ELECTRONIC SUPPLEMENTARY INFORMATION

Silver versus gold-catalyzed sequential oxidative cyclizations of unprotected 2-alkynylanilines with oxone

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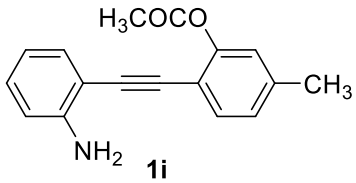
1. **General Informations**

^{1}H-NMR spectra were recorded at 400 MHz on Bruker instrument. Chemical shifts (in ppm) were referenced to tetramethylsilane (δ = 0 ppm) in $CDCl_3$ or in acetone-d_6 as an internal standard. ^{13}C-NMR spectra were recorded at 100.6 MHz and were calibrated with $CDCl_3$ (δ = 77.00 ppm) or acetone-d_6 (δ = 30.50 ppm). HRMS-ESI data were performed at the University P. et M. Curie and Università dell'Aquila on a TOF mass spectrometer. Unless otherwise stated, all starting materials, catalysts, and solvents were commercially available and were used as purchased. Reaction products were purified by flash chromatography on silica gel by elution with *n*-hexane/EtOAc mixtures. The products **1a,**[1] **1b**,[1] **1c**,[1] **1d,**[2] **1e,**[3] **1f**,[4] **1g**,[5] **1h,**[6] **1j,**[1] **1k,**[7] **1l**,[2] **1m**,[8] **1n**,[9] and **4a-c**[10] are known products and were identified by comparison of their physical and spectral data reported in the cited references.

2. Experimental procedures and characterization of products.

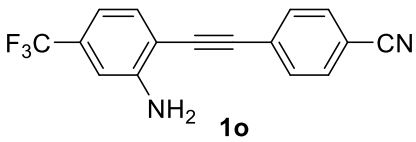
Synthesis of 2-[(2-aminophenyl)ethynyl]-5-methylphenyl acetate (1i):



1i

To a solution of 2-iodo-4-methylphenyl acetate (1.120 g, 4.06 mmol) in DMF (2.0 mL) was added $Pd(PPh_3)_2Cl_2$ (0.065 g, 0.094 mmol), Et_3N (1.8 mL) and 2- ethynylaniline (0.365 g, 3.12 mmol). After 4 h of stirring at 90 °C under N_2, 200 mL of HCl 1 M and 200 mL of EtOAc were added. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic layers were washed with water, dried over sodium sulfate, filtered and concentrated. Purification of the residue by flash chromatography (eluent: hexane/EtOAc = 95:5) afforded **1i** (0.573 g, 75% yield): ^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 2.32 (s, 6H, $OCCH_3$ and CH_3), 4.29 (bs, 2H, NH_2), 6.67-6.71 (m, 2H), 6.97-7.00 (m, 1H), 7.11-7.15 (m, 2H), 7.30 (dd, 1H, *J*=7.9 Hz, *J*=1.5 Hz), 7.36-7.37 (m, 1H); ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 20.7 (CH_3), 21.0 (CH_3), 89.7 (C), 90.5 (C), 102.4 (C), 110.9 (C), 114.3 (CH), 117.8 (CH), 121.9 (CH), 130.0 (CH), 130.2 (CH), 132.0 (CH), 133.2 (CH), 135.7 (C), 148.1 (C), 149.1 (C), 169.3 (C=O); HRMS *m/z* (ESI) positive ion, calculated for $C_{17}H_{16}NO_2$: $[M+1]^+$ 266.1176; Found: 266.1149.

Synthesis of 4-{[2-amino-4-(trifluoromethyl)phenyl]ethynyl}benzonitrile (1o):



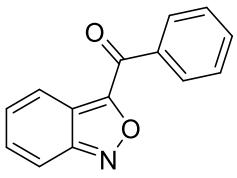
1o

To a solution of 4-iodobenzonitrile (0.790 g, 3.45 mmol) in THF (10 mL) and Et_3N (1.5 mL) were added $PdCl_2$ (0.012 g, 0.069 mmol), dppf (0.037 g, 0.069 mmol) and 2-ethynyl-5-(trifluoromethyl)aniline (0.425 g, 2.30 mmol). After 6 h of stirring at room temperature under N_2, 150 mL of HCl 1 M and 150 mL of EtOAc were added. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic layers were washed with water, dried over sodium sulfate, filtered and concentrated. Purification of the residue by flash chromatography (eluent: hexane/EtOAc = 90:10) afforded **1o** (0.526 g, 80% yield): ^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 4.48 (bs, 2H, NH_2), 6.95-6.97 (m, 2H), 7.45 (dt, 1H, *J*=7.7 Hz, *J*=0.9 Hz), 7.60-7.67 (m, 4H); ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 89.0 (C), 94.6 (C), 109.9 (q, *J*=1.5 Hz, C), 111.0 (q, *J*=4.0 Hz, CH), 112.0 (C), 114.4 (q, *J*=3.8 Hz, CH), 118.4 (CN), 123.8 (q, *J*=272.5 Hz, CF_3), 127.6 (C), 132.0 (2CH), 132.20 (2CH), 132.23 (q, *J*=32.2 Hz, C), 132.9 (CH), 148.1 (C); HRMS *m/z* (ESI) positive ion, calculated for $C_{16}H_{10}F_3N_2$: $[M+1]^+$ 287.0791; Found: 287.0766.

Typical procedure for the domino gold-catalyzed hydroamination/oxidation reaction of 2-alkynylanilines 1: $NaAuCl_4.2H_2O$ (0.010 g, 0.025 mmol) and oxone (0.314 g, 0.51 mmol) were added to a solution of 2-(*p*-tolylethynyl)aniline **1c** (0.106 g, 0.51 mmol) in CH_3CN (7 mL). The mixture was stirred at 80 °C and the reaction was monitored by TLC and GC-MS. Then, the mixture after stirring for 6 h was cooled and filtered through a pad of fluorisil. The filtrate was evaporated and subjected to column chromatography on silica gel (eluent: hexane/EtOAc = 99:1) to give 2-(*p*-tolyl)-4H-benzo[*d*][1,3]oxazin-4-one **(4c)** (0.085 g, 72% yield).

Procedure for a two-step one-pot gold-catalyzed hydroamination/oxidation 2-alkynylaniline 1a: $NaAuCl_4.2H_2O$ (0.010 g, 0.026 mmol) was added to a solution of 2-(phenylethynyl)aniline **1a** (0.103 g, 0.53 mmol) in CH_3CN (7 mL). The mixture was stirred at 80 °C for 1 h until the complete conversion of the starting **1a** into the corresponding 2-phenyl-1*H*-indole **5a** as monitored by GC-MS. Then, oxone (0.652 g, 1.06 mmol) was added and the mixture after stirring under reflux for 1 h was cooled and filtered through a pad of fluorisil. The filtrate was evaporated and subjected to column chromatography on silica gel (eluent: hexane/EtOAc = 99:1) to give 2-phenylyl-4H-benzo[*d*][1,3]oxazin-4-one **(4a)** (0.074 g, 63% yield).

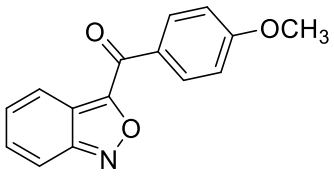
Typical procedure for silver-catalyzed oxidative cyclization of 2-alkynylanilines 1 with oxone. Synthesis of 2,1-benzisoxazol-3-yl(phenyl)methanone (6a):



6a

$AgNO_3$ (0.010 g, 0.059 mmol) and oxone (0.726 g, 1.18 mmol) were added to a solution of 2-(phenylethynyl)aniline **1a** (0.114 g, 0.59 mmol) in CH_3CN/H_2O (3.5 mL/3.5 mL). The mixture was stirred at 60 °C and the reaction was monitored by TLC and GC-MS. Then, the mixture after stirring for 1 h was cooled and 150 mL of H_2O and 150 mL of CH_2Cl_2 were added. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with water, dried over sodium sulfate, filtered and concentrated. The filtrate was evaporated and subjected to column chromatography on silica gel (eluent: hexane/EtOAc = 98:2) to give the benzo[*c*]isoxazol-3-yl(phenyl)methanone **(6a)** (0.115 g, 88% yield). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 7.24 (t, 1H, *J*=7.6 Hz), 7.38 (t, 1H, *J*=7.7 Hz), 7.54 (t, 2H, *J*=7.5 Hz), 7.64 (t, 1H, *J*=7.3 Hz), 7.71 (d, 1H, *J*=9.0 Hz), 8.09 (d, 1H, *J*=8.8 Hz), 8.27 (d, 2H, *J*=8.0 Hz); ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 115.8 (CH), 121.55 (C), 121.63 (CH), 128.4 (CH), 128.7 (2CH), 130.1 (2CH), 131.3 (CH), 133.8 (CH), 135.9 (C), 157.2 (C), 160.3 (C), 181.3 (C=O). HRMS *m/z* (ESI) positive ion, calculated for $C_{14}H_{10}NO_2$: $[M+H]^+$ 224.0706; Found: 224.0701.

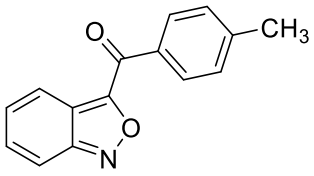
2,1-benzisoxazol-3-yl(4-methoxyphenyl)methanone (6b):



6b

^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 3.93 (s, 3H, OMe), 7.04-7.08 (m, 2H), 7.27 (ddd, 1H, *J*=8.8 Hz, *J*=6.4 Hz, *J*=0.7 Hz), 7.42 (ddd, 1H, *J*=9.1 Hz, *J*=6.4 Hz, *J*=1.0 Hz), 7.74 (ddd, 1H, *J*=9.1 Hz, *J*=1.2 Hz, *J*=0.8 Hz), 8.14 (dt, 1H, *J*=8.8 Hz, *J*=1.0 Hz), 8.34-8.37 (m, 2H); ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 55.6 (OMe), 114.2 (2CH), 115.8 (CH), 121.5 (C), 121.9 (CH), 128.1 (CH), 128.9 (C), 131.4 (CH), 132.7 (2CH), 157.3 (C), 161.0 (C), 164.3 (C), 179.8 (C=O); HRMS *m/z* (ESI) positive ion, calculated for $C_{15}H_{12}NO_3$: $[M+H]^+$ 254.0814; Found: 254.0811.

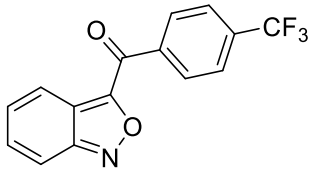
2,1-benzisoxazol-3-yl(4-methylphenyl)methanone (6c):



6c

^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 2.45 (s, 3H, Me), 7.25 (ddd, 1H, *J*=8.8 Hz, *J*=6.4 Hz, *J*=0.8 Hz), 7.34-7.37 (m, 2H), 7.39 (ddd, 1H, *J*=9.1 Hz, *J*=6.4 Hz, *J*=1.0 Hz), 7.73 (ddd, 1H, *J*=9.1 Hz, *J*=1.2 Hz, *J*=0.8 Hz), 8.11 (dt, 1H, *J*=8.8 Hz, *J*=1.1 Hz), 8.19 - 8.22 (m, 2H); ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 21.8 (Me), 115.8 (CH), 121.5 (C), 121.8 (CH), 128.3 (CH), 129.5 (2CH),130.3 (2CH), 131.3 (CH), 133.4 (C), 144.9 (C), 157.2 (C),160.6 (C),180.9 (C=O); HRMS *m*/*z* (ESI) positive ion, calculated for $C_{15}H_{12}NO_2$: $[M+H]^+$ 238.0862; Found: 238.0862.

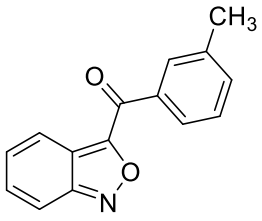
2,1-benzisoxazol-3-yl[4-(trifluoromethyl)phenyl]methanone (6d):



6d

^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 7.32 (ddd, 1H, *J*=8.8 Hz, *J*=6.5 Hz, *J*=0.8 Hz), 7.44 (ddd, 1H, *J*=9.1 Hz, *J*=6.5 Hz, *J*=1.0 Hz), 7.77 (ddd, 1H, *J*=9.1 Hz, *J*=1.2 Hz, *J*=0.8 Hz), 7.82-7.86 (m, 2H), 8.12 (dt, 1H, *J*=8.8 Hz, *J*=1.1 Hz), 8.38 - 8.41 (m, 2H); ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 116.1 (CH), 121.5 (CH), 122.0 (C), 123.6 (q, *J*=272.8 Hz, CF_3), 125.8 (q, *J*=3.7 Hz, 2CH), 129.2 (CH), 130.4 (2CH), 131.6 (CH), 134.9 (q, *J*=32.8 Hz, C), 138.7 (C), 157.4 (C), 159.7 (C), 180.3 (C=O); HRMS *m*/*z* (ESI) positive ion, calculated for $C_{15}H_9F_3NO_2$: $[M+H]^+$ 292.0579; Found: 292.0580.

2,1-benzisoxazol-3-yl(3-methylphenyl)methanone (6e):

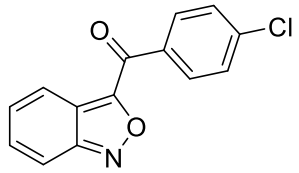


6e

^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 2.46 (s, 3H, Me), 7.27 (ddd, 1H, *J*=8.8 Hz, *J*=6.4 Hz, *J*=0.8 Hz), 7.40 (ddd, 1H, *J*=9.1 Hz, *J*=6.5 Hz, *J*=1.0 Hz), 7.44-7.47 (m, 2H), 7.74 (ddd, 1H, *J*=9.1 Hz, *J*=1.2

Hz, *J*=0.8 Hz), 8.05 - 8.09 (m, 2H), 8.11 (dt, 1H, *J*=8.8 Hz, *J*=1.1 Hz); ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 21.4 (Me), 115.8 (CH), 121.5 (C), 121.7 (CH), 127.4 (CH), 128.4 (CH), 128.6 (CH), 130.5 (CH), 131.3 (CH), 134.6 (CH), 136.0 (C), 138.6 (C), 157.2 (C), 160.5 (C), 181.6 (C=O); HRMS *m/z* (ESI) positive ion, calculated for $C_{15}H_{12}NO_2$: $[M+H]^+$ 238.0862; Found: 238.0862.

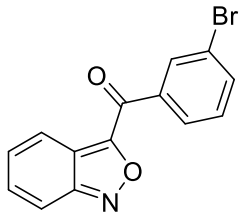
2,1-benzisoxazol-3-yl(4-chlorophenyl)methanone (6f):



6f

^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 7.30 (ddd, 1H, *J*=8.8 Hz, *J*=6.4 Hz, *J*=0.8 Hz), 7.43 (ddd, 1H, *J*=9.1 Hz, *J*=6.4 Hz, *J*=1.0 Hz), 7.52-7.56 (m, 2H), 7.75 (dt, 1H, *J*=9.1 Hz, *J*=1.0 Hz), 8.12 (dt, 1H, *J*=8.8 Hz, *J*=1.1 Hz), 8.25-8.28 (m, 2H); ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 115.9 (CH), 121.6 (CH), 121.8 (C), 128.8 (CH), 129.1 (2CH), 131.46 (CH), 131.52 (2CH), 134.2 (C), 140.5 (C), 157.2 (C), 160.0 (C), 179.9 (C=O); HRMS *m/z* (ESI) positive ion, calculated for $C_{14}H_9ClNO_2$: $[M+H]^+$ 258.0316; Found: 258.0319.

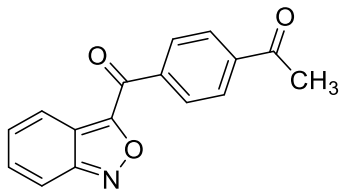
2,1-benzisoxazol-3-yl(3-bromophenyl)methanone (6g):



6g

^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 7.32 (ddd, 1H, *J*=8.8 Hz, *J*=6.5 Hz, *J*=0.8 Hz), 7.44 (ddd, 1H, *J*=9.0 Hz, *J*=6.5 Hz, *J*=1.0 Hz), 7.46 (td, 1H, *J*=7.9 Hz, *J*=0.6 Hz), 7.76-7.81 (m, 2H), 8.13 (dt, 1H, *J*=8.8 Hz, *J*=1.1 Hz), 8.26 (ddd, 1H, *J*=7.8 Hz, *J*=1.7 Hz, *J*=1.0 Hz), 8.40 (ddd, 1H, *J*=2.1 Hz, *J*=1.6 Hz, *J*=0.5 Hz); ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 116.0 (CH), 121.6 (CH), 121.9 (C), 123.0 (C), 128.7 (CH), 128.9 (CH), 130.3 (CH), 131.5 (CH), 132.9 (CH), 136.6 (CH), 137.6 (C), 157.3 (C), 159.8 (C), 179.8 (C=O); HRMS *m/z* (ESI) positive ion, calculated for $C_{14}H_9BrNO_2$: $[M+H]^+$ 301.9811; Found: 301.9813.

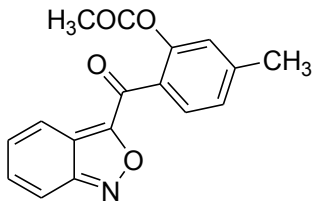
1-[4-(2,1-benzisoxazol-3-ylcarbonyl)phenyl]ethanone (6h):



6h

^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 2.70 (s, 3H, Me), 7.33 (ddd, 1H, *J*=8.8 Hz, *J*=6.5 Hz, *J*=0.8 Hz), 7.45 (ddd, 1H, *J*=9.1 Hz, *J*=6.5 Hz, *J*=1.0 Hz), 7.78 (td, 1H, *J*=9.1 Hz, *J*=1.0 Hz), 8.12-8.15 (m, 3H), 8.35-8.39 (m, 2H); ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 27.0 (CH_3), 116.0 (CH), 121.5 (CH), 121.9 (C), 128.5 (2CH), 129.0 (CH), 130.3 (2CH), 131.5 (CH), 139.2 (C), 140.5 (C), 157.3 (C), 159.9 (C), 180.7 (C=O), 197.4 (C=O); HRMS *m/z* (ESI) positive ion, calculated for $C_{16}H_{12}NO_3$: $[M+H]^+$ 266.0811; Found: 266.0814.

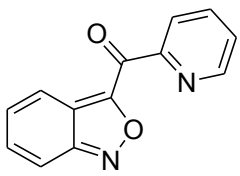
2-(2,1-benzisoxazol-3-ylcarbonyl)-5-methylphenyl acetate (6i):



6i

^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 2,12 (s, 3H, OCMe), 2.43 (s, 3H, Me), 7.16 (dt, 1H, *J*=8.3 Hz, *J*=0.4 Hz), 7.28 (ddd, 1H, *J*=8.8 Hz, *J*=6.5 Hz, *J*=0.8 Hz), 7.42 (ddd, 1H, *J*=9.1 Hz, *J*=6.5 Hz, *J*=1.0 Hz), 7.44 (ddd, 1H, *J*=8.3 Hz, *J*=2.2 Hz, *J*=0.7 Hz), 7.66 (ddd, 1H, *J*=2.2 Hz, *J*=0.7 Hz, *J*=0.4 Hz), 7.75 (ddd, 1H, *J*=9.1 Hz, *J*=1.2 Hz, *J*=0.8 Hz), 7.98 (dt, 1H, *J*=8.8 Hz, *J*=1.1 Hz); ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 20.8 (Me), 20.9 (Me), 116.0 (CH), 120.9 (C), 121.3 (CH), 123.4 (CH), 128.6 (CH), 129.3 (C), 131.1 (CH), 131.4 (CH), 134.3 (CH), 135.9 (C), 147.0 (C), 157.5 (C), 159.8 (C), 169.3 (C=O), 180.9 (C=O); HRMS *m/z* (ESI) positive ion, calculated for $C_{17}H_{14}NO_4$: $[M+1]^+$ 296.0923; Found: 296.0919.

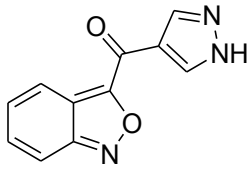
2,1-benzisoxazol-3-yl(pyridin-2-yl)methanone (6j):



6j

^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 7.29 (ddd, 1H, *J*=8.8 Hz, *J*=6.5 Hz, *J*=0.8 Hz), 7.41 (ddd, 1H, *J*=9.1 Hz, *J*=6.5 Hz, *J*=1.0 Hz), 7.60 (ddd, 1H, *J*=7.6 Hz, *J*=4.7 Hz, *J*=1.2 Hz), 7.78 (dt, 1H, *J*=9.1 Hz, *J*=1.0 Hz), 7.78 (td, 1H, *J*=7.8 Hz, *J*=1.7 Hz), 8.08 (dt, 1H, *J*=8.8 Hz, *J*=1.1 Hz), 8.21 (dt, 1H, *J*=7.9 Hz, *J*=1.1 Hz), 8.88 (ddd, 1H, *J*=4.7 Hz, *J*=1.7 Hz, *J*=0.9 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 100.6 MHz): δ = 116.1 (CH), 121.6 (C), 121.8 (CH), 124.7 (CH), 127.4 (CH), 128.6 (CH), 131.1 (CH), 137.2 (CH), 149.5 (CH), 153.2 (C), 157.3 (C), 159.9 (C), 180.7 (C=O); HRMS *m*/*z* (ESI) positive ion, calculated for $C_{13}H_9N_2O_2$: $[M+H]^+$ 225.0658; Found: 225.0659.

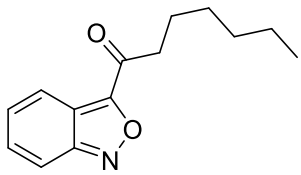
2,1-benzisoxazol-3-yl(1H-pyrazol-4-yl)methanone (6k):



6k

^{1}H-NMR (DMSO, 400 MHz): δ = 7.41 (ddd, 1H, *J*=8.8 Hz, *J*=6.4 Hz, *J*=0.6 Hz), 7.57 (ddd, 1H, *J*=9.1 Hz, *J*=6.4 Hz, *J*=1.0 Hz), 7.88 (dt, 1H, *J*=9.1 Hz, *J*=0.8 Hz), 8.08 (dt, 1H, *J*=8.8 Hz, *J*=1.0 Hz), 8.60 (bs, 2H) 13.81 (bs, 1H, NH) and ^{13}C-NMR (DMSO, 100.6 MHz): δ = 115.5 (CH), 119.6 (C), 120.2 (C), 120.9 (CH), 128.7 (CH), 132.0 (CH), 134.3 (bs, CH), 140.1 (bs, CH), 156.8 (C), 160.1 (C), 173.7 (C=O); HRMS *m*/*z* (ESI) positive ion, calculated for $C_{11}H_8N_3O_2$: $[M+H]^+$ 214.0611; Found: 214.0612.

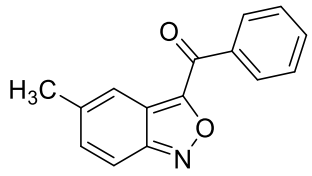
1-(2,1-benzisoxazol-3-yl)heptan-1-one (6l):



6l

^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 0.90 (t, 3H, *J*=7.1 Hz), 1.32-1.46 (m, 6H), 1.82 (qt, 2H, *J*=7.5 Hz), 3.17 (t, 2H, *J*=7.4 Hz), 7.26 (ddd, 1H, *J*=8.8 Hz, *J*=6.4 Hz, *J*=0.8 Hz), 7.40 (ddd, 1H, *J*=9.1 Hz, *J*=6.5 Hz, *J*=1.0 Hz), 7.72 (ddd, 1H, *J*=9.1 Hz, *J*=1.1 Hz, *J*=0.8 Hz), 8.05 (dt, 1H, *J*=8.8 Hz, *J*=1.1 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 100.6 MHz): δ 14.0 (CH_3), 22.5 (CH_2), 23.6 (CH_2), 28.9 (CH_2), 31.6 (CH_2), 40.2 (CH_2), 115.9 (CH), 119.1 (C), 121.3 (CH), 128.4 (CH), 131.3 (CH), 157.6 (C), 159.8 (C), 190.5 (C=O); HRMS *m*/*z* (ESI) positive ion, calculated for $C_{14}H_{18}NO_2$: $[M+H]^+$ 232.1332; Found; 232.1332.

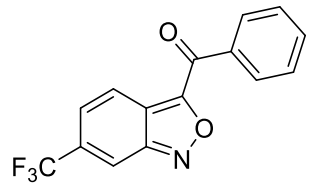
(5-methyl-2,1-benzisoxazol-3-yl)(phenyl)methanone (6m):



6m

^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 2.43 (s, 3H), 7.24 (dd, 1H, *J*=9.2 Hz, *J*=1.5 Hz), 7.55-7.58 (m, 2H), 7.64-7.68 (m, 2H), 7.88 (td, 1H, *J*=2.5 Hz, *J*=1.2 Hz), 8.27-8.30 (m, 2H); ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 22.1 (Me), 115.5 (CH), 119.0 (CH), 122.3 (C), 128.7 (2CH), 130.1 (2CH), 133.6 (CH), 134.8 (CH), 136.2 (C), 139.1 (C), 156.7 (C), 159.2 (C), 181.5 (C=O); HRMS *m/z* (ESI) positive ion, calculated for $C_{15}H_{12}NO_2$: $[M+H]^+$ 238.0862; Found: 238.0862.

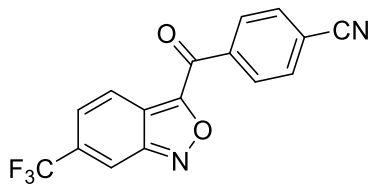
phenyl[6-(trifluoromethyl)-2,1-benzisoxazol-3-yl]methanone (6n):



6n

^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 7.44 (ddd, 1H, *J*=9.2 Hz, *J*=1.4 Hz, *J*=0.3 Hz), 7.59-7.63 (m, 2H), 7.69-7.73 (m, 1H), 8.14 (td, 1H, *J*=2.4 Hz, *J*=1.2 Hz), 8.30-8.32 (m, 3H); ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 114.9 (q, *J*=5.3 Hz, CH), 122.7 (C), 123.1 (q, *J*=273.2 Hz, CF_3), 123.9 (CH), 124.0 (q, *J*=2.7 Hz, CH), 129.0 (2CH), 130.2 (2CH), 133.7 (q, *J*=32.8 Hz, C), 134.3 (CH), 135.6 (C), 156.2 (C), 161.6 (C), 181.1 (C=O); HRMS *m/z* (ESI) positive ion, calculated for $C_{15}H_9F_3NO_2$: $[M+1]^+$ 292.0580; Found: 292.0588.

4-{[6-(trifluoromethyl)-2,1-benzisoxazol-3-yl]carbonyl}benzonitrile (6o):

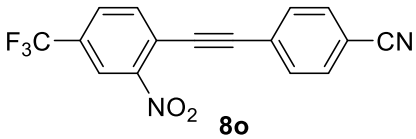


6o

^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 7.50 (dd, 1H, *J*=9.2 Hz, *J*=1.4 Hz), 7.90-7.93 (m, 2H), 8.18 (td, 1H, *J*=2.4 Hz, *J*=1.2 Hz), 8.34 (dt, 1H, *J*=9.1 Hz, *J*=0.9 Hz), 8.41-8.44 93 (m, 2H); ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 115.1 (q, *J*=5.2 Hz, CH), 117.5 (C), 117.7 (C), 123.0 (q, *J*=273.1 Hz,

CF_3), 123.5 (CH), 124.9 (q, *J*=2.7 Hz, CH), 128.8 (C), 130.5 (2CH), 132.7 (2CH), 134.0 (q, *J*=33.0 Hz, C), 138.6 (C), 156.3 (C), 160.6 (C) 179.6 (C=O); HRMS *m/z* (ESI) positive ion, calculated for $C_{16}H_8F_3N_2O_2$: $[M+1]^+$ 317.0532; Found: 317.0535.

4-{[2-nitro-4-(trifluoromethyl)phenyl]ethynyl}benzonitrile (8o):



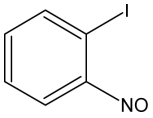
8o

^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 7.70 (s, 4H), 7.88-7.89 (m, 2H), 8.40 (ddd, 1H, *J*=2.2 Hz, *J*=1.5 Hz, *J*=0.7 Hz); ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 87.3 (C), 97.6 (C), 113.2 (C), 118.2 (CN), 121.4 (q, *J*=1.0 Hz, C), 122.4 (q, *J*=3.9 Hz, CH), 122.5 (q, *J*=273.0 Hz, CF_3), 127.9 (C), 129.5 (q, *J*=3.5 Hz, CH), 131.6 (q, *J*=34.6 Hz, C), 132.3 (2CH), 132.7 (2CH), 135.5 (CH), 149.6 (C); HRMS *m/z* (ESI) positive ion, [M+1] 317.0532; Found: 317.0529.

Synthesis of 1-nitroso-2-(phenylethynyl)benzene 9a

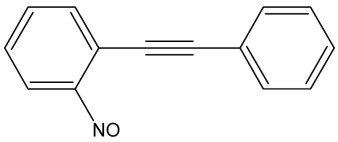
2-Iodoaniline (1.63 g, 7.45 mmol,) was dissolved in 22 ml of DCM. To this solution Oxone (8.95 g, 14.90 mmol) dissolved in 900 ml of water was added. The solution was stirred at room temperature until TLC monitoring indicated complete consumption of the starting material (2.5 h).[11] After separation of the layers, the aqueous layer was extracted with DCM twice. The combined organic layers were washed with water, dried over sodium sulfate, filtered and concentrated. Purification of the residue by flash chromatography (eluent: hexane/EtOAc = 99/1) afforded the 1-iodo-2-nitrosobenzene (0.500 g, 29%).[12] To a solution of 1-iodo-2-nitrosobenzene (0.350 g, 1.50 mmol) in DMF (2.0 mL) was added Et_3N (2.0 mL), phenyacetylene (0.183 g, 1.80 mmol), $Pd(PPh_3)_2Cl_2$ (0.021 g, 0.03 mmol) and CuI (0.006 g, 0.03 mmol). After 1 h of stirring at 80 °C under N_2, 200 mL of HCl 1 M and 200 mL of CH_2Cl_2 were added. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with water, dried over sodium sulfate, filtered and concentrated. Purification of the residue by flash chromatography (eluent: hexane/EtOAc = 95:5) afforded **9a** (0.124 g, 40% yield):

1-iodo-2-nitrosobenzene



^{1}H-NMR (Acetone-d6, 400 MHz): δ = 6.23 (dd, 1H, *J*=8.0 Hz, *J*=1.7 Hz), 7.48 (td, 1H, *J*=7.5 Hz, *J*=1.4 Hz), 7.57 (td, 1H, *J*=7.5 Hz, *J*=1.5 Hz), 8.43 (dd, 1H, *J*=7.8 Hz, *J*=1.2 Hz); ^{13}C-NMR

(Acetone-d6, 100.6 MHz): δ = 109.4 (CH), 109.7 (C), 129.6 (CH), 138.4 (CH), 142.6 (CH), 163.7 (C); HRMS *m/z* (ESI) positive ion, calculated for C_6H_4INO: $[M+1]^+$ 233.9416; Found: 233.9490



9a

^{1}H-NMR (Acetone-d6, 400 MHz): δ = 6.59-6.73 (m, 1H), 7.11-7.15 (m, 1H), 7.26-7.28 (m, 1H), 7.33-7.38 (m, 4H), 7.51-7.53 (m, 2H); ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 85.9 (C), 94.7 (C), 114.4 (CH), 118.0 (CH), 128.2 (CH), 128.4 (2CH), 129.7 (CH), 131.5 (2CH), 132.1 (CH), 133.0 (C), 133.8 (C), 147.8 (C); HRMS *m/z* (ESI) positive ion, calculated for $C_{14}H_{10}NO$: $[M+1]^+$ 208.0762; Found: 208.0802.

3. References

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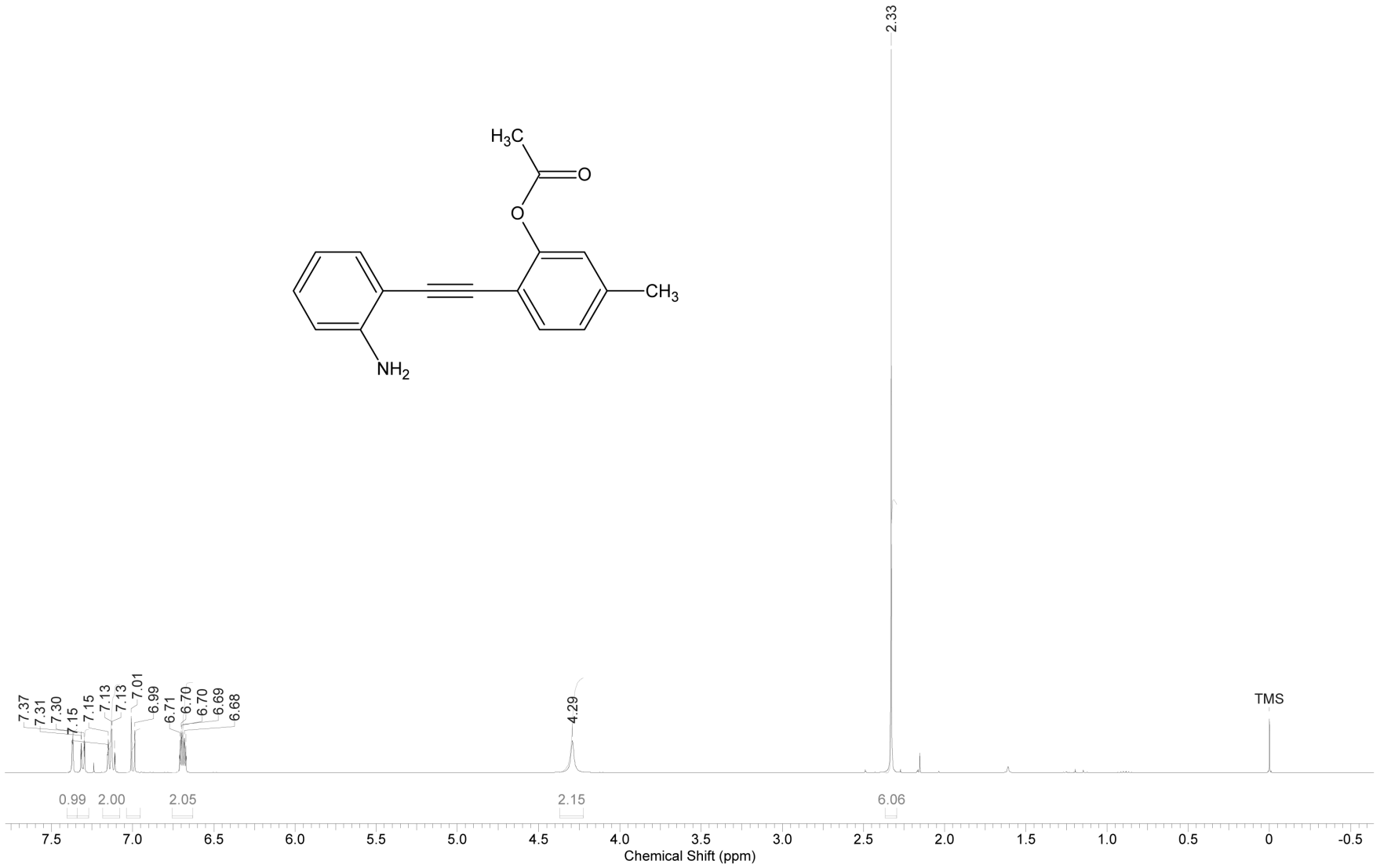
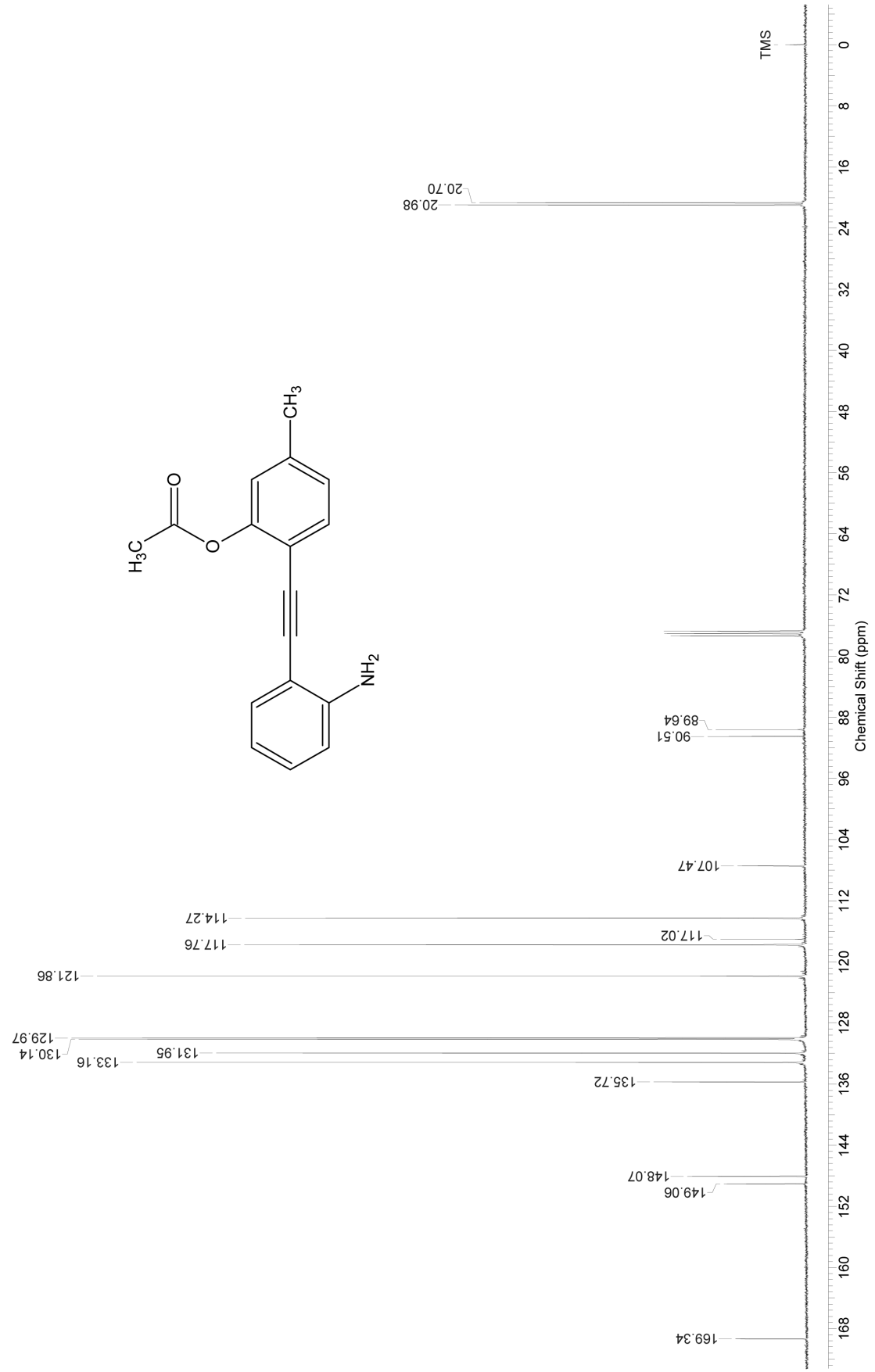
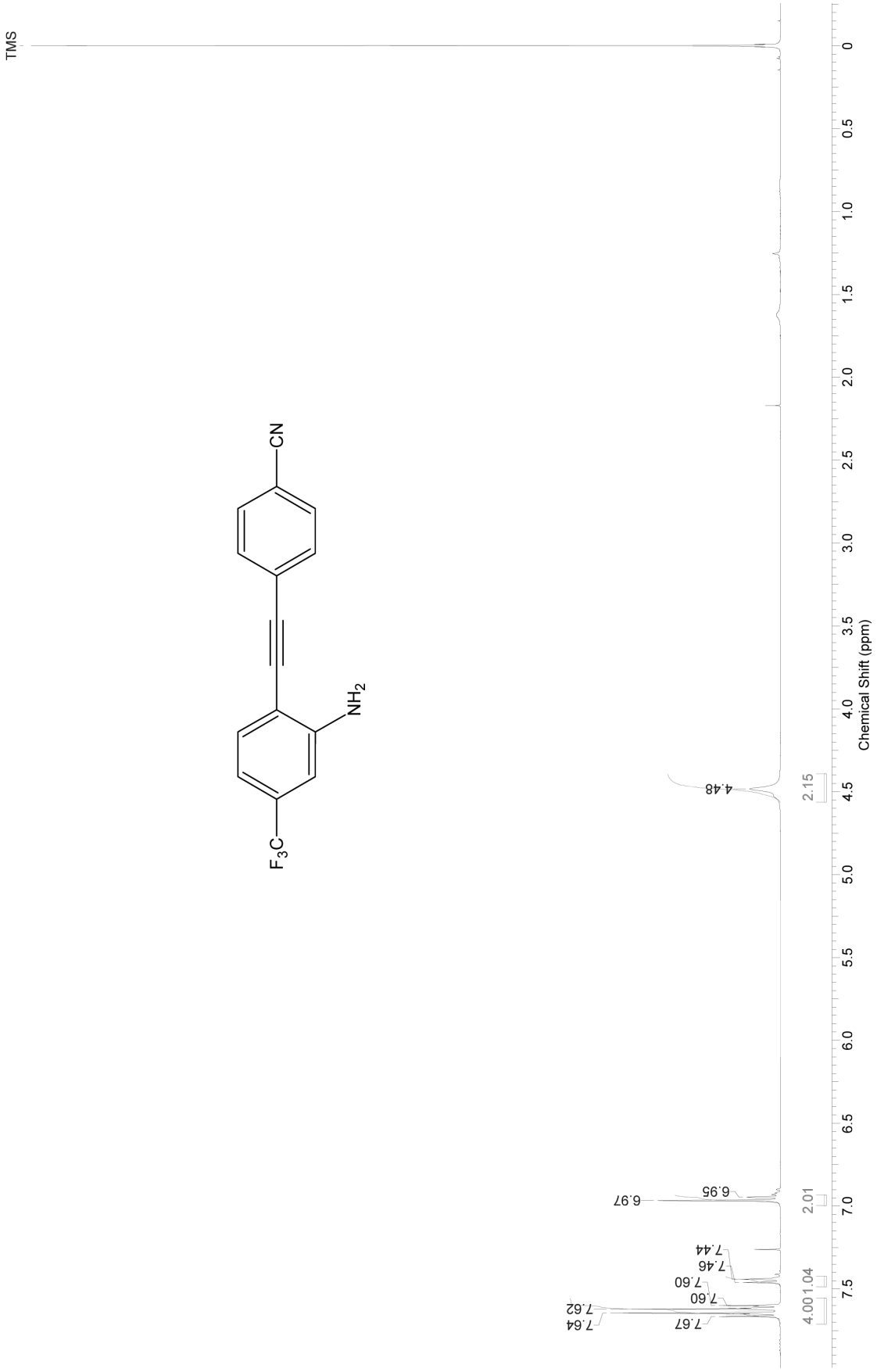
1i


2.33
H3C
O
O
CH3
NH2
7.37
7.31
7.30
7.15
7.15
7.13
7.13
7.01
6.99
6.71
6.70
6.70
6.69
6.68
4.29
TMS
0.99
2.00
2.05
2.15
6.06
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
0
-0.5
Chemical Shift (ppm)

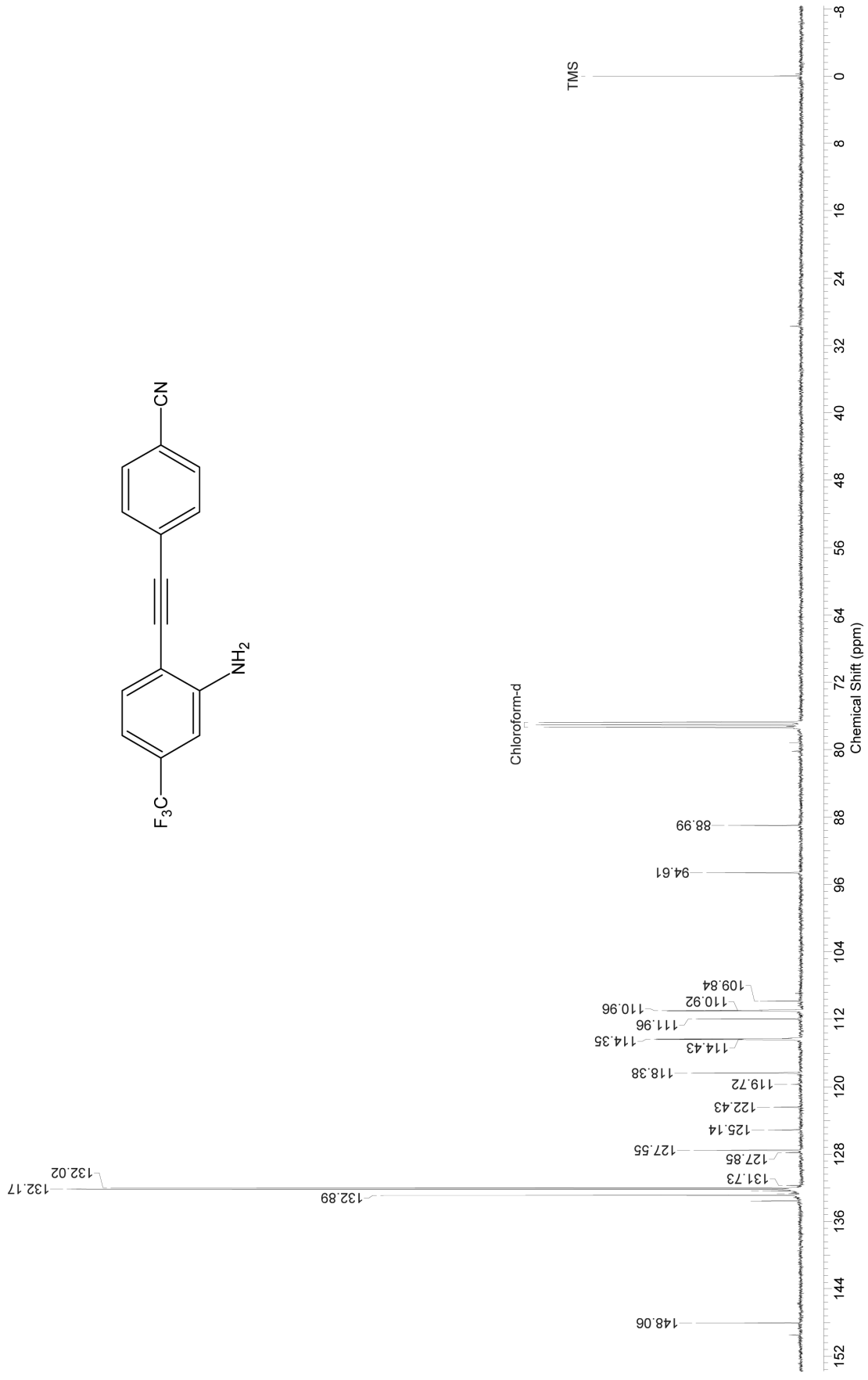
1i

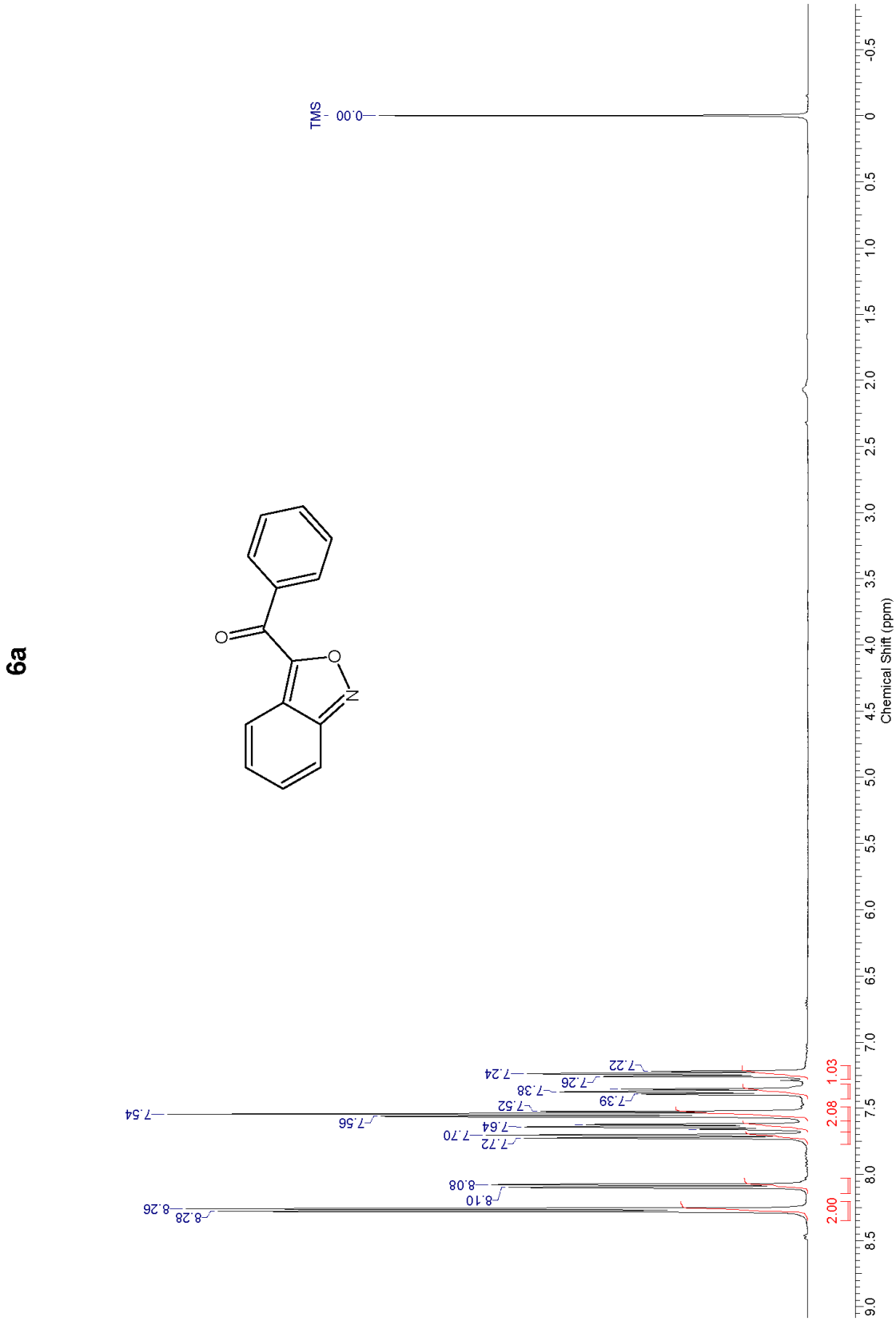

TMS
20.98
20.70
89.64
90.51
107.47
114.27
117.02
117.76
121.86
129.97
130.14
131.95
133.16
135.72
148.07
149.06
169.34
Chemical Shift (ppm)
0
8
16
24
32
40
48
56
64
72
80
88
96
104
112
120
128
136
144
152
160
168
CH3
O
O
H3C
NH2

1o

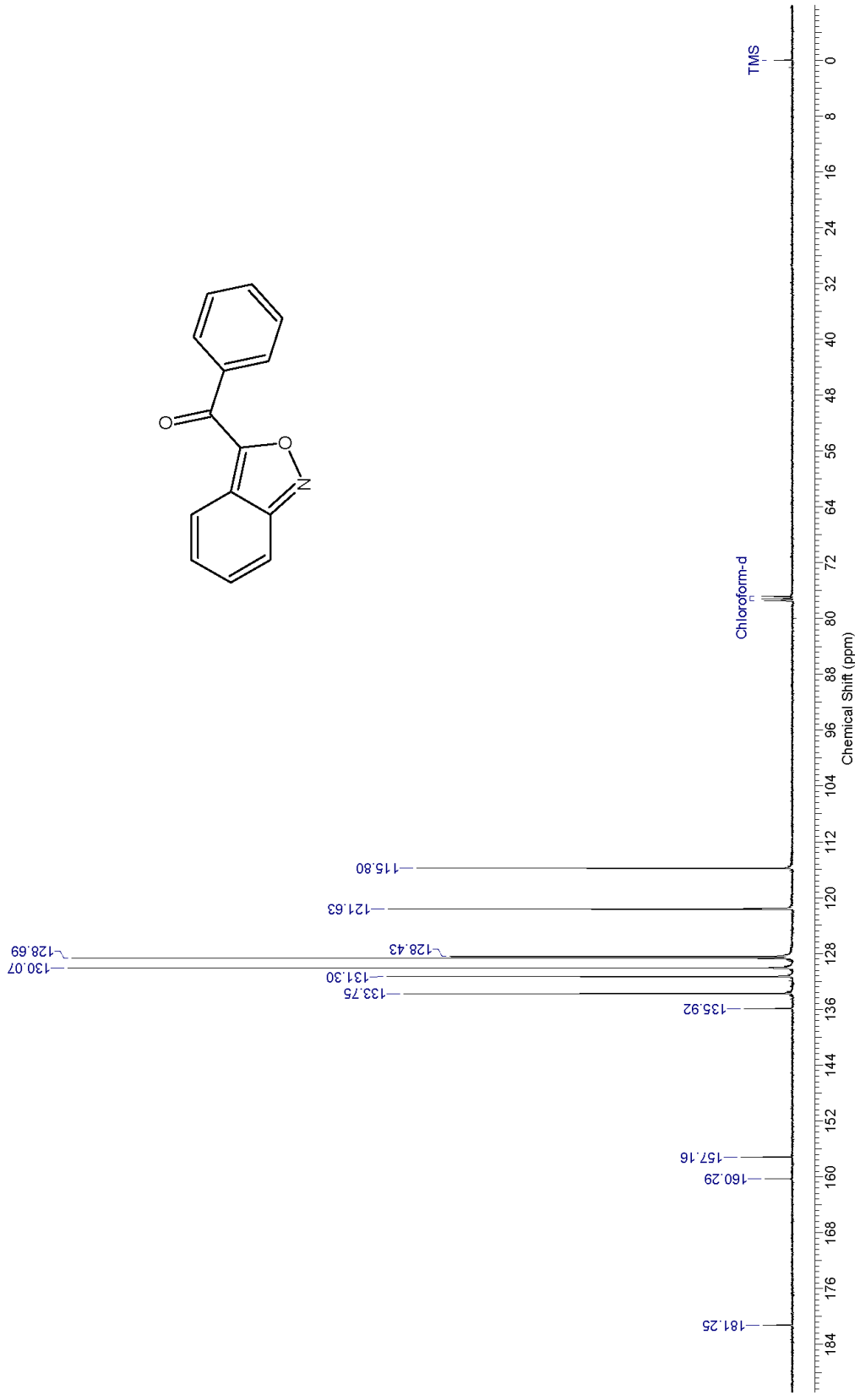

TMS
CN
NH2
F3C
4.48
6.95
6.97
7.44
7.46
7.60
7.60
7.62
7.64
7.67
2.15
2.01
4.00
1.04
Chemical Shift (ppm)

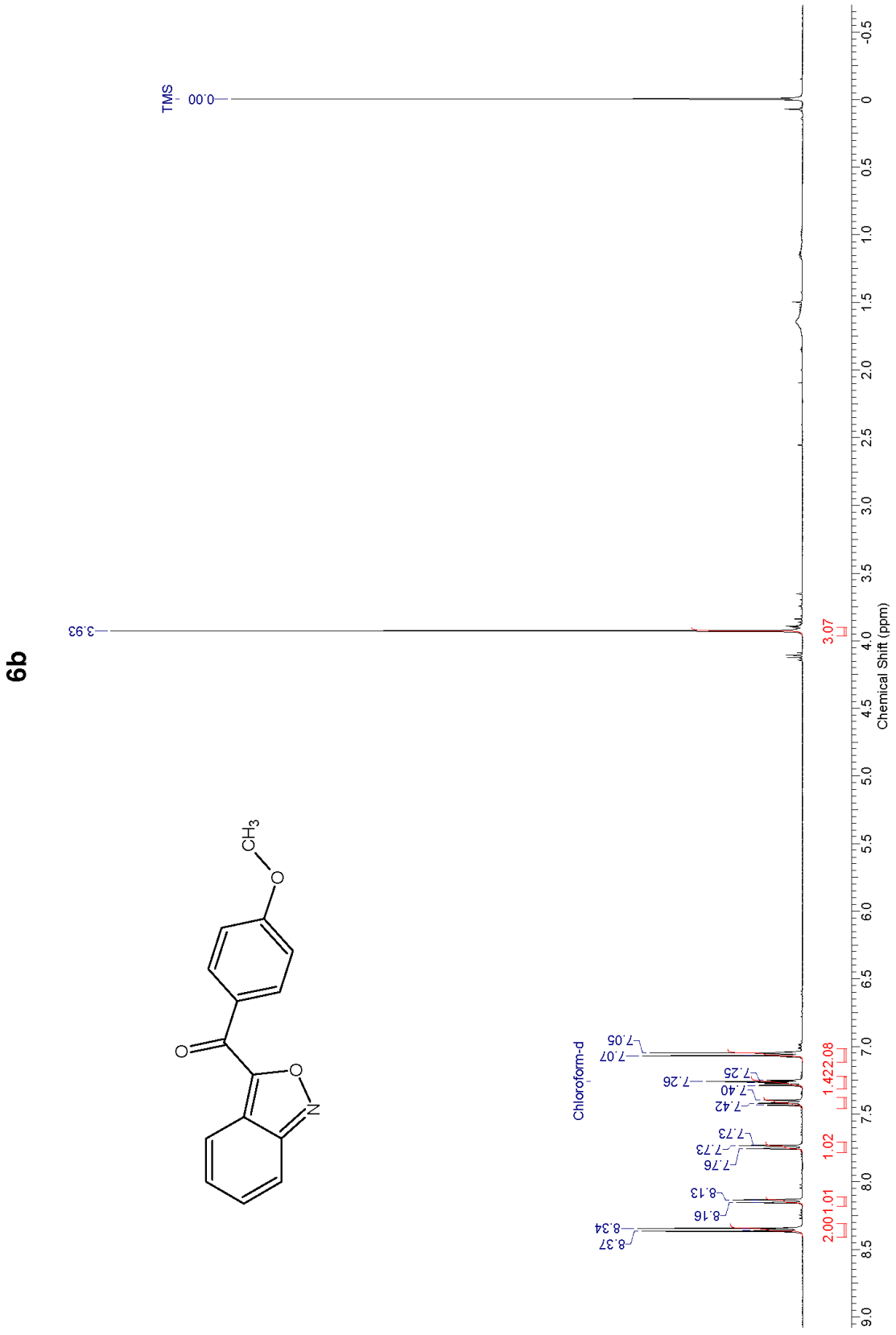
1o


CN
NH2
F3C
TMS
Chloroform-d
88.99
94.61
109.84
110.92
110.96
111.96
114.35
114.43
118.38
119.72
122.43
125.14
127.55
127.85
131.73
132.02
132.17
132.89
148.06
-8
0
8
16
24
32
40
48
56
64
72
80
88
96
104
112
120
128
136
144
152
Chemical Shift (ppm)

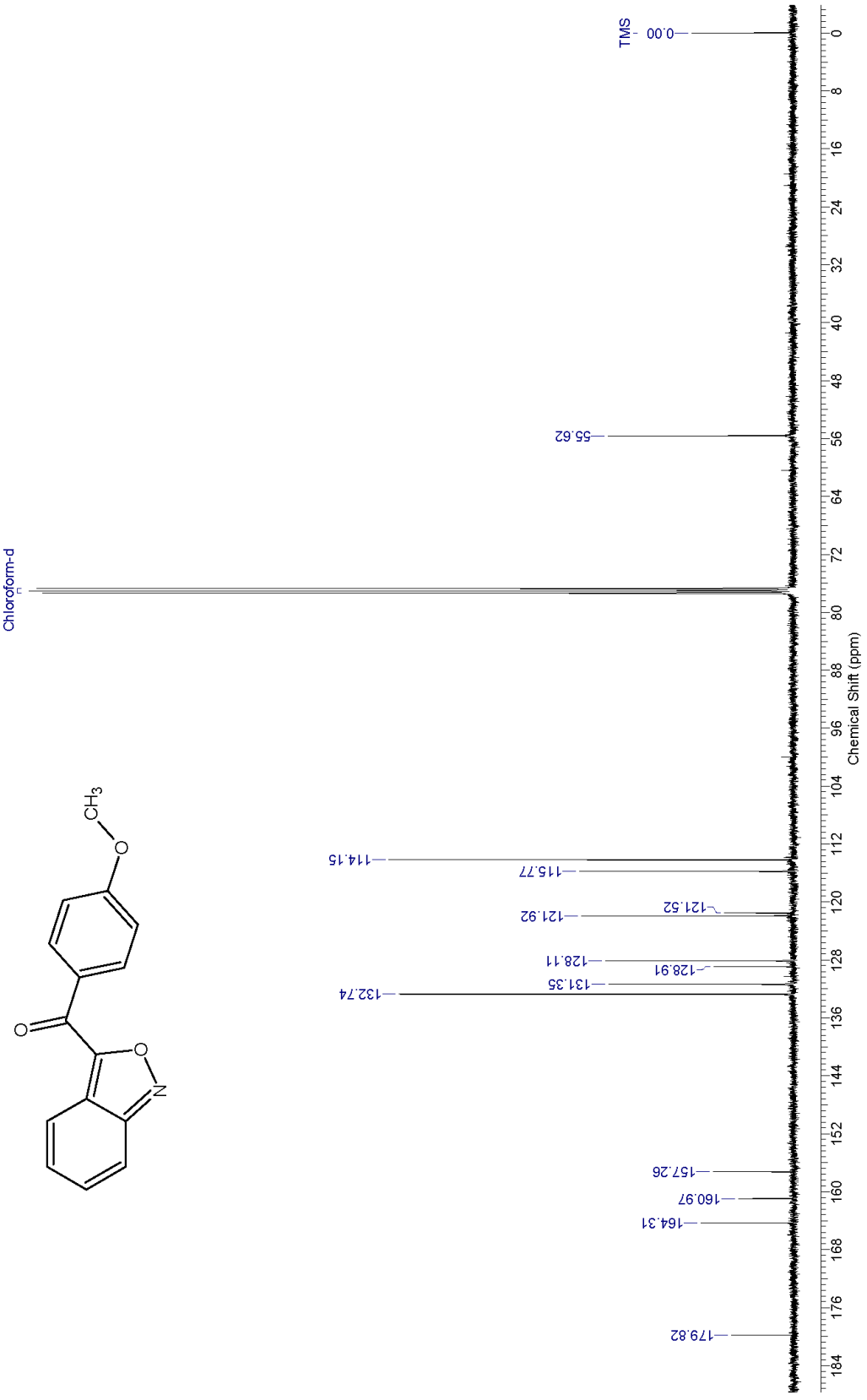

6a
TMS
0.00
8.28
8.26
8.10
8.08
7.72
7.70
7.64
7.56
7.54
7.52
7.39
7.38
7.26
7.24
7.22
2.00
2.08
1.03
Chemical Shift (ppm)

6a

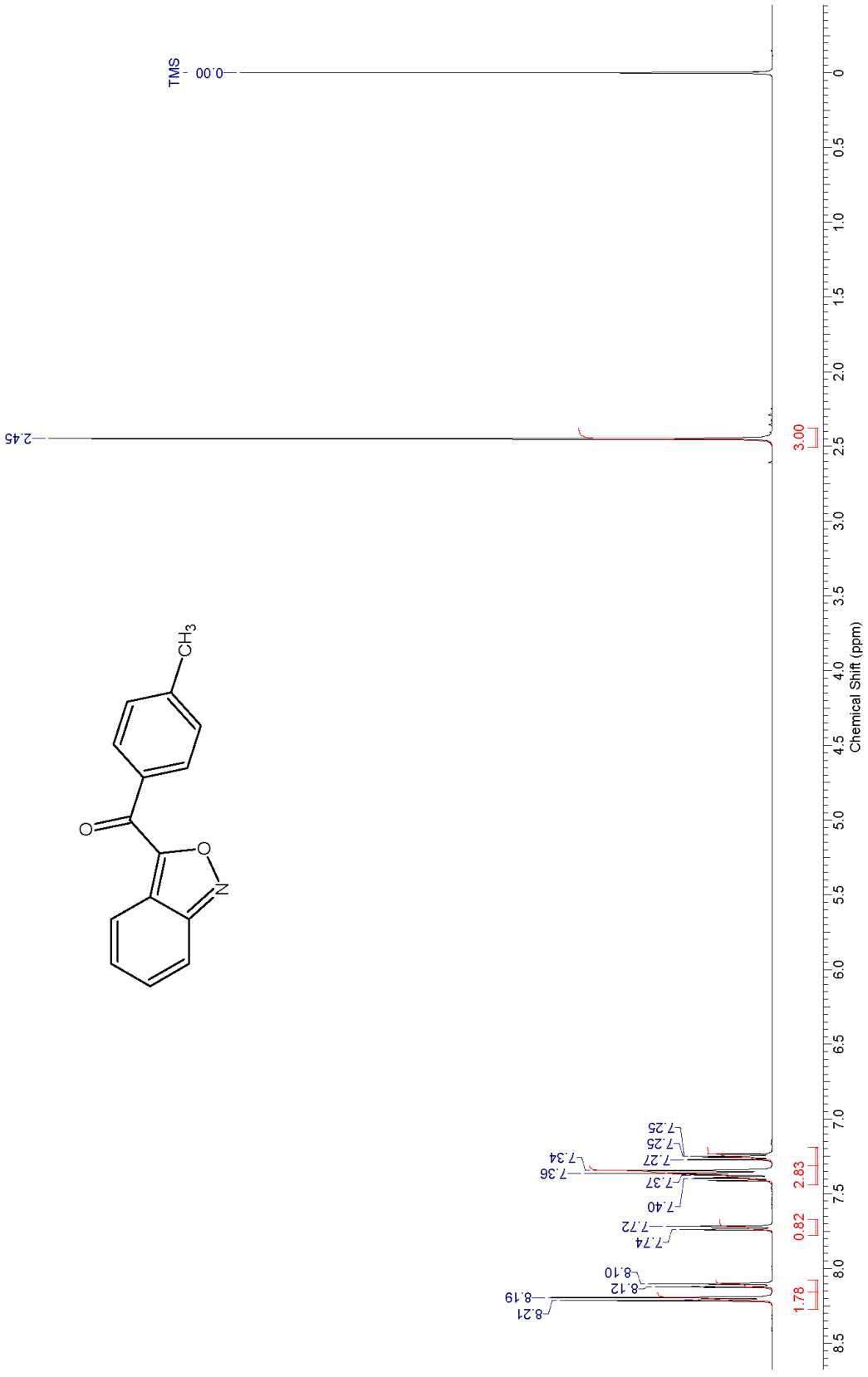

O
O
N
TMS
Chloroform-d
115.80
121.63
128.43
128.69
130.07
131.30
133.75
135.92
157.16
160.29
181.25
0
8
16
24
32
40
48
56
64
72
80
88
96
104
112
120
128
136
144
152
160
168
176
184
Chemical Shift (ppm)


6b
TMS
0.00
3.93
Chloroform-d
8.37
8.34
8.16
8.13
7.76
7.73
7.73
7.42
7.40
7.26
7.25
7.07
7.05
2.00
1.01
1.02
1.42
2.08
3.07
Chemical Shift (ppm)

6b


TMS
0.00
Chloroform-d
55.62
114.15
115.77
121.52
121.92
128.11
128.91
131.35
132.74
157.26
160.97
164.31
179.82
Chemical Shift (ppm)
0
8
16
24
32
40
48
56
64
72
80
88
96
104
112
120
128
136
144
152
160
168
176
184
CH3
O
O
O
N

6c


TMS
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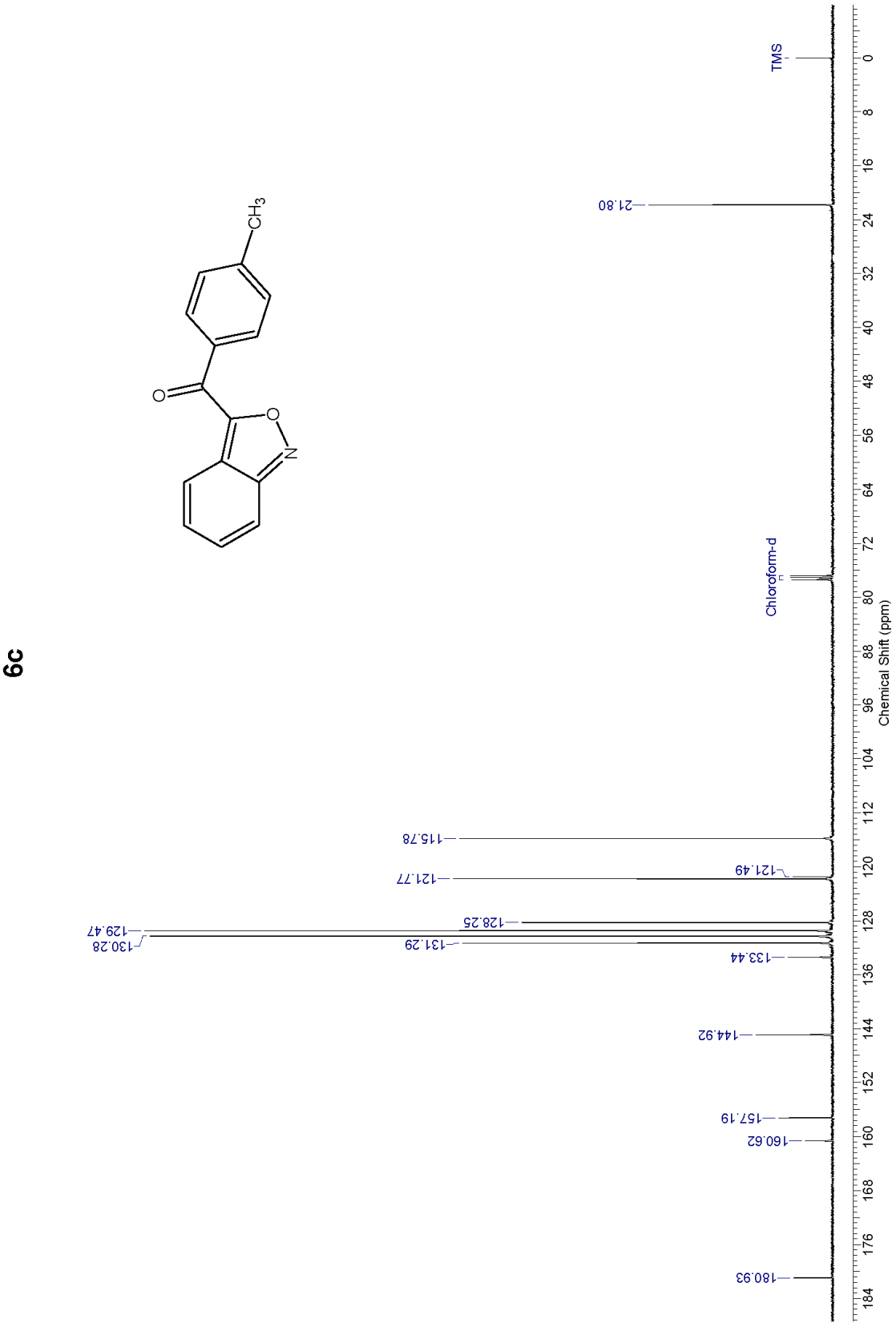
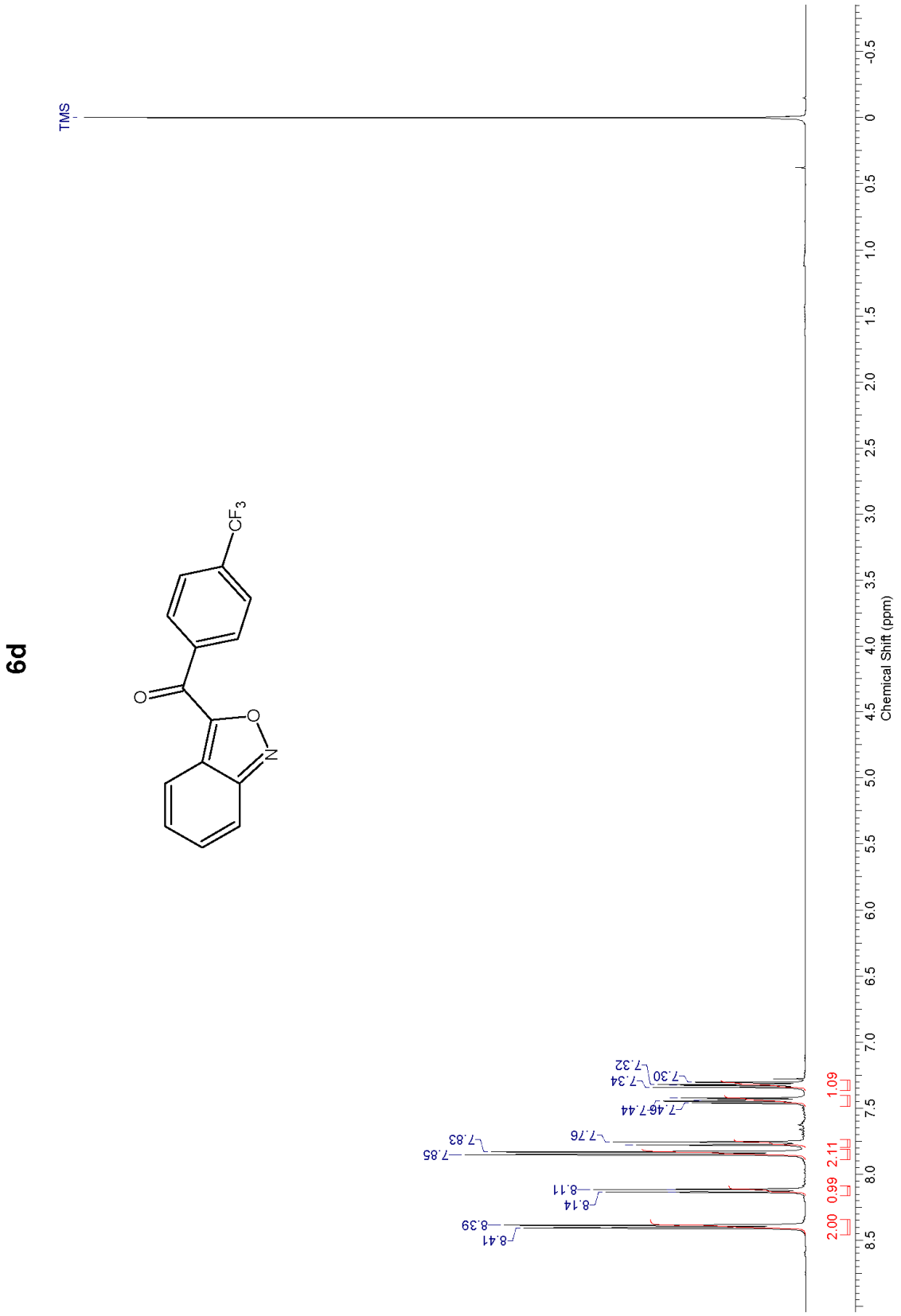
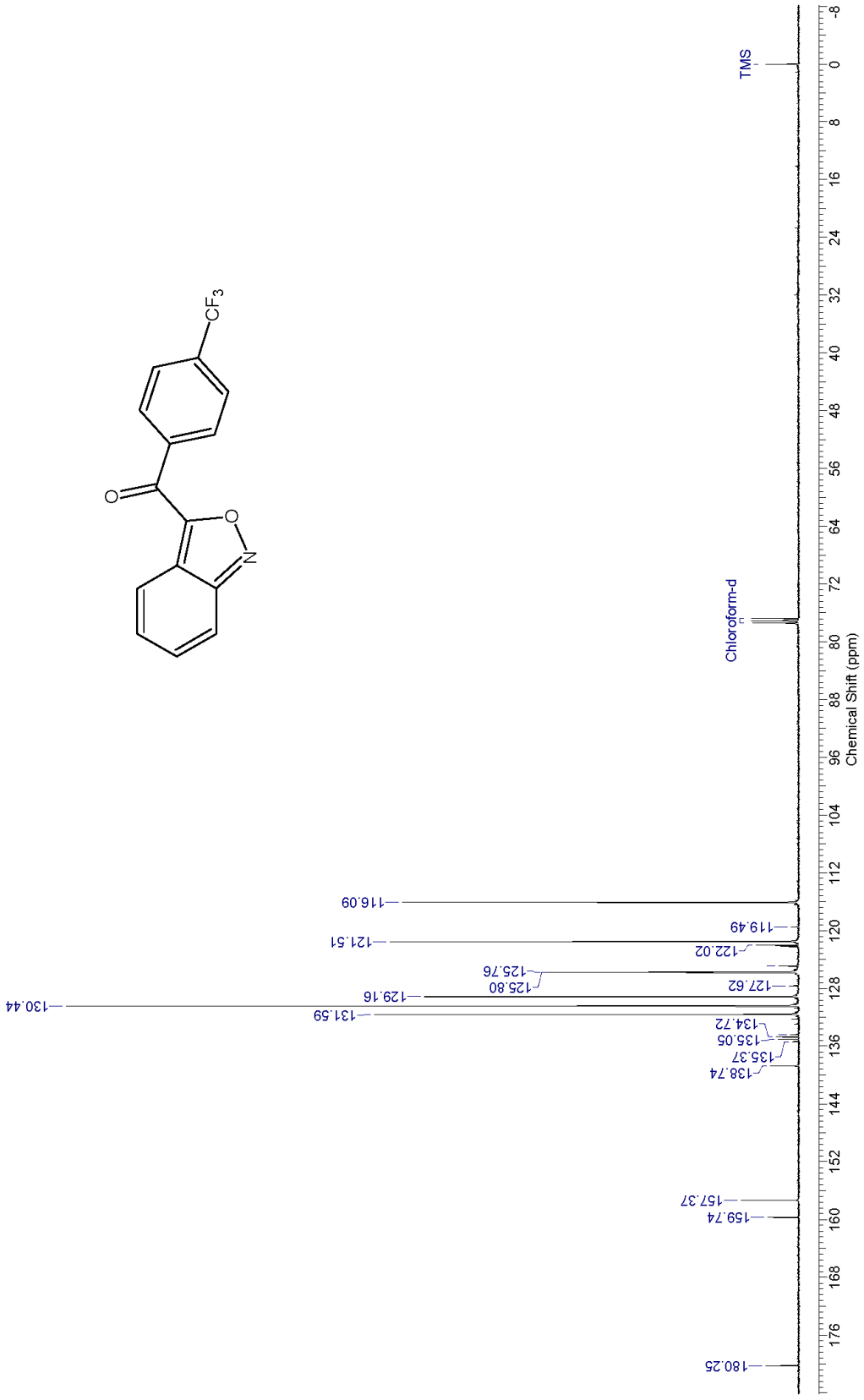
2.45
3.00
2.83
0.82
1.78
8.21
8.19
8.12
8.10
7.74
7.72
7.40
7.37
7.36
7.34
7.27
7.25
7.25
Chemical Shift (ppm)

6c

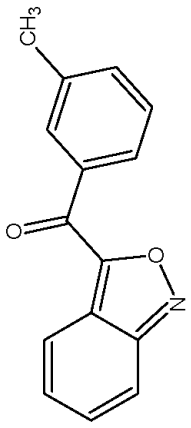

CH3
O
O
N
TMS
21.80
Chloroform-d
115.78
121.49
121.77
128.25
129.47
130.28
131.29
133.44
144.92
157.19
160.62
180.93
0
8
16
24
32
40
48
56
64
72
80
88
96
104
112
120
128
136
144
152
160
168
176
184
Chemical Shift (ppm)


6d
TMS
CF3
O
O
N
8.41
8.39
8.14
8.11
7.85
7.83
7.76
7.48
7.44
7.30
7.34
7.32
2.00
0.99
2.11
1.09
Chemical Shift (ppm)

6d


CF3
O
O
N
TMS
Chloroform-d
Chemical Shift (ppm)
180.25
159.74
157.37
138.74
135.37
135.05
134.72
131.59
130.44
129.16
125.80
125.76
121.51
122.02
119.49
116.09
127.62

6e


CH3
O
O
N

TMS
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7.46
7.48
7.42
7.44
7.40
7.38
7.28
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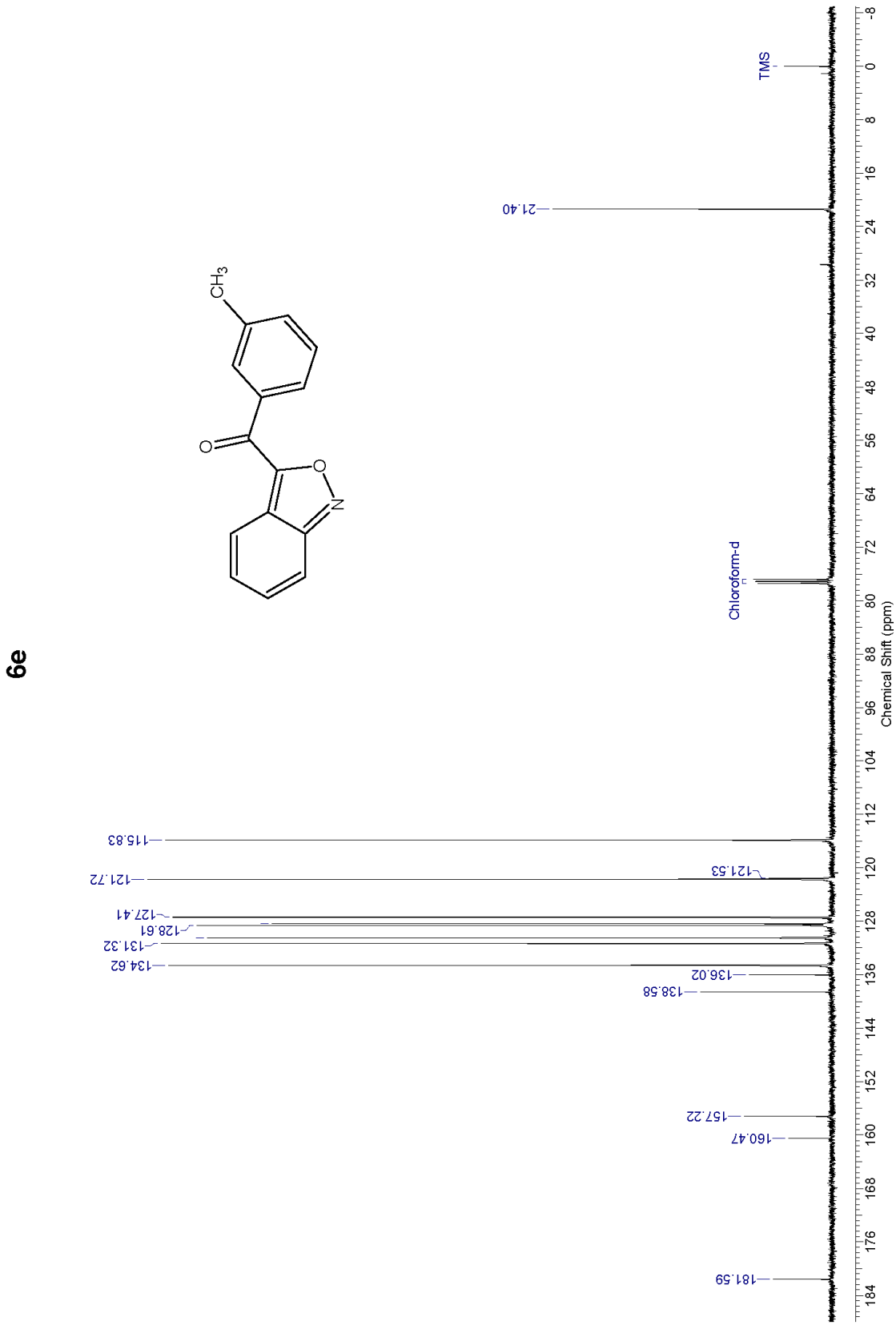
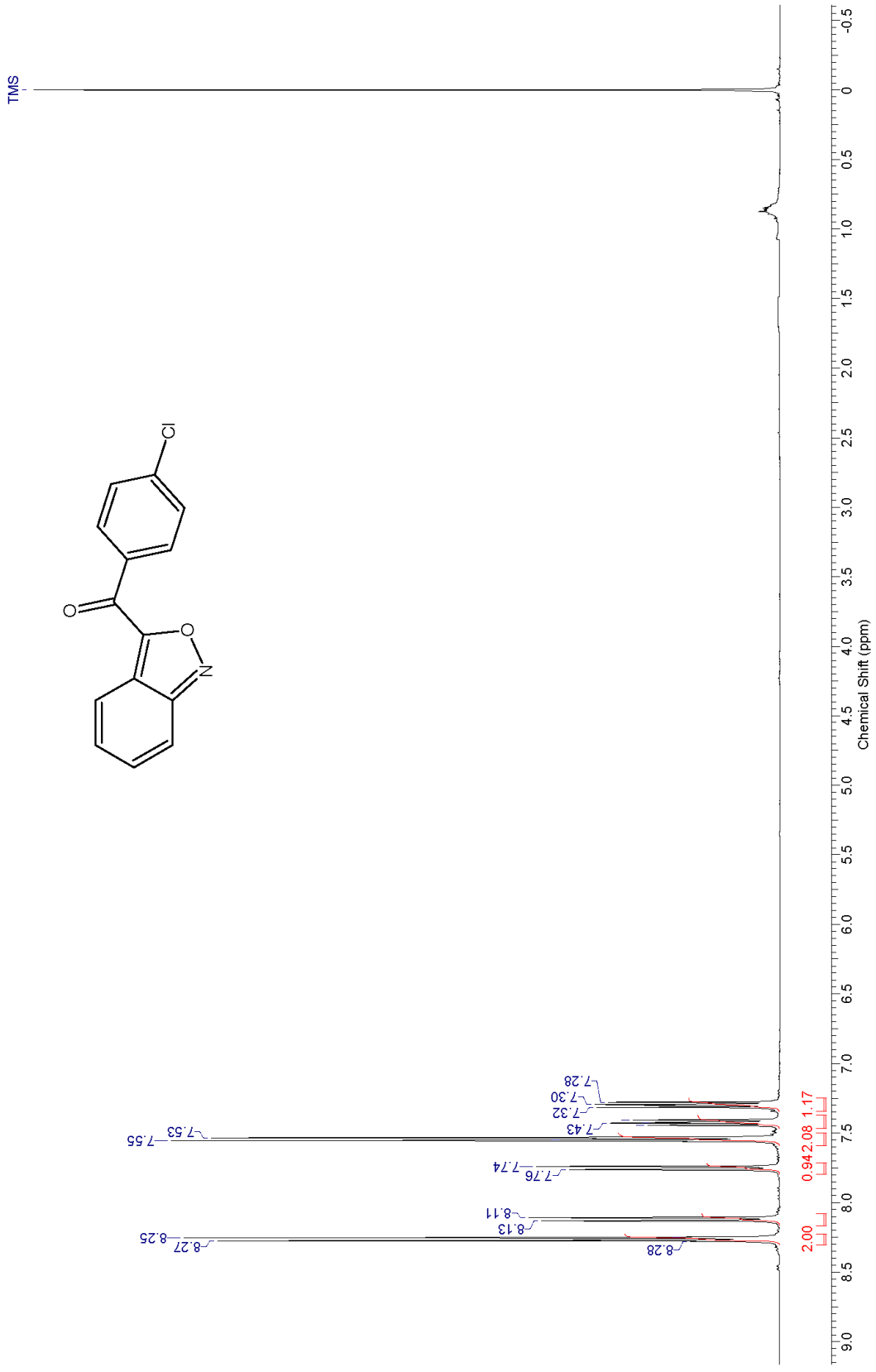
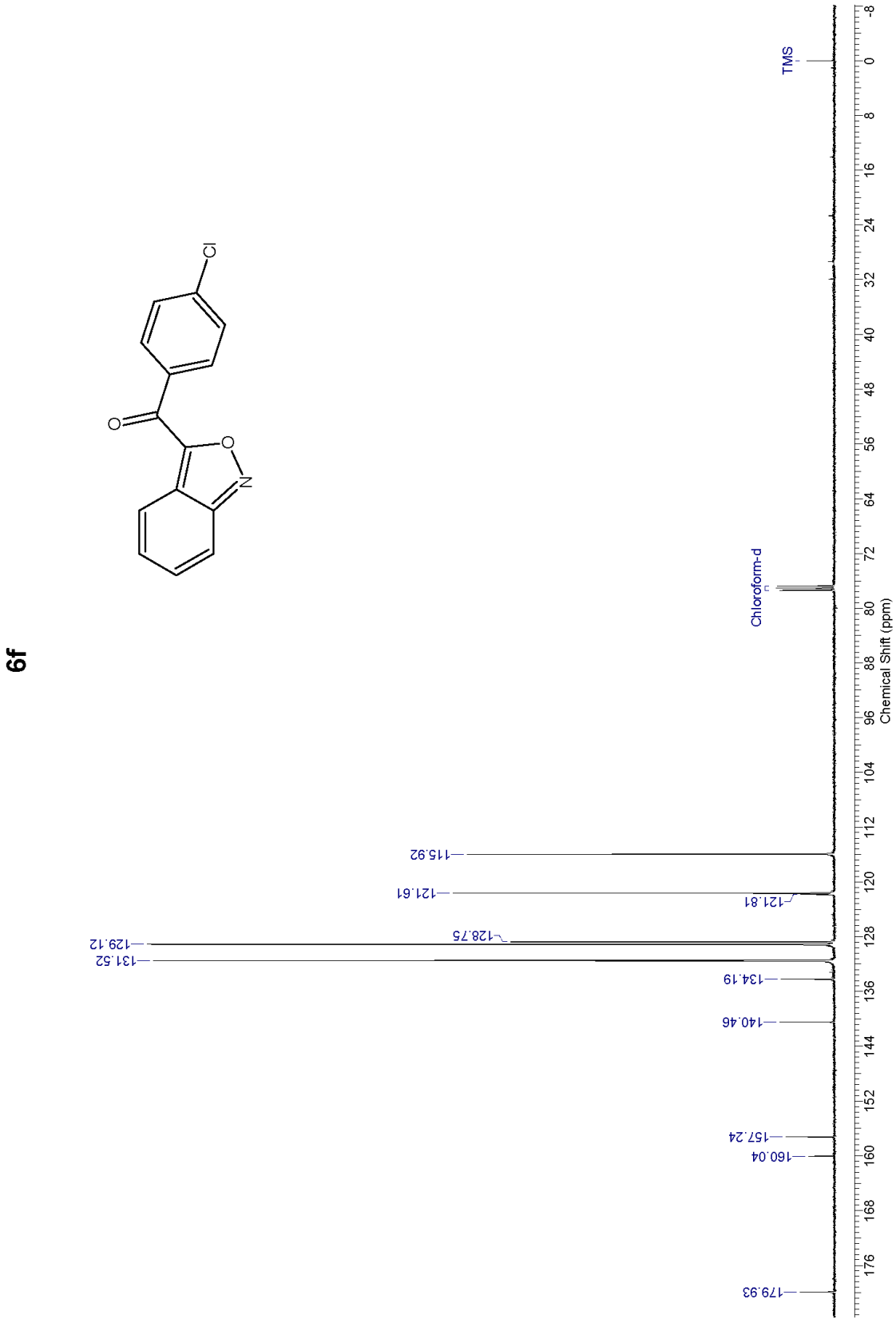
7.75
7.75
7.73
7.73
8.12
8.10
8.06
3.07
3.30
1.23
1.00
3.00
Chemical Shift (ppm)


6e
CH3
O
O
N
TMS
Chloroform-d
21.40
115.83
121.72
121.53
127.41
128.61
131.32
134.62
136.02
138.58
157.22
160.47
181.59
Chemical Shift (ppm)

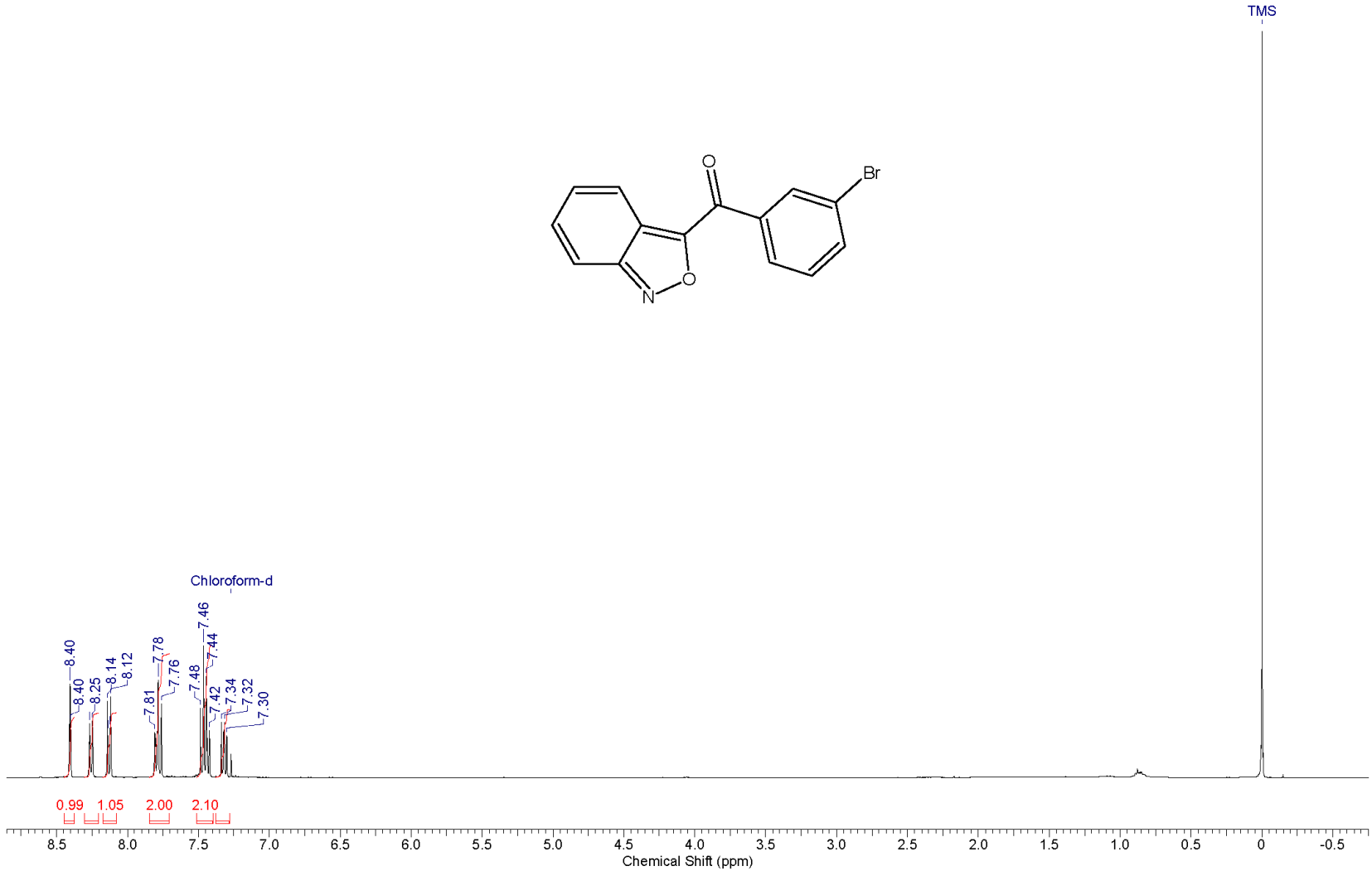
6f


Cl
O
O
N
TMS
8.28
8.27
8.25
8.13
8.11
7.76
7.74
7.55
7.53
7.43
7.32
7.30
7.28
2.00
0.94
2.08
1.17
Chemical Shift (ppm)

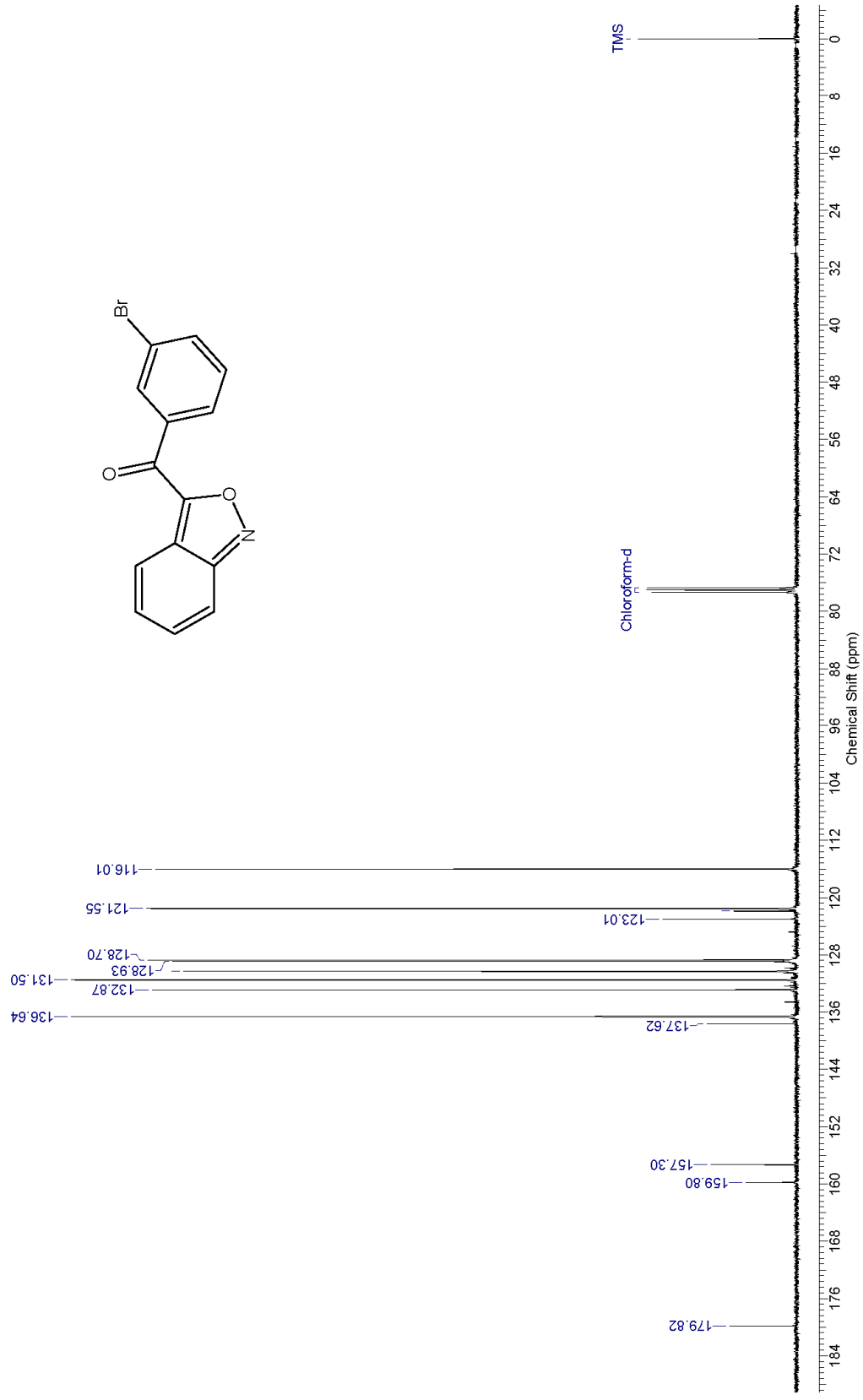
6f

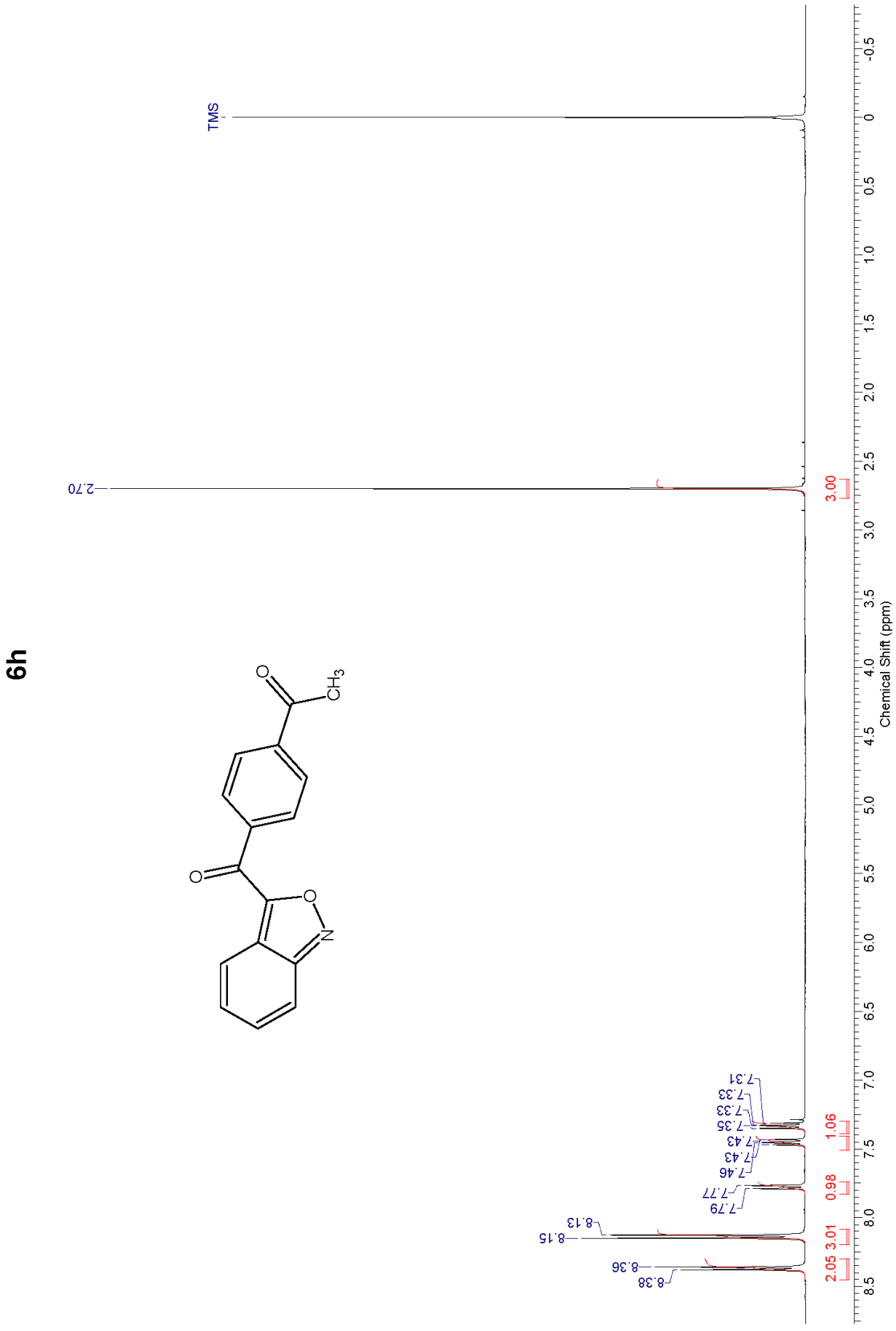

Cl
O
O
N
TMS
Chloroform-d
179.93
160.04
157.24
140.46
134.19
131.52
129.12
128.75
121.81
121.61
115.92
Chemical Shift (ppm)

6g

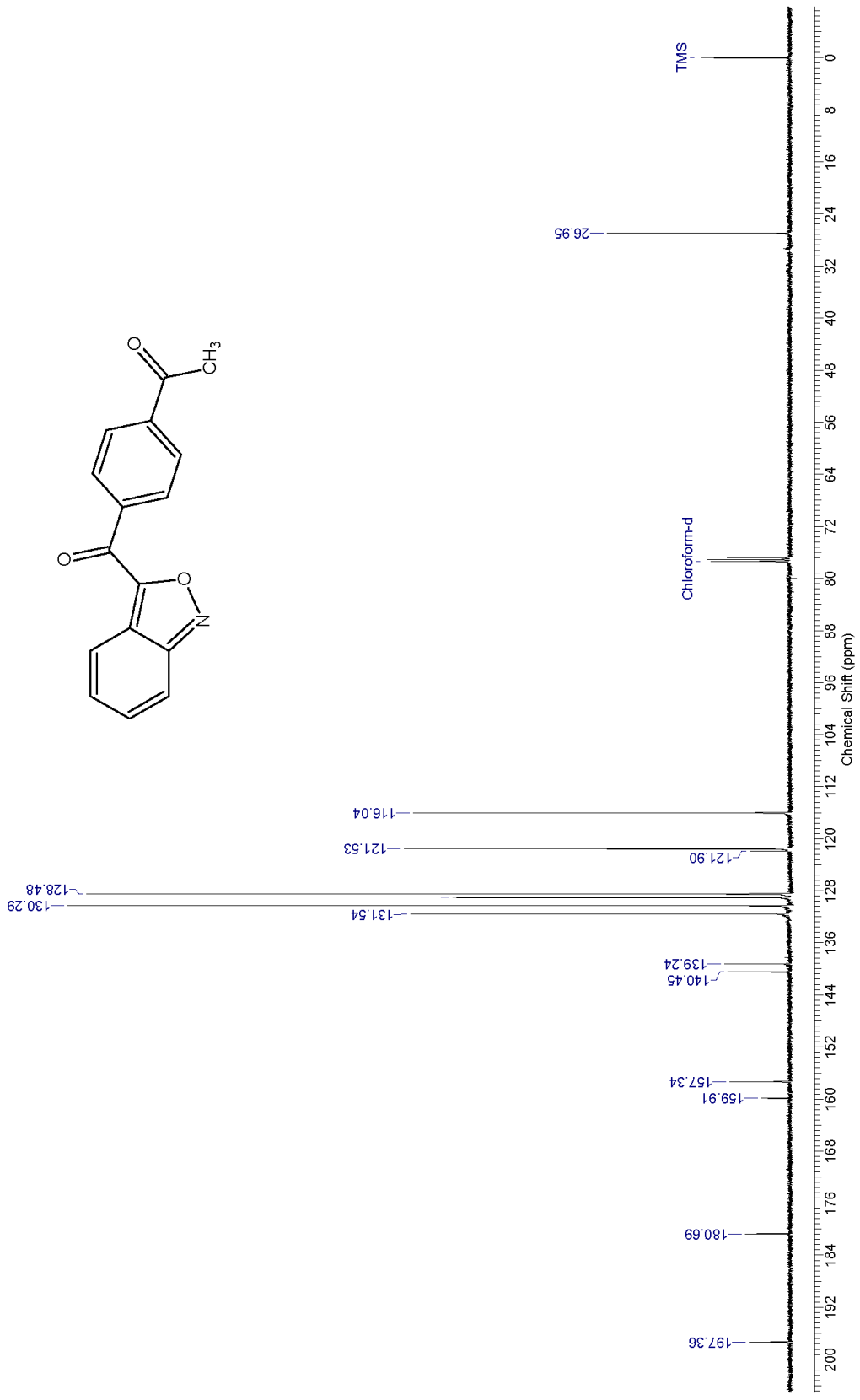

TMS
Chloroform-d
8.40
8.40
8.25
8.14
8.12
7.81
7.78
7.76
7.48
7.46
7.44
7.42
7.34
7.32
7.30
0.99
1.05
2.00
2.10
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
-0.5
Chemical Shift (ppm)

6g

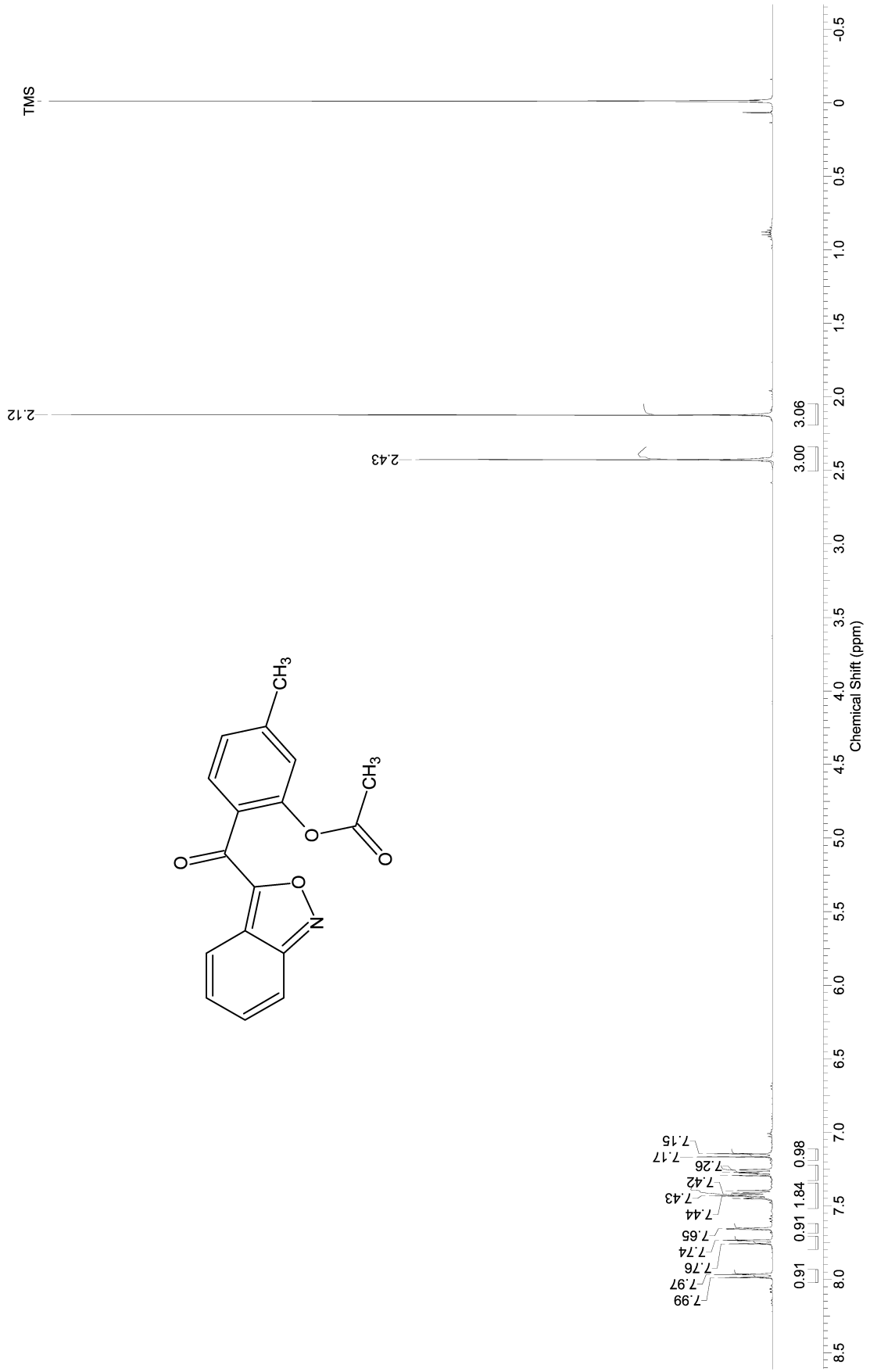

Br
O
O
N
TMS
Chloroform-d
179.82
159.80
157.30
137.62
136.64
132.87
131.50
128.93
128.70
123.01
121.55
116.01
Chemical Shift (ppm)


6h
TMS
2.70
3.00
8.38
8.36
8.15
8.13
7.79
7.77
7.46
7.43
7.43
7.35
7.33
7.33
7.31
2.05
3.01
0.98
1.06
Chemical Shift (ppm)

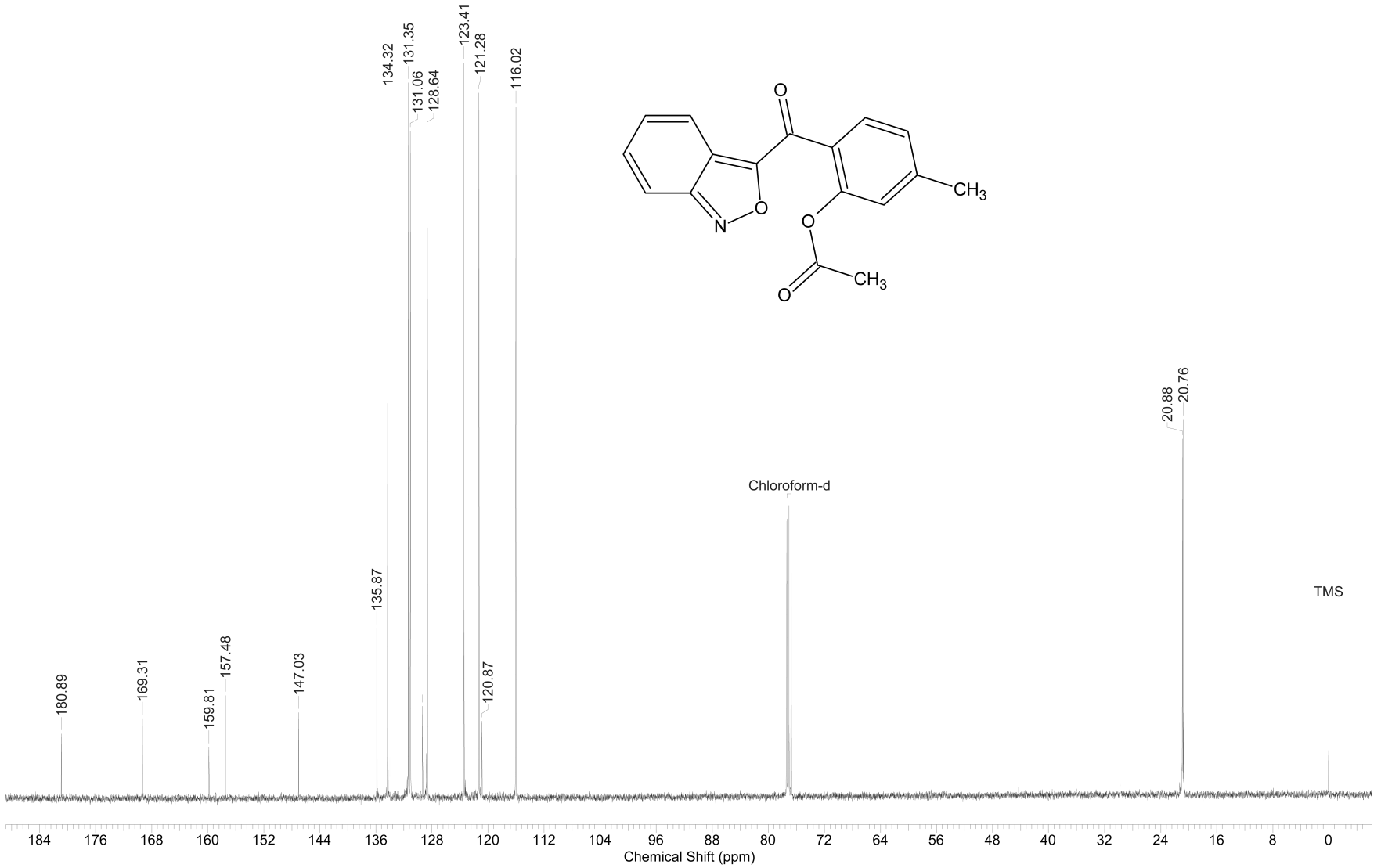
6h


O
CH3
O
O
N
TMS
26.95
Chloroform-d
116.04
121.53
121.90
128.48
130.29
131.54
139.24
140.45
157.34
159.91
180.69
197.36
0
8
16
24
32
40
48
56
64
72
80
88
96
104
112
120
128
136
144
152
160
168
176
184
192
200
Chemical Shift (ppm)

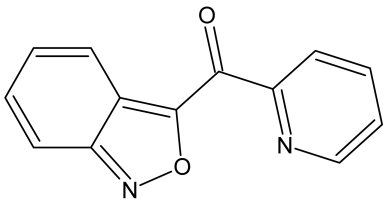
6i


TMS
2.12
2.43
7.99
7.97
7.76
7.74
7.65
7.44
7.43
7.42
7.26
7.17
7.15
0.91
0.91
1.84
0.98
3.00
3.06
Chemical Shift (ppm)

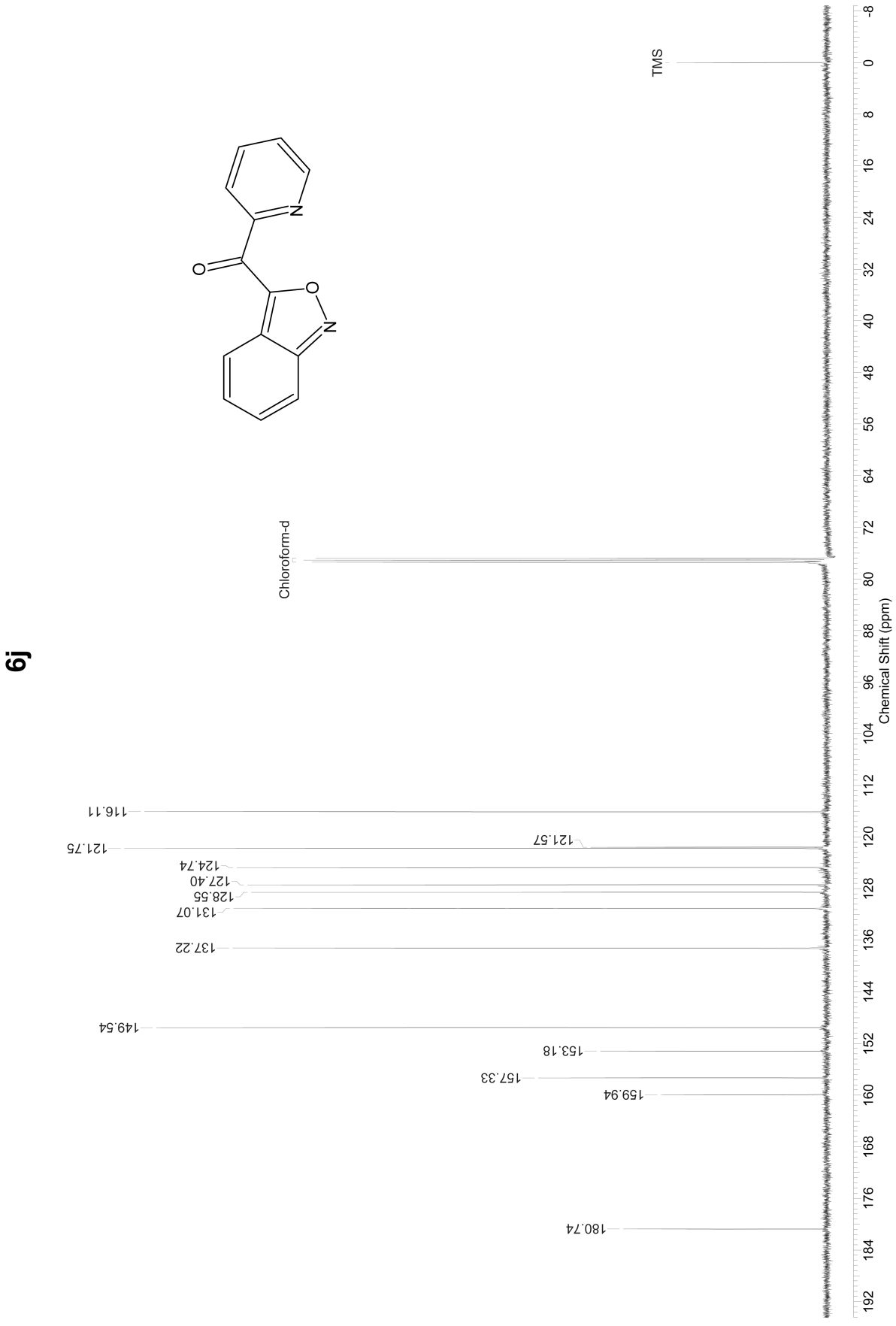
6i


134.32
131.35
131.06
128.64
123.41
121.28
116.02
O
O
N
O
O
CH3
CH3
O
20.88
20.76
Chloroform-d
TMS
135.87
180.89
169.31
159.81
157.48
147.03
120.87
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

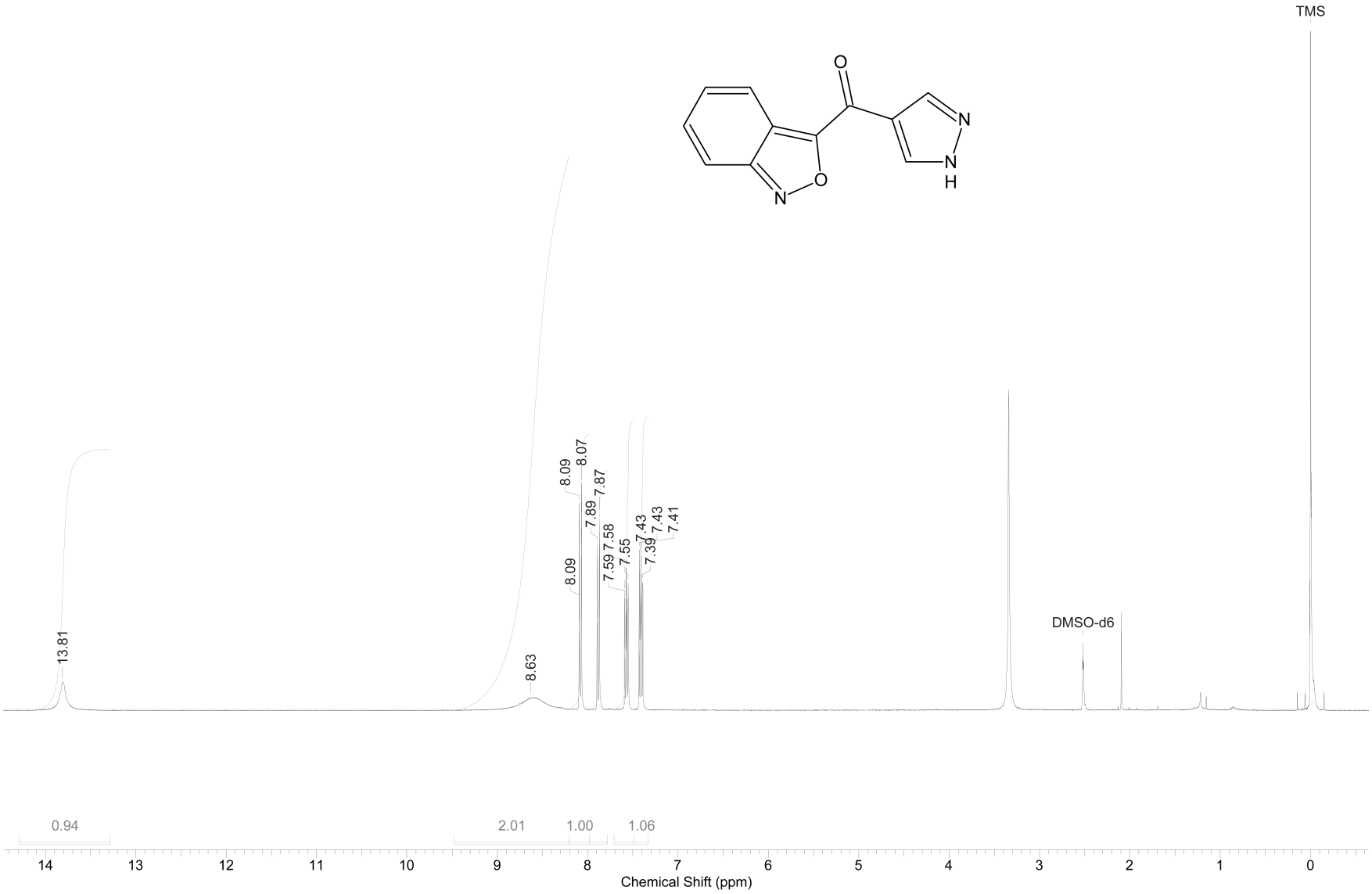
6j


O
N
O
N

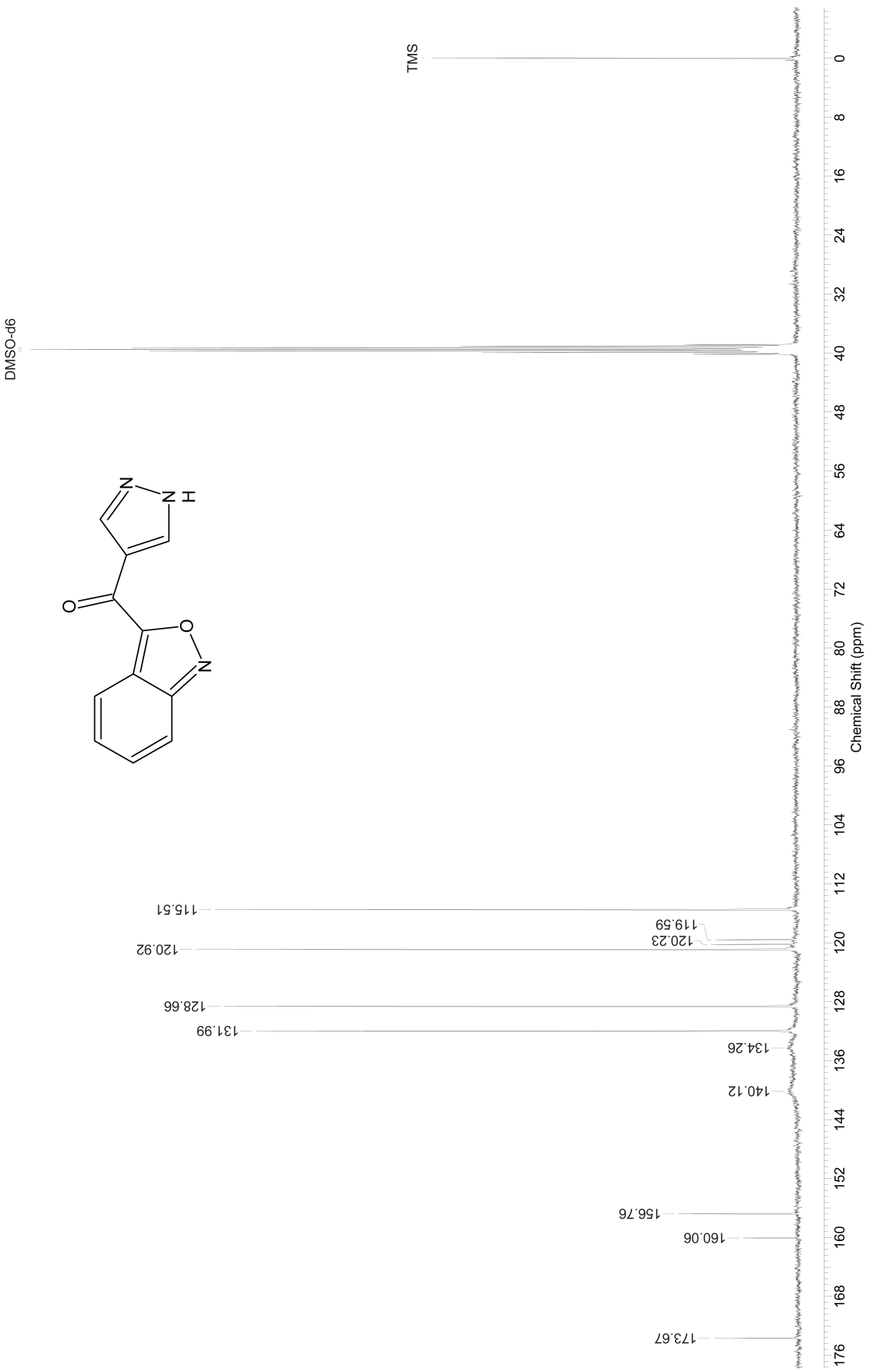
TMS
8.88
8.87
8.23
8.21
8.09
8.07
7.98
7.96
7.77
7.61
7.60
7.42
7.30
7.28
7.27
1.00
1.04
1.06
1.05
1.10
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
-0.5
Chemical Shift (ppm)


6j
TMS
Chloroform-d
180.74
159.94
157.33
153.18
149.54
137.22
131.07
128.55
127.40
124.74
121.75
121.57
116.11
-8
0
8
16
24
32
40
48
56
64
72
80
88
96
104
112
120
128
136
144
152
160
168
176
184
192
Chemical Shift (ppm)

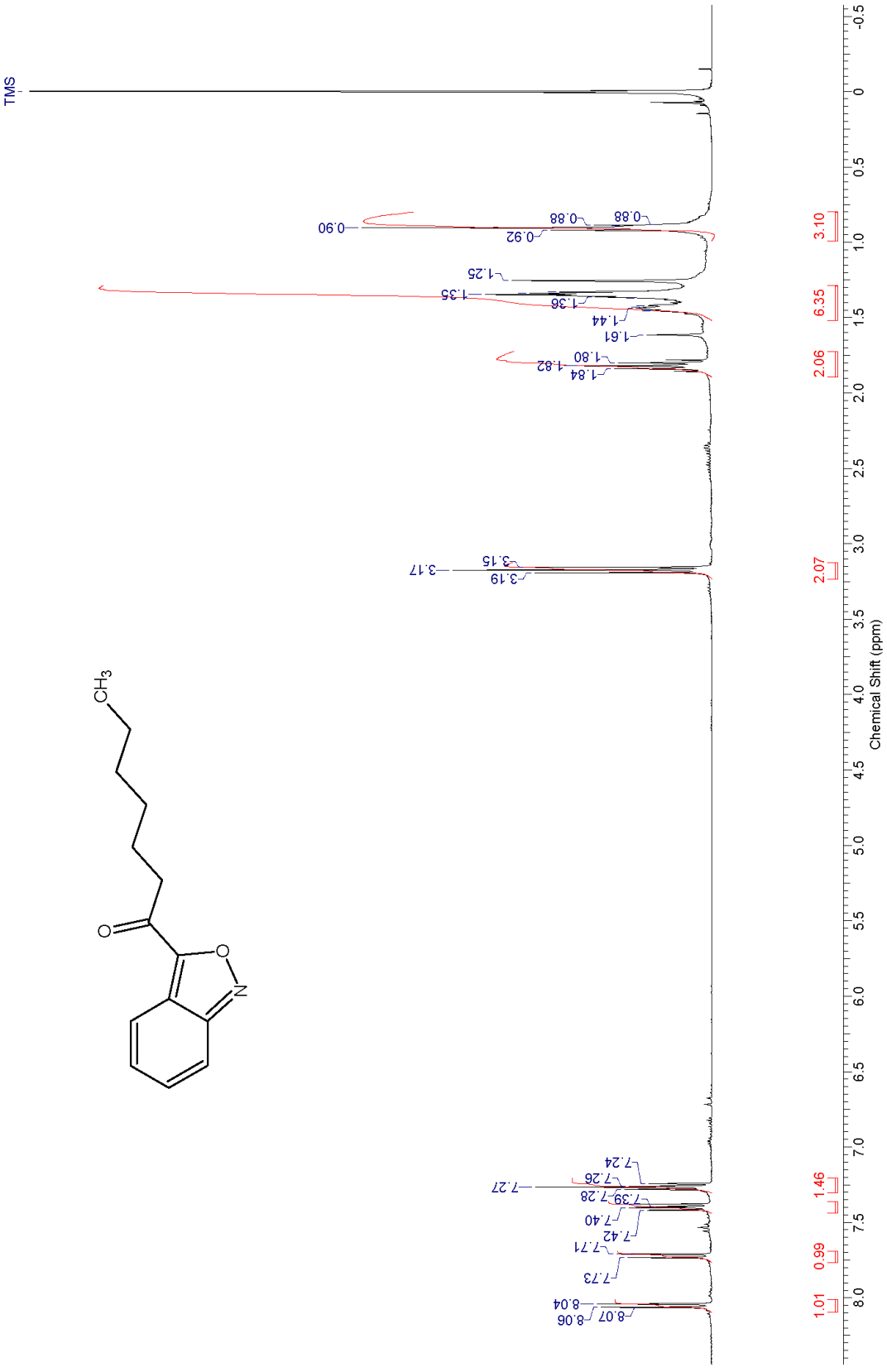
6k

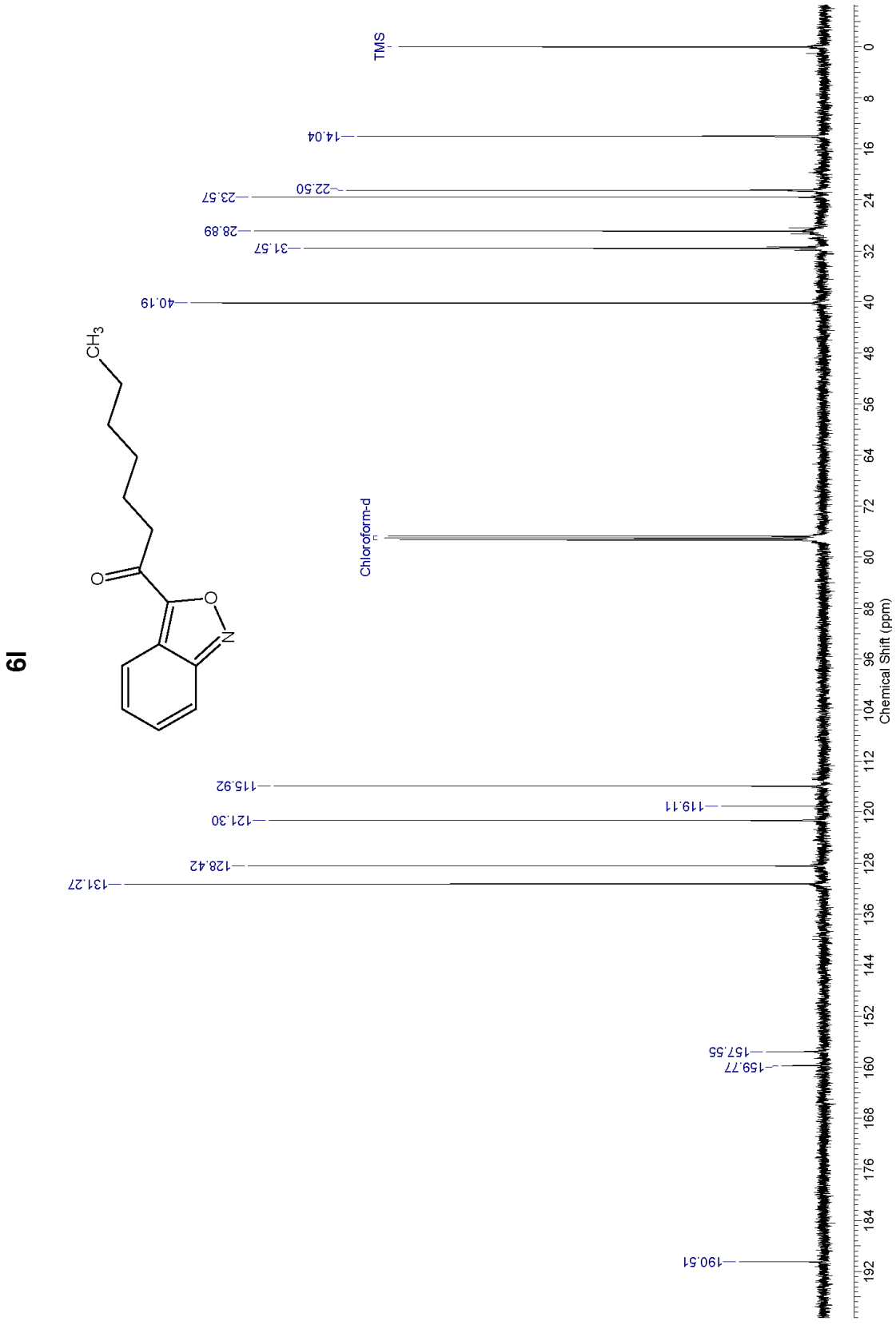

TMS
O
N
N
H
O
N
13.81
8.63
8.09
8.07
7.87
7.89
7.58
7.55
7.59
8.09
7.43
7.43
7.39
7.41
DMSO-d6
0.94
2.01
1.00
1.06
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

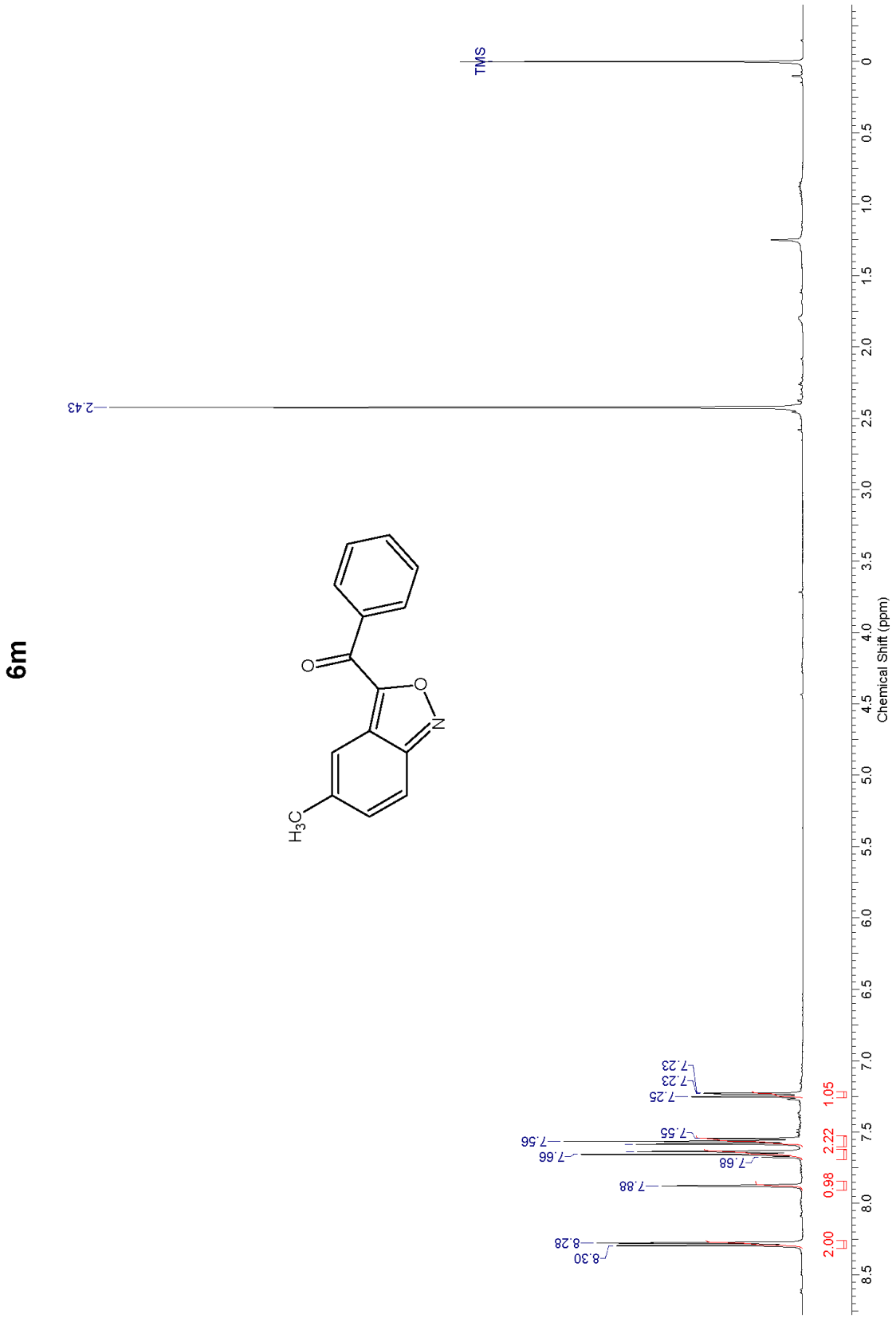
6k

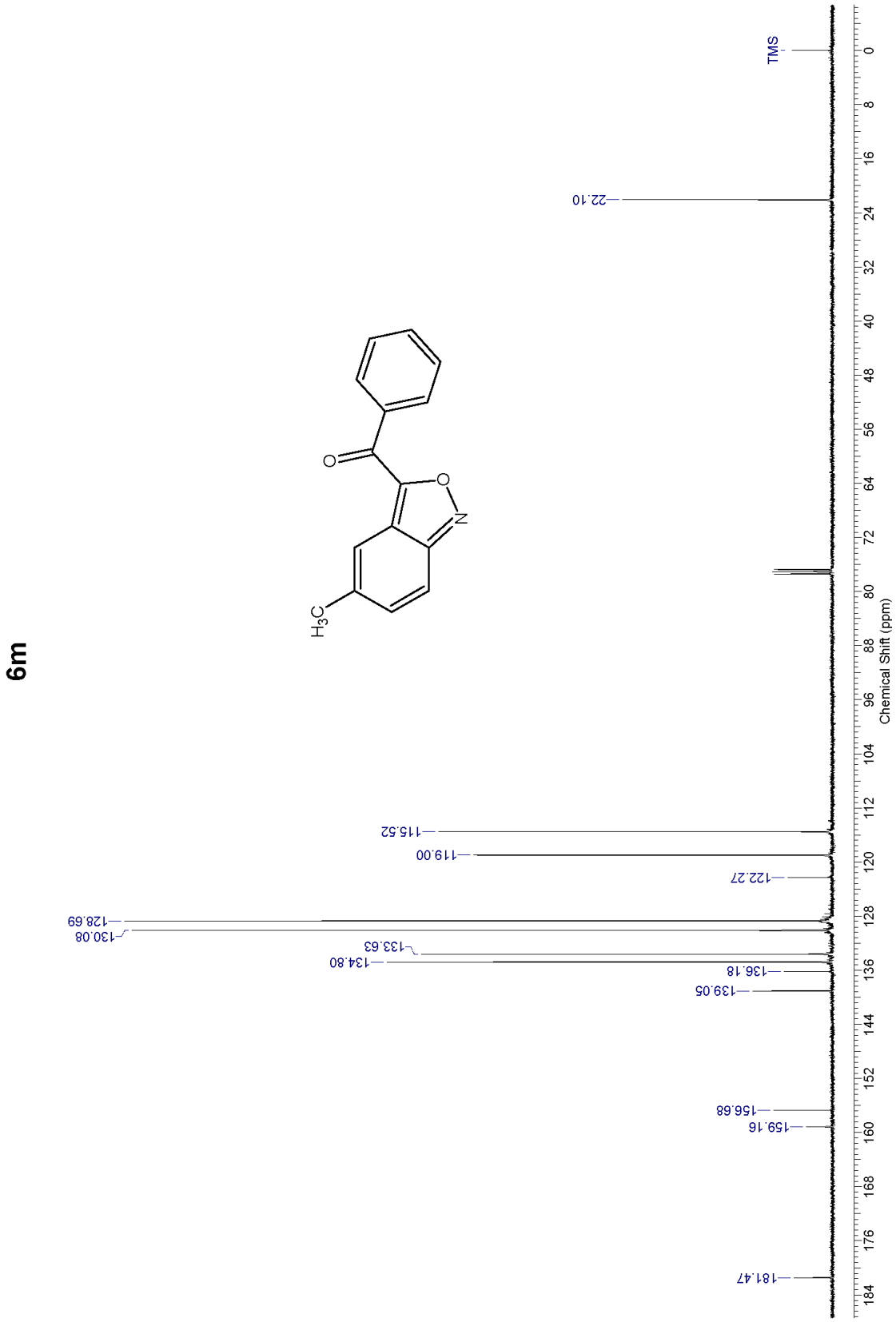

DMSO-d6
TMS
115.51
120.92
128.66
131.99
134.26
140.12
156.76
160.06
173.67
119.59
120.23
Chemical Shift (ppm)

6l

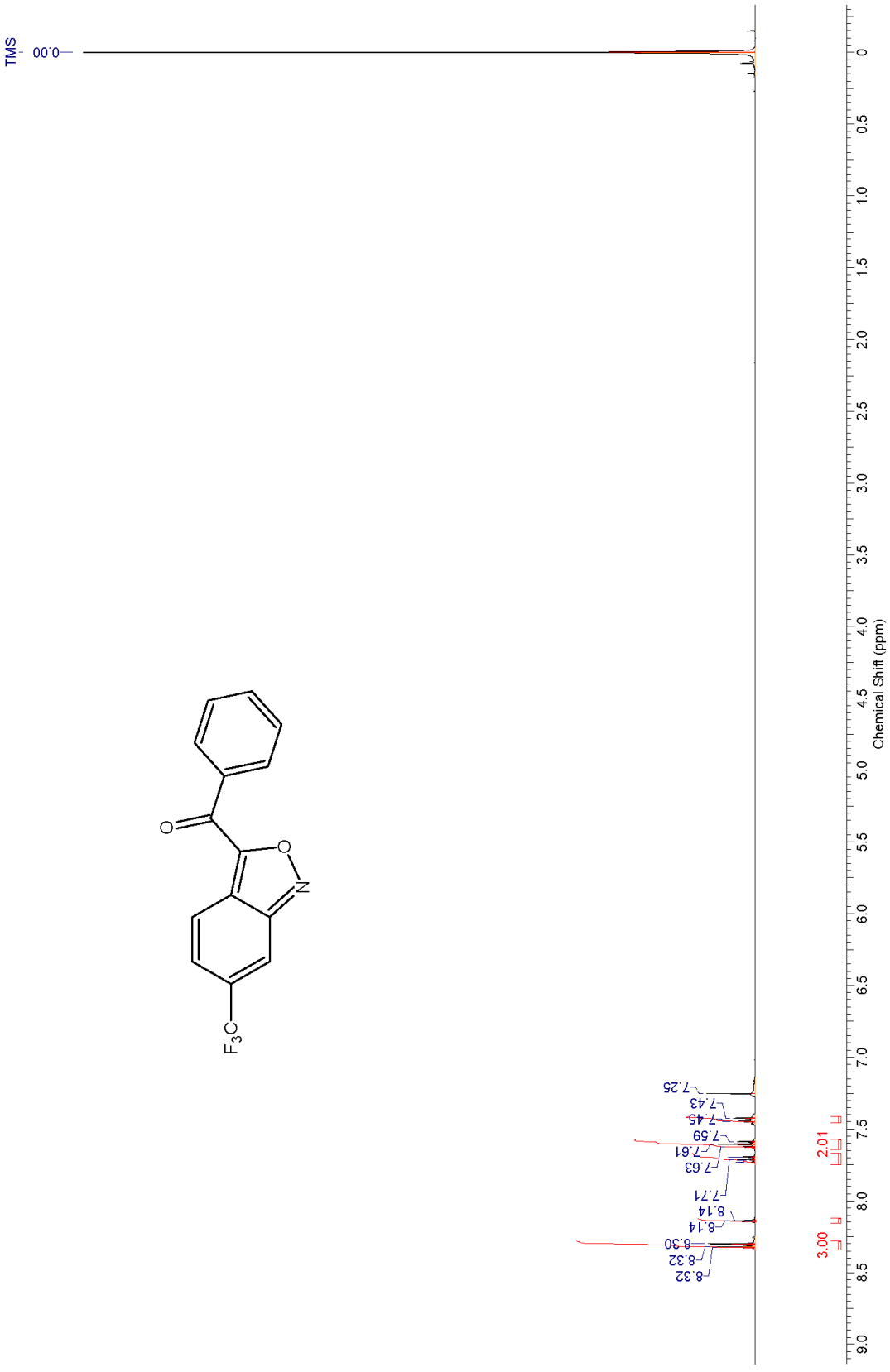

TMS
0.90
0.88
0.92
0.88
1.25
1.35
1.36
1.44
1.61
1.80
1.82
1.84
3.15
3.17
3.19
7.24
7.26
7.27
7.28
7.39
7.40
7.42
7.71
7.73
8.04
8.06
8.07
1.01
0.99
1.46
2.07
2.06
6.35
3.10
Chemical Shift (ppm)


6l
CH3
O
O
N
TMS
Chloroform-d
14.04
22.50
23.57
28.89
31.57
40.19
115.92
119.11
121.30
128.42
131.27
157.55
159.77
190.51
0
8
16
24
32
40
48
56
64
72
80
88
96
104
112
120
128
136
144
152
160
168
176
184
192
Chemical Shift (ppm)

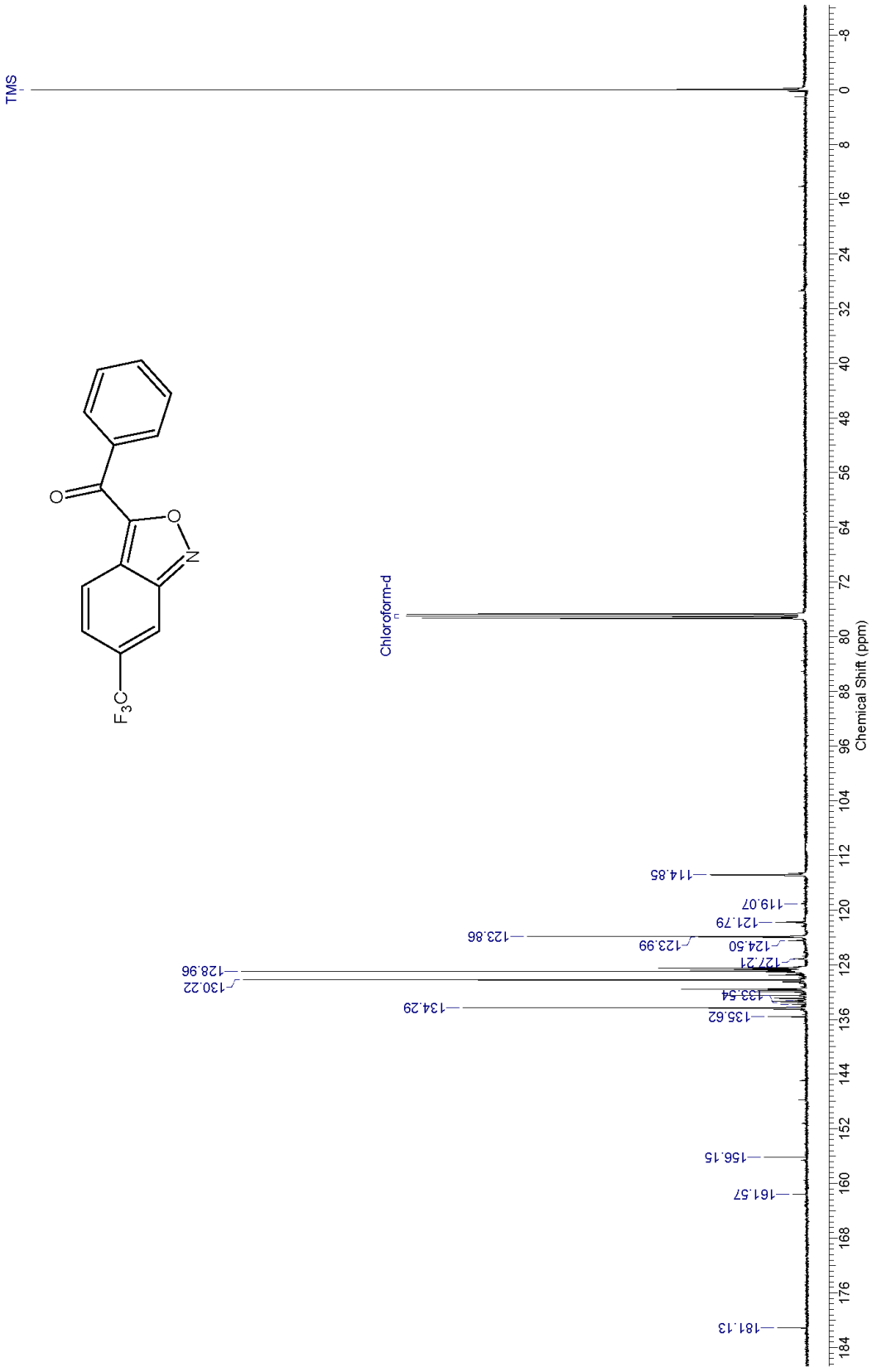

6m
TMS
2.43
7.23
7.23
7.25
7.55
7.56
7.66
7.68
7.88
8.28
8.30
2.00
0.98
2.22
1.05
Chemical Shift (ppm)


6m
TMS
22.10
115.52
119.00
122.27
128.69
130.08
133.63
134.80
136.18
139.05
156.68
159.16
181.47
Chemical Shift (ppm)
O
O
N
H3C

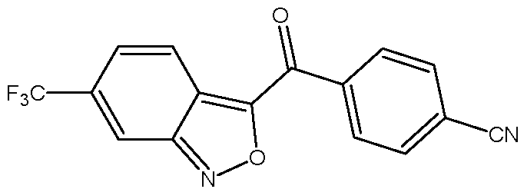
6n


TMS
0.00
8.32
8.32
8.30
8.14
8.14
7.71
7.63
7.61
7.59
7.45
7.43
7.25
3.00
2.01
Chemical Shift (ppm)

6n

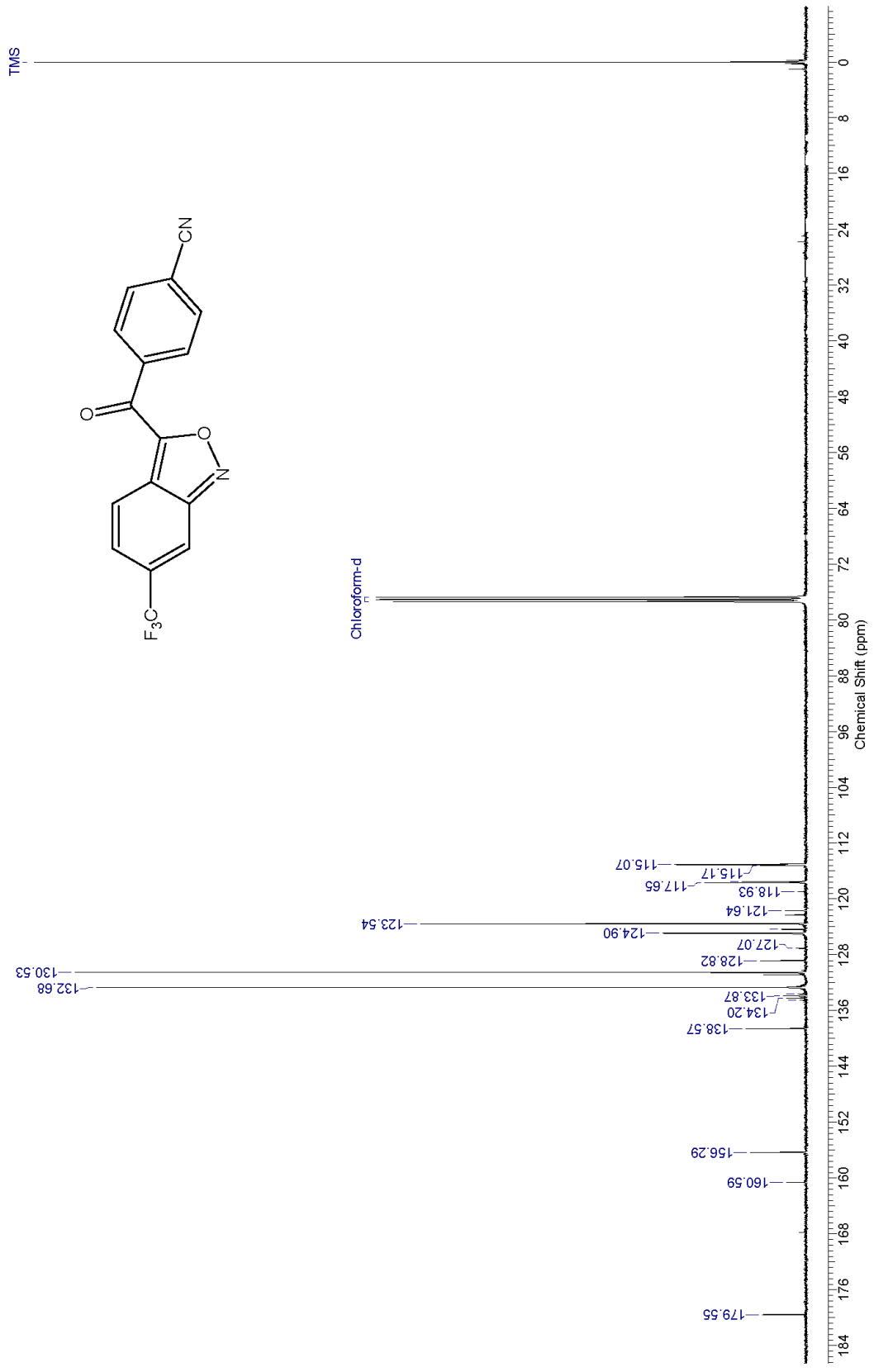

TMS
Chloroform-d
114.85
119.07
121.79
123.86
123.99
124.50
127.21
128.96
130.22
133.54
134.29
135.62
156.15
161.57
181.13
Chemical Shift (ppm)

6o

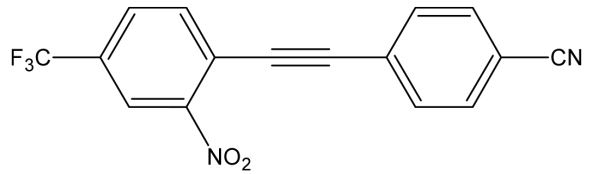

O
F3C
CN
O
N

TMS
8.44
8.42
8.33
8.18
8.18
7.93
7.91
7.90
7.52
7.49
2.00
0.98
2.03
1.06
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
0
Chemical Shift (ppm)

6o

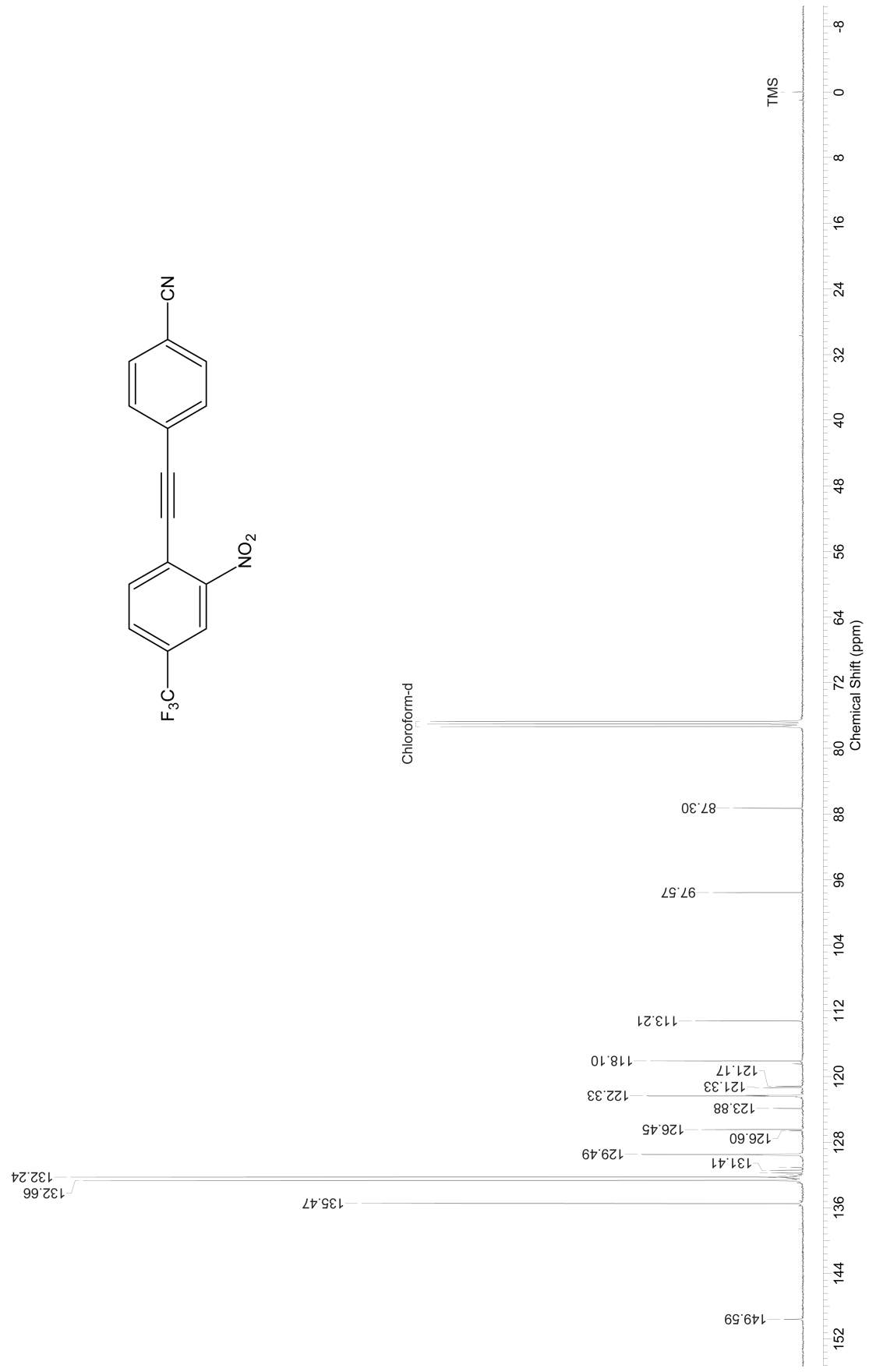

TMS
Chloroform-d
CN
O
O
N
F3C
179.55
160.59
156.29
138.57
134.20
133.87
132.68
130.53
128.82
127.07
124.90
123.54
121.64
118.93
117.65
115.17
115.07
0
8
16
24
32
40
48
56
64
72
80
88
96
104
112
120
128
136
144
152
160
168
176
184
Chemical Shift (ppm)

8o

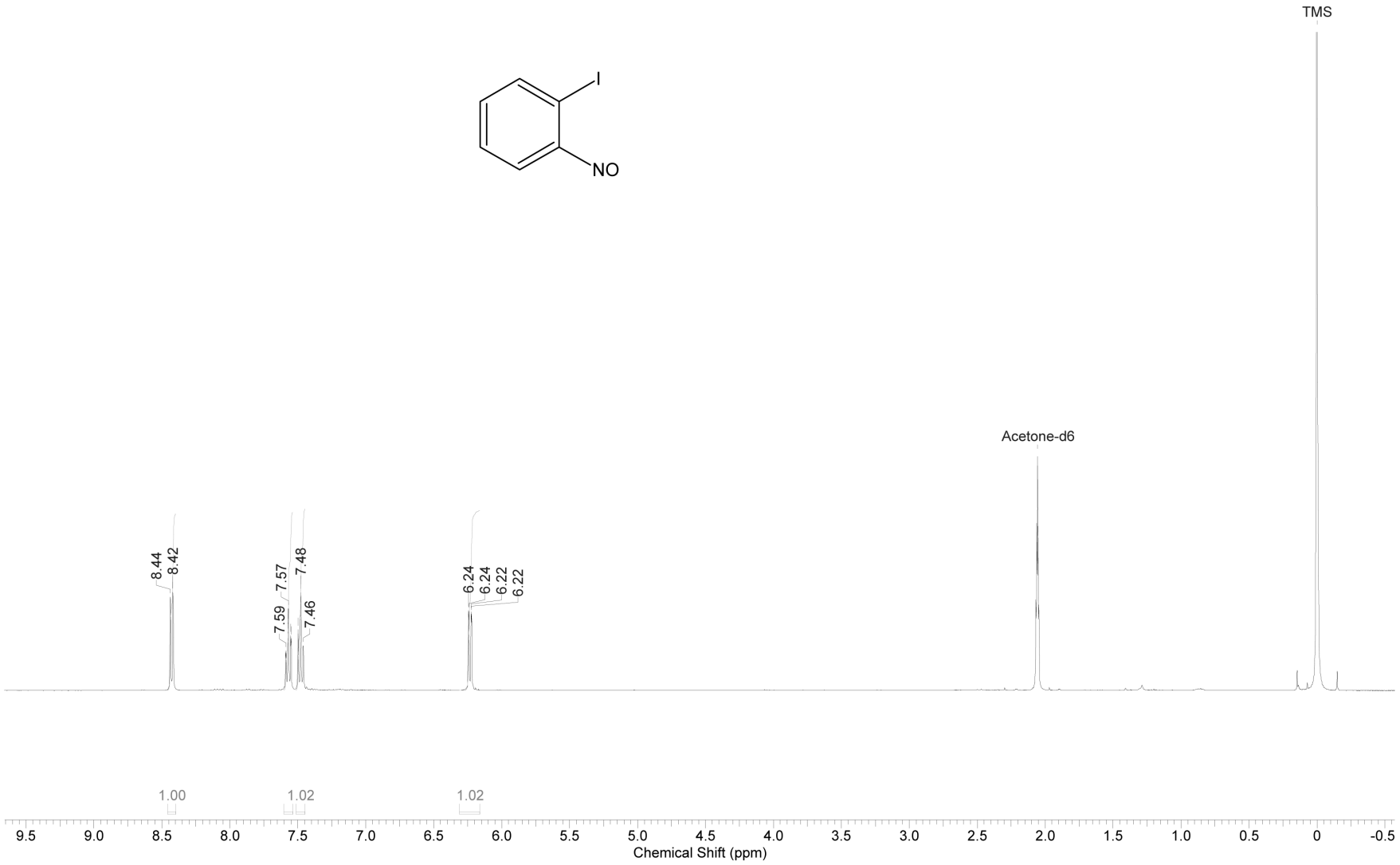

F3C
CN
NO2

TMS
7.70
7.89
8.40
1.00
2.04
4.01
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
0
-0.5
Chemical Shift (ppm)

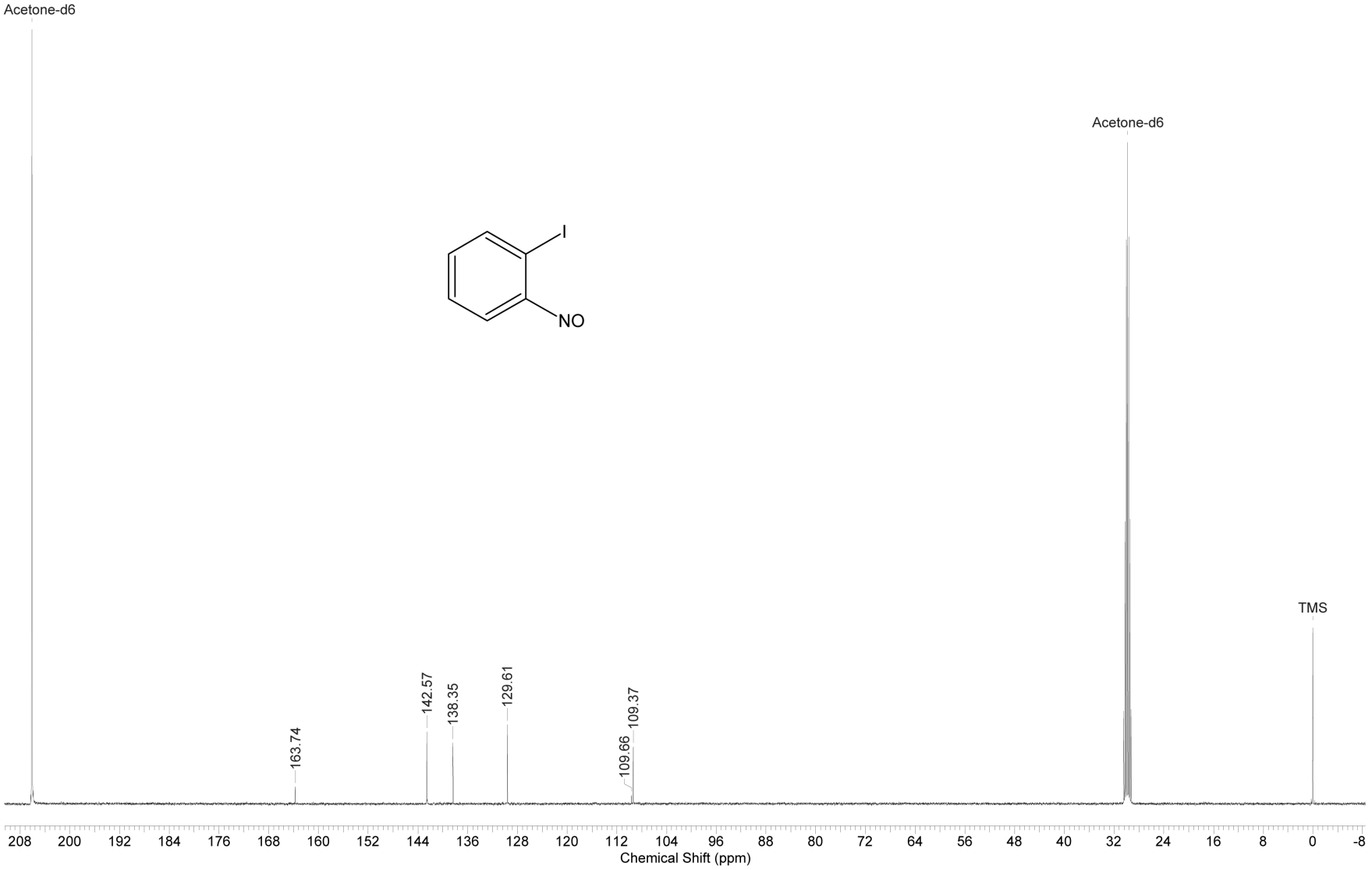
8o

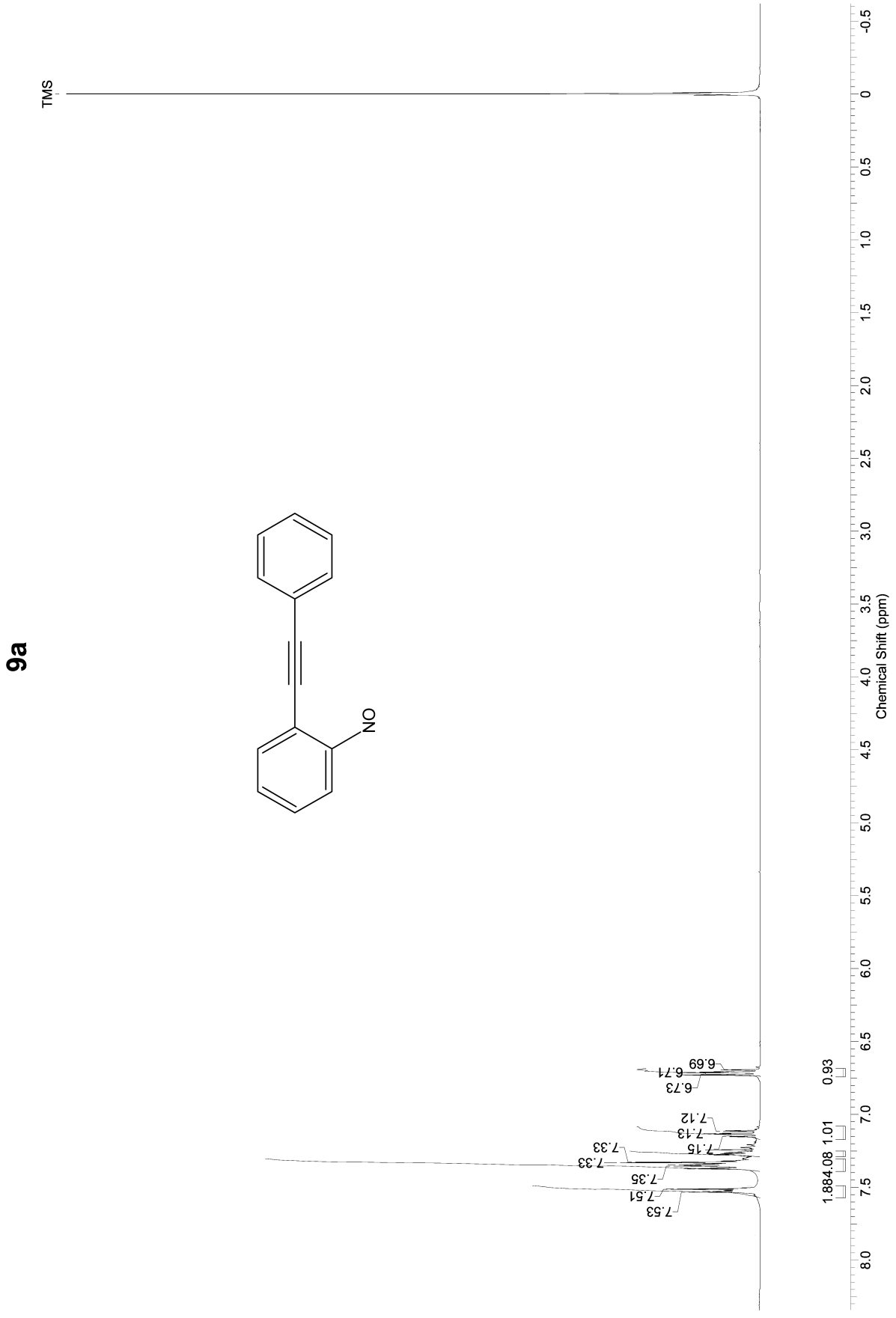

CN
NO2
F3C
Chloroform-d
TMS
149.59
135.47
132.66
132.24
131.41
129.49
126.60
126.45
123.88
122.33
121.33
121.17
118.10
113.21
97.57
87.30
Chemical Shift (ppm)

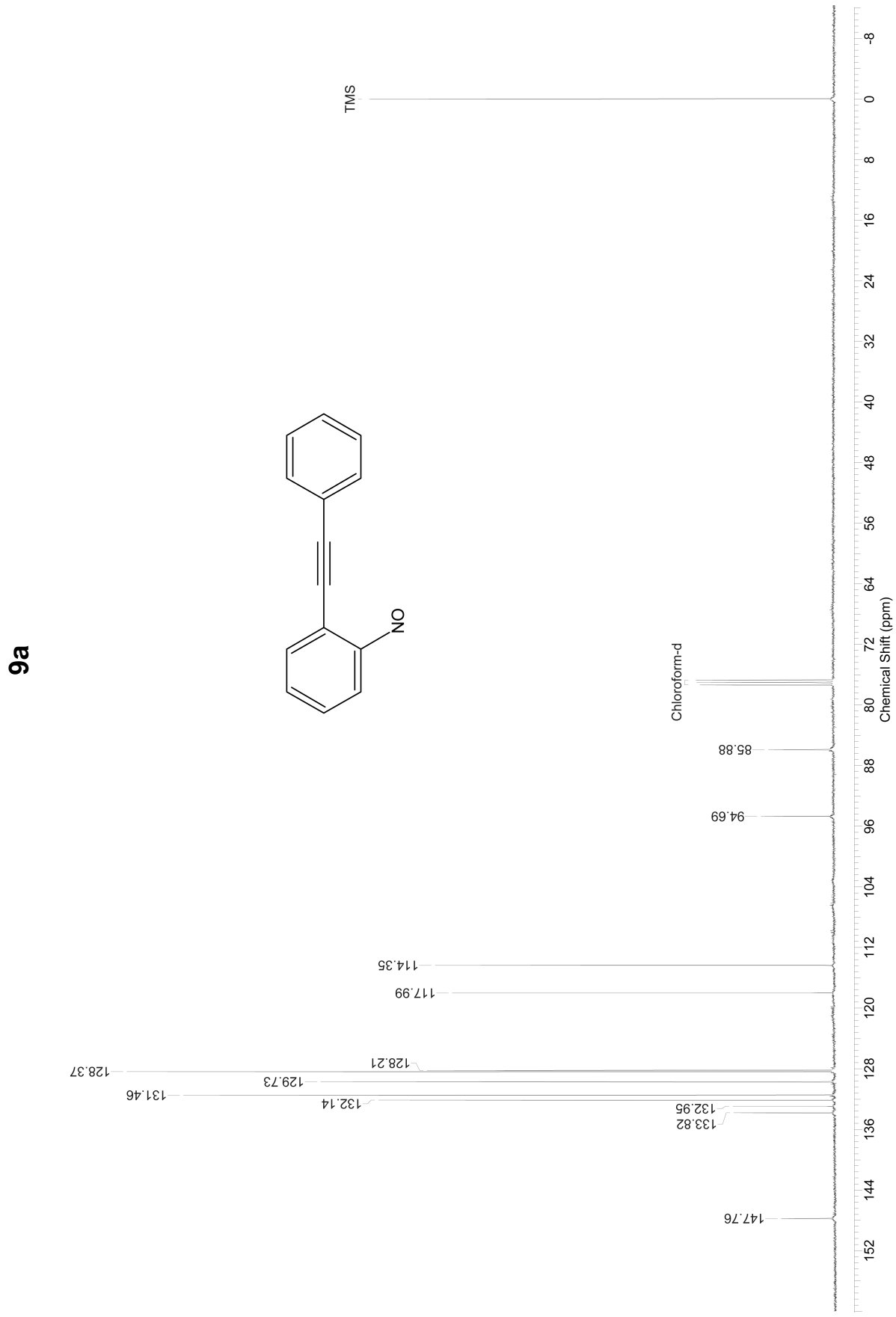
1-iodo-2-nitrosobenzene



1-iodo-2-nitrosobenzene




9a
NO
TMS
6.69
6.71
6.73
7.12
7.13
7.15
7.33
7.33
7.35
7.51
7.53
1.88
4.08
1.01
0.93
Chemical Shift (ppm)


9a
NO
TMS
Chloroform-d
85.88
94.69
114.35
117.99
128.21
128.37
129.73
131.46
132.14
132.95
133.82
147.76
-8
0
8
16
24
32
40
48
56
64
72
80
88
96
104
112
120
128
136
144
152
Chemical Shift (ppm)