Ring Opening of 2,3-, 3,4-, and 4,6-*O*-Benzylidene Acetals of Pyranosides by Photobromination with Bromotrichloromethane

Jasbir S. Chana, Peter M. Collins,* Farnoosh Farnia, and David J. Peacock

Department of Chemistry, Birkbeck College, University of London, Malet Street, London WC1E 7HX, U.K.

2,3-, 3,4-, and 4,6-*O*-Benzylidene pyranoside derivatives on photobromination in bromotrichloromethane yield bromo-deoxy-pyranoside benzoates regio- and stereo-specifically which, for the acyl derivatives of the 2,3- and 3,4-acetals, is superior to their reaction with *N*-bromosuccinimide.

Bromotrichloromethane (BTM) is a reagent known to give trichloromethyl and bromine radicals upon u.v. irradiation which initiate the free radical bromination of benzylic positions.[1] We report here on its use with benzylidenated sugars and find that upon u.v.-irradiation bromo-deoxy-sugar benzoates are produced regio- and stereo-specifically in good yields.[2] The reaction is closely related to the well known, highly successful, Hanessian–Hullar *N*-bromosuccinimide (NBS) sugar reaction[3] which involves initial homolytic bromination, see (**1**) for example, followed by heterolytic ring opening. However there are differences, some of which are advantageous, as illustrated by methyl 2-*O*-benzoyl-3,4-*O*-

Table 1. Bromination of 2,3-*O*-benzylidene-L-rhamnosides.

Benzylidene rhamnoside		Methyl 3-bromo-3-deoxyglycoside[a] Yield (%) *hν*[c]	NBS[d]	N.M.R.[b] δ (H-3)	δ (H-2)	δ (C-3)
4-*O*Bz-(**4**)	(**5**)	95	37	4.70	5.55	45.9
	(**6**)	0	52	4.70[e]	5.53[e]	48.1
4-*O*Ac-(**7**)	(**8**)	85	Low	4.53	5.48	45.8
4-*O*Me-(**9**)	(**10**)	70	80[f]	4.56	5.52	46.1
4-*O*H-(**11**)	(**12**)	37	90[g]	4.52	5.50	52.5

[a] Products (**5**), (**8**), (**10**) and (**12**) are 6-deoxy-L-altrosides whereas (**6**) is an L-rhamnoside. [b] ^1H and ^{13}C n.m.r. spectra were measured in $CDCl_3$ at 200 and 50 MHz, respectively; H-3 (t) has $J_{3,2}$ 4.0 and $J_{3,4}$ 4.0 Hz and H-2 (dd) has $J_{2,1}$ 1.0 and $J_{2,3}$ 4.0 Hz. [c] Photochemical bromination in BTM as described in the text. [d] NBS bromination as described in refs. 3 and 8. [e] For (**6**) H-3 (dd) has $J_{3,2}$ 2.4 and $J_{3,4}$ 8.8 Hz and H-2 (dd) has $J_{2,1}$ 1.3 and $J_{2,3}$ 2.4 Hz. [f] Similar to result achieved in ref. 7. [g] Similar to result achieved in ref. 8.

Table 2. Photobromination of 4,6-*O*-benzylideneglycopyranoside derivatives in bromotrichloromethane.[a]

Methyl 4,6-*O*-benzylidene glycopyranoside	M.p./°C	$[\alpha]_D$/°	Methyl 6-bromo-6-deoxyglycopyranoside 4-benzoate CH_2Br δ_C	δ_H[b]	CHOBz δ_H	$J_{4,3}J_{4,5}$	Yield (%)
α-Gluco-2,3-diacetate (**13**)[c]	88—90	+62	31.4	3.42, 3.50	5.20	9.5, 9.5	85
β-Gluco-2,3-diacetate (**14**)	161—3	−75	30.9	3.44, 3.52	5.22	9.0, 9.0	75
α-Galacto-2,3-diacetate (**15**)	103	+178		3.39, 3.44	5.82	3.5, 0.7	85
β-Galacto-2,3-diacetate (**16**)	150—2	+52	28.6	2.89, 3.10[d]	5.77[d]	3.5, 0.7	90
α-Altro-2,3-diacetate (**17**)	112—4	+48		3.30, 3.32[d]	5.44[d]	3.0, 9.0	75
α-Allo-2,3-diacetate (**18**)		+42	32.0	3.48, 3.68	5.17	4.0, 10.0	75
α-Gluco-2,3-ditosylate (**19**)			30.9	3.31, 3.38	5.38	9.5, 9.5	60[h]
α-Gluco-2,3-dimesylate (**20**)[f]	129—32	+46	31.4	3.42, 3.50	5.3 with H-3		60
α-Allo-2,3-epoxide (**21**)[g]			32.4	3.38—3.58[e]	5.30	2.0, 7.8	90[h]

[a] ^1H and ^{13}C n.m.r. spectra were measured in $CDCl_3$ at 200 and 50 MHz, respectively. [b] Two doublet of doublets. [c] NBS bromination gave half this yield (ref. 11). [d] Measured in C_6D_6. [e] A complex multiplet with H-2 and -3. [f] NBS bromination gave similar results (ref. 8). [g] NBS bromination gave similar results (ref. 8, 10). [h] Estimated from ^1H n.m.r. spectrum.

benzylidene-β-D-arabinopyranoside (**1**).† In a typical reaction two grammes of this compound, dissolved in anhydrous carbon tetrachloride (80 ml) containing bromotrichloromethane (0.5 ml), were irradiated‡ for 1.5 h whilst being agitated by the passage of dry nitrogen; t.l.c. and ^1H n.m.r. spectroscopy measured directly on the photolysate revealed that, in addition to chloroform, methyl 4-bromo-4-deoxy-2,3-di-*O*-benzoyl-α-L-xylopyranoside (**2**) was produced and this formed at least 90% of the carbohydrate material in the crude photolysate. Evaporation§ followed by chromatography gave pure (**2**),¶ (86%), $[\alpha]_D - 119°$ (CH_2Cl_2). This regio- and stereo-specific bromination is in marked contrast to the known[4] non-selective bromination of compound (**1**) under NBS conditions which affords only 30% of the 4-bromo-xyloside accompanied by 60% of the 3-bromo-arabinoside (**3**). The latter is formed by participation of the 2-*O*-benzoyl group.[4]

Photoinduced brominations of some methyl 2,3-*O*-benzylidene-α-L-rhamnopyranoside derivatives are also regio- and stereo-specific as shown in Table 1. Thus the 4-benzoate (**4**) gave the 3-bromo-altroside (**5**) in 95% yield, whereas a non-selective reaction occurred between NBS and compound (**4**), giving only 37% of the expected 3-bromo-altroside (**5**) accompanied by 52% of the 3-bromo-rhamnoside (**6**), which arose through the participation of the 4-*O*-benzoyl group. Similar participation must have taken place in the more complex reaction between NBS and methyl 2,3:4,6-di-*O*-benzylidene-α-D-mannopyranoside reported by Thiem.[5]

Photobromination of the rhamnoside 4-acetate (**7**) also gave only the 3-bromo-altroside (**8**) whereas with NBS a mixture of products was formed. Photobromination of (**7**) in the usual way but in the presence of tetra-n-butylammonium bromide (0.3 molecular equivalents), which might favour acetoxonium ion formation, was without effect on the high yield of compound (**8**). The 4-*O*-methyl-rhamnoside (**9**) gave the 3-bromo-altroside (**10**) irrespective of the method of bromination, whereas with the unprotected 4-hydroxy compound (**11**) BTM was distinctly less satisfactory than NBS.

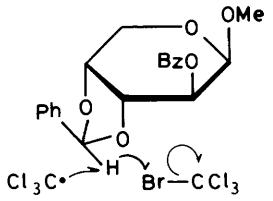
Photobromination with a wide range of 4,6-*O*-benzylidene derivatives is also successful and, as is found[8—11] with the NBS reaction, 6-bromo-6-deoxy-4-*O*-benzoyl glycopyranosides are produced as shown in Table 2. Acetoxy, tosyloxy, mesyloxy, and epoxy groups are compatible with the reaction conditions

† *Endo*-, *exo*-, or a mixture of isomers may be used, since we have shown that isomerization at the benzylidene acetal carbon atom occurs early in the reaction.

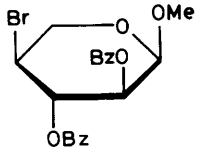
‡ Irradiations were carried out in quartz tubes situated 3 cm from a 450 W medium pressure mercury lamp.

§ Usually the only work-up necessary.

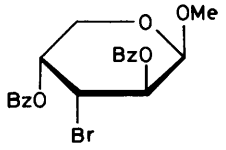
¶ All new compounds gave satisfactory elemental analyses and/or m.s. analyses, in addition to essentially first order ^1H n.m.r. spectra and clean ^{13}C n.m.r. spectra.



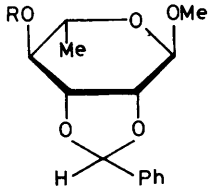
(1)



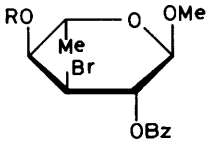
(2)



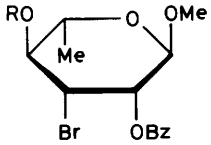
(3)



(4) R = Bz
(7) R = Ac
(9) R = Me
(11) R = H



(5) R = Bz
(8) R = Ac
(10) R = Me
(12) R = H



(6) R = Bz

Bz = benzoyl

and results with methyl 4,6-*O*-benzylidene 2,3-di-*O*-acetyl-α- and β-D-glucosides (**13**) and (**14**), α- and β-D-galactosides (**15**) and (**16**), α-D-altroside (**17**), and α-D-alloside (**18**) show that with acetyl derivatives stereo- and regio-selective opening of the 1-phenyl-2,3-dioxane ring is maintained with a wide array of stereochemical configurations.

Thus photobromination of protected benzylidenated sugars derivatives in BTM provides a useful additional method for producing bromo-deoxy-sugar benzoates. It can be carried out at room temperature or below, it offers very simple product isolation and it presents a distinct advantage for brominating molecules that possess ester groups prone to participate in the NBS reaction.

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