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Note

Oxidation of stannylene derivatives of carbohydrates using 1,3-dibromo-5,5-dimethylhydantoin

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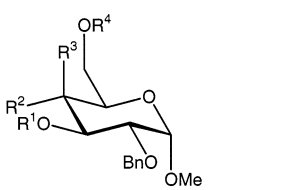
Abstract

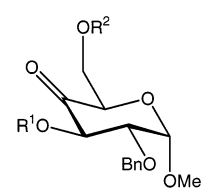
1,3-Dibromo-5,5-dimethylhydantoin (DBDMH) has been used to oxidize stannylene derivatives of monosaccharides to give hydroxy-ketones thereof. Oxidations could be performed rapidly and in good-to-excellent yields. The oxidizing reagent DBDMH thus provides a convenient alternative to existing methods.

Keywords: Carbohydrates; Oxidation; Hydantoin

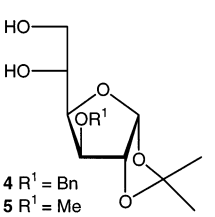
In two papers David and co-workers showed that regioselective oxidations of carbohydrate dialkyl stannylene acetals with bromine effectively produced α- or β-hydroxy-ketones [1,2]. Later, it was demonstrated that *N*-bromosuccinimide (NBS), in comparison with bromine, resulted in improved yields of α-hydroxy-ketones from carbohydrate diols [3]. These methods have been reviewed recently [4,5]. However, in our hands bromine oxidation of the dibutyl stannylene acetal derived from **2** [6] gave a 55% yield of hydroxyketone **6**. Using the same stannylene derivative, the oxidation with NBS gave a 75% yield of **6** and 15% of starting material after 1 h.



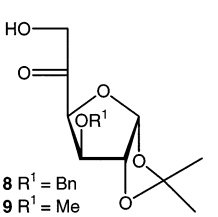
1 R^1 = Bn, R^2 = H, R^3 = OH, R^4 = H
2 R^1 = Bn, R^2 = OH, R^3 = H, R^4 = H
3 R^1 = H, R^2 = H, R^3 = OH, R^4 = Bn



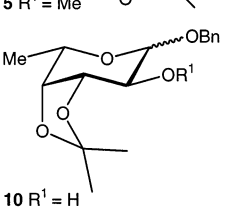
6 R^1 = Bn, R^2 = H
7 R^1 = H, R^2 = Bn



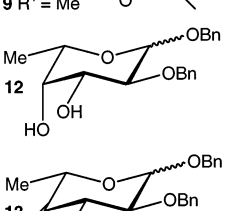
4 R^1 = Bn
5 R^1 = Me



8 R^1 = Bn
9 R^1 = Me



10 R^1 = H
11 R^1 = Bn



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1,3-Dibromo-5,5-dimethylhydantoin (DBDMH) has been used for aromatic brominations [7,8]. It should also be possible to use this reagent for oxidation reactions as an alternative to bromine or NBS. Mangholz and Vasella [9] used DBDMH in the oxidation of, e.g., *N′*-(2,3,5-tri-*O*-benzyl-α,β-D-ribofuranosyl)toluene-4-sulfonohydrazide in the presence of triethylamine as a base to give (*Z*)-*N′*-(2,3,5-tri-*O*-benzyl-D-ribofuranosylidene)toluene-4-sulfonohydrazide.

In the present study we have investigated the use of DBDMH in the oxidation of carbohydrate-activated stannylene acetals. Since DBDMH contains two bromine equivalents that can be used for oxidation, we employed a molar ratio of 0.55 and 1.0. For a comparison with the above oxidations, when **1** was activated as the dibutyl stannylene acetal and subsequently oxidized at room temperature (rt) with a 0.55 molar ratio of DBDMH, a yield of 95% of **6** was obtained within 5 min (Table 1). Compounds **2** [6], **3** [10], **4** [3] and **5** [3] were treated in the same way to give the resulting products **6**–**9**, in good-to-excellent yields (Table 1). Substrate **12** was prepared according to standard methods, viz. benzylation of the benzyl fucoside **10** [11], and subsequent deprotection of derivative **11** by acidic hydrolysis of the isopropylidene group furnished diol **12** as an α/β mixture in 83% yield, over two steps. The oxidation of **12** was performed on the α/β mixture, which led to **13** in 86% yield. NMR and MS spectral data were in agreement with postulated structures (for **6** and **7** see Ref. [3]).

The use of an equimolar ratio of DBDMH and diol led to very rapid oxidation. The reaction was complete within 1 min for all substrates. The use of a lower molar ratio of DBDMH, having two *N*-bromo groups, is sufficient since the yields using either 0.55 or an equimolar ratio of DBDMH were similar (data not shown). However, for the lower molar ratio, the reaction times are still on the order of a few minutes. In summary, DBDMH is an excellent, inexpensive and conveniently handled substitute for NBS in the oxidation of stannylene acetals of carbohydrate diols since improved yields can be obtained.

Table 1
Summary of oxidations using 0.55 molar equivalents of DBDMH

Substrate	Oxidation position	Time (min)	Product	Yield (%)
1	4	5	**6**	95
2	4	15	**6**	90
3	4	2	**7**	89
4	5	2	**8**	94
5	5	2	**9**	90
12	4	2	**13**	86

1. Experimental

General methods.—Materials were obtained from commercially available sources and used without further purification. The 1,3-dibromo-5,5-dimethylhydantoin (DBDMH) and the dibutyltin oxide were purchased from Aldrich. Solvents were dried and purified using standard methods. Concentrations were performed under reduced pressure at temperatures < 40 °C (bath). The oxidation and work-up of the oxidation products were conducted at rt if not stated otherwise. ^{13}C NMR spectra were acquired at 25 °C in $CDCl_3$ at 67 MHz on a JEOL NMR spectrometer and referenced to internal $SiMe_4$ (δ_C 0.00). High-resolution fast atom bombardment mass spectrometry (HRMS) was performed in the positive-mode at a resolution of 10,000 on a JEOL SX-102 using 3-nitrobenzyl alcohol as a matrix.

Methyl 2,3-di-O-*benzyl*-α-D-*xylo-hexopyranosid-4-ulose* (**6**).—The diol **1** (494 mg, 1.32 mmol), dibutyltin oxide (394 mg, 1.58 mmol) 1.2 equiv and 2 g of 3 Å molecular sieves were mixed in toluene or methanol (15 mL), and heated to reflux. After 3 h the solvent was concentrated under reduced pressure, and the stannylene acetal complex was dried for 0.5–1 h in vacuo. The stannylene complex was dissolved in $CHCl_3$ (10 mL) and DBDMH (0.55 equivalents) was added as a solid in one portion. After 30 s the mixture turned orange. The reaction was over after 5 min (TLC). The orange color disappeared during the course of the reaction. When one equivalent was added the reaction mixture became deep-orange within 15 s and oxidation was finished in < 1 min. The reaction mixture was filtered through

Celite into a 10% $Na_2S_2O_3$ aq. solution (10 mL). The layers were separated and the organic phase was washed twice with water (10 mL), dried and concentrated in vacuo. The remaining residue was purified by column chromatography on SiO_2 using toluene–EtOAc 6:1, followed by 3:1, which gave **6** as a colorless syrup (466 mg, 95%); $[\alpha]_D$ 75° (*c* 1.5, $CHCl_3$); ^{13}C NMR: δ 56.1, 60.6, 72.8, 73.9, 74.5, 80.0, 82.5, 98.5, 127.9–128.5, 137.6, 137.7, 203.8. HRMS: *m/z* calcd for $[M + Na]^+$ 395.1471, Found: 395.1493.

Methyl 2,3-di-O-*benzyl*-α-D-xylo-*hexopyranosid-4-ulose* (**6**).—The diol **2** (451 mg, 1.21 mmol) was oxidized as described above, which gave **6** (404 mg, 90%). For spectral data see above.

Methyl 2,6-di-O-*benzyl*-α-D-xylo-*hexopyranosid-4-ulose* (**7**).—The diol **3** (270 mg, 0.72 mmol) was oxidized as described for diol **1** to give **7** as a colorless syrup (239 mg, 89%); ^{13}C NMR: δ 56.2, 67.2, 71.5, 73.4, 73.6, 76.0, 81.4, 98.3, 127.6–137.8, 203.0. HRMS: *m/z* calcd for $[M + Na]^+$ 395.1471, Found: 395.1469.

3-O-*Benzyl-1,2*-O-*isopropylidene*-α-D-xylo-*hexofuranos-5-ulose* (**8**).—Compound **4** (618 mg, 1.99 mmol) was oxidized as described for diol **1**, to give **8** (577 mg, 94%). All spectral data were in agreement with those reported by Kong and Grindley [3]. ^{13}C NMR: δ 26.3, 26.9, 68.2, 72.6, 81.7, 83.4, 84.5, 106.0, 112.6, 127.6–128.6, 136.5, 208.2.

1,2-O-*isopropylidene-3*-O-*methyl*-α-D-xylo-*hexofuranos-5-ulose* (**9**).—Compound **5** (530 mg, 2.26 mmol) was oxidized as described for diol **1**, to give **9** (473 mg, 90%). All spectral data were in agreement with data reported by Kong and Grindley [3]. ^{13}C NMR: δ 26.3, 27.0, 58.4, 68.2, 81.2, 84.5, 85.8, 106.0, 112.6, 208.0.

Benzyl 2-O-*benzyl*-α,β-L-xylo-*hexopyranosid-4-ulose* (**13**).—A solution of **10** (1.20 g, 4.08 mmol) and benzyl bromide (0.63 ml, 5.30 mmol) in DMF (10 mL) was added to a cooled (0 °C) suspension of NaH (196 mg, 5.83 mmol) (60% in oil) in DMF (15 mL). The ice bath was removed, and the reaction mixture was stirred at ambient temperature for 1 h. The reaction was quenched with MeOH (1 mL) followed by water (25 mL). The aqueous layer was extracted twice with toluene (25 mL). Thereafter, the combined organic layers were dried ($NaSO_4$), filtered and concentrated. Crude **11** was dissolved in $CHCl_3$ (20 mL) and trifluoroacetic acid 90% aq. (5 mL) was added under stirring. After 30 min water (20 mL) was added, the mixture was stirred for 5 min, and the layers were separated. The water layer was extracted once with $CHCl_3$ (10 mL), and the combined organic layers were washed twice with saturated $NaHCO_3$ (20 mL), dried ($NaSO_4$), filtered and concentrated in vacuo. Purification of the residue by flash chromatography (SiO_2) gave **12** as a white solid (1.16 g, 83%) as an α:β mixture (2:1). ^{13}C NMR: δ 16.1, 16.2, 65.7, 69.3, 69.4, 70.3, 70.8, 71.3, 71.6, 72.2, 73.5, 74.6, 76.2, 79.0, 95.4 (C-1α), 102.3 (C-1β), 127.7–128.5, 137.4, 137.9, 138.0.

Compound **12** (303 mg, 0.88 mmol) was oxidized as described for diol **1**, to give **13** as a colorless syrup (259 mg, 86%); ^{13}C NMR: δ 13.6, 14.5, 65.3, 68.3, 70.3, 71.0, 73.0, 73.1, 74.1, 75.9, 77.2, 82.1, 84.6, 96.2 (C-1α), 101.2 (C-1β), 125.3–129.0, 136.9, 137.9, 204.7. HRMS: *m/z* calcd for $[M + Na]^+$ 365.1365, Found: 365.1328.

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