Carbohydrate Research, 60 (1978) 389–395

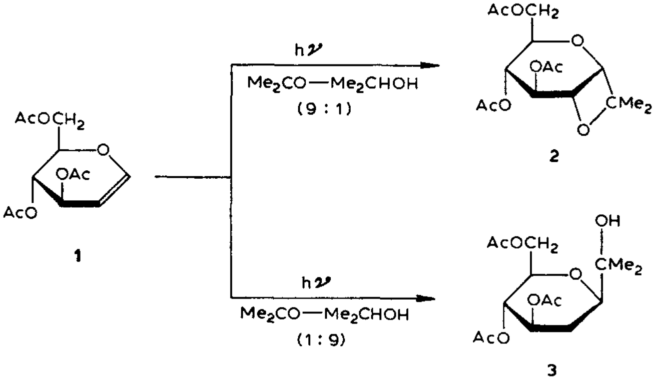
Note

Supplementary aspects in the photochemical addition of acetone to 3, 4, 6-tri-O-acetyl-D-glucal*

Younosuke Araki, Kazuo Senna, Kazuo Matsuura, and Yoshiharu Ishido
Department of Chemistry, Faculty of Science, Tokyo Institute of Technology, O-okayama, Meguro-ku, Tokyo 152 (Japan)

(Received March 4th, 1977; accepted for publication in revised form May 20th, 1977)

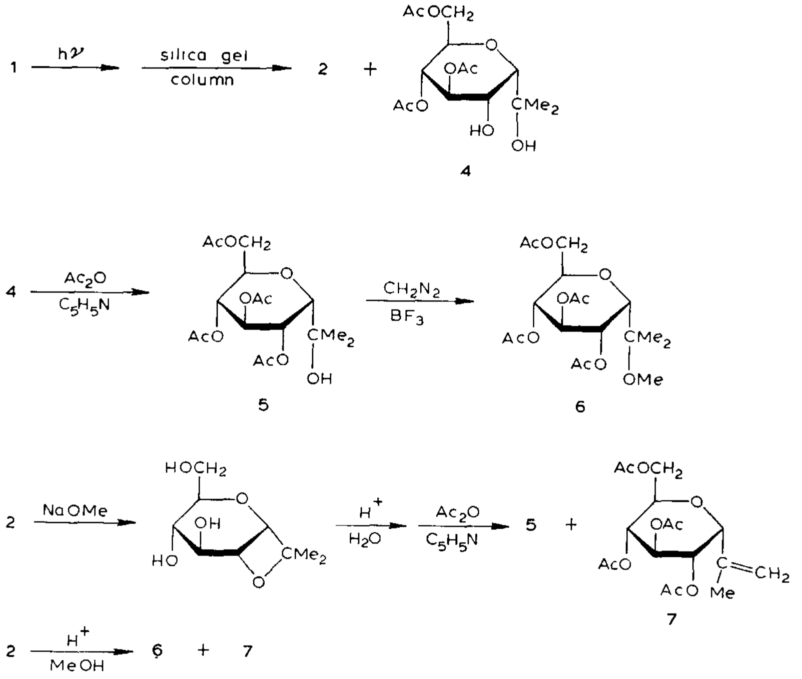
In previous papers[2], we reported the photochemical addition of acetone to 3,4,6-tri-*O*-acetyl-D-glucal (**1**) under irradiation from a high-pressure mercury lamp, leading mainly to 5,6,8-tri-*O*-acetyl-2,4:3,7-dianhydro-1-deoxy-2-*C*-methyl-D-*glycero*-D-*ido*-octitol (**2**) when 9:1 acetone–2-propanol was the solvent, whereas in 1:9 acetone–2-propanol, 5,6,8-tri-*O*-acetyl-3,7-anhydro-1,4-dideoxy-2-*C*-methyl-D-*gluco*-octitol (**3**) is formed. We now report some supplementary aspects of these photochemical additions.



Although g.l.c. showed **2** as the only product in the former photolysis, chromatographic purification on silica gel afforded **2** in only 27% yield[2]. On reexamination, we have now also isolated 43% of 5,6,8-tri-*O*-acetyl-3,7-anhydro-1-deoxy-2-*C*-methyl-D-*glycero*-D-*ido*-octitol (**4**). Compound **4** was then converted into its tetraacetate **5** and thence into the 2-*O*-methyl derivative **6** by the action of diazomethane–

---

*Part XI of a series: Synthetic Studies of Carbohydrate Derivatives by Photochemical Reactions. For Part X, see ref. 1.



boron trifluoride. Compound **6** thus obtained was identical with an authentic specimen[3] obtained from **2** by acidic methanolysis and subsequent acetylation. Based on the assumption that **4** may have been produced through hydrolysis by water occluded in the silica gel used for chromatography, an attempt was made to elute the product from the column as rapidly as possible, and this gave **2** in 48% yield. It is at present equivocal to note that purified **2** was not hydrolyzed on chromatography; the decomposition might possibly have arisen from some contaminant produced under the photochemical conditions. On the other hand, compound **5** showed unexpectedly small $J_{4,5}$, $J_{5,6}$, and $J_{6,7}$ coupling-constants (5.3 Hz each) and, therefore, the structural validity of these J values was reconfirmed by determining the n.m.r. spectrum of **5** prepared from **2** by a series of reactions, namely, deacetylation, acidic hydrolysis, and then acetylation; this sequence led to 4,5,6,8-tetra-*O*-acetyl-3,7-anhydro-1,2-dideoxy-2-*C*-methylene-D-*glycero*-D-*ido*-octitol (**7**) as a minor product. The concomitant formation of **7** in the acid-catalyzed methanolysis of **2** has previously been reported[3]; however; structural analysis by the INDOR n.m.r. technique disproved the previous assignment[3]: the broad doublet at δ 4.59 and the septet at δ 3.76 may now be assigned conclusively to H-3 and H-7, respectively (see Table I)*. As for **6**, the noticeably small values of $J_{4,5}$, $J_{5,6}$, and $J_{6,7}$ (7.5 Hz each) for the coupling constants between axial–axial protons[4] and the lowest–field resonance of the acetyl methyl near δ 2.08 for the equatorial acetyl methyl protons[5] may indicate that the compound adopts a considerably flattened ${}^4C_1$(D) conformation, or exists

---

*The septet and the broad doublet had been erroneously assigned[3] to H-3 and H-7, respectively, on the basis of the δ values of the corresponding proton signals of **5** and **6**.

TABLE I

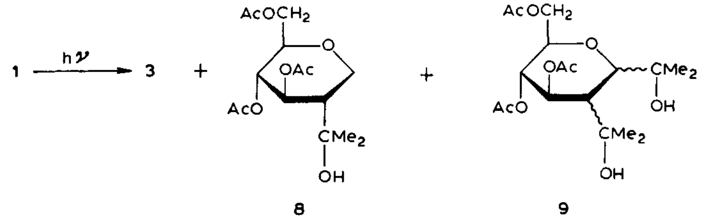
^{1}H N.M.R.-SPECTRAL DATA[a]

Compound							
5		**6**		**7**		**8**	
H-3	3.76	H-3	3.82 (3.82[b])	H-3	4.59 (*bd*)	H-1a	3.36
H-4	5.15	H-4	5.17 (5.18[b])	H-4	5.15	H-1e	4.22
H-5	5.32	H-5	5.58 (5.60[b])	H-5	5.55	H-2	2.15
H-6	4.91	H-6	4.92 (4.90[b])	H-6	5.00	H-3	5.28
H-7	4.33–4.47	H-7	4.37 } (3.95–4.50[b])	H-7	3.76	H-4	4.95
H-8 }	4.09–4.32	H-8 }	4.03–4.25 }	H-8	4.09	H-5	3.53
H-8′ }		H-8′ }		H-8′	4.24	H-6	4.07
C-Me	1.28 (2Me)	*C*-Me	1.25 (2Me) (1.25[b])	*C*-Me	1.75 (*bs*)	H-6′	4.22
O-Ac	2.04 (1Ac)	*O*-Ac	2.04 (2Ac) } (2.00–2.04[b])	$=\!<^{H}_{H}$	5.23 (*bs*)	*C*-Me	1.20 (2Me)
	2.08 (2Ac)		2.08 (2Ac) }		5.44 (*bd*)		
	2.10 (1Ac)						
		O-Me	3.27	*O*-Ac	2.03 (2Ac)	*O*-Ac	2.01 (2Ac)
					2.04 (1Ac)		2.07 (1Ac)
					2.07 (1Ac)		
$J_{3,4}$	3.5	$J_{3,4}$	4.5 (4.5[b])	$J_{3,4}$	5.4	$J_{1a,1e}$	11.5
$J_{4,5}$	5.3	$J_{4,5}$	7.5 (8[b])	$J_{4,5}$	9.0	$J_{1a,2}$	11.5
$J_{5,6}$	5.3	$J_{5,6}$	7.5 (8[b])	$J_{5,6}$	8.1	$J_{1e,2}$	4.5
$J_{6,7}$	5.3	$J_{6,7}$	7.5 (8[b])	$J_{6,7}$	9.0	$J_{2,3}$	10.5
				$J_{7,8}$	3.0	$J_{3,4}$	9.0
				$J_{7,8'}$	5.7	$J_{4,5}$	9.5
				$J_{8,8'}$	12.3	$J_{5,6}$	2.5
				$J_{=<^{H}_{H}}$	~1.5	$J_{5,6'}$	4.5
						$J_{6,6'}$	12.3

[a] Chemical shifts in p.p.m.; *J* values in Hz. [b] See ref. 3.

in equilibrium between the $^{4}C_{1}$(D) and $^{1}C_{4}$(D) conformations, in which case the former should preponderate because of its greater steric stability. On the other hand, for **5**, the three J-values (5.3 Hz each) and the acetyl methyl signals appearing at δ 2.10 (1Ac) and 2.08 (2Ac) indicated an equilibrium between the $^{4}C_{1}$ and $^{1}C_{4}$ conformations, in which the $^{1}C_{4}$ conformer might be substantially populated[†]. These n.m.r.-spectral data for **5** evidently reflect the bulkiness of the 1-hydroxy-1-methylethyl group at C-3, which is axial in the $^{4}C_{1}$(D) conformer and tends to adopt the equatorial disposition by forcing the pyranose ring to change into the $^{1}C_{4}$(D) conformation.

Two minor products were earlier detected[2] as g.l.c. peaks having retention times of 3.1 and 4.2 min, in the product from the reaction that gave the tertiary alcohol **3** in 86% yield[2]. These products were isolated by performing the reaction with a more-highly concentrated solution of **1** in 1:9 acetone–2-propanol, with subsequent column chromatography on silica gel, to give **1**, **3**, **8**, and **9** in 3 (recovery), 74, 8, and 5% yields, respectively. Although the newly isolated products **8** and **9** were contaminated by small proportions of impurities, their n.m.r. spectra provided evidence for their structure. As for **8**, H-1a, H-1e, and H-2 resonated at δ 3.36, 4.42, and 2.15, respectively, showing spin–spin coupling-constants of 11.5 Hz for $J_{1a,1e}$ and $J_{1,a2}$, 4.5 Hz for $J_{1e,2}$, and 10.5 Hz for $J_{2,3}$ (compare Table I); this product was thus confirmed to be 3,4,6-tri-*O*-acetyl-1,5-anhydro-2-deoxy-2-*C*-(1-hydroxy-1-methylethyl)-D-glucitol. The n.m.r. spectrum of **9** gave complex, overlapped signals, but the area-ratio of *C*-methyl and acetyl methyl signals (4:3) indicated that **9** was a bis(1-hydroxy-1-methylethyl) derivative. A similar minor product has also been reported in the photochemical reaction of 3-deoxy-1,2;5,6-di-*O*-isopropylidene-α-D-*erythro*-hex-3-enofuranose in acetone[6], supporting the tentative structural assignment made for **9**.



[†] An attempt at freezing out the signals of both of the individual conformers by measuring the n.m.r. spectra at lowered temperature was unsuccessful because of crystallization of the sample at −20°. The ratio was calculated by use[4] of $J_{a,a}$ = 9.63 and $J_{e,e}$ = 1.54, and the J values of 5.3 Hz afforded the ratio $^{4}C_{1}$:$^{1}C_{4}$ ≈ 47:53. Furthermore, the $\Delta\delta$ value (0.26 p.p.m.) between H-5 of **5** and **6** is of interest, although it would be premature to speculate on such scanty data.

EXPERIMENTAL

General methods. — Melting points are uncorrected. Solvents were purified prior to use. Solvent ratios given are all v/v. Irradiations were conducted externally with a 450-W high-pressure mercury lamp (Ushio Electric Inc.). ^{1}H-N.m.r. spectra were recorded with Varian HA-100 and EM-390 instruments for solutions in chloroform-*d*, with tetramethylsilane as the internal standard. G.l.c. was performed with a Hitachi Model K-53 instrument on a column of 10% of SE-30 on Chromosorb-W (60–80 mesh), with nitrogen at 1.5 atm as carrier gas; the oven temperature was 200° and the injection temperature, 300°.

*4,5,6,8-Tetra-*O*-acetyl-3,7-anhydro-1-deoxy-2-*C*-methyl-*D-glycero-D-ido-*octitol* (**5**). — (*a*) *Isolation from the second fraction obtained by column chromatography of the photoirradiated mixture.* A solution of **1** (1.00 g) in a mixture of acetone (9.9 ml) and 2-propanol (0.1 ml) was irradiated with the mercury lamp for 100 h at room temperature under nitrogen, and then evaporated *in vacuo*. The residual syrup was chromatographed on a column (35 mm inside diameter × 200 mm) of silica gel (Mallinckrodt silica gel, 100 mesh), which was eluted successively with 97:3 (1000 ml), 9:1 (500 ml), and 4:1 benzene–acetone (500 ml), to give in sequence **1** (80 mg, 8% recovered yield), 5,6,8-tri-*O*-acetyl-2,4:3,7-dianhydro-1-deoxy-2-*C*-methyl-D-*glycero*-D-*ido*-octitol (**2**) (330 mg, 27%), and 5,6,8-tri-*O*-acetyl-3,7-anhydro-1-deoxy-2-*C*-methyl-D-*glycero*-D-*ido*-octitol (**4**, 620 mg, 43%). The product **4** evidently contained an impurity, judging from the area-ratios on a gas chromatogram (**4**:impurity >9:1), and was treated with acetic anhydride (5 ml) in pyridine (20 ml) for 24 h at room temperature. The resulting mixture was poured into ice-cold water (100 ml) and stirred for 5 h. The mixture was then extracted with chloroform (2 × 30 ml, and 40 ml). The organic layers were combined and washed successively with dilute hydrochloric acid, water, aqueous sodium hydrogencarbonate and water. The organic solution, dried over anhydrous sodium sulfate, was evaporated *in vacuo* to a syrup, which was chromatographed on a column (30 × 150 mm) of silica gel, eluting with 19:1 benzene–methanol (500 ml), to give 580 mg (83% based on **4**; 36% based on **1**) of **5** as a syrup; $[\alpha]_D^{23}$ +33.4° (*c* 1.0, acetone); n.m.r. data see Table I. Retention times of **1**, **2**, **4**, and **5** in g.l.c. were 1, 2.4, 4, and 4.8 min, respectively.

Anal. Calc. for $C_{17}H_{26}O_{10}$: C, 52.30; H, 6.71. Found: C, 52.34; H, 6.97.

(*b*) *Acidic hydrolysis of* **2** *after deacetylation.* To a solution of **2** (623 mg) in methanol (50 ml) was added 2M methanolic sodium methoxide (2 ml) and the solution was stirred overnight at room temperature. The resulting solution was diluted with water (150 ml) and then eluted with water from a column of Amberlite IR-120B (H^+) resin (20 ml). The eluate and washings were combined and evaporated *in vacuo* to a colorless syrup (433 mg) that showed no carbonyl absorption band in the i.r. spectrum. The syrup was then dissolved in 5% hydrochloric acid (100 ml) and the solution was stirred overnight at room temperature. The resulting solution was diluted with water (200 ml) and the product then eluted with water from a column of Amberlite IR-45 (OH^-) resin (50 ml). The eluate and washings were combined and evaporated *in vacuo* to a pale-brown syrup (584 mg) which was dissolved in pyridine (20 ml). Upon cooling in ice–water, acetic anhydride (10 ml) was added dropwise with stirring, followed by stirring overnight at room temperature and pouring onto crushed ice (~100 g). The mixture was extracted with chloroform (50 ml × 3), and the extracts were combined and washed successively with dilute hydrochloric acid (100 ml), water (100 ml), aqueous sodium hydrogencarbonate (100 ml), and water (100 ml). The organic layer was dried with anhydrous sodium sulfate and evaporated *in vacuo* to a brown syrup (810 mg). The syrup was then chromatographed on a column (30 × 150 mm) of silica gel, eluting successively with 1:99 acetone–benzene (800 ml), and 1:99 (800 ml), and 5:95 methanol–benzene (200 ml). The first fraction thus obtained was found to contain 4,5,6,8-tetra-*O*-acetyl-3,7-anhydro-1,2-dideoxy-2-*C*-methylene-D-*glycero*-D-*ido*-octitol (**7**, 90 mg, 13%), m.p. 105.5–106° (hexane), $[\alpha]_D^{22}$ +24° (*c* 0.84, chloroform); lit.[3] m.p. 105–106° (ethyl acetate–hexane), $[\alpha]_D^{25}$ +27.6° (*c* 0.60, chloroform); n.m.r. data see Table I. Compound **5** was obtained as the second fraction in 77.5% yield (570 mg).

*4,5,6,8-Tetra-*O*-acetyl-1-deoxy-2-*C*-methyl-2-*O*-methyl*-D-glycero-D-ido-*octitol* (**6**). — (*a*) *Methylation of* **5** *with diazomethane.* The method of Gros and Gruñeiro[7] was somewhat modified by using an excess of diazomethane and diethyl ether in place of chloroform. To a cold solution of **5** (525 mg) in dried diethyl ether (~50 ml) was added a few drops of boron trifluoride diethyl etherate and then diazomethane (~15 mmol) solution in dried diethyl ether (~150 ml) with stirring and cooling; this procedure required ~4 h to complete the methylation. The precipitated mass of polyethylene was filtered off and washed with acetone (3 × 30 ml). The combined filtrate and washings were evaporated *in vacuo*. The residue was dissolved in a little ether and then the resulting solution was evaporated *in vacuo*, after which time the residue was dissolved in a little ethanol and the solution evaporated; each of these procedures was repeated several times below 40°. The resultant syrup (635 mg) was then treated with acetic anhydride–pyridine (3–5 ml), followed by conventional processing of the mixture, to give a syrup (544 mg). The syrup was chromatographed on a column (30 × 150 mm) of silica gel, successively eluting with benzene (500 ml), 2:98 acetone–benzene (600 ml), and 1:99 methanol–benzene (600 ml). This procedure gave an unidentified compound (60 mg), assumed to be polyethylene, as the first fraction. The second fraction afforded **6**, which crystallized from hexane; yield 385 mg (71%), m.p. 82.5–83° (hexane), $[\alpha]_D^{22}$ +42.6° (*c* 0.86, chloroform); lit.[3] m.p. 79–80° (hexane), $[\alpha]_D^{25}$ +45.3° (*c* 0.40, chloroform). The n.m.r.-spectral data are summarized in Table I. The third fraction afforded **5** in 18% recovery; yield (95 mg).

(*b*) *Acidic methanolysis of* **2**. By the method of Ong and Whistler[3], a solution of **2** (600 mg) in abs. methanol (60 ml) was stirred with Amberlite IR-120B (H^+) (5 ml) for 10 h under reflux. The resulting mixture was filtered and the resin was washed thoroughly with methanol (100 ml). The filtrate and washings were combined and evaporated to give a syrup (441 mg), which was treated with acetic anhydride (5 ml)–pyridine (8 ml). The resulting mixture was treated in the conventional way to give a syrup (580 mg), which was then chromatographed on a column (30 × 150 mm) of silica gel, successively eluting with 1:99 (1000 ml) and, 2:98 acetone–benzene (500 ml), and then 1:99 methanol–benzene (500 ml), to give crystals of **7**, yield 140 mg (21%), m.p. 106.5–107.5° (hexane), and syrupy **6**, which crystallized from hexane; yield 270 mg (37%), m.p. 82–83° (hexane).

*5,6,8-Tri-*O*-acetyl-2,4:3,7-dianhydro-1-deoxy-2-*C*-methyl-*D-glycero-D-ido-*octitol* (**2**); *Procedure utilizing rapid column chromatography.* — The syrup resulting from the first example in the Experimental section was chromatographed on a column of silica gel in less than two days; this step had required five days in the first instance. The chromatography gave in turn **2** (580 mg, 48%), a mixture of **2**, **4**, and an unidentified product (500 mg), and a mixture of **4** and the unidentified compound (420mg).

*Irradiation of a solution of 3,4,6-tri-*O*-acetyl-*D*-glucal* (**1**) *in acetone–2-propanol at a higher concentration.* — A solution of **1** (2.00 g, double the previously used[2] concentration) in a mixture of acetone (2.5 ml) and 2-propanol (22.5 ml) was irradiated with a mercury lamp at room temperature for 70 h under a nitrogen atmosphere, and the product was then evaporated *in vacuo*. The residual syrup was subsequently chromatographed on a column (35 × 200 mm) of silica gel, eluting in turn, with 1:19 (1000 ml), 1:9 (500 ml), and then 1:4 acetone–benzene, to give **1** (60 mg, 3% recovery), **3** (1790 mg, 74% yield), and 3,4,6-tri-*O*-acetyl-1,5-anhydro-2-deoxy-2-*C*-(1-hydroxy-1-methylethyl)-D-glucitol (**8**, 220 mg, 8% yield), and also a bis(2-hydroxy-2-propyl) derivative (**9**, 170 mg, 5% yield). Among these products, **8** and **9** evidently contained <10% of impurities, judging from the areas on their gas chromatograms. Further attempts by t.l.c. at purification of **8** and **9** were unsuccessful. G.l.c. retention times of **1**, **3**, **8**, and **9** were 1, 2.5, 3.1, and 4.2, respectively. N.m.r.-spectral data for **8** are shown in Table I.

ACKNOWLEDGMENTS

The authors thank the members of Laboratory of Organic Analysis, Tokyo Institute of Technology, for the elementary analyses, and to the Kawakami Foundation for a research grant-in-aid. They are also indebted to Mr. K. Kushida, Nippon Electric Varian, for determination of the n.m.r. spectra.

REFERENCES

1 K. Matsuura, K. Senna, Y. Araki, and Y. Ishido, *Bull. Chem. Soc. Jpn.*, 47 (1974) 1197–1200.
2 K. Matsuura, Y. Araki, and Y. Ishido, *Bull. Chem. Soc. Jpn.*, 45 (1972) 3496–3498; K. Matsuura, Y. Araki, Y. Ishido, A. Murai, and K. Kushida, *Carbohydr. Res.*, 29 (1973) 459–468.
3 K.-S. Ong and R. L. Whistler, *J. Org. Chem.*, 37 (1972) 572–574.
4 B. Coxon, *Methods Carbohydr. Chem.*, 6 (1972) 513–539.
5 F. W. Lichtenthaler and P. Emig, *Carbohydr. Res.*, 7 (1968) 121–137.
6 A. Rosenthal and K. Shudo, *J. Org. Chem.*, 37 (1972) 1608–1612.
7 E. G. Gros and E. M. Gruñeiro, *Carbohydr. Res.*, 23 (1972) 148–151.