# Enamine Chemistry. Part III.[1] Reaction of αβ-Unsaturated Acid Chlorides with Enamines of Acyclic Ketones. Preparation of Cyclohexane-1,3-diones

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Reaction of acryloyl, crotonoyl, and methacryloyl chlorides with the morpholine enamine of diethyl ketone has been shown to give 2,4-dimethyl-, 2,4,5-trimethyl-, and 2,4,6-trimethyl-cyclohexane-1,3-diones respectively. The intermediate substituted 3-morpholinocyclohex-2-enones have been isolated and characterised as their perchlorates. Acryloyl chloride and the morpholine enamine of ethyl isopropyl ketone and the dimethylamine enamine of di-isopropyl ketone gave 2,2,4-trimethyl- and 2,2,4,4-tetramethyl-cyclohexane-1,3-diones respectively. The morpholine enamine of dibenzyl ketone gave 3-morpholino-2,4-diphenyl-cyclohex-2-enone which could not be hydrolysed to the cyclohexane-1,3-dione. The mechanism of the reaction is discussed.



SINCE αβ-unsaturated acid chlorides react [2] with 1-morpholinocyclohexene to give the corresponding bicyclo[3,3,1]nonane-2,9-dione, the reaction has been applied to enamines of acyclic ketones and shown to constitute a new method for the preparation of cyclohexane-1,3-diones.

TABLE 1

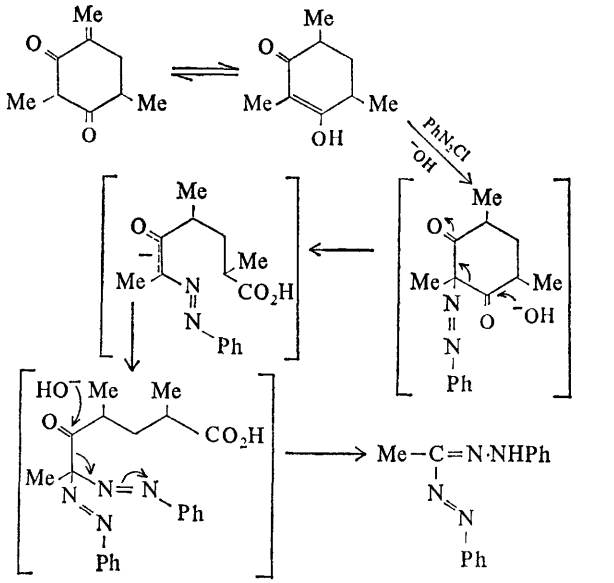
Cyclohexane-1,3-diones

| No. | Substituents | Yield (%) | M.p. | Solvent for crystn. | Found (%) C | Found (%) H | Formula | Required (%) C | Required (%) H |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 2,4-Dimethyl | 41 | 117—118° | Benzene–petroleum | 68·7 | 8·7 | $C_8H_{12}O_2$ | 68·55 | 8·6 |
| 2 | 2,4,5-Trimethyl | 8·3 | 128—129 | Benzene–petroleum | 69·9 | 8·8 | $C_9H_{14}O_2$ | 70·1 | 9·15 |
| 3 | 2,4,6-Trimethyl | 51 | 139—140 | Benzene | 70·1 | 9·0 | $C_9H_{14}O_2$ | 70·1 | 9·15 |
| 4 | 2,2,4-Trimethyl | 42·5 | Oil | (Distillation) | 49·5 | 4·2 | $C_{21}H_{22}N_8O_8$ † | 49·0 | 4·3 |
| 5 | 2,2,4,4-Tetramethyl | 3·3 | 35 | (T.l.c. on silica) * | Mass spectrum: *m/e* 168 ($M^+$) | | | | |

* Eluted with 10% acetone in benzene. † Bis-2,4-dinitrophenylhydrazone.

Treatment of 3-morpholinopent-2-ene in boiling benzene with acryloyl chloride and aqueous hydrolysis of the precipitated intermediate gave 2,4-dimethylcyclohexane-1,3-dione (41%), identical with authentic material prepared from ethyl acrylate and ethyl α-propionylpropionate.[3] Similarly, methacryloyl chloride gave 2,4,6-trimethylcyclohexane-1,3-dione, which was oxidised by chromic acid to DL-αα′-dimethylglutaric acid. Coupling of either dione with benzenediazonium chloride in alkaline solution gave 3-methyl-1,5-diphenylformazan, identical with material unambiguously synthesised [4] from acetaldehyde phenylhydrazone. This appears to be an extension of the Japp–Klingemann reaction [5] involving ring fission of the initially formed azo-dye, presumably by the reaction sequence illustrated in Scheme 1. Crotonyl chloride gave 2,4,5-trimethylcyclohexane-1,3-dione, but in much smaller yield.

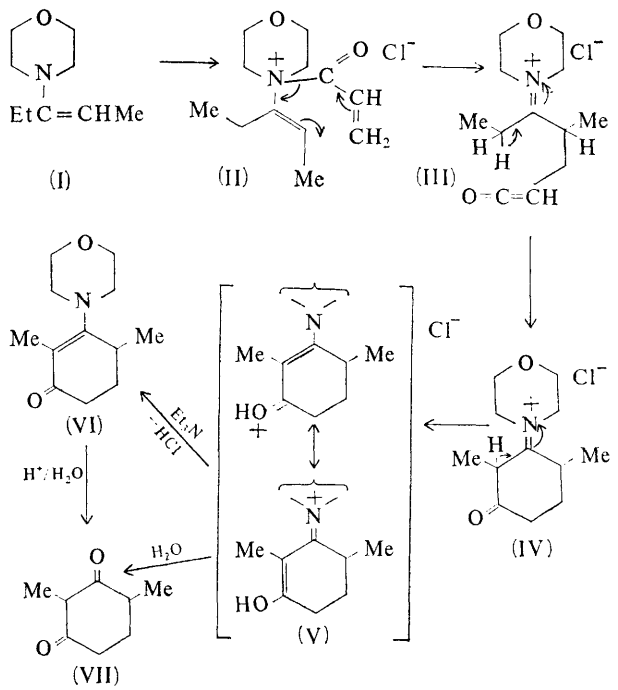
By analogy with the previously discussed [2] mechanism for the formation of bicyclo[3,3,1]nonane-2,9-dione from acryloyl chloride and 1-morpholinocyclohexene, we propose that the mechanism for the formation of the cyclohexane-1,3-diones involves initial *N*-acylation of the enamine to give the adduct (II), followed by a [3,3]sigmatropic change as illustrated in Scheme 2. Evidence for the proposed mechanistic sequence has been obtained as follows. If the reaction of acryloyl chloride with 3-morpholinopent-2-ene (I) in benzene is carried out in the presence of ethanol, ethyl 4-methyl-5-oxoheptanoate (VIII) is obtained, identical with authentic material.[6] Under identical conditions (3 min. reaction time) ethyl acrylate did not yield any detectable quantity of (VIII). This indicates that the enamine reacts with the β-position




SCHEME 1

[1] Part II, N. R. Firrell and P. W. Hickmott, *J. Chem. Soc.* (*C*), 1968, 2320.
[2] P. W. Hickmott and J. R. Hargreaves, *Tetrahedron*, 1967, **23**, 3151.
[3] S. M. McElvain, *J. Amer. Chem. Soc.*, 1929, **51**, 3124.
[4] M. Ragno and S. Bruno, *Gazzetta*, 1946, **76**, 485.
[5] A. W. Nineham, *Chem. Rev.*, 1955, **55**, 355.
[6] G. Stork, A. Brizzolara, H. Landesman, J. Szmuszkovicz, and R. Terrell, *J. Amer. Chem. Soc.*, 1963, **85**, 207.

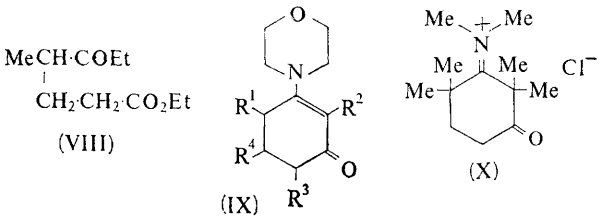
of the αβ-unsaturated acid chloride, prior to the *C*-acylation step, to give a reactive intermediate which, in the absence of other nucleophiles, cyclises to the iminium chloride (IV) with subsequent proton loss and



SCHEME 2

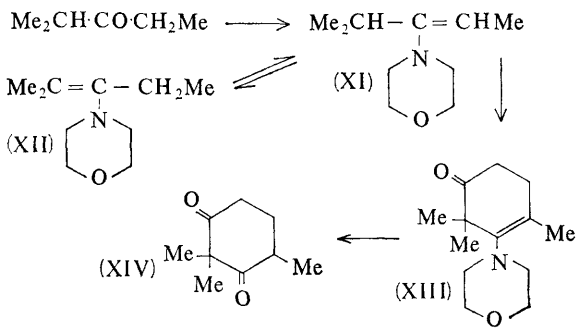
gain to give the enamino-ketone hydrochloride (V), which is hydrolysed by cold water to the dione (VII). In the presence of ethanol the reactive intermediate (III) is trapped and gives the ester (VIII) on hydrolysis. The free enamino-ketone (VI) has been isolated by treatment of the boiling suspension, obtained in the absence of ethanol, with triethylamine. Evaporation of the filtered benzene solution gave 2,4-dimethyl-3-morpholinocyclohex-2-enone (VI). The structure followed from the analytical (Table 2) and spectral data (Table 3) and from the reaction with perchloric acid to give the *O*-protonated salt (as V) (Tables 2 and 3). This follows from the work of Alt and Speziale [7] who have shown that enamino-ketones must be *O*-protonated, since if *N*-protonation occurred only enone absorption at much lower wavelength would be observed, and if *C*-protonation occurred only a weak carbonyl absorption would be observed. The corresponding enamino-ketones (IX; $R^1 = R^2 = R^4 = Me$, $R^3 = H$) and (IX; $R^1 = R^2 = R^3 = Me$, $R^4 = H$) from crotonoyl and methacryloyl chlorides, respectively, were obtained in a similar way, and could be hydrolysed to the corresponding cyclohexane-1,3-diones by mineral acid.

Reaction of acryloyl chloride with the morpholine and pyrrolidine enamines of dibenzyl ketone gave 3-morpholino-2,4-diphenylcyclohex-2-enone and 2,4-diphenyl-3-pyrrolidin-1-ylcyclohex-2-enone, respectively, which have resisted all attempts at hydrolysis to the dione.



That these structural assignments are correct follows from the spectra data (Table 3) which shows the extended conjugation of the enamino-ketone system and from conversion into the corresponding perchlorates with little change in the $\lambda_{max.}$ and ε values, as required for an *O*-protonated enamino-ketone. The reason for the inertness to hydrolysis of the 2,4-diphenyl-enamino-ketones appears to be steric in origin. The adjacent benzene rings force the morpholine ring out of the plane of the double bond and thus reduce the oribital interaction between the lone pair and the π-electrons. As a result the enamino-ketones are weakly basic and treatment of the *O*-protonated salt with water merely results in deprotonation rather than hydrolysis of the iminium group.

In the case of ethyl isopropyl ketone, n.m.r. indicated that the derived enamine was a mixture of isomers (XI) and (XII), but reaction with acryloyl chloride gave only the one product, 2,2,4-trimethylcyclohexane-1,3-dione (XIV). It is likely that the least substituted position of the enamine, which is well known to be the usual site of alkylation, attacks the β-position of the acid chloride, and that cyclisation then takes place at the more highly substituted position to give the enamine intermediate (XIII) (Scheme 3). The structure of



SCHEME 3

(XIII) followed from the spectral data [4*b*; Table 3] which showed the absence of the conjugated enamino-ketone system. Attempts to prepare the morpholine enamine of di-isopropyl ketone were unsuccessful, but the dimethylamine enamine has been prepared and prolonged reaction with acryloyl chloride and hydrolysis of the precipitated iminium ion (X) gave a small amount of 2,2,4,4-tetramethylcyclohexane-1,3-dione.

Cyclohexane-1,3-diones were not obtained from cin-

[7] G. H. Alt and A. J. Speziale, *J. Org. Chem.*, 1965, **30**, 1407.

namoyl chloride, presumably because the reduced reactivity of the β-position of the acid chloride prevents the [3,3]sigmatropic change to the corresponding reactive keten intermediate (as III). *N*-Cinnamoylmorpholine was the only identifiable product, isolated directly from the reaction mixture without addition of water being necessary.

Except for the 2,2-disubstituted derivatives, the cyclohexane-1,3-diones prepared exist mainly in the enol form. The n.m.r. spectrum of 2,4-dimethylcyclohexane-1,3-dione indicated 80% enol, and that of 2,4,6-trimethylcyclohexane-1,3-dione, 83% enol. Both these cyclohexane-1,3-diones were unstable and gave green oils with a smell of acetic acid. This decomposition has been observed before [8] and appears to be due to peroxide formation.[9]

TABLE 2

3-Morpholinocyclohex-2-enones (IX) and perchlorates

| No. | Substituents | Yield (%) | M.p. | Solvent for crystn. | Found (%) C | H | N | Formula | Required (%) C | H | N |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 2,4-Dimethyl | 46 | 56—57° | Benzene–petroleum | 68·6 | 9·3 | 6·8 | $C_{12}H_{19}O_2$ | 68·9 | 9·15 | 6·7 |
| | Perchlorate | | 175—177 | Acetone–ether | 46·3 | 6·8 | 4·65 | $C_{12}H_{20}ClNO_6$ | 46·5 | 6·5 | 4·5 |
| 2 | 2,4,5-Trimethyl | | Oil | (Chromatography †) | | | | $C_{13}H_{21}NO_2$ | | | |
| | Perchlorate | | 159—160 | Ethyl acetate–acetone | 48·5 | 7·1 | 4·4 | $C_{13}H_{22}ClNO_6$ | 48·2 | 6·85 | 4·3 |
| 3 | 2,4,6-Trimethyl | 63 | 120—121 | Ethyl acetate | 69·7 | 9·4 | 6·4 | $C_{13}H_{21}NO_2$ | 69·9 | 9·5 | 6·3 |
| | Perchlorate | | 185 | Acetone–ether | 48·4 | 7·1 | 4·2 | $C_{13}H_{22}ClNO_2$ | 48·2 | 6·85 | 4·3 |
| 4 | 2,2,4-Trimethyl * | 45 | 84 | Petroleum | 70·2 | 9·2 | 6·2 | $C_{13}H_{21}NO_2$ | 69·9 | 9·5 | 6·3 |
| 6 | 2,4-Diphenyl | 77 | 212—213 | Chloroform | 79·2 | 6·9 | 4·4 | $C_{22}H_{23}NO_2$ | 79·3 | 6·95 | 4·2 |
| | Perchlorate | | 205 (decomp.) | Acetone | 60·7 | 5·6 | 3·25 | $C_{22}H_{24}ClNO_6$ | 60·9 | 5·6 | 3·2 |
| 7 | 6-Methyl-2,4-diphenyl | 72 | 142—143 | Benzene–chloroform | 79·7 | 7·4 | 4·25 | $C_{23}H_{25}NO_2$ | 79·5 | 7·25 | 4·0 |
| 8 | 5-Methyl-2,4-diphenyl | 35 | 135—137 | (Chromatography †) | 79·5 | 7·3 | 4·25 | $C_{23}H_{25}NO_2$ | 79·5 | 7·25 | 4·0 |
| 9 | 2,4-Diphenyl ‡ | 56 | 140—141 | Ethyl acetate | 83·4 | 7·1 | 4·35 | $C_{22}H_{23}NO$ ‡ | 83·25 | 7·3 | 4·4 |
| | Perchlorate | | 189—190 | Ethyl acetate–acetone | 62·9 | 6·0 | 3·2 | $C_{22}H_{24}ClNO_5$ | 63·2 | 5·8 | 3·4 |

* Nonconjugated enamino-ketone (XIII). † Eluted with 10% ethanol–benzene on a silica column. ‡ 2,4-Diphenyl-3-pyrrolidin-1-ylcyclohex-2-en-1-one.

TABLE 3

Spectral properties of (*a*) cyclohexane-1,3-diones, (*b*) 3-morpholinocyclohex-2-enones (IX), and (*c*) perchlorates

| No. | Substituents | Infrared (cm.$^{-1}$) $\nu_{CO}$ ($CHCl_3$) | $\nu_{C=C}$ ($CHCl_3$) | Ultraviolet $\lambda_{max.}$ (EtOH) mμ | ($\varepsilon \times 10^{-3}$) | N.m.r. (τ values) Methyl protons ($CDCl_3$) |
|---|---|---|---|---|---|---|
| 1*a* | 2,4-Dimethyl ..... | 1739, 1709 | (1625 *) | 263 | (14·0) | 8·78d,(8·23s *) |
| *b* | ..... | 1630 | 1575 | 317 | (20·45) | 8·80d, 8·23s |
| *c* | ..... | | | 317 | (22·2) | |
| 2*a* | 2,4,5-Trimethyl ..... | 1745, 1710 | (1623 *) | | | |
| *b* | ..... | 1620 | 1575 | 320 | (20·2) | 8·97d, 8·80d, 8·2s |
| *c* | ..... | | | 322 | (20·8) | |
| 3*a* | 2,4,6-Trimethyl ..... | 1745, 1710 | (1623 *) | 263 | (15·4) | 8·80d,(8·28s *) |
| *b* | ..... | 1620 | 1575 | 318 | (21·0) | 8·92d, 8·80d, 8·23s |
| *c* | ..... | | | 316 | (19·8) | |
| 4*a* | 2,2,4-Trimethyl ..... | 1725, 1695 † | | 286 | (0·061) | 8·90d, 8·83s, 8·60s † |
| *b* | ‡ ..... | 1712 † | 1650 † | | | 8·84s, 8·22s |
| 5*a* | 2,2,4,4-Tetramethyl ..... | 1720, 1690 † | | | | 8·79s, 8·70s † |
| 6*b* | 2,4-Diphenyl ..... | 1612 | 1532 | 324 | (19·6) | |
| *c* | ..... | | | 325 | (25·4) | |
| 7*b* | 6-Methyl-2,4-diphenyl ..... | 1625 | 1545 | 324 | (18·2) | 8·95d |
| 8*b* | 5-Methyl-2,4-diphenyl ..... | 1625 | 1540 | 325 | (18·5) | 9·15d |
| 9*b* | 2,4-Diphenyl § ..... | 1614 | 1530 | 318 | (27·0) | |
| *c* | § ..... | | | 318 | (29·0) | |

* For enol form. † In $CCl_4$. ‡ Nonconjugated enamino-ketone (XIII). § 2,4-Diphenyl-3-pyrrolidin-1-ylcyclohex-2-enone.

## EXPERIMENTAL

*Preparation of Enamines.*—3-Morpholinopent-2-ene [required for compounds 1*a*—*c*, 2*a*—*c*, and 3*a*—*c* (Table 3)] was prepared by the method of Stork *et al.*[6] and 2-morpholino-1,3-diphenylpropene [required for compounds 6*b* and *c*, 7*b*, and 8*b* (Table 3)] by the method of Pocar, Bianchetti, and Dalla Croce.[10]

(a) 1,3-*Diphenyl-2-pyrrolidin-1-ylpropene.* A solution of dibenzyl ketone (20 g.), pyrrolidine (12 g.), and toluene-*p*-sulphonic acid (0·2 g.) in benzene (150 c.c.) was heated under reflux for 4 days under a molecular sieve. The solvent was removed and the residue distilled to give the *propene* (18·2 g., 73%), b.p. 138—142°/0·5 mm. (Found: C, 86·5; H, 7·95; N, 5·1. $C_{19}H_{21}N$ requires C, 86·65; H, 8·0; N, 5·3%), $\nu_{max.}$ (film) 1605 cm.$^{-1}$ (C=C). Compounds 9*b* and *c* (Table 3) were prepared from this enamine and acryloyl chloride.

(b) 4-*Methyl*-3-*morpholinopent-2-ene.* Titanic chloride [11] (3 c.c.) in benzene (50 c.c.) was added slowly to ethyl isopropyl ketone (5 g.) and morpholine (20 g.) in benzene

[8] E. G. Meek, J. H. Turnbull, and W. Wilson, *J. Chem. Soc.*, 1953, 812.

[9] N. J. Toivenen, T. Lewison, and H. Kivikoshi, *Acta Chem. Fennica*, 1932, **5**, 31 (*Chem. Zentr.*, 1932, **2**, 2175); R. Criegee in Houben-Weyl-Muller, 'Methoden de Organischen Chemie,' 4th edn., Thieme, Stuttgart, 1952, vol. 8, 25.

[10] D. Pocar, G. Bianchetti, and P. Dalla Croce, *Gazzetta*, 1965, **95**, 1220.

[11] W. A. White and H. Weingartern, *J. Org. Chem.*, 1967, **32**, 213.

(200 c.c.) cooled in an ice bath during 1 hr. The mixture was stirred for 24 hr., filtered, evaporated, and distilled to give the pent-2-ene (2·5 g., 30%), b.p. 93—94°/14 mm. $\nu_{max.}$ (film) 1650 cm.$^{-1}$ (C=C); n.m.r. ($CDCl_3$) indicated the presence of the more highly substituted (XII) (70%) and the less highly substituted (XI) (30%) isomers [(XII): τ 9·0 (t, Me), 8·25 (s, Me), 8·38 (s, Me), and 7·85 (q, $CH_2$); (XI): τ 8·9 (d, Me), 8·37 (d, Me), *ca.* 7·3 (overlaid m, ·CH<), and 5·3 (m, ·CH=); τ 7·35 and 6·35 (morpholine protons) in both isomers]. Compounds 4*a* and *b* (Table 3) were prepared from this enamine and acryloyl chloride.

(c) 2,4-*Dimethyl*-3-*dimethylaminopent*-2-*ene*. Titanic chloride (10 c.c.) in light petroleum (b.p. 40—60°) (100 c.c.) was added slowly to di-isopropyl ketone (11·4 g.) and distilled dimethylamine (20 c.c.) (collected in a solid carbon dioxide–acetone trap) in dry ether (500 c.c.) cooled in ice. The mixture was stirred for 10 days, filtered, evaporated, and distilled to give 2,4-dimethyl-3-dimethylaminopent-2-ene* (7·2 g., 50%), b.p. 65—67°/48 mm., $\nu_{max.}$ (film) 1665 cm.$^{-1}$ τ ($CCl_4$) 9·0 (d, 2Me), 8·4 (s, 2Me), 7·48 (s, 2Me), and 7·3 (m, $CHMe_2$). Compound 5*a* (Table 3) was prepared from this enamine and acryloyl chloride.

*Preparation of Cyclohexane*-1,3-*diones*.—The αβ-unsaturated acid chloride (0·05 mole) in dry benzene (50 c.c.) was added, with stirring, to the enamine (0·05 mole) in dry benzene (100 c.c.) at the boil during 1 hr. The mixture was then heated under reflux for 6—16 hr. and cooled; the precipitated salt was filtered off, if a solid, or separated from the benzene by decantation if an oil. The intermediate was then washed with dry benzene and hydrolysed by stirring with ice-cold water (100 c.c.) for 3 hr. The aqueous suspension was extracted with ether, and the extract was separated from any undissolved oil, dried ($MgSO_4$), and evaporated to leave the cyclohexane-1,3-dione, purified as shown in Table 1. Spectral data are listed in Table 3.

In the case of 4-methyl-3-morpholinopent-2-ene the reaction time was reduced to 1 hr., after the addition of the acryloyl chloride, and the precipitate formed consisted of enamine hydrochloride. This was filtered off and the benzene was evaporated off to leave 2,2,4-*trimethyl*-3-*morpholinocyclohex*-3-*enone* (4; Table 2). This was hydrolysed by stirring with 4N-hydrochloric acid for 12 hr. at 25° and the resulting oil was extracted with ether and distilled to give the *dione* (4; Table 1).

*Preparation of* 3-*Morpholinocyclohex*-2-*enones*.—The suspension obtained in benzene by reaction of the acid chloride with the enamine (as above), was boiled for 2 hr. and treated with triethylamine (0·1 mole); the mixture was heated under reflux (1; Table 2), or stirred while cooling down (2 and 3; Table 2), for 18 hr. Triethylamine hydrochloride was filtered off and the benzene solution was evaporated to give the corresponding 3-morpholinocyclohex-2-enone, purified as shown in Table 2. These enamino-ketones were stable to neutral hydrolysis, but were rapidly hydrolysed in acid solution to the corresponding dione (Table 1).

In the case of 2-morpholino-1,3-diphenylpropene, the suspension formed on reaction with the αβ-unsaturated acid chloride gradually evolved hydrogen chloride at the boil, so addition of triethylamine was unnecessary. The suspensions obtained from methacryloyl and crotonoyl chloride passed into solution after boiling for 18 hr. and evaporation of the solutions gave the enamino-ketones (7 and 8; Table 2). In the case of acryloyl chloride the suspended solid did not dissolve and was collected and slurried with water; the suspension was made alkaline with sodium carbonate solution and the free *enamino-ketone* was filtered off (6; Table 2). In the same way the corresponding 3-*pyrrolidin*-1-*yl derivative* (9; Table 2) was prepared from 1,3-diphenyl-2-pyrrolidin-1-ylpropene. The spectral data are listed in Table 3.

The diphenyl enamino-ketones were resistant to neutral, acidic, and basic hydrolysis; attempted hydrolysis with hot 50% sulphuric acid, caustic potash in diethylene glycol, or acetate buffer solution [6] also failed.

*Preparation of Perchlorates*.—The enamino-ketones (1, 2, and 3; Table 2) were dissolved in ether–ethanol (1 : 1) and an excess of 70% perchloric acid was added. The perchlorates separated within a few min. and were collected and recrystallised (Table 2). The enamino-ketones (6 and 9; Table 2) were dissolved in chloroform–ethanol (1 : 1) and treated in the same way. After 10—14 days the precipitated oils were separated and the solid perchlorates were obtained by trituration with ethanol or ether, followed by recrystallisation (Table 2). The spectral data are listed in Table 3.

*Reactions of Cyclohexane*-1,3-*diones*.—(a) *Coupling with diazonium salts*. A solution of benzenediazonium chloride (0·01 mole) was added slowly with stirring to a solution of 2,4-dimethylcyclohexane-1,3-dione (0·01 mole) in dilute sodium hydroxide solution [0·85 g. in water (9 c.c.)] with further additions of alkali to keep the pH in the range 7—9. After 24 hr. at 0° the red precipitate was collected and gave 3-methyl-1,5-diphenylformazan (1·08 g.), m.p. 110—112° (from ethanol) (Found: C, 70·5; H, 6·1; N, 23·6. Calc. for $C_{14}H_{14}N_4$: C, 70·5; H, 5·9; N, 23·5%), $\nu_{max.}$ ($CCl_4$) 1610 cm.$^{-1}$ (C=N). When benzene diazonium chloride (2 equiv.) was used, the yield was increased to 2·16 g. (91%). The i.r. and n.m.r. spectra were identical with those of an authentic sample, prepared from benzenediazonium chloride and acetaldehyde phenylhydrazone.[4] An identical product was obtained by coupling 2,4,6-trimethylcyclohexane-1,3-dione with benzenediazonium chloride; the 3-methyl-1,5-diphenylformazan was purified by preparative t.l.c. on silica [light petroleum (b.p. 60—80°)–ethanol–ethyl acetate (8 : 1 : 1)].

In a similar way *p*-chlorobenzenediazonium chloride (0·01 mole) and 2,4-dimethylcyclohexane-1,3-dione gave 1,5-*di*-(p-*chlorophenyl*)-3-*methylformazan* (1·0 g.), m.p. 148—150° (from aqueous ethanol) (Found: C, 54·8; H, 3·9; Cl, 23·0; N, 18·05. $C_{14}H_{12}Cl_2N_4$ requires C, 54·75; H, 3·9; Cl, 23·1; N, 18·2%) and *p*-nitrobenzenediazonium chloride (0·01 mole) gave 3-*methyl*-1,5-*di*-(p-*nitrophenyl*)*formazan* (1·95 g.) (Found: C, 51·3; H, 4·0; N, 25·2. $C_{14}H_{12}N_6O_4$ requires C, 51·2; H, 3·7; N, 25·6%).

(b) *Oxidation*. Potassium dichromate (3 g.) in 2N-sulphuric acid (10 c.c.) was added to 2,4,6-trimethylcyclohexane-1,3-dione (1·0 g.) in water (20 c.c.) and the mixture was stirred at 100° for 30 min. The suspension was cooled, made alkaline with sodium carbonate solution, and filtered, and the filtrate was acidified and extracted with ether. The ether solution was extracted with sodium hydrogen carbonate solution and the combined aqueous layers were acidified, and extracted with ether. The extract was dried and evaporated to leave a white solid (m.p. 122—128°). This was extracted with boiling benzene, filtered from a small

* Attempts to prepare the corresponding morpholine enamine by this method were unsuccessful.

amount of insoluble material, and cooled to give DL-αα′-dimethylglutaric acid (0·75 g. 73%), m.p. 137—138° (lit.,[12] m.p. 142°) (Found: C, 52·6; H, 7·5. Calc. for $C_7H_{12}O_4$: C, 52·5; H, 7·6%); $\nu_{max.}$ ($CHCl_3$) 3500—2500 (OH) and 1720 (C=O) cm.$^{-1}$, τ 8·8 (d, 2Me), 7·31 (m, 2CH), 8·0 (m, $CH_2$), and −0·5br (exchangeable, $2CO_2H$).

*Unambiguous Synthesis of* 2,4-*Dimethylcyclohexane*-1,3-*dione*.—Ethyl α-propionylpropionate (4·87 g.) was added to a cooled solution of sodium (1·45 g.) in dry ethanol (25 c.c.) with stirring at 25°, followed by ethyl acrylate (6·35 g.). The mixture was stirred at 25° for 15 min. then boiled for 6 hr. Potassium hydroxide (7·75 g.) in water (35 c.c.) was added and the mixture was heated on a steam-bath for a few min.; 4N-hydrochloric acid was then added to pH 6 and the alcohol was distilled off as rapidly as possible. The aqueous residue was treated with charcoal and filtered hot, and the filtrate was neutralised (litmus), boiled with charcoal, and filtered hot. 2N-Hydrochloric was added to the hot filtrate (to pH 3·5) and the solution was cooled; pale cream plates of 2,4-*dimethylcyclohexane*-1,3-*dione* (3·0 g., 34%) separated, m.p. 117—119° (from benzene) (Found: C, 68·7; H, 8·8. $C_8H_{12}O_2$ requires C, 68·55; H, 8·6%), i.r. and n.m.r. spectra identical with those of the product (1; Table 1) from the reaction of acryloyl chloride and 3-morpholinopent-2-ene, and mixed m.p. not depressed.

*Reaction of Acryloyl Chloride with* 3-*Morpholinopent*-2-*ene in the Presence of Ethanol*.—(*a*) Acryloyl chloride (4·52 g., 0·05 mole) in dry benzene (50 c.c.) was added with stirring to 3-morpholinopent-2-ene (7·75., 0·05 mole) and dry ethanol (6 g., 0·13 mole) in dry benzene (100 c.c.) at the boil during 3 min.; the mixture was heated under reflux for 3 min. The cooled solution was stirred with cold water (100 c.c.) for 3 hr. and extracted with ether. The extract was dried and evaporated to leave an oil (6·43 g.) which was distilled to give ethyl 4-methyl-5-oxoheptanoate (3·74 g., 41%), b.p. 118—125°/15 mm. (Found: C, 64·5; H, 9·8. Calc. for $C_{10}H_{18}O_3$: C, 64·5; H, 9·7%), $\nu_{max.}$ (film) 1748 and 1710 cm.$^{-1}$ (C=O), i.r. spectrum identical with that of authentic material prepared from ethyl acrylate and 3-morpholinopent-2-ene by boiling in ethanol for 16 hr.[6]

(*b*) Ethyl acrylate (5·0 g., 0·05 mole) was added with stirring to 3-morpholinopent-2-ene (7·75 g., 0·05 mole) and dry ethanol (6 g., 0·13 mole) in dry benzene (100 c.c.) at the boil during 3 min.; the mixture was then heated under reflux for 3 min. The cooled solution was stirred with 5% hydrochloric acid (100 c.c.) for 3 hr. and extracted with ether; the extract was dried and the ether was evaporated off to leave diethyl ketone, in which no ethyl 4-methyl-5-oxoheptanoate could be detected by t.l.c.

*Reaction of Cinnamoyl Chloride with* 3-*Morpholinopent*-2-*ene*.—Cinnamoyl chloride (8·35 g., 0·05 mole) in dry benzene (50 c.c.) was added with stirring to 3-morpholinopent-2-ene (7·75 g., 0·05 mole) in dry benzene (100 c.c.) at the boil during 45 min. The mixture was heated under reflux; after 5 hr. the evolution of hydrogen chloride was detected. The suspension was heated under reflux for a further 15 hr. and cooled, and the benzene solution decanted from the residual black oil (1·0 g.), shown by t.l.c. to consist mainly of *N*-cinnamoylmorpholine. Evaporation of the benzene solution gave a thick red oil (11·5 g.), a portion of which (5·8 g.) was stirred with cold water for 3 hr. at 25°. The mixture was extracted with ether and distilled to give *N*-cinnamoylmorpholine (2·2 g.), m.p. 89—90°. The remainder of the oil (5·7 g.) was distilled to give *N*-cinnamoylmorpholine directly (2·15 g.), b.p. 174—182°/0·6 mm., m.p. 90—91° (Found: C, 71·6; H, 6·8; N, 6·45. Calc for $C_{13}H_{15}NO_2$: C, 71·85; H, 6·95; N, 6·45%), i.r. and n.m.r. spectra identical with those of an authentic sample.[13]

We thank Miss M. Redshaw and Mr. D. J. Barraclough for i.r. and n.m.r. determinations respectively. We also thank Geigy (U.K.) Limited for grants (to J. R. H. and B. J. H.).

[8/718 *Received*, *May* 22*nd*, 1968]

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