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Note

The transformation of D-glucono-1,5-lactone into ethyl 2,3,4,6-tetra-*O*-acetyl-D-gluconate and an ethyl 2,3,4,5-tetra-*O*-acetyl-6-chloro-6-deoxyhexonate

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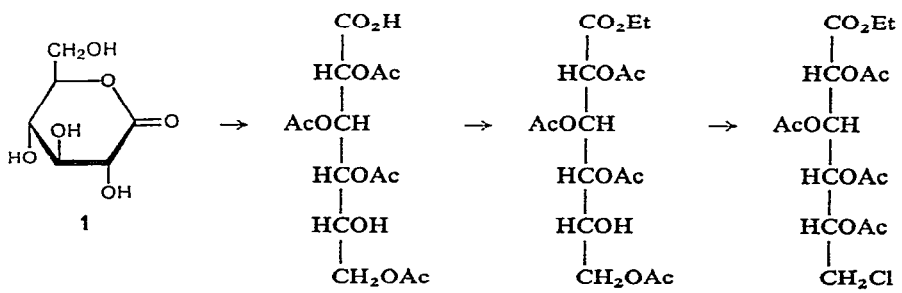
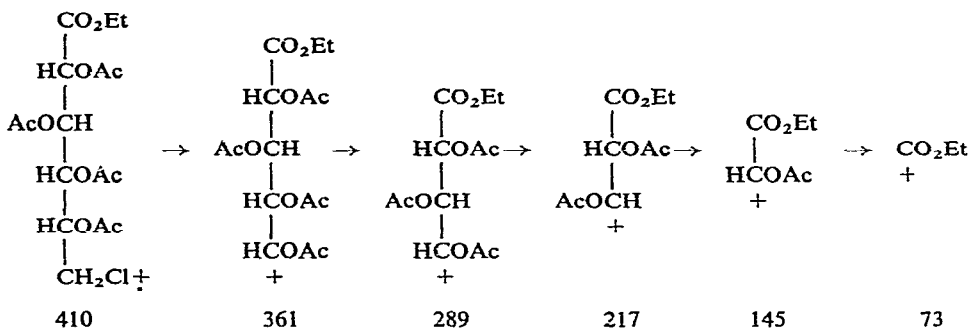
The opening of lactone rings by treatment with alcohols recently observed[1] prompts us to record similar observations. Treatment of D-glucono-1,5-lactone (**1**) with acetic anhydride in pyridine gave impure crystals which were transformed on repeated recrystallisation from ethanol into ethyl 2,3,4,6-tetra-*O*-acetyl-D-gluconate (**3**). The p.m.r. spectrum of **3** exhibited multiplets each of which had small splittings consistent with an acyclic structure, and the following signals were assigned: τ 4.73 (doublet, H-2), 4.30 and 4.84 (triplets, H-3,4), 6.16 (sextet, H-5), and 5.9 (doublet, H-6,6'). The high chemical-shift value of the signal for H-5 is consistent with the $>$CHOH grouping. The signals at τ 7.84, 7.88, 7.92, and 7.92 were assigned to four acetate substituents. Treatment of **3** with acetic anhydride–pyridine gave ethyl 2,3,4,5,6-penta-*O*-acetyl-D-gluconate[2,3]. Thus, acetylation of the lactone **1** caused ring opening to give 2,3,4,6-tetra-*O*-acetyl-D-gluconic acid (**2**) which formed the ethyl ester **3** on treatment with ethanol.



Treatment of **3** with phosphorus pentachloride gave an ethyl 2,3,4,5-tetra-*O*-acetyl-6-chloro-6-deoxyhexonate (**4**). The structure was assigned on the following evidence. The p.m.r. spectrum contained signals assigned to the various functional groups and was indicative of an acyclic compound. In contrast to **3**, the signal for H-5 had moved downfield, whereas H-2, H-3, H-4, and H-5 all resonated between

τ 4.4–5.0. Also, H-6 and H-6′ were no longer equivalent and their signals occurred as quartets shifted upfield to τ 6.34 and 6.51. Thus, it seemed that only positions 5 and 6 were modified in the conversion **3**→**4**. The i.r. spectrum of **4** showed no hydroxyl peak. The mass spectrum of **4** contained, *inter alia*, a series of peaks at *m/e* 361, 289, 217, 145, and 73 for chlorine-free fragments consistent with the sequence shown in Scheme 1, and indicative of an acyclic structure and the presence of the chlorine atom at position 6. Similar fragmentation patterns have been obtained for 2,3,4,5-tetra-*O*-acetyl-D-arabinose diethyl dithioacetal[5], hexa-*O*-acetyl-D-glucitol[6], and *aldehydo*-D-arabinose tetra-acetate[7].



Scheme 1. Partial fragmentation pattern of ethyl 2,3,4,5-tetra-*O*-acetyl-6-chloro-6-deoxyhexonate.

The rearrangement occurring in the conversion **3**→**4** has been observed in related compounds[8,9], whereby initial attack of the reagent at the group on C-5 is followed by participation by the group at C-6 which could give the 5-acetoxy-6-chloro derivative with retention of the D-*gluco* configuration (**4**) by an S_ni mechanism of chlorination[8]. If inversion of configuration occurred at C-5, the product would have the L-*ido* configuration.

EXPERIMENTAL

Acetylation of D-*glucono-1,5-lactone* (**1**). — The lactone **1** (1 g) was dissolved in dry pyridine (10 ml) and acetic anhydride (6 ml) and shaken for 1 h. After storage for a further 2 h, t.l.c. (ether) showed the presence of one product. The solution was poured on to ice and water, and the syrup resulting was separated by decantation, dissolved in chloroform, and washed with dilute hydrochloric acid, aqueous sodium hydrogen carbonate, and water. After drying ($MgSO_4$), evaporation of the solution gave a clear syrup which was crystallised from chloroform(minimum volume)–diisopropyl ether. The product (1.4 g, m.p. 99–112°) was repeatedly crystallised from ethanol to give ethyl 2,3,4,6-tetra-*O*-acetyl-D-gluconate (**3**; 1 g, 45%), m.p. 102–103°, $[\alpha]_D$ +18.7° (*c* 2, chloroform), ν_{max} 3470 cm^{-1} (HO) (Found: C, 48.8; H, 5.8. $C_{16}H_{24}O_{11}$ calc.: C, 49.0; H, 6.1%).

The ester **3** (0.5 g) was dissolved in dry pyridine (10 ml) and acetic anhydride

(10 ml) and left at room temperature for 2 days. T.l.c. (ether–light petroleum, 2:1) showed the presence of a single product. The solution was poured on to ice and water, and the product was collected and recrystallised from ethanol to give the penta-acetate (0.5 g, 90%), m.p. 104–104.5°, $[\alpha]_D$ +21.6° (*c* 2, chloroform) (Found: C, 49.6; H, 5.7. $C_{16}H_{26}O_{12}$ calc.; C, 49.8, H, 6.0%); lit.[3] m.p. 103–104°, $[\alpha]_D$ +20.5° (*c* 2, chloroform).

*Reaction of phosphorus pentachloride with ethyl 2,3,4,6-tetra-*O*-acetyl-*D*-gluconate* (**3**). — Compound **3** (1 g) and phosphorus pentachloride (3 g) were thoroughly mixed, and dry carbon tetrachloride (3 ml) was added. The mixture was heated to 90° for 4 h, and t.l.c. (ether–light petroleum, 1:1) then showed one major and many minor components. Chromatography on silica gel afforded a fraction containing the major component which crystallised from the eluent to give long needles of ethyl 2,3,4,5-tetra-*O*-acetyl-6-chloro-6-deoxy-D-hexonate (117 mg, 9%), m.p. 98–100°, $[\alpha]_D$ +15.9° (*c* 2, chloroform) (Found: C, 46.8; H, 5.6; Cl, 8.9; $C_{16}H_{23}ClO_{10}$ calc.: C, 46.8; H, 5.6; Cl, 8.65%).

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REFERENCES

1 R. M. De Lederkremer, A. F. Cirelli, and J. O. Deferrari, *Carbohyd. Res.*, 13 (1970) 9.
2 J. Miksic, *Vestn. Kralov. Ceske Spolecnosti Nauk, Cl*, 11, 18 pp. (1926); *Chem. Abstr.*, 23 (1929) 2942.
3 R. T. Major and E. W. Cook, *J. Amer. Chem. Soc.*, 58 (1936) 2474, 2477.
4 F. A. H. Rice, *J. Amer. Chem. Soc.*, 78 (1956) 3173.
5 D. C. DeJongh, *J. Amer. Chem. Soc.*, 86 (1964) 3149.
6 O. S. Chishov, L. S. Golovkina, and N. S. Vul'fson, *Khim. Prirodn. Soedin., Akad. Nauk Uz. SSR*, 2 (1966) 77; see also N. K. Kochetkov and O. S. Chizov, *Advan. Carbohyd. Chem.*, 21 (1966) 46.
7 D. C. DeJongh, *J. Org. Chem.*, 30 (1965) 453.
8 E. Pacsu and F. V. Rich, *J. Amer. Chem. Soc.*, 54 (1932) 1967; 55 (1933) 3018.
9 D. C. C. Smith, *J. Chem. Soc.*, (1956) 1244.