Enamine Chemistry. Part XVIII.[1] Reaction of Crotonoyl and Methacryloyl Chlorides with Dialkyl 4-(Pyrrolidin-1-yl)cyclohex-3-ene-1,1-dicarboxylates. One-step Synthesis of Adamantanes

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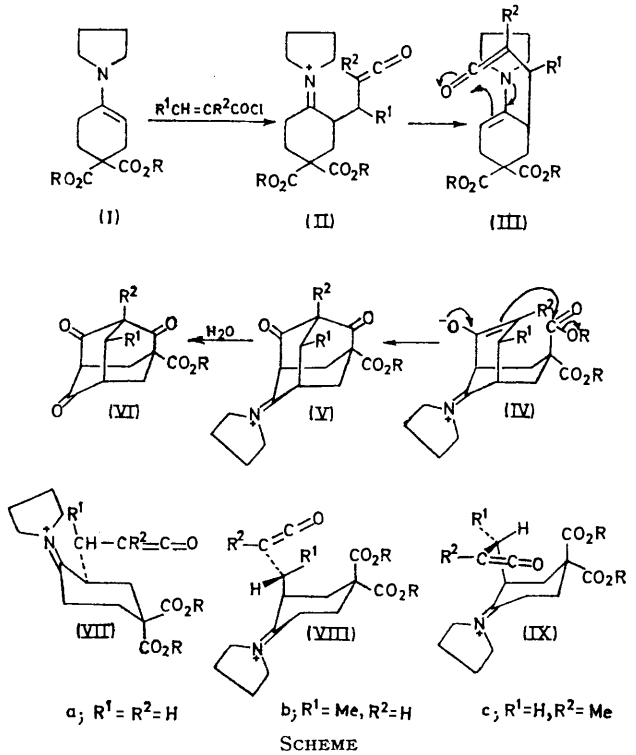
A new one-step synthesis of alkyl 2,4,6-trioxoadamantane-1-carboxylates has resulted from the reaction of crotonoyl and methacryloyl chlorides with the pyrrolidine enamines of dialkyl 4-oxocyclohexane-1,1-dicarboxylates.

THE αα′-annulation of ketones by the reaction of αβ-unsaturated acid chlorides with enamines has previously been demonstrated as a convenient synthesis of cyclohexane-1,3-diones and bi- and poly-cyclic β-diketones.[2] The recent synthesis [3] of the adamantane ring system from diethyl 4-(pyrrolidin-1-yl)cyclohex-3-ene-1,1-dicarboxylate (I; R = Et) has prompted us to apply our dione synthesis [2] to this enamine and to the corresponding methyl ester (I; R = Me).

It was considered that the reaction might involve formation of a keten intermediate (II) followed by cyclisation on to the regenerated enamine system (III) to give the enolate anion (IV) (Scheme). Internal nucleophilic attack by this enolate anion on the axial ester group would then lead to the adamantane ring system [(IV) ⟶ (V)]. These expectations have been confirmed. Various adamantane derivatives (VI) have been obtained by hydrolysis of the appropriate iminium salts (V) formed by reactions of crotonoyl and methacryloyl chlorides (but not acryloyl chloride) with the enamine (I) in boiling benzene (see Table 1).

The failure of acryloyl chloride to give an adamantane is noteworthy since in our previous work acryloyl chloride has generally given higher yields of cyclic products than have crotonoyl or methacryloyl chlorides.[2,4] The difference in behaviour indicates that the presence of an α- or β-alkyl substituent may have a profound effect on the conformation of the keten intermediates (II) and (III). We suggest that, in the case of acryloyl chloride, the 1,3-diaxial interactions between the ester and keten groups cause the keten substituent to be in an equatorial orientation (VIIa) rather than an axial orientation as in



SCHEME

(VIIIa) or (IXa), despite the severe steric interactions due to the close proximity of the α-methylene group of

[1] Part XVII, P. W. Hickmott, G. J. Miles, G. Sheppard, R. Urbani, and C. T. Yoxall, *J.C.S. Perkin I*, 1973, 1514.

[2] N. F. Firrell, P. W. Hickmott, and B. J. Hopkins, *J. Chem. Soc.* (*C*), 1970, 1477, and previous papers in this series.

[3] H. Stetter and H. G. Thomas, *Angew. Chem. Internat. Edn.*, 1967, **6**, 554.

[4] P. W. Hickmott and G. Sheppard, *J. Chem. Soc.* (*C*), 1971, 1358, 2112; *J.C.S. Perkin I*, 1972, 1038.

the pyrrolidine ring [$A^{(1,3)}$ strain][5] in conformation (VIIa).* As a consequence, intramolecular cyclisation is not possible and further reaction leads to products which we have not yet identified. This argument leads to the conclusion that, in the case of crotonoyl chloride, conformational inversion of the ring [*viz.* (VIII) ⟶ (VII)] is prevented by the presence of the β-methyl substituent in the αβ-unsaturated acid chloride residue, and the keten substituent remains in an axial orientation [*viz.* (VIII) or (IX)].† The situation is then particularly favourable for cyclisation to the adamantane since the preferred rotamer is probably as shown (IXb) with the methyl group as far as possible from the ester group, and the keten group directed over the ring.

In the case of methacryloyl chloride the situation is probably intermediate between these two extremes. Conformations (VIIc), (VIIIc), and (IXc) must exist in equilibrium, the first two [(VIIc) and (VIIIc)] leading to unidentified products and the last (IXc) to the adamantane. The population of conformation (IXc) would be expected to increase when the 1,3-diaxial interactions are reduced by use of the methyl ester (I; R = Me), instead of the ethyl ester (I; R = Et), with consequent increase in yield (Table 1).

The structures of the adamantanes follow from analytical and spectral data (Table 2). In particular the broad singlet at τ 6·3—6·4 is apparently characteristic of the adamantane-2,4,6-trione system and can only be assigned to the protons α to two ring carbonyl groups. The fact that methacryloyl chloride gives a product for which the methyl n.m.r. signal appears as a singlet confirms the formation of a carbon–carbon bond between the α-position of the acid chloride residue and one of the ester carbonyl groups.

* These interactions are reduced to $A^{(1,2)}$ strain[5] when the enamine system is regenerated from the iminium salt (VIIa).

† Irrespective of whether the keten substituent is introduced by direct axial approach of the electrophile or *via* the twist conformation arising by equatorial approach. These two possibilities will be discussed in a future publication.

EXPERIMENTAL

I.r. spectra were determined with a Perkin-Elmer 257 spectrometer, n.m.r. spectra with a Varian A60 spectrometer, and mass spectra with an A.E.I. MS 12 instrument.

Synthesis of Alkyl 2,4,6-Trioxoadamantane-1-carboxylates. General Method.—The αβ-unsaturated acid chloride (0·107 mol) in dry benzene (30 ml) was added dropwise to the dialkyl 4-(pyrrolidin-1-yl)cyclohex-3-ene-1,1-dicarboxylate[6] (0·017 mol) in boiling dry benzene (150 ml) during 1 h. The mixture was then heated under reflux for the time stated (Table 1), and cooled, and the precipitated iminium salt (V) was collected, washed with dry benzene, and hydrolysed by stirring with cold water for 3 h. The trioxoadamantane (VI) was isolated by extraction with chloroform (2 × 25 ml) and purified as stated in Table 1. Spectral data are summarised in Table 2.

TABLE 1

Synthesis of alkyl 2,4,6-trioxoadamantane-1-carboxylates (VI)

R	R¹	R²	Reflux time (h)	Yield (%)	M.p. (°C)	Solvent for cryst.	Found (%) C	Found (%) H		Required (%) C	Required (%) H
Et	Me	H	20	29	122	Benzene	64·0	6·2	$C_{14}H_{16}O_5$	63·7	6·1
Me	Me	H	2	30	129	Benzene	62·2	5·6	$C_{13}H_{14}O_5$	62·4	5·6
Et	H	Me	70	2	(Oil)	(T.l.c.†)	63·6	6·25	$C_{14}H_{16}O_5$	63·7	6·1
Me	H	Me	2	25	112	Benzene–ether	62·0	5·6	$C_{13}H_{14}O_5$	62·4	5·6

† Purified by preparative t.l.c. on silica [benzene–acetone (9 : 1) as eluant].

TABLE 2

Spectra of alkyl 2,4,6-trioxoadamantane-1-carboxylates (VI)

R	R¹	R²	M^+	$\nu_{max.}$ (Nujol)/cm⁻¹ CO_2R	$\nu_{max.}$ (Nujol)/cm⁻¹ CO	(τ) ($CDCl_3$)
Et	Me	H	264	1735	1715	5·73 (q, CH_2·CH_3), 6·38br (s, two CO·C*H*·CO), 7·35 (m, ring CH_2 and CH), 8·70 (t, CH_2·CH_3), 9·03 (d, CH_3).
Me	Me	H	250	1740	1715	6·18 (s, CO_2·CH_3), 6·37br (s, two CO·C*H*·CO), 7·35 (m, ring CH_2 and CH), 9·03 (d, CH_3).
Et	H	Me	264	1725br		5·73 (q, CH_2·CH_3), 6·3br (s, one CO·C*H*·CO), 7·0—8·0 (m, ring CH_2 and CH), 8·70 (t, CH_2CH_3), 8·70 (s, CH_3).
Me	H	Me	250	1725br		6·18 (s, CO_2·CH_3), 6·30br (s, one CO·C*H*·CO), 7·0—8·0 (m, ring CH_2 and CH), 8·70 (s, CH_3).

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[5] F. Johnson, *Chem. Rev.*, 1968, **68**, 375.
[6] H. Stetter and H. G. Thomas, *Chem. Ber.*, 1968, **101**, 1115.