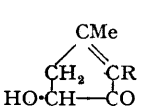
## 20. *The Structure of Pyrethrolone and Related Compounds. Part VI.*

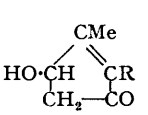
By Erich Baer and T. F. West.

Dihydrocinerolone and tetrahydropyrethrolone are inert towards lead tetra-acetate, proving the absence, from each of the ketones, of a 1 : 2-ketol system which would be cleaved quantitatively to the corresponding aldehydo-acid, consuming one mole of lead tetra-acetate per mole of compound. Cinerolone absorbed the equivalent of one mole of lead tetra-acetate by addition to the double bond in the side chain.

Staudinger and Ruzicka (*Helv. Chim. Acta*, 1924, **7**, 177) originally assigned a 1 : 2-ketol structure to pyrethrolone which appeared to form an osazone and displayed reducing properties. The alcoholic components of the pyrethrin molecules have now been shown to be a mixture of dextrorotatory and optically inactive forms of two ketols, cinerolone, $C_{10}H_{14}O_2$, and pyrethrolone,

$C_{11}H_{14}O_2$ (LaForge and Barthel, *J. Org. Chem.*, 1945, **10**, 106, 114, 222), in which the latter appears to be present to the extent of 70—80% (West, *J.*, 1946, 463). These derivatives on hydrogenation are converted into dihydrocinerolone and tetrahydropyrethrolone respectively (LaForge and Barthel, *loc. cit.*; West, *loc. cit.*). Recently, compounds identical with (±)-dihydrocinerolone (LaForge and Soloway, *J. Amer. Chem. Soc.*, 1947, **69**, 979) and (±)-tetrahydropyrethrolone (Dauben and Wenkert, *ibid.*, p. 2074) have been prepared by brominating dihydrocinerone and tetrahydropyrethrone by means of *N*-bromosuccinimide and hydrolysing the bromo-compound formed. LaForge and Soloway (*J. Amer. Chem. Soc.*, 1947, **69**, 186, 2932) assigned the structure (I, R = $[CH_2]_3{\cdot}CH_3$) to a ketone prepared by other methods which was not identical with (±)-dihydrocinerolone, and advanced this fact as indirect evidence that the *N*-bromosuccinimide had brominated dihydrocinerone in the allylic position to give the 1 : 3-ketol structure (II, R = $[CH_2]_3{\cdot}CH_3$) on hydrolysis. Dauben and Wenkert (*loc. cit.*) pointed out that, although *N*-bromosuccinimide introduces bromine into methylene groups in the α-position to the carbonyl group of saturated cyclic and acyclic ketones (Schmid and Karrer, *Helv. Chim. Acta*, 1946, **29**, 573; Djerassi and Scholz, *Experientia*, 1947, **3**, 107) and of αβ-unsaturated ketones of the mesityl oxide type (Buu-Hoï, *Experientia*, 1946, **2**, 310), substitution takes place on the allylic methylene group of $\Delta^4$-3-ketosteroids (Meystre and Wettstein, *ibid.*, p. 408). Dauben and Wenkert considered (II, R = $[CH_2]_4{\cdot}CH_3$) " the most likely structure for tetrahydropyrethrolone ", as the slow reaction of their synthetic tetrahydropyrethrolone with periodic acid indicated the absence of a 1 : 2-ketol structure.


(I.)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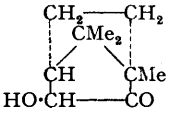
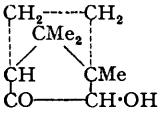

(III.)


(IV.)

Baer (*J. Amer. Chem. Soc.*, 1940, **62**, 1597; 1942, **64**, 1416) studied the reaction of 1 : 2-ketols with lead tetra-acetate, and showed that under certain conditions this reagent effects quantitative cleavage of these compounds. Thus the five-membered rings in 3-hydroxycamphor (III) and 2-hydroxy*epi*camphor (IV) are cleaved smoothly with the consumption of one mole of lead tetra-acetate per mole of the compounds. The results obtained (in moles of lead tetra-acetate consumed per mole of compound) by applying this method to samples of " natural " cinerolone, dihydrocinerolone, and tetrahydropyrethrolone (prepared by regeneration from the appropriate optically active semicarbazones) are given below in comparison with typical cyclic 1 : 2-ketols.

| | | | |
|---|---|---|---|
| Cinerolone | 1·08 | 2-Hydroxy*epi*camphor * | 1·05 |
| Dihydrocinerolone | 0·04 | *cyclo*Hexan-2-ol-1-one * | 0·98 |
| Tetrahydropyrethrolone | 0·015 | | |

* Baer, *J. Amer. Chem. Soc.*, 1942, **64**, 1419.

These results prove that the 1 : 2-ketol system cannot be present and provide strong indirect support for a 1 : 3-ketol structure in both dihydrocinerolone and tetrahydropyrethrolone (derived from the natural source) when considered with the evidence adduced by LaForge and Soloway (*loc. cit.*) and by Dauben and Wenkert (*loc. cit.*). The presence of the double bond in the side chain of cinerolone accounts for the absorption of one mole of lead tetra-acetate (Dimroth and Schweizer, *Ber.*, 1923, **56**, 1375; Fischer, Baer and Feldmann, *ibid.*, 1930, **63**, 1732) by this compound as is demonstrated by the fact that the corresponding dihydro-derivative is inert towards this reagent.

## Experimental.

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

*Tetrahydropyrethrolone.*—Tetrahydropyrethrolone semicarbazone, m. p. 192—193°, was prepared by known methods; the tetrahydropyrethrolone regenerated in the presence of cold potassium hydrogen sulphate solution (LaForge and Haller, *J. Amer. Chem. Soc.*, 1936, **58**, 1779) had 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 (Gillam and West, *J.*, 1942, 487, 672; West, *J.*, 1945, 412); $CH_3(C)$, 14·3, 14·8% (cf. LaForge and Barthel, *Ind. Eng. Chem. Anal.*, 1944, **16**, 434). In a typical experiment, this sample (89·5 mg.), dissolved in 70% v/v aqueous acetic acid (7 ml.), was mixed with a solution of lead tetra-acetate (594·7 mg. ≡ 26·85 ml. of 0·1N-sodium thiosulphate) in glacial acetic acid (25 ml.). After the mixture had been left for 24 hours at room temperature, 80 ml. of an aqueous solution containing sodium acetate (32·8 g.) and potassium iodide (4 g.) were added; the liberated iodine required 26·56 ml. of 0·1N-sodium thiosulphate ≡ 588·1 mg. lead tetra-acetate (6·6 mg. consumed). In a blank experiment the equivalent of 3·3 mg. was required.

*Cinerolone and Dihydrocinerolone.*—A sample of cinerolone semicarbazone $A_1$ prepared essentially as described by LaForge and Barthel (*J. Org. Chem.*, 1945, **10**, 106) had m. p. 202—203°; $[\alpha]_D$ − 186°

(*c*, 1 in pyridine); λλ max. 2660 A., $\epsilon$ = 18,300 and 2320 A, $\epsilon$ = 10,900; $CH_3(C)$, 12·1% (Found: C, 59·8; H, 7·5. Calc. for $C_{11}H_{17}O_2N_3$: C, 59·2; H, 7·6%). Cinerolone $A_1$ (141·8 mg.), regenerated from this semicarbazone (LaForge and Barthel, *J. Org. Chem.*, 1945, **10**, 118), was dissolved in acetic acid (70% v/v) (14 ml.) and mixed with a solution of lead tetra-acetate (933·8 mg. ≡ 42·16 ml. of 0·1N-sodium thiosulphate) in glacial acetic acid (40 ml.). After 24 hours, sodium acetate–sodium iodide solution (120 ml.) was added; the liberated iodine required 23·69 ml. of 0·1N-sodium thiosulphate ≡ 524·7 mg. lead tetra-acetate (409·1 mg. consumed). Blank, nil.

Cinerolone semicarbazone was hydrogenated to give, by known methods (LaForge and Barthel, *loc. cit.*; West *J.*, 1946, 465), dihydrocinerolone semicarbazone $A_1$, having m. p. 191—192°; $[\alpha]_D$ − 180° (*c*, 0·249 in pyridine). The dihydrocinerolone (62·2 mg.) regenerated therefrom by the method described above consumed only 6·6 mg. of lead tetra-acetate after 24 hours. (Each of the above ketones was derived from pyrethrum extracts prepared from Kenya pyrethrum flowers.) 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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