Carbohydrate Research, 64 (1978) 69–79

6-THIO- AND -SELENO-D-GALACTOSE ESTERS OF DIMETHYLARSINOUS ACID

JAMES R. DANIEL* AND RALPH A. ZINGARO
Department of Chemistry, Texas A & M University, College Station, TX 77843 (U.S.A.)
(Received April 22nd, 1977; accepted for publication in revised form, September 12th, 1977)

ABSTRACT

The syntheses of 1,2:3,4-di-*O*-isopropylidene-6-*S*-dimethylarsino-6-thio-α-D-galactopyranose (**2**), methyl 6-*S*-dimethylarsino-6-thio-D-galactopyranoside (**3**), and 1,2:3,4-di-*O*-isopropylidene-6-*Se*-dimethylarsino-6-seleno-α-D-galactopyranose (**8**) are reported. The attempted preparation of 6-*Se*-dimethylarsino-6-seleno-D-galactopyranose (**9**) is also discussed. The n.m.r. spectra of these compounds are unexceptional, except for the slight downfield shift of the arsenic methyl resonances for the selenium compound as compared to the sulfur compound, confirming previous observations. The mass spectra of these compounds showed molecular ions for **2**, **3**, and **8**. The u.v. spectra of the X–As (X=S, Se) chromophore are discussed in terms of a simplified MO model. 1,2:3,4-Di-*O*-isopropylidene-6-*S*-dimethylarsino-6-thio-α-D-galactopyranose (**2**) showed carcinostatic activity in the P388 system (mouse lymphocytic leukemia).

INTRODUCTION

Monosaccharide esters at both C-1 and C-6 are widely distributed in Nature, for instance, the 1- and 6-phosphates of D-glucose in carbohydrate metabolism, 1-*O*-benzoyl-β-D-glucose from cockroaches[1,2], 6-*O*-benzoyl-D-glucose from blueberries[3,4], and 6-*O*-acetyl-D-glucose as a metabolite of *Bacillus megaterium*[5–8]. Interest in derivatives at C-1 and C-6 has led to the synthesis of sugars where the oxygen atom occupying these positions has been replaced by sulfur[9] or selenium[10].

The synthesis and characterization of S- and Se-containing biomolecules has attracted considerable recent interest, and the fields of study have included chalcogen-containing amino acids[11], proteins[12], purines[13], and pyrimidines[14]. While the importance of sulfur in biomolecules has long been known, the essentiality of selenium to mammalian organisms has only recently been demonstrated[15]. Moreover, the recent discovery of a Se-dependent enzyme, glutathione peroxidase[12], has again demonstrated the essentiality of selenium.

*This work is in partial fulfilment of graduate-degree requirements for the Ph.D. degree from Texas A & M University.

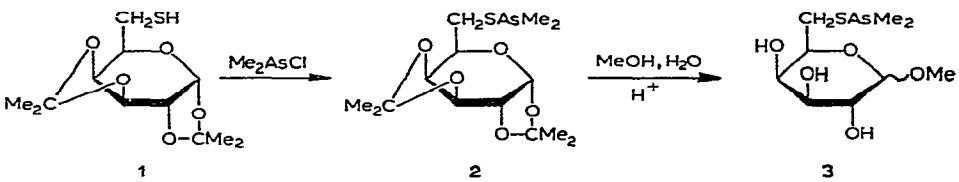
Interestingly, in the light of extensive research on chalcogen-containing amino acids, proteins, and the like, there has been relatively little work on sulfur and selenium-containing carbohydrates. The rare occurrence of natural thio sugars[16], may account for the lack of interest in this area. Very recently, however, evidence has been obtained which points strongly to the existence of naturally occurring seleno sugars in *Astragalus racemosus*[17].

Work by Zingaro[18-22] and co-workers has resulted in the preparation of thio- and seleno-D-glucose derivatives in which the chalcogen is bonded to a group VA element (phosphorus, arsenic, or antimony). Not only are these compounds interesting from a synthetic point of view, but a number of the arsenic derivatives have shown carcinostatic activity in both *in vivo* and *in vitro* tumor-screening tests. Continued interest in this field has led to the synthesis of $-SAsMe_2$ and $-SeAsMe_2$ derivatives of D-galactose at C-1, as reported elsewhere[23]. The work reported herein is concerned with the synthesis and characterization of D-galactose derivatives substituted at C-6.

DISCUSSION

The methods used for the synthesis of the 6-thiogalactose derivatives are similar to those utilized for the 6-thio-α-D-glucose derivatives. 1,2:3,4-Di-*O*-isopropylidene-6-thio-α-D-galactopyranose, prepared according to the method of Cox and Owen[9], was condensed with chlorodimethylarsine[24] in the presence of pyridine to provide the 6-dimethylthioarsino derivative, **2**. Removal of the isopropylidene groups in methanol–water (31:19 v/v) with Dowex-1 (H^+) resin gave, surprisingly, the methyl glycoside **3**.

These reactions are summarized in Scheme 1.

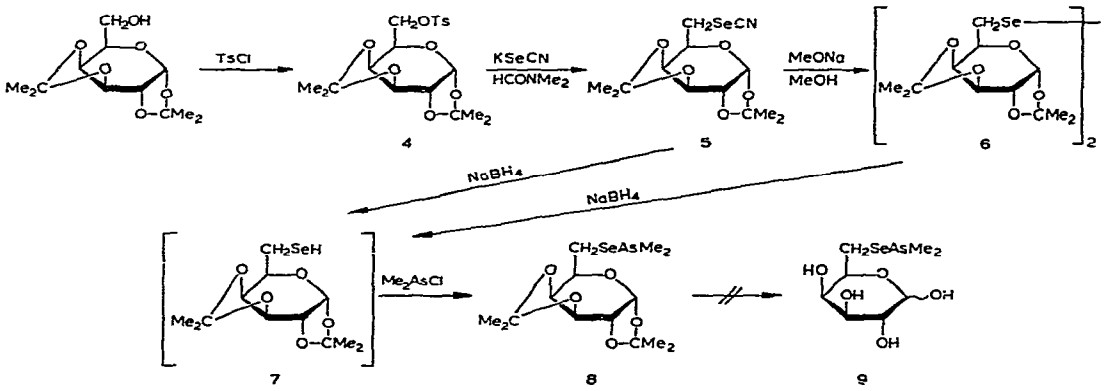


Scheme 1. Reactions leading to 6-*S*-dimethylarsino-6-thio-D-galactopyranose derivatives.

The need for stronger nucleophiles and more-stringent conditions for SN2 reactions at C-6 in D-galactose as compared to D-glucose has been noted by other workers and is thought to be due to either steric hindrance or electronic field-effects[25,26].

The synthesis of the 6-selenogalactose derivatives was approached in a variety of ways. The isopropylidenated 6-sulfonate **4** undergoes reaction with potassium selenocyanate in *N*,*N*-dimethylformamide (DMF) to produce the 6-selenocyanate, **5**. This compound may be converted into the 6,6'-diselenide (**6**) by sodium methoxide in methanol, and, after reduction with sodium borohydride, it reacts with chlorodimethylarsine to give **8**. Alternatively, **5** is reduced by sodium borohydride in DMF, treated with a small amount of methanol or ethanol to decompose the excess of

borohydride, and the 6-selenol, generated *in situ*, may be condensed with chlorodimethylarsine[24] to produce **8**. Attempts to prepare the free hydroxyl derivative **9**, by the reaction of **8** with Dowex-1 (H^+) in methanol–water, were unsuccessful. In every case, the -$AsMe_2$ group was removed together with the isopropylidene blocking groups. The reactions leading to the 6-selenogalactose derivatives are shown in Scheme 2.



Scheme 2. Reactions leading to 6-*Se*-dimethylarsino-6-seleno-D-galactopyranose derivatives.

As previously observed for both the glucose and galactose series, the selenium–arsenic bonded compounds are qualitatively less stable, both hydrolytically and oxidatively, than the sulfur–arsenic bonded compounds.

Mass spectrometry. — Mass spectrometry is an exceptionally useful tool for the elucidation of the structures of sulfur- and selenium-containing derivatives of such carbohydrates as those described herein. The selenium-containing derivatives are especially useful for elucidating the fragmentation pathways of these compounds because of the selenium-isotope distribution ratio. Natural selenium has five relatively abundant isotopes: ^{82}Se (9.2%), ^{80}Se (49.8%), ^{78}Se (23.5%), ^{77}Se (7.6%), and ^{76}Se (9.0%). This pattern of relative intensities characterizes each selenium-containing fragment in the mass spectrum of a selenium compound. Once a plausible fragmentation pathway is established for the selenium compound, a similar pathway may be searched for in the sulfur derivative. In fact, this feature should be a useful tool in interpreting the mass spectra of sulfur-containing organic compounds. This method possesses the advantages of isotopic labelling without the expense and other technical problems associated with the synthesis of isotopically labelled compounds. This chalcogen-replacement analysis does possess those disadvantages associated with synthetic organoselenium chemistry and the assumption of a common fragmentation-pathway for both the sulfur and selenium derivatives. While the occurrence of Se-containing ions at five mass-numbers presents some disadvantages because of possible overlap with other mass fragments, these overlaps may be readily recognized by careful inspection of the relative intensities of the peaks. If such regions of overlap should occur, they may be resolved by use of high-resolution mass spectrometry.

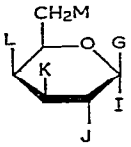
The mass spectra of compounds **2**, **3**, **5**, **6**, and **8** all showed molecular ions. The high-mass region of the spectra of **2** and **8** are somewhat similar, both exhibiting a molecular ion [S, *m/e* 380 (50%); Se, *m/e* 428 (84%)] and a relatively abundant $(M-15)^+$ fragment, [S, *m/e* 365 (69%); Se, *m/e* 413 (32%)], indicating the loss of a methyl group either from the arsenic atom or from one of the isopropylidene rings. The mass spectrum of compound **3** shows a very strong molecular ion [*m/e* 314 (100%)] and a weaker $(M-32)^+$ [*m/e* 282 (5%)], indicating loss of methanol from the galactoside, probably to form a short-lived D-galactal type of intermediate. In compounds **2**, **3**, and **8**, mass peaks are observed that may be ascribed to the formation and subsequent fragmentation of the aglycon, Me_2AsX- (X = S, Se).

Ultraviolet spectroscopy. — The u.v. spectra of these compounds are interesting in view of the fact that very little work has been done on the high-frequency spectra of organic compounds containing Group V to Group VI single bonds. In particular, no literature reference has been found that treats the spectra of organic thioarsenites or organic selenoarsenites.

The galactose derivatives described in this work that contain the As–S chromophore show λ_{max} at ~223 nm and those containing the As–Se moiety absorb at ~237 nm. Table I records the absorption maxima and molar extinction coefficients for the compounds described in this work and elsewhere[23].

TABLE I

ABSORPTION MAXIMA AND MOLAR EXTINCTION-COEFFICIENTS OF D-GALACTOSE THIO- AND SELENOARSENITES



G	*I*	*J*	*K*	*L*	*M*	λ^a_{max} *(nm)*	*(log ε)*
$SAsMe_2$	H	OAc	OAc	OAc	OAc	223	(3.61)
$SAsMe_2$	H	OH	OH	OH	OH	222	(3.78)
$SeAsMe_2$	H	OAc	OAc	OAc	OAc	237	(3.69)
H	$(Me_2)C$(O)		$(Me_2)C$(O)		$SAsMe_2$	223	(3.99)
OMe	H	OH	OH	OH	$SAsMe_2$	223	(3.64)
H	$(Me_2)C$(O)		$(Me_2)C$(O)		$SeAsMe_2$	232	(3.59)

[a]In methanol.

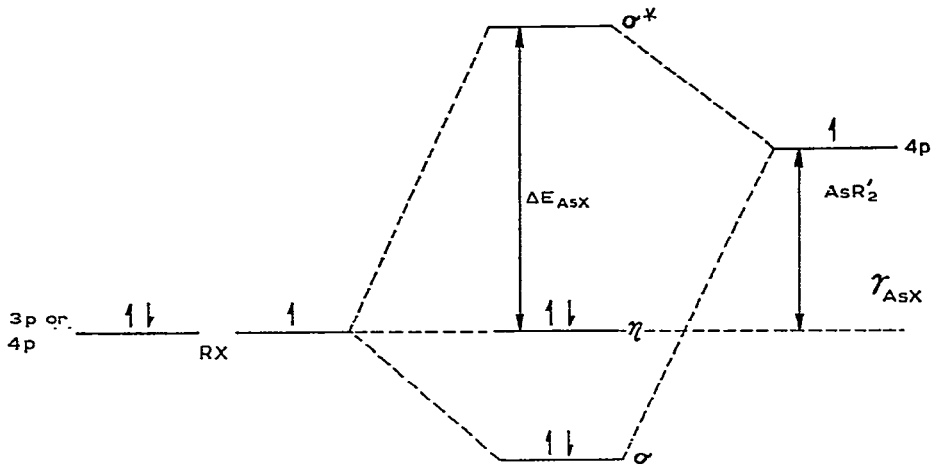


Fig. 1. An approximate MO diagram for molecules of the type RXAsR$_2'$ (X = S, Se).

The spectra of these compounds may be explained by a simplified molecular orbital (MO) model (similar to that used for disulfides and diselenides[28,29]), if it is assumed that the Group V and Group VI elements are not hybridized in these compounds. That this is a reasonable assumption is supported by the values of the bond angles of the -SAsMe$_2$ group in cacodyl disulfide[30]. The bond angles around the As and S atom are in the range 96–99°. These angles clearly indicate a decrease in the degree of sp^3 hybridization on the sulfur and arsenic atoms and an increase in the degree of bonding by pure atomic p-orbitals. An approximate MO diagram is shown in Fig. 1.

The ns (n = 3,4) electrons on both the Group V and Group VI elements are tightly bound and hence of little importance in the u.v.–visible spectra of these compounds. The assignment may now be made that, within the framework of this theory, the transition observed is an n→σ^* transition.

The electrons undergoing this excitation are in a MO that is strongly associated with the Group VI atom, so that a correlation between λ_{max} for compounds of the type RXAsR$_2'$ (X = O, S, Se, Te), and some physical property of the Group VI atom (electronegativity, ionization potential, effective nuclear charge, and the like) should be possible. A relationship of this kind would be a powerful, predictive tool for investigating the electronic structure of Group V–Group VI single bonds. However, in the absence of more data, the search for such a relationship would be difficult and if one were found its generality would be doubtful. Clearly, more investigation is needed in this area.

The red shift observed for these compounds on replacing S with Se is readily interpreted in terms of Fig. 1. When X = S, there is a larger energy-difference (γ) between the sulfur 3p and arsenic 4p lone electrons than when X = Se. In that case, the selenium 4p and arsenic 4p electrons are close in energy and γ is lowered. The relationship of the 3p lone pair on sulfur to its half-filled orbital should not be much

TABLE II

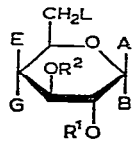
TUMOR-SCREENING DATA FOR SOME DIMETHYLARSINOUS ACID ESTERS OF 6-THIO- AND 6-SELENO-D-GALACTOSE[a,b,c]

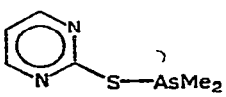
Compound	*Dose*[d]	*Toxicity day survivors*	*Control Body weight control*	*Animal-weight difference*	*T/C (%)*
2	50	5/6, 6/6	2.8, 1.8	−1.4, −1.5	110, 123
2	100	6/6, 6/6	2.8, 1.8	−2.4, −1.8	127, 126
2	200	5/6, 5/6	2.8, 1.8	−3.0, −3.2	141, 136
2	400	3/6	1.8	−0.3	
3	50	6/6	−0.2	0.4	
3	100	3/6	−0.2	−1.3	
3	200	0/6	−0.2	0.2	106
8	50	6/6	−0.2	2.7	89
8	100	6/6	−0.2	2.2	90
8	200	6/6	−0.2	1.7	92

[a]Route: intraperitoneal; [b]Interval 1 injection/day; [c]No. of injections 9; [d]Mg/kg of body weight/injection.

TABLE III

SUMMARY OF RESULTS FOR COMPOUNDS SHOWING ACTIVITY IN SCREENING TESTS FOR ANTITUMOR ACTIVITY



A	*B*	R^1	R^2	*E*	*G*	*L*	*Tumor screening test*[a]		
							1	*2*	*3*
OH	H	H	H	H	OH	$SAsMe_2$	+	+	n
OH	H	H	H	H	OH	$SeAsMe_2$	±	−	n
$SeAsMe_2$	H	Ac	Ac	H	OAc	OAc	+	±	n
$SAsMe_2$	H	H	H	H	OH	OH	+	−	n
$SAsMe_2$	H	Ac	Ac	OAc	H	OAc	n	±	n
$SAsMe_2$	H	H	H	OH	H	OH	n	±	n
H	$(Me_2C<)$		$(Me_2C<)$		H	$SAsMe_2$	n	+	n
							+	−	n
$Me_2As(S)SAsMe_2$							+	±	n
$Me_2As(O)OH$							n	−	±
$C_{16}H_{33}AsO(OH)_2$							±	±	n
CH_2-CH_2CH-$(CH_2)_4CO_2H$							n	±	n
| |									
$SAsMe_2$ $SAsMe_2$									

[a] 1 = KB5 or KB9 nasopharyngeal epidermoid carcinoma; *in vitro* cell culture. 2 = 3LE21 or PS388, lymphocytic leukemia, mice, *in vivo*. 3 = Walker carcinosarcoma, mice, *in vivo*. Notations: (+, activity confirmed), (−, inactive), ±, active, but not yet confirmed), (n, not tested in this system).

different from the similar relationship of the 4*p* lone pair on selenium to its half-filled orbital. The consequence of this ($\gamma_{AsSe} < \gamma_{AsS}$) is that ΔE_{AsSe} is less than ΔE_{AsS}, hence, a red shift is observed upon substitution by selenium.

Biochemical testing. — Previous testing has demonstrated that compounds containing the -$SAsMe_2$ group[31,32] display carcinostatic activity. Three of the compounds reported in this work were tested. Only compound **2** was found to exhibit *in vivo* carcinostatic activity in the P388 system (mouse lymphocytic leukemia). The results of these tests on some 6-thio- and 6-selenogalactose derivatives are shown in Table II.

The test animals appear to tolerate fairly high doses of this compound (50–400 mg/kg of body weight) very well. Toxic effects are noted only at very high dosages.

Table III shows those compounds tested in several test-systems that have shown presumptive (double experiment) or confirmed activity (multiple experiment). 1,2:3,4-Di-*O*-isopropylidene-6-*S*-dimethylarsino-6-thio-α-D-galactopyranose, confirmed in the P388 *in vivo* system and one of the compounds prepared in this work, is the most active compound of those shown in Table III (T/C = 141% at 200 mg/kg of body weight). The common factor among the compounds in Table III is the presence of a dialkylarsino group, primarily the -$XAsMe_2$ (X = S, Se) group. In all of the compounds tested, the S–As bonded compounds were more active than analogous Se–As derivatives, presumably because of the shorter biological and/or chemical half-life of the Se–As bonded species. Thus, the most active compounds in Table III, *in vivo*, are those containing the -$SAsMe_2$ moiety. That the dimethylarsinothio group may be the functional agent in the chemotherapeutic action of these compounds is given credence by a previous investigation that reported the inhibition of cell division of mouse fibroblasts by *S*-dimethylarsinocysteine, an amino acid containing the -$SAsMe_2$ group[32]. Clearly, there exists a relationship between the presence of the -$XAsMe_2$ moiety and the carcinostatic activity of the compounds. As the utilization and disposition of molecules by biological systems so markedly depends on subtle changes in configuration, conformation, and polarity, it would seem useful to prepare and test other biomolecules bearing the -$XAsMe_2$ group. These data could be extremely useful in helping to understand the mode of action of these compounds at the molecular level.

EXPERIMENTAL

General methods. — Evaporations were performed under diminished pressure in a Büchi Rotovapor-R rotary evaporator. Melting points were determined with a Büchi SMP-20 melting-point apparatus and are uncorrected. N.m.r. spectra were measured at 60 MHz with a Varian T-60 spectrometer. Chemical shifts refer to an internal standard of tetramethylsilane ($\delta = 0.00$) for organic solutions, and an internal standard of *tert*-butyl alcohol ($\delta = 1.20$) for aqueous solutions.

Mass spectra were recorded by Dr. Ronald Grigsby, Department of Biochemistry, Texas A&M University, with a CEC-21-110 mass spectrometer operating

at an ionizing potential of 70 eV and an ion current of 200 μA. The accelerating potential was 6 kV and the source temperature ranged from 140 to 250°.

*1,2:3,4-di-*O*-isopropylidene-6-*S*-dimethylarsino-6-thio-α-*D*-galactopyranose* (**2**). — 1,2:3,4-Di-*O*-isopropylidene-6-thio-α-D-galactopyranose (**1**, 8.4 g) was dissolved in chloroform (100 ml). Pyridine (3.5 ml) was added to this solution followed immediately by chlorodimethylarsine (3.80 ml), and the mixture was stirred overnight. The solution was treated with activated carbon, and filtered through Celite, and the filtrate was washed with five 100-ml portions of water. The organic phase was dried (magnesium sulfate) and evaporated. The yellow oil obtained was dissolved in methanol, and water was added until the solution became turbid. Cooling gave a pale-yellow solid that was dissolved in hot methanol, decolorized, and filtered through Celite. Water was added to the methanolic solution which was then cooled. The solid that crystallized was filtered off and washed with water. The yield of **2** was 6.1 g (61%) of a white solid; m.p. 64–66°; n.m.r. (60 MHz, chloroform-*d*): δ 1.35, 1.45, 1.55 (12-, 3-, 3-proton singlets, $AsMe_2$ + isopropylidene protons), 2.85 (2-proton multiplet, H-6, H-6'), 3.6–4.8 (4-proton multiplet, H-2, H-3, H-4, H-5), 5.45 (1-proton doublet, $J_{1,2}$ 3 Hz, H-1); λ_{max}^{MeOH} 223 nm (log ε 3.99).

Anal. Calc. for $C_{14}H_{25}AsO_6S$: C, 44.21; H, 6.63. Found: C, 44.49; H, 6.68.

*Methyl 6-*S*-dimethylarsino-6-thio-*D*-galactopyranoside* (**3**). — Compound **2** (2.0 g) was dissolved in methanol (50 ml) and water (30 ml) was added until turbidity persisted. Dowex-1 (H^+) ion-exchange resin (5 g) was added and the mixture was stirred for 72 h at 60°. The mixture was filtered to remove the resin, treated with activated carbon, filtered through Celite, and evaporated to a clear, colorless syrup. This syrup was taken up in the minimum volume of methanol or ethanol, and then diethyl ether or chloroform was added to permanent turbidity and the mixture was stored at 0°. The white crystals which formed were collected by filtration in a glove box under dry nitrogen because the product was extremely hygroscopic; yield 1 g (64%) of **3**; n.m.r. (60 MHz, D_2O): δ 1.4 (6-proton singlet, $AsMe_2$), 2.85 (2-proton multiplet, H-6, H-6'), 3.2–4.2 (7-proton multiplet, H-2,3,4,5, OCH_3); the H-1 signal was obscured by the solvent HOD peak.

Anal. Calc. for $C_9H_{19}AsO_5S$: C, 34.41; H, 6.09. Found: C, 34.51; H, 6.00.

*6-Deoxy-1,2:3,4-di-*O*-isopropylidene-6-selenocyanato-α-*D*-galactopyranose* (**5**). — 1,2:3,4-Di-*O*-isopropylidene-6-*O*-*p*-tolylsulfonyl-α-D-galactopyranose (**4**, 12.7 g) was dissolved in 100 ml of *N,N*-dimethylformamide, and to this solution was added potassium selenocyanate (6 g). The flask was flushed with nitrogen, and the mixture was heated for 24 h at 125°, with stirring. The dark solution was then evaporated, and the residue taken up in chloroform (150 ml). This solution was washed with four 150-ml portions of water, treated with activated charcoal, dried (magnesium sulfate), and filtered through Celite. Removal of the solvent gave 10.7 g (99%) of **5** as a bright-yellow oil. The product, as indicated by ^{1}H-n.m.r. spectroscopy, retained a small amount of *N,N*-dimethylformamide and also, because of decomposition, a satisfactory analysis was never obtained. However, n.m.r., i.r., and mass-spectral data were entirely consistent with the formulation of **5** as a 6-selenocyanate. The

product was pure enough for subsequent synthetic steps; n.m.r. (60 MHz, chloroform-*d*): δ 1.25, 1.35, 1.5 (6-, 3-, 3-proton singlets, isopropylidene protons), 2.9–3.5 (2-proton multiplet, H-6, H-6'), 3.8–4.8 (4-proton multiplet, H-2,3,4,5), 5.5 (1-proton doublet, $J_{1,2}$ 2 Hz, H-1); λ_{max}^{MeOH} 223 nm (log ε 3.22); λ_{max}^{film} 2150 cm^{-1} (-SeCN stretch); *m/e* 349 (M^+, based on ^{80}Se).

*6,6'-Diselenobis(6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-*D*-galactopyranose)* (**6**). — Compound **5** (36.8 g) was dissolved in abs. methanol (200 ml) and to this solution was added metallic sodium (2.5 g) in the form of tiny spheres. After the evolution of hydrogen had ceased, the solution was boiled for 24 h under reflux. The mixture was cooled to room temperature and the solvent was removed. The residue was taken up in chloroform (100 ml), and this solution was washed with four 125-ml portions of water, treated with activated carbon, dried over magnesium sulfate, and filtered through Celite. The diselenide **6** was obtained as 28.8 g (84%) of yellow syrup that crystallized very slowly from methanol or was purified by column chromatography on silica gel with dry ethyl ether as the eluting solvent (R_F 0.31, silica gel, Et_2O); m.p. 120–122°; n.m.r. (60 MHz, chloroform-*d*): δ 1.25, 1.35, 1.5 (6-, 3-, 3-proton singlets, CMe_2), 3.15 (2-proton multiplet, H-6,6'), 3.7–4.8 (4-proton multiplet, H-2,3,4,5), 5.5 (1-proton doublet, $J_{1,2}$ 3 Hz, H-1); λ_{max}^{MeOH} 312 nm (log ε 2.40).

Anal. Calc. for $C_{24}H_{38}O_{10}Se_2$: C, 44.73; H, 5.94. Found: C, 44.66; H, 6.00.

*1,2:3,4-di-*O*-isopropylidene-6-*Se*-dimethylarsino-6-seleno-α-*D*-galactopyranose* (**8**). — This compound was best prepared by reducing the diselenide (**6**) or the 6-selenocyanate (**5**) to the selenol (or selenolate) and then treating the latter with chlorodimethylarsine. Analytical purity was never achieved in the preparation of this compound, but n.m.r.-spectral results indicated a concentration of 85–95%.

A. Compound **6** (6.4 g) was dissolved in 50 ml of DMF, and this solution was added dropwise to a solution of sodium borohydride (1.0 g) in 50 ml of DMF at 0° under nitrogen. After 1.5 h, 2 ml of abs. methanol was added to decompose the excess of borohydride. To this solution was added, dropwise, 20 ml of DMF containing chlorodimethylarsine (2 ml). The evolution of an acidic gas (probably hydrogen chloride from the condensation of the selenol and the chloroarsine) was noted. The mixture was stirred for 24 h under nitrogen. The solvent was then removed and the syrup was dissolved in chloroform. This organic solution was washed with three 200-ml portions of water, dried (magnesium sulfate), treated with activated carbon, and filtered through Celite. The solvent was evaporated to yield 5.9 g (65%) of a yellow oil; n.m.r. (60 MHz, $CDCl_3$) δ 1.3, 1.4, 1.5 (6-, 9-, 3-proton singlets, isopropylidene protons + $AsMe_2$ protons), 2.9 (H-6, H-6' in the 6-$SeAsMe_2$ derivative), 3.1 (H-6,6' in the 6-diselenide), ratio δ 2.9 to 3.1 = 6:1 (85% conversion), 3.6–4.8 (4-proton multiplet, H-2,3,4,5), 5.5 (1-proton doublet, $J_{1,2}$ 3 Hz, H-1). N.m.r. spectra taken over a period of several days indicated that the product slowly decomposed to the 6,6'-diselenide, even when kept at 0°. Attempts to purify the compound by column chromatography with dry ethyl ether as the eluant were unsuccessful.

B. To a solution of compound **5** (8.0 g) in 40 ml of DMF was added 30 ml of DMF containing sodium borohydride (0.9 g) under nitrogen. The reduction was

allowed to proceed for 18 h. Abs. methanol (2 ml) was added to decompose the excess of borohydride and the mixture was stirred for 3 h. A solution of 20 ml of DMF containing chlorodimethylarsine (2.0 ml) was then added dropwise to the solution. Evolution of an acidic gas was noted at this time. After allowing the mixture to react for 12 h, it was evaporated and the residue was dissolved in 100 ml of dry ethyl ether. The solution was washed with two 100-ml portions of water, dried (magnesium sulfate), treated with activated carbon, and filtered through Celite. The solvent was removed and the product (5.1 g, 52%) isolated as a light-yellow syrup. The ratio of the 6-$SeAsMe_2$ derivative to the 6-diselenide was 12:1 (92% conversion) as indicated by the n.m.r. spectrum. Purification was attempted by column chromatography on silica gel employing the following solvent systems: 4:1 benzene–methanol, 99:1 benzene–acetone, and 49:1 benzene–acetone. All attempts at purification resulted in decomposition. This compound appears to be hydrolytically and oxidatively less stable than other Se–As bonded sugars, but the reason for this is not known.

Attempted preparation of 6-Se-*dimethylarsino-6-seleno-α-*D-*galactopyranose* (9). — 1,2:3,4-di-*O*-Isopropylidene-6-*Se*-dimethylarsino-6-seleno-α-D-galactopyranose (2.0 g) was dissolved in methanol (55 ml), and sufficient water (25 ml) was added to produce permanent turbidity at room temperature. Dowex-1 (H^+) ion-exchange resin (5 g) was added and the mixture was stirred and heated for 3 days at 60°. The resin was filtered off and the solvent was evaporated. The yellow residue was dissolved in a small amount of hot methanol, and dry ethyl ether was added to induce crystallization. A light-yellow solid was obtained (0.7 g, 43%) that was very hygroscopic. The n.m.r. spectrum of this solid indicated that both the isopropylidene groups and the $AsMe_2$ group had been removed. It appears that the Se–As bond is labile not only to base but also either to prolonged heating or acid, or both.

ACKNOWLEDGMENTS

This work was assisted by grants from the National Cancer Institute, Grant No. 16912, and the Robert A. Welch Foundation of Houston, Texas.

REFERENCES

1 A. Quilico, F. Piozzi, M. Pavon, and E. Mantica, *Tetrahedron*, 5 (1959) 9.
2 A. Quilico, F. Piozzi, M. Pavon, and E. Mantica, *Tetrahedron*, 5 (1959) 10.
3 E. Fischer, *Ber.*, 53 (1920) 1621–1633.
4 H. Ohle, *Biochem. Z.*, 131 (1922) 611–613.
5 R. B. Duff, D. M. Webley, and V. C. Farmer, *Nature (London)*, 179 (1957) 103–104.
6 R. B. Duff, D. M. Webley, and V. C. Farmer, *Biochem. J.*, 65 (1957) 21P.
7 R. B. Duff and V. C. Farmer, *Biochem. J.*, 70 (1958) 515–520.
8 R. B. Duff and D. M. Webley, *Biochem. J.*, 70 (1958) 520–528.
9 J. M. Cox and L. N. Owen, *J. Chem. Soc. C*, (1967) 1121–1130.
10 F. Wrede, *Hoppe-Seyler's Z. Physiol. Chem.*, 115 (1921) 284–304.
11 G. Zdansky, in D. L. Klayman and W. H. H. Gunther (Eds.), *Organic Selenium Compounds: Their Chemistry and Biology*, John Wiley & Sons, New York, 1973, pp. 579–600.
12 Howard E. Ganther, in R. A. Zingaro and W. C. Cooper (Eds.), *Selenium*, Van Nostrand Reinhold, New York, 1974, pp. 609–611.

13 H. G. MAUTNER, *Biochem. Pharmacol.*, 1 (1959) 169–173.
14 H. G. MAUTNER, S. H. CHU, J. J. JAFFE, AND A. C. SARTORELLI, *J. Med. Chem.*, 6 (1963) 36–39.
15 K. SCHWARZ AND C. M. FOLTZ, *J. Am. Chem. Soc.*, 79 (1957) 3292–3293 (see also refs. 11 and 12).
16 A. L. RAYMOND, *Adv. Carbohydr. Chem.*, 1 (1945) 129–145.
17 R. A. ZINGARO, J. PRICE, AND C. R. BENEDICT, *J. Carbohydr. Nucleos. Nucleot.*, 4 (1977) 271–279.
18 R. A. ZINGARO AND J. K. THOMSON, *Carbohydr. Res.*, 29 (1973) 147–152.
19 C. D. MICKEY, P. H. JAVORA, AND R. A. ZINGARO, *J. Carbohydr. Nucleos. Nucleot.*, 1 (1974) 291–306.
20 G. C. CHEN, R. A. ZINGARO, AND C. R. THOMPSON, *Carbohydr. Res.*, 39 (1975) 61–66.
21 C. L. BAIMBRIDGE, C. D. MICKEY, AND R. A. ZINGARO, *J. Chem. Soc., Perkin Trans. 1*, (1975) 1395–1397.
22 G. C. CHEN, J. R. DANIEL, AND R. A. ZINGARO, *Carbohydr. Res.*, 50 (1976) 53–62.
23 J. R. DANIEL AND R. A. ZINGARO, *Phosporus Sulfur*, in press.
24 G. P. VAN DER KELEN, *Bull. Soc. Chim. Belg.*, 65 (1956) 343–349.
25 J. M. SUGIHARA AND W. J. TEERLINK, *J. Org. Chem*, 29 (1964) 550–554.
26 S. NADKARNI AND N. R. WILLIAMS, *J. Chem. Soc.*, (1965) 3496–3498.
27 V. AUGER, *C. R. Acad. Sci.*, 142 (1906) 1151–1153.
28 G. BERGSON, *Ark. Kemi*, 13 (1958) 11–27.
29 G. BERGSON, G. CLAESON, AND L. SCHOTTE, *Acta Chem. Scand.*, 16 (1962) 1159–1174.
30 N. CAMERMAN AND J. TROTTER, *J. Chem. Soc.*, (1964) 219–227.
31 R. A. ZINGARO, *Chem. Scr.*, 8A (1975) 51–57.
32 H. KING AND R. J. LUDFORD, *J. Chem. Soc.*, (1950) 2086–2088.