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Energy-Conformation Studies of Hydrogen Cyanide Tetramer: A Prebiotic Precursor

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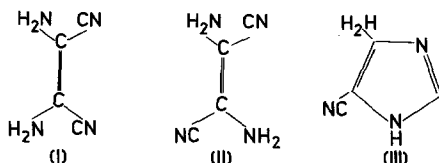
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Using the Iterative Extended Huckel Method (IEHT), we have made energy-conformation studies of the two isomers of hydrogen cyanide tetramer, a known purine precursor in prebiotic syntheses. Our results show that the *cis* isomer is more stable than the *trans* and that, for both, a totally planar conformation is most favorable, differing appreciably from the crystal structure determined by X-ray analysis. The ionization potential, dipole moment, π electron distribution and optical spectra for the tetramer have also been calculated. For all of these properties we find good agreement with experimental results. Thus encouraged by the reliability of the description obtained, we plan to use these results for further studies of the chemical reactivity of the tetramer relevant to its postulated role in prebiotic syntheses.

Mit Hilfe der iterativen erweiterten Hückel Methode (IEHT) haben wir Energie-Konformations-Untersuchungen an den beiden Isomeren der HCN-Tetrameren, das als Purinvorläufer in vorbiotischen Synthesen bekannt ist, durchgeführt. Unsere Resultate zeigen, daß das *cis*-Isomere stabiler als das *trans*-Isomere und daß für beide die planere Konformation bevorzugt ist. Diese Ergebnisse weichen stark von der mit Hilfe der Röntgenstrukturanalyse bestimmten Kristallstruktur ab. Außerdem wurden Ionisationsenergie, Dipolmoment, π -Elektronenverteilung und optische Spektren des Tetrameren berechnet. Für alle wurde gute Übereinstimmung mit experimentellen Ergebnissen gefunden.

A. Introduction and Background

Hydrogen cyanide and its small polymers have long been proposed as key precursors in the prebiotic syntheses of purines, amino acids and polypeptides [1–4]. In particular, the tetramer has been shown to undergo efficient photo-rearrangement to a purine precursor which in a dark reaction with HCN forms adenine and by hydrolysis and condensation with other nitriles forms other purines, such as guanine, diaminopurine, and xanthine [5–8]. The photochemical step has been proposed as the only efficient pathway from hydrogen cyanide to the purines which is feasible in dilute aqueous solution. Because of its importance, the complicated photochemistry of the *cis* (I) and *trans* (II) isomers of HCN tetramer involving the purine precursor ACI (III) as well as other possible intermediates has been under extensive investigation [9–11].



The tetramer has been suggested as a plausible, primordial, amino-acid condensing agent in aqueous solution [12]; and it is also thought to be an early intermediate in the formation of polymers from HCN under certain conditions [13]. These higher polymers have themselves been proposed as "foreproteins" leading by hydrolysis to polypeptides [14]. For these diverse reasons then the tetramer of HCN is considered a particularly key precursor molecule in chemical evolution.

In addition to studies exploring its role in chemical evolution, a number of other properties of the HCN tetramer have been investigated. For example, the X-ray crystal structure of the *cis* isomer (DAM I) [15] and the *trans* isomer (DAF II) [16] have been determined. While the *cis* isomer is thought to be experimentally more stable [10] both forms readily undergo photochemical interconversion [11]. The dipole moment [17] and the ionization potential [18] have both been measured for the lower energy form. Also simple Hückel, π -electron-only (SHT) molecular orbital calculations have been reported for the *cis* [15] and the *trans* [19] isomers.

Thus the HCN tetramer seemed an appropriate object of study for our continuing quantum chemical investigations of small molecules [20–23] which are considered important prebiotic precursors.

In the initial study presented here we have made a series of energy-conformation calculations to determine the most favorable isomer and conformer of the tetramer. In addition we have calculated such physical properties as dipole moment, ionization potential and electronic spectra, and compared our results with known experimental behavior.

To characterize the HCN tetramer we have used, as in the past [20, 22], the so-called Iterative Extended Hückel Theory (IEHT). The details of this approximate, all-valence-electron, semi-empirical method of solution of the molecular Schroedinger equation have been presented and discussed elsewhere [24–26]. Our method of calculation and values of input parameters are essentially those of Zerner and Gouterman [27]. Previous analysis have shown that, while this method does not pretend to give total molecular energies but rather just the valence-state-configuration energies, these latter appear to vary as the total energy with geometric variations of a given molecule [28, 29]. There are relatively few energy-conformation studies using IEHT reported in the literature [30]. Rather a simpler, less time-consuming but less reliable non-iterative EHT method has been extensively used. In our program, we automatically obtain the non-iterated energies and eigenfunction as our initial solution of the Schroedinger equation. We have uniformly found that using these zero-iteration results give much less reliable energy variations and eigenfunctions than do the charge-converged results.

B. Energy-Conformation Studies

The molecular geometries which resulted from the X-ray crystal structure determinations for the two isomers are given in Figs. 1a and 1b. Each has several interesting and unusual features. The *cis*-isomer, DAM, has no mirror plane and is twisted by 6° about the C=C bond. The bond angles of the two

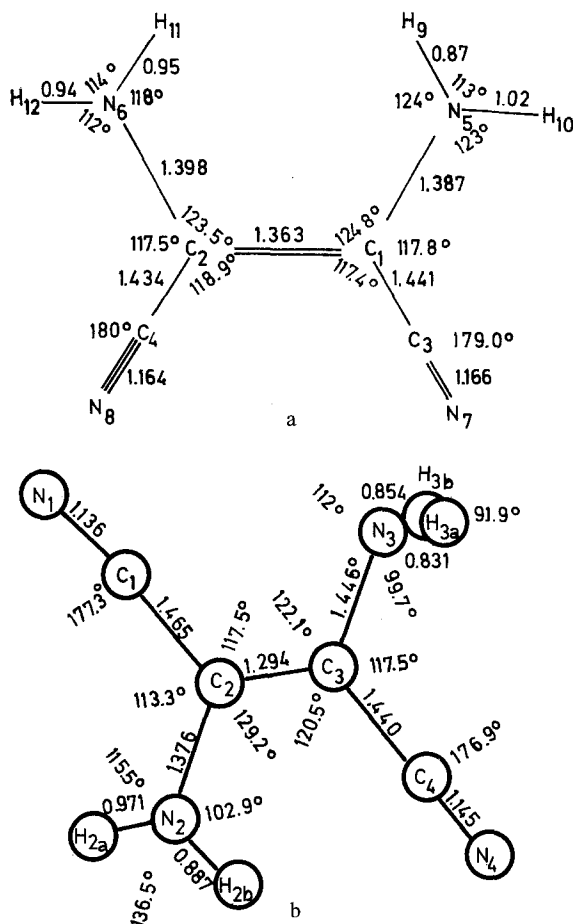


Fig. 1. a Molecular geometry of the *cis*-HCN tetramer as determined by the X-ray diffraction analysis of crystal structure (15). b Molecular geometry of the *trans*-HCN tetramer as determined by the X-ray diffraction analysis of crystal structure (16)

central ethylenic carbon atoms are highly anisotropic with two less than and one greater than 120° . The two amine groups have inequivalent geometry: one planar with anisotropic nitrogen bond angles and the other a distorted tetrahedron with the plane of the NH_2 group perpendicular to that of the remainder of the molecule and an abnormally large HNH bond angle of 114° compared to 107° in ammonia.

Interestingly, the same type of strained structure was obtained from the X-ray crystal analysis of the *trans*-isomer DAF by a different group of investigators [16]. Their results shown in Fig. 1b also yielded anisotropic ethylene carbon bond angles and one planar and one tetrahedral NH_2 group with highly anisotropic bond angles and a small HNH bond angle of 92° .

It seems highly unlikely that such distorted molecules are minimum energy conformers of the isolated molecules, i.e. the result of intramolecular interactions

Table 1. Molecular energy of HCN tetramer as a function of molecular geometry

Conformer	<i>cis</i> -isomer (I DAM) (eV)	<i>trans</i> -isomer (II DAF)
Planar	-707.83	-706.70
Exp.	-694.03	-693.50
Exp.'	-700.60	-701.90
Tetrahedral	-696.70	-697.70

alone. Since a great deal of the chemistry of the HCN tetramer relevant to prebiotic synthesis occurs either in the gas phase or dilute solution, we have made energy-conformation studies to determine the most energetically favored conformation in the isolated molecule. For each isomer the conformations chosen were: 1) the experimentally determined X-ray crystal structure (Exp); 2) an "idealized" experimental structure, (Exp') with zero twist angle and isotropic bond angles of 120° for all trivalent planar bonds and 107° for tetrahedral amine bond angles. 3) Two rotational variations with the regular bond angles of the idealized crystal structure, a totally planar one and a totally tetrahedral one, obtained by a rotation of 90° about each C-N bond in turn.

The results of these calculations are given in Table 1. We see that for both isomers the experimentally determined structure is the least stable and the completely planar conformation is the most stable. The totally tetrahedral conformation appears also to be more stable than the experimental one but less stable than the idealized experimental conformer. Thus it appears that both the bond-angle-anisotropy and the inequivalence of the two amine groups are special features of the crystal structure of the *cis* and *trans* isomers which are not shared by the isolated molecule.

We also see from Table 1, that the *cis* isomer is energetically favored over the *trans* in agreement with experimental observations. However, there does not appear to be any definitive thermodynamic estimates of the energy difference between *cis* and *trans* isomers with which to compare our estimate of 1.1 eV (25 kcal/mole).

C. Ionization Potential

Values for the lowest ionization potential of the molecule obtained from the IEHT results as the energy of the highest filled molecular orbital, are given in Table 2 for each conformer studied. We see from this table that there is only a small variation in ionization potential with conformation and from *cis* to *trans* isomer. Recently, in order to check our results, colleagues at NASA Ames Research Center have obtained an estimate of the ionization potential of the tetramer from a mass spectroscopic study of the appearance potential of the molecular ion [18]. This value is also given in Table 2. We see that the calculated ionization potentials for all conformers are lower than the experimental one, but that, except for the X-ray structure value, all fall within the limits of experimental

Table 2. Dipole moment and ionization potential of conformers of *cis*- and *trans*-HCN tetramer

Conformation	<i>cis</i> -isomer (I DAM)		<i>trans</i> -isomer (II DAF)	
	DM (Debye)	IP (eV)	DM	IP
	Calc.	Calc.	Calc.	Calc.
Planar	-7.70	10.46	0.193	10.38
Exp.	-9.47	10.14	0.956	9.74
Exp. ^a	-6.42	10.57	0.815	10.58
tetra	-5.04	10.62	0.122	10.61
	Exp.	Exp.		
Exp.	-7.78	11.2 ± 0.8		

error. In addition to providing verification of our calculation values this result might be regarded as further corroboration that the ground state in the isolated molecule is not the same as in the crystal.

D. Dipole Moments

From the molecular orbital functions resulting from the IEHT calculations, the dipole moment of each conformer was calculated. These values are also given in Table 2. We see that there is a marked distinction between the calculated values of dipole moments of the *cis* and *trans* isomer, the latter being quite small because of the symmetry of the molecule and the former having unusually large values which are quite sensitive to conformation changes.

The measured dipole moment of the tetramer in dioxane solution at 35° is -7.78 Debye. There is then excellent agreement between this measured value and our calculated value of dipole moment for the preferred planar *cis* conformer energy. The internal consistency and agreement with experiment is extremely heartening. Our results also suggest that the planar *cis*-isomer is the lowest energy form in dioxane solution with no large conformational changes in going from the isolated molecule to solution.

E. π -Electron Properties: Electron Distribution and Electronic Spectra

The HCN tetramer has 36 valence molecular orbitals and 40 valence electrons, so that in the totally paired ground state 20 molecular orbitals are filled and 16 empty. Of the 20 filled orbitals in the planar conformers, 5 are π orbitals, yielding 10 π and 30 σ electrons in the ground state tetramer with 3 empty π orbitals and 13 empty σ orbitals. The partitioning of electrons between π and σ orbitals is a result of the calculation and not an input restriction. The π electron density on each carbon and nitrogen, determined from the charge-iterated results of the IEHT calculation, is given in Table 3 for both DAM and DAF. These results may be compared to earlier, simple Hückel Theory (SHT) calculations reported for each isomer [15, 19], in which only the 8 π atomic orbitals were considered, and the number of π electrons were assumed for each molecule: 10 for DAM and 8 for DAF. The π electron distribution resulting from both of these calculations is also given in Table 3 under the heading SHT. We see that, for the *cis* isomer (DAM), the main difference is that the SHT results predict

Table 3. A comparison of π electron distribution in *cis*- and *trans*-planar HCN tetramer from SHT and IEHT calculation

Atom	SHT	IEHT	SHT	IEHT
Central C	0.97e	1.107	0.490	1.106
Nitrile C	0.76	1.025	0.781	1.023
Nitrile N	1.37	1.085	1.176	1.077
Amine N	1.89	1.782	1.553	1.793
	4.99	4.999	4.000	4.999

Table 4. π electron distribution in the 5 filled and lowest empty π -orbitals of planar HCN-tetramer

Atom/ π MO	1 (9) ^a	2 (13)	3 (16)	4 (19)	5 (20)	1 ^c (21)
<i>cis</i> -tetramer						
Central C	0.583 ^b	0.087	0.172	0.123	0.142	0.250
Nitrile C	0.275	0.514	0.224	0.008	0.003	0.188
Nitrile N	0.071	0.370	0.438	0.094	0.111	0.418
Amine N	0.071	0.028	0.165	0.775	0.744	0.144
Type π MO	C—C—C—C	C \equiv N	Deloc.	N_{amine}^{nb}	N_{amine}^{nb}	Deloc.
<i>trans</i> -isomer						
Central C	0.575	0.079	0.184	0.129	0.139	0.238
Nitrile C	0.277	0.528	0.208	0.005	0.004	0.190
Nitrile N	0.076	0.374	0.462	0.075	0.091	0.439
Amine N	0.071	0.018	0.147	0.791	0.766	0.133

^a Position of π MO in energy-ordered list of σ and π mos.

^b Fraction of π electron on atom.

^c Lowest empty molecular orbital.

an electron-deficient π orbital for the nitrile carbon and an electron rich one for the nitrile nitrogen, i.e. a fairly polar CN π bond while the IEHT results predict almost equal π electron density on the nitrile carbon and nitrogen atoms. Since an accurate dipole moment is obtained for this molecule and since the method used includes all valence electrons, it may be assumed that our π electron distribution is more accurate than the earlier one. For the DAF isomer, the π electron distributions resulting from the two methods are very different. The main discrepancies are obviously caused by the assumption of 8 rather than 10 π electrons in the earlier calculation, i.e., the *a priori* assumption of 1 π electron per atom. This assumption in the SHT calculation particularly penalizes the ethylenic carbon atoms and illustrates the disadvantage of choosing the number of π electrons as an input quantity.

Tables 4a and b describe the nature of the 5 filled and lowest empty π molecular orbitals. The lowest energy π molecular orbital (MO 9) is delocalized over the four-carbon skeleton, the next (MO 13) is a fairly localized nitrile π bond, the 3rd (MO 16) is completely delocalized on all carbon and nitrogen atoms in the molecule and the 4th and 5th, which are the two highest filled orbitals [19, 20] are nearly non-bonding amine nitrogen orbitals. The lowest empty

orbital [21], also a π orbital, is, like MO 16, delocalized on all the C and N atoms in the molecule, but primarily on the nitrile N atoms.

The π electron network appears to be relatively insensitive to *cis-trans* isomerism, with almost identical π electron distribution in each isomer.

The electronic spectra of both the *cis* and *trans* isomer have been measured in the region 2500–4500 Å at -196° K and room temperature [11]. The low temperature spectra exhibit broad absorptions with some structure and an absorption maximum of 3150 Å for the *cis* and 3350 for the *trans* isomer. There is some experimental evidence that these transitions involve charge transfer. While we can obtain transition energies only in the one electron approximation from our IEHT calculation, i.e. configuration energies uncorrected for total state formation, we can nevertheless obtain from our results some insight into the nature of the allowed transitions as well as an approximate estimate of transition energies. A series of 7 possible electronic transitions to the lowest empty orbital [21] is given in Table 5 in order of increasing energy. Included in this table are the 5 $\pi \rightarrow \pi^*$ transitions, 9, 13, 16, 19, 20→21, and the two lowest energy $\sigma \rightarrow \pi^*$ transitions 17, 18→21.

Looking at Table 5, we see that the 2 lowest energy transitions 19, 20→21 are $n(\pi) \rightarrow \pi^*$ between non-bonding and antibonding π orbitals involving about 80% charge transfer from an amine nitrogen to the other atoms of the molecule. While similar in character, these two non bonding π orbitals have somewhat different electron distributions resulting in rather different energies. We see from Table 5 that both transitions are predicted to fall within the broad range included in the experimental region, while the second corresponds very closely to the observed maxima for both *cis* and *trans* isomers. Our results also appear to confirm the suspected charge transfer nature of this transition. Also, in agreement with experiment, we calculate a small shift to higher energy of the λ_{\max} from the *trans* to the *cis* isomer.

The next two, higher energy transitions 17, 18→21 are from two, essentially non-bonding, σ , nitrile-nitrogen orbitals. These are calculated by our IEHT program to have zero values of transition moments and oscillator strengths and hence are forbidden.

The 16→21 transition noted in Table 5, is a $\pi \rightarrow \pi^*$ transition, from a delocalized π bonding to an antibonding π orbital. It is allowed but has a calculated λ_{\max} just on the high energy boundary of the experimental region. The

Table 5. Calculated ($\pi \rightarrow \pi^*$) transitions for planar *cis* (DAMI) and *trans* (DAF II) HCN tetramer spectra

MO ($i \rightarrow j$)	Transition	$\Delta\varepsilon$ (eV) _{cis}	$\Delta\varepsilon$ (eV) _{trans}	$\lambda_{\text{cis}}^{\max}$	$\lambda_{\text{trans}}^{\max}$
20→21	$n(\pi) \rightarrow \pi^*$	3.16	2.97	3900 Å	4100 Å
19→21	$n(\pi) \rightarrow \pi^*$	3.74	3.72	3200 ^a	3400 ^a
18→21	$n(\sigma) \rightarrow \pi^*$	(4.03) ¹	(3.81)	forbidden	
17→21	$n(\sigma) \rightarrow \pi^*$	(4.18)	(4.30)	forbidden	
16→21	$\pi \rightarrow \pi^*$	4.89	4.82	2500	2600
13→21	$l\pi \rightarrow \pi^*$	5.91	5.79	2000	2250
9→21	$\pi \rightarrow \pi^*$	7.31	7.15	1690	1730

^a Observed $\lambda_{\text{cis}}^{\max} = 3150$ Å, $\lambda_{\text{trans}}^{\max} = 3350$ Å.

remaining two π electron transitions are of much higher energy than the experimental range.

It appears then that the π electron orbitals obtained and their calculated energy levels can account surprisingly well for the main features of the observed spectra for both isomers.

Encouraged by the success of our model in elucidating the more physical properties of the *cis* and *trans* isomers of the HCN tetramer we are proceeding to use it for an analysis of their chemical behavior and possible role in chemical evolution.

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