Supplementary Material (ESI) for Chemical Communications

Supporting Information

Highly Enantioselective Synthesis of Isoxazoline *N*-Oxides

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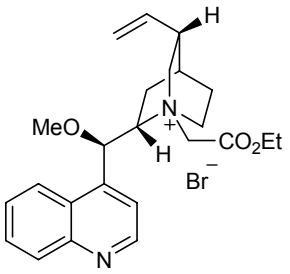
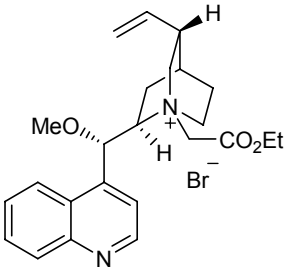
General Information. All reaction flasks were dried by flame. And all reactions were carried out under N_2 unless otherwise noted. All solvents were purified according to standard methods unless otherwise noted. All of the nitroalkenes were synthesized according to the literature[1].

^{1}H NMR and ^{13}C NMR spectra were recorded on a VARIAN Mercury 300 MHz spectrometer in chloroform-d_3 unless otherwise noted. ^{1}H NMR chemical shifts are reported in ppm with the internal TMS signal at 0.0 ppm as a standard unless otherwise noted. The data is being reported as (s = singlet, d = doublet, t = triplet, m = multiplet or unresolved, brs = broad singlet, coupling constant(s) in Hz, integration). ^{13}C NMR chemical shifts are reported in ppm with the internal chloroform signal at 77.0 ppm as a standard unless otherwise noted.

General procedure for the preparation of tertiary ammonium salt 1: A mixture of cinchonidine (cinchonine) derivative[2] (6 mmol) and ethyl bromoacetate (6 mmol) in acetone (2 mL) was stirred at room temperature over night. After the reaction was complete, the mixture was filtrate. The resulting solid was washed by ether and collected.



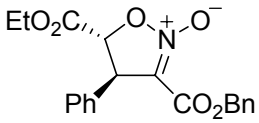
1a (solid): 24h, 95% yield; mp. 204-207 ˚C. IR (film) ν/cm^{-1} 2924 (m), 2926 (m), 1733 (s), 1219 (s). ^{1}H NMR (300MHz, $CDCl_3$/TMS): δ 9.00 (d, *J* = 4.5 Hz, 1H), 8.22 (d, *J* = 8.7 Hz, 1H), 7.80 - 7.87 (m, 2H), 7.67 - 7.73 (m, 1H), 7.50 (d, *J* = 4.2 Hz, 1H), 6.06 (d, *J* = 18.3 Hz, 1H), 5.49 – 5.57 (m, 1H), 5.20 – 5.27 (m, 2H), 4.85 – 5.03 (m, 3H), 4.29 – 4.54 (m, 6H), 3.45 (s, 3H), 2.88 (brs, 1H), 2.07 – 2.28 (m, 3H), 1.96 (t, *J* = 12.0 Hz, 1H), 1.45 (t, *J* = 7.2 Hz, 3H), 1.20 (brs, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.1, 149.7, 148.4, 139.1, 136.4, 130.6, 129.7, 127.6, 124.9, 121.6, 118.9(8), 116.7, 76.3, 63.2, 63.1, 60.1, 57.7, 57.3, 56.4, 36.9, 25.9, 25.0, 21.8, 13.9. MS (ESI, *m/z*) 395.2 (M – Br$^-$). Anal. calcd for $C_{24}H_{31}N_2O_3$: C, 60.63; H, 6.57; N, 5.89. Found: C, 60.64; H, 6.69; N, 5.78.



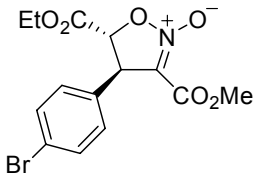
1b (solid): 24h, 85% yield; IR (film) ν/cm^{-1} 3651 (m), 3589 (m), 3568 (m), 3424 (s), 2952 (s), 1736 (s), 1639 (m), 1509 (m), 1239 (m), 924 (w). ^{1}H NMR (300MHz, $CDCl_3$ / TMS): δ 9.02 (d, *J* = 4.8 Hz, 1H), 8.20 (d, *J* = 8.1 Hz, 1H), 8.05 (d, *J* = 7.8 Hz, 1H), 7.73-7.85 (m, 2H), 7.60 (d, *J* = 4.5 Hz, 1H), 5.84-5.93 (m, 1H), 5.63 – 5.68 (m, 1H), 5.44 (d, *J* = 2.7 Hz, 1H), 5.26-5.34 (m, 2H), 4.40 – 4.72 (m, 7H), 4.25 (t, *J* =

10.2 Hz, 1H), 3.52 (s, 3H), 3.01 (brs, 1H), 2.08-2.25 (m, 3H), 1.88 (m, 1H), 1.45 (t, *J* = 7.2 Hz, 3H), 0.96-1.03 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.6, 149.3, 147.9, 138.5, 134.3, 130.0, 129.4, 127.5, 124.6, 121.7, 118.7, 117.5, 77.4, 63.8, 62.9, 59.6, 57.2, 57.1, 56.4, 36.6, 26.2, 22.9, 20.9, 13.5. MS (ESI, *m/*z) 395.2 ($M - Br^-$). HRMS (ESI) calcd for $C_{24}H_{31}N_2O_3^+$ ($M - Br^-$) 395.2338, Found: 395.23292.

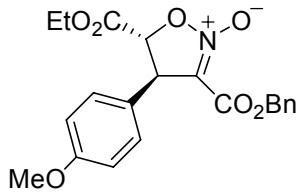
General procedure for the ammonium ylide annulation reaction (substrates 2a-2k): A mixture of salt **1** (0.22 mmol), Cs_2CO_3 (0.22 mmol) and nitroalkene **2** (0.2 mmol) was cooled to 0°C under N_2. To the mixture was then added H_2O (10 μL) and THF (2.5 mL). The reaction mixture was stirred at 0°C for the desired time. After the reaction was complete (monitored by TLC), the mixture was passed rapidly through a glass funnel with a thin layer (20 mm) of silica gel (300-400 mesh), washed with AcOEt (100 mL). The filtrate was concentrated under reduced pressure and the residue was purified by flash chromatography (EtOAc/petroleum ether/Et_3N, v/v/v, 100/500/1.8).



3a (solid): 46h, 65% yield, dr > 99/1. HPLC analysis (Chiralcel OD-H, 30/70 ^{i}PrOH/hexanes, 0.8 mL/min, 238 nm; t_r (major) = 12.75 min, t_r (minor) = 20.94 min) gave the isomeric composition of the product: 99% ee. $[\alpha]_D^{20}$ = -171.8 (c = 1.11, $CHCl_3$). mp. 82-85°C . IR (film) ν/cm^{-1} 3064 (m), 3033 (m), 2983 (m), 1743 (s), 1708 (s), 1635 (s), 1207 (m), 1148 (m), 750 (s), 699 (s). ^{1}H NMR (300 MHz, $CDCl_3$/TMS) δ 7.36-7.38 (m, 3H), 7.25-7.30 (m, 5H), 7.04-7.08 (m, 2H), 5.20 (ABd, *J* = 12.3 Hz, 1H), 5.06 (ABd, *J* = 12.3 Hz, 1H), 4.92 (d, *J* = 3.0 Hz, 1H), 4.85 (d, *J* = 3.0 Hz, 1H), 4.31 (q, *J* = 7.2 Hz, 2H), 1.32 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.0, 157.8, 137.8, 134.5, 129.3, 128.7, 128.4, 128.3, 127.9, 127.0, 108.8, 78.7, 67.2, 62.6, 52.5, 14.0. MS (ESI, *m/*z) 424.1 (M + MeOH + Na^+), 392.0 (M + Na^+), 387.1 (M + NH_4^+), 370.1 (M + H^+). Anal. calcd for $C_{20}H_{19}NO_6$: C, 65.03; H, 5.18; N, 3.79. Found: C, 65.21; H, 5.19; N, 3.51.

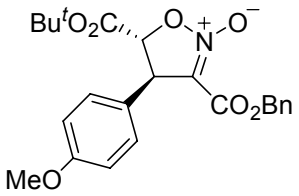


3b (solid): 34h, 74% yield; dr > 99/1. HPLC analysis (Chiralcel OD-H, 30/70 ^{i}PrOH/hexanes, 0.6 mL/min, 238 nm; t_r (major) = 18.28 min, t_r (minor) = 35.25 min) gave the isomeric composition of the product: 98% ee. $[\alpha]_D^{20}$ = -162.3 (c = 1.20, $CHCl_3$). mp. 88-90˚C . IR (film) ν/cm^{-1} 2978 (w), 2936 (w), 1740 (s), 1633 (s), 1442 (m), 1231 (s), 1011 (m), 756 (m). ^{1}H NMR (300 MHz, $CDCl_3$/TMS) δ 7.54 (ABd, *J* = 8.7 Hz, 2H), 7.23 (ABd, *J* = 8.7 Hz, 2H), 4.89 (d, *J* = 2.7 Hz, 1H), 4.83 (d, *J* = 2.4 Hz, 1H), 4.33 (q, *J* = 6.9 Hz, 2H), 3.76 (s, 3H), 1.35 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.7, 158.4, 136.7, 132.5, 128.6, 122.8, 108.5, 78.3, 62.8, 52.8, 51.9, 14.0. MS (ESI, *m/*z) 428.1 (M + 2 + MeOH + Na^+), 426.1 (M + MeOH + Na^+), 396.0 (M + 2 + Na^+), 394.0 (M + Na^+), 391.0 (M + 2 + NH_4^+), 389.0 (M + NH_4^+), 374.0 (M + 2 + H^+), 372.0 (M + H^+). Anal. calcd for $C_{14}H_{14}BrNO_6$: C, 45.18; H, 3.79; N, 3.76. Found: C, 45.28; H, 3.82; N, 3.61.

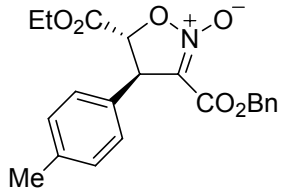


3c (solid): 44h, 65% yield; dr > 99/1. HPLC analysis (Chiralcel OD-H, 30/70 ^{i}PrOH/hexanes, 0.8 mL/min, 238 nm; t_r (major) = 17.28 min, t_r (minor) = 26.61 min) gave the isomeric composition of the product: 99% ee. mp. 87-90˚C. $[\alpha]_D^{20}$ = -163.0 (c = 1.02, $CHCl_3$). mp. 87-90˚C . IR (film) ν/cm^{-1} 2979 (m), 2904 (m), 2837 (m), 1738 (s), 1634 (s), 1538 (s), 1252 (m), 1030 (m), 838 (m), 754 (m), 698 (m). ^{1}H NMR (300 MHz, $CDCl_3$/TMS) δ 7.26-7.30 (m, 3H), 7.21 (ABd, *J* = 9 Hz, 2H), 7.11-7.12 (m, 2H), 6.88 (ABd, *J* = 9.0 Hz, 2H), 5.22 (ABd, *J* = 12 Hz, 1H), 5.09 (ABd, *J* = 12 Hz, 1H), 4.89 (d, *J* = 3.0 Hz, 1H), 4.80 (d, *J* = 3.0 Hz, 1H), 4.31 (q, *J* = 6.9 Hz, 2H), 3.82 (s, 3H), 1.33 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.1, 159.9, 158.0, 134.6, 129.9, 128.5, 128.4, 128.3, 128.0, 114.7, 109.0, 79.0, 67.3, 62.6, 55.4, 52.0, 14.1. MS (ESI, *m/*z) 454.2 (M + MeOH + Na^+), 422 (M + Na^+), 417.3(M +

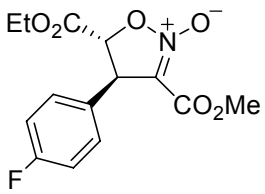
NH_4^+), 400.2 (M + H^+). Anal. calcd for $C_{21}H_{21}NO_7$: C, 63.15; H, 5.30; N, 3.51. Found: C, 63.10; H, 5.12; N, 3.33.



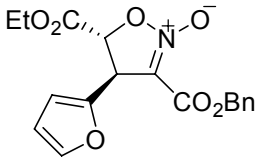
3d (solid): 38h, 56% yield; dr > 99/1. HPLC analysis (Chiralcel OD-H, 30/70 ^{i}PrOH/hexanes, 0.4 mL/min, 238 nm; t_r (major) = 19.19 min, t_r (minor) = 24.94 min) gave the isomeric composition of the product: 98% ee. ^{1}H NMR (300 MHz, $CDCl_3$/TMS) δ 7.26-7.28 (m, 3H), 7.19 (ABd, *J* = 9 Hz, 2H), 7.07-7.10 (m, 2H), 6.88 (ABd, *J* = 9.0 Hz, 2H), 5.23 (ABd, *J* = 12.3 Hz, 1H), 5.09 (ABd, *J* = 12.3 Hz, 1H), 4.78 (ABd, *J* = 3.3 Hz, 1H), 4.75 (ABd, *J* = 3.3 Hz, 1H), 3.81 (s, 3H) 1.51 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.9, 159.7, 158.0, 134.6, 130.0, 128.3, 128.2, 127.8, 114.5, 109.0, 84.0, 79.3, 67.1, 55.3, 51.9, 27.8.



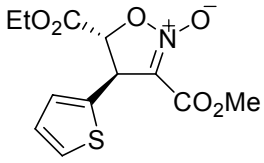
3e (solid): 37h, 77% yield; dr > 99/1. HPLC analysis (Chiralcel OD-H, 30/70 ^{i}PrOH/hexanes, 0.8 mL/min, 238 nm; t_r (major) = 11.38 min, t_r (minor) = 17.38 min) gave the isomeric composition of the product: 97% ee. $[\alpha]_D^{20}$ = -137.7 (c = 1.03, $CHCl_3$). mp. 82-83˚C . IR (film) ν/cm^{-1} 3032 (m), 2982 (s), 1738 (vs), 1709 (s), 1628 (vs), 1515 (m), 1456 (m), 1391 (m), 1361 (m), 1220 (s), 1024 (m), 818 (m), 751 (s), 698 (s). ^{1}H NMR (300 MHz, $CDCl_3$/TMS) δ 7.25-7.27 (m, 3H), 7.17 (s, 4H), 7.06-7.09 (m, 2H), 5.20 (ABd, *J* = 12.0 Hz, 1H), 5.06 (ABd, *J* = 12.0 Hz, 1H), 4.89 (d, *J* = 3.0 Hz, 1H), 4.81 (d, *J* = 3.0 Hz, 1H), 4.31 (q, *J* = 6.9 Hz, 2H), 2.36 (s, 3H), 1.32 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.0, 157.9, 138.6 , 134.8, 134.5, 129.9, 128.3, 128.2, 127.9, 126.9, 108.9, 78.7, 67.2, 62.6, 52.2, 21.1, 14.0. MS (EI, *m/*z, rel. intensity) 383 (M^+, 0.24), 91 (100.00). Anal. calcd for $C_{21}H_{21}NO_6$: C, 65.79; H, 5.52; N, 3.65. Found: C, 65.82; H, 5.70; N, 3.48.



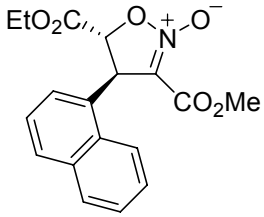
3f (solid): 34h, 79% yield, dr > 99/1. HPLC analysis (Chiralcel OD-H, 30/70 ^{i}PrOH/hexanes, 0.6 mL/min, 238 nm; t_r (major) = 14.96 min, t_r (minor) = 20.54 min) gave the isomeric composition of the product: 99% ee. $[\alpha]_D^{20}$ = -167.9 (c = 0.94, $CHCl_3$). mp. 85-87°C . IR (film) ν/cm^{-1} 2986 (m), 2938 (m), 1742 (s), 1631 (s), 1511(s), 1443 (m), 1373 (m), 1229 (m), 977 (w), 841 (m), 756 (s). ^{1}H NMR (300 MHz, $CDCl_3$/TMS) δ 7.31–7.35 (m, 2H), 7.10 (t, *J* = 8.4 Hz, 2H), 4.91 (d, *J* = 2.7 Hz, 1H), 4.85 (d, *J* = 2.7 Hz, 1H), 4.33 (q, *J* = 7.2 Hz, 2H), 3.76 (s, 3H), 1.35 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.9, 164.3 161.0, 158.5, 133.6, 133.5(5), 128.8, 128.7, 116.5, 116.2, 108.8, 78.6(5), 78.6(3), 62.7, 52.7, 51.8, 14.0. MS (ESI, *m/*z) 366.2 (M + MeOH + Na^+), 334.2 (M + Na^+), 329.2 (M + NH_4^+), 312.2 (M + H^+). Anal. calcd for $C_{14}H_{14}FNO_6$: C, 54.02; H, 4.53; N, 4.50. Found: C, 54.06; H, 4.44; N, 4.40.



3g (solid): 36h, 67% yield, dr > 99/1. HPLC analysis (Chiralcel OD-H, 30/70 ^{i}PrOH/hexanes, 0.6 mL/min, 238 nm; t_r = 15.29 min, only one peak was observed.) gave the isomeric composition of the product: > 99% ee. $[\alpha]_D^{20}$ = -84.4 (c = 1.00, $CHCl_3$). IR (film) ν/cm^{-1} 3123 (w), 2983 (m), 1739 (s), 1633 (s), 1500 (m), 1456 (m), 1393 (m), 1224 (m), 747 (m), 698 (m), 598 (m). ^{1}H NMR (300 MHz, $CDCl_3$/TMS) δ 7.22-7.39 (m, 6H), 6.35 (dd, *J* = 1.5, 3.3 Hz 1H), 6.27 (d, *J* = 3.0 Hz, 1H), 5.26 (ABd, *J* = 12.6 Hz, 1H), 5.14 (ABd, *J* = 12.6 Hz, 1H), 5.04 (s, 2H), 4.30 (q, *J* = 7.2Hz, 2H), 1.31 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.6, 157.7, 148.7, 143.1, 134.5, 128.4, 128.4, 128.0, 110.8, 108.4, 106.2, 76.0, 67.3, 62.7, 46.1, 13.9. MS (EI, *m/*z, rel. intensity) 341 (M^+-H_2O, 1.01), 91 (100.00). HRMS (ESI) calcd for $C_{18}H_{17}NO_7Na^+$ (M+Na^+) 382.0901, Found: 382.08973.

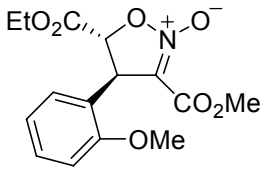


3h (solid): 41h, 79% yield; dr > 99/1. HPLC analysis (Chiralcel OD-H, 30/70 ^{i}PrOH/hexanes, 0.6 mL/min, 238 nm; t_r (major) = 14.71 min, t_r (minor) = 20.79 min) gave the isomeric composition of the product: 99% ee. $[\alpha]_D^{20}$ = -123.2 (c = 1.10, $CHCl_3$). mp. 119-121˚C . IR (film) ν/cm^{-1} 3113 (w), 2993 (w), 2909 (w), 1740 (s), 1633 (s), 1438 (m), 1230 (m), 982 (m), 751 (s), 732 (m), 546 (w). ^{1}H NMR (300 MHz, $CDCl_3$/TMS) δ 7.32 (dd, *J* = 0.9, 5.1 Hz, 1H), 7.09-7.10 (m, 1H), 7.02 (dd, *J* = 3.6, 5.4 Hz, 1H), 5.18 (d, *J* = 2.4 Hz ,1H), 5.05 (d, *J* = 2.7 Hz, 1H), 4.33 (q, *J* = 7.2 Hz, 2H), 3.80 (s, 3H), 1.35 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.5, 158.3, 139.4, 127.4, 125.9(9), 125.9(6), 108.4, 78.8, 62.7, 52.7,47.6, 13.9. MS (ESI, *m/z*) 354.1 (M + MeOH + Na^+), 322.1 (M + Na^+), 317.1 (M + NH_4^+), 300.1 (M + H^+). Anal. calcd for $C_{12}H_{13}NO_6S$: C, 48.16; H, 4.38; N, 4.68. Found: C, 48.58; H, 4.05; N, 4.63.

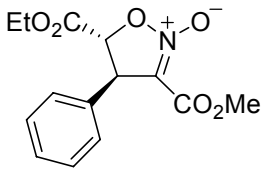


3i (solid): 39h, 68% yield; dr > 99/1. HPLC analysis (Chiralcel OD-H, 30/70 ^{i}PrOH/hexanes, 0.6 mL/min, 238 nm; t_r (major) = 20.48 min, t_r (minor) = 27.55 min) gave the isomeric composition of the product: 96% ee. $[\alpha]_D^{20}$ = -3.0 (c = 1.23, $CHCl_3$). IR (film) ν/cm^{-1} 3055(w), 2981(w), 2959 (w), 1759 (s), 1740 (s), 1633 (s), 1440 (s), 1227 (m), 1056 (w), 799 (m), 777 (m), 748 (m), 537 (m). ^{1}H NMR (300 MHz, $CDCl_3$/TMS) δ 8.25 (d, *J* = 8.4 Hz, 1H), 7.92 (d, *J* = 0.9 Hz, 1H), 7.88 (d, *J* = 8.4 Hz, 1H), 7.65 (dd, *J* = 6.3, 6.9 Hz, 1H), 7.58 (dd, *J* = 6.3, 6.6 Hz, 1H), 7.46 (t, *J* = 7.2 Hz, 1H), 7.32 (d, *J* = 6.6 Hz, 1H), 5.72 (d, *J* = 1.5 Hz, 1H), 4.88 (d, *J* = 1.8 Hz, 1H), 4.38-4.44 (m, 2H), 3.72 (s, 3H), 1.41 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.4, 158.7, 134.2, 132.8, 130.3, 129.4, 129.2, 127.1, 126.3, 125.4, 124.1, 122.5, 108.3, 78.5, 62.8, 52.8, 48.4, 14.0. MS (ESI, *m/z*) 398.1 (M + MeOH + Na^+),

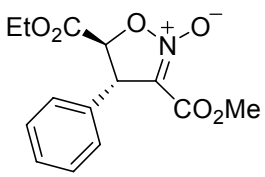
366.1 (M + Na^+), 344.1 (M + H^+). Anal. calcd for $C_{18}H_{17}NO_6$: C, 62.97; H, 4.99; N, 4.08. Found: C, 67.61; H, 4.94; N, 3.75.



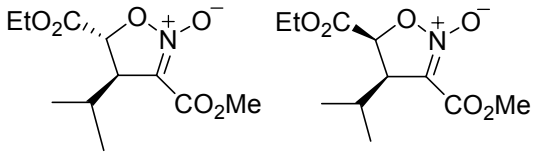
3j (solid): 36h, 54% yield; dr > 99/1. HPLC analysis (Chiralcel AD-H, 10/90 ^{i}PrOH/hexanes, 0.4 mL/min, 238 nm; t_r (major) = 28.02 min, t_r (minor) = 38.33 min) gave the isomeric composition of the product: 99% ee. $[\alpha]_D^{20}$ = -70.3 (c = 1.13, $CHCl_3$). IR (film) ν/cm^{-1} 2956 (m), 2843 (m), 1741 (s), 1708 (s), 1632 (s), 1494 (m), 1246 (m), 1026 (m), 757 (s). ^{1}H NMR (300 MHz, $CDCl_3$/TMS) δ 7.33-7.35 (m, 1H), 7.12-7.14 (m, 1H), 6.94-6.98 (m, 2H), 5.15 (d, *J* = 3.6 Hz 1H), 4.86 (d, *J* = 3.6 Hz 1H), 4.30-4.34 (m, 2H), 3.88 (s, 3H), 3.74 (s, 3H), 1.35 (t, *J* = 7.2 Hz 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.2, 158.8, 156.6, 129.9, 128.3, 125.2, 120.8, 111.0, 108.1, 78.0, 62.3, 55.5, 52.5, 47.9, 14.0. MS (ESI, *m/z*) 378.1 (M + MeOH + Na^+), 346.1 (M + Na^+), 324.1 (M + H^+). Anal. calcd for $C_{15}H_{17}NO_7$: C, 55.73; H, 5.30; N, 4.33. Found: C, 55.79; H, 5.27; N, 4.33.



3k (solid)[3]: 36h, 62% yield; dr > 99/1. HPLC analysis (Chiralcel OD-H, 30/70 ^{i}PrOH/hexanes, 0.8 mL/min, 238 nm; t_r (major) = 12.63 min, t_r (minor) = 18.44 min) gave the isomeric composition of the product: 97% ee. $[\alpha]_D^{20}$ = -228.6 (c = 1.00, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$/TMS) δ 7.27-7.43 (m, 5H), 4.93 (d, *J* = 3.6 Hz ,1H), 4.84 (d, *J* = 3.6 Hz, 1H), 4.33 (q, *J* = 7.2 Hz, 2H), 3.75 (s, 3H), 1.35 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.1, 158.6, 137.8, 129.4, 128.7, 126.9, 109.0, 78.7, 62.7, 52.7, 52.5, 14.0.



ent-3k (solid): 36h, 69% yield; dr > 99/1. HPLC analysis (Chiralcel OD-H, 30/70 ^{i}PrOH/hexanes, 0.6 mL/min, 238 nm; t_r (minor) = 15.09 min, t_r (major) = 19.74 min) gave the isomeric composition of the product: -99% ee. $[\alpha]_D^{20}$ = 216.0 (c = 0.50, $CHCl_3$).



3l (oil): 39h, 30% yield, dr = 80/20. HPLC analysis (Chiralcel OD-H, 1/15 ^{i}PrOH/hexanes, 0.5 mL/min, 238 nm; t_{r1} (major) = 28.15 min, the other peak was not observed; t_{r2} (major) = 30.30 min, t_{r2} (minor) = 33.59 min) gave the isomeric composition of the product: trans, 99% ee, cis, 88% ee. For trans-isomer: ^{1}H NMR (300 MHz, $CDCl_3$/TMS) δ 4.76 (d, *J* = 2.7 Hz, 1H), 4.22 (dq, *J* = 2.1, 6.9 Hz, 2H), 3.82 (s, 3H), 3.58 (dd, *J* = 2.1 Hz, 3 Hz, 1H), 2.33 (hepta, *J* = 3.9 Hz, 1H). 1.26 (t, *J* = 7.8 Hz, 3H), 1.02 (d, *J* = 7.2 Hz, 3H), 0.91 (d, *J* = 7.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.9, 159.0, 108.3, 72.5, 62.2, 53.5 52.6, 29.2, 19.5, 16.6, 13.9. MS (EI, *m/*z, rel. intensity) 242 (M^+-OH, 2.09), 186 (45.42), 144 (45.88), 142 (42.86), 100 (86.76), 85 (42.29), 59 (100.00), 43 (45.50), 41 (36.26). Anal. calcd for $C_{11}H_{17}NO_6$: C, 50.96; H, 6.61; N, 5.40. Found: C, 51.40; H, 6.76; N, 5.20.

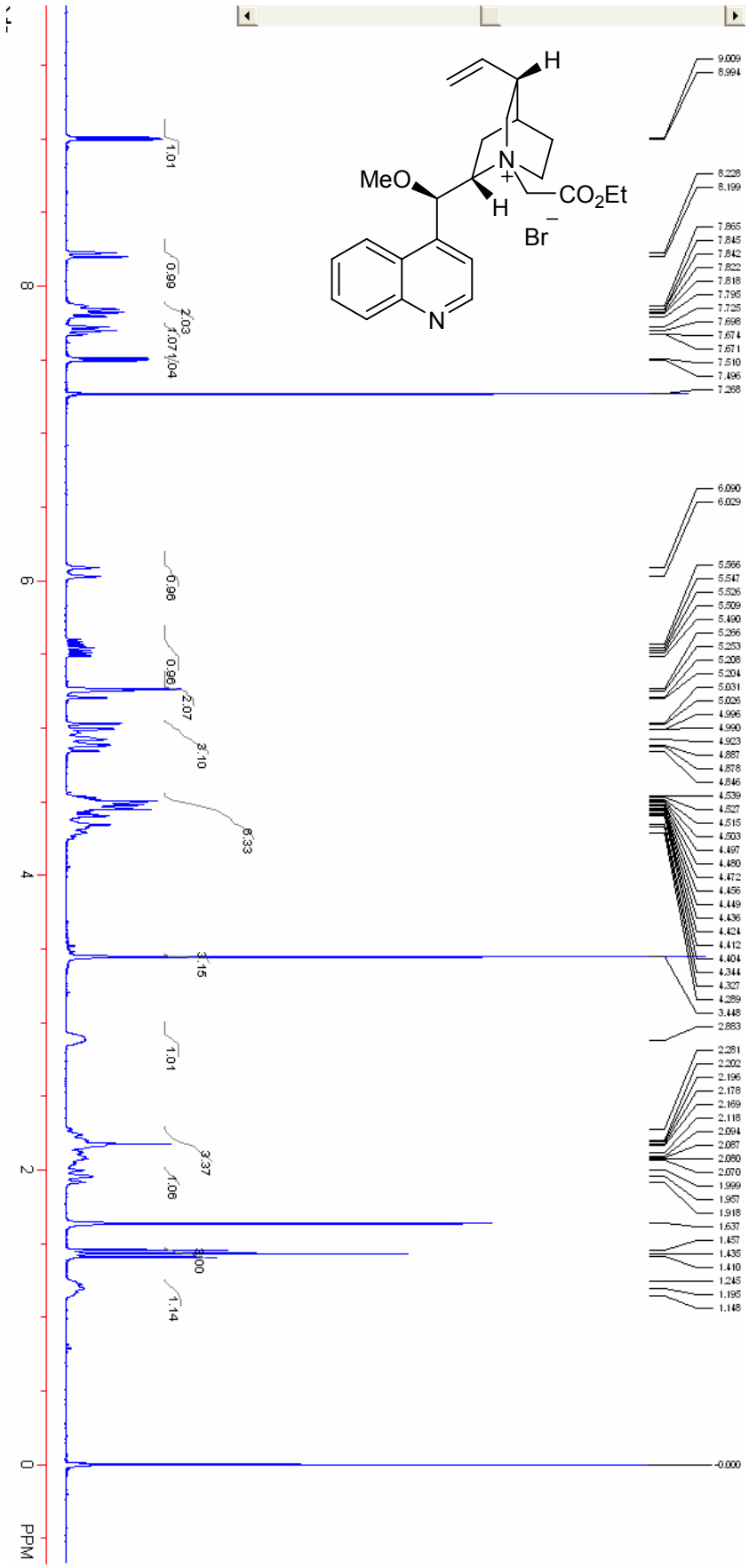
References:

1. Fornicola, R. S.; Oblinger, E.; Montgomery, J. *J. Org. Chem.* **1998**, *63*, 3528.
2. Papageo, C. D.; Ley, S. V.; Gaunt, M. J. *Angew. Chem. Int. Ed.* **2003**, *42*, 828.
3. Kaji, E.; Zen, S. *Chem. Pharm. Bull.* **1980**, *28*, 479.

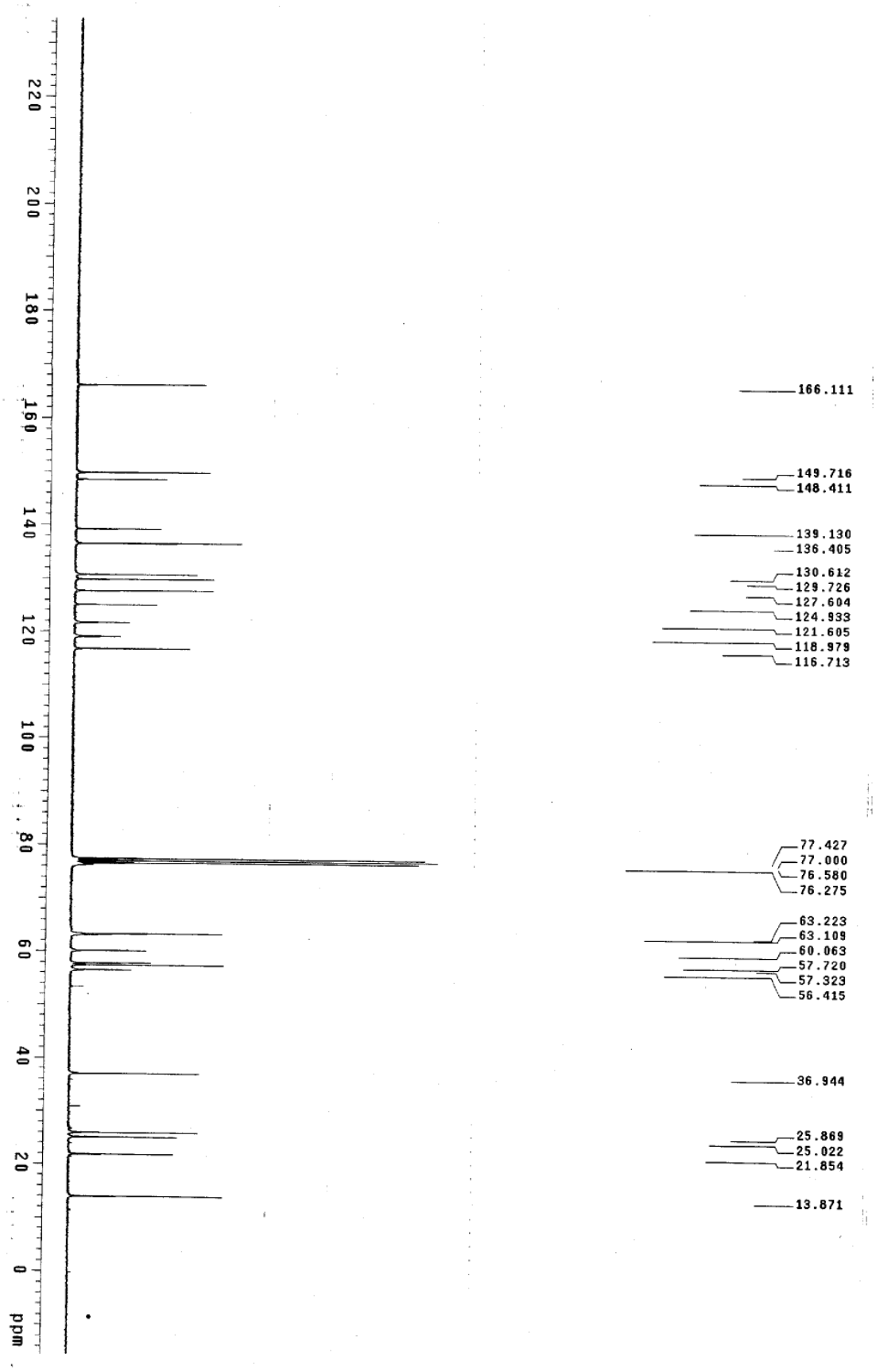
.

NMR spectra for new compounds

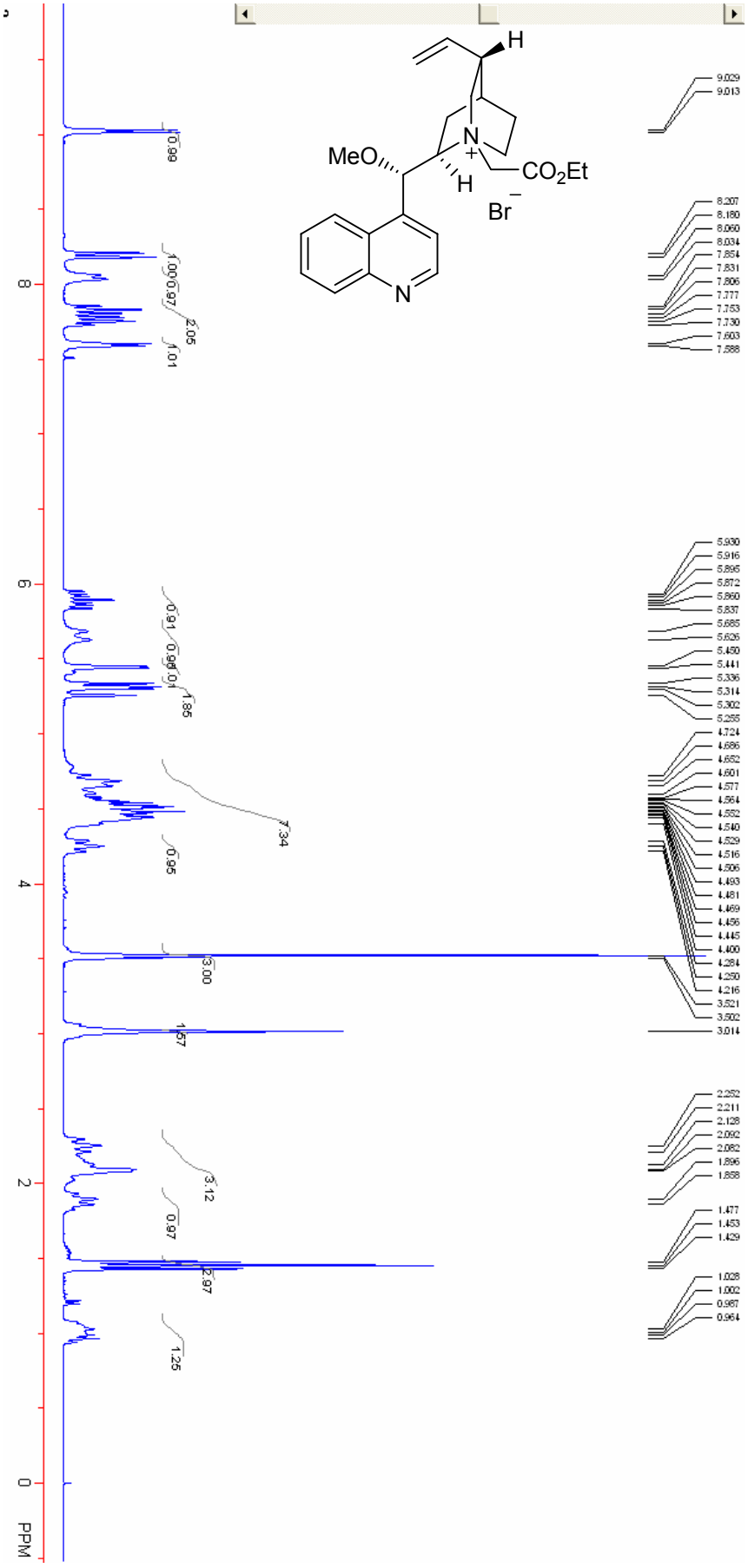
^{1}H NMR **1a**



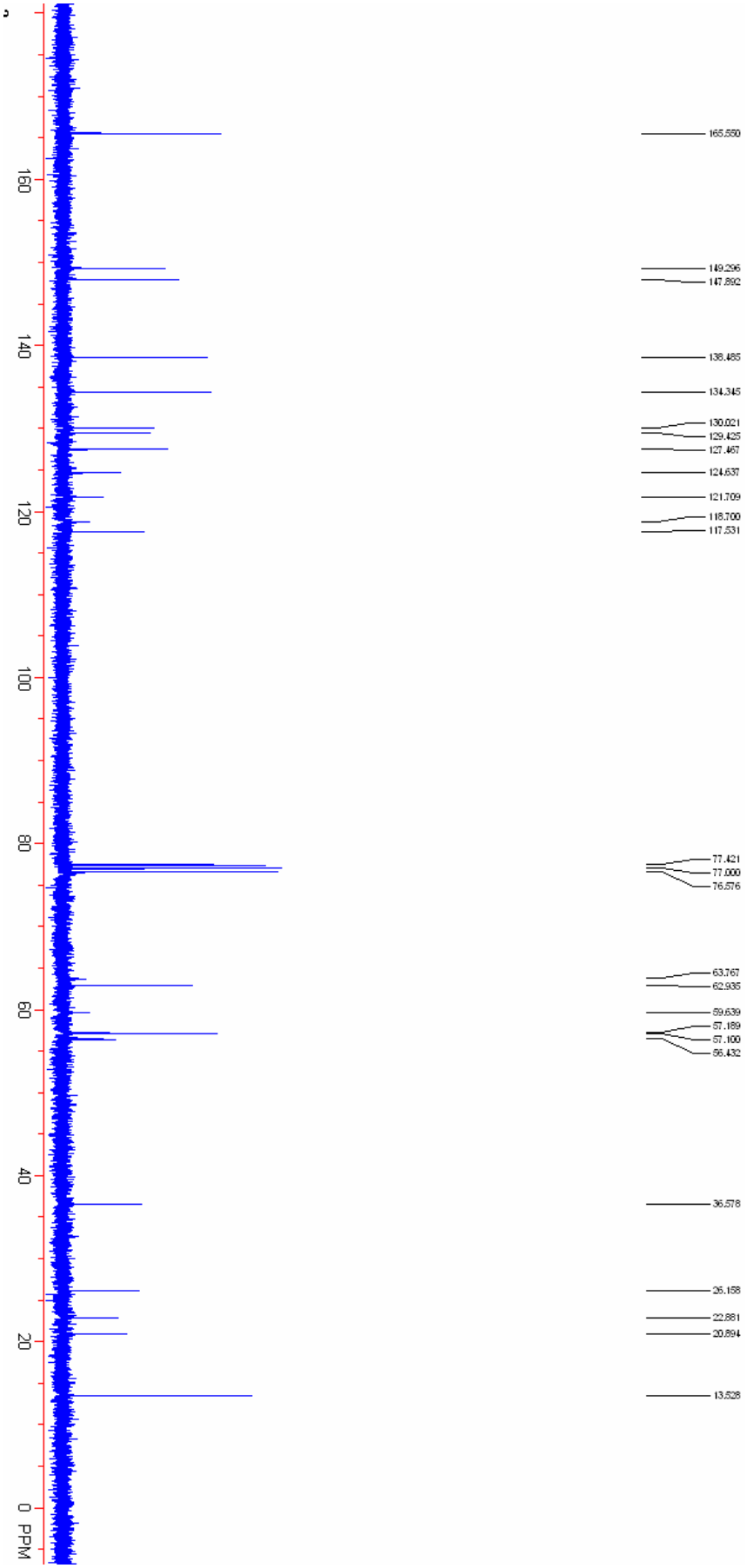
^{13}C NMR **1a**


166.111
149.716
148.411
139.130
136.405
130.612
129.726
127.604
124.933
121.605
118.979
116.713
77.427
77.000
76.580
76.275
63.223
63.109
60.063
57.720
57.323
56.415
36.944
25.869
25.022
21.854
13.871
220
200
180
160
140
120
100
80
60
40
20
0
ppm

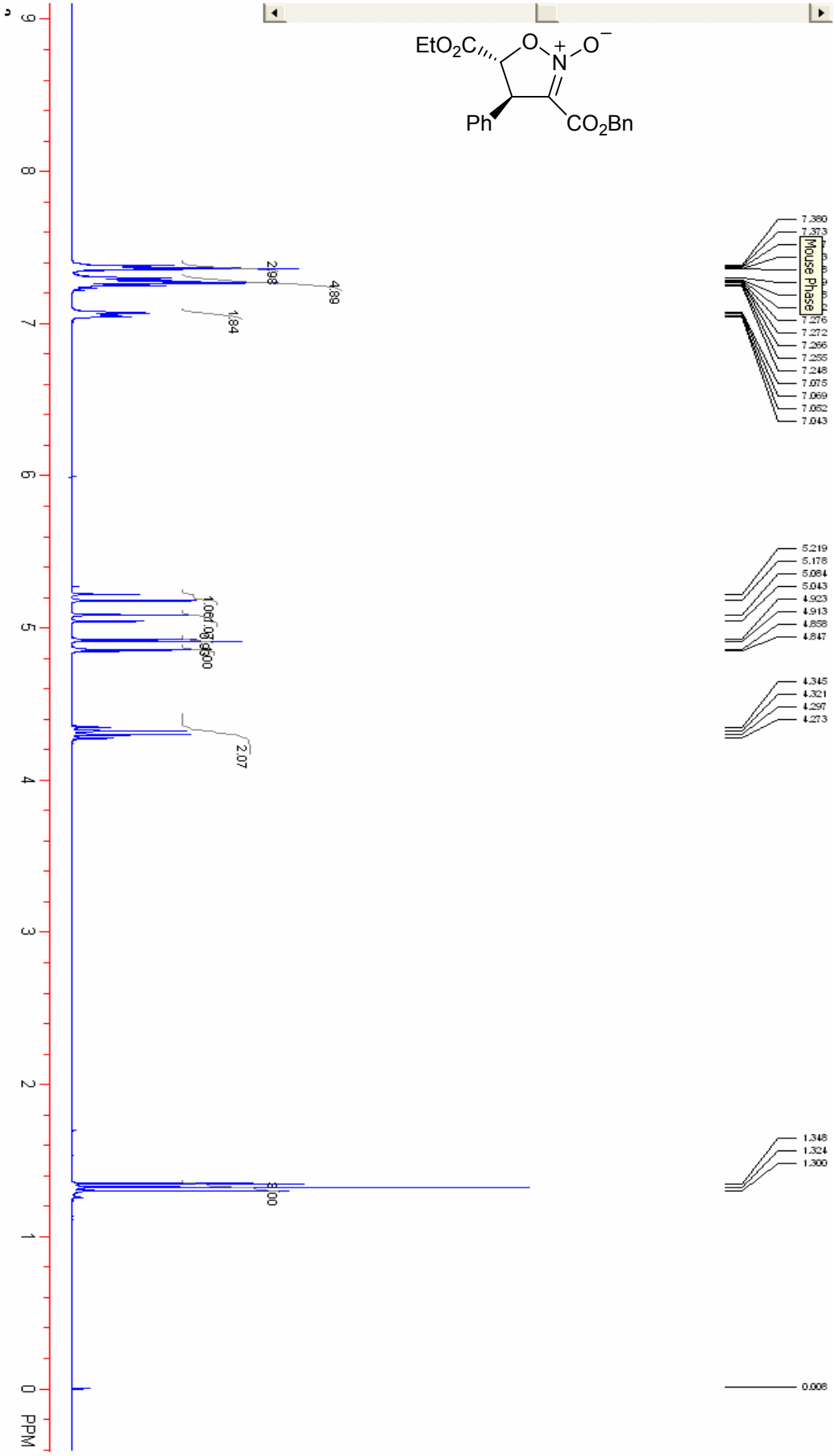
^{1}H NMR **1b**



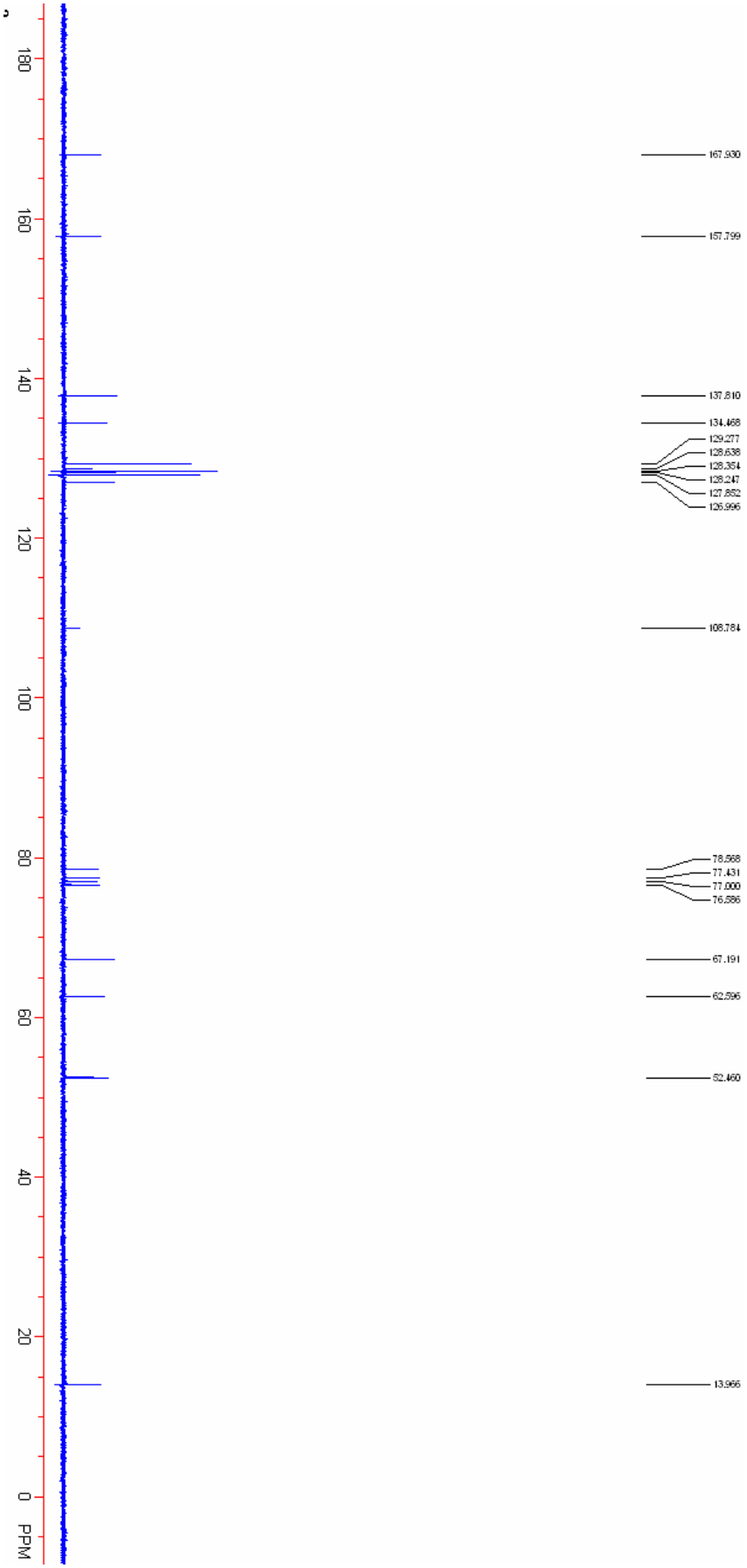
^{13}C NMR **1b**


165.550
149.296
147.892
138.485
134.345
130.021
129.425
127.467
124.637
121.709
118.700
117.531
77.421
77.000
76.576
63.767
62.935
59.639
57.189
57.100
56.432
36.578
26.158
22.881
20.894
13.528
160
140
120
100
80
60
40
20
0 PPM

^{1}H NMR **3a**



^{13}C NMR **3a**


180
160
140
120
100
80
60
40
20
0
PPM
167.930
157.799
137.810
134.468
129.277
128.638
128.354
128.247
127.882
126.996
108.784
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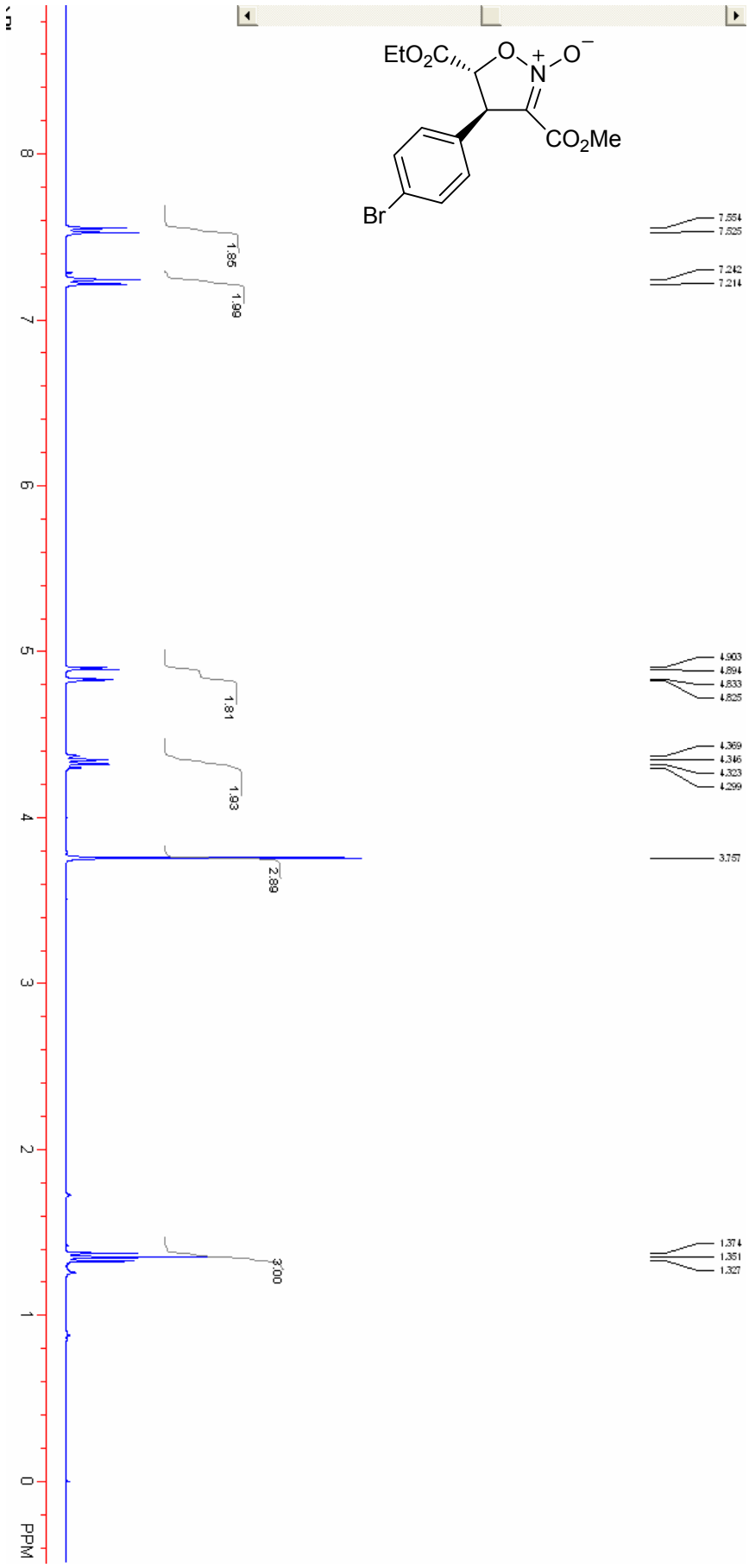
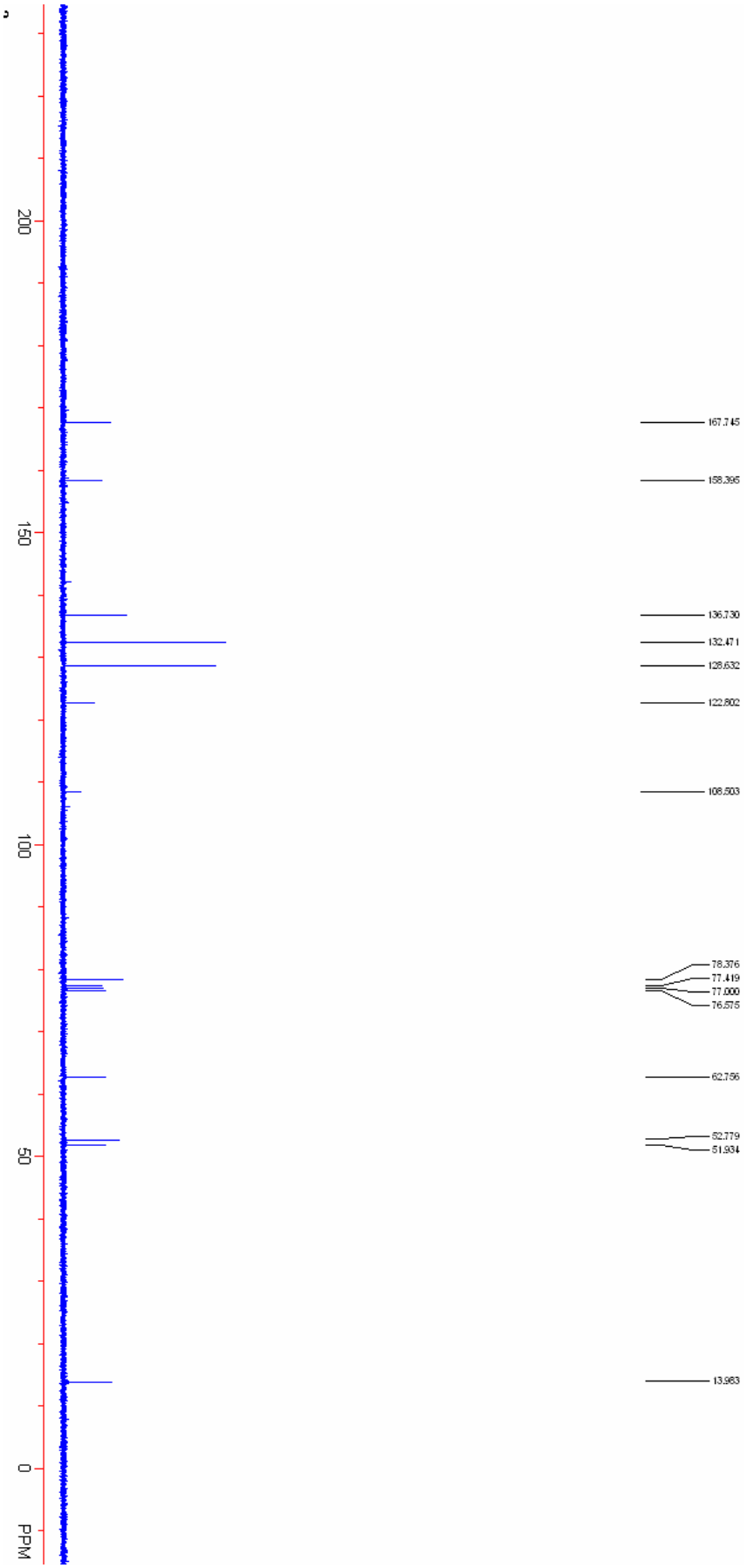
76.586
67.191
62.596
52.460
13.966

^{1}H NMR **3b**



^{13}C NMR **3b**


200
150
100
50
0
PPM
167.745
158.395
136.730
132.471
128.632
122.802
108.503
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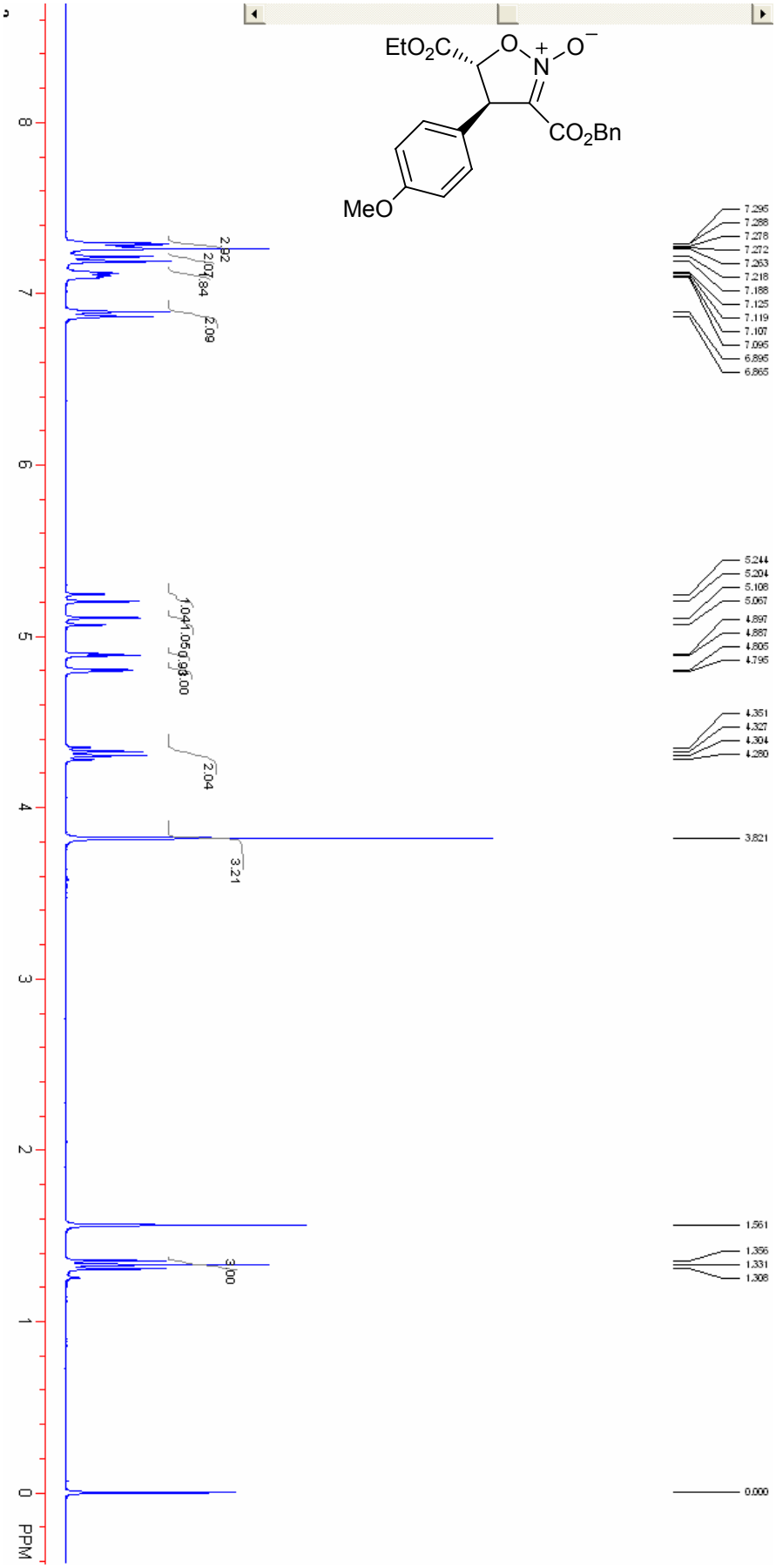
77.419
77.000
76.575
62.756
52.779
51.934
13.963

^{1}H NMR **3c**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O
N
O
CO2Bn
MeO
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7.278
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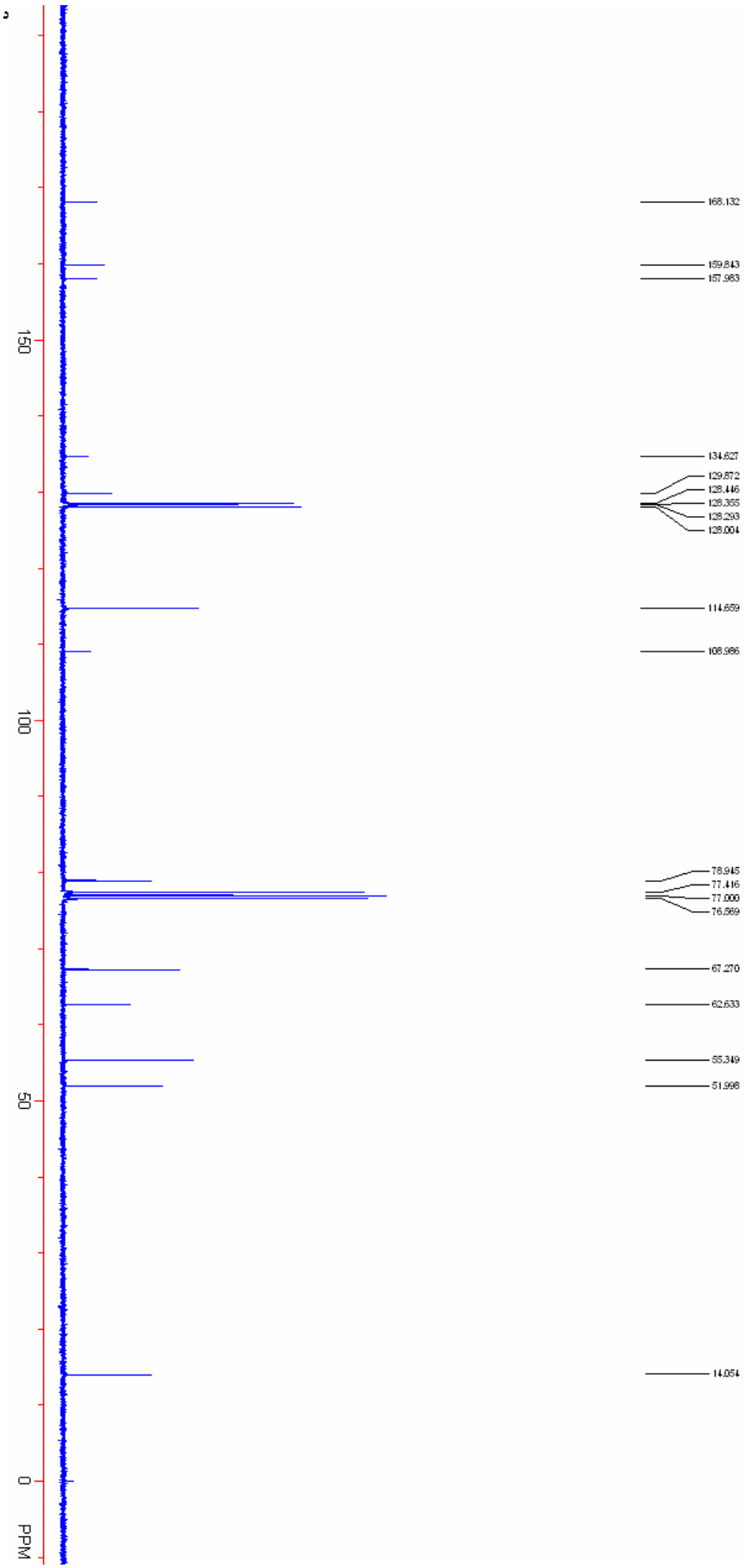
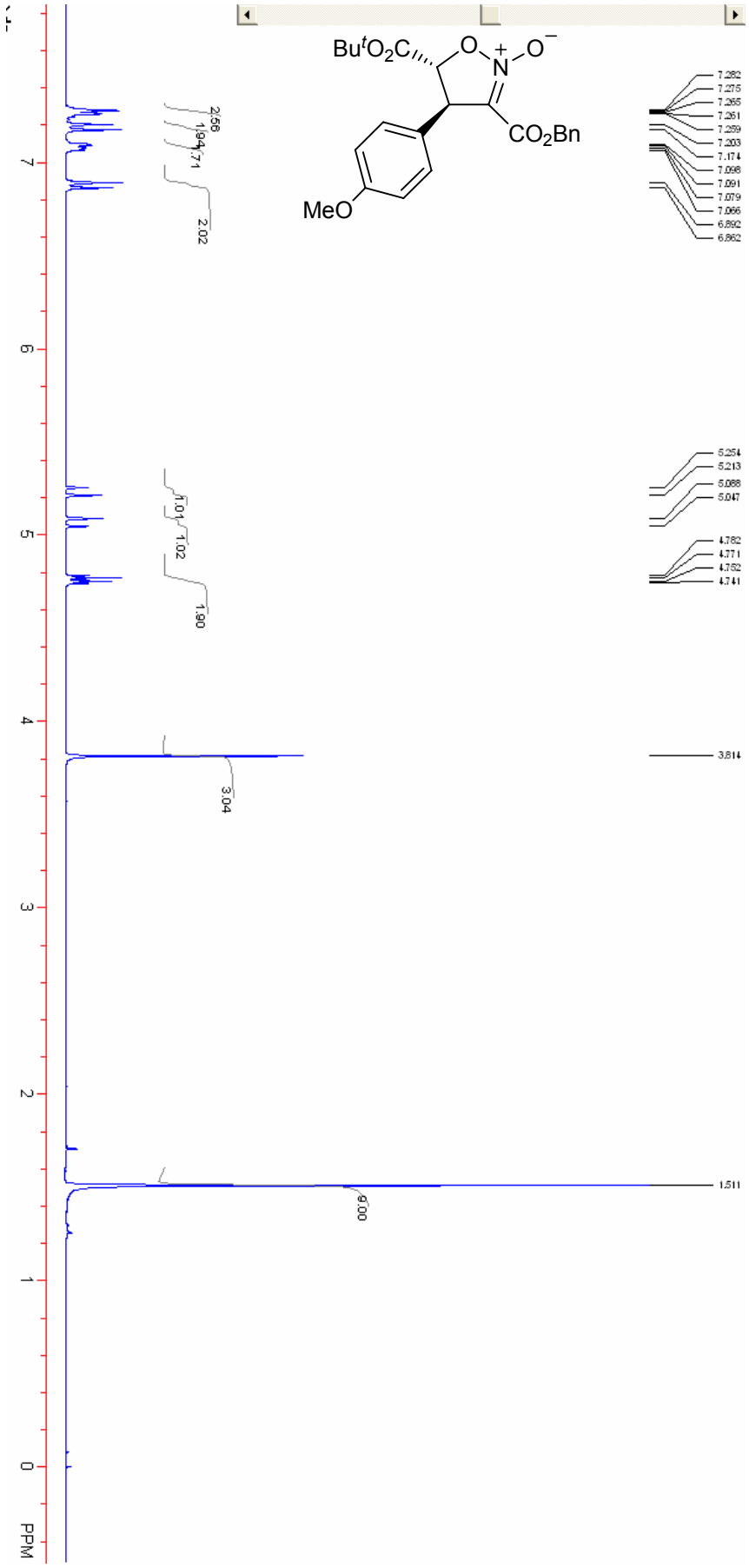
7.263
7.218
7.188
7.125
7.119
7.107
7.095
6.895
6.865
5.244
5.204
5.108
5.067
4.897
4.887
4.805
4.795
4.351
4.327
4.304
4.280
3.821
1.561
1.356
1.331
1.308
0.000
2.92
2.07
1.84
2.09
1.04
1.05
1.96
3.00
2.04
3.21
3.00
PPM

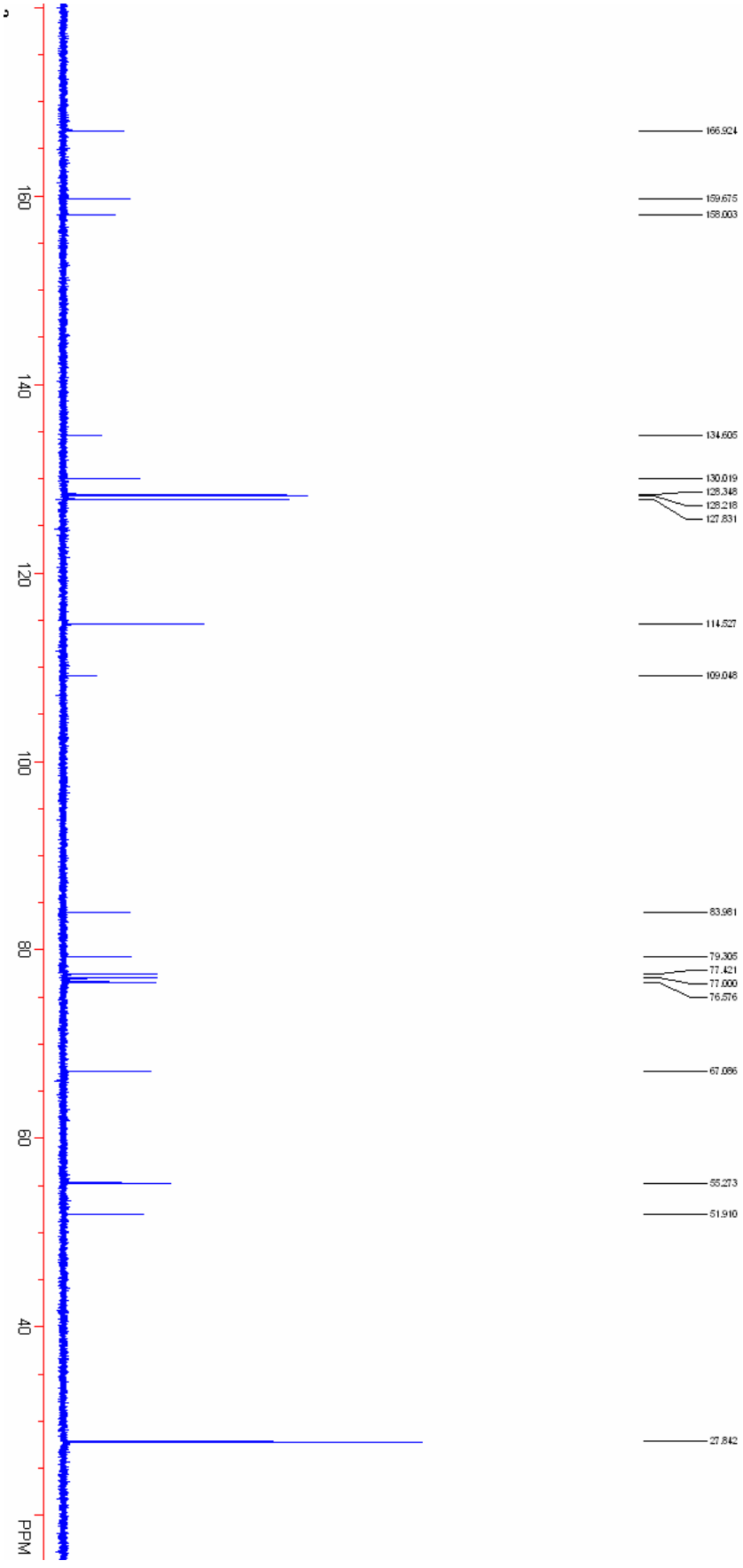
^{13}C NMR **3c**


168.132
159.843
157.983
134.627
129.872
128.446
128.355
128.293
128.004
114.659
108.986
78.945
77.416
77.000
76.569
67.270
62.633
55.349
51.998
14.054
150
100
50
0
PPM

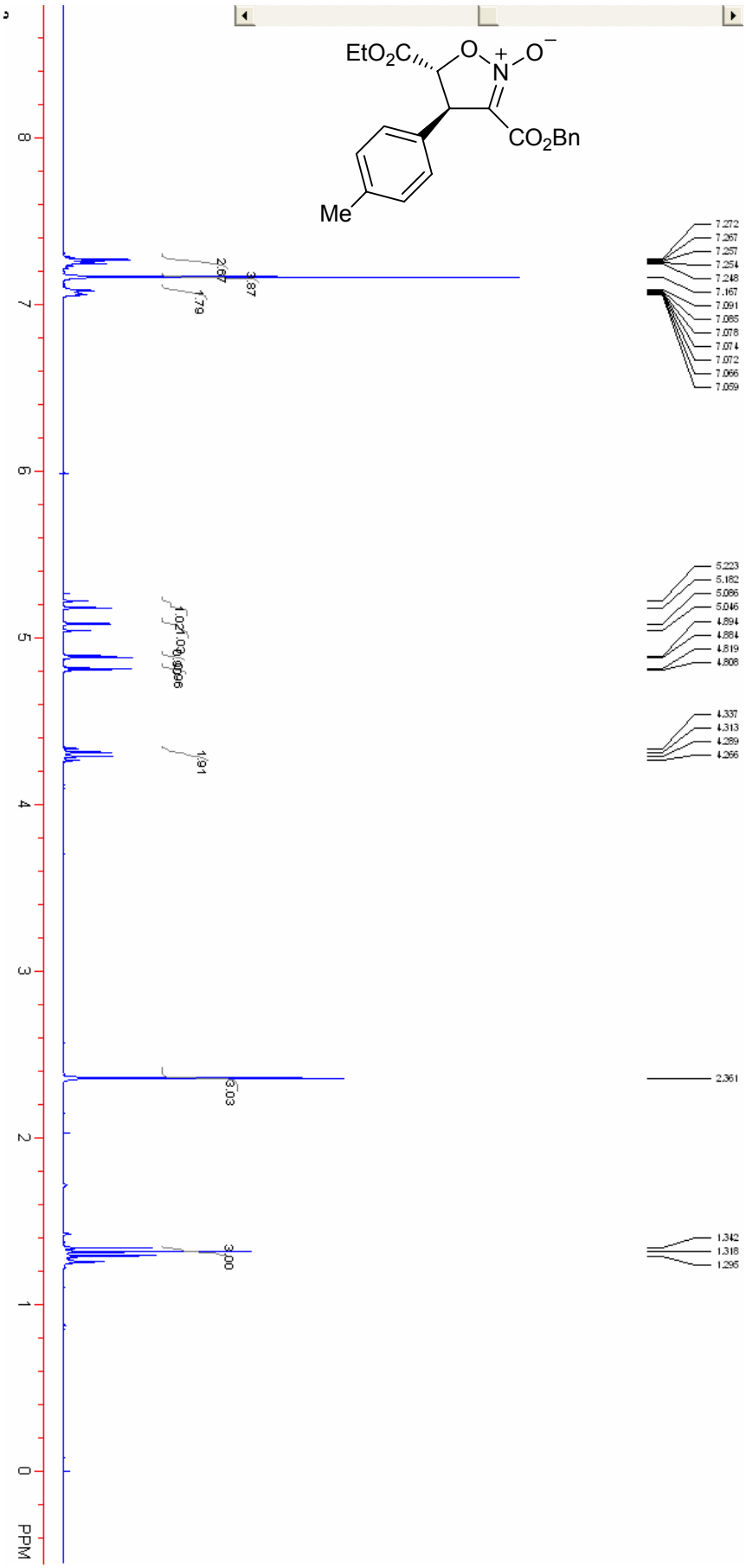
^{1}H NMR **3d**


Bu^{t}O$_2$C
O
N
O
CO$_2$Bn
MeO
7.282
7.275
7.265
7.261
7.259
7.203
7.174
7.098
7.091
7.079
7.066
6.892
6.862
5.254
5.213
5.088
5.047
4.782
4.771
4.752
4.741
3.814
1.511
2.56
1.94
1.71
2.02
1.01
1.02
1.90
3.04
9.00
PPM

^{13}C NMR **3d**



^{1}H NMR **3e**


EtO2C
O
N
O
CO2Bn
Me
7.272
7.267
7.257
7.254
7.248
7.167
7.091
7.085
7.078
7.074
7.072
7.066
7.059
5.223
5.182
5.086
5.046
4.894
4.884
4.819
4.808
4.337
4.313
4.289
4.266
2.361
1.342
1.318
1.295
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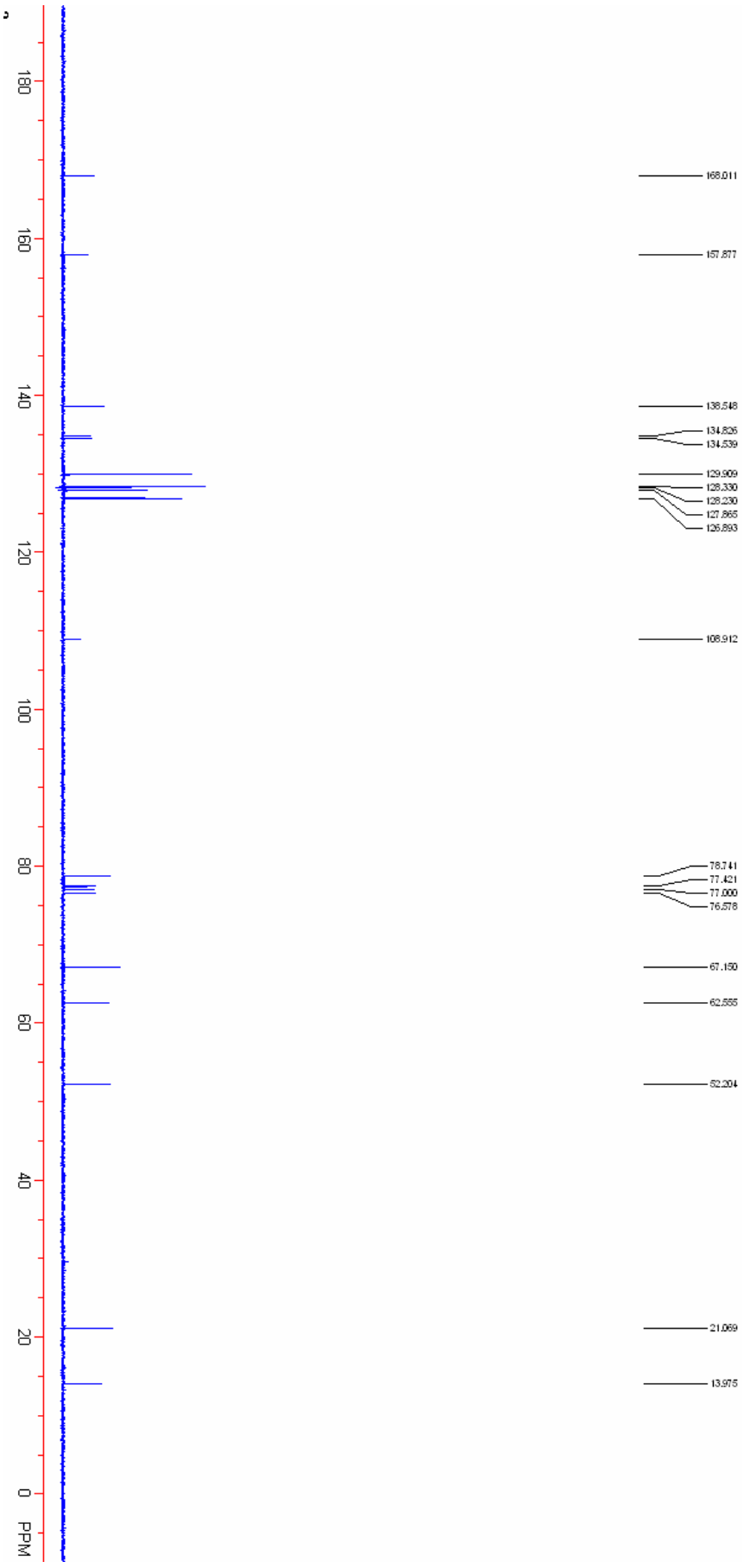
1.79
1.91
3.03
3.00
PPM

^{13}C NMR **3e**


168.011
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134.539
129.909
128.330
128.230
127.865
126.893
108.912
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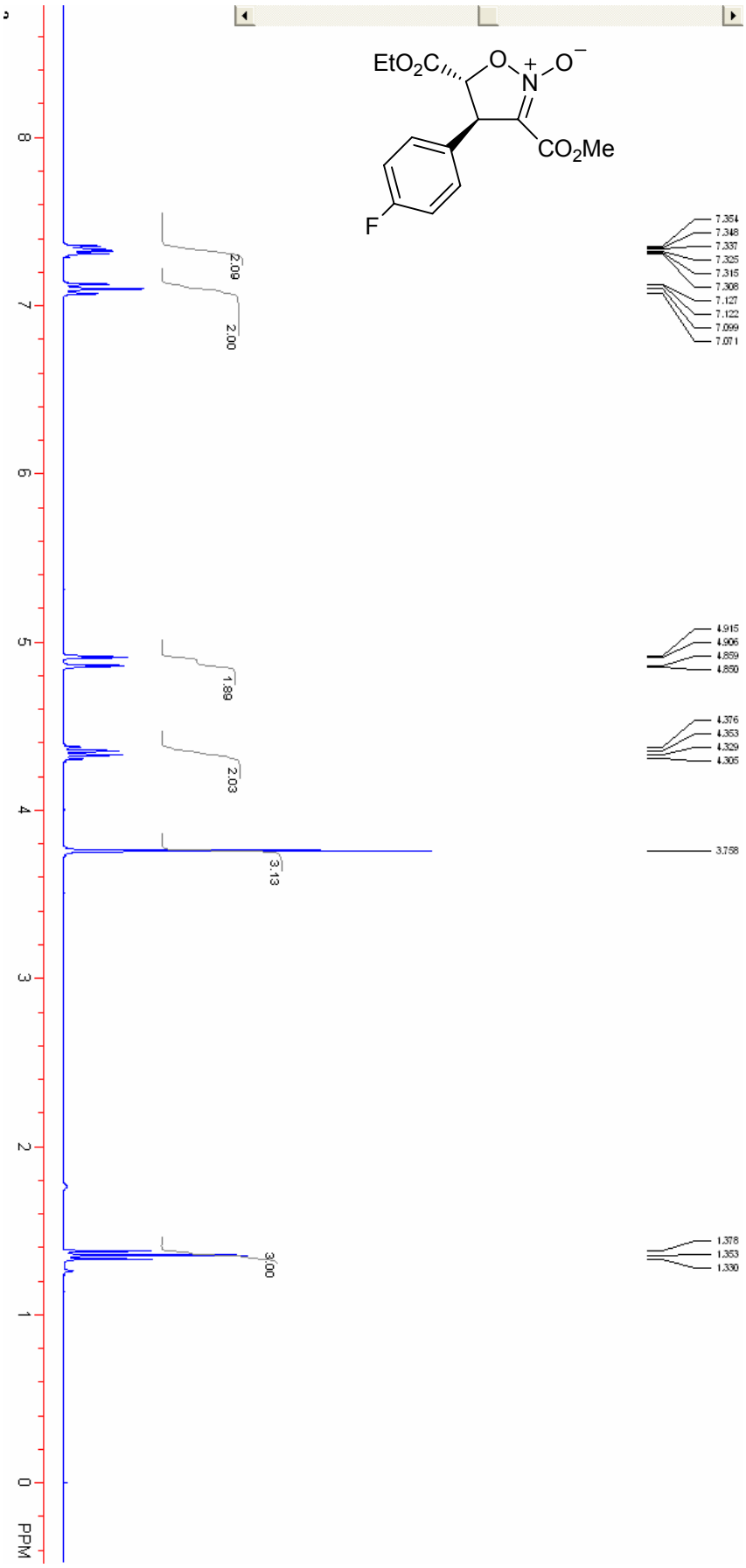
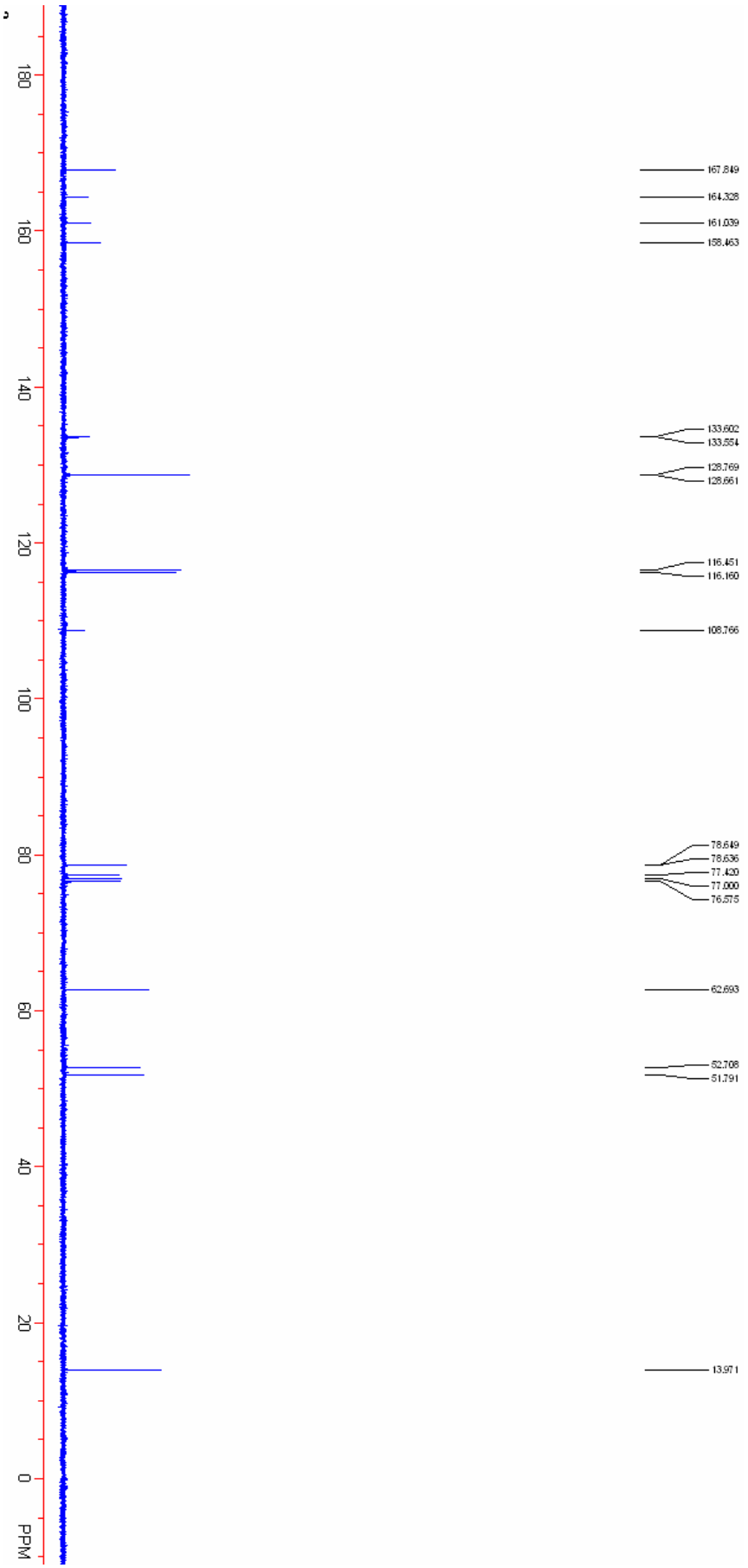
77.421
77.000
76.578
67.150
62.555
52.204
21.069
13.975
180
160
140
120
100
80
60
40
20
0
PPM

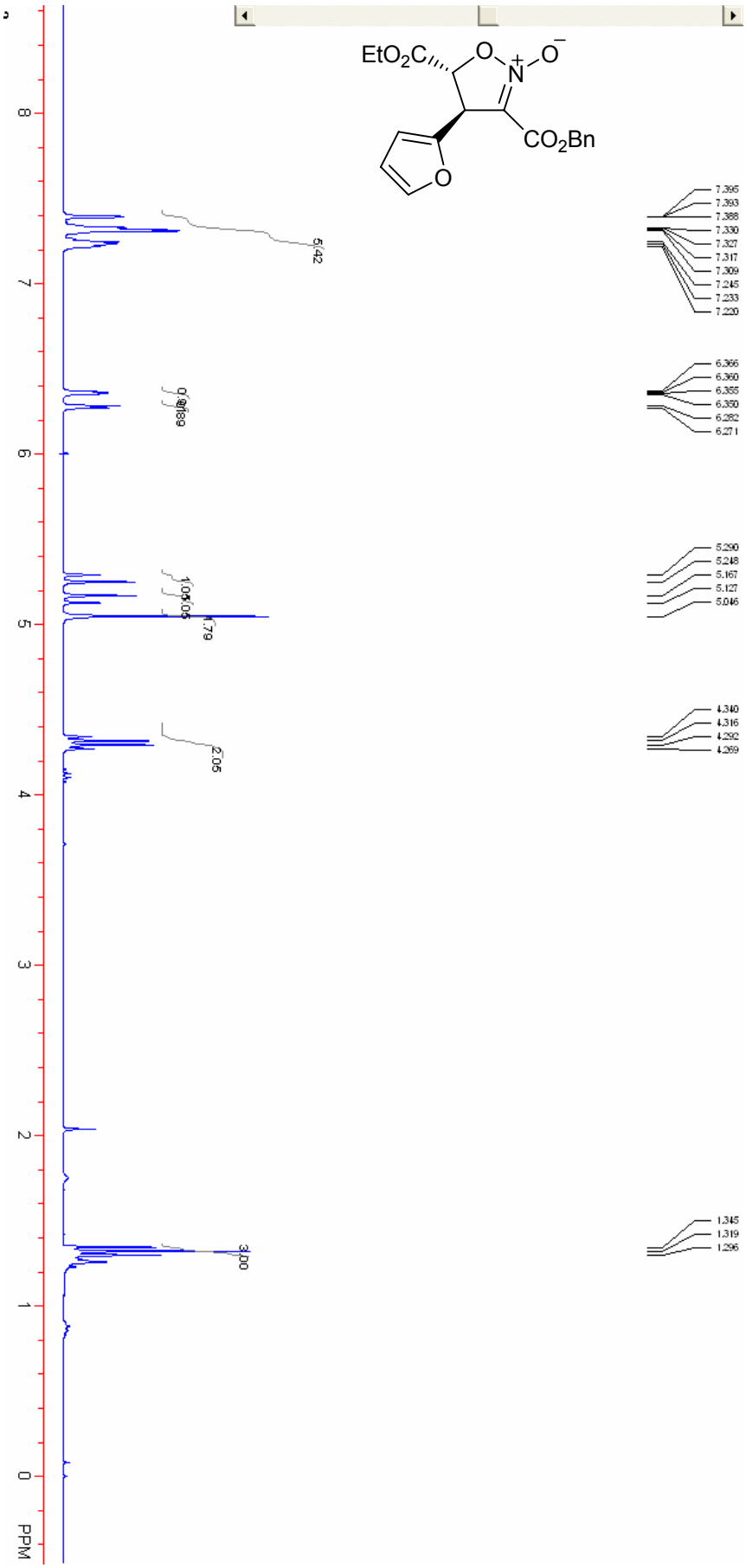
^{1}H NMR **3f**



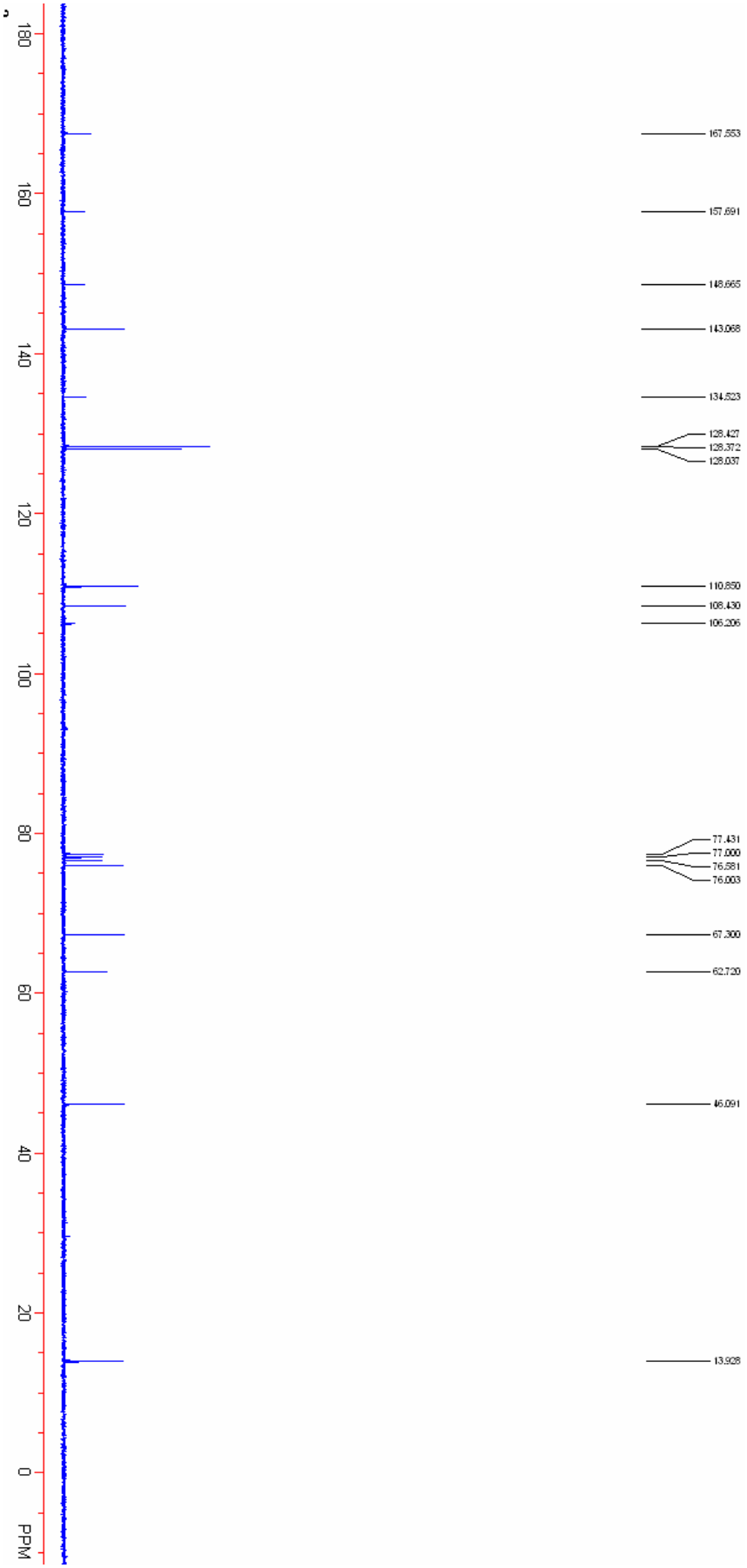
^{13}C NMR **3f**


167.849
164.328
161.039
158.463
133.602
133.554
128.769
128.661
116.451
116.160
108.766
78.649
78.636
77.420
77.000
76.575
62.693
52.708
51.791
13.971
180
160
140
120
100
80
60
40
20
0
PPM

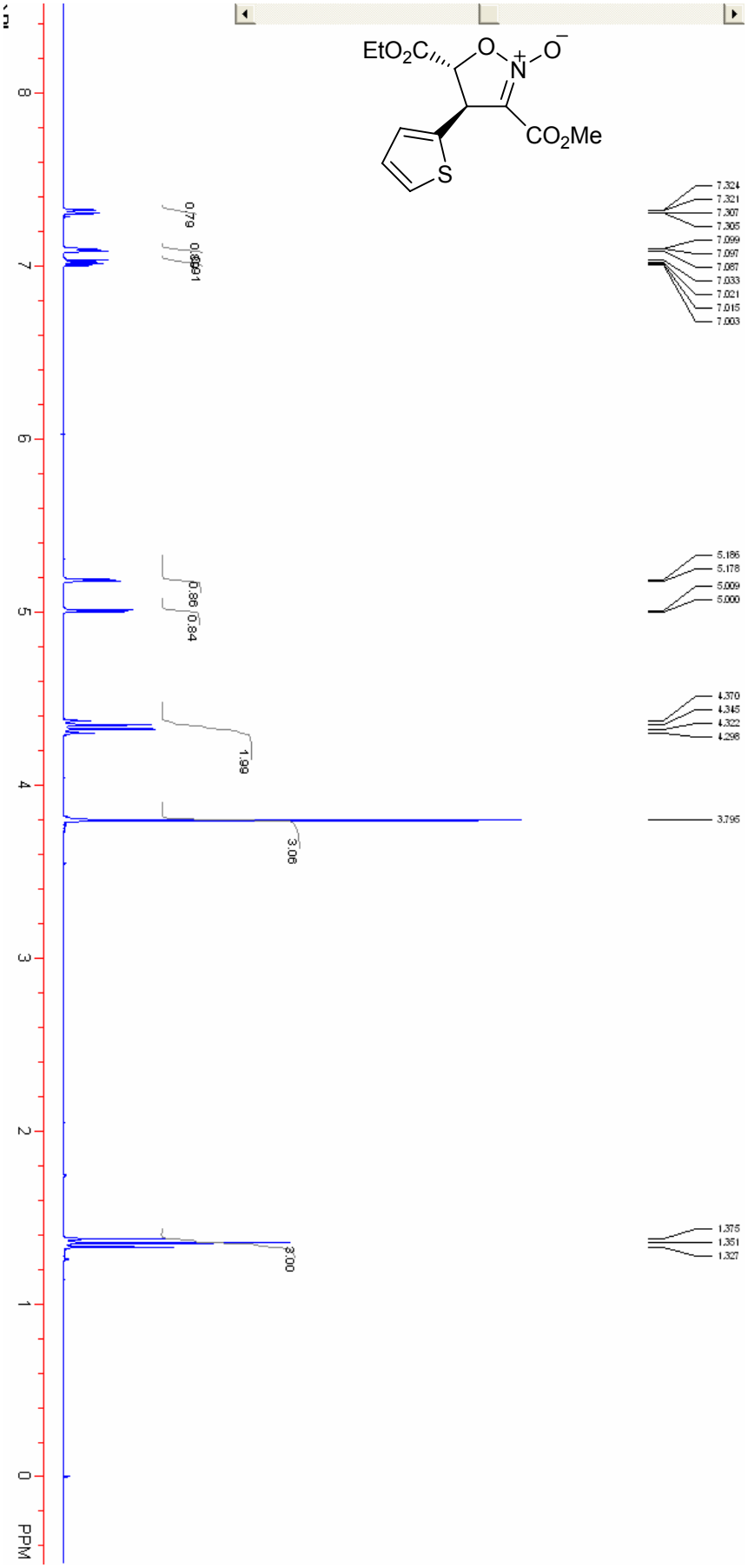
^{1}H NMR **3g**



^{13}C NMR **3g**



^{1}H NMR **3h**


EtO2C
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N
O
CO2Me
S
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7.307
7.305
7.099
7.097
7.087
7.033
7.021
7.015
7.003
5.186
5.178
5.009
5.000
4.370
4.345
4.322
4.298
3.795
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1.351
1.327
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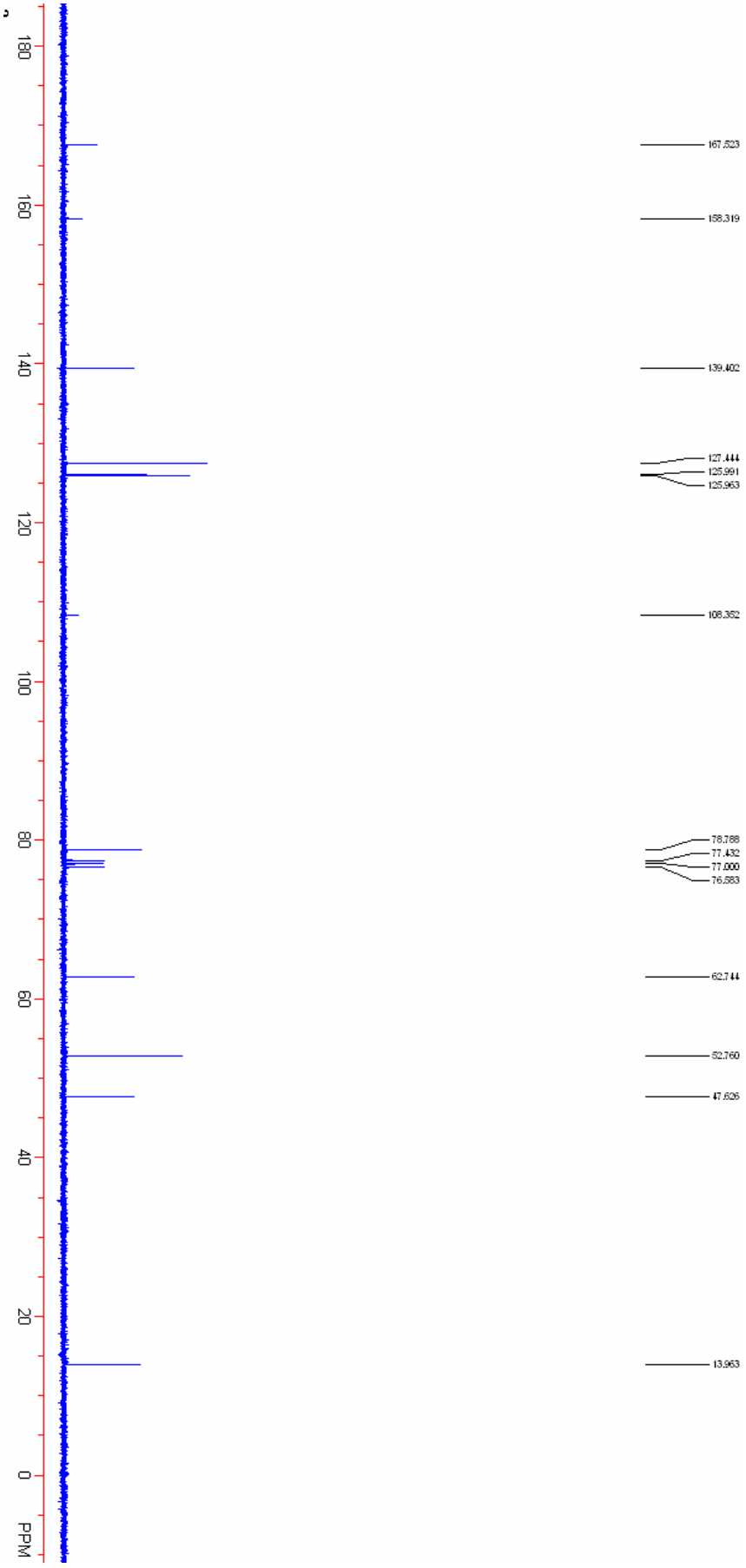
0.86
0.84
1.99
3.06
3.00
PPM

^{13}C NMR **3h**


180
160
140
120
100
80
60
40
20
0
PPM
167.523
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139.402
127.444
125.991
125.963
108.352
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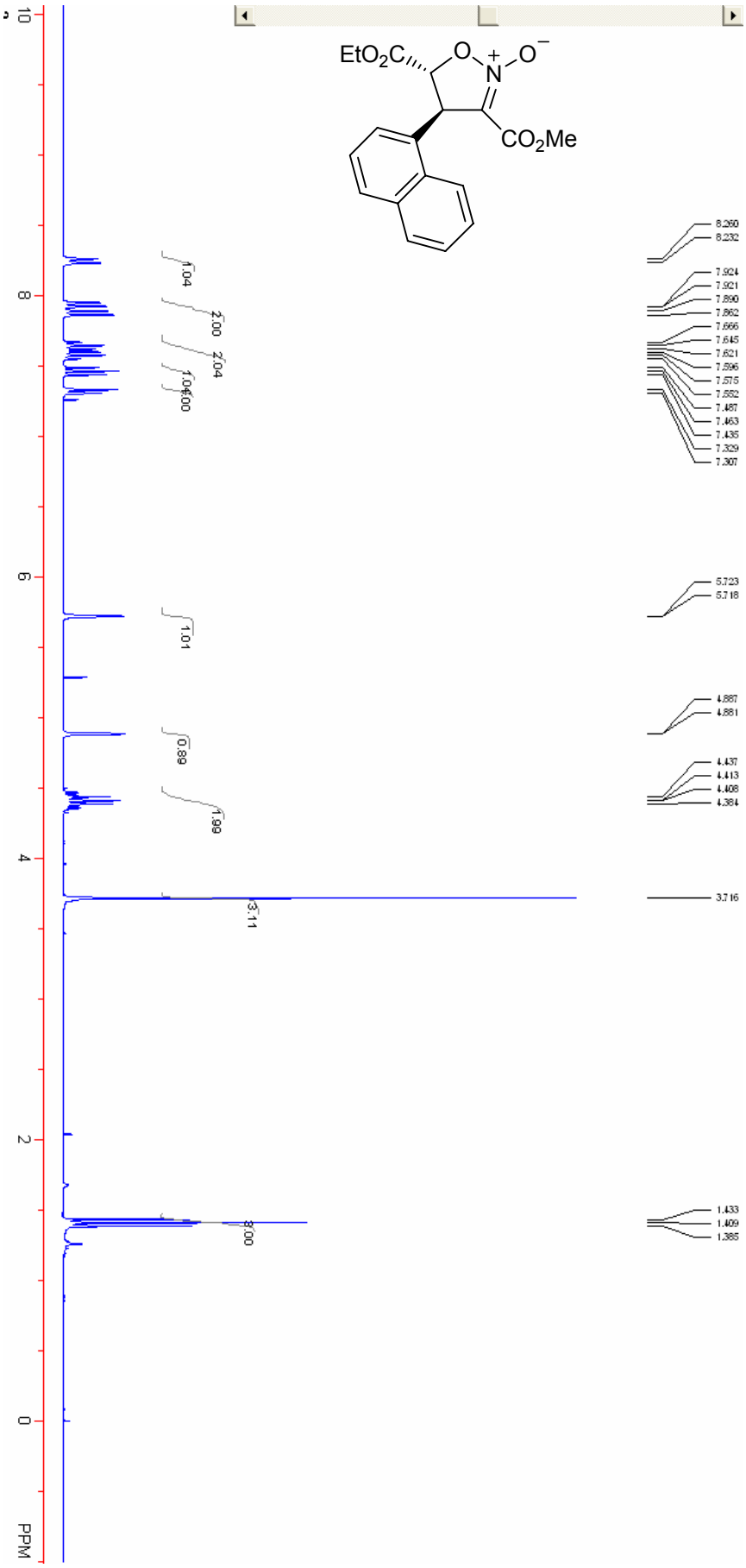
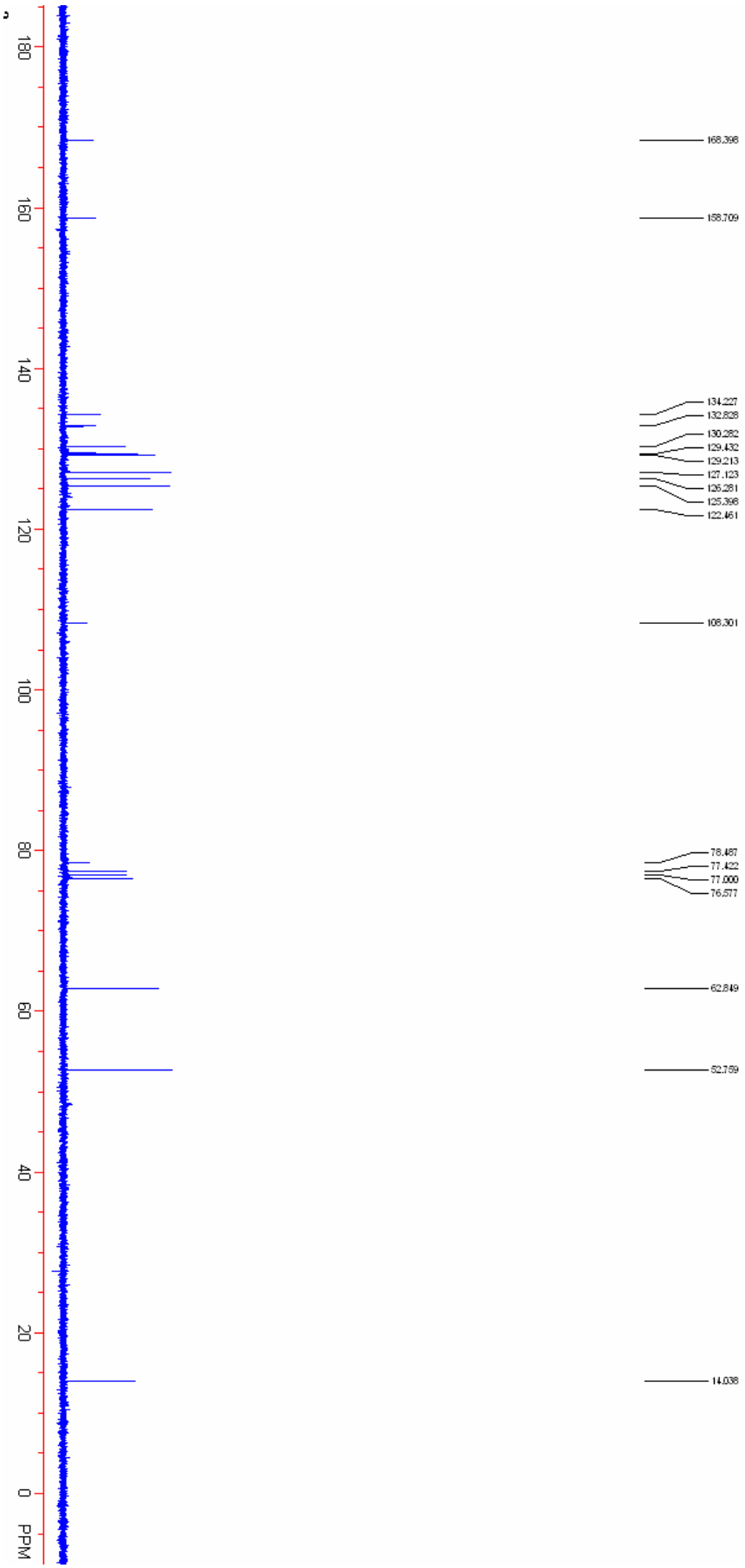
77.000
76.583
62.744
52.760
47.626
13.963

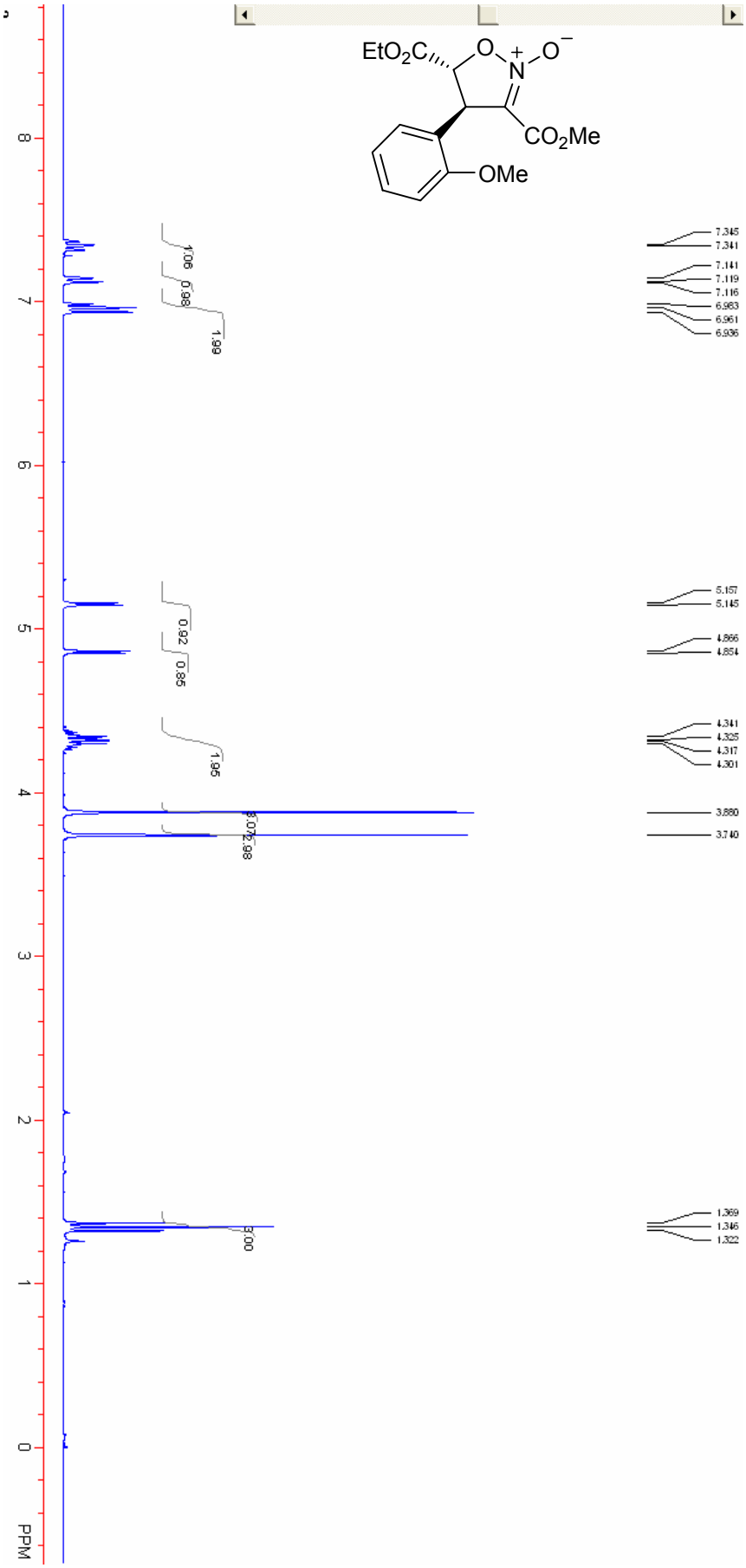
^{1}H NMR **3i**


EtO2C
O
+
N
O
−
CO2Me
8.260
8.232
7.924
7.921
7.890
7.862
7.666
7.645
7.621
7.596
7.575
7.552
7.487
7.463
7.435
7.329
7.307
5.723
5.718
4.887
4.881
4.437
4.413
4.408
4.384
3.716
1.433
1.409
1.385
1.04
2.00
2.04
1.04
1.00
1.01
0.89
1.99
3.11
8.00
10
8
6
4
2
0
PPM

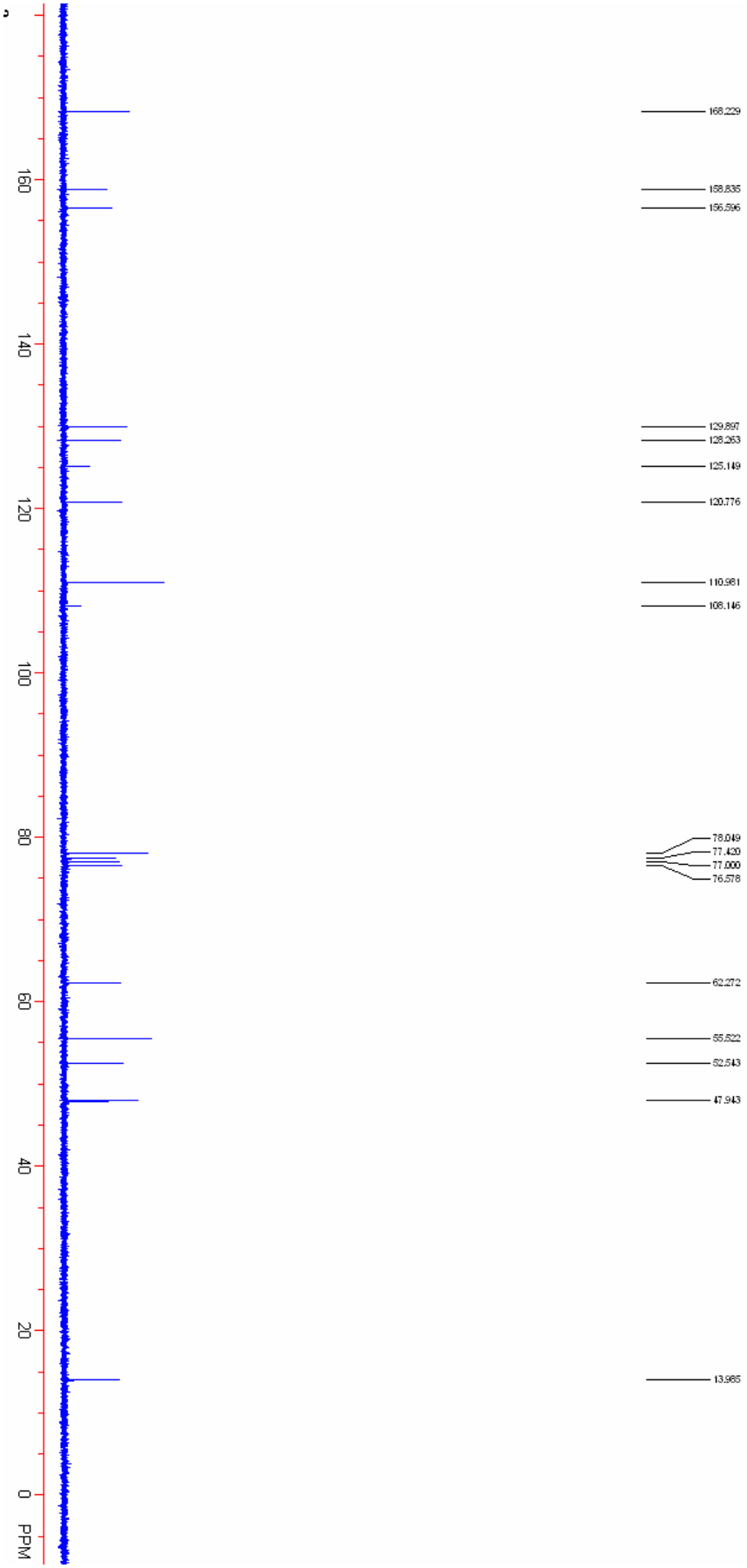
^{13}C NMR **3i**


180
160
140
120
100
80
60
40
20
0
PPM
168.398
158.709
134.227
132.828
130.282
129.432
129.213
127.123
126.281
125.398
122.461
108.301
78.487
77.422
77.000
76.577
62.849
52.759
14.038

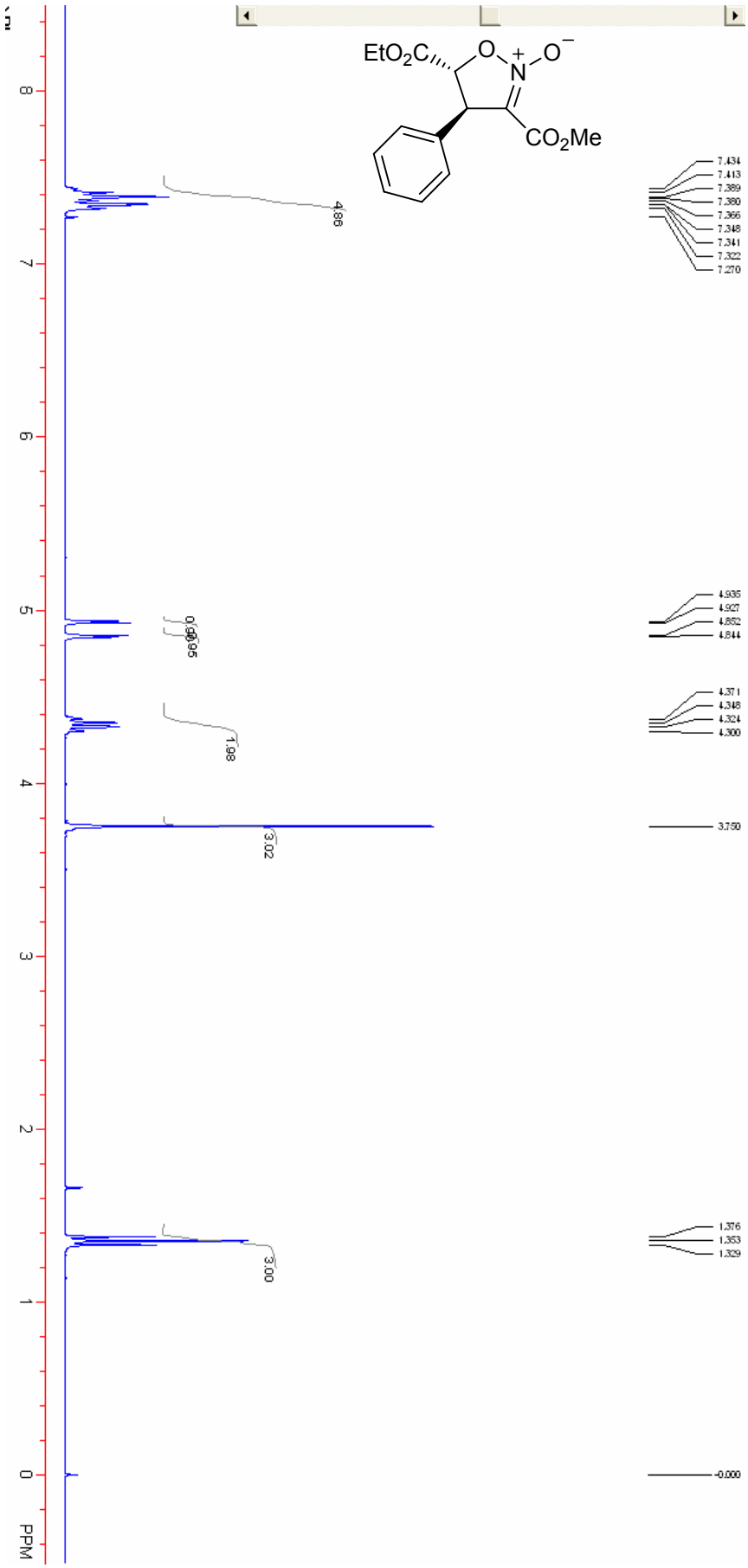
^{1}H NMR **3j**


EtO2C
O
N
O
CO2Me
OMe
7.345
7.341
7.141
7.119
7.116
6.983
6.961
6.936
5.157
5.145
4.866
4.854
4.341
4.325
4.317
4.301
3.880
3.740
1.369
1.346
1.322
1.06
0.98
1.99
0.92
0.86
1.95
8.07
2.98
3.00
PPM

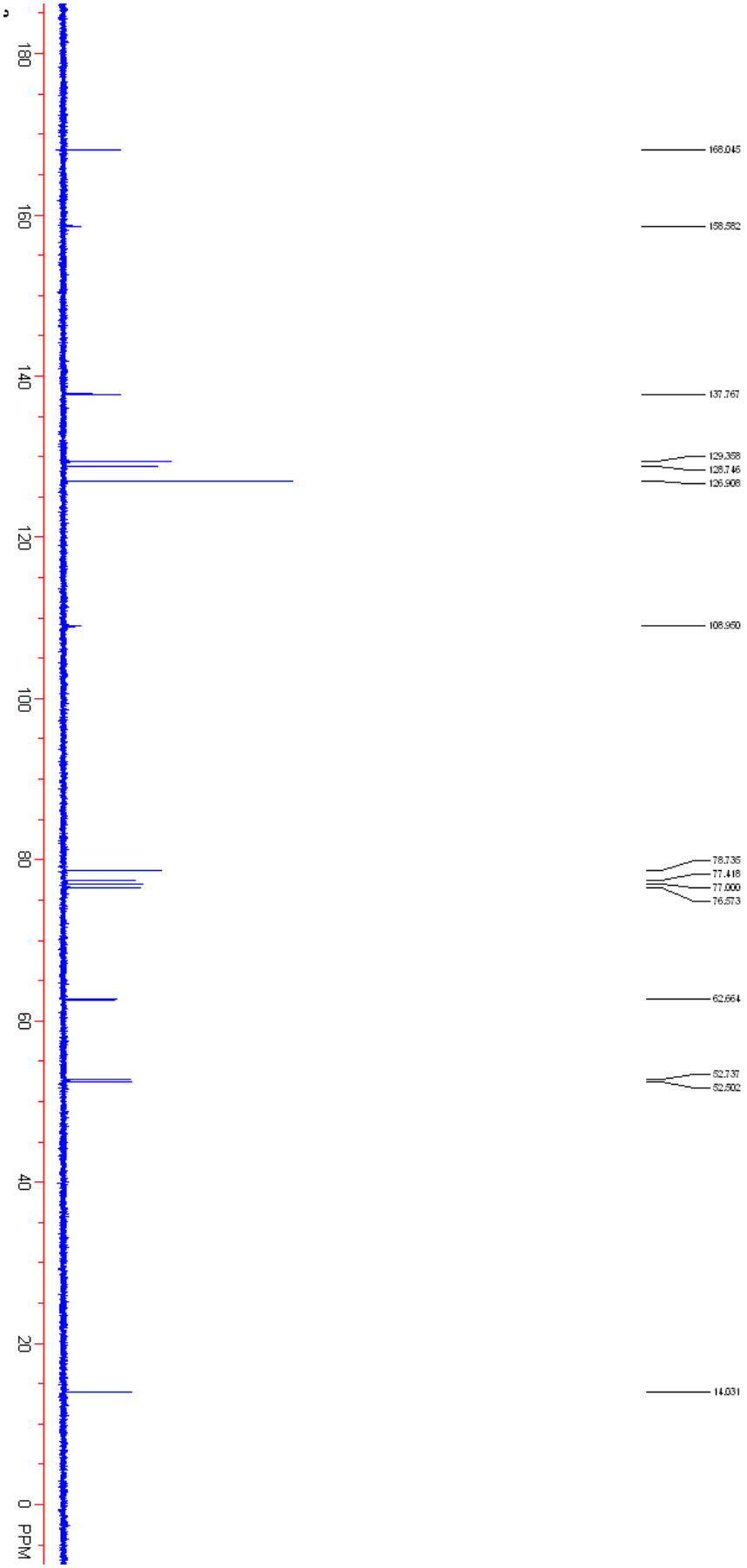
^{13}C NMR **3j**



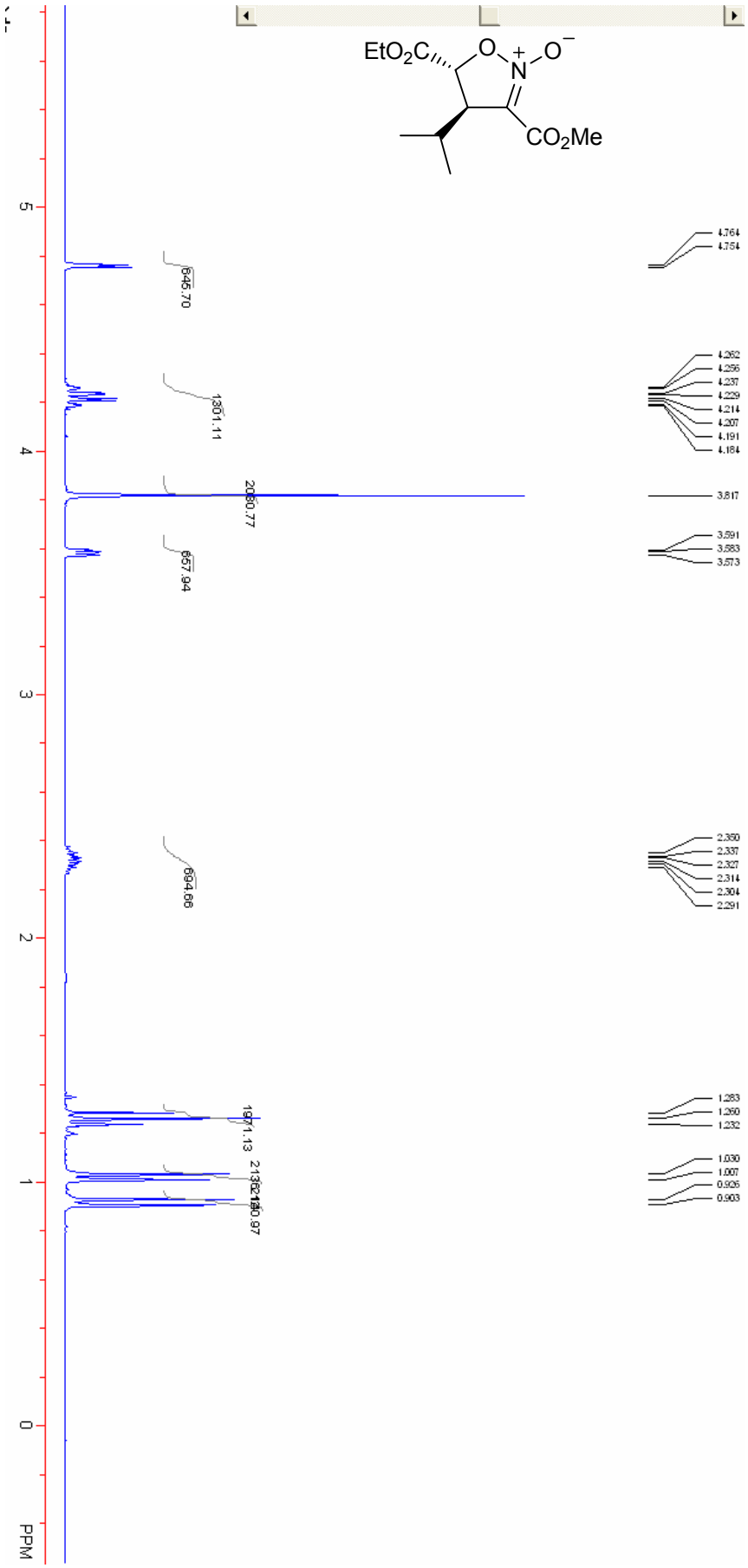
^{1}H NMR **3k**



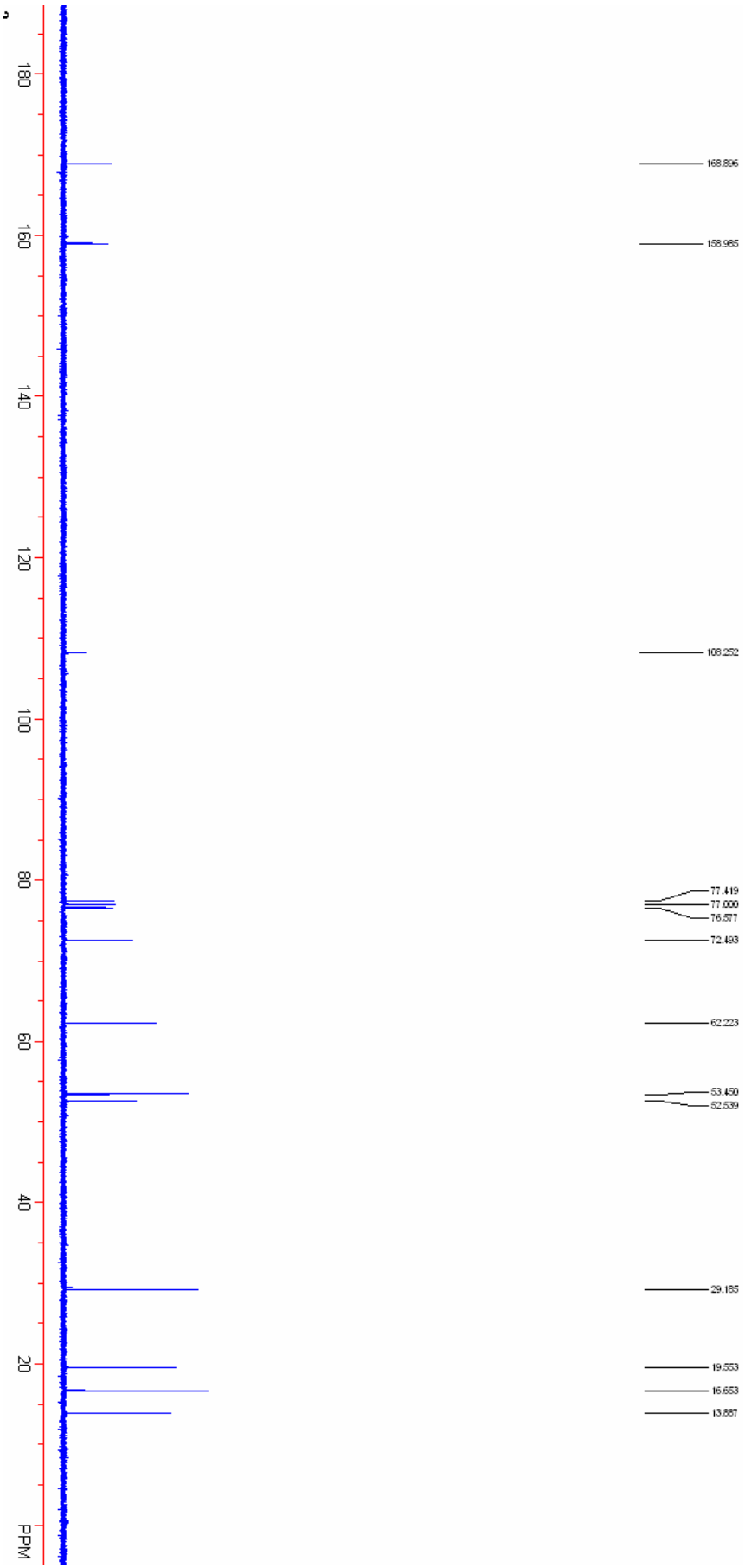
^{13}C NMR **3k**


180
160
140
120
100
80
60
40
20
0
PPM
168.045
158.582
137.767
129.358
128.746
126.908
108.960
78.735
77.418
77.000
76.573
62.664
52.737
52.502
14.031

^{1}H NMR **3l**

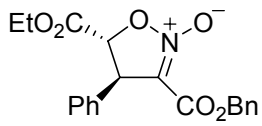


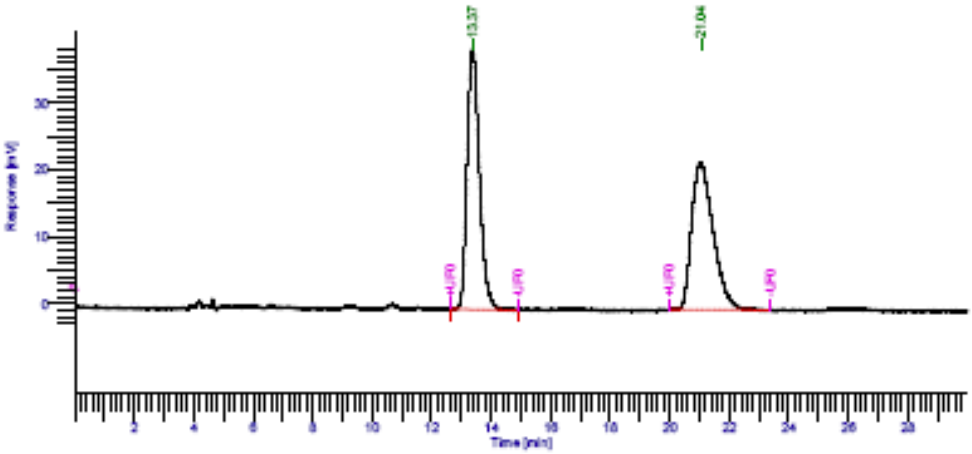
^{13}C NMR **3l**


168.896
158.985
108.252
77.419
77.000
76.577
72.493
62.223
53.450
52.539
29.185
19.553
16.653
13.887
180
160
140
120
100
80
60
40
20
PPM

Part VI: HPLC spectra for compounds 3.

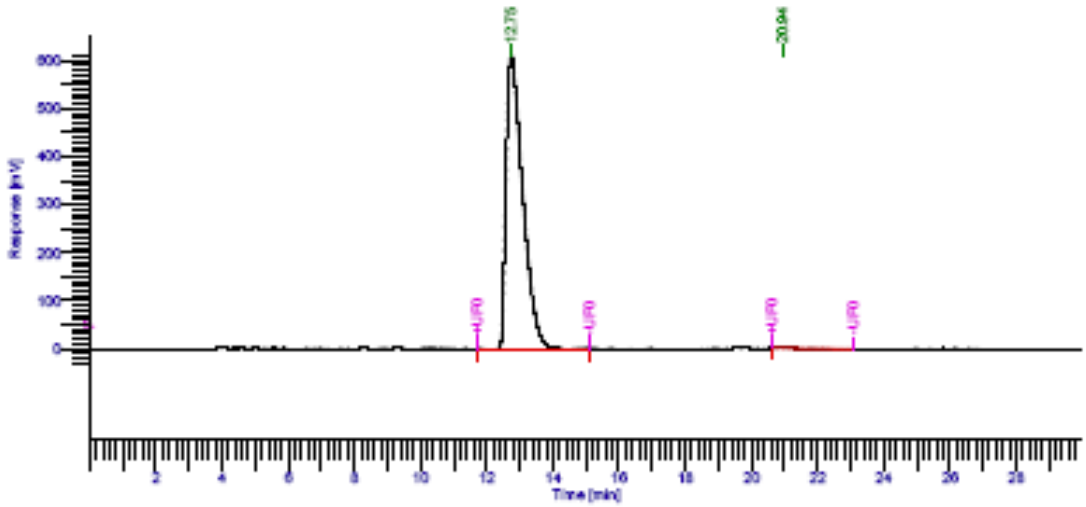
3a





Test REPORT

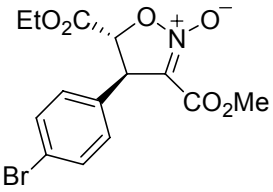
Peak #	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1	13.37	1118683.18	38962.02	50.32
2	21.04	1104403.32	22027.20	49.68
		2223086.50	60969.22	100.00

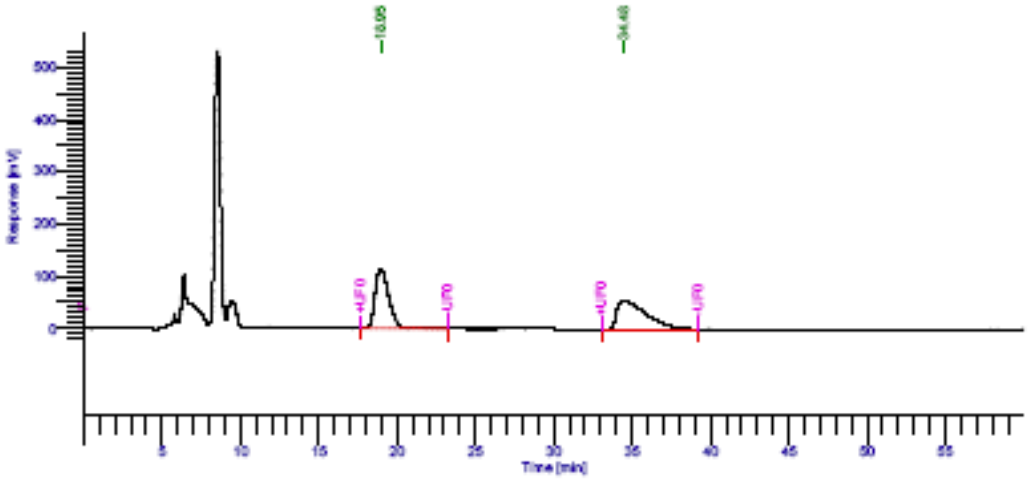


Test REPORT

Peak #	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1	12.75	21436062.96	612240.83	99.85
2	20.94	32124.38	1457.57	0.15
		21468187.34	613698.40	100.00

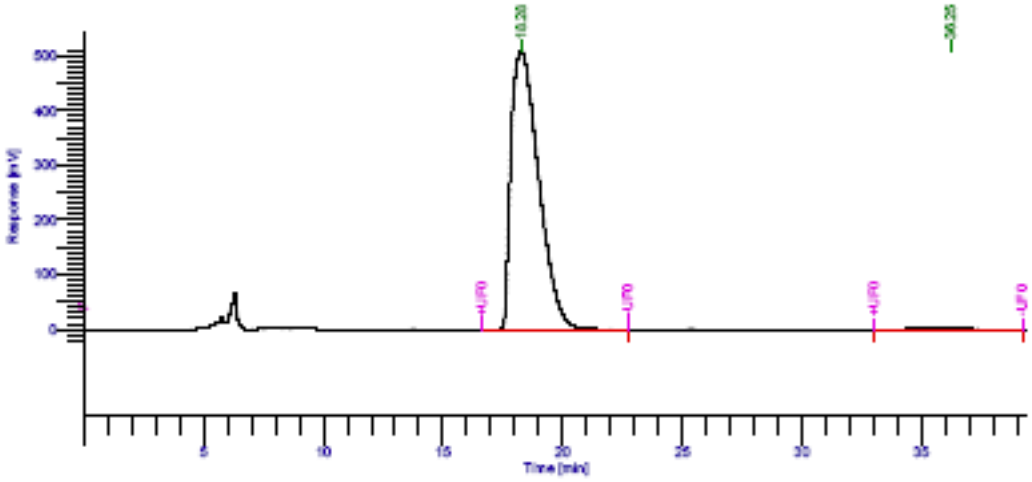
3b





Test REPORT

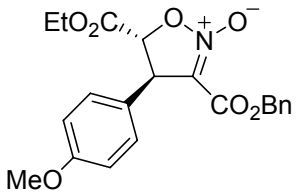
Peak #	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1	18.95	6839634.81	112711.01	49.95
2	34.48	6853475.60	54636.39	50.05
		13693310.42	167347.40	100.00

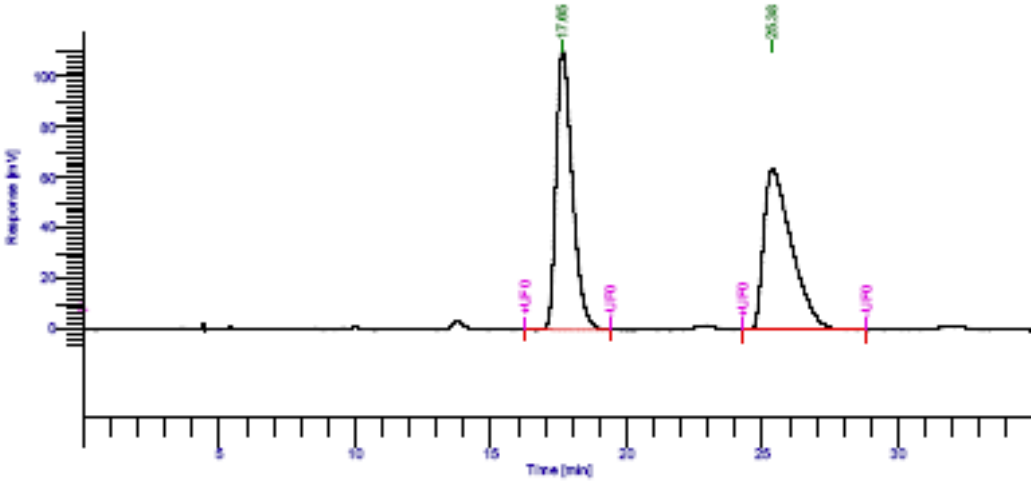


Test REPORT

Peak #	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1	18.28	40831328.59	510502.95	99.09
2	36.25	374970.83	2367.98	0.91
		41206299.42	512870.94	100.00

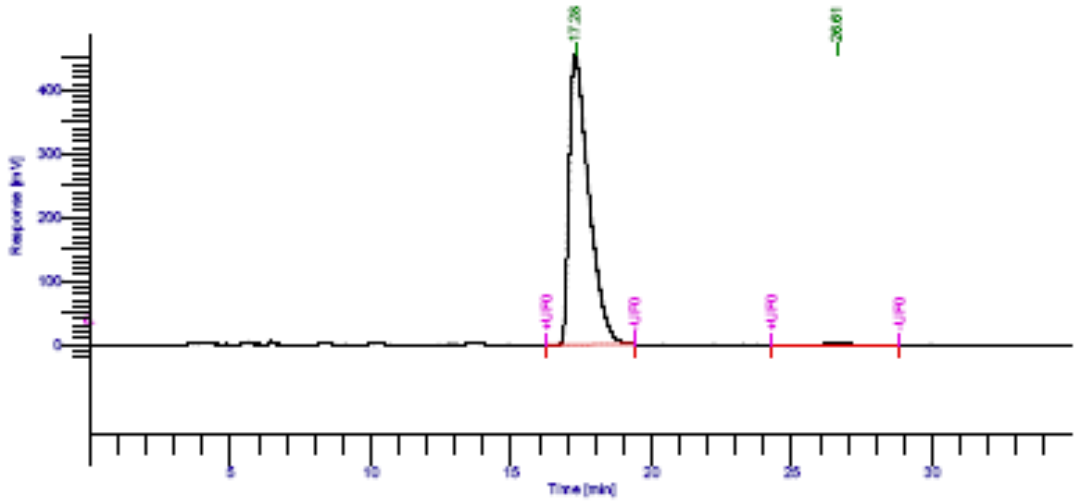
3c





Test REPORT

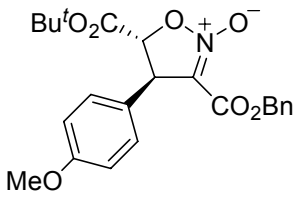
Peak #	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1	17.65	4605572.73	110629.02	50.02
2	25.38	4602021.54	63901.06	49.98
		9207594.27	174530.07	100.00

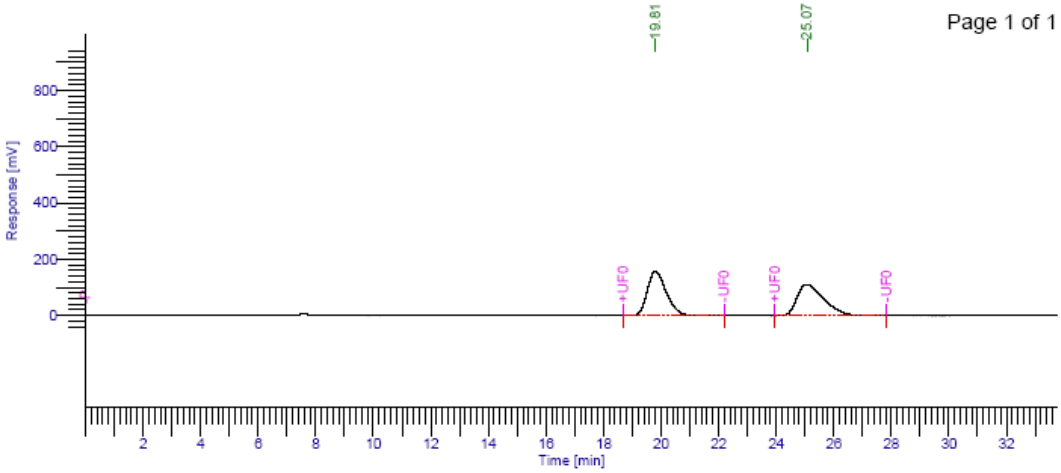


Test REPORT

Peak #	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1	17.28	22251054.25	457812.63	99.43
2	26.61	127534.57	2165.73	0.57
		22378588.82	459978.36	100.00

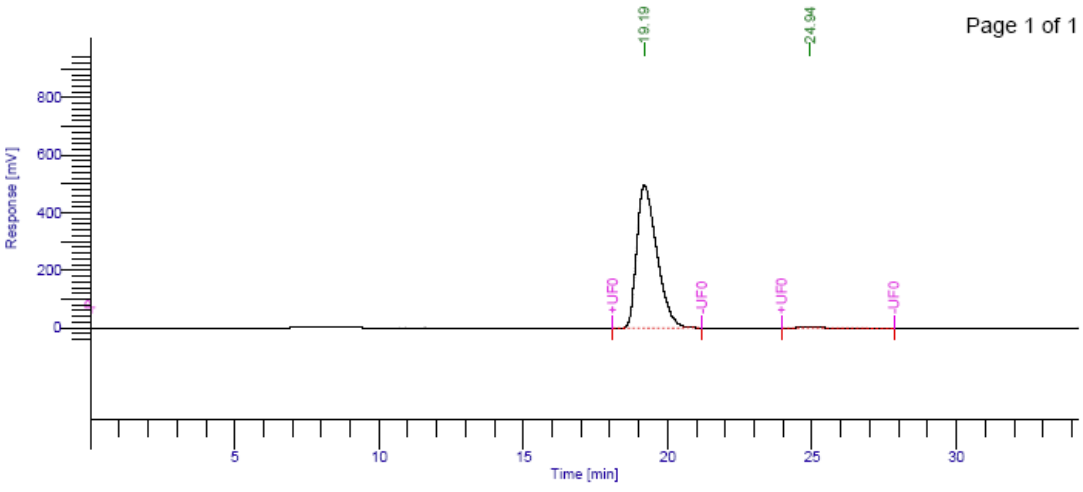
3d





zcy report

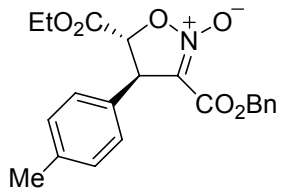
Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Norm. Area [%]
1		19.808	7286972.27	156893.54	50.02
2		25.068	7282504.40	111879.81	49.98
			14569476.68	268773.35	100.00

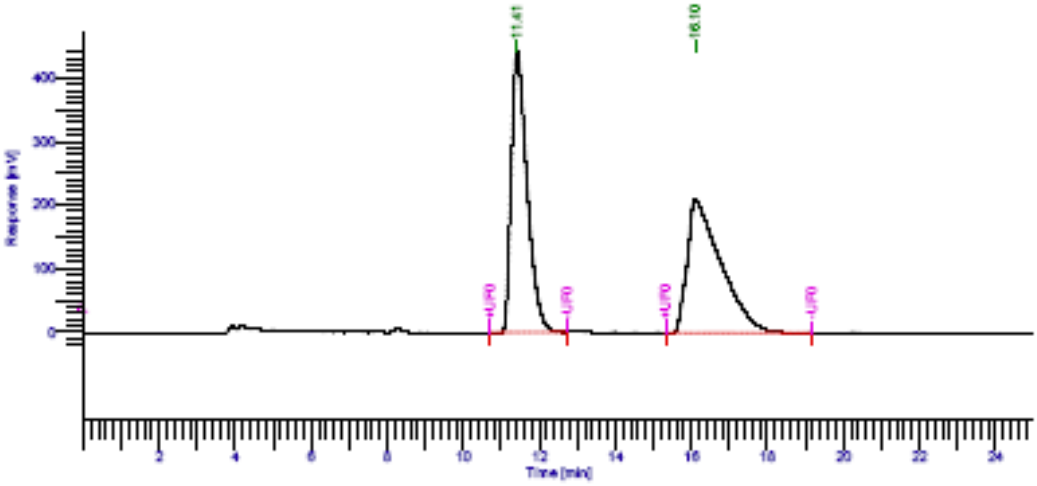


zcy report

Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Norm. Area [%]
1		19.193	24045009.44	498113.44	99.03
2		24.942	234934.10	4112.41	0.97
			24279943.54	502225.85	100.00

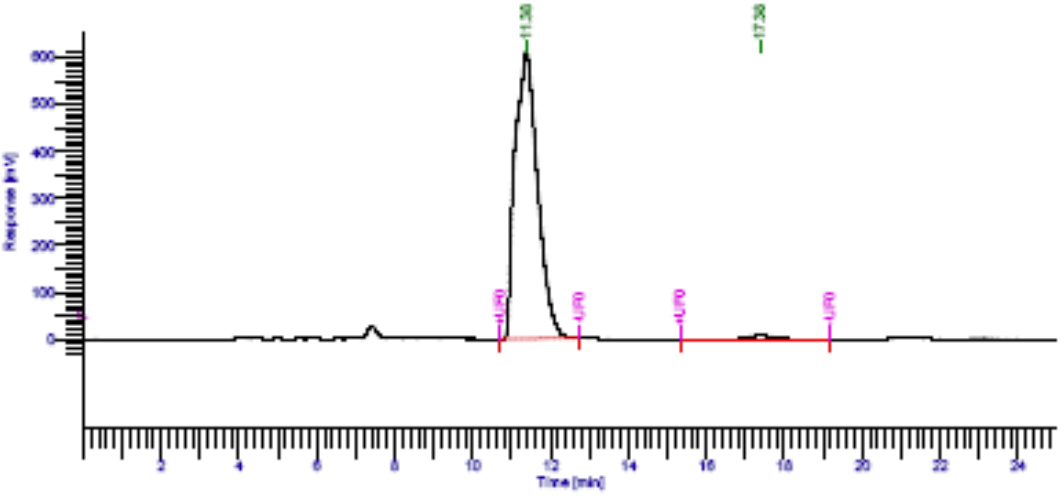
3e





Test REPORT

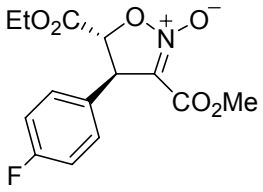
Peak #	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1	11.41	12792527.47	443430.20	49.92
2	16.10	12831674.16	209511.13	50.08
		25624201.63	652941.34	100.00

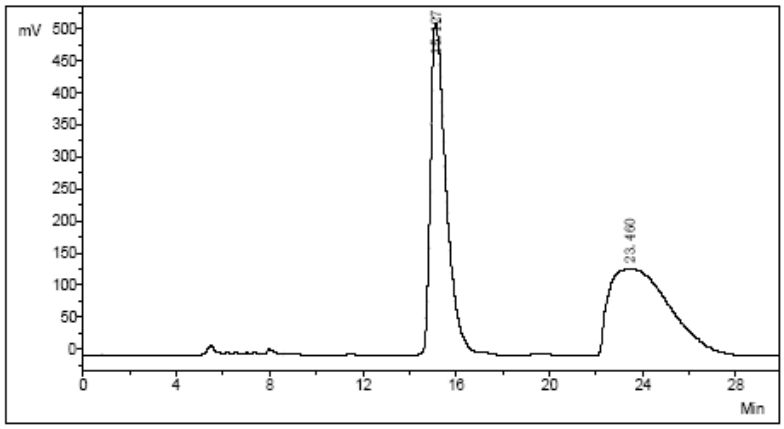


Test REPORT

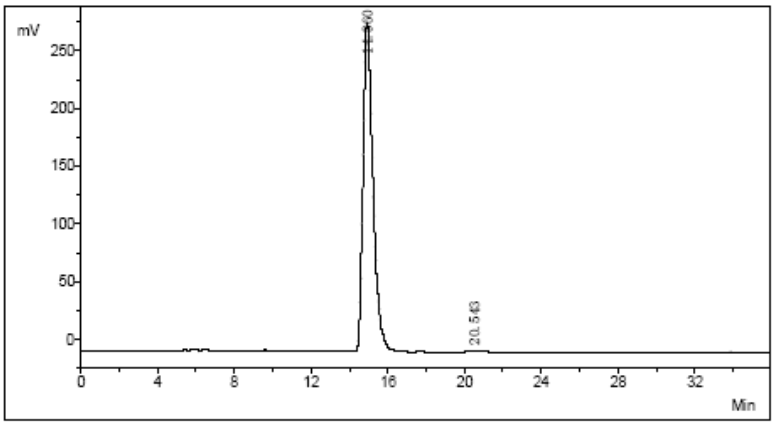
Peak #	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1	11.38	24541267.08	612694.27	98.62
2	17.38	342440.38	7384.78	1.38
		24883707.46	620279.05	100.00

3f



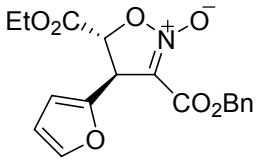


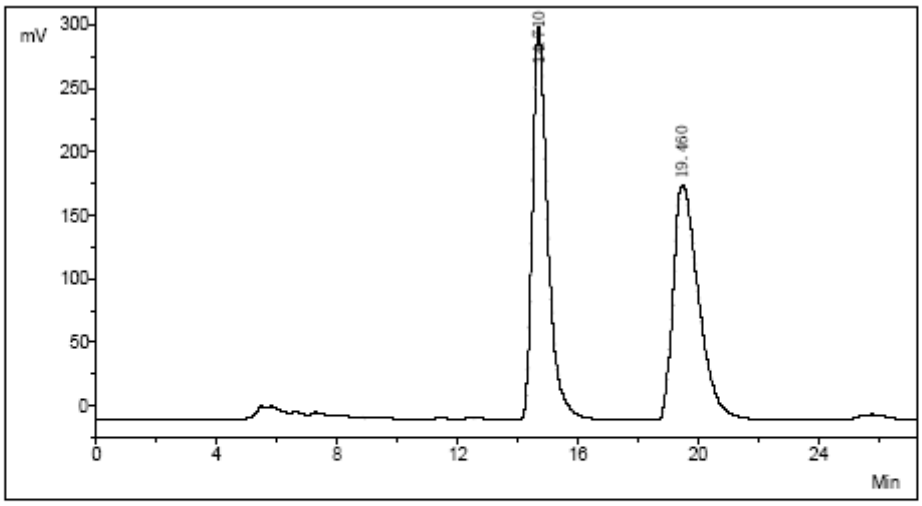
序号	峰号	组份名	保留时间	峰高	峰面积	面积百分比(%)
1	1	Unknown	15.127	516522.8	24163024.7	50.1217
2	2	Unknown	23.460	134322.0	24045665.0	49.8783
合计:				650844.8	48208689.7	100.0000



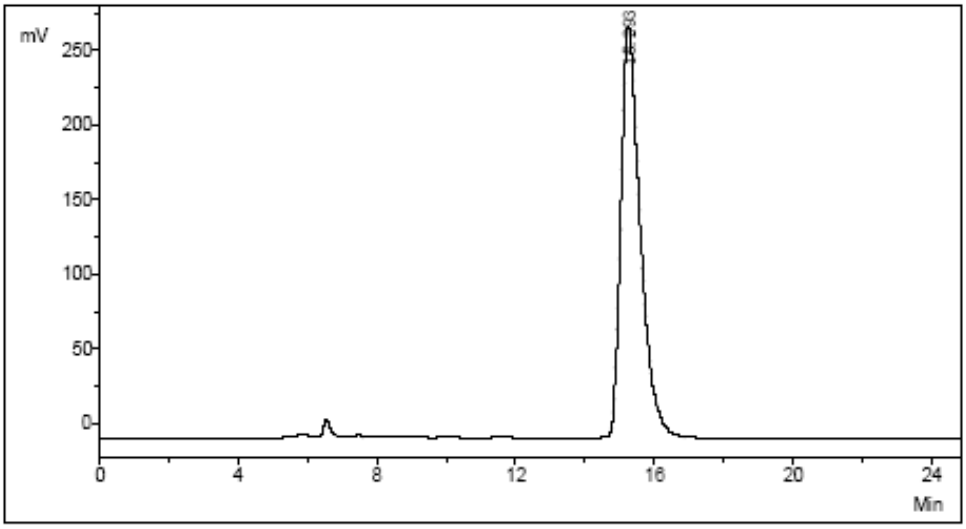
序号	峰号	组份名	保留时间	峰高	峰面积	面积百分比(%)
1	1	Unknown	14.960	281761.1	10335926.4	99.4347
2	2	Unknown	20.543	1199.3	58756.6	0.5653
合计:				282960.4	10394683.0	100.0000

3g



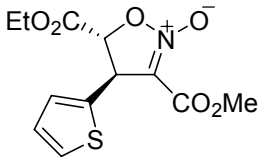


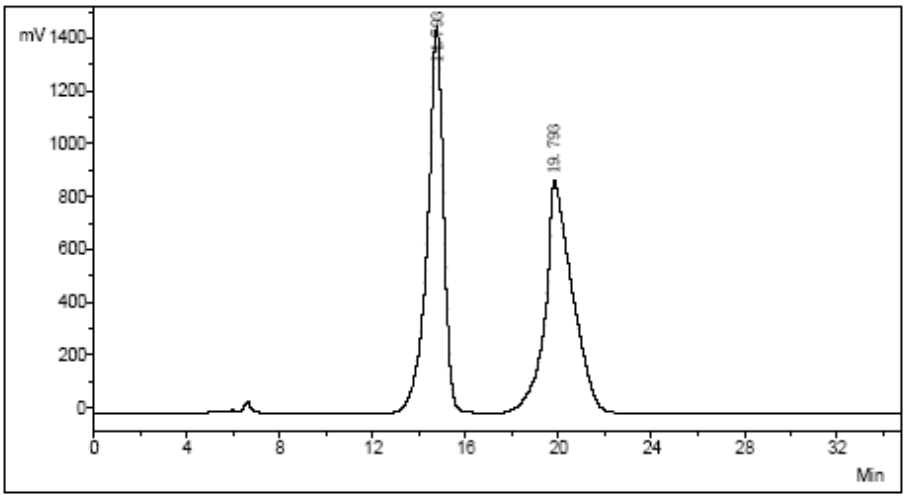
序号	峰号	组份名	保留时间	峰高	峰面积	面积百分比(%)
1	1	Unknown	14.710	307714.3	10847635.1	50.5205
2	2	Unknown	19.460	183206.3	10624099.7	49.4795
合计:				490920.7	21471734.8	100.0000



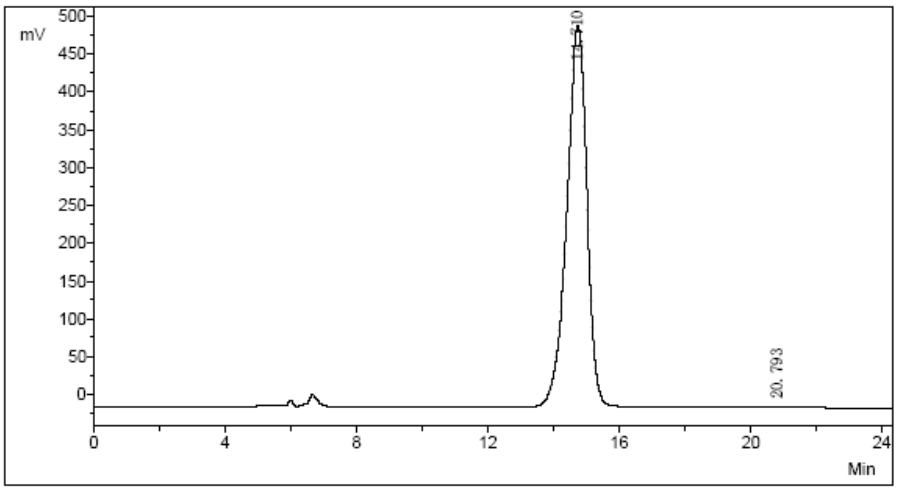
序号	峰号	组份名	保留时间	峰高	峰面积	面积百分比(%)
1	1	Unknown	15.293	271131.1	10845130.2	100.0000
合计:				271131.1	10845130.2	100.0000

3h



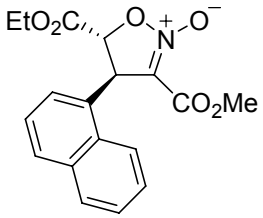


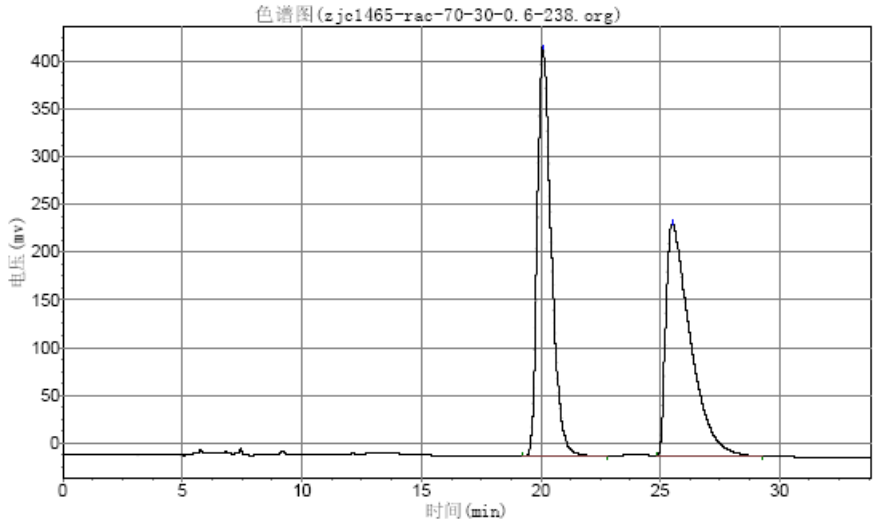
序号	峰号	组份名	保留时间	峰高	峰面积	面积百分比(%)
1	1	Unknown	14.793	1449953.8	70954876.8	49.9609
2	2	Unknown	19.793	873987.7	71065937.7	50.0391
合计:				2323941.5	142020814.5	100.0000



序号	峰号	组份名	保留时间	峰高	峰面积	面积百分比(%)
1	1	Unknown	14.710	499321.7	21541102.9	99.7006
2	2	Unknown	20.793	1110.4	64683.8	0.2994
合计:				500432.2	21605786.7	100.0000

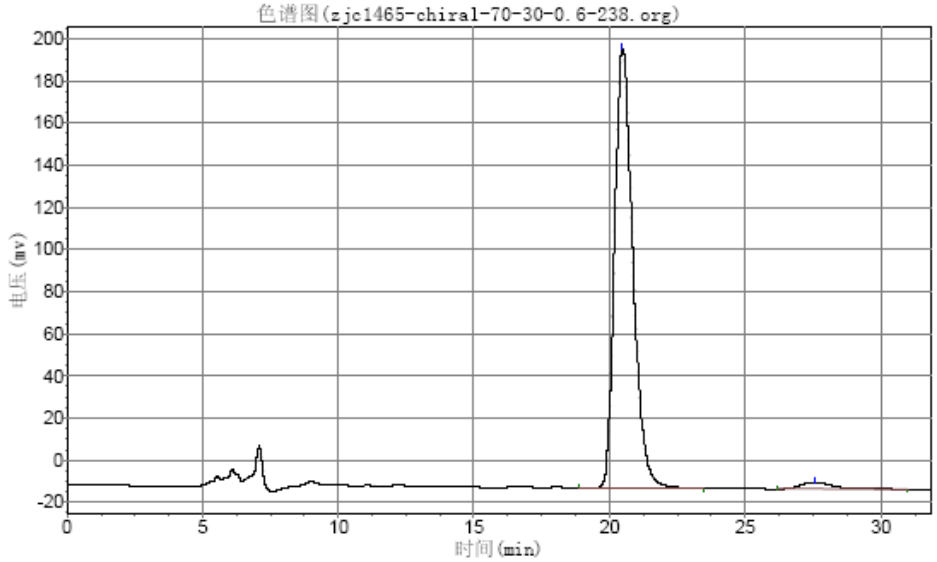
3i





分析结果表

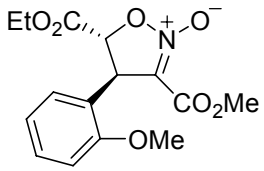
峰号	峰名	保留时间	峰高	峰面积	含量
1		20.123	427901.250	17548520.000	50.0288
2		25.523	242585.375	17528302.000	49.9712
总计			670486.625	35076822.000	100.0000

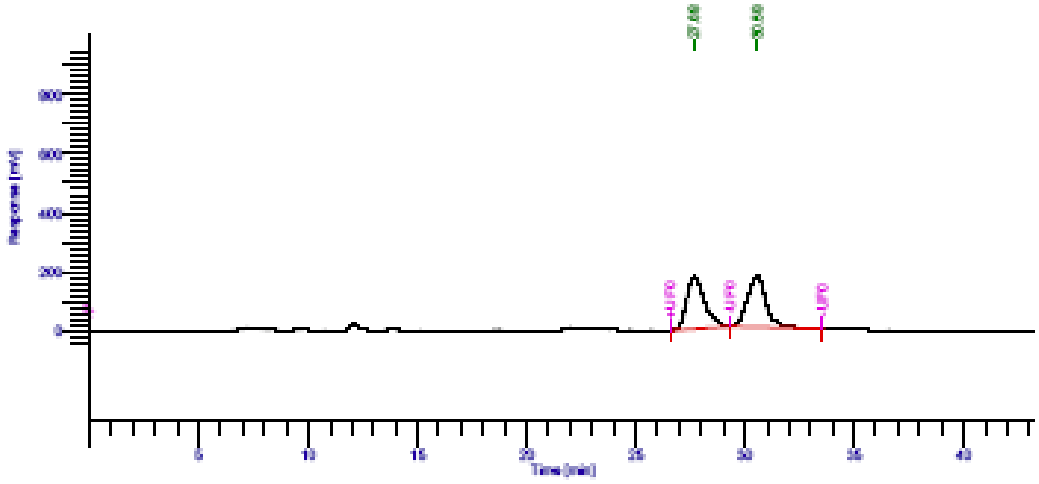


分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		20.482	208724.250	9772852.000	97.9561
2		27.547	2961.011	203912.453	2.0439
总计			211685.261	9976764.453	100.0000

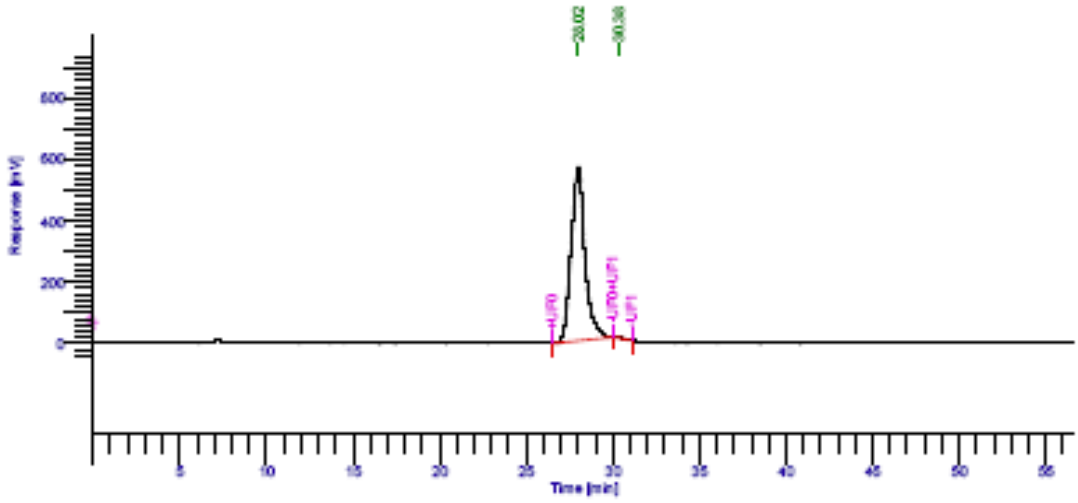
3j





Test REPORT

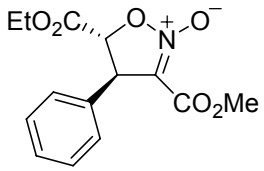
Peak #	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1	27.68	9999982.81	178021.50	49.32
2	30.59	10277043.56	174049.27	50.68
		20277026.37	352070.78	100.00

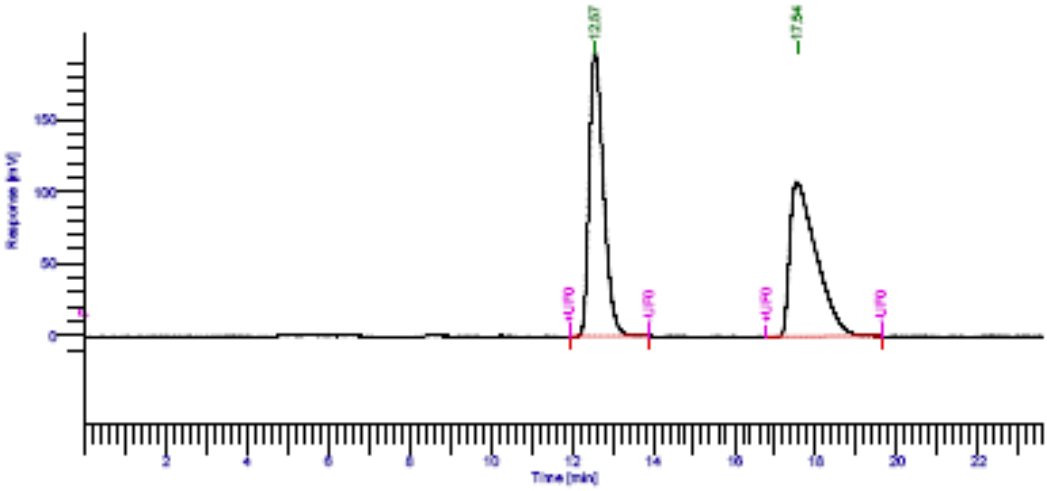


Test REPORT

Peak #	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1	28.02	31566585.39	568452.62	99.53
2	30.38	148847.40	4771.56	0.47
		31715432.79	573224.18	100.00

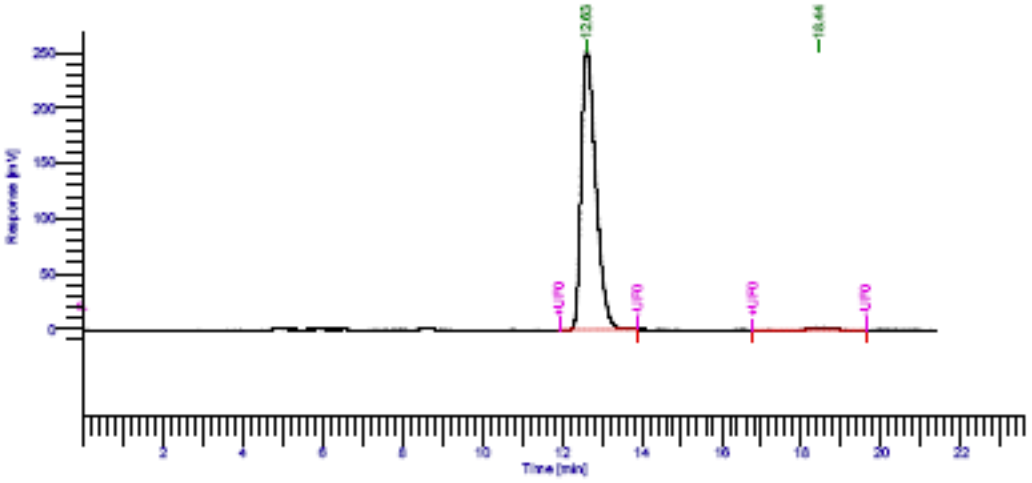
3k





Test REPORT

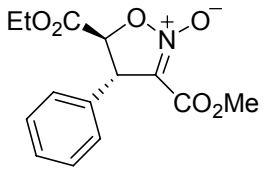
Peak #	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1	12.57	4843263.40	197631.53	49.92
2	17.54	4859037.80	107630.86	50.08
		9702301.20	305462.39	100.00

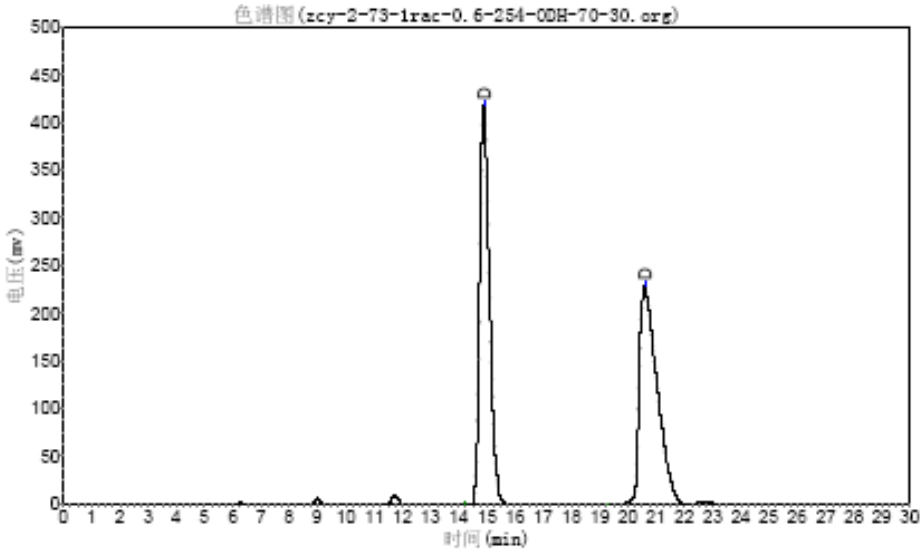


Test REPORT

Peak #	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1	12.63	6430522.01	252718.54	98.52
2	18.44	96668.03	2501.37	1.48
		6527190.04	255219.91	100.00

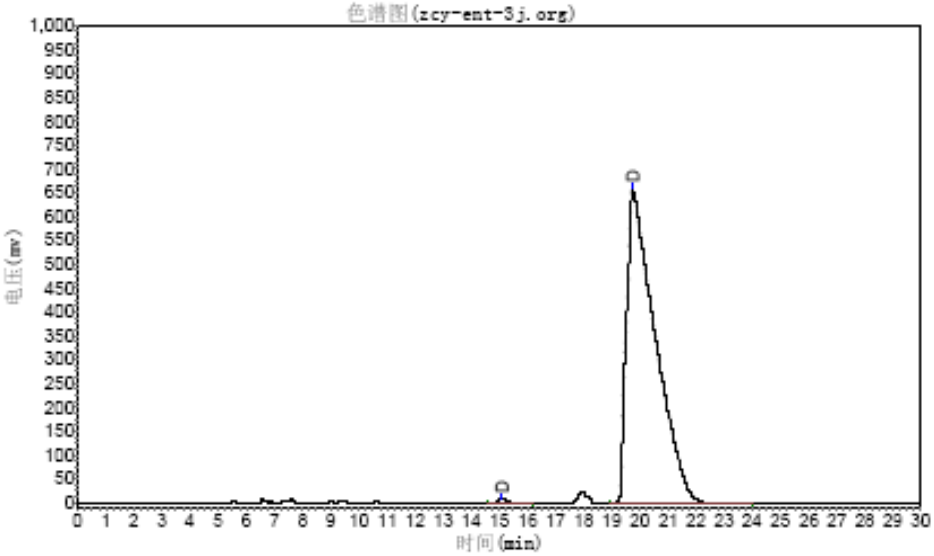
ent-3k(enantiomer of **3k**)





分析结果表

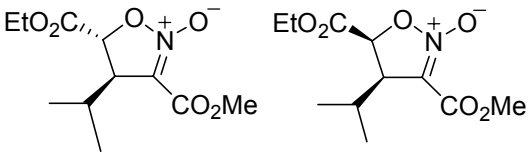
峰号	峰名	保留时间	峰高	峰面积	含量
1	D	14.898	398349.625	10263381.000	49.6784
2	D	20.598	226275.844	10396277.000	50.3216
总计			624625.469	20659658.000	100.0000

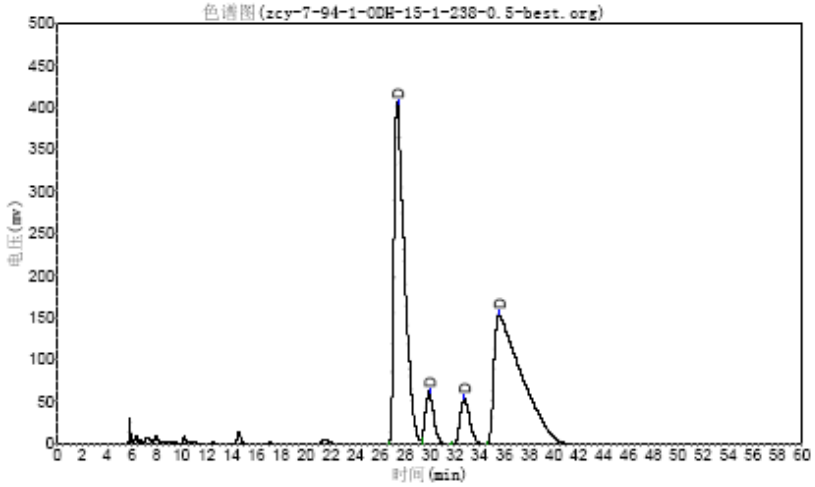


分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1	D	15.087	9150.553	222058.047	0.4703
2	D	19.743	659022.688	46993880.000	99.5297
总计			668173.240	47215938.047	100.0000

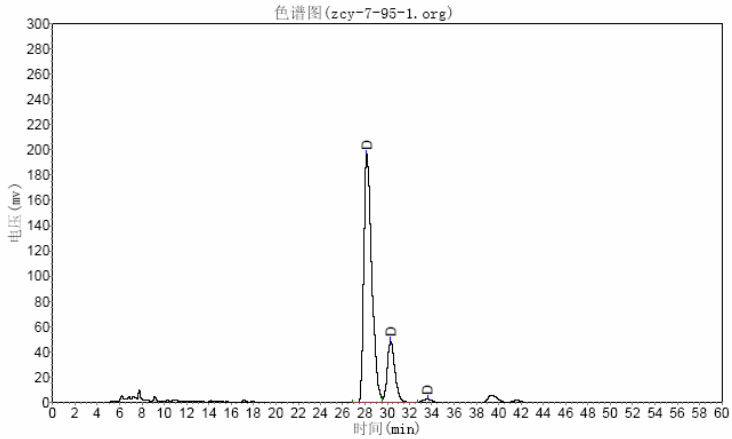
3l and **3l**’





分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1	D	27.398	405091.125	23918996.000	44.4899
2	D	29.998	62481.730	2980181.250	5.5432
3	D	32.798	54782.070	2914038.750	5.4202
4	D	35.598	154109.406	23949530.000	44.5467
总计			676464.332	53762746.000	100.0000



分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1	D	28.153	196483.297	9674590.000	79.8442
2	D	30.298	48280.922	2301147.750	18.9913
3	D	33.585	2673.118	141104.375	1.1645
总计			247437.337	12116842.125	100.0000