Tetrahedron Letters No. 21, pp 1839 - 1842, 1976. Pergamon Press. Printed in Great Britain.

THE REACTION BETWEEN N-CHLORO-N'-PHENYLAMIDINES AND ENAMINES
A NOVEL IMIDAZOLE RING SYNTHESIS

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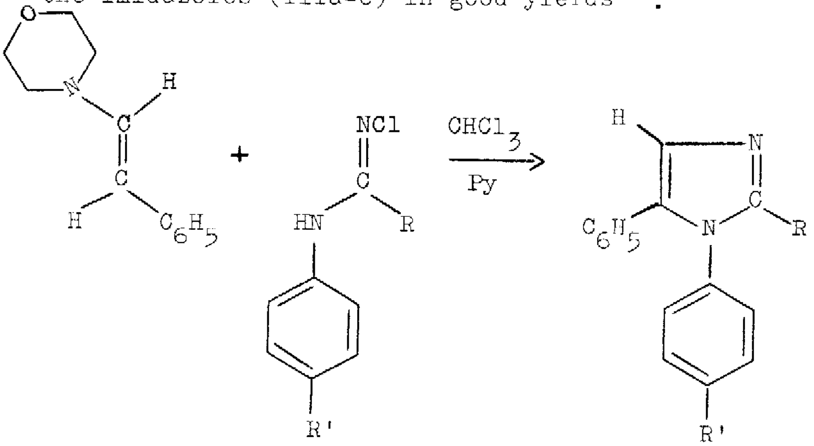
(Received in UK 2 April 1976; accepted for publication 12 April 1976)

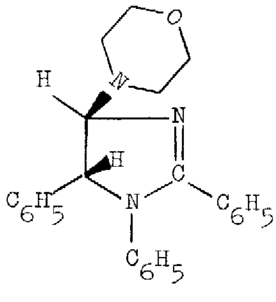
It has been reported that N-chloro-N'-phenylamidines undergo cyclisation to benzimidazoles(1) and/or rearrangement to diphenylcarbodiimides(2) upon treatment with bases.

We now report a new method for the synthesis of 1,2,5-substituted imidazoles by reaction of N-chloro-N'-phenylamidines(3) with enamines. β-morpholinostyrene (Ia) reacts with N-chloro-amidines (IIa-c) in boiling chloroform and in the presence of an equimolecular amount of pyridine affording the imidazoles (IIIa-c) in good yields(4).



Ia IIa-c

IIIa: R=C_6H_5; R'=H; m.p. 250°C
b: R=C_6H_5; R'=NO_2; m.p. 270°C
c: R=CH_3; R'=H; m.p. 122°C

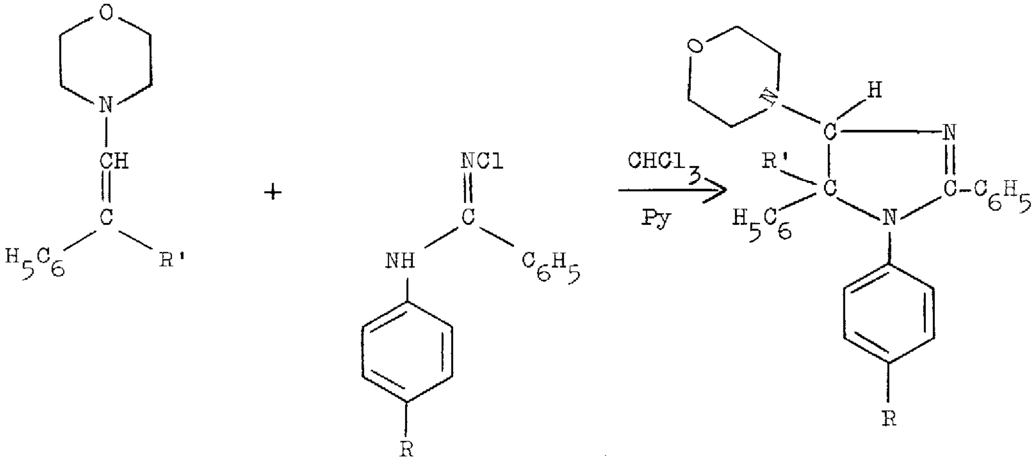


IVa: m.p. 202°C

The reaction proceeds via 4-morpholino-4,5-dihydroimidazole intermediates (IV) which easily undergo aromatisation through the elimination of the amino group. In the case of the reaction affording the imidazole IIIa, a small amount of the dihydroimidazole IVa could be isolated by thorough chromatographic separation of the reaction by-products. On heating in the presence of Py.HCl, IVa was deaminated to IIIa.

The structure of IVa was assigned on the basis of analytical and spectral data (N.M.R. and mass spectroscopy(5)). The trans configuration of the two hydrogens on C_4 and C_5 was inferred from the value of the $J_{H4-H5} = 4$ c.p.s.(6)

In the reaction between N-chloroamidines and enamines which do not bear hydrogen atoms in the β-position (Ib-c) the 4-amino-5,5-substituted imidazolines (IVb-c) were easily isolated because of the impossibility of the amine elimination(7).

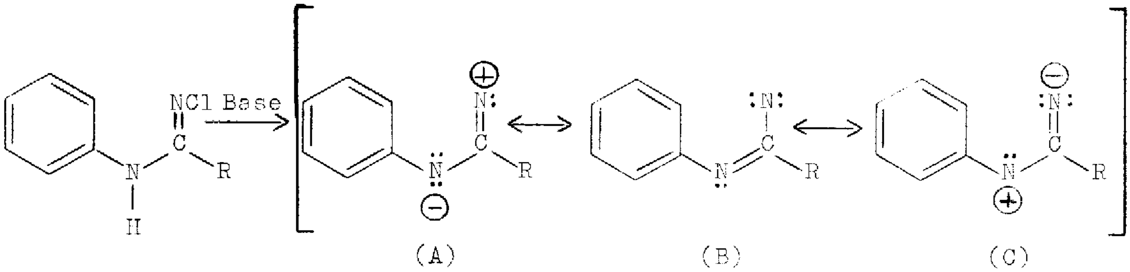


Ib: $R' = CH_3$
c: $R' = C_6H_5$

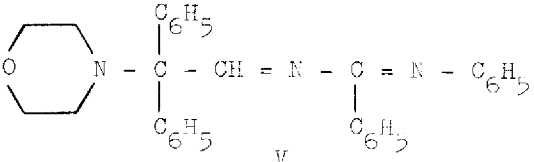
IIa-c

IVb: R=H; $R' = CH_3$; m.p. 182°C
c: R=H; $R' = C_6H_5$; m.p. 166°C
d: $R = NO_2$; $R' = CH_3$; m.p. 255°C

The results reported can be rationalized assuming that N-chlorobenzamidines give rise, in basic medium, to a reactive intermediate which reacts wit the electron rich double bond of the enamines as the 1-3 dipole of the type C.

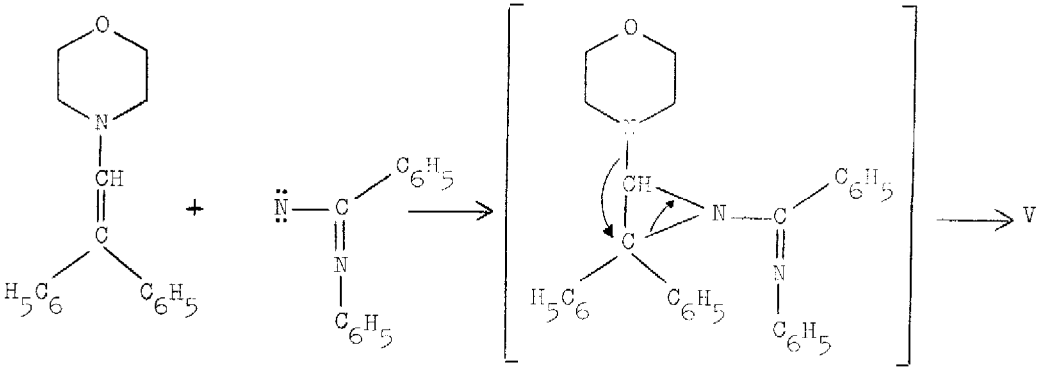


In the case of the reaction from enamine Ic, besides the imidazoline IVc a yellow product melting at 171°C was isolated whose structure was assigned as N-(2-morpholino-2,2-diphenyl)ethylidene-N'-phenyl-benzamidine (V) on the basis of the analytical and spectral data and of chemical behaviour.



V

This unusual compound probably arises from the rearrangement of an aziridine intermediate (VI) formed by direct insertion of the nitrene form (B) on the enamine double bond.



VI

The formation of V from the aminoimidazoline IVc can be excluded by the fact that a pure sample of IVc does not afford V under the reaction conditions.

Actually, at present, we cannot exclude that the intermediate VI could also rearrange to the corresponding imidazoline analogously to the well known transformation of N-acylaziridines to oxazolines(8).

Further work is in progress to establish more firmly the mechanism and to exploit the synthetic potential of this reaction.

REFERENCES AND NOTES

(1) V.J. Grenda, R.E. Jones, G. Gal and M. Sletzinger, J.Org.Chem., 30, 259 (1965).

(2) E. Haruki, T. Inaike and E. Imoto, Bull.Chem.Soc.Japan, 38, 1806 (1965).

(3) The N-chloro-N'-phenylbenzamidines were obtained almost quantitatively by reacting 0,1 moles of the amidine with 0,105 moles of N-chlorosuccinimide in dry methylene chloride at room temperature.

(4) Imidazoles IIIb and IIIc are new compounds. IIIa has been described (S. Sato et al., Bull.Chem.Soc.Japan, 40, 2938 (1967)).

(5) The mass spectra of imidazolines described agree with the known fragmentation pattern of these compounds (M. Ohashi et al., Org.Mass.Spectrom., 1, 703 (1968)).

(6) NMR data of 4-amino-imidazolines are not reported in the literature. However, this assignment is in good agreement with the Karplus equation. Moreover, a strict analogy exists between the imidazolines IV and 5-amino-v-triazolines which have already been studied (R. Stradi et al., Org. Mag.Res., 4, 247 (1972)).

(7) In the reaction involving enamine Ic, a small amount (13%) of 1,2,4,5-tetraphenylimidazole was also isolated. This compound derives from the deamination and the shift of a phenyl group from C_5 to C_4 of the imidazoline IVc under the reaction conditions.

(8) A. Hassner, S.S. Burke, J. Cheng-Fan I, J.Amer.Chem.Soc., 97, 4692 (1975) and references therein.