Competition between Ethylenic and Nitrile Groups in the Intramolecular Capture of Nitrile Imines

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o-Vinylphenylhydrazonyl chlorides (2) react with triethylamine in boiling benzene to afford cyclopropa[*c*]cinnolines (4) and [1,2,4]triazolo[1,5-*a*]quinolines (5). Under the same conditions, the structurally related compounds (7) give 1,2-benzodiazepines (10). A mechanism is proposed involving nitrile imine intermediates which cyclise through participation of the nitrile or ethylenic group.

Cyclisation reactions of nitrile imines with unsaturated compounds represent a well-established method for the construction of heterocycles.[1-3] In the case of appropriately functionalised nitrile imines, ring closure can also occur intramolecularly, thus widening the synthetic potential of these intermediates.[3,4] In this context, we were interested in the behaviour of the nitrile imines (3a—c) and (8a—c) with the aim of studying the possible competition between C=C and C≡N bonds in the intramolecular capture of the nitrile imine moiety (see Schemes 1 and 2).

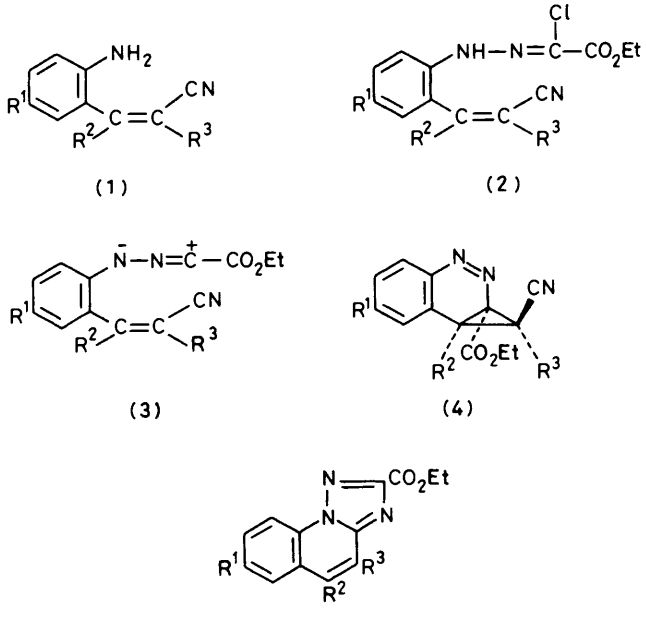
Results and Discussion

Compounds (3a—c) and (8a—c) were generated *in situ* upon treatment of the corresponding hydrazonyl chlorides (2a—c) and (7a—c) with an excess of triethylamine in boiling benzene. The latter precursors were, in turn, synthesized from the known amines (1a—c) and (6a—c) through diazotisation and coupling with ethyl 2-chloroacetoacetate. The reaction of (2a—c) and (7a—c) under the above conditions was complete within 30 min and gave the products indicated in Table 1.

The product structures were assigned on the basis of analytical and spectral data (see Table 2). In particular, while the *cis*-relationship between the cyclopropyl hydrogens of (4a) is unequivocally shown by the observed coupling constant,[5,6] the stereochemistry of (4b) follows from the chemical shift of the cyclopropyl hydrogen, which is consistent with some deshielding effect of a *cis* located phenyl group. On the other hand, the position of the R^3 substituent in (4c) is well established by its n.m.r. signal in comparison with those reported for *endo*- and *exo*-methyl groups in similar compounds.[6,7] It was ascertained by control experiments that the tricyclic compounds (4a) and (4b) are not stable in boiling benzene, both in the presence and in the absence of triethylamine, but they rearrange to (10a) and (10b) respectively. No change was observed under the same conditions in the case of (4c).

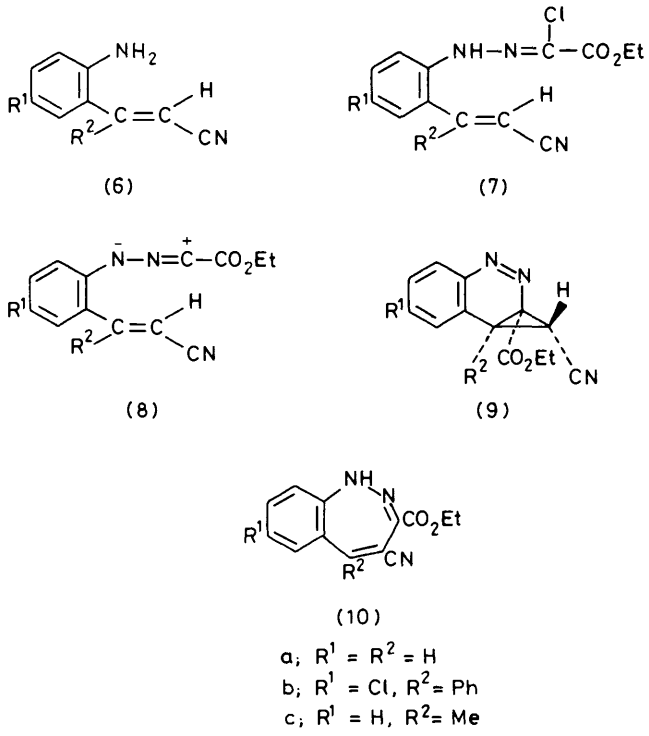
The formation of the ring-closed products (4), (5), and (10) indicates that the nitrile and ethylenic functions compete to capture intramolecularly the nitrile imine dipole. In the first case, a 1,3-cycloaddition occurs in a fashion similar to that observed in intermolecular reactions of nitrile imines with conjugated nitriles.[8] Such a pathway is actually preferred whenever the *cis*-relationship between the nitrile and aryl groups permits the intramolecular contact of the reactive centres.

As to the participation of the ethylenic bond, two different mechanisms are, in principle, conceivable: (i) 1,7-electrocyclisation to the original dipolar intermediates such as (11) or (12), which then undergo either a hydrogen shift or (potentially reversible) valence tautomerisation to give, respectively, 1,2-benzodiazepines or cyclopropa[*c*]cinnolines; (ii) intramolecular cheletropic addition to form cyclopropa[*c*]cinnolines, which may be isolable products or transient species leading to 1,2-benzodiazepines. The latter mechanism has been advanced by Padwa and Nahm for nitrile *N*-(2-vinylphenyl)imines generated *in situ* upon treatment of hydrazonyl chlorides with silver carbonate.[6] On the other hand, we have previously found that the cyclisation of similar substrates under phase-transfer conditions is better interpreted according to mechanism (i).[9] In the present case, the retention of stereochemistry observed in the formation of (4) fits well to a concerted pathway, but it is also consistent with the intermediacy of (11) as long as the reaction of this species is fast with respect to the reversal of the seven-membered ring.† Significant evidence was obtained on treating (2) with triethylamine in boiling ethanol: in this solvent, the ratios (4) : (5) in the product mixtures were much larger than those found in

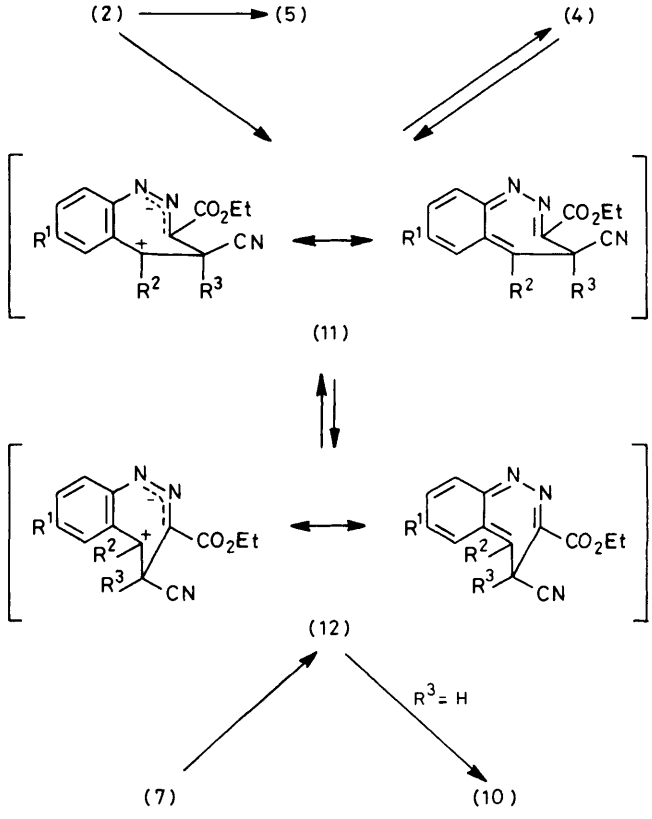


Scheme 1

† The existence of an energy barrier for the ring inversion in 1,2-diazepines is documented.[10-12]



Scheme 2



Scheme 3

Table 1. Reaction of the hydrazonyl chlorides (2) and (7) with triethylamine in boiling benzene

Compound	Products	Yields (%)	Isolation procedure [a]
(2a)	(4a)	29	A
	(5a)	53	
(2b)	(4b)	45	A
	(5b)	34	
(2c)	(4c)	14	A
	(5c)	66	
(7a)	(10a)	78	B
(7b)	(10b)	91	B
(7c)	(10c)	89	B

[a] A, Column chromatography on silica gel with 50 : 45 : 5 light petroleum–diethyl ether–triethylamine as eluant (products are given in order of elution); B, treatment of the crude product with di-isopropyl ether and subsequent filtration.

benzene, despite the presence of some (10a) and (10b) (see Experimental section). This result indicates that the parallel processes leading to (4) and (5) involve transition states of different polarity, the former being more polar than the latter. This is in harmony with the intervention of (11) before the formation of (4).

Another point is particularly worthy of note and needs rationalisation. The absence of (9) among the products arising from (7) is at variance with the obtention of (4) from (2), showing that stereoelectronic factors dictate the mode of evolution of the intermediates (11) and (12). It may be that the final 1*H*-1,2-benzodiazepines (10) derive from an intramolecular 1,5-sigmatropic hydrogen shift, which would require the spatial disposition just attained in (12), but not in (11). Hydrogen migrations through a 1,5-sigmatropic path are known to occur in rearrangements of seven-membered heterocycles.[12–14]

Experimental

M.p.s were taken with a Büchi apparatus and are uncorrected. N.m.r. spectra were obtained with a Varian EM-390 instrument, using $SiMe_4$ as an internal standard. I.r. spectra were recorded with a Perkin-Elmer 377 spectrophotometer. H.p.l.c. analyses were performed on a Millipore-Waters ' Mod. 244 with gradient ' Liquid Chromatograph.

Amines (1a),[15] (1b),[16] (1c),[15] (6a),[17] (6b),[15] and (6c) [15] were prepared according to literature methods.

Preparation of Hydrazonyl Chlorides (2a—c) *and* (7a—c).—Compounds (2a—c) and (7a—c) were prepared from the amines (1a—c) and (6a—c) following the procedure previously reported for (7a).[7] All of them were obtained in the pure state by column chromatography on silica gel with 1 : 1 light petroleum–diethyl ether as eluant (see Table 3).

Treatment of Hydrazonyl Chlorides (2a—c) *and* (7a—c) *with Triethylamine.*—(A) A solution of hydrazonyl chloride (2) or (7) (10 mmol) and triethylamine (40 mmol) in dry benzene (500 ml) was refluxed for 30 min. The mixture was washed with water, dried with Na_2SO_4, and evaporated. The residue was worked up as indicated in Table 1 to afford the products reported therein (see Table 2).

(B) A solution of hydrazonyl chloride (2) or (7) (2 mmol) and triethylamine (8 mmol) in absolute ethanol (100 ml) was refluxed for 15 min. The solvent was removed under reduced pressure, and the residue was taken up with ether, washed with water, and dried with Na_2SO_4. After evaporation of the solvent, the residue was submitted to n.m.r. analysis. In the case of (7a—c), the product was practically pure (10a—c). In the other cases, the following mixtures were obtained: (2a) gave (4a), (5a), and (10a) in the proportion 65 : 20 : 15;

Table 2. Physical, spectral, and analytical data of compounds (4), (5), and (10) [a]

Compd.	M.p. [b] (°C)	$\nu_{max.}$ (Nujol)/cm^{-1}	δ ($CDCl_3$) [c,d]	Elemental analysis (%) Found (required) C	H	N
(4a)	99 [e]	2 240, 1 730	3.48, 3.58 (2 H, AB type, *J* 9), 7.4—7.8 (3 H, m), 8.4—8.6 (1 H, m)	64.8 (64.7)	4.6 (4.6)	17.2 (17.4)
(4b)	140	2 240, 1 735	4.20 (1 H, s), 6.7—7.8 (7 H, m), 8.35 (1 H, d, *J* 8)	65.0 (64.9)	3.9 (4.0)	11.9 (11.9)
(4c)	116	2 240, 1 725	1.87 (3 H, s), 3.40 (1 H, s), 7.4—7.8 (3 H, m), 8.3—8.5 (1 H, m)	65.8 (65.9)	5.2 (5.1)	16.3 (16.5)
(5a) [f]	133	1 725	7.5—8.0 (5 H, m), 8.6—8.8 (1 H, m)	64.6 (64.7)	4.5 (4.6)	17.5 (17.4)
(5b) [f]	187	1 720	7.4—8.0 (8 H, m), 8.69 (1 H, d, *J* 8)	64.7 (64.9)	4.1 (4.0)	11.8 (11.9)
(5c) [f]	120	1 730	2.78 (3 H, d, *J* 1), 7.5—7.9 (4 H, m), 8.6—8.8 (1 H, m)	66.0 (65.9)	5.1 (5.1)	16.4 (16.5)
(10b)	225	3 280, 2 220, 1 730	6.68 (1 H, d, *J* 2.5), 6.85 (1 H, d, *J* 8), 7.2—7.6 (7 H, overlapping signals)	64.8 (64.9)	3.9 (4.0)	11.9 (11.9)
(10c)	182	3 290, 2 220, 1 740	2.57 (3 H, s), 6.75—6.95 (1 H, m), 7.1—7.5 (4 H, overlapping signals)	65.7 (65.9)	5.0 (5.1)	16.6 (16.5)

[a] Compound (10a) is described in ref. 7. [b] From di-isopropyl ether unless otherwise noted. [c] The signals of the ethyl group are not given. [d] *J* in Hz. [e] From n-pentane. [f] B. A. Dreikorn and K. E. Kramer, *Ger. Offen.*, 1973, 2 239 892 (*Chem. Abstr.*, 1973, **78**, 136304) and U.S. Patent, 1976, 3 953 457 (*Chem. Abstr.*, 1976, **85**, 29564).

Table 3. Preparation of the hydrazonyl chlorides (2) and (7) [a,b]

Compd.	Yield (%)	M.p. (°C)	δ ($CDCl_3$) [c,d]	Elemental analysis (%) Found (required) C	H	N
(2a)	45	95—96 [e]	5.62 (1 H, d, *J* 12), 7.0—7.8 (5 H, m), 8.3 (1 H, br s)	56.3 (56.2)	4.2 (4.3)	15.3 (15.1)
(2b)	74	199—200 [f]	6.10 (1 H, s), 7.3—7.8 (8 H, m), 8.1 (1 H, br s)	58.5 (58.7)	4.0 (3.9)	10.6 (10.8)
(2c)	37	111—112 [f]	2.23 (3 H, d, *J* 1.5), 7.0—7.7 (5 H, m), 8.2 (1 H, br s)	57.5 (57.6)	4.9 (4.8)	14.2 (14.4)
(7b)	66	164—165 [f]	5.62 (1 H, s), 7.2—7.7 (8 H, m), 7.9 (1 H, br s)	58.9 (58.7)	3.6 (3.9)	10.8 (10.8)
(7c)	75	68—69 [e]	2.46 (3 H, d, *J* 1.2), 5.50 (1 H, q, *J* 1.2), 7.0—7.7 (4 H, m), 8.4 (1 H, br s)	57.7 (57.6)	4.8 (4.8)	14.5 (14.4)

[a] Compound (7a) is described in ref. 7. [b] All compounds listed gave correct i.r. spectra. [c] The signals of the ethyl group are not given. [d] *J* in Hz. [e] From n-pentane. [f] From di-isopropyl ether.

(2b) gave (4b), (5b), and (10b) in the proportion 75 : 10 : 15; (2c) gave (4c) and (5c) in the proportion 65 : 35.

Conversion of (4a, b) *into* (10a, b).—A solution of (4a) (1 mmol) and triethylamine (4 mmol) in benzene (50 ml) was refluxed for 3 h. The mixture was washed with water, dried with Na_2SO_4, and evaporated. The residue was practically pure (10a) (n.m.r. analysis).

Under the same conditions (8 h), compound (4b) gave practically pure (10b).

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