*J. Am. Chem. Soc.* **1983**, *105*, 1284–1288

# Hydride Abstraction Reactions from Cycloheptatriene and 1-Carbamoylcycloheptatriene. Effect of the $CONH_2$ Group Orientation on the Reactivity Difference of the Exo and Endo Hydrogen toward Hydride Abstraction. A Quantum Chemical Study

**R. H. A. M. Brounts* and H. M. Buck**

*Contribution from the Department of Organic Chemistry, Eindhoven University of Technology, Eindhoven, The Netherlands 5600MB.* *Received July 22, 1982*

**Abstract:** Quantum chemical calculations (MINDO/3 and ab initio (STO-3G)) for the enzyme-catalyzed stereospecific hydride transfer equilibrium $RH + NAD^+ \rightleftharpoons R^+ + NADH$ have shown that it seems possible to relate the stereospecificity with an out-of-plane orientation of the $CONH_2$ group in the transition state. To generalize this model reaction for cyclic ($4n + 2$) aromatic cations, we focus our attention on the intermolecular hydride transfer from 1-carbamoylcycloheptatriene to the cyclopropenium cation. The enthalpy of activation for exo-hydride abstraction from cycloheptatriene was found to be 26 kJ mol$^{-1}$ higher than for endo-hydride transfer. For 1-carbamoylcycloheptatriene the calculations showed clearly that the difference in enthalpy of activation for endo- and exo-hydrogen transfer is more favored for endo abstraction by orientation of the carbonyl dipole toward the endo hydrogen. Orientation toward the exo hydrogen does not result in an increased selection with respect to the parent hydrocarbon.

## Introduction

Recently it has been shown[1] that it seems possible to relate the stereochemical course of the enzyme-catalyzed hydride transfer equilibrium $RH + NAD^+ \rightleftharpoons R^+ + NADH$ simply to an out-of-plane orientation of the $CONH_2$ group in the transition state (TS) of the reaction. The quantum chemical calculations were performed on hydride abstraction reactions from the model compounds 1-carbamoylcyclopropene ($CPCONH_2$) and 3-carbamoyl-1,4-dihydropyridine ($DHPCONH_2$), using the cyclopropenium cation ($CP^+$) as hydride acceptor.[2] It was found that a low-enthalpy TS corresponds to the carbonyl dipole pointing toward the hydride acceptor and a high-enthalpy TS to the carbonyl dipole pointing away from the acceptor. The difference in activation enthalpy was attributed to an electrostatic interaction between the negatively charged oxygen atom of the $CONH_2$ group and the positive charge of the hydride-accepting moiety. Thus the hydrogen atom located in a syn position with respect to the carbonyl dipole is found to be most reactive toward hydride abstraction.

In order to study out-of-plane orientation of the $CONH_2$ group for nonplanar cyclic structures, developing a cyclic ($4n + 2$) electron system, we chose 1-carbamoylcycloheptatriene ($CHTCONH_2$) as model compound for our calculations. Due to the nonplanarity of CHT, a conformational-induced difference in reactivity of the methylene hydrogen atoms is expected to be present already in $CHTCONH_2$, irrespective of the orientation of the $CONH_2$ group. For this reason, we will first report the results of our calculations on the exo- and endo-hydride abstraction reactions from CHT itself. (See Table I for abbreviations used.)

## Choice of Model and Method

As was demonstrated before,[3] intermolecular hydride transfer reactions can be well described by MINDO/3 calculations.[4] Reaction path and geometries of intermediate structures for the reaction of cyclopropene (CP) and $CPCONH_2$ with $CP^+$ as hydride acceptor showed a good correspondence for MINDO/3 and STO-3G results. Although values for activation enthalpies calculated with MINDO/3 and STO-3G may differ, trends in the overall-enthalpy surface given by both calculation methods are similar.[1] It was shown for the intermolecular hydride transfer reaction from CP to $CP^+$ that no triangular intermediate structures could be found.[3] For this and analogue reactions, the formation-enthalpy surface could conveniently be described by using linear intermediate structures. The optimized TSs described in this paper all show an (almost) linear C···H···C fragment;[5] e.g., the hydrogen to be transferred is located in the TS as a bridging atom, partially bonded to both donor (RH) and acceptor ($A^+$) (see Scheme I).

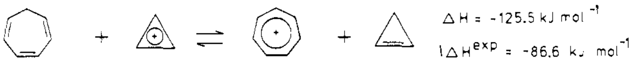
Table I. Abbreviations

| | |
|---|---|
| TS | transition state |
| rc | reaction coordinate |
| CP | cyclopropene |
| $CP^+$ | cyclopropenium cation |
| $CPCONH_2$ | 1-carbamoylcyclopropene |
| CHT | cycloheptatriene |
| $CHT^+$ | cycloheptatrienylium cation |
| $CHTCONH_2$ | 1-carbamoylcycloheptatriene |
| $CHTCONH_2^+$ | carbamoylcycloheptatrienylium cation |
| $DHPCONH_2$ | 3-carbamoyl-1,4-dihydropyridine |

Scheme I. Schematic Representation of the Hydride-Transfer Reaction Showing the Linear Arrangement in the TS

$$RH + A^+ \rightleftharpoons [R\text{---}H\text{---}A]^{+\ddagger} \rightleftharpoons R^+ + AH$$

Scheme II. Reaction Enthalpy Calculated with MINDO/3[a]



[a] $\Delta H$(exptl) was obtained from $\Delta H_f°$(exptl) values for reactants and products.[7]

Because of the large negative reaction enthalpy (see Table II and Scheme II) for the hydride transfer reaction from CHT to $CP^+$, the TS should be located early on the reaction coordinate (rc) and as a result it should resemble the reactants (Hammond postulate[6]). For this reason, we considered the reaction to proceed

---

[1] Donkersloot, M. C. A.; Buck, H. M. *J. Am. Chem. Soc.* **1981**, *103*, 6554–6558.

[2] For reasons of convenience, the abbreviations used in this paper are collected in Table I.

[3] Donkersloot, M. C. A.; Buck, H. M. *J. Am. Chem. Soc.* **1981**, *103*, 6549–6554.

[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] For $CHTCONH_2$ the $C_s$ symmetry in the TS is broken and some deviation of the linearity occurs. However, these deviations remain quite small, and in accordance with the negligible values of the bond orders between the donating and accepting carbon atoms, no tendency to form triangular intermediate structures could be visualized.

0002-7863/83/1505-1284$01.50/0

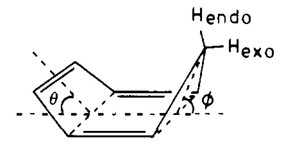


**Figure 1.** Ring puckering angles θ (40°) and φ (36°) in the boat conformation of CHT.

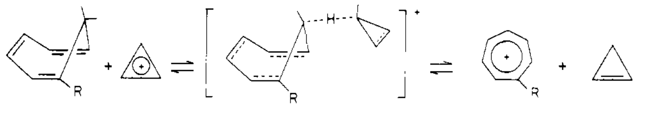


**Figure 2.** Model for the exo-hydride transfer reaction from CHT (R = H) and $CHTCONH_2$ (R = $CONH_2$) to $CP^+$.

via a nonplanar TS. However, since fully optimized MINDO/3 geometries[8] of CHT give a planar structure for the seven-membered ring, puckering had to be introduced by fixing the angles θ and φ. The values of θ and φ, as indicated in Figure 1, were 40° and 36°, respectively, based on the experimental data.[9,10] A model for the reaction, illustrated for exo-H abstraction from CHT (R = H) and $CHTCONH_2$ (R = $CONH_2$), is given in Figure 2.

It should be noted that energies and structural parameters obtained from MINDO/3 calculations for CHT (optimized except for θ = 40° and φ = 36°) are in good agreement with the experimental data. For example, the standard formation enthalpy calculated with MINDO/3, with the fixed values for θ and φ, was found to be 185.8 kJ $mol^{-1}$ ($\Delta H_f°$(exptl) = 183.7 kJ $mol^{-1}$),[7a] whereas fully optimized MINDO/3 calculations (planar conformation) give 140.4 kJ $mol^{-1}$.

We also performed calculations on CHT at the MNDO[11a] and ab initio level (STO-3G, GAUSSIAN70 program).[11b] Though the MNDO geometry, optimized with respect to all geometrical parameters, shows a boat conformation for the seven-membered ring (θ = 19° and φ = 34°), the calculated activation enthalpy for ring inversion is found to be only 4 kJ $mol^{-1}$, which is too small with regard to the experimental value[12] of about 25 kJ $mol^{-1}$. On account of this small barrier for ring inversion, the ring puckering given by the MNDO method is of minor significance and fixation of the angles θ and φ would have been necessary to describe nonplanar TSs at the MNDO level. The fully optimized STO-3G structure even shows a stronger ring puckering (θ = 21° and φ = 41°) for CHT. Very recently a theoretical study of the CHT geometry using the GAUSSIAN80 program was published.[13] The reported values for θ and φ are 27.3° and 47.7°, respectively. The total energy of the structure is 1.6 kJ $mol^{-1}$ lower than the energy of the corresponding structure reported in this paper. The energy difference between the puckered and planar CHT structures calculated with STO-3G was reported to be 21.3 kJ $mol^{-1}$, disfavoring the planar structure. So the STO-3G calculations are far superior to the semiempirical methods in describing the ring puckering. However, on account of the extension of the CHT system, it is an illusive try to localize and optimize TSs with the ab initio method. We therefore adhere to the MINDO/3 results presented in the following section.

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

| species | $\Delta H_f°$, kJ $mol^{-1}$ |
|---|---|
| CHT[a] | 185.8 |
| $CP^+$ | 1005.9 |
| $CHT^+$ | 818.2 |
| CP | 248.1 |

[a] Optimized for fixed values of θ = 40° and φ = 36°.

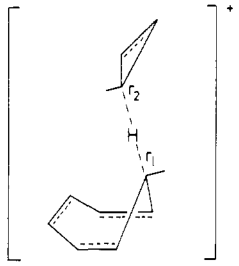


**Figure 3.** Linear intermediate structure for endo-H abstraction from CHT.

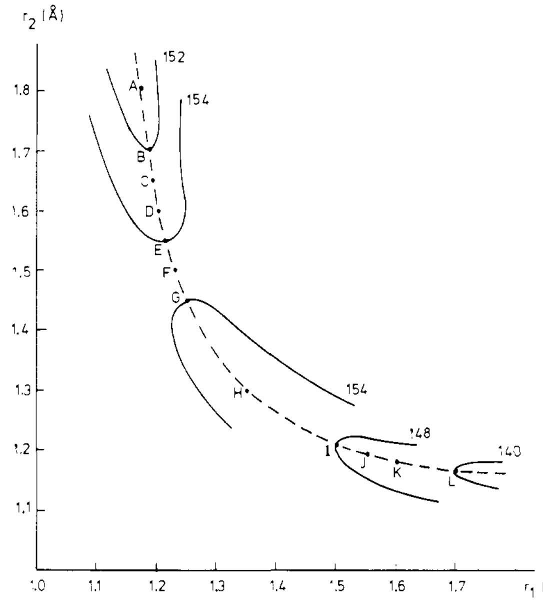


**Figure 4.** Enthalpy contour map for endo-H abstraction from CHT. Enthalpy values in kJ $mol^{-1}$ with respect to the reaction product level.

## Results and Discussion

**a. Intermolecular Hydride Transfer from Cycloheptatriene to the Cyclopropenium Cation.** The standard formation enthalpies of reactants and products for the reaction, calculated with MINDO/3, are given in Table II. The linear intermediate structures[14] for endo-H abstraction from CHT, defined as in Figure 3, allow the formation enthalpy to be described as a function of $r_1$ and $r_2$, $r_1$ and $r_2$ being the distances between the migrating hydrogen atom and the donating and accepting carbon atoms, respectively.

The enthalpy contour map for the reaction, enthalpy values plotted as a function of $r_1$ and $r_2$, is represented in Figure 4. Enthalpies are given in kJ $mol^{-1}$ with respect to the reaction product level, all structural parameters being optimized except θ and φ. The reaction path is found as a valley of varying depth in the enthalpy surface (minimum gradient reaction path). The

---

(6) Hammond, G. S. *J. Am. Chem. Soc.* **1955**, *77*, 334–338.

(7) (a) Cox, J. D.; Pilcher, G. "Thermochemistry of Organic and Organometallic Compounds"; Academic Press: New York, 1970. (b) Rosenstock, H. M.; Draxl, K.; Steiner, B. W.; Herron, J. T. *J. Phys. Chem. Ref. Data, Suppl.* **1977**, *6*, 1.

(8) (a) Bingham, R. C.; Dewar, M. J. S.; Lo, D. H. *J. Am. Chem. Soc.* **1975**, *97*, 1285–1293. (b) Bingham, R. C.; Dewar, M. J. S.; Lo, D. H. *Ibid.* **1975**, *97*, 1294–1301.

(9) Traetteberg, M. *J. Am. Chem. Soc.* **1964**, *86*, 4265–4270.

(10) (a) A semiquantitative estimate of the nonplanarity of CHT was made by Butcher[10b] from interpretation of the microwave spectrum, by using bond lengths and angles from analogous molecules. The reported values for the puckering angles are θ = 29° and φ = 50°. In this paper we adhere to the results obtained from a total molecular structure determination by electron diffraction. (b) Butcher, S. S. *J. Chem. Phys.* **1965**, *42*, 1833–1836.

(11) (a) Thiel, W. *QCPE* **1978**, *11*, 353. (b) Hehre, W. J.; Lathan, W. A.; Ditchfield, R.; Newton, M. D.; Pople, J. A. *Ibid.* **1973**, *11*, 236.

(12) (a) Anet, F. A. L. *J. Am. Chem. Soc.* **1964**, *86*, 458–460. (b) Jensen, F. R.; Smith, L. A. *Ibid.* **1964**, *86*, 956–957.

(13) Schulman, J. M.; Disch, R. L.; Sabio, M. L. *J. Am. Chem. Soc.* **1982**, *104*, 3785–3788.

(14) An eclipsed arrangement of the $CP^+$ moiety with respect to the seven-membered ring in the endo TS was not taken into consideration. On account of the proximity of the two positively charged fragments, the formation enthalpies of eclipsed intermediate structures would inevitably be much higher than for the corresponding staggered conformations.

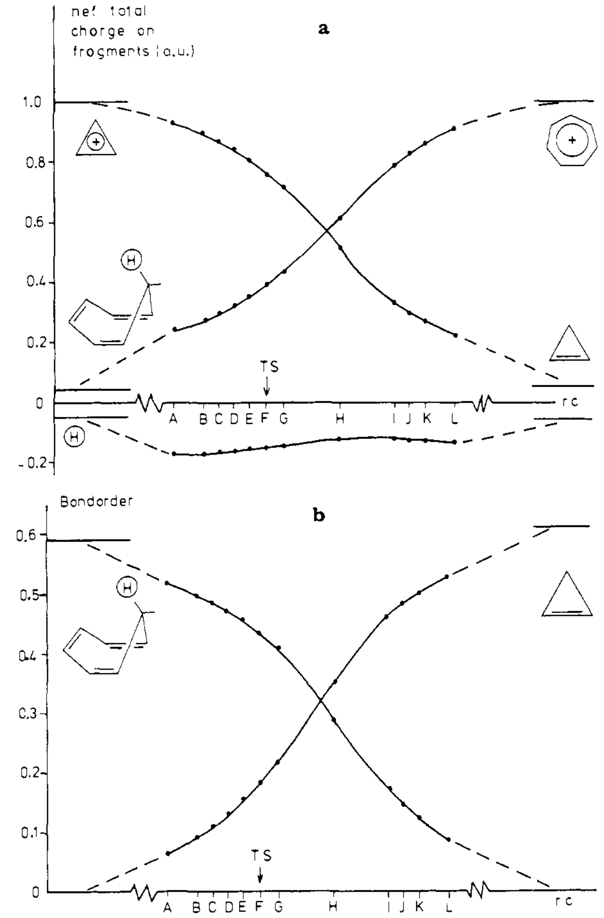


**Figure 5.** (a) Variation of the net fragmental charges along the rc for endo-H abstraction from CHT. (b) Variation of bond orders in the C···H···C fragment along the rc for endo-H abstraction from CHT.

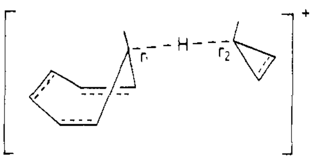


**Figure 6.** Linear intermediate structure for exo-H abstraction from CHT.

TS can be located as the structure with highest formation enthalpy on the energy profile.

Although the overall reaction involves the transfer of H$^-$ from CHT to CP$^+$, the reaction is more likely to be described as a process of simultaneous bond breaking and bond forming. This can be visualized from a plot of the total net charge on the donating and accepting moieties and the migrating hydrogen atom as they change along the rc (see Figure 5a). Figure 5b shows the variation of bond orders of the C···H···C fragment in the intermediate structures for the reaction.

In the same way, the enthalpy contour map and reaction path could be constructed for exo-H abstraction from CHT, considering an intermediate structure[15] as depicted in Figure 6. The enthalpy contour map for the reaction is given in Figure 7.

The required activation enthalpy for exo-H abstraction appears to be 55 kJ mol$^{-1}$. Comparison with the value for $\Delta H^{\ddagger}_{\text{endo}}$ = 29 kJ mol$^{-1}$ leads to the conclusion that endo-H abstraction from CHT is favored by 26 kJ mol$^{-1}$. Although this difference in $\Delta H^{\ddagger}$ may seem small, it should be mentioned that we are comparing formation enthalpies of very similar structures. The observed nonequivalency of the methylene hydrogen atoms in the hydride transfer reaction is therefore considered to be significant. As can be seen from Figures 4 and 7, the TS for endo-H abstraction (endo TS) is located earlier on the rc than the exo TS. This results in a larger total net charge in the seven-membered ring of the exo

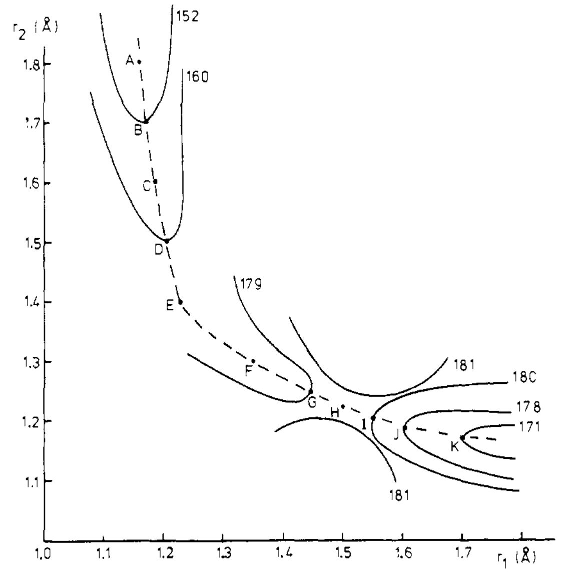


**Figure 7.** Enthalpy contour map for exo-H abstraction from CHT. Enthalpy values in kJ mol$^{-1}$ relative to the reaction product level.

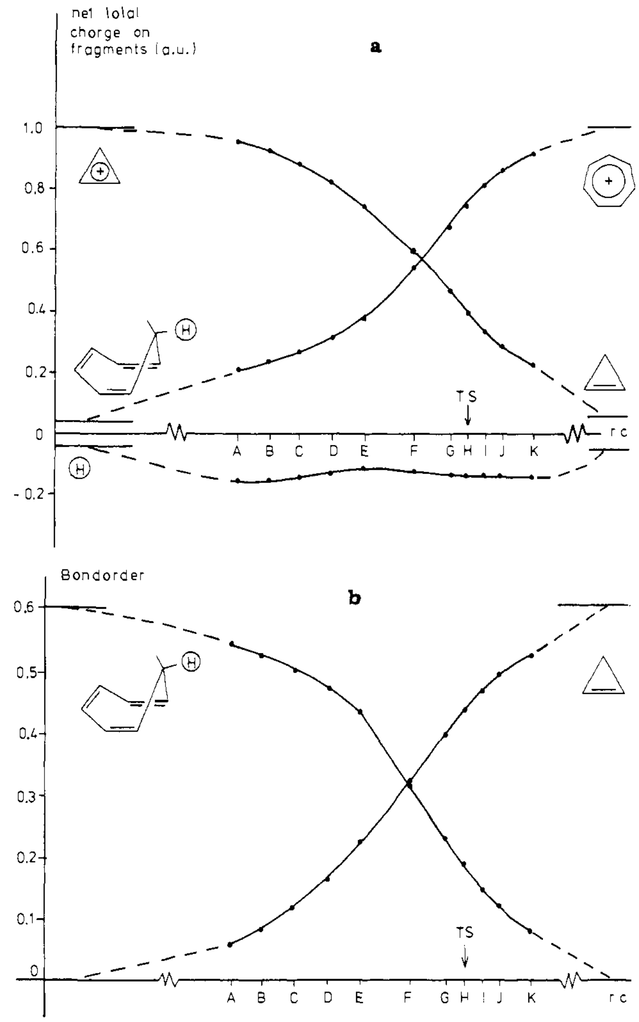


**Figure 8.** (a) Variation of the net fragmental charges along the rc for exo-H abstraction from CHT. (b) Variation of bond orders in the C···H···C fragment along the rc for exo-H abstraction from CHT.

---

(15) For a staggered conformation of the CP$^+$ moiety with respect to the CHT ring, identical results with regard to the reaction path, geometries, and energies were obtained. In this paper, an eclipsed arrangement in all exo TSs was considered.

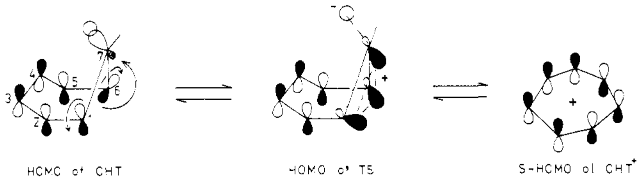


Figure 9. Model for endo-H abstraction from CHT, assuming anchimeric assistance of the HOMO of CHT.

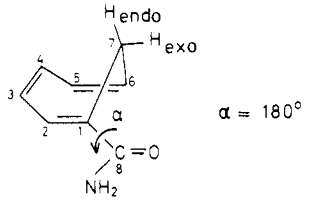


Figure 10. Out-of-plane orientation of the $CONH_2$ group in $CHTCONH_2$ indicated by $\alpha$.

TS compared to the situation for the endo TS. This is illustrated in Figure 8.

The fact that the exo TS is found relatively late on the rc should possibly have consequences for the extent of ring puckering in the TS. However, as was stated before, the underestimation of ring puckering in the MINDO/3 calculation prohibits the description of a gradually flattening of the boat conformation along the rc. Despite the possible inadequacy of describing the exo TS with fixed puckering angles, these results are essentially consistent with the experimental data we obtained in our investigations on the reactivity of the bicyclo[5.4.1]dodecapentaenylium cation and its derivatives.[16] The stereoselective course of the reactions studied was explained in terms of anchimeric assistance and orbital symmetry controlled processes. For hydride abstraction reactions from CHT, a similar model can be presented. The endo-hydride abstraction is promoted by orbital assistance of the highest occupied molecular orbital (HOMO) of the CHT $\pi$ system, leading to a three-center orbital overlap at the exo face of the TS (see Figure 9).

However, no theoretical evidence could be found for such a three-center orbital overlap in the endo TS. Probably the fixation of the puckering angles introduces a rigidity into the system, which does not allow the essential disrotatory movement of the $p_\pi$ orbitals at $C_1$ and $C_6$. Evidently, the endo TS possesses a favorable geometrical arrangement compared to the situation for the exo TS. This is also reflected in the slight deviation from planarity when $\theta$ and $\phi$ are optimized in the TS.[3] Though this deviation is small ($\theta = 3°$ and $\phi = 7°$), the seven-membered ring shows a tendency to pucker in such a way that the migrating hydrogen atom becomes located in the endo position. Besides, it is interesting to notice that MINDO/3 and STO-3G agree in a slightly smaller bond order for the $C_7$–$H_{endo}$ bond with regard to the $C_7$–$H_{exo}$ bond in CHT. On account of the rapid ring inversion, the expected stereospecificity of hydride abstraction cannot be observed for CHT itself. Experimental data may be obtained from derivatives of CHT, in which the barrier for ring inversion has become high enough to lock the boat conformation of the seven-membered ring. This can be achieved by introducing large groups or rings to the CHT system or by constructing a suitable $C_1$–$C_6$ linkage. In this context, we like to refer to earlier reports on the preferential endo-nucleophile abstraction reactions from tetraphenyltribenzocycloheptatriene derivatives.[17]

**b. Intermolecular Hydride Transfer from 1-Carbamoylcycloheptatriene to the Cyclopropenium Cation.** In order to study the effect of the carbonyl dipole orientation on the reactivity of the endo- and exo-hydrogen atom in the CHT system, we performed MINDO/3 calculations on hydride abstraction reactions from $CHTCONH_2$ for three orientations of the $CONH_2$ group with respect to the CHT ring. The orientation of the $CONH_2$ group was defined by the out-of-plane angle $\alpha$ as indicated in Figure 10. The calculations were carried out for $\alpha = 90°$, 180°, and 270°. The standard formation enthalpies (MINDO/3) for reactants and products of the reaction are collected in Table III.

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

| species | $\Delta H_f°$, kJ mol⁻¹ | species | $\Delta H_f°$, kJ mol⁻¹ |
|---|---|---|---|
| $CP^+$ | 1005.9 | CP | 248.1 |
| $CHTCONH_2$[a] ($\alpha = 90°$) | −57.0 | $CHTCONH_2^+$ ($\alpha = 90°$) | 595.2 |
| $CHTCONH_2$[a] ($\alpha = 180°$) | −33.1 | $CHTCONH_2^+$ ($\alpha = 180°$) | 623.4 |
| $CHTCONH_2$[a] ($\alpha = 270°$) | −55.9 | $CHTCONH_2^+$ ($\alpha = 270°$) | 595.2 |

[a] Optimized for $\theta = 40°$ and $\phi = 36°$.

Table IV. $\Delta(\Delta H^{\ddagger}) = \Delta H^{\ddagger}_{exo} - \Delta H^{\ddagger}_{endo}$ for Hydride Abstraction from $CHTCONH_2$

| $\alpha$, deg | $\Delta(\Delta H^{\ddagger})$, kJ mol⁻¹ |
|---|---|
| 90 | 25 |
| 180 | 44 |
| 270 | 51 |

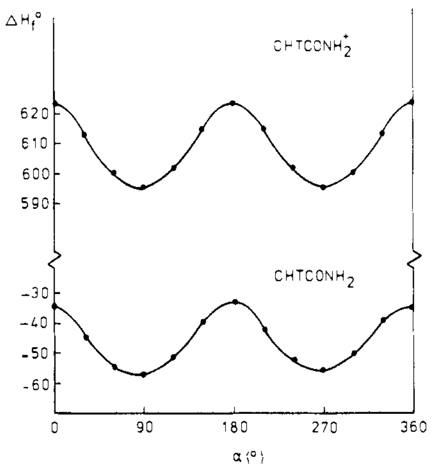


Figure 11. Standard formation enthalpies in kJ mol⁻¹ for $CHTCONH_2$ ($\theta = 40°$, $\phi = 36°$) and $CHTCONH_2^+$ (fully optimized structures) as a function of $\alpha$.

In comparison with the reported MINDO/3 results for $CPCONH_2$, $DHPCONH_2$, and corresponding cations, the $CONH_2$ group has a preference for a perpendicular orientation with respect to the $C_1$–$C_2$ bond in the hydrogen-donating molecule as well as in the hydrogen-accepting cation. The barrier for rotation is about 23 kJ mol⁻¹ in $CHTCONH_2$ ($\theta = 40°$ and $\phi = 36°$) and 28 kJ mol⁻¹ in the fully optimized cation $CHTCONH_2^+$ (see Figure 11).

The STO-3G predicts a planar conformation for $CPCONH_2$ and the corresponding cation.[1] Nevertheless, rotation barriers calculated with both semiempirical and ab initio methods are relatively low, and the $CONH_2$ group is therefore supposed to be almost freely rotating at ordinary temperature. Variation of $\alpha$ has no appreciable effect on the (original) planarity of the seven-membered ring in $CHTCONH_2^+$. Furthermore, in all structures studied, the $C_1$–$C_8$ bond was found to be single (bond length varying from 1.51 to 1.55 Å).

The relevant parts of the enthalpy surface for exo- and endo-hydride abstraction from $CHTCONH_2$ were constructed by using intermediate structures as were defined before, all geometrical parameters optimized except $\theta = 40°$, $\phi = 36°$, and $\alpha = 90°$, 180°, and 270°, respectively. Again TSs could be located as the

---

(16) Brounts, R. H. A. M.; Schipper, P.; Buck, H. M. *J Chem. Soc., Chem. Commun.* **1980**, 522–524 and forthcoming publication.

(17) Tochtermann, W. *Fortschr. Chem. Forsch.* **1970**, *15*, 378–444 and references cited therein.

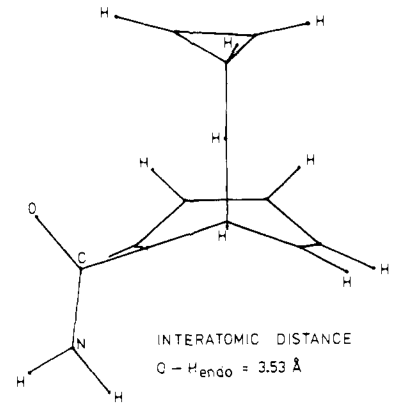


**Figure 12.** Geometry of the endo TS for $CHTCONH_2$ ($\alpha = 270°$).

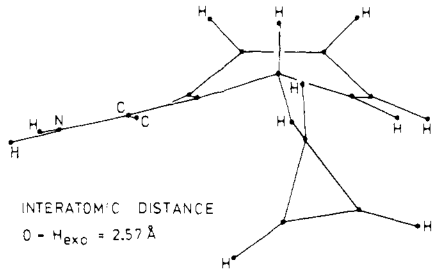
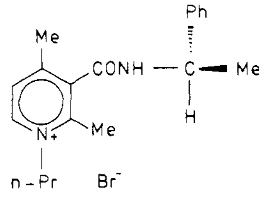


**Figure 13.** Geometry of the exo TS for $CHTCONH_2$ ($\alpha = 180°$).

structures with highest formation enthalpy on the minimum gradient reaction path. Results are collected in Table IV.

For $\alpha = 90°$, almost the same value for $\Delta(\Delta H^{\ddagger}) = \Delta H^{\ddagger}_{\mathrm{exo}} - \Delta H^{\ddagger}_{\mathrm{endo}}$ is found as in the unsubstituted CHT. Again endo-H abstraction is favored by 25 kJ $mol^{-1}$. This is not surprising since the carbonyl dipole is pointing away from the reaction center and therefore no interaction with the positively charged acceptor takes place. On the contrary, for $\alpha = 270°$, the carbonyl bond is pointing toward the endo-hydrogen atom. Consequently an electrostatical interaction in the endo TS between the negatively charged oxygen atom and the cyclopropenium moiety leads to a considerable lowering of $\Delta H^{\ddagger}_{\mathrm{endo}}$ relative to $\Delta H^{\ddagger}_{\mathrm{exo}}$, resulting in an activation enthalpy difference $\Delta(\Delta H^{\ddagger}) = 51$ kJ $mol^{-1}$. On account of the presence of the $CONH_2$ group, the intermediate structures are no longer symmetric. In the endo TS for $\alpha = 270°$, a slight bending of the cyclopropenium moiety toward the carbonyl dipole reflects the presence of the electrostatic interaction (see Figure 12).

For $\alpha = 180°$, we expected a considerable lowering of $\Delta H^{\ddagger}_{\mathrm{exo}}$ with respect to $\Delta H^{\ddagger}_{\mathrm{endo}}$ since the carbonyl dipole is now pointing toward the exo-hydrogen atom. As can be inferred from Table IV, the activation enthalpy difference for $\alpha = 180°$ is found to be 44 kJ $mol^{-1}$, still in favor of endo-H abstraction. Examination of the exo-TS geometries showed in all cases that the cyclopropenium moiety is somewhat tilted away from the $CONH_2$ group. In particular, for $\alpha = 180°$ a relatively large displacement of the migrating hydrogen atom from the original plane of symmetry (cf. CHT) is found (see Figure 13). This is probably due to the repulsion of the oxygen atom and the migrating hydrogen (net atomic charges −0.56 and −0.14 au, respectively). Consequently the structure becomes more strained, which is reflected in an enhancement of $\Delta H^{\ddagger}_{\mathrm{exo}}$ relative to $\Delta H^{\ddagger}_{\mathrm{endo}}$. Furthermore, steric hindrance of the cyclopropenium $\sigma$ frame by the $CONH_2$ group may also attribute to the large activation enthalpy for exo-H abstraction. Apparently, these effects overrule the favorable dipole–acceptor interaction in the exo TS for $\alpha = 180°$. On the contrary, in the endo TS for $\alpha = 270°$, the interatomic distance between the carbamoyl oxygen atom and the migrating hydrogen is considerably larger (see Figure 12), and here the dipole–acceptor interaction clearly dominates the process. Again the rapid ring inversion will make it impossible to examine these effects in $CHTCONH_2$ itself. But as was mentioned for CHT, the phenomena can be observed for derivatives of $CHTCONH_2$ containing a fixed puckered seven-membered ring. Experimental evidence for the stereochemical outcome introduced by the $CONH_2$ group has been recently published for hydride uptake of **1**. In that case, the CONHR group is forced out of plane by the adjacent methyl groups, resulting in one diastereoisomeric pair of compounds with a syn orientation of the hydrogen atom at $C_4$ with respect to the carbonyl bond.[18]



**1**

The reaction clearly supports the dipole–acceptor interaction mechanism and was presented as a model reaction for the stereospecific hydride transfer in the $NAD^+$/NADH equilibrium. This model can also be used as experimental verification of the increased discrimination for $H_{\mathrm{endo}}$ over $H_{\mathrm{exo}}$ in $CHTCONH_2$, by introducing bulky substituents at the $C_2$ and $C_6$ position. Since it was also demonstrated that 2,4-dimethyl-3-carbamoylpyridinium cations are also optically active when the 9*R* chirality in **1** is absent,[19] the suggestion was put forward that the absolute configuration of the carbamoylpyridinium moiety controls the stereochemistry of the hydride uptake.

## Conclusion

The MINDO/3 calculations clearly show a conformational-induced difference in reactivity between the methylene hydrogen atoms in CHT toward hydride abstraction. On account of the rapid ring inversion, stereospecific endo-H abstraction cannot be observed in practice in CHT itself. Nevertheless, the results of the calculations correspond with experimental data obtained from earlier investigations on the reactivity of the bicyclo[5.4.1]dodecapentaenylium cation and with reports on the preferential endo-nucleophile abstraction reactions from tetraphenyltribenzocycloheptatriene derivatives. For CHT and $CHTCONH_2$ MINDO/3 predicts favorable endo-H abstraction, but the difference in activation enthalpy for exo- and endo-hydride abstraction becomes more pronounced by an out-of-plane orientation of the $CONH_2$ group toward the endo-hydrogen. Due to the ring puckering in $CHTCONH_2$, the picture is somewhat more complicated than for the planar structures of $CPCONH_2$ and $DHPCONH_2$. The results of our calculations can be considered an additional support to the mechanism proposed for the stereospecific hydride transfer in the enzyme-catalyzed equilibrium $RH + NAD^+ \rightleftarrows R^+ + NADH$.

**Acknowledgment.** This investigation was supported by the Netherlands Foundation for Chemical Research (SON), with financial aid from the Netherlands Organization for the Advancement of Pure Research (ZWO). The authors thank Dr. M. C. A. Donkersloot for many helpful discussions.

**Registry No.** $CHTCONH_2$, 26902-48-7; CHT, 544-25-2; $CP^+$, 26810-74-2.

---

[18] Van Lier, P. M.; Donkersloot, M. C. A.; Koster, A. S.; van Hooff, H. J. G.; Buck, H. M. *Recl. Trav. Chim. Pays-Bas* **1982**, *101*, 119–120.

[19] van Hooff, H. J. G.; van Lier, P. M.; Bastiaansen, L. A. M.; Buck, H. M. *Recl. Trav. Chim. Pays-Bas* **1982**, *101*, 191–192.