

CCCXXI.—4-*Alkyl Derivatives of 1-Phenylcyclohexane-3 : 5-dione*.

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THE synthesis of derivatives of *cyclohexane-1 : 3-dione* by addition of compounds of the type of ethyl sodiomalonate to the double bond in ketones of the general formula $>C:CH\cdot CO\cdot CH_3$, and subsequent ring closure (Vorländer, *Ber.*, 1894, **27**, 2053), is so well known that, on reference to the literature, it was surprising to find no information as to the general applicability or otherwise of this method to ketones of the structure $>C:CH\cdot CO\cdot CH_2A$ (A = alkyl or

aryl). The only instance in which the ketone employed was not a methyl ketone is that of the synthesis of 1 : 4-dimethyl-1-ethylcyclohexane-3 : 5-dione from ethyl sodiomalonate and ϵ -methyl- Δ^{δ} -hepten- γ -one (Becher and Thorpe, J., 1922, 124, 1303).

We find that ring closure may be effected in a number of other cases in which A is an alkyl group, and the compounds now described are principally 4-alkyl derivatives of 1-phenylcyclohexane-3 : 5-dione. Thus, the 4-methyl, 4-ethyl, 4-*n*-propyl, 4-*n*-amyl, and 4-benzyl derivatives, required by one of us for the purposes of another investigation, were readily obtained by condensation of ethyl sodiomalonate with styryl ethyl, styryl *n*-propyl, styryl *n*-butyl, styryl *n*-hexyl, and styryl β -phenylethyl ketones, respectively.

Ethyl phenylacetate also was found to condense with styryl ethyl ketone in the presence of sodium ethoxide to yield 1 : 2-diphenyl-4-methylcyclohexane-3 : 5-dione (compare Borsche, *Ber.*, 1909, 42, 4498), but the corresponding reaction did not occur with styryl β -phenylethyl ketone.

EXPERIMENTAL.

Ethyl 1-Phenyl-4-methylcyclohexane-3 : 5-dione-2-carboxylate.—Styryl ethyl ketone (8 g.; 1 mol.) (Harries and Muller, *Ber.*, 1902, 35, 966) was added to a solution of ethyl sodiomalonate prepared from ethyl malonate (8 g.; 1 mol.) in dry alcohol (25 c.c.). The mixture was boiled until neutral to litmus (4 hours); on cooling, the sodium salt of the *product* separated in needles. Water was added, unchanged material removed in ether, the aqueous-alcoholic solution treated with dilute hydrochloric acid, and the precipitate washed with water and crystallised from methyl alcohol containing a little water, giving colourless prisms, m. p. 121—123°, soluble in acetone and ether and very sparingly soluble in water (yield, 79%) (Found : C, 67.8, 68.0; H, 6.7, 6.8. $C_{16}H_{18}O_4 \cdot \frac{1}{2}H_2O$ requires C, 68.1; H, 6.7%).

1-Phenyl-4-methylcyclohexane-3 : 5-dione.—The above-described ester was heated under reflux in alcoholic caustic potash (20% solution) during 2 hours, the bulk of the alcohol then distilled off, the residue acidified with dilute hydrochloric acid and the mixture boiled until evolution of carbon dioxide ceased. The *product*, which crystallised on cooling, separated from hot acetone in small colourless prisms, m. p. 212—213° (sintering at 210°) (yield, 40% calc. on the ester) (Found : C, 76.8; H, 6.9; *M*, 199. $C_{13}H_{14}O_2$ requires C, 77.2; H, 6.9%; *M*, 202).

1-Phenyl-4-ethylcyclohexane-3 : 5-dione.—Styryl propyl ketone (14.5 g.; 1 mol.) (Harries and Bromberger, *Ber.*, 1902, 35, 3088) was boiled with a solution of ethyl sodiomalonate (from 13.3 g.,

1 mol., of ethyl malonate) in absolute alcohol (40 c.c.) until the mixture was neutral to litmus (3 hours). The bulk of the alcohol was distilled off, water (200 c.c.) added, neutral material removed in ether, and the aqueous residue boiled for 2 hours with caustic potash (40 g.). After cooling, the liquid was acidified with hydrochloric acid and the liberated product was decarboxylated by further boiling until carbon dioxide ceased to be evolved. The crystals which separated on standing were washed with water, dried on tile, and recrystallised several times from methyl alcohol and acetone alternately, giving colourless plates, m. p. 200° (yield, 41%) (Found: C, 77.4; H, 7.1. $C_{14}H_{16}O_2$ requires C, 77.7; H, 7.4%).

This compound absorbed oxygen and became resinous in the air. Tendency to resinification has been noticed in other 4-substituted derivatives of dihydroresorcinol (compare Becher and Thorpe, *loc. cit.*; Farmer and Ross, J., 1925, **127**, 2362), but such liability to decomposition would not necessarily appear to depend on the presence of a substituent in the 4-position, since ethyl 1-*n*-propylcyclohexane-3:5-dione-2-carboxylate decomposes on long keeping (Sonn and Burkard, *Ber.*, 1928, **61**, 2479), and 1-benzylcyclohexane-3:5-dione is stated to resinify readily in contact with hydrolytic agents (Linstead and Williams, J., 1926, 2735).

1-Phenyl-4-*n*-propylcyclohexane-3:5-dione, obtained by the condensation of styryl butyl ketone with ethyl sodiomalonate and hydrolysis and decarboxylation of the product, crystallised readily from methyl alcohol and from acetone, forming colourless needles, m. p. 185° (yield, 35%) (Found by microanalysis: C, 77.8; H, 7.4. $C_{15}H_{18}O_2$ requires C, 78.3; H, 7.8%).

1-Phenyl-4-*n*-amylcyclohexane-3:5-dione.—Ethyl malonate (22 g.) and styryl *n*-hexyl ketone (22 g.) were condensed by means of alcoholic sodium ethoxide (from sodium, 2.34 g.), and the resulting ester (27 g.) was hydrolysed and decarboxylated as in the previous preparations. After crystallising from methyl alcohol and acetone, alternately, the product had m. p. 191° (yield, 17 g.) (Found by microanalysis: C, 79.4; H, 8.3. $C_{17}H_{22}O_2$ requires C, 79.1; H, 8.5%).

Ethyl 1-Phenyl-4-benzylcyclohexane-3:5-dione-2-carboxylate.—The following is a more convenient way of preparing styryl β -phenylethyl ketone than the somewhat lengthy process of Harries and Golnitz (*Annalen*, 1903, **330**, 233). A mixture of ethyl benzylacetoacetate (73 g.) with a solution of caustic potash (19 g.) in alcohol (190 g.) was heated under reflux on a steam-bath for 2 hours, a sodium salt separating. After removal of the alcohol the solid was acidified, and decarboxylated by boiling, and the liquid was then cooled and extracted with ether. The extract yielded 44 g. of β -phenylethyl methyl ketone, b. p. $118-122^{\circ}/15-16$ mm. It was found that the

time (3 days) required by Harries and Gollnitz (*loc. cit.*) to condense this substance with benzaldehyde could be shortened to 18 hours provided the reactants were agitated together continuously in a shaking-machine. So prepared, styryl β -phenylethyl ketone melted at 56° , and its oxime after crystallisation from alcohol had m. p. $100\text{--}103^\circ$ (Harries and Gollnitz give 53° and $95\text{--}105^\circ$, respectively).

Styryl β -phenylethyl ketone (23.6 g.) was mixed with an alcoholic solution of ethyl sodiomalonate (from ethyl malonate, 16 g., sodium, 2.5 g., and absolute alcohol, 50 c.c.) and heated on a steam-bath for 3 hours. *Ethyl 1-phenyl-4-benzylcyclohexane-3 : 5-dione-2-carboxylate*, isolated as in a previous similar preparation, formed colourless prisms, m. p. 146° , from ethyl alcohol (yield, 60%) (Found by microanalysis : C, 75.2; H, 6.0. $\text{C}_{22}\text{H}_{22}\text{O}_4$ requires C, 75.7; H, 6.3%).

This ester was converted by hydrolysis and decarboxylation into *1-phenyl-4-benzylcyclohexane-3 : 5-dione*, which crystallised from alcohol in colourless prisms, m. p. $169\text{--}170^\circ$, readily soluble in acetone and methyl alcohol, moderately easily soluble in ethyl alcohol, and sparingly soluble in benzene and in light petroleum (yield, 86% calc. on the ester) (Found : C, 81.9; H, 6.0. $\text{C}_{19}\text{H}_{18}\text{O}_2$ requires C, 82.0; H, 6.4%).

1 : 2-Diphenyl-4-methylcyclohexane-3 : 5-dione was prepared by the same general method from ethyl phenylacetate (41 g.), styryl ethyl ketone (40 g.), and sodium (5.8 g.) in dry alcohol (200 c.c.). After crystallising from boiling methyl alcohol containing a little water, it had m. p. 167° (yield, 21%). It was readily soluble in acetone, moderately easily soluble in hot benzene, and very sparingly soluble in light petroleum or ligroin (Found : C, 81.8; H, 6.4. $\text{C}_{19}\text{H}_{18}\text{O}_2$ requires C, 82.0; H, 6.4%).

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