Scheme I

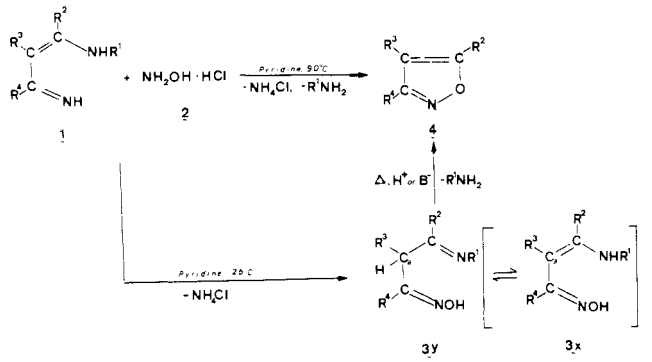

Table II. Compounds 3 from 1-Azabutadienes 1 and Hydroxylamine Hydrochloride 2[a]

3	R^1	R^2	R^3	R^4	yield, %	mp, °C
a	C_6H_5	C_6H_5	CH_3	C_6H_5	75	156-7*
b	C_6H_5	C_6H_5	CH_3	p-$CH_3C_6H_4$	83	170-3*
c	C_6H_5	C_6H_5	H	CH_3	76	131-4*
d	C_6H_5	p-ClC_6H_4	CH_3	C_6H_5	72	163-4*
e	C_6H_5	C_6H_5	H	c-C_6H_{11}	70	126-7*
f	p-$CH_3C_6H_4$	C_6H_5	CH_3	C_6H_5	75	156-7**
g	p-$CH_3C_6H_4$	C_6H_5	H	p-$CH_3C_6H_4$	87	164-5***
h	c-C_6H_{11}	C_6H_5	CH_3	C_6H_5	68	135-7*
i	c-C_6H_{11}	C_6H_5	CH_3	p-$CH_3C_6H_4$	80	120-2*

[a] See paragraph at the end of paper about supplementary material. * Recrystallized from ethanol. ** Recrystallized from hexane. *** Recrystallized from methanol.

evaporated and the residue recrystallized from ethanol to afford 2.5 g (83%) of **3b**: IR (Nujol) ν_{max} 1620, 3340 cm^{-1}; ^1H NMR ($CDCl_3$, internal Me_4Si) δ 0.8 (d, CH_3, J = 6 Hz), 2.4 (s, CH_3), 3.5 (c, 1 H), 4.9 (m, 1 OH), 6.5–7.8 (m, 14 H, Ar); ^{13}C NMR (Me_2SO-d_6, external Me_4Si) δ 15.2 (c), 21.1 (c), 51.9 (d), 100.3 (s), 116.2 (d), 117.5 (d), 126.3, 127.0, 128.0, 128.3, 128.5, 129.6, 138.4 (s), 140.0 (s), 144.8 (s), 162.3 (s). Anal. Calcd for $C_{23}H_{22}N_2O$: C, 80.7; H, 6.43; N, 8.18. Found: C, 80.55; H, 6.22; N, 8.03.

Conversions of oximes 3 into isoxazoles 4 were performed according the following procedures: (a) To a solution of **3** (5 mmol) in dry THF was added an 0.82 N ethereal solution of methyllithium (12 mL). After 1 h of stirring, the mixture was poured into ice-cooled 2 N H_2SO_4 and extracted with ether. The dry organic layer was evaporated and the residue recrystallized from hot hexane. (b) To a solution of **3** (5 mmol) in THF was added CF_3COOH (5 mmol) and the solution stirred for 30 min. Solvents were removed under reduced pressure, and the residue was recrystallized from hexane. (c) A solution of **3** (5 mmol) and 6 N H_2SO_4 (30 mL) in THF was stirred at 60 °C for 3 h, then poured into ice-cooled water, and extracted with ether. The dry organic layer was evaporated and the residue recrystallized from hexane. (d) A solution of **3** in pyridine was heated at 100 °C for 10 h. The resulting solution was poured into ice-cooled 4 N H_2SO_4, extracted with ether, dried over sodium sulfate, concentrated, and the residue recrystallized from hot hexane.

Registry No. **1a**, 71115-28-1; **1b**, 71115-31-6; **1c**, 71443-42-0; **1d**, 78946-76-6; **1e**, 84512-70-9; **1f**, 71115-24-7; **1g**, 72923-07-0; **1h**, 72923-06-9; **1i**, 71115-32-7; **1j**, 72923-09-2; **1k**, 71115-34-9; **2**, 7803-49-8; **3a**, 84850-51-1; **3b**, 84850-52-2; **3c**, 84850-53-3; **3d**, 84850-54-4; **3e**, 84850-55-5; **3f**, 84850-56-6; **3g**, 84850-57-7; **3h**, 84850-58-8; **3i**, 84850-59-9; **4a**, 10557-77-4; **4b**, 2039-49-8; **4c**, 1008-75-9; **4d**, 29329-38-2; **4e**, 16112-19-9; **4f**, 84850-60-2; **4g**, 84850-61-3; **4h**, 84850-62-4; **4i**, 84850-63-5; **4j**, 84850-64-6; **4k**, 84850-65-7.

Supplementary Material Available: Complete ^1H NMR and ^{13}C NMR data for compounds **4** and complete IR, ^1H NMR, and ^{13}C NMR data for compounds **3** (4 pages). Ordering information is given on any current masthead page.

Selective Preparation of Mono- and Diacetals of D-Mannitol

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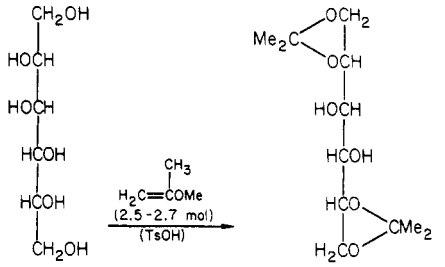
The 1,2:5,6-diisopropylidene acetal (**2**) of D-mannitol (**1**) is an important chiral precursor for natural-product synthesis; on glycol cleavage it is converted into 2 mol of 2,3-*O*-isopropylidene-D-glyceraldehyde.[1] This optically pure D-glyceraldehyde derivative is a convenient and widely used starting point for numerous syntheses[2] of optically active lipids, of various sugars, and of many non-carbohydrate, chiral molecules.

Conventional, acid-catalyzed reaction of D-mannitol (**1**) with acetone under equilibrium conditions gives[1] only modest (~40%) yields of the diacetal **2** in a rather tedious procedure that uses large quantities of solvents. Addition of 2,2-dimethoxypropane to the reagent mixture facilitates the procedure and gives **2** in 31% yield,[3] and use of 2,2-dimethoxypropane in 1,2-dimethoxyethane allows **2** to be obtained in 54–58% yield.[4]

Kinetic acetonation by use of 2-alkoxypropenes, as developed in our laboratories,[5,6] was evaluated for its practical potential in preparation of diacetal **2** from the alditol **1**.



It is shown here that the method provides a simple, large-scale procedure that gives **2** in 92% yield from **1**. Furthermore, the technique may be adapted to furnish a preparative route to the corresponding monoacetal, 1,2-*O*-isopropylidene-D-mannitol (**3**), obtainable from **1** in ~70% yield and itself also a valuable synthetic precursor.

Previous work has shown[5,6] that 2-alkoxypropenes react with sugars in *N*,*N*-dimethylformamide in the presence of a trace of acid under exclusively kinetic control; favored initial attack takes place at primary hydroxyl groups, if present, and ring-closure to stable cyclic acetals is dictated by the availability of suitably disposed hydroxyl groups

(1) (a) E. Baer and H. O. L. Fischer, *J. Biol. Chem.*, **128**, 463–500 (1939); (b) *J. Am. Chem. Soc.*, **61**, 761–765 (1939); (c) E. Baer, *ibid.*, **67**, 338–339 (1945); (d) A. Carayon-Gentile, *Bull. Soc. Chim. Biol.*, **34**, 617–618 (1952).

(2) See, for example, B. T. Golding and V. P. Ioannou, *Synthesis*, 423–424 (1977); A. H. Haines and P. Karntiang, *J. Chem. Soc., Perkin Trans. 1*, 2577–2587 (1979); K. Mori, *Tetrahedron*, **32**, 1979 (1976); H. Eibl, *Chem. Phys. Lipids*, **28**, 1 (1981).

(3) G. Kohan and G. Just, *Synthesis*, 192 (1974); these authors depicted their product as the L-iditol derivative but presumably meant it to be the D-mannitol derivative.

(4) G. J. F. Chittenden, *Carbohydr. Res.*, **84**, 350–352 (1980); **87**, 219–226 (1980).

(5) M. L. Wolfrom, A. B. Diwadkar, J. Gelas, and D. Horton, *Carbohydr. Res.*, **35**, 87–96 (1974).

(6) J. Gelas and D. Horton, *Carbohydr. Res.*, **71**, 103–121 (1979); *Heterocycles*, **16**, 1587–1601 (1981); E. Fanton, J. Gelas, D. Horton, H. Karl, R. Khan, C.-K. Lee, and G. Patel, *J. Org. Chem.*, **46**, 4057–4060 (1981).

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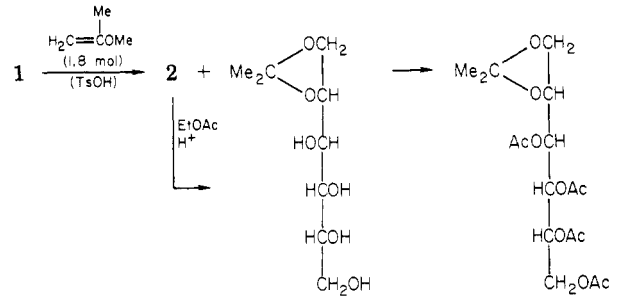
in the molecule. Initial, small-scale experiments have shown[5] that a 5 M excess of 2-ethoxypropene converts 1 into a mixture from which chromatographic resolution gave ~60% of the diacetal plus ~30% of the accompanying 1,2:3,4:5,6 triacetal.

In the optimized procedure reported here, a total amount of 2.4–2.7 molar equiv of 2-methoxypropene reagent is used during a 3-h period at 0 °C; all of the D-mannitol (1) is converted, and the diacetal product 2 crystallizes directly upon evaporation of the solution in 92% isolation yield and pure enough for most further applications.

The monoacetal 3 is readily prepared by conducting the acetonation of 1 with only 1.8 equiv of 2-methoxypropene for 3 h at 0 °C to give mainly 3 plus some diacetal 2.



3 4

Unreacted D-mannitol (1) also present is readily removed as it is insoluble in methanol containing a little ethyl acetate, and addition of more ethyl acetate leads to crystallization of the monoacetal 3. The net yield of 3 is significantly augmented by treating the mother liquors (containing a major proportion of diacetal 2) in ethyl acetate suspension with a trace of *p*-toluenesulfonic acid; this procedure converts 2 into the monoacetal 3 and allows isolation of crystalline monoacetal 3 by direct filtration. The yield of 3 is ~70% in the reaction, not taking into account the amount of starting D-mannitol (1) recovered. The high yield of monoacetal 3 may be ascribed in large measure to its low solubility in ethyl acetate, so that the proportion of 3 in the product mixture crystallizes out almost completely, and the acid-catalyzed deacetalation of the accompanying, ethyl acetate soluble diacetal 2 is arrested by crystallization from the medium at the monoacetal stage.

The monoacetal 3 was characterized directly[7] and as its tetraacetate[7] 4. The literature procedure[7] for 3 is tedious and gives only a 15% yield, and an alternative procedure[8] by way of boronate intermediates is quite complex and still does not readily give good yields.

The monoacetal 3 is of considerable synthetic interest, as its tetraacetate 4 provides access, via deacetonation and glycol cleavage, to *aldehydo*-D-arabinose tetraacetate. The acetylated *aldehydo*-aldoses so widely employed in synthesis are generally prepared in three steps by way of dithioacetal intermediates; the procedural superiority of access to the D-arabinose derivative via compound 4 is readily evident.

Experimental Section

1,2:5,6-Di-*O*-isopropylidene-D-mannitol (2). A solution of D-mannitol (1, 18.2 g, 0.1 mol) in anhydrous *N,N*-dimethylformamide (400 mL) containing 1 g of desiccant (Drierite or Sikkon) is stirred magnetically at 0 °C (ice bath[9]). 2-Methoxypropene (14.4 g, 0.2 mol) is added, followed by a catalytic amount (~0.2 g) of *p*-toluenesulfonic acid, and the mixture is stirred for ~1 h. TLC (silica gel, 1:4 methanol–chloroform) shows some unreacted starting material, which disappears upon addition of more enol ether portionwise over the next 1–2 h (0.4–0.7 equiv in 4–5 portions; total amount 2.4–2.7 equiv of reagent). The mixture is then stirred vigorously with anhydrous sodium carbonate (~5 g) for 1 h and filtered. The filtrate is then evaporated (<1 torr, 40 °C) to afford a crystalline residue of 2. The crystals are washed with a small amount of light petroleum ether, and the mixture is filtered to give 2 (24.1 g, 92%) of acceptable purity (>95% by TLC and NMR) for most further synthetic operations. Pure diacetal 2 may be obtained by recrystallization from dibutyl ether; yield 21.7 g (83%), characterized by comparison (mp, specific rotation) with literature data,[1b] by NMR spectroscopy, and by conversion into the known[8] 3,4-diacetate.

1,2-*O*-Isopropylidene-D-mannitol (3). The foregoing procedure is repeated except that only 1.8 equiv of 2-methoxypropene (10.8 g, 0.15 mol) is used in the reaction with D-mannitol (1, 18.2 g, 0.2 mol) and the reagent is added dropwise. The reaction is stopped after 3 h by addition of anhydrous sodium carbonate. Evaporation of the solution leaves an amorphous residue, TLC of which shows two products, the diacetal 2 and monoacetal 3, totgether with some unreacted 1. The residue is dissolved in anhydrous methanol (~200 mL), ethyl acetate (5–10 mL) is added, and the mixture is kept overnight, whereupon unreacted 1 precipitates out and is filtered off. Further addition of ethyl acetate (50–100 mL) leads to crystallization of the monoacetal 3; yield 5.5 g (30%) of purity >95%. Alternatively, the product mixture may be resolved more completely by column chromatography on silica gel to yield the pure monoacetal 3 as the slower migrating product (6.4 g, 35%).

The yield of monoacetal 3 may be augmented by converting the diacetal 2 in the product mixture into the monoacetal 3. The mixture obtained as described and freed from unreacted D-mannitol is dispersed in suspension in a large volume of ethyl acetate, and a few crystals of *p*-toluenesulfonic acid are added. The mixture is stirred for 1 h, triethylamine (~10 mL) is added, and the suspension is filtered to give the crystalline monoacetal 3 (11.0 g, 60%). Additional 3 may be obtained by evaporating the filtrate (which conains essentially the diacetal 2) and subjecting the recovered material once more in ethyl acetate to the action of a catalytic amount of *p*-toluenesulfonic acid. The monoacetal 3 has mp 161–163 °C, $[\alpha]^{20}_D$ +2.5° (*c* 0.1, water); lit.[8] mp 167 °C, $[\alpha]_D$ +3.5° (in water).

Acetylation of 3 with acetic anhydride–pyridine gives in 91% yield the pure tetraacetate 3: mp 104–106 °C, $[\alpha]^{21}_D$ +29° (*c* 0.1, chloroform); lit.[8] mp 107 °C, $[\alpha]_D$ +28° (in chloroform); ^{1}H NMR ($CDCl_3$) δ 4.9–5.6 m (H-3, -4, -5), 3.7–4.3 (H-1, -1′, -2, -6, -6′), 2.10, 2.07, 2.04, 2.03 (4 s, OAc), 1.37 s, 1.30 s (CMe_2).

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Registry No. 1, 69-65-8; 2, 1707-77-3; 3, 4306-35-8; 4, 76867-27-1.

(7) L. von Vargha, *Ber.*, 66, 1394–1399 (1933).
(8) C. J. Griffiths and H. Weigel, *Carbohydr. Res.*, 81, 17–21 (1980).
(9) The reaction proceeds more rapidly at room temperature, but exclusive kinetic control may not be operative at the higher temperature.

Sydnone Compounds. 18. Schmidt Reaction of 4-Acetyl-3-arylsydnones

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Although a large number of sydnone derivatives have been synthesized, attempts to prepare 4-aminosydnone or

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