254. *Tracer Studies in the Formation and Reactions of Organic Per-acids.*

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The acid-catalysed hydrolysis of performic and peracetic acid, and their acid-catalysed formation from the carboxylic acid and hydrogen peroxide, involve acyl–oxygen bond fission. The rate of the acid-catalysed hydrolysis of peracetic acid has been measured. Tracer experiments on the peracetic acid oxidation of benzophenone, 4-methoxybenzophenone, and fluorenone to the corresponding ester or lactone proved that the carbonyl-oxygen of the product came from the ketone and the ethereal oxygen from the per-acid. The course of the reaction is that observed by Doering and Dorfman for the oxidation of benzophenone by perbenzoic acid.

THE hydrolysis of peracetic acid in aqueous perchloric acid at 25·2° was followed by estimation of the per-acid iodometrically, or, as in two preliminary experiments, by following the formation of hydrogen peroxide. The hydrolysis rate was proportional to the acid concentration in the range studied (see Table 1). As the rate follows the concentration of hydroxonium ions, and not the Hammett acidity function h_0, we conclude that the transition state includes a water molecule as well as the conjugate acid of peracetic acid.[1] Added sodium perchlorate gives a small decrease in rate, but sodium perchlorate increases the acidity of perchloric acid, as measured by the Hammett acidity function,[2] and therefore should accelerate a unimolecular reaction, whose rate should follow the acidity function.[2] The absence of such an acceleration is therefore additional evidence for a bimolecular reaction.

Qualitative observations were made of the hydrolysis of performic and perbenzoic acid in aqueous perchloric acid at 25·2°. The hydrolysis of performic acid was too fast for convenient measurement since it was not possible to stop the reaction during the decomposition of the hydrogen peroxide with acid ceric sulphate or potassium permanganate. The rate was at least ten times that of the peracetic acid hydrolysis under similar conditions. The hydrolysis of perbenzoic acid was much slower than that of peracetic acid. This rate sequence is qualitatively similar to those observed for the acid hydrolysis of the methyl and ethyl esters of the corresponding carboxylic acids.

TABLE 1. *Rates of hydrolysis of peracetic acid in aqueous perchloric acid at* 25·2°.

$[HClO_4]$	0·022	0·096	0·310	0·483	0·886	1·57	1·82 *	2·16	2·57	2·73	3·16 †	3·63
10^3k_1 (min.$^{-1}$)	0·14	0·75	2·05	2·90	5·68	9·7	10·0	13·6	15·9	16·6	18·3	21·3
10^3k_A (mole^{-1} l. min.$^{-1}$)	6·4	7·8	6·6	6·0	6·4	6·2	5·5	6·3	6·2	6·1	5·7	5·9

* $[NaClO_4]$ = 0·6M. † $[NaClO_4]$ = 0·2M.

The position of bond fission in the formation and hydrolysis of performic and peracetic acid was determined with ^{18}O as a tracer. Isotopically enriched carboxylic acid was treated with 30% hydrogen peroxide in $H_2{}^{18}O$ (in the presence of sulphuric or perchloric acid) at room temperature. When equilibrium was attained the solutions were neutralised, hydrogen peroxide pumped off, and the peracid hydrolysed in $H_2{}^{18}O$; the hydrogen peroxide so formed was found to be isotopically normal. The isotopic analyses of the hydrogen

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[1] Hammett, " Physical Organic Chemistry," McGraw-Hill Book Company Inc., New York, 1940, p. 267; Bell, Dowding, and Noble, *J.*, 1955, 3106.

[2] Long and McIntyre, *J. Amer. Chem. Soc.*, 1954, **76**, 3243.

peroxide were carried out by decomposition with acid potassium permanganate and mass-spectrometric analysis of the evolved oxygen. In this decomposition it has been shown that the oxygen is derived from the hydrogen peroxide.

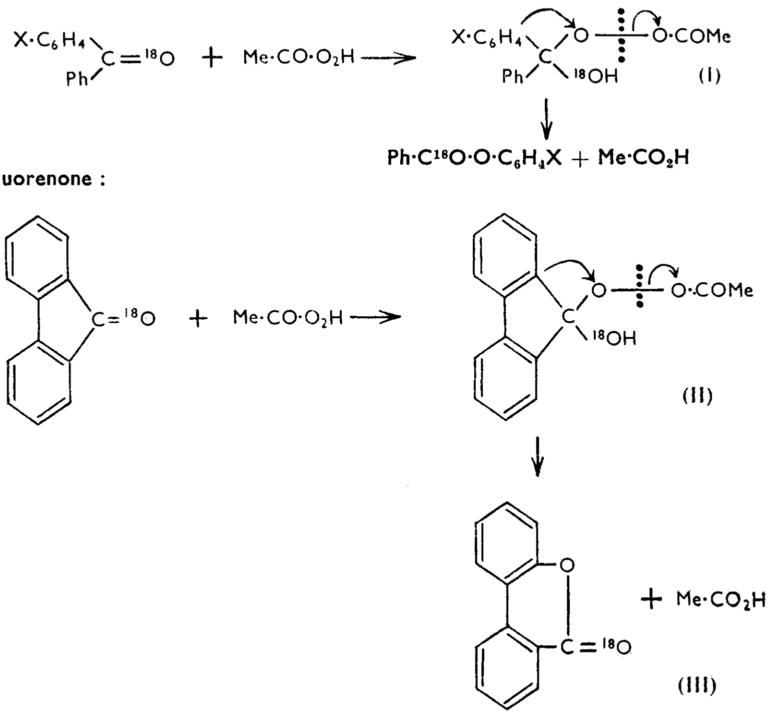
The only interpretation of this isotopic and kinetic evidence is that at no stage in formation or hydrolysis of a per-acid is the peroxide bond broken, and that the mechanism is analogous to the $A_{Ac}2$ mechanism of carboxyl esterification and hydrolysis:[3]

$$R{\cdot}CO{\cdot}O_2H_2^+ + H_2{}^{18}O \longrightarrow R{\cdot}C^{18}O{\cdot}OH_2^+ + H_2O_2$$

(In this formulation the position of the proton is assumed.)

The oxidation of benzophenone by perbenzoic acid in benzene was examined by Doering and Dorfman,[4] whose findings are in accord with the general mechanism of Criegee [5] and Robertson and Waters.[6] Mechanisms in which either the oxygen atoms of the ester became equivalent, or the per-acid formed the hydroxyl cation, OH^+, were excluded. It seemed possible that in a more ionizing solvent, and in the presence of mineral acid, other mechanisms might be observed. The oxidations of benzophenone and 4-methoxybenzophenone in acetic acid solution by peracetic acid in the presence of sulphuric acid were examined isotopically, and it was found that the ethereal oxygen was derived from the per-acid,[7] as required by the mechanism of Criegee [5] and Robertson and Waters.[6]

These observations have now been extended to the oxidation of fluorenone to give the lactone of 2′-hydroxydiphenyl-2-carboxylic acid (III). The reactions are shown in the annexed scheme. The oxidation of ketones by per-acids is acid-catalysed, as are many carbonyl-addition reactions. For simplicity the proton has been omitted in the formulations in the scheme: it is presumably located on the carbonyl-oxygen atom of the ketone.



The oxygen of the ketone and the acetic acid was isotopically enriched, and after

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[3] Day and Ingold, *Trans. Faraday Soc.*, 1941, **37**, 686.
[4] Doering and Dorfman, *J. Amer. Chem. Soc.*, 1953, **75**, 5595.
[5] Criegee, *Ann. Chim. (France)*, 1947, **127**, 560.
[6] Robertson and Waters, *J.*, 1948, 1574.
[7] Bunton, Lewis, and Llewellyn, *Chem. and Ind.*, 1954, 191.

reaction the oxygen isotopic content of the product ester or lactone was determined. This was done for phenyl benzoate and *p*-methoxyphenyl benzoate by alkaline hydrolysis in isotopically normal water. Independent experiments proved that phenyl benzoate undergoes acyl–oxygen fission under these conditions. Thus, to a first approximation, one oxygen atom of the isolated benzoic acid is the carbonyl-oxygen atom of the ester (the other coming from the water), and the oxygen of the phenol is the ethereal oxygen of the ester.

The results for the ^{18}O abundance of the ester are given in Table 2. In calculation of the results, isotopic equilibration between the oxygen atoms of the ketone, acetic acid, and water under the strongly acidic conditions of the oxidation is assumed, and isotope dilution by the acetic acid formed in the course of the oxidation is ignored. This dilution causes the isotopic abundance of the carbonyl-oxygen of the ester to be lower than that calculated for the ketone.

The oxidation of fluorenone was studied by a similar method. The isotopic abundance of the lactone was determined by pyrolysis to carbon monoxide. The lactone was hydrolysed and methylated in $H_2{}^{18}O$ to give 2′-methoxydiphenyl-2-carboxylic acid, and this acid converted into 2-hydroxydiphenyl by heating it with soda-lime. Isotopic analysis proved that the hydroxyl-oxygen, and hence the ethereal oxygen of the lactone, was isotopically normal, as is found for per-acid oxidation of open-chain ketones. Another sample of 2′-methoxydiphenyl-2-carboxylic acid was refluxed with perchloric acid in isotopically normal water to normalise the carboxyl-oxygen; isotopic analysis then gave independent evidence that the ethereal oxygen of the lactone was isotopically normal. These degradations also show that this lactone is hydrolysed in aqueous alkali with acyl–oxygen fission, and an experiment with isotopically enriched soda-lime proves that the methyl–oxygen bond is broken in the demethylation of 2-methoxydiphenyl.

TABLE 2. *Oxidation of open-chain ketones.*

Compound	Calc. isotopic abundance of ketone (atom % ^{18}O)	Isotopic abundance of product (atom %) Carbonyl oxygen *	Ethereal oxygen †
Benzophenone	0·586	0·514	0·001
,, ...	0·630	0·474	0·002
4-Methoxybenzophenone	0·720	0·560	0·004
,, ...	0·605	0·610	0·002
,, ...	0·450	0·374	0·005

* From isotopic abundance of benzoic acid. † From isotopic abundance of phenol.

Oxidation of fluorenone.

Calc. isotopic abundance of ketone (atom %)	Isotopic abundance of product (atom %) Lactone	Carbonyl oxygen *	Ethereal oxygen †
0·60	0·275	0·55	0·025%

* Taken to be twice the abundance of the lactone. † By degradation to 2-hydroxydiphenyl.

Abundance of 2′-methoxydiphenyl-2-carboxylic acid from separate oxidation with carboxyl-oxygen atoms normalised by boiling with water: 0·039 and 0·043 atoms %. Abundance of original ketone 0·95% atoms %.

These results, together with the isotopic results on the formation and hydrolysis of the per-acids, suggest that the hydroxyl cation, OH^+, is not formed, even in acidic conditions. If it were formed it should react with water, to give hydrogen peroxide, and so introduce tracer into the peroxide.

It has been suggested that oxidations by per-acids often involve intermediates containing cationic oxygen,[9] and that the intermediates [(I) and (II)], formed by per-acid oxidation at the carbonyl-carbon atom, give entities of the general formula (IV), which then rearrange to the product, thus :

(IV)

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[8] Friess and Soloway, *J. Amer. Chem. Soc.*, 1951, **73**, 3968.

[9] Leffler, *Chem. Rev.*, 1949, **45**, 385.

If such an intermediate (IV) involving cationic oxygen were formed, and had an appreciable life, the oxygen atoms could become equivalent by the ready hydrogen transfer. The fact that they do not, even in a good ionizing solvent, suggests that the intermediate (IV), if formed, has a very short life, or that the breaking of the oxygen–oxygen bond is synchronous with, and assisted by, the migration.[4, 10]

EXPERIMENTAL

Results of typical experiments on the formation and hydrolysis of per-acids are given below. All isotopic abundances are in atom % excess above normal.

Preparations.—Isotopically enriched acetic acid. Acetic anhydride (34 g.) was hydrolysed by 6 c.c. of $H_2{}^{18}O$ (abundance 2·72 atom %). Calculated abundance of acetic acid, 0·68 atom %.

Isotopically enriched formic acid. Anhydrous formic acid (12 g.) was left to equilibrate with 1·5 c.c. of $H_2{}^{18}O$ (abundance 9·1 atom %). Calculated abundance of formic acid 1·25 atom %.

Formation and Hydrolysis of Per-acids.—Enriched acetic acid was treated with 2 drops of concentrated sulphuric acid and 2 c.c. of 90% hydrogen peroxide. After 6 hr. at 20° the peracetic acid contained *ca.* 65% of total peroxide. The solution was diluted with 100 c.c. of 0·5 atom % $H_2{}^{18}O$, and the pH adjusted to 9. The liquid was then frozen, and hydrogen peroxide pumped off and decomposed with potassium permanganate. The abundance of the evolved oxygen was 0·004 atom %. The solution was then acidified, and the per-acid hydrolysed; the hydrogen peroxide had an oxygen isotopic abundance of −0·001 atom %.

The experiment with enriched formic acid was conducted in a similar manner, but on a smaller scale. The isotopic abundance of the residual hydrogen peroxide (after formation of the performic acid) was 0·002 atom %. The abundance of the hydrogen peroxide produced by hydrolysis of this performic acid in 0·5 atom % $H_2{}^{18}O$ was −0·002 atom %.

Duplicate experiments gave isotopically normal hydrogen peroxide in all cases.

An experiment in which perphthalic acid was hydrolysed in 0·5 atom % $H_2{}^{18}O$ gave hydrogen peroxide of abundance 0·002 atom %.

Kinetics of Hydrolysis of Peracetic acid.—The hydrolyses were followed in aqueous perchloric acid by first titrating the hydrogen peroxide with potassium permanganate or ceric sulphate, and then titrating the iodine liberated on addition of potassium iodide. In general the integrated first-order rate constants were calculated graphically from the peracetic acid concentrations. The rate constants of two preliminary runs ($[HClO_4]$ = 2·2M and 2·57M) were calculated from the hydrogen peroxide concentrations. The results are quoted in Table 1, and the data of a kinetic run are annexed.

$[HClO_4]$ = 2·16M. Portions (5 c.c.) were titrated with 0·0327N-potassium permanganate to destroy hydrogen peroxide, potassium iodide was added, and the iodine titrated with 0·0317N-sodium thiosulphate:

Time (min.)	0	5	10	20	30	40	50	60	70
$Na_2S_2O_3$ (c.c.)	6·63	6·44	6·20	5·34	4·64	3·90	3·54	3·10	2·74

$k_1 = 13·6 \times 10^{-3}$ (min.$^{-1}$) from plot of log $(a - x)$ against time.

Ketone Oxidation.—Benzophenone and 4-methoxybenzophenone were isotopically enriched by refluxing with acidified dioxan and $H_2{}^{18}O$. The isotopic abundances of the ketones were calculated from the isotopic abundance of the water.

The ketone was left overnight in isotopically enriched acetic acid containing sulphuric acid. This mixture was then added to a solution of isotopically normal peracetic acid in isotopically enriched acetic acid, of a composition such that the ^{18}O abundances of the ketonic and carboxylic oxygen atoms were similar in the two solutions. The isotopic abundance of the oxygen of the ketone was calculated by assuming complete isotopic equilibriation between the ketone and the acetic acid solvent. To test this assumption, some experiments were carried out with isotopically normal ketone added directly to the solution of peracetic acid in isotopically enriched acetic acid containing sulphuric acid. The solutions were then left at room temperatures for several days (the general reaction conditions of Doering and Spears[11]). The product was isolated by pouring the mixture into water, filtering, and hydrolysing the crude ester with sodium hydroxide in isotopically normal water. The oxygen isotopic abundance of the phenol

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[10] Friess, *J. Amer. Chem. Soc.*, 1949, **71**, 2571.
[11] Doering and Spears, *ibid.*, 1950, **72**, 5515.

was determined by pyrolysis *in vacuo* to carbon monoxide on heated metal gauze, or on red-hot carbon. As a test of the analytical method, some carbon monoxide samples were converted catalytically into carbon dioxide, and this gas was analysed mass-spectrometrically. The benzoic acid was converted into its silver salt, and this decarboxylated by heat *in vacuo*. All isotopic analyses were carried out mass-spectrometrically.

The lactone (III) of 2′-hydroxydiphenyl-2-carboxylic acid was isolated from oxidation of fluorenone with peracetic acid, and a portion pyrolysed to carbon monoxide. Another portion was converted into 2′-methoxydiphenyl-2-carboxylic acid by hydrolysis in $H_2{}^{18}O$ (abundance, *ca.* ½ atom %), and methylation with dimethyl sulphate.[12] This acid was then decarboxylated and demethylated by heating it with soda-lime, and the 2-hydroxydiphenyl so formed was pyrolysed to carbon monoxide and shown to be isotopically normal in oxygen. The product of another oxidation of fluorenone was similarly converted into 2′-methoxydiphenyl-2-carboxylic acid, and this acid heated with aqueous perchloric acid to remove any tracer in the carboxyl-oxygen atoms; it was assumed that the methoxyl oxygen was not affected by this treatment. The isotopic abundance of this " normalised " acid was determined by pyrolysis to carbon monoxide.

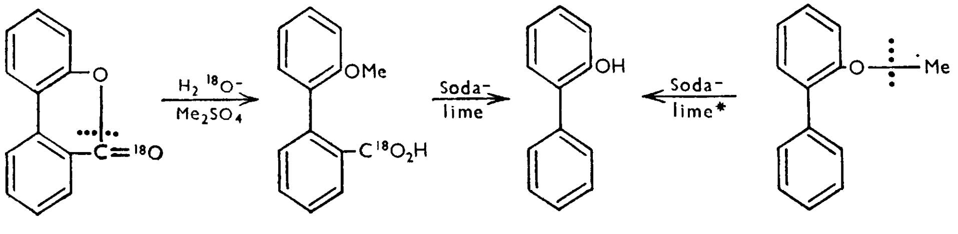
Examples of the oxidations and degradations are given below.

Benzophenone. Acetic anhydride (0·246 mole) was hydrolysed in 0·25 mole of $H_2{}^{18}O$ (abundance 2·80 atom %). A portion was added to 0·033 mole of benzophenone (abundance 1·61 atom %) with 7 c.c. of concentrated sulphuric acid, and the residue to 12 g. of 40% peracetic acid in acetic acid. The following morning the solutions were mixed and left for 4 days at room temperature. The phenyl benzoate gave phenol (abundance 0·001 atom %) and benzoic acid (abundance 0·257 atom %); the abundance calculated from that of the ketone was 0·293 atom %.

Fluorenone. Acetic anhydride (0·5 mole) was hydrolysed in 0·5 mole of $H_2{}^{18}O$ (abundance 2·80 atom %), and fluorenone (6 g.) and 10 c.c. of concentrated sulphuric acid were then added, followed by 22 g. of 40% peracetic acid in acetic acid. The solution was left at room temperature for 10 days and then poured into 250 c.c. of $H_2{}^{18}O$ (0·4 atom %). Some of the lactone was isolated, and purified (m. p. 91—92°, isotopic abundance 0·275 atom %, isotopic abundance calculated from isotopic abundance of ketone 0·30 atom %). The remainder of the lactone was hydrolysed and methylated with dimethyl sulphate in $H_2{}^{18}O$. The 2′-methoxydiphenyl-2-carboxylic acid so formed was heated with soda-lime to give 2-hydroxydiphenyl (m. p. 54—56°; isotopic abundance 0·025 atom %).

A similar oxidation with peracetic acid (formed by the reaction of acetic anhydride and 90% hydrogen peroxide) in isotopically enriched acetic acid gave a lactone which, after hydrolysis and methylation in $H_2{}^{18}O$ (*ca.* 0·5 atom % abundance), gave 2′-methoxydiphenyl-2-carboxylic acid (m. p. 152°).

After being heated for several days in 2N-perchloric acid, the 2′-methoxydiphenyl-2-carboxylic acid had m. p. 151—152°, and isotopic abundance 0·039 and 0·043 atom % (separate determinations). Demethylation of 2-methoxydiphenyl by isotopically enriched soda-lime (isotopic abundance *ca.* 0·3 atom %) gave 2-hydroxydiphenyl (m. p. 53—55°, isotopic abundance 0·003 atom %). The reactions can be represented by the annexed scheme.



(Abundance, 0·275 atoms %) **(Isotopically normal)** *** Abundance *ca.* 0·3 atom %**

The authors are indebted to Professors C. K. Ingold, F.R.S., and E. D. Hughes, F.R.S., for their valuable advice on this work.

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[*Received, September 6th,* 1955.]

[12] Rule and Bretscher, *J.*, 1927, 925.