*Derivatives of Acetoacetic Acid. Part I. The Reaction of Diketen with 1 : 2- and 1 : 3-Ketols to give γ- and δ-Lactones.**

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Diketen reacted with diacetone alcohol to give the expected acetoacetate, which, with alkali, readily cyclised to a δ-lactone. β-Hydroxy-αα-dimethylpropaldehyde and β-hydroxy-αγ-dimethylvaleraldehyde reacted with diketen in boiling toluene in the presence of a tertiary amine to give δ-lactones directly, and salicylaldehyde and *o*-hydroxyacetophenone afforded the expected coumarins. Acyloins were converted into γ-lactones by reaction with diketen. In some of the these reactions diketen could be replaced by an acetoacetic ester, but the yields were somewhat poorer.

Our extensive knowledge of the chemistry of acetoacetic esters is mostly concerned with the reactivity of the acetoacetic acid residue itself. Thus, alkylation, acylation, condensation, hydrolysis, etc., are, to a large extent, independent of the parent alcohol, which may find an explanation in the fact that all acetoacetic esters, on dilution with solvents, tend to enolise to the same extent (cf. Henecka, "Chemie der Beta-dicarbonylverbindungen," Springer-Verlag, 1950, p. 11). Nevertheless, it was considered of interest to study the chemistry of derivatives of acetoacetic acid with alcohols, and, subsequently, amines,

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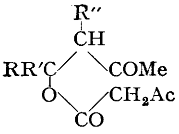
* Patents pending: B.P. Appln. 14581/1951; 10829/1952.

possessing a second functional group which might be induced to react with the acetoacetic acid residue. While many alkyl acetoacetates may be prepared by Claisen condensation or ester exchange, these methods become impracticable when applied to many complex alcohols. However, the use of diketen made available a wide range of acetoacetic esters and amides. The reaction of diketen with simple alcohols is known to be catalysed by acids (Boese, U.S.P. 2,167,168/1939) and by bases such as sodium alkoxide (Chick and Wilsmore, *J.*, 1908, 946) and tertiary amines (Pohl and Schmidt, U.S.P. 2,351,366/1944). The present paper deals with the reaction of diketen with alcohols (or phenols) possessing a keto or aldehyde group, and with the properties of the products.

Diacetone alcohol reacted smoothly with diketen at 80—90° in the presence of triethylamine to give an 85% yield of the acetoacetate (I; R = R′ = Me, R″ = H), previously obtained by Bader, Cummings, and Vogel (*J. Amer. Chem. Soc.*, 1951, **73**, 4195) in only 4% yield by prolonged ester exchange. This ester cyclised very rapidly with alkali at room temperature, giving a solid, $C_{10}H_{14}O_3$, m. p. 48°, in high yield (first observed by Mr. R. E. Graham). The ultra-violet absorption was characteristic of an αβ-unsaturated ketone, strongly suggesting the unsaturated δ-lactone (II).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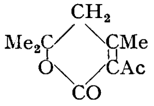
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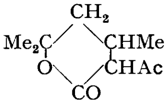
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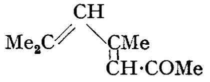
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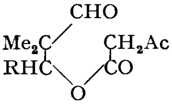
Confirmation was provided by hydrogenation, since, on absorption of one mol. of hydrogen, a solid (III) was obtained, which gave a bright violet colour with ferric chloride, characteristic of an α-substituted acetoacetic ester. Alkaline hydrolysis of (II) gave mesityl oxide and 4 : 6-dimethylhepta-3 : 5-dien-2-one (IV) (semicarbazone), although the ultra-violet spectrum indicated that there was also some 4 : 6-dimethylhepta-3 : 6-dien-2-one present. The lactone (II) was also decarboxylated to (IV) by toluene-*p*-sulphonic acid at 100°, recalling the conversion of *tert.*-butyl acetoacetates into ketones, *iso*butene, and carbon dioxide under similar conditions (Renfrow and Walker, *J. Amer. Chem. Soc.*, 1948, **70**, 3957).

Since aldols dehydrate readily to give unsaturated aldehydes (Owen, *Ann. Reports*, 1944, **41**, 146), it was not surprising that diketen and freshly distilled acetaldol, in the presence of triethylamine, gave only crotonaldehyde, acetone, and resinous products. β-Hydroxy-αα-dimethylpropaldehyde with diketen in the presence of triethylamine at 55—65° gave a mixture of the acetoacetate (V; R = H) and the lactone (VI; R = H), but in boiling toluene water was eliminated, and a 75% yield of the lactone (VI; R = H) resulted. The ultra-violet absorption was characteristic of an αβ-unsaturated ketone. Similarly, *iso*butaldehyde aldol diketen gave the unsaturated lactone (VI; R = Pr^i) in 77·5% yield.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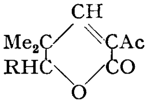
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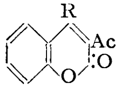
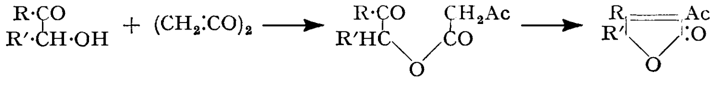
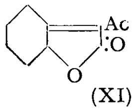

(VII)

Among aromatic compounds, salicylaldehyde reacted with diketen in boiling toluene in the presence of triethylamine to give a 45% yield of 3-acetylcoumarin (VII; R = H) although a considerable amount of salicylaldehyde was recovered; *o*-hydroxyacetophenone gave 3-acetyl-4-methylcoumarin (VII; R = Me) in 29% yield.

This direct formation of lactones prompted an attempt to prepare (II) under the same conditions, but the ester (I; R = R′ = Me, R″ = H) failed to cyclise. 4-Hydroxybutan-2-one readily reacted with diketen to give the acetoacetate (I; R = R′ = R″ = H), but this ester was unaffected by refluxing toluene in the presence of piperidinium acetate, and treatment with alcoholic alkali at low temperature gave only low-boiling products. Similarly, 4-hydroxy-3-methylpentan-2-one, possessing a secondary hydroxyl, gave an acetoacetate (I; R = R″ = Me, R′ = H) which also failed to cyclise. The ability of the ester (I; R = R′ = Me, R″ = H) to give a lactone on treatment with aqueous or alcoholic alkali seems attributable to the much lower hydrolysis or alcoholysis rate of *tert.*-alkyl esters, the esters of primary or secondary 1 : 3-keto-alcohols being hydrolysed rather than cyclised. With 1 : 3-hydroxy-aldehydes, cyclisation of the acetoacetates occurred even on heating them in the presence of triethylamine, owing to the much greater readiness of aldehydes to undergo the Knoevenagel condensation.



(VIII) (IX) (X)



(XI)

The reaction with 1 : 2-hydroxy-ketones was also investigated. Butyroin (VIII; R = R′ = Pr^n) in benzene at 60—70° reacted with diketen in the presence of triethylamine to give a mixture, but from the higher-boiling fractions was isolated an oil which analysis showed to be formed by elimination of water from one mole of diketen and one mole of butyroin. The ultra-violet spectrum supported the formulation as an unsaturated γ-lactone (X; R = R′ = Pr^n). However, since the product exhibited a purple colour with ferric chloride solution and slowly dissolved in aqueous sodium hydroxide, the prototropic rearrangement to a $\beta\gamma$-unsaturated ketone with an enolisable hydrogen must readily take place.

It therefore appeared that the acetoacetate (IX; R = R′ = Pr^n) first formed was partly converted into the lactone. Under more vigorous reaction conditions, *i.e.*, in boiling toluene with provision for the continuous removal of the water eliminated, the lactone was obtained in 80% yield. Again, (VIII; R = R′ = Et) reacted in boiling toluene with diketen to give an 84·5% yield of the lactone (X; R = R′ = Et). The ultra-violet spectrum indicated an $\alpha\beta$-unsaturated ketone although the lactone gave a purple colour with ferric chloride and slowly dissolved in aqueous alkali. Acetoin reacted similarly but the somewhat lower yield (68·5%) of lactone (X; R = R′ = Me) is probably attributable to the lower boiling point and water miscibility of the acyloin, which rendered the water-entrainment procedure less effective. On prolonged storage or after a short period of heating in alcoholic sodium acetate, this lactone gave a solid which appeared to be a dimer containing one carbonyl group.

In the reaction of lauroin (VIII; R = R′ = $C_{11}H_{23}$) the calculated quantity of water was eliminated, but the product resisted attempts at distillation and failed to give solid ketonic derivatives. With alkali a solid sodium salt slowly separated and reactions to be described in the next paper indicated that the product must have contained considerable quantities of the expected lactone (X; R = R′ = $C_{11}H_{23}$). 2-Hydroxy*cyclo*hexanone with diketen in boiling benzene in the presence of triethylamine gave the expected lactone (XI) in 34% yield.

The reaction of benzoin was similar to those encountered with aliphatic acyloins, for, while reaction at 60—70° gave a mixture, reaction in boiling toluene resulted in the elimination of water and an almost quantitative yield of the expected lactone (X; R = R′ = Ph). The product exhibited anomalous ultra-violet absorption at 3550 Å, but since the lactone was subsequently found to form a peroxide very readily in air, this may well account for the enhanced absorption (cf. Waters, *Ann. Reports*, 1945, **42**, 135).

Phenacyl alcohol (VIII; R = Ph, R′ = H) reacted with diketen, giving phenacyl acetoacetate, which in refluxing toluene, in the presence of pyridine, lost water giving the lactone (X; R = Ph, R′ = H). Phenacyl acetoacetate dissolved in aqueous alkali, and after a few minutes the sodium salt of (X; R = Ph, R′ = H) was precipitated: acidification afforded the lactone which gave a weak red colour with ferric chloride and dissolved slowly in dilute aqueous alkali.

Acetol (VIII; R = Me, R′ = H) reacted with diketen at 60—70° in the presence of triethylamine to give the acetoacetate. However, although refluxing toluene in the presence of pyridine appeared to have cyclised the ester, with elimination of water, the product resinified on attempted distillation. Treatment with cold alcoholic alkali gave rise to low-boiling products only.

Since diketen and salicylaldehyde gave 3-acetylcoumarin, a product previously obtained by Knoevenagel (*Ber.*, 1898, **31**, 732) from acetoacetic ester and salicylaldehyde, attempts were made to condense other ketols with acetoacetic ester. The catalysts employed were pyridine, piperidine, triethylamine, or their acetates, the last being generally preferable, since they permitted a higher concentration of catalyst in the boiling reaction mixture. It is probable that with the reactions involving diketen, the true catalyst was the amine acetate, since the diketen employed always contained a few units per cent. of acetic acid. It was found that by refluxing a mixture of methyl acetoacetate and toluene or xylene plus amine or amine acetate catalyst, several of the ketols previously mentioned, *e.g.*, butyroin (67·5% yield), benzoin (56% yield), and *iso*butaldehyde (57% yield), could be converted into the γ- or δ-lactones, although the yields were inferior to those obtained by using diketen.

A useful route to 1 : 2-ketols (type VIII) is the mercuric ion-catalysed hydration of acetylenic alcohols. The hydration of an alkynyl acetoacetate, followed by conversion of the ketol acetoacetate so obtained into a γ-lactone, was therfore attempted. 1-Methylprop-2-ynyl acetoacetate readily prepared by using diketen, was refluxed with mercuric chloride in aqueous ethanol, a 36% yield of the acetoacetate of acetoin being obtained. This was converted into the lactone (X; R = R′ = Me) by refluxing it in toluene containing 2—3% of piperidine.

With the exception of (X; R = Ph, R′ = H), which rapidly decolorised 2 : 6-dichlorophenolindophenol solution, the colour reactions of the lactones tested, with sodium nitroprusside and with 2 : 6-dichlorophenolindophenol (Kuehl, Linstead, and Orkin, *J.*, 1950, 2213), were in agreement with formulation as $\alpha\beta$-unsaturated lactones.

In view of the bacteriostatic properties of certain $\alpha\beta$-unsaturated ketones (cf. Haynes, *Quart. Reviews*, 1948, **2**, 46), the physiological properties of the lactones described may prove of interest.

EXPERIMENTAL

M. p.s were determined on a Kofler block and are corrected. Light-absorption determinations were carried out in ethanol.

Commercial diketen was purified by fractional distillation giving a fraction, 95—98% pure, having b. p. 57—59°/60 mm., n_D^{20} 1·4352—1·4370.

1 : 1-*Dimethyl*-3-*oxobutyl Acetoacetate*.—Diketen (85 g.) was added dropwise to an agitated mixture of diacetone alcohol (116 g.) and triethylamine (0·5 c.c.) at 80—90° during 20 min. Distillation afforded the acetoacetate (I; R = R′ = Me, R″ = H) (170 g., 85%), b. p. 78—83°/0·5 mm., n_D^{20} 1·4425 (Found: C, 60·3; H, 8·4. Calc. for $C_{10}H_{16}O_4$: C, 60·0; H, 8·05%). Bader *et al.*, *loc. cit.*, give b. p. 125—127°/10 mm., n_D^{25} 1·4424.

3-*Acetyl*-5 : 6-*dihydro*-4 : 6 : 6-*trimethyl*-1 : 2-*pyran*-2-*one* (II).—The above acetoacetate (50 g.) was added during 0·5 hr. to alcoholic potassium hydroxide (0·5N; 50 c.c.) with agitation, the temperature being kept below 25°. After a further 0·5 hr., the product was neutralised with acetic acid, concentrated, poured into water, and isolated with ether. Crystallisation of the product (42 g., 92%) from ether–light petroleum (b. p. 40—60°) gave the *pyrone* as prisms, m. p. 48° (Found: C, 66·15; H, 7·65. $C_{10}H_{14}O_3$ requires C, 65·9; H, 7·75%). Light absorption: max., 2200 A.; ε, 8000. The *semicarbazone* crystallised from *iso*propanol as prisms, m. p. 204° (decomp.) (Found: C, 55·5; H, 7·3; N, 17·7. $C_{11}H_{17}O_3N_3$ requires C, 55·2; H, 7·15; N, 17·55%). The 2 : 4-*dinitrophenylhydrazone* formed orange needles, m. p. 136°, from aqueous ethanol (Found: N, 15·6. $C_{16}H_{18}O_6N_4$ requires N, 15·5%). The above cyclisation could also be effected by addition of the ester to cold aqueous alkali; the lactone separated and was crystallised as formed.

3-*Acetyl*-3 : 4 : 5 : 6-*tetrahydro*-4 : 6 : 6-*trimethyl*-1 : 2-*pyran*-2-*one* (III).—The pyrone (II) (20 g.) was hydrogenated in *iso*propanol (200 c.c.) in the presence of Raney nickel (8 g. of paste) at 70°. Hydrogen equivalent to 0·9 double bond was absorbed in 3 hr. Isolation of the product gave the *pyrone* (III) (17 g.), b. p. 80—83°/0·1 mm., n_D^{20} 1·4670, which subsequently solidified. Crystallisation from ether–light petroleum (b. p. 40—60°) gave plates, m. p. 56—57° (Found: C, 65·3; H, 8·85. $C_{10}H_{16}O_3$ requires C, 65·2; H, 8·75%), which produced a bright violet colour with ferric chloride.

4 : 6-*Dimethylhepta*-3 : 5-*dien*-2-*one* (IV).—A mixture of the pyrone (II) (30 g.) and sodium hydroxide solution (20% ; 60 c.c.) was refluxed for 1 hr. Neutralisation with acetic acid, isolation with ether, and distillation gave mesityl oxide (3·2 g.) and a fraction, b. p. 83—86°/19 mm. (7·9 g.), redistillation of which gave two closely boiling fractions : (*a*) b. p. 78—80°/17 mm., $n_{\rm D}^{20}$ 1·4930, and (*b*) b. p. 80—83°/17 mm., $n_{\rm D}^{20}$ 1·5000, the latter being substantially pure *dienone* (IV) (Found : C, 77·8 ; H, 10·15. $C_9H_{14}O$ requires C, 78·2 ; H, 10·2%). A *semicarbazone* prepared from (*b*) formed plates, m. p. 153—154°, from aqueous methanol (Found : C, 61·85 ; H, 8·45 ; N, 21·6. $C_{10}H_{17}ON_3$ requires C, 61·5 ; H, 8·8 ; N, 21·5%). Light absorption : fraction (*a*) : max., 2850 and 2250 Å. ; ε, 12,500 and 10,700, respectively : fraction (*b*) : max., 2850 Å ; ε, 14,500.

3-*Acetyl*-5 : 6-*dihydro*-5 : 5-*dimethyl*-1 : 2-*pyran*-2-*one* (VI ; R = H).—Diketen (44 g.) was added to a stirred mixture of freshly distilled β-hydroxy-αα-dimethylpropaldehyde (51 g.) and triethylamine (0·5 c.c.) at 55—65° during 45 min., which was then heated at 60° for a further 0·5 hr., and distilled. The product (62 g.) had b. p. 144—146°/12 mm., $n_{\rm D}^{20}$ 1·4594 (Found : C, 61·8 ; H, 7·45. Calc. for $C_9H_{14}O_4$: C, 58·5 ; H, 7·6. Calc. for $C_9H_{12}O_3$: C, 64·25 ; H, 7·2%). Repetition of the experiment, with triethylamine (3 c.c.) and toluene (150 c.c.), at the b. p., gave water (6 c.c.) and, on distillation, the *pyrone* (VI ; R = H) (62·8 g., 75%), b. p. 144—148°/13 mm., $n_{\rm D}^{20}$ 1·4859 (Found : C, 64·1 ; H, 7·15. $C_9H_{12}O_3$ requires C, 64·25 ; H, 7·2%). Light absorption : max., 2300 Å ; ε, 11,800. The 2 : 4-*dinitrophenylhydrazone* crystallised from ethanol in orange needles, m. p. 183° (Found : C, 52·0 ; H, 4·35 ; N, 15·9. $C_{15}H_{16}O_6N_4$ requires C, 51·7 ; H, 4·65 ; N, 16·1%).

In this and in other experiments in which diketen was added to refluxing mixtures containing volatile amines, the diketen was introduced below the surface, otherwise some polymerisation took place on contact with the amine in the vapour.

3-*Acetyl*-5 : 6-*dihydro*-5 : 5-*dimethyl*-6-iso*propyl*-1 : 2-*pyran*-2-*one* (VI ; R = Pr^i).—β-Hydroxy-αγ-dimethylvaleraldehyde (72 g. ; prepared according to Späth, Lorenz, and Freund, *Ber.*, 1943, **76**, *B*, 1207 ; b. p. 92—96°/15 mm., $n_{\rm D}^{20}$ 1·4437) in boiling toluene (100 c.c.) containing triethylamine (3 c.c.) was treated with diketen (43·5 g.) during 45 min., and the product refluxed for a further 2 hr.: water (6·8 c.c.) was removed during the reaction. Distillation gave the *pyrone* (VI ; R = Pr^i) (79·2 g., 77·5%), b. p. 119—122°/0·5 mm., $n_{\rm D}^{20}$ 1·4870 (Found : C, 68·25 ; H, 8·35. $C_{12}H_{18}O_3$ requires C, 68·55 ; H, 8·65%). The 2 : 4-*dinitrophenylhydrazone* crystallised from acetic acid as orange needles, m. p. 162—163° (Found : C, 55·3 ; H, 5·7 ; N, 14·0. $C_{18}H_{22}O_6N_4$ requires C, 55·35 ; H, 5·7 ; N, 14·35%).

3-*Acetylcoumarin* (VII ; R = H).—Diketen (45 g.) was added during 1 hr. to an agitated refluxing mixture of salicylaldehyde (61 g.) and triethylamine (0·5 c.c.) in toluene (100 c.c.), and the mixture refluxed a further 0·5 hr., water (1 c.c.) being collected. Removal of solvents and washing of the residue with benzene–light petroleum (b. p. 40—60°) gave 3-acetylcoumarin (42 g., 45%), m. p. 122° (Knoevenagel, *loc. cit.*, gives m. p. 123°). Salicylaldehyde (19·4 g.) was recovered from the washings.

3-*Acetyl*-4-*methylcoumarin* (VII ; R = Me).—Diketen (7 g., 98%) was condensed with *o*-hydroxyacetophenone (10 g.) in toluene (80 c.c.) and triethylamine (1 c.c.), and the product worked up as described in the previous experiment (crude yield : 4·3 g.). 3-*Acetyl*-4-*methylcoumarin* formed needles (from aqueous methanol), m. p. 102—103° (Found : C, 70·9 ; H, 5·0. $C_{12}H_{10}O_3$ requires C, 71·25 ; H, 5·0%). Light absorption : max., 2800 and 3200 Å ; ε, 11,700 and 8700, respectively. The 2 : 4-*dinitrophenylhydrazone* crystallised from acetic acid in orange needles, m. p. 220—221° (Found : C, 56·3 ; H, 3·5 ; N, 14·8. $C_{18}H_{14}O_6N_4$ requires C, 56·55 ; H, 3·7 ; N, 14·65%).

3-*Oxobutyl Acetoacetate* (I ; R = R′ = R″ = H).—4-Hydroxybutan-2-one (35·2 g. ; prepared according to Hays, Hager, Engelmann, and Spurlin, *J. Amer. Chem. Soc.*, 1951, **73**, 5369) in chloroform (100 c.c.) containing trimethylamine (30% solution in methanol ; 0·5 c.c.) was treated at 60° with diketen (34·6 g.). Distillation gave the *acetoacetate*, b. p. 117—120°/0·5 mm., $n_{\rm D}^{20}$ 1·4461, which was appreciably soluble in water (Found : C, 55·4 ; H, 7·35. $C_8H_{12}O_4$ requires C, 55·8 ; H, 7·05%).

1 : 2-*Dimethyl*-3-*oxobutyl Acetoacetate* (I ; R = R″ = Me, R′ = H).—Diketen (44 g.) was added during 0·5 hr. to 4-hydroxy-3-methylpentane-2-one (58 g.) containing triethylamine (0·2 c.c.) at 65—75°, and the mixture then heated at 60° for a further 0·5 hr. Distillation gave the *acetoacetate* (86 g., 86%), b. p. 112—114°/0·5 mm., $n_{\rm D}^{20}$ 1·4460 (Found : C, 59·75 ; H, 7·9. $C_{10}H_{16}O_4$ requires C, 60·0 ; H, 8·05%).

3-*Acetyl*-2 : 5-*dihydro*-4 : 5-*dipropylfuran*-2-*one* (X ; R = R′ = Pr^n).—(*a*) Diketen (31 g.) was added to a mixture of butyroin (48 g.), benzene (50 c.c.), and triethylamine (0·5 c.c.) at

60—70° during 0·5 hr. After a further hour at 60°, the product was distilled, giving fractions (i) 29·3 g., b. p. 132—157°/15 mm., and (ii) 16·8 g., b. p. 157—164°/15 mm. The second of these was redistilled, giving the pure *lactone*, b. p. 161—163°/15 mm., n_D^{20} 1·4847 (Found: C, 68·3; H, 8·7. $C_{12}H_{18}O_3$ requires C, 68·55; H, 8·65%). Light absorption: max. 2350 and 3110 Å; ε, 12,600 and 290, respectively. The 2 : 4-*dinitrophenylhydrazone* crystallised from *iso*propanol in red needles, m. p. 127° (Found: C, 55·25; H, 5·5; N, 14·3. $C_{18}H_{22}O_6N_4$ requires C, 55·4; H, 5·7; N, 14·35%).

(*b*) Repetition of the above under reflux, but with triethylamine (3 c.c.) and toluene (100 c.c.) in place of benzene, gave water (4 c.c.; after 2 hours' reaction). Distillation of the product gave the lactone (55·8 g., 80%), b. p. 158—165°/15 mm.

3-*Acetyl*-4 : 5-*diethyl*-2 : 5-*dihydrofuran*-2-*one* (X; R = R' = Et).—The reaction of propionoin (56 g.) in toluene (100 c.c.) and triethylamine (3 c.c.) with diketen (45 g.) was carried out as in (*b*) above: 6·5 c.c. of water were collected. Distillation of the product gave the *lactone* (76·8 g., 84·5%), b. p. 140—142°/12 mm., n_D^{20} 1·4896 (Found: C, 65·7; H, 7·7. $C_{10}H_{14}O_3$ requires C, 65·9; H, 7·75%). Light absorption: max., 2300 and 3080 Å; ε, 25,100 and 710, respectively. The 2 : 4-*dinitrophenylhydrazone* formed red needles (from butanol), m. p. 140·5° (Found: C, 52·8; H, 4·8; N, 15·4. $C_{16}H_{18}O_6N_4$ requires C, 53·05; H, 5·0; N, 15·45%).

3-*Acetyl*-2 : 5-*dihydro*-4 : 5-*dimethylfuran*-2-*one* (X; R = R' = Me).—Diketen (45 g.) was condensed with freshly distilled acetoin (36 g.) and triethylamine (1 c.c.) in toluene (80 c.c.) as described above: 6 c.c. of water were removed from the decanter head during the course of the reaction. Distillation gave the pale yellow *lactone* (52 g., 68·5%), b. p. 134—138°/12 mm., n_D^{20} 1·4915 (Found: C, 62·1; H, 6·85. $C_8H_{10}O_3$ requires C, 62·35; H, 6·55%). The 2 : 4-*dinitrophenylhydrazone* formed red prisms (from aqueous acetic acid), m. p. 177° (Found: C, 50·25; H, 3·9; N, 16·7. $C_{14}H_{14}O_6N_4$ requires C, 50·3; H, 4·2; N, 16·75%).

On prolonged storage, or, rapidly, when refluxed, in ethanol (20 c.c.) with a solution of sodium acetate (1 g.) in water (5 c.c.), the lactone (X; R = R' = Me) (5 g.) gave a solid *dimer* (3·0 g.) which crystallised from aqueous methanol as needles, m. p. 240° (Found: C, 62·5; H, 7·0. $C_{16}H_{20}O_6$ requires C, 62·3; H, 6·55%). The dimer gave a 2 : 4-*dinitrophenylhydrazone* which crystallised as red needles, m. p. 270° (decomp.), from aqueous acetic acid (Found: C, 53·8; H, 5·2; N, 11·4. $C_{22}H_{24}O_9N_4$ requires C, 54·15; H, 4·95; N, 11·45%).

3-*Acetyl*-2 : 5-*dihydro*-4 : 5-*diundecylfuran*-2-*one* (X; R = R' = $C_{11}H_{23}$).—Lauroin (110 g.) in toluene (200 c.c.) containing triethylamine (3 c.c.) was treated with diketen (27 g.) as previously described, water (6 c.c.) being eliminated. Removal of solvents gave an oil (129 g.).

3-*Acetyl*-2 : 4 : 5 : 6 : 7 : 8-*hexahydrobenzofuran*-2-*one* (XI).—Diketen (29 g.) was added during 0·75 hr. to a refluxing solution of 2-hydroxy*cyclo*hexanone (28·5 g.; prepared as described by Bloink and Pausacker, *J.*, 1950, 1330) in benzene (100 c.c.) and triethylamine (0·5 c.c.), and the mixture refluxed for a further 0·5 hr.; 3 c.c. of water were eliminated. Distillation gave the *lactone*, b. p. 124—126°/0·5 mm., n_D^{20} 1·5230 (Found: 66·3; H, 6·75. $C_{10}H_{12}O_3$ requires C, 66·65; H, 6·7%). Light absorption: max., 2370 Å; ε, 10,600. The 2 : 4-*dinitrophenylhydrazone* formed red needles, m. p. 196°, from ethyl acetate (Found: N, 15·3. $C_{16}H_{16}O_6N_4$ requires N, 15·55%).

3-*Acetyl*-2 : 5-*dihydro*-4 : 5-*diphenylfuran*-2-*one* (X; R = R' = Ph).—Benzoin (53 g.) in toluene (80 c.c.) containing triethylamine (0·5 c.c.) was treated with diketen (22·5 g.) as previously described; 2·5 c.c. of water were eliminated. Removal of solvents and crystallisation of the residue (69 g.) from *iso*propanol gave the *lactone* as pale green needles, m. p. 109—110° (Found: C, 77·4; H, 4·9. $C_{18}H_{14}O_3$ requires C, 77·7; H, 5·05%). Light absorption: max., 3550 and 2900 Å; ε, 11,700 and 6700, respectively.

3-*Acetyl*-2 : 5-*dihydro*-4-*phenylfuran*-2-*one* (X; R = Ph, R' = H).—Phenacyl alcohol was prepared by Evans's method (*Amer. Chem. J.*, 1906, **35**, 120), except that it was found that phenacyl acetate was not appreciably hydrolysed by boiling water; however, 1% hydrochloric acid was effective.

Diketen (8·6 g., 98%) was added during 1 hr. to an agitated solution of phenacyl alcohol (13·6 g.) in chloroform (20 c.c.) containing trimethylamine (0·2 c.c.; 25% in methanol) at 55—60°. After a further 20 min. at 55°, the solvent was evaporated and the residue (22 g.) crystallised from methanol, giving *phenacyl acetoacetate* as needles, m. p. 88° (Found: C, 65·35; H, 5·65. $C_{12}H_{10}O_3$ requires C, 65·45; H, 5·5%). The ester gave a weak yellow colour with ferric chloride.

The ester was cyclised by two methods: (*a*) The acetoacetate (5 g.) was refluxed in toluene (25 c.c.) and pyridine (1 c.c.) for 1 hr.; water was eliminated. Removal of solvents and crystallisation of the dark residue from aqueous methanol (charcoal) gave the *lactone* (3·0 g.), as yellow-green needles, m. p. 107—108° (Found : C, 71·1; H, 4·85. $C_{12}H_{10}O_3$ requires C, 71·25; H, 5·0%). Light absorption : max., 2850 and 2250 Å; ε, 9550 and 5750, respectively.

(*b*) The ester (3 g.) was warmed for 1 hr. at 50° with methanol (10 c.c.) containing 10% aqueous sodium hydroxide (1 c.c.); isolation gave the lactone (1 g.).

Acetonyl Acetoacetate.—1-Hydroxypropan-2-one (23·5 g.), in benzene (100 c.c.) and triethylamine (0·2 c.c.), was treated with diketen (28 g., 98%) at 60—70°. Distillation gave the *acetoacetate* (23·0 g.), b. p. 98—100°/0·2 mm., n_D^{20} 1·4531 (Found : C, 53·5; H, 6·5. $C_7H_{10}O_4$ requires C, 53·15; H, 6·4%). Light absorption : max., 2300 Å; ε, 7000. When the ester was refluxed in toluene and pyridine water was eliminated and the product resinified. The *bis-2 : 4-dinitrophenylhydrazone* crystallised in orange granules, m. p. 208—209°, from aqueous acetic acid (Found : C, 43·7; H, 3·55; N, 22·0. $C_{19}H_{18}O_{10}N_8$ requires C, 44·0; H, 3·5; N, 21·6%).

Reaction of Acetoacetic Ester with Ketols.—(a) *Butyroin.* Butyroin (14·4 g.), methyl acetoacetate (11·6 g.), xylene (100 c.c.), pyridine (1 c.c.), and acetic acid (0·8 c.c.) were refluxed beneath a decanter head for 3 hr., during which 5 c.c. of aqueous alcohol were removed. Distillation gave the lactone (X; R = R′ = Pr^n) (14·2 g., 67·5%), b. p. 156—160°/12 mm., n_D^{20} 1·4835, which afforded a 2 : 4-dintrophenylhydrazone, m. p. and mixed m. p. 127°.

(b) *Benzoin.* Benzoin (53 g.), methyl acetoacetate (29 g.), piperidine (2 c.c.), and toluene (80 c.c.) were refluxed for 1·5 hr., aqueous methanol being eliminated as before. Removal of the solvent and recrystallisation of the residue from *iso*propanol gave the lactone (X; R = R′ = Ph) (39 g., 56%) as green needles, m. p. and mixed m. p. 109—110°.

(c) β-*Hydroxy-*αγ*-dimethylvaleraldehyde.*—The aldehyde (36 g.), methyl acetoacetate (35 g.), toluene (100 c.c.), piperidine (1 c.c.), and acetic acid (0·8 c.c.) were refluxed for 5 hr., 8·5 c.c. of aqueous methanol being removed from a decanter head. Distillation of the products gave the lactone (V; R = Pr^i) (29·8 g., 57%).

Hydration of 1-Methylprop-2-ynyl Acetoacetate.—Diketen (122 g., 97%) was added to an agitated mixture of but-3-yn-2-ol (98 g.) and triethylamine (0·5 c.c.) at 60—70° during 0·5 hr. Distillation gave the *acetoacetate* (177 g., 82%), b. p. 95—98°/12 mm., n_D^{20} 1·4441 (Found : C, C, 62·25; H, 6·95. $C_8H_{10}O_3$ requires C, 62·35; H, 6·55%). The ester (20 g.) was refluxed with a solution of mercuric chloride (1 g.) in aqueous ethanol (1 : 1; 50 c.c.) for 2 hr. Distillation gave α-*methylacetonyl acetoacetate* (8·0 g.), b. p. 124°/12 mm., n_D^{20} 1·4400 (Found : C, 56·15; H, 7·2. $C_8H_{12}O_4$ requires C, 55·8; H, 7·05%).

2 Hours' refluxing of the acetoacetate (8 g.) in toluene (20 c.c.) containing piperidine (0·5 c.c.) gave the lactone (X; R = R′ = Me) (6·1 g.), b. p. 135°/12 mm., shown to be identical with that previously obtained, by mixed-m. p. determinations on the 2 : 4-dinitrophenylhydrazones.

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