

Supporting Information
for
Phosphazene-catalyzed desymmetrization of cyclohexadienones
by dithiane addition

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**Experimental procedures, characterization data and copies of
¹H and ¹³C NMR spectra for final compounds**

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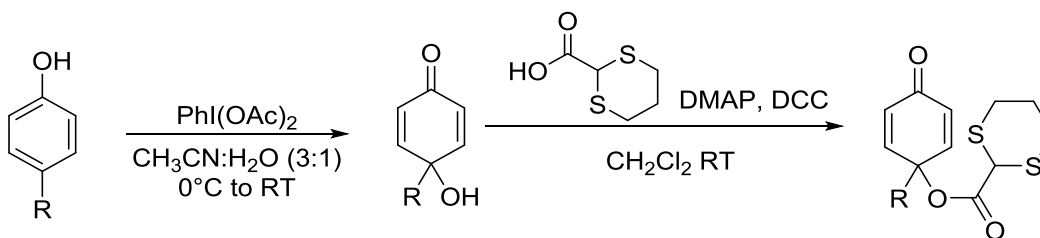
General information:

Methods: Infrared (IR) spectra were obtained using an ASI ReactIR 1000 Fourier transform infrared spectrometer. Proton and carbon magnetic resonance spectra (^1H NMR, ^{13}C NMR, ^{19}F NMR and ^{31}P NMR) were recorded on a Bruker model DRX 400 or 600 (^1H NMR at 400 MHz or 600 MHz, ^{13}C NMR at 101 MHz or 151 MHz, or a Bruker AVANCE III-OneBay500 (^{13}C NMR at 235 MHz) spectrometer with solvent resonance as the internal standard (^1H NMR: CDCl_3 at 7.26 ppm and ^{13}C NMR: CDCl_3 at 77.0 ppm). ^1H NMR data are reported as follows: chemical shift, multiplicity (s = singlet, br-s = broad singlet, d = doublet, dd = doublet of doublet, t = triplet, td = triplet of doublet, m = multiplet), coupling constants (Hz), and integration. High resolution mass spectra were obtained with a Thermo Fisher Scientific Exactive or FinniganTM LTQ-ICR FTTM (all samples prepared in methanol). Melting points were obtained using a Thomas Hoover UniMelt Capillary Melting Point Apparatus. Analytical thin layer chromatography was carried out using Whatman 0.25 mm silica gel 60 plates, Sorbent Technologies 0.20 mm Silica Gel TLC plates. Visualization was allowed by UV light, phosphomolybdic acid in ethanol, or aqueous ceric ammonium nitrate solution. Purification of the reaction products was carried out by using Siliacflash-P60 silica gel (40–63 μm) purchased from Silicycle. Yields refer to isolated yields after flash column chromatography. Since all results are the averages of two trials, the yields listed in the paper may not exactly match those listed below.

Materials: THF and DCM were purified by passing the solvent through a column of aluminum oxide under nitrogen. Dearomatization of phenol derivatives was carried out according to literature procedures.¹ 1,3-Dithiane-2-carboxylic acid was prepared according to literature procedure.² Phosphazene base P_2 -*t*-Bu solution (~2.0 M in THF) and DMAP were purchased from Sigma-Aldrich and used as received. (Diacetoxyiodo)benzene, [bis(trifluoroacetoxy)iodo]benzene, and DCC were purchased from Oakwood Chemical and used as received.

General procedure for substrate synthesis:

The substrates were prepared through a two-step synthesis on gram scale.



STEP 1 – Dearomatization of phenols¹

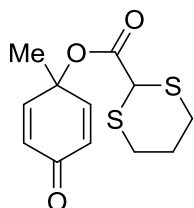
The phenol (1 equiv) was dissolved in MeCN (3 mL for 1 mmol) and H_2O (1 mL for 1 mmol); the solution was cooled to 0°C and $\text{PhI}(\text{OAc})_2$ (1.1 equiv) was slowly added as a solid. The reaction mixture was allowed stirred at ambient temperature for 18 h. The mixture was diluted with EtOAc and washed with water and brine. The combined organic phases were dried over Na_2SO_4 and the solvent was removed under reduced pressure. The crude materials thusly obtained were purified using flash column chromatography on silica gel.

STEP 2 – DCC coupling between *para*-quinols and 1,3-dithiane-2-carboxylic acid

The desired *p*-quinols (1 equiv) and 1,3-dithiane-2-carboxylic acid (1.5 equiv) were dissolved in CH_2Cl_2 ($[\text{quinol}]_0 = 1.0\text{ M}$); 4-dimethylaminopyridine (DMAP) (1 equiv) was then added to the mixture. The reaction mixture was cooled to 0°C and *N,N'*-dicyclohexylcarbodiimide (DCC) (1.1 equiv) was added. The reaction mixture was allowed to warm to rt and stirred for 18 h. After that period, the mixture was filtered through a short plug of silica gel and washed with CH_2Cl_2 . The solvent was removed under reduced pressure. The crude materials thusly obtained were purified using flash column chromatography on silica gel.

Characterization of substrates:

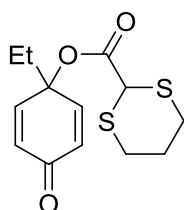
1-Methyl-4-oxocyclohexa-2,5-dien-1-yl 1,3-dithiane-2-carboxylate (1a):



The title compound was obtained in 61% yield.

White solid, mp 88-90 °C; $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 6.96 (d, J = 10.2 Hz, 2H), 6.31 (d, J = 10.2 Hz, 2H), 4.12 (s, 1H), 3.43-3.39 (m, 2H), 2.61-2.57 (m, 2H), 2.19-2.14 (m, 1H), 2.06-1.99 (m, 1H), 1.62 (s, 3H); $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 184.8, 168.3, 148.6, 128.5, 75.3, 39.0, 26.4, 25.5, 24.8; **IR** (thin film) ν 2931, 1735, 1667, 1631, 1608, 1393, 1285, 1138, 1052, 857 cm^{-1} ; **HRMS** (ESI): Calcd. For $\text{C}_{12}\text{H}_{14}\text{NaO}_3\text{S}_2^+$ ($[\text{M}+\text{Na}^+]$): 293.0277, found 293.0275; **TLC** (1:4 EtOAc/hexanes): R_f = 0.33.

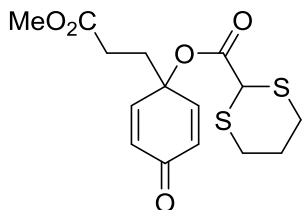
1-Ethyl-4-oxocyclohexa-2,5-dien-1-yl 1,3-dithiane-2-carboxylate (1b):



The title compound was obtained in 49% yield.

Yellow oil; $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 6.88 (d, J = 10.2 Hz, 2H), 6.36 (d, J = 10.2 Hz, 2H), 4.14 (s, 1H), 3.40 (ddd, J = 14.3, 12.2, 2.5 Hz, 1H), 2.60-2.57 (m, 1H), 2.18-2.14 (m, 1H), 2.06-1.99 (m, 1H), 1.94 (q, J = 7.5 Hz, 1H), 0.94 (t, J = 7.5 Hz, 2H). $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 185.1, 168.3, 147.6, 129.6, 78.4, 39.2, 32.2, 25.5, 24.8, 7.7; **IR** (thin film) ν 2935, 1736, 1667, 1631, 1282, 1138, 1063, 995, 915, 853 cm^{-1} ; **HRMS** (ESI): Calcd. For $\text{C}_{13}\text{H}_{16}\text{NaO}_3\text{S}_2^+$ ($[\text{M}+\text{Na}^+]$): 307.0433, found 307.0428; **TLC** (1:4 EtOAc/hexanes): R_f = 0.38.

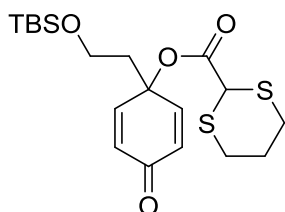
1-(3-Methoxy-3-oxopropyl)-4-oxocyclohexa-2,5-dien-1-yl 1,3-dithiane-2-carboxylate (1c):



The title compound was obtained in 49% yield.

Light yellow solid, mp 79-80 °C; $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 6.85 (d, J = 10.2 Hz, 2H), 6.34 (d, J = 10.1 Hz, 2H), 4.10 (s, 1H), 3.66 (s, 3H), 3.39-3.34 (m, 2H), 2.58-2.54 (m, 2H), 2.36-2.33 (m, 2H), 2.26-2.23 (m, 2H), 2.16-2.12 (m, 1H), 2.04-1.97 (m, 1H). $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 184.6, 172.5, 168.0, 146.7, 129.9, 52.0, 39.0, 33.8, 28.1, 25.5, 24.8; **IR** (thin film) ν 2949, 2360, 1734, 1670, 1654, 1521, 1473, 1281, 1136, 990 cm^{-1} ; **HRMS** (ESI): Calcd. For $\text{C}_{15}\text{H}_{18}\text{NaO}_5\text{S}_2^+$ ($[\text{M}+\text{Na}^+]$): 365.0488, found 365.0478; **TLC** (1:4 EtOAc/hexanes): R_f = 0.25.

1-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)-4-oxocyclohexa-2,5-dien-1-yl 1,3-dithiane-2-carboxylate (1d):

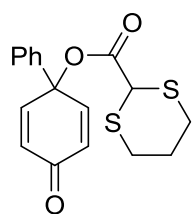


The title compound was obtained in 55% yield.

Clear oil; $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 6.98 (d, J = 10.2 Hz, 2H), 6.29 (d, J = 10.2 Hz, 2H), 4.11 (s, 1H), 3.75 (t, J = 9.0 Hz, 2H), 3.42-3.35 (m, 2H), 2.59-2.55 (m, 2H), 2.18-2.16 (m, 1H), 2.08 (t, J = 6.1 Hz, 2H), 2.04-1.95 (m, 1H), 0.87 (s, 9H), 0.03 (s, 6H). $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 185.1, 168.1, 147.9, 128.6, 57.7, 42.7,

39.2, 25.8, 25.5, 24.8, 18.1; **IR** (thin film) ν 2929, 2855, 1739, 1670, 1635, 1508, 1472, 1256, 1097, 838 cm^{-1} ; **HRMS** (ESI): Calcd. For $\text{C}_{19}\text{H}_{30}\text{NaO}_4\text{S}_2\text{Si}^+$ ($[\text{M}+\text{Na}^+]$): 437.1247, found 437.1233; **TLC** (1:4 EtOAc/hexanes): R_f = 0.32.

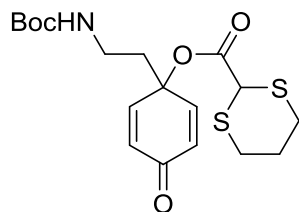
4-Oxo-[1,1'-biphenyl]-1(4H)-yl 1,3-dithiane-2-carboxylate (1e):



The title compound was obtained in 18% yield.

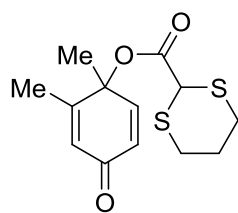
Orange solid, mp 113-114 °C; **^1H NMR** (600 MHz, CDCl_3) δ 7.41-7.46 (m, 2H), 7.41-7.34 (m, 3H), 7.06 (d, J = 10.1 Hz, 2H), 6.38 (d, J = 10.1 Hz, 2H), 4.26 (s, 1H), 3.37 (td, J = 12.0, 6.1 Hz, 2H), 2.60-2.57 (m, 2H), 2.15-2.12 (m, 1H), 2.06-1.99 (m, 1H). **^{13}C NMR** (151 MHz, CDCl_3) δ 185.3, 167.7, 146.8, 136.2, 129.2, 129.0, 128.5, 125.2, 39.6, 25.6, 24.8; **IR** (thin film) ν 2920, 2360, 1739, 1669, 1277, 1126, 994, 849, 698 cm^{-1} ; **HRMS** (ESI): Calcd. For $\text{C}_{17}\text{H}_{16}\text{NaO}_3\text{S}_2^+$ ($[\text{M}+\text{Na}^+]$): 355.0433, found 355.0425; **TLC** (1:4 EtOAc/hexanes): R_f = 0.44.

1-(2-((*tert*-Butoxycarbonyl)amino)ethyl)-4-oxocyclohexa-2,5-dien-1-yl 1,3-dithiane-2-carboxylate (1f):



The title compound was obtained in 17% yield.

White solid, mp 107-109 °C; **^1H NMR** (600 MHz, CDCl_3) δ 6.91 (d, J = 10.1 Hz, 2H), 6.32 (d, J = 10.1 Hz, 2H), 4.68 (bs, 1H), 4.10 (s, 1H), 3.22-3.21 (m, 2H), 3.22-3.21 (m, 2H), 2.58-2.54 (m, 2H), 2.14-2.11 (m, 1H), 2.08-2.05 (m, 2H), 2.03-1.95 (m, 1H), 1.41 (s, 9H). **^{13}C NMR** (151 MHz, CDCl_3) δ 184.6, 168.0, 155.6, 147.0, 129.5, 79.7, 39.6, 39.3, 35.7, 33.9, 28.4, 25.6, 24.8; **IR** (thin film) ν 3354, 2975, 2929, 1738, 1668, 1517, 1366, 1274, 1169, 859 cm^{-1} ; **HRMS** (ESI): Calcd. For $\text{C}_{18}\text{H}_{25}\text{NNaO}_5\text{S}_2^+$ ($[\text{M}+\text{Na}^+]$): 422.1066, found 422.1054; **TLC** (1:4 EtOAc/hexanes): R_f = 0.24.



1,2-Dimethyl-4-oxocyclohexa-2,5-dien-1-yl 1,3-dithiane-2-carboxylate (1g):

The title compound was obtained in 67% yield.

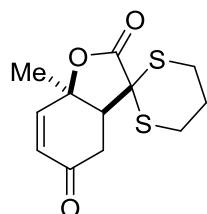
White solid, mp 120-121 °C; **^1H NMR** (600 MHz, CDCl_3) δ 6.91 (d, J = 10.2 Hz, 1H), 6.29 (dd, J = 9.9, 2.4 Hz, 1H), 6.16 (s, 1H), 4.13 (s, 1H), 3.48-3.36 (m, 2H), 2.61-2.56 (m, 2H), 2.20-2.15 (m, 1H), 2.07-1.99 (m, 1H), 2.04 (d, J = 1.2 Hz, 3H), 1.57 (s, 3H); **^{13}C NMR** (151 MHz, CDCl_3) δ 185.3, 168.0, 158.8, 149.4, 128.1, 126.8, 38.4, 26.4, 25.3, 25.3, 24.8, 17.8; **IR** (thin film) ν 2933, 1734, 1668, 1613, 1433, 1391, 1293, 1134, 1056, 885 cm^{-1} ; **HRMS** (ESI): Calcd. For $\text{C}_{13}\text{H}_{16}\text{NaO}_3\text{S}_2^+$ ($[\text{M}+\text{Na}^+]$): 307.0433, found 307.0431; **TLC** (1:4 EtOAc/hexanes): R_f = 0.25.

General procedure for intramolecular conjugate addition of dithiane:

A flame-dried 1 dram vial was charged sequentially with the dithiane-tethered cyclohexadienone (0.1 mmol, 1.0 equiv), followed by THF (1.0 mL), and then P2-*t*-Bu phosphazene (0.02 mmol, 20 mol %). The reaction was stirred at room temperature for 30 min. The reaction was quenched with saturated ammonium chloride, and the layers were separated. The aqueous layer was extracted three times with ethyl acetate, and then the combined organic phases were dried with sodium sulfate, and concentrated in vacuo. The crude materials thusly obtained were purified using flash column chromatography on silica gel using a hexane/EtOAc system (typically EtOAc/hexanes 1:9).

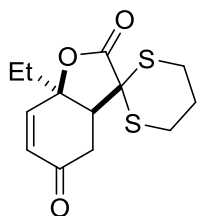
Characterization of products:

7a-Methyl-3a,7a-dihydro-2*H*-spiro[benzofuran-3,2'-[1,3]dithiane]-2,5(4*H*)-dione (2a):



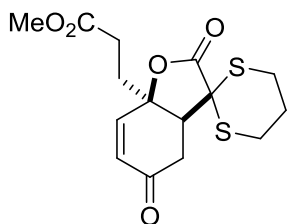
The title compound was prepared by the general procedure. White solid, mp 185-187 °C; ¹H NMR (600 MHz, CDCl₃) δ 6.79 (dd, *J* = 10.5 Hz, 1.8 Hz, 1H), 6.10 (d, *J* = 10.2 Hz, 1H), 3.99-3.94 (m, 1H), 3.42-3.37 (m, 1H), 2.99 (d, *J* = 18.6 Hz, 1H), 2.87 (d, *J* = 7.2 Hz, 1H), 2.69 (dd, *J* = 18.6 Hz, 7.8 Hz, 1H), 2.63-2.61 (m, 2H), 2.17-2.13 (m, 1H), 1.87-1.80 (m, 1H), 1.68 (s, 3H); ¹³C NMR (151 MHz, CDCl₃) δ 193.4, 171.9, 147.7, 130.0, 78.8, 52.5, 49.5, 33.4, 27.4, 26.6, 25.9, 23.6; ; IR (thin film) ν 2920, 1761, 1681, 1275, 1194, 1104, 1067, 972, 787, 734 cm⁻¹; HRMS (ESI): Calcd. For C₁₂H₁₅O₃S₂⁺ ([M+H⁺]): 271.0457, found 271.0457; TLC (2:8 EtOAc/hexanes): R_f = 0.13.

7a-Ethyl-3a,7a-dihydro-2*H*-spiro[benzofuran-3,2'-[1,3]dithiane]-2,5(4*H*)-dione (2b):



The title compound was prepared by the general procedure. White solid, mp 109-110 °C; ¹H NMR (400 MHz, CDCl₃) δ 6.80 (d, *J* = 10.5 Hz, 1H), 6.18 (d, *J* = 10.6 Hz, 1H), 4.02-3.94 (m, 1H), 3.45-3.38 (m, 1H), 3.01 (d, *J* = 18.9 Hz, 1H), 2.89 (d, *J* = 8.0 Hz, 1H), 2.68-2.61 (m, 3H), 2.20-2.13 (m, 1H), 2.04-1.98 (m, 1H), 1.94-1.89 (m, 1H), 1.87-1.81 (m, 1H), 1.09 (t, *J* = 5.0 Hz, 3H); ¹³C NMR (151 MHz, CDCl₃) δ 193.8, 172.0, 147.0, 130.8, 81.2, 50.1, 49.7, 33.8, 32.8, 27.3, 26.0, 23.7, 7.8 IR (thin film) ν 3425, 2970, 1757, 1681, 1388, 1223, 1187, 1116, 978, 9321 cm⁻¹; HRMS (ESI): Calcd. For C₁₃H₁₆NaO₃S₂⁺ ([M+Na⁺]): 307.0433, found 307.0433; TLC (2:8 EtOAc/hexanes): R_f = 0.28.

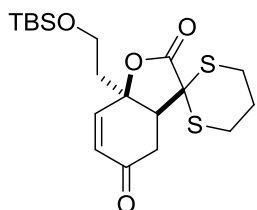
Methyl 3-(2,5-dioxo-4,5-dihydro-2H-spiro[benzofuran-3,2'-[1,3]dithian]-7a(3aH)-yl)propanoate



(2c): The title compound was prepared by the general procedure. White solid, mp 114-115 °C; $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 6.78 (dd, $J = 10.5, 1.6$ Hz, 1H), 6.17 (d, $J = 10.6$ Hz, 1H), 3.98-3.93 (m, 1H), 3.72 (s, 3H), 3.42-3.37 (m, 1H), 3.00 (d, $J = 18.9$ Hz, 1H), 2.89 (d, $J = 7.7$ Hz, 1H), 2.69 (dd, $J = 18.8, 7.8$ Hz, 1H), 2.64-2.61 (m, 2H), 2.59-2.51 (m, 2H), 2.35-2.30 (m, 1H), 2.25-2.20 (m, 1H), 2.18-2.14 (m, 1H), 1.88-1.81 (m, 1H); $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 193.3,

172.5, 171.6, 146.0, 131.1, 79.8, 52.2, 50.5, 49.3, 34.4, 33.4, 28.0, 27.3, 26.0, 23.6; **IR** (thin film) ν 2923, 2852, 1760, 1735, 1685, 1435, 1166, 1079, 972, 932 cm^{-1} ; **HRMS** (ESI): Calcd. For $\text{C}_{15}\text{H}_{19}\text{O}_5\text{S}_2\text{Si}^+$ ($[\text{M}+\text{H}^+]$): 343.0668, found 343.0663; **TLC** (3:7 EtOAc/hexanes): $R_f = 0.14$.

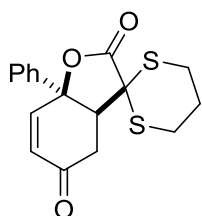
7a-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)-3a,7a-dihydro-2H-spiro[benzofuran-3,2'-[1,3]dithiane]-2,5(4H)-dione (2d):



The title compound was prepared by the general procedure. White solid, mp 135-137 °C; $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 6.78 (d, $J = 10.5$ Hz, 1H), 6.15 (d, $J = 10.5$ Hz, 1H), 3.97 (td, $J = 13.6, 2.4$ Hz, 1H), 3.89-3.86 (m, 1H), 3.80-3.76 (m, 1H), 3.43-3.93 (m, 1H), 3.35 (d, $J = 7.8$ Hz, 1H), 2.96 (d, $J = 18.8$ Hz, 1H), 2.81 (dd, $J = 18.8, 7.7$ Hz, 1H), 2.63-2.60 (m, 1H), 2.18-2.14 (m, 1H), 2.08-2.04 (m, 1H), 2.88-2.81 (m, 1H), 0.90 (s, 9H), 0.09 (s, 3H), 0.08 (s, 3H); $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 194.3,

172.2, 147.4, 130.5, 80.7, 57.7, 50.0, 49.5, 41.6, 33.5, 27.3, 26.0, 25.8, 23.7, 18.1, -5.5, -5.5; **IR** (thin film) ν 23434, 2953, 1761, 1642, 1407, 1248, 1182, 1095, 778 cm^{-1} ; **HRMS** (ESI): Calcd. For $\text{C}_{19}\text{H}_{31}\text{O}_4\text{S}_2\text{Si}^+$ ($[\text{M}+\text{H}^+]$): 415.1428, found 415.1420; **TLC** (2:8 EtOAc/hexanes): $R_f = 0.37$.

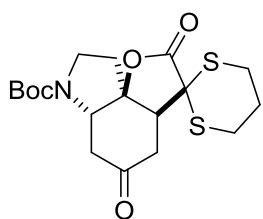
7a-Phenyl-3a,7a-dihydro-2H-spiro[benzofuran-3,2'-[1,3]dithiane]-2,5(4H)-dione (2e):



The title compound was prepared by the general procedure. White solid, mp 171-172 °C; $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 7.46-7.42 (m, 5H), 6.87 (d, $J = 10.2$ Hz, 1H), 6.40 (d, $J = 10.2$ Hz, 1H), 4.02 (t, $J = 13.2$ Hz, 1H), 3.50 (t, $J = 14.4$ Hz, 1H), 3.03 (d, $J = 7.2$ Hz, 1H), 2.99 (d, $J = 18.6$ Hz, 1H), 2.72-2.64 (m, 3H), 2.20 (m, 1H), 1.87 (q, $J = 13.2$ Hz, 1H); $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 193.8, 172.0, 145.3, 138.8, 131.5, 129.3, 129.2, 124.6, 81.7, 54.6, 49.4, 33.0, 27.4, 26.0, 23.7; **IR** (thin film) ν 22971, 2361,

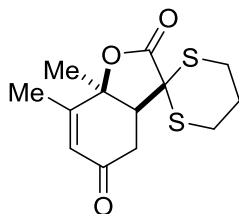
1769, 1684, 1540, 1507, 1224, 1170, 997, 799 cm^{-1} ; **HRMS** (ESI): Calcd. For $\text{C}_{17}\text{H}_{17}\text{O}_3\text{S}_2^+$ ($[\text{M}+\text{H}^+]$): 333.0614, found 333.0608; **TLC** (3:7 EtOAc/hexanes): $R_f = 0.38$.

tert-Butyl 2,5-dioxohexahydro-2H-spiro[furo[2,3-d]indole-3,2'-[1,3]dithiane]-7(3aH)-carboxylate



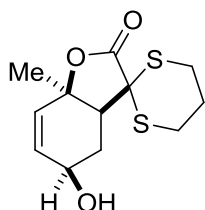
(2f): The title compound was prepared by the general procedure. Two rotamers were observed in a 56:44 ratio in the ^1H NMR spectrum. White solid, mp 196-197 °C; ^1H NMR (600 MHz, CDCl_3) δ 4.32-4.04 (m, 1H for the minor rotamer), 4.28-4.25 (m, 1H for the major rotamer) 3.77-3.58 (m, 4H), 3.19 (dd, J = 17.2, 5.8 Hz, 1H for the minor rotamer), 3.02 (dd, J = 17.1, 5.7 Hz, 1H for the major rotamer), 2.80-2.75 (m, 1H), 2.75-2.73 (m, 4H), 2.63-2.59 (m, 1H), 2.32-2.26 (m, 1H), 2.24-2.19 (m, 1H), 2.10-1.99 (m, 1H), 1.96-1.89 (m, 1H), 1.48 (s, 9H); ^{13}C NMR (151 MHz, CDCl_3) δ 205.0, 204.7, 171.2, 153.8, 153.5, 88.7, 88.0, 80.7, 60.6, 60.5, 49.3, 48.3, 48.2, 44.4, 44.0, 43.6, 42.9, 37.3, 37.2, 35.7, 34.8, 28.5, 28.4, 27.6, 27.5, 26.4, 26.3, 23.8; IR (thin film) ν 2974, 2927, 1764, 1721, 1691, 1399, 1249, 1174, 1136 975 cm^{-1} ; HRMS (ESI): Calcd. For $\text{C}_{18}\text{H}_{25}\text{NNaO}_5\text{S}_2$ ($[\text{M}+\text{Na}^+]$): 422.1067, found 422.1077; TLC (1:1 EtOAc/hexanes): R_f = 0.50.

7,7a-Dimethyl-3a,7a-dihydro-2H-spiro[benzofuran-3,2'-[1,3]dithiane]-2,5(4H)-dione (2g):



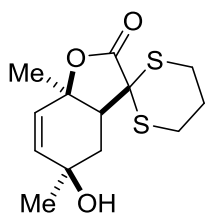
The title compound was prepared by the general procedure. Impurity present in the δ 2.73-2.67 multiplet makes integral appear as 3H. Orange-brown solid, mp 169-179 °C; ^1H NMR (600 MHz, CDCl_3) δ 5.96 (s, 1H), 3.96 (t, J = 13.8 Hz, 1H), 3.35 (t, J = 13.8 Hz, 1H), 2.98 (d, J = 19.2 Hz, 1H), 2.868 (d, J = 9.0 Hz, 1H), 2.73-2.67 (m, 1H), 2.63-2.60 (m, 2H), 2.17-2.14 (m, 1H), 2.09 (s, 3H), 1.83 (q, J = 13.2 Hz, 1H), 1.69 (s, 3H); ^{13}C NMR (151 MHz, CDCl_3) δ 193.2, 171.9, 159.3, 128.5, 81.0, 53.2, 49.5, 33.1, 27.1, 26.1, 25.7, 23.7, 18.4; IR (thin film) ν 2920, 1266, 1760, 1671, 1425, 1228, 1190, 1098, 970, 935 cm^{-1} ; HRMS (ESI): Calcd. For $\text{C}_{13}\text{H}_{17}\text{O}_3\text{S}_2$ ($[\text{M}+\text{Na}^+]$): 285.0614, found 285.0611; TLC (2:8 EtOAc/hexanes): R_f = 0.13.

Procedure for the preparation of 5-hydroxy-7a-methyl-3a,4,5,7a-tetrahydro-2H-spiro[benzofuran-3,2'-[1,3]dithian]-2-one (3) via Luche reduction of enone 2a: CeCl₃·7H₂O (1.2 equiv) and NaBH₄ (5.3 equiv) were added to a solution of the substrate (2a) in MeOH (0.2 M) at -10 °C. The reaction mixture was stirred at the same temperature for 40 min. After this period, it was quenched with 1 M HCl and extracted with EtOAc three times. The combined organic phases were dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The crude residue was purified by flash column chromatography on silica gel using EtOAc/hexanes 3:7 as the eluent.



White solid, mp 97-99 °C; ¹H NMR (600 MHz, CDCl₃) δ 5.95 (d, *J* = 10.2 Hz, 1H), 5.79 (d, *J* = 10.2 Hz, 1H), 4.20-4.16 (br, 1H), 4.00 (t, *J* = 13.8 Hz, 1H), 3.62 (t, *J* = 18.3 Hz, 1H), 2.68-2.64 (m, 2H), 2.46-2.43 (d, *J* = 12.0, 5.4 Hz, 1H), 2.41-2.37 (m, 1H), 2.22-2.18 (m, 1H), 1.98-1.90 (m, 1H), 1.86 (d, *J* = 7.2 Hz, 1H), 1.77-1.70 (m, 1H), 1.67 (s, 3H); ¹³C NMR (151 MHz, CDCl₃) δ 172.6, 134.7, 129.6, 65.4, 49.9, 49.8, 49.8, 31.3, 29.0, 28.2, 26.5, 24.3; IR (thin film) ν 3035, 2926, 1752, 1423, 1276 1189, 1148, 1061, 956, 732 cm⁻¹; HRMS (ESI): Calcd. For C₁₂H₁₇O₃S₂ ([M+Na⁺]): 273.0614, found 273.0610; TLC (6:4 EtOAc/hexanes): R_f = 0.34.

Procedure for the preparation of 5-hydroxy-5,7a-dimethyl-3a,4,5,7a-tetrahydro-2H-spiro[benzofuran-3,2'-[1,3]dithian]-2-one (4) via 1,2-addition of AlMe₃: A solution of the substrate (2a) in dry CH₂Cl₂ was added to a solution of AlMe₃ (2 M in toluene, 4 equiv) in dry CH₂Cl₂ at 0 °C. The reaction mixture was allowed to reach room temperature and kept under stirring for 3 h. After this period, it was quenched with MeOH and extracted with CH₂Cl₂ and EtOAc. The combined organic phases were dried over anhydrous Na₂SO₄ and the solvent was removed under reduced pressure.

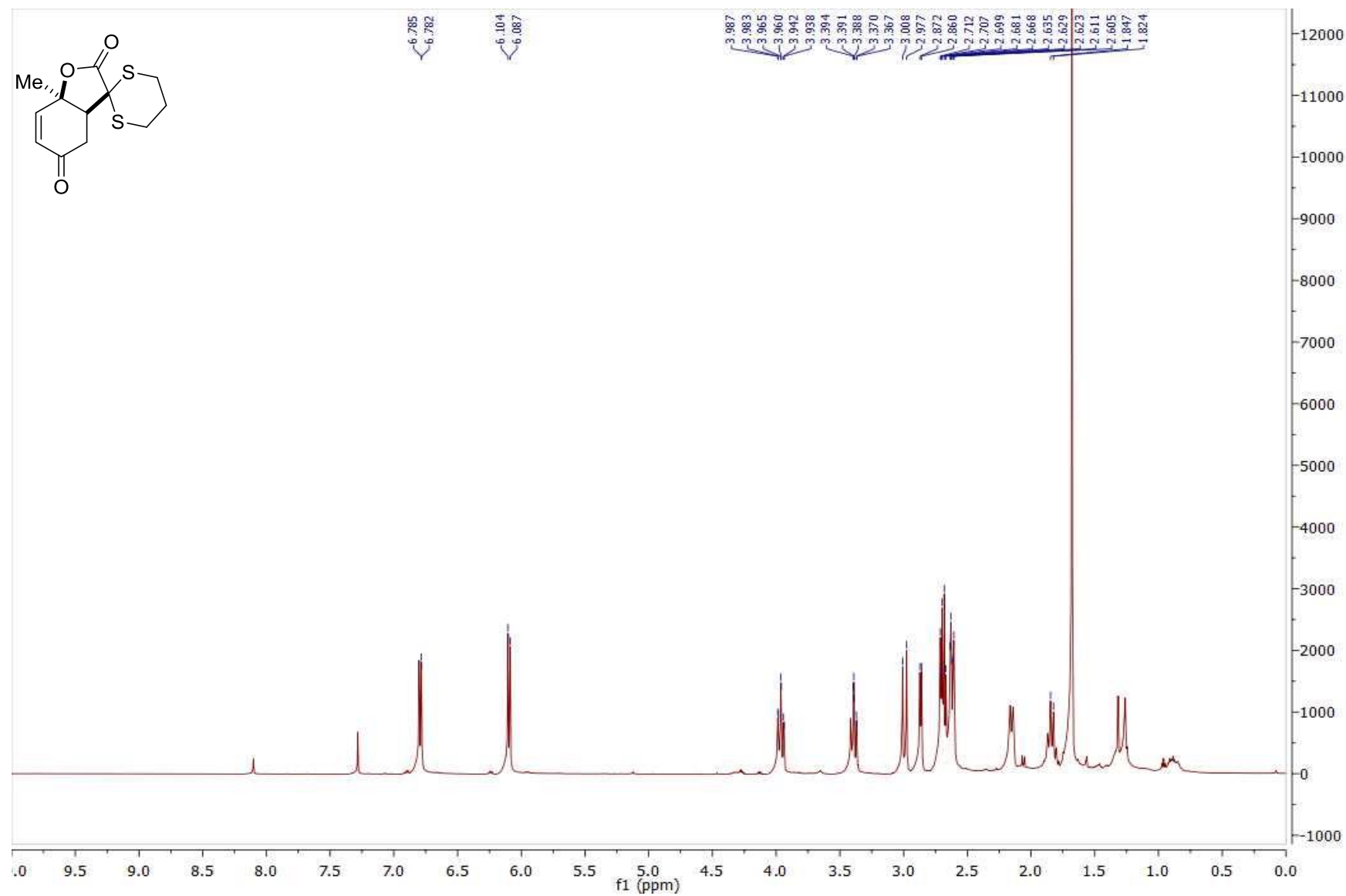


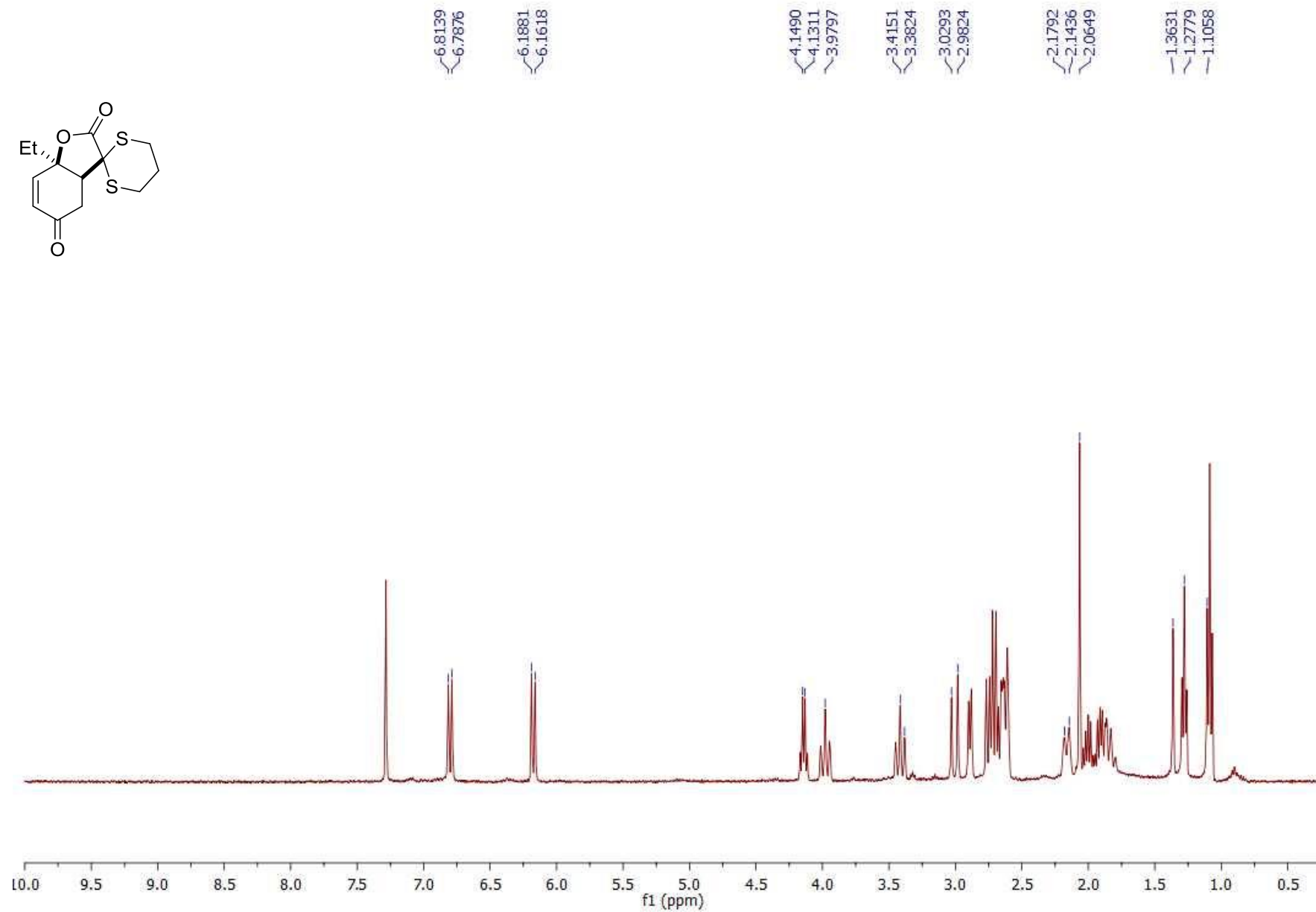
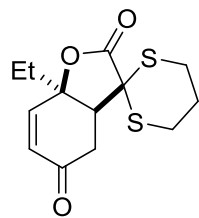
Light yellow solid, mp 179-180 °C; ¹H NMR (600 MHz, CDCl₃) δ 5.91 (dd, *J* = 10.1, 1.4 Hz, 1H), 5.67 (d, *J* = 10.1 Hz, 1H), 4.06-4.01 (m, 1H), 3.62-3.57 (m, 1H), 2.71-2.65 (m, 3H), 2.50 (dd, *J* = 12.7, 5.6 Hz, 1H), 2.23-2.16 (m, 2H), 1.95-1.91 (m, 2H), 1.70 (s, 3H), 1.28 (s, 3H); ¹³C NMR (151 MHz, CDCl₃) δ 172.7, 137.9, 128.0, 79.1, 68.9, 50.0, 36.7, 29.3, 28.3, 26.5, 26.4, 24.4; IR (thin film) ν 3433, 2960, 2088, 1752, 1643, 1373, 1280, 1193, 1151, 1055 cm⁻¹; HRMS (ESI): Calcd. For C₁₃H₁₈NaO₃S₂ ([M+Na⁺]): 309.0590, found 309.0593; TLC (4:6 EtOAc/hexanes): R_f = 0.43.

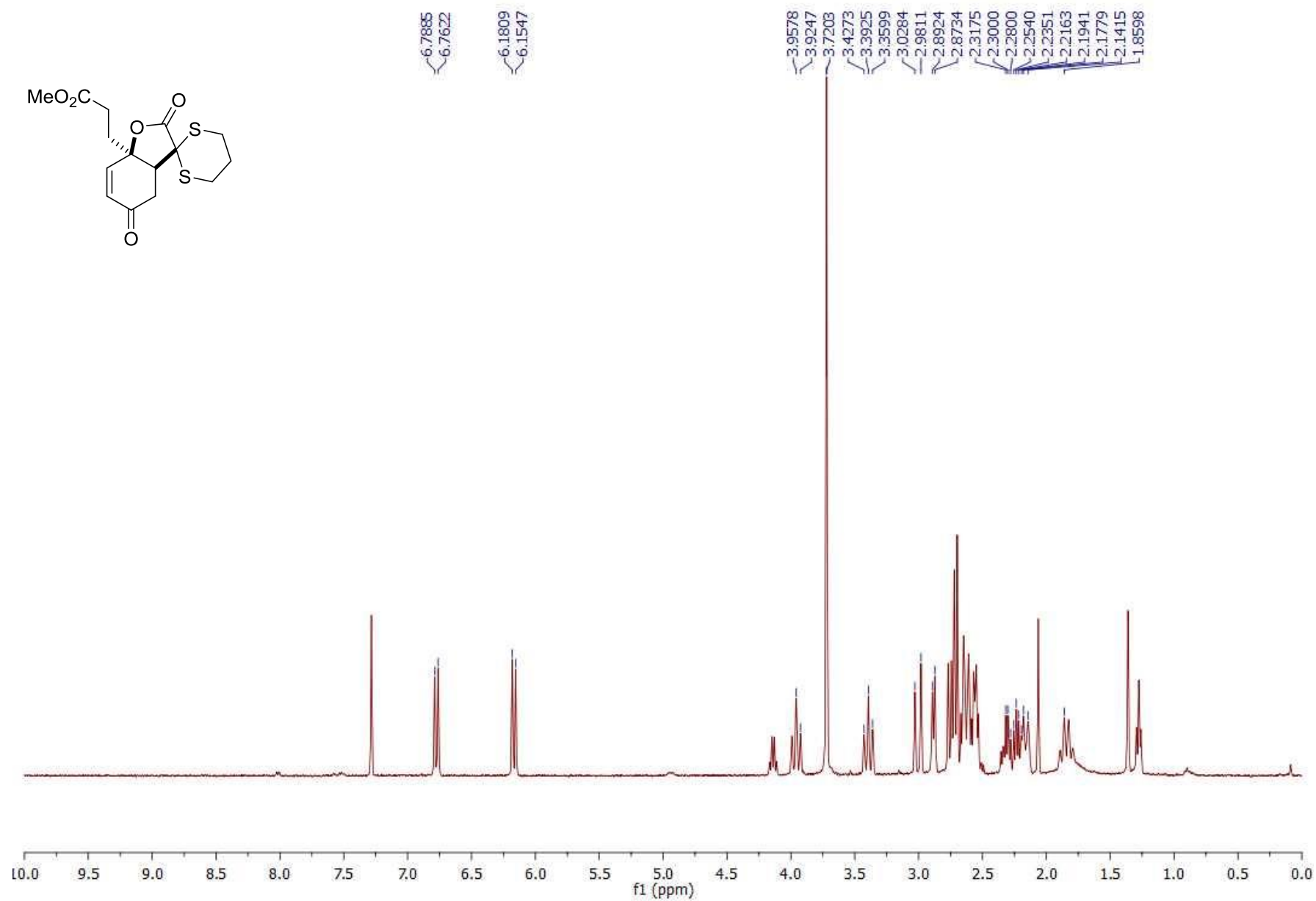
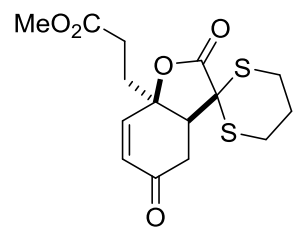
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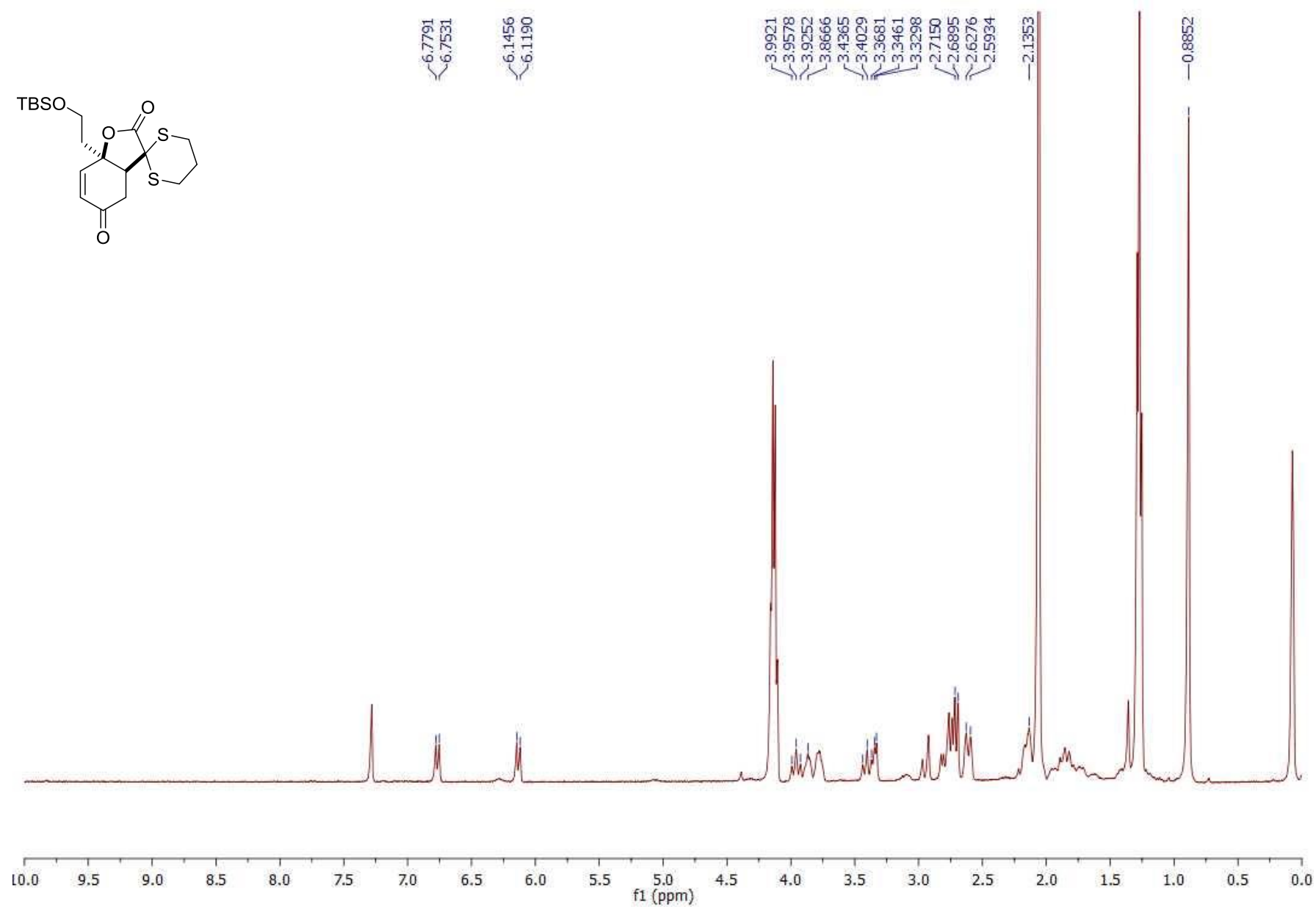
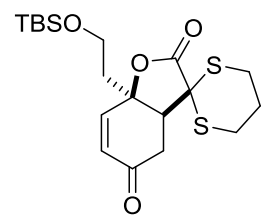
1. a) Felpin, F.-X. *Tetrahedron Lett.* **2007**, 48, 409. b) McKillop, A.; McLaren, L.; Taylor, R. J. K. *J. Chem. Soc., Perkin Trans. 1*, **1994**, 15, 2047. c) Jepsen, T. H.; Jensen, A. A.; Lund, M. H.; Glibstrup, E.; Kristensen, J. L. *ACS Med. Chem. Lett.* **2014**, 5, 766. d) Canesi, S.; Bouchu, D.; Ciufolini, M. A. *Org. Lett.* **2005**, 7, 175. e) Brown, P. D.; Willis, A. C.; Sherburn, M. S.; Lawrence, A. L. *Org. Lett.* **2012**, 14, 4537.
2. Kondoh, A.; Oishi, M.; Takeda, T.; Terada, M. *Angew. Chem., Int. Ed.* **2015**, 54, 15836.

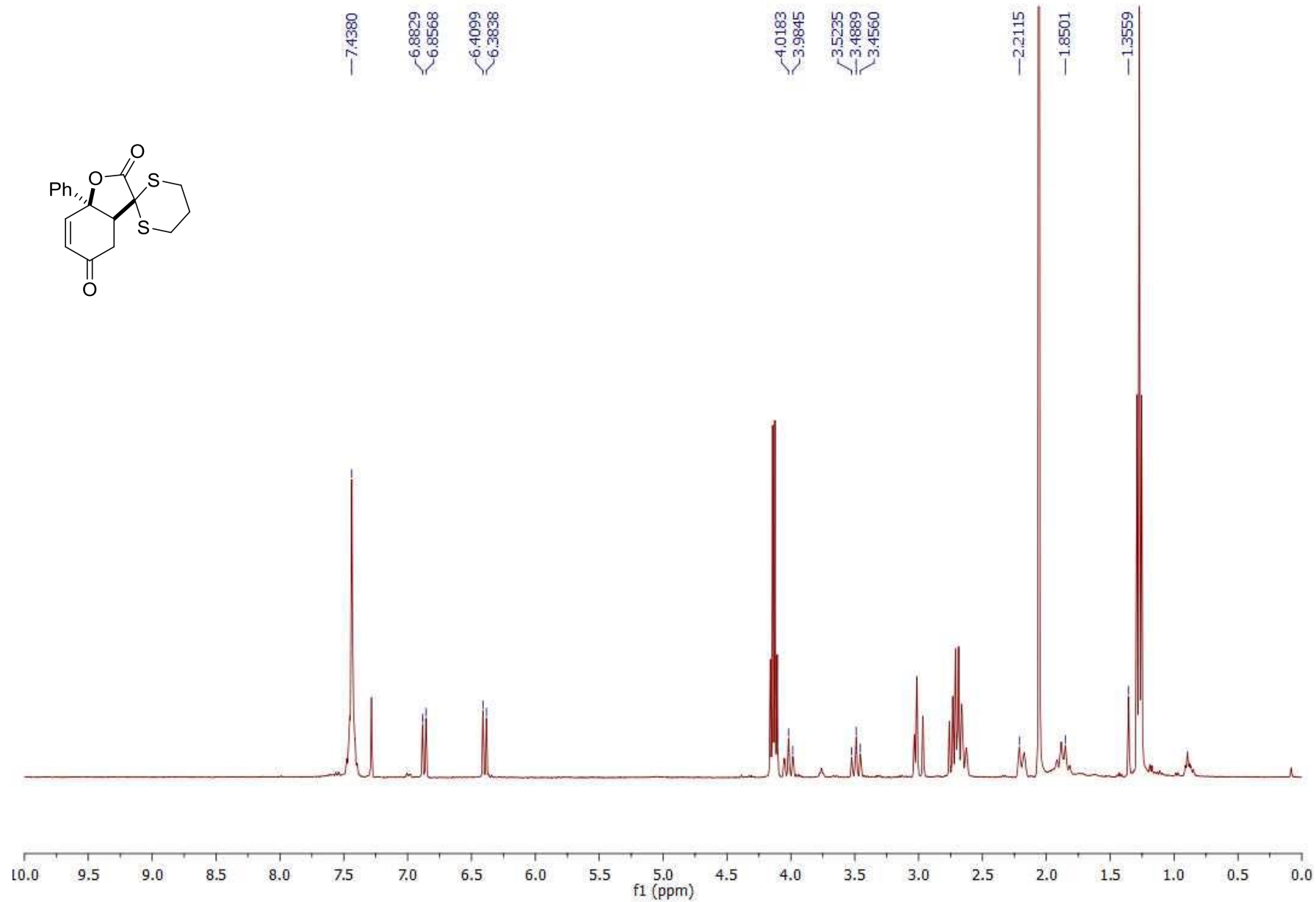
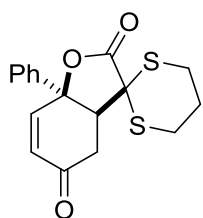
Crude ^1H NMR spectra for the desymmetrization reaction:

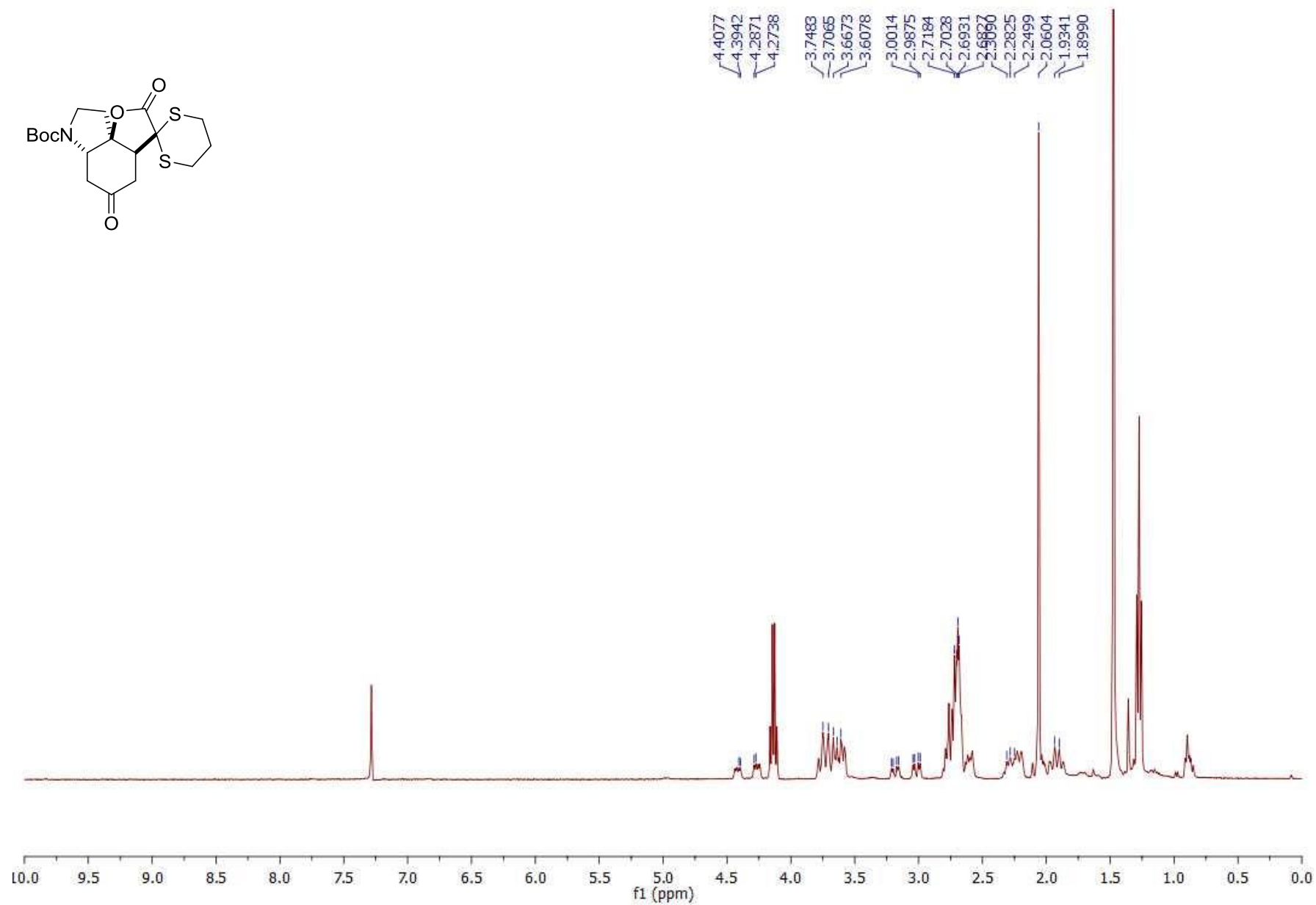
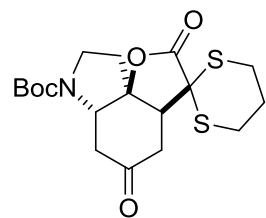


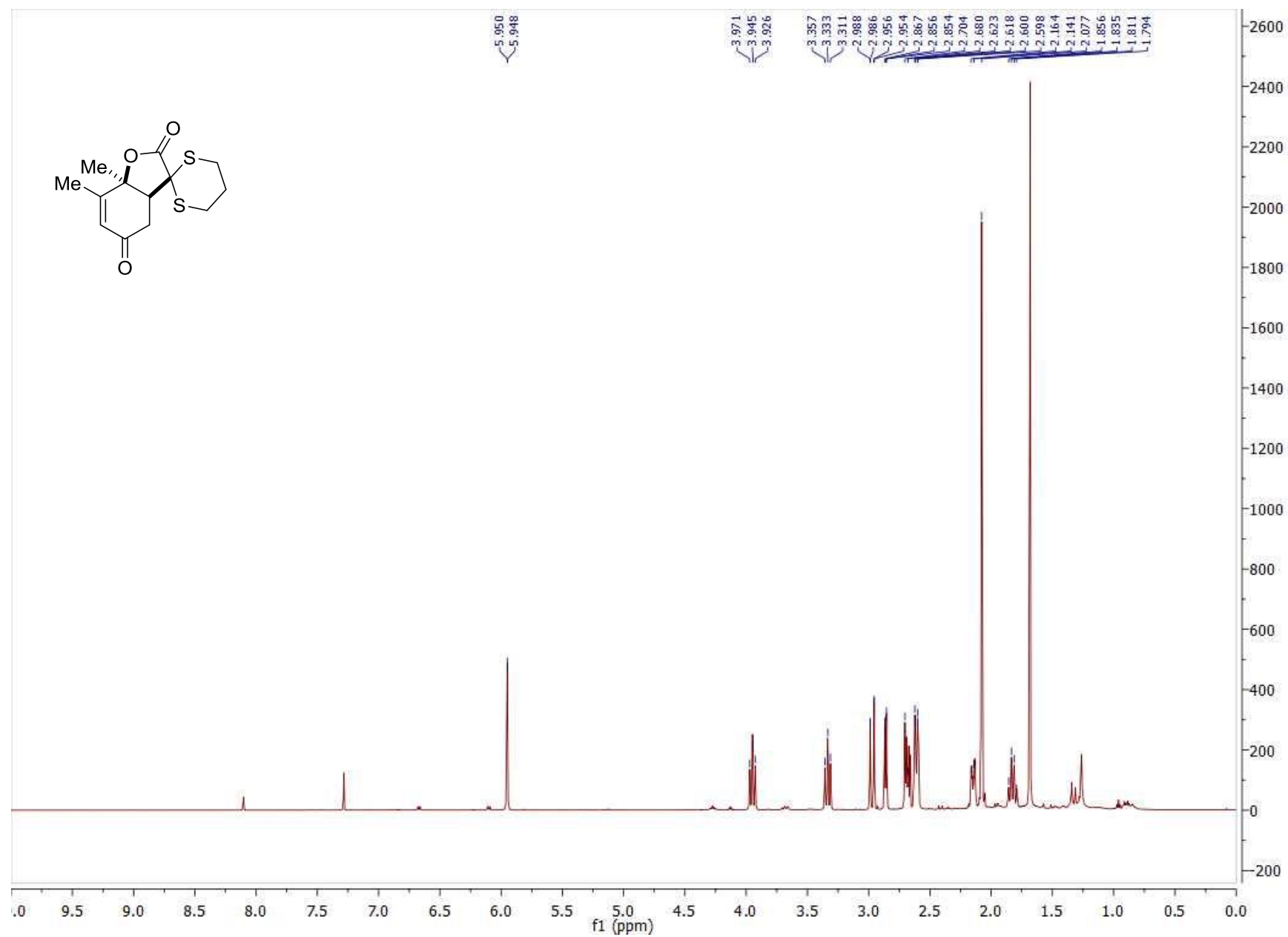




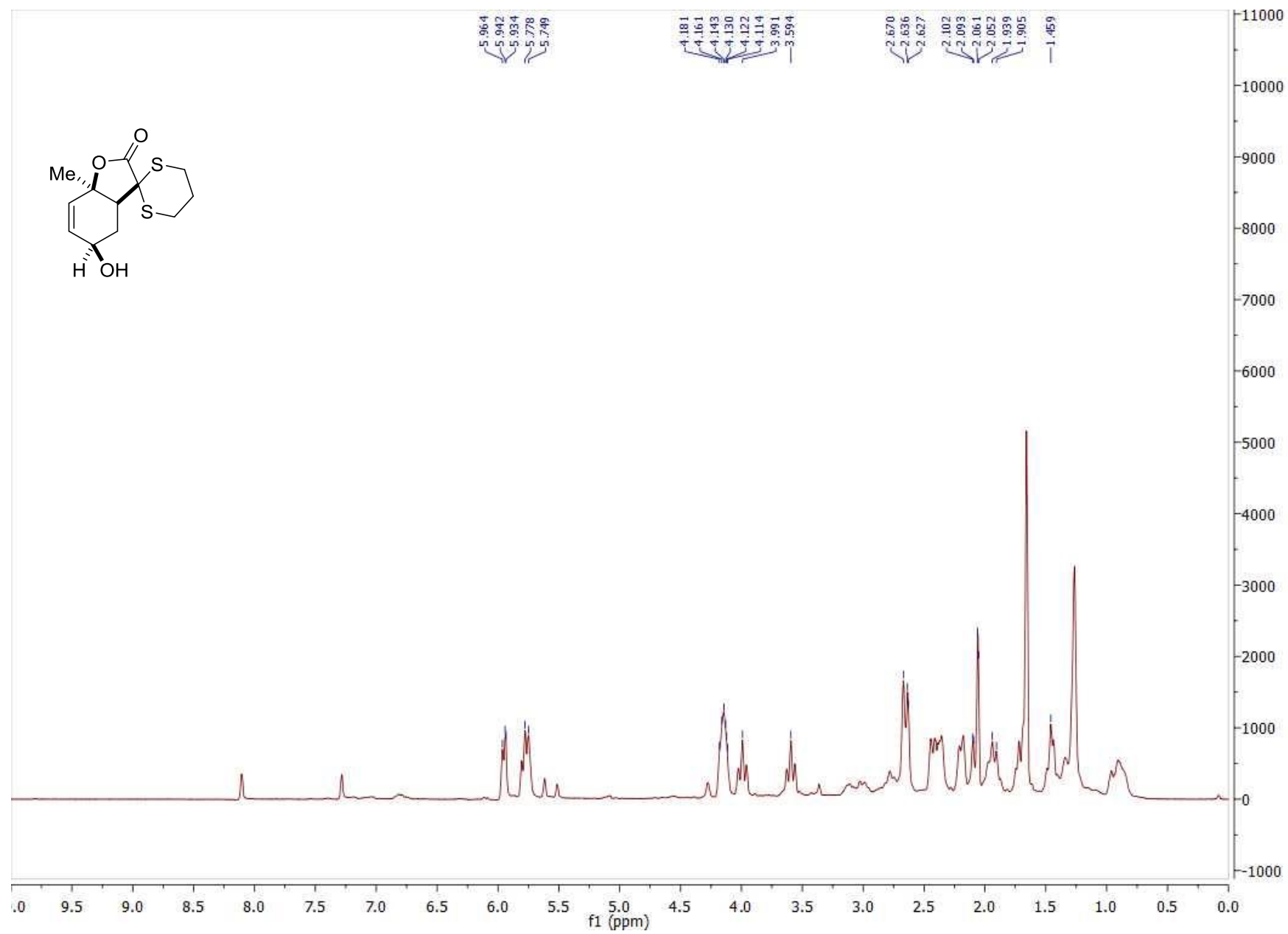








S17



S18

¹H and ¹³C NMR spectra of new compounds:

