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A QUANTUM CHEMICAL STUDY OF HCN, HNC AND CN$^-$

APPLICATION TO ASPECTS OF ORGANIC CHEMISTRY AND PREBIOTIC ORGANIC SYNTHESIS

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Abstract—Extended Hückel Self Consistent Change (EH-SCC) molecular orbital calculations have been made for some molecules of possible importance in prebiotic organic synthesis: hydrogen cyanide, hydrogen isocyanide and cyanide ion. In this paper, attention is focused on the bonding picture for these species which emerges from the calculations. Notably, isocyanide carbon appears to have very electron deficient pi orbitals as well as non-bonding electrons, and cyanide ion has essentially equal negative charge on carbon and nitrogen and no non-bonding electrons. Aspects of prebiotic organic synthesis and the organic chemistry of cyanides, isocyanides and cyanide ion are discussed in terms of these and other conclusions derived from the calculations. In addition, insight is gained into the energetics of hydrogen cyanide and hydrogen isocyanide formation from a study of the potential energy variation in the reverse process, linear stretching of the H—CN and H—NC bonds to the point of heterolytic dissociation, thus providing a basis for a discussion of the possible formation and existence of hydrogen isocyanide.

I. INTRODUCTION

In a previous paper[1] we reported some of the results of a MO calculation for HCN, HNC and CN$^-$ using the EH-SCC method. The main purpose of that study was to compare the energies and charge distributions obtained for HCN from this approximate, semi-empirical calculation with those obtained previously from more exact SCF calculations.[2-4] Specifically we calculated and compared total energies, ionization potentials, dipole moments, and electronic transitions. We also calculated the valence configuration energy variation as a function of bond angle and bond lengths in the ground and excited states of HCN. Our results correctly predicted that HCN has a linear ground state, bent excited state and is more stable than its HNC isomer. The success with this trial system, together with a general analysis of the expected behavior of valence configuration energies with conformation changes made previously by Pan and Allen, allowed the conclusion that the EH-SCC MO model can be used to predict correct relative energies for different molecular conformations for most small molecules.

The more exact MO calculations do not in general focus attention on the chemical properties of the molecules which they study. Instead, together with accurate total energy values, the emphasis in these calculations is on the more physical properties such as electric polarizability, quadrupole moments, spin interactions, and so on. In addition to energy-conformation studies, one of the main applications we wish to make of the results of the EH-SCC MO calculations is to understand and predict the nature of the bonding and chemical properties in a series of molecules such as HCN, its dimer, trimer, terramer and related small amines, nitriles and imines which may have been important as precursors in prebiotic synthesis of proteins and nucleic acids under primitive Earth conditions. Such an investigation of chemical properties is based on the use of the electron density distributions obtained from the calculated MO's in the EH-SCC MO approach. Our exploratory studies indicate that this description of electron distribution is realistic enough to warrant such use. The chemical interpretation is characterized by a regrouping of the MO results into the more classical bonding orbital picture with a description of the atomic orbitals participating in each bond. Thus the way in which the atoms form the molecule, their participation in bonding, and their expected properties in the molecule can be more easily elucidated and discussed. In this paper, we shall discuss aspects of the possible formation of HNC and describe the more chemical aspects of HCN, HNC and CN^-. The bonding analysis to be presented is based on the same MO calculation described in a previous paper[5] and is typical of the type we shall make for other molecules in this series.

II. POSSIBLE FORMATION OF HNC

Our recent calculations[1] indicate that HNC is less stable (higher binding energy) than HCN by about 2 eV or 50 kcal. mole^{-1} We have also studied the potential energy variation as the H—C bond in HCN and the H—N bond in HNC is stretched linearly. In both cases, at distances (six times the normal bond length) where H no longer interacts with CN, the original bond appears to cleave heterolytically rather than homolytically, forming H^+ and CN^- (Fig 1). According to the principle of microscopic reversibility, the reverse reactions, formation of HCN and HNC from a common ground state involving H^+ and CN^-, should follow the same energetic pathways.

Strictly speaking, activated complexes in a reaction are species of maximum free energy, but not necessarily maximum potential energy. Because of difficulties in constructing free-energy surfaces, however, we make the reasonable assumption that in the simple H^+ and CN^- system, activation entropies for the activated complexes in HCN and HNC formation are essentially the same and that the activated complexes are located at maximum potential energy.[6] The difference in potential energy between the pathways at the respective energy maxima, then, is taken to represent the difference in free energies of activation for formation of HCN and HNC from H^+ and CN^-. Accordingly, the free energy of activation for HCN formation appears to be 0·5 eV lower than that for HNC. indicating that the ratio of rate constants for the respective processes would be $k_{HCN}/k_{HNC} = 10^8$ ($T = 300°$ K). This conclusion appears valid for the gas phase.

The ground state for HCN and HNC formation is the same in the liquid phase or in aqueous media, and solvation of H^+ and CN^- ions, would certainly lower their energy relative to that in the gas phase. However, differential solvation of the respective transition states for HCN and HNC formation will lead to greater or smaller differences in activation energy for the two pathways. The states involved in formation

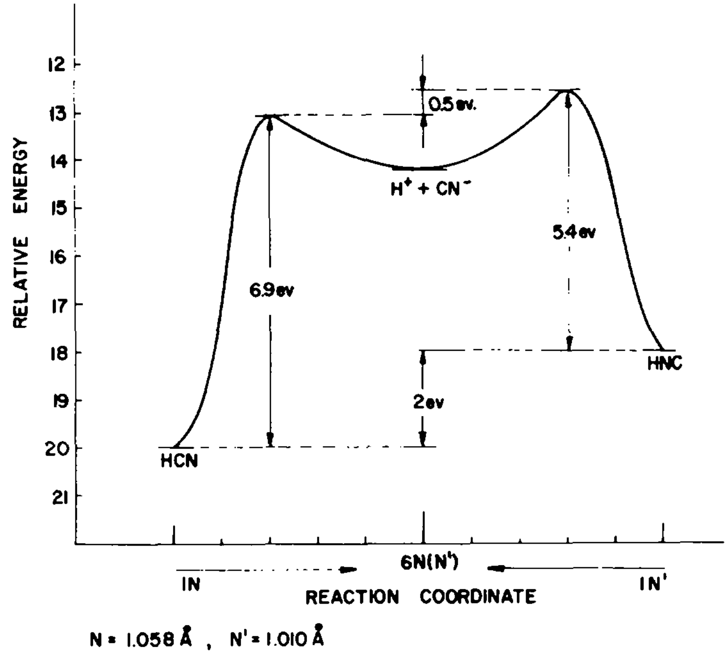


FIG 1. Variation of Potential Energy with Stretching of H—CN and H—NC Bonds.

of HCN or HNC in the gas (g) and solution (s) phase are illustrated in Fig 2. ΔG_s^0 is the free energy of solvation of H^+ and CN^-; $\Delta G_g^\dagger$ and $\Delta G^\dagger$. the free energies of activation in gas and solution, respectively; and $\Delta G_s^\dagger$. the free energy of solvation of the transition state.[7] Since

$$\Delta G_s^0(\mathrm{HCN}) = \Delta G_s^0(\mathrm{HNC}), \text{ and } \Delta G_g^\ddagger(\mathrm{HNC}) - \Delta G_g^\ddagger(\mathrm{HCN}) = 0{\cdot}5\ \mathrm{eV},$$

$$\Delta(\Delta G^\ddagger) = \Delta G^\ddagger(\mathrm{HNC}) - \Delta G^\ddagger(\mathrm{HCN}) = 0{\cdot}5\ \mathrm{eV} + [\Delta G_s^\ddagger(\mathrm{HNC}) - \Delta G_s^\ddagger(\mathrm{HCN})].$$

In liquid HCN or water, both strongly solvating by virtue of H-bonding and high dielectric constant, the free energy of solvation will be lower for the transition state with greater polarity or charge separation. Thus formation of HNC in the solution phase will be more or less favorable depending on whether the transition state is more or less polar than that for HCN formation. By inspection of the two linear transition states, $H^+ \ldots. (CN)^-$ and $H^+ \ldots. (NC)^-$, it is clear that the orientation of the cyanide ion dipole in the former case results in greater charge separation. We conclude,

$$\begin{tikzcd}
H^{\oplus}(g) + X^{\ominus}(g) \arrow[r, "\Delta G_g^\ddagger"] \arrow[d, "\Delta G_s^0"] & {[H^+ \ldots\ldots X^-](g)} \arrow[r] \arrow[d, "\Delta G_s^\ddagger"] & HX(g) \\
H^{\oplus}(s) + X^-(s) \arrow[r] & {[H^+ \ldots\ldots X^-](s)} \arrow[r] & HX(s) \arrow[u, "\Delta G_v^0"']
\end{tikzcd}$$

FIG 2. Free Energy Cycles for Combination of H^+ and X^- ($X^- = CN^-$ or NC^-) in the gas phase and in solution.

therefore, that in pure liquid HCN or in aqueous solution, formation of HCN from H^+ and CN^- is favoured over HNC by at least 0·5 eV. Thus our calculations indicate on kinetic and thermodynamic bases that at ambient temperatures formation of HNC from H^+ and CN^- in the gas phase, liquid HCN or aqueous solution phase is highly unfavorable, and that once formed HCN will not undergo transformation to HNC via dissociation to ions and recombination. In the absence of a means for generating free radicals, rearrangement via homolysis is prohibited by the high H—CN bond energy.[8] Recent calculations[9] also show that an intramolecular rearrangement of HCN to HNC must overcome a formidable 5·25 eV potential energy barrier. However, there is one report[10] that gamma-irradiation of methacrylonitrile led to rearrangement to the corresponding isonitrile in 25% yield. Generation and recombination of the free radicals were postulated. In addition, trimethylsilyl cyanide appears to be in labile equilibrium with trimethylisocyanide.[11] Whether the rearrangements involve dissociation and recombination of cyanide radical or cyanide ion is not known.

Our results are in accord with the past failures[12] to find any clear evidence for the existence of HNC in gaseous and liquid HCN or its aqueous solutions. Raman spectra of saturated aqueous solutions of HCN contained a weak band at 4·95 μ attributed to HNC.[13] Either this band, which was absent in pure HCN,[12b] was due to some impurity, or the concentration of HNC is higher in aqueous solutions than in liquid HCN. The latter explanation is unlikely in light of chemical evidence that pure liquid and aqueous solutions of HCN contained no HNC.[12a,c]

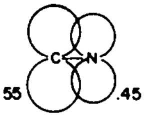
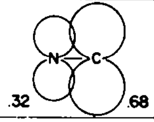
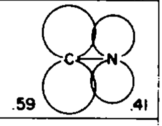
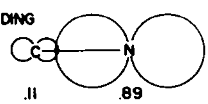
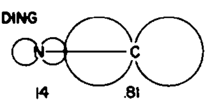
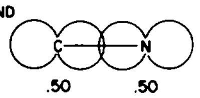
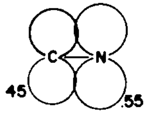
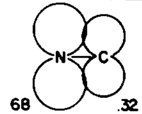
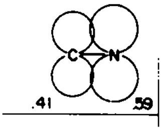
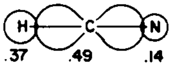
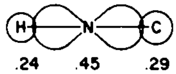
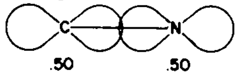
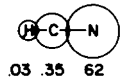
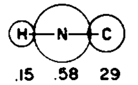
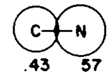
Our results do not exclude the possibility that HNC may be formed through reactions involving free radicals. Reactions of HNC with other species in the medium may then be significant. However, if it is formed or dissolved in aqueous media, HNC must react before it dissociates to H^+ and CN^-, recombination of which will yield HCN. With very few exceptions in the cases studied, weak acids in water have dissociation rate constants greater than 10^3 sec.$^{-1}$ [14] If HNC behaves as a weak acid, a reasonable assumption, a maximum half-life for dissociation of the order of 7×10^{-4} sec is expected. Clearly, other competing reactions would have to occur faster in order to leave any chemical evidence of HNC formation in aqueous media.

III. NATURE OF THE BONDING IN HCN, HNC AND CN^-

A. *Characterization of the molecular orbitals*

HCN has 10 valence atomic orbitals which when allowed to interact in molecule formation yield 10 MO's each of which are linear combinations of the original atomic orbitals (LCAO-MO's). From a calculation of the electron density contribution of each atomic orbital to each MO, these MO's can be described in terms of their bonding characteristics. Results of such an analysis of the five filled and first empty MO's for linear HCN, HNC and CN^- are presented pictorially in Table 1. The 10 valence electrons in the systems fill half of the available molecular orbitals pairwise in the ground state configuration. The lowest lying excited configurations appear to be those due to promotion of an electron from the two highest filled MO's to the lowest empty orbital. The numbers under the MO diagrams indicate the fraction of electron charge in each atomic orbital. As shown in Table 1 the electron distribution in these three linear systems is divided into the traditional pi ahd sigma orbitals. The lowest empty orbitals (6, 7) for each system are doubly degenerate, polar, anti-bonding pi orbitals with a polarity C^-—N^+. Orbitals (3) and (4) are the lower energy, π bonding partners of these orbitals and have a complementary polarity N^-—C^+, which increases from HCN to CN^- to HNC.

TABLE 1. NATURE OF MO'S IN HCN, HNC, CN^-

MO#	HCN	HNC	CN^-
6,7	$\pi(P_x, P_y)$ 	$\pi(P_x, P_y)$ 	$\pi(P_x, P_y)$ 
5	NON-BONDING Nitrile $N(P_z)$ 	NON-BONDING methylene $C(SP_z)$ 	CN σ BOND (P_z) 
4,3	$\pi(P_x, P_y)$ 	$\pi(P_x, P_y)$ 	$\pi(P_x, P_y)$ 
2	σ BOND $(S-P_z)$ 	σ BOND $(S-SP_z)$ 	σ BOND (SP_z) 
1	σ BOND S 	σ BOND S 	σ BOND S 

The three remaining filled orbitals represent the sigma electron distribution. For the CN^- ion, all three sigma orbitals indicate bonding between the C and N atoms. The highest filled orbital MO (5) is p_z-sigma, MO (2) is sp_z-sigma, and MO (I) is pure s-sigma bonding. For HCN and HNC there are only two sigma bonds. The top filled sigma orbital (5) represents an essentially non-bonding orbital for both isomers. In HCN it is 84 % localized on the cyanide nitrogen, and in HNC 81 % on the isocyanide carbon. Thus it appears that in interchanging positions in the molecule, the cyanide nitrogen and isocyanide carbon have also interchanged their non-bonding characteristics. Examination of MO's (1) and (2) for both molecules show that this interchangeable behavior is also true for their sigma bonding. In MO (2), of HCN, the carbon uses sp_z orbitals to bond to s orbitals of nitrogen and hydrogen as does the nitrogen atom in HNC. MO (1) of each molecule, is essentially an s-sigma bond between the carbon and nitrogen with slight bonding to the hydrogen atom.

B. *Atomic orbital electron densities and net atomic charges*

From a Mulliken population analysis of the electron distribution in each filled MO, as described above, the number of electrons in each atomic orbital of each atom can be calculated and the resulting net charge in the atom determined. These results are given below for HCN, HNC and CN^-

H——C——N	H——N——C	C——N
0·10 + 0·29 − 0·39	+0·22 − 0·12 − 0·11	−0·49 − 0·51

	2s	px	py	pz	2s	px	py	pz	2s	px	py	pz
N	1·50	1·11	1·11	1·68	1·28	1·36	1·36	1·10	1·46	1·18	1·18	1·67
C	1·03	0·89	0·89	0·89	1·44	0·64	0·64	1·39	1·45	0·82	0·82	1·42

These charge distributions will be further discussed in the next section.

C. *Composite valence bond picture of bonding in each species*

From a summation of the contribution of each molecular orbital to a given bond, the nature of the bonds formed by each atom can be described in terms of their "bond hybridization." This redistribution of MO's to more localized bonding orbitals is shown in Tables 2 A. B. and C for HCN. HNC and CN^- where the bonds for each atom are identified in column 1, the MO's contributing to each bond are listed in column 2, the bond character or hybridization is given in column 3, and the total number of electrons contributed by the atom to the bond is given in column 4.

Data in Table 2A show that in HCN the cyanide nitrogen uses an almost pure s orbital to form its single sigma bond with carbon, whereas its non-bonding orbital is almost pure p_z-sigma. The former orbital contains 1·52 and the latter 1·66 electrons making a total of over 3 electrons in the sigma system. This distribution of sigma electrons is quite different from the more traditional chemical description of a cyanide nitrogen which assigns one electron to a sp_z bonding orbital and 2 electrons to an equivalent sp_z non-bonding orbital. The present description of the pi bonding places about one electron in each of two cyanide pi bonds in agreement with the usual picture. The cyanide carbon's sigma bonding also does not conform to the standard valence bond picture in that, instead of two equivalent sp_z bonding orbitals, one to hydrogen and one to nitrogen, the linear carbon uses an orbital which is mostly p_z (sp^2) to bond the hydrogen and one which is almost all s to bond to the nitrogen. It has no non-bonding character, and its pi bonds have slightly less than one electron in each. The charge separation between carbon and nitrogen does agree with the conventional view of the polarized cyanide bond. The hydrogen atom acquires a slight positive charge as it bonds to either carbon or nitrogen with its only valence atomic 1s orbital.

As we have already noted, the trivalent isocyanide carbon in HNC has bonding properties similar to those of the trivalent cyanide nitrogen in HCN. Results in Table 2B indicate that the carbon atom also forms two inequivalent sigma orbitals. Its sigma bonding to nitrogen has mainly 2s character, but with somewhat less electron density than cyanide nitrogen, and its non-bonding orbital has mainly p_z character with 1·62 non-bonding electrons, almost identical to the 1·66 on the cyanide nitrogen. Its pi bonding system is qualitatively similar to that of cyanide nitrogen, but the carbon has much less electron density with 0·64 electrons in each pi bond compared to 1·11 for the cyanide nitrogen of HCN. In HNC the isocyanide nitrogen appears to have two equivalent sp_z-sigma bonds to hydrogen and carbon in contrast to the inequivalent sigma bonds of the cyanide carbon in HCN. Moreover, there are nearly

TABLE 2. BONDING PICTURE FOR EACH ATOM IN HCN, HNC AND CN$^-$: DISTRIBUTION OF ATOMIC ORBITAL ELECTRON DENSITY IN MOLECULAR ORBITALS AFTER BOND FORMATION

	Atom	Bond	MO's	Bond character	Electrons in bond
A. HCN.	N	σ bond to C	1,2	$1{\cdot}42\,s + 0{\cdot}10\,p_z$	1·52
		2 π bonds to C	3,4	$1{\cdot}11\,p_x\,(p_y)$	2·22
		non-bonding	5	$0{\cdot}08\,s + 1{\cdot}58\,p_z$	1·66
	C	σ bond to H	2	$0{\cdot}41\,s + 0{\cdot}57\,p_z$	0·98
		σ bond to N	1,5	$0{\cdot}62\,s + 0{\cdot}32\,p_z$	0·94
		2π bonds to N	3,4	$0{\cdot}89\,p_x(p_y)$	1·78
	H	σ bond to C	2	$0{\cdot}86\,s$	0·86
B. HNC.	C	σ bond to N	1,2	$1{\cdot}15\,s + 0{\cdot}06\,p_z$	1·21
		non-bonding	5	$0{\cdot}29\,s + 1{\cdot}33\,p_z$	1·62
		2π bonds to N	3,4	$0{\cdot}64\,p_x(p_y)$	1·28
	N	σ bonds to H and C	1,2	$1{\cdot}28\,s + 1{\cdot}10\,p_z$	2·38
		2π bonds to C	3,4	$1{\cdot}36\,p_x(p_y)$	2·72
		non-bonding	—	——	0·0
	H	σ bond to N	1,2	$0{\cdot}78\,s$	0·78
C. CN.	C	σ bonds to N	1,2,5	$1{\cdot}45\,s + 1{\cdot}42\,p_z$	2·87
		2π bonds to N	3,4	$0{\cdot}81\,p_x\,(p_y)$	1·62
		non-bonding	—	——	0·0
	N	σ bonds to C	1,2,5	$1{\cdot}46\,s + 1{\cdot}67\,p_z$	3·13
		2π bonds to C	3,4	$1{\cdot}19\,p_x\,(p_y)$	2·37
		non-bonding	—	——	0·0

2·4 sigma electrons in these bonds in contrast to less than 2 in the carbon sigma bonds of HCN. The two pi bonds on nitrogen are identical in nature in both isomers, but the isocyanide nitrogen has substantially more pi electron density than the cyanide carbon. The isocyanide nitrogen has no-bonding electrons which is unusual for nitrogen but similar to the normal cyanide carbon with which it has exchanged roles. For HNC the calculations place almost equivalent amounts of negative charge on nitrogen and carbon. This contradicts the conventional view that the nitrogen is electron deficient and that the isocyanide group is best depicted as $\mathrm{R{-}N\overset{+}{\equiv}C^-}$ (compare with $\mathrm{CH_3N^-{\equiv}C^+}$ below).

Table 2C contains the bonding and electron distribution obtained for CN$^-$. From the total electron density on each atom, it is clear that the extra electron (and negative charge) is equally distributed on the C and N atoms. The calculated distribution of the 4·5 electrons on C and the 5·5 electrons on N also indicates that neither atom has any non-bonding electron character. Instead, there appears to be an sp_z hybridized sigma bond with approximately three electrons from each atom in this bond, i.e., the calculations indicate a "triple sigma bond" in CN$^-$, composed of s, sp_z and p_z MO's. In addition, there are two rather polar pi bonds with substantially more electron density on N than C, that is, 0·81 electrons on carbon and 1·18 electrons on N per bond. The pi bonds are then more polar than the sigma bonds. Thus the calculations depict CN$^-$ as $\mathrm{(C{\equiv}N)^-}$, indicating three sigma, two pi bonds, no non-bonding electrons, and equal negative charge on each atom. The conventional view of CN$^-$, $\mathrm{^-\!:C{\equiv}N\!:}$, is a consequence of the concepts of electron pair bonds and integral number of bonding and non-bonding electrons. As such there is one sigma (sp_z) bond between the C and N, each atom contributing one electron to it, and two pi bonds with each contributing two electrons. Neither bond is polar. The N atom is left with two non-bonding electrons. Consequently, the extra electron acquired by CN in becoming CN^- must be formally placed on the C, giving it the total (−1) charge and also two non-bonding electrons. All the nucleophilic character of the CN^- is attributed to the non-bonding electrons on C. If the present picture of CN^- has any physical reality, it indicates that the usual bonding description is a misleading basis for explaining the chemical behavior of CN^-, even though predictions based on it are correct for the most part.

In another study[9] employing the EH method, all the charge in CN^- was located on N. Since that method tended to exaggerate charge separation,[15] whereas the present method employs charge iteration as well as an additional quadratic term in the overlap Hamiltonian, the charge distribution in CN^- depicted above is considered more reliable. Moreover, a recent SCF calculation[16] revealed a value of 0·3792D for the dipole moment of CN^-. This very low value corresponds to a 0·04 unit charge difference between C and N, in good agreement with the 0·02 charge difference shown above. From data tabulated by the same authors, it is possible to calculate the charge distribution per atom in acetonitrile and methyl isocyanide as follows:

H_3——C——C——N H_3——C——N——C

+0·25 −0·65 +0·09 −0·17   +0·24 −0·49 −0.36 +0·14

In addition the net positive charges on cyanide and isocyanide carbon appear to result from electron deficiency in pi orbitals, the isocyanide carbon containing only 0·57 electrons in each, compared to the 0·64 in HNC. Apparently, the charges on carbon and nitrogen in cyanide and isocyanide groups derived from the present EH-SCC method are in good qualitative agreement with those obtained from the SCF calculations.

IV. SOME ASPECTS OF THE CHEMISTRY OF HCN, HNC AND CN^-

A. *HCN*.

We have recently made a study of the relative basicity of amino, imino and cyanide nitrogens in a number of small related compounds and deduced that the greater the number of non-bonding electrons, the more p character—especially pi character—in them, and the greater the negative charge on the nitrogen, the more basic it is.[17] We have further deduced that very small quantitative variations in these three properties appear to manifest themselves in significant changes in basicity. On the basis of these criteria, our present calculations for HCN verify that the cyanide nitrogen is very weakly basic, much less so than ammonia, for example. In ammonia[17] the negative charge is greater than the value of −0·30 found here, the number of non-bonding electrons is 1·96 as compared to 1·66, and they are totally p electrons with some pi character.

The calculations indicate a charge on the carbon of +0·29 relative to a charge on the nitrogen of −0·39, which gives good agreement with the dipole moment. A study has not been made of the relative electrophilicity of carbon in different functional groups, thus criteria from MO calculations for the relative magnitude of this property in carbon were not established. But electrophilicity should stem directly from net electron deficiency on the atom or in specific orbitals. Both of these properties are present in HCN and the net positive charge on the carbon appears to be associated with an electron deficiency primarily in its pi-bonding orbitals. Similar conclusions can be drawn from an SCF calculation for CH_3CN[16] (see above). In accord with the greater charge on carbon in HCN, which is reflected in a greater susceptibility to nucleophilic attack on cyanide carbon than in CH_3CN, base-catalyzed polymerization is much more facile with HCN than with CH_3CN or other nitriles.[18a] The present calculations are consistent with the known electrophilicity of carbon in the cyanide group.

In the polymerization of HCN,[18, 19] considered an important process in prebiotic synthesis, formation of HCN dimer through reaction of HCN with HNC has been suggested.[18b] This reaction may be possible in the gas phase, but in liquid HCN or its aqueous solutions, it must compete with ionization of HNC. Furthermore, HCN polymerization requires either substantial energy input or base catalysis,[18] which is difficult to account for if polymerization involved HNC. In aqueous media, the rate of HCN polymerization depends on the concentration of HCN and CN$^-$, pointing to nucleophilic attack of CN$^-$ at the electron deficient carbon in HCN in the rate-determining step.*

B. *HNC.*

Unlike HNC, alkyl and aryl isocyanides have been isolated and studied extensively.[23] Apparently, except in HNC, non-bonding electrons on isocyanide carbon are not too destabilizing. Possibly delocalization of non-bonding electrons may be more extensive in RNC than HNC. Though they are more stable than HNC, organic isocyanides are still less stable than the corresponding cyanides. The thermal isomerizations of RNC to RCN are clear demonstrations of the stability difference. The isomerizations proceed at temperatures from 140° to 250°C, corresponding to energy differences of about 0·02 eV between isomers, much less than the calculated difference of 2 eV between HCN and HNC.

Comparison of data in Table 2 shows that the total electron density and net negative charge are greater on cyanide nitrogen (5·39 electrons, $-0{\cdot}39$ charge) than on isocyanide nitrogen (5·12 electrons, $-0{\cdot}12$ charge), findings which are supported by ^{14}N NMR studies of aliphatic cyanides and isocyanides.[24] Significantly, H-bonding to the isocyanide group occurs at carbon and is considered to be comparable in strength to hydrogen-bonding to nitrogen in cyanides.[25] The absence of such bonding to isocyanide nitrogen is consistent with its lack of non-bonding electrons. It follows that protonation of the isocyanide group is expected to occur at carbon. In reports[26] where protonation of isocyanide nitrogen was proposed as the initial step in reactions with ketones, oxalic acid, dimethyl sulfoxide, and a beta-keto function, equally plausible mechanistic pathways involving initial reaction at carbon can be formulated

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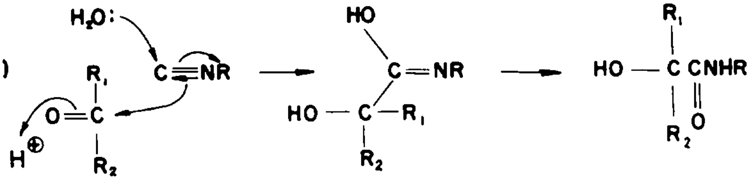
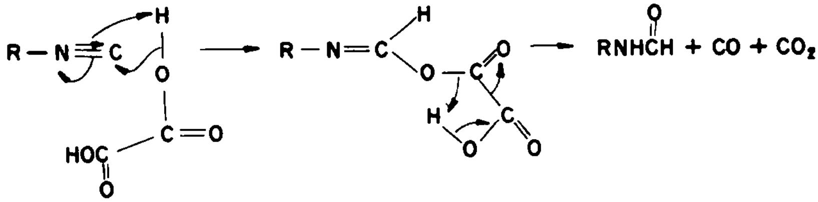
* Most reactions of HCN that are considered interesting from the prebiotic synthesis standpoint are ionic in nature. That very little attention has been paid to the free radical chemistry of HCN in the gas or condensed phase is surprising because many of the energy types presumably available on the primitive earth[20] are radical forming in nature, *e.g.* UV and gamma radiation and heat. Some interesting findings which may be the result of free radical chemistry are the formation of propionitrile during passage of a silent electric discharge through a mixture of HCN and ethylene[21] and the formation of pyrrole, pyridine, aniline and quinoline during pyrolysis of HCN and acetylene.[22]

(Eqs 1–4). On the other hand, the net negative charge and the greater electron density on isocyanide nitrogen (5·12 electrons) relative to that on cyanide carbon (3·71 electrons) mean that nucleophilic reactions at isocyanide nitrogen are much less likely. In fact organic isocyanides are known to be inert to hot aqueous alkali; and reaction with sodium amide in liquid ammonia occurs at the alpha carbon rather than at isocyanide nitrogen, yielding an amine and sodium cyanide.[27] Further examination of the results reveals that cyanide nitrogen has a larger net negative charge (−0·39) than isocyanide carbon (−0·11). Similarly, there are more non-bonding electrons with greater p-character on cyanide nitrogen (1·66 $sp^{5\cdot 6}$) than on isocyanide carbon (1·62 $sp^{4\cdot 6}$). These differences suggest greater basicity for cyanide nitrogen than isocyanide carbon (See ref. 23, however). If in this instance basicity and nucleophilicity can be related, it is not unreasonable to expect that the reactivity of isocyanide carbon may not be associated wholly with its non-bonding electrons (see below).

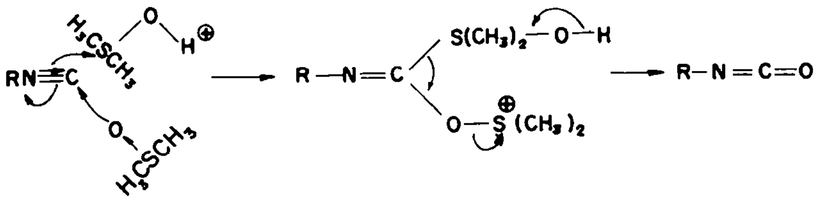
(1)



(2)



(3)



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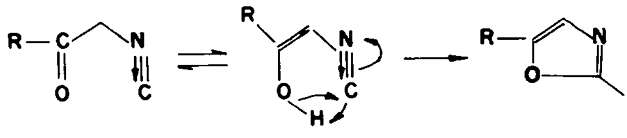
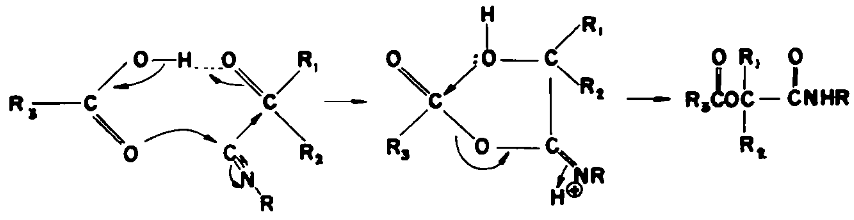
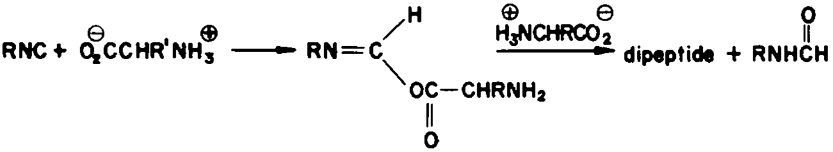


(5)



(6)



$$\mathrm{RNC} + \overset{\ominus}{\mathrm{O_2}}\mathrm{CCHR'}\overset{\oplus}{\mathrm{NH_3}} \longrightarrow \mathrm{RN{=}C}\begin{matrix}\diagup \mathrm{H} \\ \diagdown \mathrm{OC{-}CHRNH_2} \\ \quad\overset{\|}{\mathrm{O}}\end{matrix} \xrightarrow{\mathrm{H_3\overset{\oplus}{N}CHRC\overset{\ominus}{O_2}}} \text{dipeptide} + \mathrm{RNH\overset{O}{\overset{\|}{C}}H}$$

It appears that the foregoing qualitative conclusions regarding the nature of carbon and nitrogen in cyanide and isocyanide groups, based on calculations for HCN and HNC, are valid for CH_3CN and CH_3NC and other organic derivatives. Indeed the experimental support for many of the conclusions are based on the chemistry of organic cyanides and isocyanides. Thus the present bonding pictures for cyanide and isocyanide groups constitute valid models. Interestingly, the SCF calculations[16] predicted higher electron density on isocyanide than cyanide nitrogen in CH_3NC and CH_3CN (see above), a prediction which was not borne out by ^{14}N NMR experiments.[24]

The characteristic feature of isocyanides is their well-known tendency to undergo α, α addition reactions.[23] Aside from Passirini-type reactions, some oxidations with O_3 or HgO to cyanate and with sulfur to thiocyanate, and formation of transition metal complexes. many isocyanide reactions can be viewed as insertions of isocyanide carbon between X—Y bonds, where X = carbon or heteroatom and Y = hydrogen, heteroatom or X.[28] While catalysts, Lewis acids or bases, are required in some instances. many reactions occur without them. In those which are acid-catalyzed the isocyanide carbon can exhibit initially nucleophilic behavior. In uncatalyzed and base-catalyzed reactions, electrophilic behavior is possible. Thus, depending on the electronic demands made on it by other components in the reaction mixtures, the isocyanide may react initially as an electrophile or a nucleophile. In either case, the reactions it undergoes can be dissected into electrophilic and nuclephilic aspects, as will be shown below. With the reasonable presumption that the isocyanide group in HNC is a valid model for other isocyanides, examination of the bonding in HNC can provide some insight into the electronic reasons why isocyanides undergo myriad insertion reactions and why isocyanide carbon often appears to function as an electron-acceptor despite the presence of non-bonding electrons.

Although the bonding of trivalent isocyanide carbon is similar to trivalent cyanide nitrogen, there are two major differences: the isocyanide carbon has a smaller negative charge and its pi bonds are quite electron deficient, containing only 0·64 electrons each as compared to the 1·11 electrons of cyanide nitrogen. In CH_3NC (see above) the +0·14 charge and the presence of only 0·57 electron in each pi bond indicate a correspondingly more pronounced electron deficiency on the isocyanide carbon. It should be noted here that the electrophilicity of cyanide carbon is also associated with electron deficiency in its pi orbitals. The presence of non-bonding electrons and quite electron deficient pi orbitals give isocyanide carbon a dual nature which helps explain why it is peculiarly suited for its characteristic reactions. The unusual ability of isocyanides to function as pi-donor ligands in complexes with zero-valent metals may be taken as a clear reflection of their dual nature. An attractive scheme for the reactions of isocyanide carbon is depicted in Fig 3. In step (1) the non-bonding (sp_z) electrons on isocyanide carbon (in the highest filled MO) initiate nucleophilic attack on the electrophilic site, Y. As C—Y bond formation proceeds, X_1 becomes more electron rich facilitating bond formation in the same XZ plane between it and the electron deficient p_x pi orbital on the isocyanide carbon, as shown in step (2). The two steps may be sequential as indicated, reversed, or may occur as a single concerted step. In instances where hydrogen-bonding is possible ($Y = H$), the depicted sequence would be particularly favorable. In cases where initial reactivity may not be associated with the non-bonding electrons, *e.g.* base-catalyzed reactions, bond formation will initially involve the electron deficient pi orbitals (step 2). Regardless of the timing of bond formation, the MO calculations serve to point out the origin of the dual role played by isocyanide carbon during its reactions. The mechanism of the Passirini reaction has been depicted as shown in equation 5.[29] This formulation is quite analogous to the scheme depicted in Fig 3, except that X and Y (C and O, respectively) are in different molecules.

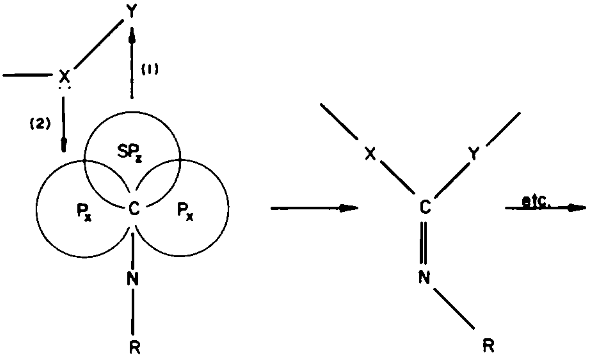


FIG 3. Scheme for Isonitrile Insertion Reactions.

When in Fig 3, $X = N$ and $Y = H$, the reaction amounts to formation of a formamidine by insertion of isocyanide carbon into the N—H bond of an amine. This reaction occurs with aryl isocyanides, but transition metal catalysts are required with alkyl isocyanides.[30] This difference in reactivity is consistent with the isocyanide functioning as an electrophile. Initial bonding (step 2 in this case) is more favorable for aryl derivatives because the inductive effect of the aromatic ring lowers the electron density of the polarizable pi orbitals at the isocyanide carbon rendering them more electron deficient and thus more reactive than in the alkyl derivatives. Delocalization of pi electrons into the aromatic ring would also lead to more electron deficient pi orbitals on carbon, but the insensitivity of $C\equiv N$ absorption in the infrared to *para* substitution in free and complexed aryl isonitriles suggests that interaction between pi orbitals on isocyanide carbon and aromatic ring is not extensive.[31] Because the non-bonding electrons in less polarizable sigma orbital are not expected to be as strongly affected by inductive or resonance effects, the net result is to increase the electrophilicity and thus the reactivity of the pi orbitals on carbon. This also explains why methyl isocyanide is a poorer pi-acceptor than aryl isocyanides in transition metal complexes[31] and why isocyanides substituted with strongly electron-attracting groups adjacent to the isocyanide group are extremely reactive.[26] Interestingly, the dual nature of the isonitrile carbon, the presence of non-bonding electrons and electron deficient orbitals, is also characteristic of the reactive carbon in methylenes,[32] to which isocyanides have been compared[32, 28a] and which also exhibit nucleophilic[33] as well as electrophilic behavior.

If HNC were formed under prebiotic conditions and if its lifetime were sufficiently long, it would be expected to undergo many of the reactions characteristic of organic isocyanides,[23] giving rise to more complex molecules. Thus HNC and other isocyanides could have contributed to the pool of organic compounds in the primeval soup. Isocyanides, like some cyanides, undergo polymerization reactions; however, these reactions are generally catalyzed by Lewis acids and yield products of the type $R'\text{—}(C\text{=}NR)\text{—}R'$[34, 35] which do not appear to be of much relevance for prebiotic synthesis. Although results were not encouraging in the only report[36] of a search for isocyanides in prebiotic-type experiments, the recent finding[10] that gamma-irradiation of cyanides results in partial rearrangement to isocyanides should renew interest in them. One potentially significant reaction which has been explored is the phosphorylation of nucleosides with alkyl isocyanides and inorganic phosphate,[36] the reaction presumably involving an imidoyl phosphate formed by addition of inorganic phosphate to the isocyanide carbon. A related reaction worth exploring is carboxyl activation of amino acids for peptide synthesis: addition of an amino acid to RNC could yield a mixed imidoyl acid anhydride, which could subsequently react with the amino group of a second amino acid molecule to produce a dipeptide and an N-formyl amine (Eq 6). Since isocyanides are relatively inert to aqueous base. addition of an amino acid may compete favorably with hydrolysis under the mildly basic (pH 8–9) conditions generally accepted for primitive waters.

C. *CN^-*.

Formation of cyanides by alkylation of cyanide ion using organic halides or esters of sulfuric and sulfonic acids is a well known synthetic route. Addition of HCN to carbon–carbon and carbon–heteroatom multiple bonds takes place, but since these reactions generally involve basic catalysis, they can also be viewed as cyanide alkylations.[37] In the present MO picture for the ambident CN^- ion, net negative charge and sigma electron density in the highest filled MO (5) are essentially the same on carbon as on nitrogen. In the next lower MO's (3) and (4), however, the pi electron density is higher on nitrogen. Thus the bonding picture for CN^- suggests that both C— and N— alkylation will occur, with the latter perhaps predominating. In fact isocyanides are formed in very low yields, if at all, except when heavy metal cyanides or transition metal cyanide complexes[38] are employed. Clearly, unaccounted factors in the calculations such as solvent, cation, and alkylating agent play influential roles in the course of alkylation.

Under conditions where product formation is kinetically controlled, coulomb attracting forces are expected to direct a polar electrophilic alkylating agent to bond at nitrogen, the site in the ambident ion with the highest electron density.[39] In cases where predominant N-alkylation is observed, the reactants include organic halide and AgCN. The silver cation presumably promotes partial ionization of the halide so that coulombic forces direct bonding of the electron rich nitrogen in CN^- to the incipient carbonium center. If incipient carbonium ion formation were not involved, the fact that CN^- is bound to metal by carbon in most cases[40] forces alkylation to occur as observed on nitrogen. If there is little or no charge on the alkylating agent, bond formation is expected to occur at carbon, the most polarizable site.[39] Since protic solvents are usually used in alkylations of alkali cyanides, "selective solvation"[41] of the electron rich nitrogen shields it from reaction and, coupled with the greater polarizability of carbon, directs bond formation almost completely to the carbon of the cyanide ion. However, even in dipolar aprotic solvents where selective solvation is minimized, alkylation of NaCN yields mostly cyanide and little isocyanide.[42] Either selective solvation persists to a significant extent or the importance of carbon polarizability is paramount or some other factor operates to produce mainly C-alkylation in dipolar aprotic solvents.

A useful interpretation of the alkylations of CN^- may be couched in terms of hard and soft acids and bases.[43] The carbon of CN^- can be viewed as the soft base end and the nitrogen as the hard. Similarly, the cations of cyanides can also be catorized as soft (Ag^+, Hg^+, Hg^{+2}, Cu^+) and hard (H^+, Li^+, Na^+, K^+) acids. Thus interaction of soft cations with carbon in CN^- is expected to be stronger than with nitrogen, and conversely, hard cations should interact more strongly with nitrogen. These expectations are experimentally verified in the solid state for the soft Ag^+ and transition metal complex ions[40] and the hard Li cation.[44] Thus it is reasonable that in solution, depending on the cation, soft or hard, either the carbon or the nitrogen, respectively, of CN^- is shielded in the $M^+(CN)^-$ ion pair from attack by the alkylating agent. In accord with this conclusion, alkylation of AgCN and transition metal complex cyanides takes place at nitrogen while alkylation of LiCN, NaCN and KCN occurs on carbon regardless of solvent, suggesting that cation proximity rather than solvation effects may be of paramount importance in determining the site of alkylation of CN^-.

The results in section II indicate that in the gas and solution phase reaction of a proton with CN^- at carbon rather than nitrogen is favored by at least 0·5 eV. Coulombic considerations apparently are not crucial in this case, otherwise HNC formation would have been favored. In the gas phase the activated complexes for HNC and HCN formation appear to occur at a separation between H^+ and CN^- of slightly over 3 angstroms (Fig 1). Since coulombic forces between two particles decrease in the gas phase as the inverse square of the separation, they may be relatively unimportant at that distance. Why a proton prefers to bond to carbon in CN^- is not obvious since H^+ is a hard acid and nitrogen is the hard end of CN^-, but may have something to do with the greater polarizability of carbon at bonding distances or the possible greater strength of the incipient H—C bond than the H—N bond.

Since HCN and CN^- occur in many prebiotic-type syntheses, alkylation of CN^- is certainly possible under prebiotic conditions and would lead to a variety of organic cyanides which could undergo further reactions to enrich the pool of organic matter in the primitive oceans. Particularly important would be Strecker-type syntheses of amino cyanides, hydrolysis of which would yield amino acids[45] and polymerization of which would afford peptide precursors.[46]

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