304. *The Active Principles of Leguminous Fish-poison Plants. Part III. The Structure of Elliptone.*

By Stanley H. Harper.

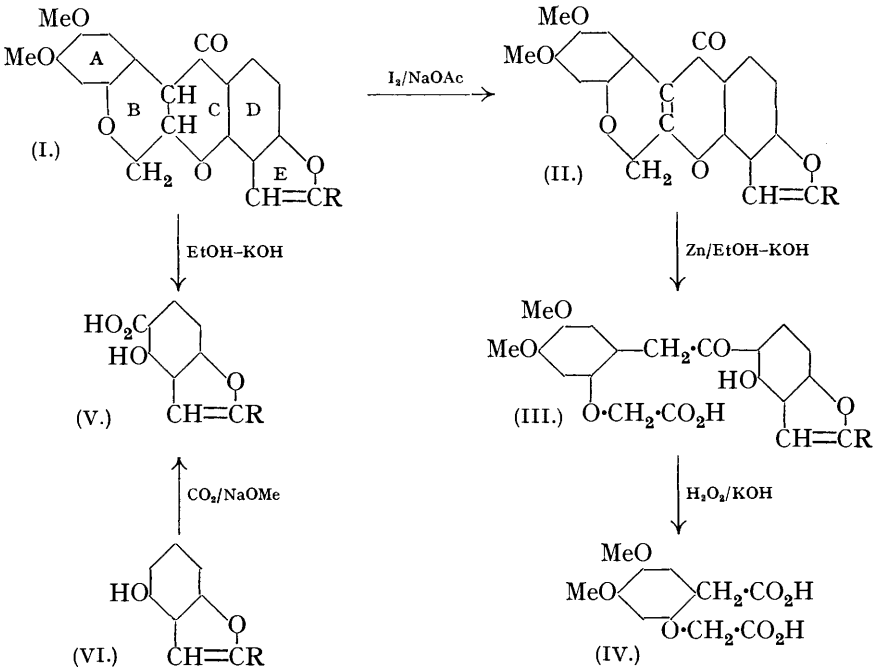
The structure advanced for elliptone (I, R = H) in Part II (this vol., p. 1099) is placed beyond doubt by degradation experiments. Dehydroelliptone with zinc and alkali yields *elliptic acid*, oxidation of which with alkaline hydrogen peroxide gives derric acid (IV). This establishes the identity of rings A, B, and C with those of rotenone and *iso*rotenone. *l*-Elliptone with alcoholic alkali gives *4-hydroxycoumarone-5-carboxylic acid* (V, R=H), whereas *iso*rotenone under the same conditions gives 4-hydroxy-2-*iso*propylcoumarone-5-carboxylic acid (*iso*tubaic acid) (V, R = Pr^{β}). This establishes the nature of rings D and E and hence that of the whole molecule.

In Part II (this vol., p. 1099) the isolation of *l*-elliptone from *Derris elliptica* root was described, and from a study of its reactions and the similarity of these with those of *iso*rotenone (I, R = Pr^{β}), it was assigned the structure (I, R = H). Degradation experiments, now described, have placed this structure beyond doubt.

Dehydrorotenone and *iso*dehydrorotenone (II, R = Pr^{β}) on treatment with zinc and alcoholic alkali (LaForge and Smith, *J. Amer. Chem. Soc.*, 1930, **52**, 1091) or with alcoholic alkali alone (Butenandt, *Annalen*, 1928, **464**, 253; Butenandt and Hildebrandt, *ibid.*, 1930, **477**, 245) add two molecules of water with opening of rings B and C to give derrisic and *iso*derrisic acid (III, R = Pr^{β}) respectively. Oxidation of these with alkaline hydrogen peroxide (LaForge and Smith, *loc. cit.*) gives derric acid (IV) by fission at the keto-group. It has now been found that dehydroelliptone ($C_{20}H_{14}O_6$) similarly adds two molecules of water, on treatment with zinc and alcoholic alkali, to give a monobasic phenolic acid ($C_{20}H_{18}O_8$) for which the name *elliptic acid* is suggested. Diazomethane in benzene–ether gives the *methyl* ester, the phenolic group remaining unattacked and so indicating that it is diortho-substituted. Oxidation of elliptic acid with alkaline hydrogen peroxide gives derric acid (IV) in good yield. It follows that the degradation has taken the same course as with rotenone and *iso*rotenone, and therefore rings A, B, and C of these are identical with those in elliptone.

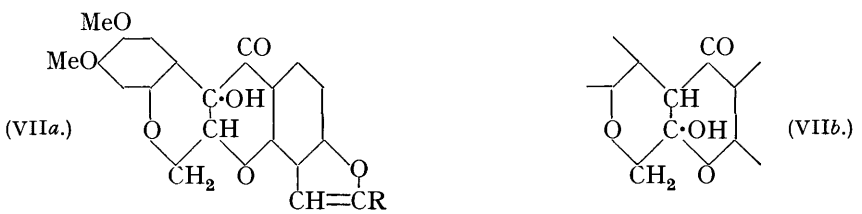
To elucidate the nature of rings D and E the action of alcoholic alkali on *l*-elliptone was studied. Cleavage of *iso*rotenone with alcoholic alkali yields *iso*tubaic acid (V, R = Pr^{β}) (Takei, Koide, and Miyajima, *Ber.*, 1930, **63**, 508; Butenandt and Hildebrandt, *loc. cit.*; Haller and LaForge, *J. Amer. Chem. Soc.*, 1930, **52**, 2480). It is now found that *l*-elliptone is similarly cleaved by alcoholic alkali to give a monobasic phenolic acid,

$C_9H_6O_4$, m. p. 221°, which gives a deep blue colour with ferric chloride and on heating above the melting point loses carbon dioxide to yield a phenol which no longer gives a colour with ferric chloride. Diazomethane in ether methylates only the carboxyl group, indicating



that the phenolic group is diortho-substituted. This acid differs from both tubaic and *iso*tubaic acids. On the basis of formula (I, R = H) for elliptone this acid should be the unknown 4-hydroxycoumarone-5-carboxylic acid (V, R = H). Synthesis of this has therefore been effected by the method used by Reichstein and Hirt (*Helv. Chim. Acta*, **1933**, **16**, 121) for *iso*tubaic acid (V, R = Pr^{β}), 4-hydroxycoumarone (VI, R = H) being carboxylated in the presence of sodium methoxide at 180°. The *4-hydroxycoumarone-5-carboxylic acid* (V, R = H) so obtained is identical with the acid formed by cleavage of *l*-elliptone, further comparison being effected through the *methyl* ester. The identification of this acid establishes the nature of rings D and E and, coupled with the formation of derric acid, places beyond doubt the structure of elliptone as being (I, R = H). It follows also that dehydroelliptone is represented by (II, R = H) and elliptic acid by (III, R = H).

It has been necessary for this work to prepare dehydroelliptone in a larger quantity than previously. After the dehydroelliptone has been separated, the mother-liquor deposits a second substance, crystallising from alcohol in colourless plates, m. p. 176°. By analogy



with rotenone and *iso*rotenone this should be the *acetate* of *elliptolone* (VII*a* or *b*), and this supposition was confirmed because alkaline hydrolysis afforded an alcohol, which on dehydration with alcoholic sulphuric acid gives dehydroelliptone. Also, the acetate, on being refluxed with alcoholic sulphuric acid, gives dehydroelliptone quantitatively, and when

heated above its m. p. it loses acetic acid to give dehydroelliptone, which solidifies and then remelts at 264°. This explains the observations of Buckley (*J. Soc. Chem. Ind.*, 1936, **55**, 285T) and of Meyer and Koolhaas (*Rec. Trav. chim.*, 1939, **58**, 207), who, in preparing the dehydro-compound, obtained from the mother-liquor a second crop which showed a double melting point, 178—264° and 176—252°, and was apparently regarded by them as a dimorphic form of the dehydro-compound.

It was shown in Part II (*loc. cit.*) that *l*- and *dl*-elliptone give α- and β-oximes depending on whether the preparation is carried out in alcohol (α) or in pyridine (β); neither of these oximes is of the *iso*oxime type described by Butenandt (*loc. cit.*). This observation has been extended to rotenone, which gives a similar pair of oximes: α-, m. p. 237°, and β-, m. p. 249°. The fact that previous workers had obtained both the β-form (Kariyone and Atsumi, *J. Pharm. Soc. Japan*, 1923, 10, m. p. 245°; Butenandt, *loc. cit.*, m. p. 249°; Wright, *J. Amer. Chem. Soc.*, 1928, **50**, 3355, m. p. 252°) and the α-form (Takei, *Ber.*, 1928, **61**, 1004, m. p. 239°) in sodium acetate–alcohol suggested that this isomerism was in reality dimorphism. This has been shown to be the case by seeding a saturated solution of rotenone α-oxime with the β-form, whereupon separation occurs entirely in this form. The author's preparations have always led to the α-form from alcohol and the β-form from pyridine. It followed that the isomerism recorded for *l*- and *dl*-elliptone oximes was probably due to dimorphism. This has been proved, for on being seeded with the β-form, the α-changes completely to the β-form, showing that the higher-melting oxime is the more stable.

Experimental.

Microanalyses are by Drs. Weiler and Strauss, Oxford. Methoxyl determinations are by the author, using Clark's semimicro-method (*J. Assoc. Off. Agric. Chem.*, 1932, **15**, 136). M. p.'s are uncorrected.

O-*Acetylelliptolone.*—*l*-Elliptone (6 g.) in boiling ethyl alcohol was oxidised with iodine as described previously (this vol., p. 1103). After cooling to room temperature the dehydroelliptone (3·3 g.) that had separated was filtered off. The filtrate was kept in a refrigerator overnight, a crop of colourless plates (1·1 g.) separating. A further crop (0·3 g.) was obtained on concentrating the mother-liquor and removing the sodium acetate that separated. The bulked crops were crystallised from ethyl alcohol to give O-*acetylelliptolone*, m. p. 175·5° [Found: C, 64·1; H, 4·5; OMe, 15·9; CH_3·CO, 8·9. $C_{20}H_{15}O_7(CO{\cdot}CH_3)$ requires C, 64·35; H, 4·4; OMe, 15·1; CH_3·CO, 10·5%]. When heated above its m. p., it evolved acetic acid to give dehydroelliptone, which crystallised and then remelted at 264°. Refluxing in 5% alcoholic sulphuric acid for 8 hours gave a quantitative yield of dehydroelliptone.

Elliptolone.—The acetyl derivative (250 mg.) was refluxed with 0·5N-alcoholic potassium hydroxide (20 c.c.) for 2 hours. The diluted solution was acidified, the precipitate taken up in ether, and the extract washed with 2% potassium hydroxide and water, dried, and evaporated. The *elliptolone* (130 mg.) crystallised from a small volume of ethyl alcohol in dense colourless prisms, m. p. 228° (Found: C, 65·3; H, 4·55; OMe, 16·9. $C_{20}H_{16}O_7$ requires C, 65·2; H, 4·4; OMe, 16·9%). Refluxing in 5% alcoholic sulphuric acid for 8 hours gave a 77% yield of dehydroelliptone.

Elliptic Acid.—Dehydroelliptone (2 g.), zinc dust (8 g.), and 15% potassium hydroxide solution (20 c.c.) in ethyl alcohol (60 c.c.) were refluxed for 2 hours. The filtered liquid was acidified (hydrochloric acid) and diluted till crystallisation commenced, *elliptic acid* (1·68 g.) separating as colourless hair-like needles. It could be recrystallised from dilute ethyl alcohol, m. p. 190°, and gave a blue-green colour with ferric chloride (Found: C, 62·1; H, 5·0; OMe, 16·35. $C_{20}H_{18}O_8$ requires C, 62·2; H, 4·7; OMe, 16·1%). The acid in benzene–ether was treated with excess of diazomethane and kept at 0° for 24 hours; after evaporation of solvent, the residue was crystallised from ethyl alcohol, yielding *methyl elliptate* as long needles, m. p. 143°, which gave a blue-green colour with ferric chloride (Found: OMe, 23·35. $C_{21}H_{20}O_8$ requires OMe, 23·25%).

Degradation to derric acid. 20-Vol. hydrogen peroxide (10 c.c.) was added slowly to elliptic acid (2 g.) in 5% potassium hydroxide solution (25 c.c.) at 60°, considerable charring occurring; the solution was heated to boiling, to decompose any excess hydrogen peroxide, cooled, and acidified. The carbonaceous precipitate was removed, and the filtrate extracted continuously with ether for 48 hours [derric acid was found to be very soluble in water, and the low yield from

derrisic acid reported by LaForge and Smith (*loc. cit.*) was probably due to incomplete extraction]. The dried ethereal extract was evaporated, and the residue, which solidified, was triturated with small portions of ether to remove coloured impurities, giving nearly pure derric acid (760 mg., 55% of the theoretical). Purification was effected by crystallisation from ethyl acetate–*cyclo*hexane (2 : 1), from which the acid separated in narrow plates, m. p. 167° (Found : OMe, 23·0. Calc. for $C_{12}H_{14}O_7$: OMe, 23·0%). Diazomethane in ether gave dimethyl derrate, which, crystallised from low-boiling petrol, had m. p. 66° (Found : OMe, 41·55. Calc. for $C_{14}H_{18}O_7$: OMe, 41·6%). An authentic specimen of derric acid was prepared by oxidation of derrisic acid (from dehydrorotenone) as described above. This and the dimethyl ester prepared from it were identical with those obtained from elliptic acid, and mixtures of the acids and of the esters respectively showed no depression of m. p.

Degradation to 4-*hydroxycoumarone*-5-*carboxylic acid*. *l*-Elliptone (5 g.) in 5% alcoholic potassium hydroxide (50 c.c.) was refluxed for 2 hours. The deep red solution was diluted, and extracted with ether several times. The aqueous layer was acidified, and the precipitated acids and phenols taken up in ether. This solution was extracted with 25-c.c. portions of 5% sodium carbonate solution. As only the first gave a green precipitate on acidification, the remaining extracts were discarded. The dried precipitate was treated with a small volume of ether and decanted from tar, and petrol (b. p. 80—100°) added to the clear solution. The ether was evaporated slowly, and the petrol solution put aside to crystallise A crop of white nodules separated which were removed by hand from accompanying amorphous precipitate. This acid (120 mg.) was purified by two sublimations in high vacuum at 150° to afford 4-*hydroxycoumarone*-5-*carboxylic acid* as colourless plates, m. p. 221°, giving a deep blue colour with ferric chloride (Found : C, 60·6; H, 3·55. $C_9H_6O_4$ requires C, 60·65; H, 3·4%). When heated above its m. p., this acid lost carbon dioxide, yielding 4-hydroxycoumarone, which did not give a colour with ferric chloride. The acid (50 mg.) in ether was treated with diazomethane till decoloration no longer occurred. After evaporation, the residue was crystallised from aqueous methyl alcohol; the resulting *methyl* ester (48 mg.), m. p. 105° (Found : OMe, 16·15. $C_{10}H_8O_4$ requires OMe, 16·15%), gave a deep blue colour with ferric chloride.

Synthesis of 4-*Hydroxycoumarone*-5-*carboxylic Acid*.—4-Hydroxycoumarone (830 mg.) (Reichstein and Hirt, *loc. cit.*) was added to sodium (200 mg.) dissolved in methyl alcohol (2 c.c.) in a small distilling-flask. The mixture was heated at 180° for 2 hours in a stream of dry carbon dioxide, methyl alcohol collecting in the receiver. The residue in the flask was dissolved in water and acidified, and the precipitate taken up in ether. 5% Sodium carbonate solution extracted the acid; it separated on acidification, and was filtered off, washed, and dried (590 mg.). After being twice sublimed in a high vacuum at 150°, the acid, m. p. 221° (Found : C, 61·1; H, 3·8%), was identical (mixed m. p.) with that obtained from elliptone (above), and its methyl ester, m. p. and mixed m. p. 105° (Found : OMe, 16·2%), was identical with the foregoing ester. The ester was recovered unchanged after being kept in ether with a large excess of diazomethane for a week at room temperature.

Rotenone α-*Oxime*.—Rotenone (5 g.), hydroxylamine hydrochloride (5 g.), and sodium acetate (6 g.) in ethyl alcohol (200 c.c.) were refluxed for 8 hours. Water was then added till crystallisation commenced. The oxime (4·02 g.) so obtained was crystallised to constant m. p. 237° from alcohol.

Rotenone β-*Oxime*.—Rotenone (5 g.), hydroxylamine hydrochloride (5 g.), and sodium carbonate (4 g.) in pyridine (100 c.c.) were refluxed for 3 hours, and the oxime (4·83 g.) obtained as above was crystallised from alcohol to constant m. p.; needles, m. p. 249°.

A hot saturated alcoholic solution of the α-oxime, on being seeded with the β-form, deposited pure β-oxime; but a similar solution of the β-oxime on seeding with the α-form deposited only the β-oxime. A hot solution of *l*-elliptone α-oxime in methyl alcohol deposited the β-oxime after seeding with that form.

I am indebted to the Ministry of Agriculture and the Colonial Development Fund for grants.

Rothamsted Experimental Station, Harpenden, Herts. [*Received, July 31st,* 1939.]