317. *Studies of the Autoxidation of Tetralin. Part I. Investigation of Autoxidation Products.*

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Several products have been isolated from the autoxidation of tetralin, the chief being α-tetralone and α-tetralol. Some of the minor products have been shown to be autoxidation products of α-tetralone, which itself forms a hydroperoxide that breaks down to a 1 : 2-diketone and then to acidic substances. *cyclo*Hexanone similarly gives *cyclo*hexanedione, and adipic acid and its hemi-aldehyde.

γ-*o*-Hydroxyphenylbutyric acid is also an autoxidation product of tetralin, and plays the important rôle of being an inhibitor of autoxidation. It can be made by oxidising α-tetralone with Caro's acid. An ionic mechanism is proposed for the formation of this substance, and, in general, for the per-acid oxidations of ketones.

IN an earlier paper (*Trans. Faraday Soc.*, 1946, **42**, 201) we pointed out that the chemical reactions concerned in the autoxidation of tetralin, and of its analogues (compare Waters, *Ann. Reports*, 1945, **42**, 130—143), can be divided into two consecutive phases, *viz.*, (I) formation of tetralin hydroperoxide, and (II) breakdown of the hydroperoxide, and showed that in the early stages of the autoxidation the *whole* of the oxygen uptake was due to the formation of tetralin hydroperoxide by a chain reaction involving free radicals. We have now found that the later stages of the autoxidation also involve the autoxidations of certain of the breakdown products of tetralin hydroperoxide, *e.g.*, α-tetralone. Some of these products too can be oxidised directly by tetralin hydroperoxide.

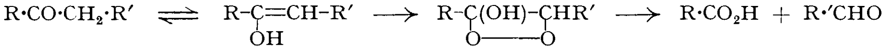
By studying separately the decomposition of pure tetralin hydroperoxide in the absence of fresh oxygen (see Part II, following paper) we have discriminated between direct and secondary oxidation processes sufficiently clearly to be able to interpret all earlier studies of the autoxidation on a much more comprehensive basis than has been possible hitherto (see Part III, this vol., p. 1585).

The Final Oxidation Products of Tetralin.—After about 80 hours of autoxidation at 76°, tetralin is converted into a viscous reddish-orange oil, containing *ca.* 25% of tetralin hydroperoxide; at an earlier stage, however, the peroxide content of the liquid is much higher (*ca.* 35—40%). Further oxygen uptake is thereafter very slow indeed.

After the remaining hydroperoxide has been destroyed by heat, the components of the resultant mixture can be separated by fractional distillation under reduced pressure, and in this way the following products have all been characterised : (1) 1 : 2-Dihydronaphthalene, comprising approximately 2% of the liquid, (2) α-tetralone, (3) α-tetralol, (4) γ-o-*hydroxyphenylbutaldehyde*, (5) γ-*o*-hydroxyphenylbutyric acid, (6) β-*o*-carboxyphenylpropionic acid, together with polymeric products which could not be distilled. The lactone of (5) is probably present in the original mixture, whilst small amounts of the α-tetralyl esters of (5) and (6) may be formed during the distillation process, since the less volatile fractions of the oil contain small amounts of saponifiable substances. All these compounds have also been obtained by thermal decomposition of tetralin hydroperoxide in the absence of oxygen.

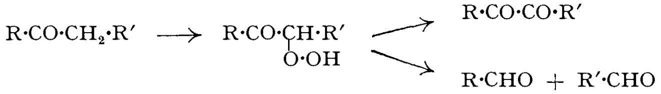
The acid (5) had been prepared from α-tetralone by oxidation with Caro's acid (Schroeter, D.R.-P. 562,827 of 1928). It is not formed by the autoxidation of α-tetralone (see below), whereas acid (6) is a major product of the autoxidation of α-tetralone. The production of both (5) and (6) indicates that α-tetralone can undergo further oxidation in two different ways. We regard (4) as a direct thermal decomposition product of tetralin hydroperoxide.

Autoxidations of Cyclic Ketones.—The foregoing work shows that the autoxidations of ketones and of hydrocarbons are interrelated. Previous studies of the autoxidation of ketones have not yielded clear information as to the nature of the autoxidation process. Jenkins (*J. Amer. Chem. Soc.*, 1935, **57**, 2733) showed that ketones of the type $R\cdot CO\cdot CH_2R'$ can autoxidise, and give strong peroxide reactions after exposure to air. He suggested that the oxygen attacked their enolic forms as follows :



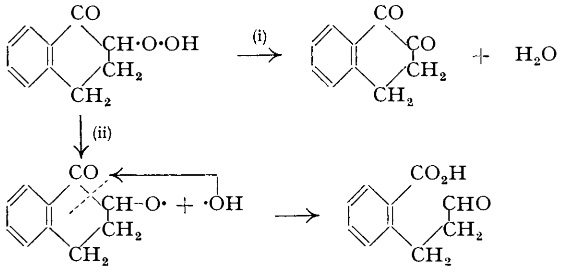
$$R\cdot CO\cdot CH_2\cdot R' \rightleftharpoons R{-}\underset{OH}{C}{=}CH{-}R' \longrightarrow R{-}\underset{O\text{———}}{C}(OH){-}\underset{O}{C}HR' \longrightarrow R\cdot CO_2H + R'\cdot CHO$$

Paquot (*Bull. Soc. chim.*, 1945, **12**, 450), however, obtained diketones, as well as aldehydes and acids, by autoxidation of a whole series of ketones in the presence of nickel phthalocyanine, and, in accordance with the theories of Farmer and his colleagues (*Trans. Faraday Soc.*, 1942, **38**, 348; 1946, **42**, 228), suggested that a carbonyl group activates an adjacent methylene group sufficiently to allow of the formation of a ketone hydroperoxide :



$$R\cdot CO\cdot CH_2\cdot R' \longrightarrow R\cdot CO\cdot \underset{O\cdot OH}{C}H\cdot R' \begin{cases} \nearrow R\cdot CO\cdot CO\cdot R' \\ \searrow R\cdot CHO + R'\cdot CHO \end{cases}$$

We have found that at 100° *cyclo*hexanone is easily autoxidised and soon gives positive peroxide tests with potassium iodide, and also an acid reaction to litmus. After 10 hours' treatment a heavy deposit of adipic acid settles out on cooling, whilst the residual liquid contains both *cyclo*hexane-1 : 2-dione and the hemi-aldehyde of adipic acid. β-Tetralone, which contains the $\cdot C_6H_4\cdot CH_2\cdot CO\cdot$ group is much more rapidly autoxidised than is α-tetralone : it yields β-*o*-carboxyphenylpropionic acid (6). α-Tetralone autoxidises *slowly* at 100°, yielding an orange-red liquid (compare tetralin itself) which gives a positive peroxide test and an acid reaction with litmus. The red liquid gave positive tests for a 1 : 2-diketone, and colour reactions with alkali indicative of β-naphthaquinol, which is a tautomeride of tetrahydronaphthalene-1 : 2-dione (compare Strauss, Bernouilly, and Mautner, *Annalen*, 1925, **444**, 165). These results accord with Paquot's conclusions, and indicate that cyclic ketones form hydroperoxides which can either (i) dehydrate to 1 : 2-diketones or (ii) undergo a more complex decomposition which leads to a carbon–carbon bond fission similar to that suggested by Walsh (*Trans. Faraday Soc.*, 1946, **42**, 269) for the breakdown of tertiary hydroperoxides :



There is no indication, even with the hydroperoxide of β-tetralone, that the second of these oxidation processes affects the fission of the Aryl–C link.

The Rôles of Secondary Products in the Autoxidation of Tetralin.—(a) *α-Tetralone.* On the technical scale ketones (*e.g.*, methyl ethyl ketone) have been employed as promoters of the autoxidation of hydrocarbons (*e.g.*, pentane; U.S.P. 2,265,948 of 1939), and often do reduce considerably the duration of the initial " induction period " in which there is very little oxygen uptake. On the other hand, Medvedev and Podyapolskaya (*J. Phys. Chem. Russia*, 1939, **12**, 719) found that the addition of α-tetralone reduced the overall rate of autoxidation of tetralin, and this has been confirmed by George and Robertson (*Proc. Roy. Soc.*, 1946, *A*, **185**, 309). Evidently the net rôle of a ketone as a promoter or as an inhibitor of autoxidation depends on (i) the relative ease of autoxidation of the hydrocarbon and the ketone concerned, and, more particularly, on (ii) the relative stabilities of their two hydroperoxides, which by their decompositions generate chain-starting hydroxyl radicals. Thus *cyclo*hexanone, which contains an active methylene group, is more easily autoxidised than *cyclo*hexane, whereas tetralin, which itself contains two active α-methylene groups, is more reactive than α-tetralone, and apparently yields a more stable hydroperoxide.

(b) *Phenolic products.* Nearly all phenols act as inhibitors in the initial stage of the autoxidation of hydrocarbons, though only certain easily oxidised ones, such as α-naphthol, are also effective once an appreciable amount of hydroperoxide has been formed (Robertson and Waters, *loc. cit.*). Bolland and ten Have (*Trans. Faraday Soc.*, 1947, **43**, 201) have shown that these typical inhibitors are themselves oxidised by chain-breaking processes. Now, the autoxidation rate of tetralin, in common with that of most naphthenic hydrocarbons (Larsen, Thorpe, and Armfield, *Ind. Eng. Chem.*, 1942, **34**, 182), begins to decrease when *ca.* 30% of the hydrocarbon has been oxidised, and becomes quite small at about the stage when, in phase (II) of the oxidation process, the phenolic secondary products (4) and (5) appear in appreciable amounts. The following table shows that γ-o-hydroxyphenylbutyric acid (5) is a marked inhibitor of the autoxidation of tetralin even if added at the stage of rapid oxygen uptake.

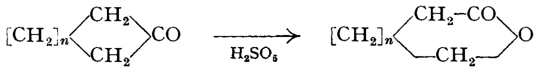
The effect of γ-o-hydroxyphenylbutyric acid on the autoxidation of tetralin at 76°.

	Oxygen uptake : ml. per 15 mins. Time after start of oxidation, mins.						
	15.	30.	45.	60.	75.	90.	105.
Partly oxidised tetralin	4·3	4·6	4·9	5·4	5·7	—	—
Same sample of tetralin plus 1 g. of acid (5)	2·2	1·9	1·7	1·4	1·0	0·9	0·5

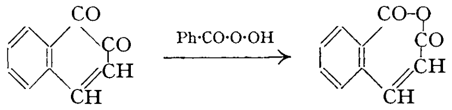
Our studies of the minor products of the autoxidation of tetralin have thus afforded a rational explanation of even the subsidiary features of oxygen-uptake measurement.

The Mechanism of Oxidation of Ketones with Hydroperoxides, including Caro's Acid.—Since γ-*o*-hydroxyphenylbutyric acid (5), one of the minor autoxidation products of tetralin, was not obtained by the autoxidation of α-tetralone, but can be obtained, in good yield by the action of Caro's acid, $HO{\cdot}O{\cdot}SO_3H$, which is of course a hydroperoxide, on α-tetralone, it probably results from the reaction between α-tetralone and tetralin hydroperoxide. If, as we believe (see Parts II and III) the thermal decomposition of tetralin hydroperoxide yields some free hydroxyl radicals, then it would be expected that it should behave as a hydrogen-abstracting, or as a hydroxylating agent, but it is difficult to reconcile radical reactions of these types with the salient facts concerning ketone oxidation with hydrogen peroxide and the per-acids, amongst which the formation of (5) from α-tetralone is quite typical.

Baeyer and Villiger (*Ber.*, 1899, **32**, 3625; 1900, **33**, 862) found that Caro's acid reacted with cyclic ketones to give cyclic lactones, carbon–carbon bond fission taking place with the addition of an atom of oxygen to the ring. The reaction has been found to be quite general; other per-acids, *e.g.*, perbenzoic, peracetic, and perphthalic acids, can be used similarly :



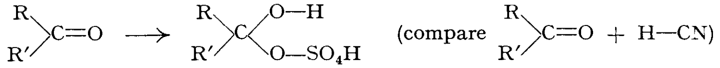
Marker (*J. Amer. Chem. Soc.*, 1940, **62**, 525, 2543) has used the reaction to convert $\geqslant C{\cdot}CO{\cdot}CH_3$ groups into $\geqslant C{\cdot}O{\cdot}CO{\cdot}CH_3$ groups, and Dilthey, Inckel, and Stephan (*J. pr. Chem.*, 1940, **154**, 219) have shown that Caro's acid converts benzophenone into phenyl benzoate. Since Aryl–CO–Alkyl is regularly converted into Aryl–O–CO–Alkyl, the mechanism of the reaction cannot involve the addition of hydroxyl radicals to the enolic form of the ketone, as suggested by Triebs (*Ber.*, 1939, **72**, 7, 1194). Again, acetone, which easily enolises in the presence of acids, is not readily oxidised by hydrogen peroxide, even in the presence of a ferrous salt, but gives quite a stable, polymeric peroxide. Moreover, Karrer and his colleagues (*Helv. Chim. Acta*, 1946, **29**, 1836; 1947, **30**, 859) have shown that the per-acids will easily oxidise unsaturated diketones to acid anhydrides which are still unsaturated, *e.g.* :



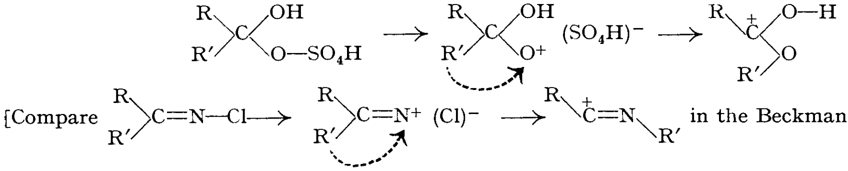
Consequently, since free hydroxyl radicals promptly attack olefinic bonds (Baxendale, Evans, and Park, *Trans. Faraday Soc.*, 1946, **42**, 155), these reactions cannot involve free hydroxyl radicals.

Now, in discussing the mode of fission of cyclic ketones, such as menthone, Baeyer and Villiger commented on the fact that the rupture of the carbon–carbon bond by Caro's acid always occurred in the same place as the rupture effected by the Beckmann rearrangement of the corresponding oximes, and suggested that both processes proceeded by a similar mechanism. This surmise gives a clear lead to a rational *ionic* mechanism for the reactions of the per-acids, which may be formulated as under :

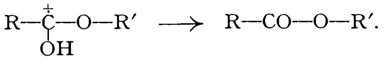
(i) The ions, H^+ and $(O{\cdot}SO_4H)^-$ of Caro's acid add to the carbonyl group of a ketone in the normal way : many ketone peroxides of this type are known.



(ii) The stable *anion* [*i.e.*, $(SO_4H)^-$ in this example] of the per-acid separates as a free entity, leaving an electron-deficient oxygen atom. This is at once stabilised by the intramolecular migration of an anionoid hydrocarbon radical.



(iii) Finally, by loss of proton, a stable lactone is formed :



$$R-\underset{OH}{\overset{+}{C}}-O-R' \longrightarrow R-CO-O-R'.$$

This interpretation accords with the order of migratory aptitudes of the different groups, and, in the case of the reactions of α-tetralone, with which this paper is more particularly concerned, explains at once why a phenolic acid (5) is produced rather than the alternative (6), which would result from any reaction sequence involving enolisation, epoxide formation (compare Stoll and Scherrer, *Helv. Chim. Acta*, 1930, **13**, 142), or free-radical reaction, such as that involved in its autoxidation.

EXPERIMENTAL.

Oxidation Products of Tetralin.—The thick oil obtained by oxidation of tetralin was carefully heated at 130—150° until all the peroxide had decomposed, and then was distilled into the following fractions under a reduced pressure of nitrogen or carbon dioxide :

(i) B. p. 88°/15 mm. : this was mainly tetralin, but colour reactions (Robertson and Waters, *J.*, 1947, 496) indicated that it also contained 1 : 2-dihydronaphthalene; the liquid rapidly absorbed bromine at 0° in amount corresponding to 2% of this substance.

(ii) B. p. 130°/13 mm. : this was a pale yellow oil of peppermint odour, from which α-tetralone was separated as the oxime, m. p. 103°. A portion was refluxed with phenyl *iso*cyanate for 2 hrs., and then steam distilled. The residue was extracted with light petroleum (b. p. 60—80°) and gave the phenylurethane of α-tetralol, m. p. and mixed m. p. 122° (*ex* EtOH). Previous workers have often failed to detect α-tetralol in this fraction of liquid. Its phenylurethane is so soluble that it cannot be separated from tetralone, etc., unless all the volatile material is first steam distilled away. Separation of α-tetralol was also effected by treating the oil with finely-ground calcium chloride. This forms a solid complex with α-tetralone which can be removed by filtration, and leaves reasonably pure α-tetralol. The complex is immediately decomposed by water.

(iii) B. p. 128°/0·4 mm. : this viscous yellow product, with aldehydic reactions (Fehling's solution and Schiff's reagent), gave a 2 : 4-*dinitrophenylhydrazone*, m. p. 149° (Found : C, 56·0; H, 4·9; N, 16·0. $C_{16}H_{16}O_5N_4$ requires C, 55·8; H, 4·7; N, 16·3%), and a bisulphite compound. Analysis of the oil agreed with that for γ-o-*hydroxyphenylbutaldehyde* (4) (Found : C, 73·2; H, 7·1. $C_{10}H_{12}O_2$ requires C, 73·1; H, 7·3%). On exposure to air the substance was slowly oxidised to the corresponding acid (5, see below), m. p. 68°.

(iv) B. p. 128—200°/0·4 mm. : this mixture could not be separated by repeated fractional distillation, probably on account of progressive lactonisation or esterification. It was acidic, and when treated with sodium hydroxide gave a transient blue-green colour and finally became brown. Acidification of the alkaline extract gave a dark brown oil which, by extraction with carbon disulphide gave a water-soluble carboxylic acid which coloured ferric chloride bluish-green and coupled to a red dye with diazotised sulphanilic acid. It was finally obtained as a solid, m. p. 68°, and proved to be identical with *γ-o*-hydroxyphenylbutyric acid, which was prepared, for comparison by Schroeter's method, as follows : 40 G. of finely powdered potassium persulphate were mixed at 0° with 40 g. of concentrated sulphuric acid and then added slowly, with vigorous mechanical stirring, to an ice-cold solution of 15 g. of α-tetralone in 40 g. of methanol. When reaction was complete, the excess of acid was neutralised, the bulk of the methanol was removed by distillation, and the residual methyl ester of (5) was extracted with ether and purified by distillation (b. p. 180°/15 mm.). The free acid, m. p. 68°, tended to lose water on heating (Found : C, 66·2; H, 6·9; equiv., 180. Calc. for $C_{10}H_{12}O_3$: C, 66·2; H, 6·7%; equiv., 180).

(v) B. p. > 200°/0·4 mm. : this was a very viscous, dark brown, liquid from which, by alkali extraction *β-o*-carboxyphenylpropionic acid, m. p. 164°, was obtained (Found : C, 62·5; H, 5·1; equiv., 100. Calc. for $C_{10}H_{10}O_4$: C, 62·0; H, 5·1%; equiv., 97). Chromatographic analysis of the residue was attempted but did not give pure products. Polymerised hydrocarbons were evidently present.

Autoxidation of cyclo*Hexanone*.—This was exceedingly slow at 76° but proceeded at 100°. After 10 hours' aeration the liquid gave a heavy crystalline deposit of adipic acid, m. p. 151°, when cooled. The filtrate from this was washed 3 times with ice-cold potassium hydroxide solution and the extract was shaken with ether to remove dissolved *cyclo*hexanone. After careful neutralisation at 0°, the solution was extracted with ether to separate cyclohexane-1 : 2-dione (compare Riley, Morley, and Friend, *J.*, 1932, 1879). The extract, after drying, gave, besides adipic acid, an oil, b. p. <100°/20 mm., which formed an oxime that gave with nickel sulphate the flocculent red precipitate characteristic of a glyoxime.

Distillation of the direct product of oxidation gave a small fraction of a carboxylic acid, b. p. 145—150°/10 mm., which also gave positive tests for the aldehyde group (Schiff's reagent, etc.). The fraction gave a dinitrophenylhydrazone which, after recrystallisation from alcohol, had m. p. 141°, identical with that obtained by Baer (*J. Amer. Chem. Soc.*, 1942, **64**, 1416) for adipic hemi-aldehyde.

Autoxidation of α-Tetralone.—This was conducted at 100° and gave an acidic orange-red product which contained peroxides. The liquid was extracted with ice-cold sodium hydroxide solution, the extract neutralised, and the liberated ketone converted into the oxime, as described above. Addition of nickel sulphate solution to this gave a reddish-brown precipitate, which was slightly soluble in chloroform, giving a pink solution.

β-Tetralone soon deposited crystals when exposed to the air, and after purification, these proved to be *β-o*-carboxyphenylpropionic acid, m. p. and mixed m. p. 164°.

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