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Molecular Modeling, X-ray Diffraction, and ^{13}C,^{77}Se CP/MAS NMR Studies of Bis(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl) Diselenide and Disulfide

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Bis(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl) diselenide (**1**) crystallized from methanol forms three polymorphs. Crystals **1a** are orthorhombic, $P2_12_12_1$, with $a = 10.143(3)$, $b = 14.413(2)$, $c = 26.290(2)$ Å, $V = 3843(1)$ Å^3, $Z = 4$, and $D_c = 1.418$ g/cm^3. Refinement using 3682 observed reflections for 435 parameters gives $R = 0.041$. Crystals **1b** are orthorhombic, $P2_12_12$, with $a = 24.180(2)$, $b = 14.0748(7)$, $c = 5.578$ (1) Å, $V = 1898.4(4)$ Å^3, $Z = 2$, and $D_c = 1.435$ g/cm^3. Refinement using 2054 reflections for 219 parameters gives $R = 0.058$. Crystals of bis(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl) disulfide (**2**) crystallized from methanol are orthorhombic, $P2_12_12_1$, with $a = 10.099(1)$, $b = 14.207(2)$, $c = 26.253(3)$ Å, $V = 3766(1)$ Å^3, $Z = 4$, and $D_c = 1.282$ g/cm^3. Refinement using 3438 reflections for 435 parameters gives $R = 0.071$. Diselenides **1a** and **1b** have molecular structures with *anti–syn* and *anti–anti* arrangements of the C–C–Se–Se–C–C backbone. Changes of geometry influence the bond lengths and angles because of the strong hyperconjugative interaction between the p-electron lone pair of selenium and the σ^*_{C-C} orbital. Molecular symmetry and molecular packing effects are studied by high-resolution solid-state ^{13}C and ^{77}Se NMR. The principal elements (δ_{ii}) of the ^{77}Se chemical shift tensors for polymorphs **1 a–c**, determined from spinning sideband intensities, are discussed in terms of local geometry. The structure of modification **1c**, which gave crystals of insufficient quality for XRD measurements, was deduced from molecular mechanics calculations and solid-state NMR.

Introduction

Disulfide bonds play an important role in the chemistry of natural products.[1,2] The S–S linkage formed at cysteine residues influences local conformation and stability in folded proteins and polypeptides.[3,4] Little attention has been paid to dichalcogenide bonds in saccharides, even though these compounds are significant in metabolism and are useful as models for structural studies.[5,6] Lees and Whitesides reported that 6,6′-dithiosucrose cyclic disulfide is a convenient compound for the study of thiol–disulfide interchange.[7] Circular dichroism of monosaccharide dichalcogenides was measured by Michalska and Snatzke.[8]

Little is known about the nature of the selenium–selenium bond in saccharides. Simple selenoorganic compounds mimic *in vitro* the enzymatic activity of glutathione peroxidase, an important system of cell defense against oxidative stress.[9,10] The modified diaryl selenides and diselenides show significant glutathione peroxidase activity.[11,12]

As part of our continuing interest in the properties of sulfur/selenium systems in the solid state[13−18] we report X-ray Diffraction (XRD) and ^{13}C and ^{77}Se magic angle spinning with cross polarization (CP/MAS) results for bis(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl) diselenide (**1**) and disulfide (**2**). We show that changes of geometry of the C–C–X–X–C–C backbone when X is in an anomeric position influence C–X bond lengths and C–C–X bond angles of β-D-glucopyranose rings because of the overlap of the p-electron lone pair of the X atom and the σ^*_{C1-C2} orbital of the sugar moiety.

^{13}C and ^{77}Se spectra are discussed in terms of crystal and molecular structures established from XRD studies. The relationship between ^{77}Se spectral parameters and

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Table 1. Crystal Data and Experimental Details

	compound **1a**	compound **1b**	compound **2**
molecular formula	$C_{28}H_{38}O_{18}Se_2$	$C_{28}H_{38}O_{18}Se_2$	$C_{28}H_{38}O_{18}S_2$
crystallographic system	orthorhombic	orthorhombic	orthorhombic
space group	$P2_12_12_1$	$P2_12_12$	$P2_12_12_1$
a (Å)	10.143(3)	24.180(2)	10.099(1)
b (Å)	14.413(2)	14.0748(7)	14.207(2)
c (Å)	26.290(2)	5.578(1)	26.253(3)
V (Å^3)	3843(1)	1898.4(4)	3766(1)
Z	4	2	4
D_c (g/cm^3)	1.418(2)	1.435(2)	1.282
μ (cm^{-1})	30.6	31.0	18.6
crystal dimensions (mm)	0.3, 0.3, 0.4	0.4, 0.4, 0.5	0.25, 0.35, 0.4
maximum 2θ (deg)	150	150	150
radiation, λ (Å)	Cu Kα, 1.54178	Cu Kα, 1.54178	Cu Kα, 1.54178
scan mode	$\omega/2\theta$	$\omega/2\theta$	$\omega/2\theta$
scan width (deg)	$0.95 + 0.14 \tan \theta$	$0.82 + 0.14 \tan \theta$	$1.14 + 0.14 \tan \theta$
hkl ranges	$h = 0\ 12$	$h = 0\ 30$	$h = -12\ 0$
	$k = 0\ 18$	$k = 0\ 17$	$k = -17\ 0$
	$l = 0\ 32$	$l = 0\ 6$	$l = 0\ 32$
DECAY correction:			
min	1.00002	1.00003	1.00028
max	1.02618	1.02372	1.07594
av	1.01235	1.01073	1.03607
no. of reflections:			
unique	4122	2184	3944
with $I \geq 3\sigma(I)$	3682	2054	3438
no. of parameters refined	435	219	435
largest diff. peak (eÅ^{-3})	0.294	0.545	0.389
largest diff. hole (eÅ^{-3})	−0.539	−0.456	−0.408
R	0.041	0.058	0.071

the distortion of selenium local geometry is described. Finally, experimental geometric parameters are compared with calculated values. The usefulness of these methods in structural analysis of dichalcogen saccharides is discussed.

Experimental Section

Bis(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl) diselenide (**1**) and disulfide (**2**) were synthesized according to established procedures.[19] Diselenide **1** was dissolved in boiling methanol. The saturated solution was brought to ambient temperature and crystals **1a** were obtained. Crystals **1b** were grown from methanol at −10 °C, and the sample was kept in refrigerator at −10 °C. Crystals **1b** and **1c** were obtained by isothermal evaporation of methanol at room temperature. Crystals **2** were crystallized from methanol at room temperature.

X-ray Diffraction. Crystal and molecular structures of diselenides **1a** and **1b** and disulfide **2** were determined using a CAD4 diffractometer. All compounds crystallize in orthorhombic systems with space group $P2_12_12_1$ for **1a** and **2** and $P2_12_12$ for **1b**. Crystal data and experimental details are shown in Table 1. Intensity data were collected at room temperature using a diffractometer with graphite-monochromatized Cu Kα radiation. Lattice constants were refined by least-squares fit of 25 reflections in a θ range of 17.6−23.9° for **1a**, 21.4−26.2° for **1b**, and 20.5−27.3° for **2**. Declines in intensities of three standard reflections (2,5,-5; 3,6,1; 3,3,-10 for **1a**, -10,-4,1; −3,-1,1; 3,6,2 for **1b**, and 2,2,-12; 4,-1,-7; 3,0,-10 for **2**) were 5.0% during 69.8 h of exposure, 4.6% during 29.2 h and 13.6% during 65.0 h respectively for **1a**, **1b**, and **2**. Because of observed loss in intensities of reflections which was, on average, 0.072% per hour in **1a**, 0.137% per hour in **1b** and 0. 210% per hour in **2**, experimental data of **1a**, **1b**, and **2** were corrected using the DECAY program.[20] A total of 3682, 2054, and 3438 observed reflections, respectively for **1a**, **1b**, and **2** [with $I \geq 3\sigma(I)$], were used to solve the structures by direct methods and to refine it by full-matrix least-squares fits using F's. Hydrogen atoms were placed geometrically at idealized positions and set as riding, with fixed isotropic thermal parameters. Anisotropic thermal parameters were refined for all non-hydrogen atoms. The final refinement converged to $R = 0.041$ in **1a**, $R = 0.058$ in **1b**, and $R = 0.071$ in **2** with respective weighting schemes $w = 1/[\sigma^2(F) + pF^2]$, where p was 0.000259, 0.003388, and 0.000882, respectively. The absolute configuration was established by use of two independent methods: calculation of the Rogers' parameter and the Hamilton test.[21,22] The obtained value of η for **1a** was equal to 0.92(6), and $\eta_{\text{inv}} = 0.936(6)$ for structure with the "opposite" configuration. The results of the Hamilton test were $N = 3247$ and $R_{\text{-ratio}} = 1.0105$, which gives the probability of the opposite structure of $\alpha < 10^{-9}$. The results of the Hamilton test ($N = 3003$ and $R_{\text{-ratio}} = 1.0020$) showed that the "opposite" structure **1b** had to be rejected with very high probability ($\alpha < 5 \times 10^{-4}$). For structure **2**, the obtained values of η were; $\eta = 1.47(9)$ and $\eta_{\text{inv}} = -1.47(10)$. The Hamilton test ($N = 1835$ and $R_{\text{ratio}} = 1.0650$) showed that the opposite structure **2** had to be rejected (probability $\alpha \ll 10^{-9}$)

Data corrections were performed with the Enraf-Nonius SDP crystallographic computing package[20] and calculations (structure solution and refinement) were carried out with SHELXTL package.[23] Scattering factors were taken from *International Tables for X-ray Crystallography*.[24]

NMR Measurements. ^1H-^{13}C and ^1H-^{77}Se CP/MAS NMR spectra were recorded on a Bruker MSL 300 NMR spectrometer at 75.496 MHz and 57.206 MHz, respectively, with high-power proton decoupling. Powdered samples of diselenide **1** and disulfide **2** were placed in a cylindrical rotor and spun at 2.0−4.5 kHz. For the ^{13}C experiments, the field strength for ^1H decoupling was 1.05 mT, and the contact time of 5 ms, a repetition time of 6s, and spectral width of 50 kHz were used. A total of 8K data points represented the FID. Spectra were accumulated 100 times which gave a reasonable signal-to-noise ratio. ^{13}C chemical shifts were calibrated indirectly using glycine set at 176.34 ppm.

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Table 2. Selected Bond Lengths (Å) and Angles (deg) in Compounds 1, 1a and 2

	compound **1a**			compound **2**	
	A	B	compound **1b**[a]	A	B
Se–Se	2.298(2)		2.325(1)	2.033(3)[b]	
Se–C1	1.960(6)	1.944(5)	1.961(7)	1.802(7)	1.805(6)[b]
C1–O1	1.425(6)	1.421(6)	1.400(8)	1.416(8)	1.416(7)
C1–C2	1.505(8)	1.520(7)	1.537(7)	1.522(10)	1.527(8)
Se–Se–C1	100.6(2)	100.9(2)	97.1(2)	103.9(2)	104.2(2)[b]
Se–C1–O1	108.0(3)	108.7(3)	106.9(4)	108.6(4)	109.4(4)[b]
Se–C1–C2	109.5(4)	116.1(4)	111.0(4)	109.8(5)	115.4(4)[b]
O1–C1–C2	110.0(4)	108.2(4)	109.8(5)	108.8(5)	107.9(5)
C1–Se–Se–C1	−81.8(2)		−109.2(3)	−82.5(3)[b]	
Se–Se–C1–O1	−85.4(3)	75.6(3)	−69.2(4)	−87.2(4)	74.7(4)[b]
Se–Se–C1–C2	154.8(3)	−46.6(4)	171.1(4)	154.1(4)	−47.2(5)[b]

[a] An asymmetric part of the unit cell of **1b** consists a half of the molecule (symmetry $-x$, $1-y$, z). [b] In compound **2**, the sulfur except selenium occurs.

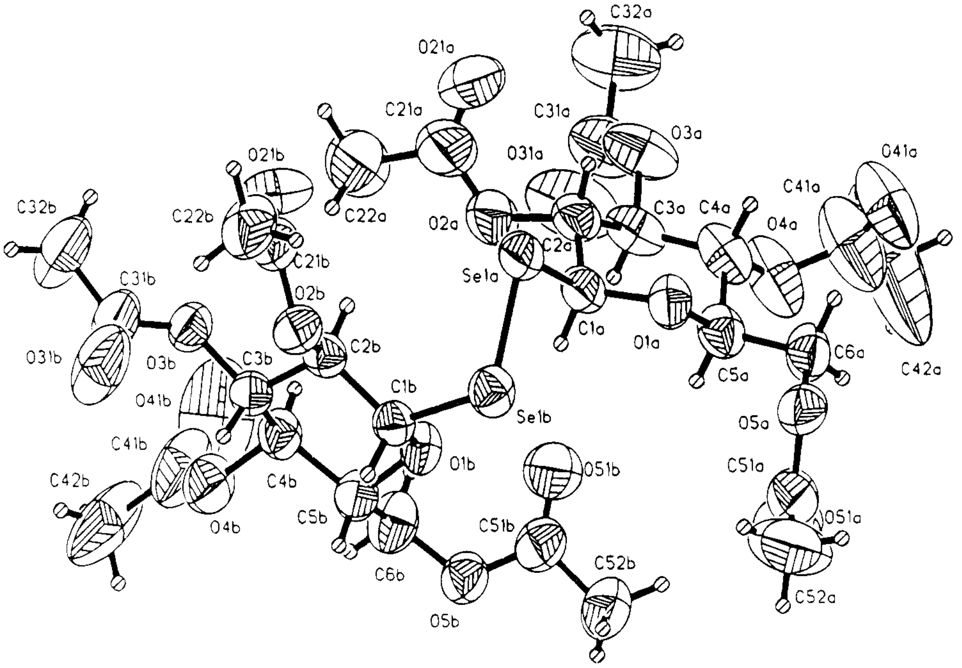

Figure 1. ORTEP plot of bis(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl) diselenide (**1a**).

The Hartmann–Hahn condition for ^{1}H-^{77}Se CP/MAS was established using powdered sample of ammonium selenate. The field strength for ^{1}H decoupling was 1.05 mT, the contact time was 5 ms, and the repetition time was 10s. A spectral width of 50 kHz was used and 8K data points were acquired. Several thousand scans were required to obtain the spectrum of diselenide **1**. The ^{77}Se chemical shifts were calibrated indirectly using ammonium selenate used as a secondary chemical shift reference standard, set at $\delta = 1040.2$ ppm.

The principal elements of the ^{77}Se chemical shift tensor and shielding parameters were determined employing the MAS-NMR program.[25] The details of the fitting routine are fully discussed elsewhere.[25,26]

The principal components δ_{ii} were used to calculate the anisotropy ($\Delta\delta$), asymmetry (η), span (Ω), and skew (κ)[27] according to the following:

If $|\delta_{11} - \delta_{\rm iso}| > |\delta_{33} - \delta_{\rm iso}|$ and $\delta_{11} > \delta_{22} > \delta_{33}$ then

$$\Delta\delta = \delta_{11} - (\delta_{22} + \delta_{33})/2 \qquad (1)$$

$$\eta = (\delta_{22} - \delta_{33})/(\delta_{11} - \delta_{\rm iso}) \qquad (2)$$

If $|\delta_{11} - \delta_{\rm iso}| < |\delta_{33} - \delta_{\rm iso}|$ and $\delta_{11} > \delta_{22} > \delta_{33}$ then

$$\Delta\delta = \delta_{33} - (\delta_{11} + \delta_{22})/2 \qquad (3)$$

$$\eta = (\delta_{22} - \delta_{11})/(\delta_{33} - \delta_{\rm iso}) \qquad (4)$$

Furthermore,

$$\Omega = \delta_{11} - \delta_{33} \qquad (5)$$

$$\kappa = 3(\delta_{22} - \delta_{\rm iso})/\Omega \qquad (6)$$

Computer Calculations. Calculations were performed with the HyperChem[28] program executed on an IBM compatible 486 (66 MHz) computer. Energy minimizations were carried out with the HyperChem default values. All molecular mechanics studies were performed with the MM$^+$ force field[29] until the root square of the gradient vector was less than 0.001 kcal/Å. The limitations of the accuracy of computational calculations should be stressed. The calculations were performed for systems in the gas phase, neglecting the crystallographic effects.

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(29) MM+ for HyperChem is derived from a public domain code developed by N. L. Allinger, referred to a MM2 (1977) and distributed by the Quantum Chemistry Program Exchange (QCPE).

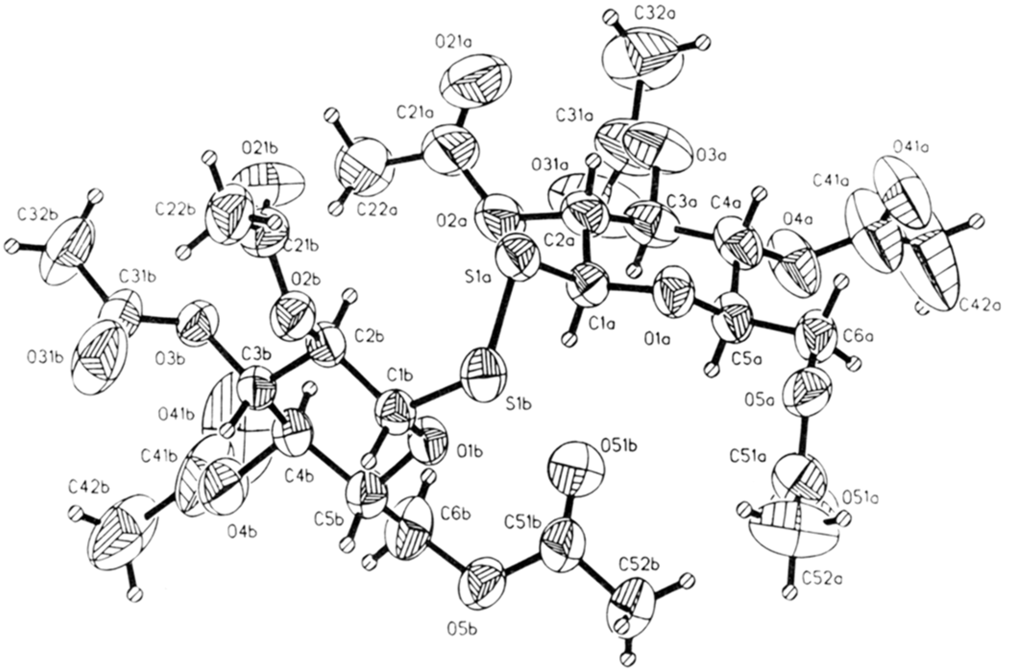


Figure 2. ORTEP plot of bis(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl) disulfide (**2**).

Table 3. Asymmetry Parameters of Six-Membered Rings in Compounds 1a, 1b, and 2

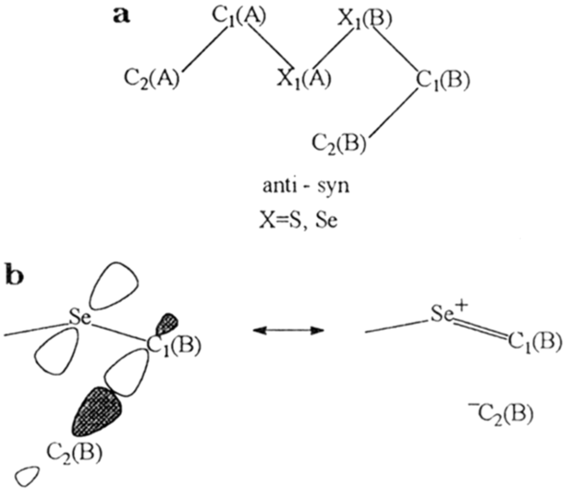
	1a			2	
	A	B	1b	A	B
ΔCs(O1)	6.6(1)	7.2(1)	1.1(1)	4.4(1)	4.9(1)
ΔCs(C1)	15.2(1)	7.2(1)	11.9(1)	13.9(1)	8.8(1)
ΔCs(C2)	8.7(1)	14.1(1)	12.4(1)	9.7(1)	13.4(1)
ΔC_2(O1−C1)	15.5(1)	1.1(1)	8.0(1)	13.0(1)	3.0(1)
$\Delta C_2(C_1-C_2)$	16.8(1)	15.0(1)	17.0(1)	16.5(1)	15.5(1)
ΔC_2(C2−C3)	2.1(1)	15.2(1)	9.6(1)	4.0(1)	13.1(1)

Results and Discussion

X-Ray Diffraction. Crystallographic data and experimental details for diselenide **1** and disulfide **2** are listed in Table 1.[50] Selected bond lengths and angles and torsional angles are given in Table 2. The thermal ellipsoidal plots and numbering schemes of diselenide **1a** and disulfide **2** are shown in Figures 1 and 2.

Compounds **1a** and **2** crystallize in the $P2_12_12_1$ space group with one molecule as asymmetric part of the unit cell. The molecular structures are similar and lie in the skew conformation. Analogies between the disulfide and diselenide linkage in other C−Se−Se−C and C−S−S−C isostructural systems were reported by Hargittai and Rozsondai.[30] The X atoms (X = S, Se) attached to six-membered rings are in equatorial positions. For both compounds, 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranose rings are bridged by disulfide or diselenide units. The conformation of the bridge involves torsional angles C−Se(S)−Se(S)−C (−81.8° for **1a** and −82.5° for **2**; Table 2). Values close to 90° are typical for dichalcogenide bonds in natural products and organic compounds.[31] The length of the disulfide bond was found to be 2.033(3) Å and reaches a value similar to the sulfur−sulfur distance between divalent sulfur atoms in noncyclic compounds.

Scheme 1[a]



[a] C2(A)−C1(A)−X1(A)−X1(B): X = S, 154.1°; X = Se, 154.8°. C2(B)−C1(B)−X1(B)−X1(A): X = S, −47.2°; X = Se, −46.6°.

The diselenide bond length was found to be 2.298(2) Å (Table 2). Twice the covalent radius of selenium according to Pauling, is 2.34 Å.[32]

The C−C−Se−Se−C−C fragment of diselenide **1a** shows several geometrical distortions. First, the bond lengths C1−Se are different (by means of the range 3σ: 1.960(6) Å and 1.944(5) Å). Second, the Se−C1−C2 bond angles are very different (109.5(4)° and 116.1(4)°). Third, the C1−O1 bond lengths and Se1−C1−O1 bond angles in A and B glucopyranoses are very similar while there are small differences (in the range 2σ) in C1−C2 bond lengths (1.505(8) Å for A and 1.520(7) Å for B). The changes of geometric parameters around C1 atoms may presumably be explained by anomeric effect and/or hyperconjugative interaction, which in generalized form refers to the torsional preferences about the C−X and

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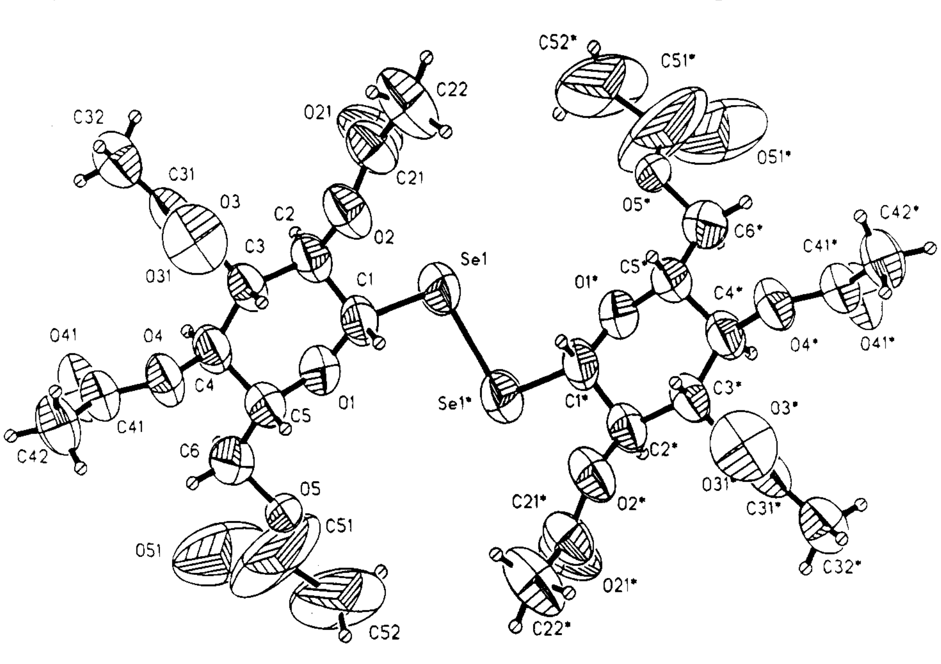

Figure 3. ORTEP plot of bis(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl) diselenide (**1b**). Half of the molecule is an asymmetric part of the unit cell; the primed atoms are from the symmetrical (−*x*,1 - *y*,*z*) moiety.

C−Y bonds in R−X−CH$_2$−Y−R′ molecules.[33] The existence of conformational effect in system containing first-row atoms has been widely accepted. The anomeric effects and hyperconjugation involving second- and lower-row atoms has been discussed by Saltzner and Schleyer.[34,35] An unusual conformation of selenium coronad and conformational equilibria of (arylseleno)-1,3-dithianes, were explained by Pinto and co-workers in terms of selenium anomeric effect.[36−39] Very recent theoretical calculations published by Kahn et al. fully confirmed the existence of anomeric stabilization for second, third and fourth row atoms.[40] Our results prompt us to speculate that oxygen at the anomeric position has no influence on the geometry of diselenide **1a**. The stereoelectronic effect from the selenium atom plays the predominant role, as the p electron lone pair of selenium affects the σ^*_{C1-C2} orbital.

As shown in Scheme 1a, the C2(A)−C1(A)−Se1(A)−Se1(B)−C1(B)−C2(B) backbone has *anti*−*syn* geometry. The appropriate torsional angles C2(A)−C1(A)−Se1(A)−Se1(B) and Se1(A)−Se1(B)−C1(B)−C2(B) are 154.8(3)° and −46.6(4)°, respectively. In the *synclinal* arrangement the p_y selenium electron lone pair is antiperiplanar to σ^*_{C1-C2} as displayed in Scheme 1b. It causes the shortening of the Se1(B)−C1(B) bond, lengthening of the C1(B)−C2(B) bond and the distortion of Se1(B)−C1(B)−C2(B) angle (116.1(4)°) from tetrahedral.

In the *anti* arrangement the p_y selenium lone pair is perpendicular to σ^*_{C1-C2}, thus overlap is not possible. As a results, the Se1(A)−C1(A) and C1(A)−C2(A) bond lengths in **1a** are not changed and the Se1(A)−C1(A)−C2(A) angle is found to be 109.5(4)°. On the other hand, the nonbonding selenium−oxygen contacts can affect the geometry of the C2(A)−C1(A)−Se1(A)−Se1(B)−C1(B)−C2(B) unit. The Se−O2 distance is 3.20 Å, marginally less than the sum of the Se and O van der Waals radii (3.4 Å). As reported by Goldstein et al.[41] the close Se−O contact is electrostatic in origin.

Although the MM$^+$ force field approach does not contain the parameters that describe the crystallographic effects, it is known that theoretical calculations roughly correspond to those obtained employing experimental techniques.[42] The conformations of the pyranose rings are kept at their fixed geometry as established by X-ray or neutron diffraction studies. Assuming that comparison of the minimum energy for *anti*−*anti*, *anti*−*syn*, and *syn*−*syn* conformations shows the probability to taking on a preferred geometry, the MM calculations were carried out (see section iii for details). Calculations reveal that all conformations have comparable energies. Careful inspection by the ^{77}Se CP/MAS technique (details in section ii) of powder patterns of diselenide **1** crystallized under different conditions has allowed us to recognize and finally select single crystals of each crystallographic form. Figure 3 shows the ORTEP plot and numbering scheme for diselenide **1b**.

Diselenide **1b** crystallizes in the $P2_12_12$ space group with half molecule as an asymmetric part of the unit cell (the second half is symmetrical by the symmetry operation −x, 1 − y, z). The C1−Se1−Se1*−C1* torsional angle is 109.2(3)°. The Se1−Se1* bond length is considerably larger than in **1a** (2.325(1) Å). This result is consistent with data which show that the dichalcogenide bond is a function of C−X−X−C torsional angle and

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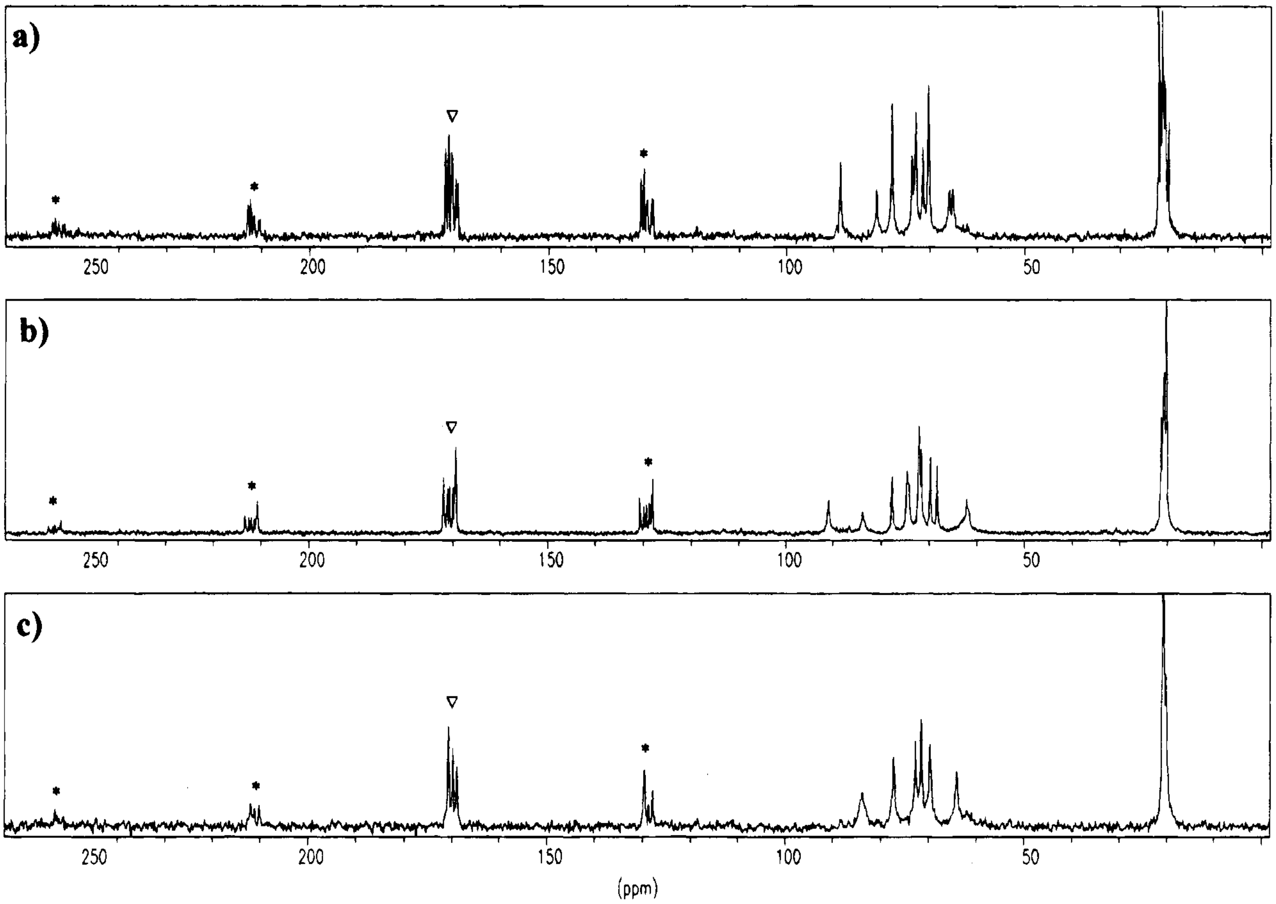

Figure 4. ^{1}H-^{13}C CP/MAS spectra of (a) bis(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl) diselenide (**1a**), (b) bis(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl) disulfide (**2**), and (c) bis(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl) diselenide (**1b**). All spectra have 8K data points with 5 Hz line broadening, a contact time of 1 ms, and 100 scans. The spinning sidebands are marked by asterisks, the isotropic lines are marked by inverted triangles.

reaches minimum close to 90°.[30] The glucopyranose rings are in the chair conformation and the selenium atoms are equatorial. The C2−C1−Se1−Se1*−C1*−C2* skeleton is found to be in the *anti−anti* arrangement. The C2−C1−Se−Se torsional angles are 171.1(4)°. The geometry of the C2−C1−Se1−Se1*−C1*−C2* backbone has apparent influence on the bond angle of the C2−C1−Se unit of **1b** (111.0(4)°). By comparing geometric parameters for **1a** and **1b** we conclude that *synclinal* arrangement and, in consequence, overlap of the selenium p lone pair and σ^*_{C1-C2}, are crucial to the distortion of the C2−C1−Se−Se−C1−C2 skeleton. Small differences in C1−O1 bond lengths (in the range of 3σ) for **1a** and **1b** are observed. For **1a**, C1−O1 distances are found to be 1.425(6) Å and 1.421(6) Å while for **1b** they are only 1.400(8) Å. The C1−C2 and Se1−C1 bond lengths for **1a** are 1.537(7) and 1.961(7) Å. It is noteworthy that molecular packing effects may also cause differences in bond lengths and bond angles.

The effect of distortion of the local geometry of the C−C−S−S−C−C backbone was observed for disulfide **2**. The C−S bond lengths were found to be very similar (1.802(7) and 1.805(6) Å) but the S−C1−C2 bond angles are different: 109.8(5)° and 115.4(4)°. These differences are related to the *anti−syn* geometry of the main skeleton. Despite several attempts we were unable to select a new crystallographic modification of disulfide **2** suitable for XRD studies.

The structural disorder and thermal vibrations of acyl groups in **1a**, **1b**, and **2** should be stressed. 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranose rings for all compounds are in the chair conformation. The asymmetry parameters used to establish the geometry of the six-membered rings are collected in Table 3.

Solid State NMR Studies. High-resolution solid-state ^{13}C NMR spectra for diselenide **1a** and disulfide **2** are shown in Figure 4, parts a and b, respectively.

The carbohydrate resonances in the ^{13}C CP/MAS spectra are found in the region of 63−93 ppm and are slightly downfield compared to those in solution. As one molecule is an asymmetric part of the unit cell, 12 signals were predicted. Because of overlap of signals only nine peaks for diselenide **1a** and 10 for disulfide **2** were seen. Anomeric carbon resonances for both compounds can be easily assigned in the solid state. Due to a different local environment of the C1 carbon in the A and B rings the signals differ by ca. 8 ppm and are found at $\delta = 81.2$ and $\delta = 89.6$ ppm in diselenide **1a** and at $\delta = 83.4$ and 91.8 ppm in disulfide **2**. Five (**1a**) and six (**2**) carbonyl resonances, found at ca. 170 ppm confirmed that one molecule per unique volume is an independent structural unit. Since large chemical shift anisotropy is characteristic for carbonyl groups, isotropic lines are symmetrically flanked by spinning sidebands at 130 and 210 ppm. A rough analysis of spinning sideband intensities suggests that the shielding parameters, Ω and κ, for carbonyl groups are very similar in both compounds. A comparison of spectra recorded in the solid state and in solution indicates that the isotropic chemical shifts of the carbonyl groups in both compounds are similar. Thus, these

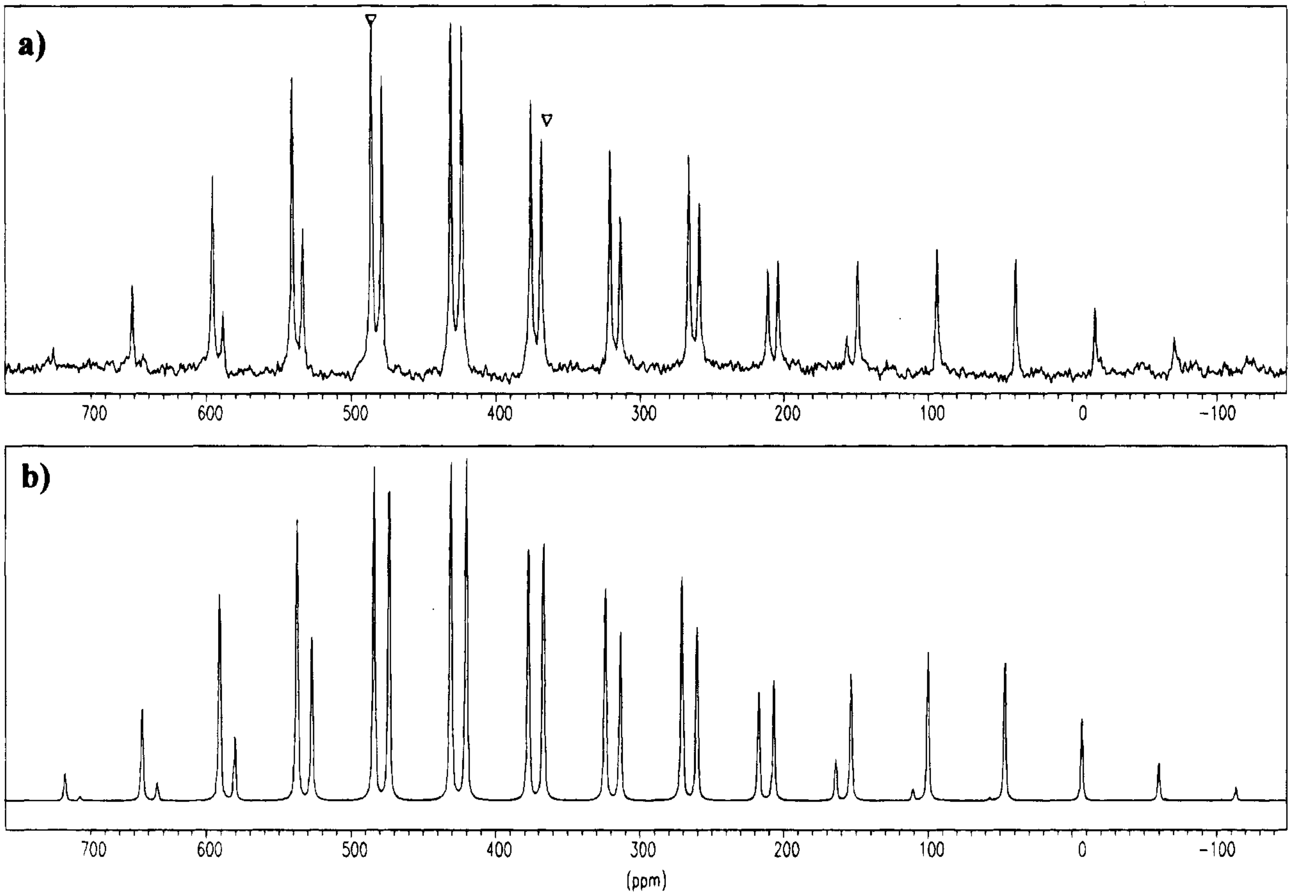

Figure 5. (a) Experimental ^{1}H-^{77}Se CP/MAS spectrum of bis(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl) diselenide (**1a**) with 8K data points, 50 Hz line broadening, 1 ms contact time, 2020 scans, and ν_{rot} = 3150 Hz; and (b) theoretical spectrum calculated with the MASNMR program commercially available from Bruker Instruments Inc. The isotropic lines are marked by inverted triangles.

Table 4. ^{77}**Se Chemical Shift Parameters for Three Polymorphs of Bis(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl) Diselenide (1)**[a]

compound	conformation	δ_{11} (ppm)	δ_{22} (ppm)	δ_{33} (ppm)	δ_{iso} (ppm)	Ω (ppm)	η	κ	$\Delta\delta$ (ppm)
diselenide **1a**	*anti*–*syn*	718	504	231	484.2	487	0.85	0.12	−380
		639	484	−22	366.9	661	0.40	0.55	−584
diselenide **1b**	*anti*–*anti*	779	434	169	460.5	610	0.83	−0.13	477
diselenide **1c**	*syn*–*syn*	844	473	225	513.9	619	0.75	−0.20	495
		731	400	118	416.2	613	0.90	−0.08	472

[a] Errors in the experimental principal components of the chemical shift tensor are ±5 ppm.

resonances are not affected by molecular packing effects and/or local distortion. The methyl group signals at 20 ppm shows six partially overlapping ^{13}C resonances. The values of the ^{13}C chemical shifts and multiplicities of peaks can be useful in studies of molecular symmetry and local geometry. Solid-state NMR and XRD provide information in this respect.

Diselenide **1b** crystallizes in the space group $P2_12_12$ with half of the molecule as an asymmetric part of the unit cell. The ^{13}C CP/MAS spectrum of diselenide **1b** (Figure 4c) shows only three carbonyl, six glucopyranose, and three methyl peaks. The anomeric carbon seen as a broad signal is found at δ = 89.3 ppm.

Our most spectacular results come from the analysis of the ^{77}Se NMR results. As shown by XRD, selenium atoms in diselenide **1a** are in two different environments and should be magnetically nonequivalent. Figure 5a displays the ^{77}Se CP/MAS spectrum of **1a** recorded at room temperature.

Isotropic ^{77}Se resonances are symmetrically surrounded by a number of spinning sidebands. The spectrum shows two sets of spinning sideband systems which correspond to crystallographically nonequivalent Se1 and Se2 sites. The MASNMR program[25] based on the Berger and Herzfeld algorithm[26] enables us to obtain the principal components of the ^{77}Se chemical shift tensors as well as the shielding parameters (see Table 4). The accuracy of the results was confirmed by comparison with the theoretical spectrum shown in Figure 5b.

The selenium nuclei of diselenide **1a** have very different chemical shift anisotropy. As shown by Collins et al.,[43] the ^{77}Se anisotropic shielding is extremely sensitive to even small departures from spherical symmetry. For lower symmetry environments the large anisotropy leads to large number of spinning sidebands. For the Se1 site, Ω is found to be 487 ppm, $\Delta\delta$ is −380 ppm, κ is 0.12, and η is 0.85, whereas for Se2 these parameters are 661 ppm, −584 ppm, 0.55 and 0.40, respectively. The isotropic values δ_{iso} are 484.2 ppm (Se1) and 366.9 ppm (Se2).

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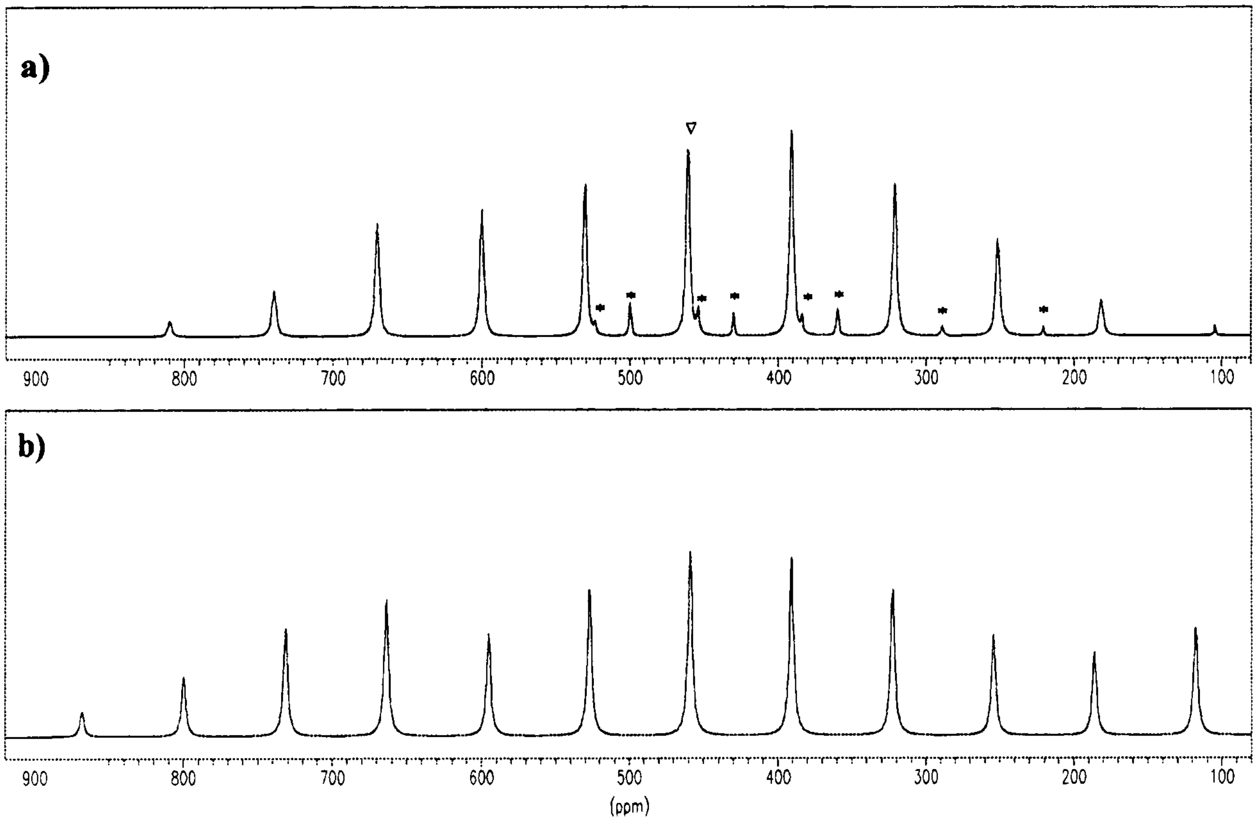

Figure 6. (a) Experimental ^{1}H-^{77}Se CP/MAS spectra of bis(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl) diselenide (**1b**) with 8K data points, 50 Hz line broadening, 1 ms contact time, 11090 scans, and ν_{rot} = 3150 Hz (asterisks denote peaks from the **1c** polymorph); and (b) theoretical spectrum calculated with the MASNMR program commercially available from Bruker Instruments Inc. The isotropic lines are marked by inverted triangles.

Figure 6a displays the ^{77}Se CP/MAS spectrum of diselenide **1b**. It is apparent that half of the molecule is an asymmetric part of the unit cell. For **1b**, the Ω is 610 ppm, $\Delta\delta$ is 477 ppm, κ is −0.13, η is 0.83, and δ_{iso} is found to be 460.5 ppm. The calculated shielding parameters for **1b** differ from those established for diselenide **1a** and are related to differences in molecular structures of both modifications.

It is known that anisotropy parameters $\Delta\delta$ and Ω reflect the distortion of molecular structure from ideal tetrahedral, whereas the asymmetry parameters η and κ correspond to asymmetry of electron-density distribution about central atom. In case of diselenides **1** the local environment of selenium is created by appropriate Se-Se-C1, Se-C1-C2, and Se-C1-O1 bond angles and bond lengths as well as p-electron lone pairs. The comparison of absolute values of $|\Delta\delta|$ for **1a** and **1b** indicate that geometry around selenium atoms for both compounds is different what is consistent with XRD results. Moreover for Se1(A) and Se1(B) sites of polymorph **1a** the significant differences in $\Delta\delta$, Ω, η, and κ are observed. These differences may presumably be explained by interaction of p-electron lone pair of Se1(B) and σ^*_{C1-C2} orbital and changes of Se shielding which causes the increase of $|\Delta\delta|$ and Ω. The values of η and κ indicate that Se shielding is not localized to a particular bond but is averaged out over the entire tetrahedral. Note that κ which carries information on the symmetry of shielding tensors is positive for *anti*−*syn* geometry and negative for *anti*−*anti* geometry.

Molecular Modeling. In order to compare relative energies of different molecular arrangements of the C2−C1−X−X−C1−C2 backbone in **1** and **2**, further results were obtained from molecular mechanics calculations.[44] The applications of force field approach in conformational analysis of oligosaccharides was reviewed by Meyers.[42] The usefulness of the MM2 program in the area of carbohydrates chemistry has been demonstrated in numerous publications.[45,46] The *anti*−*anti*, *anti*−*syn*, and *syn*−*syn* conformations were calculated with MM$^+$ program in HyperChem package.[29] The established energies and geometrical parameters are given in Tables 5 and 6, respectively.

Table 5. MM$^+$ Geometries and Energies for Diselenide 1 and Disulfide 2

	diselenide		disulfide	
conformation	energy (kcal/mol)	torsional angles[a]	energy (kcal/mol)	torsional angles[a]
anti−*syn*	98.006	−69.088 179.429	76.929	−69.183 179.492
syn−*syn*	99.259	−68.359 53.146	77.895	−68.091 55.577
anti−*anti*[b]	101.365	−179.774 178.131		

[a] Torsional angles refer to C−X−X−C unit; X = Se, S. [b] *anti*−*anti* geometry of disulfide **2** was taken as input data. After energy minimization the geometry was changed to *anti*−*syn* conformation.

From these results it is seen that diselenide **1** adopts different conformations. Two of them were assigned by XRD. Systematic inspection of crystals of diselenide **1** by ^{77}Se solid-state NMR technique has allowed the

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Table 6. Selected Geometric Parameters Taken from MM$^+$ Calculation for Diselenide 1 (a) and Disulfide 2 (b)

a. Diselenide **1**

bond lengths and bond angles	*anti–syn* A	*anti–syn* B	*syn–syn* A	*syn–syn* B	*anti–anti* A	*anti–anti* B
Se–Se	2.3204		2.3202		2.3195	
C1–O1	1.4129	1.4106	1.4331	1.4099	1.4115	1.4114
C1–Se	1.9643	1.9560	1.9672	1.9588	1.9627	1.9554
C1–C2	1.5367	1.5361	1.5366	1.53380	1.5366	1.5358
C2–C3	1.5374	1.5369	1.5383	1.5374	1.5376	1.5373
C3–C4	1.5368	1.5366	1.5360	1.5373	1.5371	1.5358
C4–C5	1.5372	1.5379	1.5386	1.5438	1.5366	1.5385
C5–C6	1.5376	1.5363	1.5381	1.5382	1.5366	1.5371
Se–Se–C1	110.93	109.70	111.41	112.33	109.04	108.70
Se–C1–O1	111.74	108.15	111.97	109.91	112.37	107.37
Se–C1–C2	116.94	111.09	116.98	114.39	115.66	111.28
O1–C1–C2	110.55	110.33	110.09	108.08	111.07	110.46
Se–Se–C1–C2	−69.08	179.42	−68.359	53.146	179.74	−178.81
C1(A)–Se–Se–C1(B)	96.10		107.47		95.99	

b. Disulfide **2**

bond lengths and bond angles	*anti–syn* A	*anti–syn* B	*syn–syn* A	*syn–syn* B
S–S	1.994		1.992	
C1–O1	1.4110	1.4094	1.4117	1.4078
C1–S	1.8015	1.8072	1.8124	1.8071
C1–C2	1.5405	1.5380	1.5398	1.5366
C2–C3	1.5396	1.5364	1.5408	1.5368
C3–C4	1.5363	1.5362	1.5362	1.5377
C4–C5	1.5368	1.5399	1.5387	1.5447
C5–C6	1.5377	1.5369	1.5380	1.5383
S–S–C1	115.33	114.53	115.61	116.60
S–C1–O1	111.75	108.70	111.84	111.94
S–C1–C2	115.52	109.34	115.85	112.43
O1–C1–C2	110.67	109.76	110.31	107.93
S–S–C1–C2	−69.18	176.49	−68.09	55.57
C1(A)–S–S–C1(B)	98.86		105.64	

identification of the third conformer (diselenide **1c**), unfortunately as mixture with diselenide **1b**. ^{13}C CP/MAS was found to be insensitive to this conformer, due to severe overlap in the ^{13}C spectra.

Figure 7a shows the spectrum of a mixture of diselenides **1c** and **1b** made under optimized conditions for growth of **1c** crystals, and Figure 7b shows the spectrum of polymorph **1c** obtained by substracting simulated spectra of **1b** from Figure 7a. In the best experiment the yield of **1c** was 68%. From ^{77}Se spectra we conclude that one independent molecule is an asymmetric part of the unit cell. Similar shielding parameters for Se1 and Se2 centers suggest resemblance of local environments for both selenium. Values of Ω and $\Delta\delta$ for **1c** are somewhat larger compared to those measured for **1b**. κ is negative as in case of *anti–anti* conformation. Although we do not have conclusive evidence we speculate that diselenide **1c** adopts *syn–syn* geometry. Assuming that ^{77}Se shielding parameters for all polymorphs reflect the local geometry of selenium centers, it seems that the hypothesis of the *syn–syn* arrangement is valid. The C–C–Se–Se torsional angles, optimized by MM method were found to be −68.36° and 53.1°.

The minimum energies for diselenide **1** and disulfide **2** differ by about 20 kcal/mol. We were not able to find a local minimum in energy for the *anti–anti* geometry of **2**. In each case the conformation was changed to an arrangement where the C–C–S–S torsional angles were close to 170° and 70° (*anti–syn*). The results of calculations presumably explain the lack of success in searching for the other polymorph of disulfide **2**.

Conclusion

When crystallized from methanol under different conditions, bis(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl) diselenide (**1**) forms three polymorphs. The crystal and molecular structures for two polymorphs were determined by XRD. In both of these, selenium atoms bonded to anomeric carbons are in an equatorial position. For polymorph **1a**, the role of oxygen is negligible and has no influence on conformation of the –O–C–Se–Se–C–O– unit. However, there is a strong effect of the selenium lone pair, causing changes in bond lengths and bond angles. To the best of our knowledge, this is the first clear example that shows the relationship between the geometric parameters and the conformation of the C–C–Se–Se–C–C backbone in organoselenium compounds.

Diselenides **1a** and **1b** crystallize in different noncentrosymmetric space groups, $P2_12_12_1$ (**1a**) and $P2_12_12$ (**1b**). The changes in molecular symmetry are immediately detected by ^{13}C and ^{77}Se CP/MAS experiments. The latter technique is particularly powerful for the study of molecular packing. Shielding parameters obtained from spinning sideband intensities correlate with the geometry around the selenium centers.

Diselenide **1c** is obtained as a mixture with **1b** and the individual structures cannot be resolved by XRD. However, some conclusions may be drawn from NMR spectra and the MM approach. Molecular mechanics calculations are a useful guide in the search for new polymorphs. The results for bis(2,3,4,6-tetra-*O*-acetyl-

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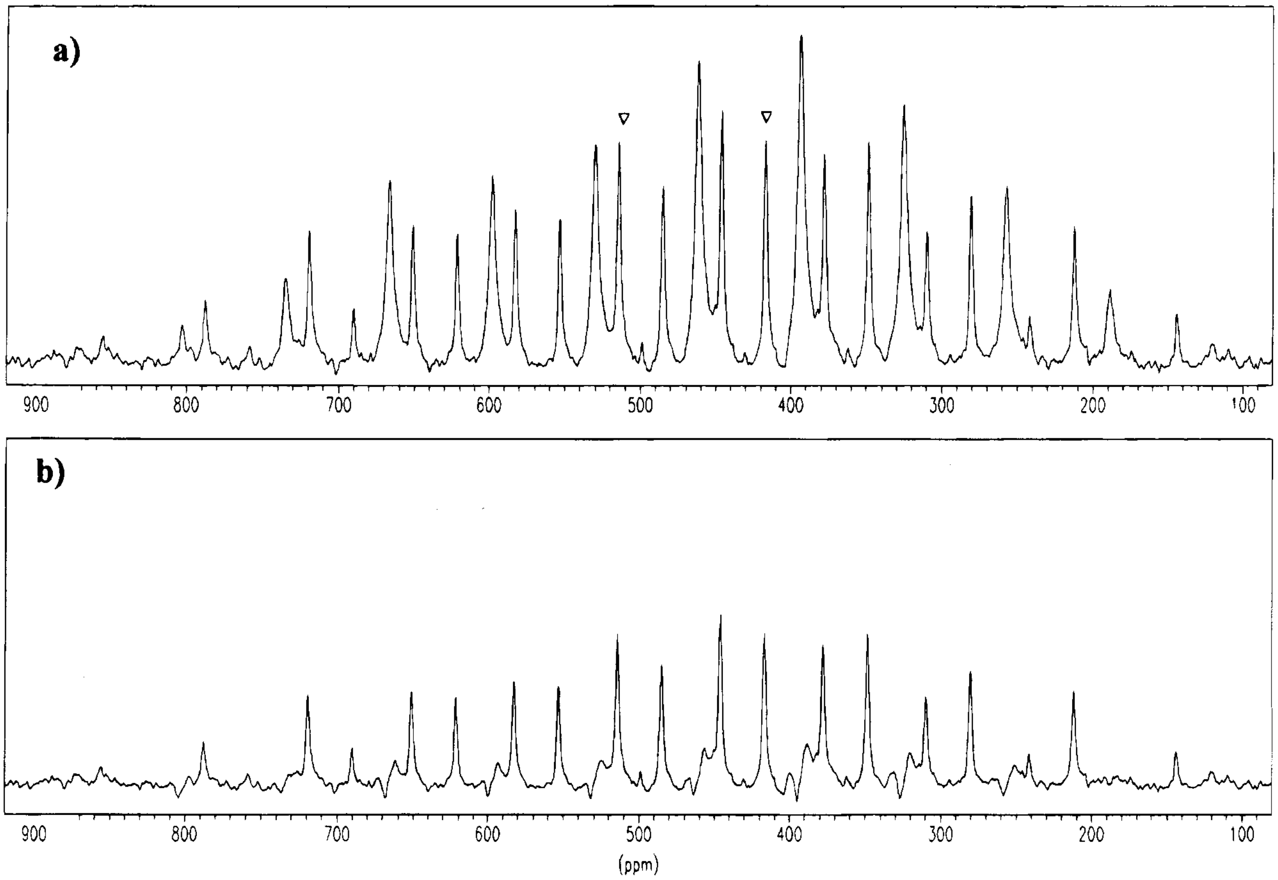

Figure 7. ^{1}H-^{77}Se CP/MAS spectra of (a) a mixture of bis(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl) diselenides **1b** and **1c** and (b) diselenide **1c** obtained by substraction of a simulated spectrum of polymorph **1b** from a. Each spectrum has 8K data points with 50 Hz line broadening, a contact time of 1 ms, 6460 scans, and ν_{rot} = 3910 Hz.

β-D-glucopyranosyl) disulfide (**2**) were less impressive because ^{77}Se CP/MAS NMR, an excellent structural tool, is inapplicable.

This work shows the power of the multitechnique approach for the study of solids. The question of polymorphism of bulk materials and ambiguity of the space groups versus solid-state NMR has attracted much attention.[47-49] Our results reveal that this phenomenon is common for organic and heteroorganic dichalcogenides. Formation of polymorphs can be caused by changes of molecular structures or by solvatation effects.[17]

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