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.

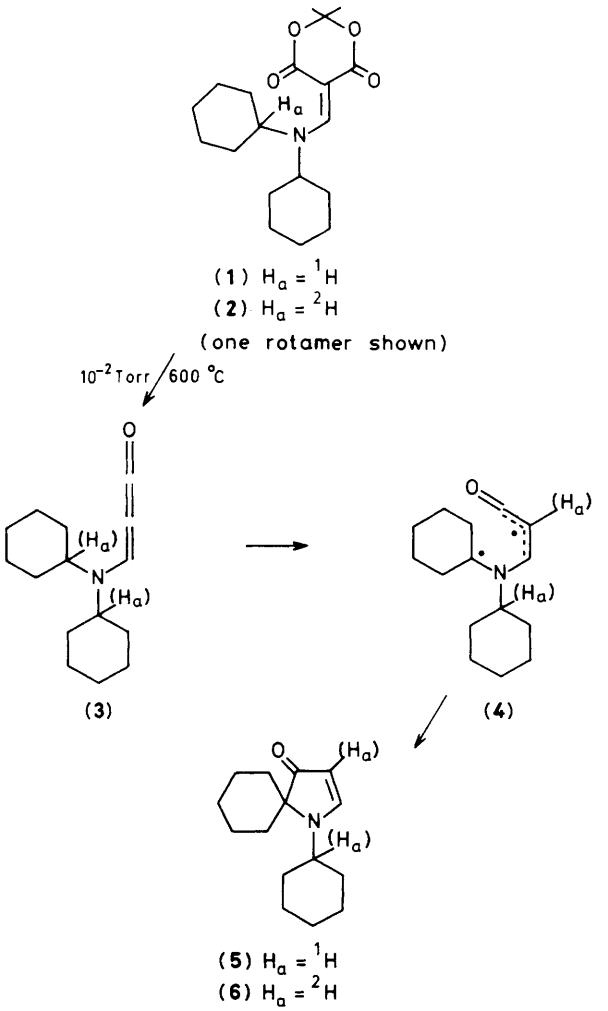
Pyrolysis of the aminomethylene Meldrum's acid derivatives (5-aminomethylene-2,2-dimethyl-1,3-dioxane-4,6-dione) (**1**), (**7**), (**11**), and (**12**) causes hydrogen transfer reactions which result in specific functionalisation of the amino substituent: tertiary amino substrates give 1,2-dihydropyrrol-3-ones (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-dihydropyrrol-3-ones, quinolin-4-ones, or enaminoenaminones. We also present a mechanistic rationalisation of this behaviour, based on the results of deuterium labelling studies.

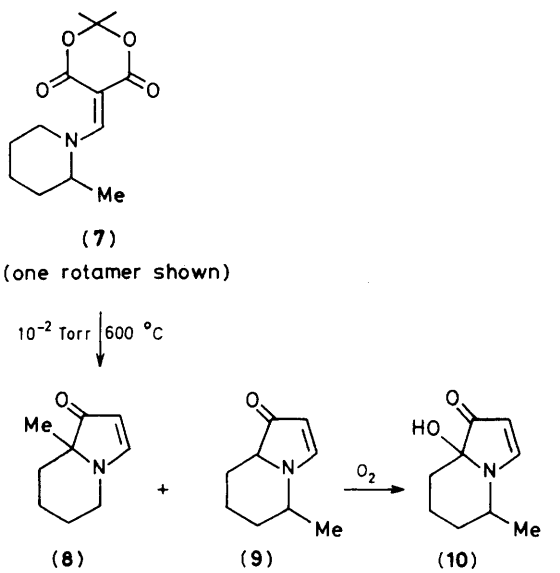
Flash vacuum pyrolysis of the dicyclohexylamino compound (**1**)† at 600 °C gave the crystalline 1,2-dihydropyrrol-3-one (**5**) in 60% yield. The heterocyclic system was characterised by ^{1}H n.m.r. [alkene signals at δ ($CDCl_3$) 7.82 (d) and 4.97 (d), ^3J 3.4 Hz], ^{13}C n.m.r. {quaternary signals 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-

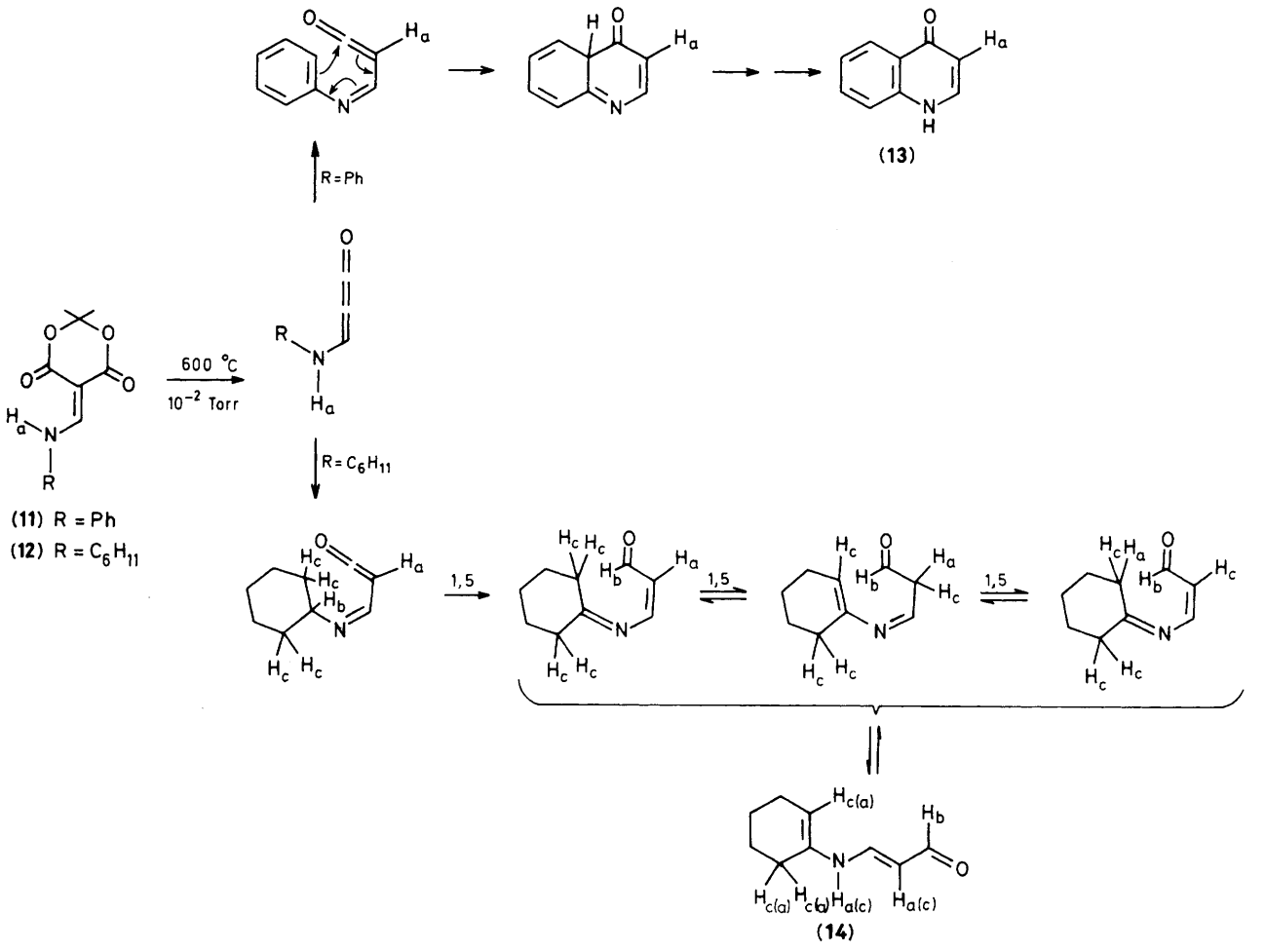


Scheme 1



Scheme 2

† 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 stabilised by its allyl and α-aminoalkyl[11–13] fragments.

In contrast, pyrolysis reactions of secondary amino derivatives, *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 mechanisms 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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