KETENIMINE CARBOXYLATE ISOMER PROTONATION

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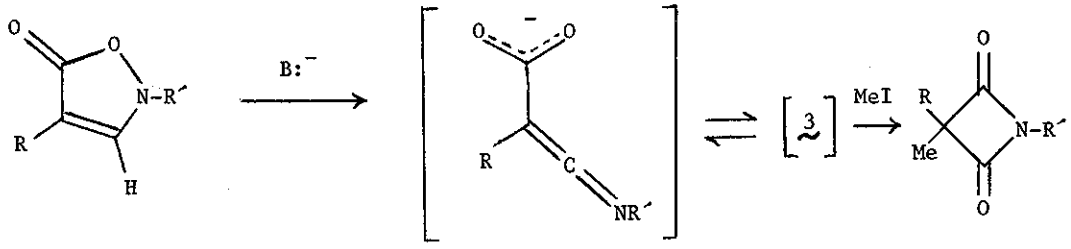
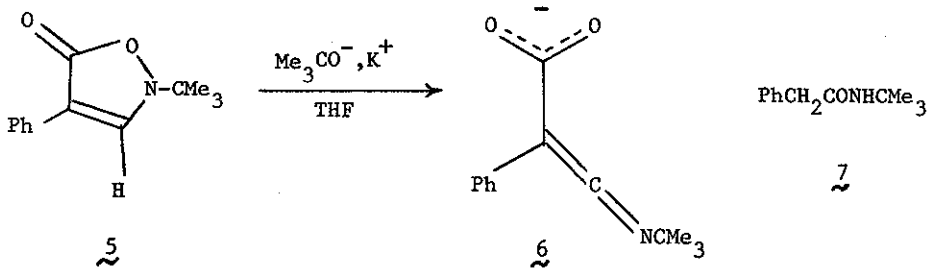
A reactive C-monosubstituted malonimide has been isolated from ring opening of a 3-unsubstituted isoxazolone followed by isomerization of the intermediate ketenimine carboxylate in HMPA, protonation, and rapid work-up.

It was recently demonstrated that basic ring opening of 3-unsubstituted isoxazolones (1) leads to ketenimine carboxylates (2). The latter were found to undergo further conversion in highly polar aprotic solvents to cyclic anions (3), which were trapped as the rearranged C-methylmalonimides (4) upon methylation (1). Using 2-tert-butyl-4-phenyl-3-isoxazolin-5-one (5), we have now established that protonation of this novel anionic system follows a similar course, leading to a reactive C-monosubstituted malonimide.



1 2 4

Since the previous work, in which ketenimines were only observed spectroscopically in solution, it has been found that the ring-opening product 6 can be isolated as the potassium salt from the reaction of 5 with potassium tert-butoxide in dry THF (0.2 M solution) by precipitation with excess hexane. The structure of the moisture-sensitive solid was confirmed by the cumulene (4.9 μ) and carboxyl (6.3 μ) ir bands (KBr).

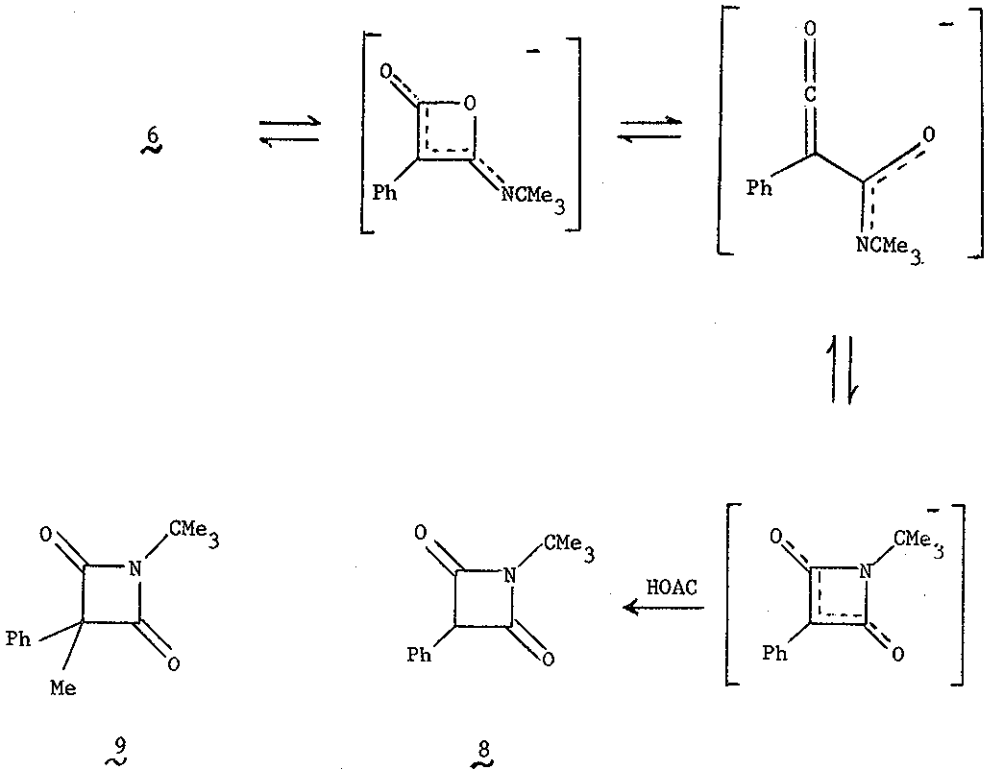


5 6 7

In contrast to the earlier methylation results, the product of protonation, after the potassium salt of 6 was allowed to stand in HMPA (approx. 2 hrs for complete cyclization), had only marginal stability in the reaction medium. Initial isolation attempts provided mainly the hydration/decarboxylation product 7, suggesting interception by moisture at some point. However, when the reaction mixture was quenched with a proton source (e.g., HOAc) and worked up immediately by partitioning between CCl_4 and water, the conjugate acid was isolated in 56 percent yield as the predominant organic-soluble product (mp 48 - 50°, after recrystallization from 30 - 60° petroleum ether).

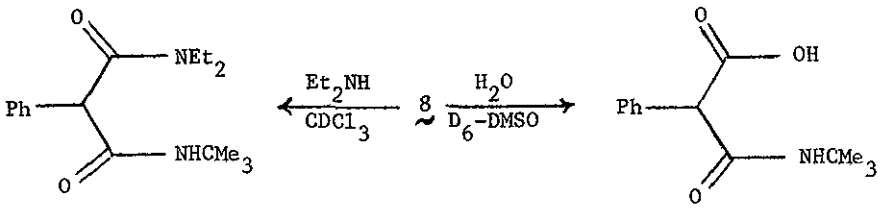
The structure 8 was assigned to the protonation product on the basis of combustion analysis, osmometric molecular weight determination, and spectral

data. The ir spectrum (CCl_4) features a prominent band at 5.75 μ, as observed for other malonimides (2). The pmr spectrum (CCl_4) contained signals at δ 1.50 (s, 9H), 4.53 (s,1H), and 7.26 (s,5H) as expected for 8. Finally, ^{13}C nmr ($CDCl_3$) showed a single low-field carbonyl carbon signal (172 ppm downfield from Me_4Si).



9 8

The striking difference in stability of 8 and the disubstituted methylation product 9 is noteworthy. In $CDCl_3$ solution, for example, nmr assay shows that 9 is inert at room temperature to added diethylamine, while 8 is rapidly converted to the diamide 10. In moist D_6-DMSO solution 8 also readily hydrolyzes to 11.



10 11

The lability of 8 suggests that the mobile proton of C-monosubstituted malonimides permits interconversion to reactive acylating agents. This feature could be partly responsible for the paucity of accounts of isolation of compounds of this type not disubstituted on the central carbon (2). Under basic conditions, reversal of the postulated (1) anionic pathway for the formation of 8 could lead to several intermediates which could account for 10 and 11 above. In support of this possibility, spectal tests have demonstrated reversion to 6, when 8 is combined with potassium tert-butoxide in THF.

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