

### 3. *Ketonic Products of the Oxidation of the cis- and trans-Forms of Ricinoleic Acid.*

(Considered in relation with the author's work on the autoxidation of the unsaturated fatty acids.)

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The hitherto unknown *cis-11-ketoheptadec-8-ene-1-carboxylic acid* ( $\lambda$ -*keto-oleic acid*) and its *trans-isomer* ( $\lambda$ -*ketoelaidic acid*) have been prepared by the chromic acid oxidation of ricinoleic and ricinelaidic acid, respectively. Both of these acids containing  $\beta\gamma$ -olefinic ketone grouping have been transformed, through their common hydrogen bromide additive product, *9-bromo-11-ketoheptadecane-1-carboxylic acid* (*u-bromo- $\lambda$ -ketostearic acid*), into the *trans*-form of their  $\alpha\beta$ -isomer, *trans-11-ketoheptadec-9-ene-1-carboxylic acid*. Some of the properties of these compounds have been studied, particularly the quantitative nature of their alkaline hydrolyses. Their reactions with semicarbazide have been studied and special interest attaches to formation, from  $\lambda$ -keto-oleic acid, of a peroxide simultaneously with an *epoxy*-derivative.

THE main purpose of these investigations was to throw further light on the formation of unsaturated ketone groups during the autoxidation of the mono-unsaturated fatty acids. The products obtained from oleic and elaidic acid, after an oxygen uptake at 60—70° of about 20% by weight, contained only a low concentration of these unsaturated keto-acids, but contained substances regarded as resulting therefrom, such as elaidic acid oxide (m. p. 55·5°) in nearly 40% yield with its monoacyl derivatives, and oily, resinous polymers. The amount of

these substances became inappreciable when it was found possible to bring about autoxidation at 45—50°. In their place appeared  $\eta$ - and  $\kappa$ -keto-oleic acids, or their *trans*-isomers, as the main autoxidation products (Ellis, *Biochem. J.*, 1936, **30**, 753 ; 1950, in the press).

The existence of different isomers of these keto-acids and the appreciable chain degradation found to accompany autoxidation led to the formation of a complex mixture of these bodies from which no pure product can, with certainty, be regarded as having been isolated. The present study of similar compounds, obtained in a pure form from ricinoleic and ricinelaic acids, confirms the evidence for the presence of the unsaturated ketonic acids as significant autoxidation products of the mono-unsaturated fatty acids; similar ketone formation has been observed for 1-methylcyclohexene (Dupont, *Bull. Soc. chim. Belg.*, 1936, **45**, 57 ; 1937, **46**, 21 ; Cook, *J.*, 1938, 1778). It was realised that carefully controlled oxidation of ricinoleic and ricinelaic acids should afford acids containing  $\beta\gamma$ -unsaturated ketone groupings in *cis*- and *trans*-forms which by the catalytic action of acids and alkalis might undergo tautomeric change to the respective  $\alpha\beta$ -forms (cf. Kon *et al.*, *J.*, 1923, 1361 etc. ; 1926, 2128). However, the *trans*- $\alpha\beta$ -form was obtained from both the *cis*- and the *trans*- $\beta\gamma$ -form by way of the hydrobromic acid additive product of the latter (cf. Blaise, *Bull. Soc. chim.*, 1905, **33**, 40).

$\lambda$ -Keto-oleic, m. p. 39°, and -elaic acid, m. p. 73°, have now been prepared by the oxidation of ricinoleic and ricinelaic acid, respectively, with chromic acid below 15°. Both keto-acids have iodine values lower than the theoretical and, although the latter acid is perfectly stable, the former rapidly autoxidises in air, even at 0°. At room temperatures  $\lambda$ -keto-oleic acid absorbs 3—4 atoms of oxygen with evolution of carbon dioxide, to form a semi-solid mass containing up to 12.5% of a peroxide (calculated as a peroxide of keto-oleic acid with one active oxygen atom), an appreciable proportion of  $\lambda$ -ketoepoxystearic acid, m. p. 112.5° (2 : 4-dinitrophenylhydrazone, m. p. 119°), and oily substances giving reactions pointing to  $\beta$ -keto-acid formation. The instability of the unsaturated ketones has usually been attributed to polymerisation rather than to autoxidation, but explosive products have sometimes been observed (Eccott and Linstead, *J.*, 1930, 905), suggestive of the peroxide formation observed in the present studies.

In the present study of the autoxidation of oleic and elaidic acid, small and not greatly varying amounts of peroxides were formed at temperatures between 45° and 100°. At the lower temperatures high yields of the unsaturated keto-acids were obtained, with little evidence of their decomposition into the coloured, resinous oils which form the greater part of the products at higher temperatures. At all temperatures within the range, elaidic acid oxide, m. p. 55.5°, was also formed from both oleic and elaidic acid (maximum yield at 60—70°), with a copious evolution of carbon dioxide and water. Some of the oily fractions isolated gave marked enol reactions and yielded carbon dioxide on hydrolysis, so that  $\beta$ -keto-acid formation is probable. The products are thus closely comparable with those obtained by autoxidation of the olefinic keto-acid studied in the course of this work, and since, for the autoxidation of oleic and elaidic acid, a preliminary formation of olefinic keto-acids has been demonstrated in the author's contemporary work (Ellis, 1950, *loc. cit.*), it seems likely that for this process there is a sequence : olefinic acid  $\longrightarrow$  olefinic keto-acid  $\longrightarrow$  olefinic keto-acid peroxide  $\longrightarrow$  peroxidation products, including an epoxide, carbon dioxide, and water with other chain-peroxidation products.

$\lambda$ -Keto-oleic and -elaic acid absorb hydrogen bromide in dry carbon tetrachloride solution (cf. Blaise, *Bull. Soc. chim.*, 1905, **33**, 40 : Eccott and Linstead, *loc. cit.*) to form the same *t*-bromo- $\lambda$ -ketostearic acid, m. p. 68°, in good yield. This is converted by aqueous potassium hydrogen carbonate at 100° into 11-ketoheptadec-9-ene-1-carboxylic acid, m. p. 50°, containing an  $\alpha\beta$ -unsaturated keto-group and considered to be the *trans*-form by analogy with the findings of the authors mentioned above.

Alkaline hydrolysis of  $\lambda$ -keto-oleic and -elaic acid afforded a 40% yield (theory 43%) of hexyl methyl ketone, the isolation of which was facilitated by the use of a simple still-head (Ellis, 1950, *loc. cit.*). The other hydrolysis product, the semialdehyde of sebamic acid, was not isolated : it appeared to have polymerised under the action of the alkali. Since methyl hexyl ketone was obtained in very similar yields by alkaline hydrolysis of both the *cis*- and the *trans*-form of the  $\beta\gamma$ -isomers and from the *trans*-form of the  $\alpha\beta$ -isomer, it seems probable that the first two acids isomerise under the influence of alkalis (cf., *e.g.*, Eccott and Linstead, *loc. cit.*).

Condensed with phenylhydrazine and then treated with sulphuric-nitrous acid, all these olefine-ketonic acids gave an intense purple pyrazoline dye. This reaction was previously regarded as specific for  $\alpha\beta$ -olefinic ketones. It is a marked reaction of the oily products

obtained by the autoxidation of the mono-unsaturated fatty acids and is given by a linseed oil film which has been exposed to the air for a few hours at room temperatures.

#### EXPERIMENTAL.

*λ*-Keto-oleic (*cis*-11-Ketoheptadec-8-ene-1-carboxylic) Acid from Ricinoleic Acid.—A solution of recently prepared ricinoleic acid (60 g.) in acetic acid (500 ml.) was cooled with occasional stirring so as to crystallise a large proportion of the acetic acid without causing the mass to set and so hinder the next operation. Chromium trioxide (14 g.) in a minimum of water and acetic acid (100 ml.) was added with vigorous stirring, and the mixture was set aside for 2 hours at room temperature. It was then mixed with half its bulk of powdered ice, and the solid product was allowed to separate over a clear lower layer. The solid (which should contain a large proportion of ice) was washed by suction with ice-cold water until colourless. It crystallised from 80% ethanol at 0° in long, thin plates (10 g.), m. p. 39° (Found: C, 72.9; H, 10.7%; I.V., 56. C<sub>18</sub>H<sub>32</sub>O<sub>3</sub> requires C, 72.9; H, 10.9%; I.V., 85.7).

*λ*-Keto-oleic acid is very soluble in all the common organic solvents and crystallises well from light petroleum. Filtration of its solution in this solvent serves to remove possible traces of the epoxide described below. This acid is very unstable in air, absorbing oxygen to form a peroxide and other substances (see below). Although it clearly reacts with semicarbazide and with 2:4-dinitrophenylhydrazine, no pure derivatives have been isolated. It gives the following sensitive test: About 1 mg. is heated for a few seconds with an equal bulk of phenylhydrazine on a slide and the cold product is rubbed into a smear with a small drop of sulphuric acid. A few crystals of sodium nitrite are allowed to react completely with a drop of sulphuric acid. On causing these two smears to run together, an intense bluish-violet mass is obtained.

When boiled with water or diluted sulphuric acid, or when heated alone at 100° for an hour, *λ*-keto-oleic acid gives a yellow oil.

*Alkaline Hydrolysis of λ*-Keto-oleic Acid.—Slow distillation of this acid with 0.03N-sodium hydroxide in the apparatus referred to above, gave a 40% yield of methyl hexyl ketone (semicarbazone, m. p. and mixed m. p. 121°), but the yields fell off with an increased concentration of alkali:

Wt. taken, g.	Alkali.	Methyl hexyl ketone, g.	Yield, %.	Yield, % corr.
0.2689	0.03N-NaOH	0.0960	36	40
0.1738	0.05N-NaOH	0.0535	31	34
0.2087	N-NaOH	0.0500	24	26
0.1510	10% KOH	0.0325	22	24
0.1958	10% K <sub>2</sub> CO <sub>3</sub>	0.0407	21	23

A blank experiment with pure methyl hexyl ketone in the same apparatus gave a 90% recovery, and the yields have been corrected accordingly, as shown in the last column. With the more concentrated alkali the hydrolytic reaction appears to be replaced in part by polymerisation. Acidification of the products remaining after distillation of the methyl hexyl ketone resulting from the less concentrated alkaline hydrolyses gave, apparently, polymers of sebacic acid semialdehyde as semi-solid oils [Found: equiv., 186. Calc. for (C<sub>10</sub>H<sub>18</sub>O<sub>3</sub>)<sub>n</sub>: equiv., 186]. This equivalent rose to 240–260 when more concentrated alkali was employed, furnishing some evidence that the lower yield of methyl hexyl ketone was caused by polymerisation of the olefinic keto-acid. No Schiff's or other aldehydic reaction could be obtained, either before or after boiling these oils with dilute sulphuric acid, nor could any sebacic acid be detected after their oxidation with potassium permanganate. In such respects these sticky oils bear a close analogy with the polymerised product which King (*J.*, 1938, 1826) obtained by the action of alkali on azelaic acid semialdehyde.

*λ*-Keto-elaidic (*trans*-11-Ketoheptadec-8-ene-1-carboxylic) Acid.—Ricinelaic acid, m. p. 52°, was prepared by exposing a layer of ricinoleic acid to nitrous fumes for about 2 days and purifying the product with dilute ethanol. This was oxidised with chromic acid in acetic acid in the manner described above. The crude product, however, was crystallised from 90% ethanol at room temperatures, unchanged ricinelaic acid being retained in the mother-liquors. *λ*-Keto-elaidic acid (30%) crystallised from ethanol in rhombic and hexagonal plates, m. p. 73° (Found: C, 72.9; H, 10.8%; I.V., 68), and gave a semicarbazone, m. p. 94° (Found: N, 12.0. C<sub>19</sub>H<sub>35</sub>O<sub>3</sub>N<sub>3</sub> requires N, 11.9%). The keto-acid was stable in air (during some months) and gave the pyrazoline test. It also gave a reddish-orange colour when treated with the phenylhydrazine and sulphuric acid alone. It was much more stable towards heat than was the *cis*-isomer, suffering only slight change during 2 hours at 100°, and afforded, though more slowly than its isomer, a 41% yield of methyl hexyl ketone on hydrolysis with 0.05N-sodium hydroxide.

9-Bromo-11-ketoheptadecane-1-carboxylic Acid.—*λ*-Keto-oleic (or elaidic) acid (1 g.) in carbon tetrachloride (10 ml.) was saturated with hydrogen bromide and the corked vessel was left in a cool place. The 9-bromo-11-ketoheptadecane-1-carboxylic acid which separated was crystallised from a filtered, light petroleum solution and then from carbon tetrachloride or 90% ethanol. It formed rods with pointed ends, often appearing as plate-like bundles (1.1 g.), m. p. 68° (Found: C, 57.2; H, 8.6; Br, 22.2. C<sub>18</sub>H<sub>33</sub>O<sub>3</sub>Br requires C, 57.3; H, 8.8; Br, 21.2%).

*trans*-11-Ketoheptadec-9-ene-1-carboxylic Acid.—The bromo-keto-acid was heated for 2 hours at 100° with 10% aqueous potassium hydrogen carbonate. After acidification the solution was extracted with light petroleum, and the residue left on evaporation of the solvent was crystallised successively from carbon tetrachloride (norite) and from ethanol. *trans*-11-Ketoheptadec-9-ene-1-carboxylic acid crystallised in well-defined hexagonal plates, m. p. 50° (Found: equiv., 297; I.V., 24. C<sub>18</sub>H<sub>32</sub>O<sub>3</sub> requires equiv., 296; I.V., 85.7). A low iodine value has been observed for *αβ*-olefinic ketones (Eccott and Linstead, *loc. cit.*). The acid gave a marked pyrazoline colour reaction, and with sulphurous acid gave a stable

oil. Hydrolysis of the acid with 0.05N-sodium hydroxide gave a 32.5% yield of methyl hexyl ketone. Autoxidation of this  $\alpha\beta$ -isomer is under investigation.

*Autoxidation of  $\lambda$ -Keto-oleic Acid.*—(a) Specimens of  $\lambda$ -keto-oleic acid, left in loosely corked tubes for several months, became sticky and did not melt completely below 100°. The peroxide values ranged from 4.3 to 12.5% (calc. as a peroxide of the original acid). Extraction of the tube contents with light petroleum gave an unstable oily product of 17% peroxide content, which resisted further purification. The solid left after the extraction with light petroleum was extracted with acetone, and the solution filtered and evaporated. The residue in ethanol yielded an epoxide in the form of well-defined hexagonal plates of  $\lambda$ -ketoepoxystearic (11-keto-8:9-epoxyheptadecane-1-carboxylic) acid, m. p. 112.5° [Found: C, 69.1; H, 10.1; equiv., 311; *M* (Rast), 336; I.V., 5.  $C_{18}H_{32}O_4$  requires C, 69.2; H, 10.3%; equiv. = *M*, 312]. The 2:4-dinitrophenylhydrazone crystallised in plates, m. p. 119° (Found: N, 11.0.  $C_{24}H_{36}O_7N_4$  requires N, 11.4%). Attempts to prepare a semicarbazone yielded an impure, yellow, amorphous substance, m. p. 201°, nearly insoluble in ethanol (Found: N, 18.2.  $C_{19}H_{35}O_4N_3$  requires N, 11.4%).

This keto-epoxy-acid was also isolated in small amount as a by-product in the preparation of  $\lambda$ -keto-elaidic acid described above, and was detected in smaller amounts in the mother-liquors from  $\lambda$ -keto-oleic acid preparations. It was isolated by means of its sparing solubility in lukewarm light petroleum. When prepared from these sources this compound may have acquired its epoxy-group by autoxidation of the ricinoleic acid used for the chromic acid oxidations.

(b)  $\lambda$ -Keto-oleic acid (0.0576 g.) was dispersed on a small, opened roll of filter paper (36 sq. cm.), placed in the upper part of a test-tube containing a little saturated aqueous barium hydroxide at the base. The air was replaced by oxygen and the tube connected with a manometer and a source of oxygen. After 55 days, at room temperatures, 6.84 ml. (17% by wt.) of oxygen had been absorbed, corresponding to the addition of 3.33 atoms of oxygen. Acidification of the alkaline solution gave 0.49 ml. of carbon dioxide. The ratio of oxygen evolved as carbon dioxide to the total oxygen uptake was 0.07 as compared with ratios of 0.2—0.4 found for the autoxidation of monounsaturated fatty acids (Ellis, *loc. cit.*).

Extraction of the main autoxidation products from the filter paper with peroxide-free ether furnished a semi-solid material containing crystals of the  $\lambda$ -ketoepoxystearic acid and 15% of peroxide.

(c)  $\lambda$ -Keto-oleic acid was autoxidised in air in the form of a thin film on a glass plate at 42°. After 24 hours, extraction with *n*-hexane gave an oil containing 27% of peroxide. A solid fraction, insoluble in the cold solvent, was identified as the ketoepoxystearic acid.

The oily products of the above autoxidations gave enol reactions, which were not given by any of the olefinic keto-acids. These oils also yielded small quantities of sodium carbonate when hydrolysed by sodium hydroxide. The presence of  $\beta$ -keto-acids in these autoxidation products was therefore indicated.

*Pyrazoline Test.*—The purple colour obtained in the tests described above was also given by the oils from the autoxidation of the monounsaturated fatty acids and by linseed oil which had been exposed to the air for a day, or for a few hours in warm weather. A film of linseed oil so treated gives with concentrated sulphuric acid a deep brown colour, masking the bluish-purple colour of the test, which was, therefore, slightly modified in this case. The autoxidised film (about 1 mg.) was mixed with phenylhydrazine (about 2 mg.). The application of very little heat sufficed to bring about a vigorous reaction. The resulting mass was taken up in a few drops of chloroform and the solution dropped on the sulphuric and nitrous acid mixture. Intense blue or purple colours were obtained in this way.

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