Note

Organomercurial carbohydrate derivatives; ^{199}Hg–^{1}H p.m.r. couplings, mass-spectral characterization, and a photochemical conversion into a deoxy analog*

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The oxymercuration of glycals has been shown[1,2] to lead to 2-deoxy-2-mercuriglycoside derivatives. Reductive cleavage of the carbon–mercury bond to afford the corresponding deoxyglycoside was demonstrated in the initial study[1] and has been re-examined in detail[3]. An interest in this laboratory in developing photochemical methods for effecting reactions of synthetic utility for specific structural modification of complex carbohydrates[4] prompted examination of the behavior of mercurial derivatives of sugars under ultraviolet irradiation.

It is here shown that photolysis of methyl 2-(acetoxymercuri)-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranoside (**1**) in methanol gives methyl 3,4,6-tri-*O*-acetyl-2-deoxy-D-*arabino*-hexopyranoside (**4**); this reaction might prove useful for synthesis of deoxy sugars in situations where a reductive procedure[1,3] would be precluded by the presence of groups labile to the reductant. Comparative study, by p.m.r. spectroscopy, of **1** and its chloromercuri analog (**2**), together with the α-D-*manno* analog (**3**) of **2**, revealed satellite peaks arising from ^{199}Hg–^{1}H coupling. The mass spectra of **1** and **2** indicate that the presence of the mercury atom modifies considerably the relative importance of the various established pathways for fragmentation of acetylated aldopyranosides.

Ultraviolet irradiation of a 0.4% solution of **1** in methanol led to separation of elemental mercury and the formation of a product migrating as a single zone on t.l.c. The product, isolated crystalline in 49% yield, was identified as the deoxy glycoside **4** by direct comparison with an authentic sample[5].

The 100-MHz p.m.r. spectrum of **1** is recorded in Fig. 1. The chemical shifts and proton–proton spin-couplings observed accord closely with the values reported by Takiura and Honda[3]. In the spectrum of the chloromercuri analog (**2**) of **1**, the antic-

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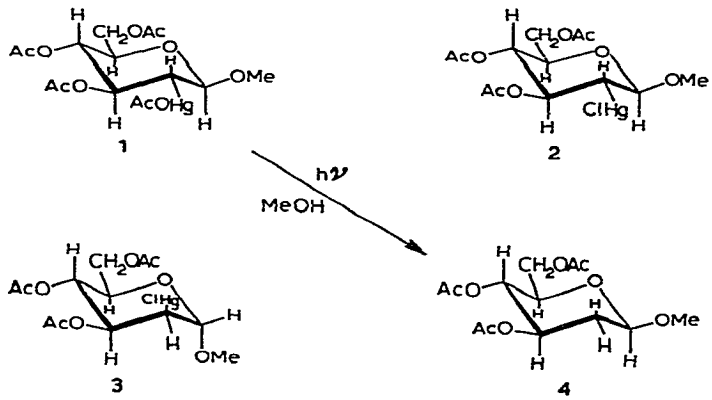


ipated decrease from 12 to 9 in the integrated intensity of the acetate resonances is observed, but alteration in the other signals is minor; the H-1 signal is moved 0.05 p.p.m. upfield, and the H-2 and H-4 signals are shifted downfield by 0.07 and 0.01 p.p.m., respectively. A similar close relationship was observed between the spectrum of methyl 2-(acetoxymercuri)-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-mannopyranoside[3] and its 2-chloromercuri analog (3).

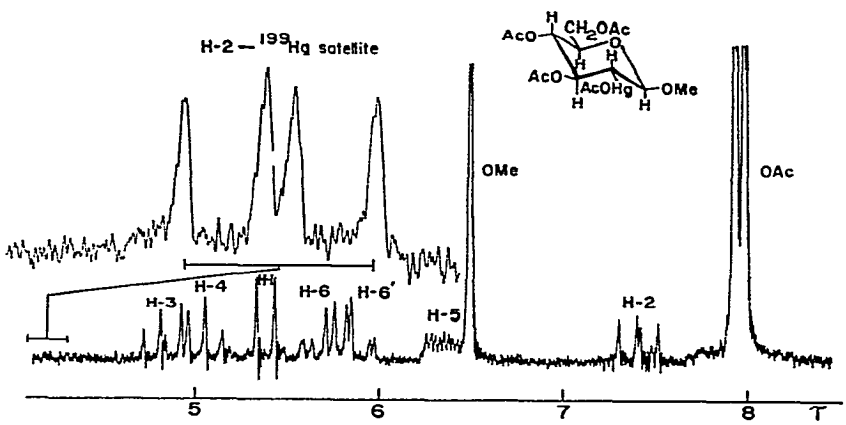


Fig. 1. The 100-MHz n.m.r. spectrum of methyl 2-(acetoxymercuri)-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranoside (1) in chloroform-*d*. The upper trace is a time-averaged (50 scans), 5-fold expansion of the downfield ^{199}Hg satellite peaks (centered at τ 4.20) of the H-2 resonance.

The upper trace depicted in Fig. 1 is the amplification of a satellite peak observed in the low-field (τ 4.20) region of the p.m.r. spectrum of **1**. It results from coupling of H-2 with ^{199}Hg. This isotope of mercury has a nuclear magnetic moment (spin ½) and an abundance of 16.9% in natural mercury. It is known that chemical shifts are insensitive to isotopic substitution in organomercurial derivatives[6], and thus the $^{2}J_{Hg,H}$ coupling constant (644 Hz) may be measured directly from the spectrum. The corresponding upfield satellite was not observed, possibly because of the proximity of the reference signal.

The 2-chloromercuri analog (**2**) of **1** exhibited a similar, low-field satellite of the H-2 resonance ($^2J_{Hg,H} = 656$ Hz) and, again, the companion, upfield resonance was obscured. The p.m.r. spectrum of the α-D-*manno* analog (**3**) of **2** exhibited a low-field satellite of the H-3 resonance ($^3J_{Hg,H} = 426$ Hz). The corresponding region ~210 Hz upfield of the H-3 resonance was obscured by other resonances; similar interference in the regions ~300 Hz to either side of the H-2 resonance precluded observation of a possible $^2J_{Hg,H}$ coupling of magnitude similar to that noted for **1** and **2**. No satellites of H-3 were observed in the spectra of **1** or **2**.

It is evident from published data[3] that there exists a dependence of proton chemical-shifts (especially of H-1 and H-3) and coupling constants upon the orientation of vicinal protons relative to the mercury atom at C-2. The observation in the spectrum of **3** of a large $^3J_{Hg,H}$ coupling for H-3, a proton antiparallel to the mercury atom, serves to reinforce this point. This conclusion has been reached, to a somewhat lesser extent, in a study of the oxymercuration products of a series of bicyclo[2.2.1]-hept-5-ene-2-*endo*-carboxylate derivatives[7]. Detailed extrapolations are at present out of the question in the absence of data on these satellite peaks in a range of examples sufficient to permit measurement of $^2J_{Hg,H}$ and $^3J_{Hg,H}$ couplings for various known geometrical relationships. The ease of obtaining organomercurials of established stereochemistry from unsaturated sugar precursors presents an attractive possibility for such a comparative study. The relative $^2J_{Hg,H}$ and $^3J_{Hg,H}$ values observed here are consistent with ratios observed for the corresponding couplings in a series of ethyl mercurials[6] and a group of norbornyl derivatives[7], although they are somewhat larger, owing, perhaps, to the particular, relatively fixed geometry in the present examples.

The mass spectra of the acetoxymercuri derivative **1** and the chloromercuri analog **2** (see Table I) showed some notable differences from those of analogous glycosides not containing mercury. A relatively strong molecular-ion peak is observed in both examples; this M^+ peak (and all other fragments containing Hg) is readily recognized as a characteristic cluster of ions whose relative intensities are determined in accordance with the natural abundance of the 7 stable isotopes of mercury (196, 0.16%; 198, 10.0%; 199, 16.9%; 200, 23.1%; 201, 13.2%; 202, 29.8%; and 204, 6.85%). The *m/e* values given here and in Table I are those corresponding to ^{198}Hg, and it is understood implicitly that each such fragment is actually observed as an isotope cluster.

The immediately striking feature of the fragmentation pathways observed is that excision of the methoxyl group from C-1 to afford a charge-delocalized, glycosyl[8] cation, a pathway known to be generally favored in the mass-spectral decomposition of glycosides having the hydroxyl groups substituted, is negligible in the mass spectrum of **2** and absent altogether from that of **1**. Ions derived from such a glycosyl ion by loss of AcOH, 2AcOH, HHgX, and HHgX+AcOH are also extremely minor, whereas *m/e* 213 ($M^+ - \cdot OMe - AcOHgX$) and *m/e* 153 (213−AcOH) are relatively more significant, although they are still rather minor. To a somewhat greater extent is observed the initial loss of the CH_2OAc group from C-5, with subsequent loss of AcOH, Ac_2O, 2AcOH, AcOHgX, HHgX, and HHgX less AcOH. The loss of ·OAc

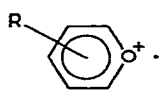
TABLE I

MAJOR FRAGMENTS RESULTING FROM ELECTRON-IMPACT IONIZATION OF COMPOUNDS 1 AND 2

m/e[a]		Intensity[b] 1	2	Assignment[c]
560		0.6		
	536[d]		0.5	$M^{\ddagger}$
529		e		
	505		0.07	$M^{\ddagger}-CH_3O\cdot$
501		0.34		
	477		0.21	$M^{\ddagger}-AcO\cdot$
487		0.08		
	463		0.11	$M^{\ddagger}-AcOCH_2\cdot$
458		0.37		
	434		e	$M^{\ddagger}-Ac_2O$
441		4.2		
	417		3.4	$M^{\ddagger}-AcO\cdot-AcOH$
427		0.34		
	403		0.1	$M^{\ddagger}-AcOCH_2\cdot-AcOH$ or $M^{\ddagger}-MeO\cdot-Ac_2O$
409		0.14		
	385		0.1	$M^{\ddagger}-MeO\cdot-2AcOH$
399		2.2		
	375		1.3	$M^{\ddagger}-AcO\cdot-Ac_2O$
385		1.3		
	361		0.3	$M^{\ddagger}-AcOCH_2\cdot-Ac_2O$
381		2.1		
	357		0.4	$M^{\ddagger}-AcO\cdot-2AcOH$
367		0.8		
	343		0.6	$M^{\ddagger}-AcOCH_2\cdot-2AcOH$
356		2.6		
	332		1.2	$M^{\ddagger}-Ac_2O-AcO^{6}CH_2\,^{5}CHO$
343		6.5		
	319		2.8	$XHgCH_2\overset{+}{C}HOAc$
315		2.2		
	291		0.7	$XHgCH_2\overset{+}{C}HOMe$
303		5.0	1.1	$M^{\ddagger}-XHg\cdot$
283		2.2		
	259		2.1	$XHgCH{=}CH^{+}$
257		2.5		
	233		0.4	XHg^{+}
244		1.6	0.7	$M^{\ddagger}-AcOHgX$
243		14.0	3.6	$M^{\ddagger}-XHg\cdot-AcOH$
229		1.6	0.64	$M^{\ddagger}-XHg\cdot-AcOMe$
213		2.6	1.1	$M^{\ddagger}-MeOHgX-AcO\cdot$
211		1.1	0.3	$M^{\ddagger}-XHg\cdot-AcOH-MeOH$
201		6.0	1.5	$M^{\ddagger}-XHg\cdot-Ac_2O$ or $M^{\ddagger}-XHg\cdot-AcOCH_2CHO$
198		49.1	7.7	$Hg^{\ddagger}$
184		6.7	2.6	$M^{\ddagger}-AcOHgX-AcOH$
183		30.0	8.8	$M^{\ddagger}-XHg\cdot-2AcOH$
171		14.0	6.8	$M^{\ddagger}-AcOHgX-AcOCH_2\cdot$
169		3.0	0.64	$M^{\ddagger}-XHg\cdot-Ac_2O-MeOH$
159		1.6	0.4	$AcO\overset{+}{C}HCH_2CH_2OAc$
158		1.6	1.1	$[AcOCH{=}CHCH_2OAc]^{\ddagger}$

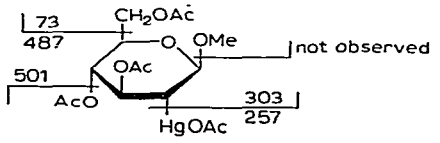
Table I (continued)

m/e[a]	*Intensity*[b] 1	2	*Assignment*[c]
157	2.6	2.3	$AcOCH{=}CH\overset{+}{C}HOAc$
153	4.0	1.4	$M^{\ddagger} - AcO\cdot - MeOHgX - AcOH$
152	4.8	2.9	$M^{\ddagger} - MeOHgX - 2AcOH$
145	4.0	3.3	Ac_3O^+
143	5.2	1.8	
142	23.9	12.3	$M^{\ddagger} - AcOHgX - Ac_2O$
141	39.0	8.8	$M^{\ddagger} - XHg\cdot - AcOH - Ac_2O$
140	3.8	0.6	
139	10.9	3.3	AcO-*py*[f]
129	30.0	15.8	$AcOCH_2\overset{+}{C}HOAc$
128	1.5	1.1	$[AcOCHCHOAc]^{\ddagger}$
127	2.6	0.8	$AcOCH{=}\overset{+}{C}OAc$
116	3.0	3.2	$[HOCH_2CH{=}CHOAc]^{\ddagger}$
115	9.4	7.9	$HO\overset{+}{C}HCH{=}CHOAc$
111	16.0	7.3	MeO-*py*[f]
110	5.2	2.6	
109	4.5	1.5	$M^{\ddagger} - XHg\cdot - Ac_2O - MeOH - AcOH$
103	4.4	2.4	Ac_2OH^+
102	1.9	1.4	
101	3.7	2.1	
100	51.2	31.7	$[CH_2{=}CHCH_2OAc]^{\ddagger}$
99	16.5	11.4	$\underbrace{OCH{=}CH-\overset{+}{C}H-CHOMe}$
98	4.1	1.1	$[\underbrace{AcOCHCH{=}CH}]^{\ddagger}$
97	12.4	4.9	HO-*py*[f]
87	26.2	18.5	$CH_3{}^+CHOAc$
85	6.3	2.8	$CH_2{=}\overset{+}{C}OAc$
81	12.8	7.9	H-*py*[f]
73	2.5	2.3	$AcOCH_2{}^+$
69	8.2	4.6	$\underbrace{OCH_2CH{=}CH}\overset{+}{C}H$
43	100	100	CH_3CO^+

[a]The *m/e* values of fragments containing Hg or Cl atoms are *calculated* for ^{198}Hg and ^{35}Cl, respectively, whereas each ion thus represented is *observed* as an "isotope cluster" of peaks; the intensity recorded for such polyisotopic species is the sum of the intensities of the members of the isotope cluster. [b]Expressed as percent of the base peak. [c]These assignments are assumed; in the fragments of **1** and **2**, X = OAc and X = Cl, respectively. [d]The offset column of figures provides the *m/e* values of fragments derived from **2** corresponding to numbers in the left-hand column for those fragments in which the substituent on the Hg atom is retained [e]Of insignificant intensity. [f]*py* designates the monosubstituted pyrilium ion,  .

(presumably the 4-OAc group or, possibly, that at C-6, as the mercury atom appears to discourage localization of charge on the adjacent carbon atoms) is observed as a third, minor series that proceeds by loss of AcOH, HHgX, or AcOHgX.

Intense ions are, however, observed corresponding to Hg^{+}, to HgX^{+}, and at *m/e* 303 ($M^{+} - HgX$), which indicates that the favored, primary-ionization process occurs at the mercury atom. The intense, odd-electron ion at *m/e* 100 may be rationalized as being formed through loss of acetic anhydride followed by simultaneous cleavage of the C-3–C-4 and C-5–O bonds. The mercurial substituent appears to favor this and a number of other processes leading to odd-electron species. The mass spectra of **1** and **2** are identical in those fragments containing no mercury atom, and exhibit the typical losses (from *m/e* 303) of AcOH, CH_2CO, and Ac_2O.



EXPERIMENTAL

*Photolysis of methyl 2-(acetoxymercuri)-3,4,6-tri-*O*-acetyl-2-deoxy-β-*D*-glucopyranoside* (**1**). — A solution of the mercuri derivative[2] **1** (2.0 g) in abs. methanol (250 ml) was irradiated at ambient temperature with a bench-type Pen Ray Ultraviolet Source (Model No. SCT-4) at a current of 0.25A. The reaction was monitored by t.l.c. on Silica Gel G with 1:1 ether–petroleum ether (b.p. 30–60°) as developer, and sulfuric acid as indicator, in which system a zone at the origin was observed for **1**. During the elapse of 20 h, the zone at the origin progressively diminished and finally disappeared completely, and there appeared concomitantly a single zone having R_F 0.54. Elemental mercury was deposited in the reaction vessel; it coalesced upon trituration with methanol, and it was recovered and dried; yield 0.50 g (70%). The methanolic solution was concentrated, and passed through a small column of Celite with elution by dichloromethane, to remove fine droplets of suspended mercury. The effluent was evaporated to dryness, the residue was dissolved in a little ethanol. petroleum ether (b.p. 65–110°) was added, and the solution was refrigerated, whereupon slow crystallization (7–10 days) ensued to give methyl 3,4,6-tri-*O*-acetyl-2-deoxy-β-D-*arabino*-hexopyranoside (**4**); yield 0.53 g (49%), m.p. 93–95° (lit.[5] m.p. 96–98°), *m/e* 303 ($M^{+} - H\cdot$), 231 ($M^{+} - \cdot CH_2OAc$), 213 ($M^{+} - \cdot OMe - HOAc$); X-ray powder diffraction data (interplanar spacings, in Å, for CuKα radiation): 8.90 s (2), 6.48 vw, 6.02 s (3), 5.26 m, 4.99 m, 4.40 s, 4.20 m, 3.92 vs (1), 3.83 m, 3.71 m, 3.53 w, 3.29 w, 3.18 m, and 3.09 w.

The product was identical, by t.l.c., mixed m.p., and X-ray diffractogram, with an authentic sample of **4**.

In a similar experiment performed on methyl 3,4,6-tri-*O*-acetyl-2-(chloromercuri)-2-deoxy-α-D-mannopyranoside[1] (1.0 g), t.l.c. monitoring showed conversion

of the starting material at the origin into a dextrorotatory, syrupy product having R_F 0.53, and metallic mercury (0.264 g, 71%) was recovered.

Spectral measurements. — N.m.r. spectra of solutions in chloroform-*d* were recorded with a Varian HA-100 spectrometer at the ambient temperature (~32°) of the probe. Internal tetramethylsilane or benzene was used as the lock signal, and all chemical shifts are referenced to the former.

Mass spectra were recorded with an AEI MS-902 high-resolution, double-focusing, mass spectrometer equipped with a direct-insertion probe, at an ionizing potential of 70 eV, and accelerating potential of 8 kV, and a source temperature of 250°.

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