1-*S*- (or *Se*)-Dimethylstibino-derivatives of 1-Thio- and 1-Seleno-β-D-glucopyranose

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The ready syntheses of 2,3,4,6-tetra-*O*-benzoyl-1-*Se*-dimethylstibino-1-seleno-, 2,3,4,6-tetra-*O*-acetyl-1-*Se*-dimethylstibino-1-seleno-, 1-*Se*-dimethylstibino-1-seleno-, 2,3,4,6-tetra-*O*-acetyl-1-*S*-dimethylstibino-1-thio-, and 1-*S*-dimethylstibino-1-thio-β-D-glucopyranose are described. N.m.r., i.r., and mass spectral properties of the compounds are reported.

THE syntheses of 1-*S*- and 1-*Se*-diorganoarsino-,[1] 1-*S*- and 1-*Se*-diorganophosphino-,[2] and 6-*S*- and 6-*Se*-diorganoarsino-[3] derivatives of 1-thio- or seleno-β-D-glucopyranose have been described. 2,3,4,6-Tetra-*O*-acetyl-1-*Se*-dimethylarsino-1-seleno-β-D-glucopyranose and 1-*S*-dimethylarsino-1-thio-β-D-glucopyranose display *in vitro* activity in the KB-9 tissue culture system.† In addition, 1-*S*-dimethylarsino-1-thio-β-D-glucopyranose has been shown to be a potent irreversible inhibitor of the muscle-glycogen debranching enzyme.[4] These observations, coupled with our interest in the chemistry of organometallic sugar derivatives have resulted in an extension of this work to include the synthesis of the antimony analogues.

The *S*- and *Se*-dimethylstibino-derivatives (IIa—e) were obtained by the reactions of tetramethyldistibine[5] with the corresponding bis-(β-D-glucopyranosyl) diselenides (Ia—c) and disulphides (Id and e).[6,7] The derivatives (IIc and e) were also produced by hydrolysis of the tetra-acetates (IIa and d) with methanolic sodium methoxide. All the products were isolated as recrystallizable solids and were stable in air. However, compounds (IIc and e) are exceedingly hygroscopic.

The i.r. absorption spectra of compounds (IIa—e) in

† N.C.I. Screening data summary reports NSC 163 665 and 163 666 (March 30, and May 11, 1973, respectively).

[1] R. A. Zingaro and J. K. Thomson, *Carbohydrate Res.*, 1973, **29**, 147.

[2] C. D. Mickey, R. A. Zingaro, and P. H. Javora, *J. Carbohydrates-Nucleosides-Nucleotides*, 1974, **1**, 291.

[3] G. C. Chen, R. A. Zingaro, and C. R. Thompson, *Carbohydrate Res.*, 1975, **39**, 61.

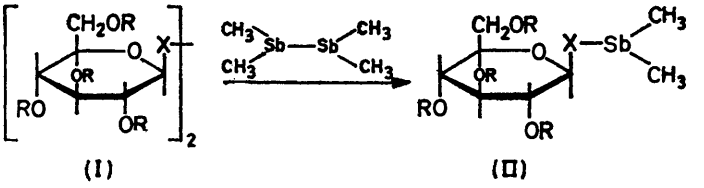
[4] T. E. Nelson, B. K. Gillard and R. A. Zingaro, paper presented to the 29th Southwest Regional Meeting, American Chemical Society, El Paso, Texas, 5th December, 1973.

[5] H. A. Meinema, H. F. Martens, and J. C. Noltes, *J. Organometallic Chem.*, 1973, **51**, 223.

[6] G. Wagner and P. Nuhn, *Arch. Pharm.*, 1964, **297**, 461.

[7] A. Thomson, M. L. Wolfrom, and E. Pacsu, *Methods Carbohydrate Chem.*, 1961, **2**, 215.

the range 500—200 cm^{-1} showed bands within the limits calculated for the antimony–chalcogen vibrations from Gordy's rule [8] [(IIa) 243, (IIb) 237, (IIc) 225 cm^{-1} (calc.[8] 234 cm^{-1}); (IId) 356, (IIe) 319 cm^{-1} (calc.[8] 338 cm^{-1})].



(I) (II)

a; X=Se, R=Ac
b; X=Se, R=Bz
c; X=Se, R=H
d; X=S, R=Ac
e; X=S, R=H

N.m.r. data (δ values [a]; 60 MHz)

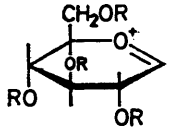
Compound	Me_2Sb	R	H-1	H-2, -4	H-3	H-6, -6′	H-5
(IIe) [b]	1.60	*d*	4.85—4.95	4.05—4.35	3.45———		———4.02
(IId) [c]	1.10	1.93, 1.96, 2.00	4.90—5.35	4.70—5.05	4.40—4.70	4.00—4.30	3.55—3.90
(IIc) [b]	1.68	*d*	*d*	4.12—4.38	3.55———		———4.08
(IIa) [c]	1.20	1.99, 2.03, 2.06, 2.10	4.90—5.35	4.80—5.03	4.65—4.80	4.05—4.40	3.55—3.90
(IIb) [c]	1.10—1.25	7.00—8.25	5.70—5.90	5.50—5.75	5.05—5.35	4.35—4.65	3.95—4.34

[a] A range of chemical shifts is provided when the signals overlap at 60 MHz. [b] Solvent D_2O. [c] Solvent $CDCl_3$. [d] Interference from solvent.

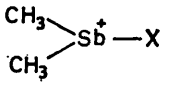
The antimony–selenium absorption occurs very close to the cut-off point of caesium iodide. Hence, it was necessary to use a thicker sample film and a slower scan rate to resolve this band.

Attempts to obtain a Raman spectrum for these compounds were unsuccessful because of their phosphorescence.

The ^1H n.m.r. data are given in the Table. The spectrum of the tetra-*O*-benzoyl-seleno-derivative (IIb) shows a well-resolved Me_2Sb doublet indicating non-equivalence of the methyl protons, which probably arises from restricted rotation about the antimony–selenium bond exacerbated by the presence of the benzoyl groups.

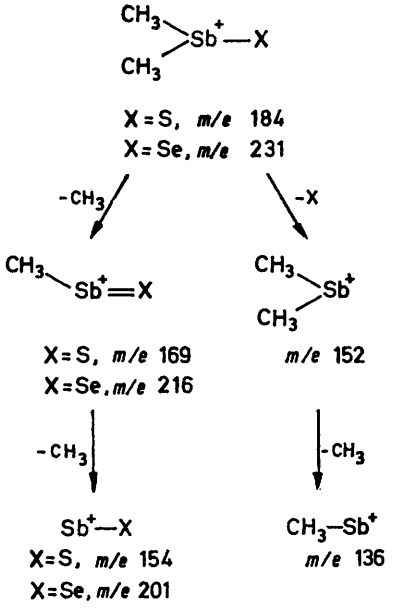


(A)



(B)

The mass spectra are characterized by cleavage at the glycosidic linkage, producing an abundance of ions derived from both the sugar unit (A) and the aglycone (B). Counterparts of the prominent mass peaks produced by fragmentation of the sugar (A) are found in the mass spectra of other monosaccharide derivatives.[1,2,9] Ions formed by fragmentation of the aglycone appear in each of the spectra. These may be accounted for by two different pathways (see Scheme), one characterized by the cleavage of the methyl–antimony bond, and the other by cleavage of the antimony–chalcogen bond followed by elimination of methyl radicals.



SCHEME

EXPERIMENTAL

Evaporations were preformed under reduced pressure. Compounds sensitive to moisture were handled in a dry-box containing phosphorus pentoxide. M.p.s were determined

[8] G. N. Chremos, Doctorial Dissertation, Texas A&M University, 1969.

[9] K. Biemann, D. C. DeJongh, and H. K. Schnoes, *J. Amer. Chem. Soc.*, 1963, **87**, 1763.

with a Thiele tube. I.r. spectra were recorded on a Beckman IR-12 spectrophotometer for thin films between caesium iodide plates. ^{1}H N.m.r. spectra were recorded at 60 MHz on a Varian T-60 instrument with tetramethylsilane as internal standard for organic solutions and external standard for aqueous solutions. Mass spectra were recorded under the supervision of Dr. R. D. Grigsby with a DuPont CEC21-110B high-resolution spectrometer operating at an ionizing potential of 70 eV and an ion current of 100 μA (accelerating voltage 8 kV; source temperatures 170—300 °C). In the analyses of the spectra of the selenium-containing compounds, allowance was made for the isotopic distribution of selenium and assignments were made using ^{80}Se as the most abundant natural isotope. Microanalyses were performed by Galbraith Analytical Laboratories, Inc., Knoxville, Tennessee.

2,3,4,6-*Tetra*-O-*benzoyl*-1-Se-*dimethylstibino*-1-*seleno*-β-D-*glucopyranose* (IIb).—Bis-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl) diselenide [6] (2.0 g, 0.001 5 mol) was dissolved in dichloromethane (10 ml) under nitrogen. Tetramethyldistibine [5] (1.5 ml) (*caution: tetramethyldistibine is exceedingly flammable and oxygen must be rigorously excluded from the system*) was injected and the solution was stirred for 12 h at room temperature. The mixture was then dried ($MgSO_4$) and filtered. The filtrate was evaporated and the resulting crystals were dried at reduced pressure for 3 h, to yield the *product* (1.75 g, 66%), having a poorly defined m.p. (Found: C, 52.95; H, 4.0. $C_{36}H_{33}O_9SbSe$ requires C, 53.3; H, 4.05%).

2,3,4,6-*Tetra*-O-*acetyl*-1-Se-*dimethylstibino*-1-*seleno*-β-D-*glucopyranose* (IIa).—Bis-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl) diselenide [6] (4.92 g, 0.006 mol) was dissolved in dichloromethane (50 ml) under nitrogen. Tetramethyldistibine [5] (7.5 ml) was injected and the solution was stirred for 12 h at room temperature. The mixture was dried ($MgSO_4$) and filtered and the filtrate evaporated at reduced pressure. The *product*, a pale yellow solid, was recrystallized once from methanol and twice from dichloromethane; yield 5.0 g (75%), m.p. 114—116° (Found: C, 35.5; H, 4.65. $C_{16}H_{25}O_9SbSe$ requires C, 34.15; H, 4.45%). Despite the fact that this preparation was repeated several times and the m.p.s and n.m.r. spectra were reproducible, the carbon analyses were consistently high and suggest contamination by starting material.

1-Se-*Dimethylstibino*-1-*seleno*-β-D-*glucopyranose* (IIc).—The tetra-acetate (IIa) (1.0 g, 0.001 8 mol) was dissolved in anhydrous methanol. The pH of the solution was adjusted to 9 (Hydrion paper) with sodium methoxide [from sodium (0.1 g, 0.044 mol) in anhydrous methanol (30 ml)] and stirred for 12 h. The solution was neutralized (Hydrion paper) with Dowex 50W-X8 resin (H^+), filtered, and evaporated under reduced pressure. The pale yellow *crystals* (58%) were dried *in vacuo* for 12 h; the m.p. was poorly defined (Found: C, 24.2; H, 4.3. $C_8H_{17}O_5SbSe$ requires C, 24.35; H, 4.3%).

Alternatively, a suspension of bis-(β-D-glucopyranosyl) diselenide [7] (1.4 g, 0.002 9 mol) in dichloromethane (15 ml) was treated, under nitrogen, with tetramethyldistibine [5] (2.2 ml). The dark yellow suspension was stirred for 12 h at room temperature and filtered, and the pale yellow solid recrystallized from anhydrous methanol. The product (2.2 g, 97%), was dried *in vacuo* for 12 h to remove the last traces of solvent.

2,3,4,6-*Tetra*-O-*acetyl*-1-S-*dimethylstibino*-1-*thio*-β-D-*glucopyranose* (IId).—Bis-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl) disulphide [7] (6.7 g, 0.009 2 mol) was dissolved in dichloromethane (30 ml) and treated with tetramethyldistibine [5] (9 ml) under nitrogen with stirring for 12 h. The mixture was dried ($MgSO_4$) and filtered and the solvent was then removed under reduced pressure. The *product* was dried *in vacuo* and recrystallized once from methanol and twice from dichloromethane; m.p. 121—123°; yield 74% (Found: C, 37.45; H, 4.7. $C_{16}H_{25}O_9SbS$ requires C, 37.3; H, 4.85%).

1-S-*Dimethylstibino*-1-*thio*-β-D-*glucopyranose* (IIe).—The tetra-acetate (IId) (2.5 g, 0.004 85 mol) was dissolved in anhydrous methanol (50 ml). The pH was adjusted to 9 (Hydrion paper) with sodium methoxide [from sodium (0.1 g, 0.044 mol) in anhydrous methanol (30 ml)]. After stirring for 12 h, the solution was neutralized (Hydrion paper) with Dowex 50W-X8 resin (H^+), filtered, and evaporated under reduced pressure. The white crystalline *product*, recrystallized from anhydrous methanol, was obtained in 71% yield; the m.p. was poorly defined (Found: C, 27.8; H, 5.0. $C_8H_{17}O_5SbS$ requires C, 27.7; H, 4.9%).

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