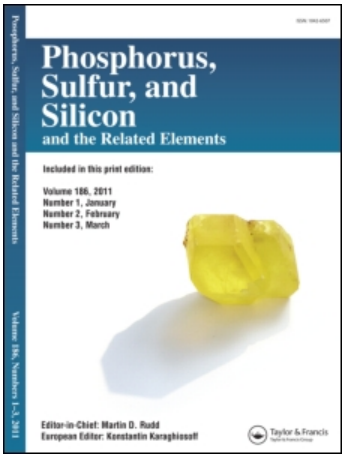


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

Structural Features of 2-S-Substituted Crystalline Tetrahydropyrans. Syntheses of 2-(2-Naphthylthiomethylthio)-Tetrahydropyran Derivatives

Kaija Sipilä[a]; Jarno Kansikas[b]
[a] Laboratory of Organic Chemistry, Department of Chemistry, University of Helsinki, Finland [b] Laboratory of Inorganic Chemistry, Department of Chemistry, University of Helsinki, Finland

Online publication date: 27 October 2010

To cite this Article Sipilä, Kaija and Kansikas, Jarno(2002) 'Structural Features of 2-S-Substituted Crystalline Tetrahydropyrans. Syntheses of 2-(2-Naphthylthiomethylthio)-Tetrahydropyran Derivatives', Phosphorus, Sulfur, and Silicon and the Related Elements, 177: 1, 19 — 31
To link to this Article: DOI: 10.1080/10426500210214
URL: http://dx.doi.org/10.1080/10426500210214

Phosphorus, Sulfur and Silicon, 2002, 177:19–31

1042-6507/02 $12.00 + .00

STRUCTURAL FEATURES OF 2-S-SUBSTITUTED CRYSTALLINE TETRAHYDROPYRANS. SYNTHESES OF 2-(2-NAPHTHYLTHIOMETHYLTHIO)-TETRAHYDROPYRAN DERIVATIVES

Kaija Sipilä[a] *and Jarno Kansikas*[b]
Laboratory of Organic Chemistry, Department of Chemistry, University of Helsinki, PO Box 55, FIN-00014 University of Helsinki, Finland [a] *and Laboratory of Inorganic Chemistry, Department of Chemistry, University of Helsinki, PO Box 55, FIN-00014 University of Helsinki, Finland* [b]

(Received June 19 2001.)

*(1*R,*2*S,*2′*R*)-1-Phenyl-2-(2-naphthylthio)-2-(tetrahydropyran-2′-ylthio)-ethanol* ***2****, (1*R,*2*S,*2′*S*)-1-phenyl-2-(2-naphthylthio)-2-(tetrahydropyran-2′-ylthio)ethanol* ***3****, and 2-[1-butyl-1-(2-naphthylthio)pentylthio]tetrahydropyrane* ***4*** *were synthesized from lithiated 2-(2-naphthylthiomethylthio)tetrahydropyran* ***1****. The X-ray single-crystal structures of* ***2–4*** *were determined and the structural features, especially S-sidechain orientation at the 2-position of the THP-ring, bond lengths, and hydrogen bonding were compared to six hydroxyalkylated 2-(phenylthiomethylthio)tetrahydropyrans.*

Keywords: 2-S-tetrahydropyran; O,S,S-acetal; synthesis; X-ray structure

INTRODUCTION

We have studied the syntheses of several new compounds that are hemithioacetals and dithioacetals at the same time. In these O,S,S-acetal structures the O atom belongs to a tetrahydropyran ring with an S-sidechain at the 2-position and the other S-atom of the dithioacetal moiety is substituted by an aryl group. The tetrahydropyran ring with an S-sidechain at the 2-position is the fundamental substructure in thioglycosides[1,2] used as glycosylating components in carbohydrate chemistry, and is also found in nature as glucosinolates in the "mustard

We thank Jorma Matikainen, Ph.D. for running the mass spectra.

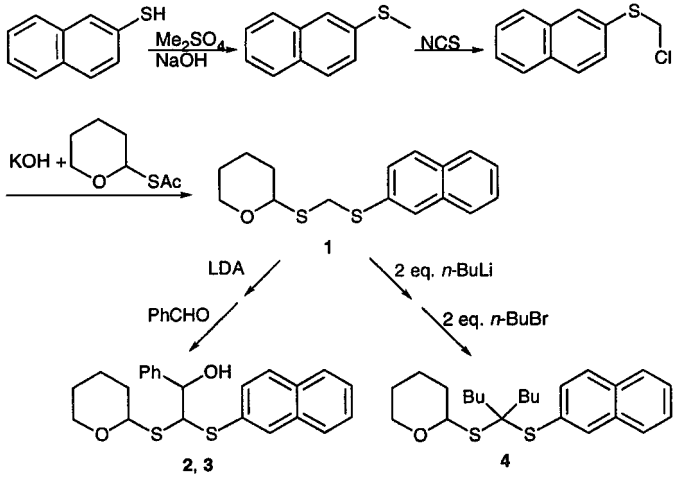
Address correspondence to Kaija Sipilä, Laboratory of Organic Chemistry, Department of Chemistry, University of Helsinki, PO Box 55, FIN-00014, University of Helsinki, Finland.

oil" of *Brassicaceae*, *Resedaceae*, *Tovariaceae*, and *Tropaeolaceae* plant families.[3]

The monoalkylations at the SCH(Li)S are diastereoselective[4] but disappointingly, in hydroxyalkylations all four diastereomers are formed in an approximately equal ratio. However, unlike the alkylation products, most of the hydroxyalkylated derivatives are crystalline. This offers an excellent opportunity to study the crystal structures of a series of new 2-thiotetrahydropyranyl derivatives. In this article we present the syntheses and structures of three novel derivatives of 2-(2-naphthylthiomethylthio)tetrahydropyran **1**; two hydroxyalkylation products (1*R*,2*S*,2′*R*)-1-phenyl-2-(2-naphthylthio)-2-(tetrahydropyran-2′-ylthio)ethanol **2**, (1*R*,2*S*,2′*S*)-1-phenyl-2-(2-naphthylthio)-2-(tetrahydropyran-2′-ylthio)ethanol **3**, and the dibutylated 2-[1-butyl-1-(2-naphthylthio)pentylthio]tetrahydropyrane **4**. Structural features of **2–4**, especially the conformations and bond lengths in the O,S,S-acetal fragment, are compared to those of six hydroxyalkylated 2-(phenylthiomethylthio)tetrahydropyrans **5–10**.[4–8]

RESULTS AND DISCUSSION

The synthesis of the tetrahydropyranyl dithioacetal derivative 2-(2-naphthylthiomethylthio)tetrahydropyrane **1** is presented in Scheme 1. 2-Methylthionaphthalene was prepared by a literature method[9] using 2-naphthalenethiol as the starting material. 2-(chloromethylthio)naphthalene was synthesized from 2-methylthionaphthalene



SCHEME 1 The preparation of 2-(2-naphthylthiomethylthio) tetrahydropyran **1** and its derivatives **2–4**.

and *N*-chlorosuccinimide according to the literature procedure.[10] The O,S,S-acetal 2-(2-naphthylthiomethylthio)tetrahydropyrane **1** was prepared in a two-step synthesis from thioacetic acid *S*-(2-tetrahydropyranyl)ester[5] and 2-(chloromethylthio)naphthalene. In the hydroxyalkylation of lithiated **1** four diastereoisomers of 1-phenyl-2-(2-naphthylthio)-2-(tetrahydropyran-2-ylthio)ethanol were formed in about equal amounts. The diastereomers were separated from the crude product by flash chromatography using Silica gel and CH_2Cl_2 elution. Two diastereomers of 1-phenyl-2-(2-napthylthio)-2-(tetrahydropyran-2-ylthio)ethanol **2** and **3** gave crystals suitable for X-ray diffraction. The dialkylated derivative 2-[1-butyl-1-(2-naphthylthio)pentylthio]tetrahydropyrane **4**, was obtained when two equivalents of *n*-BuLi and *n*-BuBr were used in the butylation of **1**. In these conditions only about 20% of the desired product, 2-[1-(2-naphthylthio)pentylthio]tetrahydropyran[4] was obtained. The reaction conditions were not optimized, and a better yield of **4** could obviously be obtained by using a two-step procedure.

X-ray single-crystal structures* of compounds **2**, **3**, and **4** with crystallographic atom labels are presented in Figure 1 and the molecular packing schemes in Figure 2. Crystal data and structure refinements are reported in Table I. Some selected structural features of **2–4** are compared to those of four diastereomeric phenylthioethanols **5–8** and two diastereomeric phenylthiopropanols **9–10** (Table II and Figure 3). An exceptional aspect of these crystal structures is that the ethanol derivatives **2** and **3**, with three stereogenic atoms, crystallize as conglomerates of enantiomeric crystals in space groups $P2_1$ and $P1$. The configurations are based on the Flack parameter[11] values of 0.15(17) and 0.014(17). The same feature appears in the ethanol derivatives of 2-(phenylthiomethylthio)tetrahydropyran; diastereomers **5**[6], **6**[7], and **8**[7] form enantiomeric crystals whereas the crystals of **7**[4] are centrocymmetric. The crystals of diastereomeric propanol derivatives **9**[5] and **10**[8] are also centrocymmetric. The dibutylated compound **4** is centrosymmetric in a space group $P2_1/c$.

Compound **2** forms intermolecularly hydrogen bonded chains where the hydroxyl group is connected to the oxygen atom of the tetrahydropyran ring of the neighboring molecule at the equivalent position $(-x, y+0.5, -z+1)$ with the O···O distance of 2.668(6) Å. Compound **3** forms similar chains with the O···O distance of 2.800(3) Å in the *a*-axis direction to the molecule at the equivalent position $(x+1, y, z)$ (Figure 2).

*The crystallographic data has been deposited at the Cambridge Crystallographic Data Centre, U.K.

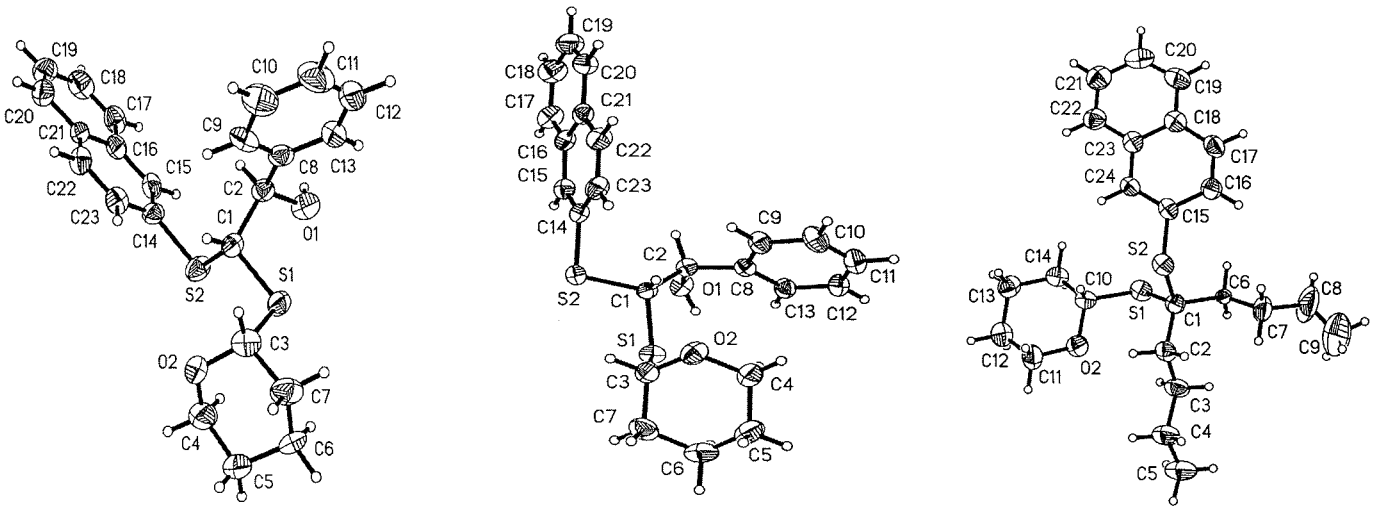


FIGURE 1 The X-ray single-crystal structures of compounds **2**, **3**, and **4** with crystallographic atom labels. Ellipsoids are drawn at the 50% probability level.

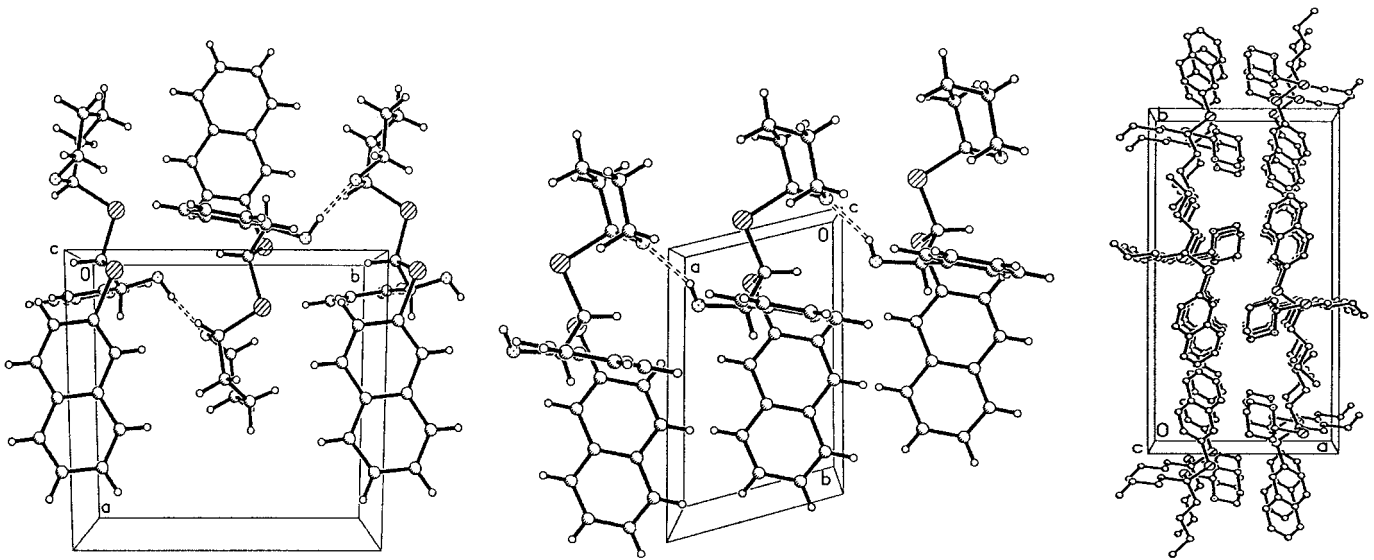
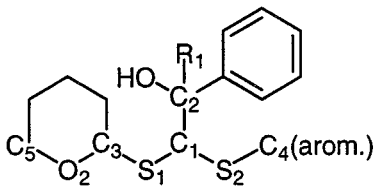


FIGURE 2 The molecular packing schemes seen in the *c*-axis direction. for compounds **2**, **3**, and **4**.

TABLE I Structure Determination Summary of **2**, **3**, and **4**

Compound code	**2**	**3**	**4**
Empirical formula	$C_{23}H_{24}O_2S_2$	$C_{23}H_{24}O_2S_2$	$C_{24}H_{33}OS_2$
Formula weight	396.54	396.54	401.62
Temperature /K	193(2)	193(2)	193(2)
Wavelength/Å	0.71073	1.5418	0.71073
Crystal system, space group	Monoclinic, $P2_1$ (No. 4)	Triclinic, $P1$ (No.1)	Monoclinic, $P\ 2_1/c$ (No. 14)
Unit cell dimensions/Å,°	$a = 9.903(2)$	$a = 5.7230(11)$	$a = 10.778(2)$
	$b = 10.564(2)$	$b = 9.2150(18)$	$b = 23.743(5)$
	$c = 10.201(2)$	$c = 10.156(2)$	$c = 9.0170(18)$
		$\alpha = 83.64(3)$	
	$\beta = 107.79(3)$	$\beta = 78.29(3)$	$\beta = 90.22(3)$
		$\gamma = 74.64(3)$	
Volume/Å^3	1016.2(4)	504.80(17)	2307.5(8)
Z, Calculated density/Mg/m^3	2, 1.296	1, 1.304	4, 1.156
Absorption coefficient/mm^{-1}	0.277	2.502	0.241
$F(000)$	420	210	868
Crystal size/mm	0.28 × 0.21 × 0.17	0.21 × 0.16 × 0.14	0.25 × 0.19 × 0.16
θ range for data collection/°	2.51 to 25.24	4.45 to 67.93	2.55 to 24.02
Index ranges	$h = 0 \rightarrow 1, k = 0 \rightarrow 12,$	$h = -6 \rightarrow 0, k = -11 \rightarrow 10,$	$h = 0 \rightarrow 12, k = -27 \rightarrow 26,$
	$l = -12 \rightarrow 11$	$l = -12 \rightarrow 11$	$l = -10 \rightarrow 10$
Reflections collected/unique	2039/1925 ($R_{int} = 0.0537$)	2026/2026	5716/3343 (R_{int}=0.1036)
Observed reflections [$I > 2\sigma(I)$]	1653	1971	1851
Data/restraints/parameters	1925/1/244	2026/3/245	3343/0/244
Goodness-of-fit (S) on F^2	1.051	1.075	1.061
Final R indices [$I > 2\sigma(I)$]	$R_1 = 0.0562$, w$R_2 = 0.1390$	$R_1 = 0.0359$, w$R_2 = 0.0897$	$R_1 = 0.0952$, w$R_2 = 0.2218$
R indices (all data)	$R_1 = 0.0677$, w$R_2 = 0.1461$	$R_1 = 0.0375$, w$R_2 = 0.0910$	$R_1 = 0.1516$, w$R_2 = 0.2549$
Absolute structure parameter	0.15(17)	0.014(17)	
Extinction coefficient		0.039(4)	
Max. and min $\Delta\rho$/eÅ^{-3}	0.730 and −0.312	0.306 and −0.284	0.440 and −0.301

TABLE II Selected Structural Features of Compounds **2–10**



2, 3, 5 – 8: $R_1 = H$
4: $C_1(Bu)_2$
9, 10: $R_1 = -CH_3$

	2	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
Bond lengths (Å)									
S1—C1	1.817(6)	1.809(3)	1.813(6)	1.814(7)	1.816(3)	1.818(3)	1.834(2)	1.829(2)	1.819(2)
S1—C3	1.818(6)	1.833(3)	1.802(6)	1.807(10)	1.794(4)	1.847(3)	1.843(3)	1.810(2)	1.828(2)
S2—C1	1.832(5)	1.829(3)	1.867(6)	1.844(9)	1.814(3)	1.827(3)	1.816(3)	1.837(2)	1.831(2)
S2—C4	1.791(5)	1.778(3)	1.790(6)	1.783(9)	1.779(3)	1.780(3)	1.783(2)	1.777(2)	1.778(3)
O2—C3	1.426(7)	1.417(4)	1.428(6)	1.428(11)	1.424(4)	1.406(4)	1.420(3)	1.436(3)	1.424(3)
O2—C5	1.441(10)	1.438(4)	1.447(7)	1.447(14)	1.433(5)	1.432(4)	1.431(3)	1.447(4)	1.431(3)
Bond angles (°)									
C1—S1—C3	102.6(3)	99.6(1)	105.5(3)	105.1(4)	101.9(2)	96.4(1)	100.5(1)	104.7(1)	101.7(1)
C1—S2—C4	101.0(2)	100.5(1)	105.4(3)	101.3(4)	101.7(2)	103.7(1)	105.0(1)	102.8(1)	99.2(1)
S1—C1—S2	107.1(3)	107.4(1)	111.3(3)	113.7(4)	114.2(2)	105.9(2)	109.2(1)	113.2(1)	107.3(1)
Torsion angles (°)									
S1—C3—O2—C5	−65.3(6)	68.7(3)	−178.7(4)	176.5(4)	−177.2(2)	69.2(3)	71.6(2)	178.9(2)	−68.2(2)
C1—S1—C3—O2	64.4(5)	−62.6(2)	−79.1(4)	79.3(4)	−80.0(3)	−60.1(2)	−64.1(2)	78.8(2)	67.0(2)
C3—S1—C1—S2	−102.4(3)	−98.7(2)	−62.8(4)	52.5(4)	−65.6(2)	−96.3(1)	−154.5(1)	50.7(1)	142.6(1)
C4—S2—C1—S1	174.7(3)	179.3(1)	−52.6(4)	70.4(4)	−67.4(2)	172.0(1)	82.1(2)	61.1(1)	72.2(2)
S-sidechain	ax	ax	eq	eq	eq	ax	ax	eq	ax
O—H—O bond	inter	inter	—	intra	intra	—	inter	intra	inter
O—O length, (Å)	2.668	2.800		2.719	2.962		2.764	2.816	2.751
Configuration									
C1, C2, C3	S,R,R	S,R,S	—	S,S,R	S,R,R	S*,R*,S*	S,S,S	S*,S*,R*	S*,R*,R*

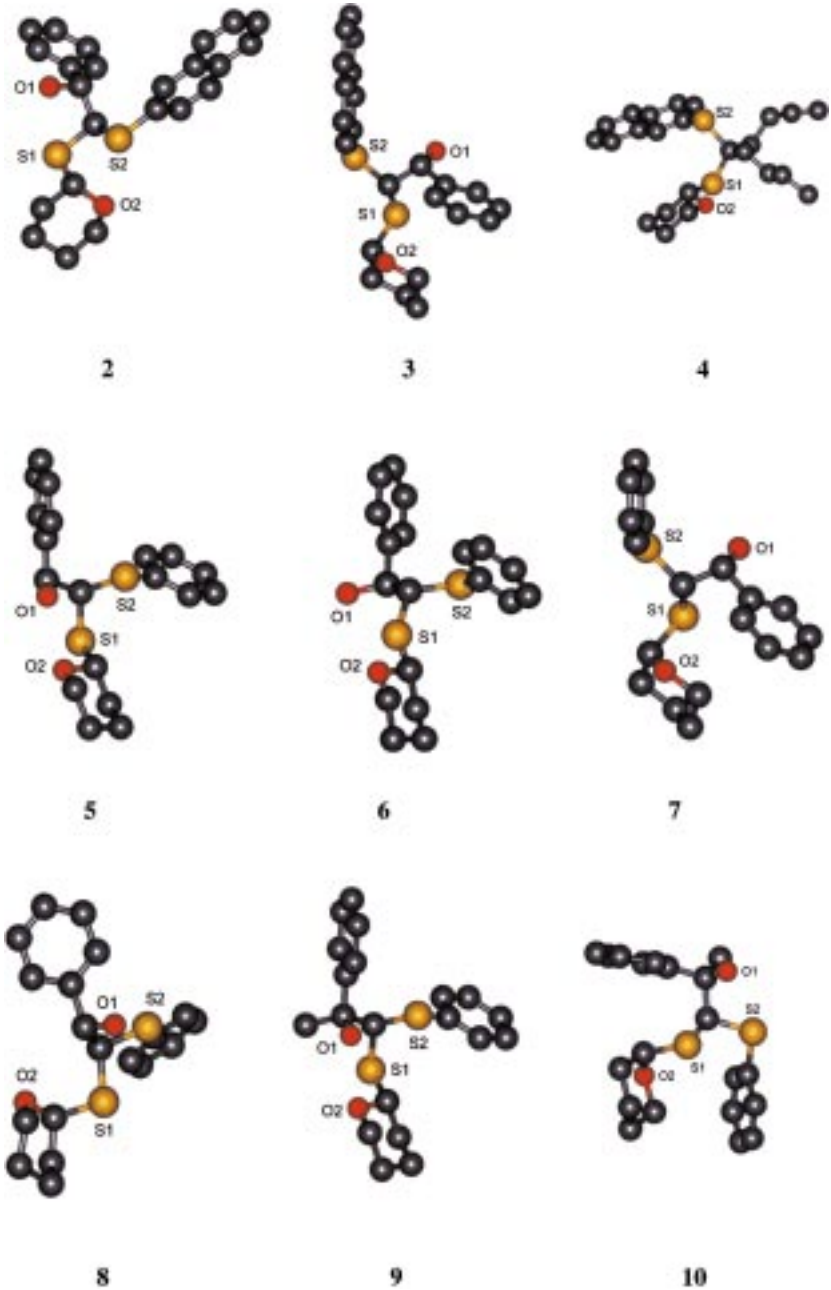


FIGURE 3 Structures of compounds **2–10**. Hydrogen atoms are omitted for clarity.

The hydroxyl group is in gauche position to both sulphur atoms in compounds **2**, **3**, **5**, and **7–10** (Figure 3). The O1···S distances range from 2.882 Å found in **2** to 3.298 Å in **8**. This variation is obvious when looking at the differences in S1—C1—C2—O1 torsion angle values of 43.6 and −73.8° in **2** and 74.5 and −45.3° in **8**. In other structures the differences in O1···S1 and O1···S2 distances and in S1—C1—C2—O1 torsion angle values are smaller. All those O···S distances are slightly below the sum of van der Waals radii of 3.32 Å,[12] but it may follow from the fact that these atoms are separated only by three covalent bonds rather than having a real hydrogen bond. In all other OH-compounds except **7** the hydroxyl group forms O—H···O hydrogen bonds, which are considerably stronger than O—H···S bonds and shift the H atom to favor H···O interaction, thus weakening the H···S hydrogen bond by moving the H-atom further from the S-atoms. Such a bifurcated hydrogen bond can be found in **3** with the O···S distance of 3.025 Å, and H···S distance of 2.75 Å which also is well below the van der Waals value 2.90 Å and the H-atom is properly oriented.

In all compounds **2–10** the O2—C3 distance in the THP ring is shorter than the O2—C5 distance (Table II). When the S-sidechain is axial the O2—C3 mean distance is only 1.421 Å whereas in the equatorially oriented compounds it is 1.429 Å. The same kind of bond shortening in glycosides with a CH_3O-sidechain (1.416 Å versus 1.428 Å) is explained by the anomeric effect.[13] The distances from S1 to C3 show large variation. There is a clear tendency for the S1—C3 bonds in the axial orientation to be longer than the S1—C1 bonds as shown by the S1—C3 values from 1.818(6) to 1.847(3) Å compared to the S1—C1 distances from 1.809(3) to 1.834(2) Å. In compounds **4–6** and **9** the equatorially orientated S1—C3 bonds of 1.794(4)–1.810(2) Å are shorter than the S1—C1 bonds of 1.813(3)–1.829(2) Å. Also, this variation of the bond lengths in axial and equatorial side chains follows very well the situation found in glycosides. The distance of S1 from the central carbon atom C1 is generally shorter than the distance of C1 from S2, which is bonded to the aromatic group. In all compounds **2–10** the bond S2—C1 is longer than S2—C4, where C4 belongs to the aromatic ring.

The axial 2-S-sidechain orientation is known to be favored in sugars and glycosides in solution because of the anomeric effect; for example in methyl D-glucoside the axial isomer predominates over the equatorial at equilibrium by about 2:1.[13] The same tendency is also seen in simple 2-alkylthiotetrahydropyrans and corresponding 2-alkylthio analogues. Most of the 2-S THP derivatives found in Cambridge Structural Database System (CSD 5.20, Oct. 2000)[14] are variously substituted carbohydrates. Among the compounds containing a THP-2-S group 13

were axially and 21 equatorially orientated. The 2-S-sidechain is axial in **2** and **3** with the C—O—C—S torsion angles 65.3(6)° and −68.7(3)° respectively. The side chains are axially oriented also in the ethanol derivatives **7** and **8** and in the propanol derivative **10**. However, there are four equatorial orientations present in these nine closely related structures. The equatorially orientated compounds **5**, **6**, and **9** have an intramolecular hydrogen bond from the hydroxyl group to the oxygen atom of the tetrahydropyranyl ring. This hydrogen bond decreases the electron density at the ether oxygen and hinders the *p*-orbital overlap with O—C bond thus diminishing the anomeric effect. In compound **4** the normal steric preference for the equatorial orientation because of the bulky side chain seems to apply. We conclude that the variation in conformational preference of 2-S substituents is a feature of isolated molecules and it is not to be attributed only to crystal packing forces.

EXPERIMENTAL

Syntheses

Tetrahydrofuran (THF) was dried by refluxing in the presence of sodium and benzophenone and distilled. Diisopropylamine was dried on KOH and distilled before use. Benzaldehyde was distilled in vacuo and *n*-butyl bromide at normal pressure. The concentration of *n*-BuLi in hexane was determined by a literature procedure.[15] Flash chromatography was carried out using Merck Silica 60 230–400 mesh. The IR spectra were measured on a Perkin Elmer Spectrum One apparatus with a Universal ATR Sampling Accessory. The NMR spectra were recorded on a Varian Gemini 200 spectrometer (chemical shifts in δ; ppm, J; Hz). The assignments are based on chemical shift data and DEPT measurements. The mass spectrum was run on a JEOL JMS-SX 102 instrument (70 eV).

2-(2-Naphthylthiomethylthio)tetrahydropyran 1

Thioacetic acid *S*-(2-tetrahydropyranyl)ester[5] (2.7g, 0.017 mol) was added to the solution of KOH (2.9 g, 0.052 mol) in dimethyl sulfoxide-water (30ml + 10 ml) at 0°C and the mixture was stirred for 30 min at 40°C. After cooling the reaction mixture in an ice bath, 3.5 g (0.017 mol) of 2-(chloromethylthio)naphthalene was slowly added and the mixture stirred at room temperature overnight. Diethyl ether (50 ml) and water were added to dissolve the white precipitate. The water phase was extracted twice with diethyl ether, the organic phase was washed with water, dried with Na_2SO_4, and evaporated to dryness. The crude product

was purified with flash chromatography (Silica gel, CH_2Cl_2) to obtain 2.9 g (59%) of 2-(2-naphthylthiomethylthio)tetrahydropyran as a light yellow syrup.

IR (ATR) 3053, 2938, 2848, 1624, 1590, 1501, 1439, 1380, 1336, 1263, 1186, 1100, 1075, 1035, 1006, 820, 741; ^{1}H NMR (200 MHz, $CDCl_3$, δ): 1.50–2.05 (m, 3 $\times$ CH_2), 3.45–3.60, and 4.05–4.20 (OCH_2), 4.22 (AB_q, 13.5 Hz, SCH_2S), 5.20 (dd, 3.6 & 5.4 Hz, OCHS), 7.40–7.55 (m, 3 arom. H), 7.70–7.90 (m, 4 arom. H); ^{13}C NMR (50 MHz, $CDCl_3$, δ): 21.5, 25.6 and 30.7 (CH_2), 35.0 (SCH_2S), 64.3 (OCH_2), 80.8 (OCHS), 125.9–133.7 (arom. C); HRMS 290.0785, calc. for $C_{16}H_{18}OS_2$ 290.0799.

1-Phenyl-2-(2-naphthylthio)-2-(tetrahydropyran-2-ylthio)ethanol 2, 3

To a solution of 2-(2-naphthylthiomethylthio)tetrahydropyran (1.2 g, 0.0041 mol) in dry THF under argon atmosphere at -78°C (dry ice-ethanol bath) 1.5 eq. of LDA (0.9 ml di-isopropylamine, 4.4 ml of 1.4 M *n*-BuLi in hexane, 5 ml of THF; $-10 - 0^\circ$C, 15 min) was slowly added and the mixture stirred for 1.25 h at that temperature. Freshly distilled benzaldehyde (0.4 g, 0.0041 mol) was added and the reaction mixture was allowed to reach room temperature by stirring overnight. The reaction was quenched with water and extracted twice with diethyl ether. The organic phase was washed with water and brine and dried with Na_2SO_4. The solvent was evaporated in the vacuum and the gummy residue (1.1 g) also containing some unreacted starting materials was purified with flash chromatography (Silica gel, CH_2Cl_2) to afford 0.8 g (50%) of 1-phenyl-2-(2-naphthylthio)-2-(tetrahydropyran-2-ylthio)ethanol as a mixture of four diastereomers. The diastereomers were separated by repeated flash chromatography using Silica gel and CH_2CI_2 elution. Flash fractions 22–35 contained diastereomer **2**, and the fractions 36–50 diastereomer **3**. After evaporation of the solvent both diastereomers were solid and they were recrystallized several times from abs. ethanol to obtain crystals suitable for X-ray analysis.

Diastereomer 2

M.p. 107°C; IR (ATR) 3328 (OH), 3058, 2936, 2840, 1583, 1492, 1336, 1261, 1187, 1098, 1061, 1030, 860, 827, 804, 753; ^{1}H NMR (200 MHz, $CDCI_3$, δ): 1.4–1.9 (m, 3 $\times$ CH_2), 3.5–3.7 & 3.9–4.1 (m, OCH_2), 4.54 (d, 7.7 Hz, OH), 4.68 (d, 4.8 Hz, SCHS), 5.07 (dd, 4.8 and 7.7 Hz, PhCH), 5.13 (m, OCHS), 7.22–7.56 (m, 8H), 7.72–7.86 (m, 3H), 7.88–7.92 (m, 1H); ^{13}C NMR (50 MHz, $CDCl_3$, δ): 22.1, 25.1, 30.9, 63.0, 66.0, 75.6, 80.0, 126.3, 126.5, 126.6, 127.5, 127.6, 127.7, 127.9, 128.1, 128.6, 129.1, 130.8, 131.6, 132.4, 133.6, 141.6.

Diastereomer 3

M.p. 127°C; IR (ATR) 3404 (OH), 3053, 2966, 2941, 1582, 1498, 1450, 1393, 1220, 1185, 1090, 1070, 1030, 862, 820, 800, 754; ^{1}H NMR (200 MHz, $CDCl_3$ δ): 1.4–2.1 (m, 3 × CH_2), 3.2–3.4 & 3.4–3.6 (m, OCH_2), 3.48 (d, 2.6 Hz, OH), 4.59 (d, 4.4 Hz, SCHS), 4.94 (dd, 2.6 & 4.4 Hz, PhCH), 5.30 (t, 4.4 Hz, OCHS), 7.20–7.42 (m, 5H), 7.44–7.58 (m, 3H), 7.72–7.92 (m, 3H); ^{13}C NMR (50 MHz, $CDCl_3$, δ): 20.6, 25.4, 30.4, 62.0, 62.7, 74.9, 81.6, 126.5, 126.6, 127.5, 127.6, 127.9, 128.7, 129.7, 131.5, 132.0, 132.5, 133.5, 140.0

2-[1-Butyl-1-(2-naphthylthio)pentylthio]tetrahydropyran 4

To the solution of 2-(2-naphthylthiomethylthio)tetrahydropyran (2.1 g, 7.2 mmol) in dry tetrahydrofuran under argon atmosphere at −78°C 13.2 ml of 1.1 M *n*-BuLi in hexane (14.5 mmol) was slowly added and the mixture stirred for 3 h. The temperature was raised to −50°C and *n*-butyl bromide (1.3 g, 14.5 mmol) was added. The reaction mixture was allowed to reach the room temperature by stirring overnight. After the usual work up, the crude product (2.7 g, containing about 20% of 2-[1-(2-naphthylthio)pentylthio]tetrahydropyran) was purified with flash chromatography (Silica gel, CH_2Cl_2) to obtain 1.9 g (66%) of **4** as a brownish syrup. After several attempts to crystallize the product from ethanol it remained a colorless, smelly resin. The soft cubic blocks were obtained after very slow evaporation of the solvent at room temperature.

M.p. 58°C; IR (ATR) 3053, 2939, 2858, 1585, 1498, 1460, 1439, 1372, 1335, 1201, 1075, 1032, 1002, 895, 816, 740; ^{1}H NMR (200 MHz, $CDCl_3$, δ): 0.9 (t, 7 Hz, 2 × CH_3), 1.2–2.2 (m, 9 × CH_2), 3.5–3.7 & 4.0–4.2 (m, OCH_2), 5.49–5.44 (m, OCHS), 7.4–7.6 (m, 3 arom. H), 7.7–7.9 (m, 3 arom. H), 8.0 (s, arom. H); ^{13}C NMR (200 MHz, $CDCl_3$, δ): 14.0 (CH_3), 22.3, 22.7, 25.6, 26.0, 26.3, 32.3, 38.0, 64.9 (OCH_2), 81.6 (OCHS), 126.3, 126.7, 127.6, 127.9, 133.5, 136.9.

Crystal Structure

X-ray data for compounds **2** and **4** were collected on a Nicolet AFC-7S and for **3** on a CAD-4 four-circle diffractometer at 193 K. Each crystal was mounted on a glass fiber using a viscose oil drop method[16] and applying some grease as an adhesive. Data reductions were done with the Texsan[17] program system for **2** and **4**, and Wingx[18] for **3**. The structures were solved by SHELXS program[19] using direct methods and full-matrix least-squares refinements on F^2 were done by SHELXL software.[20] H-atoms were positioned at calculated locations using the XP program package.[21] They were refined using a riding model where

their distances and angles to the C— or O— atoms were fixed and to their isotropic thermal parameters were applied values 1.2 and 1.5 × respective equivalent isotropic U-value of C or O. XP-program was also used to produce the illustrations.

REFERENCES

[1] H. Dehne, *Sulfur Lett*., **21,** 89 (1998).
[2] S. Oscarsson in *Carbohydrates in Chemistry and Biology*, ed. B. Ernst, G. W. Hart and P. Sinay, Wiley-VCH, Weinheim, 2000, Vol. 1, pp. 93–116.
[3] J. E. Rodman, *Systematic Botany*, **16,** 598 (1991).
[4] K. Sipilä, T. Hase, J. Koskimies, J. Matikainen, and J. Kansikas, *Phosphorus, Sulfur, and Silicon 2001*; accepted for publication.
[5] J. Kansikas, M. Leskelä, K. Sipilä, and T. Hase, *Acta Chem. Scand.*, **49,** 809 (1995).
[6] J. Kansikas, K. Sipilä, and T. Hase, *Acta Chem. Scand.*, **50,** 1147 (1996).
[7] J. Kansikas and K. Sipilä, *Acta Crystallogr*., **C56,** 1383 (2000).
[8] J. Kansikas and K. Sipilä, *Acta Crystallogr*., **E57,** 335 (2001).
[9] J. Jacques, *Bull. Soc. Chim. Fr*., **92,** 231 (1955).
[10] D. L. Tuleen and D. N. Buchanan, *J. Org. Chem*., **32,** 495 (1967).
[11] H. D. Flack, *Acta Crystallogr*., **A39,** 876 (1983).
[12] A. Bondi, *J. Phys. Chem*. **68,** 441 (1964).
[13] E. L. Eliel and S. H. Wilen, *Stereochemistry of Organic Compounds* (Wiley, New York, 1994), pp. 749–753.
[14] F. H. Allen, J. E. Davies, J. J. Galloy, O. Johnson, O. Kennard, C. F. Macrae, E. M. Mitchell, G. F. Mitchell, J. M. Smith, and D. G. Watson, *J. Chem. Inf. Comp. Sci*., **31,** 187 (1991).
[15] E. Juaristi, A. Martinez-Richa, A. Garcia-Rivera, and J. S. Cruz-Sanches, *J. Org. Chem*., **48,** 2603 (1983).
[16] T. Kottke and D. Stalke, *J. Appl. Crystallogr*., **26,** 615 (1993).
[17] TEXSAN, Single Crystal Structure Analysis Software, Molecular Structure Corporation, The Woodlands, TX (1993).
[18] L. J. Farrugia, *J. Appl. Cryst*., **32,** 837 (1999).
[19] G. M. Sheldrick, SHELXS97. *Acta Crystallogr*., **A46,** 467 (1990).
[20] G. M. Sheldrick, SHELXL97 (University of Göttingen, Germany, 1997).
[21] Bruker, SHELXTL (Release 5.1) Reference Manual. Bruker AXS, Inc., Madison, WI (1997).