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PREPARATION AND THERMAL FRAGMENTATION OF IMIDAZOLIDINES DERIVED FROM ARYL IMINES

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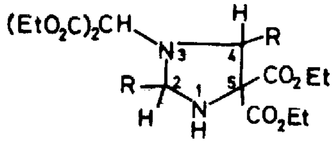
Summary. Aryl imines of diethyl aminomalonate undergo facile dimerisation to imidazolidines. Heating the imidazolidines at 110° in the presence of N-phenyl maleimide or diethyl azodicarboxylate gives pyrrolidines and triazolidines respectively via a retro 1,3-dipolar cycloaddition.

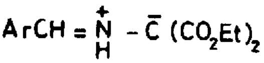
Protection of amines as their arylimine derivatives (1) allows ready deprotonation of adjacent methine or methylene groups to give (2) particularly in cases such as (1a) or (1b). These ambident anions undergo alkylation,[1] Michael addition[1] reactions and aldol condensation[2] reactions. We now report that reaction of arylaldehydes with diethyl aminomalonate hydrochloride in ethanol at 40° in the presence of 1 equiv. of sodium ethoxide gives the imidazolidines (3a-g) [e.g. (3a; 60%), m.p. 113-114°, ν_{max} (KBr) 3250 and 1745 cm.$^{-1}$]. Formation of the intermediate imine (1c) was readily demonstrated by tlc and by isolation of (1c; Ar = 5-(2-phenylthiazoyl) and (1c; Ar = p-$CF_3C_6H_4$). Formation of (3) from (1c) could involve an anionic ($4\pi + 2\pi$) cyclo addition of the type discovered and exploited by Kauffmann.[3] Thus the deprotonation of (1c) to (2; R = R^1 = CO_2Et) should be facile and cycloaddition of this 4π-anion to (1c) would give (3). Alternatively the formation of (3) might be a further example of 1,3-dipole formation via tautomerism of an X = Y - ZH system. We have recently shown that such tautomeric processes can lead to a wide range of 1,3-dipolar cycloaddition reactions.[4] The imine (1c) would undergo cycloaddition with (4). At present we cannot distinguish between these two alternatives. However, the ready formation of the imidazolidines (3a-g) is clearly due to the enhanced acidity of the methine proton of the imines (1c) since imines of α-amino acid esters (1; R=H, Me,Ph; R^1= CO_2Me) can be readily prepared and show no tendency to dimerise when only one ester group is present. Moreover a recent report of an anionic (4π + 2π) cyclodimerisation of (5) with subsequent loss of hydrogen cyanide to give imidazoles (6)[5] lends support to an anionic cycloaddition process for the formation of (3a-g).

(1) a. R=H, R'= Ph
b. R=H, R'= CO_2Me
c. R=R' = CO_2Et

(2)

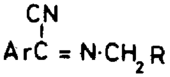


(3) a. R= 5-(2-phenylthiazoyl)
b. R= Ph
c. R= p-$NO_2C_6H_4$
d. R= p-$CF_3C_6H_4$
e. R= 2-furyl
f. R= 2-thienyl
g. R= 2-pyridyl



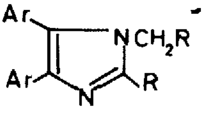
$ArCH=\overset{+}{\underset{H}{N}}-\bar{C}(CO_2Et)_2$

(4)

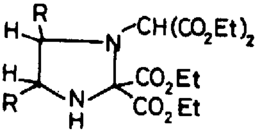


$Ar\overset{CN}{\overset{|}{C}}=N{\cdot}CH_2R$

(5)



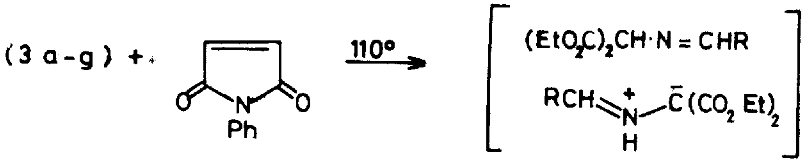
(6)

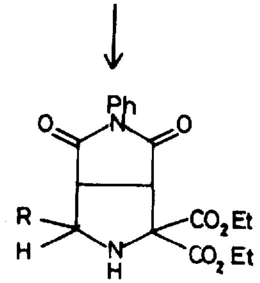


(7)

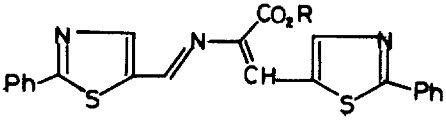
The structures of the imidazolidines were assigned on the basis of their ^1H nmr spectra. In particular the alternative imidazolidine structures (7) could be ruled out by the occurrence, in the ^1H nmr spectra of (3), of two singlets at ca. 5-6δ for the C(2) and C(4) protons of (3). Attempts to trap the intermediate [1c; Ar = 5(2-phenylthiazoyl)] with another imine by reacting 2-phenylthiazole-5-carboxaldehyde with diethyl aminomalonate in the presence of 1 mole of benzylidene aniline (50°, EtOH) gave (8; R = Et, 55%), m.p. 181-182°.

The corresponding methyl ester (8; R=Me, 66%), m.p. 208-209°, was obtained from 2-phenylthiazole-5-carboxaldehyde and glycine methyl ester in methanol [δ ($CDCl_3$) 9.29 (s, 1H), 8.20 (s, 1H), 8.09-7.99 (s + m, 5H), 7.64 (s, 1H) and 7.53-7.26 (m, 6H).

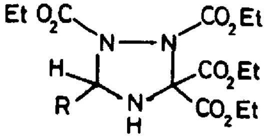




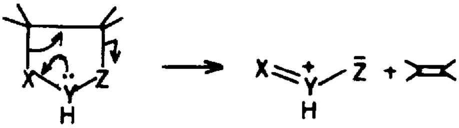
(9)



(8)



(10) a. R = 5-(2-phenylthiazoyl)
b. R = Ph



(11) (12)

When the imidazolidines (3a-g) were heated in boiling toluene with N-phenylmaleimide (2 mole), the pyrrolidines (9a-g) were formed in 40-80% yield [e.g. (7a, 51%), m.p. 176-179°, $\nu_{max.}$ (KBr) 3323, 1760 and 1740-1715 cm^{-1}]. A similar process was observed when imidazolidines (3a) and (3b) were heated in boiling toluene with diethyl azodicarboxylate (DAD). The products in this case were the triazolidines (10a and b). We have previously isolated triazolidines from cycloaddition reactions of DAD and imines of α-amino acid esters.[6] These processes are thought to involve a retro-1,3-dipolar cycloaddition reaction analogous to those observed for certain pyrrolidines[7] and pyrazolidines.[8] Thus retro-1,3-dipolar cycloadditions (11 ⟶ 12) are now established for three classes of heterocycles. Retro-1,3-anionic cycloadditions are also known.[9]

References

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