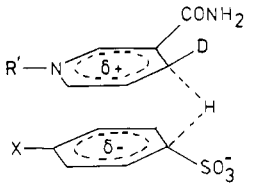
in a sandwich-type transition state:



which, at first sight, shows more resemblance with the triangular state we had to disclaim than with the linear one our study led us to adopt. However, in contrast with the positively charged hydride acceptor we used, the kinetic study was concerned with a neutral hydride acceptor with, in addition, a negatively charged substituent. Taking into consideration the importance of electrostatic contributions to the total energy of such compounds, the sandwich-type intermediate becomes an understandable variation of the linear structures of this study. Moreover, it should be noted that the main characteristic of the triangular transition state, the C(α)-C(α′) bond, is absent in the proposed sandwich-type structure. For the system cyclopropene/cyclopropenium cation MINDO/3 produces an activation enthalpy value which is low as compared with the STO-3G result. However, on other features of the enthalpy contour map, especially the reaction path and the structure of intermediates, MINDO/3 and STO-3G appear to be in good agreement, If, in all fairness, we remember that both MINDO/3 and STO-3G are approximative methods producing possible enthalpy inaccuracies of at least 5 to 10 kcal mol^{-1}, we must come to the conclusion that the overall agreement is satisfactory.

As stated earlier, the model compounds chosen for this study are, for reasons of symmetry, unable to demonstrate the interesting stereospecificity of the hydride-donation reaction of NADH. In the subsequent paper we will show that the 3-carbamoyl substituent, present in the NADH molecule, is capable of inducing different kinetic reactivities for the two α hydrogen atoms, provided the enzymatic environment locks the $CONH_2$ group in an orientation where it is rotated out of the plane of the (dihydro)pyridine ring. Although our calculations cannot be expected to give accurate results with regards to the thermodynamic aspects of the reaction, we expect our conclusions pertaining to the reaction mechanism to be substantially correct for the enzymatic hydride-transfer reaction of NAD^+/NADH.

Acknowledgment. We wish to thank Mr. W. Landa for many helpful discussions.

The Hydride-Donation Reaction of Reduced Nicotinamide Adenine Dinucleotide. 2. MINDO/3 and STO-3G Calculations on the Role of the $CONH_2$ Group in Enzymatic Reactions

M. C. A. Donkersloot* and H. M. Buck

Contribution from the Department of Organic Chemistry, Eindhoven University of Technology, Eindhoven, The Netherlands. *Received July 25, 1980*

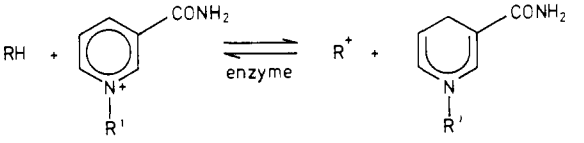
Abstract: The enzyme-catalyzed stereospecific hydride-transfer equilibrium RH + $NAD^+ \rightleftharpoons R^+$ + NADH has been studied with the help of semiempirical (MINDO/3) and ab initio (STO-3G) calculations on corresponding model compounds. It seems possible to relate the stereospecificity simply to an out-of-plane orientation of the $CONH_2$ group in the transition state of the reaction. One of the important functions of the enzyme would be to freeze the otherwise almost freely rotating $CONH_2$ group in a favorable orientation.

Introduction

During recent years the coenzyme nicotinamide adenine dinucleotide (NAD^+) has received wide-spread attention.[1] It is well known that the stereochemistry of this redox coenzyme is controlled by a number of dehydrogenation enzymes, the characteristic reaction being the transfer of a hydride ion from the substrate to the 4 position of the nicotinamide moiety of NAD^+; see Scheme I.

An, as yet, not fully understood feature of this equilibrium is the stereospecificity of the hydride transfer. This effect was demonstrated by Vennesland and Westheimer[2] for the oxidation of CH_3CD_2OH by NAD^+, catalyzed by alcohol dehydrogenase (ADH); see Scheme II. They showed that in this reaction direct transfer of $:D^-$ takes place and that this transfer is stereospecific with respect to both coenzyme and substrate. This stereospecificity is absent when the reaction is carried out under nonenzymatic conditions. In the preceding paper[3] we demonstrated that the hydride-transfer reactions with cyclopropene, 1,4-dihydropyridine, and tropilidene as hydride donors, and the cyclopropenium cation

Scheme I. Prototype of the Enzymatic Reduction of NAD^+ to NADH



Scheme II. Reduction of NAD^+ by CH_3CD_2OH with Alcohol Dehydrogenase

$$CH_3CD_2OH + NAD^+ \underset{ADH}{\rightleftharpoons} CH_3CDO + NADD + H^+$$

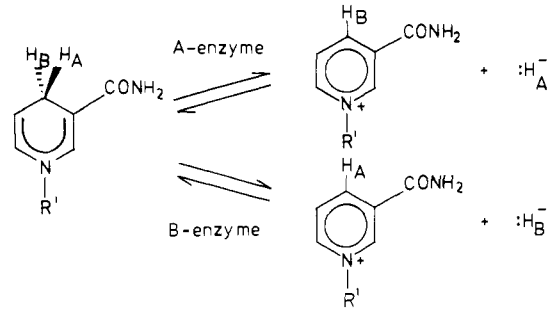
(1) Sund, H. "Pyridine Nucleotide-Dependent Dehydrogenases"; W. de Gruyter: Berlin, West Germany.

(2) Vennesland, B.; Westheimer, F. H. In "The Mechanism of Enzyme Action"; McElroy, W. D.; Glass, B., Eds.; John Hopkins Press: Baltimore, 1954.

(3) Donkersloot, M. C. A.; Buck, H. M. *J. Am. Chem. Soc.*, preceding paper in this issue.

0002-7863/81/1503-6554$01.25/0

Scheme III. Stereospecific Hydride Transfer by A- and B-Type Dehydrogenase



as acceptor, can be conveniently described with respect to a reaction coordinate which is very similar for all three equilibria. This reaction coordinate is defined on a two-dimensional formation-enthalpy-contour map with the enthalpy values plotted as a function of the two distances between the migrating hydrogen atom and the donating and accepting carbon atoms. Along this reaction coordinate the transfer of two electrons and one proton occurs in a synchronous fashion. The C···H···C chain, where the actual hydride transfer takes place, remains linear along the minimum-gradient reaction path (MGRP). We also demonstrated that MINDO/3 and STO-3G calculations for the reaction of cyclopropene and the cyclopropenium cation are compatible as regards the reaction pathway they indicate, but that MINDO/3 seems less accurate with respect to the location of the transition state and the magnitude of the activation enthalpy. In the present paper we report semiempirical (MINDO/3[4]) and ab initio (STO-3G with Gaussian 70[5]) calculations which indicate how the stereospecificity of the enzymatic hydride transfer of NAD^+/NADH can arise, that is to say, how the substrate can distinguish between the two hydrogen atoms available for transfer (H_A or H_B), dependent on the type of enzyme (A or B type); see Scheme III.

To this purpose we have extended our series of model compounds with 3-carbamoyl-1,4-dihydropyridine (CDHP)/3-carbamoylpyridinium cation (CP^+). As in the preceding paper[3] we have chosen cyclopropene/cyclopropenium cation as a convenient substrate, but we report also MINDO/3 calculations pertaining to the reaction of CP^+ with methanol as hydride donor (CH_3OH/H_2COH^+). This latter substrate is conveniently small and suitable as a model compound for the frequently encountered substrate ethanol. Finally we have performed MINDO/3 as well as STO-3G calculations on the hydride-transfer reaction of 2-carbamoylcyclopropene (CCP)/carbamoylcyclopropenium cation (CCP^+) with cyclopropene/cyclopropenium cation as substrate. This model reaction has been included to make it possible to calibrate important MINDO/3 results with STO-3G calculations.

The presence of the $CONH_2$ group enables NAD^+/NADH to react in a stereospecific manner either directly, by permanently breaking the symmetry with respect to the (dihydro)pyridine ring, or indirectly, by breaking the symmetry with respect to the plane perpendicular to the ring, thereby providing an enzyme with the possibility to distinguish between both sides of the molecule. In the first case, it is essential that both NADH and NAD^+ exist in stable chiral configurations, uncontaminated by their enantiomers. In the second case, the transition states in the enzymatic environment must be different. Both possibilities will be examined in this paper.

Results and Discussion

The first possible explanation of the difference in reactivity between H_A and H_B (see Scheme III), namely, the one based on a permanent dissymmetry of both sides of the (dihydro)pyridine ring in both NADH and NAD^+, was investigated as follows. The total standard enthalpy of formation ($\Delta H_f°$) of CDHP and CP^+ was calculated with MINDO/3 using complete structural optimization, but keeping the torsion angle (φ) around the C(3)–C-ONH_2 bond fixed at certain values. Figure 1 shows the resulting $\Delta H_f°$ as a function of φ ($\varphi = 0°$ corresponds to the oxygen of the $CONH_2$ group syn-oriented with respect to C(4); $0° < \varphi < 180°$ corresponds to the oxygen of the $CONH_2$ group being on the same side of the (dihydro)pyridine ring as H_A, etc.). The calculations established that, independent of the value of φ, in CDHP as well as in CP^+ both the (dihydro)pyridine ring and $CONH_2$ group each preserve a planar configuration at the MINDO/3 level. Although it is known that the MINDO/3 approximation has a tendency to underestimate ring puckering,[6] the outcome in this case is in agreement with CNDO/2 results, whereas EHT leads to a very flat boat-type conformation.[7] It can be seen from Figure 1 that MINDO/3 indicates a slight bias toward chirality associated with minimum enthalpy values for perpendicular orientations of the $CONH_2$ group. However, the enthalpy barriers are low enough for the rotation of the $CONH_2$ group to be almost free: for CDHP there are barriers at $\varphi = 0$ and 180° of 3.9 and 1.7 kcal mol^{-1}, respectively; for CP^+ one finds 4.6 and 3.3 kcal mol^{-1}. For CDHP comparable results are found in the literature: barriers at $\varphi =$ 0 and 180° of 5.0 and 4.5 kcal mol^{-1}, respectively (MINDO/2), and 1.5 and 3.0 kcal mol^{-1}, respectively (CNDO/2), all given with respect to a minimum enthalpy at $\varphi = 90°$, have been reported.[8] With the NDDO method a rotational barier of 1.7 kcal mol^{-1} was found at $\varphi = 90°$, the minimum enthalpy being located at $\varphi =$ 150°.[9] In view of the relatively small magnitude of these barrier

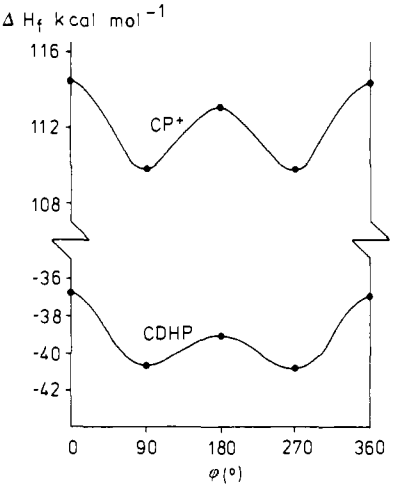


Figure 1. $\Delta H_f°$ of CDHP and CP^+ against φ.

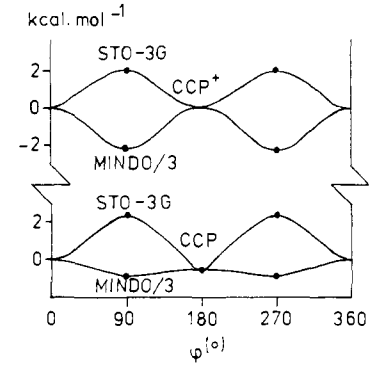


Figure 2. $\Delta H_f°$ of CCP and CCP^+ against φ, calculated with MINDO/3 and STO-3G.

(4) Dewar, M. J. S.; Metiu, H.; Student, P. J.; Brown, A.; Bingham, R. C.; Lo, D. H.; Ramsden, C. A.; Kollmar, H.; Weiner, P. *QCPE* **1975**, *11*, 279.
(5) Hehre, W. J.; Lathan, W.A.; Ditchfield, R.; Newton, M.D.; Pople, J. A. *QCPE*, **1973**, *11*, 236.
(6) Bingham, R. C.; Dewar, M.J.S.; Lo, D.H. *J. Am. Chem. Soc.* **1973**, *95*, 1285–1293.
(7) Krechl, J.; Kuthan, J. *Collect. Czech. Chem. Commun.* **1980**, *45*, 2425–2432.
(8) Kuthan, J.; Musil, L. *Collect. Czech. Chem. Commun.* **1975**, *40*, 3169–3176.

Table I. Calculated Energies for Planar Configurations of CCP and CCP$^+$

	MINDO/3[a]	STO-3G[a]
CCP	−10.70[b]	−279.94793[c]
CCP$^+$	172.37[b]	−279.17589[c]

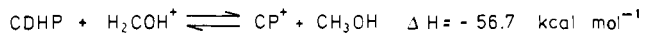
[a] MINDO/3-optimized structures (constraint $\varphi = 0°$). [b] In kcal mol^{-1}. [c] In atomic energy units.

Table II. Standard Formation Enthalpies as Calculated with MINDO/3

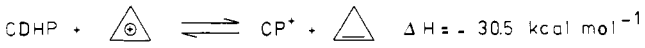
	$\Delta H_f°$[a]
CDHP	−40.81
CP$^+$	109.79
C_3H_4	59.29
$C_3H_3^+$	240.42
CH_3OH	−50.66
CH_2OH^+	156.65

[a] $\Delta H_f°$ in kcal mol^{-1} for structures fully optimized at MINDO/3 level.

Scheme IV. The Hydride-Transfer Equilibrium of CP$^+$ and Methanol



Scheme V. The Hydride-Transfer Equilibrium of CP$^+$ and Cyclopropene

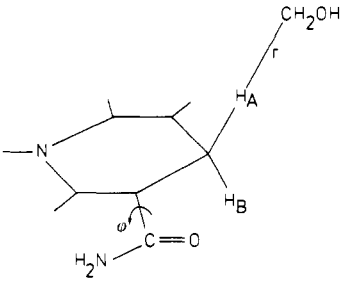


enthalpies as compared with the accuracy one can expect from semiempirical methods, we can only conclude that the barrier for the rotation of the $CONH_2$ group is very low. Experimental evidence as to the planarity of the pyridine ring and a rotation of the amide group out of the plane of the pyridine ring in crystals of N-substituted CDHP compounds[10] is interesting but of no relevance in the present context.

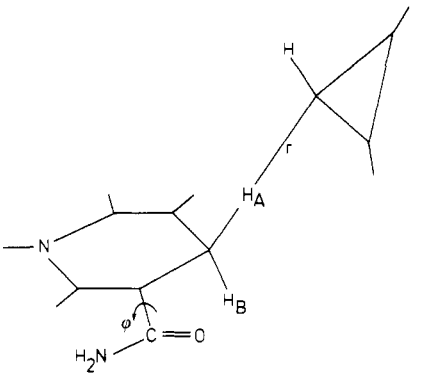
We also carried out MINDO/3 as well as STO-3G calculations for the compounds CCP and CCP$^+$. The results are shown in Figure 2, where enthalpy differences are plotted as a function of the out-of-plane torsion angle φ, defined in the same way as for Figure 1. Apart from this angle all other structure parameters were optimized with MINDO/3. The STO-3G results relate to the MINDO/3-optimized structures. Enthalpies are given with respect to the planar configurations with $\varphi = 0°$; see Table I.

From Figure 2 it can be seen that MINDO/3 predicts a perpendicular orientation for the $CONH_2$ group for both the compounds CCP and CCP$^+$, whereas STO-3G predicts these compounds to be planar, with a slight preference in CCP for the orientation with the C=O bond trans with respect to the methylene group. Although the differences between the MINDO/3 and the STO-3G results are interesting in themselves, in the present context it is sufficient to conclude that in both cases the calculated barriers are no great hindrance to occasional flipping over of the $CONH_2$ group. In summary we come to the conclusion that it is unlikely that the experimental stereospecificity of the NAD$^+$/NADH hydride-transfer reaction originates from a permanent chirality of the reactive fragments of NADH and NAD$^+$. For looking at kinetic effects we have adopted the same procedure as described in the preceding paper,[3] making use of results reported there. In particular we refer to the conclusion that for 1,4-dihydropyridine the interesting phenomena take place early on the reaction coordinate where structures are reactant-like. This could also be inferred from the calculated negative reaction enthalpy for the reactions given in Schemes IV and V. These reaction enthalpies were calculated from MINDO/3 standard formation enthalpies as collected in Table II. Consequently we constructed

Scheme VI. Transition State for the Transfer of H_A^+ from CDHP to CH_2OH^+



Scheme VII. Transition State for the Transfer of H_A^- from CDHP to $C_3H_3^+$



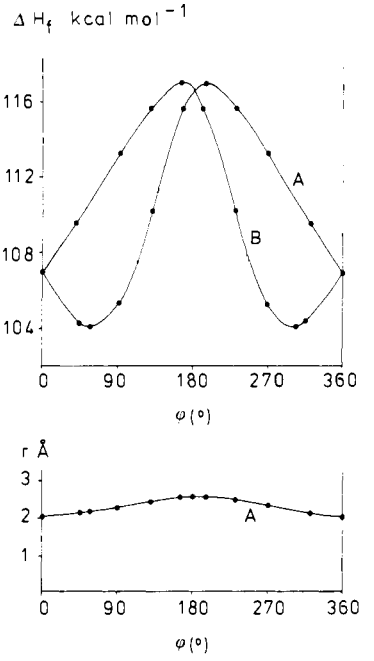


Figure 3. $\Delta H_f°$ and r of the transition state CP···H···CH_2OH^+ against φ.

the configurations as given in Schemes VI and VII and calculated the MINDO/3 formation enthalpy of these structures as a function of one parameter r, the distance between the migrating hydrogen atom and the accepting C(α) atom of the C_3H_3 and CH_2OH moieties; see Scheme VI and VII. All structure parameters except r were optimized with respect to $\Delta H_f°$. The parameter r was varied until a maximum enthalpy on the MGRP was found. The corresponding structure is the transition state.

Similarly calculated transition states but with fixed values of φ (Schemes VI and VII) were located; that is to say, for each fixed value of φ a local enthalpy maximum on the MGRP was determined with full optimization of all structural parameters but r and φ. The resulting activation enthalpies and values of r locating

(9) Hofmann, H.-J.; Kuthan, J. *Collect Czech. Chem. Commun.* **1979**, *44*, 2633–2638.

(10) Huml, K.; Jěcný, J.; Kutschabsky, L.; Reck, G. *Acta Crystallogr., Sect. B* **1979**, *35*, 444–447.

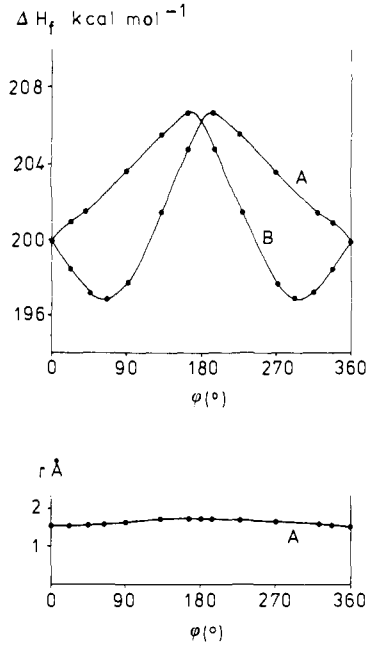
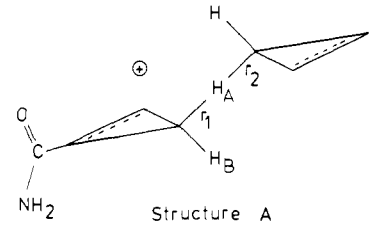


Figure 4. $\Delta H_f°$ and r of the transition state CP···H···$C_3H_3^+$ against φ.

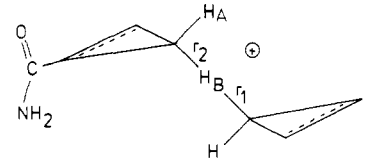
the transition states are depicted in Figures 3 and 4, where the curves A and B refer to the choice of H_A or H_B as leaving hydride ion. The transition states are very similar to those found for cyclopropene, 1,4-dihydropyridine, and tropilidene with the cyclopropenium cation.[3] However, because of the presence of the $CONH_2$ group, the C_s symmetry is broken with the result that the C···H···C bridge is no longer linear. The deformations of the linear structure remain quite small and can be described as a tilt of the C_3H_3 or CH_2OH moieties caused by a relatively strong attraction by the oxygen of the $CONH_2$ group, and a relatively small repulsion by the NH_2 of the $CONH_2$ group. It can be seen that variation of φ has a marked effect on the activation enthalpy: the enthalpy extremes are much wider apart than was found for the free molecules CDHP and CP^+. Moreover, the mutual symmetry of H_A and H_B, essentially preserved in the free molecules, is no longer there: around $\varphi = 90$ and 270° there is a significant difference in activation enthalpy for the transfer of H_A^- and H_B^-. This difference amounts to 8 kcal mol^{-1} for the combination CDHP + CH_2OH^+ and 6 kcal mol^{-1} for CDHP + $C_3H_3^+$. The origin of this enthalpy difference can easily be denoted. In the transition state CDHP interacts with a positively charged hydride acceptor, and it is the electrostatic interaction between the acceptor and the $CONH_2$ group which dominates in the interaction enthalpy. Indeed, the $CONH_2$ group, and in particular the carbonyl bond, is highly polarized according to our calculations; the carbon atom carries a (positive) net charge of +0.67, whereas the oxygen atom has a (negative) net charge of −0.61, the NH_2 group approximately making up the balance to render the $CONH_2$ group slightly positive (ca. +0.02; all charges expressed in atomic units of charge). The shape of the curves shown in Figures 2 and 3 can now be understood in terms of the interaction between the negatively charged oxygen atom of the $CONH_2$ group and the positive charge of the hydride-accepting moiety. A low-enthalpy transition state corresponds to the carbonyl dipole pointing toward the hydride acceptor and a high-enthalpy transition state to the carbonyl dipole pointing away from the acceptor. Other effects, e.g., more or less efficient HOMO–LUMO interactions, are of secondary importance. To add additional support we have also performed MINDO/3 and STO-3G calculations on intermediate structures for the reaction of CCP with the cyclopropenium cation. In particular, we looked at structures with $\varphi = 90°$, and with H_A or H_B as the leaving hydride moiety; see Schemes VIII and IX. These structures were optimized with MINDO/3, using as constraints $\varphi = 90°$ and $r_1 = r_2$. The resulting structures were taken to be representative of the transition states. A more detailed search of the enthalpy surface was not attempted in view of our earlier

Scheme VIII. Transition State for the Transfer of H_A^- from CCP to C_3H_3 with $\varphi = 90°$



Structure A

Scheme IX. Transition State for the Transfer of H_B^- from CCP to $C_3H_3^+$ with $\varphi = 90°$



Structure B

Table III. Comparison of Energies Calculated for Structures A and B (see Schemes VIII and IX) with MINDO/3 and STO-3G

	MINDO/3	STO-3G
structure A	233.95[a]	−393.54136[b]
structure B	235.80[a]	−393.53779[b]
difference	1.85[a]	2.24[a]

[a] In kcal mol^{-1}. [b] In atomic energy units.

work,[3] which demonstrated the flatness of the MINDO/3 surface along the reaction coordinate. In Table III the energies are given for the structures A and B as calculated with MINDO/3 and STO-3G. It can be seen that MINDO/3 and STO-3G both result in attributing to structure A an enthalpy which is less by ca. 2 kcal mol^{-1} as compared with structure B. Although the effect is here much smaller, the $CONH_2$ group, once fixed in a perpendicular orientation, induces the same stereospecific behavior as found in the hydride-transfer reaction of CDHP/CP^+. Moreover, the quantitative agreement between MINDO/3 and STO-3G suggests that the MINDO/3 results for the studied type of reactions are fairly reliable. Besides it should be stated that the important result is a difference between the enthalpies of two closely resembling transition states, namely, one with H_A and one with H_B as bridging atom. It seems safe to assume that many inaccuracies are cancelled in the comparison.

Conclusion

We should like to suggest now a way in which our results can be used to explain the experimental observations concerning the redox reactions of NADH as given in the Introduction. To begin with, we can understand the absence of stereospecificity displayed under nonenzymatic conditions. At normal temperatures even in the transition state the $CONH_2$ group is rotating almost freely and no stereospecificity arises. However, once the coenzyme has formed a reactive complex with a suitable enzyme the $CONH_2$ group looses the freedom to rotate, for instance, by the formation of a hydrogen bond. When the $CONH_2$ group is fixed, and most likely this will be in an out-of-plane orientation with respect to the pyridine ring, H_A and H_B may migrate to the substrate but with very different rates. This causes the reaction to be effectively stereospecific. As regards hard experimental evidence for this mechanism, one has to remember that transition states are of a notorious elusiveness. Even X-ray diffraction results of crystallized enzyme/coenzyme/substrate complexes are, strictly speaking, not relevant. Moreover, it appears very difficult from the electron-density map to distinguish between the two possible $CONH_2$ orientations in coplanar configurations, this structural detail being a matter of choice.[11] From this point of view, reaction mecha-

(11) See ref 1. We refer to a statement made by A. J. Wonacott, p 235.

nisms in which the $CONH_2$ group is supposed to remain in-plane, and therefore passive with respect to stereospecificity, seem insufficiently supported. However, our theory is at least partly sustained by Dutler's mechanism for the hydride transfer catalyzed by liver alcohol dehydrogenase.[12] He envisaged the (dihydro)pyridine ring to have enough freedom of motion to change its position during the hydrogen transfer, a movement possibly accompanied by rotation of the $CONH_2$ group out of the plane of the (dihydro)pyridine ring. However, no mention was made of an active role of the $CONH_2$ group in the reaction.

(12) See ref 1, Dutler, H., 347.

Acknowledgment. We wish to thank Mr. W. Landa and Professor L. A. AE. Sluyterman for many helpful discussions.

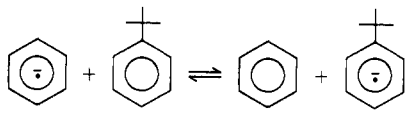
Enthalpy of Steric Inhibition to Solvation due to *tert*-Butyl Groups on an Anion Radical

Gerald R. Stevenson,* Jeanette D. Kokosinski, and Yoh-Tz Chang

Contribution from the Department of Chemistry, Illinois State University, Normal, Illinois 61761. *Received February 10, 1981*

Abstract: Electron-spin-resonance techniques have been utilized to measure the enthalpy of electron transfer from the anion radical of naphthalene ($N^{-}\cdot,K^{+}$) to 2-*tert*-butylnaphthalene (TBN) and from the anion radical of TBN ($TBN^{-}\cdot,K^{+}$) to 2,6-di-*tert*-butylnaphthalene (DTBN) in dimethoxyethane (DME). These endothermic enthalpies of electron transfer were combined with the heat of solvation of the gas-phase anion radical of naphthalene plus the gas-phase potassium cation in DME, the heats of solvation of the neutral hydrocarbons in DME, and the heats of vaporization of the hydrocarbons in a thermochemical cycle to yield the enthalpy of solvation of $(DTBN^{-}\cdot)_g + (K^{+})_g$ in DME. This enthalpy of solvation is about 17 kcal/mol less exothermic than that for $(N^{-}\cdot)_g + (K^{+})_g$ and is attributed to the steric inhibition to solvation by the *tert*-butyl groups on $DTBN^{-}\cdot$. The enthalpy of solvation of $(N^{-}\cdot)_g + (K^{+})_g$ (−162 kcal/mol) was determined by combining the enthalpy of the reaction of the DME solvated anion radical with water with a series of well-known constants in a thermochemical cycle. Thus, by utilizing a combination of calorimetric and ESR techniques a complete picture of the thermodynamic parameters controlling the stabilities of the solvated and gas-phase anion radicals of N and DTBN has been generated.

Lawler and Tabit[1] have determined the relative solution electron affinities of benzene and a series of alkyl-substituted benzenes, including *tert*-butylbenzene, based upon the free energy change for the reaction shown in reaction 1. Mixtures of carefully



(1)

$(\Delta H^{\circ})_{soln} = +1.6$ kcal/mol
$(\Delta H^{\circ})_{g} = -2.1$ kcal/mol

measured quantities of benzene and the alkyl-substituted benzene were reduced with sodium–potassium alloy in a mixture of dimethoxyethane (DME) and tetrahydrofuran (THF), and the relative intensities of the two simultaneously observed ESR spectra were used to calculate the equilibrium constant. In this manner ΔG°, which was assumed to be equal to the enthalpy of the reaction, was found to be +1.6 kcal/mol. The endothermic nature of the electron transfer (proving that the solution electron affinity of benzene is greater than that of *tert*-butylbenzene) is consistent with what was thought to be the intrinsic electron-releasing nature of the *tert*-butyl group. These authors made the statement that this endothermicity should also be observed in the gas phase, a valid assumption based upon the experimental evidence available at the time. However, 7 years later Jordan et al.[2] found that the free energy and enthalpy of the reaction depicted in eq 1 in the gas phase are opposite in sign from those in solution. In fact, the gas-phase electron affinities of *tert*-butylbenzene and benzene are −28.7 and −26.6 kcal/mol, respectively.[2]

From this work and the fact that the basicity of methoxide is greater than that of *tert*-butoxide[3] in the gas phase (the reverse of that found in solution) it is clear that the destabilizing effect that the *tert*-butyl group has upon the solvated anionic species is not due to its electron-releasing nature but is due to its ability to inhibit solvation (including ion association) of the anion. This steric inhibition of solvation and possibly ion association is evidently important enough in a thermodynamic sense to reverse the electron affinities of the gas phase and solvated benzene and *tert*-butylbenzene.

In solution, both the solvation enthalpy of the neutral and anionic species are of importance in controlling the electron transfer depicted in eq 1, but that of the anion radical is certainly of much more importance. This is, the capture of an electron from a gas-phase donor by a gas-phase acceptor (A) to yield the solvated anion radical ion pair (reaction 2) is much more exothermic than the same reaction to yield the gas-phase anion radical and cation (reaction 3). The extra exothermicity of reaction 2 is due to the

$$A_g + Na_g \rightarrow (A^{-}\cdot,Na)_{soln} \quad (2)$$

$$A_g + Na_g \rightarrow A^{-}\cdot_g + Na^{+}_g \quad (3)$$

specific anion–solvent and cation–solvent interactions as well as the ion association.

The actual heats of solvation of a series of polyacene anion radicals with the sodium cation in THF have been measured and found not to vary far from −180 kcal/mol[4] (reaction 4). The

$$A^{-}\cdot_g + Na^{+}_g \rightarrow (A^{-}\cdot,Na^{+})_{THF} \quad (4)$$

$$\Delta H^{\circ} \simeq 180 \text{ kcal/mol}$$

heat of formation of a solvated anion radical–cation ion pair from the gas-phase metal and neutral molecule (ΔH° for the reaction shown in reaction 2) can be obtained from this data by simply adding the electron affinity (EA) of the polyacene and subtracting

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