[CONTRIBUTION FROM THE DIVISION OF APPLIED BIOLOGY, NATIONAL RESEARCH COUNCIL,]

Synthesis of Some Substituted Cyclitols and Correlation of Structure with Their Spectra[1]

N. Z. STANACEV[2] AND M. KATES

Received June 29, 1960

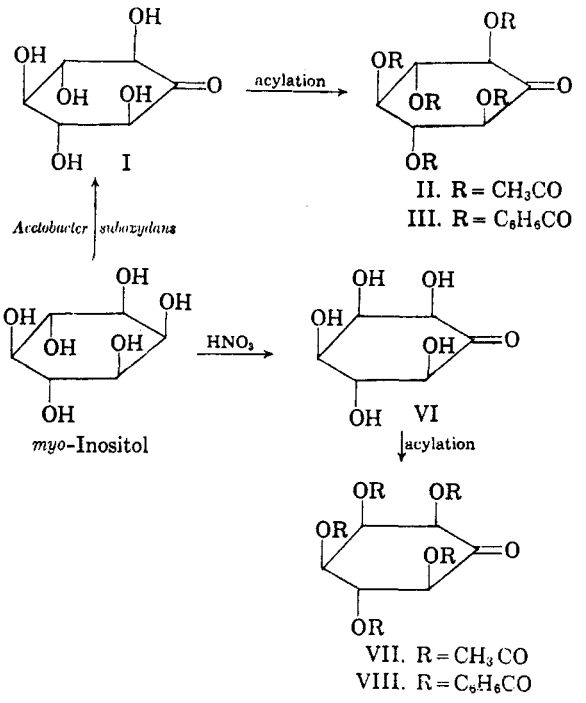
The preparation of several substituted inositols by reduction of the corresponding inososes is described. Catalytic hydrogenation of penta-*O*-acetyl- or penta-*O*-benzoyl-*myo*-inosose-2 in ethanol or dioxane, respectively, yielded the corresponding substituted *myo*-inositol (axial hydroxyl), but reduction of penta-*O*-acetyl-*myo*-inosose-2 with sodium borohydride gave the corresponding *scyllo*-epimer (equatorial hydroxyl). Reduction of penta-*O*-acetyl-DL-*epi*-inosose-2, either by catalytic hydrogenation in ethanol or with sodium borohydride, gave the corresponding substituted DL-*epi*-inositol, in which the new hydroxyl group was axial. When methanol was used as solvent for the hydrogenation of penta-*O*-acetyl-*myo*-inosose or penta-*O*-acetyl-DL-*epi*-inosose, consumption of hydrogen was very slow, and in both cases the product isolated proved to be tetraacetoxycyclohexen-2-one-1, formed presumably by elimination of acetic acid from the acetylated inososes in the presence of the alkaline platinum catalyst. The bearing of this finding on the structure of some substituted cyclitols prepared previously is discussed.

In the course of preparing partially acetylated (or benzoylated) inositols by reduction of the corresponding inososes[3] we observed that the reduction did not always proceed as expected, and that some of the compounds obtained had properties differing from those reported in the literature. We have therefore re-investigated the preparation of these compounds and have examined their constitution with the aid of their ultraviolet and infrared spectra.

Discrepancies were first encountered in the preparation of acetylated (or benzoylated) inososes. *myo*-Inositol was converted to *myo*-inosose-2 (I) through oxidation by *Acetobacter suboxydans*, and to DL-*epi*-inosose-2 (VI) by oxidation with nitric acid, following the procedures of Posternak.[4-6]

Acetylation[6] of *myo*-inosose (I) gave penta-*O*-acetyl-*myo*-inosose-2 (II) having m.p. 212°, identical with the reported value[5,6] for the high-melting form (the low-melting form (m.p. 147°) was never observed[7]).

Benzoylation[5] of I gave penta-*O*-benzoyl-*myo*-inosose-2 (III) with m.p. 221°, differing considerably from either of the two melting points (188° and 286°) previously reported[5,7]. Acetylation[4] of the DL-*epi*-inosose (VI) yielded penta-*O*-acetyl-DL-*epi*-inosose (VII) having m.p. 131°, in contrast to the reported values of 106–108°[4] or 113–115°.[6] Benzoylation[4] of VI gave penta-*O*-benzoyl-DL-*epi*-inosose-2 (VIII) with m.p. 144°, identical with that reported previously.[4]



The acylated inososes (II, III, VII, and VIII) had ester C=O and C—O— absorptions in the in-

(1) Issued as N.R.C. No. 6118.

(2) National Research Council Postdoctorate Fellow, 1958–59. Present address: Department of Biochemistry, The W. A. Noyes Laboratory, University of Illinois, Urbana, Ill.

(3) The system of nomenclature of the cyclitols used here is that devised by H. G. Fletcher, L. Anderson, and H. A. Lardy, *J. Org. Chem.*, **16**, 1238 (1951).

(4) T. Posternak, *Helv. Chim. Acta*, **19**, 1333 (1936).

(5) T. Posternak, *Helv. Chim. Acta*, **24**, 1045 (1941).

(6) T. Posternak, *Biochem. Preparations*, **2**, 57 (1952).

(7) Posternak[5] reported two forms of penta-*O*-acetyl- or penta-*O*-benzoyl-*myo*-inosose-2: a low-melting form obtained by crystallization from neutral solvent (*e.g.*, ethanol), and a high-melting form obtained by crystallization from acidic solvent (*e.g.*, acetic anhydride–sulfuric acid). Subsequently, both forms of penta-*O*-acetyl-*myo*-inosose have been found to have identical m.p. (218°) on a heated stage[19] and in a Pyrex capillary (212°),[20] and to have an identical infrared spectrum and x-ray diffraction pattern.[20] The low melting point of the ethanol-crystallized form is attributed[20,13] to elimination of acetic acid catalyzed by the alkali in the soft glass capillary used,[5] whereas the high-melting form is protected by traces of sulfuric acid adsorbed from the crystallizing medium and thus shows the true melting point of this compound.[20] Presumably, the two melting forms of the penta-*O*-benzoyl-*myo*-inosose are also identical, and the explanation given above should also account for the two forms of the pentabenzoate.

TABLE I

PRINCIPAL INFRARED ABSORPTION BANDS OF SUBSTITUTED CYCLITOLS[a]

Compound	Absorption Maxima, cm.$^{-1}$			
	OH	C=O	Ester C—O—	Fingerprint region
myo-Inosose-2 (I)	v. br	1720(s)	Absent	975(m), 930(m), 925(sh), 805(w)
DL-*epi*-Inosose-2 (VI)	v. br	1720(s)	Absent	987(m), 930(m), 908(w), 877(w), 775(w)
Penta-*O*-acetyl-*myo*-inosose-2 (II)	Absent	1767(sh), 1736(s)	1235(s)	973(m), 923(m), 905(sh), 718(w)
Penta-*O*-benzoyl-*myo*-inosose-2 (III)[b]	Absent	1765(sh), 1725(s)	1270(s)	1025(s), 1000(w), 970(m), 937(sh), 863, 855 (w), 800(w)
Penta-*O*-acetyl-DL-*epi*-inosose-2 (VII)	Absent	1770(sh), 1748(s), 1730(sh)	1235, 1225, 1210 (s)	983(m), 950(s), 928(sh), 913, 897, 887 (w), 855 (w), 760(w)
Penta-*O*-benzoyl-DL-*epi*-inosose-2 (VIII)[b]	Absent	1772(sh), 1725(s)	1270(s)	1025(s), 1000(w), 970(m), 938(w), 903(sh), 882(w), 853(w), 800(w), 755(w)
1,3,4,5,6-Penta-*O*-acetyl-*myo*-inositol (X)	3470	1748(s)	1235(s)	980(w), 938, 928 (m), 908(sh), 895(w), 883(w), 850(w)
1,3,4,5,6-Penta-*O*-benzoyl-*myo*-inositol (XII)[b]	3420	1720(s)	1270(s)	1025(s), 992(w), 970(m), 935(sh), 855(w), 800(w)
1,3,4,5,6-Penta-*O*-acetyl-scyllitol (XV)	3400	1745(s)	1230(s)	983, 975 (m), 925(s), 900(sh)
1,3,4,5,6-Penta-*O*-acetyl-DL-*epi*-inositol (XIV, XIX)	3540	1740, 1730 (s)	1245(s)	983, 973 (m), 929(s), 860(w), 785(m)
Hexa-*O*-acetyl-*myo*-inositol (IV)	Absent	1740(s)	1235(s) 1215(sh)	980(w), 947(m), 930(m), 908(w), 887(w), 870(w)
Hexa-*O*-benzoyl-*myo*-inositol (V)[b]	Absent	1725(s)	1270(s)	1025(s), 1000(w), 970(m), 935(sh), 855(w), 800(w)
Hexa-*O*-acetyl-scyllitol (XVI, XVIII)[c]	Absent	1740(s)	1250, 1235, 1224 (s)	983, 975 (m), 950(vw), 930(m), 908(sh)
Hexa-*O*-acetyl-*epi*-inositol (IX)	Absent	1745(s)	1232(s)	975(w), 947, 930, 915 (m), 860(w), 775(w)
Tetraacetoxycyclohexen-2-one-1 (XI)[d] from II and VII	Absent	1755, 1735 (s), 1708(m)	1245(sh), 1220, 1215, 1205 (s)	938(m), 933(m), 905, 895 (s), 850(w), 820(w), 750(w), 725(sh)

[a] All spectra were measured in Nujol mull with a Perkin-Elmer Model 21 spectrophotometer (double-beam), using sodium chloride optics. Abbreviations: s, strong; m, moderate; w, weak; sh, shoulder; br, broad; v. br, very broad. Bracketed frequencies indicate incompletely resolved peaks (doublets or triplets). [b] Also shows "aryl" bands at 1600(m), 1585(sh), 708(s), and 683(sh) cm.$^{-1}$, due to the benzoyl groups. [c] S. A. Barker, E J. Bourne, R. Stephens, and D. H. Whiffen, (*J. Chem. Soc.*, 4212 (1954)) have reported identical absorption frequencies below 1000 cm.$^{-1}$ for this compound. [d] Also shows C=C double bond absorption at 1655 cm.$^{-1}$

frared in the expected regions (1735–1750 cm.$^{-1}$ and 1230–1250 cm.$^{-1}$, respectively, for the acetates; 1725 cm.$^{-1}$ and 1270 cm.$^{-1}$ for the benzoates), and showed no absorption in the OH-stretching region (Table I). Surprisingly, none of the compounds had a keto C=O absorption band, expected at 1720 cm.$^{-1}$ [*cf.* the free inososes (I, VI), (Table I)], but showed a new band at 1765–1772 cm.$^{-1}$ corresponding to a vinyl ester C=O. The absence of a keto C=O band is most likely attributable to partial enolization of the keto group, together with masking by the strong ester C=O band at 1725–1750 cm.$^{-1}$ In the ultraviolet (Table II), the acetylated inososes (II, VII) showed a keto C=O band (λ_{max} 277–279 mμ; ϵ, 16–24) almost identical with that reported for the free inososes (I, VI),[8] but this band could not be detected in the spectrum of the benzoylated inososes (III, VIII) because of the strong benzene ring absorption (Table II). The spectral data presented thus establish that the acetylated inososes obtained here have the normal structures II and VII. The benzoylated inososes may also be considered to have the expected structures III and VIII, since their infrared spectra in the carbonyl region are similar to that of the acetylated inososes. It may be concluded that the penta-*O*-acetyl-*myo*-inosose[5] and the penta-*O*-benzoyl-DL-*epi*-inosose[4] obtained previously also have the expected structure, but the structure of the previously obtained penta-*O*-benzoyl-*myo*-inosose[5] and of the penta-*O*-acetyl-DL-*epi*-inosose,[4] in view of the discrepancy in their melting points, must be considered in doubt (see below).

TABLE II

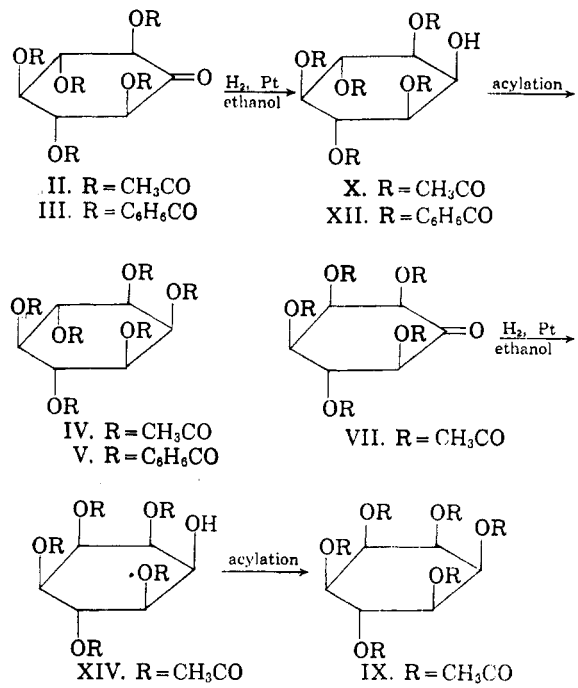
KETO CARBONYL ABSORPTION IN THE ULTRAVIOLET OF SOME SUBSTITUTED INOSOSES[a,b]

Compound	λ_{max}, mμ	Molar Extinction Coeff., ϵ
Penta-*O*-acetyl-*myo*-inosose-2 (II)[c]	279	16
Penta-*O*-acetyl-DL-*epi*-inosose-2 (VII)[c]	277	24
Tetraacetoxycyclohexen-2-one (XI):		
(1) from II	312	32
(2) from VII	312	33

[a] Spectra were measured in glacial acetic acid with a Cary UV recording spectrophotometer. [b] Keto carbonyl absorption could not be demonstrated in penta-*O*-benzoyl-*myo*-inosose-2 (III) or in penta-*O*-benzoyl-DL-*epi*-inosose-2 (VIII) because of strong aryl absorption at 274 mμ (ϵ, 5500–6000) and 282 mμ (ϵ, 4400–4900). [c] Posternak[8] reported λ_{max}, 280 mμ (ϵ, 26) for *myo*-inosose-2, and λ_{max}, 275 mμ (ϵ, 26) for DL-*epi*-inosose-2, in water.

Catalytic (platinum) hydrogenation of penta-*O*-acetyl-*myo*-inosose-2 (II) in glacial acetic acid, according to Posternak[5] gives a product with m.p. 161–162°, which is reported to be a mixture of penta-*O*-acetyl-*myo*- and penta-*O*-acetyl-*scyllo*-inositol[9]; with methanol as solvent, according to Iselin,[9] only the *myo*-isomer (m.p. 177–179°) is obtained. Hydrogenation in ethyl acetate also yields a mixture of isomers, from which the *myo*-isomer (m.p. 166–168° from methanol; 177–179° from ethanol) may be isolated.[10]

Ethanol is reported by May[10] to be the most satisfactory solvent, the hydrogenation being rapid and giving rise only to the *myo*-isomer (m.p. 174–177°) in high yield.



We found, in agreement with May,[10] that absolute ethanol is a suitable solvent for the hydrogenation of II, but the 1,3,4,5,6-penta-*O*-acetyl-*myo*-inositol (X) which we obtained had m.p. 158.5–159.5°, differing from any of the melting points reported previously.[5,9,10] Ethanol could not be used for the hydrogenation of the penta-*O*-benzoyl-*myo*-inosose (III), but the reaction was carried out readily in dioxane, and gave rise, in good yield, to 1,3,4,5,6-penta-*O*-benzoyl-*myo*-inositol (XII), having m.p. 258–260°. (Griffin and Nelson[11] reported m.p. 269° for an unspecified positional isomer of penta-*O*-benzoyl-*myo*-inositol, prepared by partial benzoylation of *myo*-inositol). The *myo*-configurations of both X and XII were established by conversion to the authentic hexa-substituted inositols, IV and V, respectively.

When penta-*O*-acetyl-DL-*epi*-inosose-2 (VII) was hydrogenated in absolute ethanol, following Posternak,[4] we obtained 1,3,4,5,6-penta-*O*-acetyl-DL-*epi*-inositol (XIV) having m.p. 140.5–141.5°, differing significantly from the m.p. 153–154° reported previously.[4] The *epi*-configuration of com-

(8) T. Posternak, *Helv. Chim. Acta*, **29**, 1991 (1946).
(9) B. Iselin, *J. Am. Chem. Soc.*, **71**, 3822 (1949).
(10) E. L. May, *J. Org. Chem.*, **17**, 286 (1952).
(11) E. G. Griffin and J. M. Nelson, *J. Am. Chem. Soc.*, **37**, 1552 (1915).

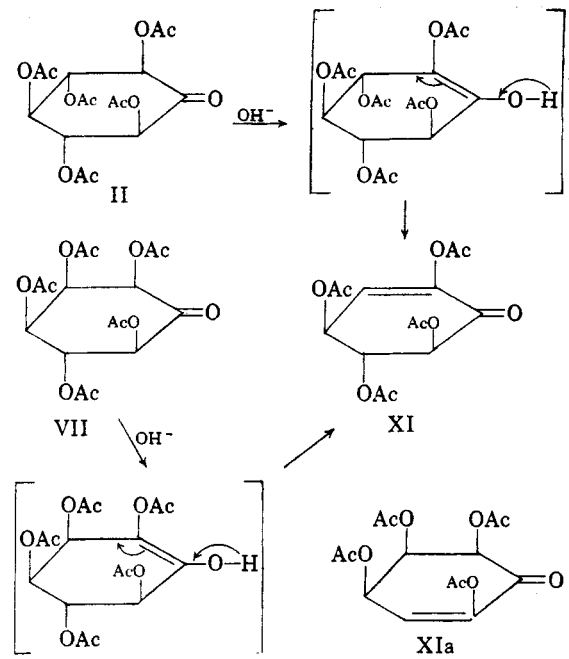
pound XIV was established by conversion to authentic hexa-*O*-acetyl-*epi*-inositol (IX).

Each of the three penta-substituted inositols (X. XII, XIV) had a well defined absorption band in the region 3400–3540 cm.$^{-1}$ attributed to hydrogen-bonded OH groups, as well as strong ester C=O and ester C—O— bands (1730–1750 cm.$^{-1}$ and 1230–1245 cm.$^{-1}$, respectively, for the acetates; 1720 cm.$^{-1}$ and 1270 cm.$^{-1}$, respectively, for the benzoate). The ester absorptions were very close to those of the corresponding hexa-substituted inositols (Table I). The above data (together with the analytical data given in Experimental section) thus show that the pentasubstituted inositols (X, XII, XIV) obtained here have the required structure and configuration, but do not eliminate the possibility that acyl-migration (from position -1 or -3 to position -2) had occurred during the hydrogenation step to produce positional isomers. The difference in melting point between the pentaacetyl inositols (X, XIV) obtained here and those obtained by previous workers,[4,5,9,10] may perhaps be due (a) to positional isomerization having occurred either in our compounds or in those obtained previously, or (b) to differences in the methods used to determine the melting points; further work is necessary to settle this question.[12]

When either penta-*O*-acetyl-*myo*- or DL-*epi*-inosose-2 (II or VII) was hydrogenated in methanol, we found that the reaction was very slow and that the products obtained were quite unexpected. The compound (XI) isolated after hydrogenation of penta-*O*-acetyl-*myo*-inosose (II) had m.p. 114–115°, while that obtained from the *epi*-isomer (VII) had m.p. 107–108° (mixed m.p. was 110–112°). However, both compounds were found to have identical infrared and ultraviolet spectra (Tables I and II) and to have the same empirical formula $C_{14}H_{16}O_9$. Furthermore, the spectral data (Tables I and II) showed that compound XI contained an α,β-unsaturated keto group [λ_{max}, 312 mμ (ϵ, 33); conjugated keto C=O band, 1708 cm.$^{-1}$; C=C band, 1655 cm.$^{-1}$ and 825 cm.$^{-1}$]. The presence of a double bond in compound XI was further confirmed by its Raman spectrum which showed a strong band at 1655 cm.$^{-1}$ It may therefore be concluded that compound XI is tetraacetoxycyclohexen-2-one-1. Such a compound has been reported to be formed by alkali-catalyzed elimination of acetic acid when the melting point of penta-*O*-acetyl-*myo*-inosose (II) (low-melting form) is determined in a soft glass capillary.[13]

(12) Anderson and Landell[22] reported that penta-*O*-acetyl-*myo*-inositol (prepared according to May[10]) melted at 166–168° in a soft glass capillary, and at 177–179° in a Pyrex capillary; the higher melting point was obtained in both types of capillary when the material was finely ground. These authors also attempted to verify the structural purity of the penta-*O*-acetyl-*myo*-inositol by oxidizing it to penta-*O*-acetyl-*myo*-inosose-2. This attempt is considered to be only partially successful since the product was isolated in 58% yield and had m.p. 147° (capillary not specified).

Formation of compound XI most likely occurred by elimination of acetic acid from the pentaacetyl inososes (II and VII) in the presence of the alkaline platinum catalyst, as follows:



This mechanism, similar to that involved in the base-catalyzed aromatization of acetylated inososes,[4,14] predicts that the structure of XI is 2,4,5,6-tetraacetoxycyclohexen-2-one-1. Also, according to this mechanism, II can give rise *only* to one stereo-isomer of tetraacetoxycyclohexanone, namely structure XI, whereas VII can theoretically also give rise to a stereoisomer with structure XIa, differing from XI in the configuration at position 5. Since the compound obtained from VII had an infrared spectrum identical with that of the compound obtained from II (Table I), and since a difference in configuration at one carbon atom is detectable in the fingerprint region (*e.g.*, compare spectra of hexa-*O*-acetyl-*myo*- and *epi*-inositols, Table I) the configuration of tetraacetoxycyclohexenone obtained from both VII and II is most likely that given by structure XI. Formation of structure XI rather than XIa from VII would probably be a consequence of the greater ease of elimination of the axial-4-acetoxy group relative to that of the equatorial-6-acetoxy group. Consistent with this is the observation that the penta-*O*-acetyl-DL-*epi*-inosose (VII) is much more rapidly converted to tetraacetoxycyclohexenone than is the *myo*-isomer (II), which does not contain an axial-acetoxy group (see Experimental section).

The similarity of the m.p. (106–108°) reported for penta-*O*-acetyl-DL-*epi*-inosose[4,6] to that of tetraacetoxycyclohexenone (XI) suggested either

(13) S. J. Angyal and L. Anderson, *Advances in Carbohydrate Chem.*, 14, 179 (1959).

(14) H. Isbell, *Ann. Rev. Biochem.*, 12, 213 (1943).

that structural changes had occurred during the purification of the penta-*O*-acetyl-DL-*epi*-inosose or that the reported m.p. was erroneous. The investigations of McCormick[15] have a bearing on this point. He prepared penta-*O*-acetyl-DL-*epi*-inosose by Posternak's procedure[4,6] and found that crystallization of the crude product from non-polar solvents gave a compound having m.p. 138–140° (block) and an infrared spectrum identical with that found here (Table I) for our penta-*O*-acetyl-DL-*epi*-inosose-2 (VII). Furthermore, he observed that repeated crystallization of the crude penta-*O*-acetyl-DL-*epi*-inosose (m.p. 135–138°) from ethanol gave a new compound having capillary m.p. 107–108° (113–115°, block). The same compound was also obtained after concentrating an ethanolic solution of penta-*O*-acetyl-*myo*-inosose-2 on the steam bath. He considered this compound to be an isomerized pentaacetyl inosose, but the identity of its infrared spectrum with that of compound XI (Table I) shows that it must have been tetraacetoxycyclohexenone. From our observations and those of McCormick[15] it may be concluded that the higher melting point (138–140°) is the correct one for penta-*O*-acetyl-DL-*epi*-inosose-2 and that the lower melting point reported by Posternak[4,6] is probably that of tetraacetoxycyclohexenone. However, it is not yet possible to decide whether the compound obtained by Posternak actually was tetraacetoxycyclohexenone, or whether determination of the melting point of penta-*O*-acetyl-DL-*epi*-inosose in a soft glass capillary gives a low value due to rapid alkali-catalyzed conversion to tetraacetoxycyclohexenone (see ref. 7). In any case, the present results indicate that prolonged exposure of the acetylated inososes to polar solvents should be avoided because of the ease with which these compounds (especially the *epi*-isomer) are converted to tetraacetoxycyclohexenone.

Reduction of the acetylated inososes with sodium borohydride was also studied. According to Barton's rule,[16] reduction of inososes with sodium borohydride should in general afford the equatorial epimer if the keto group is not sterically hindered. Raymond[17] found that sodium borohydride reduction of free *myo*-inosose-2 gave a mixture of *myo*-inositol and scyllitol, whereas reduction of DL-*epi*-inosose-2 gave only *epi*-inositol. In our work, reduction of penta-*O*-acetyl-*myo*-inosose-2 (II) with sodium borohydride at *p*H 6 yielded only penta-*O*-acetyl scyllitol (equatorial epimer). When the medium was allowed to become alkaline (*p*H 8), free scyllitol was obtained in pure form and in high yield (86%). Reduction of the penta-*O*-acetyl DL-*epi*-isomer (VII) with sodium borohydride at *p*H 3–4 gave only the 1,3,4,5,6-penta-*O*-acetyl-DL-*epi*-inositol (axial epimer).

Formation of an axial hydroxyl group by sodium borohydride reduction of free DL-*epi*-inosose-2 has been attributed[17] to steric hindrance by the axial hydroxyl group in position -4, necessitating an attack of the BH_4^- anion from the equatorial direction. Since the axial 4-acetoxy group in the penta-*O*-acetyl-DL-*epi*-inosose-2 would be expected to exert as much or more steric hindrance as a free hydroxyl, the same mechanism probably also applies to the acetylated inosose. In penta-*O*-acetyl-*myo*-inosose-2, however, all acetoxy groups are equatorial and the BH_4^- anion can thus easily approach from the axial direction, with the resulting formation of an equatorial hydroxyl group.

EXPERIMENTAL[18]

A. *Starting materials.* Because of differences in the reported properties of some of the known starting materials, full experimental details of the preparation of these compounds, and their analytical and spectral (Tables I and II) data will be given.

myo-Inosose-2 (I). This compound was prepared following the procedure of Posternak,[5,6] and had m.p. 196–197° dec.; reported m.p.[5,6] 199–202° dec.

Anal. Calcd. for $C_6H_{10}O_6$ (178.1): C, 40.44; H, 5.66. Found: C, 40.12; H, 5.75.

Penta-O-acetyl-myo-inosose-2 (II) was prepared by acetylation of I with acetic anhydride in the presence of sulfuric acid at room temperature. After recrystallization from hot acetic acid the product had m.p. 212–213°; reported m.p. 211–212°,[6] 218°,[19] 212°,[20] and 209–212°[10]; formation of compound with m.p. 147°[5,21] was not observed.

Anal. Calcd. for $C_{16}H_{20}O_{11}$ (388.3): C, 49.48; H, 5.19; $5CH_3CO$, 55.4. Found: C, 49.29; H, 5.15; CH_3CO, 53.7.

Penta-O-benzoyl-myo-inosose-2 (III). This compound was prepared following Posternak's procedure,[5] and had m.p. 221–221.5° after recrystallization from acetic anhydride. Posternak[5] reported two forms for this compound, one with m.p. 188°, and the other with m.p. 286°.

Anal. Calcd. for $C_{41}H_{30}O_{11}$ (698.65): C, 70.47; H, 4.33. Found: C, 70.17; H, 4.08.

Hexa-O-acetyl-myo-inositol (IV). *myo*-Inositol (m.p. 223–224°) was acetylated with acetic anhydride and concentrated sulfuric acid at room temperature. After recrystallization from absolute ethanol, compound IV had m.p. 210–211°; reported m.p. 212°,[5] 214–215°,[9] and 213–215°.[10]

Anal. Calcd. for $C_{18}H_{24}O_{12}$ (432.4): C, 50.00; H, 5.60; $6CH_3CO$, 59.73. Found: C, 50.00; H, 5.42; CH_3CO, 60.00.

Hexa-O-benzoyl-myo-inositol (V). *myo*-Inositol (1 g.) was heated with 10 ml. of benzoyl chloride in the presence of zinc chloride at 80–100° for 1.5 hr. The cooled reaction mixture was suspended in 25 ml. of absolute ethanol, and the insoluble material was filtered and recrystallized twice

(15) M. H. McCormick, Ph.D. thesis, University of Illinois, 1948.

(16) D. H. R. Barton, *J. Chem. Soc.*, 1027 (1953).

(17) D. Raymond, *Helv. Chim. Acta*, **40**, 492 (1957).

(18) All melting points were determined in "Kimax" capillaries using a heated block apparatus ("Culatti"-Zurich), preheated 10° below the melting point (max. error ±2°). Before analysis, all compounds were dried *in vacuo* (0.01 mm.) over potassium hydroxide for 6 hr.

(19) P. Fleury, A. Desjobert, and J. Lecocq, *Bull. Soc. Chim. Biol.*, **36**, 1301 (1954).

(20) P. Fleury, J. Lecocq, and T. Posternak, *Bull. Soc. Chim. France*, 1107 (1954).

(21) H. E. Carter, R. K. Clark, E. H. Flynn, B. Lytle, G. E. McCasland, and M. Robbins, *J. Biol. Chem.*, **174**, 415 (1948).

from acetone by addition of water; yield 2.5 g.; m.p. 265.5–266°; reported m.p., 258°.[11]

Anal. Calcd. for $C_{48}H_{36}O_{12}$ (804.8); C, 71.63; H, 4.51. Found: C, 71.47; H, 4.43.

DL-*epi-Inosose-2* (VI) was prepared according to the procedure of Posternak.[4,6] Compound VI had m.p. 198° dec.; reported m.p. 198–200° dec.[4]

Anal. Calcd. for $C_6H_{10}O_6$ (178.1): C, 40.44; H, 5.66. Found: C, 40.36; H, 5.90.

Penta-O-acetyl-DL-*epi-inosose-2* (VII) was prepared by acetylation of VI with acetic anhydride and sulfuric acid at room temperature. After recrystallization from absolute ethanol, compound VII had m.p. 130.5–131°; reported m.p. 106–108°,[4] 113–115°,[6] 138–140° (block).[15]

Anal. Calcd. for $C_{16}H_{20}O_{11}$ (388.3); C, 49.48; H, 5.19; $5CH_3CO$, 55.4. Found: C, 49.65; H, 5.31; CH_3CO, 54.92.

Penta-O-benzoyl-DL-*epi-inosose-2* (VIII) was prepared as described by Posternak.[4] Compound VIII had m.p. 144° and solubilities identical with those reported.[4]

epi-Inositol was prepared by catalytic (platinum) hydrogenation of DL-*epi*-inosose-2 (VI) in absolute ethanol. Compound VIII had m.p. 245–250°; reported m.p. 285°.[4,8]

Anal. Calcd. for $C_6H_{12}O_6$ (180.2): C, 40.00; H, 6.70. Found: C, 39.57; H, 6.63.

Hexa-O-acetyl-epi-inositol. (IX) was prepared by acetylation of *epi*-inositol with acetic anhydride in the presence of zinc chloride. The reaction mixture was cooled, and the separated crystals were recrystallized from ethanol; m.p. 185°; reported m.p. 188°,[4] and 189°.[8]

Anal. Calcd. for $C_{18}H_{24}O_{12}$ (432.4): C, 50.00; H, 5.60. Found: C, 49.70; H, 5.44.

B. *Catalytic hydrogenation. 1,3,4,5,6-Penta-O-acetyl-myo-inositol* (X). A suspension of 4.0 g. of II and 500 mg. of platinum oxide (Adams' catalyst) in 120 ml. of absolute ethanol was shaken in an atmosphere of hydrogen (*ca.* 1.1 atm.) at room temperature. After 75 hr., the theoretical amount of hydrogen was consumed. The reaction mixture was centrifuged, and the clear supernatant was evaporated to 15 ml. *in vacuo* and cooled overnight at 5°. The separated crystals (500 mg.) had m.p. 158.5–159.5°, after recrystallization from absolute ethanol.

Anal. Calcd. for $C_{16}H_{22}O_{11}$ (390.3): C, 49.23; H, 5.68; $5CH_3CO$, 55.13. Found: C, 49.16; H, 5.40; CH_3CO, 55.04.

A second crop was obtained as follows: the insoluble material plus catalyst was extracted several times with boiling absolute ethanol (total, 200 ml.), and the combined extracts were filtered, evaporated to 10 ml., and cooled overnight at 5°; yield, 500 mg.; m.p., after recrystallization from absolute ethanol, 158–159°; infrared spectrum identical with that of the first crop. Reported m.p. for penta-*O*-acetyl-*myo*-inositol is 161–162°,[5] 177–179°,[9] and 174–177°[10] (also 166–168°[10]; see Anderson and Landell[22]).

Anal. Found (for second crop): C, 49.30; H, 5.13; CH_3CO, 55.20.

Proof of configuration of (X): *Conversion to hexa-O-acetyl-myo-inositol.* Compound X was acetylated with acetic anhydride and concentrated sulfuric acid at room temperature, and the resulting compound had m.p. 210–211°, either alone or when mixed with authentic hexa-*O*-acetyl-*myo*-inositol (IV), and had an infrared spectrum identical with that of compound IV.

Tetraacetoxy-cyclohexen-2-one-1 (*XI*) *from* II. A suspension of 1.0 g. of II and 150 mg. of platinum oxide in 30 ml. of absolute methanol was shaken in an atmosphere of hydrogen as described above. The consumption of hydrogen was very slow, and after 24 hr., ethanol (30 ml.) was added, and the mixture was warmed to the boiling point and filtered. The clear filtrate was concentrated *in vacuo* to 10 ml. and cooled overnight at 5°; yield, 420 mg. of crystals with m.p. 114–115°; mixed m.p. with XI obtained from VII, 110–112°.

Anal. Calcd. for $C_{14}H_{16}O_9$ (328.2): C, 51.25; H, 4.92; $4CH_3CO$, 52.5. Found: C, 51.40, 51.50; H, 4.76, 5.36; CH_3CO, 51.9, 51.8.

The infrared spectrum of compound XI (Table I) showed a keto C=O band at 1708 cm.$^{-1}$, an ester at 1735 cm.$^{-1}$, a vinyl acetate band at 1755 cm.$^{-1}$ and C=C bands at 1655 cm.$^{-1}$ and 820 cm.$^{-1}$; OH-absorption was absent. The ultraviolet spectrum (Table II) showed the presence of a conjugated unsaturated ketone.

It should also be mentioned that when contact of II with the platinum catalyst in methanol was prolonged to 10 days, XI could no longer be isolated, but a crude product (m.p. 123.5–125°) was obtained whose analysis and spectra indicated that further elimination of acetic acid had occurred.

1,3,4,5,6-Penta-O-benzoyl-myo-inositol (XII). A suspension of 4 g. of IV and 500 mg. of platinum oxide in 150 ml. of dioxane (redistilled) was hydrogenated in a Parr hydrogenation apparatus for 2 days. The mixture was then warmed and the catalyst removed by centrifugation. The supernatant liquid was evaporated to dryness *in vacuo*, and the residue was dried over potassium hydroxide and recrystallized from dioxane; yield, 3.3 g.; m.p. 258–260°; reported m.p. 269° (for unknown isomer of penta-*O*-benzoyl-*myo*-inositol)[11]

Anal. Calcd. for $C_{41}H_{32}O_{11}$ (700.7): C, 70.27; H, 4.61. Found: C, 70.01; H, 4.80.

1,3,4,5,6-Penta-O-benzoyl-2-acetyl-myo-inositol (XIII). To confirm the presence of a free hydroxyl group in XII, this compound was acetylated by recrystallization twice from hot acetic anhydride in the presence of concentrated sulfuric acid. The product obtained had m.p. 166–167°.

Anal. Calcd. for $C_{43}H_{34}O_{12}$ (742.7): C, 69.54; H, 4.61. Found: C, 69.96; H, 4.39.

Proof of configuration of XII: *Conversion to hexa-O-benzoyl-myo-inositol.* Compound XII was benzoylated as described above for compound V, and the resulting product had m.p. 265–266°, either alone or when mixed with authentic hexa-*O*-benzoyl-*myo*-inositol (V). Its infrared spectrum was identical with that of compound V.

1,3,4,5,6-Penta-O-acetyl-DL-*epi-inositol* (XIV). A solution of 500 mg. of VII in 20 ml. of absolute ethanol was hydrogenated in the presence of 100 mg. of platinum oxide at room temperature and *ca.* 1.1 atm. After 1 hr. the theoretical amount of hydrogen was consumed. The catalyst was removed by filtration, and the filtrate was evaporated to 5 ml. and kept at 5°. The crystals obtained were recrystallized from absolute ethanol; yield 420 mg.; m.p. 140.5–141.5°; reported[4] m.p., 153–154°.

Anal. Calcd. for $C_{16}H_{22}O_{11}$ (390.3): C, 49.23; H, 5.68. Found: C, 49.31; H, 5.77.

Proof of configuration of XIV: *Conversion to hexa-O-acetyl-epi-inositol.* Compound XIV was acetylated as described for compound IX, and the resulting product had m.p. 185°, either alone or when mixed with authentic hexa-*O*-acetyl-*epi*-inositol (IX). Its infrared spectrum was identical with that of compound IX.

Anal. Calcd. for $C_{18}H_{24}O_{12}$ (432.4): C, 50.00; H, 5.60. Found: C, 49.73; H, 5.52.

Tetra-o-aceloxy-cyclohexen-2-one-1 (XI) *from VII.* A solution of 5 g. of VII in 200 ml. of absolute methanol was shaken in the presence of 500 mg. of platinum oxide in an atmosphere of hydrogen for a period of 5 hr. The catalyst was removed by filtration, and the filtrate was concentrated *in vacuo* to 10 ml. and kept at 5°. The crystals obtained (1.1 g.) were recrystallized from absolute ethanol and had m.p. 106.5–107.5° (mixed m.p. with XI obtained from II, 110–112°).

Anal. Calcd. for $C_{14}H_{16}O_9$ (328.2): C, 51.25; H, 4.92. Found: C, 51.38, 51.30; H, 4.98, 4.95.

The infrared and ultraviolet spectra (Tables I and II) of this compound were identical with those of compound XI obtained from penta-*O*-acetyl-*myo*-inosose (II). Its Raman spectrum in chloroform (156 mg./g. solvent) showed a strong band at 1655 cm.$^{-1}$ confirming the presence of a double bond, and C=O bands at 1725 cm.$^{-1}$ (strong) and 1755 cm.$^{-1}$ (moderate).

(22) L. Anderson and A. M. Landell, *J. Am. Chem. Soc.*, **76**, 6130 (1954).

It is noteworthy that after storage of penta-*O*-acetyl-DL-*epi*-inososose-2 (VII) in a test tube in the desiccator at 5° for about 10 months, the sample had darkened considerably and smelled of acetic acid; after two recrystallizations from absolute ethanol, two thirds of the sample was recovered as a compound with m.p. 108–110°, having ultraviolet and infrared spectra identical with those (Tables I and II) found for tetraacetoxycyclohexenone (XI). Storage of penta-*O*-acetyl-*myo*-inososose-2 (II) under the same conditions did not result in any detectable decomposition.

C. Reduction with sodium borohydride. 1,3,4,5,6-Penta-O-acetyl scyllitol (XV). To a suspension of 1.0 g. of II in 25 ml. of absolute methanol was added with stirring, simultaneously, a solution of 200 mg. of sodium borohydride in 25 ml. of methanol and 1*N* acetic acid to maintain the *p*H at 6. The mixture was stirred for 1 hr. at room temperature when it cleared to a slightly red solution. The latter was concentrated *in vacuo* to dryness and the residue was crystallized from hot 95% ethanol; yield 450 mg.; m.p. (after recrystallization from ethanol) 213–214°; reported,[10] m.p. 211–213°.

Anal. Calcd. for $C_{16}H_{22}O_{11}$ (390.3): C, 49.23; H, 5.68; $5CH_3CO$, 55.13. Found: C, 49.52; H, 5.75; CH_3CO, 55.38.

Proof of configuration of XV: Conversion to hexa-O-acetyl scyllitol (XVI). Compound XV was acetylated with acetic anhydride in the presence of concentrated sulfuric acid with gentle warming. The reaction mixture was cooled at 5°, and the crystals which separated were recrystallized from 95% ethanol; m.p. 301–302°; reported[5] m.p. 298–299°, 301°.[23]

The melting point of compound XVI was undepressed when mixed with hexaacetyl scyllitol (XVIII) prepared from scyllitol (see below), and both derivatives had identical infrared spectra.

Anal. Calcd. for $C_{18}H_{24}O_{12}$ (432.4): C, 50.00, H. 5.60; $6CH_3CO$, 59.73. Found: C, 49.80; H, 5.83; CH_3CO, 60.00.

Scyllitol (XVII). To a suspension of 1.0 g. of II in 25 ml. of absolute methanol was added, with stirring, a solution of 150 mg. of sodium borohydride in 25 ml. of absolute methanol. The mixture (*p*H, 8.5) was stirred for 30 min., and the resulting clear solution was acidified with 2*N* hydrochloric acid, evaporated *in vacuo* to *ca.* 5 ml., and kept at 5°. The crystals (400 mg., yield, 86%) obtained had m.p. 355–356°; reported[24] m.p. 348.5°, and 352°.[5]

Anal. Calcd. for $C_6H_{12}O_6$ (180.2): C, 40.00; H, 6.70. Found: C, 39.66; H, 6.82.

Hexa-O-acetyl scyllitol (XVIII) was prepared by acetylation of scyllitol (XVII) as described above for compound XV; m.p. after recrystallizatiln from 95% ethanol, 301–302°.

Anal. Calcd. for $C_{18}H_{24}O_{12}$ (432.4): C, 50.00; H, 5.60; $6CH_3CO$, 59.73. Found: C, 49.73; H, 5.51; CH_3CO, 59.60.

1,3,4,5,6-Penta-O-acetyl-DL-epi-inositol (XIX). To a solution of 1.0 g. of IV in 50 ml. of methanol was added simultaneously with stirring a solution of 300 mg. of sodium borohydride in 50 ml. of methanol and 1*N* sulfuric acid to maintain the *p*H at 3–4. The mixture was stirred at room temperature for 20 hr. and was then shaken with 25 g. of Amberlite MB-3 for 30 min. The resin was removed by filtration, and the clear filtrate was evaporated to dryness *in vacuo* at 40°. The residue was recrystallized twice from absolute ethanol. Yield, 460 mg.; m.p. 140–141°; reported[4] m.p., 153–154°. Compound XIX had an infrared spectrum identical with that of compound XIV.

Anal. Calcd. for $C_{16}H_{22}O_{11}$ (390.3); C, 49.23; H, 5.68. Found: C, 49.44; H, 5.53.

Proof of configuration of XIX*; Conversion to hexa-O-acetyl-epi-inositol.* Compound XIX was acetylated as described for compound IX, and the resulting product had m.p. 185°, alone or when mixed with authentic hexa-*O*-acetyl-*epi*-inositol (IX); its infrared spectrum was also identical with that of IX.

Acknowledgment. The authors are indebted to Dr. P. T. Krueger for the Raman spectrum, to Mr. C. F. Rollin for the infrared spectra, and to Mr. A. E. Castagne for the microanalyses. One of the authors (N.Z.S.) is grateful to the National Research Council of Canada for a Postdoctorate Fellowship, and to Dr. G. A. Adams for help in preparation of the manuscript. The ultraviolet spectra and some of the infrared spectra were taken in the Department of Chemistry, W. A. Noyes Laboratory, University of Illinois, with the kind permission of Professor H. E. Carter, to whom the authors express their thanks.

OTTAWA, CAN.

(23) P. Fleury and P. Balatre, *Les Inositols,* Masson et Cie, Paris, 1947, p. 82.

(24) F. Micheel, *Chemie der Zucker und Polysaccharide,* 2nd ed., Leipzig, 1956, p. 482.