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Dioxolanylium Ions Derived from Carbohydrates. II

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Reaction of methyl 2,3:4,6-di-*O*-benzylidene-α-D-mannopyranoside with triphenylmethyl fluoroborate gave the 2,3-benzoxonium ion (*2*); the 4,6-benzylidene group did not react. A similar treatment of 3-*O*-benzoyl-5,6-*O*-benzylidene-1,2-*O*-isopropylidene-α-D-glucofuranose gave the 5,6-benzoxonium ion (*5*), and 1,2:3,4-di-*O*-benzylidene-β-D-arabinopyranose yielded the 3,4-benzoxonium ion (*11*). In the latter case no hydride abstraction took place from the 1,2-benzylidene group. A study of a number of compounds showed that 4,6-, 3,5-, and 1,2-*O*-benzylidene groups, attached to pyranose or furanose rings, did not undergo hydride abstraction with triphenylmethyl fluoroborate. The reactions of the ions *2*, *5*, and *11* with water and with bromide ions were studied.

In the preceding paper[1] it was shown that benzoxonium ions could be generated by reaction of benzylidene derivatives with triphenylmethyl fluoroborate in acetonitrile solution. The dioxolanylium ring was shown to undergo *cis*-opening when hydrolysed whereas reaction with bromide ions lead to *trans*-opening and formation of bromo-deoxy sugars. In the present paper further examples of these reactions are described, mainly in the hexose series, and the behaviour of various types of benzylidene compounds towards triphenylmethyl fluoroborate has been investigated.

Treatment of methyl 2,3:4,6-di-*O*-benzylidene-α-D-mannopyranoside (*1*) with triphenylmethyl fluoroborate in acetonitrile gave the 2,3-benzoxonium ion (*2*) in quantitative yield after 16 h. The ion was quite stable and its NMR spectrum could be measured in deuterioacetonitrile (Table 1). On prolonged reaction with triphenylmethyl fluoroborate a slow decomposition took place, but no hydride abstraction from the 4,6-*O*-benzylidene group was observed. Lack of reactivity of certain types of benzylidene derivatives was found in a number of other cases. Thus the following compounds could not be induced to react with triphenylmethyl fluoroborate in acetonitrile: methyl 2,3-di-*O*-acetyl-4,6-*O*-benzylidene-α-D-glucopyranoside, methyl 2,3-di-*O*-benzoyl-4,6-*O*-benzylidene-α-D-galactopyranoside, 3,5-*O*-benzylidene-6-*O*-benzoyl-1,2-*O*-isopropylidene-α-D-glucofuranose, 1,2:4,6-di-*O*-benzylidene-3-*O*-benzoyl-α-D-glucopyranose, and 1,2:3,5-di-*O*-benzylidene-6-*O*-benzoyl-α-D-glucofuranose. From these results it appears that benzoxonium ions with 6-membered rings cannot be formed under the conditions used; the latter two examples furthermore show that 1,2-benzoxonium ions are not formed. However, while 1,2-*O*-benzylidene groups were isomerized by triphenylmethyl fluoroborate to mixtures of *endo* and *exo* isomers 4,6-*O*-benzylidene groups were completely unaffected. This was further confirmed by treating 1,2:3,4-di-*O*-benzylidene-β-D-arabinopyranose (*10*) with triphenylmethyl fluoroborate which gave the 3,4-benzoxonium ion (*11*) as the sole product. NMR spectra of the two diastereomers of *11* are shown in Table 1. The dibenzoxonium ion which could be formed by hydride abstraction from *11* was not detected. It is known to be stable in anhydrous hydrogen fluoride solution.[2]

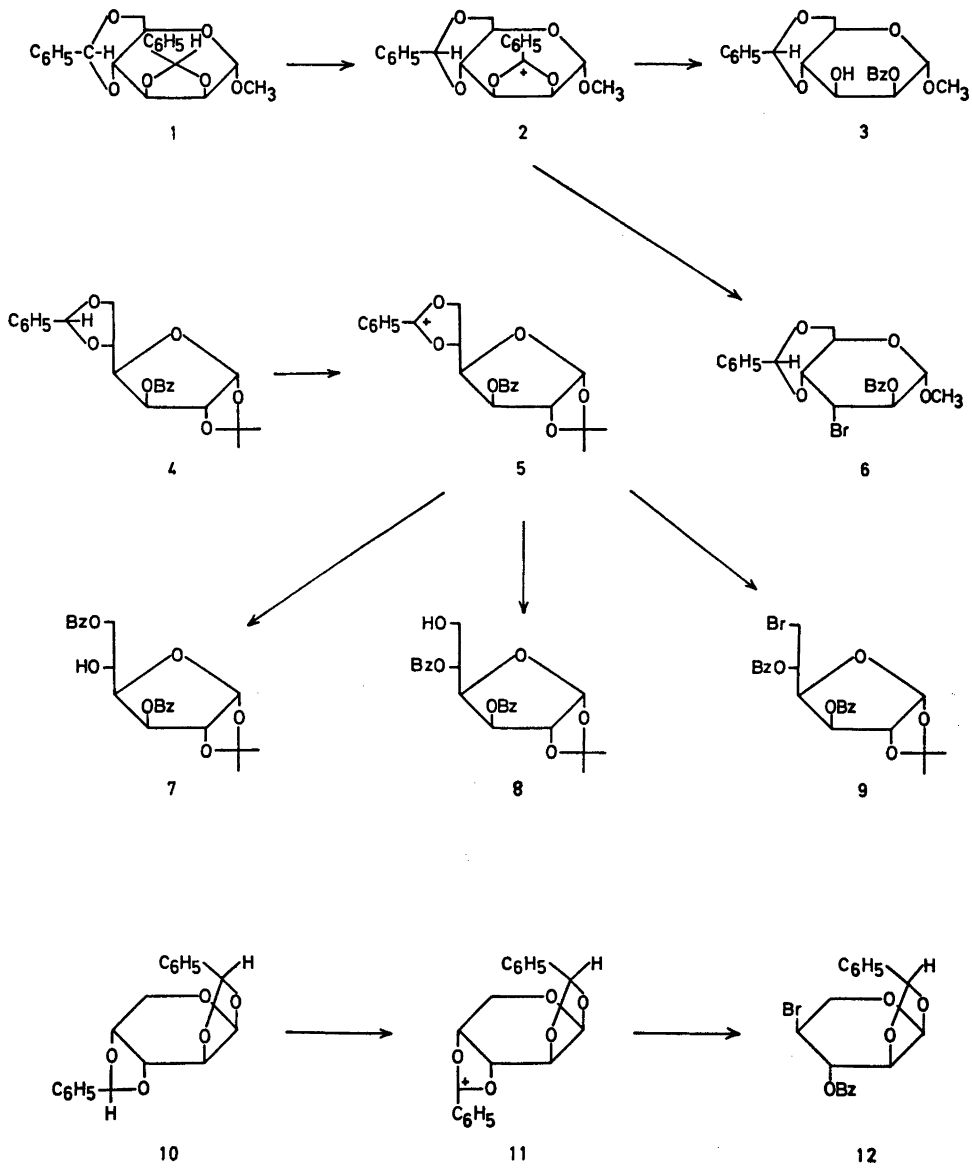
Treatment of 3-*O*-benzoyl-5,6-*O*-benzylidene-1,2-O-isopropylidene-α-D-glucofuranose (*4*) with triphenylmethyl fluoroborate rapidly gave the benzoxonium ion (*5*) as seen from its NMR spectrum in deuterioacetonitrile (Table 1). The corresponding 3-*O*-mesylated ion was obtained by Hanessian and Staub.[3] Barton *et al.*[4] have shown that isopropylidene groups will react with triphenylmethyl fluoroborate. This reac-

Table 1. Proton NMR spectra of benzoxonium ions and products prepared from them. Chemical shifts are in ppm relative to tetramethylsilane, coupling constants in Hz.

Compound	Solvent	H1	H2	H3	H4	H5	H6	H6′	J_{12}	J_{23}	J_{34}	J_{45}	J_{56}	J_{56}'	J_{66}'		
2	CD_3CN	5.59	5.75	6.27	~4.4		3.7–4.1		0	8.5	~8					OCH_3 3.54	benzylidene H 5.74
5	CD_3CN	6.15	4.80	5.66	5.24	6.27	5.76	5.62	3.7	0	3.5	2.6	9.0	8.1	9.3		isoprop. 1.55; 1.32
3	$CDCl_3$	4.76	5.37	4.2	3.7	———		4.4	1.5	3.5						OCH_3 3.33	benzylidene 5.58
7	$CDCl_3$	6.01	4.70	5.61	4.44	4.13	4.74	4.45	3.7	<0.5	2.6	9.2	2.5	5.8	11.9		isoprop. 1.34; 1.39
8	$CDCl_3$	5.98	4.65	5.55	4.82	5.46	4.07	4.03	3.7	<0.5	3.0	9.2	3.2	3.7	12.8		isoprop. 1.32; 1.59

Compound	Solvent	H1	H2	H3	H4	H5	H5′	J_{12}	J_{23}	J_{34}	J_{45}	J_{45}'	J_{55}'	benzylidene H
11 endo-H [a]	CD_3CN	5.53	4.60	5.9	5.9			5.2	1.8					5.68
11 exo-H [a]	CD_3CN	5.58	4.46	5.9	5.9	3.92–4.03		5.2	1.5					5.53
12 endo-H [a]	$CDCl_3$	5.40	3.91	5.83	3.6	———	4.0	4.2	5.3	6.9				6.31
12 exo-H [a]	$CDCl_3$	5.32	3.75	5.87	3.5	———	4.1	4.5	3.5	4.5				

[a] Assignment of structure is based on the chemical shift of the benzylidene proton.[14]



tion is, however, slower than the reaction with benzylidene groups and it was not observed. When the benzoxonium ion (*5*) was kept in acetonitrile solution in the presence of excess triphenylmethyl fluoroborate for several days a slow decomposition took place.

The benzoxonium ions were reacted with water and with bromide ions as in the preceding paper.[1] Treatment of *2* with water gave the 2-*O*-benzoate (*3*), with an axial *O*-benzoyl group, as the sole product, in agreement with the results of King and Allbutt.[5] The 5,6-benzoxonium ion (*5*) gave a mixture of the 6-*O*-benzoate (*7*) and the 5-*O*-benzoate (*8*) on hydrolysis.

Reaction of *2* with bromide ions lead to *trans*-opening of the dioxolanylium ring and gave the 3-bromo-3-deoxy-altroside (*6*) as the only product. The formation of the *trans*-diaxial product is in agreement with the results

that King and Allbutt [6] found for nucleophilic opening of dioxolanylium rings fused to bicyclic systems. The 5,6-benzoxonium ion (*5*) gave only the 6-bromo-derivative (*9*) on reaction with bromide ions.[3] Finally, the benzoxonium ion (*11*) when treated with bromide ions gave the 4-bromo-4-deoxy-L-xylose derivative (*12*) as a mixture of the two diastereomers.

EXPERIMENTAL

For details of chromatography and NMR spectroscopy see the preceding paper.[1]

Methyl 2,3:4,6-di-O-benzylidene-α-D-mannopyranoside (1). Methyl α-D-mannopyranoside (9.7 g) and benzaldehyde (11.5 g) were boiled for 10 h with *p*-toluenesulfonic acid (100 mg) in chloroform (200 ml) with a Soxhlet extractor containing 50 g of 4 Å molecular sieves. The solution was then washed with aqueous sodium hydrogencarbonate and water, dried and evaporated. The residue was crystallized from ethanol–chloroform to give 8.5 g of *1*. The mother liquor was evaporated and the residue was dissolved in chloroform and boiled for 1 h with *p*-toluenesulfonic acid (100 mg). Work up as described above gave 3.4 g of *1*. After an additional equilibration the total yield of *1* was 13.7 g, m.p. 160–175 °C. One recrystallization from ethanol-chloroform gave 11.9 g of a product with m.p. 176–177 °C (reported [7] m.p. 180–181 °C).

Conversion of benzylidene derivatives to hydroxy-benzoates

The benzoxonium ions were prepared by reaction of the benzylidene derivatives with a 10–25 % molar excess of triphenylmethyl fluoroborate in dry acetonitrile at room temp. Hydrolysis and chromatography was performed as described in the preceding paper.[1]

Methyl 2,3:4,6-di-O-benzylidene-α-D-mannopyranoside (1) (520 mg) gave the benzoxonium ion (*2*) after reaction with triphenylmethyl fluoroborate for 16 h. Hydrolysis and chromatography yielded 364 mg (67 %) of methyl 2-*O*-benzoyl-4,6-*O*-benzylidene-α-D-mannopyranoside (*3*) as a syrup, $[\alpha]_D^{21}$ −33.8° (*c* 1.3, $CHCl_3$). (Found: C 65.13; H 5.82. Calc. for $C_{21}H_{22}O_7$: C 65.27; H 5.74). An NMR spectrum (Table 1) proved the structure. Debenzoylation with sodium methoxide in methanol and recrystallization from ethanol-water gave methyl 4,6-*O*-benzylidene-α-D-mannopyranoside, m.p. 145–145.5 °C (reported [7] m.p. 146–147 °C). A mixed m.p. with an authentic sample gave no depression.

3-O-Benzoyl-5,6-O-benzylidene-1,2-O-isopropylidene-α-D-glucofuranose (4) [8] (533 mg) gave the benzoxonium ion (*5*) after reaction with triphenylmethyl fluoroborate for 1 h. Hydrolysis and chromatography yielded two products. The fast moving fraction (183 mg, 33 %) was 3,6-di-*O*-benzoyl-1,2-*O*-isopropylidene-α-D-glucofuranose (*7*), m.p. 108–110 °C, $[\alpha]_D^{20}$ −4.4° (*c* 1.7, $CHCl_3$), (reported [9] m.p. 108–109 °C, $[\alpha]_D$ −4.6°). The slow moving fraction (213 mg, 38 %) was the 3,5-di-*O*-benzoate (*8*) as a syrup, $[\alpha]_D^{21}$ −111.3° (*c* 1.6, $CHCl_3$). (Found: C 64.34; H 5.77. Calc. for $C_{23}H_{24}O_8$: C 64.48; H 5.65). Benzoylation of (*8*) with benzoyl chloride in pyridine gave 3,5,6-tri-*O*-benzoyl-1,2-*O*-isopropylidene-α-D-glucofuranose, m.p. 118–120 °C (reported [10] m.p. 119–120 °C). A mixed m.p. with an authentic sample gave no depression.

Conversion of benzylidene derivatives to bromo-deoxy-benzoates

The benzoxonium ions were prepared as described above and treated with dry tetraethylammonium bromide (3 molar equiv.) in acetonitrile for 2 h. Work up and chromatography as described in the preceding [1] paper gave the products.

Methyl 2,3:4,6-di-O-benzylidene-α-D-mannopyranoside (*1*) (552 mg) gave 388 mg (50 %) of methyl 2-*O*-benzoyl-4,6-*O*-benzylidene-3-bromo-3-deoxy-α-D-altropyranoside (*6*). Crystallization from ethyl acetate–pentane gave the pure product, m.p. 134–136 °C. (Found: C 56.25; H 4.62; Br 17.91. Calc. for $C_{21}H_{21}BrO_6$: C 56.13; H 4.71; Br 17.79). The product was identical with a sample prepared by benzoylation of methyl 4,6-*O*-benzylidene-3-bromo-3-deoxy-α-D-altropyranoside,[11] m.p. 136.5–137.5 °C, $[\alpha]_D^{21}$ +1.6° (*c* 1.5, $CHCl_3$). A mixed m.p. gave no depression.

In a separate experiment 3.3 g of *1* was converted to the 2,3-benzoxonium ion (*2*) which was treated with tetraethylammonium bromide to give the bromo-compound (*6*) in acetonitrile solution. Stirring with saturated aqueous sodium hydrogencarbonate (50 ml) for 30 min gave a crystalline precipitate which was filtered off and washed with water. Extraction with pentane (3 × 50 ml) removed most of the triphenylmethane. The product was then dissolved in ethyl acetate (50 ml) and treated with activated carbon. Evaporation of the ethyl acetate to *ca.* 10 ml and addition of pentane (40 ml) precipitated 1.75 g (43 %) of *6*, m.p. 135–137 °C. One recrystallization from ethyl acetate–pentane gave 1.60 g, m.p. 136–138 °C, $[\alpha]_D^{20}$ +1.2° (*c* 1.2, $CHCl_3$).

3-O-Benzoyl-5,6-O-benzylidene-1,2-O-isopropylidene-α-D-glucofuranose (4) (454 mg) gave after chromatography 427 mg (79 %) of 3,5-di-*O*-benzoyl-6-bromo-6-deoxy-1,2-*O*-isopropylidene-α-D-glucofuranose (*9*) as a syrup, $[\alpha]_D^{21}$ −114.5° (*c* 1.2, $CHCl_3$). (Found. C 56.41; H 4.78; Br 16.13. Calc. for $C_{23}H_{23}O_7Br$: C 56.22;

H 4.72; Br 16.26). A product obtained by benzoylation of 5-*O*-benzoyl-6-bromo-6-deoxy-1,2-*O*-isopropylidene-α-D-glucofuranose [12] had $[\alpha]_D^{21}$ −119.8° (*c* 1.4, $CHCl_3$). NMR spectra of the two products were identical.

1,2:3,4-Di-O-*benzylidene-β*-D-*arabinopyranose* [13] (10) (508 mg) gave the 3,4-benzoxonium ion (*11*) after treatment with triphenylmethyl fluoroborate for 4 h in acetonitrile solution. Reaction with tetraethylammonium bromide and work up as described above yielded 324 mg (51 %) of a mixture of the diastereomeric 3-*O*-benzoyl-1,2-*O*-benzylidene-4-bromo-4-deoxy-α-L-xylopyranoses (*12*). Crystallization from ethyl acetate (3 ml)-pentane (10 ml) gave 102 mg, m.p. 124–125 °C. Recrystallization gave the pure *endo*-H isomer, m.p. 125–126 °C, $[\alpha]_D^{21}$ −43.3° (*c* 1.7, $CHCl_3$). (Found: C 56.43; H 4.31; Br 19.72. Calc. for $C_{19}H_{17}BrO_5$: C 56.31; H 4.22; Br 19.72). The *exo*-H isomer could not be obtained pure, but preparative TLC (benzene) gave a product which contained 80 % *exo*-H isomer, allowing it to be identified through its NMR spectrum (Table 1).

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