On the Mechanism of Thermal Cyclisation of Dialkylaminomethyleneketenes to give 1*H*-Pyrrol-3(2*H*)-one Derivatives

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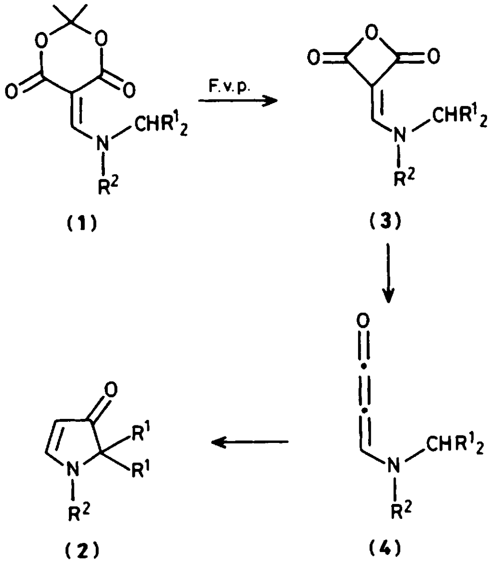
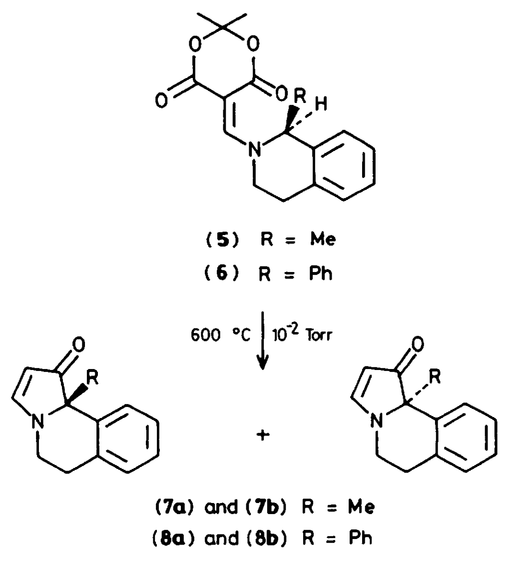
The observed loss of optical activity in the pyrrolones (**7**), (**8**), and (**10**) formed by flash vacuum pyrolysis of the chiral substrates (**5**), (**6**), and (**9**) requires that a discrete intermediate is involved in the hydrogen transfer–cyclisation steps which lead to these products.

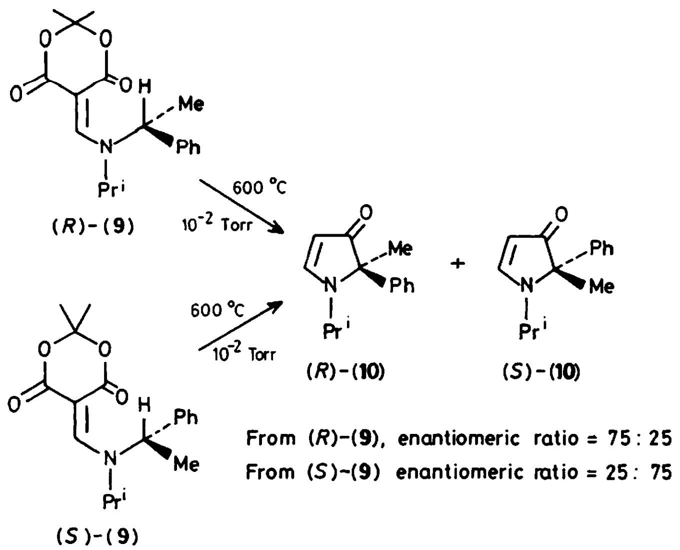
Following the initial report in 1983,[1] flash vacuum pyrolysis (f.v.p.) of aminomethylene derivatives of Meldrum's acid (**1**) has become a popular means of synthesising simple 1*H*-pyrrol-3(2*H*)-ones (**2**) (3-hydroxypyrroles) (Scheme 1).[2—4] Recently, it has been shown by spectroscopic studies that the early stages of this reaction involve stepwise elimination of acetone and carbon dioxide to give stable malonic anhydride [*cf.* (**3**)] and isolable methyleneketene [*cf.* (**4**)] derivatives, respectively.[5]



Scheme 1



Scheme 2

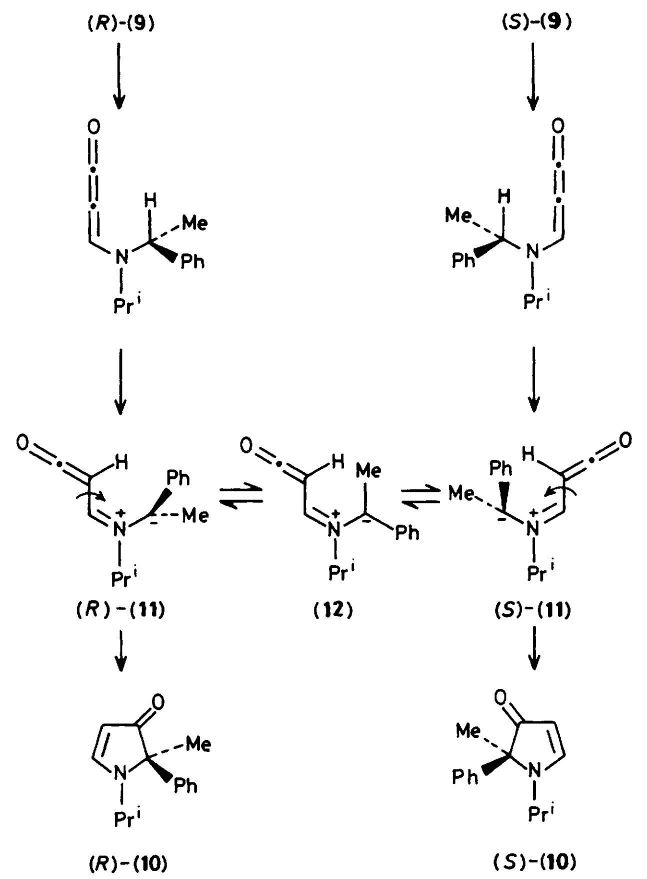


Scheme 3

We now present chemical evidence for the existence of a further intermediate on the reaction pathway, *en route* from the methyleneketene to the pyrrolone.

This transformation requires intramolecular hydrogen transfer from, and ring closure to, a site adjacent to the nitrogen atom of the methyleneketene:[6] these processes may in principle be stepwise or concerted. Accordingly, we have synthesised the optically active precursors (**5**) and (**6**)† in which a chiral centre is incorporated at the site of hydrogen transfer. Pyrolysis of these derivatives at 600 °C (10^{-2} Torr) gives the expected fused pyrrolones (**7**) and (**8**) derived solely from reaction at the benzylic site,[8] but with *complete loss of chirality*‡ (Scheme 2). Hence the ring formation from the methyleneketene cannot be concerted, and must involve an intermediate with sufficient lifetime to allow racemisation after the hydrogen transfer step.

Though we have no direct evidence for the nature of this intermediate, further information may be gained by pyrolysis of the enantiomers (*R*)- and (*S*)-(**9**) in which the geometry is not constrained by the presence of a ring, and in which *incomplete chirality loss* is observed§ (Scheme 3). These results are best explained by hydrogen transfer to the in-plane p-orbital at C(2) of the methyleneketene to give a species (*R*)- or (*S*)-(**11**) (whose chirality is maintained by an allene-like spiral geometry), and which can be intercepted by the ketene fragment before full equilibration (Scheme 4). In the cyclic cases, from (**5**) or (**6**), a low-energy, planar configuration (**12**) of the dipolar intermediate[4] would be encouraged by conformational effects in the six-membered ring.



Scheme 4

We are grateful to the S.E.R.C. for a Research Studentship (to L. C. M.).

Received, 18th August 1986; Com. 1183

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† All new compounds were characterised by their spectra and by elemental analysis. Chiral tetrahydroisoquinolines were prepared by a standard procedure,[7] and had identical physical constants to those in the literature.

‡ Analysis by ^{1}H n.m.r. spectroscopy using tris[3-(heptafluoropropylhydroxymethylene)-(+)-camphorato]europium(III) as chiral shift reagent is estimated to be accurate to ±3%.

§ Repyrolysis of an (*R*)-/(*S*)-(**10**) mixture at 600 °C (10^{-2} Torr) has demonstrated that such compounds are not racemised under these conditions. In this series, we have also shown, by examination of recovered starting material after pyrolysis at 400 °C, that the loss of stereochemistry does not take place by fortuitous equilibration of the Meldrum's acid derivatives (*R*)- and (*S*)-(**9**). At this stage, we cannot exclude fortuitous equilibration in the malonic anhydride or methyleneketene intermediates, but any such reaction can only be a reversible, intramolecular process, and would generate species at least as likely to lie on the reaction co-ordinate to the pyrrolone as to revert to starting materials.