Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Synthesis and structure of large difluoromethylene containing alicycles by ring closing metathesis (RCM)

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Supporting information:

General considerations:

Reagents, solvents and reaction conditions

All commercially available reagents were purchased and used without further purification unless otherwise stated. Complex **M_{20}** was supplied by Umicore. Complex **9** was purchased from Strem Chemicals. 2,2'-Ethylenebis(1,3-dithiane) **5a** was purchased from Alfa Aesar. *n*-Butyllithium was purchased from Acros Organics as 2.5 M solution in hexanes, and titrated against diphenylacetic acid prior to use. All reactions were conducted under an atmosphere of argon using standard vacuum line techniques. All glassware was flamedried and allowed to cool under high vacuum. PTFE flasks were oven dried (60 °C) and allowed to cool under high vacuum. Dry solvents DCM, THF were obtained from the MBraun SPS-800 Solvent Purification System, by passing the solvent through two drying columns under an argon atmosphere. Anhydrous 1,2-dichloroethane (DCE) was purchased from Sigma-Aldrich. Reaction temperatures of -78 °C to -10 °C were obtained using isopropyl alcohol bath together with LabPlant Refrigerated Immersion Probe. Temperature of 0 °C was obtained using an ice/water bath. Reactions requiring heating or reflux were carried out using a heating block with a contact thermometer.

Chromatography

Thin layer chromatography (TLC) was performed using Merck TLC silica gel 60 F_{254} aluminium-backed plates. Compounds were visualised by either UV light (254 nm) or by the use of potassium permanaganate stain or molybdenum-based stain. Column chromatography was performed using Merck silica gel 60 (40-63 μm). Gas chromatography-mass spectroscopy (GC-MS) analysis was performed on an Agilent 5890 gas chromatograph (GC) equipped with 5973N mass selective detector and 7683 injector. The GC was equipped with 30 m long Supleco MDN-35 column. The oven temperature was programmed to hold for 10 min at 50 °C, and then ramped at 10 °C/min to 280 °C, with helium flow 1 mL/min.

Nuclear magnetic resonance (NMR) spectroscopy

NMR spectra were acquired on either Bruker Avance 300 (^{1}H at 300 MHz, ^{13}C at 75 MHz, ^{19}F at 282 MHz), Bruker Avance II 400 spectrometer (^{1}H at 400 MHz, ^{13}C at 100 MHz, ^{19}F at 376 MHz), Bruker Avance 500 spectrometer or Bruker Avance III 500 (^{1}H at 500 MHz, ^{13}C 125 MHz ^{19}F at 470 MHz). Chemical shifts (δ) are reported in parts per million (ppm) and are quoted relative to the residual peak of $CDCl_3$. Coupling constants (J) are given in Hertz (Hz). ^{13}C NMR spectra were recorded with ^{1}H decoupling. Signal splitting patterns are described as: s - singlet, t - triplet, tt - triplet of triplets, ddd – doublet of doublets of doublets, ddt - doublet of doublets of triplets m - multiplet ddd.

Mass spectrometry

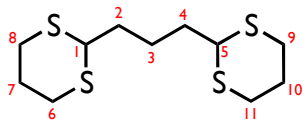
Mass spectrometric data was acquired by electron impact ionisation (EI), electrospray ionisation (ES) or chemical ionisation (CI). At the University of St Andrews LRMS and HRMS examination was carried out by Mrs. C. Horsburgh on a Waters Micromass LCT (ES) or GCT (EI/CI) spectrometers. At the EPSRC National Mass Spectrometry Service Centre, Swansea, the LRMS assessment was performed on Thermofisher DSQ-II spectrometer (EI/CI) and HRMS was performed on Finnigan MAT 95 XP (EI/CI) or Thermofisher LTQ Orbitrap XL (ES/CI). Values are reported in Daltons as a ratio of mass to charge (m/z).

Other analysis

Single crystal X-ray Diffraction analysis was carried out by Prof Alexandra M. Z. Slawin at University of St Andrews. Melting points were determined in Pyrex capillaries using a Gallenkamp Griffin Melting Point Apparatus 350 and were uncorrected. Differential scanning calorimetry (DSC) analysis of compounds **11a-d** was carried out by Mrs. S. Williamson, at the University of St Andrews on a NETZSCH DCS 204 F1 calorimeter, providing corrected melting points.

Synthesis and characterisation of the products:

2,2'-Propylenebis(1,3-dithiane) (5b)

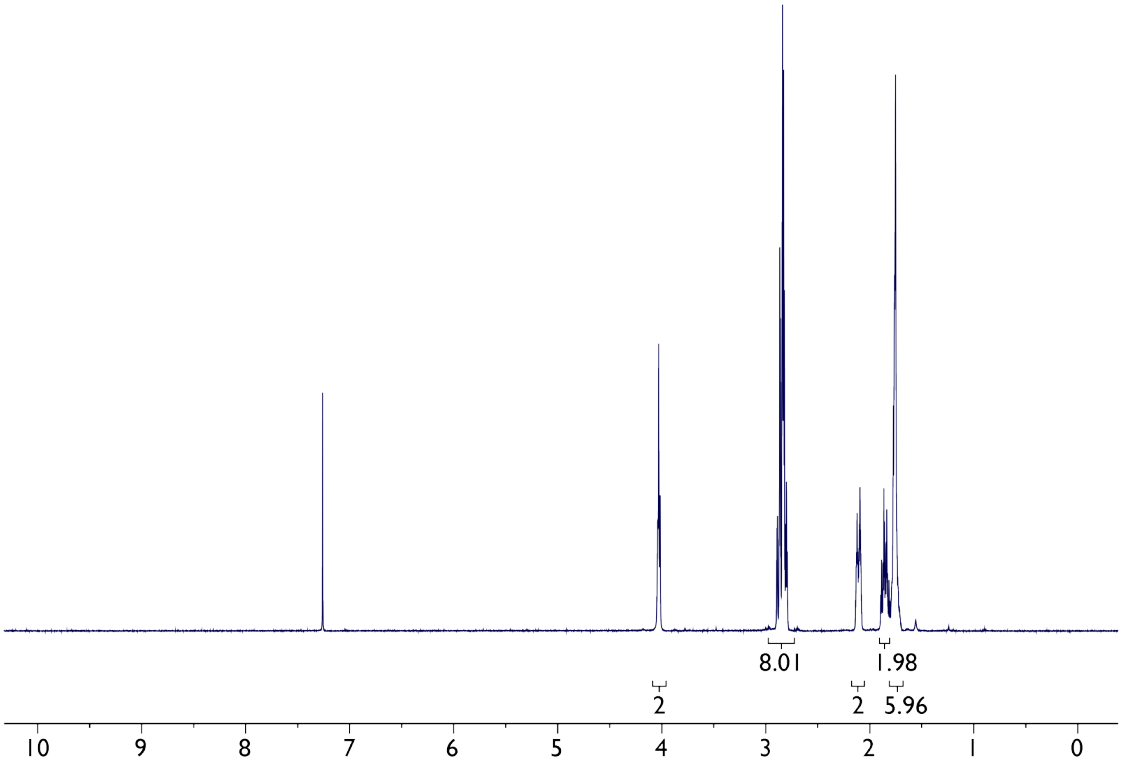


n-BuLi (49.4 mL, 2.35 M, 116.1 mmol, 1.1 eq) was added portionwise to a solution of 1,3-dithiane **4** (12.7 g, 105.6 mmol, 1 eq) in THF (250 mL) at −30 °C and stirred for 2.5 h. 1,3-Dibromopropane (4.93 mL, 48.6 mmol, 0.46 eq) was added dropwise and the mixture stirred for 2 h at −30 °C. Temperature was increased to −5 °C and stirring continued for 48 h. Reaction was quenched with saturated aqueous NH_4Cl solution (200 mL) and extracted with diethyl ether (4 × 150 mL). The organic extracts were washed with brine (150 mL), dried over $MgSO_4$, filtered and concentrated. The product was recrystallised from boiling MeOH, affording 2,2'-propylenebis(1,3-dithiane) **5b** (8.37 g, 62%) as a white crystalline solid:

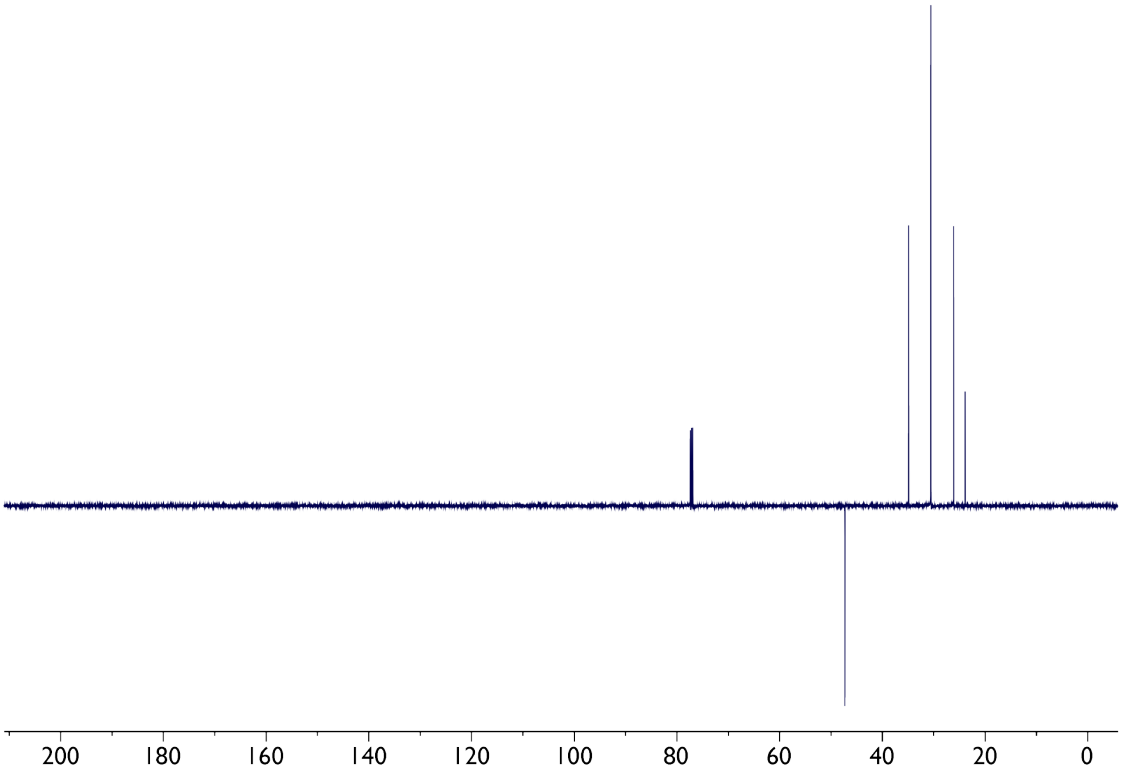
m.p. = 100-101 °C (from MeOH) (lit.[1] 101.5-102 °C); $\mathbf{R_f}$ = 0.19 (petroleum ether:Et_2O, 88:12); **^{1}H NMR** (500 MHz, $CDCl_3$) $\boldsymbol{\delta_H}$ 4.06-4.01 (2H, m, *CH-1,5*), 2.91-2.79 (8H, m, CH_2-*6,8,9,11*), 2.15-2.08 (2H, m, CH_a-*7,10*), 1.91-1.81 (2H, m, CH_b-*7,10*), 1.81-1.70 (6H, m, CH_2-*2,3,4*); **^{13}C NMR** (125 MHz, $CDCl_3$) $\boldsymbol{\delta_C}$ 47.3 (*C-1,5*), 34.9 (*C-2,4*), 30.6 (*C-6,8,9,11*), 26.2 (*C-3*), 23.9 (*C-7,10*); **HRMS** *m/z* (ES^+) Found: $[M+H]^+$ 281.0518. $C_{11}H_{21}S_4$ requires $[M+H]^+$ 281.0521.

[1] D. Seebach and E. J. Corey, *J. Org. Chem.*, 1975, **40**, 231–237.

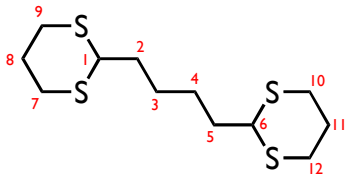
^{1}H NMR of **5b** (500 MHz, $CDCl_3$)



^{13}C NMR of **5b** (125 MHz, $CDCl_3$)



2,2'-Butylenebis(1,3-dithiane) (5c)

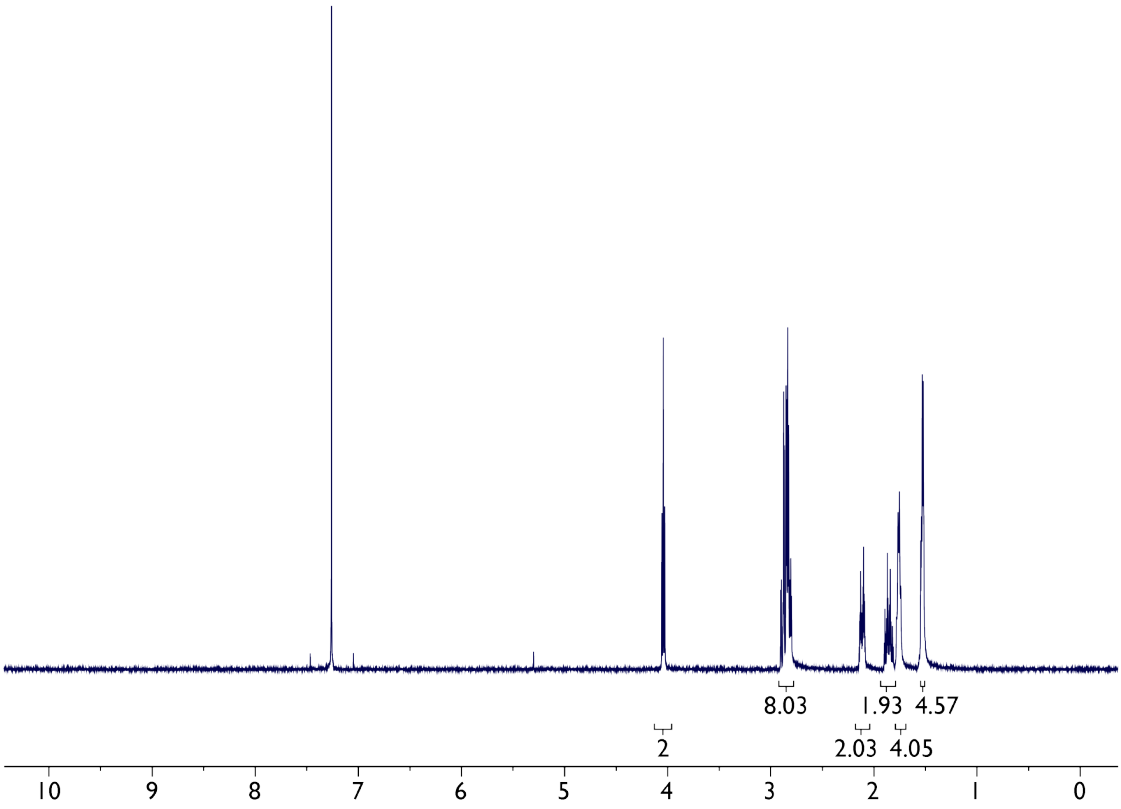


n-BuLi (46.1 mL, 2.31 M, 106.5 mmol, 1.1 eq) was added portionwise to a solution of 1,3-dithiane **4** (11.6 g, 96.5 mmol, 1 eq) in THF (250 mL) at −30 °C and stirred for 2 h. 1,4-Dibromobutane (5.6 mL, 46.9 mmol, 0.49) was added dropwise and the mixture stirred at −30 °C for 2 h. Temperature was increased to −5 °C and stirring continued for 24 h. Reaction was quenched with saturated aqueous NH_4Cl solution (200 mL) and extracted with diethyl ether (4 × 150 mL). The organic extracts were washed with brine (150 mL), dried over $MgSO_4$, filtered and concentrated. Purification over silica gel, eluting with hexane and DCM (80:20, 40:60), yielded 2,2'-butylenebis(1,3-dithiane) **5c** (8.87 g, 65%) as a white crystalline solid:

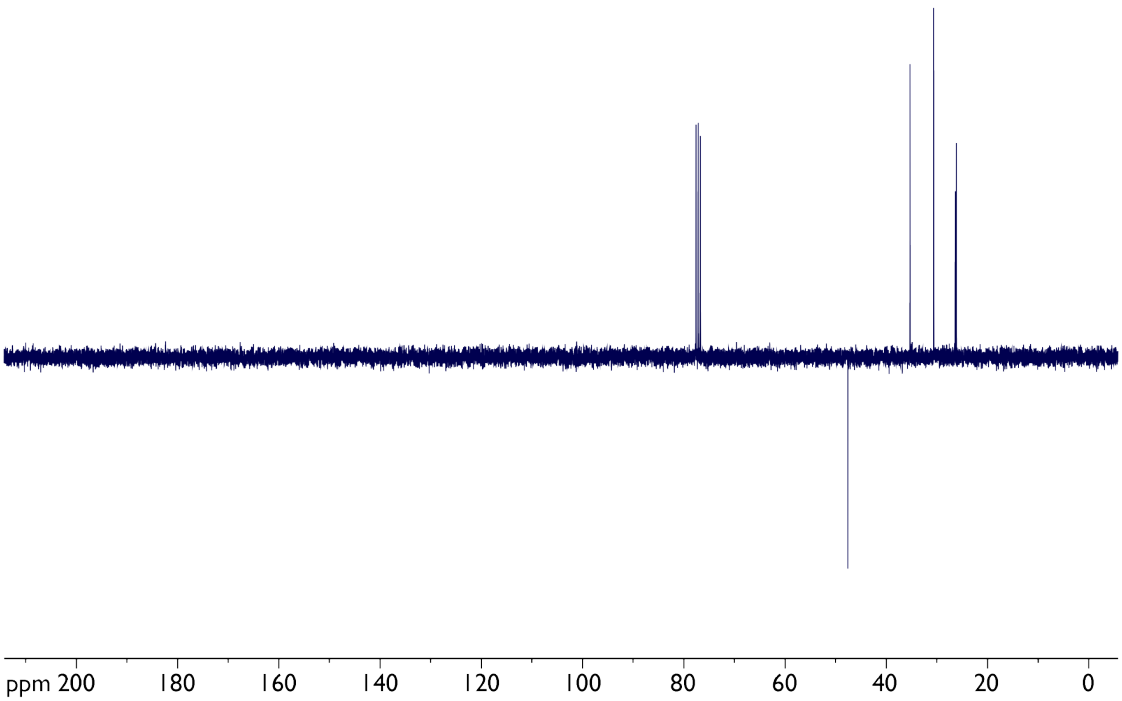
m.p. = 103-104 °C (from $CDCl_3$) (lit.[1] 102.5-103.5 °C); $\mathbf{R_f}$ = 0.20 (petroleum ether:Et_2O, 88:12); **^{1}H NMR** (500 MHz, $CDCl_3$) δ_H 4.04 (2H, t, *J* = 6.9 Hz, *CH-1,6*), 2.91-2.79 (8H, m, *CH_2-7,9,10,12*), 2.15-2.08 (2H, m, *CH_a-8,11*), 1.91-1.80 (2H, m, *CH_b-8,11*), 1.79-1.72 (4H, m, *CH_2-2,5*), 1.56-1.49 (4H, m, *CH_2-3,4*); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C 47.6 (*C-1,6*), 35.3 (*C-2,5*), 30.6 (*C-7,9,10,12*), 26.4 (*C-3,4*) 26.2 (*C-8,11*); **HRMS** *m/z* (ES^+) Found: $[M+Na]^+$ 317.0507. $C_{12}H_{22}S_4Na$ requires $[M+Na]^+$ 317.0502.

[1] D. Seebach and E. J. Corey, *J. Org. Chem.*, 1975, **40**, 231–237.

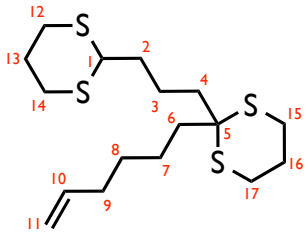
^{1}H NMR of **5c** (500 MHz, $CDCl_3$)



^{13}C NMR of **5c** (75 MHz, $CDCl_3$)



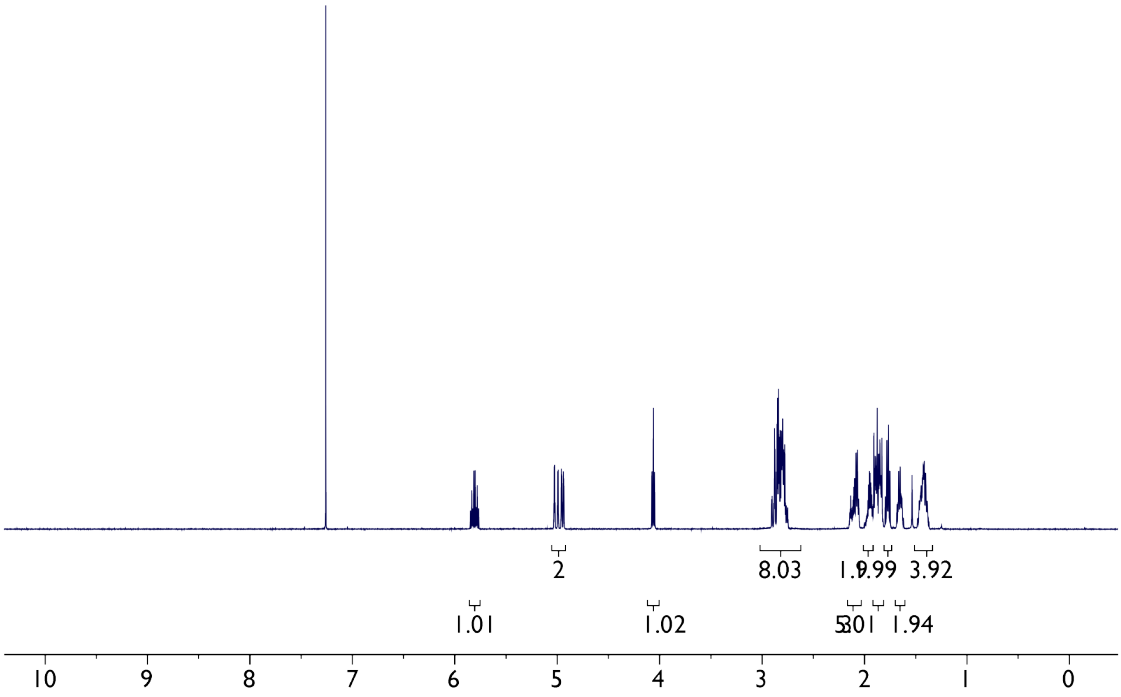
1-(2-(hex-5-enyl)-1,3-dithian-2-yl)-3-(1,3-dithian-2-yl)propane (6)



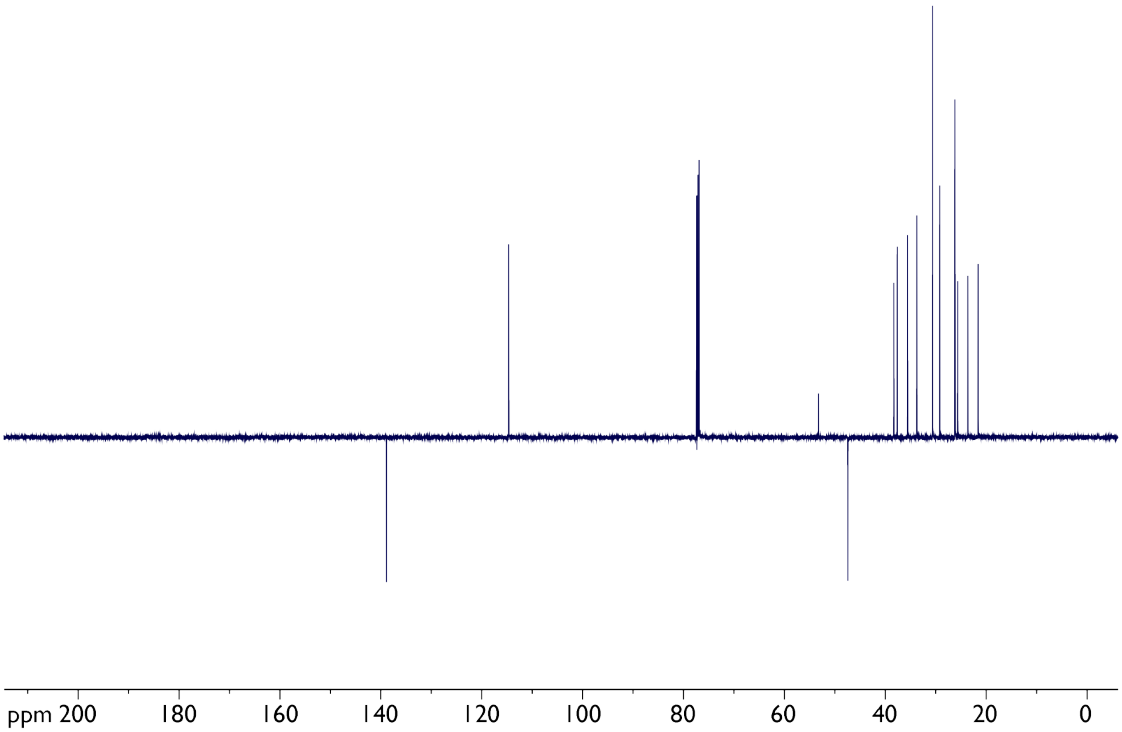
n-BuLi (4.81 mL, 2.23 M, 10.7 mmol, 1 eq) was added to a solution of 2,2'-propylenebis(1,3-dithiane) **5b** (3.01 g, 10.7 mmol, 1 eq) in THF (150 mL) at −35 °C and gradually warmed to −15 °C over 2 h. 6-Bromo-1-hexene (1.43 mL, 10.7 mmol, 1 eq) was added dropwise at −30 °C and the mixture stirred for 4 h. Reaction was quenched with saturated aqueous NH_4Cl solution (150 mL), extracted with Et_2O (4 × 150 mL). The organic extracts were washed with brine (150 mL), dried over $MgSO_4$, filtered and concentrated. Purification over silica gel, eluting with petroleum ether and Et_2O (97:3), yielded 1-(2-(hex-5-enyl)-1,3-dithian-2-yl)-3-(1,3-dithian-2-yl)propane **6** (3.19 g, 82%) as a colourless viscous oil:

R_f = 0.25 (petroleum ether:Et_2O, 88:12); **^{1}H NMR** (500 MHz, $CDCl_3$) **δ_H** 5.81 (1H, ddt, *J* = 17.1, 10.2, 6.7 Hz, *CH-10*), 5.01 (1H, ddt, *J* = 17.1, 2.1, 1.6 Hz, CH_{trans}*-11*), 4.95 (1H, ddt, *J* = 10.2, 2.1, 1.2 Hz, CH_{cis}*-11*), 4.06 (1H, t, *J* = 7.0 Hz, *CH-1*), 2.92-2.74 (8H, m, CH_2*-12,14,15,17*), 2.16-2.04 (3H, m, CH_2*-9,* CH_a*-13*), 2.01-1.91 (2H, m, CH_2*-16*), 1.91-1.81 (5H, m, CH_2*-4,6,* CH_b*-13*), 1.81-1.74 (2H, m, CH_2*-2*), 1.69-1.61 (2H, m, CH_2*-3*), 1.49-1.36 (4H, m, CH_2*-7,8*); **^{13}C NMR** (125 MHz, $CDCl_3$) **δ_C** 138.9 (*C-10*), 114.7 (*C-11*), 53.2 (*C-5*), 47.4 (*C-1*), 38.3 (*C-6*), 37.6 (*C-4*), 35.6 (*C-2*), 33.7 (*C-9*), 30.6 (*C-12,14*), 29.2 (*C-8*), 26.19 (*C-15,17*), 26.17 (*C-13*), 25.6 (*C-16*), 23.6 (*C-7*), 21.6 (*C-3*); **HRMS** *m/z* (ES^+) Found: $[M+H]^+$ 363.1299. $C_{17}H_{31}S_4$ requires $[M+H]^+$ 363.1303.

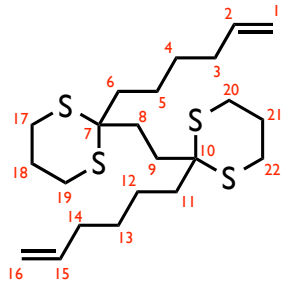
^{1}H NMR of **6** (500 MHz, $CDCl_3$)



^{13}C NMR of **6** (125 MHz, $CDCl_3$)



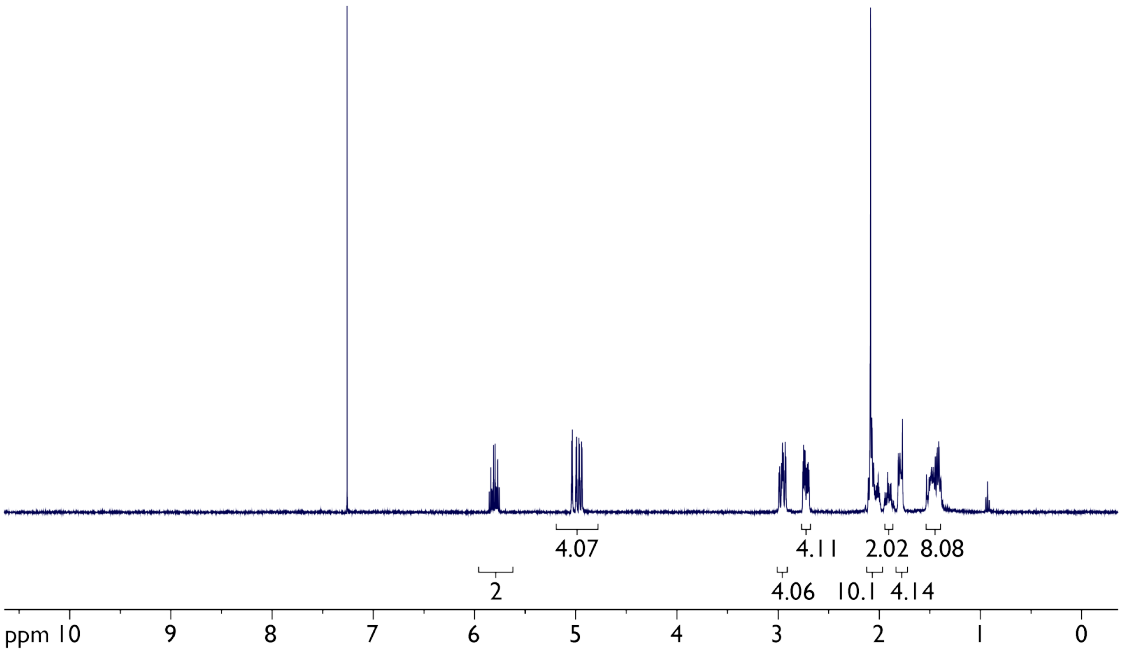
2,2'-Ethylenebis(2-(hex-5-enyl)-1,3-dithiane) (7a)



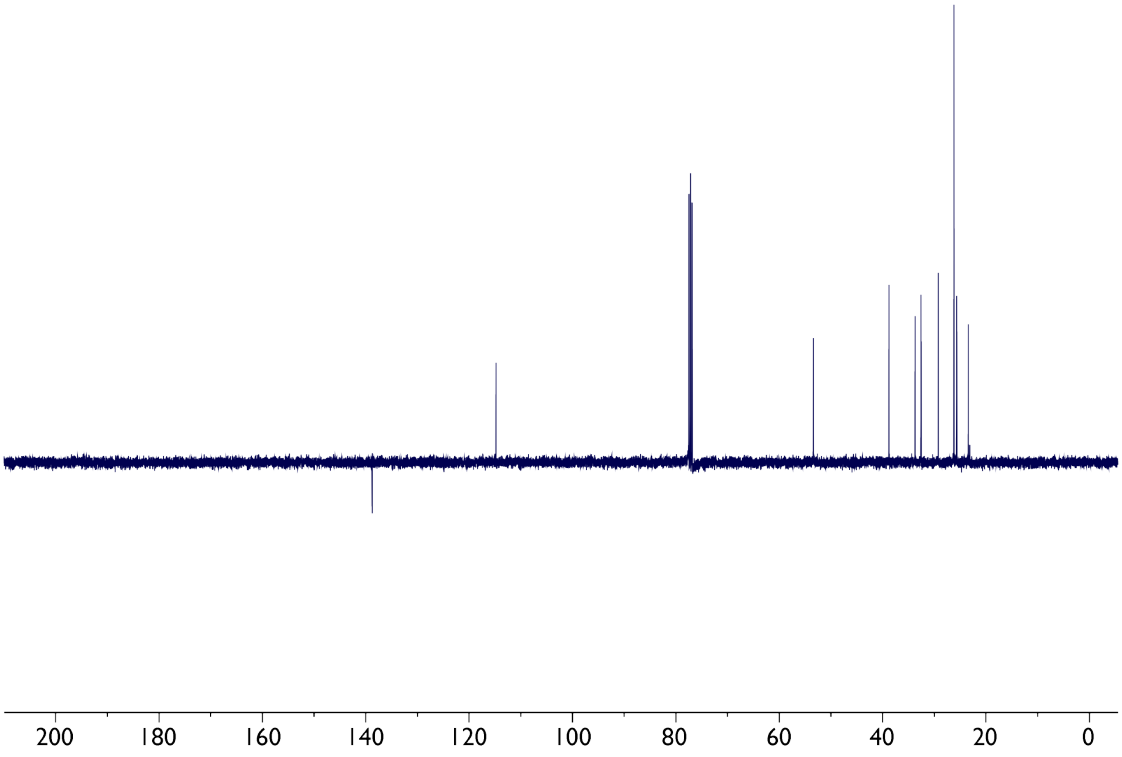
n-BuLi (31.1 mL, 2.5 M, 77.8 mmol, 2.6 eq) was added to a solution of 2,2'-ethylenebis(1,3-dithiane) **5a** (7.90 g, 29.6 mmol, 1 eq) in THF (300 mL) at −20 °C, stirred for 20 min and gradually warmed to −5 °C over 80 min. 6-Bromo-1-hexene (9.2 mL, 68.8 mmol, 2.3 eq) was added portionwise at −25 °C and the mixture stirred overnight at −5 °C. A mixture of mono- and di- alkylated products was observed (TLC/^{1}H NMR). A further aliquot of *n*-BuLi (8.35 mL, 2.5 M, 20.9 mmol, 0.7 eq) was added at −15 °C and stirred for 90 min at that temperature. 6-Bromo-1-hexene (2.78 mL, 20.8 mmol, 0.7 eq) was added dropwise −15 °C and stirred for 4 h. Deprotonation/alkylation sequence was repeated again at −15 °C using *n*-BuLi (3.50 mL, 2.5 M, 8.75 mmol, 0.3 eq) and 6-bromo-1-hexene (1.59 mL, 11.9 mmol, 0.4 eq). The reaction mixture was stirred for 4 h, warmed to 0 °C, quenched with saturated aqueous NH_4Cl solution (200 mL) and extracted with Et_2O (4 × 200 mL). The organic extracts were washed with brine (150 mL), dried over $MgSO_4$, filtered and concentrated. Purification over silica gel, eluting with petroleum ether and EtOAc (99:1, 97:3), yielded 2,2'-Ethylenebis(2-(hex-5-enyl)-1,3-dithiane) **7a** (9.34 g, 73%) as a colourless viscous oil:

R_f = 0.41 (petroleum ether:Et_2O, 88:12); **^{1}H NMR** (400 MHz, $CDCl_3$) **δ_H** 5.80 (2H, ddt, *J* = 17.1, 10.2, 6.7 Hz, *CH-2,15*), 5.01 (2H, ddt, *J* = 17.1, 2.1, 1.5 Hz, CH_{trans}*-1,16*), 4.95 (2H, ddt, *J* = 10.2, 2.1, 1.2 Hz, CH_{cis}*-1,16*), 2.96 (4H, ddd, *J* = 14.5, 10.2, 3.1 Hz, CH_a*-17,19,20,22*), 2.73 (4H, ddd, *J* = 14.6, 6.5, 3.2 Hz, CH_b*-17,19,20,22*), 2.12-1.97 (10H, m, CH_a*-18,21,* CH_2*-3,8,9,14*), 1.96-1.84 (2H, m, CH_b*-18,21*), 1.83-1.75 (4H, m, CH_2*-6,11*), 1.55-1.32 (8H, m, CH_2*-4,5,12,13*); **^{13}C NMR** (100 MHz, $CDCl_3$) **δ_C** 138.8 (*C-2,15*), 114.8 (*C-1,16*), 53.4 (*C-7,10*), 38.8 (*C-6,11*), 33.7 (*C-3,14*), 32.6 (*C-8,9*), 29.2 (*C-4,13*), 26.2 (*C-17,19,20,22*), 25.6 (*C-18,21*), 23.4 (*C-5,12*); **HRMS** *m/z* (ES$^+$) Found: $[M+Na]^+$ 453.1762. $C_{22}H_{38}S_4Na$ requires $[M+Na]^+$ 453.1749.

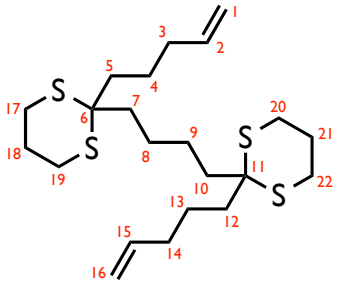
^{1}H NMR of **7a** (400 MHz, $CDCl_3$)



^{1}H NMR of **7a** (100 MHz, $CDCl_3$)



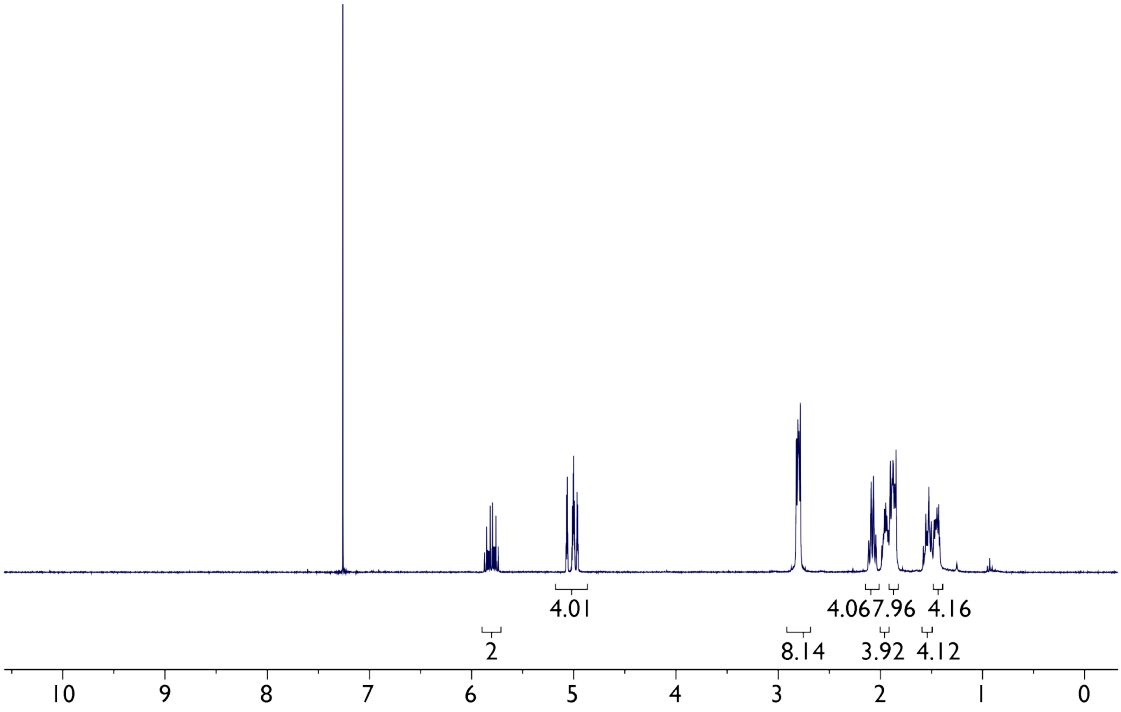
2,2'-Butylenebis(2-(pent-4-enyl)-1,3-dithiane) (7b)



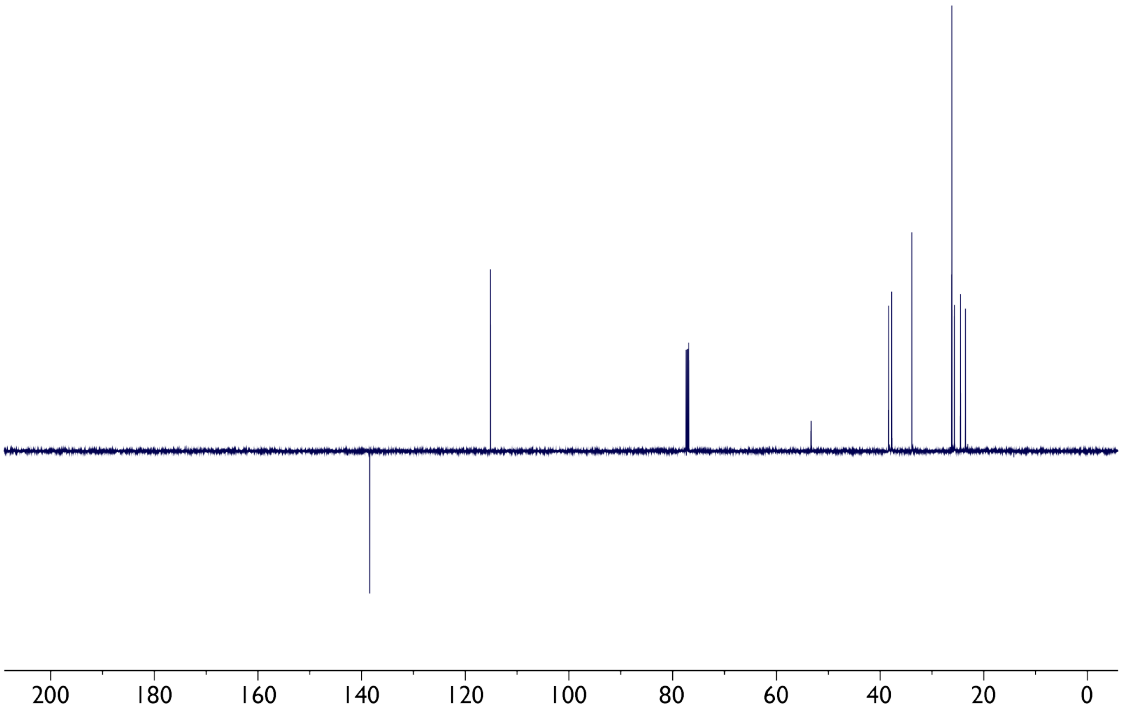
n-BuLi (17.4 mL, 2.42 M, 42.1 mmol, 3 eq) was added to a solution of 2,2'-butylenebis(1,3-dithiane) **5c** (4.14 g, 14.1 mmol, 1 eq) in THF (150 mL) at −30 °C, stirred for 30 min, and gradually warmed to −10 °C over 60 min. 5-Bromo-1-pentene (5.0 mL, 42.2 mmol, 3 eq) was added in small portions at −30 °C and the mixture stirred overnight at −30 °C. A mixture of mono- and di- alkylated products was observed (TLC/^{1}H NMR). A further aliquot of *n*-BuLi (5.81 mL, 2.42 M, 14.1 mmol, 1 eq) was added at −20 °C and stirred for 90 min at that temperature. 5-Bromo-1-pentene (1.67 mL, 14.1 mmol, 1 eq) was added dropwise −20 °C and stirred for 2 h. Deprotonation/alkylation sequence was repeated again at −15 °C using *n*-BuLi (5.81 mL, 2.42 M, 14.1 mmol, 1 eq) and 5-bromo-1-pentene (0.83 mL, 7.0 mmol, 0.5 eq). The reaction mixture was stirred for 2 h, warmed to 0 °C, quenched with saturated aqueous NH_4Cl solution (100 mL) and extracted with Et_2O (4 × 100 mL). The organic extracts were washed with brine (150 mL), dried over $MgSO_4$, filtered and concentrated. Purification over silica gel, eluting with petroleum ether and Et_2O (99:1, 98:2), yielded **7b** (4.54 g, 75%) as a colourless viscous oil:

R_f = 0.33 (petroleum ether:Et_2O, 88:12); **^{1}H NMR** (300 MHz, $CDCl_3$) **δ_H** 5.81 (2H, ddt, *J* = 17.1, 10.2, 6.7 Hz, *CH-2,15*), 5.04 (2H, ddt, *J* = 17.1, 1.9, 1.4 Hz, CH_{trans}*-1,16*), 4.98 (2H, ddt, *J* = 10.1, 1.9, 1.2 Hz, CH_{cis}*-1,16*), 2.85-2.75 (8H, m, CH_2*-17,19,20,22*), 2.13-2.03 (4H, m, CH_2*-3,14*), 2.00-1.91 (4H, m, CH_2*-18,21*), 1.91-1.82 (8H, m, CH_2*-5,7,10,12*), 1.59-1.49 (4H, m, CH_2*-4,13*), 1.49-1.41 (4H, m, CH_2*-8,9*); **^{13}C NMR** (125 MHz, $CDCl_3$) **δ_C** 138.4 (*C-2,15*), 115.2 (*C-1,16*), 53.3 (*C-6,11*), 38.3 (*C-7,10*), 37.8 (*C-5,12*), 33.9 (*C-3,14*), 26.2 (*C-17,19,20,22*), 25.6 (*C-18,21*), 24.5 (*C-8,9*), 23.5 (*C-4,13*); **HRMS** *m/z* (ES^+) Found: $[M+Na]^+$ 453.1743. $C_{22}H_{38}S_4Na$ requires $[M+Na]^+$ 453.1749.

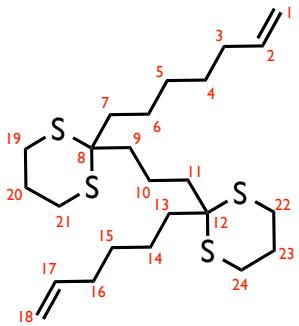
^{1}H NMR of **7b** (300 MHz, $CDCl_3$)



^{13}C NMR of **7b** (125 MHz, $CDCl_3$)



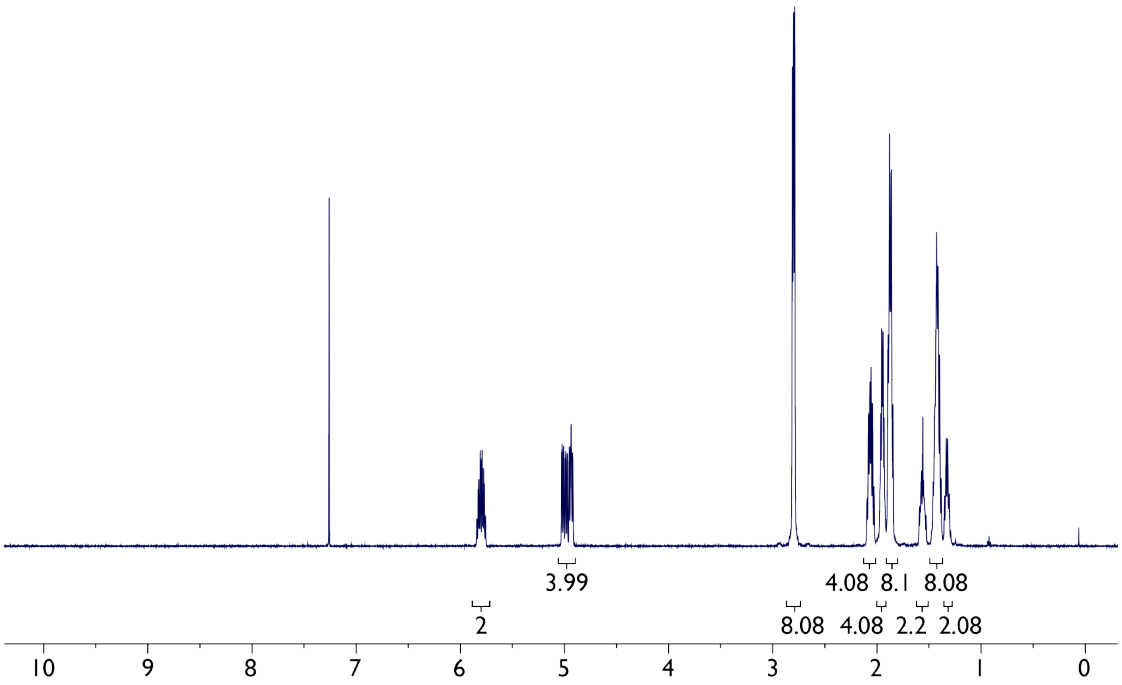
1-(2-(hept-6-enyl)-1,3-dithian-2-yl)-3-(2-(hex-5-enyl)-1,3-dithian-2-yl)propane (7c)



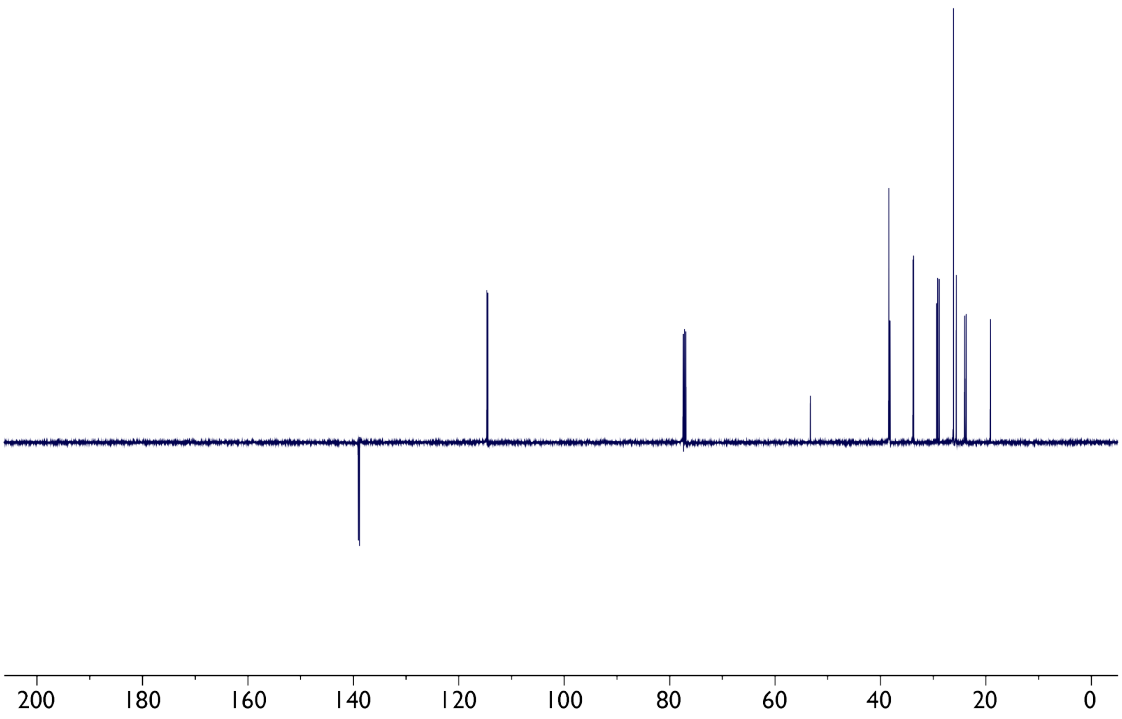
n-BuLi (4.0 mL, 2.23 M, 8.92 mmol, 1.2 eq) was added to a solution of 1-(2-(hex-5-enyl)-1,3-dithian-2-yl)-3-(1,3-dithian-2-yl)propane **6** (2.69 g, 7.42 mmol, 1 eq) in THF (70 mL) at −10 °C, gradually warmed to 0 °C and stirred for 45 min. 7-Bromo-1-heptene (1.36 mL, 8.92 mmol, 1.2 eq) was added dropwise at −10 °C. The reaction mixture was stirred for 90 min, warmed to 0 °C, quenched with saturated aqueous NH_4Cl solution (50 mL) and extracted with Et_2O (4 × 50 mL). The organic extracts were washed with brine (50 mL), dried over $MgSO_4$, filtered and concentrated. Purification over silica gel, eluting with petroleum ether and Et_2O (94:6), yielded 1-(2-(hept-6-enyl)-1,3-dithian-2-yl)-3-(2-(hex-5-enyl)-1,3-dithian-2-yl)propane **7c** (2.66 g, 78%) as a colourless viscous oil:

R_f = 0.27 (petroleum ether:Et_2O, 88:12); **^{1}H NMR** (500 MHz, $CDCl_3$) **δ_H** 5.85-5.75 (2H, m, *CH-2,17*), 5.04-4.91 (4H, m, *CH_2-1,18*), 2.85-2.75 (8H, m, *CH_2-19,21,22,24*), 2.11-2.02 (4H, m, *CH_2-3,16*), 1.99-1.91 (4H, m, *CH_2-20,23*), 1.91-1.83 (8H, m, *CH_2-7,9,11,13*), 1.61-1.51 (2H, m, *CH_2-10*), 1.49-1.37 (8H, m, *CH_2*), 1.37-1.28 (2H, m, *CH_2-11*); **^{13}C NMR** (125 MHz, $CDCl_3$) **δ_C** 139.1 (*C-2 or 17*), 138.8 (*C-2 or 17*), 114.7 (*C-1 or 18*), 114.5 (*C-1 or 18*), 53.3 (*C-8,12*), 38.4 (*CH_2*), 38.3 (*CH_2*), 38.2 (*CH_2*), 33.8 (*C-3 or 16*), 33.7 (*C-3 or 16*), 29.4 (*CH_2*), 29.2 (*CH_2*), 28.9 (*CH_2*), 26.2 (*C-19,21,22,24*), 25.6 (*C-20,23*), 24.0 (*CH_2*), 23.7, (*CH_2*), 19.2 (*C-10*); **HRMS** *m/z* (ES^+) Found: $[M+Na]^+$ 481.2054. $C_{24}H_{42}S_4Na$ requires $[M+Na]^+$ 481.2062.

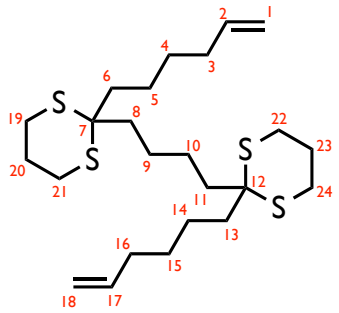
^{1}H NMR of **7c** (500 MHz, $CDCl_3$)



^{13}C NMR of **7c** (125 MHz, $CDCl_3$)



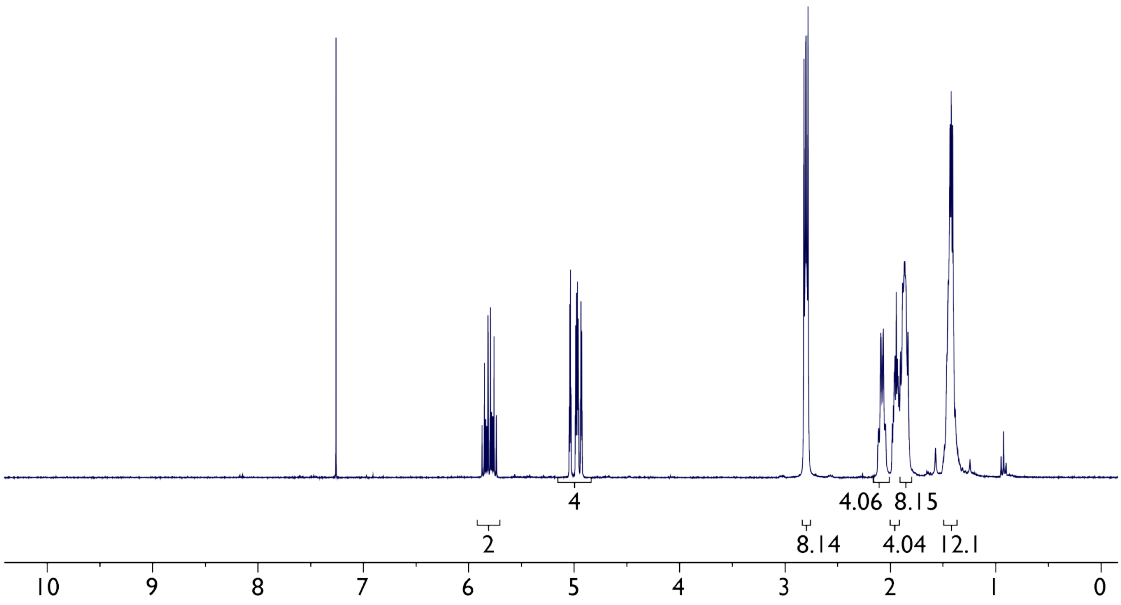
2,2'-Butylenebis(2-(hex-5-enyl)-1,3-dithiane) (7d)



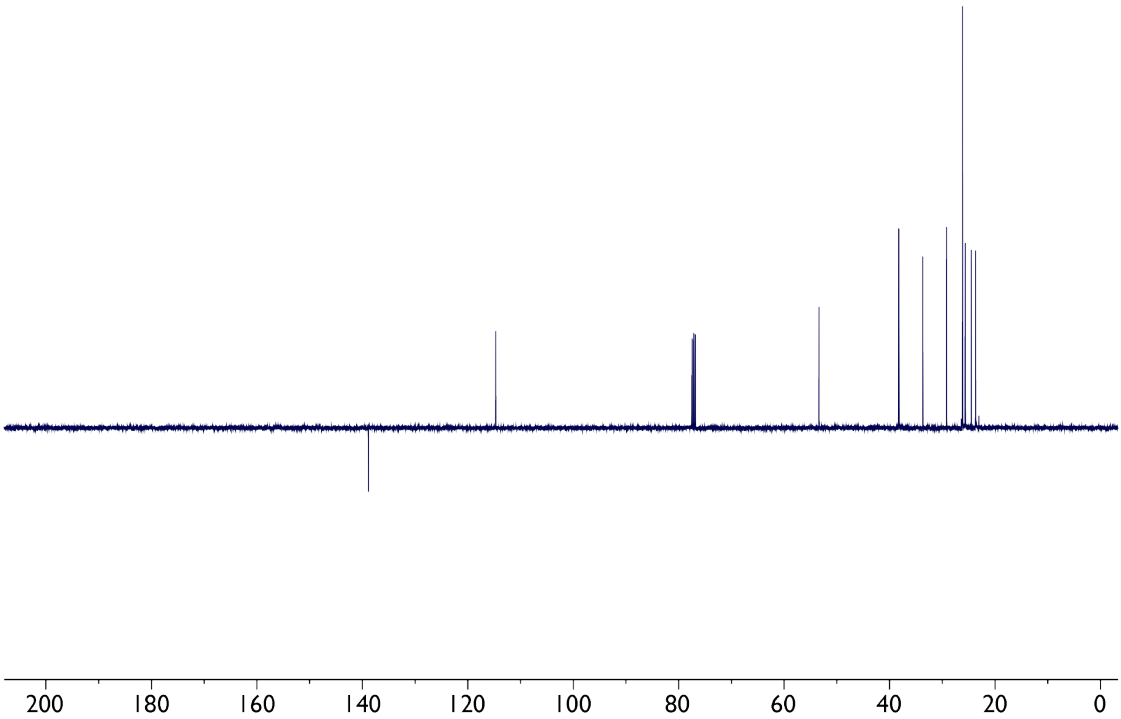
n-BuLi (15.4 mL, 2.42 M, 37.2 mmol, 3 eq) was added to a solution of 2,2'-butylenebis(1,3-dithiane) **5c** (3.65 g, 12.4 mmol, 1 eq) in THF (140 mL) at −30 °C, stirred for 30 min, and gradually warmed to −10 °C over 60 min. 6-Bromo-1-hexene (4.97 mL, 37.2 mmol, 3 eq) was added portionwise at −30 °C and the mixture stirred overnight at −30 °C. A mixture of mono- and di- alkylated products was observed (TLC/^{1}H NMR). A further aliquot of *n*-BuLi (5.12 mL, 2.42 M, 12.4 mmol, 1 eq) was added at −20 °C and stirred for 90 min at that temperature. 6-Bromo-1-hexene (1.66 mL, 12.4 mmol, 1 eq) was added dropwise −20 °C and stirred for 2 h. Deprotonation/alkylation sequence was repeated again at −15 °C using *n*-BuLi (5.12 mL, 2.42 M, 12.4 mmol, 1 eq) and 6-bromo-1-hexene (0.83 mL, 6.20 mmol, 0.5 eq). The reaction mixture was stirred for 2 h, warmed to 0 °C, quenched with saturated aqueous NH_4Cl solution (100 mL) and extracted with Et_2O (4 × 100 mL). The organic extracts were washed with brine (150 mL), dried over $MgSO_4$, filtered and concentrated. Purification over silica gel, eluting with petroleum ether and DCM (80:20, 60:40), yielded 2,2'-Butylenebis(2-(hex-5-enyl)-1,3-dithiane) **7d** (3.51 g, 62%) as a colourless viscous oil:

R_f = 0.36 (petroleum ether:Et_2O, 88:12); **^{1}H NMR** (300 MHz, $CDCl_3$) **δ_H** 5.81 (2H, ddt, *J* = 17.1, 10.2, 6.7 Hz, *CH-2,17*), 5.01 (2H, ddt, *J* = 17.1, 2.1, 1.6 Hz, CH_{trans}*-1,18*), 4.95 (2H, ddt, *J* = 10.2, 2.1, 1.2 Hz, CH_{cis}*-1,18*), 2.84-2.76 (8H, m, CH_2*-19,21,22,24*), 2.14-2.02 (4H, m, CH_2*-3,16*), 2.00-1.91 (4H, m, CH_2*-20,23*), 1.91-1.79 (8H, m, CH_2*-6,8,11,13*), 1.51-1.33 (12H, m, CH_2*-4,5,9,10,14,15*); **^{13}C NMR** (100 MHz, $CDCl_3$) **δ_C** 138.8 (*C-2,17*), 114.7 (*C-1,18*), 53.4 (*C-7,12*), 38.27 (*C-6,13 or 8,11*), 38.25 (*C-6,13 or 8,11*), 33.7 (*C-3,16*), 29.2 (*C-4,15*), 26.2 (*C-19,21,22,24*), 25.6 (*C-20,23*), 24.5 (*C-9,10*), 23.5 (*C-5,14*); **HRMS** *m/z* (Cl^+) Found: $[M+H]^+$ 459.2234. $C_{24}H_{43}S_4$ requires $[M+H]^+$ 459.2242.

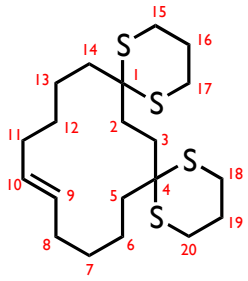
^{1}H NMR of **7d** (300 MHz, $CDCl_3$)



^{13}C NMR of **7d** (100 MHz, $CDCl_3$)



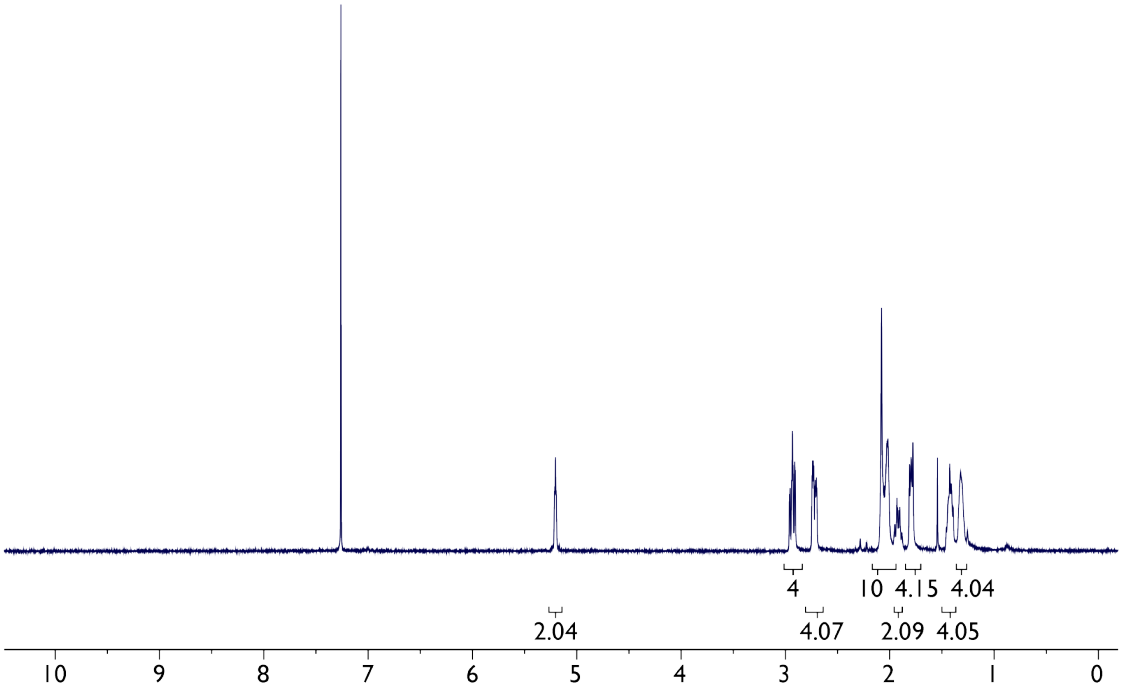
1,5,10,14-Tetrathiadispiro[5.2.5.10]tetracos-19-ene (8a)



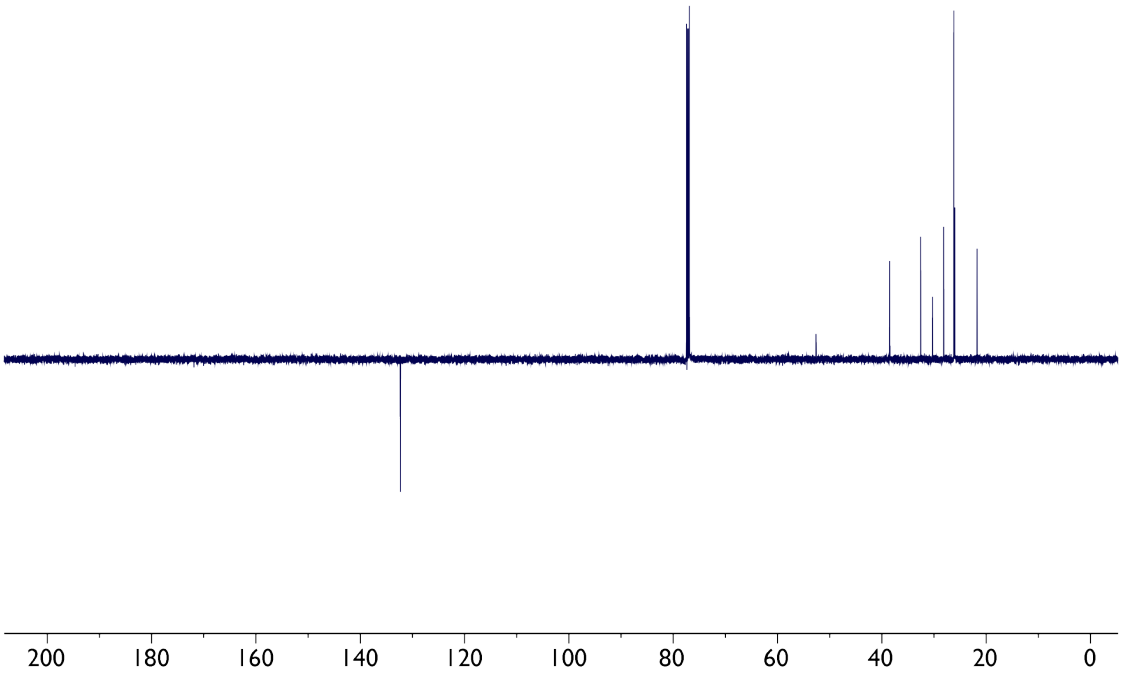
M_{20} (16 mg, 17 µmol, 1.5 mol%) was added in one portion to a solution of 2,2'-ethylenebis(2-(hex-5-enyl)-1,3-dithiane) **7a** (0.50 g, 1.16 mmol,) in DCE (29 mL, 0.04 M) and stirred for 20 h at 40 °C. The crude reaction was concentrated under reduced pressure affording a brown waxy solid. Purification over silica gel, eluting with pentane and Et_2O (95:5), yielded 1,5,10,14-tetrathiadispiro[5.2.5.10]tetracos-19-ene **8a** (0.33 g, 71%) as a white crystalline solid:

R_f = 0.35 (pentane:Et_2O, 88:12); **m.p.** = 135-136 °C (from hexane:DCM, 60:40); **^{1}H NMR** (500 MHz, $CDCl_3$) **δ_H** 5.25-5.16 (2H, m, *CH-9,10*), 2.93 (4H, ddd, *J* = 14.2, 10.7, 2.8 Hz, CH_a-*15,17,18,20*), 2.72 (4H, ddd, *J* = 14.2, 6.1, 3.2 Hz, CH_b-*15,17,18,20*), 2.12-1.97 (10H, m, CH_a-*16,19; CH_2-2,3,8,11*), 1.96-1.87 (2H, m, CH_b-*16,19*), 1.83-1.75 (4H, m, CH_2-*5,14*), 1.47-1.37 (4H, m, CH_2-*6,13*), 1.36-1.27 (4H, m, CH_2-*7,12*); **^{13}C NMR** (125 MHz, $CDCl_3$) **δ_C** 132.3 (*C-9,10*), 52.6 (*C-1,4*), 38.5 (*C-5,14*), 32.5 (*C-8,11*), 30.3 (*C-2,3*), 28.1 (*C-7,12*), 26.2 (*C-15,17,18,20*), 26.0 (*C-16,19*), 21.7 (*C-6,13*); **HRMS** *m/z* (ES^+) Found: $[M+Na]^+$ 425.1443. $C_{20}H_{34}S_4Na$ requires $[M+Na]^+$ 425.1436.

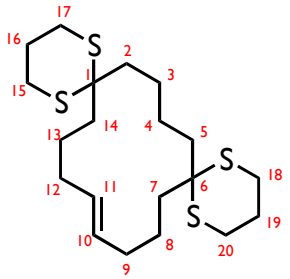
^{1}H NMR of **8a** (500 MHz, $CDCl_3$)



^{13}C NMR of **8a** (125 MHz, $CDCl_3$)



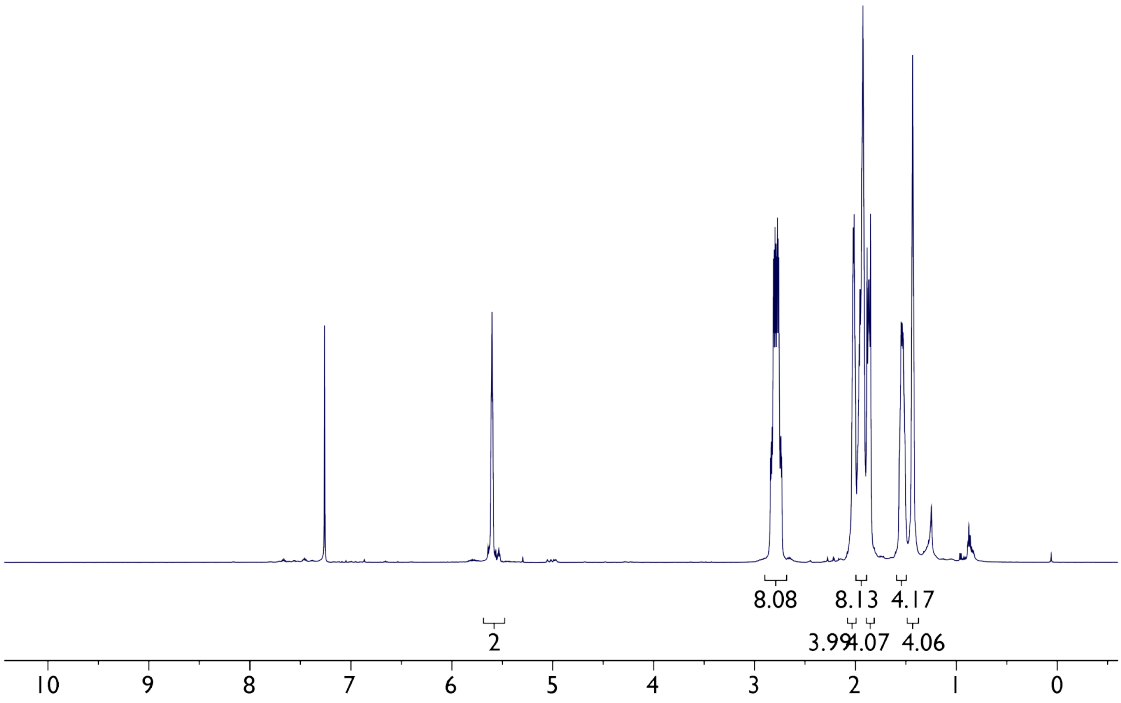
1,5,12,16-Tetrathiadispiro[5.4.5.8]tetracos-20-ene (8b)



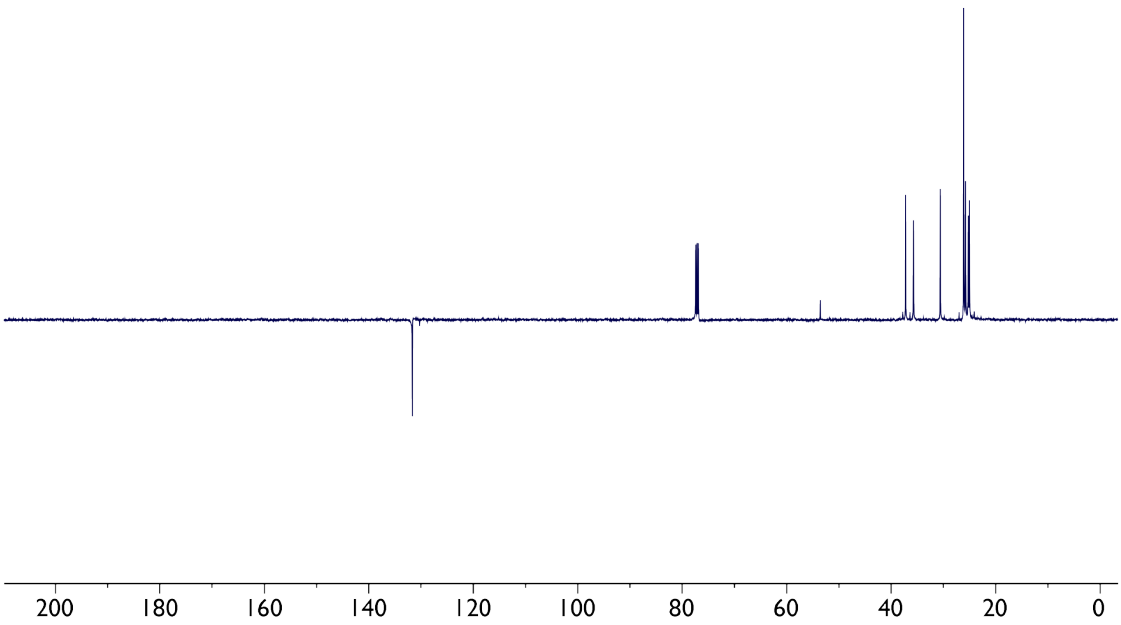
M_{20} (12 mg, 17 μmol, 0.01 eq) was added in one portion to a solution of 2,2'-butylenebis(2-(pent-4-enyl)-1,3-dithiane) **7b** (0.50 g, 1.16 mmol) in DCE (58 mL, 0.02 M) and stirred for 20 h at room temperature. The crude reaction was concentrated under reduced pressure affording a brown waxy solid. Purification over silica gel, eluting with pentane and Et_2O (95:5), afforded 1,5,12,16-tetrathiadispiro[5.4.5.8]tetracos-20-ene **8b** (0.12 g, 31%) as a white crystalline solid:

R_f = 0.22 (petroleum ether:Et_2O, 88:12); **m.p.** = 139-140 °C (from $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) **δ_H** 5.65-5.55 (2H, m, *CH-10,11*), 2.86-2.71 (8H, m, *CH_2-15,17,18,20*), 2.08-1.99 (4H, m, *CH_2-9,12*), 1.99-1.90 (8H, m, *CH_2-2,5,16,19*), 1.90-1.82 (4H, m, *CH_2-7,14*), 1.59-1.49 (4H, m, *CH_2-8,13*), 1.47-1.38 (4H, m, *CH_2-3,4*); **^{13}C NMR** (125 MHz, $CDCl_3$) **δ_C** 131.7 (*C-10,11*), 53.6 (*C-1,6*), 37.2 (*C-2,5*), 35.7 (*C-7,14*), 30.6 (*C-9,12*), 26.1 (*C-15,17,18,20*), 25.8 (*C-16,19*), 25.2 (*C-3,4*), 25.0 (*C-8,13*); **HRMS** *m/z* (ES^+) Found: $[M+Na]^+$ 425.1435. $C_{20}H_{34}S_4Na$ requires $[M+Na]^+$ 425.1436.

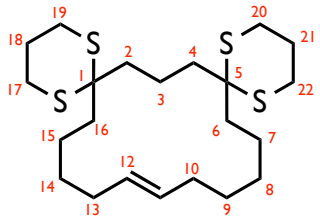
^{1}H NMR of **8b** (500 MHz, $CDCl_3$)



^{13}C NMR of **8b** (125 MHz, $CDCl_3$)



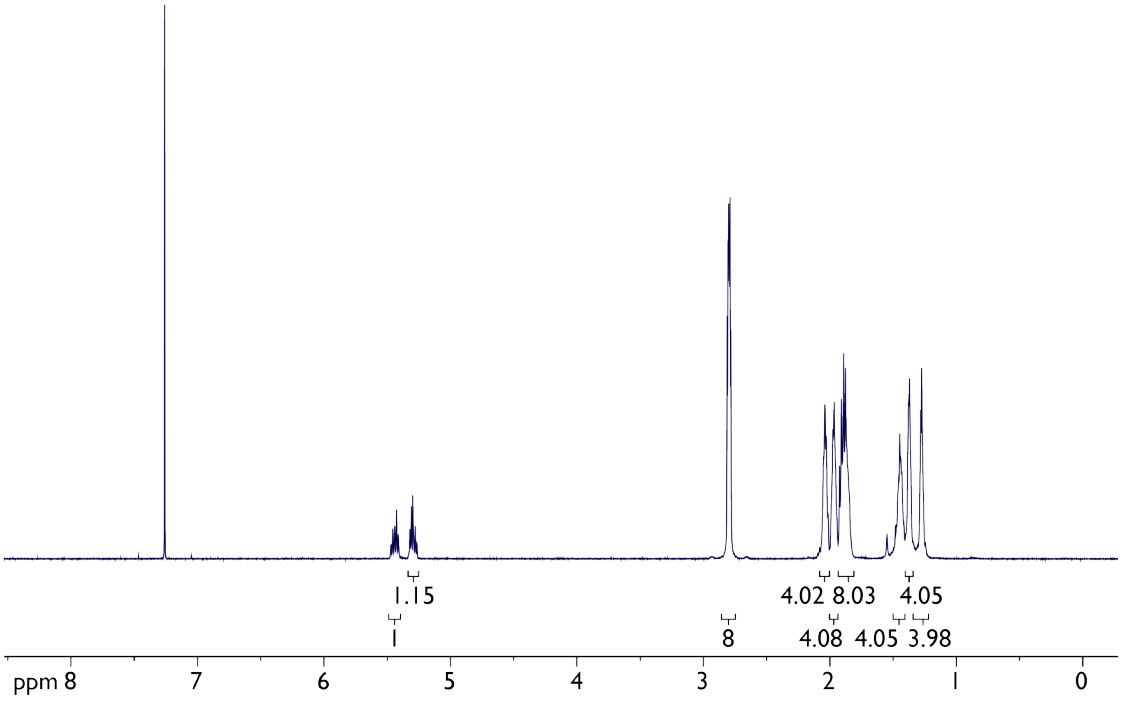
1,5,11,15-Tetrathiadispiro[5.3.5.11]hexacos-21-ene (8c)



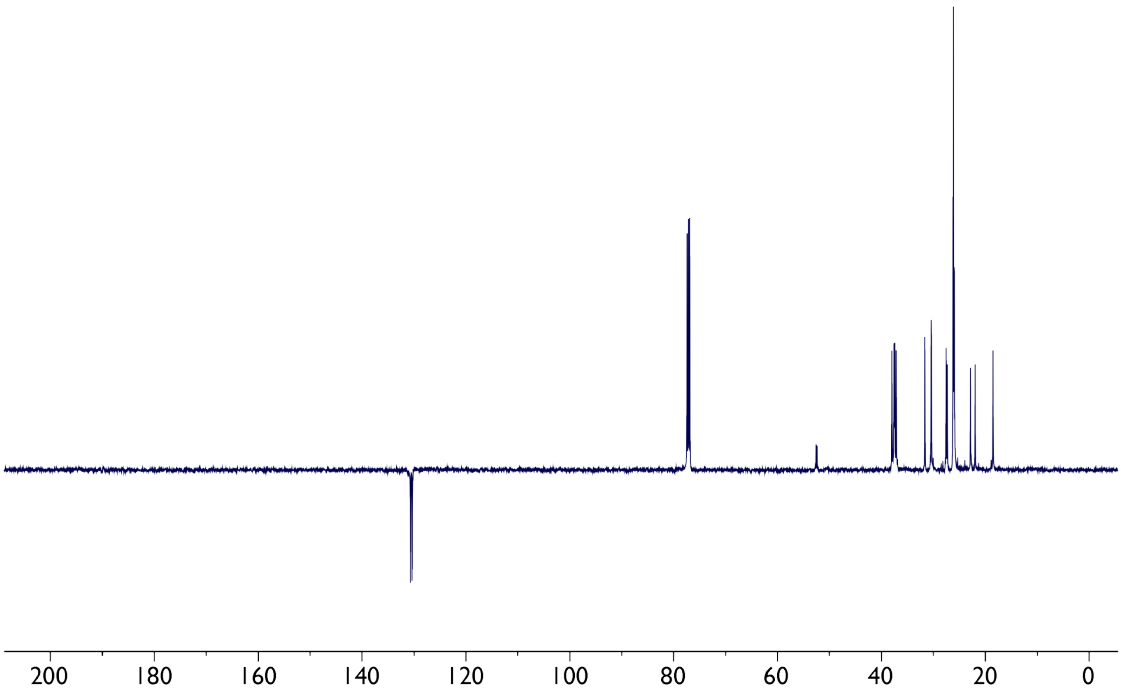
M_{20} (37 mg, 0.04 mmol, 1 mol%) was added in one portion to a solution of 1-(2-(hept-6-enyl)-1,3-dithian-2-yl)-3-(2-(hex-5-enyl)-1,3-dithian-2-yl)propane **7c** (1.80 g, 3.92 mmol) in DCE (196 mL, 0.02 M) and stirred for 16 h at RT. A further aliquot of **M_{20}** was added (37 mg, 0.04 mmol, 1 mol%) and stirring continued for 8 h. The crude reaction was concentrated under reduced pressure affording a brown waxy solid. Purification over silica gel, eluting with petroleum ether and Et_2O (97:3, 96:4), yielded 1,5,11,15-tetrathiadispiro[5.3.5.11]hexacos-21-ene **8c** (1.17 g, 69%) as a colourless viscous oil:

R_f = 0.49 (DCM); **^{1}H NMR** (500 MHz, $CDCl_3$) **δ_H** 5.48-5.40 (1H, m, *CH-11 or 12*), 5.33-5.25 (1H, m, *CH-11 or 12*), 2.83-2.77 (8H, m, *CH_2-17,19,20,22*), 2.08-2.00 (4H, m, *CH_2-10,12*), 2.00-1.94 (4H, m, *CH_2-18,21*), 1.94-1.82 (8H, m, *CH_2*), 1.49-1.41 (4H, m, *CH_2*), 1.40-1.34 (4H, m, *CH_2*), 1.31-1.24 (4H, m, *CH_2*); **^{13}C NMR** (125 MHz, $CDCl_3$) **δ_C** 130.7 (*C-11 or 12*), 130.4 (*C-11 or 12*), 52.6 (*C-1 or 5*), 52.4 (*C-1 or 5*), 38.0 (*CH_2*), 37.6 (*CH_2*), 37.4 (*CH_2*), 37.1 (*CH_2*), 31.6 (*C-10 or 13*) 30.42 (*C-10 or 13*), 30.37 (*CH_2*), 27.5 (*CH_2*), 27.3 (*CH_2*), 26.1 (*CH_2-17,19,20,22*), 26.0 (*C-18,21*), 22.8 (*CH_2*), 22.0 (*CH_2*), 18.5 (*CH_2*); **HRMS** m/z (ES^+) Found: $[M+H]^+$ 431.1923. $C_{22}H_{39}S_4$ requires $[M+H]^+$ 431.1929.

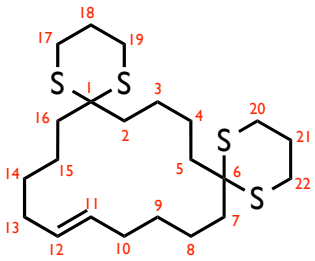
^{1}H NMR of **8c** (500 MHz, $CDCl_3$)



^{13}C NMR of **8c** (125 MHz, $CDCl_3$)



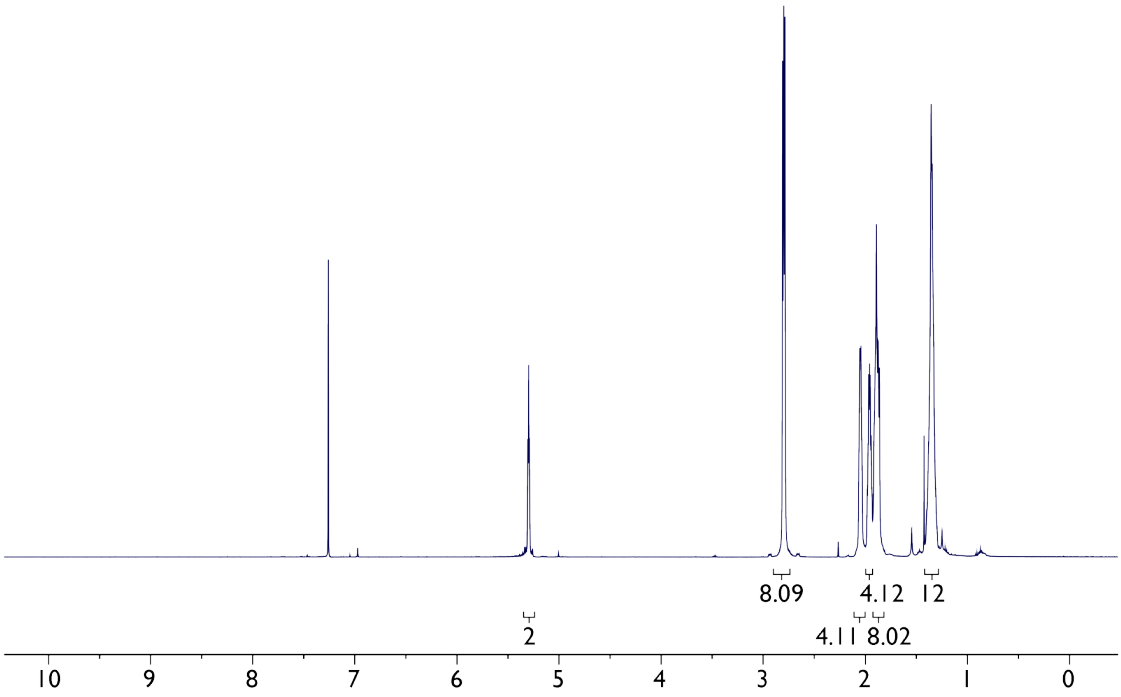
1,5,12,16-Tetrathiadispiro[5.4.5.10]hexacos-21-ene (8d)



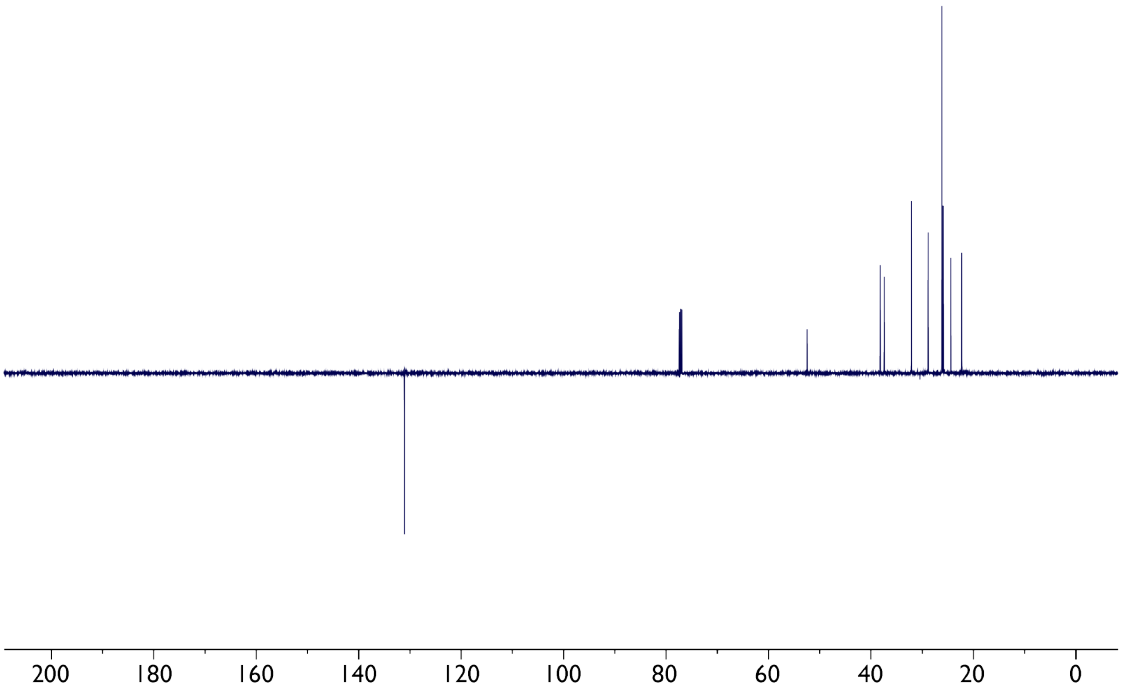
M_{20} (17 mg, 18 μmol, 1 mol%) was added in one portion to a solution of 2,2'-Butylenebis(2-(hex-5-enyl)-1,3-dithiane) **7d** (0.85 g, 1.85 mmol) in DCE (92 mL, 0.02 M) and stirred for 20 h at RT. A further aliquot of **M_{20}** was added (17 mg, 18 μmol, 1 mol%) and stirring continued for 8 h. The crude reaction was concentrated under reduced pressure affording a brown waxy solid. Purification over silica gel, eluting with petroleum ether and Et_2O (97:3), yielded 1,5,12,16-tetrathiadispiro[5.4.5.10]hexacos-21-ene **8d** (0.54 g, 68%) as a white crystalline solid:

R_f = 0.27 (petroleum ether:Et_2O, 88:12); **m.p.** = 154-156 °C (from EtOAc); **^{1}H NMR** (500 MHz, $CDCl_3$) **δ_H** 5.35-5.25 (2H, m, *CH-11,12*), 2.86-2.74 (8H, m, *CH_2-17,19,20,22*), 2.10-2.00 (4H, m, *CH_2-10,13*), 2.00-1.93 (4H, m, *CH_2-18,21*), 1.93-1.82 (8H, m, *CH_2-2,5,7,16*), 1.41-1.29 (12H, m, *CH_2-3,4,8,9,14,15*); **^{13}C NMR** (125 MHz, $CDCl_3$) **δ_C** 131.1 (*C-11,12*), 52.5 (*C-1,6*), 38.2 (*C-2,5 or 7,16*), 37.4 (*C-2,5 or 7,16*), 32.1 (*C-10,13*), 28.8 (*C-9,14*), 26.2 (*C-17,19,20,22*), 25.9 (*C-18,21*), 24.4 (*C-3,4*), 22.3 (*C-8,15*); **HRMS** *m/z* (ES^+) Found: $[M+H]^+$ 431.1919. $C_{22}H_{39}S_4$ requires $[M+H]^+$ 431.1929.

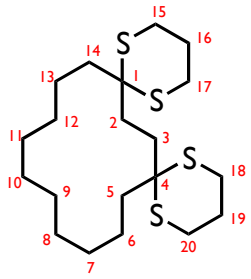
^{1}H NMR of **8d** (500 MHz, $CDCl_3$)



^{13}C NMR of **8d** (125 MHz, $CDCl_3$)



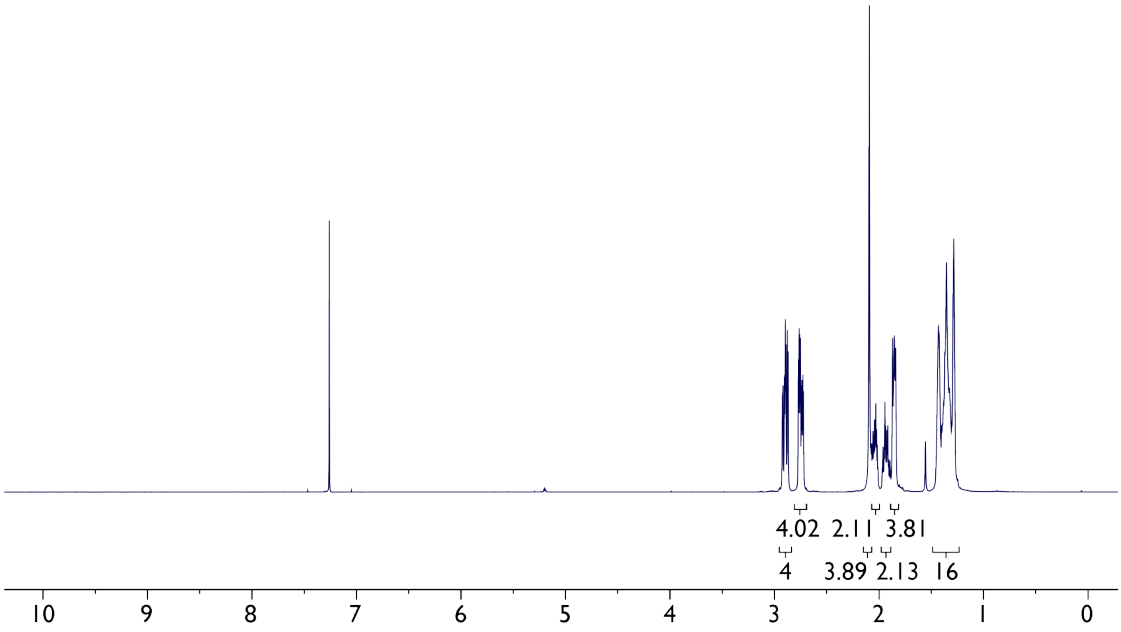
1,5,10,14-Tetrathiadispiro[5.2.5.10]tetracosane (10a)



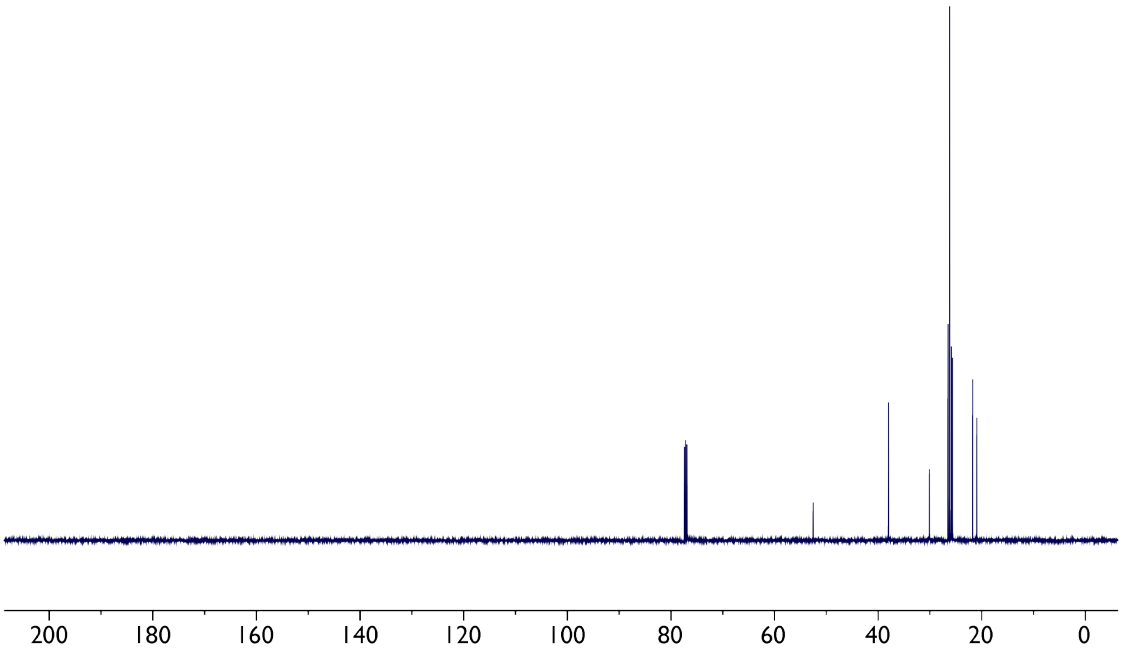
In a vial, 1,5,10,14-tetrathiadispiro[5.2.5.10]tetracos-19-ene **8a** (100 mg, 0.25 mmol) and the catalyst **9** (30 mg, 3.8 µmol, 15 mol%) were dissolved into dried DMF (2 mL), the vial was introduced inside an autoclave, and the system was pressurised with hydrogen at 10 bars. The reactor was heated at 80 °C for 48 h. The product was then extracted with a mixture of Et_2O and DCM. Purification over silica gel, eluting with DCM afforded 1,5,10,14-tetrathiadispiro[5.2.5.10]tetracosane **10a** (60 mg, 60% yield) as a white crystalline solid:

R_f = 0.30 (pentane:Et_2O, 88:12); **m.p.** = 149-150 °C (from DCM); **^{1}H NMR** (500 MHz, $CDCl_3$) **δ_H** 2.90 (4H, ddd, *J* = 14.6, 9.9, 3.0 Hz, *CH_a-15,17,18,20*), 2.75 (4H, ddd, *J* = 14.6, 6.7, 3.2 Hz, *CH_b-15,17,18,20*), 2.09 (4H, s, *CH_2-2,3*), 2.08-2.00 (2H, *CH_a-16,19*), 1.97-1.88 (2H, m, *CH_b-16,19*), 1.88-1.82 (4H, m, *CH_2-5,14*), 1.47-1.24 (16H, m, *CH_2*); **^{13}C NMR** (125 MHz, $CDCl_3$) **δ_C** 52.6 (*C-1,4*), 38.0 (*C-5,14*), 30.1 (*C-2,3*), 26.5 (*CH_2*), 26.2 (*C-15,17,18,20*), 25.9 (*C-16,19*), 25.7 (*CH_2*), 21.8 (*CH_2*), 21.0 (*CH_2*); **HRMS** m/z (ES^+) Found: $[M+H]^+$ 405.1771. $C_{20}H_{37}S_4$ requires $[M+H]^+$ 405.1773.

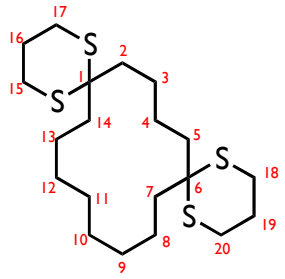
^{1}H NMR of **10a** (500 MHz, $CDCl_3$)



^{13}C NMR of **10a** (125 MHz, $CDCl_3$)



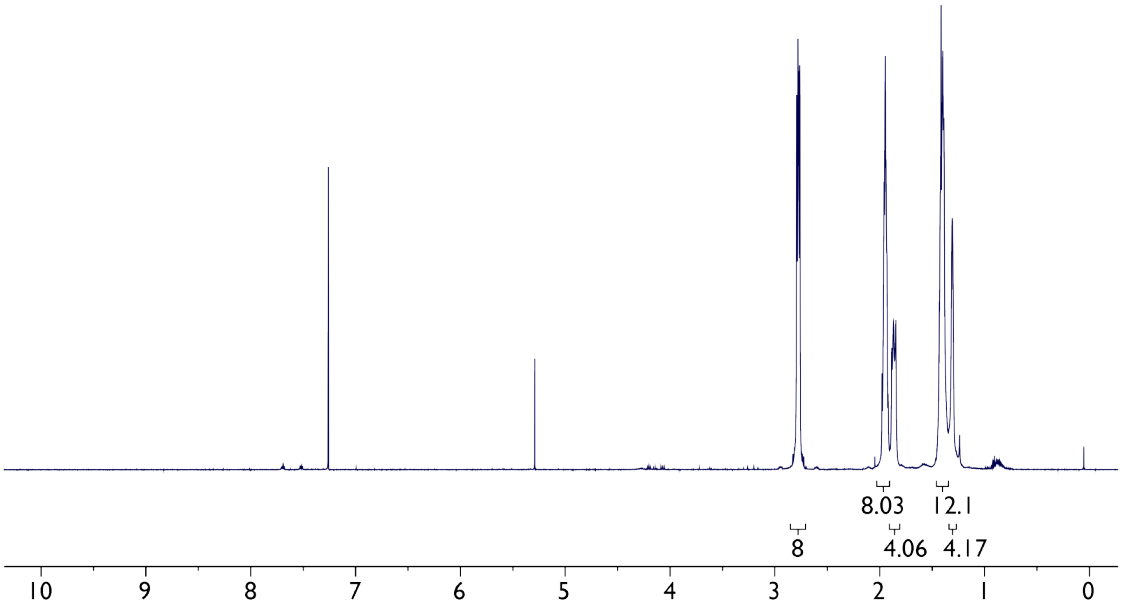
1,5,12,16-Tetrathiadispiro[5.4.5.8]tetracosane (10b)



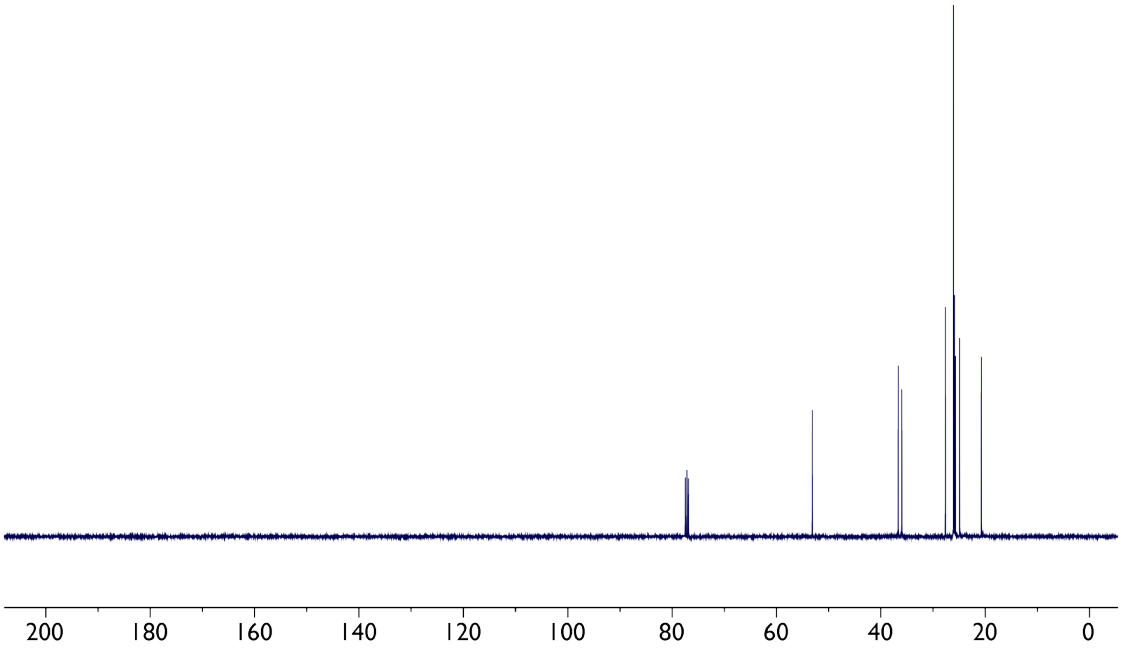
1,5,12,16-tetrathiadispiro[5.4.5.8]tetracos-20-ene **8b** (124 mg, 0.31 mmol) and the catalyst **9** (73 mg, 9.2 μmol, 30 mol%) were dissolved into dried DMF (3 mL), the vial was introduced inside an autoclave, and the system was pressurised with hydrogen at 10 bars. The reactor was heated at 80 °C for 48 h. The product was then extracted with a mixture of Et_2O and DCM. Purification over silica gel, eluting with DCM afforded 1,5,10,14-tetrathiadispiro[5.2.5.10]tetracosane **10b** (87 mg, 70% yield) as a white solid:

R_f = 0.27 (petroleum ether:Et_2O, 88:12); **m.p.** = 152-153 °C (from $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$) **δ_H** 2.83-2.72 (8H, m, *CH_2-15,17,18,20*), 2.00-1.91 (8H, m, *CH_2-7,14,16,19*), 1.90-1.81 (4H, m, *CH_2-2,5*), 1.46-1.35 (12H, m, *CH_2-3,4,8,13* and *9,12* or *10,11*), 1.34-1.28 (4H, m, *CH_2-9,12 or 10,11*); **^{13}C NMR** (100 MHz, $CDCl_3$) **δ_C** 53.1 (*C-1,6*), 36.7 (*C-7,14*), 36.0 (*C-2,5*), 27.6 (*C-8,13*), 26.1 (*C-15,17,18,20*), 25.9 (*C-16,19*), 25.7 (*CH_2*), 24.9 (*CH_2*), 20.8 (*C-3,4*); **HRMS** *m/z* (ES^+) Found: $[M+Na]^+$ 427.1593. $C_{20}H_{36}S_4Na$ requires $[M+Na]^+$ 427.1592.

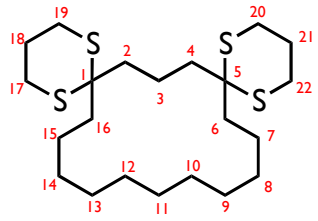
^{1}H NMR of **10b** (400 MHz, $CDCl_3$)



^{13}C NMR of **10b** (100 MHz, $CDCl_3$)



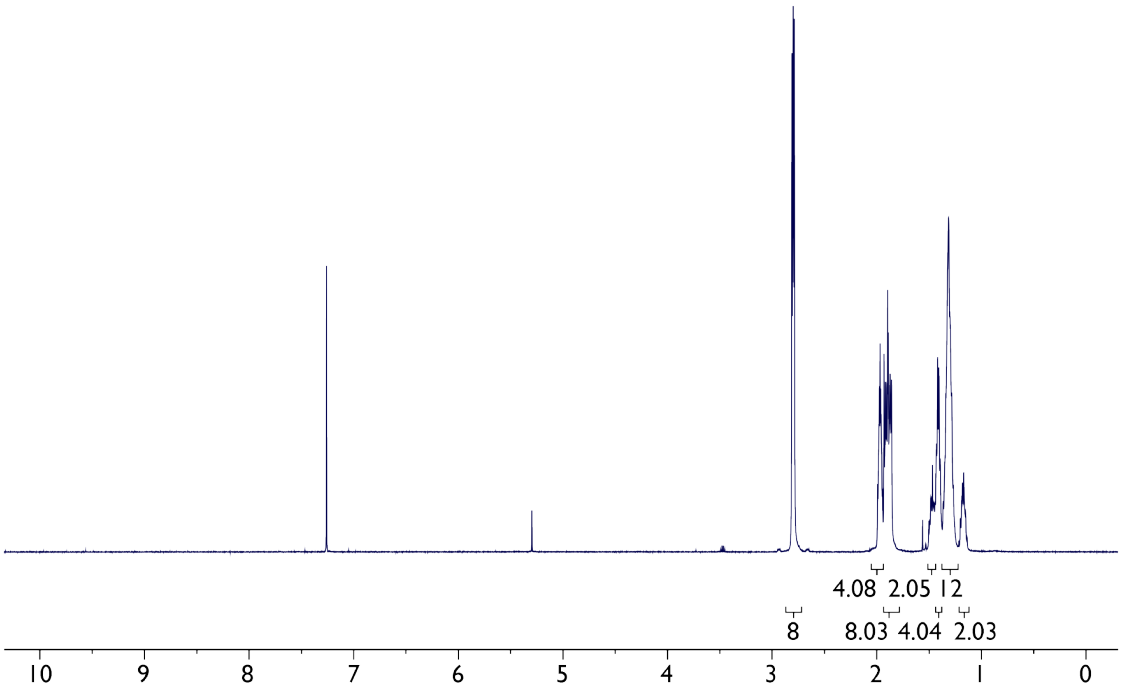
1,5,11,15-Tetrathiadispiro[5.3.5.11]hexacosane (10c)



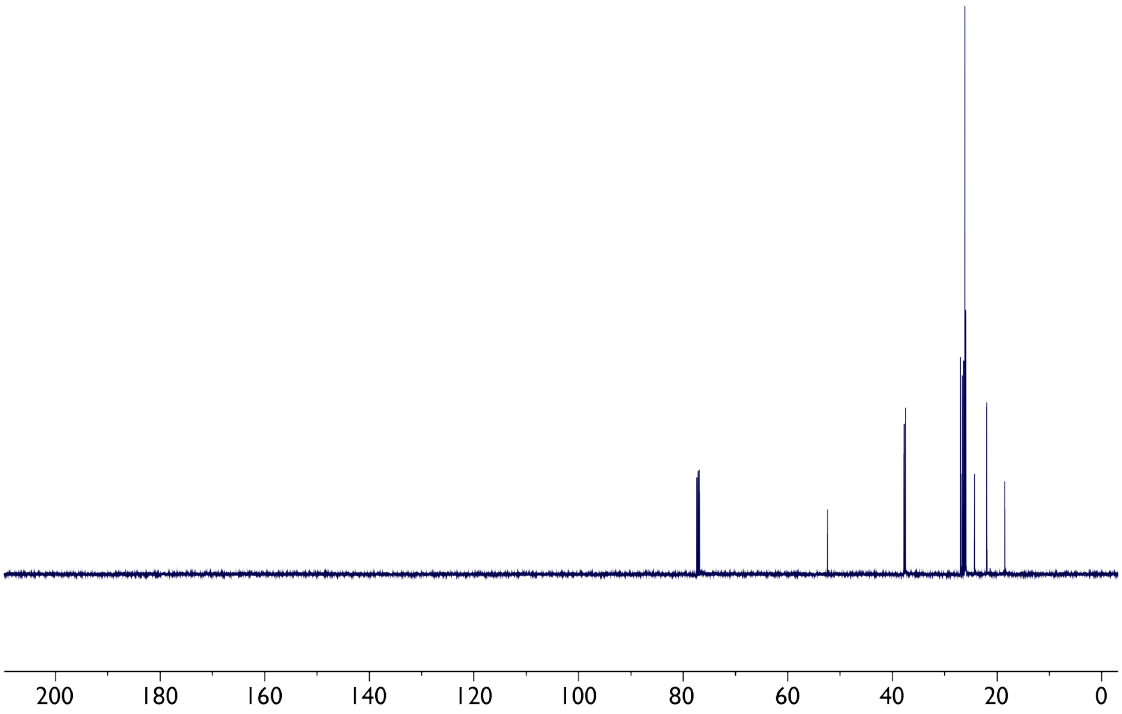
In a glass vial, 1,5,11,15-tetrathiadispiro[5.3.5.11]hexacos-21-ene **8c** (1.0 g, 2.4 mmol) and the catalyst **9** (146 mg, 18.5 μmmol, 7.6 mol%) were dissolved into dried DMF (10 mL) and placed in the autoclave. The system was pressurised with hydrogen at 10 bars. The reactor was heated at 80 °C for 48 h. The product was then extracted with a mixture of Et_2O and DCM. Purification over silica gel, eluting with DCM afforded 1,5,10,14-tetrathiadispiro[5.2.5.10]tetracosane **10c** (0.59 g, 56% yield) as a white crystalline solid:

R_f = 0.23 (petroleum ether:Et_2O, 88:12); **m.p.** = 126-128 °C (from DCM); **^{1}H NMR** (500 MHz, $CDCl_3$) **δ_H** 2.83-2.77 (8H, m, *CH_2-17,19,20,22*), 2.00-1.94 (4H, m, *CH_2-18,21*), 1.94-1.84 (8H, m, *CH_2-2,4,6,16*), 1.51-1.44 (2H, m, *CH_2-3*), 1.44-1.38 (4H, m, *CH_2-8,14*), 1.38-1.24 (12H, m, *CH_2-7,9,10,12,13,15*), 1.21-1.13 (2H, m, *CH_2-11*); **^{13}C NMR** (125 MHz, $CDCl_3$) **δ_C** 52.4 (*C-1,5*), 37.8 (*C-6,16*), 37.5 (*C-2,4*), 27.0 (*C-8,14*), 26.6 (*CH_2*), 26.4 (*CH_2*), 26.1 (*C-17,19,20,22*), 26.0 (*C-18,21*), 24.3 (*C-11*), 22.0 (*CH_2*), 18.5 (*C-3*); **HRMS** m/z (ES^+) Found: $[M+H]^+$ 433.2087. $C_{22}H_{41}S_4$ requires $[M+H]^+$ 433.2086;

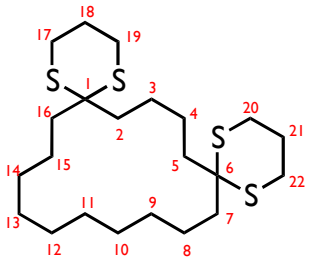
^{1}H NMR of **10c** (500 MHz, $CDCl_3$)



^{13}C NMR of **10c** (125 MHz, $CDCl_3$)



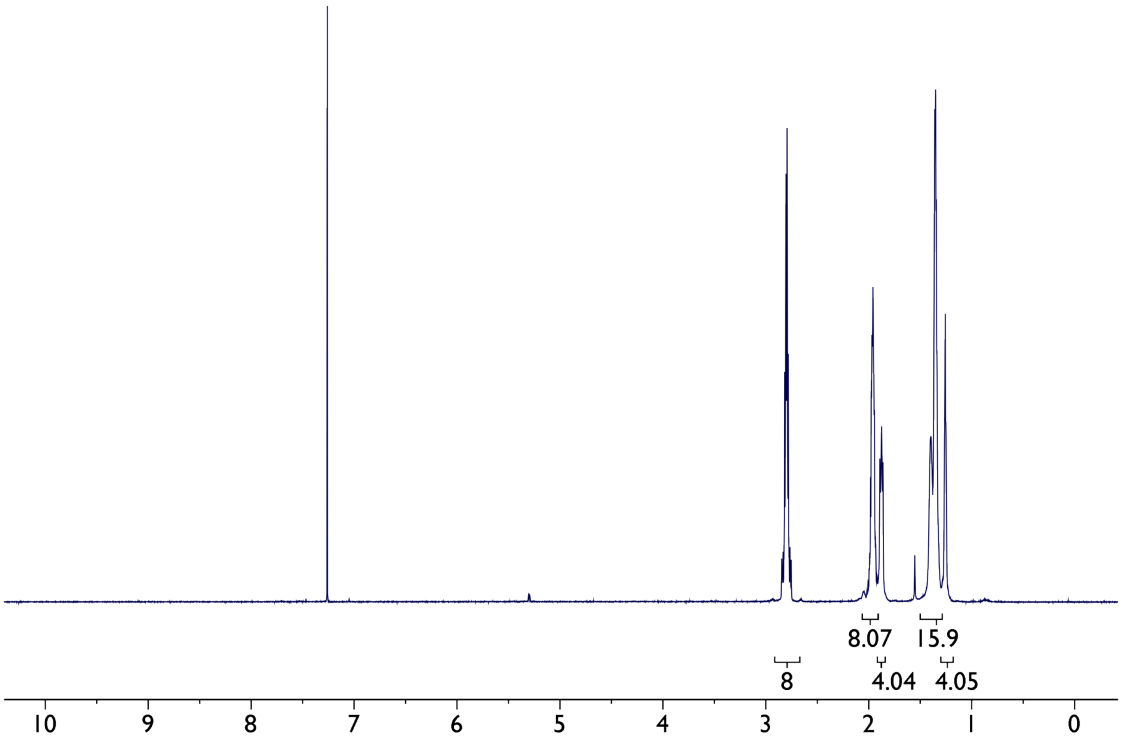
1,5,12,16-Tetrathiadispiro[5.4.5.10]hexacosane (10d)



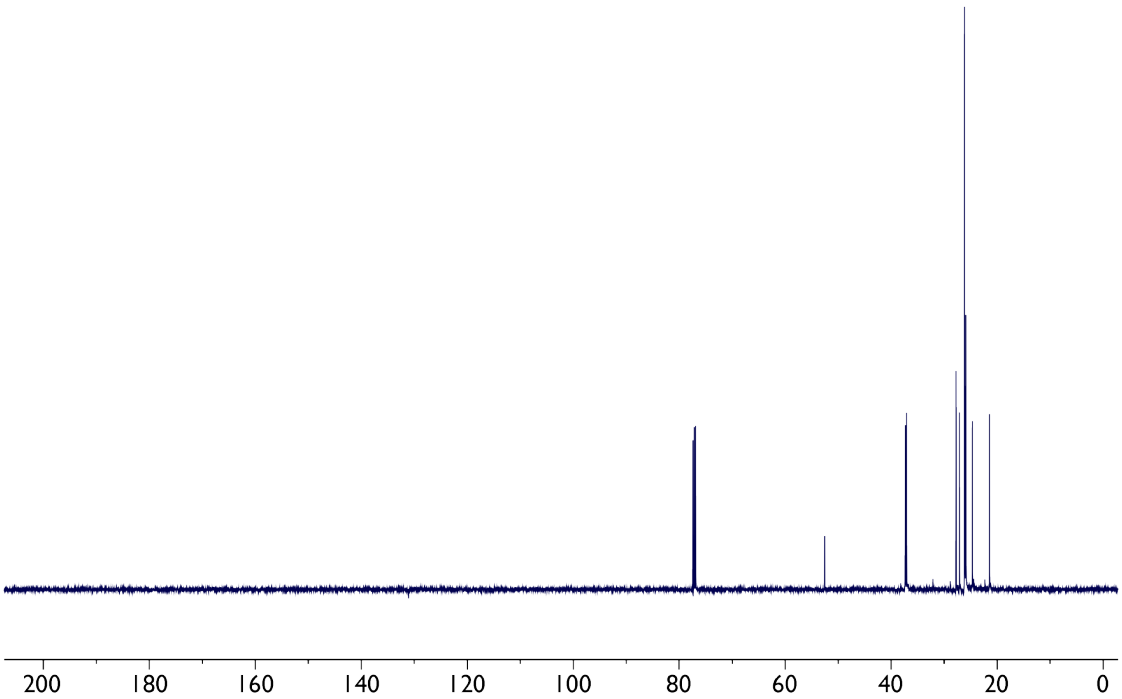
In a glass vial, 1,5,12,16-tetrathiadispiro[5.4.5.10]hexacos-21-ene **8d** (270 mg, 0.63 mmol) and the catalyst **9** (37 mg, 4.8 µmol, 7.6 mol%) were dissolved into dried DMF (4 mL), the vial was introduced inside an autoclave, and the system was pressurised with hydrogen at 10 bars. The reactor was heated at 80 °C for 48 h. The product was then extracted with a mixture of Et_2O and DCM. Purification over silica gel, eluting with DCM afforded 1,5,12,16-tetrathiadispiro[5.4.5.10]hexacosane **10d** (208 mg, 77% yield) as a white crystalline solid:

R_f = 0.17 (DCM); **m.p.** = 136-137 °C (from $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) **δ_H** 2.85-2.74 (8H, m, *CH_2-17,19,20,22*), 2.00-1.92 (8H, m, *CH_2-18,21 and 2,5 or 7,16*), 1.91-1.84 (4H, m, *CH_2-2,5 or 7,16*), 1.43-1.31 (16H, m, 4 × *CH_2*), 1.34-1.28 (4H, m, *CH_2-11,12*); **^{13}C NMR** (125 MHz, $CDCl_3$) **δ_C** 52.5 (*C-1,6*), 37.3 (*C-2,5 or 7,16*), 37.1 (*C-2,5 or 7,16*), 27.8 (*C-10,13*), 27.1 (*CH_2*), 26.2 (*C-17,19,20,22*), 26.1 (*CH_2*), 25.9 (*C-18,21*), 24.7 (*CH_2*), 21.4 (*CH_2*); **HRMS** *m/z* (ES^+) Found: $[M+H]^+$ 433.2081. $C_{22}H_{41}S_4$ requires $[M+H]^+$ 433.2086.

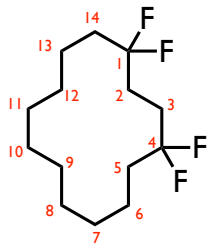
^{1}H NMR of **10d** (500 MHz, $CDCl_3$)



^{13}C NMR of **10d** (125 MHz, $CDCl_3$)



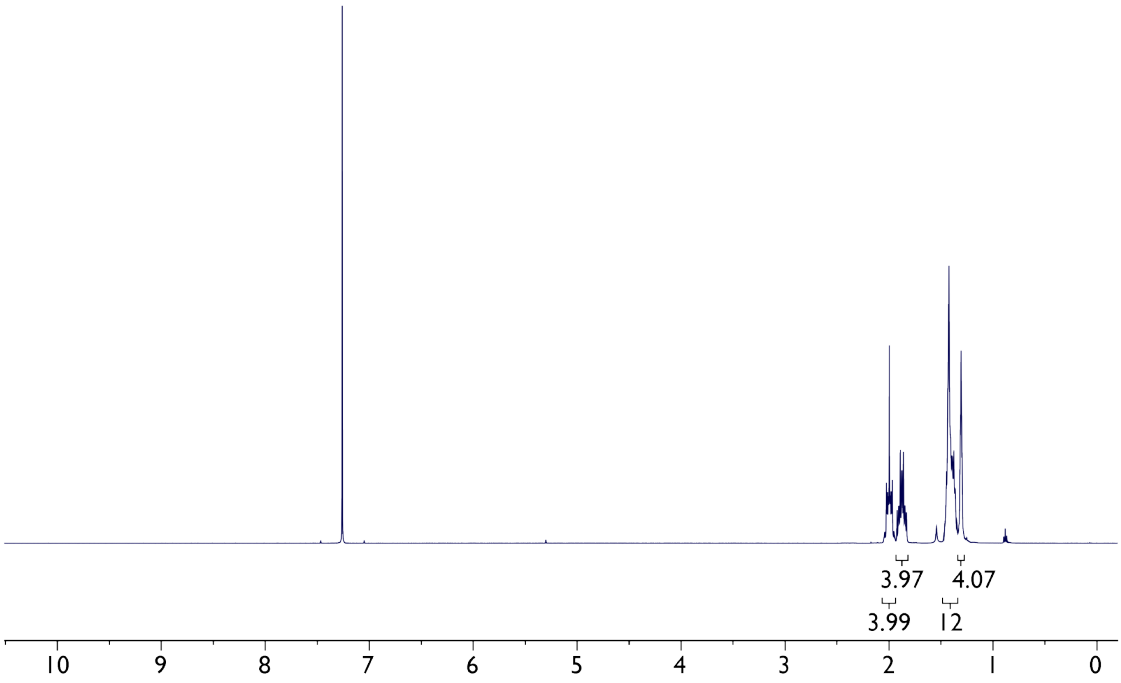
1,1,4,4-Tetrafluorocyclotetradecane (11a)



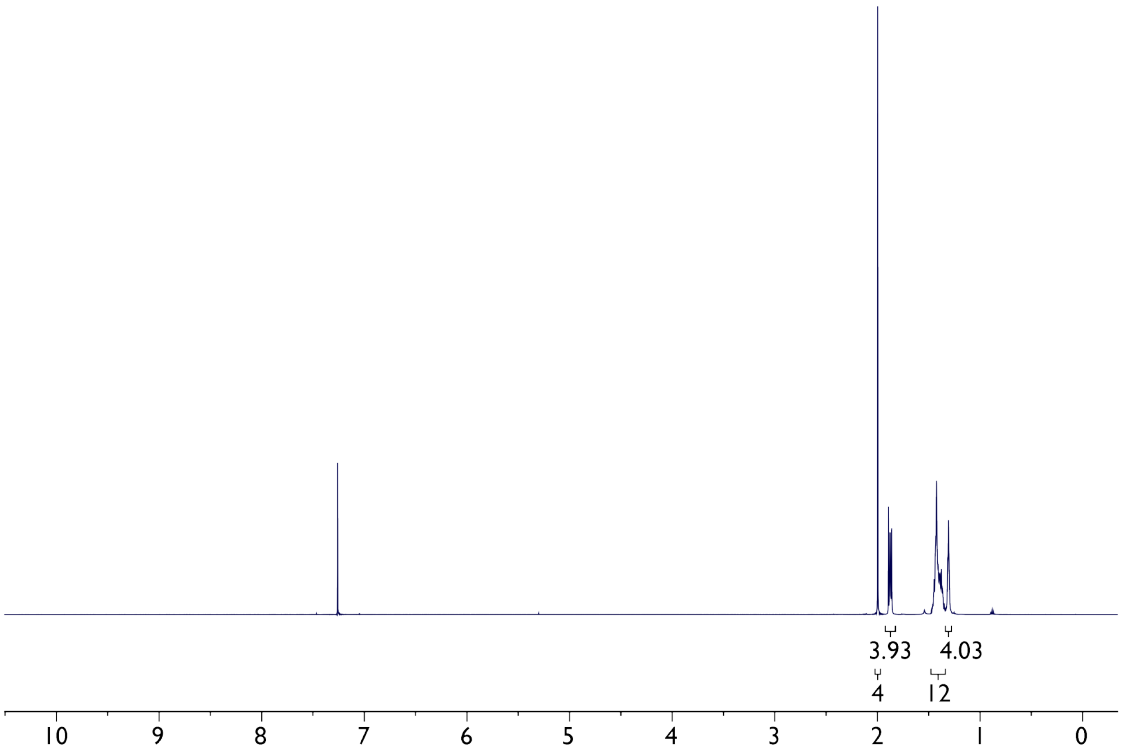
To a solution of *N*-iodosuccinimide (1.40 g, 6.22 mmol, 8 eq) in DCM (12 mL) cooled to −78 °C was added hydrogen fluoride-pyridine (2.33 mL, 89.7 mmol, 121 eq) and the resulting mixture was stirred for 5 min at −78 °C. A solution of **10a** (0.30 g, 0.74 mmol, 1 eq) in DCM (5 mL) was added dropwise to the mixture over 10 min. The reaction mixture was stirred at −78 °C for 4 h and gradually warmed to RT overnight. The crude reaction was added portionwise to a biphasic mixture of saturated aqueous $NaHCO_3$ solution (80 mL) and DCM (40 mL) at 0 °C. The aqueous layer was separated and extracted with DCM (3 × 50 mL). The organic extracts were washed with aqueous $Na_2S_2O_3$ solution (10% w/v, 2 × 80 mL), brine (100 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification over silica gel, eluting with pentane, yielded 1,1,4,4-tetrafluorocyclotetradecane **11a** (0.14 g, 68%) as a white crystalline solid:

R_f = 0.34 (pentane:DCM, 90:10); **m.p.** = 74 °C (from $CDCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) **δ_H** 2.06-1.94 (4H, m, *CH_2-2,3*), 1.93-1.81 (4H, m, *CH_2-5,14*), 1.48-1.34 (12H, m, *CH_2*), 1.33-1.27 (4H, m, *CH_2*); **^{1}H{^{19}F} NMR** (500 MHz, $CDCl_3$) **δ_H** 2.00 (4H, s, *CH_2-2,3*), 1.90-1.85 (4H, m, *CH_2-5,14*), 1.48-1.34 (12H, m, *CH_2*), 1.33-1.27 (4H, m, *CH_2*); **^{13}C NMR** (125 MHz, $CDCl_3$) **δ_C** 125.7 (t, *J* = 240.8 Hz, *C-1,4*), 34.4 (t, *J* = 25.3 Hz, *C-5,14*), 28.2 (tt, *J* =27.6, 5.2 Hz, *C-2,3*), 25.9 (*CH_2*), 25.2 (*CH_2*), 23.4 (*CH_2*), 20.9 (t, *J* = 5.4 Hz, *C-6,13*); **^{19}F{^{1}H} NMR** (470 MHz, $CDCl_3$) **δ_F** −91.59 (s, *CF_2-1,4*); **HRMS** *m/z* (EI^+) Found: $[M-HF]^{+\cdot}$ 248.1747. $C_{14}H_{23}F_3$ requires $[M-HF]^{+\cdot}$ 248.1746; **LRMS** *m/z* (EI^+) 248.18 $[M-HF]^{+\cdot}$, 228.16 $[M-2HF]^{+\cdot}$.

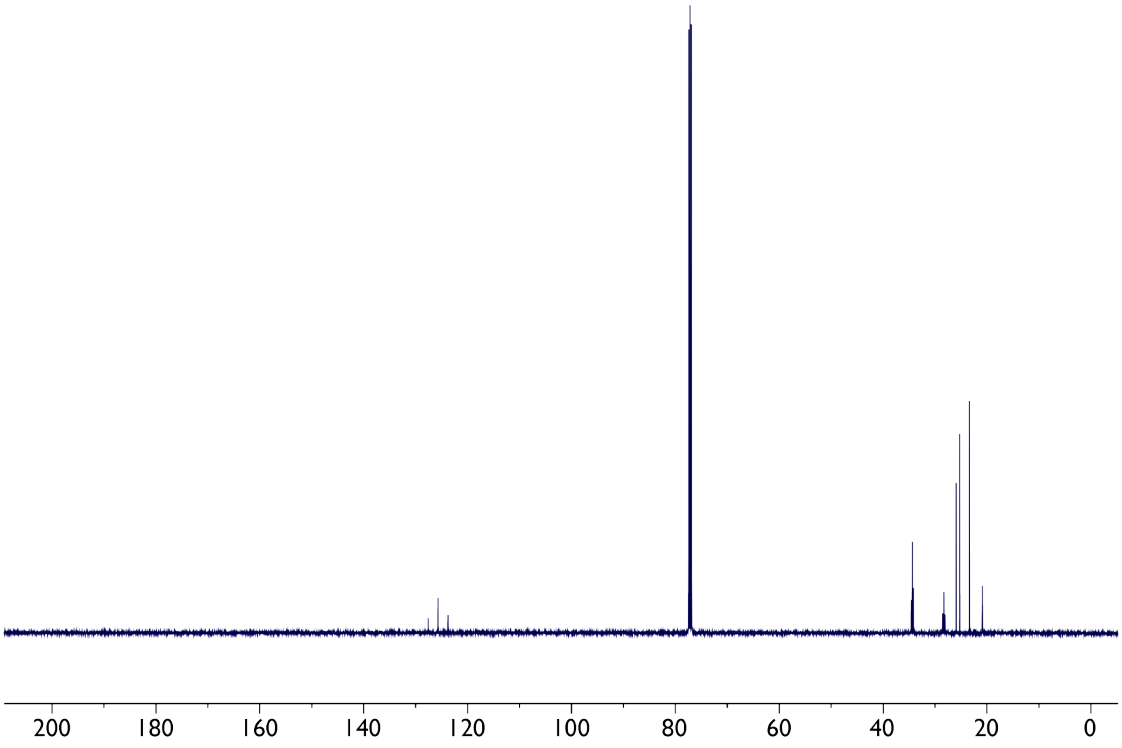
^{1}H NMR of **11a** (500 MHz, $CDCl_3$)



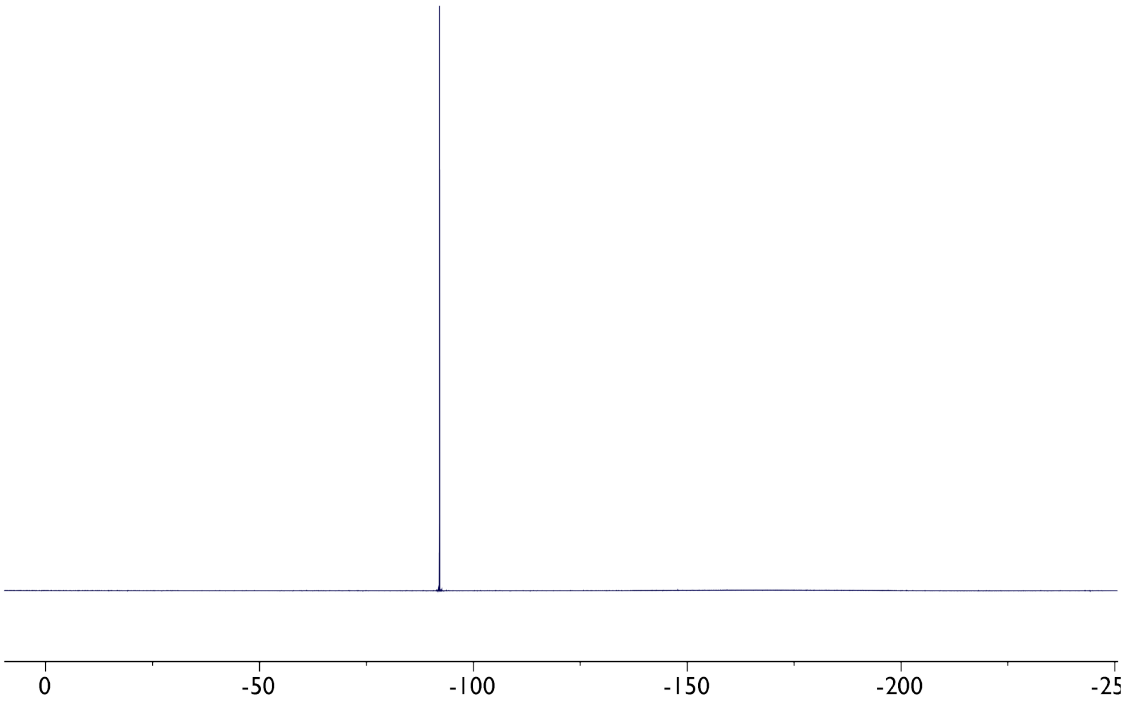
^{1}H{^{19}F)NMR of **11a** (500 MHz, $CDCl_3$)



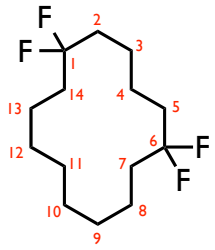
^{13}C NMR of **11a** (125 MHz, $CDCl_3$)



$^{19}F\{^{1}H\}$ NMR of **11a** (470 MHz, $CDCl_3$)



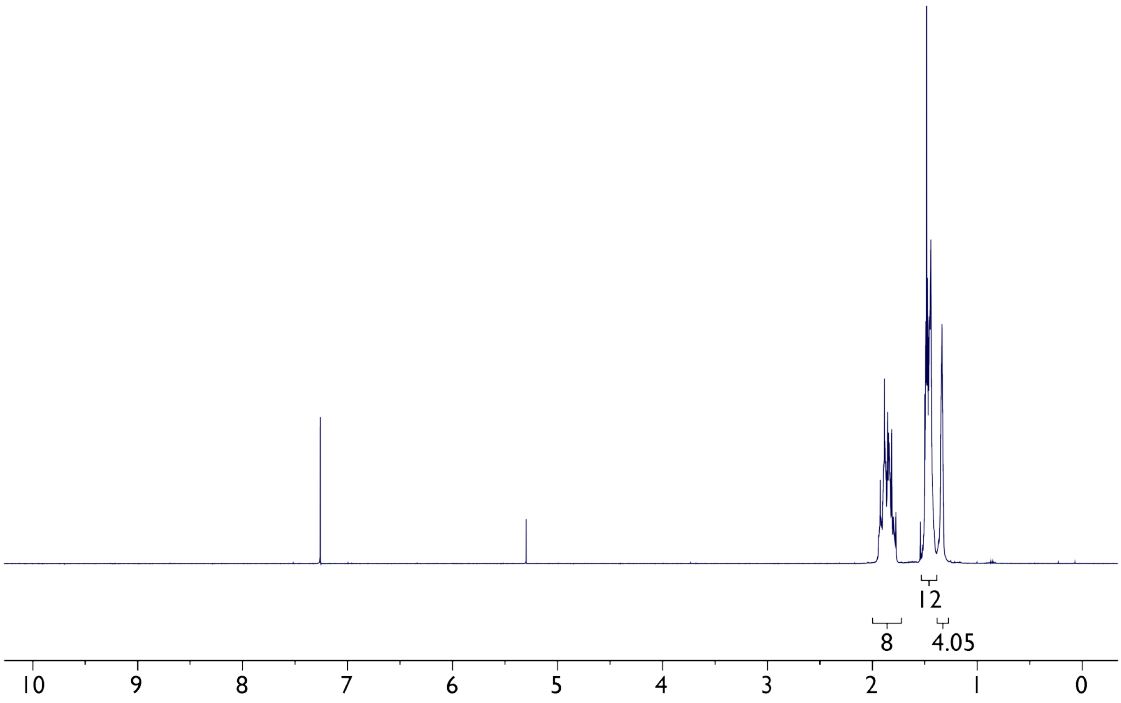
1,1,6,6-Tetrafluorocyclotetradecane (11b)



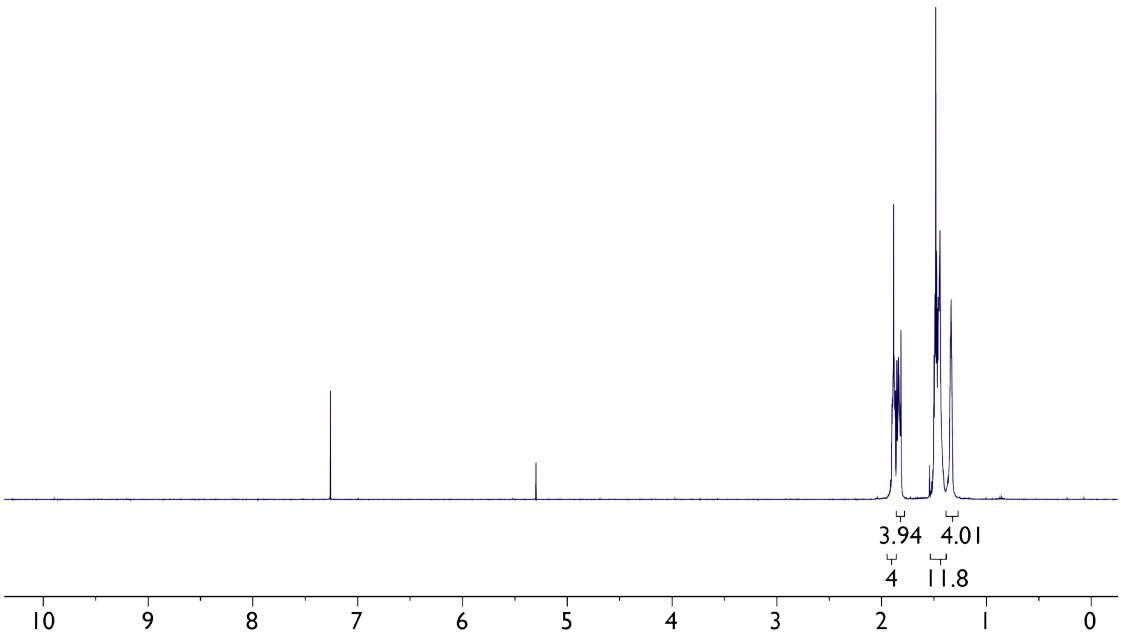
To a solution of *N*-iodosuccinimide (0.62 g, 2.76 mmol, 8 eq) in DCM (6 mL) cooled to −78 °C was added hydrogen fluoride-pyridine (1.05 mL, 40.4 mmol, 117 eq) and the resulting mixture was stirred for 5 min at −78 °C. A solution of **10b** (0.14 g, 0.35 mmol, 1 eq) in DCM (3 mL) was added dropwise to the mixture over 10 min. The reaction mixture was stirred at −78 °C for 4 h and gradually warmed to RT overnight. Crude reaction was added portionwise to a biphasic mixture of saturated aqueous $NaHCO_3$ solution (40 mL) and DCM (30 mL) at 0 °C. The aqueous layer was separated and extracted with DCM (3 × 30 mL). The organic extracts were washed with aqueous $Na_2S_2O_3$ solution (10% w/v, 2 × 50 mL), brine (80 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification over silica gel, eluting with petroleum ether and DCM (95:5), yielded 1,1,6,6-tetrafluorocyclotetradecane **11b** (0.05 g, 53%) as a white crystalline solid:

R_f = 0.38 (petroleum ether:DCM, 80:20); **m.p.** = 50 °C (from $CDCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$) **δ_H** 1.96-1.76 (8H, m, *CH_2*), 1.53-1.39 (12H, m, *CH_2*), 1.38-1.29 (4H, m, *CH_2*); **^{1}H{^{19}F} NMR** (400 MHz, $CDCl_3$) **δ_H** 1.92-1.86 (4H, m, *CH_2*), 1.86-1.80 (4H, m, *CH_2*), 1.53-1.39 (12H, m, *CH_2*), 1.38-1.29 (4H, m, *CH_2*); **^{13}C NMR** (125 MHz, $CDCl_3$) **δ_C** 126.5 (t, *J* = 240.2 Hz, *C*-1,6), 34.5 (t, *J* = 25.8 Hz, *CH_2*), 33.3 (t, *J* = 25.4 Hz, *CH_2*), 26.5 (*CH_2*), 24.5 (*CH_2*), 23.0 (t, *J* = 5.4 Hz, *CH_2*), 20.0 (t, *J* = 5.0 Hz, *CH_2*); **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$) **δ_F** −91.36 (s, *CF_2*-1,6); **HRMS** *m/z* (CI^+) Found: $[M-2HF+H]^+$ 229.1773. $C_{14}H_{23}F_2$ requires $[M-2HF+H]^+$ 229.1768; **LRMS** *m/z* (EI^+) 248.18 $[M-HF]^{+\cdot}$, 228.1 $[M-2HF]^{+\cdot}$.

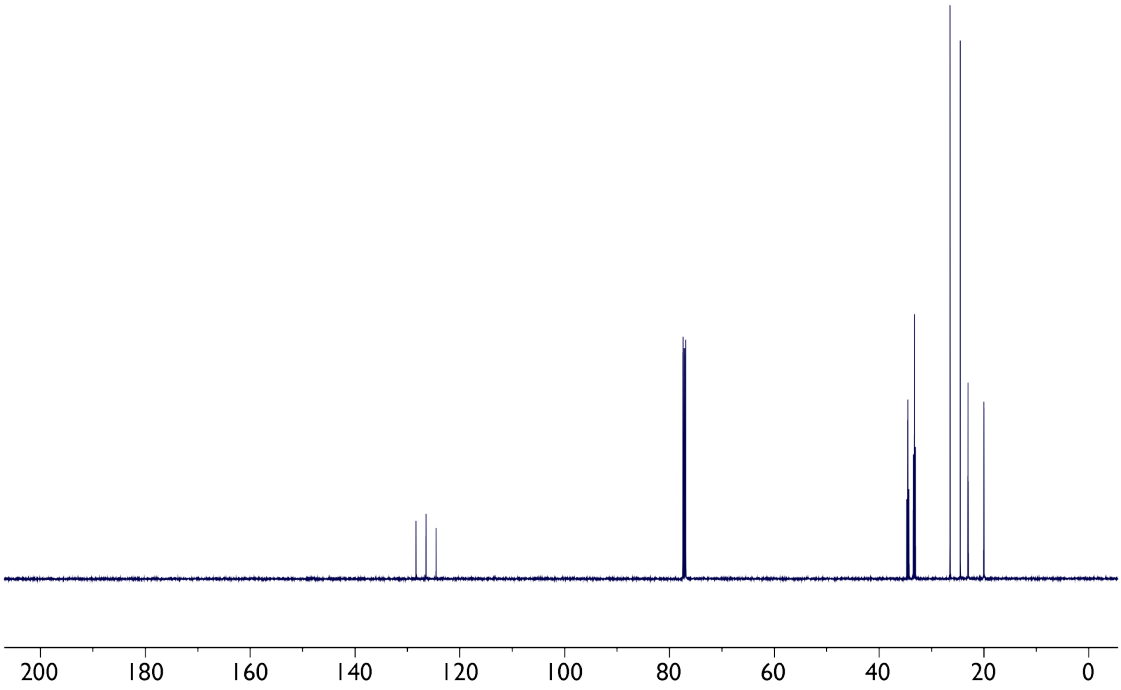
^{1}H NMR of **11b** (400 MHz, $CDCl_3$)



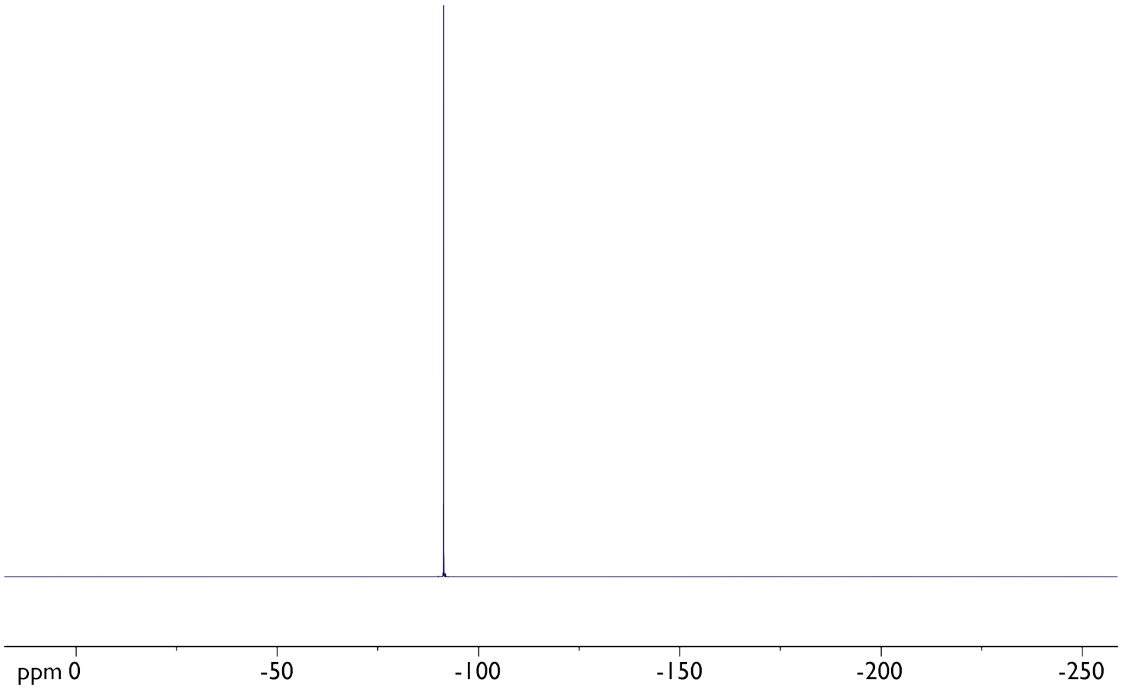
^{1}H{^{19}F} NMR of **11b** (400 MHz, $CDCl_3$)



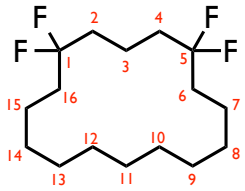
^{13}C NMR of **11b** (125 MHz, $CDCl_3$)



$^{19}F\{^{1}H\}$ NMR of **11b** (376 MHz, $CDCl_3$)



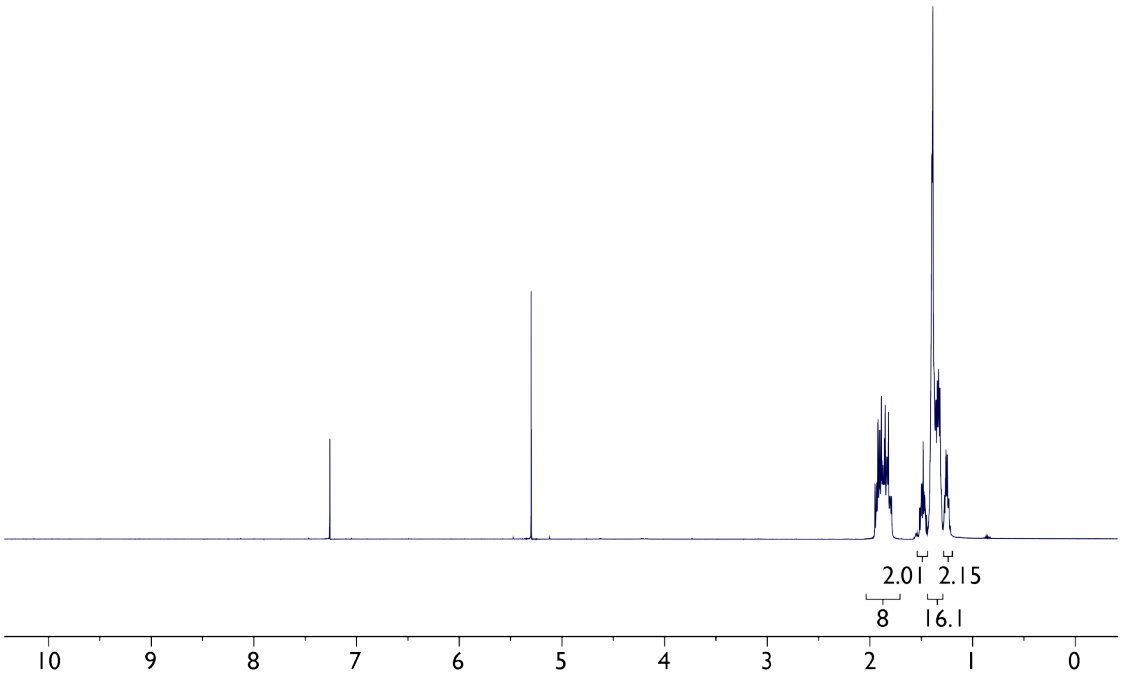
1,1,5,5-Tetrafluorocyclohexadecane (11c)



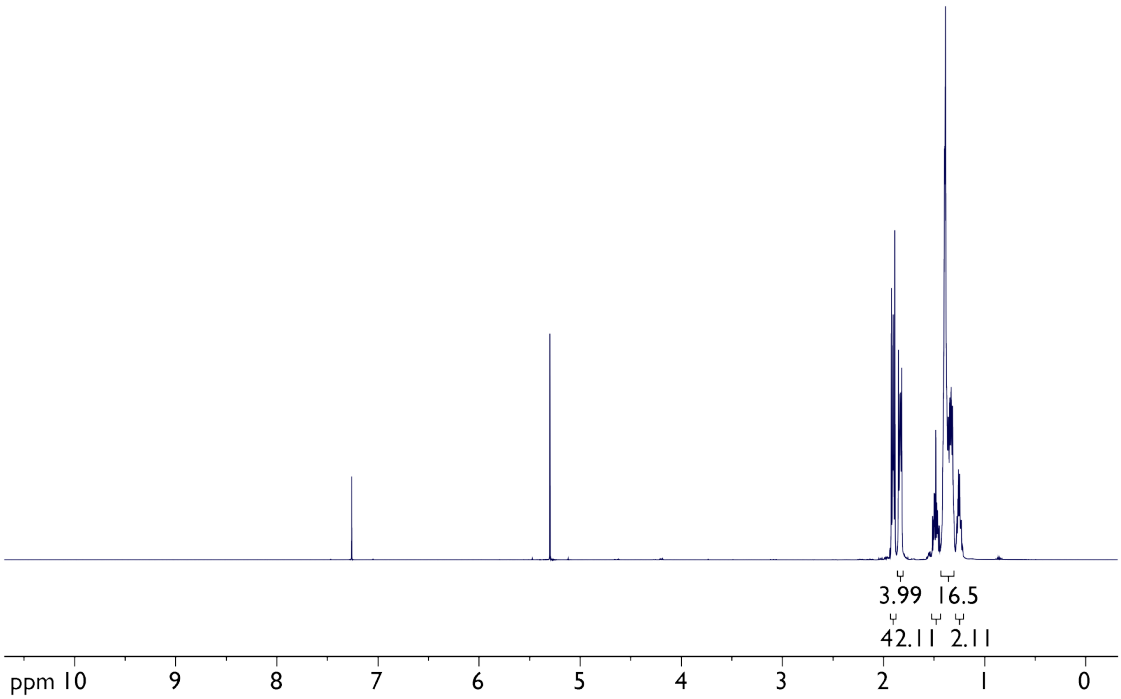
To a solution of *N*-iodosuccinimide (1.33 g, 5.96 mmol, 8 eq) in DCM (12 mL) cooled to −78 °C was added hydrogen fluoride-pyridine (2.28 mL, 87.8 mmol, 119 eq) and the resulting mixture was stirred for 5 min at −78 °C. A solution of **10c** (0.32 g, 0.74 mmol, 1 eq) in DCM (5 mL) was added dropwise to the mixture over 10 min. The reaction mixture was stirred at −78 °C for 4 h and gradually warmed to RT overnight. The crude reaction was added portionwise to a biphasic mixture of saturated aqueous $NaHCO_3$ solution (80 mL) and DCM (40 mL) at 0 °C. The aqueous layer was separated and extracted with DCM (3 × 50 mL). The organic extracts were washed with aqueous $Na_2S_2O_3$ solution (10% w/v, 2 × 80 mL), brine (100 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification over silica gel, eluting with petroleum ether and DCM (95:5), yielded 1,1,5,5-tetrafluorocyclohexadecane **11c** (0.09 g, 43%) as a white crystalline solid:

R_f = 0.83 (DCM); **m.p.** = 62.5 °C (from $CDCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) **δ_H** 1.97-1.77 (8H, m, *CH_2-2,4,6,16*), 1.53-1.44 (2H, m, *CH_2-3*), 1.43-1.29 (16H, m, *CH_2*), 1.28-1.21 (2H, m, *CH_2-11*) ; **^{1}H{^{19}F} NMR** (400 MHz, $CDCl_3$) **δ_H** 1.93-1.88 (4H, m, *CH_2-2,4*), 1.86-1.81 (4H, m, *CH_2-6,16*), 1.53-1.44 (2H, m, *CH_2-3*), 1.43-1.29 (16H, m, *CH_2*), 1.28-1.21 (2H, m, *CH_2-11*); **^{13}C NMR** (125 MHz, $CDCl_3$) **δ_C** 125.8 (t, *J* = 240.1 Hz, *C-1,5*), 34.8 (t, *J* = 26.4 Hz, *C-2,4*), 34.7 (t, *J* = 25.4 Hz, *C-6,16*), 26.7 (*CH_2*), 26.6 (*CH_2*), 26.4 (*CH_2*), 25.4 (*C-11*), 21.4 (t, *J* = 5.3 Hz, *C-7,15*), 17.9 (q, *J* = 5.9 Hz, *C-3*); **^{19}F{^{1}H} NMR** (470 MHz, $CDCl_3$) **δ_F** −91.92 (s, *CF_2*-1, 5); **HRMS** *m/z* (CI^+) Found: $[M-2HF+H]^+$ 257.2088. $C_{16}H_{27}F_2$ requires $[M-2HF+H]^+$ 257.2081; **LRMS** *m/z* (EI^+) 276.21 $[M-HF]^{+\cdot}$, 256.19 $[M-2HF]^{+\cdot}$.

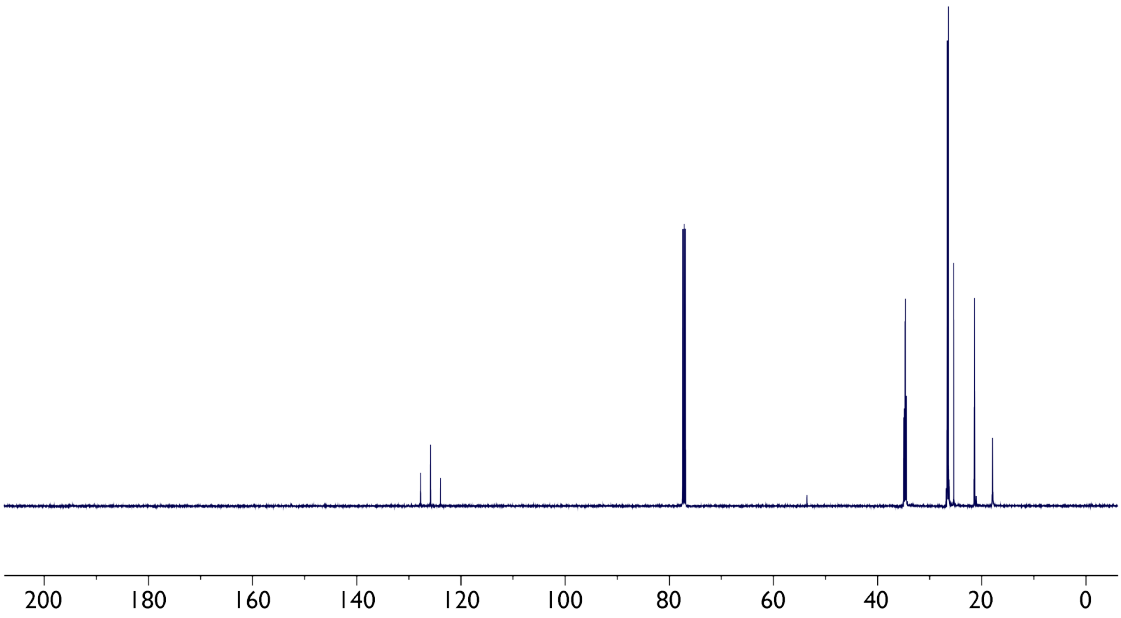
^{1}H NMR of **11c** (500 MHz, $CDCl_3$)



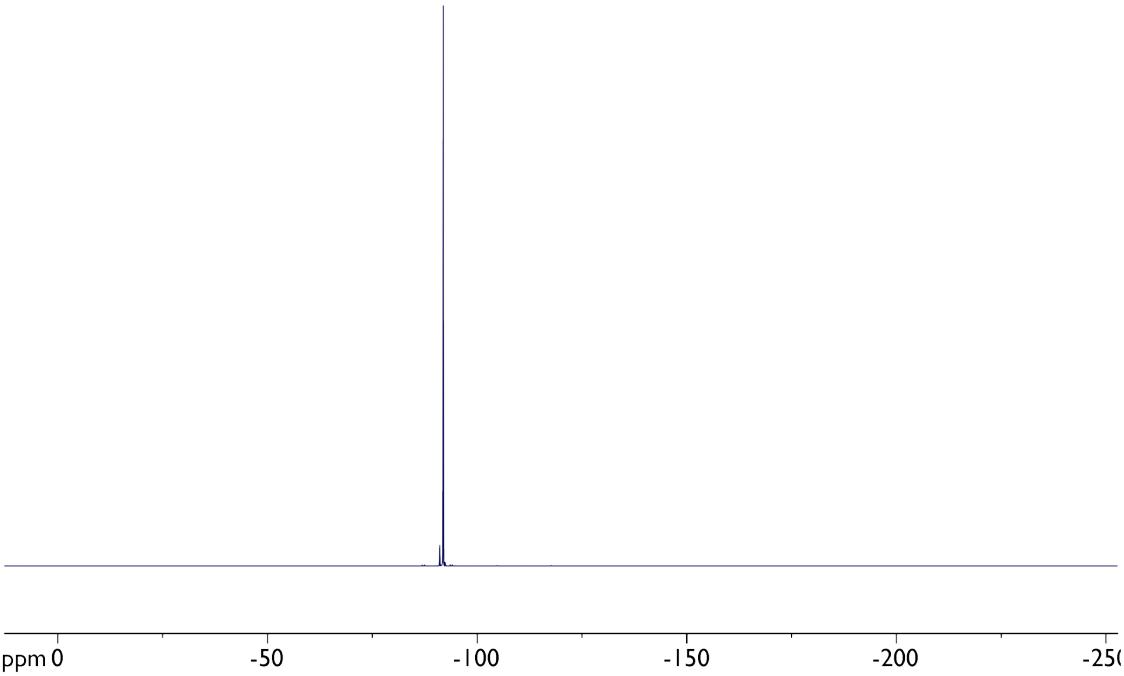
^{1}H{^{19}F} NMR of **11c** (500 MHz, $CDCl_3$)



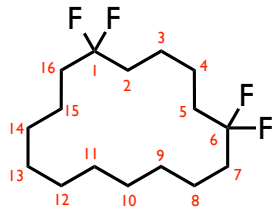
^{13}C NMR of **11c** (125 MHz, $CDCl_3$)



^{19}F{^{1}H} NMR of **11c** (470 MHz, $CDCl_3$)



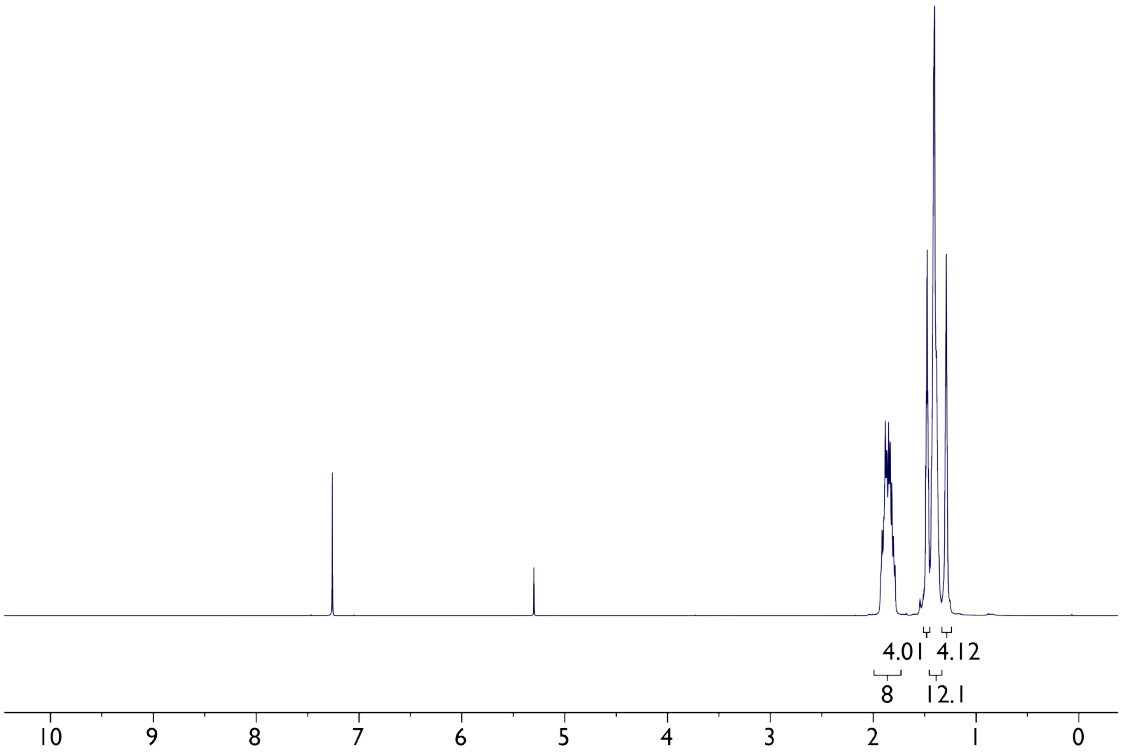
1,1,6,6-Tetrafluorocyclohexadecane (11d)



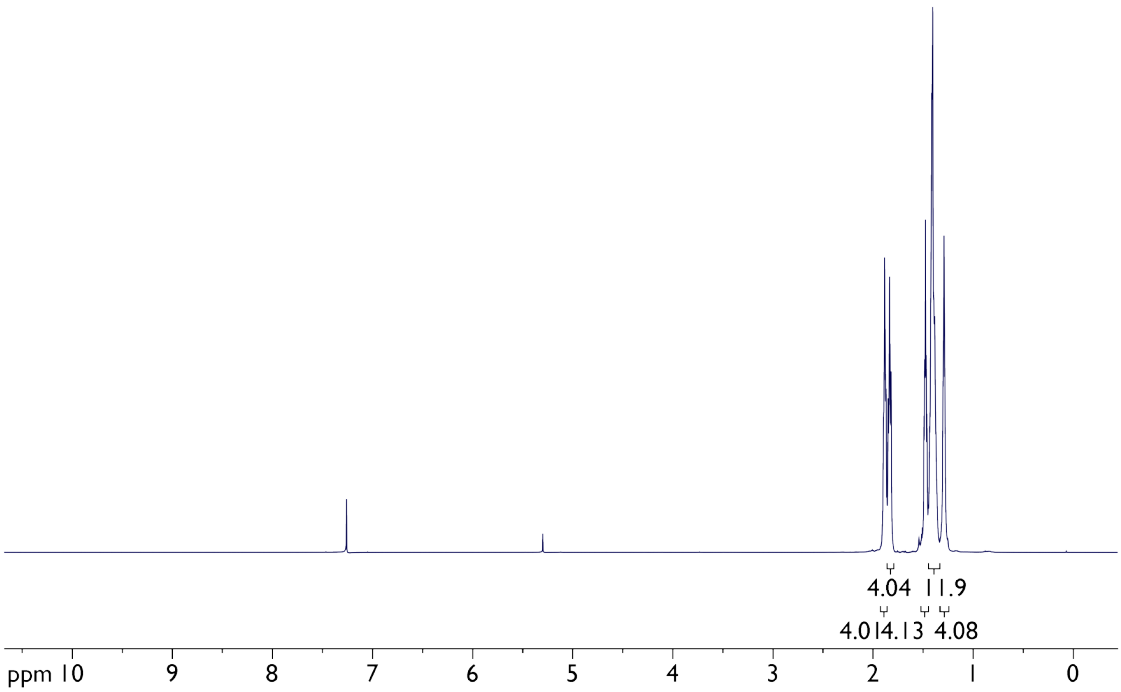
To a solution of *N*-iodosuccinimide (0.87 g, 3.87 mmol, 8 eq) in DCM (8 mL) cooled to −78 °C was added hydrogen fluoride-pyridine (1.50 mL, 57.8 mmol, 119 eq) and the resulting mixture was stirred for 5 min at −78 °C. A solution of **10d** (0.21 g, 0.49 mmol, 1 eq) in DCM (3 mL) was added dropwise to the mixture over 10 min. The reaction mixture was stirred at −78 °C for 4 h and gradually warmed to RT overnight. Crude reaction was added portionwise to a biphasic mixture of saturated aqueous $NaHCO_3$ solution (50 mL) and DCM (25 mL) at 0 °C. The aqueous layer was separated and extracted with DCM (3 × 30 mL). The organic extracts were washed with aqueous $Na_2S_2O_3$ solution (10% w/v, 2 × 50 mL), brine (80 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification over silica gel, eluting with petroleum ether, yielded 1,1,6,6-tetrafluorocyclohexadecane (0.09 g, 65%) **11d** as a white crystalline solid:

R_f = 0.82 (DCM); **m.p**. = 39.5 °C (from $CDCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$) **δ_H** 1.95-1.77 (8H, m, *CH_2-2,5,7,16*), 1.52-1.45 (4H, m, *CH_2-3,4*), 1.45-1.34 (12H, m, *CH_2*), 1.33-1.25 (4H, m, *CH_2*); **^{1}H{^{19}F} NMR** (500 MHz, $CDCl_3$) **δ_H** 1.92-1.86 (4H, m, *CH_2-2,5*), 1.86-1.80 (4H, m, *CH_2-7,16*), 1.52-1.45 (4H, m, *CH_2-3,4*), 1.45-1.34 (12H, m, *CH_2*), 1.33-1.25 (4H, m, *CH_2*); **^{13}C NMR** (125 MHz, $CDCl_3$) **δ_C** 126.2 (t, *J* = 240.2 Hz, *C-1,6*), 34.9 (t, *J* = 25.8 Hz, *C-2,5*), 34.3 (t, *J* = 25.3 Hz, *C-7,16*), 27.0 (*CH_2*), 26.8 (*CH_2*), 26.2 (*CH_2*), 23.2 (t, *J* = 5.4 Hz, *C-3,4*), 21.0 (t, *J* = 5.0 Hz, *C-8,15*); **^{19}F{^{1}H} NMR** (470 MHz, $CDCl_3$) **δ_F** −92.18 (s, *CF_2-1,6*); **HRMS** m/z (CI^+) Found: $[M-2HF+H]^+$ 257.2084. $C_{16}H_{27}F_2$ requires $[M-2HF+H]^+$ 257.2081; **LRMS** m/z (EI^+) 276.21 $[M-HF]^{+\cdot}$, 256.20 $[M-2HF]^{+\cdot}$.

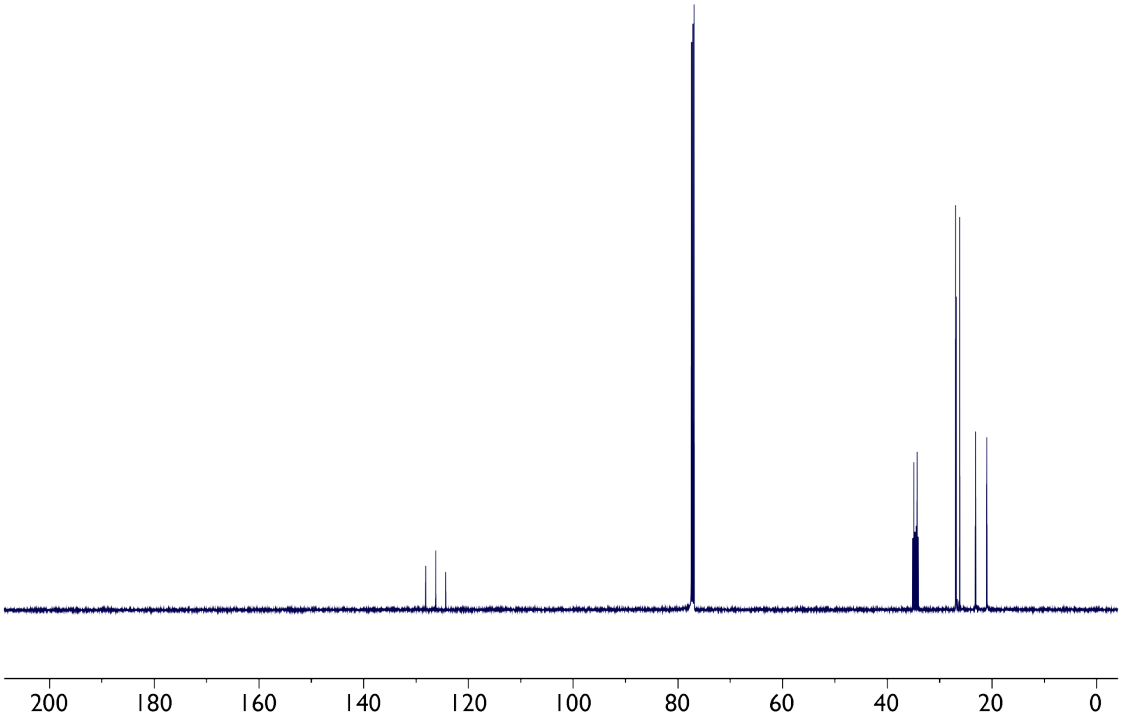
^{1}H NMR of **11d** (500 MHz, $CDCl_3$)



^{1}H{^{19}F} NMR of **11d** (500 MHz, $CDCl_3$)



^{13}C NMR of **11d** (125 MHz, $CDCl_3$)



$^{19}F\{^{1}H\}$ NMR of **11d** (470 MHz, $CDCl_3$)