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# Model Calculations of Base-Catalysed 1,3-Proton Transfer Reactions in Indene-like Systems

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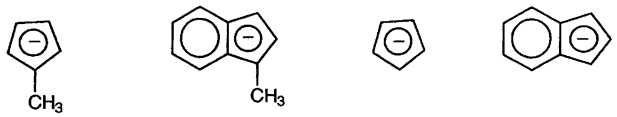
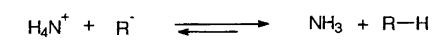
The geometries and heats of formation for stationary points on the potential energy surface (PES) for the prototropic rearrangement reactions of 1-methylcyclopentadiene and 1-methylindene, respectively, catalysed by ammonia, have been calculated by the PM3 method. The model used includes eight water molecules to simulate specific interactions of a polar solvent with the reactant molecules. After the initial transfer of the proton from the carbon acid to ammonia, the PES is found to be very flat, with almost free mobility of the ammonium ion above the 1-, 2- and 3-positions of the anions.

In the present paper, we describe hydrogen-bonded complexes (tight ion pairs) formed from the ammonium cation, on the one hand, and the methylcyclopentadienide (**1**) or 1-methylindenide (**2**) anions, on the other hand. Although **1** and **2** are carbanions substantially stabilized by π electron delocalization, the difference in basicity (expressed, e.g., in terms of the corresponding $\Delta pK_a$) between these anions and ammonia is very large. The $pK_a$



**1** **2** **3** **4**

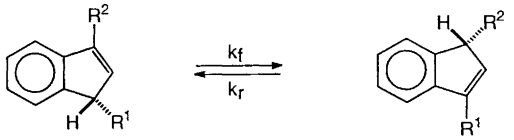
of the ammonium cation and the hydrocarbons (cyclopentadiene and indene) resulting from protonation of the parent carbanions **3** and **4** are roughly 10, 15 and 20, respectively.[1] Methyl substitution to give **1** and **2** will increase the $pK_a$, and therefore $\Delta pK_a$ by approximately one unit. Thus, at chemical equilibrium, the neutral species, i.e., ammonia plus the hydrocarbon, will predominate very substantially (Scheme 1).



*Scheme 1.*

This is also expected to be the case in the gas phase, and the reaction from left to right in Scheme 1 will most probably be a very rapid one-step proton transfer from nitrogen to carbon.

Our interest in ion pairs of the kind presented here is due to their proposed appearance as intermediates in amine-catalysed 1,3-hydron transfer reactions from carbon to carbon in allylic systems. The indene system has proved to be ideal for studies of fundamental aspects of base-promoted hydron transfer ever since 1963 when Bergson and coworkers[2] discovered the first non-enzymatic completely intramolecular and stereospecific prototropic rearrangement (Scheme 2).



*Scheme 2.*

Over the years, extensive investigations using the indene system have been performed.[3–5] Hydrogen-bonded carbanions are postulated as intermediates in essentially all hydron transfer reactions from carbons acids,[5a] and have recently been observed by spectroscopic methods.[6] The 1,3-hydron transfer in the indenes is believed to occur via at least one (probably two or maybe three) ion-pair intermediates.[7–9] In 1967, Wold and Bergson[7a] used the extended Hückel method[10] in an investigation of ion

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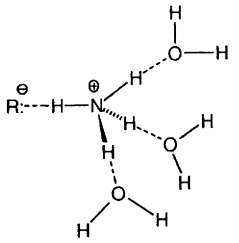
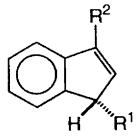
pairs between the indenide and ammonium ions. The relative stabilities of all five possible tautomeric forms of indene resulting from protonation of the corresponding non-equivalent carbon atoms in the indenide anion (**4**) were estimated. As expected, the molecule represented by formula **5** ($R^1 = R^2 = H$) was found to be much more



**6**



**5**

stable than the other tautomers. For example, 2*H*-indene, resulting from protonation at the 2-position of **4** was found to be 15–20 kcal $mol^{-1}$ higher in energy. The investigation also strongly indicated the existence of several ion-pairs. As expected, hydrogen-bonded complexes associated with carbon atoms 1 and 3, which have the largest negative net charge, were found to be energetically favoured.[7a]

A major weakness in this early study was that the ion-pair stabilizing effect of the solvent could not be taken into account. To prevent the spontaneous collapse of the ion pairs to ammonia and the hydrocarbon (cf. Scheme 1), the positions of the nitrogen atom and the mobile proton had to be treated as constant, *a priori* chosen parameters. In the present study, modern computational methods suitable for the modelling of chemical reactions were used to explore this reaction, with the ion-pair stabilizing effect of the solvent explicitly considered.

The smallest model system which would have the essential characteristics of an aromatic carbanion of the indenide type would be the cyclopentadienide anion (**3**). In the present context, however, it is desirable to perturb the fivefold symmetry of the cyclopentadienyl ion, e.g., by methyl substitution, in order to simulate the reduced symmetry of the corresponding fragment of the indenyl ion. Methyl-substituted cyclopentadiene may also serve as a simple model system for the calculation of β-secondary deuterium kinetic isotope effects (KIEs).[11]

The major part of the present study therefore utilized the methylcyclopentadienide anion (**1**) as the carbanion, where the methyl group perturbs the fivefold symmetry in **3**, making carbon atoms 1, 2 and 3 non-equivalent. Hence, in this respect, **1** simulates the 1-methylindenide anion (**2**). It should, however, be noted that in the latter, the presence of the benzene ring introduces additional effects on the electron distribution in the allylic system, which affect the relative proton affinities of positions 1, 2 and 3. This will be discussed further in the two following sections.

## Methods

Owing to the size of the systems under study, we used semiempirical rather than *ab initio* methods. Since, in the studied reaction, a strong interaction of the reaction species with the solvent was expected, including hydrogen bonds, we selected the PM3[12] parametrization of MNDO.[13] Even though this reparametrization of the MNDO method is relatively recent, the results of the original author[12] as well as our own experience[14] indicate that, in most cases, it is superior to other similar semiempirical methods for hydrogen-bonded systems and for transition states.

In order to model the experimentally studied systems,[2,3] the following simplifications were made.

(1) Ammonia was used instead of a tertiary amine. In principle, this simplification could introduce qualitative changes in the reaction mechanism, since it allows for bifurcated hydrogen bonds, not possible in a tertiary amine. In practice, however, the calculations also predict the establishment of a normal linear hydrogen bond when ammonia is used as base. However, since the basicities of ammonia and the experimentally used amines are different, their reactivities are expected to be different.

(2) In the first step, we used methylcyclopentadiene instead of 1-methylindene as a model system. As noted above, this approximation may change qualitatively the reaction profile, owing to the overestimation of the proton affinity of the carbon in position 2, as compared with position 3. In a later step, this approximation was removed.

(3) To simulate ion-pairs corresponding to minima on a PES, i.e., as reactive short-lived intermediates in the 1,3-proton transfer reaction, we had to take solvation effects into account. For a polar solvent we expected substantial specific solvation. We therefore disregarded continuum models and considered a supermolecule including eight water molecules in addition to the reaction system. In the ion-pair intermediates, three of these water molecules are hydrogen-bonded to the ammonium ion, whose remaining proton forms a loose hydrogen bond with the carbanion (**6**). The remaining five water molecules are distributed on the opposite side of the carbanion, relative to the ammonium ion. The positions of all eight water molecules were optimized at each stationary point of the reaction surface.

The calculations were done in three steps. (1) The interaction between ammonia and methylcyclopentadiene was studied in the gas phase. (2) The reaction system was solvated by eight water molecules, as described above. The potential energy surface, reaction path, and stationary points were studied in detail. All stationary points were characterized by determination of the eigenvalues of the Hessian matrices. (3) Finally, methylcyclopentadiene was replaced by 1-methylindene in a set of calculations involving only the reactant, intermediate and product states.

## Results and discussion

From an intuitive point of view, it is clear that the solvent influence on the 1,3-proton transfer reaction is decisive. The reactants and the products are neutral molecules, but the intermediate species are ion pairs. Thus, the transition states in the proton transfer reaction are partially charge-separated species. Inclusion of the polar solvent is therefore expected to have the following effects on the ion pairs and transition states.

(1) The oxygen of the water molecules solvating the ammonia will form hydrogen bonds with the ammonia protons. As a consequence, the electron density on nitrogen increases as does its basicity, thus the interactions with the migrating proton are stronger and the reaction towards the left in Scheme 1 becomes easier.

(2) Part of the negative charge on the ring is transferred to the hydrogen atoms of the water molecules hydrogen bonded to the carbanion, decreasing the basicity of the carbanion. This will also have the effect of increasing the probability of a reaction towards the left in Scheme 1.

Calculations on the non-solvated reaction system confirm that proton migration to ammonia is impossible in the gaseous phase. When the proton is removed from the ring in the direction of the ammonia molecule, the energy of the system increases monotonically, giving no probability for the reaction to the left in Scheme 1.

The inclusion of the eight water molecules dramatically changes the reaction profile, as expected. In Table 1 and Fig. 1 are shown the heats of formation of the different species in the reaction, in the presence of the water molecules.

The first stationary point of the studied reaction is a reactant complex, in which the proton is linked to the methylated carbon atom of the ring (position 1) and the free electron pair of the nitrogen is weakly linked to this proton [see Fig. 2(a)]. This complex is 10 kcal $mol^{-1}$ more stable than the isolated reactants, and constitutes a minimum in the potential energy hypersurface. The distance between the proton and the nitrogen is about 1.75 Å.

The second minimum of the potential energy surface corresponds to an ion pair, where the proton is transferred from the ring to the ammonia molecule [see Fig. 2(c)]. This is an intermediate species in the 1,3-proton transfer reaction, in which the proton is linked to a nitrogen but is still very close to the ring (about 1.83 Å). This intermediate species is calculated to be slightly more stable than the reactant complex (cf. Table 1).

*Table 1.* Heats of formation (kcal $mol^{-1}$) for different locations of the ammonia/ammonium ion above the cyclopentadiene ring, with eight water molecules from the solvent explicitly included in the calculation.

| Position | Neutral species (reactant or product complex) | Transition state (TS) | Ion pair |
|---|---|---|---|
| 1 | −427.9 | −423.1 | −428.7 |
| 2 | – | – | −429.9 |
| 3 | −430.8 | −426.0 | −429.6 |

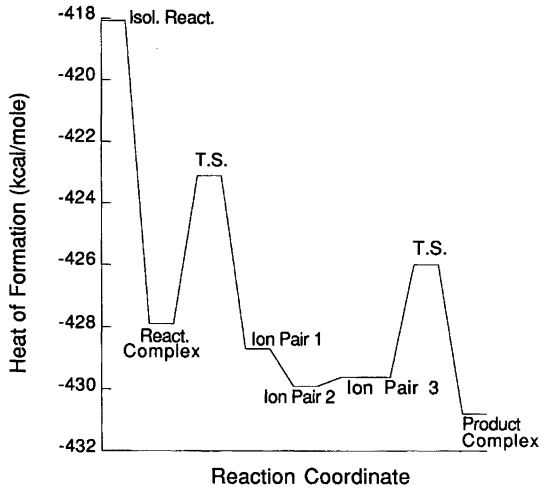



*Fig. 1.* Schematic representation of the reaction path for the 1,3-prototropic rearrangement in methylcyclopentadiene, catalysed by ammonia, calculated by the PM3 method with eight water molecules included.

Between these two minima there exists a transition state in which the proton is linked both to the ring and to the ammonia molecule [see Fig. 2(b)]. This is a maximum on the reaction profile and was located by means of the SADDLE algorithm implemented in program system MOPAC, from both minima, and later refined by the eigenvalue – following TS – search method, also implemented in this program. The energy of this transition state is about 5 kcal $mol^{-1}$ above the reactant complex.

After the ion pair is formed, the potential energy surface is very flat. This implies that this ion pair is formed between the proton and the $\pi$ electrons of the ring. No transition state was found when the ammonium ion was moved from the 1 to the 2 position to form another ion pair which, in this case (methylcyclopentadiene), is slightly more stable. This result does not agree with the expected behaviour in indene, where it is anticipated that the influence of the benzene ring reduces the stability of this ion pair.[7a] No transition state was found when the ammonium ion was further moved from the 2 to the 3 position [Fig. 3(a)]. However, a slight increase in energy (0.3 kcal $mol^{-1}$) was found in this case.

The next stationary point considered is the transition state [see Fig. 3(b)] for reprotonation at the 3-position. In this case, the activation energy is less than for the first step and the protonated complex [the reaction product, Fig. 3(c)] is the most stable species in the reaction profile. From this it is clear that, in our model, the 'slow' step is the formation of the first ion pair.

In the final stage of our modelling, we replaced the methylcyclopentadienide anion (**1**) by the 1-methylindenide anion (**2**). As can be seen in Table 1 and Fig. 1,

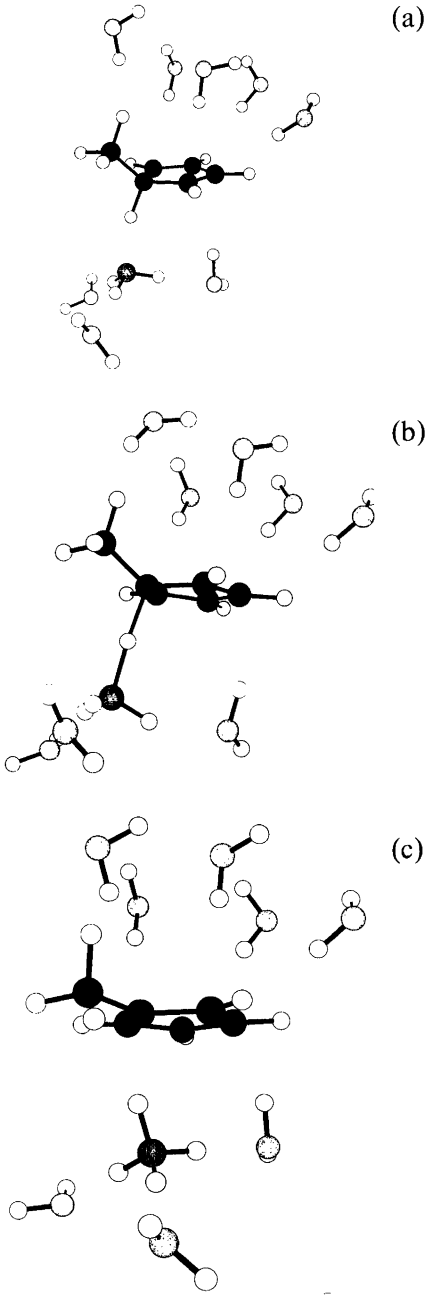



*Fig. 2.* Geometric arrangement of the reacting species and the eight surrounding water molecules at the stationary points of the potential energy surface corresponding to (a) the reactant complex (b) the first transition state and (c) the ion pair 1 in Fig. 1.

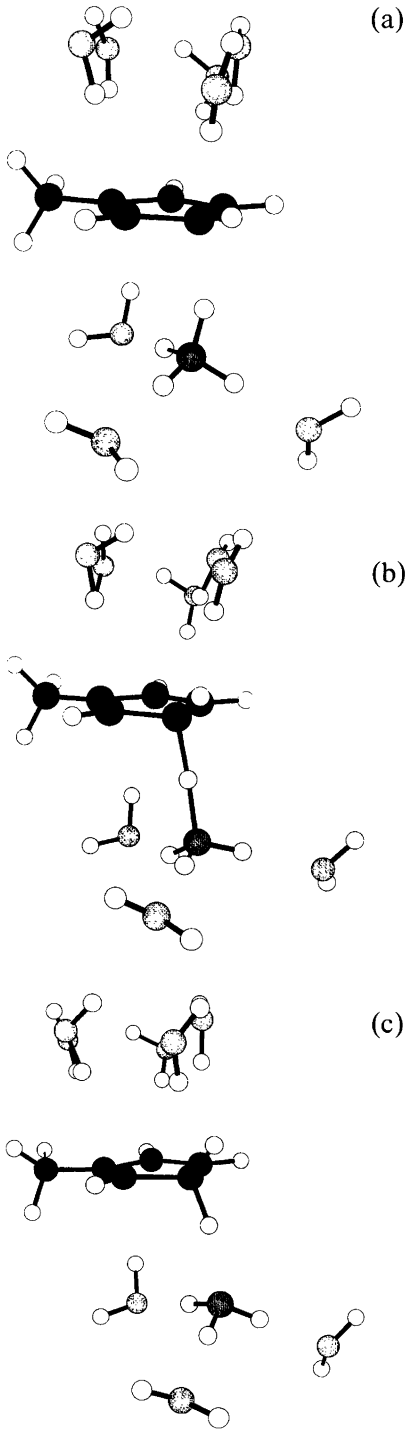



*Fig. 3.* Geometric arrangement of the reacting species and the eight surrounding water molecules at the stationary points of the potential energy surface corresponding to (a) the ion pair 3, (b) the second transition state and (c) the products in Fig. 1.

the energies of the transition states were, in the methylcyclopentadienide case, found to be close to the energies of the corresponding protonated complexes. Therefore, in the methylindenyl case, we chose to calculate only the different ion pairs in order to estimate the relative stabilities of the intermediate species in the proton-transfer reaction.

In Table 2 are shown the calculated heats of formation of all the ion pairs and protonated complexes, with methylindenide as the carbanion. From the results shown in the table, it is clear that, in the methylindenide anion, the most favoured position of protonation is the 3-position. We further see that all the ion pairs have nearly the same

*Table 2.* Heats of formation (kcal $mol^{-1}$) for different locations of the ammonia/ammonium ion above the 1-methylindene molecule, with eight water molecules from the solvent explicitly included in the calculation.

| Position | Neutral species (reactant or product complex) | Ion pair |
|---|---|---|
| 1 | −421.7 | −420.3 |
| 2 | −409.6 | −419.8 |
| 3 | −423.3 | −420.3 |

energies and that protonation in the 2-position is practically impossible, owing to the relative instability of the neutral species formed. The present results thus confirm those obtained in the previously mentioned extended Hückel calculation in Ref. 7(a).

The results in Fig. 1 contain one unsatisfactory aspect, namely that the heats of formation calculated for the ion pair intermediates are *lower* than that of the reactant complex, which disagrees with the experimentally found equilibrium (cf. Scheme 1). This obviously indicates a weakness in the model used. It is easy to trace this to the exclusive emphasis on specific solvation, as compared with the general effects of solvation, as included in, e.g., a reaction field or Monte Carlo treatment.[15] An indication that this is the root of the inadequacies of the present model is given by results from other calculations, which show that the first solvation shell contributes only about half of the solvation energy.[16] Further work is therefore needed in order to understand all the details of these reactions.

## Conclusions

The predicted mechanism for the base-catalysed 1,3-prototropic rearrangement reaction studied in the present paper includes a first, rate-determining step, in which an ion pair is formed, where the ammonium ion is weakly linked to the methylated carbon atom (position 1) via a hydrogen bond. Additional minima in the potential energy surface are found, where the base is linked to positions 2 and 3. Especially in the case of 1-methylindene, the total energies differ very little between these three locations, indicating relatively free mobility of the ammonium ion above the surface of the carbanion.

Further study is needed concerning this rapid translational motion of the ammonium ion. Of particular importance is the energetics of the transition states for this motion as compared with the activation energies for ion-pair collapse[3d,e] of the hydrogen-bonded complexes, i.e., the hydron transfer to the various carbon atoms. A firm knowledge of the rate constant ratios for ion-pair translation vs. collapse, for unsymmetrically substituted carbanions is necessary, e.g., for the interpretation of observed isotope effects ($^1H$ vs. $^2H$), in enantioselective hydron-transfer reactions of **2**.[17]

## Acknowledgements

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