Isotope Effects and Concerted Two-Hydron-Transfer between Formamidine Molecules

A Theoretical Study using the Ab Initio STO-3G Potential Energy Surface

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Dedicated to Professor Jacob Bigeleisen on the occasion of his 70th birthday

With the intention to assist mechanistic studies of two-hydron-transfer reactions using $^1H/^2H$ isotope effects we have carried out theoretical studies of the two-hydron-transfer reaction between formamidine molecules. The ab initio STO-3G potential energy surface has been calculated and all stationary points characterized by their force constant matrices. With this basis set the two hydrons are transferred concertedly and synchronously. The transition state (TS) has D_{2h} symmetry. $^1H/^2H$ isotope effects were calculated using the Bebovib-IV program. Our results deviated from predictions made from common simple vibrational models. The isotope effects are dominated by the zero-point-energy contribution. The effect due to the stretching vibrations of the initial state is to a small extent counteracted by stretching of the TS. The bending vibrations appear to play a dominant role in reducing the magnitude of the isotope effect for the two-hydron-transfer reaction to a value expected for a one-hydron-transfer reaction.

Key words: Two-hydron-transfer, Formamidine, Ab initio, STO-3G, Isotope effects.

Introduction

Reactions involving transfer of two hydrons, in which one of the hydron transfers is assisted by the other one, are common in enzyme and other catalysis [1]. There has been a large number of mechanistic studies of such reactions, and a major tool has been $^1H/^2H$ isotope effects [2]. Parallel to our experimental studies [3] of the interplay of the two hydrons being transferred, we are carrying out theoretical studies of reaction mechanisms of model systems, e.g. to assist the interpretation of observed isotope effects and to investigate the predictive power of simple vibrational models. We now wish to communicate our first results of ab initio studies of a concerted two-hydron-transfer between formamidine molecules.

It appears that using the STO-3G basis set a transition state (TS) is modelled in which the two hydrons are transferred concertedly and synchronously. This particular TS has D_{2h} symmetry. Deuterium isotope effects have been calculated from this potential-energy surface and are discussed below.

Methods

The ab initio calculations were performed with the Gaussian 86 [4] program package installed on a Digital MicroVax II Computer. The potential-energy surface was evaluated at the Hartree-Fock (HF)/STO-3G level of theory [5]. All stationary points were characterized by their force-constant matrices. The cartesian force-constant matrices from the Gaussian 86 program were used as input to a modified version of the Bebovib-IV program [6], which was used in the calculations of the isotope effects.

Results

The stationary points found correspond to the monomer (M) (C_1 symmetry), the dimer (D) (C_i symmetry) and the TS (D_{2h} symmetry) shown in Scheme 1.

Total and relative energies for the species are given in Table 1.

The structures of M (Fig. 1) and D resulting from the STO-3G basis set are nonplanar due to the pyramidal amine parts. This is not the case at higher levels (3–21G, 4–31G, 6–31G, and 6–31+G) of theory [7]. The split-valence basis sets overestimate bond

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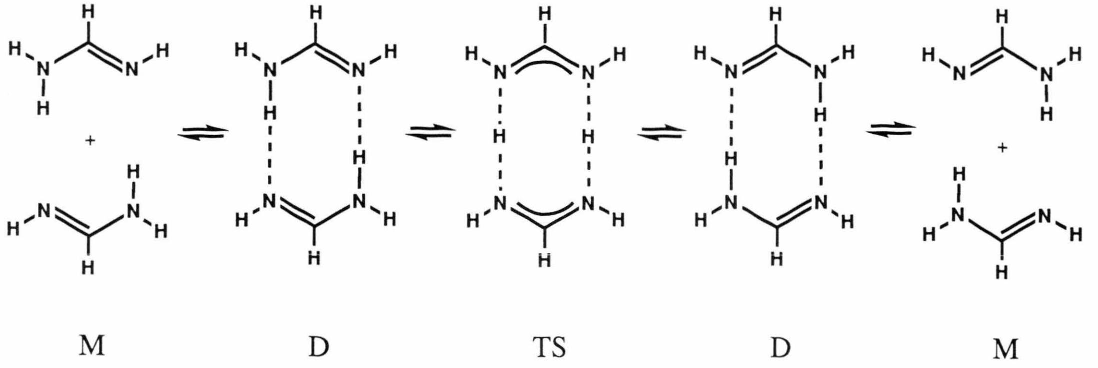


Scheme 1

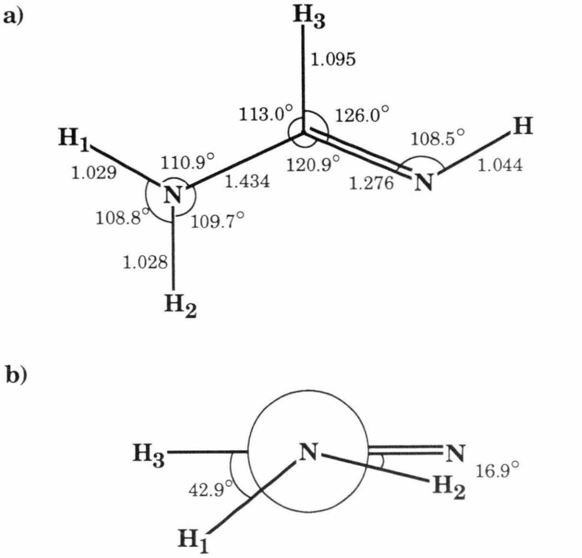


Fig. 1. Calculated equilibrium geometry for the formamidine monomer (M), C_1 structure, at STO-3G level of theory. a) Bond distances (given in Å) and bond angles. b) Dihedral angles for the amine part viewed as a Newman projection along the N–C single bond.

polarities [8], introducing a repulsive force between the nitrogen ligands which leads to a C_s structure for the monomer and a C_{2h} structure for the dimer.

The two hydrogen bonds in the dimer were found to be slightly bent ($\angle(\mathrm{NHN}) = 176.8°$) with a somewhat elongated N–H bond ($r_{\mathrm{NH}} = 1.041$ Å) compared to the corresponding bond ($r_{\mathrm{NH}} = 1.028$ Å) in the monomer (see Fig. 2), and a hydrogen-bond (H $\cdots$ N) distance of 1.786 Å.

The D_{2h} structure TS reported in Fig. 2 was verified to be a true saddlepoint. The NN-distance

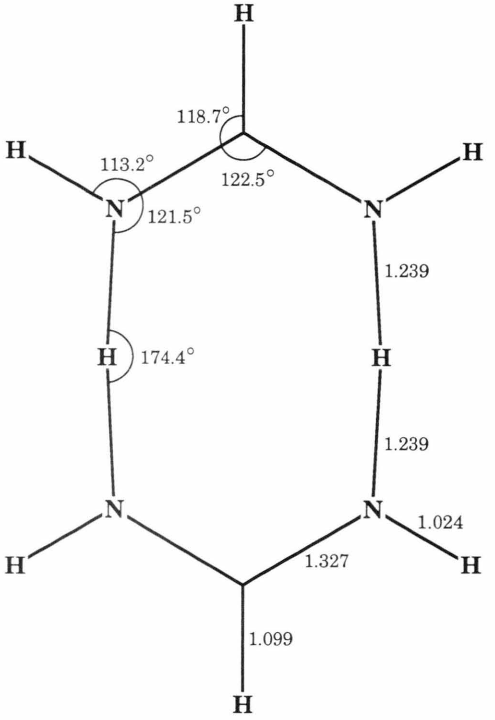


Fig. 2. Calculated equilibrium geometry for TS of D_{2h} symmetry in the two-proton transfer between formamidine molecules at STO-3G level of theory. Bond distances are given in Å.

Table 1. Summary of total and relative energies for the formamidine monomer (M), dimer (D) and transition state (TS) at the STO-3G level.

	total energy Hartree	relative energy kcal mol^{-1}
2 M	−294.30794	0
D	−294.32663	−11.7
TS	−294.31235	− 2.7

Table 2. Kinetic isotope effects for the two-hydrogen-transfer reaction between two formamidine molecules with 2 M as initial state. Temperature 25 °C.

	MMI [a]	EXC [a]	ZPE [a]	
HH/DD [b]				$\frac{\nu^{\neq}_{L(HH)}}{\nu^{\neq}_{L(DD)}} = 1.321$
Initial state (2 M)	1.3341	1.1410	3506.4	
Transition state	1.0562	1.0311	782.79	
Ratio	1.2631	1.1066	4.4793	$\frac{k_{HH}}{k_{DD}} = 6.26$
HH/HD [b]				$\frac{\nu^{\neq}_{L(HH)}}{\nu^{\neq}_{L(HD)}} = 1.157$
Initial state (2 M)	1.1550	1.0682	59.215	
Transition state	1.0277	1.0151	28.299	
Ratio	1.1239	1.0523	2.0925	$\frac{k_{HH}}{k_{HD}} = 2.47$
HD/DD [b]				$\frac{\nu^{\neq}_{L(HD)}}{\nu^{\neq}_{L(DD)}} = 1.142$
Initial state (2 M)	1.1550	1.0682	59.215	
Transition state	1.0277	1.0157	27.662	
Ratio	1.1239	1.0517	2.1407	$\frac{k_{HD}}{k_{DD}} = 2.53$

[a] Ref. [9]. – [b] Indicates type of isotopic substitution.

Table 3. Kinetic isotope effects for the two-hydron-transfer reaction between two formamidine molecules with D as initial state. Temperature 25 °C.

	MMI [a]	EXC [a]	ZPE [a]	
HH/DD [b]				$\frac{\nu^{\neq}_{L(HH)}}{\nu^{\neq}_{L(DD)}} = 1.321$
Initial state (D)	1.0561	1.1352	5540.3	
Transition state	1.0562	1.0311	782.79	
Ratio	0.9999	1.1010	7.0776	$\frac{k_{HH}}{k_{DD}} = 7.79$
HH/HD [b]				$\frac{\nu^{\neq}_{L(HH)}}{\nu^{\neq}_{L(HD)}} = 1.157$
Initial state (D)	1.0277	1.0654	74.437	
Transition state	1.0277	1.0151	28.299	
Ratio	1.0000	1.0496	2.6340	$\frac{k_{HH}}{k_{HD}} = 2.76$
HD/DD [b]				$\frac{\nu^{\neq}_{L(HD)}}{\nu^{\neq}_{L(DD)}} = 1.142$
Initial state (D)	1.0276	1.0655	74.429	
Transition state	1.0277	1.0157	27.662	
Ratio	0.9999	1.0490	2.6907	$\frac{k_{HD}}{k_{DD}} = 2.82$

[a] Ref. [9]. – [b] Indicates type of isotopic substitution.

(N···H···N) in TS is 2.474 Å and ∠(NHN) = 174.4°. The corresponding distance in D, 2.826 Å, is substantially longer.

The isotopic rate-constant ratios were calculated within the framework of the TS theory according to

$$k_H/k_D = \mathrm{MMI} \times \mathrm{EXC} \times \mathrm{ZPE}\,, \tag{1}$$

where the symbols MMI, EXC, and ZPE have their usual meaning [9]. Depending upon the choosen initial state, two sets of isotope effects can be calculated. One where the two formamidine molecules (2 M) are considered as the initial state and one where the reactant complex (D) is considered as the initial state. The former calculation gives the results presented in Table 2 and the latter calculation gives the results in Table 3.

In each table the contributions from the different factors in (1) are given together with the ratios of the imaginary frequencies and the calculated isotopic rate constant ratios.

It is also possible to calculate an equilibrium isotope effect for the formation of D. The results from such a calculation are presented in Table 4. The isotopically sensitive modes of the reactants and the TS are collected in Tables 5 and 6. The classification is based on an inspection of the eigenvectors and corresponds to the main feature of the motions of the hydrogens transferred in the reaction. Only those vibrations with an isotopic shift greater than 10 cm^{-1} have been included.

The mode corresponding to the reaction coordinate is given in Fig. 3, where the relative displacements of the atoms are shown in cartesian coordinates.

Discussion

The STO-3G surface used in this study should be seen just as a model for the surface of a concerted two-hydron-transfer reaction with a TS of D_{2h} symmetry. It is like to be a crude surface description of the

Table 4. Equilibrium isotope effects for the formation of the formamidine dimer. Temperature 25 °C.

	MMI[a]	EXC[a]	ZPE[a]	
HH/DD[b]				
Initial state (2 M)	1.3341	1.1410	3506.4	
Final state (D)	1.0561	1.1352	5540.3	
Ratio	1.2632	1.0051	0.6329	$\frac{K_{HH}}{K_{DD}}=0.804$
HH/HD[b]				
Initial state (2 M)	1.1550	1.0682	59.215	
Final state (D)	1.0277	1.0655	74.419	
Ratio	1.1239	1.0025	0.7957	$\frac{K_{HH}}{K_{HD}}=0.897$
HD/DD[b]				
Initial state (2 M)	1.1550	1.0682	59.215	
Final state (D)	1.0276	1.0654	74.429	
Ratio	1.1240	1.0026	0.7956	$\frac{K_{HD}}{K_{DD}}=0.897$

[a] Ref. [9]. – [b] Indicates type of isotopic substitution.

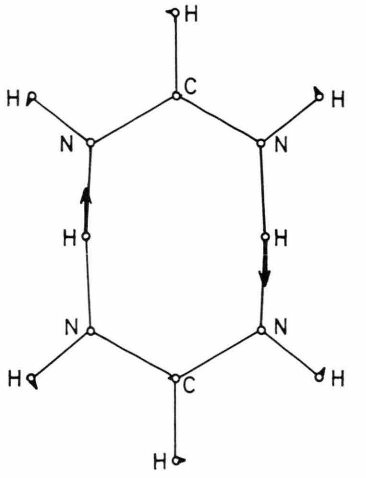


Fig. 3. Decomposition mode ($|\nu^{\neq}_{L(H)}|=1311\ \mathrm{cm}^{-1}$) of the D_{2h} transition state in the two-proton-transfer reaction between formamidine molecules.

Table 5. Summary of isotopically sensitive modes[a] in the formamidine molecule (M). Frequencies in cm^{-1}.

N–H type of motion	ν_H	ν_D
Stretching	3944, 4143	2955, 4045
	$\sum \nu_H - \sum \nu_D = 1087$	
Bending	379, 572, 826, 960, 1320, 1532, 1633, 1943, 2044	341, 530, 751, 930, 1170, 1461, 1621, 1769, 2031
	$\sum \nu_H - \sum \nu_D = 605$	

[a] Only vibrations with an isotopic shift greater than 10 cm^{-1} have been included.

two-hydron-transfer reaction between two formamidine molecules, e.g. it is well known that STO-3G gives too short hydrogen-bond distances and poor energies for species containing weak bonds of this type [10].

Before discussing the obtained ab initio results we will apply a simple vibrational model to predict the isotope effects.

a) A Simple Vibrational Model

Scheme 2 shows the stretching modes of a one-hydron transfer reaction. The initial state is a weakly

Table 6. Summary of isotopically sensitive modes[a] in TS. Frequencies in cm^{-1}.

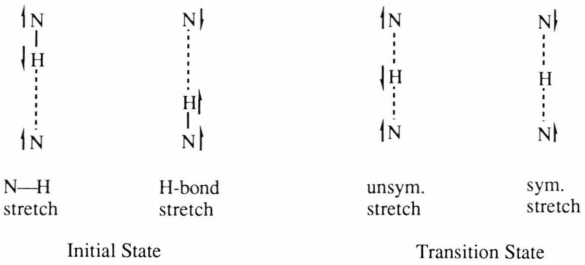
N ··· H ··· N type of motion	ν_{HH}	ν_{HD}	ν_{DD}
Stretching	1304, 1520, 2149, 2253	1287, 1457, 1978, 2177	1225, 1367, 1910, 2041
	$\sum \nu_{HH} - \sum \nu_{HD} = 327$	$\sum \nu_{HD} - \sum \nu_{DD} = 356$	$\sum \nu_{HH} - \sum \nu_{DD} = 683$
In-plane bending	766, 1385, 1543, 1731, 1974, 2181, 2204	755, 1332, 1514, 1632, 1787, 1990, 2192	745, 1292, 1509, 1553, 1704, 1821, 1821
	$\sum \nu_{HH} - \sum \nu_{HD} = 582$	$\sum \nu_{HD} - \sum \nu_{DD} = 577$	$\sum \nu_{HH} - \sum \nu_{DD} = 1159$
Out-of-plane bending	1168, 1591, 1615	1120, 1209, 1604	1109, 1144, 1238
	$\sum \nu_{HH} - \sum \nu_{HD} = 441$	$\sum \nu_{HD} - \sum \nu_{DD} = 442$	$\sum \nu_{HH} - \sum \nu_{DD} = 883$
Decomposition mode	i 1311	i 1133	i 992

[a] Only vibrations with an isotopic shift greater than 10 cm^{-1} have been included.

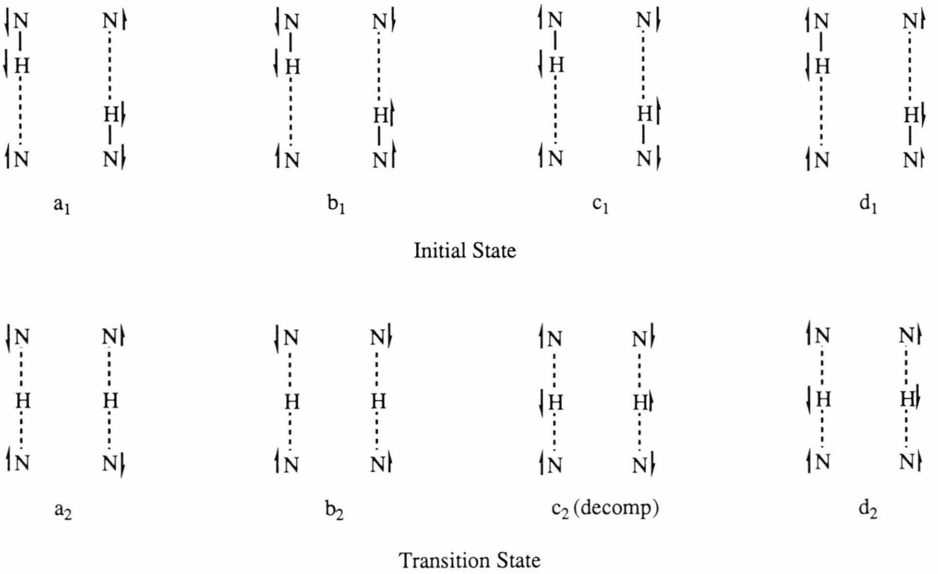
hydrogen-bonded linear complex, and the TS is linear and symmetrical. The N–H-stretch corresponds to the decomposition mode (unsym. stretch) in the transition state. The H-bond stretch, which is almost isotopically insensitive, corresponds to the isotopically insensitive symmetrical stretch of the TS. If it is assumed that the sum of the frequencies for the bending vibrations is equal for the initial- and transition states, respectively, we may conclude that the isotope effect (k_H/k_D) for the hydron-transfer is dominated by the ZPE-difference for the N–H and N–D stretching vibrations of the initial state.

For a concerted two-hydron-transfer reaction having a TS with D_{2h} symmetry, we might at a first glance predict a $k_{HH}/k_{DD} = (k_H/k_D)^2$ using assumptions similar to those for the one-hydron-transfer above, i.e. we have just multiplied the isotope effects for two one-hydron-transfers.

However, a deeper analysis still using a simple model yields a different answer. Scheme 3 shows the stretching modes of a two-hydron-transfer. The initial state is a weakly hydrogen-bonded complex and the TS has D_{2h} symmetry. There are four stretching modes for each state. The (H-bond)$_2$ stretches a_1 and b_1, which are essentially isotopic insensitive, correspond to the insensitive stretches a_2 and b_2 of the TS. The $(N-H)_2$-stretches c_1 and d_1, on the other hand, correspond to c_2 and d_2 of the TS, where c_2 corresponds to the decomposition mode. Thus for the two-hydron-transfer we may conclude that k_{HH}/k_{DD} is dominated not only by the zero-point energies (ZPE) of the $(N-H)_2$ and $(N-D)_2$ stretching vibrations c_1 and d_1 of the initial state, but we also have to take into accout the corresponding difference for d_2 of the TS. However, if we assume that the frequency for d_1 is equal to that of d_2, and again ignore any difference of sums of bending frequencies of the initial and transition states, respectively, we find that k_{HH}/k_{DD} is dominated by just the difference in ZPE of $(N-H)_2$ and $(N-D)_2$ of c_1. This frequency difference is likely to be close to the corresponding frequency difference for the one-hydron-transfer case above. Therefore we expect that k_{HH}/k_{DD} for a two-hydron-transfer is approximately equal to k_H/k_D for a one-hydron transfer and thus not equal to



Scheme 2



Scheme 3

$(k_H/k_D)^2$. Futhermore, we predict by this simple model for a concerted two-hydron-transfer via a D_{2h} TS that k_{HH}/k_{HD} ($= k_{HH}/k_{DH}$) is approximately equal to $(k_H/k_D)^{1/2}$. However, it has not been easy to see how accurate the approximations made above are.

b) Discussion of the ab initio Calculations

Our ab initio calculations have been carried out with the intention to get further insight into the factors that determine the magnitude of isotope effects of two-hydron-transfer reactions. The present model will be used to illustrate some features which we think are pertinent to isotope effects in concerted two-hydron-transfer reactions with TS's of D_{2h} symmetry.

Not unexpectedly the ZPE contribution to the isotope effect plays by far the most important role as can be seen from Tables 2 and 3. This is true for both the monodeuterated and the dideuterated species. However, the ZPE-factor is in all cases rather modest, giving rise to fairly weak isotope effects compared to what could be expected from the simple-minded model presented above. The reason behind this is that the ZPE-difference in the reactant is compensated for, to a rather large extent, by the ZPE-difference in the TS. From Tables 5 and 6, where the isotopically sensitive vibrations for the reactant and the TS are listed, it is obvious that this compensation is mainly due to isotopically sensitive bending vibrations in the TS. The highest bending vibrations (and therefore also the most isotopically sensitive vibrations) are found among the in-plane vibrations possibly due to restrictions from the cyclic structure of the TS.

This outcome is perhaps somewhat unexpected and not predicted by the simple model presented above. The importance of the bending vibrations is obviously decisive for the magnitude of the isotope effect. This will be illustrated for just one case using data from Tables 5 and 6.

From the differences in isotopic frequencies listed in Tables 5 and 6 a ZPE-factor of 4.91 (compared to 4.48 in Table 2, where all frequencies have been included) can be calculated for the HH/DD-case. In the same way a ZPE-factor based only on stretching vibrations is calculated to be 36.59. The corresponding ZPE-factor calculated from the bending frequencies is 0.1342.

These simple calculations clearly demonstrate the weak isotopic dependence of the stretching vibrations in the TS. The decisive importance of bending vibrations in the TS in reducing the isotope effect to a value expected for a one-hydron-transfer reaction is obvious.

The formation of the reactant complex results in a somewhat steeper potential for the hydrogens in the hydrogen bonds as indicated by the inverse equilibrium isotope effect (Table 4). This may be due to increased isotopic sensitivity of the in-plane vibrations as discussed for the TS.

The decomposition mode is given in Fig. 3, and as can be seen the mode is dominated by the motions of the two hydrogens although there is some coupling with the motions of the heavy atoms. This results in ratios of imaginary frequencies which are below the maximum values 1.414 ($\sqrt{2}$), 1.225 ($\sqrt{3/2}$), and 1.155 ($\sqrt{4/3}$), respectively. A calculation of a tunnel correction factor, e.g., according to Bell's formula [11] has not been performed, as the magnitude of the imaginary frequencies obtained here demand the use of at least two terms in the formula. The absolute magnitude of the calculated energy barrier needed for this is probably not reliable enough due to the limited basis set used.

The present calculations thus show that a modest isotope effect is predicted for a concerted two-hydron-transfer reaction with a TS of D_{2h} symmetry. This is not only the result of a reaction coordinate dominated by motions of heavy atoms [3] but to a great extent due to isotopically sensitive bending vibrations in the TS. Work is in progress to investigate two-hydron-transfer reactions using extended basis sets applied to the present and other systems to find out how general the conclusions from this first investigation are.

Acknowledgement

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