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Note

Oxidation of primary and secondary alcohols in partially protected sugars with the chromium trioxide–pyridine complex in the presence of acetic anhydride

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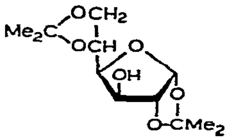
The chromium trioxide–pyridine complex[1–3] is a well-established reagent for the oxidation of primary and secondary alcohols to the corresponding carbonyl derivatives It is generally used in dichloromethane[4], which dissolves 12 5 g/100 ml at room temperature, and it is prepared *in situ*[5] Arrick and co-workers[6] have examined this reagent for the oxidation of carbohydrate derivatives Using a 12 1 molar ratio of oxidant to substrate they smoothly oxidized primary alcohols to aldehydes in yields of 53–75% The reagent was not, however, useful in oxidation of sugar derivatives containing endocyclic, isolated, secondary hydroxyl groups, *e g* , 1,2 5,6-di-*O*-isopropylidene-α-D-glucofuranose Stensio and Wachtmeister[7] observed that the oxidation with the chromium trioxide–pyridine complex was fast when performed in acetic acid The subject of oxidation in the carbohydrate field, including chromium trioxide–pyridine oxidation, has been reviewed by Butterworth and Hanessian[8]

We now report on the results of oxidation with the CrO_3 $2C_5H_5N$ complex in dichloromethane in the presence of 1 mol of acetic anhydride per mol of oxidant The oxidations were performed at room temperature with excess of the reagent Preliminary experiments with various molar ratios of reagent and hydroxyl compound demonstrated that the optimal results, with almost quantitative yields of oxidized product formed in 5–10 min, were obtained when a 4 1 ratio was used Results are presented in Table I A strong dependence of the yield upon the molar excess of oxidant used was observed for 1,2 3,4-di-*O*-isopropylidene-α-D-galactose only. With a molar ratio of 3 1 and a 30-min reaction time, the yield of 1,2 3,4-di-*O*-isopropylidene-α-D-*galacto*-hexodialdo-1,5-pyranose obtained was ~65% A molar ratio of 4 1 and a 5-min reaction time gave a 93% yield Variations in the reaction time indicated that the product is susceptible to further oxidation

A possible reason for the high yields obtained in the oxidations by adding 1 molar equivalent of acetic anhydride per mole to the chromium trioxide–pyridine complex in dichloromethane may be that the acetic anhydride facilitates the reduction of



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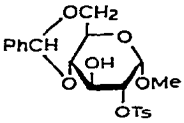

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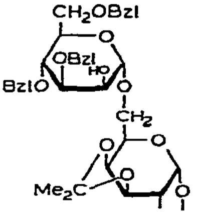

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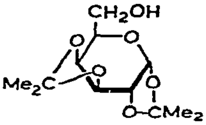

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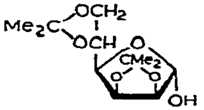

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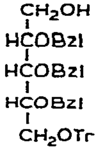

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Bzl = CH_2Ph

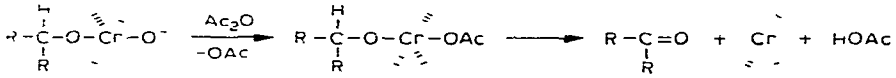
TABLE I

OXIDATION DATA

Starting material	Ref	Product	Yield (%)	$[\alpha]_D^{22}$ (CHCl$_3$) (degrees) Obs	Lit	M p (degrees) Obs	Lit
1	10	3-ulose[11, 12]	>90[a]	+123	+137[11]	low-melting, hygroscopic solid	39–40
2	13	3-ulose[14, b]	95	+71 +45 (HCONMe$_2$)	 +45 (HCONMe$_2$)	167–168	165–167
3	15	2-ulose[15]	94	+1	+1	syrup	syrup
4	16, 17	6-aldehyde[6, 18]	93[c]	−109	−111 −131	syrup	syrup
5	19, 20	1,4-lactone[21]	97	+51	−51	128	126
6	22	1-aldehyde[d]	87	+7		85–86	

[a] The weighed yield was 95% G l c revealed the presence of <5% of acetylated starting material The hydrate of the 3-ulose had $[\alpha]_D^{22}$ +40° (CHCl$_3$), lit[12] $[\alpha]_D$ +40° (CHCl$_3$) [b] N m r data (CDCl$_3$) δ 5.21 (d 1 H $J_{1,2}$ 4.2 Hz H-1) 5.09 (dd, 1 H, $J_{1,2}$ 4.2, $J_{2,4}$ 1.0 Hz, H-2) The long-range coupling was not previously noted[14] [c] To obtain maximum yield the reaction was interrupted after 5 min by adding an excess of ethanol in ethyl acetate [d] *Anal* Calc for $C_{45}H_{42}O_5$ C 81.5, H, 6.39 Found C 81.5, H 6.22

chromium(VI) from the intermediate ester as follows



in an analogous fashion to the role of acetic anhydride in methyl sulfoxide–acetic anhydride oxidation[9]

In previous oxidations of secondary hydroxyl groups in carbohydrates, the yields varied with the orientation of the hydroxyl groups, axial or equatorial in pyranoid systems and *exo* or *endo* in five-membered ring systems. The present system seems to be insensitive to steric factors.

EXPERIMENTAL

General. — Melting points are corrected. Optical rotations were determined with a Perkin–Elmer 241 polarimeter (*c* 1, throughout). I.r. spectra were recorded with a Perkin–Elmer 257 spectrometer. N.m.r. spectra were recorded with a Jeol JNM FX-100 instrument operating at 99.55 MHz in the Fourier-transform mode, for solutions in chloroform-*d* containing 0.1% of tetramethylsilane as the internal standard and lock signal. Chemical shifts were recorded on the δ scale. For all products, i.r. and n.m.r. spectra were in agreement with the postulated structures. A Perkin–Elmer 990 gas chromatograph fitted with a glass column containing 3% of OV-225 on Gas Chrom Q was used. Concentrations were performed at reduced pressure with a bath temperature below 40°. T.l.c. was performed on silica gel F_{254} (Merck) plates, sulfuric acid (8%) was used as spray reagent. Elution of oxidation products was performed with silica gel 60 (0.040–0.063 mm, Merck). The purity of all the various products was ascertained by g.l.c. or by t.l.c. in solvent systems that clearly distinguished starting materials from products.

Reagents. — Chromium trioxide (Riedel-de Haen AG, Seelze-Hannover) was kept dry in a vacuum over phosphorus pentaoxide. Analytical-grade pyridine was distilled from phosphorus pentaoxide and stored over potassium hydroxide pellets. Analytical-grade dichloromethane was distilled from phosphorus pentaoxide and stored over a molecular sieve (3 Å). Analytical-grade acetic anhydride was used.

Oxidation and work-up procedure. — Chromium trioxide (4 molar equivalents per molar equivalent of alcohol to be oxidized) was added to a stirred solution of pyridine (2 mol per mol of CrO_3) in sufficient dichloromethane to dissolve the $CrO_3 \cdot 2C_5H_5N$ complex. The reaction vessel was sealed during this operation, in order to prevent evaporation of the solvent; the heat evolved facilitated dissolution of the complex. These oxidations were performed with 0.5–3.5 g of carbohydrate derivative; in oxidations on a larger scale, a reflux condenser should be used. The mixture was stirred for 15 min to produce a deep-red solution containing only traces of unreacted CrO_3. The alcohol to be oxidized, dissolved in a small amount of dichloromethane, was added with stirring at room temperature. A tarry deposit formed at once and the colour of the mixture changed to dark-brown. Acetic anhydride (1 mol per mol of $CrO_3 \cdot 2C_5H_5N$) was added at once and the reaction was monitored by t.l.c. After a reaction time of 5–10 min, the mixture was transferred to the top of a short column of silica gel in ethyl acetate, with a layer of ethyl acetate above the gel in which chromium compounds were precipitated before elution. The product was eluted with ethyl acetate in one fraction. The colourless eluate was concentrated to near dryness. Toluene was added and the mixture concentrated again

This procedure was repeated a few times in order to remove any acetic acid and pyridine present, after which the mixture was concentrated to dryness

Note Laboratory equipment contaminated with chromium compounds is cleaned with aqueous sodium hydroxide

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