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Supporting Information

Synthesis and Application of Easily Recyclable Thiomorpholines for use in Sulfur Ylide-mediated Asymmetric Epoxidation of Aldehydes.

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Supporting Information

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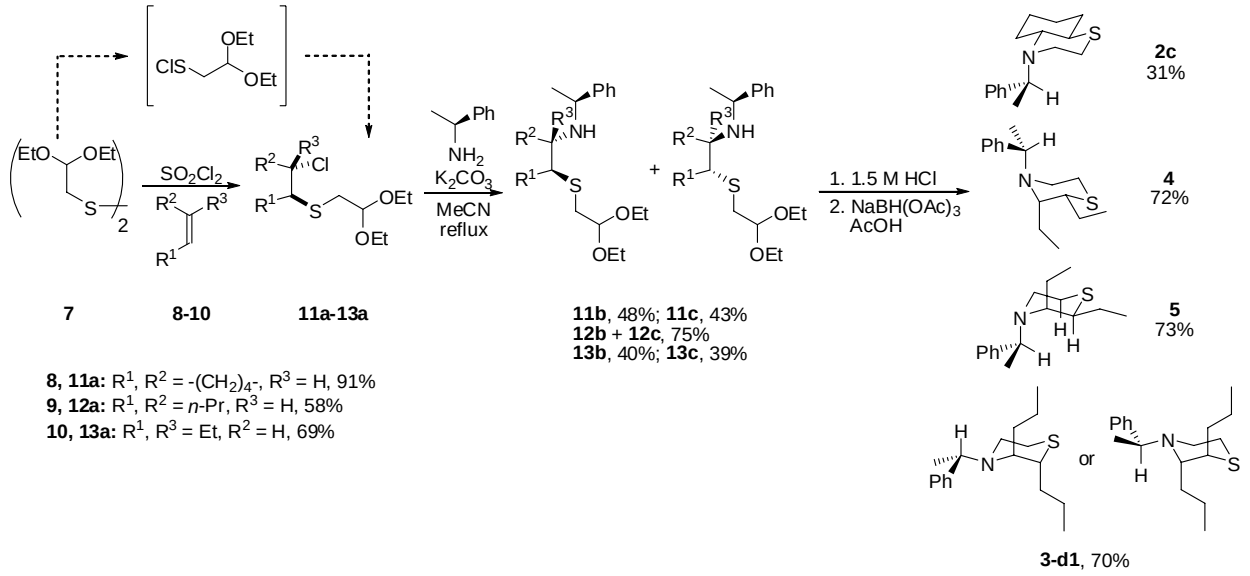
Assignment of Stereochemistry of 11–13 and 2c–5

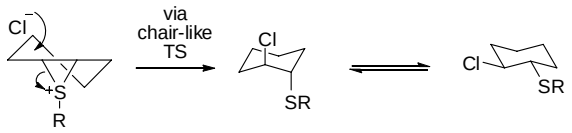
Scheme 1



Scheme 1 shows the synthesis of **2c**–**5**. The stereochemistry of **5** was determined from the X-ray crystal structure of its benzyl sulfonium salt **23**. This enabled the assignment of the absolute stereochemistry of **4.** The stereochemistries of **13b** and **13c** were deduced in turn.

β-Chlorosulfides **11a–13a** are proposed to form via a mechanism involving nucleophilic attack by chloride on an epi-sulfonium ion (Scheme 2).[1] The coupling constants of the ^{1}H NMR signals assigned to the CHS and CHCl protons (ddd, J = 7.5, 7.5, 4.5 Hz) are consistent with the proposed *trans*-relationship. The *trans*-relationship of the sulfur and nitrogen substituents of **11b** is evident from the ^{1}H NMR signals of the SCH and NCH protons on the cyclohexane ring (Table 1); both appear as ddds with two large coupling constants of 10–11 Hz and one smaller coupling (4 Hz) which is typical of protons having a *trans*-diaxial relationship in a dominant chair conformer. The sulfide group is proposed to participate in the displacement of the chloride ion giving rise to a stereoretentive displacement of chloride by the phenylethylamine.[2] In the ^{1}H NMR spectrum of **11c** one of the two NCH/SCH protons gives rise to a signal at 2.50 ppm (ddd, J = 11.5, 11.5, 4.0 Hz) which is consistent with the proposed *trans*-diaxial relationship. Compounds **12b,c** and **13b,c** are also proposed to be formed with retention of stereochemistry. The stereochemistry established for **13b,c** is consistent with these proposals.

Scheme 2 Attack by chloride on an episulfonium ion initially leading to *trans*-diaxial β-chlorosulfide.



The coupling constants of the signals assigned to the SCH and NCH protons in the ^{1}H NMR spectrum of **2c** are in agreement with the expected *trans*-diaxial relationship.[3] The phenylethyl group is predicted to sit in a pseudoaxial position in the dominant conformers of **2c** based on molecular modelling.[4] The absolute stereochemistries of the corresponding stereocenters on **11b** and **11c** were deduced from the major enantiomer of *trans*-stilbene oxide obtained when the epoxidation of benzaldehyde was carried out with **21** (see main paper). The absolute stereochemistry of the stereocenters on the octene-derived parts of **12b** and **12c** has not been determined. In the ^{1}H NMR of **3-d1** the coupling of just 2 Hz between the SCH and NCH protons is indicative of the propyl groups occupying *trans*-diaxial positions in the dominant conformation(s). This is due to highly unfavourable steric clashes between the two propyl groups in *trans*-diequatorial conformations.[5] Conformers with the propyl groups sitting in axial positions and the *N*-phenylethyl group pseudoequatorial are predicted to dominate based on molecular modelling.[4] Modelling of conformers of **4** and **5** predicted that the phenylethyl group and the ethyl group on the carbon α to nitrogen would sit in pseudoaxial positions as is observed in the crystal structure of **23**. We note that the preference for *trans*-dipropyl groups to occupy diaxial positions is not general for saturated heterocycles. Figure 1 shows the calculated[4] energy difference between the lowest energy diequatorial and diaxial conformers of various saturated heterocycles.

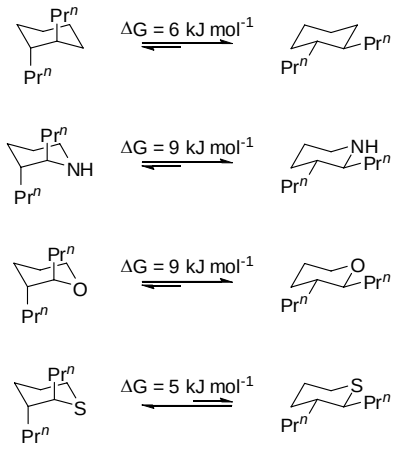


Figure 1 Calculated energy differences between the lowest energy diequatorial and diaxial conformers of *trans*-1,2-dipropylcyclohexane and *trans*-2,3-dipropyl saturated heterocycles.[4]

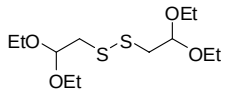
Table 1 Coupling constants between CHS and CHCl/CHN protons in 11–13 and 2c–5.

R, R	**β-chlorosulfides**	
	CHS	CHCl
-$(CH_2)_4$- **11a**	3.03 (ddd, J = 7.5, 7.5, 4.5 Hz)	4.07 (ddd, *J* = 7.5, 7.5, 4.5 Hz)
Et, Et **13a**	2.89 (ddd, *J* = 9.0, 5.5, 3.5 Hz)	4.00 (ddd, *J* = 9.0, 5.5, 3.5 Hz)
n-Pr, *n*-Pr **12a**	3.01 (ddd, *J* = 10.0, 4.0, 3.0 Hz)	4.15 (ddd, *J* = 10.0, 3.0, 3.0 Hz)
	amino-sulfides (CHS/CHN)	
-$(CH_2)_4$- **11b**	2.40 (ddd, *J* = 10.0, 10.0, 4.0 Hz), 2.58 (ddd, *J* = 11.0, 10.0, 4.0 Hz)	
-$(CH_2)_4$- **11c**	2.50 (ddd, *J* = 11.5, 11.5, 4.0 Hz), second signal obscured by overlapping signals.	
Et, Et **13b**	2.34 (ddd, *J* = 9.0, 3.0, 3.0 Hz), 2.94 (ddd, *J* = 8.0, 7.0, 3.0 Hz)	
Et, Et **13c**	2.38–2.45 (m, 1 H), 2.70 (ddd, *J* = 9.5, 5.0, 3.5 Hz)	
n-Pr, *n*-Pr **12b/c -d1**	2.88 (ddd, *J* = 10.0, 3.0, 3.0 Hz); 2.48 (ddd, *J* = 8.5, 3.0, 3.0 Hz)	
n-Pr, *n*-Pr **12b/c -d2**	2.44 (ddd *J* = 6.0, 6.0, 3.0 Hz, NCH or SCH), 2.48–2.55 (m, NCH or SCH)	
	Thiomorpholines (CHS/CHN)	
-$(CH_2)_4$- **2c**	2.26 (ddd, *J* = 12.5, 9.0, 3.5 Hz, 1 H, NCH_{ax}), 2.72 (ddd, *J* = 12.5, 9.0, 3.5 Hz, 1 H, SCH_{ax}),	
Et, Et **4**	2.70 (ddd, *J* = 8.0, 5.5, 3.0 Hz, 1 H, NCH), 3.16 (td, *J* = 7.0, 3.0 Hz, 1 H, SCH)	
Et, Et **5**	2.97 (ddd, *J* = 8.0, 4.5, 3.0 Hz, 1 H, SCH or NCH), 3.12 (ddd, *J* = 8.5, 6.5, 3.0 Hz, 1 H, NCH or SCH)	
n-Pr, *n*-Pr **3b/c**	2.51 (ddd, *J* = 7.0, 7.0, 2.0 Hz, 1 H, SCH), 3.06 (ddd, *J* = 10.0, 2.0, 2.0 Hz, 1 H, NCHPr)	
	Sulfonium Salts (CHS/CHN)	
-$(CH_2)_4$- **21 (**major)	2.59 (ddd, *J* = 10.5, 10.5, 4.0 Hz, 1 H, NC*H*CH or SCH), 3.25–3.33 (m, 2 H, C*H*, CH*H*)	
n-Pr, *n*-Pr **27**	2:1 Mixture of diastereomers. Relevant peaks not assigned.	
Et, Et, **22** (Ph)	2.93 (ddd, *J* = 11.0, 3.5, 3.5 Hz, 1H, CHEt), 3.91 (ddd, *J* = 11.0, 3.5, 3.5 Hz, 1H, CHEt)	
Et, Et **23** (Ph)	3.55 (ddd, *J* = 10.0, 5.5, 3.0 Hz, 1 H, CHEt), 3.92 (ddd, *J* = 11.0, 3.5, 3.5 Hz, 1 H, CHEt)	
Et, Et, **24** (C_6H_4Cl)	3.56 (ddd, *J* = 9.0, 5.5, 3.0 Hz, 1 H, CHEt), 3.93 (ddd, *J* = 11.0, 3.5, 3.0 Hz, 1 H, CHEt)	
Et, Et, **25** (*p*-MeC_6H_4)	3.55 (ddd, *J* = 9.0, 5.5, 3.0 Hz, 1 H, CHEt), 3.91 (ddd, *J* = 11.0, 3.5, 3.0 Hz, 1 H, CHEt)	

General Experimental Methods.

Anhydrous CH_2Cl_2, diethyl ether, and acetonitrile were obtained from a purification column composed of activated alumina (A-2); for CH_2Cl_2 a supported copper catalyst (Q-5 reactant) was also employed.[6] Chromatography: Flash chromatography was performed on silica gel (Merck Kieselgel 60 F_{254} 230-400 mesh). Infra red spectra were recorded on the neat compounds using an ATR sampling accessory on an FTIR spectrometer unless indicated otherwise. The units of the specific rotation, (deg mL)/(g dm), are implicit and are not included with the reported value. Appropriate 2D spectra are provided where 2D NMR experiments were used in the assignment of NMR spectra.

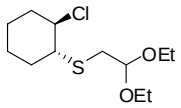
General procedure 1: preparation of aminoacetals 11b,c– 13b,c



7

A stirred solution of the disulfide **7**[7] (2.98 g, 10.0 mmol) in dry dichloromethane (50 ml) was cooled to –78 °C and sulfuryl chloride (0.88 ml, 11 mmol) was added slowly.[8] The reaction mixture was stirred for 15 min at –78 °C before the appropriate alkene (40.0 mmol) was added in one portion. The reaction mixture was stirred for a further 15 min at –78 °C and then warmed to rt. The solvent was evaporated under reduced pressure and the resulting crude β-chlorosulfide was purified by filtration through a plug of aluminium oxide (neutral, Brockmann I, standard grade) with diethyl ether/petrol ether 1:4 as eluent. The β-chlorosulfides **11a–13a** thus obtained were characterized by ^{1}H NMR and used in the next step without further purification, because they are somewhat unstable and potentially hazardous (**Caution!**).

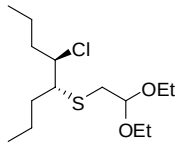
(±)-*trans*-1-Chloro-2-[(2,2-diethoxyethyl)sulfanyl]cyclohexane (11a)



11a

Cyclohexene (4.05 ml, 40.0 mmol) gave **11a** as an oil (4.00 g, 75% yield). ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.23 (t, *J* = 7.0 Hz, 6 H, $2CH_3$), 1.24–1.81 (m, 6 H), 2.20–2.38 (m, 2 H), 2.79 (dd, *J* = 13.5, 5.5 Hz, 1 H, SCH*H*), 2.85 (dd, *J* = 13.5, 5.5 Hz, 1 H, SC*H*H), 3.03 (ddd, *J* = 7.5, 7.5, 4.5 Hz, 1 H, SCH), 3.49–3.75 (m, 4 H, $2OCH_2$), 4.07 (ddd, *J* = 7.5, 7.5, 4.5 Hz, 1 H, CHCl), 4.62 (t, *J* = 5.5 Hz, 1 H, $CH(OEt)_2$).

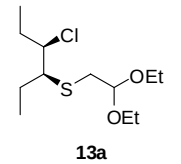
(±)-(4*R,5*R**)-4-Chloro-5-[(2,2-diethoxyethyl)sulfanyl]octane (12a)**



12a

cis-*n*-Oct-4-ene (6.23 ml, 40.0 mmol) gave **12a** as an oil (3.44 g, 58% yield). ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.95 (t, *J* = 7.0 Hz, 6 H, $2CH_3$), 1.23 (t, *J* = 7.0 Hz, 6 H, $2OCH_2CH_3$), 1.20–2.04 (m, 8 H), 2.70 (dd, *J* = 13.5, 5.5 Hz, 1 H, SC*H*H), 2.77 (dd, *J* = 13.5, 5.5 Hz, 1 H, SCH*H*), 3.01 (ddd, *J* = 10.0, 4.0, 3.0 Hz, 1 H, CHS), 3.44–3.73 (m, 4 H, $2OCH_2$), 4.15 (ddd, *J* = 10.0, 3.0, 3.0 Hz, 1 H, CHCl), 4.59 (t, *J* = 5.5 Hz, 1 H, $CH(OEt)_2$).

(±)-(3*R,4*S**)-3-Chloro-4-[(2,2-diethoxyethyl)sulfanyl]hexane (13a)**



13a

trans-Hex-3-ene (4.97 ml, 40.0 mmol) gave **13a** as an oil (3.71 g, 69% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.06 (t, *J* = 7.0 Hz, 3 H, CH_3), 1.07 (t, *J* = 7.0 Hz, 3 H, CH_3), 1.22 (t, *J* = 7.0 Hz, 6 H, 2 × OCH_2CH_3), 1.52 (m, 1 H), 1.76–1.91 (m, 2 H), 1.93–2.03 (m, 1 H), 2.73 (dd, *J* = 13.5, 5.5 Hz, 1 H,

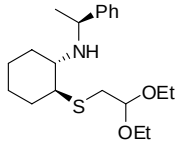
SC*H*H), 2.78 (dd, *J* = 13.5, 5.5 Hz, 1 H, SCH*H*), 2.89 (ddd, *J* = 9.0, 5.5, 3.5 Hz, 1 H, SCH), 3.51–3.73 (m, 4 H, 2 × OCH_2), 4.00 (ddd, *J* = 9.0, 5.5, 3.5 Hz, 1 H, CHCl), 4.59 (t, *J* = 5.5 Hz, 1 H, $CH(OEt)_2$).

(*S*)-α-Phenylethylamine (1.34 g, 10.5 mmol) and K_2CO_3 (1.45 g, 10.5 mmol) were added to a stirred solution of β-chlorosulfide (7.00 mmol) in dry acetonitrile (20 ml). The reaction mixture was stirred at reflux for 15 h. It was then cooled to rt, the inorganic solids were filtered off and the solvent was removed under reduced pressure. The aminoacetals **11b,c–13b,c** were obtained as diastereomeric mixtures in all cases (dr 1:1 by ^{1}H NMR of the crude products). The diastereomeric products were separated by flash chromatography as specified below and obtained as colorless oils.

(1*S*,2*S*)-2-[(2,2-Diethoxyethyl)sulfanyl]-*N*-[(1*S*)-1-phenylethyl]cyclohexanamine 11b and (1*R*,2*R*)-2-[(2,2-Diethoxyethyl)sulfanyl]-*N*-[(1*S*)-1-phenylethyl]cyclohexanamine 11c

11a (1.87 g, 7.01 mmol) gave **11b** as an oil (1.18 g, 48% yield) and **11c** as an oil (1.05 g, 43% yield). Separation of the diastereomers was achieved by flash chromatography (silica; EtOAc/PE gradient 1:6 to 1:3 to 1:1).

(1*S*,2*S*)-2-[(2,2-Diethoxyethyl)sulfanyl]-*N*-[(1*S*)-1-phenylethyl]cyclohexanamine (11b)

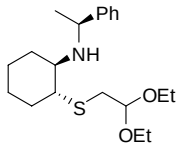


11b

R_f (EtOAc/PE 1:1) 0.52; $[\alpha]_D^{21}$ +52.0 (*c* 1.14, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.05–1.27 (m, 3 H), 1.23 (t, *J* = 7.0 Hz, 6 H, $2OCH_2CH_3$), 1.35 (d, *J* = 7.0 Hz, 3 H, $NCHCH_3$), 1.44–1.48 (m, 1 H), 1.54–1.57 (m, 1 H), 1.63–1.67 (m, 1 H), 1.73–1.79 (m, 1 H), 2.09–2.13 (m, 2 H), 2.40 (ddd, *J* = 10.0, 10.0, 4.0 Hz, 1 H, SCH or NCH), 2.58 (ddd, *J* = 11.0, 10.0, 4.0 Hz, 1 H, SCH or NCH), 2.76 (d, *J* = 5.5 Hz, 2 H, SCH_2), 3.51–3.60 (m, 2 H, OCHH), 3.64–3.72 (m, 2 H, OCHH), 3.83 (q, *J* = 7.0 Hz, 1 H, PhCH), 4.61 (t, *J* = 5.5 Hz, 1 H, $CH(OEt)_2$), 7.18–7.36 (m, 5 H, ArH); ^{13}C NMR (68 MHz, $CDCl_3$) δ 15.3 (2 × CH_3), 24.1 (CH_3), 24.4 (CH_2), 25.9 (CH_2), 33.4 (2 × CH_2), 33.6 (CH_2), 51.0 (CH), 56.8 (CH), 59.1 (CH), 61.8 (CH_2),

61.9 (CH_2), 102.9 (CH), 126.5 (3 × CH), 128.2 (2 × CH), 147.2 (C); IR ν_{max}/cm^{-1} 2926, 1446, 1054, 1008, 760; MS (CI) *m/z* (%) 352 ($M+H^+$, 100), 306 (55), 202 (35), 185 (40), 120 (50); HRMS (CI): found 352.2319; $C_{20}H_{34}NO_2S$ ($M+H^+$) requires 352.2310.

(1*R*,2*R*)-2-[(2,2-Diethoxyethyl)sulfanyl]-*N*-[(1*S*)-1-phenylethyl]cyclohexanamine (11c)

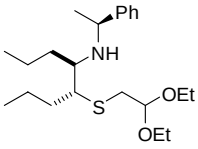


11c

R_f (EtOAc/PE 1:1) 0.29; $[\alpha]_D^{21}$ –50.6 (*c* 0.87, $CHCl_3$); ^1H NMR (270 MHz, $CDCl_3$) δ 1.04–1.35 (m, 4 H), 1.21 (t, *J* = 7.0 Hz, 3 H, OCH_2CH_3), 1.23 (t, *J* = 7.0 Hz, 3 H, OCH_2CH_3), 1.36 (d, *J* = 7.0 Hz, 3 H, $NCHCH_3$), 1.58–1.70 (m, 2 H), 1.98–2.18 (m, 3 H), 2.50 (ddd, *J* = 11.5, 11.5, 4.0 Hz, 1 H, SCH or NCH), 2.54 (dd, *J* = 13.0, 5.5 Hz, 1 H, SCH*H*), 2.61 (dd, *J* = 13.0, 5.5 Hz, 1 H, SC*H*H), 2.66 (br s, 1 H, NH), 3.40–3.57 (m, 2 H, OCHH), 3.60–3.71 (m, 2 H, OCHH), 3.90 (q, *J* = 7.0 Hz, 1 H, CHPh), 4.56 (t, *J* = 5.5 Hz, 1 H, $CH(OEt)_2$), 7.21–7.36 (m, 5 H, ArH); ^{13}C NMR (68 MHz, $CDCl_3$) δ 15.2 (2 × CH_3), 24.2 (CH_2), 25.1 (CH_3), 26.4 (CH_2), 31.8 (CH_2), 32.6 (CH_2), 33.5 (CH_2), 51.0 (CH), 54.0 (CH), 55.5 (CH), 61.4 (CH_2), 61.9 (CH_2), 102.5 (CH), 126.4 (2 × CH), 126.7 (CH), 128.4 (2 × CH), 145.2 (C); IR ν_{max}/cm^{-1} 2927, 1447, 1054, 761; MS (CI) *m/z* (%) 352 ($M+H^+$, 100), 306 (50), 202 (35), 185 (40), 120 (45); HRMS (CI): found 352.2313, $C_{20}H_{34}NO_2S$ ($M+H^+$) requires 352.2310; Anal. Calc'd for $C_{20}H_{33}NO_2S$: C, 68.33; H, 9.46; N, 3.98; found: C, 68.36; H, 9.58; N, 3.90.

(4*R*,5*R*)-5-[(2,2-Diethoxyethyl)sulfanyl]-*N*-[(1*S*)-1-phenylethyl]-4-octanamine and (4*S*,5*S*)-5-[(2,2-diethoxyethyl)sulfanyl]-*N*-[(1*S*)-1-phenylethyl]-4-octanamine, 12b/c

12a (2.07 g, 6.97 mmol) gave two diastereomers **12b/c-diastereomer 1** as an oil (0.96 g, 36% yield) and **12b/c-diastereomer 2** as an oil (1.04 g, 39% yield). Separation of the diastereomers was achieved by flash chromatography (Silica; Et_2O/PE gradient 1:15 to 1:10 to 1:3).



12b/c

12b/c-diastereomer 1

R_f (Et_2O/PE 1:5) 0.60; $[\alpha]_D^{22}$ –83.5 (*c* 0.46, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.78 (t, *J* = 7.0 Hz, 3 H, $(CH_2)_2CH_3$)), 0.95 (t, *J* = 7.0 Hz, 3 H, $(CH_2)_2CH_3$)), 1.05–1.72 (m, 9 H, 4 × CH_2, NH), 1.19 (t, *J* = 7.0 Hz, 3 H, OCH_2CH_3), 1.22 (t, *J* = 7.0 Hz, 3 H, OCH_2CH_3), 1.30 (d, *J* = 6.5 Hz, 3 H, $NCHCH_3$), 2.44 (dd, *J* = 13.5, 5.0 Hz, 1 H, SC*H*H), 2.48 (ddd, *J* = 8.5, 3.0, 3.0 Hz, 1 H, SCH or PrC*H*N), 2.54 (dd, *J* = 13.5, 6.0 Hz, 1 H, SC*H*H), 2.88 (ddd, *J* = 10.0, 3.0, 3.0 Hz, 1 H, PrC*H*N or SCH), 3.43–3.51 (m, 2 H, 2 × OC*H*H), 3.56 (dq, *J* = 9.0, 7.0 Hz, 1 H, OC*H*H), 3.64 (dq, *J* = 9.0, 7.0 Hz, 1 H, OC*H*H), 3.85 (q, *J* = 6.5 Hz, 1 H, NC*H*Ph), 4.48 (dd, *J* = 6.0, 5.0 Hz, 1 H, $CH(OEt)_2$), 7.18–7.36 (m, 5 H, ArH); ^{13}C NMR (68 MHz, $CDCl_3$) δ 14.0 (CH_3), 14.1 (CH_3), 15.3 ($2CH_3$), 19.9 (CH_2), 21.2 (CH_2), 25.0 (CH_3), 31.9 (CH_2), 32.9 (CH_2), 34.8 (CH_2), 48.7 (CH), 55.1 (CH), 57.3 (CH), 61.2 (CH_2), 62.1 (CH_2), 103.2 (CH), 126.7 (2 CH), 126.8 (CH), 128.3 (2 CH), 146.1 (C); IR ν_{max}/cm^{-1} 2958, 1453, 1053, 761; MS (CI) *m/z* (%) 382 ($M+H^+$, 75), 264 (55), 176 (100); HRMS (CI): found 382.2780, $C_{22}H_{40}NO_2S$ ($M+H^+$) requires 382.2780.

12b/c-diastereomer 2

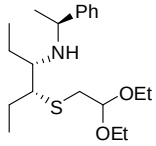
R_f (Et_2O/PE 1:5) 0.51; $[\alpha]_D^{22}$ –7.0 (*c* 0.71, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.78 (t, *J* = 7.0 Hz, 3 H, $(CH_2)_2CH_3$)), 0.91 (t, *J* = 7.0 Hz, 3 H, $(CH_2)_2CH_3$)), 1.18–1.78 (m, 8 H, 4 × CH_2), 1.20_9 (t, *J* = 7.0 Hz, 3 H, OCH_2CH_3), 1.21_4 (t, *J* = 7.0 Hz, 3 H, OCH_2CH_3), 1.31 (d, *J* = 6.5 Hz, 3 H, $NCHCH_3$), 2.44 (ddd, *J* = 6.0, 6.0, 3.0 Hz, 1 H, NCH or SCH), 2.48–2.55 (m, 1 H, NCH or SCH), 2.57 (d, *J* = 5.5 Hz, 2 H, SCH_2), 3.44–3.70 (m, 5 H, 4 × OC*H*H and NH), 3.83 (q, *J* = 6.5 Hz, 1 H, NCHPh), 4.5 (t, *J* = 5.5 Hz, 1 H, $CH(OEt)_2$), 7.15–7.38 (m, 5 H, ArH); ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.9 (CH_3), 14.3 (CH_3), 15.3 (2 CH_3), 19.7 (CH_2), 20.7 (CH_2), 24.9 (CH_3), 33.3 (CH_2), 33.7 (CH_2), 34.9 (CH_2), 50.7 (CH), 56.2 (CH), 57.6 (CH), 61.5 (CH_2), 61.8 (CH_2), 102.9 (CH), 126.7 (CH), 127.0 (2 CH), 128.1 (2 CH), 146.4 (C); IR

ν_{max}/cm^{-1} 2958, 1453, 1054, 761; MS (CI) *m/z* (%) 382 (M+H$^+$, 90), 232 (50), 176 (100); Anal. Calc'd for $C_{22}H_{39}NO_2S$: C, 69.24; H, 10.30; N, 3.67; found: C, 69.17; H, 10.39; N, 3.62.

(3*S*,4*R*)-4-[(2,2-Diethoxyethyl)sulfanyl]-*N*-[(1*S*)-1-phenylethyl]-3-hexanamine 13b and (3*R*,4*S*)-4-[(2,2-Diethoxyethyl)sulfanyl]-*N*-[(1*S*)-1-phenylethyl]-3-hexanamine 13c

13a (1.88 g, 6.99 mmol) gave **13b** as an oil (0.96 g, 39% yield) and **13c** as an oil (0.99 g, 40% yield). Separation of the diastereomers was achieved by flash chromatography (Silica; Et_2O/PE gradient 1:6 to 1:4 to 1:2).

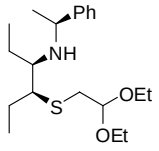
(3*S*,4*R*)-4-[(2,2-Diethoxyethyl)sulfanyl]-*N*-[(1*S*)-1-phenylethyl]-3-hexanamine 13b



13b

R_f (Et_2O/PE 1:5) 0.26; $[\alpha]_D^{21}$ –69.1 (*c* 0.81, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.84 (t, *J* = 7.0 Hz, 3 H, $CHCH_2CH_3$), 0.90 (t, *J* = 7.0 Hz, 3 H, $CHCH_2CH_3$), 1.13–1.40 (m, 2 H, 2 × C*H*H), 1.23$_9$ (t, *J* = 7.0 Hz, 6 H, 2 × OCH_2CH_3), 1.24$_3$ (t, *J* = 7.0 Hz, 6 H, 2 × OCH_2CH_3), 1.33 (d, *J* = 7.0 Hz, 3 H, $NCHCH_3$),1.42–1.60 (m, 2 H, 2 × CH*H*), 1.60 (br s, 1 H, NH), 2.34 (ddd, *J* = 9.0, 3.0, 3.0 Hz, 1 H, SCH or EtCHN), 2.74 (dd, *J* = 13.5, 5.5 Hz, 1 H, SC*H*H), 2.82 (dd, *J* = 13.5, 5.5 Hz, 1 H, SCH*H*), 2.94 (ddd, *J* = 8.0, 7.0, 3.0 Hz, 1H, EtC*H*N or SCH), 3.53–3.62 (m, 2 H, 2 × OC*H*H), 3.65–3.75 (m, 2 H, 2 × OC*H*H), 3.88 (q, *J* = 7.0 Hz, 1 H, NCHPh), 4.63 (t, *J* = 5.5 Hz, 1 H, $CH(OEt)_2$), 7.19–7.39 (m, 5 H, ArH); ^{13}C NMR (68 MHz, $CDCl_3$) δ 11.4 (CH_3), 12.7 (CH_3), 15.3 (2 × CH_3), 23.5 (CH_2), 25.3 (CH_3), 26.5(CH_2), 35.7(CH_2), 52.2 (CH), 54.9 (CH), 58.6 (CH), 61.7 (CH_2), 61.8 (CH_2), 103.2 (CH), 126.7 (CH), 127.0 (2 × CH), 128.1 (2 × CH), 146.2 (C); IR ν_{max}/cm^{-1} 2929, 1452, 1370, 1054, 761; MS (CI) *m/z* (%) 354 (M+H$^+$, 60), 187 (60), 162 (100); Anal. Calc'd for $C_{20}H_{35}NO_2S$: C, 67.94; H, 9.98; N, 3.96; found: C, 67.84; H, 10.07; N, 3.81.

(3*R*,4*S*)-4-[(2,2-Diethoxyethyl)sulfanyl]-*N*-[(1*S*)-1-phenylethyl]-3-hexanamine 13c



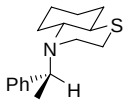
13c

R_f (Et_2O/PE 1:5) 0.07; $[\alpha]_D^{21}$ –53.1 (*c* 0.81, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.86 (t, *J* = 7.0 Hz, 3 H, $CHCH_2CH_3$), 0.97 (t, *J* = 7.0 Hz, 3 H, $CHCH_2CH_3$), 1.17 (t, *J* = 7.0 Hz, 3 H, OCH_2CH_3), 1.18 (t, *J* = 7.0 Hz, 3 H, OCH_2CH_3), 1.33 (d, *J* = 7.0 Hz, 3 H, $CHCH_3$), 1.35–1.58 (m, 3 H, 3 × C*H*H), 1.60–1.72 (m, 1 H, CH*H*), 1.73 (br s, 1 H, NH), 2.40 (dd, *J* = 13.5, 5.5 Hz, 1 H, SCH*H*), 2.38–2.45 (m, 1 H, SCH or NCHEt), 2.44 (dd, *J* = 13.5, 5.5 Hz, 1 H, SC*H*H), 2.70 (ddd, *J* = 9.5, 5.0, 3.5 Hz, 1H, SCH or NCHEt), 3.42–3.50 (m, 2 H, 2 × OC*H*H), 3.53–3.64 (m, 2 H, 2 × OCH*H*), 3.84 (q, *J* = 7.0 Hz, 1 H, NC*H*Ph), 4.49 (t, *J* = 5.5 Hz, 1 H, $CH(OEt)_2$), 7.18–7.38 (m, 5 H, ArH); ^{13}C NMR (68 MHz, $CDCl_3$) δ 10.8 (CH_3), 12.7 (CH_3), 15.19 (CH_3), 15.24 (CH_3), 23.1 (CH_2), 23.8 (CH_2), 24.4 (CH_3), 34.6 (CH_2), 52.5 (CH), 55.3 (CH), 57.5 (CH), 61.4 (CH_2), 61.8 (CH_2), 103.0 (CH), 126.7 (3CH), 128.2 (2CH), 146.0 (C); IR ν_{max}/cm^{-1} 2969, 1453, 1122, 1053, 761; MS (CI) *m/z* (%) 254 ($M+H^+$, 60), 187 (60), 162 (100); Anal. Calc'd for $C_{20}H_{35}NO_2S$: C, 67.94; H, 9.98; N, 3.96; found: C, 68.17; H, 9.99; N, 3.73.

General procedure 2: reductive amination[9]

The appropriate aminoacetal **11b,c–13b,c** (10.0 mmol) was dissolved in aqueous HCl solution (1.5 M, 140 ml) und the reaction mixture was stirred for 10 min at rt before addition of aqueous NaOH solution (3 M, 85 ml). The reaction mixture was extracted with diethyl ether (3 × 75 ml), the combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated in vacuo. The residue was dissolved in dry 1,2-dichloroethane (60 ml) and $NaBH(OAc)_3$ (3.39 g, 16.0 mmol) and glacial acetic acid (0.92 ml, 16.0 mmol) were successively added. The reaction mixture was stirred for 1 h at rt. The reaction was stopped by addition of aqueous NaOH solution (1 M, 40 ml). The organic phase was separated and the aqueous layer was extracted with diethyl ether (2 × 30 ml). The combined organic phases were washed with brine, dried over $MgSO_4$ and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography as specified in each case.

(4a*R*,8a*R*)-4-[(1*S*)-1-Phenylethyl]octahydro-2*H*-1,4-benzothiazine (2c)

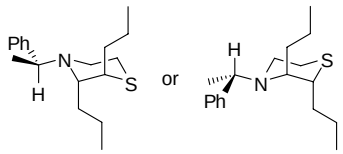


2c

11c (3.52 g, 10.0 mmol) gave **2c** as a colorless solid (0.81 g, 31%). Purification by flash chromatography (Silica; EtOAc/PE 1:6); R_f (EtOAc/PE 1:3) 0.30; m.p. 59–60 °C (petroleum ether); $[\alpha]_D^{20}$ –109.3 (*c* 0.49, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.11–1.37 (m, 4 H, 2 × CH_2), 1.44 (d, *J* = 7.0 Hz, 3 H, CH_3), 1.60–1.87 (m, 3 H, 3 × CH*H*), 2.26 (ddd, *J* = 12.0, 9.0, 3.5 Hz, 1 H, NCH_{ax}), 2.33 (ddd, *J* = 12.5, 12.5, 2.0 Hz, 1 H, NCHH_{ax}), 2.42 (ddd, *J* = 12.5, 3.0, 2.0 Hz, 1 H, SCH_{eq}H), 2.42–2.50 (m, 1 H, CH*H*), 2.72 (ddd, *J* = 12.0, 9.0, 3.5 Hz, 1 H, SCH_{ax}), 2.90 (ddd, *J* = 12.5, 12.5, 3.0 Hz, 1 H, SCHH_{ax}), 3.34 (ddd, *J* = 12.5, 3.0, 3.0 Hz, 1 H, NCHH_{eq}), 4.45 (q, *J* = 7.0 Hz, 1 H, NCHPh), 7.21–7.33 (m, 5 H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.1 (CH_3), 25.6 (CH_2), 26.0 (CH_2), 29.1 (CH_2), 30.8 (CH_2), 32.1 (CH_2), 45.6 (CH), 49.1 (CH_2), 54.7 (CH), 65.8 (CH), 126.6 (CH), 127.8 (2 × CH), 127.9 (2 × CH), 141.2 (C); IR ν_{max}/cm^{-1}

2918, 1449, 1021, 772; MS (EI) *m/z* (%) 261 (M^+, 65), 246 (25), 105 (80), 84 (100); Anal. Calc'd for $C_{16}H_{23}NS$: C, 73.51; H, 8.87; N, 5.36; found: C, 73.74; H, 9.05; N, 5.20.

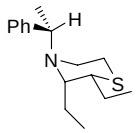
(2*R*,3*R*)-4-[(1*S*)-1-Phenylethyl]-2,3-dipropylthiomorpholine or (2*S*,3*S*)-4-[(1*S*)-1-phenylethyl]-2,3-dipropylthiomorpholine (3b/c; 3-d1)



3b **3c**

In variation to the general procedure the condensation to the intermediate enamine was achieved by stirring the aminoacetal **12b/c-diastereomer 1** (3.82 g, 10.0 mmol) for 45 min at rt in 1.5 M aqueous HCl solution/dioxane 3:2 before addition of aqueous NaOH solution and continuing as described in the general procedure; purification by flash chromatography (Silica; Et_2O/PE 1:20) gave **3b/c (3-d1)** as a colorless oil (2.04 g, 70% yield); R_f (Et_2O/PE 1:5) 0.33; $[\alpha]_D^{23}$ –36.3 (*c* 1.07, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.98 (t, *J* = 7.0 Hz, 3 H, CH_2CH_3), 0.99 (t, *J* = 7.0 Hz, 3 H, CH_2CH_3), 1.18–1.60 (m, 5 H, 5 × CH*H*), 1.21 (d, *J* = 7.0 Hz, 3 H, $CHCH_3$),1.91–2.00 (m, 1 H, C*H*H), 2.00 (ddd, *J* = 12.5, 3.0, 3.0 Hz, 1 H, $SCH_{eq}H$), 2.09–2.23 (m, 2 H, 2 × CH*H*), 2.46 (ddd, *J* = 12.5, 3.5, 3.5 Hz, 1 H, $NCHH_{eq}$), 2.51 (ddd, *J* = 7.0, 7.0, 2.0 Hz, 1 H, SCH), 2.59 (ddd, *J* = 12.5, 12.5, 2.5 Hz, 1 H, $NCH_{ax}H$), 2.80 (ddd, *J* = 12.5, 12.5, 3.5 Hz, 1 H, $SCHH_{ax}$), 3.06 (ddd, *J* = 10.0, 2.0, 2.0 Hz, 1 H, NCHPr), 3.54 (q, *J* = 7.0 Hz, 1 H, NCHPh), 7.19–7.38 (m, 5 H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0 (CH_3), 14.5 (CH_3), 20.5 (CH_2), 21.2 (CH_2), 21.7 (CH_3), 23.6 (CH_2), 25.6 (CH_2), 35.9 (CH_2), 41.4 (CH), 45.3 (CH_2), 56.7 (CH), 61.4 (CH), 126.6 (CH), 127.1 (2 × CH), 128.3 (2 × CH), 147.6 (C); IR ν_{max}/cm^{-1} 2955, 1452, 918, 762; MS (EI) *m/z* (%) 291 (M^+, 5), 248 (10), 202 (10), 188 (10), 144 (10), 105 (100); Anal. Calc'd for $C_{18}H_{29}NS$: C, 74.17; H, 10.03; N, 4.81; found: C, 74.26; H, 10.03; N, 4.82.

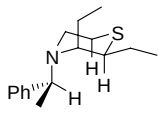
(2*R*,3*S*)-2,3-Diethyl-4-[(1*S*)-1-phenylethyl]thiomorpholine (4)



4

After purification by flash chromatography (Silica; Et_2O/PE 1:20) (**13b**) (3.54 g, 10.0 mmol) gave **4** (1.90 g, 72% yield) which solidified upon storage in the fridge; R_f (Et_2O/PE 1:20) 0.51; m.p. 40–41 °C; $[\alpha]_D^{23}$ +12.0 (*c* 1.16, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.86 (t, *J* = 7.0 Hz, 3 H, CH_2CH_3), 0.88 (t, *J* = 7.0 Hz, 3 H, CH_2CH_3),1.28 (d, *J* = 6.5 Hz, 3 H, $CHCH_3$), 1.27–1.45 (m, 3 H, 3 × C*H*H), 1.84–1.95 (m, 1 H, CH*H*), 2.10 (ddd, *J* = 12.0, 2.5, 2.5 Hz, 1 H, CHH_{eq}), 2.70 (ddd, *J* = 8.0, 5.5, 3.0 Hz, 1 H, NCH), 2.81 (ddd, *J* = 12.0, 12.0, 2.5 Hz, 1 H, CHH_{ax}), 2.88 (ddd, *J* = 12.0, 12.0, 2.5 Hz, 1 H, CHH_{ax}), 2.96 (ddd, *J* = 12.0, 2.5, 2.5 Hz, 1 H, CHH_{eq}), 3.16 (td, *J* = 7.0, 3.0 Hz, 1 H, SCH), 3.97 (q, *J* = 6.5 Hz, 1 H, NC*H*Me), 7.17–7.31 (m, 5 H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.8 (CH_3), 11.9 (CH_3), 16.9 (CH_2), 21.3 (CH_3), 24.7 (CH_2), 25.5 (CH_2), 42.8 (CH + CH_2), 58.4 (CH), 58.8 (CH), 126.7 (CH), 127.3 (2 × CH), 128.3 (2 × CH), 146.7 (C); IR ν_{max}/cm^{-1} 2963, 1451, 766; MS (EI) *m/z* (%) 263 (M^+, 5), 234 (10), 188 (13), 105 (100); HRMS (EI): found 263.1707; $C_{16}H_{25}NS$ requires 263.1708.

(2*S*,3*R*)-2,3-Diethyl-4-[(1*S*)-1-phenylethyl]thiomorpholine (5)



5

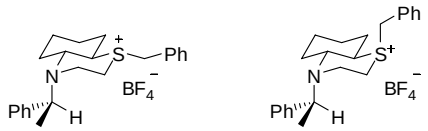
After purification by flash chromatography (Silica; EtOAc/PE 1:50) **13c** (3.54 g, 10.0 mmol) gave **5** (1.92 g, 73% yield) which solidified upon storage in the fridge; R_f (Et_2O/PE 1:20) 0.24; m.p. 28–29 °C; $[\alpha]_D^{23}$ –57.3 (*c* 1.10, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, *J* = 7.5 Hz, 3 H, CH_2CH_3), 0.89 (t, *J* = 7.5 Hz, 3 H, CH_2CH_3), 1.20 (d, *J* = 6.5 Hz, 3 H, $CHCH_3$), 1.22–1.34 (m, 2 H, 2 × C*H*H), 1.34–1.53 (m, 1 H, CH*H*), 1.92 (ddd, *J* = 13.0, 3.0, 3.0 Hz, 1 H, $CH_{eq}H$), 1.92–2.06 (m, 1 H), 2.63 (ddd, *J* = 13.0, 3.0, 3.0 Hz, 1 H, $CH_{eq}H$), 2.77 (ddd, *J* = 13.0, 13.0, 3.0 Hz, 1 H, CHH_{ax}), 2.89 (ddd, *J* = 8.0, 4.5, 3.0 Hz, 1 H, SCH or NCH), 2.94 (ddd, *J* = 13.0, 13.0, 3.0 Hz, 1 H, CHH_{ax}), 3.04 (ddd, *J* = 8.5, 6.5, 3.0 Hz, 1 H, NCH

or SCH), 4.01 (q, J = 6.5 Hz, 1 H, NCHMe), 7.10–7.30 (m, 5 H, ArH); ^{13}C NMR (68 MHz, $CDCl_3$) δ 11.9 (CH_3), 12.0 (CH_3), 16.6 (CH_2), 22.5 (CH_3), 23.5 (CH_2), 25.8 (CH_2), 41.4 (CH_2), 41.9 (CH), 57.4 (CH), 57.9 (CH), 126.7 (CH), 127.0 (2 × CH), 128.4 (2 × CH), 146.9 (C); IR ν_{max}/cm^{-1} 2966, 1453, 916, 768; MS (EI) *m/z* (%) 263 (M^+, 5), 234 (10), 188 (10), 105 (100); Anal. Calc'd for $C_{16}H_{25}NS$: C, 72.95; H, 9.57; N, 5.32; found: C, 73.31; H, 9.81; N, 5.29.

General procedure 3: preparation of sulfonium salts 21– 25

The appropriate aminosulfide **2c–5** (1.00 mmol) was dissolved in dichloromethane (1.0 ml), then benzyl bromide (0.59 ml, 5.0 mmol) and a solution of sodium tetrafluoroborate (0.55 g, 5.0 mmol) in water (1.0 ml) were added. The resulting biphasic mixture was rapidly stirred at rt for 2 d. Water (5 ml) and dichloromethane (10 ml) were added and the layers were separated. The aqueous layer was extracted with dichloromethane (3 × 10 ml). The combined organic phases were dried over $MgSO_4$ and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (Silica; EtOAc/PE gradient 1:1 to MeOH/CH_2Cl_2 1:9).

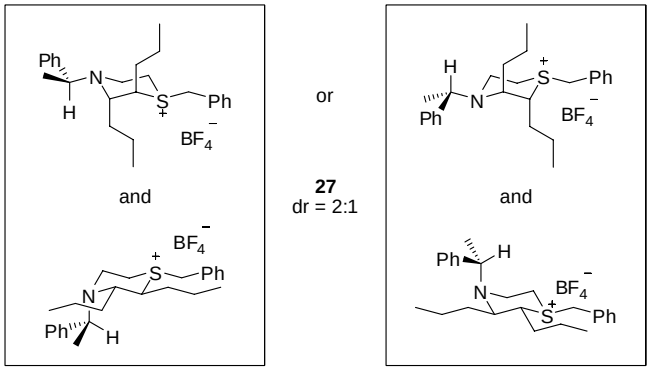
(1*R*,4a*R*,8a*R*)-1-Benzyl-4-[(1*S*)-1-phenylethyl]octahydro-2*H*-1,4-benzothiazin-1-ium tetrafluoroborate 21a and **(1*S*,4a*R*,8a*R*)-1-benzyl-4-[(1*S*)-1-phenylethyl]octahydro-2*H*-1,4-benzothiazin-1-ium tetrafluoroborate 21b**



Aminosulfide **2c** (0.261 g, 0.998 mmol) gave **21** as a mixture of diastereomers as a green foam (0.351 g, 80% yield) (d.r. 14:1 – determined by integration of the signals for the SC*H*$_2$Ph groups in the ^{1}H NMR spectrum); R_f (CH_2Cl_2/MeOH 9:1) 0.45; m.p. 75–78 °C (CH_2Cl_2); $[\alpha]_D^{22}$ –104.1 (*c* 0.49, $CHCl_3$); **21a major diastereomer**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.18–1.54 (m, 4 H), 1.37 (d, *J* = 7.0 Hz, 3 H, CHC*H*$_3$), 1.79–1.85 (m, 2 H), 2.17–2.21 (m, 1 H), 2.47 (ddd, *J* = 12.0, 12.0, 2.0 Hz, 1 H, C*H*$_{ax}$H), 2.46–2.51 (m, 1 H, CH*H*), 2.59 (ddd, *J* = 10.5, 10.5, 4.0 Hz, 1 H, NC*H*CH or SCH), 3.12 (ddd, *J* = 12.0, 12.0, 3.0 Hz, 1 H, C*H*H), 3.25–3.33 (m, 2 H, C*H*, CH*H*), 3.53 (ddd, *J* = 14.5, 4.5, 3.0 Hz, 1 H, CH*H*$_{eq}$), 4.35 (q, *J* = 7.0 Hz, 1 H, NC*H*Me), 4.71 (d, *J* = 13.5 Hz, 1 H, CH*H*Ph), 4.80 (d, *J* = 13.5 Hz, 1 H, C*H*HPh), 7.12–7.14 (m, 2 H, ArH), 7.22–7.47 (m, 8 H, ArH); **21b minor diastereomer**: δ 4.49 (d, *J* = 13.5 Hz, 1 H, CH*H*Ph) 4.60 (d, *J* = 13.5 Hz, 1 H, C*H*HPh)); **21a major diastereomer**: ^{13}C NMR (68 MHz, $CDCl_3$) δ

19.3 (CH_3), 24.2 (CH_2), 24.4 (CH_2), 28.0 (CH_2), 30.4 (CH_2), 35.8 (CH_2), 43.3 (CH_2), 44.1 (CH_2), 54.5 (CH), 54.6 (CH), 62.0 (CH), 126.3 (C), 127.2 (2 × CH), 127.3 (CH), 128.4 (2 × CH), 129.6 (2 × CH), 130.1 (CH), 130.9 (2 × CH), 140.1 (C); IR ν_{max}/cm^{-1} 2941, 1450, 1030, 912; MS (CI) *m/z* (%) 352 ([M-BF_4^-]$^+$, 5), 261 (60), 158 (60), 105 (100), 91 (90); HRMS (CI): found 352.2088; $C_{23}H_{30}NS$ ([M-BF_4^-]$^+$) requires 352.2099.

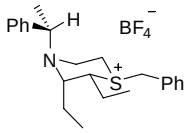
(1*R*,2*R*,3*R*) and (1*S*,2*R*,3*R*), or (1*S*,2*S*,3*S*) and (1*R*,2*S*,3*S*)-1-Benzyl-4-[(1*S*)-1-phenylethyl]-2,3-dipropylthiomorpholin-1-ium tetrafluoroborate (27)



Aminosulfide **3-d1** (0.292 g, 1.00 mmol) gave **27** as a 2:1 mixture of diastereomers, foam (0.329 g, 70%); R_f (CH_2Cl_2/MeOH 9:1) 0.46; m.p. 60–66 °C (CH_2Cl_2); $[\alpha]_D^{22}$ –42.7 (*c* 0.52, $CHCl_3$); d.r of 2:1 was determined by integration of the SC*H*$_2$Ph-group of each diastereomer in the ^{1}H NMR (400 MHz, $CDCl_3$); **major diasteromer**: δ 4.36 (d, *J* = 12.5 Hz, 1 H, C*H*HPh), 4.83 (d, *J* = 12.5 Hz, 1 H, CH*H*Ph); **minor diastereomer**: δ 4.57 (d, *J* = 12.5 Hz, 0.5 H, C*H*HPh), 4.66 (d, *J* = 12.5 Hz, 0.5 H, CH*H*Ph); ^{13}C NMR (68 MHz, $CDCl_3$) (mixture of diastereomers) δ 13.4 (CH_3), 13.5 (CH_3), 13.9 (CH_3), 13.9 (CH_3), 18.3 (CH_3), 18.9 (CH_2), 19.4(CH_2), 19.6 (CH_2), 19.9 (CH_2), 21.2 (CH_3), 25.8 (CH_2), 26.5 (CH_2), 31.2 (CH_2), 31.3 (CH_2), 34.1 (CH_2), 34.8 (CH_2), 39.6 (CH_2), 41.3 (CH_2), 42.1 (CH_2), 43.8 (CH_2), 48.8 (CH), 54.1 (CH), 56.3 (CH), 59.4 (CH), 61.0 (CH), 61.3 (CH), 126.8 (CH), 126.8$_4$ (C), 127.2 (CH), 127.5 (CH), 127.6 (CH), 128.2 (C), 128.6 (CH), 128.8 (CH), 129.4 (CH), 129.5 (CH), 129.6 (CH), 129.8 (CH), 130.4 (CH), 130.5 (CH), 142.8 (C), 144.3 (C); IR ν_{max}/cm^{-1} 2963, 1456, 1029, 765; MS (CI) *m/z* (%) 382 ([M–

$BF_4^-]^+$, 5), 292 (40), 188 (75), 105 (80), 91 (100); HRMS (CI): found 382.2554; $C_{25}H_{36}NS$ ($[M–BF_4^-]^+$) requires 382.2563.

(1*R*,2*R*,3*S*)-1-Benzyl-2,3-diethyl-4-[(1*S*)-1-phenylethyl]thiomorpholin-1-ium tetrafluoroborate (22)

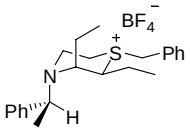


22

Aminosulfide **4** (0.263 g, 0.998 mmol) gave **22** as a beige solid (0.405 g, 92% yield); R_f (CH_2Cl_2/MeOH 9:1) 0.42; m.p. 190–192 °C (CH_2Cl_2); $[\alpha]_D^{22}$ –203.0 (*c* 1.01, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.67 (t, *J* = 7.0 Hz, 3 H, CH_2CH_3), 0.74 (t, *J* = 7.0 Hz, 3 H, CH_2CH_3), 1.26 (d, *J* = 6.5 Hz, 3H, $CHCH_3$), 1.28–1.65 (m, 3H, 3 × CH*H*Me), 1.81–1.93 (m, 1H, C*H*HMe), 2.73 (ddd, *J* = 12.0, 2.5, 2.5 Hz, 1H, $CH H_{eq}$), 2.93 (ddd, *J* = 11.0, 3.5, 3.5 Hz, 1H, CHEt), 3.13 (ddd, *J* = 16.0, 12.5, 2.0 Hz, 1H, $CH H_{ax}$), 3.42 (ddd, *J* = 12.5, 12.5, 3.0 Hz, 1H, $CH_{ax}H$), 3.53 (ddd, *J* = 16.0, 3.0, 3.0 Hz, 1H, $CH H_{eq}$), 3.91 (ddd, *J* = 11.0, 3.5, 3.5 Hz, 1H, CHEt), 4.17 (q, *J* = 6.5 Hz, 1H, C*H*Me), 4.74 (d, *J* = 13.0 Hz, 1H, C*H*HPh), 4.79 (d, *J* = 13.0 Hz, 1H, CH*H*Ph), 7.12–7.35 (m, 8H, ArH), 7.44–7.50 (m, 2H, ArH); ^{13}C NMR (68 MHz, $CDCl_3$) δ 9.6 (CH_3), 10.3 (CH_3), 18.5 (CH_2), 20.8 (CH_2), 21.5 (CH_3), 30.4 (CH_2), 37.3 (CH_2), 44.3 (CH_2), 49.9 (CH), 55.3 (CH), 56.6 (CH), 126.6 (C), 127.5 (3 × CH), 128.6 (2 × CH), 129.6 (2 × CH), 130.0 (CH), 130.8 (2 × CH), 144.0 (C); IR ν_{max}/cm^{-1} 2981, 1416, 1054, 1020, 768; MS (CI) *m/z* (%) 354 ($[M\text{-}BF_4^-]^+$, 10), 263 (55), 160 (55), 105 (100), 91 (96); HRMS (CI): found 354.2244; $C_{23}H_{32}NS$ ($[M\text{-}BF_4^-]^+$) requires 354.2250.

(1*S*,2*S*,3*R*)-1-Benzyl-2,3-diethyl-4-[(1*S*)-1-phenylethyl]thiomorpholin-1-ium tetrafluoroborate (23)

Crystals suitable for X-ray crystallography were grown by layering a chloroform solution of **23** with hexane and allowing slow diffusion.



23

Aminosulfide **5** (0.264 g, 1.00 mmol) gave **23** as a beige solid (0.367 g, 83%); R_f (CH_2Cl_2/MeOH 9:1) 0.40; m.p. 120–122 °C (CH_2Cl_2); $[\alpha]_D^{23}$ +116.1 (*c* 1.18, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.98 (t, *J* = 7.0 Hz, 3 H, CH_2CH_3), 1.02 (t, *J* = 7.5 Hz, 3 H CH_2CH_3), 1.22 (d, *J* = 6.5 Hz, 3 H, $CHCH_3$), 1.54–1.71 (m, 3 H, 3 × CH*H*Me), 1.92–2.06 (m, 1 H, C*H*HMe), 2.45 (br d, *J* = 12.0 Hz, 1 H, CH*H*), 2.84–2.93 (m, 2 H, 2 × C*H*H), 3.42 (ddd, *J* = 12.0, 8.0, 8.0 Hz, 1 H, CH*H*), 3.55 (ddd, *J* = 10.0, 5.5, 3.0 Hz, 1 H, CHEt), 3.92 (ddd, *J* = 11.0, 3.5, 3.5 Hz, 1 H, CHEt), 4.25 (q, *J* = 6.5 Hz, 1 H, CHMe), 4.72 (d, *J* = 13.0 Hz, 1 H, SCH*H*Ph), 4.77 (d, *J* = 13.0 Hz, 1 H, SCH*H*Ph), 7.10–7.33 (m, 8 H, ArH), 7.42–7.48 (m, 2 H, ArH); ^{13}C NMR (68 MHz, $CDCl_3$) δ 10.0 (CH_3), 11.0 (CH_3), 18.3 (CH_2), 21.1 (CH_2), 22.3 (CH_3), 30.1 (CH_2), 38.3 (CH_2), 44.6 (CH_2), 50.9 (CH), 54.2 (CH), 56.4 (CH), 126.5 (C), 127.0 (2 × CH), 127.3 (CH), 128.7 (2 × CH), 129.6 (2 × CH), 130.0 (CH), 130.7 (2 × CH), 144.8 (C); IR ν_{max}/cm^{-1} 2974, 1457, 1029, 773; MS (ESI) *m/z* (%) 354 ($[M\text{-}BF_4^-]^+$, 100), 250 (4), 215 (5), 118 (7); HRMS (ESI): found 354.2260; $C_{23}H_{32}NS$ ($[M\text{-}BF_4^-]^+$) requires 354.2250.

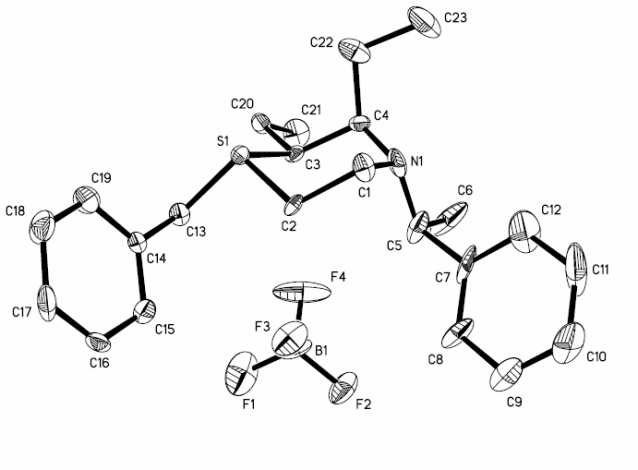
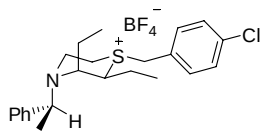


Figure 2 Solid state structure of 23. Thermal ellipsoids are drawn at the 50% probability level. Hydrogen atoms and cocrystallized dichloromethane solvent have been omitted for clarity.

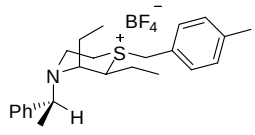
(1*S*,2*S*,3*R*)-1-(4-Chlorobenzyl)-2,3-diethyl-4-[(1*S*)-1-phenylethyl]thiomorpholin-1-ium tetrafluoroborate (24)



24

Aminosulfide **5** (0.264 g, 1.00 mmol) gave **24** as a beige solid (0.415 g, 87% yield); R_f (CH_2Cl_2/MeOH 9:1) 0.47; m.p. 170–171 °C (CH_2Cl_2); $[\alpha]_D^{21}$ +123.9 (*c* 1.24, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.99 (t, *J* = 7.0 Hz, 3 H, CH_2CH_3), 1.01 (t, *J* = 7.5 Hz, 3 H, CH_2CH_3), 1.23 (d, *J* = 6.5 Hz, 3 H, $CHCH_3$), 1.55–1.70 (m, 3 H, 3 × C*H*HMe), 1.91–2.02 (m, 1 H, CH*H*Me), 2.47 (ddd, *J* = 12.0, 2.5, 2.5 Hz, 1 H, CH*H*), 2.84–2.95 (m, 2 H, 2 × CH*H*), 3.42 (ddd, *J* = 12.0, 10.5, 6.0 Hz, 1 H, CH*H*), 3.56 (ddd, *J* = 9.0, 5.5, 3.0 Hz, 1 H, CHEt), 3.93 (ddd, *J* = 11.0, 3.5, 3.0 Hz, 1 H, CHEt), 4.28 (q, *J* = 6.5 Hz, 1 H, C*H*Me), 4.74 (s, 2 H, CH_2Ph), 7.13–7.31 (m, 7 H, ArH), 7.38–7.42 (m, 2 H, ArH); ^{13}C NMR (68 MHz, $CDCl_3$) δ 10.0 (CH_3), 11.0 (CH_3), 18.3 (CH_2), 21.2 (CH_2), 22.3 (CH_3), 30.4 (CH_2), 38.3 (CH_2), 44.0 (CH_2), 51.5 (CH), 54.4 (CH), 56.5 (CH), 125.3 (C), 127.0 (2 × CH), 127.4 (CH), 128.8 (2 × CH), 129.8 (2 × CH), 132.1 (2 × CH), 136.2 (C), 144.8 (C); IR ν_{max}/cm^{-1} 2978, 1494, 1031; MS (ESI) *m/z* (%) 391 (12), 390 ([M+2–BF_4^-)]$^+$, 37), 389 (30), 388 ([M–BF_4^-]$^+$, 100); HRMS (ESI): found 388.1874; $C_{23}H_{31}ClNS$ ([M-BF_4^-]$^+$) requires 388.1860.

(1*S*,2*S*,3*R*)-2,3-Diethyl-1-(4-methylbenzyl)-4-[(1*S*)-1-phenylethyl]thiomorpholin-1-ium tetrafluoroborate (25)



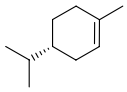
25

Aminosulfide **5** (0.265 g, 1.01 mmol) gave **25** as a beige solid (0.380 g, 83% yield); beige solid; R_f (CH_2Cl_2/MeOH 9:1) 0.53; m.p. 140–141 °C (CH_2Cl_2); $[\alpha]_D^{23}$ +160.4 (*c* 1.11, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.98 (t, *J* = 7.0 Hz, 3 H, CH_2CH_3), 1.03 (t, *J* = 7.5 Hz, 3 H, CH_2CH_3), 1.22 (d, *J* = 6.5 Hz, 3 H,

CHC*H*$_3$), 1.55–1.70 (m, 3 H, 3 × CH*H*Me), 1.94–2.05 (m, 1 H, C*H*HMe), 2.25 (s, 3 H, ArCH$_3$), 2.43 (ddd, *J* = 12.0, 2.5, 2.5 Hz, 1 H, CH*H*), 2.82–2.93 (m, 2 H, 2 × C*H*H), 3.40 (ddd, *J* = 12.0, 10.0, 6.5 Hz, 1 H, CH*H*), 3.55 (ddd, *J* = 9.0, 5.5, 3.0 Hz, 1 H, CHEt), 3.91 (ddd, *J* = 11.0, 3.5, 3.0 Hz, 1 H, CHEt), 4.25 (q, *J* = 6.5 Hz, 1 H, C*H*Me), 4.67 (d, *J* = 13.0 Hz, 1 H, C*H*HPh), 4.74 (d, *J* = 13.0 Hz, 1 H, CH*H*Ph), 7.07–7.23 (m, 5 H, ArH), 7.27–7.32 (m, 4 H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.0 (CH_3), 11.0 (CH_3), 18.3 (CH_2), 21.1 (CH_2), 21.2 (CH_3), 22.3 (CH_3), 30.1 (CH_2), 38.3 (CH_2), 44.5 (CH_2), 50.8 (CH), 54.3 (CH), 56.5 (CH), 123.2 (C), 127.0 (2 × CH), 127.3 (CH), 128.7 (2 × CH), 130.3 (2 × CH), 130.7 (2 × CH), 140.2 (C), 144.9 (C); IR ν_{max}/cm^{-1} 2971, 1453, 1054, 769; MS (CI) *m/z* (%) 368 ([M-BF_4^-]$^+$, 13), 263 (40), 160 (38), 105 (100); HRMS (CI): found 368.2415; $C_{24}H_{34}NS$ ([M-BF_4^-]$^+$) requires 368.2406.

Synthesis of aminosulfide 26

(*R*)-Menthene 15



15

A modification of the procedure described by Newhall was used.[10] *R*-limonene (5.0 g 0.037 mol, 99:1 er [Chiral GC: Supelco cyclodextrin-β column, 50 °C, major enantiomer R_t: 87.5 min, minor enantiomer R_t: 85.4 min]) was placed in a round-bottom flask equipped with a septum. PtO_2 (10 mg, 0.044 mmol) was added. Two balloons full of hydrogen were connected to the system and the solution was stirred at room temperature for approximately 8 h. The reaction was followed by ^{1}H NMR and when it was complete the solution was filtered through Celite. The resulting slightly impure oil (quantitative crude yield, contaminated with up to 15% over-reduced product – 1-isopropyl-4-methylcyclohexane) used in the next step without further purification (99:1 er; chiral GC: Supelco cyclodextrin-β column, 50 °C, major enantiomer R_t: 77.5 min, minor enantiomer R_t: 75.6). ^{1}H NMR (400 MHz, $CDCl_3$): 0.87 (d, 3H, J = 6.7 Hz, (C*H*$_3$)CHMe), 0.88 (d, 3H, J = 6.7 Hz, (C*H*$_3$)CHMe), 1.17–1.24 (m, 2H), 1.41–1.47 (m, 1H), 1.63 (s, 3H, C=CC*H*$_3$), 1.65-1.76 (m, 2H), 1.80–2.02 (m, 3H), 5.36-5.37 (m, 1H, CH=C) [lit.[11]]. ^{13}C NMR (67.5 MHz, $CDCl_3$): 19.8 (CH_3), 20.1 (CH_3), 23.6 (CH_3), 26.6 (CH_2), 29.0 (CH_2), 30.9 (CH_2), 32.4 (CH), 40.1 (CH), 121.1 (*C*H=C), 134.0 (CH=*C*). IR ν_{max}/cm^{-1} 2957, 2911, 2876, 1449, 1383, 1365, 908, 796; MS (EI) *m/z* (%) 138 (M^+, 21), 95 (75), 61 (100); HRMS (EI) $C_{10}H_{18}$ (M^+) requires: 139.1409; found: 139.1409.

(1*S*,2*S*,4*R*)-2-Iodo-4-isopropyl-1-isothiocyanato-1-methylcyclohexane 16 and **(1*S*,2*S*,4*R*)-1-iodo-4-isopropyl-2-isothiocyanato-1-methylcyclohexane 17**

16 2 : 1 **17**

The procedure of Woodgate and co-workers was used.[12] Lead (II) thiocyanate (11.34 g, 35.07 mmol) was placed under a nitrogen atmosphere in a Schlenk flask and protected from the light. Anhydrous benzene (80 ml) and then bromine (0.94 ml, 18 mmol) were added slowly. The solution was stirred at room temperature for 15 min. Iodine (4.00 g, 15.8 mmol) was placed in under a nitrogen atmosphere in another Schlenk flask protected from the light. The supernatant solution of thiocyanogen in benzene was transferred to the Schlenk flask containing the iodine, and the solution was stirred at room temperature for 15 min. Then menthene (3.60 g, 26.0 mmol) was added slowly, and the resulting solution was stirred for 16 h protected from the light, at room temperature. The reaction mixture was diluted with toluene (80 ml) and washed with water (100 ml), saturated aqueous $NaHSO_3$ solution (100 ml), saturated aqueous $NaHCO_3$ solution (100 ml) and finally brine (100 ml). The organic layer was dried with $MgSO_4$, filtered and evaporated. Column chromatography (silica gel; petroleum ether) of the crude material gave a 2:1 mixture of diastereoisomers **16** and **17** contaminated with an unidentified impurity, as a yellow oil (6.7 g, 80% combined crude yield). This material was used without further purification in the next step.

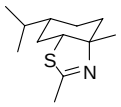
R_f: 0.52 (petroleum ether). ^{1}H NMR (400 MHz, $CDCl_3$): Major isomer **16** (characteristic peaks): 0.91 (d, 3H, J = 5.6 Hz, (C*H*$_3$)CHMe), 0.92 (d, 3 H, J = 5.6 Hz, (C*H*$_3$)CHMe), 1.58 (s, 3H, CH_3), 4.54 (dd, J = 5.6 Hz, J = 3.2 Hz, 1H, $CH_{eq}I$). Minor isomer **17** (characteristic peaks): 0.90 (d, 3H, J = 5.6 Hz, (C*H*$_3$)CHMe), 0.91 (d, 3 H, J = 5.6 Hz, (C*H*$_3$)CHMe), 2.18 (s, 3H, CH_3), 4.19 (ddd, J = 3.1 Hz, J = 3.1 Hz, J = 1.5 Hz, 1H, CH_{eq}NCS); IR ν_{max}/cm^{-1} (**16** + **17**): 2957, 2868, 2059 (NCS, broad, intense), 1451, 1435, 1369, 1173, 938.

Kugelrohr distillation (oven temperature 155 °C, 5 mm Hg) allowed the separation of the mixture of diastereomers from the unidentified impurity for further characterisation. Major isomer **16:** ^{13}C-NMR (75 MHz, $CDCl_3$) 19.9 (CH_3), 20.0 (CH_3), 25.1 (CH_2), 31.7 (CH_3/CH), 32.2 (CH_3/CH), 34.2 (CH_2), 36.6

(CH_2), 38.4 (CH), 39.3 (CH), 63.8 (C), 133.4 (NCS) Mixture of isomers: MS (CI) *m/z* (%): 265 ([M-SCN]$^+$, 39), 196([M-I]$^+$, 48), 137([M-HI-SCN]$^+$, 100); HRMS (CI) $C_{10}H_{18}I$ ([M-SCN]$^+$) requires: 265.0453; found: 265.0454;

Data are consistent with analogous reaction with 4-*tert*-butyl-1-methylcyclohexene.[12]

(3a*S*,6*R*,7a*R*)-6-Isopropyl-2,3a-dimethyl-3a,4,5,6,7,7a-hexahydro-1,3-benzothiazole 18

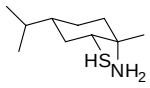


18

A modification of the procedure reported by Woodgate was used.[13] A solution of 3 M methyl magnesium bromide in diethyl ether (2.61 ml, 7.84 mmol) were added to a solution of **16** (contaminated with **17** and an unidentified impurity; 1.90 g estimated to contain 1.27 g of **16**, 3.92 mmol) in anhydrous diethyl ether (2 ml). The mixture was refluxed under nitrogen for 2 days. The reaction mixture was placed in an ice bath. A saturated solution of NH_4Cl was added very slowly until no further reaction was observed. Then, diethyl ether (10 ml) and water (10 ml) were added and the product was extracted with diethyl ether (2 × 10 ml). The crude material was purified by column chromatography (silica gel; petroleum ether and then petroleum ether/ ethyl acetate 9:1). Thiazoline **18** was obtained as a yellow oil (0.33 g, 40% yield based on **16**, unoptimized).

R_f: 0.48 (PE/EtOAc 9:1); $[\alpha]_D^{23}$ +202.4 (*c* 0.42, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): 0.84 (d, 6H, *J* = 6.8 Hz, (CH_3)$_2$CH), 0.95–1.05 (m, 2H), 1.14 (s, 3H, CH_3), 1.38–1.65 (m, 4H), 1.90–1.98 (m, 1H), 2.22 (s, 3H, CH_3C=N), 2.47 (ddd, 1H, *J* = 13.7 Hz, *J* = 3.2 Hz, *J* = 3.2 Hz, CHH_{eq}), 3.28 (dd, 1 H, *J* = 11.4 Hz, *J* = 5.9 Hz, SCH_{ax}). ^{13}C NMR (125 MHz, $CDCl_3$): 19.5 ((CH_3)$_2$CH), 21.1 (CH_3C=N), 25.3 (CH_2), 25.5 (CH_3), 32.3 (Me_2CH), 36.6 (CH_2), 37.8 (CH_2), 41.9 (CH-*i*Pr), 57.7 (CHS), 77.4 (C), 165.1 (C=N). IR ν_{max}/cm^{-1} 2947, 2927, 1740, 1619, 1435, 1367, 1214, 1138; HRMS (EI) $C_{12}H_{21}NS$ requires: 211.1395; found: 211.1386.

(1*R*,2*S*,5*R*)-2-Amino-5-isopropyl-2-methylcyclohexanethiol (19)



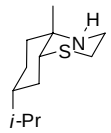
19

Thiazoline **18** (2.00 g, 9.46 mmol) was dissolved in 20 ml of 6 N HCl. The reaction mixture was heated in a sealed vessel using a microwave oven at 175 °C for 13 h (using a Biotage Initiator microwave synthesiser using an IR sensor to monitor and control temperature). After cooling, the solution was basified to pH = 12 using a 2.5 M solution of NaOH. Then the product was extracted using diethyl ether (3 × 25 ml). The organic layers were combined, dried over $MgSO_4$, filtered and evaporated. Aminothiol **19** was obtained without the need of further purification as a pale yellow oil (1.74 g, 98% yield). The aminothiol was very sensitive to oxidation and was used directly after preparation.

^{1}H NMR (270 MHz, $CDCl_3$): 0.85 (d, 6H, *J* = 6.8 Hz, $(CH_3)_2CH$), 1.12 (s, 3H, CH_3), 1.17–1.56 (m, 9H), 1.76 (ddd, 1H, *J* = 13.2 Hz, *J* = 2.8 Hz, *J* = 2.8 Hz, $CH H_{eq}$), 1.81–1.90 (m, 1H), 2.77 (dd, 1H, *J* = 12.0 Hz, *J* = 3.8 Hz, $H_{ax}CS$); ^{13}C NMR (68 MHz, $CDCl_3$): 19.9 (CH_3), 24.8 (CH_2), 30.8 (CH_3), 32.6 (Me_2CH), 37.1 (CH_2), 40.1 (CH_2), 45.2 (CH-iPr), 49.9 (CHS), 51.0 (C).

Exposure of the thiol to air gave the corresponding disulfide: $[\alpha]_D^{23}$ -97.2 (*c* 0.91, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): 0.92 (d, 6H, *J* = 6.8 Hz, $(CH_3)CH$), 0.93 (d, 6H, *J* = 6.6 Hz, $(CH_3)CH$), 1.12–1.21 (m, 4H), 1.28 (s, 6H, CH_3), 1.34–1.59 (m, 12H), 1.69 (dt, 2H, *J* = 13.4 Hz, *J* = 2.8 Hz, $CH H_{eq}$), 2.14–2.20 (m, 2H), 2.65 (dd, 2H, *J* = 12.7 Hz, *J* = 4.2 Hz, $H_{ax}CS$); ^{13}C NMR (68 MHz, $CDCl_3$): 20.0 ($(CH_3)_2CH$), 24.8 (CH_2), 30.8 (CH_3), 32.8 (Me_2CH), 33.2 (CH_2), 41.4 (CH_2), 44.9 (CHiPr), 51.9 (C), 63.9 (CHS); IR ν_{max}/cm^{-1} 2952, 2924, 2861, 1474, 1439, 1363, 1219, 738, 690; MS (CI) *m/z* (%): 373 (100), 218 (26), 186 (85), 169 (26), 154 (50); HRMS (CI) $C_{20}H_{41}N_2S_2$ ($[M+H]^+$) requires: 373.2711; found: 373.2700.

(4a*S*,7*R*,8a*R*)-7-Isopropyl-4a-methyloctahydro-2*H*-benzo[b][1,4]thiazine 20



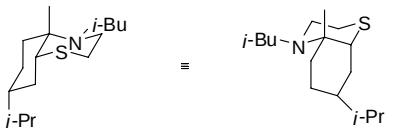
20

Freshly prepared aminothiol **19** (1.24 g, 6.62 mmol) was dissolved in anhydrous dichloromethane (50 ml) and placed in an ice bath. Anhydrous triethylamine (1.83 ml, 13.3 mmol) was added. A solution of vinyl sulfonium salt[14] **34 (**2.53 g, 7.02 mmol) in anhydrous dichloromethane (50 ml) was added slowly over 15 min. The reaction mixture was then stirred at 0 °C for 3 h. Then the ice bath was removed and the mixture stirred at room temperature overnight.

The reaction mixture was evaporated at reduced pressure and the crude material was purified by column chromatography (silica gel; ethyl acetate/petroleum ether/triethylamine 4/6/0.05) to give sulfide **20** as a pale yellow oil (1.27 g, 90% yield) which was used in the next step without further purification.

R_f: 0.24 (EtOAc/petroleum ether/NEt_3 4/6/0.05); ^{1}H NMR (400 MHz, $CDCl_3$): 0.88 (d, 3H, J = 6.8 Hz, CH_3CHMe), 0.89 (d, 3H, J = 6.8 Hz, CH_3CHMe), 1.11–1.25 (m, 4H), 1.38–1.48 (m, 2H), 1.42 (s, 3H, CH_3), 1.58–1.64 (m, 1H), 1.81–1.84 (m, 1H, SCHCHH_{eq}), 1.98 (ddd, 1H, J = 12.7 Hz, J = 12.7 Hz, J = 12.7 Hz, SCHCH_{ax}H), 2.11 (ddd, 1H, J = 13.2 Hz, J = 2.9 Hz, J = 2.9 Hz, CHH_{eq}S), 2.21 (dd, 1H, J = 12.7 Hz, J = 4.3 Hz, SCH_{ax}), 2.85 (ddd, 1H, J = 13.2 Hz, J = 13.2 Hz, J = 2.9 Hz, SCHH_{ax}), 3.04 (ddd, 1H, J = 13.2 Hz, J = 2.9 Hz, J = 2.9 Hz, NCHH_{eq}), 3.32 (ddd, 1H, J = 13.2 Hz, J = 13.2 Hz, J = 2.9 Hz, NCH_{ax}H); ^{13}C NMR (68 MHz, $CDCl_3$): 20.0 ((CH_3)$_2$CH), 22.7 (CH_2S), 24.5 (CH_2), 26.8 (CH_3), 32.8 (Me_2CH), 33.0 (CH_2CHS), 42.1 (CH_2N), 42.6 (CH_2), 43.8 (CHS), 45.3 (CH*i*Pr), 50.0 (C).

(4a*S*,7*R*,8a*R*)-4-isoButyl-7-isopropyl-4a-methyloctahydro-2*H*-1,4-benzothiazine 6



6 **6**

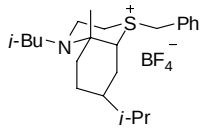
Sulfide **20** (1.27 g, 5.95 mmol) was dissolved in anhydrous dichloroethane (25 ml). Isobutyraldehyde (2.7 ml, 30 mmol) was added, followed by sodium triacetoxyborohydride (12 g, 57 mmol). The reaction

was stirred at room temperature under nitrogen overnight. A saturated aqueous solution of $NaHCO_3$ was added carefully until no further reactivity was observed, and the product was extracted with ethyl acetate (3 × 25 ml). The combined organic fractions were dried with $MgSO_4$, filtered and evaporated. The desired product **6** was obtained after purification by column chromatography (silica gel; petroleum ether) as a pale yellow oil (1.26 g, 79% yield). R_f: 0.40 (petroleum ether).

$[\alpha]_D^{23}$ +149.6 (*c* 1.15, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): 0.84 (d, 3H, *J* = 6.7 Hz, C*H*$_3$CHMe), 0.87 (d, 3H, *J* = 6.7 Hz, C*H*$_3$CHMe), 0.87 (d, 3H, *J* = 7.1 Hz, C*H*$_3$CHMe), 0.89 (d, 3H, *J* = 7.1 Hz, C*H*$_3$CHMe), 1.06 (ddd, 1H, *J* = 13.6 Hz, *J* = 13.6 Hz, *J* = 3.1 Hz, CH*H*$_{ax}$), 1.16 (s, 3H, CH_3), 1.18–1.26 (m, 2H, $(CH_2)_2$C*H*iPr, CH*H*), 1.38 (ddd, 1H, *J* = 13.6 Hz, *J* = 13.6 Hz, *J* = 2.4 Hz, CH*H*$_{ax}$), 1.42–1.48 (m, 1H, Me_2CH), 1.65 (ddd, 1H, *J* = 12.7 Hz, *J* = 5.6 Hz, *J* = 3.4 Hz, CH*H*$_{eq}$), 1.69–1.76 (m, 1H, $CHMe_2$), 1.80 (dd, 1H, *J* = 12.5 Hz, *J* = 4.8 Hz, NCH*H*iPr), 2.18–2.29 (m, 4H, SCH, C*H*HiPr, C*H*H, SCH*H*$_{eq}$), 2.39 (ddd, 1H, *J* = 12.7 Hz, *J* = 12.7 Hz, *J* = 12.7 Hz, C*H*$_{ax}$H), 2.63 (ddd, 1H, *J* = 12.8 Hz, *J* = 12.8 Hz, *J* = 3.2 Hz, NCH*H*$_{ax}$), 2.85 (ddd, 1H, *J* = 12.8 Hz, *J* = 3.2 Hz, *J* = 3.2 Hz, NCH*H*$_{eq}$), 3.11 (ddd, 1H, *J* = 12.8 Hz, *J* = 12.8 Hz, *J* = 3.2 Hz, SCH*H*$_{ax}$). ^{13}C NMR (64 MHz, $CDCl_3$): 18.1 (CH_3), 19.9 (*C*H_3CH × 2), 20.7 (*C*H_3CH), 21.3 (*C*H_3CH), 23.4 (CH_2), 24.1 (CH_2S), 26.4 (Me_2*C*H), 32.8 (*C*H_2), 32.9 (Me_2*C*H), 38.8 (CH_2), 45.7 ($(CH_2)_2$*C*HiPr), 47.0 (CH_2*C*H_2N), 48.1 (CHS), 55.3 (C), 56.0 (N*C*H_2iPr). IR ν_{max}/cm^{-1} ($CHCl_3$, film) 2947, 2810, 1467, 1367, 1260, 1100, 1067, 1024; HRMS (EI) $C_{16}H_{31}NS$ requires: 269.2177; found: 269.2173.

Synthesis of sulfonium salt 26

(1*S*,4a*S*,7*R*,8a*R*)-1-Benzyl-4-isobutyl-7-isopropyl-4a-methyloctahydro-2*H*-1,4-benzothiazin-1-ium tetrafluoroborate 26



26

Sulfide **6** (220 mg, 0.816 mmol) was dissolved in dichloromethane (4.4 ml) and benzyl bromide (0.24 ml, 2.0 mmol) was added. Then $NaBF_4$ (220 mg, 2.00 mmol) in water (1.5 ml) were added and the mixture was stirred at room temperature for three days. The organic layer was extracted with dichloromethane (3 × 5 ml), dried and evaporated. The crude material was purified by column chromatography (silica gel; CH_2Cl_2 and then CH_2Cl_2:MeOH 9:1). Sulfonium salt **26** was obtained as a white crystalline solid (259 mg, 71%).

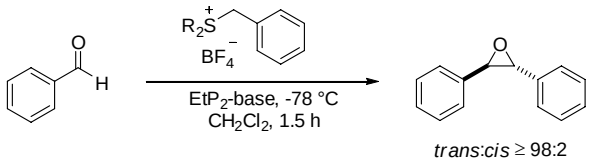
R_f: 0.68; m.p. 182–184 °C (Et_2O/CH_2Cl_2); $[\alpha]_D^{23}$ +91.8 (*c* 0.92, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): 0.90 (d, 3H, *J* = 6.5 Hz, C*H*$_3$CHMe), 0.92 (d, 3H, *J* = 6.5 Hz, C*H*$_3$CHMe) 0.93 (d, 3H, *J* = 6.8 Hz, C*H*$_3$CHMe) 0.95 (d, 3H, *J* = 6.8 Hz, C*H*$_3$CHMe), 1.22 (s, 3H, CH_3), 1.35–1.47 (m, 4H, CHiPr, C*H*H, C*H*$_2$CHiPr), 1.60–1.66 (m, 1H, Me$_2$C*H*CH), 1.70–1.81 (m, 1H, Me$_2$C*H*CH$_2$), 1.92–1.97 (m, 2H, CH*H*CHS, C*H*HiPr), 2.24–2.33 (m, 3H, CH*H*iPr, CH*H*, C*H*HCHS), 2.71 (ddd, 1H, *J* = 13.4 Hz, *J* = 13.4 Hz, *J* = 2.4 Hz, NCH*H*$_{ax}$ or SC*H*$_{ax}$H), 3.16–3.26 (m, 2 H, C*H*$_{eq}$HN, C*H*$_{eq}$HS), 3.44 (ddd, 1H, *J* = 13.4 Hz, *J* = 13.4 Hz, *J* = 3.7 Hz, SC*H*$_{ax}$H or NCH*H*$_{ax}$), 3.68 (d, 1H, *J* = 2.7 Hz, CHS), 4.37 (d, 1H, *J* = 12.7 Hz, C*H*HPh), 4.74 (d, 1H, *J* = 12.7 Hz, CH*H*Ph), 7.40-7.42 (m, 3H, ArH), 7.52-7.54 (m, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): 17.0 (CH_3), 19.3 (CH*C*H$_3$), 19.9 (CH*C*H$_3$), 20.4 (CH*C*H$_3$), 21.2 (CH*C*H$_3$), 22.0 (CH_2), 23.6 (*C*H$_2$CHS), 26.1 (CH_2*C*HMe$_2$), 31.3 (CH_2), 32.7 (CH*C*HMe$_2$), 38.9 (CH_2), 42.1 (CH_2Ph), 42.7 (CH_2), 43.8 ((CH_2)$_2$*C*HiPr), 54.6 (NCH$_2$iPr), 55.0 (SCH), 57.5 (C), 126.9 (C), 129.8 (CH), 130.0 (CH), 130.6 (CH); IR ν_{max}/cm^{-1} (film, $CHCl_3$) 3055, 2963, 1423, 1265, 1061, 896; MS (ESI+) $C_{23}H_{38}NS^+$ (M-BF_4^-) requires: 360.2719; found: 360.2718.

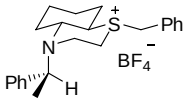
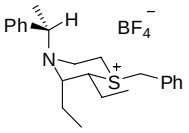
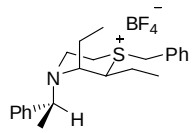
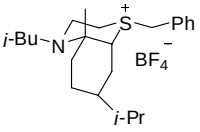
Procedures for the asymmetric epoxidation of aldehydes

Method A: Using Sulfonium Salt and EtP_2 base

EtP_2 base (77 µl, 0.23 mmol) was added with stirring to a solution of benzaldehyde (23 µl, 0.23 mmol) and the sulfonium salt **23** (0.21 mmol) in CH_2Cl_2 (1.5 ml) at –78 °C. The reaction mixture was stirred for 1.5 h at –78 °C, after which brine (3 ml) was added. The reaction mixture was extracted with Et_2O (3 × 5 ml). The combined organic extracts were extracted with aqueous HCl solution (1 M, 2 × 4 ml). The organic phase was dried over $MgSO_4$ and the solvent was removed under reduced pressure. The diastereomeric ratio of the crude product was determined by ^1H NMR (dr (*trans/cis*) ≥ 98:2 in all cases). Purification of the crude product by flash chromatography (Silica; EtOAc/PE 1:50) afforded *trans*-stilbene oxide **35a** as a colorless solid.

Table 2 Results of epoxidations of benzaldehyde with various sulfonium salts using method A.



Sulfonium salt	Yield **35a**[%]	er (*R*,*R*):(*S*,*S*)
 **21** dr = 14:1	79	85.5:14.5
 **22**	74	93:7
 **23**	79	3: 97
 **26**	86	21: 79

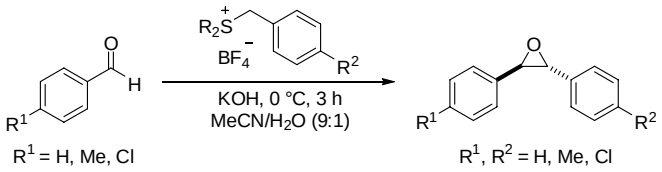
Method B: Using Sulfonium Salt and Potassium Hydroxide with Sulfide Recovery

Powdered KOH (25 mg, 0.44 mmol) was added to a solution of the sulfonium salt **23** (0.22 mmol) and the corresponding aldehyde (0.22 mmol) in MeCN/H_2O 9:1 (1.0 ml) at 0 °C without preclusion of air. The reaction mixture was stirred for 3 h at 0 °C. The organic solvent was removed under reduced pressure, the residue was redissolved in Et_2O (10 ml) and extracted with aqueous HCl solution (1 M, 2 × 5 ml). The organic phase was dried over $MgSO_4$ and the solvent was removed under reduced pressure. The

diastereomeric ratio of the crude epoxide was determined by ^{1}H NMR. Purification of the crude product by flash chromatography (Silica; EtOAc/PE 1:50) afforded the epoxides as colorless solids.

Recovery of sulfide: The combined aqueous phases were basified by addition of aqueous NaOH solution (3 M) to pH 11 and extracted with Et_2O (3 × 5 ml). The combined organic extracts were washed with brine, dried over $MgSO_4$ and the solvent was removed under reduced pressure. The sulfide **5** thus recovered was shown to be pure by ^{1}H and ^{13}C NMR.

Table 3 Results of epoxidations of benzaldehydes with various sulfonium salts using method B.

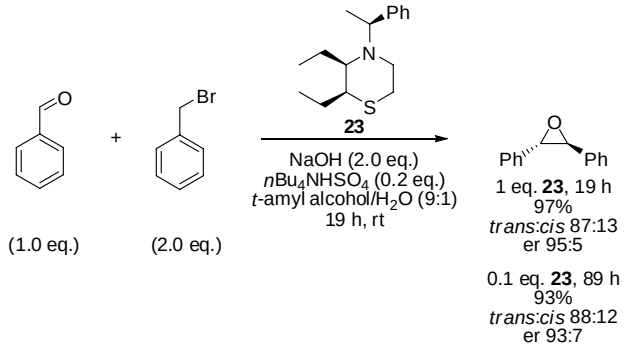


Entry	Sulfonium Salt	R^1	R^2	Yield (%)[a]	*trans*:*cis* [b]	er (*S*,*S*):(*R*,*R*)	Recovered Sulfide (%)
1 [c]	**26**	H	H	60	97:3	80:20	83
2	**23**	H	H	95	86:14	96:4	97
3	**23**	Cl	H	89	94:6	96:4	90
4	**24**	H	Cl	92	98:2	97:3	93
5	**23**	Me	H	94	89:11	96:4	96
6	**25**	H	Me	73	78:22	95:5	94

[a] combined isolated yield of *cis*- and *trans*-stilbene oxide; [b] determined by ^{1}H NMR of crude product; [c] 8 h;

Method C Using Sodium Hydroxide and in situ alkylation of Sulfide

Powdered NaOH (55 mg, 1.4 mmol) and nBu$_4$NHSO$_4$ (44 mg, 0.13 mmol) were added to a solution of sulfide **5** (0.67 mmol), benzaldehyde (69 µl, 0.68 mmol) and benzyl bromide (157 µl, 1.32 mmol) in *t*-amylalcohol/H_2O 9:1 (3.9 ml). The reaction mixture was stirred at room temperature for 19 h. The organic solvent was removed under reduced pressure, the residue was redissolved in Et_2O (10 ml) and extracted with aqueous HCl solution (1 M, 2 × 5 ml). The organic phase was dried over $MgSO_4$ and the solvent was removed under reduced pressure. The diastereomeric ratio of the crude epoxide was determined by ^{1}H NMR. Purification of the crude product by flash chromatography (Silica; EtOAc/PE 2:98) afforded the epoxide as a colorless solid.



Scheme 3 Results obtained in epoxidation of benzaldehyde using Method C.

Characterization data for Epoxides

***trans*-Stilbene oxide (35a)** and ***cis*-Stilbene oxide (35b)** [15]

35a: R_f (EtOAc/PE 1:9) 0.70; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.88 (s, 2 H), 7.26–7.42 (m, 10 H); **35b**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.28 (s, 2 H), 7.01–7.15 (m, 10 H). Enantiomeric excesses were determined by HPLC (Chiralcel OD column, UV–VIS-detector); mobile phase: 2% *i*PrOH, 98% hexane, flow rate (ml/min): 1; (*S*,*S*)-Enantiomer R_t: 8.5 min; (*R*,*R*)-Enantiomer R_t: 16.0 min. The absolute configuration was determined by comparison with literature data.[15]

2-(4-Chlorophenyl)-3-phenyloxirane 36[15]

36a (*trans* isomer): R_f (EtOAc/PE 1:9) 0.65; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.81 (d, J = 2.0 Hz, 1 H), 3.83 (d, J = 2.0 Hz, 1 H), 7.04–7.50 (m, 9 H); **36b** (*cis* isomer): ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.31 (d, J = 4.5 Hz, 1 H), 4.37 (d, J = 4.5 Hz, 1 H), 7.04–7.50 (m, 9 H); Enantiomeric excess was determined by HPLC (Chiralcel OD column, UV–VIS-detector); mobile phase: 1% *i*PrOH, 99% hexane, flow rate (ml/min): 1; (*S*,*S*)-Enantiomer R_t: 11.2 min; (*R*,*R*)-Enantiomer R_t: 13.8 min. The absolute configuration has been determined by comparison with literature data.[15]

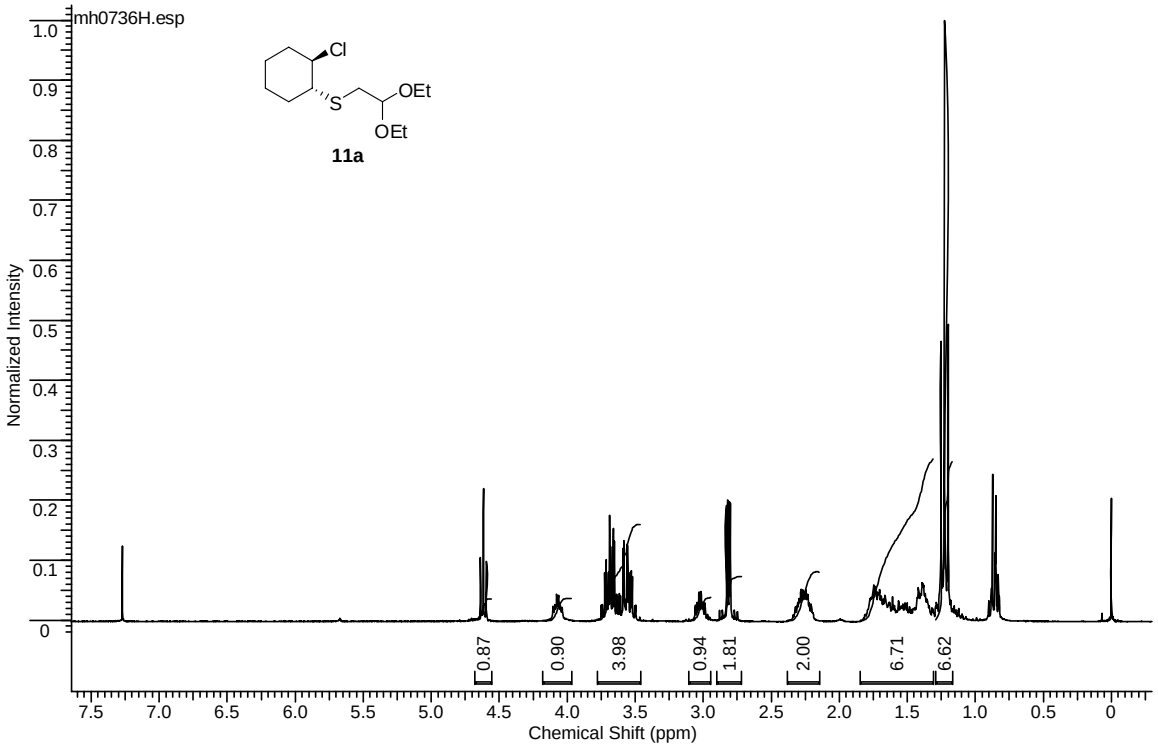
2-Phenyl-3-*p*-tolyloxirane 37[15]

37a *trans* isomer: R_f (EtOAc/PE 1:9) 0.70; ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.29 (s, 3 H), 3.75 (d, J = 2.0 Hz, 1 H), 3.78 (d, J = 2.0 Hz, 1 H), 7.16–7.44 (m, 9 H); **37b** *cis* isomer: ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.16 (s, 3 H), 4.25 (m, 2 H), 6.89–7.40 (m, 9 H); Enantiomeric excess was determined by HPLC (Chiralcel OD column, UV–VIS-detector); mobile phase: 1% *i*PrOH, 99% hexane, flow rate (ml/min): 1; (*S*,*S*)-Enantiomer R_t: 8.2 min; (*R*,*R*)-Enantiomer R_t: 12.4 min. The absolute configuration has been determined by comparison with literature data.[15]

NMR spectra

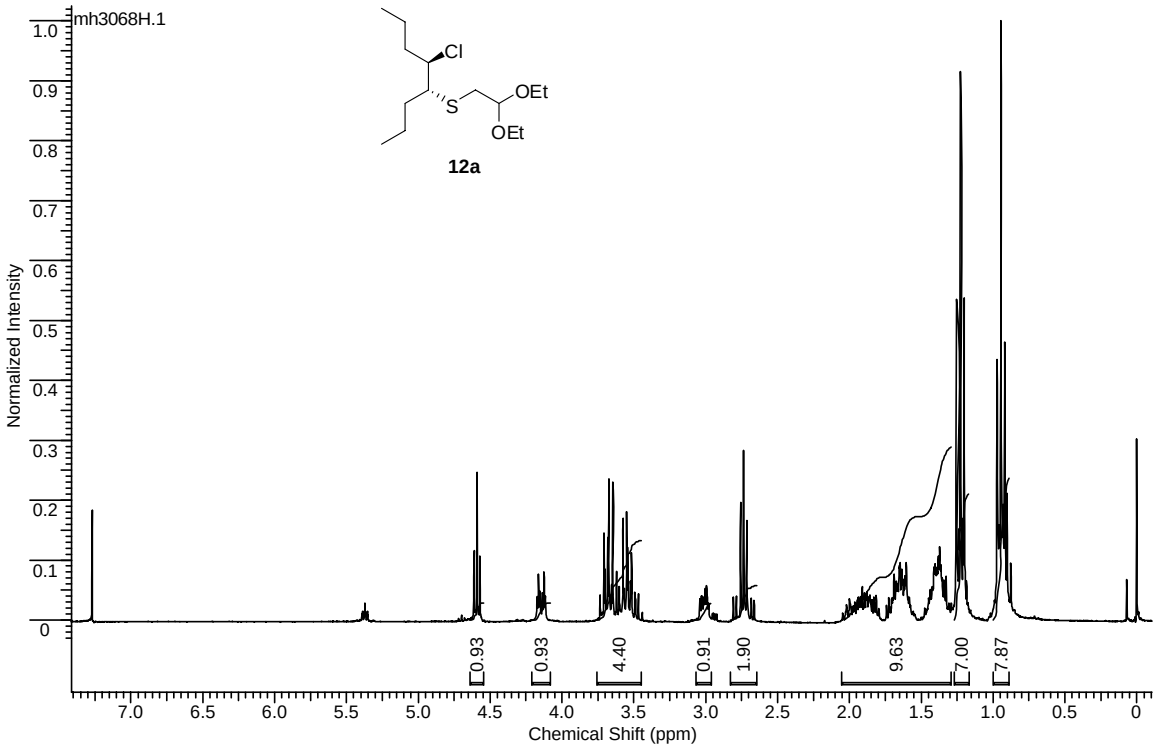
(±)-*trans*-1-Chloro-2-[(2,2-diethoxyethyl)sulfanyl]cyclohexane 11a

^{1}H NMR (270 MHz, $CDCl_3$)



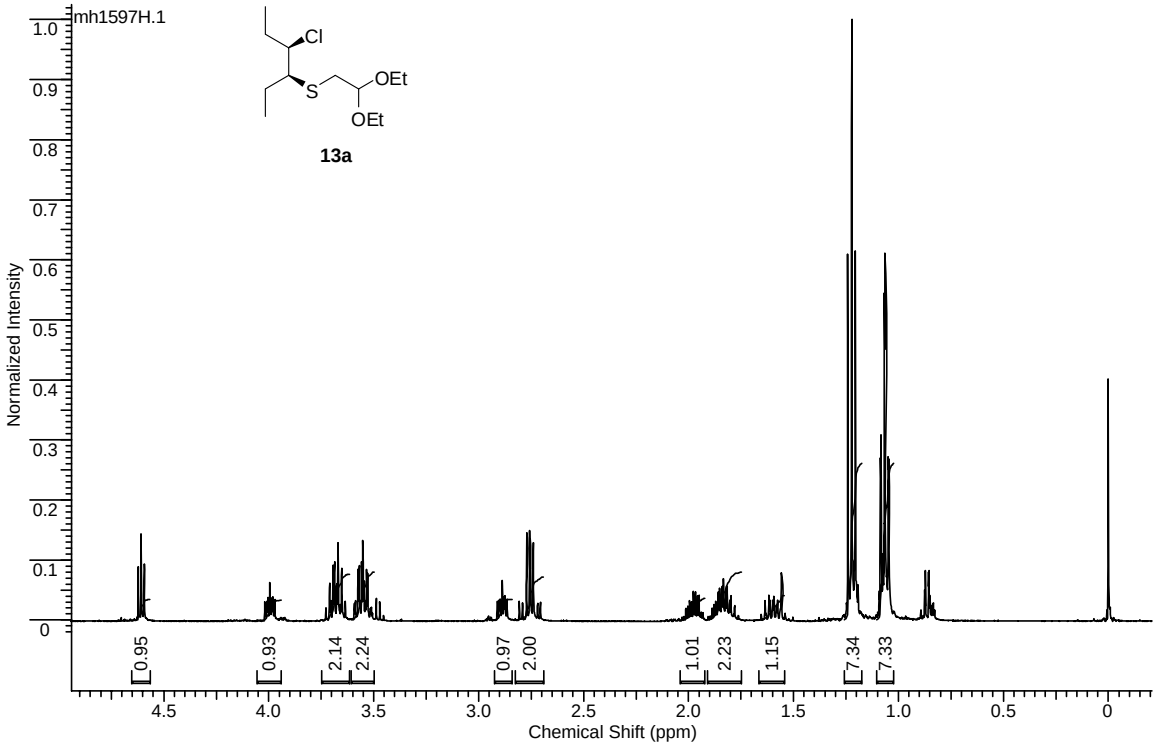
(±)-(4*R**,5*R**)-4-Chloro-5-[(2,2-diethoxyethyl)sulfanyl]octane 12a

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



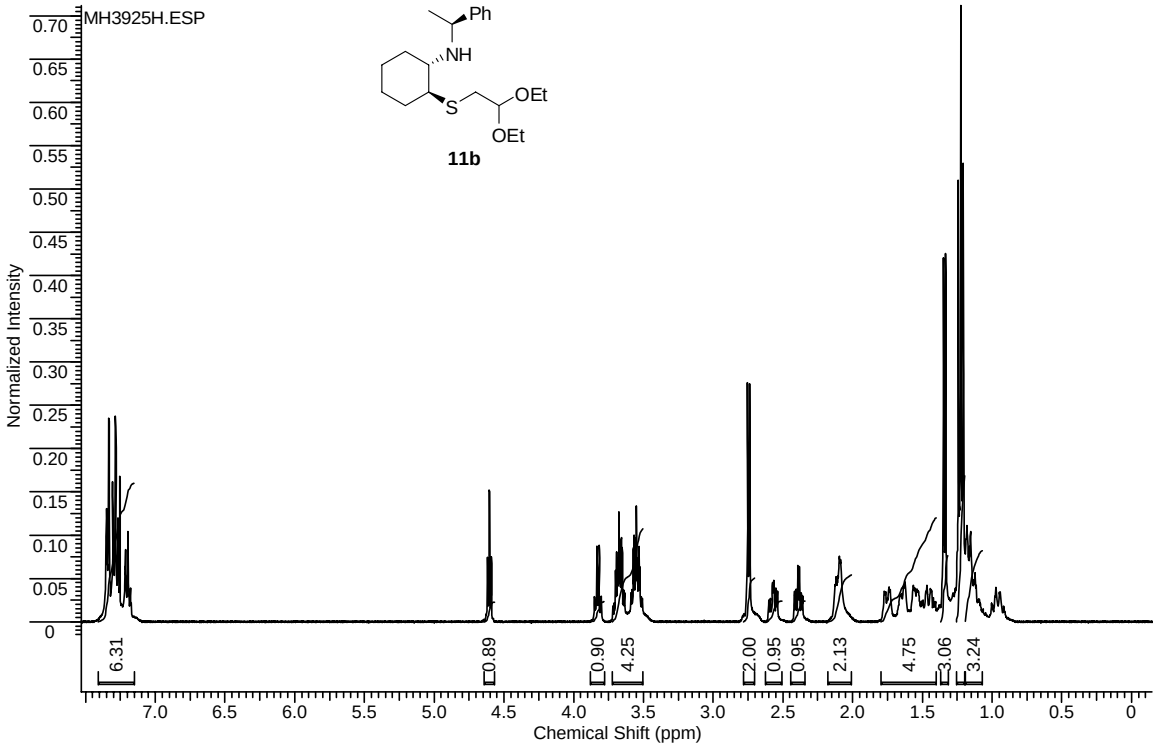
(±)-(3*R,4*S**)-3-Chloro-4-[(2,2-diethoxyethyl)sulfanyl]hexane 13a**

^{1}H NMR (270 MHz, $CDCl_3$)

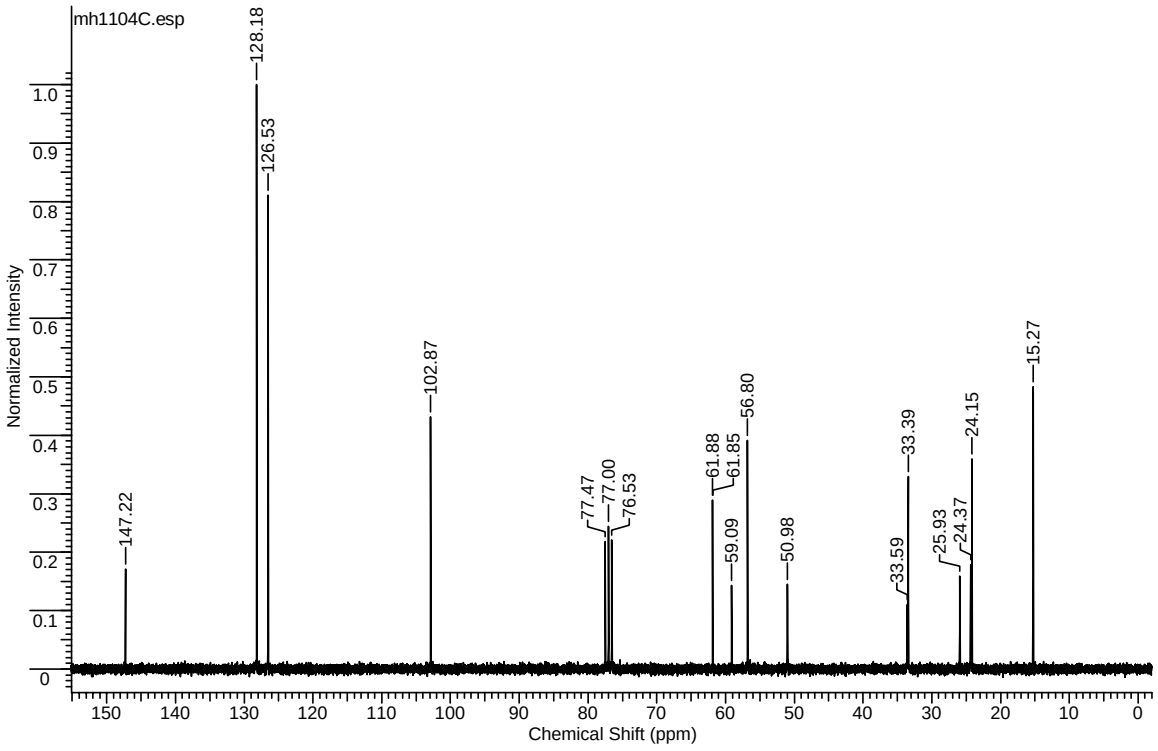


(1*S*,2*S*)-2-[(2,2-Diethoxyethyl)sulfanyl]-*N*-[(1*S*)-1-phenylethyl]cyclohexanamine 11b

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

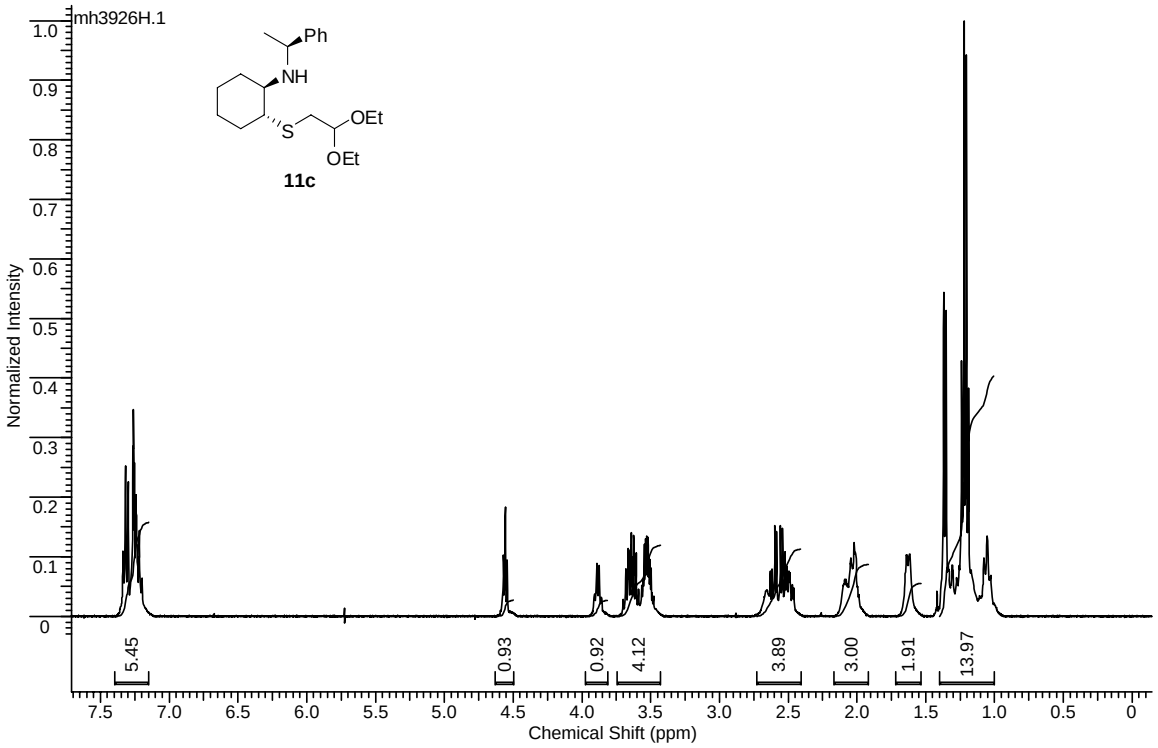


^{13}C NMR (68 MHz, $CDCl_3$)

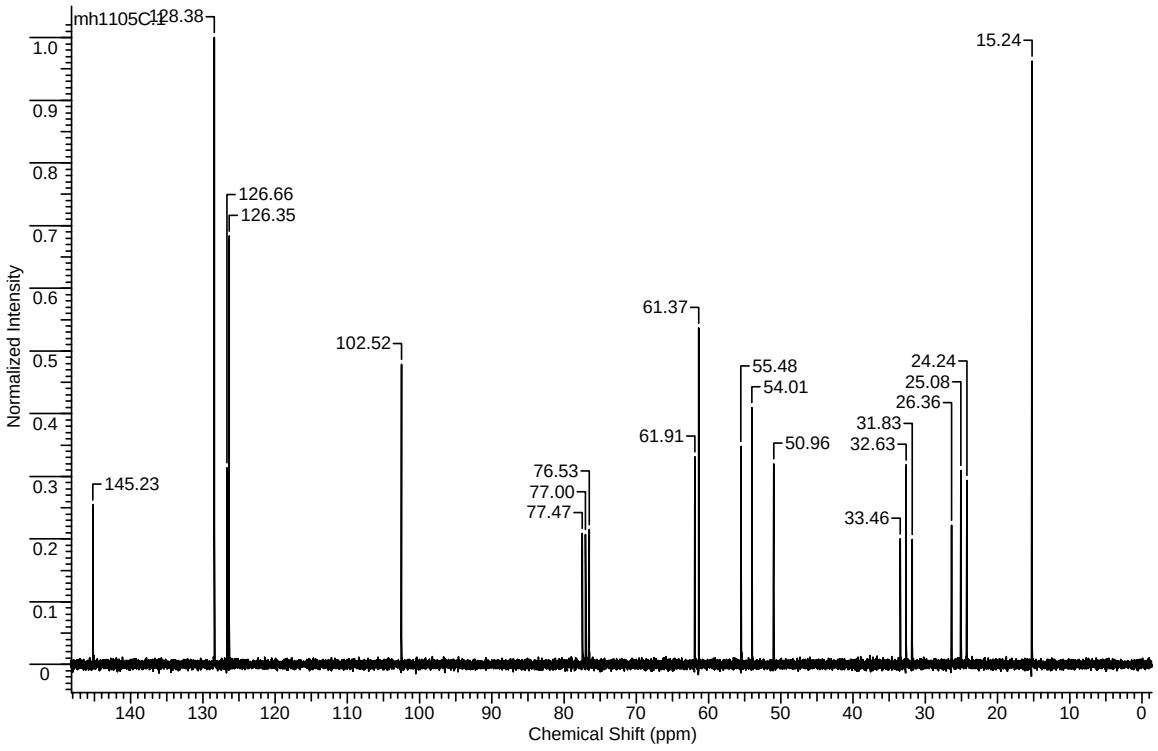


(1*R*,2*R*)-2-[(2,2-Diethoxyethyl)sulfanyl]-*N*-[(1*S*)-1-phenylethyl]cyclohexanamine 11c.

^{1}H NMR (270 MHz, $CDCl_3$)

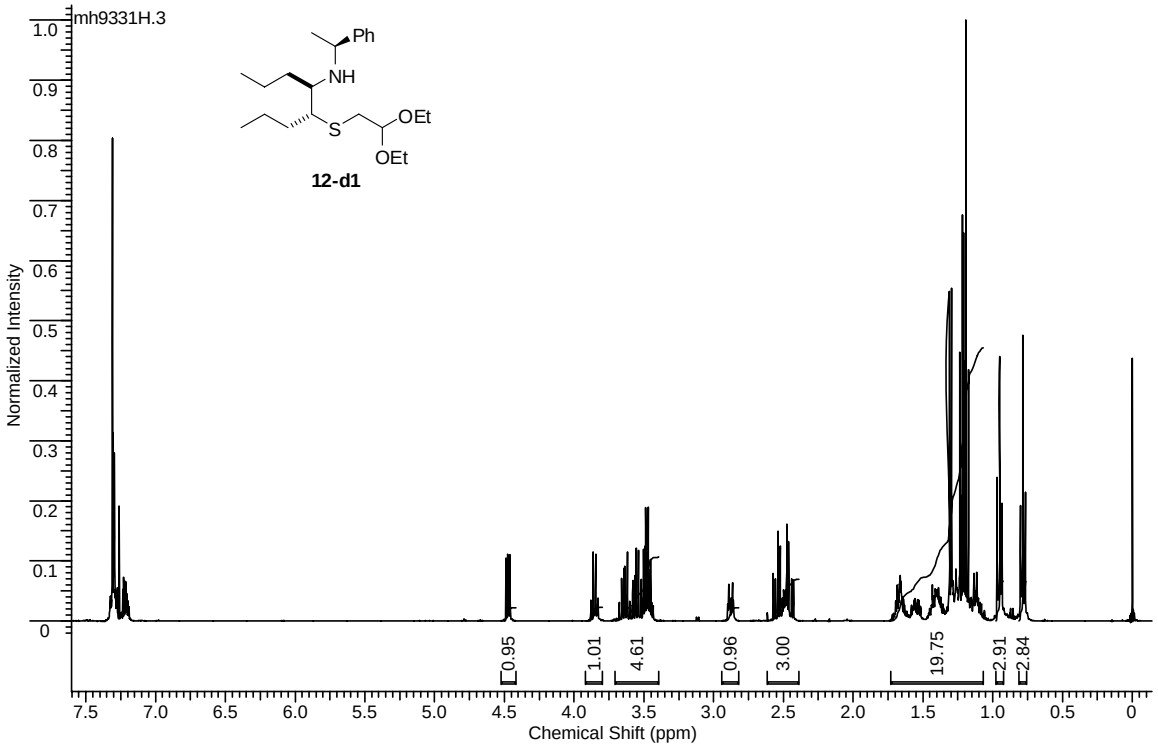


^{13}C NMR (68 MHz, $CDCl_3$)

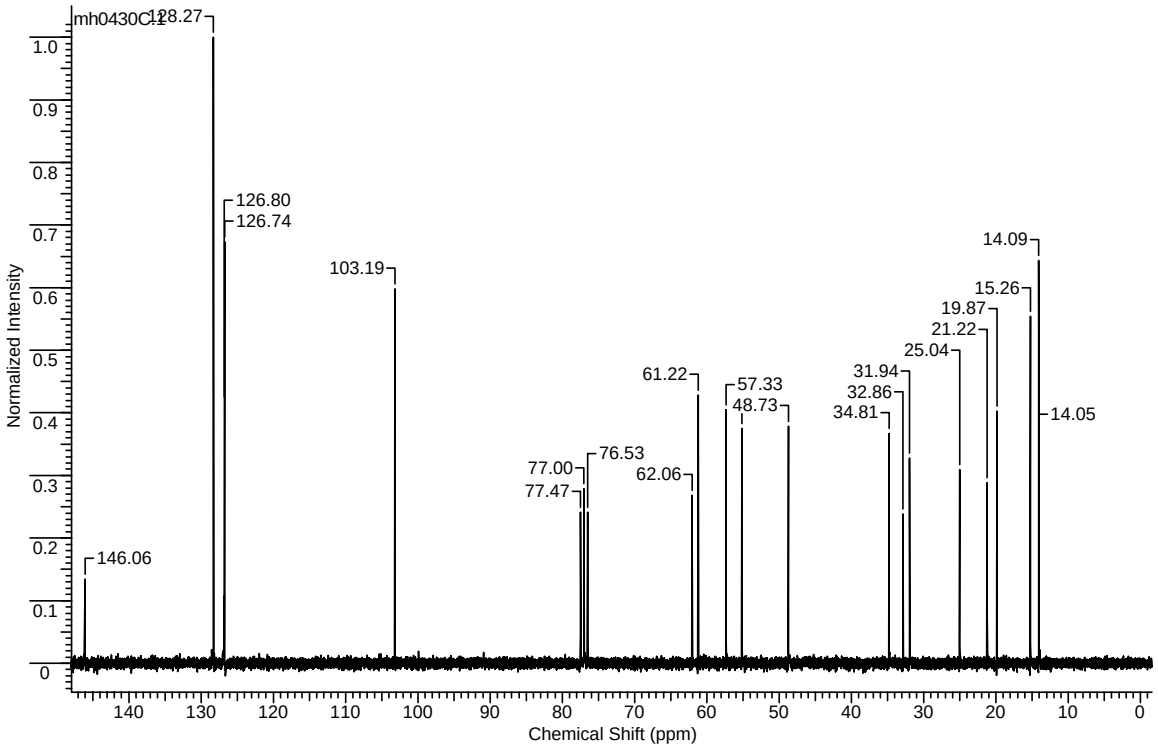


(4*R*,5*R*)-5-[(2,2-Diethoxyethyl)sulfanyl]-*N*-[(1*S*)-1-phenylethyl]-4-octanamine or (4*S*,5*S*)-5-[(2,2-diethoxyethyl)sulfanyl]-*N*-[(1*S*)-1-phenylethyl]-4-octanamine (12-diastereomer 1)

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

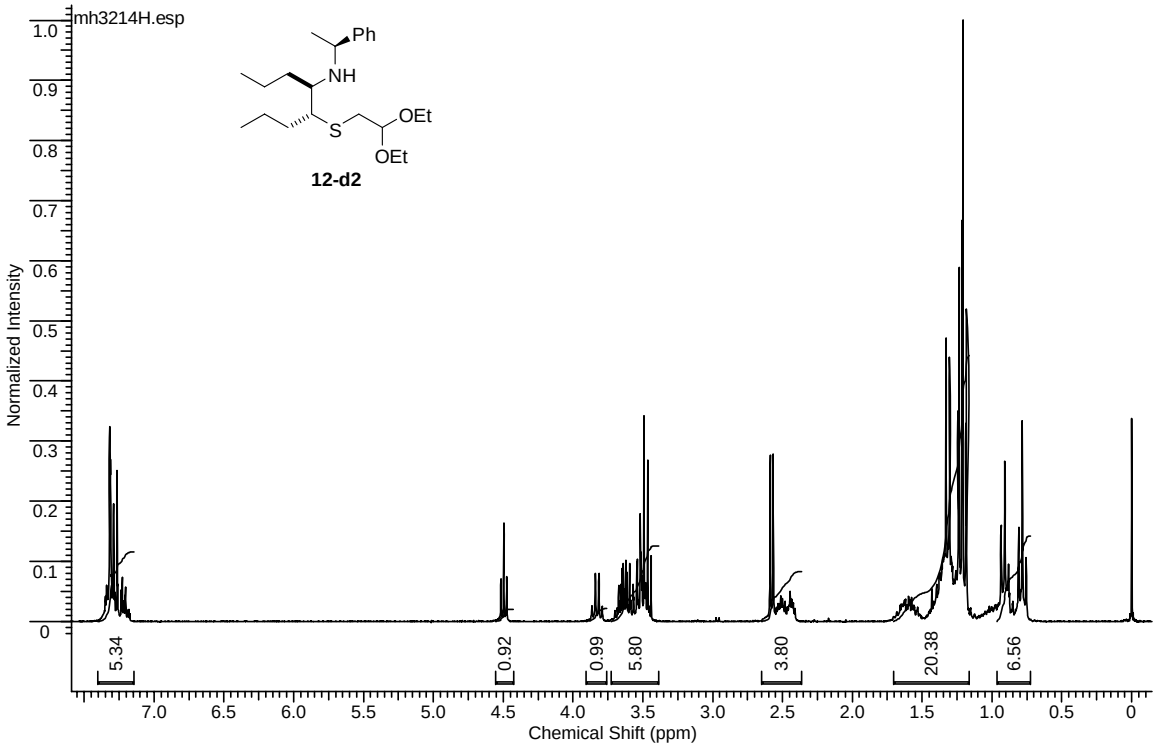


^{13}C NMR (68 MHz, $CDCl_3$)

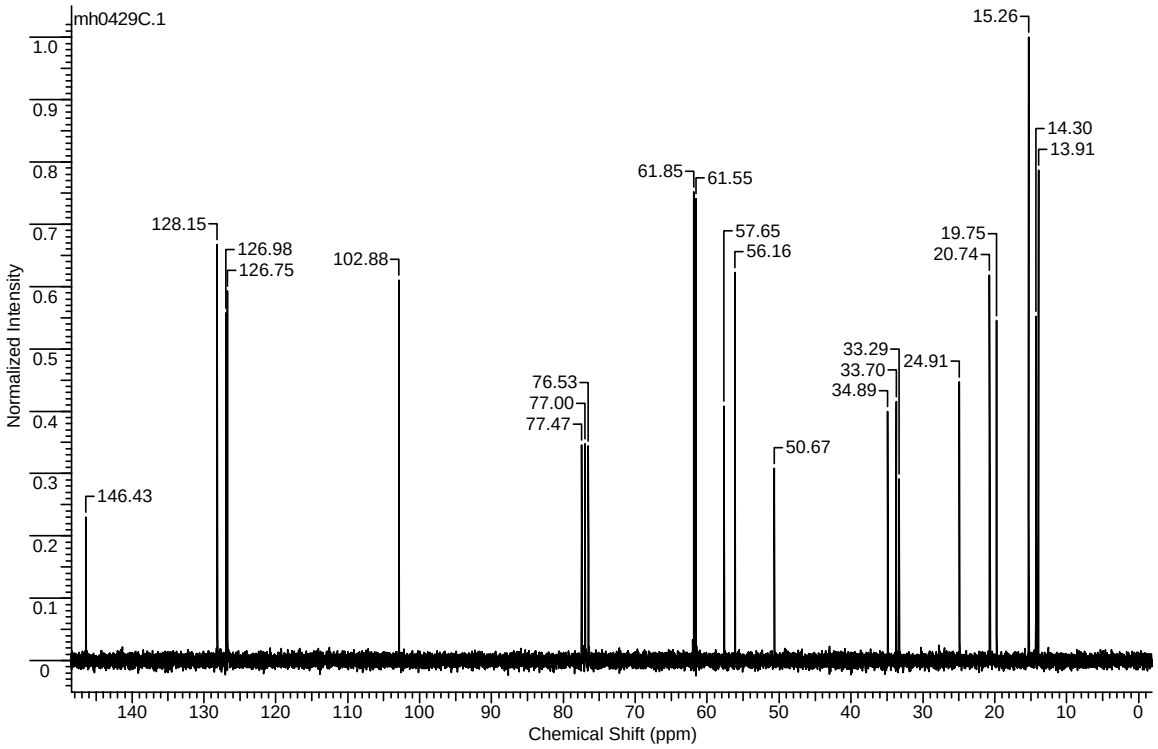


(4*R*,5*R*)-5-[(2,2-Diethoxyethyl)sulfanyl]-*N*-[(1*S*)-1-phenylethyl]-4-octanamine or (4*S*,5*S*)-5-[(2,2-diethoxyethyl)sulfanyl]-*N*-[(1*S*)-1-phenylethyl]-4-octanamine (12-diastereomer 2).

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

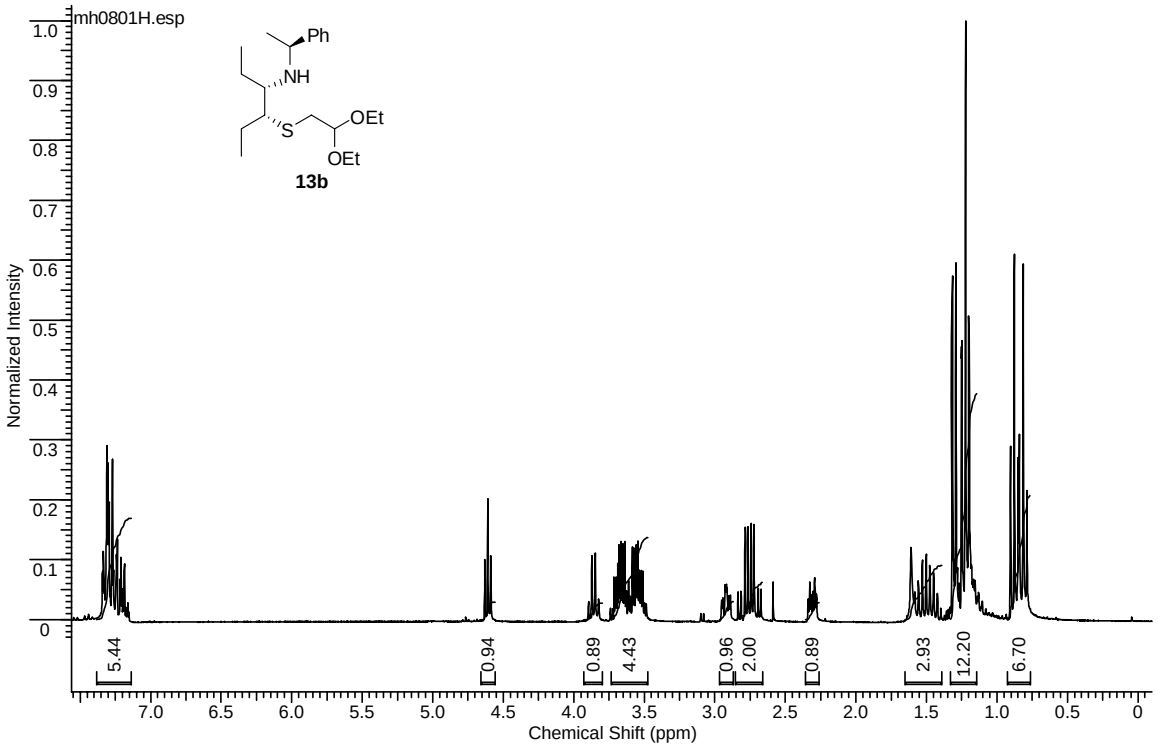


^{13}C NMR (68 MHz, $CDCl_3$)

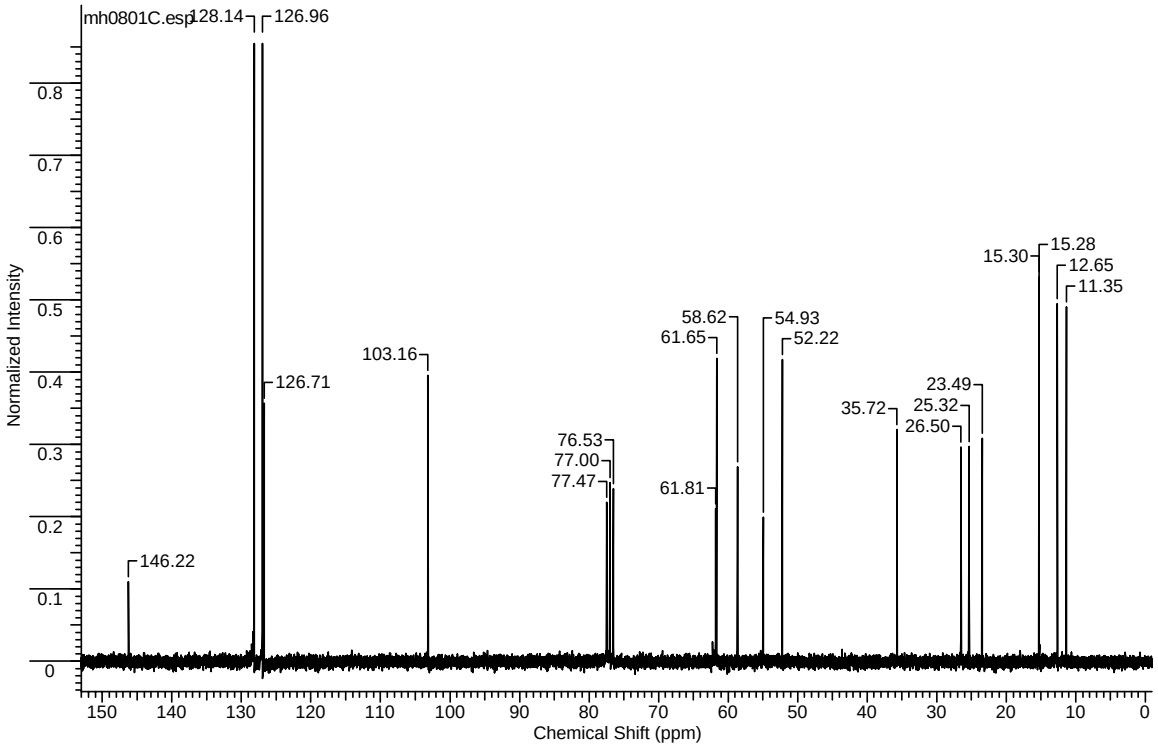


(3*S*,4*R*)-4-[(2,2-Diethoxyethyl)sulfanyl]-*N*-[(1*S*)-1-phenylethyl]-3-hexanamine 13b.

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

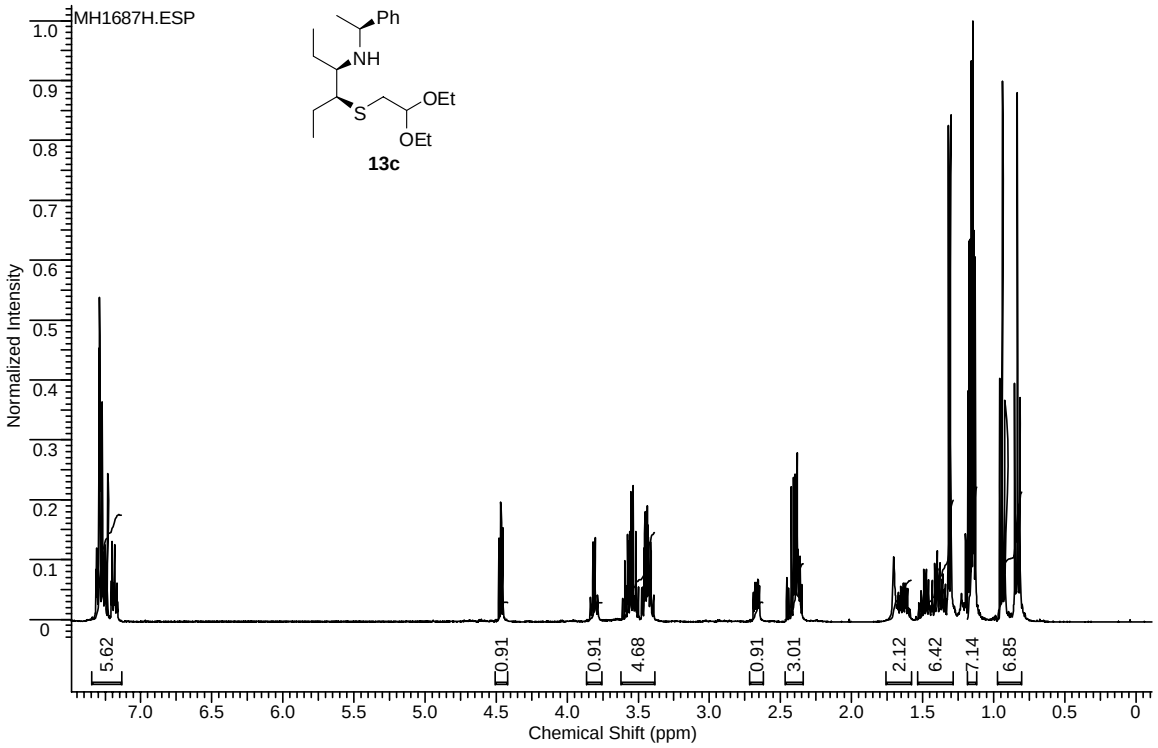


^{13}C NMR (68 MHz, $CDCl_3$)

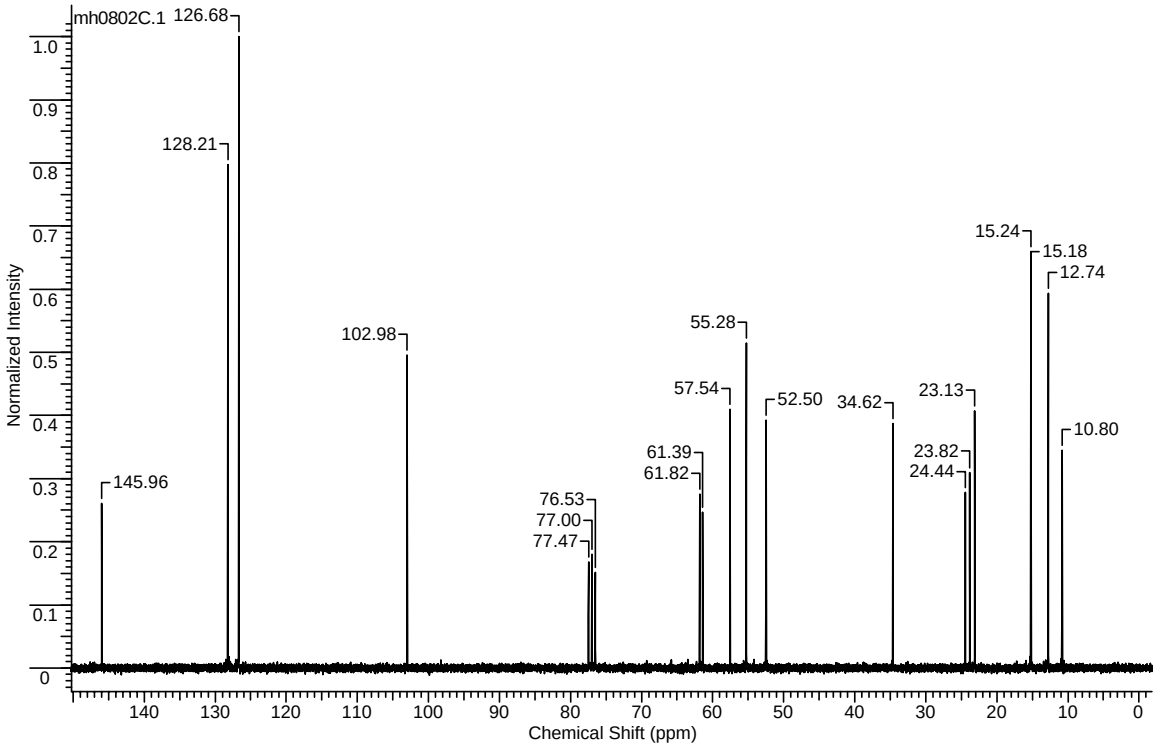


(3*R*,4*S*)-4-[(2,2-Diethoxyethyl)sulfanyl]-*N*-[(1*S*)-1-phenylethyl]-3-hexanamine 13c.

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

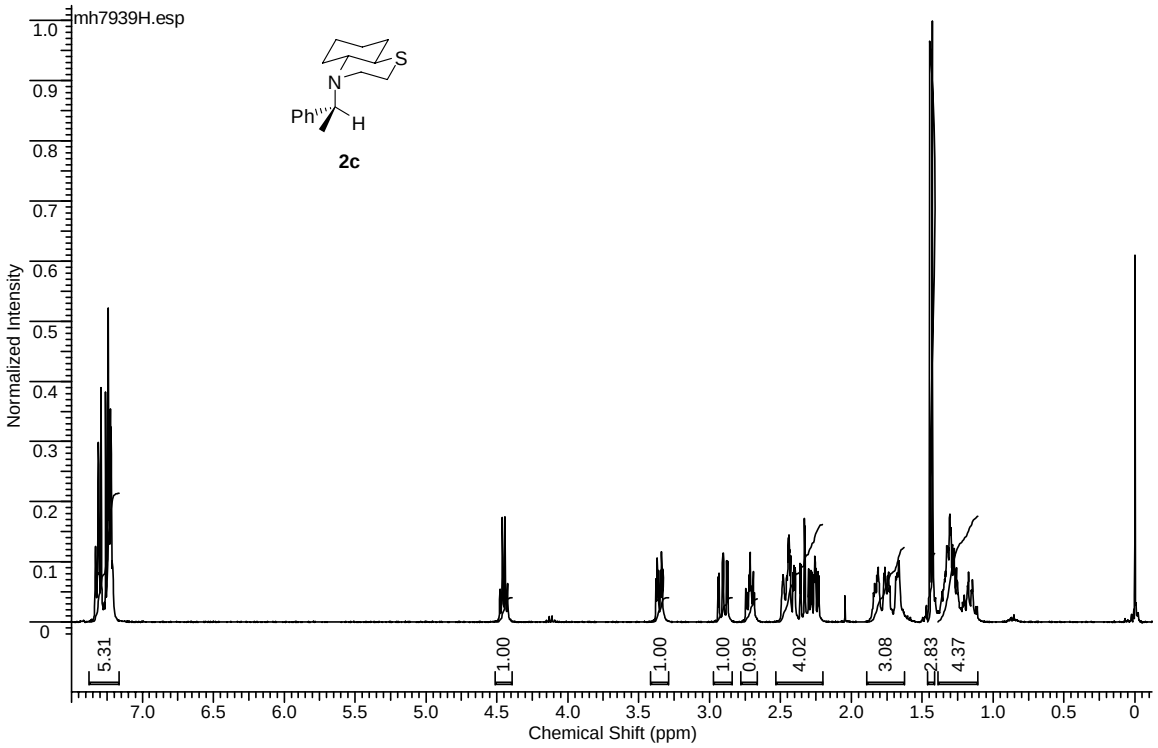


^{13}C NMR (68 MHz, $CDCl_3$)

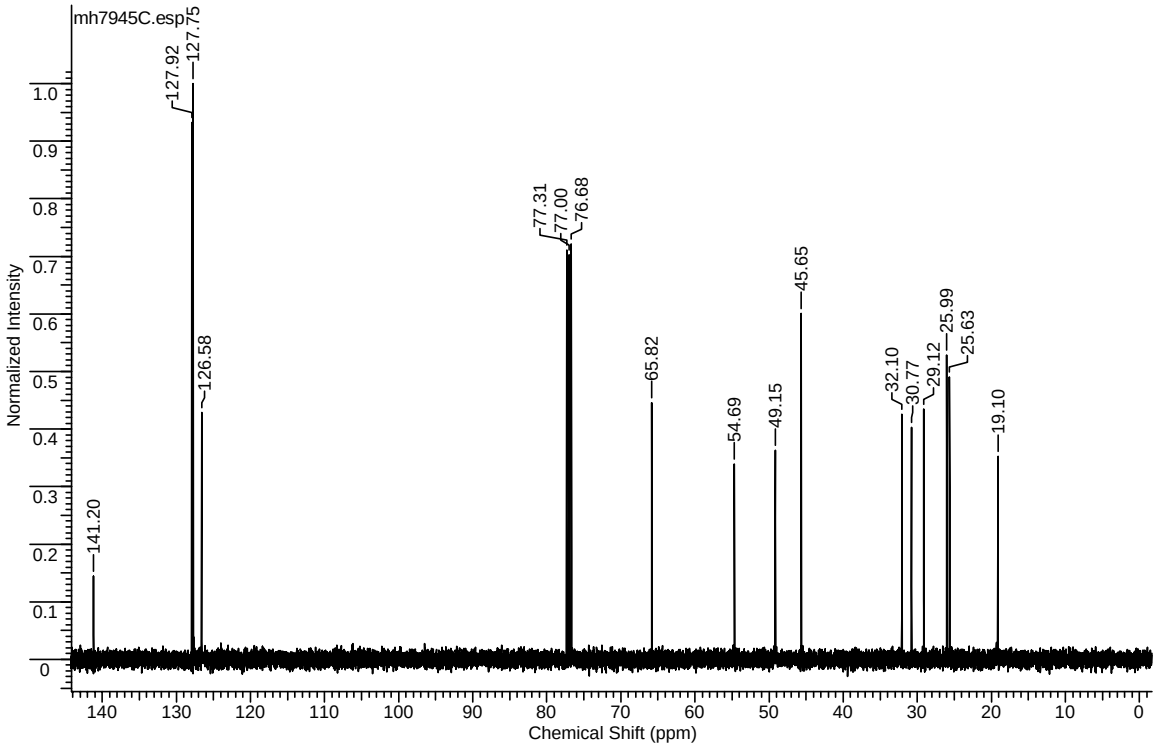


(4a*R*,8a*R*)-4-[(1*S*)-1-Phenylethyl]octahydro-2*H*-1,4-benzothiazine 2c.

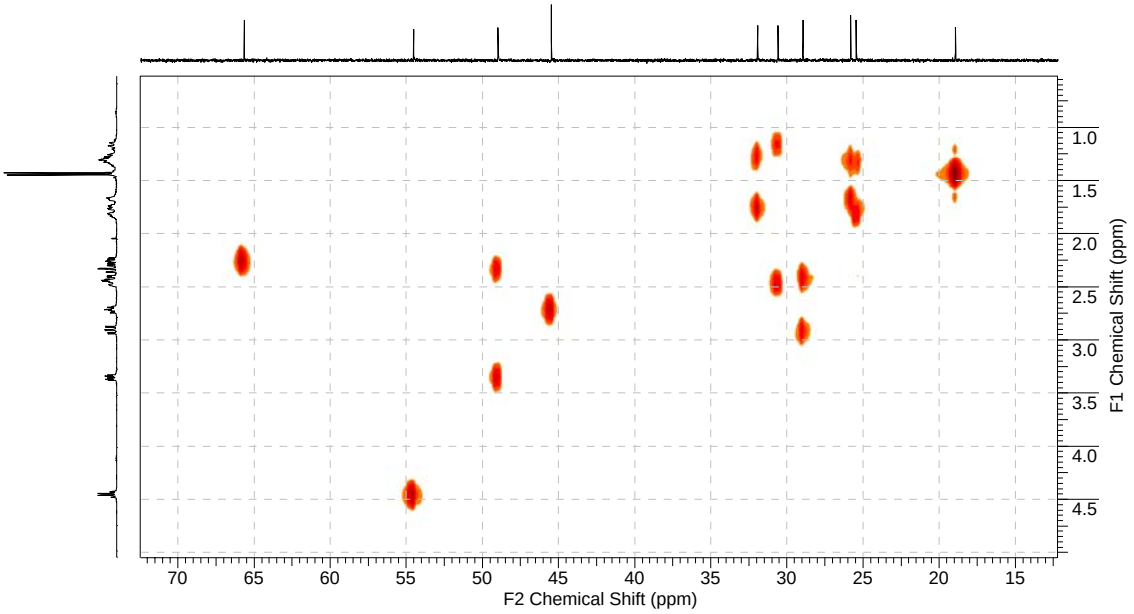
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (100 MHz, $CDCl_3$)



HMQC ($CDCl_3$)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F2 Chemical Shift (ppm)
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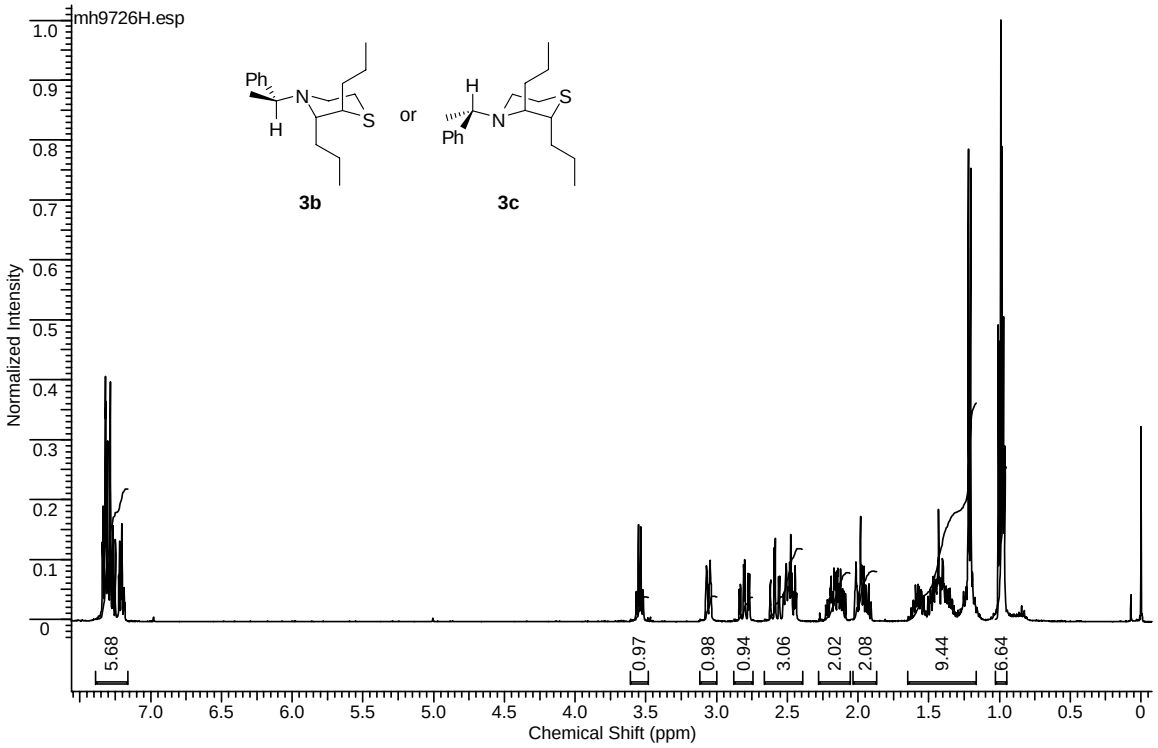
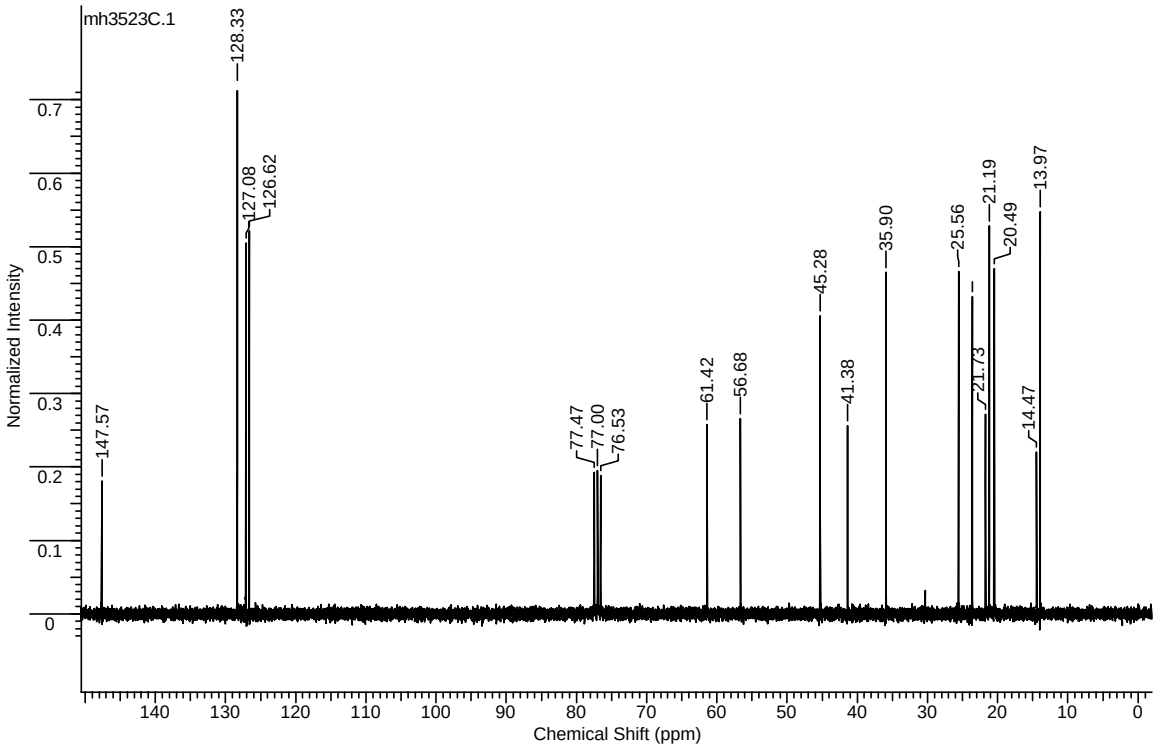
1.5
2.0
2.5
3.0
3.5
4.0
4.5
F1 Chemical Shift (ppm)

(2*R*,3*R*)-4-[(1*S*)-1-Phenylethyl]-2,3-dipropylthiomorpholine or (2*S*,3*S*)-4-[(1*S*)-1-phenylethyl]-2,3-dipropylthiomorpholine 3-d1.

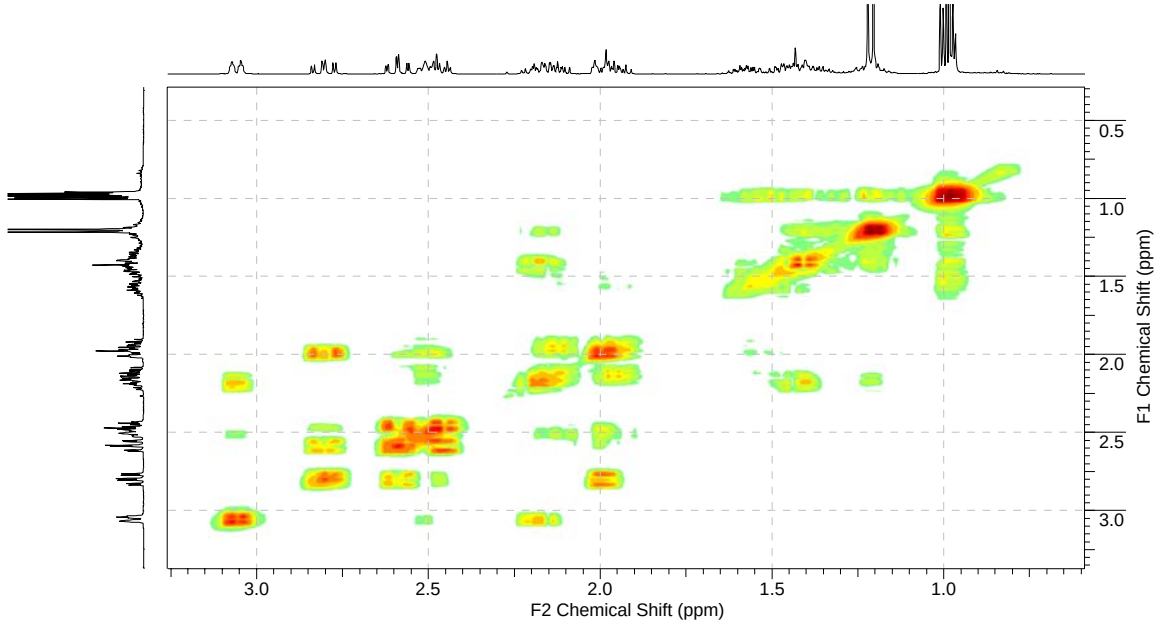
^{1}H NMR (400 MHz, $CDCl_3$)



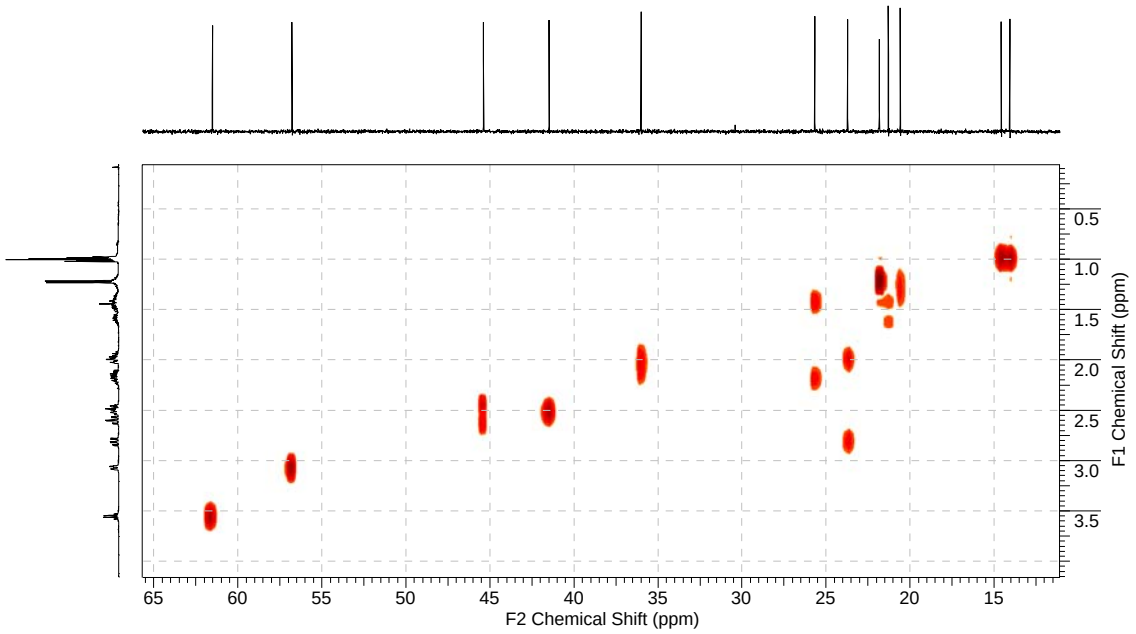
^{13}C NMR (100 MHz, $CDCl_3$)



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

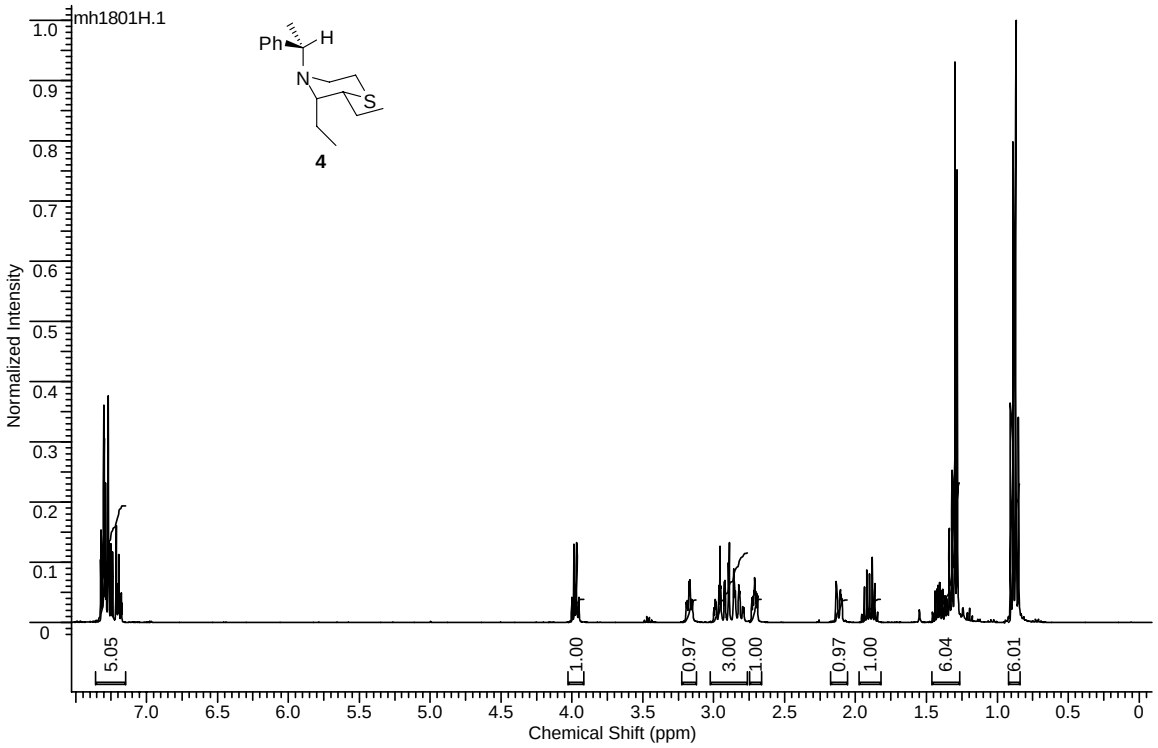


HMQC ($CDCl_3$)

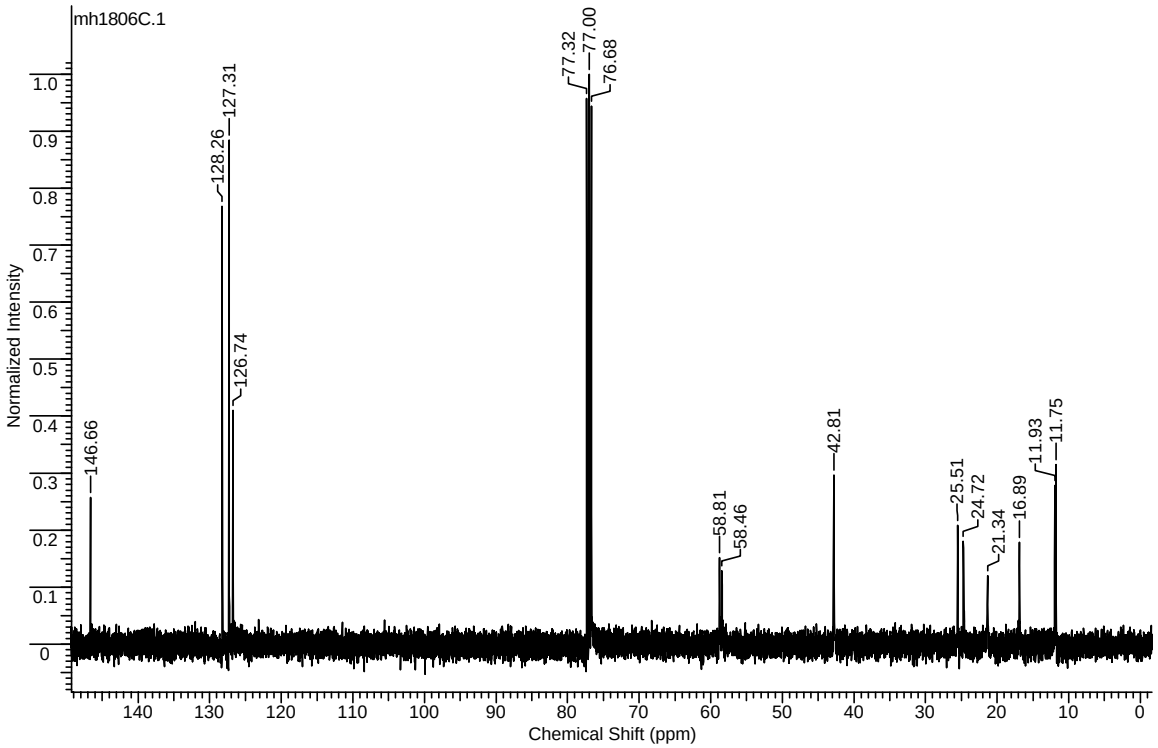


(2*R*,3*S*)-2,3-Diethyl-4-[(1*S*)-1-phenylethyl]thiomorpholine 4

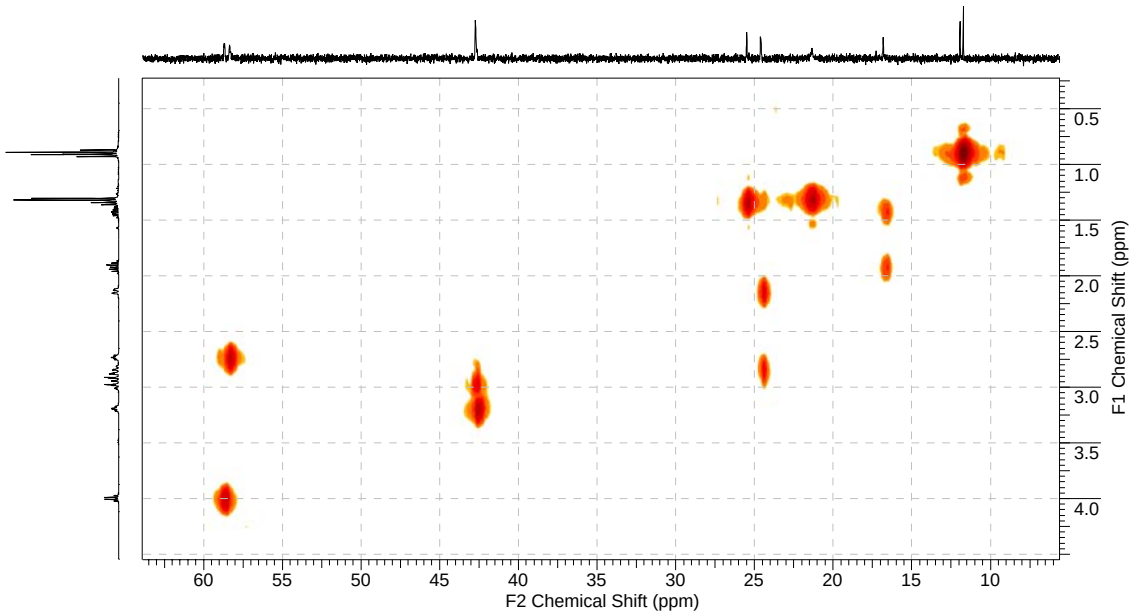
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (100 MHz, $CDCl_3$)



^{1}H-^{13}C ($CDCl_3$)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4.0
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40
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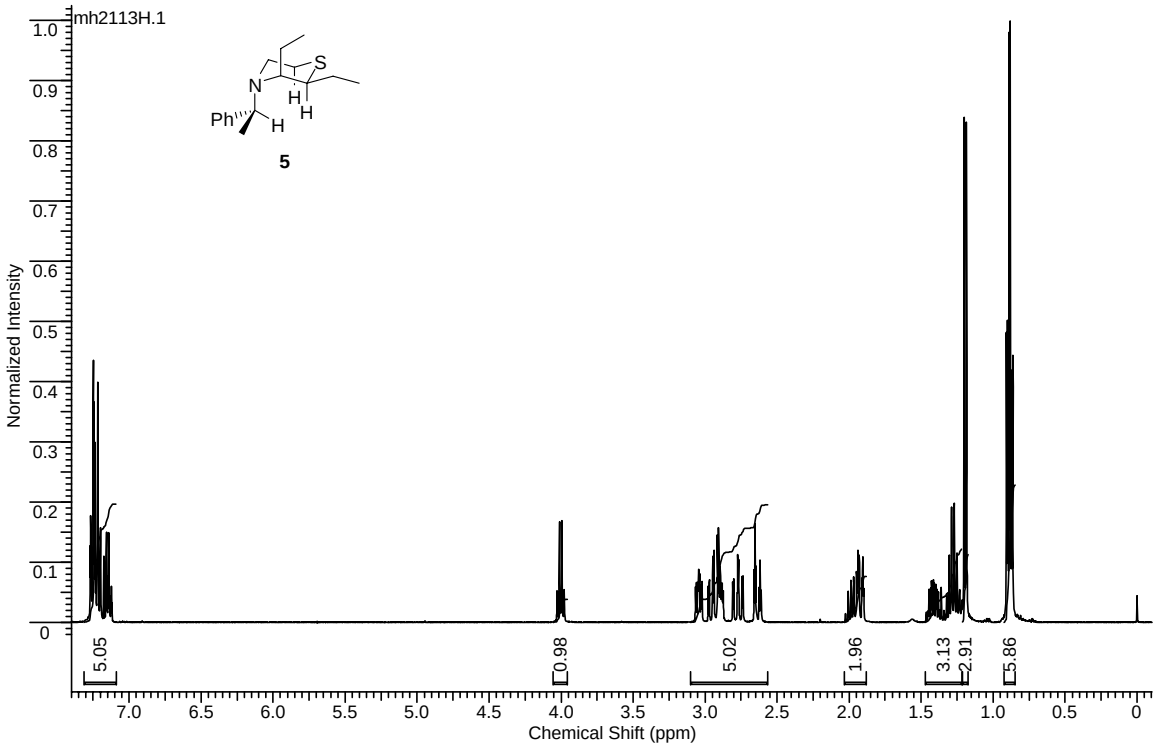
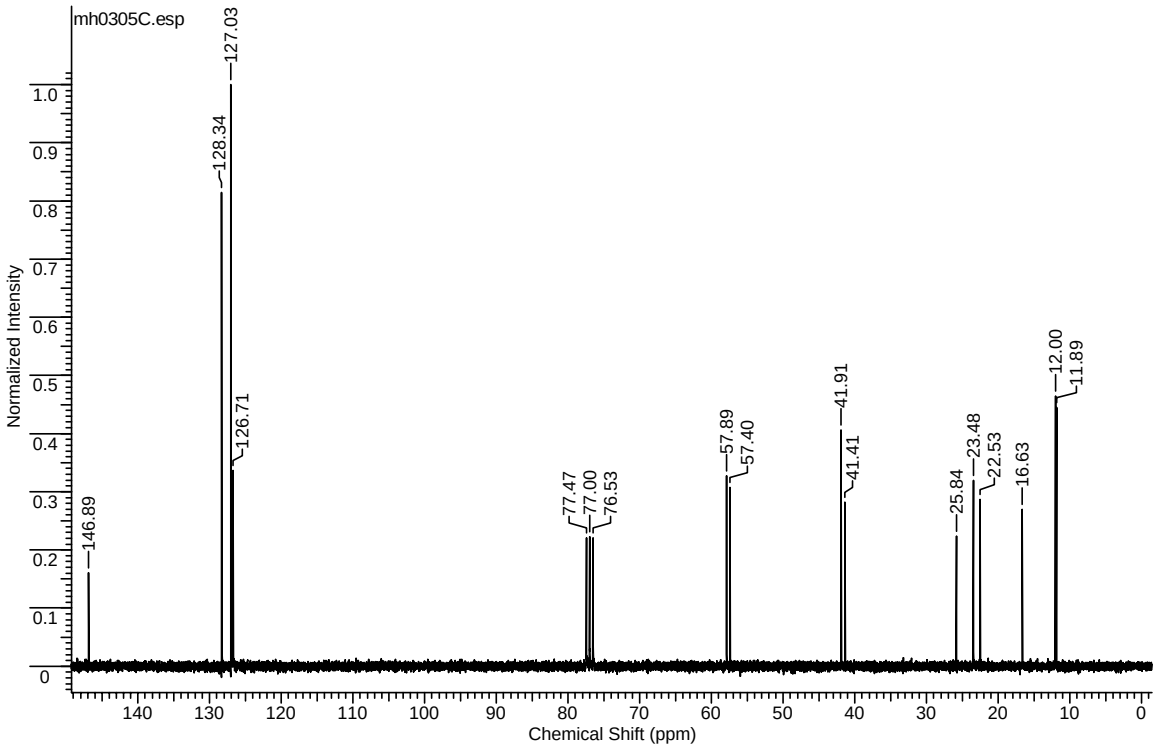
30
25
20
15
10
F2 Chemical Shift (ppm)

(2*S*,3*R*)-2,3-Diethyl-4-[(1*S*)-1-phenylethyl]thiomorpholine 5

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

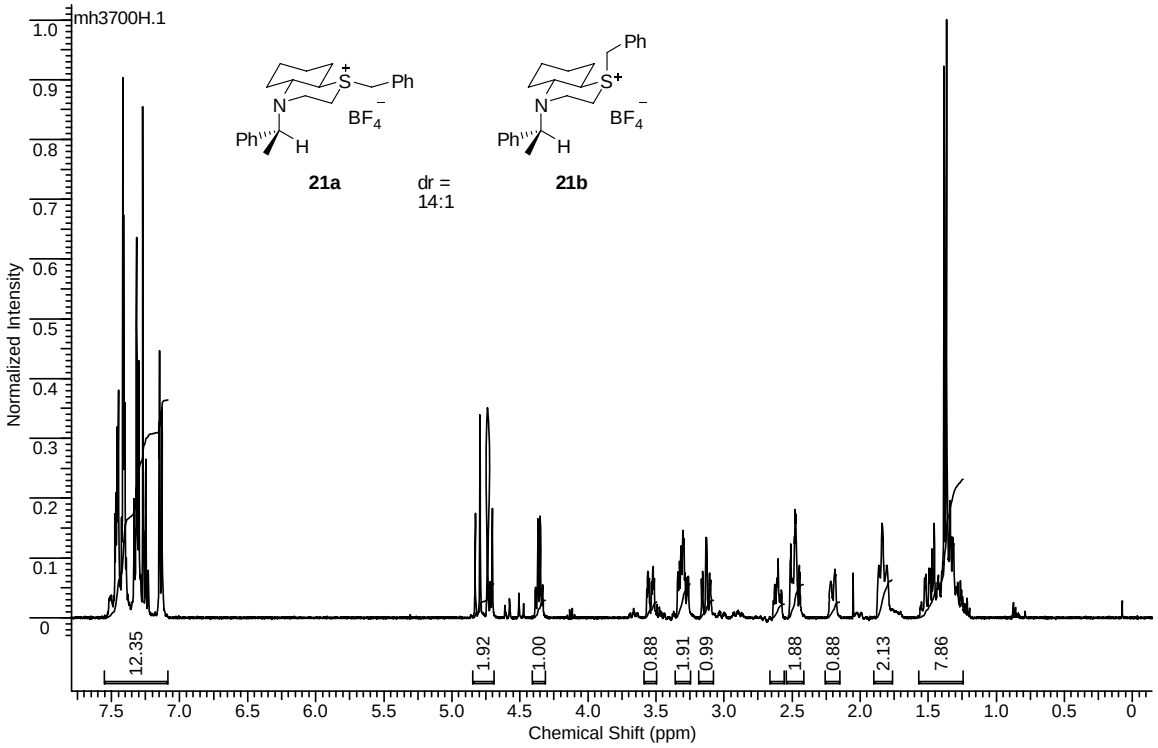


^{13}C NMR (68 MHz, $CDCl_3$)

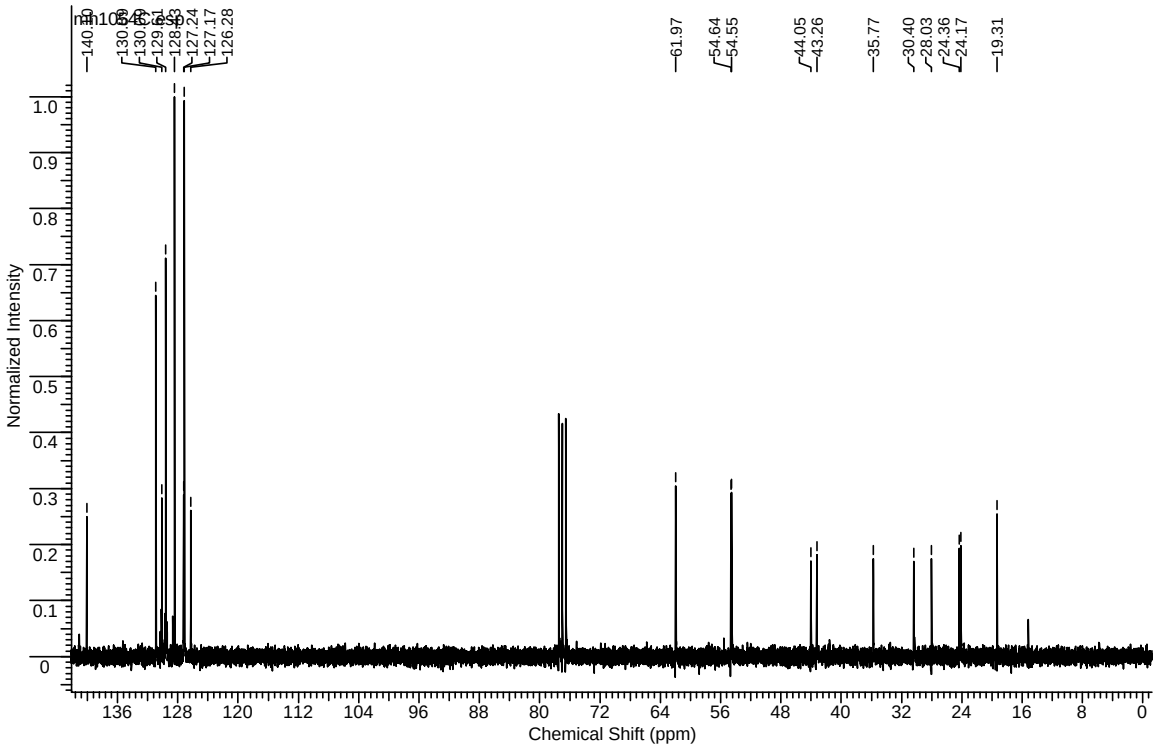


(1*R*,4a*R*,8a*R*)-1-Benzyl-4-[(1*S*)-1-phenylethyl]octahydro-2*H*-1,4-benzothiazin-1-ium tetrafluoroborate 21a and **(1*S*,4a*R*,8a*R*)-1-benzyl-4-[(1*S*)-1-phenylethyl]octahydro-2*H*-1,4-benzothiazin-1-ium tetrafluoroborate 21b**

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

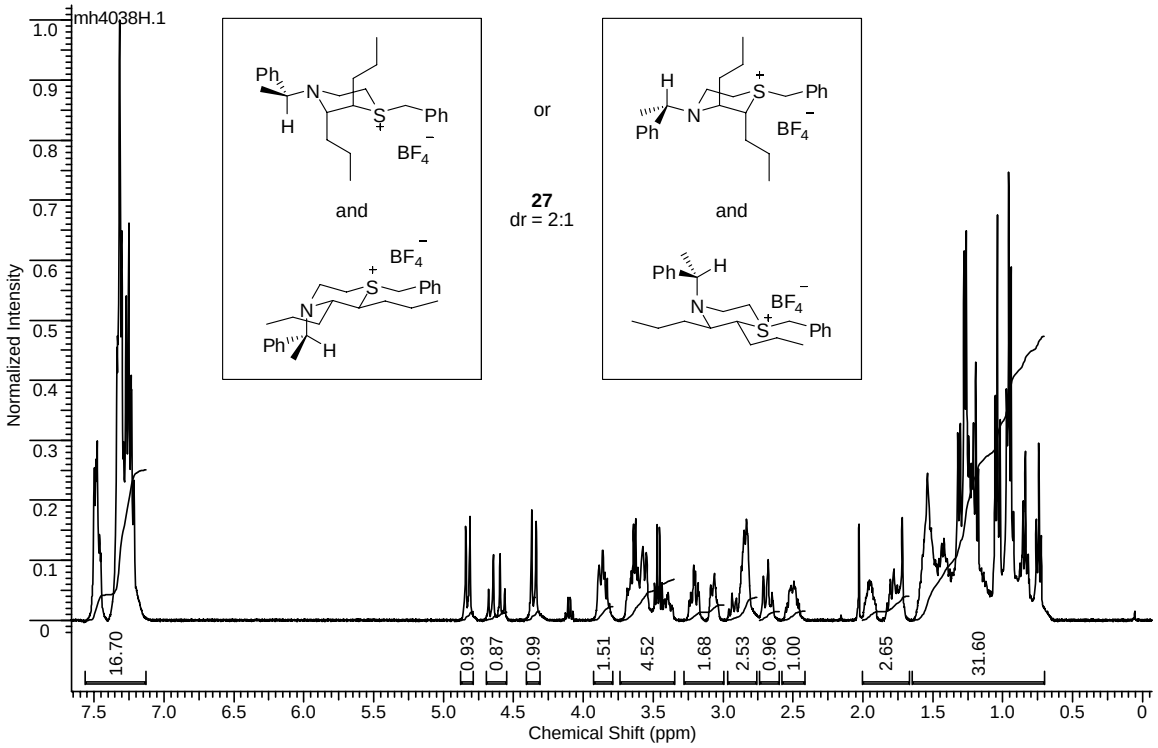


^{13}C NMR (68 MHz, $CDCl_3$)

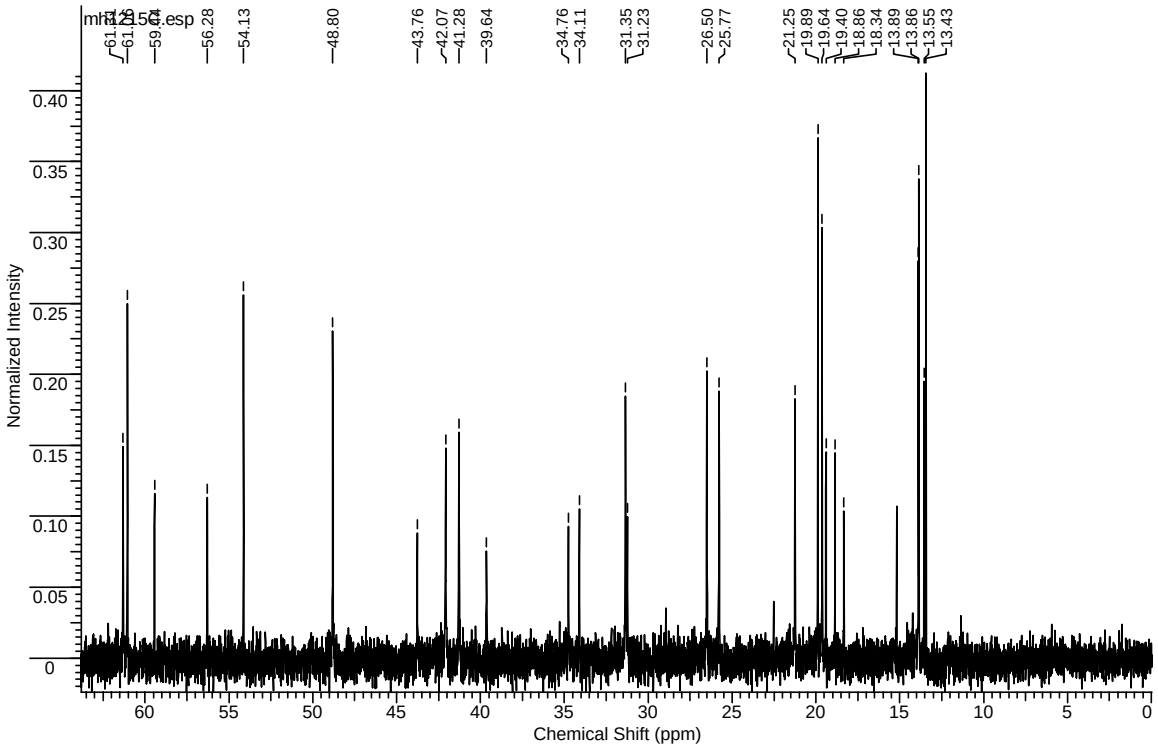


(1*R*,2*R*,3*R*) and (1*S*,2*R*,3*R*), or (1*S*,2*S*,3*S*) and (1*R*,2*S*,3*S*)-1-Benzyl-4-[(1*S*)-1-phenylethyl]-2,3-dipropylthiomorpholin-1-ium tetrafluoroborate 27

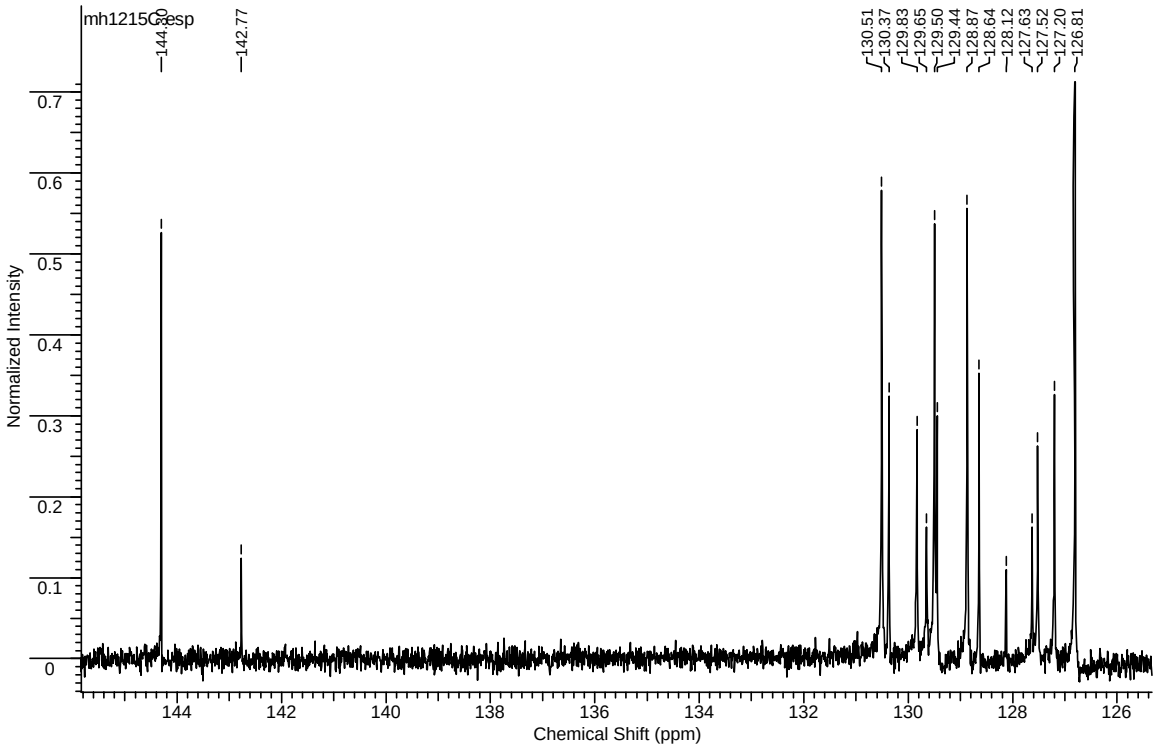
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (68 MHz, $CDCl_3$)

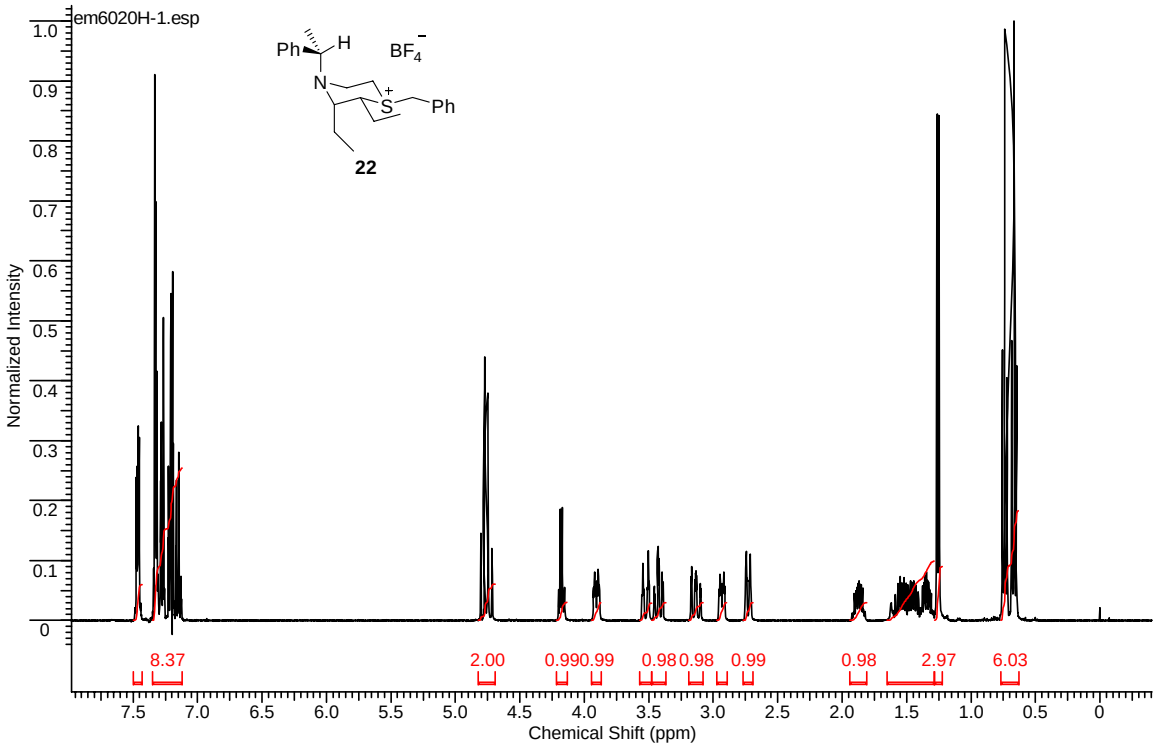


^{13}C NMR (68 MHz, $CDCl_3$)

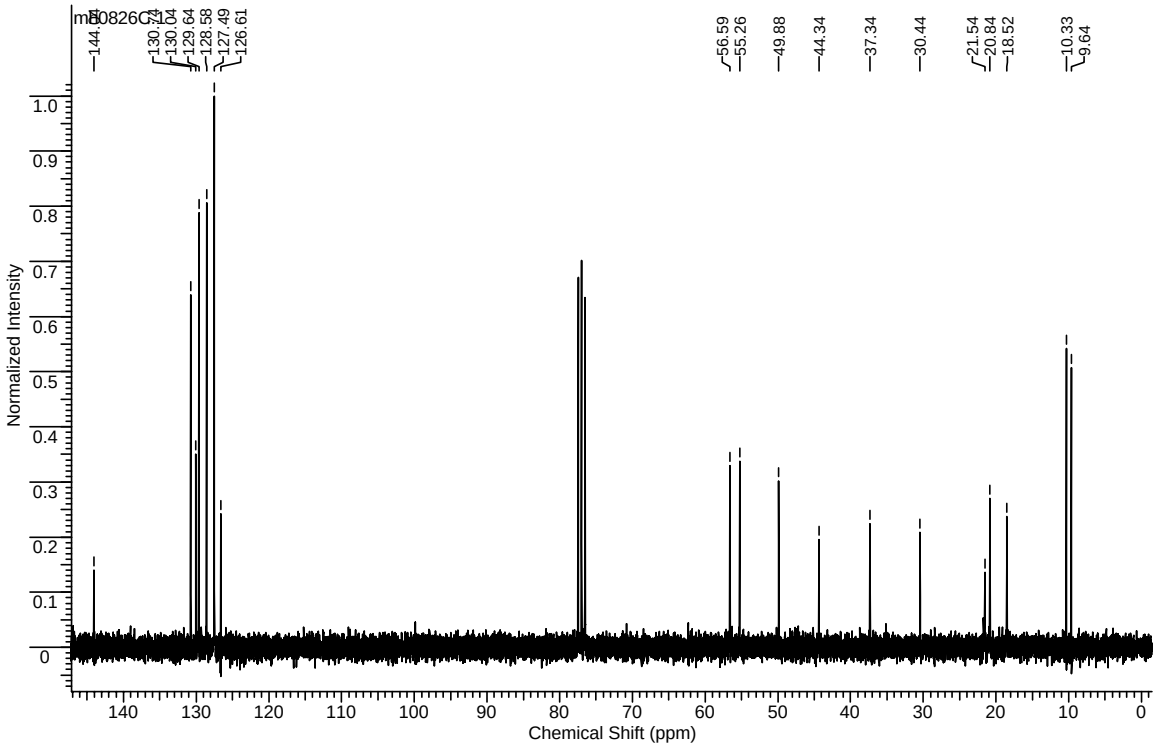


(1*R*,2*R*,3*S*)-1-Benzyl-2,3-diethyl-4-[(1*S*)-1-phenylethyl]thiomorpholin-1-ium tetrafluoroborate 22.

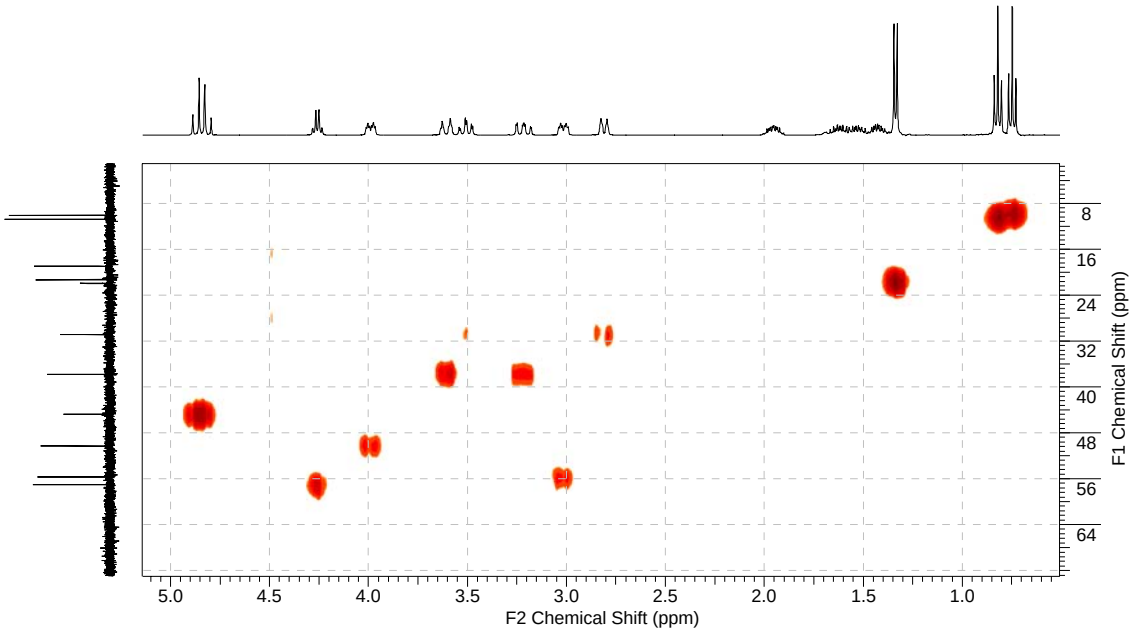
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (68 MHz, $CDCl_3$)



HMQC ($CDCl_3$)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1.5
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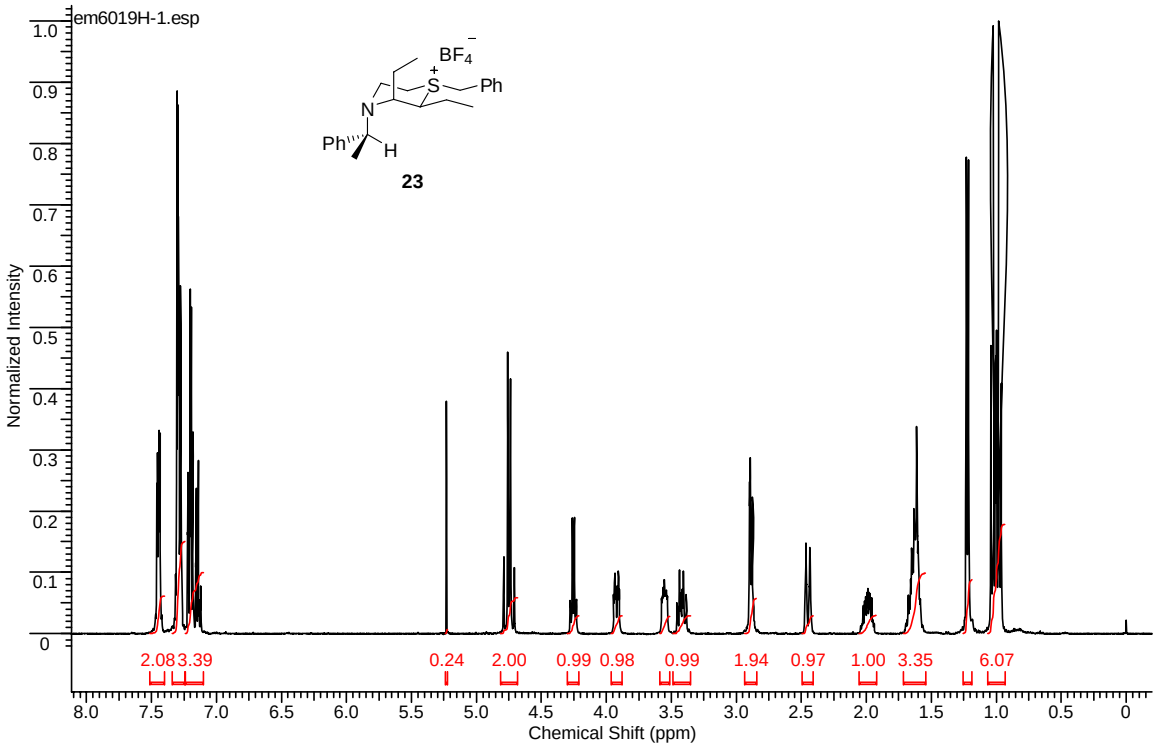
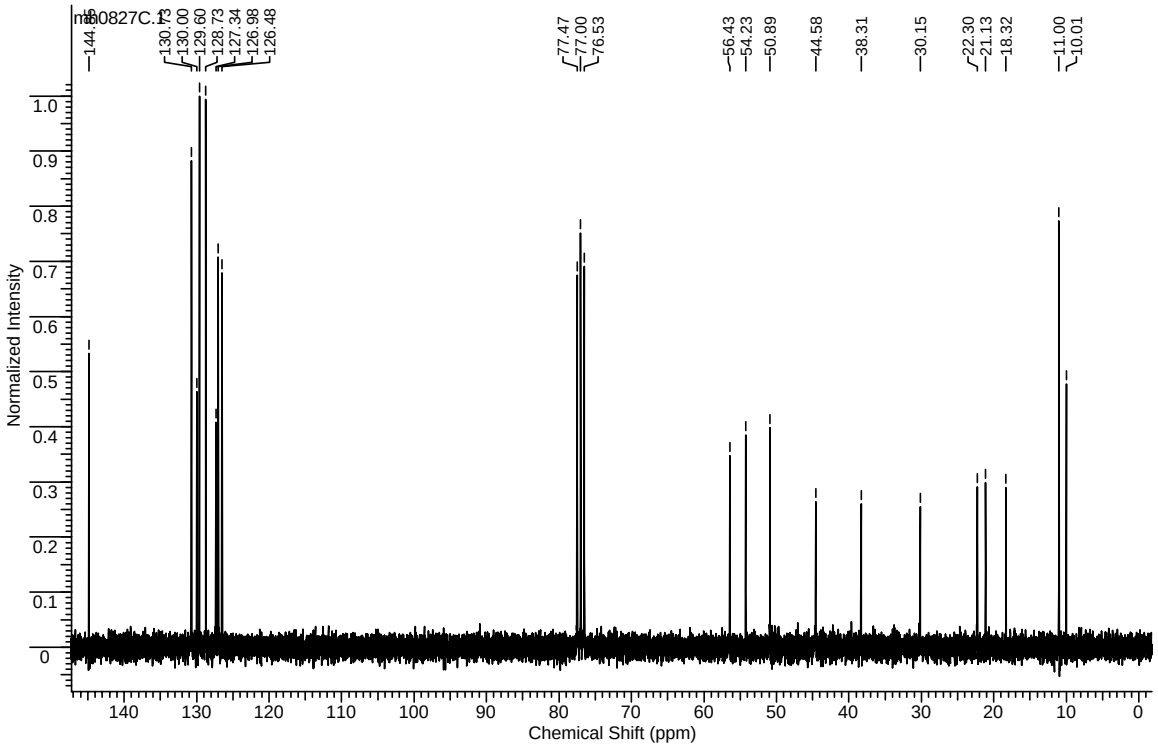
F2 Chemical Shift (ppm)

(1*S*,2*S*,3*R*)-1-Benzyl-2,3-diethyl-4-[(1*S*)-1-phenylethyl]thiomorpholin-1-ium tetrafluoroborate 23

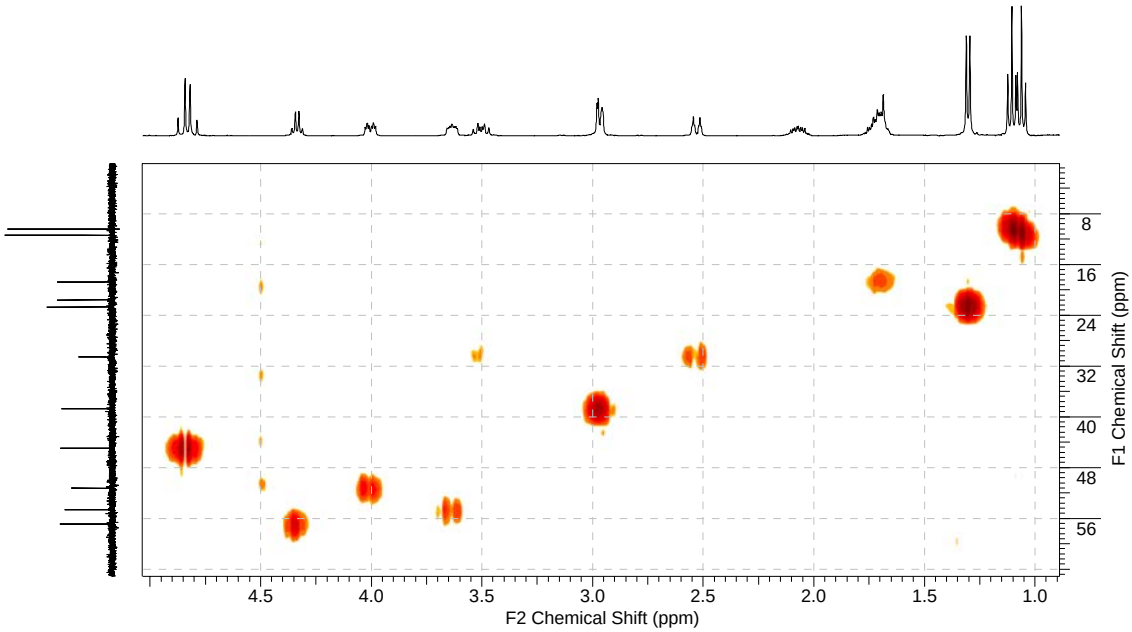
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (68 MHz, $CDCl_3$)



HMQC ($CDCl_3$)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F1 Chemical Shift (ppm)
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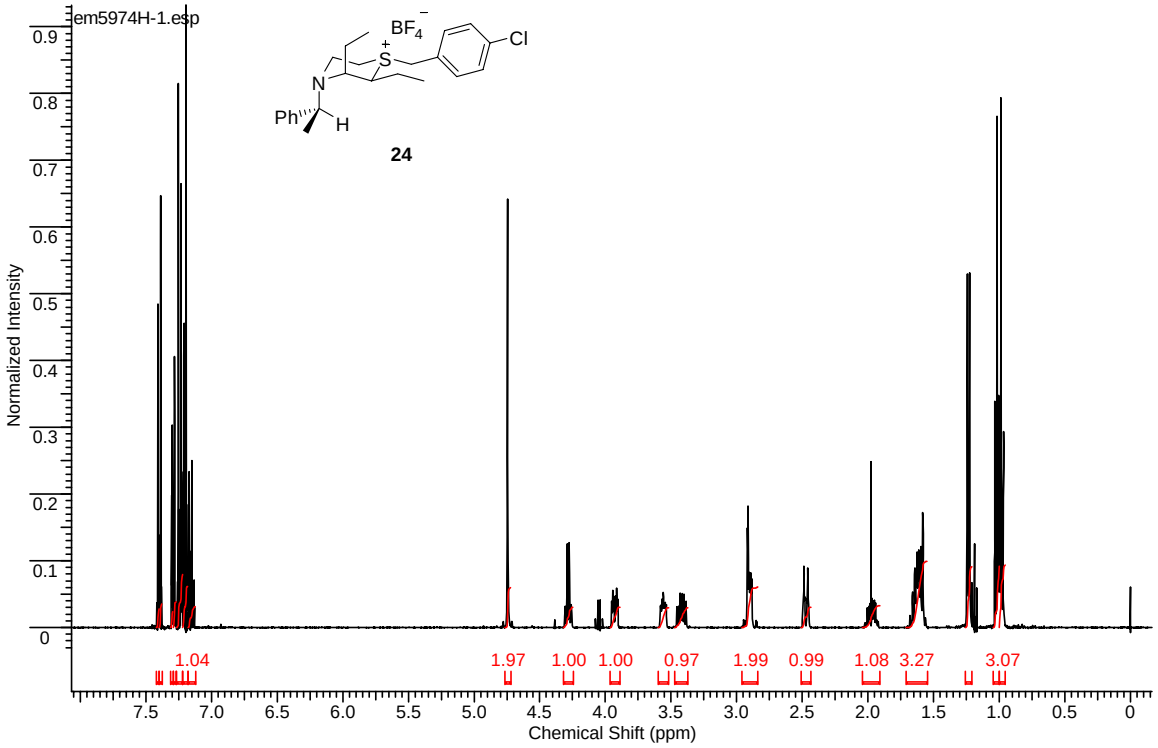
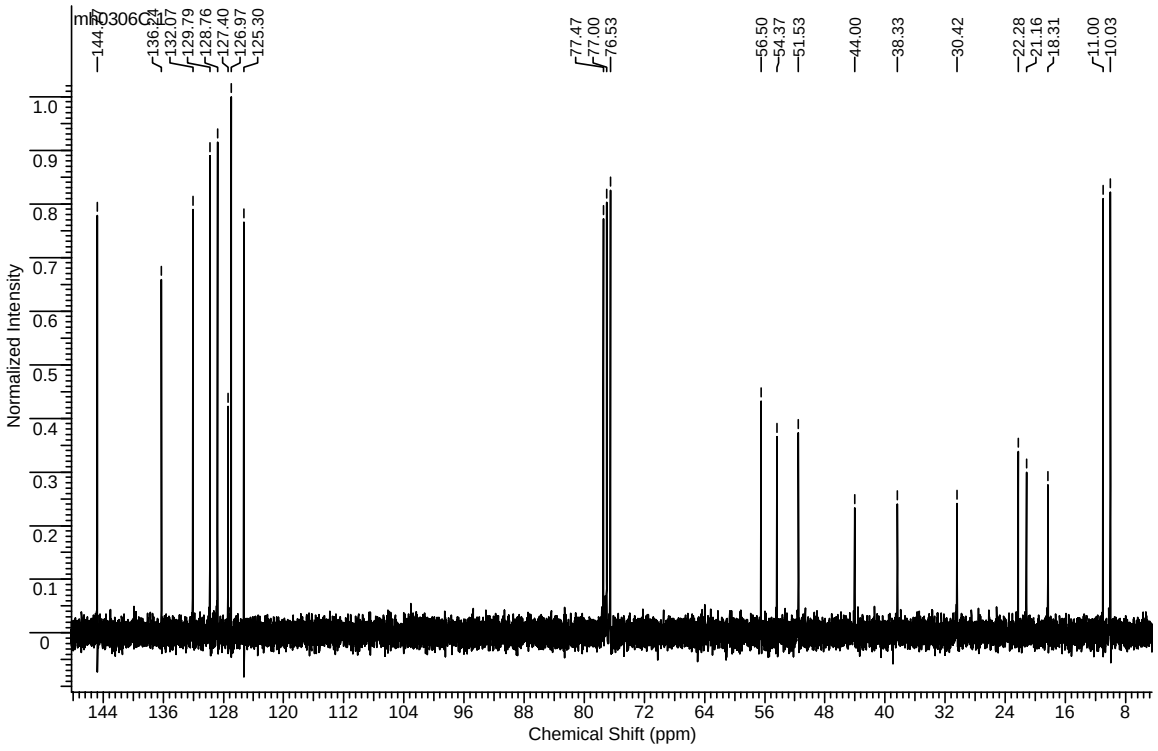
1.5
1.0
F2 Chemical Shift (ppm)

(1*S*,2*S*,3*R*)-1-(4-Chlorobenzyl)-2,3-diethyl-4-[(1*S*)-1-phenylethyl]thiomorpholin-1-ium tetrafluoroborate 24

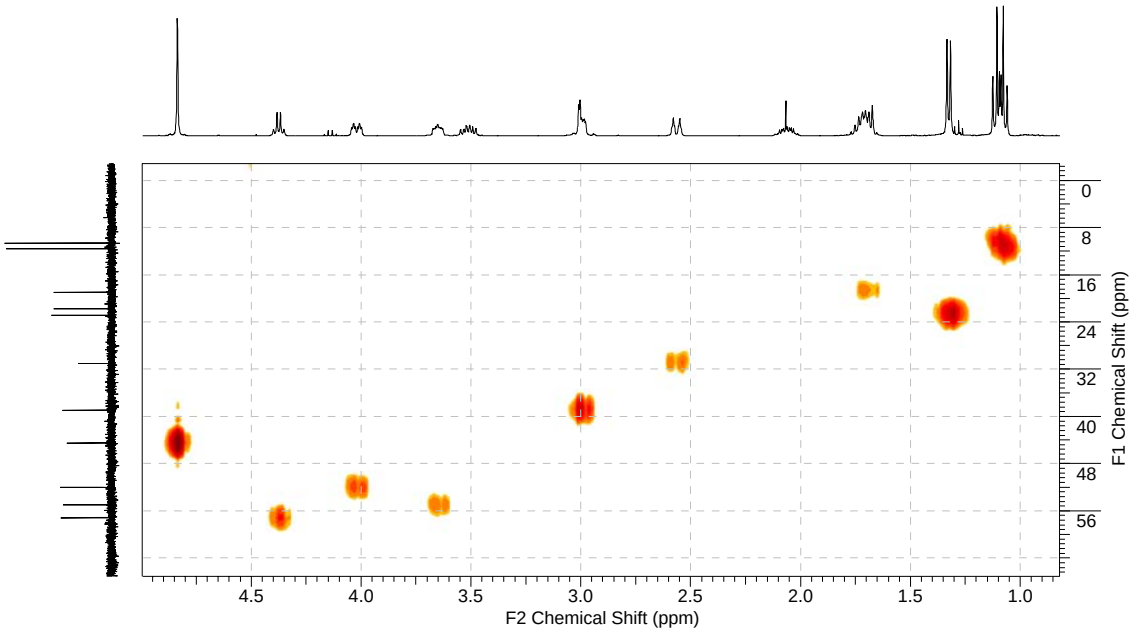
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (68 MHz, $CDCl_3$)



HMQC ($CDCl_3$)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F1 Chemical Shift (ppm)
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3.5
3.0
2.5
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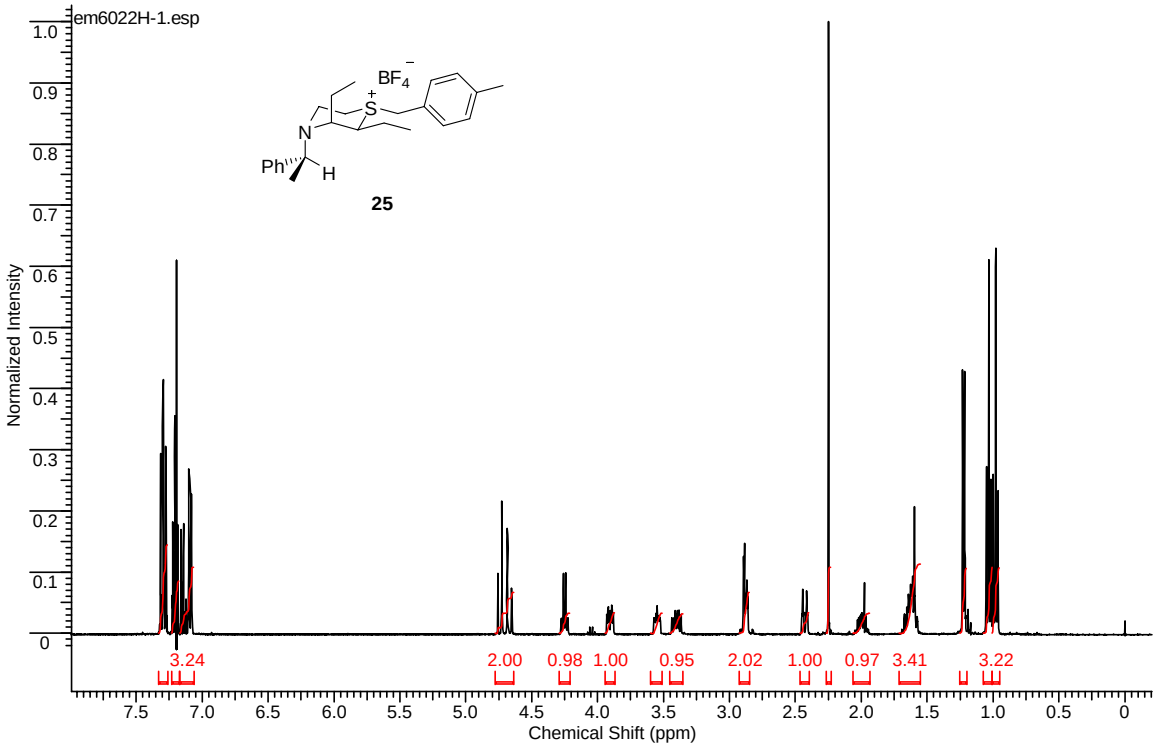
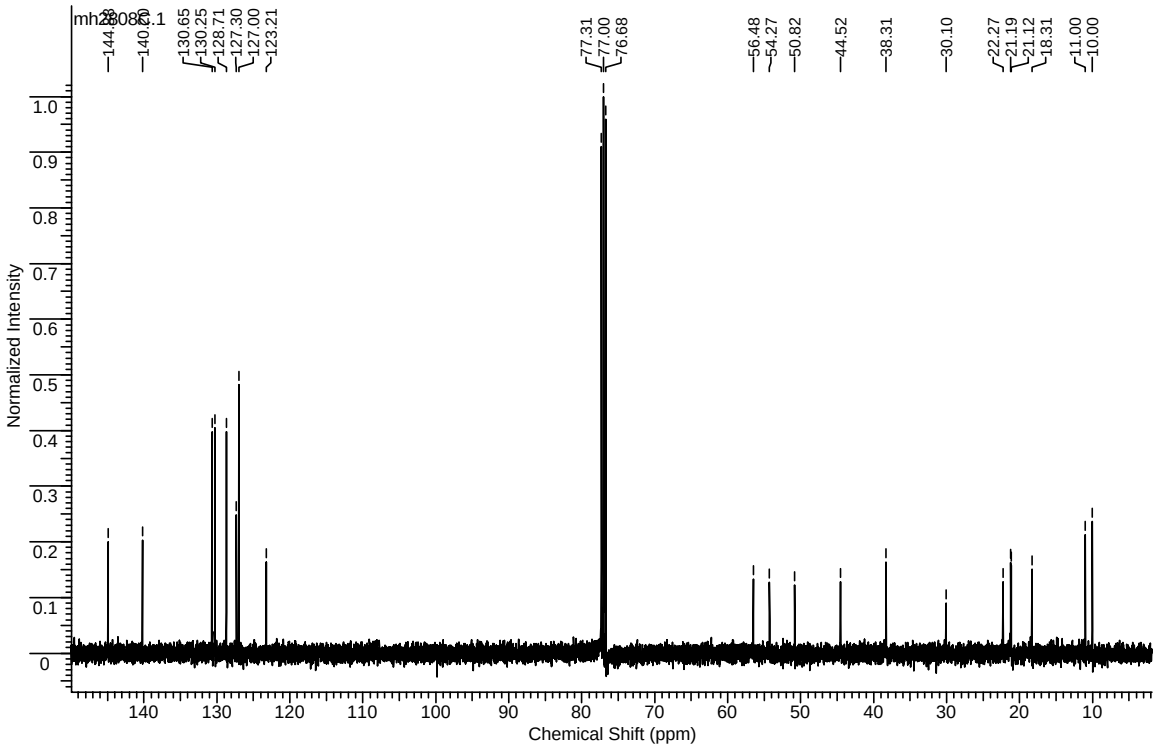
1.5
1.0
F2 Chemical Shift (ppm)

(1*S*,2*S*,3*R*)-2,3-Diethyl-1-(4-methylbenzyl)-4-[(1*S*)-1-phenylethyl]thiomorpholin-1-ium tetrafluoroborate 25

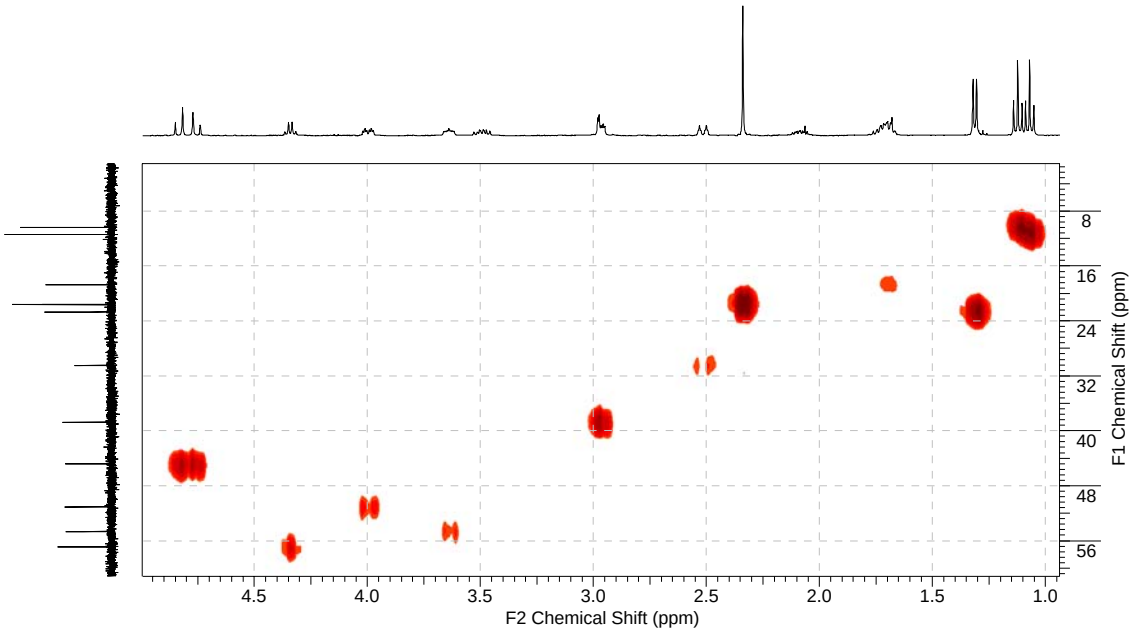
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (100 MHz, $CDCl_3$)



HMQC ($CDCl_3$)


8
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56
F1 Chemical Shift (ppm)
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4.0
3.5
3.0
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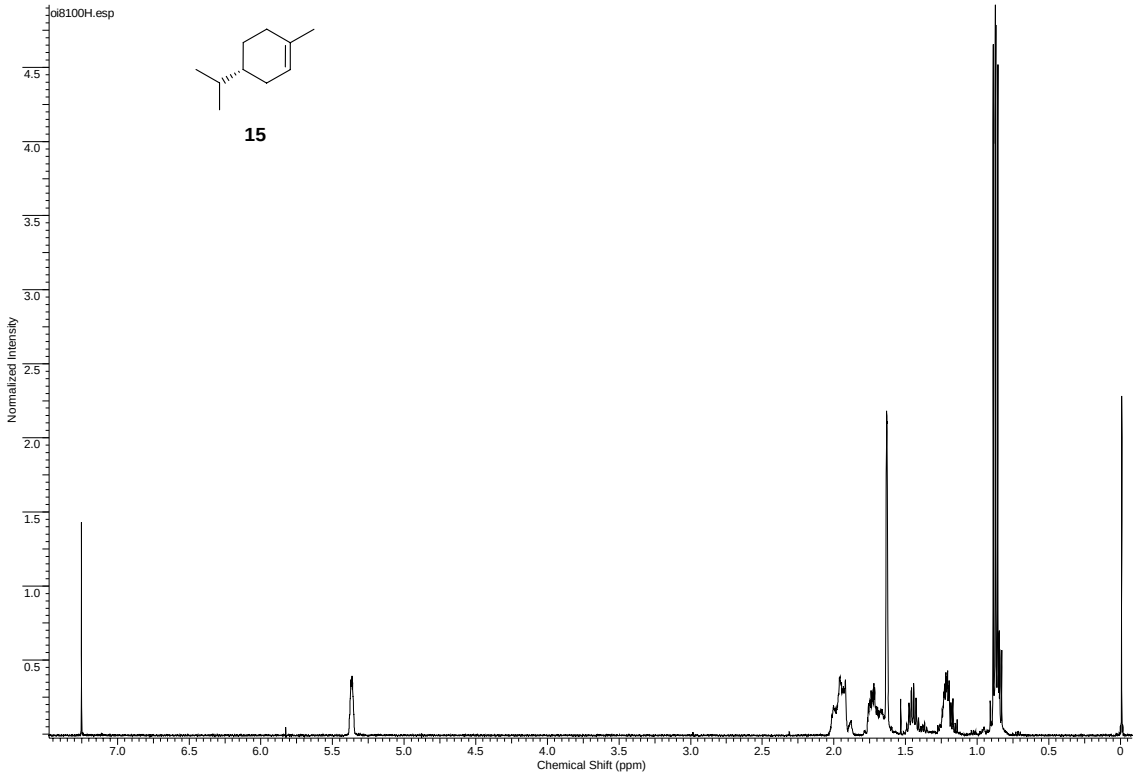
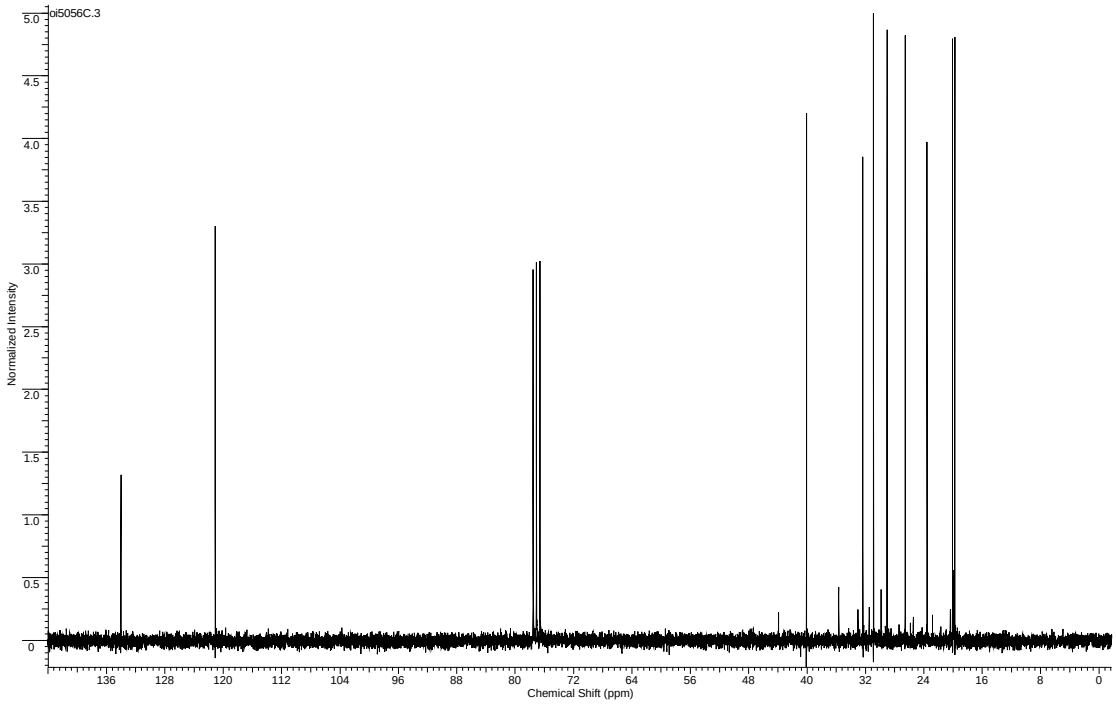
1.5
1.0
F2 Chemical Shift (ppm)

(*R*)-Menthene (15)

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

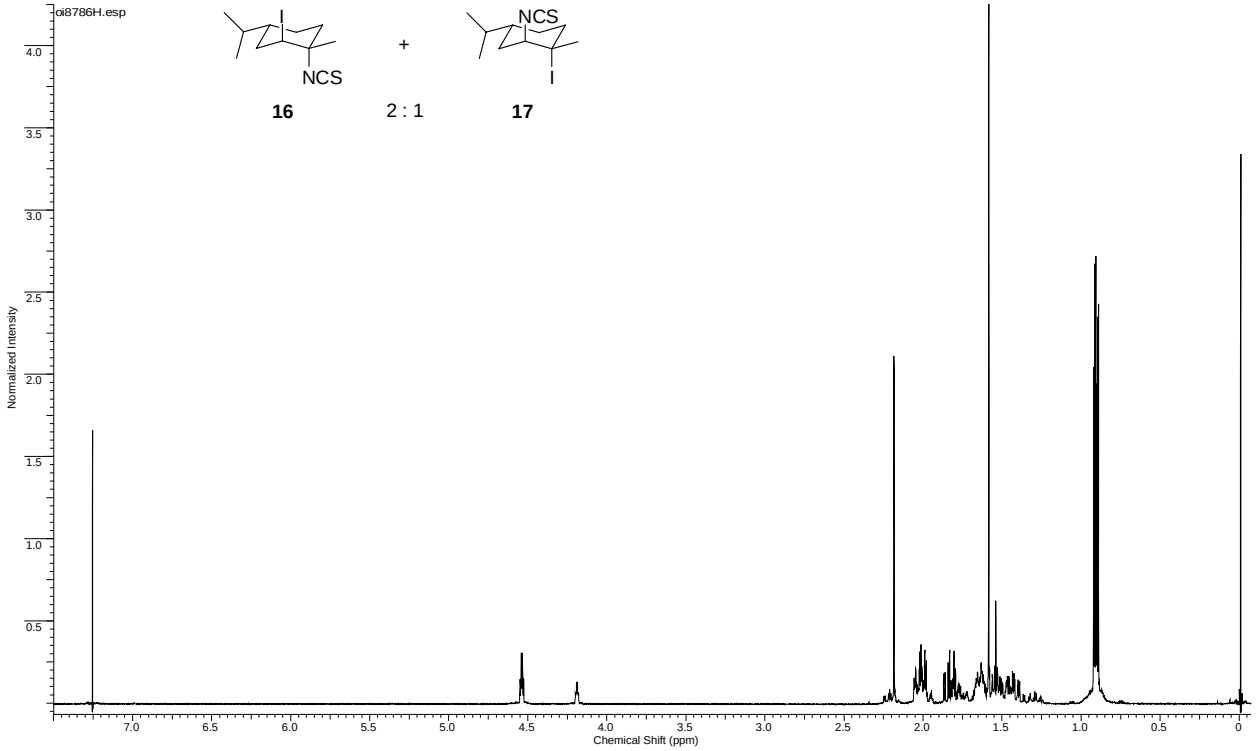


^{13}C NMR (67.5 MHz, $CDCl_3$)



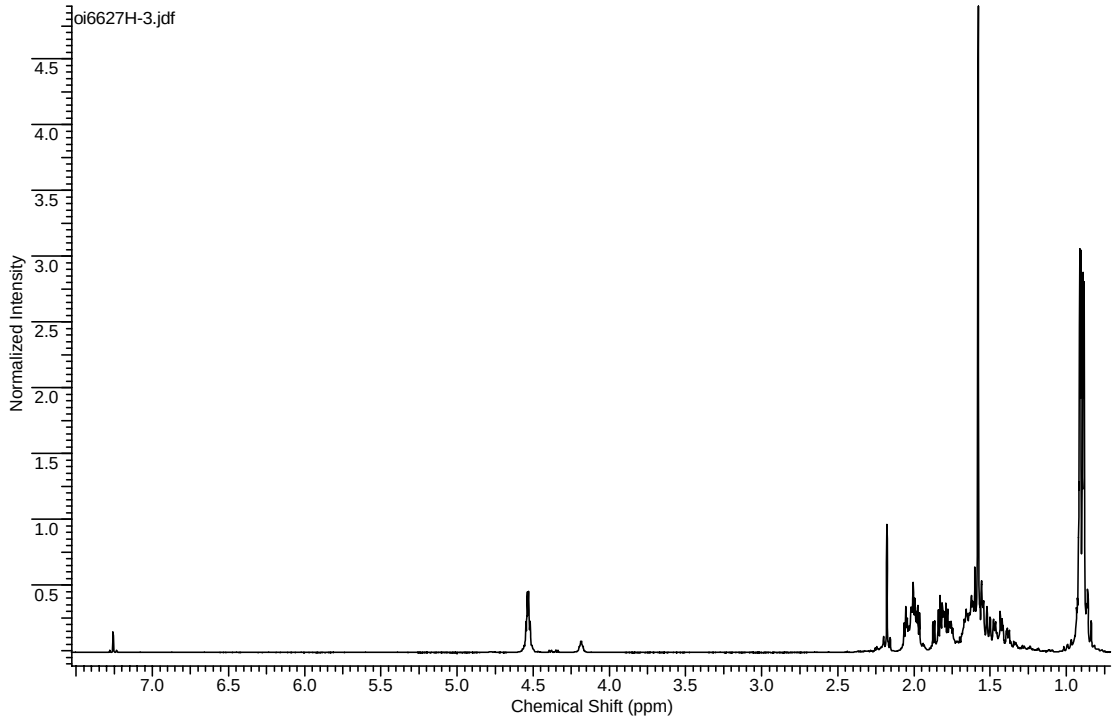
(1*S*,2*S*,4*R*)-2-Iodo-4-isopropyl-1-isothiocyanato-1-methylcyclohexane 16 and **(1*S*,2*S*,4*R*)-1-iodo-4-isopropyl-2-isothiocyanato-1-methylcyclohexane 17**

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

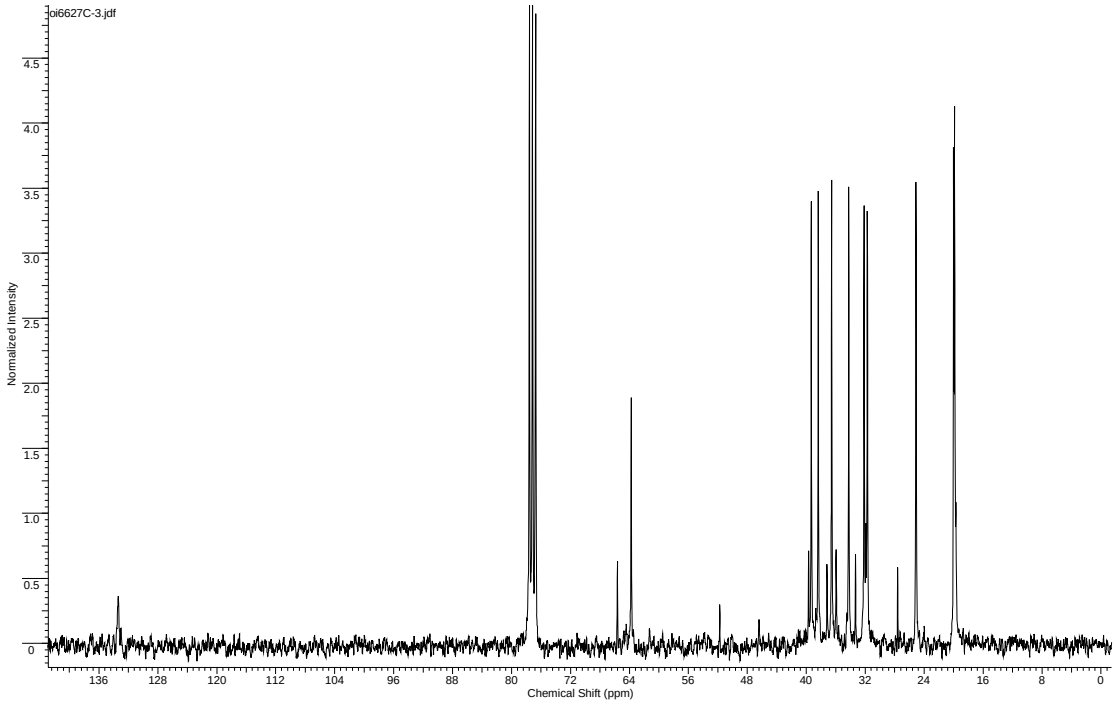


After Kugel-Rohr distillation:

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

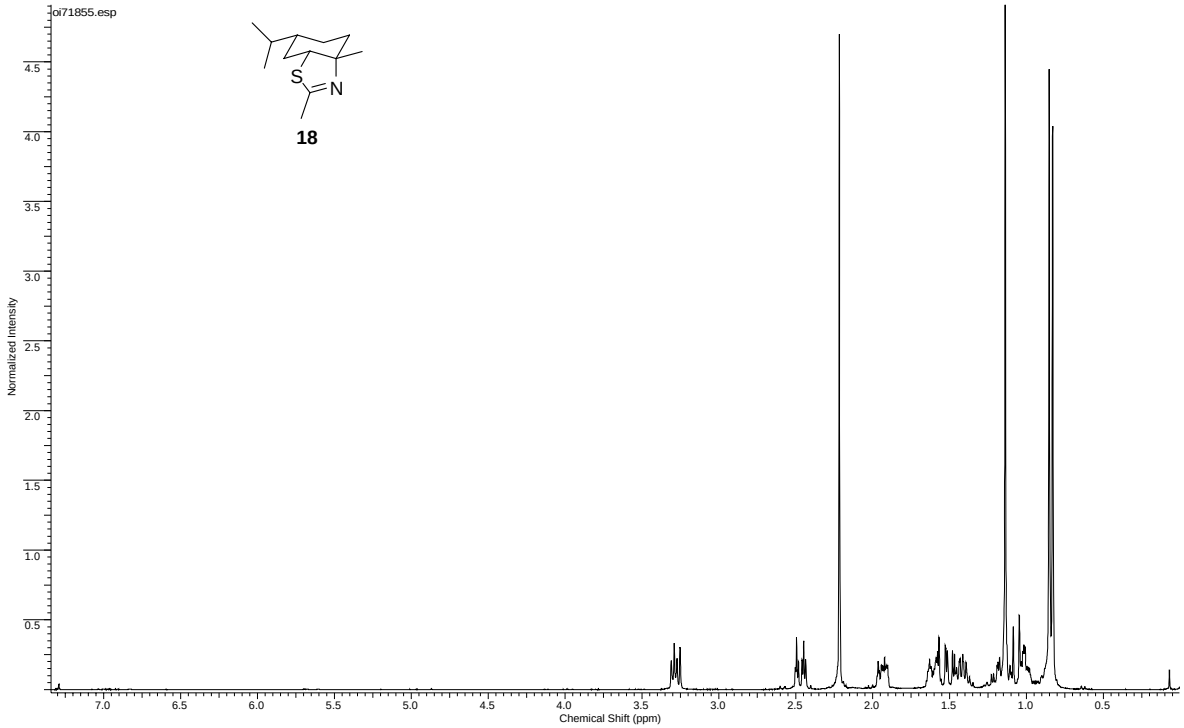


^{13}C NMR (75 MHz, $CDCl_3$)

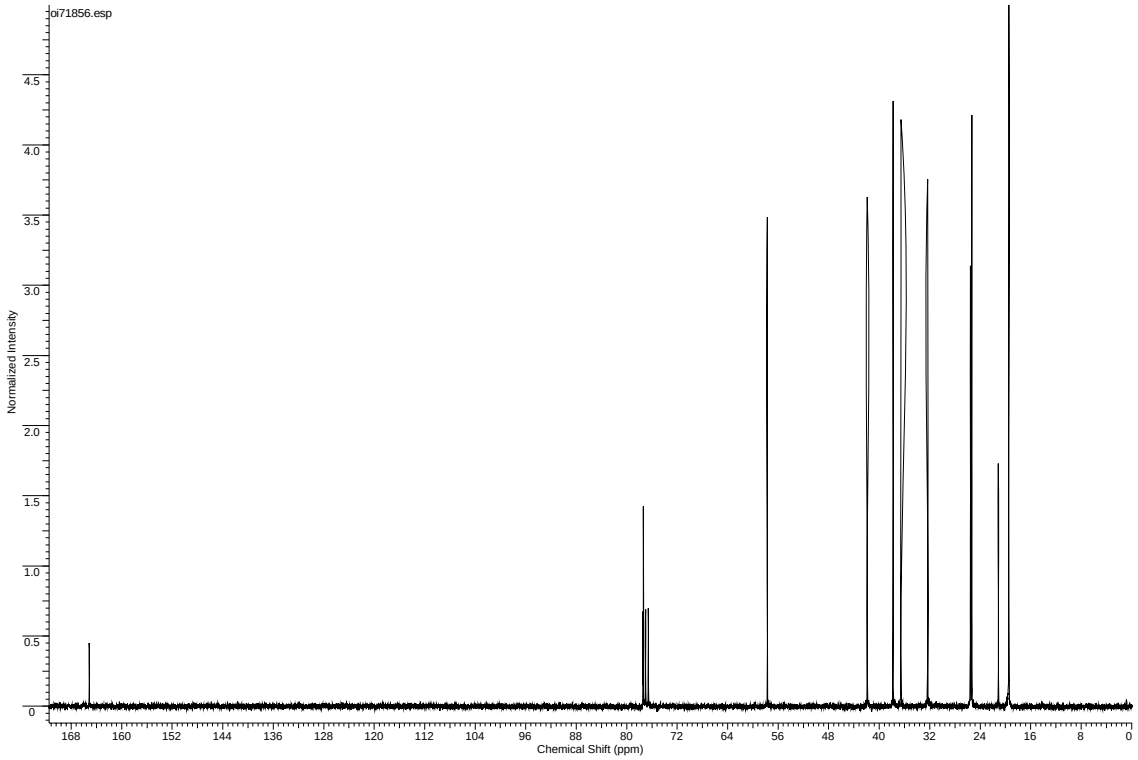


(3a*S*,6*R*,7a*R*)-6-isopropyl-2,3a-dimethyl-3a,4,5,6,7,7a-hexahydro-1,3-benzothiazole 18

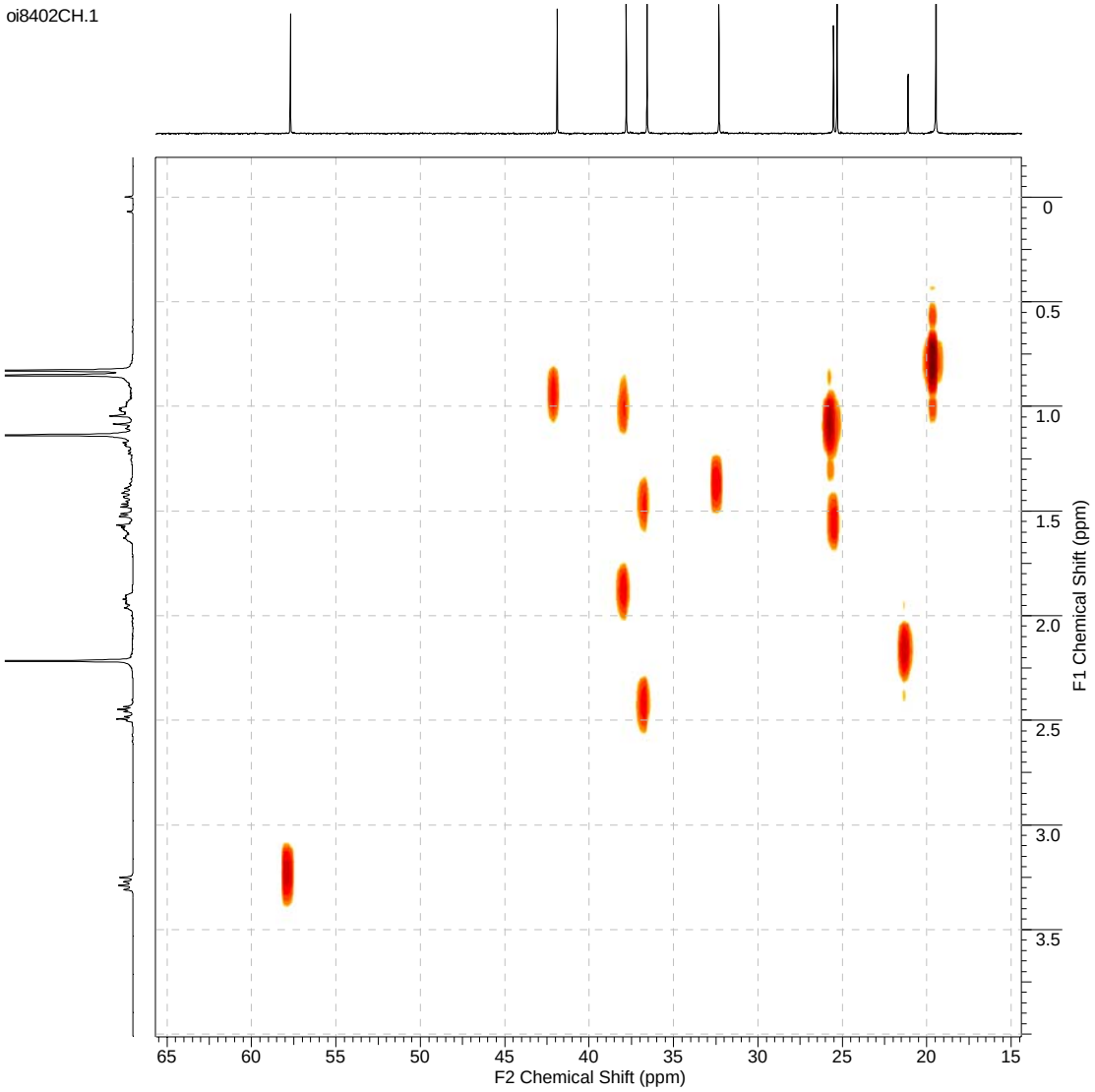
^{1}H NMR (500 MHz, $CDCl_3$)



^{13}C NMR (100 MHz, $CDCl_3$)

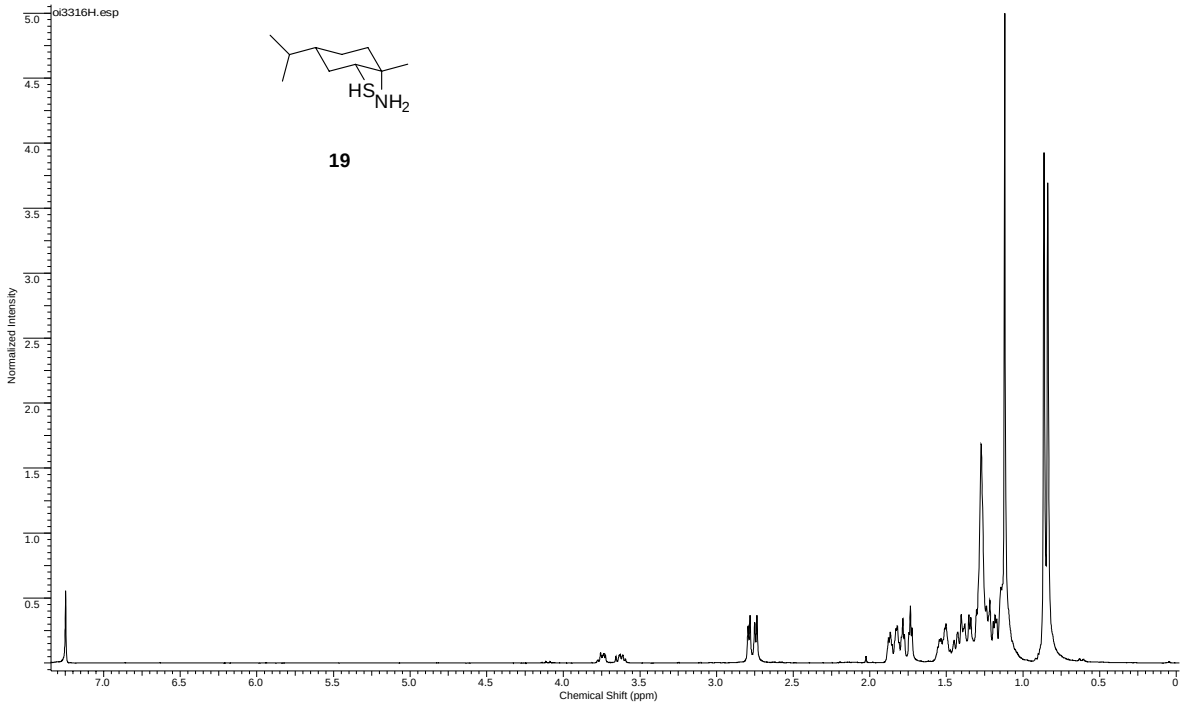


HMQC (400 MHz for ^{1}H NMR, $CDCl_3$)

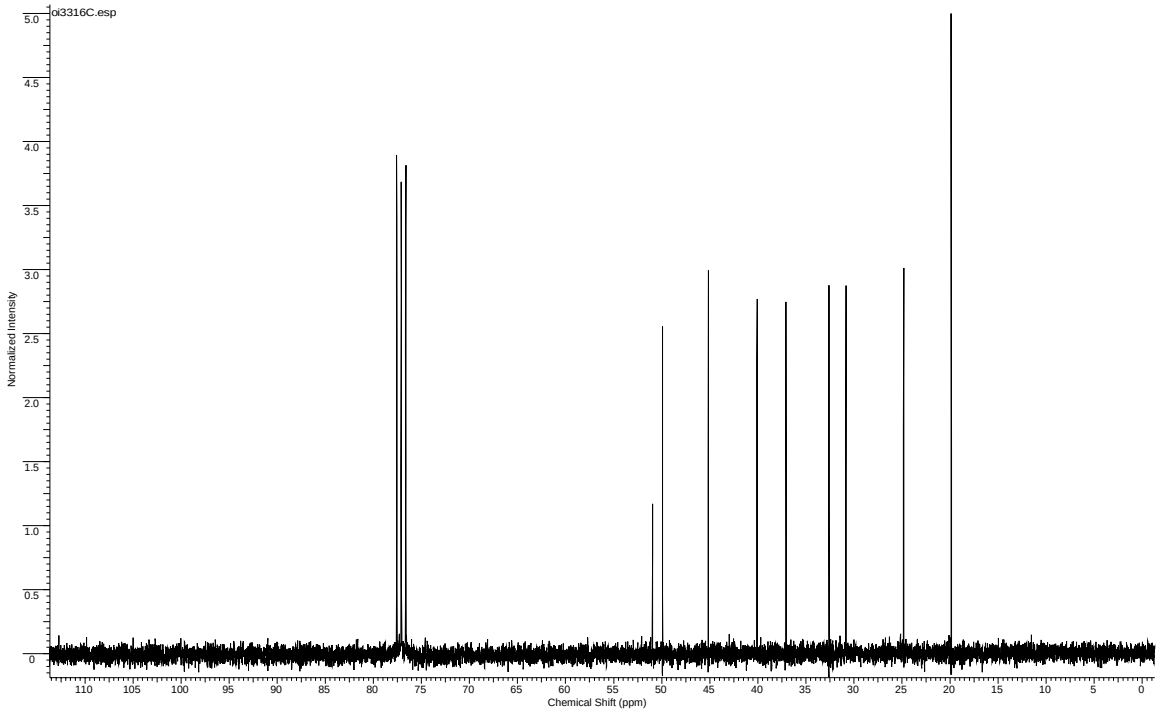


(1*R*,2*S*,5*R*)-2-Amino-5-isopropyl-2-methylcyclohexanethiol (19)

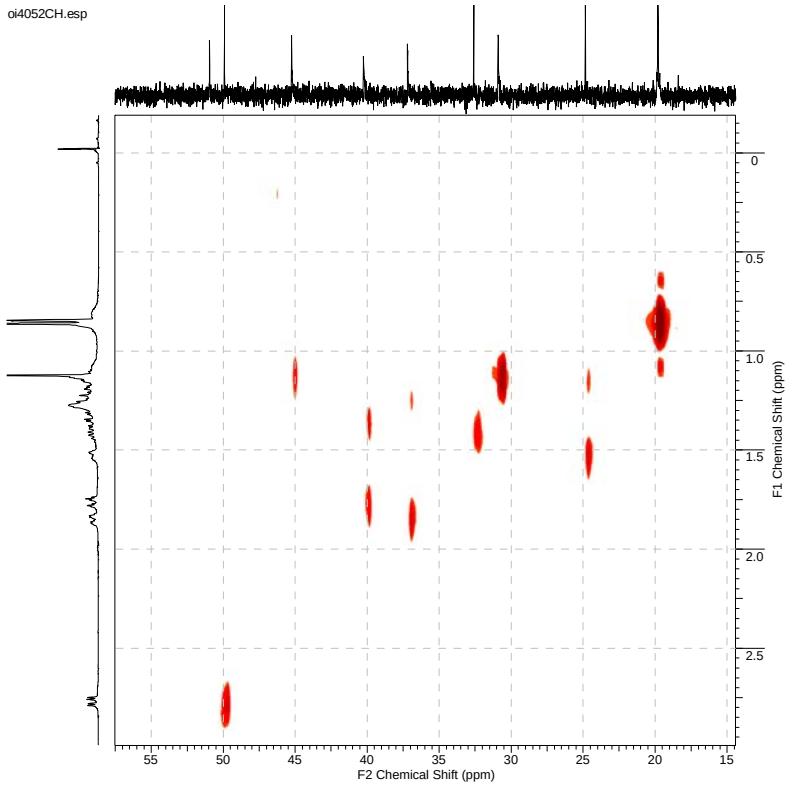
^{1}H NMR (270 MHz, $CDCl_3$)



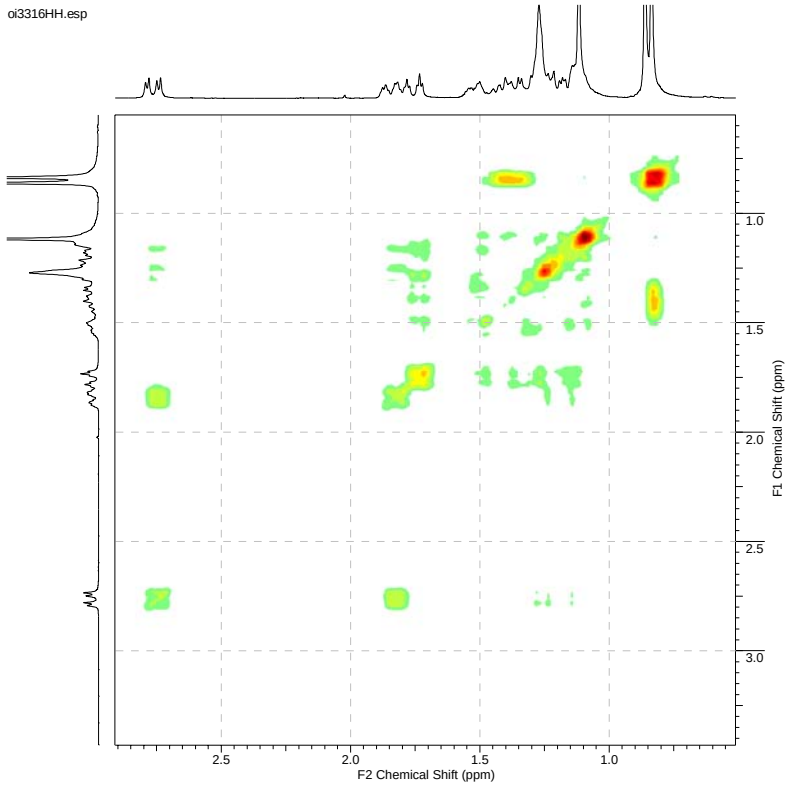
^{13}C NMR (67.5 MHz, $CDCl_3$)



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

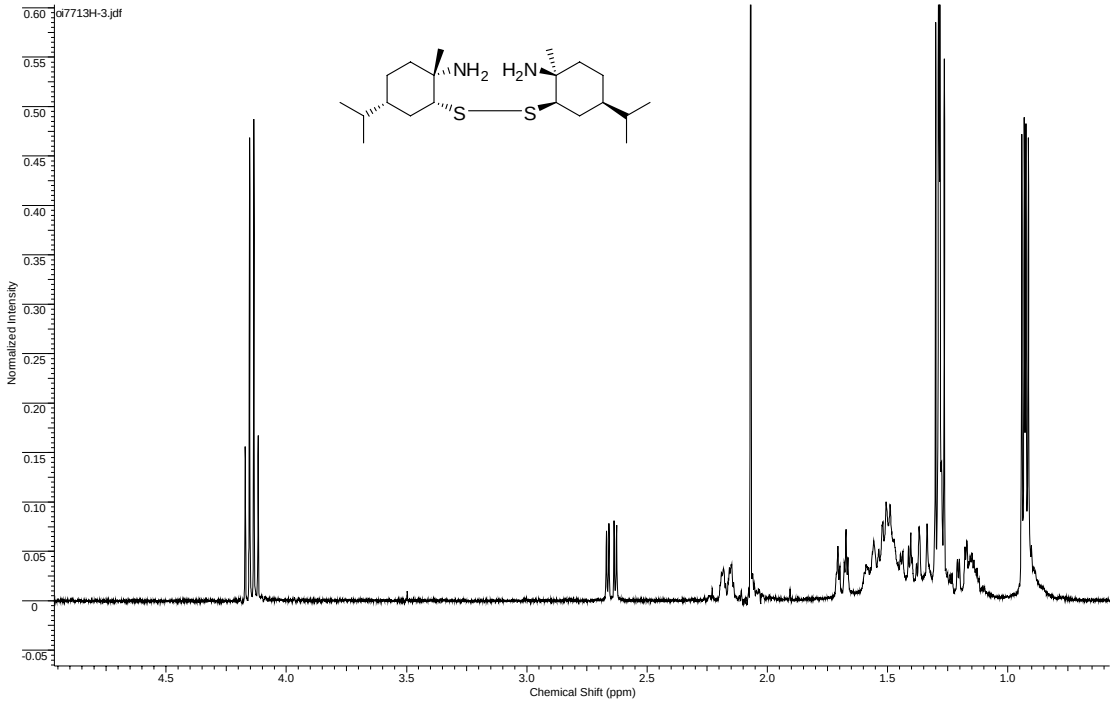


COSY (400 MHz, $CDCl_3$)

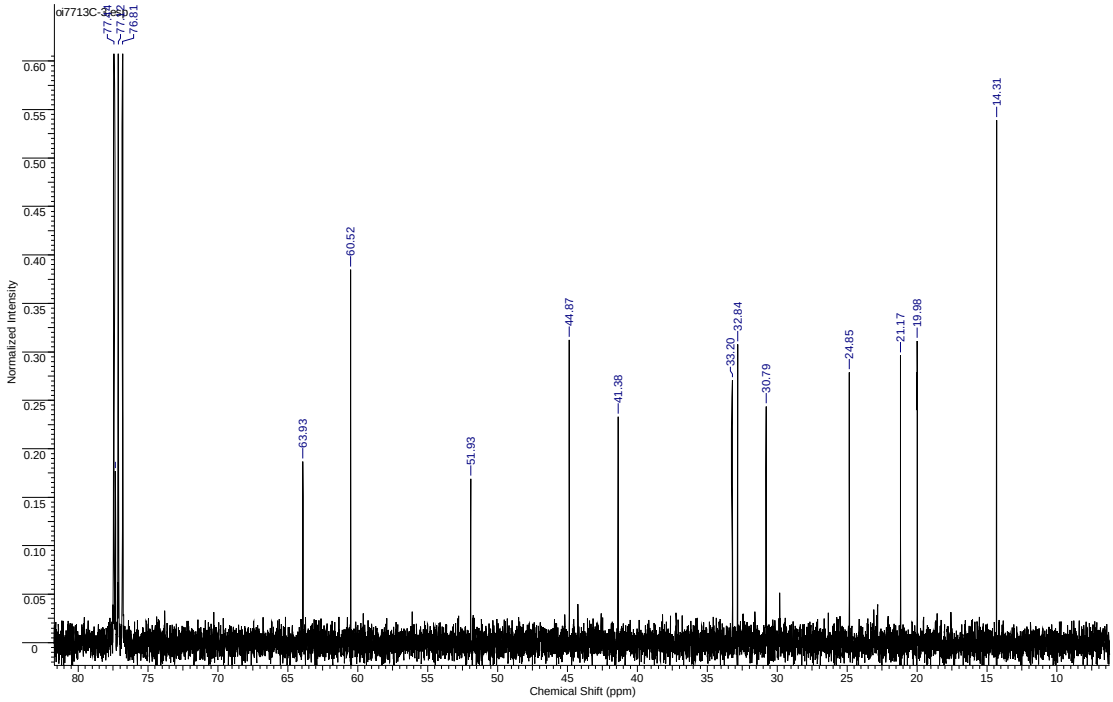


Dimerized 19

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



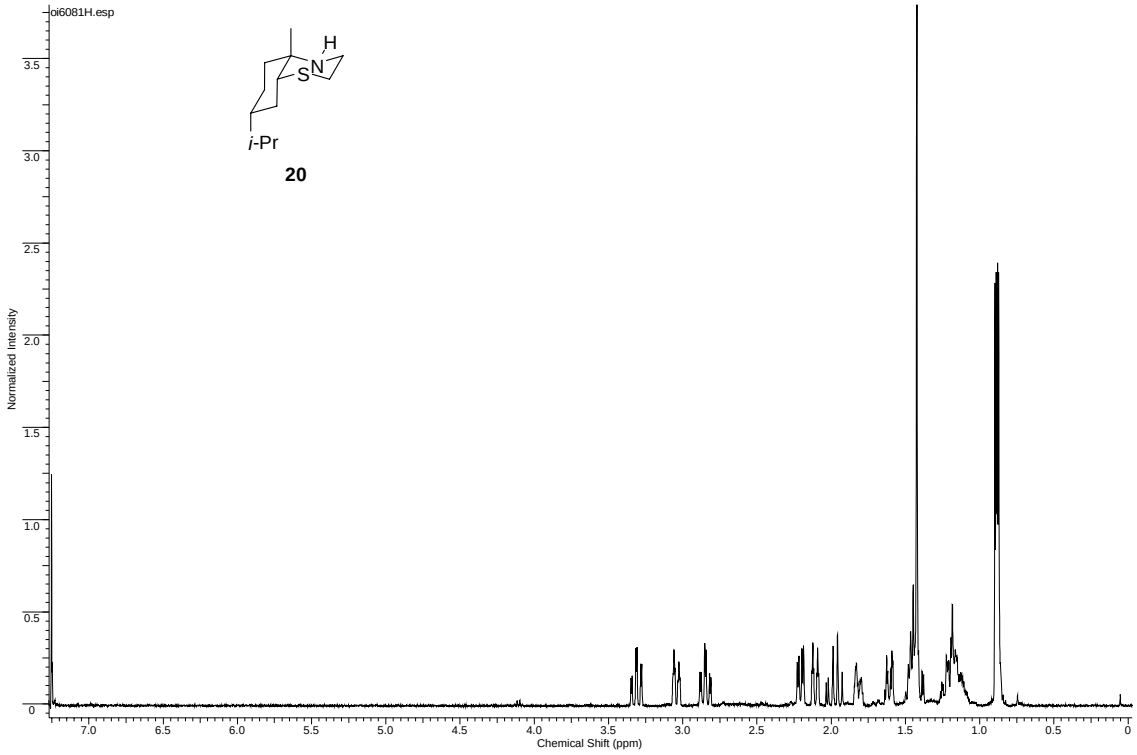
^{13}C NMR (100 MHz, $CDCl_3$)



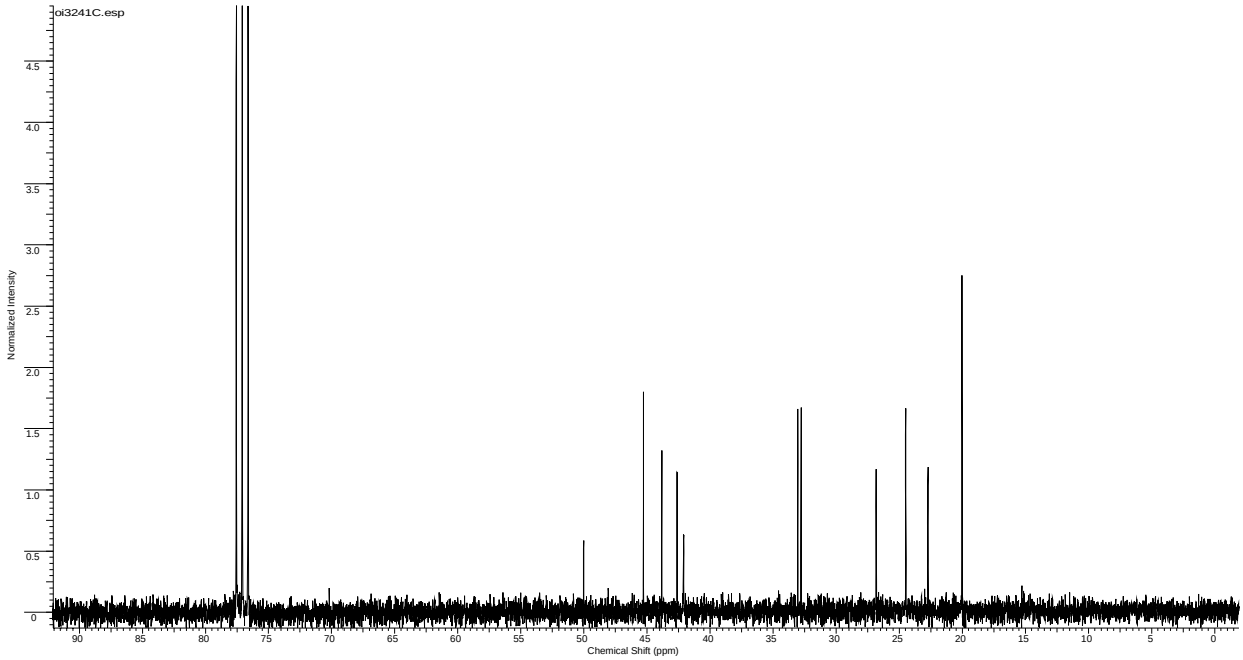
Note: peaks at 14.3, 21.17 and 60.5 are due to EtOAc.

(4a*S*,7*R*,8a*R*)-7-isopropyl-4a-methyloctahydro-2*H*-benzo[b][1,4]thiazine 20

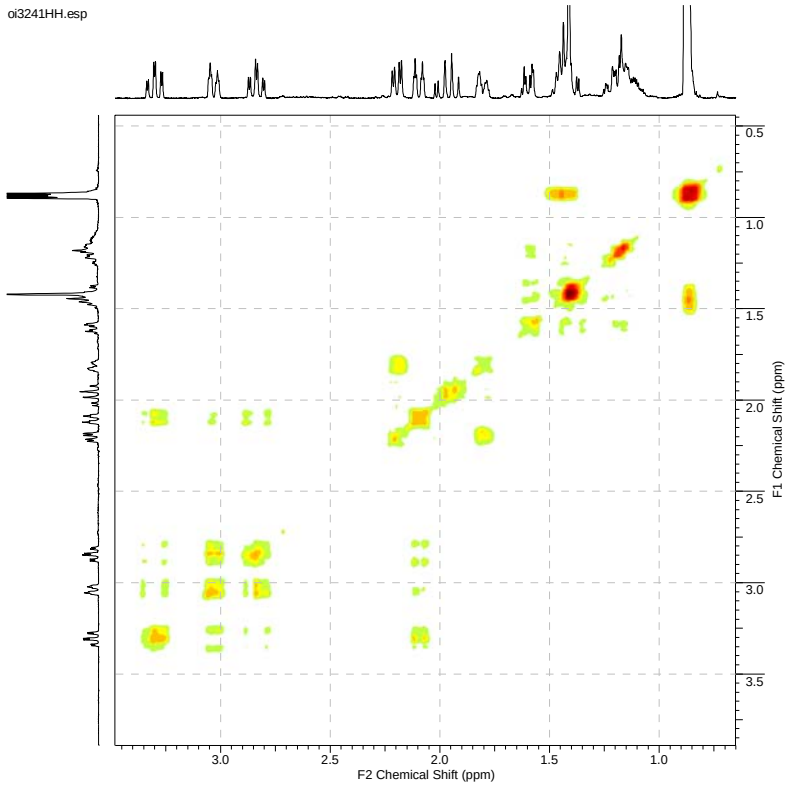
^{1}H NMR (400 MHz, $CDCl_3$)



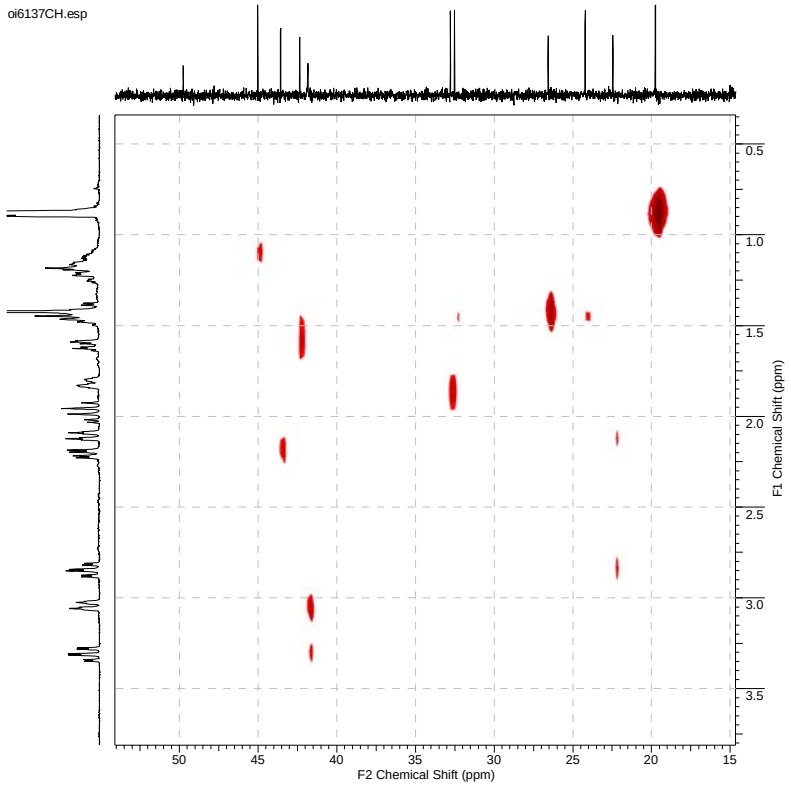
^{13}C NMR (67.5 MHz, $CDCl_3$)



COSY (270 MHz, $CDCl_3$)

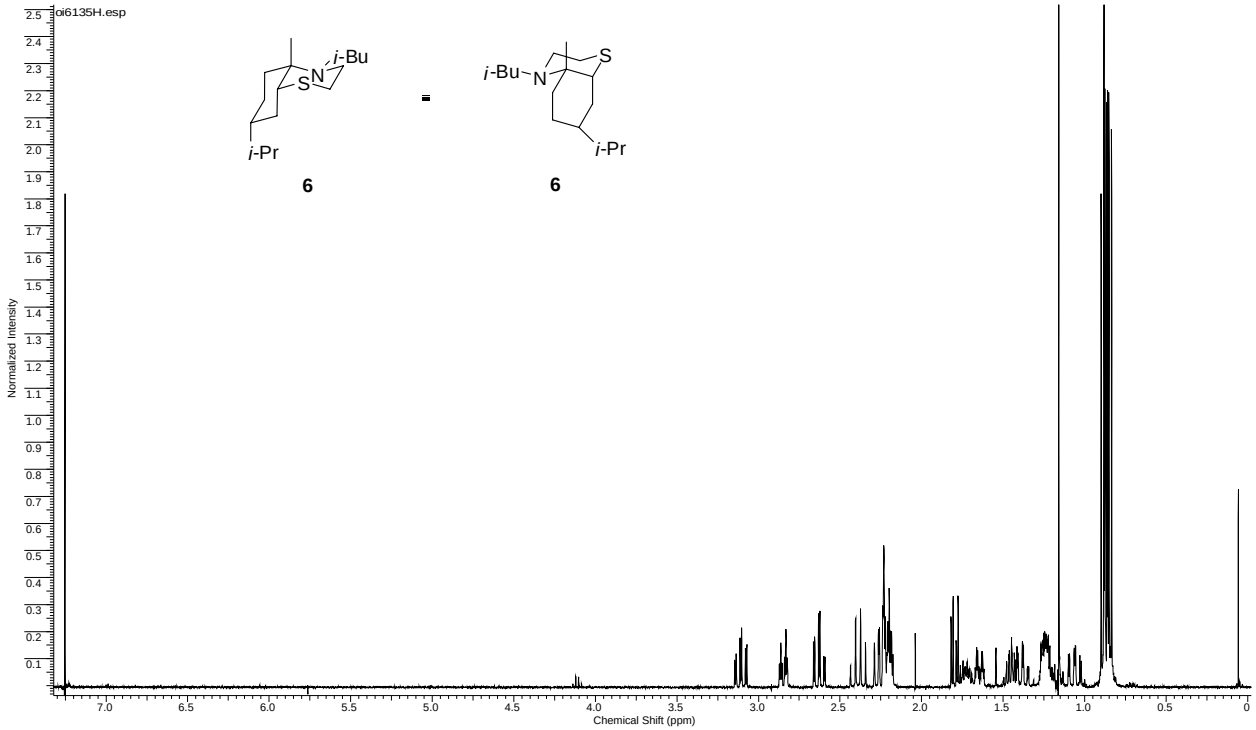


HMQC (400 MHz for ^1H NMR, $CDCl_3$)

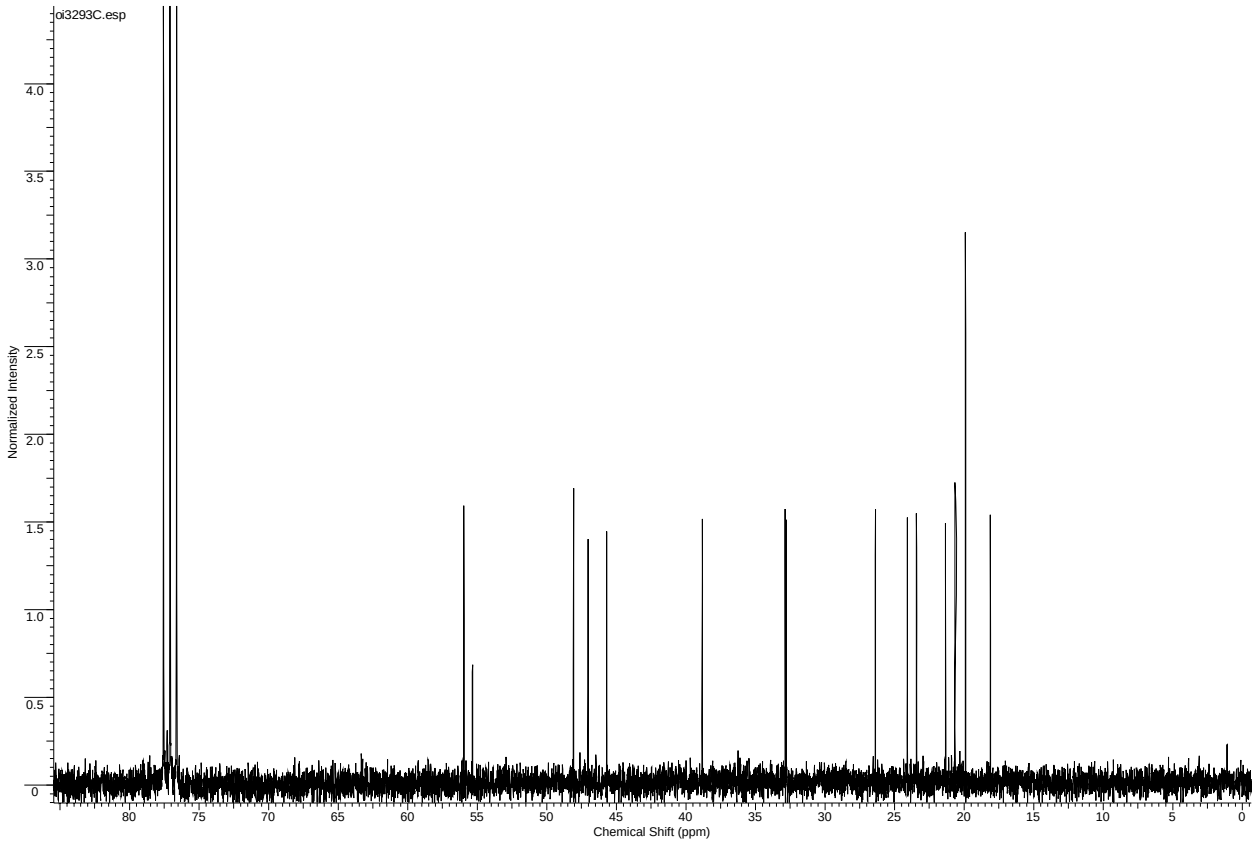


(4a*S*,7*R*,8a*R*)-4-Isobutyl-7-isopropyl-4a-methyloctahydro-2*H*-1,4-benzothiazine 6

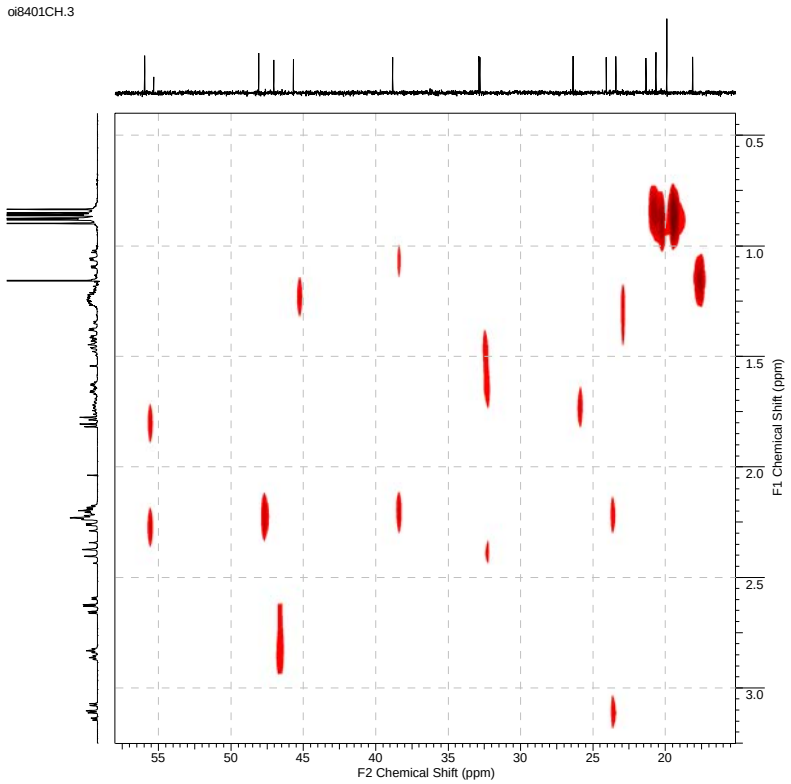
^{1}H NMR (400 MHz, $CDCl_3$)



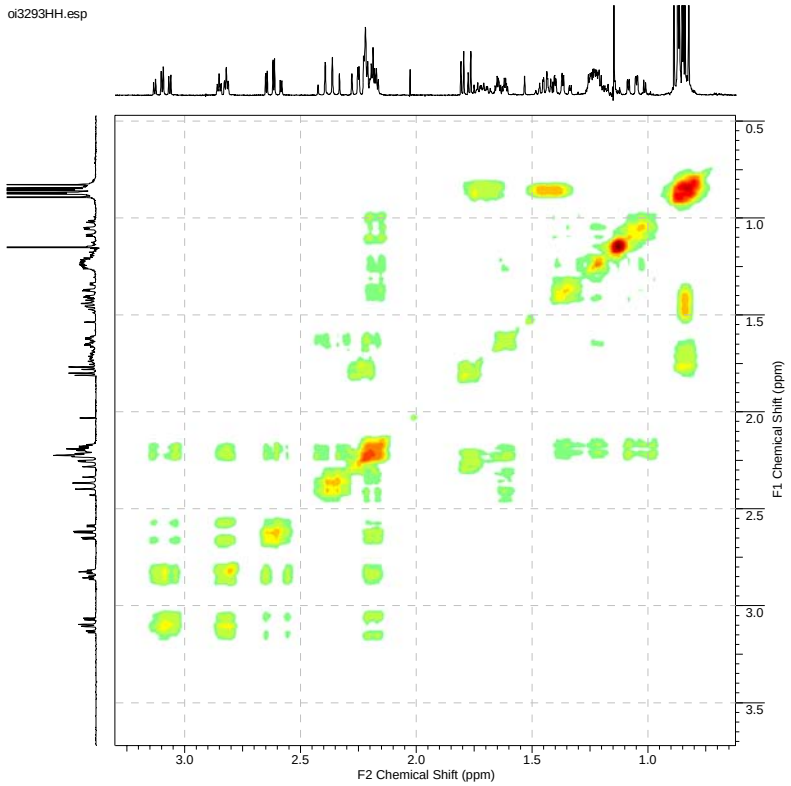
^{13}C NMR (67.5 MHz, $CDCl_3$)



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

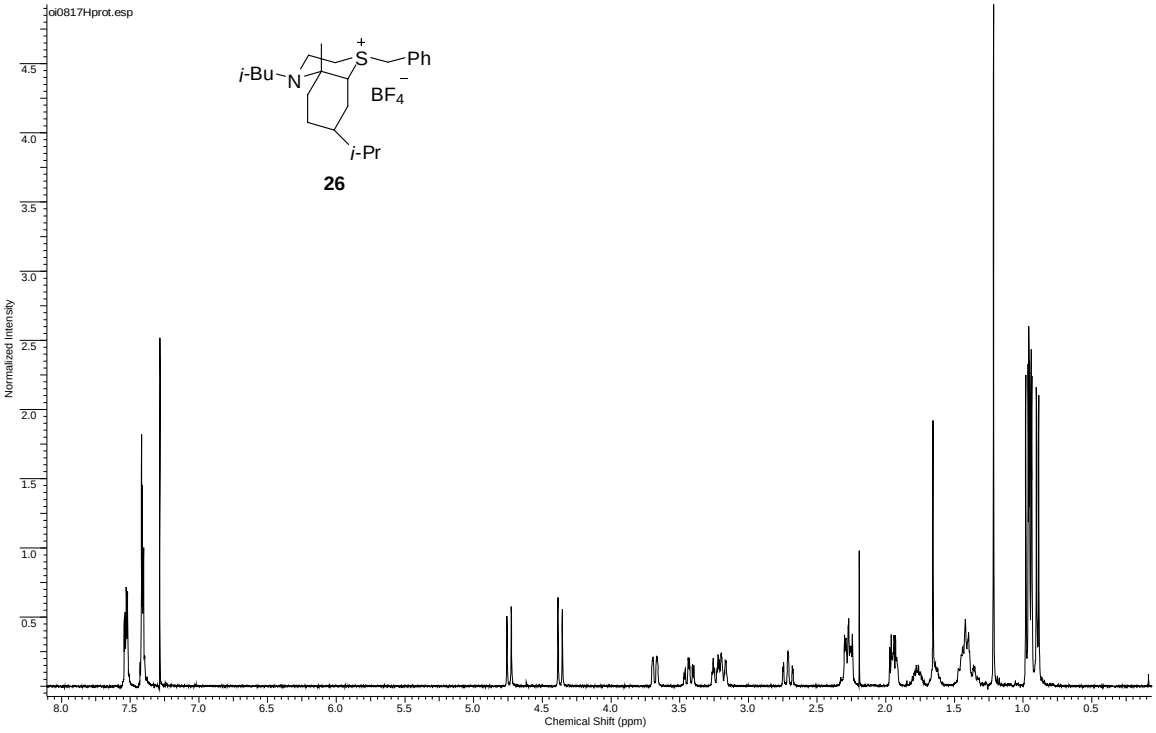


COSY (270 MHz, $CDCl_3$)

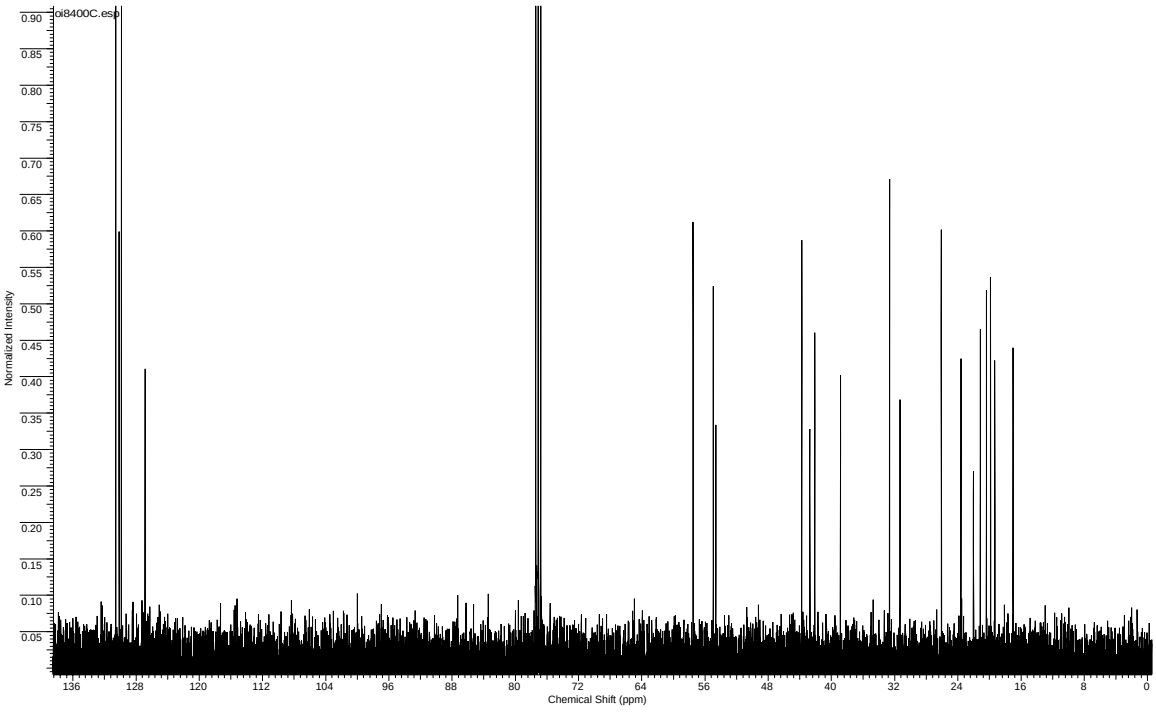


(1*S*,4a*S*,7*R*,8a*R*)-1-Benzyl-4-isobutyl-7-isopropyl-4a-methyloctahydro-2*H*-1,4-benzothiazin-1-ium tetrafluoroborate 26

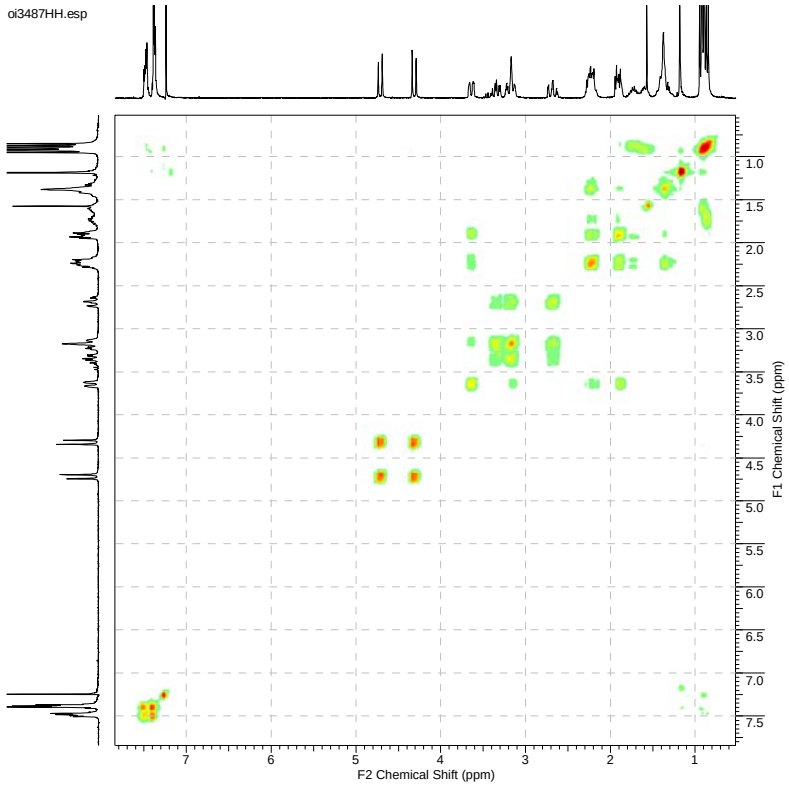
^{1}H NMR (400 MHz, $CDCl_3$)



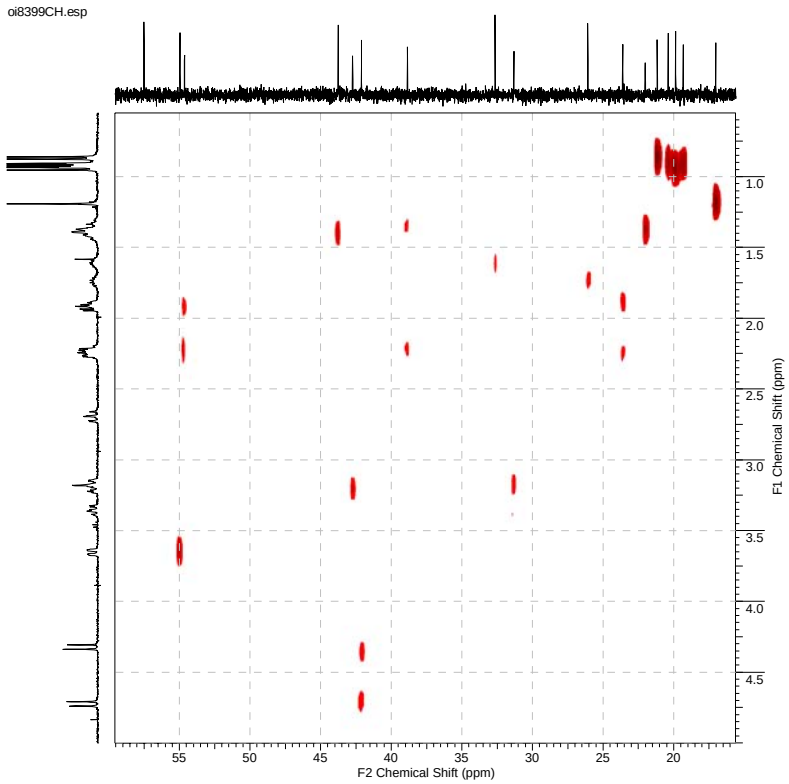
^{13}C NMR (100 MHz, $CDCl_3$)



COSY (270 MHz, $CDCl_3$)

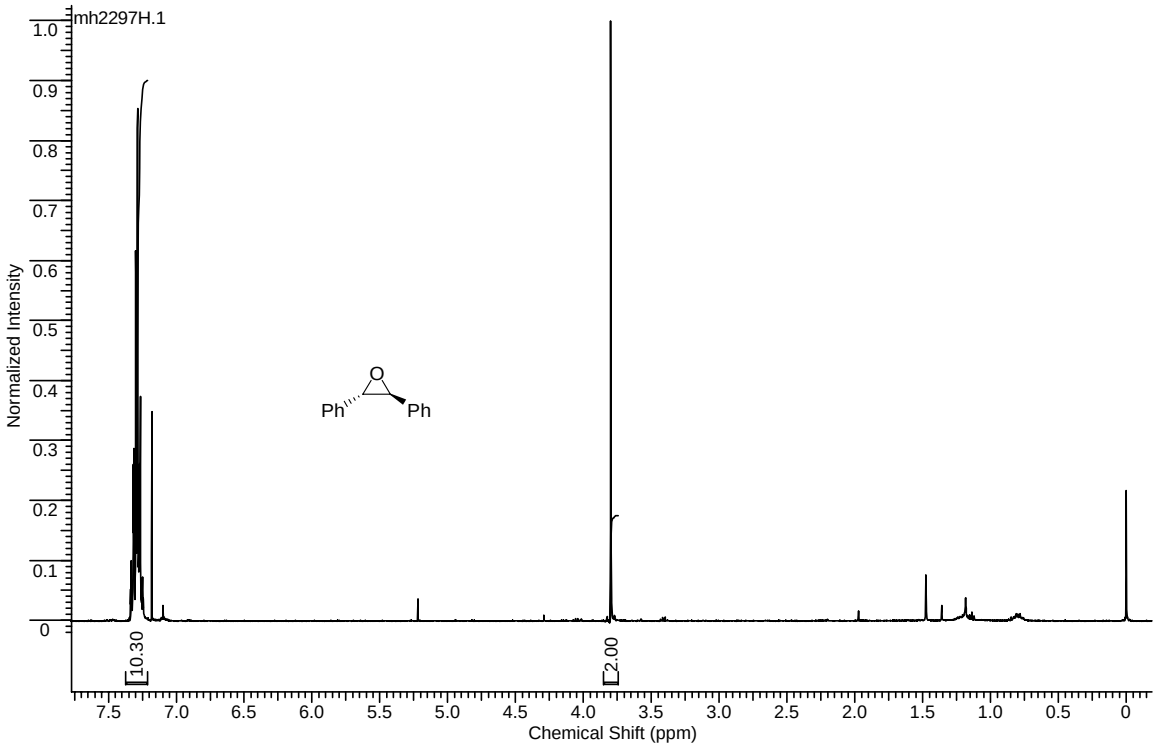


HMQC (400 MHz for ^1H NMR, $CDCl_3$)



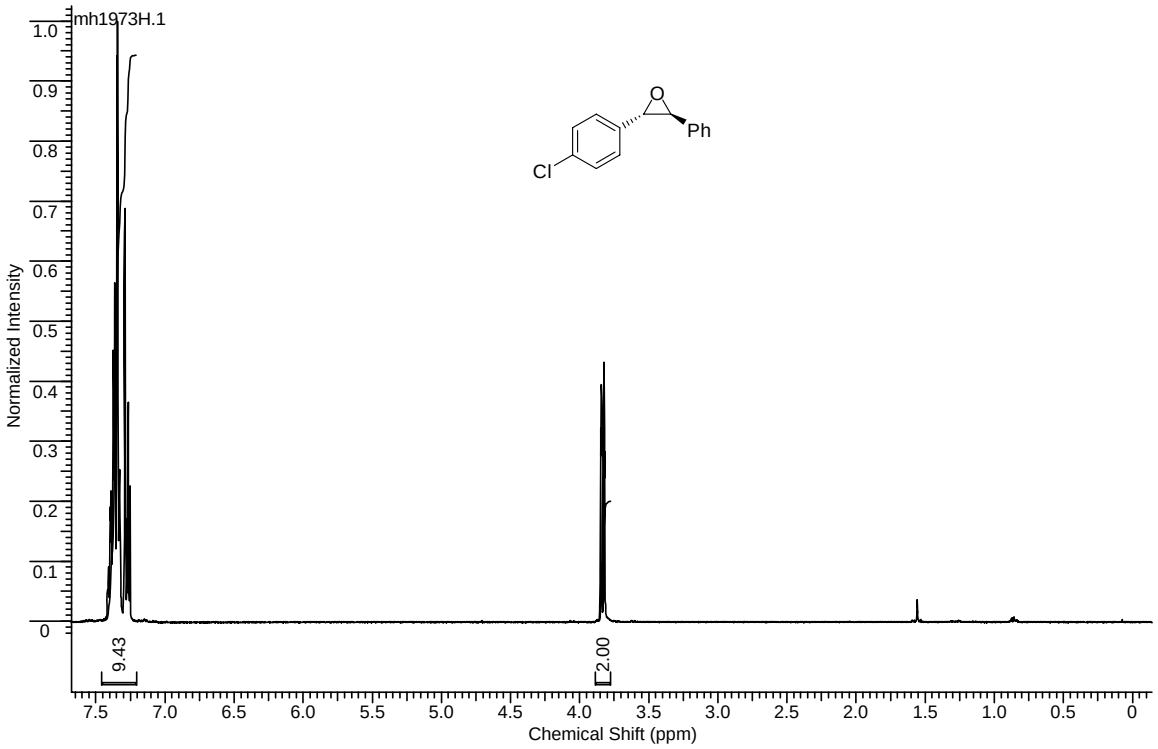
trans-Stilbene oxide (35a)

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



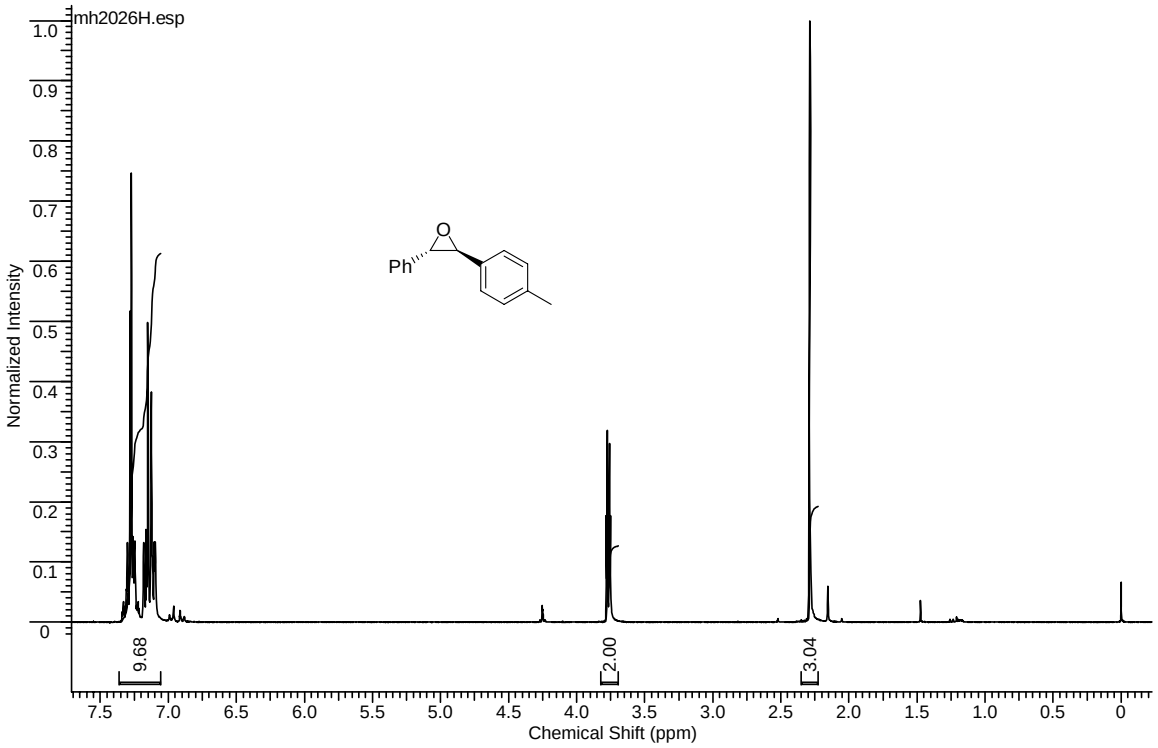
2-(4-Chlorophenyl)-3-phenyloxirane 36

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



2-Phenyl-3-*p*-tolyloxirane 37

^{1}H NMR (270 MHz, $CDCl_3$)



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[4] *MMFF molecular mechanics using Spartan '06, Copyright © 1991-2007 by Wavefunction Inc., 18401 Von Karman Avenue, Suite 370, Irvine, CA 92612.*

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X-ray Structure Report for 23

CCDC-684971 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via http://www.ccdc.cam.ac.uk/data.

Crystallographic data are presented in the Tables below. A single crystal of **23** was coated in perfluoropolyether oil and mounted on a glass fibre. X-ray measurements were made using a Bruker SMART Apex CCD area-detector diffractometer with Mo-K_α radiation (λ = 0.71074 Å).[1] Intensities were integrated[2] from several series of exposures, each exposure covering 0.3° in ω, and the total data set being almost a hemisphere. Absorption corrections were applied, based on multiple and symmetry-equivalent measurements.[3] The structure was solved by direct methods and refined by least squares on weighted F^2 values for all reflections (see Table 1).[4]

All non-hydrogen atoms were assigned anisotropic displacement parameters and refined without positional constraints. The positions of the methyl hydrogen atoms were assigned by a rotating group refinement with fixed, idealised C-H distances. All other hydrogen atoms were constrained to ideal geometries. All hydrogen atoms were assigned isotropic displacement parameters equal to 1.5 times (methyl hydrogen atoms) or 1.2 times (all other hydrogen atoms) that of their parent atom.

Bond lengths within phenyl ring C(7) – C(12) were restrained to be equal to 1.38 Å within an estimated standard deviation of 0.03 Å. The positions of atoms in this ring were also restrained to be planar and the thermal parameters of these atoms were restrained to have similar values. The C-Cl bond lengths in the disordered dichloromethane solvent molecule were restrained to a length of 1.76 Å within an estimated standard deviation of 0.03 Å.

Refinement proceeded smoothly to give the residuals shown in Table 1. Complex neutral-atom scattering factors were used.[5]

References

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3. G. M. Sheldrick. *SADABS version 2.05*, University of Göttingen: Germany, 2003.
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5. *International Tables for Crystallography*, Kluwer, Dordrecht, 1992, vol. C.

Table 1. Crystal data and structure refinement for sulfonium salt **23**.

Identification code	**23**	
Empirical formula	C23.50 H32.50 B Cl1.50 F4 N S	
Formula weight	501.05	
Temperature	100 K	
Wavelength	0.71074 Å	
Crystal system	Orthorhombic	
Space group	P 21 21 2	
Unit cell dimensions	a = 13.550(3) Å	α = 90°
	b = 22.783(5) Å	β = 90°
	c = 8.2664(17) Å	γ = 90°
Volume	2551.9(10) Å^3	
Z	4	
Density (calculated)	1.304 Mg/m^3	
Absorption coefficient	0.325 mm^{-1}	
F(000)	1052	
Crystal size	0.4 x 0.2 x 0.2 mm	
θ range for data collection	1.75 to 27.48°	
Index ranges	-16<=h<=17, -29<=k<=26, -10<=l<=10	
Reflections collected	18194	
Independent reflections	3323 [R_{int} = 0.0341]	
Completeness to θ = 27.48°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.94 and 0.84	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3323 / 46 / 302	
Goodness-of-fit on F^2	S = 1.216	
R indices [for 3281reflections with I>2σ(I)]	R_1 = 0.1148, wR_2 = 0.3138	
R indices (for all 3323 data)	R_1 = 0.1162, wR_2 = 0.3171	
Weighting scheme	$w^{-1} = \sigma^2(F_o^2) + (aP)^2 + (bP)$,	
	where $P = [\max(F_o^2, 0) + 2F_c^2]/3$	
	a = 0.1029, b = 22.8707	
Absolute structure (Flack) parameter	0.1(3)	
Largest diff. peak and hole	0.651 and -0.825 eÅ^{-3}	

Table 2. Bond lengths [Å] and angles [°] for **23**.

C(1)-N(1)	1.438(12)
C(1)-C(2)	1.538(12)
C(1)-H(1A)	0.9900
C(1)-H(1B)	0.9900
C(2)-S(1)	1.819(8)
C(2)-H(2A)	0.9900
C(2)-H(2B)	0.9900
C(3)-C(20)	1.527(12)
C(3)-C(4)	1.546(12)
C(3)-S(1)	1.828(8)
C(3)-H(3)	1.0000
C(4)-N(1)	1.479(12)
C(4)-C(22)	1.528(14)
C(4)-H(4)	1.0000
C(5)-N(1)	1.485(15)
C(5)-C(7)	1.520(14)
C(5)-C(6)	1.530(15)
C(5)-H(5)	1.0000
C(6)-H(6A)	0.9800
C(6)-H(6B)	0.9800
C(6)-H(6C)	0.9800
C(7)-C(8)	1.383(13)
C(7)-C(12)	1.41(2)
C(8)-C(9)	1.386(12)
C(8)-H(8)	0.9500
C(9)-C(10)	1.385(14)
C(9)-H(9)	0.9500
C(10)-C(11)	1.382(15)
C(10)-H(10)	0.9500
C(11)-C(12)	1.376(14)
C(11)-H(11)	0.9500
C(12)-H(12)	0.9500
C(13)-C(14)	1.504(12)
C(13)-S(1)	1.817(9)
C(13)-H(13A)	0.9900
C(13)-H(13B)	0.9900
C(14)-C(15)	1.384(14)
C(14)-C(19)	1.416(15)

C(15)-C(16)	1.425(15)
C(15)-H(15)	0.9500
C(16)-C(17)	1.341(17)
C(16)-H(16)	0.9500
C(17)-C(18)	1.419(17)
C(17)-H(17)	0.9500
C(18)-C(19)	1.381(15)
C(18)-H(18)	0.9500
C(19)-H(19)	0.9500
C(20)-C(21)	1.517(13)
C(20)-H(20A)	0.9900
C(20)-H(20B)	0.9900
C(21)-H(21A)	0.9800
C(21)-H(21B)	0.9800
C(21)-H(21C)	0.9800
C(22)-C(23)	1.544(15)
C(22)-H(22A)	0.9900
C(22)-H(22B)	0.9900
C(23)-H(23A)	0.9800
C(23)-H(23B)	0.9800
C(23)-H(23C)	0.9800
B(1)-F(2)	1.363(14)
B(1)-F(1)	1.363(16)
B(1)-F(4)	1.380(15)
B(1)-F(3)	1.404(14)
C(45)-Cl(1)#1	1.72(4)
C(45)-Cl(2)	1.763(18)
C(45)-Cl(1)	1.76(2)
C(45)-H(45)	1.0000
Cl(1)-C(45)#1	1.72(4)
Cl(2)-C(45)#1	1.54(3)
Cl(2)-Cl(2)#1	1.745(16)

N(1)-C(1)-C(2)	115.2(8)
N(1)-C(1)-H(1A)	108.5
C(2)-C(1)-H(1A)	108.5
N(1)-C(1)-H(1B)	108.5
C(2)-C(1)-H(1B)	108.5
H(1A)-C(1)-H(1B)	107.5
C(1)-C(2)-S(1)	107.4(6)

C(1)-C(2)-H(2A)	110.2
S(1)-C(2)-H(2A)	110.2
C(1)-C(2)-H(2B)	110.2
S(1)-C(2)-H(2B)	110.2
H(2A)-C(2)-H(2B)	108.5
C(20)-C(3)-C(4)	116.1(7)
C(20)-C(3)-S(1)	109.7(6)
C(4)-C(3)-S(1)	108.1(6)
C(20)-C(3)-H(3)	107.5
C(4)-C(3)-H(3)	107.5
S(1)-C(3)-H(3)	107.5
N(1)-C(4)-C(22)	113.0(8)
N(1)-C(4)-C(3)	112.1(7)
C(22)-C(4)-C(3)	113.2(8)
N(1)-C(4)-H(4)	105.9
C(22)-C(4)-H(4)	105.9
C(3)-C(4)-H(4)	105.9
N(1)-C(5)-C(7)	110.7(10)
N(1)-C(5)-C(6)	112.3(9)
C(7)-C(5)-C(6)	109.2(8)
N(1)-C(5)-H(5)	108.2
C(7)-C(5)-H(5)	108.2
C(6)-C(5)-H(5)	108.2
C(5)-C(6)-H(6A)	109.5
C(5)-C(6)-H(6B)	109.5
H(6A)-C(6)-H(6B)	109.5
C(5)-C(6)-H(6C)	109.5
H(6A)-C(6)-H(6C)	109.5
H(6B)-C(6)-H(6C)	109.5
C(8)-C(7)-C(12)	118.6(11)
C(8)-C(7)-C(5)	120.3(11)
C(12)-C(7)-C(5)	121.0(11)
C(7)-C(8)-C(9)	121.6(12)
C(7)-C(8)-H(8)	119.2
C(9)-C(8)-H(8)	119.2
C(10)-C(9)-C(8)	119.0(11)
C(10)-C(9)-H(9)	120.5
C(8)-C(9)-H(9)	120.5
C(11)-C(10)-C(9)	120.1(12)
C(11)-C(10)-H(10)	120.0

C(9)-C(10)-H(10)	120.0
C(12)-C(11)-C(10)	121.0(14)
C(12)-C(11)-H(11)	119.5
C(10)-C(11)-H(11)	119.5
C(11)-C(12)-C(7)	119.6(14)
C(11)-C(12)-H(12)	120.2
C(7)-C(12)-H(12)	120.2
C(14)-C(13)-S(1)	109.9(6)
C(14)-C(13)-H(13A)	109.7
S(1)-C(13)-H(13A)	109.7
C(14)-C(13)-H(13B)	109.7
S(1)-C(13)-H(13B)	109.7
H(13A)-C(13)-H(13B)	108.2
C(15)-C(14)-C(19)	120.8(9)
C(15)-C(14)-C(13)	119.4(9)
C(19)-C(14)-C(13)	119.8(9)
C(14)-C(15)-C(16)	117.6(10)
C(14)-C(15)-H(15)	121.2
C(16)-C(15)-H(15)	121.2
C(17)-C(16)-C(15)	122.6(9)
C(17)-C(16)-H(16)	118.7
C(15)-C(16)-H(16)	118.7
C(16)-C(17)-C(18)	119.3(9)
C(16)-C(17)-H(17)	120.4
C(18)-C(17)-H(17)	120.4
C(19)-C(18)-C(17)	120.1(11)
C(19)-C(18)-H(18)	119.9
C(17)-C(18)-H(18)	119.9
C(18)-C(19)-C(14)	119.5(11)
C(18)-C(19)-H(19)	120.3
C(14)-C(19)-H(19)	120.3
C(21)-C(20)-C(3)	110.7(8)
C(21)-C(20)-H(20A)	109.5
C(3)-C(20)-H(20A)	109.5
C(21)-C(20)-H(20B)	109.5
C(3)-C(20)-H(20B)	109.5
H(20A)-C(20)-H(20B)	108.1
C(20)-C(21)-H(21A)	109.5
C(20)-C(21)-H(21B)	109.5
H(21A)-C(21)-H(21B)	109.5

C(20)-C(21)-H(21C)	109.5
H(21A)-C(21)-H(21C)	109.5
H(21B)-C(21)-H(21C)	109.5
C(4)-C(22)-C(23)	109.7(10)
C(4)-C(22)-H(22A)	109.7
C(23)-C(22)-H(22A)	109.7
C(4)-C(22)-H(22B)	109.7
C(23)-C(22)-H(22B)	109.7
H(22A)-C(22)-H(22B)	108.2
C(22)-C(23)-H(23A)	109.5
C(22)-C(23)-H(23B)	109.5
H(23A)-C(23)-H(23B)	109.5
C(22)-C(23)-H(23C)	109.5
H(23A)-C(23)-H(23C)	109.5
H(23B)-C(23)-H(23C)	109.5
C(1)-N(1)-C(4)	112.3(8)
C(1)-N(1)-C(5)	113.2(8)
C(4)-N(1)-C(5)	114.3(8)
C(13)-S(1)-C(2)	103.0(4)
C(13)-S(1)-C(3)	101.4(4)
C(2)-S(1)-C(3)	98.6(4)
F(2)-B(1)-F(1)	110.3(10)
F(2)-B(1)-F(4)	113.0(12)
F(1)-B(1)-F(4)	107.1(11)
F(2)-B(1)-F(3)	109.5(10)
F(1)-B(1)-F(3)	110.6(11)
F(4)-B(1)-F(3)	106.4(9)
Cl(1)#1-C(45)-Cl(2)	103.1(16)
Cl(1)#1-C(45)-Cl(1)	110.2(15)
Cl(2)-C(45)-Cl(1)	119.5(16)
Cl(1)#1-C(45)-H(45)	107.8
Cl(2)-C(45)-H(45)	107.8
Cl(1)-C(45)-H(45)	107.8

Symmetry transformations used to generate equivalent atoms:

#1 -x+2,-y+2,z