Enamine Chemistry. Part XVII.[1] Reaction of αβ-Unsaturated Acid Chlorides with Enamines. Further Mechanistic Investigations. Effect of Triethylamine on the Reaction Path

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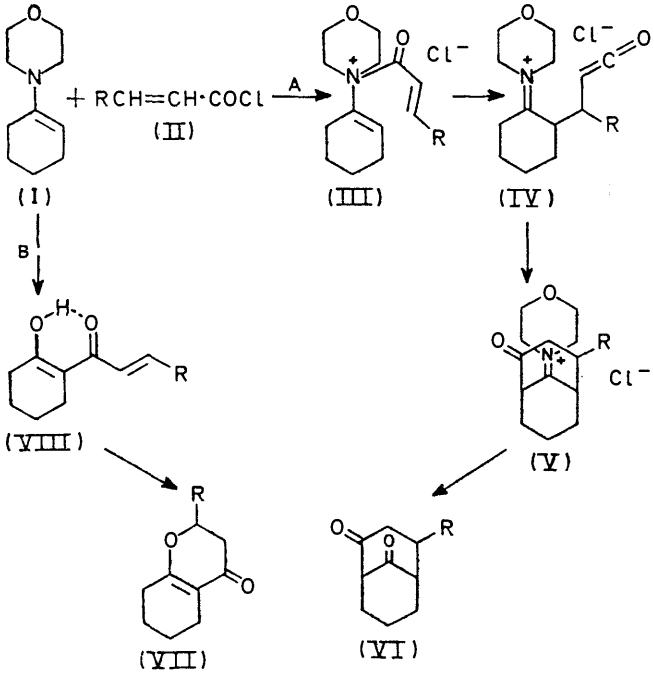
αα'-Annulation of enamines of cyclic ketones occurs on treatment with αβ-unsaturated acid chlorides in boiling benzene, to give bridged bicyclic ketones. Further evidence supports the contention that this occurs by initial *N*-acylation of the enamine followed by a [3,3]sigmatropic rearrangement. In the presence of triethylamine the course of the reaction is changed. *C*-Acylation of the enamine occurs, leading to a tetrahydrochromanone. This reaction has been shown to involve a vinylketen intermediate. The evidence available indicates that vinylketens react with enamines by a two-stage mechanism to give a zwitterionic intermediate, rather than by concerted [2 + 2] or [4 + 2] cycloaddition.

THE reaction of acryloyl and cinnamoyl chlorides with the morpholine enamine of cyclohexanone in boiling benzene has previously been shown to give the corresponding bicyclo[3.3.1]nonane-2,9-dione (VI; R = H or Ph).[2] The proposed mechanism involved initial *N*-acylation of the enamine (path A, Scheme 1) followed by



SCHEME 1

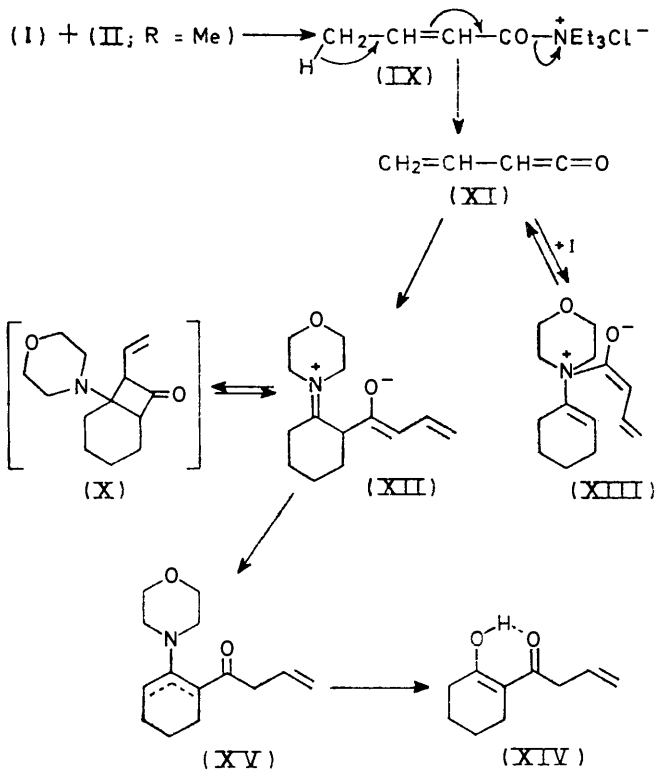
a [3,3]sigmatropic rearrangement [(III) ⟶ (IV)]. This leads to the bicyclic dione by cyclisation of the keten group onto the regenerated enamine system and hydrolysis of the precipitated iminium salt (V). Recently Gelin *et al.*[3] have reported that the reaction of acryloyl, crotonyl, and αβ- and ββ-dimethylacryloyl chlorides with the same enamine (I) in chloroform, in the presence of triethylamine, gives the corresponding tetrahydrochromanone (VII). None of the bicyclic dione (VI) was isolated. Since the tetrahydrochromanone must arise by *C*-acylation of the enamine followed by cyclisation of the enol tautomer (VIII) of the β-diketone formed on hydrolysis (path B, Scheme 1), we have reinvestigated this reaction in order to determine the reason for the change in the reaction path.

Saturated aliphatic acid chlorides possessing an α-hydrogen atom,[4] and αβ-unsaturated acid chlorides possessing a γ-hydrogen atom,[5] are known to form ketens in the presence of triethylamine. The course of the reaction between crotonoyl chloride and morpholinocyclohexene (I) can therefore be rationalised as follows. In the absence of triethylamine kinetically controlled *N*-acylation of the enamine must occur (path A, Scheme I), leading, by rearrangement and ring closure, to the bicyclic dione (VI; R = Me) which we have isolated in 48% yield by carrying out the reaction under our preferred conditions (Experimental section). In the presence of triethylamine the amine–acid chloride adduct (IX) (Scheme 2) must be formed. *N*- or *C*-Acylation of the enamine is then unlikely since the carbonyl group in the adduct (IX) is sterically hindered by the bulky tertiary amine residue. Reaction with the enamine must therefore be preceded by deprotonation to vinylketen [(IX) ⟶ (XI)]. Previous work on the reaction of adduct (IX) with large hydroxylic nucleophiles supports this contention.[5] Any *N*-acylation which now occurs must be reversible since the zwitterionic intermediate formed (XIII) does not contain the αβ-double bond in the acid chloride residue which is necessary for the [3,3]-sigmatropic rearrangement process. *C*-Acylation by the vinylketen (XI) would give the zwitterion (XII) and would be rendered irreversible by the protonation–deprotonation step [(XII) ⟶ (XV)]. Formation of the cycloadduct (X) is unlikely, for reasons to be discussed later, and in any case would be reversible.[6] In this way the reaction would be directed through the *C*-acylation path, leading, after hydrolysis and double-

[1] P. W. Hickmott, B. J. Hopkins, G. Sheppard, and D. J. Barraclough, *J.C.S. Perkin I*, 1972, 1639.
[2] P. W. Hickmott and J. R. Hargreaves, *Tetrahedron*, 1967, **23**, 3151.
[3] R. Gelin, S. Gelin, and R. Dolmazon, *Tetrahedron Letters*, 1970, 3657.
[4] W. E. Hanford and J. C. Sauer, *Org. Reactions*, 1947, **3**, 124.
[5] W. E. Truce and P. S. Bailey, *J. Org. Chem.*, 1969, **34**, 1341; T. Ozeki and M. Kusaka, *Bull. Chem. Soc. Japan*, 1966, **39**, 1995; 1967, **40**, 1232, 2686.
[6] S. Hünig and H. Hoch, *Fortschr. Chem. Forsch.*, 1970, **14**, 235.

bond migration, to the tetrahydrochromanone [(XV) ⟶ (XIV) ⇌ (VIII) ⟶ (VII)].*

Support for this rationalisation has been obtained as follows. The ^1H n.m.r. spectrum of the crude product



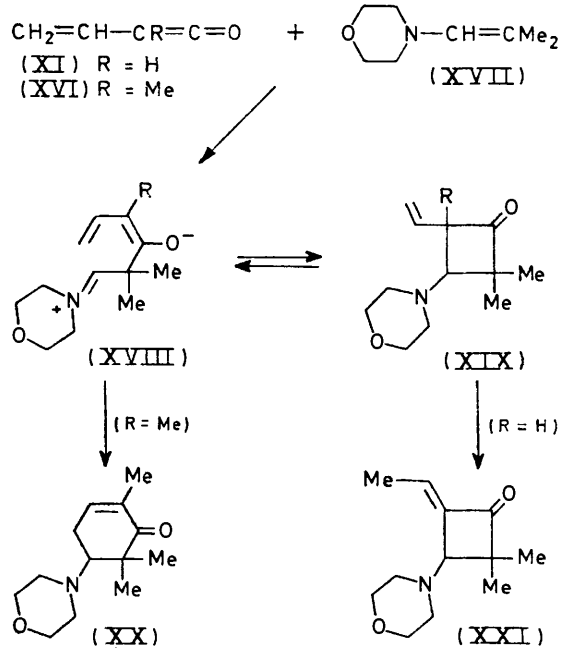
SCHEME 2

obtained before hydrolysis, from the reaction of crotonoyl chloride with morpholinocyclohexene in the presence of triethylamine, showed strong olefinic signals at τ 4·7—5·1 which we attribute to the geminal protons of the terminal double bond in (XV). Hydrolysis with dilute hydrochloric acid then gave a mixture of the enolised β-diketones (VIII; R = Me) and (XIV), with the latter predominating. Treatment of this mixture with cold concentrated hydrochloric acid resulted in quantitative conversion into the tetrahydrochromanone (VII; R = Me). The formation of 5,6,7,8-tetrahydrochroman-4-one (VII; R = H) from the reaction of acryloyl chloride with (I) in the presence of triethylamine [3] can also be attributed to keten formation. In this case either loss of the α-hydrogen atom or addition of triethylamine [7] would have to occur (to give CH_2=C=C=O or Et_3N^+·CH_2·-CH=C=O, respectively). In the latter case the αβ-unsaturated ketone side chain [in (VIII; R = H)] would be regenerated during the acidic hydrolysis of the resulting *C*-acylated enamine. However we have not been able to obtain any corroborative evidence for these suggestions.

* A similar explanation appertains to the reaction of αβ- and ββ-dimethylacryloyl chlorides with (I).

† The reaction in the absence of triethylamine has already been reported.[8]

Although cycloadducts from ketens and cyclohexanone enamines cannot be isolated, owing to ready cleavage to the acylcyclohexanone, cyclobutanones are readily obtained by cycloaddition of ketens to aldehyde enamines.[6] In an attempt to obtain further evidence for the intermediacy of vinylketen (XI) we have therefore investigated the reaction of crotonoyl chloride with morpholinoisobutene (XVII) in the presence of triethylamine.† However, a complex mixture was obtained from which no pure compound was isolated.[9] The i.r. spectrum of the crude reaction mixture showed a strong absorption at 1768 cm^{-1}, which can be attributed to the cyclobutanone (XIX; R = H), but this peak disappeared overnight and an absorption at 1735 cm^{-1} became more prominent, possibly as a result of double-bond rearrangement [(XIX) ⟶ (XXI), Scheme 3]. In an attempt to produce a thermally stable product the reaction was repeated with αβ-dimethylacryloyl chloride, since this would give a cyclobutanone containing no α-hydrogen atoms. This provided evidence for the intermediacy of methylvinylketen (XVI) in that a mixture of 2,2,4-trimethyl-3-morpholino-4-vinylcyclobutanone (XIX; R = Me) (10% yield) and 2,6,6-trimethyl-5-morpholinocyclohex-2-enone (XX) (12% yield) was obtained. The separation of this mixture by preparative t.l.c. was difficult, owing to the similarity in R_F values, but a



SCHEME 3

sufficiently pure portion of the cyclobutanone was isolated for identification purposes by removing only the leading edge of the band. The cyclohexenone was isolated by heating the mixture in toluene under reflux

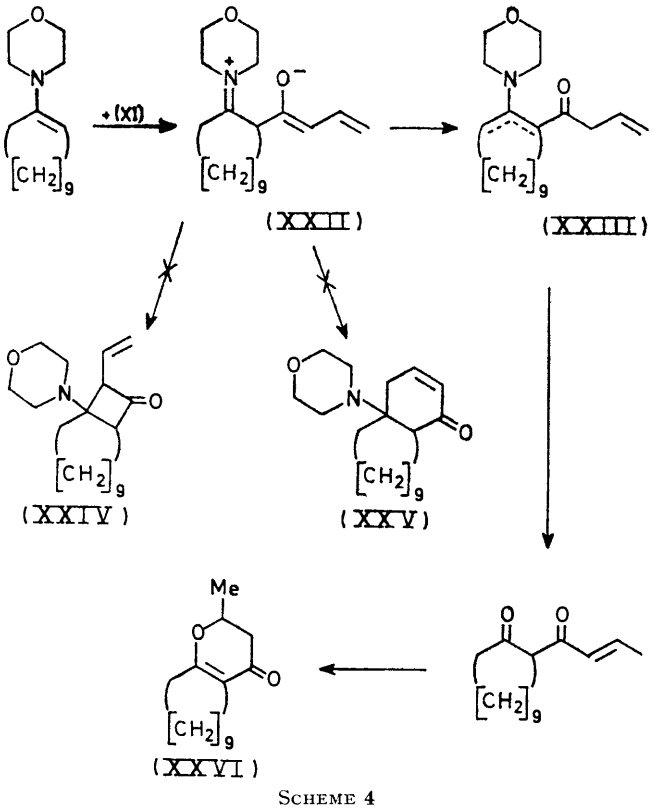
[7] P. W. Hickmott, *J. Chem. Soc.*, 1964, 883.

[8] P. W. Hickmott and B. J. Hopkins, *J. Chem. Soc.* (*C*), 1968, 2918.

[9] G. J. Miles, B.Sc. Dissertation, University of Salford, 1972.

in the presence of a catalytic amount of toluene-*p*-sulphonic acid. After 6 h the cyclobutanone carbonyl absorption had disappeared and preparative t.l.c. purification of the product gave pure 2,6,6-trimethyl-5-morpholinocyclohex-2-enone (XX). The yield of cyclohexenone (XX) was determined before and after this *treatment*, by ^{1}H n.m.r. (added triphenylmethane as reference), and was found to increase from 12 to 20%. The increased yield of cyclohexenone can be attributed to cleavage of the cyclobutanone and recyclisation of the intermediate produced [(XVIII) or the *O*-protonated derivative].

The problem of whether the cyclobutanone and cyclohexenone are being formed by competing [2 + 2] and [4 + 2] cycloadditions of the vinylketen, or by a two-step process as shown in Scheme 3, has been resolved as follows. Keten cycloadducts of large-ring enamines have been shown to undergo ring expansion rather than cleavage to the acylcycloalkanone.[6] We have therefore investigated the reaction of vinylketen (XI), produced



SCHEME 4

in situ, with 1-morpholinocyclododecene. However, the only product isolated was shown by spectroscopic evidence to be the dihydro-γ-pyrone derivative [(XXVI), Scheme 4]. None of the expected[6] ring-enlarged products or the cyclohexenone (XXV) were isolated. This indicates that the vinylketen is not reacting to any appreciable extent by a [2 + 2] or [4 + 2] cycloaddition process. The failure of the zwitterionic intermediate (XXII) to cyclise to (XXIV) or (XXV) can presumably be attributed to the enhanced stabilisation of the enolate anion system owing to the extended conjugation, and to the ease of proton transfer [(XXII) ⟶ (XXIII)]. A similar explanation has been advanced to account for the failure of phenyl- and diphenyl-keten to give ring-expanded products.[6,10] In the case of aldehyde enamines [of type (XVII)] proton transfer is not possible in the zwitterionic intermediate formed (XVIII) and nucleophilic cyclisation onto the iminium group can occur to give the cyclobutanone and cyclohexenone by competing processes (Scheme 3).

In the absence of triethylamine, crotonoyl chloride gave the enamino-ketone (XXVII) as expected from our previous work.[11]

We have also re-investigated the evidence available for the mechanism of the reaction leading to the bicyclic iminium salt (V) in the absence of triethylamine (path A, Scheme 1). If formation of the *N*-acylated enamine (III) is a necessary step in this reaction sequence, then changing the amine system of the enamine should affect the propensity for *N*-acylation and this should be reflected in the yield of bicyclic dione (VI) isolated. The results of this investigation are summarised in Table 1 for the reaction of acryloyl chloride with various cyclohexanone enamines in the absence of triethylamine. The yields of bicyclo[3.3.1]nonane-2,9-dione were determined by g.l.c. and are reproducible to ±5%. The Table shows that changing the amine system of the

TABLE 1

Effect of amine system on the reaction between cyclohexanone enamines and acryloyl chloride †

Enamine	Bicyclo[3.3.1]nonane-2,9-dione yield (%) ‡
Morpholinocyclohexene	67
Piperidinocyclohexene	32
Pyrrolidin-1-ylcyclohexene	17
Di-n-butylaminocyclohexene	20
Di-isobutylaminocyclohexene	2

† 0·01 mol in benzene (25 ml) added to 0·01 mol of enamine in boiling benzene (50 ml). Refluxed 19 h. ‡ Total yield after hydrolysis of benzene layer, and precipitate, with cold water.

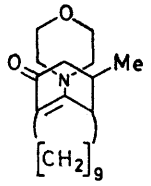
enamine from morpholine to piperidine or pyrrolidine causes a marked decrease in the yield of dione. We attribute this to an increased tendency for direct *C*-acylation and a decreased tendency for initial reaction by the acid chloride at the nitrogen atom. This must be particularly so in the case of the more reactive pyrrolidine enamine owing to the increased orbital interaction between the nitrogen lone pair and the π-electrons of the double bond in the ground state.[12] This conclusion is supported by the low yields obtained when di-n-butylamine and di-isobutylamine enamines are used. In these cases reaction at the nitrogen atom is sterically

[10] S. Hünig, H.-J. Buysch, H. Hoch, and W. Lendle, *Chem. Ber.*, 1967, **100**, 3996.

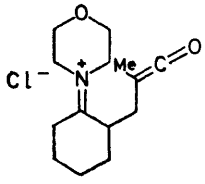
[11] R. J. Hargreaves, P. W. Hickmott, and B. J. Hopkins, *J. Chem. Soc.* (*C*), 1969, 592.

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

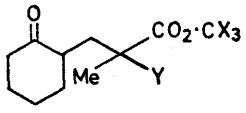
hindered,[13] but the reactivity of the β-carbon atom of the enamine is not reduced appreciably. We have demonstrated this by reaction with methyl acrylate. The



(XXVII)



(XXVIII)



(XXIX)

yield of 2-β-methoxycarbonylethylcyclohexanone (Table 2) obtained from these two hindered enamines is similar to that obtained from the morpholine enamine, but

TABLE 2

Effect of amine system on the reaction between cyclohexanone enamines and methyl acrylate

Enamine	2-β-Methoxycarbonylethylcyclohexanone yield (%) †
Morpholinocyclohexene	19(*a*)
Pyrrolidin-1-ylcyclohexene	40(*b*)
Di-n-butylaminocyclohexene	18(*a*)
Di-isobutylaminocyclohexene	18(*a*)

† After heating reactants in boiling benzene for (*a*) 90 h and (*b*) 40 h; enamine function hydrolysed with boiling water.

considerably lower than that obtained from the pyrrolidine enamine. These results further support our contention that the first step in the reaction leading to the bicyclic dione (VI) involves *N*-acylation of the enamine. The alternative possibility, that the keten intermediate (IV) is formed by direct attack by the β-position of the enamine on the β-position of the αβ-unsaturated acid chloride (an S_N2' reaction or Michael addition with subsequent expulsion of chloride anion), is therefore untenable.

Table 3 shows the effects of concentration, temperature, and solvent on the yield of bicyclic dione. On passing from high dilution to high concentration the percentage yield of dione passes through a maximum at a concentration of *ca.* 2% enamine in benzene. The low yields obtained at higher concentration can be attributed to an increased tendency for intermolecular reactions of the intermediates (III) or (IV) leading to products other than the dione. The low yields obtained under conditions of high dilution are presumably due to increased diffusion times with consequent partial decomposition or polymerisation of the acid chloride. Similarly the low yields obtained at higher temperatures (boiling toluene or mesitylene) can also be attributed to competing polymerisation of the acid chloride. The low yields obtained in chloroform or acetonitrile may be due

TABLE 3

Effects of concentration, temperature, and solvent on the reaction between acryloyl chloride † and morpholinocyclohexene

Concentration of enamine (% w/v)	Solvent	Bicyclo[3.3.1]nonane-2,9-dione yield (%) ‡
8	Benzene	34
5	Benzene	44
2	Benzene	67
1	Benzene	52
0·15	Benzene	13
2	Toluene	32
2	Mesitylene	2
2	Acetonitrile	29
2	Chloroform	37
2	Tetrahydrofuran	0

† Added to boiling solution of enamine (1 equiv.) in solvent stated. Refluxed 19 h. ‡ Total yield after hydrolysis of solvent layer, and precipitate, with cold water.

to selective solvation of the nitrogen, thus hindering the approach of the acid chloride, or to the intervention of intermolecular reactions since there was no precipitation of the intermediates [(III) or (IV)], or of the product (V), in these solvents. In tetrahydrofuran no dione was obtained, presumably owing to preferential reaction of the acid chloride with the solvent.*

Attempts to obtain spectroscopic evidence for the formation of the keten intermediate (IV) have been unsuccessful owing to broad absorption in the 2200—2700 cm^{-1} region of the i.r. spectrum, presumably attributable to the 'ammonium band' of *N*-protonated enamine present in the reaction mixture. However, we have obtained chemical evidence for the intermediacy of the keten (XXVIII), derived from the corresponding reaction with methacryloyl chloride. Addition of methacryloyl chloride to morpholinocyclohexene (I) in boiling benzene in the presence of deuteriomethanol gave the ester (XXIX; X = D) in which partial deuterium incorporation into the side chain had occurred (Y = H and D) in addition to the cyclohexanone ring. When methyl methacrylate, instead of methacryloyl chloride, was used, none of the corresponding ester (XXIX; Y = H or D, X = H) was formed.† Since interconversion of (XXIX; Y = H, X = D) and (XXIX; X = Y = D) does not occur under the experimental conditions used, the latter must arise by reaction of the keten (XXVIII) with deuteriomethanol.

Finally, the effect of an extra β-substituent in the acid chloride on the course of the reaction was investigated. Treatment of morpholinocyclohexene with 3,3-dimethylacryloyl chloride in boiling benzene gave, after mild

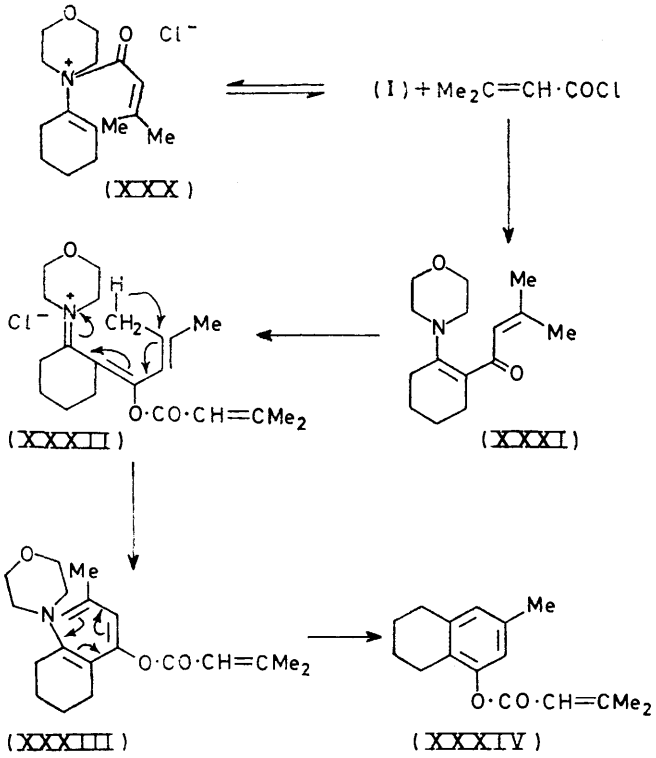
* We thank Professor H. Normant for this latter explanation.

† Under the experimental conditions used (*viz.* 3 min reaction in boiling benzene). See also refs. 2 and 14.

[13] G. Opitz, *Annalen*, 1961, **650**, 122; T. J. Curphey and J. Chao-Yu Hung, *Chem. Comm.*, 1967, 510.

[14] J. R. Hargreaves, P. W. Hickmott, and B. J. Hopkins, *J. Chem. Soc.* (*C*), 1968, 2599.

hydrolysis, a mixture of 2-(3-methylbut-2-enoyl)cyclohexanone, *N*-ββ-dimethylacryloylmorpholine and the tetrahydro-α-naphthyl ester (XXXIV) (in low yield). None of the corresponding bicyclic dione was isolated.



SCHEME 5

We attribute this to steric inhibition of the [3,3]sigmatropic rearrangement process owing to interference between the *cis*-methyl group and the axial hydrogen atoms of the cyclohexene ring [in (XXX)] when the β-carbon atom of the acid chloride residue approaches within bonding distance of the enamine double bond. This therefore renders the *N*-acylation process reversible and allows direct *C*-acylation to compete on more favourable terms. Since part of the enamine is then removed as the hydrochloride, further acylation of the resulting enaminoketone (XXXI) can occur to give the enol ester (XXXII). The formation of the tetrahydro-α-naphthyl ester (XXXIV), the structure of which follows from spectroscopic and chemical evidence (Experimental section), can therefore be attributed to electrocyclic closure of the terminally unsaturated enol ester (XXXIII) with subsequent elimination of morpholine.

EXPERIMENTAL

The i.r. spectra were determined with a Perkin-Elmer 257 spectrometer and the n.m.r. and mass spectra with Varian A60 and A.E.I. MS9 and MS12 instruments, unless stated otherwise.

Reaction of Crotonoyl Chloride with Morpholinocyclohexene.—(i) *With triethylamine.* Crotonoyl chloride (1·73 g, 0·016 mol) in dry chloroform (20 ml) was added dropwise to a stirred solution of morpholinocyclohexene (2·5 g, 0·015 mol) and dry triethylamine (1·81 g, 0·018 mol) in dry chloroform (40 ml) at 35°. The mixture was then stirred at 35° for 1 h and at ambient temperature for 20 h. A small portion was removed, filtered from triethylamine hydrochloride, and examined by n.m.r. (Discussion section). The remainder was hydrolysed with boiling 2N-hydrochloric acid (25 ml) for 5 h and cooled; the chloroform layer was washed with water (4 × 50 ml), dried ($MgSO_4$), and evaporated. The resulting yellow oil (2·5 g) was purified by preparative t.l.c. on silica (4% acetone in benzene). The first band gave a mixture (0·83 g, 34%) of enolised 2-crotonoylcyclohexanone (VIII; R = Me) and 2-but-3-enoylcyclohexanone (XIV) (M^+, 166·0990. Calc. for $C_{10}H_{14}O_2$: *M*, 166·0994), ν (film) 1660br cm^{-1} (enol), τ ($CDCl_3$) −6·95 and −6·05 [s, OH of (VIII) and (XIV), respectively, integral ratio 1 : 2], 2·7—4·3 [m, CH=CH and CH=CH_2 of (VIII) and (XIV)], 4·7—5·1 [m, =CH_2 of (XIV)], 6·75 (dm, CH_2·CH=CH), and 3·4—8·8 (methylene envelope and =CH·CH_3), and the second band gave 5,6,7,8-tetrahydro-2-methylchroman-4-one (VII; R = Me) (0·11 g, 4%), m.p. 44—45° (lit.,[3] 46°) (Found: C, 72·3; H, 8·4%; M^+, 166. Calc. for $C_{10}H_{14}O_2$: C, 71·9; H, 8·4%; M^+, 166), ν (film) 1665 (CO) and 1615 cm^{-1} (C=C), τ ($CDCl_3$) 5·50 (m, O·CH), 7·7 (m, 3 CH_2), 8·32 (m, 2 CH_2), and 8·56 (d, *J* 6 Hz, Me).

The mixture of (VIII; R = Me) and (XIV) (0·08 g) was stirred with concentrated hydrochloric acid (1 ml) at room temperature for 18 h. Dilution with water (25 ml), neutralisation (pH 6·0) with dilute sodium hydroxide, and ether extraction gave the tetrahydrochromanone (VII; R = Me) in quantitative yield, identical with that already isolated.

(ii) *Without triethylamine.* (a) *In chloroform.* Repetition of experiment (i), but without triethylamine, and hydrolysis of the reaction mixture with cold water (25 ml) for 20 h, instead of with boiling hydrochloric acid, gave an oil (2·52 g) from which only 4-*methylbicyclo*[3.3.1]*nonane*-2,9-*dione* (VI; R = Me) (0·36 g, 14%) was isolated (Found: C, 72·3; H, 8·4%; M^+, 166. $C_{10}H_{14}O_2$ requires: C, 71·7; H, 8·2%; *M*, 166), ν (film) 1728 and 1705 cm^{-1} (CO), τ ($CDCl_3$) 6·8—9·0 (methylene envelope) and 8·90 (d, *J* 6 Hz, CH_3).

(b) *In boiling benzene.* Crotonoyl chloride (1·73 g) in dry benzene (20 ml) was added dropwise to a boiling solution of the enamine (I) (2·5 g) in dry benzene (40 ml). The mixture was heated under reflux for 6 h, then cooled, and the yellow precipitate was collected, washed with dry benzene, and hydrolysed by stirring with cold water (40 ml) for 4 h. Extraction with ether gave an oil (1·9 g) which was purified by preparative t.l.c. on silica (5% acetone in benzene) to give 4-methylbicyclo[3.3.1]nonane-2,9-dione (VI; R = Me) (1·2 g, 48%) identical with that isolated in experiment (ii) (a).

Reaction of αβ-Dimethylacryloyl Chloride with 2-Methyl-1-morpholinopropene (XVII) *and Triethylamine.*—The acid chloride (1·2 g, 0·01 mol) in dry benzene (30 ml) was added to a mixture of the enamine (1·41 g, 0·01 mol) and triethylamine (2·1 g, 0·02 mol) in boiling benzene (80 ml) over 1 h and the mixture was heated under reflux for 20 h. Triethylamine hydrochloride was filtered from the cooled mixture, and the filtrate was extracted with 2N-hydrochloric acid (3 × 10 ml). The aqueous layer was separated and made alkaline with 2N-sodium hydroxide solution, and the precipitated oil was purified by preparative t.l.c. on silica (10% acetone in benzene). The ^1H n.m.r. spectrum of the first band indicated it to be a mixture of 2,2,4-trimethyl-3-morpholino-4-vinylcyclobutanone (XIX; R = Me) and 2,6,6-trimethyl-5-morpholinocyclohex-2-enone (XX). A

portion was rechromatographed (10% acetone in n-hexane as eluant) and the leading edge of the band was removed to give the *cyclobutanone* (XIX; R = Me) (5%) (Found: M^+, 223·1572. $C_{13}H_{21}O_2$ requires M, 223·1571), ν (film) 1773 cm^{-1} (CO), τ ($CDCl_3$) 3·55 (dd, J 10 and 17 Hz, CH=), 4·8 (m, CH_2=), 6·25 (m, CH_2·O·CH_2), 7·6 (m, CH_2·N·CH_2 and N·CH), 8·66 (s, two CH_3), and 8·8 (s, CH_3).

The remaining mixture of (XIX; R = Me) and (XX) and a crystal of toluene-*p*-sulphonic acid were dissolved in toluene (20 ml) and heated under reflux for 6 h until the cyclobutanone carbonyl absorption at 1773 cm^{-1} had disappeared. The toluene was removed *in vacuo* and the residual oil was purified by preparative t.l.c. (10% acetone in n-hexane) to give 2,6,6-*trimethyl*-5-*morpholinocyclohex*-2-*enone* (XX) (Found: C, 70·1; H, 9·2; N, 6·4%; M^+, 223. $C_{13}H_{21}NO_2$ requires C, 70·0; H, 9·4; N, 6·3%; M, 223), ν (film) 1670 cm^{-1}, τ ($CDCl_3$) 3·35 (m, CH=), 6·34 (m, CH_2·O·CH_2), 7·5 (m, CH_2·N·CH_2 and N·CH), 8·25 (m, CH_3·C=), and 8·78 and 8·86 (s, two CH_3).

Reaction of Crotonoyl Chloride with 1-*Morpholinocyclododecene.*—(i) *With triethylamine.* The acid chloride (2·62 g) in benzene (50 ml) was added over 1 h to the enamine (8·3 g) and triethylamine (7·0 g) in boiling dry benzene (100 ml). The mixture was heated under reflux for 20 h, cooled, and filtered from triethylamine hydrochloride, and the filtrate was evaporated *in vacuo* to an oil which was hydrolysed with boiling 2N-hydrochloric acid (1 h). The resulting oil was extracted with chloroform and distilled to give cyclododecanone and 2,3,5,6,7,8,9,10,11,12,13,14-*dodecahydro*-2-*methylcyclododeca*[b]*pyran*-4-*one* (XXVI) (1·5 g, 19%), b.p. 140° at 0·3 mmHg, which solidified (m.p. 34°) after purification by preparative t.l.c. on silica (5% acetone in benzene as eluant) (Found: C, 76·5; H, 10·8%; M^+, 250·1926. $C_{16}H_{26}O_2$ requires C, 76·8; H, 10·4%; M, 250·1932), ν (film) 1675 and 1610 cm^{-1}, τ (C_6D_6) 6·1 (m, O·CH), 7·8 (m, three CH_2), 8·7 (s, $[CH_2]_8$), and 9·0 (d, CH_3). The multiplet at τ 6·1 was resolved into two quintets at 100 MHz, and a symmetrical septet at 220 MHz, indicative of two isomers present in equal amounts, with one vicinal coupling constant of the ·O·CHMe·CH_2· group being zero.

(ii) *Without triethylamine.* Crotonoyl chloride (2·88 g) in dry benzene (50 ml) was added to 1-morpholinocyclododecene (6·91 g) in boiling benzene (150 ml) over 1 h and the mixture was heated under reflux for 20 h. The oil, which was initially precipitated, solidified and gradually dissolved in the benzene. Evaporation of the solvent and trituration of the residue with petroleum (b.p. 60—80°) gave a solid (2·7 g) which was dissolved in water; the solution was basified with 2N-sodium hydroxide to pH 8. Extraction with ether gave 14-*methyl*-15-*morpholinobicyclo*[9.3.1]*pentadec*-11(15)-*en*-12-one (XXVII) (2·5 g), m.p. 143° (from benzene–petroleum) (Found: C, 75·6; H, 10·1; N, 4·1%; M^+, 319. $C_{20}H_{33}NO_2$ requires C, 75·2; H, 10·3; N, 4·4%; M, 319), ν (Nujol) 1610 and 1530 cm^{-1}, τ ($CDCl_3$) 6·2—9·0 (complex) and 8·95 (d, J 7 Hz, Me).

Treatment of the enamino-ketone (XXVII) (0·3 g) in ether (4 ml) and ethanol (4 ml) with 70% perchloric acid (0·4 ml) gave the *perchlorate*, m.p. 198° (from acetone–ether) (Found: C, 57·4; H, 8·0; N, 3·1. $C_{20}H_{34}ClNO_6$ requires C, 57·3; H, 8·1; N, 3·3%).

Reaction of ββ-*Dimethylacryloyl Chloride with* 1-*Morpholinocyclohexene.*—The experimental procedure was as for the corresponding reaction with crotonoyl chloride [(ii) (b)]. The precipitate formed consisted only of enamine hydrochloride. The benzene filtrate was evaporated and the residual oil stirred with cold water for 3 h. Extraction with ether gave an oil (2·2 g) which was purified by preparative t.l.c. on silica (3% acetone in benzene). The second and third bands consisted of 2-(3-methylbut-2-enoyl)cyclohexanone (0·2 g) and N-ββ-dimethylacryloylmorpholine (0·33 g), respectively, identical with authentic materials. The first band contained 5,6,7,8-*tetrahydro*-3-*methyl*-1-*naphthyl* ββ-*dimethylacrylate* (XXXIV) (0·36 g, 10%) (M^+, 244·1459. $C_{16}H_{20}O_2$ requires M, 244·1463), ν (film) 1738, 1650, 1628, and 1125 cm^{-1}, τ (CCl_4) 3·3 and 3·4 (2H, s, aromatic), 4·12 (m, CH=), 7·27 and 7·52 (m, 2 CH_2), 7·73 (s, CH_3), 7·8 and 8·05 (d, J 1·5 Hz, Me_2C=), and 8·26 (m, 2 CH_2). The ^1H n.m.r. assignments were confirmed by spin decoupling experiments. Irradiation at τ 7·8 or 8·05 caused the olefinic signal at τ 4·12 to collapse to a quartet, and irradiation at both these values simultaneously converted the signal into a singlet. Irradiation at the frequency of the aromatic proton signals at τ 3·3 and 3·4 resulted in sharpening and increase in peak height of the methyl signal at τ 7·73, the peaks at τ 7·8 and 8·05 being unaffected.

The tetrahydro-α-naphthyl ester (XXXIV) (0·15 g) was heated under reflux with 10% sodium hydroxide (8 ml) for 2 h, cooled, and acidified (to Congo Red) with 2N-sulphuric acid. Sodium hydrogen carbonate was added until the solution was alkaline to litmus and extraction with ether gave 5,6,7,8-*tetrahydro*-3-*methyl*-1-*naphthol* (0·084 g), m.p. 85—87°, purified by preparative t.l.c. on silica (5% acetone in benzene as eluant) (Found: M^+, 162·1046. $C_{11}H_{14}O$ requires M, 162·1044), ν (Nujol) 3340 cm^{-1} (OH), τ ($CDCl_3$) 3·45 and 3·55 (s, two aromatic H), 7·33 (m, two CH_2), 7·75 (s, CH_3), and 8·22 (m, two CH_2). Acidification of the aqueous filtrate and extraction with ether gave ββ-dimethylacrylic acid (0·042 g), identical with authentic material.

Added in proof. Gelin *et al.* (R. Gelin, S. Gelin, and R. Dolmazon, *Bull. Soc. chim. France*, 1973, 1409.) have also concluded recently that the formation of the tetrahydrochromanone involves the intermediacy of the triethylamine–acid chloride adduct (IX) and vinylketen (XI), as we had previously suggested to them. However, their suggestion, that there is an equilibrium between (IX) and the *N*-acylated enamine (III; R = Me), we consider to be unlikely for reasons discussed in the text and since an *appreciable* quantity of bicyclic dione (VI; R = Me) would be expected to be formed in view of the ease with which the rearrangement [(III) → (IV)] is known to take place. The formation of the *cis*- and *trans*-*N*-crotonoyl- and *N*-vinylacetylmorpholines, which they have isolated in the presence of triethylamine, can be attributed to O- [or C(2)-] protonation and C–N heterolysis of (XIII) (Scheme 2).

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