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ADDITION OF DIAZOACETONITRILE TO N-BENZYLIDENE-ANILINES

SYNTHESIS AND DECOMPOSITION OF 4-CYANO-1,5-DIARYL, Δ^2-1,2,3-TRIAZOLINES[1]

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Abstract—Addition of diazoacetonitrile to *para*-substituted N-benzilidene-anilines has been studied. The addition is easier if the substituent is an electrodonating group. Products obtained are Δ^2-1,2,3-triazolines or aziridines, and enamines resulting from the decomposition of the triazolines with migration of the 5-aryl substituent. Decomposition of the triazolines under various conditions has also been studied.

Diazoacetonitrile does not appear to have many applications in the field of organic synthesis, and in particular in 1,3-dipolar cycloadditions. Addition of this reagent (1) to a series of N-benzylidene-anilines (**2a–2f**) with different substituents *para* to the aromatic nucleus was undertaken in order to explore new synthetic routes to Δ^2-1,2,3-triazolines (**3** and **4**).

Results show that the addition of diazoacetonitrile occurs at room temperature all the more readily when N-benzylidene-anilines carry *para*-electrodonating substituents. As an example, addition of **2b** is complete after 8 hr, while 80% of **2f** remained unreacted after 25 days. This situation is the reverse in the addition of diazomethane to the same derivatives[2] and implies an electrophilic attack of the diazoacetonitrile to the N-benzylidene-anilines, in the field of the 1,3-dipolar cycloadditions.[3]

With respect to the products, two possibilities can be distinguished.

Starting from **2a, b, c**, triazolines *cis*-**3a, b, c** and *trans*-**4a, b, c** are found in the reaction mixtures in about the same proportions, as can be seen from the corresponding ^{1}H NMR spectra (Table 2); although only **3a** and **3b** were isolated as pure materials. The enamines **9a, b, c** and traces of aziridines appeared at the end of the addition.

In presence of triethylamine, isomerisation of pure **3a** into **4a** was observed, NMR spectroscopy making it possible to follow the change of the protonic AB system. Taking this into account, we feel that isomerisation may occur during the addition of diazoacetonitrile to N-benzylidene-anilines.

Starting from **2d, e, f**, no triazolines were found; we think they are formed but decompose readily. Aziridines *cis*-**5d, e** are formed, in good yield as distinct from the corresponding *trans* isomer **6d, e**. Enamines **9d, e** were also produced.

The enamines **9** are formed by migration of the *p*-R^1-C_6H_4-group to the C atom carrying the cyano group. This was ascertained by independent synthesis. A few cases of such a phenyl migration in the decomposition of triazolines are known.[4]

The percentages of reagent and reaction products are related to the initial quantity of N-benzylidene-anilines; these percentages were determined by ^{1}H NMR spectroscopy of the reaction mixtures after CH_2Cl_2 removal and $CDCl_3$ addition, except for the enamines **9** where the percentages are related to isolated products. For the unreacted N-benzylidene-anilines: integration of the azomethinic proton, under 1.9τ. For the triazolines: integration of the AB system (Table 2) between 4.3 and 5.2τ.

For the aziridines: integration of the AB system (Table 2) between 6.2 and 7.2τ.

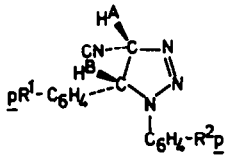
Chemical shifts are expressed in τ and are the corrected values, calculated for AB systems;[11] coupling

Table 1. Addition of diazoacetonitrile (1) to various N-benzylidene-anilines (2)

	R^1	R^2	Reaction times in days	N-benzylidenes anilines 2	Triazolines *Cis* 3 + *Tr* 4	Aziridines *Cis* 5	Aziridines *Tr* 6	Enamines 9
a	H	OCH_3	10	40%	45%	—	—	Traces
			18	15%	35%	Traces		5%
b	$N(CH_3)_2$	OCH_3	0.3	10%	60%	—	—	25%
			4	—	30%	—	—	65%
c	H	$N(CH_3)_2$	0.3	67%	22%	—	—	—
			6	20%	35%	Traces		Present
d	H	H	18	30%	—	18%	2%	10%
e	H	NO_2	25	25%	—	28%	3%	30%
f	NO_2	H	25	80%	—	—	—	—

Reaction temp.: 25°; in the dark.
Solvent: dichloromethane.

Table 2. ^{1}H NMR spectra of triazolines and aziridines at 60 Mc, 25°



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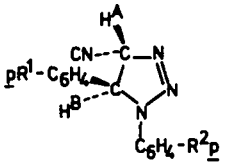

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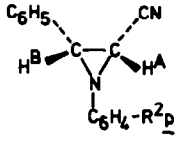
	R_1	R_2	H^A	H^B	$J_{A,B}$ *cis*	H^A	H^B	$J_{A,B}$ *trans*
a	H	OCH_3	4.41	4.67	12.9	4.40	4.68	8.9
b	$N(CH_3)_2$	OCH_3	4.56	4.80	13.1	4.79	4.97	8.8
c	H	$N(CH_3)_2$	4.63	4.89	13.3	4.84	5.08	9.2



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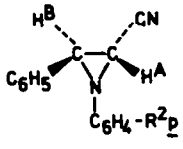

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	R^2	H^A	H^B	$J_{A,B}$ *cis*	H^A	H^B	$J_{A,B}$ *trans*
a	OCH_3	7.15	6.66	5.9 c/s	7.18	6.48	2.4 c/s
d	H	7.03	6.59	5.9 c/s	overlap with H^A of 5d	6.45	2.5 c/s
e	NO_2	6.73	6.29	5.9 c/s			

Solvent: $CDCl_3$.
Internal standard: TMS.

constants are in c/s. Assignations are based on data of the literature.[5,7,12]

The enamines **9** are likely to be generated through the intermediacy of the instable diazoalkanes **7**; the latter are generated by the departure of the acidic proton α to the cyano group and by the opening of the triazoline nuclei.

When the IR spectrum of **3a** and **3b** was taken in presence of triethylamine, strong pics which are typical of the diazo group were observed at 2082 and 2072 cm^{-1} respectively. Catalytic decomposition of these triazolines in NEt_3 leads to enamines **9a** and **9b**, faster for **3b** than **3a**. This opening of the triazolines catalysed by bases has already been observed.[4,5]

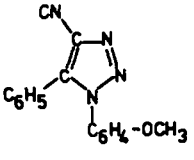
The route from diazoalkanes **7** to enamines **9** is likely through the carbenes **8**, the electrophilic character of the latter explaining the faster formation of **9b** than **9a**.

In addition to the former results, we found a small quantity of triazole **11** in the reaction of **2a** with diazoacetonitrile.[6] The structure of **12** was ascertained by comparison with an authentic sample prepared by addition of *p*-azido-anisole to phenyl-propiolonitrile.

Photochemical decomposition of the *cis*-triazoline **3a** produces the *cis*-aziridine **5a** in a 72% yield and the *trans*-aziridine **6a** in a 15% yield (determined by proton NMR spectroscopy). This good retention of configuration has been found in other photochemical decompositions of triazolines.[7]

Thermal decomposition of *cis*-triazoline **3a** in refluxing benzene gave *cis*-aziridine **5a** in a 38% yield, *trans*-aziridine **6a** in a 30% yield (proton NMR determination) and enamine **9a**, isolated in a 30% yield.

Pure *cis*-aziridine **5a** at 70° in *trans*-cinnamic nitrile gave the enamine **12** which results from the opening of the C–N bond and migration of a proton (structure ascertained through independent synthesis).



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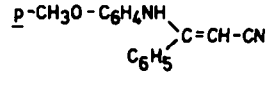

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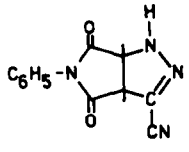
Other similar aziridines open between the two cyclic C atoms,[8] giving 5-membered cyclic adducts with suitable dipolarophiles.

We also investigated the addition of diazoacetonitrile to N-phenylmaleimide. After 6 days at normal temperature in the dark, Δ^2-pyrazoline **13** was isolated in a 65% yield.



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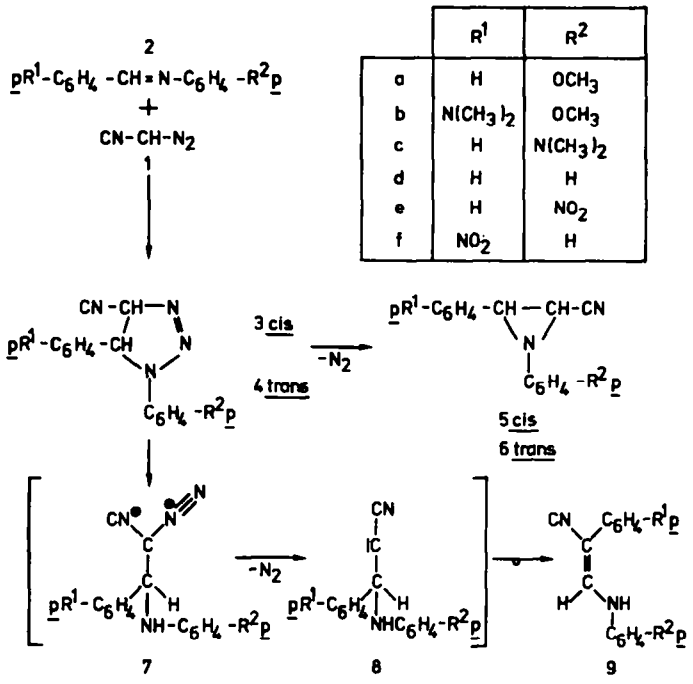
EXPERIMENTAL

^{1}N NMR spectra: JEOL 60; TMS as internal standard; IR spectra: Perkin–Elmer 327 and Beckman IR 12; UV spectra: UNICAM S.P. 800.



	R^1	R^2
a	H	OCH_3
b	$N(CH_3)_2$	OCH_3
c	H	$N(CH_3)_2$
d	H	H
e	H	NO_2
f	NO_2	H

Scheme 1.

Diazoacetonitrile (1 = DAN). Prepared by diazotation of aminoacetonitrile hydrogenosulfate,[9] the product was extracted with di- or tetra-chloromethane. This soln was neutralised (Na_2CO_3), dried one night over Na_2SO_4, filtered and utilised immediately (yield 66%). We did not purify DAN further. In every case there was an explosion during isolation.[9,13] In soln and in the dark, DAN is relatively stable. The concentrations of DAN were determined by integration of the proton at 5.57τ, in mixtures with the N-benzylidene-anilines.

N-benzylidene-anilines (2a–2f = NBA). These azomethines were prepared in usual way, condensing *p*-R^1-benzaldehydes with *p*-R^2-anilines, and recrystallization. The azomethinic proton is always well separated from the aromatic protons, below 1.77τ, in NMR spectra.

Additions of DAN to NBA

General procedure. These were carried out in the dark, at room temp. adding the DAN soln slowly to the NBA soln, all of these being well dried. Initial concentrations of NBA were 0.167 M/l, and of DAN, 0.4 M/l and were the same for **2a, b, c, e, f.** In case of **2d**, the initial concentration of DAN was 0.5 M/l. After reaction the solvent was removed *in vacuo* without warming, and the residue worked up.

Addition of DAN to **2a.** Starting from 10.5 g of **2a**, the mixture was handled following the general procedure. After 10 days an equal quantity of MeOH was added to the resulting mixture and kept 2 days at −20°. The major part the triazoline **3a** was precipitated and was filtered; another part of the remaining **3a** was precipitated by removing the MeOH *in vacuo* and adding ether and keeping the mixture at −20° for some days. The triazoline was dissolved in a 1/1 mixture of MeOH–CH_2Cl_2. This soln was slowly evaporated *in vacuo*, while stirring. 4.18 g of pure *cis* **3a** was isolated as a white powder; m.p.: 133–134°, (dec). (Found: C, 68.63; H, 5.02; N, 19.95. Calc: C, 69.05; H, 5.07; N, 20.13%); IR (KBr): (C≡N): 2250 cm^{-1}; NMR: see Table 2 for the AB system; MeO: 6.22 (singlet, 3 H); aromatic protons: 2.40–3.25 (complex, 9 H).

Triazole (**11**): a few mg of this product were crystallized from the preceding ethereal soln, after one week at −20°; m.p.: 146–150°; IR (KBr): (C≡N): 2247 cm^{-1}; (Found: C, 69.55; H, 4.38; N, 20.28; Calc: C, 69.75; H, 4.38; N, 20.02%).

Enamine **9a**: another mixture prepared as before, was treated with MeOH and ether after 18 days. This gave 3.8 g of **3a**. Ether was then removed *in vacuo* and 10 ml toluene added; on standing a few days at −20°, 600 mg of **9a** crystallized as grey cubes. (Found: C, 76.68; H, 5.60; N 10.83. Calc: C, 76.78; H, 5.64; N, 11.19%), m.p.: 149–155°; IR (KBr): (C≡N): 2205 cm^{-1}; (N–H): 3240 and 3226 cm^{-1}; (C=C): 1640 cm^{-1}; UV (EtOH): γ (max): 30200 cm^{-1}; ε: 22400.

Independent synthesis of **9a.**[10] Condensation of α-formyl, α-phenyl, acetonitrile with *p*-anisidine in refluxing xylene, evaporation of most of the solvent after 1/2 hr; and recrystallization from EtOH yielded yellow needles m.p.: 123–126°; IR (KBr): (C≡N): 2202 cm^{-1}; (N–H): 3302 and 3250 cm^{-1}; (C=C): 1645 cm^{-1}; UV (EtOH): ν (max): 29050 cm^{-1}; ε: 21900. (Found: C, 76.52; H, 5.60; N, 10.91. Calc: C, 76.78; H, 5.64; N, 11.19%).

On very slow evaporation in air, the ethanolic soln left a few grey cubes, m.p.: 150–153°; IR and UV as of **9a** from the addition of DAN to **2a** in refluxing MeOH. The grey cubes afforded yellow needles: m.p.: 120–125°; IR and UV as the preceding yellow needles. Hence these two products are probably the two possible geometrical isomers of **9a**.

Addition of DAN to **2b.** Starting from 12.7 g of **2b**, the mixture was handled following the general procedure after 8 hr. To the resulting mixture, 20 ml acetone was added; the enamine **9b** is only slightly soluble in this solvent, yield: 3.65 g, yellow-brown crystals; m.p.: 191–194° (from acetonitrile); ν (max): 29600 cm^{-1} (EtOH); m.p.: 185–188° (from dioxane); ν (max): 27500 cm^{-1} (EtOH); IR for both fractions ($CHCl_3$): (C≡N): 2197 cm^{-1}; (N–H): 3402, 3310, 3263 cm^{-1}; (C=C): 1636 cm^{-1}.

The acetonic soln was evaporated *in vacuo* and MeOH was added to the resulting mixture. After 1 day −20°, 4.2 g of *triazoline* **3b** was precipitated and was purified by dissolution in a 1/1 mixture of CH_2Cl_2 and MeOH followed by slow evaporation of the solvents *in vacuo*: white powder; m.p.: 131–135°, with dec. (Found: C, 69.05; H, 5.86; N, 21.89. Calc: C, 67.27; H, 5.96; N, 21.79%).

NMR ($DCCl_3$): see Table 2 for the AB system of the cyclic protons; Me_3O: 6.26 (st, 3 H); Me_2N: 7.09 (st, 6 H); IR: ($CHCl_3$): (CN): 2258 cm^{-1}.

On removing the MeOH *in vacuo*, adding ether to the residue, and leaving the mixture at −20° for 2 days, 1.3 g of a mixture of

70% *cis* **3b** and 30% *trans* **4b** was obtained, as can be seen from the two AB systems of the NMR spectrum. The IR spectrum of this mixture is very similar to that of the pure **3b**; we could not obtain pure **4b**.

Addition of DAN to **2c**. No product was isolated by this addition. Nevertheless, NMR spectroscopy of the mixture showed the presence of *cis*-triazolines and *trans*-**4c** (Tables 1 and 2) and IR spectroscopy, the presence of **9c** through a strong peak at 2200 cm^{-1} (CN) and a peak at 1645 cm^{-1} (C=C).

Addition of DAN to **2d**. No triazolines are shown by proton NMR spectroscopy after 6, 12 and 18 days. But aziridines were evidenced by the two AB systems of the cyclic protons (see Table 2) compared with the AB system of pure *cis* **5a**, **e** and with the data in the literature for the *trans* form.

Enamine **9d** was separated in small quantity by column chromatography on silica gel from benzene as pale yellow needles. Recrystallization from different solvents (alcohol, toluene, cyclohexane) made the m.p. vary from 125–131° to 164–167° and the ν (max) from 30250 to 32200 cm^{-1} (EtOH). (Found: C, 81.37; H, 5.39; N, 12.68. Calc: C, 81.79; H, 5.49; N, 12.72. IR ($CHCl_3$): (C≡N): 2200 cm^{-1}; (C=C): 1640 cm^{-1}; (N–H free): 3380 cm^{-1}.

Addition of DAN to **2e**. Starting from 0.05 M of **2e**, the mixture was handled following the general procedure. No triazolines were evidenced after 6, 15 and 25 days. After 25 days, $CHCl_3$ was added to the mixture, solvent in which **9e** is only slightly soluble (5.65 g). Recrystallization in acetonitrile gave orange needles of **9e**, m.p.: 274–277° with sublimation. (Found: C, 66.62; H, 4.19; N, 16.20. Calc: C, 67.91; H, 4.18; N, 15.84%). IR(KBr): (CN): 2213 cm^{-1}; (C=C): 1658 cm^{-1}; (N–H): 3306 and 3257 cm^{-1}; UV: ν (max) 25600 cm^{-1}; ϵ 31200 (EtOH).

$CHCl_3$ was removed *in vacuo* and ether added, as well as a little MeOH in order to dissolve the residue. This mixture was placed at −20° for some days. Pale yellow crystals appeared (2.73 g) which were recrystallized in ether: *cis* **5e**, m.p.: 131–134°. (Found: C, 69.52; H, 4.28; N, 15.13. Calc: C, 67.91; H, 4.18; N, 15.84%). IR ($CHCl_3$): (CN): 2260 cm^{-1}; NMR ($DCCl_3$): see Table 2 for the cyclic protons.

Photodecomposition of cis-*triazoline* **3a**. 500 mg of **3a** were placed in 10 ml CH_2Cl_2 at −15° and irradiated with a high pressure mercury lamp. N_2 evolution ceased after 20 hr. NMR spectroscopy of the mixture made it possible to find a yield of 72% *cis* **5a** and 15% of *trans* **6a**. 300 mg of **5a** were isolated by crystallization in ether as a white powder. (Found: C, 76.78; H, 5.64; N, 11.19. Calc: C, 76.01; H, 5.50; N, 11.19%). IR ($CHCl_3$): (CN): 2255 cm^{-1}; NMR ($DCCl_3$): see Table 2 for the cyclic protons; aromatic protons: 2.7 to 3.6 (complex, 9 H); MeO: 6.26 (st, 3 H).

Thermal decomposition of cis-*triazoline* **3a**. 139 mg of **3a** were dissolved in 10 ml benzene and the soln was heated under reflux until the evolution of N_2 ceased. After removal of the benzene, NMR spectroscopy in CCl_4 made it possible to find 38% of **5a** and 30% of **6a**; 30 mg of **9a** crystallized from a concentrated soln in CCl_4.

Thermal decomposition of cis-*aziridine* **5a**. 125 mg **5a** were dissolved in 5 ml *trans*-cinnamic nitrile and the soln was kept at 70° during 2 weeks. After removal of the cinnamic nitrile in high *vacuo*, the mixture was recrystallized from MeOH. 105 mg of the *enamine* **12** separated as white crystals, m.p.: 148–150°. (Found: C, 76.06; H, 5.53; N, 11.25. Calc: C, 76.78; H, 5.64; N, 11.19%). IR (KBr): (CN): 2189 cm^{-1}; (N–H): 3282 cm^{-1}; (C=C): from 1615 to 1518 cm^{-1}; UV: ν (max) 33100 cm^{-1} and 43500 cm^{-1} (EtOH); NMR ($DCCl_3$): MeO: 6.20 (st, 3 H); H to the CN group: 5.62 (st, 1 H); H animo: 4.10 (st, 1 H).

Independent synthesis of **12**. This achieved by condensation of phenyl-propriolonitrile with *p*-anisidine in abs alcohol. The product obtained had the same characteristics as **12**.

Addition of DAN to N-*phenylmaleimide*. 5.19 g of N-phenylmaleimide were dissolved in 150 ml of a soln of DAN prepared from 7.7 g of aminoacetonitrile hydrogenosulfate. This soln was kept in the dark during 6 days at normal temp. After removal of the CH_2Cl_2, the mixture was crystallized from MeOH and gave 4.8 g of *pyrazoline* **13** as white crystals, m.p.: 192–194°, with dec. (Found: C, 60.13; H, 3.31; N, 23.14. Calc: C, 60.0; H, 3.36; N, 23.33%). IR (KBr): (C≡N); 2223 cm^{-1}; (N–H): 3320 cm^{-1}; (C=C): 1705 cm^{-1}; NMR (CD_3COCD_3): the two bridge-head protons give an AB system at 5.31 and 4.76τ, T = 10.95 c/s; the animo proton appeared as a doublet at 0.8τ, and was coupled with the proton to it (4.76τ), T = 2.4 c/s; this coupling disappeared when putting D_2O in the sample. Integrations were consistent with this interpretation.

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