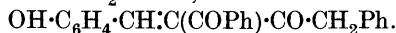


CCLVIII.—*The Relative Reactivity of Methylene Groups in 1:3-Diketones.*

By ARTHUR BERTRAM EDMUND LOVETT and ELWYN ROBERTS.

THE present investigation was designed to discover which methylene group, in a diketone of the general formula  $\text{CH}_2\text{R}\cdot\text{CO}\cdot\text{CH}_2\cdot\text{COR}'$ , would be the more reactive as regards condensation with aldehydes. Bülow and Grotowsky (*Ber.*, 1901, **34**, 1479) assumed that in  $\omega$ -phenylacetylacetophenone,  $\text{CH}_2\text{Ph}\cdot\text{CO}\cdot\text{CH}_2\cdot\text{COPh}$ , the methylene group adjacent to the benzoyl radical was the more reactive towards nitrous acid and diazo-compounds. Different aldehydes, however, behave very differently towards phenylacetylacetophenone in presence of piperidine; for instance, benzaldehyde and cinnamaldehyde give resins, but salicylaldehyde readily condenses in alcohol or benzene solution. Since the resulting *o*-hydroxybenzylidenephylacetylacetophenone is readily convertible, in good yield, into acetophenone and 3-phenylcoumarin, it must have the formula  $\text{OH}\cdot\text{C}_6\text{H}_4\cdot\text{CH}:\text{CPh}\cdot\text{CO}\cdot\text{CH}_2\cdot\text{COPh}$ , and not



The more reactive methylene group in  $\omega$ -phenylacetylacetophenone is therefore that adjacent to the phenyl group. The formation of 3-phenylcoumarin cannot be attributed to an initial hydrolysis

giving rise to phenylacetic acid and acetophenone, since phenylacetic acid does not condense with salicylaldehyde under the same conditions to give the coumarin. Furthermore, the intermediate product on continued recrystallisation from a non-aqueous solvent such as benzene gives a mixture in which 3-phenylcoumarin increasingly preponderates. It reacts with concentrated sulphuric acid and acetic anhydride to give products of undetermined constitution.

5-Methyl, 5-chloro-, 5-bromo-, 5-nitro-, 3-nitro-, 3 : 5-dichloro-, 3 : 5-dibromo-, and 3-nitro-5-methyl-salicylaldehydes condense with  $\omega$ -phenylacetylacetophenone under similar conditions to give substituted 3-phenylcoumarins, but in no case could the intermediate product be isolated. The yield of coumarin, except from salicylaldehyde and its 5-methyl derivative, was small, indicating the influence of substituents on the condensation. From 5-bromo-3-nitrosalicylaldehyde a trace only of the coumarin, and from 5-chloro-3-nitro- and 3 : 5-dinitro-salicylaldehydes no coumarin was obtained; these three aldehydes react with piperidine to give stable piperidides of undetermined constitution. Phenylacetylacetophenone and 2-hydroxy- $\alpha$ -naphthaldehyde in the presence of piperidine give, not the expected 3-phenylbenzocoumarin, but a red compound probably having formula  $C_{27}H_{18}O_2$ . 2-Hydroxy- $\alpha$ -naphthaldehyde, however, condenses with ethyl acetoacetate to give 3-acetobenzocoumarin (Knoevenagel and Schrötter, *Ber.*, 1904, **37**, 4484; compare Bülow and Grotowsky, *Ber.*, 1902, **35**, 1803).

$\omega$ -Propionyl- and butyryl-acetophenones and propionylacetone were condensed with salicylaldehyde and substituted salicylaldehydes in the presence of piperidine. Resin-like products were obtained from which no crystalline solid could be isolated. The effect of the nature of the groups R, R' on the reactivity of the methylene groups could not therefore be readily determined by this method.

In all cases the coumarins were synthesised for identification purposes by the Perkin reaction. The yield of coumarin by this method was good, in contradistinction to the poor yields obtained by condensation of aldehyde and ketone.

#### EXPERIMENTAL.

$\omega$ -Phenylacetyl-, propionyl-, and butyryl-acetophenones and propionyl-acetone were prepared by a modification of Claisen's method, a suspension of powdered sodium in xylene being used instead of anhydrous sodium ethoxide.

*Propionylacetophenone.*—The green copper salt crystallised from acetone in needles, m. p. 151—152°. The pure ketone boils at

149°/17 mm. or 151°/19 mm. Beyer and Claisen (*Ber.*, 1887, 20, 2178) give b. p. 170—172°/30—31 mm.

The *p*-nitrophenylhydrazone was obtained by heating 1.76 g. (1 mol.) of the ketone and 1.53 g. (1 mol.) of *p*-nitrophenylhydrazine at 100° for 7 hours. The product, a thick gum, when covered with 96% alcohol and kept for 3 days, set to a solid mass. It was crystallised from aqueous alcohol, in which it was fairly easily soluble, and then from light petroleum (b. p. 80—100°), fine yellow needles (1.3 g.), m. p. 67—68°, being obtained (Found: N, 13.4.  $C_{17}H_{17}O_3N_3$  requires N, 13.5%).

*Propionylacetophenoneanil.*—A mixture of 5 g. (1 mol.) of the ketone and 2.64 g. (1 mol.) of freshly distilled aniline was heated under reflux for  $\frac{1}{2}$  hour; no more water then appeared to separate. Benzene extracted from the product a dark brown, mobile oil which deposited a solid after a few days. This, after being pressed on porous porcelain, crystallised from light petroleum (b. p. 40—60°), in which it was readily soluble, in prisms (1.8 g.), m. p. 48—49° (Found: N, 5.7.  $C_{17}H_{17}ON$  requires N, 5.6%).

*Condensation of Salicylaldehydes with  $\omega$ -Phenylacetylacetophenone.*—A solution of salicylaldehyde (7.5 g.; 1 mol.) and phenylacetylacetophenone (14.6 g.; 1 mol.) in 25 c.c. of absolute alcohol was treated with piperidine (45 drops; which produced a marked development of heat and deepening of colour) and heated on the water-bath; *o*-hydroxybenzylidenephénylacetylacetophenone separated in prisms from the hot liquor. The latter was decanted, and the solid washed with alcohol and collected (13.3 g.; m. p. 171—174°) (Found: C, 80.6; H, 5.3.  $C_{23}H_{18}O_3$  requires C, 80.7; H, 5.3%). Recrystallisation from alcohol or benzene lowers the melting point. The yield of product depends upon the amount of piperidine used, the above quantity giving the maximum yield.

The mother-liquor was heated on the water-bath for a further hour; 3-phenylcoumarin (2.4 g.) separated on cooling.

If the intermediate product was not isolated, it gradually dissolved on prolonged heating (5 hours); on cooling, almost pure 3-phenylcoumarin (7.0 g.) separated, m. p. 140—141° (Found: C, 81.1; H, 4.5. Calc.: C, 81.1; H, 4.5%).

The same products were obtained on varying the molecular proportion of aldehyde and ketone.

Ethyl phenylacetate (1 mol.) and salicylaldehyde (1 mol.), on heating on the water-bath for 4 hours in presence of piperidine, gave a 16% yield of pure 3-phenylcoumarin.

In the condensations of  $\omega$ -phenylacetylacetophenone and substituted *o*-hydroxyaldehydes the same method was employed, the period of heating varying from 7 to 11 hours. In some cases the

coumarin was deposited from the hot solution. Unless otherwise stated in the following table, the coumarin was crystallised from alcohol, in which it was very sparingly soluble. The yields obtained (I) by ketone condensation and (II) by the Perkin reaction are given.

Substituted 3-phenyl- coumarin.	Form.	M. p.	% found.	% calc.	Yield. (I), (II).
6-Chloro- .....	Pale yellow prisms	199°	Cl, 14.3	13.8	25 40
6-Bromo- .....	"	189—191	Br, 26.6	26.5	25 62
6-Nitro- .....	Yellow prisms	251—253	N, 5.3	5.3	4 60
6-Methyl- .....	Pale yellow needles	146—147.5	{ C, 80.2 H, 5.1	{ 80.4 5.1	{ 42 40
8-Nitro- .....	"	236—239	N, 5.3	5.3	4 65
6 : 8-Dichloro- ...	Colourless needles *	193—194.5	Cl, 24.5	24.5	16 27
6 : 8-Dibromo- ...	"	186—187.5	Br, 42.3	42.1	trace 30
6 : 8-Dinitro- .....	Pale yellow needles *	244—246	N, 8.9	9.0	0 60
6-Chloro-8(?)nitro-	Yellow needles	212—214	Cl, 11.6	11.7	0 70
6-Bromo-8-nitro-	Plates †	228—230	Br, 22.8	23.1	trace 74
8-Nitro-6-methyl-	Yellow needles	180—182	N, 5.0	5.0	12.5 44

\* From acetic acid.

† From acetic anhydride.

**3 : 5-Dinitrosalicylaldehyde.**—The mixture of 3- and 5-nitrosalicylaldehydes (33 g.) obtained by the nitration of salicylaldehyde (von Miller, *Ber.*, 1887, **20**, 1927) was added cautiously, with cooling in ice and salt, to a mixture (100 g.) of concentrated sulphuric acid (2 parts) and nitric acid (*d* 1.5; 1 part). After 30 minutes the nitration mixture was poured on ice, and the yellow product was washed with ice-water, dried, and crystallised three times from benzene, giving lemon-yellow prisms (20 g.), m. p. 58—60° (Found : N, 13.1.  $C_7H_4O_6N_2$  requires N, 13.2%). Its constitution was proved by oxidising it by alkaline permanganate to 3 : 5-dinitrosalicylic acid.

**5-Chloro-3(?)nitrosalicylaldehyde.**—A solution of 8.1 g. of 5-chlorosalicylaldehyde in 100 c.c. of glacial acetic acid was slowly treated at 60—70° with nitric acid (*d* 1.42; 8 c.c.). The solution was then cooled slowly, the yellow, crystalline product removed, the filtrate diluted with 100 c.c. of water, and the precipitated solid collected. The combined product was crystallised twice from light petroleum (b. p. 80—100°), from which it separated in yellow needles (5.5 g.), m. p. 105—107° (Found : Cl, 17.4.  $C_7H_4O_4NCl$  requires Cl, 17.6%). The constitution of this aldehyde was inferred by analogy, since 5-bromosalicylaldehyde nitrates under identical conditions (von Auwers and Bürger, *Ber.*, 1898, **31**, 3934) to give 5-bromo-3-nitrosalicylaldehyde.

**Condensation of 2-Hydroxy- $\alpha$ -naphthaldehyde and  $\omega$ -Phenylacetylacetophenone.**—A solution of 2.4 g. (1 mol.) of the ketone, 1.72 g. (1 mol.) of the aldehyde, and 7 drops of piperidine in 5 c.c. of

absolute alcohol was heated on the water-bath for 2 hours. On cooling, no separation of solid occurred. The mixture was then heated for a further 9 hours; on cooling, a red crystalline mass was now obtained. After being washed with spirit, this crystallised from alcohol, in which it was very sparingly soluble (1 g. in 200 c.c.), in small, deep blood-red prisms (0.9 g.), m. p. 155—156.5° (Found : C, 86.8; H, 4.9.  $C_{27}H_{18}O_2$  requires C, 86.6; H, 4.8%).

The authors desire to thank the Research Fund Committee of the Chemical Society for a grant which has partly defrayed the cost of this investigation.

EAST LONDON COLLEGE,  
UNIVERSITY OF LONDON.

[Received, May 15th, 1928.]

---