the filtrate was warmed and evaporated under reduced pressure. A chloroform solution of the residue was washed with dilute sulphuric acid and then with dilute sodium carbonate solution. The solution was dried (sodium sulphate) and evaporated. The residue, a yellow oil, distilled under reduced pressure, yielded an almost colorless oil (230 mg), b.p. 70–72°/10^{-1} mm, showing strong absorption at 1644 cm^{-1} in the infrared. Anal. Calc. for $C_{13}H_{17}ON$: C, 76.81; H, 8.43; N, 6.89. Found: C, 76.98; H, 8.43; N, 6.84.

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1. G. V. D. TIERS. J. Phys. Chem. **62**, 1151 (1958).
2. J. A. POPLE, W. G. SCHNEIDER, and H. J. BERNSTEIN. Can. J. Chem. **35**, 1060 (1957).
3. S. MCLEAN, K. PALMER, and L. MARION. Can. J. Chem. **38**, 1547 (1960).
4. G. M. BENNET and M. M. HAFEZ. J. Chem. Soc. 287 (1941).

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SCISSION OF STERICALLY HINDERED *vic*-DIOLS*

H. R. GOLDSCHMID† AND A. S. PERLIN

The scission of *vic*-diols by lead tetraacetate (1) and periodic acid (2, 3) is strongly rate dependent on the stereochemistry of the glycol group attacked. This property has led to the view (4), now generally accepted, that the reaction usually involves formation of a coplanar cyclic intermediate complex between the glycol and oxidant. Complexing of this type is unlikely to occur if the projected valency angle of the glycol group is held rigidly in the region of 120–180° (5, 6, 7). Such a steric arrangement is found in several compounds that contain a *trans*-glycol group situated in a fused or bridged ring system, and the fact that these compounds fail to react with lead tetraacetate or periodate is in excellent agreement with the concept of the cyclic intermediate.‡ In this group of sterically hindered glycols are 1,6-anhydro-β-D-glucofuranose and -α-D-galactofuranose (8), the two *trans*-2,3-camphanediols (9), cholestane-3β,6β,7α-triol (10), 4,6-*O*-benzylidene methyl α-D-altropyranoside (11), and 2,6-anhydro-β-D-fructofuranose (12).

Steric effects that are strongly evident for oxidations with lead tetraacetate in acetic acid were noted by Hockett and Mowery (13) to be much less marked when pyridine was used as solvent. This observation suggested that the steric requirements for lead tetraacetate oxidation are less critical in pyridine than under the more usual reaction conditions, and prompted us to test the stability of the sterically hindered glycols towards lead tetraacetate in pyridine. Several of these compounds have now been examined and found, in fact, to be oxidized readily (Table I). That the reactions constitute true glycol cleavage is indicated by the degradation of 4,6-*O*-benzylidene methyl α-D-altropyranoside (I) (as well as the corresponding D-glucoside) to the dialdehyde isolated, as the hemialdal hydrate

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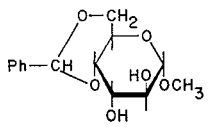
‡*Trans-9,10-Decalindiol also appears unable to attain such a transition state but is nevertheless oxidized by lead tetraacetate, possible via an acyclic pathway (7). However, this compound resists attack by periodate (10).*



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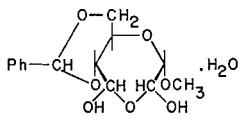

II

TABLE I

Scission of *vic*-diols by lead tetraacetate in pyridine (moles of oxidant consumed/mole at 0° C)

Time (minutes)	2,6-Anhydro-β-D-fructofuranose		*trans*-2-Exo-3-endo-camphanediol*	
	(2 moles)†	(4.5 moles)	(3 moles)	(4.5 moles)
15	0.11	0.60	0.35	0.83
30	0.19	0.69	0.42	0.93
60	0.29	0.81	0.50	1.00
180	0.44	1.02	—	1.06
480	0.57	1.30	—	1.08

	4,6-*O*-Benzylidene methyl α-D-glycopyranoside	
	D-Altro-	D-Gluco-
	(5 moles)	
5	0.51	1.01
15	0.71	1.02
30	0.82	1.07
60	1.03	—
180	1.04	1.16

	Ethyl β-D-fructofuranoside and derivatives			
	1,6-Di-*O*-trityl-‡		1,6-Di-*O*-tosyl-	Glycoside‡
	(1.6 moles)§	(5 moles)	(1.7 moles)§	(2.0 moles)
15	0.54	1.02	—	0.88
30	0.63	0.98	0.95	1.03
60	0.72	1.00	0.96	1.18
90	0.74	—	1.04	1.21

*Closely similar data were obtained for the 2-endo-3-exo-isomer.
†Figures in parentheses give the number of moles of lead tetraacetate used per mole of substrate.
‡Closely similar data were obtained for the α-anomer.
§Temperature, 25° C.

(II) (14), formed by periodate oxidation of 4,6-*O*-benzylidene methyl α-D-glucopyranoside* (14, 15, 16).†

A normally "slow" diol (17), *trans*-1,2-cyclopentanediol, was very rapidly oxidized, the observed uptake being 0.9 to 1.0 mole of lead tetraacetate per mole in 5 minutes reaction time, irrespective of whether the excess of oxidant used was 0.25, 1.0, or 3.0 moles per mole. By contrast, the rate of oxidation of the hindered diols fell off sharply at well below

4,6-O-Benzylidene methyl α-D-glucopyranoside is oxidized at an unusually slow rate by periodate (11, 16). It also is extremely resistant to attack by lead tetraacetate in acetic acid, a property that is exhibited also by e,e trans-diols situated on 1,4-bonded central units of oligosaccarides (18). In pyridine, however, the benzylidene derivative is rapidly oxidized by lead tetraacetate (Table I and Experimental section).

†*Cholestane-3β,6β,7α-triol (10) (a sample of which was kindly provided by Prof. S. J. Angyal) is more resistant to oxidation than the other compounds examined: the observed rate of lead tetraacetate uptake (mole/mole(min)) was 0.34 (15), 0.55 (90), and 0.80 (360). This result contrasts strongly with the behavior of I (Table I), which also contains a diaxal glycol group, and may be related to the greater rigidity of ring B in the cholestane derivative than of the pyranoside ring in I.*

the theoretical level if an excess of only 1 to 2 moles of lead tetraacetate was used (Table I). With an excess of 3 to 4 moles the data were much more satisfactory (Table I). The marked drop in reaction rate at the lower level of concentration may possibly be related to Criegee's suggestion (4) that acetic acid, formed in the reduction of lead tetraacetate to the diacetate, can depress the rate of oxidation in a solvent other than acetic acid by a mass-action effect. Such an effect would be most readily apparent with the most highly hindered glycols.

Although the stoichiometry of the various reactions examined is close to the theoretical value under suitable conditions, slow overoxidation is always evident (Table I). Because of this non-specific overoxidation several hydroxylated compounds, other than 1,2-glycols, were examined. In this group were 1,2,3,4- and 2,3,4,6-tetra-*O*-acetyl-D-glucopyranose; 1,3-dihydroxypropane; 1,3-dihydroxy-2,2-dimethylpropane; pentaerythritol; 1,6-dihydroxyhexane; 2,5-dihydroxyhexane; and 1,3,6-trihydroxyhexane. Of these compounds, only 1,3-dihydroxypropane was attacked to a significant degree during the period of 1 to 2 hours (Table I) required for complete oxidation of the hindered glycols, the consumption in 2 hours reaction time being 0.12 mole of lead tetraacetate per mole. With a more prolonged oxidation period (8 to 24 hours), several of the compounds reduced a small proportion of oxidant (0.1 to 0.2 mole/mole), and with pentaerythritol the consumption reached a value of 0.6 mole/mole in 24 hours. It is clear, therefore, that in testing for the presence of a 1,2-diol group in an unknown compound with lead tetraacetate in pyridine, prolonged reaction periods should be avoided.

Pyridine is particularly suitable for the glycol-cleavage oxidation of certain classes of compounds which might be unstable or poorly soluble in media used more commonly. Hockett and co-workers (13, 19) first employed this solvent for lead tetraacetate oxidation of sucrose and trityl ethers of methyl D-arabopyranoside, compounds unstable in acetic acid. Similarly, we have found these conditions of oxidation useful for determining the structure of trityl- and tosyl-derivatives of ethyl α- and β-D-fructofuranoside (12). The 1,6-ditrityl ether of these glycosides exhibited behavior that is characteristic of the highly hindered diols described above, in that their oxidation rates dropped sharply when a small excess of lead tetraacetate was used (Table I). As shown by Smith and co-workers (20), periodate oxidation may be inhibited when a trityl or phenyl group is in close proximity to the *vic*-diol, the effect being attributed to steric interference. However, interference by bulky substituents does not appear to account fully for the retarded oxidation rate of the ditrityl-D-fructofuranosides, because the corresponding 1,6-ditosyl derivative reacts readily and quantitatively (Table I).

EXPERIMENTAL

Lead tetraacetate was dried *in vacuo* over solid potassium hydroxide, and pyridine was freshly distilled over solid potassium hydroxide.

Measurement of Lead Tetraacetate Uptake

The stopping solution (1) used (per milliliter of reaction mixture) contained potassium iodide (1.0 g), sodium acetate (2.7 g, anhydrous) in water (10 ml). Acetic acid (3 ml) was added to the stopping solution immediately before an aliquot of the oxidation mixture in order to complete the liberation of iodine. A bulky yellow precipitate is formed when lead tetraacetate in pyridine is mixed with the stopping solution; determination of the iodine with thiosulphate was facilitated by adding starch indicator at the outset, the suspension being titrated until the pea-green color was discharged.

In a typical experiment, 2,6-anhydro-β-D-fructofuranose (13.0 mg) in pyridine (4 ml) was treated at 0° C with a solution of lead tetraacetate (160 mg) in pyridine (6 ml). (The solution of lead tetraacetate in pyridine is deep brown in color, and the intensity of the color diminishes as oxidant is used up.) At chosen intervals, 1-ml portions of the reaction mixture were transferred to the stopping solution, and the liberated iodine was titrated immediately with thiosulphate.

Oxidation of 4,6-O-Benzylidene Methyl α-D-Altropyranoside (I)

To a solution of the benzylidene glycoside (282 mg) in pyridine (15 ml), lead tetraacetate (1.32 g) was added. After 25 minutes at room temperature the reaction mixture was treated with oxalic acid dihydrate (4.0 g) and a few drops of water. The precipitate was filtered off, the filtrate concentrated *in vacuo* at 45° C, and the residue obtained was taken up in hot aqueous acetone. A crystalline product (201 mg) was deposited from the cooled solution, and after recrystallization from aqueous acetone the product II (14) had a melting point of 130–133° C and $[\alpha]_D^{27}$ +62.8° (*c*, 1.9, pyridine). Calculated for $C_{14}H_{18}O_7 \cdot H_2O$: C, 53.16%; H, 6.37%. Found: C, 53.25%; H, 6.44%.

On treatment with hot phenylhydrazine acetate the product yielded glyoxal bis-phenylhydrazone, m.p. 164–166° C, undepressed.

The above hemialdal hydrate furnished a bis-cyclohexylamine derivative (14) with a melting point of 115–117° C and $[\alpha]_D^{27}$ −32.6° (*c*, 1.2, pyridine). Calculated for $C_{26}H_{38}O_4N_2$: C, 70.55%; H, 8.65%. Found: C, 70.48%; H, 8.86%.

Oxidation of 4,6-O-Benzylidene Methyl α-D-Glucopyranoside

The benzylidene glycoside (282 mg) was treated in pyridine (10 ml) with lead tetraacetate (618 mg) for 15 minutes at room temperature. Excess oxidant was reduced with oxalic acid, and the reaction mixture was worked up, affording compound II (14), m.p. 130–133° C, undepressed, and $[\alpha]_D^{27}$ +63.0° (*c*, 1.8, pyridine). Calculated for $C_{14}H_{18}O_7 \cdot H_2O$: C, 53.16%; H, 6.37%. Found: C, 53.54%; H, 6.16%.

On treatment with hot phenylhydrazine acetate the product yielded glyoxal bis-phenylhydrazone, m.p. 164–166° C, undepressed.

The derived bis-cyclohexylamine derivative (14) had a melting point of 115–117° C, undepressed and $[\alpha]_D^{27}$ −31.9° (*c*, 1.2, pyridine). Calculated for $C_{26}H_{38}O_4N_2$: C, 70.55%; H, 8.65%. Found: C, 70.56%; H, 8.59%.

The X-ray powder diagrams obtained from the above hemialdal hydrate and its bis-cyclohexylamine derivative were indistinguishable from the corresponding materials obtained from 4,6-*O*-benzylidene methyl α-D-altropyranoside.

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1. R. CRIEGEE. Ber. **64**, 260 (1931).
2. L. MALAPRADE. Bull. soc. chim. France, **39**, 325 (1926).
3. P. F. FLEURY and J. LANGE. Compt. rend. **195**, 1395 (1932).
4. R. CRIEGEE, L. KRAFT, and B. RANK. Ann. **507**, 159 (1933).
5. R. E. REEVES. *In* Advances in carbohydrate chemistry. Vol. 6. Academic Press, Inc., New York. 1951. p. 107.
6. R. J. DIMLER. *In* Advances in carbohydrate chemistry. Vol. 7. Academic Press, Inc., New York. 1952. p. 37.

7. R. CRIEGEE, E. HÖGER, G. HUBER, P. KRUCK, F. MARKTSCHEFFEL, and H. SCHELLENBERGER. Ann. **599**, 81 (1956).
8. R. J. DIMLER, H. A. DAVIS, and G. E. HILBERT. J. Am. Chem. Soc. **68**, 1377 (1946).
9. S. J. ANGYAL and R. J. YOUNG. J. Am. Chem. Soc. **81**, 5467 (1959).
10. S. J. ANGYAL and R. J. YOUNG. J. Am. Chem. Soc. **81**, 5251 (1959).
11. J. HONEYMAN and C. J. G. SHAW. J. Chem. Soc. 2454 (1959).
12. H. R. GOLDSCHMID and A. S. PERLIN. Can. J. Chem. This issue.
13. R. C. HOCKETT and D. F. MOWERY, JR. J. Am. Chem. Soc. **65**, 403 (1943).
14. R. D. GUTHRIE and J. HONEYMAN. J. Chem. Soc. 2441 (1959).
15. J. W. ROWEN, R. E. REEVES, and F. H. FORZIATI. J. Am. Chem. Soc. **73**, 4484 (1951).
16. J. BADDILEY, J. G. BUCHANAN, and L. SZABO. J. Chem. Soc. 3826 (1954).
17. R. CRIEGEE, E. BÜCHNER, and W. WALTHER. Ber. **73**, 571 (1940).
18. A. S. PERLIN and A. R. LANSDOWN. Can. J. Chem. **34**, 451 (1956).
19. R. C. HOCKETT and M. ZIEF. J. Am. Chem. Soc. **72**, 2130 (1950).
20. E. F. GARNER, I. J. GOLDSTEIN, R. MONTGOMERY, and F. SMITH. J. Am. Chem. Soc. **80**, 1206 (1958).

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