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REACTION OF α,β-UNSATURATED ACID CHLORIDES WITH ENAMINES—I

PREPARATION OF BICYCLO(3.3.1)NONAN-2,9-DIONES

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Abstract—A new method for the preparation of bicyclo(3,3,1)nonan-2,9-diones involves the reaction of α,β-unsaturated acid chlorides with enamines. Bicyclo(3,3,1)nonan-2,9-dione, 1-methylbicyclo-(3,3,1)nonan-2,9-dione, and 6,6,8,8-tetramethylbicyclo(3,3,1)nonan-2,9-dione have been obtained from the reaction of acryloyl chloride with the morpholine enamine of the corresponding cyclohexanone Cinnamoyl chloride gives varying amounts, depending upon the conditions, of 2-cinnamoylcyclohexanone and a bis-compound, formed by reaction of a second molecule of enamine with the β-position of the acid chloride residue, in addition to 4-phenylbicyclo(3,3,1)nonan-2,9-dione. A mechanism has been proposed and confirmatory evidence obtained.

PRELIMINARY work[1] has shown that the reaction of α,β-unsaturated acid chlorides with enamines gives a mixture of compounds, one of which, isolated in very small yield, was tentatively assigned the bicyclic diketone structure I and another the bis-compound II. Further work has confirmed this conclusion and developed the reaction into a synthetic method for the preparation of bicyclo(3.3.1)nonan-2,9-diones. Of the two methods previously reported for the preparation of this bicyclic system directly, the one[2] has been shown to be incorrect[3] and the other,[4] involving the cyclization of 1-substituted-β-2-oxocyclohexylpropionic acids in tetralin in the presence of *p*-toluenesulphonic acid, failed to yield bicyclo(3.3.1)nonan-2,9-dione in our hands and thus appears to be applicable only when a large α-substituent (e.g. benzyl) is present. Such a group would provide steric assistance to the reaction by favouring that conformation in which the carboxyethyl group is axial and thus favourably placed for reaction with the α′-position of the cyclohexanone ring. Recently Cope *et al.*[5] have modified Stork and Landesman's[6] preparation of 2-N-pyrrolidinylbicyclo-(3.3.1)nonan-9-one, formed by the reaction of acrolein with 1-N-pyrrolidinylcyclohexene, to give β-2-oxocyclohexylpropionaldehyde which was then cyclized to bicyclo(3.3.1)nonan-2-ol-9-one (III). In order to establish the identity of our product we have oxidized the keto alcohol III with Jones reagent to give bicyclo(3.3.1)nonan-2,9-dione, identical to the product[1,3] from the reaction of acryloyl chloride with 1-N-morpholinocyclohexene in every respect.

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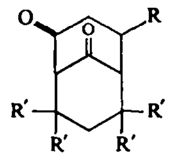
[1] P. W. Hickmott, *Proc. Chem. Soc.* 287 (1964).
[2] A. N. Kost and L. G. Ovseneva, *Zh. obshch Khim.* 32, 3983, (1962).
[3] J. R. Hargreaves and P. W. Hickmott, *Tetrahedron Letters* 4173 (1966).
[4] R. Fusco and F. Tenconi, *Tetrahedron Letters* 1313 (1965).
[5] A. C. Cope, D. L. Nealy, P. Scheiner and G. Wood, *J. Am. Chem. Soc.* 87, 3130 (1965).
[6] G. Stork and H. K. Landesman, *J. Am. Chem. Soc.* 78, 5130, (1956).



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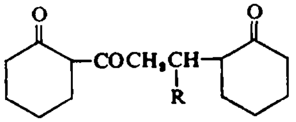

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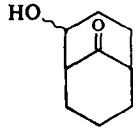

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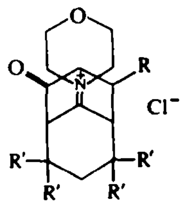

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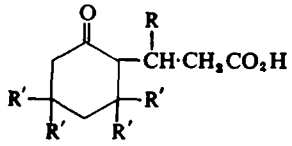

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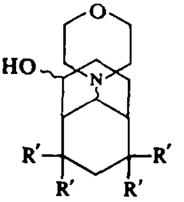

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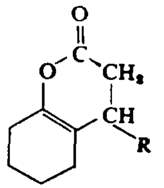


VII

The effect of the reaction conditions on the yield and purity of the bicyclic dione I is summarized in Table 1. Under the original conditions,[1] in which acryloyl chloride was added to 1-N-morpholinocyclohexene in benzene at low temperatures, followed by prolonged boiling, a complex mixture of products was obtained from which only bicyclo(3.3.1)nonan-2,9-dione was isolated in very small yield. When the addition is carried out at the boil, in equimolecular proportions, a high yield of the bicyclic dione I is obtained in a relatively pure state. The initial product is an unstable adduct IV which is decomposed by water to give the bicyclic dione, and by acid or alkali to give the corresponding β-2-oxocyclohexylpropionic acid (V). Evidence for the structure of the adduct has been obtained from the reaction of acryloyl chloride and the morpholine enamine of 3,3,5,5-tetramethylcyclohexanone. In this case the adduct was sufficiently stable to be isolated and crystallised as the less soluble iodide. Analysis and spectroscopic data agree with the proposed structure IV (R = H, R′ = Me) and reduction by sodium borohydride gave VI (R′ = Me). Decomposition

TABLE 1. EFFECT OF REACTION CONDITIONS ON YIELD OF 1-METHYLBICYCLO-(3.3.1)NONAN-2,9-DIONE

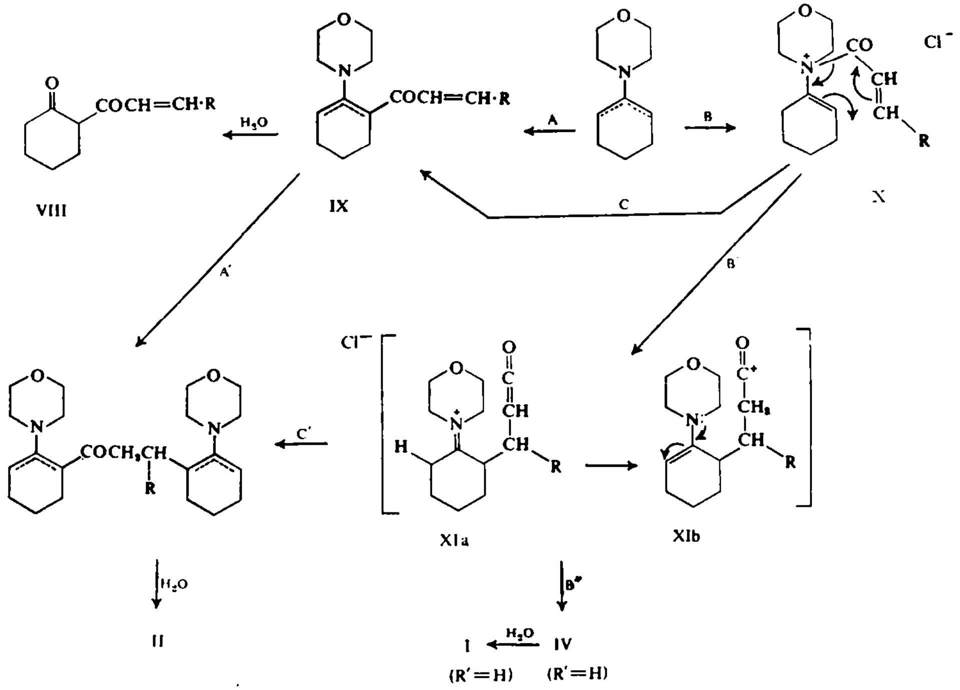
Solvent	Addition time*	Addition temp	Reaction time	Reaction temp	Yield %	M.p.
Benzene	75 min	Reflux	21 hr	Reflux	87	37·5°
Benzene	79	Reflux	2 hr	Reflux	77	37
Benzene	4	Reflux	21 hr	Reflux	71	36–37
Benzene	4	Reflux	4 min	Reflux	50	37
Benzene	70	49°	21 hr	49°	41	38
Toluene	75	Reflux	21 hr	Reflux	21	35
Benzene	65	0–10°	21 hr	Reflux	17	37
Benzene	25	5°	21 hr	Reflux	< 5†	—

* A soln of acryloyl chloride was added to a 0·5 M soln of enamine in equimolecular proportions.
† Two equivs of enamine used.

of the adduct with warm water gave a mixture of β-2-oxo-4,4,6,6-tetramethylcyclohexylpropionic acid (V, R = H, R′ = Me) and 6,6,8,8-tetramethylbicyclo(3.3.1)nonan-2,9-dione (I, R = H, R′ = Me), separated by chromatography on alumina.

Cinnamoyl chloride, on cold addition to excess of the enamine in benzene followed by prolonged boiling and decomposition of the resulting mixture with water, gave 4-phenylbicyclo(3.3.1)nonan-2,9-dione (I, R = Ph, R′ = H) and 2(β-2-oxocyclohexyl-β-phenylpropionyl)cyclohexanone (II, R = Ph). The latter was isolated in either keto or enol form, depending on the method of separation. Distillation gave the enol, m.p. 107–109° (immediate $FeCl_3$ colouration), $\nu_{CO}^{CCl_4}$ 1710 cm^{-1}; 1620–1575 cm^{-1} [intramol. H-bonded ·CO·C:C(OH)·], whereas treatment with cold n-propanol gave the keto tautomer, m.p. 161–163°, lowered to m.p. 145–147° on crystallization from ethanol (no $FeCl_3$ colouration, $\nu_{CO}^{CHCl_3}$ 1710, 1690 cm^{-1}) and converted into the enol by heating in tetrachloroethane. Hot addition* of cinnamoyl chloride to an equivalent of the enamine (at 80°) gave an increased yield of bicyclic dione (I, R = Ph, R′ = H). The latter was rapidly hydrolysed by alkali to β-2-oxocyclohexyl-β-phenylpropionic acid (V, R = Ph, R′ = H). This ready fission of the bicyclo(3.3.1)nonan-2,9-dione ring system, which initially[1] led us to consider the enol lactone VII as a possible structure for this compound, has been noted previously.[4,7] The possible reaction paths which we favour in the formation of these compounds are illustrated below.

C-acylation (Path A) leads to the formation of the acylated enamine IX which cannot be involved in the formation of the bicyclic dione ring system whatever the



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* 'Hot addition' used in this context differentiates between this and the cold addition process.

[7] J. D. Connolly, R. McCrindle and K. H. Overton, *Chem. Comm.* 162 (1965); G. I. Fujimoto and J. Pavlos, *Tetrahedron Letters* 4477 (1965).

orientation of the enamine double bond with respect to the carbonyl group.[8] Further reaction of IX, as an electrophilic olefin, can take place with free enamine (Path A′), thus accounting for the formation of the bis-compound II. N-acylation (Path B) results in the formation of the tertiary amine-acid chloride complex X which can react further (Path B′) to give a ketene XIa or acylium ion XIb intermediate formed via a cyclic transition state (as depicted in X) or intermolecularly by Michael addition of free enamine. The situation (axial substitution of bridging group) is now favourable for further intramolecular reaction (Path B″) to give the bicyclic dione, with possible intermolecular competition (Path C′) to give some bis-compound II. A further possibility is that the acylated enamine IX may be formed from the complex X (Path C) by intra- or intermolecular pathway. This will be favoured when the reactivity of the β-position in the α,β-unsaturated acid chloride is lowered (as when R = Ph).

Confirmatory experimental evidence for the proposed reaction paths has been obtained. The complex X (R = Ph) has been isolated at low temperatures and identified by treatment with water to give cinnamic acid. Addition to boiling benzene and subsequent decomposition with water gave a mixture of bicyclic dione I (R = Ph, R′ = H) and 2-cinnamoylcyclohexanone VIII (R = Ph). Similarly the complex from acryloyl chloride X (R = H) gave the dione as the main and only identifiable product in boiling benzene, in the dry state at 110°, or in boiling benzene in the presence of excess enamine; when added to a boiling benzene solution of a different enamine (1-N-morpholino-6-methylcyclohexene) bicyclo(3.3.1)nonan-2,9-dione was formed, but no 1-methylbicyclo(3.3.1)nonan-2,9-dione was detected, indicating that conversion of the complex X to XI, and hence to the adduct IV, is an intramolecular process as depicted (in X) and not intermolecular Michael addition of free enamine. The formation of a reactive intermediate (XIa or XIb) has been demonstrated in the case of acryloyl chloride by carrying out the additon to the enamine in boiling benzene in the presence of ethanol. A high yield of ethyl β-2-oxocyclohexylpropionate was obtained. Under the same conditions (Experimental) ethyl acrylate gave none of this compound (by GLC), proving that β-alkylation of the enamine is taking place before C-acylation of the enamine (or O-acylation of alcohol) to give a reactive intermediate XI. The ketene group, having been introduced into an axial position, will be favourably situated for aiding proton loss from the imminium ion (XIa → XIb) and for cyclization to the bicyclononane derivative IV. Alternatively proton loss and gain may take place concurrently with β-alkylation without the intermediacy of a ketene. Addition of cinnamoyl chloride to enamine in the presence of ethanol gave only ethyl cinnamate, due to the lower reactivity of the β-position. Further evidence for the β-alkylation process preceding C-acylation in bicyclic dione formation has been obtained from the reaction of acryloyl chloride with the morpholine enamine of 2-methylcyclohexanone. The only product isolated, in 80–90% yield, was 1-methylbicyclo(3.3.1)nonan-2,9-dione (Me singlet at 8·96 τ). Structure confirmation was obtained by hydrolysis to β-2-oxo-3-methylcyclohexylpropionic acid (Me doublet at 9·0 τ). Gurowitz and Joseph[9] have shown that the commonly held belief that enamines of 2-alkyl cyclic ketones exist as the isomer with the least substituted double bond does not generally

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[8] This follows from the observation that only 1-methylbicyclo(3.3.1)nonan-2,9-dione was formed, in 87% yield, from the morpholine enamine of 2-methylcyclohexanone. Prior C-acylation, at the least substituted α-position, would lead to 5-methylbicyclo(3.3.1)nonan-2,9-dione.

[9] W. D. Gurowitz and M. A. Joseph, *Tetrahedron Letters* 4433 (1965).

hold for cyclohexanone derivatives, except in the case of pyrrolidine enamines. The reasons they advance for this can only be applicable in the ground state since in the transition state of enamine reactions orbital overlap between the lone pair and the π-electrons must be of predominant importance. Therefore, the least substituted α-position must be the first to be attacked, for steric reasons.* Finally, in the case of cinnamoyl chloride the alternative (path C) becomes more favourable and appreciable quantities of cinnamoyclyclohexanone can be isolated together with bicyclic dione. In the presence of excess enamine the intermediate acylated enamine is converted to the bis compound II with consequent reduction in the yield of cinnamoylcyclohexanone.

Attempts to convert bicyclo(3.3.1)nonan-2,9-dione to the hydrocarbon have been made, but without success; further work on the chemistry of bicyclo(3.3.1)nonan-2,9-dione is in progress and will be reported in due course.

EXPERIMENTAL

UV and IR spectra were measured on Unicam S.P. 800 and Perkin–Elmer 221 spectrophotometers respectively and NMR spectra on a Varian HA 100 instrument. GLC was carried out on the Pye Argon chromatograph with a polyethylene glycol adipate column at 150°.

Reaction of acryloyl chloride with 1-N-*morpholinocyclohexene*

(a) Acryloyl chloride (18·5 ml) was added to 1-N-morpholinocyclohexene (79 g) in dry benzene (300 ml) with stirring and cooling below 25°. After refluxing overnight the ppt was collected, washed with dry benzene and stirred with ice-cold water for 3 hr. The resulting oil was extracted with ether, dried, volatiles removed *in vacuo* and the residual oil purified by chromatography on silica gel (20% methylene dichloride in benzene). Distillation (0·4 mm) gave *bicyclo*(3,3,1)*nonan*-2,9-*dione* (0·4 g) as an oil which failed to solidify. (Found: C, 71·3; H, 7·9. $C_9H_{12}O_2$ requires; C, 71·05; H, 7·9%.) The IR spectrum showed $\nu_{C=O}^{film}$ 1725, 1700 cm^{-1} and the NMR spectrum (CCl_4) consisted of a complex band at 7·0–8·4 τ. Nothing else was isolated in a sufficiently pure state for identification, either from the column or the benzene filtrates.

Hydrolysis of the ppt with boiling 2N HCl, instead of cold water, gave β-2-oxocyclohexylpropionic acid (10 g), b.p. 166–168°/3 mm, m.p. 64–65°, undepressed by admixture with authentic material, (Found: C, 63·4; H, 8·0. Calc. for $C_9H_{14}O_3$: C, 63·5; H, 8·2%.)

(b) Acryloyl chloride (4·6 g) in dry benzene (50 ml) was added to 1-N-morpholinocyclohexene (8·35 g) in dry benzene (75 ml) over 1 hr *at the boil*. After refluxing overnight the mixture was cooled and the ppt collected, washed with dry benzene and stirred for 3 hr with ice-cold water (100 ml). The oil was ether extracted and sublimed at 100°/0·5 mm to give bicyclo(3,3,1)nonan-2,9-dione (3·4 g, 45%) as a waxy solid, m.p. 117° (Found: C, 70·9; H, 7·8. $C_9H_{12}O_2$ requires: C, 71·05; H, 7·9%), $\nu_{C=O}^{CCl_4}$ 1735, 1710 cm^{-1}, λ_{max}^{MeOH} 281 mμ (log ε 1·84). The IR[10] and NMR spectra were identical with those of the product from (a). A bis-2,4-dinitrophenylhydrazone was obtained, m.p. 266° from AcOEt–acetone. (Found: C, 49·0; H, 4·0; N, 21·6. $C_{21}H_{20}N_8O_8$ requires: C, 49·2; H, 3·9; N, 21·9%.)

Oxidation of bicyclo(3,3,1)*nonan-2-ol-9-one*

Bicyclo(3,3,1)nonan-2-ol-9-one[5] (5·25 g) in acetone (90 ml) was cooled in ice and a slight excess of Jones reagent (8N CrO_3 in dil H_2SO_4) added dropwise over 10 min. with cooling. The mixture was

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* Evidence that the most substituted position may be attacked appreciably [H. O. House and M. Schellenbaum, *J. Org. Chem.* **28**, 34, (1963); R. D. Campbell and J. A. Jung, *Ibid.* **30**, 3711 (1965)] has not been substantiated by other workers [S. K. Malhotra and F. Johnson, *Tetrahedron Letters* 4027, 1965; R. Helmers, *Acta. Chem. Scand.* **19**, 2139 (1965)]. The acylation of 1-N-morpholino-6-methylcyclohexene has been shown to give the 2-butyryl derivative (65% yield) [S. Hünig and M. Salzwedel, *Chem. Ber.* **99**, 823 (1966)] and we have confirmed that no 6-acyl derivative can be detected in the crude reaction product before distillation.

[10] Solvent dependence of the carbonyl stretching absorption has been noted previously [Ref. 3 and G. Eglinton, J. Martin and W. Parker, *J. Chem. Soc.* 1243 (1965)].

poured into ice-cold water (600 ml) and extracted with ether. The ether extracts were washed with sat NaClaq and sat $NaHCO_3$aq, dried, and evaporated to give bicyclo(3,3,1)nonan-2,9-dione (2·0 g) as a waxy solid which was purified by chromatography on silica (10% EtOH in benzene), m.p.117°. The IR and NMR spectra were identical with those of the above product from b. (Found: C, 70·7; H, 8·05. $C_9H_{12}O_2$ requires: C, 71·05; H, 7·9%.)

Reaction of cinnamoyl chloride with 1-N-*morpholinocyclohexene*

(a) Cinnamoyl chloride (29 g) in dry benzene (50 ml) was added slowly to 1-N-morpholinocyclohexene in dry benzene (100 ml) with stirring and cooling below 25°. The mixture was stirred and refluxed overnight and the ppt collected, washed with benzene and stirred with ice-cold water (400 ml) for 3 hr. The resulting oil was separated, dried, and dissolved in cold n-propanol (50 ml). After 1week crystals of the pure *diketo* form of *2(β-2-oxocyclohexyl-β-phenylpropionyl) cyclohexanone* (0·25g) were obtained, m.p. 161–163°, (Found: C, 76·8; H, 8·0. $C_{21}H_{26}O_3$ requires: C, 77·3; H, 8·0%.) The IR spectrum showed $\nu_{\mathrm{C=O}}^{\mathrm{CCl_4}}$ 1710, 1690 cm^{-1} and no bands at ~1600 cm^{-1}. Crystallization from EtOH or glacial AcOH gave a lower melting form, m.p. 145–147°, which was identical spectroscopically with the high melting form. (Found: C, 77·1; H, 7·8. $C_{21}H_{26}O_3$ requires: C, 77·3; H, 8·0%.) Neither form gave a $FeCl_3$ colouration. Evaporation of the n-propanol gave an oil which was distilled to give *4-phenylbicyclo*(3,3,1)*nonan*-2,9-*dione* (4·0 g, 10%) as an oil, b.p. 162–166°/0·05 mm which failed to solidify. (Found: C, 78·9; H, 7·2. $C_{15}H_{16}O_2$ requires: C, 78·95; H, 7·0%) [mass spectrum gave molecular ion 228 (M.W.228), $\nu_{\mathrm{C=O}}^{\mathrm{chf}}$ 1730, 1705 cm^{-1}] and the *enol* form of 2(β-2-oxocyclohexyl-β-phenylpropionyl) cyclohexanone (3·5 g), b.p. 230–235°/0·05 mm, m.p. 107–109° from petroleum ether. (Found: C, 77·0; H, 7·6. $C_{21}H_{26}O_3$ requires: C, 77·3; H, 8·0%.) The latter gave an immediate violet colour with alcoholic $FeCl_3$aq and the IR spectrum showed $\nu_{\mathrm{C=O}}^{\mathrm{CCl_4}}$ 1710(S) and intramolecular H-bonded —CO·C:C·(OH)—group at 1620—1575 (m) cm^{-1}. Both the diketo forms, in tetrachloroethane, on boiling for 10 min gave an IR spectrum identical with that of the enol.

The dione I (R = Ph, R′ = H; 1·3 g) dissolved in 2N NaOH (100 ml) on boiling for 5 min, and β-2-oxocyclohexyl-β-phenylpropionic acid (0·5 g) was obtained on acidification of the cooled solution, m.p. 130–132° (Lit.[11] 126–128°). (Found: C, 73·1; H, 7·7. Calc. for $C_{15}H_{18}O_3$: C, 73·2; H, 7·3%.) The NMR spectrum showed a complex band at 7·2–8·85 τ (cyclohexyl ring), a doublet at 7·25 τ (—CH_2·CO_2—), a multiplet at 6·51 τ (—CH·Ph—), a multiplet at 2·78 τ (benzene ring), and a broad band at 0·16 τ (CO_2H).

(b) Cinnamoyl chloride (16·7 g) in benzene (100 ml) was added over 1 hr to a stirred boiling soln of 1-N-morpholinocyclohexene (16·7 g) in benzene (150 ml) and the mixture refluxed for 21 hr. The ppt was washed with benzene and stirred with cold water for 3 hr. The resulting oil was extracted with ether, dried, and distilled to give 4-phenylbicyclo(3,3,1)nonan-2,9-dione (11·0 g, 48%) as a solid, m.p. 52°, (Found: C, 78·75; H, 7·0. $C_{15}H_{16}O_2$ requires: C, 78·95; H, 7·0%.) $\nu_{\mathrm{CO}}^{\mathrm{CCl_4}}$ 1735, 1714 cm^{-1}, $\lambda_{\mathrm{max}}^{\mathrm{MeOH}}$ 278 mμ (log ε 3·17), 360 mμ (log ε 2·76).

(c) Cinnamoyl chloride (8·35 g) in benzene (50 ml) was added to a boiling soln of 1-N-morpholinocyclohexene (8·35 g) in benzene (75 ml) over 3 min. The mixture was refluxed for 3 min, cooled, stirred with cold water (100 ml) for 3 hr, and the benzene layer separated and evaporated down to give 11·38 g oil. Chromatography of 1·5 g of this oil on silica (benzene–trace EtOH) gave 2-cinnamoylcyclohexanone (0·15 g), m.p. 92°, as the first fraction. (Found: C, 78·8; H, 6·95. Calc. for $C_{15}H_{16}O_2$: C, 78·95; H, 7·0%.) The IR spectrum was identical with that of authentic material.[12]

(d) Cinnamoyl chloride (0·835 g) in benzene (50 ml) was added to a boiling soln of 1-N-morpholinocyclohexene (0·835 g) in benzene (75 ml) over 1½ hr, refluxed overnight, cooled, and filtered. The solid, on hydrolysis with cold water, gave 4-phenylbicyclo(3.3.1)nonan-2,9-dione (0·41 g) and the filtrate, after stirring with cold water for 3 hr, was evaporated down to give 0·71 g crude 2-cinnamoylcyclohexanone (identified by TLC with authentic material[12]), contaminated with a trace of the dione and two other minor constituents.

The experiment was repeated and after refluxing overnight a further quantity of 1-N-morpholinocyclohexene (0·835 g) in benzene (10 ml) was added and the mixture refluxed a further 48 hr. The ppt gave 0·3 g of 4-phenylbicyclo(3.3.1)nonan-2,9-dione on hydrolysis, and the filtrate 1·23 g of oil consisting (TLC) of some dione, the bis compound II in both tautomeric forms, and only a trace of 2-cinnamoyl cyclohexanone.

[11] P. Cordier and M. Meszaros, *C.R. Acad. Sci. Paris* **255**, 1125 (1962).

[12] B. O. Linn and C. R. Hauser, *J. Am. Chem. Soc.* **78**, 6066 (1956).

Reaction of acryloyl chloride with 1-N-*morpholino*-3,3,5,5,-*tetramethylcyclohexene*

(a) A soln of 3,3,5,5-tetramethylcyclohexanone (30·8 g), morpholine (26·1 g) and *p*-toluenesulphonic acid (0·2 g) in benzene (75 ml) was refluxed for 20 hr, the water formed being azeotroped off by means of a Dean & Stark head. The mixture was concentrated and the residue distilled to give 1-N-*morpholino*-3,3,5,5-*tetramethylcyclohexene* (39 g), b.p. 95–100°/0·7 mm. (Found: C, 75·05; H, 11·4; N, 6·4. $C_{14}H_{25}NO$ requires: C, 75·3, H, 11·3; N, 6·3%.)

(b) Acryloyl chloride (4·6 g) in benzene (50 ml) was added slowly (1 hr) to a stirred soln of 1-N-morpholino-3,3,5,5-tetramethylcyclohexene (11·15 g) in benzene (75 ml) at the boil and the mixture refluxed for 20 hr. The ppt (14·5 g) was unaffected by cold water, and boiling water or dil HCl gave a quantitative yield of *β-2-oxo-4,4,6,6-tetramethylcyclohexylpropionic acid* (V, R = H, R′ = Me), m.p. 112–114° from benzene. (Found: C, 69·1; H, 9·8. $C_{13}H_{22}O_3$ requires: C, 69·0; H, 9·8%.) The adduct (5 g) was stirred with water (50 ml) at 45° for 96 hr to give a mixture of V (R = H, R′ = Me) and I(R = H, R′ = Me), separated on alumina (with EtOH) to give 6,6,8,8-*tetramethylbicyclo*(3.3.1)-*nonan*-2,9-*dione* (0·55 g), m.p. 78° from petroleum. (Found: C, 74·8; H, 9·7. $C_{13}H_{20}O_2$ requires: C, 75·0; H, 9·7%.) $\nu^{\mathrm{CCl_4}}_{\mathrm{C=O}}$ 1727, 1705 cm⁻¹, $\lambda^{\mathrm{MeOH}}_{\mathrm{max}}$ 285 mμ (log ε 2·04).

(c) Evidence that the ppt from (b) was the *bicyclic morpholinium chloride* (IV) was obtained by addition of a conc soln of NaI (0·5 g) to a cold conc soln of the adduct (1·05 g) in water. The less soluble *iodide* (1·0 g) was precipitated immediately and was recrystallized from aqueous EtOH. (Found: C, 50·25; H, 7·0; N, 3·5; I, 31·3. $C_{17}H_{28}NO_2I$ requires: C, 50·4; H, 7·0; N, 3·45; I, 31·3%.) $\nu^{\mathrm{KBr}}_{\mathrm{CO}}$ 1715 cm⁻¹; $\nu^{\mathrm{KBr}}_{\mathrm{C:N^+}}$ 1625 cm⁻¹. Confirmation was obtained by adding $NaBH_4$ (3·74 g) over 30 min to the adduct (6·26 g) in water (50 ml) at 0–5° and the mixture stirred for 20 hr while warming up to room temp. Ether extraction gave 2-*hydroxy*-6,6,8,8-*tetramethyl*-9-N-*morpholino-bicyclo*(3.3.1)*nonane* (4·55 g), m.p. 124–126° from petroleum. (Found: C, 72·4; H, 11·0; N, 5·0. $C_{17}H_{31}NO_2$ requires: C, 72·6; H, 11·1; N, 5·0%.) The IR spectrum showed $\nu^{\mathrm{Chf}}_{\mathrm{O-H}}$ 3620, 3450 cm⁻¹ and no bands at 1800–1600 cm⁻¹.

Reaction of acryloyl chloride with 1-N-*morpholino-6-methylcyclohexene*

Acryloyl chloride (4·6 g) in benzene (50 ml) was added slowly (70 min) to a boiling soln of 1-N-morpholino-6-methylcyclohexene (9·05 g) in benzene (75 ml), and the mixture refluxed for 21 hr. The cooled suspension was stirred with water for 3 hr, the benzene separated and the aqueous layer extracted with ether. Evaporation of the combined dried ether and benzene soln gave crude 1-*methyl-bicyclo*(3.3.1)*nonan*-2,9-*dione* (8·1 g, 97%), purified by sublimation at 100°/0·4 mm to give the pure bicyclic dione (7·3 g, 87%), m.p. 37·5°. (Found: C, 72·2; H, 8·5. $C_{10}H_{14}O_2$ requires: C, 72·3; H, 8·5%.) $\nu^{\mathrm{CCl_4}}_{\mathrm{CO}}$ 1738, 1714 cm⁻¹, $\lambda^{\mathrm{MeOH}}_{\mathrm{max}}$ 291 mμ (log ε 1·77). The NMR spectrum (in CCl_4) showed a complex band equivalent to 11H (bicyclononane ring) and a singlet (3H) at 8·96 τ (Me). Acid hydrolysis of the dione or the intermediate adduct gave β-2-oxo-3-methylcyclohexylpropionic acid, m.p. 71–72°. (Found: C, 65·3; H, 8·7 Calc. for $C_{10}H_{16}O_3$: C, 65·2; H, 8·75.%) The NMR spectrum (in $CDCl_3$) showed the Me group as a doublet (J = 6·7 c/s) at 9·0 τ and ruled out the alternative structure for the acid (β-1-methyl-2-oxocyclohexylpropionic acid) and confirmed that the Me group was in position 1 (not 5) in the bicyclic dione.

The yield of bicyclic dione was found to be drastically affected by variation in reaction conditions, as summarized in Table 1.

Reactions of the acid chloride-enamine complex (X)

In most cases the products were not isolated, but were identified by TLC on silica using two solvent systems (benzene:EtOH–99:1 and benzene:AcOEt–9:1 for X, R = Ph; benzene:EtOH–9:1 and toluene:AcOEt–8:2 for X, R = H), authentic specimens of the products identified being developed on the same plate.

Solution A. Acryloyl chloride (4 ml), dry benzene (50 ml); Solution B: 1-N-Morpholinocyclohexene (8·35 g), dry benzene (75 ml); Solution C: Cinnamoyl chloride (8·35 g), dry benzene (50 ml).

(a) Solution A (2·7 ml) was added to soln B (4·2 ml) at 5° over 3 min with stirring. The resulting suspension was centrifuged in the same reaction vessel, the benzene layer decanted and the ppt* washed with dry benzene (3 × 10 ml) until free of acryloyl chloride. The solid was then suspended in benzene

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* This ppt refers to the acid chloride-enamine complex X not the imminium ion adduct IV obtained at higher temperatures.

and the suspension added to boiling benzene (12 ml) and refluxed for 1 hr, cooled and stirred with cold water (10 ml) for 3 hr. The benzene was separated and evaporated to give almost pure bicyclo-(3.3.1)nonan-2,9-dione (0·275 g). When the ppt was hydrolysed with water, instead of adding to boiling benzene, only a very small amount of the dione was detected.

(b) The ppt* from (a) was washed and added to 1-N-morpholinocyclohexene (4 g) in (1) 40 ml benzene and (11) 10 ml benzene at the boil. Hydrolysis, as for (a), gave bicyclo(3.3.1)nonan-2,9-dione in each case, with a trace amount of other products of higher R_F value.

(c) The ppt* from (a) was washed and added to a boiling soln of 1-N-morpholino-6-methylcyclohexene (4 ml) in benzene (10 ml) and refluxed for 3 hr, cooled and hydrolysed. TLC showed the presence of bicyclo(3.3.1)nonan-2,9-dione, and traces of compounds with higher R_F values, but no 1-methylbicyclo(3.3.1)nonan-2,9-dione was detected, showing that the conversion of the complex to the intermediate adduct IV is an intramolecular process as depicted in X. When the ppt was added to the 1-N-morpholino-6-methylcyclohexene soln at room temp, and the mixture left for 24 hr before adding to boiling benzene, a mixture of both possible diones (bicyclo(3.3.1)nonan-2,9-dione and 1-methylbicyclo(3.3.1)nonan-2,9-dione) was obtained, with the former predominating.

(d) The ppt* from (a) was dried *in vacuo* below 20° and then heated to 110° for 3 hr. Hydrolysis gave bicyclo(3.3.1)nonan-2,9-dione and traces of compounds of higher R_F values.

(e) Soln C (2·9 ml) was added to soln B (4·2 ml) over 2 min at 5° with stirring. The resulting suspension was centrifuged in the same reaction vessel, the benzene layer decanted and the solid washed with dry benzene (5 × 10 ml) by shaking vigorously, centrifuging, and decanting the benzene after each addition. The solid was resuspended in benzene, and the suspension added to boiling benzene, and refluxed with stirring for 3 hr. Hydrolysis with cold water gave a mixture of 4-phenylbicyclo(3.3.1)nonan-2,9-dione and 2-cinnamoylcyclohexanone.

(f) Soln C (2·9 ml) was added to soln B (4·2 ml) over 2 min at 5° and left 5 days at room temp. On hydrolysis with water no 4-phenylbicyclo(3.3.1)nonan-2,9-dione, and only a trace of 2-cinnamoylcyclohexanone, was detected.

(g) The ppt* (1·9 g) (obtained by mixing soln C and B) was stirred with cold water for 3 hr, made alkaline with $NaHCO_3$ and ether extracted. Acidification of the aqueous layer gave 0·6 g crude acid, m.p. 128–129° (after crystallization), IR spectrum identical with, and m.p. undepressed on admixture with, cinnamic acid.

Reaction of acryloyl chloride with 1-N-*morpholinocyclohexene in the presence of ethanol*

Acryloyl chloride (3·97 ml) in dry benzene (50 ml) was added over 3 min to a soln of 1-N-morpholinocyclohexene (8·35 g) and EtOH (5 ml) in benzene (75 ml) at the boil and the mixture refluxed for a further 3 min, cooled and stirred with water (100 ml) at 0–5° for 3 hr. The mixture was extracted with ether to give 7·58 g oil shown by GLC to consist of approximately 90% ethyl β-2-oxocyclohexylpropionate (retention times relative to methyl laevulinate: ethyl β-2-oxocyclohexylpropionate 4·18; product 4·18).

Reaction of ethyl acrylate with 1-N-*morpholinocyclohexene*

Ethyl acrylate (5 g) in benzene (50 ml) was added to 1-N-morpholinocycolhexene (8·35 g) and EtOH (5 ml) in benzene (75 ml) over 3 min at the boil and refluxed for a further 3 min, cooled, stirred with cold water for 3 hr and ether extracted to give a yellow oil (8·57 g). The oil was not identified, but was shown to contain no ethyl β-2-oxocyclohexylpropionate (by GLC) or bicyclo(3.3.1)nonan-2,9-dione (by TLC). The experiment was repeated in the presence of HCl (0·05 mole HCl gas in 5 ml EtOH added after the ethyl acrylate). A yellow oil (3·2 g) was again obtained which was shown by GLC to contain a very small amount (approx 1%) of ethyl β-2-oxocyclohexylpropionate, thus proving that the large yield of ethyl β-2-oxocyclohexylpropionate obtained from the reaction of acryloyl chloride and 1-N-morpholinocyclohexene in the presence of EtOH was not obtained by the prior formation of ethyl acrylate.

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[*] This ppt refers to the acid chloride-enamine complex X not the imminium ion adduct IV obtained at higher temperatures.

Reaction of cinnamoyl chloride and 1-N-*morpholinocyclohexene in the presence of ethanol*

This reaction was carried out under the same conditions as the corresponding reaction with acryloyl chloride. The product was shown (by TLC) to consist mainly of ethyl cinnamate and contained no ethyl β-2-oxocyclohexyl-β-phenylpropionate. Distillation gave ethyl cinnamate, b.p. 141°/12 mm (7·9 g, 89·5%). The IR spectrum was identical with that of authentic material.

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