# New synthesis of (±)-cyclohexene-1,3/2,4-tetrol (conduritol-B)

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1,4,5,6-Tetra-*O*-acetyl-myoinositol is reacted with *N,N'*-thiocarbonyl diimidazole to give 1,4,5,6-tetra-*O*-acetyl-myoinositol-2,3-thionocarbonate. This is desulfurized with trimethyl phosphite to yield tetra-*O*-acetyl-(±)-cyclohexene-1,3/2,4-tetrol (tetra-*O*-acetyl-conduritol-B).

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Although a method for the preparation of tetra-*O*-acetyl-(±)-cyclohexene-1,3/2,4-tetrol (tetra-*O*-acetyl-conduritol-B, **4**) from myoinositol has been described (1), the low yields of the intermediate bromoquercitol-A pentaacetates obtained in our laboratory, especially in large scale preparations, prompted us to examine the possibility of synthesizing the compound by the method of Corey and Winter (2).

The readily available 1,4,5,6-tetra-*O*-acetyl-myoinositol (**1**) (3) was reacted with *N,N'*-thiocarbonyl diimidazole (**2**) (4) to give 1,4,5,6-tetra-*O*-acetyl-myoinositol-2,3-thionocarbonate (**3**). Treatment of **3** with trimethyl phosphite provided tetra-*O*-acetyl-(±)-cyclohexene-1,3/2,4-tetrol (**4**) which was characterized both by nuclear magnetic resonance (n.m.r.) spectroscopy and *O*-deacetylation to conduritol-B (**5**).

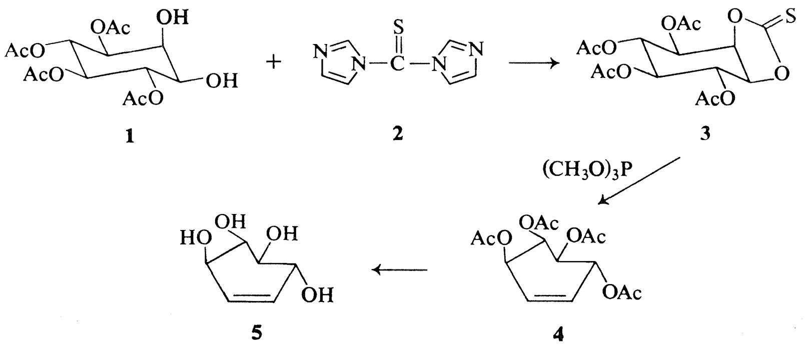
## Experimental

Melting points were determined on a heating stage and are uncorrected. Infrared spectra were measured with a Perkin–Elmer Model 137 "Infracord" infrared spectrophotometer. Nuclear magnetic resonance spectra were measured at 60 Mc.p.s. with a Varian A60 n.m.r. spectrometer. Chemical shifts are given in τ values and refer to spectra measured in deuteriochloroform, with tetramethylsilane as the internal standard.

### *1,4,5,6-Tetra-O-acetyl-myoinositol-2,3-thionocarbonate (3)*

1,4,5,6-Tetra-*O*-acetyl-myoinositol (**1**) (3) was prepared as a monohydrate. The compound was dried over phosphorus pentoxide and further dehydrated by dissolving in tetrahydrofuran and drying over phosphorus pentoxide. The amorphous solid obtained after removal of the solvent *in vacuo* was again dried.

Thiophosgene (14.6 ml, 0.191 mole) was added dropwise to a stirred solution of freshly dried imidazole (52.0 g, 0.764 mole) in anhydrous acetone (1040 ml) under anhydrous conditions. The temperature of the mixture was maintained at 25–28°. After 90 min the precipitated imidazole hydrochloride was collected by filtration and in the filtrate was dissolved the previously dried 1,4,5,6-tetra-*O*-acetyl-myoinositol (**1**, 66.4 g, 0.19 mole). The mixture was refluxed under anhydrous conditions for 2 h. The solvent was removed and the residual yellow solid dissolved in ethyl acetate. The solution was extracted with 3.6 *N* hydrochloric acid (106.4 ml) in order to remove imidazole. The organic phase was washed successively with water, a saturated solution of sodium bicarbonate, and water. After drying the solution over anhydrous sodium sulfate, the solvent was removed and the crystalline residue recrystallized from hot ethanol. The colorless crystals were isolated, washed with cold



ethanol, and dried. The yield of **3** was 32.05 g (40%), m.p. 166–168°; $\nu_{max}$(Nujol) 1750 (C=O), 1160 $cm^{-1}$ (C=S); n.m.r. data: τ 7.84–7.91, 4 *O*-acetyl groups, 4.53–5.03, 6 ring hydrogens.

Anal. Calcd. for $C_{15}H_{18}O_{10}S$: C, 46.14; H, 4.65; S, 8.21. Found: C, 46.66; H, 4.58; S, 8.09.

### *Conduritol-B Tetraacetate (4)*

A solution of 1,4,5,6-tetra-*O*-acetyl-myoinositol-2,3-thionocarbonate (**3**, 27.65 g, 0.071 mole) in trimethyl phosphite (200 ml) was refluxed under nitrogen for 5 h. The solvent was removed and to the clear oily residue was added water (200 ml). After seeding, the mixture was set aside a few minutes when crystallization started. The mixture was refrigerated overnight. The crystals were collected, washed with water, and dried. The product still smelled of trimethyl phosphite and, therefore, was washed thoroughly with *n*-hexane and recrystallized from ethanol–water. The compound, m.p. 85–85.5°, was obtained in a yield of 81% (18.02 g) (reported (1) m.p. 91–92.5°, corrected); $\nu_{max}$(Nujol) 1750 $cm^{-1}$ (C=O); n.m.r. data: τ 7.95–7.99, 4 *O*-acetyl groups, 4.34–4.83, 6 protons, multiplets.

### *Conduritol-B (5)*

Triethylamine (4 ml) was added to a solution of conduritol-B tetraacetate (**4**, 5 g, 15.92 mmole) dissolved in 70% aqueous methanol (50 ml) and the mixture was set aside 6 h with occasional shaking. The solvents were removed and the residual white solid dried over phosphorus pentoxide. Recrystallization from hot methanol and benzene afforded colorless crystals of **5** (74%), m.p. 199.5–201° (reported (1) m.p. 204.5–205°, corrected).

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# The heat of formation of the norbornyl cation

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The heat of formation of the norbornyl ion has been evaluated from experimental data. This was compared to the heats of formation of various formulations of the norbornyl ion computed by quantum mechanical methods.

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A recent report on the heats of formation of several possible formulations for the norbornyl ion calculated by quantum mechanical methods (1) prompts us to report an evaluation of the enthalpy of formation of the $C_7H_{11}^+$ ion, which occurs in the mass spectrum of norbornyl bromide (2).

This ion was presumed to be the norbornyl cation and its appearance potential in the mass spectrometer was observed to be 10.26 ± 0.05 eV (2). The appearance potential of an ion is related to its heat of formation by eq. [1].

$$[1]\quad \text{A.P.} = \Delta H_f(C_7H_{11}^+) + \Delta H_f(\text{Br}) - \Delta H_f(C_7H_{11}\text{Br})$$

For $\Delta H_f$(Br) we have adopted the value $+26.73 \pm 0.11$ kcal/mole found in the literature (3). There does not appear to be any direct measurement of $\Delta H_f$ for norbornyl bromide but Bedford *et al.* have reported a value of $-22.01 \pm 0.65$ kcal/mole for $\Delta H_f^0$ of bicyclo[2,2,1]heptane (cryst) (4) which, combined with the value of 13 ± 2 kcal/mole for $\Delta H_{\text{sublimation}}$ reported by Chiang *et al.* (5), leads to $\Delta H_f$ for bicyclo[2,2,1]heptane (gas) $= -9.91 \pm 2.65$ kcal/mole. Using bond dissociation data from the literature (3, 6, 7), we have computed the heat of reaction for the bromination of bicyclo[2,2,1]heptane via the process outlined in reaction [2]

$$[2]\qquad C_7H_{12} + Br_2 \rightarrow C_7H_{11}Br + HBr$$

In computing this heat of reaction we have assumed the dissociation energies of the C—H and C—Br bonds at C-2 in the norbornyl system to be the same as those reported for $(CH_3)_2$-CH—H and $(CH_3)_2$CH—Br, viz. 94.5 ± 1 and

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