Carbohydrate Research, 48 (1976) 139–142
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Note

Cleavage of per-*O*-acetylated *N*-arylglycopyranosylamines with dichloromethyl methyl ether*

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(Received July 22nd, 1975; accepted for publication in revised form, December 31st, 1975)

Per-*O*-acetylated glycosides of various types can be cleaved selectively with dichloromethyl methyl ether to give the acetylated glycosyl chlorides in good yield[1–5]. We now report an extension of this method to *N*-arylglycopyranosylamine derivatives. As the reactivity of these glycosylamines towards electrophilic reagents is greater than that of the oxygen analogues, it was expected that their glycosyl bonds would be cleaved easily with dichloromethyl methyl ether.

We have found that various per-*O*-acetylated *N*-arylglycopyranosylamines are readily converted by the dichloromethyl methyl ether–zinc chloride reagent into the corresponding acetylated glycopyranosyl chlorides. Thus, 2,3,4,6-tetra-*O*-acetyl-*N*-*p*-nitrophenyl-D-glucopyranosylamine afforded *p*-nitroaniline and 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl chloride. However, other monosaccharide glycosylamines gave complicated reaction mixtures from which the sugar component could not be isolated by crystallization.

In the cleavage reactions of the per-*O*-acetylated *N*-arylglycosylamine derivatives of lactose and cellobiose, the corresponding acetylated α-glycosyl chlorides were obtained in satisfactory yields, independently of the type of aglycon. However, the maltose derivative gave a syrupy glycosyl chloride which could be converted into the crystalline octa-*O*-acetyl-β-maltose. The results of these experiments are summarized in Tables I and II.

The amine component of the glycoside was converted into a complex mixture of products, and the oxalic acid test[6] revealed the presence of aryl isocyanide. In the acidic reaction mixture containing zinc chloride, most of the highly reactive aryl isocyanide reacts further[7].

No aryl isocyanide was formed from the weakly basic *N*-*p*-nitrophenyl derivatives, and *p*-nitroaniline was isolated. The presence of *p*-nitroformanilide in the reaction mixture was also demonstrated. Thus, it is postulated that the primary decomposition product of the aglycon is the corresponding formanilide derivative

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*Selective Cleavage of Glycosides: Part VI. For Part V, see Ref. 5.

TABLE I

CLEAVAGE OF HEPTA-*O*-ACETYL-*N*-ARYL-LACTOSYLAMINES[a]

Aryl group[b]	*Reaction conditions*		*Reaction product Hepta-O-acetyl-α-lactosyl chloride*[c]				
	Time (min)	*Temp. (degrees)*	*Yield (%)*	*M.p. (degrees)*	$[\alpha]_D$[d] *(degrees)*	*Found Cl*	*Calc. Cl*
Phenyl	30	65	43	140–141	+85	5.49	5.42
p-Tolyl	40	75	44	140–141	+89	5.60	
p-Bromophenyl	60	70	57	144–145	+88	5.62	
p-Chlorophenyl	45	70	57	142–143	+89	5.72	
p-Nitrophenyl	45	70	41	145	+87	5.56	

[a]Anomer mixtures containing small amounts of α anomer. [b]The amount of the starting material was 1 g. [c]Lit.[1]: m.p. 121°, 144°; $[\alpha]_D$ +83.9° (chloroform). [d]In chloroform.

TABLE II

CLEAVAGE OF HEPTA-*O*-ACETYL-*N*-ARYL-CELLOBIOSYLAMINES[a]

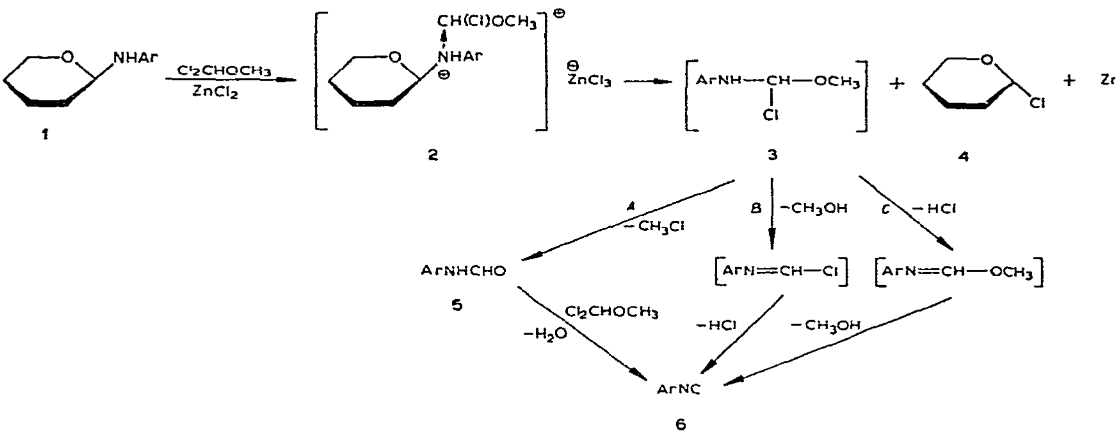
Aryl group[b]	*Reaction conditions*		*Reaction product Hepta-O-acetyl-α-cellobiosyl chloride*[c]				
	Time (min)	*Temp. (degrees)*	*Yield (%)*	*M.p. (degrees)*	$[\alpha]_D$[d] *(degrees)*	*Found Cl*	*Calc. Cl*
Phenyl	50	65	65	189–190	+72	5.48	5.42
p-Tolyl	60	70	59	178–179	+74	5.63	
p-Bromophenyl	45	70	69	190–192	+74	5.75	
p-Chlorophenyl	60	65	69	191–192	+71	5.65	
p-Methoxyphenyl	40	70	68	182–183	+73	5.36	
p-Nitrophenyl	40	75	52	191–192	+72	5.47	

[a]Anomer mixtures containing small amounts of α anomer. [b]The amount of the starting material was 1 g. [c]Lit.[13]: m.p. 178°, 187°, 200°; $[\alpha]_D$ +73° (chloroform). [d]In chloroform.

which, by the action of dichloromethyl methyl ether, is dehydrated to yield the aryl isocyanide; the reagent did not dehydrate *p*-nitroformanilide.

The selective decomposition of per-*O*-acetylated *N*-arylglycopyranosylamines (**1**) by dichloromethyl methyl ether–zinc chloride could involve an ammonium-type complex **2**. Decomposition of **2** yields the glycosyl chloride **4** and the cleavage product **3** of the aglycon which is then converted into the corresponding formanilide derivative **5**. Loss of water from **5** yields **6** (Path *A*). The formation of **6** from **3** may also occur through paths *B* and *C*.

Hydrogen chloride is evolved in the reaction between dichloromethyl methyl ether and zinc chloride[1]. However, it was found that although zinc chloride–hydrogen chloride cleaves the glycosidic linkage of the *N*-arylglycosylamine derivatives of the disaccharides, this reaction is not selective and no crystalline sugar derivative could be isolated. These observations indicate that a reaction mediated by zinc chloride–hydrogen chloride does not occur.



$$\text{ArNHCHO} + \text{Cl}_2\text{CHOCH}_3 \xrightarrow[\text{CHCl}_3]{\text{Et}_3\text{N}} \text{ArNC} + \text{HCOOCH}_3 + 2\,\text{HCl}$$

Dichloromethyl methyl ether, in the presence of mercuric chloride or boron trifluoride etherate[8], cleaves only partly and non-selectively the glycosidic linkage of per-*O*-acetylated *N*-arylglycosylamines.

EXPERIMENTAL

Anomeric per-*O*-acetylated *N*-arylglycosylamines enriched in β anomers were prepared by known methods. The purity of the product was checked by t.l.c. on Silica Gel G, using light petroleum–acetone–ethyl acetate (4:1:1) and light petroleum–acetone (5:1), with detection by charring with 5% sulphuric acid in ethanol. Nitrogen-containing substances were located with the glucose–phosphoric acid reagent[9]· Solutions were dried over sodium sulphate and concentrated under diminished pressure at <40°.

*Cleavage of per-*O*-acetylated *N*-aryl-lactosyl- and -cellobiosyl-amine.* — Per-*O*-acetylated *N*-arylglycosylamine (1 g) was treated with dichloromethyl methyl ether (2.5–3.0 ml) and anhydrous zinc chloride (0.1 g) under the conditions specified in Tables I and II. The reaction mixture was then concentrated to dryness and the residue was dissolved in chloroform (20 ml); *p*-nitroaniline and *p*-nitroformanilide could be detected (t.l.c.) at this stage. The solution was washed with ice-cold water, aqueous potassium hydrogen carbonate, and ice-cold water until neutral. The presence of aryl isocyanide at this stage was proved by the formation of carbon dioxide on shaking the solution with aqueous oxalic acid[6]; no aryl isocyanide was formed from *p*-nitrophenyl derivatives. The dried chloroform solution was concentrated and the residue was recrystallized from ethanol (see Tables I and II). For the *p*-nitrophenyl derivatives, *p*-nitroaniline (~50%) could be isolated from the mother liquor.

*Cleavage of hepta-*O*-acetyl-*N*-arylmaltosylamine.* — The title compound (1 g) was cleaved as described above, and the crude glycosyl halide (the presence of which was confirmed by t.l.c.) was converted into the peracetate with acetic anhydride (10 ml) and silver acetate (1 g) at 100°. The mixture was worked-up in the usual manner and the product was crystallized from ethanol (twice) to give octa-*O*-acetyl-β-maltose (30%), m.p. 157–159°, $[\alpha]_D$ +62° (*c* 1, chloroform); lit.[10]: m.p. 158–161°, $[\alpha]_D$ +62.6° (chloroform).

Reactions of formanilide. — (*a*) A solution of formanilide (10 g, 82.6 mmol) in anhydrous chloroform (50 ml) was treated for 20 min with triethylamine (25 ml) and dichloromethyl methyl ether (10.44 g, 90.8 mmol), the temperature of the reaction mixture being kept at 40–50°. The mixture was washed with aqueous potassium hydrogen carbonate and ice–water, then dried, and fractionally distilled to give phenyl isocyanide (1.93 g, 23%), b.p. 75–80°/25 torr. The product was converted by the Passerini reaction[11] into diphenylformamidine, m.p. and mixture m.p.139–140°; lit.[12] m.p. 138–140°.

(*b*) Formanilide (0.13 g) was heated with dichloromethyl methyl ether (3 ml) and anhydrous zinc chloride (0.1 g) at 70° for 35–40 min. The mixture was concentrated and the residue, after being triturated in water (5 ml), was extracted with ether (10 ml). The extract, which contained phenyl isocyanide (oxalic acid test[6]), was neutralized by washing with aqueous potassium hydrogen carbonate. Formanilide and aniline could then be detected (t.l.c.).

(*c*) *p*-Nitroformanilide (0.5 g) was treated with dichloromethyl methyl ether (4 ml) and anhydrous zinc chloride (0.1 g) on a boiling water-bath for 1 h. The reaction mixture was then concentrated to dryness and the residue was dissolved in chloroform–acetone (3:1, 20 ml); the oxalic acid test[6] indicated *p*-nitrophenyl isocyanide to be absent. The solution was then neutralized with solid potassium hydrogen carbonate and concentrated to dryness, and the residue was crystallized from ethanol (8 ml) to give *p*-nitroformanilide (0.2 g, 40%), m.p. and mixture m.p. 198°. *p*-Nitroanaline (0.22 g, 52%), m.p. 144–145°, was isolated from the mother liquor.

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