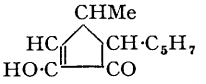
19. *The Structure of Pyrethrolone and Related Compounds. Part I.*

By T. F. West.

The preparation of the enolic forms of pyrethrolone has been investigated, and light absorption data are recorded for *iso*pyrethrolone enol which indicate that the formula suggested by Haller and LaForge (*J. Org. Chem.*, 1938, **3**, 543) is incorrect. The data for samples of tetrahydro*iso*pyrethrolone enol prepared from the *iso*enol or directly from tetrahydropyrethrolone show that tautomeric changes can take place in alcoholic solution. This observation is of special interest in view of the double-bond shifts tentatively postulated (Gillam and West, J., 1942, 671) to explain the preparation of dihydrojasmone from the pyrethrins themselves or tetrahydropyrethrolone.

Staudinger and Ruzicka (*Helv. Chim. Acta*, 1924, **7**, 212) observed that when pyrethrolone was boiled in a dilute solution of sodium methoxide it was converted into two enols which could be separated readily by distillation. Both compounds were shown to possess the empirical formula $C_{11}H_{14}O_2$, the lower-boiling one being regarded as a dehydropyrethrolone of suggested structure (I), and the other being assumed to be a polymer of this.

The description dehydropyrethrolone was based on the incorrect emprical formula $C_{11}H_{16}O_2$ for pyrethrolone. LaForge and Haller (*J. Amer. Chem. Soc.*, 1936, **58**, 1061) subsequently showed that its correct formula was $C_{11}H_{14}O_2$, so dehydropyrethrolone was not an oxidation product but was formed by rearrangement of pyrethrolone.



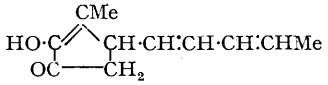
Pyrethrolone enol (I.)

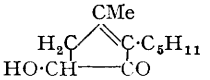
*iso*Pyrethrolone enol (II.)

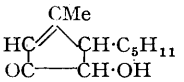
On the basis of the examination of hydrogenation products, Haller and LaForge (*J. Org. Chem.*, 1938, **3**, 543) assigned structure (II) to the higher-boiling compound, and used the names pyrethrolone enol for (I) and *iso*pyrethrolone enol for (II). By the hydrogenation of (II) these workers obtained tetrahydro*iso*pyrethrolone enol, which, from the observed analytical constants, appeared to be identical with the enol prepared directly from tetrahydropyrethrolone by treatment with dilute alcoholic potassium hydroxide.

Although the light-absorption data for pyrethrolone enol (Gillam and West, preceding paper) are in agreement with the formula (I), that suggested by LaForge and Haller for *iso*pyrethrolone enol (II), which shows maximum absorption at 2400 A., is clearly incorrect because the system O:C·C:C·C:C·C:C is involved if the side chain CH:CH·CH:CHMe be accepted for the *iso*enol. This would obviously be expected to absorb at considerably longer wave-lengths.

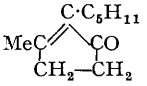
The light-absorption data thus preclude the presence of a double bond, certainly between C atoms 2 and 3 and almost as certainly between 4 and 3 in the *cyclo*pentenolone ring of the molecule of *iso*pyrethrolone enol, and to accord with the chemical evidence adduced by Haller and LaForge (*J. Org. Chem.*, 1938, **3**, 543) it appears to be necessary to assign a tentative structure (III) to this compound.

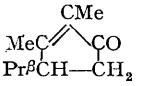

(III.)


(IV.)

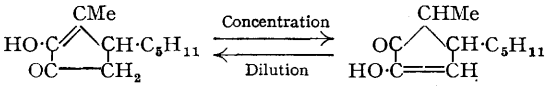

(V.)

For tetrahydropyrethrolone, LaForge and his collaborators have suggested formula (IV), whereas Gillam and West tentatively suggested (V). The latter formulation appears to be supported by the light-absorption data; *e.g.*, the closely analogous trisubstituted αβ-unsaturated ketones dihydrojasmone (VI) and *iso*thujone (VII) exhibit $\lambda_{max.}$ at 2370 and 2375 A. respectively, whilst tetrahydropyrethrolone has its $\lambda_{max.}$ at 2320 A. This would suggest a di- rather than a tri-substituted αβ-unsaturated ketone, hence (V) rather than (IV). In the case of tetrahydro*iso*pyrethrolone enol, accurate deduction is complicated by the presence of the hydroxyl

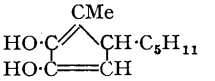
(VI.) 

 (VII.)

group on the chromophore. However, it is an interesting observational fact that in slightly weaker solutions (order 0·005%) some tetrahydro*iso*pyrethrolone enol preparations have their absorption maxima displaced to

Trisubstituted (VIII.)  Disubstituted (IX.)

longer wave-lengths (2610 A.) (see Experimental). This may be due to a reversible equilibrium between the di- and the tri-substituted form, (VIII) and (IX), or may even be due to changes of the type (VIII) ⇄ (X) ⇄ (IX). This phenomenon was not observable with solutions of the acetate of tetrahydro*iso*pyrethrolone enol or of the enols themselves, presumably because of the masking effect of the absorption due to the conjugated dienoid system present in the side chain in the latter case.


(X.)

In this connection, however, it may be significant that the analytical data obtained for various samples of *iso*pyrethrolone enol showed considerable variation and were never closely in accord with a formula $C_{11}H_{14}O_2$ in spite of vigorous purification and many experiments. Separation of the enols, by taking advantage of the fact that pyrethrolone enol does not form an acetate under the conditions employed for the acetylation of *iso*pyrethrolone enol and regeneration of the *iso*pyrethrolone enol from the acetate, gave no better result. Haller and LaForge (*J. Org. Chem.*, 1938, **3**, 543) did not record analytical data for their sample of *iso*pyrethrolone enol but stated that " the fraction boiling from 155—160° (0·7 mm.) (*iso*pyrethrolone enol) has been analysed by Staudinger and Ruzicka and found to correspond to the formula $C_{11}H_{14}O_2$." The variation in the carbon and hydrogen content was reflected in the wide differences in the intensity of light absorption displayed by different samples of the *iso*pyrethrolone enol (cf. Experimental; lowest $\varepsilon = 15{,}000$, highest 27,000). However, no evidence for the presence of the trienone system was obtained in any of the samples examined, since, although the ε values showed considerable variation, $\lambda_{max.}$ was unchanged at 2400 A. within experimental error.

Experimental.

(Analyses are by Drs. Weiler and Strauss, Oxford.)

Pyrethrolone.—A mixture of the semicarbazones of pyrethrins I and II (20 g.), dissolved in methyl alcohol (109 ml.), was mixed with 0·5N-sodium methoxide (132 ml.) and water (6·6 ml.) (Haller and LaForge *J. Org. Chem.*, 1936, **1**, 38). After standing for a week at 0°, the crude pyrethrolone semicarbazone obtained as described by Haller and LaForge was recrystallised from methyl alcohol; 1·7 g. of insoluble material were rejected, and the pyrethrolone semicarbazone obtained (9 g.) had m. p. 208°. The pyrethrolone (6·2 g.) regenerated from the semicarbazone (15 g.) so prepared in the presence of cold potassium hydrogen sulphate solution and ether in an atmosphere of carbon dioxide (*idem, J. Amer. Chem. Soc.*, 1937, **59**, 1678) had b. p. 164—166°/2 mm., n_D 1·5420.

iso*Pyrethrolone Enol and its Acetate.*—Maximum yields of *iso*pyrethrolone enol were obtained as described in the preceding paper (but by using 90% w/w aqueous methyl alcohol instead of 90% w/v), the pyrethrolone (6·2 g.), having b. p. 164—166°/2 mm., $n_D^{20°}$ 1·5420; only 0·1 g. of unchanged pyrethrolone was recovered. The crude product (5·8 g.), a viscous reddish oil, was distilled and suitable fractions redistilled to give *iso*pyrethrolone enol (1·2 g.), b. p. 165°/1 mm., $n_D^{21°}$ 1·5445, showing maximum absorption at 2400 A. ($\varepsilon = 27{,}600$) (Found: C, 72·0; H, 8·0. Calc. for $C_{11}H_{14}O_2$: C, 74·15; H, 7·9%). Small variations in method reduced the proportion of *iso*pyrethrolone enol obtained; *e.g.*, use of 90% w/v alcohol gave the same weight of crude enol but only 0·47 g. of purified enol.

A solution of *iso*pyrethrolone enol (0·4 g.) in acetic anhydride (1·6 g.) was heated on the water-bath, and the acetate

purified substantially as described by Haller and LaForge (*J. Org. Chem.*, 1938, **3**, 543). The *iso*pyrethrolone enol acetate (0·25 g.) had b. p. 143°/1·5 mm., $n_D^{21°}$ 1·5010, $\lambda_{max.}$ 2310 A., $\varepsilon = 19{,}300$ (Found: C, 70·5; H, 7·9. Calc. for $C_{13}H_{16}O_3$: C, 70·9; H, 7·3%). When a solution of pyrethrolone enol (0·35 g.) in acetic anhydride (1·4 g.) was treated in the same manner, only unchanged pyrethrolone enol (0·28 g.) was recovered; the enol before treatment had b. p. 105—106°/1 mm., $n_D^{21°}$ 1·5132, $\lambda_{max.}$ 2435 A., $\varepsilon = 15{,}000$ (Found: C, 74·2; H, 7·8%), the recovered oil having b. p. 104°/1·5 mm., $n_D^{22°}$ 1·5110, $\lambda_{max.}$ 2440 A., $\varepsilon = 16{,}800$ (Found: C, 73·5; H, 7·8%).

The data for the samples of *iso*pyrethrolone enol and its acetate obtained by similar methods are given below.

Sample No.	Name.	B. p./1 mm.	n_D.	Found. C, %.	Found. H, %.	$\lambda_{max.}$, A.	$\varepsilon_{max.}$
40/3	*iso*Enol	167—168°	1·5395 (23°)	72·45	8·1	2420	16,500
81/3	*iso*Enol	160—166	1·5428 (25°)	73·0	8·1	2400	18,900
2/4	*iso*Enol	165	1·5445 (21°)	—	—	2390	26,500
3/4	Acetate	140	1·5007 (20°)	70·9	7·3	2300	18,300

On the basis of these experiments the *iso*pyrethrolone enol fraction obtained by one fractional distillation from the mixture of enols was purified by taking advantage of this difference in reactivity towards acetic anhydride of pyrethrolone enol and the *iso*enol. The crude *iso*pyrethrolone enol (1·6 g.) was heated with acetic anhydride (6·4 g.) on the steam-bath for 4 hours, the excess anhydride distilled off under reduced pressure, and the acetylated product poured into water and extracted with ether. The ethereal solution was washed successively with 5% sodium hydrogen carbonate solution and brine, and the oil obtained by removing the solvent was twice distilled to give *iso*pyrethrolone enol acetate (0·87 g.), b. p. 122—124°/0·5 mm., $n_D^{20°}$ 1·5017, $\lambda_{max.}$ 2310 A. ($\varepsilon = 14.300$) (Found: C, 70·9; H, 8·1%). This acetate (0·8 g.) was heated under reflux (water-bath) with a solution of sodium (0·13 g.) in methyl alcohol (12 ml.) for 1 hour Water (11 ml.) was added, the methyl alcohol distilled off under reduced pressure, and this aqueous alkaline solution thoroughly extracted with ether. The alkaline solution was then acidified in the presence of ether by 5 ml. of 10% sulphuric acid. The *iso*-pyrethrolone enol (0·6 g.) recovered from the ether had b. p. 162°/1·5 mm., $n_D^{22°}$ 1·5438, $\lambda_{max.}$ 2395 A., $\varepsilon = 16{,}500$ (Found: C, 72·4; H, 8·45%).

*Tetrahydro*iso*pyrethrolone Enol.*—(a) *From* iso*pyrethrolone enol.* 250 Mg. of *iso*pyrethrolone enol were hydrogenated in ethyl acetate solution by means of a reduced platinum oxide catalyst, and worked up as described by Haller and LaForge (*J. Org. Chem.*, 1938, **3**, 543); the tetrahydro*iso*pyrethrolone enol (60 mg.) had b. p. 145°/0·5 mm., $n_D^{18°}$ 1·5080, $\lambda_{max.}$ 2460 A. ($\varepsilon = 11{,}300$) in 0·025% solution and 2545 A. ($\varepsilon = 10{,}800$) in 0·005% solution (same solvent) (Found: C, 73·7; H, 10·4. Calc. for $C_{11}H_{18}O_2$: C, 72·5; H, 9·9%). A second sample prepared as above had b. p. 155—156°/1 mm., $n_D^{20°}$ 1·5127, $\lambda_{max.}$ 2430 A. ($\varepsilon = 17{,}000$) at a concentration of 0·017% in ethyl alcohol, which was changed to 2615 A. ($\varepsilon = 17{,}000$) at 0·0003% (Found: C, 74·4; H, 10·2%). A third sample showed maximum at 2435 A. ($\varepsilon = 20{,}600$) at a concentration of 0·005% in alcohol.

(b) *From tetrahydropyrethrolone.* Tetrahydropyrethrolone (2·3 g.), b. p. 137—138°/1·5 mm., $n_D^{20°}$ 1·4898, showing maximum absorption at 2320 A. ($\varepsilon = 12{,}400$), was dissolved in alcohol (95% v/v; 575 ml.), zinc dust (3·45 g.) added, and potassium hydroxide (10% solution, 17·5 ml.) added dropwise over 30 minutes to the well-stirred boiling mixture; by following Haller and LaForge's procedure (*loc. cit.*), 0·9 g. of unreacted tetrahydropyrethrolone was recovered. The experiment was repeated with recovered ketone three times, and the alkaline solutions of the enol bulked. By acidification 1·9 g. of crude tetrahydro*iso*pyrethrolone enol were obtained. A sample purified by rigorous fractional distillation had b. p. 155°/1 mm., $n_D^{20°}$ 1·5049, and showed maximum absorption at 2435 A. ($\varepsilon = 16{,}400$) in 0·01% solution, but in 0·0005% solution $\lambda_{max.}$ was displaced to 2560 A. (Found: C, 72·3; H, 10·4%).

A second sample of tetrahydro*iso*pyrethrolone enol prepared from tetrahydropyrethrolone had b. p. 150—152°/0·5 mm., $n_D^{20°}$ 1·5069, $\lambda_{max.}$ 2470 A. ($\varepsilon = 15{,}200$) in 0·00064% solution (alcohol) and 2435 A. ($\varepsilon = 18{,}300$) in 0·0013% solution.

*Tetrahydro*iso*pyrethrolone Enol Acetate.*—The enol (0·4 g.), dissolved in acetic anhydride (1·6 g.), was heated on the water-bath for 4 hours, and the product worked up as described by Haller and LaForge (*loc. cit.*). The acetate obtained (0·18 g.) had b. p. 116°/1 mm., $n_D^{20°}$ 1·4801, $\lambda_{max.}$ 2363 A., $\varepsilon = 17{,}400$ (Found: C, 70·3; H, 8·8. Calc. for $C_{13}H_{20}O_3$: C, 69·6; H, 8·9%). A second sample had b. p. 120—121°/1·5 mm., $n_D^{20°}$ 1·4740, $\lambda_{max.}$ 2365 A., $\varepsilon = 12{,}300$ (Found: C. 69·5; H, 8·9%), and a third sample b. p. 116°/1 mm., $n_D^{23°}$ 1·4777, $\lambda_{max.}$ 2365 A., $\varepsilon = 20{,}200$.

Diosphenol Acetate.—Diosphenol (10 g.), acetic anhydride (30 g.), and sodium acetate (1 g.) were heated under reflux for 1 hour, the product poured into water, and the precipitated oil washed repeatedly with hot water and dilute sodium bicarbonate solution (cf. Semmler and McKenzie, *Ber.*, 1906, **39**, 1167; Auwers, *Ber.*, 1924, **57**, 1106). The acetate purified by distillation (9·7 g.) had b. p. 109°/2 mm., $n_D^{21°}$ 1·4833, $d_{15°}^{15°}$ 1·037, $\lambda_{max.}$ 2400 A., $\varepsilon = 12{,}400$ (Found: C, 68·3; H, 8·5. Calc. for $C_{12}H_{18}O_3$: C, 68·6; H, 8·6%).

Determinations of absorption spectra were made in ethyl-alcoholic solution on a Hilger E_3 quartz spectrograph in conjunction with a Spekker photometer.

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