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Preliminary communication

Cyclic carbonates as protecting groups in cyclitol chemistry

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In the past [1] and more recently [2] cyclic carbonates have been widely used as protecting groups in carbohydrate chemistry. The methods recommended [3–6] for the preparation of cyclic carbonates involve reaction of the diol with phosgene, triphosgene, or chloroformates in pyridine, with carbonyldiimidazole, or with diethyl or diphenyl carbonate and base.

The reaction of an excess of ethylene carbonate (**1**) with a vicinal diol at 120°C for 30 min in the presence of a trace of $NaHCO_3$ has been used for the preparation of glycerol 1,2-carbonate (**2**) [7] and of the cyclic carbonates of the anomers of methyl 5-*O*-benzyl-D-ribofuranoside [8].

Under these conditions, **1** gave a product **4** [1] with 1,4,5,6-tetra-*O*-benzyl-*myo*-inositol (**3**) [9,10] whereas 1,2,3,6-tetra-*O*-benzyl-*myo*-inositol (**5**) [11] was recovered unchanged. This indicated that only axial–equatorial (*cis*) vicinal diols of the cyclohexane ring formed cyclic carbonates under these conditions. This was confirmed when 1,4-di-*O*-benzyl-*myo*-inositol (**6**) [12,13] gave the carbonate **7** which was isolated (80% yield, slightly contaminated with tetraol **6**) by dilution of the cooled reaction mixture with water, in which ethylene carbonate is soluble, followed by filtration of the product. Column chromatography on silica gel (ethyl acetate) gave pure **7** (mp 172–174°C), which has been prepared previously [12] (mp 165–167°C), in admixture with the bis-carbonate **8**, on reaction of **6** with phosgene in pyridine. The diol **7** gave a syrupy

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[1] All of the compounds described are racemic and all new compounds gave satisfactory elemental analyses.

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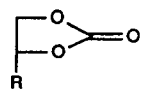
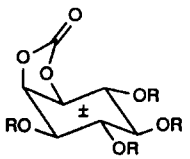
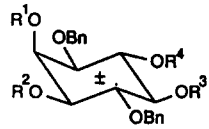
diacetate **9** [^{1}H NMR ($CDCl_3$): δ 2.02, 2.04 (2 s, each 3 H, 2 Ac), 3.84 (t, 1 H, J 2.4 Hz), 4.25 (dd, 1 H, J 3.7 and 9.2 Hz)]. Treatment of **7** with 2,2-dimethoxypropane and an acid catalyst gave **10** (mp 193–195°C) in near quantitative yield and this on basic hydrolysis gave 1,4-di-*O*-benzyl-5,6-*O*-isopropylidene-*myo*-inositol (**11**) identical with the material prepared previously [14] in low yield (together with its stereoisomer **12**) by kinetic acetonation of the tetraol **6**.



1 R = H
2 R = CH_2OH



13 R = H
14 R = Ac



3 $R^1 = R^2 = H$; $R^3 = R^4 = Bn$
4 $R^1,R^2 = CO$; $R^3 = R^4 = Bn$
5 $R^1 = R^2 = Bn$; $R^3 = R^4 = H$
6 $R^1 = R^2 = R^3 = R^4 = H$
7 $R^1,R^2 = CO$; $R^3 = R^4 = H$
8 $R^1,R^2 = R^3,R^4 = CO$
9 $R^1,R^2 = CO$; $R^3 = R^4 = Ac$
10 $R^1,R^2 = CO$; $R^3,R^4 = CMe_2$
11 $R^1 = R^2 = H$; $R^3,R^4 = CMe_2$
12 $R^1,R^2 = CMe_2$; $R^3 = R^4 = H$

Bn = CH_2Ph

The diol **11** has been used [14–16] for the preparation of intermediates for the synthesis of 1D-*myo*-inositol 1,4,5-trisphosphate and its analogues, and the preparative route described above from the tetraol **6** should make it readily available in bulk. On the preparative scale there is no need to remove the small amount of tetraol **6** from the carbonate **7** since **11** is readily purified in the final stage. We have also described [17] routes for the preparation of both enantiomers of the diol **12** and thus both enantiomers of the tetraol **6** are available by acid hydrolysis of the enantiomers of **12**.

The simple technique described above for the specific introduction of a cyclic carbonate on to the vicinal, *cis*-diol of *myo*-inositol derivatives should be applicable to many other cyclitol derivatives, to provide useful intermediates in this very active field of research.

Hydrogenolysis of the benzyl groups from **7** in glacial acetic acid over Pd–C gave the previously undescribed *myo*-inositol 1,2-carbonate (**13**) [mp 165°C, dec with elimination of gas; ^{13}C NMR (D_2O): δ (measured from Me of internal acetone taken as 0) 39.0, 41.7, 41.9, 42.8, 48.1, 50.3, 125.8]. Acetylation of **13** gave the tetraacetate **14** [mp 140–142 °C (from ethyl acetate–light petroleum); ^{1}H NMR ($CDCl_3$): δ 2.08, 2.09, 2.15, 2.16 (4 s, each 3 H, 4 Ac)].

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