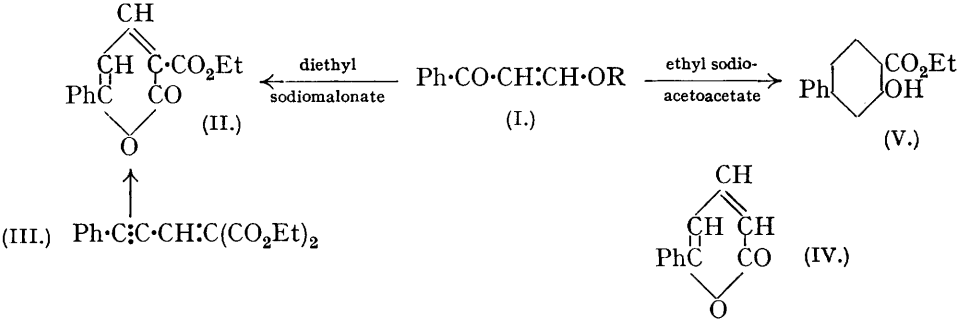
27. *Some Observations on Alkyl Ethers of Hydroxymethyleneacetophenone.*

By James Walker.

According to the literature the *O*-alkylation of hydroxymethyleneacetophenone is not a facile process. The *methyl* and the ethyl ether have, however, been prepared. The latter on condensation with ethyl sodiomalonate yielded *ethyl* 6-*phenylcoumalin*-3-*carboxylate*, and the former on treatment with ethyl sodioacetoacetate gave *ethyl* 3-*hydroxydiphenyl*-4-*carboxylate*. 3-*Hydroxydiphenyl*-4-*carboxylic acid* and 3-hydroxydiphenyl were also prepared.

Von Auwers has commented (*Ber.*, 1938, **71**, 2082) on the difficulty of preparing alkyl ethers of hydroxymethyleneacetophenone and pointed out that he and Schmidt (*Ber.*, 1925, **58**, 536) succeeded in preparing the ethyl ether, following failure by Claisen. Sen and Mondal (*J. Indian Chem. Soc.*, 1928, **5**, 627) attempted to prepare the methyl and the ethyl ether, but were unable to obtain pure specimens; in any case, the boiling point (120—130°/45 mm.) of their supposed methyl ether does not bear comparison with that (145—147°/12 mm.) of the authentic substance described below, and their ethyl compound was merely described as a " coloured liquid " yielding acetophenone on hydrolysis and no constants were quoted.

The lability of these ethers makes the attainment of satisfactory yields difficult, but the *methyl* (I; R = Me) and the ethyl (I; R = Et) representative have been prepared. Ethoxymethyleneacetophenone (I; R = Et), on treatment with ethyl sodiomalonate, yielded an unstable product, passing, with loss of alcohol, into *ethyl 6-phenylcoumalin-3-carboxylate* (II), probably identical with the compound stated, with no details beyond melting point (107—108°), by Claisen (*Ber.*, 1903, **36**, 3671) to result from the action of dilute sulphuric acid on ethyl phenylpropargylidenemalonate (III). The compound (II) is a possible laboratory precursor of the natural product 6-phenylcoumalin (IV), but no convenient method of effecting the necessary conversion, (II) ⟶ (IV), was, however, disclosed by exploratory experiments.



Methoxymethyleneacetophenone (I; R = Me), on condensation with ethyl sodioacetoacetate, yielded *ethyl 3-hydroxydiphenyl-4-carboxylate* (V). The free *acid* was prepared and subsequent decarboxylation gave 3-hydroxydiphenyl.

EXPERIMENTAL.

Methoxymethyleneacetophenone (I; R = Me).—(a) Crude sodio-derivative (68 g.) of hydroxymethyleneacetophenone (v. Auwers and Schmidt, *loc. cit.*, p. 535) was dissolved in absolute alcohol (200 c.c.) and refluxed with methyl iodide (40 c.c.; 1·5 mols.) until the mixture had a neutral reaction (approx. 1½ hours). The solvent was largely removed under diminished pressure, and the residue mixed with water and extracted with ether. The extract was washed with very dilute sodium hydroxide solution and then with water, dried (anhydrous sodium sulphate), and evaporated. The product (37 g.) was fractionally distilled under diminished pressure and a fraction (22·2 g.), b. p. 100—160°/16 mm. (mainly 150°/16 mm.), was collected, leaving a considerable tarry residue. On further fractionation the distillate yielded the *methyl* ether as a faintly yellow oil (14·5 g.), b. p. 145—147°/12 mm., $n_{\mathrm{D}}^{14^\circ}$ 1·5688 (Found: C, 74·2; H, 6·4; OMe, 19·6. $C_{10}H_{10}O_2$ requires C, 74·1; H, 6·2; OMe, 19·2%). Rectangular plates separated from the oil on standing.

(b) Crude sodio-derivative (45 g.) of hydroxymethyleneacetophenone was dissolved in water (100 c.c.) and shaken mechanically with a slight deficit of methyl sulphate (21·2 c.c.; 85% of 1 mol.) for 24 hours. The whole was mixed with water, and an ethereal extract manipulated as above. The pure product (11 g.) distilled at 140—145°/11 mm., $n_{\mathrm{D}}^{11^\circ}$ 1·5750. There was again a considerable tarry residue in the preliminary fractionation.

Ethoxymethyleneacetophenone (I; R = Et).—This was prepared by method (a) above, ethyl iodide being used. The product (*ca.* 25% yield) had properties in agreement with those recorded by v. Auwers and Schmidt (*loc. cit.*).

Ethyl 6-Phenylcoumalin-3-carboxylate (II).—Ethoxymethyleneacetophenone (8·3 g.) in absolute alcohol (10 c.c.) was added to an absolute-alcoholic solution (50 c.c.) of ethyl sodiomalonate (8·1 g. of ester; 1·15 g. of sodium) cooled in a freezing mixture. A golden-yellow colour developed immediately and deepened to reddish-orange in a few hours while a small amount of solid separated. After 24 hours ice-water was added and the heavy oil precipitated was extracted with ether, dried (anhydrous sodium sulphate), and recovered as a light brown oil (16·7 g.); this, on distillation under reduced pressure, appeared to undergo decomposition with separation of a low-boiling liquid (presumably alcohol, though not examined); subsequently a fraction (5·1 g.) was collected, b. p. 185—195°/0·3 mm., as a yellow oil which crystallised spontaneously. The *ethyl* ester (II) was extremely readily soluble in all the common solvents except ether and light petroleum. Crystallisation from a small volume of ether afforded long, lemon-yellow, prismatic needles, m. p. 105—106° (Found: C, 68·8; H, 5·0. $C_{14}H_{12}O_4$ requires C, 68·8; H, 4·9%). The ester possessed the peculiar property of showing a strong green fluorescence in the crystalline state but was non-fluorescent in solution or in the fused supercooled state.

Ethyl 3-*Hydroxydiphenyl*-4-*carboxylate* (V).—Ethyl acetoacetate (8·6 c.c.; 1 mol.) was converted into the sodio-derivative with powdered sodium (1·56 g.) in dry benzene (50 c.c.) and then, after thorough cooling, treated with methoxymethyleneacetophenone (11 g.; 1 mol.), which was washed into the mixture with a little dry benzene. Two orange-coloured layers were formed, the lower being somewhat viscous. After 40 hours at room temperature the mixture was refluxed for an hour, cooled, and shaken with dilute acetic acid. The separated benzene layer, dried (anhydrous sodium sulphate) and evaporated, yielded a crude brown oil (18·1 g.), which was distilled in a vacuum. After removal of fore-runnings a colourless viscous oil (7·0 g.) distilled at 165—195°/0·3 mm. (mainly 190°/0·3 mm.) and crystallised completely on being cooled and scratched. The *ethyl* ester (V) separated from alcohol in stellate clusters of colourless prisms, m. p. 44—45° (Found: C, 74·3; H, 5·8. $C_{15}H_{14}O_3$ requires C, 74·4; H, 5·8%). With aqueous alcoholic ferric chloride a port-wine colour was developed.

3-*Hydroxydiphenyl*-4-*carboxylic Acid*.—The foregoing ester (0·5 g.) in methyl-alcoholic solution (6 c.c.) was warmed with 30% aqueous potassium hydroxide (3 c.c.; 5 mols.) under reflux on the water-bath for 20 minutes. Dilution with water caused separation of the potassium salt; this was redissolved by warming, and dilute hydrochloric acid liberated the free acid, which was collected in a centrifuge, washed with water, and dried over phosphoric oxide in a vacuum desiccator (yield, 0·45 g.). Recrystallisation from glacial acetic acid or, better, 85% acetic acid afforded small, compact, colourless prisms, m. p. 207—208° (Found: C, 72·9; H, 4·6. $C_{13}H_{10}O_3$ requires C, 72·9; H, 4·7%). The *acid* gave a purple colour with ferric chloride in aqueous alcoholic solution.

3-*Hydroxydiphenyl*.—The above acid underwent only partial decarboxylation when heated, and the following method was adopted. The acid (0·56 g.) was refluxed (metal-bath, 270°) in quinoline (5 c.c.) with copper chromite (0·1 g.) (Adkins and Connor, *J. Amer. Chem. Soc.*, 1931, **53**, 1092; cf. Reichstein, Grüssner, and Zschokke, *Helv. Chim. Acta*, 1932, **15**, 1067) for 25 minutes. The cooled mixture, in ethereal solution, was filtered through norit and washed repeatedly with dilute mineral acid to remove quinoline, with sodium bicarbonate solution to remove any unchanged acid, and finally thrice with potassium hydroxide solution to recover the phenol. The crude phenol (0·44 g.), recovered from the caustic alkali washings, was treated with norit in aqueous alcoholic solution and then recovered (0·37 g.) by means of ether. The compound separated from light petroleum (b. p. 60—80°) in long colourless needles, m. p. 74—75° alone and in admixture with an authentic specimen (m. p. 74—75°) kindly supplied by Dr. D. H. Hey (Found: C, 84·7; H, 5·9. Calc. for $C_{12}H_{10}O$: C, 84·7; H, 5·9%). Errera and La Spada (*Gazzetta*, 1905, **35**, ii, 552) and Jacobson and Loeb (*Ber.*, 1903, **36**, 4085) record m. p. 75° and 78° respectively.

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