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Note

A mild and rapid conversion of sugar dithioacetals into the corresponding dimethyl acetals by *N*-bromosuccinimide–methanol

DUŠAN MILJKOVIĆ*, MIRJANA POPSAVIN, VELIMIR POPSAVIN, NADA VUKOJEVIĆ,
Institute of Chemistry, Faculty of Sciences, University of Novi Sad, Dr. I. Djuričića 4a, 21000 Novi Sad (Yugoslavia)

JÁNOS HARANGI
Institute of Biochemistry, L. Kossuth University, H-4010 Debrecen (Hungary)

AND MARIANNA MÁK
Central Research Institute of Chemistry, Hungarian Academy of Sciences, H-1525 Budapest (Hungary)

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The known procedures for the conversion of carbohydrate dithioacetal derivatives into the corresponding dimethyl acetals[1–4] have certain disadvantages, including long times of reaction at elevated temperature and removal of the last traces of mercury salts. These procedures are not satisfactory for dithioacetals having reactive functional groups.

The recent findings[5] that some sugar dialkyl dithioacetals undergo a smooth oxidative hydrolysis to the corresponding *aldehydo*-sugars on treatment with *N*-bromosuccinimide prompted an investigation of the possible use of this reagent for direct dethioacetalation of diethyl dithioacetal derivatives (**3**, **4**, and **9**) of D-arabinose and D-glucose into the corresponding dimethyl acetals (**5**, **6**, and **10**).

N-Bromosuccinimide in dry methanol at 0° rapidly converted **3**, **4**, and **9** into the corresponding dimethyl acetal derivatives. Thus, 2,3,4-tri-*O*-acetyl-5-*O*-toluene-*p*-sulfonyl-D-arabinose diethyl dithioacetal (**3**) gave 70% of **5**. Treatment[6] of D-arabinose diethyl dithioacetal (**1**) with mesyl chloride (triethylamine, dichloromethane, 0°) afforded the unstable tetramesylate **4**, which was promptly treated with *N*-bromosuccinimide in methanol to give **6** (68% from **1**). Treatment of **7** with ethanethiol (conc. hydrochloric acid, room temperature) gave the unstable dithioacetal **8** which, with 2,2-dimethoxypropane (toluene-*p*-sulfonic acid, room temperature)[7], gave 5,6-di-*O*-benzoyl-2,4-*O*-isopropylidene-3-*O*-toluene-*p*-sul-

*Author for correspondence.

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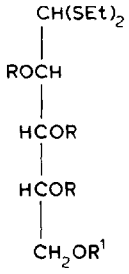
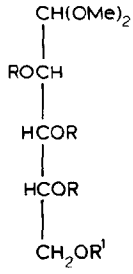
fonyl-D-glucose diethyl dithioacetal (**9**, 60% from **7**). Reaction of **9** with *N*-bromosuccinimide in methanol gave 76% of **10**.

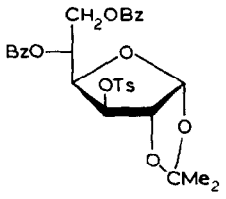
An advantage of the new dethioacetalation procedure is the short time of reaction at low temperatures, so that dithioacetal–dimethyl acetal conversions of sugar derivatives possessing additional highly reactive functional groups can be effected.





1 R = R¹ = H
2 R = H, R¹ = Ts
3 R = Ac, R¹ = Ts
4 R = R¹ = Ms

5 R = Ac, R¹ = Ts
6 R = R¹ = Ms



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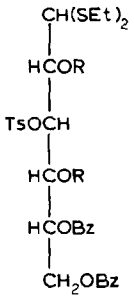
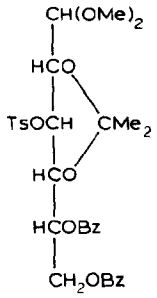


8 R = H
9 R = Me_2C



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EXPERIMENTAL

General methods. — Melting points (uncorrected) were determined with a Büchi SMP-20 apparatus. Optical rotations were measured on solutions in chloroform with a Polamat A (Karl-Zeiss Jena) automatic polarimeter. The ^1H- and ^{13}C-n.m.r. spectra were recorded on solutions in $CDCl_3$ (internal Me_4Si) with a Brüker WP 200 SY instrument. Mass spectra were obtained with an MS-902 mass spectrometer (70 eV, 190°). T.l.c. was performed on Kieselgel 60 (Merck), using

A, benzene–acetone (21:4); *B*, dichloromethane–ethyl acetate (8:1); *C*, benzene–acetone (9:1); and *D*, cyclohexane–acetone (7:3).

*2,3,4-Tri-*O*-acetyl-5-*O*-toluene-*p*-sulfonyl-*D*-arabinose diethyl dithioacetal* (**3**). — To a solution of 5-*O*-toluene-*p*-sulfonyl-D-arabinose diethyl dithioacetal[8] (2.6 g, 6.34 mmol) in dry pyridine (12 mL) was added acetic anhydride (24 mL) (at 0°). The mixture was stored at room temperature for 24 h, then poured onto ice (~200 g), acidified with hydrochloric acid (5:1) to pH 2, and extracted with dichloromethane (3 × 50 mL). The combined extracts were washed with saturated aq. sodium hydrogencarbonate and water, dried (Na_2SO_4), and concentrated. Column chromatography [silica gel (60 g), cyclohexane–acetone (19:1, 9:1)] of the residue (3.3 g) gave **3** (3.12 g, 92%) as a colorless syrup, $[\alpha]_D$ +21° (*c* 6.6), R_F 0.8 (solvent *A*). Mass spectrum: *m/z* 536 (0.1, M^+), 460 (0.4, M^+ − AcOH), 172 (100, $HOTs^+$), 135 (65, $CH(SEt)_2^+$), 91 (100, $C_6H_4CH_3^+$).

*2,3,4-Tri-*O*-acetyl-5-*O*-toluene-*p*-sulfonyl-*D*-arabinose dimethyl acetal* (**5**). — A suspension of *N*-bromosuccinimide (20.42 g, 114.74 mmol) in dry methanol (40 mL) was added in portions to a solution of **3** (10.25 g, 19.12 mmol) in dry methanol (40 mL) at −10°. The mixture was stirred vigorously for 10 min, then poured onto ice (800 g), and stirred for 0.5 h at room temperature. The resulting suspension was extracted with chloroform (5 × 100 mL), and the combined extracts were washed successively with saturated aq. Na_2SO_3, aq. $NaHCO_3$, and water, dried (Na_2SO_4), and concentrated. Column chromatography [silica gel (80 g), benzene–acetone (19:1)] of the residue (9 g) gave **5** (6.37 g, 70%), isolated as a colorless syrup, $[\alpha]_D$ +20° (*c* 2.1), R_F 0.48 (solvent *A*). N.m.r. data: ^1H, δ 7.775–7.162 (m, 4 H, aromatic), 5.4 (dd, 1 H, $J_{3,4}$ 8.5, $J_{2,3}$ 2.8 Hz, H-3), 5.075 (dd, 1 H, $J_{1,2}$ 6.5 Hz, H-2), 5.0 (ddd, 1 H, $J_{4,5a}$ 5, $J_{4,5b}$ 3 Hz, H-4), 4.2 (d, 1 H, H-1), 4.125 (dd, 1 H, $J_{5a,5b}$ 11.5 Hz, H-5b), 3.387 (dd, 1 H, H-5a), 3.3 and 3.225 (2 s, 6 H, 2 OMe), 2.375 (s, 3 H, Ts*Me*), 2.0 and 1.95 (2 s, 9 H, 3 Ac); ^{13}C, δ 129.814–128.034 (aromatic), 101.967 (C-1), 68.775, 68.478, and 68.049 (C-2,3,4), 67.172 (C-5), 55.43 and 53.444 (2 OCH_3), 21.579 and 20.604 (3 CH_3CO_2). Mass spectrum: *m/z* 476 (0.4; M^+), 75 [100; $CH(OMe)_2^+$].

*2,3,4,5-Tetra-*O*-methanesulfonyl-*D*-arabinose dimethyl acetal* (**6**). — To a stirred solution of D-arabinose diethyl dithioacetal[9] (4 g, 15.6 mmol) in dry dichloromethane (80 mL) at −10° was added freshly distilled triethylamine (13.28 mL, 56.03 mmol) and mesyl chloride (7.48 mL, 96.03 mmol), whereupon the temperature was raised to 0°. Stirring was continued for 10 min, and the mixture was diluted with dichloromethane (100 mL), washed successively with cold water, aq. hydrochloric acid (10%), saturated aq. $NaHCO_3$, and saturated aq. NaCl, dried (Na_2SO_4), and concentrated at ~25° (bath). The crude product **4** [8.98 g, an unstable yellow oil, R_F 0.65 (solvent *B*)] was dissolved immediately in dry methanol (40 mL), the solution was cooled to −4°, and a suspension of *N*-bromosuccinimide (8.34 g, 46.8 mmol) in dry methanol (30 mL) was added with stirring that was continued for an additional 3 min at 0°. Work-up, as described for **5**, gave crude **6**, isolated as a yellow oil. Crystallization from dichloromethane–hexane gave **6** (5.4

g, 68.3%), m.p. 108°, $[\alpha]_D$ +34° (*c* 2.7), R_F 0.46 (solvent *B*). N.m.r. data: ^1H, δ 5.375–5.225 (m, 2 H, H-3,4), 4.775 (dd, 1 H, $J_{2,3}$ 6.25, $J_{1,2}$ 4 Hz, H-2), 4.65 (d, 1 H, H-1), 4.65 (dd, 1 H, $J_{5a,5b}$ 11.5, $J_{4,5a}$ 3 Hz, H-5a), 4.425 (dd, 1 H, $J_{4,5b}$ 7.5 Hz, H-5b), 3.556 and 3.534 (2 s, 6 H, 2 OMe), 3.237, 3.202, 3.188, and 3.132 (4 s, 12 H, 4 Ms); ^{13}C, δ 103.022 (C-1), 77.219, 76.993, and 76.176 (C-2,3,4), 65.774 (C-5), 56.611 and 55.901 (2 OCH_3), 38.722, 38.331, 38.197, and 37.145 (4 CH_3SO_2).

Anal. Calc. for $C_{11}H_{14}O_{24}S_4$: C, 25.95; H, 4.71; S, 25.15. Found: C, 25.69; H, 4.87; S, 24.11.

*5,6-Di-*O*-benzoyl-2,4-*O*-isopropylidene-3-*O*-toluene-*p*-sulfonyl-*D*-glucose diethyl dithioacetal* (**9**). — To a solution of 5,6-di-*O*-benzoyl-1,2-*O*-isopropylidene-3-*O*-toluene-*p*-sulfonyl-α-D-glucofuranose[10] (0.1783 g, 0.31 mmol) in ethanethiol (4 mL) was added conc. hydrochloric acid (2 mL). The mixture was stirred for 5 days at room temperature, $PbCO_3$ (8 g) and water (30 mL) were added, and stirring was continued for 0.5 h at room temperature. The precipitate was collected and washed with dichloromethane (60 mL). The organic phase was separated, the aqueous phase was re-extracted with dichloromethane (3 × 20 mL), and the combined extracts were dried (Na_2SO_4) and concentrated. Column chromatography [silica gel (30 g), cyclohexane–acetone (4:1)] of the crude product gave **8** (0.159 g, 79.85%), isolated as a colorless unstable syrup, $[\alpha]_D$ −34° (*c* 1.2). A solution of freshly isolated **8** (0.1364 g, 0.21 mmol), 2,2-dimethoxypropane (5 mL), and toluene-*p*-sulfonic acid (0.013 g) was stirred for 22 h at room temperature, then diluted with dichloromethane (50 mL), washed with saturated aq. $NaHCO_3$ (2 × 10 mL), dried (Na_2SO_4), and concentrated. Column chromatography [silica gel (5 g), cyclohexane–acetone (9:1)] of the residue (0.15 g) gave **9** (0.105 g, 72.3%), isolated as a colorless syrup, $[\alpha]_D$ −66° (*c* 1), R_F 0.65 (solvent *C*). N.m.r. data: ^1H, δ 8.087–7.3 (m, 14 H, aromatic), 5.467 (bs, 1 H, H-3), 5.215 (ddd, 1 H, $J_{5,6a}$ 3, $J_{5,6b}$ 2, $J_{4,5}$ 9 Hz, H-5), 4.795 (dd, 1 H, $J_{6a,6b}$ 12.5 Hz, H-6b), 4.585 (dd, 1 H, H-6a), 4.41 (dd, 1 H, $J_{4,3}$ ~1 Hz, H-4), 4.08 (d, 1 H, $J_{1,2}$ 11 Hz, H-1), 3.86 (dd, $J_{2,3}$ ~1 Hz, H-2), 2.82–2.58 (m, 4 H, 2 SCH_2CH_3), 2.422 (s, 3 H, Ts*Me*), 1.425 (s, 6 H, CMe_2), 1.265 and 1.21 (2 t, 6 H, *J* 7.5 Hz, 2 SCH_2CH_2); ^{13}C, δ 133.013–126.905 (aromatic), 100.505 (CMe_2), 74.568, 71.567, 70.476, and 70.261 (C-2,3,4,5), 61.911 (C-6), 51.457 (C-1), 29.018 and 18.66 [$C(CH_3)_2$], 25.813 and 24.396 (2 SCH_2CH_3), 21.5 ($SO_2C_6H_4CH_3$), 14.274 and 14.198 (2 SCH_2CH_3).

*5,6-Di-*O*-benzoyl-2,4-*O*-isopropylidene-3-*O*-toluene-*p*-sulfonyl-*D*-glucose dimethyl acetal* (**10**). — Following the procedure described above for **5**, a suspension of *N*-bromosuccinimide (0.079 g, 0.48 mmol) in dry methanol (1.5 mL) and a solution of **9** (0.08 g, 0.11 mmol) in ice-cold dry methanol (1.5 mL) afforded crude **10**. Column chromatography [silica gel (5 g), cyclohexane–acetone (4:1)] gave **10** (0.056 g, 76.09%), isolated as a colorless syrup, $[\alpha]_D$ −67° (*c* 1.78), R_F 0.27 (solvent *D*). N.m.r. data: ^1H, δ 8.10–7.312 (m, 14 H, aromatic), 5.17–5.11 (m, 2 H, H-3,5), 4.767 (dd, 1 H, $J_{6a,6b}$ 12.5, $J_{6b,5}$ 2 Hz, H-6b), 4.62–4.54 (m, 2 H, H-1,6a), 4.455 (dd, 1 H, $J_{4,5}$ 9, $J_{4,3}$ ~1 Hz, H-4), 4.017 (dd, 1 H, $J_{2,1}$ 7.5, $J_{2,3}$ ~1 Hz, H-2), 3.41 and 3.364 (2 s, 6 H, 2 OMe), 2.414 (s, 3 H, TsMe), 1.425 (s, 6 H, CMe_2); ^{13}C, δ 133.013–

127.677 (aromatic), 100.99 (C-1), 100.0 (CMe_2), 71.25, 70.542, 70.281, and 69.627 (C-2,3,4,5), 61.717 (C-6), 54.824 and 52.31 (2 OCH_3), 29.021 and 18.424 [$C(CH_3)_2$], 21.55 ($SO_2C_6H_4CH_3$).

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