Electronic Supplementary Material (ESI) for ChemComm.

SUPPORTING INFORMATION

FOR

An Umpolung Approach toward *N*-Aryl Nitrone Construction: Phosphine-Mediated Addition of 1,2-Dicarbonyls to Nitroso Electrophiles

Aditi P. Chavannavar, Allen G. Oliver and Brandon L. Ashfeld*

Department of Chemistry and Biochemistry, University of Notre Dame
251 Nieuwland Science Hall, Notre Dame, IN 46556

bashfeld@nd.edu

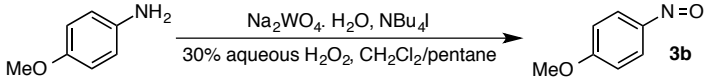
Contents

1. GENERAL

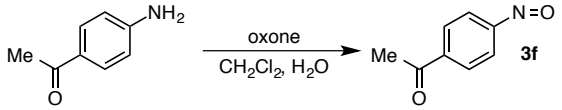
Solvents and reagents were ACS reagent grade and used without further purification unless noted below. Dimethylformamide (DMF), tetrahydrofuran (THF), dichloromethane (CH_2Cl_2) and diethyl ether (Et_2O) were passed through a column of molecular sieves and stored under argon. All reactions were carried out in flame-dried glassware under an argon atmosphere unless otherwise specified. Nitrosobenzene **3a**, methyl benzoylformate **1a** and trisaminophosphine were purchased and used without purification. Nitrosoarenes **3c**,[1] **3d**,[2] **3e**,[3] **3h**[4] were prepared according to literature procedures.

^{1}H Nuclear magnetic resonance (NMR) spectra were obtained at either 400 or 500 MHz, and ^{13}C NMR spectra at 100, 125 or 150 MHz. Chemical shifts are reported in parts per million (ppm, δ), and referenced to residual solvent or tetramethylsilane (TMS). Coupling constants are reported in Hertz (Hz). Spectral splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet; p, pentet; m, multiplet; comp, complex; app, apparent; hom, higher order multiplet; and br, broad. Infrared (IR) spectra were obtained using a Thermo Electron Nicolet 380 FT-IR using a silicon (Si) crystal in an attenuated total reflectance (ATR) tower and reported as wavenumbers (cm^{-1}). High and Low resolution electrospray ionization (ESI) measurements were made with a Bruker MicroTOF II mass spectrometer. Analytical thin layer chromatography (TLC) was performed using EMD 250 micron 60 F_{254} silica gel plates, visualized with UV light and stained with a *p*-anisaldehyde solution. Flash column chromatography was performed according to Still's procedure (Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923) using EMD 40-63 μm 60Å silica gel.

2. EXPERIMENTAL PROCEDURES

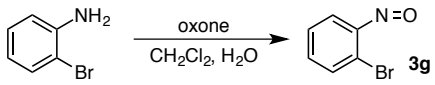


4-Nitrosoanisole (3b): $Na_2WO_4.H_2O$ (134 mg, 0.406 mmol), H_2O_2 (30% aqueous solution, 3mL, 26.4 mmol) and tetrabutylammonium iodide (45 mg, 0.121 mmol) were added sequentially to a solution of *p*-anisidine (500 mg, 4.06 mmol) in CH_2Cl_2/pentane (1:1, 20 mL) at room temperature. The reaction was stirred for 3 h and the resulting mixture was then diluted with CH_2Cl_2 (25 mL) and washed with H_2O (3 x 30 mL). The organic layer was dried (Na_2SO_4) and concentrated under reduced pressure. The resulting crude mixture was purified by flash chromatography eluting with hexanes/EtOAc (4:1) to provide 223 mg (40%) of **3b** as a green oil whose spectral data (^{1}H NMR, ^{13}C NMR) matched that reported in the literature.[5] IR (neat) 3013, 2944, 2842, 1596, 1581, 1502, 1448, 1410, 1330, 1256 cm^{-1}; HRMS (ESI) *m/z* 138.0543 [$C_7H_8NO_2$ (M+H) requires 138.0550].



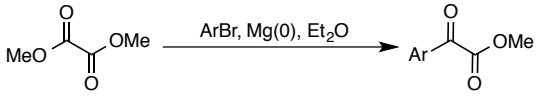
4-Acetylnitrosobenzene (3f): A solution of oxone (4.2 g, 13.7 mmol) in H_2O (25 mL) was added to a solution of 4′-aminoacetophenone (500 mg, 3.70 mmol) in CH_2Cl_2 (10 mL) at room temperature and stirred for 1.5 h. The reaction mixture was diluted with CH_2Cl_2 (15 mL) and extracted with H_2O (3 x 30 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure to provide 353 mg (64%) of **3f** as a yellow solid that was used without further purification. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7 8.15 (d, *J* = 8.2 Hz, 2H), 7.90 (d, *J* = 8.2 Hz, 2H), 2.64 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.3, 164.2, 141.1, 129.8, 129.8, 120.9, 120.9, 27.3; IR (neat) 3097, 3039, 1682, 1595, 1461,

1409, 1358, 1304, 1263, 1246 cm^{-1}; HRMS (ESI) *m/z* 150.0535 [$C_8H_8NO_2$ (M+H) requires 150.0550]; decomposed at 109 ˚C.

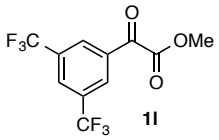


3g

2-Bromonitrosobenzene (3g): A solution of oxone (1.78 g, 5.89 mmol) in water (25 mL) was added to 2-bromoaniline (500 mg, 2.90 mmol) dissolved in CH_2Cl_2 (6 mL) and the reaction stirred at room temperature for 20 h when TLC indicated complete consumption of the aniline. The reaction mixture was diluted with CH_2Cl_2 (25 mL) and extracted with H_2O (3 x 30 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure to provide 530 mg (98%) of **3g** as a brown solid that was used without further purification. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.0 Hz, 1H), 7.53 (dt, *J* = 8.0, 7.9, 1.3 Hz, 1H), 7.26 (t, *J* = 7.9 Hz, 1H), 6.20 (dd, *J* = 8.0, 1.3 Hz, 1H); ^{13}C NMR (100 MHz) δ 161.4, 136.9, 135.4, 133.4, 127.5, 109.2; IR (neat) 3091, 3038, 1704, 1598, 1497, 1466, 1348, 1257, 1216, 1196 cm^{-1}; HRMS (ESI) *m/z* 185.9553 [C_6H_5BrNO (M+H) requires 185.9549]; mp 100 ˚C.

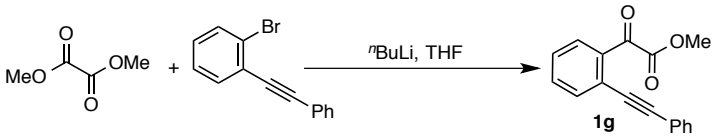


General procedure for the synthesis of substituted α-ketoesters: Clean, dry Mg turnings (3.75 mmol) were added to a solution of aryl bromide (3.41 mmol) in Et_2O (12 mL) at room temperature under a N_2 atmosphere and then heated at reflux for 1.5-2 h until complete consumption of the Mg was observed. The resulting solution was allowed to cool to room temperature by removal of the oil bath, then added dropwise via cannula to a solution of dimethyl oxalate (483 mg, 4.09 mmol) in Et_2O (25 mL) that was precooled to –78 ˚C. The mixture was stirred for 1 h, allowed to warm to room temperature by removal of the cooling bath, and stirred for an additional 2 h. The reaction was quenched with saturated aqueous NH_4Cl (25 mL), the layers were separated, and the organic fraction was washed with H_2O (3 x 30 mL). The organic phase was dried (Na_2SO_4) and concentrated under reduced pressure. The resulting crude mixture was purified by flash chromatography eluting with hexanes/EtOAc (4:1) to provide the title α-ketoester. The spectral data (^{1}H NMR, ^{13}C NMR, IR, MS) for α-ketoesters **1j**,[6] **1k**,[6] **1m**[6] and **1n**[7] matched literature values.

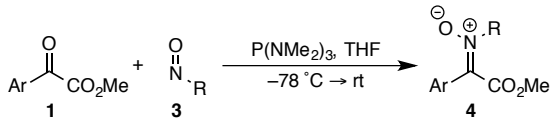


1l

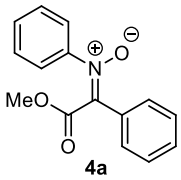
Methyl 2-(3,5-bis(trifluoromethyl)phenyl)-2-oxoacetate (1l): The synthesis of **1l** was performed on a 3.41 mmol scale of the 1,3-bis(trifluoromethyl)-5-bromobenzene with a total reaction time of 5 h. Purification by flash chromatography eluting with hexanes/EtOAc (5:1) provided 532 mg (52%) of **1l** as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (d, *J* = 0.4 Hz, 2H), 8.12 (s, 1H), 4.00 (s, 3H); NMR (100 MHz) δ 182.4, 162.1, 134.4, 133.3 (q, *J* = 136 Hz, 2C), 130.3 (d, *J* = 12.8 Hz, 2C), 127.9 (t, *J* = 14 Hz), 124.1, (q, *J* = 1084 Hz, 2C), 53.4; IR (neat) 3093, 2963, 1740, 1703, 1617, 1456, 1439, 1380, 1275, 1166 cm^{-1}; HRMS (ESI) *m/z* 323.0095, [$C_{11}H_6F_6NaO_3$ (M+Na) requires 323.0113].



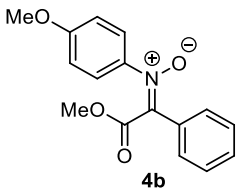
Methyl 2-oxo-2-(2-(phenylethynyl)phenyl)acetate (1g): ^{n}BuLi (0.674 μL, 1.2 mmol, 1.2 M in hexanes) was added dropwise to a solution of aryl bromide[8] (180 μL, 1.0 mmol) in dry THF (2 mL) under a N_2 atmosphere at -78 ˚C and stirred for 15 mins. The resulting solution was cannulated into a solution of dimethyl oxalate (130 mg, 1.1 mmol) in Et_2O (1.5 mL) that was precooled to -78 ˚C. The reaction was then warmed to 0 ˚C and quenched with saturated NH_4Cl (10 mL), diluted with Et_2O (10 mL) and extracted with H_2O (3 x 15 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure. The resulting crude mixture was purified by flash chromatography eluting with hexanes/ethyl acetate (4:1) to provide 148 mg (56%) of the α-ketoester **1g** as a clear oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 7.8 Hz, 1H), 7.59 (d, *J* = 7.4 Hz, 1H), 7.56-7.51 (m, 3H), 7.42 (t, *J* = 7.58 Hz, 1H), 7.35-7.30 (m, 3H), 3.76 (s, 3H); ^{13}C NMR (100 MHz) δ 187.7, 164.4, 135.4, 133.6, 133.5, 131.9, 131.9, 130.2, 129.3, 128.8, 128.7, 128.7, 124.0, 122.4, 97.0, 86.4, 53.3; IR (neat) 3064, 2953, 2845, 2215, 1738, 1690, 1590, 1492, 1443, 1298 cm^{-1}; HRMS (ESI) *m/z* 265.0852, [$C_{17}H_{13}O_3$ (M+H) requires 265.0859].



General procedure for the synthesis of nitrones: Neat $P(NMe_2)_3$ (125 mg, 0.699 mmol) was added dropwise to a solution of **1** (0.560 mmol) in THF (2.8 mL) at –78 ˚C and stirred for 10 min. Then **3** (0.466 mmol) was added in one portion and the reaction allowed to warm up to room temperature in the dry-ice acetone bath over 2 h followed by continued stirring until full consumption of nitrosobenzene **3** was observed by thin layer chromatography (ca. 12 h). The mixture was concentrated under reduced pressure and the crude residue was purified by flash chromatography eluting with the indicated solvent system to provide the title compound **4**. Unless otherwise stated, nitrone **4** was obtained as solely the *E*-isomer as determined by ^{1}H NMR analysis.

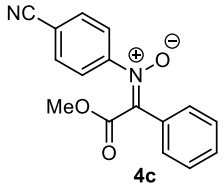


(E)-*N*-(2-Methoxy-2-oxo-1-phenylethylidene)aniline oxide (4a): The redox condensation of **1a** with **3a** was performed on a 0.5 mmol scale with a reaction time of 11 h. Purification by flash chromatography eluting with hexanes/EtOAc (3:1) provided 101 mg (85%) of **4a** as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (dd, *J* = 7.2, 2.6 Hz, 2H), 7.51-7.44 (m, 8H), 3.55 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.7, 148.6, 140.7, 131.1, 130.4, 129.8, 129.4, 129.4, 128.8, 128.8, 128.7, 128.7, 123.4, 123.4, 53.2; IR (neat) 3061, 2952, 1730, 1714, 1592, 1575, 1492, 1432, 1348, 1306 cm^{-1}; HRMS (ESI) *m/z* 256.0982, [$C_{15}H_{14}NO_3$ (M+H) requires 256.0968]; mp 88 ˚C.



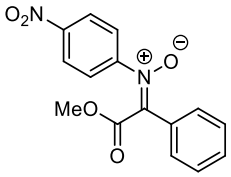
4b

(*E*)-4-Methoxy-*N*-(2-methoxy-2-oxo-1-phenylethylidene)aniline oxide (4b): The redox condensation of **1a** with **3b** was performed on a 0.4 mmol scale with a reaction time of 11 h. Purification by flash chromatography eluting with hexanes/EtOAc (3:1) provided 86 mg (85%) of **4b** as a yellow oil in a 1:1 mixture of *E*/*Z* isomers. The geometry of **4b** was determined by analysis of the 500 MHz ^{1}H NMR spectra (***E*-4b**: 3.61 (s, 3 H); ***Z*-4b**: 3.76 (s, 3 H)). Upon storing at 0˚C, the isolated ***Z*-4b** underwent 100% conversion to ***E*-4b** over 72 h. ***E*-4b**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14-8.09 (m, 2H), 7.53-7.41 (m, 5H), 6.92 (d, *J* = 8.9 Hz, 2H), 3.84 (s, 3H), 3.61 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.9, 160.9, 142.0, 140.3, 130.9, 129.6, 128.7, 128.7, 128.6, 128.6, 124.8, 124.8, 114.4, 114.4, 55.8, 53.1; ***Z*-4b**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (d, *J* = 8.7 Hz, 2H), 7.25-7.20 (m, 3H), 7.10 (dd, *J* = 7.2, 1.7 Hz, 2H), 6.75 (d, *J* = 8.7 Hz, 2H), 3.95 (s, 3H), 3.76 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.9, 160.8, 139.4, 139.0, 130.2, 129.7, 129.1, 129.1, 129.0, 129.0, 126.1, 126.1, 114.2, 114.2, 55.7, 53.3; IR (neat) 3058, 3039, 2951, 1732, 1603, 1572, 1524, 1501, 1435, 1344, 1299 cm^{-1}; HRMS (ESI) *m/z* 286.1095 [$C_{16}H_{16}NO_4$ (M+H) requires 286.1074]; mp 138 ˚C.



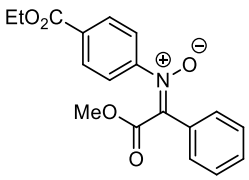
4c

(*E*)-4-Cyano-*N*-(2-methoxy-2-oxo-1-phenylethylidene)aniline oxide (4c): The redox condensation of **1a** with **3c** was performed on a 0.45 mmol scale with a reaction time of 11 h. Purification by flash chromatography eluting with hexanes/EtOAc (3:1) provided 100 mg (79%) of **4c** as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (dd, *J* = 6.7, 2.9 Hz, 2H), 7.76 (d, *J* = 8.4 Hz, 2H), 7.60 (d, *J* = 8.4 Hz, 2H), 7.50-7.46 (m, 3H), 3.62 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.1, 151.2, 141.4, 133.6, 133.6, 131.6, 130.6, 129.0, 129.0, 128.8, 128.8, 124.4, 124.4, 117.6, 114.3, 53.5; IR (neat) 3094, 3038, 2954, 2228, 1740, 1704, 1598, 1496, 1439, 1348, 1260 cm^{-1}; HRMS (ESI) *m/z* 281.0888 [$C_{16}H_{13}N_2O_3$ (M+H) requires 281.0921]; mp 134 ˚C.



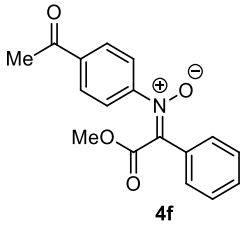
4d

(*E*)-*N*-(2-Methoxy-2-oxo-1-phenylethylidene)-4-nitroaniline oxide (4d): The redox condensation of **1a** with **3d** was performed on a 0.33 mmol scale with a reaction time of 10 h. Purification by flash chromatography eluting with hexanes/EtOAc (3:1) provided 73 mg (74%) of **4d** as a brown oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (d, *J* = 8.9 Hz, 2H), 8.07 (dd, *J* = 6.5, 3.2 Hz, 2H), 7.67 (d, *J* = 8.9 Hz, 2H), 7.51-7.49 (m, 3H); ^{13}C NMR (100 MHz) δ 164.0, 152.5, 148.4, 141.5, 131.7, 129.3, 129.1, 129.1, 128.8, 128.8, 125.1, 125.1, 124.6, 124.6, 53.5; IR (neat) 3111, 3063, 2954, 1730, 1692, 1613, 1593, 1529, 1434, 1347, 1267 cm^{-1}; HRMS (ESI) *m/z* 301.0782 [$C_{15}H_{13}N_2O_5$ (M+H) requires 301.0819].



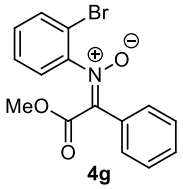
4e

(*E*)-4-(Ethoxycarbonyl)-*N*-(2-methoxy-2-oxo-1-phenylethylidene) aniline oxide (4e): The redox condensation of **1a** with **3e** was performed on a 0.28 mmol scale with a reaction time of 10 h. Purification by flash chromatography eluting with hexanes/EtOAc (3:1) provided 70 mg (77%) of **4e** as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, *J* = 8.5 Hz, 2H), 8.11 (dd, *J* = 6.6, 3.1 Hz, 2H), 7.56 (d, *J* = 8.5 Hz, 2H), 7.48-7.46 (m, 3H), 4.40 (q, *J* = 7.1 Hz, 2H), 3.58 (s, 3H), 1.40 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz) δ 165.4, 164.3, 151.4, 141.1, 132.2, 131.3, 130.9, 130.9, 129.1, 128.9, 128.9, 128.7, 128.7, 123.4, 123.4, 61.7, 53.3, 14.5; IR (neat) 2982, 2950, 1736, 1710, 1602, 1574, 1519, 1434, 1339, 1269 cm^{-1}; HRMS (ESI) *m/z* 328.1173 [$C_{18}H_{18}NO_5$ (M+H) requires 328.1179]; mp 95 ˚C.



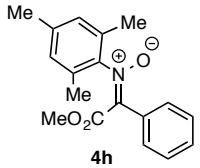
4f

(*E*)-4-Acetyl-*N*-(2-methoxy-2-oxo-1-phenylethylidene) aniline oxide (4f): The redox condensation of **1a** with **3f** was performed on a 0.47 mmol scale with a reaction time of 10 h. Purification by flash chromatography eluting with hexanes/EtOAc (3:1) provided 110 mg (79%) of **4f** as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ8.09 (dd, *J* = 6.4, 3.0 Hz, 2H), 8.02 (d, *J* = 8.2 Hz, 2H), 7.57 (d, *J* = 8.2 Hz, 2H), 7.46-7.45 (m, 3H), 3.57 (s, 3H), 2.61 (s, 3H); ^{13}C NMR (100 MHz) δ 196.7, 164.3, 151.5, 141.1, 138.2, 131.4, 129.7, 129.7 129.0, 128.9, 128.9, 128.7, 128.7, 123.7, 123.7, 53.4, 27.0; IR (neat) 3097, 2956, 2925, 1727, 1686, 1597, 1508, 1433, 1348, 1263 cm^{-1}; HRMS (ESI) *m/z* 298.1075 [$C_{17}H_{16}NO_4$ (M+H) requires 298.1074]; mp 106 ˚C.



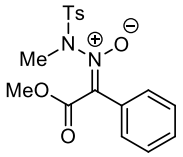
4g

(*E*)-2-Bromo-*N*-(2-methoxy-2-oxo-1-phenylethylidene)aniline oxide (4g): The redox condensation of **1a** with **3g** was performed on a 0.27 mmol scale with a reaction time of 11 h. Purification by flash chromatography eluting with hexanes/EtOAc (3:1) provided 40 mg (45%) of **4g** as a brown oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (dd, *J* = 6.5, 2.6 Hz, 2H), 7.66 (d, *J* = 7.9 Hz, 1H), 7.52-7.46 (m, 4H), 7.42 (t, *J* = 7.6 Hz, 1H), 7.31 (dt, *J* = 7.6, 1.3 Hz, 1H), 3.60 (s, 3H); ^{13}C NMR (100 MHz) δ 163.3, 147.3, 141.8, 133.8, 131.1, 130.9, 129.3, 129.3, 129.1, 129.1, 128.6, 128.4, 125.5, 116.9, 53.2; IR (neat) 3060, 2951, 2850, 1725, 1577, 1510, 1488, 1433, 1338, 1276 cm^{-1}; HRMS (ESI) *m/z* 334.0081 [$C_{15}H_{13}BrNO_3$ (M+H) requires 334.0073].



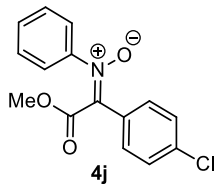
4h

(*E*)-*N*-(2-Methoxy-2-oxo-1-phenylethylidene)-2,4,6trimethylaniline oxide (4h): The redox condensation of **1a** with **3h** was performed on a 0.34 mmol scale with a reaction time of 12 h. Purification by flash chromatography eluting with hexanes/EtOAc (4:1) provided an inseparable mixture of **4h** and dimethyl 2,3-diphenyloxirane-2,3-dicarboxylate. A 6% yield of **4h** was determined by ^{1}H NMR analysis using 1,3,5-trimethoxybezene as an internal standard. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (dd, *J* = 7.2, 2.3 Hz, 2H), 7.50-7.45 (m, 3H), 6.89 (s, 2H), 3.54 (s, 3H), 2.34 (s, 6H), 2.29 (s, 3H); ^{13}C NMR (100 MHz) δ 163.3, 147.3, 141.8, 133.8, 131.1, 130.9, 129.3, 129.3, 129.1, 129.1, 128.6, 128.4, 125.5, 116.9, 53.2; IR (neat) 3063, 2953, 2843, 1740, 1602, 1494, 1434, 1377, 1277, 1233 cm^{-1}; HRMS (ESI) *m/z* 298.1440 [$C_{18}H_{20}NO_3$ (M+H) requires 298.1438].



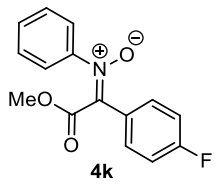
4i

(*E*)-Diazald® nitrone (4i): The redox condensation of **1a** with **3i** was performed on a 0.23 mmol scale with a reaction time of 12 h. Purification by flash chromatography eluting with hexanes/EtOAc (4:1) provided 66 mg (78%) of **4i** as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (dd, *J* = 7.5, 1.2 Hz, 2H), 7.86 (d, *J* = 8.1 Hz, 2H), 7.48-7.43 (m, 3H), 7.37 (d, *J* = 8.1 Hz, 2H), 4.04 (s, 3H), 3.11 (s, 3H), 2.47 (s, 3H); ^{13}C NMR (100 MHz) δ 162.9, 145.7, 131.8, 130.5, 130.5, 130.0, 129.7, 129.7, 129.4, 128.9, 128.9, 128.8, 128.8, 127.2, 53.7, 36.6, 21.9; IR (neat) 3056, 2923, 2852, 1736, 1595, 1551, 1435, 1365, 1349, 1265 cm^{-1}; HRMS (ESI) *m/z* 385.0805 [$C_{17}H_{18}N_2O_5SNa$ (M+Na) requires 385.0829]; mp 143 ˚C.



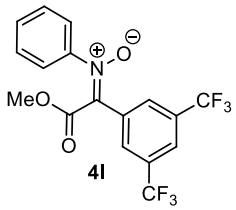
4j

(*E*)-*N*-(1-(4-Chlorophenyl)-2-methoxy-2-oxoethylidene)aniline oxide (4j): The redox condensation of **1j** with **3a** was performed on a 0.25 mmol scale with a reaction time of 12 h. Purification by flash chromatography eluting with hexanes/EtOAc (4:1) provided 55 mg (76%) of **4j** as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, *J* = 8.8 Hz, 2H), 7.51-7.41 (m, 7H), 3.55 (s, 3H); ^{13}C NMR (100 MHz) δ 164.4, 148.6, 136.7, 130.5, 130.1, 130.1, 129.5, 129.5, 128.9, 128.9, 127.8, 124.5, 123.3, 123.3, 53.2; IR (neat) 3075, 3055, 2957, 1709, 1589, 1509, 1489, 1427, 1339, 1266 cm^{-1}; HRMS (ESI) *m/z* 290.0588 [$C_{15}H_{13}NO_3Cl$ (M+H) requires 290.0578]; mp 118 ˚C.



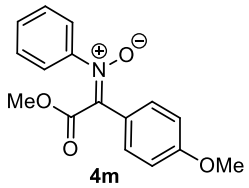
4k

(*E*)-*N*-(1-(4-Fluorophenyl)-2-methoxy-2-oxoethylidene)aniline oxide (4k): The redox condensation of **1k** with **3a** was performed on a 0.32 mmol scale with a reaction time of 12 h. Purification by flash chromatography eluting with hexanes/EtOAc (4:1) provided 60 mg (69%) of **4k** as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22-8.18 (m, 2H), 7.51-7.42 (m, 5H), 7.18-7.11 (m, 2H), 3.54 (s, 3H); ^{13}C NMR (100 MHz) δ 164.9 (d, J = 172 Hz) , 162.5, 148.5, 131.2 (d, J = 36 Hz, 2C), 130.4, 129.5, 129.5, 125.6 (d, J = 16 Hz, 1C), 123.3, 123.3, 115.8 (d, J = 88 Hz, 2C), 53.2; IR (neat) 3066, 2923, 2853, 1727, 1599, 1503, 1481, 1435, 1345, 1271 cm^{-1}; HRMS (ESI) *m/z* 274.0882 [$C_{15}H_{13}NO_3F$ (M+H) requires 274.0874]; mp 90 ˚C.



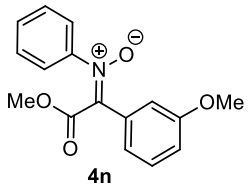
4l

(*E*)-*N*-(1-(3,5-Bis(trifluoromethyl)phenyl)-2-methoxy-2-oxoethylidene)aniline oxide (4l): The redox condensation of **1l** with **3a** was performed on a 0.25 mmol scale with a reaction time of 12 h. Purification by flash chromatography eluting with hexanes/EtOAc (4:1) provided 55 mg (56%) of **4l** as a yellow amorphous solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (s, 2H), 7.95 (s, 1H), 7.56-7.48 (m, 5H), 3.59 (s, 3H); ^{13}C NMR (100 MHz) δ163.4, 148.6, 137.8, 132. 3 (q, J = 134 Hz, 2C), 131.5, 130.9, 129.6, 129.6, 128. 9(d, J = 13.2 Hz, 2C), 124.1, (t, J = 14.4 Hz), 123.1, 123.1, 123.0 (q, J = 1084 Hz, 2C), 53.4 ; IR (neat) 3103, 2958, 1732, 1618, 1593, 1484, 1435, 1385, 1331, 1277, 1131 cm^{-1}; HRMS (ESI) *m/z* 392.0738 [$C_{17}H_{12}F_6NO_3$ (M+Na) requires 392.0716].



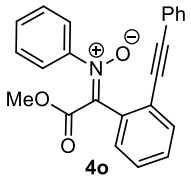
4m

(*E*)-*N*-(2-Methoxy)-1-(4-methoxyphenyl)-2-oxoethylidene)aniline oxide (4m): The redox condensation of **1m** with **3a** was performed on a 0.26 mmol scale with a reaction time of 12 h. Purification by flash chromatography eluting with hexanes/EtOAc (4:1) provided 32 mg (44%) of **4m** as an amorphous solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1H NMR 8.21 (d, J = 9.2 Hz, 2H), 7.52-7.48 (m, 2H), 7.46-7.42 (m, 3H), 6.98 (d, J = 9.2 Hz, 2H), 3.87 (s, 3H), 3.55 (s, 3H); ^{13}C NMR (100 MHz) δ 164.9, 161.6, 148.5, 140.6, 132.8, 130.7, 130.7, 130.1, 129.4, 129.4, 123.5, 123.5, 114.0, 114.0, 55.6, 53.1; IR (neat) 3006, 2951, 2839, 1729, 1602, 1569, 1507, 1455, 1348, 1247 cm^{-1}; HRMS (ESI) *m/z* 286.1090 [$C_{16}H_{16}NO_4$ (M+H) requires 286.1074].



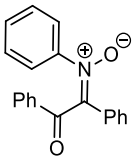
4n

(*E*)-*N*-(2-Methoxy)-1-(3-methoxyphenyl)-2-oxoethylidene)aniline oxide (4n): The redox condensation of **1n** with **3a** was performed on a 0.26 mmol scale with a reaction time of 12 h. Purification by flash chromatography eluting with hexanes/EtOAc (4:1) provided 38 mg (52%) of **4n** as a 5:1 mixture of isomers. The geometry of **4n** was determined by analysis of the 500 MHz ^{1}H NMR spectra (***E*-4n**: 3.56 (s, 3 H); ***Z*-4n**: 3.60 (s, 3 H)). For the major (*E*)- isomer; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03-8.00 (m, 1H), 7.52-7.43 (m, 5H), 7.37 (t, *J* = 8.1Hz, 2H), 7.03 (ddd, *J* = 8.1, 2.6, 0.8 Hz, 1H), 3.85 (s, 3H), 3.56 (s, 3H); ^{13}C NMR (100 MHz) δ 164.6, 159.6, 148.6, 140.8, 130.4, 130.0, 129.6, 129.4, 129.4, 123.4, 123.4, 121.4, 117.7, 113.5, 55.6, 53.1; For the minor (*Z*)-isomer; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (dd, *J* = 2.6, 1.8 Hz, 2H), 7.35-7.31 (m, 3H), 7.13 (t, *J* = 8.0 Hz, 1H), 6.80 (ddd, *J* = 8.0, 2.0, 0.8 Hz, 1H), 6.71 (ddd, *J* = 8.0, 2.0, 0.8 Hz, 1H), 6.62-6.59 (m, 1H), 3.99 (s, 3H), 3.60 (s, 3H); ^{13}C NMR (100 MHz) δ 163.6, 159.7, 148.6, 140.8, 130.8, 130.3, 130.0, 129.3, 129.3, 124.5, 124.5, 121.6, 116.1, 114.2, 55.4, 53.4; IR (neat) 3061, 2951, 2836, 1727, 1594, 1576, 1486, 1428, 1338, 1252 cm^{-1}; HRMS (ESI) *m/z* 286.1093 [$C_{16}H_{16}NO_4$ (M+H) requires 286.1074].



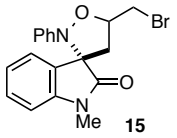
4o

(*E*)-*N*-(2-Methoxy-2-oxo-1-(2-(phenylethynyl)phenyl)ethylidene)aniline oxide (4o): The redox condensation of **1g** with **3a** was performed on a 0.22 mmol scale with a reaction time of 12 h. Purification by flash chromatography eluting with hexanes/EtOAc (3:1) provided 49 mg (63%) of **4o** as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87-7.81 (m, 1H), 7.66 (dd, *J* = 7.5, 1.4 Hz, 1H), 7.52-7.43 (m, 9H), 7.31 (dd, *J* = 5.1, 1.7 Hz, 3H), 3.58 (s, 3H); ^{13}C NMR (100 MHz) δ 163.5, 149.0, 139.2, 133.3, 132.8, 131.8, 131.8, 130.3, 129.9, 129.9, 129.3, 129.3, 128.8, 128.7, 128.7, 128.6, 123.8, 123.3, 123.3, 122.9, 94.6, 87.2, 53.1; IR (neat) 3057, 2951, 2216, 1724, 1597, 1492, 1467, 1335, 1265, 1212 cm^{-1}; HRMS (ESI) *m/z* 356.1273 [$C_{23}H_{18}NO_3$ (M+H) requires 356.1281].



12

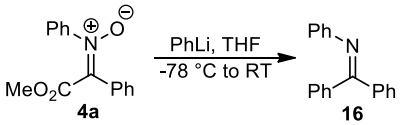
(*E*)-*N*-(2-oxo-1,2-diphenylethylidene)aniline oxide (12): The redox condensation of **11** (118 mg, 0.56 mmol) with **3a** was performed on a 0.46 mmol scale with a reaction time of 12 h. Purification by flash chromatography eluting with hexanes/EtOAc (2:1) provided 60 mg (43%) of **12** as a pale brown solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, *J* = 7.3 Hz, 2H), 7.62 (t, *J* = 7.3 Hz, 1H), 7.53 (t, *J* = 7.5 Hz, 4H), 7.41-7.34 (m, 4H), 7.28-7.18 (m, 2H), 7.14 (dd, *J* = 8.0, 1.0 Hz, 2H); ^{13}C NMR (100 MHz) δ 190.5, 145.9, 135.1, 134.3, 130.6, 130.5, 129.8, 129.5, 129.5, 129.4, 129.4, 129.3, 129.3, 129.2, 129.2, 129.2, 129.1, 129.1, 124.7, 124.7; IR (neat) 3059, 2922, 1771, 1662, 1594, 1580, 1534, 1482, 1447, 1348 cm^{-1}; HRMS (ESI) *m/z* 302.1151 [$C_{20}H_{16}NO_2$ (M+H) requires 302.1176]; mp 124 ˚C.



15

5′-(Bromomethyl)-1-methyl-2′-phenylspiro[indoline-3,3′-isoxazolidin]-2-one (15) and (*E*)-*N*-(1-methyl-2-oxoindolin-3-ylidene)aniline oxide (4p): The redox condensation of **13** (60 mg, 0.37 mmol) with **3a** was performed on a 0.34 mmol scale with a reaction time of 12 h. Purification by flash chromatography eluting with hexanes/EtOAc (2:1) provided 35 mg (41%) of the intermediate nitrone **4p** as a 11:1 mixture of isomers The geometry of **4p** was determined by analysis of the 500 MHz ^{1}H NMR spectra (***E*-4p**: 3.19 (s, 3 H); ***Z*-4p**: 3.31 (s, 3 H). For the major isomer, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50-8.44 (m, 1H), 7.56-7.40 (m, 6H), 7.15 (dt, *J* = 7.7, 0.7 Hz, 1H), 6.85 (d, *J* = 7.7 Hz, 1H), 3.19 (s, 3H); For the major isomer, ^{13}C NMR (100 MHz) δ 159.8, 146.7, 142.4, 134.2, 132.5, 130.9, 129.6, 129.3, 129.3, 125.4, 123.9, 123.9, 123.3, 108.2, 26.2; For the minor isomer, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (dd, *J* = 5.6, 1.5 Hz, 1H), 7.50-7.40 (m, 3H), 7.36 (ddd, *J* = 7.8, 1.1, 0.6 Hz, 1H), 7.23 (d, *J* = 7.4 Hz, 1H), 7.02-6.97 (m, 1H), 6.76 (dt, *J* = 7.6, 0.6 Hz, 1H), 6.62-6.60 (m, 1H), 3.31 (s, 3H); ^{13}C NMR (100 MHz) δ 159.8, 146.7, 142.4, 134.8, 131.3, 130.6, 128.8, 126.3, 125.5, 123.4, 122.8, 118.3, 118.0, 109.4, 26.6; IR (neat) 3057, 2933, 1728, 1702, 1605, 1539, 1467, 1372, 1327, 1293 cm^{-1}; HRMS (ESI) *m/z* 253.0968 [$C_{15}H_{13}N_2O_2$ (M+H) requires 253.0972]; mp 161 ˚C.

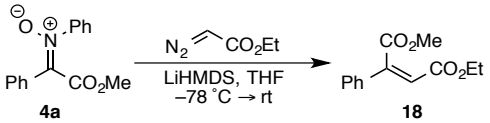
Allyl bromide (16 mg, 0.134 mmol) was added to a solution of **4p** (20 mg, 0.08 mmol) in toluene (3 mL) at room temperature, the mixture was heated to 80 ˚C, and stirred for 8 h. After allowing the reaction to cool to room temperature by removal of the oil bath, the solvent was removed under reduced pressure. The crude residue was purified by flash chromatography eluting with hexanes/EtOAc (3:1) to provide 19 mg (64%) of **15** as a 1:1 mixture of diastereomers. **Diastereomer A:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (dd, *J* = 7.4, 0.7 Hz, 1H), 7.25 (dt, *J* = 7.7, 1.2 Hz, 1H), 7.07-7.01 (m, 3H), 6.89-6.84 (m, 1H), 6.78-6.71 (m, 3H), 4.80 (qd, *J* = 7.5, 6.1 Hz, 1H), 3.89 (dd, *J* = 9.9, 6.1 Hz, 1H), 3.76 (dd, *J* = 9.9, 7.5 Hz, 1H), 3.10 (s, 3H), 2.85 (dd, *J* = 6.1, 2.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.7, 146.2, 143.4, 129.8, 129.8, 128.4, 128.3, 124.8, 123.9, 123.3, 117.6, 108.5, 108.5, 76.6, 73.2, 46.5, 33.4, 26.5; **Diastereomer B:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (dd, *J* = 7.4, 0.7 Hz, 1H), 7.30 (dt, *J* = 7.7, 1.2 Hz, 1H), 7.12-7.02 (m, 3H), 6.91-6.85 (m, 1H), 6.76-6.71 (m, 3H), 4.96 (dq, *J* = 6.9, 5.3 Hz, 1H), 3.79 (dd, *J* = 10.3, 5.3 Hz, 1H), 3.71 (dd, *J* = 10.3, 6.9 Hz, 1H), 3.04 (dd, *J* = 12.7, 6.9 Hz, 1H), 3.06 (s, 3H), 2.67 (dd, *J* = 12.7, 6.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.7, 146.7, 143.8, 130.0, 128.5, 128.5, 127.9, 124.8, 123.9, 123.4, 117.4, 117.4, 108.6, 75.9, 73.3, 46.2, 33.3, 26.3; IR (neat) 3057, 2925, 2853, 1719, 1612, 1598, 1490, 1470, 1372, 1348 cm^{-1}; HRMS (ESI) *m/z* 373.0524 [$C_{18}H_{18}N_2O_2Br$ (M+H) requires 373.0546].



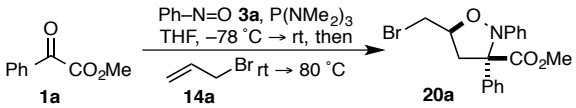
4a **16**

Benzophenone imine (16): PhLi (136 μL, 0.245 mmol, 1.8 M solution in Bu_2O) was added dropwise to a solution of **4a** (30 mg, 0.118 mmol) in THF (2.5 mL) under a N_2 atmosphere at -78 ˚C and the reaction stirred at -78 ˚C for 1 h and then at room temperature for 1.5 h. The reaction mixture was quenched with saturated aqueous NH_4Cl (15 mL), diluted with EtOAc (10 mL), and washed with H_2O (3 x 10 mL). The organic phase was dried (Na_2SO_4) and concentrated under reduced pressure. The resulting crude mixture was purified by flash chromatography eluting with hexanes/EtOAc (4:1) to provide 21 mg (71%) of **16**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79-7.74 (m, 2H), 7.48 (ddd, *J* = 6.3, 3.7, 1.2 Hz, 1H), 7.44-7.39 (m, 2H), 7.33-7.25 (m, 3H), 7.18-7.11 (m, 4H), 6.93 (dd, *J* = 13.7, 1.1 Hz, 1H), 6.73 (dd, *J* = 8.4, 1.1 Hz, 2H); ^{13}C NMR (100 MHz) δ 168.4, 151.5, 139.9, 136.5, 130.9, 129.7, 129.7,

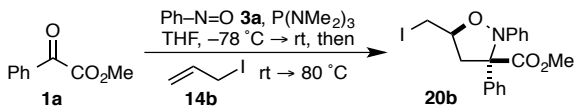
129.5, 129.5, 128.8, 128.7, 128.7, 128.4, 128.4, 128.1, 128.1, 123.4, 121.2, 121.2; IR (neat) 3058, 3027, 2925, 1795, 1737, 1659, 1619, 1591, 1482, 1445, 1317, 1290 cm^{-1}; HRMS (ESI) *m/z* 258.1270 [$C_{19}H_{16}N$ (M+H) requires 258.1277].



2-Phenyl fumarate (18): LiHMDS (170 μL, 0.176 mmol, 1 M solution in THF) was added dropwise to a solution of **4a** (30 mg, 0.118 mmol) and ethyl diazoacetate (20 mg, 0.177 mmol) in THF (2.5 mL) at -78 ˚C and stirred for 1 h. The reaction was allowed to warm to room temperature and stirring continued for an additional 1 h. The resulting solution was quenched with saturated aqueous NH_4Cl (15 mL), diluted with EtOAc (10 mL) and washed with H_2O (3 x 10 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure. The resulting crude mixture was purified by flash chromatography eluting with hexanes/EtOAc (4:1) to provide 18 mg (66%) of **18** in a 10:1 mixture of *E*/*Z* isomers. The geometry of **18** was determined by analysis of the 500 MHz ^{1}H NMR spectra (***E*-18**: 7.03 (s, 1 H); ***Z*-18**: 6.31 (s, 1 H)). ***Z*-18**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52-7.44 (m, 2H), 7.41 (t, *J* = 7.1 Hz, 3H), 6.31 (s, 1H), 4.24 (q, *J* = 7.1 Hz, 2H), 3.95 (s, 3H), 1.32 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz) δ 168.6, 165.2, 148.8, 133.5, 130.8, 129.2, 129.2, 126.9, 126.9, 117.8, 61.2, 52.9, 14.4; The ^{1}H NMR and ^{13}C NMR for the *E*-isomer matched reported values.[9] IR (neat) 2983, 2904, 1736, 1714, 1624, 1448, 1369, 1349, 1286, 1166 cm^{-1}; HRMS (ESI) *m/z* 257.0797 [$C_{13}H_{14}NaO_4$ (M+Na) requires 257.0784].

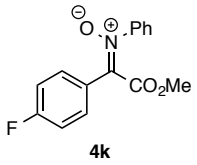


Methyl 5-(bromomethyl)-2,3-diphenylisoxazolidine-3-carboxylate (20a): Neat $P(NMe_2)_3$ (125 mg, 0.699 mmol) was added dropwise to a solution of **1a** (92 mg, 0.560 mmol) in THF (2.8 mL) at –78 ˚C and stirred for 10 min. Then **3a** (50 mg, 0.466 mmol) was added in one portion and the reaction allowed to warm up to room temperature in the dry-ice acetone bath over 2 h. Stirring was continued for 8 h, then **14a** (96 mg, 0.792 mmol) was added. The reaction was heated to 60 ˚C, stirred for 10 h, and the solvent was removed under reduced pressure. The crude mixture was purified by flash chromatography eluting with hexanes/EtOAc (3:1) to provide 93 mg (53%) of **20a** as a 2:1 mixture of diastereomers. The stereochemistry of the two isomers was assigned based on ROESY experiment. **Diastereomer A (major):** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50-7.47 (m, 2H), 7.37-7.33 (m, 3H), 7.15-7.10 (m, 2H), 6.96-6.91 (m, 3H), 4.59 (dq, *J* = 7.4, 6.0 Hz, 1H), 3.66 (dd, *J* = 10.2, 6.0 Hz, 1H), 3.56 (dd, *J* = 10.2, 7.4 Hz, 1H), 3.50 (s, 3H), 3.26 (dd, *J* = 12.7, 7.4 Hz, 1H), 2.82 (dd, *J* = 12.7, 7.4 Hz, 1H); ^{13}C NMR (100 MHz) δ 171.4, 147.0, 139.5, 128.8, 128.6, 128.6, 128.3, 128.3, 127.8, 127.8, 123.2, 118.0, 118.0, 78.5, 76.2, 52.6, 49.3, 31.5; **Diastereomer B (minor):** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52-7.47 (m, 2H), 7.42-7.36 (m, 3H), 7.17-7.11 (m, 2H), 6.96-6.92 (m, 3H), 4.72 (tt, *J* = 7.4, 5.9 Hz, 1H), 3.63 (dd, *J* = 8.8, 7.4 Hz, 1H), 3.59 (dd, *J* = 8.8, 5.9 Hz, 1H), 3.50 (s, 3H), 3.40 (dd, *J* = 10.3, 7.4 Hz, 1H), 2.54 (dd, *J* = 10.3, 5.9 Hz, 1H); ^{13}C NMR (100 MHz) δ 170.9, 147.5, 139.4, 128.6, 128.4, 128.4, 128.2, 128.2, 127.4, 127.4, 122.9, 117.4, 117.4, 78.8, 76.8, 52.5, 50.2, 33.9; IR (neat) 3059, 3026, 1729, 1596, 1489, 1448, 1432, 1225, 1155 cm^{-1}; HRMS (ESI) *m/z* 398.0340 [$C_{18}H_{18}BrNaNO_3$ (M+Na) requires 398.0362].

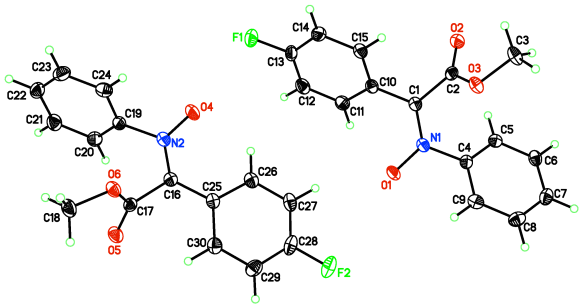


Methyl 5-(bromomethyl)-2,3-diphenylisoxazolidine-3-carboxylate (20b): Neat $P(NMe_2)_3$ (125 mg, 0.699 mmol) was added dropwise to a solution of **1a** (92 mg, 0.560 mmol) in THF (2.8 mL) at –78 ˚C and stirred for 10 min. Then **3a** (50 mg, 0.466 mmol) was added in one portion and the reaction allowed to warm up to room temperature in the dry-ice acetone bath over 2 h. Stirring was continued for 8 h, then **14b** (133 mg, 0.792 mmol) was added. The reaction was heated to 60 ˚C, stirred for 10 h, and the solvent was removed under reduced pressure. The crude mixture was purified by flash chromatography eluting with hexanes/EtOAc (3:1) provided 101 mg (51%) of **20b** as a 2:1 mixture of diastereomers. The stereochemistry of the two isomers was assigned based on ROESY experiment. **Diastereomer A (major):** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (dd, *J* = 8.1, 1.5 Hz, 2H), 7.39-7.32 (m, 3H), 7.16-7.10 (m, 2H), 6.94-6.90 (m, 3H), 4.52 (dq, *J* = 7.4, 5.8 Hz, 1H), 3.48 (s, 3H), 3.43 (d, *J* = 5.8 Hz, 1H), 3.38 (d, *J* = 7.4 Hz, 1H), 3.21 (dd, *J* = 12.5, 7.4 Hz, 1H), 2.82 (dd, *J* = 12.5, 7.4 Hz, 1H); ^{13}C NMR (100 MHz) δ 171.4, 147.1, 139.7, 128.8, 128.5, 128.5, 128.3, 128.3, 127.7, 127.7, 123.1, 117.8, 117.8, 78.8, 76.6, 52.5, 50.6, 3.9. **Diastereomer B (minor):** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51-7.47 (m, 2H), 7.42-7.30 (m, 3H), 7.17-7.10 (m, 2H), 6.96-6.91 (m, 3H), 4.71 (tt, *J* = 7.5, 6.1 Hz, 1H), 3.60 (dd, *J* = 12.8, 7.5 Hz, 1H), 3.48 (s, 3H), 3.36 (d, *J* = 6.1 Hz, 1H), 3.25 (d, *J* = 7.5 Hz, 1H), 2.50 (dd, *J* = 12.8, 6.1 Hz, 1H); ^{13}C NMR (100 MHz) δ 171.0, 147.6, 139.4, 128.5, 128.4, 128.4, 128.2, 128.2, 127.4, 127.4, 122.8, 117.3, 117.3, 79.2, 77.4, 52.5, 51.4, 7.6; IR (neat) 3060, 3027, 2950, 1729, 1596, 1489, 1448, 1431, 1227, 1182 cm^{-1}; HRMS (ESI) *m/z* 446.0211 [$C_{18}H_{18}INaNO_3$ (M+Na) requires 446.0224].

3. CRYSTAL SUMMARY FOR NITRONE 4K



4k



DISCUSSION

The compound crystallizes as colorless plate-like crystals. There are four molecules of the compound in the unit cell of the primitive, centrosymmetric, triclinic space group P-1. Although there are two crystallographically independent molecules in the asymmetric unit, they are chemically identical and only differ in minor variations of torsion angles and derived parameters (bond distances and angles).

The structure of the compound: methyl (*N*-oxy-*N*-phenylimino)(*p*-fluorophenyl)acetate is as expected. The N1-C1 and N2-C16 bond distances (1.3220(16) and 1.3180(16) Å, respectively see Table of Bond Distances) are indicative of a formal double bond. By contrast, the N1-O1 and N2-O4 distances (1.2876(13) and 1.2857(14) Å, respectively) are typical for N=O distances, indicating some delocalization of the bonds. Bond angles and remaining bond distances are otherwise as expected.

CRYSTAL SUMMARY

Crystal data for $C_{15}H_{12}FNO_3$; M_r = 273.26; Triclinic; space group P-1; *a* = 10.1802(5) Å; *b* = 10.4053(5) Å; *c* = 13.1475(6) Å; α = 90.7253(19)°; β = 108.2012(17)°; γ = 106.1890(19)°; V = 1262.93(11) $Å^3$; Z = 4; T = 120(2) K; λ(Mo-Kα) = 0.71073 Å; μ(Mo-Kα) = 0.110 mm^{-1}; d_{calc} = 1.437g.cm^{-3}; 18678 reflections collected; 5348 unique (R_{int} = 0.0199); giving R_1 = 0.0350, wR_2 = 0.0880 for 4389 data with [I>2σ(I)] and R_1 = 0.0469, wR_2 = 0.0947 for all 5348 data. Residual electron density (e^-.$Å^{-3}$) max/min: 0.232/-0.265.

An arbitrary sphere of data were collected on a colorless plate-like crystal, having approximate dimensions of 0.589 × 0.371 × 0.056 mm, on a Bruker Kappa X8-APEX-II diffractometer using a combination of ω- and φ-scans of 0.5°.[10] Data were corrected for absorption and polarization effects and analyzed for space group determination. The structure was solved by intrinsic phasing methods and expanded routinely.[11] The model was refined by full-matrix least-squares analysis of F^2 against all reflections. All non-hydrogen atoms were refined with anisotropic thermal displacement parameters. Unless otherwise noted, hydrogen atoms were included in calculated positions. Thermal parameters for the hydrogens were tied to the isotropic thermal parameter of the atom to which they are bonded (1.5 × for methyl, 1.2 × for all others).

Table 1. Crystal data and structure refinement for **4k**.

Identification code	**4k**
Empirical formula	$C_{15}H_{12}FNO_3$
Formula weight	273.26
Temperature	120(2) K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	P-1
Unit cell dimensions	a = 10.1802(5) Å α = 90.7253(19)°
	b = 10.4053(5) Å β = 108.2012(17)°
	c = 13.1475(6) Å γ = 106.1890(19)°
Volume	1262.93(11) $Å^3$
Z	4
Density (calculated)	1.437 $g.cm^{-3}$
Absorption coefficient (μ)	0.110 mm^{-1}
F(000)	568
Crystal color, habit	colorless, plate
Crystal size	0.589 × 0.371 × 0.056 mm^3
θ range for data collection	1.640 to 26.712°
Index ranges	$-12 \le h \le 12$, $-13 \le k \le 12$, $-16 \le l \le 16$
Reflections collected	18678
Independent reflections	5348 [R_{int} = 0.0199]
Completeness to θ = 25.242°	100.0 %
Absorption correction	Numerical
Max. and min. transmission	1.0000 and 0.9255
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5348 / 0 / 363
Goodness-of-fit on F^2	1.037
Final R indices [I>2σ(I)]	R_1 = 0.0350, wR_2 = 0.0880
R indices (all data)	R_1 = 0.0469, wR_2 = 0.0947
Extinction coefficient	n/a
Largest diff. peak and hole	0.232 and -0.265 $e^-.Å^{-3}$

Table 2. Atomic coordinates and equivalent isotropic displacement parameters ($Å^2$) for **4k**. U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U(eq)
F(1)	0.18247(10)	0.55059(9)	0.56509(6)	0.032(1)
O(1)	0.35813(10)	0.47881(10)	1.05070(8)	0.024(1)
O(2)	0.15223(11)	0.82267(10)	0.99957(8)	0.024(1)
O(3)	0.04621(10)	0.64335(9)	1.06926(7)	0.020(1)
N(1)	0.29651(11)	0.56410(11)	1.07070(9)	0.017(1)
C(1)	0.22452(13)	0.62544(13)	0.99543(10)	0.017(1)
C(2)	0.13971(14)	0.70924(13)	1.02243(10)	0.018(1)
C(3)	-0.03418(16)	0.72292(15)	1.10072(12)	0.026(1)
C(4)	0.31764(13)	0.59237(13)	1.18436(10)	0.017(1)
C(5)	0.35573(13)	0.72323(13)	1.23018(10)	0.018(1)
C(6)	0.37893(14)	0.74622(14)	1.33931(11)	0.021(1)
C(7)	0.36558(14)	0.63933(15)	1.40066(11)	0.023(1)
C(8)	0.32958(15)	0.50876(15)	1.35405(11)	0.024(1)
C(9)	0.30613(14)	0.48426(14)	1.24510(11)	0.021(1)
C(10)	0.21859(14)	0.60975(13)	0.88294(10)	0.017(1)
C(11)	0.33510(14)	0.59407(13)	0.85459(11)	0.021(1)
C(12)	0.32385(15)	0.57683(14)	0.74723(11)	0.024(1)
C(13)	0.19524(16)	0.57328(13)	0.66975(11)	0.022(1)
C(14)	0.07845(15)	0.58987(14)	0.69385(11)	0.022(1)
C(15)	0.09156(14)	0.60933(13)	0.80148(11)	0.020(1)
F(2)	0.38934(10)	0.13873(10)	1.02867(7)	0.035(1)
O(4)	0.25238(11)	0.29288(9)	0.54157(8)	0.026(1)
O(5)	0.32561(10)	-0.11445(10)	0.54350(8)	0.025(1)
O(6)	0.09408(10)	-0.11385(9)	0.47395(7)	0.020(1)
N(2)	0.24390(12)	0.17044(11)	0.51600(9)	0.019(1)
C(16)	0.25792(13)	0.07816(13)	0.58297(10)	0.017(1)
C(17)	0.23312(14)	-0.05984(13)	0.53145(10)	0.017(1)
C(18)	0.05635(16)	-0.24114(14)	0.40986(11)	0.025(1)
C(19)	0.22239(14)	0.13846(13)	0.40220(10)	0.018(1)
C(20)	0.33528(15)	0.12009(14)	0.37260(11)	0.022(1)
C(21)	0.31465(16)	0.09547(15)	0.26392(12)	0.026(1)
C(22)	0.18295(17)	0.08838(14)	0.18767(11)	0.026(1)
C(23)	0.07120(16)	0.10663(15)	0.21952(11)	0.026(1)
C(24)	0.09068(15)	0.13335(14)	0.32709(11)	0.023(1)
C(25)	0.29224(13)	0.09901(13)	0.69934(10)	0.017(1)
C(26)	0.31091(14)	0.22175(14)	0.75515(11)	0.020(1)
C(27)	0.34401(14)	0.23547(15)	0.86590(11)	0.023(1)
C(28)	0.35827(15)	0.12595(15)	0.92017(11)	0.024(1)
C(29)	0.34232(15)	0.00342(15)	0.86974(11)	0.025(1)
C(30)	0.30899(14)	-0.01003(14)	0.75916(11)	0.021(1)
H(3A)	-0.0907	0.6710	1.1427	0.039
H(3B)	-0.0997	0.7456	1.0361	0.039
H(3C)	0.0336	0.8059	1.1446	0.039
H(5A)	0.3659	0.7962	1.1877	0.021

H(6A)	0.4040	0.8355	1.3720	0.025
H(7A)	0.3813	0.6557	1.4754	0.028
H(8A)	0.3210	0.4360	1.3968	0.029
H(9A)	0.2826	0.3951	1.2126	0.025
H(11A)	0.4225	0.5952	0.9093	0.025
H(12A)	0.4033	0.5677	0.7275	0.028
H(14A)	-0.0085	0.5881	0.6384	0.026
H(15A)	0.0130	0.6226	0.8201	0.024
H(18A)	-0.0493	-0.2784	0.3804	0.038
H(18B)	0.0966	-0.3042	0.4552	0.038
H(18C)	0.0962	-0.2270	0.3506	0.038
H(20A)	0.4251	0.1242	0.4255	0.027
H(21A)	0.3912	0.0834	0.2418	0.031
H(22A)	0.1690	0.0710	0.1133	0.031
H(23A)	-0.0194	0.1007	0.1669	0.031
H(24A)	0.0151	0.1480	0.3491	0.027
H(26A)	0.3007	0.2968	0.7164	0.024
H(27A)	0.3566	0.3190	0.9035	0.027
H(29A)	0.3539	-0.0703	0.9099	0.030
H(30A)	0.2972	-0.0942	0.7229	0.026

Table 3. Anisotropic displacement parameters ($Å^2$) for **4k**.
The anisotropic displacement factor exponent takes the form:
$-2\pi^2[h^2a^{*2}U_{11} + ... + 2hka^*b^*U_{12}]$

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
F(1)	0.0485(6)	0.0335(5)	0.0202(4)	0.0032(4)	0.0169(4)	0.0162(4)
O(1)	0.0263(5)	0.0246(5)	0.0241(5)	-0.0004(4)	0.0071(4)	0.0158(4)
O(2)	0.0336(6)	0.0224(5)	0.0237(5)	0.0059(4)	0.0132(4)	0.0134(4)
O(3)	0.0178(5)	0.0179(5)	0.0276(5)	-0.0008(4)	0.0102(4)	0.0053(4)
N(1)	0.0159(5)	0.0172(6)	0.0188(5)	-0.0007(4)	0.0050(4)	0.0056(4)
C(1)	0.0143(6)	0.0175(6)	0.0179(6)	-0.0008(5)	0.0043(5)	0.0039(5)
C(2)	0.0166(6)	0.0203(7)	0.0132(6)	-0.0010(5)	0.0017(5)	0.0054(5)
C(3)	0.0245(7)	0.0243(7)	0.0337(8)	-0.0017(6)	0.0146(6)	0.0099(6)
C(4)	0.0123(6)	0.0205(7)	0.0164(6)	0.0000(5)	0.0037(5)	0.0050(5)
C(5)	0.0140(6)	0.0186(6)	0.0197(6)	0.0022(5)	0.0051(5)	0.0045(5)
C(6)	0.0174(6)	0.0219(7)	0.0212(7)	-0.0028(5)	0.0058(5)	0.0048(5)
C(7)	0.0196(7)	0.0313(8)	0.0182(6)	0.0018(6)	0.0073(5)	0.0067(6)
C(8)	0.0219(7)	0.0256(7)	0.0244(7)	0.0082(6)	0.0077(6)	0.0061(6)
C(9)	0.0179(6)	0.0180(7)	0.0252(7)	0.0021(5)	0.0056(5)	0.0047(5)
C(10)	0.0180(6)	0.0141(6)	0.0187(6)	-0.0002(5)	0.0061(5)	0.0034(5)
C(11)	0.0187(6)	0.0203(7)	0.0236(7)	0.0018(5)	0.0073(5)	0.0060(5)
C(12)	0.0257(7)	0.0224(7)	0.0289(7)	0.0040(6)	0.0157(6)	0.0087(6)
C(13)	0.0338(8)	0.0166(7)	0.0178(6)	0.0008(5)	0.0121(6)	0.0069(6)
C(14)	0.0242(7)	0.0205(7)	0.0190(7)	0.0005(5)	0.0034(5)	0.0071(6)
C(15)	0.0186(6)	0.0203(7)	0.0216(7)	0.0005(5)	0.0073(5)	0.0068(5)

F(2)	0.0405(5)	0.0436(6)	0.0174(4)	-0.0013(4)	0.0101(4)	0.0060(4)
O(4)	0.0385(6)	0.0161(5)	0.0281(5)	0.0009(4)	0.0131(5)	0.0109(4)
O(5)	0.0224(5)	0.0279(5)	0.0266(5)	-0.0032(4)	0.0034(4)	0.0137(4)
O(6)	0.0173(5)	0.0164(5)	0.0245(5)	-0.0019(4)	0.0050(4)	0.0042(4)
N(2)	0.0182(6)	0.0180(6)	0.0206(6)	0.0002(4)	0.0066(4)	0.0058(4)
C(16)	0.0139(6)	0.0183(6)	0.0189(6)	0.0012(5)	0.0051(5)	0.0047(5)
C(17)	0.0176(6)	0.0195(7)	0.0155(6)	0.0028(5)	0.0065(5)	0.0060(5)
C(18)	0.0251(7)	0.0197(7)	0.0262(7)	-0.0064(6)	0.0028(6)	0.0049(6)
C(19)	0.0211(6)	0.0148(6)	0.0179(6)	0.0015(5)	0.0061(5)	0.0045(5)
C(20)	0.0192(7)	0.0241(7)	0.0228(7)	0.0020(5)	0.0059(5)	0.0075(6)
C(21)	0.0287(8)	0.0269(8)	0.0262(7)	0.0020(6)	0.0134(6)	0.0098(6)
C(22)	0.0364(8)	0.0211(7)	0.0193(7)	0.0036(5)	0.0097(6)	0.0065(6)
C(23)	0.0247(7)	0.0244(7)	0.0233(7)	0.0046(6)	0.0010(6)	0.0068(6)
C(24)	0.0199(7)	0.0224(7)	0.0270(7)	0.0048(6)	0.0071(6)	0.0084(6)
C(25)	0.0127(6)	0.0184(6)	0.0200(6)	-0.0008(5)	0.0061(5)	0.0024(5)
C(26)	0.0155(6)	0.0214(7)	0.0231(7)	-0.0009(5)	0.0053(5)	0.0055(5)
C(27)	0.0168(6)	0.0263(7)	0.0238(7)	-0.0067(6)	0.0062(5)	0.0047(6)
C(28)	0.0187(7)	0.0351(8)	0.0162(6)	-0.0026(6)	0.0073(5)	0.0014(6)
C(29)	0.0256(7)	0.0255(7)	0.0228(7)	0.0055(6)	0.0094(6)	0.0028(6)
C(30)	0.0204(7)	0.0186(7)	0.0229(7)	-0.0003(5)	0.0079(5)	0.0014(5)

Table 4 Bond lengths [Å] for **4k**.

atom-atom	distance	atom-atom	distance	
F(1)-C(13)	1.3524(15)	O(1)-N(1)	1.2876(13)	O(2)-
C(2)	1.2036(16)	O(3)-C(2)	1.3296(16)	O(3)-
C(3)	1.4516(15)	N(1)-C(1)	1.3220(16)	N(1)-
C(4)	1.4555(16)	C(1)-C(10)	1.4663(17)	C(1)-
C(2)	1.4951(17)	C(4)-C(5)	1.3806(18)	C(4)-
C(9)	1.3873(18)	C(5)-C(6)	1.3856(18)	C(6)-
C(7)	1.3832(19)	C(7)-C(8)	1.384(2)	C(8)-
C(9)	1.3846(19)	C(10)-C(15)	1.3968(18)	C(10)-
C(11)	1.3982(18)	C(11)-C(12)	1.3852(19)	C(12)-
C(13)	1.376(2)	C(13)-C(14)	1.3756(19)	C(14)-
C(15)	1.3860(18)	F(2)-C(28)	1.3574(15)	O(4)-
N(2)	1.2857(14)	O(5)-C(17)	1.2009(15)	O(6)-
C(17)	1.3297(16)	O(6)-C(18)	1.4484(16)	N(2)-
C(16)	1.3180(16)	N(2)-C(19)	1.4627(16)	C(16)-
C(25)	1.4578(17)	C(16)-C(17)	1.5003(18)	C(19)-
C(24)	1.3812(19)	C(19)-C(20)	1.3815(18)	C(20)-
C(21)	1.3873(19)	C(21)-C(22)	1.382(2)	C(22)-
C(23)	1.386(2)	C(23)-C(24)	1.379(2)	C(25)-
C(26)	1.3999(18)	C(25)-C(30)	1.4077(18)	C(26)-
C(27)	1.3841(19)	C(27)-C(28)	1.370(2)	C(28)-
C(29)	1.374(2)	C(29)-C(30)	1.3815(19)	C(3)-
H(3A)	0.9800	C(3)-H(3B)	0.9800	C(3)-
H(3C)	0.9800	C(5)-H(5A)	0.9500	C(6)-

H(6A)	0.9500	C(7)-H(7A)	0.9500	C(8)-
H(8A)	0.9500	C(9)-H(9A)	0.9500	C(11)-
H(11A)	0.9500	C(12)-H(12A)	0.9500	C(14)-
H(14A)	0.9500	C(15)-H(15A)	0.9500	C(18)-
H(18A)	0.9800	C(18)-H(18B)	0.9800	C(18)-
H(18C)	0.9800	C(20)-H(20A)	0.9500	C(21)-
H(21A)	0.9500	C(22)-H(22A)	0.9500	C(23)-
H(23A)	0.9500	C(24)-H(24A)	0.9500	C(26)-
H(26A)	0.9500	C(27)-H(27A)	0.9500	C(29)-
H(29A)	0.9500	C(30)-H(30A)	0.9500	

Symmetry transformations used to generate equivalent atoms:

Table 5 Bond angles [°] for **4k**.

atom-atom-atom	angle	atom-atom-atom	angle	
C(2)-O(3)-C(3)	114.71(10)	O(1)-N(1)-C(1)	123.29(11)	O(1)-
N(1)-C(4)	114.42(10)	C(1)-N(1)-C(4)	122.25(10)	N(1)-
C(1)-C(10)	122.23(11)	N(1)-C(1)-C(2)	120.13(11)	C(10)-
C(1)-C(2)	117.58(11)	O(2)-C(2)-O(3)	124.38(12)	O(2)-
C(2)-C(1)	122.56(12)	O(3)-C(2)-C(1)	113.00(11)	C(5)-
C(4)-C(9)	121.82(12)	C(5)-C(4)-N(1)	120.55(11)	C(9)-
C(4)-N(1)	117.54(11)	C(4)-C(5)-C(6)	118.80(12)	C(7)-
C(6)-C(5)	120.08(13)	C(6)-C(7)-C(8)	120.54(13)	C(7)-
C(8)-C(9)	120.02(13)	C(8)-C(9)-C(4)	118.72(13)	C(15)-
C(10)-C(11)	119.02(12)	C(15)-C(10)-C(1)	118.71(11)	C(11)-
C(10)-C(1)	122.27(11)	C(12)-C(11)-C(10)	120.38(12)	C(13)-
C(12)-C(11)	118.57(12)	F(1)-C(13)-C(12)	118.42(12)	F(1)-
C(13)-C(14)	118.52(12)	C(12)-C(13)-C(14)	123.05(12)	C(13)-
C(14)-C(15)	117.96(12)	C(14)-C(15)-C(10)	120.99(12)	C(17)-
O(6)-C(18)	116.53(10)	O(4)-N(2)-C(16)	125.81(11)	O(4)-
N(2)-C(19)	114.21(10)	C(16)-N(2)-C(19)	119.93(11)	N(2)-
C(16)-C(25)	125.86(12)	N(2)-C(16)-C(17)	115.24(11)	C(25)-
C(16)-C(17)	118.89(11)	O(5)-C(17)-O(6)	125.26(12)	O(5)-
C(17)-C(16)	124.39(12)	O(6)-C(17)-C(16)	110.31(10)	C(24)-
C(19)-C(20)	122.03(12)	C(24)-C(19)-N(2)	118.43(11)	C(20)-
C(19)-N(2)	119.48(11)	C(19)-C(20)-C(21)	118.59(13)	C(22)-
C(21)-C(20)	120.17(13)	C(21)-C(22)-C(23)	120.10(13)	C(24)-
C(23)-C(22)	120.46(13)	C(23)-C(24)-C(19)	118.63(13)	C(26)-
C(25)-C(30)	118.09(12)	C(26)-C(25)-C(16)	123.71(12)	C(30)-
C(25)-C(16)	118.19(12)	C(27)-C(26)-C(25)	121.03(13)	C(28)-
C(27)-C(26)	118.51(13)	F(2)-C(28)-C(27)	118.64(13)	F(2)-
C(28)-C(29)	118.37(13)	C(27)-C(28)-C(29)	122.98(13)	C(28)-
C(29)-C(30)	118.37(13)	C(29)-C(30)-C(25)	121.01(13)	O(3)-
C(3)-H(3A)	109.5	O(3)-C(3)-H(3B)	109.5	H(3A)-
C(3)-H(3B)	109.5	O(3)-C(3)-H(3C)	109.5	H(3A)-

C(3)-H(3C)	109.5	H(3B)-C(3)-H(3C)	109.5	C(4)-
C(5)-H(5A)	120.6	C(6)-C(5)-H(5A)	120.6	C(7)-
C(6)-H(6A)	120.0	C(5)-C(6)-H(6A)	120.0	C(6)-
C(7)-H(7A)	119.7	C(8)-C(7)-H(7A)	119.7	C(7)-
C(8)-H(8A)	120.0	C(9)-C(8)-H(8A)	120.0	C(8)-
C(9)-H(9A)	120.6	C(4)-C(9)-H(9A)	120.6	C(12)-
C(11)-H(11A)	119.8	C(10)-C(11)-H(11A)	119.8	C(13)-
C(12)-H(12A)	120.7	C(11)-C(12)-H(12A)	120.7	C(13)-
C(14)-H(14A)	121.0	C(15)-C(14)-H(14A)	121.0	C(14)-
C(15)-H(15A)	119.5	C(10)-C(15)-H(15A)	119.5	O(6)-
C(18)-H(18A)	109.5	O(6)-C(18)-H(18B)	109.5	H(18A)-
C(18)-H(18B)	109.5	O(6)-C(18)-H(18C)	109.5	H(18A)-
C(18)-H(18C)	109.5	H(18B)-C(18)-H(18C)	109.5	C(19)-
C(20)-H(20A)	120.7	C(21)-C(20)-H(20A)	120.7	C(22)-
C(21)-H(21A)	119.9	C(20)-C(21)-H(21A)	119.9	C(21)-
C(22)-H(22A)	119.9	C(23)-C(22)-H(22A)	119.9	C(24)-
C(23)-H(23A)	119.8	C(22)-C(23)-H(23A)	119.8	C(23)-
C(24)-H(24A)	120.7	C(19)-C(24)-H(24A)	120.7	C(27)-
C(26)-H(26A)	119.5	C(25)-C(26)-H(26A)	119.5	C(28)-
C(27)-H(27A)	120.7	C(26)-C(27)-H(27A)	120.7	C(28)-
C(29)-H(29A)	120.8	C(30)-C(29)-H(29A)	120.8	C(29)-
C(30)-H(30A)	119.5	C(25)-C(30)-H(30A)	119.5	

Symmetry transformations used to generate equivalent atoms:

Table 6. Torsion angles [°] for **4k**.

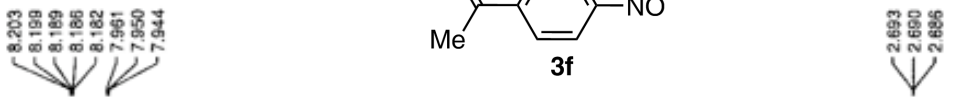
atom-atom-atom-atom	angle	atom-atom-atom-atom	angle	
O(1)-N(1)-C(1)-C(10)	-5.12(19)	C(4)-N(1)-C(1)-C(10)	172.18(11)	O(1)-
N(1)-C(1)-C(2)	172.00(11)	C(4)-N(1)-C(1)-C(2)	-10.70(18)	C(3)-
O(3)-C(2)-O(2)	-5.21(18)	C(3)-O(3)-C(2)-C(1)	177.63(11)	N(1)-
C(1)-C(2)-O(2)	129.25(14)	C(10)-C(1)-C(2)-O(2)	-53.50(17)	N(1)-
C(1)-C(2)-O(3)	-53.54(16)	C(10)-C(1)-C(2)-O(3)	123.71(12)	O(1)-
N(1)-C(4)-C(5)	133.93(12)	C(1)-N(1)-C(4)-C(5)	-43.59(17)	O(1)-
N(1)-C(4)-C(9)	-42.52(15)	C(1)-N(1)-C(4)-C(9)	139.96(13)	C(9)-
C(4)-C(5)-C(6)	-1.87(18)	N(1)-C(4)-C(5)-C(6)	-178.16(11)	C(4)-
C(5)-C(6)-C(7)	0.78(19)	C(5)-C(6)-C(7)-C(8)	0.2(2)	C(6)-
C(7)-C(8)-C(9)	-0.2(2)	C(7)-C(8)-C(9)-C(4)	-0.82(19)	C(5)-
C(4)-C(9)-C(8)	1.89(19)	N(1)-C(4)-C(9)-C(8)	178.29(11)	N(1)-
C(1)-C(10)-C(15)	145.19(13)	C(2)-C(1)-C(10)-C(15)	-32.00(17)	N(1)-
C(1)-C(10)-C(11)	-34.25(19)	C(2)-C(1)-C(10)-C(11)	148.57(12)	C(15)-
C(10)-C(11)-C(12)	-0.7(2)	C(1)-C(10)-C(11)-C(12)	178.69(12)	C(10)-
C(11)-C(12)-C(13)	-1.1(2)	C(11)-C(12)-C(13)-F(1)	-177.17(12)	C(11)-
C(12)-C(13)-C(14)	1.9(2)	F(1)-C(13)-C(14)-C(15)	178.24(12)	C(12)-
C(13)-C(14)-C(15)	-0.8(2)	C(13)-C(14)-C(15)-C(10)	-1.1(2)	C(11)-
C(10)-C(15)-C(14)	1.8(2)	C(1)-C(10)-C(15)-C(14)	-177.61(12)	O(4)-

N(2)-C(16)-C(25)	-3.0(2)	C(19)-N(2)-C(16)-C(25)	174.34(11)	O(4)-
N(2)-C(16)-C(17)	175.96(11)	C(19)-N(2)-C(16)-C(17)	-6.71(16)	C(18)-
O(6)-C(17)-O(5)	-8.60(18)	C(18)-O(6)-C(17)-C(16)	173.45(10)	N(2)-
C(16)-C(17)-O(5)	112.67(14)	C(25)-C(16)-C(17)-O(5)	-68.30(17)	N(2)-
C(16)-C(17)-O(6)	-69.36(14)	C(25)-C(16)-C(17)-O(6)	109.67(12)	O(4)-
N(2)-C(19)-C(24)	-69.78(15)	C(16)-N(2)-C(19)-C(24)	112.59(14)	O(4)-
N(2)-C(19)-C(20)	107.46(13)	C(16)-N(2)-C(19)-C(20)	-70.17(16)	C(24)-
C(19)-C(20)-C(21)	-0.2(2)	N(2)-C(19)-C(20)-C(21)	-177.31(12)	C(19)-
C(20)-C(21)-C(22)	-0.6(2)	C(20)-C(21)-C(22)-C(23)	0.4(2)	C(21)-
C(22)-C(23)-C(24)	0.7(2)	C(22)-C(23)-C(24)-C(19)	-1.5(2)	C(20)-
C(19)-C(24)-C(23)	1.2(2)	N(2)-C(19)-C(24)-C(23)	178.37(12)	N(2)-
C(16)-C(25)-C(26)	1.9(2)	C(17)-C(16)-C(25)-C(26)	-176.98(11)	N(2)-
C(16)-C(25)-C(30)	-177.42(12)	C(17)-C(16)-C(25)-C(30)	3.67(17)	C(30)-
C(25)-C(26)-C(27)	-0.39(19)	C(16)-C(25)-C(26)-C(27)	-179.74(12)	C(25)-
C(26)-C(27)-C(28)	0.02(19)	C(26)-C(27)-C(28)-F(2)	-179.37(12)	C(26)-
C(27)-C(28)-C(29)	0.5(2)	F(2)-C(28)-C(29)-C(30)	179.24(12)	C(27)-
C(28)-C(29)-C(30)	-0.7(2)	C(28)-C(29)-C(30)-C(25)	0.2(2)	C(26)-
C(25)-C(30)-C(29)	0.26(19)	C(16)-C(25)-C(30)-C(29)	179.64(12)	

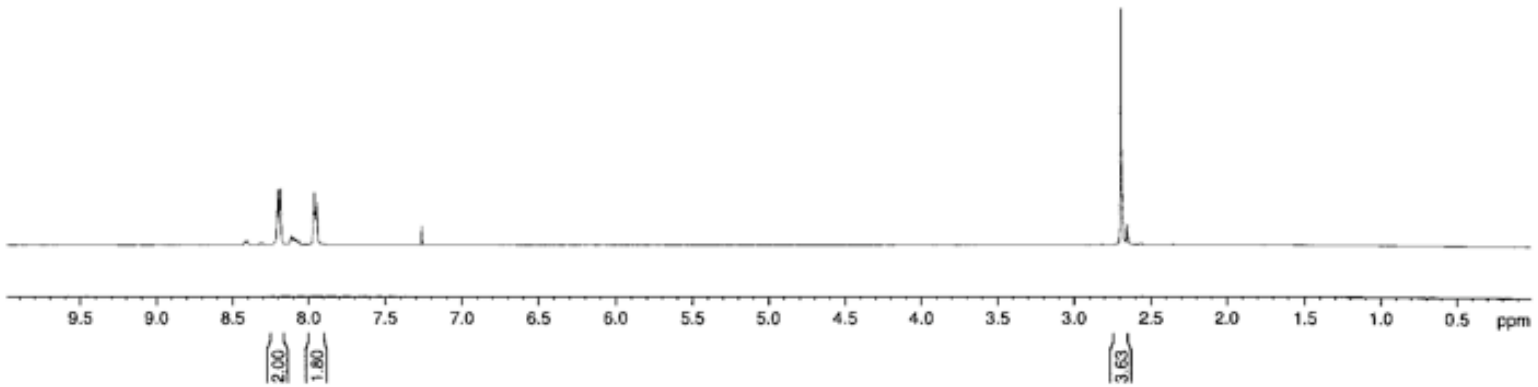
Symmetry transformations used to generate equivalent atoms:

4. REFERENCES

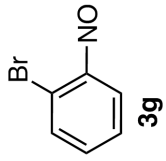
1. Rueck-Braun, K.; Zarwell, S. *Tetrahedron Letters* **2008**, *49*, 4020.
2. Tibiletti, F. *et. al. Tetrahedron* **2010**, *66*, 1280.
3. Blackburn, O. A.; Coe, B. J.; Helliwell, M. *Organometallics* **2011** , *30*, 4910.
4. Bordoloi, A.; Halligudi S. B. *Adv. Synth. Catal*. **2007**, *349*, 2085.
5. Jurok, R.; Hodacova, J.; Eigner, V.; Dvorakova, H.; Setnicka, V.; Cibulka, R. *Eur. J. Org. Chem.,* **2013,** *34,* 7724.
6. Wang, Z.; Zha, Z.; Zhang, Z.; Su, J. *Chem. Eur. J.* **2013**, *19*, 17711.
7. Gravel, M.; Langdon, S. M.; Thai, K.; Bilodeau, F. *Org. Lett.* **2013**, *15*, 2214.
8. Ishida, T.; Kikuchi, S.; Tsubo, T.; Yamada, T. *Org. Lett*. **2013**, *15*, 848.
9. Hansen, J. H. *et. al. Angew. Chem., Int. Ed.* **2011**, *50*, 2544.
10. Bruker AXS. (2008). *APEX-2*. Bruker-Nonius AXS, Madison, Wisconsin, USA.
11. Sheldrick, G. M. *Acta Cryst.*, **2008**, *A64*, 112.


8.203
8.199
8.189
8.186
8.182
7.961
7.950
7.944
O
Me
NO
2.693
2.690
2.686

3f

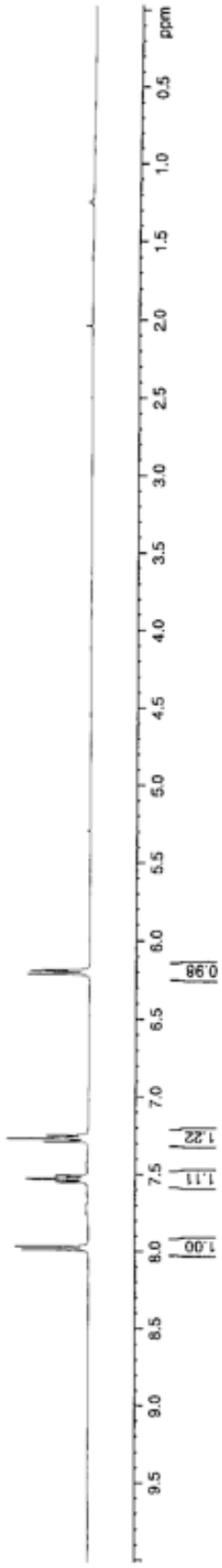

9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
2.00
1.80
3.63

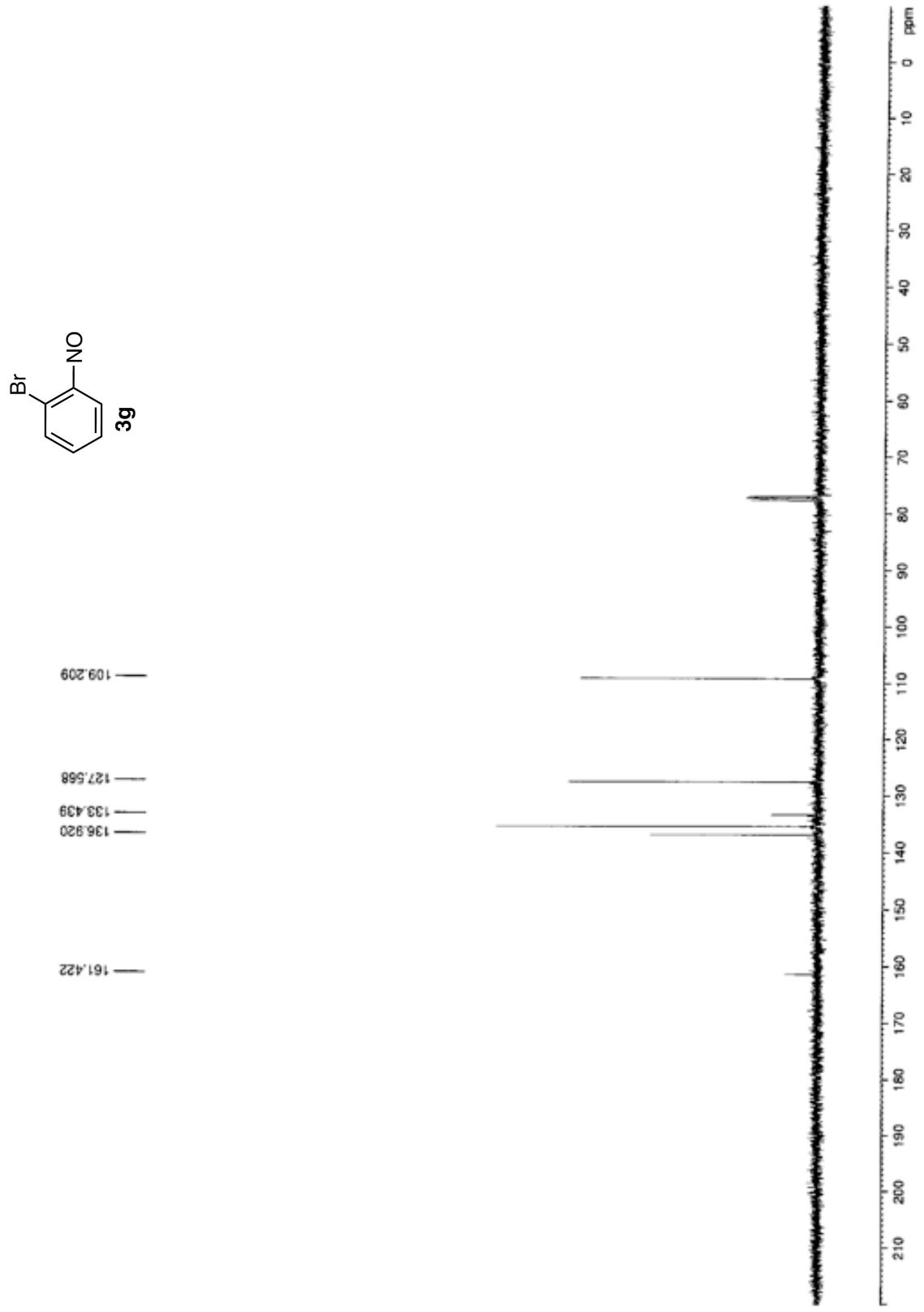
27.330
120.955
129.896
141.117
164.199
197.322
NO
O
Me
3f
ppm


Br
NO

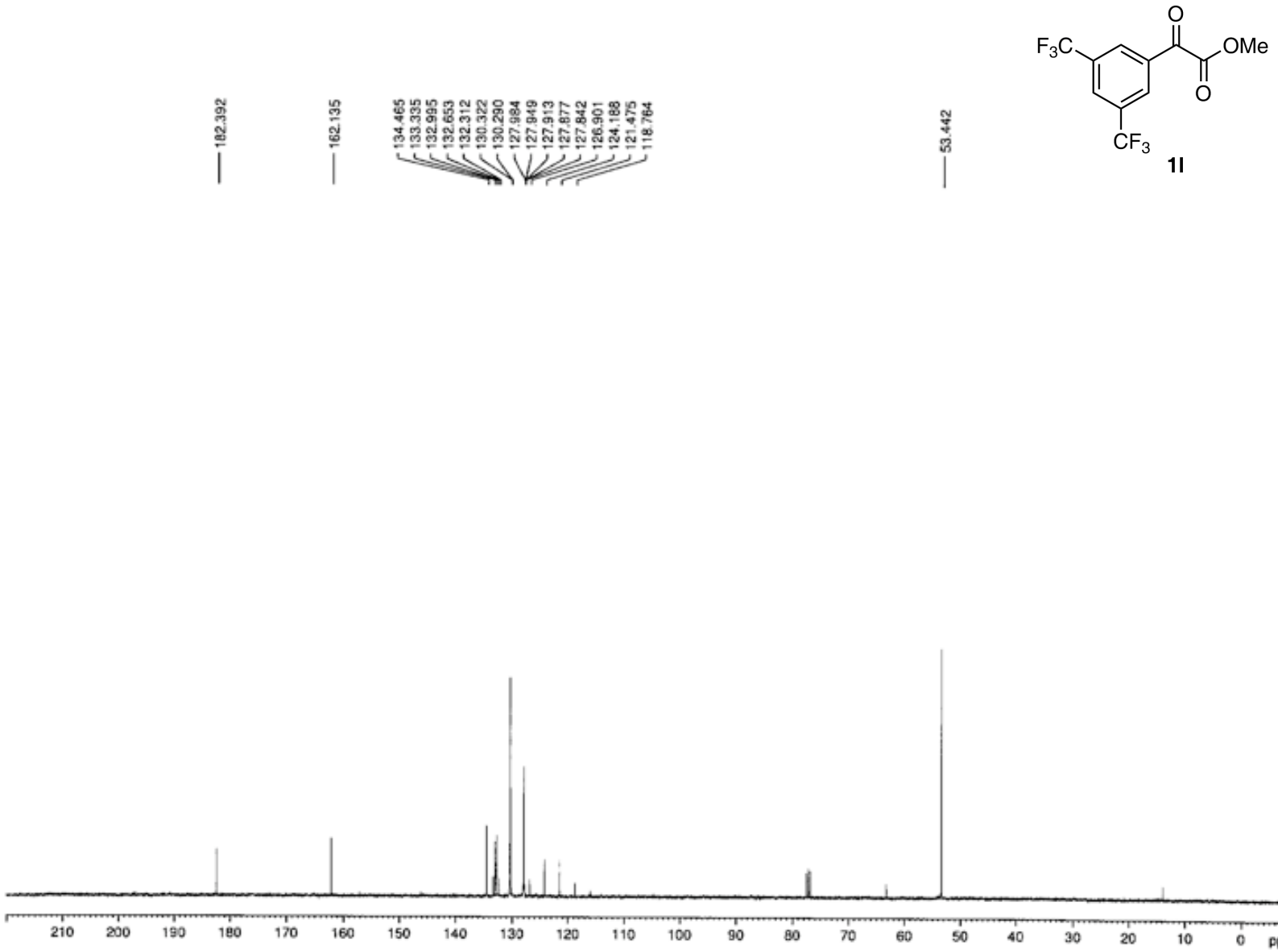
3g

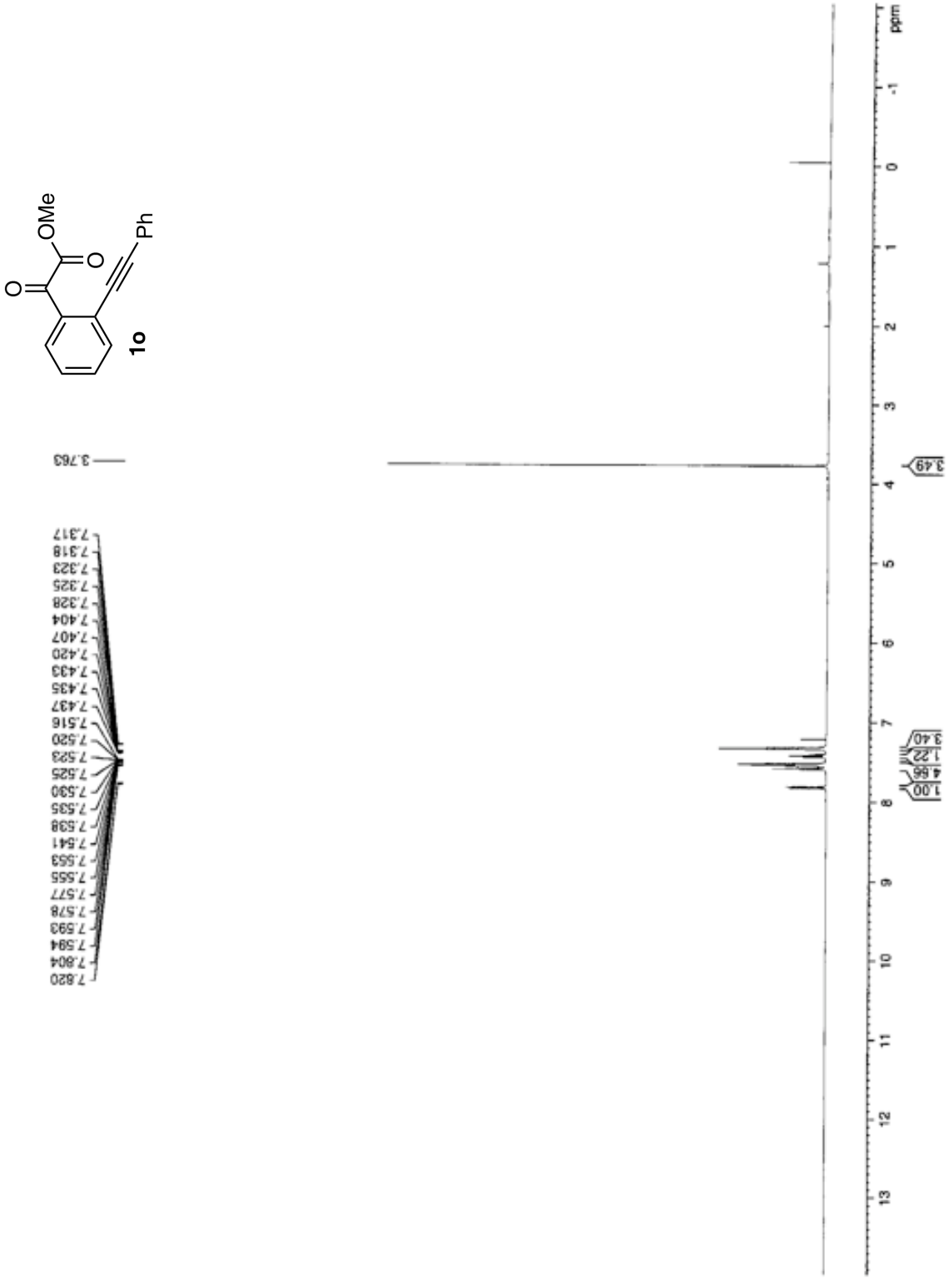

8.208
8.204
8.188
8.184
7.986
7.966
7.547
7.543
7.527
7.526
7.509
7.505
7.284
7.245

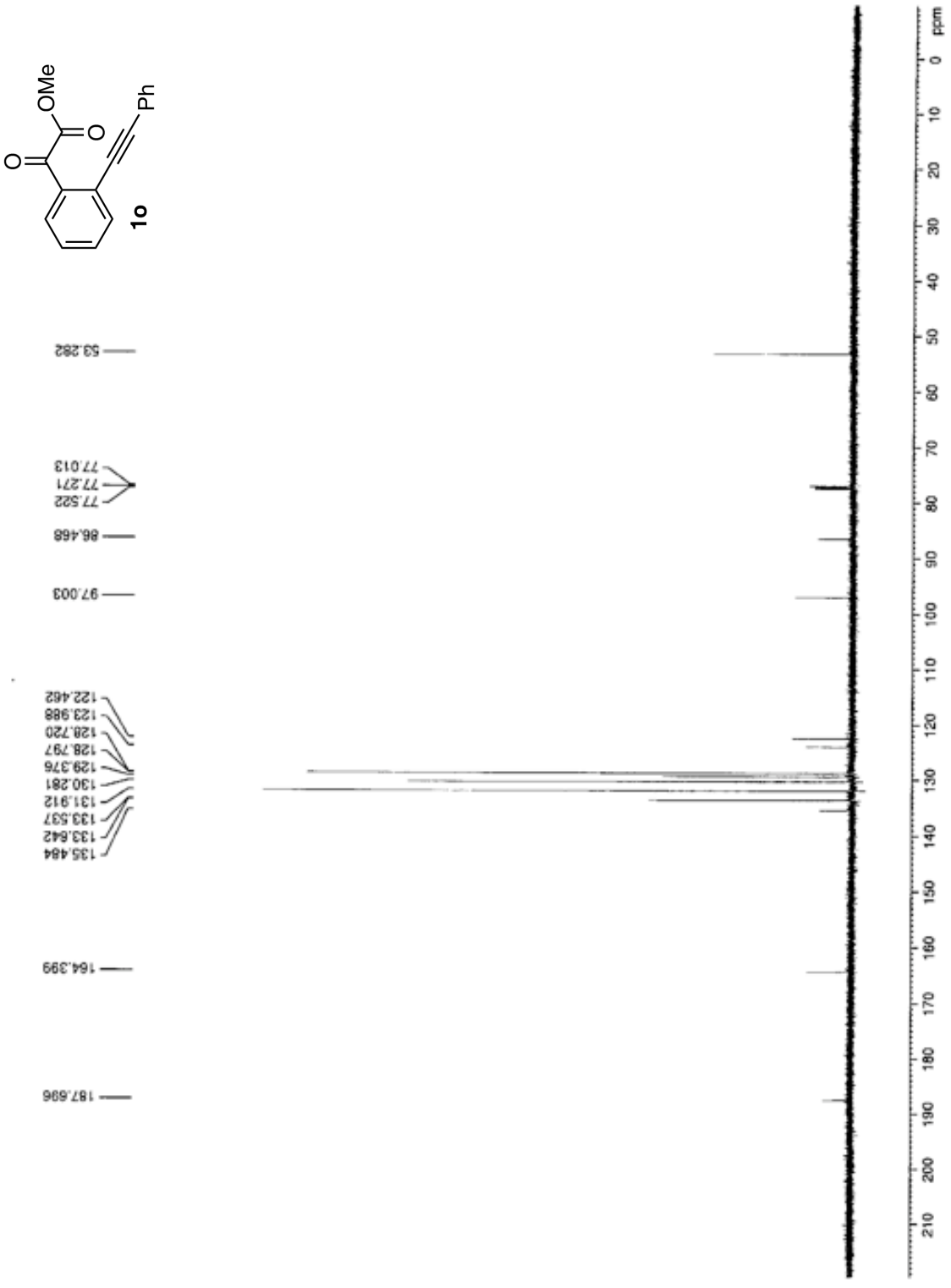

ppm
0.98
1.22
1.11
1.00


Br
NO
3g
109.209
127.568
133.439
136.820
161.422
ppm

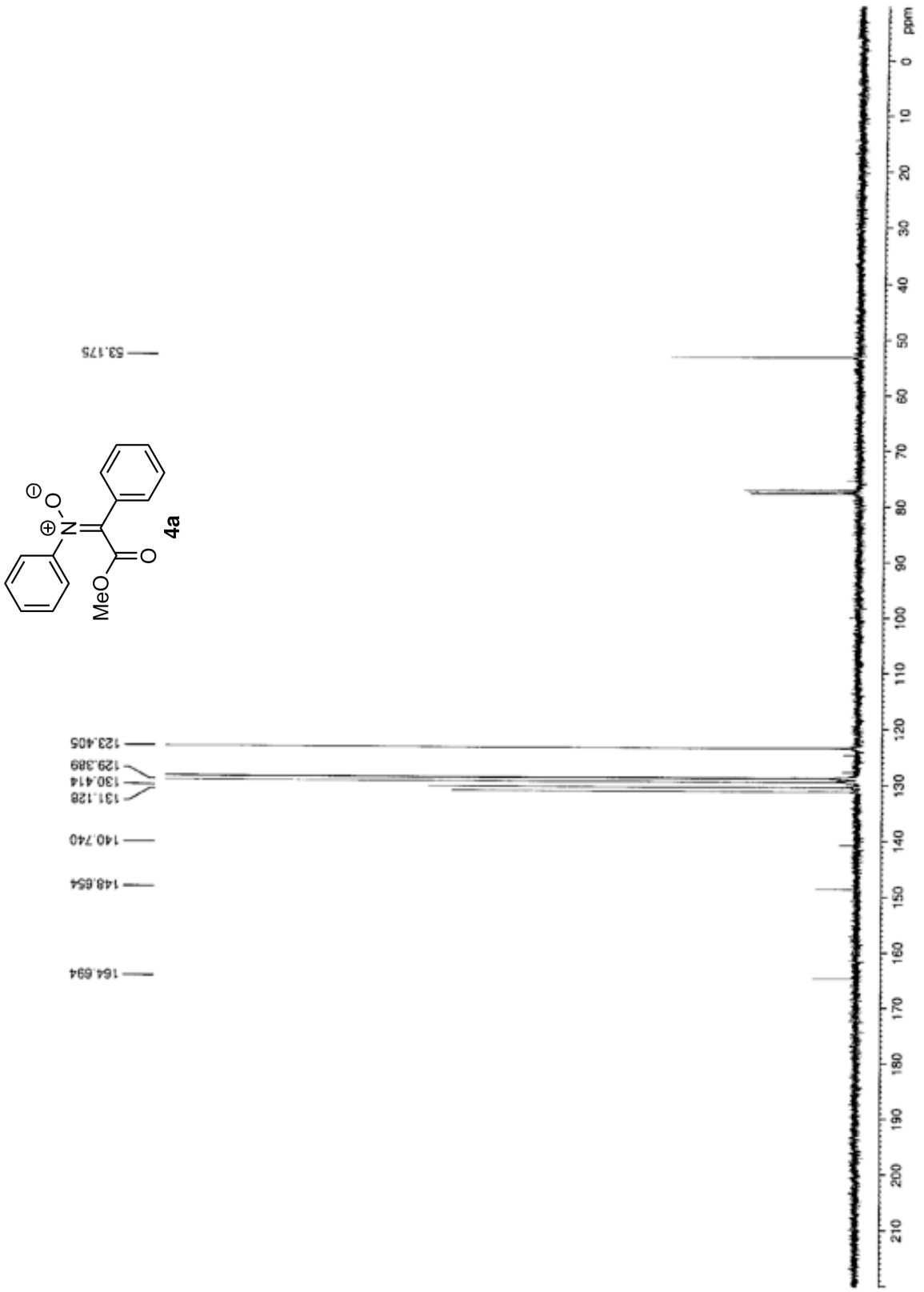
4.000
8.122
8.512
8.511
OMe
O
O
F3C
CF3
1l
3.76
1.09
2.00
ppm

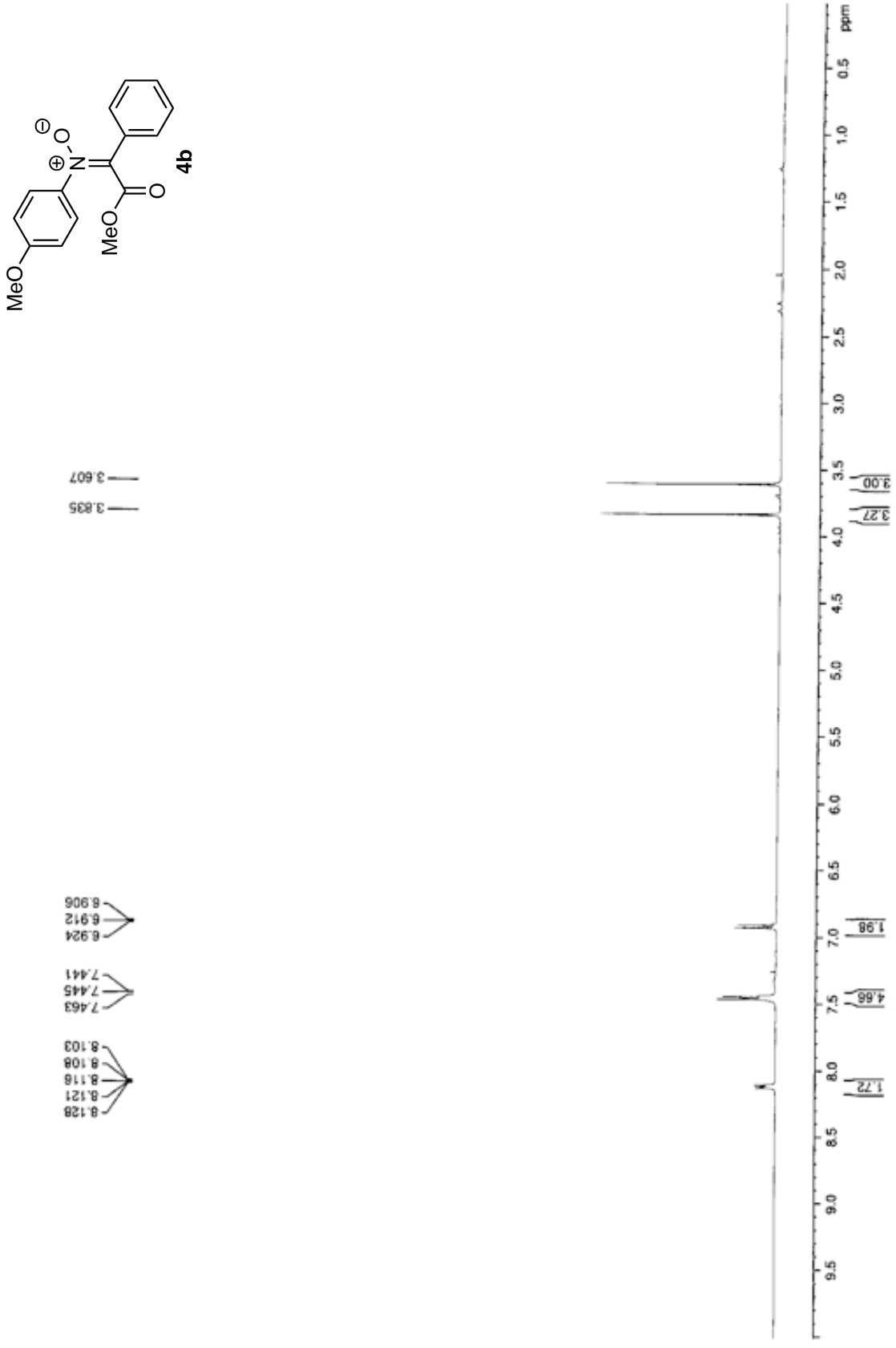

182.392
162.135
134.465
133.335
132.995
132.653
132.312
130.322
130.290
127.984
127.949
127.913
127.877
127.842
126.901
124.188
121.475
118.764
53.442
F3C
O
OMe
O
CF3
1l
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

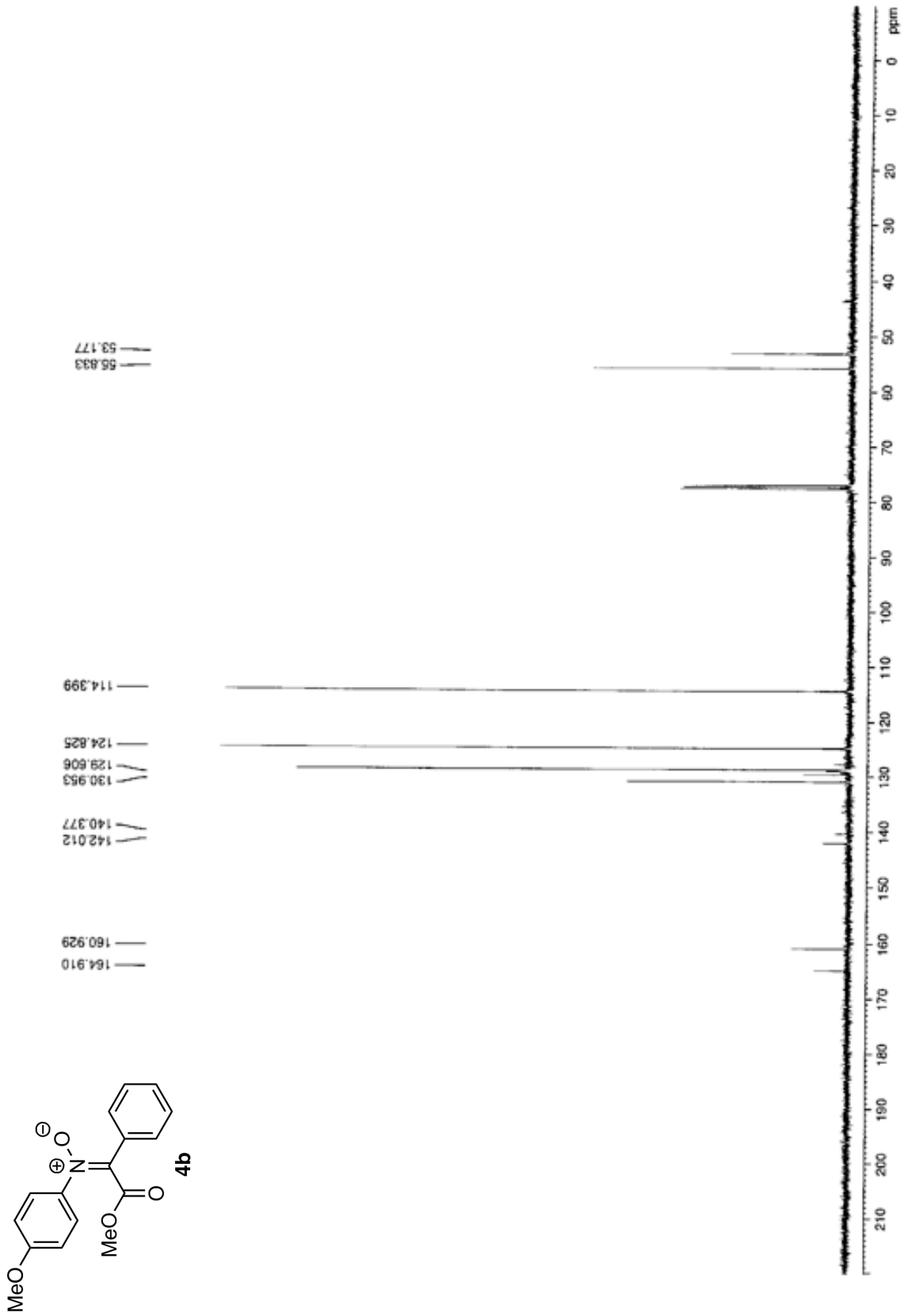

OMe
O
O
Ph
1o
3.763
7.317
7.318
7.323
7.325
7.328
7.404
7.407
7.420
7.433
7.435
7.437
7.516
7.520
7.523
7.525
7.530
7.535
7.538
7.541
7.553
7.555
7.577
7.578
7.593
7.594
7.804
7.820
3.49
3.40
1.22
4.66
1.00
ppm

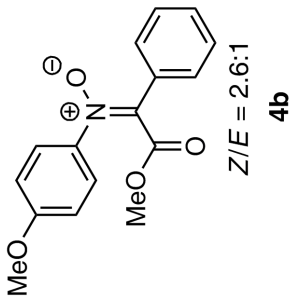

OMe
O
O
Ph
1o
53.282
77.013
77.271
77.522
86.468
97.003
122.462
123.988
128.720
128.797
129.376
130.281
131.912
133.537
133.642
135.484
164.399
187.696
ppm
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210

4a
MeO
O
N
3.556
7.436
7.439
7.442
7.445
7.453
7.455
7.457
7.462
7.470
7.472
7.475
7.479
7.485
7.492
7.494
7.497
7.504
7.508
7.512
7.515
7.519
8.127
8.133
8.141
8.144
8.147
8.150
8.152
3.51
8.65
2.00
ppm


4a
MeO
O
53.175
123.405
129.389
130.414
131.128
140.740
148.654
164.694
ppm


4b
MeO
MeO
3.607
3.835
8.906
8.912
8.924
7.441
7.445
7.463
8.103
8.108
8.116
8.121
8.128
3.00
3.27
1.98
4.66
1.72
ppm

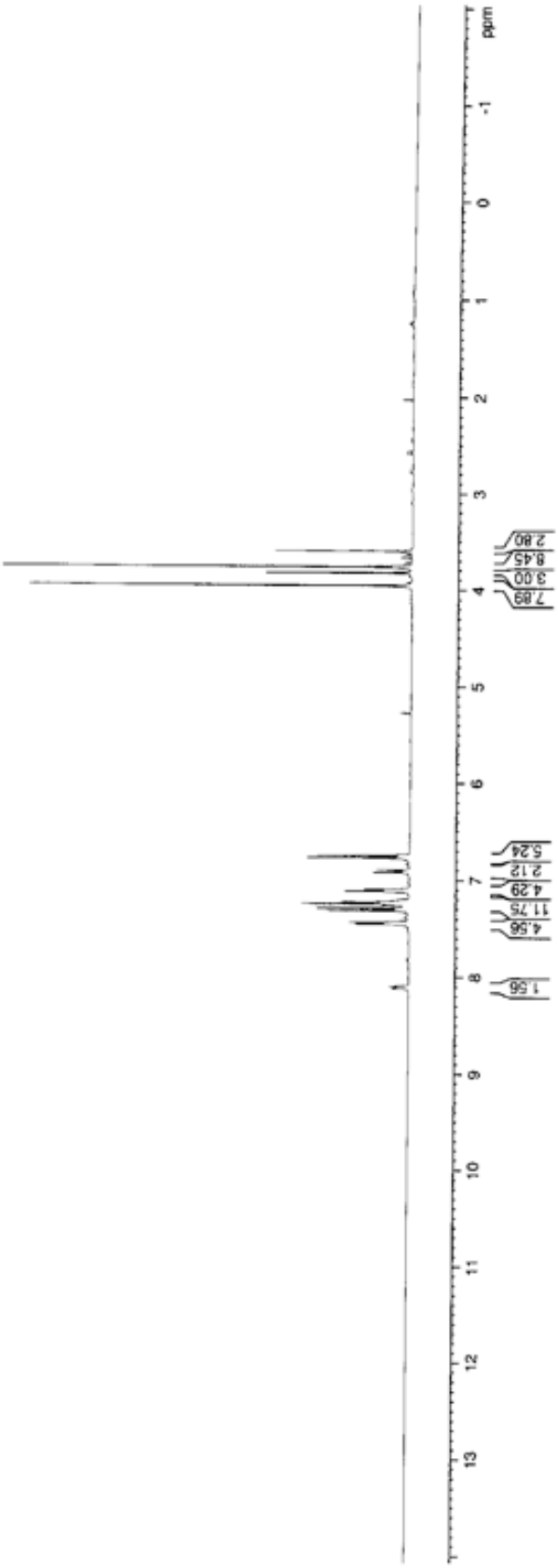

53.177
55.833
114.399
124.825
129.606
130.953
140.377
142.012
160.929
164.910
ppm
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210
MeO
MeO
4b

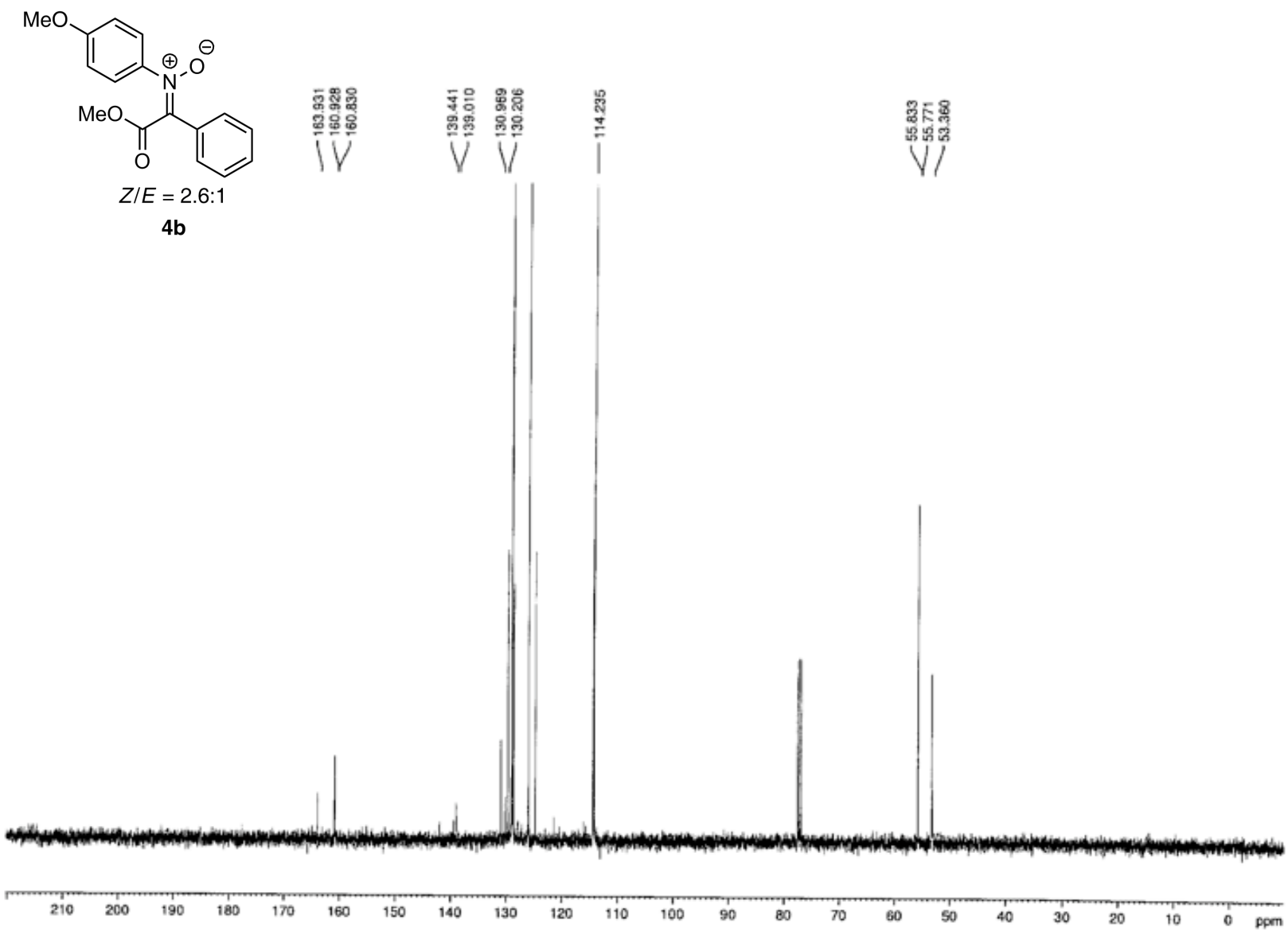

MeO
MeO
O

Z/*E* = 2.6:1

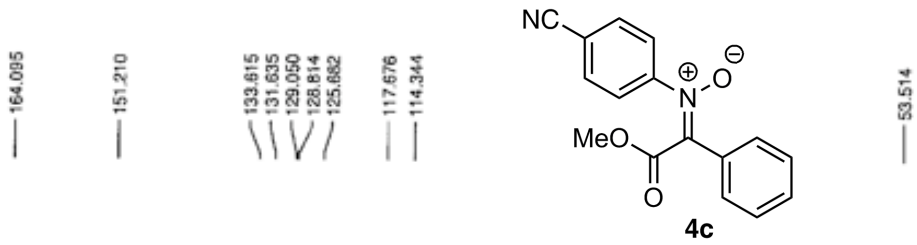
4b

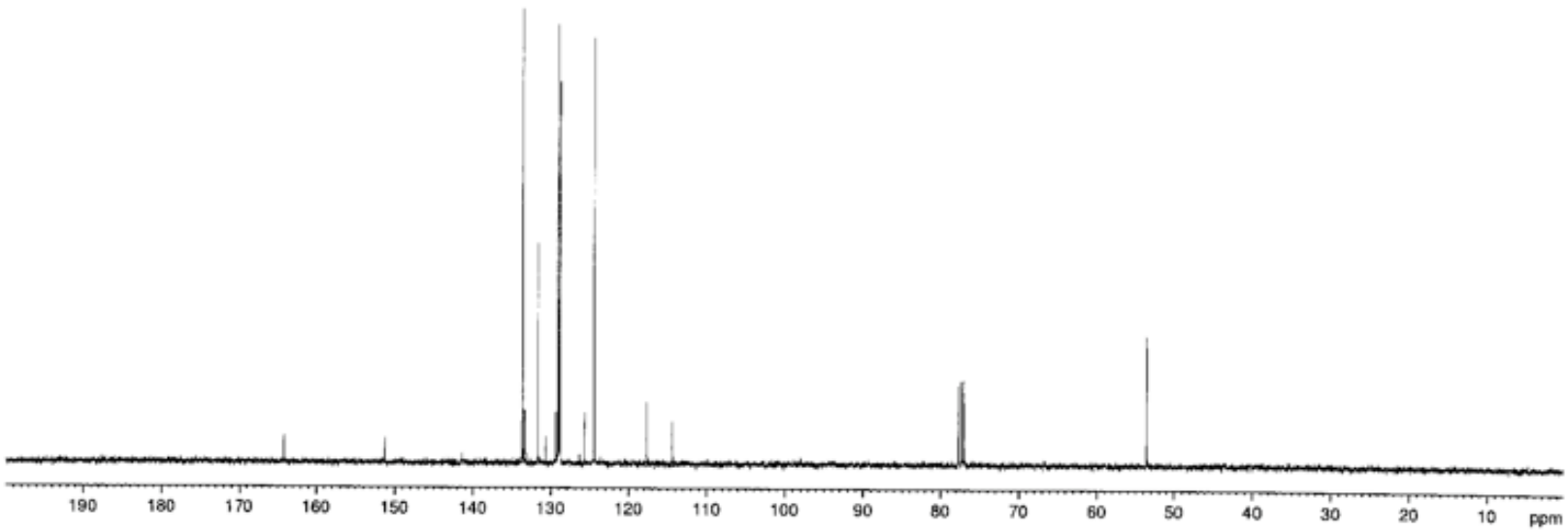

3.759
3.952
8.116
8.109
8.106
8.096
8.092
7.450
7.435
7.430
7.312
7.290
7.258
7.254
7.241
7.224
7.215
7.210
7.209
7.115
7.112
7.097
7.092
6.918
6.896
6.768
6.746


ppm
7.89
3.00
8.45
2.80
5.24
2.12
4.29
11.75
4.56
1.56

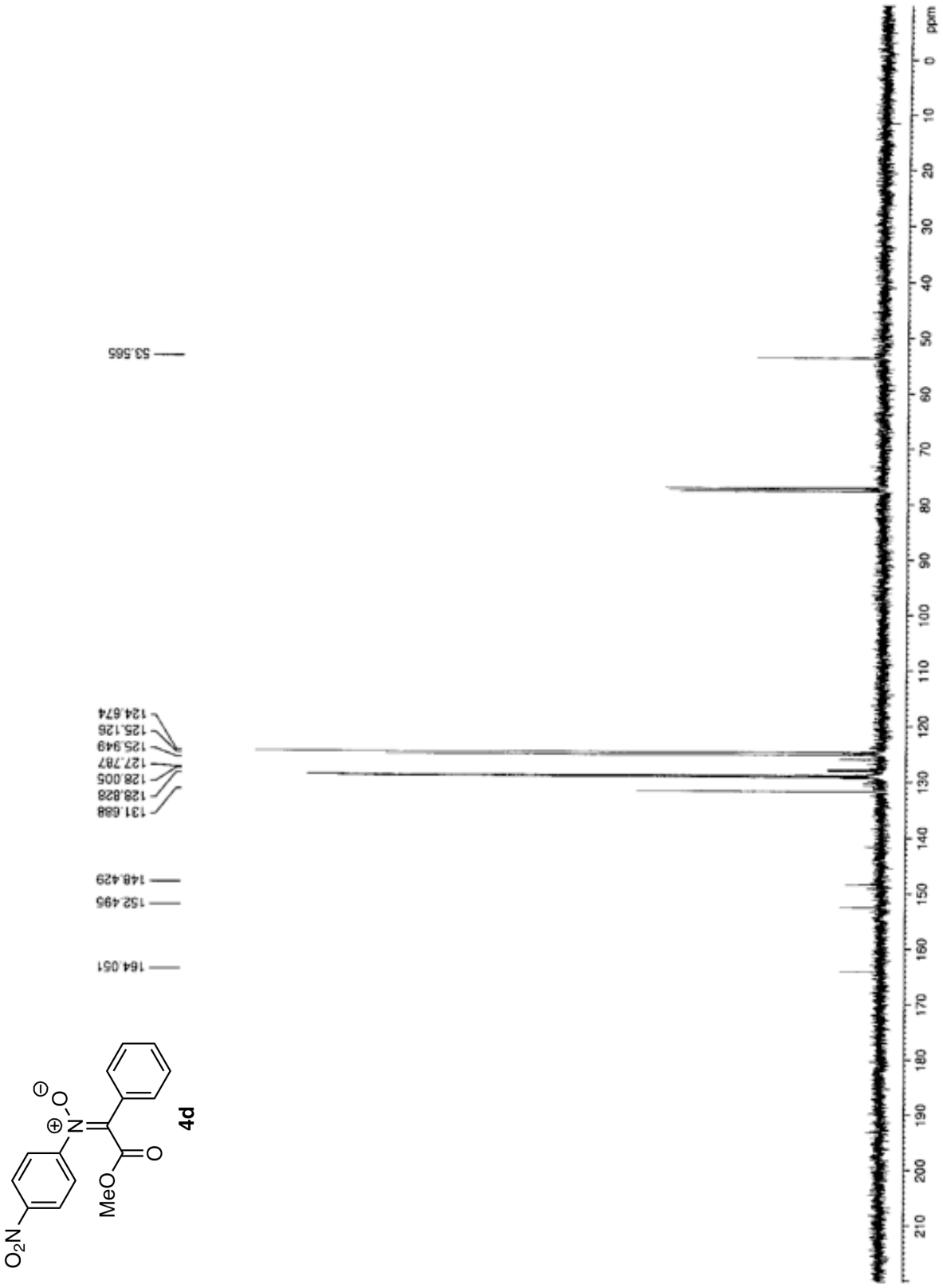

MeO
MeO
O
N
O
O
Z/E = 2.6:1
4b
163.931
160.928
160.830
139.441
139.010
130.969
130.206
114.235
55.833
55.771
53.360
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

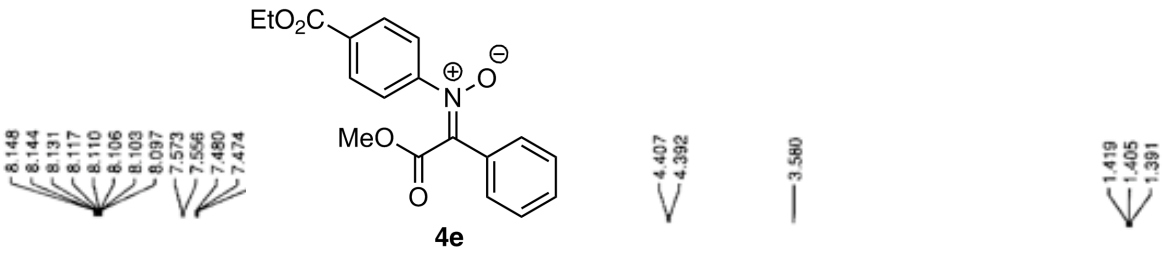
4c
NC
MeO
O
O
N
O
3.619
8.078
8.073
8.063
8.054
7.770
7.749
7.615
7.594
7.495
7.489
7.478
3.35
2.00
1.93
2.02
3.43
ppm


164.095
151.210
133.615
131.635
129.050
128.814
125.682
117.676
114.344
53.514
NC
MeO
O
4c

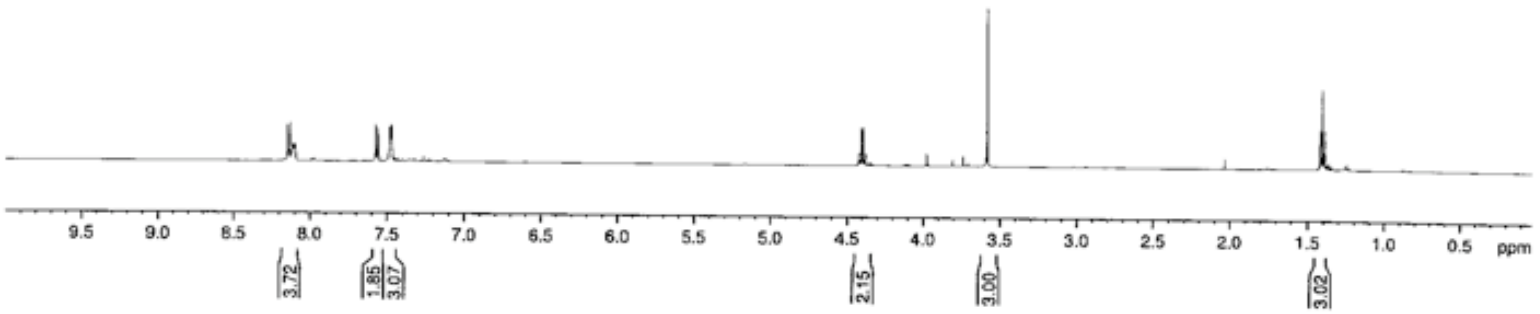

190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

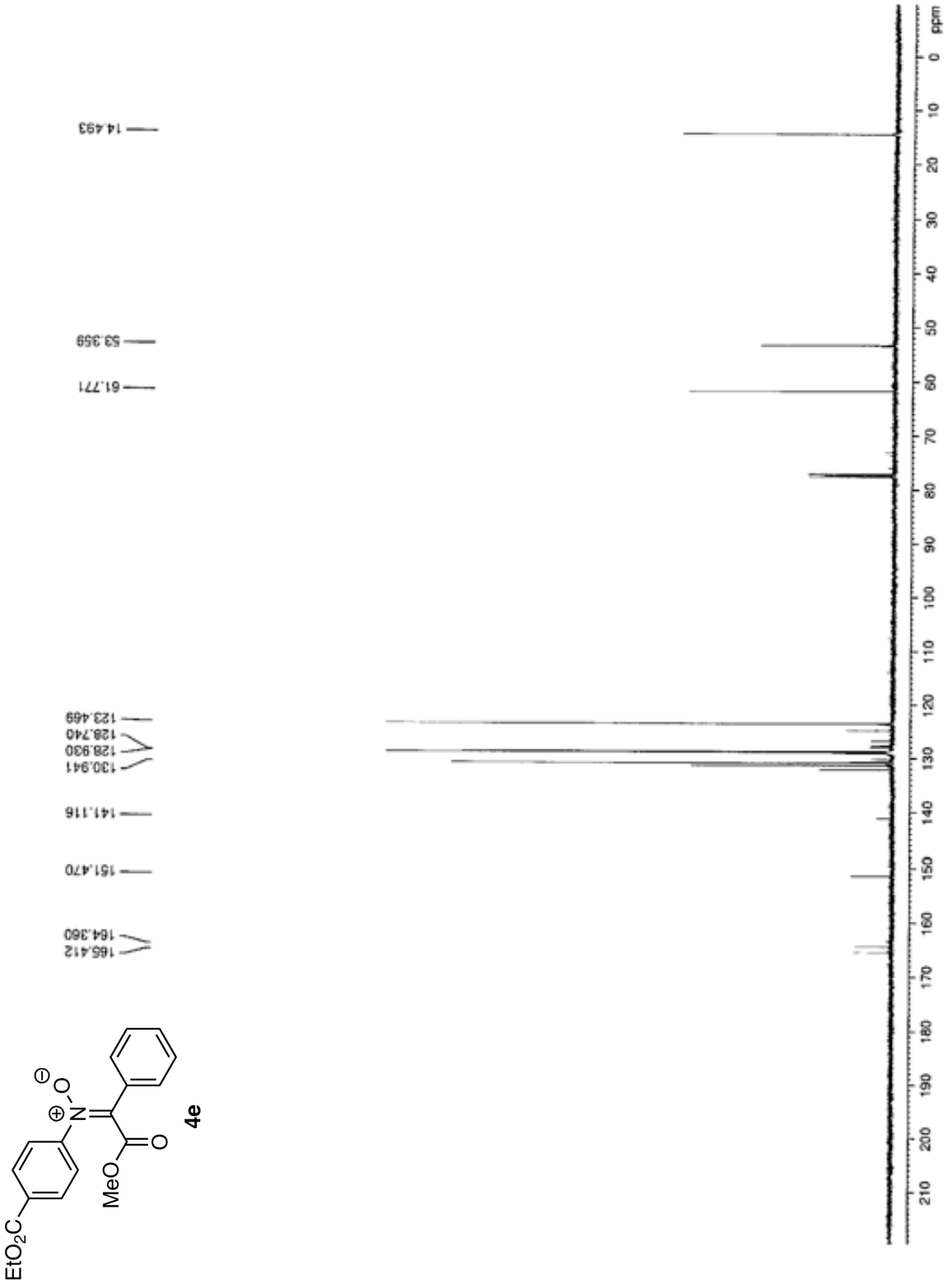
4d
MeO
O
O2N
3.639
8.344
8.322
8.084
8.079
8.071
8.060
7.882
7.860
7.509
7.503
7.494
7.492
3.46
2.10
3.56
2.03
2.00
ppm

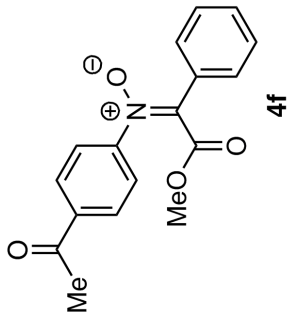

4d
MeO
O
O
N
O
O2N
164.051
152.495
148.429
131.688
128.828
128.005
127.787
125.949
125.126
124.874
53.565
ppm
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210


8.148
8.144
8.131
8.117
8.110
8.106
8.103
8.097
7.573
7.556
7.480
7.474
EtO2C
MeO
O
4.407
4.392
3.580
1.419
1.405
1.391

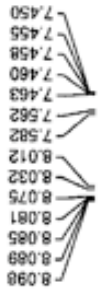
4e

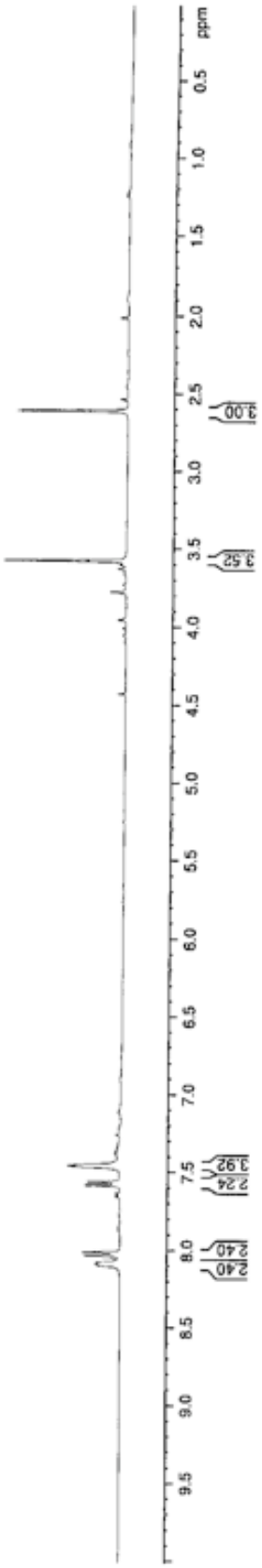

9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
3.72
1.85
3.07
2.15
3.00
3.02

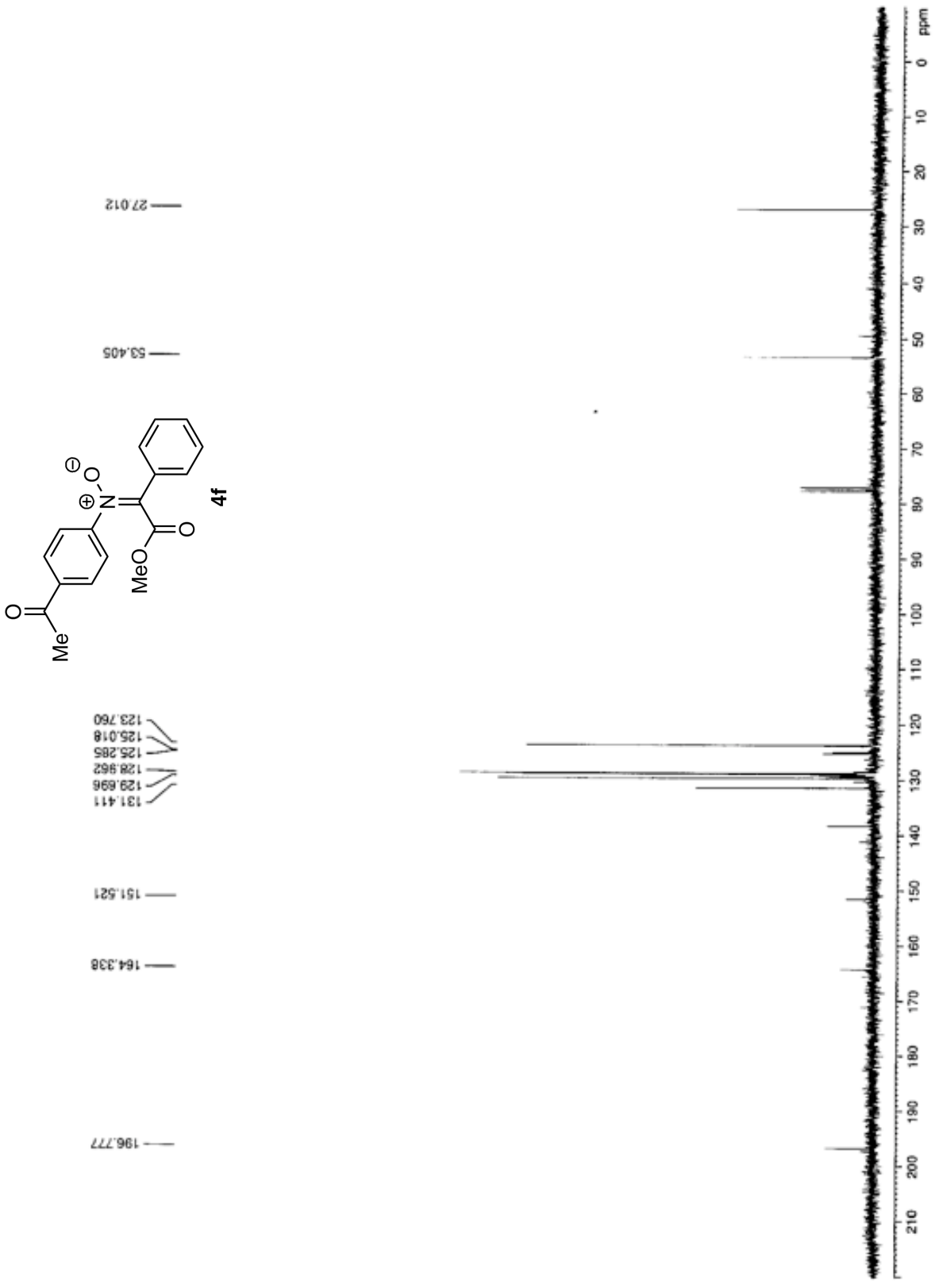

14.493
53.359
61.771
123.469
128.740
128.930
130.941
141.116
151.470
164.360
165.412
4e
MeO
EtO2C
ppm

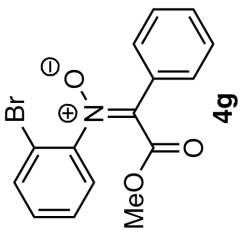

Me
O
MeO
O
O
4f

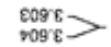

2.607
2.605
3.574
3.573


7.450
7.455
7.458
7.460
7.463
7.562
7.582
8.012
8.032
8.075
8.081
8.085
8.089
8.098

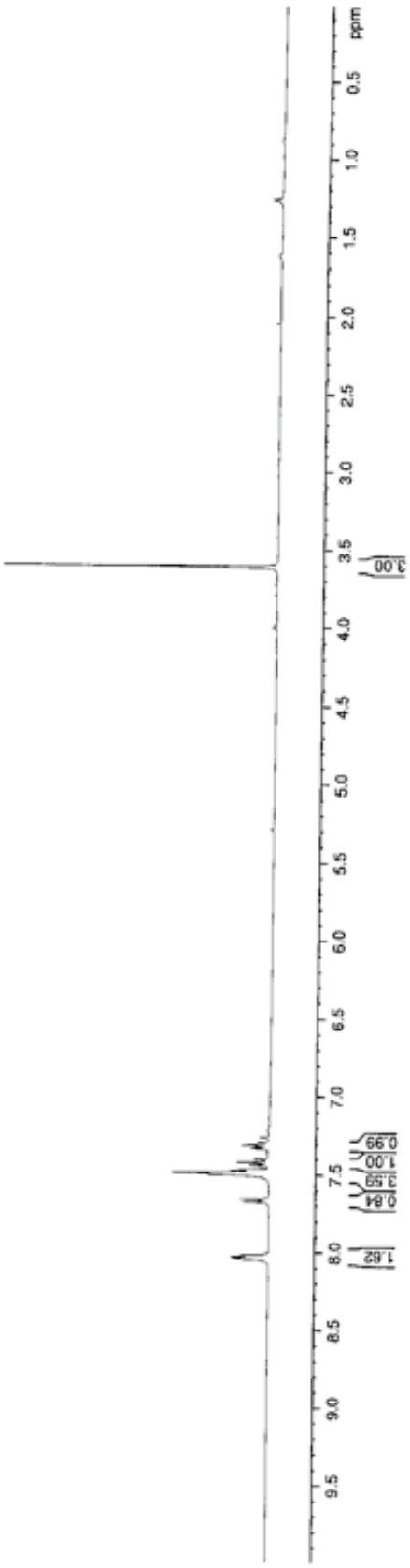

3.00
2.52
1.92
2.24
2.40
2.40
ppm

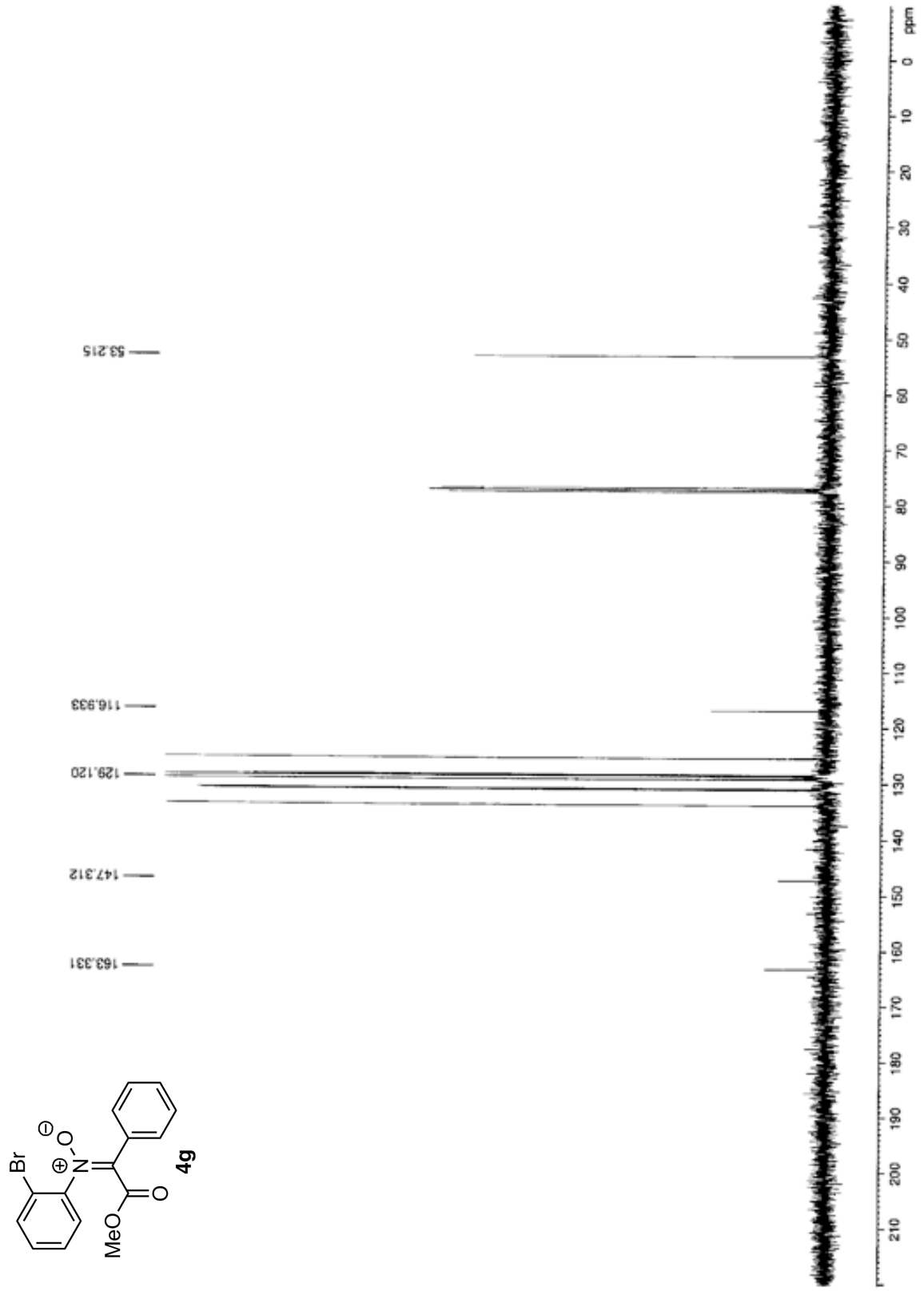

4f
Me
MeO
O
O
O
O
N
27.012
53.405
123.760
125.018
125.285
128.962
129.696
131.411
151.521
164.338
196.777
ppm
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210

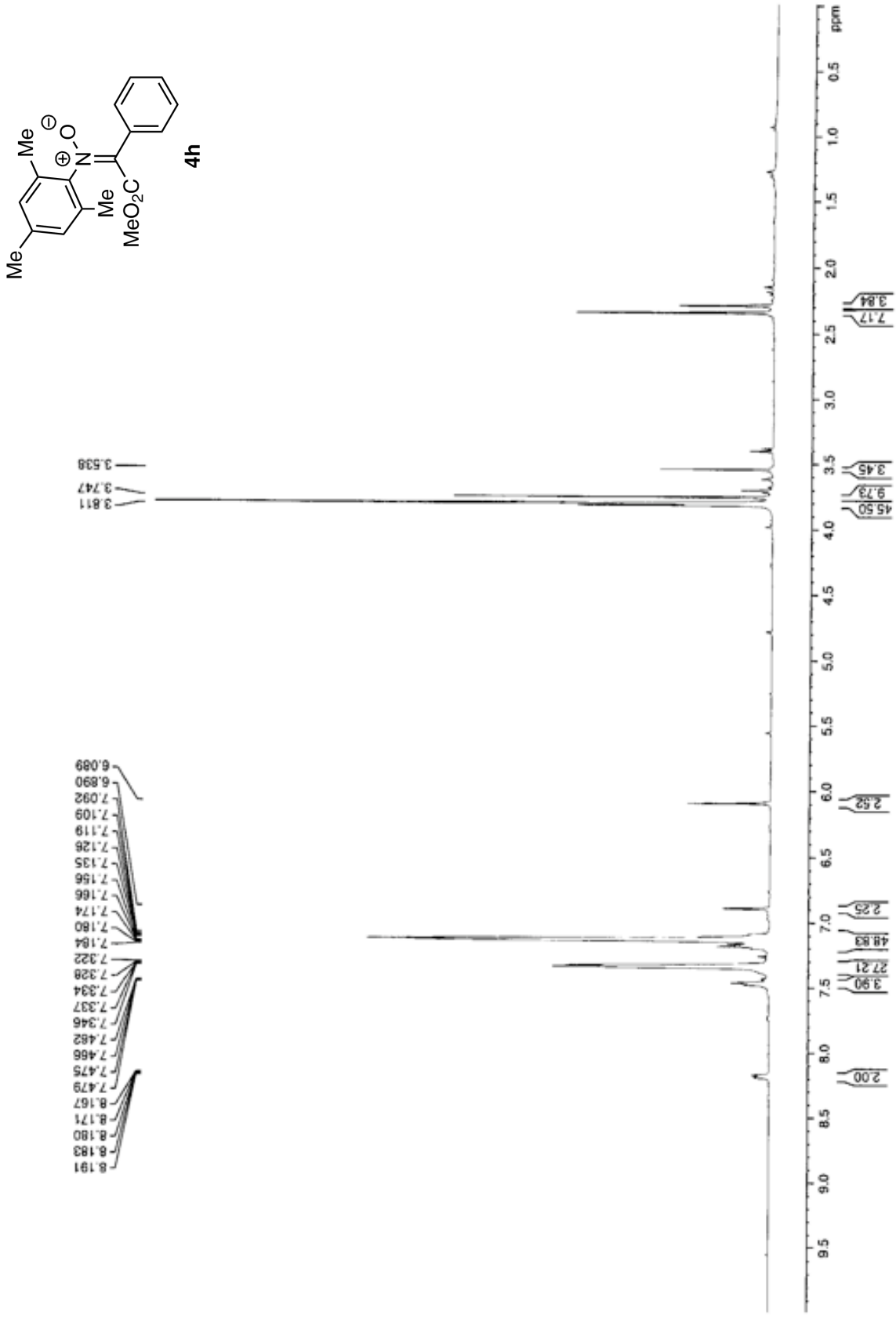

Br
MeO
O
4g

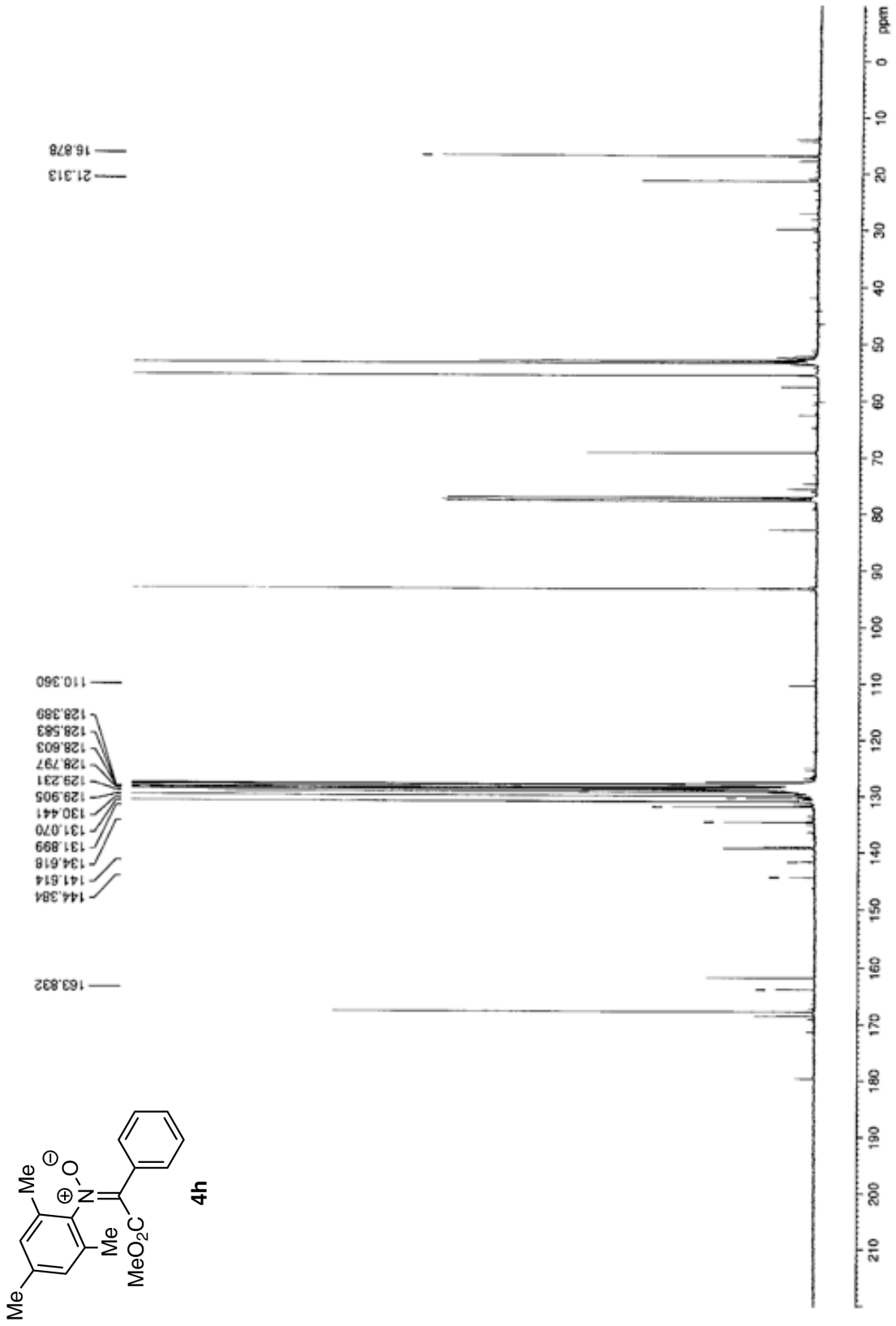

3.604
3.603


7.258
7.259
7.289
7.291
7.307
7.310
7.311
7.326
7.327
7.330
7.400
7.420
7.438
7.471
7.654
7.674
8.019
8.020
8.024
8.034
8.043

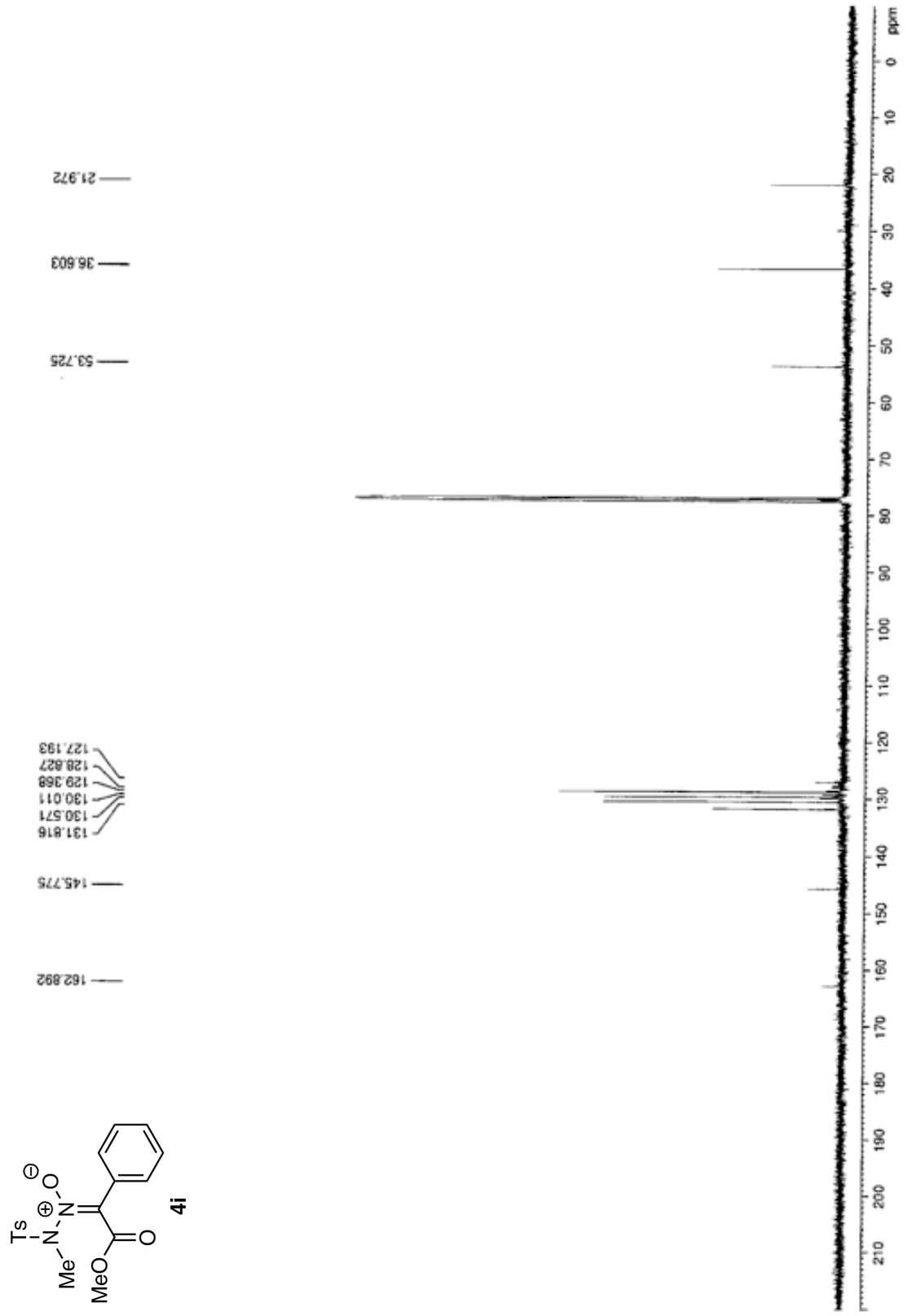

ppm
3.00
1.62
0.84
3.59
1.00
0.99


53.215
116.933
129.120
147.312
163.331
ppm
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210
Br
O
N
O
MeO
4g


4h
Me
Me
Me
MeO2C
3.538
3.747
3.811
6.089
6.890
7.092
7.109
7.119
7.126
7.135
7.156
7.166
7.174
7.180
7.184
7.322
7.328
7.334
7.337
7.346
7.482
7.486
7.475
7.479
8.167
8.171
8.180
8.183
8.191
2.00
3.90
27.21
48.83
2.25
2.52
45.50
9.73
3.45
7.17
3.84
ppm

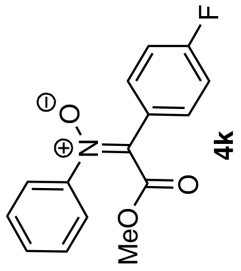

16.878
21.313
110.360
128.389
128.583
128.603
128.797
129.231
129.905
130.441
131.070
131.899
134.618
141.614
144.384
163.832
ppm
Me
Me
Me
MeO2C
4h

Ts
Me
MeO
4i
2.470
3.110
4.035
8.072
8.057
8.054
7.872
7.851
7.463
7.445
7.384
7.384
ppm
3.67
3.53
3.49
1.26
2.25
2.28
2.00


21.972
36.603
53.725
127.193
128.827
129.368
130.011
130.571
131.816
145.775
162.892
ppm
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210
Ts
Me
MeO
4i

Cl
MeO
O
4j
3.548
8.124
8.101
7.484
7.475
7.464
7.462
7.456
7.450
7.442
7.438
7.419
3.47
2.00
7.43
ppm

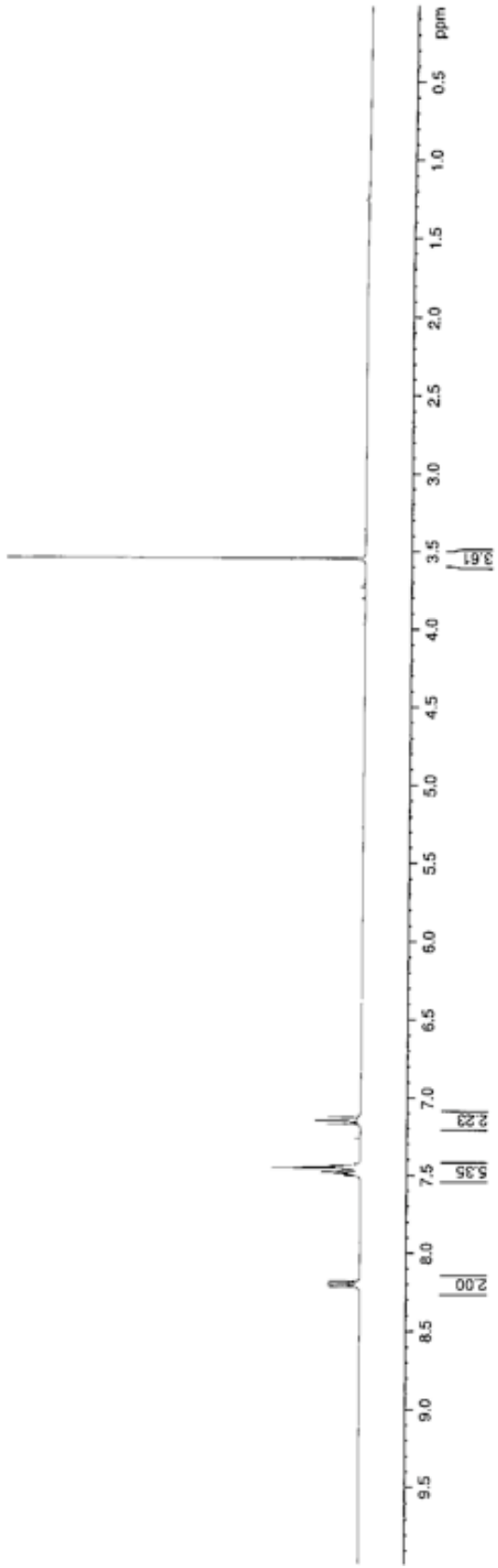
53.272
123.322
124.530
127.828
128.959
129.508
130.185
136.753
148.599
164.396
Cl
MeO
O
4j
ppm

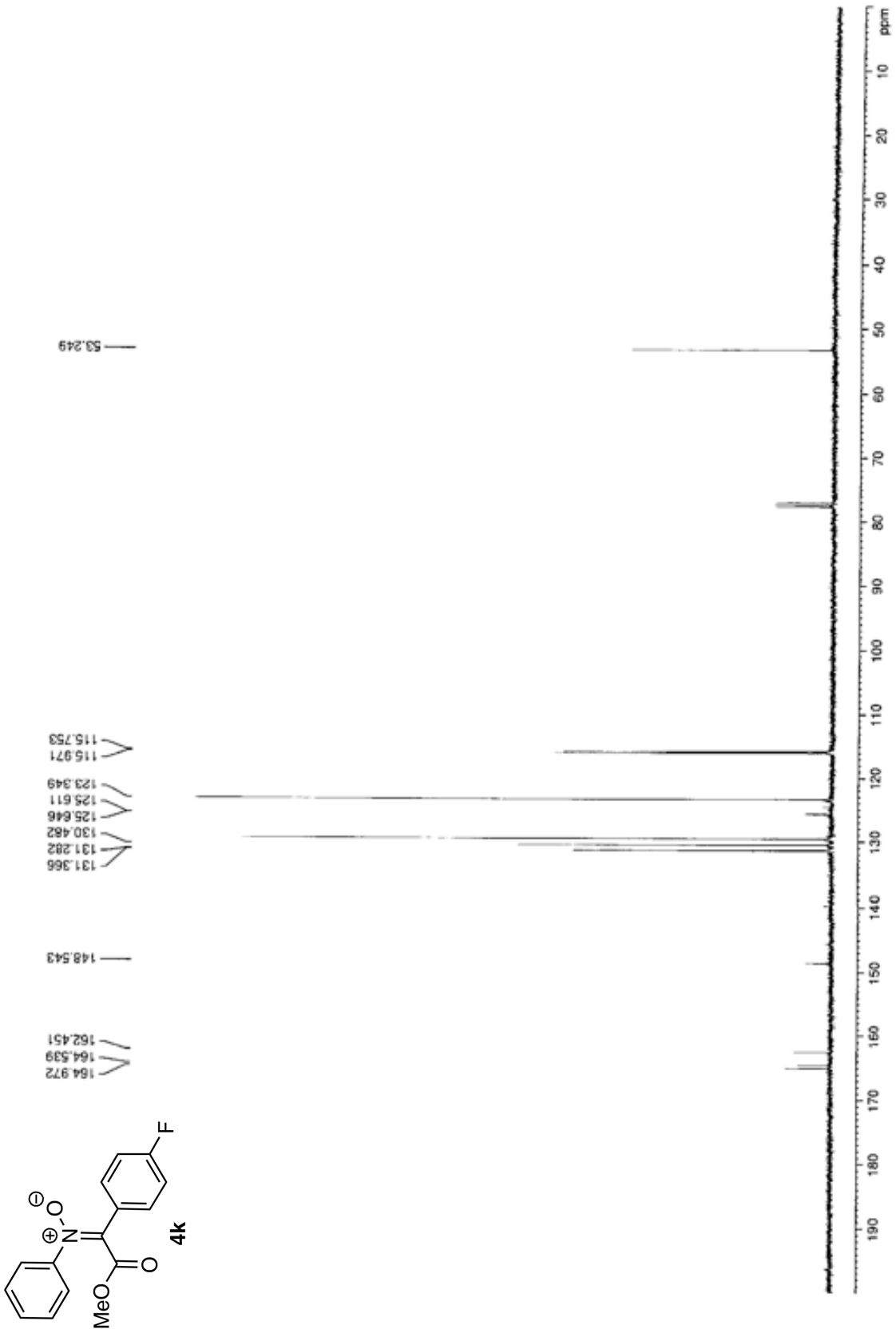

F
O
N
O
MeO
O

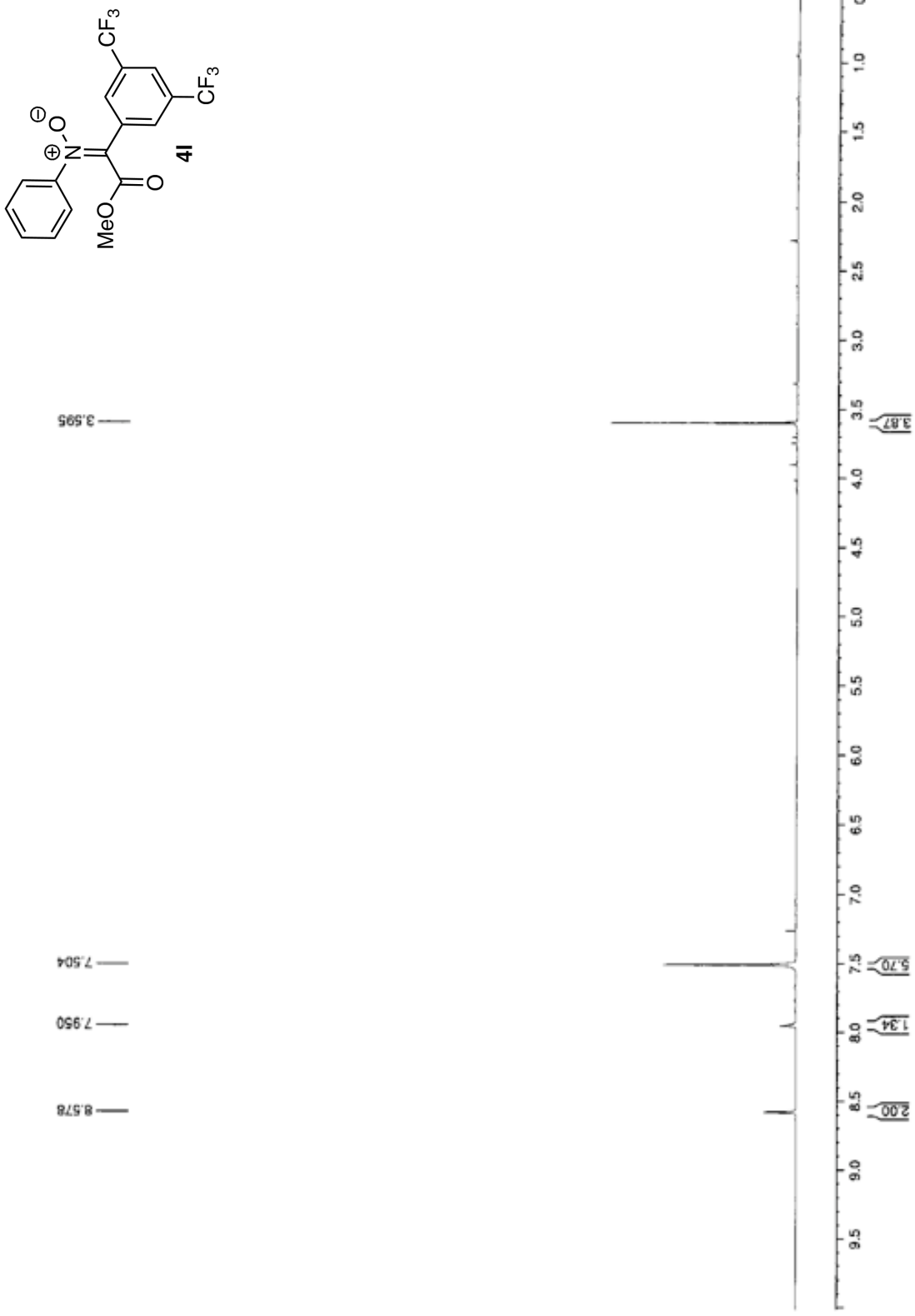
4k

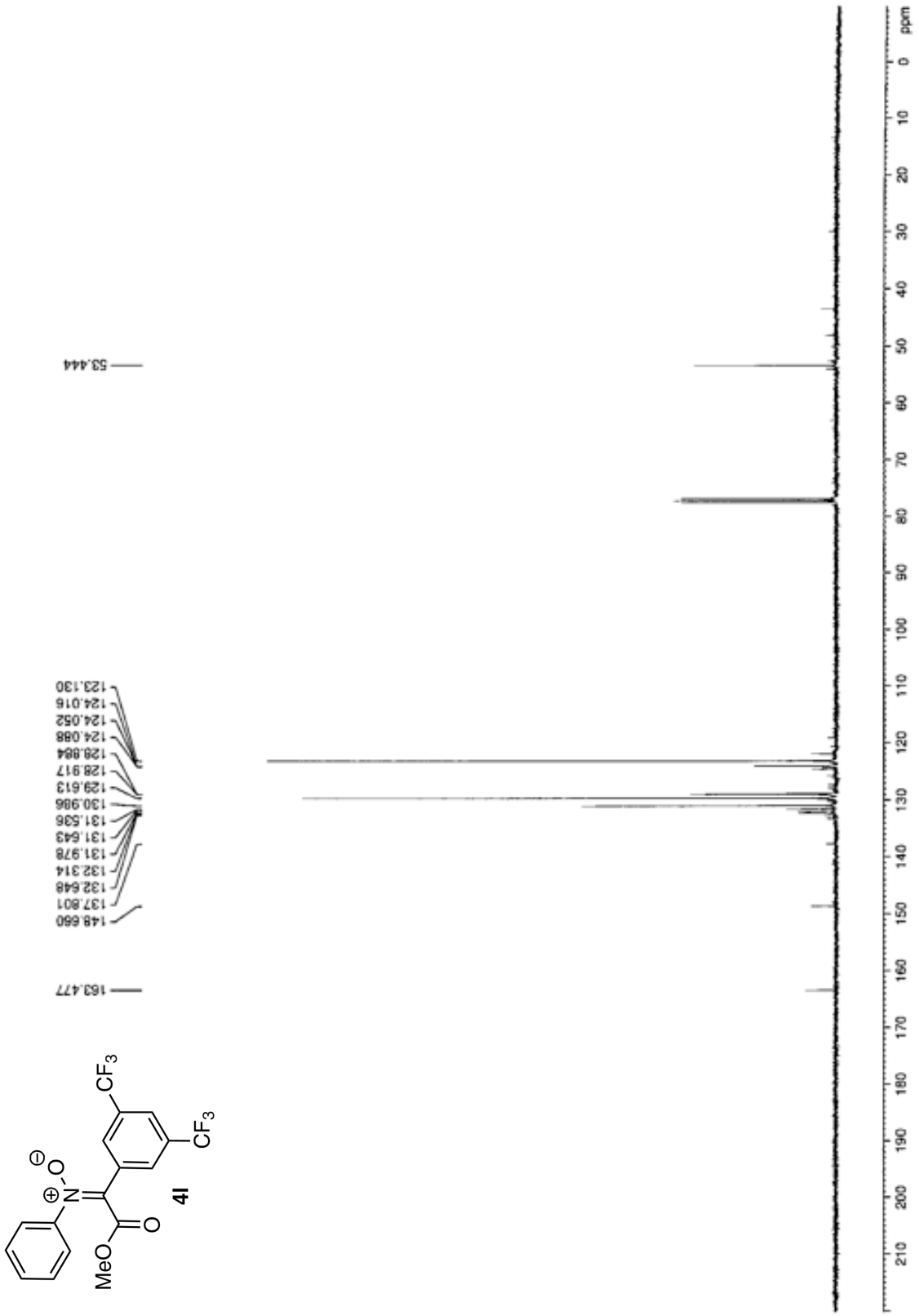

8.218
8.213
8.205
8.201
8.199
8.195
8.187
8.182
7.502
7.495
7.491
7.489
7.486
7.484
7.479
7.477
7.466
7.461
7.456
7.451
7.448
7.445
7.440
7.436
7.434
7.167
7.161
7.149
7.146
7.144
7.141
7.129
7.123


3.544


ppm
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
8.5
9.0
9.5
3.61
2.23
5.35
2.00


4k
MeO
O
O
N
F
53.249
115.753
115.971
123.349
125.611
125.646
130.482
131.282
131.366
148.543
162.451
164.539
164.972
ppm


CF3
CF3
O
N
O
MeO
O
4l
3.595
7.504
7.950
8.578
3.87
5.70
1.34
2.00
ppm

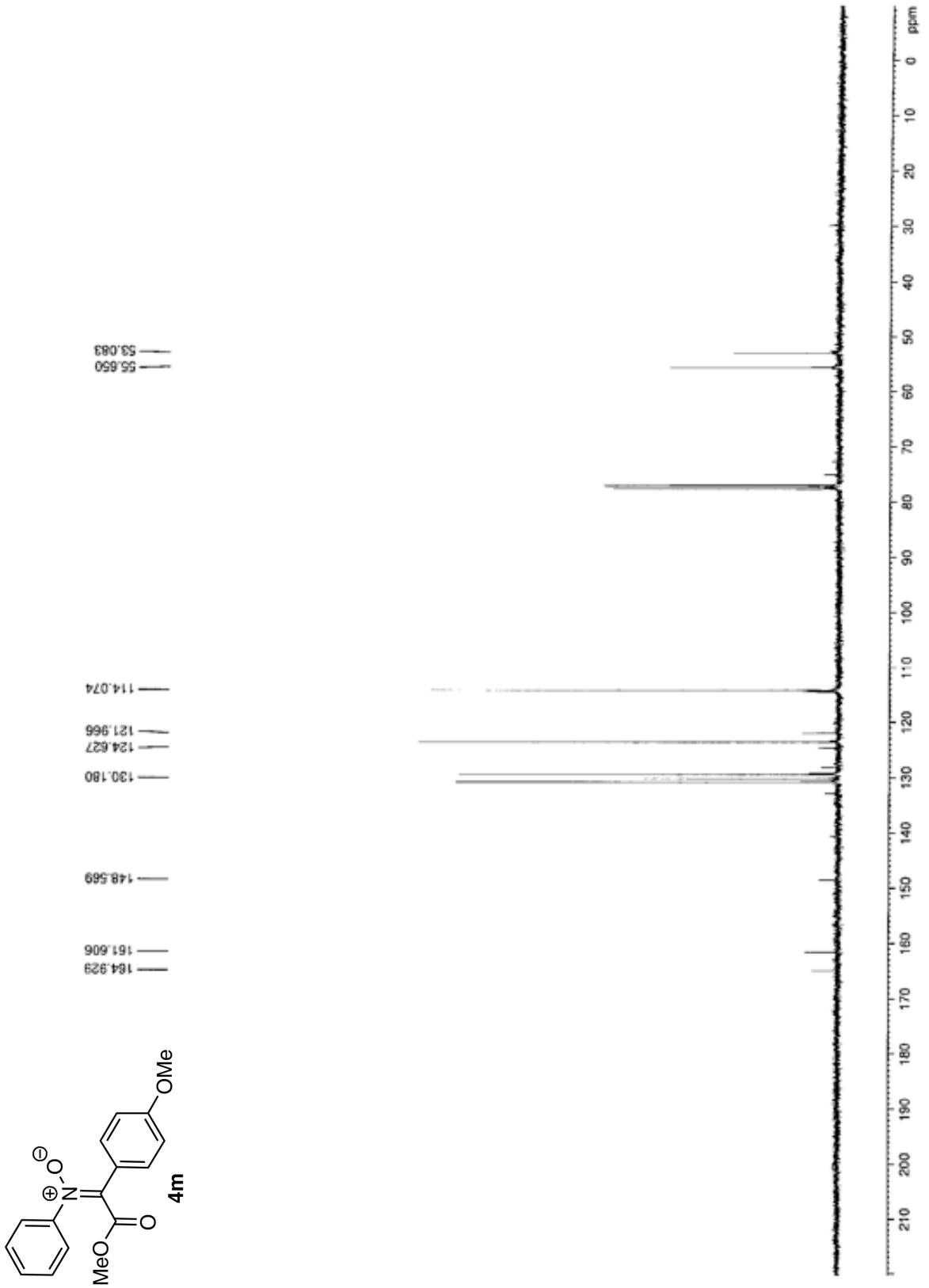

CF3
CF3
MeO
O
O
N
4l
163.477
148.660
137.801
132.648
132.314
131.978
131.643
131.536
130.986
129.613
128.917
128.884
124.088
124.052
124.016
123.130
53.444
ppm

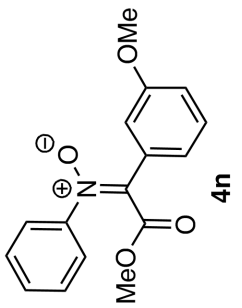
OMe
MeO
O
4m

3.550
3.872

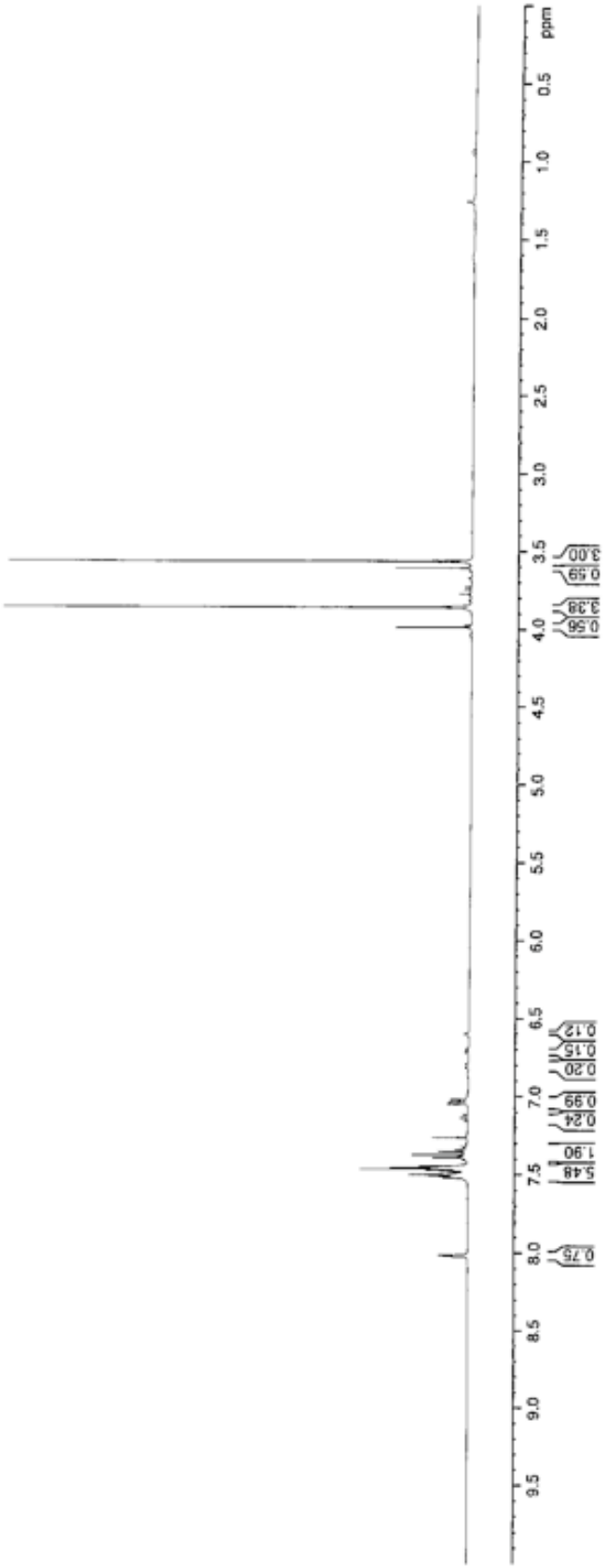
6.966
6.989
7.428
7.432
7.436
7.445
7.449
7.451
7.488
7.492
7.495
7.499
7.504
7.513
8.200
8.206
8.218
8.223

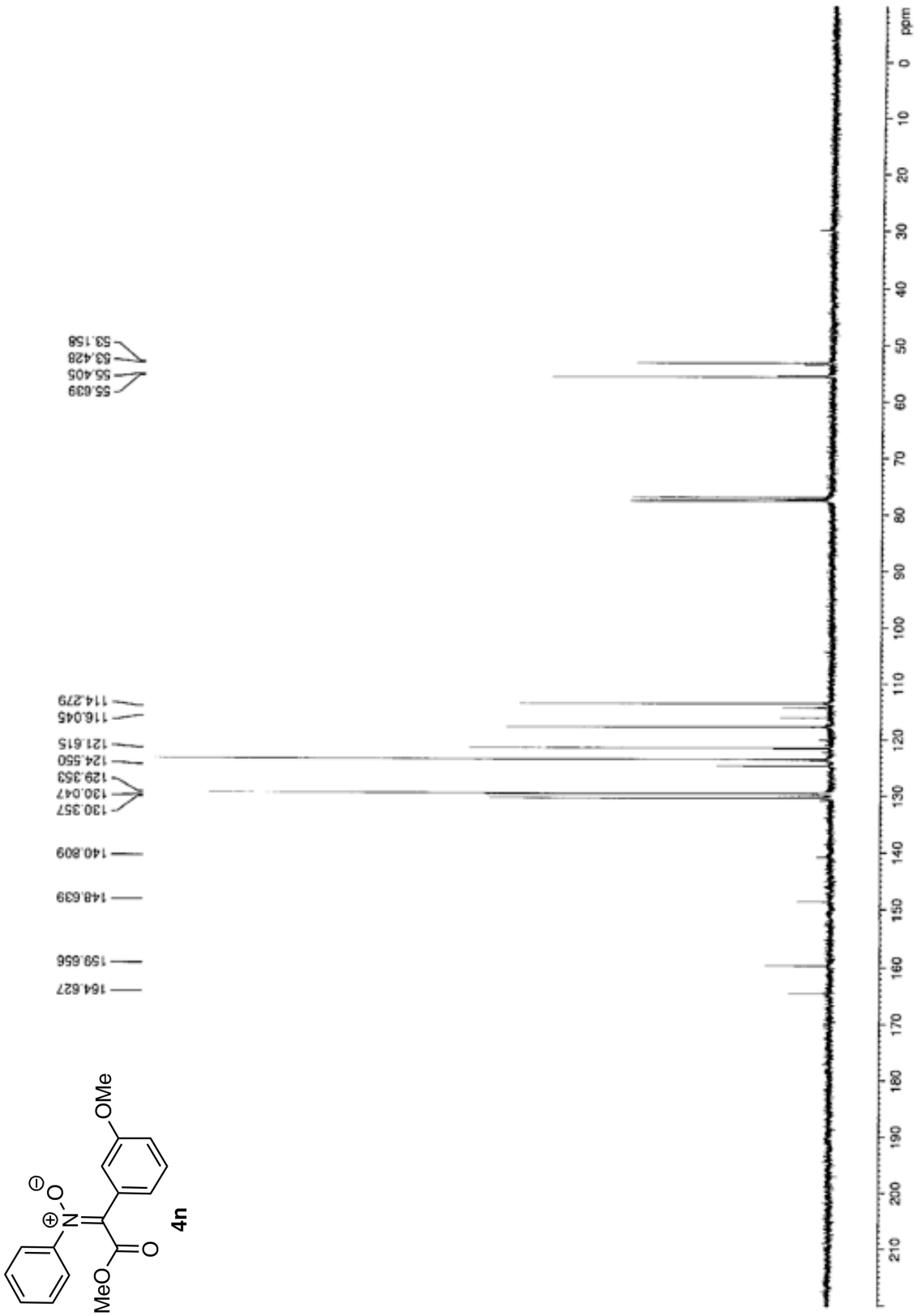
3.00
3.43
2.24
4.82
1.69
ppm


53.083
55.850
114.074
121.966
124.627
130.180
148.569
161.606
164.929
OMe
MeO
O
4m
ppm

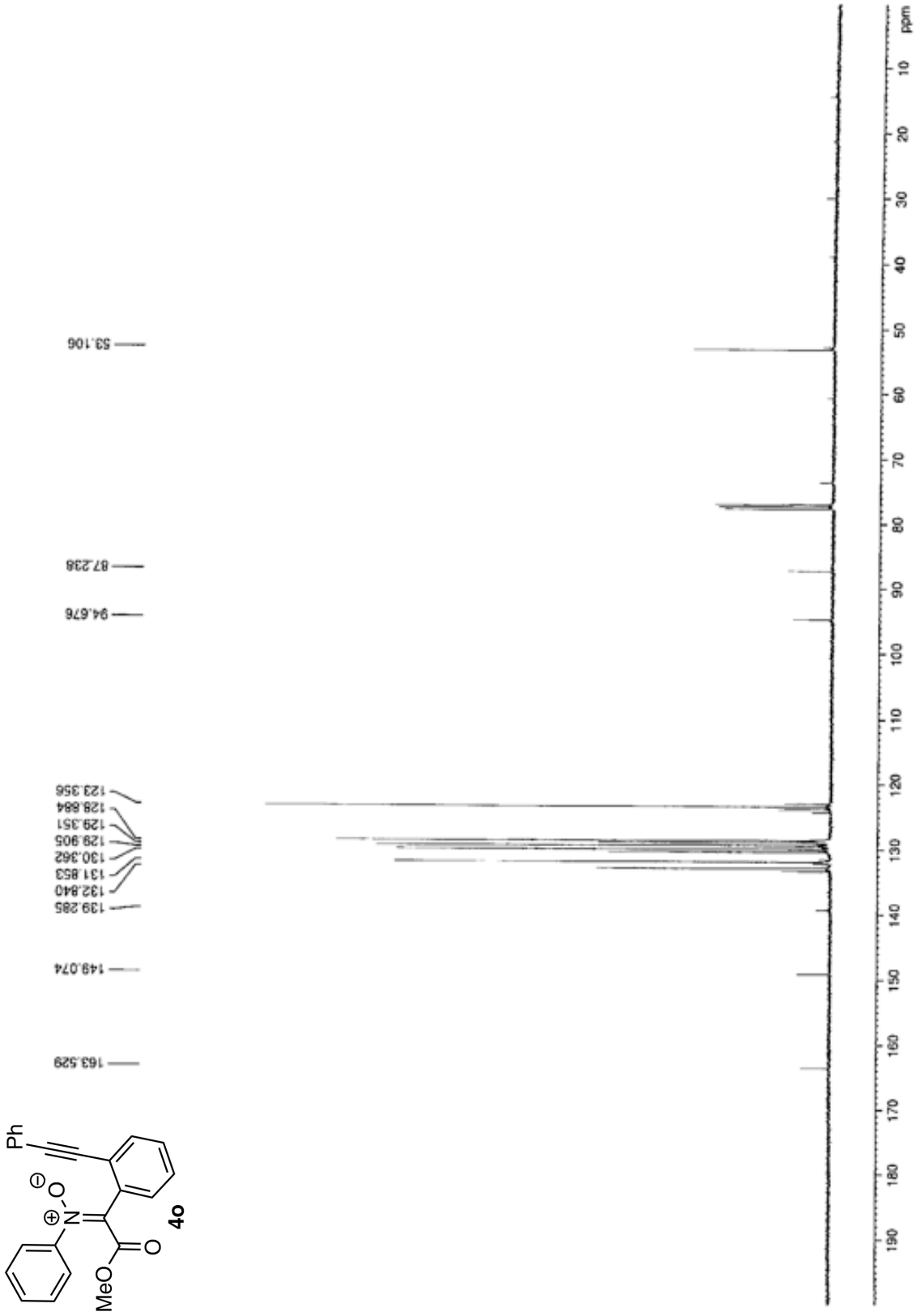

OMe
MeO
O
4n

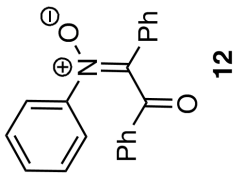

3.604
3.986
6.693
6.695
6.697
6.699
6.712
6.714
6.716
6.719
6.786
6.788
6.792
6.794
6.807
6.809
6.813
6.815
7.015
7.017
7.021
7.024
7.035
7.038
7.042
7.044
7.115
7.135
7.155
7.259
7.303
7.319
7.323
7.326
7.333
7.337
7.344
7.350
7.359
7.370
7.382
7.390
7.398
7.403
7.407
7.436
7.439
7.444
7.449
7.454
7.458
7.461
7.470
7.472
7.474
7.476
7.481


ppm
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
8.5
9.0
9.5
3.00
0.59
2.38
0.56
0.12
0.15
0.20
0.24
0.99
5.48
1.90
0.75


OMe
MeO
O
4n
164.627
159.656
148.639
140.809
130.357
130.047
129.353
124.550
121.615
116.045
114.279
55.039
55.405
53.428
53.158
ppm

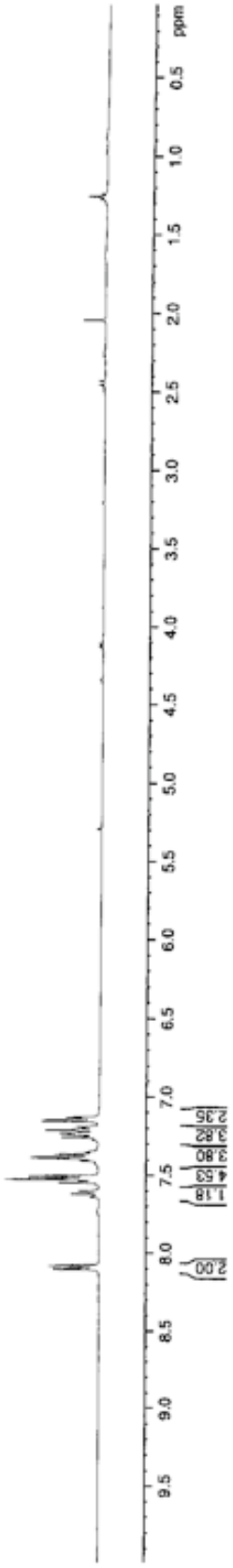
Ph
MeO
O
4o
3.578
7.259
7.300
7.302
7.304
7.313
7.317
7.442
7.446
7.462
7.465
7.470
7.473
7.478
7.482
7.491
7.504
7.506
7.511
7.650
7.653
7.668
7.672
7.832
7.834
7.836
7.850
7.854
3.50
1.00
1.12
9.79
2.29
ppm

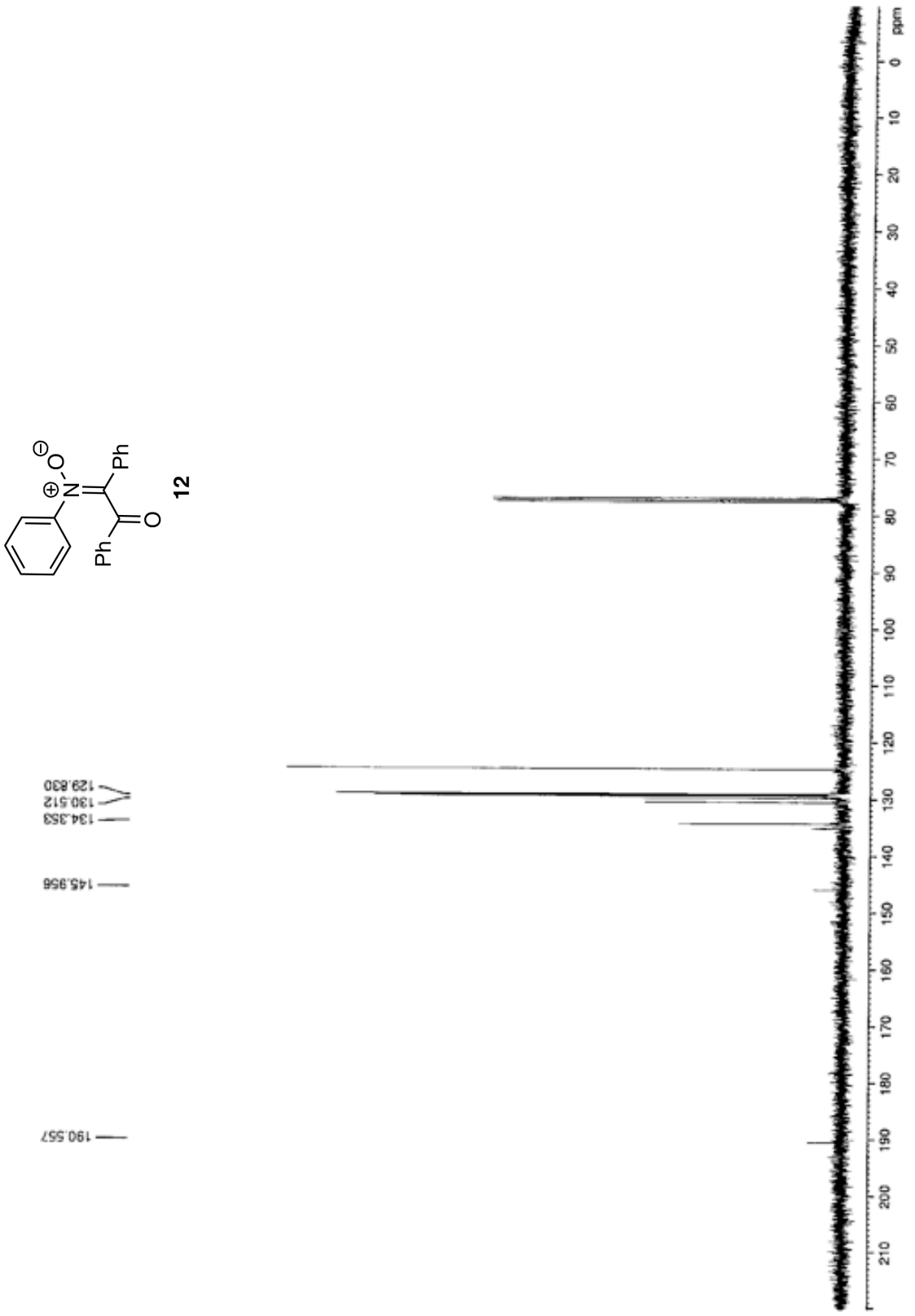

Ph
MeO
O
4o
53.106
87.238
94.676
123.356
128.884
129.351
129.905
130.362
131.853
132.840
139.285
149.074
163.529
ppm

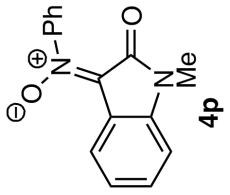


12

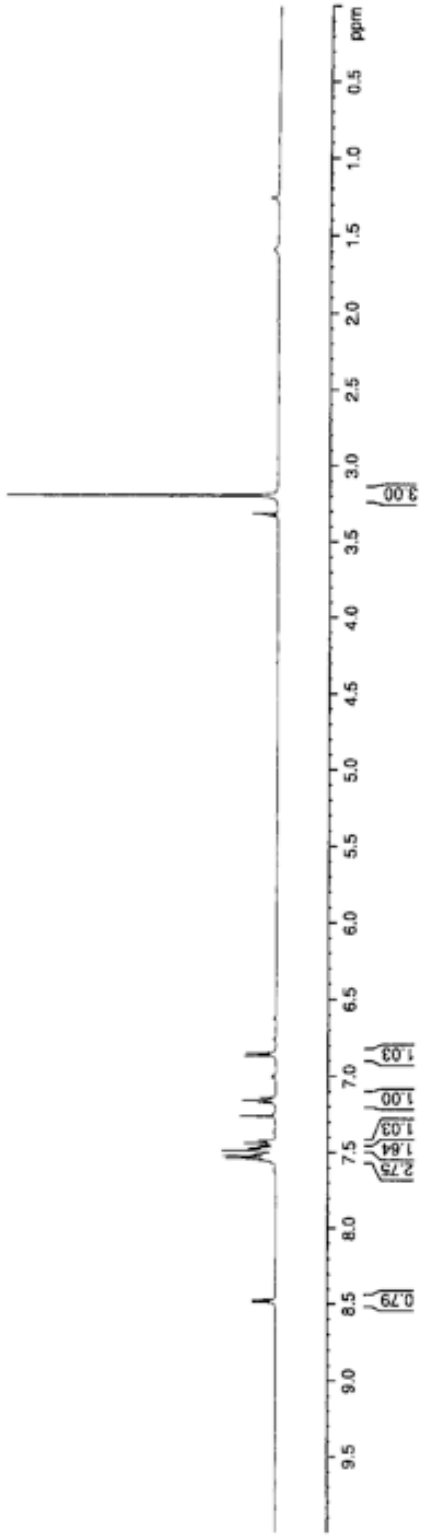

8.101
8.100
8.082
7.619
7.600
7.545
7.526
7.507
7.387
7.369
7.258
7.240
7.232
7.213
7.196
7.155
7.153
7.136
7.132

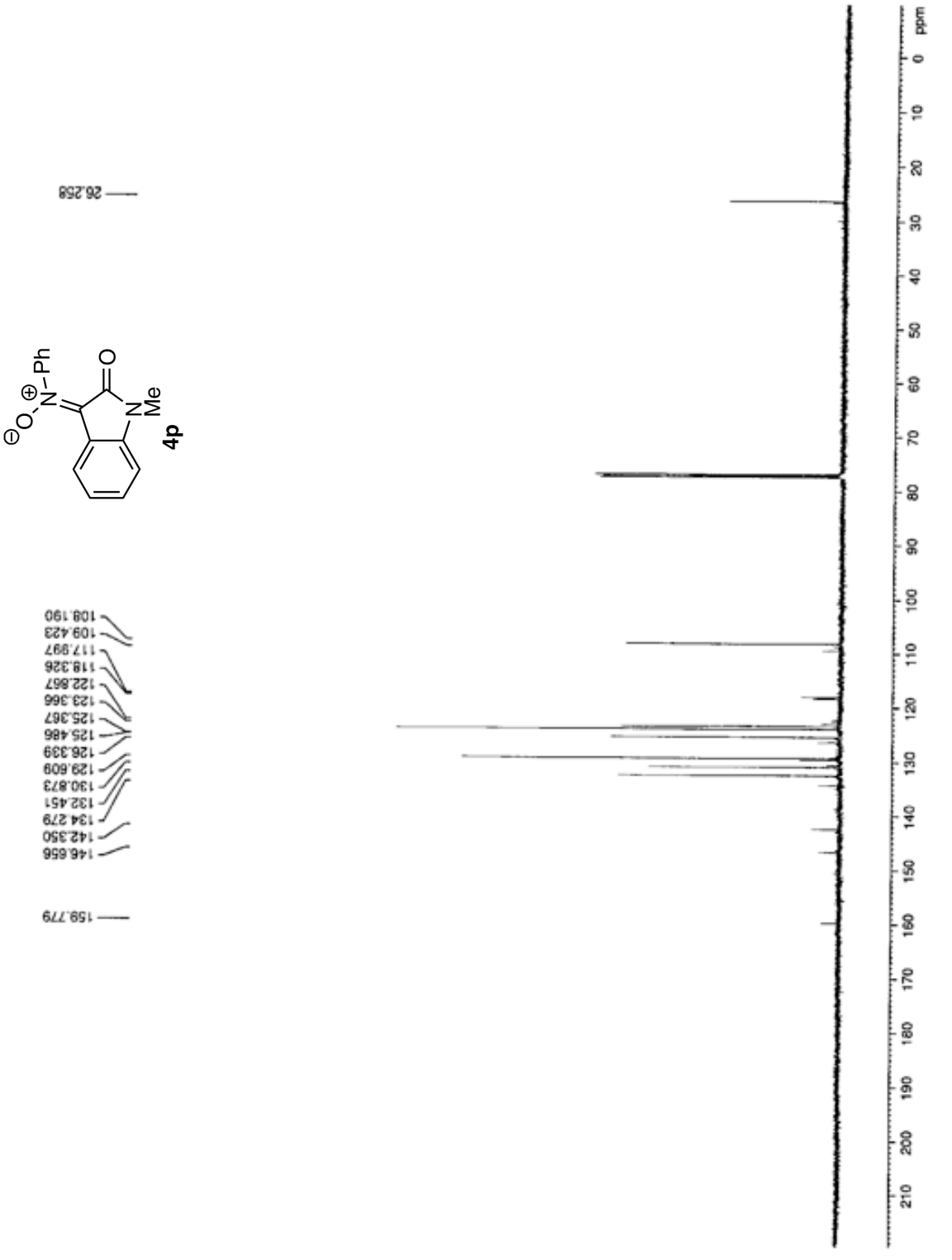

2.00
1.18
4.53
3.80
3.82
2.25
ppm

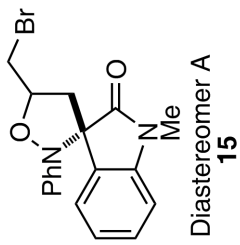

12
190.557
145.956
134.353
130.512
129.830
ppm



4p

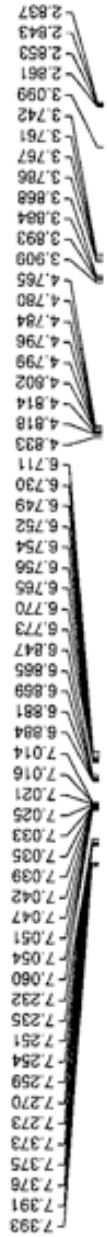


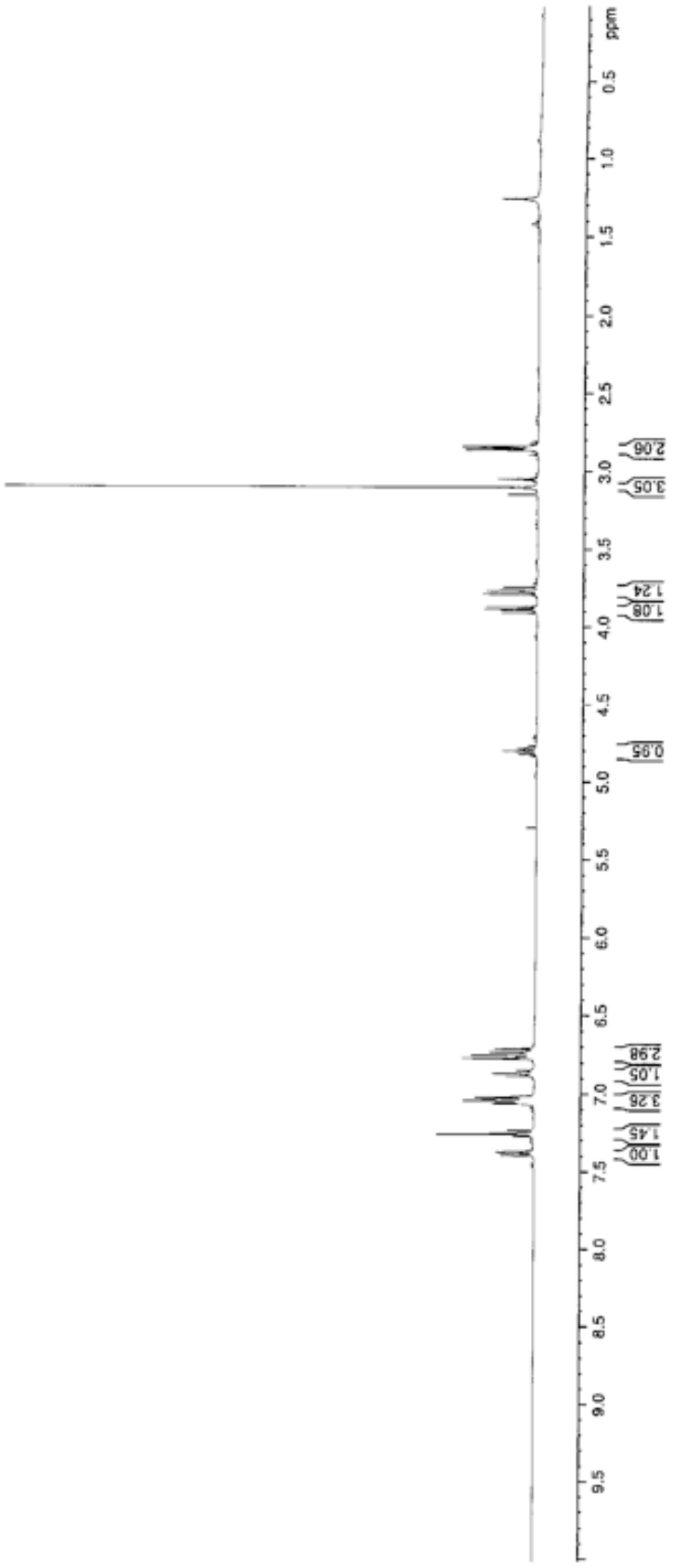

26.258
159.779
146.656
142.350
134.279
132.451
130.873
129.609
126.339
125.486
125.367
123.366
122.867
118.326
117.997
109.423
109.190
Ph
O
Me
4p
ppm

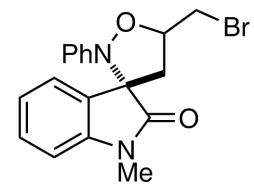


Diastereomer A

15

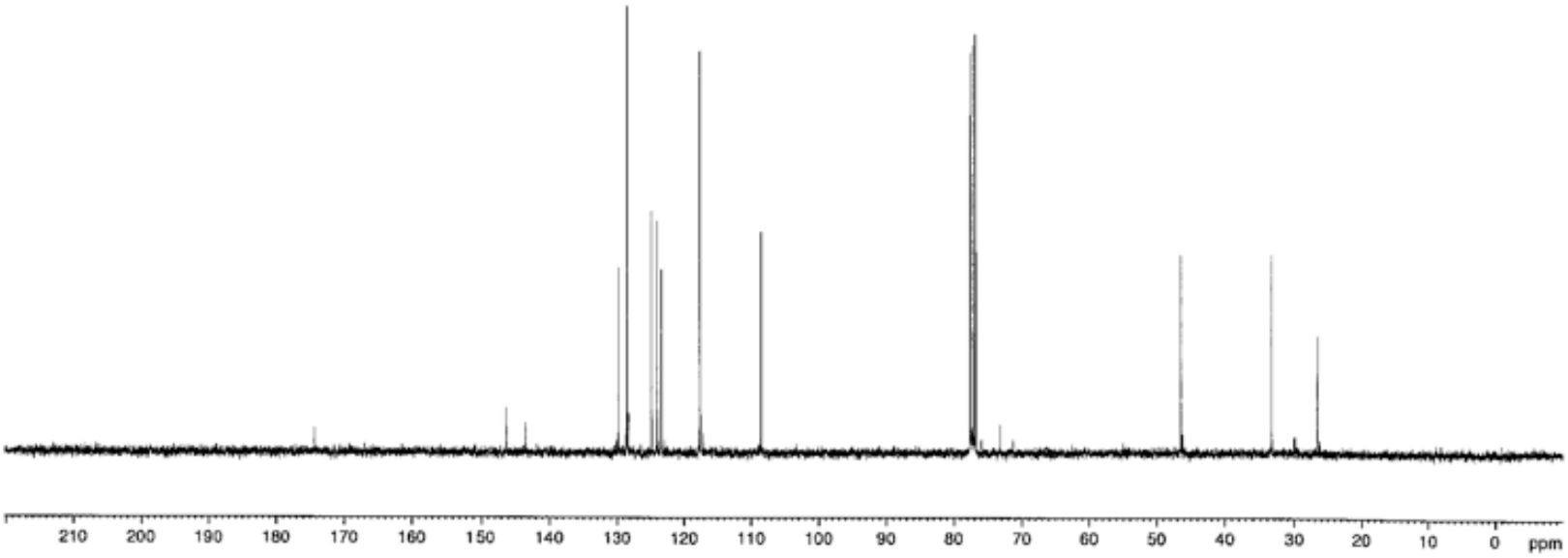


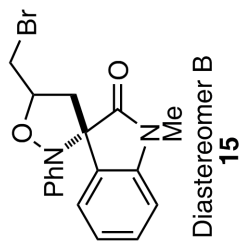




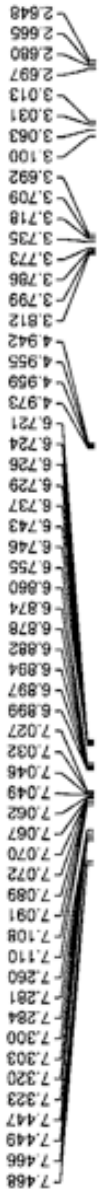
Diastereomer A
15

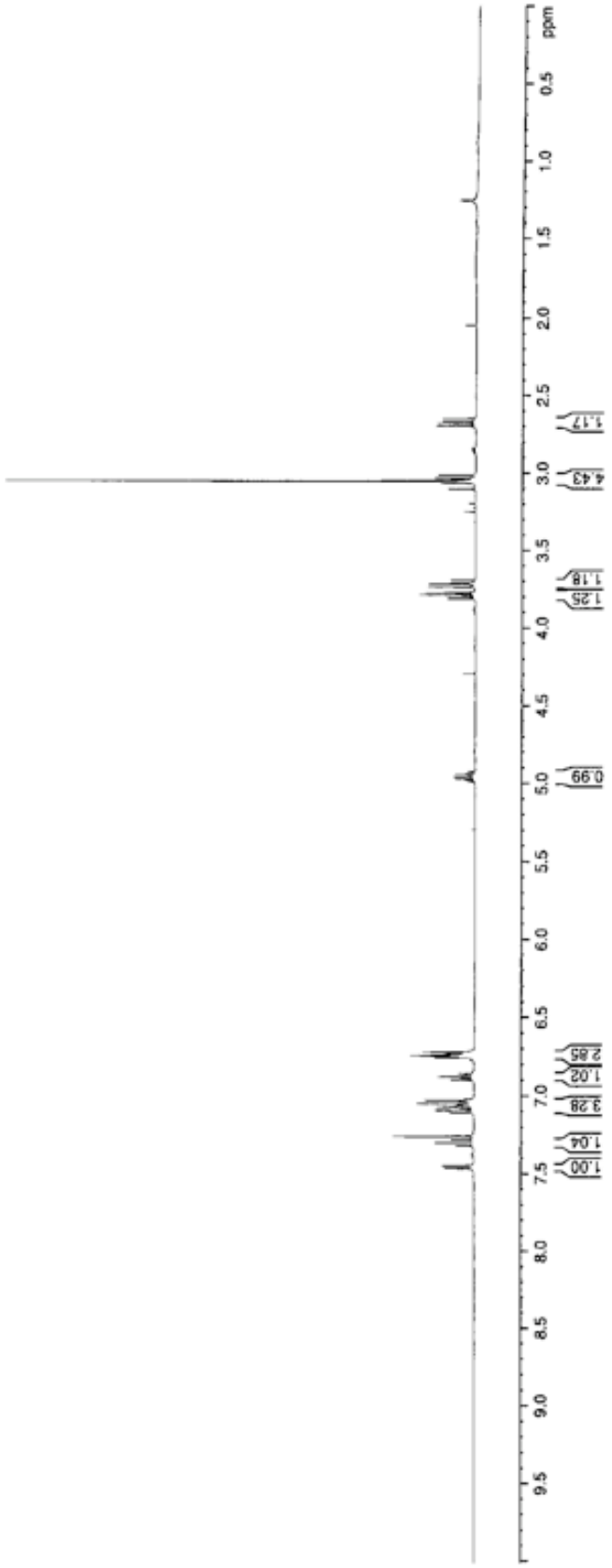
174.374
146.280
143.471
129.819
124.804
123.974
123.353
108.528
73.195
46.484
33.404
26.536

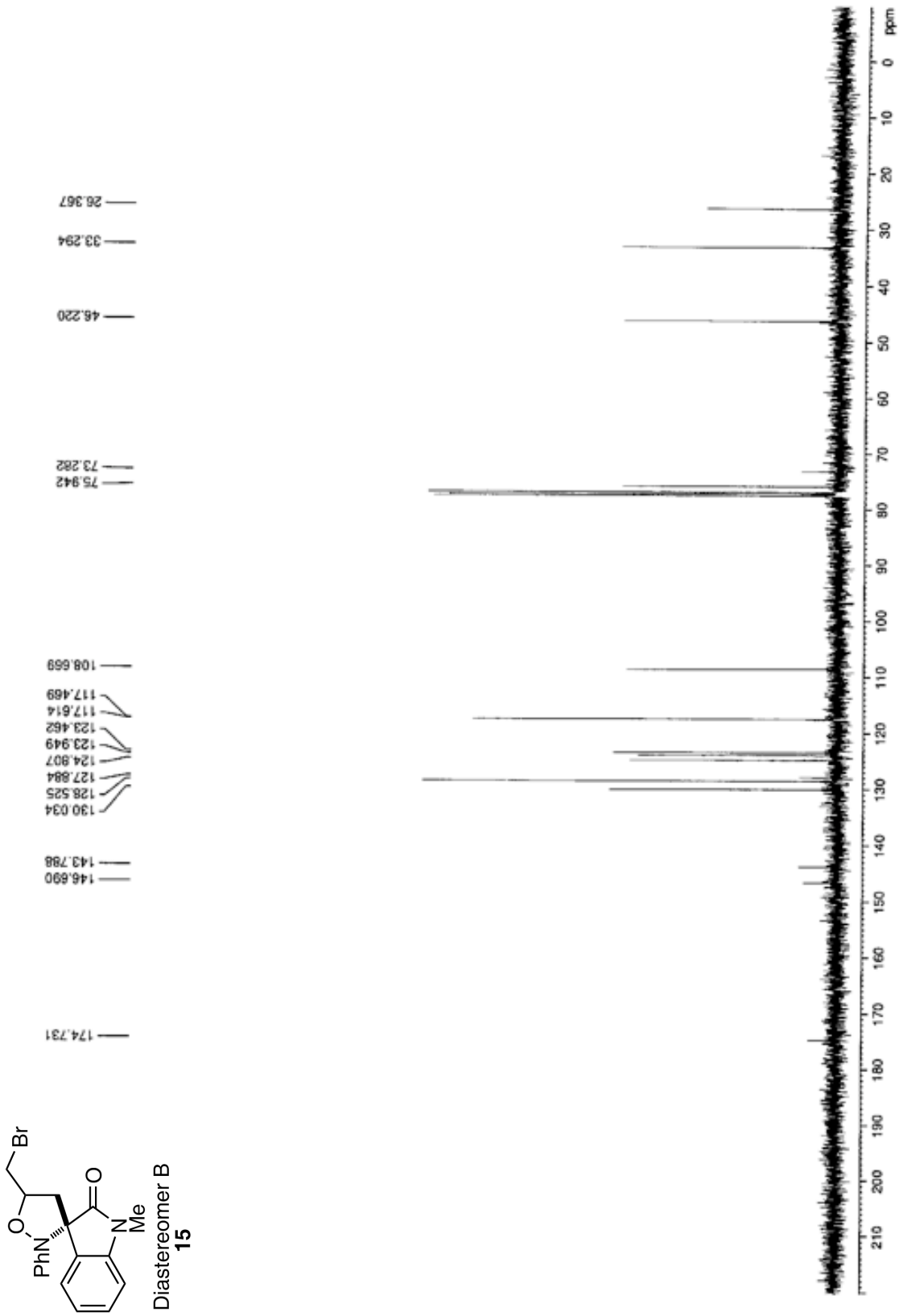




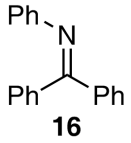
Diastereomer B
15



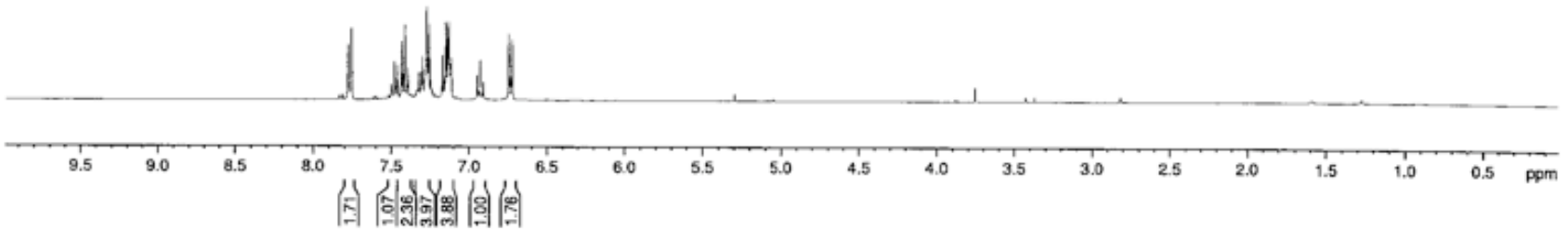



26.367
33.294
46.220
73.282
75.942
108.669
117.469
117.614
123.462
123.949
124.807
127.884
128.525
130.034
143.788
146.690
174.731
Br
O
O
PhN
N
Me
Diastereomer B
15
ppm

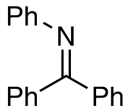

7.770
7.761
7.756
7.752
7.497
7.479
7.464
7.460
7.457
7.431
7.428
7.416
7.412
7.399
7.394
7.391
7.323
7.309
7.300
7.289
7.283
7.276
7.272
7.266
7.259
7.249
7.244
7.189
7.184
7.150
7.148
7.140
7.136
7.130
7.124
7.122
7.116
6.946
6.943
6.927
6.909
6.746
6.743
6.738
6.725
6.722


Ph
N
Ph
Ph

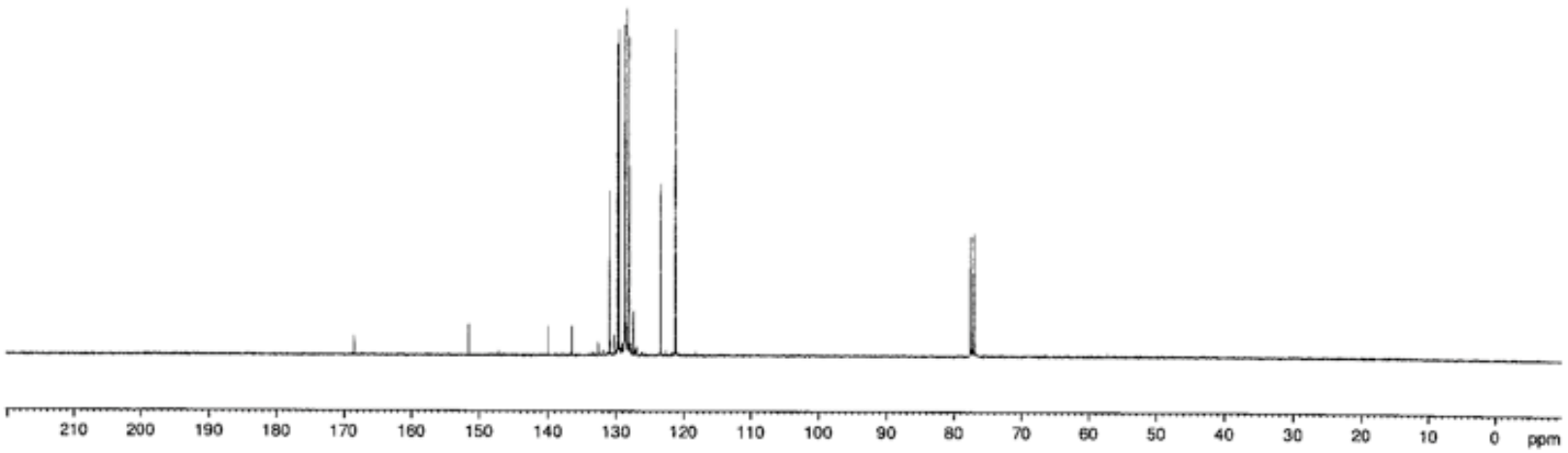
16

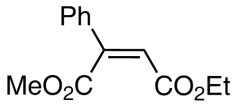

9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.71
1.07
2.36
3.97
3.88
1.00
1.78


168.455
151.519
139.948
136.500
130.934
129.754
129.561
128.782
128.694
128.433
128.172
128.125
127.498
123.366
121.171


Ph
N
Ph
Ph

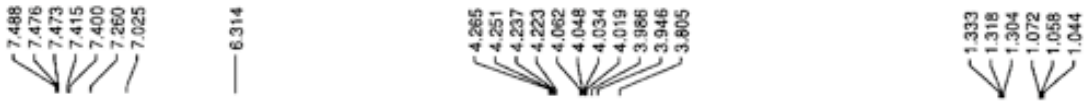
16

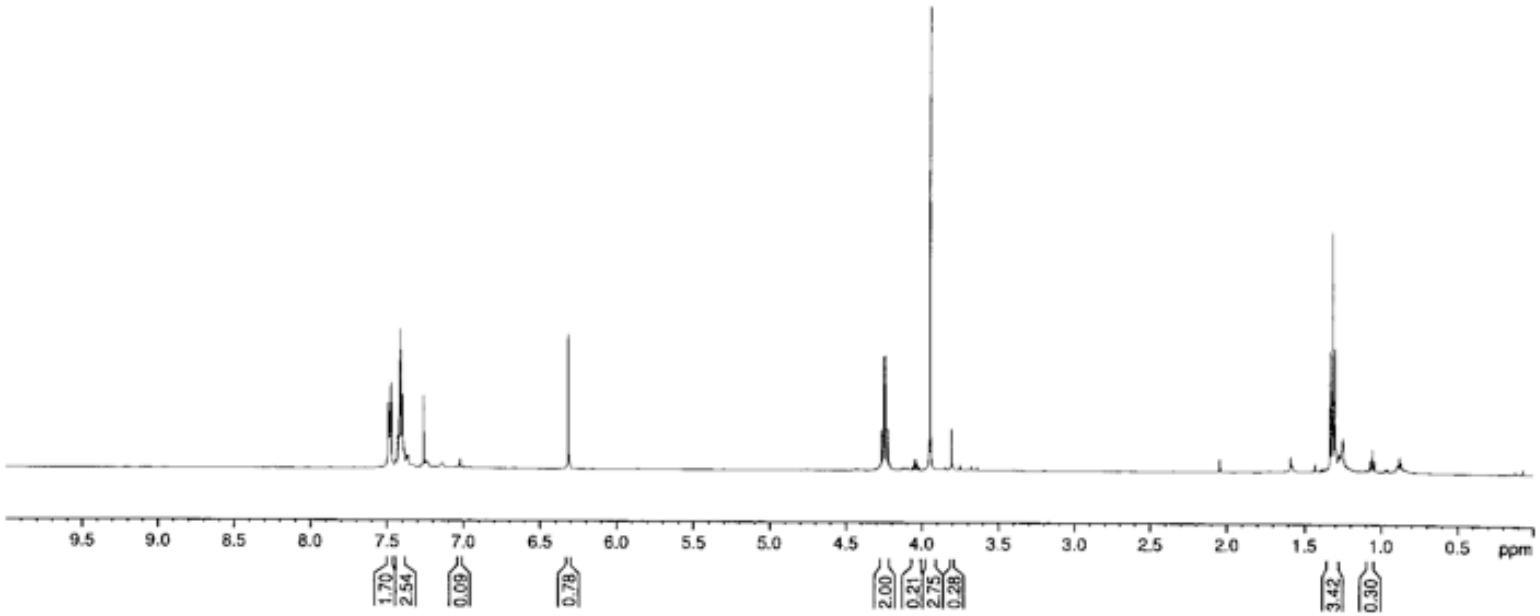

210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

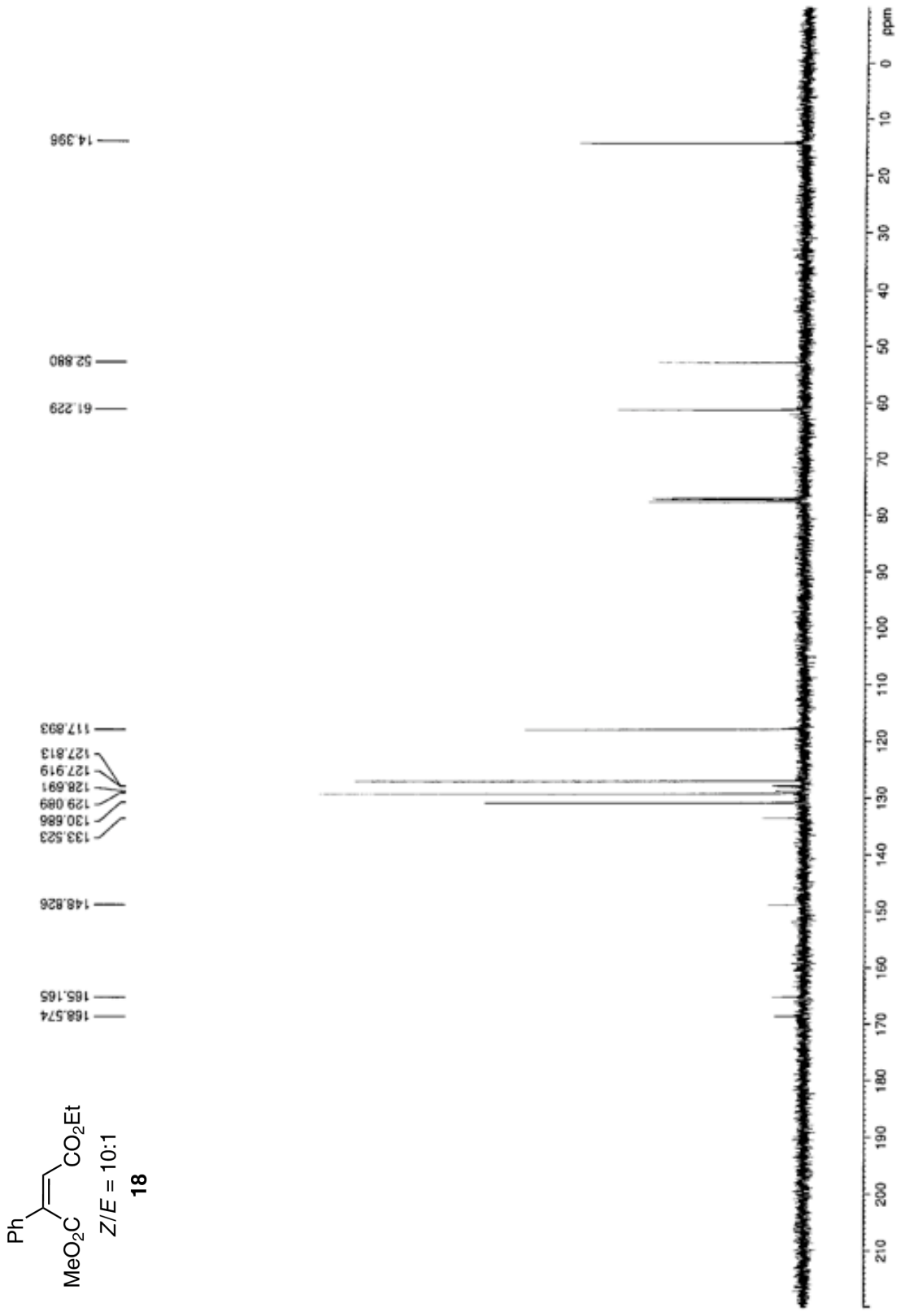

Ph
MeO2C
CO2Et

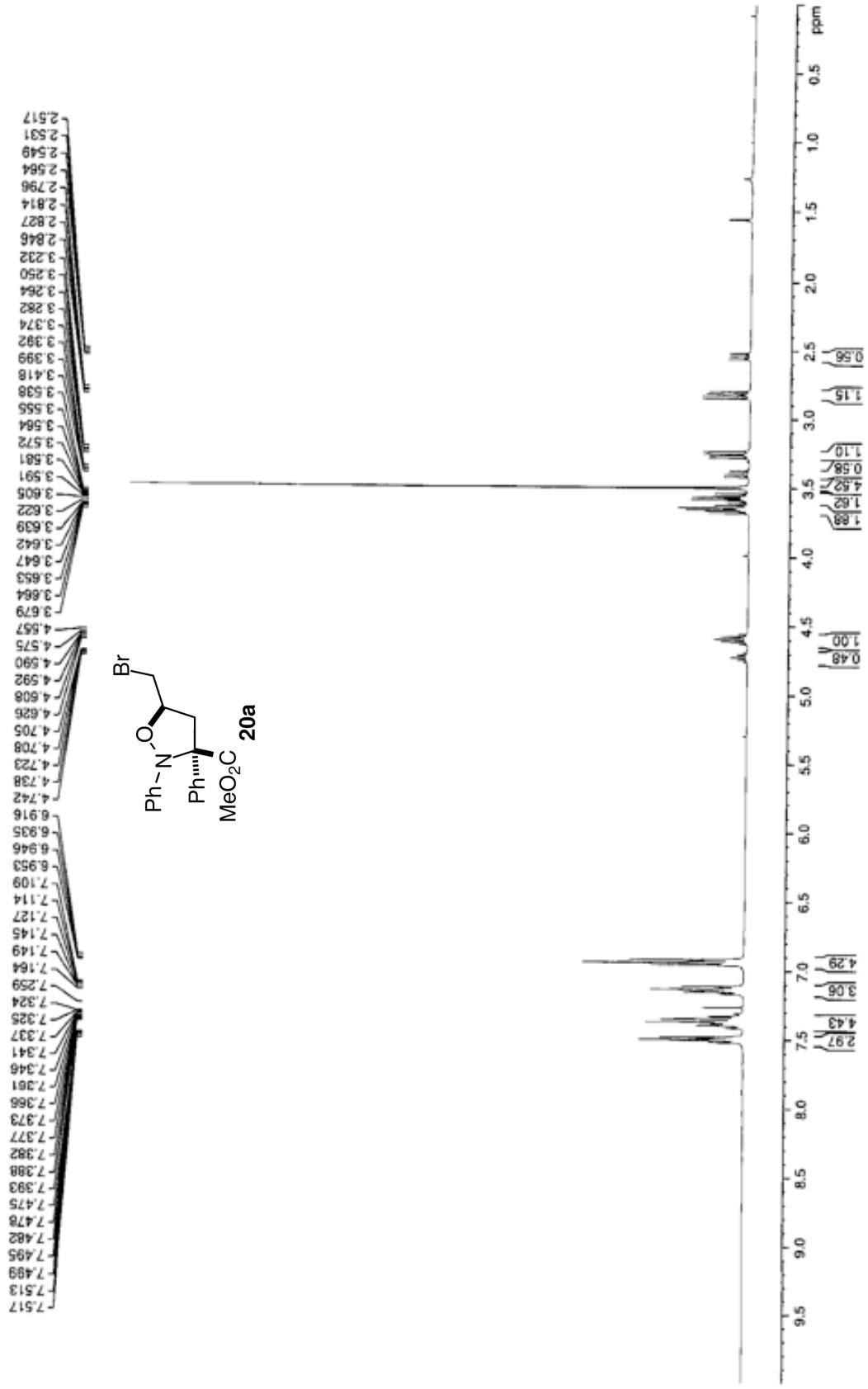
Z/*E* = 10:1

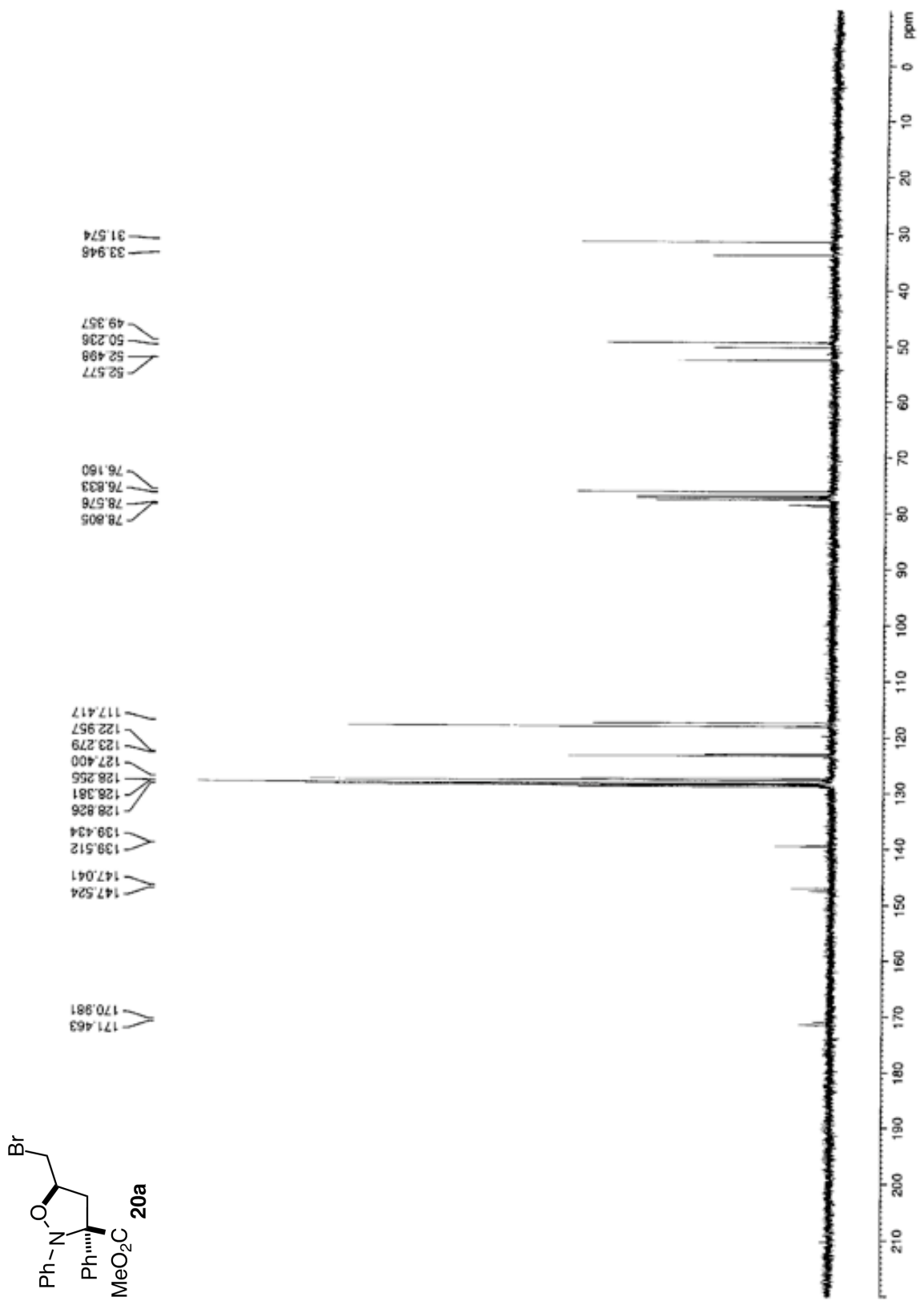
18

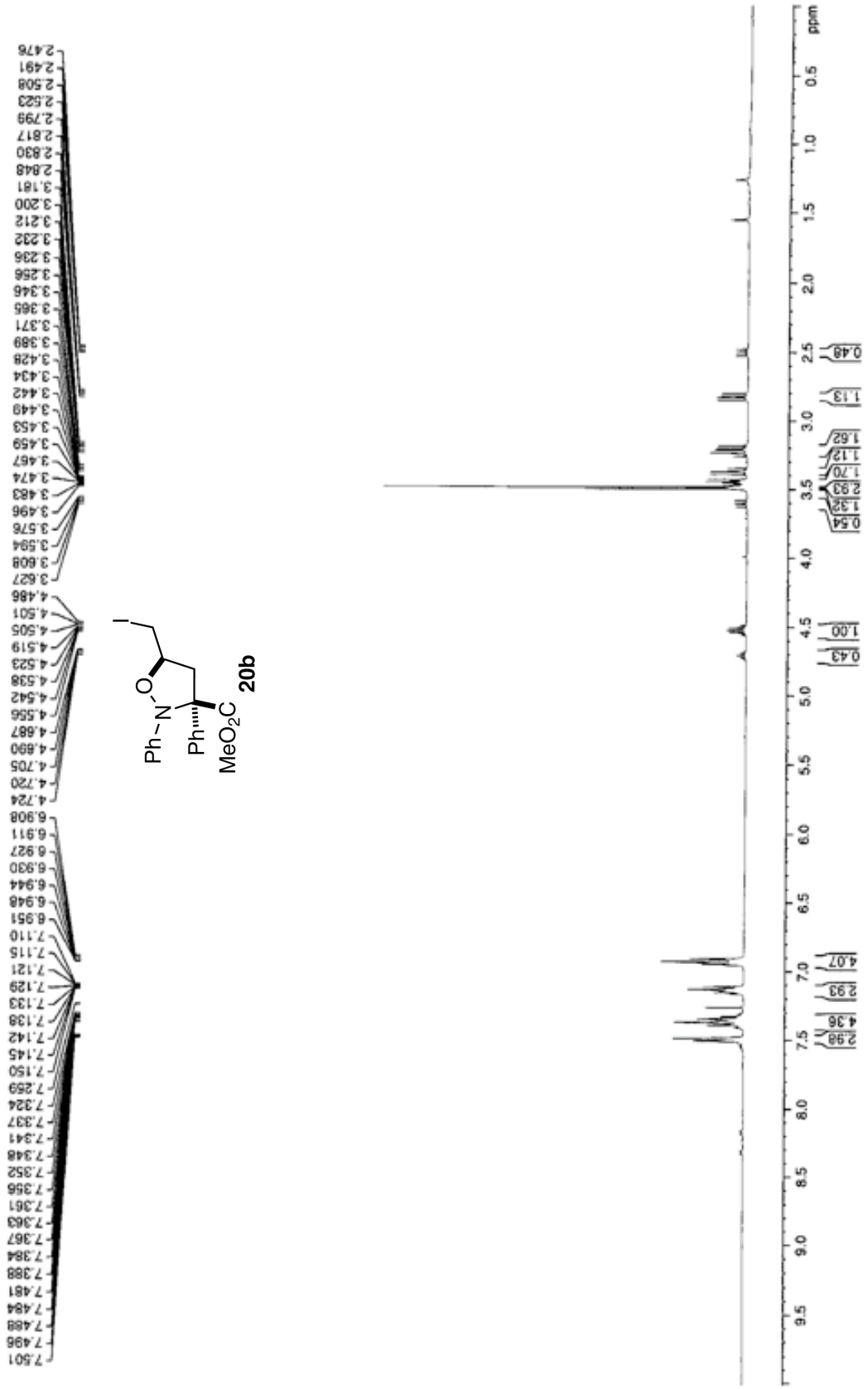

7.488
7.476
7.473
7.415
7.400
7.260
7.025
6.314
4.265
4.251
4.237
4.223
4.062
4.048
4.034
4.019
3.986
3.946
3.805
1.333
1.318
1.304
1.072
1.058
1.044


9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.70
2.54
0.09
0.78
2.00
0.21
2.75
0.28
3.42
0.30


Ph
MeO2C
CO2Et
Z/E = 10:1
18
168.574
165.165
148.826
133.523
130.686
129.089
128.691
127.919
127.813
117.893
61.229
52.880
14.396
ppm


Br
O
N
Ph
Ph
MeO2C
20a
ppm


Br
O
N
Ph
Ph
MeO2C
20a
171.463
170.981
147.524
147.041
139.512
139.434
128.826
128.381
128.255
127.400
123.279
122.957
117.417
78.805
78.576
76.833
76.160
52.577
52.498
50.236
49.357
33.946
31.574
ppm


20b

3.896
7.628
50.639
51.445
52.513
52.555
76.631
77.464
78.876
79.213
117.315
117.859
122.850
123.181
125.771
128.954
129.055
129.857
131.843
139.452
139.694
147.165
147.647
171.045
171.462
Ph
N
O
Ph
MeO2C
20b
ppm