Oxidation of 1,4-Diols to Lactones[1]

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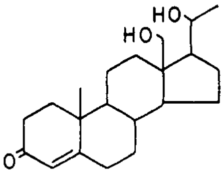
Received July 31, 1962

A study is presented of the oxidation of a variety of 1,4-diols using several oxidizing agents. A γ-lactone is formed in all cases except where stereochemical orientation prohibits it. The formation of the γ-lactone is thought to proceed through an intermediate hemiacetal which is readily oxidized to the corresponding lactone. The formation of lactone requires the vicinal hydroxymethyl groups to be essentially coplanar. Where the coplanarity is prohibited further oxidation products are obtained.

There are several known reactions in which lactones have been generated from diols. Dehydrogenation catalysts are reported to be successful.[3-7] A direct oxidation on 3-methyl-1,4-heptanediol with dichromate–acetic acid provides the γ-lactone in 80% yield.[8] Further Nussbaum, *et al.*, have converted the steroidal diol (I) into a lactone by oxidation[9] and Rothman, *et al.*, have shown that hecolyl alcohol (II) can be converted into 3-dihydrohecololactone[10] by the Sarett procedure[11] in 86% yield. It is important to note that one of the hydroxyls in the reactions not involving dehydrogenation catalysts is either secondary or tertiary. Hence the results are not as surprising as the present cases where both are primary.



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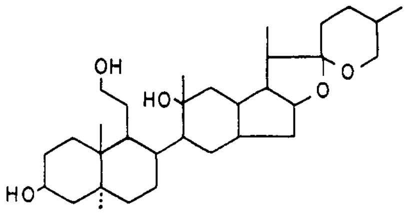
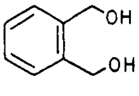


II

In attempts to prepare dialdehydes from 1,4-diols, the oxidation of alcohols using the Sarett procedure was brought under investigation. *o*-Xylene-α,α′-diol (III) formed none of the desired phthalaldehyde when treated with the chromium trioxide–pyridine complex; instead, the reaction produced phthalide (V). The high yield of this conversion prompted a thorough investigation to determine the full scope of the reaction.

The models, other than *o*-xylene-α,α′-diol, chosen for study were *cis*-1,4-butenediol, 1,4-butanediol, and the two cyclopentanediols, VI and VII. The last two alcohols were included to determine the influence of stereochemical factors on the oxidation.



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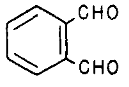

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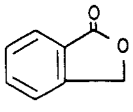

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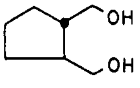

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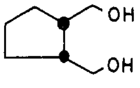

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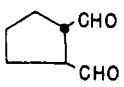
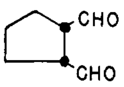


VIII



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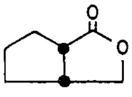

X

The γ-lactones corresponding to the 1,4-diols were obtained in good yield for the first three systems, whereas, only in trace quantities for the cyclopentanediols. Interestingly, each of the cyclic diols (VI and VII) gave the same dialdehyde (VIII) as the major product. No evidence was found for the formation of a *cis* aldehyde (IX). The yields of lactone decreased according to the sequence: *o*-xylene-α,α′-diol > butenediol > butanediol. To determine further whether the reaction was specific only with chromium trioxide–pyridine, the reaction was conducted with two other oxidizing agents, sodium dichromate and potassium permanganate. The γ-lactone was formed in even higher yields in these cases, the work ups less tedious and the reaction times reduced. In contrast to the Sarett oxidation, the *cis* diol (VII) now gave the lactone (X) when oxidized with sodium dichromate.

The mechanism suggested[10] for the oxidation of I is also consistent with these experimental data. One hydroxyl group is first oxidized with subsequent collapse of the neighboring alcohol to form the hemiacetal. This acetal then undergoes further oxidation to the lactone as illustrated in Figure 1. The last step of the mechanism is supported by the known fact that hemiacetals can be oxidized by the chromic anhydride complex to the corresponding lactones.[12]

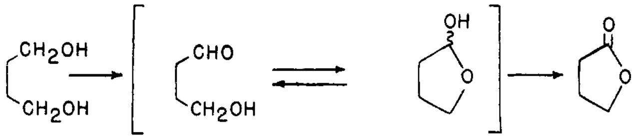

Figure 1

Since hemiacetal formation is an equilibrium reaction, stereochemical factors should be important in the lac-

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[1] The financial support by a Frederick Gardner Cottrell Grant from the Research Corp. is gratefully acknowledged. This material was presented in part before the 54th Meeting of the North Dakota Academy of Science, Fargo, N. D., May 4-5, 1962.

[2] Abstracted from the M.S. thesis of R. J. Perkins, University of North Dakota, 1962.

[3] J. W. Reppe, *Chem. Industries*, **57**, 458 (1945).

[4] J. G. M. Bremmer and D. G. Jones (Imperial Chem. Ind.), British Patent 583,344 (December 16, 1946).

[5] L. P. Kyrides and F. B. Zienty, *J. Am. Chem. Soc.*, **68**, 1385 (1946).

[6] L. E. Schniepp and H. H. Geller, *ibid.*, **69**, 1545 (1947).

[7] J. A. Berson and W. M. Jones, *J. Org. Chem.*, **21**, 1325 (1956).

[8] C. Glacet, *Ann. chim.*, [12] **2**, 293 (1947).

[9] A. L. Nussbaum, F. E. Carlon, E. P. Oliveto, E. Townley, P. Kabasakalian, and D. H. R. Barton, *Tetrahedron*, **18**, 373 (1962).

[10] E. S. Rothman, M. E. Wall, and C. R. Eddy, *J. Am. Chem. Soc.*, **76**, 527 (1954).

[11] G. I. Poos, G. E. Arth, R. E. Beyler, and L. H. Sarett, *ibid.*, **75**, 427 (1953).

[12] D. H. R. Barton, J. M. Beaton, L. E. Geller, and M. M. Pechet, *ibid.*, **83**, 4076 (1961).

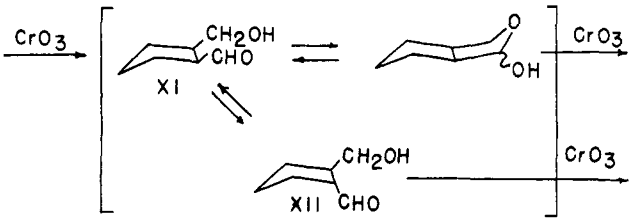

Figure 2

tone formation. With *o*-xylene-α,α'-diol (III) and *cis*-1,4-butenediol, the vicinal hydroxymethyl groups are held rigidly in the same plane facilitating collapse to the hemiacetal. In the case of 1,4-butanediol, the probability that the two groups will be in the necessary orientation for formation of the intermediate hemiacetal prior to oxidation is less. As a consequence the presence of aldehyde in the oxidation products of the latter reaction is expected and, indeed, obtained.

The formation of the *trans* dialdehyde from VI and VII also can be rationalized from the mechanism. In both these compounds the hydroxylmethyl groups have fixed orientations in space. Because the configuration of the *trans* diol (VI) inhibits cyclization of the intermediate to the hemiacetal (based on studies of molecular models[13] and the related bicyclo[3,3,0]octanes[14]), the corresponding dialdehyde is the favored product. On the same basis the *cis* diol (VII), analogous in stereochemistry to the unsaturated alcohols, should give the lactone. However, this oxidation produces products of *trans* stereochemistry. It is noteworthy that the monoaldehyde (XI) contains an equilibratable hydrogen alpha to a carbonyl function and that it is isomerized to the corresponding *trans* form (XII) in the presence of the base pyridine.

The extent of formation of lactone opposed to aldehyde generation would be dependent upon the reactive rate of the reactions illustrated in Figure 2. In chromium trioxide–pyridine the *cis* to *trans* isomerization is more rapid than the cyclization with oxidation accounting for the observed products. In the presence of a stronger oxidizing agent the oxidation process portrayed in Figure 1 is now expediated and the lactone formation more than successfully competes with the isomerization. Therefore when the *cis* diol (VII) is oxidized with sodium dichromate in acid media, the lactone is produced exclusively. This evidence strengthens the postulated sequence above and discards the alternate possibility of direct oxidation to the *cis* dialdehyde with subsequent isomerization to the *trans* species in the generation of IX from VII.[15]

Experimental[16]

Oxidation of *o*-Xylene-α,α'-diol with Chromium Trioxide–Pyridine.—A solution of the chromic anhydride–pyridine complex was prepared by the procedure of Sarett from 5.1 g. (51 mmoles) of chromium trioxide and 50 ml. of pyridine. To the bright yellow slurry of complex, a solution of 0.7 g. (5 mmoles) of *o*-xylene-α,α'-diol in 10 ml. of pyridine was added. The resulting mixture was well mixed and shaken intermittently over a 20-min. period and then allowed to stand at room temperature overnight. The reaction was hydrolyzed with water (50 ml.) and filtered to remove the inorganic residue. The filtrate was extracted three times with a 1:1 benzene–ether mixture; the combined organic layers were dried over magnesium sulfate and the solvent removed on a steam bath at reduced pressure. The residue (565 mg., 84.6%) was recrystallized from petroleum ether to afford 400 mg. (60%) of phthalide, m.p. 74–75.5° (lit.,[17] m.p. 73–74°). The infrared spectrum had a band at 5.62 μ appropriate for a γ-lactone.

Oxidation of 1,4-Butanediol with Chromium Trioxide–Pyridine.—In the same manner as described for *o*-xylene-α,α'-diol, 1,4-butanediol (0.9 g.) was treated with the chromium trioxide–pyridine complex. Evaporation of the benzene–ether afforded a thick brown oil; infrared analysis showed bands at 5.58 μ (γ-lactone) and 5.81 μ (aldehyde). The crude butyrolactone was separated by gas phase chromatography. There were two major components, identified as butyrolactone and pyridine by comparison of their retention times to those of authentic samples; 75 seconds at 190° on an *n*-decylphthalate column for butyrolactone. The yield of lactone was 34% which was determined from the gas chromatogram.

Oxidation of *cis*-1,4-Butenediol with Chromium Trioxide–Pyridine.—A pyridine solution of *cis*-1,4-butenediol (11.4 mmoles, Gaf Chemical Co.) was oxidized as above. The reaction afforded 51% of the α,β-unsaturated γ-lactone. The yield was determined by comparison of the area under the gas chromatogram to that of the standard butyrolactone. This requires the assumption that the heat conductivities of the two lactones are equal. The identity was based on the infrared spectrum which exhibited a γ-lactone carbonyl band at 5.60 μ and a double bond band at 6.25 μ.

Oxidation of the *trans* Diol(VI) with Chromium Trioxide–Pyridine.—Oxidation of VI (350 mg.) with chromium trioxide–pyridine produced an oil. Infrared analysis revealed the absence of a γ-lactone in the oil and the presence of a carbonyl band at 5.80 μ. The 2,4-dinitrophenylhydrazone of the oil was identical to that of the same derivative of the *trans* aldehyde (VI from an independent synthesis) m.p. 240° dec.; mixed m.p. 238–240° dec.

Oxidation of *o*-Xylene-α,α'-diol with Sodium Dichromate.—A solution of 1.38 g. (10 mmoles) of *o*-phthalyl alcohol in water (10 ml.) was chilled to 0° in an ice bath while a mixture of 4.78 g. (20 mmoles) of sodium dichromate and 3 ml. of concentrated sulfuric acid in water (10 ml.) was added. The solution was warmed to room temperature and allowed to stand for 3 hr. After dilution with 50 ml. of water the solution was extracted with ether. The combined ether extracts, after drying, afforded 1.28 g. (95%) of phthalide.

Oxidation of the *cis* Diol (V) with Sodium Dichromate.—A chilled solution of 100 mg. (8 mmoles) of the *cis* diol was treated in the same manner as above. The clear liquid (85 mg.) obtained after evaporation of the ether was analyzed by infrared. The material consisted mainly of the γ-lactone (5.61 μ) with the estimated over-all yield of 60% (infrared).

Oxidation of *o*-Xylene-α,α'-diol with Potassium Permanganate.—A solution of 1.38 g. (10 mmoles) of *o*-xylene-α,α'-diol and 3.18 g. (20 mmoles) of potassium permanganate in 20 ml. of water was allowed to stand at room temperature for 8 hr. The purple color of the permanganate was discharged within the first 10 min. After dilution with water, the solution was extracted with ether. After drying and removal of the solvent, 71% of phthalide was found, m.p. 74–75°.

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[13] Brode and Boord atom models.

[14] J. W. Barrett and R. P. Linstead, *J. Chem. Soc.*, 436 (1935).

[15] The intermediate formation of a cyclic ester between chromium trioxide and 1,2-diols is a subject of controversy [see H. Kwart, J. A. Ford, Jr., and G. C. Corey, *J. Am. Chem. Soc.*, **84**, 1252 (1962)]. We have been successful in the preparation of II and VII by using selenium dioxide *via* an intermediate cyclic ester formation with subsequent decomposition with heat. Although cyclic chromic ester formation in the present cases cannot be ruled out unambiguously, the ester must either be short lived or absent.

[16] All melting points are corrected.

[17] J. H. Gardner and C. A. Naylor, Jr., *Org. Syn.*, **XVI**, 71 (1936).