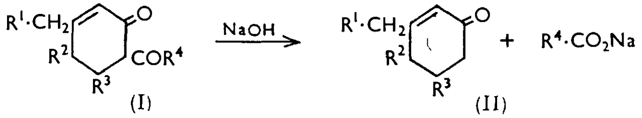
330. *The Hydrolysis of 6-Acylcyclohex-2-enones and the Base-catalysed Rearrangement of Cyclohex-2-enones.*

By R. N. Lacey.

6-Acylcyclohex-2-enones may be hydrolysed with aqueous sodium hydroxide to cyclohex-2-enones with elimination of the 6-acyl group. 3,4-Disubstituted derivatives, however, give an ~1 : 1 mixture of two isomeric cyclohex-2-enones arising from simultaneous hydrolysis and ring-opening followed by re-cyclisation; further contact with boiling sodium hydroxide induces a further change to an equilibrium mixture of unequal amounts of the two isomers. The interconversion of a variety of substituted cyclohex-2-enones in boiling alkali has been studied kinetically, and velocity and equilibrium constants have been established. At equilibrium, 2,3- and 3,4-dialkylcyclohex-2-enones, were in all cases preponderant over the corresponding 3-alkyl- or 3,6-dialkyl-substituted isomers. Possible explanations are proposed and some implications of the present work in connection with earlier literature of cyclohex-2-enone synthesis are pointed out.

The synthesis of 6-acylcyclohex-2-enones (I) by the condensation of 1,3-diketones with αβ-unsaturated ketones in the presence of alkaline catalysts has been described in an earlier paper.[1] These products behaved as enolisable 1,3-diketones with aqueous alkali; addition to boiling 10% aqueous sodium hydroxide typically gave a clear solution which became cloudy after a few seconds, a substantial oily layer separating in 2—3 min. Hydrolysis of three compounds (I; $R^1 = R^2 = H$, $R^4 = Me$, $R^3 = H$, Me, or Ph) proceeded simply to give 60—70% yields of the known cyclohexenones (II) with elimination of the acetyl group, as shown below. Similarly, the benzoyl derivative (I; $R^1 = R^2 = R^3 = H$, $R^4 = Ph$) gave 3-methylcyclohex-2-enone and benzoic acid. It was particularly noted that the product contained no 3-phenylcyclohex-2-enone (see below).



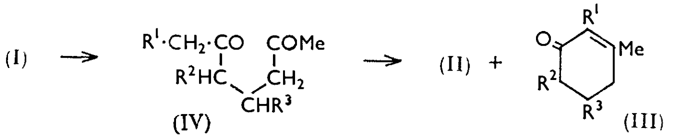
However, hydrolysis of 6-acylcyclohexones with substituents in the 4-position ($R^2 \neq H$) gave products which showed that the above representation was a considerable simplification

---

[1] Lacey, *J.*, 1960, 1625.

of the reaction. The neutral products from the hydrolysis of compound (I; $R^1 = R^2 = R^4 =$ Me, $R^3 =$ H) in boiling 10% aqueous sodium hydroxide for 0·5 hr. constituted a series of fractions which were shown by gas–liquid chromatography to consist essentially of two components (A and B). Spectroscopic examination of the higher-boiling component (B) showed it to be of the type (II) [$\nu_{max.}$ C:O (str.) 1672 cm.$^{-1}$, C:C (str.) 1626 cm.$^{-1}$, δ-CH 876 cm.$^{-1}$; $\lambda_{max.}$ 2350 Å]. The lower-boiling component (A), however, although clearly a cyclohex-2-enone, had markedly different spectral properties [$\nu_{max.}$ C:O (str.) 1664 cm.$^{-1}$, C:C (str.) 1641 cm.$^{-1}$, δ-CH (weak) 876 cm.$^{-1}$ (typical of the 2-hydrogen atom); $\lambda_{max.}$ 2420 Å]. Component (A) was catalytically dehydrogenated to 2,3,6-trimethylphenol and treatment of its oxime with acetic anhydride–acetyl chloride–pyridine (an established technique [2] for the conversion of cyclohexenones into *N*-acetylanilines) gave *N*-acetyl-2,3,6-trimethylaniline; similar treatment of material (B) gave *N*-acetyl-3-ethyl-4-methylaniline. Products (A) and (B) were thus identified as 2,3,6-trimethyl- (III; $R^1 = R^2 =$ Me, $R^3 =$ H) and 3-ethyl-4-methyl-cyclohex-2-enone (II; $R^1 = R^2 =$ Me, $R^3 =$ H) respectively.

Hydrolysis of 6-acetyl-4-ethyl-3-methylcyclohex-2-enone (I; $R^1 = R^3 =$ H, $R^2 =$ Et, $R^4 =$ Me) similarly gave a mixture of ketones. The higher-boiling one, separated in not better than 80% purity, was shown by the above method to have structure (II; $R^1 = R^3 =$ H, $R^2 =$ Et) as expected from the simple hydrolysis mechanism given earlier, whereas the lower-boiling ketone was a " rearranged " cyclohexenone, separated in 90% purity and shown to have structure (III; $R^1 = R^3 =$ H, $R^2 =$ Et). The acetyldimethyl derivative (I; $R^1 = R^3 =$ H, $R^2 = R^4 =$ Me) gave a mixture of two ketones on hydrolysis comprising compound (II; $R^1 = R^3 =$ H, $R^2 =$ Me) and the " rearranged " ketone (III; $R^1 = R^3 =$ H, $R^2 =$ Me), which was only partially resolved by distillation; gas–liquid chromatography readily separated the two ketones, however, and conversion into the respective *N*-acetylanilines provided identification.



The formation of two products from acetylcyclohexenones (I) may be formally explained as shown above, the two ketones being the products arising from the two possible ways in which a hypothetical αε-diketone (IV), postulated as intermediate, may cyclise. The diketones (I) in which $R^1 = R^2 =$ H can be hydrolysed to give only one product no matter which way the " intermediate " (IV) may cyclise. The possibility that the diketone (I) in which R^4 is not methyl may give two products is discussed below.

Kinetic experiments in which the diketone (I) was added to a 100% molar excess of boiling 10% aqueous sodium hydroxide, samples of the supernatant ketone layer being removed at intervals for analysis, were carried out for the three instances in which two products were formed. It was shown: (*a*) that hydrolysis is rapid and gives in all cases a product which at the instant of hydrolysis contains substantial quantities of the " rearranged " ketone (III) (see Table 1), and (*b*) that the mixture of cyclohexenones undergoes a slower change in composition giving ultimately a preponderance of (III) in equilibrium with (II). The alkylation of diketone (I; $R^1 = R^2 = R^3 =$ H, $R^4 =$ Me) with methyl iodide and sodium ethoxide followed by hydrolysis had given a mixture of ketones with $R^1 = R^3 =$ H, $R^2 =$ Me [(III) 72·4%, (II) 23·9%], closely approximating to the equilibrium composition in this instance.[1] Hydrolysis of diketones of the type (I) with mineral acids was found to be slow and accompanied by the formation of tar. Hydrolysis of compound (I; $R^1 = R^3 =$ H, $R^2 = R^4 =$ Me) with aqueous-ethanolic hydrogen chloride, however, gave

---

[2] Beringer and Ugelow, *J. Amer. Chem. Soc.*, 1953, **75**, 2635.

a small conversion into a cyclohexenone mixture which was predominantly (75%) of type (II).

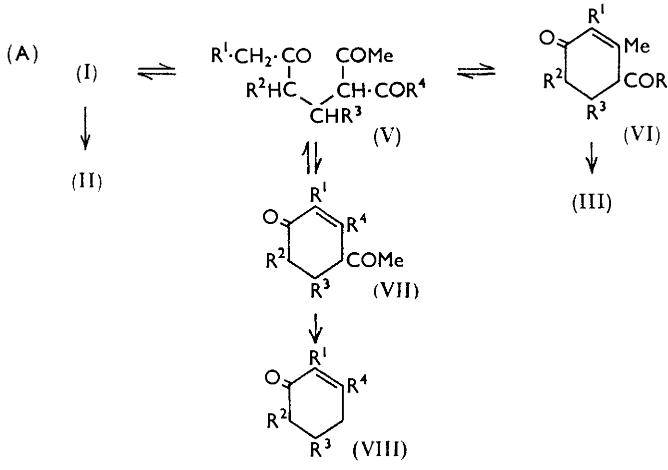
TABLE 1. *Composition* (%) *of mixed cyclohexenones formed on hydrolysis of the diketone* (I).

	$t = 0$		Final values	
	(II)	(III)	(II)	(III)
(I; $R^1 = R^2 = R^4 = Me, R^3 = H$)	63	37	3·5	96·5
(I; $R^1 = R^3 = H, R^2 = Et, R^4 = Me$)	54	46	20	80
(I; $R^1 = R_3 = H, R^2 = R^4 = Me$)	61	39	25·5	74·5

The kinetic evidence rules out the possibility that the hydrolysis of the diketone (I) might first give the monoketone (II), which would subsequently partially rearrange to its isomer (III). The possibility that the ring opens before hydrolysis may also be excluded; two schemes might be considered as annexed.

Mechanism A supposes the formation of a triketone (V) which may recyclise in three ways. The reactions (V) ⟶ (VI) ⟶ (III) would probably be slow since compound (VI) is not a β-diketone. Now, route (V) ⟶ (VII) ⟶ (VIII) would lead to 3-phenylcyclohex-2-enone when compound (I; $R^1 = R^2 = R^3 = H$, $R^4 = Ph$) was the starting material, but this is not formed; in the preparation of this starting material it is probable that some of the isomer (VII) was formed and was removed by purification through the copper salt; hydrolysis of the *crude* product did, indeed, give some 3-phenylcyclohex-2-enone (*ca.* 25% of the total cyclohexenones produced).

(A)

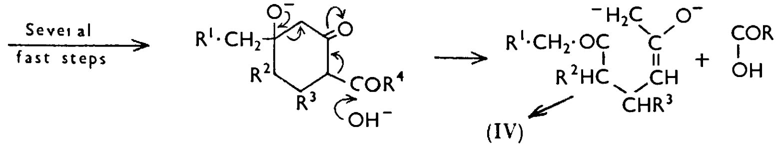


(B) (I) ⟶ (V) ⟶ (IV) ⟶ (II) + (III)

Mechanism B requires that the triketone (V) hydrolyses to the diketone (IV) which may then cyclise to (II) and (III). This mechanism may be rejected since (*a*) if R^4 were Ph, it is to be expected that the acetyl group rather than the benzoyl group would be eliminated by hydrolysis, *e.g.*, ethyl α-benzoylacetoacetate gives ethyl benzoylacetate on hydrolysis rather than ethyl acetoacetate (such hydrolysis would give a 3-phenylcyclohex-2-enone), and (*b*) the triketone (V) is certainly the intermediate in the formation of diketones of the type (I) [1] but, except in the single instance of the condensation of acetylacetone and methyl vinyl ketone, (V) exists in an equilibrium with its two precursors which is most unfavourable to (V). Thus (V), if formed, would be converted into the respective αβ-unsaturated ketone and 1,3-diketone used in the preparation of (I).

The evidence is consistent with a *simultaneous* reversed aldol condensation and hydrolysis of the 6-acyl group; addition of water to the cyclic double bond should proceed rapidly and would then leave the ring-carbonyl group free to play its rôle in attracting electrons from the 6-acyl group, thus facilitating hydrolysis.

(I)



(IV)

The interconversion of a variety of alkylcyclohexenones [(II) $\rightleftharpoons$ (III)] in boiling aqueous 5% sodium hydroxide was studied. In addition to the three pairs of isomers arising from the hydrolyses described, other 3-alkylcyclohex-2-enones, prepared from 3-ethoxycyclohex-2-enone and the appropriate Grignard reagent,[3] and 2-alkylcyclohex-2-enones [4] were also studied. All the results could be satisfactorily analysed in terms of a reversible interconversion, the forward and the backward reactions being both of first-order. If a is the mole fraction of the more stable product, *i.e.*, [III]/([II] + [III]), then whether the reaction takes place in the oil phase or in the aqueous layer, provided that the reaction does not proceed so rapidly that the rate of mass transfer between the phases significantly influences the overall rate, we have for a reversible first-order reaction:

$$\text{(II)} \underset{k_{\text{III}}}{\overset{k_{\text{II}}}{\rightleftharpoons}} \text{(III)};\ K = \frac{k_{\text{II}}}{k_{\text{III}}}$$

$$\mathrm{d}a/\mathrm{d}t = k_{\text{II}}(1 - a) - k_{\text{III}} = ak_{\text{III}}[K - a(K + 1)]$$

whence, a plot of $-\ln[K - a(K + 1)]$ against t should give a straight line of slope $k_{\text{III}}(K + 1)$, from which value k_{III} and k_{II} can be determined. K was determined by two methods: (i) successive approximation with various values of K to select the one that gave the best straight line and (ii) protracted equilibration to determine the value of a at equilibrium (a_e), whence $K = a_e/(1 - a_e)$; the two methods gave good agreement. The results obtained from the hydrolysis of the diketones (I) were plotted similarly to give good straight lines which, by extrapolation, gave the values $a_{t=0}$ recorded in Table 1 and gave velocity constants in fair agreement with those obtained in experiments in which the isolated cyclohexenones themselves were treated with boiling alkali.

The velocity constants for the rates of conversion of (II) and (III) are set out to show the effects of substituents (R^3 = H throughout).

TABLE 2. *Kinetic data for the interconversion* (II) $\rightleftharpoons$ (III) *with boiling* 5% *sodium hydroxide solution* (*probable accuracy* ±10%).

R^1 = H:	R^2 =	Me	Et	Pr^i	R^1 = Me:	R^2 = H	Me
10^2k_{II} (hr.$^{-1}$)		115	38	16·5		180	61·5
10^2k_{III} (hr.$^{-1}$)		40	9·5	1·45		15	2·15
K		2·9	4·0	11·5		12·0	28·5
R^2 = H:	R^1 =	Me	Et	Pr^n	R^2 = Me:	R^1 = H	Me
10^2k_{II} (hr.$^{-1}$)		180	27	11		115	61·5
10^2k_{III} (hr.$^{-1}$)		15	4·2	2·7		40	2·15
K		12·0	6·4	4·0		2·9	28·5

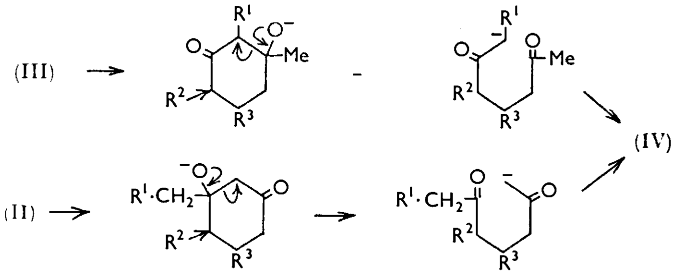
The effects may be summarised as follows: (*a*) increase in the molecular weight of substituent in R^1 decreases both k_{II} and k_{III}, affecting k_{II} markedly more than k_{III}, *i.e.*, stabilising (II) with respect to (III), *except* in the instance where H is replaced by Me when k_{III} is sharply reduced and (III) is highly preponderant at equilibrium; (*b*) increase

---

[3] Woods, Griswold, Armbrecht, Blumenthal, and Plapinger, *J. Amer. Chem. Soc* , 1949, **71**, 2028.
[4] Smith and Rouault, *J. Amer. Chem. Soc.*, 1943, **65**, 631.

in the weight of substituent in R^2 reduces both k_{II} and k_{III}; k_{III} is influenced rather more than k_{II}, particularly when $R^2 = \text{Pr}^i$. Since the kinetic results from the hydrolysis of acetylcyclohexenones (I) show that both products (II) and (III) are formed initially in roughly equal amounts, it appears that the two forward reactions from a common intermediate, *e.g.*, (IV), must both be rapid and have approximately the same rates. The controlling steps must therefore be the reverse reactions, *i.e.*, hydration of the double bond and the de-aldolisation. The reason for the greater stability of the 2,3-dialkylcyclohexenones (III), particularly if $R^1 = \text{Me}$, must lie in the stabilisation of the double bond by hyperconjugation; in the isomer (II) the double bond bears only one substituent whereas there are two in isomer (III). The general decrease in reaction rates with increasing weight of substitution may be ascribed to inductive ($+I$) and electromeric effects ($+E$) of the alkyl groups on the nucleophilic addition to the double bond and the nucleophilic de-aldolisation. The greater stability of the 3,6-dialkylcyclohexenones (III) than of the 3,4-isomers (II) and the fact that substitution in R^2, which can affect only the de-aldolisation step, has such a pronounced effect on k_{II} and k_{III}, particularly the latter, is more difficult to explain. The effect of substituents on simple de-aldolisation is by no means well established [5] but it seems possible to ascribe the influence of R^2 to its inductive ($+I$) effect on the de-aldolisation step which would inhibit the conversion of (III) rather than of (II); the pronounced effect of $R^2 = \text{Pr}^i$ might be thus explained, although the size of the effect and the remoteness of R^2 from the unsaturated systems suggest that other influences are under observation.

The observation that 3-alkylcyclohexenones are subject to rearrangement under the influence of alkaline catalysts sheds some doubt on the purity and even the identity of several previously reported materials of this type. Melikyan and Tatevosyan [6] prepared a series of alkylcyclohexenones (III; $R^1 = R^3 = \text{H}$, $R^2 = \text{Pr}^i$, Bu^n, $\text{Me}_2\text{CH}{\cdot}\text{CH}_2{\cdot}\text{CH}_2$) by the condensation of 1,3-dichloroprop-2-ene with the appropriate α-alkylacetoacetic ester followed by cyclisation with acid and removal of ethoxycarbonyl by prolonged refluxing



with methanolic potassium hydroxide. It is certain that these products must have contained some of the less stable isomers (II). A similar criticism must also apply to the work of Downes, Gill, and Lions [7] whose synthesis of cyclohexenones also involved a final treatment with boiling alkali. The piperitone syntheses by Walker [8] and Henecka [9] must have given a mixture containing some 4-isopropyl-3-methylcyclohex-2-enone. The several reported preparations of 2,3-dimethylcyclohex-2-enone by alkylation of compound (II; $R^1 = R^3 = \text{H}$, $R^2 = \text{CO}_2\text{Et}$) ("Hagemann's ester") followed by alkaline hydrolysis [4,10,11] would give chiefly the desired product but, in addition, 3—4% of the

---

[5] Ingold, "Structure and Mechanism in Organic Chemistry," Bell, London, 1953, p. 683.

[6] Melikyan and Tatevosyan, *J. Gen. Chem.* (*U.S.S.R.*), 1951, **21**, 696.

[7] Downes, Gill, and Lions, *J. Amer. Chem. Soc.*, 1950, **72**, 3464.

[8] Walker, *J.*, 1935, 1585.

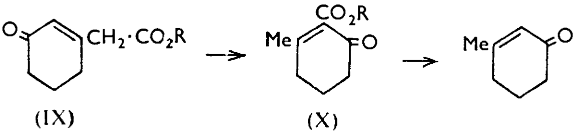
[9] Henecka, *Chem. Ber.*, 1949, **82**, 415.

[10] Copp and Simonsen, *J.*, 1940, 415.

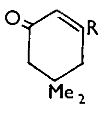
[11] Bergmann and Weizmann, *J. Org. Chem.*, 1939, **4**, 266.

isomer (II; $R^1 = Me$, $R^2 = R^3 = H$), which may, however, be readily separated by fractional distillation, would be formed. The method of Décombe, described in several publications [12,13] and claimed to be of general application, which involves the reaction of various 2-chloroethyl ketones with acetoacetic ester (or an α-substituted derivative) and completed in refluxing aqueous barium hydroxide, must be suspect since this reagent is capable of rearranging cyclohexenones (see p. 1647). It seems probable, for instance, that preparations of the ketones (II; $R^1 = R^3 = H$, $R^2 = Me$) from 4-chloro-3-methylbutan-2-one and ethyl acetoacetate, and of the ketone (III; $R^1 = R^3 = H$, $R^2 = Me$) from 4-chlorobutan-2-one and ethyl α-acetylpropionate, would give the same equilibrium mixture (25·5% and 74·5% respectively). Similarly the ketone (III; $R^1 = R^3 = H$, $R^2 = Et$) can have been only 80% pure, the balance being the isomer (II). The procedure of Cologne and Dreux,[14] involving condensation of methyl ketones with formaldehyde or with 3-methylbut-3-en-2-one in the presence of alkali, seems to be capable of giving mixtures of ketones but, of the examples quoted, only the reaction of 3-methylbut-3-en-2-one and acetone could do so. In this instance the product was purified through the semicarbazone and, from physical properties quoted, appears to have been pure (III; $R^1 = R^3 = H$, $R^2 = Me$).

Grewe, Nolte, and Rotzoll [15] observed that the ester (IX; R = Et) was hydrolysed with alkali to an acid, presumed to be (IX; R = H), which was readily decarboxylated to 3-methylcyclohex-2-enone. The present work suggests that the ester may first rearrange to the β-keto-ester (X), the ready hydrolysis and decarboxylation of which would be in accordance with expectations. Clemo and his co-workers,[16] following earlier work by Crossley and Gilling,[17] studied the hydrolysis of the substituted malonic ester (XI) in acid and in alkali and found that hydrolysis is accompanied by decarboxylation to give a cyclohexenone described as 3-ethyl-5,5-dimethylcyclohex-2-enone (XII). It was suspected that this product might have been 2,3,5,5-tetramethylcyclohex-2-enone but repetition of the work and comparison with a sample of (XII) prepared by the action of ethylmagnesium bromide on 3-ethoxy-5,5-dimethylcyclohex-2-enone showed that the material had been correctly described. It was further shown, moreover, that cyclohexenones such as (XII) and (XIII) were quite unaffected by prolonged contact with boiling aqueous sodium hydroxide under conditions sufficient to afford substantially complete rearrangement of 3-alkylcyclohex-2-enones (II) (lacking the 5,5-dimethyl substituents) to 2,3-dialkyl derivatives. 2,3,5,5-Tetramethylcyclohex-2-enone was similarly inert to boiling alkali. This surprising contrast in behaviour may possibly be due to a steric effect, the gem-dimethyl group conferring such rigidity on the cyclohexene conformation that de-aldolisation is rapidly followed by re-aldolisation to the starting material. The rapid hydrolysis–decarboxylation of (XI) may be explained by supposing the ring to open in the course of a de-aldolisation to give a β-keto-acid which may be decarboxylated and subsequently re-cyclise.



(IX) (X)



(XI) : $R = CMe(CO_2Et)_2$
(XII) : R = Et
(XIII) : $R = Bu^n$

Examination of the action of boiling 25% sulphuric acid, a reagent used by Blaise and Maire [18] in the final stage of a cyclohexenone synthesis, showed that it is capable of effecting

---

[12] Décombe, *Compt. rend.*, 1936, **202**, 1685; 1937, **205**, 680; *Bull. Soc. chim. France*, 1945, **42**, 651.
[13] Capon, Claudon, Cornubert, Lemoine, and Vivant, *Bull. Soc. chim. France*, 1958, 847.
[14] Colonge and Dreux, *Compt. rend.*, 1950, **231**, 1504.
[15] Grewe, Nolte, and Rotzoll, *Chem. Ber.*, 1956, **89**, 600.
[16] Clemo, Cocker, and Hornsby, *J.*, 1946, 616.
[17] Crossley and Gilling, *J.*, 1909, **95**, 24.
[18] Blaise and Maire, *Compt. rend.*, 1907, **144**, 572.

rearrangement (II) $\rightleftharpoons$ (III), but that the rate of conversion of (II) is much less than with 5% sodium hydroxide (about one-thirtieth in the example chosen).

EXPERIMENTAL

M. p.s are corrected. Ultraviolet-light absorptions were measured for ethanol solutions. Gas–liquid chromatography was carried out on a column (8 ft. of 6 mm.-bore tubing) packed with 20% Apiezon M on Celite (60—80 mesh); nitrogen was used as carrier gas and the column was maintained at 156°. A hydrogen-flame detector was used; analyses are based on area measurements of recorder chart peaks.

6-Acetyl-3-methylcyclohex-2-enone.—The diketone (I; $R^1 = R^2 = R^3 = H$, $R^4 = Me$) (10 g.) was refluxed with 10% aqueous sodium hydroxide (50 ml.) for 0·5 hr.; the oil immediately dissolved but droplets reappeared within 2—3 min. Isolation of the product with ether gave 3-methylcyclohex-2-enone (4·4 g.), b. p. 79°/13 mm., n_D^{20} 1·4938, $\lambda_{max.}$ 2330 Å (ε 13,500) (semicarbazone, m. p. 198°) [(lit.,[19] b. p. 78·5—79°/12 mm., n_D^{20} 1·4930; semicarbazone, m. p. 199—200°)].

6-Acetyl-3,5-dimethylcyclohex-2-enone.—The diketone (I; $R^1 = R^2 = H$, $R^3 = R^4 = Me$) (10 g.) on hydrolysis as described above gave 3,5-dimethylcyclohex-2-enone (5·2 g.), b. p. 91—92°/13 mm., n_D^{20} 1·4838, $\lambda_{max.}$ 2330 Å (ε 13,000), which afforded a semicarbazone, m. p. and mixed m. p. 180° (Knoevenagel [20] gives m. p. 179—180°), and had an infrared spectrum identical with that of an authentic sample.

6-Acetyl-3-methyl-5-phenylcyclohex-2-enone.—The diketone (I; $R^1 = R^2 = H$, $R^3 = Ph$, $R^4 = Me$) (15·4 g.) on hydrolysis as described above gave 3-methyl-5-phenylcyclohex-2-enone (8·5 g.), b. p. 123°/0·8 mm., n_D^{20} 1·5665, m. p. 31—32°, $\lambda_{max.}$ 2330 Å (ε 16,500), identical with an authentic specimen.[21]

6-Benzoyl-3-methylcyclohex-2-enone.—The diketone (I; $R^1 = R^2 = R^3 = H$, $R^4 = Ph$) (10 g.) on hydrolysis as above gave 3-methylcyclohex-2-enone (2·8 g.), b. p. 80°/13 mm. (infrared spectroscopy of the crude product before distillation showed that 3-phenylcyclohex-2-enone was not present; limit of detection 3%). Acidification of the aqueous layer from the hydrolysis gave benzoic acid (3·85 g.).

6-Acetyl-3-ethyl-4-methylcyclohex-2-enone.—The diketone (I; $R^1 = R^2 = R^4 = Me$, $R^3 = H$) (120 g.) was refluxed for 0·5 hr. with 10% aqueous sodium hydroxide (600 ml.), and the product obtained on isolation with ether was distilled at a high reflux ratio through a 30 in. column packed with glass helices. The following fractions were obtained: (*a*) b. p. 93—99°/15 mm. (9·8 g.), n_D^{20} 1·4900, (*b*) b. p. 99—100°/13 mm. (18·0 g.), n_D^{20} 1·4905, (*c*) b. p. 100—106°/13 mm. (13·6 g.), (*d*) b. p. 106—108°/13 mm. (20·2 g.), n_D^{20} 1·4976. Chromatography showed the fractions to be mixtures of two compounds: (*a*) 72% A, 27% B, (*b*) 65·5% A, 33·5% B, (*d*) 6% A, 94% B. Light-absorption max. were at: (*a*) 2420 (ε 12,000) and (*d*) 2350 Å (ε 13,500) (Found for fraction *b*: C, 78·4; H, 10·3. Calc. for $C_9H_{14}O$: C, 78·2; H, 10·2%).

Fraction (*a*) was identified as predominantly 2,3,6-trimethylcyclohex-2-enone (III; $R^1 = R^2 = Me$, $R^3 = H$) by dehydrogenation in refluxing biphenyl (equal weight) for 3 hr. with 10% of palladium–barium sulphate (5% Pd) catalyst. Isolation by extraction into alkali gave 2,3,6-trimethylphenol (6%), m. p. and mixed m. p. 62° (lit.,[22] m. p. 62°). Conversion of fraction (*a*) (5 g.) through the oxime into the acetanilide by the method of Beringer and Ugelow [2] and crystallisation of the product from aqueous ethanol gave *N*-acetyl-2,3,6-trimethylaniline (3·6 g.), m. p. 187° (lit.,[23] m. p. 186°). Fraction (*a*) gave the *semicarbazone* of 2,3,6-trimethylcyclohex-2-enone (III; $R^1 = R^2 = Me$, $R^3 = H$) as prisms, m. p. 207° (from aqueous ethanol) (Found: C, 61·9; H, 8·5; N, 21·7. $C_{10}H_{17}ON_3$ requires C, 61·55; H, 8·8; N, 21·5%). A sample of this ketone was prepared by 7 hours' refluxing of diketone (I; $R^1 = R^2 = R^4 = Me$, $R^3 = H$) (10 g.) with aqueous sodium hydroxide (50 ml.); the product had b. p. 88—90°/12 mm., n_D^{20} 1·4880; gas–liquid chromatography showed 92·4% purity with 5·1% of isomer (II; $R^1 = R^2 = Me$, $R^3 = H$).

---

[19] Bowman, Ketterer, and Dinga, *J. Org. Chem.*, 1952, **17**, 563.
[20] Knoevenagel, *Annalen*, 1897, **297**, 165.
[21] Montgomery and Dougherty, *J. Org. Chem.*, 1952, **17**, 823.
[22] Morgan and Pette, *J.*, 1934, 418.
[23] Mayer, *Ber.*, 1887, **20**, 972.

Fraction (*d*) was identified as substantially pure 3-ethyl-4-methylcyclohex-2-enone (II; $R^1 = R^2 =$ Me, $R^3 =$ H) by conversion into *N*-acetyl-3-ethyl-4-methylaniline, m. p. 88° (lit.,[22] m. p. 88°). The *semicarbazone* formed needles, m. p. 170°, from aqueous ethanol (Found: C, 61·75; H, 8·45; N, 21·7. $C_{10}H_{17}ON_3$ requires C, 61·55; H, 8·8; N, 21·5%).

Fraction (*b*) gave a mixture of the above two acetanilides which was resolved by chromatography on alumina and elution with benzene–chloroform (1 : 1).

6-Acetyl-4-ethyl-3-methylcyclohex-2-enone.—The diketone (I; $R^1 = R^3 =$ H, $R^2 =$ Et, $R^4 =$ Me) (80 g.) was refluxed with 10% aqueous sodium hydroxide (320 ml.) for 0·5 hr.; the product was isolated and fractionally distilled as in the previous example to give fractions (*a*) 97—100°/13 mm. (14·3 g.), n_D^{20} 1·4850; (*b*) 100—104°/13 mm. (12·7 g.), n_D^{20} 1·4865; (*c*) b. p. 104—107°/13 mm. (10·5 g.), n_D^{20} 1·4893; (*d*) b. p. 107—109°/13 mm. (1·6 g.), n_D^{20} 1·4899. Gas–liquid chromatography indicated compositions: (*a*) 90% A, 8% B; (*c*) 32% A, 67% B; (*d*) 20% A, 80% B. An intermediate fraction, giving an analysis 61% A, 39% B, gave (Found: C, 77·9; H, 10·35. Calc. for $C_9H_{14}O$: C, 78·2; H, 10·2%), showed $\lambda_{max.}$ 2350 Å (ε 14,500). Fraction (*a*) gave *6-ethyl-3-methylcyclohex-2-enone semicarbazone* (ketone = component A) as plates, m. p. 170°, from aqueous ethanol (Found: C, 61·95; H, 8·65; N, 21·1. $C_{10}H_{17}ON_3$ requires C, 61·55; H, 8·8; N, 21·5%); fraction (*d*) gave *4-ethyl-3-methylcyclohex-2-enone semicarbazone* (ketone = component B) as plates m. p. 147°, from aqueous methanol (Found: C, 61·0; H, 9·2; N, 21·6%).

Fraction (*a*) (4 g.) was converted through the oxime into the acetanilide; purification by chromatography on alumina and crystallisation from benzene–light petroleum (b. p. 60—80°) gave *N*-acetyl-2-ethyl-5-methylaniline (0·9 g.), m. p. 142·5° (lit.,[24] m. p. 142°).

Fraction (*c*) (4 g.) gave *N*-acetyl-4-ethyl-3-methylaniline (0·95 g.), prisms, m. p. 87·5° [from light petroleum (b. p. 60—80°)] (lit.,[22] m. p. 90°).

6-Acetyl-3,4-dimethylcyclohex-2-enone.—The diketone (I; $R^1 = R^3 =$ H, $R^2 = R^4 =$ Me) (100 g.) was added rapidly to boiling 10% sodium hydroxide solution (500 ml.); dissolution was rapid but within 20 sec. oil started to separate. After 10 minutes' boiling, the product was rapidly cooled and the oil isolated with ether. The oil (58 g.) was distilled as before, to give the following: (*a*) b. p. 86°/12 mm. (9·1 g.), n_D^{20} 1·4875; (*b*) b. p. 86—88°/12 mm. (7·1 g.), n_D^{20} 1·4885; (*c*) b. p. 88—91°/12 mm. (12·8 g.); and (*d*) b. p. 91—93°/12 mm. (14·8 g.), n_D^{20} 1·4913. Gas–liquid chromatography showed compositions: (*a*) 77·0% A, 22·0% B; (*b*) 67·5% A, 31·8% B; and (*d*) 33·5% A, 63·0% B. An intermediate fraction having composition 68% A and 31% B (Found: C, 77·35; H, 9·35. Calc. for $C_8H_{12}O$: C, 77·4; H, 9·75%), showed $\lambda_{max.}$ 2330 Å (ε 14,200).

Component A was shown to be 3,6-dimethylcyclohex-2-enone (III; $R^1 = R^3 =$ H, $R^2 =$ Me) Fraction (*a*) (5 g.) was dehydrogenated in refluxing biphenyl (15 g.) for 3 hr. by 5% palladium–barium sulphate (0·5 g.). Isolation by extraction with alkali gave a crude phenol (2·3 g.) which, after several recrystallisations from light petroleum (b. p. 40—60°), gave 2,5-dimethylphenol, m. p. and mixed m. p. 74·5—75·5° (lit.,[25] m. p. 74·5°). Conversion *via* the oxime gave *N*-acetyl-2,5-dimethylaniline, m. p. and mixed m. p. 139° (lit.,[26] m. p. 139°).

Component B was shown to be 3,4-dimethylcyclohex-2-enone (II; $R^1 = R^3 =$ H, $R^2 =$ Me). Fraction (*d*) (5 g.) gave a mixture of oximes and thence a mixture (5·6 g.) of substituted acetanilides. Chromatography on alumina in chloroform–benzene (1 : 1) gave *N*-acetyl-3,4-dimethylaniline (2·4 g.), needles (from aqueous ethanol), m. p. and mixed m. p. 96—97° (lit.,[27] m. p. 96—98°).

Hydrolysis of the diketone (I; $R^1 = R^3 =$ H, $R^2 = R^4 =$ Me) (10 g.) in boiling ethanol (20 ml.) and concentrated hydrochloric acid (10 ml.) for 3 hr. gave a fraction (2·0 g.), b. p. 94—99°/13 mm., n_D^{20} 1·4931, consisting of (II; $R^1 = R^3 =$ H, $R^2 =$ Me) 75% and (III; $R^1 = R^3 =$ H, $R^2 =$ Me) 25%, followed by some starting material (2·3 g.) and high-boiling material.

Hydrolysis of 6-Acetylcyclohex-2-enones (I).—The ketone was rapidly added to boiling aqueous 10% w/w sodium hydroxide (2 equivs.) in nitrogen. Samples were removed at timed intervals from the supernatant oil layer; these were washed with water, the mixture being just neutralised to phenolphthalein with dilute sulphuric acid, and dried (Na_2SO_4) before analysis by gas–liquid chromatography. Results are tabulated.

---

[24] Rinkes, *Rec. Trav. chim.*, 1945, **64**, 205.
[25] Jacobsen, *Ber.*, 1878, **11**, 27.
[26] Noelting, Witt, and Forel, *Ber.*, 1885, **8**, 2665.
[27] Jacobsen, *Ber.*, 1884, **17**, 161.

(i) (I; $R^1 = R^2 = R^4 = Me$, $R^3 = H$):

Time (min.)	10	20	30	60	120
a	0·436	0·478	0·540	0·653	0·802

$a_e = 0{\cdot}965$; $K = 28{\cdot}5$; $k_{II} = 0{\cdot}615$ hr.$^{-1}$; $k_{III} = 2{\cdot}15 \times 10^{-2}$ hr.$^{-1}$; $a_{t=0} = 0{\cdot}37$.

(ii) (I; $R^1 = R^3 = H$, $R^2 = Et$, $R^4 = Me$):

Time (min.)	30	60	120	180
a	0·555	0·590	0·665	0·720

$a_e = 0{\cdot}80$; $K = 4{\cdot}0$; $k_{II} = 0{\cdot}37$ hr.$^{-1}$; $k_{III} = 9{\cdot}25 \times 10^{-2}$ hr.$^{-1}$; $a_{t=0} = 0{\cdot}46$.

(iii) (I; $R^1 = R^3 = H$, $R^2 = R^4 = Me$):

Time (min.)	10	20	30	60	120
a	0·477	0·538	0·593	0·694	0·740

$a_e = 0{\cdot}745$; $K = 2{\cdot}9$; $k_{II} = 1{\cdot}3$ hr.$^{-1}$; $k_{III} = 0{\cdot}45$ hr.$^{-1}$; $a_{t=0} = 0{\cdot}39$.

Rearrangement of Alkylcyclohex-2-enones, (II) $\rightleftharpoons$ (III).—Procedure was that used in hydrolysis experiments except that 5% w/w aqueous sodium hydroxide (*ca.* 1·3N; 5 ml. per g. of ketone) was used.

(II; $R^1 = R^2 = Me$, $R^3 = H$):

Time (hr.)	0	0·5	1	2	3	4	5	6	7
(i) *a*	0·149	—	0·420	0·726	0·816	0·895	0·936	—	0·946
(ii) [a] *a*	0·027	0·16	0·354	0·584	0·752	0·852	0·916	—	—
(iii) [b] *a*	0·027	—	0·044	—	0·064	—	—	0·092	—

$a_e = 0{\cdot}965$; $K = 28{\cdot}5$; (i) $k_{II} = 0{\cdot}615$ hr.$^{-1}$; $k_{III} = 2{\cdot}15 \times 10^{-2}$ hr.$^{-1}$. (ii) $k_{II} = 0{\cdot}54$ hr.$^{-1}$; $k_{III} = 1{\cdot}90 \times 10^{-2}$ hr.$^{-1}$.

[a] Experiment (ii): the sodium hydroxide solution was replaced by N-barium hydroxide. [b] Experiment (iii): the sodium hydroxide solution was replaced by 25% w/w sulphuric acid.

(II or III; $R^1 = R^3 = H$, $R^2 = Et$):

Time (hr.)	0	0·5	1	2	3	4	5
(i) *a*	0·330	0·438	0·538	0·652	0·706	0·745	0·782
(ii) [a] *a*	0·885	0·862	0·842	0·810	0·798	0·805	—

$a_e = 0{\cdot}80$; $K = 4{\cdot}0$; (i) $k_{II} = 0{\cdot}39$ hr.$^{-1}$; $k_{III} = 9{\cdot}8 \times 10^{-2}$ hr.$^{-1}$. (ii) $k_{II} = 0{\cdot}5$ hr.$^{-1}$; $k_{III} = 0{\cdot}125$ hr.$^{-1}$.

[a] Experiment (ii), in which the starting material was already close in composition to that expected at equilibrium, is intrinsically less accurate than (i).

(II; $R^1 = R^3 = H$, $R^2 = Me$):

Time (hr.)	0	0·5	1	2	3
a	0·347	0·540	0·670	0·723	0·738

$a_e = 0{\cdot}745$; $K = 2{\cdot}9$; $k_{II} = 1{\cdot}15$ hr.$^{-1}$; $k_{III} = 0{\cdot}40$ hr.$^{-1}$.

(II or III; $R^1 = Me$, $R^2 = R^3 = H$):

Time (hr.)	0	0·5	1	2	3
(i) [a] *a*	0·0	0·504	0·760	0·903	0·920 [c]
(ii) [b] *a*	1·0	0·942	0·928	—	—

$a_e = 0{\cdot}923$; $K = 12{\cdot}0$; (i) $k_{II} = 1{\cdot}8$ hr.$^{-1}$; $k_{III} = 0{\cdot}15$ hr.$^{-1}$. (ii) $k_{II} = 1{\cdot}55$ hr.$^{-1}$; $k_{III} = 0{\cdot}13 \times 10^{-2}$ hr.$^{-1}$.

[a] Compound (II; $R^1 = Me$, $R^2 = R^3 = H$) had b. p. 93—96°/12 mm., n_D^{20} 1·4945 (lit.,[3] b. p. 56—57°/0·8 mm., n_D^{20} 1·4913); gas-liquid chromatography showed 95·1% purity; isomer (III; $R^1 = Me$, $R^2 = R^3 = H$) was absent; six minor impurities persisted throughout the run. [b] Compound (III; $R^1 = Me$, $R^2 = R^3 = H$) had b. p. 84—85°/10 mm., n_D^{20} 1·4988 (lit.,[4] b. p. 80—84°/19 mm., b. p. 78—78·5°/8 mm., n_D^{20} 1·4995), and $\lambda_{max.}$ 2420 Å (ε 14,500); 94·2% purity with none of the isomer (II; $R^1 = Me$, $R^2 = R^3 = H$). [c] A portion of the end-product of run (i) had $\lambda_{max.}$ 2420 Å (ε 12,500) and gave a semicarbazone, m. p. 219° alone and on admixture with the semicarbazone of (III; $R^1 = Me$, $R^2 = R^3 = H$) (lit.,[4] m. p. 222°).

(II; $R^1 = Et$, $R^2 = R^3 = H$):

Time (hr.)	0	0·5	1	2	3	4	6	20
(i) [a] *a*	0·045	0·150	0·220	0·385	0·525	0·615	—	—
(ii) [a] *a*	0·032	0·143	0·220	0·415	—	0·633	0·734	0·865

$a_e = 0{\cdot}865$; $K = 6{\cdot}4$; (i) $k_{II} = 0{\cdot}26$ hr.$^{-1}$; $k_{III} = 4{\cdot}05 \times 10^{-2}$ hr.$^{-1}$. (ii) $k_{II} = 0{\cdot}275$ hr.$^{-1}$; $k_{III} = 4{\cdot}3 \times 10^{-2}$ hr.$^{-1}$.

[a] Compound (II; $R^1 = Et$, $R^2 = R^3 = H$) had b. p. 110—113°/13 mm., n_D^{20} 1·4896 (lit.,[3] b. p. 59—60°/0·4 mm., n_D^{20} 1·4876); a typical batch had 93·9% purity, with 4·4% of isomer (III; $R^1 = Et$, $R^2 = R^3 = H$); $\lambda_{max.}$ 2360 Å (ε 14,800).

(II; $R^1 = Pr^n$, $R^2 = R^3 = H$):

Time (hr.)	0	0·5	1	2	4	6	24
a	0·05	0·045	0·082	0·18	0·32	0·44	0·76

$a_e = 0{\cdot}80$; $K = 4{\cdot}0$; $k_{II} = 0{\cdot}11$ hr.$^{-1}$; $k_{III} = 2{\cdot}7 \times 10^{-2}$ hr.$^{-1}$.

Compound (II; $R^1 = Pr^n$, $R^2 = R^3 = H$) had b. p. 76—78°/0·6 mm., n_D^{20} 1·4877 (lit.,[3] b. p. 83—84°/1 mm., n_D^{20} 1·4865); $\lambda_{max.}$ 2360 Å (ε 15,800); 91·2% purity, with 5·1% of isomer (III; $R^1 = Pr^n$, $R^2 = R^3 = H$).

(III; $R^1 = R^3 = H$, $R^2 = Pr^i$):

Time (hr.)	0	1	2	3	4	24
a	1·00	0·99	0·98	0·96	0·95	0·92

$a_e = 0{\cdot}92$; $K = 11{\cdot}5$; $k_{II} = 0{\cdot}165$ hr.$^{-1}$; $k_{III} = 1{\cdot}45 \times 10^2$ hr.$^{-1}$.

Piperitone (supplied by Givaudan et Cie.) was fractionally distilled to give a main fraction, b. p. 111°/15., n_D^{20} mm., 1·4847. Gas–liquid chromatography showed 94·8% purity, with none of the isomer (II; $R^1 = R^3 = H$, $R^2 = Pr^i$). The identity of the isomer (II; $R^1 = R^3 = H$, $R^3 = Pr^i$) was not rigorously established but was strongly indicated by its retention time in chromatography compared with that of piperitone, and by the fact that this component was formed in a manner kinetically consistent with this formation.

3-*Ethyl*-5,5-*dimethylcyclohex*-2-*enone* (XII).—3-Ethoxy-5,5-dimethylcyclohex-2-enone (50 g.) was treated with ethylmagnesium bromide (from 11 g. of magnesium) in ether (200 ml.). Isolation gave 3-ethyl-5,5-dimethylcyclohex-2-enone (XII) (24 g.), b. p. 62—66°/1 mm., n_D^{20} 1·4806, $\lambda_{max.}$ 2360 Å (ε 12,700) [semicarbazone, plates, m. p. 180°, from aqueous ethanol (Found: C, 63·15; H, 9·05; N, 20·6. Calc. for $C_{11}H_{19}ON_3$: C, 63·2; H, 9·15; N, 20·1%) (lit.,[16,17] m. p. 197°)]. Samples prepared by the alkaline-[17] or acid-hydrolysis[16] of the ester (XI) were identical with the above. Examination of the material obtained after 24 hours' refluxing of the ketone with 5% aqueous sodium hydroxide showed it to be at least 92% unchanged.

Alkylation of isophorone with methyl iodide in the presence of sodium t-pentyloxide (Conia[28]) gave a product, b. p. 107—113°/18 mm., n_D^{20} 1·4815, containing (infrared analysis) 10—15% of isophorone and *ca.* 40% of ketone (XII), the balance being 2,3,5,5-tetramethylcyclohex-2-enone (lit.,[28] b. p. 90°/8 mm., n_D^{21} 1·4798). 20 hours' refluxing with 5% sodium hydroxide solution was without effect on this composition.

3-*Butyl*-5,5-*dimethylcyclohex*-2-*enone* (XIII).—A preparation, in which the general method of Woods *et al.*[3] was applied to 3-ethoxy-5,5-dimethylcyclohex-2-enone (0·2 mole) which was treated with butylmagnesium bromide, gave a product (19·8 g.), b. p. 86—93°/0·8 mm., shown by gas–liquid chromatography and infrared examination to contain about 25% of starting material. 24 hours' boiling with 5% sodium hydroxide solution removed the contaminant and gave 3-*butyl*-5,5-*dimethylcyclohex*-2-*enone*, b. p. 80°/0·7 mm., n_D^{20} 1·4788 (Found: C, 79·8; H, 11·3. $C_{12}H_{20}O$ requires C, 79·95; H, 11·2%), $\lambda_{max.}$ 2375 Å (ε 16,500), which formed a *semicarbazone* as plates, m. p. 148°, from aqueous ethanol (Found: C, 65·6; H, 9·75; N, 17·45. $C_{13}H_{23}ON_3$ requires C, 65·8; H, 9·75; N, 17·7%). Spectroscopic and gas–liquid chromatographic examination, and preparation and comparison of derivatives, confirmed the final product as identical with the major component in the mixture before alkali-treatment; no evidence for the formation of 3,5,5-trimethyl-2-propylcyclohex-2-enone was obtained (limit of detection *ca.* 1%).

With regard to this and the preceding two papers, the author acknowledges with gratitude the help given by Mr. P. Bullock and Mr. H. Jowitt with gas–liquid chromatography, by Mr. W. R. Ward with spectroscopic analyses and their interpretation, and by Professor N. B. Chapman generally. He thanks the Management of The Distillers Company Limited (Chemical Division) for permission to publish these papers.

CHEMICAL DIVISION, THE DISTILLERS COMPANY LIMITED,
HEDON, HULL.

[*Received, October 27th*, 1959.]

---

[28] Conia, *Bull. Soc. chim. France*, 1954, 690.