Synthesis of Spiro[4.5]trienones by Intramolecular *ipso*-Halocyclization of 4-(*p*-Methoxyaryl)-1-alkynes

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Supporting Information

General. The ^{1}H and ^{13}C NMR spectra were recorded at 300 and 75.5 MHz or 400 and 100 MHz respectively. All melting points are uncorrected. High resolution mass spectra were recorded on a Kratos MS50TC double focusing magnetic sector mass spectrometer using EI at 70 eV. All reagents were used directly as obtained commercially unless otherwise noted.

Synthesis of Starting Materials.

Compounds **1**, **5**, **7**, **9**, and **13** were prepared by the following general reaction conditions. To a solution of *N*-(4-methoxyphenyl)trifluoromethanesulfonamide[1] (1.28 g, 5.0 mmol), PPh_3 (5.5 mmol) and the corresponding propargylic alcohol (5.5 mmol) in anhydrous THF (50 mL) at 0 ^{o}C was added diethyl azodicarboxylate (5.5 mmol). The resulting solution was stirred at 0 ^{o}C for 1 h and an additional 3 h at room temperature. The mixture was washed with brine (50 mL) and the organic layer was dried over Na_2SO_4, filtered, and the solvent removed under reduced pressure. The residue was purified by chromatography on a silica gel column to afford the corresponding product.

***N*-(4-Methoxyphenyl)-*N*-(3-phenylprop-2-yn-1-yl)trifluoromethanesulfonamide (1).** The indicated compound was prepared as a yellow oil from 3-phenyl-2-propyn-1-ol in a 70 % yield. The reaction mixture was

chromatographed using 5:1 hexane/EtOAc. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.78 (s, 3H), 4.70 (s, 2H), 6.91-6.94 (m, 2H), 7.29-7.41 (m, 7H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 44.76, 55.72, 82.35, 86.90, 114.98, 122.18, 128.68, 129.20, 129.63, 130.96, 131.95, 160.65; IR (CH_2Cl_2) 3060, 3008, 2967, 2938, 2841 cm^{-1}; HRMS *m/z* 369.0651 (calcd for $C_{17}H_{14}F_3NO_3S$, 369.0646).

***N*-(4-Methoxyphenyl)-*N*-[3-(4-methoxyphenyl)prop-2-yn-1-yl)trifluoromethanesulfonamide (5).** The indicated compound was prepared as an orange oil from 3-(4-methoxyphenyl)-2-propyn-1-ol in a 98 % yield. The reaction mixture was chromatographed using 5:1 hexane/EtOAc. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.73 (s, 3H), 3.74 (s, 3H), 4.66 (s, 2H), 6.79-6.82 (d, *J* = 9.0 Hz, 2H), 6.88-6.91 (d, *J* = 8.7 Hz, 2H), 7.28-7.31 (d, *J* = 8.7 Hz, 2H), 7.36-7.39 (d, *J* = 9.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 44.84, 55.42, 55.61, 80.99, 86.93, 114.19, 114.90, 129.66, 130.95, 133.44, 160.38, 160.63; IR (CH_2Cl_2) 2963, 2842, 2220, 1606, 1508, 1390 cm^{-1}; HRMS *m/z* 399.0758 (calcd for $C_{18}H_{16}F_3NO_4S$, 399.0752).

***N*-[3-(4-Acetylphenyl)prop-2-yn-1-yl]-*N*-(4-methoxyphenyl)trifluoromethanesulfonamide (7).** The indicated compound was prepared as a yellow oil from 1-[4-(3-hydroxy-1-propynyl)phenyl]ethanone in a 95 % yield. The reaction mixture was chromatographed using 3:1 hexane/EtOAc. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.54 (s, 3H), 3.77 (s, 1H), 4.74 (s, 2H), 6.92-6.95 (d, *J* = 9.0 Hz, 2H), 7.39-7.45 (m, 4H), 7.86-7.89 (d, *J* = 9.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.05, 44.61, 60.48, 85.59, 85.94, 114.95, 118.24, 122.53, 126.74, 128.43, 129.42, 130.83, 131.97, 136.98, 160.65, 197.27 (extra peak due to F splitting); IR ($CHCl_3$) 3057,

2971, 2846, 1682, 1606, 1511, 1398 cm^{-1}; HRMS *m/z* 411.0759 (calcd for $C_{19}H_{16}F_3NO_4S$, 411.0752).

***N*-(2-Heptynyl)-*N*-(4-methoxyphenyl)trifluoromethanesulfonamide (9).** The indicated compound was prepared as a colorless oil from 2-heptyn-1-ol in a 80 % yield. The reaction mixture was chromatographed using 10:1 hexane/EtOAc. ^1H NMR ($CDCl_3$, 300 MHz) δ 0.87-0.92 (t, *J* = 7.2 Hz, 3H), 1.28-1.49 (m, 4H), 2.13-2.19 (m, 2H), 3.79 (s, 3H), 4.47 (s, 2H), 6.90-6.95 (d, *J* = 7.2 Hz, 2H), 7.32-7.37 (d, *J* = 7.2 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 13.63, 18.40, 21.96, 30.55, 44.39, 55.57, 73.22, 87.84, 113.99, 114.73, 118.28, 122.57, 126.86, 129.61, 130.86, 160.49 (extra peaks are due to F-splitting); IR (CH_2Cl_2) 2962, 2872, 2236, 1607, 1513, 1395 cm^{-1}; HRMS *m/z* 349.0965 (calcd for $C_{15}H_{18}F_3NO_3S$, 349.0959).

***N*-[3-(Cyclohex-1-en-1-yl)-1-methylprop-2-ynyl]-*N*-(4-methoxyphenyl)trifluoromethanesulfonamide (13).** The indicated compound was prepared as a light yellow oil from 4-(1-cyclohexen-1-yl)-3-butyn-2-ol in an 84 % yield. The reaction mixture was chromatographed using 5:1 hexane/EtOAc. ^1H NMR ($CDCl_3$, 400 MHz) δ 1.37-1.39 (d, *J* = 7.2 Hz, 3H), 1.55-1.63 (m, 4H), 2.05-2.08 (m, 4H), 3.80 (s, 3H), 5.25-5.26 (q, *J* = 7.2 Hz, 1H), 6.06 (s, 1H), 6.90-6.93 (d, *J* = 8.8 Hz, 2H), 7.32-7.34 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.39, 21.97, 22.16, 25.57, 25.62, 28.82, 50.30, 55.42, 83.81, 88.10, 114.13, 118.58, 119.80, 121.79, 125.50, 132.91, 135.70, 160.55 (extra peaks due to F splitting); IR (CH_2Cl_2) 2985, 2936, 2838, 2224, 1731, 1512, 1386 cm^{-1}; HRMS *m/z* 387.1121 (calcd for $C_{18}H_{20}F_3NO_3S$, 387.1116).

***N*-(4-Methoxyphenyl)-*N*-[3-(trimethylsilyl)prop-2-yn-1-yl)]trifluoromethanesulfonamide (11).** To a solution of (3-bromo-1-

propynyl)trimethylsilane in CH_3CN was added 4 equiv of 4-methoxyaniline. After being stirred for 20 h under N_2, the reaction was quenched by adding brine. The reaction mixture was extracted with Et_2O. The extracts were dried over $MgSO_4$ and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (5:1 hexane/EtOAc) on silica gel to afford *N*-[3-(trimethylsilyl)prop-2-yn-1-yl]-4-methoxyaniline in a 53 % yield as a yellow oil. To a solution of *N*-[3-(trimethylsilyl)prop-2-ynyl]-4-methoxyaniline (699 mg, 3.0 mmol) and NEt_3 (364 mg, 3.6 mmol) in CH_2Cl_2 (5 mL) was added Tf_2O (1.02 g, 3.6 mmol) at –78 ^oC. The reaction mixture was quenched with aq $NaHCO_3$ and the reaction mixture was extracted twice with CH_2Cl_2. The extracts were dried over $MgSO_4$ and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (5:1 hexane/EtOAc) on silica gel to afford compound **11** (931 mg, 85 % yield) as a yellow oil. ^1H NMR ($CDCl_3$, 300 MHz) δ 0.15 (s, 9H), 3.82 (s, 3H), 4.47 (s, 2H), 6.91-6.94 (d, J = 9.0 Hz, 2H), 7.34-7.36 (d, J = 9.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 0.00, 45.00, 56.00, 93.05, 98.72, 115.10, 118.53, 122.81, 129.87, 131.30, 160.93 (extra peaks due to F splitting); IR (CH_2Cl_2) 2963, 2842, 1610, 1515, 1398 cm^{-1}; HRMS *m/z* 365.0734 (calcd for $C_{14}H_{18}F_3NO_3SSi$, 365.0729).

Compounds **15** and **17** were prepared using the following general reaction conditions. To a solution of the corresponding *N*-arylacetamide (3.0 mmol) in anhydrous THF (10 mL) was added NaH (9.0 mmol, 60 % dispersion in mineral oil) at room temperature. After being stirred for 15 min, 3-bromo-1-phenyl-1-propyne (4.5 mmol) in 5 ml THF was added dropwise. TLC was used to monitor the completion of the reaction. The reaction was cooled to 0 ^oC upon completion and quenched with satd NH_4Cl, and

extracted twice with EtOAc. The organic layer was washed with water and brine, dried over $MgSO_4$, and concentrated in vacuo. The residue was purified by column chromatography on silica gel to afford the corresponding product.

***N*-(4-Methoxyphenyl)-*N*-(3-phenylprop-2-yn-1-yl)acetamide (15).** The indicated compound was prepared as an orange oil from *N*-(4-methoxyphenyl)acetamide in a 55 % yield. The reaction mixture was chromatographed using 1:1 hexane/EtOAc. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.81 (s, 3H), 3.75 (s, 3H), 4.62 (s, 2H), 6.87-6.89 (d, J = 8.8 Hz, 2H), 7.17-7.21 (m, 5H), 7.28-7.29 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 22.44, 38.98, 55.48, 83.98, 84.85, 114.77, 122.89, 128.24, 129.40, 131.67, 134.98, 159.38, 170.47; IR (CH_2Cl_2) 3056, 2959, 2935, 2841, 1663, 1514, 1392 cm^{-1}; HRMS *m/z* 279.1263 (calcd for $C_{18}H_{17}NO_2$, 279.1259).

***N*-[4-(Dimethylamino)phenyl]-*N*-(3-phenylprop-2-yn-1-yl)acetamide (17).** The indicated compound was prepared as a slightly, red sticky oil from *N*-[4-(dimethylamino)phenyl]acetamide in a 52 % yield. The reaction mixture was chromatographed using 2:1 hexane/EtOAc. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.88 (s, 3H), 2.96 (s, 6H), 6.68-6.71 (d, J = 6.9 Hz, 2H), 7.13-7.16 (d, J = 6.9 Hz, 2H), 7.24-7.26 (m, 3H), 7.35-7.38 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 22.66, 39.31, 40.69, 83.87, 85.48, 112.80, 123.31, 128.34, 128.41. 129.01, 131.20, 131.91, 150.34, 171.13; IR (CH_2Cl_2) 3045, 2919, 2812, 1609, 1661, 1524 cm^{-1}; HRMS *m/z* 292.1580 (calcd for $C_{19}H_{20}N_2O$, 292.1576).

1-(4-Methoxyphenyl)-4-phenyl-3-butyn-2-one (18). To a cooled suspension (ice bath) of PCC (4.31 g, 20.0 mmol) in CH_2Cl_2 (200 mL) was slowly added a solution of 2-(4-methoxyphenyl)ethanol (15.0 mmol) in CH_2Cl_2 (10 mL). The mixture was stirred

at that temperature for 2 h, then warmed up to room temperature for another 2 h. The mixture was filtered through celite and the solvent was removed under vacuum. The reaction mixture was chromatographed using 5:1 hexane/EtOAc to give (4-methoxyphenyl)acetaldehyde as a colorless oil in a 75 % yield. To a solution of phenylacetylene (10.0 mmol) in anhydrous 30 mL THF at 0 ^{o}C was added *n*-BuLi (10 mmol, 2.5M in hexane) under N_2. The resulting solution was stirred at that temperature for 1 h. Then (4-methoxyphenyl)acetaldehyde (5.0 mmol) in 10 ml of THF was added to the solution under an inert atmosphere. The resulting solution was stirred at room temperature for 2 h. Brine (30 mL) was then added to quench the reaction and the solution was extracted twice with diethyl ether (2 x 30 mL). The solvent was removed under vacuum, and the reaction mixture was chromatographed using 5:1 hexane/EtOAc to obtain 1-(4-methoxyphenyl)-4-phenyl-3-butyn-2-ol as a light orange oil in an 80 % yield. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.91 (s, 1H), 2.99-3.01 (d, J = 6.3 Hz, 2H), 3.71 (s, 3H), 4.71 (m, 1H), 6.80-6.83 (d, J = 8.7 Hz, 2H), 7.16-7.26 (m, 5H), 7.35-7.38 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 43.57, 55.50, 64.07, 85.95, 90.18, 114.09, 122.96, 128.61, 128.70, 129.08, 131.21, 131.95, 158.79; IR (CH_2Cl_2) 3310, 1609 cm^{-1}; HRMS *m/z* 252.1154 (calcd for $C_{17}H_{16}O_2$, 252.1150). To the solution of 1-(4-methoxyphenyl)-4-phenyl-3-butyn-2-ol (2.0 mmol) in 10 mL of CH_2Cl_2 was added Dess-Martin periodinane (2.4 mmol). The mixture was stirred for 12 h. The reaction was diluted with another 20 mL of CH_2Cl_2. The organic layer was washed with 20 mL of aq satd $Na_2S_2O_3$, 20 mL of aq satd $NaHCO_3$ and brine. The organic layer was dried over $MgSO_4$, and concentrated in vacuo. The residue was purified by column chromatography on silica gel by 10:1 hexane/EtOAc to afford compound **18** in a 90 % yield as a colorless oil. ^{1}H NMR

($CDCl_3$, 400 MHz) 3.78 (s, 3H), 3.86 (s, 2H), 6.89-6.91 (d, J = 8.8 Hz, 2H), 7.21-7.23 (d, J = 8.8 Hz, 2H), 7.32-7.35 (m, 2H), 7.40-7.47 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 51.39, 55.33, 87.82, 92.76, 114.24, 119.93, 125.24, 128.67, 130.87, 130.98, 133.15, 159.03, 185.66; IR ($CHCl_3$) 3068, 2935, 2228, 1701, 1609, 1511 cm^{-1}; HRMS *m/z* 250.0997 (calcd for $C_{17}H_{14}O_2$, 250.0994).

4-Methoxyphenyl 3-phenyl-2-propynoate (20). To a solution of 4-methoxyphenol (10.0 mmol) in CH_2Cl_2 (5 mL) was added 3-phenyl-2-propynoic acid (10.0 mmol), DMAP (1.0 mmol), and a solution of DCC (10 mmol) in 1 mL of CH_2Cl_2 at 0 ^oC. After 2 h, the precipitate was filtered off and the filtrate was washed with H_2O, dried over $MgSO_4$, and concentrated in vacuo. The product was obtained as a yellow solid in a 62 % yield by direct recrystallization of the mixture. The spectral properties were identical with those previously reported.[4]

***N*-(4-Methoxyphenyl)-3-phenyl-2-propynamide (22).** This compound was prepared using the procedure used for compound **20**, except 4-methoxyaniline was used instead of 4-methoxyphenol. Compound **22** was obtained as a white solid in a 74 % yield. The spectral properties were identical with those previously reported.[5]

4-(4-Phenyl-3-butynyl)anisole (24). This compound was prepared by the Sonogashiro reaction of 4-(3-butynyl)anisole with phenyl iodide. 4-(3-Butynyl)anisole was prepared as follows. *n*-Butyllithium (3.3 mmol, 1.1 equiv, 2M in hexanes) was added at –78 ^oC to 1-trimethylsilyl-1-propyne (3.6 mmol, 1.2 equiv) in dry THF (30 mL). After stirring at –78 ^oC for 2 h, 4-methoxybenzyl iodide (248 mg, 3.0 mmol) in dry THF (10 ml) was added and the mixture was stirred at –78 ^oC for 1 h. The reaction mixture was allowed to reach room temperature and brine (30 mL) was then added to quench the

reaction. The solution was extracted twice using diethyl ether (2 x 30 mL). The solvent was removed under vacuum to obtain crude [4-(4-methoxyphenyl)-1-butynyl]trimethylsilane, which was directly employed in the next step. To the silane was added 20 mL of methanol and KOH (3.6 mmol, 1.2 equiv). The solution was stirred overnight, neutralized by adding 1N HCl, and extracted with ether. Removal of the solvent and flash chromatography on silica gel using 40:1 hexane/EtOAc afforded 4-(3-butynyl)anisole in an 80 % yield as an oil. The spectral properties were identical with those previously reported.[2] To a solution of Et_3N (30 mL), $PdCl_2(PPh_3)_2$ (2 mol %), 3.0 mmol of 4-(3-butynyl)anisole, and 1.2 equiv of iodobenzene (stirring for 3 min beforehand) was added CuI (1 mol %). The reaction mixture was flushed with Ar and the flask was then sealed. The mixture was stirred at room temperature and the reaction was monitored by TLC to establish completion of the reaction. The resulting solution was filtered, washed with satd aq NaCl solution, and extracted with diethyl ether. The combined ether fractions were dried over $MgSO_4$ and concentrated under vacuum to yield the crude product, which was purified by flash chromatography on silica gel using 40:1 hexane/EtOAc. The spectral properties were identical with those previously reported.[3]

General Procedure for Iodocyclization by ICl (Conditions A). 0.3 Mmol of the alkyne and 3 mL of CH_2Cl_2 were placed in a vial. Then the vial was sealed, flushed with N_2 and cooled to –78 ^oC. 2 Equiv of ICl in 1 mL of CH_2Cl_2 were added dropwise to the vial for 10 minutes. The reaction mixture was stirred at –78 ^oC for another 10-30 min. The reaction mixture was then quickly quenched with 20 mL of satd aq $Na_2S_2O_3$ and extracted twice with EtOAc. The organic layers were dried over $MgSO_4$ and filtered.

The solvent was evaporated under reduced pressure and the product was isolated by chromatography on a silica gel column.

3-Iodo-4-phenyl-1-trifluoromethanesulfonyl-1-azaspiro[4.5]deca-3,6,9-trien-8-one (3). The reaction mixture was chromatographed using 5:1 hexane/EtOAc to afford 88 % of the product as a light yellow solid: mp 166-167 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.69 (s, 2H), 6.16-6.19 (d, *J* = 10.0 Hz, 2H), 6.81-6.84 (d, *J* = 10.0 Hz, 2H), 6.98-7.01 (m, 2H), 7.28-7.34 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 63.47, 74.19, 90.01, 128.53, 129.26, 129.66, 130.40, 131.57, 144.21, 144.34, 183.62; IR (CH_2Cl_2) 3054, 2927, 2856, 1675, 1400 cm^{-1}; HRMS *m/z* 480.9461 (calcd for $C_{16}H_{11}F_3INO_3S$, 480.9457).

3-Iodo-4-(4-methoxyphenyl)-1-trifluoromethanesulfonyl-1-azaspiro[4.5]deca-3,6,9-trien-8-one (6). The reaction mixture was chromatographed using 5:1 hexane/EtOAc to afford 84 % of the product as a light yellow solid: mp 140-141 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.78 (s, 3H), 4.69 (s, 2H), 6.19-6.21 (d, *J* = 10.0 Hz, 2H), 6.81-6.85 (m, 4H), 6.95-6.97 (d, *J* = 10.0 Hz, 2H), 8.22-8.26 (m, 2H), 8.70 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 55.25, 63.32, 74.06, 89.97, 113.95, 118.14, 121.36, 123.58, 130.34, 130.58, 144.01, 144.48, 160.34, 183.71 (extra peaks due to F splitting); IR (CH_2Cl_2) 3054, 2955, 2842, 1674, 1511, 1398 cm^{-1}; HRMS *m/z* 510.9571 (calcd for $C_{17}H_{13}F_3INO_4S$, 510.9562).

4-(4-Acetylphenyl)-3-iodo-1-trifluoromethanesulfonyl-1-azaspiro[4.5]deca-3,6,9-trien-8-one (8). The reaction mixture was chromatographed using 3:1 hexane/EtOAc to afford 89 % of the product as a white solid: mp 160-161 ^{o}C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.59 (s, 3H), 4.73 (s, 2H), 6.20-6.23 (d, *J* = 9.9 Hz, 2H), 6.87-6.90 (d, *J* = 9.9 Hz, 2H), 7.15-7.17 (d, *J* = 6.6 Hz, 2H), 7.15-7.17 (d, *J* = 6.6 Hz, 2H); ^{13}C

NMR ($CDCl_3$, 75 MHz) δ 26.85, 63.79, 74.35, 90.96, 128.61, 129.90, 130.70, 136.43, 137.89, 143.57, 144.10, 183.53, 197.36; IR ($CHCl_3$) 3056, 2926, 2856, 1676, 1394 cm^{-1}; HRMS *m/z* 522.9572 (calcd for $C_{18}H_{13}F_3INO_4S$, 522.9562).

4-Butyl-3-iodo-1-trifluoromethanesulfonyl-1-azaspiro[4.5]deca-3,6,9-trien-8-one (10). The reaction mixture was chromatographed using 10:1 hexane/EtOAc to afford a 75 % yield of the product as a light yellow solid: mp 118-119 ^oC; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.86-0.88 (t, *J* = 7.2 Hz, 3H), 1.26-1.38 (m, 4H), 1.83-1.87 (m, 2H), 4.55 (s, 2H), 6.34-6.37 (d, *J* = 10.0 Hz, 2H), 6.68-6.71 (d, *J* = 10.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 13.60, 22.80, 28.26, 30.96, 63.11, 74.13, 86.87, 118.08, 121.30, 130.15, 142.78, 144.90, 184.05 (extra peaks due to F splitting); IR (CH_2Cl_2) 2978, 2930, 2871, 1676, 1401 cm^{-1}; HRMS *m/z* 460.9776 (calcd for $C_{14}H_{15}F_3INO_3S$, 460.9770).

3-Iodo-1-trifluoromethanesulfonyl-4-trimethylsilyl-1-azaspiro[4.5]deca-3,6,9-trien-8-one (12). The reaction mixture was chromatographed using 3:1 hexane/EtOAc to afford a 58 % yield of the product as a white solid: mp 154-155 ^oC; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.32 (s, 9H), 4.57 (s, 2H), 6.39-6.42 (d, *J* = 10.0 Hz, 2H), 6.57-6.59 (d, *J* = 10.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ-1.82, 62.92, 77.30, 100.90, 118.02, 121.24, 131.28, 144.82, 148.30, 184.14 (extra peaks due to F splitting); IR (CH_2Cl_2) 2959, 1674, 1394 cm^{-1}; HRMS *m/z* 476.9544 (calcd for $C_{13}H_{15}F_3INO_3Si$, 476.9539).

4-(Cyclohex-1-en-1-yl)-3-iodo-1-trifluoromethanesulfonyl-1-azaspiro[4.5]deca-3,6,9-trien-8-one (14). The reaction mixture was chromatographed using 10:1 hexane/EtOAc to afford an 83 % yield of the product as a white solid: mp 131-132 ^oC; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.49-1.64 (m, 7H), 1.87-2.02 (m, 4H), 4.87-4.89 (m, 1H), 5.45 (s, 1H), 6.25-6.28 (m, 2H), 6.62-6.73 (m, 2H); ^{13}C NMR ($CDCl_3$, 300

MHz) δ 21.22, 22.31, 25.02, 28.42, 68.70, 74.68, 77.27, 97.36, 129.68, 133.25, 144.50, 184.09 (one sp^3 carbon missing due to overlap); IR (CH_2Cl_2) 2934, 1673, 1398 cm^{-1}; HRMS *m/z* 498.9932 (calcd for $C_{17}H_{17}F_3INO_3S$, 498.9926).

1-Acetyl-3-iodo-4-phenyl-1-azaspiro[4.5]deca-3,6,9-trien-8-one (16). The reaction mixture was chromatographed using EtOAc to afford a 66 % yield of the product as a white solid (conformational isomers). ^1H NMR ($CDCl_3$, 400 MHz) δ 1.97 and 2.11 (s, 3H), 4.65 (s, 2H), 6.15-6.17 (d, *J* = 10.0 Hz, 1H), 6.21-6.23 (d, *J* = 10.0 Hz, 1H), 6.70-6.72 (d, *J* = 10.0 Hz, 1H), 6.81-6.84 (d, *J* = 10.0 Hz, 1H), 6.96-6.98 (m, 2H), 7.24-7.30 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.71, 22.80, 62.52, 62.68, 71.36, 71.77, 90.64, 93.35, 128.22, 128.33, 129.16, 129.26, 129.39, 129.62, 130.00, 130.53, 132.25, 132.37, 143.30, 145.31, 146.73, 146.89, 168.01, 168.97, 183.61, 184.59; IR (CH_2Cl_2) 3048, 2926, 2863, 1665, 1394 cm^{-1}; HRMS *m/z* 391.0076 (calcd for $C_{17}H_{14}INO_2$, 391.0069).

General Procedure for the Iodo/bromocyclization by Br_2/I_2 (Conditions B). 0.3 Mmol of the *N*-(2-alkynyl)-4-methoxyanilide, 0.60 mmol of $NaHCO_3$, and 3 mL of MeCN were placed in a vial. 2 Equiv of Br_2/I_2 in 1 mL of CH_3CN were added dropwise to the vial. The reaction mixture was stirred for 10 min (Br_2) or 1-12 h (I_2). The reaction mixture was then quenched with 20 mL of satd aq $Na_2S_2O_3$ and extracted twice with EtOAc. The organic layers were dried over $MgSO_4$ and filtered. The solvent was evaporated under reduced pressure and the product was isolated by chromatography on a silica gel column.

3-Bromo-4-phenyl-1-trifluoromethanesulfonyl-1-azaspiro[4.5]deca-3,6,9-trien-8-one (4). The reaction mixture was chromatographed using 5:1 hexane/EtOAc to afford a 92 % yield of the product as a white solid: mp 142-143 ^oC; ^1H NMR ($CDCl_3$, 300

MHz) δ 4.73 (s, 2H), 6.21-6.24 (d, *J* = 10.2 Hz, 2H), 6.85-6.88 (d, *J* = 10.2 Hz, 2H), 7.06-7.09 (m, 2H), 7.32-7.35 (m, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 59.45, 74.23, 115.69, 128.55, 129.19, 129.58, 129.70, 130.57, 138.35, 144.12, 183.53; IR (CH_2Cl_2) 3054, 2927, 2852, 1676 cm^{-1}; HRMS *m/z* 432.9602 (calcd for $C_{16}H_{11}BrF_3NO_3S$, 432.9595).

3-Iodo-4-phenylspiro[4.5]deca-3,6,9-triene-2,8-dione (19). The reaction mixture was chromatographed using 3:1 hexane/EtOAc to afford a 98 % yield of the product as a purple solid: mp 129-131 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.98 (s, 2H), 6.34-6.37 (d, *J* = 10.0 Hz, 2H), 6.81-6.84 (d, *J* = 10.0 Hz, 2H), 7.26-7.29 (m, 2H), 7.36-7.42 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 43.40, 54.30, 106.23, 127.00, 128.60, 130.47, 130.65, 134.13, 148.87, 176.22, 184.40, 199.41; IR (CH_2Cl_2) 3058, 2930, 2853, 1732, 1670, 1624 cm^{-1}; HRMS *m/z* 361.9809 (calcd for $C_{16}H_{11}IO_2$, 361.9804).

3-Iodo-4-phenyl-1-oxaspiro[4.5]deca-3,6,9-triene-2,8-dione (21). The reaction mixture was chromatographed using 3:1 hexane/EtOAc to afford a 100 % yield of the product as a white solid: mp 174-175 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.38-6.41 (d, *J* = 10.0 Hz, 2H), 6.67-6.69 (d, *J* = 10.0 Hz, 2H), 7.35-7.48 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 85.17, 88.11, 127.32, 129.04, 130.24, 131.16, 132.08, 141.66, 166.86, 168.66, 183.60; IR (CH_2Cl_2) 3066, 2936, 1783, 1704, 1668, 1638, 1393 cm^{-1}; HRMS *m/z* 363.9602 (calcd for $C_{15}H_9IO_3$, 362.9597).

3-Iodo-4-phenyl-1-azaspiro[4.5]deca-3,6,9-triene-2,8-dione (23). The reaction mixture was chromatographed using 3:1 hexane/EtOAc to afford a 84 % yield of the product as a white solid: decomposes at 195 ^{o}C; ^{1}H NMR (*d*$_6$-acetone, 400 MHz) δ 6.24-6.27 (d, *J* = 10.0 Hz, 2H), 6.94-6.96 (d, *J* = 10.0 Hz, 2H), 7.37-7.43 (m, 5H), 8.23 (s,

1H); ^{13}C NMR (d_6-acetone, 100 MHz) δ 66.72, 98.99, 128.07, 128.42, 129.58, 130.62, 132.89, 145.73, 160.70, 168.58, 183.79; IR (CH_2Cl_2) 3196, 3066, 1693, 1673, 1638 cm^{-1}; HRMS *m/z* 362.9761 (calcd for $C_{15}H_{10}INO_2$, 362.9756); Anal. Calcd for $C_{15}H_{10}INO_2$: C, 49.61; H, 2.78; N, 3.86; Found: C, 49.35; H, 3.03; N, 4.03.

General Procedure for the Iodo/bromocyclization of 4-(4-phenylbut-3-ynyl)anisole (Conditions C). 0.3 Mmol of 4-(4-phenylbut-3-ynyl)anisole, 0.6 mmol of NaOMe, 4 mL of MeOH, and 2 mL of CH_2Cl_2 were placed in a vial and the solution was cooled to -78 ^{o}C. 5 Equiv of Br_2/ICl in 1 mL of CH_2Cl_2 were added dropwise to the vial. The reaction mixture was stirred for 10 min and then quickly quenched with 20 mL of satd aq $Na_2S_2O_3$ and extracted twice with EtOAc. The organic layers were dried over $MgSO_4$ and filtered. The solvent was evaporated under reduced pressure and the product was isolated by chromatography on a silica gel column.

2-Iodo-1-phenylspiro[4.5]deca-1,6,9-trien-8-one (25). The reaction mixture was chromatographed using 5:1 hexane/EtOAc to afford a 93 % yield of the product as a light yellow solid (Conditions C): mp 124-125 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.32-2.35 (t, *J* = 7.2 Hz, 1H), 3.05-3.08 (t, *J* = 7.2 Hz, 1H), 6.20-6.22 (d, *J* = 10.0 Hz, 2H), 6.88-6.90 (d, *J* = 10.0 Hz, 2H), 7.09-7.11 (m, 2H), 7.26-7.28 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 37.53, 43.47, 56.86, 98.89, 128.01, 128.20, 128.37, 129.14, 135.69, 147.87, 151.64, 185.57; IR (CH_2Cl_2) 2944, 2858, 1620 cm^{-1}; HRMS *m/z* 348.0019 (calcd for $C_{16}H_{13}IO$, 348.0011).

2-Bromo-1-phenylspiro[4.5]deca-1,6,9-trien-8-one (26). The reaction mixture was chromatographed using 5:1 hexane/EtOAc to afford a 98 % yield of the product as a light yellow solid (Conditions C): mp 129-130 ^{o}C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.28-

2.33 (t, *J* = 7.2 Hz, 1H), 3.00-3.05 (t, *J* = 7.2 Hz, 1H), 6.22-6.25 (d, *J* = 10.2 Hz, 2H), 6.90-6.94 (d, *J* = 10.2 Hz, 2H), 7.16-7.19 (m, 2H), 7.25-7.28 (m, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 36.17, 39.45, 56.88, 123.52, 128.14, 128.39, 128.54, 129.36, 134.12, 141.37, 152.23, 185.72; IR (CH_2Cl_2) 3038, 2944, 2858, 1665, 1620 cm^{-1}; HRMS *m/z* 300.0155 (calcd for $C_{16}H_{13}BrO$, 300.0150); Anal. Calcd for $C_{16}H_{13}BrO$: C, 63.81; H, 4.35. Found: C, 63.47; H, 4.70.

5,6-Diphenyl-2-(trifluoromethanesulfonyl)spiro[benz[*e*]isoindoline-1,1'-[2.5]cyclohexadien-4'-one (27). To a solution of **3** (0.25 mmol) in 4 mL of DMF in a vial was added diphenylacetylene (0.50 mmol), $Pd(OAc)_2$ (5 mol %), *n*-Bu_4NCl (0.75 mmol) and NaOAc (0.50 mmol). The vial was flushed with N_2 and closed. The reaction mixture was heated to 100 ^{o}C for 12 h, cooled to room temperature, diluted with 25 ml of ether, washed with 25 mL of satd aq NaCl, dried over $MgSO_4$ and filtered. The solvent was evaporated under reduced pressure. The reaction mixture was chromatographed using 5:1 hexane/EtOAc to afford a 46 % yield of the product as a yellow solid: mp 254-255 ^{o}C ; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.84 (s, 2H), 6.49-6.52 (d, *J* = 9.0 Hz, 2H), 6.98-7.05 (m, 6H), 7.16-7.20 (m, 7H), 7.34-7.40 (m, 2H), 7.56-7.59 (m, 1H), 7.72-7.75 (m, 1H); ^{13}C NMR ($CDCl_3$, 400 MHz) 55.76, 71.90, 121.49, 126.75, 127.06, 127.32, 127.45, 127.58, 127.90, 128.39, 128.44, 128.61, 129.22, 130.15, 130.83, 132.78, 133.64, 134.22, 137.55, 137.82, 142.01, 145.91, 184.77; IR ($CHCl_3$) 3061, 2921, 2835, 1674, 1632, 1398 cm^{-1}; HRMS *m/z* 531.1129 (calcd for $C_{30}H_{20}F_3NO_3S$, 531.1116).

References

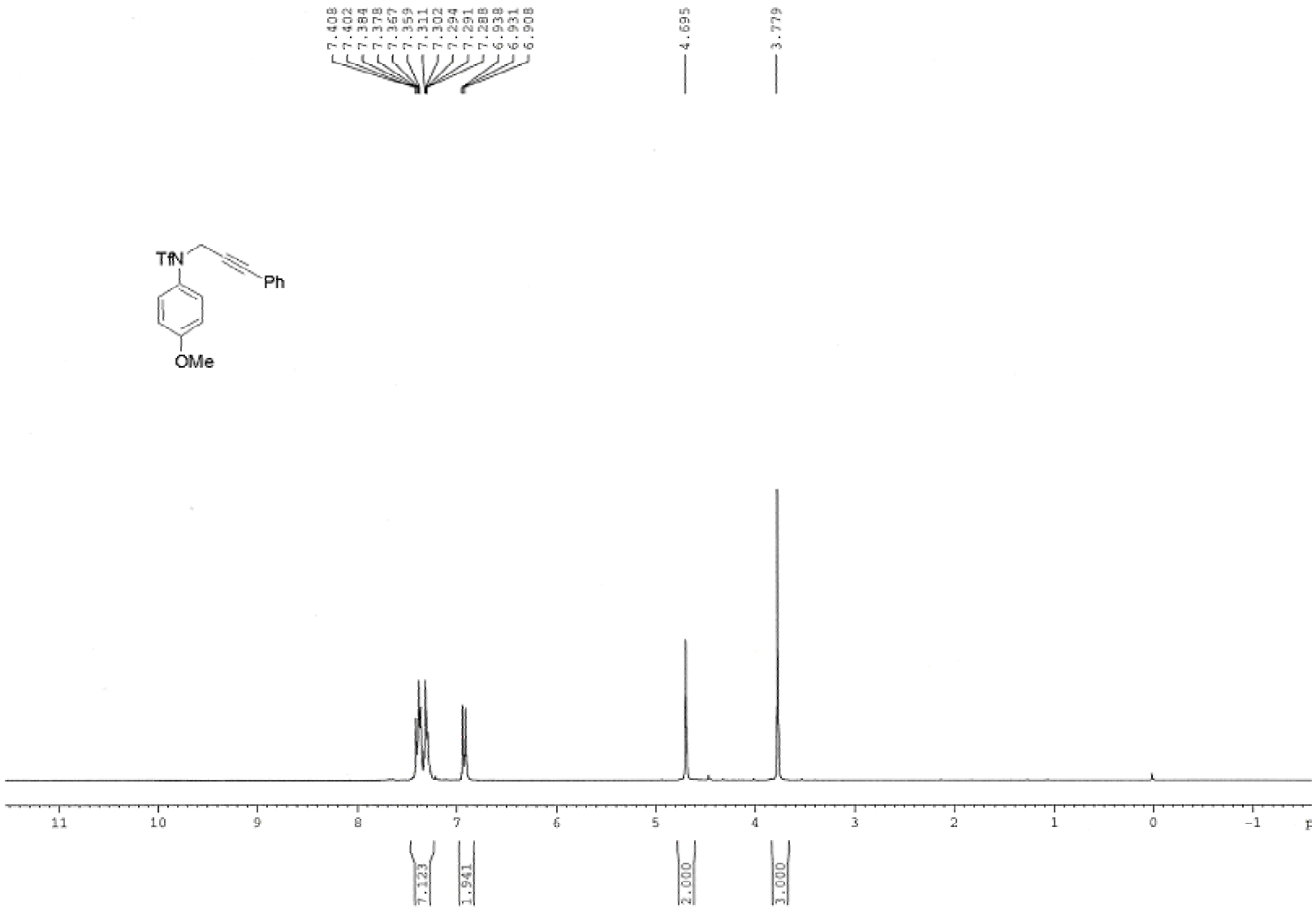
(1) Inoue, J.; Cui, Y.-S.; Sakai, O.; Nakamura, Y.; Kogiso, H.; Kador, P. F. *Bioorg. Chem.* **2000**, *8*, 2167.

(2) Satoh, T.; Hayashi, Y.; Yamakawa, K. *Bull. Chem. Soc. Jpn.* **1993**, *66*, 1866.

(3) Ma, S.; Wang, L. *J. Org. Chem.* **1998**, *63*, 3497.

(4) Shi, Z.; He, C. *J. Org. Chem.* **2004**, *69*, 3669.

(5) Barreau, M.; Ponsinet, G. *Synthesis*, **1987**, 262.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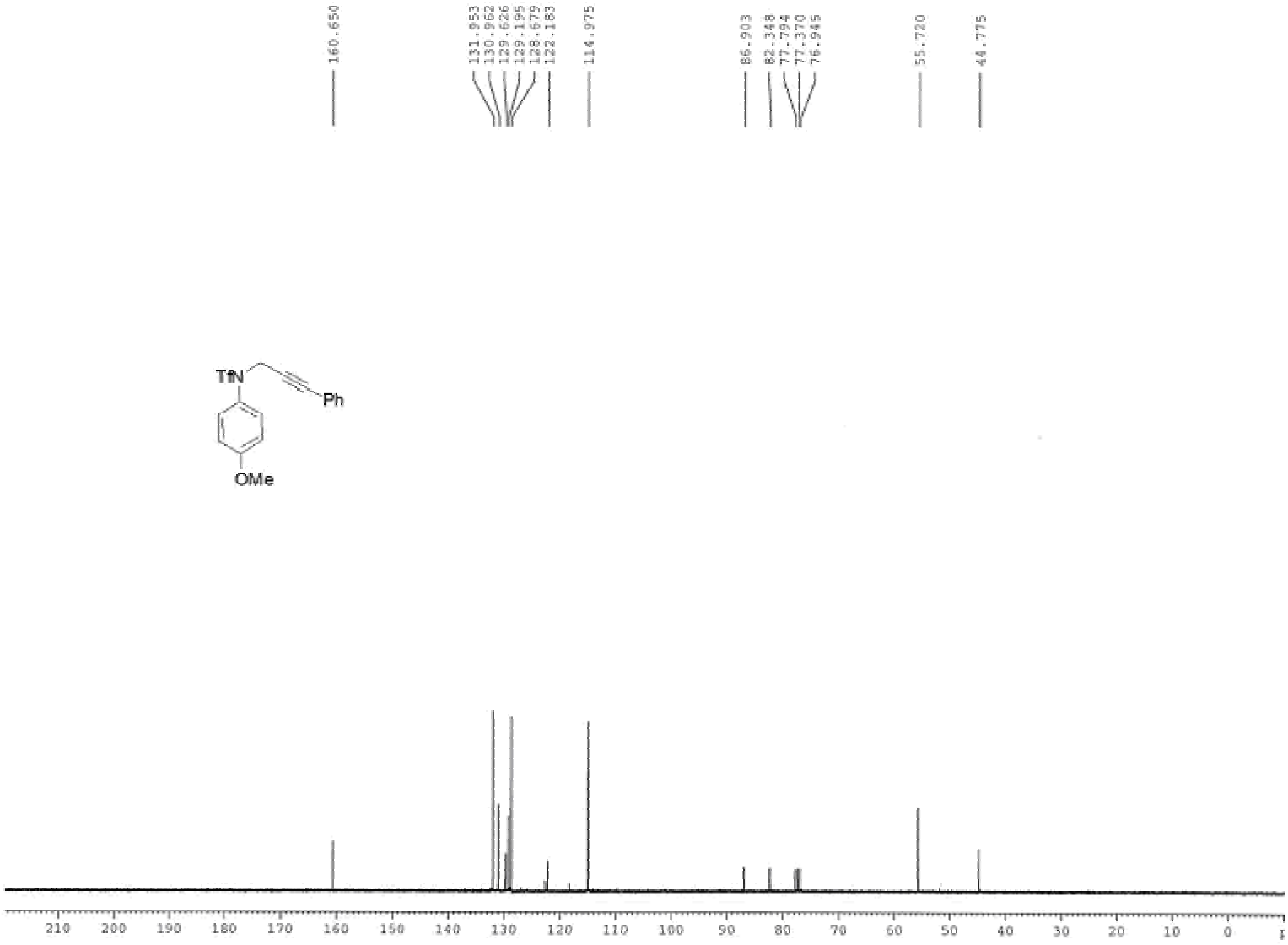
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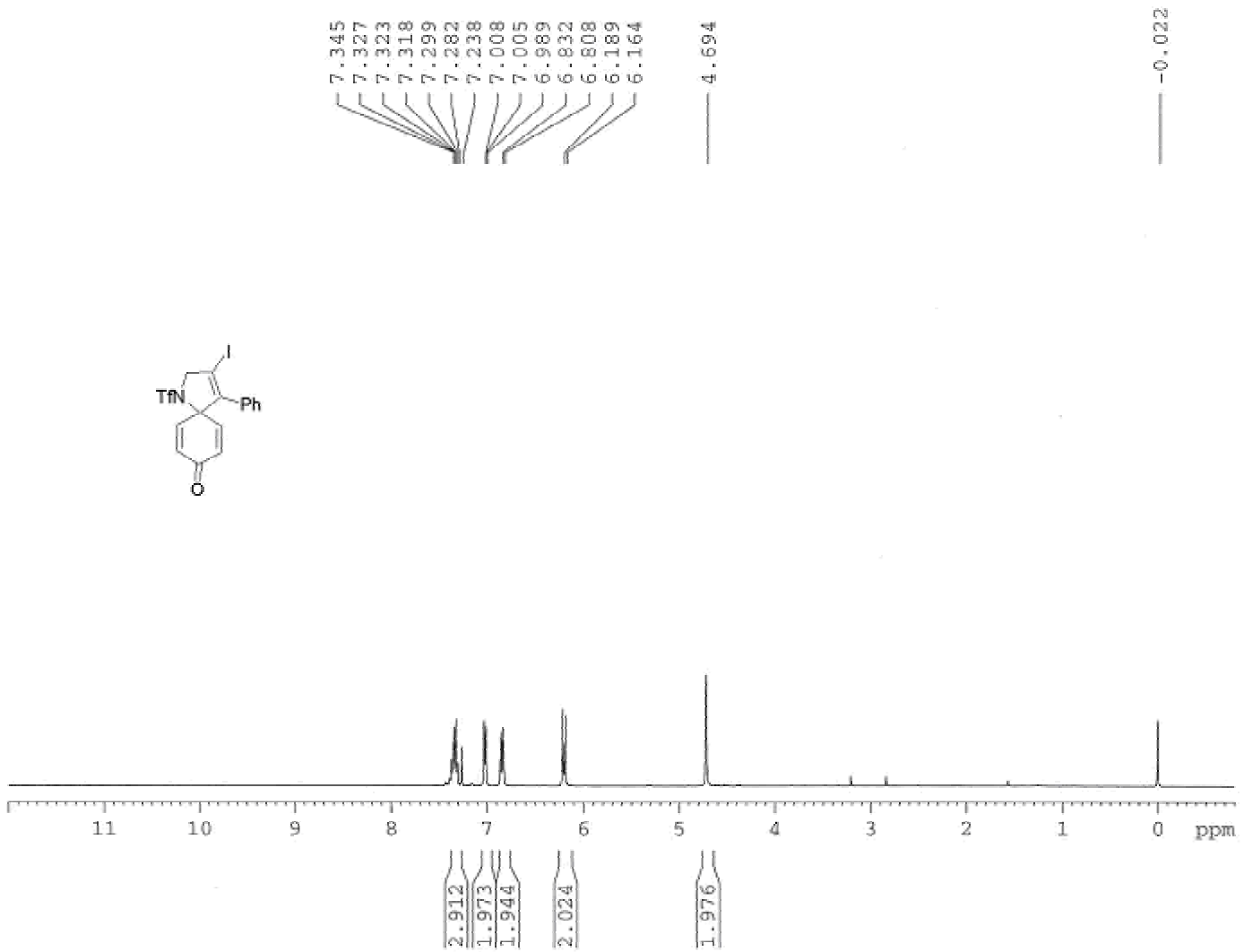
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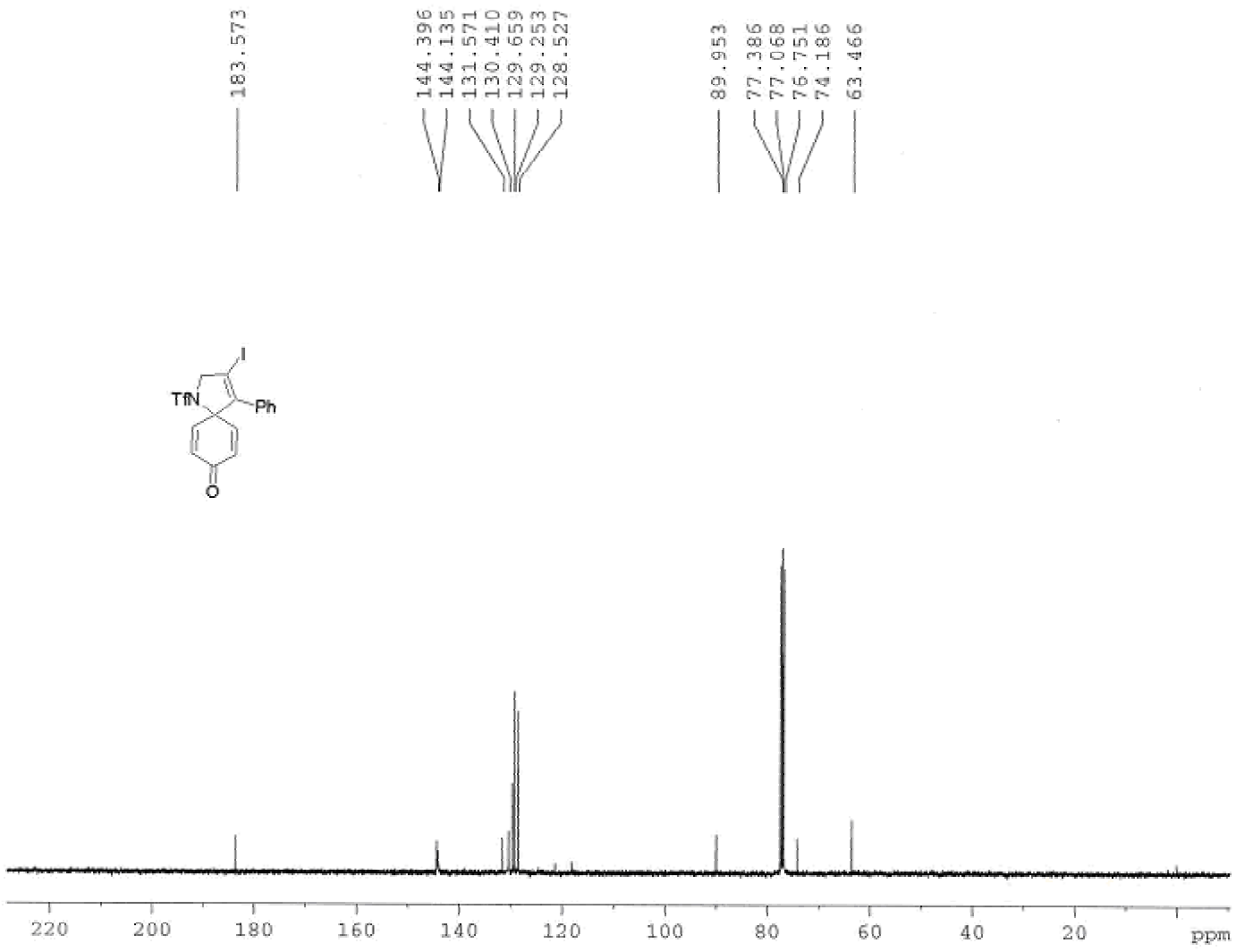
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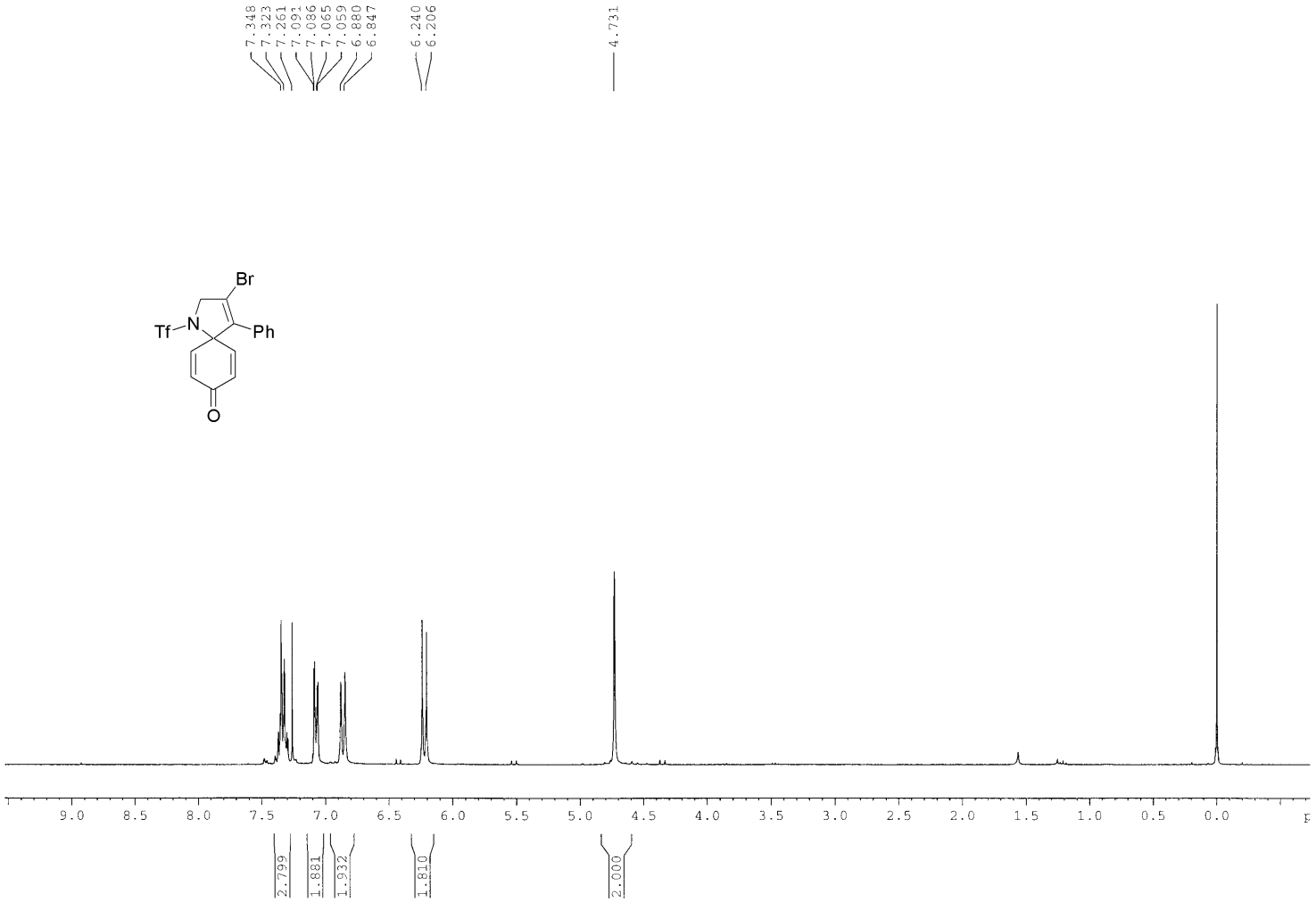
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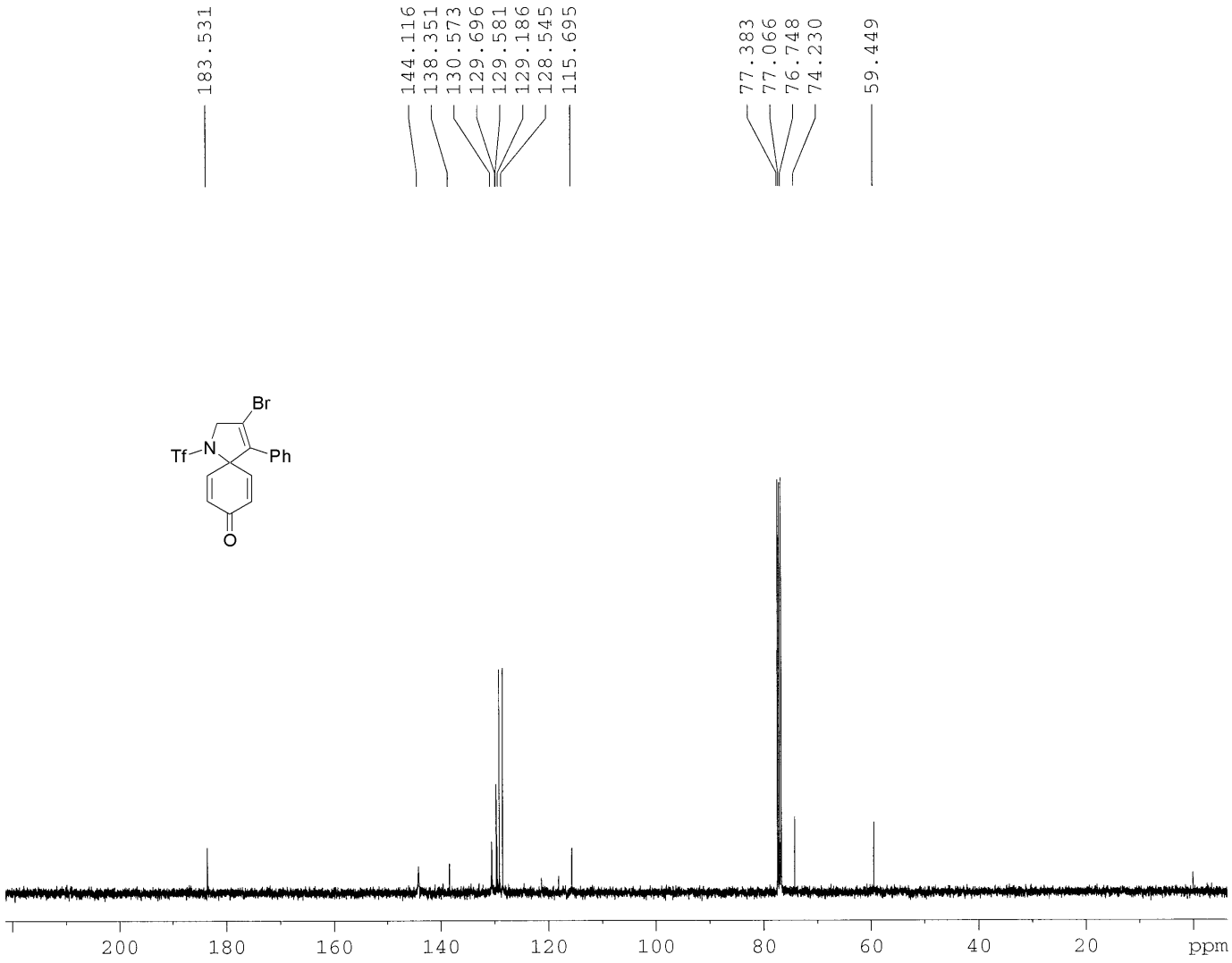
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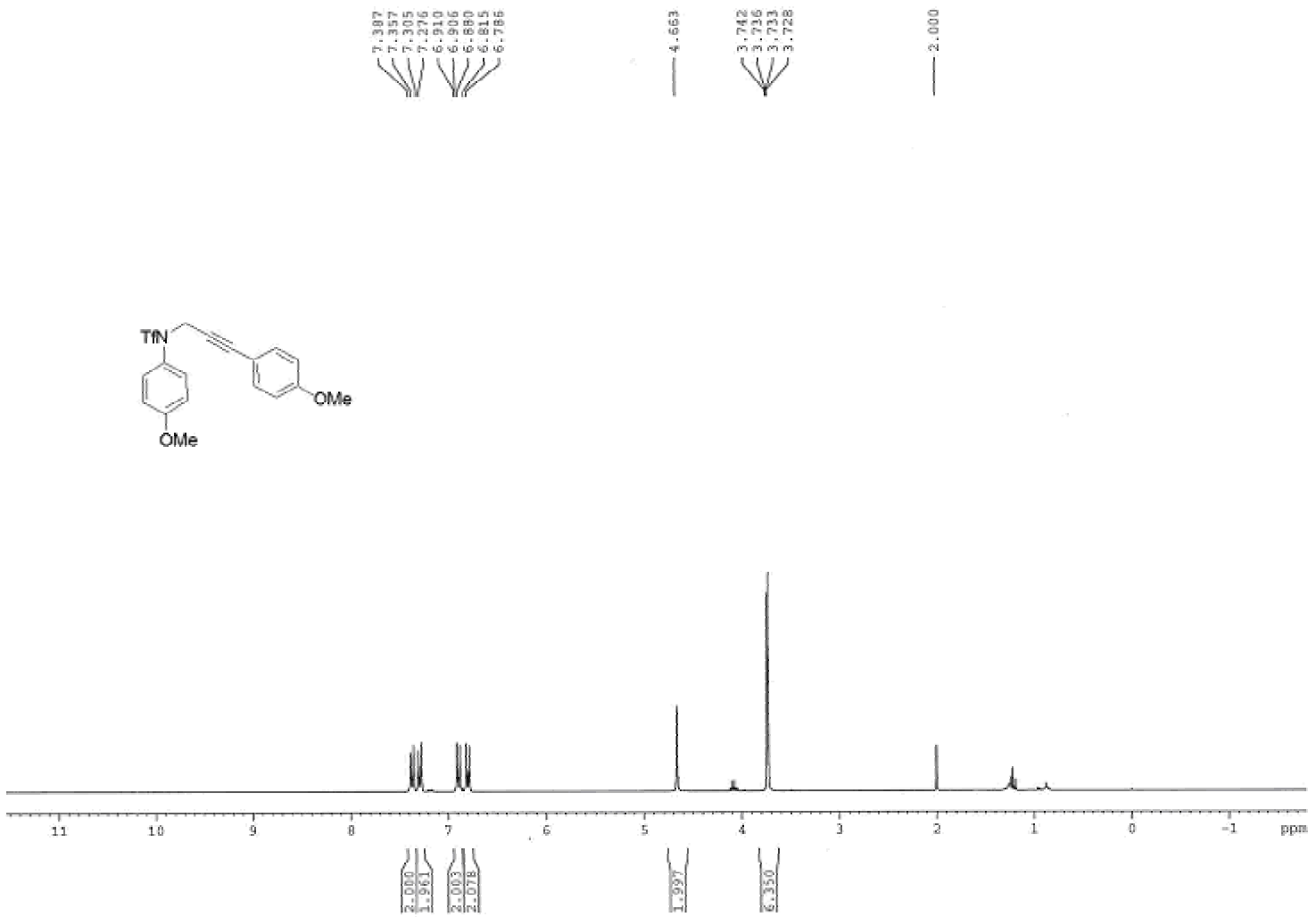
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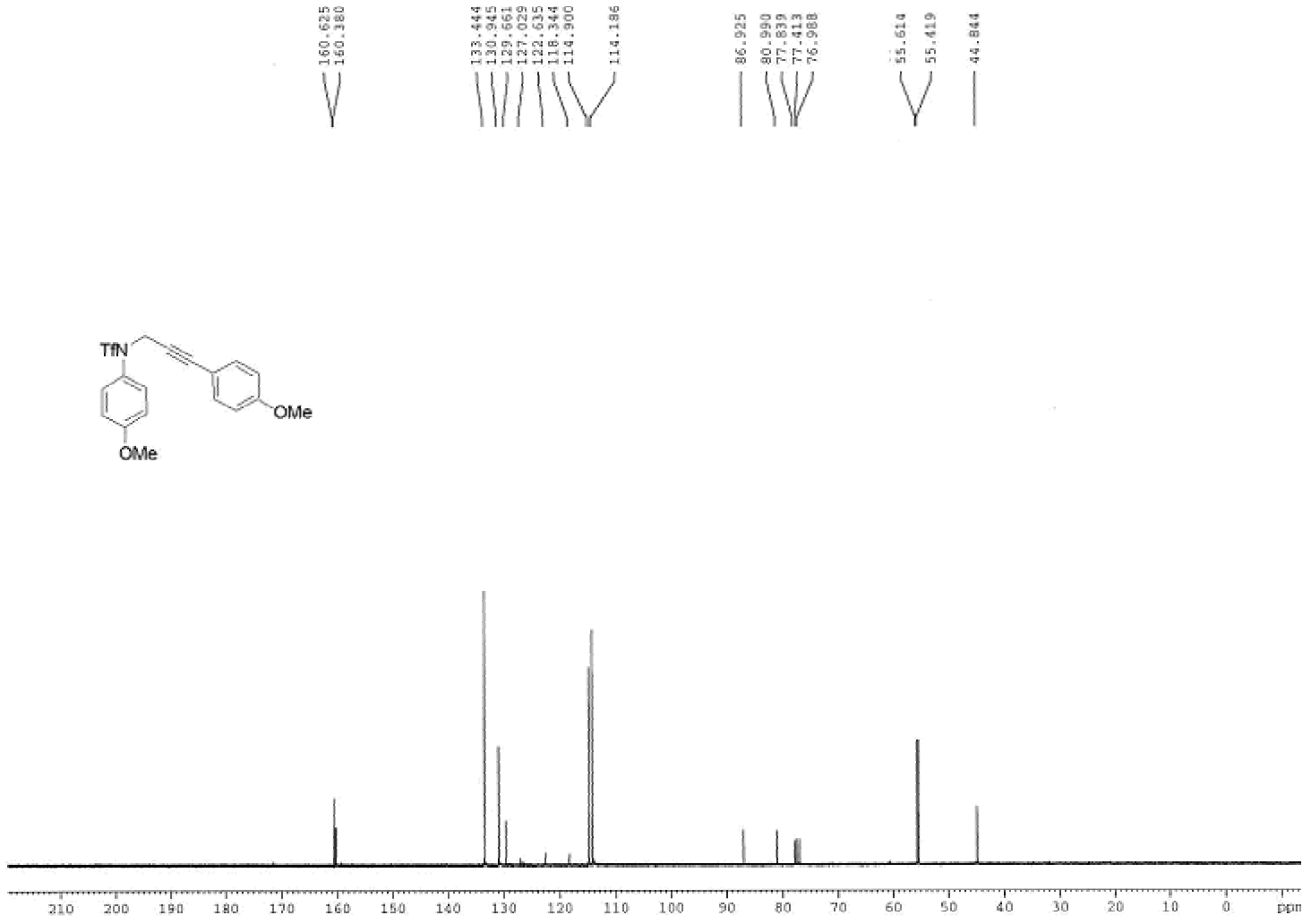
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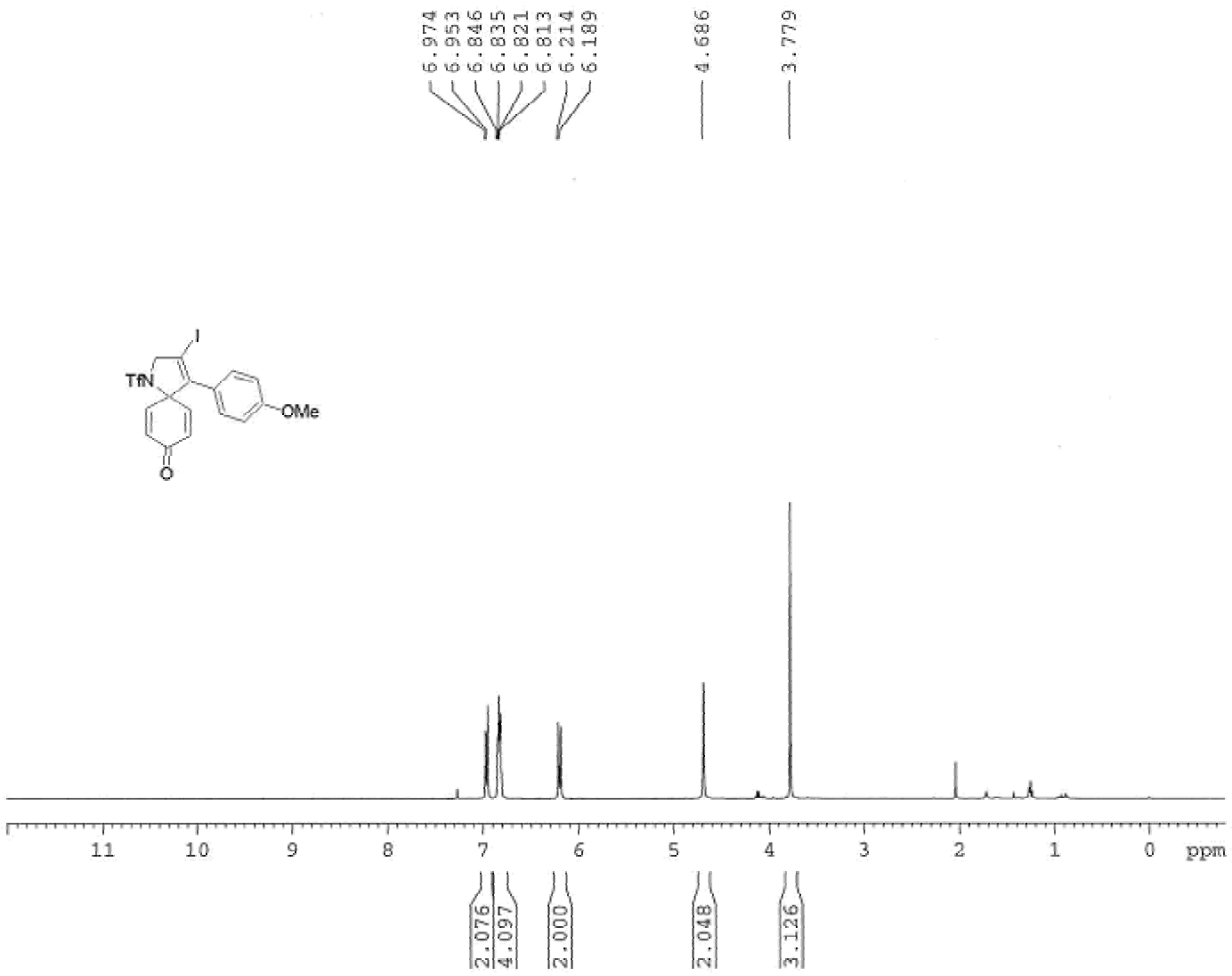
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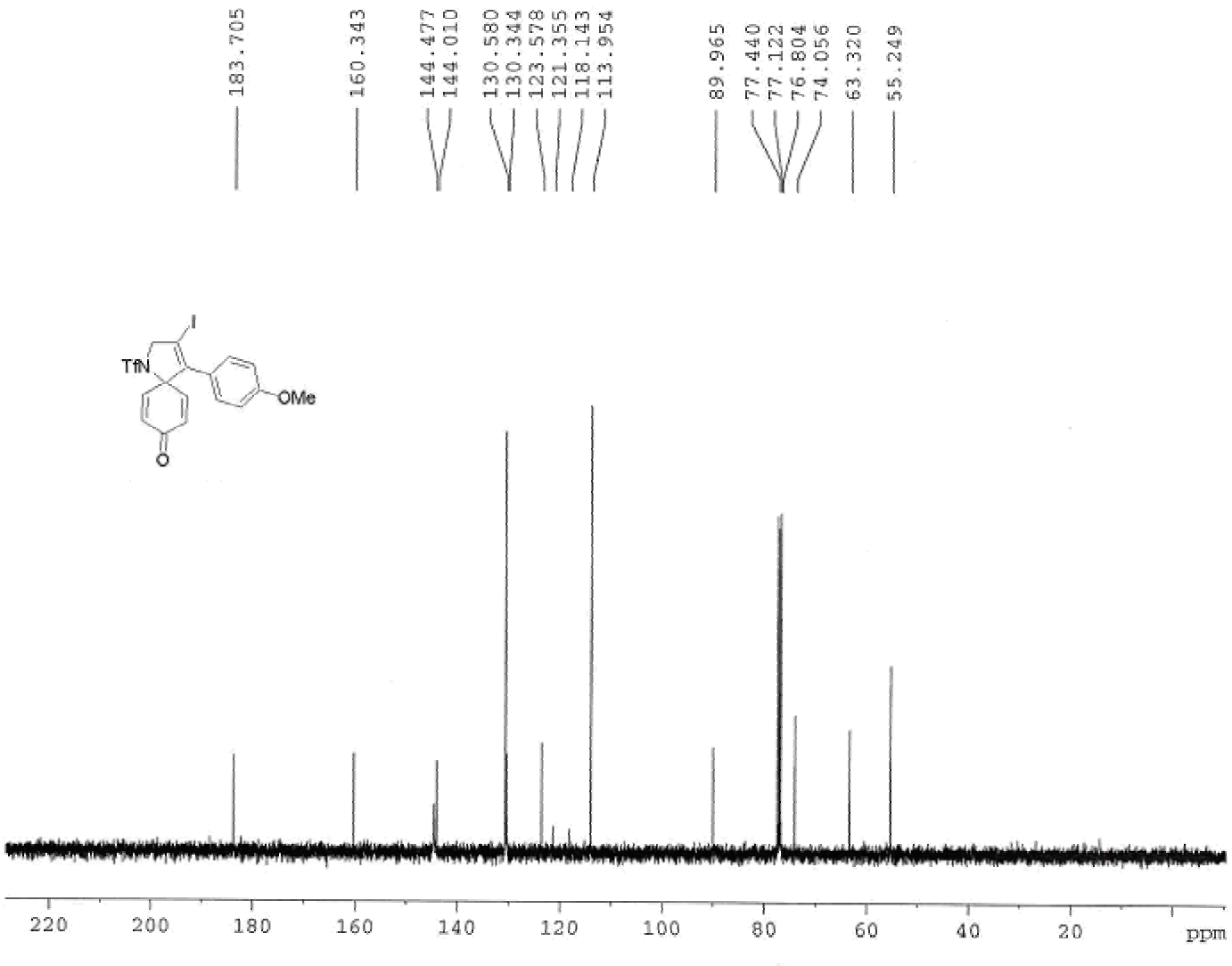
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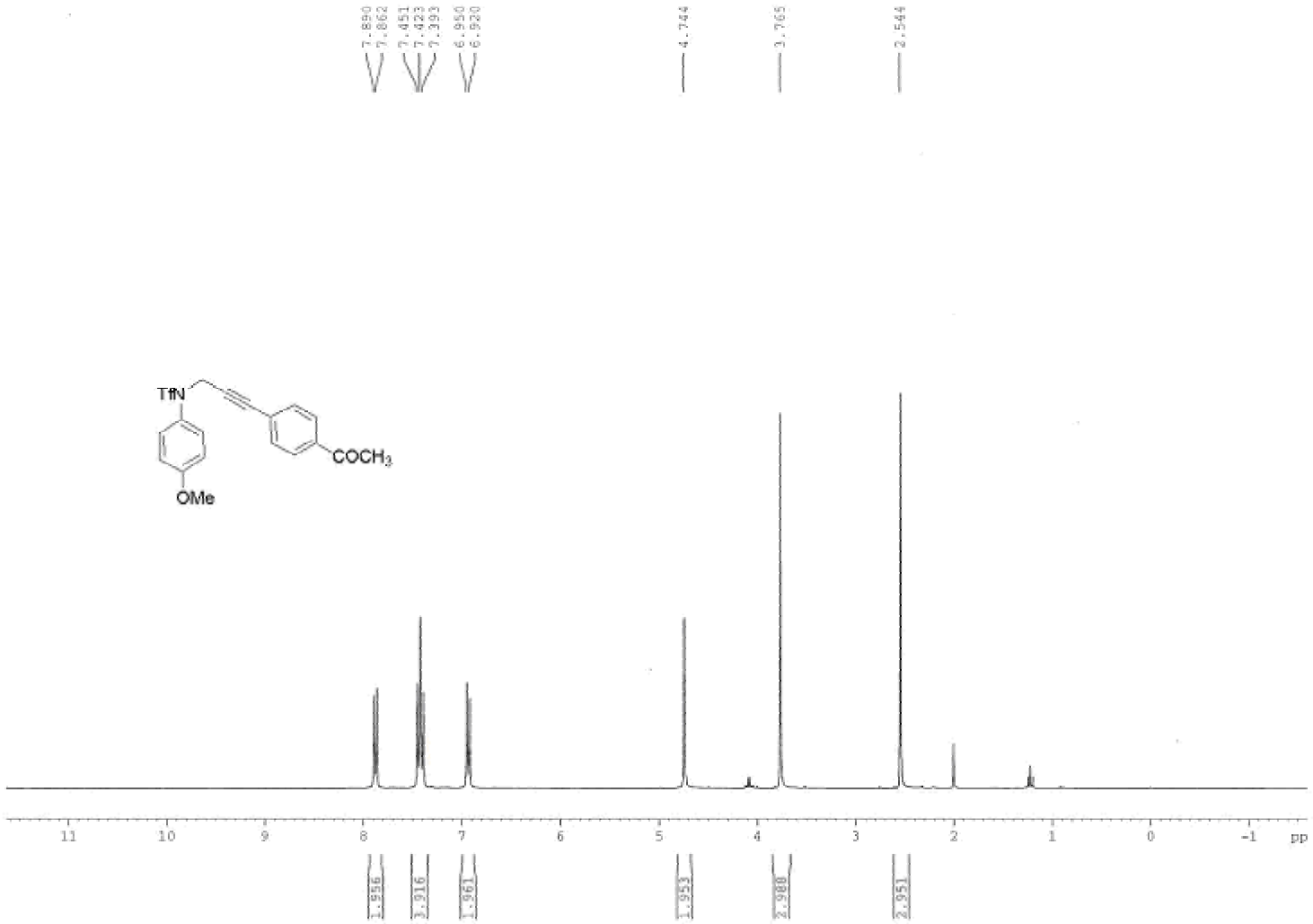
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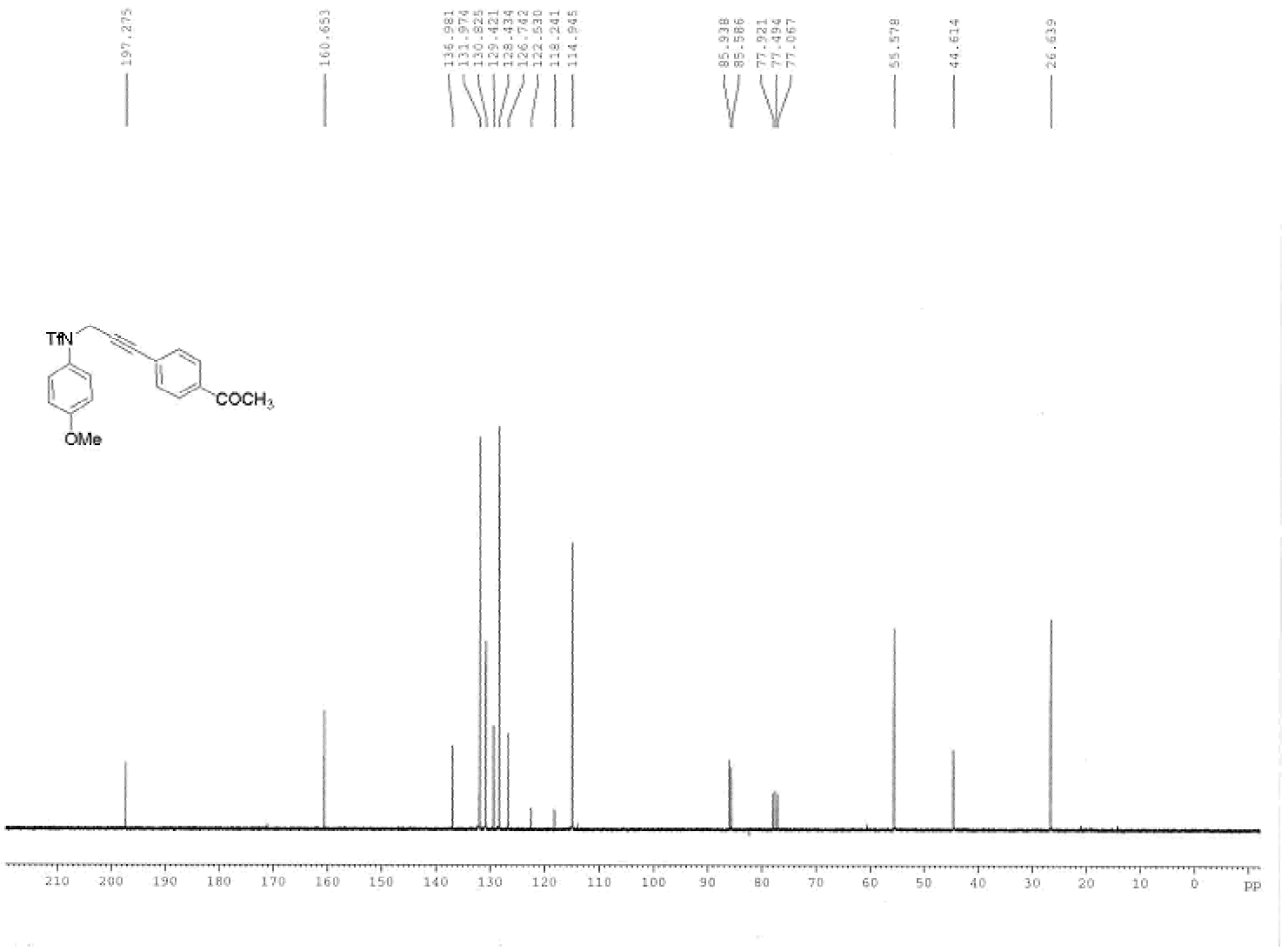
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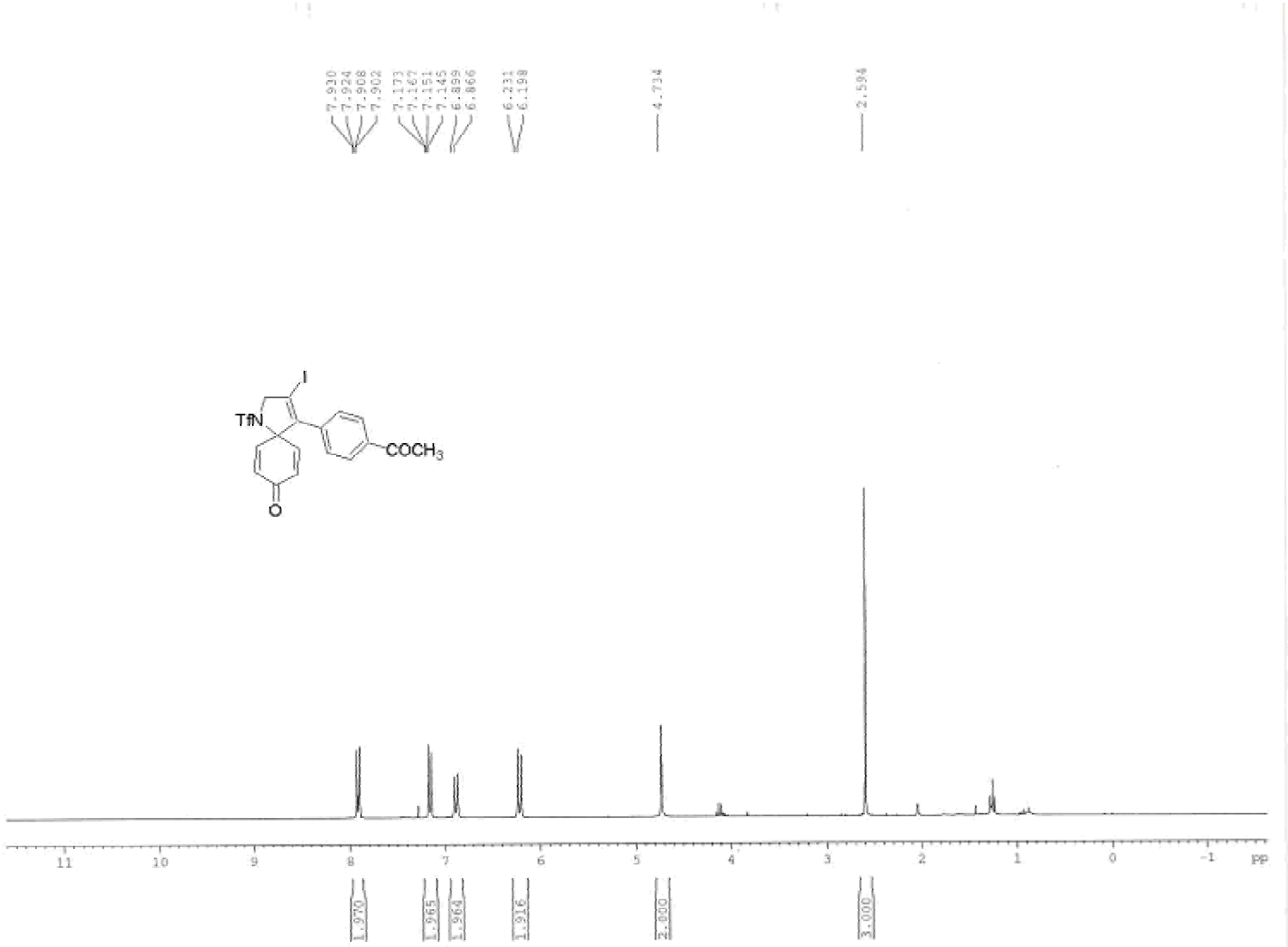
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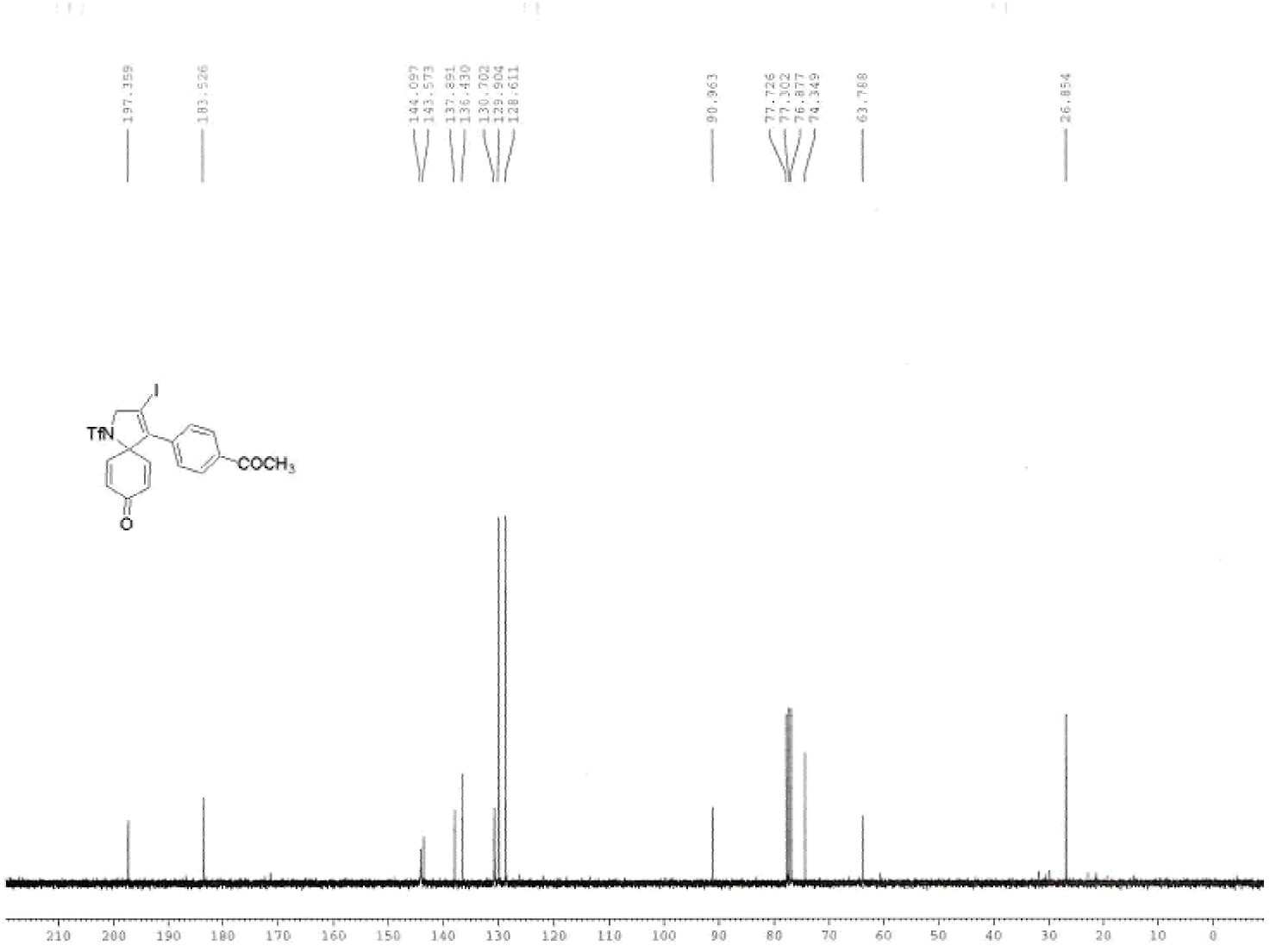
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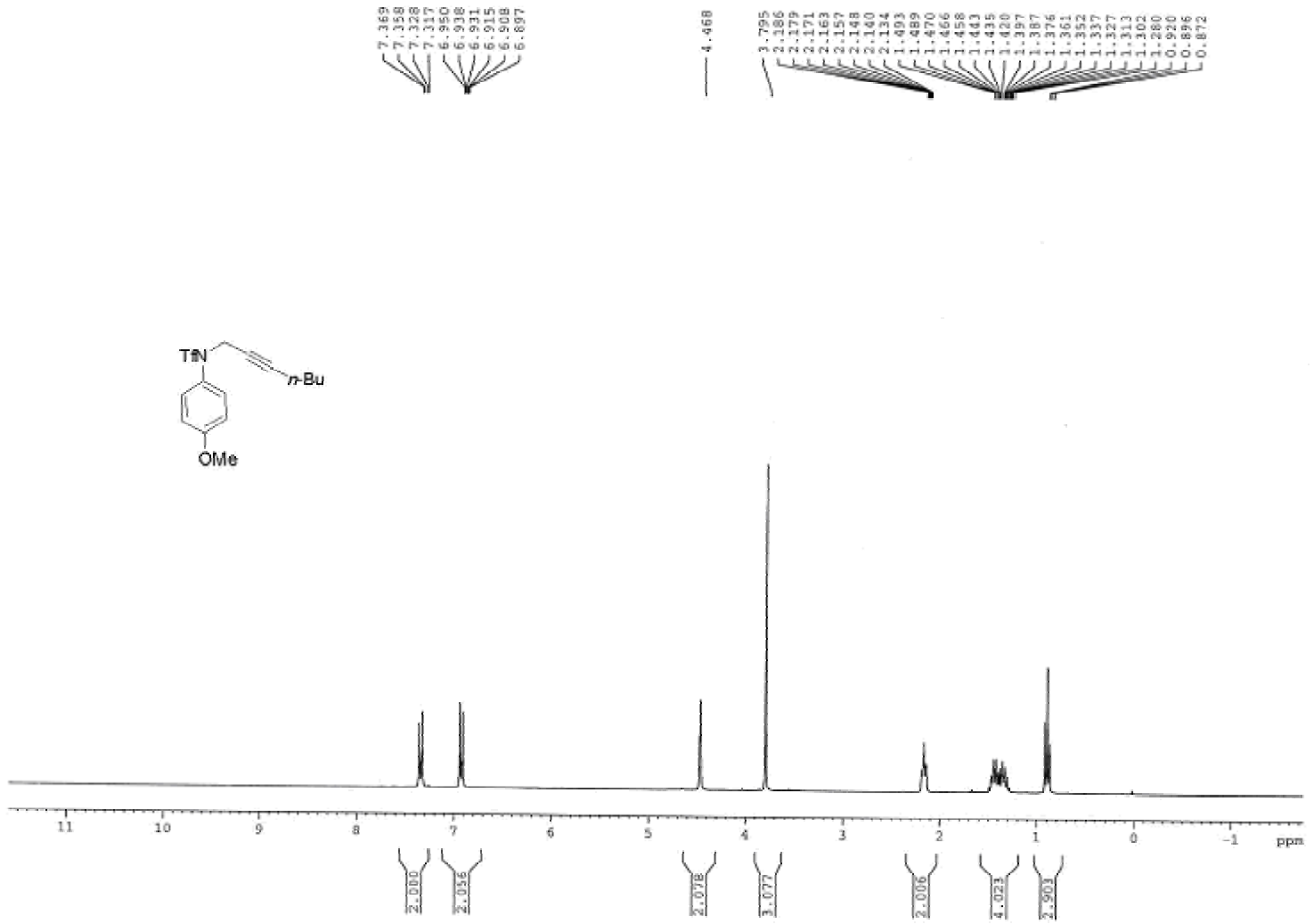
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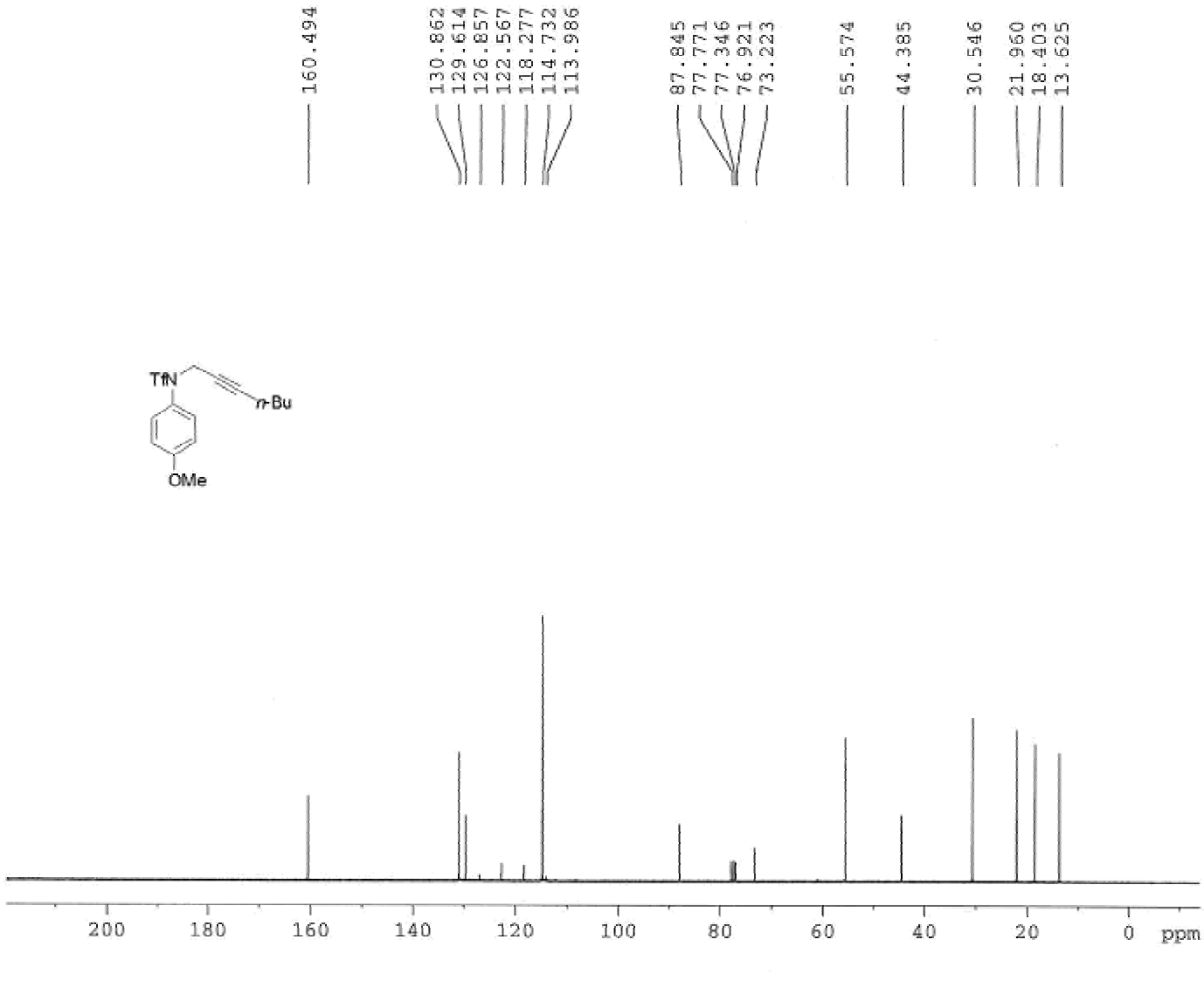
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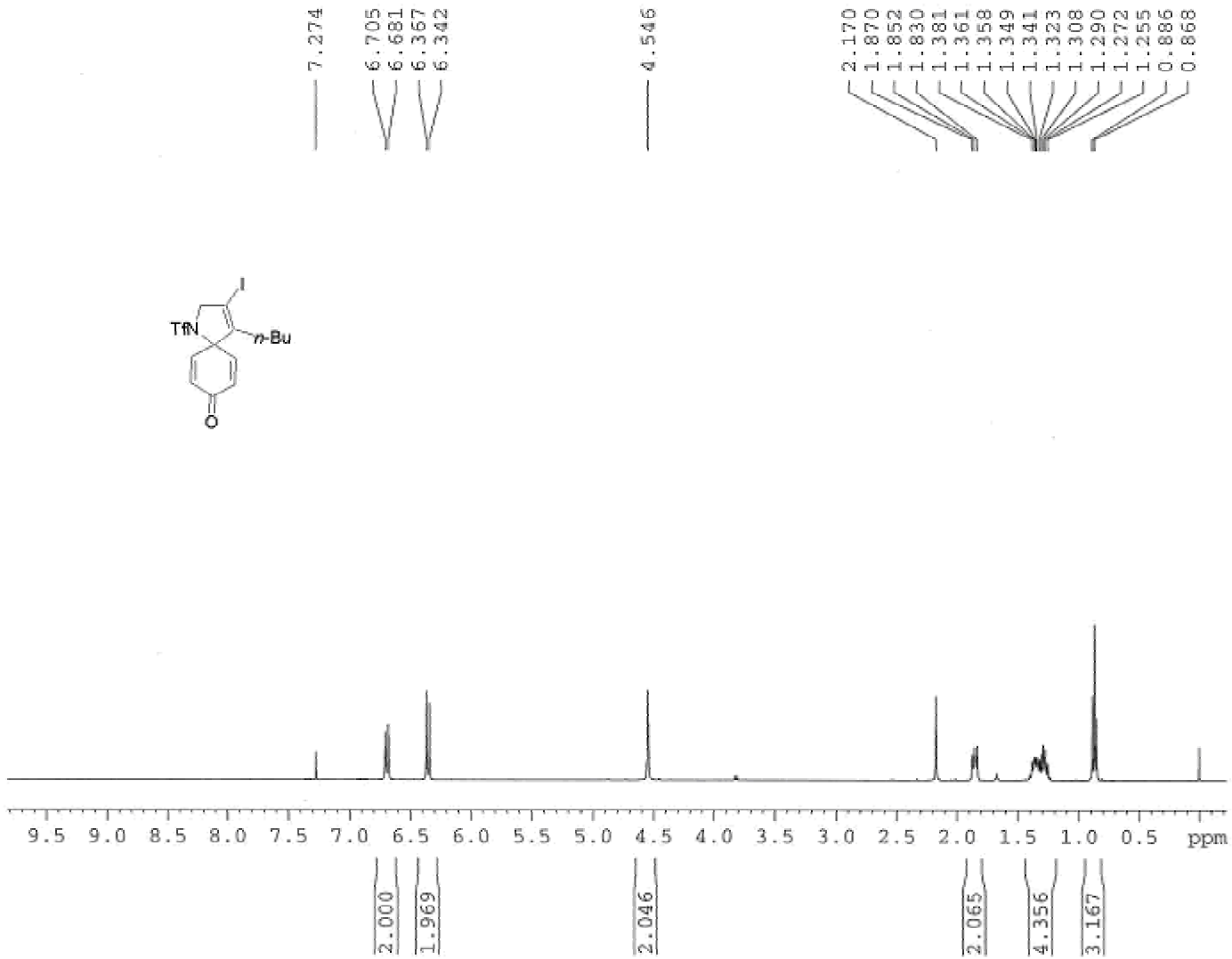
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1.358
1.349
1.341
1.323
1.308
1.290
1.272
1.255
0.886
0.868
Ts
N
n-Bu
O
I
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
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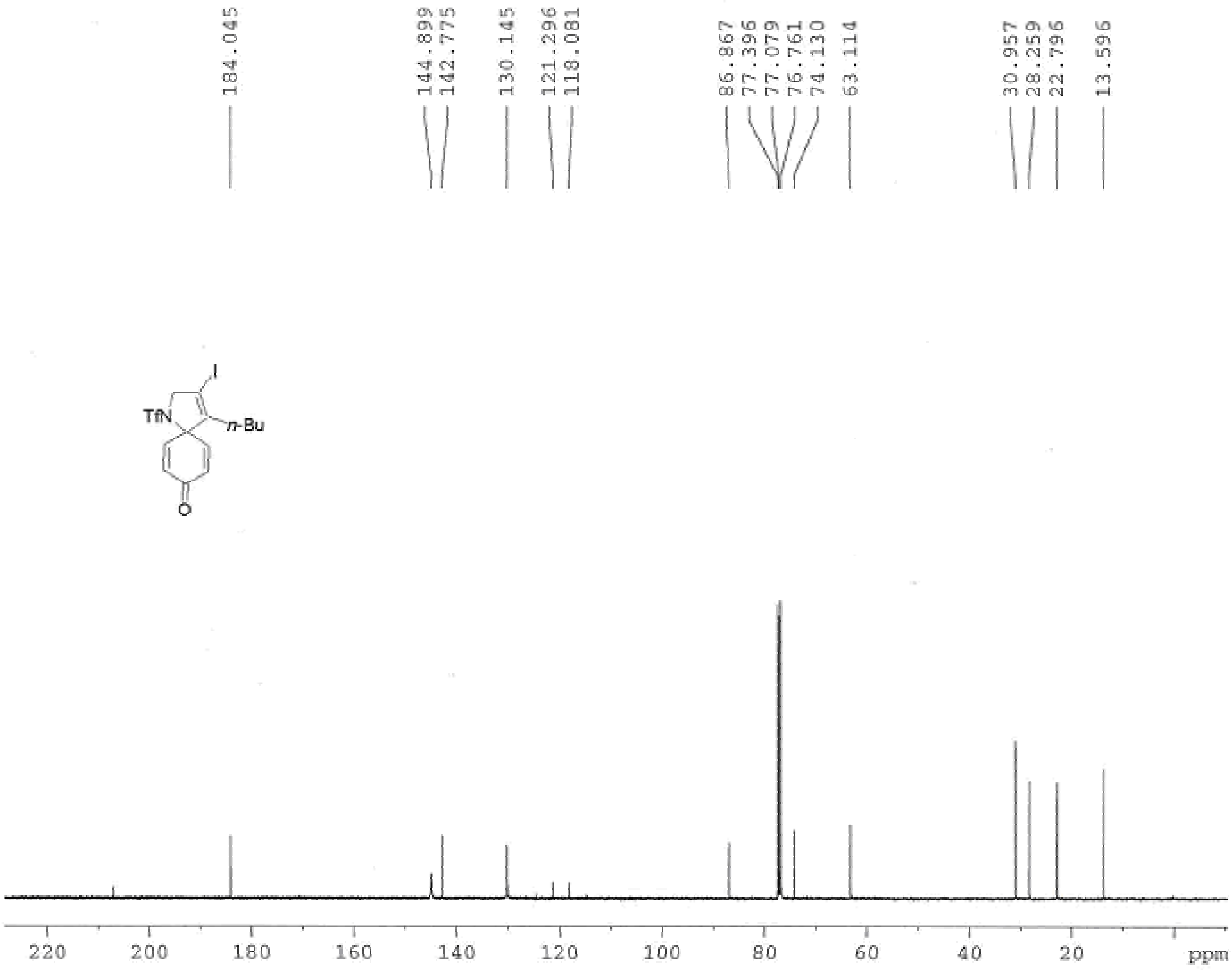
2.065
4.356
3.167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144.899
142.775
130.145
121.296
118.081
86.867
77.396
77.079
76.761
74.130
63.114
30.957
28.259
22.796
13.596
I
TfN
n-Bu
O
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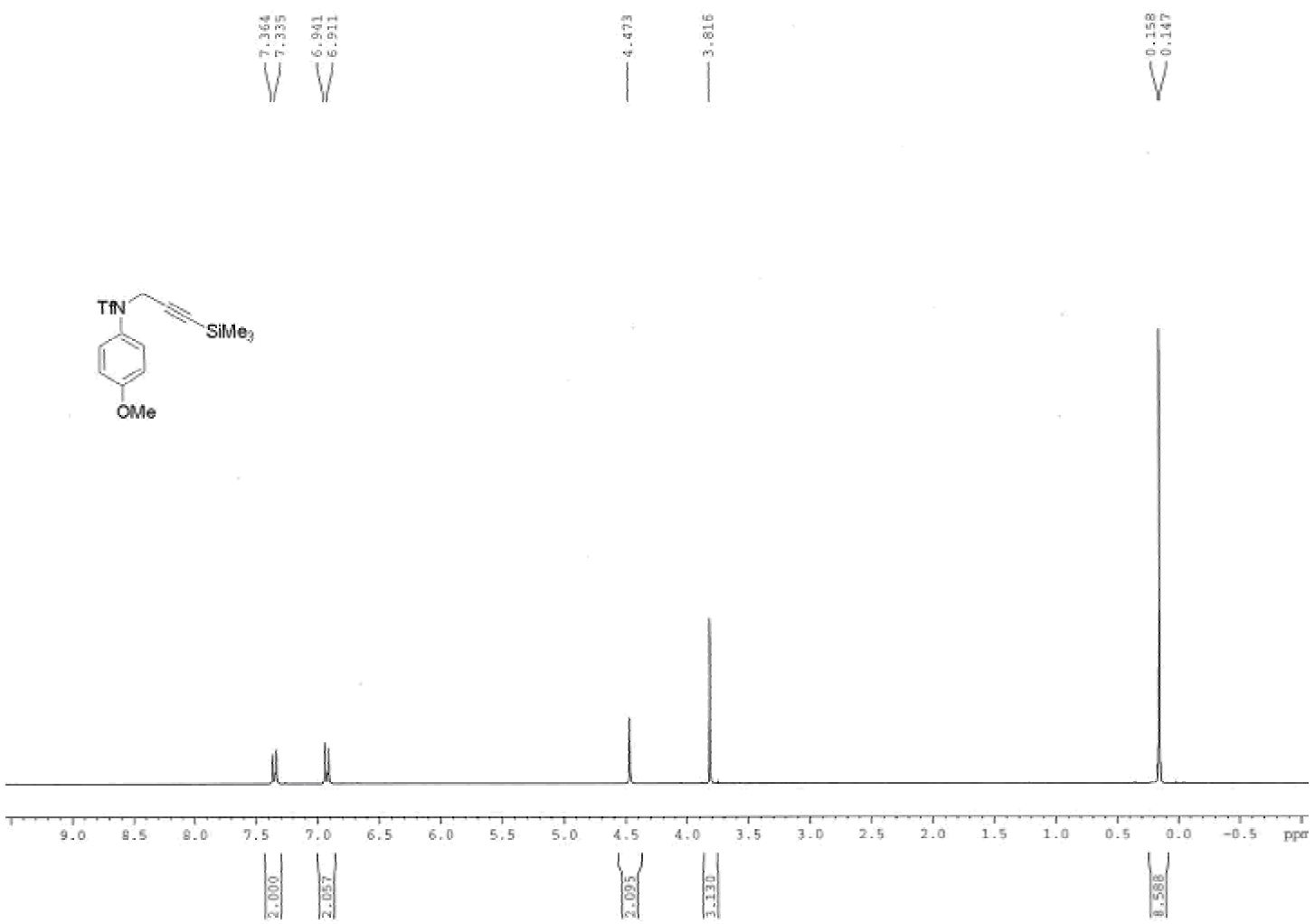
160
140
120
100
80
60
40
20
ppm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7.355
6.941
6.911
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3.816
0.158
0.147
TfN
SiMe3
OMe
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
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ppm
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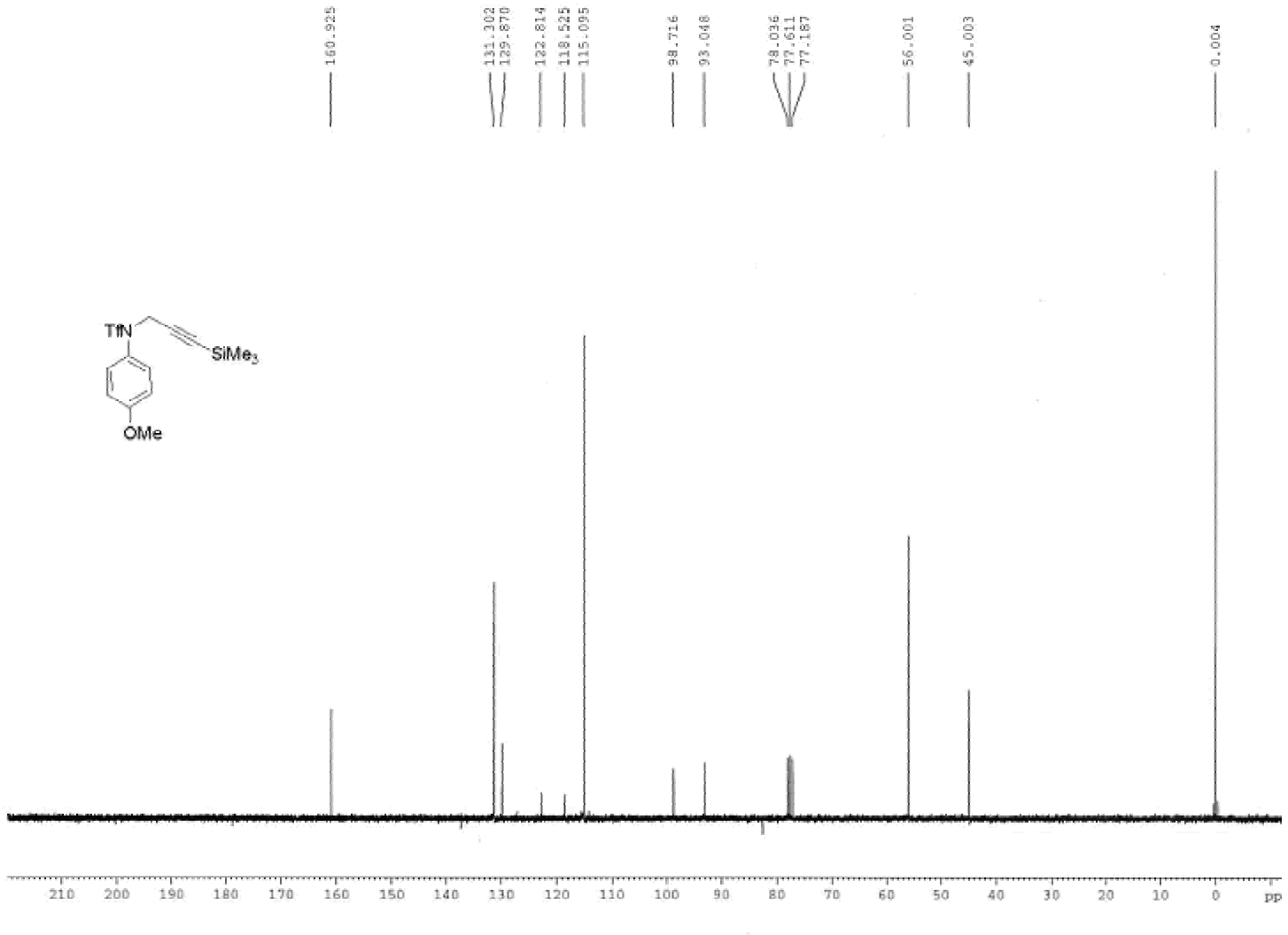
2.005
3.130
8.588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131.302
129.870
122.814
118.525
115.095
98.716
93.048
78.036
77.611
77.187
56.001
45.003
0.004
TfN
SiMe3
OMe
210
200
190
180
170
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140
130
120
110
100
90
80
70
60
50
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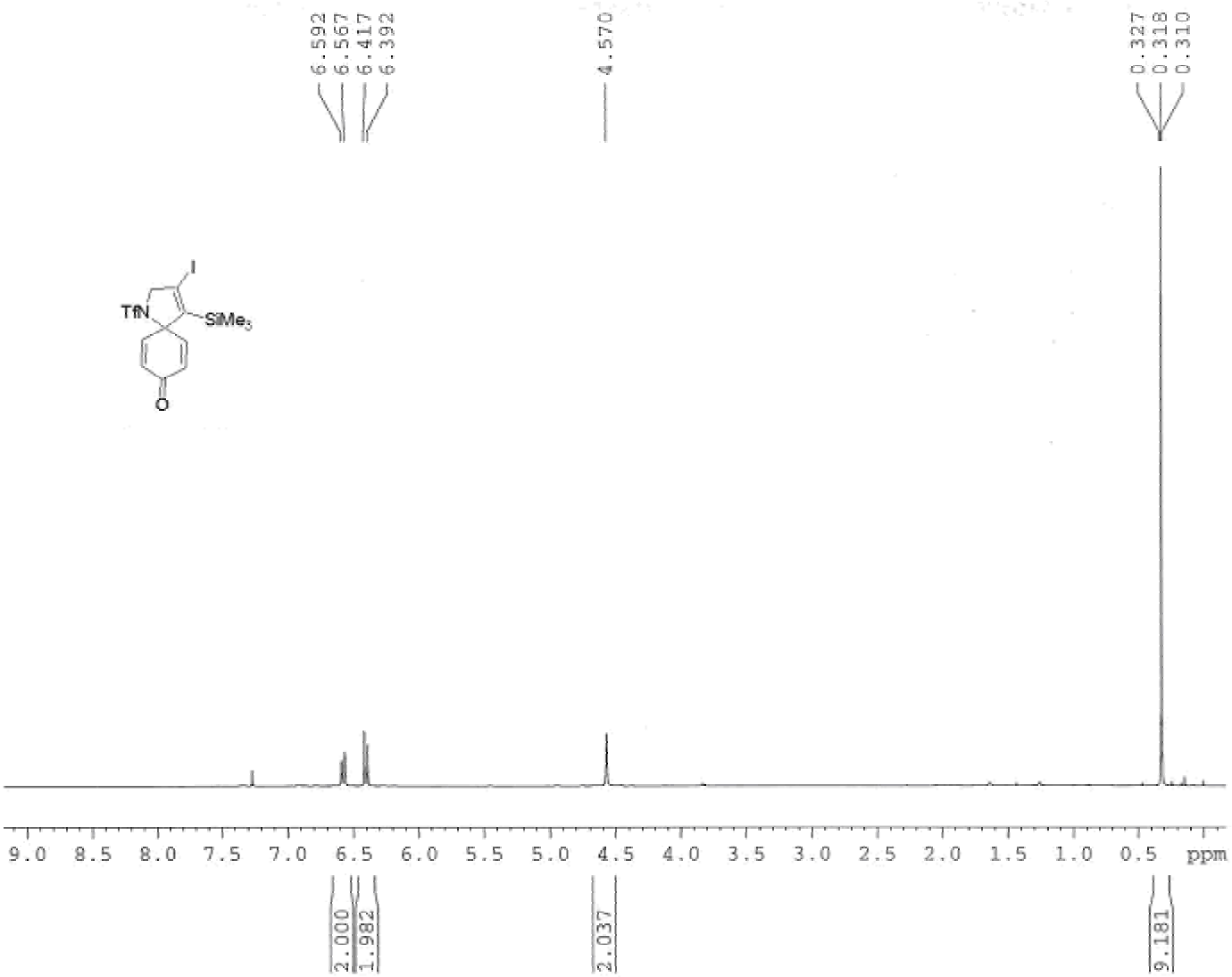
30
20
10
0
ppm


6.592
6.567
6.417
6.392
4.570
0.327
0.318
0.310
I
TfN
SiMe3
O
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
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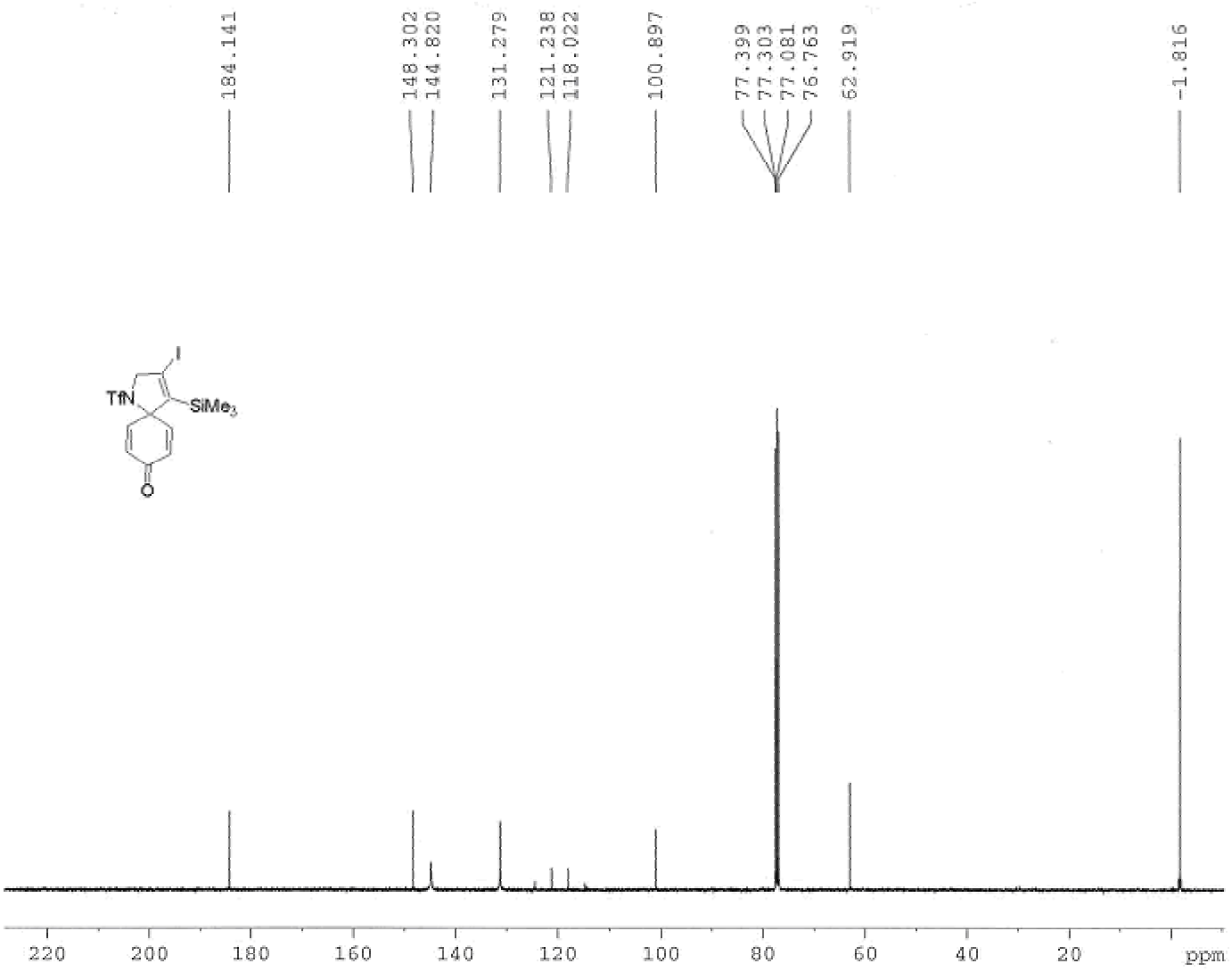
1.982
2.037
9.181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148.302
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77.399
77.303
77.081
76.763
62.919
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TfN
SiMe3
O
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200
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160
140
120
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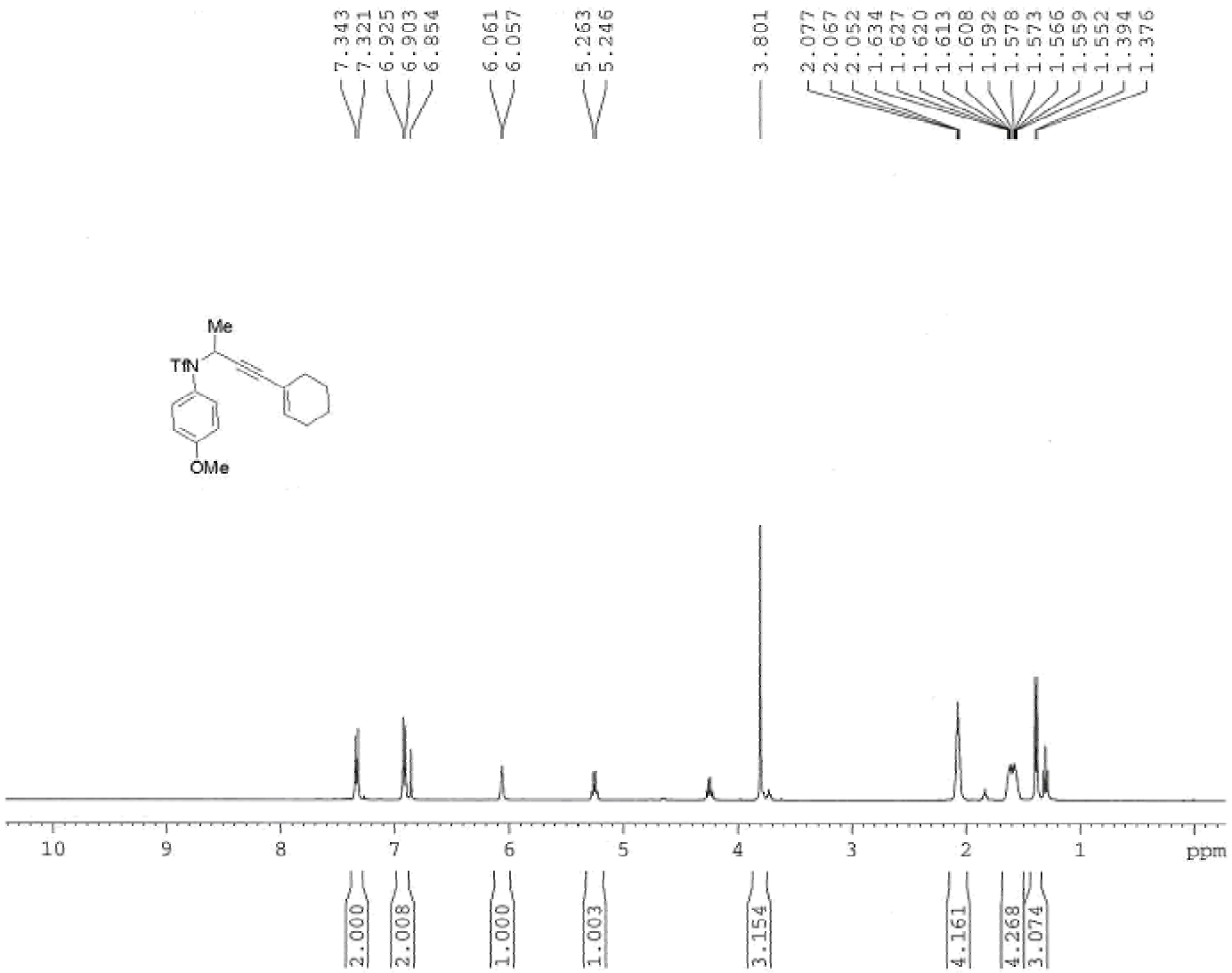
80
60
40
20
ppm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6.925
6.903
6.854
6.061
6.057
5.263
5.246
3.801
2.077
2.067
2.052
1.634
1.627
1.620
1.613
1.608
1.592
1.578
1.573
1.566
1.559
1.552
1.394
1.376
Me
TfN
OMe
10
9
8
7
6
5
4
3
2
1
ppm
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1.000
1.003
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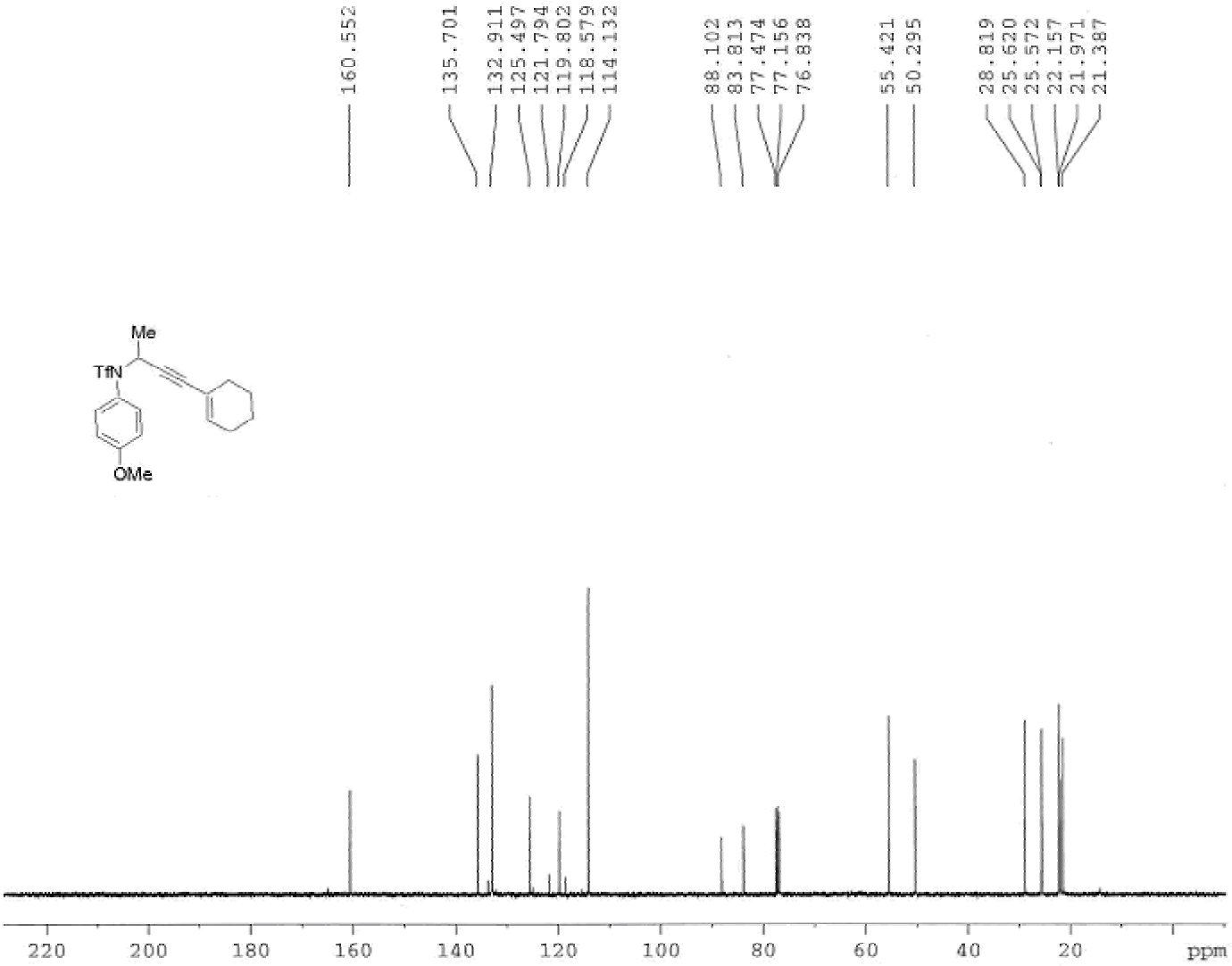
4.161
4.268
3.074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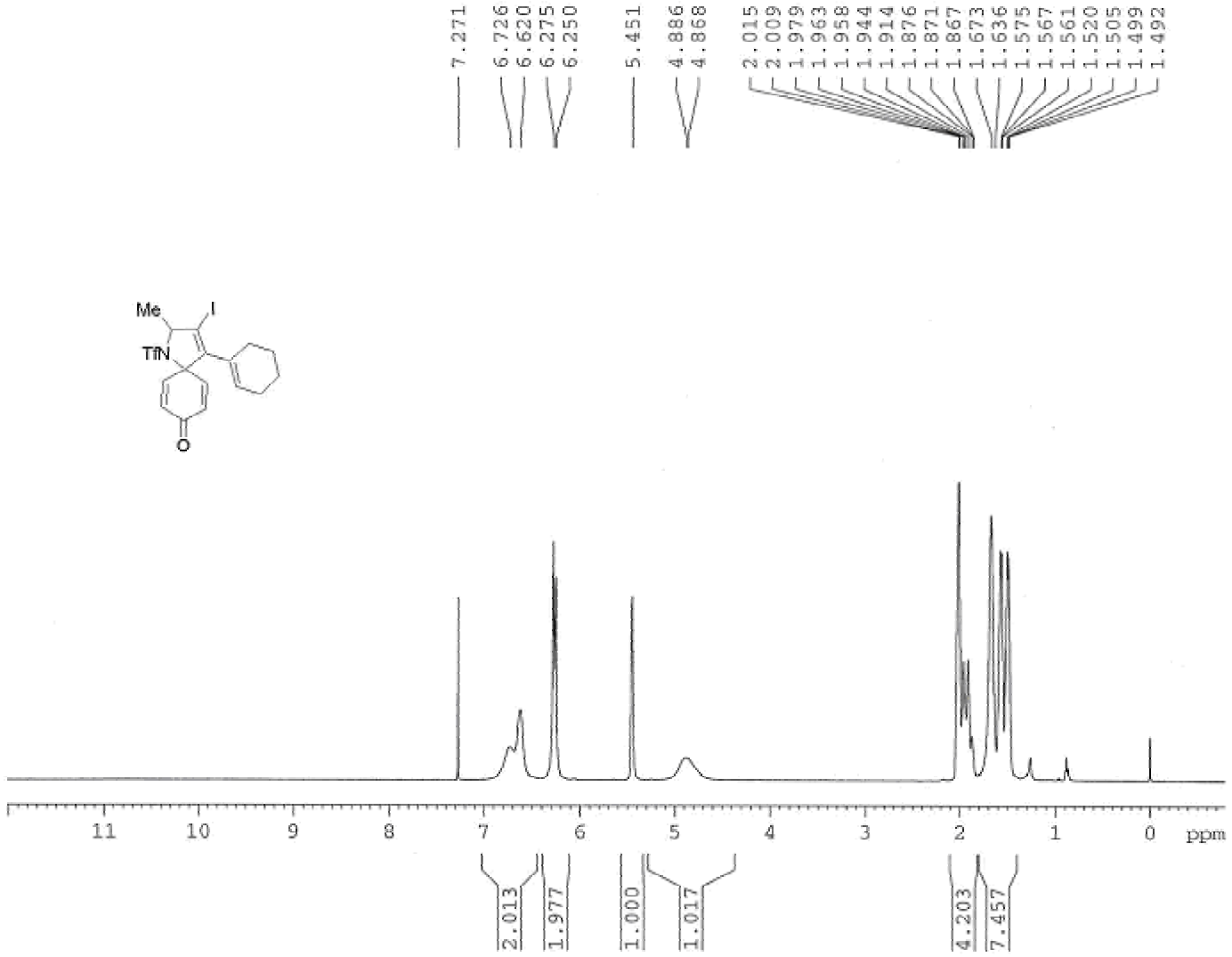
132.911
125.497
121.794
119.802
118.579
114.132
88.102
83.813
77.474
77.156
76.838
55.421
50.295
28.819
25.620
25.572
22.157
21.971
21.387
Me
TfN
OMe
220
200
180
160
140
120
100
80
60
40
20
ppm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6.726
6.620
6.275
6.250
5.451
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4.868
2.015
2.009
1.979
1.963
1.958
1.944
1.914
1.876
1.871
1.867
1.673
1.636
1.575
1.567
1.561
1.520
1.505
1.499
1.492
Me
I
TfN
O
11
10
9
8
7
6
5
4
3
2
1
0
ppm
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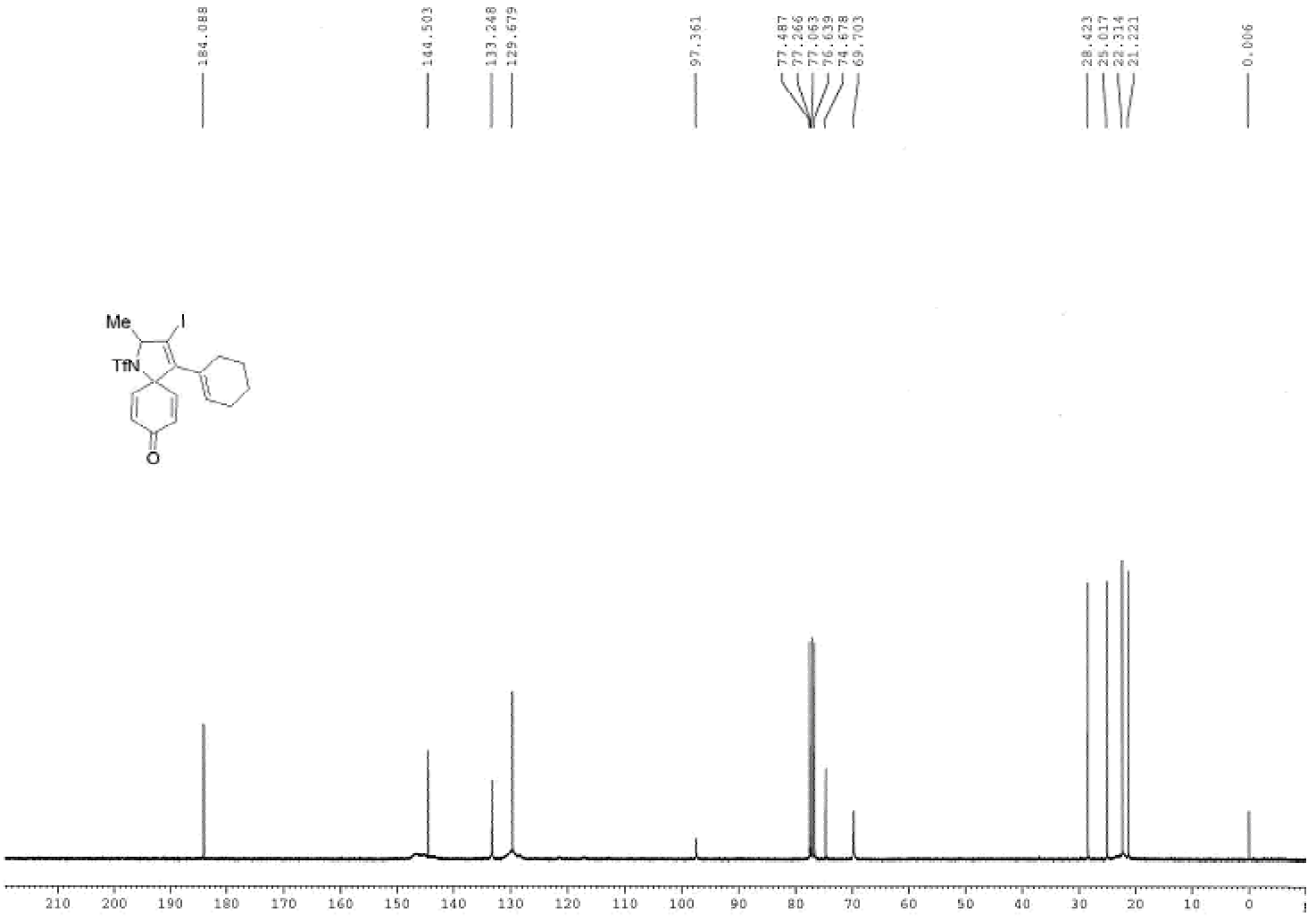
1.017
4.203
7.457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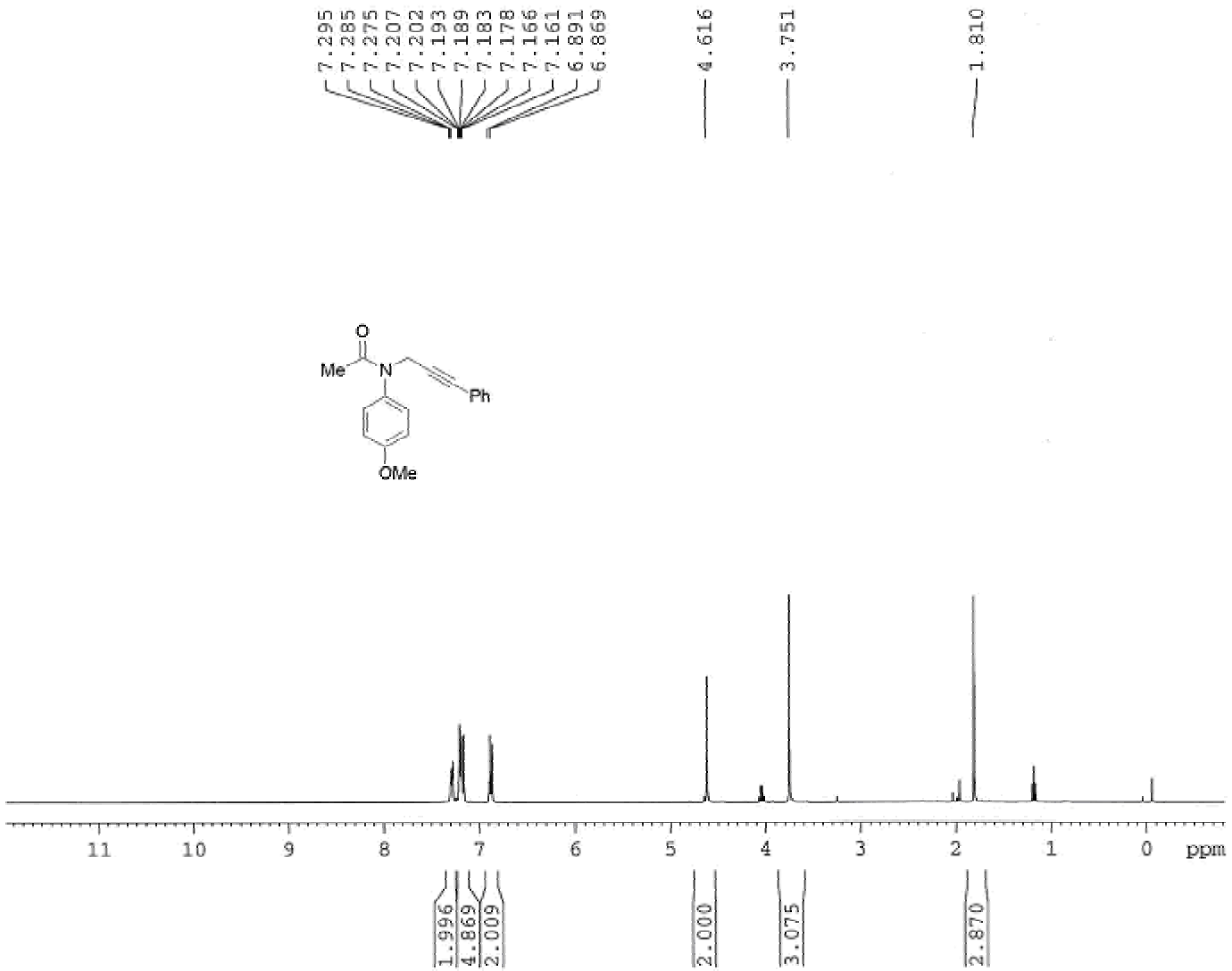
77.266
77.063
76.639
74.678
69.703
28.423
25.017
22.314
21.221
0.006
Me
I
TfN
O
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0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7.275
7.207
7.202
7.193
7.189
7.183
7.178
7.166
7.161
6.891
6.869
4.616
3.751
1.810
O
Me
N
Ph
OMe
11
10
9
8
7
6
5
4
3
2
1
0
ppm
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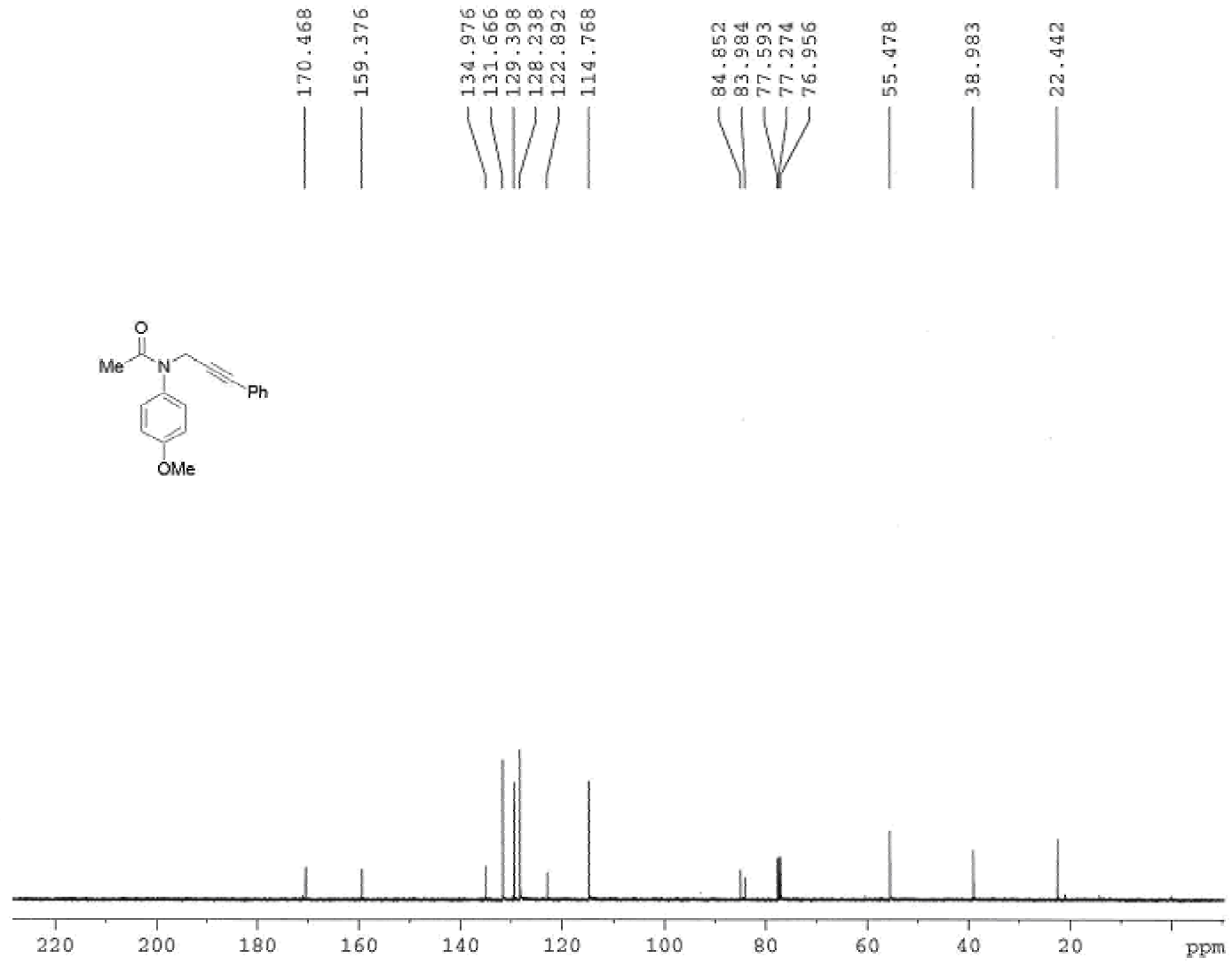
2.009
2.000
3.075
2.870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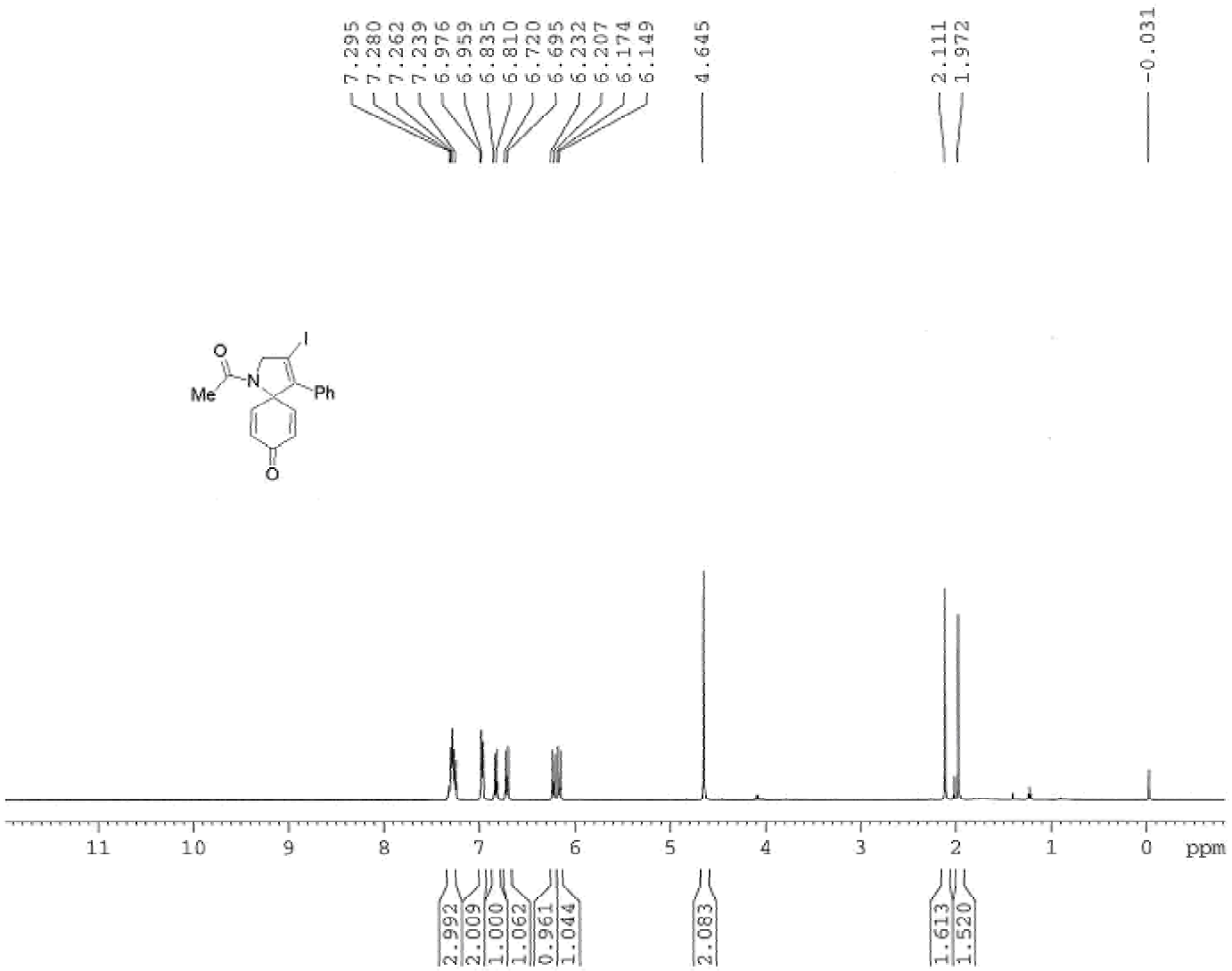
128.238
122.892
114.768
84.852
83.984
77.593
77.274
76.956
55.478
38.983
22.442
O
Me
N
Ph
OMe
220
200
180
160
140
120
100
80
60
40
20
ppm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7.262
7.239
6.976
6.959
6.835
6.810
6.720
6.695
6.232
6.207
6.174
6.149
4.645
2.111
1.972
-0.031
O
I
Me
N
Ph
O
11
10
9
8
7
6
5
4
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ppm
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1.000
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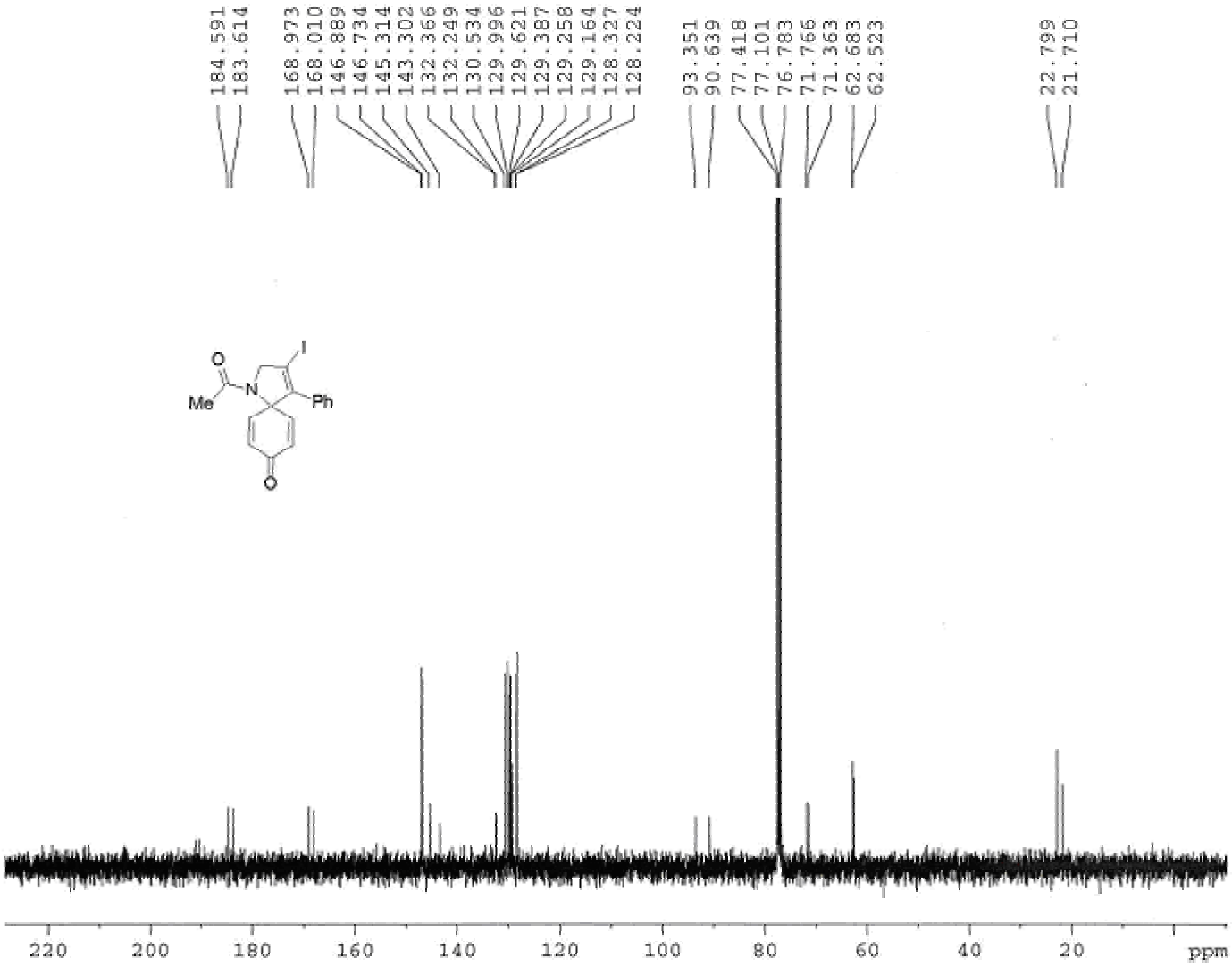
1.613
1.520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145.314
143.302
132.366
132.249
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129.996
129.621
129.387
129.258
129.164
128.327
128.224
93.351
90.639
77.418
77.101
76.783
71.766
71.363
62.683
62.523
22.799
21.710
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N
Me
I
Ph
O
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200
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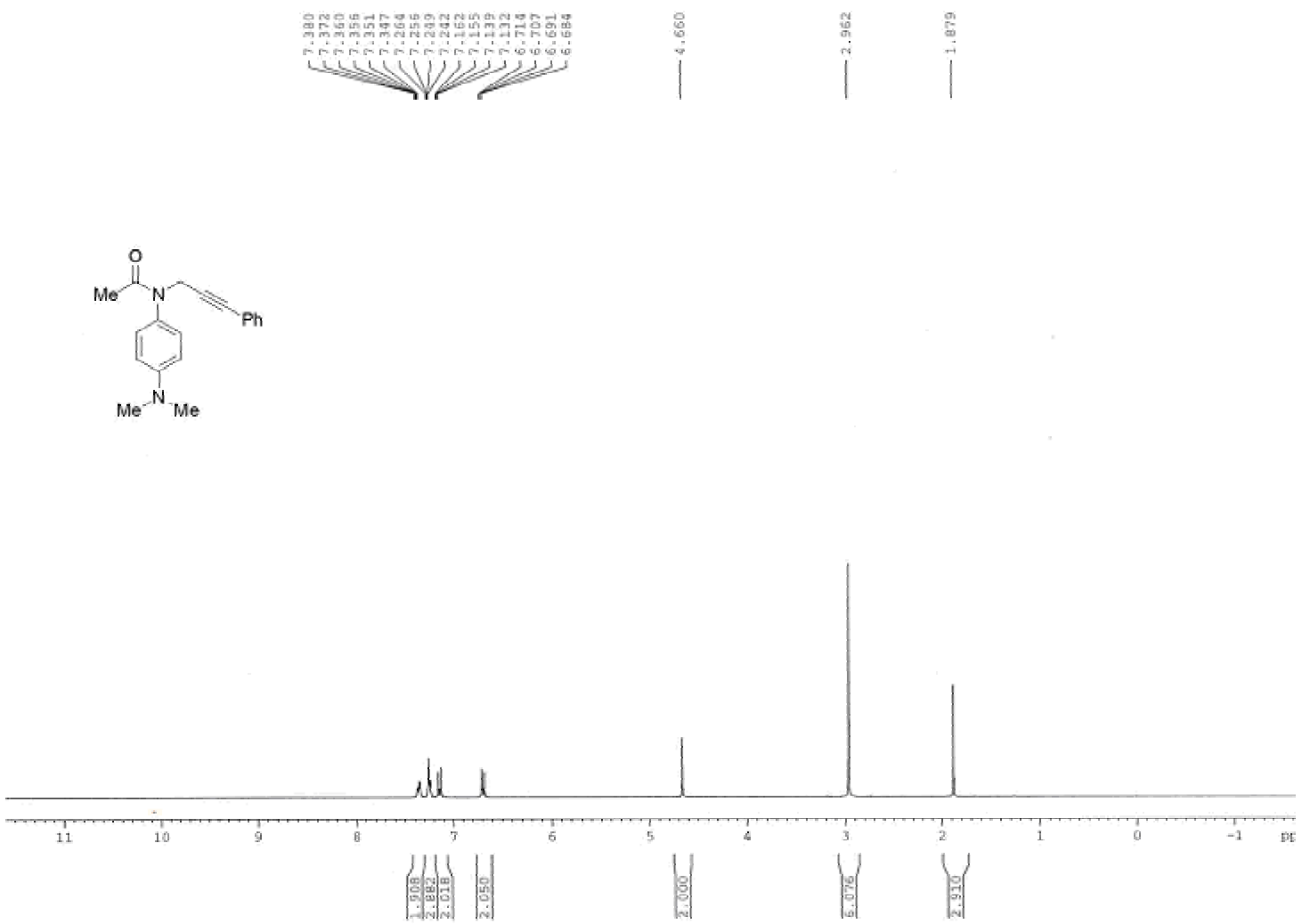
140
120
100
80
60
40
20
ppm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7.360
7.356
7.351
7.347
7.264
7.256
7.249
7.242
7.162
7.155
7.139
7.132
6.714
6.707
6.691
6.684
4.660
2.962
1.879
O
Me
N
Ph
Me
N
Me
11
10
9
8
7
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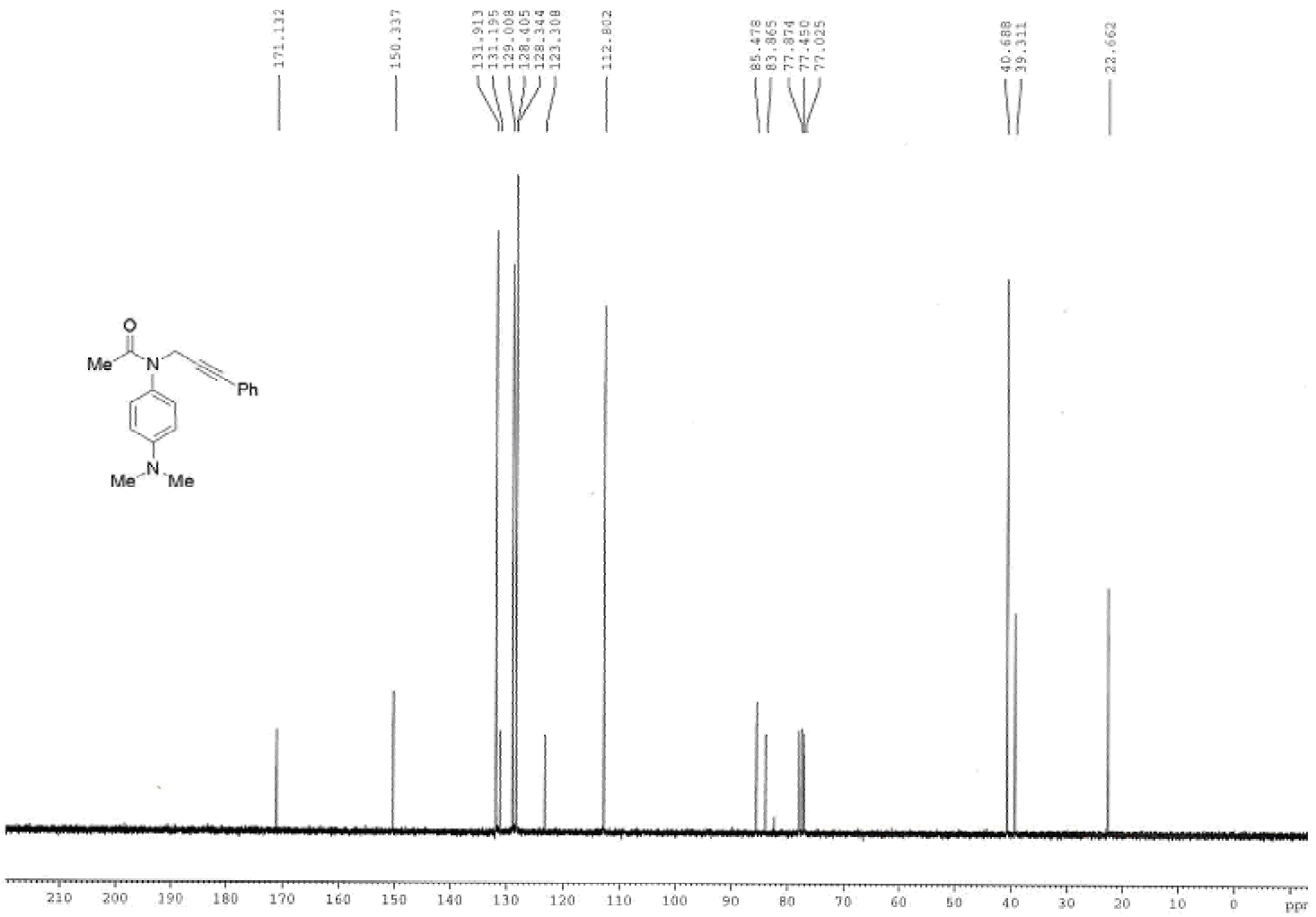
2.910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128.344
123.308
112.802
85.478
83.865
77.874
77.450
77.025
40.688
39.311
22.662
Me
N
Ph
Me
N
Me
210
200
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50
40
30
20
10
0
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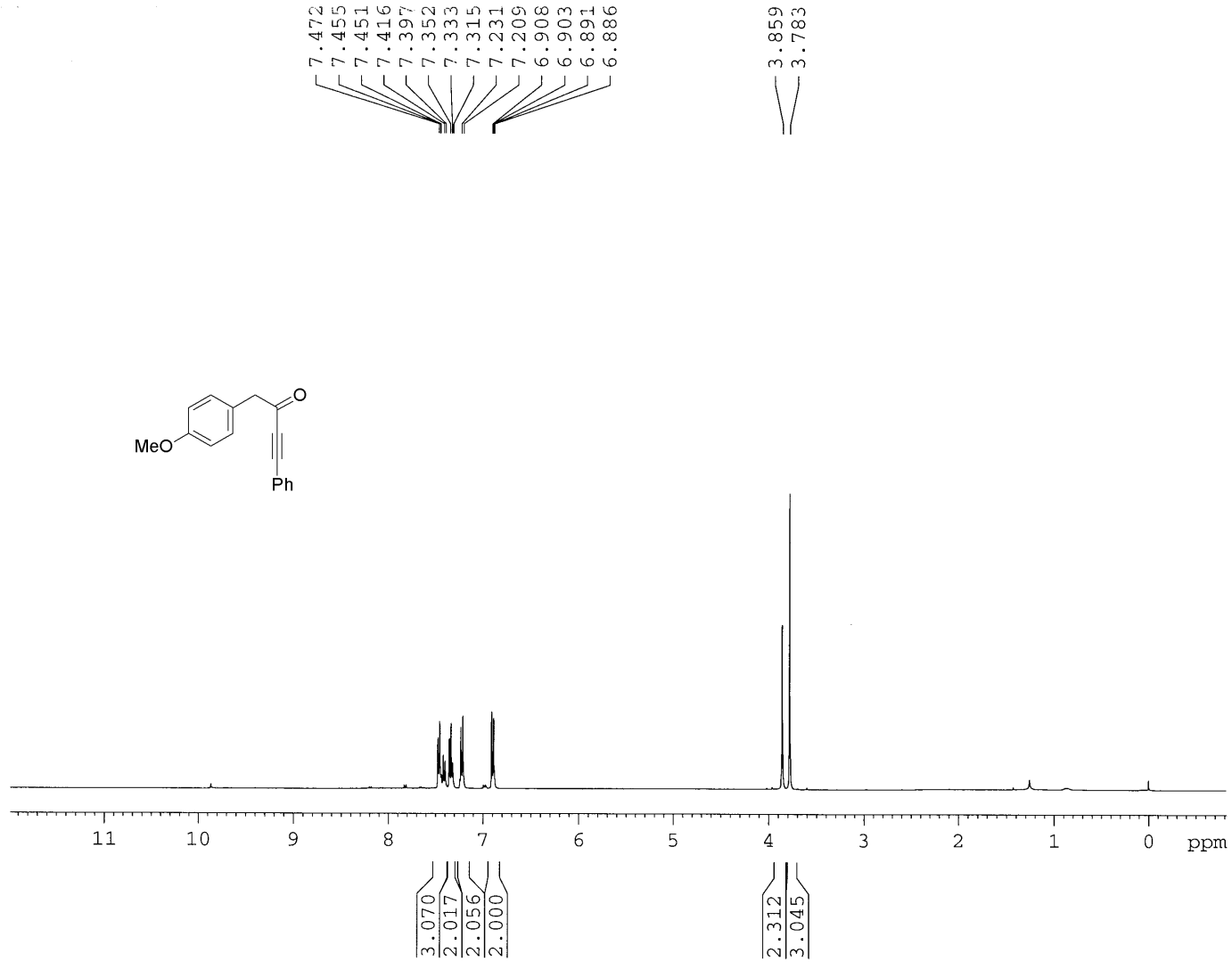
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7.315
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7.209
6.908
6.903
6.891
6.886
3.859
3.783
MeO
O
Ph
11
10
9
8
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6
5
4
3
2
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2.017
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2.000
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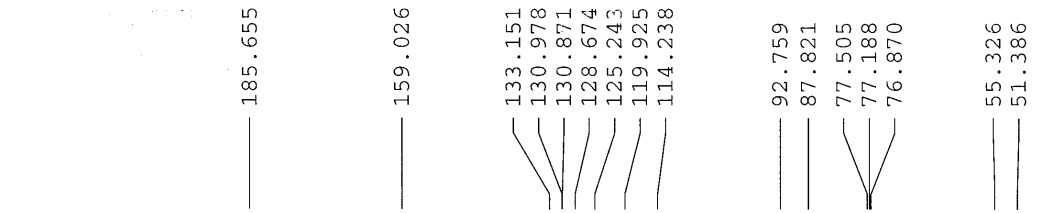
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77.505
77.188
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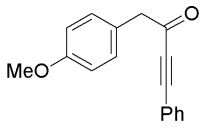
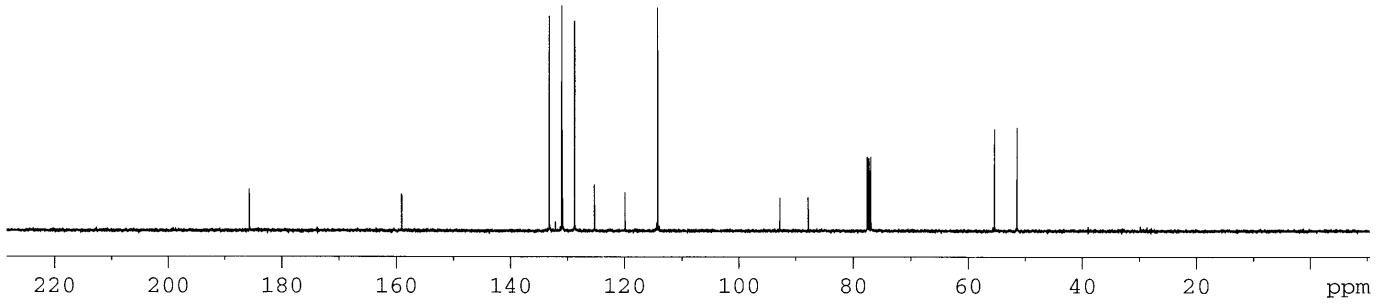
55.326
51.386


O
MeO
Ph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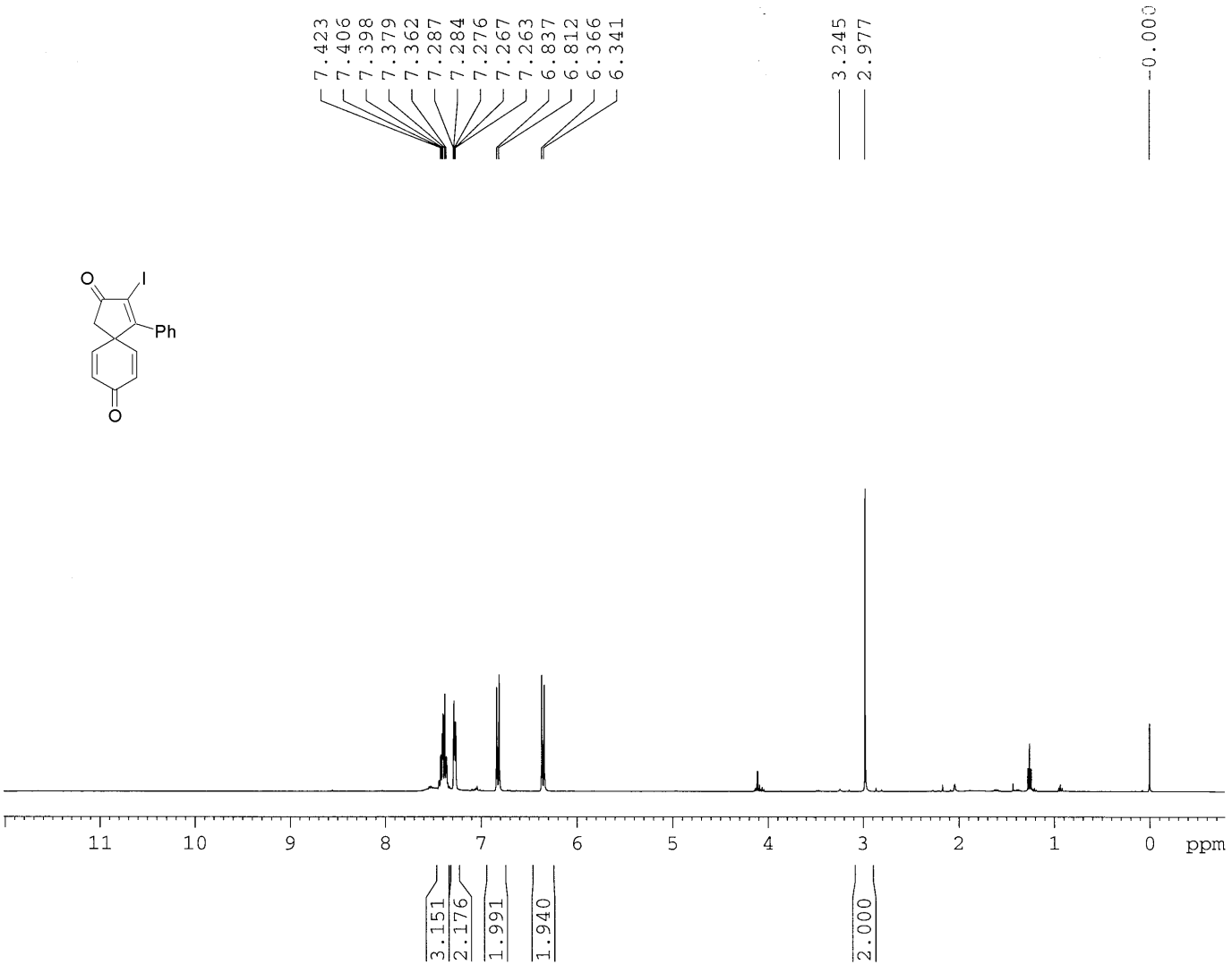
200
180
160
140
120
100
80
60
40
20
ppm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7.284
7.276
7.267
7.263
6.837
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6.341
3.245
2.977
-0.000
O
I
Ph
O
11
10
9
8
7
6
5
4
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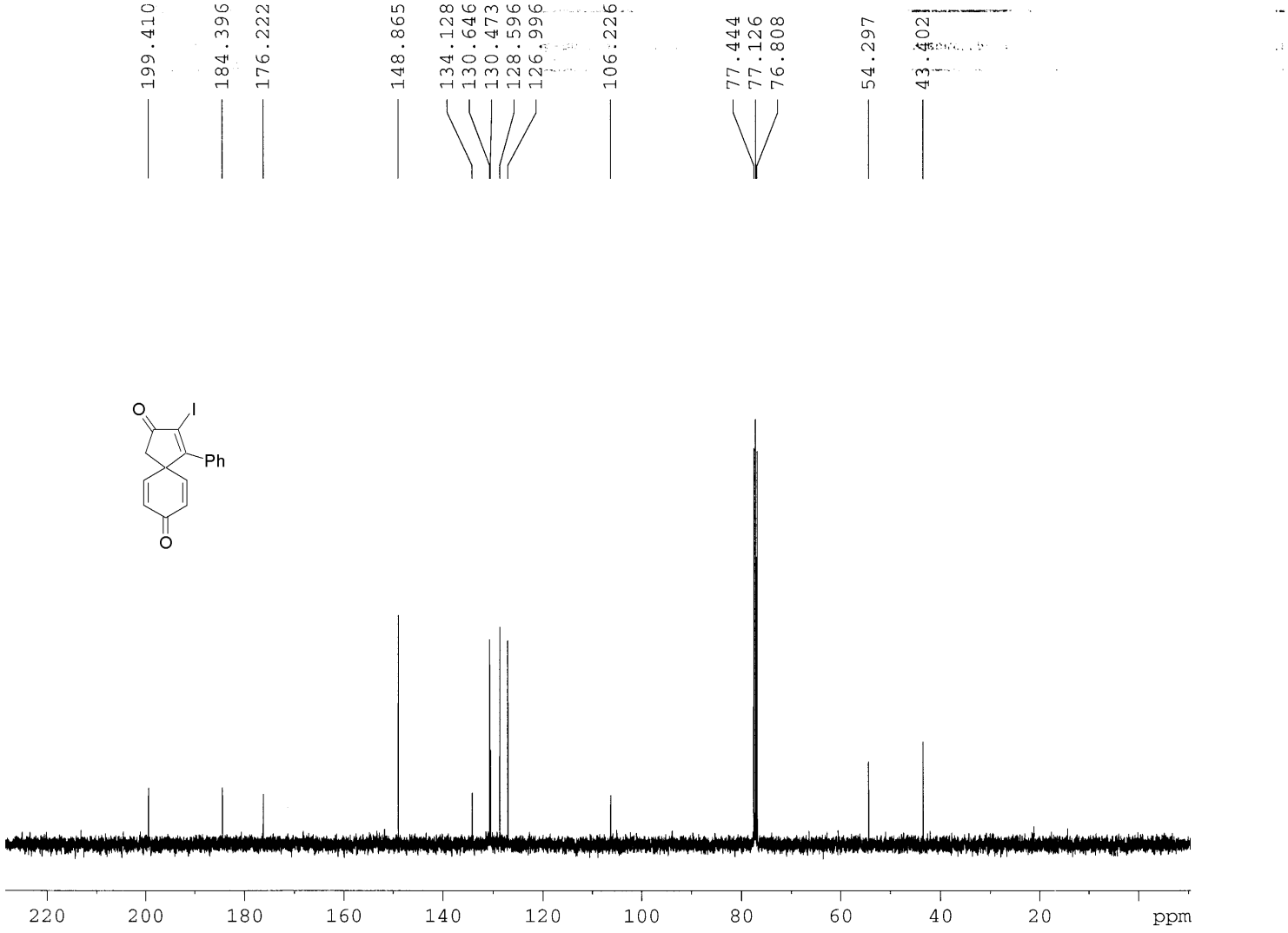
1.940
2.000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130.473
128.596
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77.444
77.126
76.808
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43.402
O
I
Ph
O
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140
120
100
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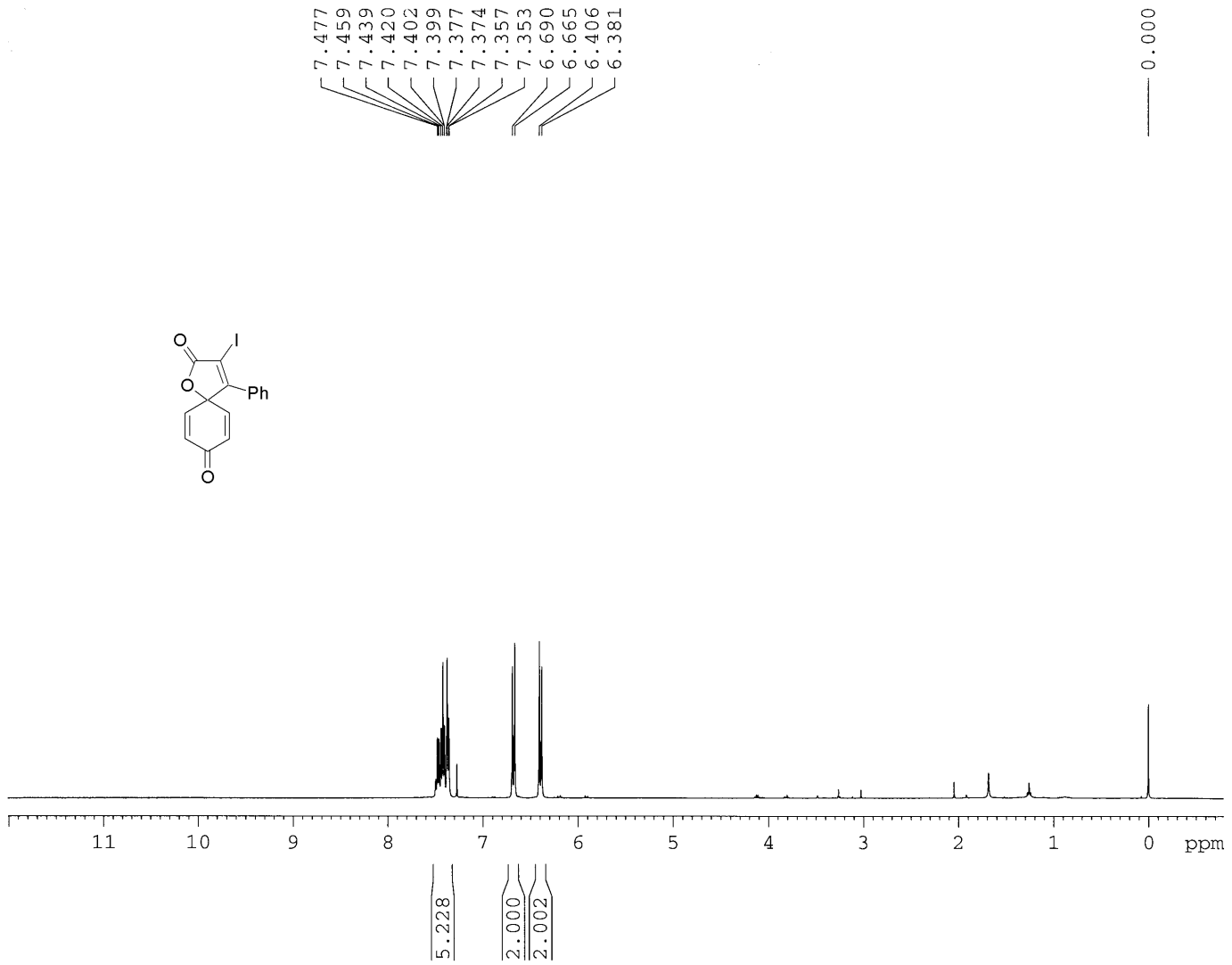
60
40
20
ppm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7.353
6.690
6.665
6.406
6.381
0.000
O
I
O
Ph
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10
9
8
7
6
5
4
3
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1
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ppm
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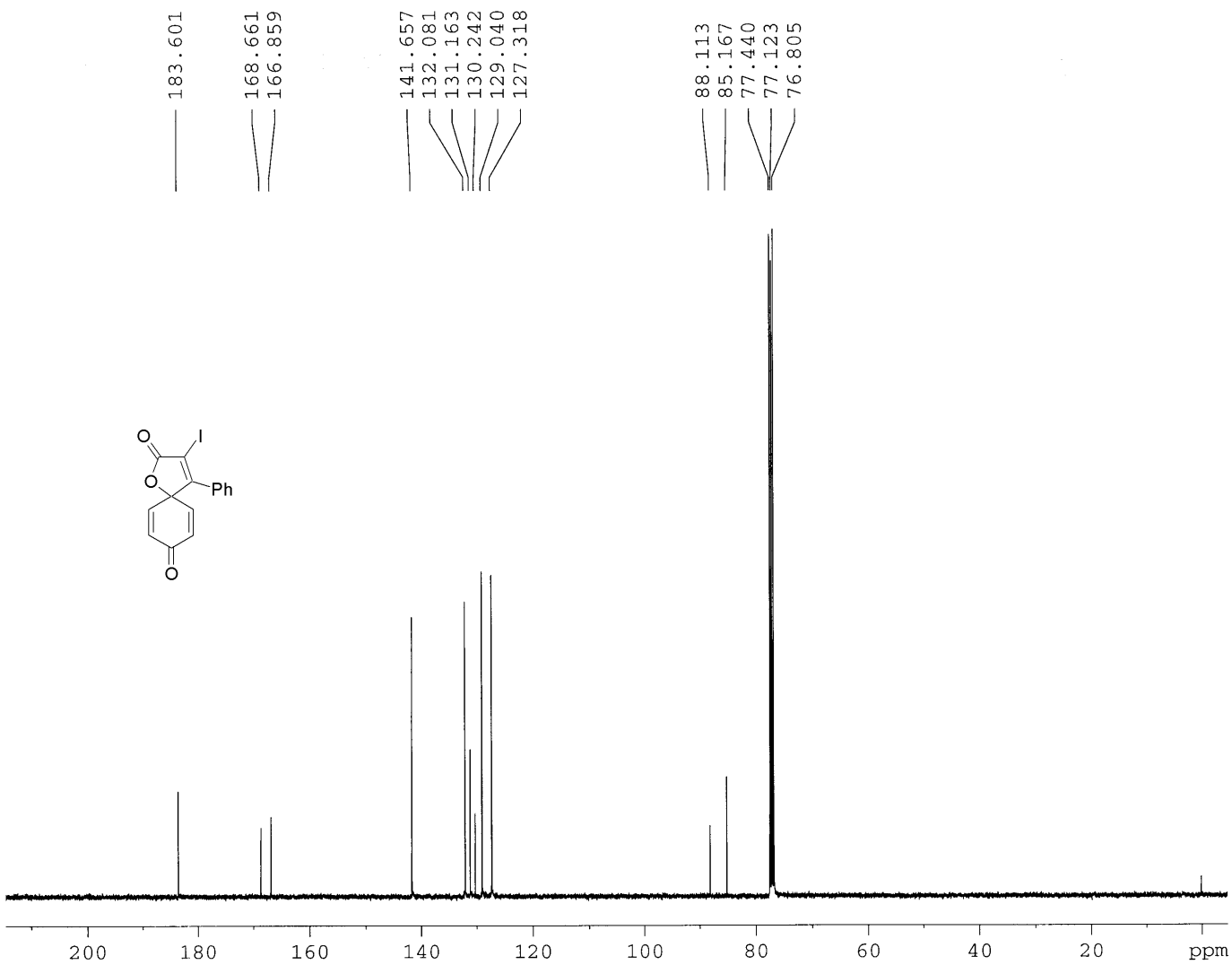
2.000
2.002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131.163
130.242
129.040
127.318
88.113
85.167
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O
I
O
Ph
O
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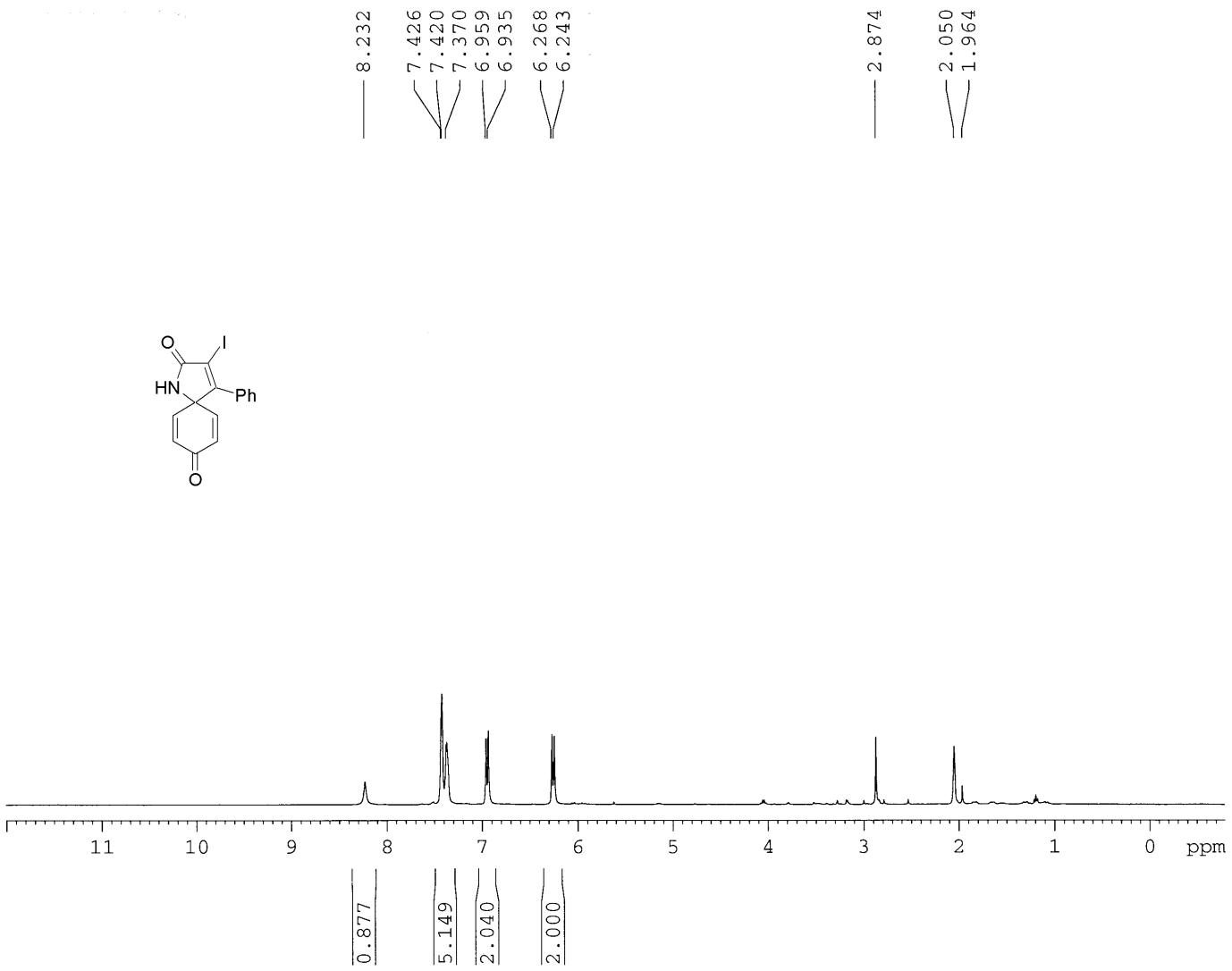
140
120
100
80
60
40
20
ppm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6.935
6.268
6.243
2.874
2.050
1.964
O
I
HN
Ph
O
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10
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7
6
5
4
3
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0
ppm
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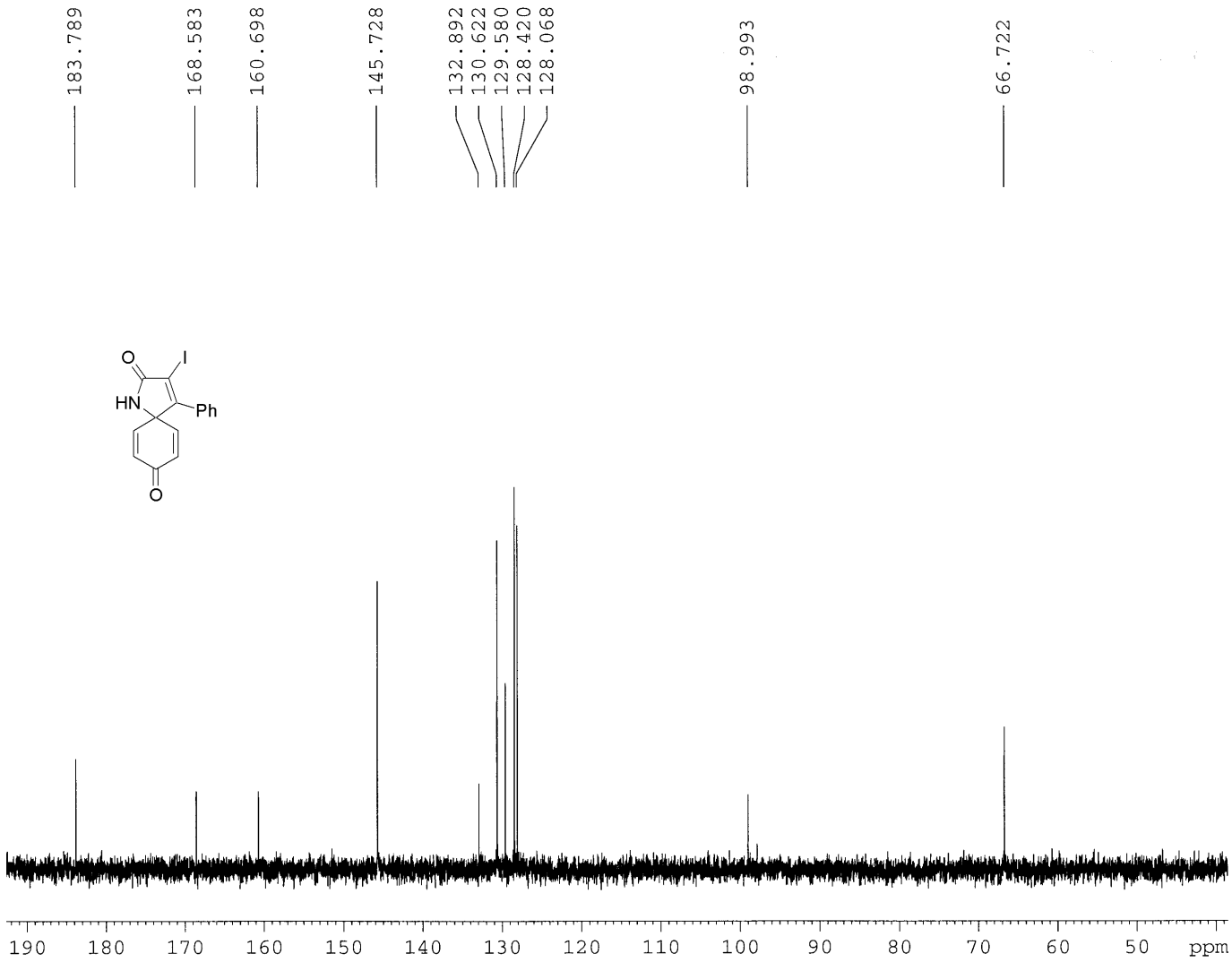
2.000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128.420
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110
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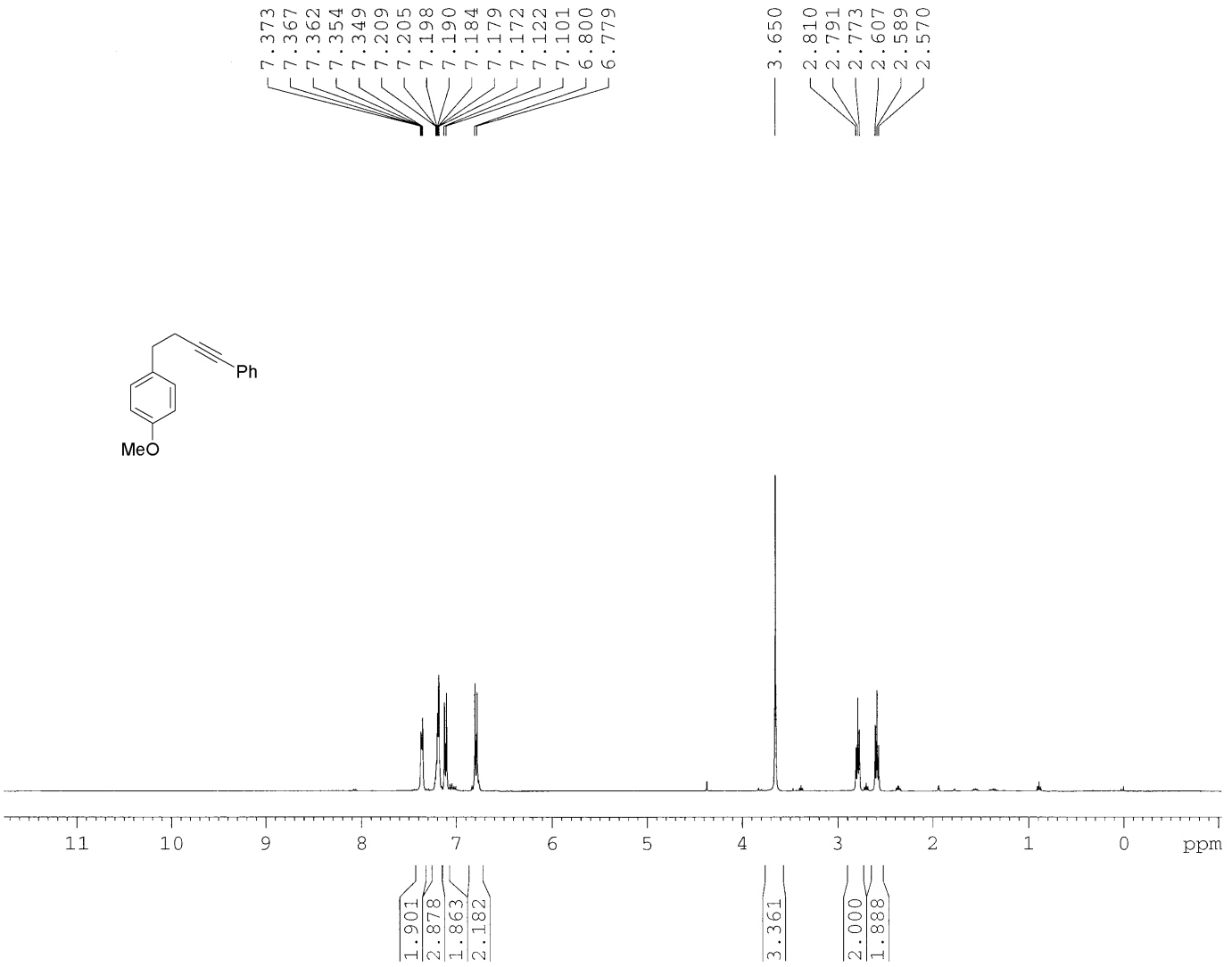
60
50
ppm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7.198
7.190
7.184
7.179
7.172
7.122
7.101
6.800
6.779
3.650
2.810
2.791
2.773
2.607
2.589
2.570
Ph
MeO
11
10
9
8
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4
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1
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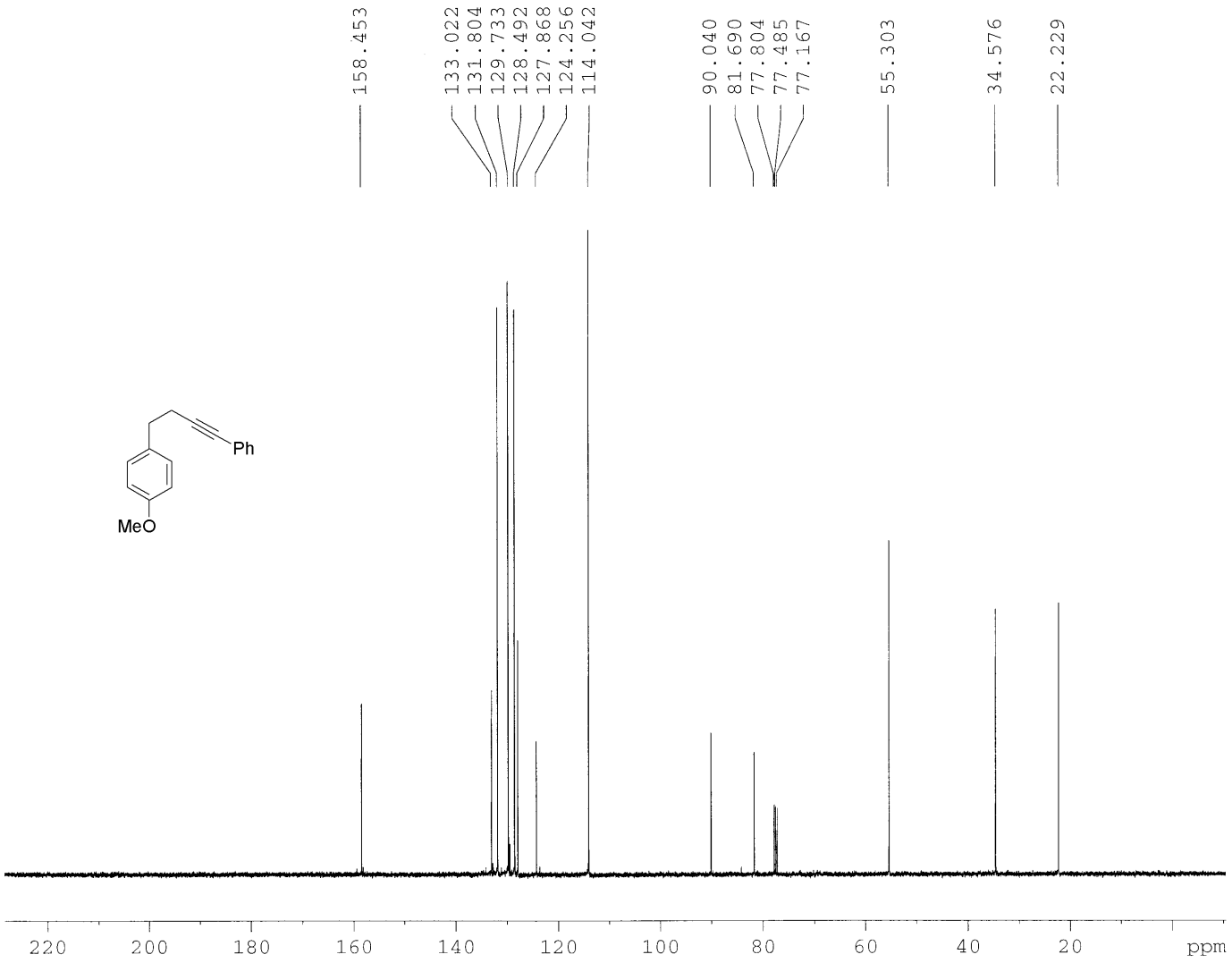
2.000
1.888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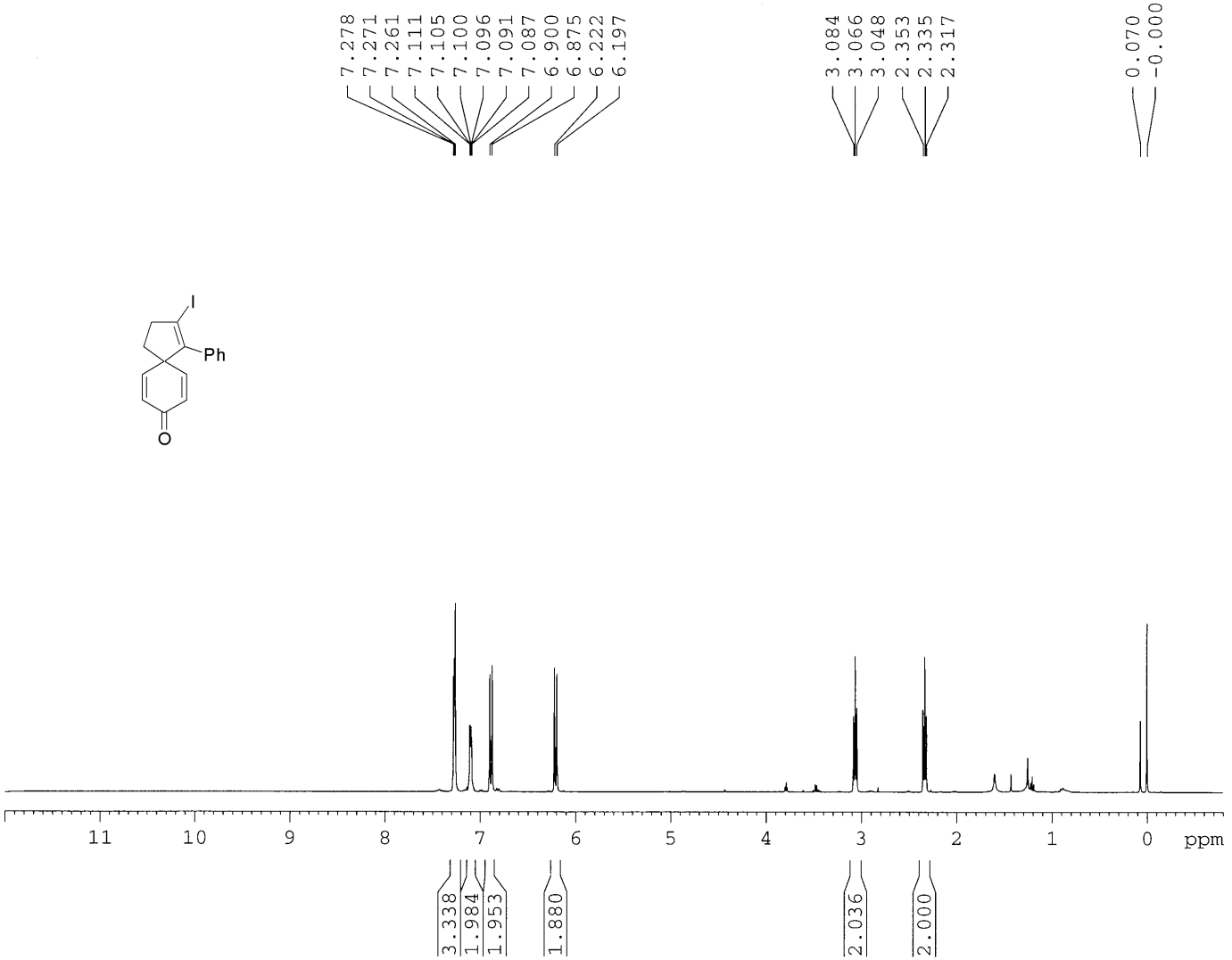
129.733
128.492
127.868
124.256
114.042
90.040
81.690
77.804
77.485
77.167
55.303
34.576
22.229
Ph
MeO
220
200
180
160
140
120
100
80
60
40
20
ppm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7.100
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7.091
7.087
6.900
6.875
6.222
6.197
3.084
3.066
3.048
2.353
2.335
2.317
0.070
-0.000
I
Ph
O
11
10
9
8
7
6
5
4
3
2
1
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ppm
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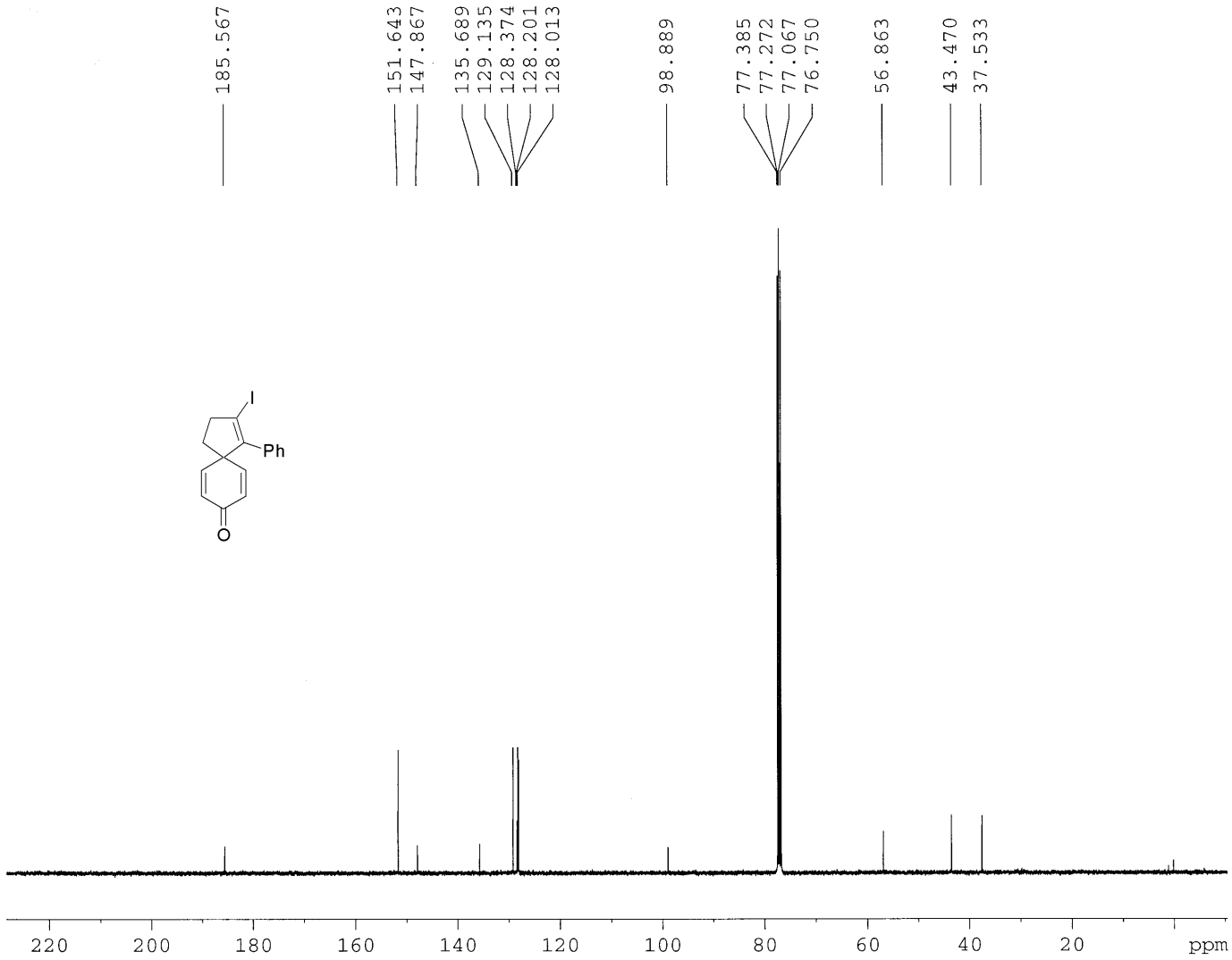
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Ph
O
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20
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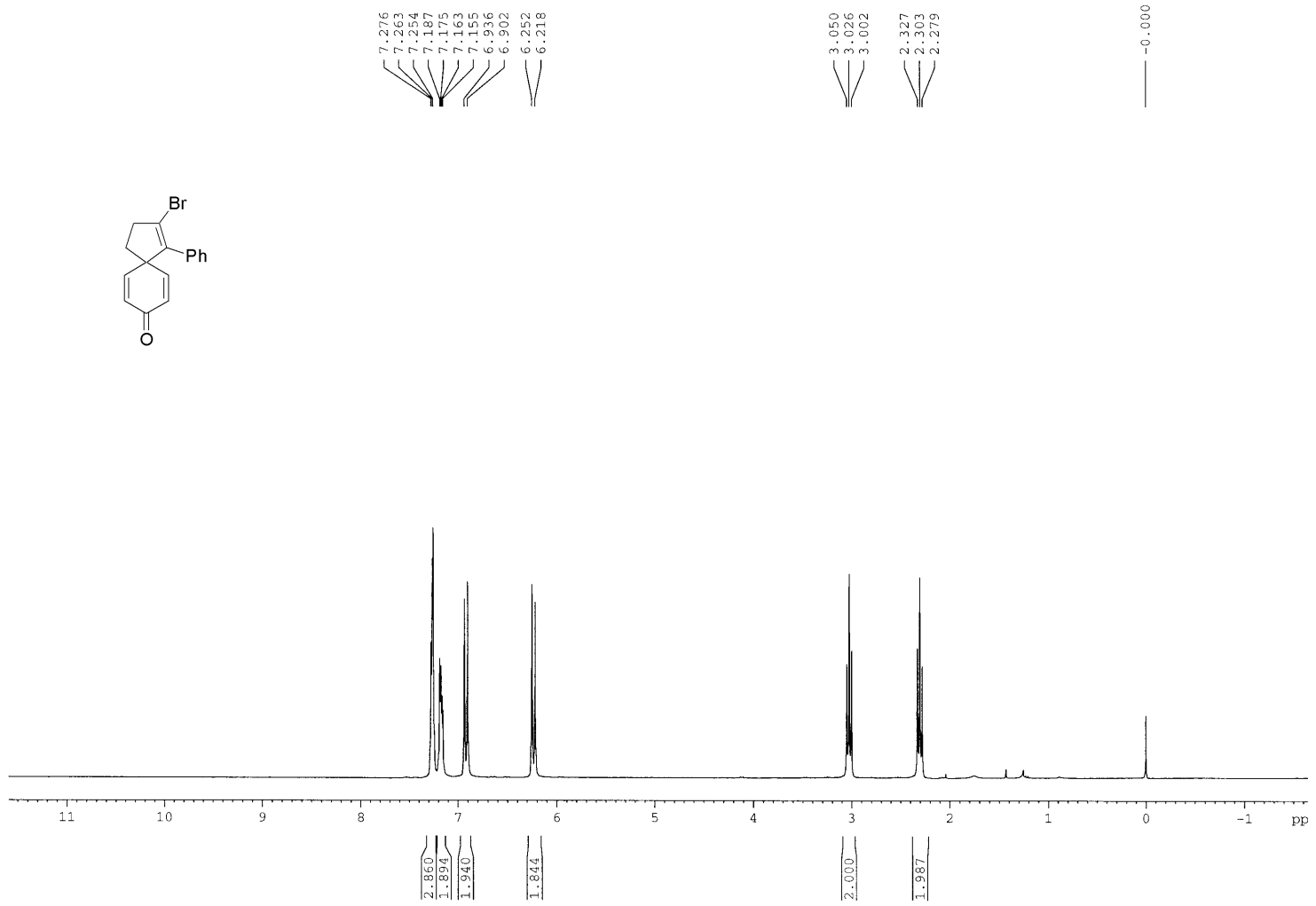
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3.026
3.002
2.327
2.303
2.279
-0.000
Br
Ph
O
11
10
9
8
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1
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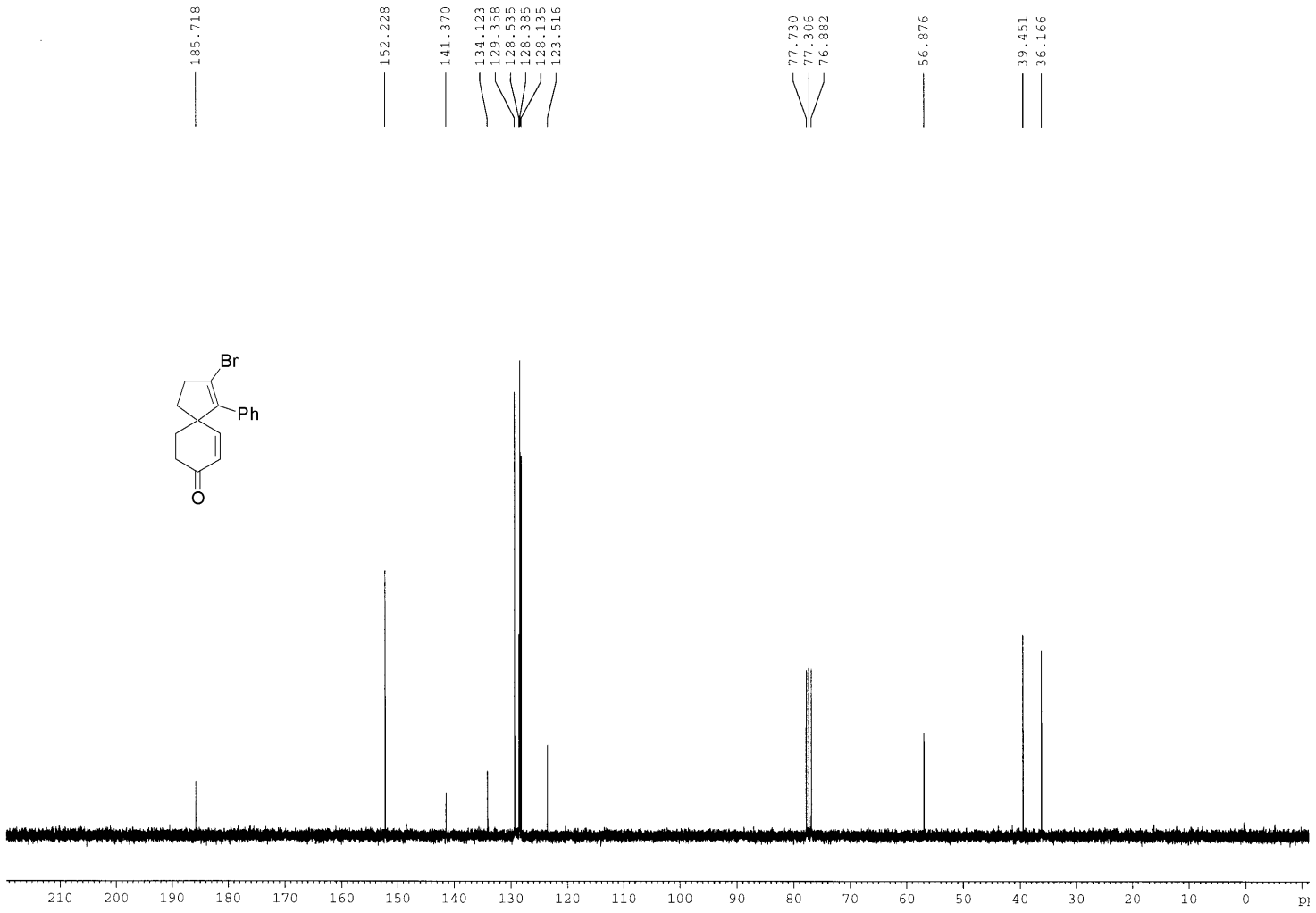
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76.882
56.876
39.451
36.166
Br
Ph
O
210
200
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10
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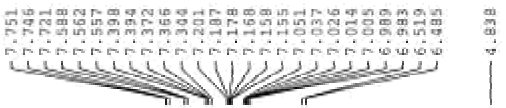
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7.562
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7.366
7.360
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7.168
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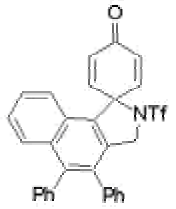
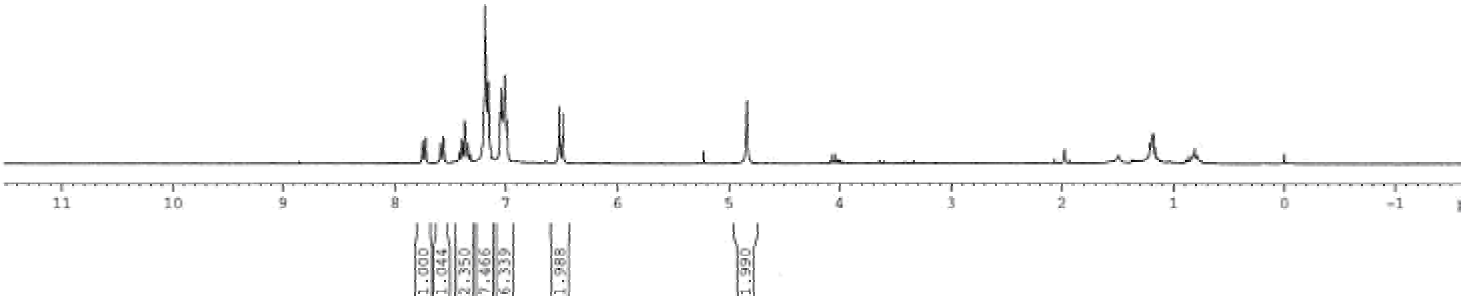

O
NTf
Ph
Ph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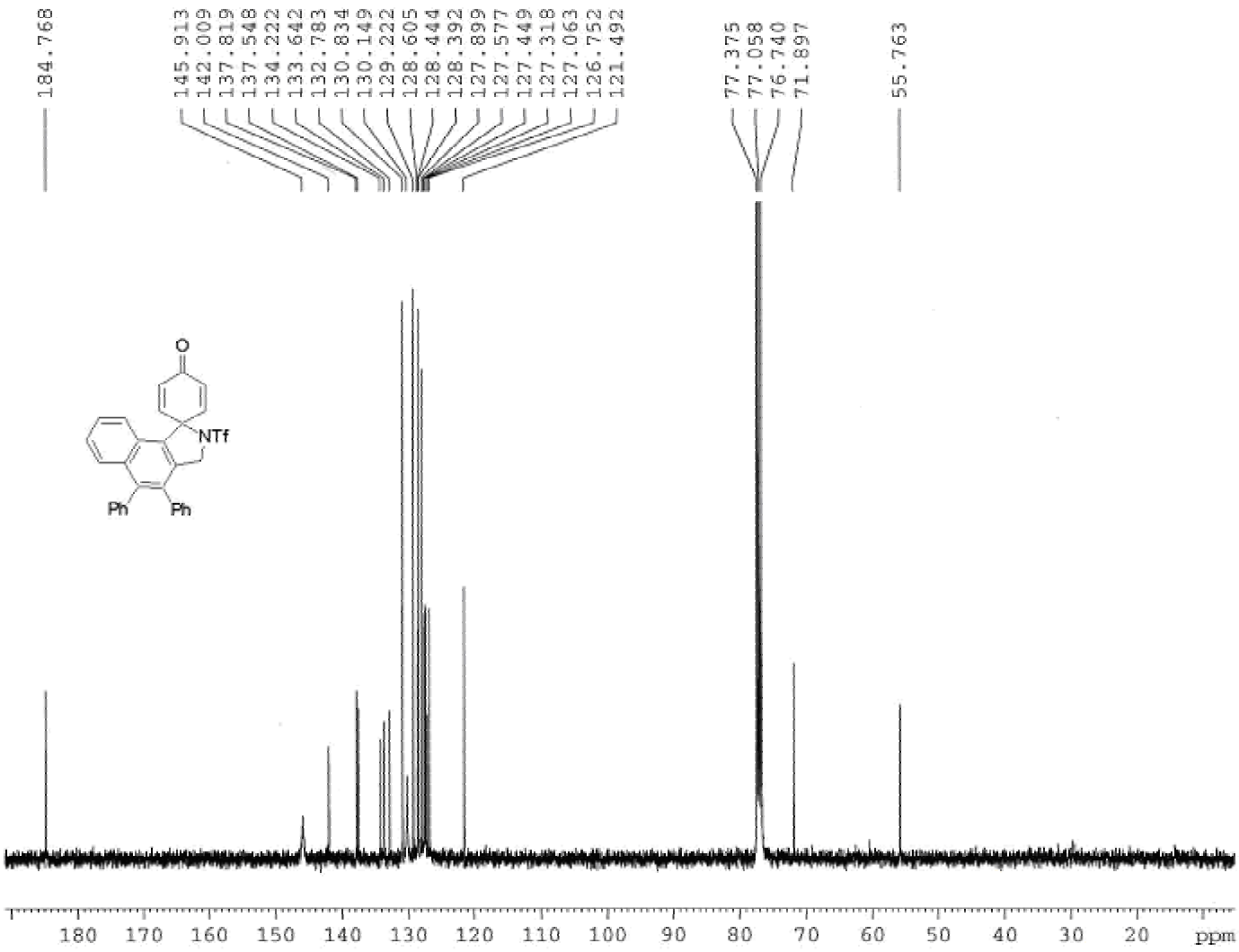
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O
NTf
Ph
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ppm