

STRUCTURE OF "CARBONYL CYANIDE PHENYLHYDRAZONES" AS EVIDENCED BY MULTINUCLEAR NMR

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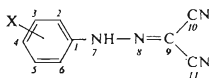
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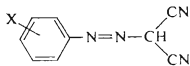
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The structure of "carbonyl cyanide phenylhydrazones" has so far not been settled. The substances possess, according to a multinuclear NMR measurements, a phenylhydrazone grouping. This finding enabled us to propose the denomination phenylhydrazonopropanedinitriles for these compounds.

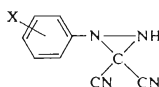
"Carbonyl cyanide phenylhydrazones" exhibit bacteriostatic, antituberculous, trichomonastic, antifungal, insecticide, and fasciolicide effects¹⁻⁴. They are highly effective inhibitors of oxidative phosphorylation⁵⁻⁷, since they are able to decouple mitochondrial oxidation from phosphorylation; this leads to a failure of adenosine triphosphate synthesis. Although these substances are a useful tool for investigating the bioenergetic processes⁷⁻¹⁰, the molecular mechanism of their action remains undissolved. The prerequisite for a successful study of the biochemical reaction mechanisms is doubtlessly the knowledge of the structure of reactants. Carbonyl cyanide phenylhydrazones can be classified according to the majority of proposals into phenylhydrazones *I* (ref.²), azobenzenes *II* (ref.¹) or diaziridines *III* (ref.^{11,12}), nevertheless the X-ray analysis¹³ of crystals evidences the structure *I*.



I



II



III

X — substituent

This paper deals with the structure elucidation of the unsubstituted compound (X = H) in solution from its ¹H, ¹³C and ¹⁵N NMR spectra.

EXPERIMENTAL

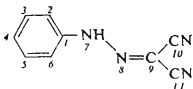
Carbonyl cyanide phenylhydrazones were obtained by diazotization of aniline with NaNO_2 followed by a copulation of the diazonium salt with malonodinitrile, *cf.*¹. The purity of the final product (m.p. 147°C) was verified by chromatography. The ^{15}N -labelled derivatives were prepared from $\text{Na}^{15}\text{NO}_2$ (90% ^{15}N) or ^{15}N -aniline (90% ^{15}N , Isocomerz, GDR). Measured were 1M solutions in acetone or hexadeuterioacetone (Uvasol, Merck). All spectra were measured on a JEOL FX-100 spectrometer, operating at 99.60 MHz for protons, 25.47 MHz for carbons and 10.08 MHz for nitrogen, equipped with a multinuclear probe. The internal deuterium or external lithium lock was employed. The ^1H and ^{13}C NMR chemical shifts are relative to tetramethylsilane, the ^{15}N NMR chemical shifts to nitromethane (indirectly through the absolute ^1H NMR resonance of tetramethylsilane, *cf.* ref.¹⁴) as internal standards.

RESULTS AND DISCUSSION

The ^1H NMR spectrum of the sample measured at 22°C in deuterioacetone shows a complex multiplet at δ 7.2–7.6 due to a spin system of aromatic protons and a broad singlet at δ 11.9 ascribable to one proton. This proton is active, since its signal

TABLE I

The NMR spectral parameters of carbonyl cyanide phenylhydrazones at 22°C



Location	Chemical shifts, δ			$J(^{13}\text{C}-^{15}\text{N})$, Hz ^a	
	^1H	^{13}C	^{15}N	$\text{N}_{(7)}$	$\text{N}_{(8)}$
1	—	142.1	—	18.6	6.3
2, 6	—	117.1	—	1.8	2.0
3, 5	7.2–7.6	130.5	—	2.3	1
3	—	126.8	—	—	—
7	11.9	—	—199.5 ^b	—	—
			—205.0		
8	—	—	—5.0 ^b	—	—
			—5.5		
9	—	86.5	—	1.4	7.6
10	—	114.2	—	2.0	1
11	—	109.8	—	3.9	11.8

^aThe constant values were read from expanded spectra of a digital resolution 0.125 Hz; ^b at –75°C.

disappeared after addition of $^2\text{H}_2\text{O}$; as it follows, the azo structure, which does not imply an acidic hydrogen, is little probable. The ^{13}C NMR spectrum is in line with this suggestion. Signals of aromatic and nitrile carbons have characteristic chemical shifts in the ^{13}C NMR spectrum and can be unambiguously identified (Table I). The remaining signal at δ 86.4 belongs to the carbon bearing the nitrile grouping. The off-resonance multiplicity¹⁵ reveals that this carbon does not bear any proton and consequently, it excludes the structure *II*. Its position in the spectrum, however, does not offer an unequivocal information enabling to decide whether the particular carbon is sp^2 or sp^3 hybridized, in other words to exclude one of the structures *I* or *III*. The key factor for structure elucidation of carbonyl cyanide phenylhydrazones is the determination of the nitrogen atom to which the proton is linked. The determination is based upon the magnitude of the ^1H — ^{15}N spin-spin interaction of a ^{15}N -labelled derivative either by the ^1H or ^{15}N NMR methods. The coupling constant between the directly bound ^1H and ^{15}N atoms makes between 60 and 100 Hz. The two-bond coupling, on the other hand, is always smaller than 20 Hz (ref.¹⁶). The exchange of the proton between the NH group of carbonyl cyanide phenylhydrazone and the solvent complicates the determination; it effectively averages the interaction to zero at room temperature. Cooling of the sample in a solvent without an interchangeable deuterium can retard this exchange and the interaction can be observed. As shown by the experiment, the ^1H — ^{15}N spin-spin interaction at -75°C was seen only with derivatives obtained from the labelled aniline ($J = 93$ Hz). This means that the NH structural element is directly bound to the aromatic ring and therefore, carbonyl cyanide phenylhydrazone is related to phenylhydrazones *I* at -75°C . The value of the coupling constant is in a good agreement with data published¹⁷ for other phenylhydrazone derivatives. The question is, whether this structure dominates at an ambient temperature, too. The answer can offer a comparison of the ^{15}N NMR chemical shift values recorded at various temperatures. The chemical shifts at -85°C were found to be $\delta -199.5$ (N-phenyl), $\delta -5.5$ ($-\text{N}=\text{C}$), and $\delta -205.0$, $\delta -5.5$ at room temperature, respectively. These temperature changes of chemical shifts are relatively small¹⁶ and consequently, the structure at both temperatures is the same.

The ^{13}C — ^{15}N spin-spin interactions are in full accordance with those reported¹⁸ for the proposed structure *I*. The two-bond interaction $\text{N}_{(8)}-\text{CN}$ transmitted through the double bond is stereospecific¹⁸ and makes it possible to distinguish mutually the nitrile groups in the ^{13}C NMR spectrum. The coupling constant with the *cis* nitrile with respect to the lone electron pair at nitrogen $\text{N}_{(8)}$ has a greater value.

It could be, therefore, concluded that the substance under investigation has a phenyl hydrazone structure; its denomination as carbonyl cyanide phenylhydrazone is generally incorrect; the real structure of this class of compounds is better described by the term phenylhydrazonopropanedinitrile.

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