Carbohydrate Research, 128 (1984) 11–20
Elsevier Science Publishers B.V., Amsterdam – Printed in The Netherlands

REMOVAL OF SUGAR DITHIOACETAL GROUP WITH *N*-BROMOSUCCINIMIDE

MOMČILO MILJKOVIĆ, DANIEL DROPKIN, PETER HAGEL, AND MARGARET HABASH-MARINO
Department of Biological Chemistry, The Milton S. Hershey Medical Center, The Pennsylvania State University, Hershey, Pennsylvania 17033 (U.S.A.)

(Received May 11th, 1983; accepted for publication, July 10th, 1983)

ABSTRACT

Oxidative removal of the dithioacetal group of several protected sugar and 2-acylamido-2-deoxy sugar dialkyl dithioacetals with *N*-bromosuccinimide in 97% aqueous acetone or 1:1 (v/v) 2-methyl-2-propanol–acetone was compared with removal with mercury dichloride–mercury(II) oxide or mercury dichloride–cadmium carbonate. In general, removal with *N*-bromosuccinimide proceeded more rapidly, and, with one exception, yields were higher than or equal to those obtained with the method using mercury salt.

INTRODUCTION

In his classic paper on the conversion of various aldoses into their diethyl dithioacetals, Fischer[1] noted that the parent sugar can be regenerated from its dithioacetal derivative by the action of, *inter alia*, mercury(II) chloride. Thus, he pioneered today's most often used route for the synthesis of substituted aldehydo sugars. Since its first application[2], this approach has been modified and improved. Thus, it was found that neutralization of the hydrochloric acid formed during the removal of the thioacetal group with cadmium carbonate[3] or yellow mercuric oxide[4], results in a higher yield. The suggestion[5] that cadmium carbonate also serves as a promoter of dethioacetalation was disputed by Corey and Erickson[6] who successfully used calcium carbonate as a substitute for cadmium carbonate.

The conversion of the diethyl dithioacetal of 2-acylamido-2-deoxy sugars into the corresponding *aldehydo*-2-amino-2-deoxy sugars by mercury(II) chloride and cadmium carbonate or yellow mercuric oxide was controversial at the time we undertook this investigation. Kent[7] and Whitehouse *et al.*[8] reported the preparation of 2-acetamido-3,4,5,6-tetra-*O*-acetyl-2-deoxy-*aldehydo*-D-glucose by treating the corresponding diethyl dithioacetal with mercuric chloride and cadmium carbonate in 30% aqueous acetone. Harmon *et al.*[9] demonstrated, however, that this procedure led to the formation of the unsaturated 2-acetamido-4,5,6-tri-*O*-acetyl-2,3-dideoxy-*aldehydo*-D-*erythro*-hex-2-enose (**1**) by way of the intermediate oxazoline **2**. Repetition of Whitehouse *et al.*[8] procedure in our laboratory confirmed the findings of Harmon *et al.*[9].

0008-6215/84/$ 03.00

TABLE I

REACTION CONDITIONS FOR REMOVAL OF THIOACETAL GROUP OF COMPOUNDS **4**, **7**, **10**, **12**, **14**, **17**, **19**, **22**, **24**, AND **28**

Compound	*Reagent*[a]	*Solvent*[b]	*Reaction*		*Compound formed*		*Chromatography*	
			Temp.[c]	*Time*	*Struct.*	*Yield(%)*[d]	*Ratio of silica gel to substance*[e]	*Eluent*
4	NBS	B	0°	3 min	**5**	33	50:1	19:1 benzene–methanol
	$HgCl_2$–HgO	A	R.t.	12 h	**5**	59	50:1	19:1 benzene–methanol
7	$HgCl_2$–$CdCO_3$	A	R.t.	8 h	**8**	52	40:1	19:1 benzene–methanol
10	NBS–$CdCO_3$	B	0°	3 min	**11**	85		19:1 benzene–methanol
	$HgCl_2$–HgO	A	R.t	24 h	**11**			
12	NBS	A	0°	3 min	**13**	49	40:1	19:1 benzene–methanol
	$HgCl_2$–HgO	A	R.t.	12 h	**13**	39	40:1	19:1 benzene–methanol
14	$HgCl_2$–$CdCO_3$	A	R t.	14 h	**15**	79		
17	NBS–$CdCO_3$	A	0°	3 min	**18**	77		
	$HgCl_2$–$CdCO_3$	A	R.t.	48 h	**18**	79		3:1 hexane–acetone
19	NBS	A	0°	5 min	**20**	90	25:1	
22	NBS	A	0°	3 min	**23**	71		
24	$HgCl_2$–HgO	A	R.t.	14 h	**25**	81		
28	NBS	A	0°	7 min	**29**	82	45:1	8:1 hexane–acetone
	$HgCl_2$–HgO	A	0°	30 min	**29**	82	80:1	15:1 benzene–ethyl acetate

[a]NBS, *N*-bromosuccinimide. [b](A): 97% aqueous acetone, (B) 1:1 acetone–2-methyl-2-propanol. [c]R.t., room temperature. [d]After chromatography on silica gel. [e]All silica gel used for chromatography was impregnated with 25% (w/w) of water.

On the basis of earlier findings[1,10–12] that dithioacetals undergo oxidative hydrolysis on treatment with bromine and that carbon–sulfur bond cleavage prepondérates in the reaction of alkyl sulfides with excess *N*-bromo- or *N*-chloro-succinimide in anhydrous methanol[13] or in water[14], Corey and Erickson[6] developed a method for the oxidative hydrolysis of 1,3-dithiane derivatives by *N*-halosuccinimides to give the corresponding carbonyl compounds.

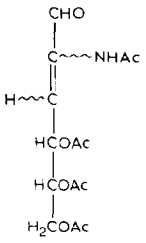
The difficulties that we encountered in our early attempts* to prepare various protected *aldehydo*-2-acylamido-2-deoxyhexoses from corresponding dialkyl dithioacetals by use of mercuric chloride–cadmium carbonate, and the highly successful oxidative dethioacetalation of 1,3-dithians with *N*-halosuccinimides[6] prompted us to investigate the use of *N*-bromosuccinimide for the removal of thioacetal groups of properly protected 2-acylamido-2-deoxy sugar dialkyl dithioacetals, and appropriately protected sugar dialkyl dithioacetals. The results of these studies are reported herein.

RESULTS AND DISCUSSION

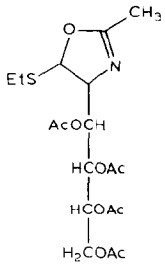
N-Bromosuccinimide used in slight excess over the calculated amount (3 and 2.5 mol per mol of aminodeoxy sugar and sugar dialkyl dithioacetal, respectively) in 97% aqueous acetone at 0° promoted a rapid (3 min) removal of the thioacetal groups of **17**, **19**, **22**, and **28** to give the corresponding *aldehydo*-sugars **18**, **20**, **23**, and **29** in yields ranging from 71 to 90% (Table I). Thus, the dethioacetalation of **17** by *N*-bromosuccinimide should be preferred to that by mercuric chloride–cadmium carbonate as it was completed within only 3 min, whereas latter reagent required 48 h. Both reactions gave the corresponding *aldehydo*-sugar **18** in practically the same yield (77 and 79%, see Table I).

The oxidative dethioacetalation of dialkyl dithioacetals with *N*-bromosuccinimide is influenced by the solvent used as the reaction medium. Thus, in 1:1 (v/v) 2-methyl-2-propanol–acetone, the dithioacetal **4** was converted into the corresponding aminodeoxy-*aldehydo*-sugar **5** within 3 min at 0°. Although some decomposition of **5** was noticed during the processing, this reaction medium proved to be superior to 97% aqueous acetone. In the latter solvent, the homogenous aminodeoxy-*aldehydo*-sugar **5** was obtained in only 33% yield after chromatog-

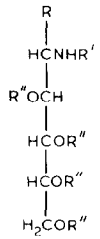
*In the repetition of Whitehouse *et al.*[8] procedure to dethioacetalate 2-acetamido-3,4,5,6-tetra-*O*-acetyl-2-deoxy-D-glucose diethyl dithioacetal with mercuric chloride–mercuric oxide in 97% aqueous acetone at room temperature, the reaction progress was monitored by t.l.c. (in 9:1, v/v, benzene–methanol). It was found that, after 12 h, the starting diethyl dithioacetal **4** had completely disappeared and 2-acetamido-3,4,5,6-tetra-*O*-acetyl-2-deoxy-*aldehydo*-D-glucose (**5**) was formed as the sole product. If, however, the reaction proceeded beyond 12 h, formation of the unsaturated *aldehydo*-D-glucose derivative **1** was noticed. The concentration of this unsaturated sugar steadily increased with time, until it became the only reaction product (89% after chromatography on silica gel in 19:1 benzene–methanol). At about the same time, Benzing and Perry[15] reported the successful dethioacetalation of 2-acetamido-2-deoxy-3,4:5,6-di-*O*-isopropylidene-D-glucose diethyl dithioacetal with mercuric chloride–mercuric oxide in 95% aqueous acetone. They obtained, in a 57% yield, a product that gave a single spot on t.l.c. in 9:1 benzene–methanol.



1



2

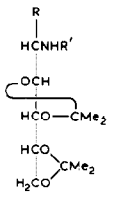


3 R = $(EtS)_2CH$, R' = Ac, R'' = H
4 R = $(EtS)_2CH$, R' = R'' = Ac
5 R = CHO, R' = R'' = Ac
6 R = $(EtS)_2CH$, R' = Ts, R'' = H
7 R = $(EtS)_2CH$, R' = Ts; R'' = Ac
8 R = CHO, R' = Ts, R'' = Ac
9 R = $(iPrS)_2CH$, R' = Ts, R'' = H
10 R = $(iPrS)_2CH$, R' = Ts, R'' = Ac
11 R = CHO, R' = Ts, R'' = Ac

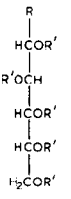
raphic purification. It is interesting that the dethioacetalation of **4** is slower when both 2-methyl-2-propanol and acetone are anhydrous, which suggests that the presence of water in the reaction mixture is important. Another example for the influence of the reaction medium was given by the diisopropyl dithioacetal **10**. When it was treated with 3 equiv. of *N*-bromosuccinimide in 97% aqueous acetone, a mixture of products was obtained, whereas treatment in 1:1 (v/v) 2-methyl-2-propanol–acetone gave the corresponding aminodeoxy-*aldehydo*-sugar **11** in 85% yield (after chromatography on silica gel) as a homogenous syrup. It is interesting that the diisopropyl dithioacetal **10** did not react with an excess of mercuric chloride–mercuric oxide in aqueous acetone over a 24-h period at room temperature. This large difference in the reactivity of diisopropyl dithioacetals toward both reagents suggests that 2-propanethiol may be a valuable reagent for carbonyl group protection in molecules containing more than one carbonyl group.

After completion of the reaction, the excess of *N*-bromosuccinimide is usually destroyed by adding 1:1 (w/w) sodium thiosulfate–sodium hydrogencarbonate and stirring the suspension for a short time at room temperature. However, this method cannot be used for destroying excess *N*-bromosuccinimide after dethioacetalation of 2-acetamido-2-deoxy sugar dialkyl dithioacetals, since the 2-acylamido-2-deoxy-*aldehydo*-sugars are exceptionally labile and undergo β-elimination in even weakly basic solutions. Therefore, in such cases, the best way to destroy the residual *N*-bromosuccinimide in the reaction mixture is by adding 1:1:2 (w/w) $Na_2S_2O_3$–NaH_2PO_4–Na_2HPO_4 and stirring the suspension for a short time at room temperature.

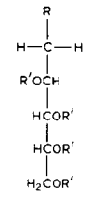
Contrary to published data[16], the quantitative removal of *N*-bromosuccinimide from the reaction mixture by extraction of chloroform or ether solutions



12 R = $(EtS)_2CH$, R′ = Ac
13 R = CHO; R′ = Ac
14 R = $(EtS)_2CH$, R′ = Ts
15 R = CHO, R′ = Ts

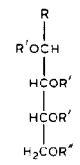


16 R = $(EtS)_2CH$, R′ = H
17 R = $(EtS)_2CH$; R′ = Ac
18 R = CHO, R′ = Ac
19 R = $(EtS)_2CH$; R′ = Me
20 R = CHO; R′ = Me



21 R = $(EtS)_2CH$, R′ = H
22 R = $(EtS)_2CH$, R′ = Ac
23 R = CHO, R′ = Ac
24 R = $(EtS)_2CH$, R′ = Me
25 R = CHO, R = Me

iPr = isopropyl



26 R = $(EtS)_2CH$, R′ = R″ = H
27 R = $(EtS)_2CH$, R′ = H, R″ = Tr
28 R = $(EtS)_2CH$, R′ = Me, R″ = Tr
29 R = CHO, R′ = Me, R″ = Tr

of *aldehydo*-sugar or aminodeoxy-*aldehydo*-sugar derivatives with water was found to be generally unsuccessful. The aldehydic forms of sugars and aminodeoxy sugars are considerably hydrated in the presence of water and, thus, much more soluble in water as hydrates. Consequently, water extraction resulted in a significant loss of product. The best way to quantitatively remove the *N*-bromosuccinimide was found to be by chromatography on silica gel*. It was found that nonpolar *aldehydo*-sugars, such as **20** and **25**, will survive rapid column-chromatography if the eluent contains an alcohol. The role of the alcohol in stabilizing *aldehydo*-sugars has not been determined at the present, but we believe it likely that it adds to the carbonyl carbon of the sugar aldehyde with formation of a hemiacetal; thus, H-2 becomes much less acidic because of the absence of CO-1, and the product can survive these chromatographic conditions.

More labile *aldehydo*-sugars, particularly aminodeoxy-*aldehydo*-sugars could not be chromatographed on fully active silica gel. However, they could be purified on silica gel deactivated with water. Studies with the peracetylated 2-acetamido-2-deoxy-*aldehydo*-sugar **4** showed that a water content of up to 17% (w/w) did not protect the sugar from significant β-elimination, whereas product separation was poor if the silica gel was deactivated with 29% (w/w) of water. The optimal results were obtained with a silica gel containing 25% (w/w) of water. Owing to difficult slurry formation, column packing with silica gel containing 25% of water was somewhat tricky. As expected, a noticeable loss of resolution was observed, as compared to fully active silica gel, and separations on wet silica gel could not be clearly anticipated from the chromatographic behavior of crude, dethioacetalation-reaction mixtures on t.l.c. plates. Differences, however, tended to be minor. An additional stabilization of the *aldehydo*-aminodeoxy sugars was observed when the eluent contained an alcohol (methanol or ethanol).

With the exception of the dethioacetalation of dithioacetal **4** where the mercuric chloride–mercuric oxide procedure afforded the aminodeoxy-*aldehydo*-sugar

*Albrecht *et al.*[17] recommended *aldehydo*-sugar not to be purified by chromatography on silica gel owing to difficulties in eluting intact materials from the column, an observation generally confirmed in our laboratory.

5 in considerably higher yield as compared to *N*-bromosuccinimide procedure, the dethioacetalation of dithioacetals **10, 12, 17,** and **28** with *N*-bromosuccinimide gave either the same or better yield of the corresponding *aldehydo*-sugars than use of mercuric salts, but the total inertness of the diisopropyl dithioacetal **10** toward mercuric chloride–cadmium carbonate had not been expected. The much greater lability of the aldehyde forms of 2-acetamido-2-deoxy sugars, as compared to those of 2-hydroxylated sugars or their 2-deoxy analogs, is of interest. We believe that the exceptional tendency of the first-mentioned compounds to undergo β-elimination lies in the partial, double-bond character of the C–N amide bond, which increases the acidity of H-2. This is supported by the observation that 2-deoxy-2-*p*-toluenesulfonamido-*aldehydo*-sugars are not as labile as the 2-carboxamido-2-deoxy-*aldehydo*-sugars, and that they do not readily undergo β-elimination during chromatography on silica gel or in weakly alkaline solution (sodium hydrogen-carbonate).

The greatest advantage of dethioacetalation with *N*-bromosuccinimide as compared to mercuric salts lies in the very short time required at 0°.

EXPERIMENTAL

General methods. — Melting points are uncorrected. Optical rotations were determined with a Cary 60 spectropolarimeter for solutions in a 1.0-cm cell. Infrared spectra were recorded with a Perkin–Elmer infrared spectrophotometer Model 267, and n.m.r. spectra for solutions in (^{2}H) chloroform with Bruker WM-360 and Varian T-60 spectrometers with tetramethylsilane as the internal standard. Silica gel (<0.08 mm) used for all column chromatography was obtained from E. Merck (Darmstadt, W. Germany). All solvent mixtures are v/v. 2-Acetamido-2-deoxy-3,4:5,6-di-*O*-isopropylidene-D-glucose diethyl dithioacetal (**12**) was prepared according to the procedure of Yoshimura and Sato[18], 2,3,4,5,6-penta-*O*-acetyl-D-glucose dithioacetal (**17**) according to the procedure of Schneider *et al.*[19], 2,3,4,5,6-penta-*O*-methyl-D-glucose diethyl dithioacetal (**19**) according to the procedure of Levene and Meyer[2], and 2-deoxy-D-*arabino*-hexose diethyl dithioacetal (**21**) and 3,4,5,6-tetra-O-*acetyl-2-deoxy-D-arabino*-hexose diethyl dithioacetal (**22**) according to the procedure of Bolliger[20].

2-Acetamido-3,4,5,6-tetra-O-*acetyl-2-deoxy*-D-*glucose diethyl dithioacetal* (**4**)*. — This compound was prepared by acetylation of 2-acetamido-2-deoxy-D-glucose diethyl dithioacetal (**3**) with acetic anhydride–pyridine for 2 days at room temperature. The isolated crude product was purified by chromatography on silica

*In their first paper, Wolfrom *et al.*[21] reported m.p. 126–127° and $[\alpha]_D^{22}$ −32° (chloroform) for **4**. Kent[7] reported for **4** m.p. 160–161° and $[\alpha]_D^{23}$ +2° (chloroform); this was disputed by Wolfrom and Anno[22] who reported as corrected values for **4** m.p. 75–77° and $[\alpha]_D$ +1°. These findings, however, were disputed by Whitehouse *et al.*[8] who reported for **4** m.p. 177° and $[\alpha]_D^{20}$ −30.6° (*c* 0.5, chloroform). Our m.p. determination is in agreement with Wolfrom and assoc. values, m.p. 76–77°.

gel (using a 10:1 silica gel-to-substrate ratio). Elution with 49:1 benzene–methanol gave **4** as a white, crystalline material, m.p. 76–77°.

*3,4,5,6-Tetra-*O*-acetyl-2-deoxy-2-*p*-toluenesulfonamido-*D*-glucose diethyl dithioacetal* (**7**). — 2-Deoxy-2-*p*-toluenesulfonamido-D-glucopyranose[23] (2.5 g, 7.5 mmol) was suspended in freshly distilled anhydrous ethanethiol (25 mL). Freshly fused anhydrous zinc chloride (8.0 g) was added, and the mixture kept for 36 h at room temperature. It was then poured into saturated, aqueous sodium hydrogencarbonate solution, and both the precipitate and filtrate were exhaustively washed with hexane in order to remove the excess of ethanethiol. The precipitate and the aqueous filtrate were extracted with chloroform, and the combined chloroform extract was dried ($MgSO_4$), and evaporated *in vacuo*, to yield a white crystalline product (**6**, 2.5 g, 75%; ref. 18).

Crude **6** (2.00 g, 4.56 mmol) was dried in high vacuum and acetylated (without further purification and characterization) with 2:1 (v/v) anhydrous pyridine–acetic anhydride (15 mL). The solution was kept overnight at room temperature, an excess of methanol added, and the mixture kept for additional 30 min at room temperature and then evaporated *in vacuo*. The partially solid residue was chromatographed on silica gel (40 g). Elution with 24:1 benzene–methanol afforded one major product (2.41 g, 87%) as a colorless syrup which crystallized after 2 weeks, m.p. 78–79°. An analytical sample was prepared by recrystallization from ether–hexane, m.p. 80.5–81°; $[\alpha]_D^{27}$ −5.0° (*c* 1.12, chloroform); ^{1}H-n.m.r.: δ 7.82–7.28 (m, 4 H, arom.), 5.61 (dd, 1 H, $J_{3,4}$ 4.27 Hz, H-3), 5.35 (dd, 1 H, $J_{4,5}$ 7.02 Hz, H-4), 5.15 (ddd, 1 H, $J_{5,6a}$ 2.75, $J_{5,6b}$ 5.49 Hz, H-5), 5.08 (d, 1 H, NH), 4.29 (dd, 1 H, $J_{6a,6b}$ 12.51 Hz, H-6a), 4.12 (dd, 1 H, H-6b),4.00 (ddd, 1 H, $J_{2,3}$ 5.49, $J_{2,NH}$ 9.77 Hz, H-2), 3.81 (d, 1 H, $J_{1,2}$ 3.66 Hz, H-1), 2.70–2.54 (m, 2 H, CH_2CH_3), 2.48–2.43 (m, 2 H, CH_2CH_3), 2.41 (s, 3 H, SO_2 $C_6H_4CH_3$), 2.15, 2.06, 2.05, 2.02 (4 s, 12 H, 4 $COCH_3$), 1.25 and 1.12 (2 t, 6 H, 2 CH_2CH_3).

Anal. Calc. for $C_{25}H_{37}NO_{10}S_3$: C, 49.41; H, 6.14. Found: C, 49.64; H, 6.12.

*3,4,5,6-Tetra-*O*-acetyl-2-deoxy-2-*p*-toluenesulfonamido-*D*-glucose diisopropyl dithioacetal* (**10**). — 2-Deoxy-2-*p*-toluenesulfonamido-D-glucopyranose[23] (3.00 g, 9.0 mmol) was dissolved in freshly distilled 2-propanethiol (50 mL), and freshly fused zinc chloride (10 g) added to the solution. After being kept for 36 h at room temperature, the mixture was poured into saturated aqueous sodium hydrogencarbonate, and the precipitate filtered off. Both the precipitate and the aqueous filtrate were exhaustively extracted with hexane to remove 2-propanethiol, and then both extracted with chloroform. The combined chloroform extract was dried (anhydrous $MgSO_4$), and then evaporated *in vacuo* to yield the diisopropyl dithioacetal **9** as a chromatographically homogenous syrup (3.9 g, 93%) that was directly acetylated with acetic anhydride–pyridine to give only one major product (**10**) as evidenced by t.l.c. in 8:1 benzene–ethyl acetate. An excess of methanol was added and the mixture kept for 30 min at room temperature and evaporated *in vacuo*. The crude product was chromatographed on silica gel (with a 30:1 silica gel-to-substance ratio). Elution with 16:1, 12:1, and 8:1 benzene–ethyl acetate gave

chromatographically homogeneous **10** as white crystals, m.p. 110°. An analytical sample was prepared by recrystallization from acetone–hexane, m.p. 113–114; $[\alpha]_D^{27}$ −2.7° (*c* 1.11, chloroform); ^{1}H-n.m.r.: δ 7.83–7.28 (m, 4 H, arom.), 5.62 (dd, 1 H, $J_{3,4}$ 4.58 Hz, H-3), 5.32 (dd, 1 H, $J_{4,5}$ 6.4 Hz, H-4), 5.13 (ddd, 1 H, $J_{5,6a}$ 3.05, $J_{5,6b}$ 5.80 Hz, H-5), 5.11 (d, 1 H, NH), 4.29 (dd, 1 H, $J_{6a,6b}$ 12.51 Hz, H-6a), 4.13 (dd, 1 H, H-6b), 3.98 (ddd, 1 H, $J_{2,3}$ 5.19, $J_{2,NH}$ 9.46 Hz, H-2), 3.93 (d, 1 H, $J_{1,2}$ 3.66 Hz, H-1), 3.08 and 2.88 (2 m, 2 H, *J* 6.71 Hz, 2 C*H*Me$_2$), 2.41 (s, 3 H, $SO_2C_6HCH_3$), 2.13, 2.05, 2.04, and 2.01 (4 s, 12 H, 4 $COCH_3$), and 1.29, 1.26, 1.19, and 1.12 (4 d, 12 H, *J* 6.71 Hz, 2 $CH(CH_3)_2$.

Anal. Calc. for $C_{27}H_{41}NO_{10}S_3$: C, 51.00; H, 6.50. Found: C, 51.05; H, 6.28.

*2-Deoxy-3,4:5,6-di-*O*-isopropylidene-2-*p*-toluenesulfonamido-*D*-glucose diethyl dithioacetal* (**14**). — 2-Deoxy-2-*p*-toluenesulfonamido-D-glucose diethyl dithioacetal[18] (**6**, 3.49 g, 7.94 mmol) was dissolved in 1:1 anhydrous acetone–2,2-dimethoxypropane (40 mL). Conc. sulphuric acid (1 mL) was added, and the mixture was kept for 2 h at room temperature and then poured into saturated aqueous barium hydroxide solution. The suspension was evaporated *in vacuo*, the dry residue extracted several times with chloroform, and the combined chloroform extract evaporated *in vacuo*. The yellow, syrupy residue was purified by chromatography on silica gel (85 g). Elution with 59:1 benzene–ethyl acetate gave one major product as a pale yellow syrup (3.63 g, 88%) which spontaneously crystallized, m.p. 80–82°. Another chromatography of this material on silica gel (80 g) with 12:1 hexane–acetone as eluent gave a chromatographically homogenous, colorless solid (3.40 g, 82%), m.p. 83–84°. An analytical sample was prepared by recrystallization from hexane, m.p. 85–85.5°; $[\alpha]_D^{27}$ +20.1° (*c* 1.01, chloroform); ^{1}H-n.m.r.: δ 7.78 and 7.31 (2 d, 4 H, *J* 8.24 Hz, $SO_2C_6H_4CH_3$), 5.49 (d, 1 H, $J_{2,NH}$ 9.97 Hz, NH), 4.54 (d, 1 H, $J_{1,2}$ 7.93 Hz, H-1), 4.1, 3.9, 3.7, and 3.5 (4 m, 6 H, H-2, -3, -4, -5, -6a, and -6b), 2.55–2.49 (m, 4 H, 2 CH_2CH_3), 2.43 (s, 3 H, $SO_2C_6H_4CH_3$), 1.42, 1.40, 1.34, and 1.32 [4 s, 12 H, 2 $C(CH_3)_2$], and 1.19 and 1.15 (2 t, 6 H, *J* 7.32 Hz, 2 CH_2CH_3).

Anal. Calc. for $C_{23}H_{37}NO_6S_3$: C, 53.15; H, 7.17. Found: C, 53.32; H, 6.95.

*2-Deoxy-3,4,5,6-tetra-*O*-methyl-*D*-arabino-hexose diethyl dithioacetal* (**24**). — A solution of 2-deoxy-D-*arabino*-hexose diethyl dithioacetal (**21**, 2.0 g, 7.4 mmol) in anhydrous *N,N*-dimethylformamide (15 mL) was added dropwise to a suspension of sodium hydride (1.36 g of a 50% oil suspension, 28 mmol) in anhydrous *N,N*-dimethylformamide (10 mL), under a nitrogen atmosphere. After being kept for 1 h at room temperature, the light-grey solution was cooled in an ice-bath and methyl iodide (3.7 mL, 39.9 mmol) was slowly added. The mixture was kept for 30 min in an ice-bath, and then brought to room temperature. After 1 h at room temperature, t.l.c. indicated the absence of starting material and the presence of only one reaction product; at this point, an excess of methanol was added (to destroy excess methyl iodide) and the mixture was kept for an additional 20 min at room temperature. The reaction mixture was evaporated *in vacuo*, water added (20 mL) to the residue, and the mixture extracted with chloroform (3 × 30 mL). The com-

bined chloroform extract was dried ($MgSO_4$) and evaporated *in vacuo*, and the yellow syrupy residue chromatographed on silica gel (50 g). Elution with 12:1 hexane–acetone gave **24** as a colorless syrup (2.03 g, 84%), $[\alpha]_D^{27}$ +5.8° (*c* 1.11, chloroform); ^{1}H-n.m.r.: δ 3.42 (s, 6 H, 2 OCH_3), 3.40 and 3.36 (2 s, 6 H, 2 OCH_3), 2.70 (br. dd, 4 H, *J* 7.0 Hz, 2 CH_2CH_3), 2.1 (m, 2 H, H_2-2), and 1.26 (t, 6 H, *J* 7.0 Hz, 2 CH_2CH_3).

2,3,4-Tri-O-methyl-5-O-triphenylmethyl-D-arabinose diethyl dithioacetal (**28**). — To sodium hydride (278 mg of a 55% oil suspension, 6.4 mmol) washed with two 4-mL portions of hexane in a nitrogen atmosphere, was added dropwise, over 20 min with constant stirring, a solution of 5-*O*-triphenylmethyl-D-arabinose diethyl dithioacetal (740 mg, 1.49 mmol; prepared[24] from D-arabinose diethyl dithioacetal[25]) in anhydrous *N*,*N*-dimethylformamide (20 mL). The stirring was continued for 1 additional h at room temperature, and the reaction mixture cooled to 0°. Methyl iodide (0.83 mL; 13.37 mmol) was added dropwise with a syringe over a 5-min period, and the reaction mixture stirred for 75 min at 0°. At this point, t.l.c. (in 20:1 benzene–ethyl acetate) indicated the presence of only one reaction product in addition to traces of starting material. The reaction was quenched by adding an excess of methanol at 0°, and the mixture was diluted with water (50 mL) and extracted with chloroform (3 × 40 mL). The combined chloroform extract was washed with water (75 mL), dried ($MgSO_4$), and evaporated *in vacuo*. The residue was chromatographed on silica gel (60 g). Elution with 50:1 benzene–ethyl acetate afforded chromatographically homogenous **28** (727 mg, 90%) as a very mobile liquid, $[\alpha]_D^{27}$ −1.8° (*c* 1.69, chloroform); ^{1}H-n.m.r.: δ 7.55–7.20 (m, 4 H, arom.), 4.05 (dd, 1 H, $J_{3,4}$ 7.94 Hz, H-3), 4.04 (d, 1 H, $J_{1,2}$ 7.9 Hz, H-1), 3.59 (dd, 1 H, $J_{2,3}$ 2.75 Hz, H-2), 3.57, 3.45, and 3.28 (3 s, 9 H, 3 OCH_3), 3.53 (dd, 1 H, $J_{5a,5b}$ 10.38 Hz, H-5a), 3.40 (ddd, 1 H, $J_{4,5a}$ 2.44, $J_{4,5b}$ 4.27 Hz, H-4), 3.10 (dd, 1 H, H-5b), 2.82–2.62 (m, 4 H, 2 CH_2CH_2), and 1.28 and 1.27 (2 t, 6 H, *J* 7.32 Hz, 2 CH_2CH_3).

Anal. Calc. for $C_{31}H_{40}O_4S_2$: C, 68.85; H, 7.46. Found: C, 68.81; H, 7.41.

General procedure for preparation of aldehydo-*glycoses from fully blocked glycose dithioacetals with* N-*bromosuccinimide. — (a) In acetone–water**. A suitably blocked glycose dithioacetal** (0.05–10 mmol) dissolved in a small amount of acetone (1–3 mL) was added to a solution of *N*-bromosuccinimide (2 mmol) in ice-cold, 97% aqueous acetone (25 mL), and the mixture vigorously stirred for 2 min (3 min if more than 1 mmol of dithioacetal is used), at 0°, Finely ground 1:1 (w/w) sodium thiosulfate–sodium hydrogencarbonate (2 g) was added, and stirring continued for 2–3 h if aldehyde is sufficiently stable under this condition at 0°. Salts were filtered off and washed with acetone, and the combined filtrate and washings evaporated, at or <30°. The residue was dissolved in chloroform, the chloroform solution washed with water (4 times), dried ($MgSO_4$) and evaporated to dryness (at or <30°).

---

*97% Aqueous acetonitrile has also been successfully used.

**This procedure is not suitable for *O*-benzyl derivatives.

(b) In acetone–2-methyl-2-propanol. A suitably blocked glycose dithioacetal* (0.1–1.3 mmol) dissolved in a small amount of acetone (1–3 mL), was added to a cold (0°) solution (30 mL) of *N*-bromosuccinimide (2 mmol) in 1:1 acetone–2-methyl-2-propanol. The mixture was vigorously stirred for 20–30 min at 0°. Quenching and processing were as described under (a).

REFERENCES

1 E. FISCHER, *Ber.*, 27 (1894) 673–679.
2 P. A. LEVENE AND G. M. MEYER, *J. Biol. Chem.*, 69 (1926) 175–180; *ibid.*, 74 (1927) 695–699.
3 M. L. WOLFROM, *J. Am. Chem. Soc.*, 51 (1929) 2188–2193; *ibid.*, 52 (1930) 2464–2473; M. L. WOLFROM AND C. C. CHRISTMAN, *J. Am. Chem. Soc.*, 58 (1936) 39–43; M. L. WOLFROM, L. J. TANGHE, R. W. GEORGE, AND S. W. WAISBROT, *J. Am. Chem. Soc.*, 60 (1938) 132–134; M. L. WOLFROM, M. KONIGSBERG, AND D. I. WEISBLAT, *J. Am. Chem. Soc.*, 61 (1939) 574–576
4 E. PACSU AND J. W. GREEN, *J. Am. Chem. Soc.*, 58 (1936) 1823–1824; J. W. GREEN AND E. PACSU, *ibid.*, 59 (1937) 1205–1210.
5 B. HOLMBERG, *J. Prakt. Chem.*, 135 (1932) 57–100.
6 E. J. COREY AND B. W. ERICKSON, *J. Org. Chem.*, 36 (1971) 3553–3560.
7 P. W. KENT, *Research*, 3 (1950) 427–428.
8 M. W. WHITEHOUSE, P. W. KENT, AND C. A. PASTERNAK, *J. Chem. Soc.*, (1954) 2315–2317.
9 R. E. HARMON, G. WELLMAN, AND S. K. GUPTA, *Abstr. Pap. Am. Chem. Soc. Meet., 163rd*, (1972) Carb 24.
10 J. C. A. CHIVERS AND S. SMILES, *J. Chem. Soc.*, (1928) 697–702.
11 B. GAUTHIER AND C. VANISCOTTE, *Bull. Soc. Chim. Fr.*, (1956) 30–35 and previous papers.
12 F. WEYGAND, H. J. BESTMANN, AND H. ZIEMANN, *Chem. Ber.*, 91 (1958) 1040–1043; F. WEYGAND, H. J. BESTMANN, H. ZIEMANN, AND E. KLIEGER, *ibid.*, 91 (1958) 1043–1049.
13 R. HARVILLE AND S. F. REED, JR., *J. Org. Chem.*, 33 (1968) 3976–3977.
14 W. TAGAKI, K. KIKUKAWA, K. ANDO, AND S. OAE, *Chem. Ind. (London)*, (1964) 1624–1626.
15 L. BENZING AND M. B. PERRY, *Can. J. Chem.*, 56 (1978) 691–693.
16 The Merck Index 9th edn., Merck and Co., Rahway, N.J., 1976, p. 185, monograph 1441.
17 H. P. ALBRECHT, D. B. REPKE, AND J. G. MOFFATT, *J. Org. Chem.*, 38 (1973) 1836–1840.
18 J. YOSHIMURA AND T. SATO, *Nippon Kagaku Zasshi*, 80 (1959) 1479–1483; *C.A.*, 55 (1961) 5355i.
19 W. SCHNEIDER, J SEPP, AND O. STIEHLER, *Ber.*, 51 (1918) 220–234
20 H. R. BOLLIGER, *Helv. Chim. Acta*, 34 (1951) 989–991.
21 M. L. WOLFROM, R. U. LEMIEUX, AND S. M. OLIN, *J. Am. Chem. Soc.*, 71 (1949) 2870–2873.
22 M. L. WOLFROM AND K. ANNO, *J. Am. Chem. Soc.*, 74 (1952) 6150–6151.
23 F. MICHEEL AND E. MICHAELIS, *Chem Ber.*, 91 (1958) 188–194.
24 W. BRISTOW AND B. LYTHGOE, *J. Chem. Soc.*, (1949) 2306–2309.
25 M. L. WOLFROM, D. I. WEISBLAT, W. H. ZOPHY, AND S. W. WAISBROT, *J. Am. Chem Soc.*, 63 (1941) 201–203.

*This procedure is not suitable for *O*-benzyl derivatives.