

N-CYANOAMIDES. TAUTOMETRIC STRUCTURE, IONIZATION, AND CONFORMATION

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Received February 24th, 1975

N-Cyanobenzamide (*IVa*) and its ring substituted derivatives *IVb-d* exist in the tautomeric amidic form as follows from their IR and UV spectra under various conditions. Hence they represent a class of true N-acids, more acidic than the corresponding carboxylic acids. The similarity to carboxylic acids and to hydroxamic acids is reflected in the Hammett correlations of p*K* values and of log *k* of the reaction with diphenyldiazomethane. The conformation of N-cyanobenzamides as determined from the dipole moments in solution is *Z*, i.e. the same as that of N-alkylamides, in spite of the opposite electrical character of the cyano and alkyl groups.

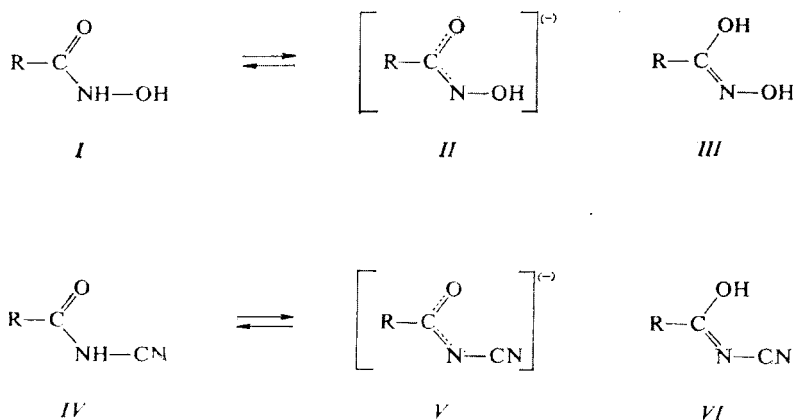
The acidic properties of N-acids have been relatively little investigated, although some recent studies¹⁻⁴ revealed that these acids are more acidic and more common than generally assumed. In particular the whole group of hydroxamic acids *I* — except possibly some very weakly acidic derivatives — is to be classified as N-acids since the NH hydrogen dissociates more easily than the OH hydrogen⁵. This case is relatively complex since there are two possible tautomeric forms of the acid (*I*, *III*) and three of the anion; a detailed investigation was necessary⁶⁻⁸ to prove that the dissociation is actually represented by the equilibrium $I \rightleftharpoons II$.

In this paper we are dealing with N-cyanoamides as simpler model compounds, which can exist in two tautomeric forms only (*IV*, *VI*) while the structure of their anion is unambiguous (*V*). The results will be compared with the previous ones concerning hydroxamic acids⁶⁻⁸ and could serve as their additional support. The N-cyanoamides themselves^{9,10} as well as their acidic properties¹⁰ are known; hence this study has been restricted to aromatic derivatives *IVa-d*.

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RESULTS AND DISCUSSION

Structure and tautomerism. Although N-cyanobenzamides seem to have been well characterized in previous studies^{9,10}, we wanted first to confirm that they are monomeric and not contaminated by polymeric material. The mass spectra of *IVa* (and *IVc*) excluded this possibility but a perceivable amount of the hydrated compound — N-benzoylurea — was observed even in purified samples. To check the possibility of contamination we prepared this compound¹¹ and investigated the IR spectra of its mixtures with *IVa*. On this basis as well as from the elemental analysis we can with certainty exclude a contamination by 3% or more.



a, R = C₆H₅; *b*, R = 3-NO₂C₆H₄; *c*, R = 4-BrC₆H₄; *d*, R = 4-CH₃C₆H₄

The problem of tautomeric structure, *IV* or *VI*, was investigated by the IR and UV spectroscopy. The IR spectra of *IVa* in Nujol and in various solvents (Table I) revealed the C=O and N—H bands as well as an N—D band after deuteration; no trace of an O—H or O—D absorption was detected. According to the experience reached with hydroxamic acids^{8,12} the deuterium bands are particularly relevant while the C=O frequency of a conjugated system O=C=N need not differ too much from the C=N frequency. To obtain a convincing proof even from the carbonyl region, we used methyl N-cyanobenzimidate (*VII*) as a model with the fixed tautomeric structure *VI*. We prepared it from methyl benzimidate and bromocyan and checked its structure by ¹H NMR spectroscopy (OCH₃, δ = 3.50 p.p.m.). The frequency of its C=N band differs clearly from C=O in *IVa* (Table I). In the field of hydroxamic acids similar results were obtained^{8,12} by comparison of benzohydroxamic acid (*Ia*) with (*Z*)-O-methylbenzohydroxamic acid (*VIII*), but the C=O frequency of the former was lowered by an intramolecular hydrogen bond.

In the $^1\text{H-NMR}$ spectra of *IVa-d* in dimethyl sulphoxide a very broad peak appears in the region 10–11 p.p.m. which cannot be safely assigned to the NH or to the OH hydrogen. Some hydroxamic acids show a similarly situated, more distinct peak¹³.

Electronic spectra of N-cyanobenzamides *IVa-d* show one absorption maximum in the region of 224–250 nm according to the substitution (Table II). This corresponds to the spectra of similarly substituted benzohydroxamic acids or even benzamides. For the unsubstituted compounds the maximum is situated at 229–238 nm and may be connected with the conjugated system $\text{C}_6\text{H}_5\text{CO}$. The tautomeric structure *VI* involves a longer conjugated system $\text{C}_6\text{H}_5\text{C}=\text{NO}$; the maximum of the model compound *VII* is actually shifted to longer wavelengths and approaches that of benzaldoxime.

In the alkaline solution the absorption maxima of N-cyanobenzamides are shifted bathochromically up to the values of 256–260 nm (Table II). Even this behaviour is in evidence for the tautomeric form *IV*; if the dissociation were expressed by the equilibrium $\text{VI} \rightleftharpoons \text{V}$, the maxima would not be appreciably shifted. Benzohydroxamic acids *I* exhibit a similar bathochromic shift with ionization⁷, even the absorption of the anion lies almost at the same wavelength.

Hence the results of the two methods suggest *IV* to be the only or the prevailing tautomeric structure; these methods would be, of course, unable to detect the presence of structure *VI* in an amount of several percent or less.

Ionization. Since the anion of N-cyanoamides has the unambiguous structure *V*, the dissociation constants (Table III) are related to the equilibrium $\text{IV} \rightleftharpoons \text{V}$. In comparison with the corresponding carboxylic acids having hydroxyl in place of the NHCN group, N-cyanoamides are stronger acids by c. 1 pK unit; when compared with hydroxamic acids they are stronger by almost 6 pK units. Hence the CN group as a second substituent is able to compensate for the less electronegativity of nitrogen compared with oxygen, while the hydroxyl group is not. It is the possibility of two-fold substitution which gives some N-acids such an acidity that they are comparable to the strong O-acids^{1,4}. When we regard *IVa* as a disubstituted ammonia, we can evaluate the substituent effects by referring to the pK values of benzamide¹⁴ (pK = 14–15) and cyanamide¹⁵ (pK 10.27). Although these old values are not completely dependable, it is clear that the effects of substituents are not additive, N-cyano-

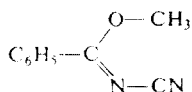
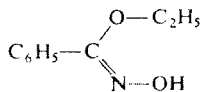
*VII**VIII*

TABLE I
Characteristic Vibrations of N-Cyanobenzamide *IVa* and of Some Model Compounds (cm^{-1})

Compound	Solvent	$\nu(\text{C}=\text{O})$	$\nu(\text{N}-\text{H})$	$\nu(\text{N}-\text{D})^a$	$\nu(\text{C}\equiv\text{N})$
<i>IVa</i>	dioxan	1 735	3 280	2 480	2 330
<i>IVa</i>	tetrahydrofuran	1 730	3 160	2 450	2 350
<i>IVa</i>	chloroform	1 730	3 240	2 450	2 300
<i>IVa</i>	acetonitrile	1 720	3 100	2 480	2 300
<i>IVa</i>	Nujol	1 685	3 260	2 480	2 330
<i>VII</i>	Nujol	1 620 ^b	—	—	2 320
<i>Ia</i> ^c	dioxan	1 670	^d	2 443	—
<i>VIII</i> ^c	dioxan	1 641 ^b	^d	—	—

^a In deuterated molecules; ^b $\nu(\text{C}\equiv\text{N})$; ^c ref.^{8,12}; ^d the band is obscured by the hydrogen bonded O—H band.

TABLE II
Electronic Spectra of N-Cyanobenzamides *IVa-d* and of Model Compounds

Compound	λ , nm (log ϵ)	
	0.1M-HCl	0.1M-KOH
<i>IVa</i>	238 (4.15)	256 (4.31)
<i>IVb</i>	224 (4.55)	260 (4.49)
<i>IVc</i>	237 (4.51)	260 (4.56)
<i>IVd</i>	250 (4.35)	258 (4.50)
<i>Ia</i>	230 (3.94)	267 (3.90)
<i>Id</i>	239 (4.22)	265 (3.96)
Benzamide	229 (4.13)	228 (4.21)
4-Toluamide	239 (4.23)	240 (4.33)
<i>VII</i>	258 (4.28)	—
<i>VIII</i>	244 ^a (3.94)	269 ^b (4.01)
(<i>E</i>)-Benzaldoxime	250 (4.10)	—

^a In 50% ethanol, ref.⁸; ^b in 50% ethanol with NaOH (0.1M), ref.⁸

benzamide being by some 8 pK units weaker acid than expected. Similar behaviour is observed with other N-acids⁴.

The restricted number of substituents does not allow to determine the Hammett constant ρ for substituted N-cyanobenzamides more precisely. In water the rough estimate is $\rho = 0.9$, in 80% methyl cellosolve a somewhat more precise value of 1.73 is obtained. For pK's in 50% methanol $\rho = 1.32$ was determined¹⁰. The values in water and in 80% methyl cellosolve are virtually identical with those for benzoic acids (1 and 1.68, respectively) or for benzohydroxamic acids^{6,17} (0.98 and 1.70); in all the cases the ionization proceeds on the second atom from the benzene nucleus.

In all respects N-cyanoamides behave similarly as the corresponding hydroxamic acids. This close resemblance represents an additional evidence that even the latter belong to the N-acids, at least in typical examples.

Reaction with diphenyldiazomethane. As a further measure of acidity (the so-called kinetic acidity) we have measured the rate of the reaction of *IVa-d* with diphenyldiazomethane. In acetone solution the N-benzhydryl derivative is the only expected product, nevertheless, we isolated the product of reaction of *IVa* on the preparative scale and checked its structure by its IR spectrum (ν_{CO} , 1725 cm^{-1}). The rate constants in Table III are higher than those of the corresponding benzoic acids, as expected from the lower pK values. The ρ constant of 0.86 is markedly lower than that for benzoic acids in the same solvent¹⁸ (1.93). The two values are, however, based on a small number of points and particularly the latter seems to be too high.

A general parallelism has been observed between pK and $\log k$ of the reaction with

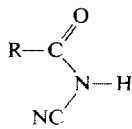
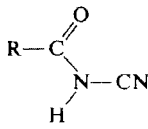
TABLE III
Some Physico-chemical Constants of N-Cyanobenzamides *IVa-d*

Compound	pK		$\log k_2$ DDM ^b	∞P_2^c cm^3	$R_D^{20 d}$ cm^3	μ^e D	$\mu_{\text{calc. D}}$	
	H ₂ O	MCS ^a					E	Z
<i>IVa</i>	2.93 ^f	3.88	-0.36	734	38.7	5.83 (5.81)	1.73	6.00
<i>IVb</i>	2.55	2.62	0.26	^g	—	^g	—	—
<i>IVc</i>	^g	3.31	-0.01	651	46.4	5.42 (5.40)	3.20	4.66
<i>IVd</i>	3.40	4.04	-0.44	838	43.3	6.23 (6.20)	1.50	6.26

^a 80% methyl cellosolve by weight; ^b second-order rate constants of the reaction with diphenyldiazomethane (acetone, 30°C) $1 \text{ mol}^{-1} \text{ min}^{-1}$; ^c molar polarization in benzene (25°C) extrapolated to zero concentration; ^d molar refraction calculated from Vogel's increments¹⁶; ^e dipole moments (in benzene) with a correction for atomic polarization of 5% (or 15%, in parentheses) of the R_D value; ^f ref.¹⁰ gives pK 2.71; ^g insufficiently soluble.

diphenyldiazomethane for the whole class of O-acids¹⁹. The correlation is, however, closer for restricted subgroups of structurally more similar compounds, so that the whole picture split into separate, nearly parallel lines. When N-cyanoamides are included, they form an additional line and fit into the overall pattern.

Conformation. The problem of conformation of N-cyanoamides resembles that of secondary amides²⁰ or of hydroxamic acids²¹. Owing to the partial double character of the C≡N bond, two planar forms are *a priori* possible (*IVE*, *IVZ*). The decision in favour of *IVZ* was made on the basis of dipole moments in solution (Table III). The calculated moments were obtained by vector addition of the following bond moments (see²¹): C≡N 3.6 D, C=O 2.5 D, C—N 0.45 D, H—N 1.31 D. The bond angles used were ∠C—C—O 124°, ∠C—C—N 115°, ∠C—N—C 124°, ∠N—N—C 115°. The decision is unambiguous in the case of derivatives *IVa* and *IVd*; the worse agreement in the case of *IVc* may be connected with its low solubility, making the experimental value less dependable.

*IV E**IV Z*

The *Z* conformation found is the same as for the salt of N-cyanourea in crystal²² and agrees with the conformation of almost all secondary amides²⁰, in spite of the opposite electrical character of the CN and alkyl groups. This allowed us to test simply the importance of electrostatic effects in determining conformation. Recently the electrostatic energy of the *E* and *Z* conformers of methyl formate has been calculated from gross atomic charges obtained by population analysis²³. Not only the preference of the *Z* form was correctly predicted but even the energy difference. This led up to renew the idea²⁴ of electrostatic forces controlling conformation. We got similar results for methyl benzoate, even when the gross atomic charges were calculated simply from bond moments and bond lengths, and the calculation was checked by comparison with the experimental dipole moment. The same approach is still successful for N-methylbenzamide, although the calculated energy difference is too low, and for N,N-dimethylbenzohydrazide (the conformation *E* prevails, see²⁵) when all possible positions on the N—N bond are taken into account. However, for N-cyanobenzamide the approach fails completely, predicting clearly the wrong conformation *E*. We conclude that this simplified concept^{23,24} overestimates the electrostatic energy and its importance for the conformation.

EXPERIMENTAL

Substituted N-cyanobenzamides were prepared by the extraction of calcium cyanamide from technical nitrolime and by a subsequent acylation^{10,26}. N-Cyanobenzamide (*IVa*) m.p. 143°C (lit.¹⁰ m.p. 142°C). N-Cyano-3-nitrobenzamide (*IVb*) m.p. 164°C (lit.¹⁰ 151°C); for C₈H₅N₃O₃ (191.2) calculated: 50.27% C, 2.64% H, 21.98% N; found: 50.49% C, 2.78% H, 22.01% N. N-Cyano-4-methylbenzamide (*IVd*) m.p. 166°C (lit.²⁶ 155°C); for C₉H₈N₂O (160.2) calculated: 67.49% C, 5.03% H, 17.49% N; found: 67.19% C, 5.13% H, 17.66% N. N-Cyano-4-bromobenzamide (*IVc*) yield 56%, m.p. 187°C (acetone). For C₈H₅BrNO₂ (225.1) calculated: 42.69% C, 2.24% H, 12.45% N; found: 42.30% C, 2.24% H, 12.48% N. [N-D]N-Cyanobenzamide was prepared by crystallization from dioxan-deuteriumoxide in an atmosphere of nitrogen, m.p. 147°C. For C₈H₅DN₂O (147.1) calculated: 65.30% C, 3.43% H, 19.05% N; found: 65.21% C, 3.64% H, 19.17% N.

Methyl N-cyanobenzimidate (VII). A solution of methyl benzimidate (2.7 g) and bromocyan (1.06 g) in ether (100 ml) was left 3 days at room temperature, filtered, the solvent evaporated and the product distilled *in vacuo*. Yield 0.67 g (42%) b.p. 150–153°C/2 Torr, $n_D^{20} = 1.5335$; the purity was checked by ¹H-NMR spectroscopy and TLC. For C₉H₈N₂O (160.2) calculated: 67.50% C, 5.04% H, 17.50% N; found: 67.42% C, 5.26% H, 17.12% N. In a patent literature²⁷ b.p. 115–125°C/0.3 Torr is given for a product prepared from methyl *ortho* benzate.

Kinetic runs. Reaction of diphenyldiazomethane²⁸ with N-cyanoamides (*IVa–d*) in purified acetone²⁹ was followed at 30°C under pseudomonomolecular conditions at the initial concentration $4 \cdot 10^{-3}$ of diphenyldiazomethane and $5 \cdot 10^{-2}$ of *IV*. The concentration of diphenyldiazomethane was measured spectrophotometrically at the wavelength 525 nm in a 1 cm cell on the apparatus Zeiss VSU-2.

N-Cyano-N-benzhydrylbenzamide. To a solution of *IVa* (1.46 g) in ether (30 ml) a solution diphenyldiazomethane (1.94 g) in pentane (50 ml) was added and the mixture left at room temperature overnight. After evaporation of solvents the residue was crystallized from chloroform–hexane; yield 35%, m.p. 165°C. For C₂₁H₁₆N₂O (314.4) calculated: 80.75% C, 5.16% N, 8.97% N; found: 80.49% C, 5.04% H, 8.66% N. The IR spectrum shows bands at 1725 cm⁻¹ (C=O), 2320 cm⁻¹ (C≡N), 1275 cm⁻¹ (C–N).

Physical measurements. Apparent dissociation constants were determined by potentiometric titration using the Beckmann Research pH-meter, a glass electrode Radiometer G 2222 and a calomel electrode Radiometer K 4112 DP. Titration by 0.1M aqueous tetramethylammonium hydroxide was carried out at 25 ± 0.1°C under nitrogen saturated with solvent vapour; concentration of the substrate was $5 \cdot 10^{-2}$.

Electronic spectra were recorded on a UNICAM SP-800 spectrophotometer, IR spectra on a Spectromom 2000 and ¹H NMR spectra on a Tesla BS 487 A apparatus. Mass spectra were measured in the Institute of Organic Chemistry and Biochemistry, Czechoslovak Academy of Sciences, Prague, on an AEI 902 spectrometer (direct inlet, temperature of the ion source 120–160°C, electron energy 70 eV). Dipole moments were measured in the Department of physical Chemistry, Institute of Chemical Technology, Prague, by the method described previously²¹.

We are indebted to Professor M. Večeřa who rendered possible the experimental work in the Department of Organic Chemistry, Institute of Chemical Technology, Pardubice, and Dr K. Kalfus for valuable advices concerning potentiometry. Thanks are also due to Dr L. Dolejš for measuring and discussing the mass spectra and Mrs M. Kuthanová for measuring the dipole moments. Elemental analyses were carried out by the staff of Department of Analytical Chemistry, Institute of Chemical Technology, Pardubice.

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Translated by the author (O. E.).