Anomalous Oxidative Dimerisation of Some Carbohydrate Primary Alcohols with $CrO_3,2C_5H_5N$

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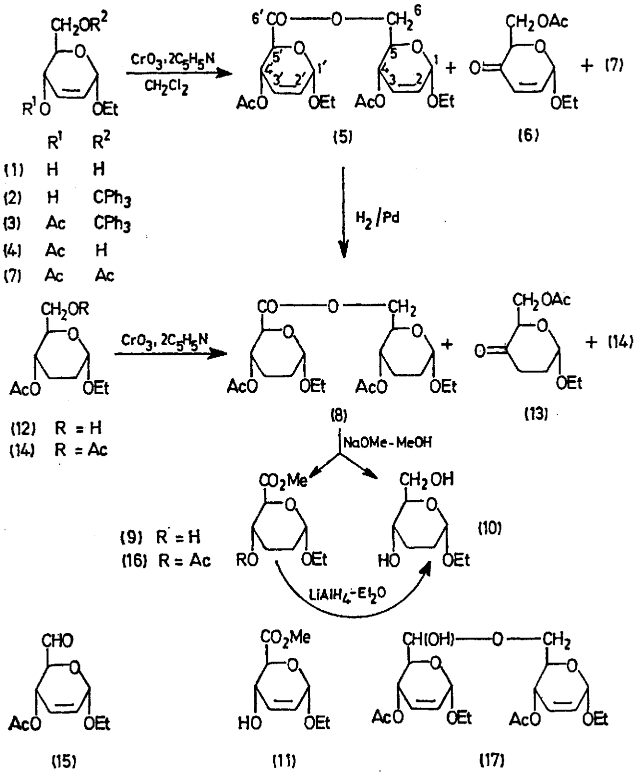
Summary The hydroxymethyl group of some carbohydrate molecules undergoes oxidative dimerisation with CrO_3,$2C_5H_5N$, there being no evidence of an intermediate aldehyde having formed prior to the dimerisation.

The complex $CrO_3,2C_5H_5N$ is widely regarded as the reagent of choice for the oxidation of alcohols, the process occurring either rapidly and cleanly, or not at all.[1] It has been widely tested with carbohydrate substrates,[2,3] and accumulated experience indicates that hydroxymethyl groups invariably furnish aldehydes.[2a] In view of this we report an anomalous case where the product of hydroxymethyl oxidation is not an aldehyde, but a dimeric ester.



Compound (4),†‡ prepared from the diol (1) *via* (2) and (3), was oxidised with 12 equiv. of $CrO_3,2C_5H_5N$ prepared beforehand[1b] or *in situ*,[1c] and yielded three components, none of which was an aldehyde, which were isolated by silica column chromatography. The major product, obtainable in 23% yield, was judged to be the dimer (5); m.p. 53—53·5°, $[\alpha]^{23}_{D}$ + 118·8° (*c* 2·05, $CHCl_3$), *m/e* 428. The mass spectrum and the 60 MHz n.m.r. spectrum of (5) ($CDCl_3$; Me_4Si) showed two acetate and two ethoxy groups. At 220 MHz, all protons except the four olefinic ones were resolved. A clean doublet at δ 4·51 assignable to 5'-H demonstrated the absence of C-6 hydrogens and facilitated the recognition of 4'-H. The C-5 and two C-6 protons on the other ring appeared (δ 4·12—4·41) as the ABC portion of a complex ABCX pattern at the expected chemical shift, and were coupled to 4-H (δ 5·23). The protons of the uronate ring resonated at lower field than the analogous protons of the other ring, the olefinic protons being excepted.

Two other products were found to be the known compounds (6) (1·3% yield) and (7) (5%).[5] The former obviously arises from intramolecular acetyl migration followed by oxidation while the latter must be the product of intermolecular acetyl migration.

Chemical proof of structure (5) was obtained by hydrogenation of the double bond to give (8) and methanolysis to yield the known diol (10) and the uronate ester (9). The structure of the latter [as (9) or the mono-acetate (16)] was evident from 220 MHz n.m.r. and i.r. spectroscopy, and was confirmed chemically by $LiAlH_4$ reduction to (10). Methanolysis of (5) without prior hydrogenation afforded (1); however the uronate portion (11) did not survive silica chromatography.

In order to test whether the double bond was in any way responsible for the unusual behaviour of (4), the dihydro-derivative (12) was oxidized similarly. Three parallel products (8), (13), and (14) were obtained in yields of 5, 17, and 4% respectively. Thus, the anomalous reaction occurred although the yield of the dihydro-dimer (8) was less.

Compound (4) also behaves unusually toward other oxidizing agents. With the Et_3N–$C_5H_5NSO_3$–Me_2SO reagent, for example, substrates having a C-4–C-5–C-6 unit as in (4), normally undergo oxidation with β-elimination to give an unsaturated aldehyde. However (4) was unaffected by this reagent after 30 min. With the Pfitzer–Moffatt reagent,[7] an appreciable amount of (4) was unchanged after 24 h although several products had been formed, which did not, however, include aldehydes, or (5) or (6).

The conversion of (4) and (12) into (5) and (8) respectively is, to the best of our knowledge, unprecedented for $CrO_3,2C_5H_5N$ oxidations. The outcome is reminiscent of a Tischenko reaction,[8] which would require formation of the expected aldehyde (15) and its subsequent intermolecular redox to give (5). Alternatively, the aldehyde (15) and the starting alcohol (4) could react to give a hemiacetal (17), which then could undergo oxidation to the uronate ester (8). However, since both these possible mechanisms ought to be applicable to any primary alcohol, it is not clear why the result is not generally observed. Further, the process is rapid, the dimers being detectable immediately on t.l.c. without any evidence of an aldehyde intermediate.

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† In view of the possibility of acetyl migration, the alcohol (4) was confirmed as being primary by retritylation to (3).

‡ All compounds gave satisfactory elemental and spectroscopic analyses.

[1] (a) R. Ratcliff and R. Rodehorst, *J. Org. Chem.*, 1970, **35**, 4000; (b) J. C. Collins, W. W. Hess, and F. J. Frank, *Tetrahedron Letters*, 1968, 3363; (c) C. A. Hendrick, F. Schaub, and J. B. Siddal, *J. Amer. Chem. Soc.*, 1972, **94**, 5374.

[2] (a) R. E. Arrick, D. S. Baker, and D. Horton, *Carbohydrate Res.*, 1973, **26**, 411; (b) P. M. Collins, *ibid.*, 1969, **11**, 125.

[3] B. Fraser Reid, D. L. Walker, and M. B. Yunker, unpublished results.

[4] B. Fraser-Reid and B. Boctor, *Canad. J. Chem.*, 1969, **47**, 393.

[5] (a) B. Fraser-Reid, A. McLean, E. W. Usherwood, and M. Yunker, *Canad. J. Chem.*, 1970, **48**, 2877; (b) R. J. Ferrier and N. Prasad, *J. Chem. Soc.* (*C*), 1969, 570, 575.

[6] D. M. Mackie and A. S. Perlin, *Carbohydrate Res.*, 1972, **67**, 24.

[7] K. E. Pfitzer and J. G. Moffatt, *J. Amer. Chem. Soc.*, 1965, **87**, 5661, 5670.

[8] C. A. Buehler and D. E. Pearson, 'Survey of Organic Synthesis,' Wiley, New York, 1970, p. 853.