STEREOSPECIFICITY IN ANIONIC 1,1-ADDITION TO ISOCYANIDES. A RE-EXAMINATION OF THE $(H^- + HN\equiv C)$ POTENTIAL ENERGY SURFACE

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The potential energy surface for the addition of the hydride ion to hydrogen isocyanide reported previously was re-examined. An improved energy surface was explored at the MP2/6–31 + + G** level while relative energies were estimated at the MP4SDTQ/6–311 + + G** level and corrected for zero-point vibrational contributions. The calculated results show the existence of transition structures for both *cis* and *trans*-additions of H⁻ to the carbon end of HN≡C even though the corresponding barrier heights are small. These transition structures did not exist at a lower level of theory (HF/4–31G) employed previously.

The *cis* addition is calculated to be favoured over the *trans* addition by 10 kcal mol⁻¹. The overall addition is thus strongly stereoselective, if not purely stereospecific. This result confirms our previous analysis of the stereoelectronic effect in the addition–elimination process involving imidoyl anions as intermediates. Recent experimental work on the addition of OH⁻ to ArN≡C is discussed.

INTRODUCTION

In recent years, new synthetic routes to isocyanides (RN≡C) have resulted in increased interest in the use of this functional group in organic synthesis.[1] Isocyanides undergo 1,1-addition to hydrogen compounds (HX) at their mono-coordinated carbon atom, under a variety of experimental conditions, to yield substituted imines (RN=CHX) as the first step in most of their chemical transformations. The stereochemistry of the reaction between isocyanide and a nucleophilic agent has been shown to be strongly dependent on the nature of nucleophile and the reaction medium.[2–6]

As a model for addition reactions in which anions act as nucleophilic agents, we previously examined,[3] using *ab initio* molecular orbital calculations, the following reaction:
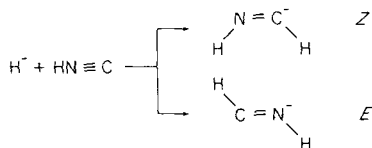
Calculated results suggested that the anionic addition is stereospecific giving the less stable isomer *Z* as the kinetic product. In other words, the anionic addition to isocyanides was predicted to have a large stereoelectronic effect.

Recently, Cunningham[7] reported an experimental study of the reaction of hydroxide ion with aromatic isocyanides. In that work, isocyanide (I) has been found to react in alkaline aqueous dioxane to give formamide (IV). The linear dependence of the observed rate constants on hydroxide ion concentration and the positive value of the ρ parameter suggest a direct attack of OH⁻ on the carbon end of I to yield II and III successively as reaction intermediates.

As far as the addition mechanism is concerned, Cunningham[7] also suggested that the proton transfer (to carbon giving III) is concerted with nucleophilic OH⁻ attack. Although no information on the conformation of the system II–III was given in Ref. 7, the

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$$Ar-N\equiv C + OH^- \longrightarrow \left[Ar\sim N=\overset{..}{C}OH \right] \overset{H^+}{\longrightarrow} \left[Ar\sim N = C\overset{H}{\underset{OH}{\diagdown}} \right]$$

I   II   III

$$Ar\overset{\diagdown}{\underset{H}{\diagup}}N-C\overset{H}{\underset{O}{\diagdown}}$$

IV

assumption of a concerted mechanism implies the possible formation of both the E and Z isomers of the imine III.[5] Accordingly, the anionic addition in solution might not be stereospecific, which is in conflict with our theoretical prediction based on MO calculations.[3]

Faced with this situation, we wished to refine the theoretical results by performing higher level calculations. Our earlier investigation[3] in fact suffered a computational limitation. Although the relative energies between stationary points were estimated using correlated wavefunctions at the fourth-order Møller–Plesset perturbation theory with the $6-31+G^{**}$ basis set (including diffuse and polarization functions), the potential energy surface of the system was explored only at the Hartree–Fock level with the split-valence 4–31G basis set (without diffuse and polarization functions). Although no transition structures for addition can be located at the HF/4–31G level, the shape of the corresponding (HCNH)$^-$ potential energy surface allowed a large stereoelectronic effect to be predicted. For instance, consider the intermolecular distance R joining the hydride ion to the carbon end of HNC. We have found that when the H$^-$ anion attacks the terminal carbon, even at large values of $R(R \geqslant 2\cdot5$ Å), the hydrogen isocyanide already becomes strongly bent (angle HNC $\approx 120°$) and the supermolecule adopts the Z structure. In this region of the energy surface only the Z form exists; the E form is found to be repulsive. At around $R \approx 2\cdot2$ Å, the E structure begins to form but the Z structure is still more favoured in energy and then remains so until the formation of the anion $(R \approx 1\cdot4$ Å). In other words, early on there appears on the energy surface a distinct valley which leads the supermolecule to the formation of the less stable Z anion.

However, recent theoretical studies[8,9] on anionic additions to ethylene and formaldehyde indicated that transition structures for addition may exist at higher levels of theory. If the latter do exist, the stereochemical course of the reaction should depend on their relative energies. In order to verify whether our earlier analysis of the stereochemistry of anionic 1,1-addition to isocyanides remains valid, we re-examined the potential energy surface of the H$^-$ + HNC system at an appropriate level of calculation. We found that although the shape of the energy surface is modified fundamentally with the existence of the transition structures for both

cis and trans additions, the overall stereochemical course remains unchanged with respect to our previous finding.[3]

CALCULATION

Ab initio MO calculations were carried out by using the Gaussian 82 program.[10] Geometrical parameters of points on the potential energy surface were determined at both Hartree–Fock SCF and second-order Møller–Plesset perturbation theory (MP2) levels[11] with the $6-31++G^{**}$ and $6-311++G^{**}$ basis sets[12] (+ + denotes a set of diffuse s functions on H and sp functions on C and N). Harmonic vibrational frequencies were computed at the HF/$6-31++G^{**}$ level in order to characterize stationary points as minima and transition structures and to estimate the zero-point vibrational contributions (ZPEs) to relative energies. The latter were obtained from single-point calculations at the fourth-order Møller–Plesset perturbation theory[13] with the $6-311++G^{**}$ basis set.

RESULTS AND DISCUSSION

Stationary points on the (H$_2$CN)$^-$ potential energy surface considered in this work are listed in Figure 1. Geometrical parameters of these points optimized at the HF/$6-31++G^{**}$, HF/$6-311++G^{**}$ and MP2/$6-31++G^{**}$ levels are summarized in Table 1. Calculated total, zero-point vibrational and relative energies are summarized in Table 2. A schematic profile showing the (HCNH)$^{-1}$ potential energy surface is

Figure 1. Stationary points relevant in the study of the H$^-$ + NH≡C addition

Table 1. Geometrical parameters of species considered at three levels of theory[a]

Species[b]	Parameter	HF/6-31 + + G**	HF/6-311 + + G**	MP2/6-31 + + G**
HNC (1)	C—N	1·154	1·150	1·186
	N—H	0·985	0.985	0·999
TS cis addition (2)	C—N	1·214	1·210	1·233
	N—H	0·994	0·994	1·006
	C—H	2·006	2·018	2·176
	HNC	120·4	119·7	125·0
	NCH	104·8	104·7	103·8
cis HCNHU⁻ (3)	C—N	1·296	1·294	1·320
	N—H	1·018	1·017	1·041
	C—H	1·141	1·141	1·141
	HNC	113·1	112·8	112·8
	NCH	111·3	111·3	111·2
TS trans addition (4)	C—N	1·201	1·196	1·217
	N—H	1·003	1·003	1·009
	C—H	2·356	2·390	2·543
	HNC	116·4	115·1	126·3
	NCH	106·4	106·2	104·7
trans-HCNH⁻ (5)	C—N	1·295	1·293	1·323
	N—H	1·010	1·010	1·024
	C—H	1·123	1·125	1·123
	HNC	108·5	108·4	107·2
	HCN	107·2	107·2	106·0
TS inversion (6)	C—N	1·266	1·264	1·283
	N—H	0·974	0·974	0·993
	C—H	1·183	1·183	1·191
	HNC	178·8	179·0	184·5
	HCN	111·1	111·1	112·8

[a] Bond lengths in Å and bond angles in degrees.
[b] Parameters are defined in Fig. 1.
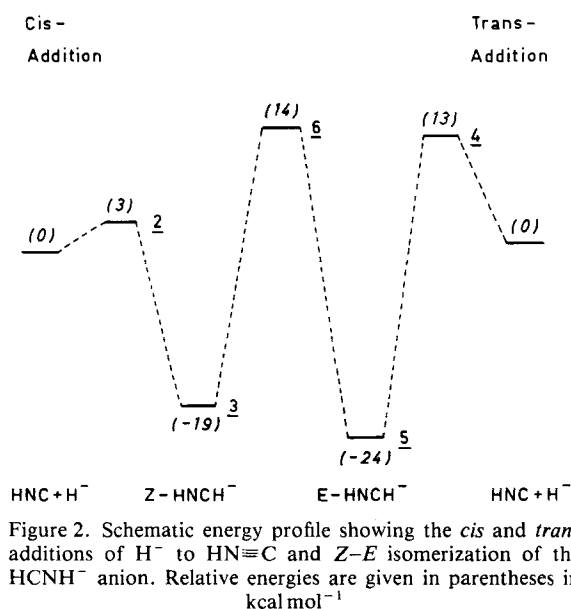
Figure 2. Schematic energy profile showing the cis and trans additions of H⁻ to HN≡C and Z–E isomerization of the HCNH⁻ anion. Relative energies are given in parentheses in kcal mol⁻¹

displayed in Figure 2. Unless noted otherwise, the energies discussed hereafter are obtained from the MP4SDTQ/6-311 + + G**//MP2/6-31 + + G** relative energies and corrected for zero-point energy contributions.

Compared with our earlier results using the HF/4–31G level, the most interesting feature of this work is perhaps the existence of transition structures for both cis addition (2) and trans-addition (4) of the hydride ion to the carbon end of HN≡C. These have been located at all three levels considered, with and without electron correlation. Such a change emphasizes again the crucial role of diffuse functions in exploring potential energy surfaces of molecular anions.

As seen in Table 1, there are marginal changes in structural parameters following extension of the basis set from the valence double-zeta (6–31 + + G**) to the valence triple-zeta (6–311 + + G**). The largest change occurs in the reaction coordinate C···H of 4 (an increase of 0·034 Å). As expected, correlation corrections introduced at the MP2 model result in bond elongation, especially for multiple bonds and intermolecular distances, with respect to the HF values.

Table 2. Relative energies of the (HCNH)⁻ stationary points at different levels of theory

Species[a]	HF/6-31++G**	HF/6-311++G**	MP2/6-31++G**	MP2/6-311++G**	MP4/6-311++G**	ZPE[c]	Estimated[d]
HCN(1)+H⁻[b]	0·0	0·0	0·0	0·0	0·0	9·6	0·0
TS cis addition (2)	7·8	7·6	4·6	3·7	2·0	10·5	2·9
(Z)-HCNH⁻ (3)	-13·0	-13·5	-24·6	-25·9	-24·3	14·7	-19·2
TS trans addition (4)	17·6	17·2	15·8	14·8	13·0	9·5	12·9
(E)-HCNH⁻ (5)	-19·0	-19·3	-30·5	-31·7	-29·7	15·4	-23·9
TS inversion (6)	24·2	23·8	10·1	9·1	11·5	12·1	14·0
ΔE (Z−E)	6·0	5·8	5·9	5·8	5·4		4·7
ΔE^* (inversion from Z)	37·2	37·3	34·7	35·0	35·8		33·2

[a] Using geometries given in Table 1.
[b] Total energies (hartree) of the reference (HNC + H⁻) calculated at five levels considered are −93·35259, −93·37165, −93·65532 (full sets of MOs), −93·67912 (frozen cores) and −93·71440 (frozen cores) respectively.
[c] Zero-point energies (in kcal mol⁻¹). The ZPEs obtained at HF/6-31++G** are systematically multiplied by 0·9 in order to account for the usual overestimation of the vibrational frequencies at this level.
[d] Including MP4 relative energies and ZPEs.

For instance, the most dramatic bond lengthening on incorporation of electron correlation is found for the C $\cdots$ H distances in both transition structures 2 and 4 (by $0\cdot17-0\cdot19$ Å). Some significant variations in bond angles can also be noted in transition structures (up to $10°$ in the HNC angle in 6). The correlation-induced changes in minima structures are shown to be less important.

A recent analysis[14] of the performance of both HF and MP2 methods for geometry of the formyl anion (CHO⁻, isoelectronic with HCNH⁻) suggests that the real r_0 distances in minima structures might lie between the HF and MP2 optimized values. Overall, the geometry changes noted above are consistent with recent studies[8,9] on anionic nucleophilic additions which showed, among other things, that corresponding transition structures are sensitive to the quality of wavefunctions. More extensive computations including larger amounts of correlation energy are no doubt necessary to obtain more accurate geometrical parameters for the transition structures being considered. Unfortunately, full geometry optimization at such levels (e.g. MCSCF–CI with larger basis sets) are beyond our present computational resources. Nevertheless, it should be stressed that the changes in geometrical parameters imply only minute consequences with respect to relative energies.

Perhaps more important than the observed changes in geometries is the associated modification of the shape of potential energy surface. First, we note that the H⁻ + HNC system remains exothermic but the extent of exothermicity found here is much smaller than reported previously.[3] In fact, the present MP2/6–31 + + G** value of $30\cdot5$ kcal mol⁻¹ for the energy difference between the isolated system (H⁻ + HNC) and the E anion 5 (cf. Table 2) is much smaller than the previous MP2/6–31 + G** value of $73\cdot9$ kcal mol⁻¹.[3] This discrepancy appears to arise from the lack of diffuse functions on the anionic centre H⁻ in Ref. 3. Such a lack renders the hydride anion unrealistically hard with respect to the adduct and gives as a consequence a large exothermicity for the addition. In this work, we find the isolated system H⁻ + HN≡C lies $19\cdot2$ and $23\cdot9$ kcal mol⁻¹ above the Z anion 3 and the E anion 5, respectively. Thus, the E carbanion 5 is about $4\cdot7$ kcal mol⁻¹ more stable than its Z isomer 3. The relevant Z/E isomerization occurs via the transition structure for N-inversion 6 and has a substantial barrier of $33\cdot2$ kcal mol⁻¹ (Figure 2). The latter relative energies computed at various levels (cf. Table 2) are not very different from those reported in Ref. 3 (computed up to MP4SDQ/6–31 + G** without ZPE corrections). The barrier heights for the cis-addition (giving the Z anion 3) and trans addition (yielding the E anion 5) are estimated to be $2\cdot9$ and $12\cdot9$ kcal mol⁻¹, respectively.

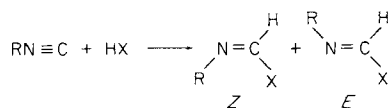Hence there is a difference of $10\cdot0$ kcal mol⁻¹ in activation energy in favour of the cis over the trans

addition (Figure 2). In addition, the computed barrier height of $2\cdot9$ kcal mol⁻¹ is too small to be real. The results in Table 2 indicate that this quantity tends to be reduced as the wavefunctions expand further. It might just disappear following a larger extension of the basis set and correlation energy. In any case, the cis addition exhibits a small barrier height and is always the preferred process. In other words, the addition of H⁻ to HN≡C is either stereospecific or, at least, strongly stereoselective. This result in general lends further support for our previous analysis based on lower levels of computations.[3] Such a stereoelectronic effect can simply be rationalized in terms of a concerted movement of electron pairs about the isocyanide as the nucleophile approaches the carbon end.[3]

Our calculated results are primarily valid for reactions which occur in gas phase. In solution, chemical systems may behave differently owing to the medium effect. In this regard, we should point out that kinetic results reported in Ref. 7 are not clear as to whether proton transfer is concerted with nucleophilic OH⁻ attack. The increase in reaction rates with increasing water content in the solvent suggests a concerted mechanism through a transition state such as V, but the apparent lack of a significant solvent isotope effect is, on the contrary, consistent with little (or no) proton transfer from the solvent. However, several assumptions with regard to the solvent isotope effect on other equilibria have to be made before coming to this conclusion. Questions can thus be posed on the rate-determining step and the role of water molecules in the transformation.
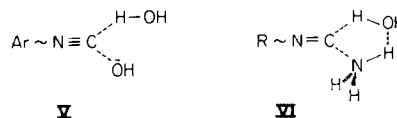
Recent experimental and theoretical studies[5,6] on the addition of amines to isocyanides showed that one or two water molecules can act as a bifunctional catalyst via a transition structure of type VI. In this case, the addition was shown to be non-stereospecific, yielding both Z and E isomers of the imine adduct. Hence the key information which would allow the mechanism of the anionic addition to isocyanide to be identified is the conformation of the primary adduct (III) (see above). Exclusive formation of the less stable Z isomer would suggest a stepwise carbanion mechanism, whereas the existence of both Z and E isomers would indicate a concerted mechanism. Because of the rapid conversion of the hydroxyimine III to formamide IV in aqueous solution, the use of hydroxide anion as nucleophilic agent may not be ideal for determining the conformation of the former. Further appropriate experiments are therefore desirable.

Table 3. Stereochemistry of 1,1-additions to isocyanides

$$RN \equiv C + HX \longrightarrow \underset{Z}{\overset{H}{\underset{R}{\diagup}}N=C\overset{R}{\underset{X}{\diagdown}}} + \underset{E}{\overset{R}{\underset{H}{\diagdown}}N=C\overset{H}{\underset{X}{\diagup}}}$$

Reaction conditions	Nature of nucleophile	Stereochemistry[a]	
		Experimental	Theoretical
Acidic, metal-catalysed	$H^+, M^+/X^-$	Stereospecific[2]	Stereospecific[3,15]
Neutral	HX	Non-stereospecific[4]	Non-stereospecific[5]
Anionic	X^-		Stereospecific[3]
Radical	$X^{\cdot}$		Non-stereospecific[6]

[a] Stereospecific indicates the formation of the less stable (Z)-imine in the kinetic step and non-stereospecific indicates the formation of both Z and E isomers.

CONCLUSION

The potential energy surface fo the $H^- + HNC$ system has been re-examined. Relative energies estimated at the $MP4/6-311++G^{**}$ level using the $MP2/6-31++G^{**}$-optimized geometries show that transition structures for both cis and trans additions exist on the energy surface, even though corresponding barrier heights are small. The cis addition is calculated to be favoured over the trans process by about $10 \, kcal \, mol^{-1}$. The overall addition is thus stereospecific or, at least, strongly stereoselective. This result confirms our previous analysis of the stereoelectronic effect in the addition—elimination reactions involving imidoyl anions (II) as intermediates.[3] Hence the addition of an anionic agent to isocyanide is predicted to be completely different from that involving a neutral nucleophile. The present knowledge on the stereochemistry of 1,1-addition reactions to isocyanides in the kinetic steps found either experimentally or theoretically is summarized in Table 3. To complete this table, experimental work with the aim of determining the mechanism and the stereochemistry in both anionic and radical additions to isocyanides is required.

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