concentrated and the residue distilled in vacuum to give 0.38 g. (72%) of crystalline caprolactam. The product had infrared spectrum identical to that of an authentic sample of caprolactam.

Effect of hydrogen fluoride on cyclohexanone oxime. A sample of cyclohexanone oxime (1.01 g.) was subjected to the same treatment as its benzoate as described above. In this case, the methylene chloride soluble fraction crystallized immediately on removal of solvent to give 0.23 g. (23%) of crude cyclohexanone oxime, m.p. 87°. No traces of caprolactam were detected. Since removal of hydrogen fluoride was accomplished by 150 hr. pumping at near 1μ pressure, sublimation of the oxime may account for the poor recovery.

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Periodate Oxidation of Compounds Related to Malondialdehyde

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The methylene carbon of malondialdehyde bis(dimethyl)acetal and 2-deoxy-D-glucose (D-arabino-2-deoxyhexose) is oxidized to carbon dioxide *via* malondialdehyde, hydroxymalondialdehyde, and mesoxdialdehyde. Evidence is presented that this is the common oxidation route for compounds producing malondialdehyde and hydroxymalondialdehyde.

In a study of the periodate oxidation of polyvinyleneglycol (polyhydroxymethylene) and vinylene glycol–vinyl alcohol copolymers, (derived from the hydrolysis of vinylene carbonate–vinyl acetate copolymer) it became necessary to clarify the overoxidation of malondialdehyde and hydroxymalondialdehyde by periodate solutions. Although overoxidations have been studied, there are few data which show the simultaneous formation of products and consumption of periodate and some inconsistencies appear in the literature.

For orientation, we investigated the periodic acid oxidation of glucose, mannitol, inositol, glycerol and tartaric acid, and in addition, studied the oxidation of malondialdehyde bis(dimethyl) acetal and 2-deoxy-D-glucose, two compounds the oxidation of which has not been previously reported.

Under the reaction conditions reported in the experimental section, glycerol consumed 2.0 molar equivalents of periodic acid and produced 1.0 mol. of titratable acid in 1 hr. and the product and oxidant concentrations remained unchanged over a 30 hr. period. Mannitol consumed nearly 5.0 (or 4.9) mole of periodic acid in 10 hr. but produced less than the theoretical amount of titratable acid, 3.7 mole rather than 4.0. Over a 70 hr. period the yield of acid increased slightly and the periodate consumption rose to slightly more than the theoretical amount 5.1 rather than 5.0.[2] We interpret this to mean that a slight amount of overoxidation occurs probably by the mechanism discussed below. Inositol was studied with less precision but gave evidence of overoxidation as has been reported previously and is to be discussed below. The consumption of periodate and formation of acid by glucose was quantitative in 30 hr. and unchanged over an additional 40 hr. when the reaction was carried out with periodic acid but was not quantitative with sodium periodate because of formate ester formation. The oxidation of tartaric acid (Fig. 1) consumed the theoretical 3.0 mole of periodate in

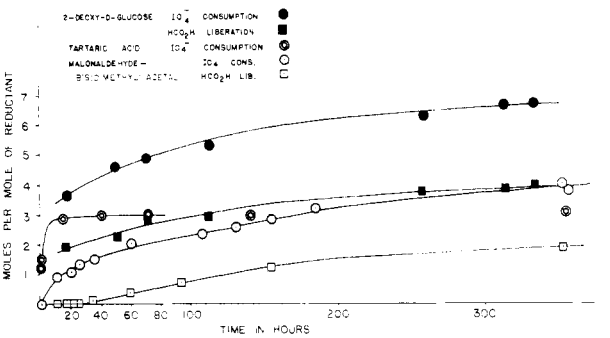

Figure 1. Oxidation of some model compounds with 0.0125*M* periodic acid

less than 20 hr. but no more over 350 hr. of reaction time. Similarly the titratable acid remained unchanged over 350 hr. In this selection of polyhydric alcohols, aldehydes and acids, there was therefore no evidence of side reactions except in those cases that might produce hydroxymalondialdehyde as an intermediate, and furthermore formic acid was stable to periodate (or more correctly, mixtures of periodate and iodate[2]) over the entire 350 hr. period of our experiments.

According to published data on the rate of hydrolysis of malondialdehyde bis(dimethyl) acetal

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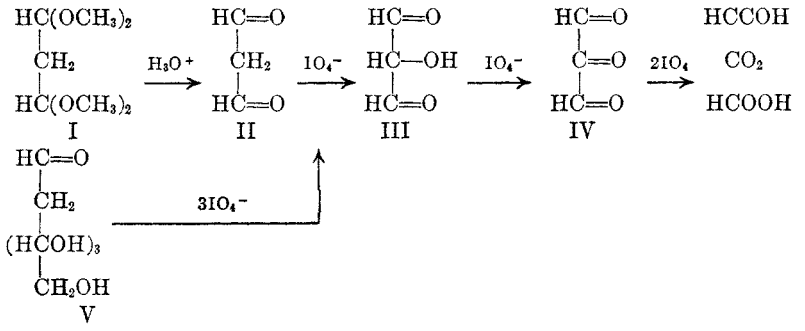
(1) Abstracted from a portion of a thesis presented by Herman L. Marder in partial fulfillment of the requirements of the Ph.D. degree at Syracuse University. Present address: Textile Fibers Dept., Pioneering Research Division, Wilmington 98, Delaware. E. I. du Pont de Nemours and Company.

(2) T. Halsall, E. Hirst, and J. Jones, *J. Chem. Soc.*, 1427 (1947).

with aqueous acid,[3] under our oxidation conditions the compound should be converted essentially completely to the free aldehyde in 5 hr. The oxidation with periodic acid, shown on Fig. 1, should therefore differ little, if at all, from that of the free aldehyde. In about 10 hr. malondialdehyde added as the bis-(dimethyl) acetal had consumed 1 mole of periodate but no formic acid was produced. Indeed no formic acid was produced until nearly 1.5 mol. of oxidant were consumed. The oxidation proceeded slowly to limiting values very close to 4 mol. of oxidant consumed and 2 mol of acid formed. These observations suggest that the periodate oxidation of malondialdehyde proceeds via the following route, and that III is not cleaved to formic acid directly.



The same reaction sequence explains in large measure our observations on the oxidation of 2-deoxy-D-glucose. This compound reacted very rapidly with three mole of oxidant according to the accepted mode of reaction of 1,2,3,4 tetraols, and then more slowly the oxidant consumption increased to a limiting value of about 6.7 mole per mole of reactant. At the same time the titratable acid which is near 2 mole per mole of reactant early in the reaction gradually increased to a limiting value of slightly less than 4 mole. In a separate experiment 0.82 mole of carbon dioxide per mole of reductant was produced after 600 hr. of reaction in the dark. The corresponding theoretical values for periodate consumption, formic acid liberation and carbon dioxide formation 7, 4, and 1 for the reaction sequence above are in good agreement with the experimental. It is however not possible to eliminate entirely other reaction sequences. As the methylene C_2 carbon atom is α to a hemiacetal hydroxyl, which probably complexes most readily with periodate, and is also in a six membered ring, which in the diketone series makes it more susceptible to oxidation, oxidation of the deoxysugar to glucose or mannose may compete with the glycol split of the trans 3,4-glycol group. Twenty percent of such a reaction occurring concurrently would still give limiting values of 6.8, 4.2, 0.8 mole also in fair agreement with our results.

(3) Data from Kay Fries Technical Bulletin, Kay Fries Chemical Co., N. Y.

The mechanism proposed for the oxidation of malondialdehyde by Huebner, Ames and Bubl[4] is in conflict with our results. They assumed that malondialdehyde oxidized via hydroxymalondialdehyde to 3 mole of formic acid with the consumption of 3 mole of periodate. However, their experimental data supporting this view are meager. The malondialdehyde was formed from digitoxose. A total of 6.1 mole of oxidant was consumed rather than the 5 mole required for their mechanism. It is not clear whether formic acid was determined to be present in the quantity proposed (4 mole from digitoxose) or merely assumed to be that amount. The carbon dioxide observed as a product of reaction was assumed to be the result of overoxidation of formic acid, formaldehyde, or acetaldehyde, the primary products. However, these products are stable to periodate when proper reaction conditions are maintained. It is probable therefore that digitoxose actually oxidizes by the mechanism proposed above.

The proposed reaction sequence which assumes instead that the active methylene carbon of malondialdehyde is oxidized via a carbonyl oxidation state to carbon dioxide is not entirely novel. It is analogous or equivalent to that proposed by Wolfrom and Bobbitt[5] for the oxidation of cyclic β-diketones, by Potter and Hassid[6] for the overoxidation of reducing end groups in starch, cellulose and maltose, and especially by Schwarz[7] for the oxidation of myoinositol. In the last case, glyoxylic acid is shown to be an intermediate in the oxidation of the tricarbonyl compound to carbon dioxide and formic acid.

As some fraction of mannitol,[2] fructose,[8] inositose,[9] 1,2,4,5-tetrahydroxycyclohexane,[10] and do-

(4) C. Huebner, S. Ames, and E. Bubl, *J. Am. Chem. Soc.*, **68**, 1621 (1946).

(5) M. L. Wolfrom and J. Bobbitt, *J. Am. Chem. Soc.*, **78**, 2489 (1956).

(6) A. L. Potter and W. Z. Hassid, *J. Am. Chem. Soc.*, **70**, 3489 (1948).

(7) J. Schwarz, *Chem. and Ind. (London)*, 1388 (1955).

(8) Y. Khouvine and G. Arragon, *Compt. Rend.*, **212**, 167 (1941).

(9) D. Sprinson and E. Chargaff, *J. Biol. Chem.*, **164**, 433 (1946).

(10) G. McCasland and E. Horswill, *J. Am. Chem. Soc.*, **76**, 2373 (1954).

decitol[11] would be expected to oxidize via malondialdehyde, or hydroxymalondialdehyde, this reaction should be considered in any interpretation of the periodate oxidation of these compounds. For example, if the simplifying assumption is made that the rate of cleavage of glycol carbon bonds is equivalent to the rate of cleavage of hydroxyaldehyde carbon bonds, 5.5% of the carbon in dodecitol should appear as carbon dioxide. Wolfrom found a consumption of 11.5 mole of periodate instead of the theoretical values of eleven and only 9.5 mole of formic acid instead of 10. His failure to find carbon dioxide is understandable if a terminal assay of the acidic solutions was used. Our results on polyvinylene glycol and its vinyl alcohol copolymer are consistent with this interpretation of the periodate oxidation and will be published elsewhere.

EXPERIMENTAL

All periodate oxidations were carried out in the dark at room temperature using paraperiodic acid (H_5IO_6) or occasionally sodium meta periodate ($NaIO_4$). Sufficient sample to reduce 1 mmol. of oxidant was weighed into a 100 ml. volumetric flask, and enough .05–.1M oxidant solution to give 1.25 mmol. of oxidant was added and the flask was diluted to the mark. At the same time a blank containing the identical amount of oxidant was prepared. After the sample was observed to be dissolved, aliquots were withdrawn at intervals for titration. This procedure was followed in all cases except for the oxidations of mannitol and glycerol where the initial oxidant concentrations were .0045 and .01M respectively, and consequently less sample was used.

Oxidant consumption was determined by the method of Malaprade.[12] A 5 ml. aliquot was added to a 125 ml. Erlenmeyer flask containing a few crystals of iodate-free potassium iodide in 20 ml. of distilled water. Two drops of 6N hydrochloric acid were then added and the liberated iodine was immediately titrated with .02N thiosulfate to a Thyodene (Fisher Scientific Co. substitute for starch indicator) endpoint. The difference between the titer of the blank and the sample, $\bar{D}$, is a measure of the oxidant consumed by the sample; Periodate consumed = $10\ \bar{D}\ N_{(thio)}$.

The formic acid liberated during the oxidation was estimated by the total acidity of the solutions according to the iodometric procedure of Hallsall, Hirst and Jones.[2] The iodometric procedure was checked by titrations with 0.02N barium hydroxide solutions to a phenophthalein endpoint and good agreement was obtained.

A terminal assay of the carbon dioxide evolved in periodic acid oxidations was performed using the high vacuum technique of Levy and Szwarc.[13,14]

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SYRACUSE 10, N. Y.

(11) M. L. Wolfrom, W. W. Binkley, C. C. Spenser, and B. W. Lew, *J. Am. Chem. Soc.*, **73**, 3357 (1951).

(12) L. Malaprade, *Compt. Rend.*, **186**, 392 (1928); *Bull. soc. chim. France*, **43**, 683 (1928).

(13) M. Levy and M. Szwarc, *J. Am. Chem. Soc.*, **76**, 5981 (1954); **77**, 1949 (1955).

(14) M. Szwarc, *J. Polymer Sci.*, **16**, 367 (1955); *J. Chem. Phys.*, **22**, 1621 (1954).

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Preparation and Properties of N^{α}-Acyl Lysine Esters[1]

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The syntheses of the free bases, N^{α}-tosyl-L-lysine methyl ester, m.p. 93–95°, and N^{α}-tosyl-DL-lysine benzyl ester, m.p. 104°, are described. A number of other N^{α}-acyl lysine esters, obtained as hygroscopic hydrochlorides or hydrobromides, have also been prepared.

It has recently been suggested that the proximate metabolite of the carcinogen *N*-(2-fluorenyl)acetamide which is bound to proteins is the *o*-quinone imine, 1,2-fluorenoquinone-2-imine,[2,3] and that the ϵ-amino group of lysine is implicated in the binding reaction.[4] N^{α}-acyl lysine esters in which the ϵ-amino group is free and the carboxyl and the α-amino group are protected, were therefore desired for a study of their reactions with model quinone imides.[5] A search of the literature showed that such N^{α}-acyl lysine esters have not been prepared and we have therefore undertaken the synthesis of a number of these lysine derivatives.[6] Since recent evidence indicates that peptide linkages involving

(1) Supported by grants from the National Cancer Institute, U. S. Public Health Service (C-2571), and the Minnesota Division of the American Cancer Society.

(2) H. T. Nagasawa, M. A. Morgan, and H. R. Gutmann, *Biochim. et Biophys. Acta*, **28**, 665 (1958).

(3) H. T. Nagasawa and H. R. Gutmann, *J. Biol. Chem.*, **234**, 1593 (1959).

(4) C. C. Irving and H. R. Gutmann, *Federation Proc.*, **18**, 252 (1959).

(5) H. R. Gutmann, J. G. Burtle, and H. T. Nagasawa, *J. Am. Chem. Soc.*, **80**, 5551 (1958).

(6) While this work was in progress, the synthesis of N^{α}-tosyl-L-lysine ethyl ester hydrochloride and N^{α}-tosyl-L-lysine benzyl ester hydrochloride were reported (D. L. Swallow, I. M. Lockart, and E. P. Abraham, *Biochem. J.*, **70**, 359 (1958)).