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Note

A convenient synthesis of peracetylated glycosyl halides using bismuth(III) halides as catalysts

Jean-Louis Montero *, Jean-Yves Winum, Alain Leydet, Mehrnaz Kamal, André A. Pavia, Jean-Pierre Roque

Laboratoire de Chimie Biomoléculaire Associé au CNRS; Université de Montpellier II, CC073 Place E. Bataillon, F-34095 Montpellier, France

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Abstract

A new halogenation procedure for peracetylated glycopyranosides is reported, using bismuth(III) halides and halogenosilanes under very mild conditions. © 1997 Elsevier Science Ltd.

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Glycosyl halides are of interest for the formation of the glycosidic bond. They have been used in the generation of anomeric carbocations [1], radicals [2] or carbanions [3].

The basic procedures for the preparation of acetylated glycosyl chloride involves the use of dry hydrogen chloride in various solvents: ether [4], acetyl chloride [5] or dioxane [6]. Other methods involve a Lewis acid such as aluminium chloride [5], zinc chloride [7] or titanium tetrachloride [8], or a secondary α-chloroenamine [9]. The use of standard chlorination reagents such as phosphorus pentachloride [10] or thionyl chloride [11,12], under various conditions, has also been reported.

Preparation of acetylated glycosyl bromide may be achieved similarly using dry hydrogen bromide in glacial acetic acid [13,14] or treatment of the peracetylated glycoside with bromine in the presence of red phosphorus [15]. The reaction of bromo- or iodotrimethylsilane at reflux also results in the corresponding bromides or iodides of mono- and di-saccharides [16,17].

We now report a new procedure for the halogenation of glycosyl peracetates under very mild conditions.

This approach, recently described by Dubac [18] for the halogenation of alcohols, involves a catalytic amount of bismuth(III) halides (5% mol) in the presence of halogenosilanes in dichloromethane. Bismuth(III) halides are good activators of the silicon–halide bond and convert halogenosilanes into halogenation reagents, presumably via halodealkylation of carboxylic esters.

In the first step, a SiX–BiX_3 interaction seems to occur, leading to a silicenium cation which binds to the oxygen atom of the carbonyl of the acetyl group [16]. The latter is removed by attack of BiX_4^- on the α-carbon atom in a nucleophilic substitution process (Scheme 1).

* Corresponding author.

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Table 1
Yields, melting points, optical rotation, FABMS, and analytical data for acetylated glycosyl halides

Acetylated α-D-glycopyranosyl halide	Reagent	Crude yield (%)	mp $[\alpha]_D$ (A: CH_2Cl_2; B: $CHCl_3$)	mp [lit.] $[\alpha]_D$ ($CHCl_3$)	FABMS: $[M+H]^+$, $[M+Na]^+$, $[2M+H]^+$	Analytical data
Glucopyranosyl						
bromide	$BiBr_3$	98	83–85 °C	88–89 °C [15]	413, 435, 820	Calcd: C, 40.89; H, 4.66
	Me_3SiBr		+187.5° (*c* 2, A)	+198° (*c* 2)		Found: C, 40.75; H, 4.57
chloride	$BiCl_3$	99	72–74 °C	75–76 °C [19]	367, 389, 733	Calcd: C, 45.85; H, 5.22
	$MeSiCl_3$		+159.8° (*c* 2.2, A)	+166° (*c* 1)		Found: C, 45.69; H, 5.16
iodide	BiI_3	99	102–105 °C	108 °C [16]	459, 481, 917	Calcd: C, 36.70; H, 4.18
	Me_3SiI		+218° (*c* 2.1, A)	+233° (*c* 1)		Found: C, 36.49; H, 4.12
Galactopyranosyl						
bromide	$BiBr_3$	99	79–81 °C	84–85 °C [20]	413, 435, 820	Calcd: C, 40.89; H, 4.66
	Me_3SiBr		+209.8° (*c* 3.8, B)	+217° (*c* 1)		Found: C, 40.72; H, 4.59
chloride	$BiCl_3$	98	71–73 °C	76 °C [7]	367, 389, 733	Calcd: C, 45.85; H, 5.22
	$MeSiCl_3$		+170.6° (*c* 3,3, B)	+176.9° (*c* 1)		Found: C, 45.70; H, 5.18
iodide	BiI_3	98	oil	oil [16]	459, 481, 917	Calcd: C, 36.70; H, 4.18
	Me_3SiI		+219.7° (*c* 2.9, B)	+235° (*c* 1.7)		Found: C, 36.09; H, 4.03
Mannopyranosyl						
bromide	$BiBr_3$	99	48–50 °C	53–54 °C [13]	413, 435, 820	Calcd: C, 40.89; H, 4.66
	Me_3SiBr		+121.0° (*c* 3.0, B)	132.2° (*c* 1)		Found: C, 40.68; H, 4.60
chloride	$BiCl_3$	98	75–77 °C	81 °C [7]	367, 389, 733	Calcd: C, 45.85; H, 5.22
	$MeSiCl_3$		+84.5° (*c* 1.1, B)	+90.8° (*c* 1)		Found: C, 45.72; H, 5.17
iodide	BiI_3	98	oil	oil [16]	459, 481, 917	Calcd: C, 36.70; H, 4.18
	Me_3SiI		+188.0° (*c* 1.2, B)	+190° (*c* 1)		Found: C, 36.20; H, 4.01
Maltosyl						
bromide	$BiBr_3$	90	109–111 °C	112–113 °C [21]	721 $[M+Na]^+$, 619 $[M-Br]^+$	Calcd: C, 44.65; H, 5.04
	Me_3SiBr		+174.0° (*c* 1.0, B)	+180° (*c* 1)		Found: C, 44.90; H, 5.24
chloride	$BiCl_3$	99	116–118 °C	122 °C [7]	677 $[M+Na]^+$, 642 $[M-Cl]^+$	Calcd: C, 47.68; H, 5.39
	$MeSiCl_3$		+152° (*c* 1.0, B)	+159° (*c* 1)		Found: C, 47.32; H, 5.34
iodide	BiI_3	90	oil [a]		769 $[M+Na]^+$, 577 $[M-I-OAc]^+$	Calcd: C, 41.84; H, 4.73
	Me_3SiI		+204° (*c* 1.0, B)			Found: C, 41.64; H, 4.68

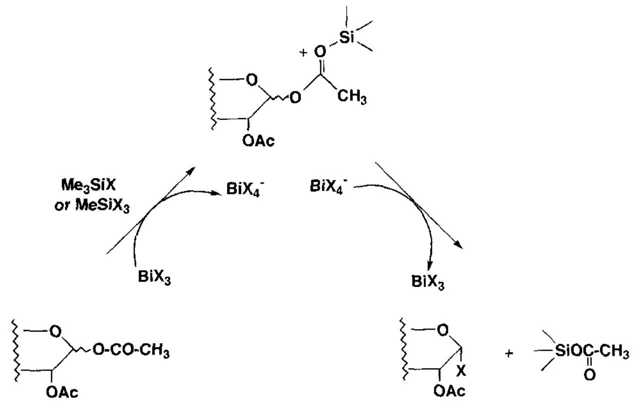
[a] This compound was particularly instable.

Table 2
^{1}H NMR spectral data for acetylated glycosyl halides

Acetylated glycopyranosyl halide	CH_3–CO–	H-1	H-2	H-3	H-4	H-5, H-6, H-6′
Glycopyranosyl						
bromide	2.0	6.55	4.75	5.5	5.1	4.1–4.2
	m, 12H	d, J 4 Hz	dd, J 4 Hz	t, J 10 Hz	t, J 10 Hz	m
chloride	2.0	6.25	4.9	5.5	5.1	4.1–4.2
	m, 12 H	d, J 4 Hz	dd, J 4 Hz	t, J 10 Hz	t, J 10 Hz	m
iodide	2.0	7.04	4.3	5.47	5.2	4.1–4.2
	m, 12 H	d, J 4 Hz	dd, J 4 Hz	t, J 10 Hz	t, J 10 Hz	m
Galactopyranosyl						
bromide	2.0	6.65	4.9	5.35	5.45	4.45, t, H-5, J 6 Hz
	m, 12 H	d, J 4 Hz	dd, J 4 Hz	dd, J 4 Hz	d, J 3 Hz	4.15, m, H-6, H-6′
chloride	2.0	6.3	5.2	5.35	5.45	4.45, t, H-5, J 6 Hz
	m, 12 H	d, J 4 Hz	dd, J 4 Hz	dd, J 4 Hz	d, J 3 Hz	4.1, m, H-6, H-6′
iodide	2.0	7.05	4.35	5.25	5.45	4.2
	m, 12 H	d, J 4 Hz	dd, J 4 Hz	dd, J 4 Hz	d, J 3 Hz	m
Mannopyranosyl						
bromide	2.0	6.25	5.35	5.65	5.25	4.15, m, H-5
	m, 12 H	d, J 1 Hz	dd, J 2 Hz	dd, J 3 Hz	m	4.05, dd, J 2 Hz, H-6
						4.25, dd, J 5 Hz, H-6′
chloride	2.0	5.95	5.35	5.55	5.3	4.1–4.2
	m, 12 H	d, J 1 Hz	dd, J 2 Hz	dd, J 3 Hz	m	m
iodide	2.0	6.65	5.45	5.75	5.35	3.95, m, H-5
	m, 12 H	d, J 1 Hz	dd, J 2 Hz	dd, J 3 Hz	m	4.1, dd, J 2 Hz, H-6
						4.35, dd, J 5 Hz, H-6′

Table 3
^{1}H NMR spectral data for acetylated maltosyl halides

Acetylated maltosyl halide	CH_3–CO–	H-4	2 H-6, 2 H-6′, H-5′, H-4′	H-5	H-2′	H-2	H-3′	H-1′	H-3	H-1
maltosyl bromide	2.0	3.6	4.0	4.4	4.6	4.9	5.1	5.4	5.4	6.5
	m, 21 H	t, *J* 10 Hz	m	m	dd, *J* 4 Hz	dd, *J* 4 Hz	t, *J* 10 Hz	d, *J* 4 Hz	t, *J* 10 Hz	d, *J* 4 Hz
maltosyl chloride	2.0	3.7	4.0–4.3	4.5	4.8	4.95	5.1	5.3	5.45	6.2
	m, 21 H	t, *J* 10 Hz	m	m	dd, *J* 4 Hz	dd, *J* 4 Hz	t, *J* 10 Hz	d, *J* 4 Hz	t, *J* 10 Hz	d, *J* 4 Hz
maltosyl iodide	2.0	3.7	3.9–4.2	4.4	4.6	4.9	5.0	5.3	5.4	6.9
	m, 21 H	t, *J* 10 Hz	m	m	dd, *J* 4 Hz	dd, *J* 4 Hz	t, *J* 10 Hz	d, *J* 4 Hz	t, *J* 10 Hz	d, *J* 4 Hz



Scheme 1. Proposed mechanism for halogenation of glycose acetates with bismuth(III) halides.

This reaction was applied to D-glucopyranose, D-galactopyranose, D-mannopyranose, and maltose peracetates (Table 1). The procedure was carried out at room temperature in dichloromethane and was readily performed in the presence of 5% mol of bismuth(III) halides. The reaction was monitored by TLC and reached completion after 0.5–2 h. The yield was generally equal to 95% or higher. The workup is easy and the products are sufficiently pure for further use without purification. In each case, chemical-shift data showed that only the α-anomer of the glycosyl halides was formed during halogenation.

All structural assignments were ascertained by NMR spectroscopy and by FABMS (Tables 2 and 3). The reaction was similarly applied to 2,3,4,6-tetra-*O*-acetyl-D-glucopyranose resulting in the corresponding glucopyranosyl chloride or bromide in almost quantitative yield.

Taking into account that the reaction is carried out very easily under mild conditions and gives a rather pure compound (without chromatography) in good yield, the present method is an interesting alternative in the synthesis of glycosyl halides.

1. Experimental

General methods.—Melting points were determined using a Büchi 530 apparatus. ^{1}H NMR spectra were determined with an AC 250 Bruker spectrometer. FAB mass spectra were recorded in the positive ion mode on a JEOL DX 300 mass spectrometer, with *m*-nitrobenzyl alcohol (NBA) as matrix. E. Merck Silica Gel 60 F_{254} (0.25 mm) plates were employed for analytical TLC. Compounds were revealed by UV light (254 nm), or iodine and 20% aq H_2SO_4 sprayings. Microanalyses were performed in the analytical department of the CNRS (ENSCM-Montpellier).

General procedure for the preparation of acetylated glycosyl halides.—To a stirred solution of a pentaacetylated hexopyranose (1 equiv, 0,5 g) or octaacetylated disaccharide (1 equiv) and BiX_3 (X = Cl, Br, I) (0.05 equiv) in 5 mL CH_2Cl_2, was added under N_2, $(CH_3)_3SiX$ (4 equiv) (X = Br or I) or CH_3SiX_3 (X = Cl). The reaction was stirred at room temperature and monitored by TLC (reaction times between 0.5 and 2 h) then poured into cold satd $NaHCO_3$ soln and extracted twice with CH_2Cl_2. The combined organic layers were dried over anhyd Na_2SO_4. Filtration and evaporation of the solvent under reduced pressure gave the desired compound in > 95% yield (Tables 1–3).

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