Synthesis of Some New D-Gulopyranose Derivatives

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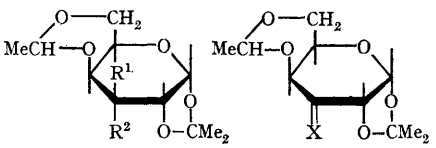
THE oxidation of carbohydrate compounds with an isolated secondary hydroxyl group, to the corresponding ketone, using dimethyl sulphoxide (DMSO) in the presence of acetic anhydride[1] or phosphorus pentoxide[2] has recently received considerable attention.[3–7] The reagent has been found to be particularly useful with compounds containing labile blocking groups since it is essentially neutral. Reduction of the ketone formed from the reaction has made it possible to obtain some new and otherwise difficult to prepare sugar derivatives.[4,5,7]

The chemistry of D-gulose and its derivatives have remained relatively unexplored mainly due to its inaccessibility, although a route from 1,2,5,6-di-*O*-isopropylidene-D-glucofuranose is now available.[8] A synthesis from a derivative of D-galactopyranose is outlined below using these oxidising agents.

Oxidation of 4,6-*O*-ethylidene-1,2-*O*-isopropylidene-D-galactopyranose[9] with DMSO in the presence of either acetic anhydride or phosphorus pentoxide yielded 4,6-*O*-ethylidene-1,2-*O*-isopropylidene-D-*xylo*-3-hexulopyranose (II);† m.p. 62—63°, $[\alpha]_D^{21}$ −47° (*c* 0·6 in $CHCl_3$); $\nu_{C=O}$ 1740 cm.$^{-1}$ in yields of 44 and 63% respectively. The product which crystallized from CCl_4–cyclohexane, was

† All new compounds reported had satisfactory analyses.

characterised as the *p*-nitrophenylhydrazone (III), m.p. **188—189°**; $[\alpha]_D^{21}$ + **466°** (*c* **0·44 in** $CHCl_3$). It is interesting to note the abnormally high positive rotation of (III) compared with the relatively small negative rotation of the parent keto-compound (II). Reduction of (II) with sodium borohydride in ethanol gave **4,6-*O*-ethylidene-1,2-*O*-isopropylidene-D-gulopyranose** (IV), m.p. **133—134°**; $[\alpha]_D^{21}$ **−19°** (*c* **0·64** in $CHCl_3$). Reduction of the crude oxidation product, without prior isolation of (II), followed by chromatography on silica gel in ether, gave (IV) in **58—65%** yield. The reduction appeared to be stereospecific as no trace of the parent D-galactose compound (I) could be found in the crude reduction mixture.



(I) $R^1 = OH$, $R^2 = H$ (II) $X = O$
(IV) $R^1 = H$, $R^2 = OH$ (III) $X = N{\cdot}NH{\cdot}C_6H_4{\cdot}NO_2$-*p*
(V) $R^1 = O{\cdot}CH_2{\cdot}SMe$, $R^2 = H$
(VI) $R^1 = H$, $R^2 = OTs$

The major by-product of the reaction was **4,6-*O*-ethylidene-1,2-*O*-isopropylidene-3-*O*-methylthiomethyl-D-galactopyranose** (V), b.p. **148—152°/0·5** mm.; $[\alpha]_D^{21}$ + **15·5°** (*C* **0·84** in $CHCl_3$). Derivatives of this type have been isolated from similar oxidations.[7] The D-gulose derivative (IV) was characterised as its **3-*O*-toluene-*p*-sulphonate** (VI), m.p. **138—139°** (decomp.); $[\alpha]_D^{21}$ + **34·6°** (*c* **0·75** in DMF).

The D-*gulo*-configuration of (IV) was shown by acid hydrolysis and comparison of the product by paper chromatography with that from the acid hydrolysis of authentic methyl **α-D-gulopyranoside**. The only products detectable in each case were D-gulose and **1,6-anhydro-β-D-gulopyranose**. The configuration was confirmed by hydrolysis of (IV) in **80%** acetic acid at **100°** for **3—4** hr. to yield syrupy D-gulose, which was characterised as its phenylhydrazone, m.p. **141—143°**, (lit.,[10] m.p. **143°**).

The reaction described above provides a reliable new route to derivatives of D-gulopyranose, and compares favourably with that mentioned earlier,[8] which also yields several other products.

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