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REACTIONS OF TETRA-*O*-ACETYL-β-D-GLUCOPYRANOSYLSULFENYL BROMIDE*†

R. H. BELL, D. HORTON**, AND MARTHA J. MILLER‡
Department of Chemistry, The Ohio State University, Columbus, Ohio 43210 (U.S.A.)
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ABSTRACT

Tetra-*O*-acetyl-β-D-glucopyranosylsulfenyl bromide (**2**) has a bivalent sulfur atom that exhibits electrophilic character. With such sulfur nucleophiles as benzenethiol and α-toluenethiol, the sulfenyl bromide **2** reacts to give mixed disulfides (**5** and **6**, respectively) and, with such arylamines as aniline or *o*-chloroaniline, the sulfur atom of **2** attacks the nucleophilic nitrogen atom to give sulfenamides (**7** and **8**, respectively). Addition of **2** to the double bond of cyclohexene gives *trans*-2-bromo-1-(tetra-*O*-acetyl-β-D-glucopyranosylthio)cyclohexane (**3**); the 3′,3′,6′,6′-tetradeuterated analog was prepared by use of cyclohexene-*3,3,6,6-d*$_4$. With *N,N*-dimethylaniline, the sulfenyl bromide **2** reacts by attack at the *para* position to give *p*-(dimethylamino)-phenyl tetra-*O*-acetyl-1-thio-β-D-glucopyranoside (**1**), although a concurrent, major reaction-pathway gives bis(tetra-*O*-acetyl-β-D-glucopyranosyl) disulfide (**4**). With phenol and various enolizable ketones, the sulfenyl bromide **2** reacts to give the disulfide **4** in high yield. The structures assigned to the products were confirmed by n.m.r. spectroscopy. Such glycosylsulfenyl halides as **2** thus offer a potential route to a wide range of thio sugar derivatives by reactions with thiols, amines, and alkenes.

RESULTS AND DISCUSSION

The accompanying paper[1] describes reactions leading to the formation of tetra-*O*-acetyl-β-D-glucopyranosylsulfenyl bromide (**2**), including a convenient preparative method for obtaining **2** in quantities of 50–100 millimoles. At the time when the sulfenyl bromide **2** was first described[2], the suggestion was made that it might be useful in various types of synthetic reaction based on attack by an electrophilic, bivalent sulfur atom on a site of high electron-density. Experimental support for

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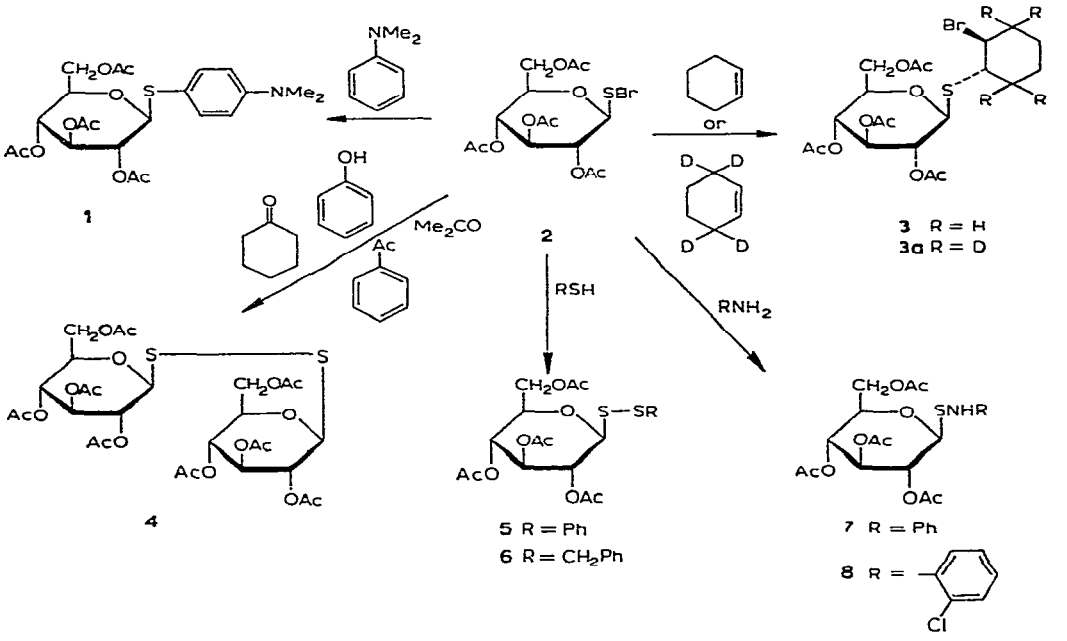
**To whom inquiries should be addressed.
‡Undergraduate Research Participant, 1964–1965.

these predictions has been the subject of a brief report[3]. The present paper records detailed studies of the reaction of the sulfenyl bromide **2** with various thiols, aromatic amines, an alkene, an aromatic system activated for electrophilic attack, various ketones, and phenol.

Reaction of **2** *with thiols.* — Treatment of the sulfenyl bromide **2** with an excess of benzenethiol in carbon tetrachloride for 1 h at room temperature gave the glucosyl phenyl disulfide **5** in high yield. Similar treatment of **2** with α-toluenethiol gave the benzyl analog (**6**), also in high yield. The structures of **5** and **6** are established by the elemental analyses, spectral data, and optical rotatory data recorded in the Experimental section. The n.m.r. spectra of **5** and **6** at 100 MHz in chloroform-*d* (see Tables I and II) showed the H-1, 2, 3, and 4 signals as multiplets perturbed by second-order effects, as anticipated[4] for this type of system.



The facility with which **2** reacts with thiols to give such disulfides as **5** and **6** makes the reaction a useful one for identifying the reactive sulfenyl halide **2** (and related analogs) by "trapping" it as a stable derivative[1,3].

Addition of **2** *to cyclohexene.* — The sulfenyl bromide **2** reacted readily with cyclohexene to give a high yield of a crystalline product whose elemental analysis showed it to be an adduct of the two reactants. A minor side-product was bis(tetra-*O*-acetyl-β-D-glucopyranosyl) disulfide (**4**). The adduct was formulated as *trans*-2-bromo-1-(tetra-*O*-acetyl-β-D-glucopyranosylthio)cyclohexane (**3**) by analogy with the established[5] *trans* mode of addition of simple sulfenyl halides to alkenes; further support for this configuration was provided by n.m.r. spectral data.

A (±) pair of enantiomorphic products will result from *trans*-addition of a

non-dissymmetric sulfenyl halide to a cyclic alkene. *trans*-Addition of an optically active sulfenyl halide, such as **2**, to cyclohexene will generate a pair of products that are related as diastereoisomers. The relative proportions of the two diastereoisomers formed will depend on the magnitude of the asymmetric inductive effect[6] in the reaction. Strong asymmetric induction would cause one diastereoisomer to preponderate; if the effect is weak, the two diastereoisomers will be formed in almost equal amounts.

On recrystallization from ether–petroleum ether, the adduct **3** did not behave as a mixture separable by fractional recrystallization; this observation indicated that **3** was either a single diastereoisomer or a cocrystallized mixture of the two diastereoisomers as a molecular complex or solid solution. Consideration of molecular models afforded no evidence suggesting strong asymmetric induction in the addition of **2** to cyclohexene, and, since the yield of crystalline product was high (66%), the occurrence of a cocrystallized mixture of diastereoisomers was suspected. Strong supporting evidence for this supposition was provided by n.m.r. spectroscopy.

The 100-MHz n.m.r. spectrum of the adduct **3** in chloroform-*d* (see Tables I and II) shows the signals of H-1,2,3, and 4 of the sugar moiety as a multiplet (τ 4.67–5.38), the H-6 signals at τ 5.83, and the H-5 signal at τ 6.27; these assignments follow from detailed studies already reported[4] for acetylated 1-thio-*β*-D-glucopyranose derivatives. A broad, one-proton multiplet, with bands centered at τ 5.41 and 5.63, may be assigned to H-2′ of the cyclohexane moiety*; this is the spectral region where the proton of a C–CHBr–C system in a 6-membered ring is observed[7]. Another one-proton multiplet, at τ 6.68, is assigned to H-1′ by analogy with observations[8] on the proton of a C–CHSR–C group in a 6-membered ring-system. The signals of the methylene protons in the cyclohexane moiety are observed as a complex "envelope" at high field.

Detailed analysis of the H-1′ and H-2′ signals was not possible, because these protons show, in addition to vicinal ($J_{1',2'}$) coupling, further couplings to their adjacent methylene groups (at C-6′ and C-3′, respectively). To clarify the n.m.r. spectral interpretation, the adduct (**3a**) of **2** with cyclohexene-*3,3,6,6-d*$_4$ was prepared. In this product, the signals of H-1′ and H-2′ were observed unperturbed by strong couplings to the vicinal (CD_2) groups at C-6′ and C-3′, respectively, because H–D couplings[9] are only 15.4% of the magnitude of the corresponding H–H couplings.

In chloroform-*d*, the H-2′ signal of **3a** was observed, not as one doublet (showing the $J_{1',2'}$ coupling), but as *two* doublets, at τ 5.43 (splitting, 5.0 Hz) and at τ 5.65 (splitting, 5.5 Hz), of approximately equal intensity. The splittings were confirmed to arise from spin-coupling ($J_{1',2'}$), because they were of the same magnitude in the 60-MHz spectrum. The separation of the doublets was 22 Hz in the 100-MHz spectrum, and 13 Hz in the 60-MHz spectrum; as these separations are proportional to the spectrometer frequency, the spacing between the two doublets is a true chemical-shift, and not the result of signal multiplicity[10]. In addition, the separation of the two

*Primed numbers refer to the cyclohexane moiety.

doublets was changed by changing the solvent; in acetone-d_6 at 100 MHz, the separation was 14 Hz.

The appearance of *two*, independent H-2′ signals provides strong indication that compound **3a** (and therefore **3**) is a 1:1 mixture of two closely related, molecular species, presumably the diastereoisomeric *trans*-adducts. Complementary evidence is provided by analysis of the H-1′ signal, and by spin-decoupling experiments on the H-1′ and H-2′ resonances. In chloroform-*d* at 100 MHz, the H-1′ signal of **3a** is observed as two overlapping doublets, at τ 6.69 (splitting 5.0 Hz) and τ 6.72 (splitting 5.5 Hz); the splittings are the same in the 60-MHz spectrum, and arise, therefore, from spin coupling ($J_{1',2'}$), whereas the separation of the doublets is a chemical-shift effect, because it is diminished from ~3 Hz (at 100 MHz) to ~2 Hz in the 60-MHz spectrum. In acetone-d_6 at 100 MHz, only one doublet (spacing, ~5.5 Hz) is observed for H-1′, indicating that, in this solvent, the chemical shift of H-1′ is the same for both species present in **3a**.

Spin-decoupling experiments (see Fig. 1) were performed at 100 MHz with solutions of **3a** in chloroform-*d* and also in acetone-d_6. In each case, irradiation of the

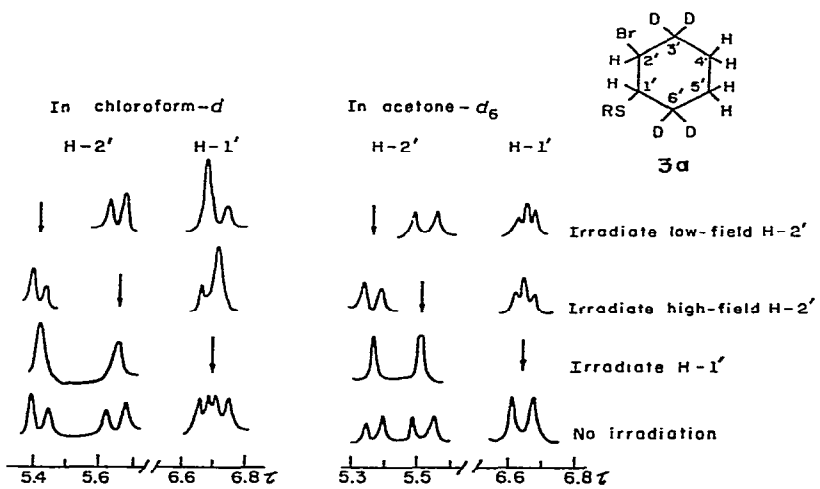


Fig. 1. Spin decoupling of the H-1′ and H-2′ signals in the 100-MHz, n.m.r. spectra of 2-bromo-(tetra-*O*-acetyl-β-D-glucopyranosylthio)cyclohexane-3′,3′,6′,6′-d_4 (3a) in chloroform-*d* and acetone-d_6.

H-1′ signals caused collapse of both H-2′ doublets into singlets. Irradiation of the low-field, H-2′ doublet did not perturb the higher-field, H-2′ doublet, but one of the H-1′ doublets collapsed to a singlet in the chloroform-*d* spectrum. As the H-1′ doublets coincided in acetone-d_6, the effect was observed by the appearance of a central singlet flanked by a doublet, to give an apparent triplet. Irradiation of the higher-field, H-2′ doublet did not perturb the low-field, H-2′ doublet, but collapse of the corresponding H-1′ doublet took place.

The foregoing data establish that **3** (and **3a**) contain approximately equal amounts of two species that are differentiable by n.m.r. spectroscopy. The possibility

that hindered rotation is involved is considered remote, because the H-1′ and H-2′ signals in the spectrum of **3** in hexachloroacetone[11] showed no indication of collapse as the temperature was raised from 20 to 105°.

The observed $J_{1',2'}$ couplings (5.0 and 5.5 Hz) accord with formulation of the two forms of **3a** (and therefore **3**) as the diastereoisomeric *trans*-adducts. Had the adducts been *cis*, the $J_{1',2'}$ coupling would have been only 3–3.5 Hz, because of the *gauche* relationship of H-1′ and H-2′ (axial–equatorial or equatorial–axial) in either chair conformation of the cyclohexane ring. In the *trans*-adduct, the favored chair conformer of the cyclohexane moiety (equatorial S and Br) would have H-1′ and H-2′ antiparallel, giving a coupling of ~8 Hz, and this value would be diminished by any substantial contribution from the less-favored conformer, having H-1′ and H-2′ diequatorial ($J_{1',2'}$ 1-2 Hz), in rapid equilibrium[12] with the favored form.

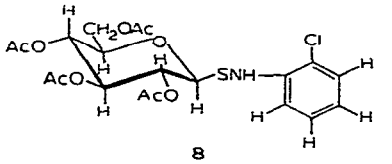
Formulation of **3** as a diastereoisomeric mixture of *trans*-adducts has not been verified independently by chemical degradations.

Reaction of **2** *with amines.* — The sulfenyl bromide **2** reacted readily with aniline to give the crystalline sulfenamide **7** in 82% yield. *o*-Chloroaniline reacted similarly to give the corresponding sulfenamide (**8**). In each case, a trace of the disulfide **4** accompanied the sulfenamide. The elemental analyses of the products established that they had been formed by condensation of one molecule of the amine with one molecule of sulfenyl bromide, with the loss of a molecule of hydrogen bromide. This evidence does not prove the sulfenamide structure, because attack of **2** on the aryl ring-positions cannot be excluded. The n.m.r. spectra provided clear confirmation of the sulfenamide structure, because, in each compound, a one-proton singlet was observed (at τ 4.76 for **7** and at τ 4.24 for **8**, with chloroform-*d* as solvent) that could be assigned to the NH proton of a sulfenamide, because it was exchanged slowly when the sample was deuterated. Furthermore, in the region for aryl protons, compound **7** showed five protons, and **8** showed four protons, thus proving that substitution on the aryl nucleus had not taken place.

The n.m.r. spectra for **7** (see Fig. 2) and **8** were closely similar, and were analyzed completely for the ring protons on the sugar moiety by first-order inspection (see Tables I and II). The assignments were verified by spin decoupling. A striking feature of the spectra is the exceptionally high field-position of the H-1 signal, which is upfield of the H-2, H-3, and H-4 signals and is close to the H-6 signals. Because the H-1 signal is shifted away from the H-2, H-3, and H-4 signals, it is possible to analyze the latter signals readily. In most of the acetylated derivatives of 1-thio-*β*-D-glucopyranose, the proximity of the H-1 signal to those of H-2, H-3, and H-4 makes detailed spectral analysis difficult[4]. It has not been established whether the unusual shielding of H-1 in **7** and **8** is an inductive effect of the sulfenamide group, or whether it is the effect of the location of H-1 in the shielding region of the π-cloud above or below the aromatic ring.

Reaction of **2** *with an activated aryl derivative.* — The sulfenyl bromide **2** was allowed to react in a carbon tetrachloride medium with two molar equivalents of *N*,*N*-dimethylaniline. The latter was selected as an activated, aromatic molecule that

readily undergoes substitution, principally at the *para* position, by electrophilic reagents. The major product isolated was, however, the disulfide[13] **4** (yield 62%), although the anticipated product, *p*-(dimethylamino)phenyl tetra-*O*-acetyl-1-thio-β-D-glucopyranoside (**1**), was formed simultaneously, in low yield. The structure of the product **1** was readily apparent from the data of elemental analysis and n.m.r.



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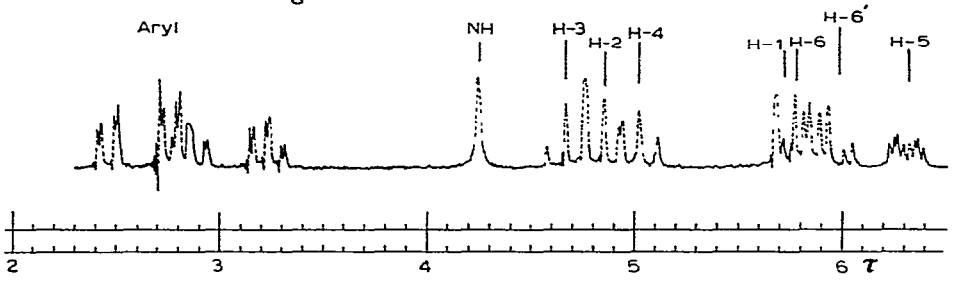
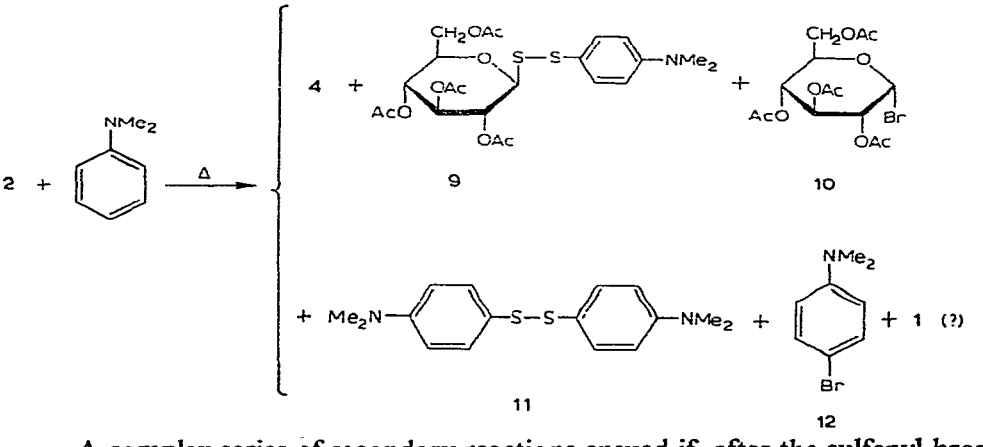


Fig. 2. The low-field portion of the 100-MHz, n.m.r. spectrum of 2-chloro-1-(tetra-*O*-acetyl-β-D-glucopyranosylsulfenamido)benzene (**8**) in chloroform-*d*.

spectroscopy; the spectrum was amenable to first-order analysis of the carbohydrate portion, and the assignments (see Tables I and II) were confirmed by spin decoupling. Chemical confirmation of the structure of **1** was obtained by independent synthesis through coupling of tetra-*O*-acetyl-α-D-glucopyranosyl bromide with *p*-dimethylaminobenzenethiol, as first described by Montgomery, Richtmyer, and Hudson[14]. The procedure was improved by preparing the thiol from *p*-(dimethylamino)phenyl thiocyanate by reduction with lithium aluminum hydride instead of tin and acid.



A complex series of secondary reactions ensued if, after the sulfenyl bromide **2** had been treated with two molar proportions of *N*,*N*-dimethylaniline, the reaction

TABLE I

CHEMICAL-SHIFT DATA FOR 1-THIO-β-D-GLUCOPYRANOSE DERIVATIVES[a]

Compound	*Chemical shifts (τ) and signal multiplicities*[b]								*Aryl protons (integral)*	*Other protons*
	H-1	*H-2*	*H-3*	*H-4*	*H-5*	*H-6a*	*H-6b*	*OAc (integral)*		
1[c]	5.51d	5.13t	4.80t	5.02t	6.34m	5.75q	5.87q	7.89, 7.91, 7.99, 8.01	2.58, 2.67, 2.72, 3.32, 3.40(4)	7.00(6) (NMe_2)
3	4.67—5.38(4)				6.27m	5.83m		7.89, 7.99(6), 8.02	5.41m, 5.63m (H-2')[d] 6.68m (H-1')[d]	7.55—8.65(8) [$(CH_2)]_4$
3a	4.67—5.38(4)				6.27m	5.83m		7.90, 7.97, 7.98, 8.02	5.43d, 5.65d (H-2')[d], 6.69d, 6.72d (H-1')[d]	8.22—8.65(4) [$(CH_2)_2$]
3a[e]	4.65—5.21(4)				5.71—6.16			7.99, 8.03(6), 8.08	5.37d, 5.51d (H-2')[d], 6.64d (H-1')[d]	8.27—8.65(4) [$(CH_2)_2$]
5	4.63—5.00(3) and 5.29—5.50(1)				6.26o	5.81q	5.95q	7.97(6), 7.98, 8.00	2.33—2.47 and 2.61—2.80(5)	
6	4.58—4.99(3) and 5.42—5.58(1)				6.29o	5.70q	5.97q	7.92, 7.95, 7.96, 7.98	2.70(5)	5.97(2) (SCH_2)
7[c]	5.72d	4.85t	4.68t	5.02t	6.31o	5.73q	5.95q	7.86, 7.99(6), 8.08	2.74—3.27(5)	4.76(1) (NH)[f]
8[c]	5.72d	4.86t	4.68t	5.01t	6.31o	5.78q	5.98q	7.84, 7.98(6), 8.08	2.40—2.50, 2.70—2.96, 3.15—3.30(4)	4.24(1) (NH)[f]
9	4.69—4.98(3) and 5.32—5.43(1)				6.26m	5.72q	5.90q	7.92, 7.97, 8.00, 8.04	2.47, 2.56, 2.74, 3.38, 3.47(4)	7.04(6) (NMe_2)

[a]Data taken, unless otherwise stated, from 100-MHz spectra measured in chloroform-*d*. [b]Signals are singlets unless a range or multiplicity (d, doublet; m, multiplet; o, octet; q, quartet; t, triplet) is given. [c]Assignments verified by spin decoupling. [d]Protons on cyclohexyl moiety. [e]In acetone-d_6. [f]Signal disappears after deuteration for 3 days, or after shaking the solution with D_2O and a trace of tributylamine[22] for 1 min.

TABLE II

FIRST-ORDER COUPLING-CONSTANTS FOR 1-THIO-β-D-GLUCOPYRANOSE DERIVATIVES[a]

Compound	*Coupling constants in Hz*[b]						
	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6a}$	$J_{5,6b}$	$J_{6a,6b}$
1	9.5	9.5	8.8	9.3	3	4.5	13
3[c]	*d*	*d*	*d*	*d*	*d*	*d*	*d*
3a[c]	*d*	*d*	*d*	*d*	*d*	*d*	*d*
3a[c,e]	*d*	*d*	*d*	*d*	*d*	*d*	*d*
5	*d*	*d*	*d*	9	4.0	2	12
6	*d*	*d*	*d*	9	4.5	2	12
7	9.4	9.5	9.5	9.6	2.7	4.2	12.2
8	9.3	9.5	9.3	9.6	2.5	4.1	12.2
9	*d*	*d*	*d*	*d*	4.5	2.6	12.3

[a]The data refer to 100-MHz spectra and solutions in chloroform-*d*. [b]H-6a and H-6b are the protons on C-6 of the sugar moiety resonating at lower and higher field, respectively. [c]See Fig. 1 and Discussion for details of coupling of H-1′ and H-2′. [d]Not measured because of second-order effects. [e]In acetone-d_6.

mixture (presumably containing the product **1**; *N,N*-dimethylaniline hydrobromide; probably, the disulfide **4**; and, possibly, other products) was heated for 20 min at a relatively high temperature (105°). Fractionation of the reaction mixture gave, in addition to bis(tetra-*O*-acetyl-β-D-glucopyranosyl) disulfide (**4**), *p*-bromo-*N,N*-dimethylaniline (**12**), bis(*p*-dimethylaminophenyl) disulfide (**11**), tetra-*O*-acetyl-α-D-glucopyranosyl bromide (**10**), and a product closely resembling the adduct **1** in its n.m.r. spectral data, but containing an additional sulfur atom; it was formulated as *p*-(dimethylamino)phenyl tetra-*O*-acetyl-β-D-glucopyranosyl disulfide (**9**). These products probably arise by a series of metathetical reactions between primary reaction products, and free-radical bromination of the amine by **2** is a possible route to **12**. The factors controlling the distribution of these products were not investigated.

Reaction of **2** *with ketones and phenol.* — To determine whether the sulfenyl bromide **2** would react with enolizable ketones by attack of sulfur at the α-position to the carbonyl group, separate experiments were conducted with **2** and acetophenone, acetone, and cyclohexanone, respectively. In each case, the reaction gave bis(tetra-*O*-acetyl-β-D-glucopyranosyl) disulfide (**4**) in high yield. Possibly, free-radical bromination of the ketones provides a more favored reaction-pathway than electrophilic attack by sulfur on the enolic forms of the ketones. The disulfide **4** was also obtained in high yield in the reaction between the sulfenyl bromide **2** and phenol, and no product of attack on the aryl ring by sulfur was detected.

EXPERIMENTAL

General. — The general procedures used in this paper are the same as those given in the preceding paper[1].

Phenyl tetra-O-acetyl-β-D-glucopyranosyl disulfide (**5**). — To a suspension of tetra-*O*-acetyl-β-D-glucopyranosylsulfenyl bromide (**2**) that had been prepared[1] from tetra-*O*-acetyl-1-*S*-acetyl-1-thio-β-D-glucopyranose (2.08 g, 5.1 mmoles) in carbon tetrachloride (60 ml) was added benzenethiol (1 ml, 9.8 mmoles) in carbon tetrachloride (9 ml), and the mixture was kept, with occasional swirling, for 1 h at room temperature. The resultant, clear solution was washed successively with water (100 ml), aqueous sodium hydrogen carbonate (100 ml), and water, dried (magnesium sulfate), and evaporated to give a crystalline residue. Recrystallization from ethanol gave **5** as needles; yield 1.85 g (63%), m.p. 123–124°, $[\alpha]_D^{1.5}$ −241 ±1° (*c* 1.9, chloroform); R_F 0.87; λ_{max}^{KBr} 5.72 (OAc), 6.32, 6.77, 6.96 (aryl), and 9.12 μm (aryl C–S); λ_{max}^{EtOH} 287 (ε 3,300) (shoulder), 274 (3,800), 236 (10,300), and 207 nm (12,300); n.m.r. data, see Tables I and II; X-ray powder diffraction data: 13.91 vw, 10.91 vs (1), 9.46 w, 8.93 w, 6.93 vw, 7.14 vw, 6.37 vw, 5.87 vw, 5.50 s (3,3), 5.26 s (2), 4.98 m, 4.78 s (3,3), 4.43 w, 4.20 m, 3.95 m, 3.72 m, and 3.62 m. The product was homogeneous by t.l.c.

Anal. Calc. for $C_{20}H_{24}O_9S_2$: C, 50.83; H, 5.12; S, 13.57. Found: C, 50.53; H, 5.12; S, 13.40.

The mother liquors contained a major and a minor component, having the chromatographic characteristics of **5** and the disulfide **4**, respectively.

Benzyl tetra-O-acetyl-β-D-glucopyranosyl disulfide (**6**). — The procedure of the foregoing experiment was used, but with α-toluenethiol (1 ml, 8.4 mmoles) instead of benzenethiol. The crude product, obtained as an oil, crystallized spontaneously. Recrystallization from ethanol–petroleum ether gave **6** as white, fluffy needles, yield 1.68 g (68%), m.p. 117–118° (a form having m.p. 94–95° was also encountered[3]), $[\alpha]_D^{21}$ −185 ±1° (*c* 2,3, chloroform); R_F 0.88; λ_{max}^{KBr} 5.72 (OAc), 6.71, and 6.90 μm (aryl); λ_{max}^{EtOH} 271 (ε 2,200), 220 (11,000) (shoulder), and 208 nm (14,000); n.m.r. data, see Tables I and II; X-ray powder diffraction data: 12.66 m, 11.26 m, 10.25 w, 9.28 s (2), 7.34 w, 6.59 vvw, 5.48 vs (1,1), 4.96 vs (1,1), and 4.68 vs (1,1).

Anal. Calc. for $C_{21}H_{26}O_9S_2$: C, 51.84; H, 5.39; S, 13.18. Found: C, 51.99; H, 5.29; S, 13.28.

T.l.c. of the mother liquors revealed a major component having the same mobility as **6**, together with a trace of a product having the chromatographic characteristics of the disulfide **4**.

trans-*2-Bromo-1-(tetra-O-acetyl-β-D-glucopyranosylthio)cyclohexane* (**3**). — A suspension of the sulfenyl bromide **2** (22.27 g, 50.2 mmoles, prepared[1] from 20.00 g of tetra-*O*-acetyl-1-*S*-acetyl-1-thio-β-D-glucopyranose) in carbon tetrachloride (200 ml) was shaken for 1 h at room temperature with a solution of cyclohexene (5.1 ml, 50.3 mmoles) in carbon tetrachloride (10 ml). The resulting, clear solution was washed successively with water (100 ml), saturated aqueous sodium hydrogen carbonate (100 ml), and water, dried (magnesium sulfate), and evaporated to a syrup. The syrup was dissolved in the minimal volume of ether, and petroleum ether was added to incipient turbidity. The product **3** had a tendency to separate as an oil, but, by careful manipulation, it could be obtained as colorless, stout needles; yield (in 5 crops) 15.0 g (57%, raised to 66% by chromatographic isolation of further **3** from the mother

liquors), m.p. 86–87° (87–88° after one recrystallization), $[\alpha]_D^{22}$ −22.0 ±1.0° (*c* 2.8, chloroform); R_F 0.88 (chromatographically homogeneous); λ_{max}^{KBr} (Perkin–Elmer Model 337 spectrometer) 5.70, 5.76 (OAc), 11.17 (axial H at C-1), 13.58, and 13.84 μm (equatorial[15] C–Br); λ_{max}^{EtOH} 274 (ε 70) (shoulder), 242 (290) (shoulder), 224 (1025) (shoulder), and 207 nm (1300); n.m.r. data, see Tables I and II; X-ray powder diffraction data: 10.19 m, 7.01 m, 6.22 m, 5.29 vs (1), 5.00 s (3), 4.72 vw, 4.45 vw, 4.22 s (2,2), 4.05 vw, 3.90 w, 3.75 vw, 3.56 vw, 3.44 s (2,2), 3.24 w, 3.10 w, 3.01 vw, and 2.86 w.

Anal. Calc. for $C_{20}H_{29}BrO_9S$: C, 45.72; H, 5.56; Br, 15.21; S, 6.10. Found: C, 45.88; H, 5.26; Br, 14.99; S, 6.36.

The mother liquors were combined and evaporated. T.l.c. of the residue indicated the presence of two components, having the characteristics of **3** and the disulfide **4**. Column-chromatographic fractionation gave **3** as the faster-moving component, obtained crystalline from ether–petroleum ether, yield 2.018 g (9%), m.p. 82–85°. The slower-moving component was crystallized from ether–petroleum ether to give bis(tetra-*O*-acetyl-β-D-glucopyranosyl) disulfide (**4**); yield 303 mg (1.7%), m.p. (after one recrystallization) 139–140°, identical with an authentic sample by mixed m.p., elemental analysis, and comparative i.r. spectra.

When the experiment was conducted on a 2-gram scale, the yield of **3** isolated by direct crystallization was 73%.

trans-*2-Bromo-1-(tetra*-O-*acetyl-β*-D-*glucopyranosylthio)cyclohexane*-3,3,6,6-d_4 (**3a**). — This compound was prepared by the route used for **3**, but with 489 mg of the sulfenyl bromide **2** and 96 mg of cyclohexene-*3,3,6,6-d_4* (Ref. 16), and the deuterated derivative **3a** was obtained, m.p. and mixed m.p. with **3**, 85–86°; n.m.r. data: see Tables I and II and Fig. 1.

Tetra-O-*acetyl-β*-D-*glucopyranosylsulfenamidobenzene* (**7**). — To a suspension of the sulfenyl bromide (3.24 g, 7.3 mmoles) in carbon tetrachloride (40 ml) was added aniline (1.4 ml, 15.4 mmoles), and the mixture was kept for 1 h at room temperature. Water (100 ml) was added to the cloudy, yellow, reaction mixture, and the mixture was shaken. The organic layer was separated, and treated by the procedure used in the preparation of compound **5**. The resultant syrup was dissolved in ether (50 ml), and the solution was decolorized with carbon, and concentrated, and petroleum ether was added to opalescence. Refrigeration of the solution gave **7** as colorless, fine needles; yield 2.76 g (83%), m.p. (after one recrystallization) 116–117°, $[\alpha]_D^{21}$ −330 ±2° (*c* 2.4, chloroform); R_F 0.85 (homogeneous); λ_{max}^{KBr} 5.72 (OAc), 6.23, and 6.70 μm (aryl); λ_{max}^{EtOH} 288 (ε 2,000) (shoulder), 244 (10,300), and 206 nm (13,900); n.m.r. data, see Tables I and II; X-ray powder diffraction data: 12.53 vvw, 10.13 vs (1), 7.16 w, 6.40 w, 5.69 w, 5.31 s (2), 5.14 m, 4.49 m, 4.27 m, 3.96 w, 3.67 m, and 3.52 m.

Anal. Calc. for $C_{20}H_{25}NO_9S$: C, 52.73; H, 5.53; N, 3.08; S, 7.04. Found: C, 52.78; H, 5.45; N, 3.28; S, 6.85.

T.l.c. of the mother liquors indicated the presence of **7** and of a minor component having the mobility of the disulfide **4**.

2-Chloro-1-(tetra-O-*acetyl-β*-D-*glucopyranosylsulfenamido)benzene* (**8**). — To a

suspension of **2** (5.11 g, 11.5 mmoles) in carbon tetrachloride (70 ml) was added *o*-chloroaniline (3 ml, 28.4 mmoles) in carbon tetrachloride (7 ml). A white solid separated at once. After 1 h at room temperature, the suspension was filtered to remove the insoluble amine salt, and the filtrate was treated by the procedure used for compound **5**. The resultant syrup was kept for 12 h at 30° under vacuum to remove traces of solvent, and was then dissolved in anhydrous ether (10 ml). Petroleum ether was added to opalescence, a crystal nucleus was added, and the solution was refrigerated for 18 h to give **8** as colorless needles; yield 2.36 g (42%), m.p. (after one recrystallization) 84–85°, $[\alpha]_D^{21}$ −311 ±2° (*c* 3.9, chloroform); R_F 0.87; λ_{max}^{KBr} 5.72 (OAc), 6.25, 6.80 (aryl), and 7.34 μm (secondary arylamine); λ_{max}^{EtOH} 295 (ε 5,000) (shoulder), 276 (8,000) (shoulder), 244 (14,000), and 210 nm (25,000); n.m.r. data, see Fig. 2 and Tables I and II; X-ray powder diffraction data: 12.58 w, 9.99 m, 8.15 m, 6.63 m, 6.28 m, 5.91 w, 5.51 vw, 5.28 w, 5.00 vw, 4.77 vs (1,1), 4.29 vs (1,1), 4.01 s (2), 3.70 m, 3.35 w, and 3.16 m.

Anal. Calc. for $C_{20}H_{24}ClNO_9S$: C, 49.03; H, 4.94; Cl, 7.24; N, 2.86; S, 6.55. Found: C, 48.91; H, 4.94; Cl, 7.34; N, 3.10, S, 6.66.

T.l.c. of the mother liquors revealed a major component corresponding to **8**, and a trace of a product chromatographically indistinguishable from the disulfide **4**.

p-(*Dimethylamino*)*phenyl tetra*-O-*acetyl-1-thio-β*-D-*glucopyranoside* (**1**). — *A. From sulfenyl bromide* **2** *and* N,N-*dimethylaniline.* To a suspension of the sulfenyl bromide **2** (2.972 g, 6.7 mmoles) in carbon tetrachloride (50 ml) was added *N,N*-dimethylaniline (2 ml, 15.8 mmoles); the mixture turned green. After 1 h at room temperature, the mixture was evaporated (bath temperature <43°), and the resultant syrup was dissolved in dichloromethane (100 ml). The solution was treated by the procedure used in the preparation of compound **5**. The resultant, green syrup was dissolved in ether, and petroleum ether was added to opalescence. Several crops of crystals were collected; the first three (total yield 1.522 g, 62%, m.p. 126–127°) were recrystallized to give pure bis(tetra-*O*-acetyl-β-D-glucopyranosyl) disulfide **4** (1.348 g), m.p. 141–142°, indistinguishable from an authentic sample[1] by t.l.c., i.r. spectra, and X-ray powder diffraction pattern. The fourth and fifth crystal fractions, yield 206 mg, were shown by t.l.c. to contain **4** as a minor component, together with a principal component (**1**) having R_F 0.81. Recrystallization (twice) from ethanol gave **1** as colorless needles, m.p. 150°, $[\alpha]_D^{20}$ −54.7 ±2° (*c* 0.9, chloroform) (lit.[14] m.p. 150–151°, $[\alpha]_D^{20}$ −47° in chloroform); R_F 0.81; λ_{max}^{KBr} 5.72 (OAc), 6.23 and 6.68 μm (aryl); λ_{max}^{EtOH} 276 (ε 12,500) and 208 nm (16,900); n.m.r. data, see Tables I and II; X-ray powder diffraction data: 15.63 vw, 12.71 vw, 10.58 vs (1,1), 8.48 vs (1,1), 6.96 m, 5.60 m, 5.27 m, 5.00 m, 4.74 w, 4.51 w, 4.39 s (2,2), 4.23 s (2,2), and 4.04 w.

Anal. Calc. for $C_{22}H_{29}NO_9S$: C, 54.64; H, 6.05; N, 2.90; S, 6.63. Found: C, 54.87; H, 6.11; N, 3.21; S, 6.96.

B. From tetra-O-*acetyl-α*-D-*glucopyranosyl bromide and* p-*dimethylaminobenzenethiol.* The procedure of Montgomery, Richtmyer, and Hudson[14] was modified. *p*-Dimethylaminophenyl thiocyanate[17] (18 g, 101 mmoles) in dry ether (200 ml) was added with stirring to a suspension of lithium aluminium hydride (4.0 g, 105 mmoles)

in dry ether (200 ml) that was maintained at 0°, and stirring was continued for 45 min. The mixture was processed by the general procedure[18] used for the reduction of nitriles with lithium aluminum hydride. The resultant, ethereal solution was decanted from the gray-white residue, and evaporated to give *p*-dimethylaminobenzenethiol (9.0 g, 59 mmoles). The latter was not further purified, because of the ease with which it undergoes oxidative dimerization, and it was condensed immediately with tetra-*O*-acetyl-α-D-glucopyranosyl bromide (20 g 48.6 mmoles) by the general method of Purves[19]. Evaporation of the yellow, turbid reaction-mixture gave a yellow syrup, which was partitioned between dichloromethane (100 ml) and water (100 ml). The turbid mixture was filtered, and the organic phase was separated, dried (magnesium sulfate), and evaporated to give a yellow syrup. Crystallization of the syrup from ether–petroleum ether gave **1**; yield 5.2 g (22%), m.p. (after recrystallization) 149–150°, identical by mixed m.p., i.r. spectrum, and X-ray powder diffraction pattern with **1** prepared by method *A*.

Reaction of sulfenyl bromide **2** *with* N,N-*dimethylaniline to give* p-(*dimethylamino*)*phenyl tetra*-O-*acetyl-β*-D-*glucopyranosyl disulfide* (**9**). — To a suspension of **2** (3.086 g, 7.0 mmoles) in carbon tetrachloride (50 ml) was added *N,N*-dimethylaniline (2 ml, 15.8 mmoles), and the mixture was kept for 0.5 h at 30°. The resultant solution was evaporated to a syrup at ~90°, the syrup was dissolved in dichloromethane (100 ml), and the solution was processed as described for compound **5**. The syrup obtained showed major components having R_F 0.88 and 0.51 (t.l.c.). The mixture was subjected to column chromatography. The first fractions eluted from the column were evaporated to a syrup that was distilled at 180° (bath)/0.15 torr to give *p*-bromo-*N,N*-dimethylaniline (**12**); yield 0.168 g, m.p. 52–54° (lit.[20] m.p. 54.7°), R_F 0.99 (detected very slowly by sulfuric acid).

Anal. Calc. for $C_8H_{10}BrN$: C, 48.02; H, 4.89; Br, 39.82; N, 7.00. Found: C, 47.85; H, 4.89; Br, 39.94; N, 7.09.

The product was identical with an authentic sample of **12** by mixed m.p. and by i.r. and n.m.r. spectra.

Continued elution of the column gave a chromatographically homogeneous component, R_F 0.88, that crystallized from ethanol to give the disulfide **9** as pale-yellow needles; yield 307 mg (8.5%), m.p. (after one recrystallization) 156–157°, $[\alpha]_D^{22}$ −324 ±3° (*c* 1.6, chloroform); R_F 0.9; λ_{max}^{KBr} 5.72 (OAc), 6.25, and 6.65 μm (aryl); λ_{max}^{EtOH} 311 (ε 11,500), 268 (8,800), and 208 nm (12,700); n.m.r. data, see Tables I and II; X-ray powder diffraction data: 16.50 vvw, 15.22 vvw, 10.84 vs (1), 8.48 s (3,3) 7.76 w, 6.76 vvw, 6.05 w, 5.74 vvw, 5.40 m, 5.09 m, 4.80 s (2), 4.41 w, 4.22 w, 4.06 s, (3,3), 3.78 s (3,3), and 3.68 m.

Anal. Calc. for $C_{22}H_{29}NO_9S_2$: C, 51.25; H, 5.67; N, 2.72; S, 12.44. Found: C, 51.06; H, 5.78; N, 2.97; S, 12.13.

Continued elution of the column gave, first, a mixture of components having R_F 0.88 and 0.50, and then the component having R_F 0.50, alone; from the latter fractions, the crystalline disulfide **4** was obtained, yield 1.11 g (44%), m.p. (after

recrystallization from ethanol) 141–142°, identical with authentic **4** by mixed m.p., i.r. and n.m.r. spectra, and X-ray powder diffraction pattern.

A second experiment was performed under similar conditions, except that 5.0 g (11.3 mmoles) of **2** and 5 ml (39.4 mmoles) of *N,N*-dimethylaniline was used, and the initial syrupy product was heated for ~20 min at 105°/0.2 torr. Column-chromatographic fractionation of the product gave, in the early fractions, bis(*p*-dimethylaminophenyl) disulfide (**11**), isolated crystalline from ether; yield 566 mg, m.p. 117.5–118.5° (lit.[21] m.p. 118°).

Anal. Calc. for $C_{16}H_{20}N_2S_2$: C, 63.11; H, 6.62; N, 9.20; S, 21.06. Found: C, 63.18; H, 6.56; N, 9.20; S, 20.98.

Further elution of the column gave fractions that contained tetra-*O*-acetyl-α-D-glucopyranosyl bromide (**10**), yield 2.155 g (46%), identical with an authentic sample by i.r. and n.m.r. spectra.

The next compound to be eluted from the column was the disulfide **9**, yield 324 mg (6%), identical with the product obtained in the preparation already described. Subsequent fractions yielded the disulfide **4**, yield 446 mg (5%), m.p. 141–142°.

In a third experiment, the reaction between **2** (1.17 g) and 2 equivalents of *N,N*-dimethylaniline was allowed to proceed for 60 h at 30°, and the product was isolated without heating it above 40°. Fractionation gave the monosulfide **1** (188 mg, 15%), and the disulfide **4** (579 mg, 60%).

Reaction of sulfenyl bromide **2** *with* (*a*) *acetophenone*, (*b*) *acetone*, (*c*) *cyclohexanone, and* (*d*) *phenol.* — Suspensions of the sulfenyl bromide **2** in carbon tetrachloride were treated, in separate experiments, with the following ketones or enols, in the molar proportions indicated (relative to 0.1 mole of **2**): acetophenone (1.0 mole) acetone (4.4 moles), cyclohexanone (1.0 mole), and phenol (1.1 moles). The reaction mixtures were kept for 1–3 h at room temperature, and then processed by the general procedures used for isolating coupling products formed from **2**. In each of the four experiments, the principal product, isolated crystalline in 70%, 63%, 76%, and 75% yield, respectively, was bis(tetra-*O*-acetyl-β-D-glucopyranosyl) disulfide (**4**), m.p. 142–143°, identical with an authentic sample by mixed m.p., i.r. spectrum, and X-ray powder diffraction data.

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