REACTION OF THE 2-NITROENAMINE IN ACID

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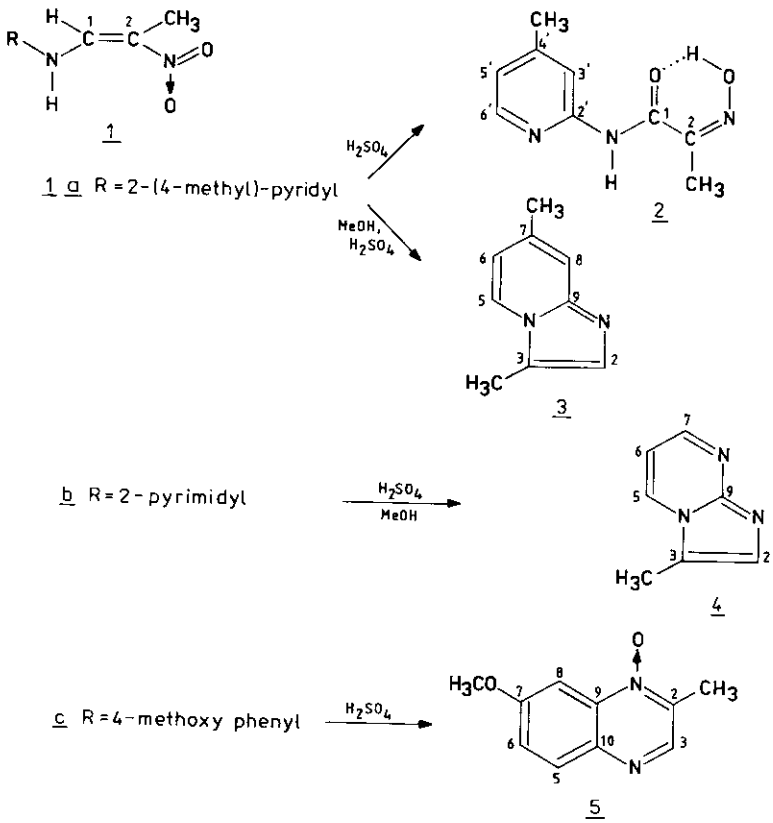
Abstract - 2-Nitroenamines bearing heteroaryl substituents on enamine nitrogen rearrange in acids to amidooxime of the pyruvic acid or give the products of the intramolecular cyclization, di- and triaza-indenes, whereas N-aryl substituted substrates yield quinoxaline oxides. Nitronic acid of the 2-nitroenamine is suggested as a primary reactive species in acid solution. ^{13}C and ^{15}N NMR data are discussed which provide the evidence for this intermediate.

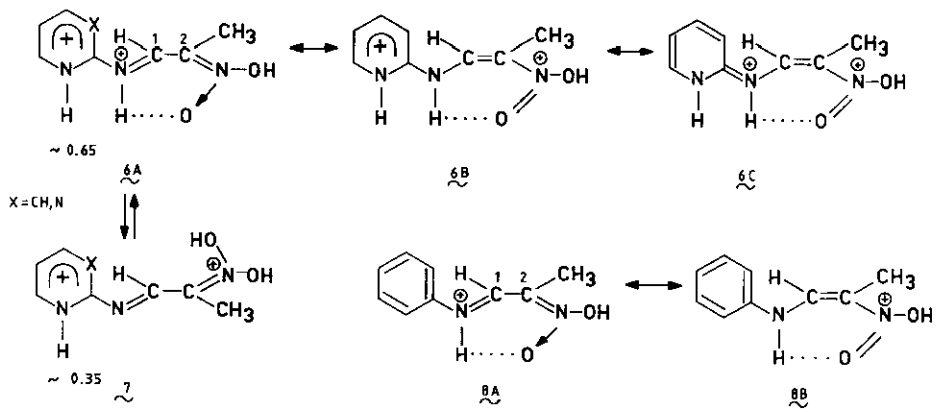
The nitroaliphatic compounds[1] and nitroenamines[2] have recently attracted a widespread interest as useful intermediates in organic synthesis. We have turned our attention to the transformations of the nitro group under acidic conditions in parent nitroenamines[3] bearing the heteroaryl or aryl substituents on nitrogen atom since such reactions have not yet been exploited[2,4] whereas they are important synthetically for nitroalkanes (Nef reaction[5,6]) as useful route to aldehydes, ketones, hydroxamic acids and carboxylic acids.

We have found now that 2-nitroenamines containing heteroaromatic or oxy substituted aromatic base at enamine nitrogen atom undergo, under acidic conditions, rearrangements depicted in Scheme I. Two experimental conditions have been checked: dissolution of 1 in cold (0 - 10°C), concentrated sulfuric acid and in boiling 40% H_2SO_4 solution in methanol. After dilution the reaction mixture with water, neutralization and extraction with chloroform, chromatography on silica gel was applied. Products 3, 4 and 5 were isolated in 70%, 90% and 10% yield, respectively, while 2 was separated after neutralization as white crystals in 50% yield. The structure of compounds 2 - 5 was determined by IR, ^{1}H, ^{13}C NMR and elemental analyses (Table 1).

Spectroscopic studies of a few compounds using variable temperature ^{1}H, ^{13}C and ^{15}N NMR spectra of nitroenamines 1 in TFA solutions allow for suggestion that nitronic acid of the structure 6, 8 in Scheme 2 is a primary reactive species in solution. The presence of the nitronic acid of the structure 6 in TFA solution of nitroenamines with heteroaromatic substituent on enamine nitrogen atom is primarily indicated by the ^{15}N NMR (comp. item 1a in Table 2) which show characteristic low frequency shift of ca. 100 ppm on protonation of the pyridine nitrogen. Furthermore, the presence of the two acidic protons in nitroenamine moiety is confirmed by the observation of the doublet of the enamine nitrogen in the proton coupled ^{15}N NMR spectrum on one hand, $^{1}J(N,H) = 94$ Hz,



Scheme 1



Scheme 2

and strong high frequency shift of 14 ppm for C^1 carbon atom in ^{13}C NMR on the other hand. The latter effect, together with ^{15}N NMR chemical shifts, can be explained as derived from the protonation of a nitro group inducing bonding described mainly by the structure 6B.

In the case of nitroenamines with aromatic substituent on enamine nitrogen atom (comp. item 1c in Table 2) ^{15}N and ^{13}C NMR chemical shifts are consistent with the nitronic acid with bonding best

Table 1 IR and NMR spectral data of compounds 2 - 5[a]

No.	IR (oil film) ν (cm^{-1})	^1H NMR ($CDCl_3$/TMS int.) δ (ppm)	^{13}C NMR ($CDCl_3$/TMS int.) δ (ppm)
2	3340, 3145, 3030, 2940, 1685, 1650, 1610, 1570, 1530, 1500, 1040	2.2 (s, 3H, C^2-CH_3); 2.4 (s, 3H, $C^{4'}$-CH_3); 7.0 (d, 1H, J=5 Hz, $C^{5'}$-H); 8.2 (d, 1H, J=5 Hz, $C^{6'}$-H); 8.2 (s, 1H, $C^{3'}$-H); 9.4 (bs, 1H, NH); 13.7 (s, 1H, OH)	9.3 (C^2-CH_3); 21.6 ($C^{4'}$-CH_3); 115.9 ($C^{3'}$); 121.2 ($C^{5'}$); 145.9 ($C^{6'}$); 150.2 (C^1); 151.4 (C^2); 151.7 ($C^{4'}$); 162.5 ($C^{2'}$)
3	2890, 1645, 1500, 1450, 1120	2.3 (s, 6H, C^3-CH_3, C^7-CH_3); 6.6 (d, 1H, J=6.8 Hz, C^6-H); 7.4 (s, 2H C^2-H, C^8-H); 7.8 (d, 1H, J=6.8 Hz, C^5-H)	8.7 (C^3-CH_3); 21.0 (C^7-CH_3); 114.9 (C^6); 115.8 (C^8); 119.1 (C^3); 122.1 (C^5); 130.6 (C^2); 133.8 (C^7); 145.5 (C^9)
4	2950, 1615, 1495, 1430, 1265, 1130	2.5 (s, 3H, C^3-CH_3); 6.9 (m, 1H, J= 6.1 Hz, J=4.1 Hz, C^6-H); 7.5 (s, 1H, C^2-H); 8.3 (m, 1H, J=6.1 Hz, J=2.5 Hz, C^5-H*); 8.4 (m, 1H, J=4.1 Hz, J=2.5 Hz, C^7-H*)	8.9 (C^3-CH_3); 108.5 (C^6); 118.6 (C^3); 131.2 (C^5); 133.0 (C^2); 148.3 (C^9); 148.5 (C^7)
5	2920, 1500, 1280, 1220	2.7 (s, 3H, C^2-CH_3); 4.2 (s, 3H, OCH_3); 7.6 (m, 1H, J=9 Hz, J=3 Hz, C^6-H); 8.1 (d, 1H, J=3 Hz, C^8-H); 8.2 (d, 1H, J=9 Hz, C^5-H); 8.9 (s, 1H, C^3-H)	15.4 (C^2-CH_3); 56.2 (OCH_3); 97.0 (C^8); 123.4 (C^6); 131.3 (C^3); 138.0 139.8, 140.5 (C^2,C^9,C^{10})*, 144.2 (C^5); 161.6 (C^7)

a Elemental analyses for all compounds are in satisfactory agreement with calculated values. Signals marked with asterisk can be interchanged.

described by structure 8A. Low frequency shift of the nitrogen atom signal of a nitro group in comparison with its position in neutral molecule indicates the increase of the double bond character in the C^2-N bond. The same conclusion can be drawn regarding bonding in C^1-N bond basing on the observation of a strong high frequency shifts of the signals of both atoms on protonation in TFA solution.

Two sets of signals of unequal intensity are observed in the NMR spectra (see Table 2), most probably, as judged on the basis of the chemical shifts and ^{15}N,H H,H spin - spin coupling constants, this process reflects the equilibrium shown in Scheme 2 [7].

As shown in Scheme 1 different products can be obtained depending on the substituent at the enamine nitrogen and acid used. The former dependence can be rationalized on the basis of the spectro-

Table 2 ^{13}C and ^{15}N chemical shifts, δ(ppm), of 1a in neutral (N) and TFA (C) solutions[a,b]

No.	Form	$N_{sp}3$	C^1	C^2	NO_2	C^2-CH_3	$N_{sp}2$	$C^{2'}$	$C^{3'}$	$C^{4'}$	$C^{5'}$	$C^{6'}$	Other
	Z	-246.9	134.4	121.6		16.4		150.7	112.7	150.4	120.8	148.2	4'-CH_3,20.9
1a N	E	-256.9			-3.0		-111.1						
	Z	-268.0	148.6	122.7	-4.2	16.3	-215.8	133.0	114.3	164.8	129.4	138.9	22.9
C	E	-33.8	148.6	122.7	-3.3	11.6	-217.2	131.6	114.3	164.9	129.1	138.9	22.9
								C_i	C_o	C_m	C_p		
	E	-259.9	139.6	119.1	+1.6	11.2		134.0	114.8	118.3	159.9		OCH_3, 55.3
1c[c] N	Z	-247.3	139.6	122.7		15.8		132.7	114.8	118.3	156.6		55.3
	C;Z	-209.6	146.3	124.8	-38.1	15.5		131.1	116.5	121.5	160.3		56.3

a ^{13}C NMR spectra in neutral medium were obtained in $CDCl_3$ whereas ^{15}N NMR spectra were obtained in DMSO solution. ^{15}N NMR spectra were calibrated against CH_3NO_2 as chemical shift reference.

b The spectra in TFA were obtained below room temperature from solutions of 0.1 g of the solute dissolved in 0.5 ml of C_6D_6 used for lock signal and 1.5 ml of TFA with internal TMS.

c ^{15}N NMR data are cited for N-phenyl derivative.

scopic results confirming the different chemical behaviour of the nitro group in 6 and 8. In the case of substrates represented by 1a, 1b the chemical character is best represented by structure 6B containing easily removable nitronium ion whereas substrate 1c is best represented in solution as nitronic acid 8A. Consequently the substrate 1c gives quinoxaline N-oxide 5 as a product of condensation between the nitronic moiety with electron rich aromatic ring.

Two types of products can be obtained depending on the used medium. Splitting off of nitrous acid from species 6 in methanolic sulfuric acid in the case of 1a, 1b gives vinylic cation which cyclizes to 3 or 4, and this process may be facilitated by the charge distribution as in 6C. Alternatively, a simple acid catalysed cyclization, between C^2 carbon atom and protonated aromatic nitrogen atom in 6, followed by elimination of nitrous acid, seems to also be plausible. In neat sulfuric acid these cyclizations may not be possible for the substrates of the 1a type; the formation of 2 can be the result of the intramolecular redox reaction in 6 or 7 or may proceed through series of steps creating amide function using intramolecular or external oxygen sorce.

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7. Slow rotation around C^1-C^2 bond in 6 can also be taken into account as giving rise to the doubling of the NMR signals. However, dramatic differences in the chemical shifts of the enamine nitrogen atom (comp. item 1a form C in Table 2), characteristic for the enamine (-268.0) and imine (-33.8) hybridization gives strong evidence that slow tautomerization of a proton is reflected in the NMR spectra. ^{1}H NMR chemical shifts of the C^1-H and C^2-CH_3 groups and ^{13}C NMR chemical shift of the latter are indicative of the configuration Z and E in the 6 and 7 respectively, this observation was used when drawing the equilibrium in Scheme 2. Apparently, the tautomerization of a proton is accompanied by a fast change of configuration around C^1-C^2 bond.
Full account of the spectroscopic studies will be published in a forthcoming paper.

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