v-Triazolines. XI (1). Rearrangement of 1-Aryl-4,5-diamino-4,5-dihydro-v-triazoles

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The reaction of arylazides with 1,2-diaminoethylenes (**1a-b**) or α,β-diaminostyrenes (**1c-f**) gave *N*-(1,2-diaminoethylideneanilines (**2a-e**) and *N*-(1,2-diamino-2-phenylethylidene)anilines (**2g-i**), respectively. These amidine derivatives are formed through the rearrangement of unstable 1-aryl-4,5-diamino-*v*-triazolines. The regiospecificity of the cycloaddition reaction has been elucidated on the basis of the products obtained.

J. Heterocyclic Chem., 16, 289 (1979).

The reaction between enamines and arylazides generally gives 1-aryl-5-amino-*v*-triazolines (2).

As a part of our continuing interest in the chemistry of *v*-triazolines we reacted some 1,2-diaminoethylenes with some arylazides in order to investigate this synthetic approach to the hitherto unknown 1-aryl-4,5-diamino-*v*-triazolines.

Although the effect of the substituents at C_4 of the triazolines ring has been extensively investigated in the case of alkyl, aryl and strongly electron withdrawing groups (3), the effect of electron releasing groups has not been studied until now.

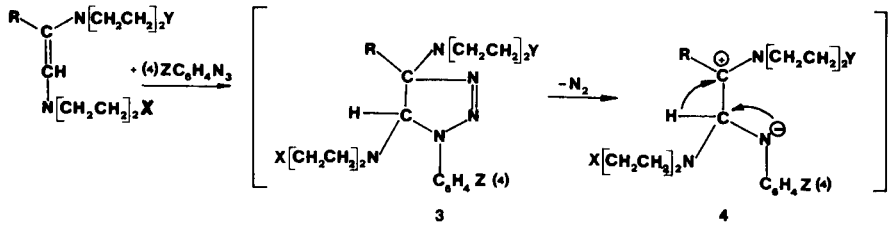
The 1,2-diaminoethylenes **1a-f** were prepared according to the literature (4). Their configuration is known and indicated in Scheme 1. The arylazides were reacted with **1a-b** at room temperature in benzene solution whereas enamines **1c-f** required refluxing for several hours. Nitrogen evolution was observed in all cases and aminoacetamidines **2a-e** or aminophenylacetamidines **2f-i**, respectively, were obtained in good yield. The structure of the amidine obtained was assigned on the basis of analytical (C, H, N) and spectral data (ir, ^{1}H-nmr and Mass spectrometry).

The relevant chemical shift values of **2a-2i** are shown in Table 1.

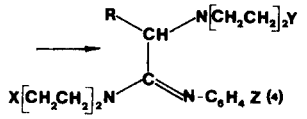
As expected, the *N*-methylene protons of the amidine amine group resonate at a lower field as a consequence of the possibility of p-π overlapping which results in a greater deshielding of the adjacent protons. This made it possible to distinguish between the two amine residues and to assign the structure to amidines **2g-h**.

The mass spectra of the amidines **2a-2i** (Scheme 2)

SCHEME 1



1a : R = H; X = Y = O (E)
1b : R = H; X = Y = CH_2 (E)
1c : R = Ph; X = Y = O (E/Z≃1:1)
1d : R = Ph; X = CH_2; Y = O (E/Z≃1:1)
1e : R = Ph; X = O; Y = CH_2 (E/Z≃1:1)
1f : R = Ph; X = Y = CH_2 (E/Z≃1:1)



2a : R = H	Z = NO_2	X = Y = O
2b : R = H	Z = NO_2	X = Y = CH_2
2c : R = H	Z = CN	X = Y = O
2d : R = H	Z = Cl	X = Y = O
2e : R = H	Z = Cl	X = Y = CH_2
2f : R = C_6H_5	Z = NO_2	X = Y = O
2g : R = C_6H_5	Z = NO_2	X = CH_2; Y = O
2h : R = C_6H_5	Z = NO_2	X = O ; Y = CH_2
2i : R = C_6H_5	Z = NO_2	X = Y = CH_2

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SCHEME 2

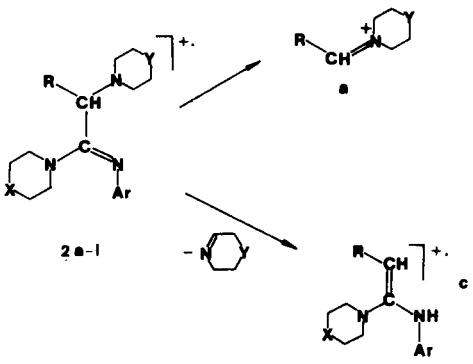
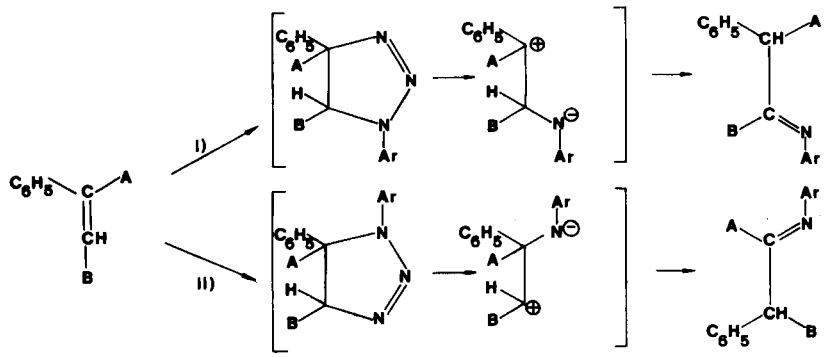


Table 1

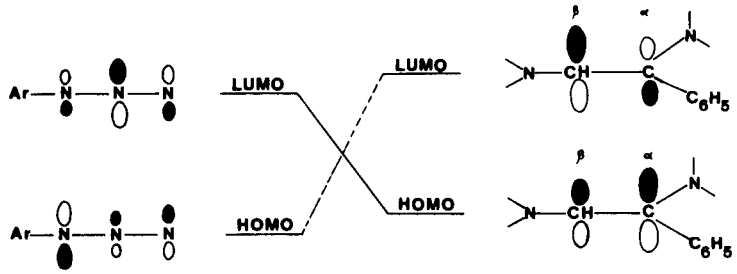
Chemical Shifts (δ from TMS, Deuteriochloroform Solution) of the Amino Group *N*-Methylenes in Amidines **2a-i**

2	$X[CH_2CH_2]_2N$-CH-R-C(= Ar)-$N[CH_2CH_2]Y$	
a	1.98	3.43
b	2.03	3.43
c	2.28	3.55
d	2.25	3.50
e	2.20	3.40
f	2.30	3.27
g	2.36	3.60
h	2.36	3.30
i	2.40	3.56

SCHEME 3



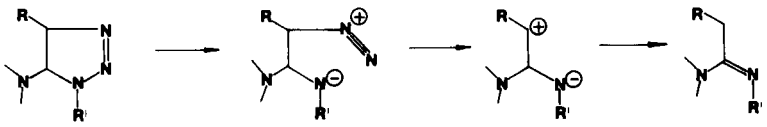
SCHEME 4



show, in addition to the molecular ions, significant peaks which indicate that the main fragmentation patterns are the cleavage of the C-C bond and the cyclic amine elimination through McLafferty rearrangement. By analogy with known cases (5) the formation mechanism of the above amidines can be formulated as depicted in Scheme 1. The unstable triazoline intermediates readily (6) rearrange through ring cleavage and nitrogen elimination. The orientation of the cycloaddition reaction of arylazides to the enamine double bond is well established on electron grounds and experimental evidence. Of course, in the case of enamines **1d** and **1e** the extension of the known regiospecificity is not obvious since both carbon atoms at the double bond have an enamine character.

Scheme 3 shows that when the two amine residues are identical (A = B) the same amidine is formed whichever orientation prevails. However, when A is different from B, path i) and ii) should lead to different amidines. The results obtained are consistent with path i). The observed regiospecificity of the cycloaddition reaction

SCHEME 5



can be explained on the following grounds.

From an examination of molecular models, the greater ability to achieve p-π overlapping of the nitrogen atom in the β position with respect to the phenyl group, both in the *E* and *Z* isomers, is evident. Accordingly, the stereochemical course of the azide addition to the double bond of α-β-diaminostyrenes should be established by the greater electron density on the α carbon atom (7).

Also the frontier molecular orbital approach (Scheme 4) agrees with the observed regiospecificity.

Because of the presence of two amino groups the difference between the c_α and c_β values of HOMO of the enamines in the dominant interaction with LUMO of the azide could be too small to justify the observed regioselectivity. However, in this reaction the HOMO azide-LUMO enamine interaction also gives the some regioisomer because of the combined effect of the amino and the phenyl groups (in β and in α positions respectively) which enhance, c_β value with respect to c_α one.

The somewhat surprising fragility of the 4,5-diaminotriazoline ring can be rationalized by the following considerations.

The rearrangement of 5-amino-*v*-triazolines to amidines is one of the typical transformations of the triazoline ring which represents the main or a secondary process according to the nature of the ring substituent (5).

As shown in scheme 5 the rearrangement process occurs through cleavage of the N_1-N_2 bond followed by nitrogen elimination. The first step should be clearly facilitated by a strong withdrawing group at N_1 whereas diazonium ions are destablized by electron releasing substituents. Thus a combined push (by R) - pull (by R') action can be considered mainly responsible for this rearrangement process.

Accordingly, it has been found that triazolines with a strongly withdrawing group (arylsulfonyl (5), CN (9), 2,4-dinitrophenyl (10)) at N-1 and an alkyl group at C-4 are very unstable and generally not isolable compounds; besides, when R' is less electron withdrawing as, for example, 4-nitrophenyl, 4-cyanophenyl and 4-chlorophenyl (11), the triazoline adducts are easily isolable and undergo rearrangement only at high temperature.

The enhanced lability of the 1-aryl-4,5-diaminotriazolines studied in this work is clearly brought about by the 4-amino residue which, making the nitrogen loss from the diazo form easier, adds its pushing action to the pulling action of the aryl substituent of N-1.

EXPERIMENTAL

Melting points are uncorrected. Nmr spectra were recorded with a Varian A-60 spectrometer operating at 60 MHZ in deuteriochloroform with TMS as the internal standard. Mass spectra were recorded with a Perkin-Elmer 270 mass spectrometer at an ionizing energy of 70 eV, using the direct inlet technique with a probe temperature of 130-150° (12).

N-(1,2-Diaminoethylidene)anilines (**2a-e**). General Method.

A solution of 1,2-diaminoethylenes (**1a-b**, 0.01 mole) was dissolved in benzene dried over molecular sieves (20 ml.) and the solution mixed with the azide (0.01 mole) dissolved in benzene (10 ml.). The reaction mixture was stirred at room temperature and under nitrogen atmosphere until no more azide was detected by tlc. Removal of solvent under vacuum and crystallization from a suitable solvent gave the pure compounds.

Compound **2a**.

This compound was a yellow powder, m.p. 191-192° (from ethanol), yield 82%; ms: 334 (M^+, 0.2%); 249 (c, 25.0%); 234 (b, 2.3%); 100 (a, 100%).

Anal. Calcd. for $C_{16}H_{22}N_4O_4$: C, 57.45; H, 6.65; N, 16.75. Found: C, 57.80; H, 6.70; N, 16.75.

Compound **2b**.

This compound was a yellow powder, m.p. 124° (from isopropyl ether), yield 78%; ms: 330 (M^+, 0.2%); 247 (C, 24.5%); 232 (b, 1.6%); 98 (a, 100%).

Anal. Calcd. for $C_{18}H_{26}N_4O_2$: C, 65.45; H, 8.0; N, 16.95. Found: C, 65.35; H, 7.95; N, 16.95.

Compound **2c**.

This compound was a white-cream powder, m.p. 164° (from isopropyl ether/2-propanol), yield 78%; ms: 314 (M^+, 0.4%); 229 (C, 27.5%); 214 (b, 4.5%); 100 (a, 100%).

Anal. Calcd. for $C_{17}H_{22}N_4O_2$: C, 64.95; H, 7.0; N, 17.85. Found: C, 64.80; H, 7.15; N, 17.60.

Compound **2d**.

This compound was a white-cream powder, m.p. 146° (from isopropyl ether), yield 74%, ms: 323 (M^+, 0.4%); 238 (C, 19.7%); 223 (b, 8.0%); 100 (a, 100%).

Anal. Calcd. for $C_{16}H_{22}ClN_3O_2$: C, 59.35; H, 6.80; N, 13.0. Found: C, 59.60; H, 6.85; N, 12.95.

Compound **2e**.

This compound was a pale yellow powder, m.p. 78-80° (from petroleum ether), yield 64%; ms: 319 (M^+, 0.2%), 236 (C, 20%); 221 (b, 7%); 98 (a, 100%).

Anal. Calcd. for $C_{18}H_{26}ClN_3$: C, 67.60; H, 8.15; N, 13.15.

Found: C, 67.25; H, 7.85; N, 12.95.

N-(1,2-Diamino-2-phenylethylidene)-4-nitroanilines (**2f-i**). General Method.

A solution of α-β-diaminostyrene (**1c-f**, 0.01 mole) in benzene dried over molecular sieves (20 ml.) was mixed with 4-nitrophenylazide (1.64 g., 0.01 mole) dissolved in dry benzene (10 ml.) and refluxed under nitrogen for 8 hours. Removal of solvent under vacuum and crystallization or chromathographic purification on a silica gel column (**2e, 2f**) gave the pure compound.

Compound **2f**.

This compound was a yellow crystalline product, m.p. 166° (from ethanol) yield 87%; ms: 410 (M^+, 0.3%); 325 (c, 15.5%); 234 (b, 1.8%); 176 (a, 100%).

Anal. Calcd. for $C_{22}H_{26}N_4O_4$: C, 64.35; H, 6.40; N, 13.65. Found: C, 64.45; H, 6.35; N, 13.75.

Compound **2g**.

This compound was a yellow crystalline powder, m.p. 160° (from ethanol), yield 76%; ms: 408 (M^+, 0.2%); 323 (c, 13.6%); 232 (b, 1.9%); 176 (a, 100%).

Anal. Calcd. for $C_{23}H_{28}N_4O_3$: C, 67.65; H, 6.90; N, 13.70. Found: C, 67.75; H, 6.75; N, 13.85.

Compound **2h**.

This compound was a pale yellow powder, m.p. 138-140° (from ethanol), yield 70%; ms: 408 (M^+, 0.2%); 325 (c, 13.0%); 234 (b, 0.6%); 174 (a, 100%).

Anal. Calcd. for $C_{23}H_{28}N_4O_3$: C, 67.65; H, 6.90; N, 13.70. Found: C, 67.35; H, 6.75; N, 13.50.

Compound **2i**.

This compound was a pale yellow powder, m.p. 161° (from isopropyl ether), yield 70%; ms: 406 (M^+, 0.4%); 323 (c, 12.1%); 232 (b, 0.9%); 174 (a, 100%).

Anal. Calcd. for $C_{24}H_{30}N_4O_2$: C, 70.90; H, 7.45; N, 13.8. Found: C, 70.75; H, 7.25; N, 13.95.

REFERENCES AND NOTES

(1) Part X: L. M. Rossi and P. Trimarco, *Synthesis*, **10**, 743 (1978).

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(4) L. Duhamel, P. Duhamel, H. Malandain and D. Lefèvre, Bull. Soc. Chim. *France*, 4642 (1967); P. Duhamel, L. Duhamel, J. L. Klein and A. Jarry, *ibid.*, 4423 (1968).

(5) P. Dalla Croce, and R. Stradi, *Tetrahedron*, **33**, 865 (1977) and references therein.

(6) The intermediate triazolines could not be isolated. Their rearrangement occurs so rapidly that nmr monitoring of the reaction mixture did not allow detection of signals unequivocally associated with the triazoline structure.

(7) The reported results of the acidic hydrolysis of these enamines also lead to the same conclusions (8).

(8) L. Duhamel, and N. Marcelle, *Tetrahedron*, **31**, 2691 (1975).

(9) R. M. Scribner, *Tetrahedron Letters*, 4737 (1967).

(10) R. Fusco, G. Bianchetti and D. Pocar, *Gazz. Chim. Ital.*, **91**, 933 (1961).

(11) R. Stradi, and D. Pocar, *ibid.*, **99**, 1131 (1969); D. Pocar, unpublished results.

(12) We would like to thank dr. B. Gioia for helpful discussion on the analysis of mass spectra.