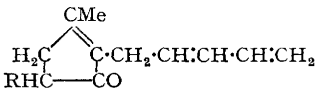
103. *The Structure of Pyrethrolone and Related Compounds. Part IV.*

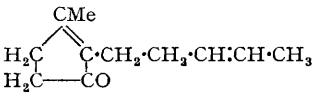
By T. F. West.

On treatment in ethereal solution with aluminium amalgam, pyrethrolone is converted into pyrethrone or dihydropyrethrone as main product according to the conditions. Under suitable conditions *d*- and *i*-pyrethrolone methyl ether are demethylated to give pyrethrone. This ketone contains the same chromophoric system as the parent pyrethrolone. Dihydropyrethrone and dihydrojasmone contain similar αβ-unsaturated ketonic groupings. Evidence is presented to cause rejection of the formulations (III) and (IV) previously advanced for pyrethrolone, and the anomalous reactions and light-absorption data (Gillam and West, J., 1942, 671; 1944, 49; West, J., 1944, 51, 239, 642) can be explained by accepting LaForge and Barthel's view (*J. Org. Chem.*, 1944, **9**, 242, in press) that pyrethrolone is heterogeneous.

Attempts to prepare pyrethrone (LaForge and Haller, *J. Org. Chem.*, 1938, **2**, 546) gave unsatisfactory results, and experiments were made using specially purified ether, to which controlled amounts of water and methyl alcohol were added, and various reaction periods. The reaction mixture afforded according to the conditions employed either dihydropyrethrone (semicarbazone, m. p. 203—205°) or pyrethrone (semicarbazone, m. p. 216—218°). Contrary to the conclusion of LaForge and Barthel (*J. Org. Chem.*, 1944, **9**, 242), the light-absorption data (for the ketones themselves and their semicarbazones) showed that pyrethrolone and pyrethrone contain similar light-absorbing systems (Gillam and West, J., 1942, 671; 1944, 49), and hence, if it be accepted that pyrethrolone consists mainly of the compound (I, R = OH), the main constituent of pyrethrone must be formulated as (I, R = H) and the data are in accord with formulation (II) for dihydropyrethrone.

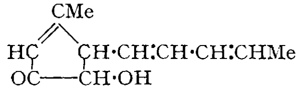
(I.)

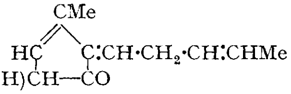


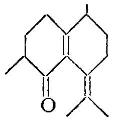


(II.)

Under suitable conditions both the *i*- and the *d*-form of pyrethrolone methyl ether were demethylated (cf. Birch, J., 1944, 430) to form pyrethrone. The terminal methyl values (Barthel and LaForge, *Ind. Eng. Chem. Anal.*, 1944, **16**, 434) have been recorded for the various compounds examined but the results are difficult to interpret; for instance, pyrethrone regenerated from its semicarbazone gave terminal methyl equivalent to 1·25 mols. of acetic acid per mol. of compound, the corresponding value for dihydropyrethrone, dihydrojasmone, and tetrahydropyrethrolone being 1·74, 1·94, and 1·76 mols., respectively. Evidence in support of the criticism (LaForge and Barthel, *loc. cit.*) of formulation (III) for pyrethrolone (Gillam and West, *loc. cit.*) has now been obtained by the isolation of the semicarbazone of hexahydropyrethrone directly from the hydrogenation products of the semicarbazone of tetrahydropyrethrolone acetate when the possibility of interchange of the >CO and the >CH(OH) group is precluded. More recently structure (IV) (West, J., 1944, 239) was advanced


(III.)


(IV.)


(V

for pyrethrolone in an attempt to overcome some of the difficulties inherent in the formulæ advanced previously. Dr. F. B. LaForge (private communication) has now directed attention to the existence of the compound (V) which contains a similar chromophoric system and displays maximum light absorption at 2650 A. with log $\varepsilon = 4{\cdot}25$ (in alcohol) (Plattner and Magyer, *Helv. Chim. Acta*, 1941, **24**, 191). It is clear that a number of the difficulties raised by the formulations suggested for pyrethrolone (Gillam and West, *loc. cit.*; West, *loc. cit.*; LaForge and Acree, *J. Org. Chem.*, 1942, **7**, 418) can be explained now that it has been ascertained that pyrethrolone is a mixture of αβ-unsaturated *cyclo*pentenolone derivatives differing with respect to the nature of the side chain (LaForge and Barthel, *loc. cit.*) and (IV) need no longer be considered.

EXPERIMENTAL.

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

Treatment of Pyrethrolone with Aluminium Amalgam.—(*a*) Pyrethrolone (15 g.), b. p. 134—138°/1·1 mm., $n_D^{20°}$ 1·5350, in ether dried by distillation over sodium (900 ml.) was poured on freshly prepared aluminium amalgam (45 g.), and the mixture kept for 15 hours at room temperature in a dry atmosphere (cf. LaForge and Haller, *J. Org. Chem.*, 1938, **2**, 546). The oil recovered from the ether was distilled, giving two fractions, each of which was identified as unchanged pyrethrolone.

(*b*) Pyrethrolone (6 g.), b. p. 137—138°/1·1 mm., $n_D^{20°}$ 1·5430, dissolved in dry ether (360 ml.), was added to aluminium amalgam (18 g.). After 6 hours, water (3 ml.) was added with shaking, followed after 12 hours by a further addition of 3 ml. of water. In this experiment the ethereal solution was kept in contact with the amalgam for 42 hours and in all 21 ml. of water were added in small quantities at intervals. The oil (5·7 g.) obtained on removal of the ether was steam-distilled, and the steam-volatile oil, $n_D^{20°}$ 1·5116 (0·72 g.), obtained with light petroleum gave a semicarbazone, m. p. 190—194°, raised by two recrystallisations from methyl alcohol to 201—203°; mixed m. p. with dihydropyrethrone semicarbazone [m. p. 203—205° (decomp.); prepared from pyrethrone] 202—204°. The semicarbazone (0·1 g.), dissolved in methyl alcohol (60 ml.), was hydrogenated in the presence of a reduced platinum oxide catalyst; 10·1 ml. of hydrogen at N.T.P. were absorbed in 5 mins. (no further absorption after 20 mins.) ($C_{12}H_{19}ON_3|^{=}$ requires 10·1 ml.). The reduced solution gave on concentration a semicarbazone (70 mg.), m. p. 171—174°, raised by one recrystallisation from benzene to 174—175°, not depressed on admixture with dihydrojasmone semicarbazone (m. p. 175—176°).

(*c*) Pyrethrolone (4 g.), b. p. 139—141°/1·2 mm., $n_D^{20°}$ 1·5379, in ether containing water (1·3% v/v) and methyl alcohol (1·5% v/v) (240 ml.) was poured on aluminium amalgam (12 g.), and after reaction had proceeded during 15 hours, the ethereal solution was treated essentially as described under (*b*). The oil recovered from the ethereal solution was distilled, giving a product (1·7 g.), b. p. 80—123°/0·7 mm., $n_D^{20°}$ 1·5204; no second fraction was obtained, the residue (2 g.) being resinous. This oil (1·5 g.), treated as described by LaForge and Haller (*loc. cit.*), gave a semicarbazone (1·6 g.), m. p. 201—204°, giving pyrethrone semicarbazone (0·65 g.), m. p. 217—219° (decomp.), after two recrystallisations from ethyl alcohol.

(*d*) Pyrethrolone (10 g.), b. p. 140—144°/1·3 mm., $n_D^{20°}$ 1·5402, $[\alpha]_D^{20°}$ 9·9° (*c*, 11·35 in alcohol), λ max. 2285 A., $\varepsilon = 22{,}500$ [Found: C, 73·8; H, 8·3; $CH_3(C)$, 13·1. Calc. for $C_{11}H_{14}O_2$: C, 74·15; H, 7·9%], in ether containing water (1·3%) and methyl alcohol (1·5%) (600 ml.) was treated with aluminium amalgam (30 g.) during 15 hours and worked up, giving a fraction (6·1 g.), b. p. 80—135°/0·7 mm., $n_D^{20°}$ 1·5246 [Found: C, 75·4; H, 9·1; $CH_3(C)$, 13·2%], λ max. 2285 A., $E_{1\,cm.}^{1\%}$ 1,100 ($\varepsilon = 17{,}800$, if $M = 162$), This was fractionated in a 20-ml. flask (Shrader and Ritzer, *Ind. Eng. Chem. Anal.*, 1939, **11**, 54):

Frn.	B.p./0·5 mm.	$n_D^{20°}$.	Wt. (g).	Found.*		λ max., A.	ε max.	*M* taken.	$CH_3(C)$ %.
				C, %.	H, %.				
1	60—75°	1·5158	1·00	80·15	9·95	2285	16,900	162	16·8
2	75—95	1·5270	0·80	79·9	9·4	2290	22,000	162	10·8
3	95—105	1·5269	0·48	77·9	9·2	2290	22,500	162	15·2
4	105—120	1·5202	1·16	72·6	9·8	2285	14,400	162	18·2
5	120—125	1·5272	1·00	73·5	8·9	2280	15,700	178	15·6
Residue	—	—	1·00						

* Calc. for pyrethrone, $C_{11}H_{14}O$: C, 81·5; H, 8·6%. For dihydropyrethrone, $C_{11}H_{16}O$: C, 80·5; H, 9·75%. For pyrethrolone, $C_{11}H_{14}O_2$: C, 74·15; H, 7·9%.

Fraction 1 (0·64 g.) gave a semicarbazone (0·78 g.), m. p. 210—212°, raised by two recrystallisations from ethyl alcohol to 216—217° [Found: N, 19·3; $CH_3(C)$, 7·4. Calc. for $C_{12}H_{17}ON_3$: N, 19·2%], λλ max. 2315 A., $\varepsilon = 22{,}100$, and 2660 A., $\varepsilon = 21{,}900$. Fraction 2 (0·4 g.) gave a semicarbazone (0·36 g.), m. p. 211—214°, raised by recrystallisation to 216—217° [Found: N, 18·6; $CH_3(C)$, 6·6%], λλ max. 2320 A., $\varepsilon = 21{,}000$, and 2665 A., $\varepsilon = 20{,}700$. Fraction 3 (0·15 g.) gave a semicarbazone (0·13 g.), m. p. 210—212°, raised by recrystallisation to 214—216° [Found: N, 18·0;

CH_3(C), 6·5%], λλ max. 2305 A., ε = 22,000, and 2665 A., ε = 19,600. Fraction 4 (0·75 g.) gave a semicarbazone (0·75 g.), m. p. 196° (indef.; sintering at 138°), recrystallised to give pyrethrone semicarbazone (0·1 g.), m. p. 216—218° [Found: N, 19·8; CH_3(C), 6·8%], λλ max. 2300 A., ε = 24,500, and 2665 A., ε = 20,500. Fraction 5 gave pyrethrolone semicarbazone, m. p. 207—208°, not depressed by admixture with the original pyrethrolone semicarbazone, m. p. 206—208° [Found: N, 17·6; CH_3(C), 9·5. Calc. for $C_{12}H_{17}O_2N_3$: N, 17·9%], λλ max. 2300 A., ε = 20,800, and 2650 A., ε = 19,400. The recrystallisation liquors were bulked and by concentration, in addition to a small amount of pyrethrone and dihydropyrethrone semicarbazones, a benzene-insoluble product was finally obtained. This was dissolved in methyl alcohol (5 ml.), and to the filtered solution ether (20 ml.) was added, giving a product (30 mg.), m. p. 147—151° (Found: C, 49·2; H, 8·3; N, 25·4%), λ max. 2295 A., $E^{1\%}_{1\,\mathrm{cm.}}$ 900. It was not identified, but from the light-absorption data it seems unlikely that it is the semicarbazone of an αβ-unsaturated ketone (location usually near 2650 A.), and the absorption is probably a summation due to the chromophores ($>\mathrm{C}{:}\overset{|}{\mathrm{C}}-\overset{|}{\mathrm{C}}{:}\mathrm{C}<$) and ($\cdot\mathrm{CR{:}N\cdot NH\cdot CO\cdot NH_2}$). It may be an impure semicarbazido-semicarbazone of an αβ-unsaturated ketone with a conjugated side chain. (Calc. for pyrethrone semicarbazido-semicarbazone, $C_{13}H_{22}O_2N_6$: C, 53·1; H, 7·5; N, 28·6%.) Each of the fractions 1—4 was hydrogenated in the presence of platinum oxide, and dihydrojasmone (identified by crystalline derivatives) obtained from the solution.

Pyrethrone semicarbazone (2·9 g.), m. p. 216—218°, subjected to steam-distillation in the presence of oxalic acid solution (10%) (LaForge and Haller, *J. Org. Chem.*, 1938, **2**, 553), gave regenerated pyrethrone (1·8 g.), b. p. 90—91°/0·75 mm., $n_D^{20°}$ 1·5282, α_D ± 0°, $d_{15·5°}^{15·5°}$ 0·973, λ max. 2297 A., ε = 28,000 [Found: C, 80·9; H, 8·9; CH_3(C), 11·4. Calc. for $C_{11}H_{14}O$: C, 81·5; H, 8·6%]. The semicarbazone of the regenerated ketone had m. p. 217—219°, not depressed by admixture with the starting material.

Dihydropyrethrone.—Hydrogen bromide was passed into a cooled solution of the regenerated pyrethrone (1·3 g.) in acetic acid (6·5 ml.) until the weight had increased by 0·88 g. This mixture was cooled overnight, acetic acid (6·5 ml.) added, the solution heated on the water-bath, and zinc dust (5 g.) added during 30 mins. The product was diluted with water, the oil extracted with ether, the ether removed, and the residue steam-distilled (cf. LaForge and Haller, *J. Org. Chem.*, 1938, **2**, 554). The oil (1·1 g.) extracted from the distillate with light petroleum had $n_D^{20°}$ 1·4916, λ max. 2380 A., ε = 10,600, and gave, after recrystallisation from methyl alcohol, pyrethrone semicarbazone, m. p. 203—205°, λ max. 2665 A., ε = 23,600 (this is consistent with the semicarbazone of an αβ-unsaturated ketone without any appreciable diene component) (Found: N, 18·1. Calc. for $C_{12}H_{19}ON_3$: N, 19·0%). The semicarbazone (0·1 g.) in methyl alcohol (45 ml.), hydrogenated in the presence of a reduced platinum oxide catalyst, absorbed 9·8 ml. of hydrogen at N.T.P. (Calc. for $C_{12}H_{19}ON_3|^{=}$: 10·1 ml.), and by concentration of the solution dihydrojasmone semicarbazone was obtained, m. p. 175—176° after recrystallisation from benzene. Dihydropyrethrone regenerated from the semicarbazone had b. p. 85—86°/0·6 mm., $n_D^{20°}$ 1·5010, $[\alpha]_D$ ± 0° (*c*, 3 in alcohol), λ max. 2350 A., ε = 14,300 [Found: C, 80·4; H, 10·2; CH_3(C), 15·9. Calc. for $C_{11}H_{16}O$: C, 80·5; H, 9·75%].

Hydrogenation of Tetrahydropyrethrolone Acetate Semicarbazone.—Tetrahydropyrethrolone (1·5 g.), b. p. 126—127°/0·8 mm., $n_D^{20°}$ 1·4932, $\alpha_D^{20°}$ 10·2°, was heated with acetic anhydride (6 g.) on the water-bath for 4 hours. The acetic acid produced and the excess of acetic anhydride were removed by fractionation under reduced pressure, and the crude acetate distilled to give *tetrahydropyrethrolone acetate* (1·65 g.), b. p. 117°/1·3 mm., $n_D^{20°}$ 1·4761, $\alpha_D^{20°}$ 27·4°, $d_{15·5°}^{15·5°}$ 1·016, λ max. 2300 A., ε = 11,750 (Found: C, 70·0; H, 8·9. $C_{13}H_{20}O_3$ requires C, 69·6; H, 8·9%). The *semicarbazone* had m. p. 140—141°, λ max. 2655 A., ε = 20,700 (Found: C, 59·6; H, 8·9. $C_{14}H_{23}O_3N_3$ requires C, 59·8; H, 8·2%). In a typical experiment tetrahydropyrethrolone acetate semicarbazone (3 g.) in methyl alcohol (350 ml.) was hydrogenated in the presence of a platinum oxide catalyst (0·75 g.) for 2¾ hours, absorbing 500 ml. of hydrogen at N.T.P. (Calc. for $2H_2$: 480 ml.). The filtered solution was concentrated (20 ml.), giving a white crystalline product (0·29 g.), m. p. 187° (sintering at 183°), which after two recrystallisations from methyl alcohol gave hexahydropyrethrone semicarbazone (Haller and LaForge, *J. Org. Chem.*, 1937, **2**, 49) (0·12 g.), m. p. 195—196°, $[\alpha]_D^{20°}$ ± 0° (*c*, 7·34 in alcohol) (Found: C, 63·6; H, 9·7; N, 18·1. Calc. for $C_{12}H_{23}ON_3$: C, 64·0; H, 10·2; N, 18·7%).

Dihydrojasmone.—Tetrahydropyrethrolone [regenerated from semicarbazone, m. p. 192—193° (LaForge and Haller, *J. Amer. Chem. Soc.*, 1936, **58**, 1777)], b. p. 124°/0·6 mm., $n_D^{20°}$ 1·4912, $\alpha_D^{20°}$ 9·8°, λλ max. 2320 A., ε = 11,800, and 3130 A., ε = 65, CH_3(C), 14·3, 14·8% (cf. Barthel and LaForge, *Ind. Eng. Chem. Anal.*, 1944, **16**, 434), with thionyl chloride (LaForge and Haller, *loc. cit.*) gave 5-chlorotetrahydropyrethrone, b. p. 98—100°/0·6 mm., $n_D^{20°}$ 1·4950, $\alpha_D^{20°}$ 23·8°, λλ max. 2350 A., ε = 10,600, and 3090 A., ε = 55 (Found: Cl, 18·0. Calc. for $C_{11}H_{17}OCl$: Cl, 17·7%). By proceeding essentially as described by LaForge and Haller (*loc. cit.*), this was reduced to dihydrojasmone, b. p. 82°/1 mm., $n_D^{20°}$ 1·4805, $[\alpha]_D^{20°}$ ± 0° (*c*, 10 in alcohol), λλ max. 2360 A., ε = 13,300, and 3050 A., ε = 55 [Found: C, 79·3; H, 10·4; CH_3(C), 17·5, 17·2. Calc. for $C_{11}H_{18}O$: C, 79·5; H, 10·8%]. The semicarbazone had m. p. 175—176° after recrystallisation from benzene, and *dihydrojasmone* 2 : 4-*dinitrophenylhydrazone*, prepared by the usual method and recrystallised from ethyl alcohol, had m. p. 121—122° (Found: N, 16·4. $C_{17}H_{22}O_4N_4$ requires N, 16·2%).

Treatment of i- *and* d-*Pyrethrolone Methyl Ethers.*—*i*-Pyrethrolone methyl ether (10 g.) (West, J., 1944, 239), b. p. 100—102°/1·2 mm., $n_D^{20°}$ 1·5091, α_D ± 0°; OMe, 15·7; CH_3(C), 14·6%, in dry ether (600 ml.) was added to freshly prepared aluminium amalgam (30 g.). Water (12 ml.) was added with shaking, and the mixture kept at room temperature during 15 hours; then a further 4 ml. of water were added with shaking, and the mixture kept for a further 25 hours. The pleasant-smelling, viscous oil obtained from the ether was fractionated:

Frn.	B. p./0·9 mm.	$n_D^{20°}$.	Wt. (g.).	Frn.	B. p./0·9 mm.	$n_D^{20°}$.	Wt. (g.).
1	64—74°	1·4933	0·2	5	88—93°	1·5100	0·52
2	74—80	1·4984	0·27	6	94—98	1·5128	0·27
3	81—83	1·5020	0·58	Resin	—	—	6·9
4	84—88	1·5052	0·36				

Fraction 1 (0·1 g.) gave a semicarbazone (90 mg.), m. p. 164—171°, raised by two recrystallisations from methyl alcohol to 180—183°, which was not further examined. Each of the fractions 2—6 gave pyrethrone semicarbazone of which the m. p. was not depressed upon admixture with the semicarbazone, m. p. 217—219°, obtained from the pyrethrone derived from pyrethrolone.

d-Pyrethrolone methyl ether (West, J., 1944, 239), $[\alpha]_D^{20°}$ 83·3°, $n_D^{20°}$ 1·5142; OMe, 16·3; (CH_3)C, 16·4%, under similar conditions gave fractions from which pyrethrone semicarbazone was obtained.

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

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