569. *The Pyrethrins and Related Compounds. Part VI.*[1] *The Structures of the " Enols " of Pyrethrolone* [2]

By M. ELLIOTT

2-Alkenyl-3-methylcyclopent-2-en-4-olones such as cinerolone and allethrolone, which have no conjugated double bonds in the side chain, are converted by sodium methoxide in methanol into enolic forms of the corresponding cyclopentane-1,4-diones. Their side chains are unaltered. Under the same conditions, pyrethrolone, with a conjugated *cis*-pentadienyl side chain, gives mainly a cyclopentene-1,4-dione with oxidation of the hydroxyl group and reduction of one of the side-chain double bonds.

STAUDINGER and RUZICKA [3] and other investigators [4-7] found that when " pyrethrolone " was boiled with methanolic sodium methoxide, two fractions, soluble in aqueous alkali and easily separated by distillation, were obtained. The interpretation of their results is complicated, for it is now known that they worked with mixtures of pyrethrolone (Ia), cinerolone (Ib),[8] and possibly " jasmololone " (Ic).[9] * Pure (+)-pyrethrolone (from the hydrate [1]) is here shown to produce a mixture of 3-methyl-2-pent-2′- and -2-pent-4′-enylcyclopent-2-ene-1,4-diones (IIa and b, respectively) (b. p. *ca.* 80°/0·05 mm.) and 3-methyl-2-*cis*-penta-2′,4′-dienylcyclopentane-1,4-dione (IIIa) (b. p. *ca.* 150°/0·05 mm.). Under the same conditions cinerolone gives only 2-*cis*-but-2′-enyl-3-methylcyclopentane-1,4-dione (IIIb).

The lower-boiling fraction from pyrethrolone (Ia) formed a bis-2,4-dinitrophenylhydrazone [10] as well as a monosemicarbazone [3,4,6,10] and had spectra [$\lambda_{max.}$ 244 mμ (ε 13,000); $\nu_{max.}$ 1749, 1709 cm.$^{-1}$] characteristic of cyclopentenediones, which show two peaks in the C=O stretching vibration region [11,12] and give very insoluble monosemicarbazones rapidly even in the absence of pyridine or sodium acetate.[11] Although these properties indicated that the fraction was a cyclopentenedione it differed from the diketone (IIc) obtained by oxidation (chromium trioxide in acetone [13]) of pyrethrolone (Ia) but the refractive index, ultraviolet, and infrared absorption were very close to those of the cyclopentenedione (IId) from allethrolone [8] (Id). The elemental analyses [3,4,6,10] agreed well only with $C_{11}H_{14}O_2$, which, if a cyclopentenedione ring is present permits only one double bond in the side chain. In agreement, the infrared spectrum showed no " pip " at 1600 cm.$^{-1}$ which is a sensitive indication of the presence of the diene,[14] and the ultraviolet absorption at 226 mμ was relatively low. This evidence, and the isolation of formaldehyde after ozonolysis,[10] led to the structure (IIb) for this compound, which was supported by the preparation of an almost identical diketone by the oxidation (manganese dioxide in chloroform [11]) of a specimen of 3-methyl-2-pent-4′-enylcyclopent-2-en-4-olone.[15] The

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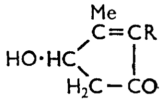
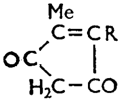
* The new ester found recently in pyrethrum extract [9] has been named " jasmolin-II." Therefore the name jasmol*olone* follows for its alcoholic constituent (cf. pyrethr*olone* and pyrethr*in*-II).

[1] Part V, M. Elliott, *J.*, 1964, 5225.
[2] Preliminary account, M. Elliott, *Proc. Chem. Soc.*, 1960, 406.
[3] H. Staudinger and L. Ruzicka, *Helv. Chim. Acta*, 1924, **7**, 212.
[4] H. L. Haller and F. B. LaForge, *J. Org. Chem.*, 1939, **3**, 543.
[5] A. E. Gillam and T. F. West, *J.*, 1942, 671.
[6] A. E. Gillam and T. F. West, *J.*, 1944, 49.
[7] T. F. West, *J.*, 1944, 51.
[8] For leading references, see L. Crombie and M. Elliott, *Fortschr. Chem. org. Naturstoffe*, 1961, **19**, 120.
[9] P. J. Godin, R. J. Sleeman, M. Snarey, and E. M. Thain, *Chem. and Ind.*, 1964, 371.
[10] This work.
[11] M. Elliott and K. A. Jeffs, unpublished results.
[12] C. H. DePuy and E. F. Zaweski, *J. Amer. Chem. Soc.*, 1959, **81**, 4920; C. H. DePuy and C. E. Lyons, *ibid.*, 1960, **82**, 631; C. H. DePuy and P. R. Wells, *ibid.*, p. 2910.
[13] P. Bladon, J. M. Fabian, H. B. Henbest, H. P. Koch, and G. W. Wood, *J.*, 1951, 2402.
[14] M. Elliott, *J. Appl. Chem.*, 1961, **11**, 19.
[15] L. Crombie and S. H. Harper, *J.*, 1952, 869.

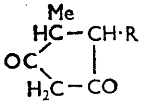
nuclear magnetic resonance spectrum [16] fully confirmed this structure for the cyclopentenedione ring system [CH_3·C=, 7·98 τ, singlet; CH_2, 7·14 τ, singlet] but revealed that the pent-4′-enyl side chain [CH_2, 7·8 τ, complex; CH_2·CH_2·CH_2, 8·3 τ, complex; CH_2, 5·0 τ, complex; C*H*=, 4·5 τ, complex] was admixed with 15—25% (based on relative areas of peaks at 9, 8·3, and 6·8 τ) of pent-2′-enyl compound (=C·CH_2C=, 6·83 τ, doublet; C*H*=C*H*, 4·5 τ, complex; CH_2C, 7·8 τ, complex; CH_3, 9·06 τ, triplet). This is the side chain in



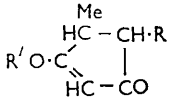
(I) (a) R = $CH_2·CH\overset{c}{=}CH·CH=CH_2$
(b) R = $CH_2·CH\overset{c}{=}CH·Me$
(c) R = $CH_2·CH\overset{c}{=}CH·Et$
(d) R = $CH_2·CH=CH_2$
(e) R = C_5H_{11}



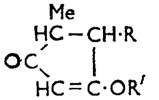
(II) (a) R = $CH_2·CH\overset{c}{=}CH·Et$
(b) R = $(CH_2)_3·CH=CH_2$
(c) R = $CH_2·CH\overset{c}{=}CH·CH=CH_2$
(d) R = $CH_2·CH=CH_2$



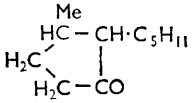
(III) (a) R = $CH_2·CH\overset{c}{=}CH·CH=CH_2$
(b) R = $CH_2·CH\overset{c}{=}CH·Me$
(c) R = $CH_2·CH\overset{c}{=}CH·Et$
(d) R = C_5H_{11}



(IV) (a) R = $CH_2·CH\overset{c}{=}CH·CH=CH_2$, R′ = Ac
(b) R = $CH_2·CH\overset{c}{=}CH·CH=CH_2$, R′ = H
(c) R = $CH_2·CH=CH_2$, R′ = H



(V)



(VI)

jasmolin II,[9] whose n.m.r. spectrum shows peaks at the same positions as the minor ones in the spectrum of the lower-boiling fraction.[17] The related cyclopentenone and cyclopentenolone were synthesised by Crombie and Harper.[15] The n.m.r. spectrum also showed that not more than a trace of any pent-3′-enyl isomer (the product of 1,4-addition of hydrogen or rearrangement of the other isomers) could have been present, for there was no indication of the doublet at 8·35 τ which the system CH=CH·Me (found in cinerin I and cinerin II) would have produced.[16] Therefore, in forming the lower-boiling enol, hydrogen adds preferentially, but not exclusively, to the internal bond of the conjugated diene. As expected, very little low-boiling fraction was obtained from allethrolone (Id) [10] or from tetrahydropyrethrolone (Ie) in the presence of zinc dust.[4,7]

Gillam and West [6] assumed the absorption at 226 mμ in the semicarbazone from the lower-boiling compound ($\lambda_{max.}$ 226, 308·5 mμ) to indicate the presence of a diene side chain, but the semicarbazone of allethredione (IId) has $\lambda_{max.}$ 226 and 305 mμ [10] so both these bands are characteristic of the keto-semicarbazone itself.

This cyclopentenedione fraction was earlier [4] called pyrethrolone "enol" because it was soluble in aqueous alkali but there is no evidence that cyclopentenedione itself [12] or 2,3-dialkyl- and -alkenyl-cyclopentenediones [11] can enolise. These compounds are probaby acidic because the anion gains stability by delocalisation of its charge. The absence of hydroxyl groups to participate in intermolecular hydrogen bonding is consistent with the relatively low boiling point of the cyclopentenediones examined here and elsewhere.

(+)-Pyrethrolone produced only a little high-boiling fraction,[10] of which allethrolone (Id) [10] and pyrethrolone mixed with cinerolone [3,4,6,7] gave much higer yields. Now that pyrethrolone and related alcohols are recognised as β-, not α-ketols,[8] the published evidence on these high-boiling compounds shows them to be cyclopentane-1,4-diones (III, R = alkenyl), in equilibrium with enolic forms (IV and V; R = alkenyl, R′ = H). This

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[16] A. Bramwell, L. Crombie, M. Elliott, and N. F. Janes, unpublished results.
[17] Dr. P. J. Godin, personal communication.

formulation is supported by the shift in $\lambda_{max.}$ of the tetrahydro-derivative (IIId) from 243·5 to 256 mμ with alteration in concentration of the spectroscopic solution [7] and by the formation of the enol acetate (IVa) readily hydrogenated to a mixture of the *cis* and *trans* forms of 2-amyl-3-methylcyclopentanone (VI), isolated as the semicarbazones.[4] The preferred enolic form must therefore be (IVb) in the solvents examined. The products from pyrethrolone and allethrolone showed a strong band at *ca.* 1560 cm.$^{-1}$, as did the spectrum of cyclopentane-1,3-dione [18] indicating conjugate chelation in a β-diketone.[19] The physical properties of the high-boiling fraction from allethrolone were like those described for 2-ethyl-4-propylcyclopentane-1,3-dione [20] and the nuclear magnetic resonance spectrum [16] in carbon tetrachloride [CH_3, 8·8 τ, doublet; 4H, complex doublet and multiplet, 7—8 τ; H, singlet 4·81 τ; 1 vinyl H, complex, 4·25 τ; 2 terminal vinyl H (side chain), 4·92 τ; absorption at —3 τ (enolic proton)] confirmed this general formulation. Because absorption intensity at low field was equivalent to a complete proton, the structure was deduced to be 2-allyl-4-hydroxy-3-methylcyclopent-4-enone (IVc) in the solvent used.

The high-boiling cyclopentanedione (IIIa) from pyrethrolone retained a diene side chain, unlike the lower-boiling fraction. This was deduced from a comparison of its neutral ($\lambda_{max.}$ 230 mμ) and alkaline ($\lambda_{max.}$ 232, 262 mμ) spectra with those of the compound (IVc) from allethrolone [neutral, $\lambda_{max.}$ 243 mμ; alkaline $\lambda_{max.}$ 260 mμ; no max. nor inflexion at 230—240 mμ]. In the enol from pyrethrolone, the absorption by the conjugated diene [21] overlaps that of the ring in neutral ethanol, but in alkali the single absorption band of the cyclopentenedione ring at 260 mμ, shown by the compound (IVc) from allethrolone, is clearly separated from that of the diene.

The name "isopyrethrolone *enol*" [4] was therefore more appropriate to the higher-boiling compounds [3-7] but most of the fraction was probably derived from cinerolone (Ib), and by analogy with the product from allethrolone (Id) it had the cyclopentanedione structure (IIIb, and related enolic forms). Pyrethrolone, having a conjugated diene side chain, is unstable and so preferential survival of cinerolone is to be expected under the alkaline conditions used to prepare the "enols." Thus, for one carefully purified sample, West [7] recorded an analysis (C, 72·0; H, 8·0%) more in agreement with a compound from cinerolone (C, 72·3; H, 8·5%) than with one from pyrethrolone (C, 74·15; H, 7·9%).

The neutral cyclopentenolones therefore rearrange to either of the two types of acidic products in alkaline conditions. Formally, with either "enol," the secondary alcohol is dehydrogenated and hydrogen is added to a double bond, either in the ring in the case of the cyclopentanediones, or in the side chain when the cyclopentenedione is produced. Probably, hydrogen is transferred intermolecularly to give the cyclopentenedione from pyrethrolone, for it is difficult to envisage the mechanism of a prototropic shift from the ring and along the side chain to the terminal double bond. On the other hand, the cyclopentanedione is more likely to be produced in an endocyclic rearrangement. The results do not indicate whether the system methanol–formaldehyde–sodium methoxide (cf. Meerwein–Pondorff reaction with isopropylalcohol and acetone) takes part in the formation of the diketones from the cyclopentenolones. However, transfer of hydrogen from the secondary alcoholic group occurs to an appreciable extent only when a double bond activated by conjugation with another is sterically accessible. Allethrolone (Id) is not oxidised [11] in neutral solution by the hydrogen acceptor 2,3-dichloro-5,6-dicyanobenzoquinone,[22] so alkaline conditions may be necessary to favour the stability of the anions from the cyclopentane- and cyclopentene-diones. The results suggest that hydrogen

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[18] J. H. Boothe, R. G. Wilkinson, S. Kurshner, and J. H. Williams, *J. Amer. Chem. Soc.*, 1953, **75**, 1732.

[19] L. J. Bellamy, "The Infra-red Spectra of Complex Molecules," Methuen, London, 1958, p. 142.

[20] R. B. Woodward and E. R. Blout, *J. Amer. Chem. Soc.*, 1943, **65**, 562.

[21] M. Elliott, *J.*, 1964, 1854.

[22] E. A. Braude, A. G. Brook, and R. P. Linstead, *J.*, 1954, 3569; E. A. Braude, R. P. Linstead, and K. R. Wooldridge, *J.*, 1956, 3070; D. Burn, V. Petrow, and G. O. Weston, *Tetrahedron Letters*, 1960, No. 9, 14.

transfer to give a cyclopentenedione and rearrangement to a cyclopentanedione are competing reactions when possible (with pyrethrolone) but in the absence of the diene side chain (allethrolone and cinerolone) only rearrangement takes place.

Earlier studies of these compounds [3-7] were probably complicated by the use of mixtures of pyrethrolone and cinerolone, when the pyrethrolone diene side chain could accept hydrogen from the secondary alcoholic group of cinerolone.

EXPERIMENTAL

For general methods, see Part III.[23] Nuclear magnetic resonance spectra [16] were determined for deuterochloroform or carbon tetrachloride solutions using a Perkin-Elmer R.10 Spectrometer at 60 Mc./sec., with tetramethylsilane as internal standard.

The " Enols " of Pyrethrolone.—(+)-Pyrethrolone, freshly isolated by dehydration of the monohydrate [1] (14·9 g., 0·084 mol.), was boiled for 21 hr. with sodium (2·28 g., 0·099 mol.) dissolved in methanol (210 ml.). After evaporation of most of the methanol on a steam-bath *in vacuo*, the residue was diluted with water and neutral products were removed in ether. The aqueous phase was acidified (Congo Red) with hydrochloric acid and the liberated compounds were extracted into ether, dried (Na_2SO_4), and distilled at 3×10^{-3} mm., after removal of solvent:

Fraction no.	B. p.	n_D^{20}	Wt. (g.)	C (%)	H (%)
1	98—104°	1·5152	0·4	74·3	7·75
2	104—109	1·5167	0·8	74·4	7·9
3	109—150	1·5192	0·7	73·95	7·95
4	150—156	1·5488	1·2	73·5	8·1
			Calc. for $C_{11}H_{14}O_2$:	74·1	7·9

Fraction 1 had $\lambda_{max.}$ 244 mμ (ε 13,500) [lit.,[6] b. p. 102°/1 mm.; n_D^{24} 1·5100; $\lambda_{max.}$ 244 mμ (ε 12,600)], $\nu_{max.}$ 2930s, 1742s, 1705s, 1640m, 1600w, 1440m, 1380s, 1330m, 1260s, 1185s, 1105m, 995w, 970m, 920s cm.$^{-1}$. The semicarbazone (fraction 1) (cf. Gillam and West [6]) had m. p. 256° (from acetic acid); $\lambda_{max.}$ 224 and 306 mμ (ε 13,100 and 18,100) [lit.,[6] m. p. 255—256°; $\lambda_{max.}$ 226—227 and 308·5—309 mμ (ε 12,000—17,600 and 16,500—20,600)] (Found: C, 60·0; H, 7·0; N, 17·9. Calc. for $C_{12}H_{17}O_2N_3$: C, 61·3; H, 7·3; N, 17·9%). The *bis*-2,4-*dinitrophenylhydrazone* (0·25 g.) was obtained by warming fraction 1 (0·12 g.) with Brady's reagent (10 ml.) and was recrystallised from methanol–chloroform; very dark red crystals, m. p. 202° (Found: C, 50·6; H, 4·0; N, 20·4. $C_{23}H_{22}O_8N_8$ requires C, 51·5; H, 4·1; N, 20·5%). Fraction 4 had $\lambda_{max.}$ 230 mμ (ε 22,200), λ_{infl} 240 mμ (ε 19,950), neutral; $\lambda_{max.}$ 232, 262 mμ (ε 17,900, 18,900), alkaline; $\nu_{max.}$ 1560s (C=O), 1000m, 909m ($CH=CH_2$) cm.$^{-1}$.

Ozonolysis.—Fraction 2 (0·22 g.) in carbon tetrachloride (25 ml.) was treated with ozonised oxygen for 1 hr. (no further uptake of ozone). After addition of water and agitation, the aqueous layer was separated and set aside with saturated aqueous dimedone solution. Formaldehyde dimethone derivative (0·117 g., m. p. 184°, raised to 188—189° on recrystallisation and not depressed on admixture with authentic material) separated after 20 min.

3-*Methyl*-2-cis-*penta*-2′,4′-*dienylcyclopentane*-1,4-*dione*.—Pyrethrolone hydrate [1] (5·5 g.) in acetone (10 ml.) was treated during 15 min. at 0° with 5 ml. of a solution [13] from chromic oxide (26·7 g.) and sulphuric acid (21·3 ml.) diluted with water to 100 ml. After adding water the products were taken up in ether, which was extracted thoroughly with potassium hydroxide (0·1N). The alkaline extracts were acidified and the liberated oil was taken into ether, dried (Na_2SO_4), and distilled at 10^{-4} mm., after evaporation of solvent, to give the required *diketone*, 0·28 g., b. p. mainly 100—112°; n_D^{20} 1·5488; $\lambda_{max.}$ 226 mμ (ε 28,000); $\lambda_{infl.}$ 240 mμ (ε 21,300); $\nu_{max.}$ 1745s, 1705s, 1600 " pip," 1260s, 1005s, 917s cm.$^{-1}$ (Found: C, 75·0; H, 6·8. $C_{11}H_{12}O_2$ requires C, 75·0; H, 6·9%).

The *semicarbazone* darkened and decomposed without melting up to 300° and was too insoluble in ethanol for spectroscopy (Found: C, 62·0; H, 5·55; N, 17·7. $C_{12}H_{15}O_2N_3$ requires C, 61·8; H, 6·5; N, 18·0%).

Oxidation of 3-*Methyl*-2-*pent*-4′-*enylcyclopent*-2-*en*-4-*olone*.—The ketol [15] (0·56 g.) was shaken for 15 min. only [11] with manganese dioxide [24] in chloroform (80 ml.). After filtration, the solvent

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[23] M. Elliott, *J.*, 1964, 888.

[24] J. Attenburrow, A. F. B. Cameron, J. H. Chapman, R. M. Evans, B. A. Hems, A. B. A. Jansen, and T. Walker, *J.*, 1952, 1094.

was evaporated and the crude diketone was distilled, b. p. 140°/15 mm., n_D^{20} 1·5070; $\lambda_{max.}$ 244 mμ (ε 13,100). This infrared spectrum showed absorption bands identical in position with those of the lower-boiling enol (above) and differed only from the alcoholic starting material in lacking absorption at 3400s, 1093m, 1055s, and 1018m cm.$^{-1}$ (OH). This crude diketone (Found C, 72·8; H, 7·8%) was converted without purification into the semicarbazone, m. p. 248° (decomp.) (from acetic acid); mixed m. p. with semicarbazone from " enol," 254° (Found: C, 60·3; H, 7·2; N, 17·9°). The bis-2,4-dinitrophenylhydrazone had m. p. 203°, mixed m. p. with derivative from " enol," 201°.

Reaction of Allethrolone with Sodium Methoxide.—By a procedure similar to that used for pyrethrolone, allethrolone (9·2 g., 0·06 mol.) with sodium (1·5 g., 0·065 mol.) in methanol (150 ml.) gave 2-*allyl*-3-*methylcyclopentane*-1,4-*dione* (5·4 g.) as a very viscous yellow liquid, b. p. 136—138°/0·3 mm.; n_D^{20} 1·5296; $\lambda_{max.}$ 243 mμ, neutral (ε 16,700); $\lambda_{max.}$ 260 mμ, alkaline (ε 25,400); $\nu_{max.}$ 1640s, 1560s, broad, 995m, 917m, cm.$^{-1}$ (Found: C, 71·3; H, 8·05. $C_9H_{12}O_2$ requires C, 71·0; H, 7·95%). The small forerun (0·07 g.) showed only very weak absorption at 1740 cm.$^{-1}$

I thank Dr. A. Bramwell and Professor L. Crombie for determinations of n.m.r. spectra, which are part of a joint study,[17] Professor S. H. Harper for a gift of pent-4-enylrethrolone, and Dr. T. F. West for helpful discussion.

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