Fischer Indole Reaction in Batch and Flow Employing a Sulfonic Acid Resin: Synthesis of Pyrido[2,3-*a*]carbazoles

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GENERAL INFORMATION

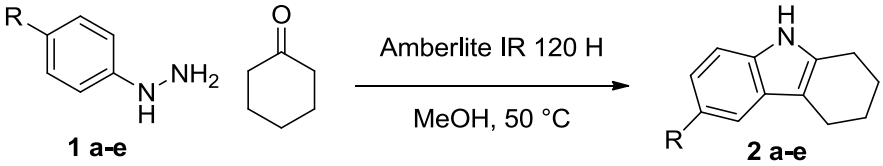
All reactions were carried out under an argon atmosphere in dry solvents under anhydrous conditions. Drying of organic extracts during workup of reactions was performed over anhydrous Na_2SO_4 except where otherwise stated. Evaporation of solvents was accomplished with a rotatory evaporator. Analytical thin layer chromatography was performed on SiO_2 (Merck silica gel 60 F_{254}) or on glass-backed plates pre-coated with silica and the spots were located with aqueous $KMnO_4$ or *p*-anisaldehyde. Chromatography refers to flash chromatography and was carried out on SiO_2 (silica gel 60 ACC, 35-75 µm, 230-240 mesh ASTM). NMR spectra were recorded in $CDCl_3$ on a Varian Mercury 400 MHz or Varian VNMRS 400 MHz. Chemical shifts of ^1H and ^{13}C NMR spectra are reported in ppm downfield (δ) from Me_4Si. All NMR data assignments are supported by COSY and HSQC experiments.

Melting points were performed on recrystallized solids and are uncorrected.

EXPERIMENTAL PROCEDURES

Batch Reactions

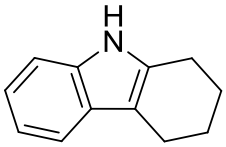
General procedure A:



1 a-e **2 a-e**

To a stirring solution of cyclohexanone (1 equiv) and solid acid catalyst Amberlite IR 120 H® (5 equiv w/w) in MeOH (0.1-0.5 M) at 50 °C, was added phenylhydrazine **1** or phenylhydrazine hydrochloric salt **1·HCl** (1.1 equiv). The mixture was left stirring at 50 °C for the indicated time. After cooling, the reaction mixture was filtered and the resin was washed with CH_2Cl_2 and MeOH and the crude product was purified by crystallization from MeOH/H_2O to afford the pure carbazole.

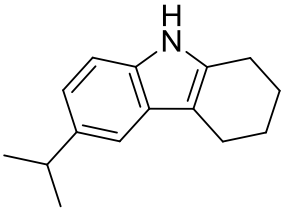
2,3,4,9-Tetrahydro-1*H*-carbazole (2a)



Following the general procedure using cyclohexanone (260 µL, 2.5 mmol) and phenylhydrazine **1a** (270 µL, 2.75 mmol) for 1 h, **2a** was isolated as a pale yellowish solid (415 mg, 97%) whose data proved consistent with the literature.[1]

Mp**:** 115-119 °C (lit.[1a] 119-120 °C); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.85-1.98 (m, 4H), 2.70-2.76 (m, 4H), 7.06-7.16 (m, 2H), 7.28 (br d, *J* = 7.5 Hz, 1H), 7.48 (br d, *J* =7.5 Hz, 1H) 7.63 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.1, 23.36, 23.40, 23.44, 110.3, 110.4, 117.9, 119.2, 121.1, 128.0, 134.2, 135.8

6-Isopropyl-2,3,4,9-tetrahydro-1*H*-carbazole (2b)



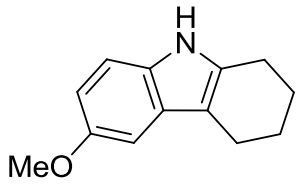
Following the general procedure using cyclohexanone (230 µL, 2.2 mmol) and *p*-isopropylphenylhydrazine hydrochloride salt **1b·HCl** (467 mg, 2.4 mmol) for 1.5 h, **2b** was isolated as a pale yellowish solid (445 mg, 95%) whose data proved consistent with the literature.[2]

Mp: 67-69 °C (lit.[2] 68-70 °C); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.34 (d, *J* = 7.0 Hz, 6 H), 1.87-1.98 (m, 4H), 2.69-2.77 (m, 4H), 3.04 (hep, *J* = 7.0 Hz, 1H), 7.04 (dd, *J* = 8.5, 2.0 Hz, 1H), 7.20 (d, *J* = 8.5 Hz, 1H), 7.34 (d, *J* = 2.0 Hz, 1H), 7.53 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.1, 23.39, 23.40, 23.5, 24.9, 34.4, 110.0, 110.2, 114.8, 120.1, 128.0, 134.3, 134.4, 140.0

[1] a) Welch W. M., *Synthesis*, **1977**, *9*, 645-646 b) Sun K., Liu S., Bec P. M., and Driver T. G., *Ang. Chem. Int. Ed.* **2011**, *50*, 1702-1706

[2] Yeung C. S., Ziegler R. E., Porco J. A., Jr. and Jacobsen E. N., *J. Am. Chem. Soc.*, **2014**, *136,* 13614-13617

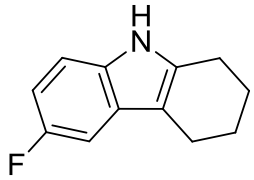
6-Methoxy-2,3,4,9-tetrahydro-1*H*-carbazole (2c)



Following the general procedure using cyclohexanone (230 µL, 2.2 mmol) and *p*-methoxyphenylhydrazine hydrochloride salt **1c·HCl** (442 mg, 2.5 mmol) for 2 h, **2c** was isolated as a pale pink solid (389 mg, 93%) whose data proved consistent with the literature.[3a]

Mp: 89-90 °C (lit. 91-92 °C); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.83-1.95 (m, 4H), 2.65-2.75 (m, 4H), 3.87 (s, 3H), 6.78 (dd, *J* = 8.5, 2.5 Hz, 1H), 6.94 (d, *J* = 2.5 Hz, 1H), 7.16 (d, *J* = 8.5 Hz, 1H), 7.56 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.1, 23.3, 23.4, 23.5, 56.1, 100.4, 110.1, 110.6, 111.1, 128.3, 130.9, 135.2, 154.0

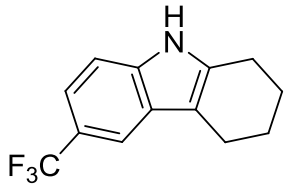
6-Fluoro-2,3,4,9-tetrahydro-1*H*-carbazole (2d)



Following the general procedure using cyclohexanone (230 µL, 2.2 mmol) and *p*-fluorophenylhydrazine hydrochloride salt **1d·HCl** (408 mg, 2.5 mmol) for 2 h, **2d** was isolated as a pale yellowish solid (389 mg, 93%) whose data proved consistent with the literature.[3]

Mp: 103-104 °C (lit.[3] 106-108 °C); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.83-1.96 (m, 4H), 2.64-2.74 (m, 4H), 6.85 (td, *J* = 9.5, 2.5 Hz, 1H), 7.10 (dd, *J* = 9.5, 2.5 Hz, 1H), 7.17 (dd, *J* = 9.0, 4.5 Hz, 1H), 7.65 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.0, 23.2, 23.3, 23.4, 103.0 (d, *J* = 23.5 Hz), 108.9 (d, *J* = 26.0 Hz), 110.6, 110.8 (d, *J* = 9.5 Hz), 128.3, 132.2, 136.3, 157.9 (d, *J* = 232 Hz)

6-Trifluoromethyl-2,3,4,9-tetrahydro-1*H*-carbazole (2e)



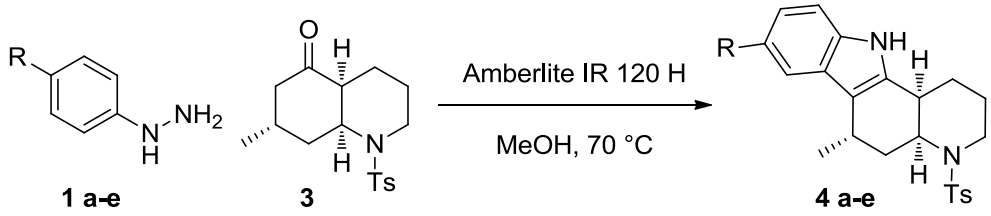
Following the general procedure using cyclohexanone (104 µL, 1 mmol), *p*-trifluoromethylphenylhydrazine **1e** (1.05 g, 6.0 mmol) and Amberlite IR 120 H (2.7g) for 3 h, filtration on silica with 10% EtOAc /hexane prior to crystallization affords **2e** as brown yellow solid (220 mg, 92%) whose data proved consistent with the literature.[4]

^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.85-1.98 (m, 4H), 2.70-2.77 (m, 4H), 7.30-7.38 (m, 2H), 7.75 (s, 1H), 7.83 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 20.8, 23.1, 23.2, 23.3, 110.5, 111.2, 115.5 (q, *J* = 4.2 Hz), 117.9 (q, *J* = 3.6 Hz), 121.6 (q, *J* = 31.4 Hz), 125.7 (q, *J* = 269.6 Hz), 127.4, 136.1, 137.1

[3] a) Chen J. and Hu Y., *Synth. Comm.* **2006,** *36*, 1485 b) Sun K., Liu S., Bec P. M., and Driver T. G., *Ang. Chem. Int. Ed.* **2011**, *50*, 1702-1706

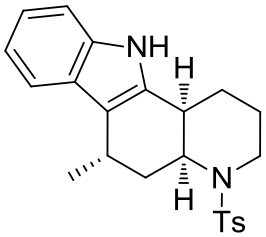
[4] Desroses M., Wieckowski K., Stevens M. and Odell L. R., *Tetrahedron Lett.* **2011**, *52*, 4417-4420

General procedure B:



A stirring solution of phenylhydrazine (10 equiv) and solid acid catalyst Amberlite IR 120 H® (10 equiv w/w with respect to **3**) in MeOH (0.05-0.1 M) was mixed for 5 min at 70 °C. To this mixture was added ketone **3** (1 equiv). The mixture was left stirring at 70 °C for 24 h. After cooling, the reaction mixture was filtered and the resin was washed with CH_2Cl_2 and MeOH and the crude product was purified by crystallization from cold MeOH or cold CH_2Cl_2 to afford the pure carbazole product.

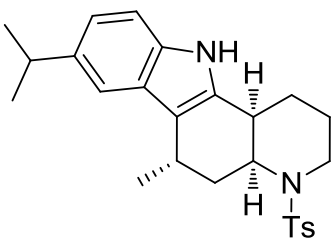
(4a*RS*,6*RS*,11b*RS*)-6-Methyl-4-(4-methylphenylsulfonyl)-2,3,4,4a,5,6,11,11b-octahydro-1*H*-pyrido[3,2-*a*]carbazole (4a)



Following the general procedure B using phenylhydrazine **1a** (915 µL, 9.33 mmol), 5-oxodecahydroquinoline **3** (300 mg, 0.93 mmol) and Amberlite IR 120 H® (3 g) for 20 h, **4a** was isolated as a pale yellow solid (320 mg, 88%) further crystallization from $CHCl_3$ and dichloroethane afforded pale yellow crystal.

Mp: 213-215 °C; ^{1}H NMR (COSY, $CDCl_3$, 400 MHz): δ 1.28-1.38 (m, 1H, H-5eq), 1.32 (d, *J* = 7.2 Hz, 3H, H-12), 1.53-1.61 (m, 2H, H-1 and H-2), 1.65-1.70 (m, 1H, H-2), 1.92-2.01 (m, 1H, H-1), 2.31 (ddd, *J* = 12.8, 12.8, 6.0 Hz, 1H, H-5ax), 2.45 (s, 3H, H-17), 2.88 (ddd, *J* = 10.4, 5.2, 5.2 Hz, 1H, H-11b), 2.97 (ddd, *J* = 12.8, 12.8, 2.8 Hz, 1H, H-3ax), 3.21 (br quint, *J* = 7.0 Hz, 1H, H-6), 3.95 (br d, *J* = 13.2 Hz, 1H, H-3eq), 4.56 (ddd, *J* = 13.2, 5.2, 3.2 Hz, 1H, H-4a), 7.05-7.15 (m, 2H, H-8 and H-9), 7.27 (d, *J* = 8.0 Hz, 1H, H-10), 7.31 (d, *J* = 8.0 Hz, 2H, H-15), 7.47 (d, *J* = 7.6 Hz, 1H, H-7), 7.66 (br s, 1H, H-11), 7.76 (d, *J* = 8.4 Hz, 2H, H-14); ^{13}C NMR (100 MHz, HSQC, $CDCl_3$): δ 21.2 (C-12), 21.5 (C-17), 24.7 (C-2), 25.8 (C-6), 27.7 (C-1), 28.4 (C-5), 34.2 (C-11b), 40.5 (C-3), 49.1 (C-4a), 110.7 (C-10), 113.5 (C-6a), 118.3 (C-7), 119.3 (C-8), 121.5 (C-9), 126.5 (C-6b), 127.0 (C-14), 129.7 (C-15), 135.8 (C-10a), 136.2 (C-13), 138.5 (C-16), 143.1 (C-11a); HRMS: m/z calcd for $C_{23}H_{27}N_2O_2S$ $(M + H)^+$ 395.1788, found 395.1801

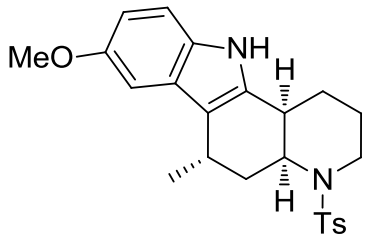
(4a*RS*,6*RS*,11b*RS*)-8-Isopropyl-6-methyl-4-(4-methylphenylsulfonyl)-2,3,4,4a,5,6,11,11b-octahydro-1*H*-pyrido[3,2-*a*]carbazole (4b)



Following the general procedure B using *p*-isopropylphenylhydrazine **1b** (467 mg, 3.11 mmol), 5-oxodecahydroquinoline **3** (100 mg, 0.31 mmol) and Amberlite IR 120 H® (1.00 g) for 20 h **4b** was isolated after trituration in cold MeOH and recrystallization in dichloroethane as a white solid (103 mg, 84%).

Mp:161-163 °C; ^{1}H NMR (COSY, $CDCl_3$, 400 MHz): δ 1.25-1.35 (m, 1H, H-5eq), 1.30 (br d, *J* = 6.8 Hz, 6H, 2 x CH_3 *i*Pr), 1.33 (d, *J* = 7.2 Hz, 3H, H-12), 1.52-1.59 (m, 2H, H-1 and H-2), 1.62-1.68 (m, 1H, H-2), 1.92-1.98 (m, 1H, H-1), 2.30 (ddd, *J* = 13.2, 13.2, 6.4 Hz, 1H, H-5ax), 2.45 (s, 3H, H-17), 2.85 (ddd, *J* = 11.6, 5.0, 5.0 Hz, 1H, H-11b), 2.91-3.05 (m, 2H, H-3ax & CH *i*Pr), 3.20 (br quint, *J* = 7.2 Hz, 1H, H-6), 3.94 (br d, *J* = 12.4 Hz, 1H, H-3eq), 4.56 (ddd, *J* = 13.2, 5.0, 3.2 Hz, 1H, H-4a), 7.02 (dd, *J* = 8.4, 2.0 Hz, 1H, H-9), 7.20 (br d, *J* = 8.4 Hz, 1H, H-10), 7.27-7.37 (m, 3H, H-7 & H-15), 7.56 (br s, 1H, H-11), 7.76 (d, *J* = 8.4 Hz, 2H, H-14); ^{13}C NMR (100 MHz, HSQC, $CDCl_3$): δ 21.2 (C-12), 21.5 (C-17), 24.68 (C-2), 24.75 (CH_3 *i*Pr), 25.8 (C-6), 27.7 (C-1), 28.5 (C-5), 34.25 (CH *i*Pr), 34.28 (C-11b), 40.5 (C-3), 49.1 (C-4a), 110.5 (C-10), 113.3 (C-6a), 115.3 (C-7), 120.5 (C-9), 126.5 (C-6b), 127.0 (C-14), 129.7 (C-15), 134.8 (C-10a), 136.0 (C-8),138.5 (C-13), 140.2 (C-16), 143.0 (C-11a); HRMS: m/z calcd for $C_{26}H_{33}N_2O_2S$ $(M + H)^+$ 437.2257, found 437.2256

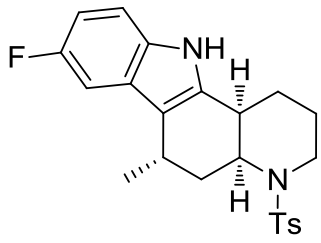
(4a*RS*,6*RS*,11b*RS*)-8-Methoxy-6-methyl-4-(4-methylphenylsulfonyl)-2,3,4,4a,5,6,11,11b-octahydro-1*H*-pyrido[3,2-*a*]carbazole (4c)



A stirring solution of *p*-methoxyphenylhydrazine hydrochloride **1c** (380 mg, 2.17 mmol), and solid acid catalyst Amberlite IR 120 H® (350 mg, 5 equiv w/w with respect to **3**) in MeOH (2.1 mL, 0.1M) was mix for 5 minutes at 70 °C. On this mixture was added the 5-oxodecahydroquinoline **3** (70 mg, 0.22 mmol). The mixture was left stirring at 70 °C for 24 h. After cooling, the reaction mixture was filtered and the resin was washed with CH_2Cl_2 and MeOH and the crude product was purified by chromatography (10-25-50% EtOAc/hexane) to afford 69 mg of a mixture **4c**/**7c** in a ratio 33/67 (yield of **4c:** 24%). (NMR data of **4c** were determined by removing signals of **7c**).

^{1}H NMR (COSY, $CDCl_3$, 400 MHz): δ 1.28-1.35 (m, 1H, H-5eq), 1.31 (d, *J* = 7.2 Hz, 3H, H-12), 1.50-1.62 (m, 2H, H-1 and H-2), 1.62-1.70 (m, 1H, H-2), 1.92-2.00 (m, 1H, H-1), 2.31 (ddd, *J* = 12.8, 12.8, 6.0 Hz, 1H, H-5ax), 2.44 (s, 3H, H-17), 2.80-2.88 (m, 1H, H-11b), 2.92-3.02 (m, 1H, H-3ax), 3.12-3.20 (m, 1H, H-6), 3.83 (s, 3H, OMe), 3.95 (br d, *J* = 12.8 Hz, 1H, H-3eq), 4.55 (ddd, *J* = 13.2, 5.2, 2.8 Hz, 1H, H-4a), 6.78 (dd, *J* = 8.4, 2.4 Hz, 1H, H-9), 6.91 (d, *J* = 2.4 Hz, 1H, H-7), 7.16 (d, *J* = 8.4 Hz, 1H, H-10), 7.31 (d, *J* = 8.0 Hz, 2H, H-15), 7.53 (br s, 1H, H-11), 7.75 (d, *J* = 8.4 Hz, 2H, H-14); ^{13}C NMR (100 MHz, HSQC, $CDCl_3$): δ 21.0 (C-12), 21.5 (C-17), 24.7 (C-2), 25.8 (C-6), 27.8 (C-1), 28.5 (C-5), 34.3 (C-11b), 40.5 (C-3), 49.1 (C-4a), 56.0 (OMe), 100.9 (C-7), 111.0 (C-9), 111.4 (C-10), 113.4 (C-6a), 126.9 (C-6b), 127.0 (C-14), 129.7 (C-15), 131.3 (C-10a), 136.8 (C-13),138.5 (C-16), 143.0 (C-11a), 153.9 (C-8); HRMS: m/z calcd for $C_{24}H_{29}N_2O_3S$ $(M + H)^+$ 425.1893, found 425.1881

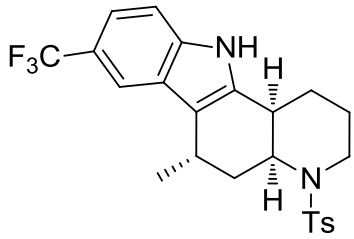
(4a*RS*,6*RS*,11b*RS*)-8-Fluoro-6-methyl-4-(4-methylphenylsulfonyl)-2,3,4,4a,5,6,11,11b-octahydro-1*H*-pyrido[3,2-*a*]carbazole (4d)



Following the general procedure B using *p*-fluorophenylhydrazine **1d** (392 mg, 3.11 mmol), 5-oxodecahydroquinoline **3** (100 mg, 0.31 mmol) and Amberlite IR 120 H® (1.00 g) for 20 h, **4d** was isolated after trituration in cold MeOH and recrystallization in dichloroethane as a white solid (96 mg, 75%).

Mp: 242-244 °C; ^{1}H NMR (COSY, $CDCl_3$, 400 MHz): δ 1.25-1.35 (m, 1H, H-5eq), 1.29 (d, *J* = 6.8 Hz, 3H, H-12), 1.52-1.63 (m, 2H, H-1 and H-2), 1.63-1.73 (m, 1H, H-2), 1.92-2.02 (m, 1H, H-1), 2.30 (ddd, *J* = 12.8, 12.8, 6.2 Hz, 1H, H-5ax), 2.45 (s, 3H, H-17), 2.87 (ddd, *J* = 11.6, 5.0, 5.0 Hz, 1H, H-11b), 2.96 (br t, *J* = 12.8 Hz, 2H, H-3ax), 3.14 (br quint, *J* = 6.8 Hz, 1H, H-6), 3.94 (br d, *J* = 12.8 Hz, 1H, H-3eq), 4.54 (ddd, *J* = 13.2, 5.2, 3.2 Hz, 1H, H-4a), 6.86 (ddd, *J* = 8.8, 8.8, 2.4, Hz, 1H, H-9), 7.09 (dd, *J* = 9.0, 2.4 Hz, 1H, H-7), 7.17 (dd, *J* = 8.8, 4.4 Hz, 1H, H-10), 7.31 (d, *J* = 8.4 Hz, 1H, H-15), 7.64 (br s, 1H, H-11), 7.75 (d, *J* = 8.4 Hz, 2H, H-14); ^{13}C NMR (100 MHz, HSQC, $CDCl_3$): δ 21.0 (C-12), 21.5 (C-17), 24.7 (C-2), 25.7 (C-6), 27.7 (C-1), 28.3 (C-5), 34.3 (C-11b), 40.4 (C-3), 49.0 (C-4a), 103.4 (d, *J* = 23.3 Hz, C-7), 109.5 (d, *J* = 26.1 Hz, C-9), 111.2 (d, *J* = 9.6 Hz, C-10), 113.8 (C-6a), 126.9 (C-6b), 127.0 (C-14), 129.7 (C-15), 132.7 (C-10a), 137.8 (C-13), 138.4 (C-16), 143.1 (C-11a), 157.7 (d, *J* = 234.4 Hz, C-8); HRMS: m/z calcd for $C_{23}H_{26}FN_2O_2S$ $(M + H)^+$ 413.1694, found 413.1684

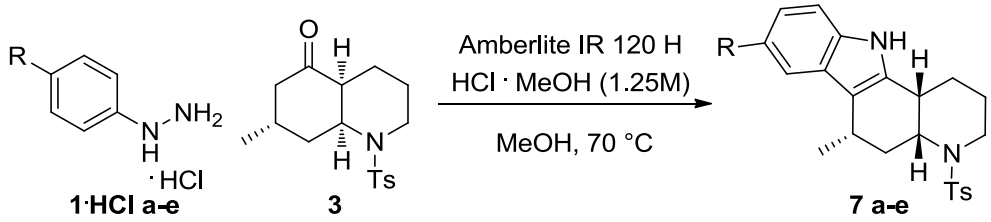
(4a*RS*,6*RS*,11b*RS*)-8-Trifluoromethyl-6-methyl-4-(4-methylphenylsulfonyl)-2,3,4,4a,5,6,11,11b-octahydro-1*H*-pyrido[3,2-*a*]carbazole (4e)



Following the general procedure B using *p*-trifluoromethylphenylhydrazine **1e** (548 mg, 3.11 mmol), 5-oxodecahydroquinoline **3** (100 mg, 0.31 mmol) and Amberlite IR 120 H® (1.00 g) for 72 h. Purification by chromatography (10-25-50% EtOAc/hexane) followed by trituration in cold MeOH allowed to obtain a mixture **4e**/**7e** in a ratio 75/25 (yield of **4e**: 8 mg, 5.5%). Another fraction was isolated 19 mg containing 50% of **4e**/**7e** 1/2. The remaining part corresponding to hydrazone and 5-oxodecahydroquinoline **3** (yield of **4e** combined: 8%). (NMR data of **4e** were determined by removing signals of **7e**).

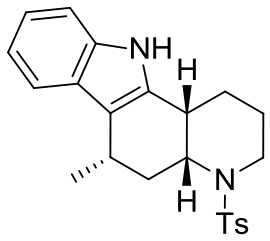
^{1}H NMR (COSY, $CDCl_3$, 400 MHz): δ 1.28-1.35 (m, 1H, H-5eq), 1.32 (d, *J* = 6.8 Hz, 3H, H-12), 1.52-1.63 (m, 2H, H-1 & H-2), 1.66-1.73 (m, 1H, H-2), 1.95-2.05 (m, 1H, H-1), 2.31 (ddd, *J* = 13.2, 13.2, 6.8 Hz, 1H, H-5ax), 2.45 (s, 3H, H-17), 2.89-3.08 (m, 2H, H-3ax & H-11b), 3.22 (quint, *J* = 6.8 Hz, 1H, H-6), 3.95 (br d, *J* = 12.4 Hz, 1H, H-3eq), 4.57 (ddd, *J* = 13.2, 5.2, 2.8 Hz, 1H, H-4a), 7.28-7.38 (m, 4H, H-7, H-10 & H-15), 7.70-7.74 (m, 3H, H-9 & H-14), 7.89 (br s, 1H, H-11); ^{13}C NMR (100 MHz, HSQC, $CDCl_3$): δ 21.3 (C-12), 21.5 (C-17), 24.7 (C-2), 25.6 (C-6), 27.7 (C-1), 28.2 (C-5), 34.3 (C-11b), 40.4 (C-3), 48.9 (C-4a), 110.9 (C-7), 114.4 (C-6a), 115.9 (d, *J* = 4.1 Hz, C-9), 118.3 (d, *J* = 3.4 Hz, C-10), 121.8 (q, *J* = 31.6 Hz, C-8), 125.3 (q, *J* = 269.6 Hz, C-18), 125.9 (C-6b), 127.0 (C-14), 129.8 (C-15), 137.7 (C-13 & C-10a), 138.4 (C-16), 143.2 (C-11a); HRMS: m/z calcd for $C_{24}H_{26}F_3N_2O_2S$ $(M + H)^+$ 463.1662, found 463.1675

General procedure C:



A stirring solution of phenylhydrazine hydrochloride **1·HCl** (2.5 equiv), solid acid catalyst Amberlite IR 120 H® (10 equiv w/w with respect to **3**) and 5-oxodecahydroquinoline **3** (1 equiv) in HCl/MeOH (1.25 M, 30 equiv) was stirred at 70 °C for the indicated time. After cooling, the reaction mixture was filtered and the resin was washed with CH_2Cl_2 and MeOH. The excess hydrazine salt was removed by precipitation in cold dichloromethane and the crude product was purified by precipitation from cold MeOH to afford the pure carbazole product.

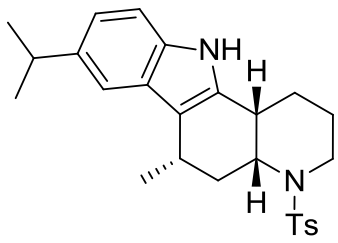
(4a*RS*,6*SR*,11b*RS*)-6-Methyl-4-(4-methylphenylsulfonyl)-2,3,4,4a,5,6,11,11b-octahydro-1*H*-pyrido[3,2-*a*]carbazole (7a)



Following the general procedure C using phenylhydrazine hydrochloride **1a·HCl** (61 mg, 0.42 mmol), 5-oxodecahydroquinoline **3** (54 mg, 0.17 mmol) and Amberlite IR 120 H® (500 mg) for 3 h, **7a** was isolated as a pale yellow solid (62 mg, 92%) further crystallization from $CHCl_3$ and DCE afforded pale yellow crystals.

Mp: 205-207 °C; ^{1}H NMR (COSY, $CDCl_3$, 400 MHz): δ 1.41 (d, *J* = 6.8 Hz, 3H, H-12), 1.45-1.52 (m, 1H, H-2), 1.60-1.72 (m, 2H, H-1 & H-2), 1.75-1.93 (m, 2H, H-5), 1.95-2.02 (m, 1H, H-1), 2.44 (s, 3H, H-17), 2.78 (ddd, *J* = 12.0, 4.8, 4.8 Hz, 1H, H-11b), 3.05 (ddd, *J* = 13.4, 13.4, 2.4 Hz, 1H, H-3ax), 3.10-3.24 (m, 1H, H-6), 3.92 (br d, *J* = 13.4 Hz, 1H, H-3eq), 4.36 (ddd, *J* = 12.8, 4.8, 3.6 Hz, 1H, H-4a), 7.05-7.15 (m, 2H, H-8 & H-9), 7.27 (d, *J* = 7.6 Hz, 1H, H-10), 7.30 (d, *J* = 8.4 Hz, 1H, H-15), 7.61 (d, *J* = 7.6 Hz,1H, H-7), 7.68 (br s, 1H, H-11), 7.75 (d, *J* = 8.4 Hz, 2H, H-14); ^{13}C NMR (100 MHz, HSQC, $CDCl_3$): δ 21.3 (C-12), 21.5 (C-17), 24.5 (C-2), 28.14 (C-1), 28.32 (C-6), 32.3 (C-5), 34.0 (C-11b), 40.5 (C-3), 52.4 (C-4a), 110.7 (C-10), 113.1 (C-6a), 119.3 (C-8), 119.9 (C-7), 121.3 (C-9), 126.6 (C-6b), 127.0 (C-14), 129.7 (C-15), 136.1 (C-10a), 136.3 (C-13), 138.5 (C-16), 143.1 (C-11a); HRMS: m/z calcd for $C_{23}H_{27}N_2O_2S$ $(M + H)^+$ 395.1788, found 395.1805

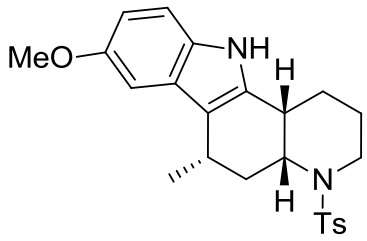
(4a*RS*,6*SR*,11b*RS*)-8-Isopropyl-6-methyl-4-(4-methylphenylsulfonyl)-2,3,4,4a,5,6,11,11b-octahydro-1*H*-pyrido[3,2-*a*]carbazole (7b)



Following the general procedure C using *p*-isopropylphenylhydrazine hydrochloride **1b·HCl** (145 mg, 0.78 mmol), 5-oxodecahydroquinoline **3** (100 mg, 0.31 mmol) and Amberlite IR 120 H® (1.00 g) for 3 h, **7b** was isolated after trituration in cold MeOH and recrystallization in DCE as a white solid (119 mg, 88%).

^{1}H NMR (COSY, $CDCl_3$, 400 MHz): δ 1.29 (dd, *J* = 7.5, 1.6 Hz, 6H,2 x CH_3 *i*Pr), 1.40 (d, *J* = 6.8 Hz, 3H, H-12), 1.43-1.53 (m, 1H, H-2), 1.53-1.68 (m, 2H, H-1 & H-2), 1.72-1.90 (m, 2H, H-5), 1.91-1.99 (m, 1H, H-1), 2.42 (s, 3H, H-17), 2.74 (ddd, *J* = 12.0, 4.8, 4.8 Hz, 1H, H-11b), 2.91-3.15 (m, 3H, CH *i*Pr, H-3ax & H-6), 3.89 (br d, *J* = 13.6 Hz, 1H, H-3eq), 4.32 (ddd, *J* = 12.8, 4.8, 3.6 Hz, 1H, H-4a), 7.01 (bd, *J* = 8.4 Hz 1H, H-9), 7.18 (d, *J* = 8,4 Hz, 1H, H-10), 7.28 (d, *J* = 8.4 Hz, 2H, H-15), 7.43 (bs, 1H, H-7), 7.66 (s, 1H, H-11), 7.73 (d, *J* = 8.4 Hz, 2H, H-14); ^{13}C NMR (100 MHz, HSQC, $CDCl_3$): δ 21.3 (C-12), 21.5 (C-17), 24.4 (C-2), 24.7 (CH_3 *i*Pr), 24.8 (CH_3 *i*Pr), 28.1 (C-1), 28.3 (C-6), 32.3 (C-5), 34.0 (C-11b), 34. 3 (CH *i*Pr), 40.5 (C-3), 52.5 (C-4a), 110.5 (C-10), 112.7 (C-6a), 116.9 (C-7), 120.3 (C-9), 126.6 (C-6b), 126.8 (C-14), 129.7 (C-15), 134.9 (C-10a), 136.4 (C-8), 138.5 (C-13), 139.9 (16), 143.0 (C-11a); HRMS: m/z calcd for $C_{26}H_{33}N_2O_2S$ $(M + H)^+$ 437.2257, found 437.2256

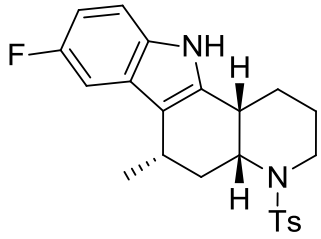
(4a*RS*,6*SR*,11b*RS*)-8-Methoxy-6-methyl-4-(4-methylphenylsulfonyl)-2,3,4,4a,5,6,11,11b-octahydro-1*H*-pyrido[3,2-*a*]carbazole (7c)



Following the general procedure C using *p*-methoxyphenylhydrazine hydrochloride **1c·HCl** (136 mg, 0.78 mmol), 5-oxodecahydroquinoline **3** (100 mg, 0.31 mmol) and Amberlite IR 120 H® (1.00 g) for 6 h, **7c** was isolated after purification by chromatography (10-25-50% EtOAc/hexane) followed by trituration in cold MeOH as a light pink solid (75 mg, 57%).

^{1}H NMR (COSY, $CDCl_3$, 400 MHz): δ 1.40 (d, *J* = 6.8 Hz, 3H, H-12), 1.45-1.52 (m, 1H, H-2), 1.60-1.72 (m, 2H, H-1 & H-2), 1.75-1.95 (m, 2H, H-5), 1.95-2.02 (m, 1H, H-1), 2.44 (s, 3H, H-17), 2.74 (ddd, *J* = 12.0, 5.0, 5.0 Hz, 1H, H-11b), 3.05 (ddd, *J* = 13.6, 13.6, 2.4 Hz, 1H, H-3ax), 3.10-3.20 (m, 1H, H-6), 3.84 (s, 3H, CH_3O), 3.94 (br d, *J* = 13.6 Hz, 1H, H-3eq), 4.34 (ddd, *J* = 12.8, 5.0, 3.6 Hz, 1H, H-4a), 6.79 (dd, *J* = 8.8, 2.4, Hz, 1H, H-9), 7.07 (d, *J* = 2.4 Hz, 1H, H-7), 7.15 (d, *J* = 8.8 Hz,1H, H-10), 7.29 (d, *J* = 8.4 Hz, 2H, H-15), 7.51 (br s, 1H, H-11), 7.74 (d, *J* = 8.4 Hz, 2H, H-14); ^{13}C NMR (100 MHz, HSQC, $CDCl_3$): δ 21.2 (C-12), 21.5 (C-17), 24.4 (C-2), 28.15 (C-1), 28.24 (C-6), 32.3 (C-5), 34.1 (C-11b), 40.5 (C-3), 52.4 (C-4a), 56.1 (CH_3O), 102.8 (C-7), 110.8 (C-9), 111.2 (C-10), 113.0 (C-6a), 126.96 (C-14), 127.01 (C-6b), 129.7 (C-15), 131.5 (C-10a), 137.1 (C-13), 138.6 (C-16), 143.0 (C-11a), 153.7 (C-8); HRMS: m/z calcd for $C_{24}H_{29}N_2O_3S$ $(M + H)^+$ 425.1893, found 425.1881

(4a*RS*,6*SR*,11b*RS*)-8-Fluoro-6-methyl-4-(4-methylphenylsulfonyl)-2,3,4,4a,5,6,11,11b-octahydro-1*H*-pyrido[3,2-*a*]carbazole (7d)

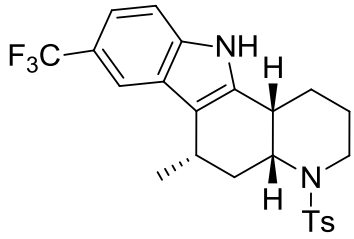


Following the general procedure C using *p*-fluorophenylhydrazine hydrochloride **1d·HCl** (127 mg, 0.78 mmol), 5-oxodecahydroquinoline **3** (100 mg, 0.31 mmol) and Amberlite IR 120 H® (1.00 g) for 3 h, **7d** was isolated after trituration in cold MeOH and recrystallization in DCE as a white solid (101 mg, 82%).

^{1}H NMR (COSY, $CDCl_3$, 400 MHz): δ 1.37 (d, *J* = 6.4 Hz, 3H, H-12), 1.46-1.53 (m, 1H, H-2), 1.58-1.72 (m, 2H, H-1 & H-2), 1.73-1.92 (m, 2H, H-5), 1.94-2.03 (m, 1H, H-1), 2.44 (s, 3H, H-17), 2.78 (ddd, *J* = 12.0, 5.0, 5.0 Hz, 1H, H-11b), 3.04 (ddd, *J* = 13.2, 13.2, 2.4

Hz, 1H, H-3ax), 3.08-3.16 (m, 1H, H-6), 3.91 (ddd, *J* = 13.2, 2.4, 2.4 Hz, 1H, H-3eq), 4.34 (ddd, *J* = 12.4, 5.0, 3.6 Hz, 1H, H-4a), 6.86 (ddd, *J* = 9.0, 9.0, 2.6 Hz, 1H, H-9), 7.16 (dd, *J* = 9.0, 4.4 Hz, 1H, H-10), 7.24 (dd, *J* = 9.6, 2.6 Hz, 1H, H-7), 7.30 (br d, *J* = 8.4 Hz,2H, H-15), 7.64 (s, 1H, H-11), 7.74 (br d, *J* = 8.4 Hz, 2H, H-14); ^{13}C NMR (100 MHz, HSQC, $CDCl_3$): δ 21.0 (C-12), 21.5 (C-17), 24.5 (C-2), 28.1 (C-1), 28.2 (C-6), 32.2 (C-5), 34.1 (C-11b), 40.5 (C-3), 52.3 (C-4a), 105.0 (d, *J* =23.9 Hz, C-7), 109.4 (d, *J* = 26.1 Hz, C-9), 111.1 (d, *J* = 9.9 Hz, C-10), 113.4 (C-6a), 126.9 (C-6b), 127.0 (C-14), 129.7 (C-15), 132.8 (C-10a), 138.1 (C-13), 138.5 (C-16), 143.1 (C-11a), 157.5 (d, *J* = 233.8 Hz, C-8); HRMS: m/z calcd for $C_{23}H_{26}FN_2O_2S$ $(M + H)^+$ 413.1694, found 413.1695

(4a*RS*,6*SR*,11b*RS*)-8-Trifluoromethyl-6-methyl-4-(4-methylphenylsulfonyl)-2,3,4,4a,5,6,11,11b-octahydro-1*H*-pyrido[3,2-*a*]carbazole (7e)

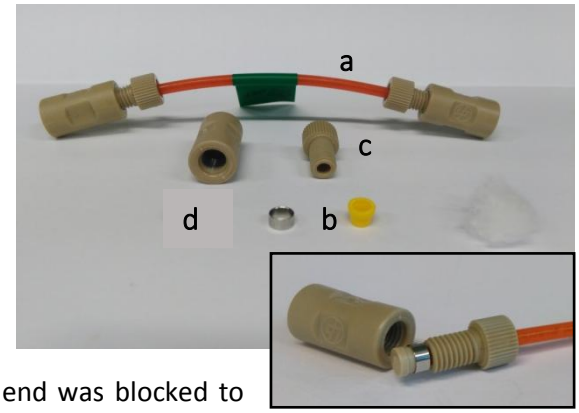


Following the general procedure C using *p*-trifluoromethylphenylhydrazine hydrochloride **1e·HCl** (166 mg, 0.78 mmol), 5-oxodecahydroquinoline **3** (100 mg, 0.31 mmol) and Amberlite IR 120 H® (1.00 g) for 24 h, **7e** was isolated after purification by chromatohraphy (10-25-50% EtOAc/hexane) followed by trituration in cold MeOH as a white solid (15 mg, 10.5%) and the recovered filtrate 50 mg containing 15% of the product (Yield of **7e** combined : 16%).

^{1}H NMR (COSY, $CDCl_3$, 400 MHz): δ 1.40 (d, *J* = 6.8 Hz, 3H, H-12), 1.47-1.53 (m, 1H, H-2), 1.62-1.71 (m, 2H, H-1 & H-2), 1.72-1.92 (m, 2H, H-5), 1.97-2.07 (m, 1H, H-1), 2.44 (s, 3H, H-17), 2.84 (ddd, *J* = 12.0, 4.8, 4.8 Hz, 1H, H-11b), 3.03 (ddd, *J* = 13.2, 13.2, 2.4 Hz, 1H, H-3ax), 3.12 (br quint, *J* = 6.8 Hz, 1H, H-6), 3.90 (br d, *J* = 13.2 Hz, 1H, H-3eq), 4.36 (ddd, *J* = 12.8, 4.8, 3.6 Hz, 1H, H-4a), 7.28-7.38 (m, 4H, H-7, H-10 & H-15), 7.74 (d, *J* = 8.4 Hz, 2H, H-14), 7.86 (s, 1H, H-9), 7.96 (s, 1H, H-11); ^{13}C NMR (100 MHz, HSQC, $CDCl_3$): δ 21.2 (C-12), 21.5 (C-17), 24.5 (C-2), 28.06 (C-1), 28.13 (C-6), 31.9 (C-5), 34.1 (C-11b), 40.5 (C-3), 52.2 (C-4a), 110.8 (C-7), 114.0 (C-6a), 117.3 (d, *J* = 4.2 Hz, C-9), 118.1 (d, *J* = 3.3 Hz, C-10), 121.6 (q, *J* = 31.6 Hz, C-8), 125.4 (q, *J* = 269.8 Hz, C-18), 126.0 (C-6b), 126.9 (C-14), 129.8 (C-15), 137.8 (C-10a), 138.0 (C-13), 138.4 (C-16), 143.2 (C-11a); HRMS: m/z calcd for $C_{24}H_{26}F_3N_2O_2S$ $(M + H)^+$ 463.1662, found 463.1669

Synthesis of indoles in flow

Cartridge assembly:



Both ends of 10-cm Tefzel® (ETFE) tubing (1/8'' OD, 1/16" ID, **a**) were blocked with cotton wool, fitted with assembled flat bottom super flangeless fittings + metal ferrules (1/8'' OD, P-359, IDEX, **b**) and male nut parts (LT-215, IDEX, **c**). These connections were mounted onto flat unions (P-703-01, IDEX, **d**). For the filling of the cartridges, only one end was blocked at first, the cartridge was filled with the catalyst (~100 mg) employing vacuum suction and after, the other end was blocked to seal the cartridge.

Microreactor setup:

All gas-tight syringes (5 mL, B-247, FutureChemistry Holding BV) were mounted on syringe pumps (B-230, FutureChemistry Holding BV) and connected to Tefzel® tubing (1/16'' OD, 1529, IDEX) via female Luer adapters (P-628, IDEX). Throughout the flow system, all the tubing (Tefzel® 1/16'' OD, 1529, IDEX) was assembled with super flangeless nut connections (P-287, IDEX) and assembled ferrules (P-259, IDEX) in order to achieve leak-free fluid connections. Also, a 5 bar back pressure regulator (B-444, FutureChemistry Holding BV) guaranteed pressurization inside the system before eluting into a collection flask (see Figure 1).

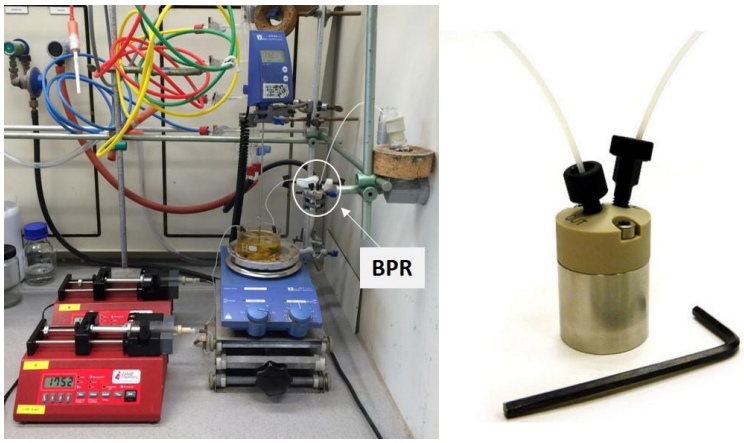


Figure 1. Flow set-up including back pressure regulator (detail, right).

Flow general procedure C:

Two feed solutions were employed: stream A containing the ketone in solution, and stream B containing the hydrazine in solution both driven by syringe pumps ($\phi_A = \phi_B$). These were mixed in a PEEK T-mixer connection (P-713, IDEX) before entering the microreactor (consisting of a ETFE cartridge packed with Amberlite® IR 120 H) at 70 °C for 10 to 60 minutes. By removing the solvent *in vacuo*, the desired indole products were obtained. In some cases, further purification was achieved by recrystallization CH_2Cl_2 or methanol.

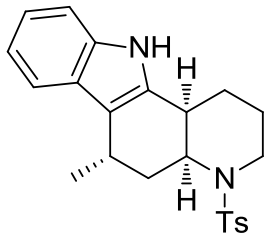
Full characterization of the indole products can be found within the general procedure for the preparation of the title compounds in batch.

Calculation for reactions performed under flow conditions:

For the reactions performed in flow, yields were calculated taking into account the total moles of product obtained (n(Collected Product)), the flow rate (ϕSM) and the concentration ([SM]) of the starting material and the overall collection time (t(Collection)), as shown in the equation below.

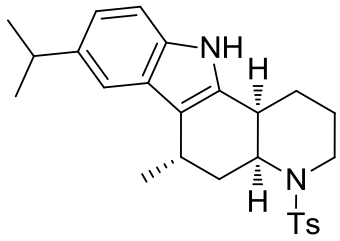
$$\eta_{Flow}\ (\%) = \frac{n\ (Collected\ Product)}{[SM]\ \times\ \phi_{SM}\ \times\ t_{(Collection)}} \times 100$$

(4a*RS*,6*RS*,11b*RS*)-6-Methyl-4-(4-methylphenylsulfonyl)-2,3,4,4a,5,6,11,11b-octahydro-1*H*-pyrido[3,2-*a*]carbazole (4a)



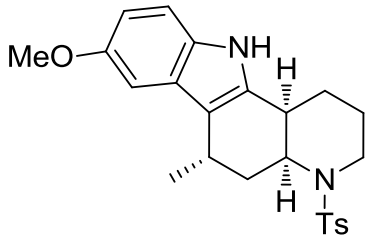
Following the flow general procedure C using 5-oxodecahydroquinoline **3** (0.05 M in MeOH/AcOH/DCE 4/2/4) and phenylhydrazine **1a** (0.5 M in MeOH/AcOH 1/1) with reaction time = 20 min, total flow = 15.00 µL·min^{-1} and collecting for 2 h (2 mL of ketone), product **4a** was isolated as a pale yellow solid (31.2 mg, 76%).

(4a*RS*,6*RS*,11b*RS*)-8-Isopropyl-6-methyl-4-(4-methylphenylsulfonyl)-2,3,4,4a,5,6,11,11b-octahydro-1*H*-pyrido[3,2-*a*]carbazole (4b)



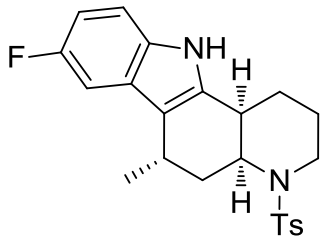
Following the flow general procedure C using a 30 cm cartridge (inner volume 300 µL) 5-oxodecahydroquinoline **3** (0.05 M in MeOH/AcOH/DCE 4/2/4) and *p*-isopropylphenylhydrazine hydrochloride salt **1b·HCl** (0.5 M in MeOH/AcOH 1/1) with reaction time = 30 min, total flow = 10.00 µL·min^{-1} and collecting for 2 h (2 mL of ketone), the crude ^{1}H NMR spectrum showed full conversion to **4b** which was isolated as a pale yellow solid (32 mg, 75%).

(4a*RS*,6*RS*,11b*RS*)-8-Methoxy-6-methyl-4-(4-methylphenylsulfonyl)-2,3,4,4a,5,6,11,11b-octahydro-1*H*-pyrido[3,2-*a*]carbazole (4c)



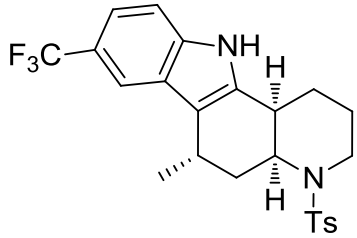
Following the flow general procedure C using a 1 m cartridge (inner volume 1 mL), 5-oxodecahydroquinoline **3** (0.02 M in MeOH/AcOH/DCE 4/4/2) and *p*-methoxyphenylhydrazine hydrochloride salt **1c·HCl** (0.2 M in MeOH) with reaction time = 60 min, total flow = 16.00 µL·min^{-1} and collecting for 2 h (2 mL of ketone), the crude ^{1}H NMR spectrum showed 55 % conversion to **4c** with the remaining part corresponding to a mix hydrazone/ 5-oxodecahydroquinoline.

(4a*RS*,6*RS*,11b*RS*)-8-Fluoro-6-methyl-4-(4-methylphenylsulfonyl)-2,3,4,4a,5,6,11,11b-octahydro-1*H*-pyrido[3,2-*a*]carbazole (4d)



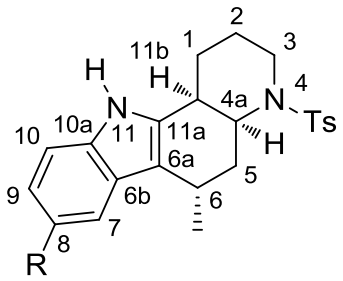
Following the flow general procedure C using a 1 m cartridge (inner volume 1 mL), 5-oxodecahydroquinoline **3** (0.01 M in MeOH/AcOH/DCE 4/5/1) and *p*-fluorophenylhydrazine hydrochloride salt **1d·HCl** (0.1 M in MeOH) with reaction time = 60 min, total flow = 16.00 µL·min^{-1} and collecting for 2 h (2 mL of ketone), the crude ^{1}H NMR spectrum showed 42% conversion to **4d** with the remaining part corresponding to a mix hydrazone/ 5-oxodecahydroquinoline.

(4a*RS*,6*RS*,11b*RS*)-8-Trifluoromethyl-6-methyl-4-(4-methylphenylsulfonyl)-2,3,4,4a,5,6,11,11b-octahydro-1*H*-pyrido[3,2-*a*]carbazole (4e)



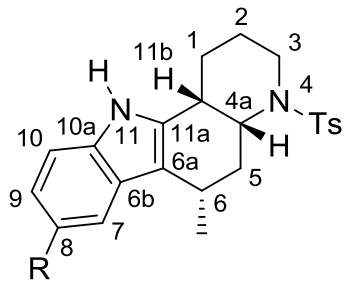
Following the flow general procedure C using a 1 m cartridge (inner volume 1 mL), 5-oxodecahydroquinoline **3** (0.04 M in AcOH/DCE 8/2) and *p*-trifluoromethylphenylhydrazine **1e** (0.4 M in MeOH) with reaction time = 60 min, total flow = 16.00 µL·min^{-1} and collecting for 2 h (2 mL of ketone), the crude ^{1}H NMR spectrum showed 22% conversion to **4e** with the remaining part corresponding to a mix hydrazone/ 5-oxodecahydroquinoline.

Table 1. ^{1}H NMR data of 6-Methyl-4-(4-methylphenylsulfonyl)-1*H*-2,3,4,4a,5,6,11,11b-octahydropyrido[3,2-*a*]carbazoles



Series **4**

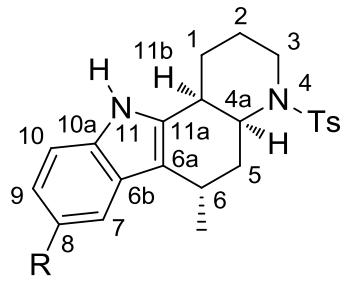
		4a H	**4b** *i*Pr	**4c** OMe	**4d** F	**4e** CF_3
H-1		1.53-1.61 (m) 1.92-2.01 (m)	1.52-1.59 (m) 1.92-1.98 (m)	1.50-1.62 (m) 1.92-2.00 (m)	1.52-1.63 (m) 1.92-2.02 (m)	1.52-1.63 (m) 1.95-2.05 (m)
H-2		1.53-1.61 (m) 1.65-1.70 (m)	1.52-1,59 (m) 1.62-1.68 (m)	1.50-1.62 (m) 1.62-1.70 (m)	1.52-1.63 (m) 1-63-1.73 (m)	1.52-1.63 (m) 1.66-1.73 (m)
H-3	ax	2.97 (ddd, 12.8, 12.8, 2.8)	2.91-3.05 (m)	2.92-3.02 (m)	2.96 (br t, 12.8)	2.89-3.08 (m)
	eq	3.95 (br d, 13.2)	3.94 (br d, 12.4)	3.95 (br d, 12.8)	3.94 (br d, 12.8)	3.95 (br d, 12.4)
H-4a		4.56 (ddd, 13.2, 5.2, 3.2)	4.56 (ddd, 13.2, 5.0, 3.2)	4.55 (ddd, 13.2, 5.2, 2.8)	4.54 (ddd, 13.2, 5.2, 3.2)	4.57 (ddd, 13.2, 5.2, 2.8)
H-5	ax	2.31 (ddd, 12.8, 12.8, 6.0)	2.30 (ddd, 13.2, 13.2, 6.4)	2.31 (ddd, 12.8, 12.8, 6.0)	2.30 (ddd, 12.8, 12.8, 6.2)	2.31 (ddd, 13.2, 13.2, 6.8)
	eq	1.28-1.38 (m)	1.25-1.35 (m)	1.28-1.35 (m)	1.25-1.35 (m)	1.28-1.35 (m)
H-6		3.21 (quint, 7.0)	3.20 (quint, 7.2)	3.12-3.20 (m)	3.14 (quint, 6.8)	3.22 (quint, 6.8)
H-7		7.47	7.27-7.37	6.91	7.09	7.28-7.38
H-8		7.05-7.15	---	---	---	---
H-9		7.05-7.15	7.02	6.78	6.86	7.70-7.74
H-10		7.27	7.20	7.16	7.17	7.28-7.38
H-11		7.66	7.56	7.53	7.64	7.89
H-11b		2.88 (ddd, 11.4, 5.2, 5.2)	2.85 (ddd, 11.6, 5.0, 5.0)	2.80-2.88 (m)	2.87 (ddd, 11.6, 5.0, 5.0)	2.89-3.08 (m)
Me		1.32 (d, 7.2)	1.33	1.31	1.29	1.32
H-14		7.76	7.76	7.75	7.75	7.70-7.74
H-15		7.31	7.27-7.37	7.31	7.31	7.28-7.38
Me-Ts		2.45	2.45	2.44	2.45	2.45
Other			1.30 & 2.91-3.05 (*i*Pr)	3.84 (OCH_3)		



Series **7**

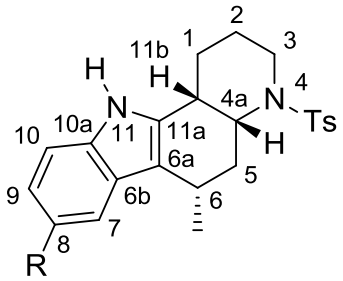
		7a H	**7b** *i*Pr	**7c** OMe	**7d** F	**7e** CF_3
H-1		1.60-1.72 (m) 1.95-2.02 (m)	1.53-1.68 (m) 1.91-1.99 (m)	1.60-1.72 (m) 1.95-2.02 (m)	1.58-1.72 (m) 1.94-2.03 (m)	1.62-1.71 (m) 1.97-2.07 (m)
H-2		1.42-1.52 (m) 1.60-1.72 (m)	1.43-1.53 (m) 1.53-1.68 (m)	1.45-1.52 (m) 1.60-1.72 (m)	1.46-1.53 (m) 1.58-1.72 (m)	1.47-1.53 (m) 1.62-1.71 (m)
H-3	ax	3.05 (ddd, 13.4, 13.4, 2.4)	2.91-3.15 (m)	3.05 (ddd, 13.6, 13.6, 2.4)	3.04 (ddd, 13.2, 13.2, 2.4)	3.03 (ddd, 13.2, 13.2, 2.4)
	eq	3.92 (br d, 13.4)	3.89 (br d, 13.6)	3.94 (br d, 13.6)	3.91 (br d, 13.2)	3.90 (br d, 13.2)
H-4a		4.36 (ddd, 12.8, 4.8, 3.6)	4.32 (ddd, 12.8, 4.8, 3.6)	4.34 (ddd, 12.8, 5.0, 3.6)	4.34 (ddd, 12.4, 5.0, 3.6)	4.36 (ddd, 12.8, 4.8, 3.6)
H-5		1.75-1.93 (m)	1.72-1.90 (m)	1.75-1.95 (m)	1.73-1.92 (m)	1.72-1.92 (m)
H-6		3.10-3.24 (m)	2.91-3.15 (m)	3.10-3.20 (m)	3.08-3.16 (m)	3.12 (quint, 6.8)
H-7		7.61	7.43	7.07	7.24	7.28-7.38
H-8		7.05-7.15	---	---	---	---
H-9		7.05-7.15	7.01	6.79	6.86	7.86
H-10		7.27	7.18	7.15	7.16	7.28-7.38
H-11		7.68	7.66	7.51	7.64	7.96
H-11b		2.78 (ddd, 12.0, 4.8, 4.8)	2.74 (ddd, 12.0, 4.8, 4.8)	2.74 (ddd, 12.0, 5.0, 5.0)	2.78 (ddd, 12.0, 5.0, 5.0)	2.84 (ddd, 12.0, 4.8, 4.8)
Me		1.41 (d, 6.8)	1.40 (d, 6.8)	1.40 (d, 6.8)	1.37 (d, 6.4)	1.40 (d, 6.8)
H-14		7.75	7.73	7.74	7.74	7.74
H-15		7.30	7.28	7.29	7.30	7.28-7.38
Me-Ts		2.44	2.42	2.44	2.44	2.44
Other			1.29 & 2.91-3.15 (*i*Pr)	3.84 (OCH_3)		

Table 2. ^{13}C NMR data of 6-Methyl-4-(4-methylphenylsulfonyl)-1*H*-2,3,4,4a,5,6,11,11b-octahydropyrido[3,2-*a*]carbazoles



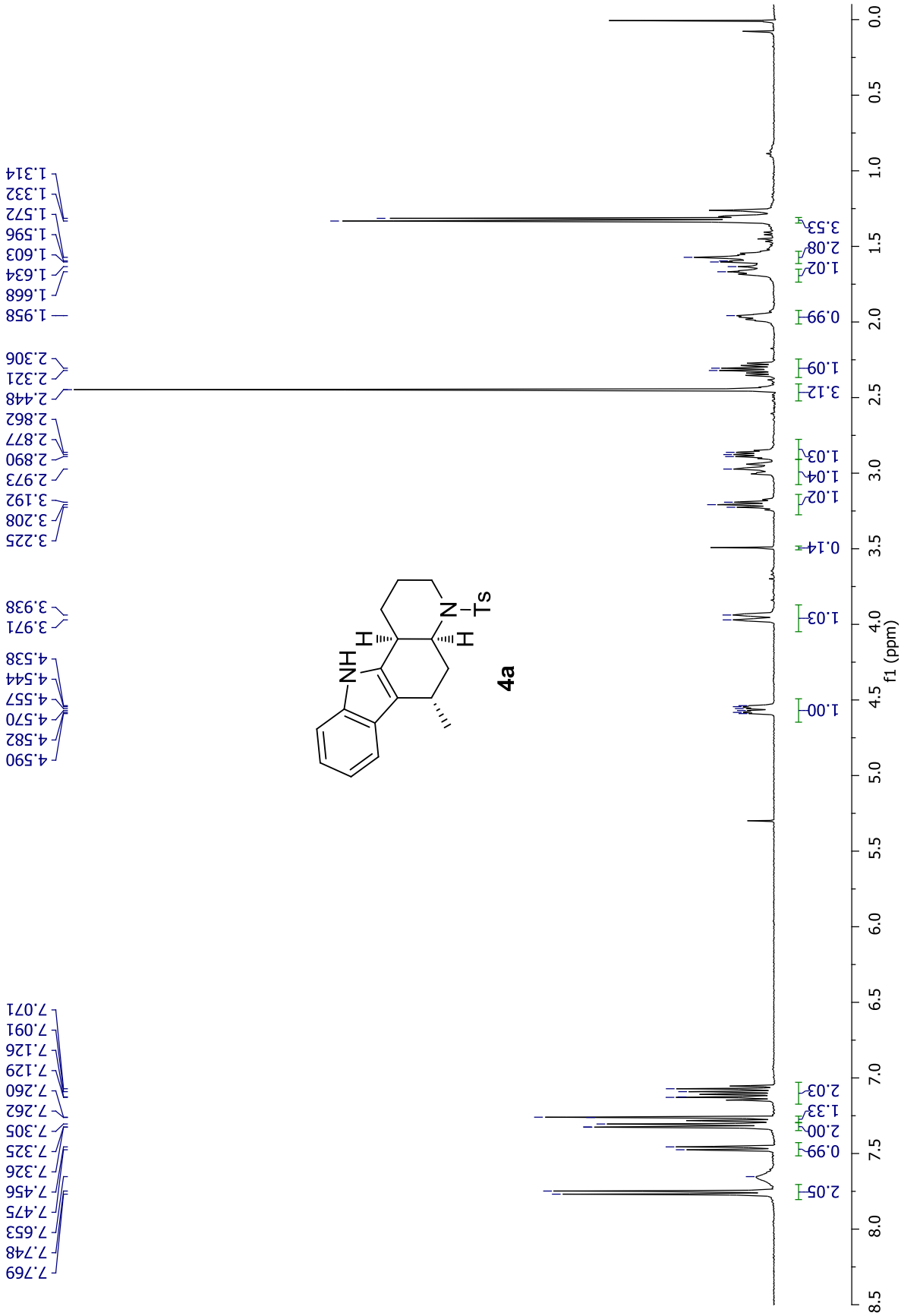
Series **4**

	4a H	**4b** *i*Pr	**4c** OMe	**4d** F	**4e** CF_3
C-1	27.7	27.7	27.8	27.7	27.7
C-2	24.7	24.7	24.7	24.7	24.7
C-3	40.5	40.5	40.5	40.4	40.5
C-4a	49.1	49.1	49.1	49.0	48.9
C-5	28.4	28.5	28.5	28.3	28.2
C-6	25.8	25.8	25.8	25.7	25.6
C-6a	113.5	113.3	113.4	113.8	114.4
C-6b	126.5	126.5	126.9	126.9	125.9
C-7	118.3	115.3	100.9	103.4	110.9
C-8	119.3	136.0	153.9	157.7	121.6
C-9	121.5	120.5	111.0	109.5	115.9
C-10	110.7	110.5	111.4	111.2	118.3
C-10a	135.8	134.8	131.3	132.7	137.7
C-11a	143.1	143.0	143.0	143.1	143.2
C-11b	34.2	34.3	34.3	34.3	34.3
Me	21.2	21.2	21.0	21.0	21.3
Me-Ts	21.5	21.5	21.5	21.5	21.6
C-13	136.2	138.5	136.8	137.8	137.8
C-14	127.0	127.0	127.0	127.0	127.0
C-15	129.7	129.7	129.7	129.7	129.8
C-16	138.5	140.2	138.5	138.4	138.4
Other		24.8 & 34.3 (*i*Pr)	56.0 (OCH_3)		125.3 (CF_3)



Series **7**

	7a H	**7b** *i*Pr	**7c** OMe	**7d** F	**7e** CF_3
C-1	28.1	28.1	28.2	28.1	28.1
C-2	24.5	24.4	24.4	24.5	24.5
C-3	40.5	40.5	40.5	40.5	40.5
C-4a	52.4	52.5	52.4	52.3	52.2
C-5	32.3	32.3	32.3	32.2	31.9
C-6	28.3	28.3	28.2	28.2	28.1
C-6a	113.1	112.7	113.0	113.4	114.0
C-6b	126.6	126.6	127.01	126.9	126.0
C-7	119.9	116.9	102.8	105.0	110.8
C-8	119.3	136.4	153.7	157.5	121.6
C-9	121.3	120.3	110.8	109.4	117.3
C-10	110.7	110.5	111.2	111.1	118.1
C-10a	136.1	134.9	131.5	132.8	137.8
C-11a	143.1	143.0	143.0	143.1	143.2
C-11b	34.0	34.0	34.1	34.1	34.1
Me	21.3	21.3	21.2	21.0	21.2
Me-Ts	21.5	21.5	21.5	21.5	21.5
C-13	136.3	138.5	137.1	138.1	138.0
C-14	127.0	126.8	126.96	127.0	126.9
C-15	129.7	129.7	129.7	129.7	129.8
C-16	138.5	139.9	138.6	138.5	138.4
Other		24.7 & 34.3 (*i*Pr)	56.1 (OCH_3)		125.3 (CF_3)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2.321
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1.603
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1.572
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1.314
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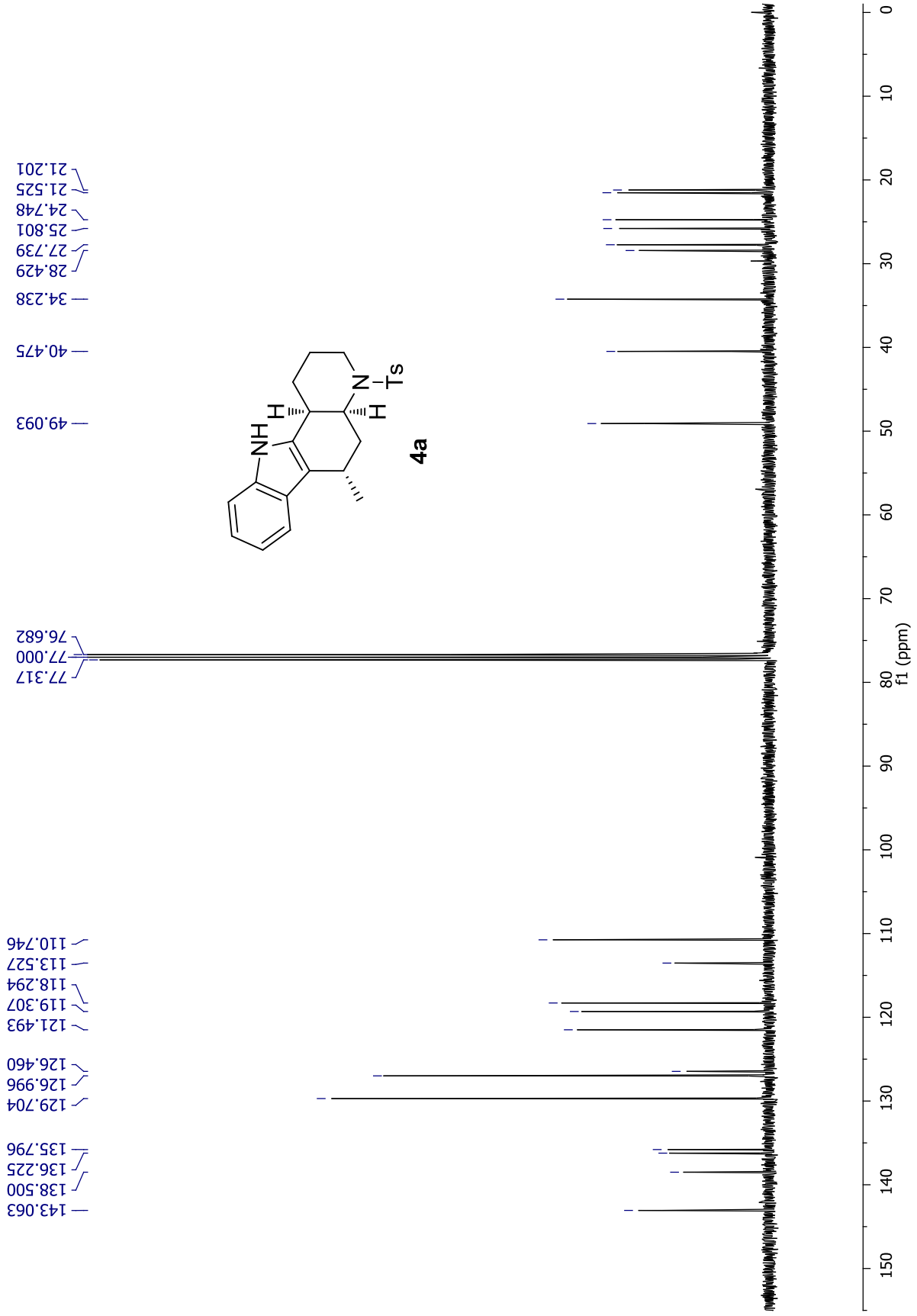
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H
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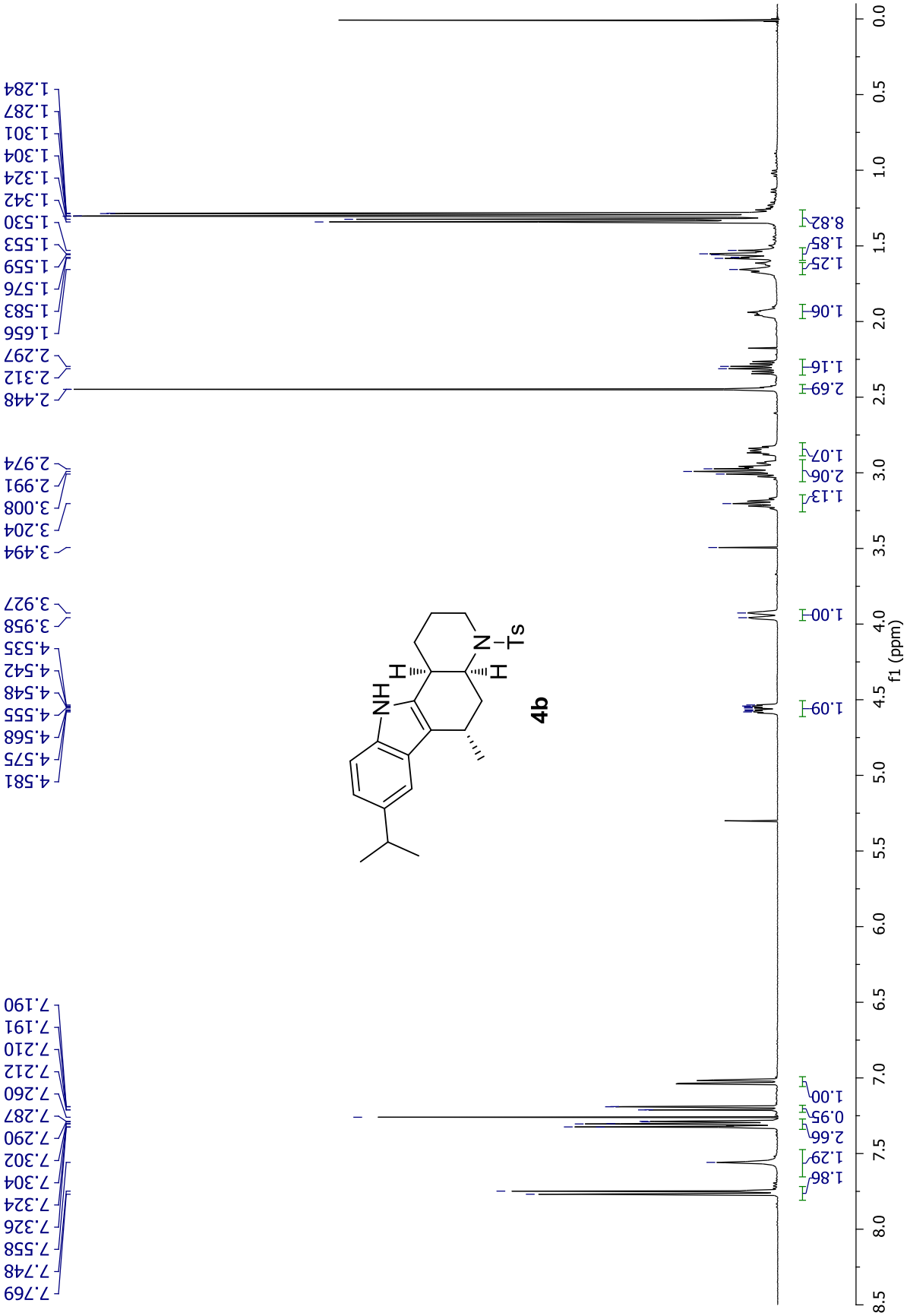
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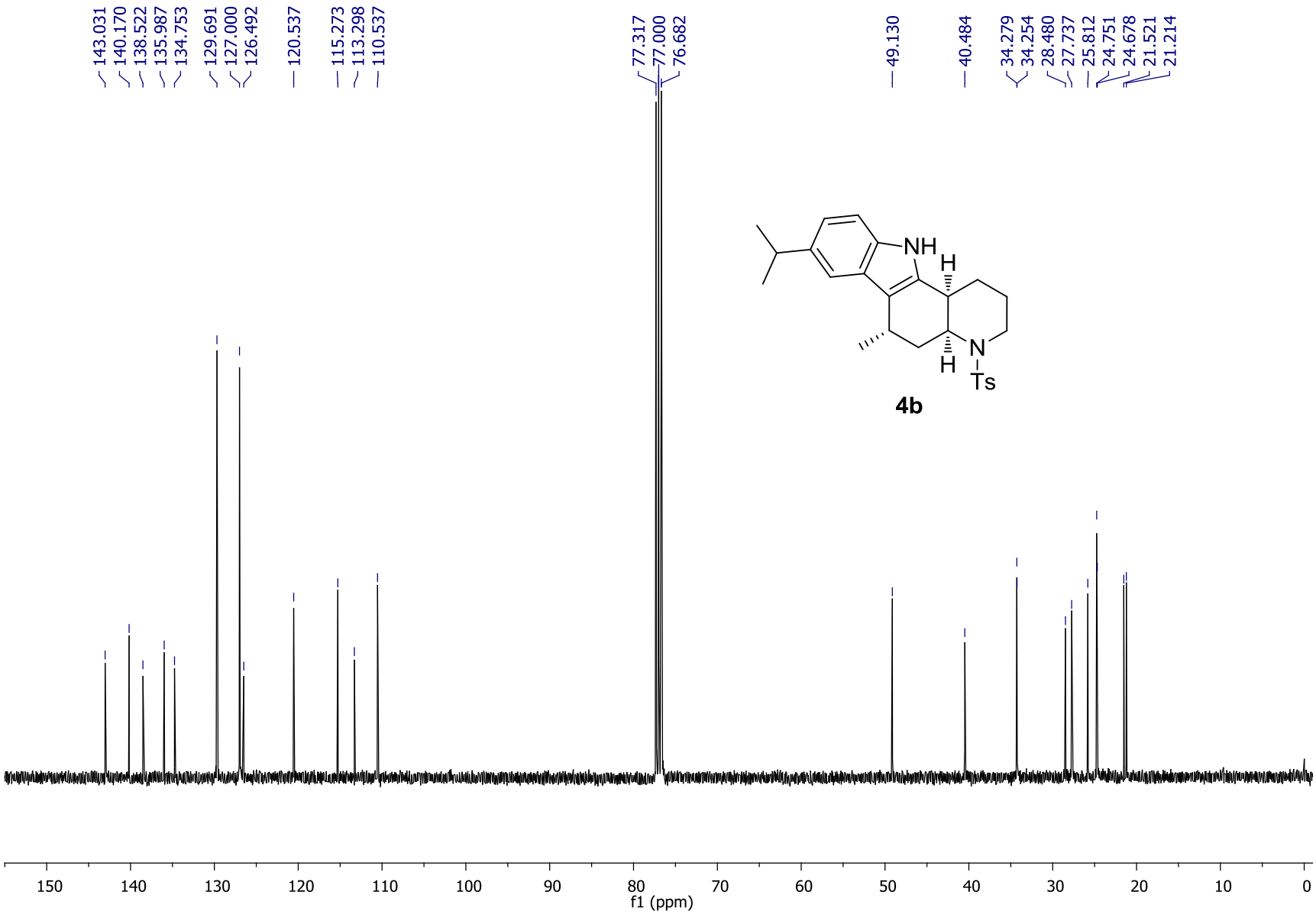
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H
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N
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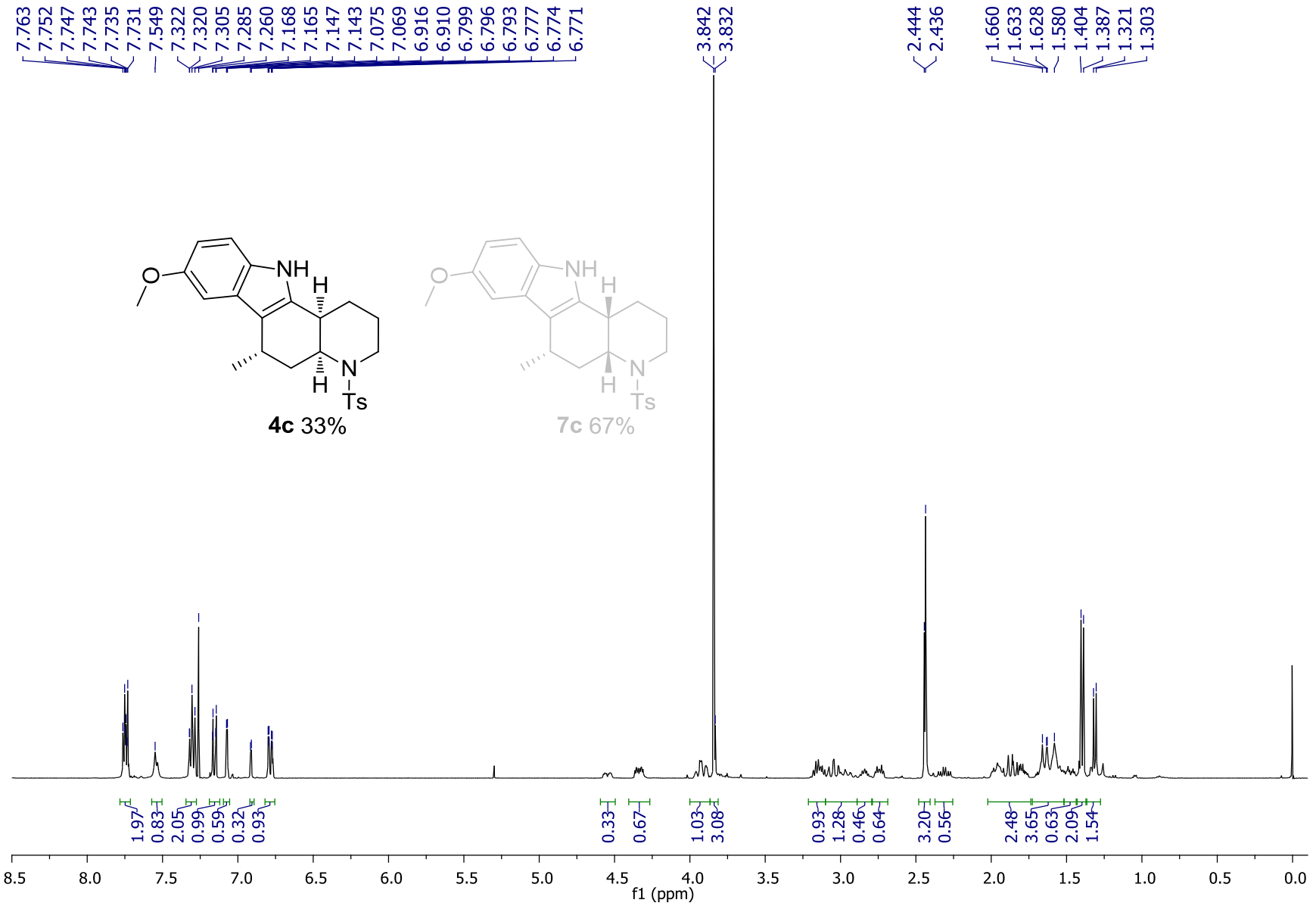
f1 (ppm)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6.799
6.796
6.793
6.777
6.774
6.771
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3.832
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1.633
1.628
1.580
1.404
1.387
1.321
1.303
O
NH
H
H
N
Ts
4c 33%
7c 67%
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0.83
2.05
0.99
0.59
0.32
0.93
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0.67
1.03
3.08
0.93
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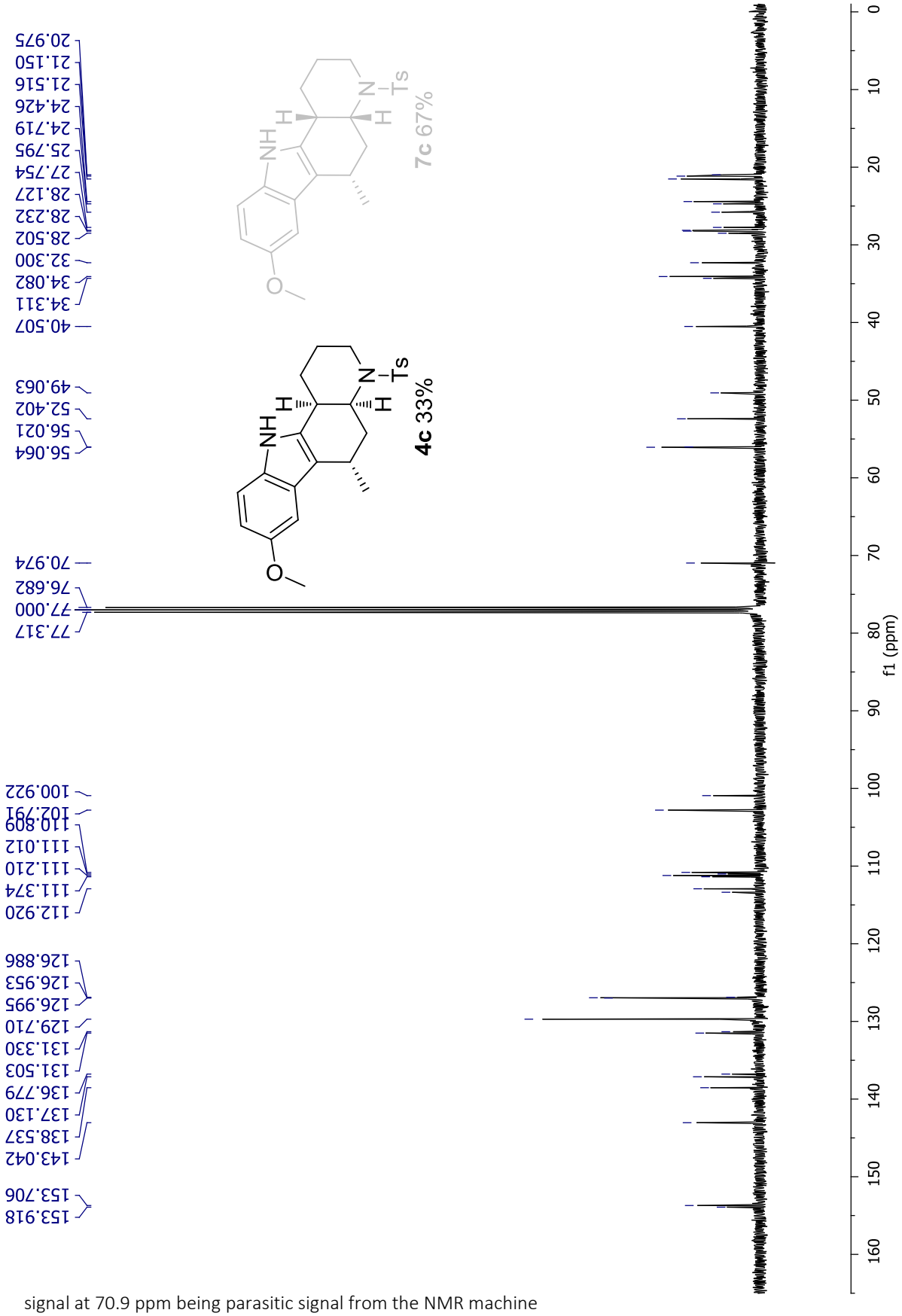
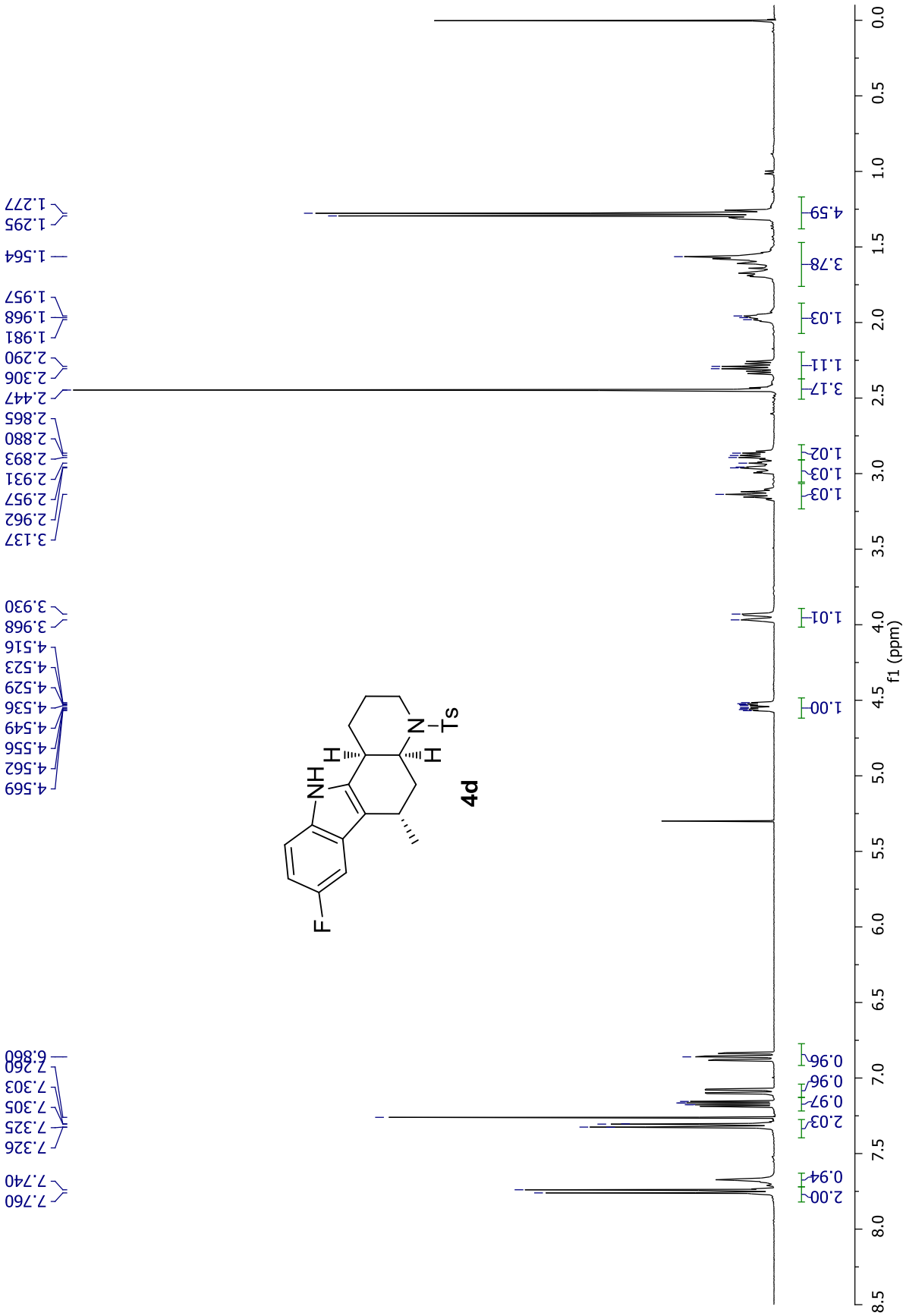
f1 (ppm)



signal at 70.9 ppm being parasitic signal from the NMR machine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1.11
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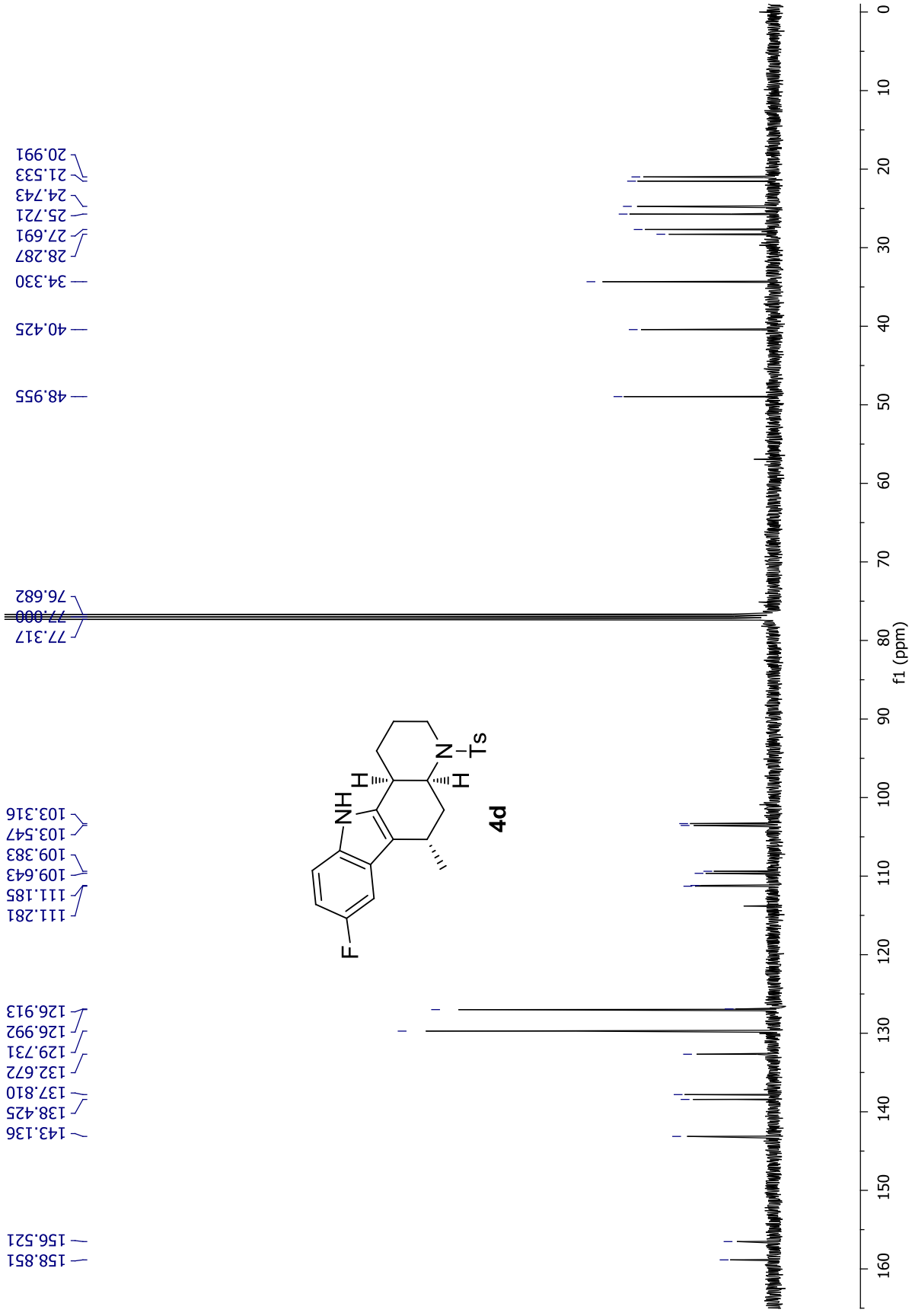
0.94
2.00
f1 (ppm)
4d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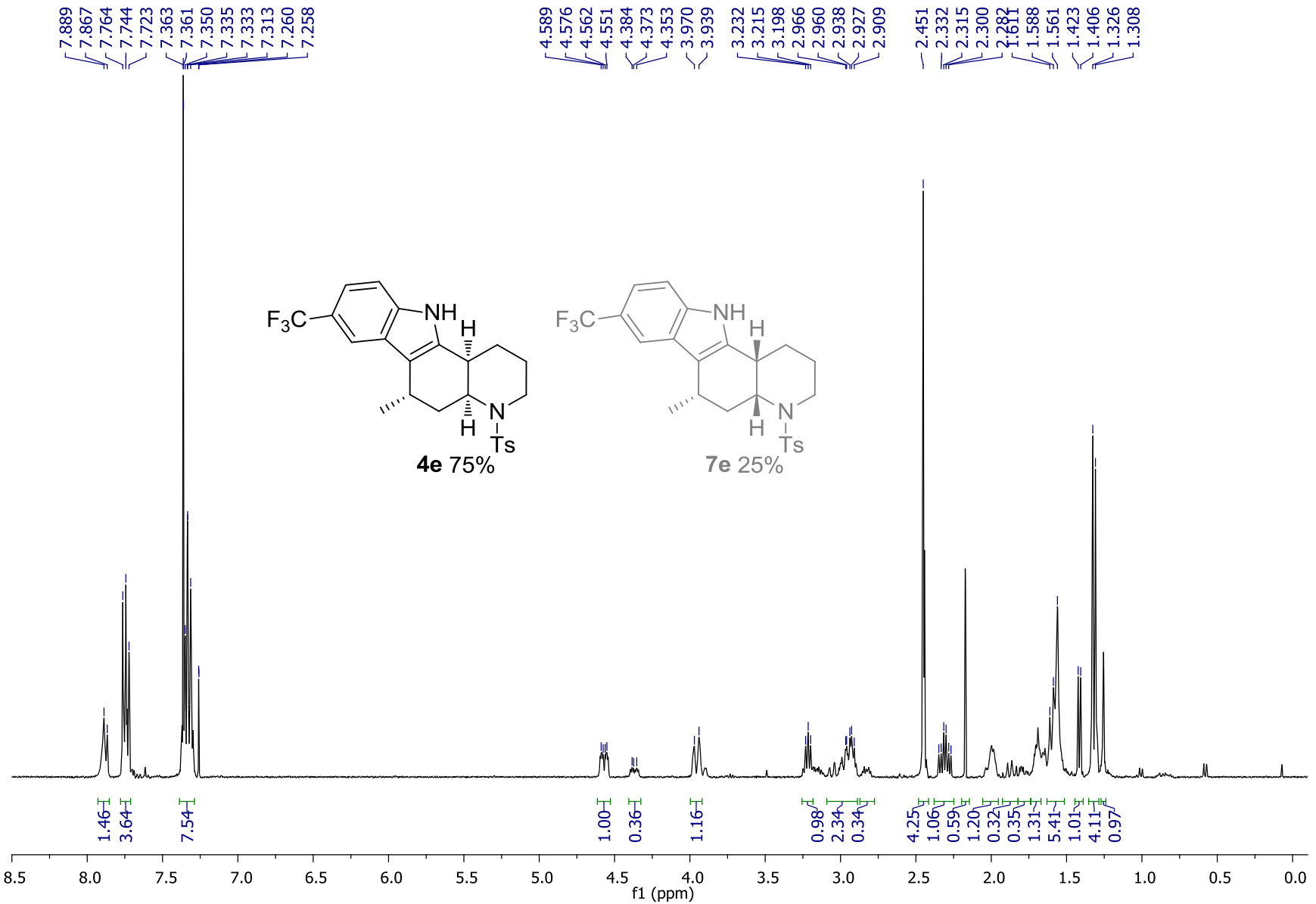
4d
f1 (ppm)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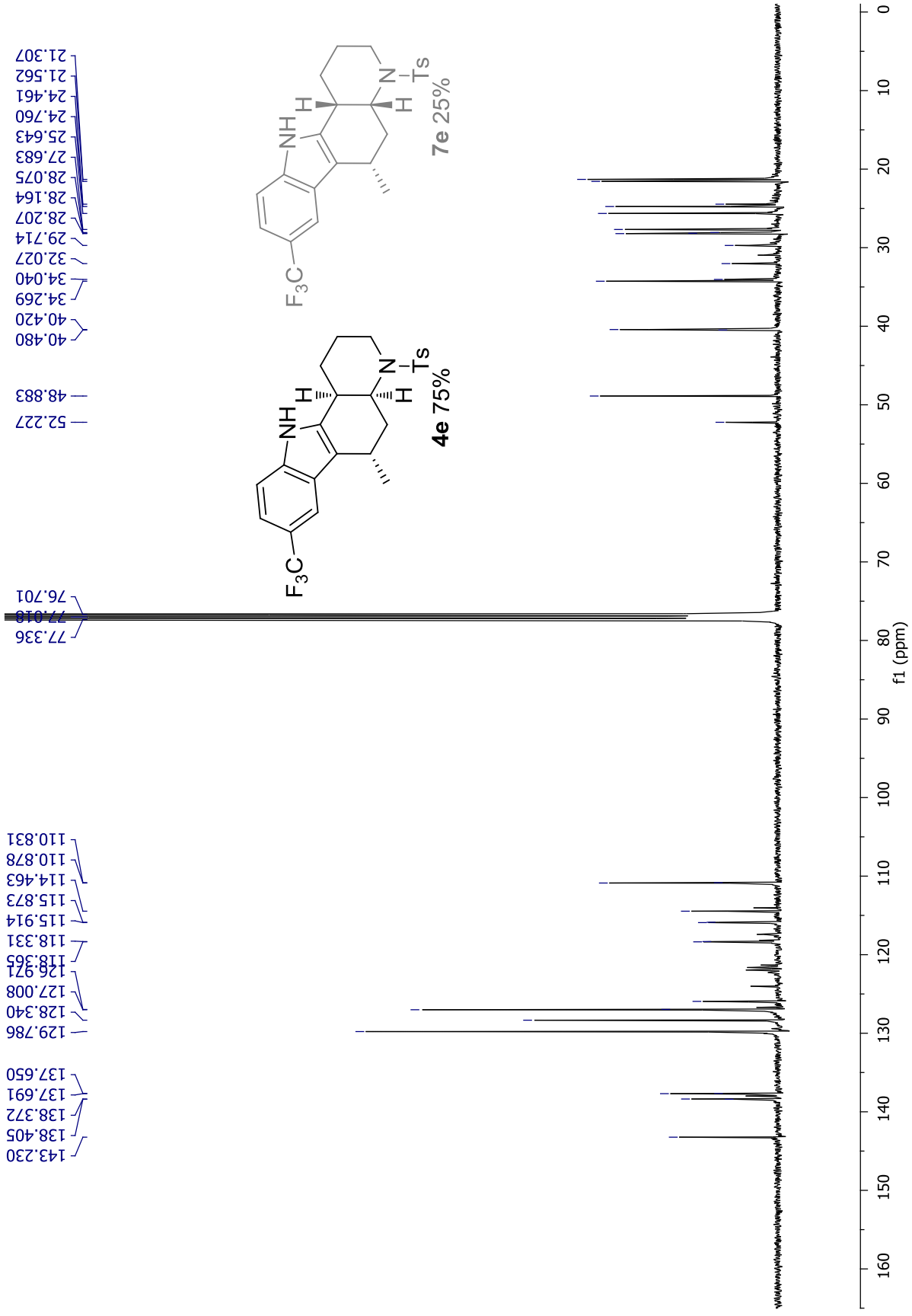
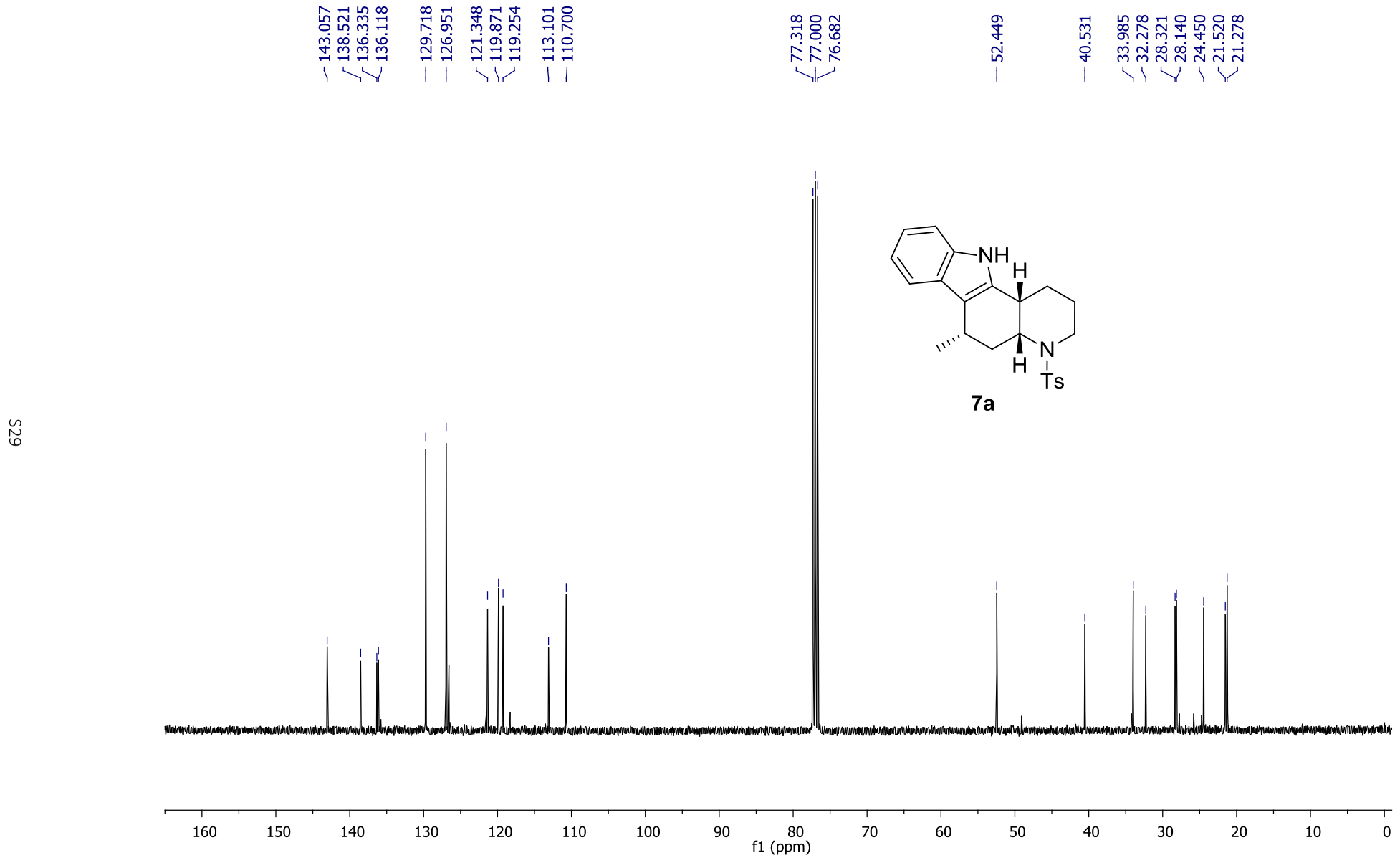
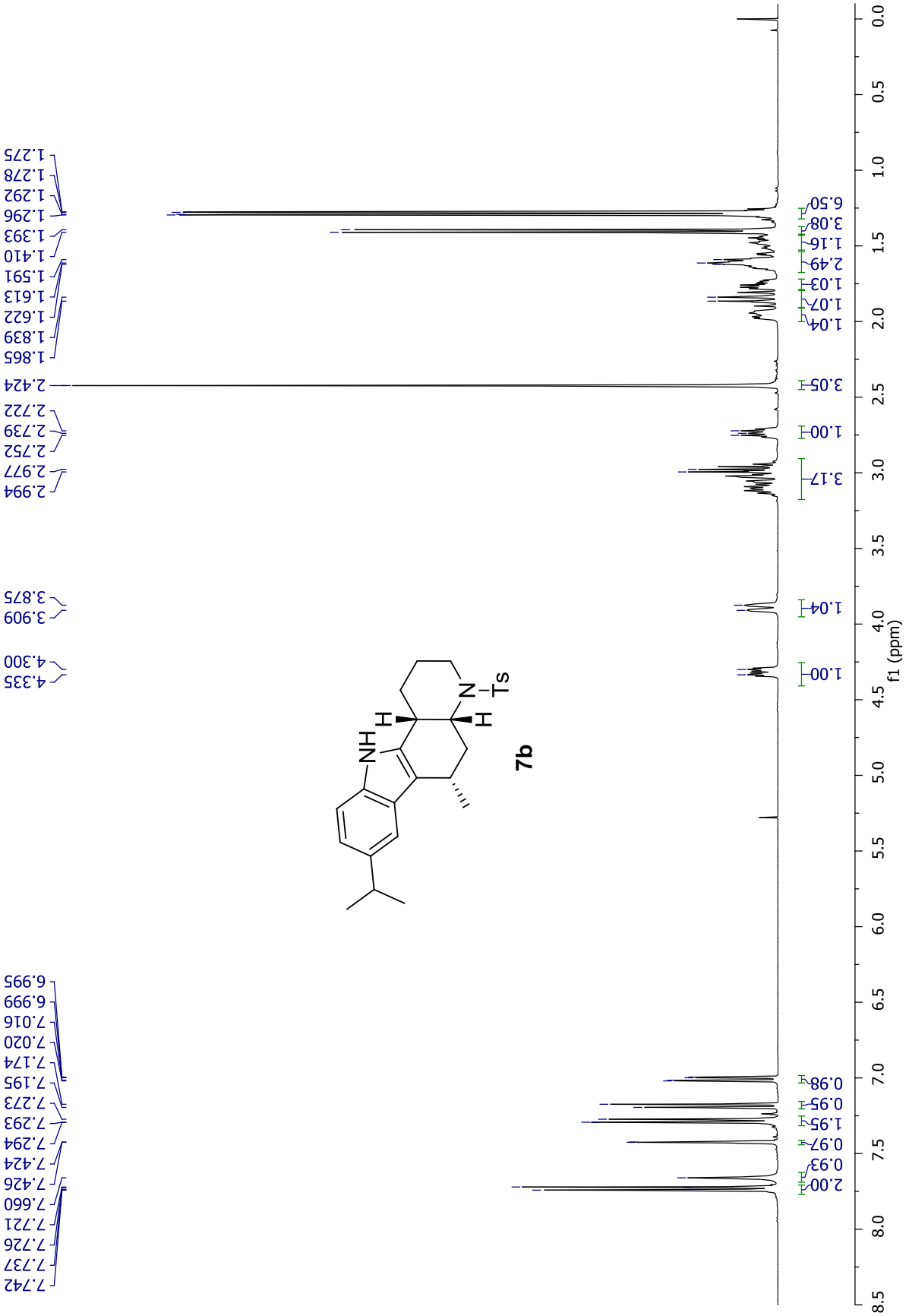
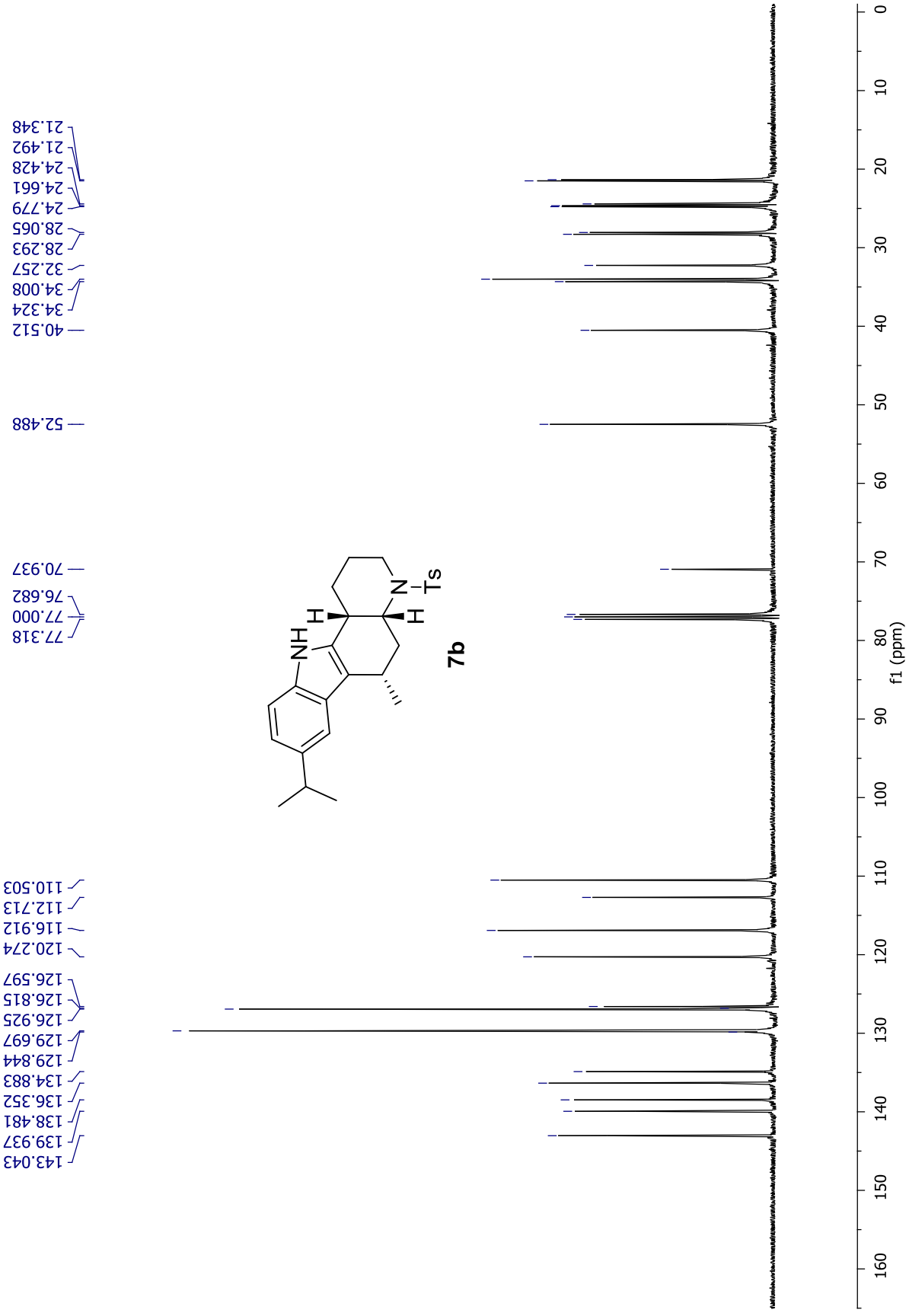
4.551
4.384
4.373
4.353
3.970
3.939
3.232
3.215
3.198
2.966
2.960
2.938
2.927
2.909
2.451
2.332
2.315
2.300
2.282
1.611
1.588
1.561
1.423
1.406
1.326
1.308
F3C
NH
H
H
N
Ts
4e 75%
F3C
NH
H
H
N
Ts
7e 25%
1.46
3.64
7.54
1.00
0.36
1.16
0.98
2.34
0.34
4.25
1.06
0.59
1.20
0.32
0.35
1.31
5.41
1.01
4.11
0.97
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
f1 (ppm)


143.230
138.405
138.372
137.691
137.650
129.786
128.340
127.008
126.971
118.365
118.331
115.914
115.873
114.463
110.878
110.831
77.336
77.018
76.701
52.227
48.883
40.480
40.420
34.269
34.040
32.027
29.714
28.207
28.164
28.075
27.683
25.643
24.760
24.461
21.562
21.307
4e 75%
7e 25%
f1 (ppm)

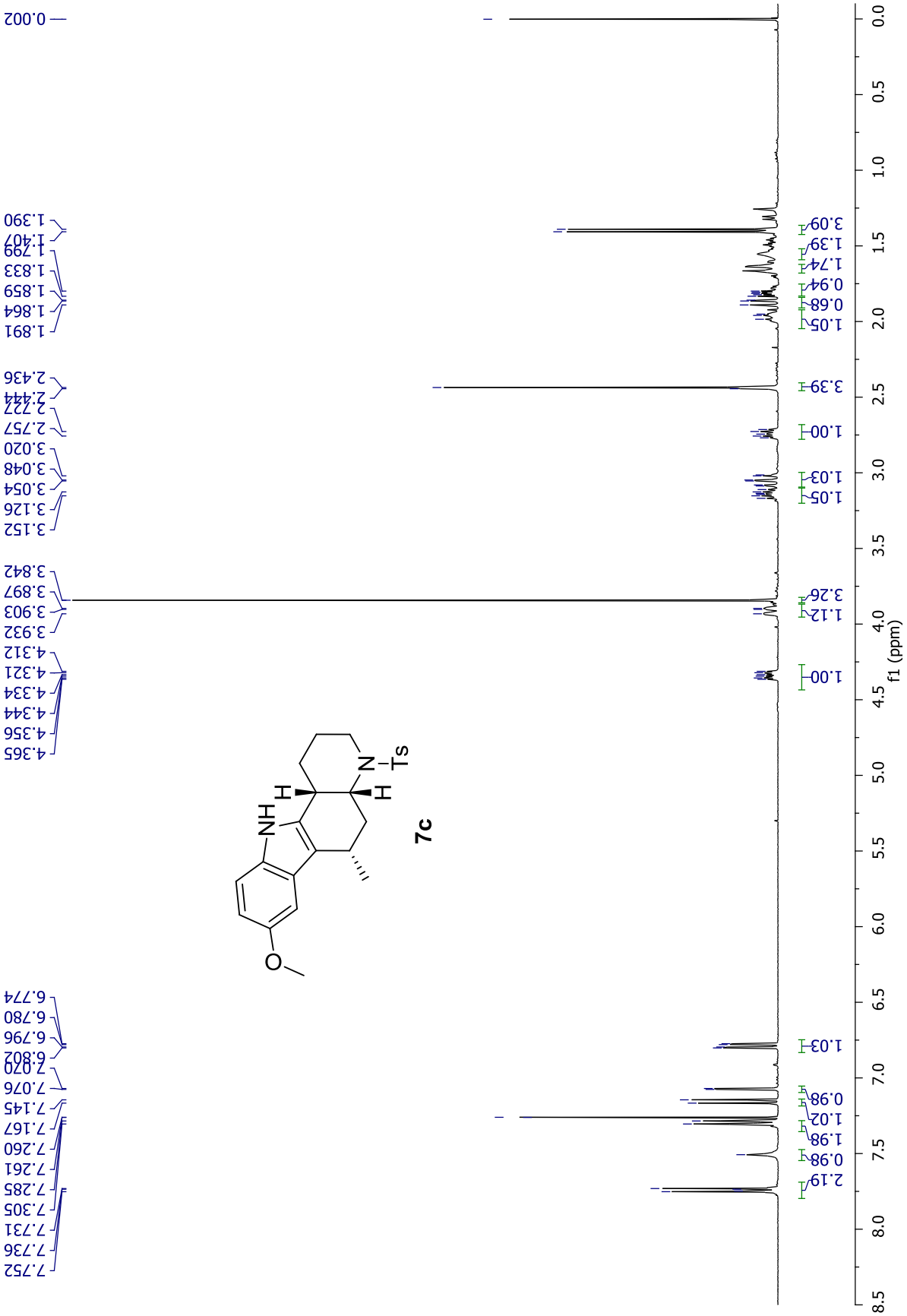
7.760
7.739
7.314
7.312
7.292
7.291
7.262
7.260
4.382
4.373
4.361
4.350
4.338
4.329
3.943
3.938
3.932
3.904
3.172
3.146
3.055
3.049
3.022
2.791
2.761
2.442
1.895
1.868
1.863
1.800
1.791
1.666
1.638
1.422
1.405
2.23
1.01
1.01
2.75
0.98
2.25
1.01
1.09
1.00
1.13
1.07
1.00
3.38
1.12
1.13
1.89
2.02
0.81
3.24
f1 (ppm)
7a

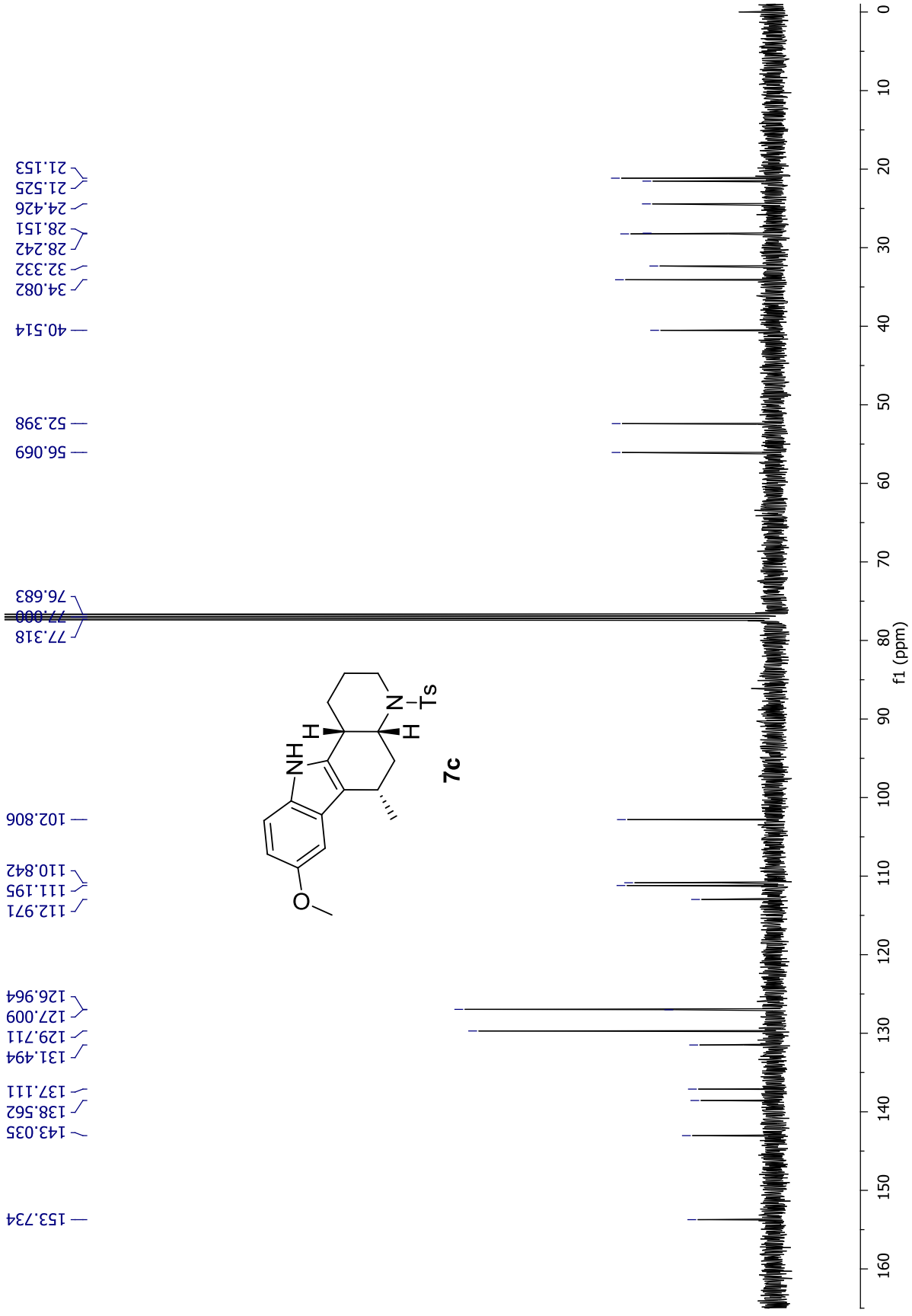

143.057
138.521
136.335
136.118
129.718
126.951
121.348
119.871
119.254
113.101
110.700
77.318
77.000
76.682
52.449
40.531
33.985
32.278
28.321
28.140
24.450
21.520
21.278
NH
H
N
H
Ts
7a
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7b
f1 (ppm)



signal at 70.9 ppm being parasitic signal from the NMR machine


7c
f1 (ppm)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143.035
138.562
137.111
131.494
129.711
127.009
126.964
112.971
111.195
110.842
102.806
77.318
77.000
76.683
56.069
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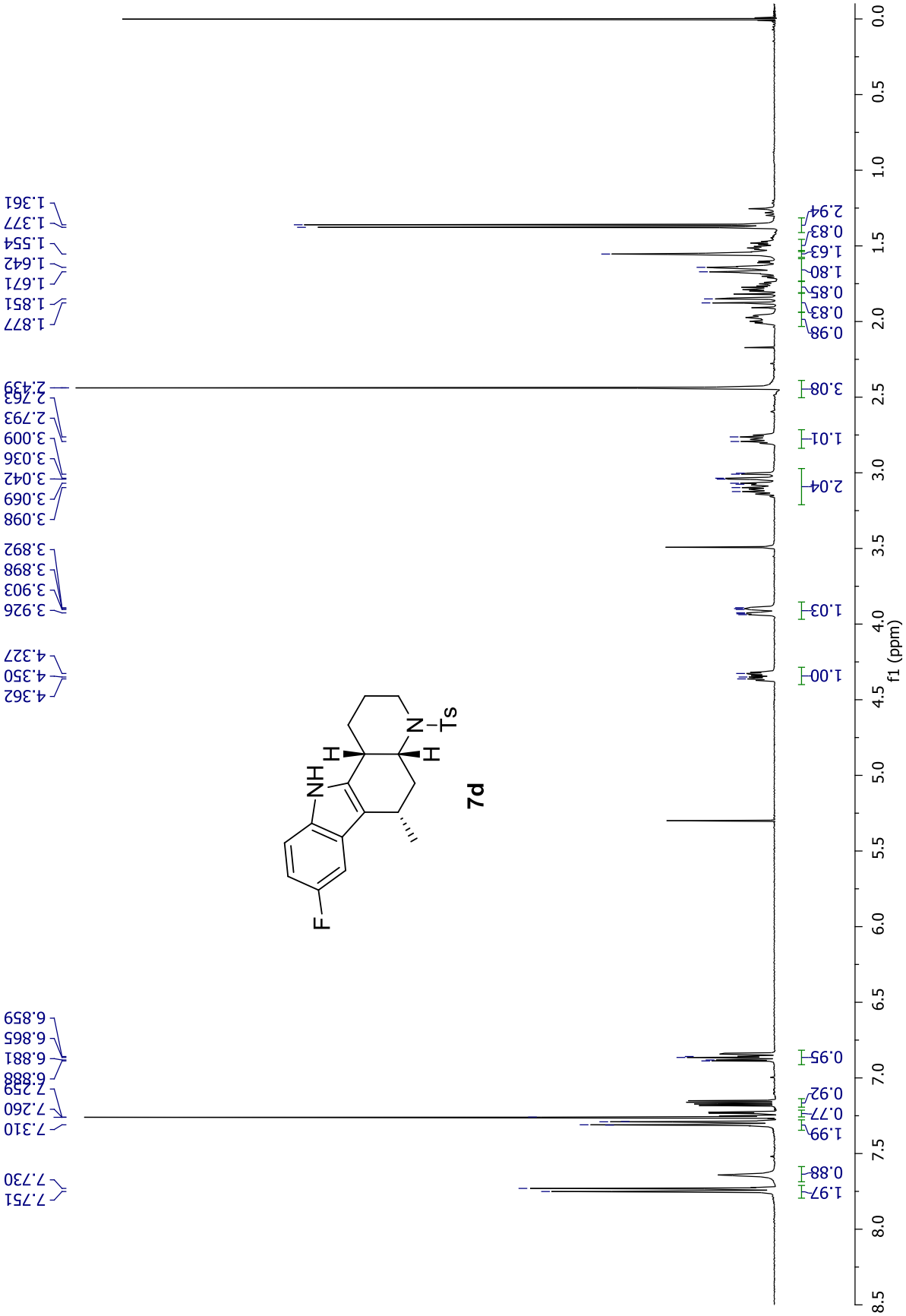
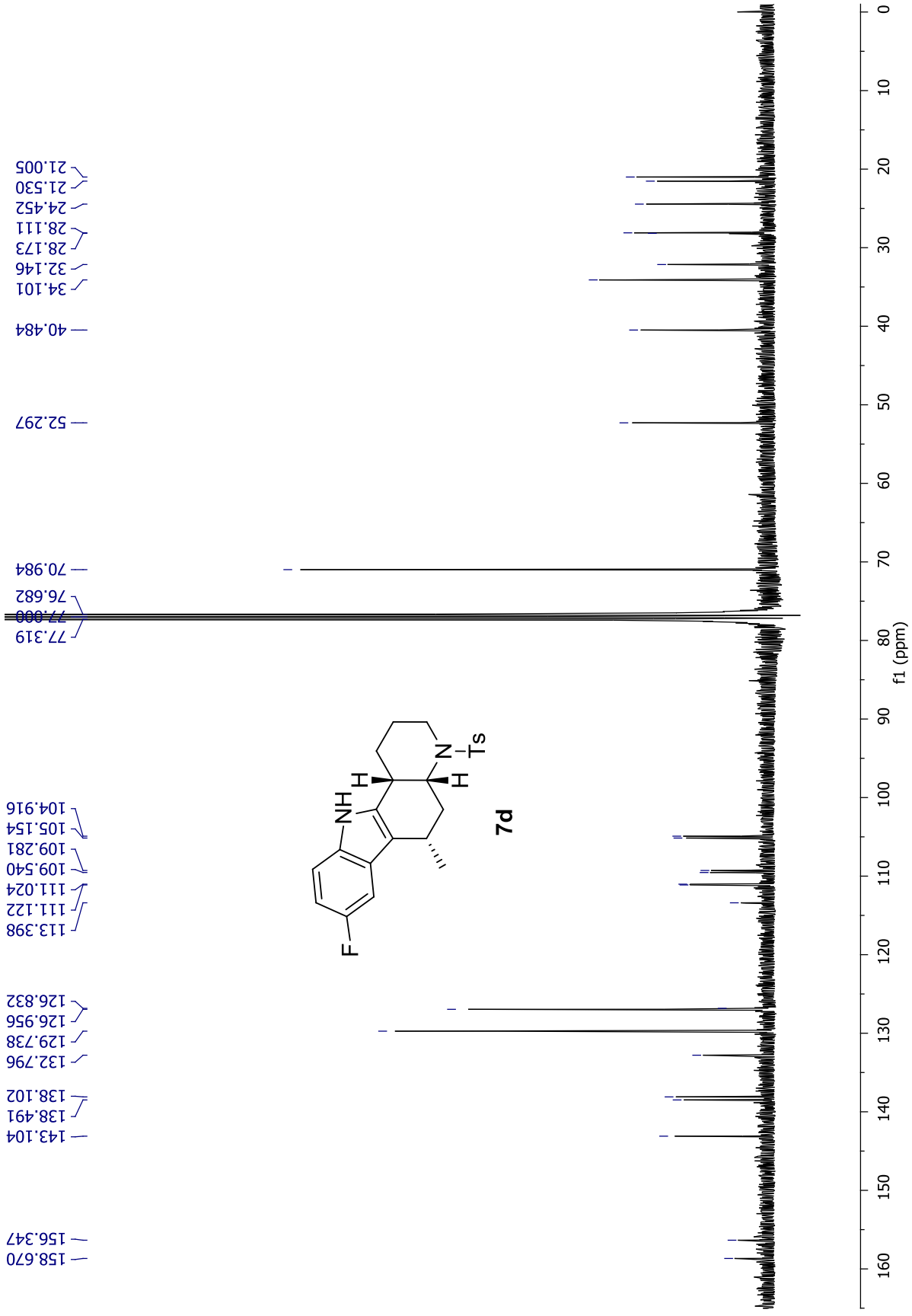
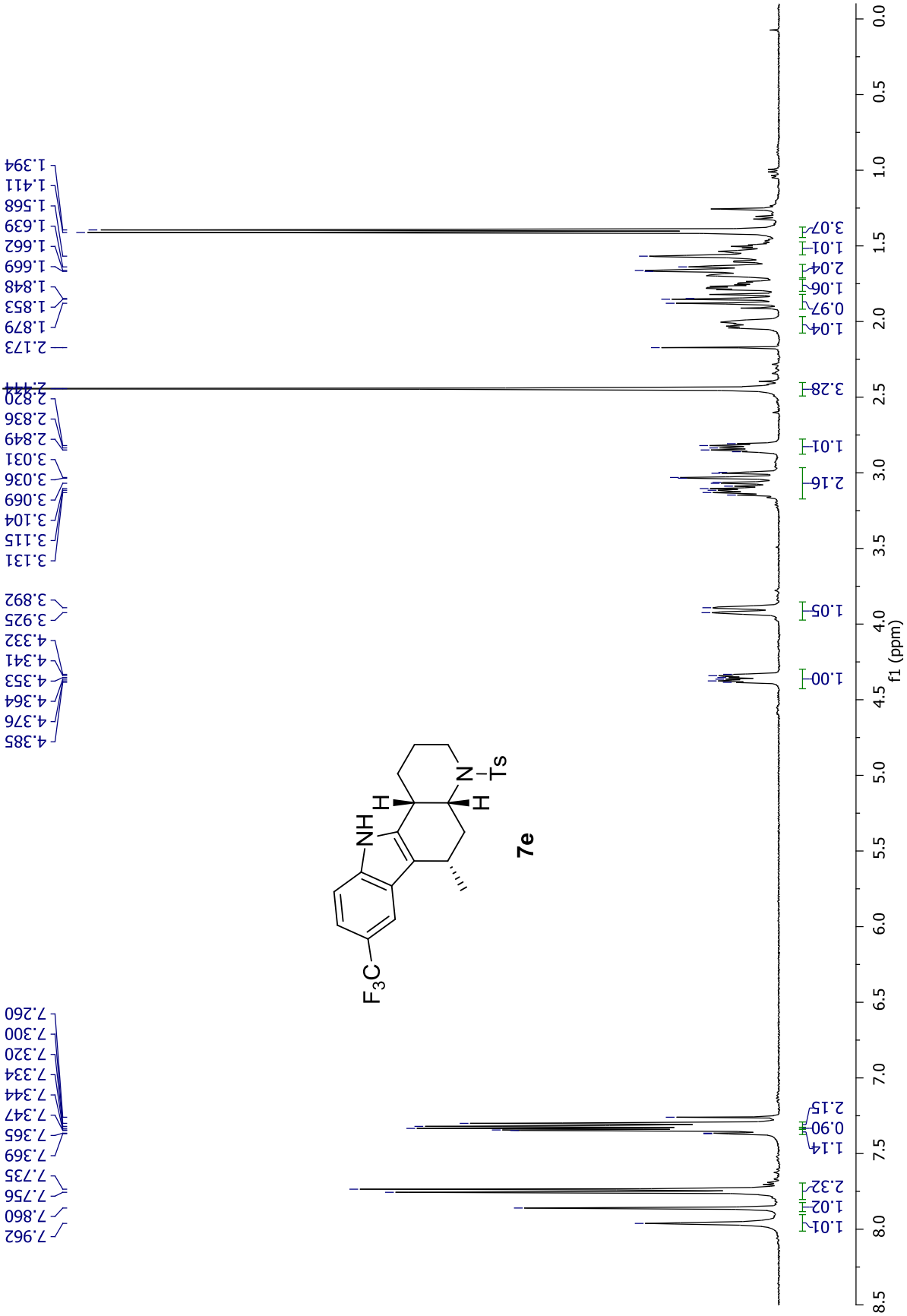
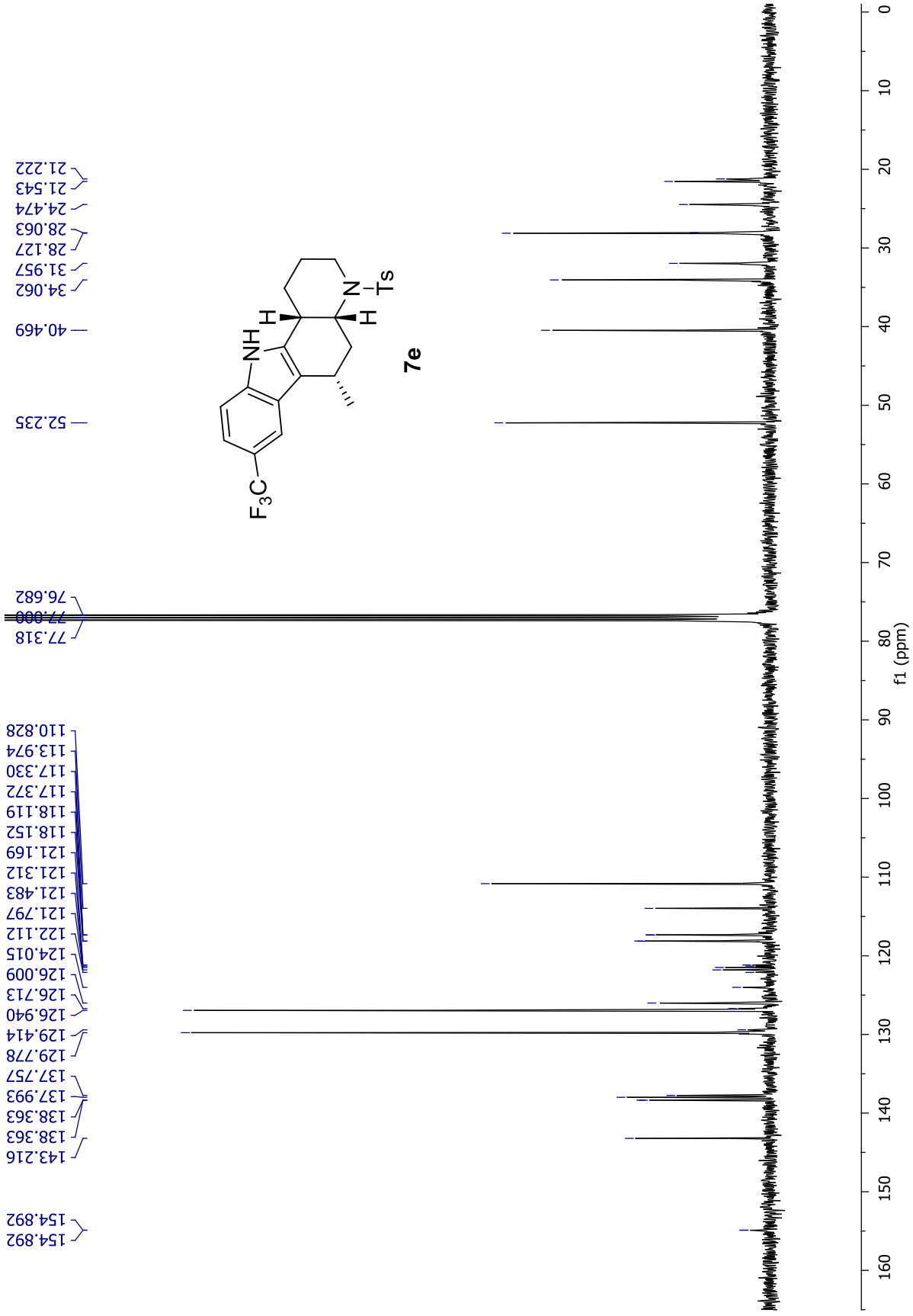
28.151
24.426
21.525
21.153
7c
f1 (ppm)


7d
f1 (ppm)



signal at 70.9 ppm being parasitic signal from the NMR machine


7.962
7.860
7.756
7.735
7.369
7.365
7.347
7.344
7.334
7.320
7.300
7.260
4.385
4.376
4.364
4.353
4.341
4.332
3.925
3.892
3.131
3.115
3.104
3.069
3.036
3.031
2.849
2.836
2.820
2.173
1.879
1.853
1.848
1.669
1.662
1.639
1.568
1.411
1.394
3.07
1.01
2.04
1.06
0.97
1.04
3.28
1.01
2.16
1.05
1.00
2.15
0.90
1.14
2.32
1.02
1.01
f1 (ppm)
7e


21.222
21.543
24.474
28.063
28.127
31.957
34.062
40.469
52.235
76.682
77.000
77.318
110.828
113.974
117.330
117.372
118.119
118.152
121.169
121.312
121.483
121.797
122.112
124.015
126.009
126.713
126.940
129.414
129.778
137.757
137.993
138.363
138.363
143.216
154.892
154.892
f1 (ppm)
7e

X-Ray Crystallographic Data

X-Ray crystallographic Data for compound **4a**

CCDC 1476675 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif

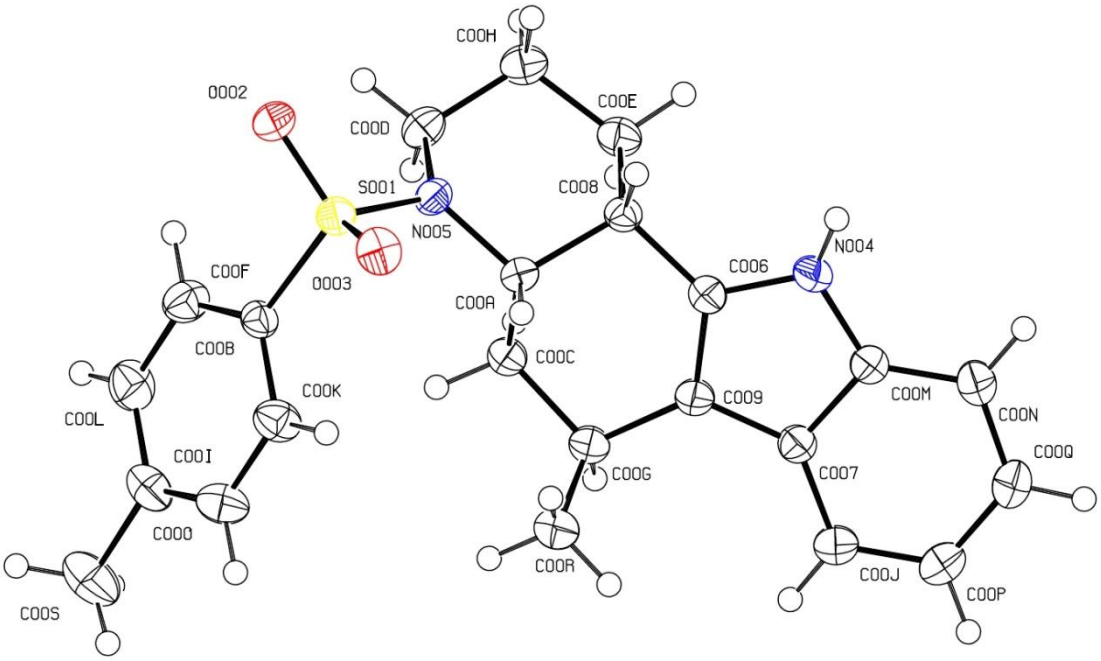


Table 3. Crystal data and structure refinement for **4a**.

Identification code	p1585c	
Empirical formula	C23 H26 N2 O2 S	
Formula weight	394.52	
Temperature	208 K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 21/c (No. 14)	
Unit cell dimensions	a = 14.776(3) Å	α= 90°.
	b = 9.354(2) Å	β= 94.17(3)°.
	c =14.360(3) Å	γ = 90°.
Volume	1979.5(7) $Å^3$	
Z	4	
Density (calculated)	1.324 Mg/m^3	
Absorption coefficient	0.185 mm^{-1}	
F(000)	840	
Crystal size	0.07 x 0.25 x 0.53 mm^3	
Theta range for data collection	2.6 to 27.5°.	

Table 4. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for p1585c. Parameters of the non-Hydrogen atoms for: p1585c P 21/c R = 0.05
U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
S001	0.40290(3)	0.77954(6)	0.57944(3)	0.0259(1)
O002	0.48372(8)	0.86539(16)	0.59223(9)	0.0326(4)
O003	0.38857(9)	0.66776(15)	0.64496(8)	0.0318(4)
N004	0.33093(11)	0.24063(19)	0.33126(11)	0.0282(5)
N005	0.40455(10)	0.70656(17)	0.47755(10)	0.0250(5)
C006	0.31249(12)	0.3774(2)	0.36039(12)	0.0245(6)
C007	0.17961(12)	0.2719(2)	0.31596(12)	0.0265(6)
C008	0.38393(11)	0.4809(2)	0.39469(12)	0.0225(6)
C009	0.22112(12)	0.4012(2)	0.35133(12)	0.0261(6)
C00A	0.33633(11)	0.5964(2)	0.44869(12)	0.0240(6)
C00B	0.30839(12)	0.8933(2)	0.57866(12)	0.0245(6)
C00C	0.25294(12)	0.6550(2)	0.39099(13)	0.0283(6)
C00D	0.44791(13)	0.7774(2)	0.40104(13)	0.0297(6)
C00E	0.43421(12)	0.5454(2)	0.31441(12)	0.0289(6)
C00F	0.31183(14)	1.0302(2)	0.54148(13)	0.0339(7)
C00G	0.17858(12)	0.5410(2)	0.37577(14)	0.0309(6)
C00H	0.49788(12)	0.6652(2)	0.34870(13)	0.0308(6)
C00I	0.15359(14)	1.0631(3)	0.56712(13)	0.0348(7)
C00J	0.09007(13)	0.2272(2)	0.29436(13)	0.0339(7)
C00K	0.22838(13)	0.8419(2)	0.61037(13)	0.0332(7)
C00L	0.23504(15)	1.1133(2)	0.53682(14)	0.0388(7)
C00M	0.25027(13)	0.1735(2)	0.30409(13)	0.0279(6)
C00N	0.23431(14)	0.0357(2)	0.27137(14)	0.0372(7)
C00O	0.15184(14)	0.9269(3)	0.60395(13)	0.0370(7)
C00P	0.07417(14)	0.0894(3)	0.26361(15)	0.0405(7)
C00Q	0.14492(14)	-0.0050(3)	0.25177(14)	0.0419(8)
C00R	0.12054(14)	0.5294(3)	0.45857(16)	0.0467(8)
C00S	0.06945(15)	1.1552(3)	0.55820(16)	0.0512(9)