CHEMISTRY LETTERS, pp. 119-122, 1982.

THE REACTIONS OF NITRILE IMINES WITH AMINO- AND OXO- SUBSTITUTED AZOLES

Hassan A. ELFAHHAM, Kamal U. SADEK, Galal E. H. ELGEMEIE, and Mohamed H. ELNAGDI

Department of Chemistry, Faculty of Science, Minia University, Minia and Cairo University, Giza, A.R.Egypt

The behavior of several amino and hydroxy azoles toward nitrile imines and hydrazonyl halides is reported.

Nitrile imines, usually synthesised in situ by base catalysed elimination of hydrogen halide from hydrazonyl halides, are reactive intermediates that found extensive utility in heterocyclic syntheses.[1] However, the reaction of these reactive intermediates with amino azoles and with azolones have not been investigated.

As a part of our program directed for development of new simple procedures for synthesis of fused azoles[2] we have investigated the reaction of nitrile imines with cyclic amidines and with azolones.

Thus in a typical procedure, a suspension of equimolecular amounts (20 mmoles) of 5-amino-3-phenylpyrazole (Ia) and benzphenylhydrazonyl chloride (II) in ethanol (30 ml) is treated with triethylamine (20 mmoles) and refluxed for 1-3 hrs (TLC control). Removal of ethanol, washing with petroleum ether, and trituration with ethanol afforded product of molecular formula $C_{22}H_{16}N_4$. The same product was formed on treatment of II with 5-hydroxy-3-phenylpyrazole (Ib) under the same condition. We took four alternative theoretically possible structures into consideration (cf. structures III-VI). Structures III and IV could be readily eliminated based on ^1H NMR which revealed absence of resonance at δ 5-6 ppm of pyrazole proton. Spectral data, however, seemed of little help for discriminating IV and VI. Structure V was established for the reaction product based on identity with authentic specimen.[3] The formation of V from the reaction of Ia,b with II

may be assumed to proceed either via alkylation of Ia,b and subsequent cyclization (Route A) or via 1,3-dipolar addition of the generated nitrile imine (Route B). It seemed most likely that the reaction proceeds via route B as alkylation sequence would afford acyclic intermediates like VII and VIII. Such intermediates could not be traced in the mother liquor. It is expected, as experienced by us, that cyclization of VII or VIII into III or V cannot take place under reaction condition and needs only drastic condition to be effected.[4)]

In contrast to the behavior of Ia,b , 3-methyl-5-hydroxypyrazole (Ic) reacted with II under the same experimental condition to yield the pyrazolo[1,5-c]-1,2,4-triazole derivative III; R= CH_3. The reaction is assumed to proceed in this case via route C. The isomeric structures V and VI were ruled out based on ^{1}H NMR which revealed pyrazole CH proton at δ 5 ppm. Moreover structure IV was also eliminated based on stability of the reaction product toward reagent reported to effect cleavage of 1,2,3-triazole derivatives.[5)]

The behavior of several other cyclic amidines and heterocyclic ketones toward II was investigated. Products resulting from substitution at the heterocyclic active site by the benzphenylhydrazonyl residue were obtained. Thus, from reaction of II with 4-aminoantipyrine (IX), 2-aminobenzimidazole (X), the amidrazones XI and XII were obtained. The structures of these amidrazones are inferred from analytical and spectral (IR and ^{1}H NMR) data.

Also 1-phenyl-3-methyl-2-pyrazolin-5-one (XIII) and rhodanine (XIV) afforded the corresponding hydrazone derivatives XV and XVI.

The behavior of 2-oxopropanophenylhydrazonyl chloride (XVII) toward aminoheterocycls and hydroxyazoles has been also investigated. In contrast to the observed formation of 2+3→5 cycloadduct from reaction of II with Ia, compound XVII reacted with Ia to yield a product for which structures XVIII or XIX seemed theoretically possible. Structure XVIII was, however, readily eliminated based on ^{1}H NMR which revealed the presence of resonance for pyrazole 4-H. The formation of XIX from reaction of XVII with Ia is similar to recently reported formation of the pyrazolo[1,5-c]-imidazole derivative on reacting of Ia with benzoylarylhydrazonyl bromides.[6)]

Although under variety of conditions, we failed to isolate products from reaction of Ib,c with XVII. Compound XIII reacted smoothly with XVII to yield

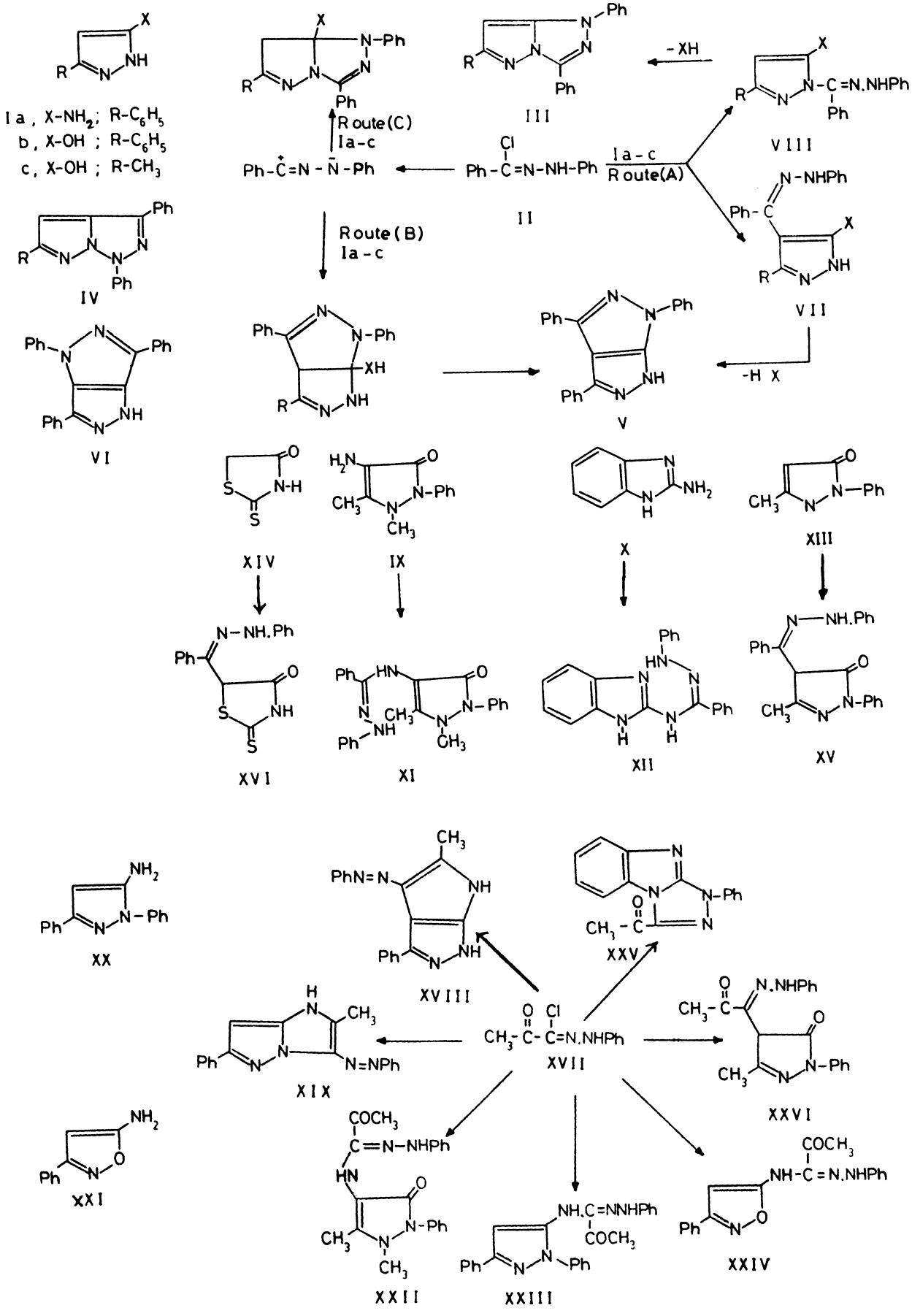
Ia, X-NH2; R-C6H5
b, X-OH ; R-C6H5
c, X-OH ; R-CH3
Route(C)
Ia-c
Route(B)
Ia-c
Ia-c
Route(A)
-XH
-H X
III
VIII
II
IV
VI
V
VII
XIV
IX
X
XIII
XVI
XI
XII
XV
XX
XVIII
XXV
XIX
XVII
XXVI
XXI
XXII
XXIII
XXIV

Table 1. List of Compounds III, V, XI, XII, XV, XVI, XIX, and XXII-XXVI

Comp.	Recrystallization from	Mp (°C)	Yield (%)	Mol.formula (MW)	Comp.	Recrystallization from	Mp (°C)	Yield (%)	Mol.formula (MW)
III	Ethanol	100	91	$C_{17}H_{14}N_4$ (274.33)	XIX	Ethanol	155	66	$C_{18}H_{15}N_5$ (301.4)
V	Dioxan	192	74	$C_{22}H_{16}N_4$ (336.4)	XXII	Ethanol	138	69	$C_{20}H_{21}N_5O_2$ (363.4)
XI	Ethanol	210	86	$C_{24}H_{23}N_5O$ (397.4)	XXIII	Ethanol	154	76	$C_{24}H_{21}N_5O$ (395.4)
XII	Chloroform	236	55	$C_{20}H_{17}N_5$ (327.35)	XXIV	Ethanol	188	44	$C_{18}H_{16}N_4O$ (320.4)
XV	Ethanol	200	85	$C_{23}H_{20}N_4O$ (368.4)	XXV	Ethanol	195	65	$C_{16}H_{12}N_4O$ (276.3)
XVI	Ethanol	114	92	$C_{16}H_{12}N_3OS_2$ (326.35)	XXVI	Ethanol	185	90	$C_{19}H_{18}N_4O$ (334.4)

hydrazone derivative XXVI. Now the behavior of several other aminoazole derivatives toward several hydrazonyl halides is under investigation.

The results indicate that nitrile imine can add to the double bond in amino and hydroxy heterocyclic derivatives. However, the nature of the end product depends on the nature of nitrile imine, nature of substituent on heterocyclic ring and nature of heterocyclic ring.

The analytical and spectral data (IR and ^{1}H NMR) of all synthesised compounds were in a good agreement with proposed structures.

ACKNOLWEDGEMENT Galal E. H. ELGEMEIE is indepted to the Ministry Education for granting a fellowship.

REFERENCES

1) S. Y. HONG and J. E. BALDWIN, Tetrahedron, 24, 3787 (1968).

2) M. H. ELNAGDI and H. WAMHOFF, Chemistry Letters, 419 (1981).

3) C. A. ROJAHN, Chem. Ber., 55B, 291, (1922).

4) A. H. HARHASH, M. H. ELNAGDI, N. S. T. HUSSEIN, and S. M. FAHMY, Indian J. Chem., 11b, 1, (1973). Also M. H. ELNAGDI, unpublished data.

5) G. K. BUCKLEY, J. Chem. Soc., 1850 (1954).

6) H. M. HASSANEEN, A. SHETTA, and A. S. SHAWALI, J. Heterocycl. Chem., 17, 1185 (1980).

(Received October 3, 1981)