328. *6-Acetylcyclohex-2-enones: The Condensation of β-Diketones with αβ-Unsaturated Ketones.**

By R. N. LACEY.

Acetylacetone readily condenses in the presence of alkali with methyl vinyl ketone and several homologues to give 6-acetylcyclohex-2-enone derivatives. The products may be catalytically dehydrogenated to *o*-acetylphenols, which are also produced by the action of bromine. Hydrogenation gives 2-acetylcyclohexanones, alkylation of the cyclohexenones takes place at the 6-position, and, as typical 1,3-diketones, 6-acetylcyclohex-2-enone derivatives show the expected reactions with ferric chloride, cupric salts, and guanidine. Spectroscopic results are reported; gas–liquid chromatography shows the products to consist of mixtures of isomers, believed to be keto–enol tautomers.

MICHAEL addition of β-diketones to αβ-unsaturated ketones has not received study since the early work of Scholtz.[1] This author condensed acetylacetone with benzylideneacetophenone in the presence of aqueous sodium hydroxide and obtained the substituted cyclohexenone (II) which he suggested had been formed by hydrolysis of the 6-acetylcyclohex-2-enone (I) first formed. Condensation of benzylideneacetophenone with benzoylacetone similarly gave 3,5-diphenylcyclohex-2-enone (II); in no case studied was a 6-acetylcyclohex-2-enone derivative isolated, and it may be noted that the examples selected by Scholtz do not permit an unequivocal selection to be made between hypothetical intermediate (II) and (*e.g.*, III from benzylideneacetophenone and acetylacetone).

It has been established that addition of ethyl acetoacetate and its homologues to αβ-unsaturated ketones gives 6-ethoxycarbonylcyclohex-2-enone derivatives, *i.e.*, β-keto-esters, not δ-keto-esters, whether (*a*) the reaction is carried out in two stages to

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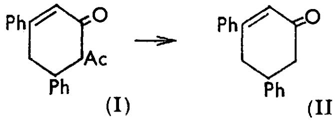
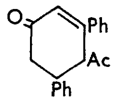
* B.P. Appln. 13,143/1958.

[1] Scholtz, *Ann. Pharm.*, 1916, **254**, 547.

give first the Michael adduct, which is then cyclised by the Claisen hydrogen chloride–diethylaniline technique [2] or by acid or alkali,[3,4] or (*b*) the condensation is carried out in one step in the presence of sodium ethoxide.[5] Orientation of the addition is similar if the $\alpha\beta$-unsaturated ketone is replaced by a precursor; thus, piperitone (6-isopropyl-3-methylcyclohex-2-enone) has been synthesised by condensing ethyl α-isopropylacetoacetate with



(I) (II)



(III)

methyl vinyl ketone,[3] 4-chlorobutan-2-one,[6] 4-diethylaminobutan-2-one,[7] or 1,3-dichlorobut-2-ene,[8] followed, in all cases, by removal of the ethoxycarbonyl group.

In a few instances acetylacetone has been condensed with Mannich bases of the type $R\cdot CO\cdot CHR'\cdot CH_2\cdot NR''_2$, and the expected 6-acetylcyclohex-2-enone derivatives have been obtained.[9,10] 2-Methylcyclohexan-1,3-dione has been condensed with methyl vinyl ketone or 4-diethylaminobutan-2-one, to give a 1,5-diketone,[11] but here the formation of the 1,3-diketone is sterically impossible. The addition of isopropenyl methyl ketone to butan-2-one and to acetone, giving 3,4,6-trimethyl- and 3,6-dimethyl-cyclohex-2-enone respectively has been described by Cologne and Dreux.[12] Condensation of acraldehyde with acetylacetone in the presence of basic catalysts has been claimed by Smith [13] to give 6-acetylcyclohex-2-enone, but the present author has been unable to repeat this preparation.

The condensation of acetylacetone and isopropenyl methyl ketone proceeded very simply when the reactants were boiled in the presence of sodium methoxide and water eliminated was allowed to distil off; sodium and sodium hydroxide were effective catalysts; quinoline and sodium acetate were without effect. The product, obtained in 72—75% yield, showed a strong blue colour with ferric chloride and formed a crystalline copper salt. No solid ketonic derivatives were formed but the infrared spectrum showed two bands, at 1703 and 1672 cm.$^{-1}$, and two broad bands, at 1630 and 1590 cm.$^{-1}$, varying in intensity in different samples; these indicated the presence of two carbonyl groups, one being conjugated, and two enolic groupings. Regeneration of the diketone from the crystalline copper salt and comparison of the product so obtained with the material obtained directly from the condensation showed that the latter was essentially a pure compound with variable proportions of keto- and enol forms. Comparison by infrared and ultraviolet spectroscopy (Tables 1 and 2) and by gas–liquid chromatography (Table 3) indicated the presence of three main components, one of which disappeared on storage. The results were consistent with the formulation as (IV), together with the two enol forms (V) and (VI), and with a mechanism involving first a reversible Michael addition to afford the intermediate (VIII) and then an aldol condensation.

Substantially identical procedures gave the expected cyclohexenones from acetylacetone with methyl vinyl ketone, ethylideneacetone, benzylideneacetone, 2-methylpent-1-en-3-one (VII; $R^1 = Et$, $R^2 = Me$, $R^3 = H$), and 3-ethylbut-3-en-2-one (VII; $R^1 = Me$, $R^2 = Et$,

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[2] Blaise and Maire, *Bull. Soc. chim. France*, 1908, **3**, 418.
[3] Henecka, *Chem. Ber.*, 1949, **82**, 112.
[4] Buchta and Satzinger, *Chem. Ber.*, 1959, **92**, 468.
[5] Abdullah, *J. Indian Chem. Soc.*, 1935, **12**, 62.
[6] Walker, *J.*, 1935, 1585.
[7] Downes, Gill, and Lions, *J. Amer. Chem. Soc.*, 1950, **72**, 3464.
[8] Melikyan and Tatevosyan, *J. Gen. Chem.* (*U.S.S.R.*), 1951, **21**, 696.
[9] Gill, James, Lions, and Potts, *J. Amer. Chem. Soc.*, 1952, **74**, 4923.
[10] Novello, Christy, and Sprague, *J. Amer. Chem. Soc.*, 1953, **75**, 1330.
[11] Swaminathan and Newman, *Tetrahedron*, 1958, **2**, 88.
[12] Cologne and Dreux, *Compt. rend.*, 1950, **231**, 1504.
[13] Smith, U.S.P. 2,516,729.

$R^3 =$ H). Mesityl oxide and 2-acetylcyclohexene failed to react. Spectroscopic data and the results of gas–liquid chromatography are presented in Tables 1—3.

TABLE 1. *6-Acylcyclohex-2-enones: light absorption data (in ethanol) (λ in Å).*

		$\lambda_{max.}$	ε	$\lambda_{max.}$	ε	$\lambda_{min.}$	ε
(IX; $R^1 = R^2 = R^4 =$ Me, $R^3 =$ H)	[a]	3350	4100	2390	8200	2720	1300
		3340	4400	2360	8550	2720	1600
(IX; $R^1 = R^4 =$ Me, $R^2 = R^3 =$ H)	[a]	3360	4700	2460	7250	2750	710
		3350	5500	2420	7750	2750	320
(IX; $R^1 = R^3 = R^4 =$ Me, $R^2 =$ H)	[a]	3340	3600	2350	11,200	2740	500
		3340	5150	2370	10,400	2730	750
(IX; $R^1 = R^4 =$ Me, $R^3 =$ Ph, $R^2 =$ H) ...	[a]	3400	6000	2350	9700	2780	1300
		3370	5400	2320	8700	2790	1250
(IX; $R^1 =$ Et, $R^2 = R^4 =$ Me, $R^3 =$ H) ...	[a]	3360	4700	2460	7250		
		3350	5500	2420	7750	2750	320
(IX; $R^1 = R^4 =$ Me, $R^2 =$ Et, $R^3 =$ H) ...		3375	3540	2360	10,300	2780	1000
(IX; $R^1 =$ Me, $R^2 = R^3 =$ H, $R^4 =$ Ph) ...	[a]	3450	5150	2430	21,300	2850	2040
(IX; $R^1 =$ Ph, $R^2 = R^3 =$ H, $R^4 =$ Me) ...	[b]	3600	12,500	2860	12,500	—	—
				2200	9700		

[a] Where two sets of figures are given, the second refers to material purified through the Cu salt.
[b] Ref. 9.

TABLE 2. *6-Acylcyclohex-2-en-1-ones: light absorption data (in* N/10-NaOH *in* 90% *ethanol–water) (λ in Å).*

		$\lambda_{max.}$	ε	$\lambda_{max.}$	ε	$\lambda_{min.}$	ε
(IX; $R^1 = R^2 = R^4 =$ Me, $R^3 =$ H)	[a]	3550	8850	2360	10,600	2700	2800
		3500	9000	2360	10,700	2700	2000
(IX; $R^1 = R^4 =$ Me, $R^2 = R^3 =$ H)	[a]	3540	12,650	2350	14,400	2720	1250
		3540	12,700	2350	13,000	2740	500
(IX; $R^1 = R^3 = R^4 =$ Me, $R^2 =$ H)	[a]	3500	12,500	2360	12,950	2750	950
		3530	13,000	2370	10,600	2740	65
(IX; $R^1 = R^4 =$ Me, $R^3 =$ Ph, $R^2 =$ H) ...	[a]	3530	10,800	2350	17,200	2870	3400
		3530	11,300	2360	12,000	2810	1550
(IX; $R^1 =$ Me, $R^2 = R^3 =$ H, $R^4 =$ Ph) ...	[a]	3640	12,400	2300	15,300	2900	1000
(IX; $R^1 =$ Ph, $R^2 = R^3 =$ H, $R^4 =$ Me) ...	[b]	3890	13,700	2710	18,400	—	—

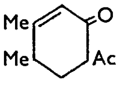
[a, b] See Table 1.

TABLE 3. *6-Acetylcyclohex-2-en-1-ones: gas–liquid chromatography.*[a]

		Crude product (%)	Purified through the Cu salt (%)	
(IX; $R^1 = R^2 = R^4 =$ Me, $R^3 =$ H)	A	29·5	24·2	23·2[b]
	B	28·0	24·1	—
	C	37·6	48·4	70·8
(IX; $R^1 = R^4 =$ Me, $R^2 = R^3 =$ H)	A	3·4	3·4	
	B	9·8	2·4	
	C	88·3	93·5	
(IX; $R^1 = R^3 = R^4 =$ Me, $R^2 =$ H)		96·8	94·9	
(IX; $R^1 =$ Et, $R^2 = R^4 =$ Me, $R^3 =$ H)	A	15·8	14·4	
	B	76·9	76·1	
(IX; $R^1 = R^4 =$ Me, $R^2 =$ Et, $R^3 =$ H)	A	51·7	—	
	B	42·3		

[a] The main components, A, B, C, only are listed, in order of increasing retention time. [b] After one month's storage.

Methyl vinyl ketone reacted readily in the cold in the presence of sodium methoxide, to give the intermediate triketone (VIII; $R^1 = R^4 =$ Me, $R^2 = R^3 =$ H) which was converted into the acetylcyclohexenone by heating it in the presence of the same catalyst with elimination of water. Boiling aqueous alkali converted the triketone into 3-methylcyclohex-2-enone by cyclisation and hydrolytic elimination of an acetyl group. Other vinyl ketones, *e.g.*, isopropenyl methyl ketone, failed to undergo addition with acetylacetone in the cold, and the formation of acetylcyclohexenones (IX) at elevated temperatures in these cases must be attributed to disturbance of an unfavourable equilibrium between (VII) and (VIII) by loss of water. In the case of mesityl oxide the tendency for Michael addition is even less, and no conversion into acetylcyclohexenone was observed. This pattern of behaviour is closely similar to the Michael addition of ethyl acetoacetate to αβ-unsaturated ketones.[14]



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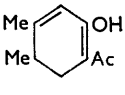

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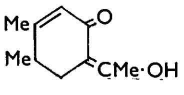

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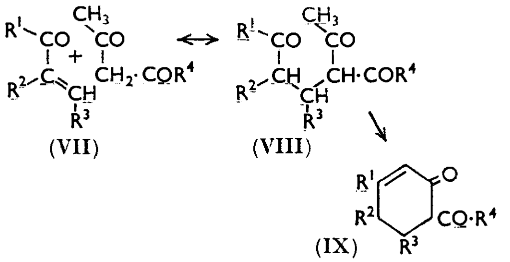


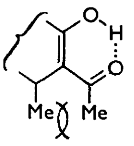
(VII) (VIII) (IX)

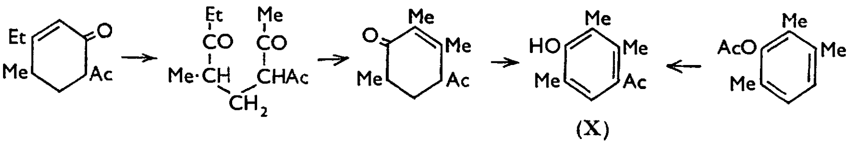
Benzoylacetone and methyl vinyl ketone under the general reaction conditions gave a mixture of ketones. Purification through the copper salt gave compound (IX; $R^1 = Me$, $R^4 = Ph$, $R^2 = R^3 = H$). The crude product appeared, from spectroscopic evidence, to contain some 4-benzoyl-3-methylcyclohex-2-enone formed by the alternative mode of cyclisation of the intermediate (VIII).

Hydrogenation of the products was not exhaustively studied; the cyclohexenones (IX; $R^1 = R^4 = Me$, $R^2 = R^3 = H$) and (IX; $R^1 = R^3 = R^4 = Me$, $R^2 = H$) were both selectively hydrogenated over palladium–barium sulphate to give the expected acetylcyclohexanones.

The two acetylcyclohexanones showed an interesting, markedly different tendency to enolise, as shown by their infrared spectra in carbon tetrachloride. Whereas 2-acetyl-5-methylcyclohexanone behaved as a highly enolised β-diketone (*ca.* 80% enol), 2-acetyl-3,5-dimethylcyclohexanone showed little enolisation (*ca.* 20% enol). Amongst the acetylcyclohexenones, the dimethyl compound (IX; $R^1 = R^2 = R^4 = Me$, $R^2 = H$) appeared to show no marked spectroscopic differences from other compounds in this series but it is noteworthy that in the vapour phase (Table 3) it appeared to exist in a single (ketonic ?) form. The possibility that the adjacent methyl group may sterically inhibit the coplanar, hydrogen-bonded enol form as shown in the annexed structure, is pointed out.

Proof of the structural formulæ proposed was supplied by dehydrogenation over palladium–barium sulphate. Conversions into aromatic compounds were incomplete and in several cases the corresponding acetylcyclohexanones, evidently arising from the disproportionation of the starting material, were detected. Fair yields of the expected *o*-acetylphenols were, however, obtained in all cases. 2-Acetyl-5-ethyl-4-methylphenol was obtained crystalline on dehydrogenation of the cyclohexenone (IX; $R^1 = Et$, $R^2 = R^4 = Me$, $R^3 = H$); earlier workers[15] report this material to be an oil. This dehydrogenation was anomalous in giving, in addition to the *o*-acetylphenol mentioned, a substantial yield of 4-acetyl-2,3,6-trimethylphenol (X), the structure of which was indicated by ultraviolet spectroscopy [$\lambda_{max.}$ 2785 Å, ε 11,000; cf. 2-acetyl-4,5-dimethylphenol, $\lambda_{max.}$ 2630 (ε 12,600), 3360 Å (ε 4250) and strong end-absorption] and by infrared





(X)

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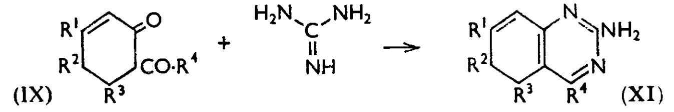
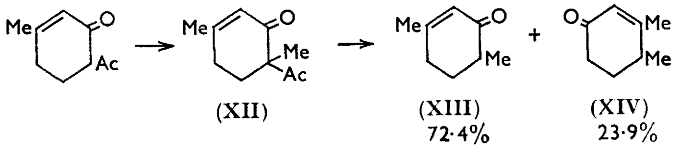
[14] Henecka, " Chemie der beta-Dicarbonylverbindungen," Springer-Verlag, Berlin, 1950.
[15] Auwers and Mauss, *Ber.*, 1928, **61**, 1496.

spectroscopy [$\nu_{max.}$ 1680 cm.$^{-1}$ (C : O), with a strong OH band and a weak band at 879 cm.$^{-1}$ indicative of heavy aromatic substitution] and proved by unambiguous synthesis by the Fries rearrangement of 2,3,6-trimethylphenyl acetate. A sample of compound (IX; R^1 = Et, R^2 = R^4 = Me, R^3 = H) purified through the crystalline copper salt also gave some 4-acetyl-2,3,6-trimethylphenol, although in lower yield than with the unpurified ketone: this surprising result indicates rearrangement through a reverse aldol reaction under the conditions of the dehydrogenation.



Treatment of the acetylcyclohexenones with bromine in carbon tetrachloride–acetic acid gave intermediate bromo-compounds which readily lost hydrogen bromide to give the expected *o*-acetyl-phenols. The method was particularly successful with 6-acetyl-3-phenylcyclohex-2-enone which was thus dehydrogenated to 4-acetyl-3-hydroxybiphenyl in high yield. The cyclohexenone (IX; R^1 = Et, R^2 = R^4 = Me, R^3 = H) in this instance gave only the expected *o*-acetylphenol. Ultraviolet absorption data for 2-acetyl-3,5-dimethylphenol show a shift to lower wavelengths and a reduction of intensities due to steric interaction between the acetyl group and the adjacent methyl group (see above).

The 6-acetylcyclohexenones behaved as normal 1,3-diketones when treated with guanidine; compounds (IX; R^1 = R^4 = Me, R^2 = R^3 = H) and (IX; R^1 = R^4 = Me, R^2 = Et, R^3 = H) condensed with guanidine carbonate in boiling ethanol to give the expected 2-aminopyrimidine derivatives (2-amino-5,6-dihydroquinazolines).



Alkylation of 6-acetylcyclohex-2-enones as their sodium salts in ethanol resulted, as expected, in substitution at the 6-position. The reaction was accompanied in the cases studied by hydrolysis of the 6-acetyl group; alkylation of the diketone (IX; R^1 = R^4 = Me, R^2 = R^3 = H) with benzyl chloride gave 6-benzyl-3-methylcyclohex-2-enone in fair yield directly. Alkylation of the same diketone with methyl iodide gave 6-acetyl-3,6-dimethylcyclohex-2-enone, which gave a solid ketonic derivative and exhibited the spectroscopic properties of a non-enolised diketone. The final ketone was readily hydrolysed with aqueous alkali but the product, although mainly the expected 3,6-dimethylcyclohex-2-enone (71·4%), also contained 3,4-dimethylcyclohex-2-enone (23·9%).

The nature of the hydrolysis products (XIII and XIV) does not discredit the structure proposed for the alkylation product. It has been shown that the two cyclohexenone derivatives are rapidly interconvertible in the presence of alkali; this interconversion and the hydrolysis of 6-acylcyclohex-2-enone derivatives are described in the following paper.

Alkylation of the cyclohexenone (IX; R^1 = R^2 = R^4 = Me, R^3 = H) with methyl iodide gave a mixture of the expected 6-methyl diketone and its hydrolysis product; this mixture was hydrolysed directly to 3,4,6-trimethylcyclohex-2-enone, the structure of which was established by dehydrogenation to 3,4,6-trimethylphenol.

EXPERIMENTAL

M. p.s are corrected. Gas–liquid chromatographic analyses were carried out with nitrogen as carrier gas and a hydrogen-flame detector. An 8 ft. × 6 mm. column packed with Apiezon M (20%) on Celite (60—80 mesh) and heated in a bath at 196° was used. Analyses are based on recorder peak-area measurements.

6-*Acetyl*-3,4-*dimethylcyclohex*-2-*enone* (IX; $R^1 = R^2 = R^4 = Me$, $R^3 = H$).—A mixture of acetylacetone (60 g., 0·6 mole), isopropenyl methyl ketone (42 g., 0·5 mole), and sodium methoxide (1·0 g.) was boiled beneath a small decanter head with a reflux condenser which enabled entrained water to be collected and removed. The temperature of the mixture rose from 120° to 174° during 15 min.; after 2 hours' heating the reaction temperature was 206° and 10·0 ml. of an aqueous layer had been collected from the decanter. The residue was taken up in ether, washed with 10% sulphuric acid followed by water, and isolated, to give the *cyclohexenone* (60·1 g., 72·5%), b. p. 133—135°/14 mm., n_D^{20} 1·519—1·525 (Found: C, 72·1; H, 8·15. $C_{10}H_{14}O_2$ requires C, 72·3; H, 8·5%), which gave a blue colour with aqueous ferric chloride. The *copper derivative* crystallised as a green powder, m. p. 144—145°, from light petroleum (b. p. 60—80°) [Found: C, 61·5; H, 6·9. $Cu(C_{20}H_{26}O_4)$ requires C, 61·05; H, 6·65%].

Other catalysts were successfully used. Sodium (0·5 g.) gave a 73·5% yield; sodium hydroxide (0·5 g.) gave a 61·5% yield; sodium and quinoline were ineffective.

A sample of the above cyclohexenone was purified through the copper salt to give an oil, b. p. 135—138°/14 mm., n_D^{20} 1·5240, in 70% overall recovery.

Acetylacetone (60 g.), isopropenyl methyl ketone (37 g.), and sodium methoxide (0·5 g.), when kept for 24 hr. in the cold, afforded no condensation products.

6-*Acetyl*-3-*methylcyclohex*-2-*enone* (IX; $R^1 = R^4 = Me$, $R^2 = R^3 = H$).—Acetylacetone (60 g., 0·6 mole), methyl vinyl ketone (35 g., 0·5 mole), sodium methoxide (1·0 g.), and quinol (0·1 g.) were heated together as described above. After 2 hr., the reaction temperature was 210° and 8 ml. of an aqueous layer had been collected. Isolation as before gave the *cyclohexenone* (43·0 g., 56·5%), b. p. 126—130°/13 mm., n_D^{20} 1·525—1·528 (Found: C, 71·35; H, 7·95. $C_9H_{12}O_2$ requires C, 71·05; H, 7·95%). The *copper derivative* formed dark green needles, m. p. 169°, from benzene–light petroleum (b. p. 60—80°) [Found: C, 58·9; H, 6·05. $Cu(C_{18}H_{22}O_4)$ requires C, 59·1; H, 6·1%].

The cyclohexenone (1·5 g.) and guanidine carbonate (0·9 g.) were refluxed in ethanol (5 ml.) for 4 hr. Addition of water gave 2-*amino*-5,6-*dihydro*-4,7-*dimethylquinazoline* (XI; $R^1 = R^4 = Me$, $R^2 = R^3 = H$) which crystallised as needles, m. p. 160—161°, from water (Found: C, 68·4; H, 7·65; N, 23·9. $C_{10}H_{13}N_3$ requires C, 68·55; H, 7·5; N, 23·95%). The ketone was purified through the copper salt to give an oil, b. p. 126—127°/17 mm., n_D^{20} 1·5267, in 50% overall recovery.

In a similar experiment in which sodium methoxide was replaced by calcium oxide (2 g.), the reaction was slower; after 3·5 hours' heating, a 34% yield was obtained.

3-*Acetylheptane*-2,6-*dione*.—Methyl vinyl ketone (30 g.) was added during 20 min. to a stirred mixture of acetylacetone (60 g.) and a solution of sodium methoxide (from 0·2 g. of sodium and 5 ml. of methanol), the temperature being kept at 25—30°. After 24 hr. at room temperature, the product was washed with dilute sulphuric acid and isolated, to give the *triketone* (VIII; $R^1 = R^4 = Me$, $R^2 = R^3 = H$) (32·9 g.), b. p. 97—101°/0·8 mm., n_D^{20} 1·4594, giving a deep reddish-purple with aqueous ferric chloride (Found: C, 63·75; H, 8·75. $C_9H_{14}O_3$ requires C, 63·5; H, 8·3%). The ketone (10 g.) immediately dissolved in cold aqueous 10% sodium hydroxide (40 ml.) but an oil was rapidly deposited on warming. After 1 hour's refluxing the product was isolated, to give 3-methylcyclohex-2-enone (4·0 g.), b. p. 79°/13 mm., identified by its infrared spectrum. The ketone (10 g.) was heated at 180—200° (bath) in the presence of sodium methoxide (0·1 g.) for 2 hr.; water distilled; isolation gave the cyclohexenone (IX; $R^1 = R^4 = Me$, $R^2 = R^3 = H$) in 70% yield.

6-*Acetyl*-3,5-*dimethylcyclohex*-2-*enone* (IX; $R^1 = R^3 = R^4 = Me$, $R^2 = H$).—Acetylacetone (60 g., 0·6 mole), ethylideneacetone (42 g.; 83% pure, the remainder being mesityl oxide), and sodium methoxide (1 g.) were heated as previously described. The reaction temperature rose from 155° to 190° during 4 hr.; 8·8 ml. of aqueous layer were collected. Isolation gave the *cyclohexenone* (49·5 g., 84% yield on ethylideneacetone), b. p. 128—132°/11 mm., n_D^{20} 1·517—1·520 (Found: C, 72·95; H, 8·4. $C_{10}H_{14}O_2$ requires C, 72·3; H, 8·5%). The *copper salt* formed green needles, m. p. 159—160°, from light petroleum (b. p. 60—80°) [Found: C, 61·1; H, 6·55. $Cu(C_{20}H_{26}O_4)$ requires C, 61·05; H, 6·65%]. Purification of the ketone through the copper salt gave an oil, b. p. 133—134°/13 mm., n_D^{20} 1·5168, in 65% overall recovery.

6-*Acetyl*-3-*methyl*-5-*phenylcyclohex*-2-*enone* (IX; $R^1 = R^4 = Me$, $R^3 = Ph$, $R^2 = H$).—Acetylacetone (75 g., 0·75 mole), benzylideneacetone (73 g., 0·5 mole), and sodium methoxide (1 g.) were heated together as before. In 1·5 hr. the reaction temperature rose to 182° and 10 ml. of an aqueous layer were collected. Isolation gave the *cyclohexenone* (76 g., 66·5%),

b. p. 140—148°/1 mm., n_D^{20} 1·579—1·581 (Found: C, 78·8; H, 7·45. $C_{15}H_{16}O_2$ requires C, 78·9; H, 7·05%). The *copper salt* formed dark green needles, m. p. 218—219°, from benzene–light petroleum (b. p. 80—120°) [Found: C, 69·35; H, 5·95. $Cu(C_{30}H_{30}O_4)$ requires C, 69·55; H, 5·85%]; purification of the ketone through this salt gave an oil, b. p. 145—146°/1 mm., n_D^{20} 1·5841, in 77% overall recovery.

6-Acetyl-3-ethyl-4-methylcyclohex-2-enone (IX; R^1 = Et, R^2 = R^4 = Me, R^3 = H).—Acetylacetone (87·5 g., 0·875 mole), 2-methylpent-1-en-3-one (68·5 g., 0·7 mole), and sodium methoxide (3 g.) were heated as before; in 5·5 hr. 12·6 ml. of an aqueous layer were collected and the final temperature was 210°. Isolation gave the *cyclohexenone* (78·2 g., 62%), b. p. 149—158°/15 mm., n_D^{20} 1·520 to 1·509 (Found: C, 73·1; H, 8·6. $C_{11}H_{16}O_2$ requires C, 73·3; H, 8·95%). The *copper salt* crystallised as a green powder, m. p. 156—157°, from benzene–light petroleum (b. p. 60—80°) [Found: C, 62·6; H, 7·0. $Cu(C_{22}H_{30}O_4)$ requires C, 62·6; H, 7·15%], and purification through this salt gave the ketone, b. p. 142—147°/12 mm., n_D^{20} 1·5237, in 59% overall recovery.

6-Acetyl-4-ethyl-3-methylcyclohex-2-enone (IX; R^1 = R^4 = Me, R^2 = Et, R^3 = H).—Acetylacetone (96 g., 0·96 mole), 3-ethylbut-3-en-2-one (78·5 g.; b. p. 71°/150 mm., n_D^{20} 1·4288), and sodium methoxide (1 g.) were heated for 4 hr.; an aqueous layer (15·7 ml.) was decanted and the reaction temperature rose to 220°. Isolation gave the *cyclohexenone* (102·3 g., 71%), b. p. 146—155°/13 mm., n_D^{20} 1·511—1·506 (Found: C, 73·8; H, 8·95. $C_{11}H_{16}O_2$ requires C, 73·3; H, 8·95%). The cyclohexenone (1·8 g.) and guanidine carbonate (0·9 g.) in 1 : 1 aqueous ethanol (10 ml.) were refluxed together for 3 hr. A solid crystallised on cooling and recrystallisation from ethyl acetate gave *2-amino-6-ethyl-5,6-dihydro-4,7-dimethylquinazoline* (XI; R^2 = Et, R^1 = R^4 = Me, R^3 = H) as needles, m. p. 158—160° (Found: C, 70·45; H, 8·3; N, 20·75. $C_{12}H_{17}N_3$ requires C, 70·9; H, 8·45; N, 20·65%). The copper salt was too soluble in light petroleum and other solvents for purification.

6-Benzoyl-3-methylcyclohex-2-enone (IX; R^1 = Me, R^2 = R^3 = H, R^4 = Ph).—A mixture of benzoylacetone (65 g.), methyl vinyl ketone (42 g.), and sodium methoxide (0·5 g.) was heated for 4 hr.; the reaction temperature rose to 180° and water (5 ml.) was collected. Isolation gave an oil (55·8 g.), b. p. 179—200°/4·5 mm., whose copper salt (33 g.) crystallised as a red powder (from benzene), m. p. 208—208·5° [Found: C, 69·05; H, 5·15. $Cu(C_{28}H_{26}O_4)$ requires C, 68·75; H, 5·35%], and with dilute sulphuric acid gave the *diketone* (25·0 g.) b. p. 150—155°/1 mm., n_D^{20} 1·5980 (Found: C, 78·8; H, 6·6. $C_{14}H_{14}O_2$ requires C, 78·45; H, 6·6%). The infrared spectrum showed a sharp C=O band at 1670 cm.$^{-1}$ and a broad band at 1580 cm.$^{-1}$. Comparison with the spectrum of the crude distilled product showed this to be about 60% pure; a band at 1692 cm.$^{-1}$ shown by the latter was ascribed to 4-benzoyl-3-methylcyclohex-2-enone.

2-Acetyl-5-methylcyclohexanone.—6-Acetyl-3-methylcyclohex-2-enone (20 g.) in ethanol (60 ml.) was agitated in hydrogen in the presence of 5% palladium–barium sulphate. Absorption (3·1 l. at 17°/754 mm.; 99%) ceased after 1 hr. The product, the *acetylcyclohexanone* (15 g.), had b. p. 114—120°/13 mm., n_D^{20} 1·5030 (Found: C, 69·8; H, 8·8. $C_9H_{14}O_2$ requires C, 70·1; H, 9·15%). A *copper salt* was obtained, crystallising in green prisms, m. p. 198—198·5°, from benzene–light petroleum (b. p. 100—120°) [Found: C, 58·2; H, 7·0. $Cu(C_{18}H_{26}O_4)$ requires C, 58·45; H, 7·1%]. The oil had $\lambda_{max.}$ in EtOH 2910 Å (ε 7000), but in 0·1N-NaOH in 90% ethanol, 3120 Å (ε 16,800). The infrared spectrum was that of a highly enolised β-diketone.

2-Acetyl-3,5-dimethylcyclohexanone.—6-Acetyl-3,5-dimethylcyclohex-2-enone (20 g.) was hydrogenated as above; absorption (2·65 l. at 18°/755 mm.; 92%) was complete in 2 hr. Isolation gave the *acetylcyclohexanone* (15 g.), b. p. 122—126°/15 mm., n_D^{20} 1·4756 (Found: C, 71·1; H, 9·45. $C_{10}H_{16}O_2$ requires C, 71·4; H, 9·6%), which afforded a *copper salt*, crystallising in pale green needles, m. p. 141—142°, from light petroleum (b. p. 60—80°) [Found: C, 60·85; H, 7·5. $Cu(C_{20}H_{30}O_4)$ requires C, 60·35; H, 7·6%]. The oil had $\lambda_{max.}$ in EtOH 2910 Å (ε 2700), in 0·1N-NaOH in 90% ethanol, 3120 Å (ε 15,000). The infrared spectrum in carbon tetrachloride showed only *ca.* 20% of enolisation.

6-Acetyl-3-methylcyclohex-2-enone.—The diketone (15 g.) was refluxed with 5% palladium–barium sulphate (0·1 g.) for 30 min. Distillation gave an oil (11·5 g.), b. p. 113—117°/13 mm., shown by infrared analysis to contain 60% of 2-acetyl-5-methylphenol, the remainder being chiefly 2-acetyl-5-methylcyclohexanone. The product formed a *2,4-dinitrophenylhydrazone* which gave orange needles (from ethyl acetate), m. p. 238° undepressed on admixture with a sample of derivative made from authentic 2-acetyl-5-methylphenol (Found: C, 54·9; H, 4·3; N, 16·5. $C_{15}H_{14}O_5N_4$ requires C, 54·65; H, 4·25; N, 16·95%).

6-*Acetyl*-3,4-*dimethylcyclohex*-2-*enone*.—The diketone (5 g.) was refluxed for 30 min. with palladium–barium sulphate (0·05 g.). The catalyst was removed and the product crystallised from light petroleum (b. p. 40—60°), to give 2-acetyl-4,5-dimethylphenol (1·26 g.), m. p. and mixed m. p. 71·5—72·5° (lit.,[16] gives m. p. 71°). Light absorption, see text.

Other 6-acylcyclohex-2-en-1-ones were dehydrogenated similarly (5 g. of diketone and 0·05 g. of catalyst) with the following results:

Compound (IX)						
R^1	R^2	R^3	R^4	Product	g.	m.p.
Me	H	Me	Me	2-Acetyl-3,5-dimethylphenol [a]	2·42	58—59°
Me	Et	H	Me	2-Acetyl-4-ethyl-5-methylphenol [b]	2·2	96·5—97
Et	Me	H	Me	4-*Acetyl*-2,3,6-*trimethylphenol* [c]	0·5	132—133
				2-Acetyl-5-ethyl-4-methylphenol [d]	0·3	52
Me	H	H	Ph	2-Benzoyl-5-methylphenol [e]	0·3	59·5—60

[a] Undepressed with authentic specimen; lit.,[17] m. p. 57—58°. $\lambda_{max.}$ 2610 (ε 5600), 3050 (ε 2180), 2200 Å (ε 1320). [b] Undepressed with authentic specimen; lit., m. p. 96—97°. $\lambda_{max.}$ 2635 (ε 12,700), 3360 Å (ε 4180): strong end absorption. [c] From light petroleum (b. p. 40—60°) (Found: C, 73·8; H, 8·0. $C_{11}H_{14}O_2$ requires C, 74·15; H, 7·9%). Light absorption, see text. [d] Plates from light petroleum (b. p. 40—60°) (Found: C, 74·2; H, 7·65. Calc. for $C_{11}H_{14}O_2$: C, 74·15; H, 7·9%); lit.,[15] an oil. $\lambda_{max.}$ 2635 (ε 12,900), 3370 Å (ε 4210): strong end absorption. [e] Isolated by distillation, b. p. 141—146°/1 mm., and crystallisation from methanol as needles; undepressed with authentic specimen, lit.,[18] m. p. 63°.

4-*Acetyl*-2,3,6-*trimethylphenol*.—2,3,6-Trimethylphenyl acetate (b. p. 118°/12 mm.; 8·9 g.) was heated rapidly with powdered anhydrous aluminium trichloride (7 g.) at 165—170° (bath), at which temperature the bath was held for 15 min. The product was cooled and treated with crushed ice and dilute hydrochloric acid. Isolation with ether gave 4-acetyl-2,3,6-trimethylphenol (8·4 g.), m. p. 128·5—130°, which on crystallisation from ether had m. p. and mixed m. p. 132—133°.

Brominations.—6-*Acetyl*-3-*methylcyclohex*-2-*enone*. To a stirred solution of the diketone (5 g.) in carbon tetrachloride (20 ml.) at 20° was added a 16% w/v solution of bromine in acetic acid (32 ml.) during 30 min. The mixture was stirred for 1 hr. at 20° and for 1 hr. at 30°; hydrogen bromide was evolved. The product, distilled under reduced pressure, gave an oil (2·5 g.), b. p. 80—83°/0·9 mm., shown by infrared analysis to contain 90% of 2-acetyl-5-methylphenol.

6-*Acetyl*-3,4-*dimethylcyclohex*-2-*enone*. The diketone (6·7 g.) gave an oil (3·0 g.), b. p. 90—91°/1 mm., which partially crystallised. Recrystallisation from light petroleum (b. p. 40—60°) gave 2-acetyl-4,5-dimethylphenol,[16] m. p. and mixed m. p. 71°.

6-*Acetyl*-3-*ethyl*-4-*methylcyclohex*-2-*enone*. The diketone (7·2 g.) gave an oil (3·5 g.), b. p. 110°/2 mm., which partially solidified. Crystallisation from light petroleum (b. p. 40—60°) gave 2-acetyl-5-ethyl-4-methylphenol as plates (1·35 g.), m. p. 51—51·5° alone or mixed with a sample obtained by catalytic dehydrogenation.

6-*Acetyl*-4-*ethyl*-3-*methylcyclohex*-2-*enone*. The diketone (7·2 g.) gave, after distillation, an oil, b. p. 110—119°/2 mm., which crystallised from light petroleum (b. p. 60—80°) to give 2-acetyl-4-ethyl-5-methylphenol [18] as needles (1·33 g.), m. p. and mixed m. p. 95·5—96·5°.

6-*Acetyl*-3-*phenylcyclohex*-2-*enone*. The diketone (8·6 g.) was treated with bromine as previously described. Removal of solvents and crystallisation from light petroleum (b. p. 60—80°) gave 4-acetyl-3-hydroxybiphenyl (7·0 g.), m. p. 85—86°, which, after repeated crystallisation, had m. p. and mixed m. p. 91° (lit.,[19] m. p. 90·5—91·5°).

Alkylations.—6-*Acetyl*-3-*methylcyclohex*-2-*enone*. (*a*) The diketone (30·4 g.) was added to a solution of sodium ethoxide in ethanol (from 4·6 g. of sodium and 100 ml. of ethanol), and the solution of the sodium salt was treated with methyl iodide (30 g.). The mixture was refluxed for 3 hr. and acidified with acetic acid. The bulk of the ethanol was distilled off, water was added, and the product isolated to give two main fractions: (i) b. p. 94—102°/15 mm. (6·2 g.) and (ii) b. p. 122—124°/15 mm. (8·6 g.). Redistillation of (ii) gave 6-*acetyl*-3,6-*dimethylcyclohex*-2-*enone* (XII), $\nu_{max.}$ 1712 (C:O), 1670 (C:O), 1638 cm.$^{-1}$ (C:C), $\lambda_{max.}$ 2340 (ε 11,400), 3230 Å (ε 150), b. p. 120°/10 mm., n_D^{20} 1·4955 (Found: C, 71·75; H, 8·7. $C_{10}H_{14}O_2$ requires C, 72·3;

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[16] Auwers, Bundesman, and Wieners, *Annalen*, 1926, **447**, 186.
[17] Auwers, *Ber.*, 1915, **48**, 92, 1707.
[18] Rosenmund and Schnurr, *Annalen*, 1928, **460**, 85.
[19] Bradsher, Brown, and Porter, *J. Amer. Chem. Soc.*, 1954, **76**, 2359.

H, 8·5%), giving a *bis-2,4-dinitrophenylhydrazone* as a red powder, m. p. 232—233° (from aqueous dioxan) (Found: C, 50·15; H, 4·4. $C_{22}H_{22}O_8N_8$ requires C, 50·2; H, 4·2%).

The diketone (XII) (12·8 g.) was hydrolysed for 3 hr. with a refluxing solution of sodium hydroxide (5 g.) in 1 : 1 aqueous ethanol (50 ml.). Isolation gave an oil (8·3 g.), b. p. 89—91°/14 mm., n_D^{20} 1·4873, shown by gas–liquid chromatography to contain 72·4% of (XIII) and 23·9% of (XIV). The nature of these products was established in unpublished work.

Fraction (i) above was shown to be a mixture of (XIII) and (XIV) with about 25% of the diketone (XII).

(*b*) The diketone (IX; $R^1 = R^4 =$ Me, $R^2 = R^3 =$ H) (28 g.) was alkylated as in (*a*), methyl iodide being replaced by benzyl chloride (25 g.). Isolation gave 6-benzyl-3-methylcyclohex-2-enone (20·5 g.), b. p. 182—185°/12 mm., n_D^{20} 1·5525, $\lambda_{max.}$ 2330 Å (ε 14,000) (lit.,[8] b. p. 125—127°/2 mm., $n_D^{27.75}$ 1·5511) (Found: C, 83·55; H, 8·2. Calc. for $C_{14}H_{16}O$: C, 83·95; H, 8·05%) which formed a *2,4-dinitrophenylhydrazone* crystallising as red needles, m. p. 150·5—151°, from propan-2-ol (Found: C, 63·0; H, 5·3. $C_{20}H_{20}O_4N_4$ requires C, 63·15; H, 5·3%), and a semicarbazone as prisms, m. p. 192°, from ethanol (lit.,[8] m. p. 189—190°).

6-Acetyl-3,4-dimethylcyclohex-2-enone.—The diketone (33 g.) in ethanol (100 ml.) containing sodium ethoxide (from 4·6 g. of sodium) was treated with methyl iodide (30 g.), and the mixture refluxed for 1 hr. Acidification of the product with acetic acid and isolation gave two main fractions: (i) b. p. 97—100°/14 mm. (7·7 g.) and (ii) b. p. 142—150°/14 mm. (10·1 g.), n_D^{20} 1·4940.

The entire product (27 g.) was hydrolysed by refluxing it for 3 hr. with a solution of sodium hydroxide (10 g.) in 1 : 1 v/v aqueous ethanol (100 ml.). Isolation gave 3,4,6-trimethylcyclohex-2-enone (14·1 g.), b. p. 96—99°/14 mm., n_D^{20} 1·4872 (Found: C, 78·05; H, 10·05. Calc. for $C_9H_{14}O$: C, 78·2; H, 10·2%), giving a semicarbazone, m. p. 179·5—181°, as a powder from aqueous ethanol (Cologne and Dreux [12] give b. p. 212°/745 mm., n_D^{17} 1·484, and a semicarbazone, m. p. 192°). A portion of the ketone (5 g.) was dehydrogenated by refluxing it in biphenyl (15 g.) with 5% palladium–barium sulphate (0·5 g.) for 3 hr. Isolation by extraction with alkali and subsequent acidification gave a crude solid (1·2 g.), which after several recrystallisations from light petroleum (b. p. 40—60°) gave 3,4,6-trimethylphenol, m. p. and mixed m. p. 70—71°.

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