Carbohydrate Research, 65 (1978) 159–165

Note

Photochemical addition of 2-propanol and of acetone to methyl 5-deoxy-2,3-*O*-isopropylidene-β-D-*erythro*-pent-4-enofuranoside*

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)

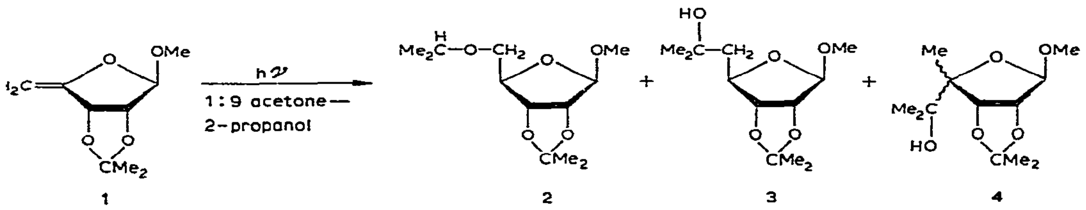
(Received November 4th, 1977; accepted for publication, December 10th, 1977)

Methyl 5-deoxy-2,3-*O*-isopropylidene-β-D-*erythro*-pent-4-enofuranoside (**1**) had been found to be reactive enough with 1,3-dioxolane under irradiation to give many isomers, with little stereoselectivity, and separation of the products was thus extremely difficult, although the reaction was over within a short time[2]. We now report the results of an investigation on the photochemical addition to **1** of 2-propanol and of acetone, respectively; this was done in order to elucidate the reactivity and selectivity of **1** (under the conditions used) in connection with the generalization[3] that an unsaturated sugar derivative gives (*a*) a tertiary alcohol derivative as an adduct with the (1-hydroxy-1-methylethyl) radical in the reaction in 1:9 acetone–2-propanol, and (*b*) an oxetane derivative as a product of cycloaddition of acetone to the unsaturated sugar derivative in the reaction in 9:1 acetone–2-propanol or in 1:9 acetone–*tert*-butyl alcohol.

First, **1** was irradiated in 1:9 acetone–2-propanol, and t.l.c. and g.l.c. of the resulting mixture showed the presence of over five species, because of the low stereoselectivity of this reaction. After evaporation of the solution, chromatographic separation on a column of silica gel afforded methyl 5-*O*-isopropyl-2,3-*O*-isopropylidene-β-D-ribofuranoside (**2**) (6%), methyl 5,7-dideoxy-2,3-*O*-isopropylidene-6-*C*-methyl-β-D-*ribo*-heptofuranoside (**3**) (19%), and methyl 6-deoxy-2,3-*O*-isopropylidene-4,5-di-*C*-methyl-β-D-*ribo*(or α-L-*lyxo*)-hexofuranoside (**4**) (5%). Of the three products, **2** and **4** were found to contain small proportions of other products with unestablished structures. The rest of the unseparable syrupy products, obtained in ~50% yield, was found to be a mixture of 1:1 adducts that, from its n.m.r. spectrum, may be the isomers of **2**, **3**, and/or **4**. By studying the variation of n.m.r.-spectral pattern throughout the series of chromatographic fractions, this syrup was deduced to contain at least three kinds of adducts. However, their separation was

---

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



unsuccessful, despite repeated application of preparative, thin-layer and column chromatography.

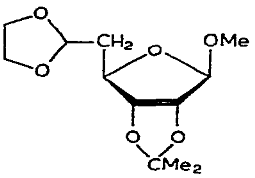
TABLE I

N.M.R.-SPECTRAL DATA FOR COMPOUNDS 2, 3, AND 4

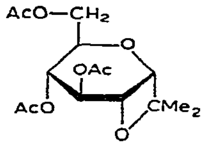
2	3	4	*Assignment*
(*p.p.m.*)	(*p.p.m.*)	(*p.p.m.*)	
4.95 (s)	4.89 (s)	5.18 (d)	H-1
4.70 (d)	4.53 (d)	4.47 (q)	H-2
4.56 (d)	4.66 (q)	4.89 (d)	H-3
4.30 (q)	4.22 (oct)		H-4
3.25–3.40 (m)	1.81 (q)		H-5
	2.08 (q)		H-5′
3.30 (s)	3.33 (s)	3.43 (s)	OCH_3
1.30 (s)	1.30 (s)	1.26 (s)	CCH_3
1.45 (s)	1.30 (s)	1.32 (s)	
	1.31 (s)	1.35 (s)	
	1.46 (s)	1.36 (s)	
		1.56 (s)	
1.15 (d) 1.15 (d)			$OCH(CH_3)_2$
4.1 (m)			$OCH(CH_3)_2$
	2.87 (bs)	3.75 (bs)	OH

Coupling constant	2 (*Hz*)	3 (*Hz*)	4 (*Hz*)
$J_{1,2}$	0	0	4.3
$J_{2,3}$	6.0	6.0	6.5
$J_{3,4}$	0	3.5	
$J_{4,5}$	6.0	4.5	
$J_{4,5'}$	9.0	9.0	
$J_{5,5'}$		15.0	
J_{H,CH_3}	6.3		

The structures of **2**, **3**, and **4** were determined from their n.m.r.-spectral data, shown in Table I. In the spectrum of **2**, there is no signal arising from a free hydroxyl group, and there was essentially no change on addition of deuterium oxide. Moreover, the $J_{1,2}$ (0 Hz), $J_{2,3}$ (6.0 Hz), and $J_{3,4}$ (0 Hz) values correspond well to those of methyl 2,3-*O*-isopropylidene-β-D-ribofuranoside[4]. These data made possible the assigning of a structure to **2**. The structure of **3** was assigned from the data for a broad singlet, at δ ~2.87, that disappeared on addition of deuterium oxide, and from the coupling constants of $J_{1,2}$ (0 Hz), $J_{2,3}$ (6.0 Hz), and $J_{3,4}$ (3.5 Hz), which correspond well to those of the ethylene acetal[2] (**5**) of methyl 5-deoxy-2,3-*O*-isopropylidene-β-D-*ribo*-hexodialdo-1,4-furanoside 6-aldehydrol, obtained by the photochemical addition of 1,3-dioxolane to **1**. The structure of **4** was assigned from the data for a broad singlet at δ ~3.75 (which also disappeared on addition of deuterium oxide), five *C*-methyl signals, no signals corresponding to H-4, and $J_{1,2}$ (4.3 Hz), which may indicate a highly strained structure, but it was impossible to establish the chirality at C-4.



5



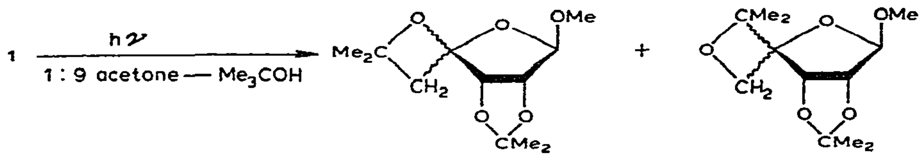
6

The formation of **2** in this reaction is of great interest; it may have been produced by the addition of an isopropoxy radical, as it may be assumed that an isopropoxy group should be introduced at C-4 in the photochemical, polar addition-reaction†. Such a product has never been obtained in the reactions of other unsaturated sugar derivatives[2,3,6]. In this case, the starting material is extremely reactive, so that it is sufficiently susceptible to attack by the isopropoxy radical formed in traces in the reaction system.

Photochemical reaction of **1** in 1:9 acetone–*tert*-butyl alcohol was next performed; t.l.c. and g.l.c. of the resultant mixture showed the formation of at least two species of products. However, attempted separation thereof by chromatography on a column of silica gel was unsuccessful. As unexpected fission of an oxetane ring had been encountered during the chromatographic purification of 5,6,8-tri-*O*-acetyl-2,4:3,7-dianhydro-1-deoxy-2-*C*-methyl-D-*glycero*-D-*ido*-octitol (**6**), because of hydrolysis to the corresponding diol derivative[7], an attempt at fractional distillation of the products under diminished pressure was made; this was successful, and gave **1** (6% recovery), methyl (4*S* or 4*R*)-4,6-anhydro-5,7-dideoxy-2,3-*O*-isopropylidene-6-*C*-

---

†Polar addition of lactonitrile to **1** under photoirradiation resulted in (1-cyanoethoxyl)ation at C-4 (*cf.*, ref. 5).



7 8

methyl-β-D-*erythro*-heptofuranosid-4-ulose (7) (3% yield, containing a small proportion of 8), and methyl 6-deoxy-2,3-*O*-isopropylidene-5-*C*-methyl-4-*C*,5-*O*-methylene-β-D-*ribo* (or α-L-*lyxo*)-hexofuranoside (8) (44% yield).

The structures of 7 and 8 were deduced from the n.m.r.-spectral data given in Table II. The oxetane structures of both 7 and 8 were confirmed by the spectra,

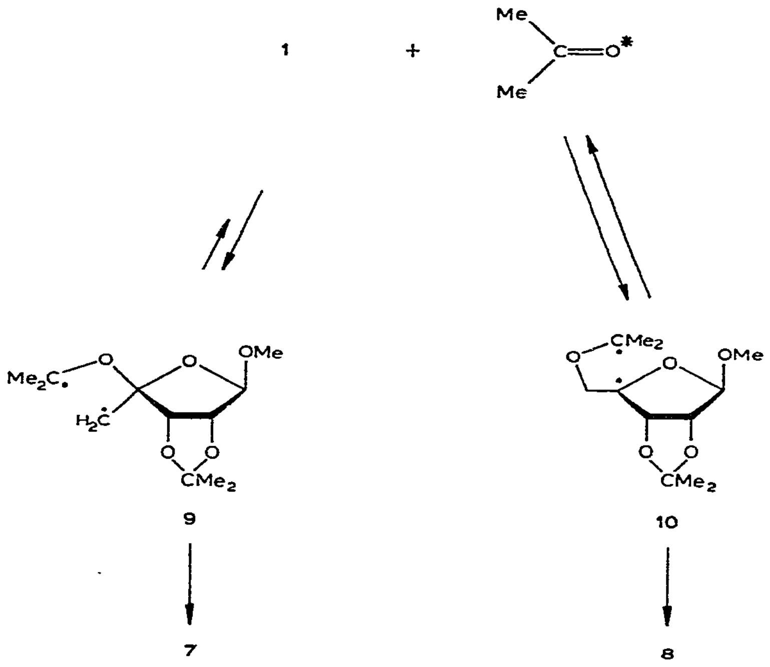
TABLE II

N.M.R.-SPECTRAL DATA FOR COMPOUNDS 7 AND 8

7	8	*Assignment*
(p.p.m.)	*(p.p.m.)*	
4.96 (s)	4.85 (s)	H-1
4.63 (bs)	4.50 (d)	H-2
	5.06 (d)	H-3
2.46 (d)	4.46 (d)	methylene
2.85 (d)	4.68 (d)	
3.42 (s)	3.40 (s)	OCH_3
1.33 (s)	1.36 (s)	CCH_3
1.38 (s)	1.36 (s)	
1.43 (s)	1.36 (s)	
1.50 (s)	1.39 (s)	
	7	8
Coupling constant	*(Hz)*	*(Hz)*
$J_{2,3}$		5.5
$J_{\text{methylene}}$	12.5	8.0

involving 12-proton signals corresponding to four *C*-methyl groups, no signals corresponding to H-4, no signals corresponding to free hydroxyl groups, and giving no substantial change on addition of deuterium oxide, as well as the fact that the oxetane ring is susceptible to hydrolysis in chromatography on silica gel[7]. The *C*,*C*-methylene structure of 7 was assigned from the data for the H-5 (δ 2.46) and H-5′ (δ 2.85) signals appearing at high field. Moreover, the *C*,*O*-methylene structure of **8** was assigned from those for methylene proton signals (δ 4.46 and 4.68). However, we could not assign the configuration at C-4 of **7** and **8**.

The formation of **7** together with **8** in this reaction is of interest in connection with the potential factors giving rise to **7**. A biradical intermediate has been assumed in oxetane formation by photocycloaddition[8]; the electron-deficient carbonyl oxygen atom of ketones in the photoexcited (n−π*) triplet state may attack the olefinic carbon atom having the higher electron-density, to give an intermediary biradical, followed by its ring closure to afford the oxetane structure. The reaction path from **1** to **8** (see Scheme 1) may be the same, involving the attack of photoexcited acetone on C-5, which should be the more electronegative (judging from the electronic effect of the ring-oxygen atom), to give biradical **10**, and then to give **8** by ring closure. By postulating a potential repulsion between the isopropyl substituent and the furanose ring, the possibility of retro-reaction to give **1** and acetone may be assumed, and, thus, there may have been the possibility of attack, to a small extent, of the excited acetone on C-4, giving **7** *via* the biradical **9**, followed by its ring closure. This consideration of stereochemical factors led to another assumption, namely, that the isopropoxyl group should lie on the "β-side" of the furanose ring, because of the steric effect of the bulky 2,3-*O*-isopropylidene grouping in cis ring-junction with the



Scheme 1

ring. Therefore, the configuration of C-4 of **7** may be *S*, and that of that of **8** may be *S* (*β*-D-*ribo*).

It is concluded that the photoaddition of 2-propanol or acetone to **1** is slightly more stereoselective than that of 1,3-dioxolane[2] to **1**, but each gives so many products (or involves some side reactions) as to make their separation difficult.

EXPERIMENTAL

General. — Acetone, 2-propanol, and *tert*-butyl alcohol were purified as usual. Methyl 5-deoxy-2,3-*O*-isopropylidene-*β*-D-*erythro*-pent-4-enofuranoside (**1**) was prepared according to the established method[9]. Irradiations were conducted externally in a Pyrex-glass test-tube at a distance of ~5 cm, with a 450-W, high-pressure, mercury lamp (Ushio Electric Inc.), the lamp and tubes being cooled with running water during the irradiation. A reaction mixture was placed in the tube, which was stoppered after passing argon gas for 30 min. T.l.c. was performed on Merck TLC aluminum sheets coated with silica gel 60 F_{254}, with 9:1 benzene–acetone as the developer. N.m.r. spectra were recorded with a Varian EM-390 instrument for solutions in deuteriochloroform, with tetramethylsilane as the internal standard, and the spectra obtained were analyzed by the double-resonance or the INDOR technique. G.l.c. was performed with a Hitachi K-53 instrument on a column (1 m) of 10% of SE-30 on Chromosorb-W (60–80 mesh), with nitrogen at 0.8 atm. as the carrier gas; oven temperature, 150°, and injection temperature, 250°. Retention times are given with reference to that of **1** as unity. Specific rotations were determined with a Carl Zeiss Photoelectric Precision Polarimeter (±0.005°), and $[\alpha]_D$ was calculated from α_{546} and α_{578} by the Drude equation.

*Methyl 5-O-isopropyl-2,3-O-isopropylidene-β-*D-*ribofuranoside* (**2**), *methyl 5,7-dideoxy-2,3-O-isopropylidene-6-C-methyl-β-*D-ribo-*heptofuranoside* (**3**), *and methyl 6-deoxy-2,3-O-isopropylidene-4,5-di-C-methyl-β-*D-ribo(*or* α-L-lyxo)-*hexofuranoside* (**4**). — A solution of **1** (1.00 g) in acetone (1 mL)–2-propanol (9 mL) was irradiated for 30 h, and the resulting mixture was evaporated *in vacuo* to a syrup. The syrupy residue was chromatographed on a column (3 × 30 cm) of silica gel (Wakogel C-300), with successive elution with benzene (500 mL), and 99:1 (1 L), 49:1 (1 L), 97:3 (1 L), and 24:1 benzene–acetone (1 L), giving, in turn, **2** (80 mg, 6% recovery), **3** (250 mg, 19% yield), and **4** (65 mg, 5% yield). Mixtures of isomers were eluted after the fraction containing **2** (a trace), and before and after the fraction containing **4**; these totalled 650 mg (~50%). Thus isolated, compounds **2** and **4** were shown by n.m.r. spectroscopy to contain 5–10% of their respective isomers. Compound **3** had $[\alpha]_D^{22}$ −74.2° (*c* 1.0, acetone); R_F values of **2**, **3**, and **4** in t.l.c.: 0.85, 0.65, and 0.60, respectively (1:0.9); retention times of **2**, **3**, and **4** (relative to **1**) in g.l.c.: 2.0, 5.0, and 5.0, respectively; the n.m.r.-spectral data for **2**, **3**, and **4** are given in Table I.

Anal. Calc. for $C_{12}H_{22}O_5$: C, 58.51; H, 9.00. Found for **3**: C, 58.50; H, 8.88.

Methyl (4S *or* 4R)-*4,6-anhydro-5,7-dideoxy-2,3-O-isopropylidene-6-C-methyl-β-*D-erythro-*heptofuranosid-4-ulose* (**7**) *and methyl 6-deoxy-2,3-O-isopropylidene-5-C-*

*methyl-4-*C,*5-*O*-methylene-β-*D-ribo(*or* α-L-lyxo)*-hexofuranoside* (**8**). — A solution of **1** (3.00 g) in acetone (7 mL)–*tert*-butyl alcohol (63 mL) was divided into seven aliquots, and each was placed in a tube into which argon gas was passed. The solutions resulting after irradiation for 80 h were combined, and evaporated *in vacuo* to a syrup. The syrupy residue was transferred to a semi-micro apparatus for fractional distillation, and distilled at low pressure, giving **1** (180 mg, 6% recovery), **7** (120 mg, 3% yield), and **8** (1.73 g, 44% yield); **7** contained ~10% of **8**. Boiling points of **1**, **7**, and **8**: 32–33°/40 Pa (~0.3 mmHg), 36–40°/40 Pa, and 40–43°/40 Pa, respectively. Compound **8** had $[\alpha]_D^{22}$ −37° (*c* 1.0, acetone). R_F values of **7** and **8** in t.l.c.: 0.8 and 0.7, respectively (**1**: 0.9), and retention times of **7** and **8** (relative to **1**) in g.l.c.: 2.6 and 3.2, respectively. The n.m.r.-spectral data are given in Table II.

Anal. Calc. for $C_{12}H_{20}O_5$: C, 59.00; H, 8.25. Found for **8**: C, 59.08; H, 8.38.

ACKNOWLEDGMENTS

The authors thank the members of the Laboratory of Organic Analysis, Department of Chemistry, Tokyo Institute of Technology, for making the elementary analyses, and Mr. Katsuhiko Kushida, Application Laboratory, Nippon Electric Varian, for recording the n.m.r. spectra.

REFERENCES

1 Y. Araki, K. Nishiyama, K. Senna, K. Matsuura, and Y. Ishido, *Carbohydr. Res.*, 64 (1978) 119–126.

2 K. Matsuura, K. Nishiyama, K. Yamada, Y. Araki, and Y. Ishido, *Bull. Chem. Soc. Jpn.*, 46 (1973) 2538–2542.

3 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; Y. Araki, K. Senna, K. Matsuura, and Y. Ishido, *ibid.*, 64 (1978) 109–117.

4 P. A. Levene and E. T. Stiller, *J. Biol. Chem.*, 104 (1934) 299–306.

5 K. Matsuura, K. Senna, Y. Araki, and Y. Ishido, *Bull. Chem. Soc. Jpn.*, 47 (1974) 1197–1200.

6 K. Matsuura, Y. Araki, Y. Ishido, and S. Satoh, *Chem. Lett.*, (1972) 849–852.

7 Y. Araki, K. Senna, K. Matsuura, and Y. Ishido, *Carbohydr. Res.*, 60 (1978) 389–395.

8 D. R. Arnold, *Adv. Photochem.*, 6 (1968) 301–423.

9 L. Hough, R. Khan, and B. A. Otter, *Adv. Chem. Ser.*, 74 (1968) 138.