Supporting Information

Nucleophilic Addition of Organozinc Reagents to 2-Sulfonyl Cyclic Ethers: Stereoselective Synthesis of Manassantins A and B

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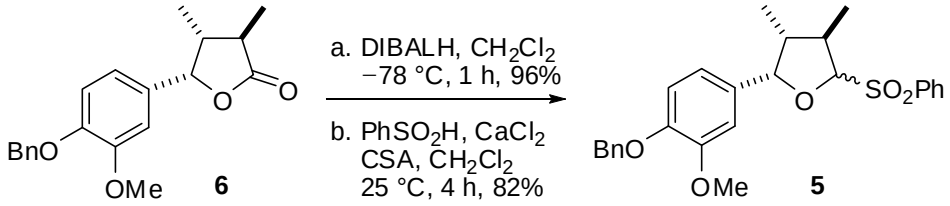
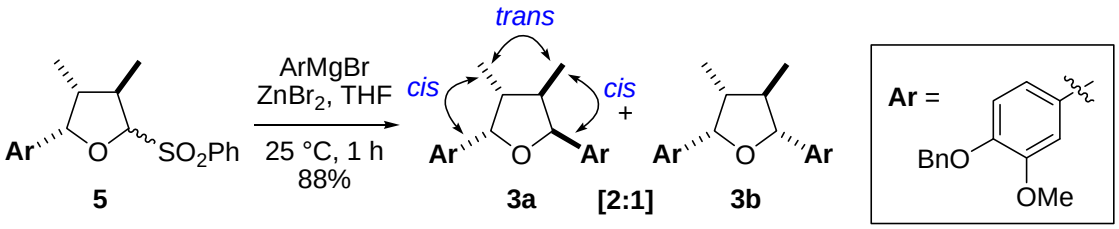


[DIBALH Reduction] To a cooled (–78 °C) solution of lactone **6** (298.7 mg, 0.915 mmol) in CH_2Cl_2 (5 mL, 0.183 M) was added dropwise DIBALH (1.10 mL, 1.0 M solution in toluene, 1.10 mmol). After being stirred at the same temperature for 1 h, the reaction was quenched with MeOH (0.5 mL). H_2O (2 mL) and 2 N NaOH (2 mL) were added and the resulting mixture was stirred at 25 °C for 1 h. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL). The combined organic layers were dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, hexanes/EtOAc, 2/1) to afford lactol (287.1 mg, 96%) as a colorless oil. **[Sulfonylation]** To a solution of stirred solution of the above lactol (142.3 mg, 0.433 mmol) in CH_2Cl_2 (5 mL) was added $PhSO_2H$ (123.1 mg, 0.866 mmol), camphorsulfonic acid (catalytic amount), and $CaCl_2$ (140.0 mg) at 25 °C. After being stirred at the same temperature for 4 h, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ (5 mL) and diluted with EtOAc (10 mL). The layers were separated, and the aqueous layer was extracted with EtOAc (2 × 10 mL). The combined organic layers were washed with brine, and dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, hexanes/EtOAc, 2/1) to afford a 3:1 diastereomeric mixture of sulfone **5** as a white foam (161.3 mg, 82%): **[For Major Diastereomer]** R_f 0.40 (hexanes/EtOAc, 4/1); ^1H NMR (400 MHz, $CDCl_3$) δ 7.93 (dd, J = 8.0, 1.2 Hz, 2 H), 7.61 (dd, J = 7.2, 7.2 Hz, 1 H), 7.53 (dd, J

= 8.0, 7.2 Hz, 2 H), 7.26–7.41 (m, 5 H), 6.79 (d, *J* = 8.0 Hz, 1 H), 6.60 (d, *J* = 2.0 Hz, 1 H), 6.56 (d, *J* = 8.0, 2.0 Hz, 1 H), 5.50 (d, *J* = 8.8 Hz, 1 H), 5.11 (s, 4 H), 5.05 (d, *J* = 7.2 Hz, 1 H), 3.84 (s, 3 H), 2.84–2.96 (m, 1 H), 2.38–2.50 (m, 1 H), 1.56 (d, *J* = 7.2 Hz, 3 H), 0.68 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.3, 147.5, 138.4, 136.9, 133.5, 132.6, 129.0, 128.8, 128.4, 127.7, 127.1, 118.6, 113.6, 110.3, 96.1, 86.0, 70.9, 55.9, 43.5, 42.2, 14.3, 12.1; HRMS (FAB) found 452.1656 [calcd for $C_{26}H_{28}O_5S$ $(M)^+$ 452.1657]

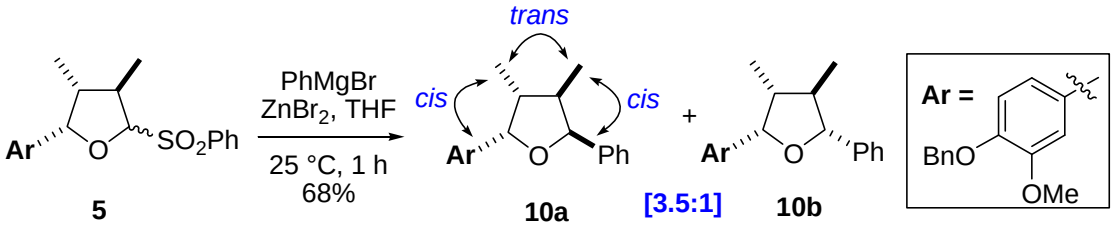
Preparation of 2,3-*Cis*-3,4-*Trans*-4,5-*Cis*-Tetrahydrofuran 3a



To a solution of $ZnBr_2$ (1 mL, 0.26 M in THF) was added dropwise 4-benzyloxy-3-methoxyphenylmagnesium bromide (1.66 mL, 0.30 M in THF, 0.50 mmol) at 25 °C and the resulting mixture was stirred for 30 min before sulfone **5** (98.1 mg, 0.217 mmol) in THF (2 mL) was added dropwise. After being stirred for 1 h, the reaction mixture was cooled to 0 °C, quenched with saturated aqueous NH_4Cl, and diluted with EtOAc. The layers were separated, and the aqueous layer was extracted with EtOAc (2 × 10 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, hexanes/EtOAc, 4/1) to afford a 2:1 mixture of 2,3-*cis*-3,4-*trans*-4,5-*cis*-tetrahydrofuran **3a** and 2,3-*cis*-3,4-*trans*-4,5-*trans*-tetrahydrofuran **3b** as a colorless oil (102.1 mg, 88%), which was purified again by column chromatography (silica gel, hexanes/EtOAc, 7/1) to afford 2,3-*cis*-3,4-*trans*-4,5-*cis*-

tetrahydrofuran **3a** (59.2 mg, 52%) and 2,3-*cis*-3,4-*trans*-4,5-*trans*-tetrahydrofuran **3b** (28.3 mg, 25%) and a mixture of **3a** and **3b** (12.0 mg, 11%): **[For 3a]** R_f 0.43 (hexanes/EtOAc, 4/1); $[\alpha]^{24.7}_D$ = –35.3 (*c* 1.00, $CHCl_3$) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24–7.45 (m, 10 H), 6.84–6.86 (m, 4 H), 6.76 (d, *J* = 8.0 Hz, 2 H), 5.41 (d, *J* = 5.6 Hz, 2 H), 5.14 (s, 4 H), 3.89 (s, 6 H), 2.19–2.29 (m, 2 H), 0.68 (d, *J* = 6.4 Hz, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.7, 147.3, 137.6, 135.0, 128.8, 128.1, 127.6, 118.7, 114.1, 110.5, 83.8, 71.5, 56.4, 44.3, 15.1; HRMS (FAB) found 524.2570 [calcd for $C_{34}H_{36}O_5$ $(M)^+$ 524.2563]; **[For 3b]** R_f 0.40 (hexanes/EtOAc, 4/1); $[\alpha]^{30}_D$ = –20.1 (*c* 0.80, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28–7.47 (m, 10 H), 7.10 (d, *J* = 1.6 Hz, 1 H), 6.98 (dd, *J* = 7.2, 2.0 Hz, 1 H), 6.80–6.91 (m, 4 H), 5.18 (s, 2 H), 5.15 (s, 2 H), 5.12 (d, *J* = 8.4 Hz, 1 H), 4.42 (d, *J* = 9.6 Hz, 1 H), 3.92 (s, 3 H), 3.85 (s, 3 H), 2.55 (dddd, *J* = 9.2, 7.2, 7.2, 7.2 Hz, 1 H), 1.74–1.82 (m, 1 H), 1.07 (d, *J* = 7.2 Hz, 3 H), 0.67 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.6, 149.2, 147.7, 147.1, 137.2, 134.4, 134.0, 128.44, 128.41, 127.7, 127.23, 127.18, 119.1, 118.5, 113.9, 113.6, 110.9, 110.5, 87.2, 83.0, 71.0, 55.94, 55.87, 47.7, 45.9, 14.97, 14.88; IR (neat) 2955, 2869, 1511 cm^{-1}; HRMS (FAB) found 524.2571 [calcd for $C_{34}H_{36}O_5$ $(M)^+$ 524.2563]

Preparation of 2,3-*Cis*-3,4-*Trans*-4,5-*Cis*-Tetrahydrofuran 10a

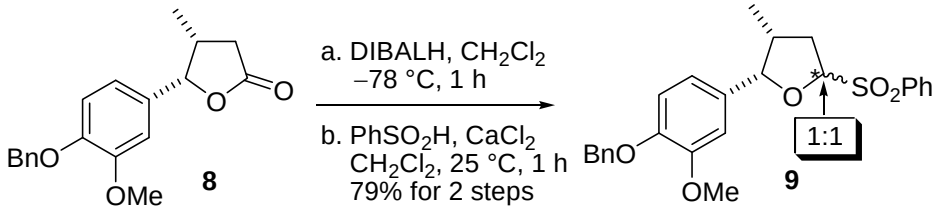


5 **10a** **[3.5:1]** **10b**

To a solution of $ZnBr_2$ (1 mL, 0.12 M in THF, 0.12 mmol) was added dropwise phenylmagnesium bromide (0.19 mL, 1.0 M in THF, 0.19 mmol) at 25 °C and the resulting mixture was stirred at the same temperature for 30 min before sulfone **5** (21.9 mg, 0.048 mmol)

in THF (1 mL) was added dropwise. After being stirred for 1 h, the reaction mixture was cooled to 0 °C, quenched with saturated aqueous NH_4Cl, and diluted with EtOAc. The layers were separated, and the aqueous layer was extracted with EtOAc (2 × 10 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, hexanes/EtOAc, 4/1) to afford a 3.5:1 mixture of 2,3-*cis*-3,4-*trans*-4,5-*cis*-tetrahydrofuran **10a** and 2,3-*cis*-3,4-*trans*-4,5-*trans*-tetrahydrofuran **10b** as a colorless oil (12.7 mg, 68%): **[10a]** R_f 0.31 (hexanes/EtOAc, 9/1); $[\alpha]^{30}_D = -30.1$ (*c* 0.64, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24–7.46 (m, 10 H), 6.90 (s, 1 H), 6.89 (d, *J* = 8.4 Hz, 1 H), 6.79 (dd, *J* = 8.4, 2.0 Hz, 1 H), 5.50 (d, *J* = 6.8 Hz, 1 H), 5.46 (d, *J* = 6.4 Hz, 1 H), 5.16 (s, 2 H), 3.92 (s, 3 H), 2.22–2.36 (m, 2 H), 0.70 (d, *J* = 6.8 Hz, 3 H), 0.68 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.3, 147.0, 141.4, 137.3, 134.7, 128.4, 127.86, 127.70, 127.3, 126.8, 126.2, 118.4, 113.8, 110.2, 83.69, 83.57, 71.1, 56.0, 43.83, 43.75, 14.69, 14.61; IR (neat) 2962, 2873, 1512 cm^{-1}; HRMS (FAB) found 388.2040 [calcd for $C_{26}H_{28}O_3$ $(M)^+$ 388.2038]; **[10b]** R_f 0.29 (hexanes/EtOAc, 9/1); $[\alpha]^{29}_D = -73.7$ (*c* 0.89, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26–7.53 (m, 10 H), 6.93 (d, *J* = 1.6 Hz, 1 H), 6.81–6.88 (m, 2 H), 5.15 (s, 2 H), 5.14 (d, *J* = 10.4 Hz, 1 H), 4.47 (d, *J* = 9.2 Hz, 1 H), 3.88 (s, 3 H), 2.20–2.32 (m, 1 H), 1.74–1.84 (m, 1 H), 1.08 (d, *J* = 6.8 Hz, 3 H), 0.65 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.3, 147.2, 141.0, 137.3, 134.4, 128.47, 128.37, 127.74, 127.61, 127.3, 126.4, 119.2, 113.7, 110.9, 87.4, 83.1, 71.1, 55.9, 48.3, 46.1, 15.0; HRMS (FAB) found 388.2035 [calcd for $C_{26}H_{28}O_3$ $(M)^+$ 388.2038];

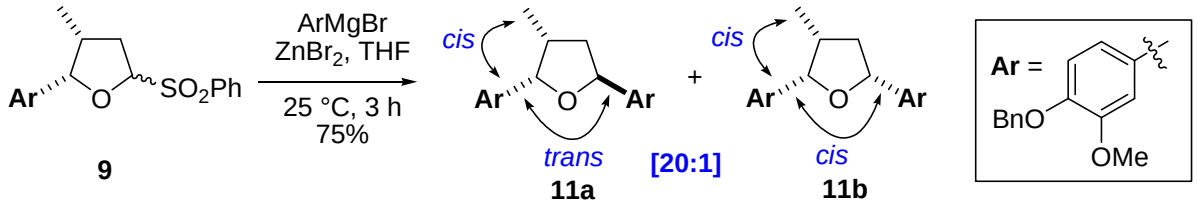
Preparation of Sulfone 9



[DIBALH Reduction] To a cooled (–78 °C) solution of lactone **8**[1] (272.5 mg, 0.872 mmol) in CH_2Cl_2 (10 mL, 0.087 M) was added dropwise DIBALH (1.02 mL, 1.0 M solution in toluene, 1.02 mmol). After being stirred at the same temperature for 1 h, the reaction was quenched with MeOH (0.5 mL). H_2O (2 mL) and 2 N NaOH (2 mL) was added and the resulting mixture was stirred at 25 °C for 1 h. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL). The combined organic layers were dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. This crude lactol was carried to the next step without further purification. HRMS (FAB) found 314.1517 [calcd for $C_{19}H_{22}O_4$ $(M)^+$ 314.1518]

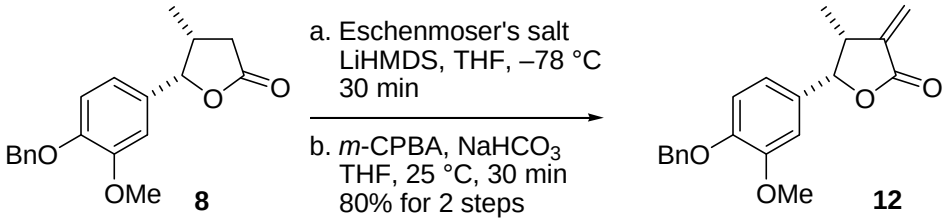
[Sulfonylation] To a solution of stirred solution of lactol in CH_2Cl_2 (2 mL) was added $PhSO_2H$ (495.9 mg, 3.488 mmol) and $CaCl_2$ (193.5 mg, 1.74 mmol) at 25 °C. After 1 h, the reaction was quenched with saturated aqueous $NaHCO_3$ (5 mL) and diluted with Et_2O (10 mL). The layers were separated, and the aqueous layer was extracted with EtOAc (2 × 10 mL). The combined organic layers were washed with brine, and dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, hexanes/EtOAc, 2/1) to afford a 1:1 diastereomeric mixture of sulfone **9** as a white foam (302.5 mg, 79%): R_f 0.50 (hexanes/EtOAc, 2/1); IR (neat) 2928, 2869, 2870, 1513 cm^{-1}; HRMS (FAB) found 438.1501 [calcd for $C_{26}H_{26}O_5S$ $(M)^+$ 438.1501]

Preparation of 2,3-*Cis*-2,5-*Trans*-Tetrahydrofuran 11a



To a solution of $ZnBr_2$ (1 mL, 0.771 M in THF) was added dropwise 4-benzyloxy-3-methoxyphenylmagnesium bromide (4.28 mL, 0.3 M in THF, 1.28 mmol) at 25 °C and the resulting mixture was stirred at the same temperature for 30 min before sulfone **9** (112.9 mg, 0.257 mmol) in THF (2 mL) was added dropwise. After being stirred for 1 h, the reaction mixture was cooled to 0 °C, quenched with saturated aqueous NH_4Cl, and diluted with EtOAc. The layers were separated, and the aqueous layer was extracted with EtOAc (2 × 10 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, hexanes/EtOAc, 7/1) to afford 2,3-*cis*-2,5-*trans*-tetrahydrofuran **11a** as a colorless oil (102.1 mg, 75%): R_f 0.68 (hexanes/EtOAc, 3/1 developed twice); $[\alpha]^{29}_D$ = –73.7 (*c* 0.89, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27–7.45 (m, 10 H), 6.76–6.97 (m, 6 H), 5.31 (dd, *J* = 7.2, 7.2 Hz, 1 H), 5.30 (d, *J* = 6.4 Hz), 5.15 (s, 4 H), 3.90 (s, 6 H), 2.58 (ddddd, *J* = 6.4, 6.4, 6.4, 6.4, 6.4 Hz, 1 H), 2.16–2.19 (m, 2 H), 0.70 (d, *J* = 7.2 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.5, 149.2, 147.0, 146.8, 137.5, 137.1, 133.7, 128.2, 127.5, 127.1, 127.0, 118.0, 127.2, 113.8, 113.6, 109.9, 109.1, 83.9, 79.0, 70.9, 55.8, 42.7, 38.2, 14.8; IR (neat) 2932, 1510 cm^{-1}; HRMS (FAB) found 510.2401 [calcd for $C_{33}H_{34}O_5$ $(M)^+$ 510.2406]

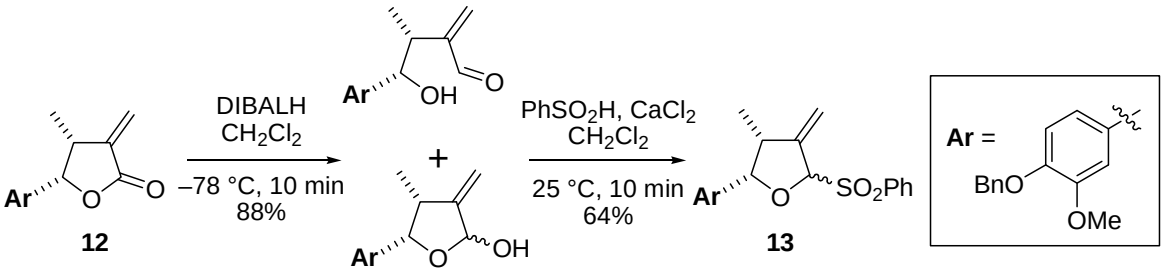
Preparation of Lactone 12



[Mannich Reaction] To a cooled (–78 °C) solution of lactone **8** (83.7 mg, 0.268 mmol) in THF (2 mL, 0.134 M) was added LiHMDS (0.536 mL, 1.0 M solution in THF, 0.536 mmol). The resulting mixture was stirred at the same temperature for 30 min and Eschenmoser's salt (148.7 mg, 0.804 mmol) in THF (1 mL) was added. After being stirred at the same temperature for another 15 min, the reaction mixture was quenched with saturated aqueous NH_4Cl solution, and diluted with CH_2Cl_2. The layers were separated, and the aqueous layer was extracted with (2 × 15 mL). The combined organic layers were dried over anhydrous Na_2SO_4, and concentrated *in vacuo* to afford the crude amine. This amine was carried to the next step without further purification. **[Elimination]** To a solution of the above amine in THF (4 mL) and saturated aqueous $NaHCO_3$ (2 mL) was added *m*-CPBA (231.2 mg, max. 78%, 1.05 mmol) at 0 °C. The resulting mixture was allowed to warm to 25 °C for 30 min, and quenched with saturated aqueous $NaHCO_3$ solution and saturated aqueous Na_2SO_3 solution. The layers were separated, and the aqueous layer was extracted with EtOAc (2 × 15 mL). The combined organic layer was washed with 2 N NaOH and brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, hexanes/EtOAc, 2/1) to afford lactone **12** as a colorless oil (69.2 mg, 80% for two steps): R_f 0.48 (hexanes/EtOAc, 2/1); $[\alpha]^{30}_D$ = +33.1 (*c* 1.86, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26–7.43 (m, 5 H), 6.85 (d, *J* = 8.4 Hz, 1 H), 6.62–6.67 (m, 2 H), 6.30 (d, *J* = 2.4 Hz, 1 H),

5.53–5.56 (m, 2 H), 5.12 (s, 2 H), 3.84 (s, 3 H), 3.33–3.41 (m, 1 H), 0.80 (d, J = 7.2 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 149.5, 148.1, 140.1, 136.8, 129.2, 128.4, 127.7, 127.2, 121.4, 118.4, 113.6, 109.5, 82.0, 70.9, 55.9, 38.9, 15.2; IR (neat) 1764, 1516 cm^{-1}; HRMS (FAB) found 324.1360 [calcd for $C_{20}H_{20}O_4$ $(M)^+$ 324.1362]

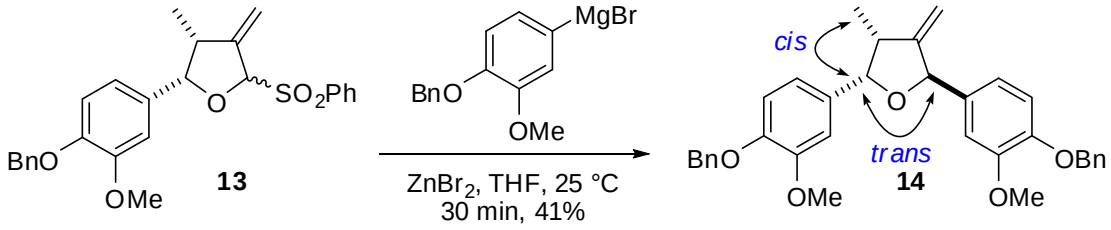
Preparation of Sulfone 13



[DIBALH Reduction] To a cooled (–78 °C) solution of lactone **12** (101.1 mg, 0.312 mmol) in CH_2Cl_2 (8 mL, 0.039 M) was added DIBALH (0.312 mL, 1.0 M solution in toluene, 0.312 mmol). After being stirred at the same temperature for 10 min, the reaction was quenched with MeOH. Then H_2O and 2 N NaOH was added and the resulting mixture was stirred at 25 °C for 1 h. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL). The combined organic layers were dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, hexanes/EtOAc, 2/1) to afford a mixture of lactol and aldehyde as a colorless oil (89.7 mg, 88%). **[Sulfonylation]** To a stirred solution of a mixture of lactol and aldehyde (28.5 mg, 0.0873 mmol) in CH_2Cl_2 (3 mL, 0.029 M) were added $PhSO_2H$ (16.1 mg, 0.114 mmol) and $CaCl_2$ (29.1 mg, 0.262 mmol) at 25 °C. After being stirred at the same temperature for 10 min, the reaction mixture was quenched with saturated aqueous $NaHCO_3$, and diluted with Et_2O (15 mL). The layers were separated, and the aqueous layer was extracted with EtOAc (2 × 10 mL). The combined organic layers were

washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, hexanes/EtOAc/Et_3N, 3/1/0.01) to afford sulfone **13** as a white foam (24.0 mg, 64%): R_f 0.61 (hexanes/EtOAc, 2/1); **[For Major Diastereomer]** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 7.2 Hz, 2 H), 7.63 (d, *J* = 7.2, 7.2 Hz, 1 H), 7.54 (dd, *J* = 7.2, 7.2 Hz, 2 H), 7.25–7.45 (m, 5 H), 6.80 (d, *J* = 8.4 Hz, 1 H), 6.63 (s, 1 H), 6.58 (d, *J* = 8.4 Hz, 1 H), 5.74 (s, 1 H), 5.52 (d, *J* = 8.0 Hz, 1 H), 5.47 (s, 1 H), 5.42 (s, 1 H), 5.11 (s, 2 H), 3.82 (s, 3 H), 3.21–3.26 (m, 1 H), 0.71 (d, *J* = 7.2 Hz, 3 H).

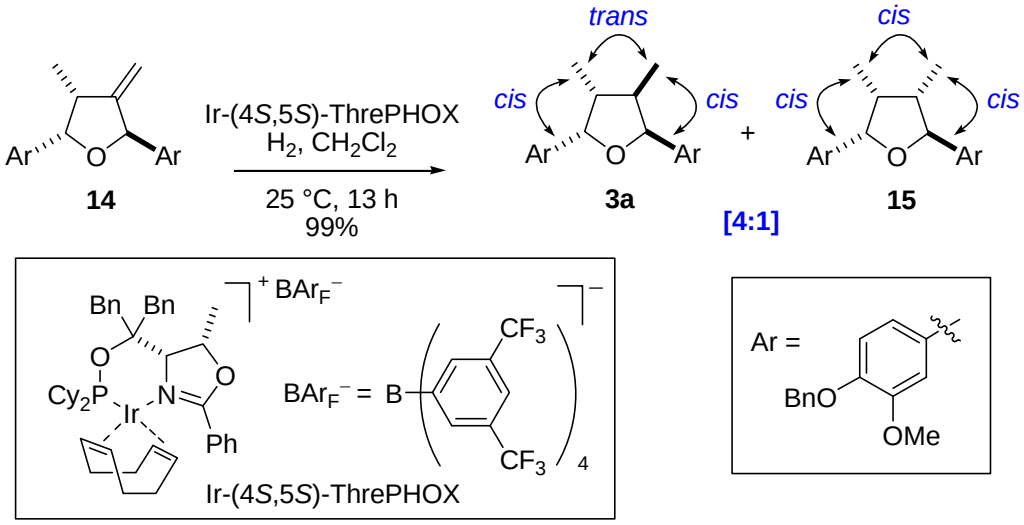
Preparation of 2,3-*Cis*-2,5-*Trans*-Tetrahydrofuran 14



To a solution of $ZnBr_2$ (1 mL, 0.22 M in THF) was added dropwise 4-benzyloxy-3-methoxyphenylmagnesium bromide (2.78 mL, 0.16 M, 0.44 mmol) at 25 °C. The resulting mixture was stirred at the same temperature for 30 min before sulfone **13** (40.0 mg, 0.088 mmol) in THF (1 mL) was added dropwise. After being stirred at 25 °C for 30 min, the reaction mixture was cooled to 0 °C, quenched with saturated aqueous NH_4Cl, and diluted with EtOAc. The layers were separated, and the aqueous layer was extracted with EtOAc (2 × 10 mL). The combined organic layers were washed with brine, and dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, hexanes/EtOAc, 6/1) to afford 2,3-*cis*-2,5-*trans*-tetrahydrofuran **14** as a colorless oil (19.1 mg, 41%): R_f 0.57 (hexanes/EtOAc, 7/1 × 3); $[\alpha]^{30}_D$ = +39.2 (*c* 0.32, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26–7.44 (m, 10 H), 6.73–6.99 (m, 6 H), 6.30 (d, *J* = 2.4 Hz, 1 H), 5.76 (d, *J* = 7.2

Hz, 1 H), 5.66 (s, 1 H), 5.15 (s, 2 H), 5.14 (s, 2 H), 5.05 (s, 1 H), 4.99 (s, 1 H), 3.90 (s, 3 H), 3.88 (s, 3 H), 3.08–3.13 (m, 1 H), 0.81 (d, J = 7.2 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.7, 149.6, 149.4, 147.7, 147.4, 137.2, 135.5, 133.3, 128.5, 127.7, 127.26, 127.21, 119.0, 118.6, 113.8, 110.6, 110.3, 106.7, 83.6, 82.5, 71.0, 56.0, 42.2, 14.3; HRMS (FAB) found 522.2409 [calcd for $C_{26}H_{26}O_5S$ $(M)^+$ 522.2406].

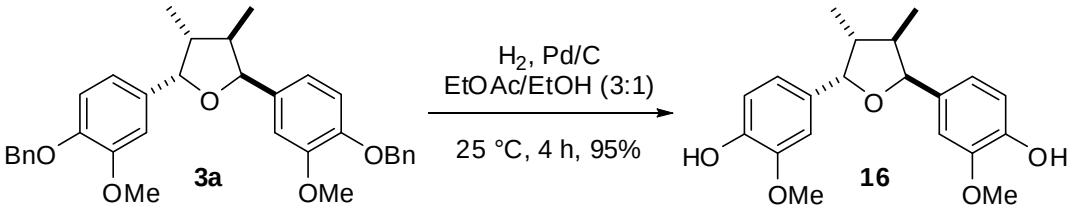
Preparation of 2,3-*Cis*-3,4-*Trans*-4,5-*Cis*-Tetrahydrofuran 3a via Asymmetric Hydrogenation of 14 with Ir-(4*S*,5*S*)-ThrePHOX



To a solution of **14** (107.1 mg, 0.205 mmol) in CH_2Cl_2 (5 mL) was added **Ir-(4*S*,5*S*)-ThrePHOX** (3.5 mg, 0.002 mmol) at 25 °C under H_2 atmosphere, and the reaction mixture was stirred at the same temperature for 1 h. An addition of **Ir-(4*S*,5*S*)-ThrePHOX** (3.5 mg, 0.002 mmol) was repeated two times every 1 h, and the reaction mixture was stirred further for 10 h before concentrated *in vacuo*. The residue was filtrated through a pad of silica gel (hexanes/EtOAc, 3/1) to afford a 4:1 mixture of 2,3-*cis*-3,4-*trans*-4,5-*cis*-tetrahydrofuran **3a** and 2,3-*cis*-3,4-*cis*-4,5-*trans*-tetrahydrofuran **15,** which was purified by column

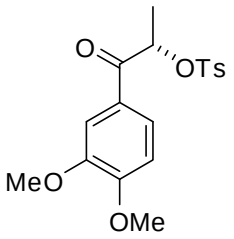
chromatography (silica gel, hexanes/EtOAc, 10/1) to afford 2,3-*cis*-3,4-*trans*-4,5-*cis*-tetrahydrofuran **3a** (66.3 mg, 62%), 2,3-*cis*-3,4-*cis*-4,5-*trans*-tetrahydrofuran **15** (19.9 mg, 18%), and a mixture of **3a** and **15** (20.1 mg, 19%). **[For 2,3-*cis*-3,4-*cis*-4,5-*trans*-tetrahydrofuran 15]** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26–7.44 (m, 10 H), 6.97 (s, 1 H), 6.94 (s, 1 H), 6.81–6.85 (m, 3 H), 6.78 (d, *J* = 8.0 Hz, 1 H), 5.44 (d, *J* = 4.0 Hz, 1 H), 5.148 (s, 2 H), 5.142 (s, 2 H), 4.64 (d, *J* = 8.8 Hz, 1 H), 3.90 (s, 3 H), 3.88 (s, 6 H), 2.36–2.48 (m, 2 H), 0.99 (d, *J* = 5.2 Hz, 3 H), 0.61 (d, *J* = 6.4 Hz, 3 H).

Preparation of Bis-Phenol 16



To a stirred solution of bis-benzyl ether **3a** (112 mg, 0.21 mmol) in EtOAc/EtOH (3:1, 4 mL) was added 10% palladium on activated carbon (22.4 mg, 20 wt %). The resulting mixture was stirred under H_2 atmosphere at 25 °C for 4 h. The reaction mixture was then filtered through celite with EtOAc and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, hexanes/EtOAc, 3/1) to afford bis-phenol **16** as a colorless oil (70 mg, 95%): R_f 0.33 (hexanes/EtOAc, 2/1); $[\alpha]^{24.7}_D$ = –35.3 (*c* 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.88 (d, *J* = 8.0 Hz, 2 H), 6.82 (s, 2 H), 6.75 (d, *J* = 8.0 Hz, 2 H), 5.63 (s, 2 H), 5.41 (d, *J* = 6.0 Hz, 2 H), 3.87 (s, 6 H), 2.18–2.28 (m, 2 H), 0.67 (d, *J* = 6.0 Hz, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.6, 144.7, 133.7, 119.4, 114.2, 109.2, 83.9, 56.3, 44.3, 15.0; IR (neat) 3420, 2964, 2932, 1515, 1269, 1035 cm^{-1}; HRMS (FAB) found 344.1617 [calcd for $C_{20}H_{24}O_5$ $(M)^+$ 344.1624]

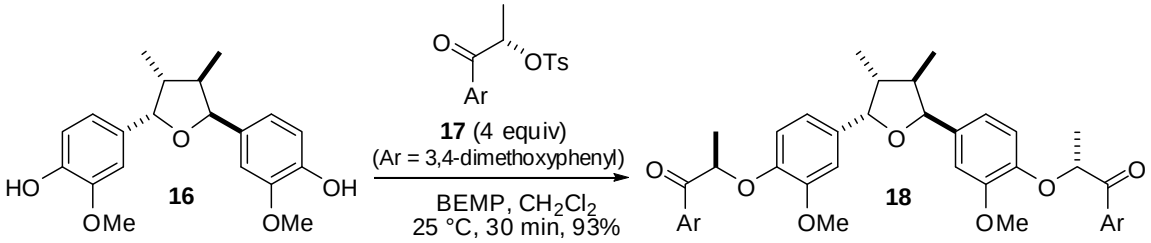
(*S*)-α-Tosyl Aryl Ketone 17[2]



17

$[\alpha]^{28.2}_{D}$ = +2.76 (*c* 0.54, $CHCl_3$); R_f 0.52 (hexanes/EtOAc, 3/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.6 Hz, 2 H), 7.56 (dd, *J* = 8.4, 2.0 Hz, 1 H), 7.42 (s, 1 H), 7.24 (d, *J* = 8.4 Hz, 2 H), 6.86 (d, *J* = 8.4 Hz, 1 H), 5.75 (ddd, *J* = 6.8, 6.8, 6.8 Hz, 1 H), 3.92 (s, 3 H), 3.89 (s, 3 H), 2.39 (s, 3 H), 1.55 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.4, 154.3, 149.6, 145.3, 133.9, 130.1, 128.2, 127.0, 123.9, 111.2, 110.4, 56.47, 56.34, 22.0, 19.2; IR (neat) 2961, 1684, 1514, 1263, 1173, 1017, 927 cm^{-1}; HRMS (FAB) found 364.0981 [calcd for $C_{18}H_{20}O_6S$ $(M)^+$ 364.0981]

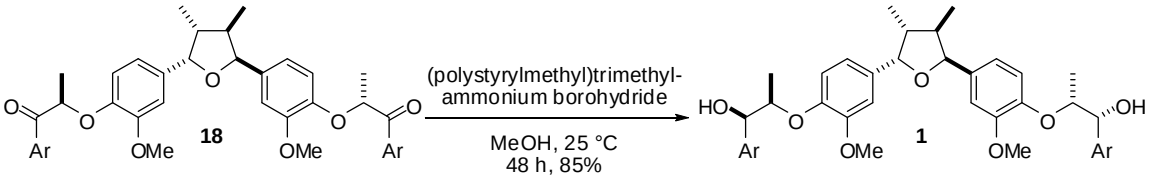
Preparation of Bis-Ketone 18



To a cooled (0 °C) solution of bis-phenol **16** (29.8 mg, 0.086 mmol) in dry CH_2Cl_2 (1.0 mL, 0.086 M) was added dropwise 2-*tert*-butylimino-2-diethylamino-1,3-dimethylpherhydro-1,3,2-diazaphosphorine (BEMP, 30 μL, 0.10 mmol). The resulting mixture was stirred at the same temperature for 10 min before **17** (126.0 mg, 0.346 mmol) in CH_2Cl_2 (1.0 mL) was added. The reaction mixture was allowed to warm to 25 °C for 30 min with stirring, quenched with

saturated aqueous NH_4Cl solution, and diluted with CH_2Cl_2 (2 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 10 ml). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, hexanes/EtOAc, 2/1) to afford **18** as a colorless oil (64.4 mg, 93%): R_f 0.26 (hexanes/EtOAc, 1/1); $[\alpha]^{24.7}_D$ = +13.9 (*c* 0.23, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77–7.82 (m, 2 H), 7.64–7.66 (m, 2 H), 6.85 (d, *J* = 8.4 Hz, 2 H), 6.79 (dd, *J* = 8.8, 1.6 Hz, 1 H), 6.73–6.76 (m, 2 H), 6.66 (dd, *J* = 8.4, 1.6 Hz, 2 H), 5.38 (ddd, *J* = 6.8, 6.8, 6.8 Hz, 2 H), 5.32 (d, *J* = 6.0 Hz, 2 H), 3.91 (s, 6 H), 3.89 (s, 6 H), 3.81 (s, 6 H), 2.14–2.20 (m, 2 H), 1.68 (d, *J* = 6.8 Hz, 6 H), 0.59 (d, *J* = 6.0 Hz, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.1, 153.9, 150.0, 149.3, 146.1, 135.9, 127.8, 124.1, 118.8, 116.1, 115.9, 111.6, 110.8, 110.4, 83.7, 78.7, 56.4, 56.3, 44.4, 19.6, 15.1; IR (neat) 2963, 1684, 1594, 1512, 1264, 1022 cm^{-1}; HRMS (FAB) found 728.3193 [calcd for $C_{42}H_{48}O_{11}$ $(M)^+$ 728.3197]

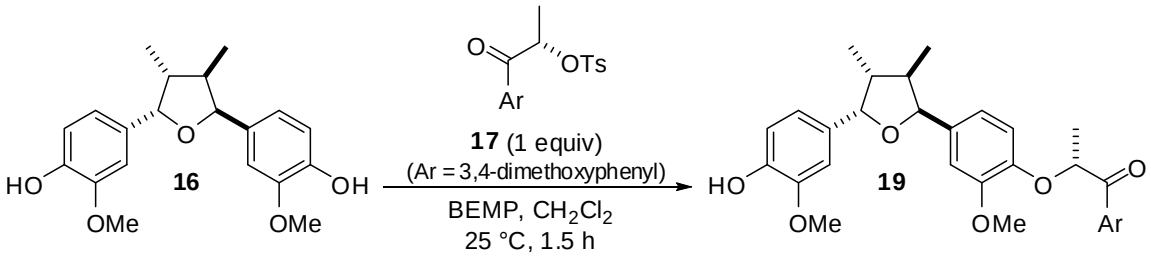
Preparation of Manassantin A (1)



To a solution of bis-ketone **18** (14.0 mg, 0.019 mmol) in MeOH (0.5 mL) was added polymer-supported borohydride (2.5~5.0 mmol BH_4/g resin, 132 mg, 0.33~0.66 mmol). The reaction mixture was stirred with gentle agitation at 25 °C for 48 h. The polymer beads were then removed by filtration and the filtrate was concentrated *in vacuo* to afford a 6:1 diastereomeric mixture of manassantin A and (7*S*,7‴*S*)-epimer, which was then purified by column chromatography (silica gel, hexanes/EtOAc/MeOH, 2/1/0.01) to afford **1** as a white solid (12.0

mg, 85%): R_f 0.18 (hexanes/EtOAc, 2/1); $[\alpha]^{32.2}_D = -107.9$ (*c* 0.18, $CHCl_3$) ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.82–7.00 (m, 12 H), 5.46 (d, *J* = 6.0 Hz, 2 H), 4.64 (d, *J* = 8.4 Hz, 2 H), 4.08–4.16 (m, 2 H), 3.93 (s, 6 H), 3.89 (s, 6 H), 3.88 (s, 6 H), 2.25–2.33 (m, 2 H), 1.17 (d, *J* = 6.4 Hz, 6 H), 0.72 (d, *J* = 6.4 Hz, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.5, 149.00, 148.84, 146.5, 136.5, 132.5, 120.0, 118.7, 110.9, 110.0, 84.2, 83.4, 78.4, 55.9, 44.1, 17.1, 14.8; IR (neat) 3594, 2961, 1506, 1262, 1140, 1028 cm^{-1}; HRMS (FAB) found 732.3506 [calcd for $C_{42}H_{52}O_{11}$ $(M)^+$ 732.3510]

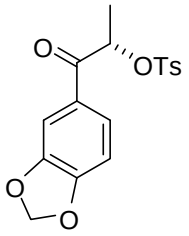
Preparation of Mono-Ketone 19



To a cooled (0 °C) solution of **16** (20 mg, 0.058 mmol) in dry CH_2Cl_2 (0.5 mL) was added BEMP (16.8 μL, 0.058 mmol). The resulting mixture was stirred at 25 °C for 5 min before tosylate **17** (21 mg, 0.058 mmol) in CH_2Cl_2 (1 mL) was added. The reaction mixture was stirred at the same temperature for 1.5 h, quenched with saturated aqueous NH_4Cl solution, and diluted with CH_2Cl_2 (2 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified via column chromatography, (silica gel, hexanes/EtOAc, 2/1) to afford **19** (9 mg, 29%) in addition to **16** (10 mg, 50%) and **18** (9 mg, 21%): $[\alpha]^{28.1}_D = -25.1$ (*c* 0.39, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80–7.85 (m, 1 H), 7.67–7.65 (m, 1 H), 6.76–6.94 (m, 7 H), 5.55 (s, 1 H), 5.36–5.44

(m, 3 H), 3.94 (s. 3 H), 3.92 (s. 3 H), 3.88 (s. 3 H), 3.85 (s. 3 H), 2.19–2.26 (m, 2 H), 1.71 (d, *J* = 6.8 Hz, 3 H), 0.66 (d, *J* = 6.8 Hz, 3 H), 0.64 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.7, 153.5, 149.6, 148.9, 146.2, 145.7, 144.4, 135.6, 133.3, 127.4, 123.6, 119.0, 118.4, 115.8, 113.9, 111.2, 110.5, 110.0, 108.8, 83.5, 83.3, 78.3, 56.0, 55.9, 44.0, 19.2, 14.7; IR (neat) 3442, 1682 cm^{-1}; HRMS (FAB) found 537.2469 [calcd for $C_{31}H_{37}O_8$ $(M+1)^+$ 537.2488].

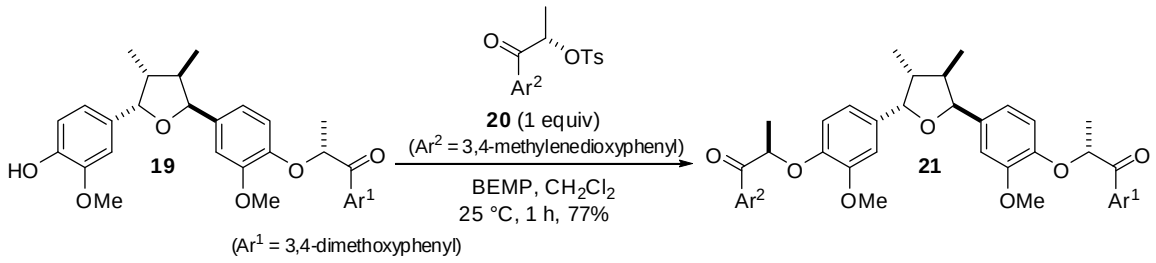
(*S*)-α-Tosyl Aryl Ketone 20[2]



20

$[\alpha]^{28.3}_D$ = –13.0 (*c* 0.40, $CHCl_3$); R_f 0.53 (hexanes/EtOAc, 3/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.4 Hz, 2 H), 7.48 (d, *J* = 8.4 Hz, 1 H), 7.30 (s, 1 H), 7.24 (d, *J* = 8.8 Hz, 2 H), 6.80 (d, *J* = 8.0 Hz, 1 H), 6.01 (s, 2 H), 5.66 (ddd, *J* = 7.2, 7.2, 7.2 Hz, 1 H), 2.38 (s, 3 H), 1.53 (d, *J* = 7.2 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.1, 152.8, 148.7, 145.3, 133.8, 130.1, 128.6, 128.3, 125.6, 108.8, 108.4, 102.4, 77.6, 22.0, 19.2; IR (neat) 2977,1712, 1376, 1121 cm^{-1}; HRMS (FAB) found 349.0749 [calcd for $C_{17}H_{17}O_6S$ $(M+1)^+$ 349.0746].

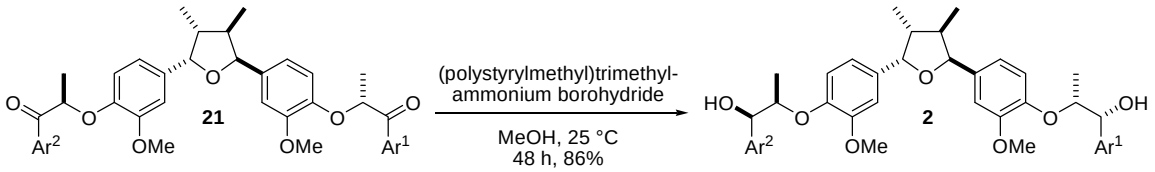
Preparation of Bis-Ketone 21



To a cooled (0 °C) solution of **19** (24.3 mg, 0.045 mmol) in CH_2Cl_2 (0.5 mL) was added

dropwise BEMP (0.027 mL, 0.094 mmol). The resulting mixture was stirred at the same temperature for 10 min before tosylate **20** (15.7 mg, 0.045 mmol) was added. The reaction mixture was allowed to warm to 25 °C for 1 h with stirring, quenched with saturated aqueous NH_4Cl, and diluted with CH_2Cl_2. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 5 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography, (silica gel, hexanes/EtOAc, 2/1) to afford **21** as a colorless oil (24.8 mg, 77%): R_f 0.42 (hexanes/EtOAc, 1/1); $[\alpha]^{28.2}_D = -10.4$ (*c* 0.41, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74–7.82 (m, 2 H), 7.65 (dd, *J* = 3.6, 2.0 Hz, 1 H), 7.58 (dd, *J* = 4.8, 2.0 Hz, 1 H), 6.72–6.88 (m, 6 H), 6.671 (d, *J* = 8.4 Hz, 1 H), 6.666 (d, *J* = 8 Hz, 1 H), 6.01 (s, 2 H), 5.32–5.41 (m, 4 H), 3.92 (s, 3 H), 3.90 (s, 3 H), 3.82 (s, 6 H), 2.12–2.22 (m, 2 H), 1.69 (d, *J* = 6.4 Hz, 3 H), 1.65 (d, *J* = 6.8 Hz, 3 H), 0.60 (d, *J* = 6.0 Hz, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.1, 197.6, 153.9, 152.3, 150.1, 150.0, 149.3, 148.4, 146.1, 146.0, 136.1, 135.9, 129.4, 127.8, 125.7, 124.0, 118.8, 116.5, 116.1, 111.6, 110.8, 110.4, 109.2, 108.3, 102.2, 83.7, 78.77, 78.66, 56.40, 56.27, 44.4, 19.53, 19.36, 15.1; IR (neat) 2963, 1684, 1511, 1261, 1036 cm^{-1}; HRMS (FAB) found 713.2957 [calcd for $C_{41}H_{45}O_{11}$ $(M+1)^+$ 713.2962].

Preparation of Manassantin B (2)



Ar^1 = 3,4-dimethoxyphenyl, Ar^2 = 3,4-methylenedioxyphenyl

To a stirred solution of **21** (24.8 mg, 0.035 mmol) in MeOH (1.5 mL) was added polymer-supported borohydride (2.5~5.0 mmol BH_4/g resin, 400 mg, 1.0~2.0 mmol) and the reaction

mixture was stirred with gentle agitation at 25 °C for 48 h. The polymer beads were then removed by filtration and the filtrate was concentrated *in vacuo* to afford a 5.4:1 diastereomeric mixture (21.4 mg, 86%) of manassantin B (**2**) and (7*S*,7‴*S*)-epimer, which was then purified by column chromatography (silica gel, hexanes/EtOAc/MeOH, 2/1/0.01) to afford manassantin B (**2)** as a white solid (13.3 mg, 53%) and a mixture (8.1 mg, 33%) of **2** and (7*S*,7‴*S*)-epimer: R_f 0.32 (hexanes/EtOAc/MeOH, 2/1/0.01); $[\alpha]^{29.5}_D = -108.4$ (*c* 0.22, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.74–7.01 (m, 12 H), 5.93 (s, 2 H), 5.45 (d, *J* = 6 Hz, 2 H), 4.65 (d, *J* = 8.0 Hz, 1 H), 4.62 (d, *J* = 8.8 Hz, 1 H), 4.04–4.16 (m, 4 H), 3.93 (s, 3H), 3.92 (s, 3 H), 3.89 (s, 3 H), 3.88 (s, 3 H), 2.23–2.32 (m, 2 H), 1.12–1.18 (dd, *J* = 5.6, 5.6 Hz, 6 H), 0.72 (d, *J* = 5.2, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.0, 150.8, 149.4, 149.2, 148.1, 147.8, 146.8, 137.0, 136.90, 134.4, 132.9, 121.5, 120.4, 119.3, 119.1, 111.2, 110.5, 110.4, 108.5, 107.9, 101.4, 84.6, 84.5, 83.8, 78.8, 56.3, 44.6, 17.5, 17.3, 15.3; IR (neat) 3725, 2959, 1508, 1259, 1035 cm^{-1}; HRMS (FAB) found 716.3196 [calcd for $C_{41}H_{48}O_{11}$ $(M)^+$ 716.3197].

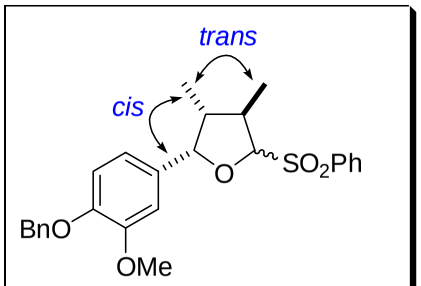
Reference

1. Kim, H.; Wooten, C. M.; Park, Y.; Hong, J. *Org. Lett.* **2007**, *9*, 3965–3968.

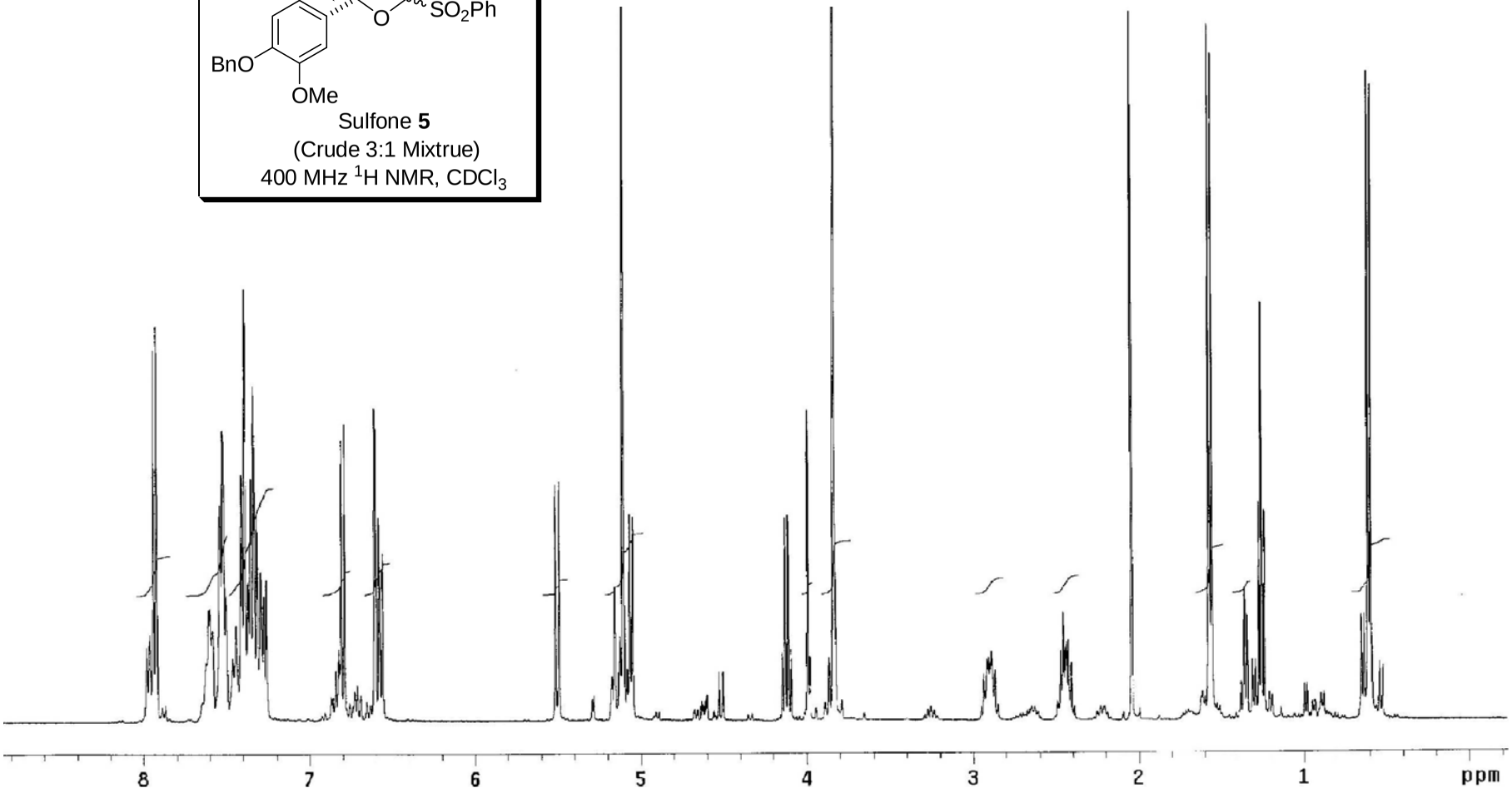
2. Lee, A.-L.; Ley, S. V. *Org. Biomol. Chem.* **2003**, *1*, 3957–3966.

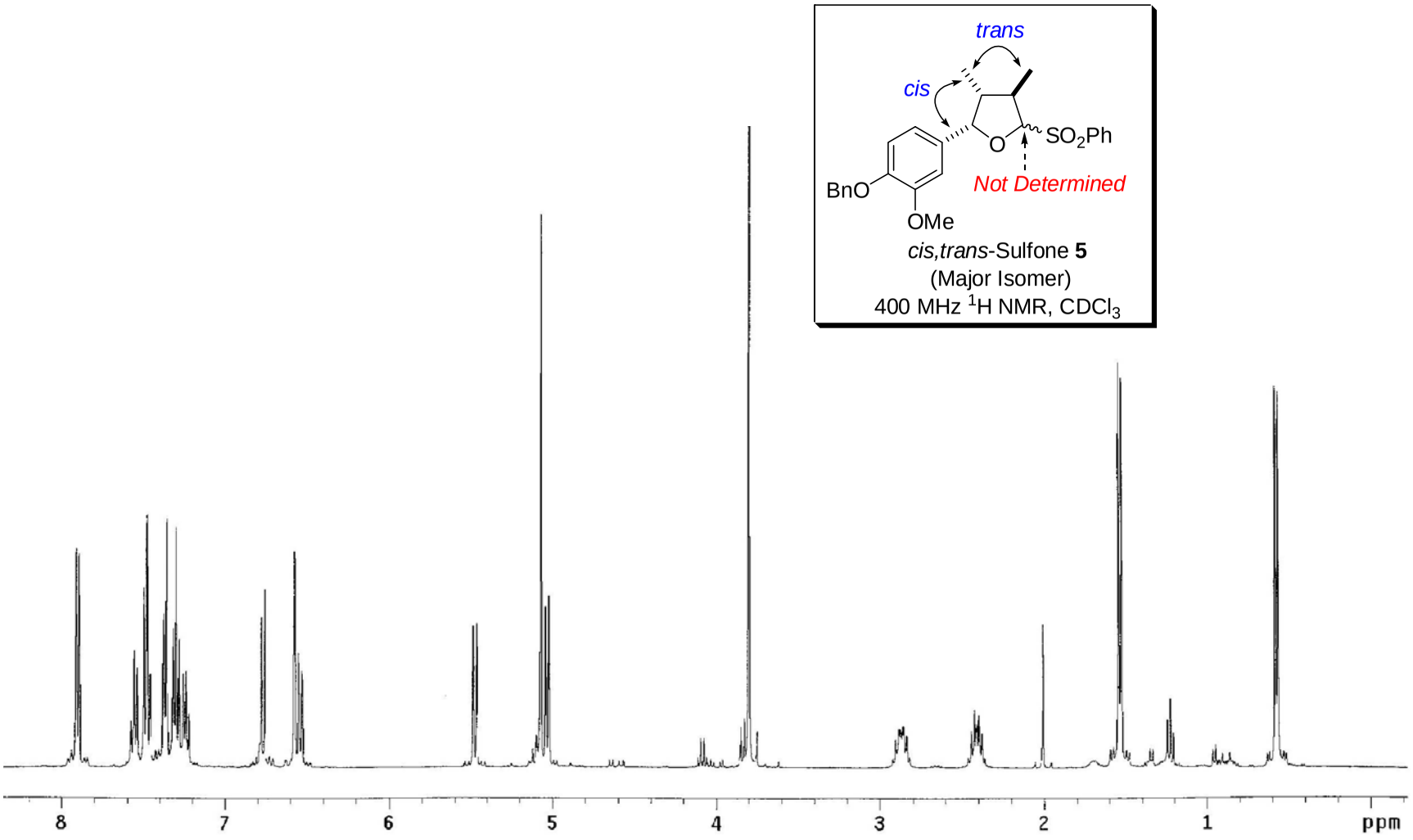
Determination of HIF-1 Inhibition Using the Luciferase Imaging

4T1-ODD-Luc cells (a gift from Dr. Chuan-Yuan Li), stably transfected with the oxygen-dependent-degradation (ODD) domain of HIF-1α and a firefly luciferase reporter, were seeded in the 24-well plate at a density of 10^5 cells/well. After 16-hour incubation, cells were treated with 240 μM of Cobalt (II) Chloride (Sigma-Aldrich, St. Louis, MO, USA) and serially diluted compounds for 24 h. To measure the luciferase signals, luciferin (150 mg/mL) was added and the plates were imaged using the Xenogen IVIS imaging system and associated Living Image software (Xenogen, Alameda, CA). Luciferase expression/activity was detected and quantified as relative light units (RLUs). Results are means ± SD, n = 3.



Sulfone **5**
(Crude 3:1 Mixtrue)
400 MHz ^{1}H NMR, $CDCl_3$

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O
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BnO
OMe
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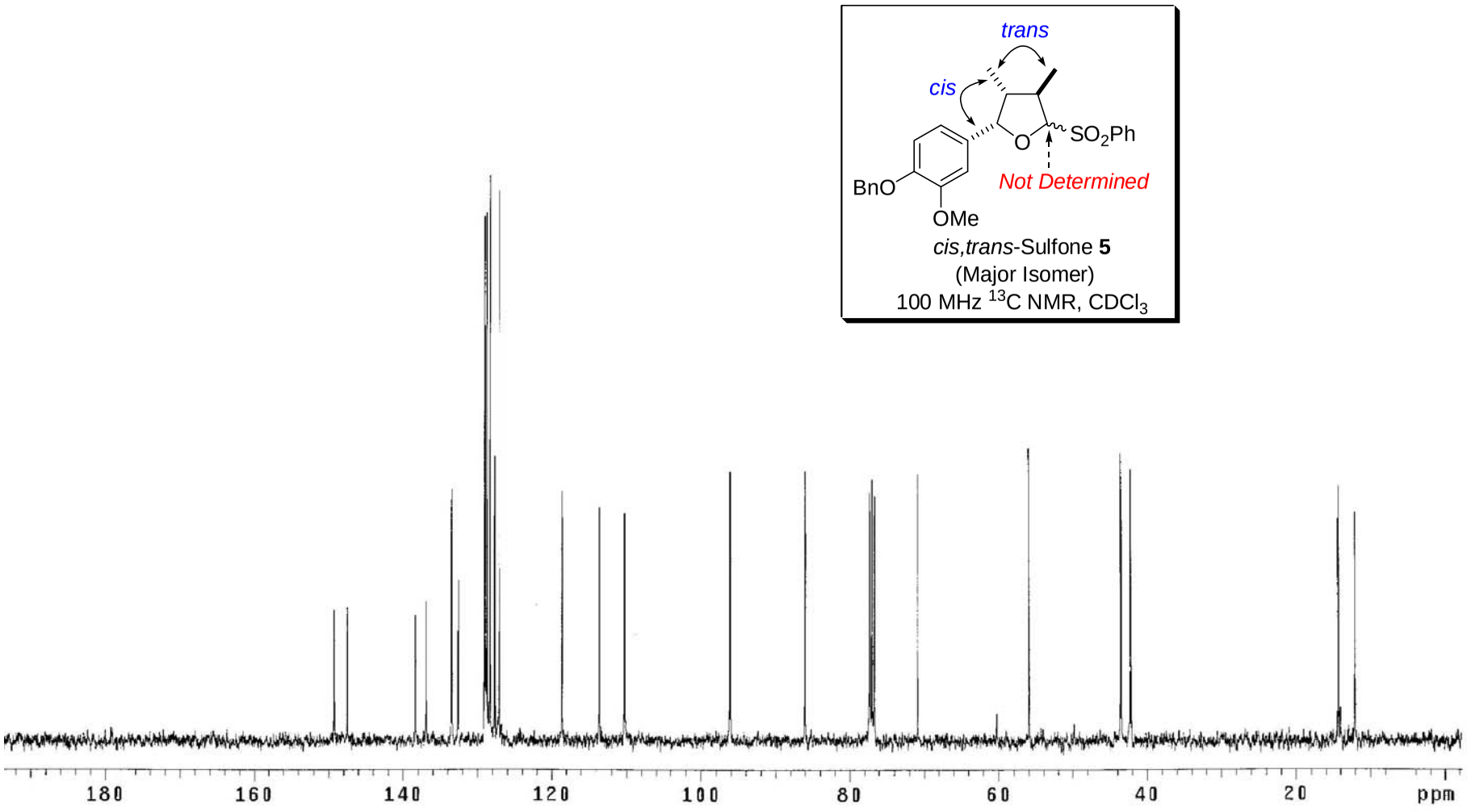
7
6
5
4
3
2
1
ppm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O
Not Determined
BnO
OMe
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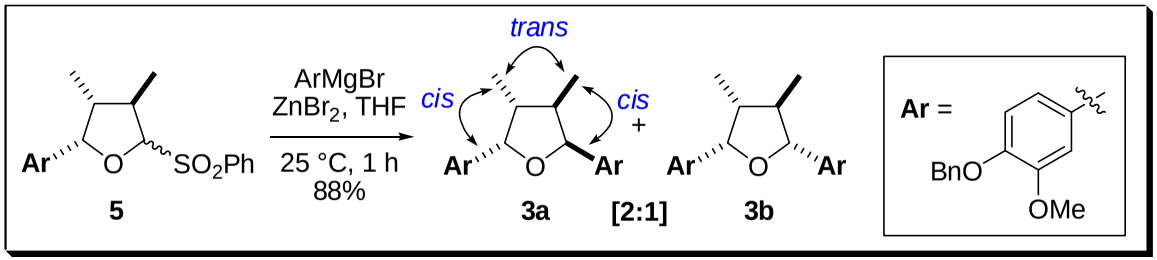
140
120
100
80
60
40
20
ppm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cis
+
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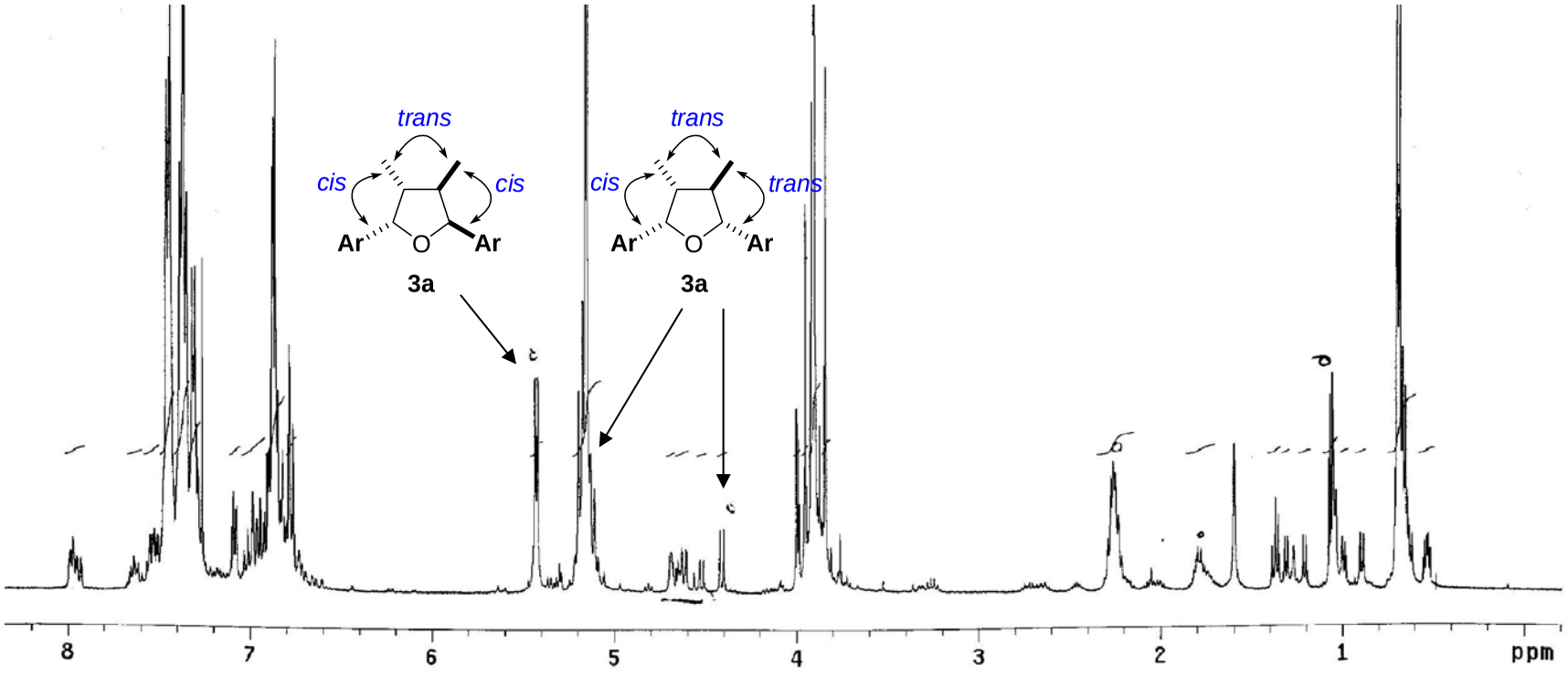
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3a
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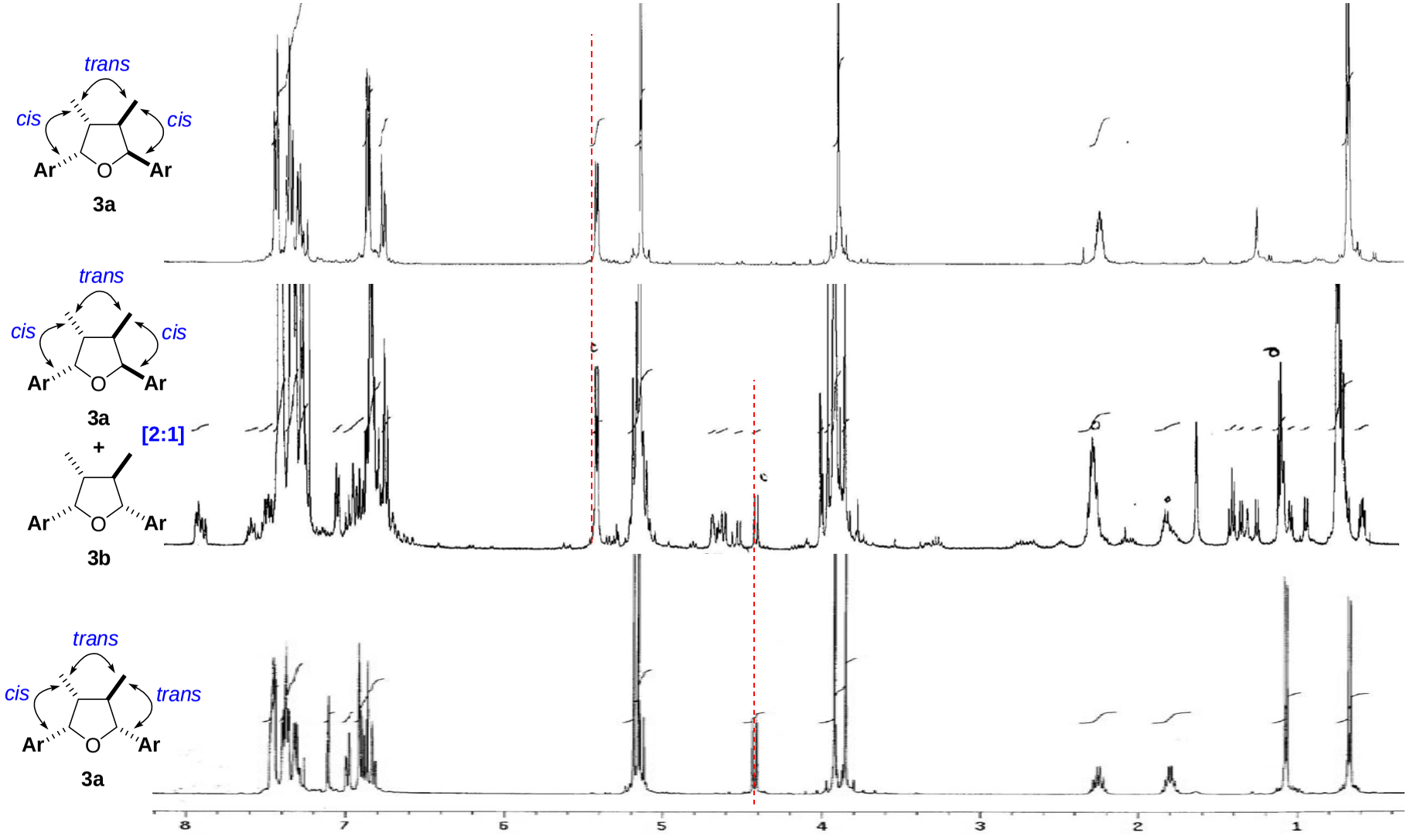
ppm


trans
cis
cis
Ar
O
Ar
3a
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cis
cis
Ar
O
Ar
3a
[2:1]
+
Ar
O
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3b
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cis
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8
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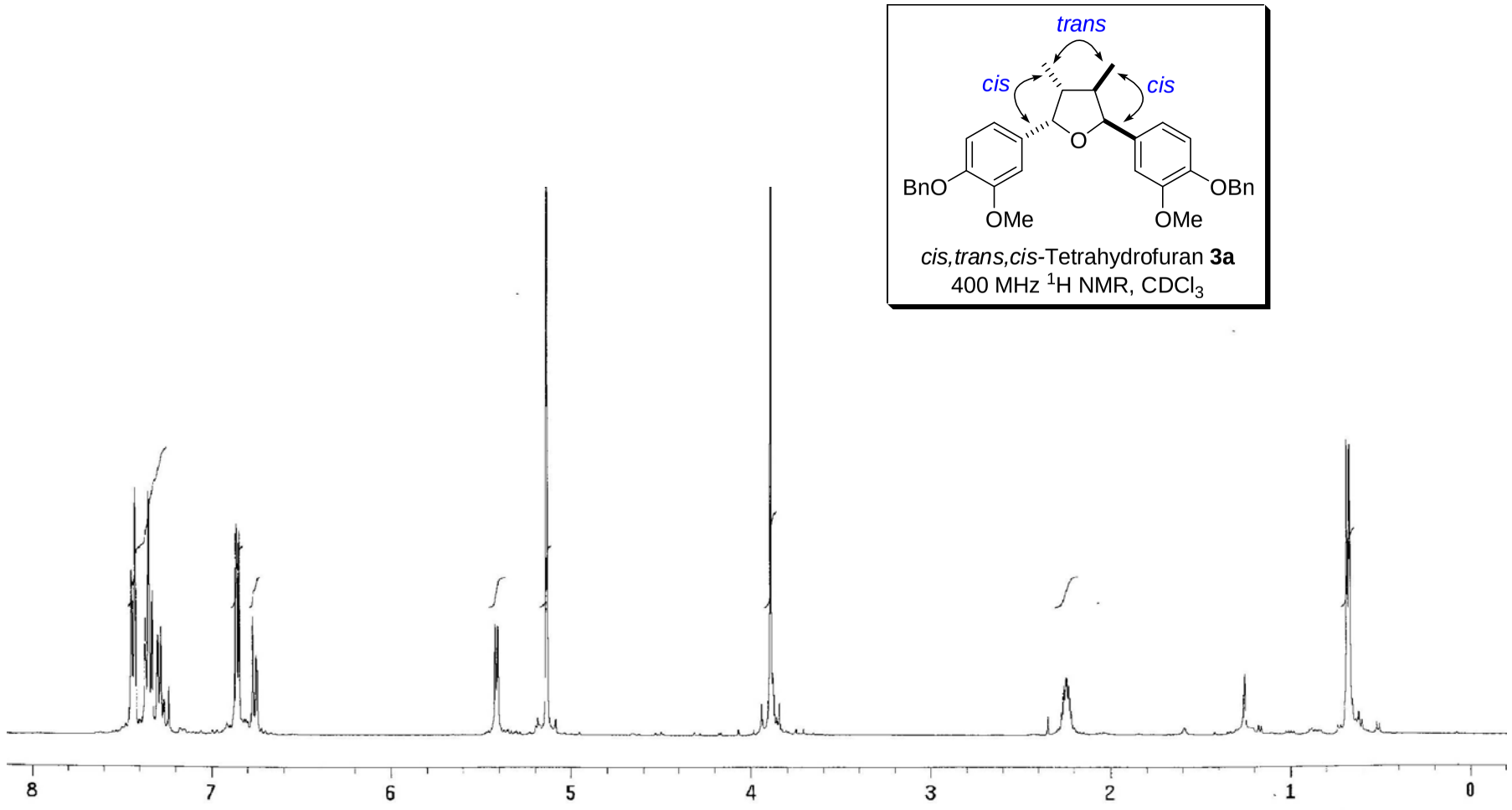
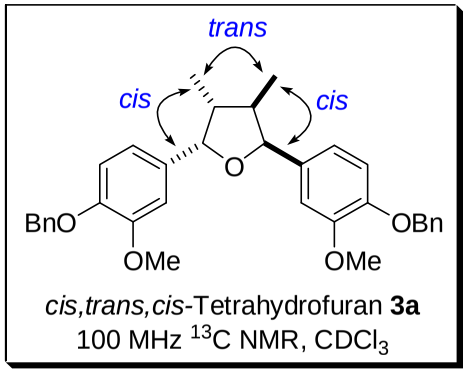
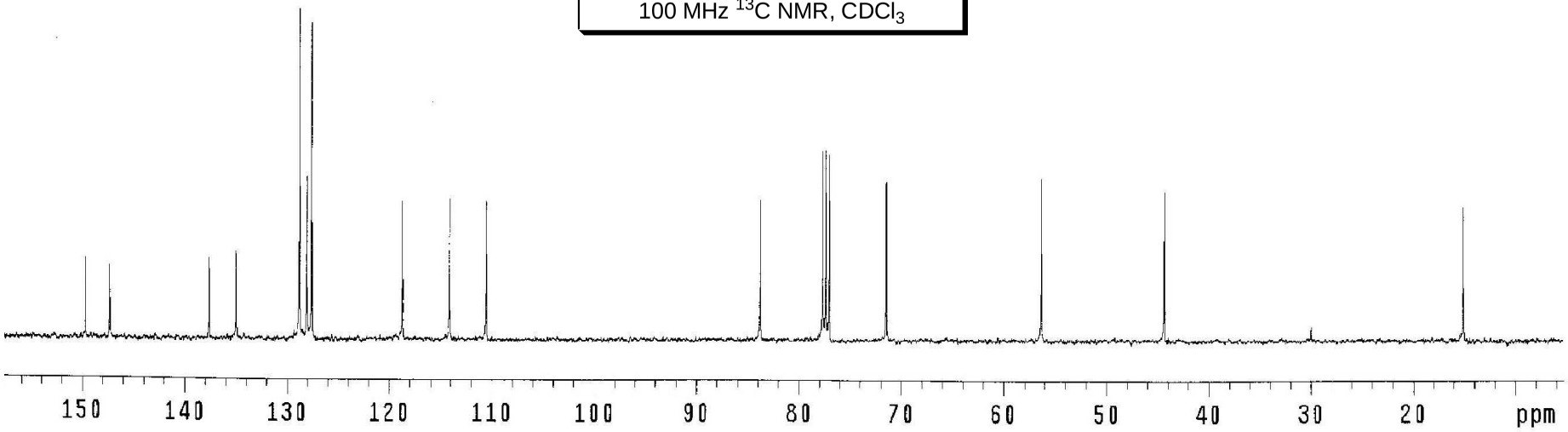
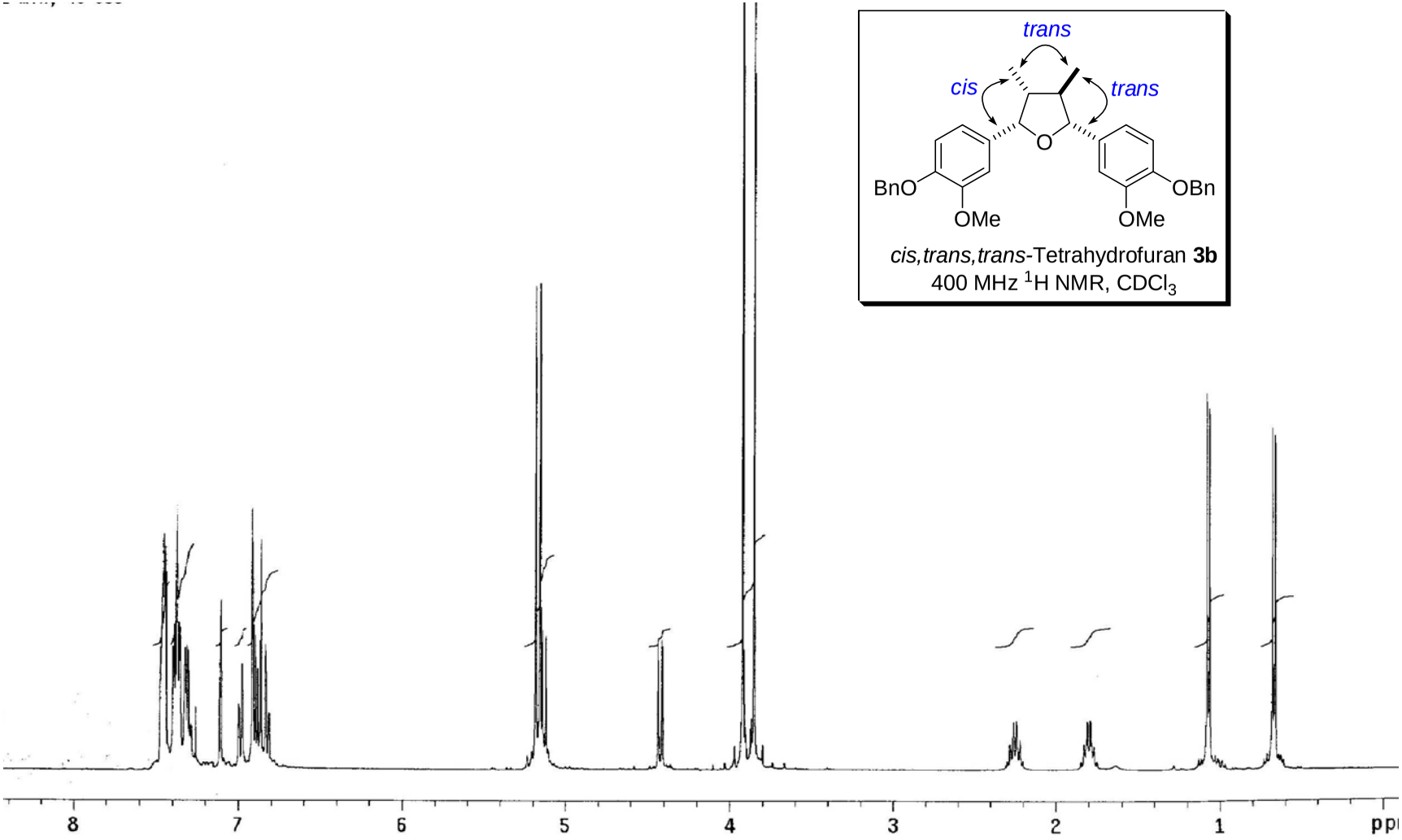


cis,trans,cis-Tetrahydrofuran **3a**
400 MHz ^{1}H NMR, $CDCl_3$

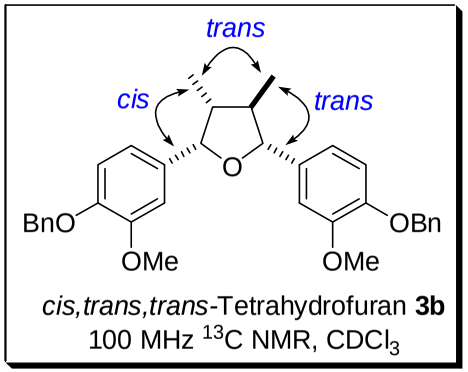


cis,trans,cis-Tetrahydrofuran **3a**
100 MHz ^{13}C NMR, $CDCl_3$

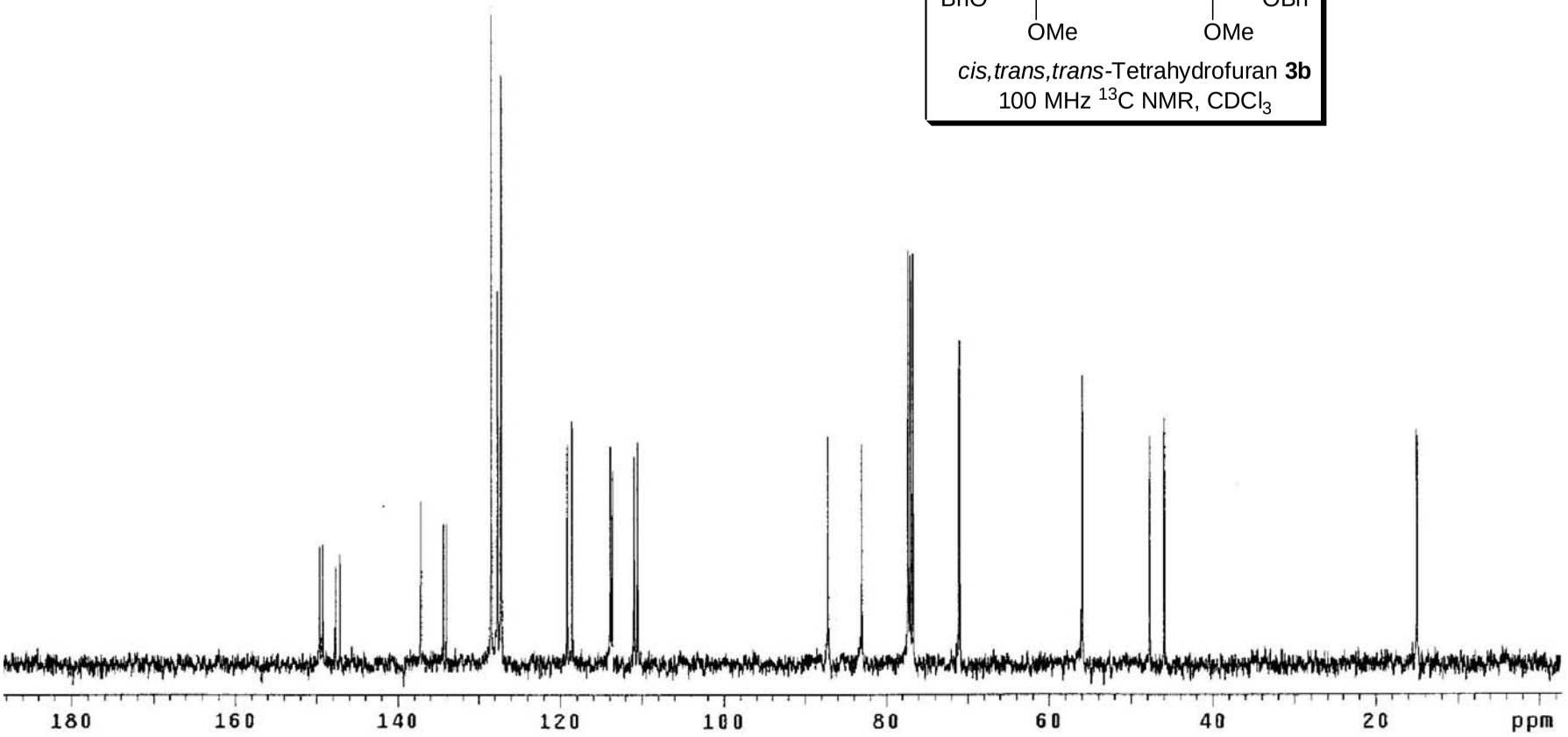


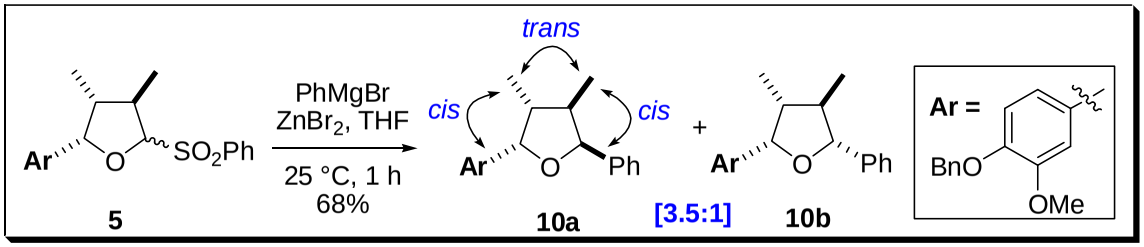


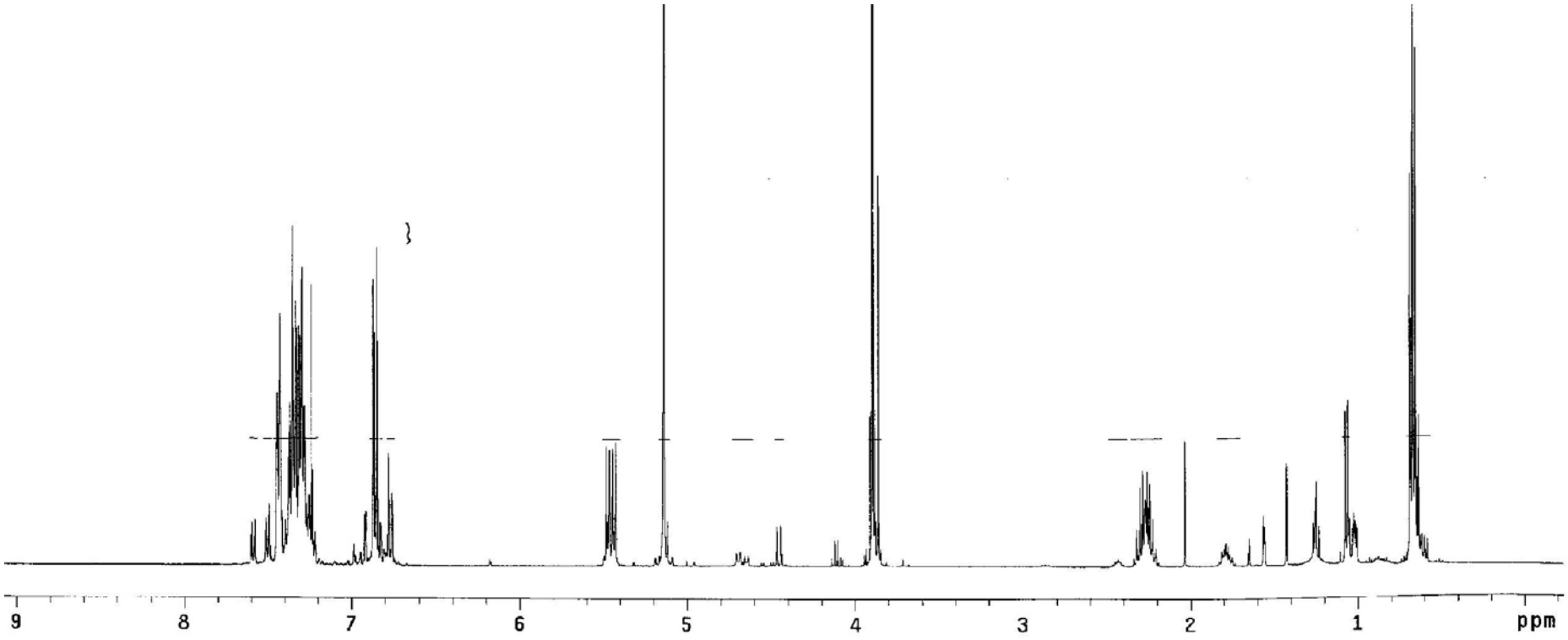
cis,trans,trans-Tetrahydrofuran **3b**
400 MHz ^{1}H NMR, $CDCl_3$

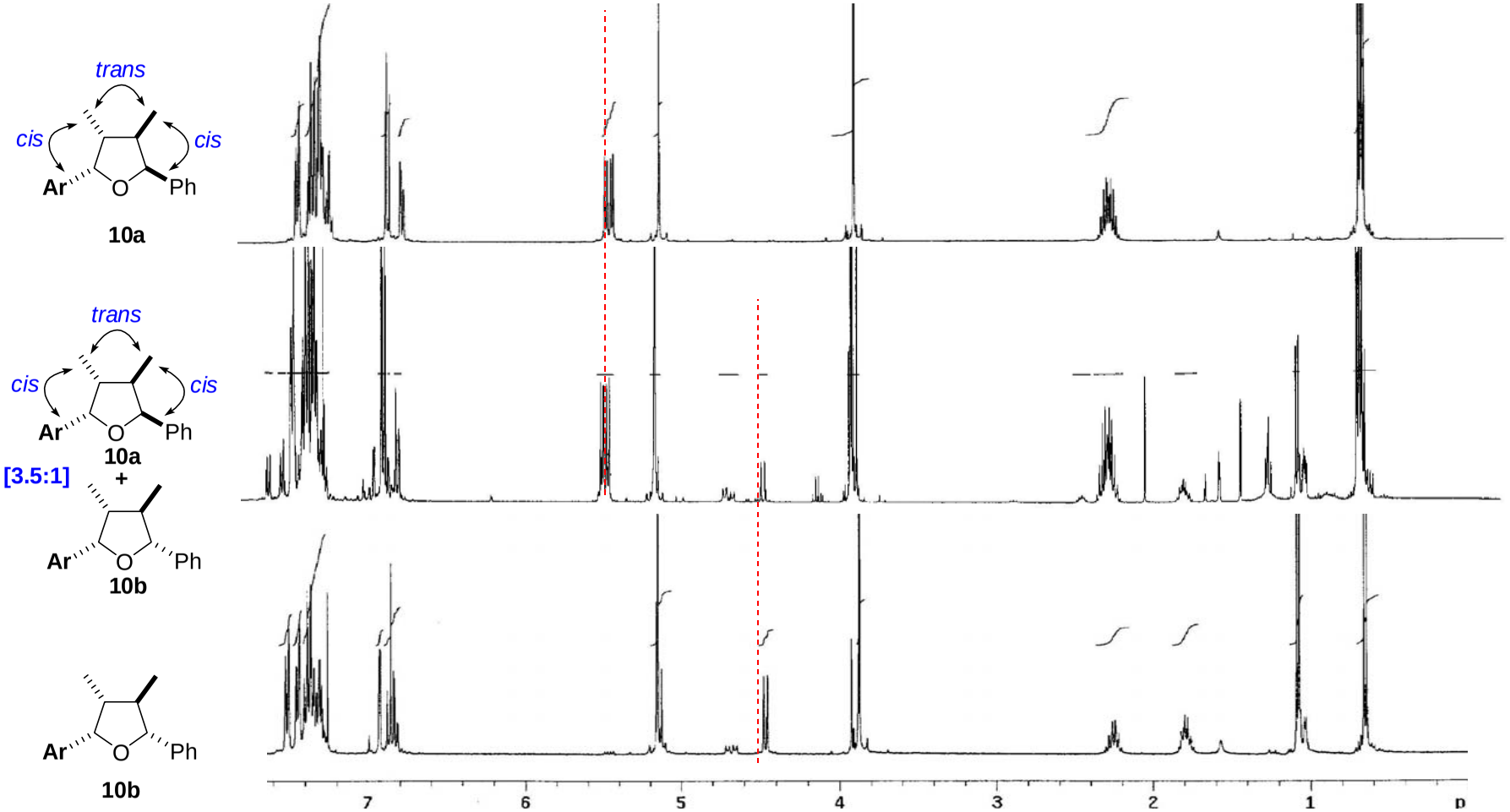


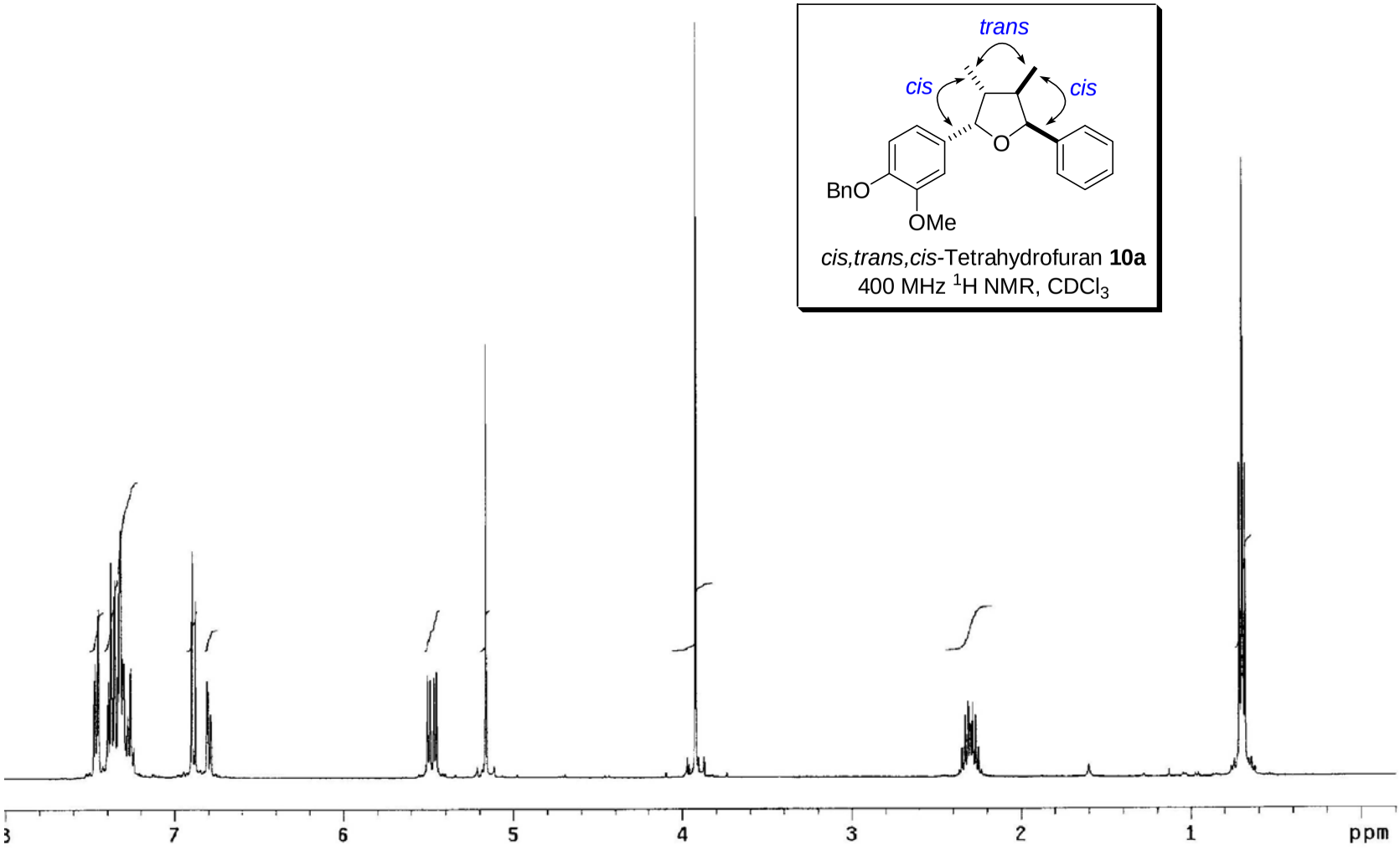
cis,trans,trans-Tetrahydrofuran **3b**
100 MHz ^{13}C NMR, $CDCl_3$

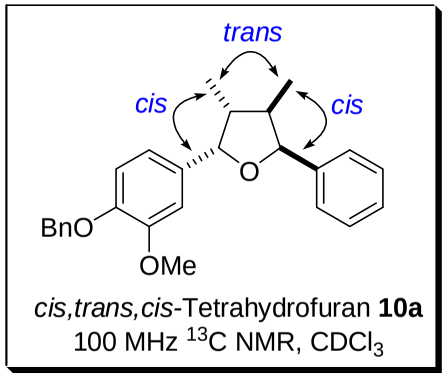



trans
cis
cis
Ar
O
SO2Ph
PhMgBr
ZnBr2, THF
25 °C, 1 h
68%
Ph
+
Ar =
BnO
OMe
5
10a
[3.5:1]
10b

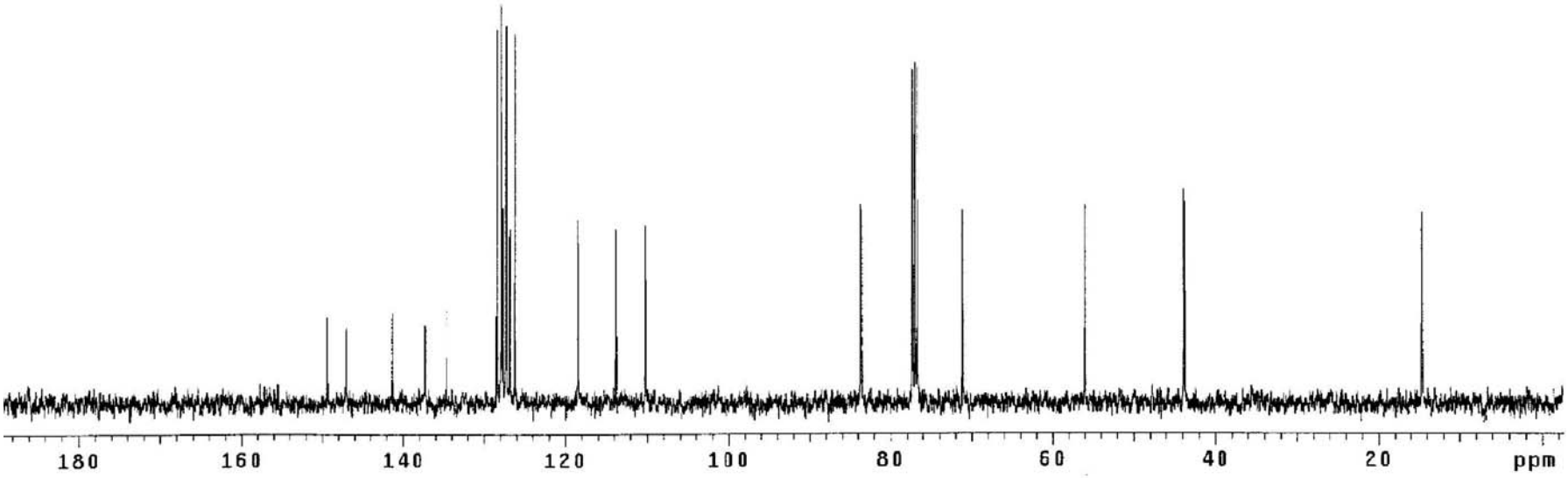

9
8
7
6
5
4
3
2
1
ppm

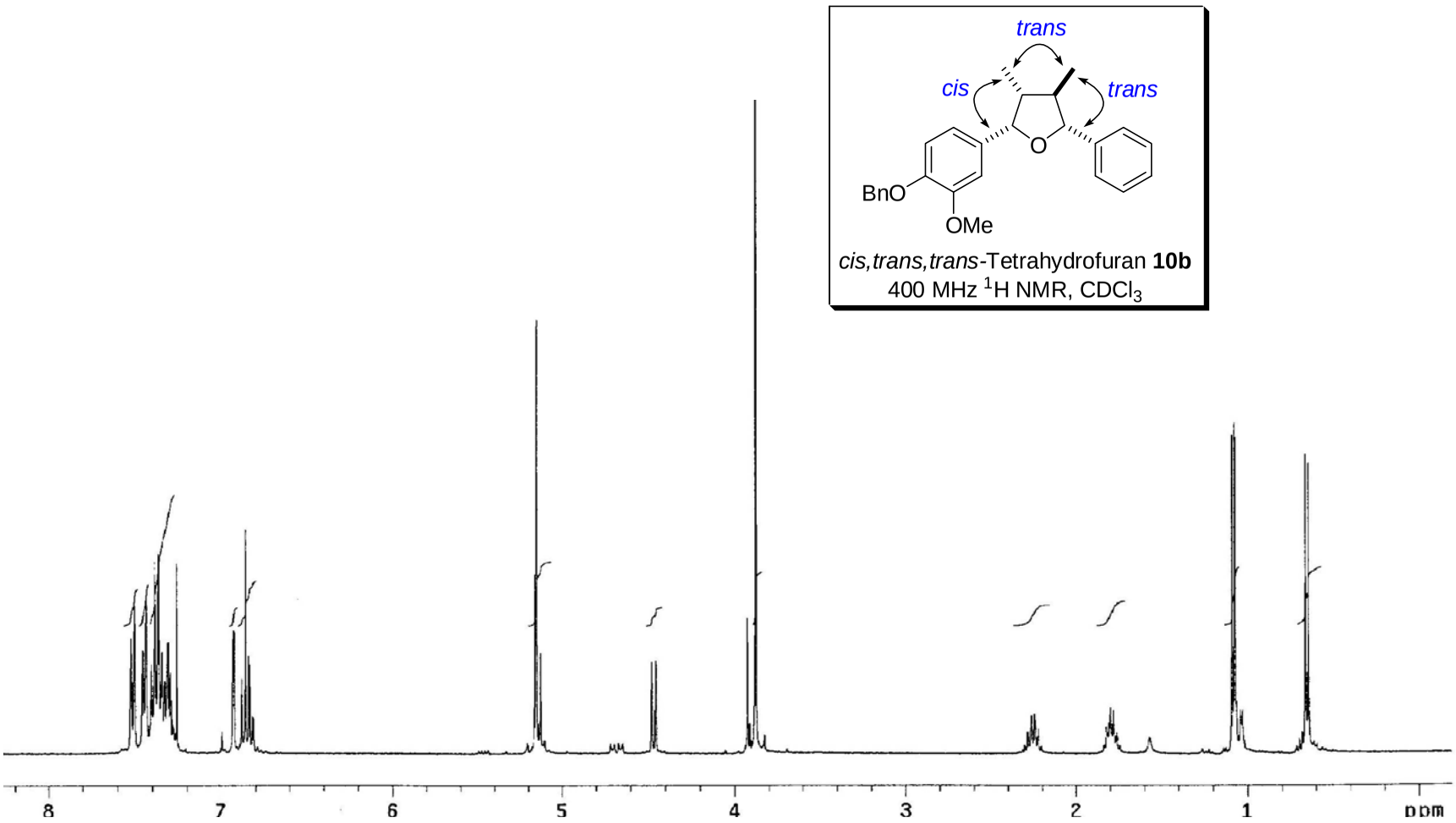

trans
cis
cis
Ar
O
Ph
10a
trans
cis
cis
Ar
O
Ph
10a
[3.5:1]
+
Ar
O
Ph
10b
Ar
O
Ph
10b
7
6
5
4
3
2
1
p


trans
cis
cis
O
BnO
OMe
cis,trans,cis-Tetrahydrofuran 10a
400 MHz 1H NMR, CDCl3
7
6
5
4
3
2
1
ppm

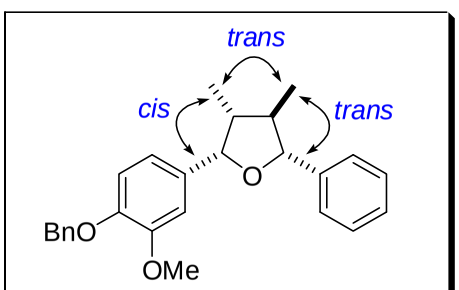


cis,trans,cis-Tetrahydrofuran **10a**
100 MHz ^{13}C NMR, $CDCl_3$

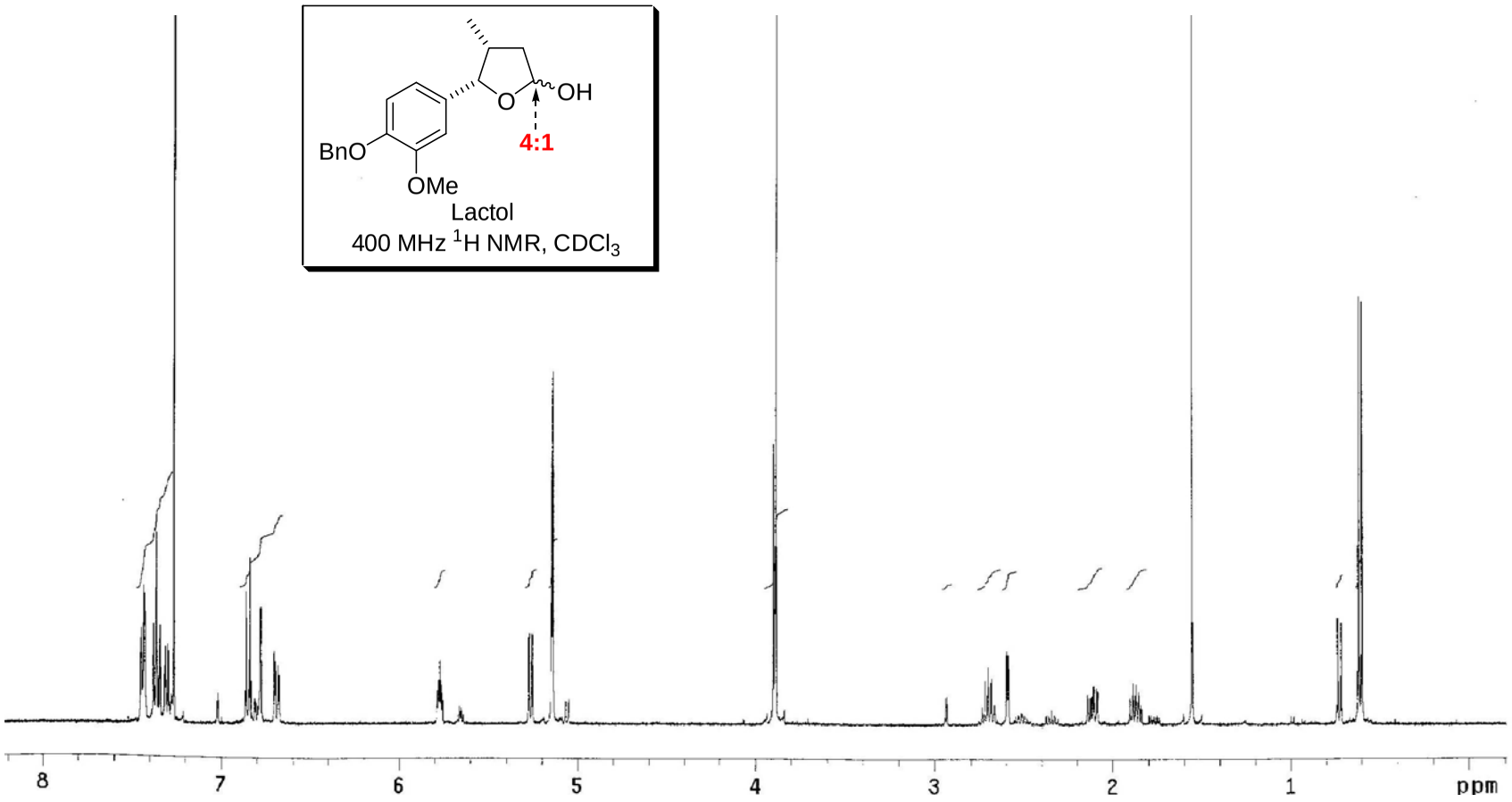


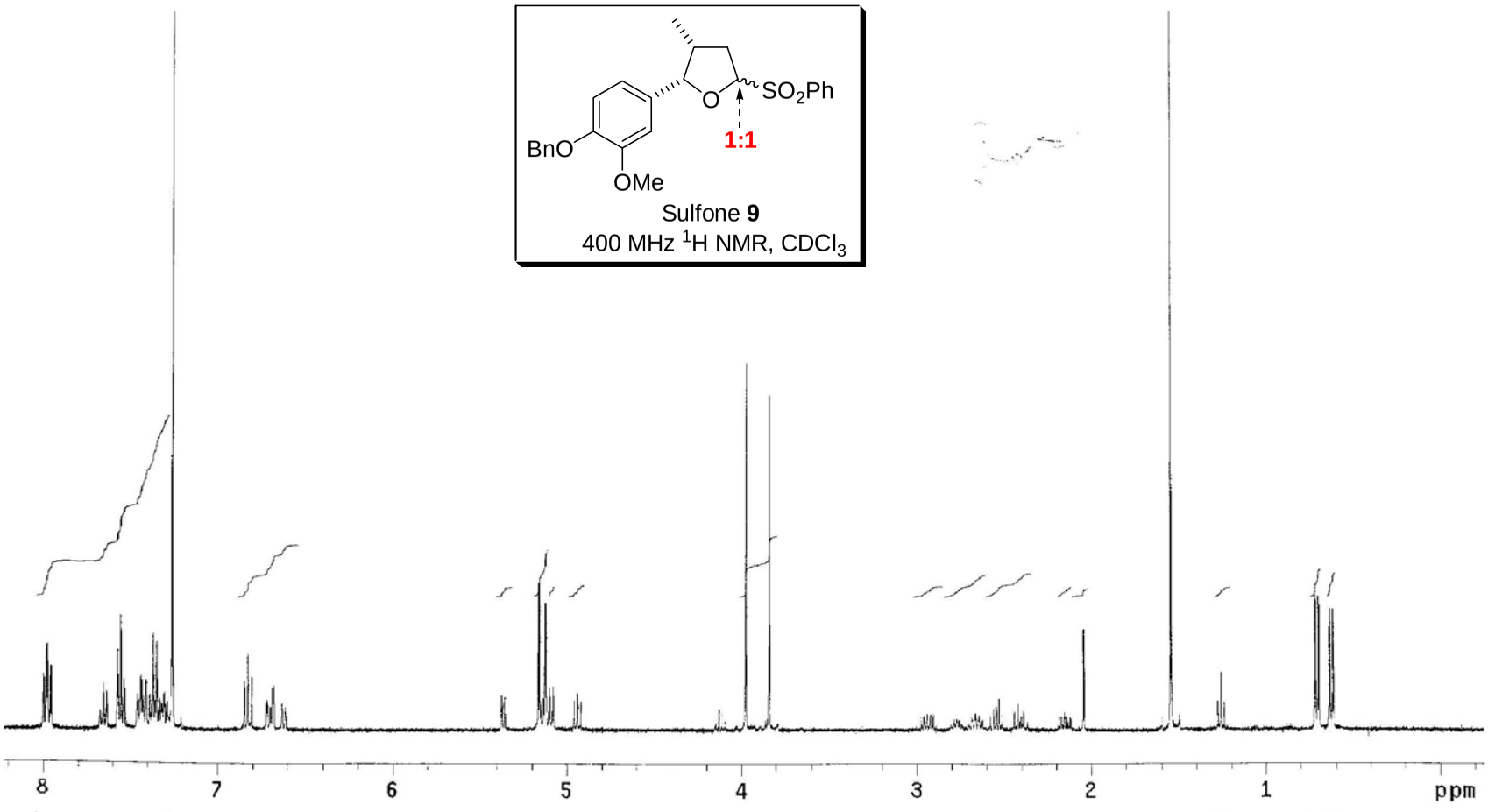


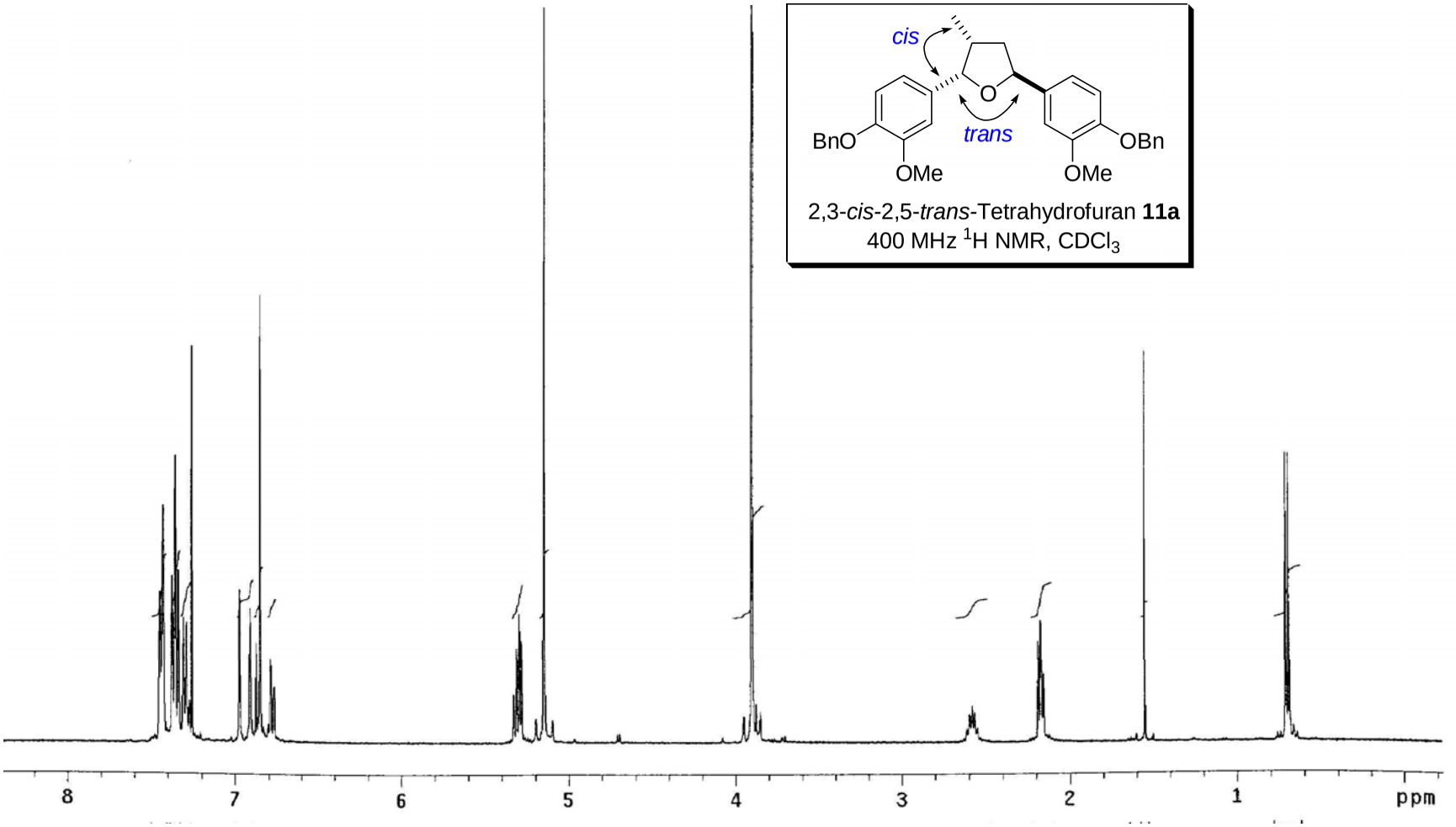
cis,trans,trans-Tetrahydrofuran **10b**
400 MHz ^{1}H NMR, $CDCl_3$



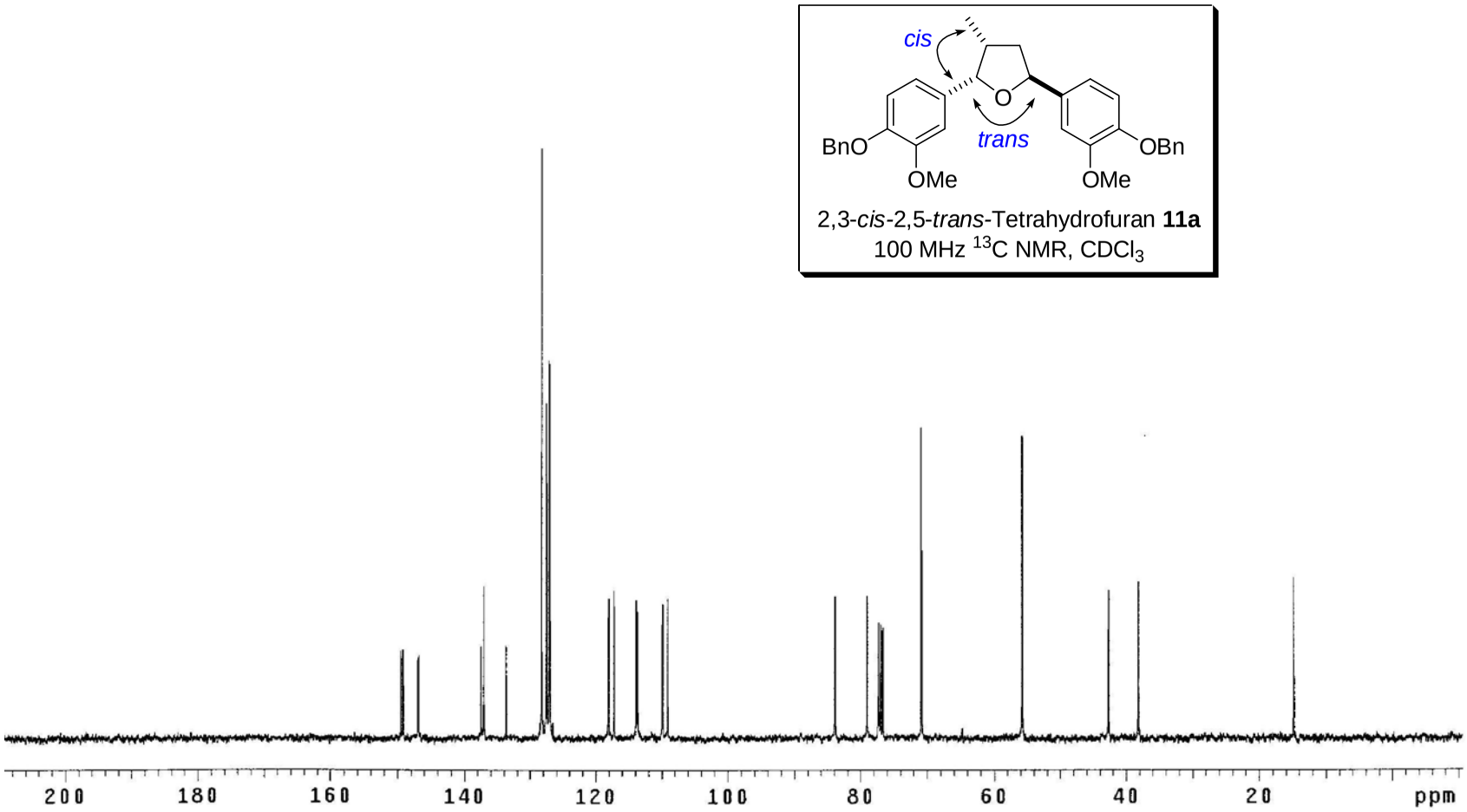
cis,trans,trans-Tetrahydrofuran **10b**
100 MHz ^{13}C NMR, $CDCl_3$

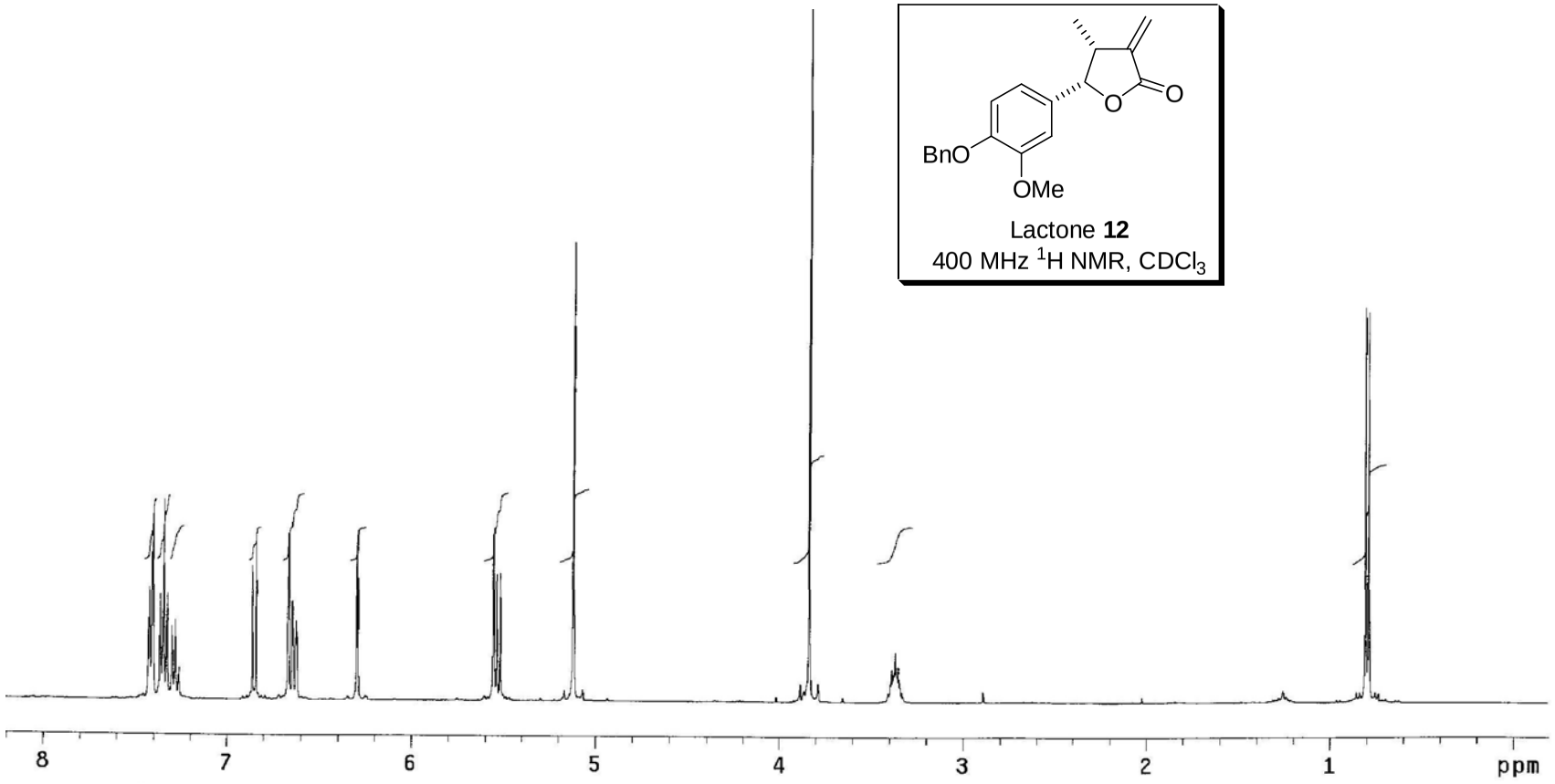

OH
O
4:1
BnO
OMe
Lactol
400 MHz ^{1}H NMR, $CDCl_3$
8
7
6
5
4
3
2
1
ppm

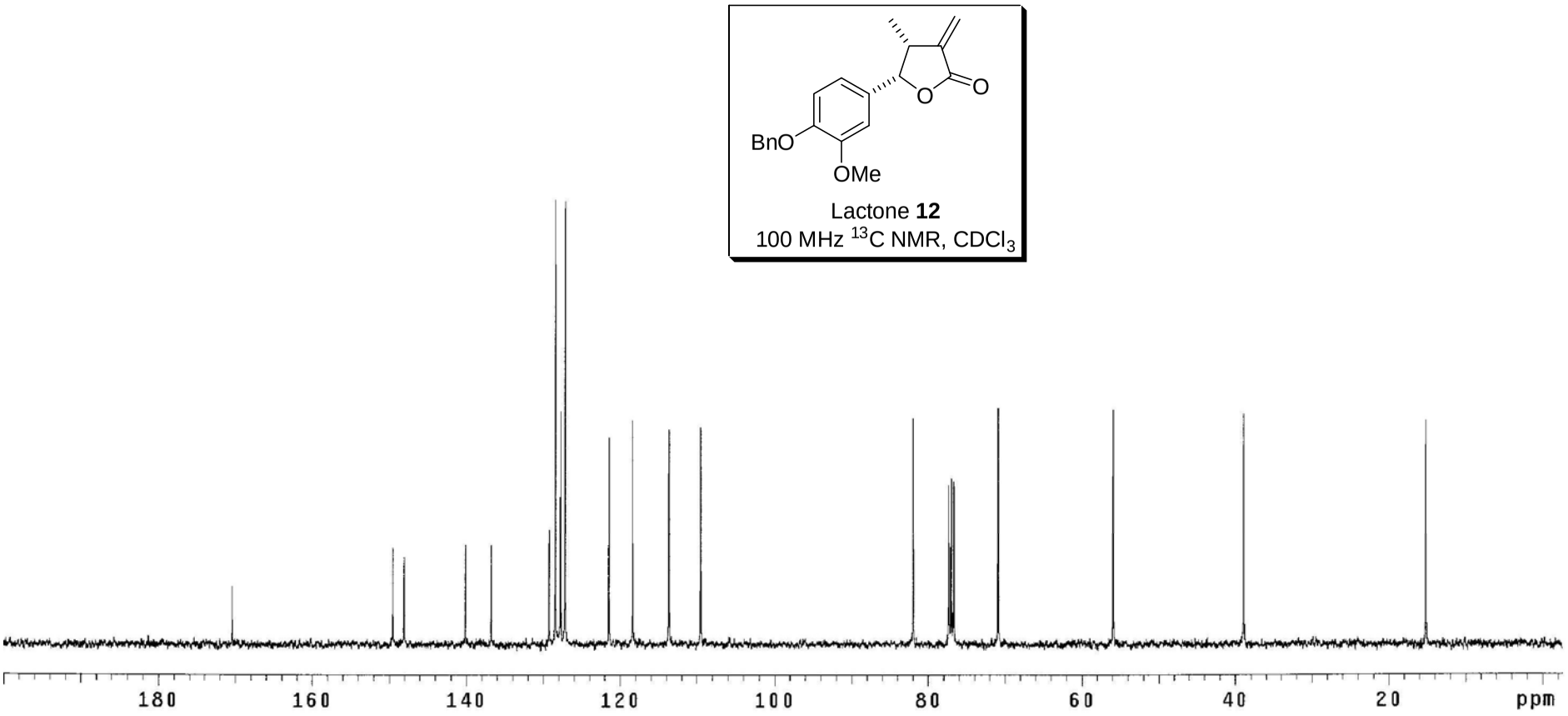

BnO
OMe
O
SO2Ph
1:1
Sulfone 9
400 MHz 1H NMR, CDCl3
8
7
6
5
4
3
2
1
ppm

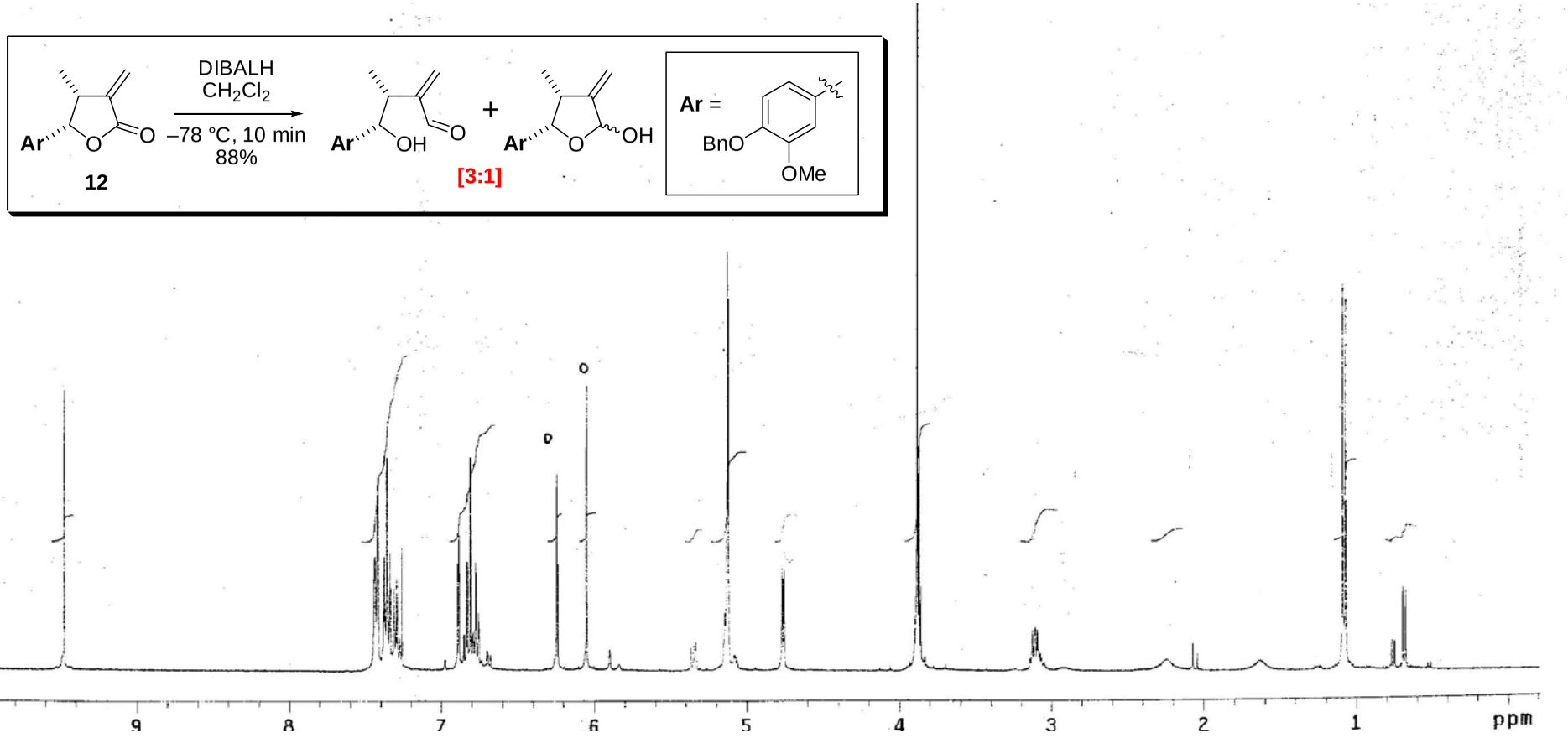


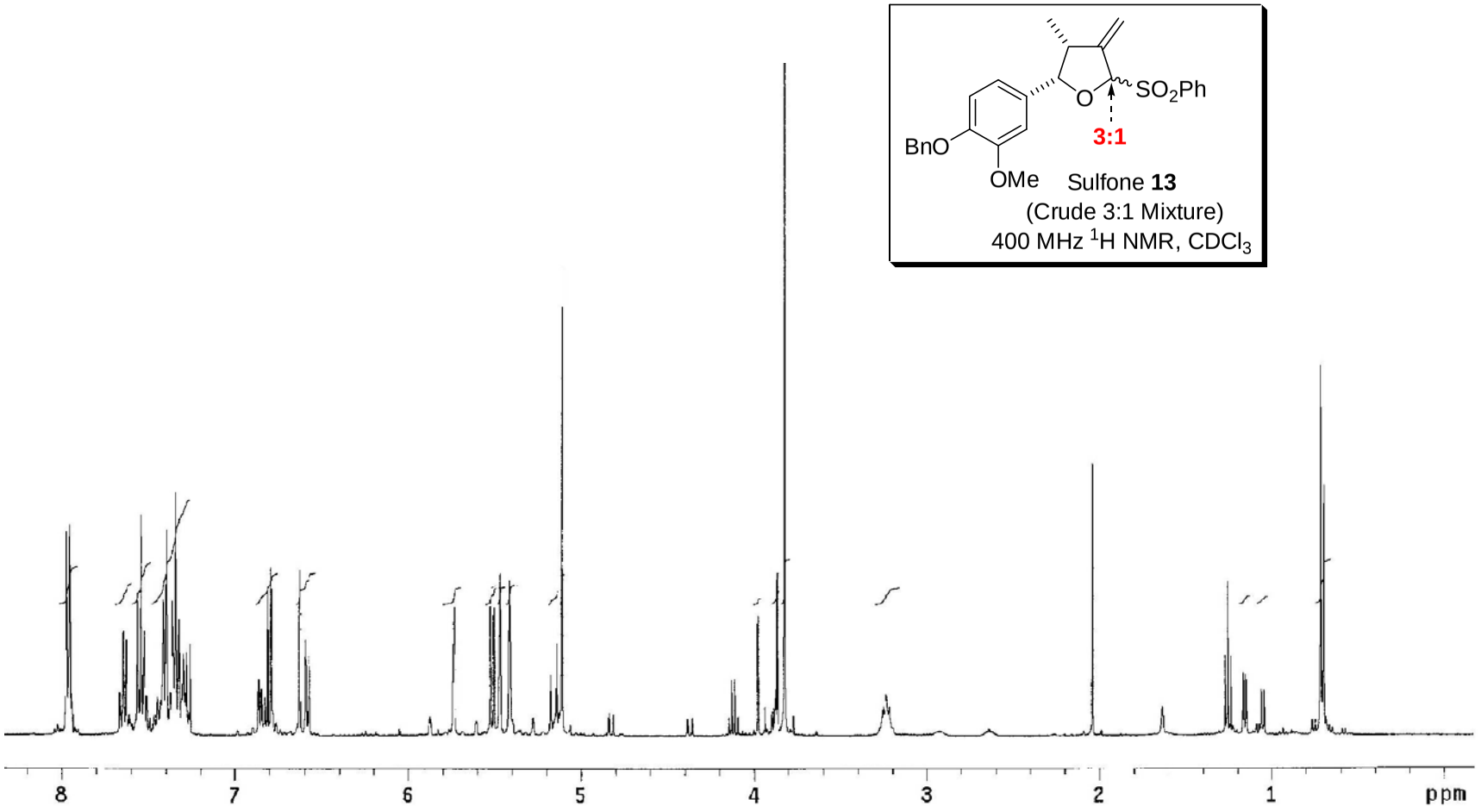
2,3-*cis*-2,5-*trans*-Tetrahydrofuran **11a**
400 MHz ^{1}H NMR, $CDCl_3$

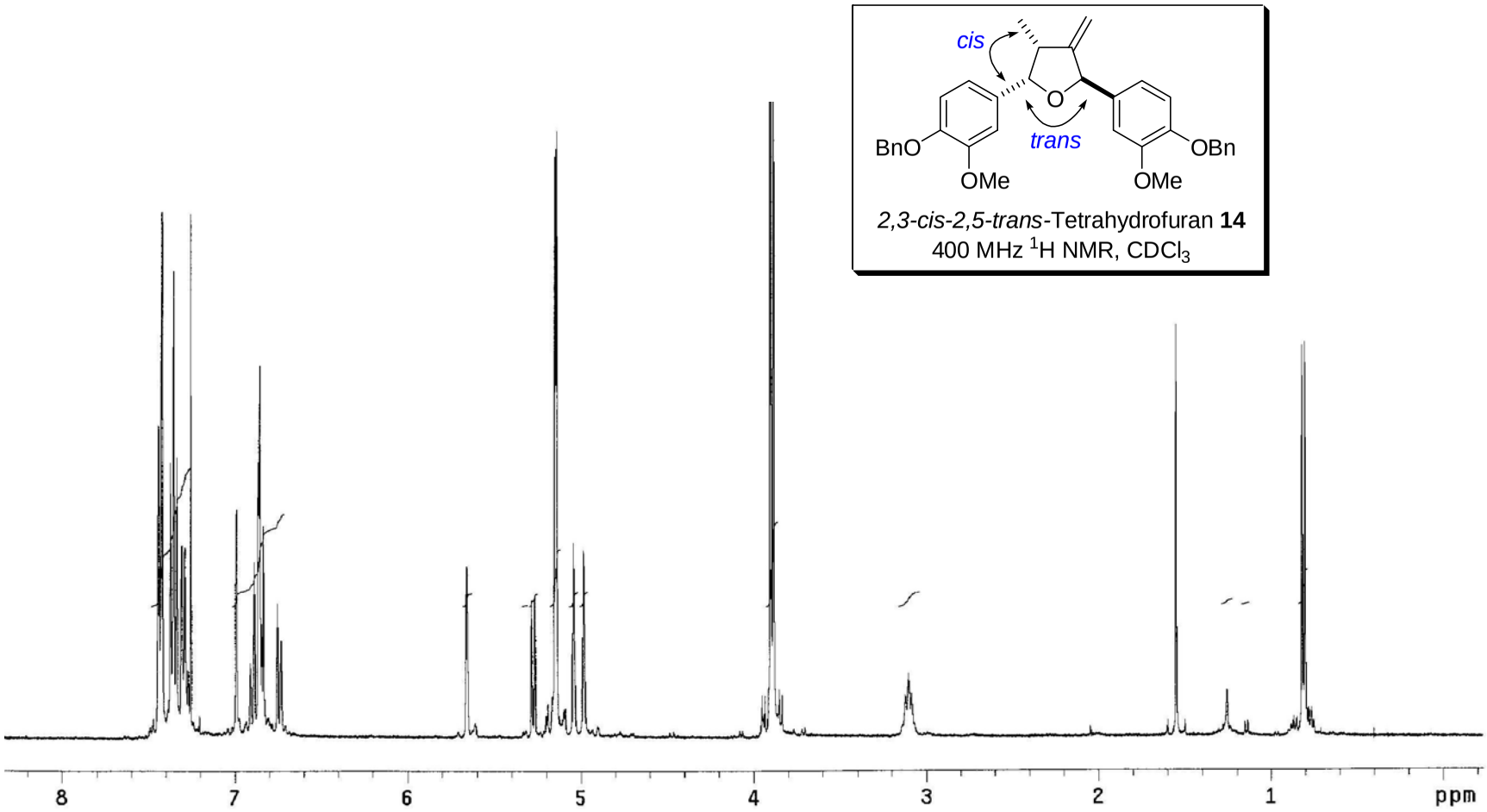

cis
trans
O
BnO
OMe
OMe
OBn
2,3-*cis*-2,5-*trans*-Tetrahydrofuran **11a**
100 MHz ^{13}C NMR, $CDCl_3$
200
180
160
140
120
100
80
60
40
20
ppm


BnO
OMe
O
O
Lactone **12**
400 MHz ^{1}H NMR, $CDCl_3$
8
7
6
5
4
3
2
1
ppm

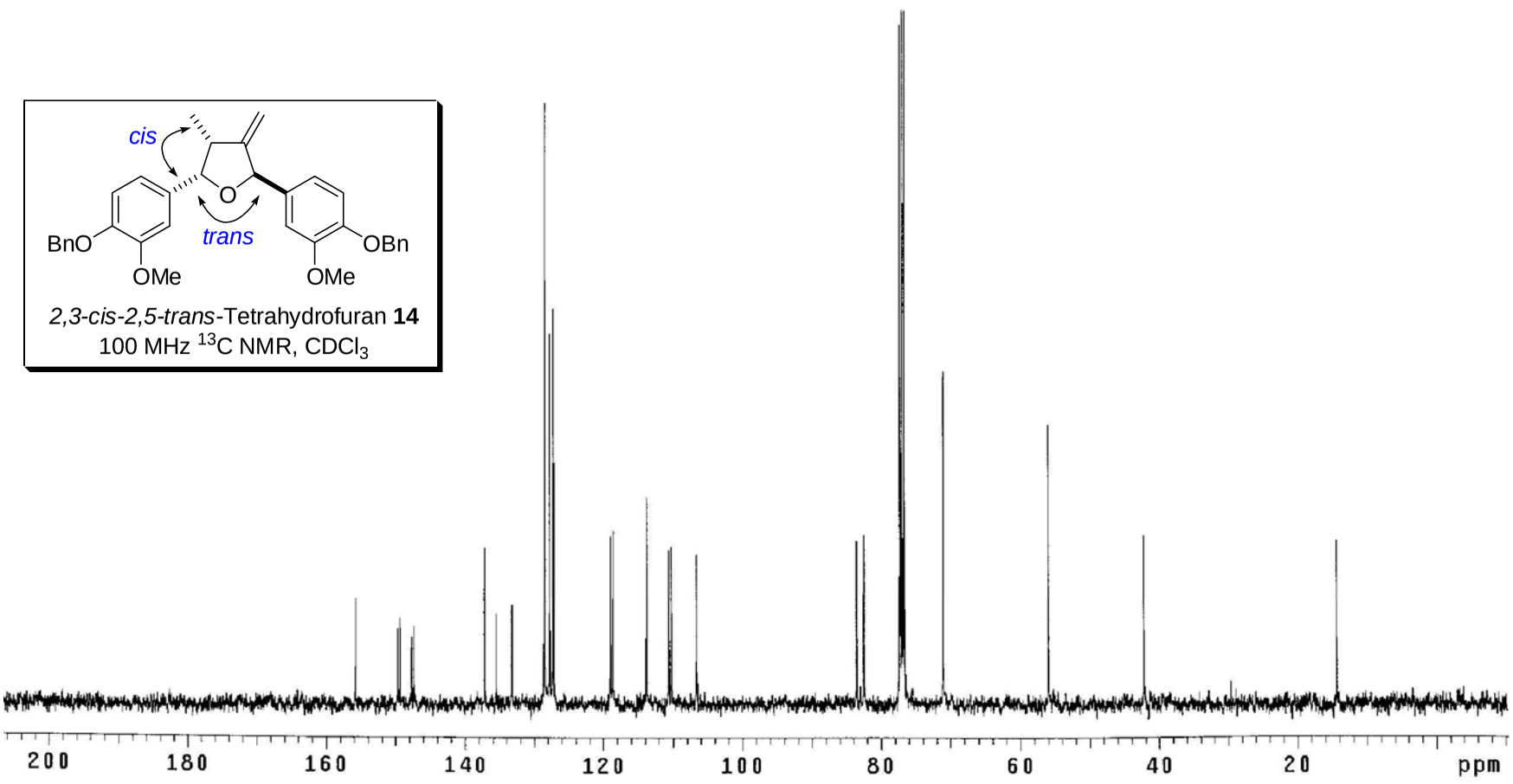

BnO
OMe
O
O
Lactone **12**
100 MHz ^{13}C NMR, $CDCl_3$
180
160
140
120
100
80
60
40
20
ppm


DIBALH
CH_2Cl_2
–78 °C, 10 min
88%
Ar
O
12
OH
[3:1]
Ar =
BnO
OMe
10
9
8
7
6
5
4
3
2
1
ppm

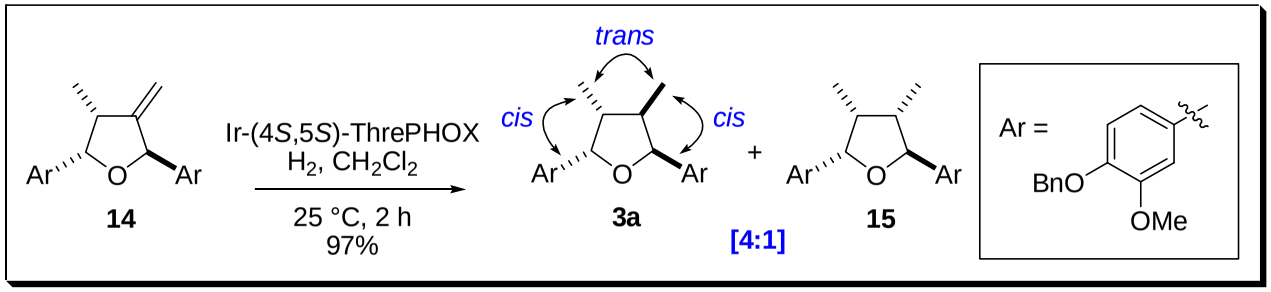

SO2Ph
O
3:1
BnO
OMe
Sulfone 13
(Crude 3:1 Mixture)
400 MHz 1H NMR, CDCl3
8
7
6
5
4
3
2
1
ppm

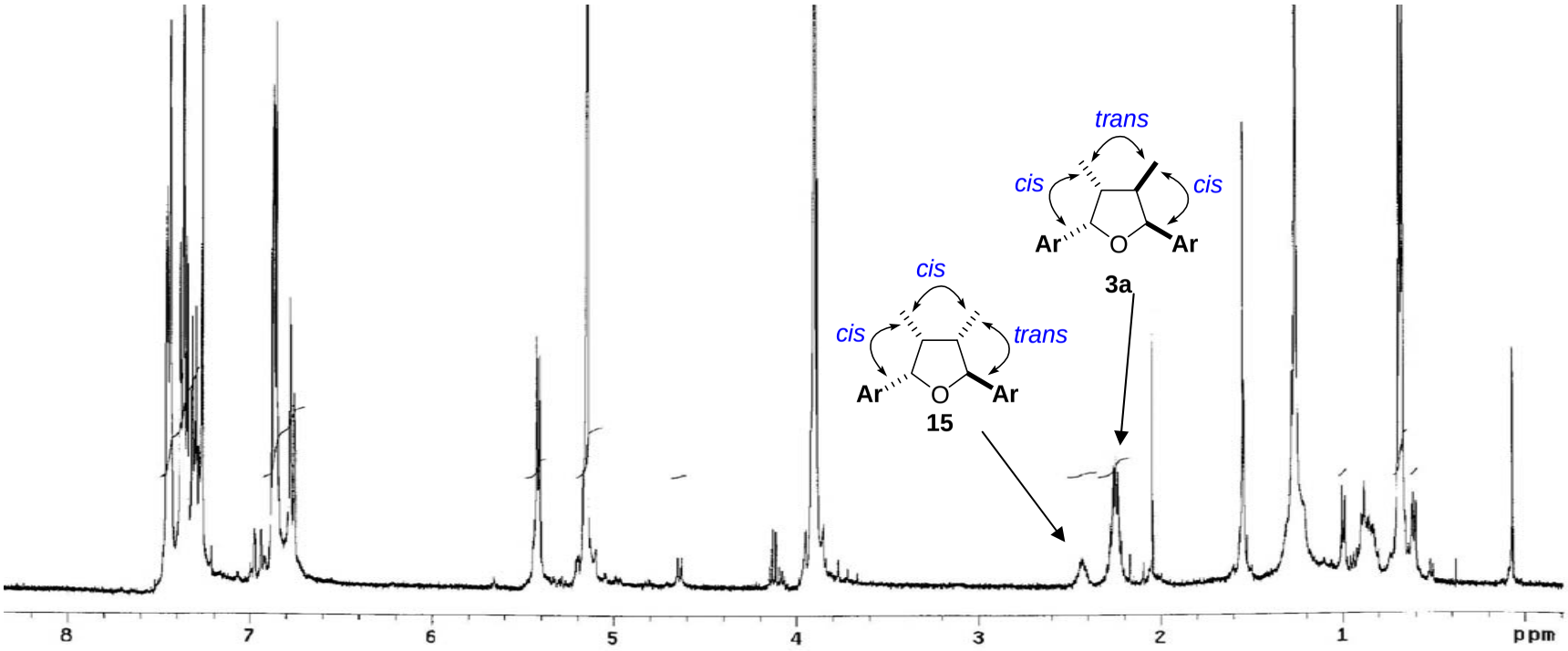


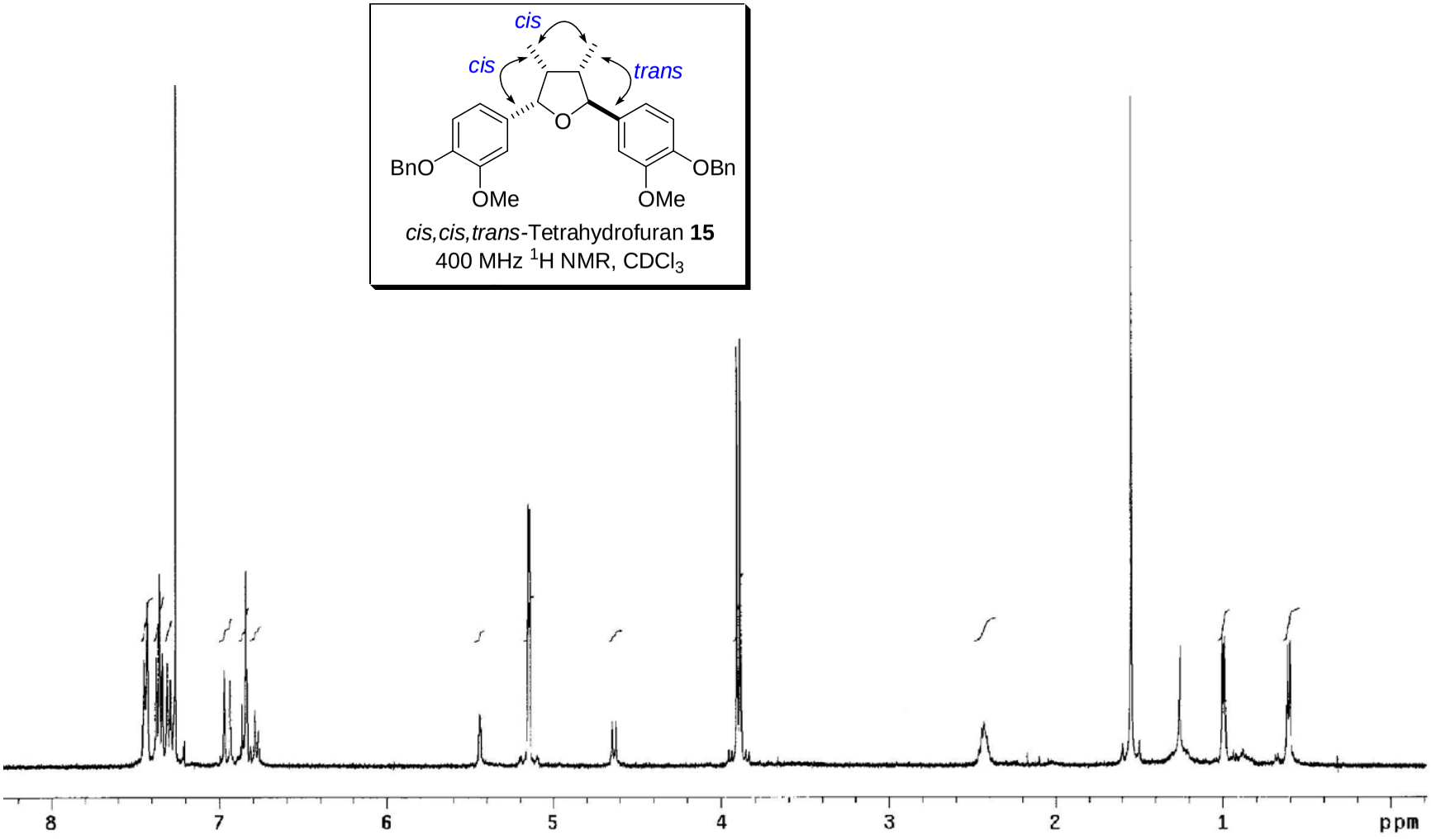
2,3-cis-2,5-trans-Tetrahydrofuran **14**
400 MHz ^{1}H NMR, $CDCl_3$



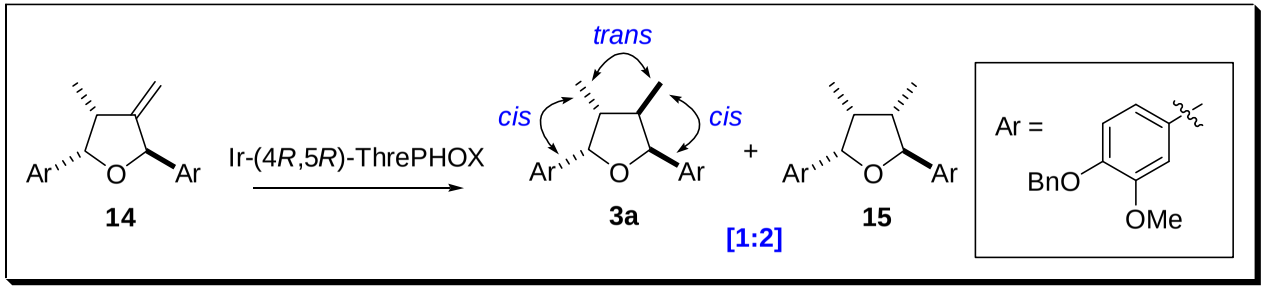
2,3-cis-2,5-trans-Tetrahydrofuran **14**
100 MHz ^{13}C NMR, $CDCl_3$

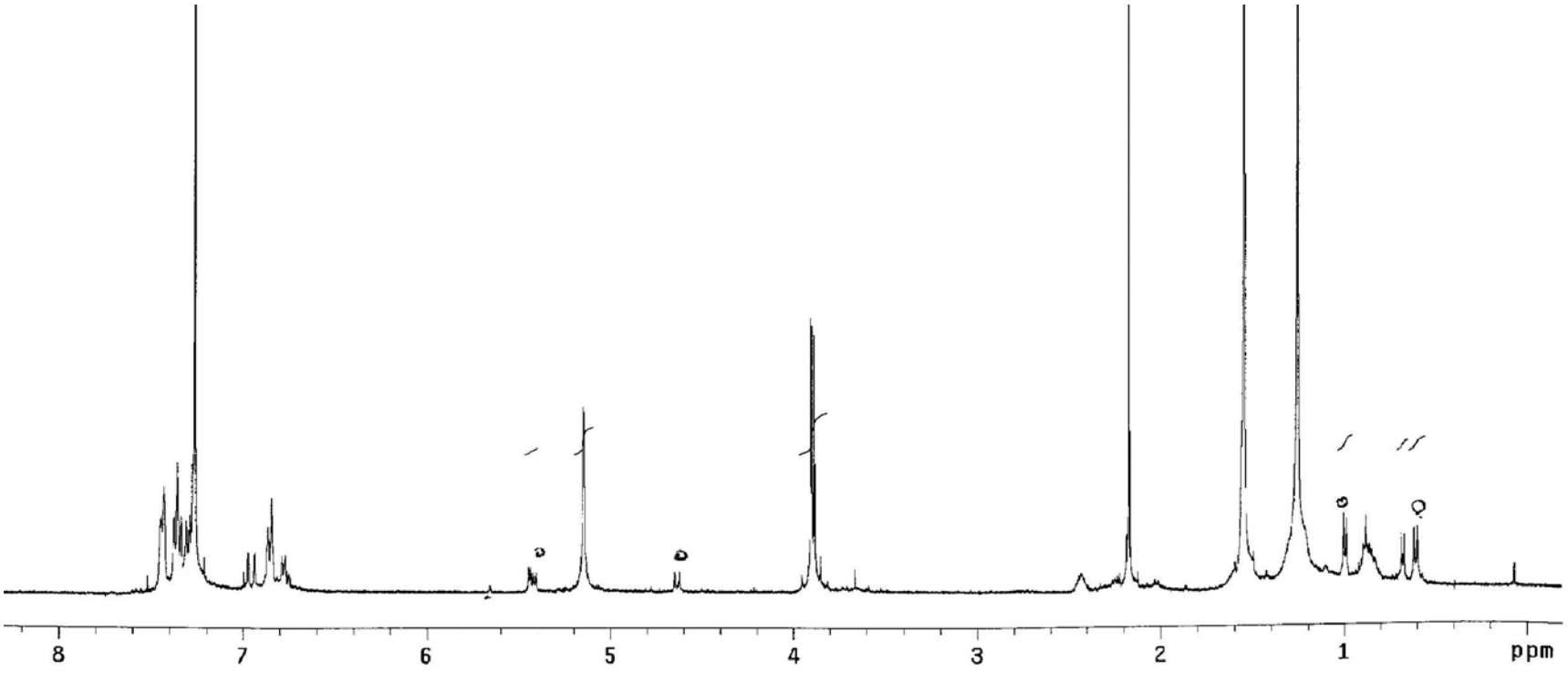

trans
cis
cis
Ar
O
Ar
14
Ir-(4S,5S)-ThrePHOX
H2, CH2Cl2
25 °C, 2 h
97%
3a
[4:1]
15
Ar =
BnO
OMe

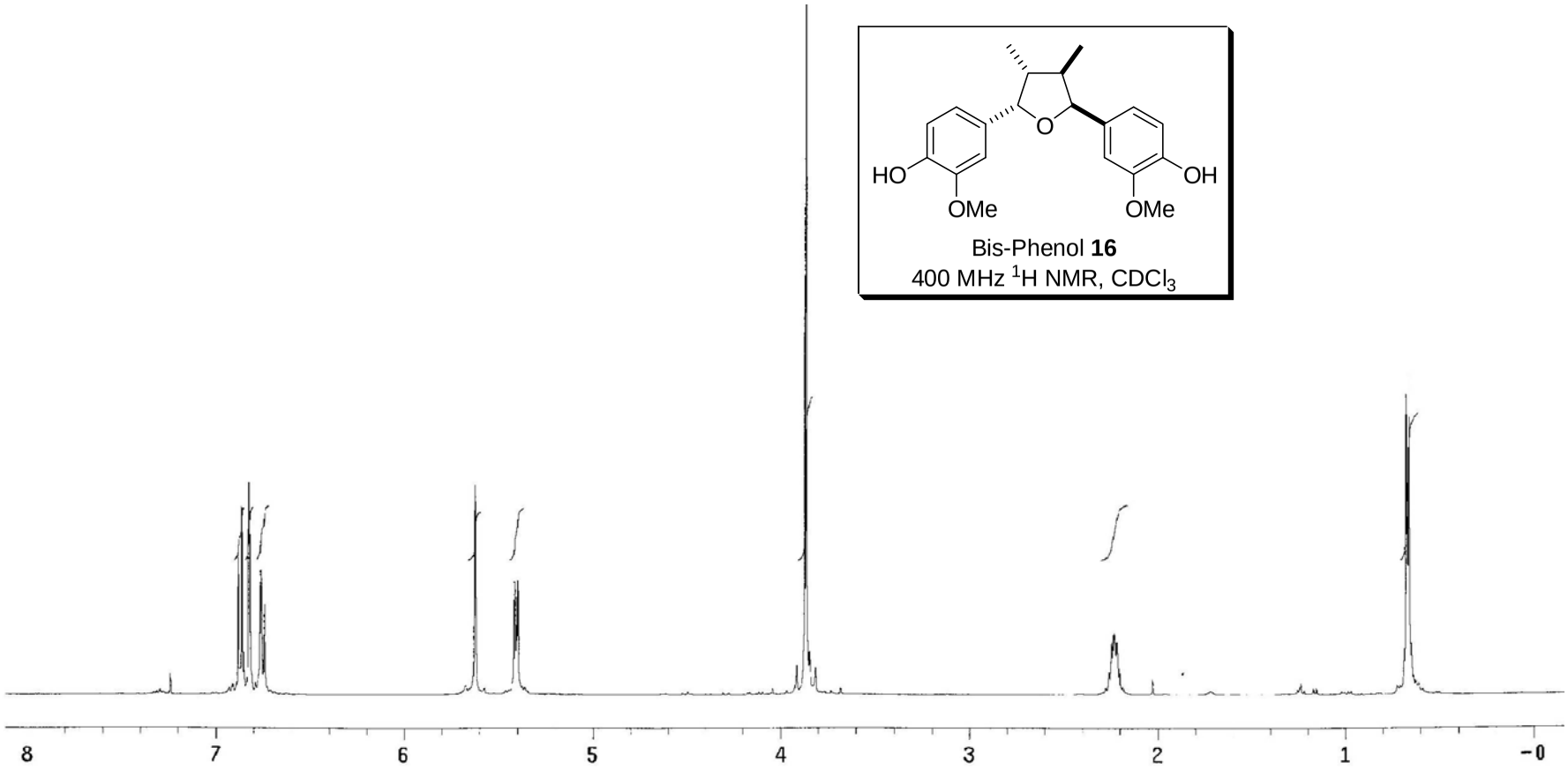

trans
cis
cis
Ar
O
Ar
3a
cis
cis
trans
15
8
7
6
5
4
3
2
1
ppm



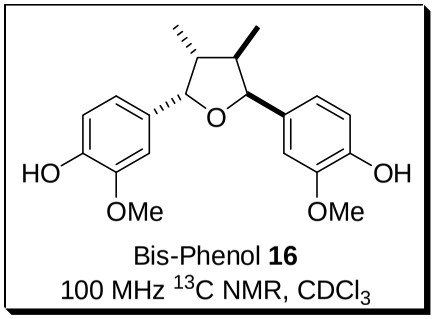
cis,cis,trans-Tetrahydrofuran **15**
400 MHz ^{1}H NMR, $CDCl_3$


trans
cis
cis
Ar
O
Ar
14
Ir-(4R,5R)-ThrePHOX
3a
+
15
[1:2]
Ar =
BnO
OMe

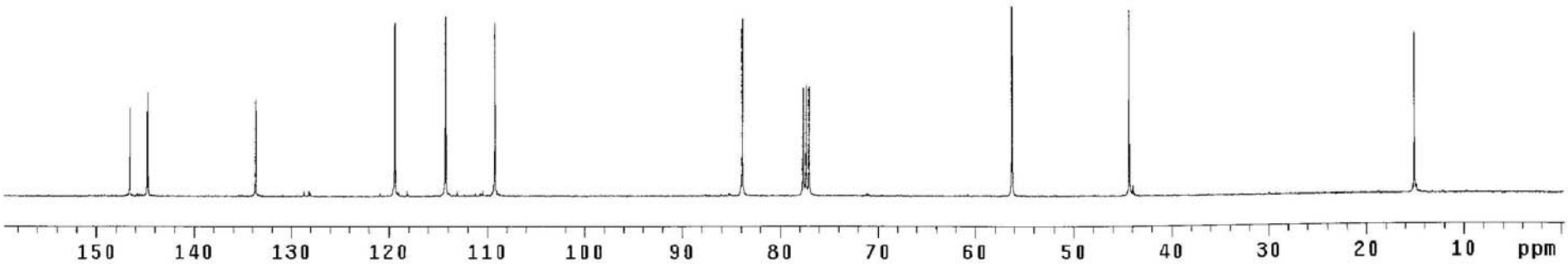

8
7
6
5
4
3
2
1
ppm

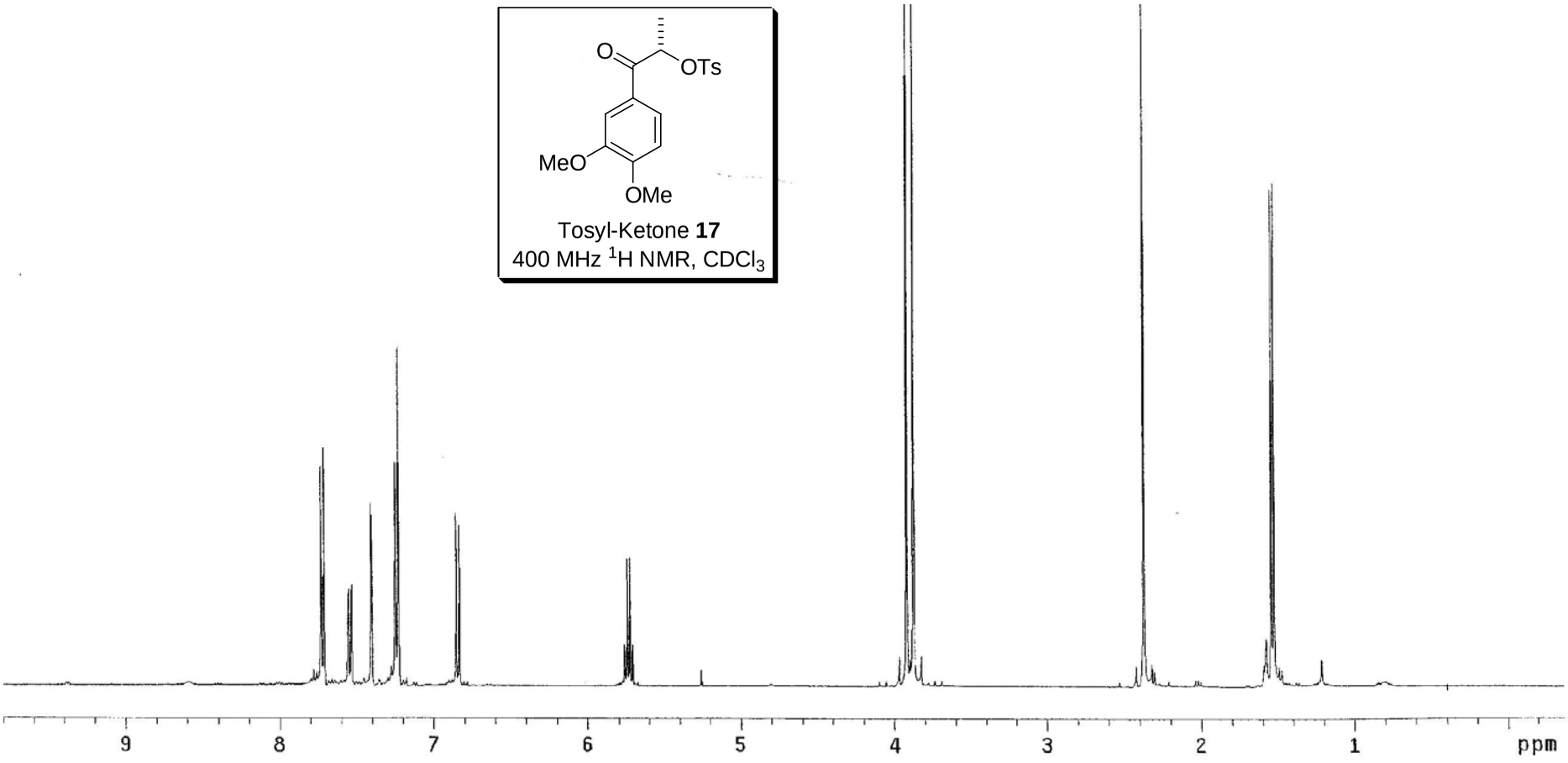


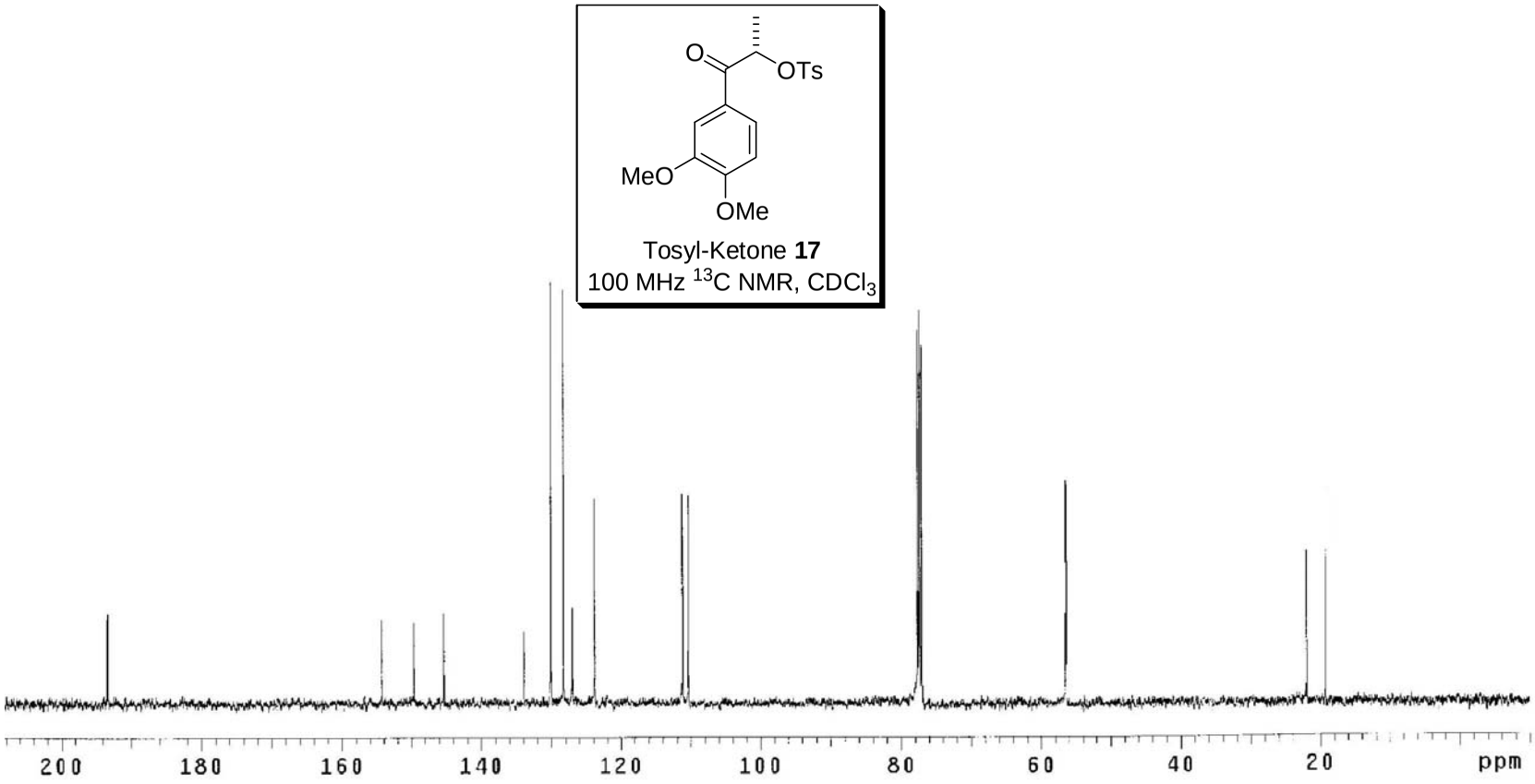
Bis-Phenol **16**
400 MHz ^{1}H NMR, $CDCl_3$

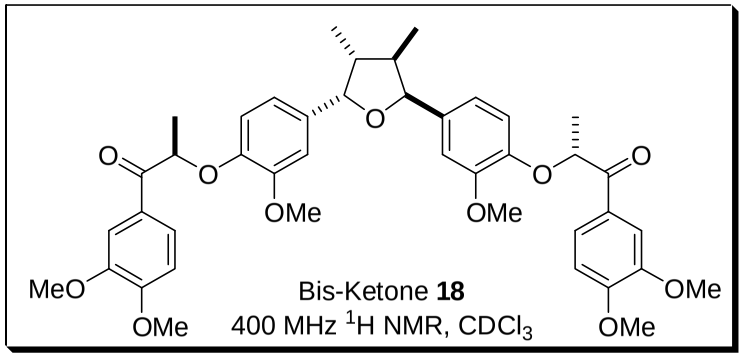


Bis-Phenol **16**
100 MHz ^{13}C NMR, $CDCl_3$

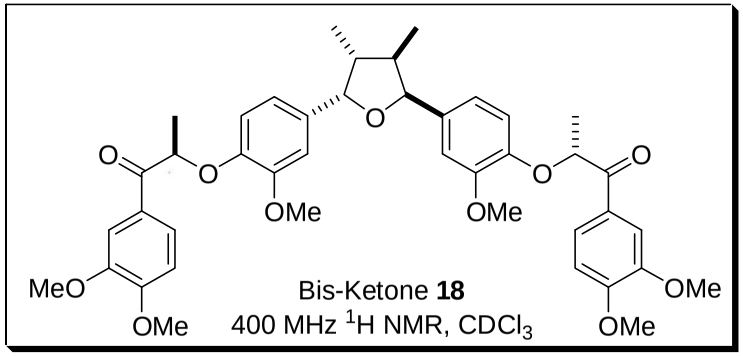



O
OTs
MeO
OMe
Tosyl-Ketone **17**
400 MHz ^{1}H NMR, $CDCl_3$
9
8
7
6
5
4
3
2
1
ppm

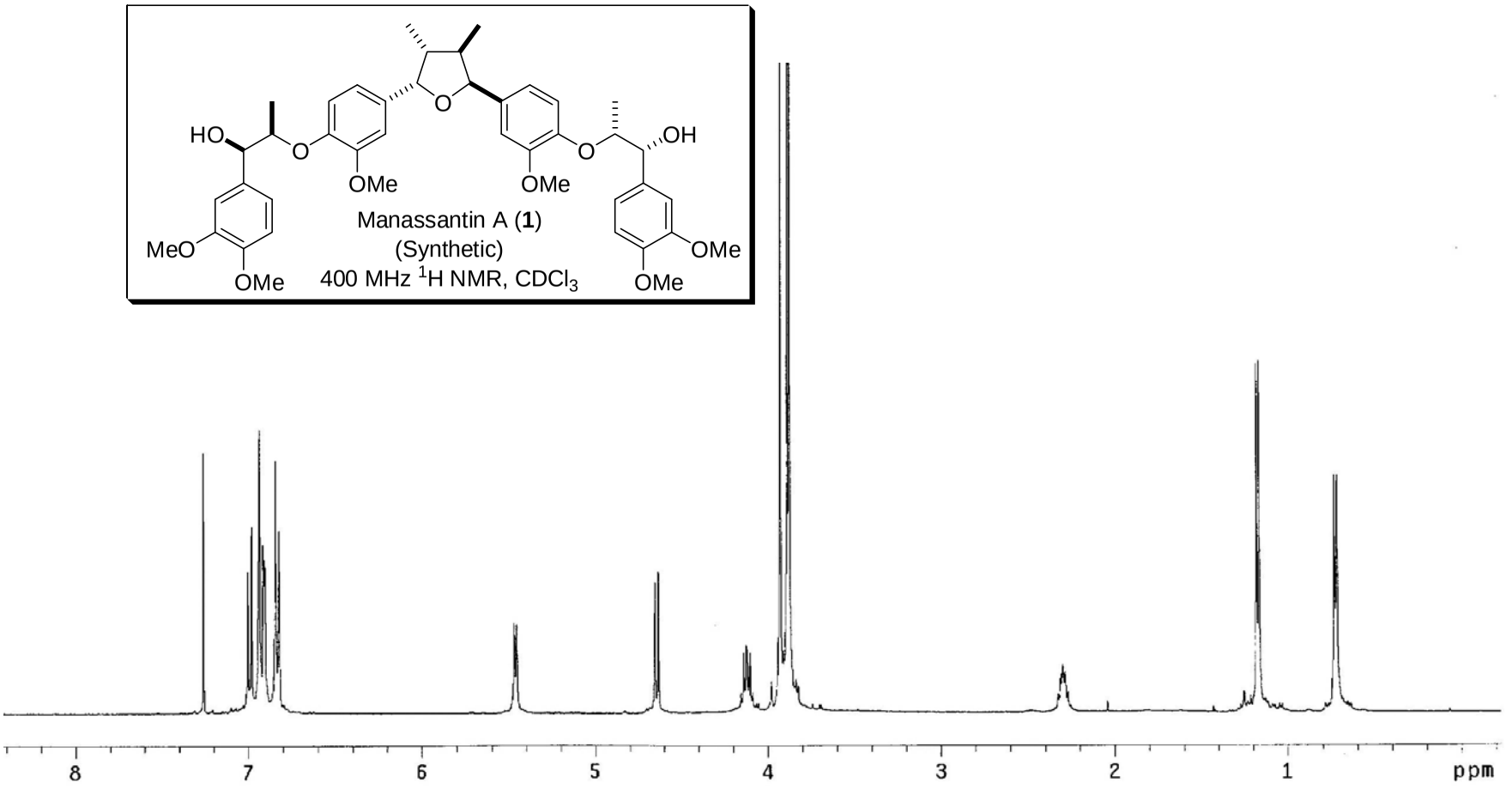

O
OTs
MeO
OMe
Tosyl-Ketone 17
100 MHz 13C NMR, CDCl3
200
180
160
140
120
100
80
60
40
20
ppm

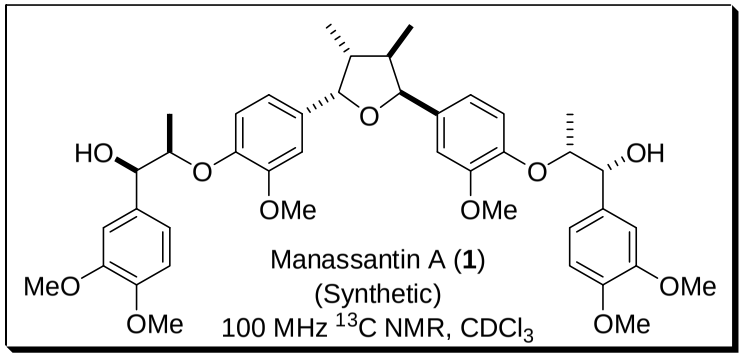


Bis-Ketone **18**
400 MHz ^{1}H NMR, $CDCl_3$

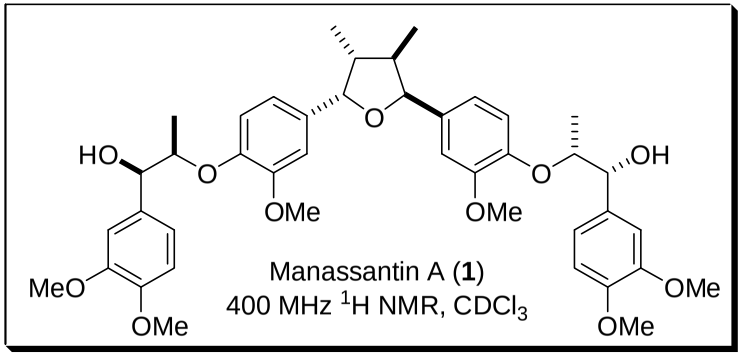


Bis-Ketone **18**
400 MHz ^{1}H NMR, $CDCl_3$


HO
O
OMe
O
OMe
OH
MeO
OMe
OMe
OMe
Manassantin A (1)
(Synthetic)
400 MHz 1H NMR, CDCl3
8
7
6
5
4
3
2
1
ppm

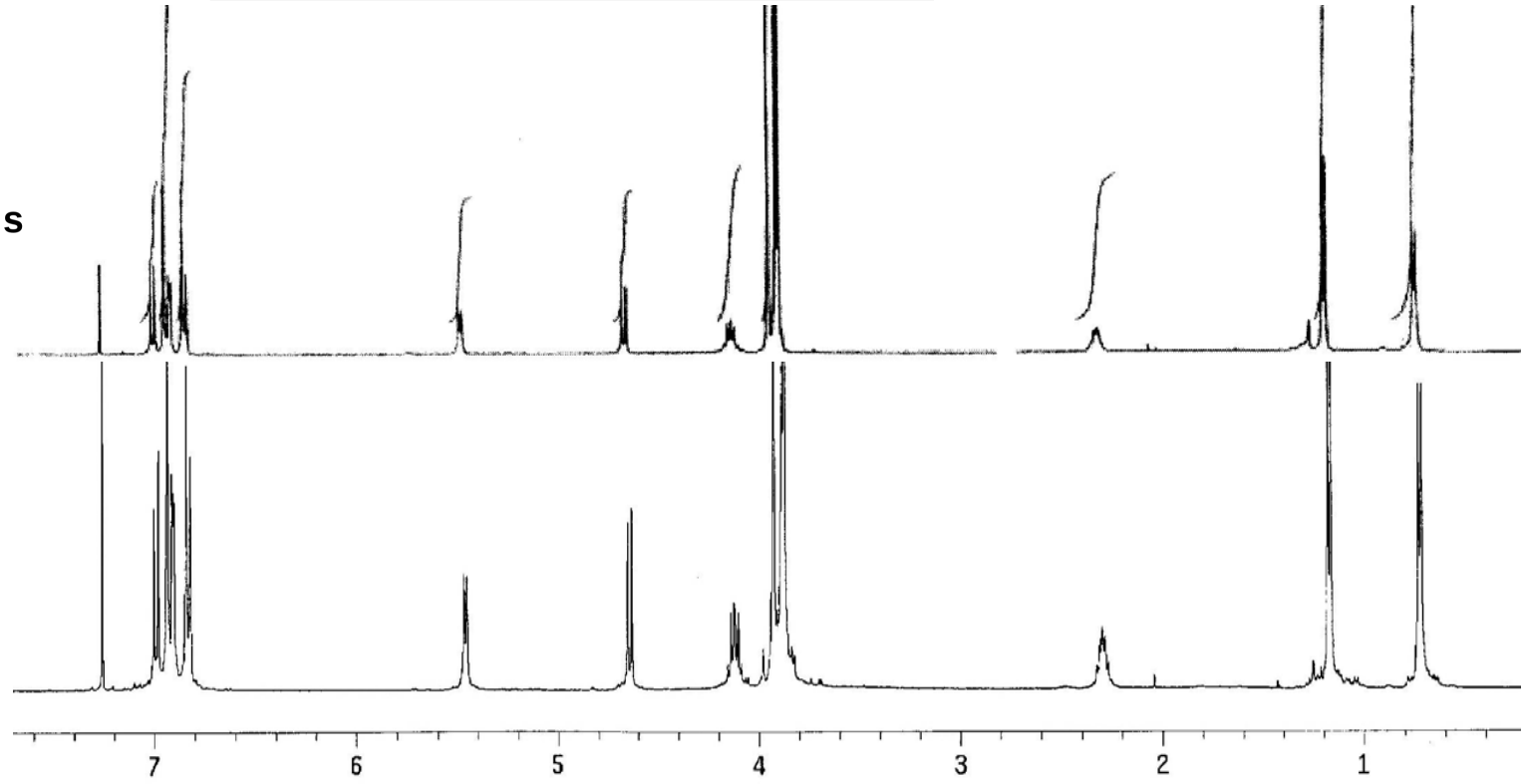

HO
O
OMe
O
O
OMe
OH
MeO
OMe
OMe
OMe
Manassantin A (1)
(Synthetic)
100 MHz 13C NMR, CDCl3

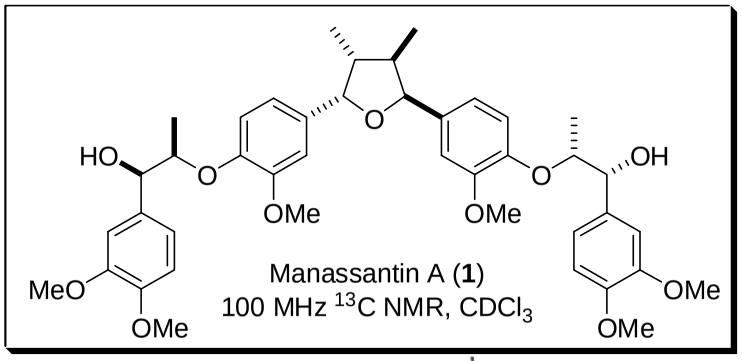
180
160
140
120
100
80
60
40
20
ppm



Hanessian's Synthetic

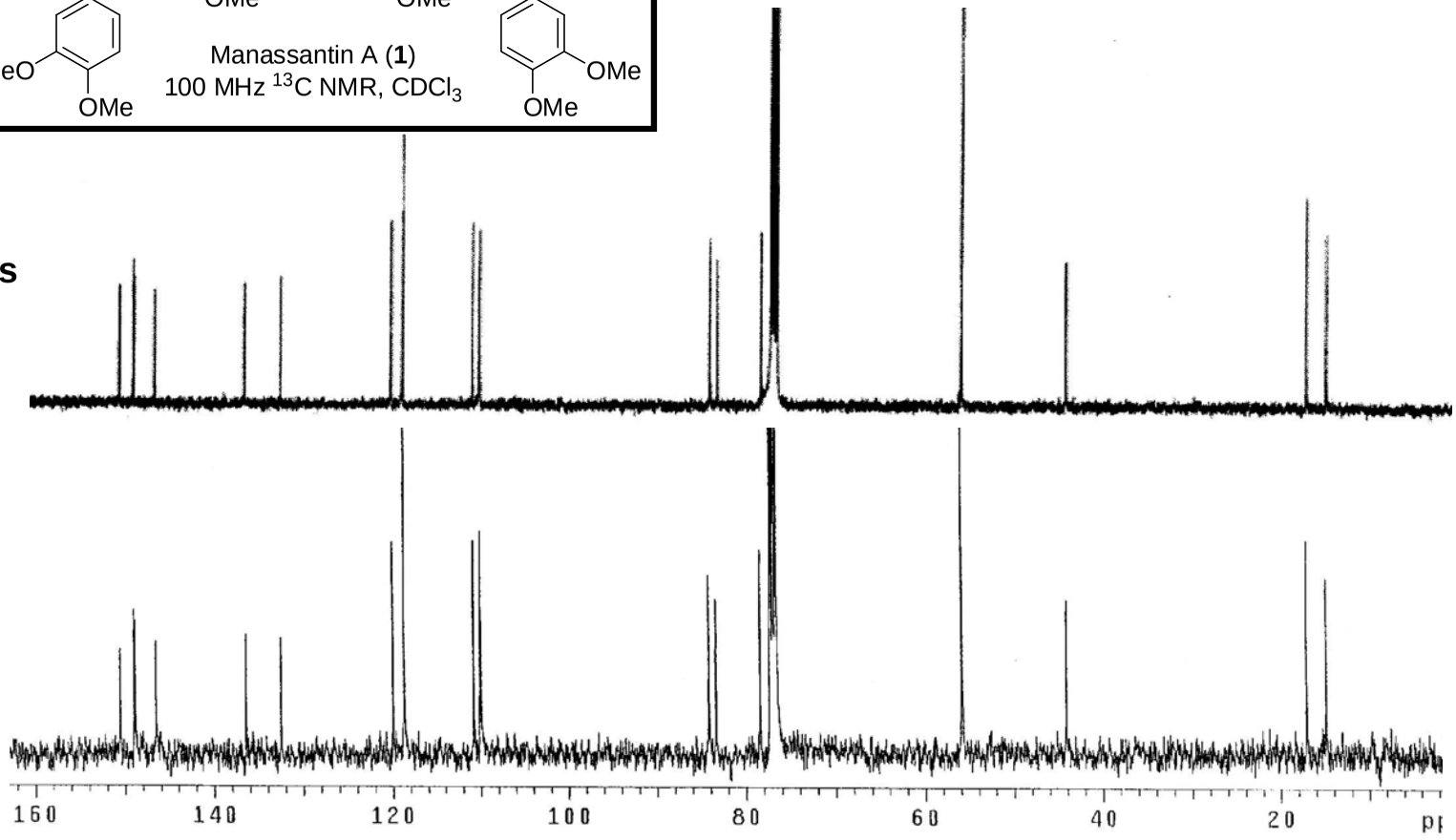
Hong's Synthetic

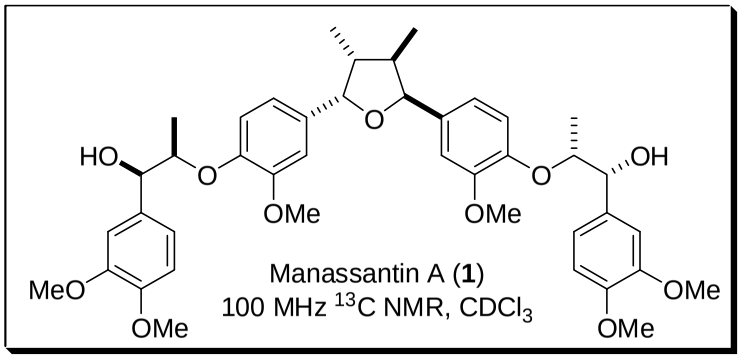




Hanessian's Synthetic

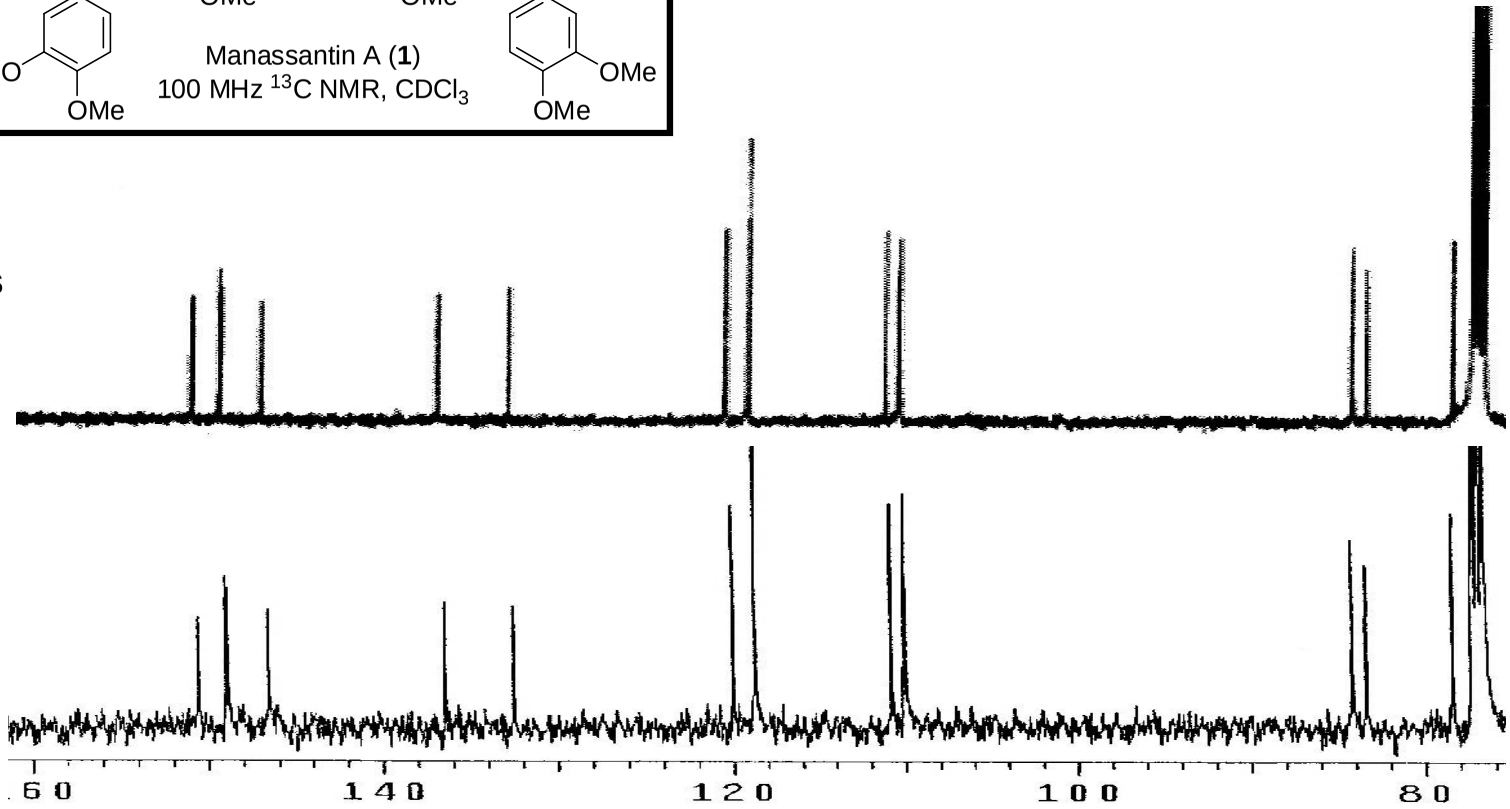
Hong's Synthetic

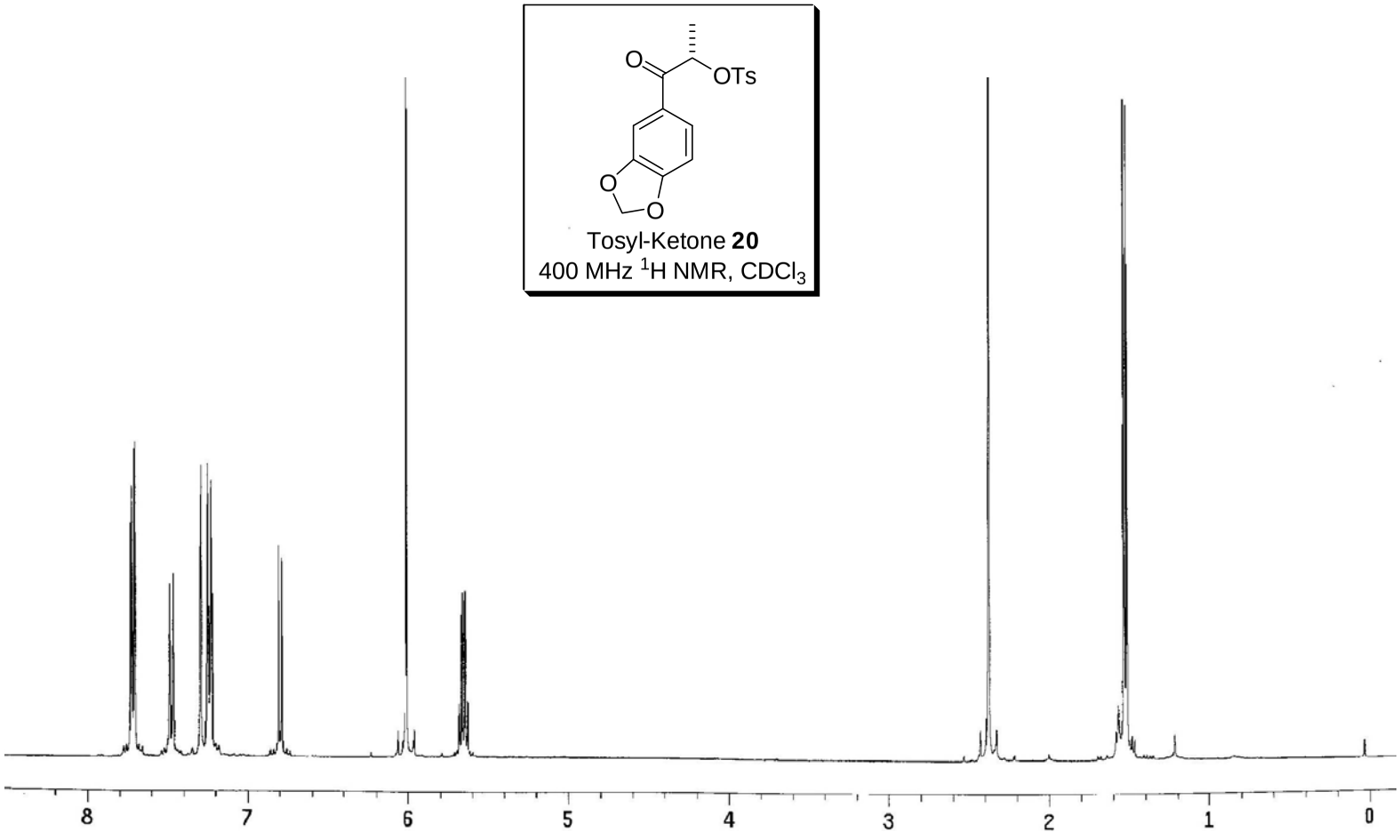


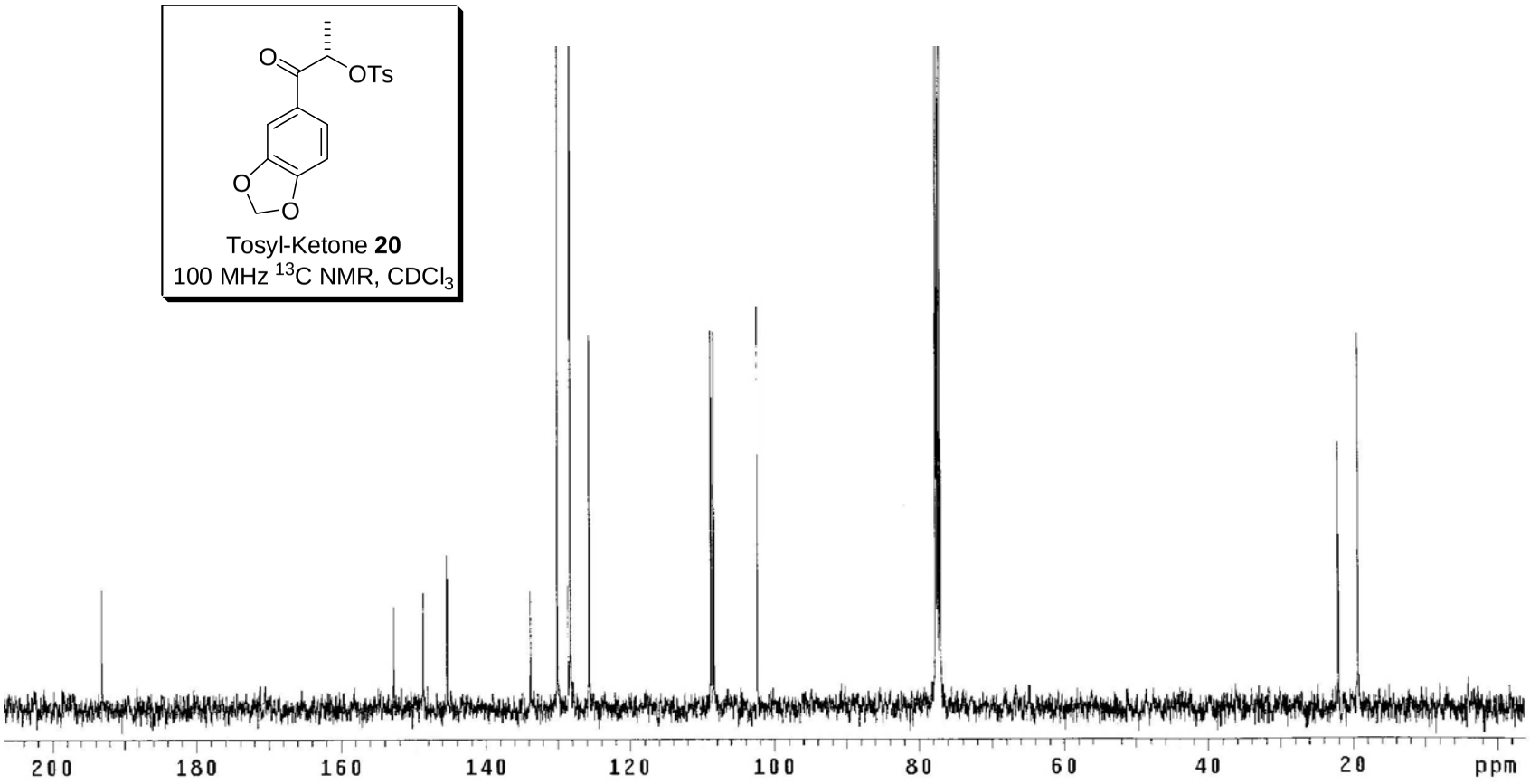


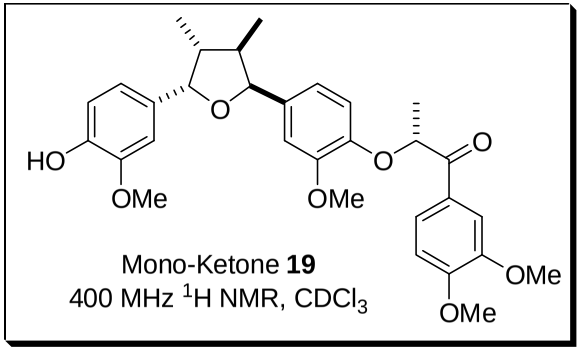
Hanessian's Synthetic

Hong's Synthetic

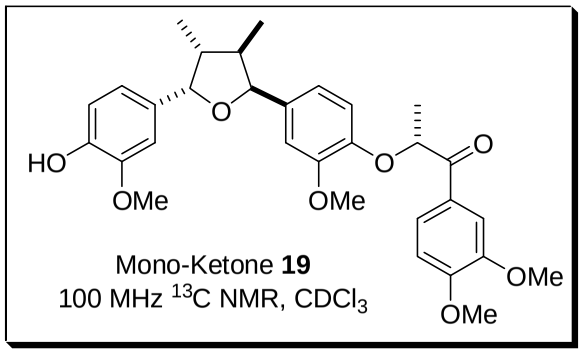



O
OTs
O
O
Tosyl-Ketone **20**
400 MHz ^{1}H NMR, $CDCl_3$
8
7
6
5
4
3
2
1
0

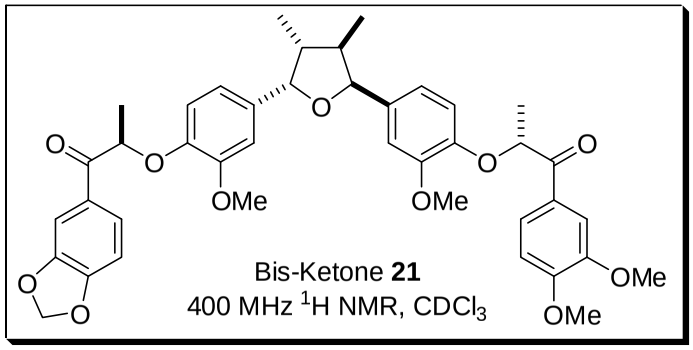

O
OTs
O
O
Tosyl-Ketone **20**
100 MHz ^{13}C NMR, $CDCl_3$
200
180
160
140
120
100
80
60
40
20
ppm



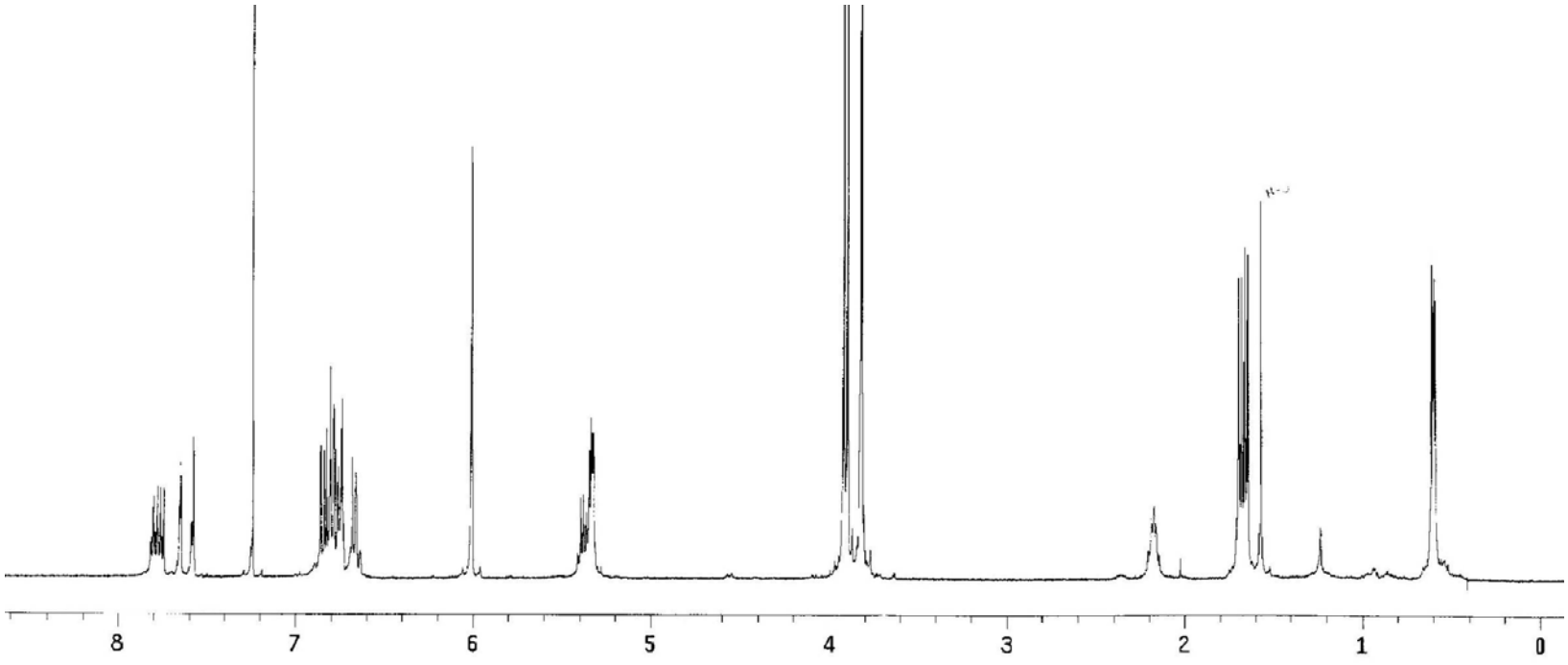
Mono-Ketone **19**
400 MHz ^{1}H NMR, $CDCl_3$

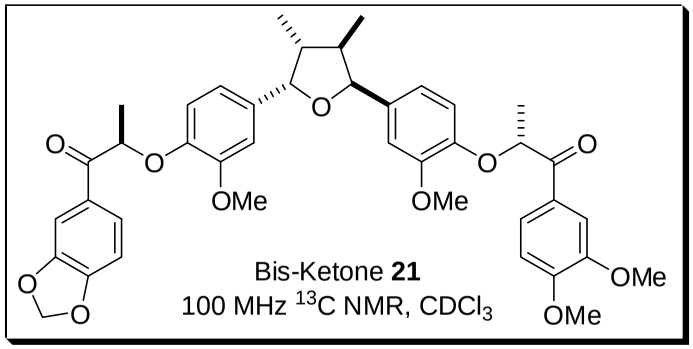


Mono-Ketone **19**
100 MHz ^{13}C NMR, $CDCl_3$

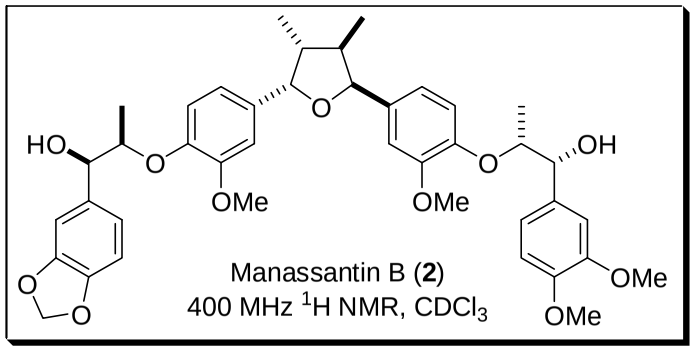


Bis-Ketone **21**
400 MHz ^{1}H NMR, $CDCl_3$

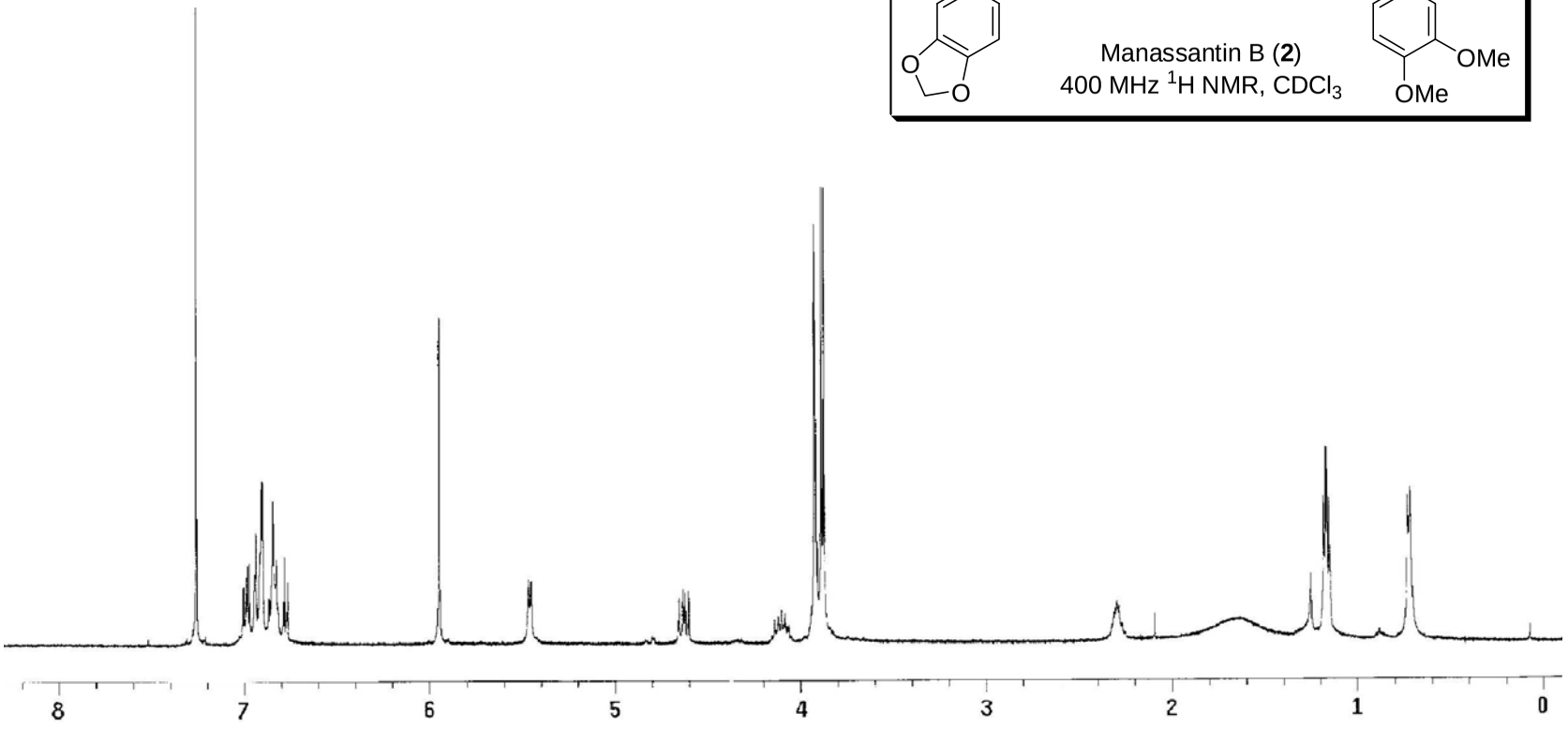


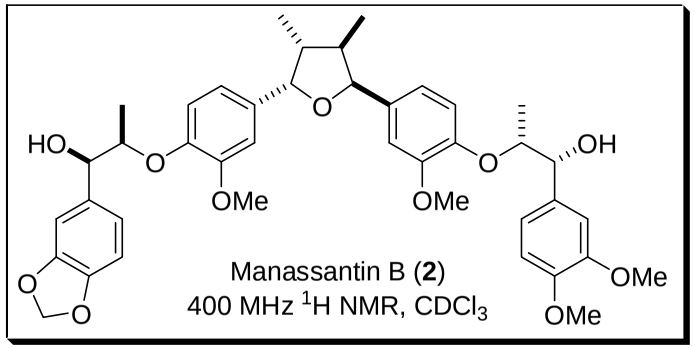

O
O
O
O
O
O
OMe
OMe
OMe
OMe
Bis-Ketone **21**
100 MHz ^{13}C NMR, $CDCl_3$

200
180
160
140
120
100
80
60
40
20
ppm



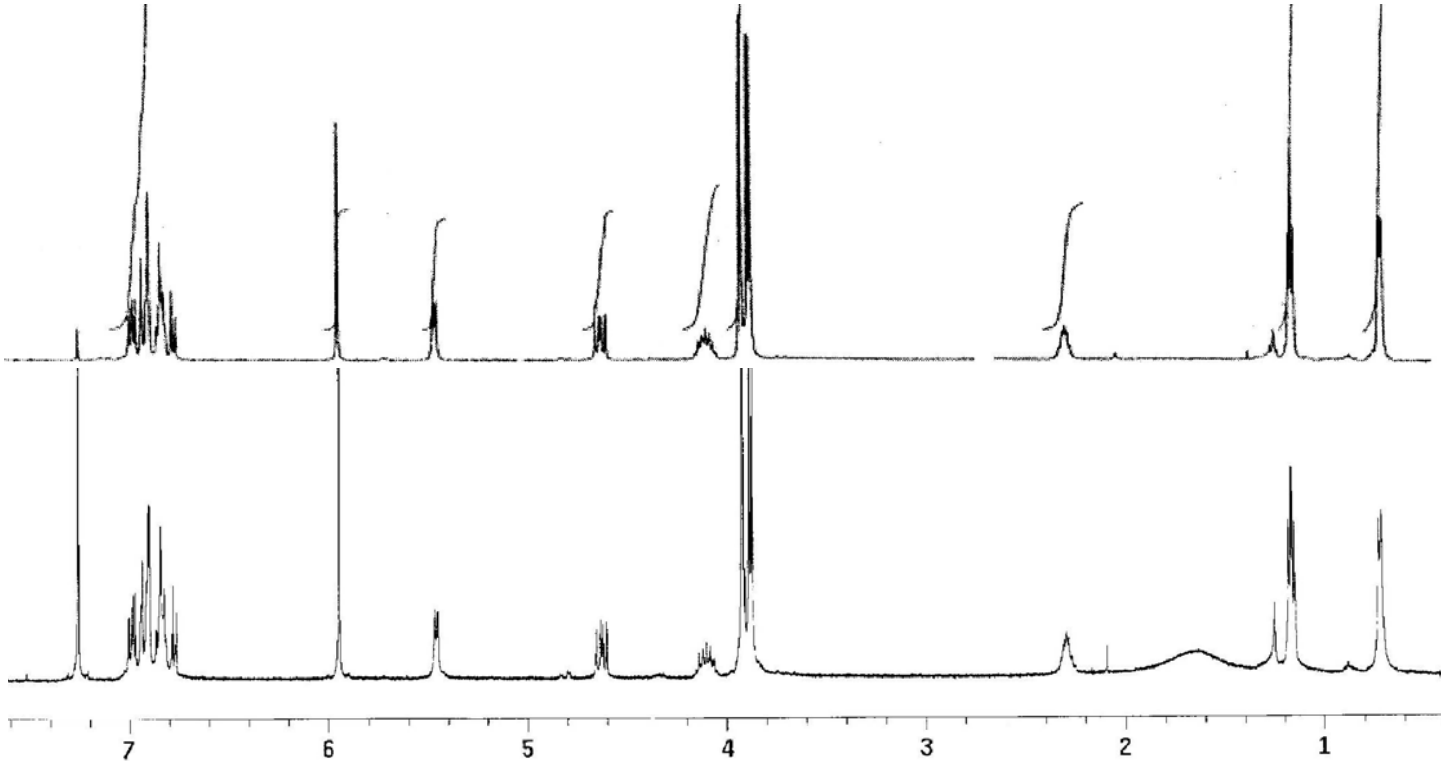
Manassantin B (**2**)
400 MHz ^{1}H NMR, $CDCl_3$

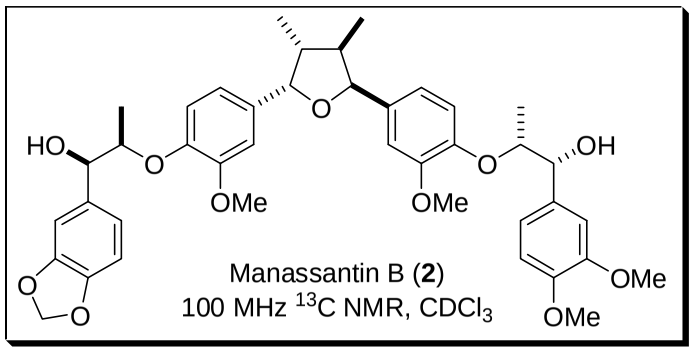




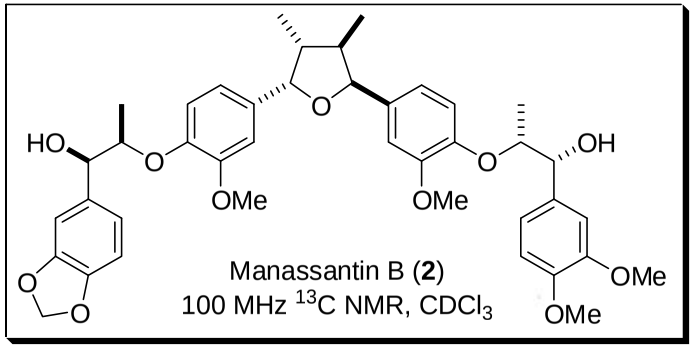
Hanessian's Synthetic

Hong's Synthetic



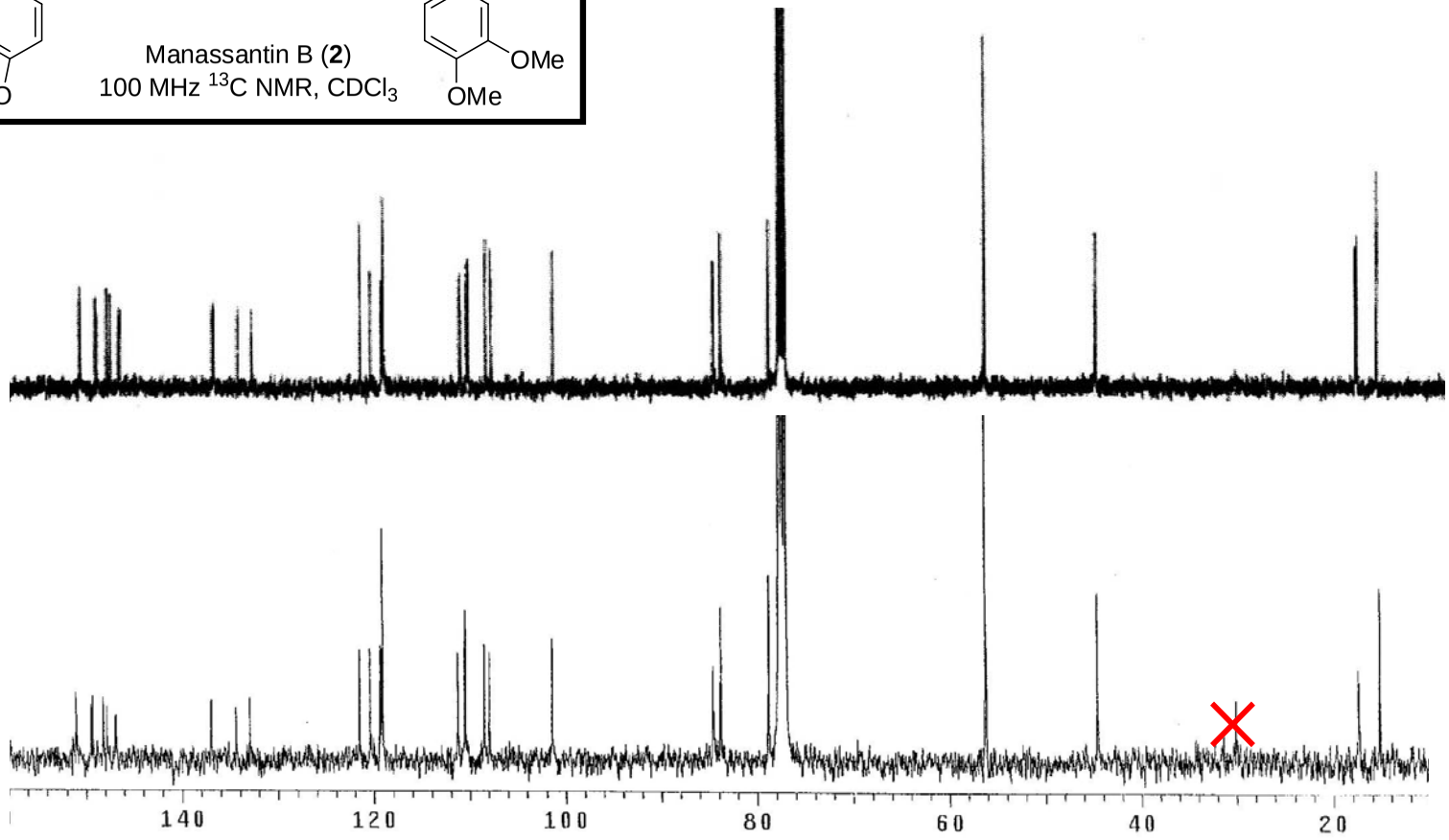

HO
O
OMe
O
OMe
O
OH
O
O
OMe
OMe
Manassantin B (2)
100 MHz 13C NMR, CDCl3

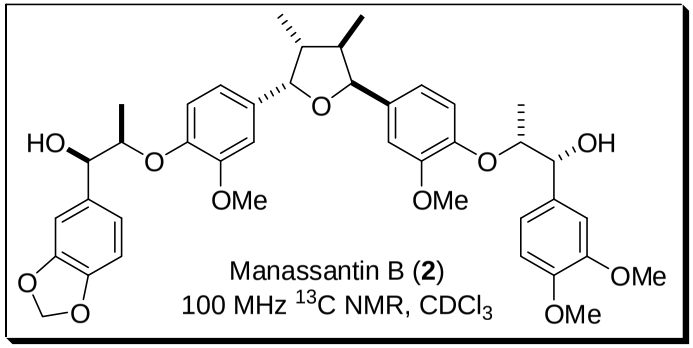
180
160
140
120
100
80
60
40
20
ppm



Hanessian's Synthetic

Hong's Synthetic





Hanessian's Synthetic

Hong's Synthetic