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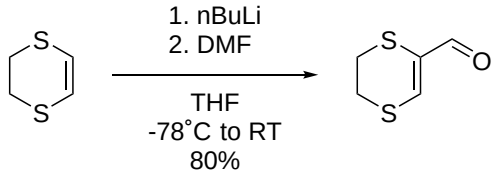
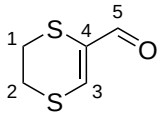
Unless otherwise stated, all reactions were performed in flame dried glassware, using a magnetically stirred Teflon stir bar under argon atmosphere. All the reagents and solvents (HPLC grade) were used without any further purification, with the exception of dichloromethane that had been distilled over CaH_2 prior to use. Synthesized products and intermediates were added under argon atmosphere and protected from light, stored at -25°C. Reactions were monitored by thin layer chromatography (TLC), with SIL G25 UV254 TLC plates with silica gel of 0.25 mm in thickness. The TLC plates were developed using an anisaldehyde stain solution (5% para-anisaldehyde and 1% sulfuric acid in ethanol). Column chromatography was performed with ROCC N.V. silica (particle size of from 0.060 to 0.200 mm). Petroleum ether (PE) (boiling point range 40-60°C) was used as the standard apolar mobile phase, typically enriched with a gradient of ethyl acetate. ^{1}H Nuclear Magnetic Resonance (NMR) spectra were recorded with a resolution of 300, 400 or 500 MHz. The chemical shifts (δ) are expressed in ppm and the residual solvent peak was used as the internal standard ($CDCl_3$: δH = 7.26 ppm; δC = 77.16 ppm). The multiplicity of the signals were designated by the following abbreviations: s, singlet; d, doublet; t, triplet; q, quadruplet; m, multiplet; br broadened; band, several overlapping signals; AB, AB system with strongly skewed signals. Mass spectra (MS) were run with an Agilent ESI single quadrupole type detector VL. High resolution mass spectra (HRMS) are recorded on an Agilent Accurate-Mass Quadrupole Time-of-Flight mass spectrometer.

1 Synthesis of dithioallyl-cation precursors and optimisation of their reaction with styrene

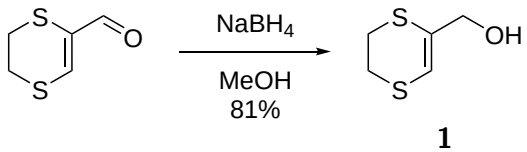
1.1 (5,6-dihydro-1,4-dithiin-2-yl)methanol (DHDT-MeOH) (1)



(5,6-dihydro-1,4-dithiin-2-yl)methanol (DHDT-MeOH) **1** is prepared in a two-step procedure starting from 5,6-dihydro-1,4-dithiin (DHDT). A solution of DHDT (33.78 mmol, 1 equiv.) in THF (60 mL) is prepared and cooled to -78°C before *n*BuLi (2.5M in hexanes, 40.54 mmol, 1.2 equiv.) is added dropwise. After two hours, DMF (3.66 ml, 47.30 mmol, 1.4 equiv.) is added and the resulting mixture is allowed to warm up to room temperature over the period of 2.5 hours. When the dithiin starting material is fully consumed as judged by TLC, the reaction mixture is quenched with a saturated solution of sodium bicarbonate and extracted using CH_2Cl_2. The combined organic layers are subsequently washed with brine and dried over sodium sulfate. Upon flash chromatography (gradient: 10% to 25% EtOAc in petroleum ether), pure (5,6-dihydro-1,4-dithiin-2-yl)aldehyde (4.06 g, 80% yield) is obtained as a yellow-orange oil.



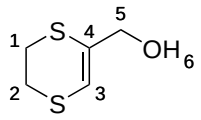
Formula: $C_5H_6OS_2$
Molar mass: 146.22 g/mol
R_f (20% ethyl acetate in hexanes): 0.33
^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm): 9.22 (s, 1H, C5-H), 7.38 (s, 1H, C3-H), 3.35-3.29 (m(AB), 2H, S$-CH_2-CH_2-$S), 3.21-3.15 (m(AB), 2H, S$-CH_2-CH_2-$S)
^{13}C-NMR (75 MHz, $CDCl_3$): δ (ppm): 186.5 (C5-H), 140.7 (C3-H), 131.2 (C_q4), 28.6 (S$-CH_2-CH_2-$S), 24.6 (S$-CH_2-CH_2-$S)
HSQC ($CDCl_3$): 186.5 x 9.22, 140.7 x 7.38, 28.6 x 3.35-3.29/3.21-3.15, 24.6 x 3.35-3.29/3.21-3.15
LCMS (ES): calculated for $C_5H_7OS_2^+$ [M+H$^+$]: 147.0; found: 147.0
IR ν_{max} (cm^{-1}): 1649 (s), 1531 (s), 1147 (s), 1119 (s), 852 (s)



1

5,6-dihydro-1,4-dithiine-2-carbaldehyde (17.78 mmol, 1 equiv.) is dissolved in dry methanol (40 mL) and cooled to -20°C. Sodium borohydride (1.01 g, 26.67 mmol, 1.5 equiv.) is added

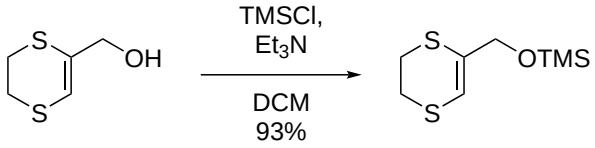
portionwise over the course of 10-15 minutes, after which the reaction mixture is allowed to warm back up to room temperature over a 90 minute period. When all aldehyde is consumed, the reaction is quenched with a saturated solution of sodium bicarbonate. Extraction of the organic layer using CH_2Cl_2, followed by washing with brine, drying over sodium sulfate and concentration *in vacuo* resulted in DHDT-MeOH **1** (2.16 g, 81% yield) as a yellow oil, requiring no further purification. All spectroscopic data matches those reported in literature.[1]



1

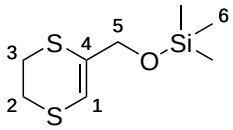
Formula: $C_5H_8OS_2$
Molar mass: 148.24 g/mol
^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm): 6.23 (s, 1H, C3-H), 4.10 (s(br), 2H, C5-H_2), 3.23-3.18 (band, 4H, S$-CH_2-CH_2-$S)
^{13}C-NMR (75 MHz, $CDCl_3$): δ (ppm): 127.8 (C_q4), 112.6 (C3-H), 67.6 (C5-H_2), 26.7 + 26.4 (S$-CH_2-CH_2-$S)
HSQC ($CDCl_3$): 112.6 x 6.23, 67.7 x 4.10, 26.7 x 3.23-3.18, 26.4 x 3.23-3.18

1.2 ((5,6-dihydro-1,4-dithiin-2-yl)methoxy)trimethylsilane (12)



1 **12**

A mixture of triethylamine (7.6 ml, 54.7 mmol, 3 equiv.) and TMSCl (4.5 ml, 36.5 mmol, 2 equiv.) is added dropwise to a solution of DHDT-MeOH **1** (2.70 g, 18.2 mmol, 1 equiv.) in CH_2Cl_2 (46 ml). The reaction mixture is stirred at room temperature until all starting material is consumed, as judged by TLC. The reaction mixture is cooled to 0°C and quenched with water (40 ml). The organic phases are separated before the aqueous phase is extracted with CH_2Cl_2 (3 x 75 ml). The combined organic phases are dried over anhydrous sodium sulfate. After concentration *in vacuo*, title compound **12** (3.74 g, 93% yield) is obtained as a yellow liquid upon flash chromatography using 5% ethyl acetate in petroleum ether.

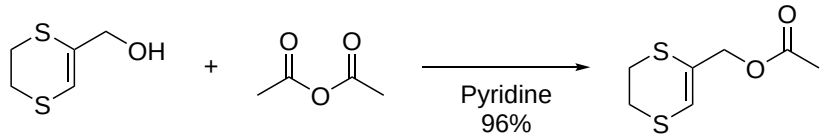


12

Formula: $C_8H_{16}OS_2Si$
Molar mass: 220.42 g/mol

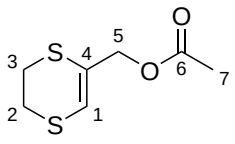
R_f (5% ethyl acetate in petroleum ether): 0.50
^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm): 6.17 (s, 1H, C1-H), 4.10 (d, 2H, J = 1.1 Hz, C5-H_2), 3.21-3.12 (band, 4H, S$-CH_2-CH_2-$S), 0.15 (s, 9H, C6-H_3)
^{13}C-NMR (75 MHz, $CDCl_3$): δ (ppm): 127.7 (C_q4), 111.1 (C1-H), 67.3 (C5-H_2), 26.9 (S$-CH_2-CH_2-$S), 26.6 (S$-CH_2-CH_2-$S), -0.3 (C6-H_3)
HSQC ($CDCl_3$): 111.1 x 6.17, 67.3 x 4.1, 26.9 x 3.21-3.12, 26.6 x 3.21-3.12, -0.3 x 0.155
LCMS (ESI): calculated for $C_5H_7S_2^+$ [M-OSi$(CH_3)_3$]$^+$: 131.0; found: 131.1
IR ν_{max} (cm^{-1}): 2953 (w), 1248 (m), 1109 (m), 1064 (m), 835 (s)

1.3 ((5,6-dihydro-1,4-dithiin-2-yl)methyl acetate (13)



1 **13**

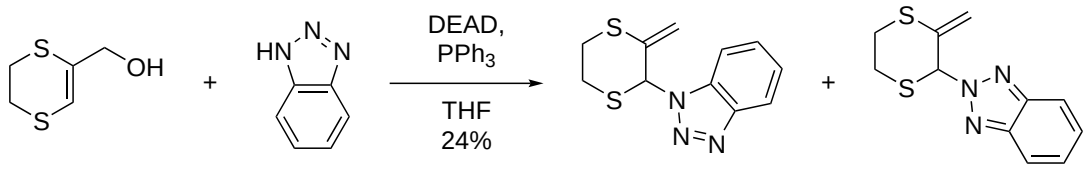
A solution of DHDT-MeOH (274.3 mg, 1.85 mmol, 1 equiv.) in pyridine (9.3 mL) is cooled to 0°C before acetic anhydride (0.21 ml, 2.22 mmol, 1.2 equiv.) is added dropwise. The resulting mixture is allowed to warm up to room temperature. When all starting material is consumed as judged by TLC, the reaction mixture is concentrated *in vacuo*. The resulting oil is purified via flash chromatography (eluent: 5% to 8% ethyl acetate in pentane) to afford title compound **13** as a clear oil (345 mg, 96%) that solidifies in the freezer.



13

Formula: $C_7H_{10}O_2S_2$
Molar mass: 190.28 g/mol
R_f (10% ethyl acetate in petroleum ether): 0.45
^{1}H-NMR (400 MHz, $CDCl_3$): δ (ppm): 6.29 (s, 1H, C1-H), 4.55 (s, 2H, C5-CH_2), 3.18 (m, 4H, C2-CH_2 and C3-CH_2), 2.09 (s, 3H, C7-CH_3)
^{13}C-NMR (101 MHz, $CDCl_3$): δ (ppm): 170.9 (C_q6), 122.8 (C_q4), 116.4 (C1-H), 68.6 (C5-H_2), 26.8 (C3-H_2), 26.3 (C4-H_2), 21.1 (C7-H_3)
HSQC ($CDCl_3$): 116.4 x 6.29, 68.6 x 4.55, 26.8 x 3.18, 26.3 x 3.18, 21.1 x 2.09
LCMS (ESI): calculated for $C_5H_7S_2^+$ [M-$C_2H_3O_2$]$^+$: 131.0; found: 131.1
IR ν_{max} (cm^{-1}): 2925 (w), 1731 (s), 1578 (w), 1375 (m), 1213 (s), 1023 (m), 958 (m), 788 (m)

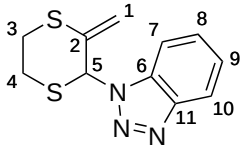
1.4 1-(3-methylene-1,4-dithian-2-yl)-1H-benzo[d][1,2,3]triazole (15a) and 2-(3-methylene-1,4-dithian-2-yl)-2H-benzo[d][1,2,3]triazole (15b)



1 **15a** **15b**

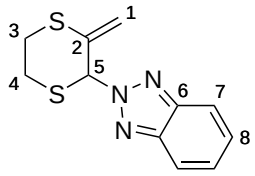
ratio 1:1

Following the procedure outlined by Mitsunobu *et al.*,[2] a solution of DHDT-methanol **1** (0.74 g, 4.99 mmol, 1 equiv.), diethyl azodicarboxylate (0.78 mL, 4.99 mmol, 1 equiv.) and benzotriazole (594 mg, 4,99 mmol, 1 equiv.) in THF (5 mL) is prepared at room temperature. In a dropwise fashion, triphenylphosphine (1.31 g, 4.99 mmol, 1 equiv.) in THF (5 mL) is added and the resulting mixture is left to stir overnight. When all starting material is consumed as judged by TLC, a saturated aqueous solution of sodium bicarbonate (10 mL) is added. The layers are separated and the organic phase is extracted with CH_2Cl_2 (3 x 10 mL) and washed with brine (4 mL). The resulting organic phase is dried over anhydrous sodium sulphate and concentrated *in vacuo*. After precipitation and filtration of residual triphenylphosphine oxide using cold petroleum ether, the obtained crude mixture is purified using flash chromatography (eluent gradient: 7% to 12% ethyl acetate in petroleum ether), affording cation precursors **15a** (151 mg, 12%) and **15b** (186 mg, 15%) as amorphous solids, in low yield.



15a

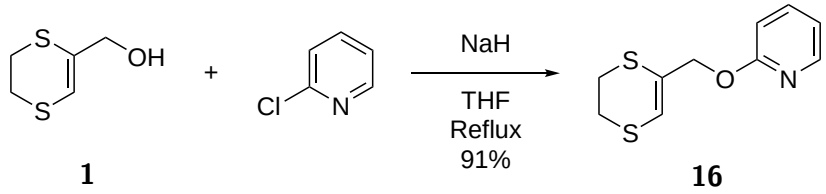
Formula: $C_{11}H_{11}N_3S_2$
Molar mass: 249.35 g/mol
R_f (15% ethyl acetate in petroleum ether): 0.39
^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm): 8.09 (dt, 1H, J = 8.2, 1.0 Hz, C10-H), 7.68 (dt, 1H, J = 8.2, 1.0 Hz, C7-H), 7.49 (ddd, 1H, J = 8.2, 7.0, 1.1 Hz, C8-H), 7.39 (ddd, 1H, J = 8.2, 7.1, 1.1 Hz, C9-H), 6.60 (s, 1H, C5-H), 5.55 (s, 1H, C1-HH), 4.97 (s, 1H, C1-HH), 3.55 (ddd, 1H, J = 13.7, 7.6, 2.6 Hz, C4-HH), 3.37-3.25 (band, 1H, C4-HH), 3.25-3.09 (band, 2H, C3-H_2)
^{13}C-NMR (75 MHz, $CDCl_3$): $a\delta$ (ppm): 146.4 (C_q11), 135.7 (C_q2), 132.3 (C_q6), 127.7 (C8-H), 124.4 (C9-H), 120.5 (C10-H), 118.5 (C1-H_2), 111.3 (C7-H), 61.1 (C5-H), 32.5 (C4-H_2), 30.7 (C3-H_2)
HSQC ($CDCl_3$): 127.7 x 7.49, 124.4 x 7.39, 120.5 x 8.09, 118.5 x 5.55, 118.5 x 4.97, 111.3 x 7.68, 61.1 x 6.60, 32.5 x 3.55, 32.5 x 3.37-3.25, 30.7 x 3.25-3.09
HRMS (ESI): calculated for $C_{11}H_{12}N_3S_2^+$ [M+H$^+$]: 250.0467; found: 250.0476
IR ν_{max} (cm^{-1}): 2910 (m), 1449 (m), 1410 (m), 1276 (m), 818 (s), 742 (s)



15b

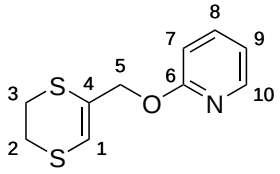
Formula: $C_{11}H_{11}N_3S_2$
Molar mass: 249.35 g/mol
Rf (15% ethyl acetate in petroleum ether): 0.44
^{1}H-NMR (400 MHz, $CDCl_3$): δ (ppm): 7.95-7.89 (m, 2H, CH_{Ar}), 7.43-7.38 (m, 2H, CH_{Ar}), 6.43 (s, 1H, C5-H)), 5.63 (s, 1H, C1-*H*H), 5.43 (s, 1H, C1-H*H*), 3.85 (ddd, 1H, J = 13.3, 10.7, 2.4 Hz, C4-*H*H), 3.30 (ddd, 1H, J = 12.7, 10.4, 2.3 Hz, C3-*H*H), 3.12-2.99 (band, 2H, C4-H*H* + C3-H*H*)
^{13}C-NMR (101 MHz, $CDCl_3$): δ (ppm): 144.5 (C_q6), 135.7 (C_q2), 127.0 (C7/8-H), 120.6 (C1-H_2), 118.6 (C7/8-H), 66.7 (C5-H), 32.1 (C3-H_2), 27.4 (C4-H_2)
HSQC ($CDCl_3$): 127.0 x 7.43-7.38, 120.6 x 5.63, 120.6 x 5.43, 118.6 x 7.95-7.89, 66.7 x 6.43, 32.1 x 3.30, 32.1 x 3.08, 27.4 x 3.85, 27.4 x 3.03
HRMS (ESI): calculated for $C_{11}H_{12}N_3S_2^+$ [M+H$^+$]: 250.0467; found: 250.0472
IR ν_{max} (cm^{-1}): 2924 (s), 1408 (m), 1259 (m), 857 (s)

1.5 2-((5,6-dihydro-1,4-dithiin-2-yl)methoxy)pyridine (16)



1 **16**

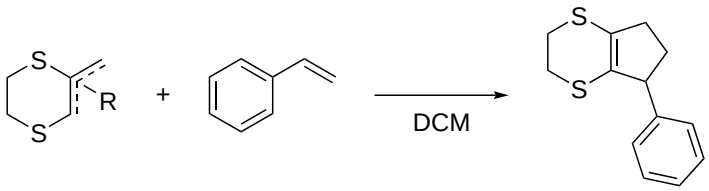
DHDT-methanol **1** (1.31g, 8.84 mmol, 1 equiv.) in THF (15 mL) is added to a suspension of sodium hydride (687 mg, 60% disperion in mineral oil, 10.61 mmol, 1.2 equiv.) in THF (25 mL) at 0°C. Following addition of 2-chloro pyridine (1.25mL, 13.26 mmol, 1.5 equiv.), the reaction mixture is left to reflux for 24h. When all starting material is consumed, as judged by TLC, the reaction is slowly quenched with saturated aqueous sodium bicarbonate. Upon extraction using CH_2Cl_2 (3 x 40mL), the combined layers are washed with brine (20mL) and dried over anhydrous sodium sulfate. The obtained mixture is concentrated *in vacuo* and subjected to pentane-acetonitrile extraction to remove residual mineral oil. The combined acetonitrile phases are concentrated *in vacuo*. Purification via flash chromatography (gradient: 8% to 12% EtOAc in hexanes) results in an inseparable mixture of product **16** and residual 2-chloro pyridine. The latter is removed through co-evaporation with toluene (5 x 15mL), yielding pure title compound **16** (1.19g, 91% yield) as a clear orange oil which solidifies into an amorphous solid upon storage in the freezer.



16

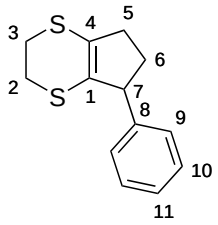
Formula: $C_{10}H_{11}NOS_2$
Molar mass: 225.32 g/mol
R_f (15% ethyl acetate in petroleum ether): 0.60
^{1}H-NMR (400 MHz, $CDCl_3$): δ (ppm): 8.14 (m, 1H, C10-H), 7.57 (m, 1H, C8-H), 6.87 (m, 1H, C9-H), 6.79 (m, 1H, C7-H), 6.37 (s (br), 1H, C1-H), 4.84 (d, 2H, J = 0.8 Hz, C5-H_2), 3.25-3.16 (band, 4H, S$-CH_2-CH_2-$S)
^{13}C-NMR (101 MHz, $CDCl_3$): δ (ppm): 163.4 (C_q6), 146.8 (C10-H), 138.8 (C8-H), 124.1 (C_q4), 117.2 (C9-H), 115.0 (C1-H), 111.5 (C7-H), 70.0 (C5-H_2), 27.0 (S$-CH_2-CH_2-$S), 26.5 (S$-CH_2-CH_2-$S)
HSQC ($CDCl_3$): 146.8 x 8.14, 138.8 x 7.57, 117.2 x 6.87, 115.0 x 6.37, 111.5 x 6.79, 70.0 x 4.84, 27.0 x 3.25-3.16, 26.5 x 3.25-3.16
LCMS (ES): calculated for $C_{10}H_{12}NOS_2^+$ [M+H^+]: 226.0; found: 226.1
IR ν_{max} (cm^{-1}): 2926 (w), 1591 (m), 1425 (s), 1241 (s), 774 (s)

1.6 Screening of different dithioallyl cation precursors



2a

General cycloaddition procedure A solution of the DHDT-building block (0.4 mmol, 1 equiv.) and styrene (69 μL, 0.6 mmol, 1.5 equiv.) is prepared in CH_2Cl_2 (5 mL). To this mixture, the activating agent (1 mmol, 2.5 equiv.) is added at once ($Ga(OTf)_3$ is added in portions) and the reaction mixture is left to stir vigorously. Once all starting material is consumed, as judged by TLC, a satured sodium bicarbonate (5 mL) is added at once. The aqueous phase is separated and extracted using CH_2Cl_2 (3 x 5 mL), after which the combined organic phases are washed using brine (2 mL) and dried over anhydrous sodium sulfate. The resulting crude mixture is purified via flash chromatography using 1% ethyl acetate in petroleum ether, resulting in pure cycloadduct **2a**.



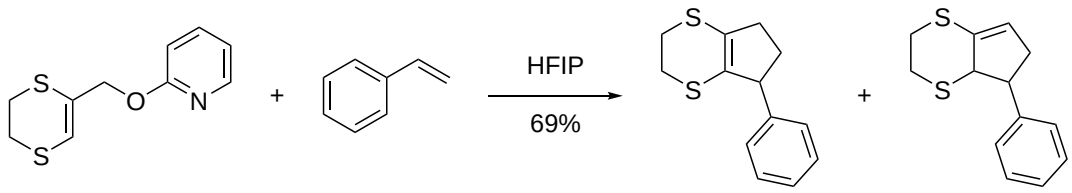
2a

Formula: $C_{13}H_{14}S_2$
Molar mass: 234.38 g/mol
^{1}H-NMR (400 MHz, $CDCl_3$): δ (ppm): 7.34-7.29 (m, 2H, C10-H), 7.25-7.18 (m, 3H, C9-H and C11-H), 3.86 (dd, 1H, J = 8.3, 6.2, 1.8 Hz, C7-H), 3.22-3.10 (band, 4H, S$-CH_2-CH_2-$S), 2.69-2.49 (m, 2H, C5-H_2), 2.47-2.37 (m, 1H, C6-HH), 1.89-1.79 (m, 1H, C6-HH)

Exp.	R-group	Activating agent (AA)	Equiv. AA	Temperature (°C)	Yield (Isolated)
1.[a]	OH	TFA	2	-78 to RT	62%
2.[b]	OH	$Ga(OTf)_3$	0.2	20	21%
3.[b]	OTMS	$Ga(OTf)_3$	0.2	20	33%
4.[c]	OH	$ZnBr_2$	2.5	20	24%
5.	OAc	$ZnBr_2$	2.5	20	51%
6.[c]	*N*-1-benzotriazole	$ZnBr_2$	2.5	20	26%
7.[c]	*N*-2-benzotriazole	$ZnBr_2$	2.5	20	36%
8.[c]	**2-pyridone**	**$ZnBr_2$**	**2.5**	**20**	**96%**
9.	2-pyridone	HFIP	20[d]	20	69%

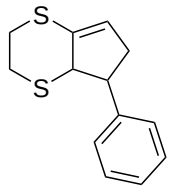
a. Performed by Hullaert and Winne[1]; b. Inspired by Callebaut et al.[3]; c. Inspired by Katritzky[4]; d. Solvent-free experiment

The formation of 5-phenyl-2,3,4a,6-tetrahydro-5H-cyclopenta[b][1,4]dithiine (2a')



16 **2a**
ratio 8:1

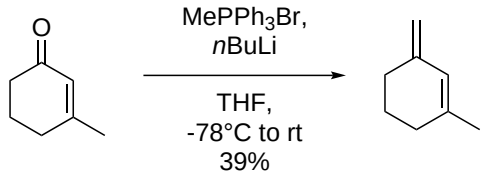
To a mixture of DHDT-pyridone **16** (116.3 mg, 0.516 mmol, 1 equiv.) and styrene (80 μL, 0.774 mmol, 1.5 equiv.), HFIP (0.5 mL, 4.76 mmol, ca. 10 equiv.) is added in a dropwise fashion. When all starting material is consumed, as judged by TLC, the solvent is co-evaporated using chloroform (3 x 0.5 mL). The resulting crude mixture is purified with flash chromatography using a 1% solution of ethyl acetate in petroleum ether, yielding an inseparable mixture of isomers.



^{1}H-NMR (400 MHz, $CDCl_3$): δ (ppm): 7.35-7.18 (band, 5H, $C_{Ar}H$), 5.99 (dt, 1H, J = 2.6, 1.3 Hz), 4.2-4.16 (m, 1H), 3.93-3.86 (dt, 1H, J = 8.8, 6.0 Hz), 3.08-3.00 (m, 1H), 2.97-2.68 (band, 5H)

2 Optimisation and exploration of single-*trans*-locked 1,3-diene substrates

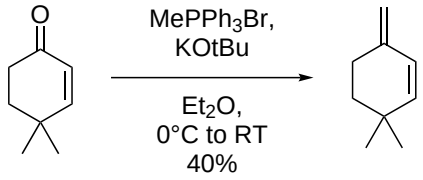
1-methyl-3-methylenecyclohex-1-ene (17)



17

To a suspension of methyltriphenylphosphonium bromide (7.94 g, 22.21 mmol, 1.2 equiv.) in THF (30 mL) at -78°C, *n*BuLi (8.9 mL, 2.5M in hexanes, 22.21 mmol, 1.2 equiv.) is added in a dropwise fashion. The resulting yellow-red suspension is gently warmed to 0°C before being cooled back to -50°C, at which point a cooled solution of 3-methyl-2-cyclohexenone (2.1 mL, 18.51 mmol, 1 equiv.) in THF (10 mL) is added dropwise. The reuslting mixture is allowed to warm to room temperature and is left to stir for 24 hours before being diluted with petroleum ether (40 mL). The phosphine oxides are allowed to settle in the fridge before the organic phase is repeatedly filtered, concentrated and washed with cold petroleum ether to remove residual phosphine oxides. The resulting yellow liquid is filtered over a small plug of silica and eluted with pentane to afford 1-methyl-3-methylene-cyclohexene **17** (923 mg, 39% yield) as a transparent liquid. All obtained spectroscopic data matches the reported literature.[5] This product is stored in the freezer to avoid degradation. Always recheck purity before use!

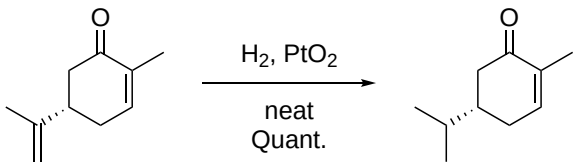
3,3-dimethyl-6-methylenecyclohex-1-ene (18)



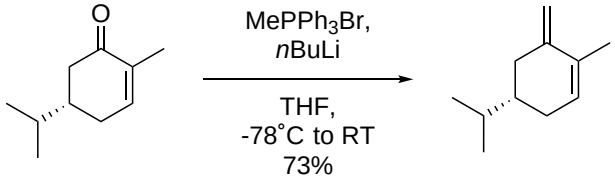
18

Following the procedure outlined by Larsen *et al.*,[6] potassium tert-butoxide (2.04 g, 18.24 mmol, 1.2 equiv.) is added to a suspension of methyltriphenylphosphonium bromide (6.52 g, 18.24 mmol, 1.2 equiv.) in Et_2O (20 ml). The resulting yellow slurry is cooled to 0°C before a solution of 4,4-dimethylcyclohex-2-en-1-one (2 ml, 15.20 mmol, 1 equiv.) in Et_2O (10 ml) is added in a dropwise fashion. The resulting reaction mixture is allowed to warm back to room temperature. After overnight stirring, the mixture is diluted using pentane (60 ml) and filtered over basic alumina, resulting in pure diene **18** as a clear liquid (748 mg, 40% yield). All spectroscopic data matches those reported in literature. This product is stored in the freezer to avoid degradation. Always recheck purity before use!

(S)-4-isopropyl-1-methyl-6-methylenecyclohex-1-ene (19)

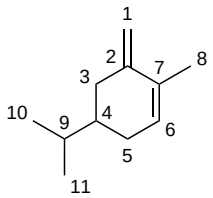


(S)-5-isopropyl-2-methylcyclohex-2-en-1-ene is prepared in a two-step procedure starting from (+)-carvone. Following the procedure of Sorensen,[7] platinum(IV)oxide (45 mg, 0.2 mmol, 0.2 equiv.) is added to (+)-carvone (15.7 ml, 100 mmol, 1.0 equiv.). The reaction mixture is degassed under vacuum before being put under hydrogen atmosphere. Reaction conversion is followed using H-NMR spectroscopy. After 20h, the mixture is filtered through a short pad of silica gel with ethyl acetate to give dihydrocarvone as a light brown oil in quantitative yield, showing experimental properties identical to those reported in literature.



19

To a suspension of methyltriphenylphosphonium bromide (2.83 g, 7.92 mmol, 1.2 equiv.) in anhydrous THF (9 mL) at -78°C, *n*BuLi (3.16 mL, 2.5M in hexanes, 7.92 mmol, 1.2 equiv.) is added in a dropwise fashion. The resulting yellow-red suspension is gently warmed to 0°C before a cooled solution of dihydrocarvone (1.00 g, 6.60 mmol, 1 equiv.) in THF (4 mL) is added dropwise. The resulting mixture is left to stir at room temperature for 24 hours before being diluted with petroleum ether. The phosphine oxides are allowed to settle in the fridge before the organic phase is repeatedly filtrated over celite, concentrated and washed with cold petroleum ether to remove residual phosphine oxides. (S)-4-isopropyl-1-methyl-6-methylenecyclohex-1-ene **19** (0.73 g, 73% yield) is obtained as a transparent oil after filtration over a plug of silica and elution with pentane. This product is stored in the freezer to avoid degradation. Always recheck purity before use!

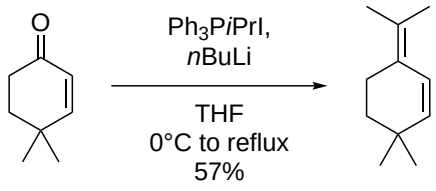


19

Formula: $C_{11}H_{18}$
Molar mass: 150.27 g/mol
R_f (Petroleum ether): 0.91
^{1}H-NMR (400 MHz, $CDCl_3$): δ (ppm): 5.68 (s, 1H, C6-H), 4.86 (s, 1H, C1-*H*H), 4.76 (s, 1H, C1-H*H*), 2.42 (dt, 1H, J = 14.1, 2.1 Hz, C3-*H*H), 2.15 (dt, 1H, J = 17.6, 5.1 Hz, C5-*H*H), 2.04 (dddd, 1H, J = 14.1, 12.1, 2.7, 1.6 Hz, C3-H*H*), 1.93-1.83 (band, 1H, C5-H*H*), 1.81 (s,

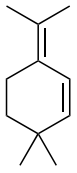
3H, C8-H_3), 1.57-1.37 (band, 1H, C4-H), 1.48 (h, 1H, J = 6.6 Hz, C9-H), 0.91 (d, 3H, J = 6.6 Hz, C10/11), 0.89 (d, 3H, J = 6.6 Hz, C10/11)
^{13}C-NMR (101 MHz, $CDCl_3$): δ (ppm): 145.6 (C_q7), 132.6 (C_q2), 128.3 (C6-H), 107.8 (C1-H_2), 41.3 (C9-H), 36.2 (C3-H_2), 32.2 (C4-H), 30.2 (C5-H_2), 20.1 (C8-H_3), 19.8 (C10/11-H_3), 19.4 (C10/11-H_3)
HSQC ($CDCl_3$): 128.3 x 5.68, 107.8 x 4.86, 107.8 x 4.76, 41.3 x 1.48, 36.2 x 2.42, 36.2 x 2.04, 32.2 x 1.57-1.37, 30.2 x 2.15, 30.2 x 1.93-1.83, 20.1 x 1.81, 19.8 x 0.91/0.89, 19.4 x 0.91/0.89
GCMS (EI) [m/z]*:* peak (at 9.80): 150 ($M^{+\bullet}$, 48), 135 ($M^{+\bullet}$ – CH_3, 36), 121 ($M^{+\bullet}$ – C_2H_5, 17), 107 ($M^{+\bullet}$ – C_3H_7, 100), 91 ($M^{+\bullet}$ – C_4H_{11}, 83), 79 ($M^{+\bullet}$ – C_5H_{11}, 83)
IR ν_{max} (cm^{-1}): 2955 (m), 1606 (m), 1438 (m), 1366 (m), 885 (s), 873 (s)

2.1 4,4,6',6'-tetramethyl-2',3',6',7'-tetrahydrospiro[cyclohexane-1,5'-cyclopenta[b][1,4]-di-thiin]-2-ene (21)



20

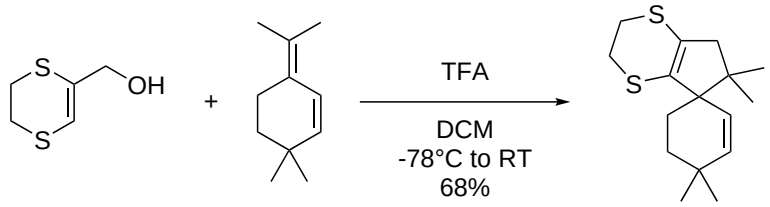
The title compound **21** is prepared in a two-step procedure starting from 4,4-dimethylcyclohex-2-en-1-one. Isopropyltriphenylphosphonium iodide (1.73 g, 4 mmol, 1.2 equiv.) is suspended in anhydrous THF (5 ml) and cooled to 0°C. A solution of *n*-butyllithium (2 ml, 5 mmol, 2.5M in hexanes, 1.5 equiv.) is added dropwise and the mixture is allowed to warm up to room temperature. After 30 min, a solution of 4,4-dimethylcyclohex-2-en-1-one (0.44 ml, 3.3 mmol, 1 equiv.) in anhydrous THF (2 ml) is added dropwise and the resulting mixture is heated to reflux conditions. After 3 h, the reaction mixture is cooled to room temperature before being diluted with petroleum ether (7 ml). The phosphine oxides are allowed to settle for 24 h in the fridge before the organic phase is repeatedly filtrated over celite, concentrated *in vacuo*. 3,3-dimethyl-6-(propan-2-ylidene)cyclohex-1-ene **20** is obtained as a transparent liquid after filtration over a plug of silica using pentane (355 mg, 80 m% in pentane, 57% yield).



20

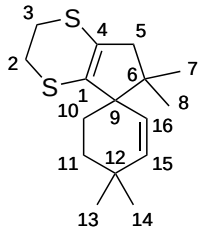
Formula: $C_{11}H_{18}$
Molar mass: 150.27 g/mol
R_f (Petroleum ether): 0.82
^{1}H-NMR (400 MHz, $CDCl_3$): δ (ppm): 6.31 (d, 1H, J = 10.1 Hz, –C*H*=CH –), 5.46 (d, 1H, J = 10.1 Hz, –CH=C*H* –), 2.34 (t(br), 2H, J = 6.5 Hz, –C=C–CH_2), 1.78 (s, 3H, –CH_3), 1.75 (s, 3H, –CH_3), 1.50 (t(br), 2H, J = 6.5 Hz, =C–CH_2–C*H*$_2$ –), 1.01 (s, 6H,

$CH_3-C_q-CH_3$)
^{13}C-NMR (101 MHz, $CDCl_3$): δ (ppm): 138.8 (C_q), 137.1 (CH), 127.1 (CH), 126.2 (C_q), 122.8 (C_q), 36.9 (CH_2), 29.0 (CH_3), 23.3 (CH_2), 20.5 (CH_3), 19.5 (CH_3)



1 **20** **21**

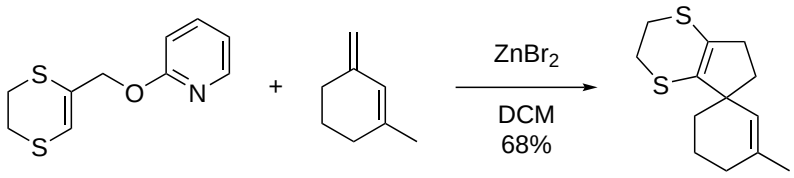
A solution of DHDT-methanol **1** (74 mg, 0.5 mmol, 1 equiv.) and diene **20** (141 mg, 0.75 mmol, 80 m% in pentane, 1.5 equiv.) in anhydrous CH_2Cl_2 (5) is prepared and cooled to -78°C. A fresh solution of trifluoroacetic acid (76 μL, 1 mmol, 2.0 equiv.) in CH_2Cl_2 (0.5 ml) is prepared and added dropwise before the cooled mixture is allowed to warm back up to room temperature. When all starting material is consumed, as judged by TLC, a saturated solution of sodium bicarbonate (5 ml) is added at once. The layers are separated and the aqueous phase is extracted using CH_2Cl_2 (3 x 5 ml). The combined organic phases are washed with brine (2 ml) and dried over anhydrous sodium sulfate. After removal of the solvent *in vacuo*, pure title compound **21** is obtained as an amorphous solid after flash chromatography using 10% EtOAc in petroleum ether (96 mg, 68% yield).



21

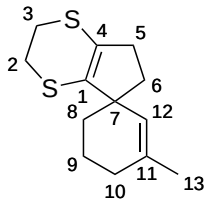
Formula: $C_{16}H_{24}S_2$
Molar mass: 280.49 g/mol
R_f (10% ethyl acetate in petroleum ether): 0.90
^{1}H-NMR (400 MHz, $CDCl_3$): δ (ppm): 5.59 (d(AB), 1H, J = 10.2 Hz, $-CH{=}CH-$), 5.28 (d(AB), 1H, J = 10.2 Hz, $-CH{=}CH-$), 3.17-3.09 (band, 4H, $S-CH_2-CH_2-S$), 2.30 (d(AB), 1H, J = 14.7 Hz, $SC{=}CHH-$), 2.16 (d(AB), 1H, J = 14.7 hz, $SC-CHH$), 1.70-1.56 (band, 3H, $(Me)_2C-CH_2-CHH$), 1.52-1.41 (m, 1H, $(Me)_2C-CH_2-CHH$), 1.03 (s, 3H, $-CH_3$), 1.01 (s, 3H, $-CH_3$), 0.99 (s, 3H, $-CH_3$), 0.96 (s, 3H, $-CH_3$)
^{13}C-NMR (101 MHz, $CDCl_3$): δ (ppm): 139.4 (CH), 128.8 (C_q), 127.0 (CH), 120.0 (C_q), 56.1 (C_q), 50.4 (CH_2), 43.8 (C_q), 34.8 (CH_2), 30.8 (C_q), 29.6 (CH_3), 29.3 (CH_3), 27.2 (CH_2), 27.1 (CH_2), 25.0 (CH_3), 24.7 (CH_3), 24.0 (CH_2)
HRMS (ESI): calculated for $C_{16}H_{25}S_2^+$ [M+H$^+$]: 281.1392; found: 281.1403

2.2 3-methyl-2',3',6',7'-tetrahydrospiro[cyclohexane-1,5'-cyclopenta[b][1,4]dithiin]-2-ene (22)



16 **17** **22**

To a solution of DHDT-pyridone **16** (80 mg, 0.392 mmol, 1 equiv.) and 1-methyl-3-methylene-cyclohexene **17** (58 mg, 0.566 mmol, 1.5 equiv.) in CH_2Cl_2 (5 ml), anhydrous zinc bromide (209 mg, 0.930 mmol, 2.37 equiv.) is added. After stirring for 1 hour at room temperature, TLC-analysis shows no presence of substrate, at which point the reaction mixture is quenched using a saturated solution of sodium bicarbonate (5 ml). The precipitates are filtered off before the organic layer is extracted using CH_2Cl_2 (3 x 5 ml). The combined organic layers are washed with brine (2 ml), dried over anhydrous sodium sulfate and concentrated *in vacuo*. The resulting crude is subjected to flash chromatography (1% to 2% EtOAc in petroleum ether) to yield pure cycloadduct **22** (68 mg, 94% pure, 68% yield) as a thick oil.

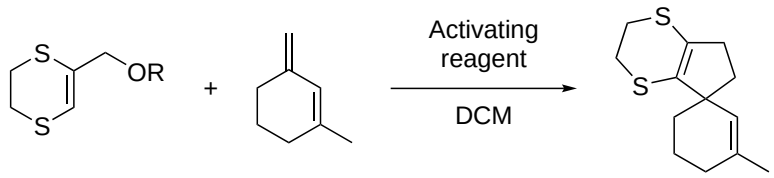


22

Formula: $C_{13}H_{18}S_2$
Molar mass: 238.41 g/mol
R_f (Petroleum ether): 0.25
^{1}H-NMR (500 MHz, $CDCl_3$): δ (ppm): 5.14 (s, 1H, C12-H), 3.16-3.06 (m, 4H, S$-CH_2-CH_2-$S), 2.49-2.42 (dt, 1H, J = 15, 7.9 Hz, C5-HH), 2.39-2.33 (ddd, 1H, J = 15, 8.8, 3.4 Hz, C5-HH), 1.98-1.89 (band, 1H, C10-HH), 1.85-1.71 (band, 4H, C6-H_2 and C9-HH and C10-HH), 1.68 (s, 3H, C13-H_3), 1.63 (dd, 1H, J = 12.3, 2.5 Hz, C8-HH), 1.60-1.54 (band, 1H, C9-HH), 1.50-1.45 (band, 1H, C8-HH)
^{13}C-NMR (125 MHz, $CDCl_3$): δ (ppm): 135.9 (C_q11), 130.3 (S-C=C-S), 127.6 (C12-H), 120.7 (S-C=C-S), 53.5 (C_q7), 36.7 (C6-H_2), 35.3 (C5-H_2), 31.5 (C8-H_2), 29.8 (C10-H_2), 27.2 (S$-CH_2-CH_2-$S), 26.8 (S$-CH_2-CH_2-$S), 24.1 (C13-H_3), 20.9 (C9-H_2)
HSQC ($CDCl_3$): 127.6 x 5.14, 36.7 x 1.85-1.71, 35.3 x 2.49-2.42, 35.3 x 2.39-2.33, 31.5 x 1.63, 31.5 x 1.50-1.45, 29.8 x 1.98-1.89, 29.8 x 1.85-1.71, 27.2 x 3.16-3.06, 26.8 x 3.16-3.06, 24.1 x 1.68, 20.9 x 1.85-1.71, 20.9 x 1.60-1.54
HRMS (ESI): [m/z]: [M+H^+] calculated: 239.0923; found: 239.0926
IR ν_{max} (cm^{-1}): 2918 (s), 2845 (m), 1587 (w), 1437 (m), 1412 (m), 1374 (w), 1285 (m), 1162 (w), 1117 (w), 1088 (w), 915 (m), 834 (m), 738 (m)

Screening of different dithioallyl cation precursors

To our delight, we found that the expected spirocyclic product 22 could be obtained from diene 17 using the new aprotic reaction conditions (see table below, entry 3). For comparison, not a trace of the cycloadduct can be observed after reaction under normal protic reaction conditions (entry 1). Other aprotic reaction conditions also gave some of the expected spirocyclic adduct, but with much lower efficiency (entry 2).

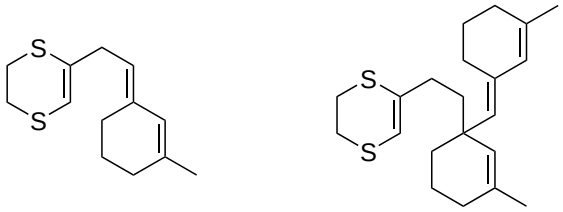


17 **22**

Experimental procedure DHDT-cation precursor (1 equiv.) and diene **17** (1.5 equiv.) are dissolved in CH_2Cl_2 (0.66 M) at 20°C. A freshly prepared solution of TFA (2 equiv.) in CH_2Cl_2 (1/10th of the cation precursor-styrene solution) is added dropwise, or the solid activating reagent is added in one portion. When the DHDT-compound is consumed, as judged by TLC, the reaction is quenched using an equal volume of saturated aqueous sodium bicarbonate. Next, the phases are separated and the aqueous phase is extracted using CH_2Cl_2 (3 x reaction volume). The combined organic phases are washed with a saturated brine solution (1/10th of the combined organic phases) before being dried over anhydrous sodium sulfate. The mixture is subject to flash chromatography (gradient: 1% to 2% EtOAc in petroleum ether) to yield cycloadduct **22** as a viscous oil.

Exp.	**R-group**	**Activating Agent**	**Diene conversion**
1.	-OH	TFA	0% (Polymers)
2.	-OTMS	$Ga(OTf)_3$	26% (Impure)
3.	-O(2-Pyr)	$ZnBr_2$	51% (pure, 68% yield)

*Entry 2. resulted in an inseparable mixture of adduct **22** together with multiple side products, of which the GCMS-results are described below:*



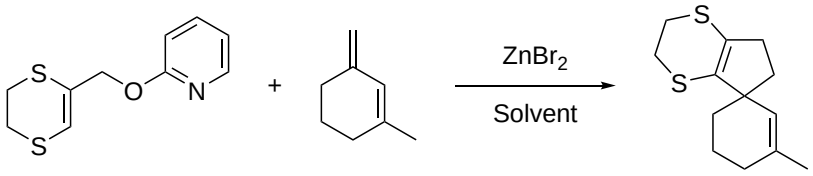
22a **22b**

GCMS (EI): Compounds 22 + 48: *major peak* (at 15.58): m/z 238 ($M^{+\bullet}$, 27), 223 ($M^{+\bullet}$ – CH_3, 100); *minor peak 1* (at 15.95): m/z 238 ($M^{+\bullet}$, 100), 223 ($M^{+\bullet}$ – CH_3, 4), 210 ($1^{+\bullet}$ – C_2H_4, 4), 182 ($1^{+\bullet}$ – C_4H_8, 73), 167 ($1^{+\bullet}$ – C_5H_{11}, 61); *minor peak 2* (at 16.11): m/z 238 ($M^{+\bullet}$, 23), 170 ($M^{+\bullet}$ – C_5H_8, 100); **Compound 49:** *minor peak 1* (at 19.54): m/z 346 ($M^{+\bullet}$, 10), 109 ($C_8H_{13}^+$, 100); *minor peak 2* (at 19.63): mz 346 ($M^{+\bullet}$, 8), 223 ($C_{12}H_{15}S_2^+$, 13), 109 ($C_8H_{13}^+$, 100); *minor peak 3* (at 19.87): m/z 346 ($M^{+\bullet}$, 17), 223 ($C_{12}H_{15}S_2^+$, 100); *minor peak 4* (at 19.90): m/z 346 ($M^{+\bullet}$, 67), 331 ($M^{+\bullet}$ – CH_3, 100), 109 ($C_8H_{13}^+$, 63); *minor peak 5* (at 19.94): m/z 346 ($M^{+\bullet}$, 65), 331 ($M^{+\bullet}$ – CH_3, 100), 223 ($C_{12}H_{15}S_2^+$, 69), 170 ($C_8H_{10}S_2^+$, 21), 109 ($C_8H_{13}^+$, 55); *minor peak 6* (at 20.20): m/z 346 ($M^{+\bullet}$, 8), 109 ($C_8H_{13}^+$, 100); *minor peak 7* (at 20.56): m/z 346 ($M^{+\bullet}$, 100), 238 ($C_{13}H_{18}S_2^+$, 23), 223 ($C_{12}H_{15}S_2^+$, 17), 209 ($C_{11}H_{13}S_2^+$, 21), 183 ($C_9H_{11}S_2^+$, 59), 170 ($C_8H_{10}S_2^+$, 69), 109 ($C_8H_{13}^+$, 52)

Due to the high sensitivity of the exocyclic diene motif, reaction optimisation is aimed at maximizing substrate conversion into the corresponding spiroadduct. Initial substrate concentration and zinc bromide equivalents mimic procedures outlined by Katritzky *et al.*[4], while the DHDT-pyridone:substrate ratio imitates previous in-house experiments.[1] We next optimised these parameters to achieve a reliable and high conversion of the diene.

Optimisation of various reaction parameters with the aim to maximize diene conversion and spirocyclic adduct yield

While initial reaction conditions employ an excess of substrate, the reactive diene motif can generally be considered as the most valuable element in this synthetic transformation, and the dithioallyl precursor is a reagent. Optimizing the reaction conditions was consequently aimed at maximizing conversion of diene into the corresponding spiroadduct.



17 **22**

Experimental procedure A A solution of DHDT-pyridone **16** and 1-methyl-3-methylenecyclohexene (1 equiv.) in acetonitrile is prepared. The total volume of acetonitrile is such that the final diene concentration is 0.1 M. To this solution, solid zinc bromide salts are added in one portion, discoloring to a dark brown shortly after addition. When all starting material is consumed, as judged by TLC, the reaction mixture is quenched using saturated sodium bicarbonate. Following extraction using CH_2Cl_2, the combined organic phases are washed using brine and dried over sodium sulfate. NMR yield is determined using 1,3,5-trimethoxybenzene

as an internal NMR-standard.

Experimental procedure B A mixture of 1-methyl-3-methylene-cyclohexene (1 equiv.) and zinc bromide salts is suspended in acetonitrile (2/3 of total volume), resulting in a cloudy white reaction mixture. The total volume of acetonitrile is such that the final diene concentration is 0.1 M. To this, DHDT-pyridone **16** in acetonitrile (1/3 of total volume) is added in a dropwise fashion, turning more transparent as the addition goes on. When all starting material is consumed, as judged by TLC, the reaction mixture is quenched using saturated sodium bicarbonate. Following extraction using CH_2Cl_2, the combined organic phases are washed using brine and dried over sodium sulfate. NMR yield is determined using 1,3,5-trimethoxybenzene as an internal NMR-standard.

Exp.	DHDT (16) (Equiv.)	$ZnBr_2$ (Equiv.)	Solvent (0.1M diene)	Temp. (°C)	Time (h)	Procedure	NMR yield[a]
3.	0.67	1.67	CH_2Cl_2	20	0.5	A	51%
4.	0.67	1.67	ACN	20	0.5	A	53%
5.	0.67	1.67	Toluene	20	2.5	A	3%
6.	0.67	1.67	THF	20	24	A	20%
7.	0.67	1	ACN	20	0.5	A	47%
8.	0.67	0.74	ACN	20	0.5	A	27%
9.	0.67	0.33	ACN	20	4	A	27%
10.	0.67	0.067	ACN	20	24	A	14%
11.	1	1.1	ACN	20	0.5	A	49%
12.	1	1.5	ACN	20	0.5	A	55%
13.	1.5	1.65	ACN	20	0.5	A	61%
14.	1.5	2.25	ACN	20	0.5	A	57%
15.	1.5	1.65	ACN	20	0.5	B	63%
16.[b]	1.5	1.65	ACN	20	0.5	B	52%
17.[c]	1.5	1.65	ACN	0	0.5	B	47%
18.[d]	1.5	1.65	ACN	0	0.5	B	43%
19.	1.5	1.65	ACN	30	0.5	B	41%
20.	1.5	1.65	ACN	40	0.5	B	32%
21.	1.5	1.65	ACN	50	0.5	B	24%
22.[e]	**1.5**	**1.65**	**ACN**	**20**	**0.5**	B	**66%**
23.[f]	1.5	1.65	ACN	20	0.5	B	46%
24.[g]	1.5	1.65	ACN	20	0.5	B	51%
25.[h]	1.5	1.65	ACN	20	0.5	B	44%
26.[i]	1.5	1.65	ACN	20	0.5	B	57%

*a. Diene conversion into spiroadduct; b. Addition of cation precursor **16** over a 30' period; c. Reaction flask immediately removed from ice bath once DHDT-pyridone **16** is added; d. Reaction flask is allowed to warm up slowly in the ice bath; e. Diene addition using 10:1 acetonitrile:CH_2Cl_2; f. Diene addition using anhydrous hexane; g. Total diene concentration is 0.05 M; h. Contains 1 equivalent of 2-pyridone as chain stopper; i. Fresh batch of zinc bromide salts used*

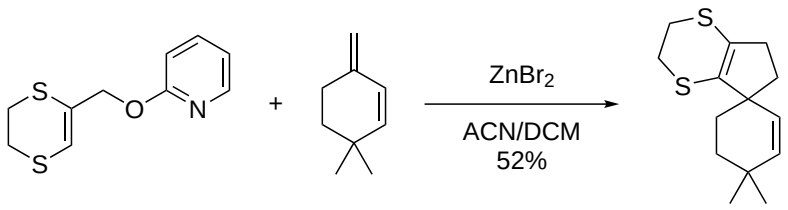
In experiments 3-5, it was noted that the added zinc bromide salts does not fully dissolved until several minutes after addition. Using THF in entry 6 attempted to homogenise the reaction mixture immediately.
Entries 7 and 8, although not performing equally well, require the same reaction time to fully

consume all diene starting material (based on TLC analysis). This observation led to vary both diene-to-DHDT ratios, from which the best results were obtained through condition 13.

We next switched our experimental protocol. In experimental procedure A, the Lewis acid is added last, while in procedure B the dithioallyl cation precursor **16** is added last.

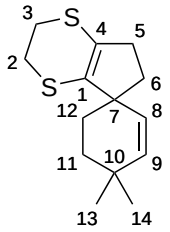
At low reaction temperatures (entries 17-18), the reaction mixture remains cloudy.
Increasing the reaction temperatures increasingly favors competitive diene polymerisation over spiroadduct formation: entries 19-21 each resulted in progressively more discolored reaction mixtures at the time of quenching, with NMR-analysis of the corresponding crude showing increased formation of oligomeric side products.
Finally, some minor variations to experimental procedure B were explored. Typically, hydrocarbons show decreased solubility in ACN, potentially resulting in incomplete transfer and uptake of diene **17** into the reaction flask. Employing CH_2Cl_2 (entry 23) results in a slightly higher conversion.
To suppress the loss of diene starting material to competitive polymerisation reactions, increased dilution of the reaction mixture (entry 24) or adding a chain stopper (entry 25) were employed.

2.3 4,4-dimethyl-2',3',6',7'-tetrahydrospiro[cyclohexane-1,5'-cyclopenta[b][1,-4]dithiin]-2-ene (23)



16 **17** **23**

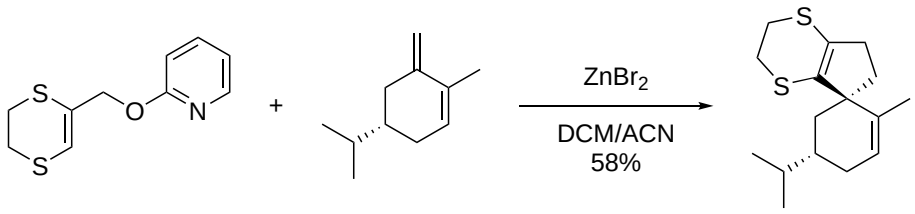
To a suspension zinc bromide (456 mg, 2.03 mmol, 1.65 equiv.) in acetonitrile (4 mL) is added a solution of 3,3-dimethyl-6-methylenecyclohex-1-ene (150 mg, 1.23 mmol, 1 equiv.) in acetonitrile (4 mL) and CH_2Cl_2 (0.4 mL). A solution of DHDT-pyridone **16** (415 mg, 1.84 mmol, 1.5 equiv.) in acetonitrile (4 mL) is prepared and added dropwise, resulting in a transparent reaction mixture. After 2h, no more DHDT-pyridone **16** is observed on TLC and a second portion (100 mg, 0.44 mmol, 0.38 equiv.) is added. After further 6h, when all diene starting material is consumed as judged by TLC, saturated aqueous sodium bicarbonate (12 mL) is added. Both phases are separated and the aqueous phase is extracted using CH_2Cl_2 (3 x 12 mL). The combined organic phases are washed using brine (5 mL) and dried over anhydrous sodium sulfate. Following concentration *in vacuo*, flash chromatography using 1% EtOAc in pentane affords pure title compound **23** as a white, amorphous solid (168 mg, 52% yield).



23

Formula: $C_{14}H_{20}S_2$
Molar mass: 252.43 g/mol
R_f (5% EtOAc in petroleum ether): 0.66
^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm): 5.52 (dd, 1H, J = 9.9 Hz, 1.2 Hz, C9-H), 5.27 (dd, 1H, J = 9.9, 1.1 Hz, C8-H), 3.17-3.08 (m, 4H, S–CH_2–CH_2–S), 2.54-2.32 (band, 2H, C5-H_2), 1.94-1.68 (band, 3H, C6-H_2 and C12-*H*H), 1.60-1.38 (band, 3H, C11-H_2 and C12-H*H*), 1.01 (s, 3H, C13-H_3), 0.97 (s, 3H, C14-H_3)
^{13}C-NMR (75 MHz, $CDCl_3$): δ (ppm): 139.1 (C9-H), 130.7 (C8-H), 129.4 (C_q1), 121.3 (C_q4), 53.3 (C_q7), 36.2 (C6-H_2), 35.4 (C5-H_2), 35.2 (C11-H_2), 31.4 (C_q10), 30.7 (C14-H_3), 28.8 (C12-H_2), 28.5 (C13-H_3), 27.3 (S–CH_2–CH_2–S), 26.8 (S–CH_2–CH_2–S)
HSQC ($CDCl_3$): 139.1 x 5.52, 130.7 x 5.27, 36.2 x 1.94-1.68, 35.4 x 2.54-2.32, 35.2 x 1.60-1.38, 30.7 x 0.97, 28.8 x 1.94-1.68, 28.8 x 1.60-1.38, 28.5 x 1.01, 27.3 x 3.17-3.08, 26.8 x 3.17-3.08
HRMS (ESI): [m/z]: calculated for $C_{14}H_{21}S_2^+$ [M+H$^+$]: 253.1079; found: 253.1080
IR ν_{max} (cm^{-1}): 2950 (s), 2918 (s), 1585 (w), 1464 (m), 1174 (m), 851 (m), 778 (s)

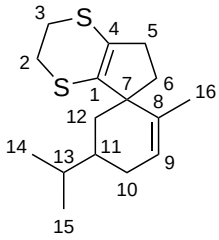
2.4 (1R,5S)-5-isopropyl-2-methyl-2',3',6',7'-tetrahydrospiro[cyclohexane-1,5'-cyclopenta-[b][1,4]dithiin]-2-ene (24)



16 **19** **24**
dr 95:5

To a suspension of zinc bromide (115 mg, 0.509 mmol, 1.63 equiv.) in acetonitrile (2 mL) is added a solution of (S)-4-isopropyl-1-methyl-6-methylenecyclohex-1-ene **19** (47 mg, 0.312 mmol, 1 equiv.) in acetonitrile (1 mL) and CH_2Cl_2 (0.2 mL), followed by the dropwise addition of DHDT-pyridone **16** (101 mg, 0.448 mmol, 1.44 equiv.) in acetonitrile (1 mL). When monitoring the reaction via TLC shows the presence of diene **19** in the absence of any DHDT-pyridone **16**, a subsequent portion of DHDT-pyridone **16** (50 mg, 0.225 mmol, 0.75 equiv.) in acetonitrile (0.5 ml) is added dropwise. In total, 4 of these portions are added over a total reaction time of 72 h. When all diene **19** is consumed, as judged by TLC, the reaction mixture is quenched with saturated aqueous sodium bicarbonate (5 mL) and extracted using CH_2Cl_2 (3 x 5 mL). The combined organic phases are washed using brine (2 mL) and dried over anhydrous sodium sulfate. The resulting crude is purified via flash chromatography (gradient: 0% to 2% ethyl acetate in pentane), resulting in pure cycloadduct **24** (50 mg, 58% yield), an amorphous solid,

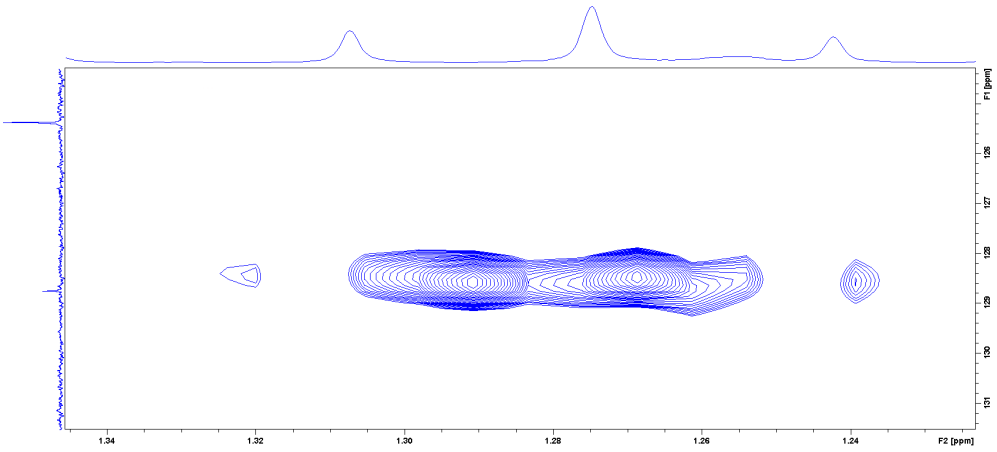
as the clear main diastereomer, integrating for 95%. A small peak which can tentatively be assigned to a diastereomer integrated for only 5%. Assignment of this minor impurity was not possible due to its low intensity, but it is likely to be the diastereomer.

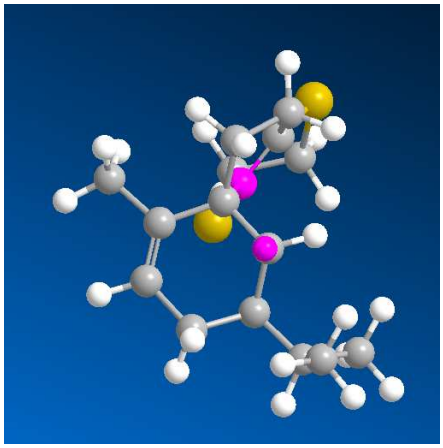


24

Formula: $C_{16}H_{24}S_2$
Molar mass: 280.49 g/mol
R_f (Petroleum ether): 0.26
^{1}H-NMR (400 MHz, $CDCl_3$): δ (ppm): 5.58 (dt, 1H, C9-H, J = 5.7, 1.4 Hz), 3.23-3.00 (m, 4H, S$-CH_2-CH_2-$S), 2.56-2.39 (band, 2H, C5-H_2), 2.10 (ddd, 1H, C6-*H*H, J = 12.9, 8.7, 4.9 Hz), 2.04 (m(br), 1H, C10-*H*H), 1.94 (dt, 1H, C12-*H*H, J = 13.0, 2.5 Hz), 1.77 (m(br), 1H, C11-H), 1.63 (m, 2H, C6-H*H* + C10H*H*), 1.59 (s(br), 3H, C16-H_3)), 1.39 (sx, 1H, C13-H, J = 6.7 Hz), 1.28 (t, 1H, C12-H*H*, J = 13.1 Hz), 0.89 (d, 3H, C14/15-H_3, J = 6.7 Hz), 0.86 (d, 3H, C14/15-H_3, J = 6.7 Hz)
^{13}C-NMR (101 MHz, $CDCl_3$): δ (ppm): 136.9 (C_q8), 128.7 (C_q1), 125.4 (C9-H), 121.4 (C_q4), 57.0 (C_q7), 42.2 (C12-H_2), 38.4 (C11-H), 36.6 (C5-H_2), 36.3 (C6-H_2), 32.7 (C13-H), 29.3 (C10-H_2), 27.3 (S$-CH_2-CH_2-$S), 27.2 (S$-CH_2-CH_2-$S), 20.1 (C14/15-H_3), 19.6 (C14/15-H_3), 19.0 (C16-H_3)
HSQC ($CDCl_3$): 125.4 x 5.58, 42.2 x 1.94, 42.2 x 1.28, 38.4 x 1.77, 36.6 x 2.56-2.39, 36.3 x 2.10, 36.3 x 1.63, 32.7 x 1.39, 29.3 x 2.04, 29.3 x 1.63, 27.3 x 3.23-3.00, 27.2 x 3.23-3.00, 20.1 x 0.89, 19.6 x 0.86, 19.0 x 1.59
HRMS (ESI): [m/z]: Calculated for $C_{16}H_{25}S_2^+$ [M+H^+]: 281.1392; found: 281.1386
IR ν_{max} (cm^{-1}): 2950 (s), 2908 (s), 1584 (m), 1439 (m), 1362 (m), 1282 (m), 1043 (w), 918 (s), 835 (s)

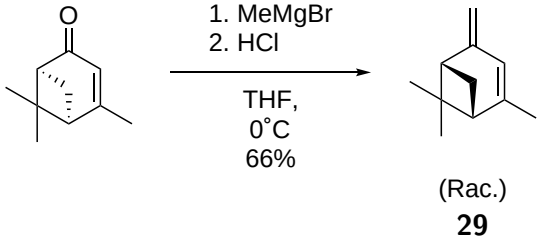
Important HMBC signal: 128.7 x 1.28



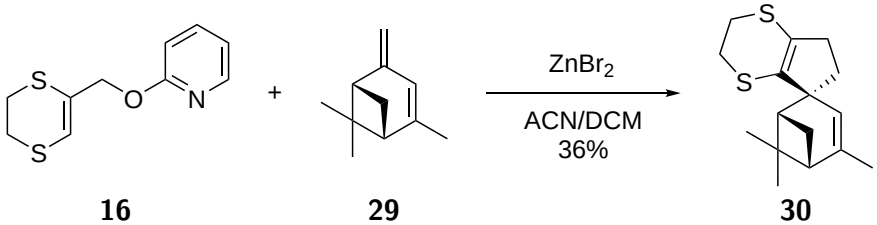


This observed cross-peak (^{4}J-coupling between the pink highlighted hydrogen and carbon atoms) can only occur when their respective bond angle nears to 180°. This determines the quaternary spirocenter to be substituted as shown above.

2.5 (1R,2R,5R)-4,6,6-trimethyl-2',3',6',7'-tetrahydrospiro[bicyclo[3.1.1]heptane-2,5'-cyclopenta[b][1,4]dithiin]-3-ene (30)

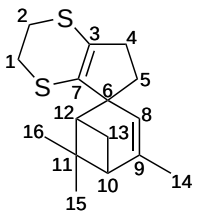


The title compound **30** is prepared in a two-step procedure starting from verbenone. (-)-Verbenone (5.2 mL, 33.93 mmol, 1 equiv.) is dissolved in freshly distilled THF (60 mL) and is placed in an ice bath at 0°C. A commercial solution of methyl magnesium bromide (3 M, 17 mL, 51 mmol, 1.5 equiv.) is added dropwise and the mixture is left to stir for 1.5 h, allowing the reaction mixture and ice bath to heat up slowly to room temperature. The resulting solution is poured into a vigorously stirred solution of aqueous HCl (1 M, 60 mL) and immeadiately extracted three times using CH_2Cl_2 (3x 60 mL). The combined organic phases are washed with brine (30 mL) and dried over anhydrous sodium sulfate. Upon filtration to the salts and removal of the solvent, the resulting oil is filtered over silica using pentane to obtain pure, racemic 2,6,6-trimethyl-4-methylenebicyclo[3.1.1]hept-2-ene **29** as a transparant colorless liquid (3.57 g, 66% yield). All spectroscopic data matches those reported in literature.[8]



Zinc bromide (927 mg, 4.12 mmol, 1.65 equiv.) is suspended with racemic diene **50** (370 mg,

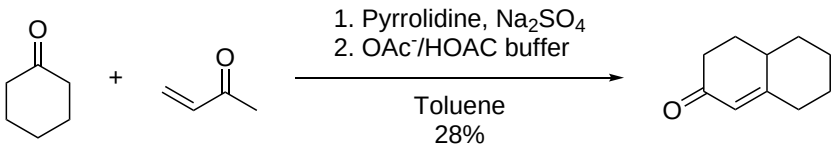
2.5 mmol, 1 equiv.) in a mixture of acetonitrile (17 mL) and CH_2Cl_2 (2 mL). To this opaque white suspension is added a solution of DHDT-pyridone **16** (844 mg, 3.74 mmol, 1.5 equiv.) in acetonitrile (8 mL) in a dropwise fashion, resulting in a transparent reaction mixture. When all diene starting material is consumed, as judged by TLC, the reaction mixture is quenched using saturated aqueous sodium bicarbonate (25 mL) and extracted with CH_2Cl_2 (3 x 25 mL). The combined organic phases are washed with brine (10 mL) and dried over anhydrous sodium sulfate. Removal of the solvent and purification via flash chromatography (0% - 5% EtOAc in pentane) results in cycloadduct **30** (200.1 mg, 36% yield) as an amorphous solid.



30

Formula: $C_{16}H_{22}S_2$
Molar mass: 278.47 g/mol
R_f (5% ethyl acetate in petroleum ether): 0.71
^{1}H-NMR (400 MHz, $CDCl_3$): δ (ppm): 5.11 (s (br), 1H, C8-H), 3.23-2.97 (band, 4H, S−CH_2−CH_2−S), 2.47-2.38 (m, 1H, C4-*H*H), 2.37-2.28 (band, 2H, C4-H*H* and C??), 2.09 (td, 1H, J = 5.9, 1.7 Hz, C10/12-H), 1.98 (ddd, 1H, J = 12.7, 8.1, 3.5 Hz, C??), 1.93-1.85 (m, 2H, C???), 1.89 (t, 1H, J = 8.8 Hz, C???), 1.73 (s, 3H, C14-H_3), 1.30 (s, 3H, C15/16-H_3), 0.96 (s, 3H, C15/16-H_3)
^{13}C-NMR (101 MHz, $CDCl_3$): δ (ppm): 145.3 (C_q??), 129.1 (C_q3/7), 122.8 (C8-H), 122.4 (C_q3/7), 60.2 (C_q6), 51.0 (C10/12-H), 47.3 (C10/12-H), 44.0 (C_q11), 35.5 (C4-H_2), 34.8 (C5/13-H_2), 31.9 (C5/13-H_2), 27.4 (S−CH_2−CH_2−S or C15/16-H_3), 27.3 (S−CH_2−CH_2−S or C15/16-H_3), 27.2 (S−CH_2−CH_2−S or C15/16-H_3), 24.3 (C15/16-H_3), 23.3 (C15/16-H_3)
HSQC ($CDCl_3$): 122.8 x 5.11, 51.0 x 2.09, 47.3 x 1.93-1.85 or 1.89, 35.5 x 2.47-2.38, 35.5 x 2.37-2.28, 34.8 x 1.98, 34.8 x 1.93-1.85 or 1.89, 31.9 x 2.37-2.28, 31.9 x 1.93-1.85 or 1.89, 27.4 x 3.23-2.97 or 1.30, 27.3 x 3.23-2.97 or 1.30, 27.2 x 3.23-2.97 or 1.30, 24.3 x 0.96, 23.3 x 1.73
HRMS (ESI): [m/z]: calculated for $C_{16}H_{23}S_2^+$ [M+H^+]: 279.1236; found: 279.1230
IR ν_{max} (cm^{-1}): 2911 (s), 1737 (m), 1582 (m), 1342 (m), 1237 (s), 1129 (w), 821 (w)

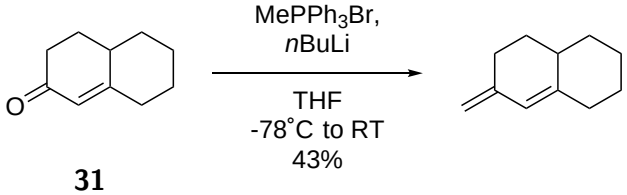
2.6 2,3,4',4a',5',6,6',7,7',8'-decahydro-3'H-spiro[cyclopenta[b][1,4]-dithiine-5,-2'-naphthalene] (32)



31

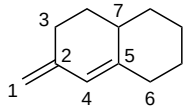
The title compound **32** is prepared in a three-step procedure starting from cyclohexanone. Following a slightly modified procedure of Yasui *et al.*,[9] pyrrolidine (12.09 mL, 144.88 mmol, 1.2 equiv.) is added to a solution of cyclohexanone (12.5 mL, 120.73 mmol, 1 equiv.) in anydrous

toluene (120 mL). The resulting mixture is refluxed overnight with a Dean-Stark trap. The solvent is removed *in vacuo*, and the supernatant is separated from the brown solids to be redissolved in anhydrous toluene (175 mL). To this vigorously stirred solution, methyl vinyl ketone (10.28 mL, 126.77 mmol, 1.05 equiv.) is added. After overnight refluxing, a buffer of NaOAc (5.12 g), AcOH (10.2 mL) en H_2O (10.2 mL) is added and refluxing is continued for 4 hours. The organic layer is seperated and subsequently washed with 1M HCl (175 mL), saturated sodium bicarbonate (175 mL), and brine (20 mL), before being dried over anhydrous sodium sulfate. The obtained solution is concentrated *in vacuo* before being purified via flash chromatography using 15% MTBE in petroleum ether. 4,4a,5,6,7,8-hexahydronaphthalen-2(3H)-one **31** (5.02 g, 28% yield) is obtained as a yellow liquid. All spectroscopic data matches those reported in literature. This enone slowly degrades into a thick brown oil while stored in the freezer. Always recheck purity of older batches before use!

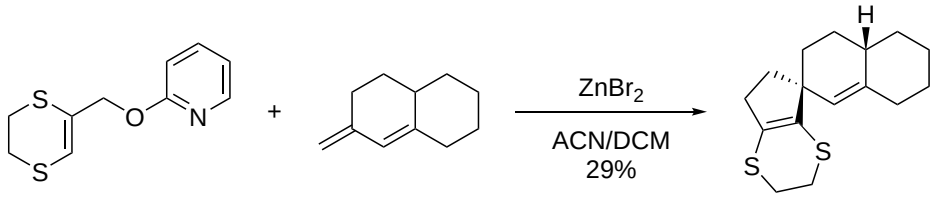


31

To a suspension of methyltriphenylphosphonium bromide (4.00 g, 11.18 mmol, 1.2 equiv.) in anhydrous THF (13 mL)fat -78°C, *n*BuLi (4.47 mL, 2.5M in hexanes, 11.18 mmol, 1.2 equiv.) is added in a dropwise fashion. The resulting yellow-red suspension is gently warmed to 0°C before a cooled solution of 4,4a,5,6,7,8-hexahydronaphthalen-2(3H)-one **31** (1.4 g, 9.32 mmol) in THF (6 mL) is added dropwise. The resulting mixture is left to stir at room temperature for 24 hours before being diluted with petroleum ether. The phosphine oxides are allowed to settle in the fridge before the organic phase is repeatedly filtrated over celite, concentrated and washed with cold petroleum ether to remove residual phosphine oxides. 7-methylene-1,2,3,4,4a,5,6,7-octahydronaphthalene (608 mg, 43% yield) is obtained as a transparent oil after filtration over a plug of silica and elution with pentane. This product is stored in the freezer to avoid degradation. Always recheck purity before use!

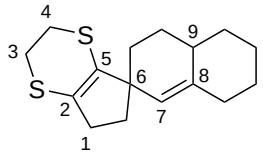


Formula: $C_{11}H_{16}$
Molar mass: 148.25 g/mol
R_f (Petroleum ether): 0.8
^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm): 5.90 (s (br), 1H, C4-H), 4.69 (s (br), 1H, C1-H*H*), 4.63 (s (br), 1H, C1-H*H*), 2.36-2.29 (dt, 1H, J = 14.3, 4.7 Hz, C3-*H*H), 2.29-2.23 (m, 1H, C6-*H*H), 2.23-2.15 (m, 1H, C3-H*H*), 2.14-2.01 (band, 2H, C6-H*H* and C7-H), 1.93-1.72 (band, 3H, -CH_2-), 1.45-1.20 (band, 4H, -CH_2-), 1.04 (m, 1H, -CH_2-)
^{13}C-NMR (75 MHz, $CDCl_3$): δ (ppm): 145.6 (C_q5), 144.6 (C_q2), 123.1 (C4-H), 108.3 (C1-H), 37.1 (C7-H), 35.4 (C6-H_2), 35.1 (-*C*H_2-), 31.1 (-*C*H_2-), 30.0 (C3-H_2), 27.7 (-*C*H_2-), 26.4 (-*C*H_2-)
HSQC ($CDCl_3$): 123.1 x 5.9, 108.3 x 4.69, 108.3 x 4.63, 37.1 x 2.14-2.01, 35.4 x 2.29-2.23, 35.4 x 2.14-2.01, 35.1 x 1.93-1.72, 35.1 x 1.04, 31.1 x 1.45-1.20, 30.0 x 2.36-2.29, 30.0 x 2.23-2.15, 27.7 x 1.93-1.72, 27.7 x 1.45-1.20, 26.4 x 1.93-1.72, 26.4 x 1.45-1.20
GCMS (EI) [m/z]*:* peak (at 11.65): 148 ($M^{+\bullet}$, 69), 133 (45), 105 (64), 91 (100), 77 (35)
IR ν_{max} (cm^{-1}): 2921 (s), 2852 (m), 1641 (w), 1447 (w), 875 (s), 610 (w)



16 **32** (Rac.) *dr* 5:1

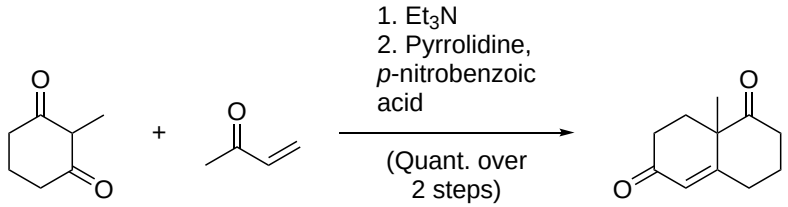
To a suspension of zinc bromide (1.10 g, 4.88 mmol, 1.65 equiv.) in acetonitrile (15 ml) is added a solution of diene **51** (434 mg, 2.93 mmol, 1 equiv.) in acetonitrile (15 mL) and CH_2Cl_2 (1.5 ml), followed by a solution of DHDT-pyridone **16** (1 g, 4.44 mmol, 1.5 equiv.) in acetonitrile (15 mL). When all diene is consumed as judged by TLC, the reaction is quenched with a saturated solution of sodium bicarbonate (45 mL) and subsequently extracted with CH_2Cl_2 (3 x 45 mL). The combined organic phases are washed with brine (20 mL) and dried over anhydrous sodium sulfate before removing the solvent under reduced pressure. The resulting crude reaction mixture is purified using flash chromatography (eluent: 0% - 2% ethyl acetate in pentane), resulting in pure cycloadduct **32** (234 mg, 29% yield) as a thick yellow oil. Title compound **32** showed NMR-data consistent with one major diastereomer, but a distribution of poorly resolved shoulders indicated the presence of a minor diasteromer, integrating in a 5:1 ratio, but this could not be assigned due to overlap of signals.



32

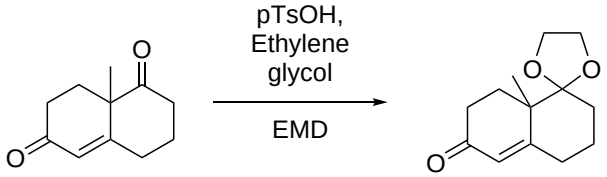
Formula: $C_{16}H_{22}S_2$
Molar mass: 278.47 g/mol
R_f (Petroleum ether): 0.25
^{1}H-NMR (400 MHz, $CDCl_3$): δ (ppm): 5.12 (t (br), 1H, J = 1.6 Hz, C7-H), 3.16-3.09 (m, 4H, S–CH_2–CH_2–S), 2.50-2.40 (m, 1H, C1-*H*H), 2.40-2.32 (ddd, 1H, J = 14.9, 8.5, 3.9 Hz, C1-H*H*), 2.19 (dp, 1H, J = 12.7, 2.0 Hz, -C*H*H-), 2.07-1.64 (band, 10H -CH_2-), 1.48-1.17 (band, 4H, C9-H and -CH_2-)
^{13}C-NMR (101 MHz, $CDCl_3$): δ (ppm): 143.3 (C_q8), 130.0 (C_q2), 124.7 (C7-H), 120.6 (C_q5), 53.3 (C_q6), 37.2 (C9-H), 37.1 (*C*H_2), 36.3 (*C*H_2), 35.4 (C1-H_2), 35.1 (*C*H_2), 30.5 (*C*H_2), 29.0 (*C*H_2), 28.9 (*C*H_2), 27.7 (*C*H_2), 27.0 (S–CH_2–CH_2–S), 26.9 (S–CH_2–CH_2–S)
HSQC ($CDCl_3$): 124.7 x 5.12, 37.2 x 1.48-1.17, 37.1 x 2.07-1.64, 36.3 x 2.19, 36.3 x 2.07-1.64, 35.4 x 2.50-2.40, 35.4 x 2.40-2.32, 35.1 x 2.07-1.64, 30.5 x 2.07-1.64, 30.5 x 1.48-1.17, 29.0 x 2.07-1.64, 28.9 x 1.48-1.17, 27.7 x 2.07-1.64, 27.0 x 3.16-3.09, 26.9 x 3.16-3.09
HRMS (ESI): [m/z]: calculated for $C_{16}H_{23}S_2^+$ [M+H^+]: 279.1236; found: 279.1230
IR ν_{max} (cm^{-1}): 2919 (s), 2848 (m), 1592 (w), 1443 (m), 1415 (w), 1284 (m), 1096 (w), 919 (w), 842 (m), 756 (m), 733 (w), 690 (w)

2.7 8a'-methyl-2,3,3',4',6,7,8',8a'-octahydro-2'H,7'H-dispiro[cyclopenta[b][1,-4]dithiine-5,6'-naphthalene-1',2"-[1,3]dioxolane] (34)



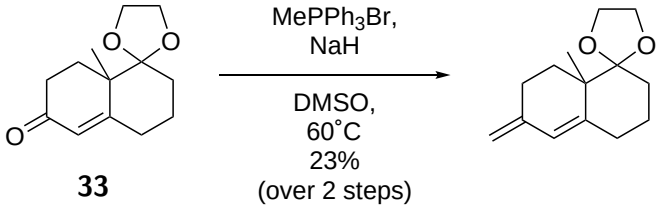
The title compound **34** is prepared in a five-step procedure starting from 2-methyl-1,3-cyclohexanedione. Based on the procedure described by Bradshaw *et al.*,[10] a mixture of 2-methylcyclohexane-1,3-dione (6 g, 47.56 mmol, 1 equiv.), methyl vinyl ketone (4.5 mL, 55.17 mmol, 1.15 equiv.) and triethyl amine (0.66 mL, 1 mol%) is stirred vigorously. After 16h, the resulting dark oil is dissolved using EtOAc (50 mL), dried over anhydrous sodium sulfate and concentrated *in vacuo* in a round-bottom flask.

Following the procedure described by Almasi *et al.*,[11] pyrrolidine (0.2 mL, 5 mol%) and *p*-nitrobenzoic acid (397 mg, 5 mol%) are added to the obtained viscous mixture. After vigorous overnight stirring, the reaction is quenched using water (200 mL) and transferred to a separatory funnel containing EtOAc (200 mL). The obtained organic phase is dried using anhydrous sodium sulfate and concentrated *in vacuo*. Purification via flash chromatography using a 1:1 mixture of EtOAc and petroleum ether results in the solid Wieland-Miescher ketone **52** (8.47 g, quantitative over 2 steps). All obtained spectroscopic data matches those reported in literature.



33

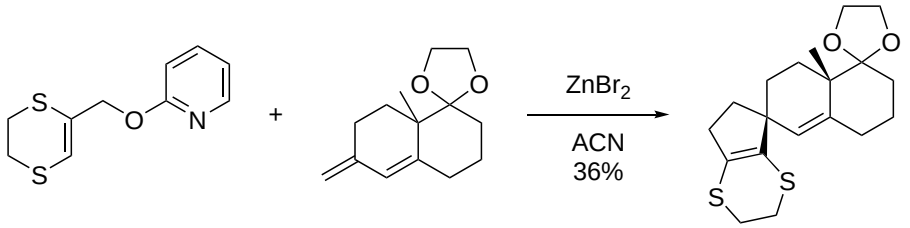
Mimicking the procedure outlined by Meinwald *et al.*,[12] Wieland-Miescher ketone (1.45 g, 8.15 mmol, 1 equiv.) is mixed together with 2-methyl-2-ethyl-1,3-dioxolane (5.6 ml, 44.82 mmol, 5.5 equiv.), ethylene glycol (0.1 ml, 1.79 mmol, 0.22 equiv.) and *p*-toluenesulfonic acid monohydrate (98 mg, 0.571 mmol, 7 mol%) at room temperature. After about 30 h, when all starting material is consumed as judged by TLC, the reaction is quenched by dropwise addition of triethylamine (0.08 ml, 0.574 mmol, 7 mol%), diluted with toluene (15 ml) and washed with water (15 ml) before being dried over anhydrous sodium sulfate. The solvent is stripped under reduced pressure and the resulting crude reaction mixture is used in the following reaction without subsequent purification.



33

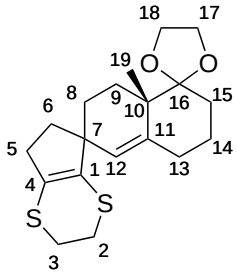
Following a procedure outlined by Bosch *et al.*,[12] a suspension of sodium hydride (60% dispersion

in mineral oil, 489 mg, 12.25 mmol, 1.50 equiv.) in anhydrous DMSO (5.5 ml) is stirred at 70°C until all evolution of hydrogen gas stopped (45 min). Once the mixture has cooled back to room temperature, anhydrous DMSO (11 ml) is added before methyltriphenylphosphonium bromide (4.40 g, 12.32 mmol, 1.5 equiv) is added at once, resulting in a yellow-orange mixture. After 30 minutes of stirring, a solution of acetal **33** in anhydrous DMSO (5.5 ml) is added in a dropwise fashion. The resulting green reaction mixture is stirred overnight at 60°C before being poured in ice-water (ca. 20 ml). Upon extraction with pentane (4 x 40 ml), the combined organic phases are washed with 1:1 H_2O-DMSO (3 x 20 ml) and brine (15 ml) before being dried over anhydrous sodium sulfate. The solvent is removed *in vacuo* and the resulting crude is purified via flash chromatography, with basic alumina I as solid phase and using pentane as eluent, to yield solid diene (410 mg, 23% yield over 2 steps). All spectroscopic data matches those reported in literature. This product is stored in the freezer to avoid degradation. Always recheck purity before use!



16 **34** (Rac.)

Zinc bromide (380 mg, 1.69 mmol, 1.65 equiv.) is suspended with diene (230 mg, 1.04 mmol, 1 equiv.) in acetonitrile (7 ml) and CH_2Cl_2 (0.7 ml). To this white opaque mixture, a solution of DHDT-pyridone **16** (341 mg, 1.51 mmol, 1.45 equiv.) in acetonitrile (3.5 ml) is added in a dropwise fashion, resulting in a transparent reaction mixture. When no more cation precursor **16** is present in the reaction mixture, as judged by TLC, subsequent batches of DHDT-pyridone are added at 2h, 8h and 24h of total reaction time in portions of 100 mg (0.444 mmol, 0.43 equiv.), 200 mg (0.888 mmol, 0.85 equiv.) and 200 mg (0.888 mmol, 0.85 equiv.) respectively. When all diene starting material is consumed, as judged by TLC, the reaction mixture is quenched using saturated aqueous sodium bicarbonate (10 ml) and extracted with CH_2Cl_2 (3 x 10 mL). The combined organic phases are washed with brine (5 ml) and dried over anhydrous sodium sulfate. Removal of the solvent *in vacuo* and purification via flash chromatography (eluent: 2% to 5% EtOAc in pentane) results in pure title compound **34** as a white amorphous solid (126 mg, 36% yield).

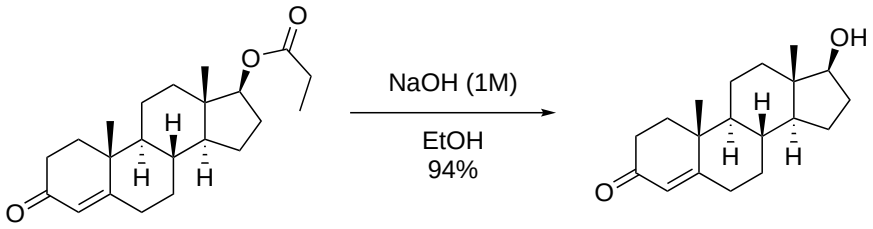


34

Formula: $C_{19}H_{26}O_2S_2$
Molar mass: 350.54 g/mol
R_f (5% EtOAc in petroleum ether): 0.18

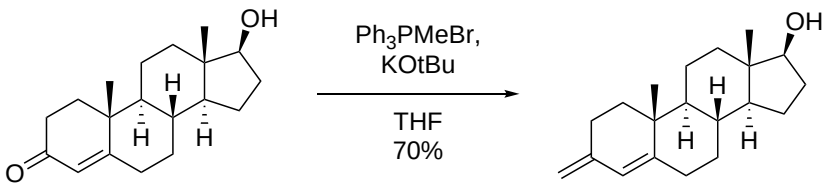
^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm): 5.21 (d, 1H, J = 1.6 Hz, C12-H), 4.00-3.90 (m, 4H, C17-H_2 and C18-H_2), 3.13 (m, 4H, S–CH_2–CH_2–S), 2.40 (dt, 2H, J = 6.9, 3.3 Hz, C5-H_2), 2.30-2.21 (band, 1H, C13-HH), 2.21-2.15 (m, 1H, C9-HH), 2.00 (d (br), 1H, J = 13.8 Hz, C13-HH), 1.91 (ddd, 1H, J = 13.1, 7.7, 3.8 Hz, C8-HH), 1.78 (t, 2H, J = 7.0 Hz, C6-H_2), 1.70-1.52 (band, 4H, C14-H_2 and C15-H_2), 1.46 (ddd, 1H, J = 13.4, 10.4, 3.6 Hz, C8-HH), 1.27 (ddd, 1H, J = 10.3, 7.3, 3.5 Hz, C9-HH), 1.16 (s, 3H, C19-H_3)
^{13}C-NMR (75 MHz, $CDCl_3$): δ (ppm): 142.6 (C_q11), 130.1 (C_q1), 127.8 (C12-H), 120.0 (C_q4), 113.6 (C_q16), 65.2 (C17-H_2 and C18-H_2), 52.9 (C_q7), 43.2 (C_q10), 38.1 (C6-H_2), 35.2 (C5-H_2), 31.3 (C8/13/14/15), 31.2 (C8/13/14/15), 27.9 (C9-H_2), 26.9 (C2-H_2 and C3-H_2), 23.7 (C14/15), 23.5 (C19-H_3)
HSQC ($CDCl_3$): 127.8 x 5.21, 65.2 x 4.00-3.90, 38.1 x 1.78, 35.2 x 2.4, 31.3 x 1.70-1.52, 31.2 x 1.70-1.52, 27.9 x 2.21-2.15, 27.9 x 1.27, 26.9 x 3.13, 23.7 x 1.70-1.52, 23.5 x 1.16
HRMS (ESI): [m/z]: calculated for $C_{19}H_{27}O_2S_2^+$ [M+H$^+$]: 351.1447; found: 351.1448
IR ν_{max} (cm^{-1}): 2922 (s), 3853 (m), 1415 (w), 1287 (m), 1149 (m), 1120 (s), 1059 (s), 953 (s), 867 (m), 659 (w)

2.8 (8R,9S,10R,13S,14S,17S)-10,13-dimethyl-1,2,2',3',6,6',7,7',8,9,10,11,12,13,-14,15,16,17-octadecahydrospiro[cyclopenta[a]-phenanthrene-3,5'-cyclopenta[b][1,4]dithiin]-17-ol (36)



35

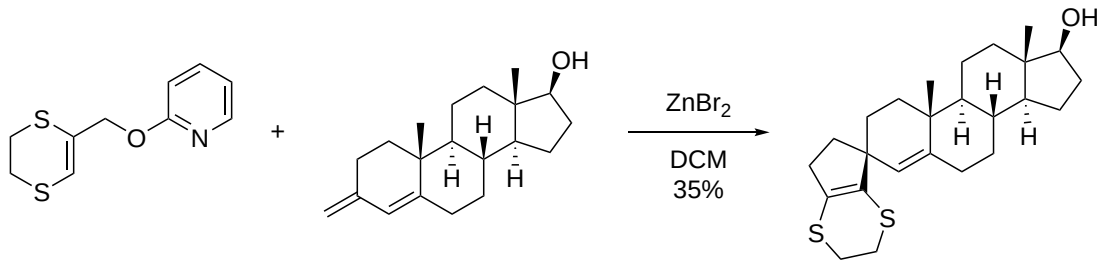
The title compound **36** is prepared in a three-step procedure starting from testosterone propionate. To a solution of testosterone propionate (1.488 g, 4.32 mmol, 1 equiv.) in absolute ethanol (21.6 mL), aqueous sodium hydroxide (4.75 mL, 1M, 4.75 mmol, 1.1 equiv.) is added. The reaction mixture is left to stir at 30°C for 24h. When the starting material is consumed as judged by TLC, the reaction mixture is poured into vigorously stirred aqueous HCl (22 mL, 1M) and immediately extracted using CH_2Cl_2 (3 x 20 mL). The combined organic phases are washed using a saturated brine solution (8 mL) and dried over anhydrous sodium sulfate. The mixture is purified using flash chromatography (eluent: 30% to 35% ethyl acetate in petroleum ether), obtaining in pure testosterone **35** (1.17 g, 94% yield) as a white solid.



35

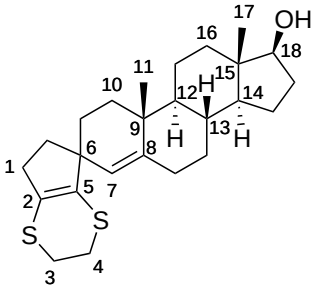
A suspension of methylphosphonium bromide (1.486 g, 4.161 mmol, 1.2 equiv.) in anhydrous

THF (7 mL) is vigorously stirred before potassium *tert*-butoxide (506 mg, 4.507 mmol, 1.3 equiv.) is added in a single portion. The resulting yellow mixture is left to stir for 30 minutes, at which point it is cooled to 0°C and testosterone (1 g, 3.47 mmol, 1 equiv.) is added at once. The resulting mixture is allowed to warm up to room temperature and is left to stir for 3 days. Upon dilution with petroleum ether (10 mL), the phosphine oxides are allowed to settle for 24h in the freezer. These precipitates are removed via repeated filtration over celite, concentration *in vacuo* and washing with cold petroleum ether. Pure diene (797 mg, 80% yield) is obtained upon flash chromatography over neutral alumina (eluent: 20% to 30% EtOAc in pentane) as a white solid. All spectroscopic data matches those reported in literature.[13] This product is stored in the freezer to avoid degradation. Always recheck purity before use!



16 **36**

A suspension of diene (200 mg, 0.70 mmol, 1 equiv.) and zinc bromide (259 mg, 1.15 mmol, 1.65 equiv.) in CH_2Cl_2 (5 mL) is prepared, to which a solution of DHDT-pyridone **16** (236 mg, 1.05 mmol, 1.5 equiv.) in CH_2Cl_2 (2.5 mL) is added dropwise, resulting in a transparent mixture. After 1.5h and 4h of stirring, when no more cation precursor **16** is observed on TLC, subsequent portions (100 mg, 0.42 mmol, 0.6 equiv.) in CH_2Cl_2 (1 mL) are added. When no more diene starting material is observed, as judged by TLC, the reaction is quenched using saturated sodium bicarbonate (8 mL). The two phases are separated and the aqueous phase is extracted using CH_2Cl_2 (3 x 8 mL). The combined organic phases are washed using saturated brine (3 mL) and dried over anhydrous sodium sulfate. Removal of the solvent under reduced pressure and purification via flash chromatography (eluent: 8% to 25% EtOAc in pentane) afford pure title compound **23** as a white powder (103 mg, 35% yield).

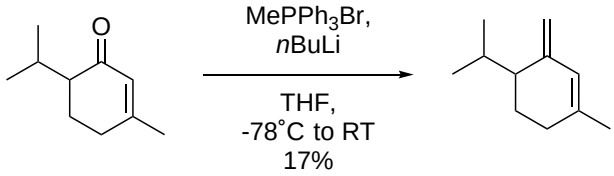


36

Formula: $C_{25}H_{36}OS_2$
Molar mass: 417.69 g/mol
R_f (15% EtOAc in petroleum ether): 0.19
^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm): 5.03 (s, 1H, C7-H), 3.63 (t, 1H, J = 8.6 Hz, C18-H), 3.24-3.06 (m, 4H, S–CH_2–CH_2–S), 2.51-2.42 (m, 1H, C1-*H*H), 2.40-2.32 (m, 1H, C1-H*H*), 2.28-2.16 (td, 1H, J = 13.6, 4.6 Hz, -C*H*H-), 2.11-1.99 (band, 2H, –CH_2–), 1.86-1.69 (band, 6H, C10-*H*H, C16-*H*H and –CH_2–), 1.64-1.52 (band, 4H, C10-H*H* and –CH_2–), 1.51 (s (br),

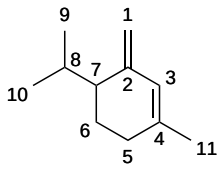
1H, C13-H), 1.49-1.18 (band, 2H, $-CH_2-$), 1.09 (dd, 1H, J = 13.4, 4.7 Hz, C16-HH), 1.00 (s, 3H, C11-H_3), 0.99 (band, 3H, C12-H, C14-H and $-CH_2-$), 0.76 (s, 3H, C17-H_3)
^{13}C-NMR (75 MHz, $CDCl_3$): δ (ppm): 146.9 (C_q8), 129.6 (C_q2/5), 125.0 (C7-H), 120.5 (C_q2/5), 82.1 (C18-H), 53.7 (C12-H), 53.1 (C_q6), 50.8 (C_q14), 43.1 (C_q15), 38.9 (-CH_2-), 37.0 (C_q9), 36.8 (C16-H_2), 36.3 (C13-H), 35.2 (C1-H_2), 35.0 (C10-H_2), 33.3 (-CH_2-), 32.7 (-CH_2-), 31.1 (-CH_2-), 30.7 (-CH_2-), 27.2 (-CH_2-), 27.0 (-CH_2-), 23.5 (-CH_2-), 21.3 (-CH_2-), 19.8 (C11-H_3), 11.2 (C17-H_3)
HSQC ($CDCl_3$): 125.0 x 5.03, 82.1 x 3.63, 53.7 x 0.99, 38.9 x 1.86-1.69, 36.8 x 1.86-1.69, 36.8 x 1.09, 36.3 x 1.51, 35.3 x 2.51-2.42, 35.5 x 2.40-2.32, 35.0 x 1.86-1.69, 35.0 x 1.64-1.52, 33.3 x 1.86-1.69, 33.3 x 0.99-0.85, 32.7 x 2.28-2.16, 32.7 x 2.11-1.99, 31.1 x 1.86-1.69, 31.1 x 1.64-1.52, 30.7 x 2.11-1.99, 30.7 x 1.49-1.18, 27.2 x 3.24-3.06, 27.0 x 3.24-3.06, 23.5 x 1.64-1.52, 23.5 x 1.49-1.18, 21.3 x 1.64-1.52, 21.3 x 1.49-1.18, 19.8 x 1.00, 11.2 x 0.76
HRMS (ESI): [m/z]: calculated for $C_{25}H_{37}OS_2^+$ [M+H^+]: 417.2280; found: 417.2288
IR ν_{max} (cm^{-1}): 3361 (w (br)), 2901 (s), 2845 (s), 1438 (m), 1131 (w), 1055 (m), 860 (w)

2.9 4-isopropyl-1-methyl-3-methylenecyclohex-1-ene (38)



37 **38**

To a suspension of methyltriphenylphosphonium bromide (2.49 g, 6.96 mmol, 1.2 equiv.) in anhydrous THF (8 ml) at -78°C, nBuLi (2.78 ml, 2.5M in hexanes, 6.96 mmol, 1.2 equiv.) is added in a dropwise fashion. The resulting yellow-red suspension is gently warmed to 0°C before a cooled solution of piperitone (1 ml, 5.80 mmol, 1 equiv.) in THF (3.5 ml) is added dropwise. The resulting mixture is left to stir at room temperature for 24 hours before being diluted with petroleum ether. The phosphine oxides are allowed to settle in the fridge before the organic phase is repeatedly filtrated over celite, concentrated and washed with cold petroleum ether to remove residual phosphine oxides. 4-isopropyl-1-methyl-3-methylenecyclohex-1-ene **53** (168 mg, 17% yield) is obtained as a transparent oil after filatration over a plug of silica and elution with pentane.



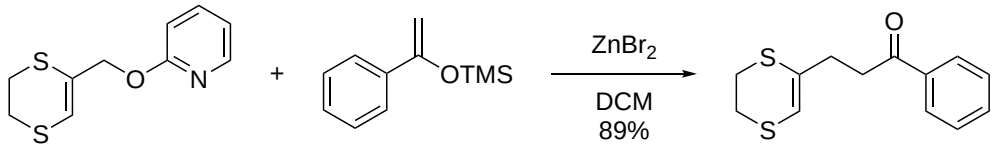
38

Formula: $C_{11}H_{18}$
Molar mass: 150.27 g/mol
R_f (Petroleum ether): 0.87
^{1}H-NMR (400 MHz, $CDCl_3$): δ (ppm): 5.86 (s (br), 1H, C3-H), 4.74 (s (br), 1H, C1-HH), 4.63 (s (br), 1H, C1-HH), 2.15-2.03 (band, 1H, C5-HH), 1.94-1.86 (m, 2H, C5-HH and C7-H), 1.86-1.78 (m, 1H, C6-HH), 1.74 (s (br), 3, C11-H_3), 1.72-1.67 (m, 1H, C8-H), 1.67-1.62 (m, 1H,

C6-HH), 0.91 (d, 3H, J = 6.6 Hz, C9-H_3), 0.90 (d, 3H, J = 6.6 Hz, C10-H_3)
^{13}C-NMR (101 MHz, $CDCl_3$): δ (ppm): 146.6 (C_q2), 138.0 (C_q4), 124.9 (C3-H), 109.3 (C1-H_2), 46.1 (C7-H), 27.7 (C5-H_2), 27.0 (C8-H), 24.7 (C6-H_2), 23.7 (C11-H_3), 21.9 (C10-H_3), 20.0 (C9-H_3)
HSQC ($CDCl_3$): 124.9 x 5.86, 109.3 x 4.74, 109.3 x 4.74, 46.1 x 1.94-1.86, 27.7 x 2.15-2.03, 27.7 x 1.94-1.86, 27.0 x 1.72-1.67, 24.7 x 1.86-1.78, 24.7 x 1.67-1.62, 23.7 x 1.74, 21.9 x 0.90, 20.0 x 0.91
GCMS (EI): (at 4.69): m/z 150 ($M^{+\bullet}$, 53), 135 (M^{+3} – CH_3, 100), 107 ($M^{+\bullet}$ – C_2H_4, 88), 91 ($M^{+\bullet}$ – C_3H_8, 45), 79 ($M^{+\bullet}$ – C_4H_8, 15), 77 ($M^{+\bullet}$ – C_4H_{10}, 15), 41 ($M^{+\bullet}$ – C_7H_{10}, 13)
IR ν_{max} (cm^{-1}): 2956 (m), 1650 (w), 1452 (w), 1152 (w), 998 (w), 876 (s), 663 (w)

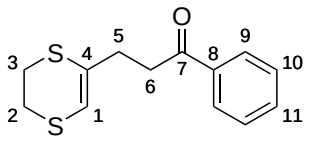
3 Other substrate types

3.1 3-(5,6-dihydro-1,4-dithiin-2-yl)-1-phenylpropan-1-one (40)



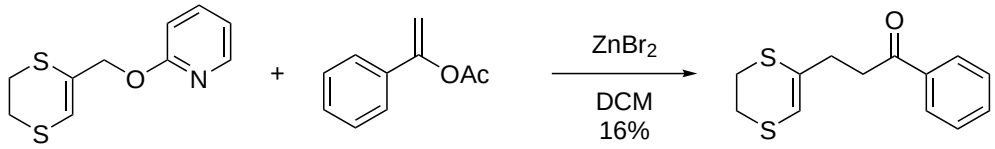
16 **39** **40**

DHDT-pyridone **16** (76 mg, 0.338 mmol, 1 equiv.) and 1-phenyl-1-trimethylsiloxyethylene (0.11 mL, 0.536 mmol, 1.5 equiv.) are dissolved in CH_2Cl_2 (5 ml) at room temperature. To this solution, anhydrous zinc bromide (232 mg, 1.03 mmol, 3 equiv.) is added at once. the progress of the reaction is monitored on TLC, and when all starting material is consumed, the reaction mixture is quenched using saturated aqueous sodium bicarbonate. The formed white precipitate is removed by filtration over celite using CH_2Cl_2 and the obtained layers are separated. The aqueous phase is extracted using CH_2Cl_2 (3 x 5 ml), the combined organic phases are washed with brine (3 mL) and dried over anhydrous sodium sulfate. The obtained phase is concentrated *in vacuo*. Purification using flash chromatography (gradient: 1.5% - 2% ethyl acetate in petroleum ether) yields compound **40** (79 mg, 89%) as a colourless oil.



40

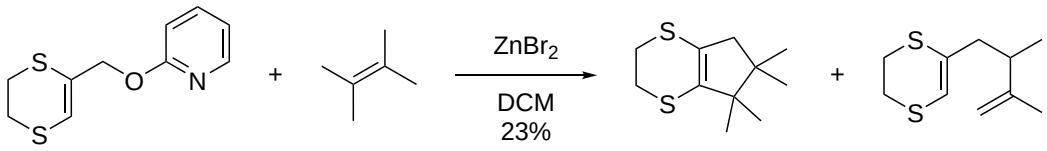
Formula: $C_{13}H_{14}OS_2$
Molar mass: 250.37 g/mol
R_f (15% ethyl acetate in petroleum ether): 0.63
^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm): 7.97 (d, 1H, J = 8.4 Hz, CH_{Ar}), 7.57 (t, 2H, J = 7.5 Hz, CH_{Ar}), 7.46 (t, 2H, J = 7.3 Hz, CH_{Ar}), 5.99 (s, 1H, C1-H), 3.21-3.07 (band, 4H, S–CH_2–CH_2–S), 3.20 (t, 2H, J = 7.59 Hz, C5-H), 2.63 (t, 2H, J = 7.66 Hz, C6-H)
^{13}C-NMR (75 MHz, $CDCl_3$): δ (ppm): 199.2 (C_q7), 137.0 (C_q4), 133.2 (C_{Ar}H), 128.8 (C_{Ar}H), 128.5 (C_q8) 128.2 (C_{Ar}H), 110.0 (C1-H), 38.0 (C5-H_2), 34.0 (C6-H_2), 27.8 (S–CH_2–CH_2–S), 26.1 (S–CH_2–CH_2–S)
HSQC ($CDCl_3$): 133.2 x 7.57, 128.8 x 7.46, 128.5 x 7.97, 110.0 x 5.99, 38.0 x 3.2, 34.0 x 2.63, 27.8 x 3.21-3.07, 26.1 x 3.21
HRMS (ESI): calculated for $C_{13}H_{15}OS_2^+$ [M+H$^+$]: 251.0559; found: 251.0556
IR ν_{max} (cm^{-1}): 1680 (s), 1595 (m), 1446 (m), 1359 (m), 1266 (s)



16 **40**

DHDT-pyridone **16** (79 mg, 0.352 mmol, 1 equiv.) and (1-phenyl)vinylacetate (89 mg, 0.547 mmol, 1.5 equiv.) are dissolved in CH_2Cl_2 (5 ml) at room temperature. To this solution, anhydrous zinc bromide (214 mg, 0.951 mmol, 2.7 equiv.) is added at once. When all starting material is consumed, as judged by TLC, the reaction mixture is quenched using saturated aqueous sodium bicarbonate. The formed white precipitate is removed by filtration over celite using CH_2Cl_2 and the obtained layers are separated. The aqueous phase is extracted using CH_2Cl_2 (3 x 5 ml), the combined organic phases are washed with brine (3 mL) and dried over anhydrous sodium sulfate. The obtained phase is concentrated *in vacuo*. Purification using flash chromatography (gradient: 1.5% to 2% ethyl acetate in petroleum ether) yields ketone **40** as a colourless oil (20 mg, 16%).

3.2 5,5,6,6-tetramethyl-2,3,6,7-tetrahydro-5H-cyclopenta[b][1,4]dithiine (42) and 5-(2,2,3-trimethylbut-3-en-1-yl)-2,3-dihydro-1,4-dithiine (43)

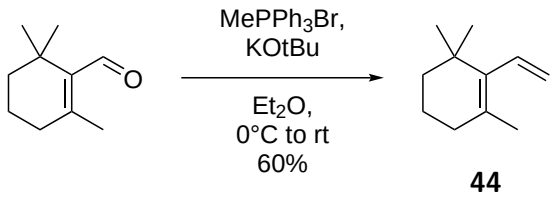


16 **41** **42** **43**

ratio 3:4

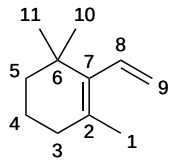
DHDT-pyridone **16** (89 mg, 0.396 mmol, 1 equiv.) and 2,3-dimethyl-2-butene (70 μL, 0.589 mmol, 1.5 equiv.) are dissolved in CH_2Cl_2 (5 ml) at room temperature. To this solution, anhydrous zinc bromide (198 mg, 0.878 mmol, ca. 2.5 equiv.) is added at once. The reaction progress is monitored on TLC, and when all starting material is consumed, the reaction mixture is quenched using saturated aqueous sodium bicarbonate. The formed white precipitate is removed by filtration over celite using CH_2Cl_2 and the obtained layers are separated. The aqueous phase is extracted using CH_2Cl_2 (3 x 5 ml), the combined organic phases are washed with brine (3 mL) and dried over anhydrous sodium sulfate. The obtained phase is concentrated *in vacuo*, resulting in a viscous oil. Purification using flash chromatography with petroleum ether yields an impure fraction of cycloadducts **42** and **43** in a 2:1 ratio (20 mg, 23% yield). The NMR-data matches the spectra reported in literature.[1]

3.3 (4aR,5R)-7-methyl-5-(2,6,6-trimethylcyclohex-1-en-1-yl)-2,3,4a,6-tetrahydro-5H-cy-clopenta[b][1,4]dithiine (46)



44

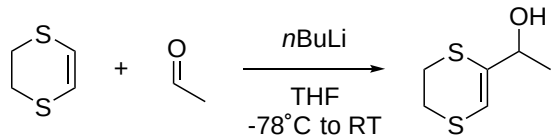
The title compound **46** is prepared in a two-step synthesis starting from cyclocitral. To a suspension of methyltriphenylphosphonium bromide (5.31 g, 14.87 mmol, 1.2 equiv.) in anhydrous Et_2O (20 mL) at 0°C, potassium *tert*-butoxide (1.67 g, 14.87 mmol, 1.2 equiv.) is added in a single portion. The resulting yellow mixture is left to stir for 30 min, after which a solution of cyclocitral (2 mL, 12.39 mmol, 1 equiv.) in anhydrous (4 mL) is added dropwise. The reaction mixture is allowed to warm up to room temperature. Upon overnight stirring, the contents in the reaction flask are diluted with pentane (20 mL). The formed precipitates are filtered over celite and washed using pentane, and the combined organic phases are concentrated *in vacuo*. Pure 1,3,3-trimethyl-2-vinylcyclohex-1-ene **44** (1.12 g, 60% yield) is subsequently obtained at a transparent liquid after flash chromatography over basic alumina using pentane.



44

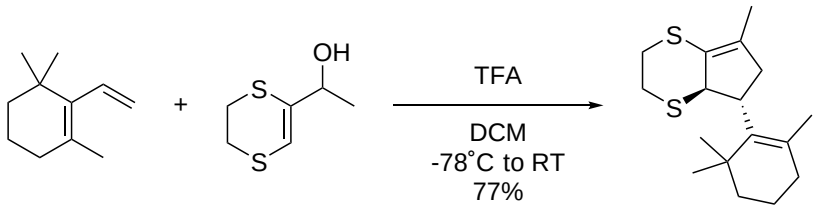
Formula: $C_{11}H_{18}$
Molar mass: 150.27 g/mol
R_f (Petroleum ether): 0.9
^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm): 6.21 (ddd, 1H, J = 17.7, 11.3, 0.9 Hz, C8-H), 5.23 (dd, 1H, J = 11.2, 2.7 Hz, C9-*H*H), 4.97 (dd, 1H, J = 17.7, 2.6 Hz, C9-H*H*), 1.99 (t(br), 2H, J = 6.2 Hz, C3-H_2), 1.70 (d, 3H, J = 0.7 Hz, C1-H_3), 1.67-1.57 (band, 2H, C4-H_2), 1.49-1.43 (band, 2H, C5-H_2), 1.01 (s, 6H, C10-H_3 + C11-H_3)
^{13}C-NMR (75 MHz, $CDCl_3$): δ (ppm): 138.5 (C_q7), 135.6 (C8-H), 128.6 (C_q2), 118.0 (C9-H_2), 39.6 (C5-H_2), 33.9 (C_q6), 32.9 (C3-H_2), 28.8 (C10-H_3 + C11-H_3), 21.5 (C1-H_3), 19.4 (C4-H_2)
HSQC ($CDCl_3$): 135.6 x 6.21, 118.0 x 5.23, 118.0 x 4.97, 39.6 x 1.49-1.43, 32.9 x 1.99, 28.8 x 1.01, 21.5 x 1.70, 19.4 x 1.67-1.57
GCMS (EI) [m/z]*:* peak at (4.37): 150 ($M^{+\bullet}$, 30), 135 ($M^{+\bullet}$ – CH_3, 100), 107 ($M^{+\bullet}$ – C_3H_7, 41), 93 ($M^{+\bullet}$ – C_4H_9, 41), 79 ($M^{+\bullet}$ – C_5H_{11}, 38), 65 ($M^{+\bullet}$ – C_6H_{13}, 8), 55 ($M^{+\bullet}$ – C_7H_{11}, 18), 43 ($M^{+\bullet}$ – C_8H_{11}, 12), 41 ($M^{+\bullet}$ – C_8H_{13}, 25), 27 ($M^{+\bullet}$ – C_9H_{15}, 10), 18 ($M^{+\bullet}$ – $C_{10}H_{12}$, 4)
IR ν_{max} (cm^{-1}): 2918 (s), 2866 (m), 1621 (w), 1458 (m), 1360 (w), 991 (m), 913 (s)

A solution of DHDT (2.93 g, 25 mmol, 1 equiv.) in anhydrous THF (50 ml) is cooled to -78°C. A solution of *n*-butyllithium (13 ml, 2.5M in hexanes, 32.5 mmol, 1.3 equiv.) is added dropwise and the mixture is left to stir for 2 h, ensuring the temperature never rises above -50°C. Acetaldehyde (2.8 ml, 50 mmol, 2 equiv.) is added dropwise and the resulting mixture is allowed to warm up to room temperature overnight. When all starting material is consumed, as judged by TLC, the reaction is quenched using saturated sodium bicarbonate (50 ml) and both phases



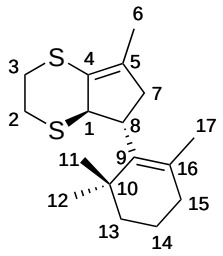
45

are separated. Upon extraction of the aqueous phase using Et_2O (3 x 50 ml), the combined organic phases are washed using brine (20 ml) and dried over anhydrous sodium sulfate. Purification via flash chromatography (eluent: 10% to 20 % EtOAc in petroleum ether) results in pure compound **45** (3.37 g, 83% yield) as a yellow oil, with all data matching the reported literature.[14] This product is stored in the freezer as a solution in CH_2Cl_2 to avoid degradation. Always recheck purity of older batches before use!



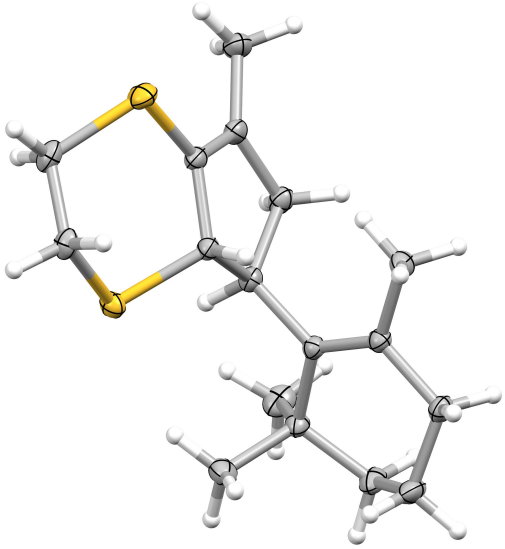
44 **45** (Rac.) **46**

A solution of DHDT-compound **45** (30 mg, 0.185 mmol, 1 equiv.) and diene (56 mg, 0.37 mmol, 2 equiv.) in CH_2Cl_2 (2 ml) is prepared and cooled to -78°C. At this temperature, a freshly prepared solution of TFA (28 μl, 0.37 mmol, 2 equiv.) in CH_2Cl_2 (0.2 ml) is added dropwise and the resulting mixture is allowed to gradually warm to room temperature. When all starting material is consumed, as judged by TLC, a saturated solution of sodium bicarbonate (2 ml) is added at once. The layers are separated and the aqueous phase is extracted using CH_2Cl_2 (3 x 2 ml). The combined organic phases are washed using a saturated brine solution (1 ml) and dried over sodium sulfate and concentrated *in vacuo*. Flash chromatography using 2% EtOAc in petroleum ether affords pure adduct **46** (42 mg, 77% yield) as a crystalline solid. A small amount of this compound (20 mg) was redissolved in a minimal amount of hexane (HPLC grade). This solution was allowed to evaporate at normal atmosphere. After the formation of a small amount of crystals, X-ray intensity data was collected at 100 K, on an Agilent Supernova Dual Source (Cu at zero) diffractometer equipped with an Atlas CCD detector using w scans and CuKa (l = 1.54184 Å) radiation. The images were interpreted and integrated with the program CrysAlisPro [1].[15] Using Olex2 [2],[16] the structure was solved by direct methods using the ShelXS structure solution program and refined by full-matrix least-squares on F2 using the ShelXL program package [3].[17] Non-hydrogen atoms were anisotropically refined and the hydrogen atoms in the riding mode with isotropic temperature factors fixed at 1.2 times U(eq) of the parent atoms (1.5 times for methyl groups). For 46, the asymmetric unit has chirality at C1 (S), C7 (S). But obviously, because of the centro-symmetric space group, also the inverse configuration is present in the crystal structure. The structure is confirmed by XRD.

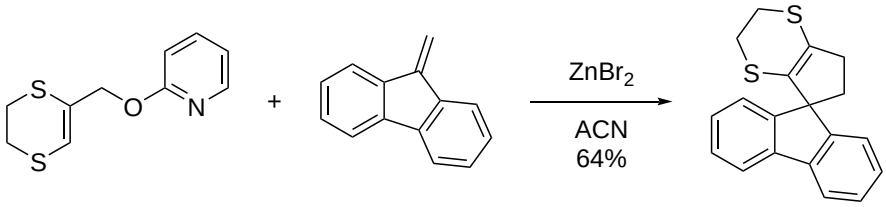


46

Formula: $C_{17}H_{26}S_2$
Molar mass: 294.52 g/mol
R_f (10% EtOAc in petroleum ether): 0.87
^{1}H-NMR (500 MHz, $CDCl_3$): δ (ppm): 3.94 (s (br), 1H, C1-H), 3.13 (ddd, 1H, J = 14.0, 12.2, 2.2 Hz, C2-HH), 2.96 (ddd, 1H, J = 12.6, 12.2, 2.4 Hz, C3-HH), 2.88 (ddd, 1H, J = 14.0, 4.2, 2.4 Hz, C2-HH), 2.74 (ddd, 1H, J = 12.6, 4.2, 2.2 Hz, C3-HH), 2.69-2.60 (band, 2H, C7-HH and C8-H), 2.35-2.26 (m, 1H, C7-HH), 1.96-1.84 (band, 2H, C15-H_2), 1.79 (s, 3H, C6-H_3), 1.59-1.51 (band, 3H, C13-HH and C14-H_2), 1.46 (s, 3H, C17-H_3), 1.37 (m, 1H, C13-HH), 1.04 (s, 3H, C11-H_3), 0.93 (s, 3H, C12-H_3)
^{13}C-NMR (125 MHz, $CDCl_3$): δ (ppm): 141.4 (C_q9), 139.0 (C4/5) 129.0 (C_q16), 123.0 (C4/5), 55.7 (C1-H), 45.6 (C7-H_2), 42.1 (C8-H), 39.9 (C13-H_2), 35.3 (C_q10), 34.0 (C15-H_2), 30.5 (C2-H_2), 30.3 (C3-H_2), 29.0 (C12-H_3), 28.6 (C11-H_3), 20.7 (C17-H_3), 19.6 (C14-H_2), 14.9 (C6-H_3)
HSQC ($CDCl_3$): 55.7 x 3.94, 45.6 x 2.69-2.60, 45.6 x 2.35-2.26, 42.1 x 2.69-2.60, 39.9 x 1.59-1.51, 39.9 x 1.37, 34.0 x 1.96-1.84, 30.5 x 3.13, 30.5 x 2.88, 30.3 x 2.96, 30.3 x 2.74, 29.0 x 0.93, 28.6 x 1.04, 20.7 x 1.46, 19.6 x 1.59-1.51, 14.9 x 1.79
Melting point: 81.0-83.0°C
XRD (Crystal system: monoclinic; Space group: $P2_{1/c}$ (No. 14)): a = 10.1865(3) Å , b = 8.18900(17) Å, c = 19.2034(4) Å, β = 96.644(2), V = 1591.14(7) Å^3, Z = 4, T = 100 K, ρ_{calc} = 1.229 g cm^{-3}, μ(Cu-Kα) = 2.887 mm^{-1}, F(000) = 640, 23284 reflections measured, 3250 unique (R_{int} = 0.0366) which were used in all calculations. The final *R1* was 0.0295 ($I > 2\sigma(I)$) and *wR2* was 0.0810 (all data).
CCDC 2287211 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/structures.

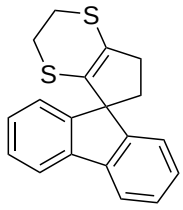


2,3,6,7-tetrahydrospiro[cyclopenta[b][1,4]dithiine-5,9'-fluorene] (47)



16 **47**

A suspension of 9-methylene-fluorene (89.1 mg, 0.50 mmol, 1 equiv.) and zinc bromide (186 mg, 0.82 mmol, 1.65 equiv.) in acetonitrile (3.5 ml) is prepared at room temperature, to which a solution of cation precursor **16** (169.0 mg, 0.75 mmol, 1.5 equiv.) in acetonitrile (1.5 ml) is added dropwise. The progress of the reaction is monitored via TLC analysis. After 24 h, 48 h and 72 h, extra portions of DHDT-pyridone **16** (77.1 mg, 0.25 mmol, 0.5 equiv.) in acetonitrile (1 ml) are added in a dropwise fashion. After a further 24 h of stirring, the reaction is quenched using saturated sodium bicarbonate (5 ml). The two phases are separated, and the aqueous phase is extracted using CH_2Cl_2 (3 x 5 ml). The combined organic phases are washed using brine (2 ml) and dried over anhydrous sodium sulfate before removing the solvent *in vacuo*. Title adduct **47** was obtained as a white crystalline solid (90 mg, 64% yield) after purification via flash chromatography with pentane. All spectroscopic data matches those reported in literature.[1]



47

Formula: $C_{19}H_{16}S_2$
Molar mass: 308.46 g/mol
^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm): 7.73-7.68 (ddd, 2H, J = 7.2, 1.5, 0.8 Hz), 7.41-7.27 (band, 6H), 3.21-3.16 (m, 2H), 2.9-2.91 (band, 4H), 2.44-2.38 (m, 2H)

Bibliography

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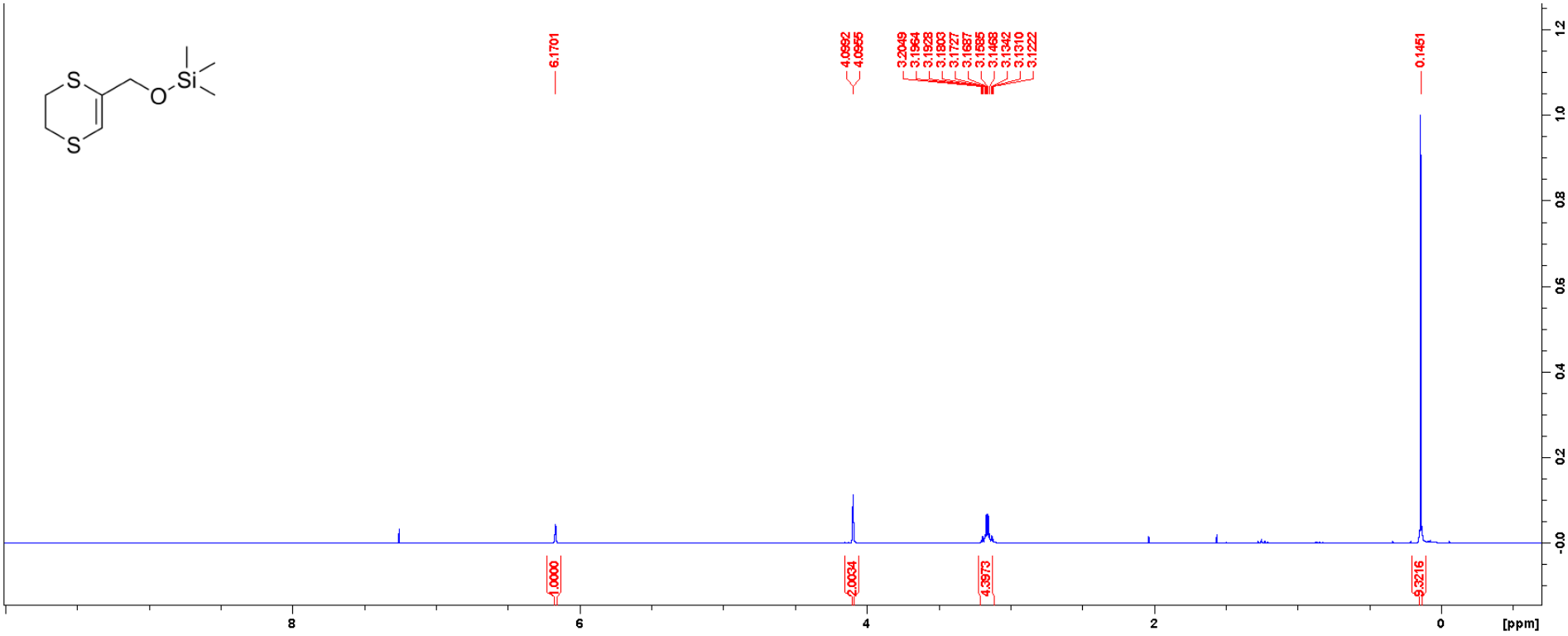
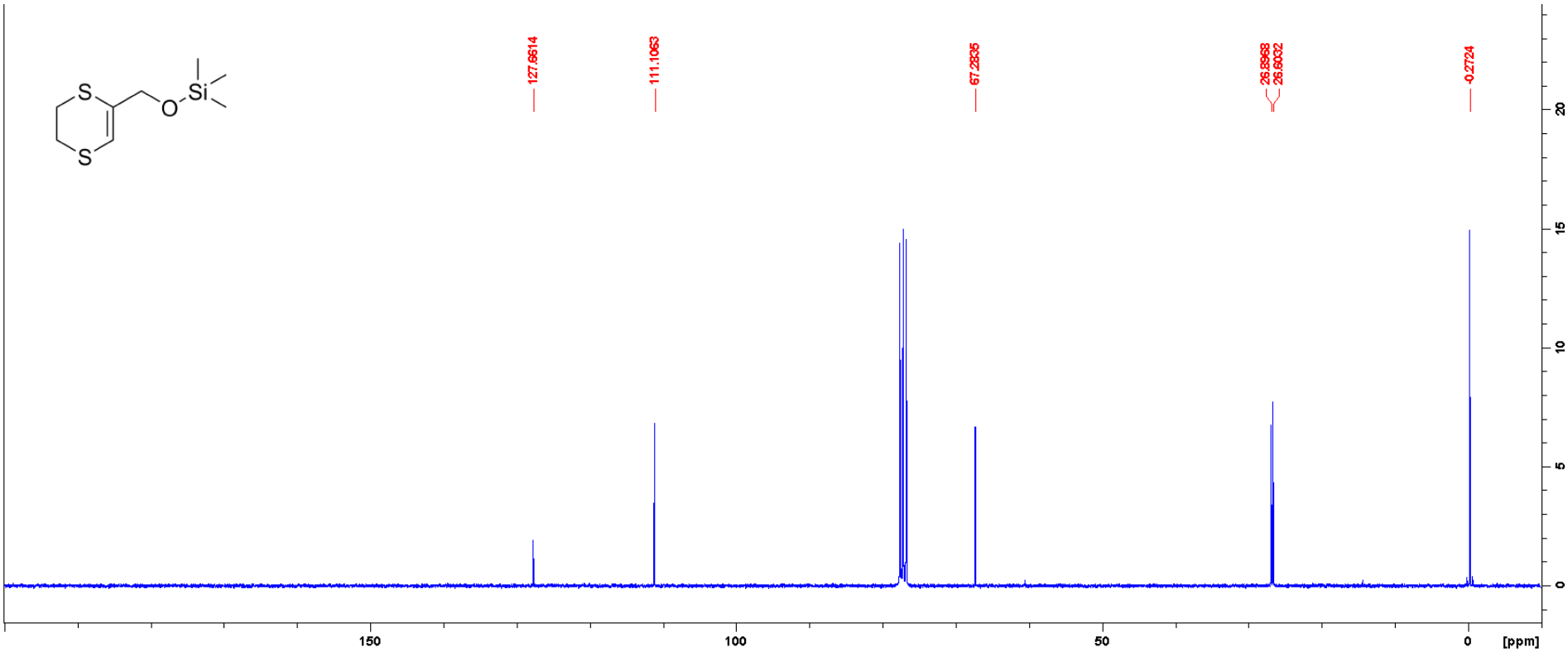
((5,6-dihydro-1,4-dithiin-2-yl)methoxy)trimethylsilane (12)
^{1}H-NMR (300 MHz, $CDCl_3$)



^{13}C-NMR (75 MHz, $CDCl_3$)



((5,6-dihydro-1,4-dithiin-2-yl)methyl acetate (13)
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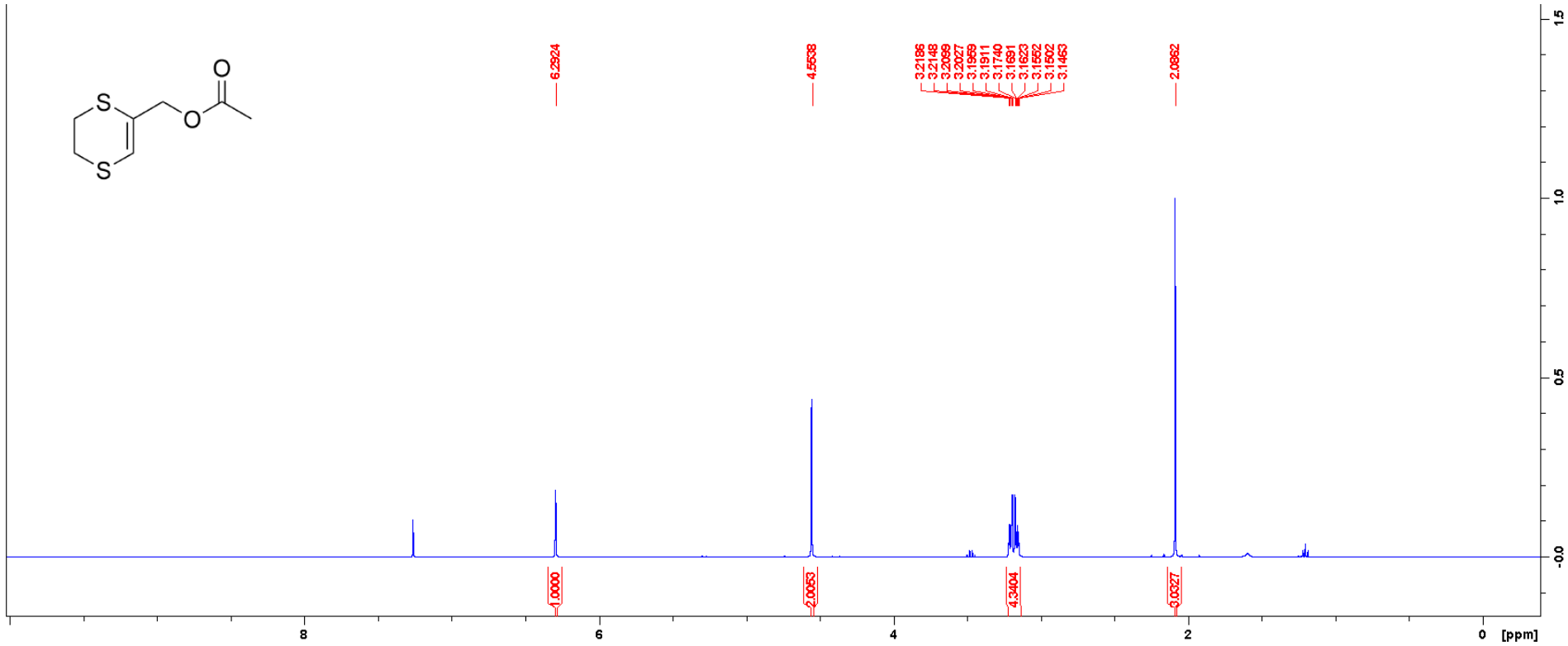

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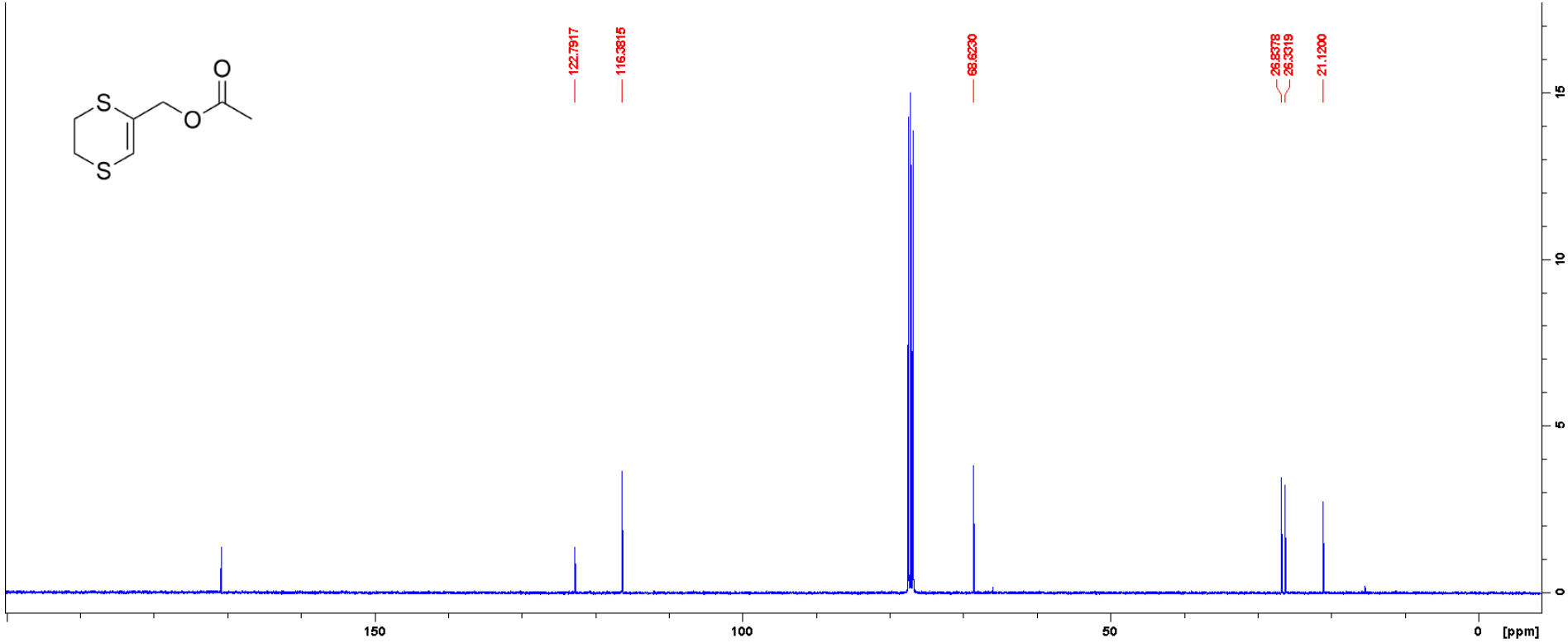
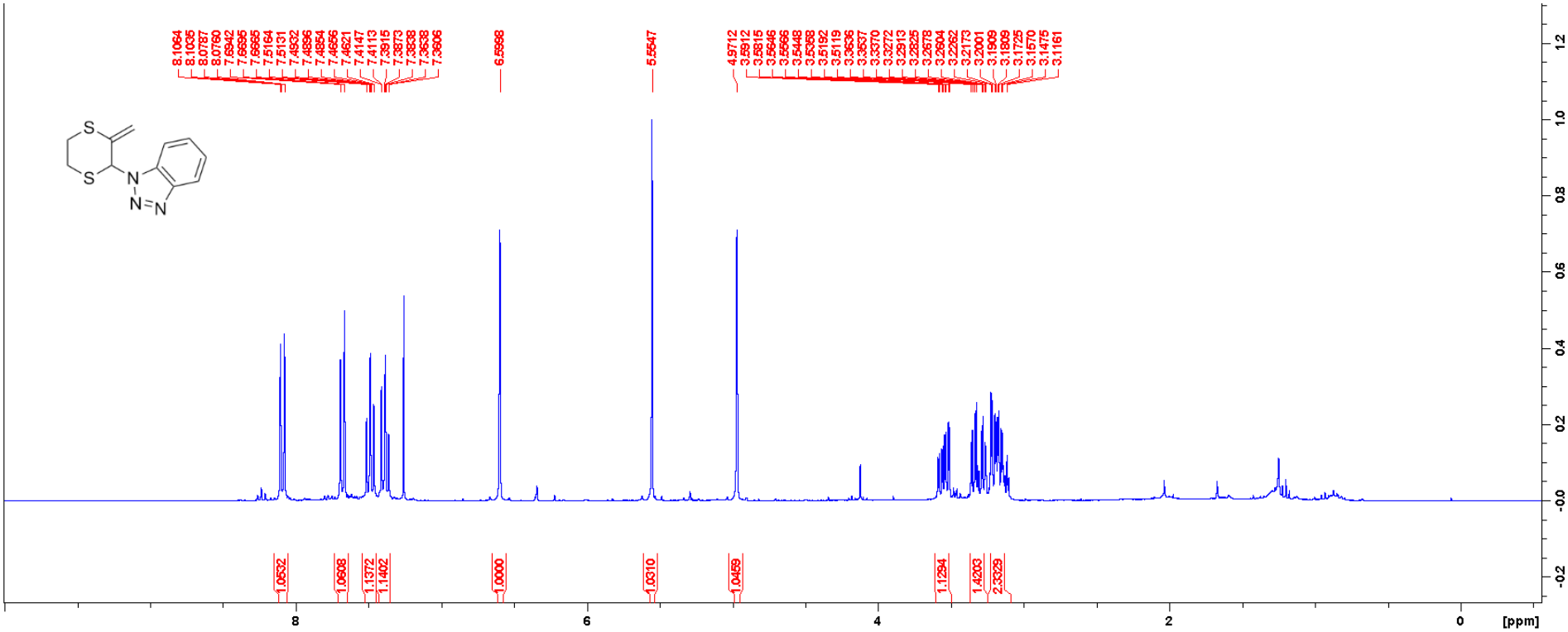
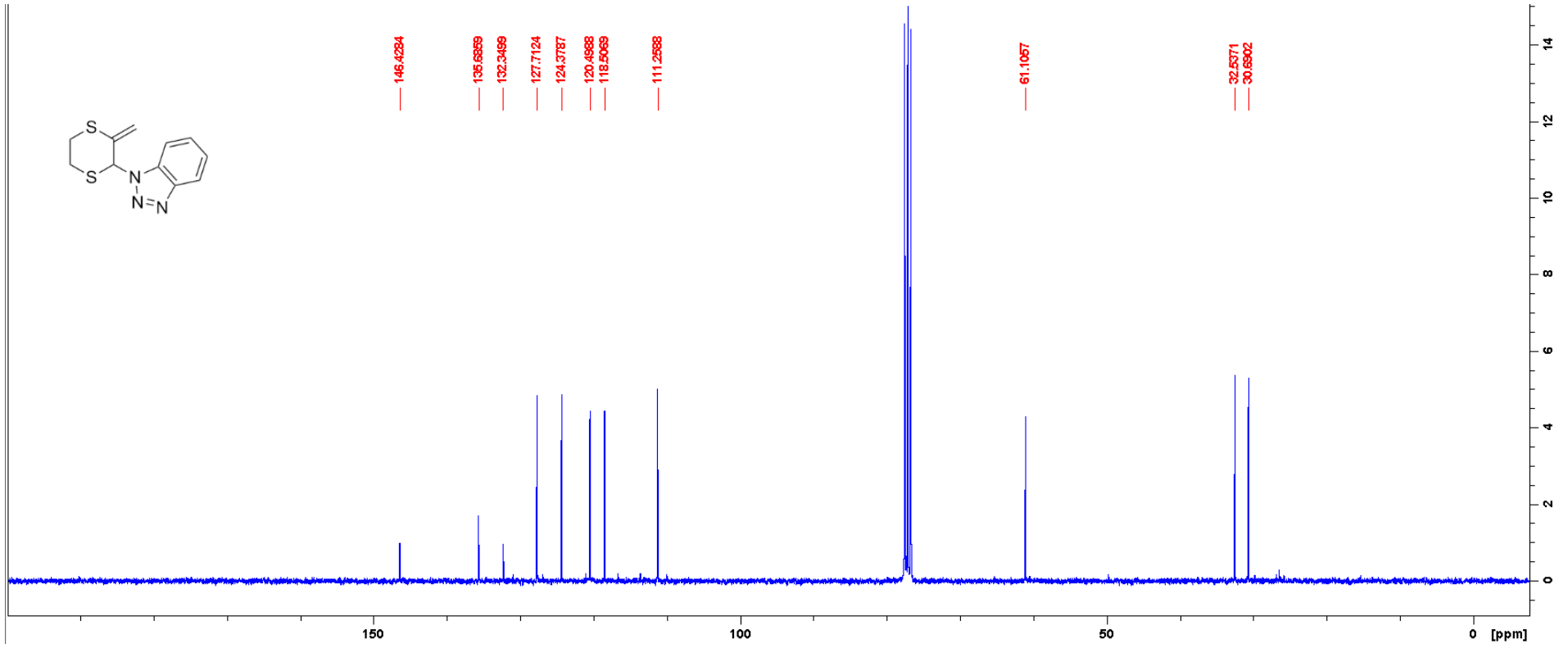


1-((5,6-dihydro-1,4-dithiin-2-yl)methyl)-2H-benzo[d][1,2,3]triazole (15a)

^{1}H-NMR (300 MHz, $CDCl_3$)

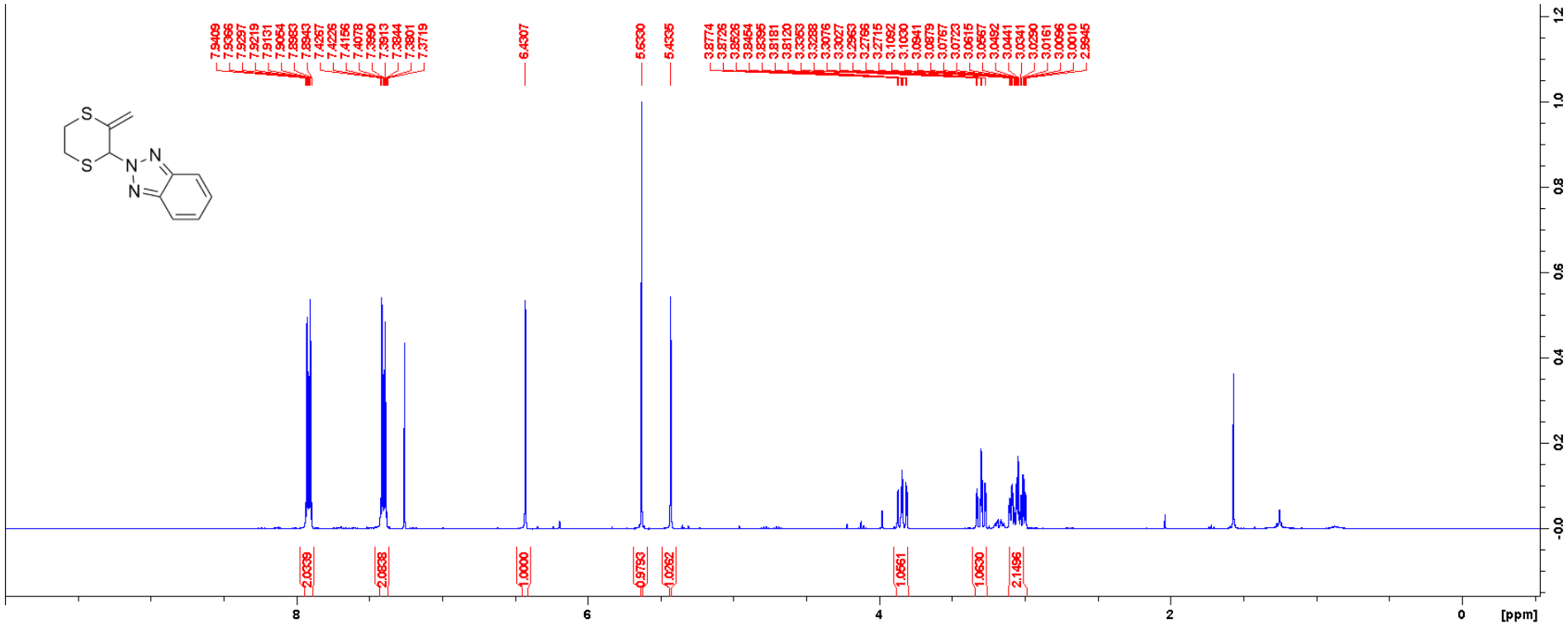


^{13}C-NMR (75 MHz, $CDCl_3$)

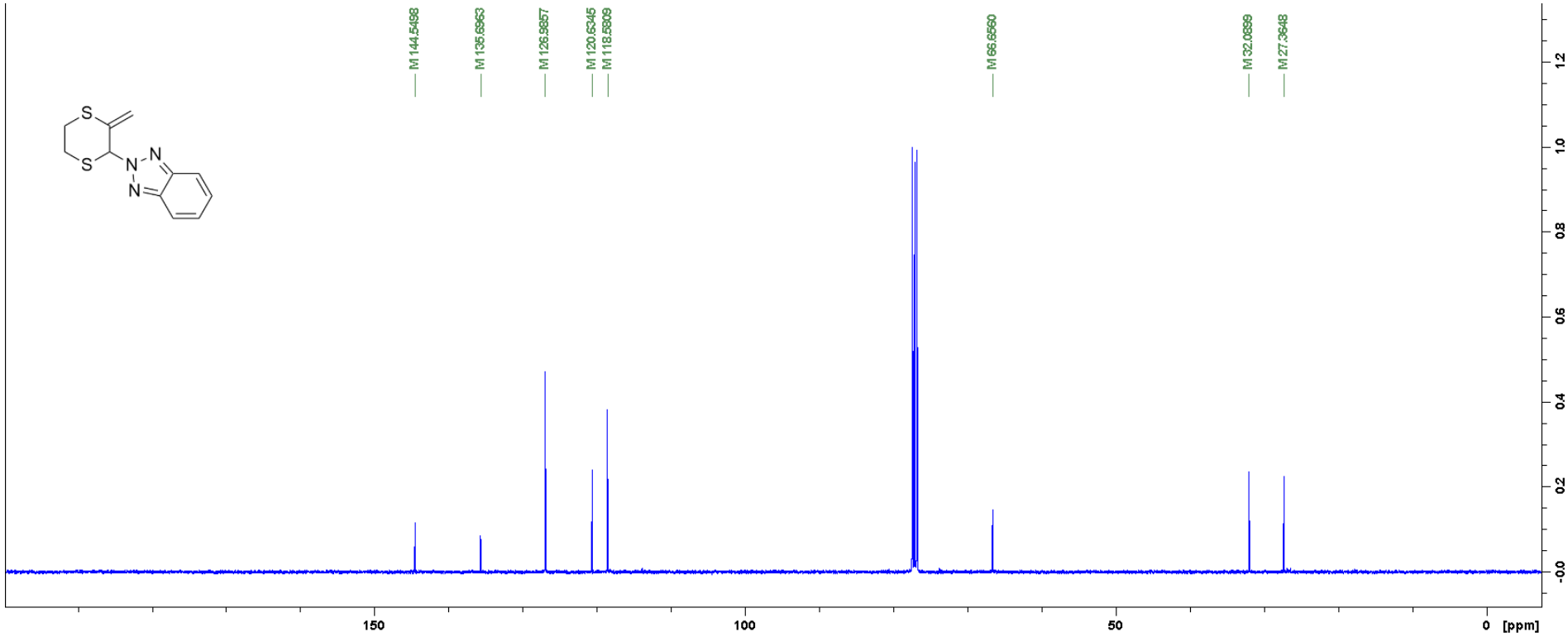


2-((5,6-dihydro-1,4-dithiin-2-yl)methyl)-2H-benzo[d][1,2,3]triazole (15b)

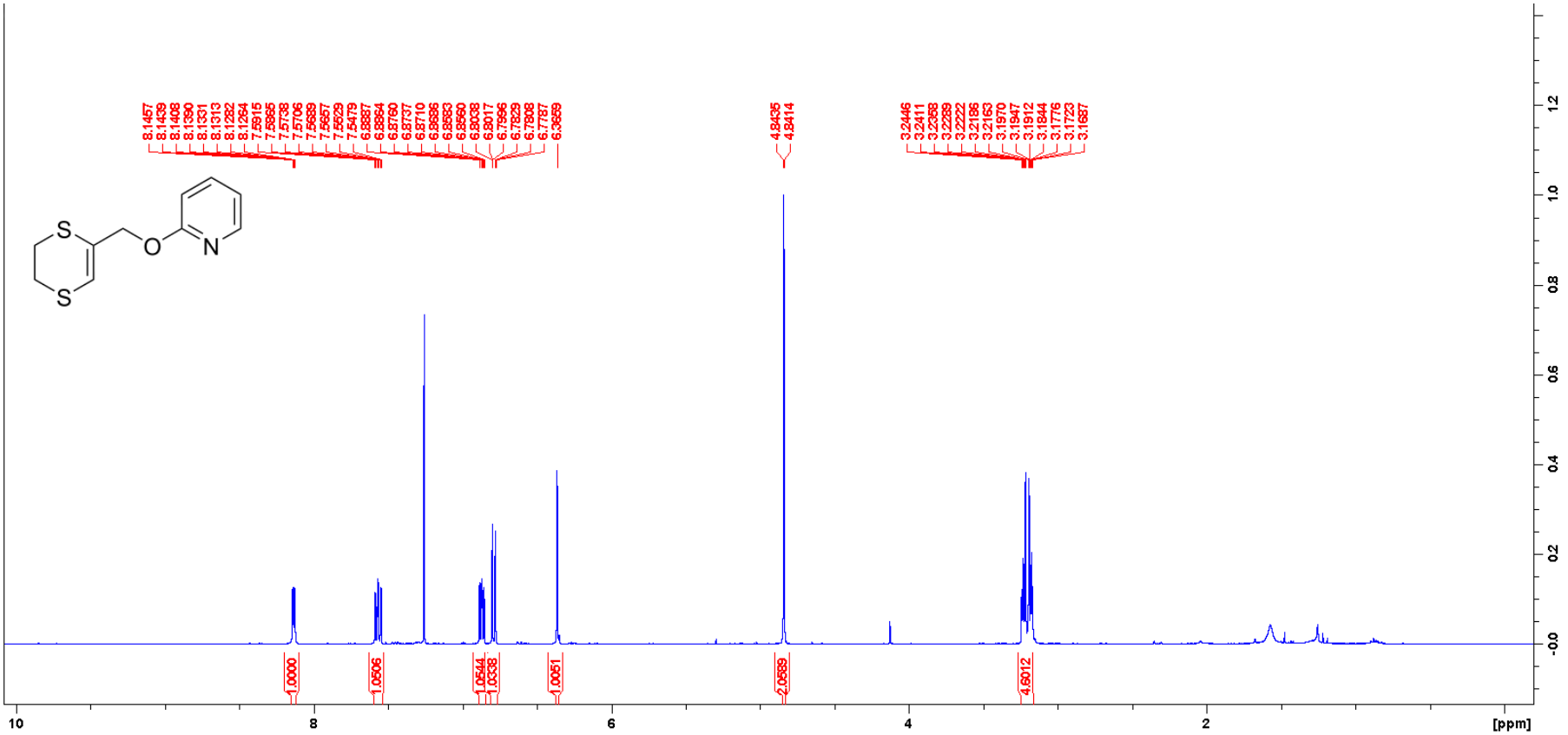
^{1}H-NMR (400 MHz, $CDCl_3$)



^{13}C-NMR (101 MHz, $CDCl_3$)



2-((5,6-dihydro-1,4-dithiin-2-yl)methoxy)pyridine (16)
^{1}H-NMR (400 MHz, $CDCl_3$)



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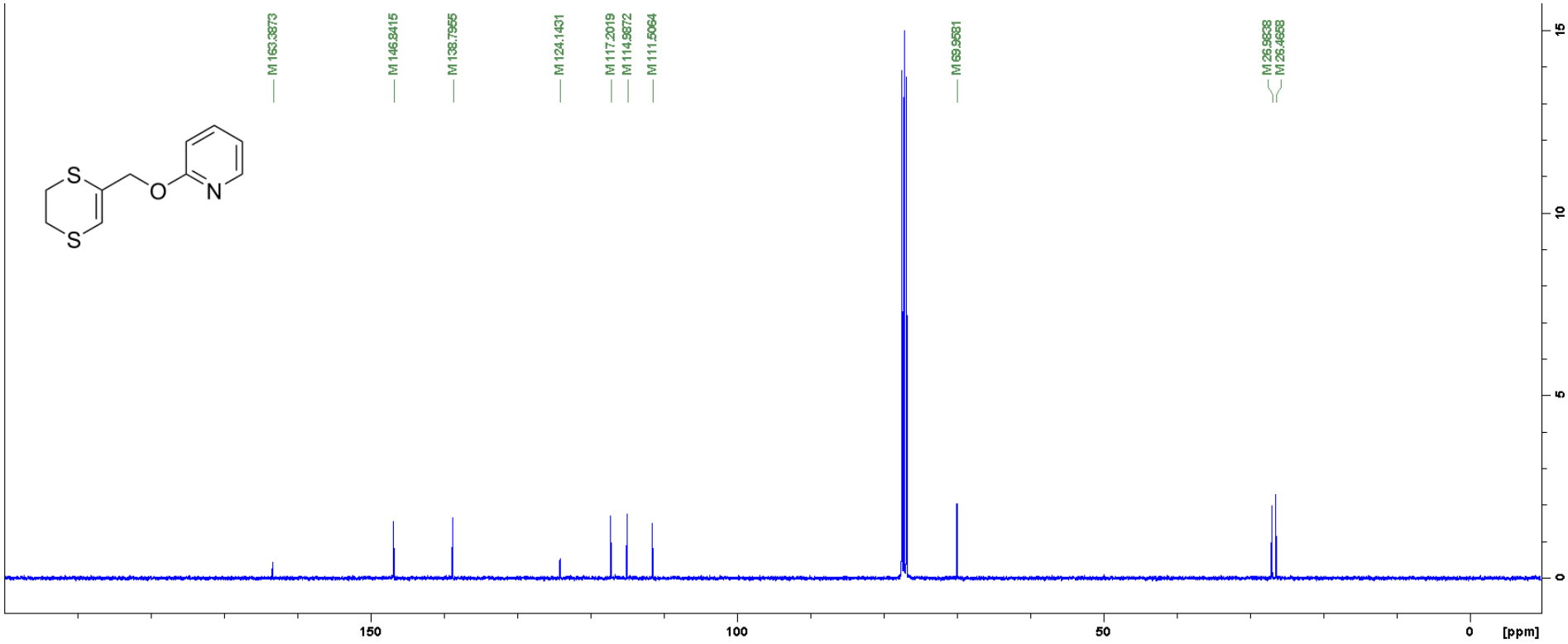
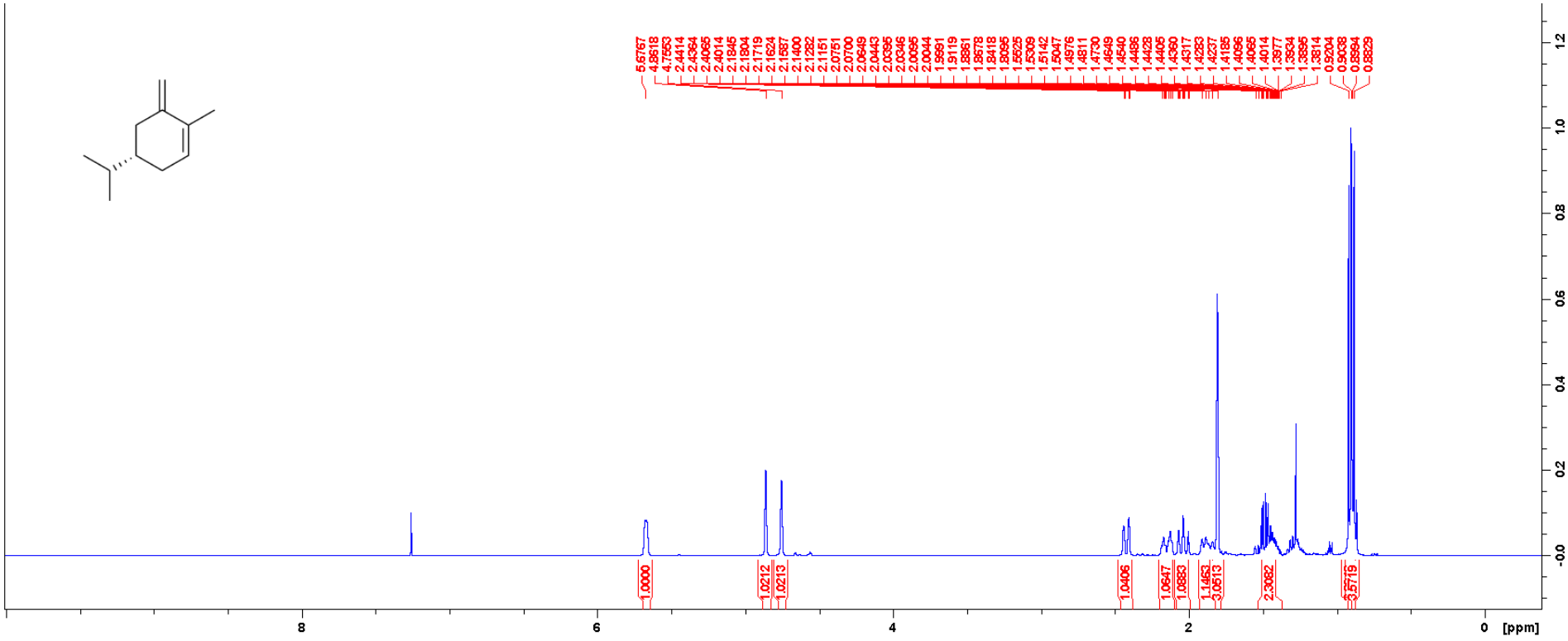


(S)-4-isopropyl-1-methyl-6-methylenecyclohex-1-ene (19)
^{1}H-NMR (400 MHz, $CDCl_3$)



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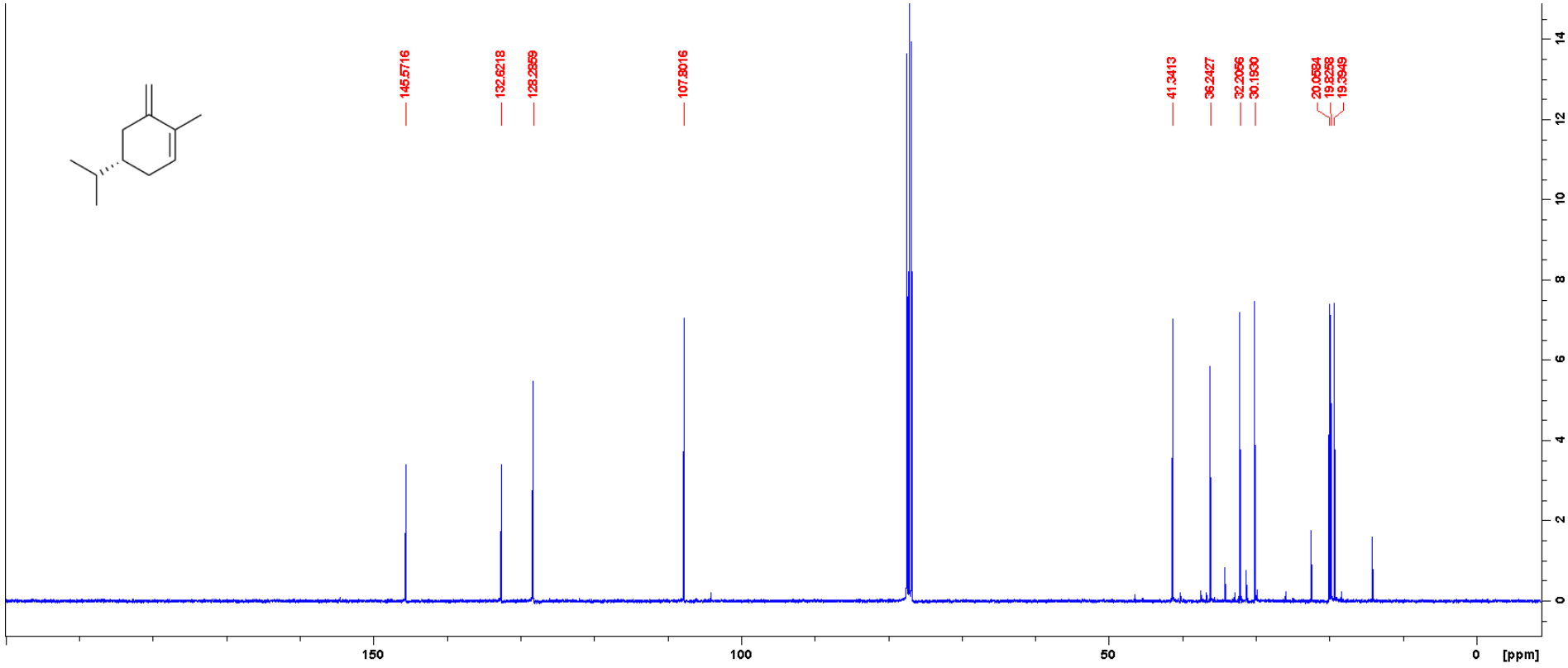
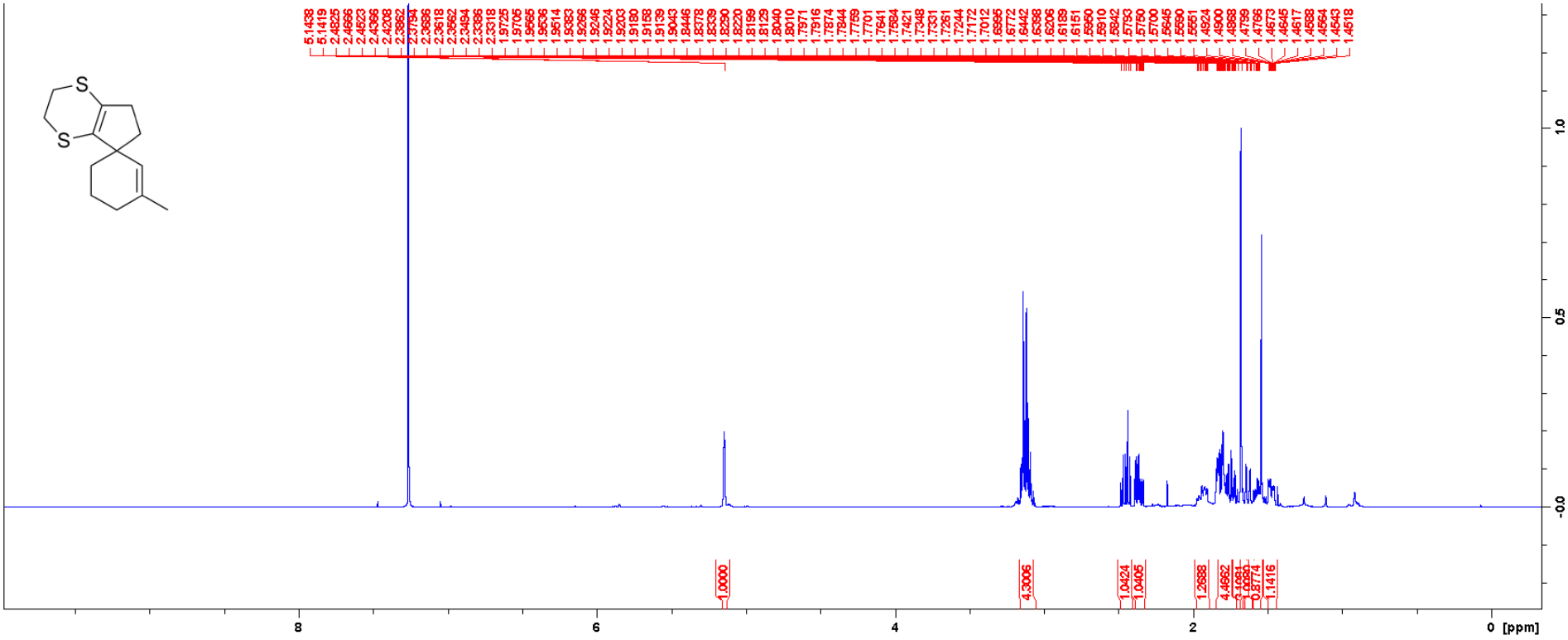
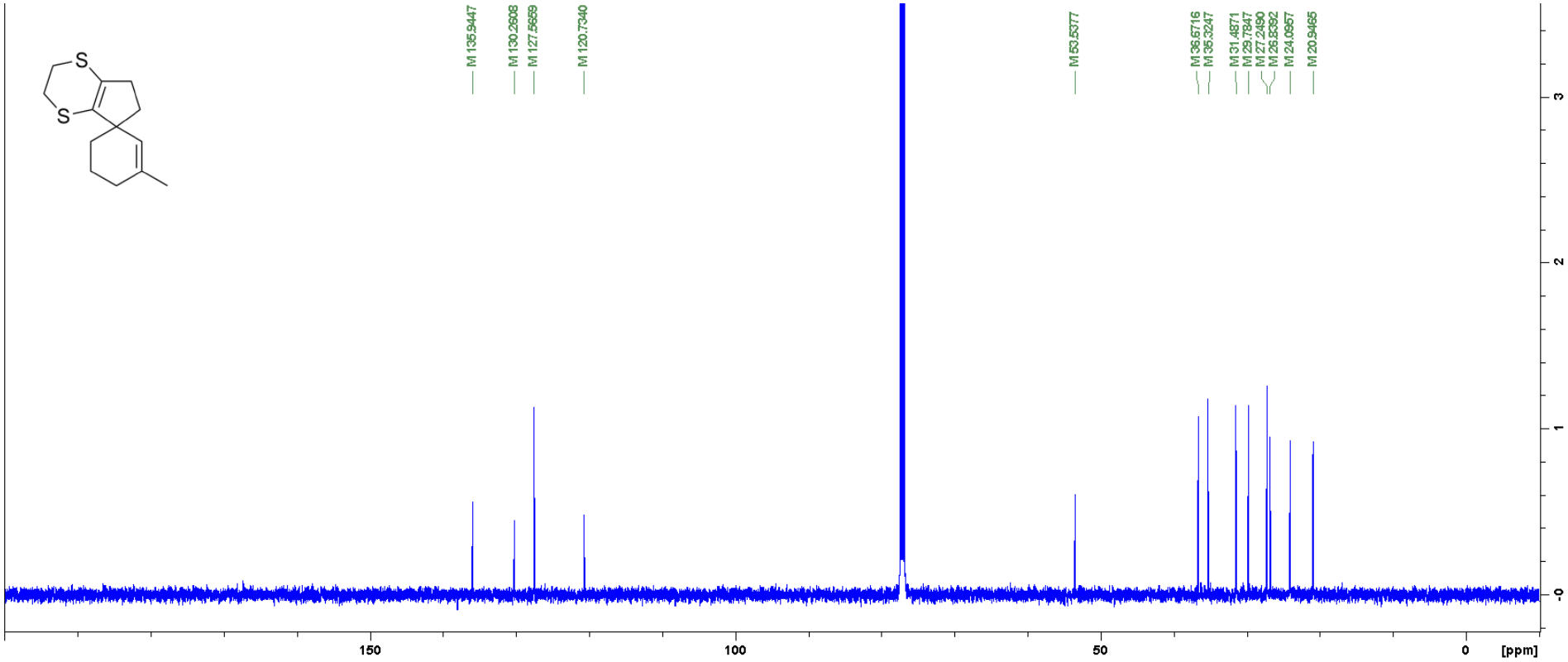


3-methyl-2',3',6',7'-tetrahydrospiro[cyclohexane-1,5'-cyclopenta[b][1,4]dithiin]-2-ene (22)

^{1}H-NMR (500 MHz, $CDCl_3$)



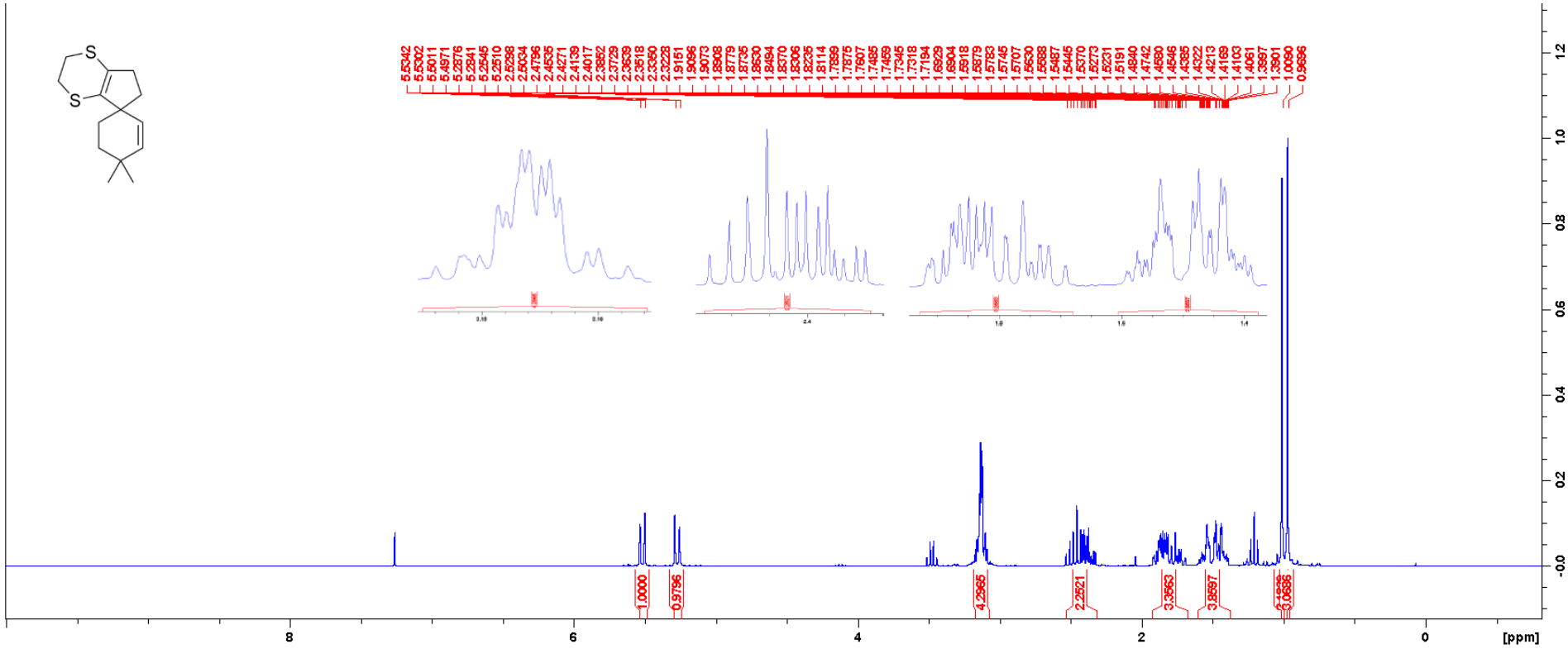
^{13}C-NMR (125 MHz, $CDCl_3$)



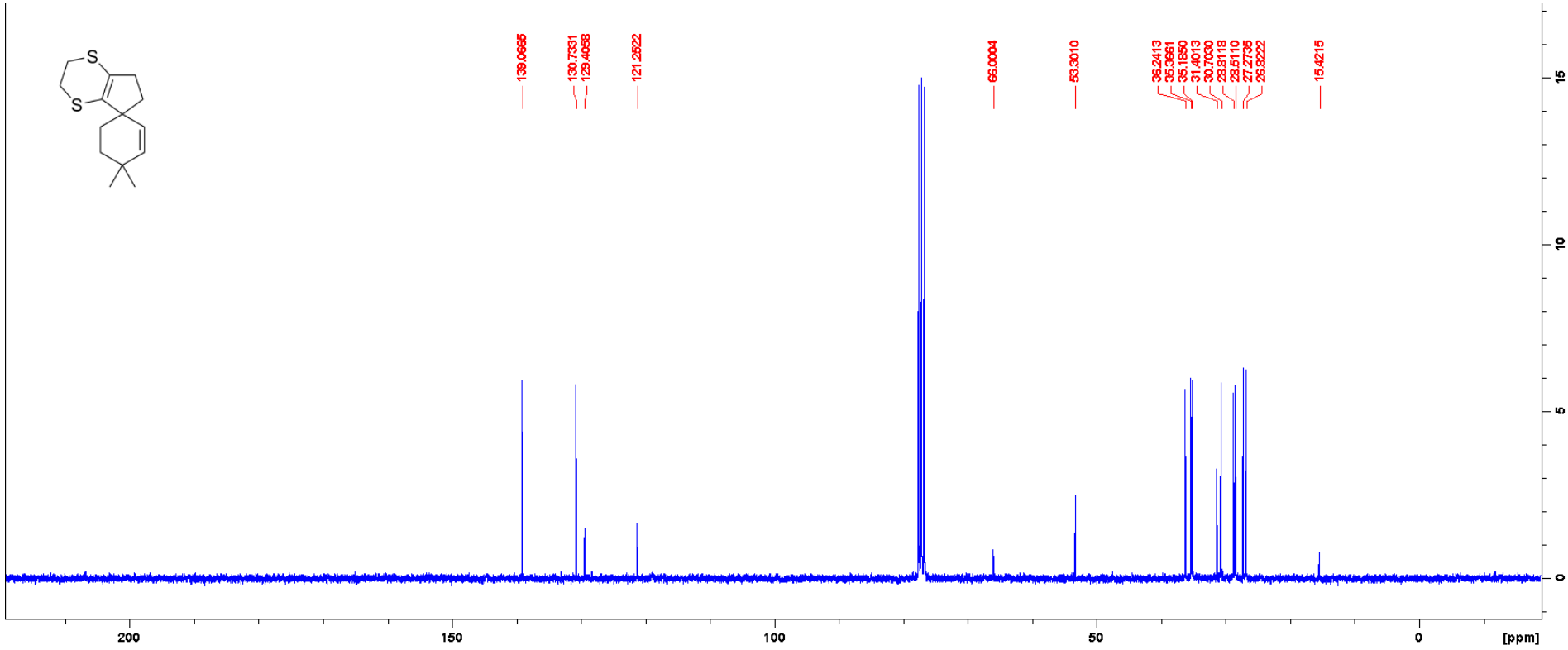
4,4-dimethyl-2',3',6',7'-tetrahydrospiro[cyclohexane-1,5'-cyclopenta[b][1,4]dithiin]-2-ene (23)

^{1}H-NMR (300 MHz, $CDCl_3$)

Contains residual Et_2O (q @ 3.48 ppm, t @ 1.21 ppm)



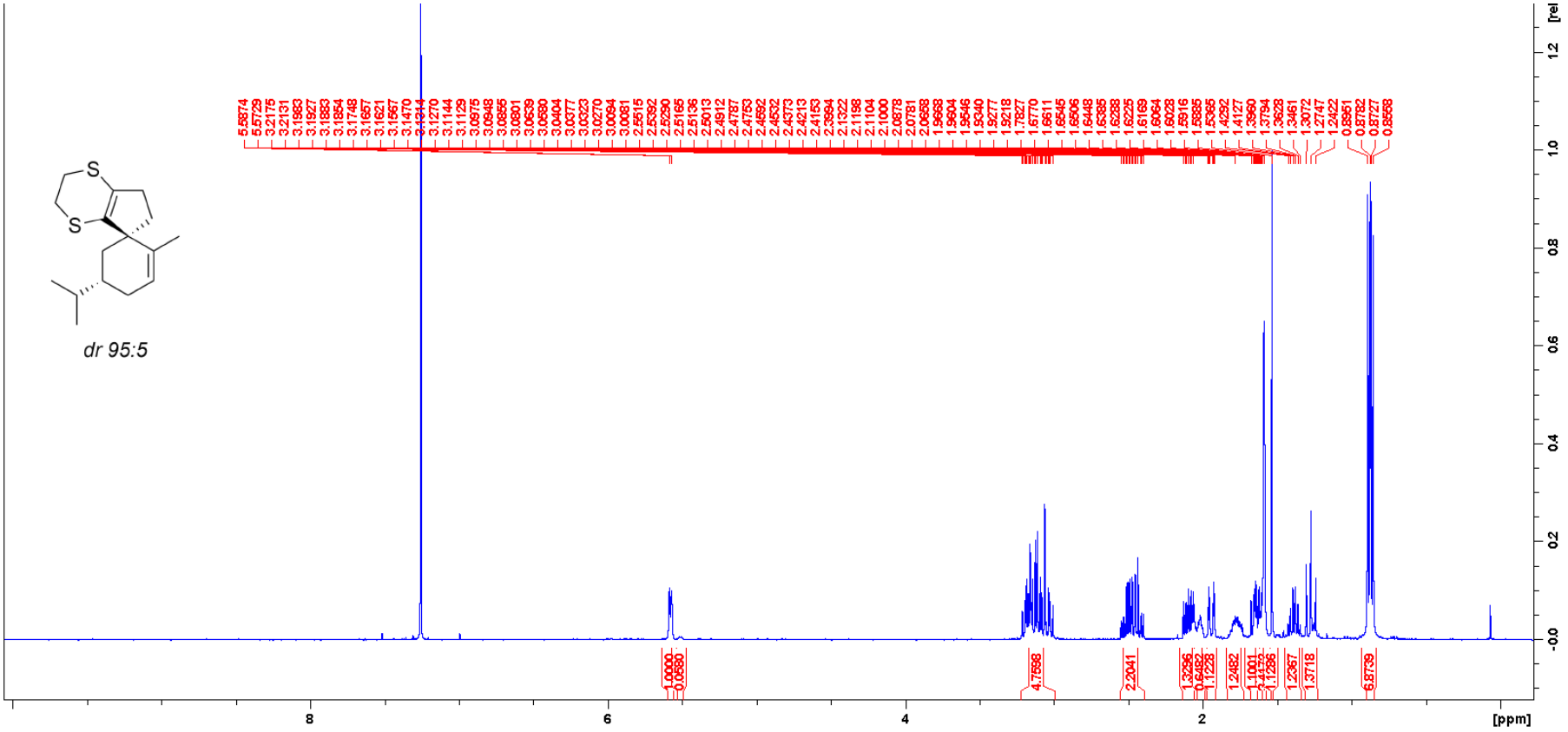
^{13}C-NMR (75 MHz, $CDCl_3$)



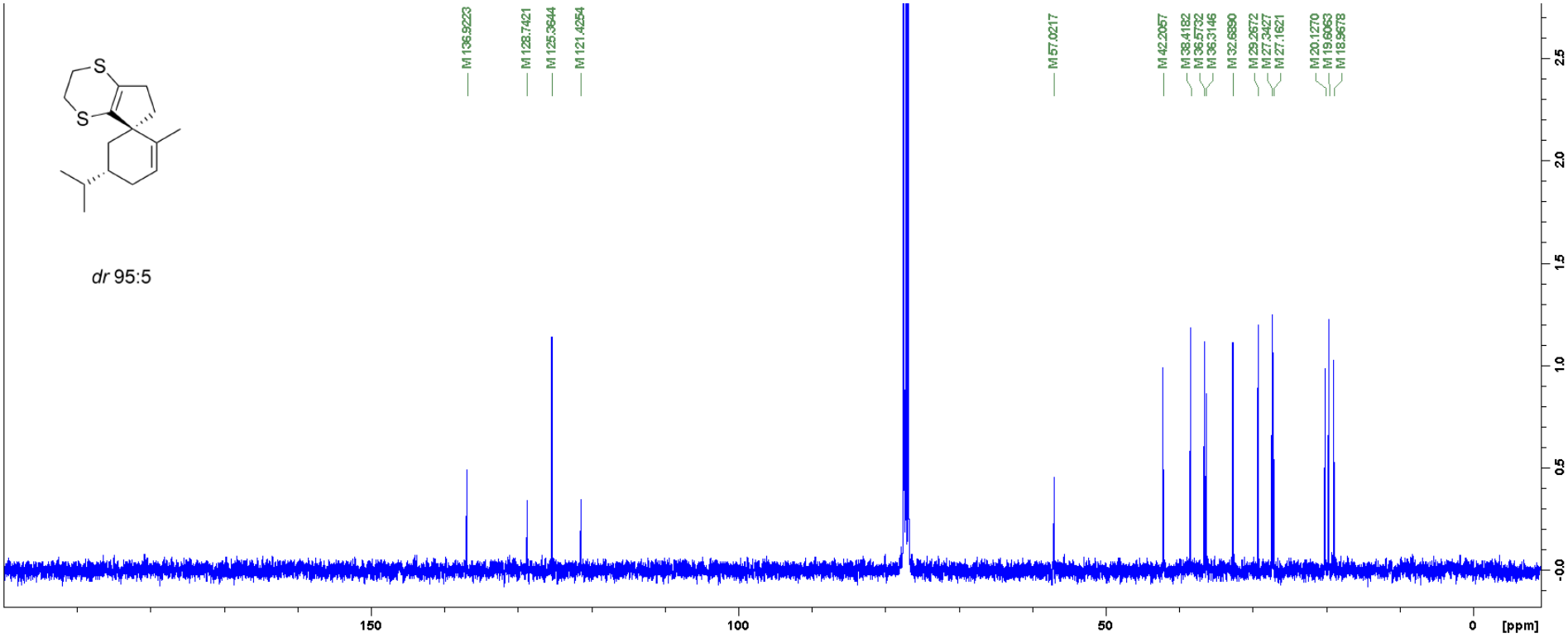
(1R,5S)-5-isopropyl-2-methyl-2',3',6',7'-tetrahydrospiro[cyclohexane-1,5'-cyclopenta[b][1,4]dithiin]-2-ene (24)

^{1}H-NMR (400 MHz, $CDCl_3$)

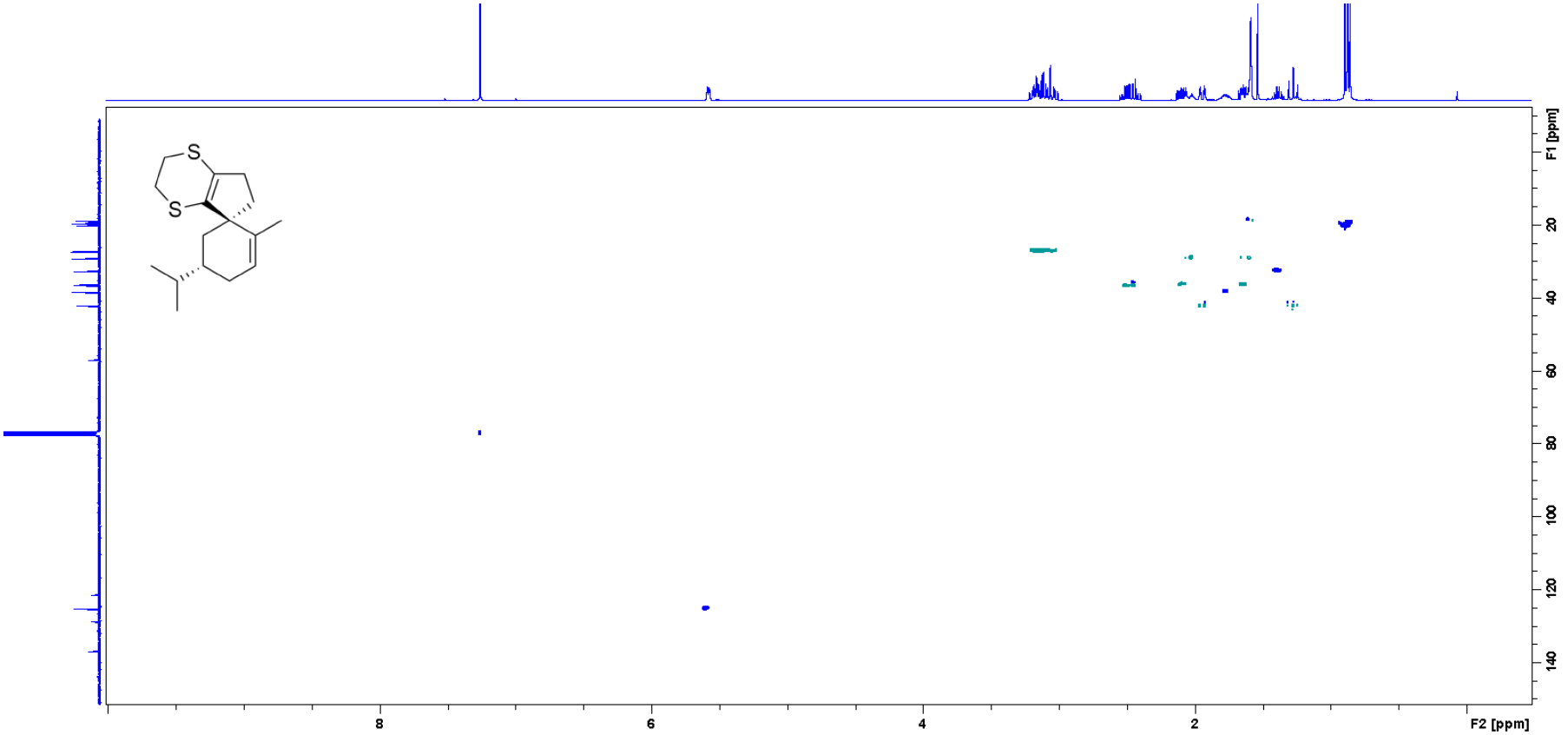
Contains residual water (s (br) @ 1.56 ppm) and CH_2Cl_2 (s @ 5.3 ppm)



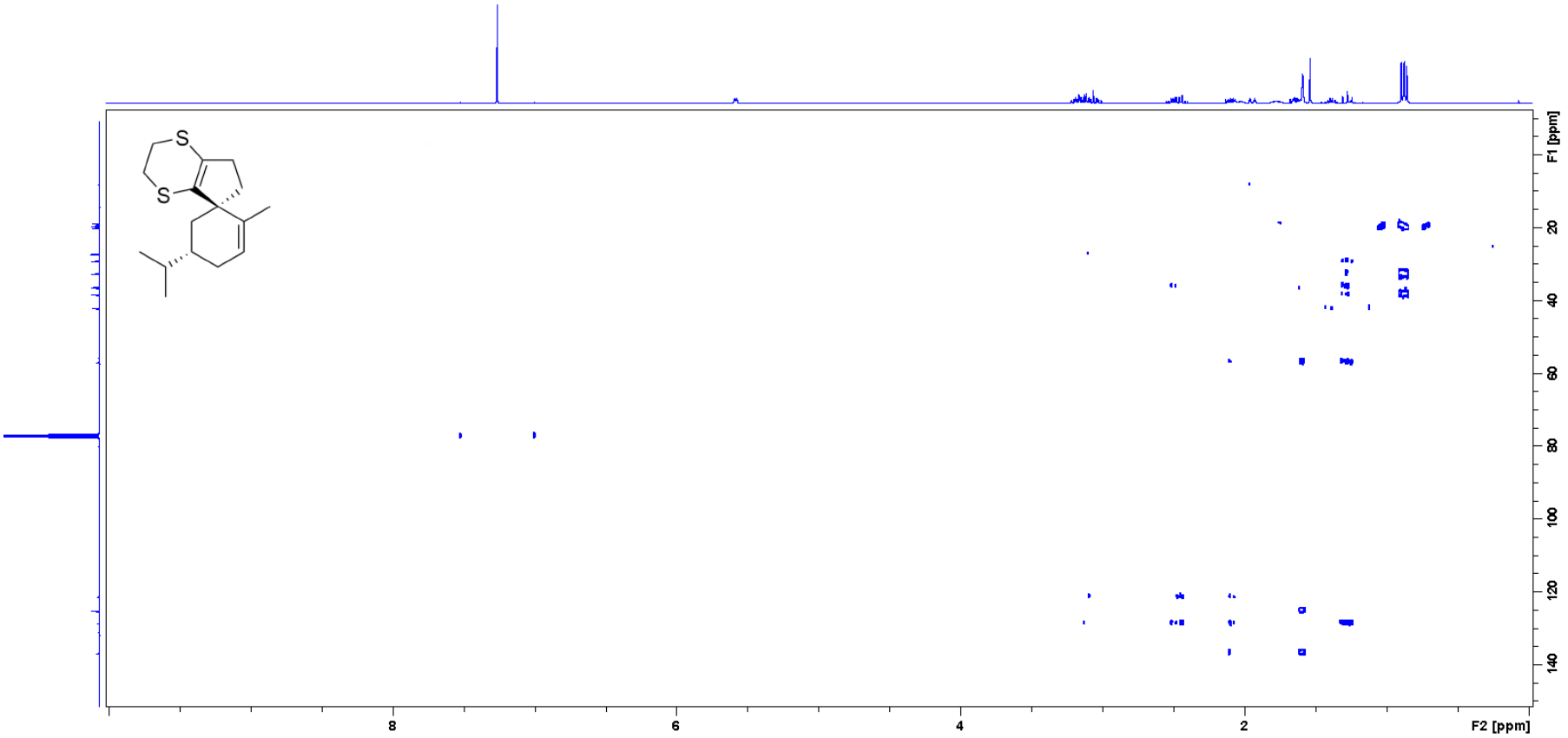
^{13}C-NMR (101 MHz, $CDCl_3$)



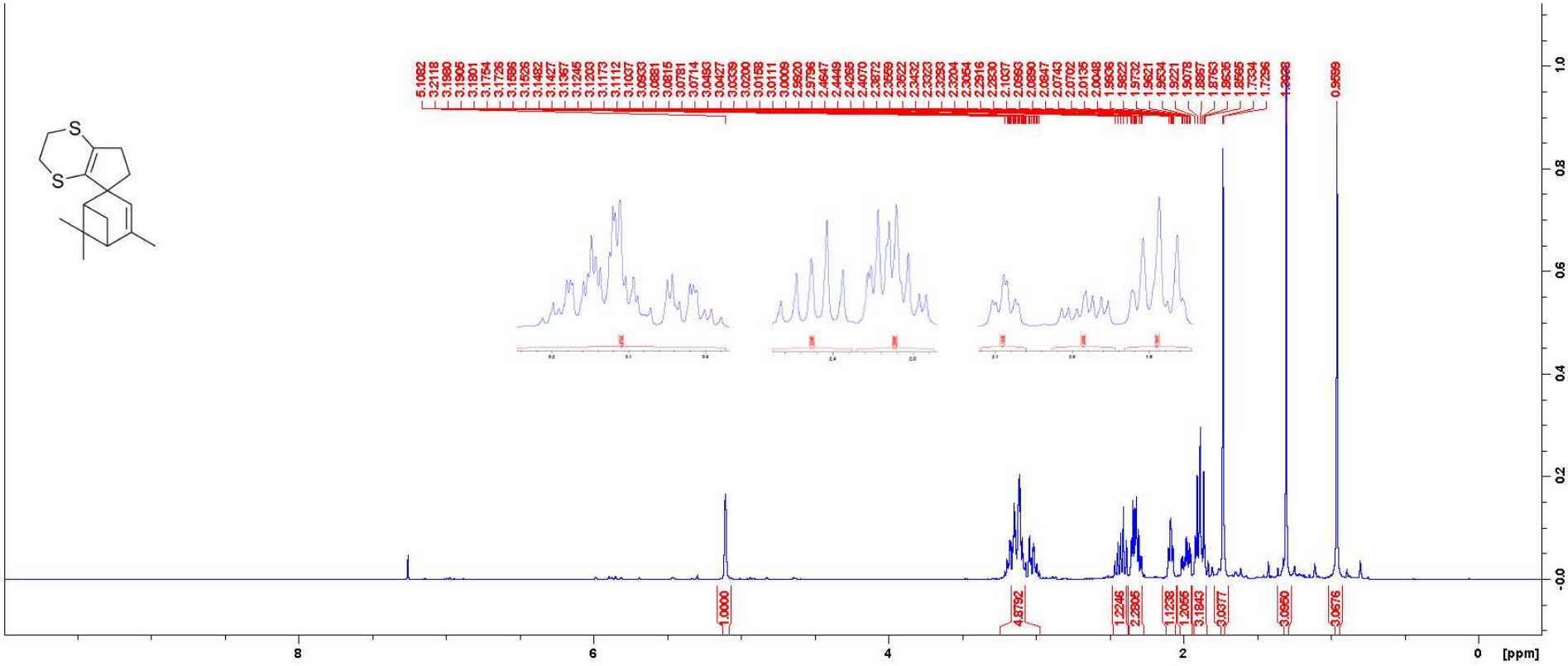
HSQC-spectrum ($CDCl_3$)



HMBC-spectrum ($CDCl_3$)



(1R,2R,5R)-4,6,6-trimethyl-2',3',6',7'-tetrahydrospiro[bicyclo[3.1.1]heptane-2,5'-cyclopenta[b][1,4]dithiin]-3-ene (30)
^{1}H-NMR (400 MHz, $CDCl_3$)



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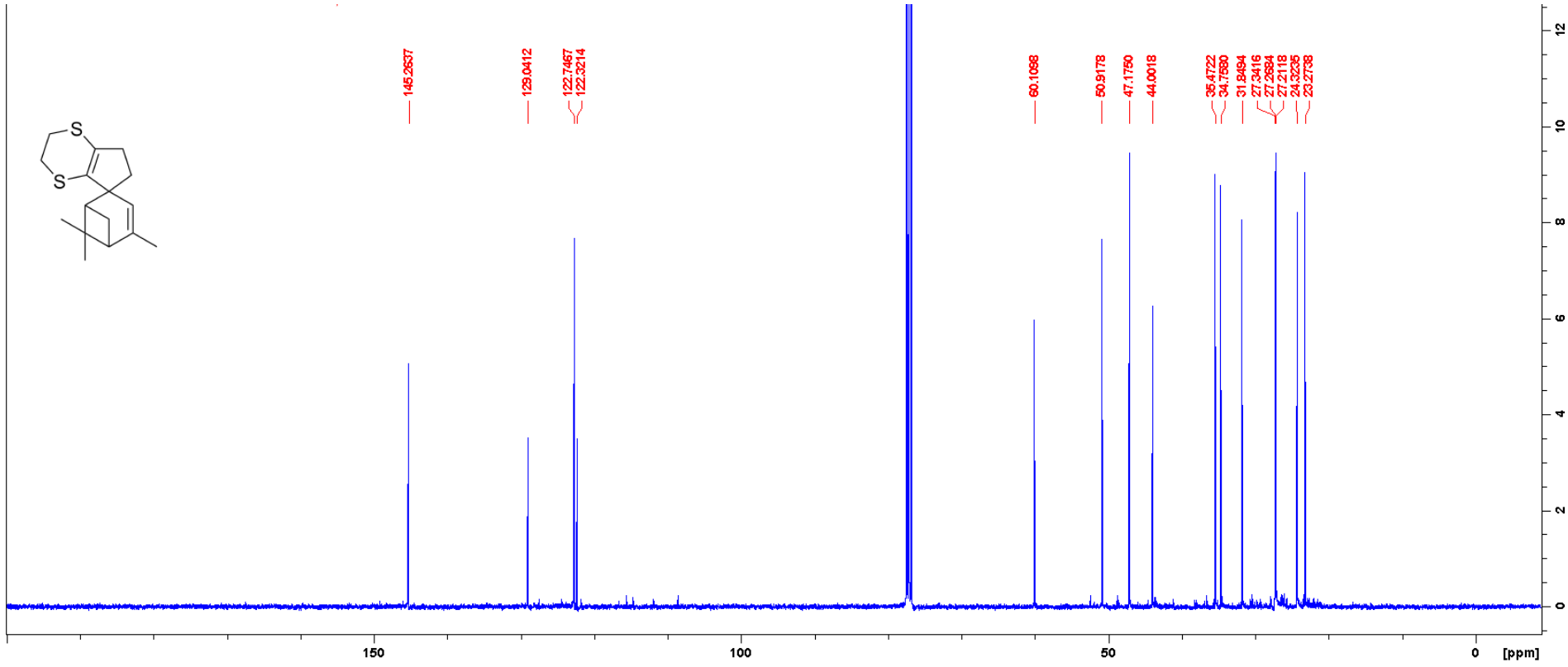
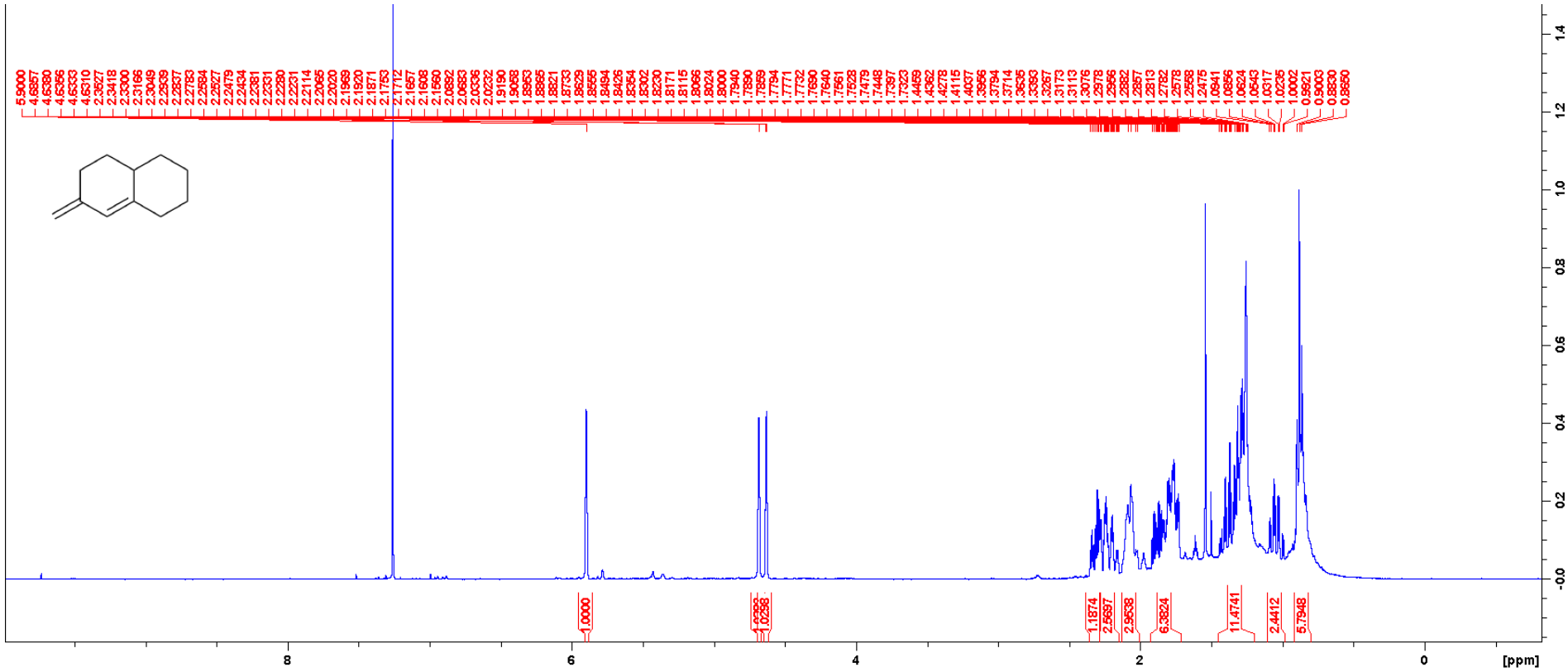
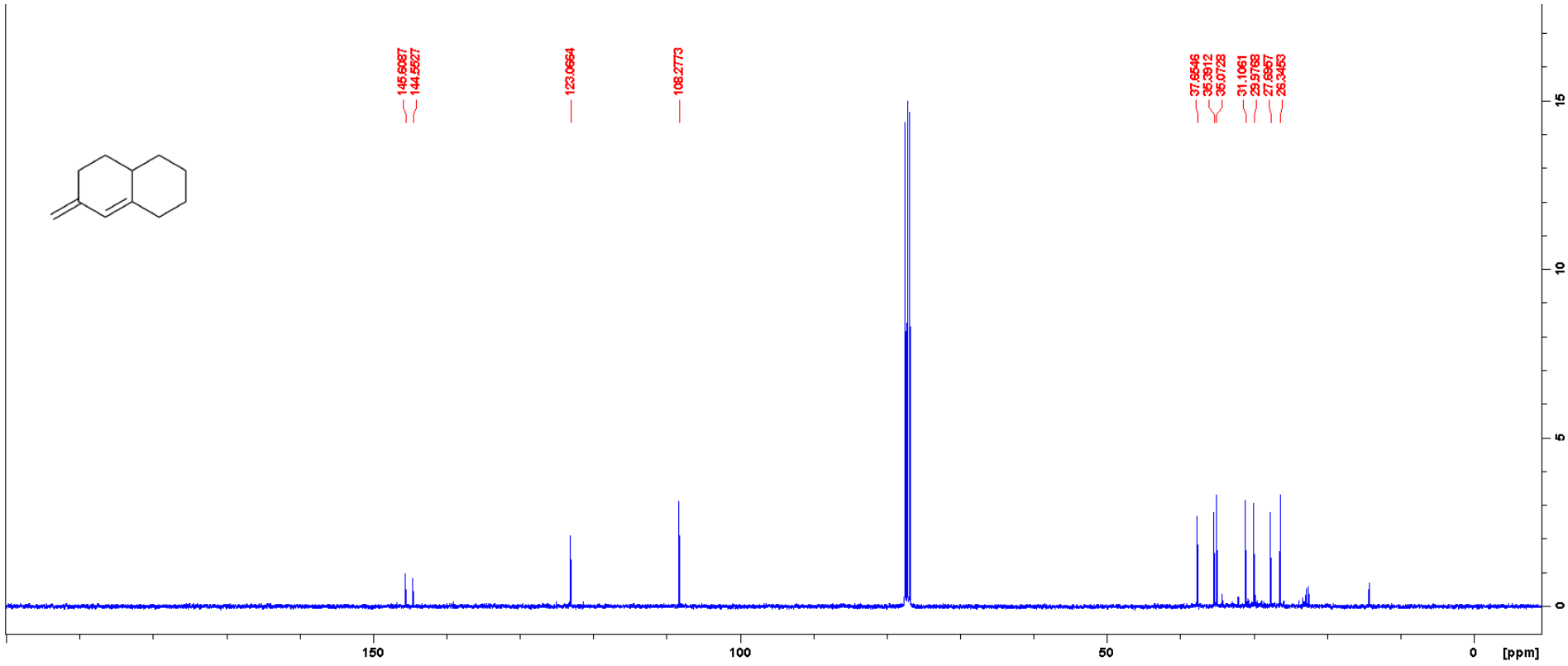


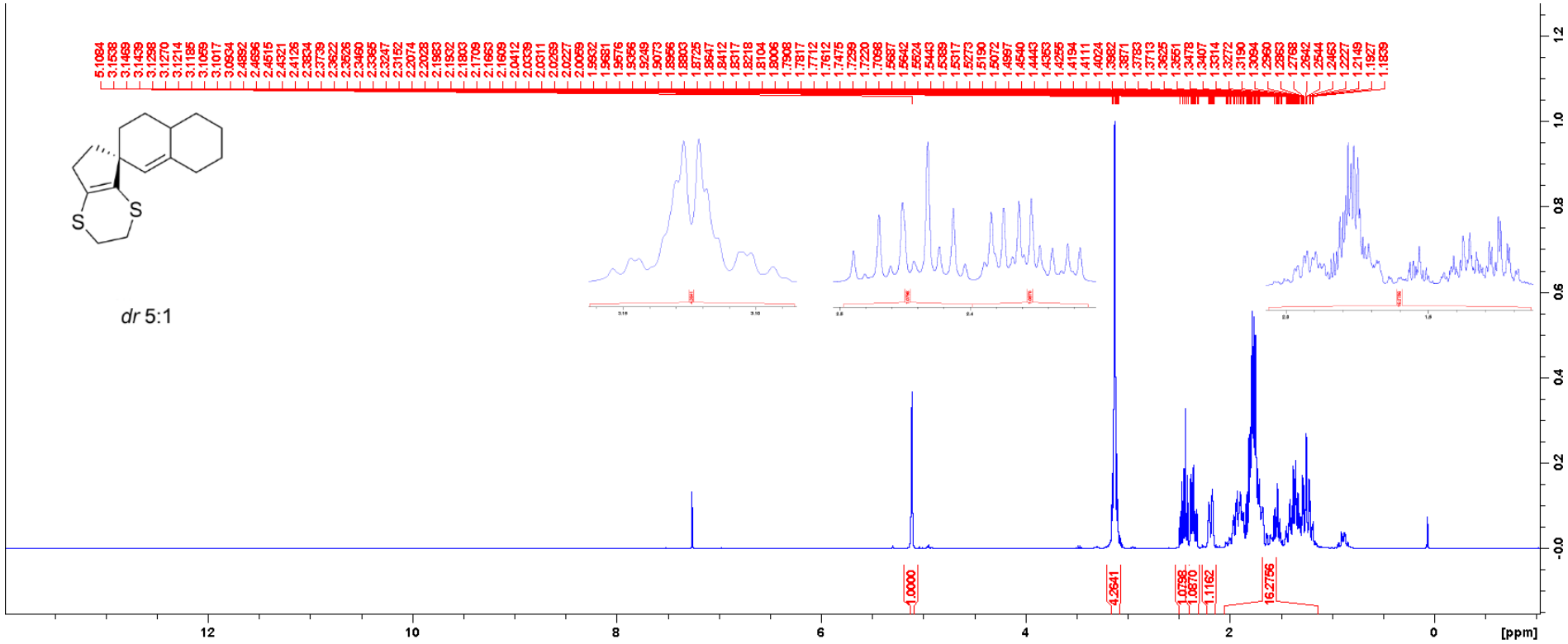
7-methylene-1,2,3,4,4a,5,6,7-octahydronaphthalene
^{1}H-NMR (300 MHz, $CDCl_3$)



^{13}C-NMR (75 MHz, $CDCl_3$)



2,3,4',4a',5',6,6',7,7',8'-decahydro-3'H-spiro[cyclopenta[b][1,4]dithiine-5,2'-naphthalene] (32)
^{1}H-NMR (400 MHz, $CDCl_3$)
Contains residual water (s (br) @ 1.56 ppm)



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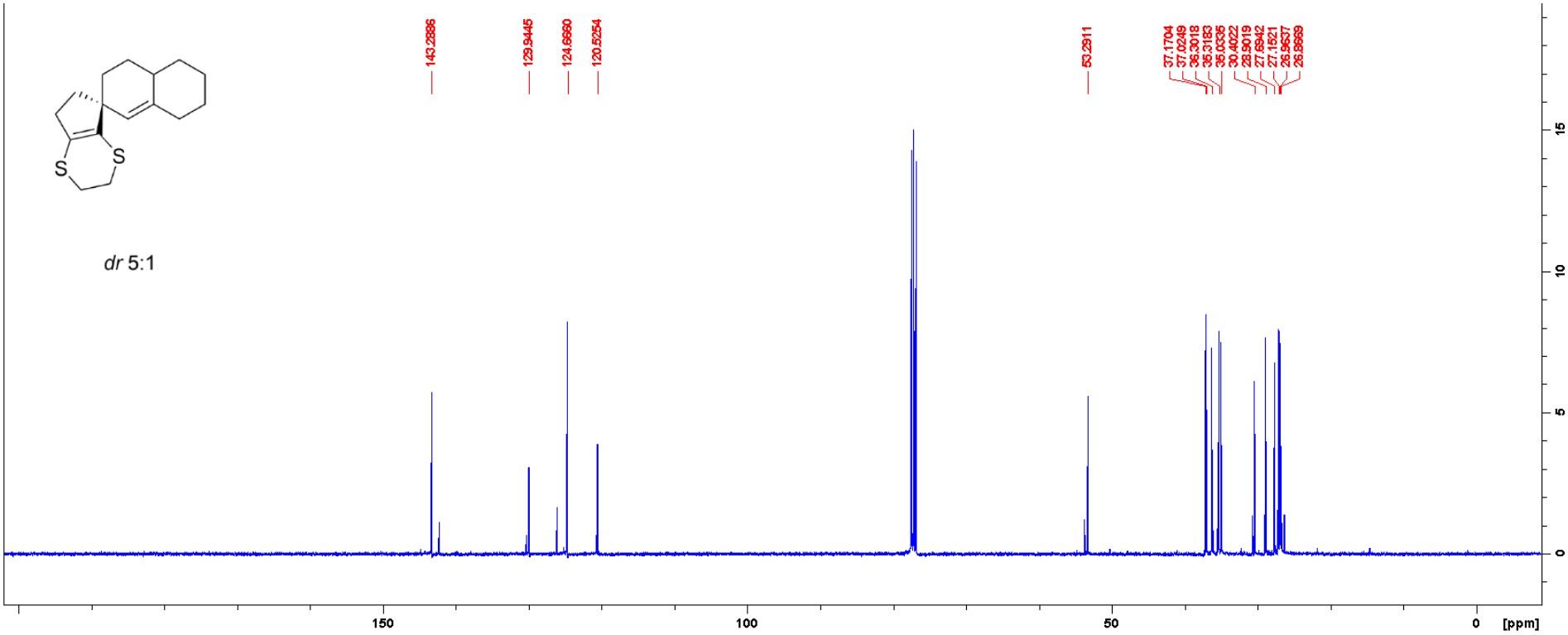
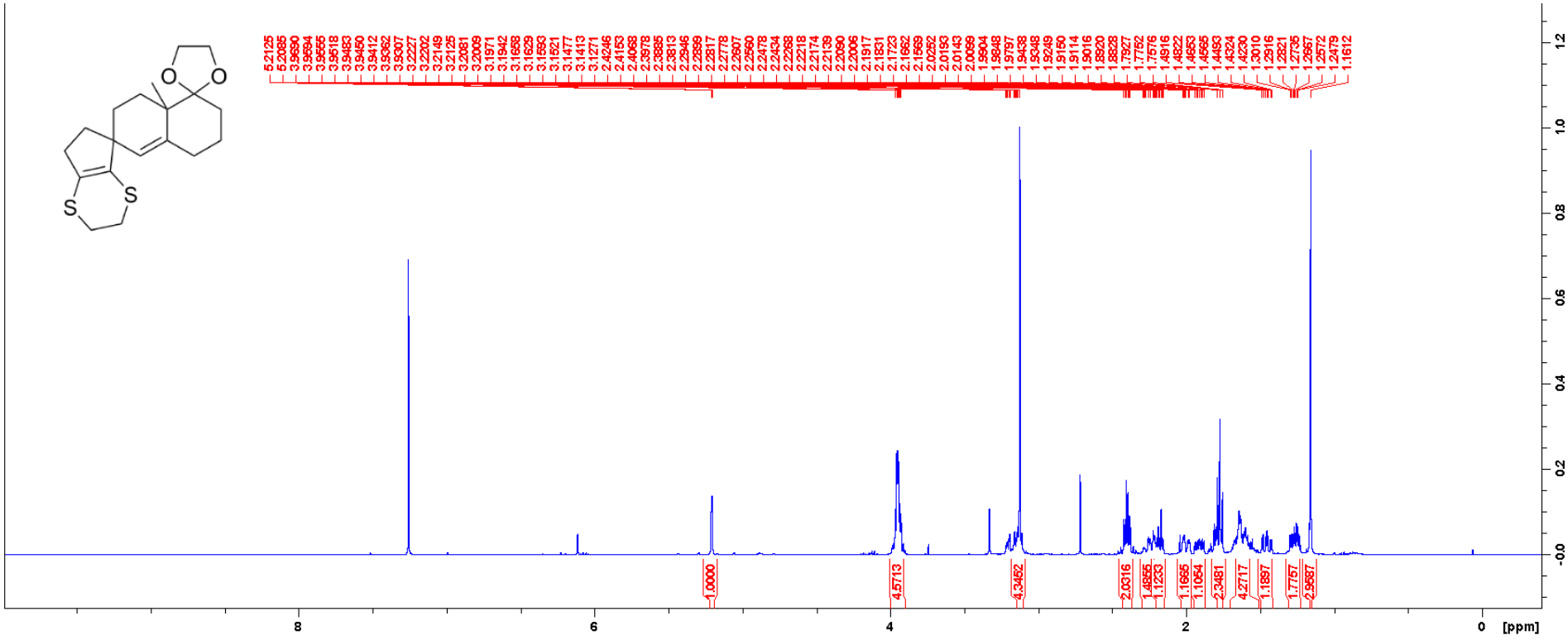


8a'-methyl-2,3,3',4',6,7,8',8a'-octahydro-2'H,7'H-dispiro[cyclopenta[b][1,4]dithiine-5,6'-naphthalene-1',2"-[1,3]dioxolane] (34)
^{1}H-NMR (400 MHz, $CDCl_3$)



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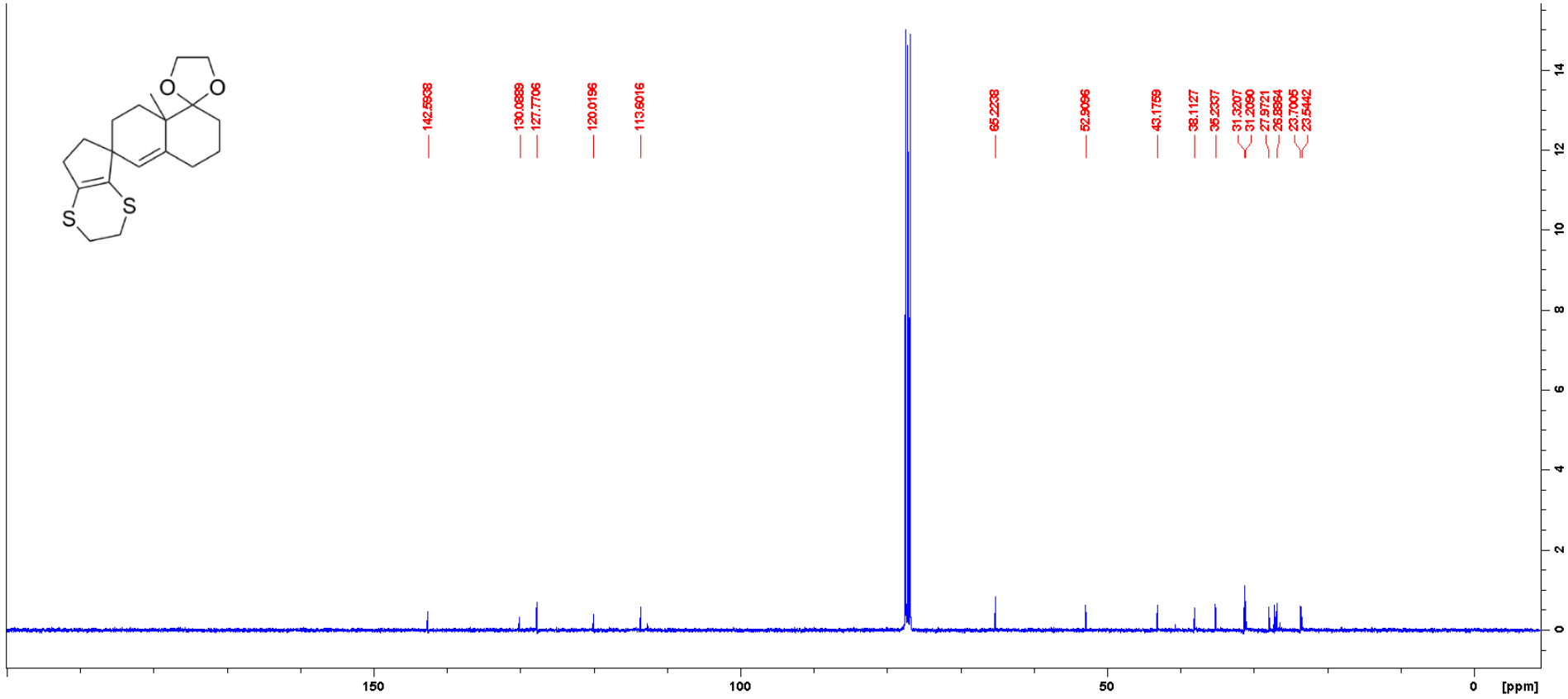
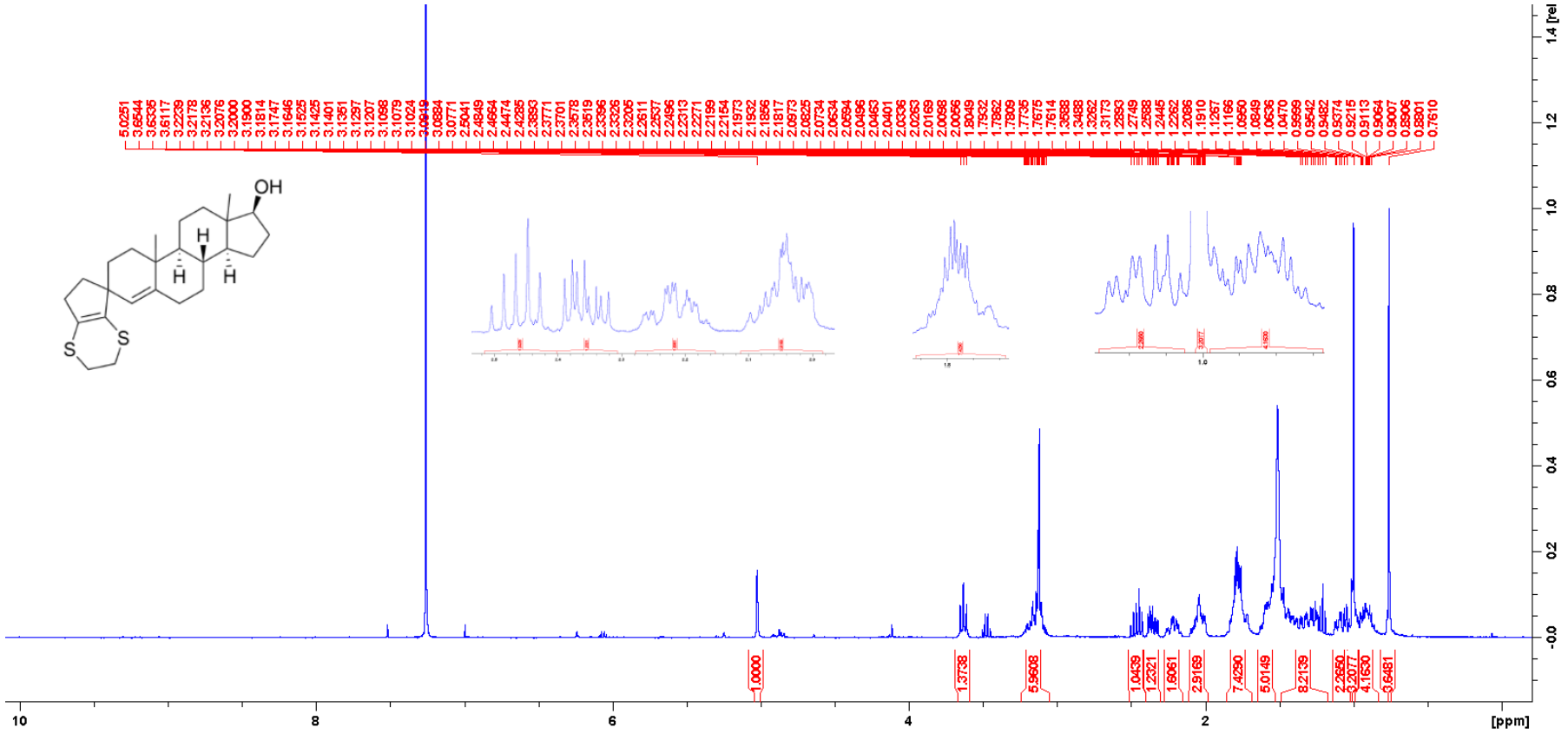


(8R,9S,10R,13S,14S,17S)-10,13-dimethyl-1,2,2',3',6,6',7,7',8,9,10,11,12,13,14,15,16,17-octadecahydrospiro[cyclopenta[a]phenanthrene-3,5'-cyclopenta[b][1,4]dithiin]-17-ol (36)

^{1}H-NMR (400 MHz, $CDCl_3$)

Contains residual Et_2O (q @ 3.48 ppm, t @ 1.21 ppm) and H_2O (s (br) @ 1.56 ppm)



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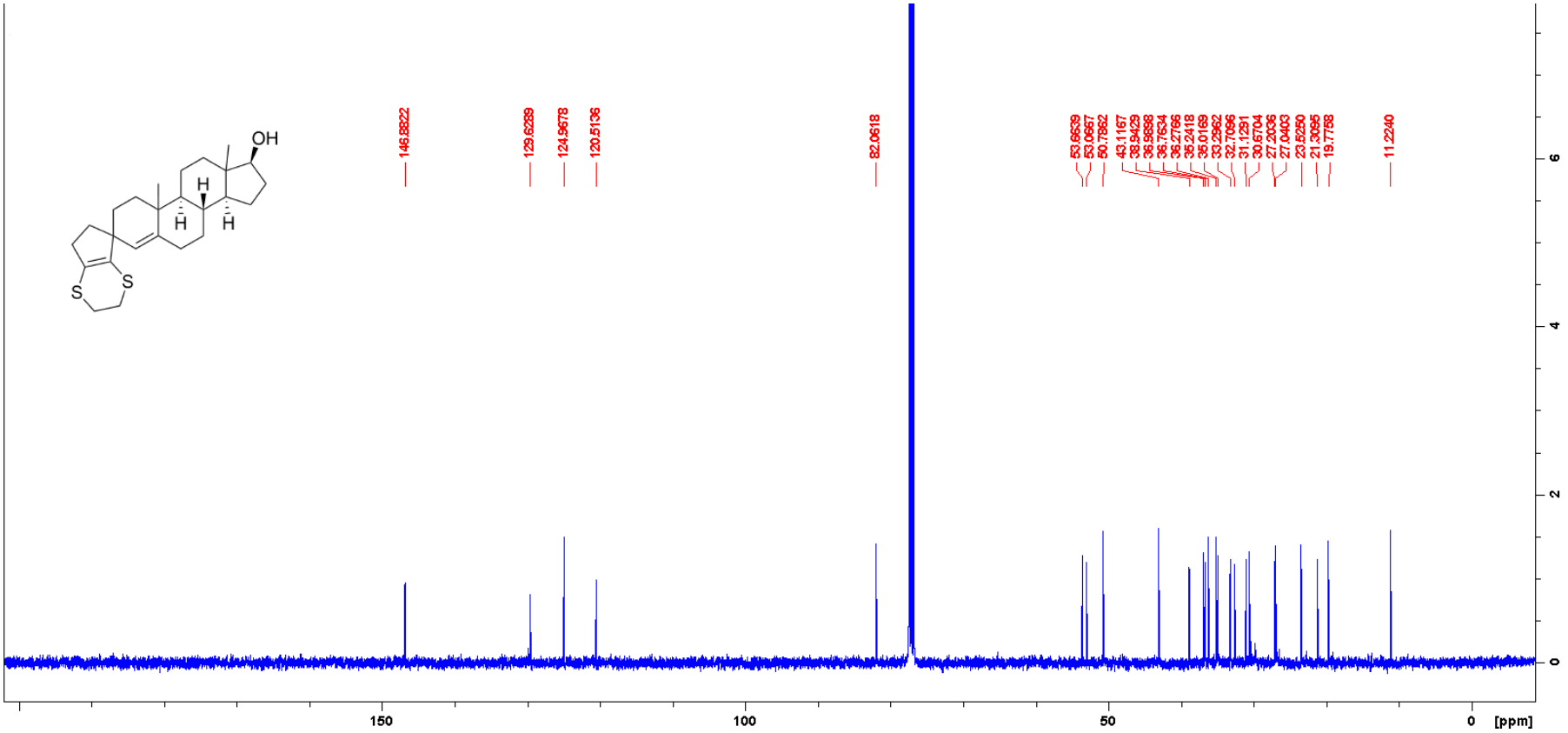
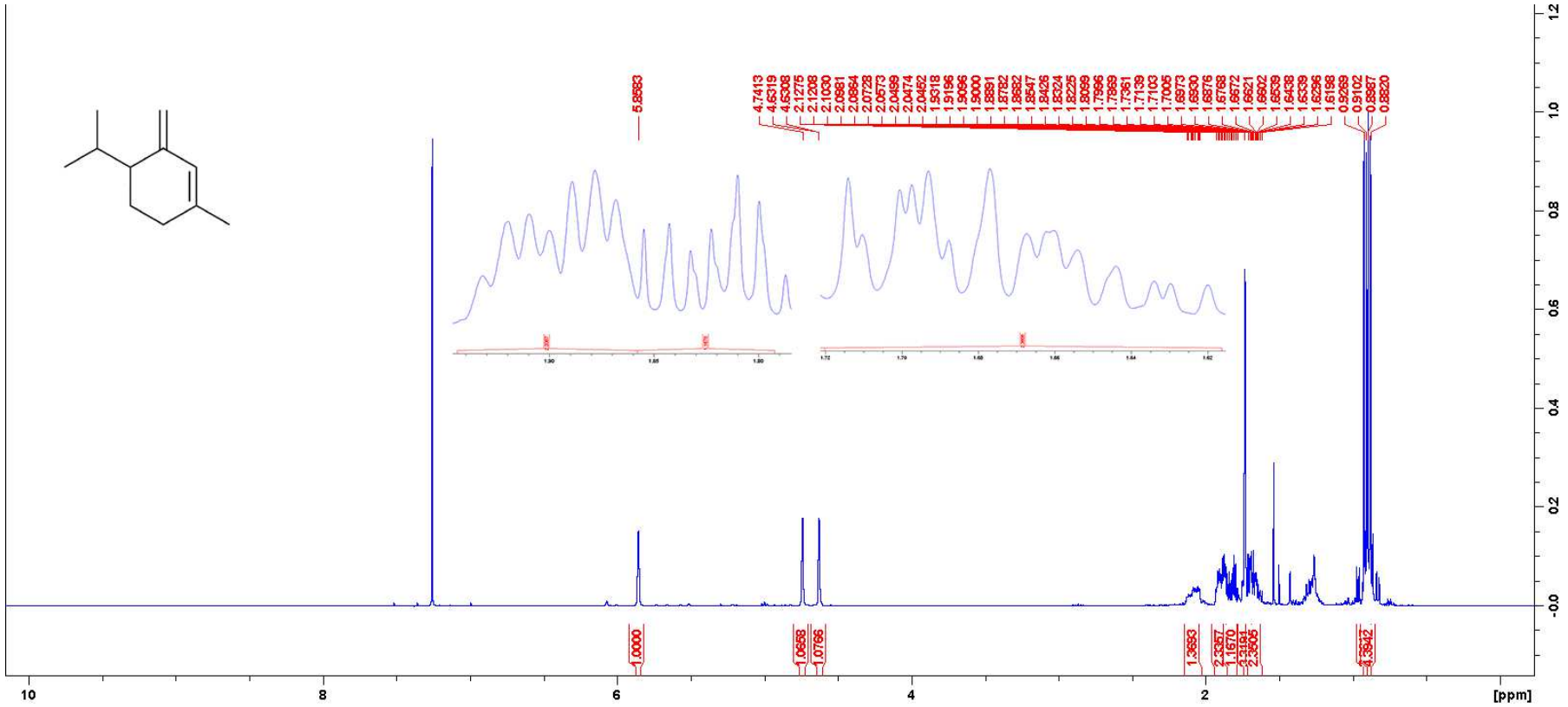


4-isopropyl-1-methyl-3-methylenecyclohex-1-ene (38)
^{1}H-NMR (400 MHz, $CDCl_3$)
Contains residual H_2O (s (br) @ 1.56 ppm)



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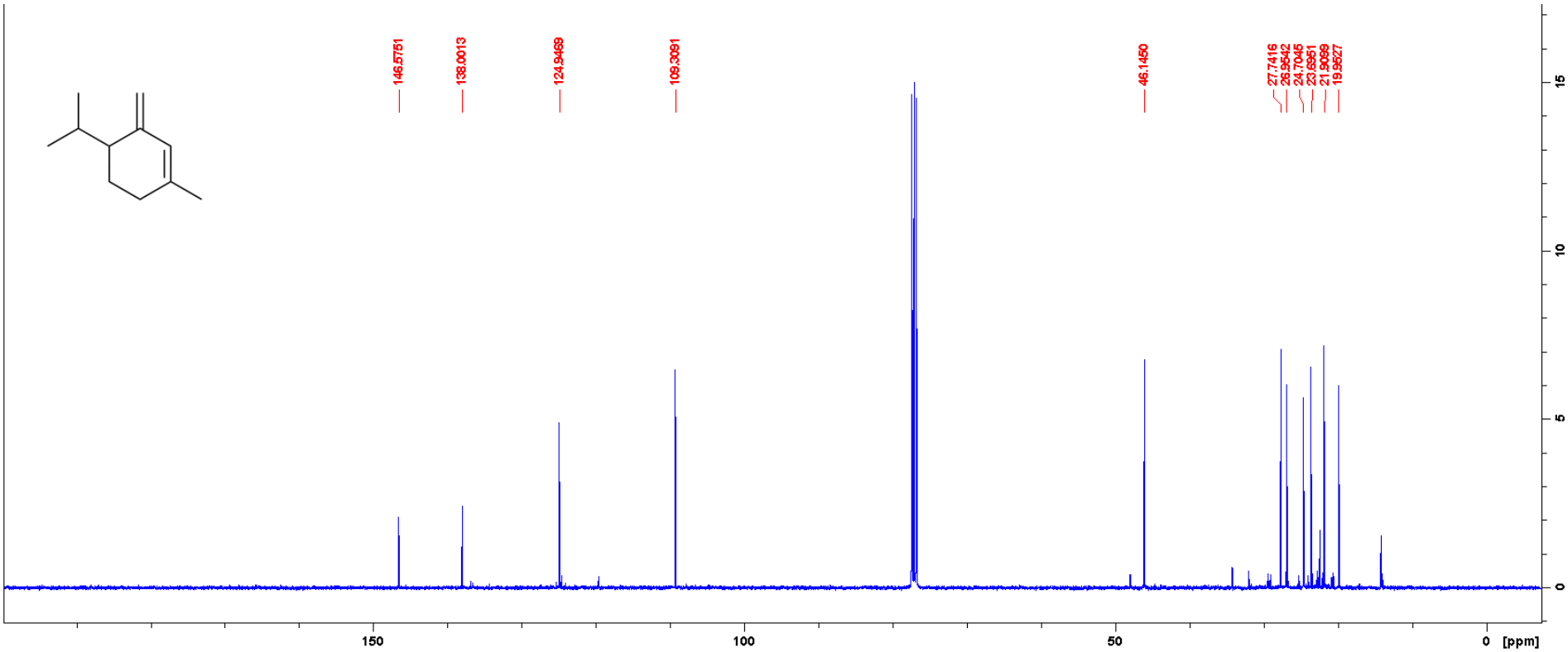
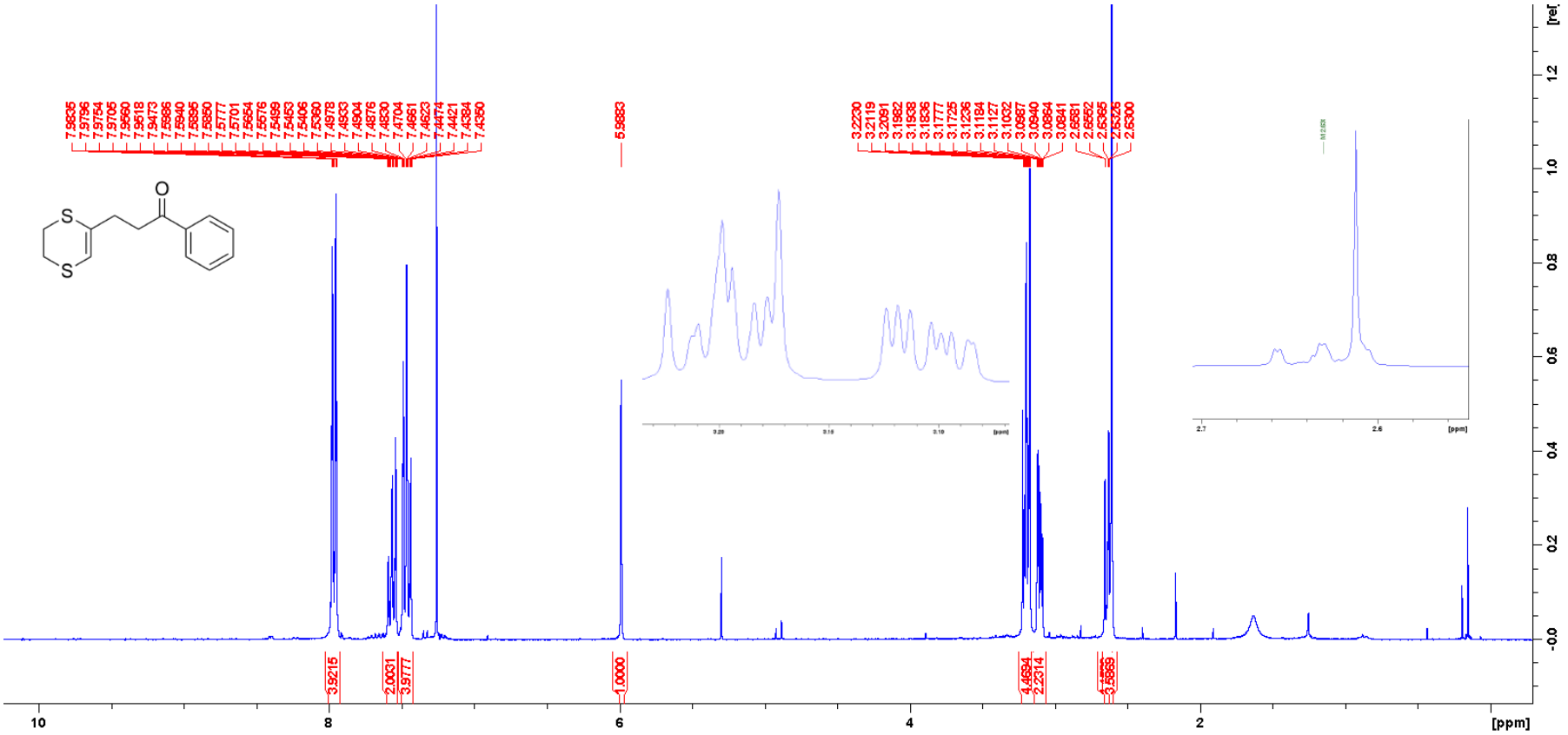


3-(5,6-dihydro-1,4-dithiin-2-yl)-1-phenylpropan-1-one (40)
^{1}H-NMR (300 MHz, $CDCl_3$)
Contains residual acetophenone (s @ 2.61 ppm)



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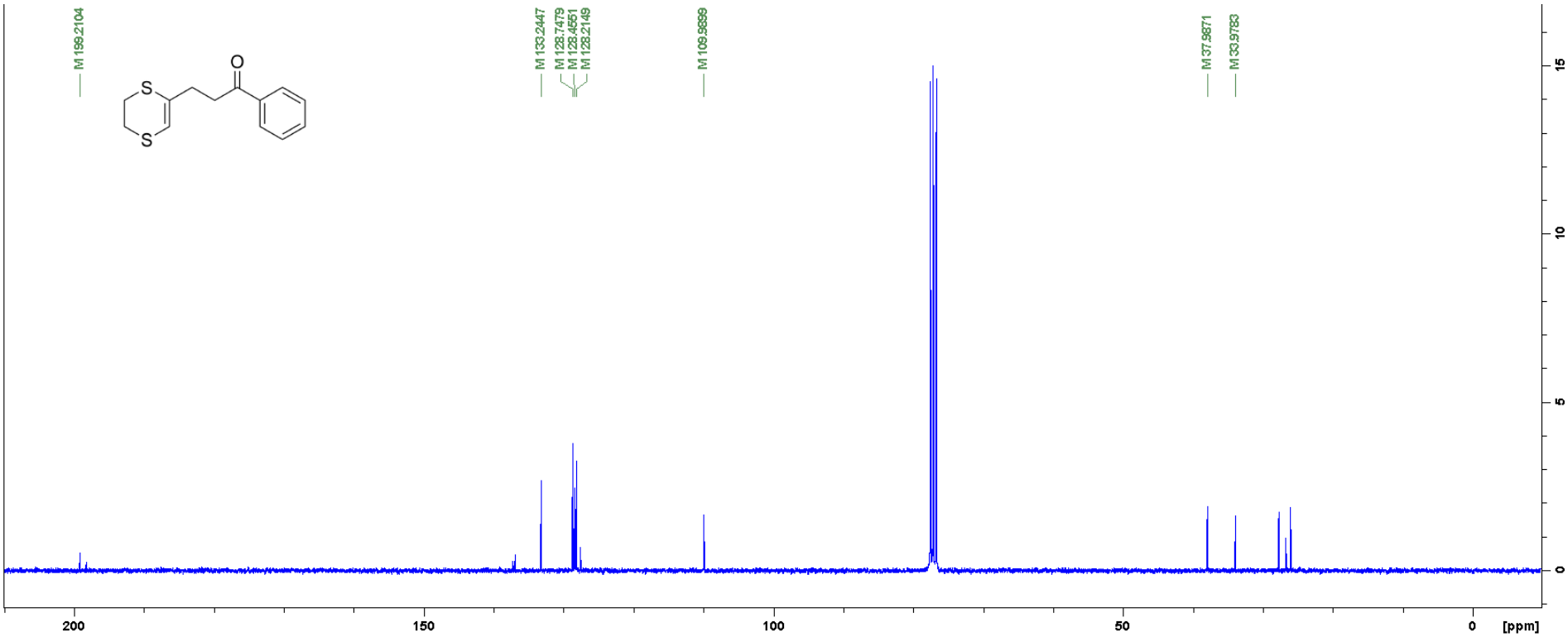
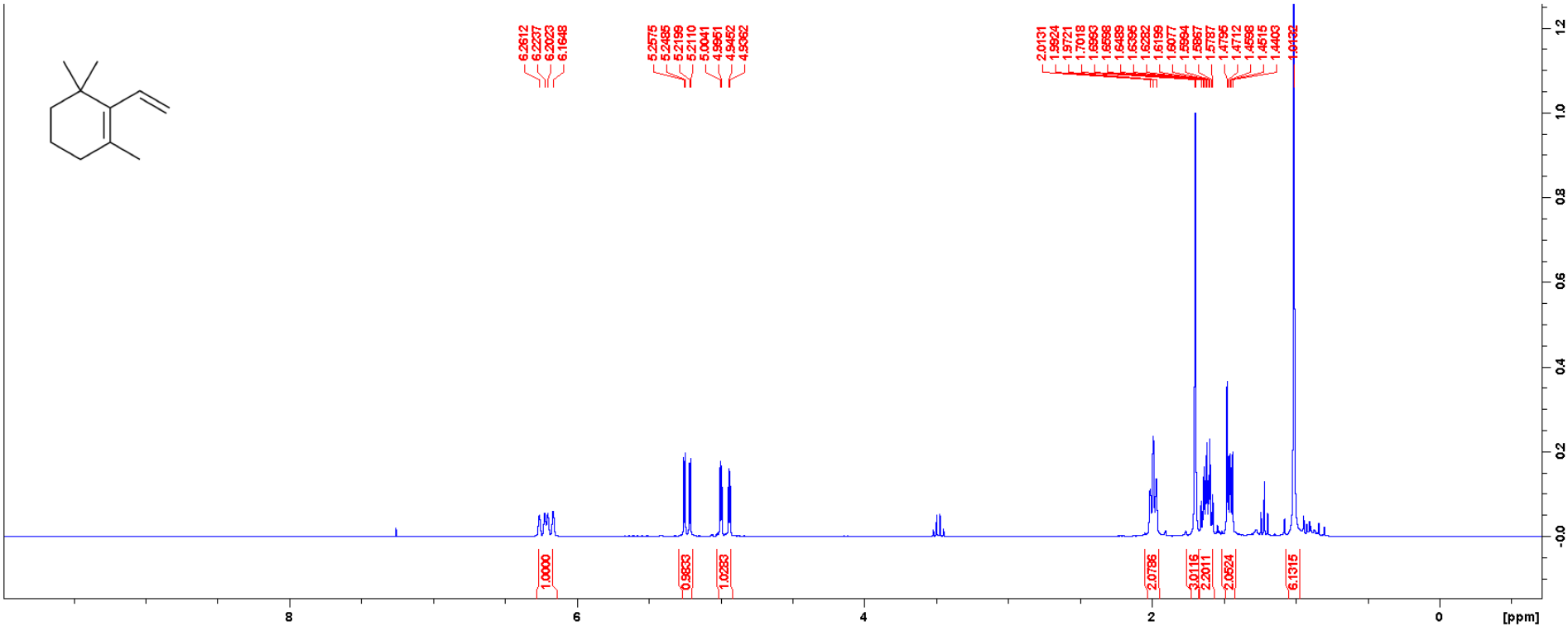
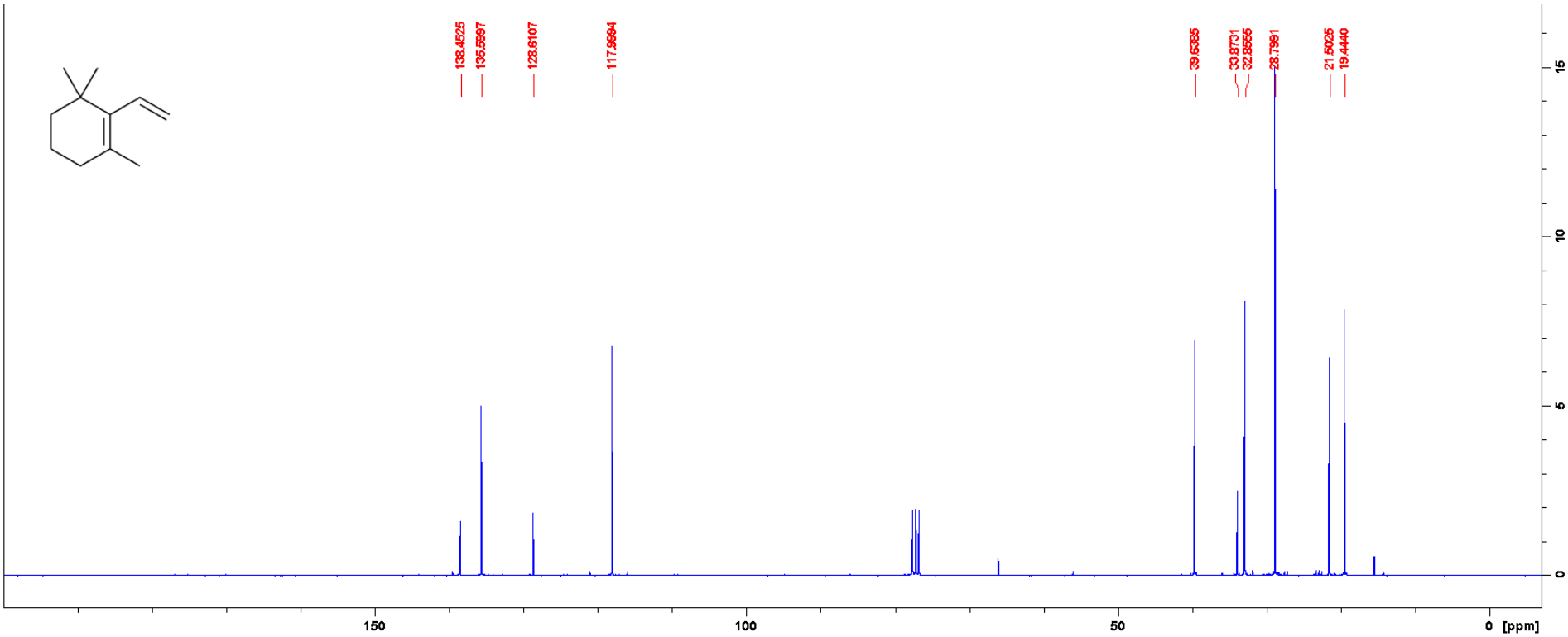


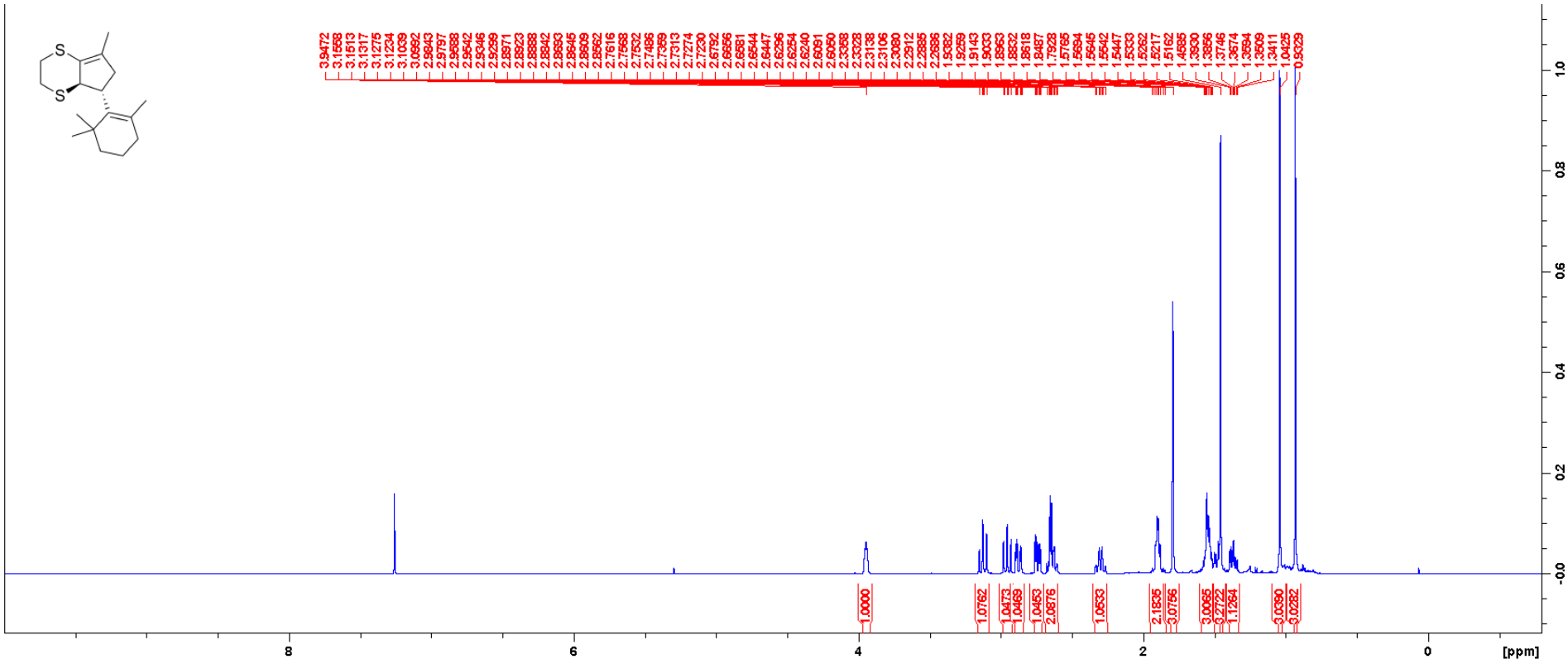
1,3,3-trimethyl-2-vinylcyclohex-1-ene (44)
^{1}H-NMR (300 MHz, $CDCl_3$)
Contains residual Et_2O (q @ 3.48 ppm, t @ 1.21 ppm)



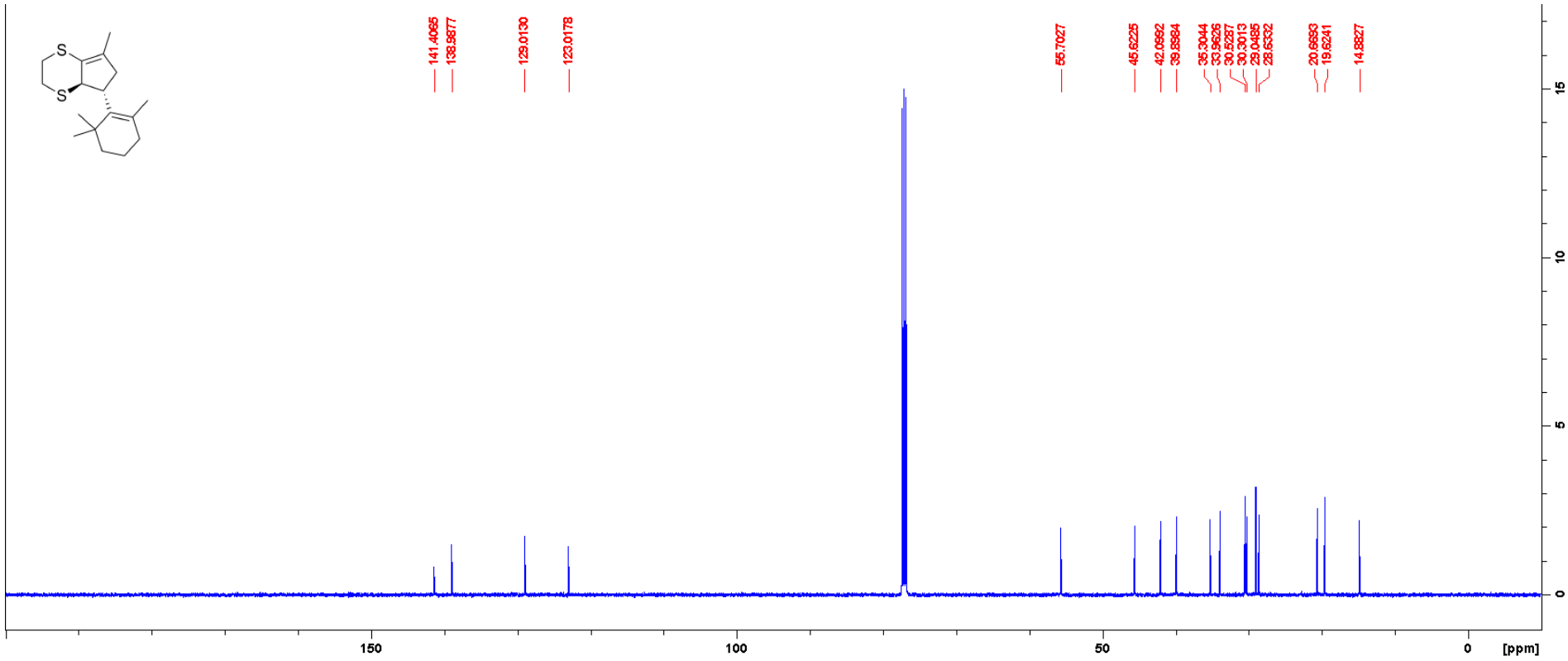
^{13}C-NMR (75 MHz, $CDCl_3$)



(4aR,5R)-7-methyl-5-(2,6,6-trimethylcyclohex-1-en-1-yl)-2,3,4a,6-tetrahydro-5H-cy-clopenta[b][1,4]dithiine (46)
^{1}H-NMR (500 MHz, $CDCl_3$)



^{13}C-NMR (125 MHz, $CDCl_3$)



2,3,6,7-tetrahydrospiro[cyclopenta[b][1,4]dithiine-5,9'-fluorene (47)
^{1}H-NMR (300 MHz, $CDCl_3$)
Contains residual H_2O (s (br) @ 1.56 ppm)