CCCXIV.—*The Hydrolytic Fission of Some Substituted Dibenzoylmethanes.*

By WILLIAM BRADLEY and ROBERT ROBINSON.

IN the present communication, we submit an account of a quantitative study of the hydrolysis of unsymmetrical derivatives of dibenzoylmethane by means of 1% aqueous sodium hydroxide. A diketone, $R\cdot CO\cdot CH_2\cdot CO\cdot R_1$, usually yields a mixture of $R\cdot CO_2H$, $R\cdot CO\cdot CH_3$, $R_1\cdot CO_2H$ and $R_1\cdot CO\cdot CH_3$, and the plan has been adopted of estimating the proportions of the carboxylic acids which are formed. The reactions examined were carried to completion and concordant results were obtained in the analysis and in control experiments. Calculations from the data recorded in the experimental section lead to the results in the following table which shows the number of molecules of $R\cdot CO_2H$ and $R_1\cdot CO_2H$, respectively, derived from 100 molecules of each of the various diketones, $R\cdot CO\cdot CH_2\cdot CO\cdot R_1$.

R.	R_1.	$R\cdot CO_2H$.	$R_1\cdot CO_2H$.
o-Methoxyphenyl.	Phenyl.	82·1	17·9
m- ,, ,,	,,	61·9	38·1
p- ,, ,,	,,	50·2	49·8
p-*iso*Propoxyphenyl.	,,	33·0	67·0
m-Chlorophenyl.	,,	66·4	33·6
p- ,, ,,	,,	63·7	36·3
m-Nitrophenyl.	,,	82·3	17·7
p- ,, ,,	,,	80·7	19·3
2 : 4-Dimethoxyphenyl.	,,	74·7	25·3
3 : 4- ,, ,, ,,	,,	50·8	49·2
m-Methoxyphenyl.	*p*-Methoxyphenyl.	79·0	21·0
3 : 4 : 5-Trimethoxyphenyl.	Phenyl.	68·8	31·2
m-Methoxyphenyl.	3 : 4-Dimethoxyphenyl.	40·1	59·9
p- ,, ,,	3 : 4- ,, ,, ,,	34·2	65·8

α-Anisoylpropiophenone gave 61·1 and 38·9 mols. of anisic and benzoic acids, respectively.

With two exceptions, the stronger * of the acids which might be formed was found to be produced in the greater relative amount, but the existence of any exceptions at all shows that no such simple analysis of the effects of the substituents is possible. Especially striking is the fact that anisic and benzoic acids are obtained in different proportions by the hydrolysis of ω-anisoylacetophenone, $MeO\cdot C_6H_4\cdot CO\cdot CH_2\cdot CO\cdot Ph$, and α-anisoylpropiophenone,

$$MeO\cdot C_6H_4\cdot CO\cdot CHMe\cdot CO\cdot Ph.$$

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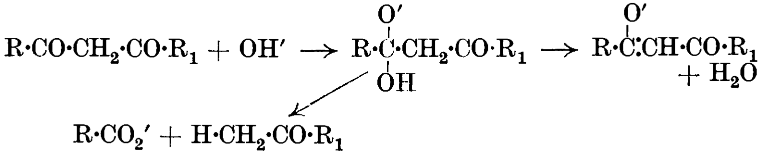
* As a matter of fact, the dissociation constants of some of the acids concerned have not yet been determined, but in every such case strong analogies are available which enable us to estimate the limits of probable values. For example, the strength of *m*-methoxybenzoic acid has not been directly determined, but it should be slightly stronger than benzoic acid in view of the fact that veratric acid is slightly stronger than anisic acid.

It became apparent that the condition of the tautomeric system in the dibenzoylmethanes has an important bearing on the direction of the hydrolytic fission, and that this should be the case follows also from a consideration of the probable mechanism of the reaction. In this connexion, the following suggestions appear to accord best with modern conceptions. (1) The hydrolytic fission of dibenzoylmethanes is a reaction characteristic of the diketonic phases and does not occur in the keto-enolic modifications. Satisfactory evidence is available in support of this proposition and it will suffice to note that compounds of fixed open-chain β-diketonic structure are readily hydrolysed by alkalis whereas substances having fixed keto-enolic structures and related to β-diketones are relatively stable to hydroxyl ions. (2) On account of the consideration given in (1), the extent of enolisation, great as it is, and the nature of the enols do not affect the result of hydrolytic fission except as mentioned below. (3) The hydrolysis is probably the result of the decomposition of a complex anion formed from the diketone and hydroxyl ion :



$$R{\cdot}CO{\cdot}CH_2{\cdot}CO{\cdot}R_1 + OH' \longrightarrow R{\cdot}\overset{O'}{\underset{OH}{C}}{\cdot}CH_2{\cdot}CO{\cdot}R_1 \longrightarrow R{\cdot}\overset{O'}{C}{:}CH{\cdot}CO{\cdot}R_1 + H_2O$$
$$\swarrow$$
$$R{\cdot}CO_2' + H{\cdot}CH_2{\cdot}CO{\cdot}R_1$$

The complex ion may undergo other transformations of which the most important is the formation of the enolic modifications as illustrated in the above scheme. (4) Hence the chief factors controlling the direction of the change are (*a*) the rates of formation of the two possible complex anions, $R{\cdot}CO'(OH){\cdot}CH_2{\cdot}CO{\cdot}R_1$ and

$$R{\cdot}CO{\cdot}CH_2{\cdot}CO'(OH){\cdot}R_1,$$

and (*b*) the extent to which each of these breaks down with the formation of carboxylate ions. The factor (*a*) should be connected with the relative degree of positive polarity exhibited by the carbonyl groups and therefore with the dissociation constants of the acids $R{\cdot}CO_2H$ and $R_1{\cdot}CO_2H$. As we have already pointed out, a great majority of our experimental results are in accord with this view. A second group of factors influencing (*a*) concerns the nature of the reagent and the solvent, but in the present series these conditions are approximately constant. If, in a certain time, x and x' hydroxyl ions become attached to the groups $R{\cdot}CO{\cdot}$ and $R_1{\cdot}CO{\cdot}$, respectively, and if ax and $a'x'$ represent the numbers of the resulting complex ions respectively which, chiefly by formation of the enols, do not undergo fissions, then we find :

$$R{\cdot}CO_2H \text{ obtained}/R_1{\cdot}CO_2H \text{ obtained} = (1 - a)x/(1 - a')x'.$$

It is beyond our power in the present state of knowledge to develop this expression in any exact manner from a theoretical point of view, but its form shows that the results we have recorded above are not necessarily opposed to the theory. The ratio x/x' may be connected in some relatively simple manner with the dissociation constants of the acids $R\cdot CO_2H$ and $R_1\cdot CO_2H$, and on the most plausible assumptions of this kind (*e.g.*, that $x/x' = \log K/K'$) we find that the remarkable effect of the substitution of methyl for hydrogen in ω-anisoylacetophenone is susceptible of a simple explanation. The introduction of the methyl group decreases the extent to which each of the complex ions breaks down into a related enol, but this effect is proportionately greater in the case of the formation of the enol, $Ph\cdot CO\cdot CMe{:}C(OH)\cdot C_6H_4\cdot OMe$ than in that of the enol, $Ph\cdot C(OH){:}CMe\cdot CO\cdot C_6H_4\cdot OMe$. In other words, the inhibition of the production of an enol is more efficient in the case of the weaker enol. The assumption that the enol mentioned first above is the weaker is justified by the consideration that the mechanism of the formation of $-C(O)' = CH-$ from $-CO\cdot CH_2-$ should be analogous to that of $-CO'_2$ from $-CO\cdot OH$ and by the fact that anisic acid is weaker than benzoic acid. We do not here attempt a more detailed discussion of the results, since experiments are in progress which should enable us to evaluate approximately the ratio x/x'.

EXPERIMENTAL.

ω-Anisoylacetophenone.—This substance has been prepared by the action of sodium ethoxide on anisylideneacetophenone dibromide (Pond and Maxwell, *J. Amer. Chem. Soc.*, 1899, **21**, 966). We obtained it by the condensation of ethyl anisate with acetophenone or of ethyl benzoate with *p*-acetylanisole, the latter process giving the better yield. Powdered sodamide (5 g.) was quickly added to a solution of *p*-acetylanisole (15·4 g.) and ethyl benzoate (15·4 g.) in dry ether (70 c.c.). When the vigorous reaction subsided the mixture was heated on the steam-bath for 4 hours. The bulky sodio-derivative was collected, washed with ether, added to ice-cold dilute acetic acid, and the diketone taken up in ether. On prolonged shaking of the extract with aqueous cupric acetate, a voluminous precipitate of the copper derivative was obtained (26·5 g.). The substance crystallises from benzene in minute, green needles, m. p. 241° (decomp.) (Pond and Maxwell, *loc. cit.*, give 247—249°). On decomposition with dilute sulphuric acid in presence of ether the free anisoylacetophenone was obtained (22·5 g.). The m. p. after crystallisation from alcohol was 132° (Found : MeO, 12·3. Calc. for $C_{16}H_{16}O_3$: MeO, 12·2%).

Phenylanisyldiveratrocopyrine (compare Lawson, Perkin, and

Robinson, J., 1924, **125**, 648) was readily obtained by condensation of the diketone with diaminoveratrone in boiling acetic acid solution. It is very sparingly soluble and crystallises from hot alcohol in almost colourless needles, m. p. 352° (decomp.). The bright yellow *hydrochloride* crystallises in needles and is readily soluble in water. The *acetate* is more stable than that of diphenyldiveratrocopyrine, but is decomposed by water with formation of the free base.

The hydrolysis of ω-anisoylacetophenone (1·75 g.) was effected by gentle warming with 1% aqueous sodium hydroxide (27·55 c.c. = 1 mol.) until the separation of the simple ketones appeared to be complete. Finally the solution was boiled until the odour of acetophenone and acetylanisole was faint. The last traces of neutral material were removed by extraction with ether and the aqueous solution was concentrated to 5—7 c.c. and acidified at 0° by means of 32% hydrochloric acid (1·2 c.c.). The precipitate was collected, washed with ice-cold 10% hydrochloric acid and dried in a desiccator over sulphuric acid and sodium hydroxide to constant weight (Found: MeO, 11·4, 11·5, 11·4%, whence anisic acid in the mixture = 55·9%). All the diketones were hydrolysed in a similar manner and in all cases the reaction was smooth and complete. In no case did the solubility of one of the acids in water reach a value which could materially influence the results (*e.g.*, benzoic acid at 0°, 0·17; anisic acid at 25°, 0·0226%). Particular attention was directed to the technique of the estimations of methoxyl, and control experiments showed that a slightly modified Zeisel-Perkin method is capable of considerable accuracy (Found in anisic acid: MeO, 20·37, 20·39. Calc.: 20·395%).

ω-2-*Methoxybenzoylacetophenone*.—14·6 G. of the copper derivative of this substance resulted from the condensation of ethyl *o*-methoxybenzoate (18 g., b. p. 261—262°) with acetophenone (12 g.) in ethereal solution in presence of sodamide (5 g.). The diketone is readily soluble in most organic solvents and crystallises from ethyl alcohol in rosettes of slender, pale yellow needles, m. p. 65° (Found: C, 75·7; H, 5·5. $C_{16}H_{14}O_3$ requires C, 75·5; H, 5·6%). The alcoholic solution becomes deep red on the addition of ferric chloride. The *copper* derivative crystallises from benzene in short, pale green prisms, m. p. 196—197° (decomp.). The diketone reacts slowly with diaminoveratrone and, after 40 hours in boiling glacial acetic acid, a small yield of *phenyl-2-methoxyphenyldiveratrocopyrine* can be isolated. The base crystallises from alcohol in microscopic needles, m. p. 308°. The *hydrochloride* crystallises in clusters of orange-yellow needles, and the yellow solution of the *acetate* in acetic acid is not decolorised on dilution with water nor is any free base precipitated. In this respect, the substance differs markedly from the isomeric anisylphenyldiveratrocopyrine. The hydrolysis of the diketone by means of the calculated amount of 1% aqueous sodium hydroxide gave a mixture of benzoic acid and *o*-methoxybenzoic acid (Found: MeO, 17·2, 17·6%, whence *o*-methoxybenzoic acid = 85·1%).

ω-3-*Methoxybenzoylacetophenone.*—*m*-Tolyl methyl ether (40 g.) was oxidised on the steam-bath by a solution of potassium permanganate (50 g.) and sodium carbonate (50 g.) in water (2 litres) and when the reaction was completed potassium permanganate (100 g.) dissolved in water (2 litres) was gradually introduced during 5—6 hours. About 8—10 g. of the unchanged ether and 22—25 g. of pure *m*-methoxybenzoic acid were obtained. The acid gave a good yield of the ethyl ester, b. p. 280—283° (or 204°/139 mm.), on treatment with boiling 4% alcoholic hydrogen chloride. Starting from ethyl *m*-methoxybenzoate (13·7 g.), acetophenone (9·1 g.) and sodamide (4 g.), the usual method led to the production of 6 g. of the *copper* derivative of ω-3-methoxybenzoylacetophenone. This crystallised from benzene in small, square, sage-green plates, m. p. 215°. The diketone itself was purified by distillation (b. p. 157—159°/18 mm.) and by crystallisation from alcohol in almost colourless plates, m. p. 59·5° (Found: C, 75·7; H, 5·5. $C_{16}H_{14}O_3$ requires C, 75·5; H, 5·6%). The substance is readily soluble in most organic solvents and gives an immediate blood-red coloration with alcoholic ferric chloride. *Phenyl-3-methoxyphenyldiveratrocopyrine* crystallises from *n*-butyl alcohol in faintly yellow needles, m. p. 315°; it is intermediate in basic character between the isomerides mentioned above, which it resembles in most respects. On hydrolysis of the diketone in the usual manner, a mixture of *m*-methoxybenzoic and benzoic acids was obtained (Found: MeO, 13·7, 13·6%, whence *m*-methoxybenzoic acid = 66·9%).

α-*Anisoylpropiophenone.*—Smedley (J., 1910, **97**, 1492) has commented on the difficulty experienced in alkylating dibenzoylmethane by a direct method and we have been unable to find conditions for the methylation of ω-anisoylacetophenone. Unsuccessful experiments were made in alcoholic solution and with the sodium and copper derivatives of the diketone in benzene. This is merely the extreme case of the operation of a tendency already apparent in the case of ethyl benzoylacetate which is far more difficult to alkylate than is ethyl acetoacetate (compare Hope and Perkin, J., 1909, **95**, 2042). The desired substance can be obtained by the condensation of ethyl benzoate and *p*-methoxypropiophenone under the usual conditions, but not a trace could be isolated as the result of a similar experiment with ethyl anisate and propiophenone. *p*-Methoxypropiophenone has been obtained by Gattermann (*Ber.*, 1890, **23**, 1199) and the following modification of the method constitutes a considerable improvement: Powdered aluminium chloride (105 g.) was added to a mixture of anisole (75 g.) and carbon disulphide (200 c.c.); thereafter, propionyl chloride (67 g.) was introduced during 20—30 minutes. The product was isolated in the known manner and 70—75 g., b. p. 178—180°/46 mm., were obtained. The condensation of *p*-methoxypropiophenone (16·5 g.) and ethyl benzoate (16 g.) in ethereal solution by means of sodamide (5 g.) proceeded very readily in the cold and gave a copious deposit of the sodio-derivative from which 8 g. of the crude diketone were obtained in the usual way. The ethereal filtrate treated with a further quantity (2·5 g.) of sodamide gave as much again of the crude product. *α-Anisoylpropiophenone* crystallises from alcohol in pale yellow plates, m. p. 56·5° (Found: C, 75·3; H, 5·4. $C_{17}H_{16}O_3$ requires C, 76·1; H, 6·0%). In some other cases persistent low values for carbon and hydrogen were experienced using copper oxide tubes, but at a later stage the difficulty was overcome by the use of lead chromate tubes. This diketone gives a blood-red coloration with ferric chloride in alcoholic solution, its *copper* derivative is readily soluble in benzene and very sparingly soluble in methyl alcohol, from a hot solution in which it crystallises in flat-pointed prisms, m. p. 218°. An interesting confirmation of the constitution of the compound is derived from the fact that it does not yield a copyrine derivative on attempted condensation with diaminoveratrone. The diketone is more readily soluble in, and more readily hydrolysed by, 1% aqueous sodium hydroxide than ω-anisoylacetophenone. The acid mixture from the hydrolysis consisted of benzoic and anisic acids (Found: MeO, 13·5, 13·5%, whence anisic acid = 66·3%).

p-iso*Propoxybenzoic Acid.*—Sodium (4·8 g.) was dissolved in dry *iso*propyl alcohol (70 c.c.) and *p*-bromophenol (40 g.) added to the solution. After the introduction of *iso*propyl iodide (35 g.) the liquid was boiled under reflux until it was neutral (about 7 hours). After the usual processes the *p*-bromophenyl *iso*propyl ether (45·5 g.) was collected at 230—234°. This ether (22·8 g.) reacted readily in ethereal solution with magnesium (2·6 g.), previously activated by means of methyl iodide, and carbon dioxide was passed through the product for 5 hours. The acid was isolated, crystallised from hot water and dried at 100° (Found: C, 66·6; H, 6·8. $C_{10}H_{12}O_3$ requires C, 66·6; H, 6·7%). The substance separates from water in colourless, elongated, hexagonal plates, m. p. 161°. The *ethyl* ester is a colourless oil, b. p. 279—280°, and on condensation with acetophenone in the presence of sodium a small yield of the dibenzoylmethane (copper derivative, m. p. 227—228°, see below) was obtained. It is better to proceed from ethyl benzoate and *p-iso*propoxyacetophenone.

p-iso*Propoxyacetophenone*.—This substance, m. p. 38—39°, b. p. 152—153°/18 mm., has been obtained in small yield from phenyl *iso*propyl ether, b. p. 182—183°, by condensation with acetyl chloride in carbon disulphide solution and in the presence of aluminium chloride. The chief product was *p*-hydroxyacetophenone and it is apparent that dealkylation is far more facile in this case than in that of *p*-methoxyacetophenone, since the analogous preparation of the latter ketone proceeds satisfactorily. The result is in full accord with the requirements of the theory of the general polar effect of alkyl groups. The ketone was prepared by the action of *iso*propyl bromide (6·5 g.) on the sodium salt of *p*-hydroxyacetophenone (from 7 g. of the phenol) in boiling *iso*propyl alcoholic solution (20 c.c.) for 48 hours. 5 G. of a neutral oil, b. p. 153°/26 mm., solidifying to large colourless crystals, m. p. 38—39°, were isolated. The substance crystallises from light petroleum in plates and dissolves in sulphuric acid to a crimson solution (Found : C, 74·0; H, 7·9. $C_{11}H_{14}O_2$ requires C, 74·1; H, 7·8%).

ω-4-iso*Propoxybenzoylacetophenone*.—The condensation of *p-iso*propoxyacetophenone (5 g.) and ethyl benzoate (5 g.) in ether (15 c.c.) was carried out with the help of granulated sodium * (0·65 g.) in 3 days. The isolation was through the copper derivative, the formation of which is very slow in comparison with that of most dibenzoylmethanes. On the other hand, the chlorodibenzoylmethanes form their copper derivatives with great readiness and we connect these phenomena with the relative strengths of the enols as acids. *Copper* iso*propoxybenzoylacetophenone* crystallises from benzene in short, pale green needles, m. p. 228° (Found : Cu, 10·3. $C_{36}H_{34}O_6Cu$ requires Cu, 10·2%). The free diketone crystallises from light petroleum in pale yellow, flat, pointed needles, m. p. 73° (Found : C, 76·6; H, 6·3. $C_{18}H_{18}O_3$ requires C, 76·6; H, 6·4%). This substance is readily soluble in most organic solvents and its alcoholic solution develops an intense crimson coloration on the addition of ferric chloride. *Phenyl*-4-iso*propoxyphenyldiveratrocopyrine* crystallised in pale yellow needles when water was slowly added to a hot solution in acetic acid. The base does not melt below 355° and its *hydrochloride* crystallises in orange needles which are soluble in water. The hydrolysis of *iso*propoxybenzoylacetophenone was carried out under the usual conditions and a mixture of benzoic acid and *p-iso*propoxybenzoic acid was isolated (Found : equivalent, 141·7, 140·7, whence benzoic acid = 57·9%). It may be mentioned here that *p*-ethoxybenzoic acid, obtained from

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* In most cases we prefer to employ sodamide, but this reagent varies very much in quality and, encountering unsatisfactory material, we turned for a time to the use of sodium.

p-ethoxyphenyl magnesium bromide, has been esterified and condensed with acetophenone.

ω-p-*Ethoxybenzoylacetophenone* crystallises from light petroleum in pale yellow, elongated, quadrilateral plates, m. p. 68°.

ω-*Piperonoylacetophenone* is readily obtained from ethyl piperonylate and acetophenone and crystallises from alcohol in clusters of short, pale yellow needles, m. p. 85·5° (Found: C, 71·8; H, 4·6. $C_{16}H_{12}O_4$ requires C, 71·7; H, 4·5%). The *copper* derivative crystallises from benzene in small, pale green needles, m. p. 179°. *Phenylpiperonyldiveratrocopyrine* crystallises from alcoholic acetic acid in pale yellow needles, m. p. 328°.

ω-3-*Chlorobenzoylacetophenone.*—*m*-Chlorobenzoic acid was prepared from *m*-aminobenzoic acid by an application of the Sandmeyer reaction. A mixture of ethyl *m*-chlorobenzoate (9·2 g., b. p. 245°), acetophenone (7 g.), ether (25 c.c.) and granulated sodium (1·2 g.) was made at 0° and kept for 3 days. The *copper* derivative (yield, 4 g.), which was isolated in the usual manner, crystallises from benzene in needles, m. p. 254°. The diketone itself separated from alcohol in very pale yellow needles, m. p. 70° (Found: C, 69·5; H, 4·2; Cl, 13·7. $C_{15}H_{11}O_2Cl$ requires C, 69·6; H, 4·3; Cl, 13·7%). The alcoholic solution develops an intense red coloration on the addition of ferric chloride. In sulphuric acid, a bright yellow solution is obtained, whereas the alkyloxydibenzoylmethanes (and acetophenones) give a deep crimson solution. *Phenyl-3-chlorophenyldiveratrocopyrine* crystallises from alcoholic acetic acid in elongated, diamond-shaped plates which do not fuse below 355°. The *hydrochloride* crystallises in yellow needles, easily soluble in cold water. On hydrolysis of the diketone under the standard conditions, a mixture of benzoic and *m*-chlorobenzoic acids was obtained (Found: Cl, 16·2, 16·3%, whence *m*-chlorobenzoic acid = 71·7%).

ω-4-*Chlorobenzoylacetophenone.*—The substance was obtained by Bodforss (*Ber.*, 1918, **51**, 216) by the action of alcoholic potassium hydroxide on *p*-chlorobenzylideneacetophenone dibromide. Ethyl *p*-chlorobenzoate (13 g., b. p. 236—238°) was condensed with acetophenone (8·7 g.) in ethereal solution (20 c.c.) by means of granulated sodium (1·7 g.) at 0°. The *copper* derivative (4 g.) was obtained as usual and this substance crystallises from benzene in pale green needles, m. p. 271°. The β-diketone has m. p. 89° as stated by Bodforss. *Phenyl-4-chlorophenyldiveratrocopyrine* closely resembles the isomeride mentioned above and does not fuse at 370°. The hydrolysis of the diketone gave a mixture of *p*-chlorobenzoic and benzoic acids (Found: Cl, 17·8, 17·8%, whence *p*-chlorobenzoic acid = 78·5%).

ω-3-*Nitrobenzoylacetophenone.*—An attempted condensation of ethyl *m*-nitrobenzoate with acetophenone was unsuccessful, but the substance was obtained by the method of Bodforss (*Ber.*, 1916, **49**, 2803). The *copper* derivative was found to be very sparingly soluble in benzene, but readily soluble in pyridine to a deep green solution from which bluish-green crystals of a solvated compound separate. These lose pyridine at 63—65°. The *copper* derivative is deposited free from solvent from aqueous pyridine and has m. p. 298°. *Phenyl*-3-*nitrophenyldiveratrocopyrine* crystallises from dilute acetic acid in pale yellow needles, m. p. 324°. The *hydrochloride*, long, bright yellow needles, is soluble in dilute hydrochloric acid, but is dissociated in contact with water. On hydrolysis the diketone yields a mixture of benzoic acid and *m*-nitrobenzoic acid (Found : C, 52·8, 52·8%, whence *m*-nitrobenzoic acid = 86·4%).

ω-4-*Nitrobenzoylacetophenone.*—Ethyl *p*-nitrobenzoate and acetophenone afford this diketone in very poor yield under the usual conditions. Wieland (*Ber.*, 1904, **37**, 1148) has, however, obtained the diketone from *p*-nitrobenzylideneacetophenone dibromide and we have utilised this process. The *copper* derivative crystallises from pyridine in vivid emerald-green needles, which lose pyridine at 149° and then melt at 305° (Found : loss at 160°, 11·9. $C_{30}H_{20}O_8N_2Cu,C_5H_5N$ requires C_5H_5N, 12·0%). *Phenyl*-4-*nitrophenyldiveratrocopyrine* darkens but does not melt at 355°. It forms a viscous solution in concentrated hydrochloric acid from which orange needles of the *hydrochloride* are deposited. On washing with water, the salt is decomposed with formation of the free base. Hydrolysis of the diketone under the standard conditions was effected, but it is much more difficult than in any other case examined. Doubtless this is due to the enhanced stability of the anion from the enolic modification, which is the result of the entry of the nitroxyl group. The case recalls that of the somewhat similarly constituted 4 : 4′-dinitrodiphenylcarbamide which is exceedingly resistant to hydrolysis by alkaline solutions. The acid mixture had m. p. 206—226° and obviously consisted mainly of *p*-nitrobenzoic acid (Found : C, 53·0, 53·1%, whence *p*-nitrobenzoic acid = 85·1%).

ω-2 : 4-*Dimethoxybenzoylacetophenone* (compare Perkin and Schiess, J., 1904, **85**, 164; Robinson and Turner, J., 1918, **113**, 876).—The *copper* derivative has m. p. 193° when freed from the molecular proportion of benzene with which it crystallises. Condensation of the diketone with diaminoveratrone occurs readily in boiling acetic acid solution. *Phenyl*-2 : 4-*dimethoxyphenyldiveratrocopyrine* crystallises from alcohol, in which it is sparingly soluble, in slender needles, m. p. 296°. The striking effect of a methoxyl, *o*-situated in the phenyl groups, on the basicity of the derivative, is again observed. The solution of this substance in glacial acetic acid gives no precipitate on dilution with water. On hydrolysis under the standard conditions, 2 : 4-dimethoxybenzoylacetophenone gave a mixture of 2 : 4-dimethoxybenzoic and benzoic acids (Found : MeO, 27·8%, whence 2 : 4-dimethoxybenzoic acid = 81·5%).

ω-*Veratroylacetophenone.*—Acetoveratrone gave poor results in β-diketone syntheses, but ethyl veratrate is a satisfactory starting-point. The condensation with acetophenone has been already described (Gulland and Robinson, J., 1925, **127**, 1493). *Phenylveratryldiveratrocopyrine* is obtained in excellent yield and crystallises from a mixture of nitrobenzene and alcohol in pale yellow needles, m. p. 289°. The *hydrochloride* crystallises in orange needles readily soluble in water, whilst the yellow solution in glacial acetic acid becomes colourless and deposits the free base on dilution with water. Hydrolysis of the diketone was carried out in the usual manner (Found : MeO, 19·9, 20·1, 20·2%, whence veratric acid = 60·6%).

ω-3-*Methoxybenzoyl*-4-*methoxyacetophenone.*—Employing *p*-acetylanisole (6 g.), ethyl *m*-methoxybenzoate (7 g.), sodamide (2 g.) and ether (20 c.c.), a ready condensation occurred and the *copper* derivative (6·5 g.), which crystallises from benzene in pale green needles, m. p. 218°, was isolated in the usual manner. The diketone separates from light petroleum in aggregates of pale yellow, flat needles, and from alcohol in plates, m. p. 91° (Found : C, 71·9; H, 5·7. $C_{17}H_{16}O_4$ requires C, 71·8; H, 5·7%). The substance is readily soluble in most organic solvents and develops a deep red coloration with ferric chloride in alcoholic solution. 3-*Methoxyphenylanisyldiveratrocopyrine* crystallises from alcohol in nearly colourless needles, m. p. 290—293°. The yellow *acetate* is hydrolysed in presence of water. On hydrolysis, the diketone yields a mixture of anisic acid and *m*-methoxybenzoic acid, which was thermally analysed.

Mixtures of Anisic and m-*Methoxybenzoic Acids.*

% Anisic acid ……	62·92	57·44	49·90	45·77	35·3
F. p. ………………	153·3°	149·3°	141·3°	135·2°	115·2°

Composition of the Hydrolysis Product.

Wt. of product in g.	Wt. of anisic acid added in g.	F. p.	% of anisic acid.	% of anisic acid in hydrolysis product.
1·0109	0·3924	143·5°	51·87	23·90
1·0109	0·4761	145·5	53·63	21·62
1·0109	0·5933	149·7	57·75	20·76

3 : 4 : 5-*Trimethoxybenzoylacetophenone.*—Ethyl 3 : 4 : 5-trimethoxybenzoate (12 g.) and acetophenone (6 g.) were condensed to-

gether in ethereal solution (50 c.c.) by means of powdered sodamide (2·5 g.). A very vigorous reaction ensued and after 1 hour this was completed by gentle heating. The *copper* derivative (7·3 g.) was isolated in the usual manner and found to crystallise from benzene in minute green needles, m. p. 254° (Found: Cu, 9·3. $C_{36}H_{36}O_{10}Cu$ requires Cu, 9·3%); on decomposing this in the usual manner with dilute sulphuric acid in the presence of ether, the β-diketone was obtained and crystallised from ether and from alcohol in canary-yellow plates, m. p. 97° (Found: C, 68·6; H, 5·9. $C_{18}H_{18}O_5$ requires C, 68·8; H, 5·8%). The ferric chloride reaction in alcoholic solution is blood-red. *Phenyl*-3 : 4 : 5-*trimethoxyphenyldiveratrocopyrine* is very sparingly soluble and crystallises on the addition of alcohol to its yellow solution in acetic acid in pale yellow needles, m. p. 323°. The *hydrochloride* crystallises in yellow needles, soluble in water, whilst dilution of an acetic acid solution of the *acetate* causes the precipitation of the free base. On hydrolysis, the diketone furnished a mixture of benzoic and 3 : 4 : 5-trimethoxybenzoic acids (Found: MeO, 34·8, 34·7%, whence trimethoxybenzoic acid = 79·2%).

ω-3-*Methoxybenzoyl*-3 : 4-*dimethoxyacetophenone*.—Ethyl *m*-methoxybenzoate and acetoveratrone react very slowly together in conjunction with sodium or sodamide, but on long standing a good yield of the diketone is obtained. Sodium (1·25 g.) cut in thin clean slices was added to a dry ethereal solution of acetoveratrone (9 g.) and ethyl *m*-methoxybenzoate (9 g.). After 3 weeks, the entire product was gradually added to ice-cold dilute acetic acid and the *copper* derivative (7 g.) isolated as in other cases. This substance crystallises from benzene, in which it is sparingly soluble, in pale green needles, m. p. 223°. The diketone was obtained in the usual manner and crystallised from alcohol in elongated prisms, m. p. 78·5° (Found: C, 68·8; H, 5·7. $C_{18}H_{18}O_5$ requires C, 68·8; H, 5·8%). The crystals of this substance have a curious conical, almond-like shape; they are coloured crimson by sulphuric acid and then dissolve to a yellow solution. Addition of ferric chloride to an alcoholic solution produces a blood-red coloration. *Veratryl*-m-*methoxyphenyldiveratrocopyrine* is readily obtained by the general method and crystallises from *n*-butyl alcohol in almost colourless, slender needles, m. p. 301·5°. The *hydrochloride* crystallises in orange needles. The substance is more strongly basic than diphenyldiveratrocopyrine but less strongly basic than phenyl-2-methoxyphenyldiveratrocopyrine. On hydrolysis of the diketone, a mixture of *m*-methoxybenzoic acid and veratric acid was obtained (Found: MeO, 26·2, 26·5, 26·8%, whence veratric acid = 44·5%).

ω-*Anisoyl*-3 : 4-*dimethoxyacetophenone*.—This diketone has been obtained from ethyl anisate and acetoveratrone using either sodium or sodamide, but the process is slow. A much more facile reaction occurs between ethyl veratrate and *p*-acetylanisole and this was effected as in previous examples. The *copper* derivative crystallises from benzene in pale green needles, m. p. 238° and the β-diketone crystallises from alcohol in lemon-yellow, pointed, almond-shaped needles, m. p. 97° (Found : C, 69·0; H, 5·8. $C_{18}H_{18}O_5$ requires C, 68·8; H, 5·8%). The behaviour towards solvents, ferric chloride, and sulphuric acid was normal. *Veratrylanisyldiveratrocopyrine*, m. p. 300°, is obtained in only a small yield under the usual conditions; the *acetate* crystallises from acetic acid in slender yellow needles. On hydrolysis, the β-diketone gave a mixture of anisic and veratric acids (Found : MeO, 30·4, 30·0, 29·5%, whence veratric acid = 69·8%).

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THE UNIVERSITY, MANCHESTER. [*Received, June* 28*th*, 1926.]