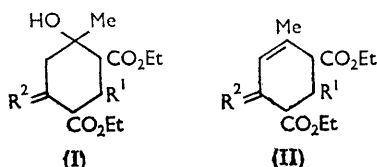


The Reaction of 2,4-Diethoxycarbonyl-5-hydroxy-5-methyl-3-phenylcyclohexanone with 2,4-Dinitrophenylhydrazine

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The reactions of one racemate of 2,4-diethoxycarbonyl-5-hydroxy-5-methyl-3-phenylcyclohexanone with 2,4-dinitrophenylhydrazine have been reinvestigated.

RABE¹ reported that condensation of benzaldehyde with ethyl acetoacetate led to three racemates of 2,4-diethoxycarbonyl-5-hydroxy-5-methyl-3-phenylcyclohexanone (I; R¹ = Ph, R² = O), which he designated β_1 , β_2 , and β_3 , and that the major product, β_1 , m. p. 149–150°, could be separated by crystallisation from ethanol.

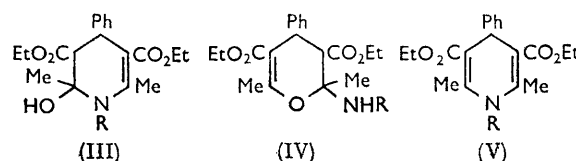


In our hands the condensation gave a mixture of five compounds, from which the major component, m. p. 154–156°, was obtained, chromatographically pure, by crystallisation from ethanol. This material had an n.m.r. spectrum in agreement with the β -hydroxy-ketone structure (I; R¹ = Ph, R² = O) which confirmed earlier evidence^{2,3} in favour of this cyclic structure.

The β -hydroxy-ketone (I; R¹ = Ph, R² = O) behaved towards 2,4-dinitrophenylhydrazine in a manner exactly analogous to the β -hydroxy-ketone (I; R¹ = Me, R² = O) studied by us previously.⁴ At room temperature the 2,4-dinitrophenylhydrazone (I; R¹ = Ph, R² = N·NH·C₆H₃[NO₂]₂), (P), m. p. 226–228°, was obtained. Dehydration of hydrazone (P) gave two isomeric derivatives (II; R¹ = Ph, R² = N·NH·C₆H₃[NO₂]₂) of the corresponding $\alpha\beta$ -unsaturated ketone (II; R¹ = Ph, R² = O), (Q), m. p. 173–174°, and (R), m. p. 151–154°, and several other unidentified minor products. Treatment of the $\alpha\beta$ -unsaturated ketone (II; R¹ = Ph, R² = O), obtained by dehydration of (I; R¹ = Ph, R² = O) gave hydrazone (Q), together with a second, minor, product.

Kuss and Karrer⁵ have previously investigated the reaction of 2,4-dinitrophenylhydrazine with a compound, m. p. 150–151°, which they obtained by the condensation of benzaldehyde with ethyl acetoacetate, and which they formulated as diethyl 4-phenyl-2,6-dioxoheptane-3,5-dicarboxylate. They reported two products; one, (A), C₂₅H₂₈N₄O₉, m. p. 194–196°, was obtained under mild conditions, and the other (B), C₂₅H₂₆N₄O₈, m. p. 169–170°, under more vigorous, dehydrating, conditions. The former was tentatively formulated as either (III; R = NH·C₆H₃[NO₂]₂) or (IV; R = NH·C₆H₃[NO₂]₂), and the latter as (V; R = NH·C₆H₃[NO₂]₂).

Through the courtesy of Professor Karrer, we have now compared his samples (A) and (B) with our hydrazones (P) and (Q), respectively. No sample of Professor Karrer's starting material has survived, but there can be little doubt from its mode of preparation and purification that it was identical with our own, and had the cyclic structure (I; R¹ = Ph, R² = O). Compound (A) in our hands did not melt at 194–196°, as reported,⁵ but at 223–225°. After recrystallisation it had m. p. 226–228° and was identical (i.r., t.l.c.) with hydrazone (P). Compound (B) was shown by t.l.c. to be essentially identical with hydrazone (Q) but to be contaminated with a trace of (P) which cannot be removed by recrystallisation. The apparent differences



between our products and those of Kuss and Karrer are thus resolved.

The formulation of our products as 2,4-dinitrophenylhydrazones is supported by their n.m.r. spectra, which closely resemble those⁴ of the 2,4-dinitrophenylhydrazones derived from the cyclic ketones (I and II; R¹ = Me, R² = O), and are incompatible with structures (III), (IV), and (V). The n.m.r. spectrum of (P) shows absorption due to the two ester methyl groups and to one other methyl group, whereas both (III) and (IV) should show absorption due to a total of four methyl groups. The n.m.r. spectrum of (Q) shows absorption due to a vinylic proton and to only one methyl group attached to a double bond, ruling out the symmetrical structure (V), so that, as far as we are aware, the only authentic derivative of *N*-anilino-1,4-dihydropyridine is now that reported⁶ by Lloyd and Wasson.

EXPERIMENTAL

For general directions see the earlier Paper.⁴

Starting Materials.—2,4-Diethoxycarbonyl-5-hydroxy-5-methyl-3-phenylcyclohexanone (I; R¹ = Ph, R² = O), m. p. 154–156° (lit.^{1,3} 149–150°; 157–158°), τ 9.20 (4-ester CH₃, triplet, 3H), 8.97 (2-ester CH₃, triplet, 3H), 8.65 (5-CH₃, singlet, 3H), and 7.35 (6-CH₂, singlet 2H), 6.30 (OH, singlet, 1H), was prepared by Rabe's method.¹ On dehydration with ethanolic hydrogen chloride¹ it gave 4,6-diethoxycarbonyl-3-methyl-5-phenylcyclohex-2-enone

¹ P. Rabe, *Annalen*, 1900, **313**, 129.

² P. Rabe and F. Elze, *Annalen*, 1902, **323**, 83.

³ I. L. Finar, *J. Chem. Soc.*, 1961, 674.

⁴ T. D. Binns and R. Brettle, *J. Chem. Soc. (C)*, 1966, 336.

⁵ L. Kuss and P. Karrer, *Helv. Chim. Acta*, 1957, **40**, 740.

⁶ D. Lloyd and F. I. Wasson, *J. Chem. Soc. (C)*, 1966, 1086.

(III; $R^1 = \text{Ph}$, $R^2 = \text{O}$), m. p. $88-91^\circ$ (lit.,¹ $86-87^\circ$), τ 9.04 and 9.01 (each ester- CH_3 , triplets, 6H), 8.01 (3- CH_3 , singlet, 3H), and 3.91 (2-H, singlet, 1H). Both ketones ran as single spots on t.l.c.

2,4-Dinitrophenylhydrazones.—The β -hydroxy-ketone (I; $R^1 = \text{Ph}$, $R^2 = \text{O}$) (1.74 g.) was treated with 2,4-dinitrophenylhydrazine (1.0 g.) in diglyme (25 ml.) containing acetic acid (3 ml.) at room temperature. Crystals separated on standing and, after recrystallisation alternately from carbon tetrachloride and benzene, gave a 2,4-dinitrophenylhydrazone (P), m. p. (taken very slowly) $226-228^\circ$, λ_{max} 362 m μ (ϵ_{max} 23,300), τ 9.20 (4-ester CH_3 , triplet, 3H), 8.91 (2-ester CH_3 , triplet, 3H), and 8.56 (5- CH_3 , singlet, 3H) (Found: C, 56.6; H, 5.2; N, 10.7. $\text{C}_{25}\text{H}_{28}\text{N}_4\text{O}_9$ requires C, 56.6; H, 5.4; N, 10.6%). The $\alpha\beta$ -unsaturated ketone (II; $R^1 = \text{Ph}$, $R^2 = \text{O}$) on treatment with Brady's reagent gave a crude product, which on crystallisation from ethanol and then carbon tetrachloride gave a 2,4-dinitrophenyl-

hydrazone (Q), m. p. $173-174^\circ$, λ_{max} 376 m μ (ϵ_{max} 30,500), τ 8.95 (ester CH_3 , triplet 6H), 7.93 (3- CH_3 , singlet, 3H), and 3.50 (2-H, singlet, 1H) (Found: C, 59.0; H, 5.3; N, 11.0. $\text{C}_{25}\text{H}_{26}\text{N}_4\text{O}_8$ requires C, 58.7; H, 5.2; N, 11.0%). 2,4-Dinitrophenylhydrazone (P) (1.0 g.) in ethanol (45 ml.) containing sulphuric acid (0.1 ml.) was heated under reflux for 3.5 hr. Crystals separated, on cooling, which on recrystallisation from ethanol, and then carbon tetrachloride, had m. p. and mixed m. p. $173-174^\circ$ with hydrazone (Q). T.l.c. on the remaining material gave a second 2,4-dinitrophenylhydrazone (R), m. p. $151-154^\circ$ (from ethanol), λ_{max} 382 m μ (ϵ_{max} 28,600), τ 8.97 and 8.92 (each ester CH_3 , triplets, 6H), 7.97 (3- CH_3 , singlet, 3H), and 3.65 (2-H, singlet, 1H) (Found: C, 58.8; H, 5.0; N, 11.0%).

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