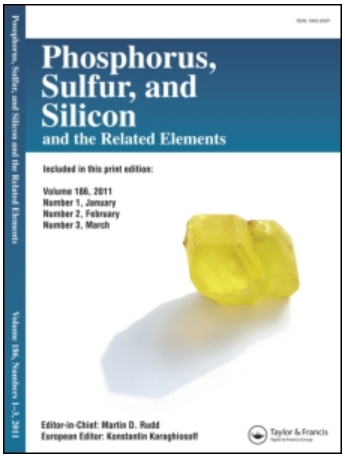

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Diastereoselectivity in Reactions of Lithiated 2-Phenylthiomethylthiotetrahydropyrans

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DIASTEREOSELECTIVITY IN REACTIONS OF LITHIATED 2-PHENYLTHIOMETHYLTHIOTETRAHYDROPYRANS

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Diastereoselectivities of up to 95:5 in alkylations of lithiated O,S,S-acetals are rationalized by the locked conformation of the five-membered ring caused by lithium-to-oxygen coordination. The relative configurations of the two diastereomers obtained in benzylation of lithiated 2-(phenylthiomethylthio)tetrahydropyran were confirmed by comparison with reference compounds of known stereochemistry obtained by benzylic reduction of crystalline hydroxyalkylated derivatives.

Keywords: Crystal structure; Li—O coordination; O,S,S-acetal; synthesis

INTRODUCTION

Organolithium compounds may be stabilized by aggregation, solvation by polar solvents, or intra- or intermolecular complexation.[1,2] Intramolecular bonding between lithium and a free electron pair on nitrogen or oxygen in reaction intermediates often controls the regio- or stereochemistry of the reaction.[3–6]

Dithioacetals are widely used in organic synthesis as protecting groups[7] and acyl anion synthons.[8] We have synthesized new dithioacetal structures that are also hemithioacetals and studied their lithiations and diastereoselectivity in the subsequent reactions with electrophiles. The diastereoselectivity was expected to be enhanced by the

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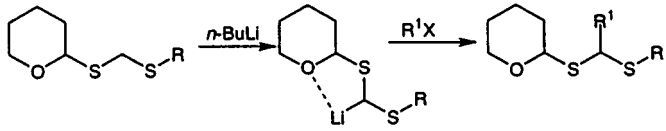


SCHEME 1 The lithium-to-oxygen coordination of cyclicO,S,S-acetals.

locked conformation of the five-membered ring caused by lithium-to-oxygen coordination (Scheme 1).[9,10]

In 2-substituted heterocyclohexanes an equatorial side chain is usually favored because of the repulsive interaction between the axial substituent at C-2 and the synaxial hydrogen at C-6.[3] However, the anomeric effect in 2-alkylthiotetrahydropyrans is reported to cause a slight preference for the axial form, which is diminished by increasing solvent polarity and decreasing temperature.[11] Thus under the lithiation conditions (THF, -78°C) the equatorial side chain is expected to be favored allowing the lithium to coordinate intramolecularly (Figure 1). It is possible, however, that the chelated structure may include a solvent molecule or another substrate molecule to saturate the coordination sphere of Li^{+}.[12] The species I with the large SPh and S-THP groups situated *anti* to each other should be favored over species II where these groups are *gauche*. It is known that alkylation of lithio sp^3 carbanions α to sulfur takes place with retention of configuration[13–15] thus, leading preferentially to R^*R^* diastereomer. The same diastereomer would also be formed from the chelated lithio compound in which the side chain is axial with respect to the dihydropyran ring. However, this intermediate is likely to react more slowly with electrophiles because the reaction site is more crowded.

RESULTS AND DISCUSSION

The dithioacetal compounds **1–10** were prepared by one-pot reactions of the thioacetic acid esters and the α-chlorosulfides (Table I). The esters were hydrolysed with potassium hydroxide in dimethyl

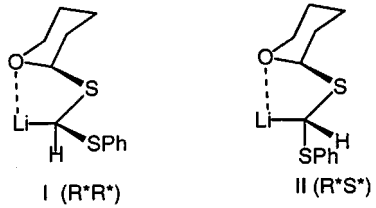
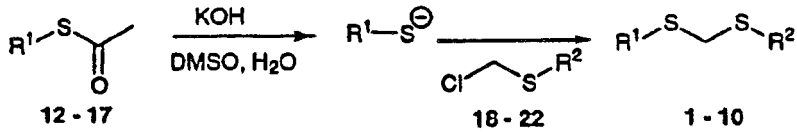
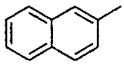
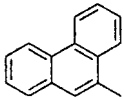
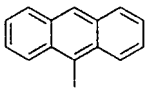
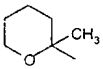
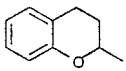
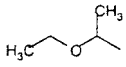
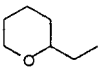


FIGURE 1 The intramolecular lithium-to-oxygen coordination of **1** with *anti* (I) and *gauche* (II) conformations of the large substituent at sulphur atoms.

TABLE I The Preparation of Dithioacetals **1–10** from the Thioacetic Acid Esters **12–17** and the α-Chlorosulfides **18–22**



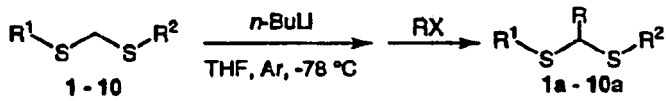
12 - 17 **18 - 22** **1 - 10**

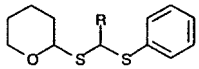
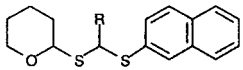
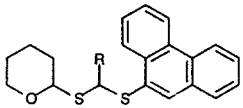
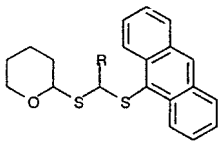
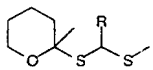
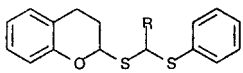
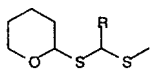
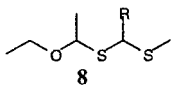
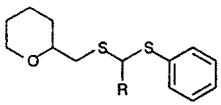
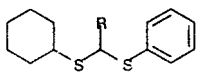
R^1	$R^1SC(O)CH_3$	R^2	$ClCH_2SR^2$	$R^1SCH_2SR^2$
	**12**		**18**	**1** (79%, flash)
	**12**		**19**	**2** (59%, flash)
	**12**		**20**	**3** (45%, flash)
	**12**		**21**	**4** (59%, flash)
	**13**		**22**	**5** (76%, crude)
	**14**		**18**	**6** (38%, flash)
	**12**		**22**	**7** (43%, dist.)
	**15**		**22**	**8** (56%, dist.)
	**16**		**18**	**9** (45%, flash)
	**17**		**18**	**10** (76%, crude)

sulfoxide-water solution at 0°C. Yields were mostly moderate but the reaction conditions were only optimized for the synthesis of 2-(phenylthiomethylthio)tetrahydropyran **1**.[17] The dithioacetals were deprotonated by *n*-butyllithium at −78°C in tetrahydrofuran and reacted with halides or carbonyl compounds.

Diastereoselectivities of up to 95:5 were found in alkylations of the cyclic O,S,S-acetals **1–7** where a five-membered ring can be formed by lithium-to-oxygen coordination (Table II). The alkylation of the open-chain hemithio-dithioacetal **8** also gives high diastereoselectivity

TABLE II The Alkylation of Dithioacetals **1–10**



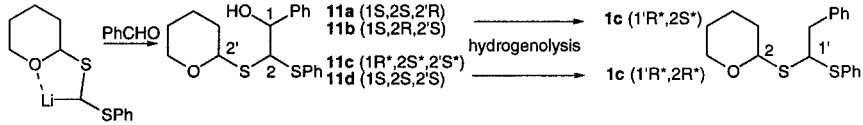
Dithioacetal R=H	Alkylation; yield (purified or crude by GC)	Ratio of diastereomers (GC)
 **1**	**1a** R=CH_3; 80% (GC)	87:13
	1b R=$(CH_2)_3CH_3$; 85% (GC)	90:10
	1c R=CH_2Ph; 64% (GC)	87:13
	1d R=$Si(CH_3)_3$; 67%(GC)	82:18
 **2**	**2a** R=$(CH_2)_3CH_3$; 70%(GC)	95:5
 **3**	**3a** R=CH_3; 71% (GC)	87:13
	3b R=$(CH_2)_3CH_3$; 51% (GC)	91:9
 **4**	**4a** R=$(CH_2)_3CH_3$; 34% (flash)	84:16
 **5**	**5a** R=CH_3; 33% (dist.)	68:32
 **6**	**6a** R=$(CH_2)_3CH_3$; 47% (flash)	85:15
 **7**	**7a** R=CH_3; 84% (GC)	70:30
	7b R=$(CH_2)_3CH_3$; 58% (dist.)	70:30
 **8**	**8a** R=CH_3; 74% (GC)	80:20
	8b R=$(CH_2)_3CH_3$; 51% (dist.)	85:15
 **9**	**9a** R=CH_3; 73% (flash)	55:45
	9b R=$(CH_2)_3CH_3$; 70% (flash)	56:44
 **10**	**10a** R=$CH(CH_3)CH_2CH_3$; 57% (GC)	50:50[a]

[a]Diastereomers could not be separated by GC, the ratio estimated to be 1:1 by ^1H NMR; SCHS.

possibly due to the more flexible structure allowing easier intramolecular coordination. A methyl group at the THP-C-2 (**5**) diminishes the selectivity, because there is a strong repulsive syn-axial interaction between the methyl and hydrogen in the chelate ring, which is likely to hinder the coordination of lithium to THP oxygen. In 2-(phenylthiomethylthiomethyl)tetrahydropyran **9** the lithium-to-oxygen coordination is apparently much weaker, and very little diastereoselectivity is seen. These results strongly indicate that the diastereoselectivity is dependent on the presence of an oxygen atom at a favorable distance. However, the intramolecular coordination seems not to facilitate the reaction to any great extent. The cyclohexyldithioacetal derivative **10** was deprotonated with *n*-BuLi and alkylated with 2-bromobutane in a comparable yield.

The diastereomeric ratios of the alkylation products determined by GC either from crude or purified product did not vary remarkably. For example, the diastereomeric ratio of **1c** by GC was 87:13 for the crude and 88:12 for the flash purified product. Practically the same ratio of diastereomers (86:14) was also seen from the ^{1}H NMR spectrum (OCHS at δ5.3 and 4.9). The yields in alkylation reactions have not been optimized. There was no evidence of deprotonation at the 2-position of the tetrahydropyranyl ring with *n*-BuLi. The pKa values calculated by CAMEO[16] in DMSO for the 2-positions are 35–39 and for the central methylene position 29–31.

Somewhat unexpectedly, the diastereoselectivity was completely lost in reactions of lithiated **1** with acetophenone[17] or benzaldehyde[18] (Scheme 2) and almost equal amounts of product diastereomers were found. We assume that the carbonyl oxygen of the electrophile is able to break up the intramolecular coordination of the lithio compound



SCHEME 2 The reaction of lithio-**1** with benzaldehyde and the deoxygenation of the ethanol derivatives **11**.

prior to the addition reaction. The structures of the compounds **11a–d** were determined by X-ray crystallography. The remarkable crystallographic feature of these diastereomers is that **11a**,[18] **11b**,[19] and **11d**[19] crystallize in noncentrosymmetric spacegroups as conglomerates of enantiomeric crystals whereas **11c** is racemic. The crystal structure determination of **11c** is described in the experimental section of this article and the structure is represented in Figure 2. In **11a** and **11b**

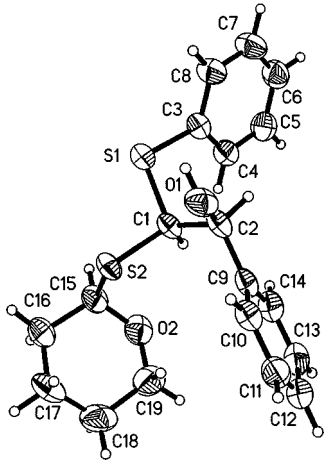


FIGURE 2 X-ray structure of **11c** with crystallographic atomic labelling. Ellipsoids are drawn at 50% probability level. Selected bond lengths (Å) and angles (°) with e.s.d.s in parentheses: S(1)-C(1) 1.827(3), S(1)-C(3) 1.780(3), S(2)-C(1) 1.818(3), S(2)-C(15) 1.847(3); S(1)-C(1)-S(2) 105.9(2), C(1)-S(2)-C(3) 103.66(13), C(1)-S(2)-C(15) 96.42(13), S(1)-C(1)-C(2) 112.4(2).

the S-sidechain is equatorial and the hydroxyl group is intramolecularly hydrogen bonded to oxygen. The vicinal ^{1}H NMR coupling constants for OCHS calculated by MacroModel[20] using Karplus equation and the crystal data are 11.2 and 2.7 Hz for **11a**, and 11.4 and 2.9 Hz for **11b**, respectively. Compounds **11c** and **11d** have axial side chains in the crystalline state and the calculated coupling constants are 5.5 and 1.2 Hz for **11c**, and 5.9 and 1.1 Hz for **11d**, respectively. The NMR measurements indicate that the corresponding observed couplings in $CDCl_3$ solution are 7.5 and 8.3 Hz for **11a**, 7.4 and 3.2 Hz for **11b**, 4.3 and 4.3 Hz for **11c**, and 5.7 and 3.9 Hz for **11d**. Clearly, these figures prove that both equatorial and axial conformations exist in solution.

The conformational equilibria may be estimated from the sum of vicinal coupling constants according De Hoog and Havinga.[11] We calculated the conformational energies ($-\Delta G^\circ$) of 2-hydroxy-2-phenyl-1-phenylthioethylthio group using the measured vicinal couplings of OCHS and the calculated reference values (see above) for the pure equatorial and pure axial conformer: 1.1 kJ, 0.14 kJ, −2.9 kJ, and −1.2 kJ for **11a–d**, respectively. Intramolecular hydrogen bonding seems to favor the equatorial conformer opposing the anomeric effect. Furthermore, these conformational energies are about the same magnitude as the ones calculated theoretically by MINTA[21,22] for the diastereomers of deoxygenated compound **1c**: 1.8 kJ for R^*R^* and 0.5 kJ for

R^*S^*, respectively. Interestingly, these calculations predict an 1.3 kJ energy difference for different diastereoisomers. Thus conformational equilibria for compounds **11** are determined by anomeric effect, the degree of hydrogen bonding, and the configuration of stereocenters in the S-sidechain. Not surprisingly, the conformer, which crystallises out is also the major conformer in solution.

The next task was to establish if the stereochemistry of the main alkylation products would be consistent with the lithium-to-oxygen coordination assumption. Attempts to assign the configuration by NMR techniques were unsuccessful due to the flexibility of the molecules. X-ray analysis could not be used because none of the alkylation products was crystalline. A reference compound to solve the configuration of **1c** at the stereocenters could be obtained by benzylic deoxygenation of the ethanol derivatives **11** (Scheme 2). Conventional reduction methods for secondary alcohols via derivatives such as tosylate, mesylate, halogen, or thiolate could not be used because the sterically hindered OH group was rather unreactive. Radical reactions were not applicable because the PhS group is easily removed.[23] Direct hydrogenation with palladium catalyst did not work, but some deoxygenated product could be obtained by refluxing **11** with lithium aluminium hydride and aluminium chloride in diethyl ether.[24] The low yield is explained by the ability of the reagent to break down the hemithioacetal moiety into thioether.[25–28] The major diastereomer of **1c** was identified by GC and NMR to be identical to (*1′R**,*2R**)-2-(2′-phenyl-1′-phenylthioethylthio)tetrahydropyran obtained by the reduction of **11c**. The benzylic deoxygenation of **11a** gave (*1′R**,*2S**)-)-2-(2′-phenyl-1′-phenylthioethylthio)tetrahydropyran, which was identical with the minor diastereomer of **1c** (Scheme 2).

Free energy calculations with MINTA[21] show that R^*R^* isomer of **1c** is 0.7 kJ/mol more stable than the R^*S^* diastereomer. Thus the thermodynamically more stable isomer is produced selectively in the reaction of lithio-**1** with benzyl bromide, in agreement with the explanation (see Scheme 1) presented above.

In conclusion, these results strongly support our original postulate that the diastereoselectivity in alkylations of the new hemithio dithioacetal compounds is enhanced by the locked conformation of the five-membered ring caused by lithium-to-oxygen coordination.

EXPERIMENTAL

The NMR spectra were recorded on a Bruker 500 Avance, Varian INOVA 300 or Varian Gemini 200 spectrometer (chemical shifts in δ;

ppm, J; Hz). The alkylation products **1a–10a** were analyzed as mixtures of diastereomers and the spectral data is given for the major diastereomer, if not otherwise mentioned. The assignments are based on chemical shift data and DEPT measurements. HMQC measurement was used for compound **11c**.

Mass spectra were run on a JEOL JMS-SX 102 instrument (70eV). GC analyses were run with HP 6890 gas chromatograph with HP-5 column (10 m) or Micromat apparatus with SE-54 column (20 m) both with FID detector. Flash chromatography was carried out using Merck Silica 60 230–400 mesh. Tetrahydrofuran (THF) was dried and distilled over CaH_2 or Na with benzophenone before use. DMF was dried and distilled in vacuum over CaH_2. The concentration of *n*-BuLi in hexane was determined by a literature procedure.[29] The melting point was determined in an open capillary tube with an Electrothermal apparatus and is uncorrected.

Preparation of Starting Materials

Thioacetic acid *S*-2-tetrahydropyranyl ester **12** was obtained from thioacetic acid and 3,4-dihydro-2*H*-pyran by a previously reported method.[17] The corresponding procedure was used for the synthesis of thioacetic acid *S*-(1-ethoxyethyl)ester **15**.[30] Thioacetic acid *S*-(2-methyl tetrahydropyran-2-yl)ester **13**, thioacetic acid *S*-l-benzopyran-2-yl ester **14**[31] and thioacetic acid *S*-(tetrahydropyran-2-ylmethyl)ester **16**[32] were prepared by the reaction of the potassium or sodium salt of thioacetic acid with 2-chloro-2-methyl tetrahydropyran,[33] 2-chloro-1-benzopyran **23**[31] and the commercially available 2-(chloromethyl)tetrahydropyran respectively. Thioacetic acid *S*-cyclohexyl ester **17** was prepared by the free radical addition of thioacetic acid to cyclohexene.[34]

Chloromethylthiobenzene **18** and chloromethylthiomethane **22** were purchased from Aldrich. 2-(Chloromethylthio)naphthalene **19** was prepared by a literature method[35] and the same procedure was applied for the synthesis of 9-(chloromethylthio)phenanthrene **20** using N-chlorosuccinimide and 9-methylthiophenanthrene.[36] The methyl group in 9-methylthioanthracene could not be chlorinated by NCS, instead, 9-(chloromethylthio)anthracene (**21**) was prepared by applying the patent of Goralski and Burk,[37] using 9-anthracenethiol[38] as the starting material.

Dithioacetals 3–10 : General Procedure

The thioacetic acid ester, 30 mmol, was added to a solution of 2.1 eq. of KOH in 45 ml of DMSO and 15 ml of H_2O, and the mixture was stirred for 15 min at 0°C and 30 min at room temperature. $ClCHSCH_2R$ (R =

phenyl, methyl, 2-naphthyl, 9-phenanthryl, 9-anthracenyl), 30 mmol, was added during 10 min at 0°C and the mixture allowed to reach room temperature with stirring overnight. Water was added and the mixture extracted with diethyl ether. The organic phase was washed with water and brine, dried with Na_2SO_4 and the solvent was evaporated.

2-(Phenanthren-9-ylthiomethylthio)tetrahydropyran 3

From thioacetic acid *S*-(2-tetrahydropyranyl)ester **12** and crude 9-(chloromethylthio)phenathrene **20**. Purification by flash chromatography (silica gel, CH_2Cl_2); 45%; δ_H(200 MHz; $CDCl_3$) 1.40–2.00 (m, 3 × CH_2), 3.36–3.55 & 3.95–4.10 (m, OCH_2), 4.18 (ABq, *J* 13.2, SCH_2S), 5.19 (m, OCHS), 7.50–7.57 (m, 4H), 7.75–7.85 (m, 1 H), 7.93 (s, 1 H), 8.45–8.75 (m, 3 H); δ_c(50 MHz; $CDCl_3$) 21.4 (C-4), 25.5 (C-5), 30.6 (C-3), 35.0 (SCH_2S), 64.2 (OCH_2), 80.9 (OCHS), 122.5, 123.0, 125.5, 126.7, 126.8, 128.1, 129.0, 130.1, 130.6, 131.2, 131.5 (arom. C); HRMS 340.0944, calc. for $C_{20}H_{20}OS_2$ 340.0956.

2-(Anthracen-9-ylthiomethylthio)tetrahydropyran 4

From thioacetic acid *S*-(2-tetrahydropyranyl)ester **12** (13 mmol) and 9-(chloromethylthio)anthracene **21** (17 mmol); yield 87%. Purification by flash chromatography (silica gel, CH_2Cl_2); 59%; δ_H(200 MHz; $CDCl_3$) 1.42–1.95 (m, 3 × CH_2), 3.38–3.50 & 3.90–4.04 (m, OCH_2), 4.05 (ABq, *J* 12.8, SCH_2S), 5.15–5.22 (m, OCHS), 7.44–7.65 (m, 4H), 7.96–8.04 (d-like m, 2 H), 8.48 (s, 1 H), 8.84–8.96 (d-like m, 2 H); δ_c(50 MHz; $CDCl_3$) 21.5 (C-4), 25.5 (C-5), 30.6 (C-3), 37.7 (SCH_2S), 64.4 (OCH_2), 81.2 (OCHS), 124.8, 125.4, 126.8, 126.9, 127.7, 129.0, 129.4, 131.8, 134.6 (arom. C); HRMS 340.0941, calc. for $C_{20}H_{20}OS_2$ 340.0956.

2-Methyl-2-(methylthiomethylthio)tetrahydropyran 5

From thioacetic acid *S*-(2-methyltetrahydropyran-2-yl)ester **13** and chloromethylthiomethane **22**; yield 76%; δ_H(200 MHz; $CDCl_3$) 1.50–1.95 (m, 3 × CH_2), 1.62 (s, CH_3), 2.23 (s, SCH_3), 3.62 (AB_q, *J* 12.9), 3.60–3.74 & 3.88–4.05 (m, OCH_2); δ_c(50 MHz; $CDCl_3$) 15.7 (SCH_3), 19.5 & 25.0 & 32.2 (CH_2), 31.1 (CH_3), 37.0 (SCH_2S), 62.2 (OCH_2), 86.4 (OCS); MS: no $M.^+$ observed (m/z 192).

2-(Methylthiomethylthio)tetrahydropyran 7

From thioacetic acid *S*-(2-tetrahydropyranyl)ester **12** and chloromethylthiomethane **22**, yield 90%. Purification by distillation; b.p. 90°C/2.4 mbar, yield 43%; δ_H(200 MHz; $CDCl_3$) 1.53–2.15 (m, 3 × CH_2), 2.19 (s, SCH_3), 3.48–3.62 & 4.02–4.16 (m, OCH_2), 3.74 (AB_q, *J* 13.6, SCH_2S), 5.13 (m, OCHS); δ_c(50 MHz; $CDCl_3$) 15.0 (SCH_3), 21.5 & 25.5 & 30.7 (CH_2), 35.5 (SCH_2S), 64.4 (OCH_2), 80.3 (OCHS); HRMS 178.0484, calc. for $C_7H_{14}OS_2$ 178.0486.

1-Ethoxy-1-methylthiomethylthioethane 8

From thioacetic acid *S*-(l-ethoxyethyl) ester **15** and chloromethylthiomethane **22**; 98%. Purification by distillation; b.p. 53–54°C/1.1 mbar; yield 56%; δ_H(200 MHz; $CDCl_3$) 1.22 (t, *J* 7.0, C*H*$_3$CH$_2$O), 1.56 (d, *J* 6.5, CHC*H*$_3$), 2.20 (s, SCH_3), 3.46–3.80 (m, OCH_2), 3.71 (AB_q, *J* 13.5, SCH_2S), 4.88 (q, *J* 6.5, OCHS); δ_c(50 MHz; $CDCl_3$) 15.0 & 15.2 (CH_3), 22.0 (CH_3), 34.3 (SCH_2S), 62.3 (OCH_2), 80.4 (OCHS); HRMS 166.0509, calc. 166.0486 for $C_6H_{14}OS_2$.

2-(Phenylthiomethylthiomethyl)tetrahydropyran 9

From thioacetic acid-*S*-(tetrahydropyran-2-ylmethyl)ester **16** and chloromethylthiobenzene **18**; yield 96%. Purification by flash chromatography (silica gel, CH_2Cl_2); yield 45%; δ_H(200 MHz; $CDCl_3$) 1.24–1.80 (m, 3 × CH_2), 2.66–2.87 (m, CHC*H*$_2$S), 3.36–3.54 (m, OCH_2), 3.74–4.06 (m, OCH), 4.10 (s, SCH_2S), 7.2–7.5 (m, arom. H); δ_c(50 MHz; $CDCl_3$) 23.2 & 26.2 & 31.7 (CH_2), 37.6 (THP-CH_2), 39.1 (SCH_2S), 69.0 (OCH_2), 78.0 (OCH), 127.2, 129.3, 130.7, 135.8 (arom. C); HRMS 254.0791, calc. for $C_{13}H_{18}OS_2$254.0799.

Cyclohexylthiomethylthiobenzene 10

From thioacetic acid *S*-cyclohexyl ester **17** and chloromethylthiobenzene **18**; yield 76%; δ_H(200 MHz; $CDCl_3$) 1.20–2.10 (m, 4 × CH_2), 2.93 (m, CHS), 4.1 (s, SCH_2S), 7.18–7.45 (arom. H); δ_c(50 MHz; $CDCl_3$) 25.6 & 25.9 & 26.0 (CH_2), 32.8 & 33.1 (SC*C*H$_2$), 35.9 (SCH_2S), 43.2 (CHS), 126.6, 128.8, 130.3, 135.7 (arom. C); HRMS 238.0842, calc. for $C_{19}H_{18}S_2$ 238.0850.

Alkylation of 1–10: General Procedure

The dithioacetals were deprotonated with 1.1 eq. 2 M *n*-BuLi at −78°C in dry THF under argon atmosphere. The mixture was stirred for 1 h at −78°C, 1 eq. RX added dropwise and the reaction mixture stirred overnight allowing it slowly to reach room temperature. The reaction mixture was quenched with water and extracted with diethyl ether. The organic phase was washed with water and brine, dried with Na_2SO_4 and the solvent evaporated.

2-(1-Phenylthioethylthio)tetrahydropyran 1a

From 2-(phenylthiomethylthio)tetrahydropyran **1**[17] (4.2 mmol) and MeI; yield 0.9 g (80%). Purification by flash chromatography (silica gel, CH_2Cl_2); yield 0.13 g (64%); δ_H(200 MHz; $CDCl_3$) 1.5–2.0 (3 × CH_2), 1.58 (d, *J* 7.0, CH_3), 3.46–3.60 & 3.98–4.14 (m, OCH_2), 4.45 (q, *J* 7.0, SCHS), 5.21–5.26 (m, OCHS), 7.25–7.55 (m, arom. H); δ_c(50 MHz;

$CDCl_3$) 21.8 & 25.7 & 30.7 (CH_2), 23.1 (CH_3), 47.7 (SCHS), 64.8 (OCH_2), 82.0 (OCS), 128.1, 129.2, 133.8, 134.3 (arom. C); HRMS 254.0793, calc. for $C_{13}H_{18}OS_2$ 254.0799.

2-(1-Phenylthiopentylthio)tetrahydropyran **1b**

From **1** (4.2 mmol) and *n*-BuBr; yield 1.04 g (85%). Purification by flash chromatography (silica gel, CH_2Cl_2); yield 0.55 g (45%). Major diastereomer: δ_H(500 MHz; $CDCl_3$)* 0.82 (t, *J* 7.3, CH_3), 1.24 & 1.27 (m, Bu-H-4), 1.45 & 1.51 (m, Bu-H-3), 1.56 (m, THP-H-5), 1.81 & 1.75 (m, Bu-H-2), 1.75 & 1.56 (m, THP-H-4), 1.67 m & 1.92 (m, THP-H-3), 3.46 & 4.02 (m, THP-H-6,), 4.31 (m, *J* 5.9, 7.3, SCHS), 5.20 (m, *J* 3.8, 6.1, OCH*S*), 7.22 (*p*-H: m), 7.27 (*m*-H; m), 7.44 (*o*-H; m); δ_c(125 MHz; $CDCl_3$) 14.15 (CH_3), 21.94 (THP-C-4), 22.48 (Bu-C-4), 25.90 (THP-C-5), 29.35 (Bu-C-3), 30.95 (THP-3-C), 36.10 (Bu-C-2), 53.72 (SCHS), 64.56 (OCH_2), 81.83 (OCHS), 127.78 *p*-C), 129.03 (*m*-C), 133.31 (*o*-C), 134.98 (arom. C-S). Minor diastereomer: δ_H(500 MHz; $CDCl_3$) 0.86 (t, *J* 7.3, CH_3), 1.27 & 1.29 (m, Bu-H-4), 1.46 & 1.52 (m, Bu-H-3), 1.52 (m, THP-H-5), 1.75 & 1.56 (m, THP-H-4), 1.66 & 1.90 (m, THP-H-3), 1.90 (m, Bu-H-2), 3.44 m & 3.91 (m, THP-H-6), 4.19 (t, *J* 7.0, SCHS), 5.14 (t-like m, *J* 5, OCHS), 7.22 (m, *p*-H), 7.27 (m, *m*-H), 7.44 (m, *o*-H); δ_c(125 MHz; $CDCl_3$) 14.20 (CH_3), 21.62 (THP-C-4), 22.48 (Bu-C-4), 25.86 (THP-C-5), 29.62 (Bu-C-3), 31.65 (THP-3-C), 36.64 (Bu-C-2), 53.94 (SCHS), 64.15 (OCH_2), 81.59 (OCHS), 127.52 *para*-C), 129.01 (*meta*-C), 132.51 (*ortho*-C), 134.94 (arom. C—S); HRMS 296.1261, calc. for $C_{16}H_{24}OS_2$ 296.1269.

2-(2-Phenyl-1-phenylthioethylthio)tetrahydropyran **1c**

From **1** (4.2 mmol) and $PhCH_2Br$; GC yield 64%. A sample for spectroscopy was purified by flash chromatography (silica gel, CH_2Cl_2); δ_H(200 MHz; $CDCl_3$) 1.40–2.10 (m, 3 × CH_2), 3.00–3.26 (m, $PhCH_2$), 3.30–3.42 & 3.66–3.80 (m, OCH_2), 4.51–4.54 (t-like m, SCHS), 5.28–5.32 (m, OCHS), 7.15–7.55 (m, arom. H); δ_c(50 MHz; $CDCl_3$) 20.7 (C-4), 25.2 (C-5), 30.0 (C-3), 42.0 ($PhCH_2$), 54.0 (SCHS), 62.7 (OCH_2), 80.9 (OCHS), 126.2, 127.2, 128.1, 128.5, 129.2, 132.6, 134.4, 137.6 (arom. C); HRMS 330.1104, calc. for $C_{19}H_{22}OS_2$ 330. 1112.

*Chemical shifts obtained from mixtures of major and minor diastereomer by combined use of 2D ^{1}H-^{1}H COSY and ^{1}H-^{13}C COSY correlation diagrams (Bruker AMX500, $CDCl_3$); Dr. Tõnis Pehk, Institute of Chemical Physics and Biophysics, Akademia tee 23 EE0026 Tallinn, Estonia.

Trimethyl[phenylthio(tetrahydropyran-2-ylthio)methyl]-silane **1d**

From **1** (2.1 mmol) and $(CH_3)_3SiCl$; yield 0.47 g (71%), GC purity 95%; δ_H(200 MHz; $CDCl_3$) 0.16 (s, CH_3), 1.20–2.00 (m, CH_2), 3.28–3.32 & 3.85–4.00 (m, OCH_2), 3.88 (s, SCHS), 4.90–5.00 (m, OCHS), 7.00–7.60 (m, arom. H); δ_c(50 MHz; $CDCl_3$) −2.8 (3 × CH_3), 21.0 (C-4), 24.8 (C-5), 29.8 (C-3), 37.7 (SCS), 63.6 (OCH_2), 79.7 (OCHS), 126.0, 128.1, 130.4, 136.7 (arom.C); HRMS 312.1024, calc. for $C_{15}H_{24}OS_2Si$ 312.1038.

2-[1-(2-Naphthylthio)pentylthio]tetrahydropyran **2a**

From **2**[39] (4.8 mmol) and *n*-BuBr; yield 1.2 g (70%). Purified by flash chromatography (silica gel, CH_2Cl_2-hexane 1:1), 0.7 g (42%); δ_H(200 MHz; $CDCl_3$) 0.86 (t, *J* 7, CH_3), 1.20–2.10 (m, 6 × CH_2), 3.45–3.62 & 4.05–4.16 (m, OCH_2), 4.42–4.51 (m, SCHS), 5.25–5.34 (m, OCHS), 7.40–7.65 (m, 3 arom. H), 7.70–7.90 (m, 3 arom. H), 7.9 (s, arom.H); δ_c(50 MHz; $CDCl_3$) 13.9 (CH_3), 21.6 & 22.3 & 25.6 & 28.9 & 30.7 & 36.1 (CH_2), 53.1 (SCHS), 64.4 (OCH_2), 81.6 (OCHS), 126.0, 126.4, 127.5, 127.6, 128.3, 130.0, 131.5, 132.4, 133.6 (arom. C); HRMS 346.1414, calc. for $C_{20}H_{26}OS_2$ 346.1425.

2-[1-(Phenanthren-9-ylthio)ethylthio]tetrahydropyran **3a**

From **3** (1.8 mmol) and MeI; yield GC yield 71%; δ_H(200 MHz; $CDCl_3$) 1.4–2.05 (m, 3 × CH_2), 1.59 (d, *J* 7.0, CH_3), 3.46–3.62 & 4.00–4.20 (m, OCH_2), 4.60 (q, *J* 7.0, SCHS), 5.34 (dd, *J* 3.8, 6.6, OCHS), 7.5–7.7 (m, 4 × arom. H), 7.80–7.90 (m, arom. H), 8.1 (s, H-10), 8.60–8.75 (m, 3 arom. H); δ_c(50 MHz; $CDCl_3$) 21.7 (C-4), 22.9 (CH_3), 25.5 (C-5), 30.6 (C-3), 46.8 (SCHS), 64.8 (OCH_2), 81.6 (OCHS), 122.5, 122.9, 126.4, 126.87, 126.89, 127.2, 128.4, 130.2, 130.7, 131.4, 132.3, 134.4 (arom. C); HRMS 354.1125, calc. for $C_{21}H_{22}OS_2$ 354.1112.

2-[1-(Phenanthren-9-ylthio)pentylthio]-tetrahydropyran **3b**

From **3** (1.8 mmol) and *n*-BuBr; GC yield 51%. Purification by flash chromatography (silica gel, CH_2Cl_2); yield 0.26 g (37%); δ_H(200 MHz; $CDCl_3$) 0.80 (t, *J* 7.3; CH_3), 1.10–2.05 (m, 6 × CH_2), 3.41–3.55 & 3.98–4.14 (m, OCH_2), 4.55 (dd, *J* 5.1, 7.3, SCHS), 5.23 (dd, *J* 3.7 & 6.3, OCHS), 7.54–7.76 (m, 4 × arom. H), 7.80–7.90 (m, arom. H), 8.06 (s, H-10), 8.60–8.75 (m, 3 arom. H); δ_c(50 MHz; $CDCl_3$) 13.8 (CH_3), 21.6, 22.2, 25.5, 28.8 & 30.7 & 35.6 (CH_2), 52.8 (SCHS), 64.5 (OCH_2), 81.5 (OCHS), 122.5, 122.9, 126.3, 126.8, 126.87, 126.89, 127.1, 128.3, 130.3, 130.7, 131.5, 132.2, 133.6 (arom. C); HRMS 396.1596, calc. for $C_{24}H_{28}OS_2$ 396.1582.

2-[1-(Anthracen-9-ylthio)-pentylthio]tetrahydropyran 4a

From **4** (2.1 mmol) and *n*-BuBr. Purification by flash chromatography (silica gel, CH_2Cl_2) 0.28 g (34%). The NMR sample in $CDCl_3$ decomposes to anthraquinone in 2–3 days at room temperature; δ_H(200 MHz; $CDCl_3$) 0.68 (t, *J* 7.2, CH_3), 1.10–1.95 (m, 6 × CH_2), 3.38–3.52 & 3.96–4.10 (m, OCH2), 4.51 (t, *J* 5.8, SCHS), 5.14–5.22 (m, OCHS), 7.48–7.55 (m, 4 × arom. H), 7.98–8.04 (m, 2 × arom. H), 8.5 (s, H-10), 8.97 (m, 2 × arom. H); δ_c(50 MHz; $CDCl_3$) 14.0 (CH_3), 22.1 & 22.5 & 25.8 & 28.9 & 31.0 & 35.8 (CH_2), 53.9 (SCHS), 65.2 (OCH_2), 81.6 (OCHS),126.8, 126.9, 127.4, 127.5, 129.2, 129.6, 132.1, 132.4, 135.3 (arom. C). MS: no M^+. observed (m/z 396).

2-Methyl-2-(1-methylthioethylthio)tetrahydropyran 5a

From **5** (2.6 mmol) and MeI, partially decomposes in distillation; yield 0.18 g (33%), b.p. 70°C/1 mbar; δ_H(200 MHz; $CDCl_3$) 1.50–1.95 (3 × CH_2; m), 1.63 (s, CH_3), 1.68 (d, *J* 7.0, $SCHCH_3$), 2.22 (s, SCH_3), 3.60–3.73 & 4.00–4.20 (m, OCH_2), 3.93 (q, *J* 7.0, SCHS); δ_c(50 MHz; $CDCl_3$) 14.0 & 25.2 & 31.0 (CH_3), 19.6 & 25.3 & 37.5 (CH_2), 43.2 (SCS), 62.3 (OCH_2), 87.4 (OCS). MS: no M^+. observed (m/z 206).

2-(Phenylthiopentylthio)-1-benzopyran 6a

From **6**[31] (10.0 mmol) and *n*-BuBr, purified by flash chromatography (silica gel, CH_2Cl_2-hexane 3:2), 0.17 g (47%); δ_H(200 MHz; $CDCl_3$) 0.80 (t, *J* 7, CH_3), 1.10–1.58 (m, 2 × CH_2), 1.68–1.92 (m, CH_2), 1.98–2.43 (m, CH_2), 2.66–3.08 (m, $PhCH_2$), 4.47 (t, *J* 7, SCHS), 5.88 (t, *J* 4, OCHS), 6.76–6.94 & 7.02–7.42 & 7.46–7.60 (m, 9 arom. H); δ_c(50 MHz; $CDCl_3$) 13.9 (CH_3), 22.1 & 22.5 & 26.8 & 28.8 & 35.7 (CH_2), 53.9 (SCHS), 80.0 (OCHS), 117.4, 121.0, 127.2, 127.7, 128.8, 129.5, 133.3 (arom. C); HRMS 344.1243, calc. for $C_{20}H_{24}OS_2$ 344.1269.

2-(1-Methylthioethylthio)tetrahydropyran 7a

From **7** (2.8 mmol) and MeI. Purification by Kugelrohr distillation (130°C/1.5 mbar); yield 0.24 g (44%); δ_H(200 MHz; $CDCl_3$) 1.50–2.00 (m, 3 × CH_2), 1.61 (d, *J* 7.2, CH_3), 2.12 (s, SCH_3), 3.48–3.62 & 4.00–4.13 (m, OCH_2), 4.12 (q, *J* 7.2, SCHS), 5.05–5.15 (m, OCHS); δ_c(50 MHz; $CDCl_3$) 11.7 & 22.4 (CH_3), 22.0 & 25.6 & 30.9 (CH_2), 45.3 (SCHS), 64.9 (OCH_2), 82.2 (OCHS); HRMS 192.0652, calc. for $C_8H_{16}OS_2$ 192.0643.

2-(1-Methylthiopentylthio)tetrahydropyran 7b

From 2-(methylthiomethylthio)tetrahydropyran **7** (2.8 mmol) and *n*-BuBr. Purification by Kugelrohr distillation (150°C/1.0 mbar); yield 0.38 g (58%); δ_H(200 MHz; $CDCl_3$) 0.91 (t, *J* 7, CH_3), 1.20–2.02 (m, 6 × CH_2), 2.08 (s, SCH_3), 3.48–3.62 & 4.02–4.16 (m, OCH_2), 3.97

(t, J 7.1, SCHS), 5.13–5.20 (m, OCHS); δ_c(50 MHz; $CDCl_3$) 11.5 & 13.9 (CH_3), 21.9 & 22.3 & 25.6 & 29.6 & 30.9 & 34.8 (CH_2), 50.93 (SCHS), 50.9 (SCHS), 64.7 (OCH_2), 81.7 (OCHS); HRMS 234.1105, calc. for $C_{11}H_{22}OS_2$ 234.1112.

1-Ethoxy-1-(1-methylthioethylthio)ethane **8a**

From **8** (18 mmol) and MeI. Purification by Kugelrohr distillation (120°C/1.8 mbar); yield 0.17 g (56%); δ_H(200 MHz; $CDCl_3$) 1.22 (t, J 7.0, CH_3), 1.53 (d, J 6.5, $OCHCH_3$), 1.61 (d, J 7.1, $SCHCH_3$), 2.13 (s, SCH_3), 3.48–3.82 (m, OCH_2), 4.08 (q, J 7.1, SCHS), 4.98 (m, J 6.5); δ_c(50 MHz; $CDCl_3$) 12.0 & 15.2 & 21.7 & 22.7 (CH_3), 45.4 (SCHS), 62.0 (OCH_2), 81.3 (OCHS); HRMS 180.0632, calc. for $C_7H_{16}OS_2$ 180.0643.

1-(1-Ethoxyethylthio)-1-methylthiopentane **8b**

From **8** (3.0 mmol) and *n*-BuBr. Purification by Kugelrohr distillation (150°C/1.5 mbar); yield 0.34 g (51%); δ_H(200 MHz; $CDCl_3$) 0.89 (t, J 7.1, CH_3), 1.19 (t, J 7.0, CH_3CH_2O), 1.49 (d, J 6.5, $OCHCH_3$), 1.20–1.80 (m, 3 × CH_2), 2.07 (s, SCH_3), 3.48–3.80 (m, OCH_2), 3.90 (t, J 7.0, SCHS), 4.99 (q, J 6.5, OCHS); δ_c(50 MHz; $CDCl_3$) 12.1 & 14.4 & 15.6 & 22.0 (CH_3), 22.6 & 29.9 & 35.6 (CH_2), 51.5 (SCHS), 62.1 (OCH_2), 81.4 (OCHS); HRMS 222.1118, calc. for $C_{10}H_{22}OS_2$ 222.1112.

2-(1-Phenylthioethylthiomethyl)tetrahydropyran **9a**

From **9** (1.2 mmol) and MeI; 0.23 g (73%); δ_H(200 MHz; $CDCl_3$) 1.20–1.90 (m, 3 × CH_2) 1.56 (d, J 6.9, CH_3), 2.68–3.02 (m, CH_2S), 3.35–3.55 (m, CH_2O), 3.94–4.02 (m, OCH), 4.35 (q, J 6.9, SCHS), 7.28–7.45 (m, arom. H); δ_c(50 MHz; $CDCL_3$) 23.8 (CH_3), 24.2 & 26.7 & 32.2, (CH_2), 38.4 (CH_2S), 51.1 (SCHS), 69.5 (OCH_2), 78.1 (OCH), 127.5, 128.8, 132.9, 133.1 (arom. C); HRMS 268.0969, calc. for $C_{14}H_{20}OS_2$ 268.0956.

2-(1-Phenylthiopentylthiomethyl)tetrahydropyran **9b**

From **9** (1.2 mmol) and *n*-BuBr; 0.26 g (70%); δ_H(200 MHz; $CDCl_3$) 0.90 (t, J 7.3, CH_3), 1.10–1.98 (m, 6 × CH_2), 2.60–2.98 (m, CH_2S), 3.35–3.55 (m, OCH_2), 3.92–4.03 (m, OCH), 4.15–4.25 (m, SCHS), 7.10–7.58 (m, arom. H); δ_c(50 MHz; $CDCl_3$) 13.9 (CH_3), 22.1 & 23.2 & 25.7 & 29.1 & 31.1 & 31.3 (CH_2), 37.1 (SCH_2), 55.5 (SCHS), 68.5 (OCH_2), 127.4, 128.7, 132.8, 134.5 (arom. C); HRMS 310.1439, calc. for $C_{17}H_{26}OS_2$ 310.1425.

(1-Cyclohexylthio-2-methylbutylthio)benzene **10a**

From **10** (2 mmol) and 2-BrBu; GC yield 57%; diastereomers could not be separated. The ratio of the diastereomers was estimated to be

1:1 from ^{1}H NMR; δ 4.2 & 4.3 (SCHS); δ_H(200 MHz; $CDCl_3$) 0.8–2.05 (m, 2 × CH_3, 6 × CH_2, CH), 2.75–3.0 (m, CHS), 4.2 & 4.3 (d, *J* 3, SCHS, for 2 diastereomers), 7.2–7.5 (arom. C). δ_c(50 MHz; $CDCl_3$) 11.8 (CH_3), 15.0 (CH_3), 25.6 & 25.7 & 27.0 & 33.0 & 33.1 & 33.7 (6 × CH_2), 39.4 (CHS), 43.5 (CH), 59.5 (SCHS), 126.9, 128.7, 131.8, 136.0 (arom. C); HRMS 294.1491, calc. for $C_{17}H_{26}S_2$ 294.1476.

Thioacetic Acid S-(2-methyltetrahydropyran-2-yl)ester 13

Sodium hydride (2.2 g of 60% dispersion in mineral oil) was washed several times with *n*-hexane under argon atmosphere and suspended to 20 ml of THF. To that suspension 3.6 g (47 mmol) of thioacetic acid in 10 ml of THF was slowly added with stirring at 0–5°C. A solution of 6.3 g (47 mmol) 2-chloro-2-methyltetrahydropyran[33] in 5 ml of THF was slowly added at the same temperature and the mixture was allowed to reach room temperature with stirring overnight. After the usual work-up (H_2O, extracted with diethyl ether, washed with $NaHCO_3/H_2O$ and H_2O, dried with Na_2SO_4, and the solvent evaporated) the crude product (yield 60%) was used without further purification; δ_H(200 MHz; $CDCl_3$) 1.45–1.95 (m, 3 × CH_2), 1.81(s, CH_3), 2.31 (s, $SCOCH_3$), 3.85 (m, OCH_2). MS: no $M.^+$ observed (m/z 174).

9-(Chloromethylthio)phenanthrene 20

The mixture of 9-(methylthio)phenanthrene[36] (3.0 g, 13 mmol) and *N*-chlorosuccinimide (1.8 g, 13 mmol) in 80 ml of dry carbon tetrachloride was stirred at room temperature overnight. The precipitate was filtered off and the solvent evaporated to get 3.3 g (95%) of an yellow gum, 9-(chloromethylthio)phenanthrene containing about 30% of 9-chloro-10-(methylthio)phenanthrene.* The product was used without further purification; δ_H(200 MHz; $CDCl_3$) 5.04 (s, SCH_2Cl), 7.58–7.78 (m, 4H), 7.87–7.94 (m, 1 H), 8.15 (s, 1 H), 8.44–8.52 (m, 1 H), 8.64–8.77 (m, 2 H); δ_c(50 MHz; $CDCl_3$) 50.7 (SCH_2Cl), 122.6, 123.0, 123.2, 125.6, 126.5, 127.1, 127.6, 128.0, 128.7, 133.0 (arom. C).

9-(Chloromethylthio)anthracene 21

Bromochloromethane (50 ml) was stirred with 0.5 g (8, 9 mmol) of KOH, and 1.87 g (8.9 mmol) of 9-anthracenethiol was added. Tetrabutylammonium bromide (0.15 g, 0, 5 mmol) was added, the mixture was stirred for 20 min, refluxed for 30 min, and cooled to room temperature.

*Pure 9-chloro-10-(methylthio)phenanthrene was isolated by flash chromatography during the purification of **3**. The crystal structure and spectral data will be published later.

The white precipitate was filtered off and the solvent was evaporated in vacuo; yellow powder (1.75 g, 76%) was used without purification; δ_H(200 MHz; $CDCl_3$) 4.96 (s, CH_2), 7.41–7.62 (m, 4 arom. H), 7.98–8.10 (d-like m, 2 arom. H), 8.57 (s, 1 arom. H), 8.80–8.90 (m, 2 arom. H); δ_c(50 MHz; $CDCl_3$) 53.0 (SCH_2Cl), 125.4, 126.5, 127.0, 128.9, 130.3, 131.7, 134.7 (arom. C). MS: no $M.^+$ observed (m/z 258).

(1′R,2R*)-2-(2′-phenyl-1′-phenylthioethylthio)-tetrahydropyran, 1c Major Diastereomer, by Deoxygenation*

To a stirred suspension of 0.1 g (2.54 mmol) of $LiAlH_4$ in 8 ml of diethyl ether under an argon atmosphere, 0.34 g (2.54 mmol) of anhydrous granular $AlCl_3$ dissolved in 8 ml of diethyl ether was added and the mixture stirred for 10 min at room temperature. **11c** (0.08 g; 0.23 mmol) in 4 ml of diethyl ether was added via syringe at such a rate as to cause a gentle reflux, and the reaction mixture refluxed with stirring for 3 h. After cooling, the excess reagent was decomposed by slow addition of 2 ml of ice-cold water followed by 3 ml of 2 M HCl. The organic phase was separated and the grey aqueous material extracted with ether. The ether solutions were washed with 10% $NaHCO_3$, water and brine, dried with Na_2SO_4 and evaporated to dryness. The oily residue (0.07 g) was analyzed with GC to contain 14% (*1′R*,2R**)-2-(2′-phenylthioethylthio)tetrahydropyran. The rest consisted of **11c** (13%) and unidentified side products. The crude product was purified with flash chromatography (Silica gel, CH_2Cl_2+hexane 9+1). In GC analysis the purified product contained 89% (*1′R*,2R**)-2-(2′-phenyl-1′-phenylthioethyl-thio)tetrahydropyran; δ_H(200 MHz; $CDCl_3$) 1.40–2.10 (m, 3 × CH_2), 3.00–3.24 (m, $PhCH_2$), 3.30–3.43 & 3.66–3.80 (m, OCH_2), 4.49–4.57 (t, *J* 6.2, SCHS), 5.28–5.32 (m, OCHS), 7.15–7.55 (m, arom. H); δ_c(50 MHz; $CDCl_3$) 21.2 (C-4), 25.6 (C-5), 30.4 (C-3), 42.3 ($PhCH_2$), 54.4 (SCHS), 63.4 (OCH_2), 81.4 (OCHS), 126.6, 127.2, 128.1, 128.8, 129.5, 133.0, 134.4, 137.5 (arom. C); HRMS 330.1122, calc. 330.1112 for $C_{19}H_{22}OS_2$.

(1′R,2S*)-2-(2′-Phenyl-1′-phenylthioethylthio)-tetrahydropyran, 1c Minor Diastereomer, by Deoxygenation*

By applying the procedure above 0.24 g (6.35 mmol) of $LiAlH_4$, 0.85 g (6.35 mmol) of $AlCl_3$ and 0.2 g (0.58 mmol) **11a** gave an oily residue (0.19 g) which was analyzed with GC to contain 8% (*1′R*,2S**)-2-(2′-phenylthioethylthio)tetrahydropyran. The rest consisted of **11a** and smaller amounts of unidentified side products. The reduction product was purified twice with flash chromatography (Silica gel,

CH_2Cl_2 + hexane 2 + 1) to obtain a pure sample for MS and ^1H NMR analysis; δ_H(200 MHz; $CDCl_3$) 1.40–1.9 (m, 3 × CH_2), 3.18–3.24 (d-like m, $PhCH_2$), 3.32–3.50 & 3.81–3.96 (m, OCH_2), 4.42 (t, *J* 7.3, SCHS), 4.87 (t, *J* 4.6, OCHS), 7.1–7.5 (10H, m, arom. H); δ_c(125 MHz; $CDCl_3$) 21.0 (C-4), 25.6 (C-5), 31.1 (C-3), 43.4 ($PhCH_2$), 54.3 (SCHS), 63.6 (OCH_2), 81.7 (OCHS), 126.7, 127.4, 128.2, 128.8, 129.5, 132.7, 138.5 (arom. C); HRMS 330.1126, calc. 330.1112 for $C_{19}H_{22}OS_2$.

The Isolation of 1-Phenyl-2-phenylthio-2-(tetrahydropyran-2′-ylthio)ethanol Diastereomers **11a–d**

When lithio-**1** is treated with benzaldehyde all four diastereoisomeric ethanol derivatives are formed[18] and can be isolated by semipreparative HPLC. The experiments were performed with an ISCO model 2350 liquid chromatograph equipped with a Shimadzu SPD-6A UV spectrophotometric detector and a Shimadzu C-R6A Chromatopac. Components were monitored measuring the absorption at 254 nm. The column used was Lichrocart Si 60 (250 × 10 mm ID), 5 μm. The mobile phase was 2% ethyl acetate in dichloromethane; flow rate, 7 ml min^{-1}. The relative amounts and retention times are for **11a** 21%, retention time 5.9 min; **11b** 21%, 6.6 min; **11c** 35%, 7.5 min; and for **11d** 23%, 10.9 min, respectively. Compounds **11a** and **11b** were readily crystallized from ethanol, but crystals of the isomers **11c** and **11d** were extremely slowly grown after atmospheric evaporation of the solvent.

(1R,2S*,2′S*)-1-phenyl-2-phenylthio-2-(tetrahydropyran-2′-ylthio)ethanol* **11c**

The diastereomer **11c** was prepared, isolated and crystallised as reported above. The melting point is 102–103°C, δ_H(300 MHz; $CDCl_3$) 1.30–2.05 (m, 3 × CH_2), 3.20–3.26 & 3.38–3.53 (m, OCH_2), 3.47 (d, *J* 2.7, OH), 4.49 (d, *J* 4.5, SCHS), 4.90 (dd, *J* 4.5, 2.7, PhCH), 5.24 (t, *J* 4.3, OCHS), 7.1–7.5 (m, arom. H); δ_c(75 MHz; $CDCl_3$) 20.7 (THP-C-4), 25.4 (THP-C-5), 30.4 (THP-C-3), 62.2 (SCHS), 62.7 (OCH_2), 74.8 (OCHPh), 81.6 (OCHS), 126.5, 127.6, 127.9, 129.1, 132.8, 134.2, 140.0 (arom. C).

The X-ray Crystal Structure of (1R,2S*,2′S*)-1-phenyl-2-phenylthio-2-(tetrahydropyran-2′-ylthio)ethanol* **11c***

The crystal was mounted using a viscose oil drop method. Diffraction data were collected on a Rigaku AFC7S diffractometer at 193(2) K using graphite monochromated Mo*Kα* radiation (λ = 0.71073 Å) and $\omega/2\theta$

*The crystallographic data (no CCDC 155438) is deposited to the Cambridge Crystallographic Data Centre, U.K.

scans. The data were processed with TEXSAN software.[40] The structure was solved with SHELXS97,[41] refined with SHELXL97[42] and graphics was produced with SHELXTL/PC[43] software. All data were used in full-matrix least-squares refinement on F^2. Hydrogen atoms were at calculated positions and refined using a riding model.

Crystal data. $C_{19}H_{22}O_2S_2$, $M_r = 346.49$, monoclinic, $a = 9.614(2)$, $b = 19.734(4)$, $c = 9.172(2)$ Å, $\beta = 93.45(3)^\circ$, $V = 1737.0(6)$ Å^3, $T = 193(2)$ K, space group $P2_1/c$ (no. 14), $Z = 4$, $\mu(\mathrm{Mo}K\alpha) = 0.313$ mm^{-1}, 3425 independent reflections. The final R-values were (all data) $R_1 = 0.0764$ and $wR_2 = 0.224$.

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