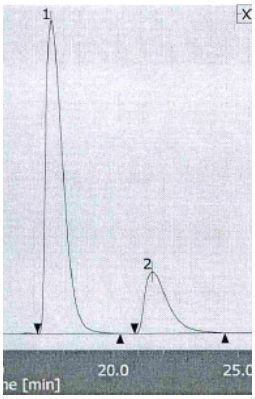
HPLC using an AS-H column (*n*-hexane/*i*-PrOH = 95/5, flow rate 1.0 mL/min, λ = 254 nm)



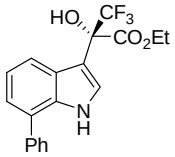
No.	tR (min)	Area (%)	High (%)
1	17.792	48.866	60.712
2	20.942	51.134	39.288



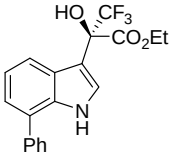
No.	tR (min)	Area (%)	High (%)
1	17.425	10.742	15.901
2	20.508	89.258	84.099



No.	tR (min)	Area (%)	High (%)
1	17.542	79.100	83.638
2	21.588	20.900	16.362

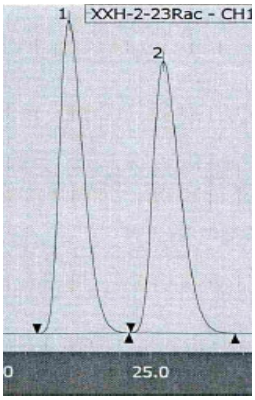


(*S*)-2p

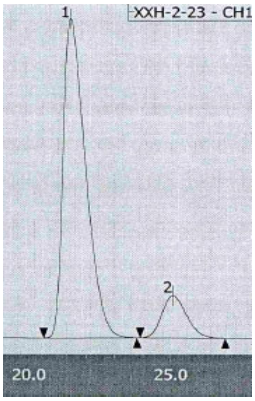


(*R*)-2p

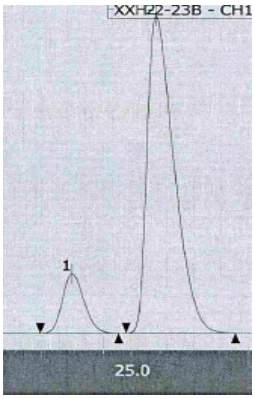
HPLC using an OD-H column (*n*-hexane/*i*-PrOH = 95/5, flow rate 1.0 mL/min, λ = 254 nm)



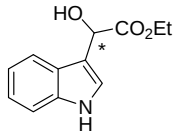
No.	tR (min)	Area (%)	High (%)
1	22.375	50.055	53.558
2	25.433	49.945	46.442



No.	tR (min)	Area (%)	High (%)
1	21.500	87.251	88.367
2	25.075	12.749	11.633

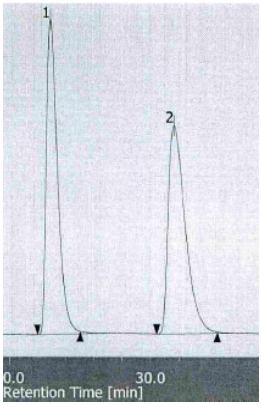


No.	tR (min)	Area (%)	High (%)
1	22.925	12.784	15.698
2	25.842	87.216	84.302

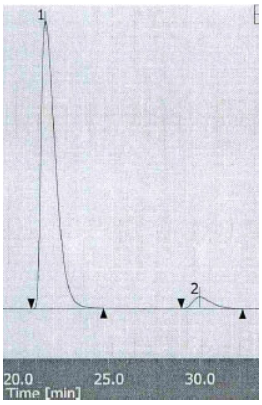


3a

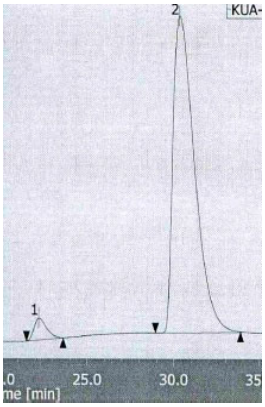
HPLC using an AS-H column (*n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm)



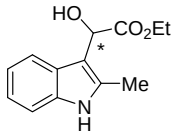
No.	tR (min)	Area (%)	High (%)
1	22.933	50.045	60.213
2	31.658	49.955	39.787



No.	tR (min)	Area (%)	High (%)
1	21.600	94.896	96.093
2	29.967	5.104	3.907

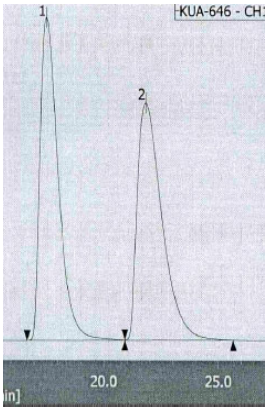


No.	tR (min)	Area (%)	High (%)
1	22.217	3.930	6.539
2	30.350	96.070	93.461

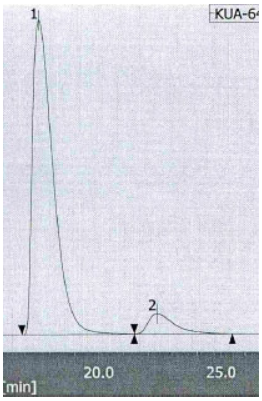


3b

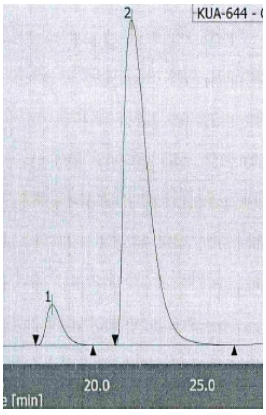
HPLC using an AS-H column (*n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm)



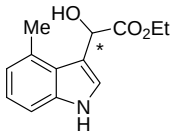
No.	tR (min)	Area (%)	High (%)
1	17.533	50.007	57.658
2	21.825	49.993	42.342



No.	tR (min)	Area (%)	High (%)
1	17.608	92.310	93.906
2	22.375	7.690	6.094

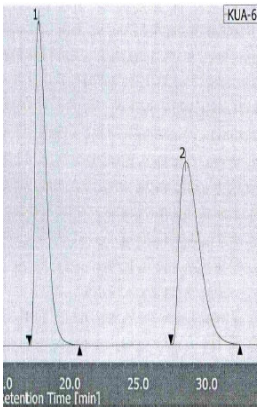


No.	tR (min)	Area (%)	High (%)
1	17.900	7.379	11.078
2	21.675	92.621	88.922

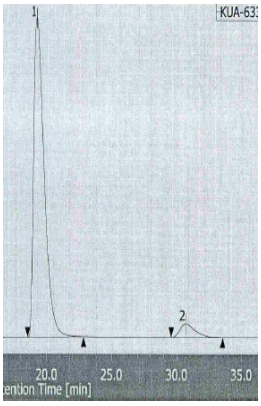


3d

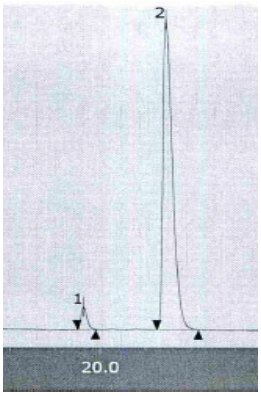
HPLC using an AS-H column (*n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm)



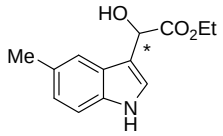
No.	tR (min)	Area (%)	High (%)
1	17.692	50.349	63.960
2	28.458	49.651	36.040



No.	tR (min)	Area (%)	High (%)
1	19.292	94.270	95.859
2	30.675	5.730	4.141

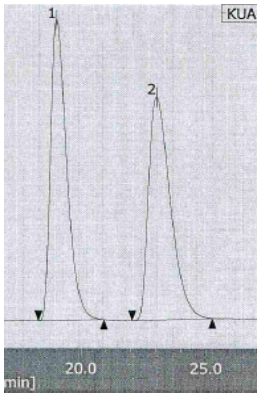


No.	tR (min)	Area (%)	High (%)
1	18.133	4.255	6.881
2	27.308	95.745	93.119

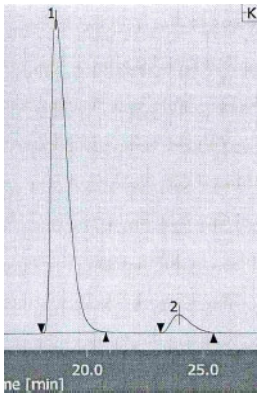


3e

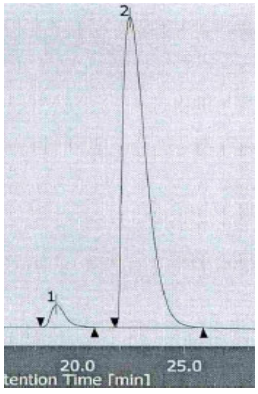
HPLC using an AS-H column (*n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm)



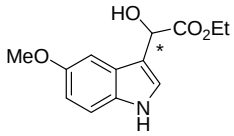
No.	tR (min)	Area (%)	High (%)
1	19.025	49.992	57.488
2	23.025	50.008	42.512



No.	tR (min)	Area (%)	High (%)
1	18.733	93.537	94.537
2	23.967	6.466	5.463

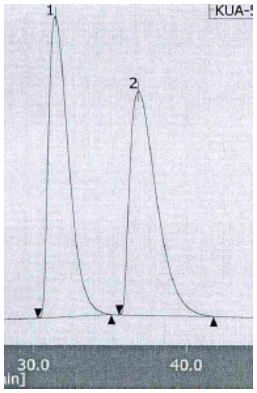


No.	tR (min)	Area (%)	High (%)
1	18.992	4.432	6.881
2	22.492	95.568	93.119

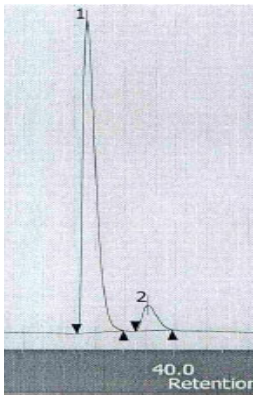


3f

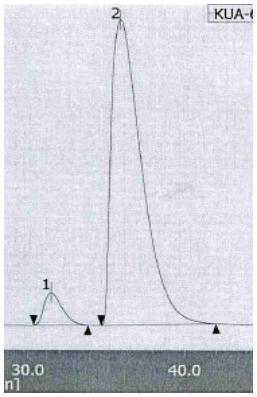
HPLC using an AS-H column (*n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm)



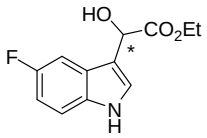
No.	tR (min)	Area (%)	High (%)
1	31.442	50.159	57.415
2	36.867	49.841	42.585



No.	tR (min)	Area (%)	High (%)
1	31.383	91.368	92.401
2	37.450	8.632	7.599

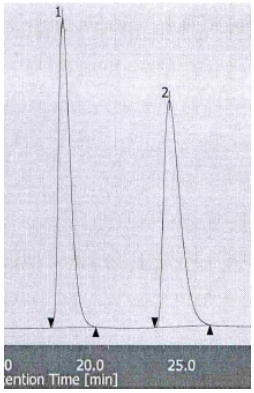


No.	tR (min)	Area (%)	High (%)
1	31.475	5.925	9.594
2	35.917	94.075	90.406

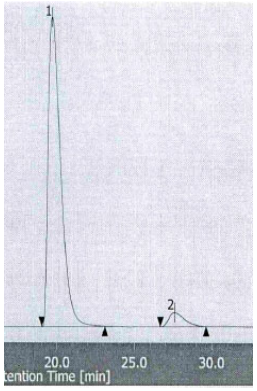


3g

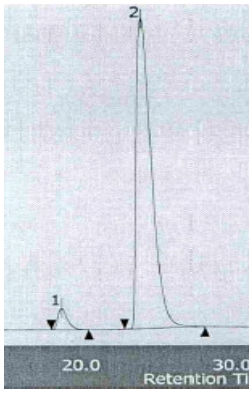
HPLC using an AS-H column (*n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm)



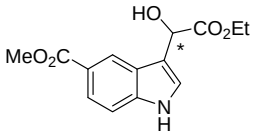
No.	tR (min)	Area (%)	High (%)
1	18.508	49.947	57.785
2	24.325	50.053	42.215



No.	tR (min)	Area (%)	High (%)
1	19.675	94.707	95.563
2	27.600	5.293	4.437

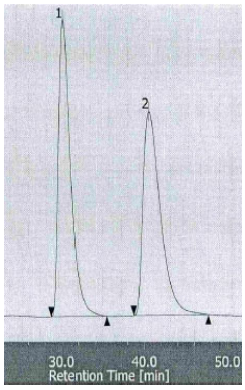


No.	tR (min)	Area (%)	High (%)
1	18.733	4.123	6.509
2	24.092	95.877	93.491

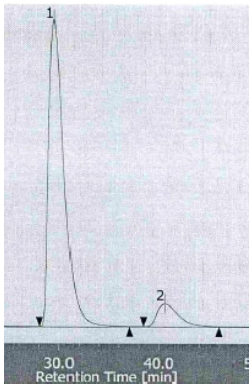


3r

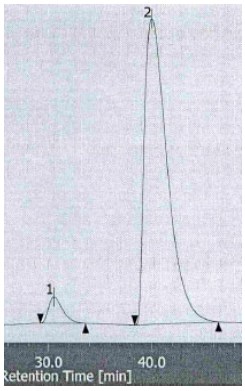
HPLC using an AS-H column (*n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm)



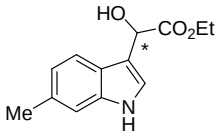
No.	tR (min)	Area (%)	High (%)
1	30.192	50.261	59.395
2	40.583	49.739	40.605



No.	tR (min)	Area (%)	High (%)
1	29.442	90.348	92.827
2	40.575	9.652	7.173

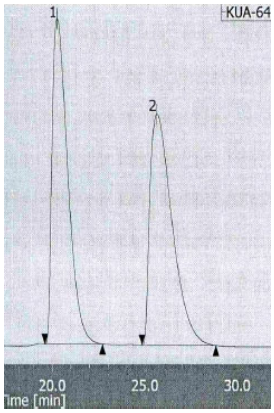


No.	tR (min)	Area (%)	High (%)
1	30.517	5.190	7.988
2	40.058	94.810	92.012

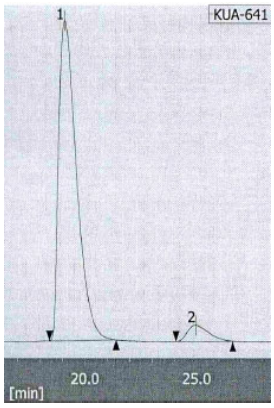


3k

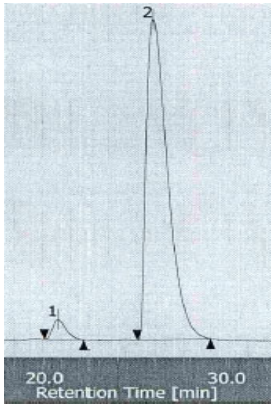
HPLC using an AS-H column (*n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm)



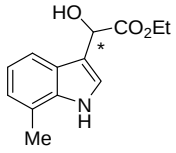
No.	tR (min)	Area (%)	High (%)
1	20.300	49.851	58.486
2	25.658	50.149	41.514



No.	tR (min)	Area (%)	High (%)
1	19.108	94.310	95.225
2	24.958	5.690	4.775

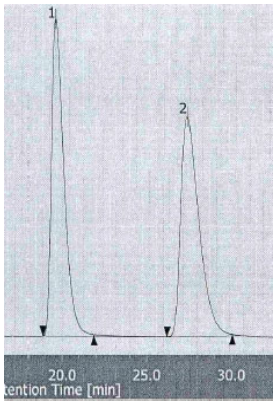


No.	tR (min)	Area (%)	High (%)
1	20.750	3.822	5.937
2	25.983	96.178	94.063

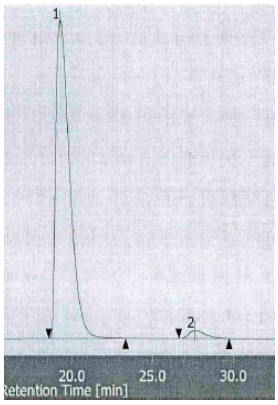


3l

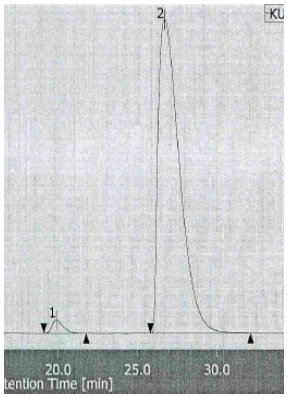
HPLC using an AS-H column (*n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm)



No.	tR (min)	Area (%)	High (%)
1	19.675	50.059	58.980
2	27.425	49.941	41.020

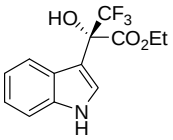


No.	tR (min)	Area (%)	High (%)
1	19.308	96.961	97.476
2	27.633	3.039	2.524

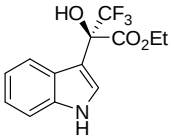


No.	tR (min)	Area (%)	High (%)
1	19.883	2.252	4.047
2	26.750	97.748	95.953

Catalytic enantioselective F-C alkylation of 1a with ethyl trifluoropyruvate in Solkane® 365/227:

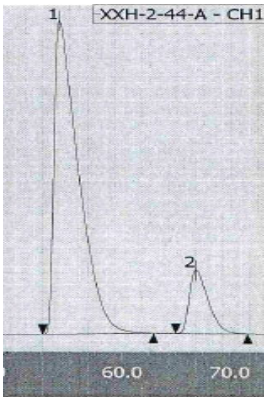


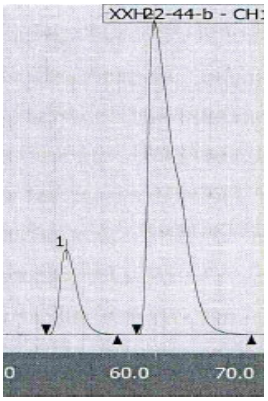
(*S*)-2a



(*R*)-2a

HPLC using an OD-H column (*n*-hexane/*i*-PrOH = 95/5, flow rate 0.5 mL/min, λ = 254 nm)

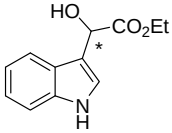




No.	tR (min)	Area (%)	High (%)
1	55.400	86.423	83.173
2	65.500	13.577	16.827

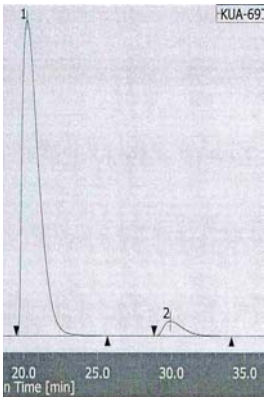
No.	tR (min)	Area (%)	High (%)
1	55.225	14.263	21.394
2	61.800	85.737	78.606

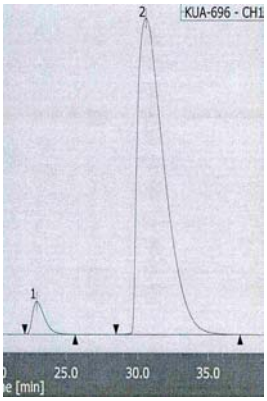
Catalytic enantioselective F-C alkylation of 1a with ethyl glyoxylate in Solkane® 365/227:



3a

HPLC using an AS-H column (*n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm)

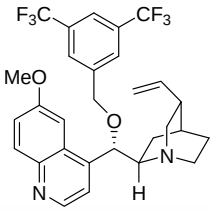




No.	tR (min)	Area (%)	High (%)
1	20.267	94.781	95.565
2	29.908	5.219	4.435

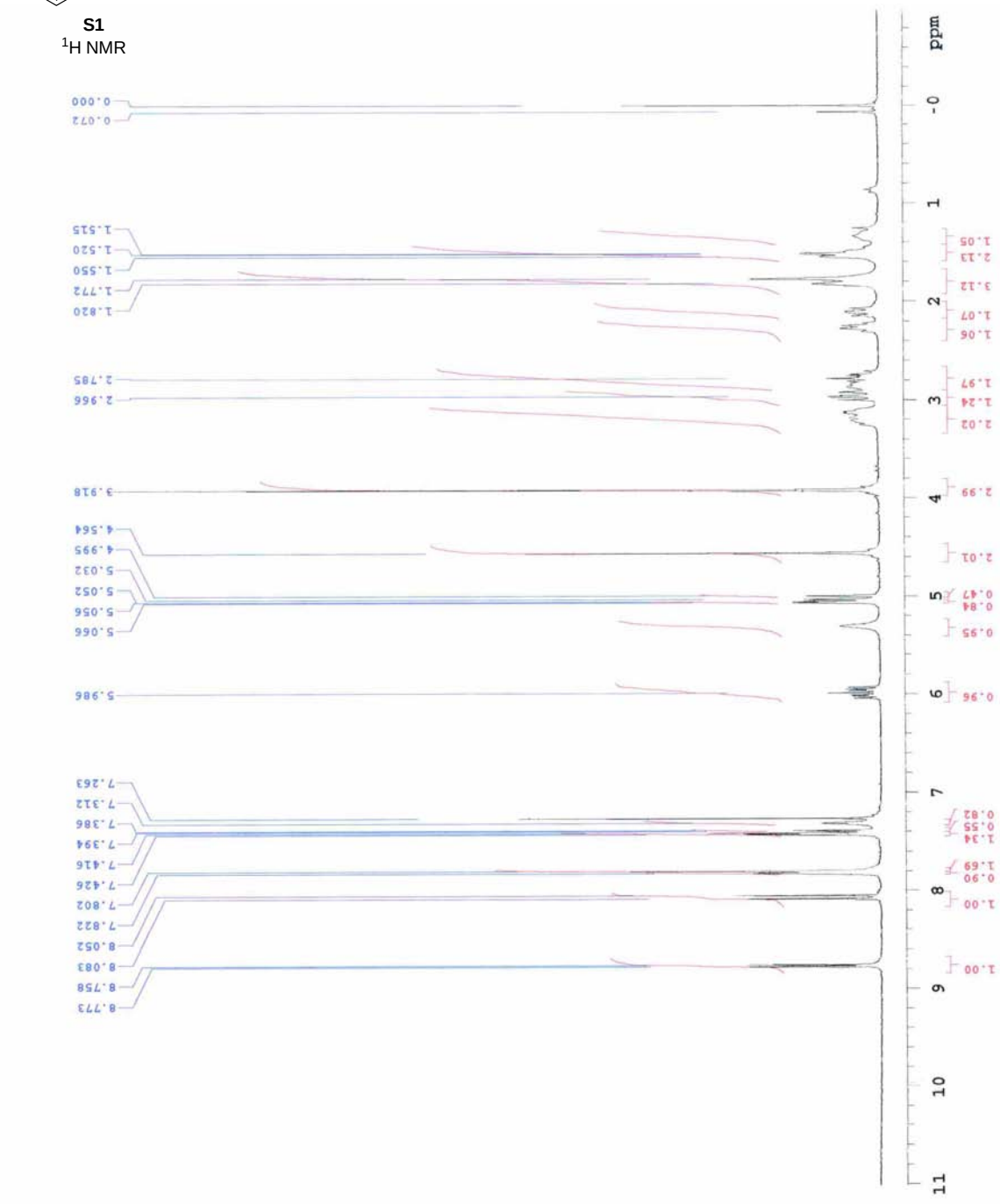
No.	tR (min)	Area (%)	High (%)
1	22.950	4.469	9.399
2	30.583	95.531	90.601

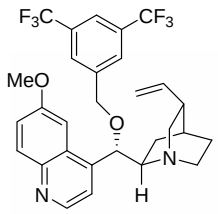
11. NMR spectrum chart:



S1

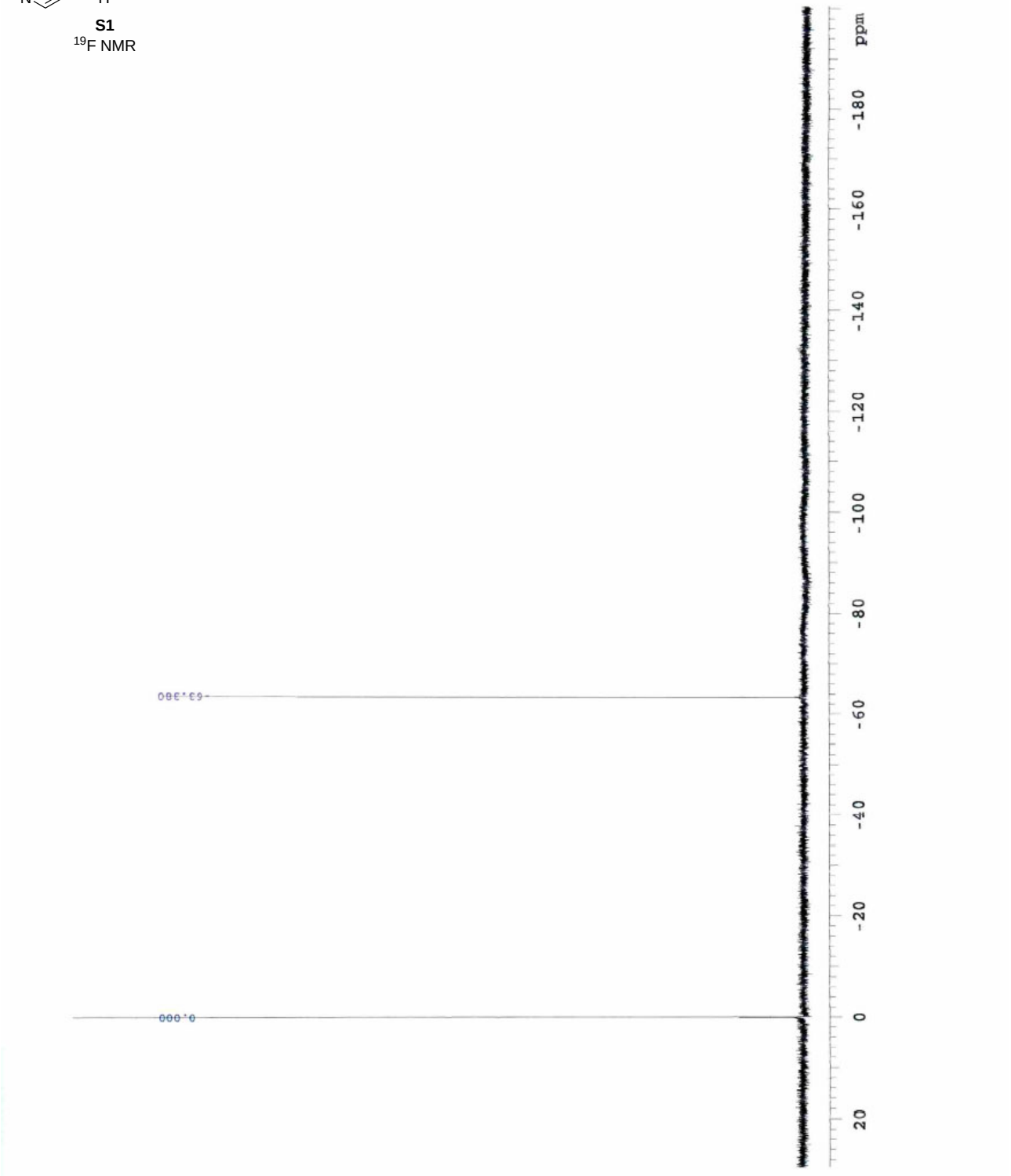
^{1}H NMR



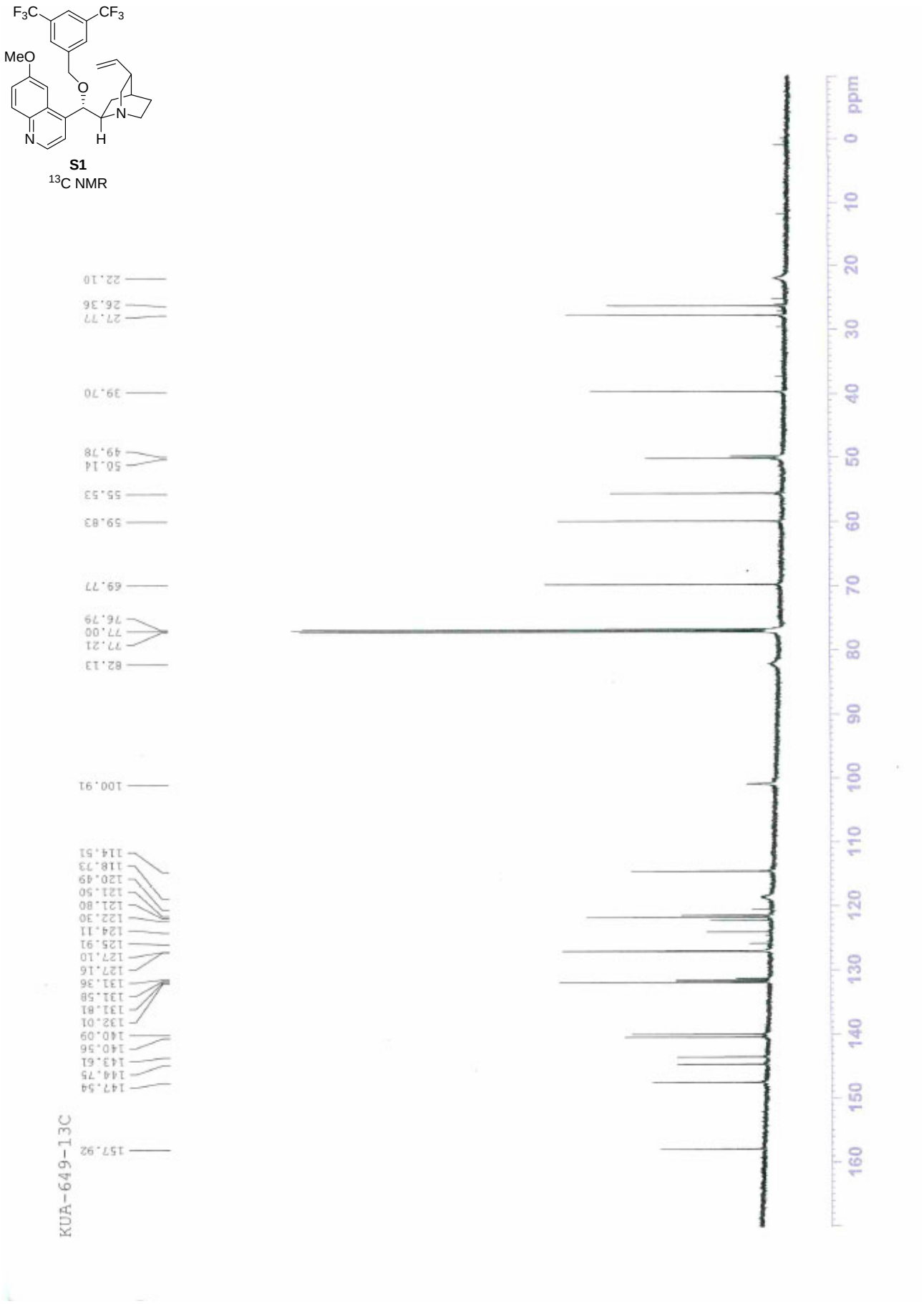

F3C
CF3
MeO
O
N
N
H

S1

^{19}F NMR


-63.380
0.000
ppm
-180
-160
-140
-120
-100
-80
-60
-40
-20
0
20

12.


F3C
CF3
MeO
O
N
N
H
S1
13C NMR
22.10
26.36
27.77
39.70
49.78
50.14
55.53
59.83
69.77
76.79
77.00
77.21
82.13
100.91
114.51
118.73
120.49
121.50
121.80
122.30
124.11
125.91
127.10
127.16
131.36
131.58
131.81
132.01
140.09
140.56
143.61
144.75
147.54
157.92
KUA-649-13C
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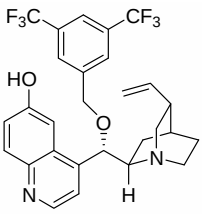
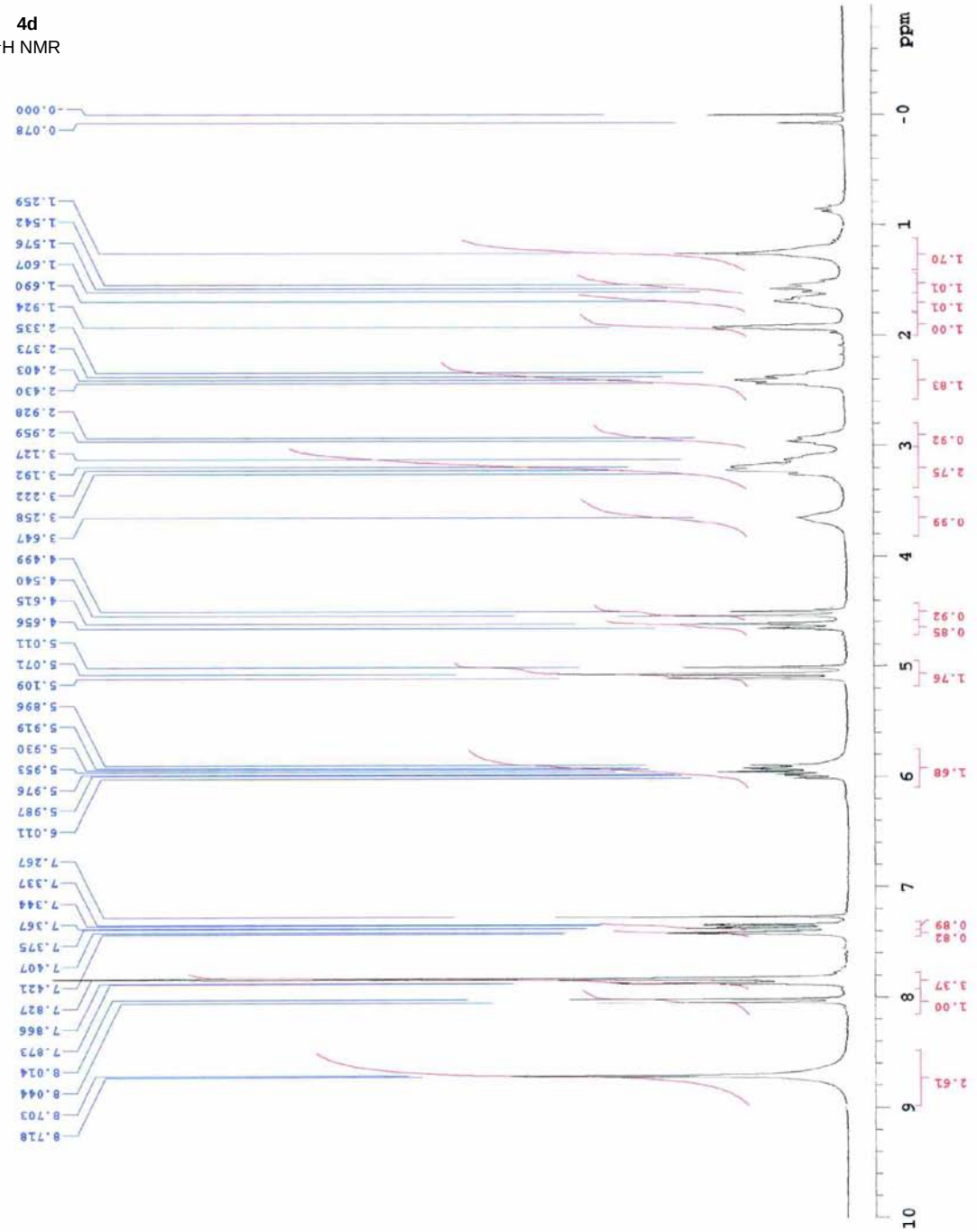
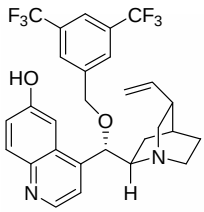
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160



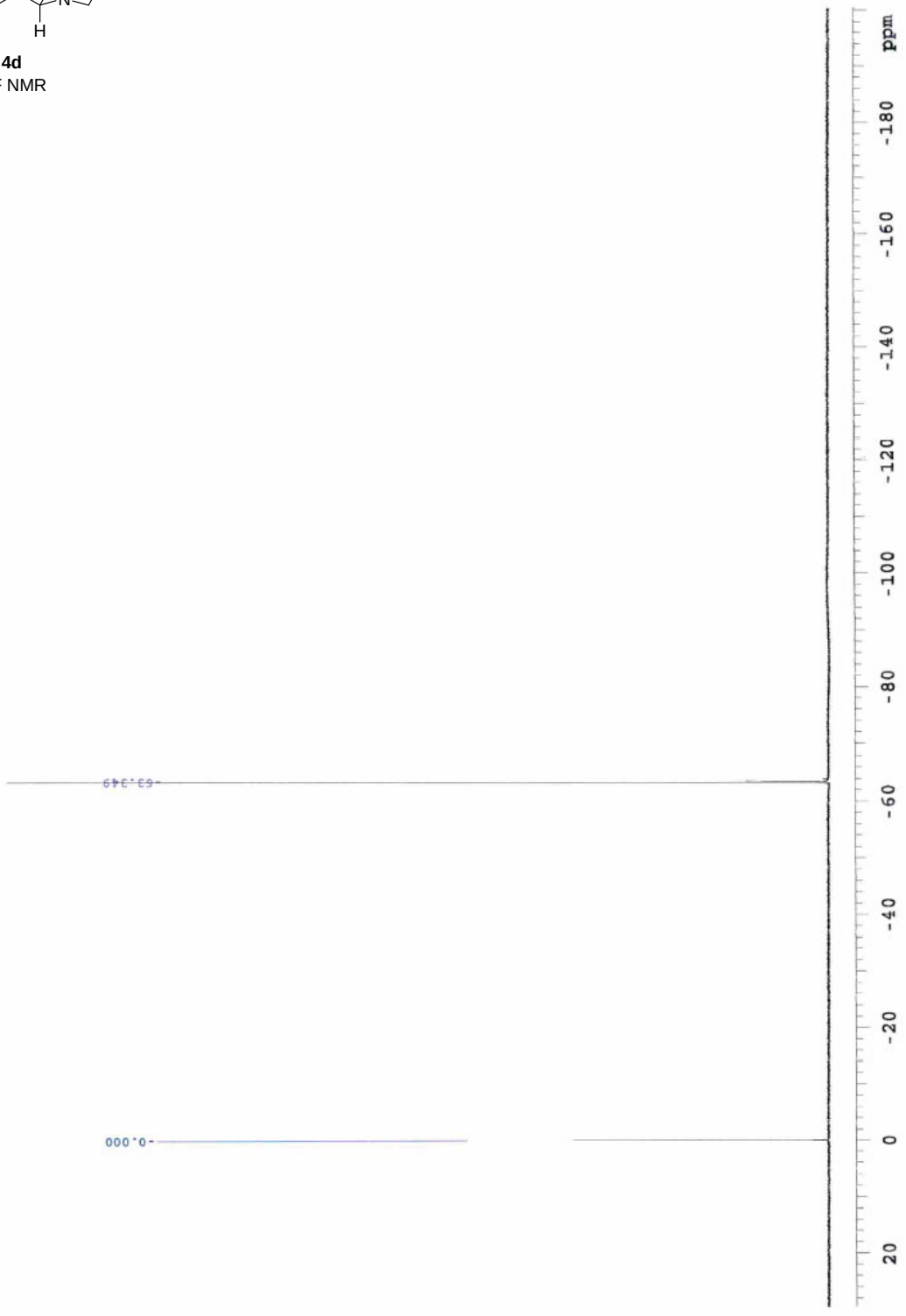
4d

^{1}H NMR




F3C
CF3
HO
O
N
N
H

4d
^{19}F NMR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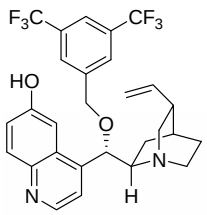
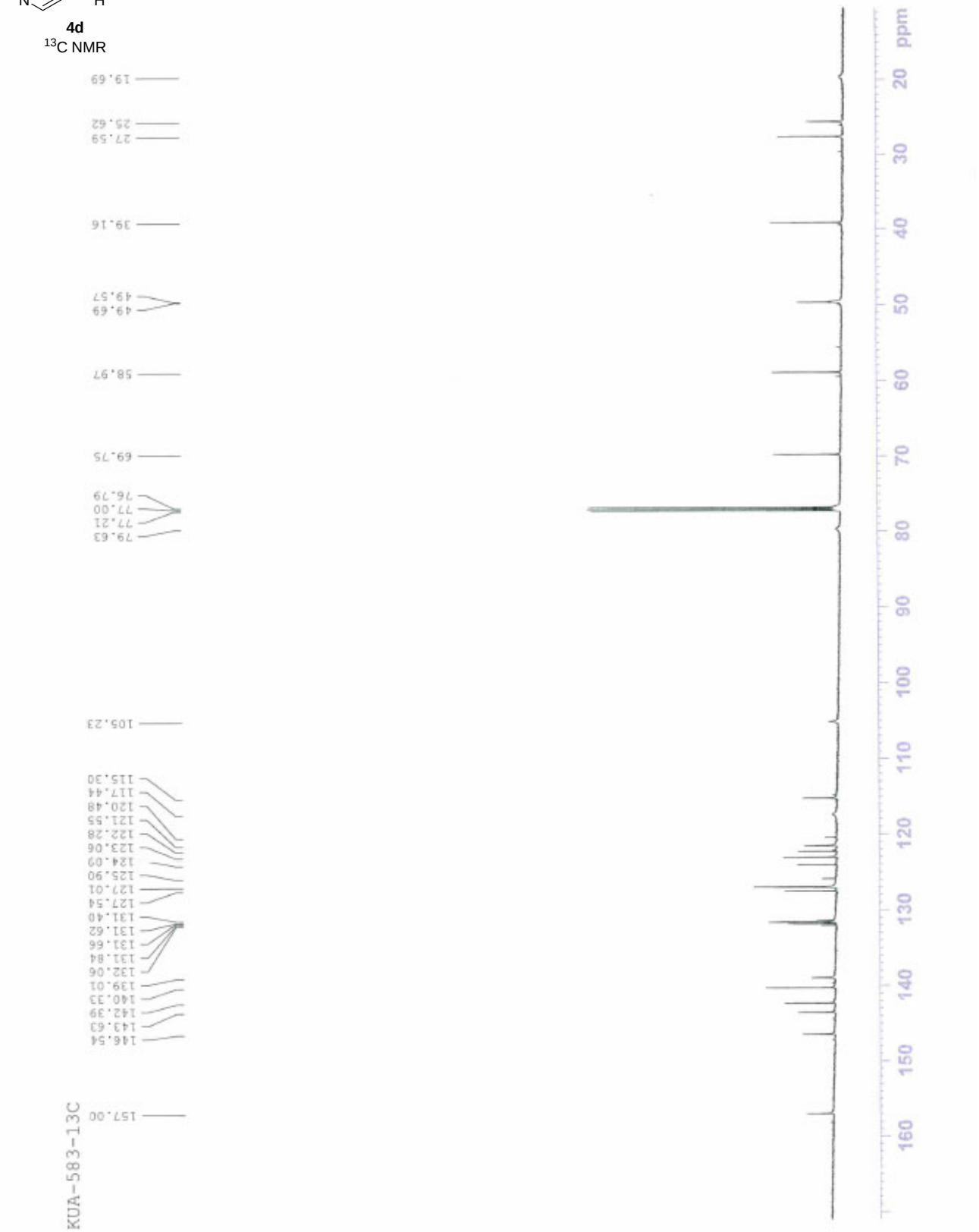
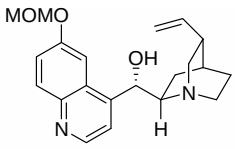
ppm
-180
-160
-140
-120
-100
-80
-60
-40
-20
0
20


F3C
CF3
HO
O
N
N
H

4d

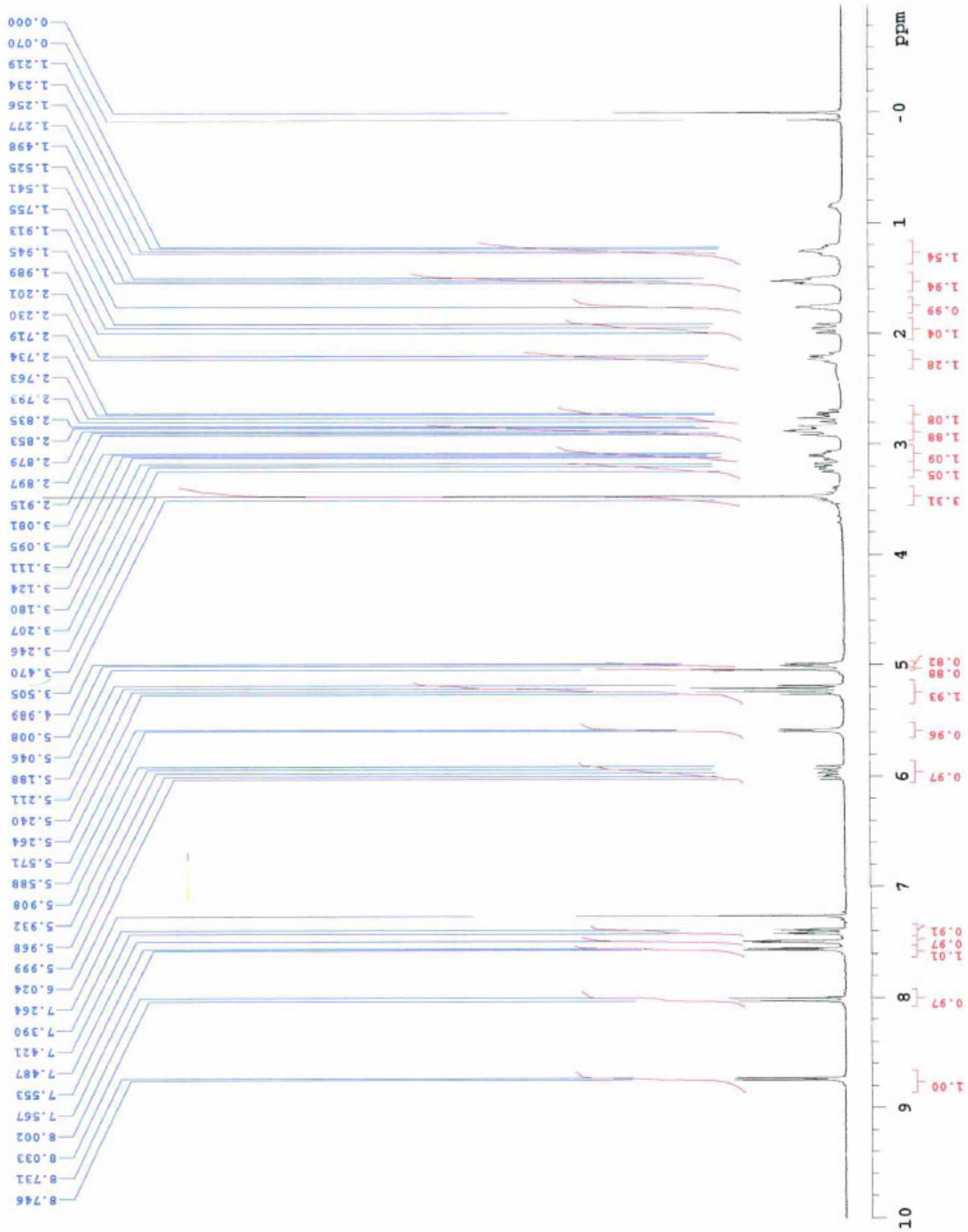
^{13}C NMR

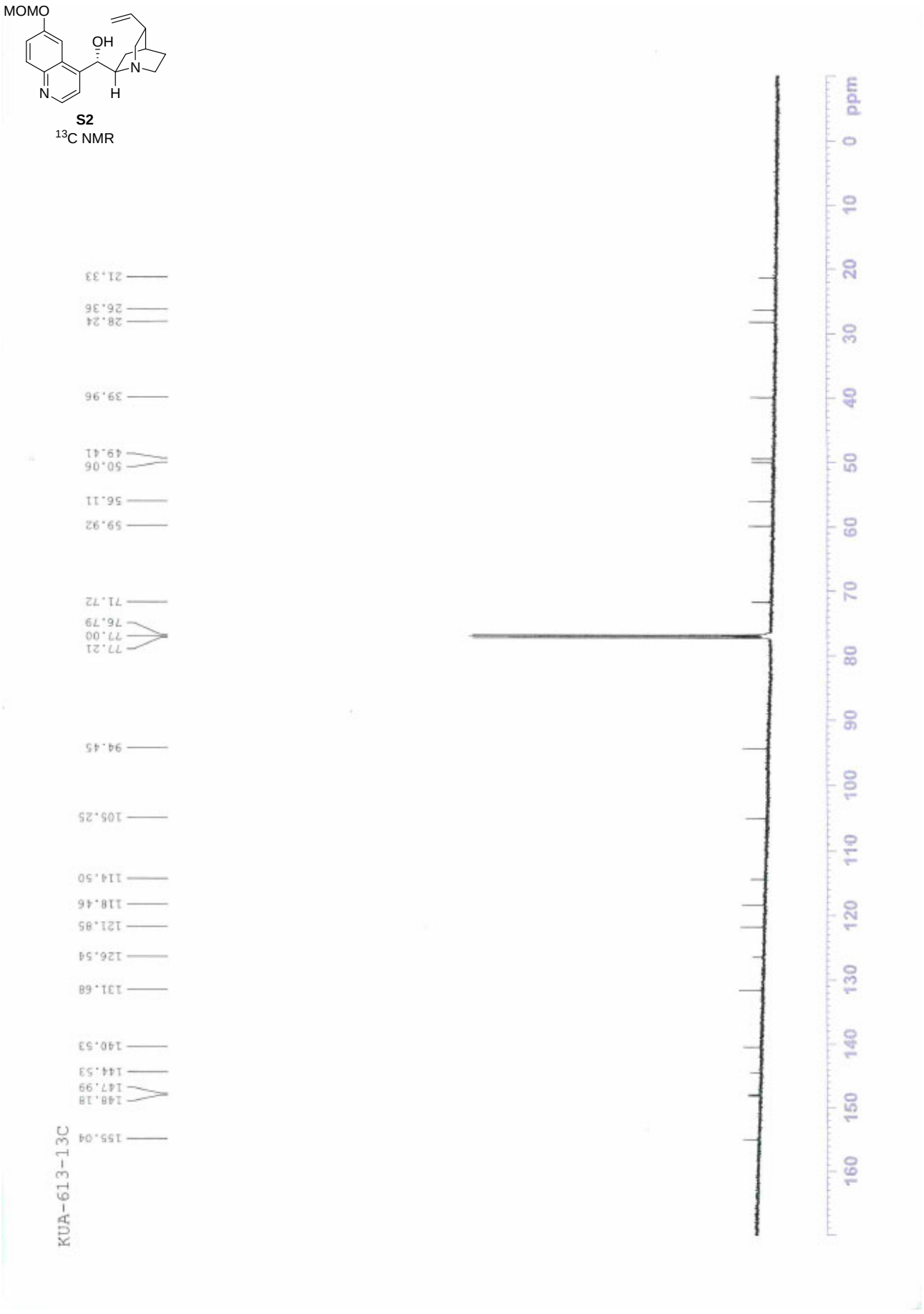

19.69
25.62
27.59
39.16
49.57
49.69
58.97
69.75
76.79
77.00
77.21
79.63
105.23
115.30
117.44
120.48
121.55
122.28
123.06
124.09
125.90
127.01
127.54
131.40
131.62
131.66
131.84
132.06
139.01
140.33
142.39
143.63
146.54
157.00
KUA-583-13C
ppm
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160



S2

^{1}H NMR




MOMO
OH
N
N
H
S2
13C NMR
21.33
26.36
28.24
39.96
49.41
50.06
56.11
59.92
71.72
76.79
77.00
77.21
94.45
105.25
114.50
118.46
121.85
126.54
131.68
140.53
144.53
147.99
148.18
155.04
KUA-613-13C
ppm
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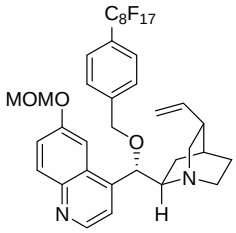
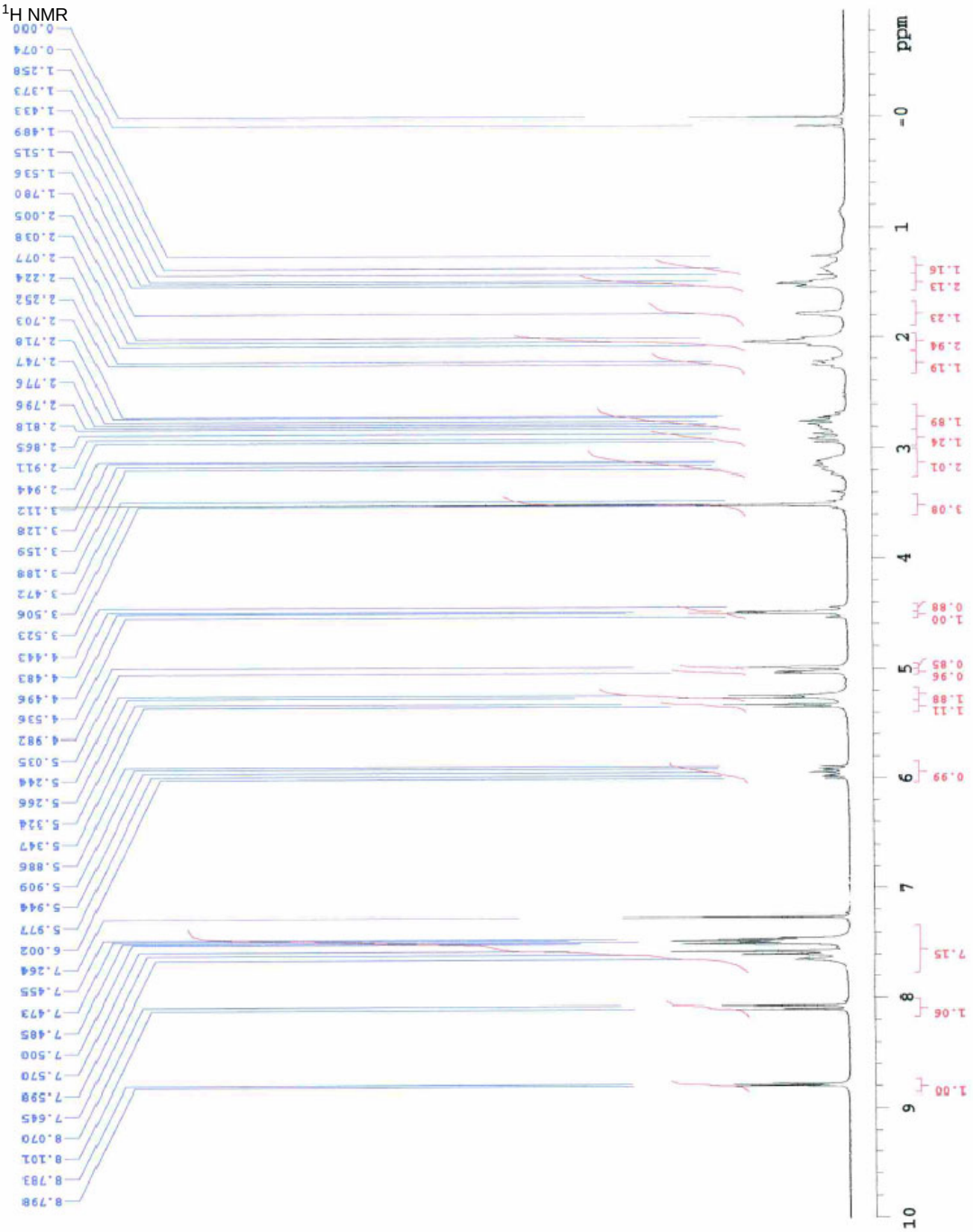
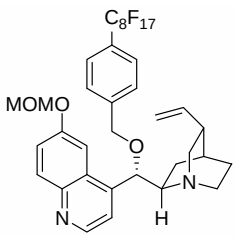
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160



S3

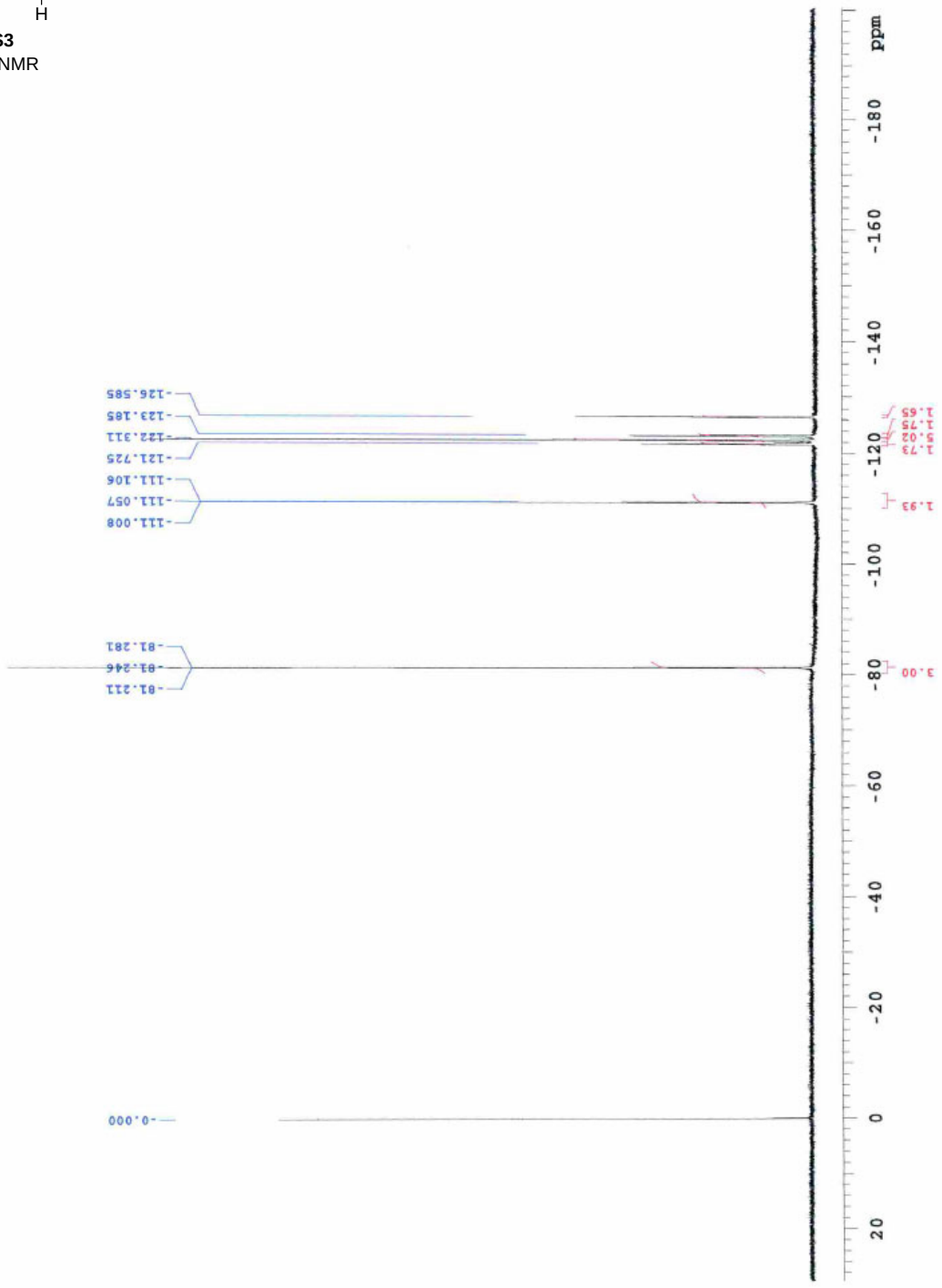
^{1}H NMR

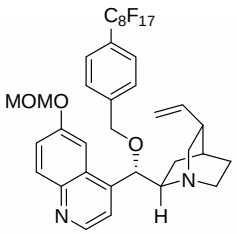



C8F17
MOMO
O
N
N
H

S3

^{19}F NMR

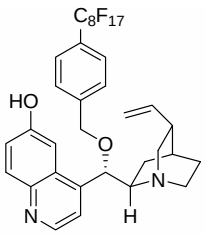

ppm
-180
-160
-140
-120
-100
-80
-60
-40
-20
0
20
-126.585
-123.185
-122.311
-121.725
-111.106
-111.057
-111.008
-81.281
-81.246
-81.211
-0.000
1.65
1.75
5.02
1.73
1.93
3.00


C8F17
MOMO
O
N
N
H

S3

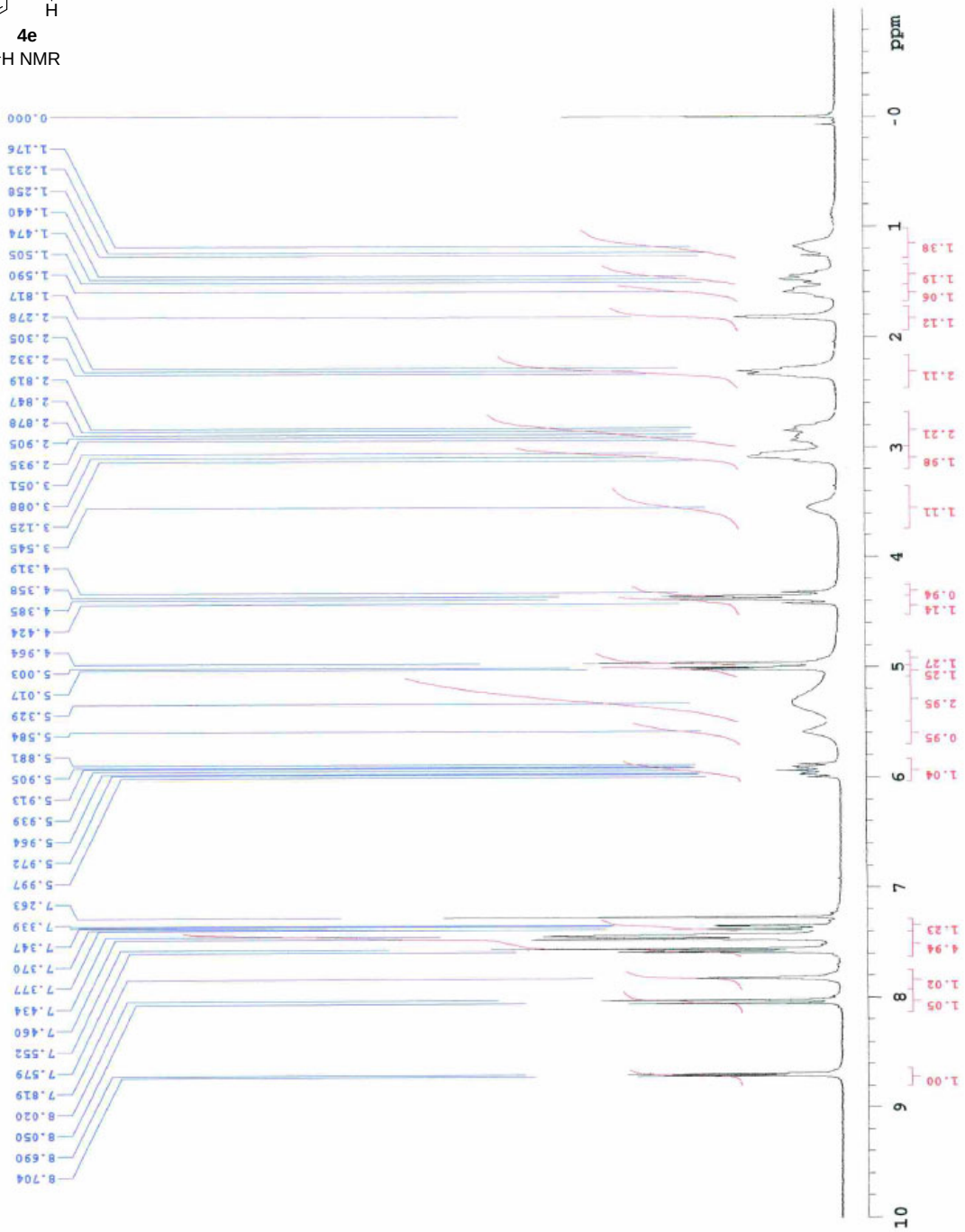
^{13}C NMR

22.38
26.35
27.98
39.75
49.27
49.95
56.10
60.25
70.44
76.79
77.00
77.21
80.88
94.57
105.39
114.41
118.77
122.14
126.84
126.89
126.93
127.37
127.60
128.02
128.18
128.34
131.91
140.32
142.18
144.77
144.98
148.12
155.29
KUA-616-13C
0 ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170


C8F17
HO
O
N
N
H

4e

^{1}H NMR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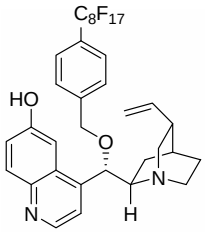
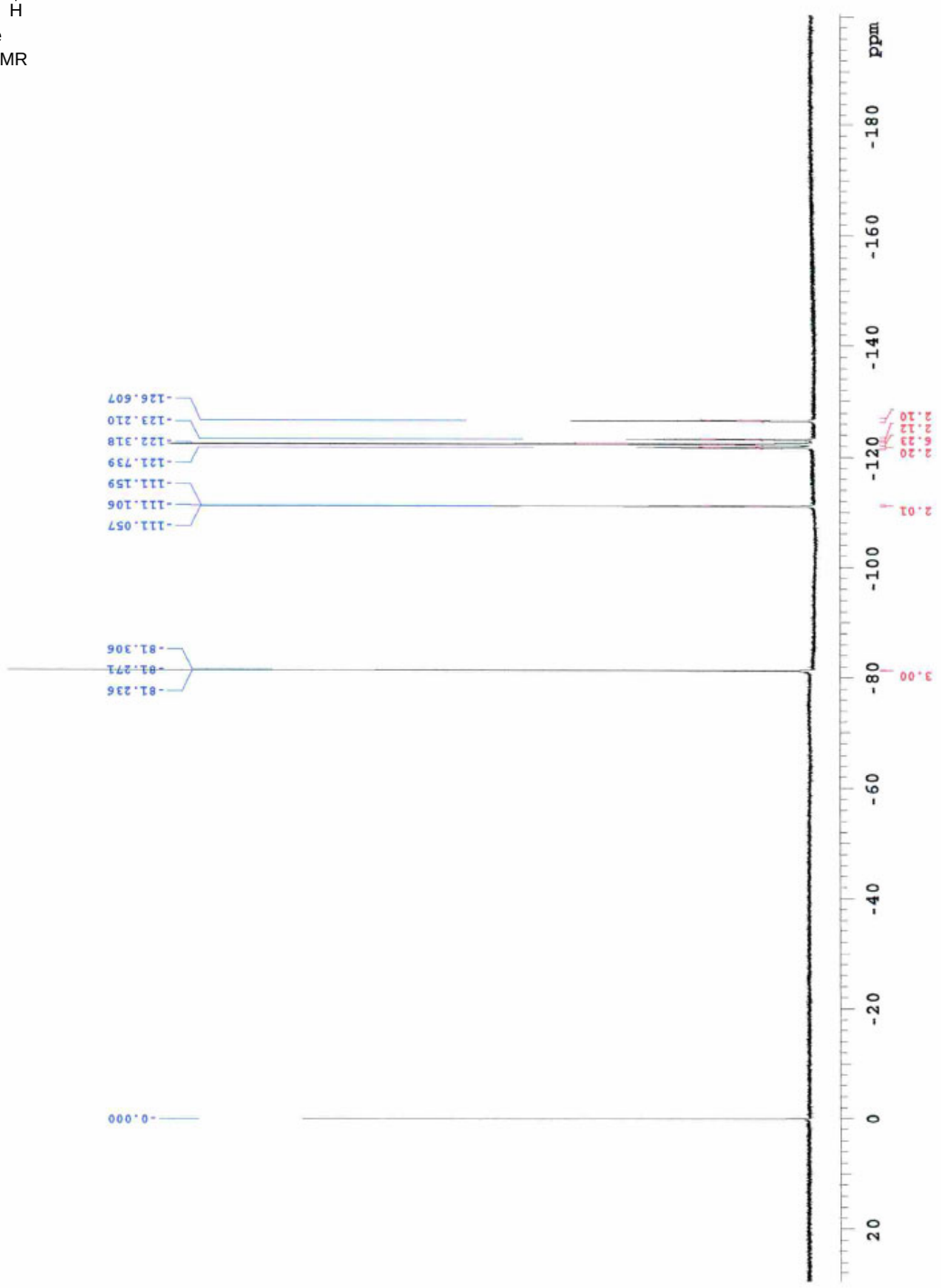
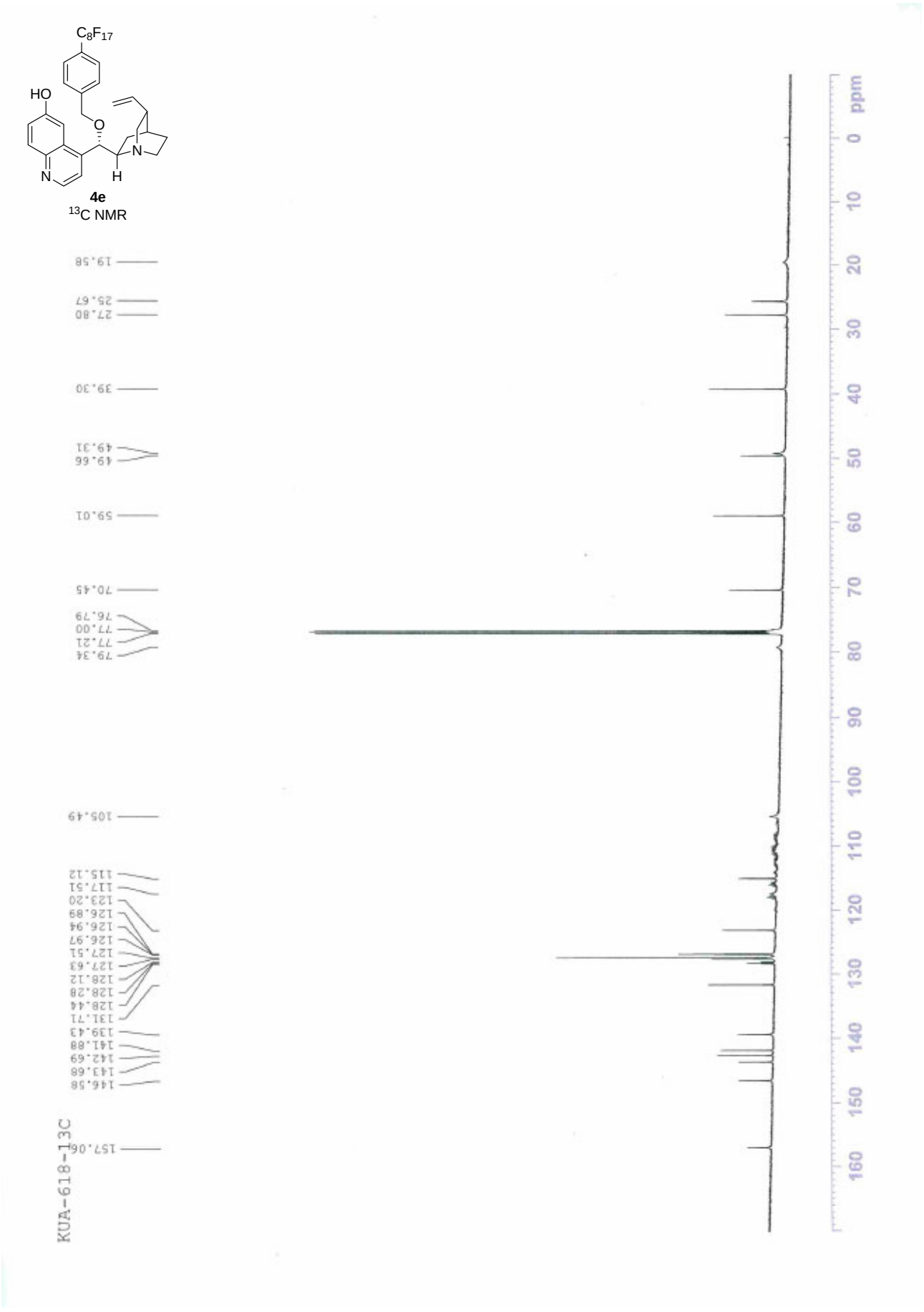
1.231
1.258
1.440
1.474
1.505
1.590
1.817
2.278
2.305
2.332
2.819
2.847
2.878
2.905
2.935
3.051
3.088
3.125
3.545
4.319
4.358
4.385
4.424
4.964
5.003
5.017
5.329
5.584
5.881
5.905
5.913
5.939
5.964
5.972
5.997
7.263
7.339
7.347
7.370
7.377
7.434
7.460
7.552
7.579
7.819
8.020
8.050
8.690
8.704
1.38
1.19
1.06
1.12
2.11
2.21
1.98
1.11
0.94
1.14
1.27
1.25
2.95
0.95
1.04
1.23
4.94
1.02
1.05
1.00

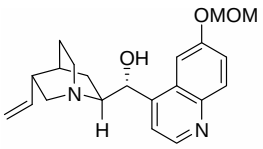


4e

^{19}F NMR

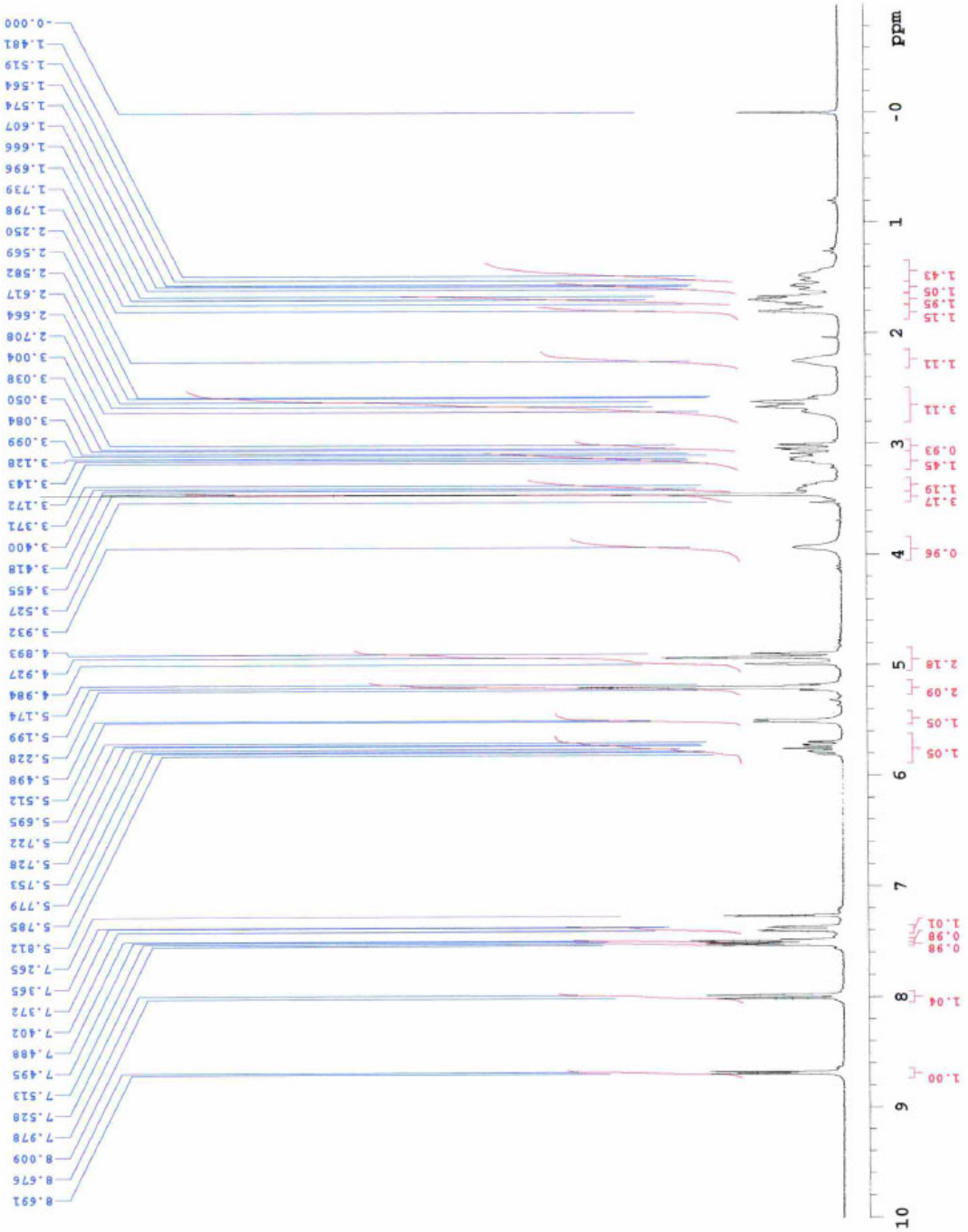


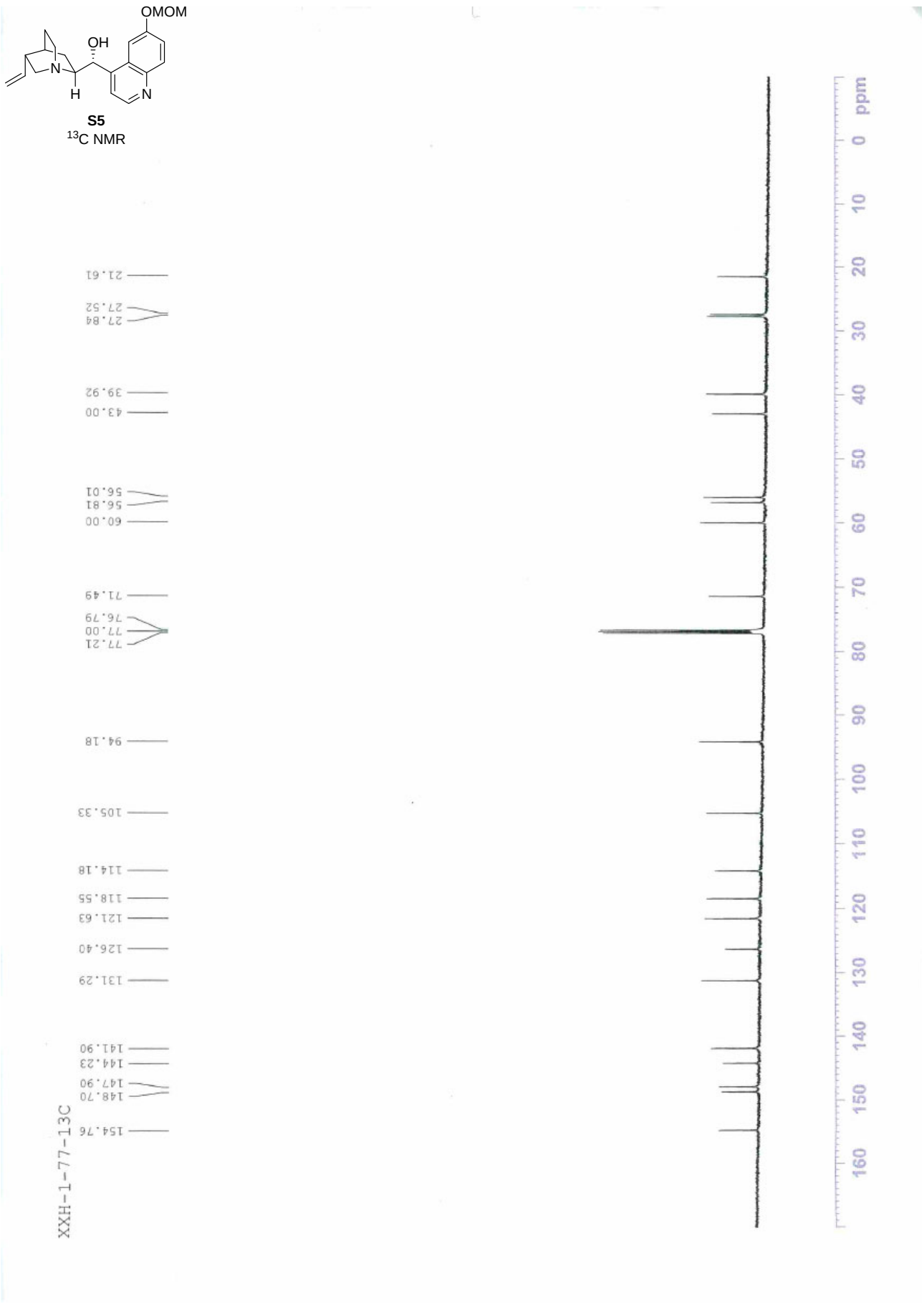

C8F17
HO
O
N
N
H
4e
13C NMR
19.58
25.67
27.80
39.30
49.31
49.66
59.01
70.45
76.79
77.00
77.21
79.34
105.49
115.12
117.51
123.20
126.89
126.94
126.97
127.51
127.63
128.12
128.28
128.44
131.71
139.43
141.88
142.69
143.68
146.58
157.06
KUA-618-13C
ppm
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160

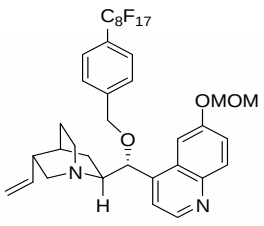


S5

^{1}H NMR

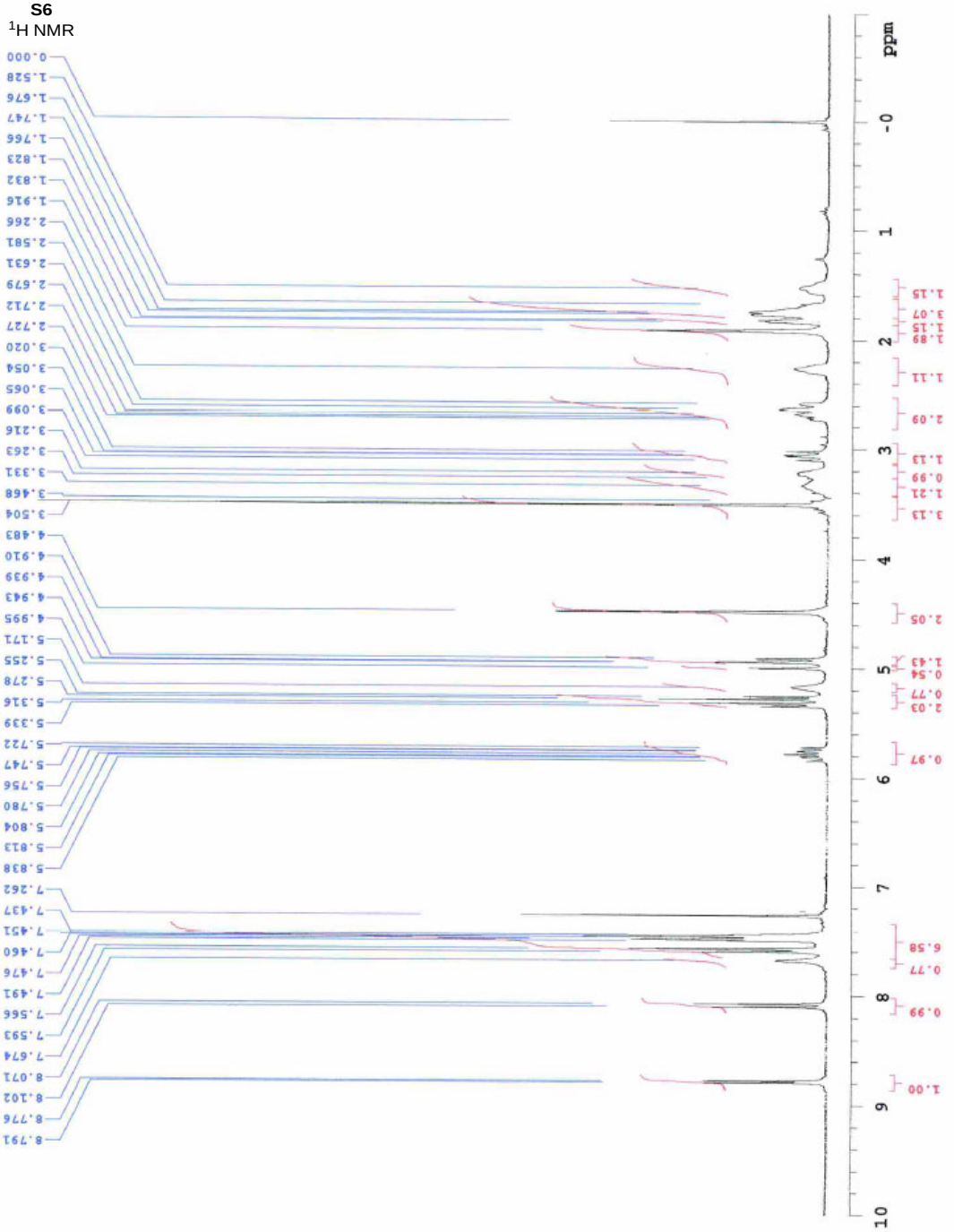


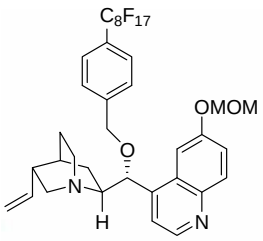

OMOM
OH
N
H
N
S5
13C NMR
21.61
27.52
27.84
39.92
43.00
56.01
56.81
60.00
71.49
76.79
77.00
77.21
94.18
105.33
114.18
118.55
121.63
126.40
131.29
141.90
144.23
147.90
148.70
154.76
XXH-1-77-13C
0 ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160



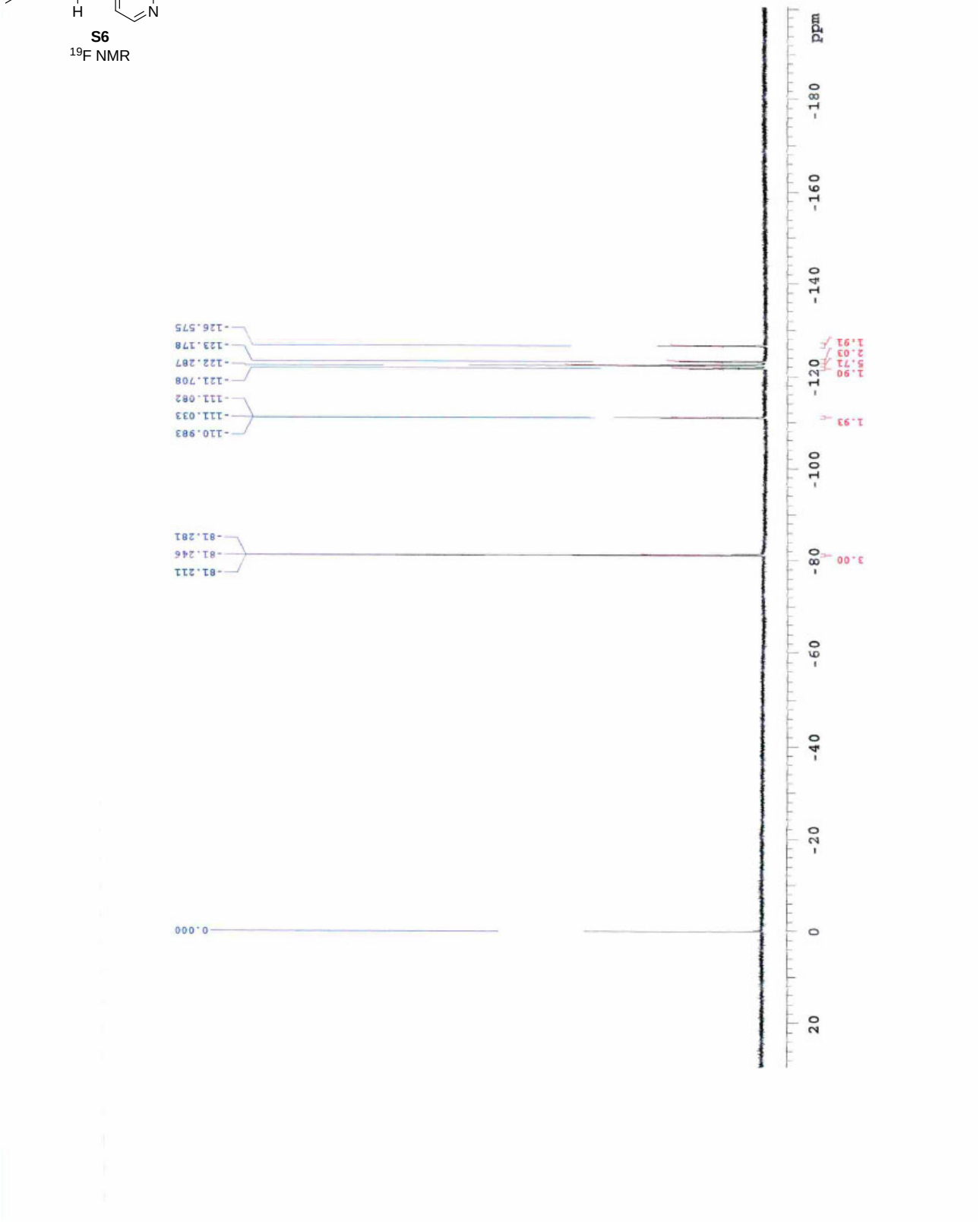
S6

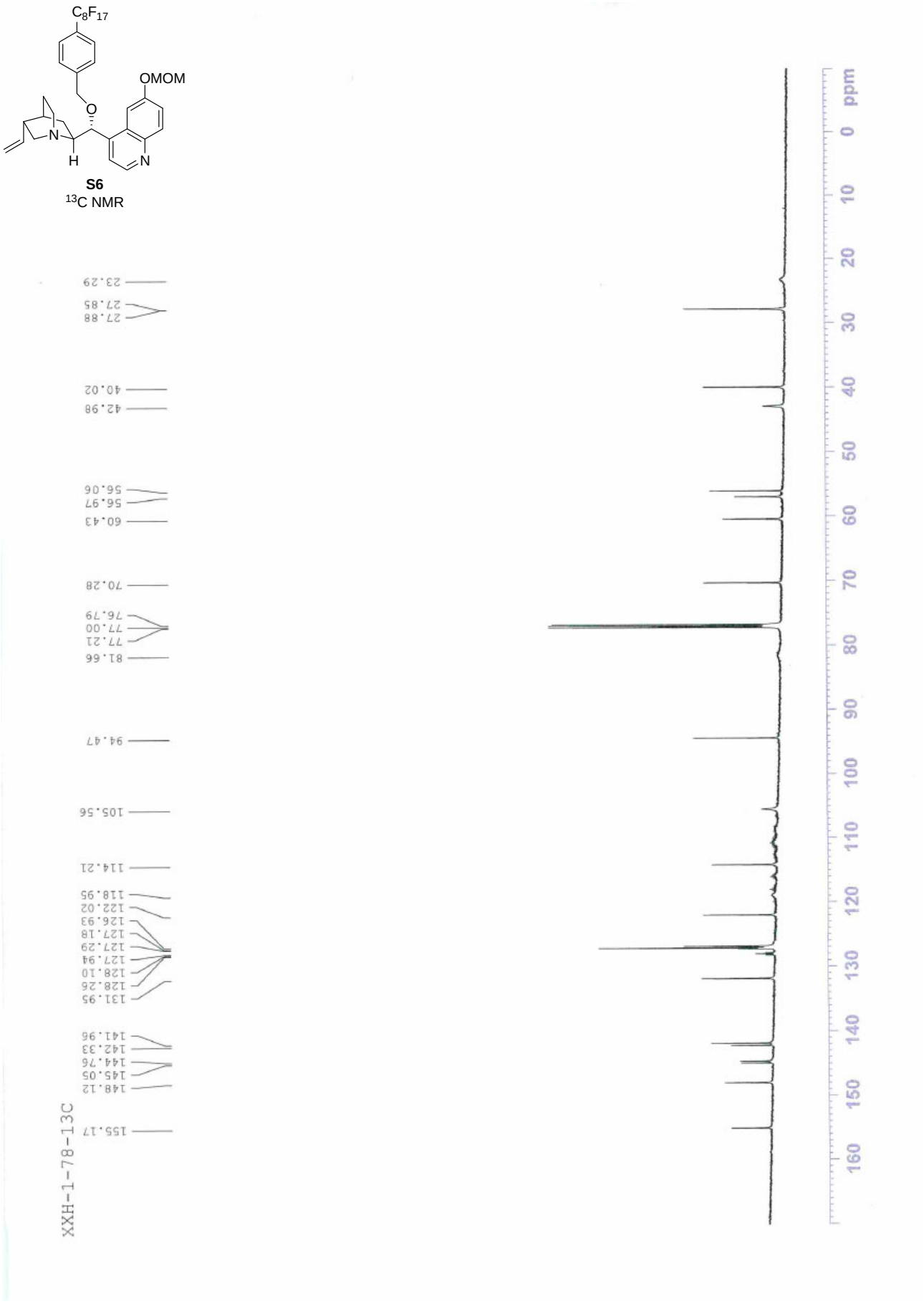
^{1}H NMR

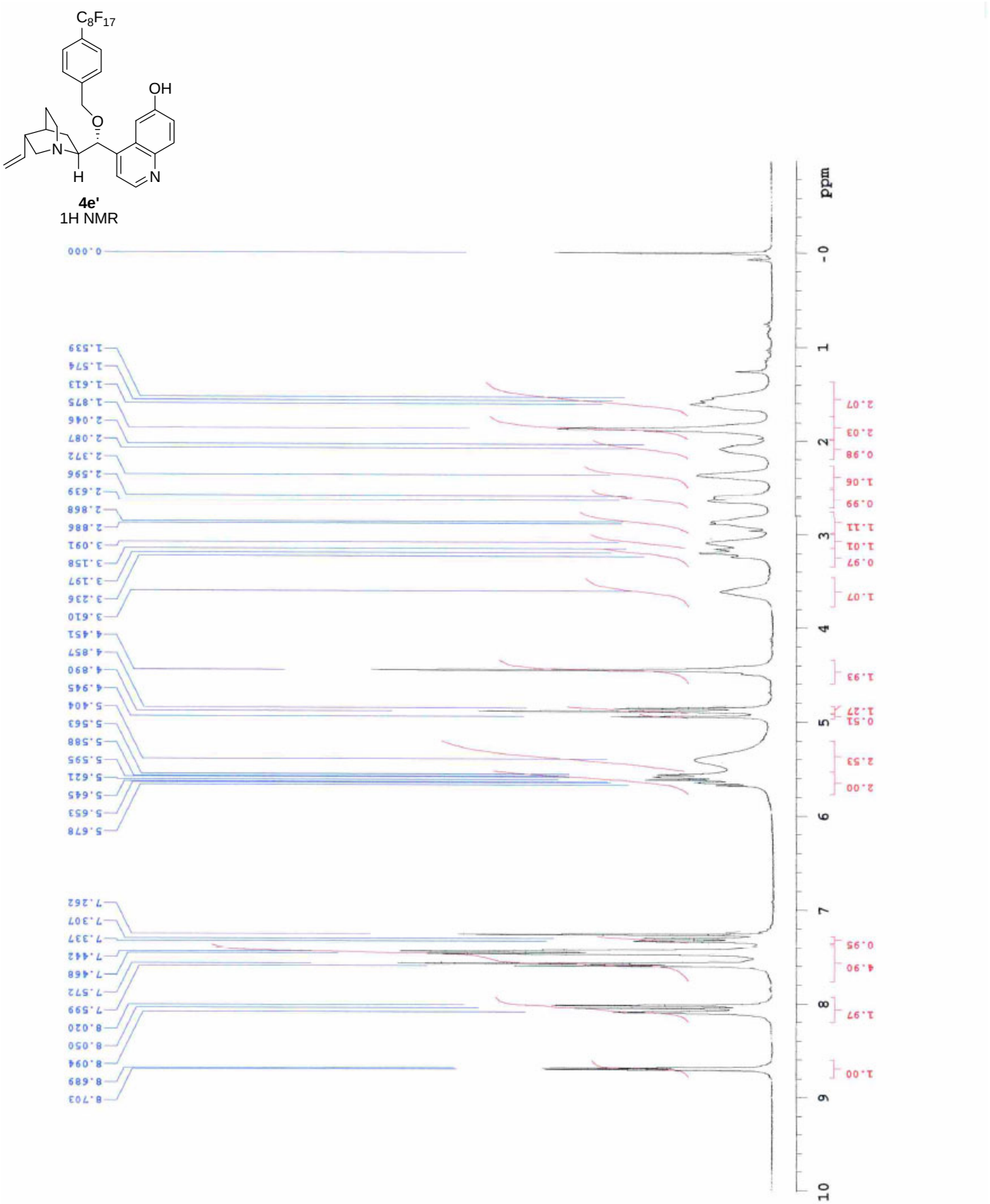


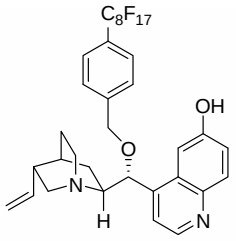

C8F17
OMOM
O
N
H
N

S6
^{19}F NMR


ppm
-180
-160
-140
-120
-100
-80
-60
-40
-20
0
20
-126.575
-123.178
-122.287
-121.708
-111.082
-111.033
-110.983
-81.281
-81.246
-81.211
0.000
1.91
2.03
5.71
1.90
1.93
3.00

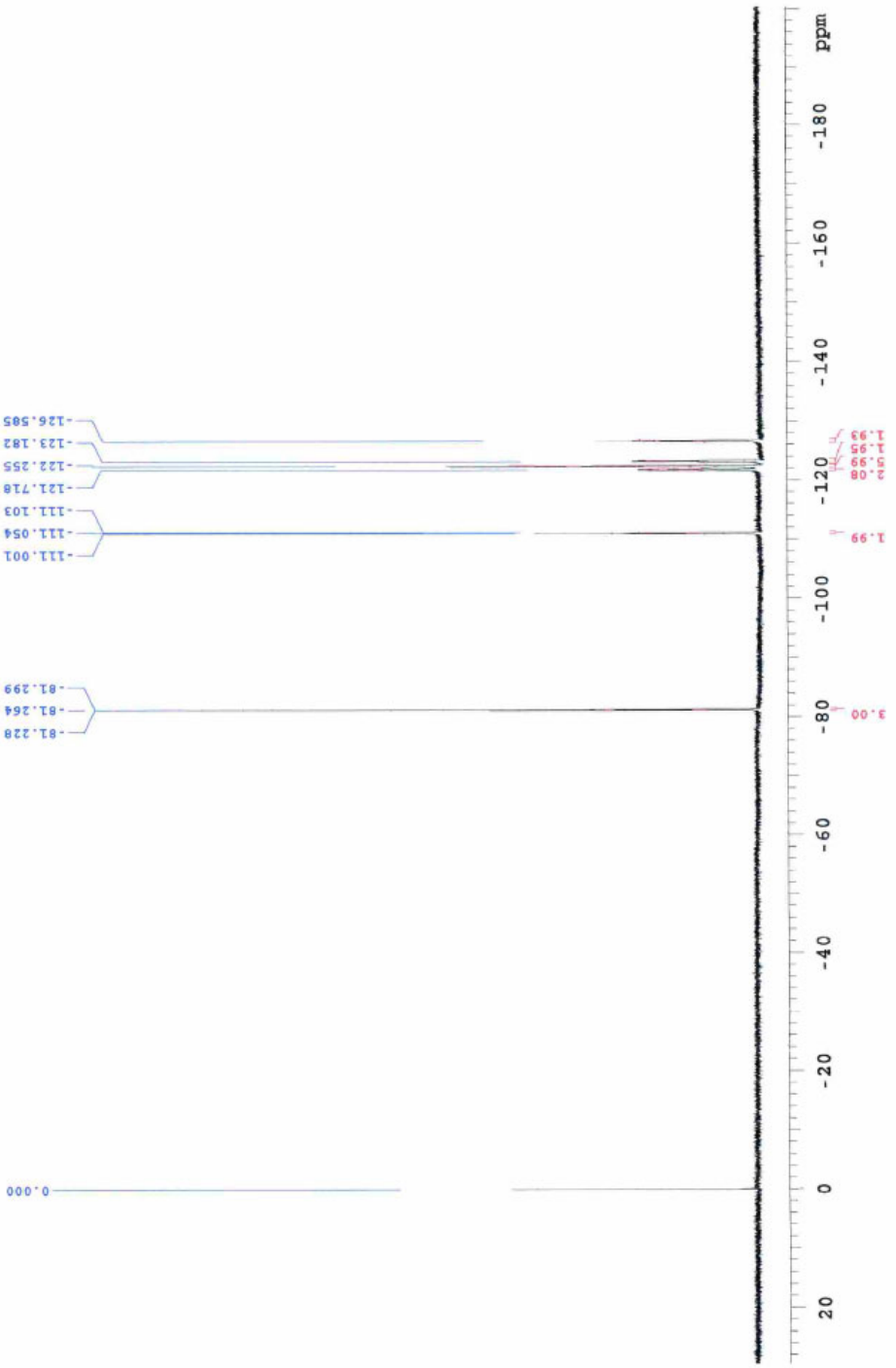

C8F17
OMOM
O
N
H
N
S6
13C NMR
23.29
27.85
27.88
40.02
42.98
56.06
56.97
60.43
70.28
76.79
77.00
77.21
81.66
94.47
105.56
114.21
118.95
122.02
126.93
127.18
127.29
127.94
128.10
128.26
131.95
141.96
142.33
144.76
145.05
148.12
155.17
XXH-1-78-13C
0 ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160

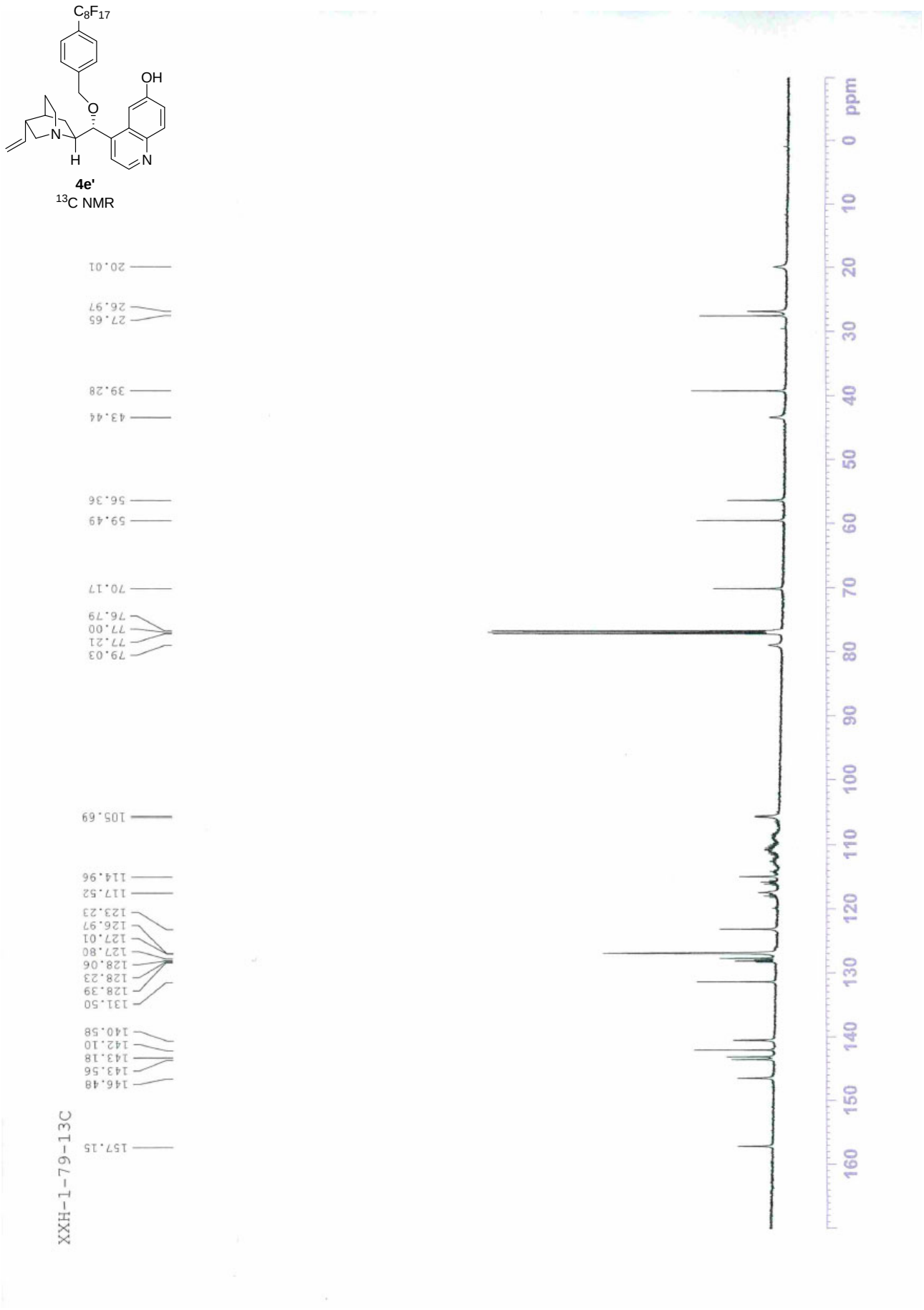

C8F17
OH
O
N
H
N
4e'
1H NMR
ppm

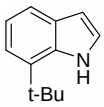

C_8F_{17}
OH
O
N
H
N

4e'

^{19}F NMR

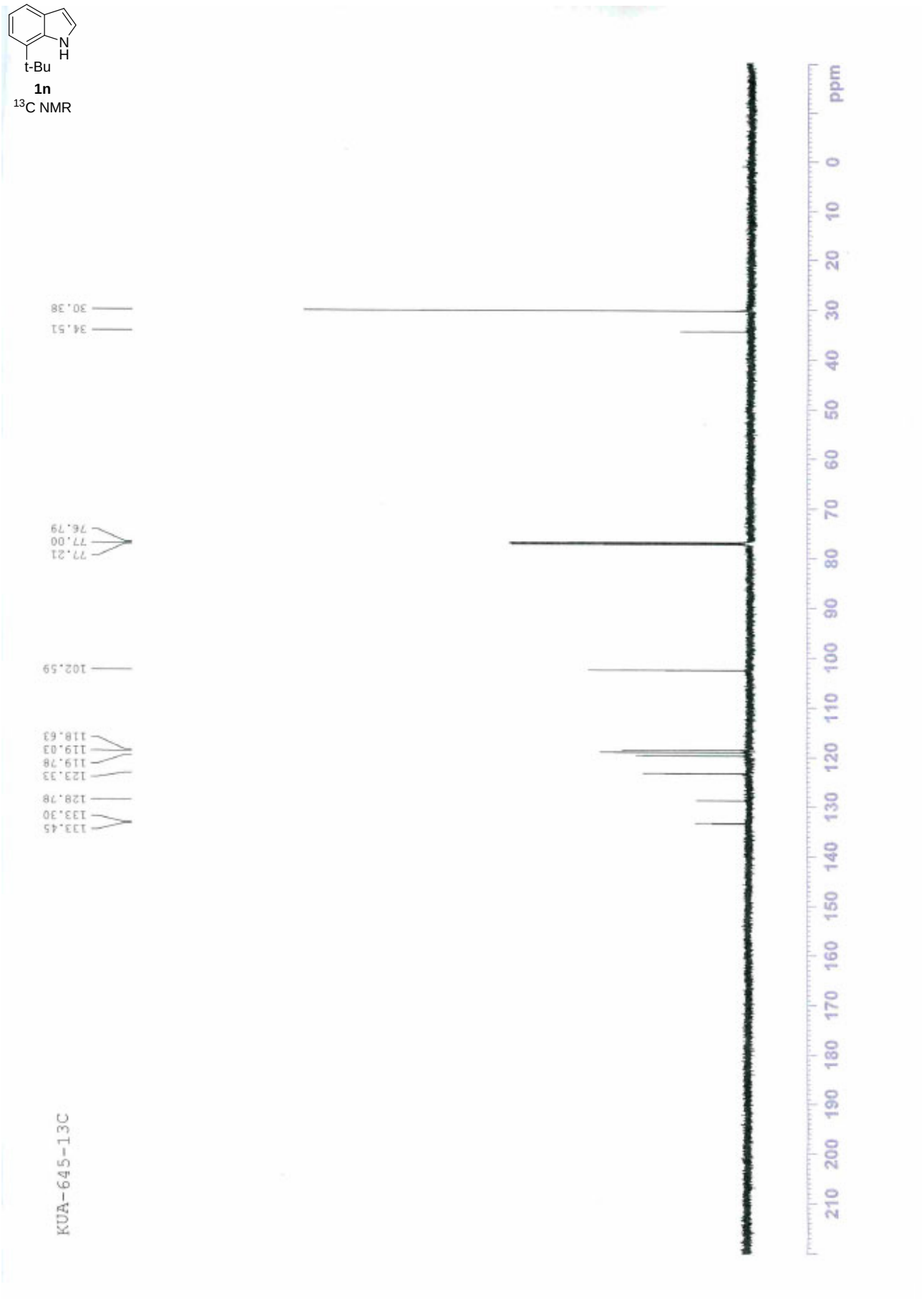

-126.585
-123.182
-122.255
-121.718
-111.103
-111.054
-111.001
-81.299
-81.264
-81.228
0.000
ppm
-180
-160
-140
-120
-100
-80
-60
-40
-20
0
20
1.93
1.95
5.99
2.08
1.99
3.00

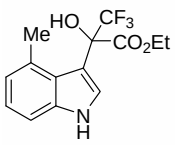

C8F17
OH
O
N
H
N
4e'
13C NMR
20.01
26.97
27.65
39.28
43.44
56.36
59.49
70.17
76.79
77.00
77.21
79.03
105.69
114.96
117.52
123.23
126.97
127.01
127.80
128.06
128.23
128.39
131.50
140.58
142.10
143.18
143.56
146.48
157.15
XXH-1-79-13C
ppm
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160



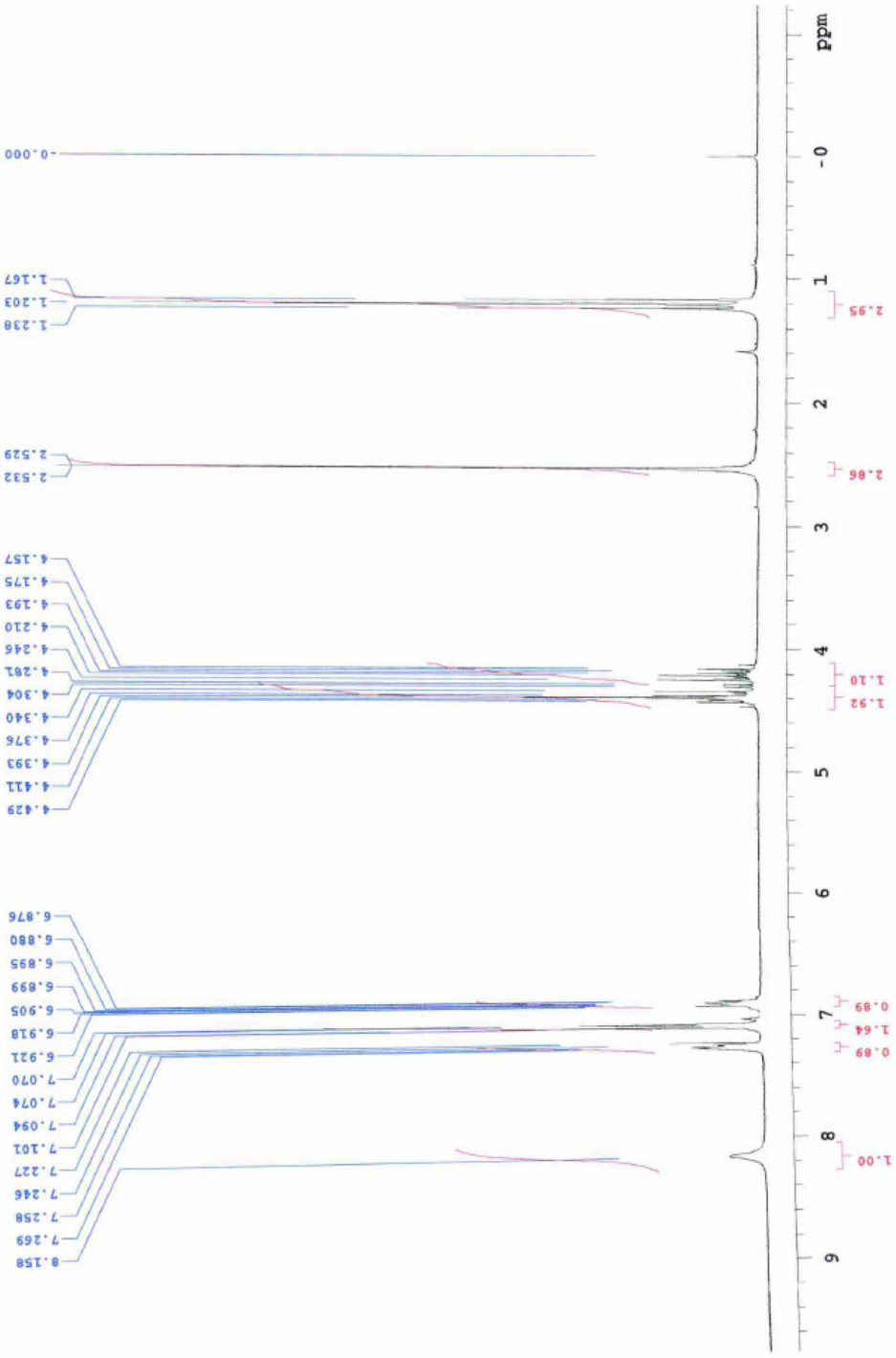
1n

^{1}H NMR


t-Bu
1n
13C NMR
30.38
34.51
76.79
77.00
77.21
102.59
118.63
119.03
119.78
123.33
128.78
133.30
133.45
KUA-645-13C
ppm
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210


Me
HO
CF3
CO2Et
N
H

2d
^{1}H NMR


ppm
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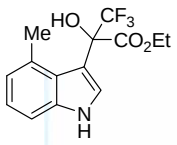
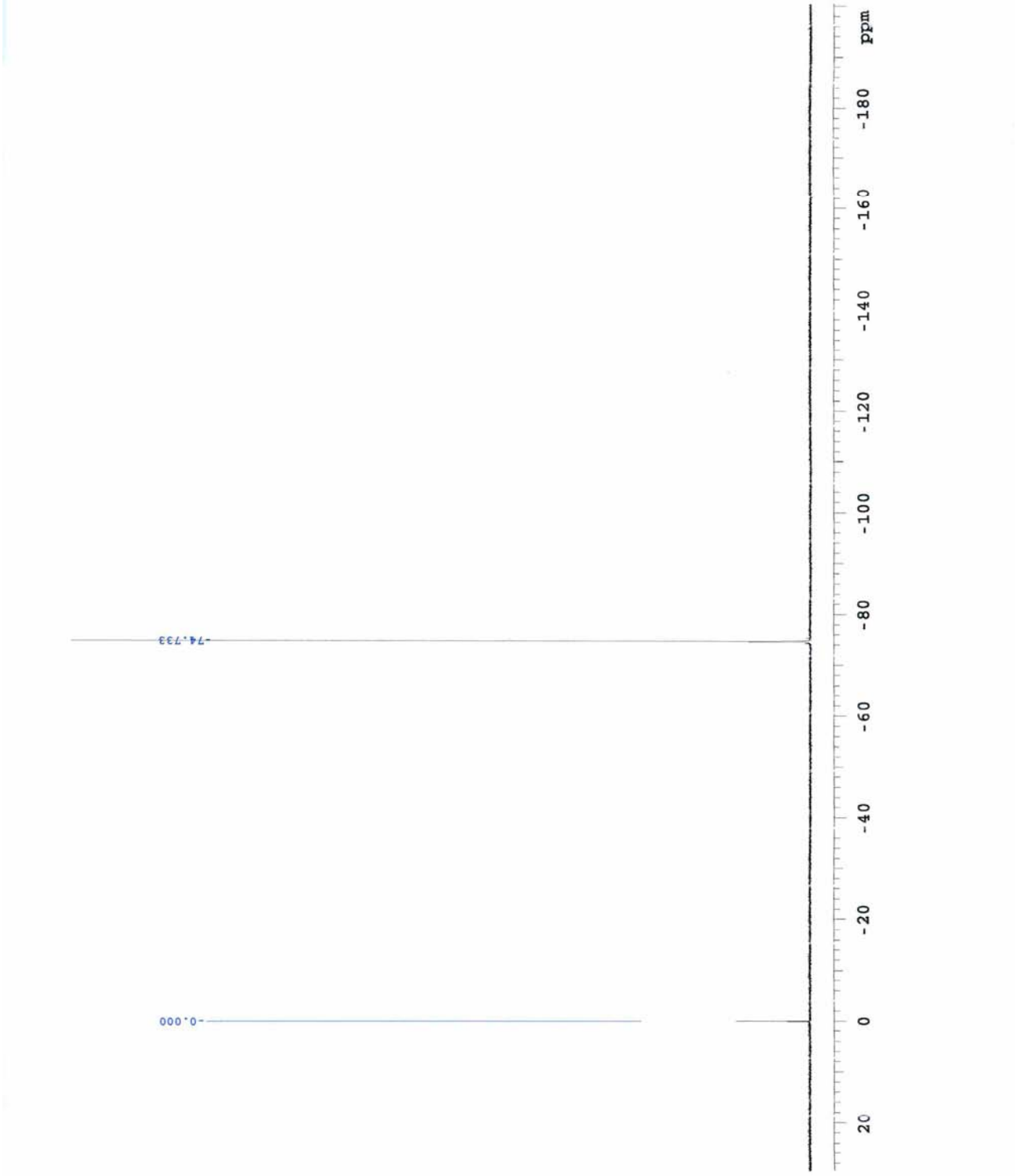
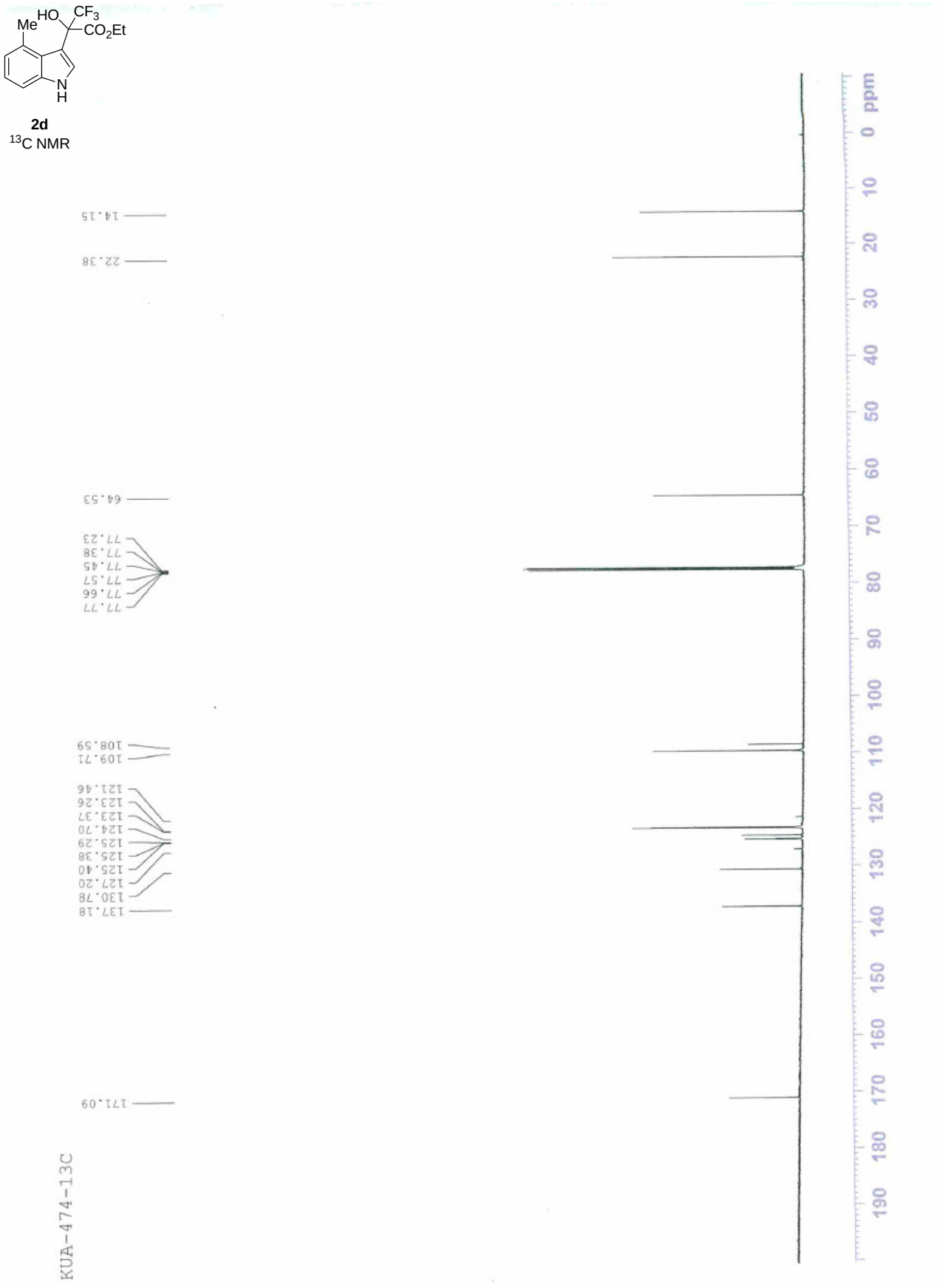
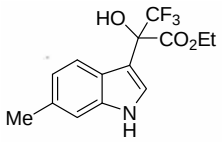
1.167
1.203
1.238
2.529
2.532
4.157
4.175
4.193
4.210
4.246
4.281
4.304
4.340
4.376
4.393
4.411
4.429
6.876
6.880
6.895
6.899
6.905
6.918
6.921
7.070
7.074
7.094
7.101
7.227
7.246
7.258
7.269
8.158
2.95
2.86
1.10
1.92
0.89
1.64
0.89
1.00


Me
HO
CF3
CO2Et
N
H

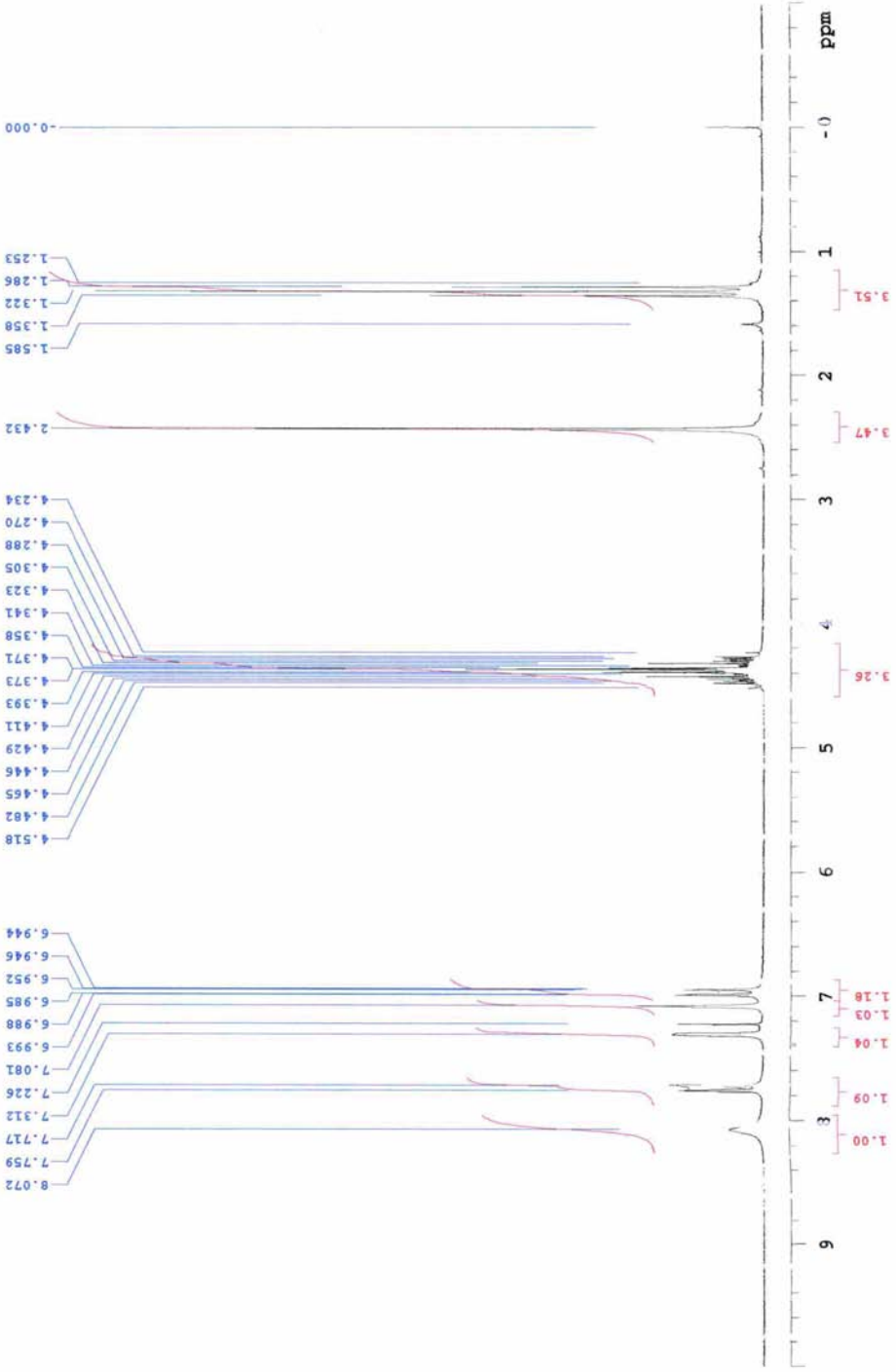
2d
^{19}F NMR


-74.733
-0.000
ppm
-180
-160
-140
-120
-100
-80
-60
-40
-20
0
20


Me
HO
CF3
CO2Et
N
H
2d
13C NMR
14.15
22.38
64.53
77.23
77.38
77.45
77.57
77.66
77.77
108.59
109.71
121.46
123.26
123.37
124.70
125.29
125.38
125.40
127.20
130.78
137.18
171.09
KUA-474-13C
0 ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190


HO
CF3
CO2Et
Me
N
H

2k
^{1}H NMR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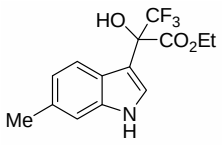
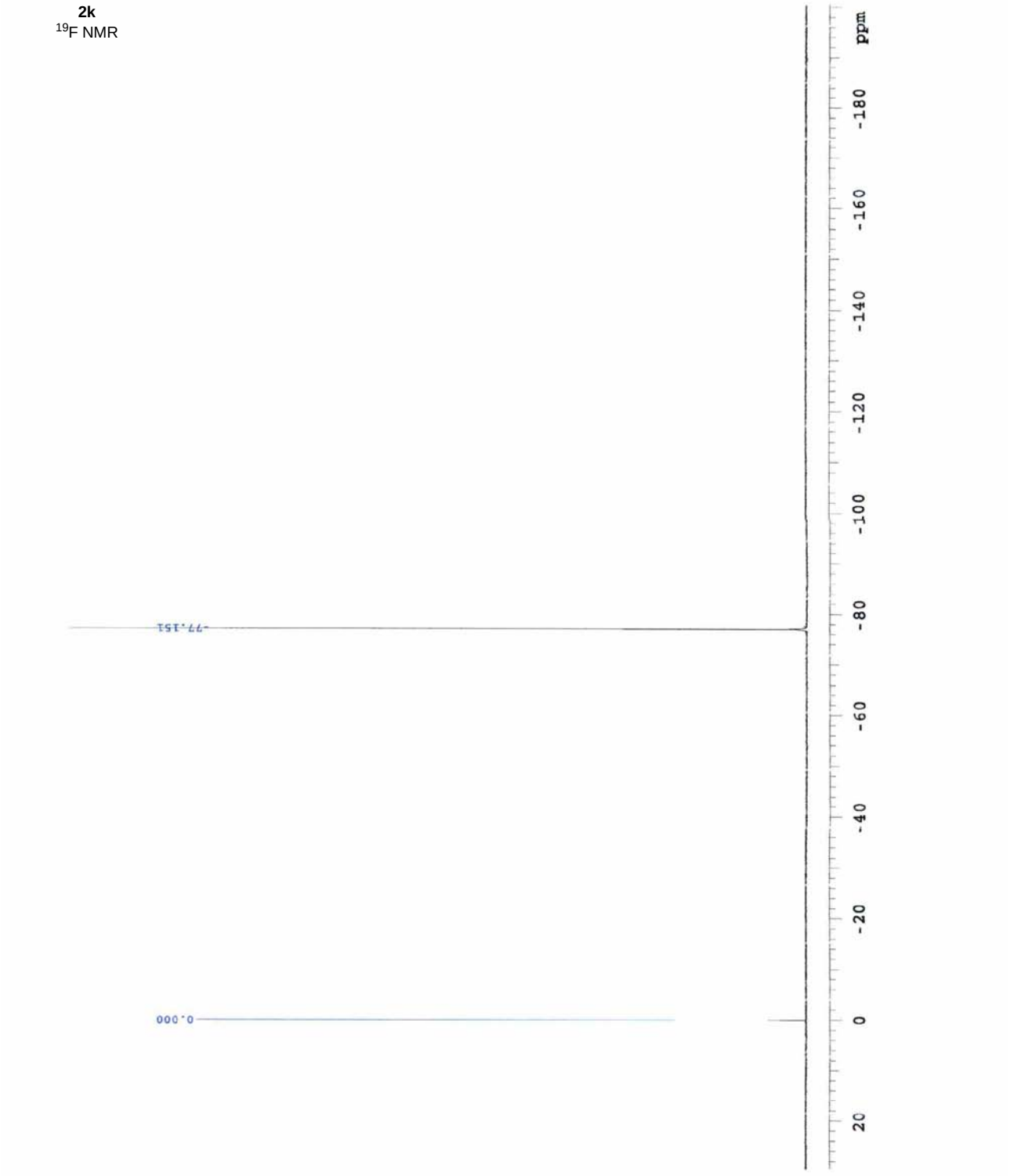
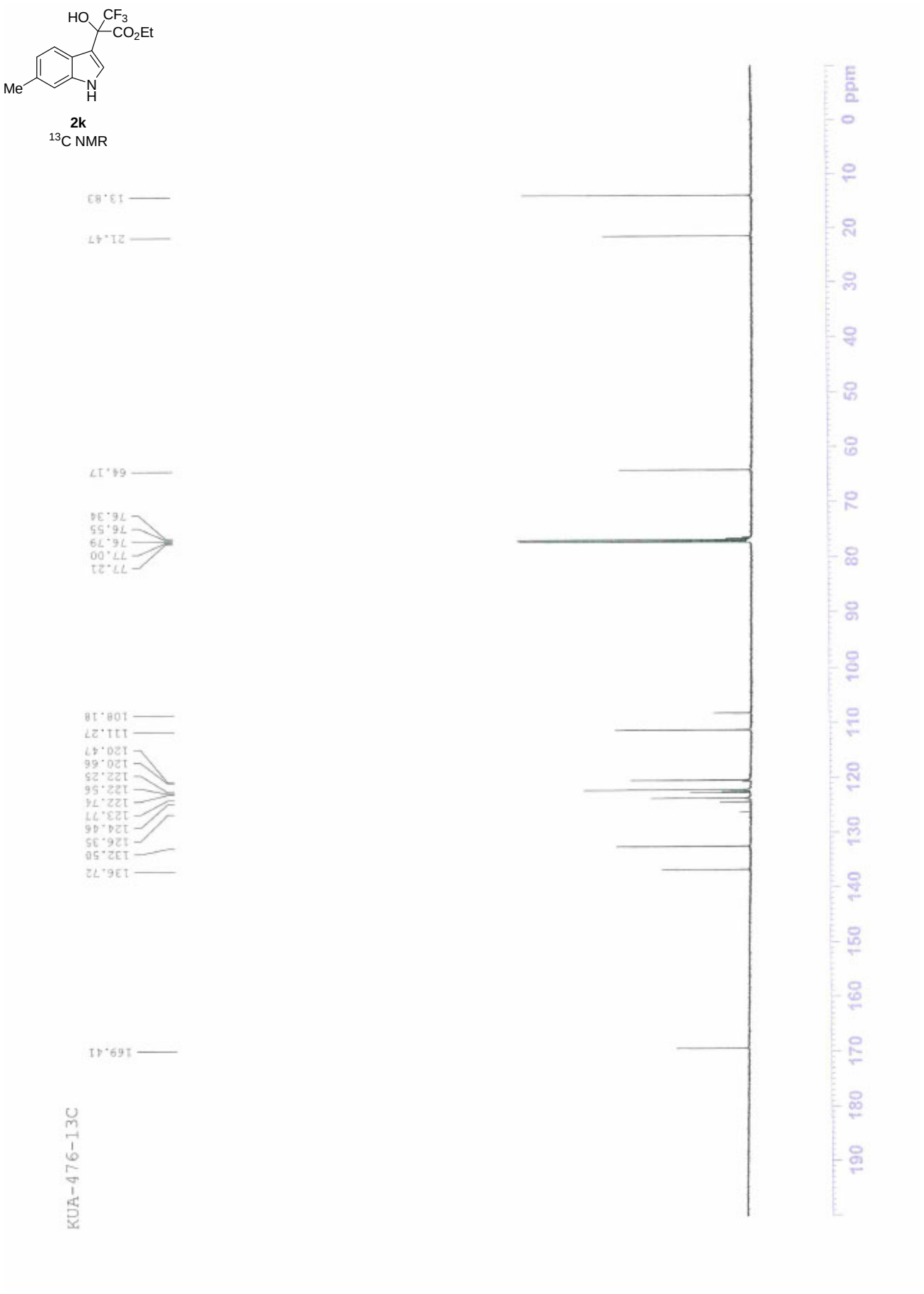
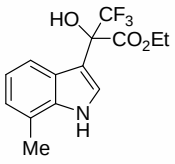
1.286
1.322
1.358
1.585
2.432
4.234
4.270
4.288
4.305
4.323
4.341
4.358
4.371
4.373
4.393
4.411
4.429
4.446
4.465
4.482
4.518
6.944
6.946
6.952
6.985
6.988
6.993
7.081
7.226
7.312
7.717
7.759
8.072
3.51
3.47
3.26
1.18
1.03
1.04
1.09
1.00


HO
CF3
CO2Et
Me
N
H

2k
^{19}F NMR

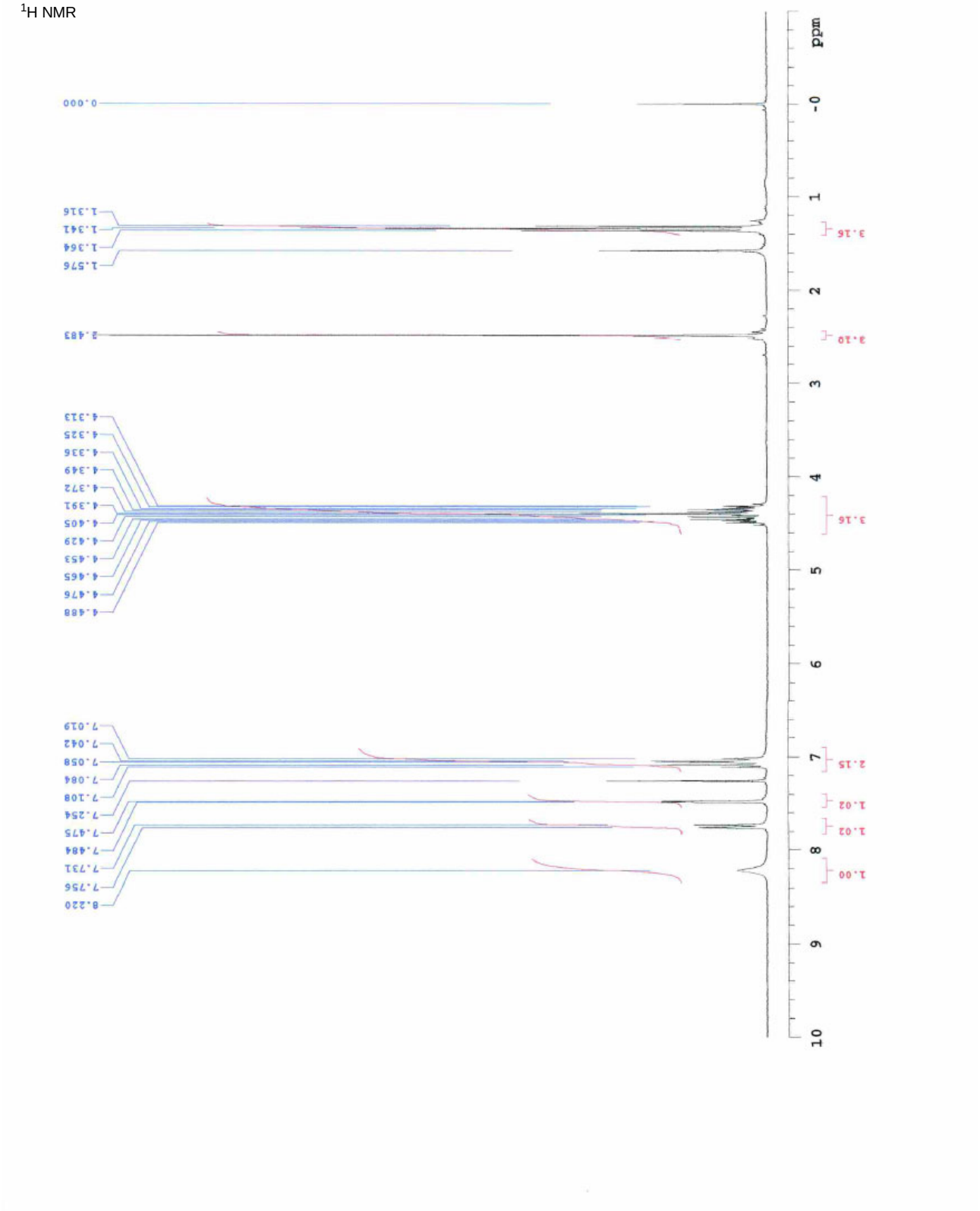

-77.151
0.000
ppm
-180
-160
-140
-120
-100
-80
-60
-40
-20
0
20


HO
CF3
CO2Et
Me
N
H
2k
13C NMR
13.83
21.47
64.17
76.34
76.55
76.79
77.00
77.21
108.18
111.27
120.47
120.66
122.25
122.56
122.74
123.37
124.46
126.35
132.50
136.72
169.41
KUA-476-13C
0 ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190


HO
CF3
CO2Et
N
H
Me

2l

^{1}H NMR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1.576
2.483
4.313
4.325
4.336
4.349
4.372
4.391
4.405
4.429
4.453
4.465
4.476
4.488
7.019
7.042
7.058
7.084
7.108
7.254
7.475
7.484
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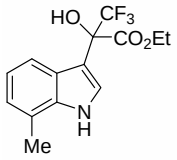
7.756
8.220
ppm
3.16
3.19
3.16
2.15
1.02
1.02
1.00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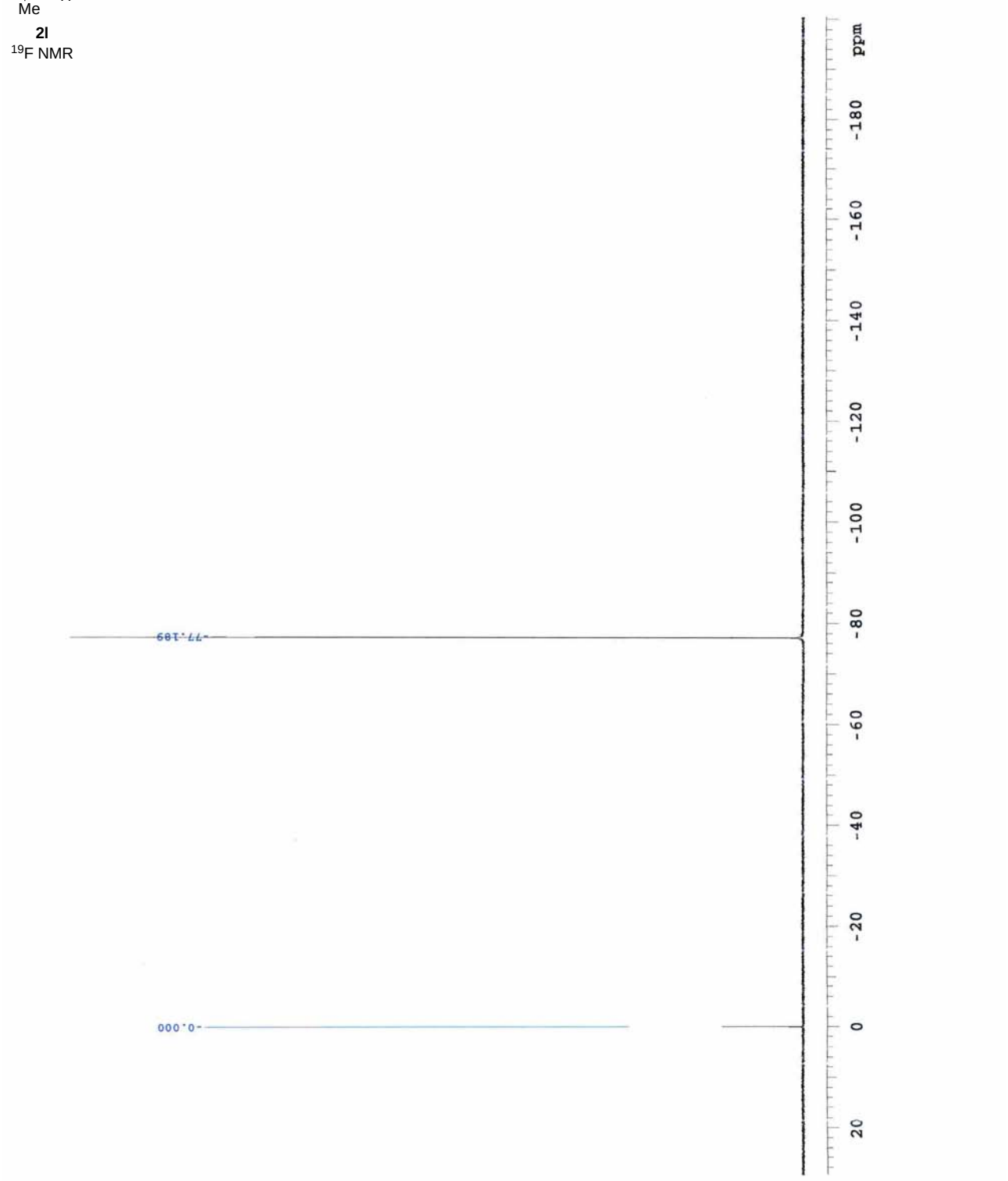
CF3
CO2Et
N
H
Me

2l

^{19}F NMR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-100
-80
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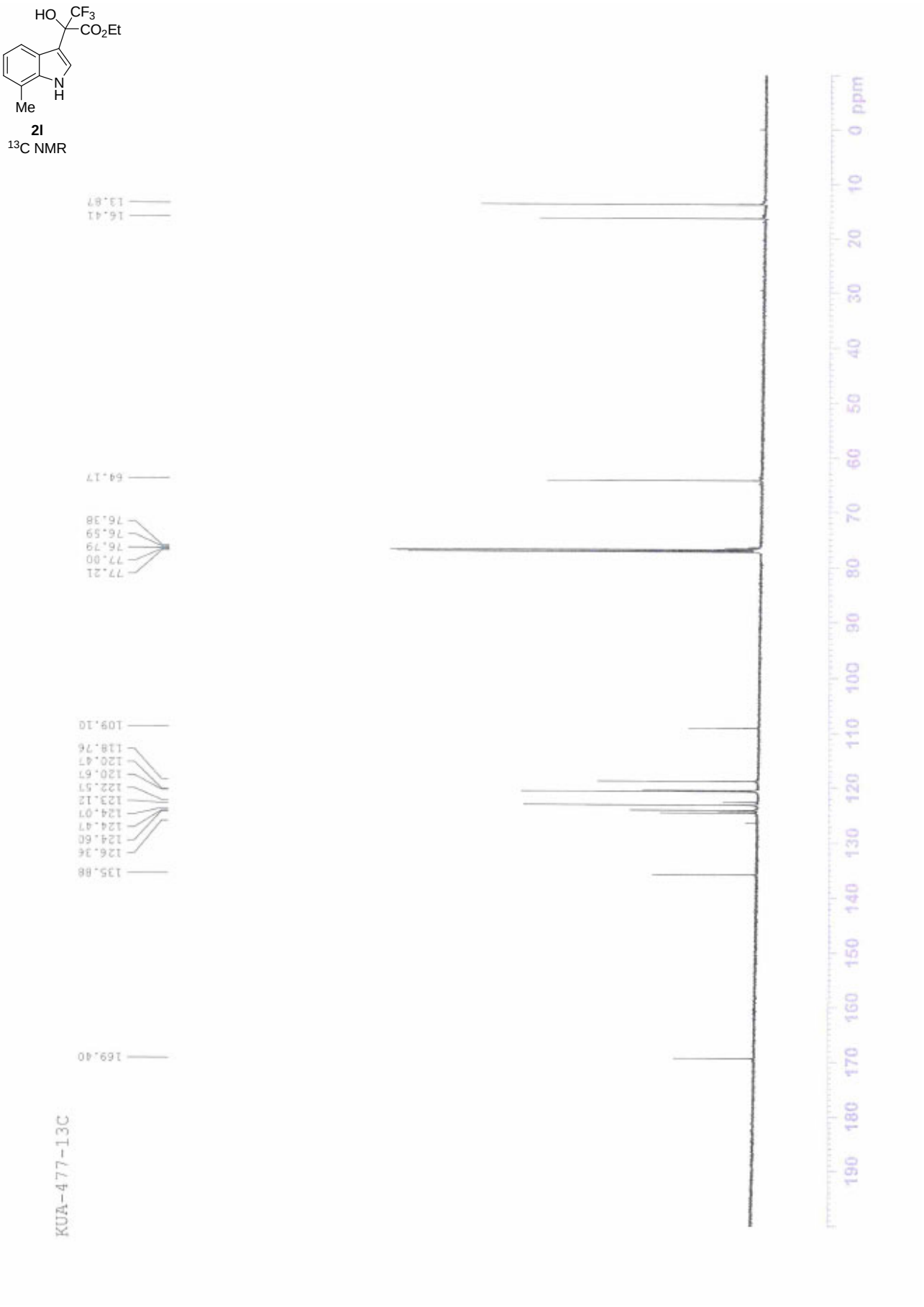
20


HO
CF3
CO2Et
N
H
Me
2l
13C NMR
13.87
16.41
64.17
76.38
76.59
76.79
77.00
77.21
109.10
118.76
120.47
120.67
122.57
123.12
124.07
124.47
124.60
126.36
135.88
169.40
KUA-477-13C
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40
50
60
70
80
90
100
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120
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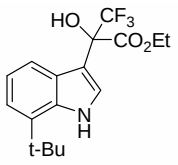
150
160
170
180
190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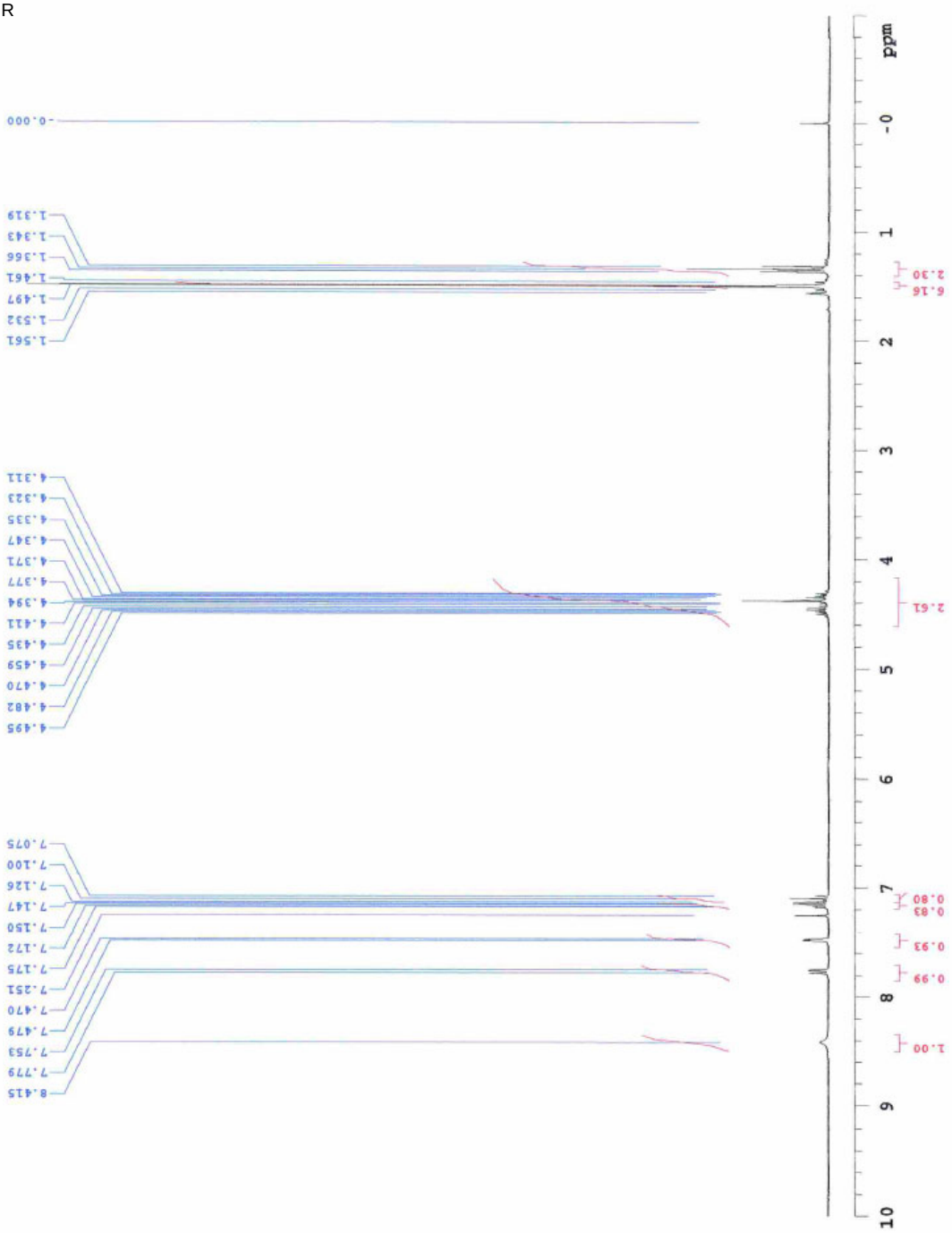
CF3
CO2Et
N
H
t-Bu

2n

^{1}H NMR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2
3
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5
6
7
8
9
10
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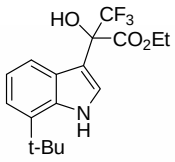
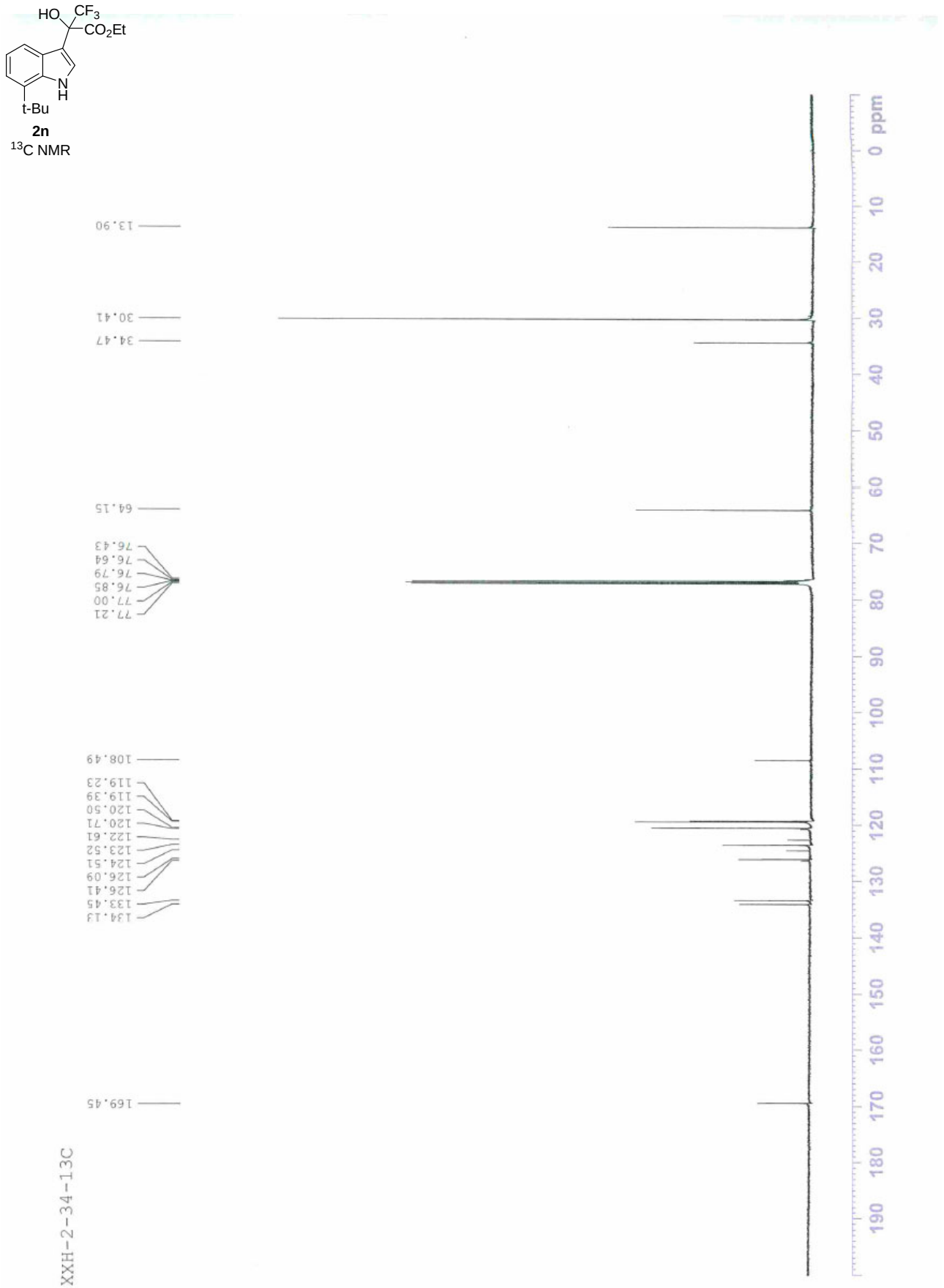
6.16
2.61
0.80
0.83
0.93
0.99
1.00



2n

^{19}F NMR


HO
CF3
CO2Et
N
H
t-Bu
2n
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30.41
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64.15
76.43
76.64
76.79
76.85
77.00
77.21
108.49
119.23
119.39
120.50
120.71
122.61
123.52
124.51
126.09
126.41
133.45
134.13
169.45
XXH-2-34-13C
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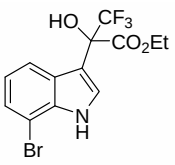
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190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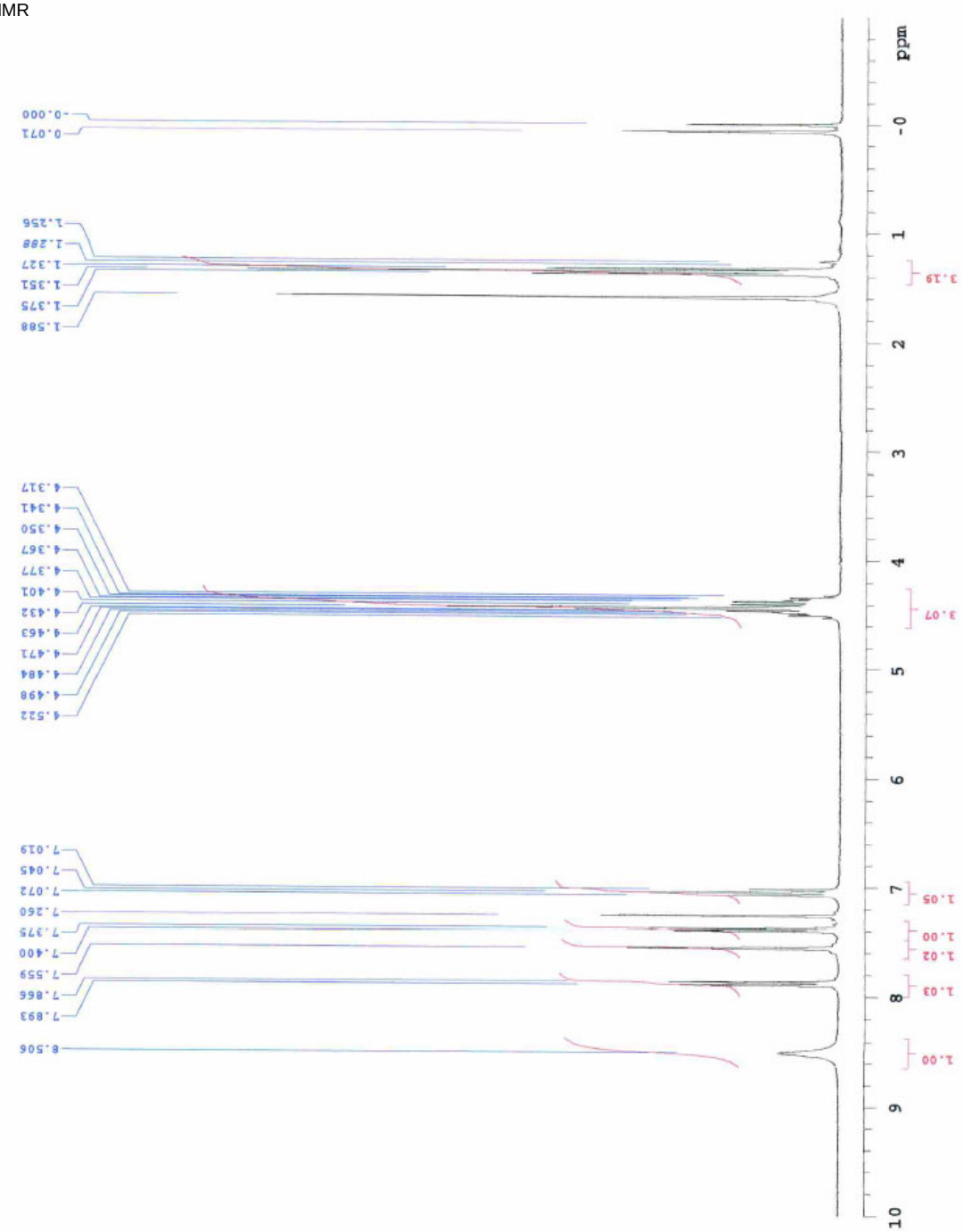
CF3
CO2Et
N
H
Br

2o

^{1}H NMR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1.327
1.351
1.375
1.588
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4.341
4.350
4.367
4.377
4.401
4.432
4.463
4.471
4.484
4.498
4.522
7.019
7.045
7.072
7.260
7.375
7.400
7.559
7.866
7.893
8.506
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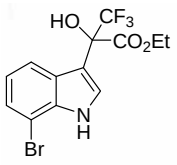
3.07
1.05
1.00
1.02
1.03
1.00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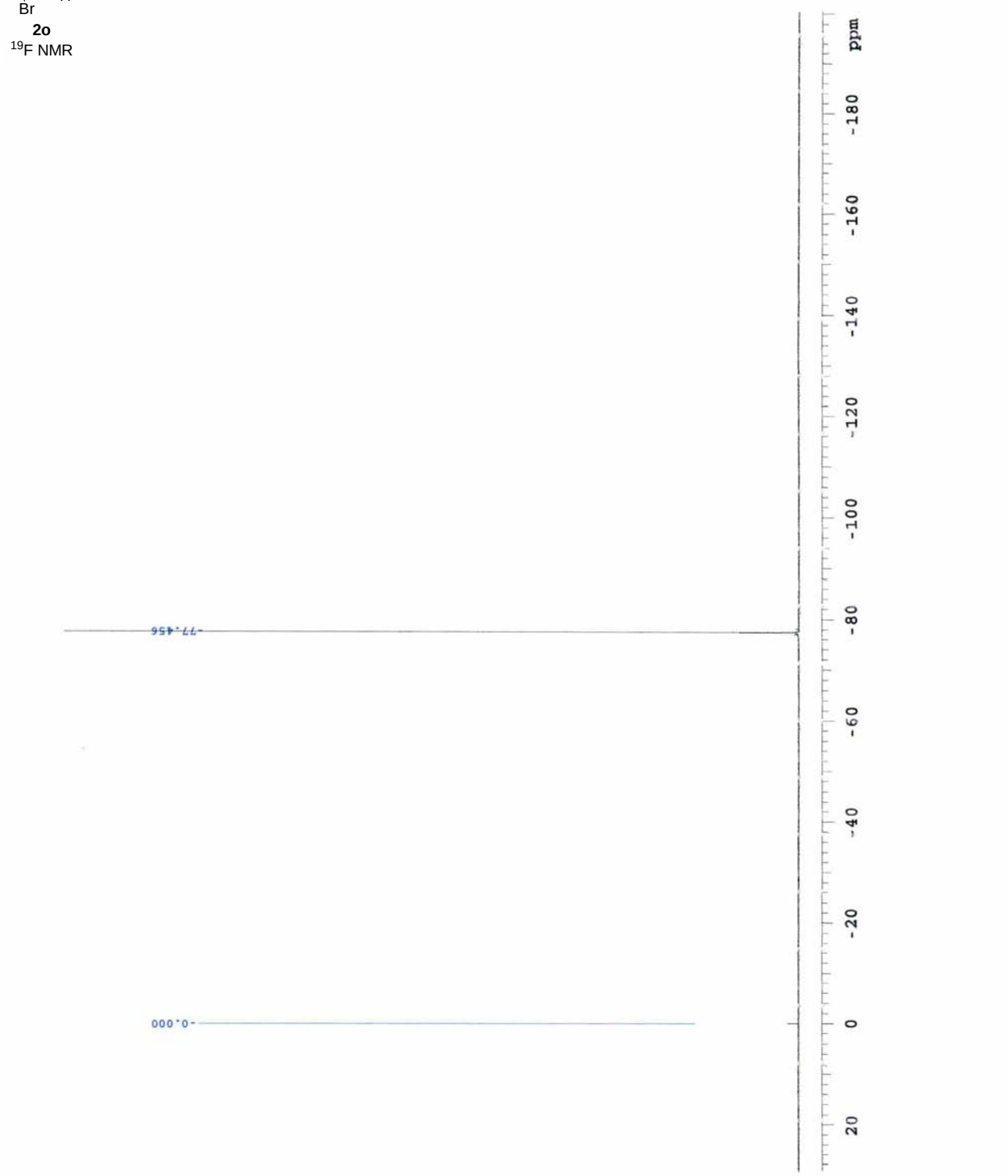
CF3
CO2Et
N
H
Br

2o

^{19}F NMR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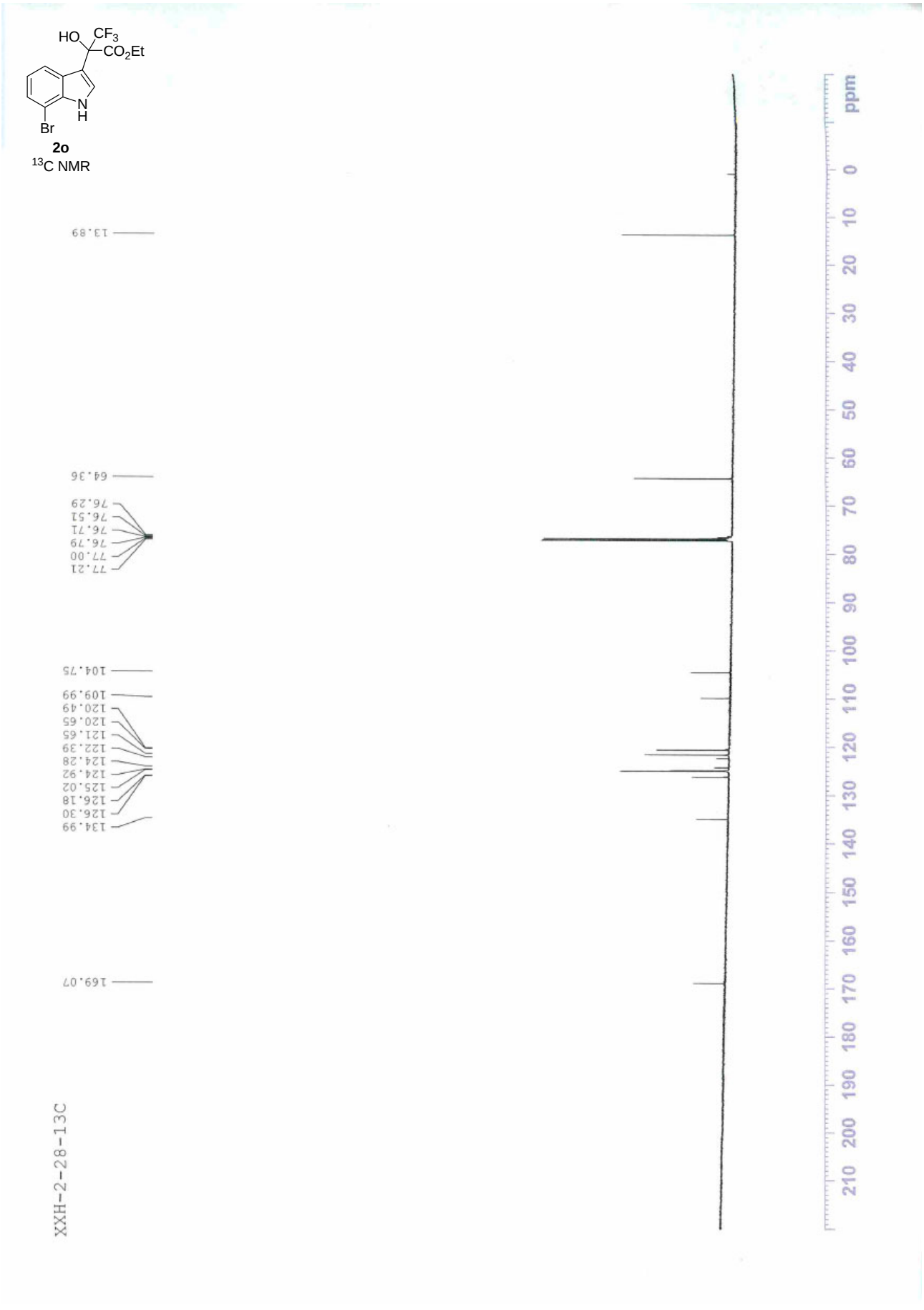
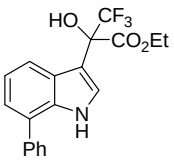
-60
-80
-100
-120
-140
-160
-180


HO
CF3
CO2Et
N
H
Br
2o
13C NMR
13.89
64.36
76.29
76.51
76.71
76.79
77.00
77.21
104.75
109.99
120.49
120.65
121.65
122.39
124.28
124.92
125.02
126.18
126.30
134.99
169.07
XXH-2-28-13C
ppm
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210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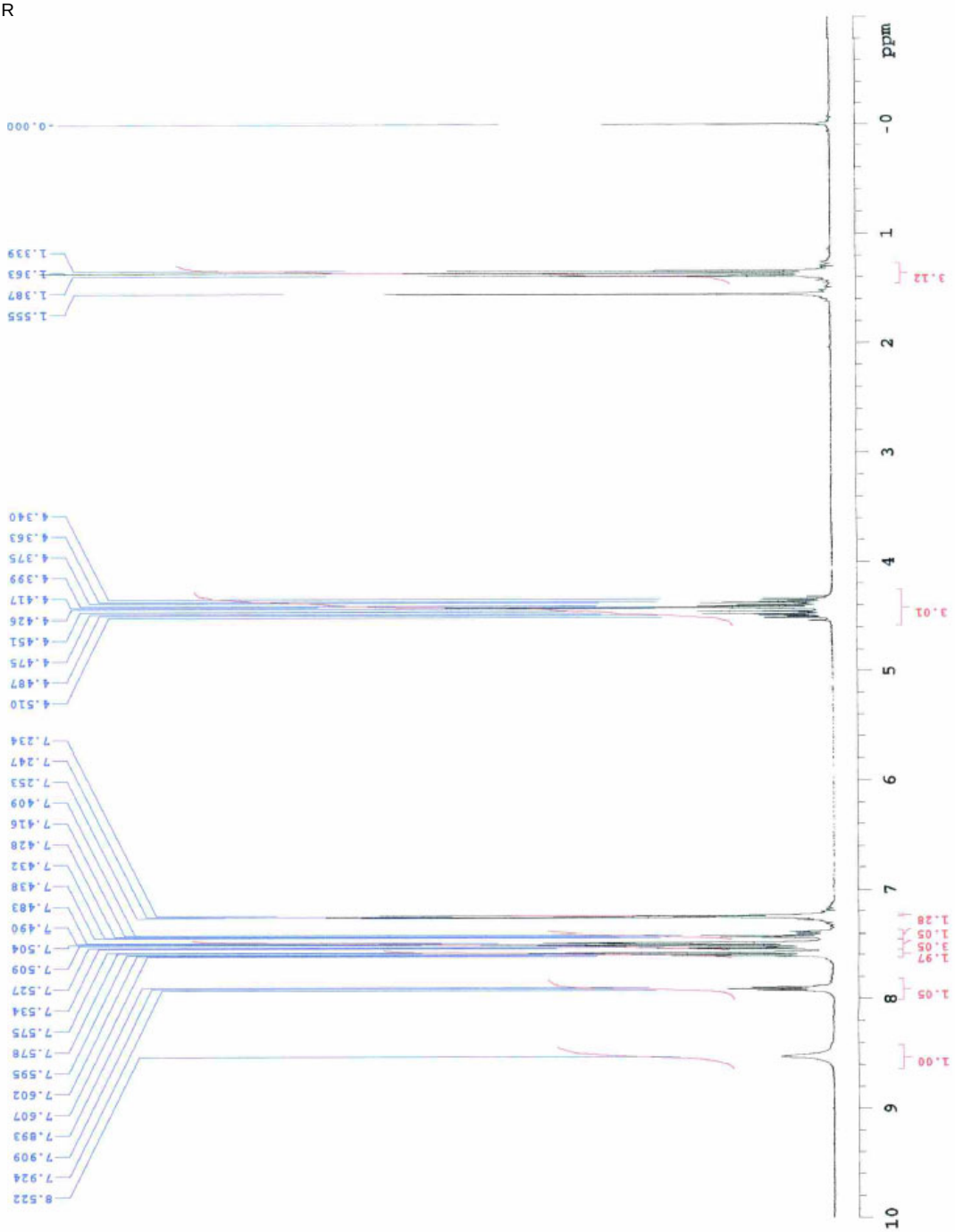
CF3
CO2Et
N
H
Ph

2p

^{1}H NMR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3
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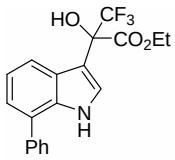
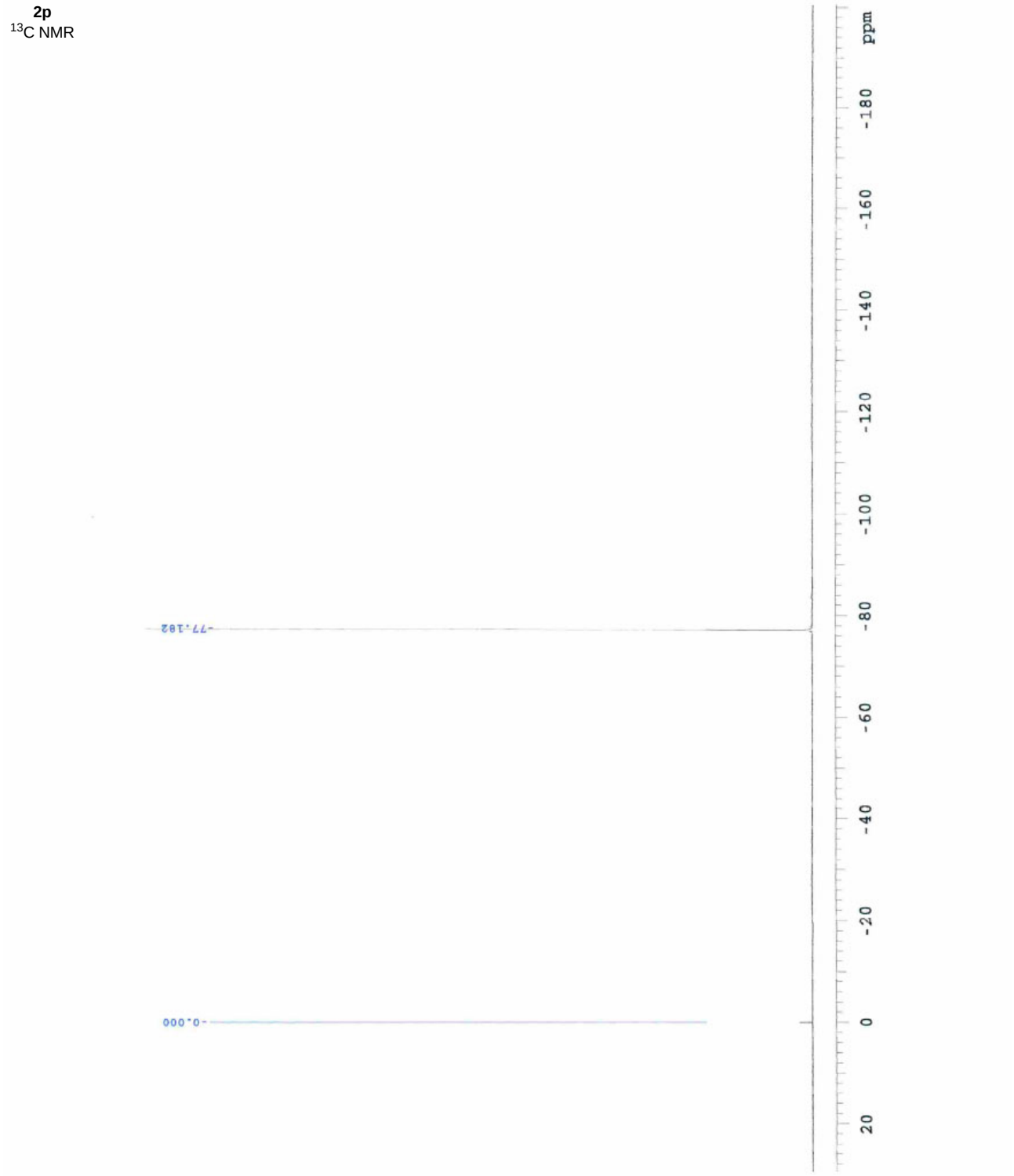
5
6
7
8
9
10
3.22
3.01
1.28
1.05
3.05
1.97
1.05
1.00


HO
CF3
CO2Et
N
H
Ph

2p

^{13}C NMR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-40
-20
0
20
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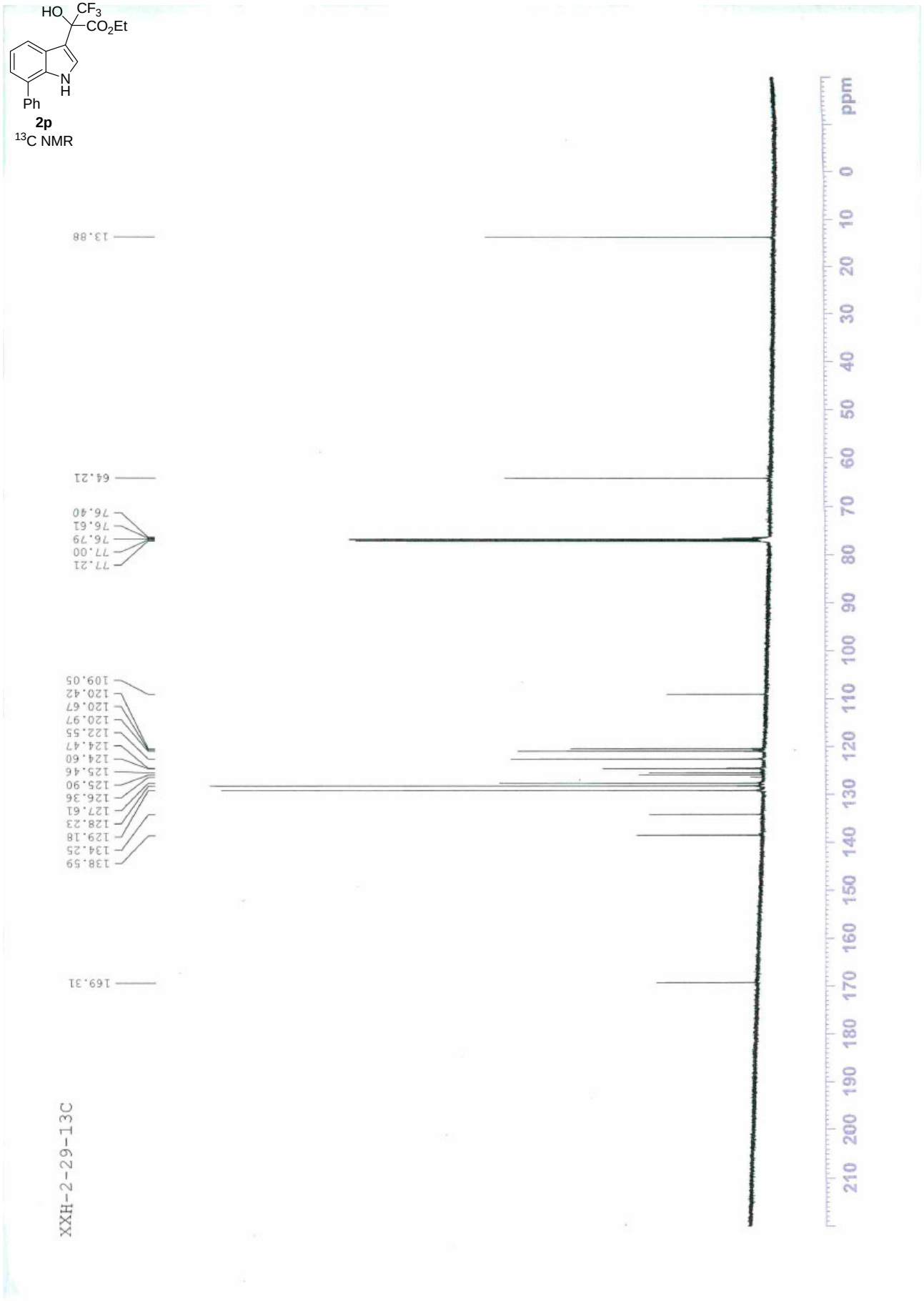
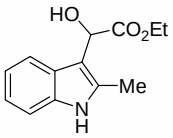
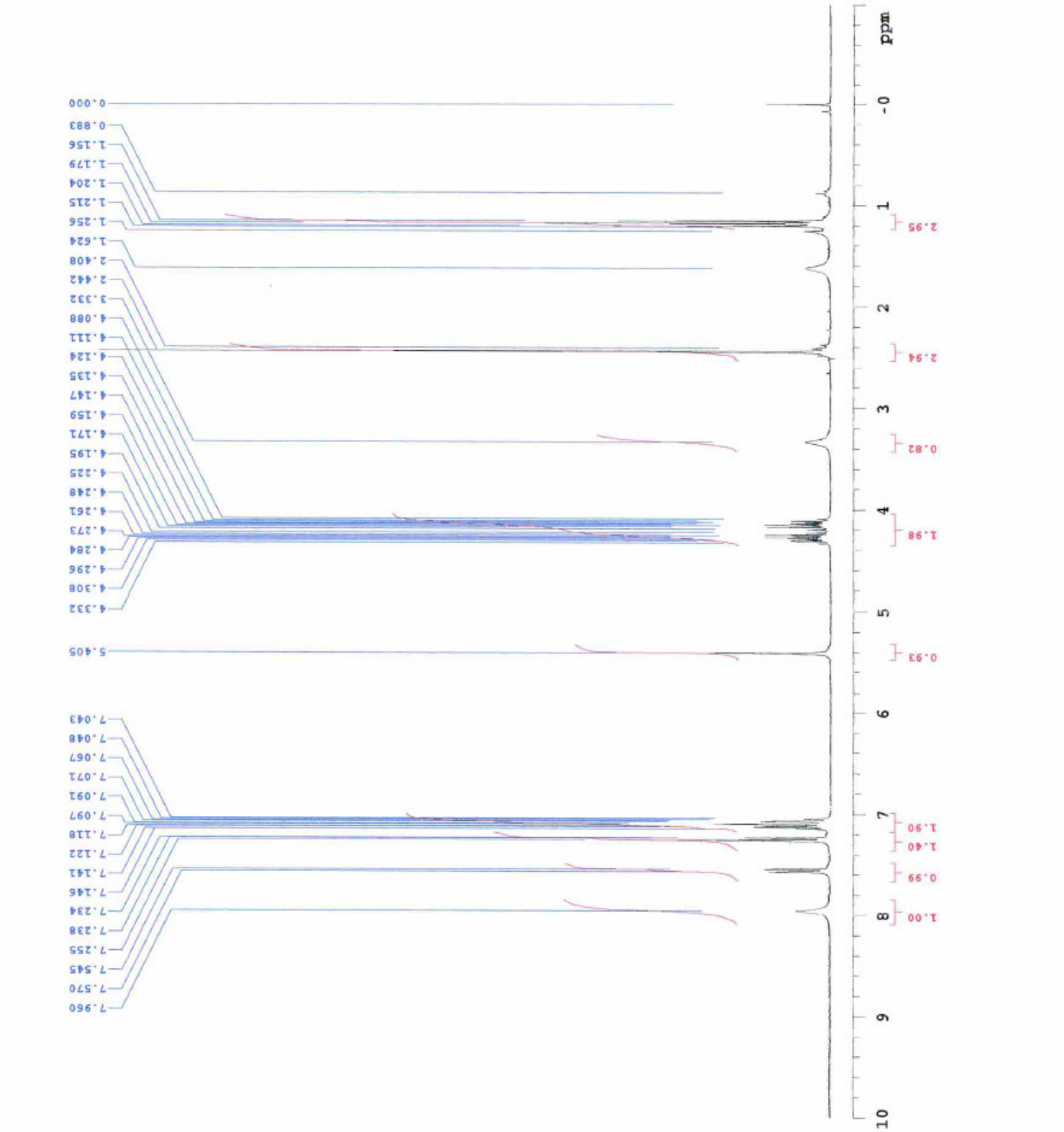
0.000




HO
CO2Et
Me
N
H

3b

^{1}H NMR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1.215
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2.442
3.332
4.088
4.111
4.124
4.135
4.147
4.159
4.171
4.195
4.225
4.248
4.261
4.273
4.284
4.296
4.308
4.332
5.405
7.043
7.048
7.067
7.071
7.091
7.097
7.118
7.122
7.141
7.146
7.234
7.238
7.255
7.545
7.570
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ppm
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0.93
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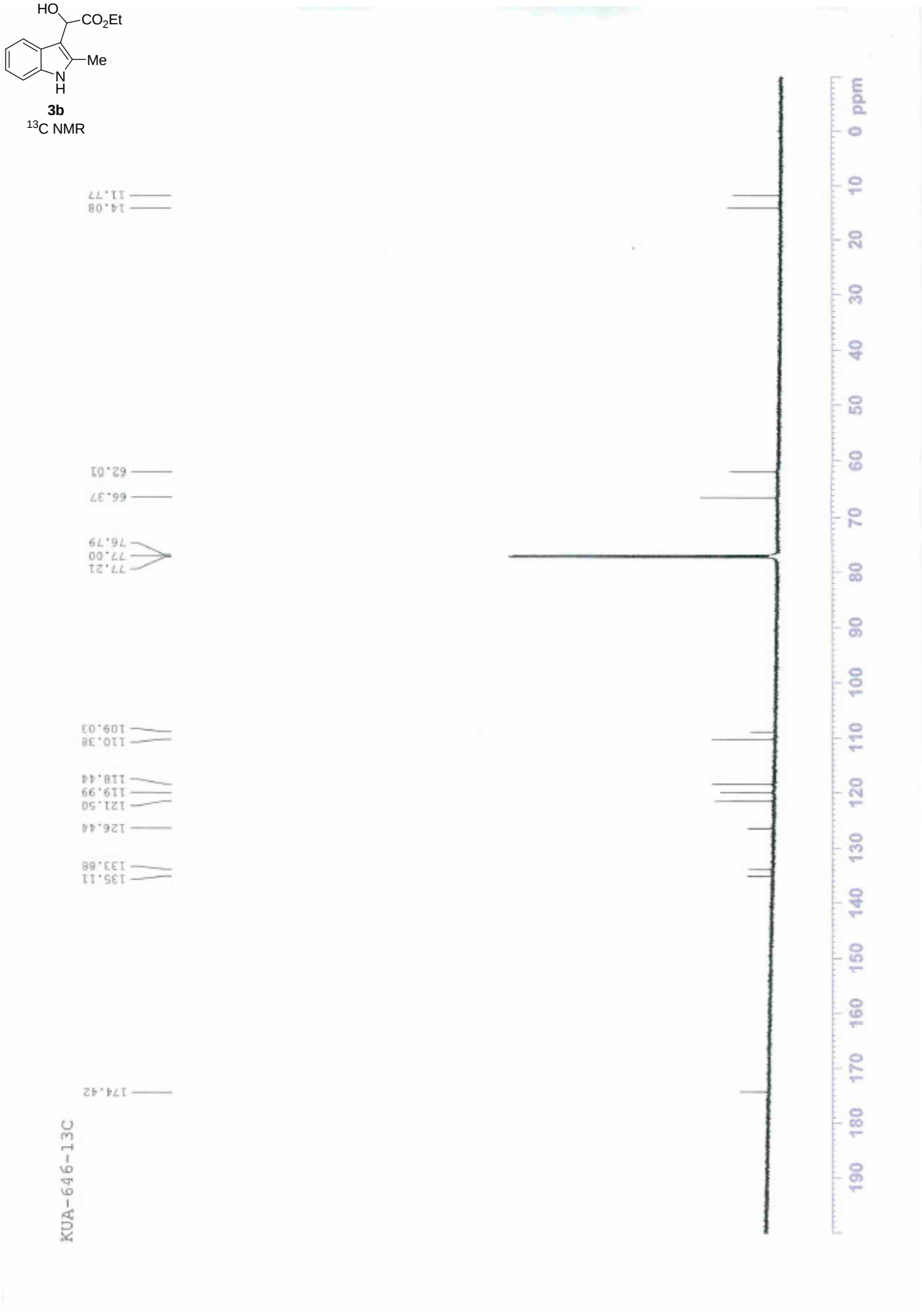
0.99
1.00


HO
CO2Et
Me
N
H
3b
13C NMR
11.77
14.08
62.01
66.37
76.79
77.00
77.21
109.03
110.38
118.44
119.99
121.50
126.44
133.88
135.11
174.42
KUA-646-13C
0 ppm
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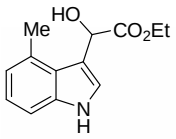
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190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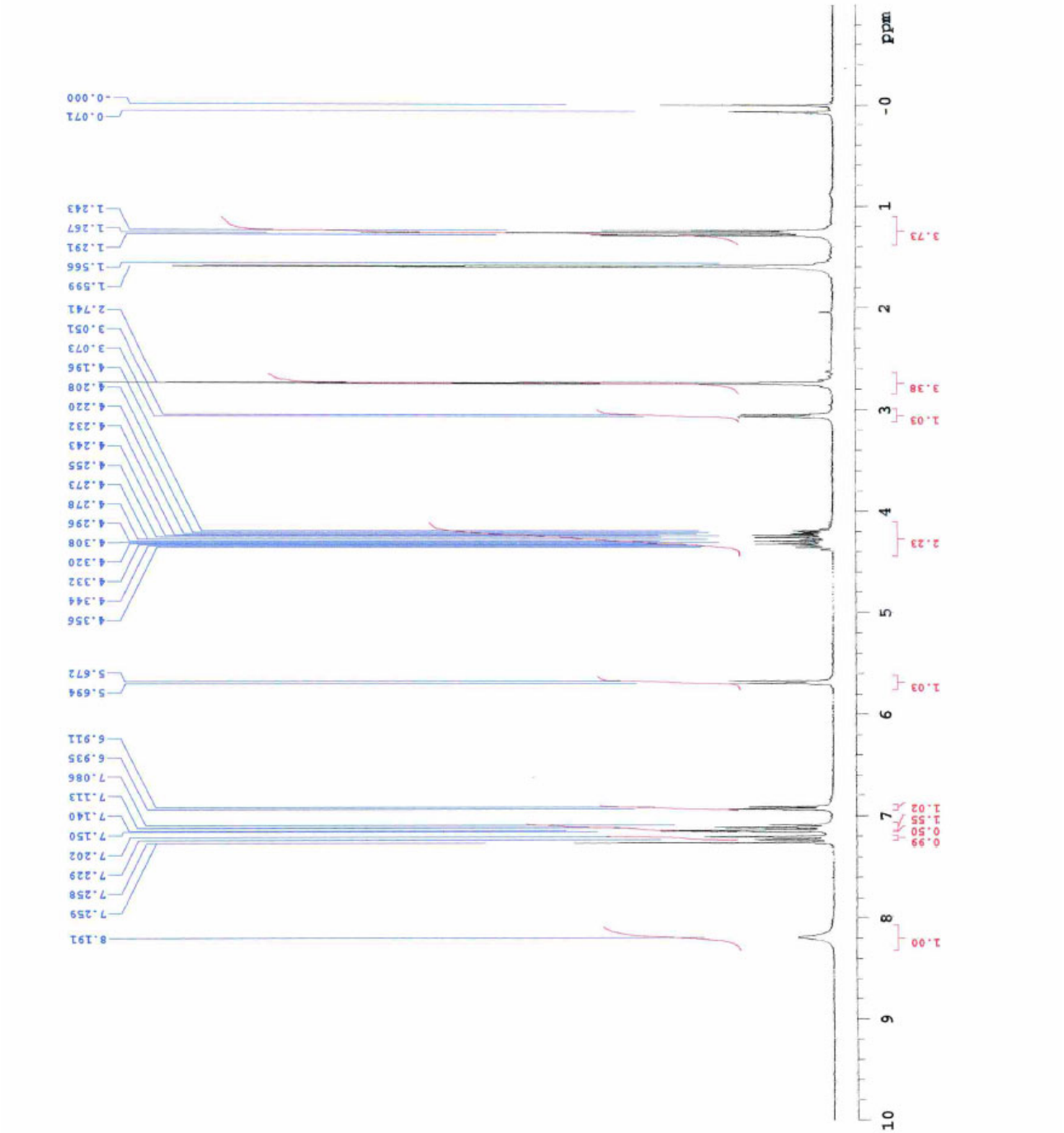
Me
CO2Et
N
H

3d
^{1}H NMR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3.073
4.196
4.208
4.220
4.232
4.243
4.255
4.273
4.278
4.296
4.308
4.320
4.332
4.344
4.356
5.672
5.694
6.911
6.935
7.086
7.113
7.140
7.150
7.202
7.229
7.258
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3.38
1.03
2.23
1.03
1.03
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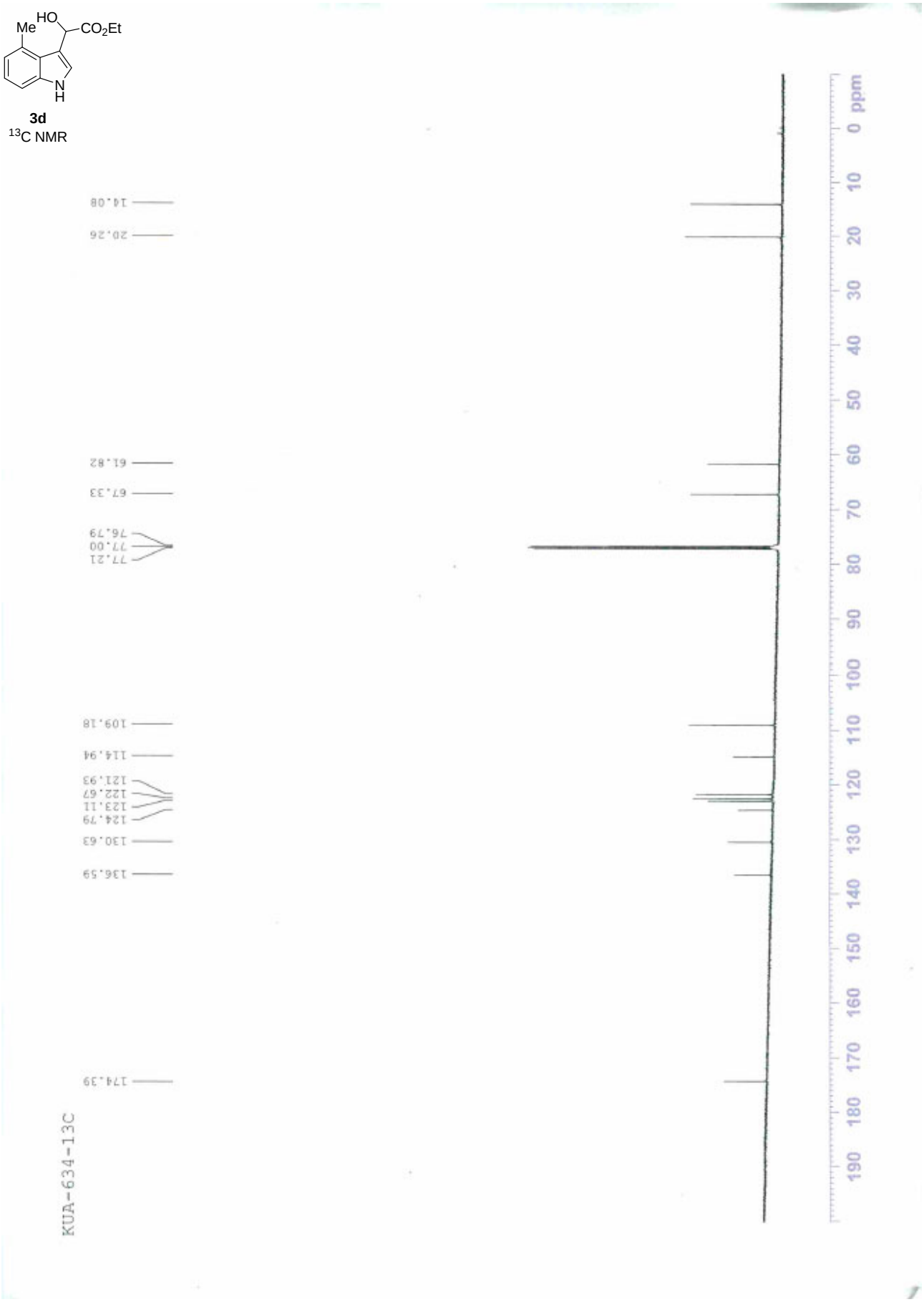
0.50
0.99
1.00


Me
HO
CO2Et
N
H
3d
13C NMR
14.08
20.26
61.82
67.33
76.79
77.00
77.21
109.18
114.94
121.93
122.67
123.11
124.79
130.63
136.59
174.39
KUA-634-13C
0 ppm
10
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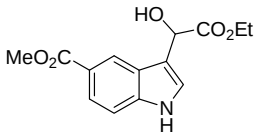
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190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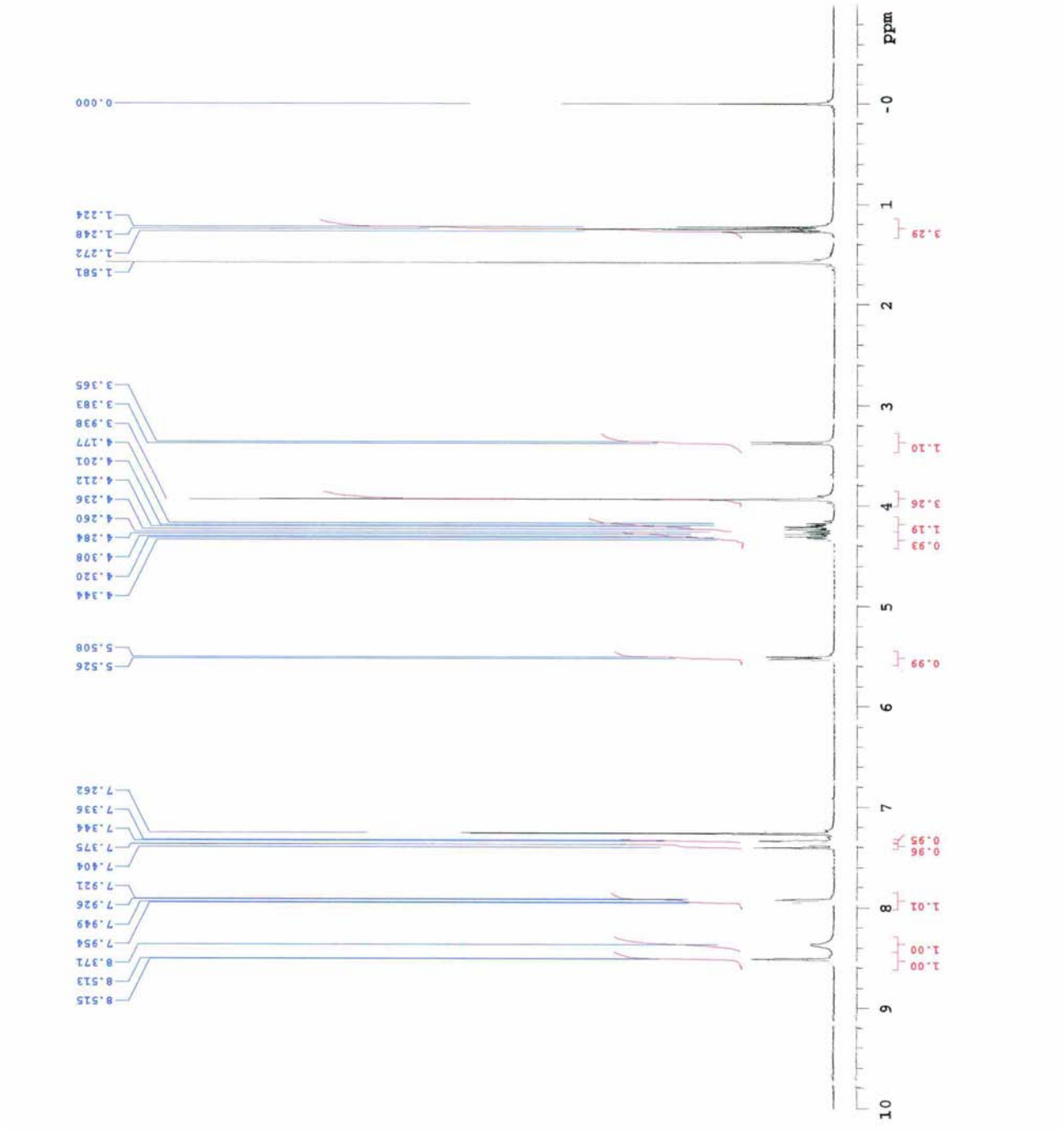
CO2Et
MeO2C
N
H

3r
^{1}H NMR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4.284
4.308
4.320
4.344
5.508
5.526
7.262
7.336
7.344
7.375
7.404
7.921
7.926
7.949
7.954
8.371
8.513
8.515
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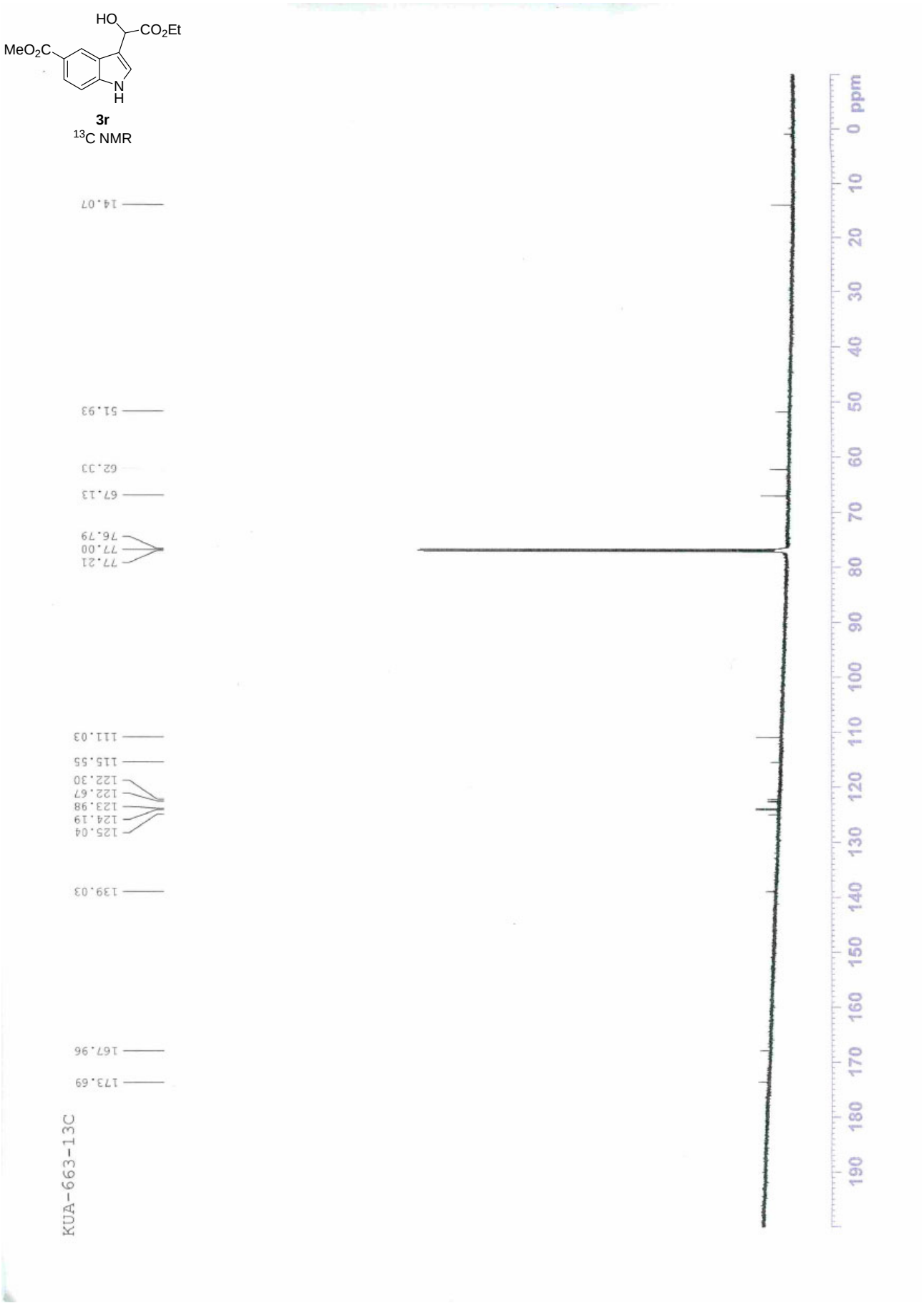
3.26
1.19
0.93
0.99
0.95
0.96
1.01
1.00
1.00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CO2Et
MeO2C
N
H
3r
13C NMR
14.07
51.93
62.33
67.13
76.79
77.00
77.21
111.03
115.55
122.30
122.67
123.98
124.19
125.04
139.03
167.96
173.69
KUA-663-13C
0 ppm
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40
50
60
70
80
90
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120
130
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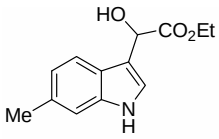
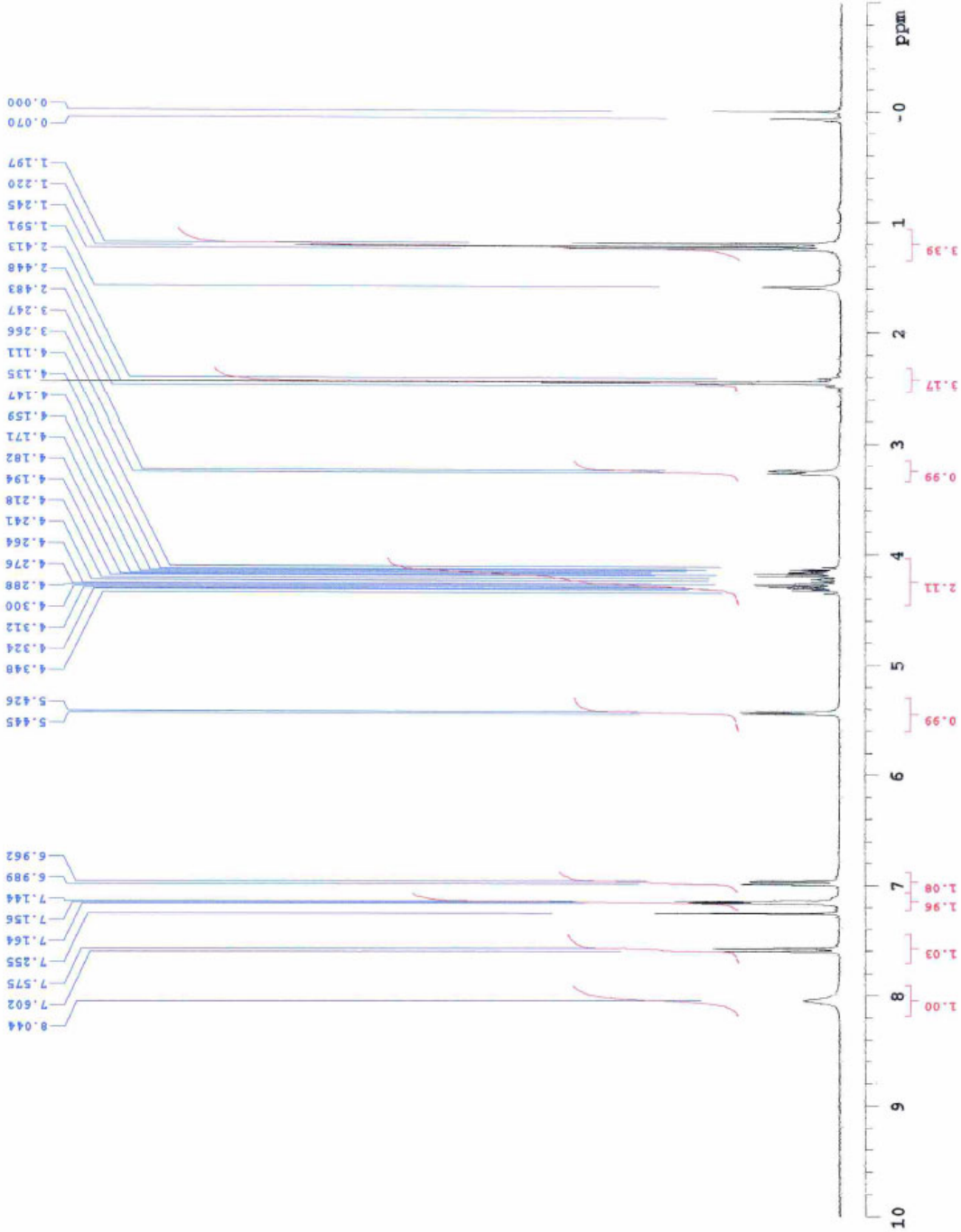
190


HO
CO2Et
Me
N
H

3k

^{13}C NMR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4.182
4.194
4.218
4.241
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4.276
4.288
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4.348
5.426
5.445
6.962
6.989
7.144
7.156
7.164
7.255
7.575
7.602
8.044
3.39
3.17
0.99
2.11
0.99
1.08
1.96
1.03
1.00


HO
CO2Et
Me
N
H
3k
13C NMR
14.06
21.62
61.98
67.34
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77.00
77.21
111.25
113.65
119.03
121.87
122.59
123.13
132.34
136.90
174.05
KUA-645-13C
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50
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80
90
100
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120
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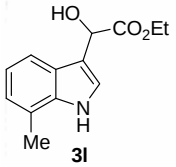
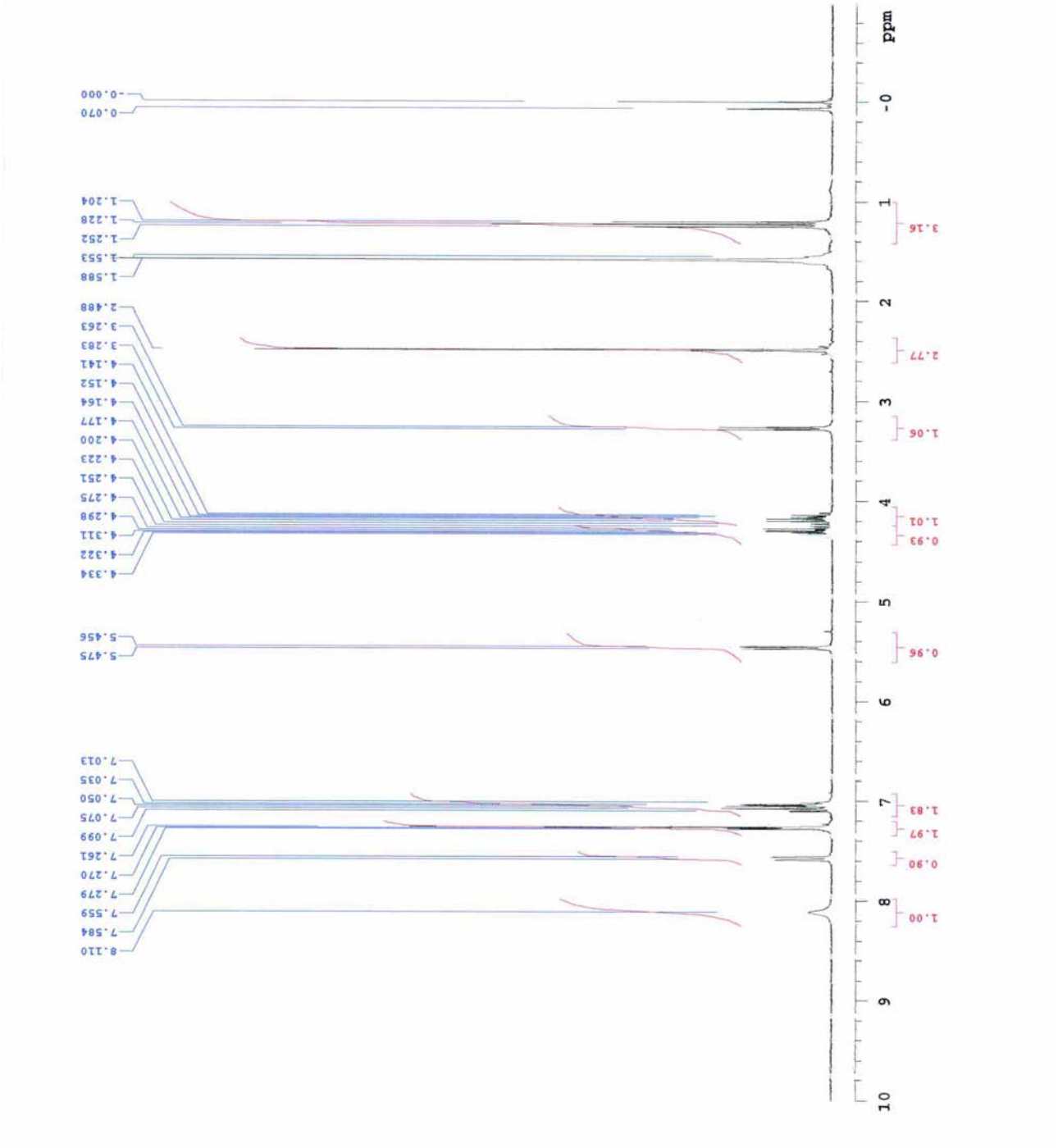
180
190


HO
CO2Et
N
H
Me

3l

^{1}H NMR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3.283
4.141
4.152
4.164
4.177
4.200
4.223
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4.275
4.298
4.311
4.322
4.334
5.456
5.475
7.013
7.035
7.050
7.075
7.099
7.261
7.270
7.279
7.559
7.584
8.110
3.16
2.77
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1.01
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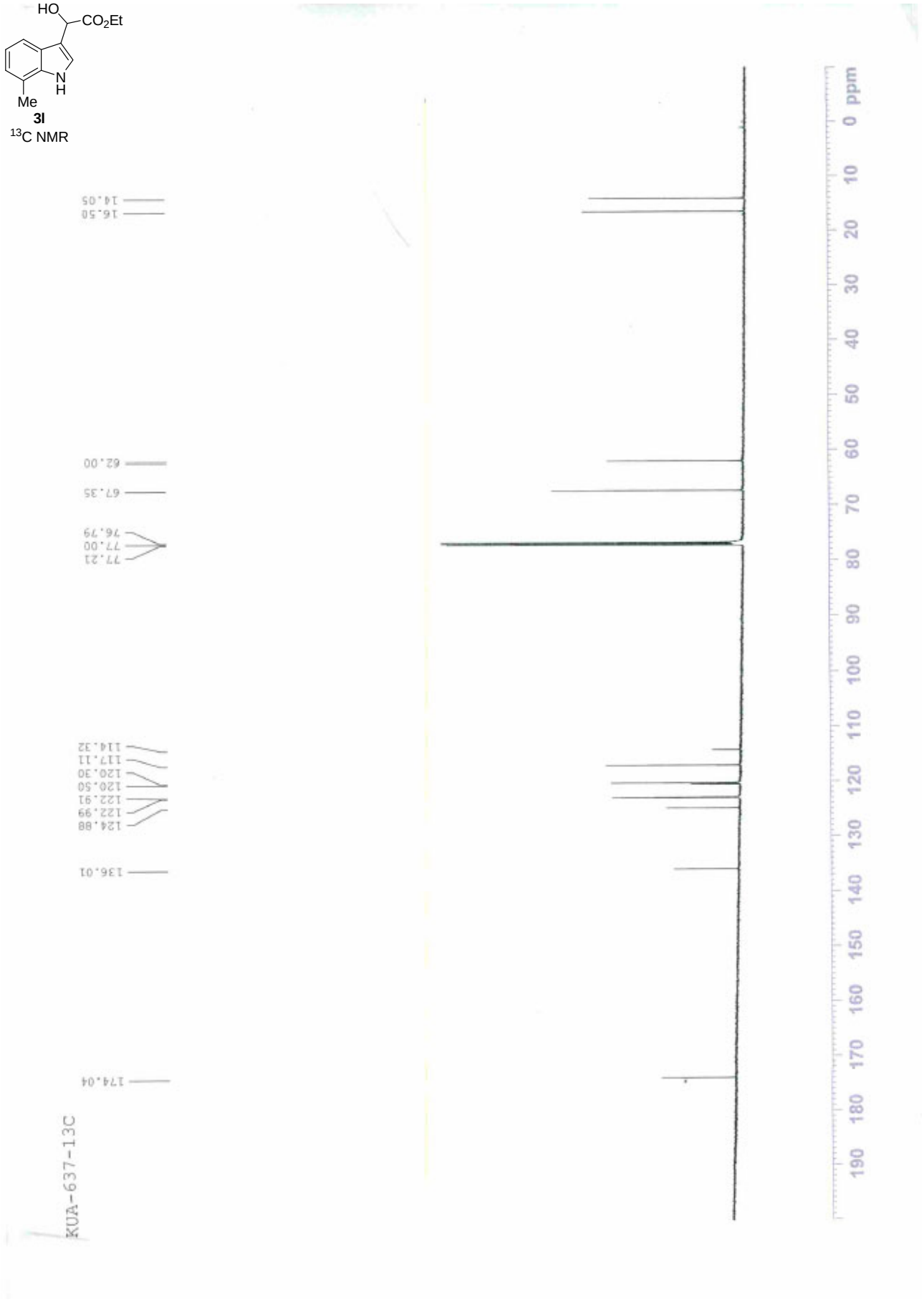
0.96
1.83
1.97
0.90
1.00


HO
CO2Et
N
H
Me
3l
13C NMR
14.05
16.50
62.00
67.35
76.79
77.00
77.21
114.32
117.11
120.30
120.50
122.91
122.99
124.88
136.01
174.04
KUA-637-13C
0 ppm
10
20
30
40
50
60
70
80
90
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130
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170
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