87. *Calythrone.*

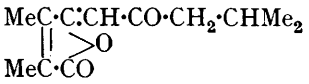
By A. R. PENFOLD and J. L. SIMONSEN.

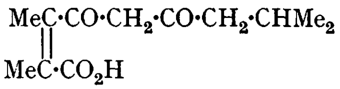
A ketone, *calythrone*, $C_{12}H_{16}O_3$, has been separated from the essential oil obtained from *Calythrix tetragona*. It yields on oxidation with sodium hypobromite in alkaline solution bromoform, *iso*valeric acid and dimethylmaleic anhydride. The ketone must therefore be represented by the structure (I).

DURING an investigation of the essential oil from *Calythrix tetragona, var. "A,"* and *C. virginata* from Queensland, extraction with aqueous alkali yielded a sodium salt, from which, by decomposition with acid, a yellow oil having the composition $C_{12}H_{16}O_3$ was obtained. This oil, for which the name *calythrone* is proposed, gave with ferric chloride an intense port-wine coloration and it was characterised by the preparation of the orange *sodium* salt, m. p. 196°, referred to above, a sage-green *copper* derivative, m. p. 208—210°, and a *dioxime anhydride*, $C_{12}H_{18}O_3N_2$, m. p. 135°. The general reactions of the ketone suggested that it was a β-diketone, which is a somewhat rare constituent of essential oils, since up to the present only three have been described, namely, angustione and dehydroangustione (Penfold, *J. Proc. Roy. Soc., New South Wales*, 1924, **57**, 300; Gibson, Penfold, and Simonsen, J., 1930, 1184; Cahn, Gibson, Penfold, and Simonsen, J., 1931, 286) and leptospermone (Penfold, *J. Proc. Roy. Soc., New South Wales*, 1921, **45**, 51; Johnson and Short, *Rep. Austr. Assoc. Sci.*, 1923, **16**, 223; Gardner, *J. Soc. Chem. Ind.*, 1924, **43**, 34 T; 1925, **44**, 828 T; Short, *ibid.*, 1926, **45**, 967; Briggs, Penfold, and Short, J., 1938, 1193).

This conclusion appeared at first to be supported by the observation that on oxidation with sodium hypobromite in alkaline solution calythrone gave, in addition to bromoform and *iso*valeric acid, a crystalline substance, $C_6H_6O_3$, m. p. 94—95°, which was readily volatile in steam, and in very small amount a *bromo-acid*, $C_7H_8O_3Br_2$, m. p. 129°. The substance $C_6H_6O_3$ seemed to be a keto-acid, since it was soluble in aqueous sodium carbonate and gave a *semicarbazone*, m. p. 238°, a p-*nitrophenylhydrazone*, m. p. 214°, and a 2 : 4-*dinitrophenylhydrazone*, decomp. 253—255°. Reduction of the substance catalytically gave *meso*-*s*-dimethylsuccinic acid and by the Clemmensen reagent the *dl*-acid, these acids being identified by direct comparison with authentic specimens and by analysis. On oxidation with potassium permanganate a quantitative yield of pyruvic acid was obtained, this acid being characterised by its colour reactions (β-naphthol and sodium nitroprusside) and by the preparation of the *p*-nitrophenylhydrazone, m. p. 219—220°, and the 2 : 4-dinitrophenylhydrazone, m. p. 215—216°. These results suggested that the substance was dimethylmaleic anhydride, m. p. 96°, and a direct comparison with this anhydride and with its derivatives showed this to be the case. There can therefore be no doubt that calythrone must be represented by the structure (I) and that the β-diketonic properties which it shows are due to the opening of the lactone ring to give (II).

(I.)





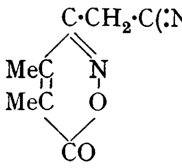
$$\begin{array}{l}\text{MeC·CO·CH}_2\text{·CO·CH}_2\text{·CHMe}_2\\ \;\|\\ \text{MeC·CO}_2\text{H}\end{array}$$

(II.)

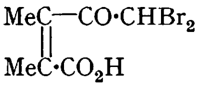
It is hoped at a later date to provide a synthetic proof for the structure now advanced.

As would be anticipated from the triple conjugation, the molecular refraction, $[R_L]_D$ 58·78, shows a considerable exaltation over that, 58·15, calculated for (I).

Analysis of the copper derivative indicates that it must be a co-ordination compound derived from (I) without ring fission, but the sodium derivative is a true salt of the diketonic acid (II). The dioxime anhydride referred to above, which was only obtained in poor yield, is evidently also derived from (II), the dioxime which is first formed losing water with the formation of the oxazine (III).

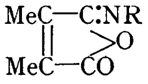


(III.)

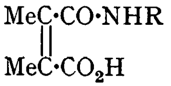


$$\begin{array}{l}\text{MeC—CO·CHBr}_2\\ \;\|\\ \text{MeC·CO}_2\text{H}\end{array}$$

(VIII.)

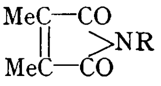


(IV.)

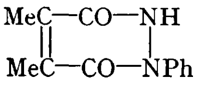


$$\begin{array}{l}\text{MeC·CO·NHR}\\ \;\|\\ \text{MeC·CO}_2\text{H}\end{array}$$

(V.)



(VI.)



(VII.)

So far as we are aware the pseudo-ketonic reactions of dimethylmaleic anhydride have not been recorded previously. The aqueous solution of the anhydride reacts very rapidly with semicarbazide acetate, *p*-nitrophenylhydrazine acetate and with 2 : 4-dinitrophenylhydrazine sulphate to yield crystalline derivatives. These are readily soluble in aqueous sodium carbonate and are therefore probably represented by (IV), dissolving in alkali to give the salts of (V). If they had the alternative and *a priori* more probable structure (VI), they would be neutral. We suggest, therefore, that these derivatives of dimethylmaleic anhydride correspond in structure to the oximes of phthalic anhydride (Brady, Baker, Goldstein, and Harris, J., 1928, 529) and that they are not comparable with the cyclic azine (VII) prepared by Otto and Holst (*J. pr. Chem.*, 1890, **42**, 68) by heating the phenylhydrazine salt of the acid phenylhydrazide of dimethylmaleic anhydride.

The bromo-acid $C_7H_8O_3Br_2$, obtained only in quantity sufficient for analysis, is probably the keto-acid (VIII).

EXPERIMENTAL.

The orange sodium salt (4·5 g.), as separated from the essential oil, was suspended in ether and decomposed by shaking with dilute sulphuric acid. The ethereal extract was well washed with water and dried and the oil (3·3 g.) remaining after removal of the solvent was distilled under diminished pressure, b. p. 145—147°/15 mm. It was redistilled for analysis, b. p. 142°/14 mm., $d_{25°}^{25°}$ 1·0531, $n_D^{25°}$ 1·5203 (Found : C, 69·6; H, 7·6. $C_{12}H_{16}O_3$ requires C, 69·2; H, 7·7%). *Calythrone* is a pale yellow, mobile oil with an unpleasant odour reminiscent of a lower fatty acid. It is acid to litmus and is readily soluble in aqueous ammonia. The *sodium* salt crystallised from water in long, orange-coloured, prismatic needles, m. p. 110—111°, which contained solvent, since when dried at 100° the salt became lighter in colour and had m. p. 196° (Found : C, 57·8; H, 6·7; Na, 9·6. $C_{12}H_{17}O_4Na$ requires C, 58·1; H, 6·8; Na, 9·3%). The *copper* derivative, readily prepared by shaking a ligroin solution of the ketone with aqueous copper acetate, crystallised from benzene in sage-green needles, m. p. 208—210° [Found : C, 60·5; H, 6·25. $(C_{12}H_{15}O_3)_2Cu$ requires C, 60·3; H, 6·3%]. For the preparation of the *dioxime anhydride* a mixture of the ketone (0·4 g.), hydroxylamine hydrochloride (0·55 g.), and potassium hydroxide (0·45 g.) in water (4 c.c.) with sufficient alcohol to give a clear solution was heated on the water-bath for 2 hours. Addition of water to the cooled solution precipitated a crystalline solid (0·15 g.), m. p. *ca.* 130°. The anhydride was dissolved in aqueous sodium hydroxide, precipitated with carbon dioxide, and recrystallised from water, separating in fine needles, m. p. 135° (Found : C, 60·9; H, 7·4. $C_{12}H_{18}O_3N_2$ requires C, 60·5; H, 7·5%).

Oxidation of Calythrone.—To a suspension of the sodium salt (5 g.) in aqueous sodium hydroxide cooled in ice, a solution of sodium hypobromite (sodium hydroxide 7·5 g.; bromine, 15 g.; water, 75 c.c.) was added. Considerable heat was generated and the sodium salt gradually dissolved. After 1 hour the bromoform was separated, the excess of hypobromite removed by sulphur dioxide, and the solution acidified. An oil separated which partly solidified. After saturation with ammonium sulphate, the solution was extracted with ether, the solvent evaporated from the dried extract, and the residual oil distilled in steam, the distillate crystallising in the receiver. The steam distillate was made alkaline, concentrated, acidified, and extracted with ether. The oil (2·3 g.) remaining after the removal of the solvent was mixed with ligroin (b. p. 40—60°), the solid (A) collected, and the filtrate distilled, yielding an oil, b. p. 173—176°/770 mm., which was identified as *iso*valeric acid by the preparation of the *p*-phenylphenacyl ester, m. p. 77—78° both alone and in admixture (Found : C, 76·6; H, 6·8. Calc. for $C_{19}H_{20}O_3$: C, 77·0; H, 6·7%). The solid (A), m. p. 92°, crystallised from *cyclo*hexane or dilute methyl alcohol in fine needles, m. p. 94—95° both alone and in admixture with dimethylmaleic anhydride (Found : C, 57·3; H, 5·1. Calc. for $C_6H_6O_3$: C, 57·1; H, 4·8%). The *methyl* p-*phenylphenacyl* ester, prepared by treating the anhydride with the phenacyl bromide (1 mol.) and the equivalent amount of potassium hydroxide solution and recrystallisation of the product from methyl alcohol, was obtained in woolly needles, m. p. 95° (Found : C, 71·6; H, 5·8. $C_{21}H_{20}O_5$ requires C, 71·6; H, 5·7%). The *semicarbazone*, which formed very rapidly, crystallised from water in long prisms, decomp. 238° or, if rapidly heated, 248°. It did not give good analytical figures; the two distinct preparations analysed yielded the same result (Found : C, 46·6; H, 5·2. $C_7H_9O_3N_3$ requires C, 45·9; H, 4·9%). The p-*nitrophenylhydrazone* crystallised from dilute acetic acid (50%) in long needles, m. p. 214° (Found : C, 55·1; H, 4·4; N, 16·0. $C_{12}H_{11}O_4N_3$ requires C, 55·2; H, 4·2; N, 16·1%). It dissolved in aqueous sodium carbonate to give a pale red solution. The 2 : 4-*dinitrophenylhydrazone* crystallised from ethyl acetate in yellow prisms, decomp. 253—255° (Found : C, 47·1; H, 3·4. $C_{12}H_{10}O_6N_4$ requires C, 47·0; H, 3·3%).

The aqueous residue from the steam distillate gave on evaporation an oil (0·2 g.), which partly crystallised and was readily soluble in aqueous sodium carbonate. After draining on porous porcelain, the *acid* crystallised from benzene–ligroin in prisms, m. p. 129° (Found : C, 28·2; H, 3·1; Br, 53·2. $C_7H_8O_3Br_2$ requires C, 28·0; H, 2·6; Br, 53·3%). It did not react with carbonyl reagents.

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