352. *The Reaction of Periodic Acid with α-Ketols, α-Diketones, and α-Ketonealdehydes.*

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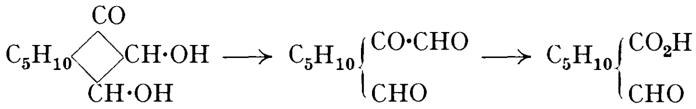
It is known from the work of Malaprade (*Compt. rend.*, 1928, **186**, 382) and of Fleury and Lange (*ibid.*, 1932, **195**, 1395; *J. Pharm. Chim.*, 1933, **17**, 409) that polyhydric alcohols containing hydroxyl groups attached to adjacent carbon atoms react with periodic acid according to the general equation

$$R\cdot[CH\cdot OH]_n\cdot R + (n + 3)HIO_4 = 2R\cdot CHO + H_2O + (n - 2)H\cdot CO_2H + (n + 3)HIO_3.$$

Fleury and Lange (*loc. cit.*) observed an analogous reaction with dihydroxyacetone, and the course of the oxidation is regarded by Criegee, Kraft, and Rank (*Annalen*, 1933, **507**, 159) as involving intermediate esterification of a hydroxyl group with paraperiodic acid, H_5IO_6.

The reaction has been applied by Birkinshaw, Charles, and Clutterbuck (*Biochem. J.*, 1931, **25**, 1527) to the determination of butane-2 : 3-diol, which reacts quantitatively according to the above equation to give 2 mols. of acetaldehyde; the interaction of tetrahydroterrein (I), the reduction product of terrein (cf. Raistrick and Smith, *Biochem. J.*, 1935, **29**, 606), led on the other hand to formation of the aldehydo-acid (III), 2 atoms of oxygen being utilised and 1 mol. of formic acid eliminated.



(I.) (II.) (III.)

It was therefore concluded that the keto-aldehyde (II) which was the expected product of the reaction had interacted with a second molecule of periodic acid, and the supposition was confirmed by the observation that methylglyoxal reacted with periodic acid to give 1 mol. each of acetic and formic acid.

It has since been found that the reaction is generally applicable to α-ketols and α-diketones; thus acetoin and benzoin give respectively acetaldehyde + acetic acid and benzaldehyde + benzoic acid, whilst diacetyl and benzil (more slowly) yield respectively 2 mols. each of acetic and benzoic acid. *p*-Toluoylphenylcarbinol (Weissberger *et al.*, *Annalen*, 1930, **478**, 112) yields *p*-toluic acid and benzaldehyde, indicating that in the scission of the ketol the carbinol group becomes CHO and the carbonyl group CO_2H.

The reaction has been utilised to confirm the suggested structures of the phenolic acids $C_{10}H_8O_6$ and $C_{10}H_{10}O_6$ produced by *Penicillium brevi-compactum* Dierckx (cf. Oxford and Raistrick, *Biochem. J.*, 1933, **27**, 634), which give respectively 1 mol. each of 3 : 5-dihydroxyphthalic + acetic acid and 1 mol. each of 6-aldehydo-2 : 4-dihydroxybenzoic + acetic acid; furthermore the benzfuroin of Fischer (*Annalen*, 1882, **211**, 228) yields with periodic acid 1 mol. each of benzaldehyde and pyromucic acid and must therefore be furoylphenylcarbinol as suggested by Werner and Detscheff (*Ber.*, 1905, **38**, 71).

The reactions described above are in accordance with the extension of his earlier work recently published by Malaprade (*Bull. Soc. chim.*, 1934, **1**, 833).

Experimental.

In each case, two experiments were carried out, the first, with about 1 millimol. of substance, to determine the amount of oxygen absorbed, and the second, with about 10 millimols., to determine the acidic substances produced and the nature of the products.

(a) *Determination of Oxygen absorbed.*—The method was essentially that of Malaprade (*loc. cit.*, 1928). A standard solution of potassium periodate was prepared (about 3 g./l.) such that on acidification and addition of excess of potassium iodide it yielded an approximately *N*/10-solution of iodine (calculated on the original volume). A known amount of substance to be oxidised (usually about 1 millimol.) was treated with 100 ml. of the periodate solution and 10 ml. of 2*N*-sulphuric acid. The mixture was kept at room temperature for 24 hours, an excess of potassium iodide added, and the liberated iodine titrated with *N*/10-thiosulphate. The amount of substance oxidised must be such that this final titration figure is greater than 75 ml., since this corresponds to the total reduction of the HIO_4 to HIO_3. The difference between a blank titration of the reagent and this final titration gives the oxygen absorbed in the reaction. The results are summarised in Table I.

TABLE I.

Substance oxidised.	Wt., mg.	I_2 absorbed, *N*/10.	Theo. absorption for 1 atom O used.	Percentage of theo.
Methylglyoxal, $CH_3{\cdot}CO{\cdot}CHO$	77·8	19·45	21·6	90
Diacetyl, $CH_3{\cdot}CO{\cdot}CO{\cdot}CH_3$	54·2* in 50 ml. H_2O	11·0	12·6	87
Acetoin, $CH_3{\cdot}CO{\cdot}CH(OH){\cdot}CH_3$	87·4	20·0	19·85	101
Benzoin, $C_6H_5{\cdot}CO{\cdot}CH(OH){\cdot}C_6H_5$	151·8* in 100 ml. EtOH	13·8	14·3	97
p-Toluoylphenylcarbinol, $CH_3{\cdot}C_6H_4{\cdot}CO{\cdot}CH(OH){\cdot}C_6H_5$	253·5* in 50 ml. EtOH	22·75	22·4	101
Dihydroxyacetone, $CH_2(OH){\cdot}CO{\cdot}CH_2{\cdot}OH$	59·9	13·1	13·3	98
Hydrated 3 : 5-dihydroxy-2-carboxybenzoyl methyl ketone	125·2	8·85	10·34	85
Benzfuroin, $C_4H_3O{\cdot}CO{\cdot}CH(OH){\cdot}C_6H_5$	109·7	8·75	10·85	81

* In these cases, the recorded amount of solvent was used in addition to the 100 ml. of reagent used in each case.

(b) *Determination of the Acid produced.*—The method employed was similar to that of Malaprade (*loc. cit.*, 1934). In our experiments the exact amount of potassium periodate calculated from the corresponding experiment in section (a) was used. Under these conditions it was found that the simple glycols, *e.g.*, butane-2 : 3-diol, gave no acid, that the α-ketols gave 1 equivalent, and the α-diketones and α-ketonealdehydes 2 equivalents of acid. Provided, therefore, that the reaction is complete or almost so, as indicated by the oxygen absorption, the acid figure gives an indication of the type of compound oxidised.

The results are summarised in Table II.

TABLE II.

Substance oxidised.	Wt., g.	Solvent, ml.	KIO_4, g.	2*N*-H_2SO_4, ml.	Acidity after reaction.		No. of equivs.
					N-Acid, ml.	Theo. for 1 equiv.	
Methylglyoxal	0·5761	Water 500	1·8399	50	14·1	8·0	1·76
Diacetyl	1·0042	Water 1000	2·685	120	21·0	11·65	1·80
Acetoin	0·874	Water 400	2·295	100	10·1	9·92	1·02
Benzoin	1·0008	Water 500, EtOH 500	1·085	100	4·5	4·72	0·95
Dihydroxyacetone	1·0008	Water 1000	2·558	100	10·4	11·19	0·93
Hydrated 3 : 5-dihydroxy-2-carboxybenzoyl methyl ketone	0·9646	Water 200	0·8429	40	15·2	3·98	3·82*
Benzfuroin	0·7968	Water 300, EtOH 250	0·9069	50	3·80	3·94	0·96

* With thymolphthalein, titration being carried to a blue colour, 3 : 5-dihydroxyphthalic acid behaves almost as a tribasic acid. Thus 90·6 mg. required 12·2 ml. of *N*/10-sodium hydroxide, corresponding to an equiv. of 74·3 ($C_8H_6O_6$, as a tribasic acid, requires 66 and as a dibasic acid 99).

Benzil.—The reaction with benzil differed from all the other reactions studied in being very much slower: after 24 hours the amount of oxygen absorbed only corresponded to 48% of one atom, and even after 2 weeks was only 80% of the theoretical. The acid formation was correspondingly slower and only benzoic acid could be isolated. The unoxidised portion of the benzil was recovered in an aliquot portion of the reaction mixture by precipitation as the dinitrophenylhydrazone, m. p. 193°. The reaction thus appears to be similar to the others described in this paper but takes place very much more slowly.

I. *Methylglyoxal.*—The titrated solution was acidified with 2*N*-sulphuric acid and distilled in a vacuum several times to a small bulk and the combined distillates, after treatment with silver carbonate to remove hydriodic acid, and with hydrochloric acid to remove any excess of silver, were neutralised and evaporated to 200 ml.

A. The formic acid in 100 ml. of this solution, determined by Fincke's method (*Biochem. Z.*, 1913, **51**, 253), corresponded to 1·44 g. of Hg_2Cl_2 (theo. for 1 mol., 1·89 g.).

B. The formic acid present in the second 100 ml. of this solution was destroyed by the silver method, and the volatile acid recovered by distillation; acetic acid in the distillate was identified as *p*-phenylphenacyl ester (Drake and Bronitsky, *J. Amer. Chem. Soc.*, 1930, **52**, 3715).

II. *Diacetyl.*—The neutralised solution was acidified and steam-distilled. The distillate, after the treatment with silver carbonate and with hydrochloric acid, was redistilled, yielding a solution which contained approximately 2 equivs. of acetic acid (identified as above).

III. *Acetoin.*—A stream of air was passed through the titrated reaction mixture into bubblers containing Brady's 2 : 4-dinitrophenylhydrazine reagent. A copious precipitate was formed, which after recrystallisation from alcohol melted at 165° and did not depress the m. p. of authentic acetaldehydedinitrophenylhydrazone.

After removal of the aldehyde, the solution was acidified and distilled in a vacuum, and acetic acid identified in the distillate as above.

IV. *Benzoin.*—Brady's reagent was added to the solution, and the precipitated benzaldehydedinitrophenylhydrazone filtered off and dried; weight 1·2 g. (theo. for 1 mol., 1·33 g.).

After removal of the benzaldehyde, benzoic acid was recovered from the solution by steam-distillation, neutralisation of the distillate, and evaporation to remove the alcohol, followed by acidification and ether extraction.

V. p-*Toluoylphenylcarbinol.*—This compound was kindly supplied by Dr. Arnold Weissberger. On addition of Brady's reagent to the oxidation solution, 330 mg. of benzaldehydedinitrophenylhydrazone were obtained (theo. for 1 mol., 321 mg.).

The solution remaining after filtration of this dinitrophenylhydrazone was evaporated several times to a low bulk in a vacuum, and the distillates neutralised and concentrated in a vacuum. The solution was then acidified and extracted three times with ether. After removal of the ether 150 mg. of *p*-toluic acid were obtained (identified by titration and by mixed m. p. with an authentic specimen). The theoretical weight, assuming 1 molecule of *p*-toluic acid was formed, was 152·5 mg.

VI. *Dihydroxyacetone.*—The products, as shown by Fleury and Lange (*loc. cit.*, 1932), were formaldehyde and glycollic acid. In our case the formaldehyde was separated as the dinitrophenylhydrazone from the oxidation experiment by addition of Brady's reagent.

VII. *Hydrated* 3 : 5-*Dihydroxy*-2-*carboxybenzoyl Methyl Ketone* (Oxford and Raistrick, *loc. cit.*).—The solution was acidified and steam-distilled in a vacuum to a low bulk several times. The distillate contained acetic acid (identified as above). The residue was extracted continuously with ether, the ethereal solution dried over anhydrous magnesium sulphate, and the ether removed; the product, after recrystallisation from chloroform–light petroleum, melted at 194° and did not depress the m. p. of authentic 3 : 5-dihydroxyphthalic acid.

VIII. 3 : 5-*Dihydroxy*-2-*carboxyphenylacetylcarbinol* (Oxford and Raistrick, *loc. cit.*).—In this case, the reaction was extremely complex, the figures for oxygen uptake and acid production not corresponding to a molecular process. From the solution, however, with Brady's reagent was isolated a *dinitrophenylhydrazone* which crystallised from aqueous alcohol in long hexagonal platelets, m. p. 270° (decomp.) [Found (Schoeller): C, 44·4; H, 3·4; N, 14·5. $C_{13}H_{10}O_8N_4,H_2O$ requires C, 44·2; H, 3·2; N, 14·7%]. The compound was soluble in sodium bicarbonate solution and was presumably the hydrate of the dinitrophenylhydrazone of 6-aldehydo-2 : 4-dihydroxybenzoic acid. The solution also contained some acetic acid, isolated as above as the *p*-phenylphenacyl ester. These facts show that the side chain of the acid $C_{10}H_{10}O_6$ at any rate in part had the acetylcarbinol structure.

IX. *Benzfuroin* (Fischer, *loc. cit.*).—The benzaldehyde produced was separated as the dinitrophenylhydrazone. The filtrate after removal of benzaldehyde was distilled to a low bulk in a vacuum several times and the combined distillates were neutralised and concentrated in a vacuum. The solution was finally acidified and extracted continuously with ether. The extract on removal of the ether gave a crystalline acid which, after several sublimations, had m. p. 132° and did not depress the m. p. of authentic pyromucic acid.

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