

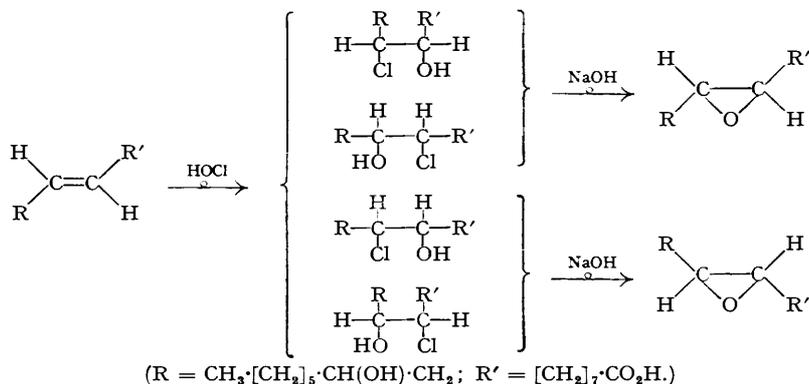
**566.** *trans*-8 : 9-Epoxy-11-ketoheptadecane-1-carboxylic Acid and *cis*-10 : 11-Diketoeptadec-8-ene-1-carboxylic Acid, with Some Observations on the Ultra-violet Absorption Spectra of These and Related Compounds.

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*trans*-8 : 9-Epoxy-11-ketoheptadecane-1-carboxylic acid ( $\lambda$ -ketoelaidic acid oxide), m. p. 84°, has been prepared by chromic acid oxidation of a mixture of diastereoisomeric ricinelaidic acid oxides, and its properties have been studied. The compound, m. p. 112.5°, resulting from the autoxidation of  $\lambda$ -keto-oleic acid and previously thought to be the corresponding epoxide, has now been identified as *cis*-10 : 11-diketoeptadec-8-ene-1-carboxylic acid ( $\mu$  $\lambda$ -diketo-oleic acid). The absorption spectra of these and certain related compounds have been examined.

It has already been shown (King, *Nature*, 1949, **164**, 706; Swern *et al.*, *Analyt. Chem.*, 1947, **19**, 414) that the absorption of hydrogen chloride from ether or dioxan by simple 1 : 2-epoxides is more or less quantitative. Nothing is known, however, of the effect on this absorption of the presence of a neighbouring carbonyl group or double bond. In the search for suitable keto-epoxides, it was decided to attempt the preparation of the  $\lambda$ -keto-derivatives of oleic acid oxide and elaidic acid oxide, since these might be synthesised from the readily accessible ricinoleic acid and ricinelaidic acid respectively. A study of the properties of these and related substances was particularly desirable in view of their possible occurrence in autoxidation processes (Ellis, *J.*, 1950, 9).

Ricinelaidic acid oxide, m. p. 64°, was prepared by Smit (*Rec. Trav. chim.*, 1930, **49**, 681) by oxidising methyl ricinelaidate with perbenzoic acid and hydrolysing the product. A similar substance, m. p. 64—67°, has now been obtained from ricinelaidic acid by the addition of hypochlorous acid, followed by treatment of the chlorohydrins with dilute alkali. The product is undoubtedly a mixture of diastereoisomeric epoxides (cf. King, *J.*, 1949, 1817), and is optically active.



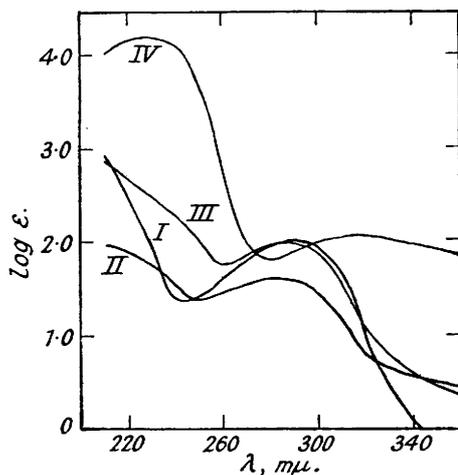
Mild oxidation of the epoxide mixture with chromium trioxide in acetic acid affords ( $\pm$ )-*trans*-8 : 9-epoxy-11-ketoheptadecane-1-carboxylic acid ( $\lambda$ -ketoelaidic acid oxide), m. p. 84° (oxime, m. p. 78°), which was found to absorb only 70% of the theoretical amount of hydrogen chloride from dioxan or ether. So low a result must be attributed to the presence of the carbonyl group, since ricinelaidic acid oxide itself absorbs hydrogen chloride nearly quantitatively under similar conditions to form a mixture of chlorohydrins, m. p. 86—91°. This observation clearly imposes a serious limitation on the accuracy of epoxide determinations based on this principle.

$\lambda$ -Ketoelaidic acid oxide does not absorb ultra-violet light strongly at wave-lengths exceeding 200 m $\mu$ ., but exhibits a weak band in ethanol at 282 m $\mu$ . ( $\epsilon_{\text{max}}$ , 38). Slow distillation of the epoxide with *N*- or 0.1*N*-sodium hydroxide affords a 12% yield of octan-2-one, to be compared with 26—34% of the same ketone given by  $\lambda$ -keto-oleic (or -elaidic) acid under similar conditions (Ellis, *loc. cit.*). In the pyrazoline test (*idem, ibid.*), hitherto regarded as specific for the groups  $\cdot\text{CO}\cdot\text{CH}\cdot\text{CH}\cdot$  and  $\cdot\text{CO}\cdot\text{CH}_2\cdot\text{CH}\cdot\text{CH}\cdot$ , it gives an intense violet colour even in the cold. In common with other ketones containing the  $\cdot\text{CO}\cdot\text{CH}_2\cdot$  group, it develops a purple colour with 3 : 5-dinitrobenzoic acid in aqueous-ethanolic sodium hydroxide, although the test is more sensitive for

$\lambda$ -ketoelaidic acid and still more so for  $\lambda$ -keto-oleic acid, of which 1  $\mu$ g. in 0.1 ml. of ethanol may just be detected.  $\lambda$ -Ketoelaidic acid oxide reduces Fehling's solution slowly on boiling, probably on account of the formation of reducing substances on alkaline hydrolysis, a view which is supported by the fact that the readily hydrolysable  $\lambda$ -keto-oleic and -elaidic acids reduce Fehling's solution rapidly, whereas ricinelaidic acid and its epoxide are without action.

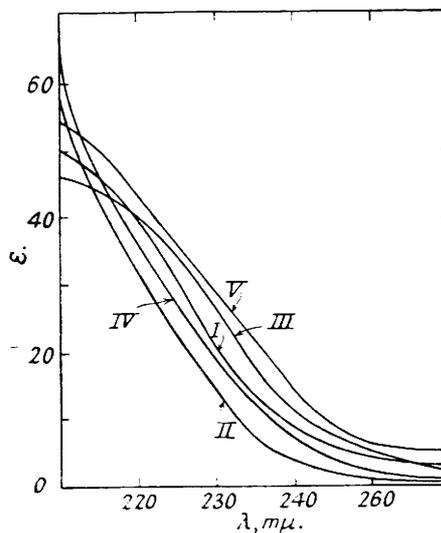
Efforts to prepare the isomeric *cis*-8:9-epoxy-11-ketoheptadecane-1-carboxylic acid ( $\lambda$ -keto-oleic acid oxide) from  $\lambda$ -keto-oleic acid by way of the chlorohydrins or by oxidation with perbenzoic acid have proved unsuccessful. The alternative route from ricinoleic acid by way of its epoxide appears equally unsatisfactory. It was observed by Ellis (*loc. cit.*) that  $\lambda$ -keto-oleic acid readily undergoes autoxidation in air at warm room temperature to yield a peroxide of unknown constitution, together with a considerable proportion of crystalline product, m. p. 112.5°, which was thought to be an epoxyketostearic acid, but whose constitution remained uncertain in view of the fact that it could not be hydrolysed to the corresponding dihydroxyketostearic acid (private communication). Evidence has now been adduced to show that this crystalline product is the unsaturated diketo-acid, *cis*-10:11-diketoheptadec-8-ene-1-carboxylic acid ( $\kappa\lambda$ -diketo-oleic acid), the methylene group in position 10 having undergone autoxidation.

FIG. 1.



- I.  $\lambda$ -Ketoelaidic acid.  
 II.  $\lambda$ -Ketoelaidic acid oxide.  
 III.  $\lambda$ -Keto-oleic acid.  
 IV.  $\kappa\lambda$ -Diketo-oleic acid.

FIG. 2.



- I. Oleic acid oxide.  
 II. Elaidic acid.  
 III. Elaidic acid oxide.  
 IV. Ricinoleic acid.  
 V. Ricinoleic acid oxide.

$\kappa\lambda$ -Diketo-oleic acid has a nearly theoretical iodine value and gives a disemicarbazone and a 2:4-dinitrophenylosazone. It absorbs a small amount of hydrogen chloride from organic solvents, a property which, as will be shown elsewhere, is shared by certain other compounds containing the group  $\cdot\text{CH}:\text{CH}\cdot\text{CO}\cdot$  or  $\cdot\text{CH}:\text{CH}\cdot\text{CH}_2\cdot\text{CO}\cdot$ . The presence of the chromophore  $\cdot\text{CO}\cdot\text{CO}\cdot\text{CH}:\text{CH}\cdot$  is strongly supported by spectroscopic evidence, since the ultra-violet absorption spectrum in ethanol, unlike that of  $\lambda$ -ketoelaidic acid oxide, exhibits an intense absorption band at  $\lambda$  228  $m\mu$ . ( $\epsilon_{\text{max}}$ . 16,000) as well as a weak subsidiary band at  $\lambda$  318  $m\mu$ . ( $\epsilon_{\text{max}}$ . 115). The spectrum thus closely resembles those of crotonaldehyde and diacetylene,  $\text{CH}_3\cdot\text{CO}\cdot\text{CH}:\text{CH}\cdot\text{CO}\cdot\text{CH}_3$  (Bowden *et al.*, *J.*, 1946, 39; Braude, *J.*, 1945, 490), containing conjugated systems involving one or more carbonyl groups.

For the purposes of comparison, the ultra-violet light absorption, in ethanol, of a number of other related compounds has also been investigated. The results (Figs. 1 and 2) are summarised in the following Table. Of the compounds examined, only the keto-acids exhibit well-defined maxima and minima within the wave-band 210—400  $m\mu$ . The remainder absorb ultra-violet light to an insignificant extent at wave-lengths exceeding 250  $m\mu$ ., and, as might be expected, epoxidation of the ethylenic acids appears to reduce the intensity of absorption. The absorption

	$\epsilon_{(210 \text{ m}\mu)}^*$	$\lambda_{\text{max.}} (\text{m}\mu)$	$\epsilon_{\text{max.}}$	$\lambda_{\text{min.}} (\text{m}\mu)$	$\epsilon_{\text{min.}}$
$\lambda$ -Ketoelaidic acid, m. p. 73° .....	925	287	100	244	27
$\lambda$ -Ketoelaidic acid oxide, m. p. 84° .....	97	282	38	250	25
$\lambda$ -Keto-oleic acid, m. p. 40° .....	800	285	93	260	37
$\kappa\lambda$ -Diketo-oleic acid, m. p. 112.5° .....	10,750	228	16,000	280	62
		318	115		
Elaidic acid, m. p. 44.5° .....	58	—	—	—	—
Elaidic acid oxide, m. p. 55.5° .....	46	—	—	—	—
Oleic acid oxide, m. p. 59.5° .....	50	—	—	—	—
Ricinelaic acid, m. p. 52° .....	70	—	—	—	—
Ricinelaic acid oxide, m. p. 64—67° ...	54	—	—	—	—

\* Lowest wave-length recorded.

spectra of oleic and elaidic acid epoxides have already been investigated by Holman *et al.* (*J. Amer. Chem. Soc.*, 1945, 67, 1285), but only down to a wave-length of 240  $\text{m}\mu$ . It is noteworthy that the values here found for the molecular extinction coefficient of elaidic acid, which was very carefully purified, are somewhat lower than those recorded by Rusoff *et al.* (*ibid.*, p. 673).

## EXPERIMENTAL.

*Ricinelaic Acid Oxides* (8 : 9-Epoxy-11-hydroxyheptadecane-1-carboxylic Acids).—Dilute hydrochloric acid was added dropwise, with vigorous shaking, to a solution of ricinelaic acid (30 g.) in 1.3M-sodium hypochlorite (115 ml.) and water (1.5 l.) until the solution was slightly acid. Free chlorine and excess of hypochlorous acid were destroyed by addition of aqueous sodium sulphite, the solution was further acidified with hydrochloric acid, and the sticky mixture of chlorohydrins washed by decantation. The product was dissolved in *n*-sodium hydroxide (300 ml.), and the solution left for several hours and then boiled for a few minutes. Acidification of the cooled solution with dilute sulphuric acid, extraction with ether, and precipitation with 2 vols. of *n*-hexane afforded a mixture of stereoisomeric ricinelaic acid oxides (11.5 g.; m. p. 58—61°), which on further crystallisation from ether-hexane and from ethanol separated as thin, rod-like plates (7.5 g.), m. p. 64—67°,  $[\alpha]_D^{25}$  in ethanol  $-22^\circ$  ( $l = 2$ ,  $c = 1.0$ ) (Found: equiv., 314; C, 68.5; H, 10.6; oxiran-O, 4.9%. Calc. for  $\text{C}_{18}\text{H}_{34}\text{O}_4$ : equiv., 314; C, 68.8; H, 10.9; oxirane-O, 5.1%). Hydrolysis of the epoxides with boiling *n*-sodium hydroxide for 5 hours gave a 30% yield of 8 : 9 : 11-trihydroxyheptadecane-1-carboxylic acid (probably a mixture of two stereoisomers), m. p. 136—137.5°.

*Chlorodihydroxystearic Acids from Ricinelaic Acid Oxides*.—Concentrated hydrochloric acid (10 ml.) was shaken with ricinelaic acid oxides (6.5 g.) in ether (120 ml.) for 1 hour, after which the washed and dried ethereal solution was treated with 2 vols. of *n*-hexane and cooled at 0°. The mixture of 8-chloro-9 : 11-dihydroxy- and 9-chloro-8 : 11-dihydroxy-heptadecane-1-carboxylic acids separated from ether-hexane as needles (2.2 g.), m. p. 86—91° (Found: C, 61.6; H, 10.0; Cl, 9.8%; equiv., 352. Calc. for  $\text{C}_{18}\text{H}_{35}\text{O}_4\text{Cl}$ : C, 61.6; H, 10.1; Cl, 10.1%; equiv., 351), from which the original epoxides were recovered in good yield on treatment with 2*N*-sodium hydroxide at room temperature for 2 hours.

*$\lambda$ -Ketoelaidic Acid Oxide* (trans-8 : 9-Epoxy-11-ketoheptadecane-1-carboxylic Acid).—A solution of chromium trioxide (3 g.) in water (6 ml.) and acetic acid (16 ml.) was added gradually to ricinelaic acid oxides (10 g.) in acetic acid (80 ml.), the temperature being kept below 15°. The solution was then left at room temperature for 1½ hours, diluted and cooled.  *$\lambda$ -Ketoelaidic acid oxide* crystallised from ethanol in rhombic and hexagonal plates (4 g.), m. p. 84° (Found: C, 69.2; H, 10.4; oxiran-O, 3.7%; equiv., 311.  $\text{C}_{18}\text{H}_{35}\text{O}_4$  requires C, 69.2; H, 10.3; oxiran-O, 5.1%; equiv., 312), sparingly soluble in ether at 0° and rather sparingly soluble in warm light petroleum. The *oxime* crystallised from ethanol in long, thin rhombic plates, m. p. 78° (Found: N, 4.4%; equiv., 327.  $\text{C}_{18}\text{H}_{35}\text{O}_4\text{N}$  requires N, 4.3%; equiv., 327).

*$\lambda$ -Ketoelaidic acid oxide* slowly reduced boiling Fehling's solution and developed a purple colour with 3 : 5-dinitrobenzoic acid in aqueous-ethanolic sodium hydroxide. It also gave the pyrazoline test (Ellis, *loc. cit.*) in the cold: thus 0.1 mg., rubbed with a trace of phenylhydrazine on a glass slide and then treated with 1 drop of a 5% (w/v) solution of sodium nitrite in sulphuric acid, gave immediately an intense violet colour which persisted for at least 5 minutes. Under these conditions,  *$\lambda$ -keto-oleic acid* gave no definite purple or violet colour. When slowly distilled with *n*- or 0.1*N*-sodium hydroxide,  *$\lambda$ -ketoelaidic acid oxide* gave a yield of ca. 12% of octan-2-one (2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 61°); the remaining hydrolysis products reduced Fehling's solution, gave a mixture of solid products when treated with 2 : 4-dinitrophenylhydrazine, and contained no epoxide, but were not further identified. The epoxide reacted readily with 2 : 4-dinitrophenylhydrazine to give an oil.

*$\lambda$ -Keto-oleic* (cis-11-Ketoheptadec-8-ene-1-carboxylic Acid).—This acid, prepared from ricinoleic acid substantially as described by Ellis (*loc. cit.*), crystallised from *n*-hexane in long, thin plates, m. p. 40° [Found: C, 72.3; H, 10.8%; equiv., 295; I.V., (Wijs, 1 hour), 131. Calc. for  $\text{C}_{18}\text{H}_{32}\text{O}_3$ : C, 72.9; H, 10.9%; equiv., 296; I.V., 85.6]. 1 ml. of a mixture of 2 vols. of 1% ethanolic 3 : 5-dinitrobenzoic acid and 1 vol. of 10% aqueous sodium hydroxide, added to 0.1 ml. of ethanol containing 0.1 mg. of  *$\lambda$ -keto-oleic acid*, developed a deep purple colour within a few minutes. As little as 1  $\mu\text{g}$ . of the keto-acid could be detected by this means, the test being about 100 times more sensitive for the keto-acid than for octan-2-one.

*$\kappa\lambda$ -Diketo-oleic* (cis-10 : 11-Diketoheptadec-8-ene-1-carboxylic Acid).— *$\lambda$ -Keto-oleic acid* (6 g.), melted and absorbed on filter paper (12 × 50 cm.), was incubated in air at 37° for 5 days. The autoxidised product was extracted with light petroleum (75 ml.; b. p. 40—60°) at room temperature and then with several lots of boiling ethanol (100 ml. in all). The latter, diluted with ¼ vol. of water and cooled at 0°, deposited  *$\kappa\lambda$ -diketo-oleic acid* (1.5 g.), which crystallised from ethanol in nearly colourless hexagonal

plates, m. p. 112.5° (Found : C, 69.5; H, 9.6%; equiv., 308; I.V., 78.3.  $C_{18}H_{30}O_4$  requires C, 69.6; H, 9.7%; equiv., 310; I.V., 81.7). The *disemicarbazone* separated as a canary-yellow microcrystalline powder, m. p. 212° (decomp.), very sparingly soluble in all the usual solvents (Found : C, 56.5; H, 8.4; N, 20.8.  $C_{20}H_{36}O_4N_6$  requires C, 56.6; H, 8.5; N, 19.8%). The 2:4-*dinitrophenylosazone* crystallised from ethanol-chloroform in small bright red rods, m. p. 154° (softening at 140°) (Found : N, 16.6.  $C_{30}H_{38}O_{10}N_8$  requires N, 16.7%), and gave an intense violet colour with ethanolic sodium hydroxide.

Diketo-oleic acid reduced Fehling's solution readily on heating and gave a deep red colour in the dinitrobenzoic acid test. Its solution in aqueous sodium hydroxide had a yellow colour, intensified on boiling, with decomposition of the diketo-acid but without the formation of volatile ketone. In the pyrazoline test in the cold it gave a transient red colour, changing to blue, green, and yellow-brown. Both  $\lambda$ -keto- and  $\mu\lambda$ -diketo-oleic acid absorbed a little hydrogen chloride from organic solvents, giving apparent oxirane-oxygen values of 0.5—0.75%. The diketo-acid in ethanol gave an absorption band of high intensity in the ultra-violet at 228  $m\mu$ . and a subsidiary band at 318  $m\mu$ .

Elaidic acid, crystallised repeatedly from acetic acid and from methanol, had m. p. 44.5° (Found : I.V., 90.0; equiv., 282.5. Calc. for  $C_{18}H_{34}O_2$ : I.V., 89.9; equiv., 282.5). Ricinelaidic acid was prepared by thoroughly stirring a mixture of freshly prepared ricinoleic acid (60 ml.) with concentrated nitric acid (4 ml.) and powdered sodium nitrite (2 g.) and leaving it for 48 hours. The semi-crystalline mass was drained on a Buchner funnel, washed with a little cold light petroleum, and crystallised successively from methanol, *n*-hexane, and again from methanol, giving the pure acid (36 g.), m. p. 52° (Found : equiv., 298.7. Calc. for  $C_{18}H_{34}O_2$ : equiv., 298.5). Oleic acid oxide, m. p. 59.5°, was obtained from dihydroxy-stearic acid, m. p. 132° (King, *J.*, 1942, 390), and elaidic acid oxide, m. p. 55.5°, from elaidic acid by the hypochlorous acid method (King, *J.*, 1949, 1820).  $\lambda$ -Ketoelaidic acid, m. p. 73°, was prepared from ricinelaidic acid (Ellis, *loc. cit.*) (Found : equiv., 295.1. Calc. for  $C_{18}H_{32}O_3$ : equiv., 295.1).

*Ultra-violet Absorption Spectra.*—These were measured in ethanol, a Model S.P.500 Unicam Spectrophotometer being used.

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