

## The Formation of Enaminoenaminones from *N*-Alkylaminomethylene Derivatives of Meldrum's Acid<sup>1</sup>

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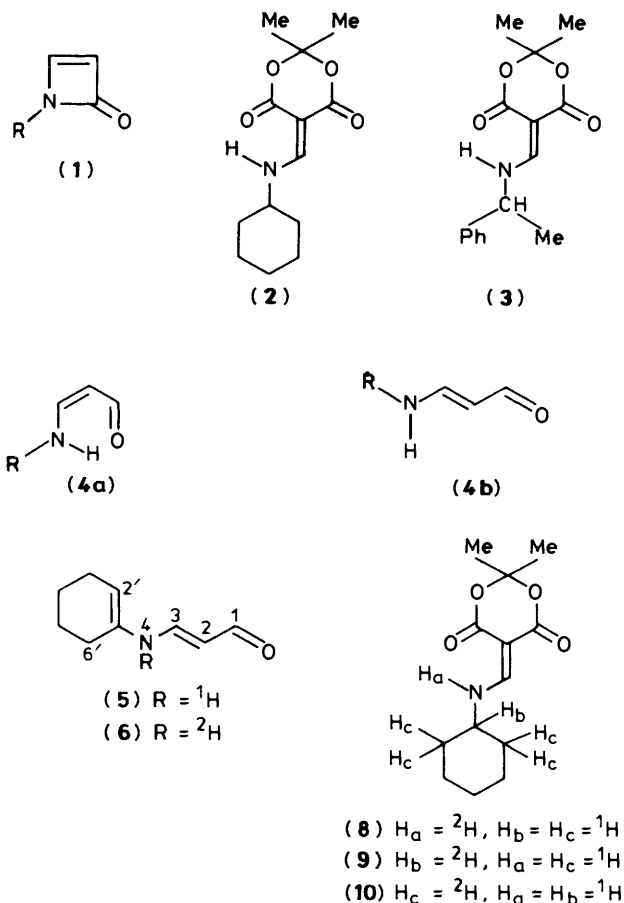
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Gas-phase pyrolysis of aminomethylene derivatives of Meldrum's acid [*e.g.* (2)], gives enaminoenaminones [*e.g.* (5)]. Deuterium labelling studies have shown that the mechanism involves tautomerism of the initial methyleneketene intermediate to an iminoketene, followed by a sequence of 1,5-hydrogen shifts.

We have shown that 5- and 6-membered ring unsaturated lactams<sup>2-4</sup> can be obtained conveniently by pyrolysis of Meldrum's acid<sup>5</sup> (2,2-dimethyl-1,3-dioxane-4,6-dione) derivatives which have an appropriate amino-containing substituent at the 5-position. A logical extension of this work is the attempted preparation of derivatives of the unusual azetin-2-one system<sup>6</sup> (1), for which the obvious precursors are the well-known 5-alkylaminomethylene compounds, *e.g.* (2) and (3). These are readily prepared by treatment of the alkylamine with the condensation product of Meldrum's acid and triethyl orthoformate.<sup>7</sup> In the event, the course of the pyrolysis reaction was diverted prior to cyclisation by efficient hydrogen transfer processes which led to a product isomeric with the expected azetinone. In this paper, we give details of the spectra and the structure determination of these products, and also present the results of deuterium labelling experiments which have established the reaction mechanism.

Flash vacuum pyrolysis at 600 °C of the *N*-cyclohexyl derivative (2) gave, at the exit point of the furnace, prior to the liquid nitrogen trap, a crystalline product, *m/z* 151, in 90% yield. The <sup>1</sup>H n.m.r. spectrum (100 MHz) of this compound in CDCl<sub>3</sub> showed, in addition to aliphatic resonances at δ<sub>H</sub> 1.4–2.3 and a broad triplet at δ<sub>H</sub> 5.24, three well-defined multiplets, at δ 5.00 (dd, *J* 2.2 and 7.2 Hz), 6.88 (oct., *J* 3.2, 7.2, and 13.0 Hz), and 9.00 (dd, *J* 2.0 and 3.0 Hz), together with an NH resonance at δ<sub>H</sub> 11.71 and some minor peaks. This coupling pattern is characteristic of the *Z-s-Z* rotamer of an *N*-monosubstituted enaminoenaminone system (4a) which is known to be the predominant form in chloroform solution.<sup>8</sup> Such enaminoenones adopt the *E-s-E* configuration (4b) exclusively when [<sup>2</sup>H<sub>4</sub>]methanol is used as solvent,<sup>8</sup> and the totally different coupling pattern which is thus observed (see Experimental section) allows confirmation of the present assignment. The environment of the proton which gives rise to the olefinic triplet (δ<sub>H</sub> 5.24) was clarified by the <sup>13</sup>C n.m.r. spectrum of the pyrolysis product in [<sup>2</sup>H<sub>4</sub>]methanol. This showed one olefinic CH signal (δ<sub>C</sub> 109.31 p.p.m.), one quaternary olefinic signal (δ<sub>C</sub> 137.03 p.p.m.), and just four signals in the sp<sup>3</sup> region, in addition to the peaks expected for the enaminoenone system. This information unambiguously identifies the structure as the enaminoenaminone (5), which clearly arises by transfer of two cyclohexyl hydrogen atoms to the central double bond of the methyleneketene (7), which is the standard intermediate in Meldrum's acid pyrolyses.<sup>9</sup> We have studied the mechanism of this unusual hydrogen transfer by specific deuterium labelling at nitrogen, and at the 1- and 2-positions of the cyclohexyl ring [structures (8)–(10)].

The [N-<sup>2</sup>H]-compound (8) was generated *in situ* by recrystallisation of the <sup>1</sup>H analogue (2) from [<sup>2</sup>H]methanol in the inlet system of the pyrolysis apparatus.<sup>4</sup> The mono-deuterated compound (9) was prepared from [1-<sup>2</sup>H]cyclohexylamine, which was itself obtained by lithium aluminium deuteride reduction of cyclohexanone oxime.<sup>10</sup> In a similar



fashion, the [<sup>2</sup>H<sub>4</sub>]-compound (10) was obtained from [2,2,6,6-<sup>2</sup>H<sub>4</sub>]cyclohexylamine, which was itself made by lithium aluminium hydride reduction of [2,2,6,6-<sup>2</sup>H<sub>4</sub>]cyclohexanone oxime, after exchange of cyclohexanone with deuterium oxide under basic conditions.<sup>10</sup> The specificity of these procedures was confirmed by the <sup>2</sup>H n.m.r. spectra of the final products (9) and (10) (see Experimental section).

The results of the pyrolyses are shown in the Table, together with that of a re-pyrolysis of the [<sup>2</sup>H]enaminoenaminone (6). As can be seen, the deuterium label is typically scrambled amongst four sites of the product, and the analysis is based on the results of the <sup>2</sup>H n.m.r. spectra of the pyrolysates, with percentage incorporations calculated from computer 'integral' values. Despite broad lines, the <sup>2</sup>H n.m.r. chemical shifts of the C<sup>2</sup>H nuclei were consistent to within 0.04 p.p.m. with the corresponding <sup>1</sup>H signals, and even the notoriously variable

OH signals were within 0.08 p.p.m. The signal at  $\delta_{\text{H}}$  ( $[\text{}^2\text{H}_4]\text{MeOH}$ ) 2.25 was assigned as being that due to 6'-H as follows. The saturated cyclohexyl protons resonate at 200 MHz in four well-defined regions ( $\delta_{\text{H}}$  2.25, 2.19, 1.85, and 1.70) of which the two multiplets to high frequency must be due to 3'- and 6'-H. Spin decoupling at  $\delta_{\text{H}}$  2.19, but *not* at  $\delta_{\text{H}}$  2.25, causes collapse of the olefinic triplets at  $\delta_{\text{H}}$  5.44 (2'-H) to a singlet, and so the peaks at  $\delta_{\text{H}}$  2.25 and 2.19 are assigned as 6'- and 3'-H, respectively.

A key observation from the Table is that the  $\text{N}^2\text{H}$  moiety of compound (8) is scrambled amongst four positions in the product (5), and that the central position (2-H) of the enaminone carries most of the label. This is consistent with rapid tautomerisation of the methyleneketene (7) to an iminoketene (11) which is now set up for an allowed 1,5-hydrogen shift of  $\text{H}_b$  to generate 1-H in a tautomer (12) of the final enaminone (5). In agreement with this, pyrolysis of the  $\alpha$ -deuteriated compound (9) gives a product with deuterium

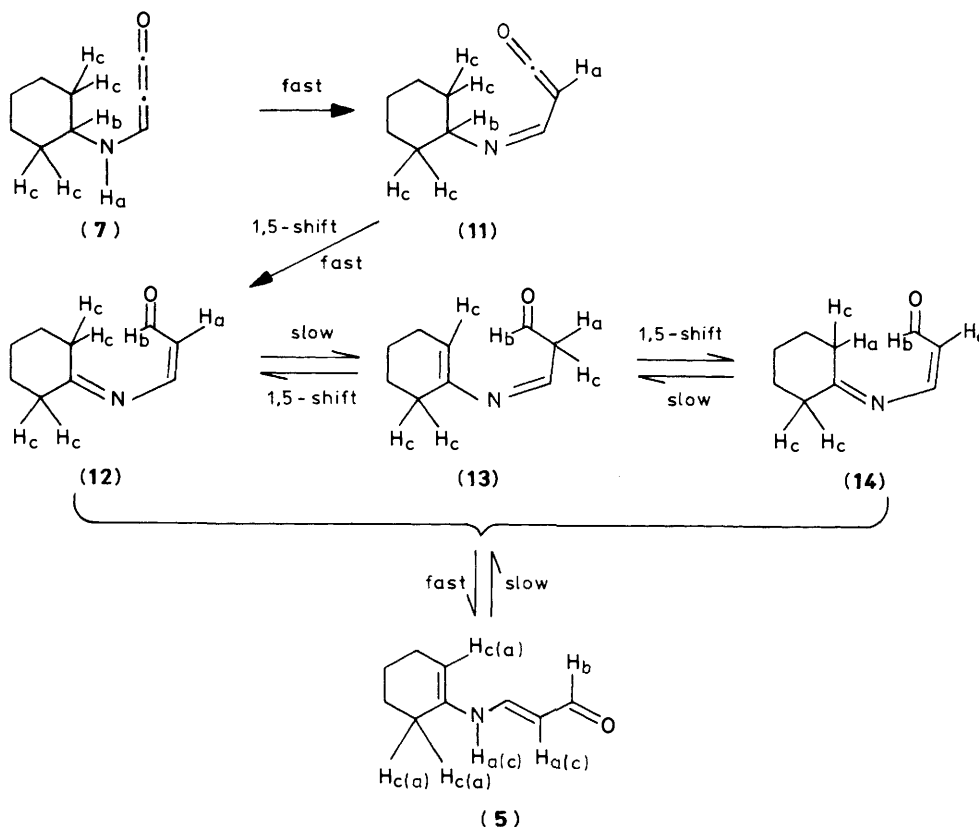
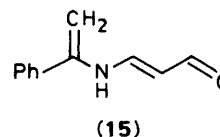
almost exclusively located in the 1-position (Scheme). That the incorporation of the  $\text{N}^2\text{H}$  from compound (8) into the cyclohexyl moiety proceeds *via* a *slow* sequence of 1,5-hydrogen shifts interconverting isomers (12), (13), and (14) (Scheme) was shown by the pyrolysis of the  $\beta$ -deuteriated compound (10). In this case, only a small amount of deuterium (11%) is located at position 2, with the remainder of the label distributed equally between positions 4, 2', and 6' of (5). Significantly, re-pyrolysis of the *N*-deuteriated enaminoenaminone (6) produces a very similar distribution in the final product, though the NH moiety remains heavily labelled (39%). This suggests that regression to an imine tautomer is slow and that structure (12) or (14) is formed in preference to (13). These results also exclude the interconversion of (12) and (13) *via* (5), and are consistent with the mendeic  $^{11}$  character of the enaminone conjugated system.

The small amounts of residual label at positions 2, 2', 4, and 6' from the precursor (9) show a similar distribution to that of the re-pyrolysed product from compound (6) (Table). It is possible that, in the former case, small amounts of deuterium liberated by unidentified side-reactions have become incorporated as the  $\text{N}^2\text{H}$  moiety.

The mechanism of the Scheme is similar to that proposed by Chuche,<sup>12</sup> who has found that C-substituted enaminoenaminones are the major products from iminoketenes, generated directly by pyrolysis of enaminoesters. The present sequence is an equally convenient method of preparing the C-unsubstituted systems, for which the key precursors are monoalkylamines

**Table.** Deuterium incorporation in the enaminoenaminone (5) by pyrolysis of the precursors (8)–(10) and (6) at 600 °C

Chemical shift [ $^2\text{H}_4$ ]/[ $^1\text{H}_4$ ] Methanol	Assignment	Precursor, and percentage $^2\text{H}$ incorporation in (5)			
		(8)	(9)	(10)	(6)
9.01	1-H		81		
7.70	3-H				
5.54	2-H	30	1	11	8
5.44	2'-H	16	3	21	15
4.92	4-H	20	7	20	39
2.25	6'-H	2 × 17	2 × 4	2 × 24	2 × 19



**Scheme.**

with at least one hydrogen atom on  $\alpha$ - and  $\beta$ -carbon atoms. As a second example, the phenyl derivative (**15**) was unexceptionally obtained from (**3**).

### Experimental

Unless otherwise stated,  $^1\text{H}$ ,  $^2\text{H}$ , and  $^{13}\text{C}$  n.m.r. spectra were recorded at 80, 55, and 20 MHz respectively.  $J_{\text{CH}}$  Values were obtained from  $^1\text{H}$ -coupled  $^{13}\text{C}$  n.m.r. spectra. Ether refers to diethyl ether.

**5-(2-Cyclohexyl-2-azaethylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (2).**—Prepared in 70–80% yield by the literature method,<sup>7</sup> by heating Meldrum's acid (2,2-dimethyl-1,3-dioxane-4,6-dione) (20 mmol) and triethyl orthoformate (20 ml) under reflux for 2 h, followed by addition of cyclohexylamine (40 mmol) and continued heating under reflux for a further 2 h, this derivative had m.p. 149–151 °C (lit.,<sup>7</sup> 153–154.4 °C),  $\delta_{\text{H}}(\text{CDCl}_3)$  9.50 (1 H, br s), 8.16 (1 H, d,  $^3J$  14.9 Hz), 3.30 (1 H, br s), 1.70 (6 H, s), and 1.0–2.1 (10 H, m);  $\delta_{\text{C}}(\text{CDCl}_3)$  165.29 (q), 163.75 (q), 157.23, 104.16 (q), 83.75 (q), 58.61, 33.01, 26.52, 24.52, and 24.01 p.p.m.;  $m/z$  253 ( $M^+$ , 74%), 196 (56), 195 (33), 177 (34), 151 (100), and 70 (94).

**5-{2-([ $^1\text{H}$ ]Cyclohexyl)-2-azaethylidene}-2,2-dimethyl-1,3-dioxane-4,6-dione (9).**—A solution of cyclohexanone oxime (1.0 g, 9 mmol) in dry ether (160 ml) containing [ $^2\text{H}_4$ ]lithium aluminium hydride (2.0 g) was heated under reflux for 30 min. The solution was cooled, and a saturated aqueous solution of sodium sulphate was added until no reaction occurred. The ether layer was separated, and the remaining solids were thoroughly washed with ether. The combined organic layers were dried ( $\text{MgSO}_4$ ) and the solvent was removed to give crude [ $^1\text{H}$ ]cyclohexylamine<sup>10</sup> (0.54 g, 73%), which was treated, without purification, with the product from Meldrum's acid (0.4 g, 2.8 mmol) and triethyl orthoformate (3 ml) as above. The labelled cyclohexylamine derivative so obtained (0.54 g, 77%) had m.p. 149–151 °C,  $m/z$  254 ( $M^+$ , 97%), 197 (73), 196 (35), 152 (100), and 70 (82); it had no peaks in the range  $\delta$  3–4 in its  $^1\text{H}$  n.m.r. spectrum [ $\delta$  ( $^2\text{H}$ ) (MeOH) 3.54].

**5-{2-([2,2,6,6- $^2\text{H}_4$ ]Cyclohexyl)-2-azaethylidene}-2,2-dimethyl-1,3-dioxane-4,6-dione (10).**—Cyclohexanone (1.0 g, 10 mmol) was heated under reflux for 4 h in dilute sodium deuterioxide solution [from sodium (0.06 g) and deuterium oxide (10 ml)]. Hydroxylamine hydrochloride (2.0 g) and sodium acetate (4.0 g) were added to the cooled mixture, which was then warmed to 70 °C for 10 min. [2,2,6,6- $^2\text{H}_4$ ]Cyclohexanone oxime<sup>10</sup> (1.0 g, 87%) crystallised on cooling and was filtered and thoroughly dried, before being reduced to [2,2,6,6- $^2\text{H}_4$ ]cyclohexylamine using lithium aluminium hydride (3.0 g) in ether (200 ml) as described above. The crude amine (0.69 g, 78%) was treated as before with the condensation product from Meldrum's acid (0.5 g, 3.5 mmol) and triethyl orthoformate (4 ml) to yield the labelled cyclohexylamino derivative (0.61 g, 68%), m.p. 149–151 °C,  $m/z$  257 ( $M^+$ , 76%), 200 (60), 199 (49), 155 (100), and 71 (64);  $\delta_{\text{H}}(\text{CDCl}_3)$  9.50 (1 H, br s), 8.12 (1 H, d), 3.30 (1 H, d), 1.66 (6 H, s), and 1.2–2.0 (6 H, m);  $\delta$  ( $^2\text{H}$ ) (MeOH) 2.00 (2  $^2\text{H}$ , s) and 1.49 (2  $^2\text{H}$ , s).

**2,2-Dimethyl-5[2-( $\alpha$ -methylbenzyl)-2-azaethylidene]-1,3-dioxane-4,6-dione (3).**—1-Phenylethylamine (12.10 g, 0.1 mol) was added to the solution obtained by heating Meldrum's acid (7.41 g, 0.05 mol) and triethyl orthoformate (50 ml) under reflux for 2 h. Heating was continued for a further 2 h, and the 2-azaethylidene derivative (**3**) (9.00 g, 62%) crystallised on cooling, m.p. 113–116 °C (from ethanol);  $\delta_{\text{H}}(100 \text{ MHz}; \text{CDCl}_3)$  9.80 (1 H, br s), 8.17 (1 H, d), 7.2–7.4 (5 H, m), 4.72 (1 H, apparent

quint), 1.67 (6 H, s), and 1.67 (6 H, d);  $\delta_{\text{C}}(\text{CDCl}_3)$  165.25 (q), 163.54 (q), 157.54, 140.08 (q), 128.91, 128.20, 125.82, 104.28 (q), 84.38 (q), 58.97, 26.56, and 22.18 p.p.m.;  $m/z$  275 ( $M^+$ , 27%), 218 (19), 217 (20), 173 (24), 144 (46), 105 (100), and 77 (39) (Found: C, 65.7; H, 6.25; N, 5.1.  $\text{C}_{15}\text{H}_{17}\text{NO}_4$  requires C, 65.45; H, 6.2; N, 5.1%).

**3-(Cyclohex-1-enylamino)acrylaldehyde (5)—5-(2-Cyclohexyl-2-azaethylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (2)** (2.06 g, 8 mmol) was sublimed at 160 °C and  $10^{-2}$  Torr during 3 h through the furnace tube (35  $\times$  2.5 cm) which was maintained at 600 °C. The product (1.11 g, 90%) which was a crystalline solid, could be purified by recrystallisation from toluene or by sublimation at  $10^{-1}$  Torr to give the aldehyde (**5**), m.p. 113–115 °C (after sublimation),  $\delta_{\text{H}}(200 \text{ MHz}, [^2\text{H}_4]\text{MeOH})$  9.01 (1 H, d,  $^3J$  9.1 Hz), 7.70 (1 H, d,  $^3J$  12.4 Hz), 5.54 (1 H, dd,  $^3J$  9.1 and 12.4 Hz), 5.44 (1 H, t,  $^3J$  3.6 Hz), 4.92 (> 1 H, NH), and residual OH of solvent), 2.25 (2 H, m), 2.19 (2 H, m), 1.85 (2 H, m), and 1.70 (2 H, m);  $\delta_{\text{C}}([^2\text{H}_4]\text{MeOH})$  192.00 ( $^1J_{\text{CH}}$  164.4,  $^3J_{\text{CH}}$  6.0 Hz), 155.31 ( $^1J_{\text{CH}}$  163.5 Hz), 137.03 (q), 109.31 ( $^1J_{\text{CH}}$  ca. 152 Hz), 104.49 ( $^1J_{\text{CH}}$  157.6,  $^2J_{\text{CH}}$  21.8 Hz), 25.81, 24.84, 23.23, and 23.11 p.p.m.;  $m/z$  151 ( $M^+$ , 100%), 122 (49), 94 (72), 80 (36), 70 (28), 54 (23), and 41 (28). (Found: C, 71.6; H, 8.4; N, 9.45.  $\text{C}_9\text{H}_{13}\text{NO}$  requires C, 71.5; H, 8.6; N, 9.25%).

**Pyrolysis of Deuteriated 5-(2-Cyclohexyl-2-azaethylidene)-2,2-dimethyl-1,3-dioxane-4,6-diones and Related Precursors.**—These pyrolyses were carried out on a small scale<sup>13</sup> (0.4–0.5 mmol), and the conditions are reported as follows: deuteriated derivative, quantity pyrolysed, inlet temperature, furnace temperature, pressure range, and pyrolysis time. The entire pyrolysate was dissolved in methanol for analysis by  $^2\text{H}$  n.m.r. spectroscopy (Table). [ $\text{N-}^2\text{H}$ ] (0.13 g, 0.5 mmol), 160 °C, 600 °C,  $3 \times 10^{-3}$  Torr, 1 h; [ $^1\text{H}$ ]cyclohexyl (0.1 g, 0.4 mmol), 170 °C, 600 °C,  $3\text{--}7 \times 10^{-2}$  Torr, 1 h; [2,2,6,6- $^2\text{H}_4$ ]cyclohexyl (0.1 g, 0.4 mmol), 170 °C, 600 °C,  $1\text{--}3 \times 10^{-2}$  Torr, 0.5 h; and 3-(cyclohex-1-enyl) [ $\text{N-}^2\text{H}$ ] aminoacrylaldehyde (0.08 g, 0.5 mmol), 90 °C, 600 °C,  $5\text{--}10 \times 10^{-3}$  Torr, 1 h.

**3-(1-Phenylethylidene)aminoacrylaldehyde (15).**—The methylbenzyl derivative (**3**) (2.05 g, 7.5 mmol) was sublimed at 150 °C and  $10^{-2}$  Torr during 2 h through the furnace tube, which was maintained at 600 °C. The majority of the pyrolysate was an orange-coloured crystalline solid (1.21 g), which was carefully recrystallised from ethanol to give the aldehyde (**15**) (0.60 g, 46%), m.p. 100–104 °C,  $\delta_{\text{H}}([^2\text{H}_4]\text{MeOH})$  9.13 (1 H, d,  $^3J$  8.8 Hz), 7.78 (1 H, d,  $^3J$  12.9 Hz), 7.4–7.6 (5 H, m), 5.72 (1 H, dd,  $^3J$  8.8 and 12.9 Hz), and 5.00 (m, confused with residual OH peak of solvent);  $\delta_{\text{C}}([^2\text{H}_4]\text{MeOH})$  193.19 ( $^1J_{\text{CH}}$  166.0,  $^3J_{\text{CH}}$  6.4 Hz), 157.20 ( $^1J_{\text{CH}}$  165.0 Hz), 146.83 (q), 137.39 (q), 130.21, 129.63, 127.93, 107.00 ( $^1J_{\text{CH}}$  158.7,  $^2J_{\text{CH}}$  22.3, 2.2 Hz), and 96.83 p.p.m. (br t in fully coupled spectrum);  $m/z$  173 ( $M^+$ , 56%), 144 (100), 104 (60), 103 (40), and 77 (48) (Found: C, 76.1; H, 6.15; N, 8.35.  $\text{C}_{11}\text{H}_{11}\text{NO}$  requires C, 76.3; H, 6.35; N, 8.1%).

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