Supporting Information

Synthesis of 1-Substituted Isoquinolines by Heterocyclization of TosMIC Derivatives: Total Synthesis of Cassiarin A

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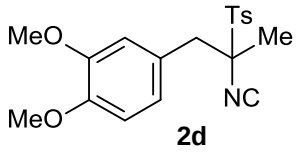
Experimental details and characterization data for compounds: 2d, 4a–i, 5a–d, 6a–c, 2e, 6d, 7 and 8. General information

Reagents of the highest commercial quality were purchased and used without further purification, unless otherwise stated. Reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm E. Merck silica gel plates (60FS-254) using UV light for visualization. Column chromatography was performed using silica gel (60 F254, 70–200 mm) as the stationary phase. All melting points were determined in open capillary tubes on a Stuart Scientific SMP3 melting point apparatus. IR spectra were obtained on a Perkin–Elmer FTIR spectrum 2000 spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded on either a Varian Mercury VX-300, Varian Unity 300 or Varian Unity 500 MHz spectrometer at room temperature. Chemical shifts are given in ppm (δ) downfield from TMS. Coupling constants (*J*) are in hertz (Hz) and signals are described as follows: s, singlet; d, doublet; t, triplet; br, broad; m, multiplet; ap, apparent etc. High-resolution analysis (TOF) was performed on an Agilent 6210 time-of-flight LC/MS. The α-benzyl TosMIC derivatives **2a** 4-[2-isocyano-2-[(4-methylphenyl)sulfonyl]-3-phenylpropyl]-1,2-dimethoxybenzene, **2b** 4-[2-isocyano-2-[(4-methylphenyl)sulfonyl]butyl]-1,2-dimethoxybenzene and **2c** 4-[2-isocyano-2-[(4-methylphenyl)sulfonyl]pent-4-enyl]-1,2-dimethoxybenzene,[12] the isoquinolines **4d**[17] and **7**,[14b] the benzyl bromide **9**[16] and Cassiarin A **8**[14b] have been described previously. The derivatives **2** and **6** are not completely stable and must be stored in a freezer at –10 to –20 ºC.

[17] Weisbach, J. A.; Kirkpatrick, J. L.; Macko, E.; Douglas, B. *J. Med. Chem.* **1968**, *11*, 760–764.

Preparation of α-benzyl TosMIC derivative 2d

4-[2-Isocyano-2-[(4-methylphenyl)sulfonyl]propyl]-1,2-dimethoxybenzene (2d)

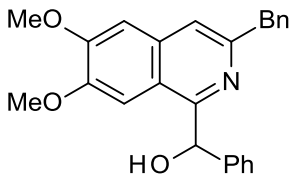


2d

A solution of NaOH (40% in H_2O, 7.5 mL) was added to a stirred solution of 4-(bromomethyl)-1,2-dimethoxybenzene (231 mg, 1 mmol), TosMIC (**1**, 195 mg, 1 mmol) and tetrabutylammonium iodide (TBAI, 74 mg, 0.2 mmol) in CH_2Cl_2 (7.5 mL) at 0 ºC and the reaction mixture was vigorously stirred at the same temperature for 1 h. The reaction mixture was warmed up to room temperature and methyl iodide (852 mg, 0.37 mL, 6 mmol) was added. Stirring was maintained at the same temperature for 24 h. Water (10 mL) was added and the two layers were separated. The aqueous layer was extracted with CH_2Cl_2. The combined organic layers were dried with anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to give the crude product, which was purified by flash chromatography [silica gel, hexane/EtOAc (8:2)] to give pure compound **2d** as a pale-yellow solid (255 mg, 71%); mp 128–130 °C; υ_{max}(KBr)/cm^{-1} 2960, 2936, 2129, 1593, 1516, 1329, 1239, 1144, 1023, 819; δ_H (500 MHz; $CDCl_3$; Me_4Si) 1.53 (3 H, s, C*H*$_3$), 2.50 (3 H, s, C*H*$_3$), 3.18 (1 H, d, *J* = 13.6 Hz, C*H*$_2$), 3.24 (1 H, d, *J* = 13.6 Hz, C*H*$_2$), 3.89 (6 H, s, 2OC*H*$_3$), 6.79 (1 H, br s), 6.80 (1 H, dd, *J* = 8.7, 2.0 Hz), 6.84 (1 H, d, *J* = 8.7 Hz),7.45 (2 H, d, *J* = 8.0 Hz, C(3, 5 arom)H), 7.93 (2 H, d, *J* = 8.0 Hz, C(2, 6 arom)H); δ_C (125 MHz; $CDCl_3$; Me_4Si) 20.1, 21.6, 38.8, 55.7, 55.8, 78.8, 111.0, 113.5, 122.9, 124.1, 129.2, 129.8 (2C), 131.2 (2C), 146.4, 148.7, 148.8, 164.6 (N=*C*:); HRMS (ESI-TOF) *m*/*z* calcd. for $C_{19}H_{22}NO_4S$ $[M + H]^+$ 360.1264 found: 360.1281.

Preparation of isoquinolines 4a–j, **5a–d** and **6a–c**

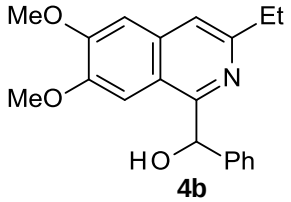
(3-Benzyl-6,7-dimethoxy-1-isoquinolyl)-phenyl-methanol (4a)



4a

A solution of $AlEt_2Cl$ (1M in hexane, 2 mmol, 2.00 mL) was added dropwise over 5 min to a stirred solution of α-benzyl TosMIC derivative **2a** (435 mg, 1 mmol) and benzaldehyde (212 mg, 2 mmol, 0.20 mL) in dry CH_2Cl_2 (10 mL) at 0 ºC under an argon atmosphere. The reaction mixture was stirred at the same temperature for a further 15 min. The reaction mixture was warmed up to room temperature and stirred for 18 h. Saturated aq. $NaHCO_3$ (20 mL) was added and the reaction mixture was stirred at room temperature for 30 min. The product was extracted with CH_2Cl_2 and the organic layer was dried with Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by chromatography [silica gel, hexane/EtOAc (8:2)] to give compound **4a** as a yellow solid (308 mg, 80%); mp 139–140 °C; υ_{max} (KBr)/cm^{-1} 3259, 2965, 1574, 1279, 703; δ_H (300 MHz; $CDCl_3$; Me_4Si) 3.77 (3 H, s, OC*H*$_3$), 3.92 (3 H, s, OC*H*$_3$), 4.34 (2 H, s, C*H*$_2$Ph), 6.16 (1 H, s), 6.95 (1 H, s), 7.03 (1 H, s), 7.21–7.40 (11 H, m); δ_C (75 MHz; $CDCl_3$; Me_4Si) 43.8, 55.7, 55.9, 72.6, 103.0, 105.0, 117.9, 119.1, 126.3, 127.7 (2C), 127.8, 128.5 (2C), 128.6 (2C), 129.4 (2C), 134.4, 139.8, 143.4, 149.3, 150.2, 152.6, 155.9; HRMS (ESI-TOF) *m*/*z* calcd. for $C_{25}H_{24}NO_3$ $[M + H]^+$ 386.1750 found: 386.1738.

(3-Ethyl-6,7-dimethoxy-1-isoquinolyl)-phenyl-methanol (4b)

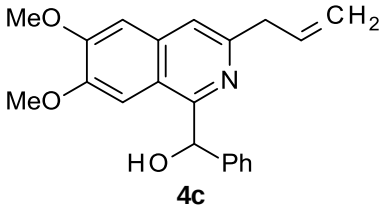


4b

A solution of $AlEt_2Cl$ (1M in hexane, 2 mmol, 2.00 mL) was added dropwise during 5 min to a stirred solution of α-benzyl TosMIC derivative **2b** (373 mg, 1 mmol) and

benzaldehyde (212 mg, 2 mmol, 0.20 mL) in dry CH_2Cl_2 (10 mL) at 0 ºC under an argon atmosphere. The reaction mixture was stirred at the same temperature for a further 15 min. The reaction mixture was warmed up to room temperature and stirred for 18 h. Saturated aq. $NaHCO_3$ solution (20 mL) was added and the reaction mixture was stirred at room temperature for 30 min. The product was extracted with CH_2Cl_2 and the organic layer was dried with Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by chromatography [silica gel, hexane/EtOAc (8:2)] to give compound **4b** as a white solid (320 mg, 99%); mp 109–111°C; υ_{max} (KBr)/cm^{-1} 3295, 2966, 1576, 1510, 1417, 1214, 705; δ_H (500 MHz; $CDCl_3$; Me_4Si) 1.43 (3 H, t, *J* = 7.5 Hz, CH_2CH_3), 3.00 (2 H, q, *J* = 7.5 Hz, CH_2CH_3), 3.76 (3 H, s, OCH_3), 3.95 (3 H, s, OCH_3), 6.14 (1 H, s), 6.99 (1 H, s), 7.02 (1 H, s), 7.22 (1 H, t, *J* = 7.3 Hz), 7.28 (2 H, t, *J* = 7.7 Hz), 7.32–7.36 (3 H, m); δ_C (125 MHz; $CDCl_3$; Me_4Si) 13.9, 30.4, 55.7, 55.9, 72.6, 103.1, 104.8, 116.6, 119.0, 127.7 (2C), 127.8, 128.6 (2C), 134.4, 143.6, 149.1, 152.5, 152.6, 155.6; HRMS (ESI-TOF) *m*/*z* calcd. for $C_{20}H_{22}NO_3$ $[M + H]^+$ 324.1594 found: 324.1603.

(3-Allyl-6,7-dimethoxy-1-isoquinolyl)-phenyl-methanol (4c)

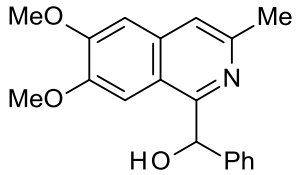


4c

A solution of $AlEt_2Cl$ (1M in hexane, 2 mmol, 2.00 mL) was added dropwise over 5 min to a stirred solution of α-benzyl TosMIC derivative **2c** (385 mg, 1 mmol) and benzaldehyde (212 mg, 2 mmol, 0.20 mL) in dry CH_2Cl_2 (10 mL) at 0 ºC under an argon atmosphere. The reaction mixture was stirred at the same temperature for a further 15 min. The reaction mixture was warmed up to room temperature and stirred for 18 h. Saturated aq. $NaHCO_3$ solution (20 mL) was added and the reaction mixture was stirred at room temperature for 30 min. The product was extracted with CH_2Cl_2 and the organic layer was dried with Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by chromatography [silica gel, hexane/EtOAc (8:2)] to give compound **4c** as a yellow oil (312 mg, 93%); υ_{max} (KBr)/cm^{-1} 3295, 2936, 1575, 1509,

1421, 1256, 1161, 702; δ_H (500 MHz; $CDCl_3$; Me_4Si) 3.75–3.78 (5 H, m), 3.95 (3 H, s, OC*H*$_3$), 5.18–5.26 (2 H, m), 6.15 (1 H, s), 6.16–6.24 (1 H, m), 7.00 (1 H, s), 7.02 (1 H, s), 7.23 (1 H, tt, *J* = 7.2, 2.3 Hz), 7.29 (2 H, t, *J* = 7.7 Hz), 7.33–7.37 (3 H, m); δ_C (125 MHz; $CDCl_3$; Me_4Si) 41.9, 55.7, 55.9, 72.6, 103.1, 104.9, 116.7, 117.5, 119.2, 127.7 (2C), 127.8, 128.6 (2C), 134.4, 136.0, 143.5, 149.2, 149.3, 152.7, 155.9; HRMS (ESI-TOF) *m*/*z* calcd. for $C_{21}H_{22}NO_3$ $[M + H]^+$ 336.1594 found: 336.1588.

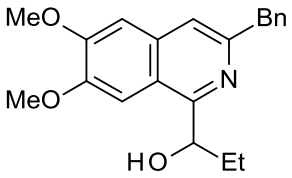
(6,7-Dimethoxy-3-methyl-1-isoquinolyl)-phenyl-methanol (4d)



4d

A solution of $AlEt_2Cl$ (1M in hexane, 2 mmol, 2.00 mL) was added dropwise during 5 min to a stirred solution of α-benzyl TosMIC derivative **2d** (359 mg, 1 mmol) and benzaldehyde (212 mg, 2 mmol, 0.20 mL) in dry CH_2Cl_2 (10 mL) at 0 ºC under an argon atmosphere. The reaction mixture was stirred at the same temperature for a further 15 min. The reaction mixture was warmed up to room temperature and stirred for 18 h. Saturated aq. $NaHCO_3$ solution (20 mL) was added and the reaction mixture was stirred at room temperature for 30 min. The product was extracted with CH_2Cl_2 and the organic layer was dried with Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by chromatography [silica gel, hexane/EtOAc (8:2)] to give compound **4d** as a yellow solid (291 mg, 94%); mp 143–144 °C; υ_{max} (KBr)/cm^{-1} 3297, 3007, 1575, 1508, 1416, 1255, 1018, 708; δ_H (500 MHz; $CDCl_3$; Me_4Si) 2.70 (3 H, s, C*H*$_3$), 3.75 (3 H, s, OC*H*$_3$), 3.94 (3 H, s, OC*H*$_3$), 6.14 (1 H, s), 6.96 (1 H, s), 7.00 (1 H, s), 7.22 (1 H, t, *J* = 7.1 Hz), 7.28 (2 H, t, *J* = 7.6 Hz), 7.30–7.36 (3 H, m); δ_C (125 MHz; $CDCl_3$; Me_4Si) 23.7, 55.7, 55.9, 72.6, 103.1, 104.6, 117.9, 118.8, 127.7 (2C), 127.8, 128.6 (2C), 134.4, 143.5, 147.4, 149.1, 152.6, 155.6; HRMS (ESI-TOF) *m*/*z* calcd. for $C_{19}H_{20}NO_3$ $[M + H]^+$ 310.1438 found: 310.1435.

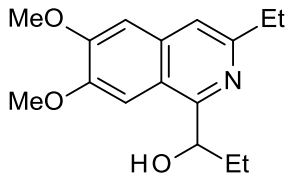
1-(3-Benzyl-6,7-dimethoxy-1-isoquinolyl)propan-1-ol (4e)



4e

A solution of $AlEt_2Cl$ (1M in hexane, 2 mmol, 2.00 mL) was added dropwise during 5 min to a stirred solution of α-benzyl TosMIC derivative **2a** (435 mg, 1 mmol) and propionaldehyde (116 mg, 2 mmol, 0.14 mL) in dry CH_2Cl_2 (10 mL) at 0 ºC under an argon atmosphere. The reaction mixture was stirred at the same temperature for additional 15 min. The reaction mixture was warmed up to room temperature and stirred for 18 h. Saturated aq. $NaHCO_3$ solution (20 mL) was added and the reaction mixture was stirred at room temperature for 30 min. The product was extracted with CH_2Cl_2 and the organic layer was dried with Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by chromatography [silica gel, hexane/EtOAc (8:2)] to give compound **4e** as a yellow oil (273 mg, 81%); υ_{max} (NaCl)/cm^{-1} 3367, 2962, 2931, 1624, 1508, 1225, 872; δ_H (500 MHz; $CDCl_3$; Me_4Si) 0.97 (3 H, t, *J* = 7.4 Hz, CH_2CH_3), 1.67–1.77 (1 H, m), 2.00–2.08 (1 H, m), 3.97 (3 H, s, OCH_3), 4.00 (3 H, s, OCH_3), 4.25 (2 H, s, CH_2Ph), 5.28 (1 H, dd, *J* = 7.1, 3.6 Hz, CHOH), 5.42 (1 H, br s, OH), 6.99 (1 H, s), 7.13 (1 H, s), 7.19 (1 H, s), 7.21–7.25 (1 H, m), 7.28–7.35 (4 H, m); δ_C (125 MHz; $CDCl_3$; Me_4Si) 9.5, 31.3, 43.8, 55.9 (2C), 70.3, 102.2, 105.3, 117.3, 118.8, 126.2, 128.5 (2C), 129.2 (2C), 134.2, 139.8, 149.5, 150.6, 152.8, 158.0; HRMS (ESI-TOF) *m*/*z* calcd. for $C_{21}H_{24}NO_3$ $[M + H]^+$ 338.1750 found: 338.1738.

1-(3-Ethyl-6,7-dimethoxy-1-isoquinolyl)propan-1-ol (4f)

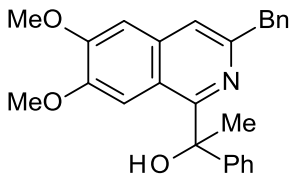


4f

A solution of $AlEt_2Cl$ (1M in hexane, 2 mmol, 2.00 mL) was added dropwise during 5 min to a stirred solution of α-benzyl TosMIC derivative **2b** (373 mg, 1 mmol) and

propionaldehyde (116 mg, 2 mmol, 0.14 mL) in dry CH_2Cl_2 (10 mL) at 0 ºC under an argon atmosphere. The reaction mixture was stirred at the same temperature for a further 15 min. The reaction mixture was warmed up to room temperature and stirred for 18 h. Saturated aq. $NaHCO_3$ solution (20 mL) was added and the reaction mixture was stirred at room temperature for 30 min. The product was extracted with CH_2Cl_2 and the organic layer was dried with Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by chromatography [silica gel, hexane/EtOAc (7:3)] to give compound **4f** as a yellow oil (222 mg, 81%); υ_{max} (NaCl)/cm^{-1} 3393, 2965, 1450, 1420; δ_H (500 MHz; $CDCl_3$; Me_4Si) 0.96 (3 H, t, *J* = 7.4 Hz, CH_2CH_3), 1.34 (3 H, t, *J* = 7.6 Hz, CH_2CH_3), 1.67–1.75 (1 H, m), 2.00–2.06 (1 H, m), 2.90 (2 H, q, *J* = 7.6 Hz, CH_2CH_3), 4.01 (3 H, s, OCH_3), 4.02 (3 H, s, OCH_3), 5.27 (1 H, dd, *J* = 7.2, 3.3 Hz, CHOH), 7.04 (1 H, s), 7.13 (1 H, s), 7.27 (1 H, s); δ_C (125 MHz; $CDCl_3$; Me_4Si) 9.5, 13.8, 29.6, 30.5, 31.4, 55.9, 70.2, 102.2, 105.1, 115.8, 118.6, 134.2, 149.3, 152.7, 153.2, 157.7; HRMS (ESI-TOF) *m*/*z* calcd. for $C_{16}H_{22}NO_3$ $[M + H]^+$ 276.1594 found: 276.1601.

1-(3-Benzyl-6,7-dimethoxy-1-isoquinolyl)-1-phenyl-ethanol (4g)

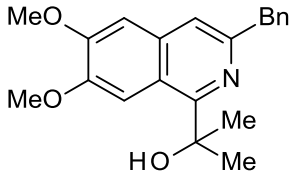


4g

A solution of $AlEt_2Cl$ (1M in hexane, 2 mmol, 2.00 mL) was added dropwise during 5 min to a stirred solution of α-benzyl TosMIC derivative **2a** (435 mg, 1 mmol) and acetophenone (240 mg, 2 mmol, 0.23 mL) in dry CH_2Cl_2 (10 mL) at 0 ºC under an argon atmosphere. The reaction mixture was stirred at the same temperature for a further 15 min. The reaction mixture was warmed up to room temperature and stirred for 18 h. Saturated aq. $NaHCO_3$ solution (20 mL) was added and the reaction mixture was stirred at room temperature for 30 min. The product was extracted with CH_2Cl_2 and the organic layer was dried with Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by chromatography [silica gel, hexane/EtOAc (8:2)] to give compound **4g** as a yellow oil (319 mg, 80%); υ_{max} (NaCl)/cm^{-1} 3418, 2931, 2112, 1466,

1215, 702; δ_H (500 MHz; $CDCl_3$; Me_4Si) 2.08 (3 H, s, C*H*$_3$), 3.52 (3 H, s, OC*H*$_3$), 3.91 (3 H, s, OC*H*$_3$), 4.33 (2 H, s, C*H*$_2$Ph), 6.85 (1 H, s), 6.93 (1 H, s), 7.18–7.44 (10 H, m), 7.64 (1 H, s); δ_C (125 MHz; $CDCl_3$; Me_4Si) 27.5, 43.9, 55.6, 55.8, 74.2, 105.1, 105.3, 118.3, 118.4, 126.3, 126.8 (2C), 127.4, 128.4 (2C), 128.6 (2C), 129.3 (2C), 135.4, 139.7, 146.7, 148.6, 149.4, 152.2, 160.2; HRMS (ESI-TOF) *m*/*z* calcd. for $C_{26}H_{26}NO_3$ $[M + H]^+$ 400.1906 found: 400.1899.

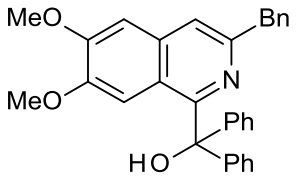
2-(3-Benzyl-6,7-dimethoxy-1-isoquinolyl)propan-2-ol (4h)



4h

A solution of $AlEt_2Cl$ (1M in hexane, 2 mmol, 2.00 mL) was added dropwise during 5 min to a stirred solution of α-benzyl TosMIC derivative **2a** (435 mg, 1 mmol) and acetone (116 mg, 2 mmol, 0.15 mL) in dry CH_2Cl_2 (10 mL) at 0 ºC under an argon atmosphere. The reaction mixture was stirred at the same temperature for a further 15 min. The reaction mixture was warmed up to room temperature and stirred for 18 h. Saturated aq. $NaHCO_3$ solution (20 mL) was added and the reaction mixture was stirred at room temperature for 30 min. The reaction was extracted with CH_2Cl_2, dried with Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by chromatography [silica gel, hexane/EtOAc (7:3)] to give pure compound **4h** as a yellow oil (307 mg, 91%); υ_{max} (NaCl)/cm^{-1} 3277, 2970, 2829, 1570, 1220, 1026, 777; δ_H (500 MHz; $CDCl_3$; Me_4Si) 1.81 (6 H, s, 2C*H*$_3$), 3.98 (3 H, s, OC*H*$_3$), 4.01 (3 H, s, OC*H*$_3$), 4.25 (2 H, s, C*H*$_2$Ph), 7.00 (1 H, s), 7.15–7.21 (2 H, m), 7.21–7.26 (1 H, m), 7.30–7.35 (4 H, m), 7.51 (1 H, s); δ_C (125 MHz; $CDCl_3$; Me_4Si) 30.3 (2C), 43.7, 55.8, 55.9, 71.3, 105.1, 105.7, 117.9, 118.2, 126.3, 128.5 (2C), 129.3 (2C), 135.5, 139.5, 148.8, 149.5, 152.2, 161.1; HRMS (ESI-TOF) *m*/*z* calcd. for $C_{21}H_{24}NO_3$ $[M + H]^+$ 338.1750 found: 338.1739.

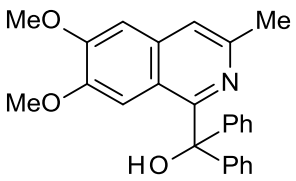
(3-Benzyl-6,7-dimethoxy-1-isoquinolyl)diphenyl-methanol (4i)



4i

A solution of $AlEt_2Cl$ (1M in hexane, 2 mmol, 2.00 mL) was added dropwise during 5 min to a stirred solution of α-benzyl TosMIC derivative **2a** (435 mg, 1 mmol) and benzophenone (364 mg, 2 mmol) in dry CH_2Cl_2 (10 mL) at 0 ºC under an argon atmosphere. The reaction mixture was stirred at the same temperature for a further 15 min. The reaction mixture was warmed up to room temperature and stirred for 18 h. Saturated. aq. $NaHCO_3$ solution (20 mL) was added and the reaction mixture was stirred at room temperature for 30 min. The reaction was extracted with CH_2Cl_2, dried with Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by chromatography [silica gel, hexane/EtOAc (8:2)] to give pure compound **4i** as a white solid (249 mg, 54%); mp 154–156 °C; υ_{max} (KBr)/cm^{-1} 3245, 2958, 1508, 1251, 1156, 1013, 705; δ_H (500 MHz; $CDCl_3$; Me_4Si) 3.38 (3 H, s, OC*H*$_3$), 3.93 (3 H, s, OC*H*$_3$), 4.32 (2 H, s, C*H*$_2$Ph), 6.85 (1 H, s), 6.94 (1 H, s), 7.20–7.39 (15 H, m), 8.22 (1 H, s); δ_C (125 MHz; $CDCl_3$; Me_4Si) 43.7, 55.7, 55.9, 80.2, 104.9, 106.6, 118.8, 120.6, 126.4 (2C), 127.3 (2C), 127.9 (4C), 128.6 (2C), 128.8 (4C), 129.3 (2C), 135.6, 139.4, 145.8, 148.7, 149.8, 152.2, 158.7; HRMS (ESI-TOF) *m*/*z* calcd. for $C_{31}H_{28}NO_3$ $[M + H]^+$ 462.2062 found: 462.2034.

(6,7-Dimethoxy-3-methyl-1-isoquinolyl)diphenyl-methanol (4j)

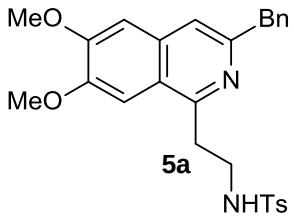


4j

A solution of $AlEt_2Cl$ (1M in hexane, 2 mmol, 2.00 mL) was added dropwise during 5 min to a stirred solution of α-benzyl TosMIC derivative **2d** (359 mg, 1 mmol) and benzophenone (364 mg, 2 mmol) in dry CH_2Cl_2 (10 mL) at 0 ºC under an argon

atmosphere. The reaction mixture was stirred at the same temperature for a further 15 min. The reaction mixture was warmed up to room temperature and stirred for 18 h at the same temperature. Saturated aq. $NaHCO_3$ solution (20 mL) was added and the reaction mixture was stirred at room temperature for 30 min. The reaction was extracted with CH_2Cl_2, dried with Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by chromatography [silica gel, hexane/EtOAc (8:2)] to give pure compound **4j** as a white solid (227 mg, 59%); mp 184–186°C; υ_{max} (KBr)/cm^{-1} 3269, 2954, 1507, 1251, 1220, 1011, 771; δ_H (500 MHz; $CDCl_3$; Me_4Si) 2.67 (3 H, s, C*H*$_3$), 3.36 (3 H, s, OC*H*$_3$), 3.97 (3 H, s, OC*H*$_3$), 6.82 (1 H, s), 6.97 (1 H, s), 7.22–7.29 (6 H, m), 7.36–7.40 (4 H, m), 8.27 (1 H, s); δ_C (125 MHz; $CDCl_3$; Me_4Si) 23.6, 55.6, 55.9, 80.1, 104.5, 106.5, 118.9, 120.2, 127.3 (2C), 127.9 (4C), 128.8 (4C), 135.6, 146.0 (2C), 146.9, 148.5, 152.3, 158.4; HRMS (ESI-TOF) *m*/*z* calcd. for $C_{25}H_{24}NO_3$ $[M + H]^+$ 386.1750 found: 386.1741.

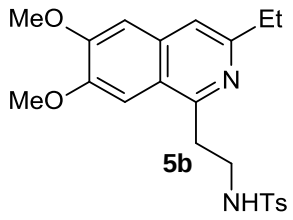
***N*-[2-(3-Benzyl-6,7-dimethoxy-1-isoquinolyl)ethyl]-4-methyl-benzenesulfonamide (5a)**



A solution of $AlEt_2Cl$ (1M in hexane, 4 mmol, 4.00 mL) was added dropwise during 5 min to a stirred solution of α-benzyl TosMIC derivative **2a** (435 mg, 1 mmol) and *N*-tosylaziridine (788 mg, 4 mmol) in dry CH_2Cl_2 (10 mL) at 0 ºC under an argon atmosphere. The reaction mixture was stirred at the same temperature for additional 15 min. The reaction mixture was warmed up to room temperature and stirred for 72 h. Saturated aq. $NaHCO_3$ solution (20 mL) was added and the reaction mixture was stirred at room temperature for 2 h. The reaction was extracted with CH_2Cl_2, dried with Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by chromatography [silica gel, hexane/EtOAc (6:4)] to give pure compound **5a** as a yellow oil (448 mg, 94%); υ_{max} (NaCl)/cm^{-1} 3280, 2923, 1572, 1508, 1253, 1159, 813; δ_H (300 MHz; $CDCl_3$; Me_4Si) 2.34 (3 H, s, C*H*$_3$), 3.34 (2 H, t, *J* = 5.6 Hz, CH_2CH_2), 3.52 (2 H,

q, *J* = 5.6 Hz, NHC*H*$_2$CH$_2$), 3.97 (3 H, s, OC*H*$_3$), 3.98 (3 H, s, OC*H*$_3$), 4.18 (2 H, s, C*H*$_2$Ph), 6.28 (1 H, t, *J* = 5.6 Hz, N*H*), 6.95 (1 H, s), 7.11 (1 H, s), 7.15–7.19 (3 H, m), 7.22–7.35 (5 H, m), 7.61 (2 H, d, *J* = 8.1 Hz, C(2, 6 arom)H); δ_C (75 MHz; $CDCl_3$; Me_4Si) 21.4, 32.4, 41.1, 43.8, 56.0 (2C), 102.7, 105.1, 116.9, 121.1, 126.3, 126.8 (2C), 128.6 (2C), 129.0 (2C), 129.4 (2C), 133.8, 137.4, 140.0, 142.8, 149.8, 151.0, 153.0, 155.3; HRMS (ESI-TOF) *m*/*z* calcd. for $C_{27}H_{29}N_2O_4S$ $[M + H]^+$ 477.1841 found: 477.1843.

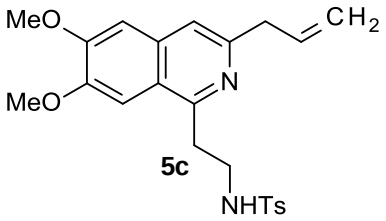
_N_-[2-(3-Ethyl-6,7-dimethoxy-1-isoquinolyl)ethyl]-4-methylbenzenesulfonamide (5b)



A solution of $AlEt_2Cl$ (1M in hexane, 4 mmol, 4.00 mL) was added dropwise during 5 min to a stirred solution of α-benzyl TosMIC derivative **2b** (373 mg, 1 mmol) and *N*-tosylaziridine (788 mg, 4 mmol) in dry CH_2Cl_2 (10 mL) at 0 ºC under an argon atmosphere. The reaction mixture was stirred at the same temperature for a further 15 min. The reaction mixture was warmed up to room temperature and stirred for 72 h. Saturated aq. $NaHCO_3$ solution (20 mL) was added and the reaction mixture was stirred at room temperature for 2 h. The reaction was extracted with CH_2Cl_2, dried with Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by chromatography [silica gel, hexane/EtOAc (6:4)] to give pure compound **6b** as a yellow oil (410 mg, 99%); υ_{max} (KBr)/cm^{-1} 3291, 2965, 2929, 1509, 1327, 1160, 1094; δ_H (500 MHz; $CDCl_3$; Me_4Si) 1.33 (3 H, t, *J* = 7.6 Hz, CH$_2$C*H*$_3$), 2.38 (3 H, s, C*H*$_3$), 2.85 (2 H, q, *J* = 7.6 Hz, C*H*$_2$CH$_3$), 3.36 (2 H, t, *J* = 5.3 Hz, CH$_2$C*H*$_2$), 3.52 (2 H, q, *J* = 5.3 Hz, NHC*H*$_2$CH$_2$), 3.99 (3 H, s, OC*H*$_3$), 4.00 (3 H, s, OC*H*$_3$), 6.52–6.62 (1 H, m), 6.98 (1 H, s), 7.13 (1 H, s), 7.22 (1 H, s), 7.23 (2 H, d, *J* = 8.1 Hz, C(3, 5 arom)H), 7.75 (2 H, d, *J* = 8.1 Hz, C(2, 6 arom)H); δ_C (125 MHz; $CDCl_3$; Me_4Si) 14.1, 21.4, 30.8, 32.4, 41.2, 55.9, 56.0, 102.6, 105.0, 115.4, 121.0, 127.0 (2C), 129.6 (2C), 133.7, 137.3, 143.0, 149.5,

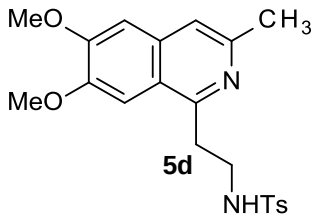
152.7, 154.0, 155.3; HRMS (ESI-TOF) *m*/*z* calcd. for $C_{22}H_{27}N_2O_4S$ $[M + H]^+$ 415.1686 found: 415.1687.

_N_-[2-(3-Allyl-6,7-dimethoxy-1-isoquinolyl)ethyl]-4-methyl-benzenesulfonamide (5c)



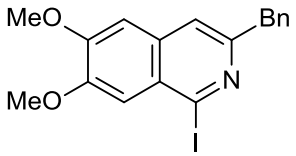
A solution of $AlEt_2Cl$ (1M in hexane, 4 mmol, 4.00 mL) was added dropwise during 5 min to a stirred solution of α-benzyl TosMIC derivative **2c** (385 mg, 1 mmol) and *N*-tosylaziridine (788 mg, 4 mmol) in dry CH_2Cl_2 (10 mL) at 0 ºC under an argon atmosphere. The reaction mixture was stirred at the same temperature for a further 15 min. The reaction mixture was warmed up to room temperature and stirred for 72 h. Saturated aq. $NaHCO_3$ solution (20 mL) was added and the reaction mixture was stirred at room temperature for 2 h. The reaction was extracted with CH_2Cl_2, dried with Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by chromatography [silica gel, hexane/EtOAc (6:4)] to give pure compound **5c** as a yellow oil (247 mg, 58%); υ_{max} (NaCl)/cm^{-1} 3300, 2938, 1573, 1509, 1428, 1327, 1160, 1094; δ_H (500 MHz; $CDCl_3$; Me_4Si) 2.37 (3 H, s, C*H*$_3$), 3.33 (2 H, t, *J* = 5.7 Hz, CH_2CH_2), 3.47–3.54 (2 H, m, $NHCH_2CH_2$), 3.58 (2 H, d, *J* = 6.8 Hz, $CHCH_2$), 3.98 (3 H, s, OCH_3), 3.99 (3 H, s, OCH_3), 5.14–5.21 (2 H, m), 6.02–6.10 (1 H, m), 6.55 (1 H, br s, N*H*), 6.97 (1 H, s), 7.11 (1 H, s), 7.22 (1 H, s), 7.23 (2 H, d, *J* = 8.1 Hz, C(3, 5 arom)H)), 7.74 (2 H, d, *J* = 8.1 Hz, C(2, 6 arom)H); δ_C (125 MHz; $CDCl_3$; Me_4Si) 21.4, 32.5, 41.1, 42.2, 56.0 (2C), 102.6, 105.0, 116.5, 116.7, 121.1, 126.9 (2C), 129.5 (2C), 133.6, 136.3, 137.4, 142.9, 149.7, 150.4, 152.7, 155.5; HRMS (ESI-TOF) *m*/*z* calcd. for $C_{23}H_{27}N_2O_4S$ $[M + H]^+$ 427.1685 found: 427.1689.

***N*-[2-(6,7-Dimethoxy-3-methyl-1-isoquinolyl)ethyl]-4-methyl-benzenesulfonamide (5d)**



A solution of $AlEt_2Cl$ (1M in hexane, 4 mmol, 4.00 mL) was added dropwise during 5 min to a stirred solution of α-benzyl TosMIC derivative **2d** (359 mg, 1 mmol) and *N*-tosylaziridine (788 mg, 4 mmol) in dry CH_2Cl_2 (10 mL) at 0 ºC under an argon atmosphere. The reaction mixture was stirred at the same temperature for a further 15 min. The reaction mixture was warmed to room temperature and stirred for 72 h. Saturated aq. $NaHCO_3$ solution (20 mL) was added and the reaction mixture was stirred at room temperature for 2 h. The reaction was extracted with CH_2Cl_2, dried with Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by chromatography [silica gel, hexane/EtOAc (6:4)] to give pure compound **5d** as a yellow oil (320 mg, 80%); υ_{max} (NaCl)/cm^{-1} 3286, 2924, 1572, 1509, 1428, 1326, 1252, 1160, 1094; δ_H (500 MHz; $CDCl_3$; Me_4Si) 2.38 (3 H, s, C*H*$_3$), 2.58 (3 H, s, C*H*$_3$), 3.37 (2 H, t, *J* = 5.8 Hz, CH_2CH_2), 3.47–3.52 (2 H, m, NHC*H*$_2$CH$_2$), 4.00 (3 H, s, OC*H*$_3$), 4.01 (3 H, s, OC*H*$_3$), 6.40 (1 H, br s, N*H*), 6.95 (1 H, s), 7.15 (1 H, s), 7.23 (2 H, d, *J* = 6.7 Hz, C(3, 5 arom)H), 7.25 (1 H, s), 7.75 (2 H, d, *J* = 6.7 Hz, C(2, 6 arom)H); δ_C (125 MHz; $CDCl_3$; Me_4Si) 21.4, 23.8, 32.6, 41.4, 43.8, 56.0, 56.1, 102.7, 104.8, 116.9, 120.9, 126.9 (2C), 129.5 (2C), 133.8, 137.2, 143.0, 148.4, 149.7, 153.0, 155.0; HRMS (ESI-TOF) *m*/*z* calcd. for $C_{21}H_{25}N_2O_4S$ $[M + H]^+$ 401.1529 found: 401.1531.

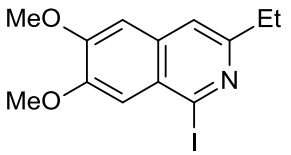
3-Benzyl-1-iodo-6,7-dimethoxy-isoquinoline (6a)



6a

A solution of α-benzyl TosMIC derivative **2a** (435 mg, 1 mmol) and *N*-iodosuccinimide (450 mg, 2 mmol) in dry CH_2Cl_2 (10 mL) under an argon atmosphere was vigorously stirred at room temperature for 18 h. The reaction mixture was cooled down to 0 ºC and LiHMDS (1M in *tert*-butyl methyl ether, 4 mL, 4 mmol) was added dropwise. The stirring was continued at the same temperature for 15 min and then at room temperature for 3 h. The mixture was quenched with water (10 mL), extracted with CH_2Cl_2, dried with Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by chromatography [silica gel, hexane/EtOAc (7:3)] to give pure compound **6a** as a yellow solid (389 mg, 96%); mp 155–156 °C; υ_{max} (KBr)/cm^{-1} 2961, 2929, 1558, 1508, 1244, 1211, 1143, 834; δ_H (500 MHz; $CDCl_3$; Me_4Si) 3.96 (3 H, s, OCH_3), 4.04 (3 H, s, OCH_3), 4.25 (2 H, s, CH_2Ph), 6.84 (1 H, s), 7.07 (1 H, s), 7.23–7.29 (1 H, m), 7.29–7.34 (5 H, m); δ_C (125 MHz; $CDCl_3$; Me_4Si) 43.6, 56.1, 56.2, 104.8, 110.9, 118.3, 124.2, 126.3, 126.4, 128.6 (2C), 129.4 (2C), 133.1, 139.2, 150.9, 153.4, 154.4; HRMS (ESI-TOF) *m*/*z* calcd. for $C_{18}H_{17}INO_2$ $[M + H]^+$ 406.0299 found: 406.0299.

3-Ethyl-1-iodo-6,7-dimethoxy-isoquinoline (6b)

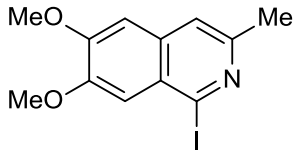


6b

A solution of α-benzyl TosMIC derivative **2b** (373 mg, 1 mmol) and *N*-iodosuccinimide (450 mg, 2 mmol) in dry CH_2Cl_2 (10 mL) under an argon atmosphere was vigorously stirred at room temperature for 18 h. The reaction mixture was cooled down to 0 ºC and LiHMDS (1M in *tert*-butyl methyl ether, 4 mL, 4 mmol) was added dropwise. The stirring was continued at the same temperature for 15 min and then at room temperature for 3 h. The mixture was quenched with water (10 mL), extracted with CH_2Cl_2, dried

with Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by chromatography [silica gel, hexane/EtOAc (7:3)] to give pure compound **6b** as an orange solid (288 mg, 84%); mp 147–148 °C; υ_{max} (KBr)/cm^{-1} 2964, 2361, 1590, 1241, 868; δ_H (300 MHz; $CDCl_3$; Me_4Si) 1.33 (3 H, t, *J* = 7.6 Hz, CH_2CH_3), 2.89 (2 H, q, *J* = 7.6 Hz, CH_2CH_2), 4.01 (3 H, s, OCH_3), 4.05 (3 H, s, OCH_3), 6.93 (1 H, s), 7.25 (1 H, s), 7.31 (1 H, s); δ_C (75 MHz; $CDCl_3$; Me_4Si) 14.0, 30.5, 56.1, 56.3, 104.7, 111.0, 116.9, 124.1, 126.2, 133.3, 150.7, 153.4, 156.8; HRMS (ESI-TOF) *m*/*z* calcd. for $C_{13}H_{15}INO_2$ $[M + H]^+$ 344.0143 found: 344.0142.

1-Iodo-6,7-dimethoxy-3-methyl-isoquinoline (6c)

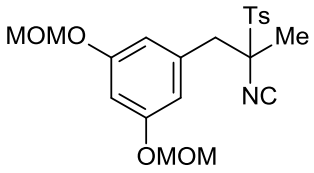


6c

A solution of α-benzyl TosMIC derivative **2d** (359 mg, 1 mmol) and *N*-iodosuccinimide (450 mg, 2 mmol) in dry CH_2Cl_2 (10 mL) under an argon atmosphere was vigorously stirred at room temperature for 18 h. The reaction mixture was cooled down to 0 ºC and LiHMDS (1M in *tert*-butyl methyl ether, 4 mL, 4 mmol) was added dropwise. The stirring was continued at the same temperature for 15 min and then at room temperature for 24 h. The mixture was quenched with water (10 mL), extracted with CH_2Cl_2, dried with Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by chromatography [silica gel, hexane/EtOAc (8:2)] to give pure compound **6c** as a white solid (234 mg, 71%); mp 159–161 °C; υ_{max} (KBr)/cm^{-1} 3004, 2967, 2914, 1503, 1413, 1247, 1151, 1015; δ_H (500 MHz; $CDCl_3$; Me_4Si) 2.57 (3 H, s, CH_3), 3.98 (3 H, s, OCH_3), 4.01 (3 H, s, OCH_3), 6.84 (1 H, s), 7.18 (1 H, s), 7.23 (1 H, s); δ_C (125 MHz; $CDCl_3$; Me_4Si) 23.6, 56.0, 56.2, 104.3, 110.9, 118.3, 124.0, 126.0, 133.1, 150.6, 151.2, 153.3; HRMS (ESI-TOF) *m*/*z* calcd. for $C_{12}H_{13}INO_2$ $[M + H]^+$ 329.9987 found: 329.9991.

Total synthesis of Cassiarin A (8): Synthesis of 2e, 6d, 7 and 8

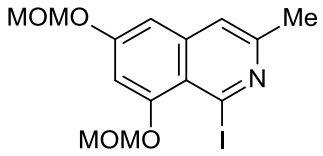
1-[2-Isocyano-2-[(4-methylphenyl)sulfonyl)propyl]-3,5-*bis*(methoxymethoxy)benzene (2e)



2e

A solution of NaOH (40% in H_2O, 3.5 mL) was added to a stirred solution of 1-bromomethyl-3,5-*bis*(methoxymethoxy)benzene **9**[16] (291 mg, 1 mmol), TosMIC (**1**, 195 mg, 1 mmol) and tetrabutylammonium iodide (TBAI, 74 mg, 0.2 mmol) in CH_2Cl_2 (3.5 mL) at 0 ºC. The reaction mixture was vigorously stirred at 0 ºC for 1 h. The reaction mixture was warmed up to room temperature and methyl iodide (852 mg, 0.37 mL, 6 mmol) was added. Stirring was maintained at the same temperature for 18 h. Water (7 mL) was added and the two layers were separated. The aqueous layer was extracted with CH_2Cl_2. The combined organic layers were dried with anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to give a crude product. The crude product was purified by flash chromatography [silica gel, hexane/EtOAc (8:2)] to give pure **2e** as a white solid (298 mg, 71%); mp 103–105 °C; υ_{max}(KBr)/cm^{-1} 2963, 2902, 2124, 1592, 1471, 1324, 1146, 1051, 1019; δ_H (300 MHz; $CDCl_3$; Me_4Si) 1.51 (3 H, s, C*H*$_3$), 2.45 (3 H, s, C*H*$_3$), 3.12 (1 H, br d, *J* = 3.5 Hz, C*H*$_2$), 3.40 (6 H, s, 2OC*H*$_3$), 5.06 (2 H, d, *J* = 6.8 Hz, O*CH*$_2$O), 5.11 (2 H, d, *J* = 6.8 Hz, O*CH*$_2$O), 6.56 (2 H, d, *J* = 2.2 Hz); 6.66 (1 H, t, *J* = 2.2 Hz), 7.40 (2 H, d, *J* = 8.1 Hz, C(3, 5 arom)H), 7.87 (2 H, d, *J* = 8.1 Hz, C(2, 6 arom)H); δ_C (75 MHz; $CDCl_3$; Me_4Si) 20.0, 21.6, 39.1, 55.8 (2C), 78.5, 94.2 (2C), 104.2, 111.9 (2C), 128.9, 129.7 (2C), 131.1 (2C), 133.9, 146.4, 158.0 (2C), 164.8 (N=*C:*); HRMS (ESI-TOF) *m*/*z* calcd. for $C_{21}H_{26}NO_6S$ $[M + H]^+$ 420.1474 found: 420.1456.

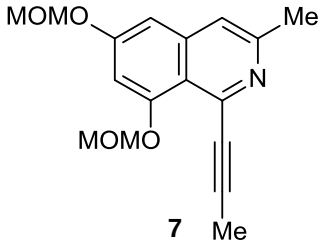
1-Iodo-6,8-*bis*(methoxymethoxy)-3-methyl-isoquinoline (6d)



6d

A solution of α-benzyl TosMIC derivative **2d** (419 mg, 1 mmol) and *N*-iodosuccinimide (450 mg, 2 mmol) in CH_2Cl_2 (30 mL) was vigorously stirred under an argon atmosphere at room temperature for 22 h. Tetrabutylammonium iodide (TBAI, 74 mg, 0.2 mmol) and aq. NaOH solution (40% in H_2O, 33 mL) were added and the reaction mixture was vigorously stirred at the same temperature for 5 h. Water (250 mL) was added and the two layers were separated. The aqueous layer was extracted with CH_2Cl_2, and combined organic layers were dried with Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by chromatography [silica gel, hexane/EtOAc (9:1)] to give pure compound **6d** as a colorless oil (334 mg, 86%); υ_{max} (NaCl)/cm^{-1} 2957, 2828, 1621, 1558, 1470, 1374, 1276, 1151, 835; δ_H (300 MHz; $CDCl_3$; Me_4Si) 2.54 (3 H, s, C*H*$_3$), 3.47 (3 H, s, OC*H*$_3$), 3.57 (3 H, s, OC*H*$_3$), 5.23 (2 H, s, OC*H*$_2$O), 5.33 (2 H, s, OC*H*$_2$O), 6.80 (1 H, d, *J* = 2.3 Hz), 6.85 (1 H, d, *J* = 2.3 Hz), 7.17 (1 H, s); δ_C (75 MHz; $CDCl_3$; Me_4Si) 23.5, 56.4, 56.9, 93.8, 94.2, 101.8, 103.2, 112.2, 117.2, 118.4, 140.5, 152.7, 153.3, 158.6; HRMS (ESI-TOF) *m*/*z* calcd. for $C_{14}H_{17}INO_4$ $[M + H]^+$ 390.0197 found: 390.0179.

6,8-*Bis*(methoxymethoxy)-3-methyl-1-prop-1-ynyl-isoquinoline (7)

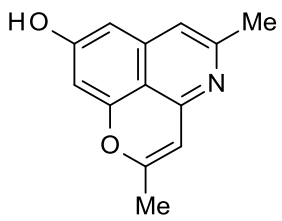


7

cis-1-Bromo-1-propene (145 mg, 0.10 mL, 1.2 mmol) was dissolved in dry THF (2 mL) under an argon atmosphere. The solution was cooled to –78 °C and *n*-BuLi (1.63 M in hexane, 1 mL, 1.63 mmol) was added. The resulting mixture was stirred at –78 °C for 1 h. Water (0.03 mL) was added and the temperature was allowed to rise to 0 °C. The

mixture was stirred for additional 30 min. To the mixture was added a solution of iodide **6c** (78 mg, 0.2 mmol) in THF (1.4 mL), $Pd(PPh_3)_2Cl_2$ (7 mg, 0.01 mmol), CuI (4 mg, 0.02 mmol), and *i*-Pr_2NH (1 mL). The resulting mixture was stirred at room temperature for 24 h. The reaction was quenched by addition of saturated aq NH_4Cl solution (6 mL). The mixture was extracted with Et_2O and the combined organic layers were dried with Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by chromatography [silica gel, hexane/EtOAc (6:4)] to give pure compound **6c** as a white solid (52.3 mg, 87%); mp 104–106 °C (Lit 105–106 °C);[14b] δ_H (300 MHz; $CDCl_3$; Me_4Si) 2.15 (3 H, s, C*H*$_3$), 2.56 (3 H, s, C*H*$_3$), 3.47 (3 H, s, OC*H*$_3$), 3.56 (3 H, s, OC*H*$_3$), 5.22 (2 H, s, OC*H*$_2$O), 5.30 (2 H, s, OC*H*$_2$O), 6.71 (1 H, d, *J* = 2.2 Hz), 6.81 (1 H, d, *J* = 2.2 Hz), 7.20 (1 H, s).

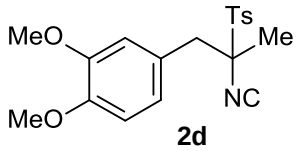
Cassiarin A (2,5-dimethyl-pyrano[2,3,4-*ij*]isoquinolin-8-ol) (8)[14b]



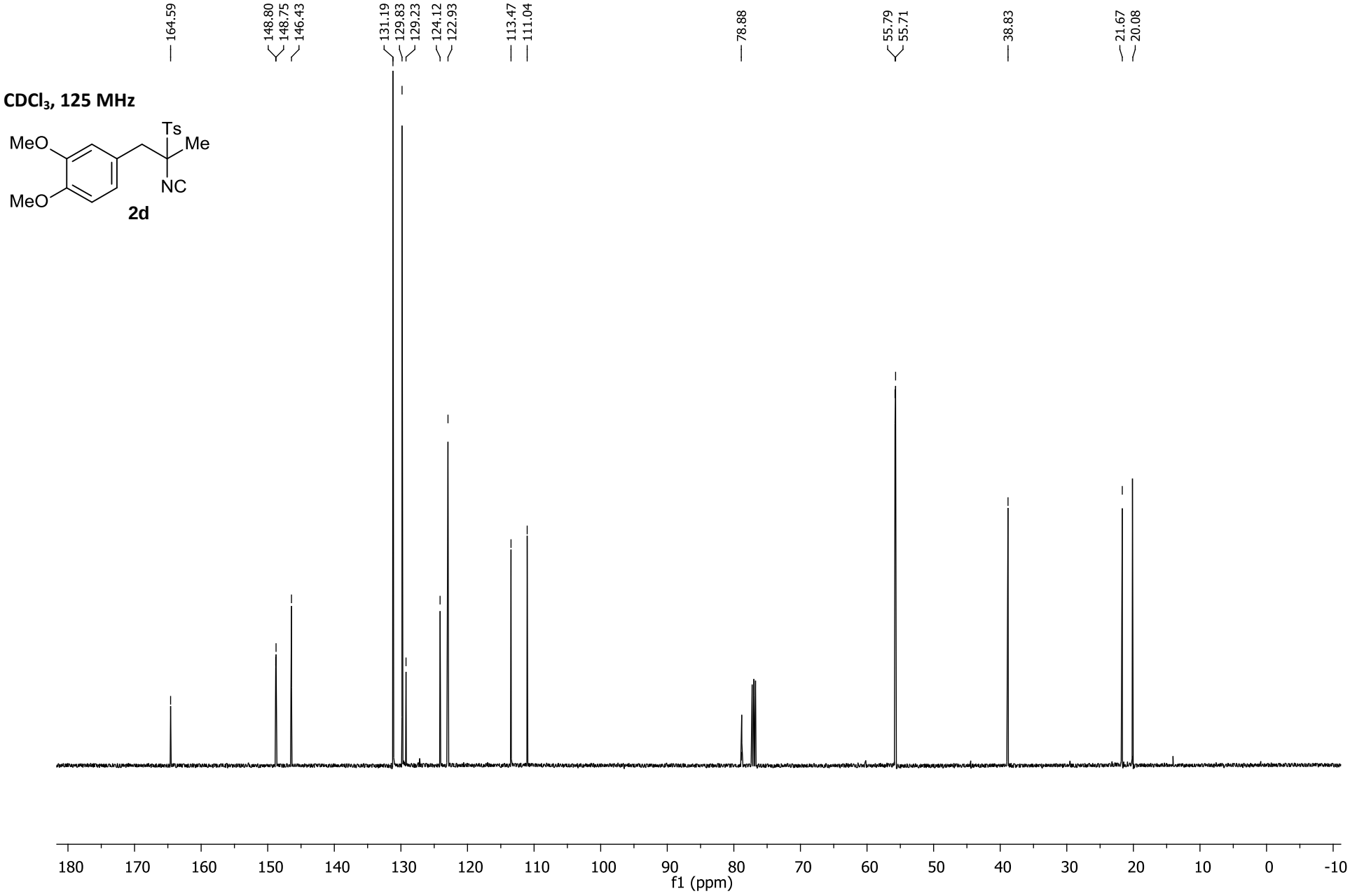
Cassiarin A (8)

To a solution of alkyne **7** (106 mg (0.35 mmol) in MeOH (7 mL) was added aq. HCl solution (10% in H_2O, 2.5 mL) and the resulting mixture was stirred at room temperature for 30 h. The solvents were evaporated to give a yellow solid residue. To the residue were added aq. ammonia solution (10% in H_2O, 18 mL) and a mixture of $CHCl_3$/MeOH ((4:1), 5 mL) and the resulting mixture was vigorously stirred for 1 h. The solvents were evaporated and the residue was extracted with $CHCl_3$/MeOH (4:1). The extract was purified by column chromatography [silica gel, $CHCl_3$/MeOH (9:1)] to give 74.5 mg (100%) of cassiarin A as a yellow solid; mp >240 °C (decomp) (Lit >240 °C (decomp);[14b] The spectroscopic data for **8** are identical to those of the isolated natural product.[13] δ_H (300 MHz; $CDCl_3$:CD_3OD (1:1); Me_4Si) 2.28 (3 H, s, C*H*$_3$), 2.38 (3 H, s, C*H*$_3$), 6.16 (1 H, s), 6.56 (1 H, s), 6.57 (1 H, s), 6.84 (1 H, s).

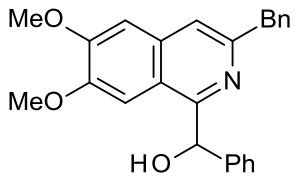
$CDCl_3$, 500 MHz



2d

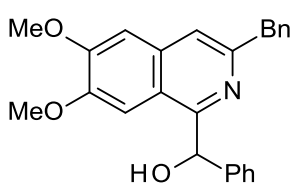

164.59
148.80
148.75
146.43
131.19
129.83
129.23
124.12
122.93
113.47
111.04
78.88
55.79
55.71
38.83
21.67
20.08
CDCl3, 125 MHz
MeO
MeO
Ts
Me
NC
2d
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

$CDCl_3$, 300 MHz

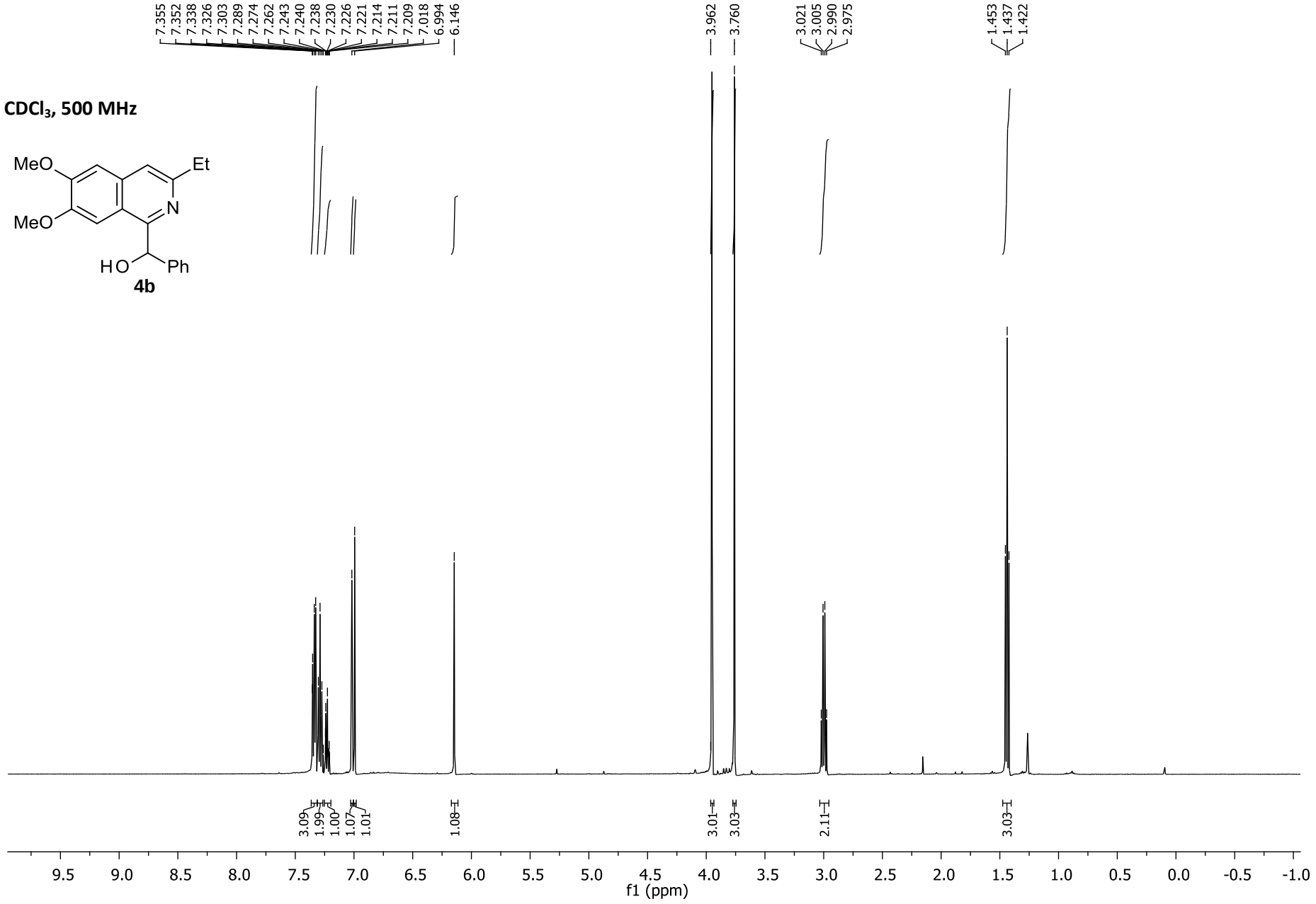


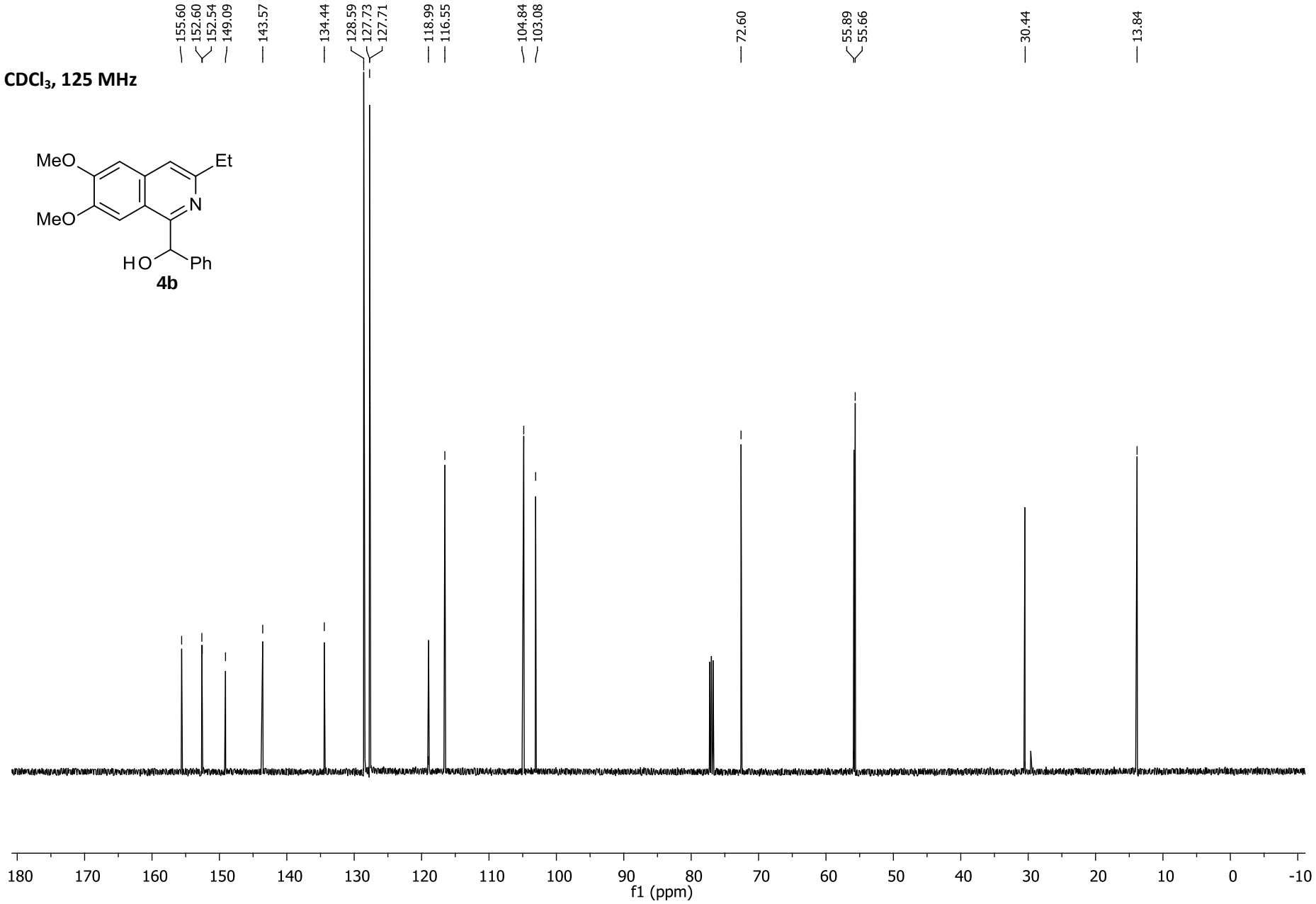
4a

$CDCl_3$, 75 MHz

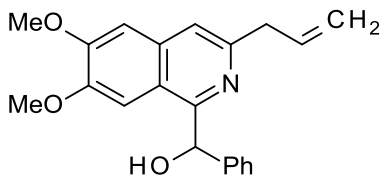


4a

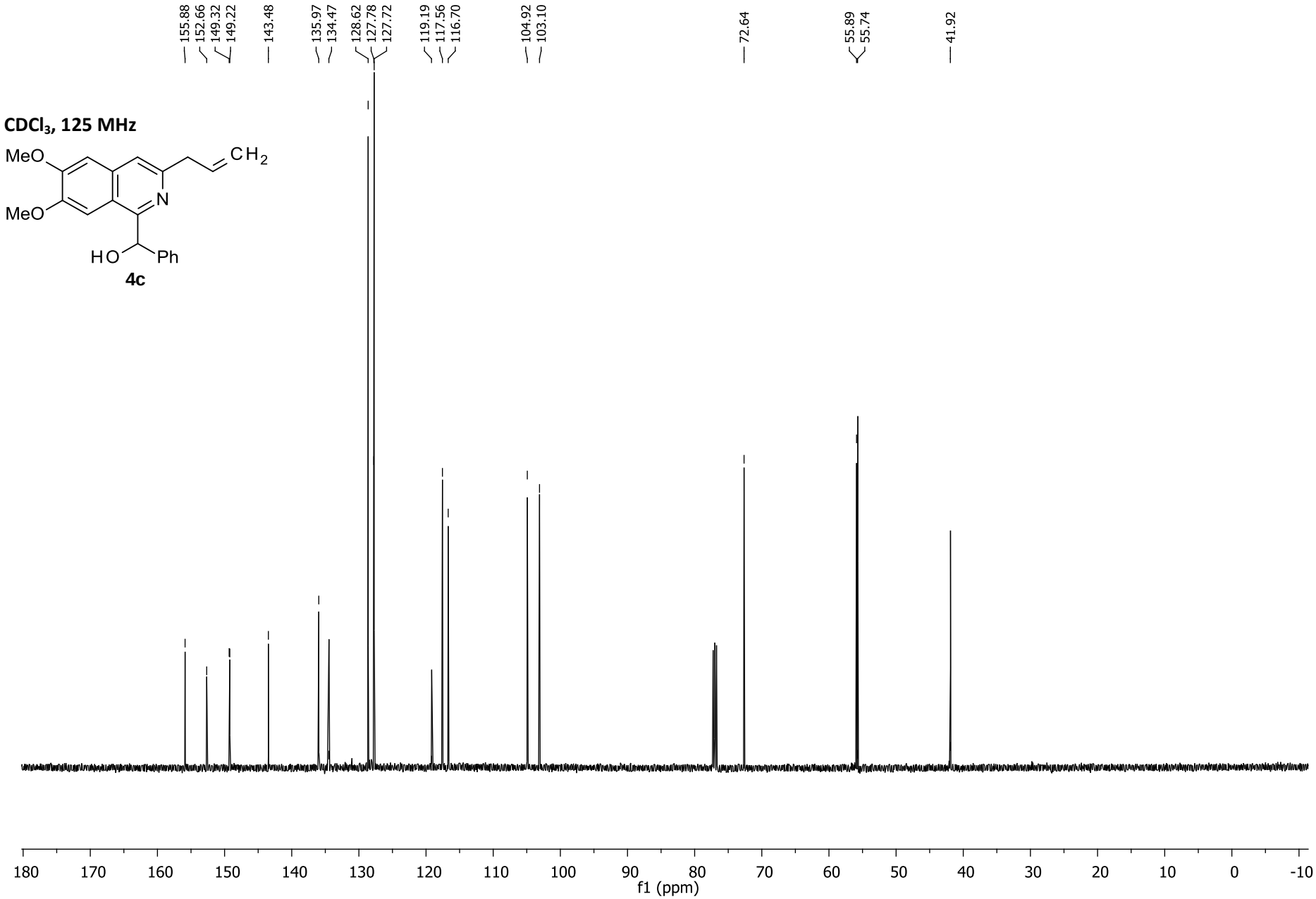

7.355
7.352
7.338
7.326
7.303
7.289
7.274
7.262
7.243
7.240
7.238
7.230
7.226
7.221
7.214
7.211
7.209
7.018
6.994
6.146
3.962
3.760
3.021
3.005
2.990
2.975
1.453
1.437
1.422
CDCl3, 500 MHz
MeO
MeO
Et
N
HO
Ph
4b
3.09
1.99
1.00
1.07
1.01
1.08
3.01
3.03
2.11
3.03
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)


155.60
152.60
152.54
149.09
143.57
134.44
128.59
127.73
127.71
118.99
116.55
104.84
103.08
72.60
55.89
55.66
30.44
13.84
CDCl3, 125 MHz
MeO
MeO
Et
N
HO
Ph
4b
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

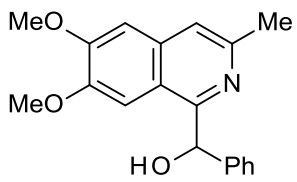
$CDCl_3$, 500 MHz



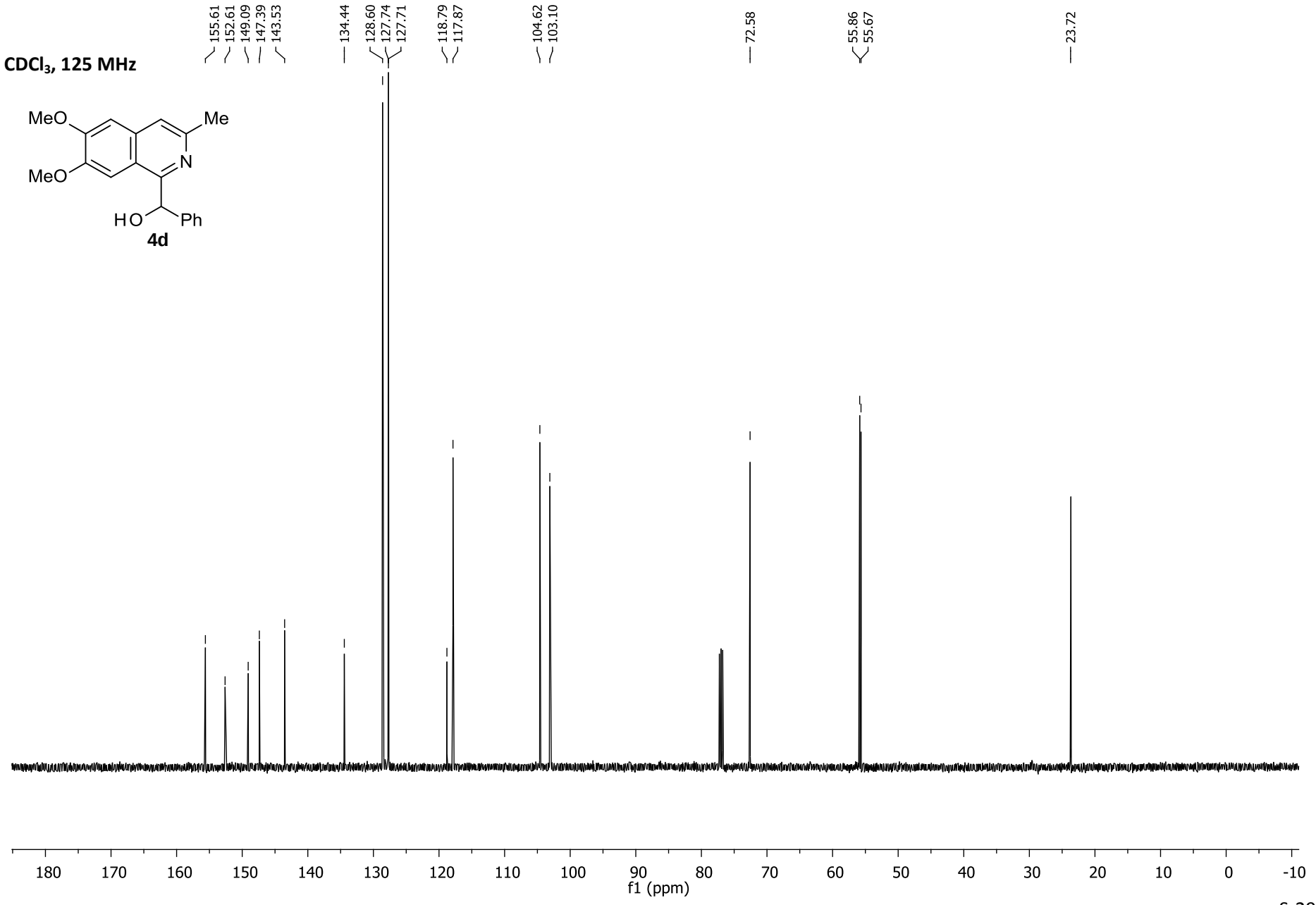
4c

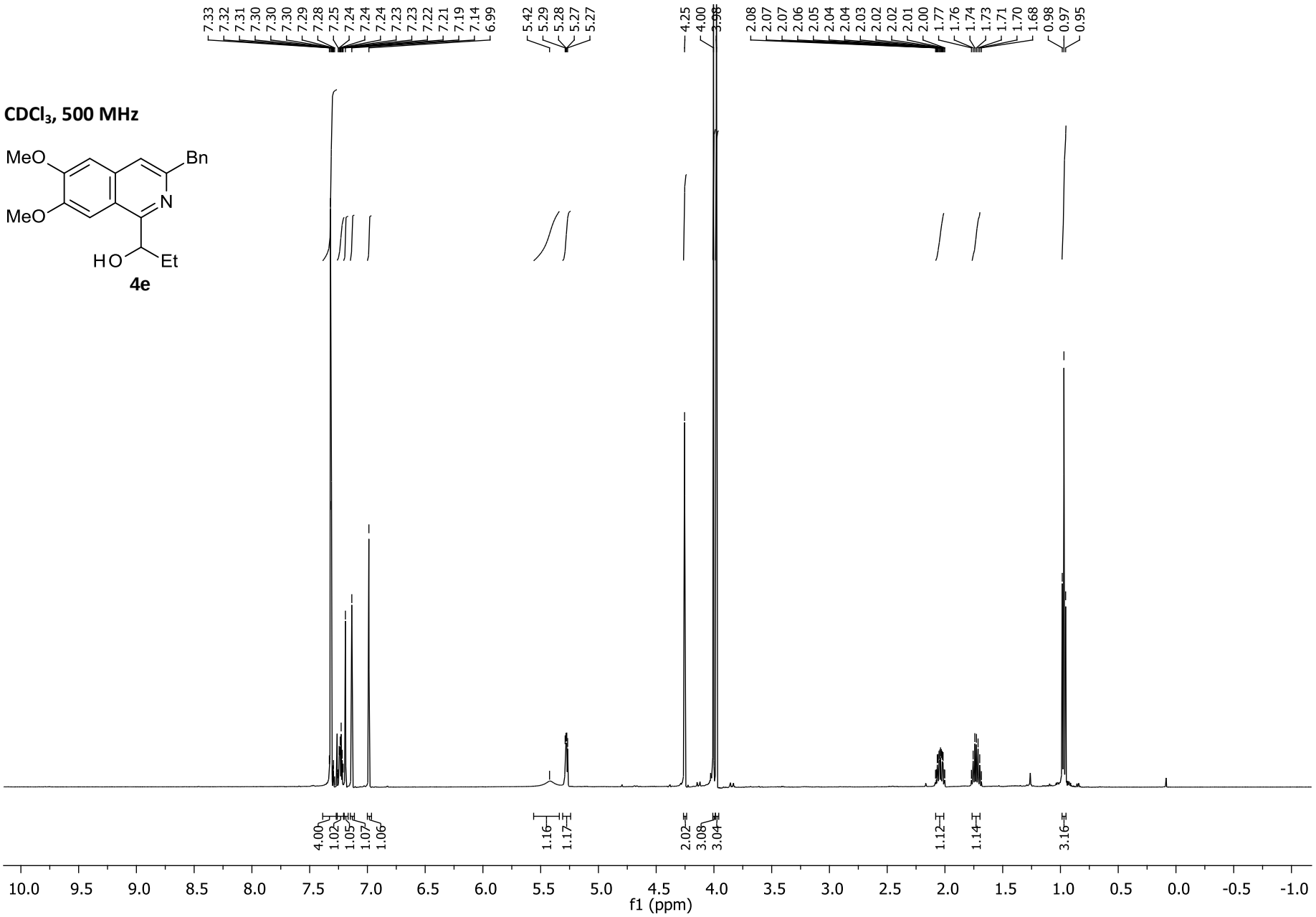

155.88
152.66
149.32
149.22
143.48
135.97
134.47
128.62
127.78
127.72
119.19
117.56
116.70
104.92
103.10
72.64
55.89
55.74
41.92
CDCl3, 125 MHz
MeO
MeO
CH2
N
HO
Ph
4c
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

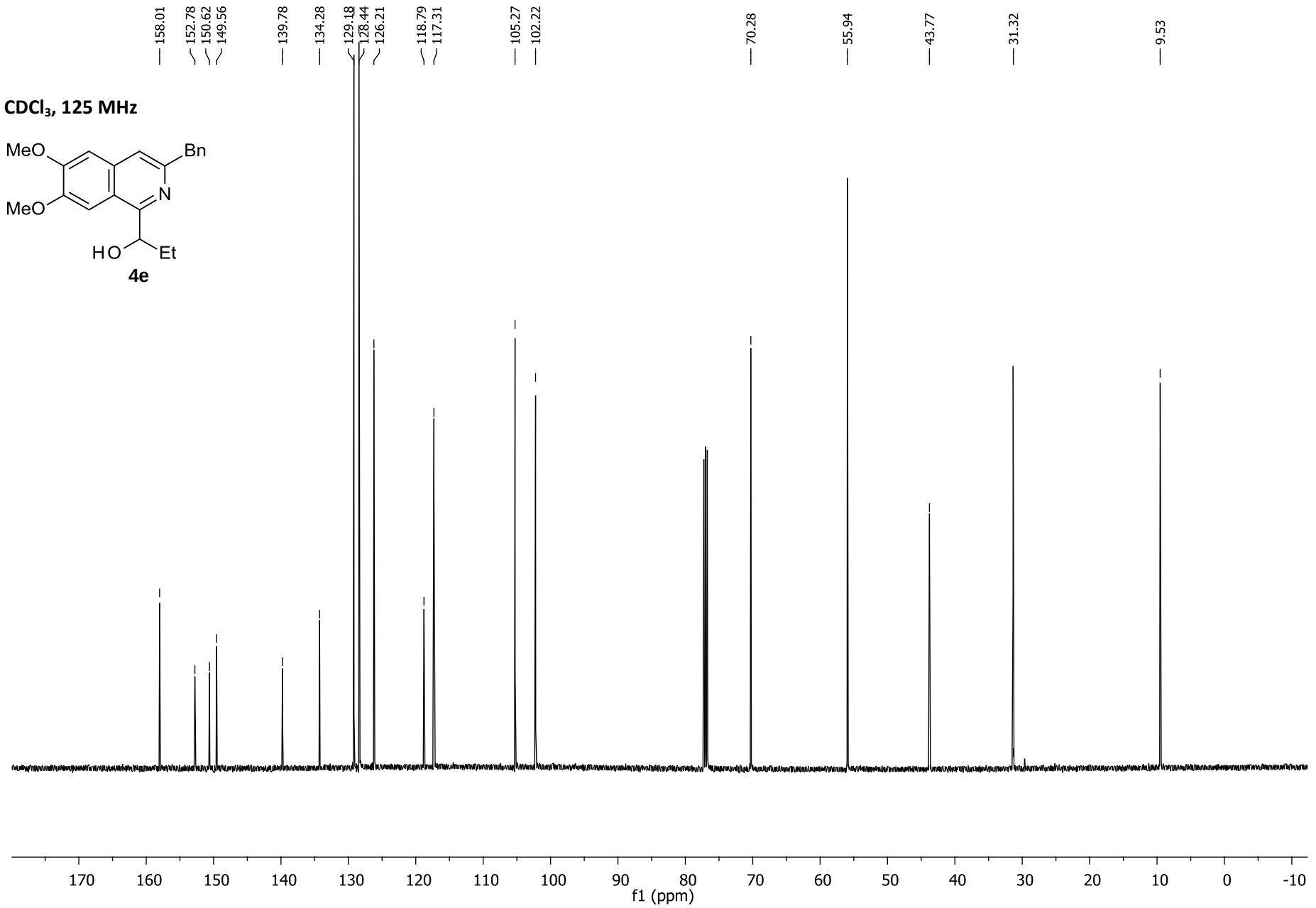
$CDCl_3$, 500 MHz



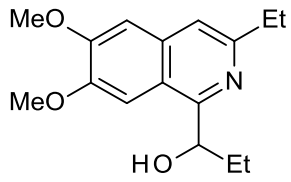
4d


CDCl3, 125 MHz
MeO
MeO
Me
N
HO
Ph
4d
155.61
152.61
149.09
147.39
143.53
134.44
128.60
127.74
127.71
118.79
117.87
104.62
103.10
72.58
55.86
55.67
23.72
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


CDCl3, 500 MHz
MeO
MeO
Bn
N
HO
Et
4e
7.33 7.32 7.31 7.30 7.30 7.30 7.29 7.28 7.25 7.24 7.24 7.24 7.23 7.23 7.22 7.21 7.19 7.14 6.99
5.42 5.29 5.28 5.27 5.27
4.25 4.00 3.98
2.08 2.07 2.07 2.06 2.05 2.04 2.04 2.03 2.02 2.02 2.01 2.00 1.77 1.76 1.74 1.73 1.71 1.70 1.68 0.98 0.97 0.95
4.00 1.02 1.05 1.07 1.06
1.16 1.17
2.02 3.08 3.04
1.12 1.14
3.16
10.0 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 -0.5 -1.0
f1 (ppm)


158.01
152.78
150.62
149.56
139.78
134.28
129.18
128.44
126.21
118.79
117.31
105.27
102.22
70.28
55.94
43.77
31.32
9.53
CDCl3, 125 MHz
MeO
MeO
Bn
N
HO
Et
4e
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

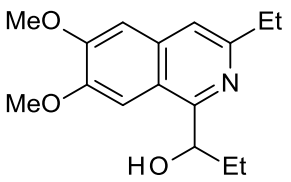
$CDCl_3$, 500 MHz



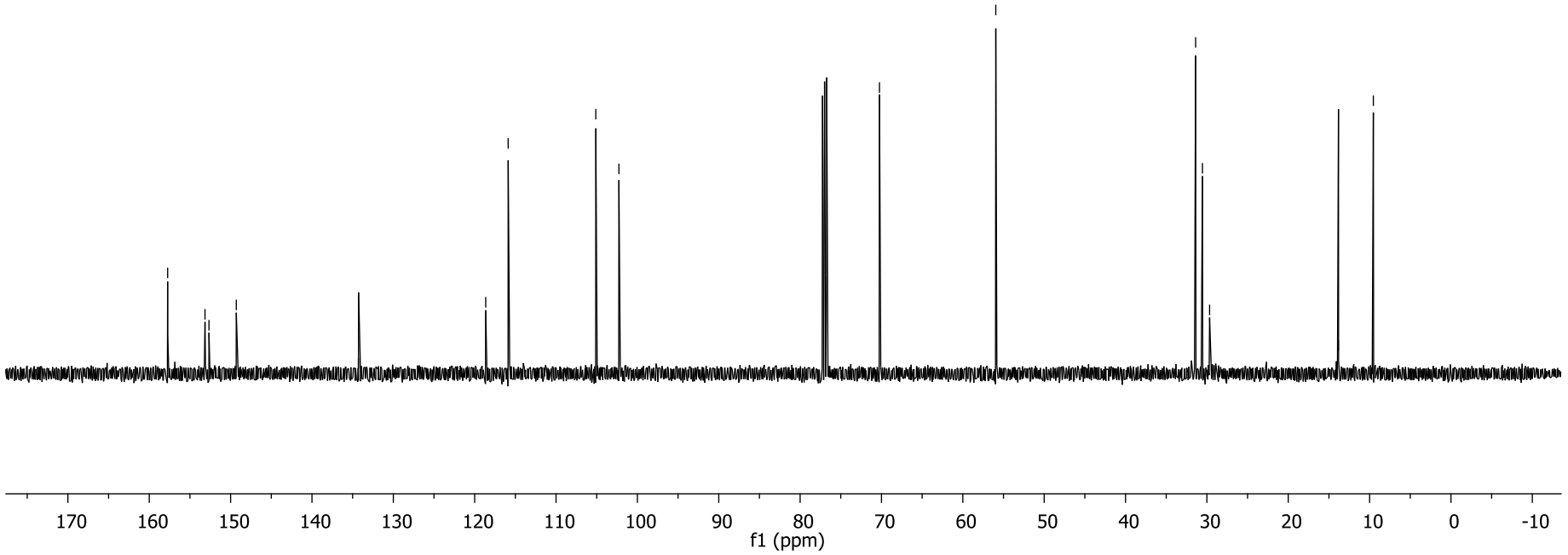
4f

157.74
153.15
152.66
149.30
134.30
118.64
115.88
105.11
102.27
70.25
55.95
31.38
30.54
29.67
13.84
9.54

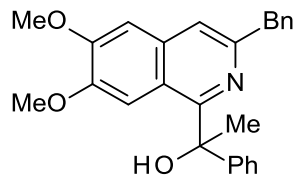
$CDCl_3$, 125 MHz



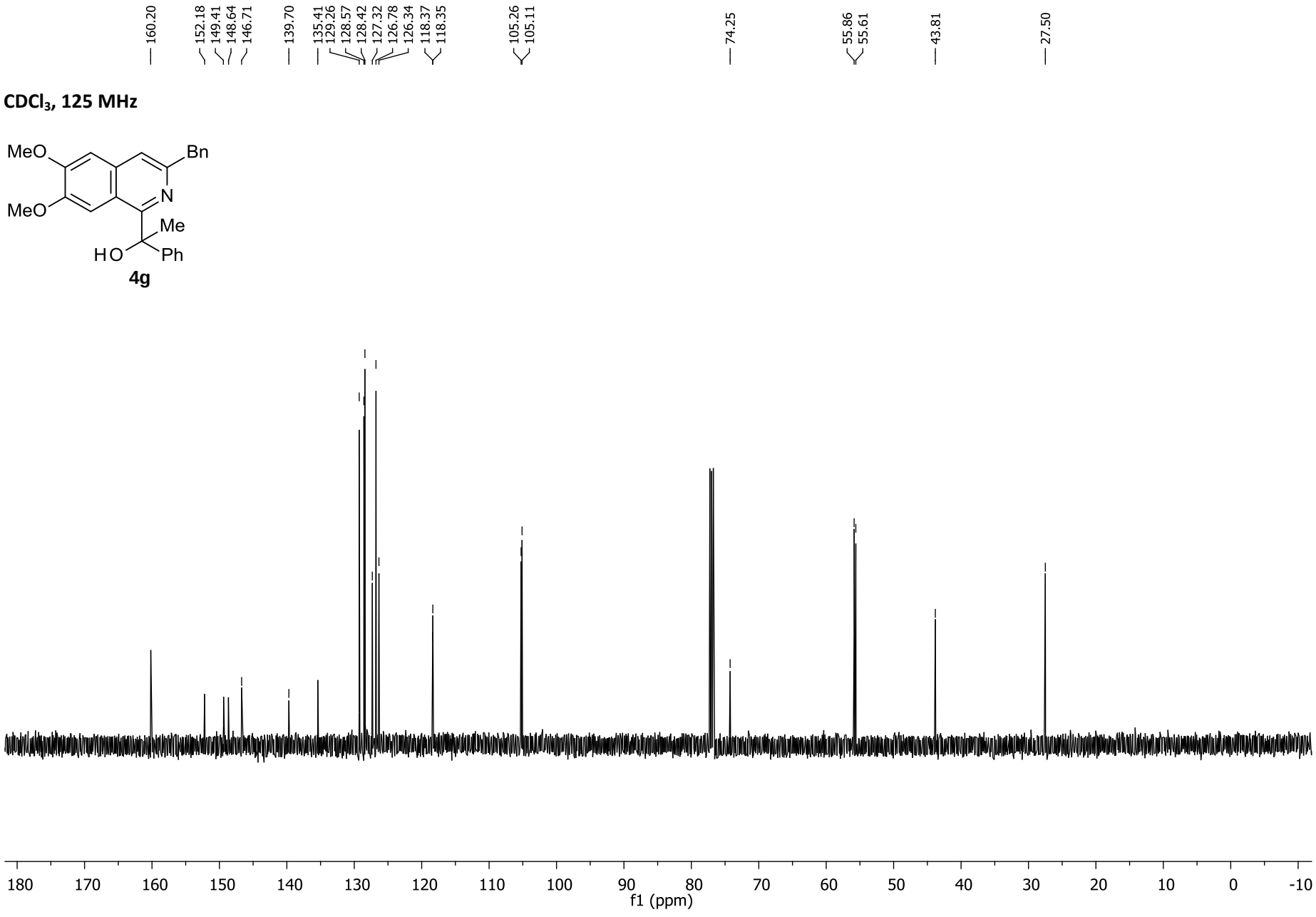
4f



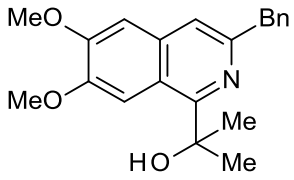
$CDCl_3$, 500 MHz



4g

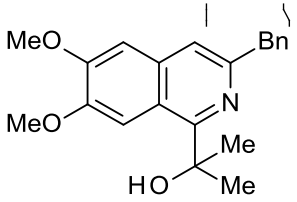

160.20
152.18
149.41
148.64
146.71
139.70
135.41
129.26
128.57
128.42
127.32
126.78
126.34
118.37
118.35
105.26
105.11
74.25
55.86
55.61
43.81
27.50
CDCl3, 125 MHz
MeO
MeO
Bn
N
Me
HO
Ph
4g
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

$CDCl_3$, 500 MHz



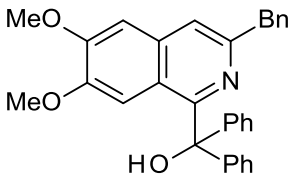
4h

$CDCl_3$, 125 MHz



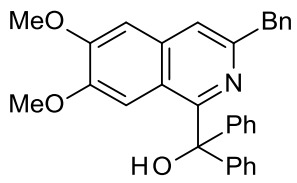
4h

$CDCl_3$, 500 MHz

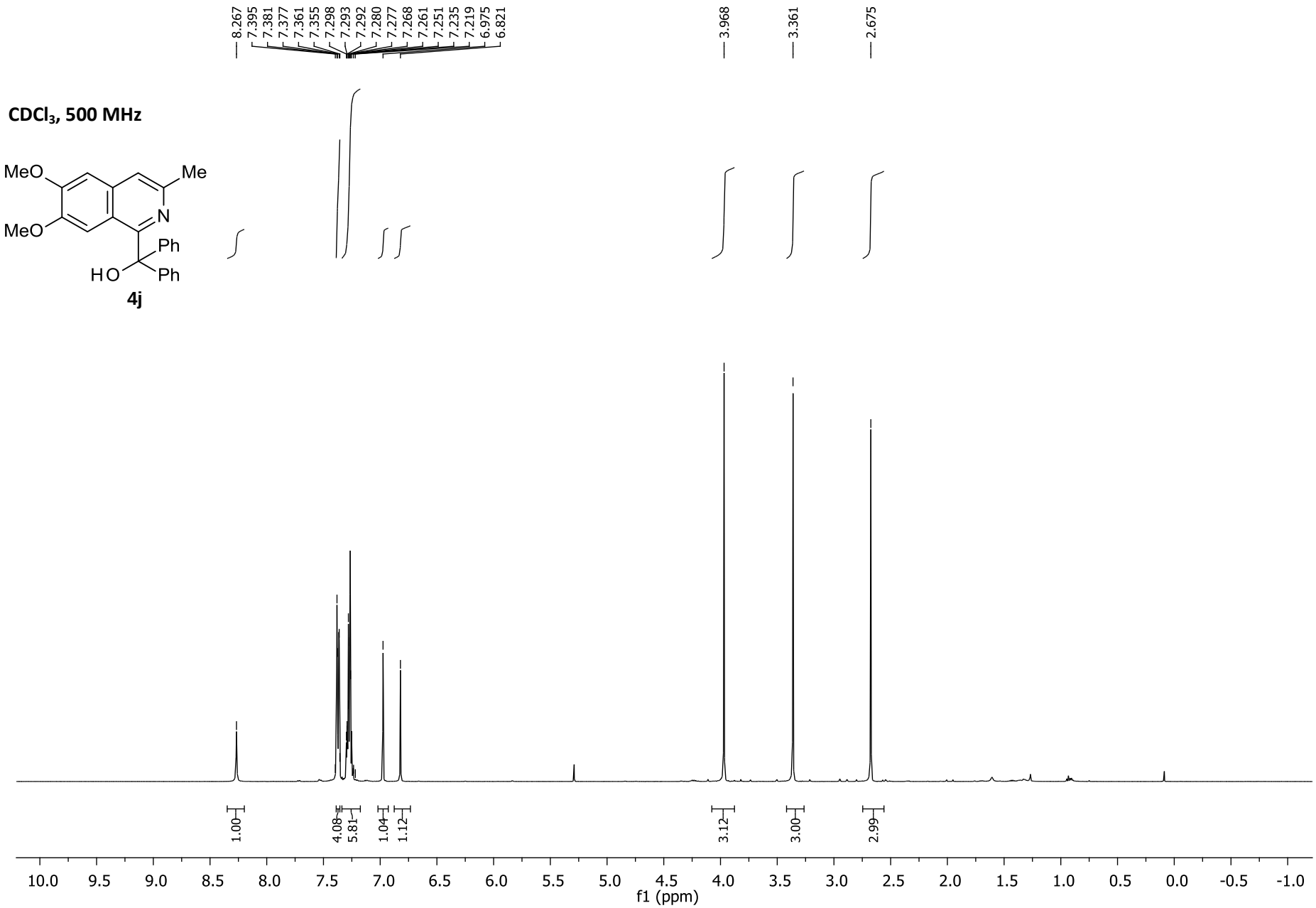


4i

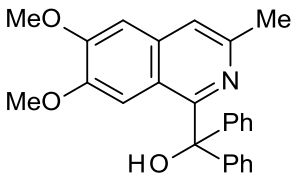
$CDCl_3$, 125 MHz



4i

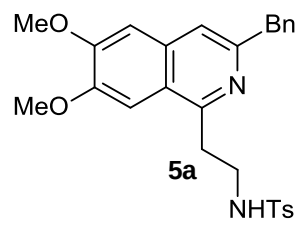

8.267
7.395
7.381
7.377
7.361
7.355
7.298
7.293
7.292
7.280
7.277
7.268
7.261
7.251
7.235
7.219
6.975
6.821
3.968
3.361
2.675
CDCl3, 500 MHz
MeO
MeO
Me
N
Ph
HO
Ph
4j
1.00
4.08
5.81
1.04
1.12
3.12
3.00
2.99
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

$CDCl_3$, 125 MHz

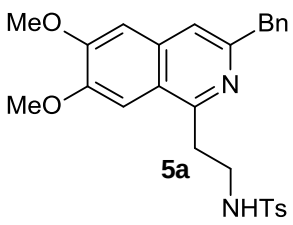


4j

$CDCl_3$, 300 MHz

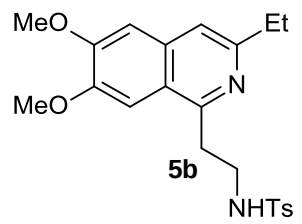


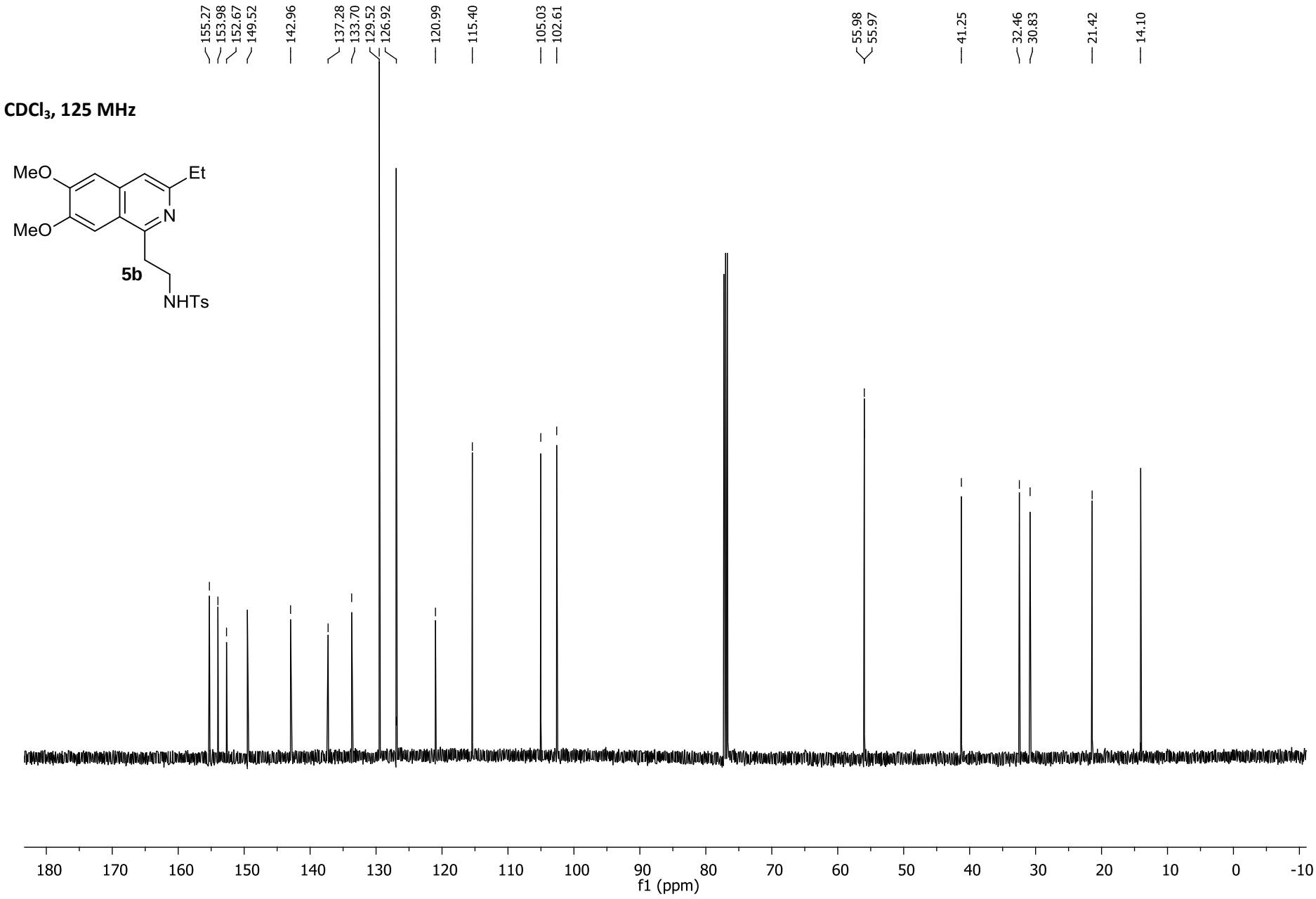
$CDCl_3$, 75 MHz


MeO
MeO
Bn
N
5a
NHTs

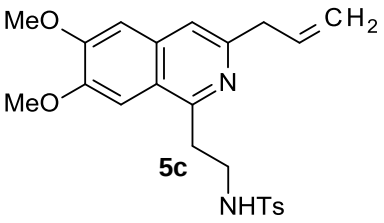
155.30
152.98
151.02
149.83
142.83
139.78
137.42
133.79
129.03
128.66
126.80
126.37
121.15
116.94
105.14
102.65
56.00
43.76
41.05
32.44
21.38
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

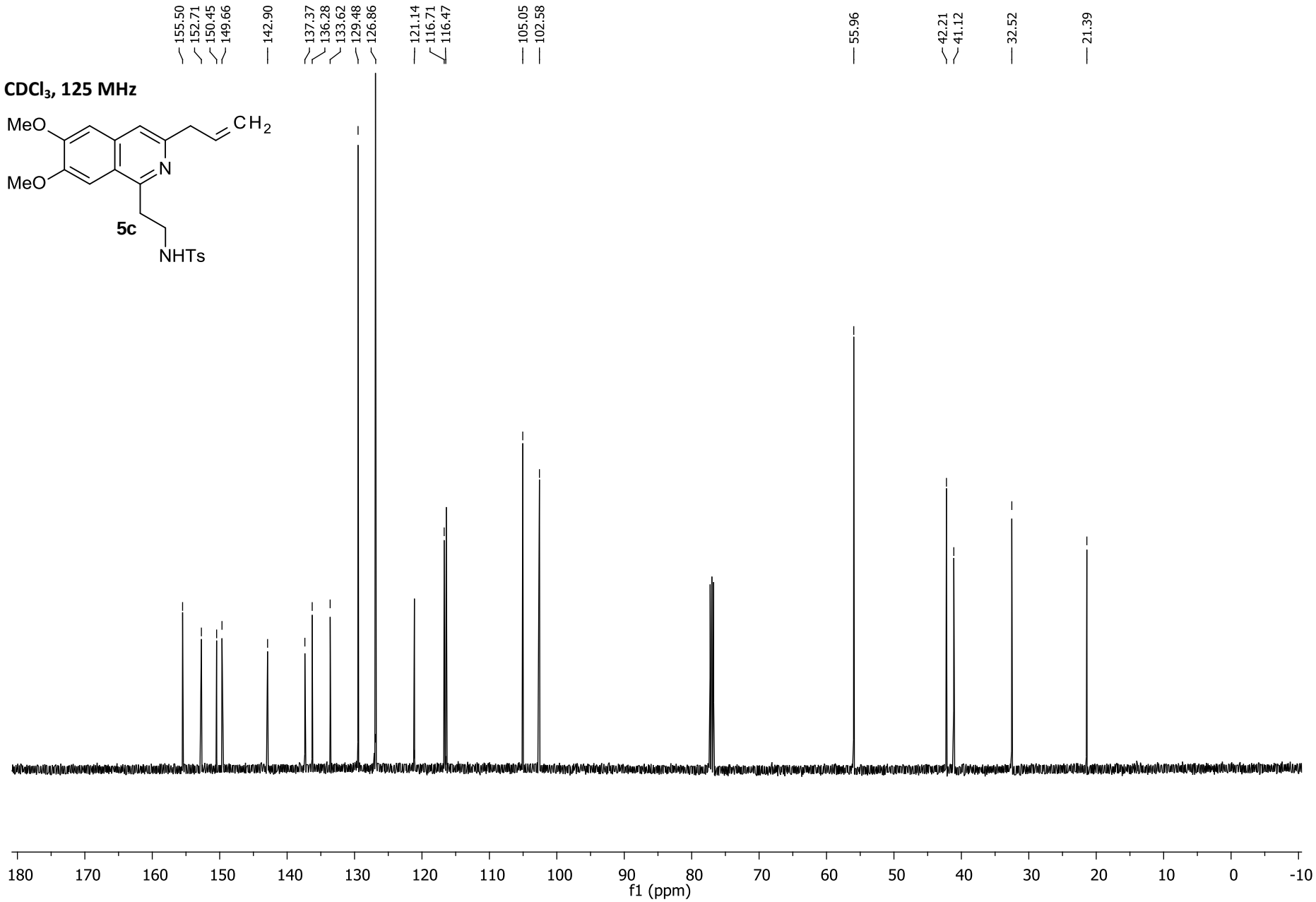
$CDCl_3$, 500 MHz



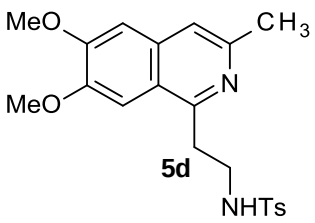

155.27
153.98
152.67
149.52
142.96
137.28
133.70
129.52
126.92
120.99
115.40
105.03
102.61
55.98
55.97
41.25
32.46
30.83
21.42
14.10
CDCl3, 125 MHz
MeO
MeO
Et
N
5b
NHTs
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

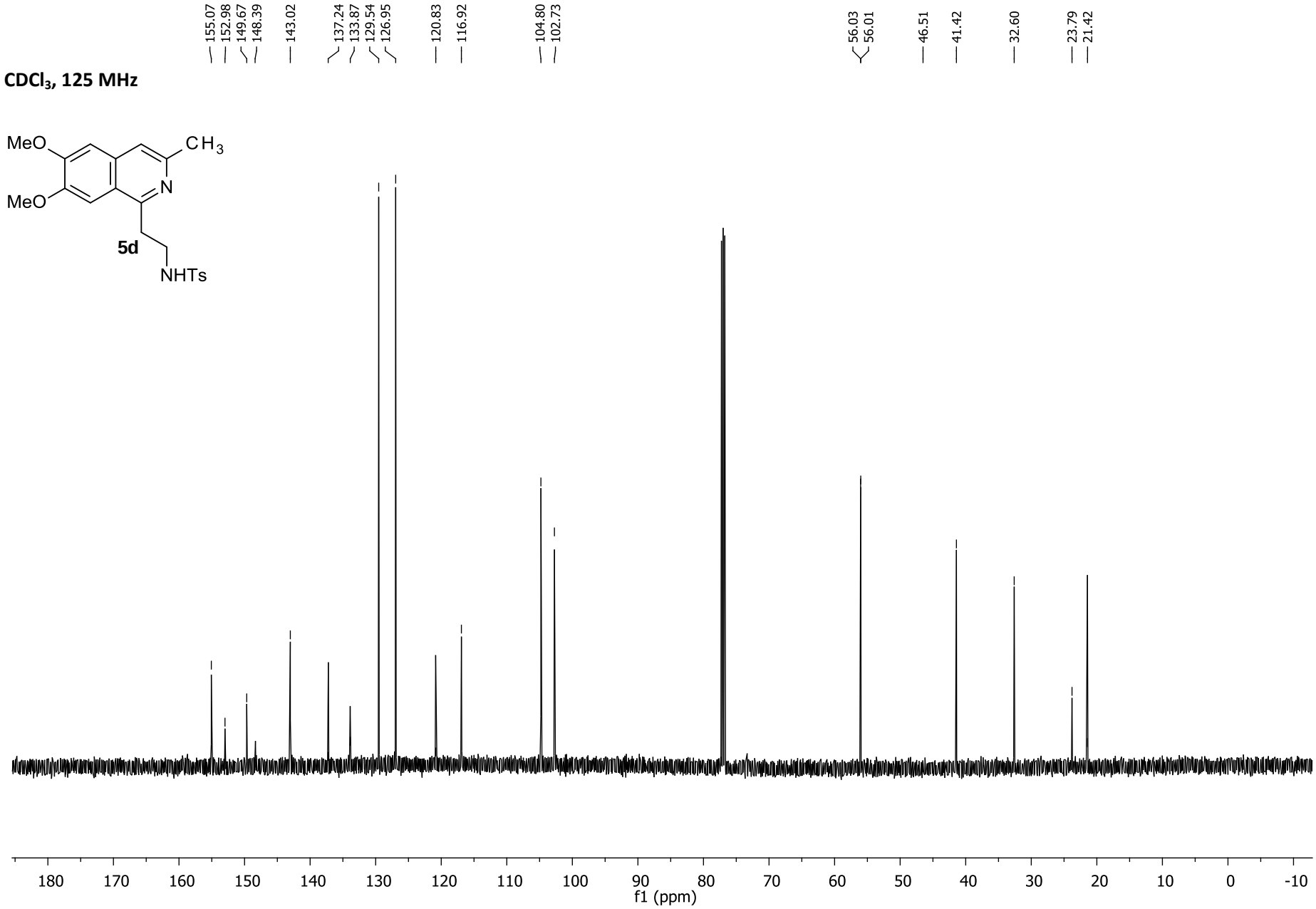
$CDCl_3$, 500 MHz



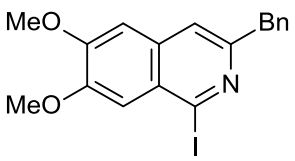

155.50
152.71
150.45
149.66
142.90
137.37
136.28
133.62
129.48
126.86
121.14
116.71
116.47
105.05
102.58
55.96
42.21
41.12
32.52
21.39
CDCl3, 125 MHz
MeO
MeO
N
CH2
5c
NHTs
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

$CDCl_3$, 500 MHz

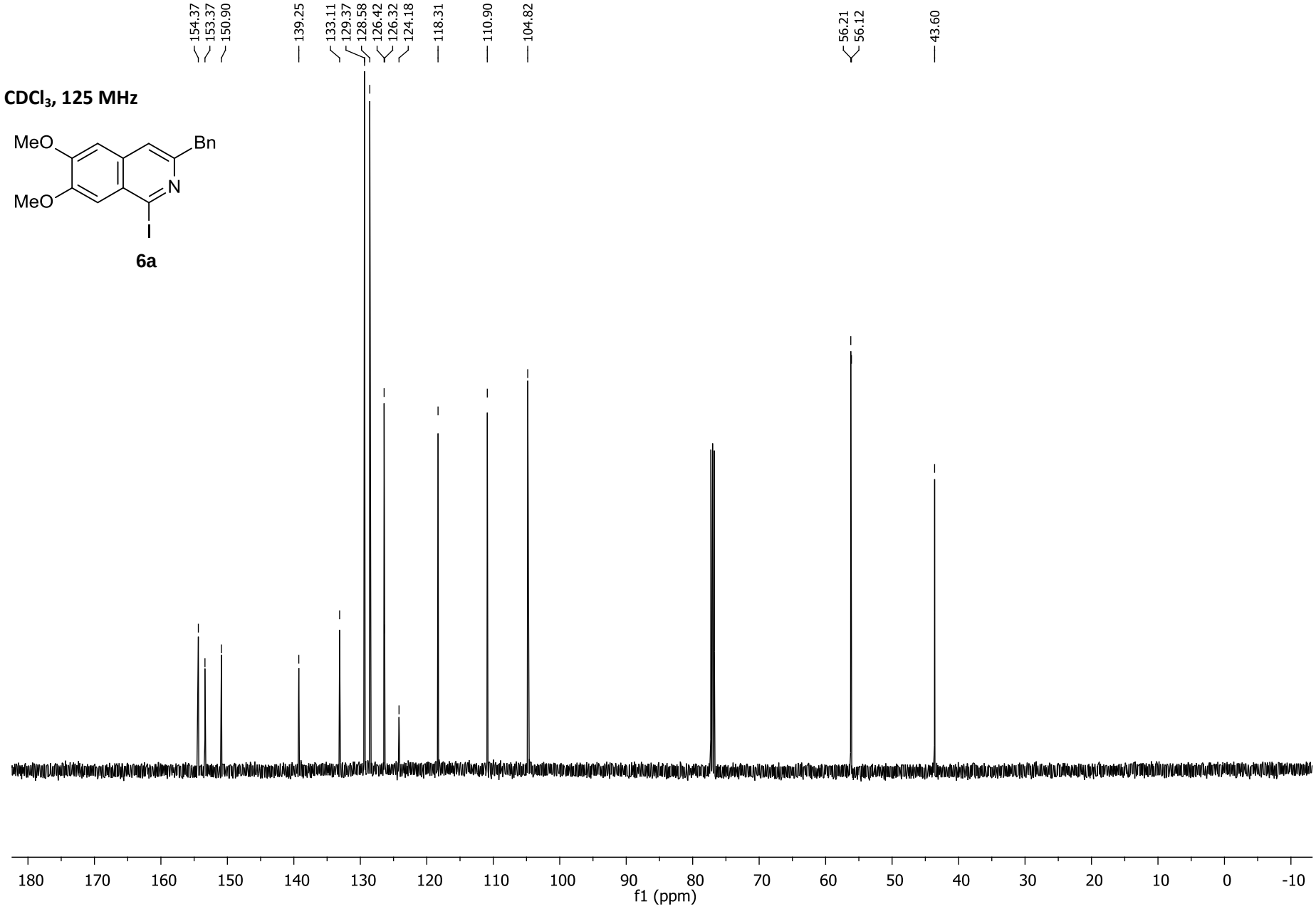



155.07
152.98
149.67
148.39
143.02
137.24
133.87
129.54
126.95
120.83
116.92
104.80
102.73
56.03
56.01
46.51
41.42
32.60
23.79
21.42
CDCl3, 125 MHz
MeO
MeO
CH3
N
5d
NHTs
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

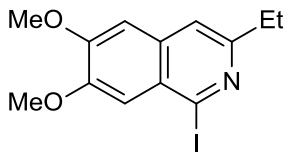
$CDCl_3$, 500 MHz



6a

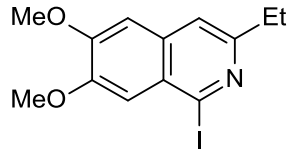

154.37
153.37
150.90
139.25
133.11
129.37
128.58
126.42
126.32
124.18
118.31
110.90
104.82
56.21
56.12
43.60
CDCl3, 125 MHz
MeO
MeO
Bn
N
I
6a
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

$CDCl_3$, 300 MHz



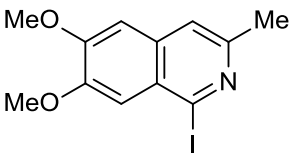
6b

$CDCl_3$, 75 MHz

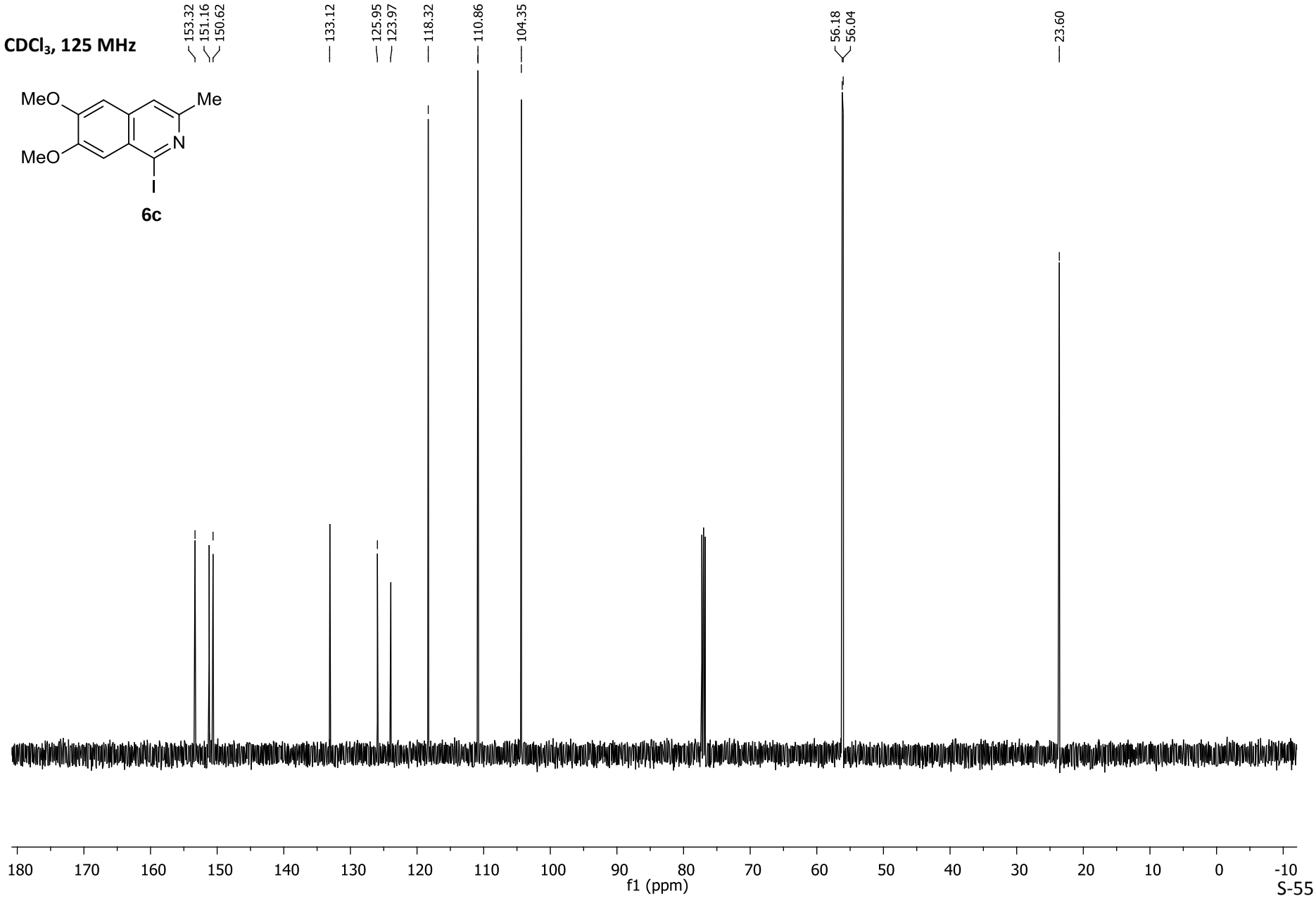


6b

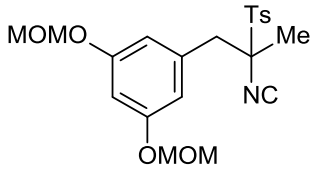
$CDCl_3$, 500 MHz



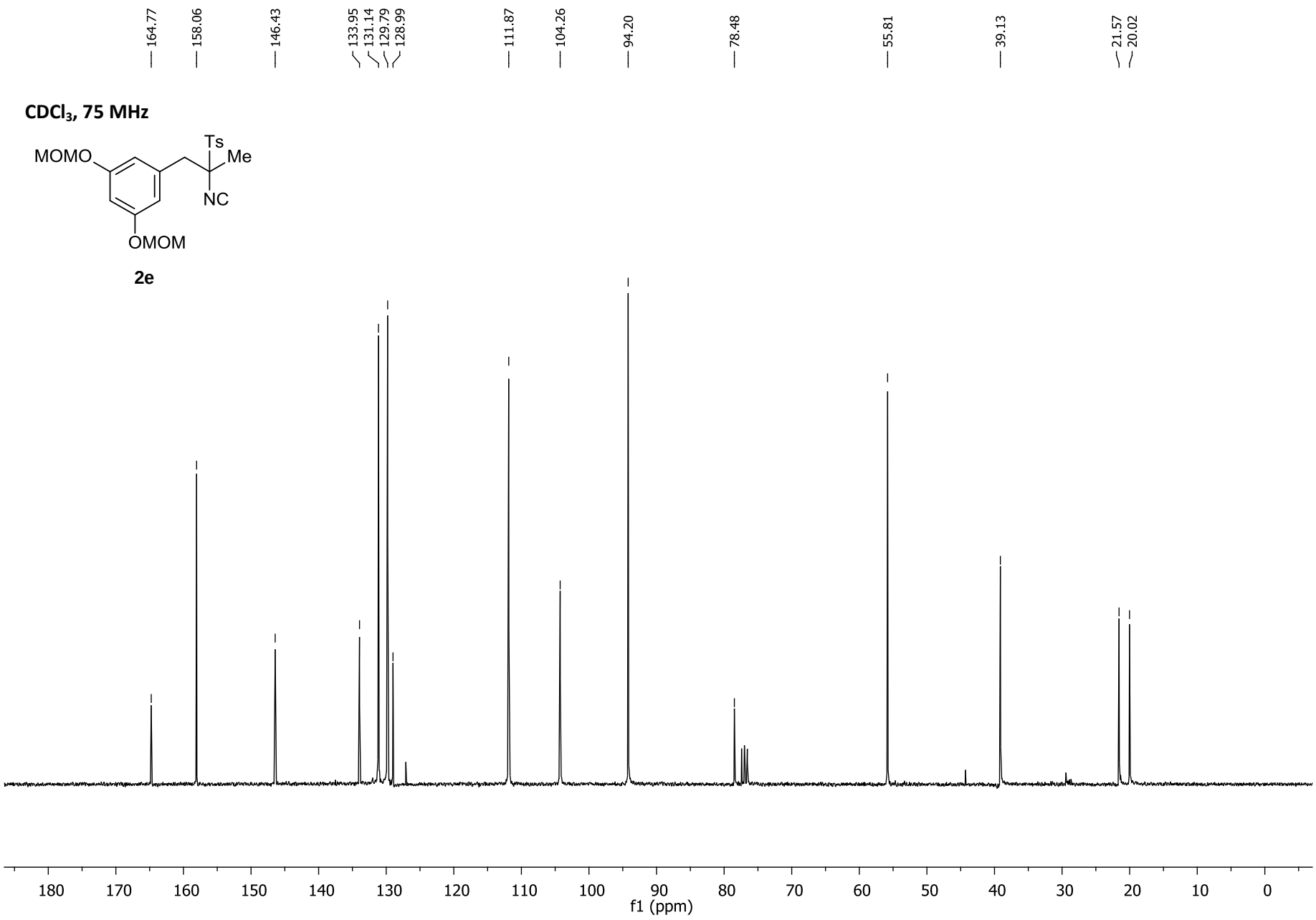
6c


CDCl3, 125 MHz
153.32
151.16
150.62
133.12
125.95
123.97
118.32
110.86
104.35
56.18
56.04
23.60
MeO
MeO
Me
N
I
6c
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

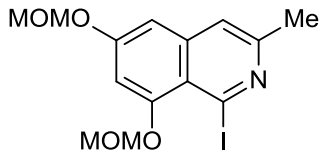
$CDCl_3$, 300 MHz



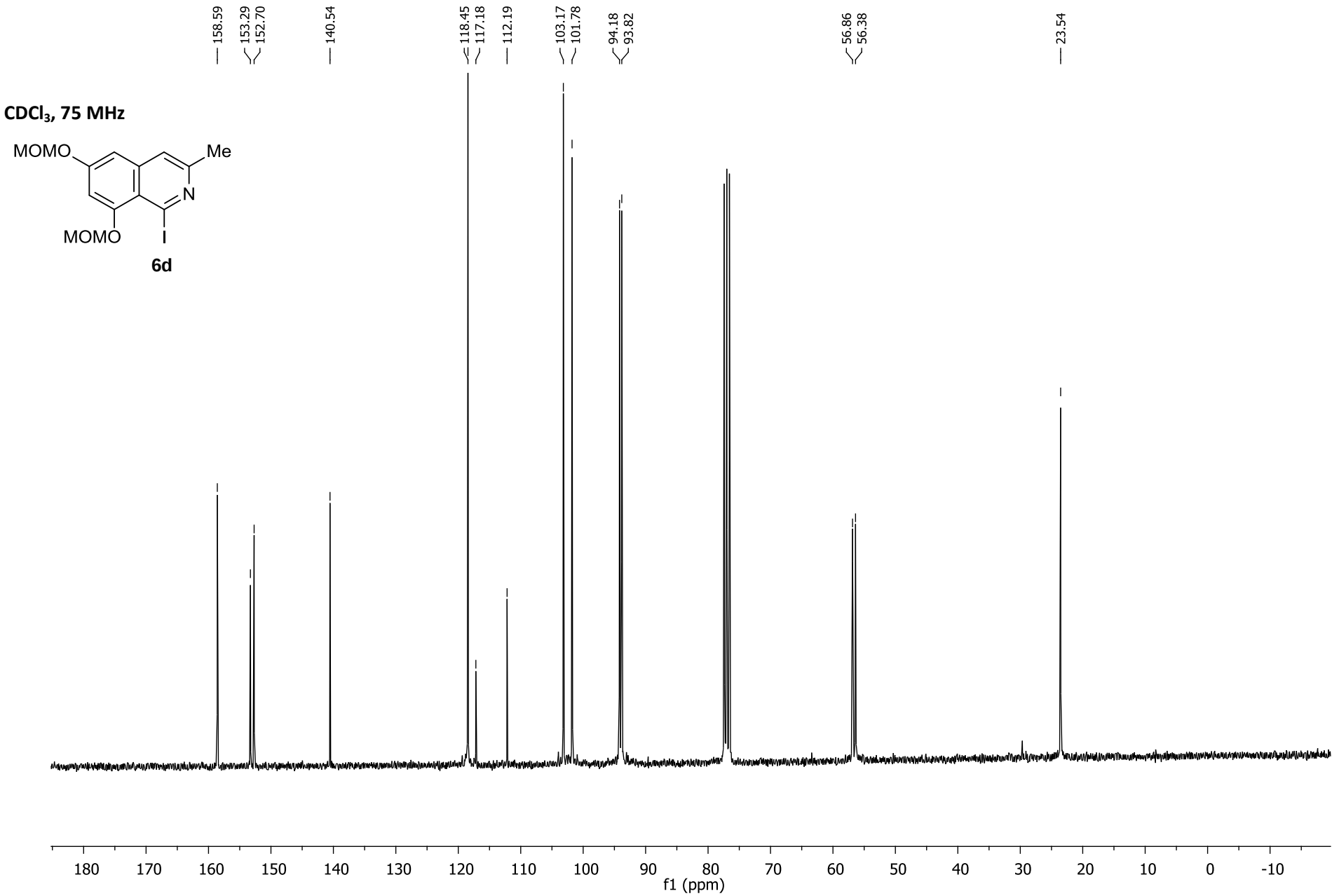
2e


164.77
158.06
146.43
133.95
131.14
129.79
128.99
111.87
104.26
94.20
78.48
55.81
39.13
21.57
20.02
CDCl3, 75 MHz
MOMO
Ts
Me
NC
OMOM
2e
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

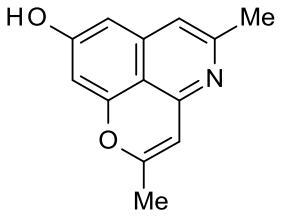
$CDCl_3$, 300 MHz



6d


158.59
153.29
152.70
140.54
118.45
117.18
112.19
103.17
101.78
94.18
93.82
56.86
56.38
23.54
CDCl3, 75 MHz
MOMO
Me
N
MOMO
I
6d
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

$CDCl_3$: CD_3OD (1:1), 300 MHz



Cassiarin A (8)