Thermal Functionalisation of Nitrogen Substituents: Formation of Dihydropyrrol-3-ones, Quinolin-4-ones, and Enaminoenaminones by Gas-phase Hydrogen Transfer Reactions

Helen J. Gordon, Jane C. Martin, and Hamish McNab*

Department of Chemistry, University of Edinburgh, West Mains Road, Edinburgh EH9 3JJ, U.K.

Pyrolysis of the aminomethylene Meldrum's acid derivatives (5-aminomethylene-2,2-dimethyl-1,3-dioxane-4,6-dione) (1), (7), (11), and (12) causes hydrogen transfer reactions which result in specific functionalisation of the amino substituent: tertiary amino substrates give 1,2-dihydropyrrol-3-ones (60%) by ring closure, while secondary amino substrates give quinolin-4-ones (90%) or enaminoenaminones (90%).

Pyrolysis of Meldrum's acid (2,2-dimethyl-1,3-dioxane-4,6-dione) derivatives[1] containing pendant amino functions is a useful general synthesis of lactams.[2-4] We now describe examples in which this process is unexpectedly and totally suppressed by diverse, yet highly efficient hydrogen transfer reactions which lead to excellent syntheses of 1,2-dihydro-pyrrol-3-ones, quinolin-4-ones, or enaminoenaminones. We also present a mechanistic rationalisation of this behaviour, based on the results of deuterium labelling studies.

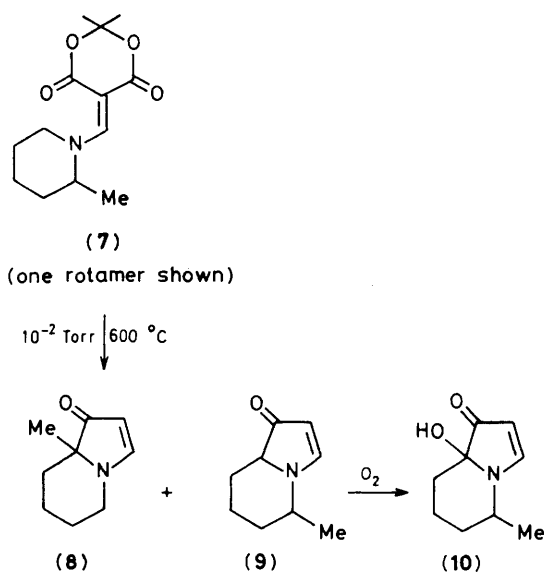Flash vacuum pyrolysis of the dicyclohexylamino compound
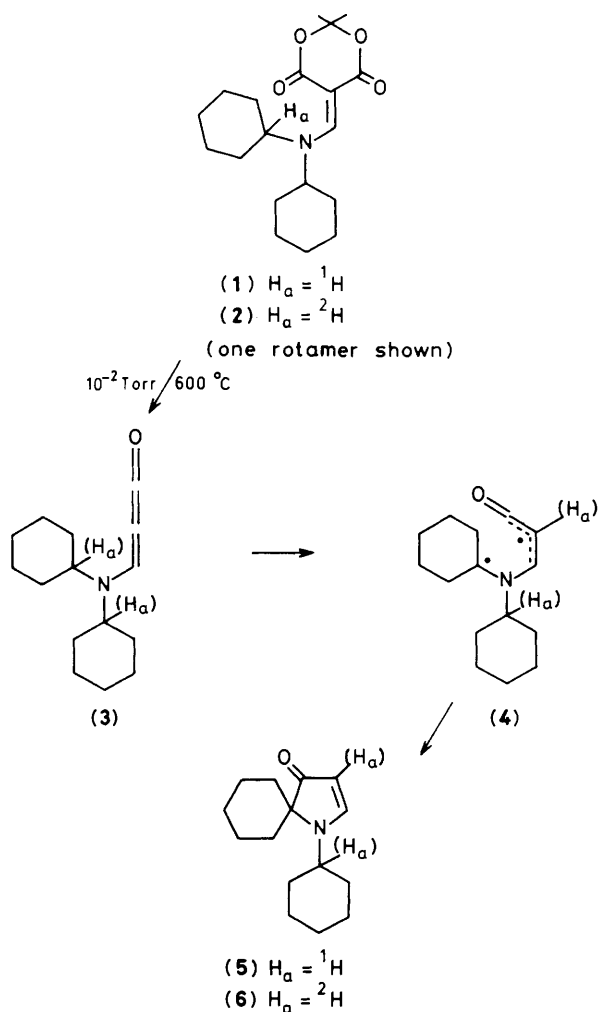
(1)† at 600 °C gave the crystalline 1,2-dihydropyrrol-3-one (5) in 60% yield. The heterocyclic system was characterised by ^{1}H n.m.r. [alkene signals at δ (CDCl$_3$) 7.82 (d) and 4.97 (d), ^3J 3.4 Hz], ^{13}C n.m.r. {quaternary signals at δ (CDCl$_3$) 205.60 [C(3)] and 67.96 p.p.m. [C(2)]}, and u.v. spectroscopy (λ_{max} 328 nm; *cf.* ref. 5). The fate of the α-hydrogen atom H$_a$ was confirmed by the pyrolysis of the deuterium labelled compound (2) (Scheme 1).‡ This experiment also allows a direct measurement of the deuterium isotope effect for the reaction (1.58 ± 0.02 at 600 °C), which is of the correct order for a rate-determining hydrogen transfer at high temperature.[6,7]

Pyrolysis of the piperidino derivative (7) proceeded in similar fashion to give equal quantities of the isomeric indolizin-1-ones (8) and (9),§ also in *ca.* 60% total yield (Scheme 2). Hydrogen transfer from the tertiary site is therefore preferred over the secondary site on a statistical basis.

These unusual reactions (Schemes 1 and 2) allow thermal functionalisation with high specificity at a site α- to an *unactivated* nitrogen atom.[9,10] This behaviour may be rationalised by hydrogen transfer from the methyleneketene[1] inter-


(1) H$_a$ = ^{1}H
(2) H$_a$ = ^{2}H

(one rotamer shown)

10^{-2} Torr / 600 °C

(3)

(4)

(5) H$_a$ = ^{1}H
(6) H$_a$ = ^{2}H

Scheme 1

(7)

(one rotamer shown)

10^{-2} Torr | 600 °C

(8)   +   (9) $\xrightarrow{O_2}$ (10)

Scheme 2

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† Unless otherwise stated, all new compounds gave consistent spectra and microanalyses.

‡ All labelling experiments were examined by ^{1}H and ^{2}H n.m.r. spectroscopy. Details of these results, and of the preparations of the substrates will be given in a full paper.

§ Compound (9) was characterised as (10), which is formed spontaneously on exposure to air (*cf.* ref. 8).
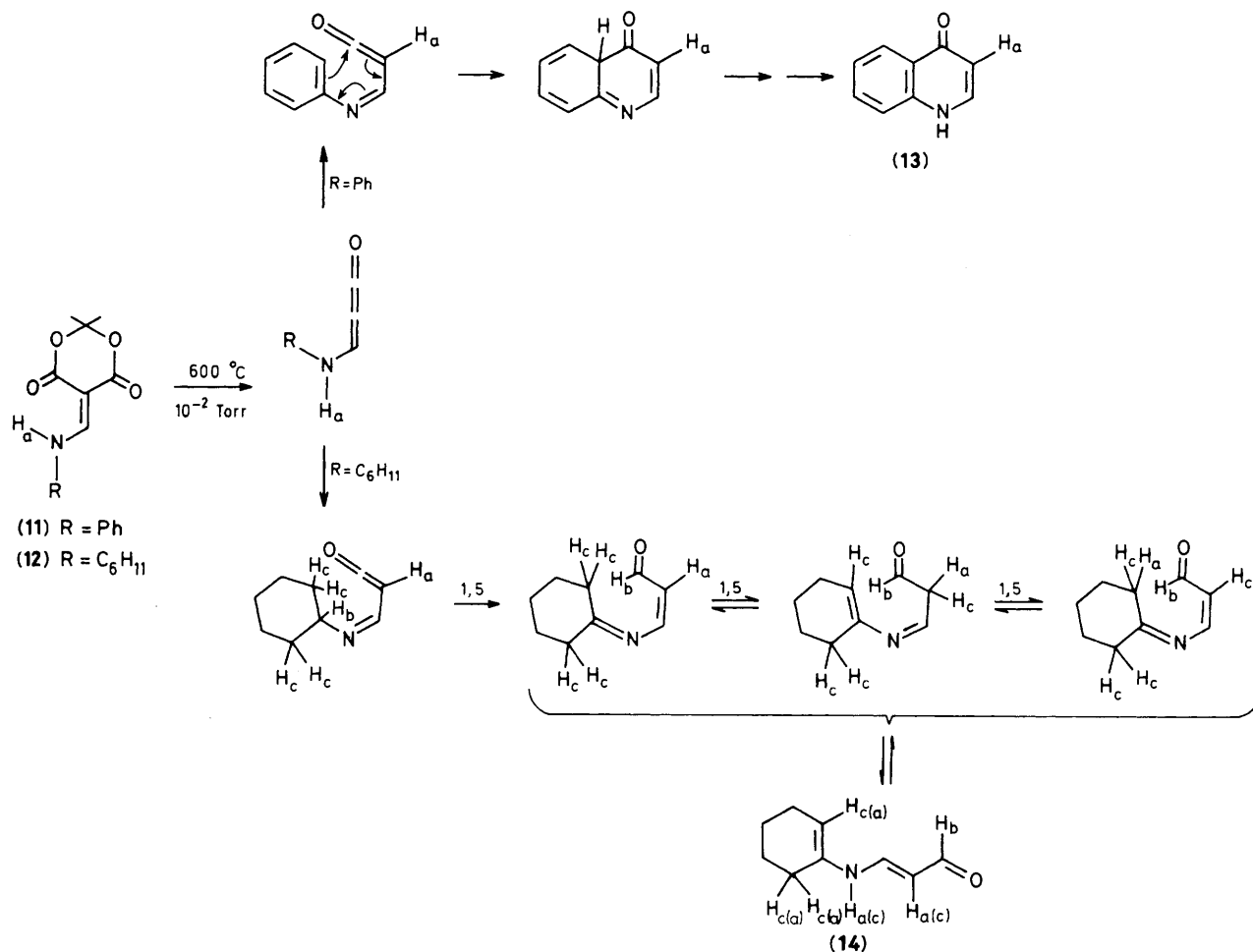
Scheme 3

mediate (3) to give the diradical (4), which is doubly stabil-ised by its allyl and α-aminoalkyl[11—13] fragments.

In contrast, pyrolysis reactions of secondary amino deriva-tives, e.g. (11)[14] and (12),[14] are controlled by tautomerisation[15] of the intermediate to an iminoketene. This may be trapped by an aromatic ring to give quinolin-4-one [(13); 90%, m.p. 203—205 °C (lit.[16] 201 °C)], or by sequences of 1,5-hydrogen shifts (as previously suggested for related reactions[17]) to give the enaminoenaminone (14) (90%). The conjugated system of (14) was characterised by spectroscopic comparison with related compounds;[18] the position of unsaturation in the ring was established by [13]C n.m.r. spectroscopy, which showed signals due to one methine, and one quaternary carbon atom, in addition to those of the enaminone system. The mechan-isms of Scheme 3 are fully supported by deuterium labelling of H_a, H_b, and H_c respectively. The exclusive location of H_b at the 1-position of the enaminone, in complete contrast to Scheme 2, confirms the deep-seated mechanistic differences between the pyrolyses of the secondary and tertiary substrates (12) and (1).

Further work is in progress to examine and extend the synthetic potential of these reactions and their products. In particular, the availability of 1,2-dihydropyrrol-3-ones in two steps from the appropriate amine has clear advantages over earlier methods of preparation.[19]

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