J. Phys. Chem. A **2004,** *108,* 5649−5654

Dyotropic Rearrangements of Dihalogenated Hydrocarbons: A Density Functional Theory Study

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Received: December 1, 2003; In Final Form: May 3, 2004

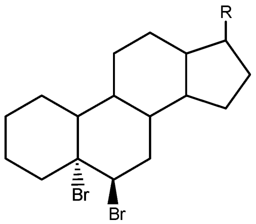
A series of dyotropic rearrangements for dihalogenated hydrocarbons have been investigated by using the B3LYP/6-311++G(d,p) method. In all cases, an ethylenic transition state has been located. The activation energy of the basic dyotropic rearrangement of chlorine migration is calculated to be 41.9 kcal/mol. Both conjugation and hyperconjugation effects lead to a delocalization of the newly formed π electrons in the transition state and therefore facilitate the rearrangement. For the dichlorinated cycloalkane series, it has been shown that the variation of the activation energy simply depends on the ring strain. In contrast, the dyotropic rearrangements of dichloro-cycloalkenes possess some complexity. In particular, the dyotropic reaction of 5,6-dichlorocyclohexa-1,3-diene is predicted to have an anomalous lower barrier, which can be attributed, to a great extent, to the aromaticity of the transition state. Similarly, due to the involvement of antiaromaticity in the transition states, the dyotropic migration barriers of 3,4-dichlorocyclobutene are found to be significantly higher than those of the corresponding dichlorinated cycloalkanes. Two possibly competitive processes, thermal elimination and sigmatropic migration, have been examined for some systems. The results suggest that the sigmatropic migration often possesses a lower barrier and therefore needs to be scrutinized to predict the observable dyotropic process. In addition, the dyotropic bromine migrations have also been investigated and predicted to have a much lower activation energy, indicating that the dyotropic rearrangement is more likely to occur in the dibrominated compounds. A mixed dyotropic rearrangement in which the chlorine and the bromine interchange their positions has proven to be feasible with the activation energy lying between that of the dyotropic chlorine migration and that of the dyotropic bromine migration.

Introduction

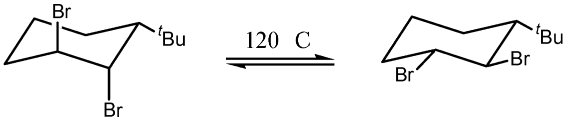
A considerable amount of examples of dyotropic rearrangement have been accumulated[1−8] in the literature during the past three decades since Reetz first introduced the terminology in 1972.[9] Reactions of this type have enriched our knowledge of orbital symmetry conservation of concerted processes.[10] Moreover, some of them provide synthetic utility.[11−14] For example, the dyotropic shift of 4-cyclohexyl β-lactone to 7-oxaspiro[5,4]-decan-8-one has been demonstrated to be a facile route in the synthesis of spiro butyrolactones, a pharmacologically important subunit in a number of naturally occurring products and in several drugs.[11,15,16] Although the orbital symmetry rules established by Woodward and Hoffmann[17] have contributed much to our understanding of the mechanisms of dyotropic shifts,[10] they are incapable of providing quantitative information. Theoretical calculation permits us to obtain a desirably revealing picture of a chemical reaction and has been applied successfully to predict the structure of transition states and the configuration of products for numerous sigmatropic rearrangements. However, few such works on dyotropic rearrangement have been found, and they have been focused primarily on dyotropic hydrogen shifts.[1,4,18]

The first example of dyotropic halogen migration can be tracked back about a century ago when Mauthner[19] reported an intramolecular isomerization of dibromo-cholestane (Scheme 1). A later mechanistic study[20] has suggested that the isomerization proceeds via a four-membered transition state and can be considered as a dyotropic reaction. Another dyotropic halogen migration reported is the thermal mutarotation of *trans*-2,3-dibromo-*tert*-butylcyclohexane (Scheme 2).[21] Deyà et al.[22] have confirmed this process through semiempirical quantum chemical (AM1) calculations. To the best of our knowledge, no other example of the dyotropic halogen migration is available in the literature, although such rearrangements are predicted to be symmetrically allowed according to the orbital symmetry rules.[10]

SCHEME 1



SCHEME 2



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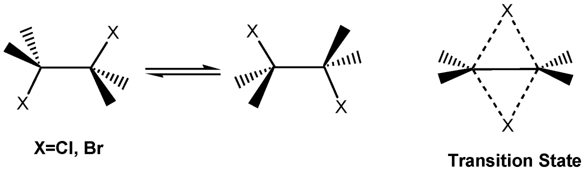
10.1021/jp037659m CCC: $27.50

TABLE 1: Dichlorinated Reactants, Their Calculated Activation Energies (in kcal/mol) of Dyotropic Migration $\Delta E^{\ddagger}$, Sigmatropic Migration $\Delta E_s^{\ddagger}$, and the Elimination Process ($\Delta E_{\text{elim}}^{\ddagger}$), the Bond Length of $C^{\alpha}-C^{\beta}$, and the Average $C^{k}-Cl^{m}$ Distances (in angstroms)

	reactant	$\Delta E^{\ddagger\ a}$	$\Delta E_s^{\ddagger\ a,b}$	$\Delta E_{\text{elim}}^{\ddagger\text{ThinSpace}a}$	$R(C^{\alpha}-C^{\beta})$	$R(C^{k}-Cl^{m})$
1	1,2-dichloroethane	41.9		57.6[c]	1.4136	2.3081
2	1,2-dichloropropane	38.4		48.8	1.4211	2.3401
3	3,4-dichlorobut-1-ene	34.8	40.7	41.7	1.4260	2.3651
4	(1,2-dichloroethyl)-benzene	34.3		41.6	1.4277	2.3794
5	2,3-dichloropropene	52.6			1.3871	2.3446
6	1,2-dichlorocyclopropane	67.5			1.3764	2.3477
7	1,2-dichlorocyclobutane	46.8			1.4281	2.3652
8	1,2-dichlorocyclopentane	35.0		45.9	1.4252	2.3726
9	1,2-dichlorocyclohexane	35.9		48.4	1.4296	2.3798
10	1,2-dichlorocycloheptane[d]	33.1			1.4347	2.3860
11	1,2-dichlorocyclooctane[e]	35.7			1.4356	2.3950
12	3,4-dichlorocyclobutene	57.6			1.4401	2.4101
13	3,4-dichlorocyclopentene	35.2	37.4	48.7	1.4326	2.4161
14	3,4-dichlorocyclohexene	34.1	39.3	39.0	1.4316	2.4161
15	4,5-dichlorocyclohexene	34.4		48.8	1.4260	2.3696
16	5,6-dichlorocyclohexa-1,3-diene	25.1	34.1 (22.7)	26.3	1.4394	2.4462
17	5,6-dichlorocyclohepta-1,3-diene	31.6	31.0 (26.6)		1.4349	2.4166
18	6,7-dichlorocyclohepta-1,4-diene	28.7			1.4354	2.4279
19	7,8-dichlorocycloocta-1,3,5-triene	34.8			1.4319	2.4179

[a] Zero-point vibrational energy is included. [b] Activation energies of the 1,3-sigmatropic shift; those of the 1,5-shift are give in parentheses. [c] Reference 37. [d] Reference 29a. [e] Reference 29b.



(a) (b)

Figure 1. Schematic diagrams of (a) the dyotropic rearrangement of halogen migration, and (b) the transition state.

In view of the fact that the dyotropic halogen migration may alter the stereochemistry of a compound significantly (see Figure 1a) and the importance of stereochemistry, it is of interest to understand the type of reaction in more detail. Indeed, it has been reported previously that the haloalkane 1,2-dibromo-3-chloropropane, one of the important environmental pollutants, may show enantioselectivity in its metabolism and/or toxicities.[23] For this purpose, potential energy surfaces of a series of dihalogenated hydrocarbons have been investigated in this study. The effects of substitutions, ring strains, and different migrating halogen atoms on the dyotropic migration rates, as well as competitions of the dyotropic reaction with the thermal elimination and the single sigmatropic processes, have been examined.

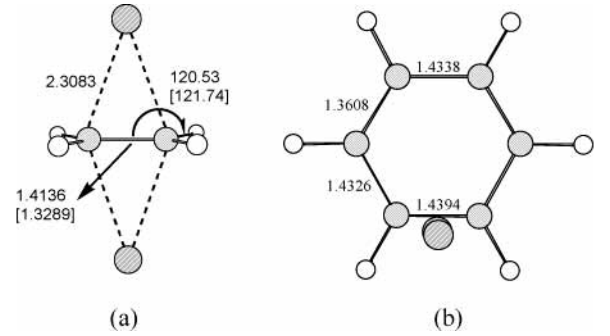
Computational Method

All calculations were performed with Gaussian 98 code[24] compiled on alpha Unix workstations and PC-Linux systems.[25] The hybrid density functional method, B3LYP,[26,27] was chosen because of its agreeable record in studying a variety of concerted reactions including the sigmatropic chlorine shifts.[28] Geometries were optimized with the standard basis set 6-311++G(d,p) and with the gradient method without any symmetry constraint. For some cyclic systems with complicated ring conformational variation, such as 1,2-dichlorocyclooctane, only the ring conformation of the most stable dechlorinated form was considered.[29] Nevertheless, there are still several distinct structures with respect to the position of the halogens. For these species, B3LYP/6-31G(d) calculations were performed to obtain the most stable structure, and then this structure was taken as the reactant and submitted to subsequent calculations at higher levels of theory. All stationary points and transition states were characterized by frequency calculations at the B3LYP/6-311++G(d,p) level of theory with no imaginary frequency and a unique one, respectively. The intrinsic reaction coordinate (IRC) calculation[30] was carried out for the basic dyotropic chlorine shift of 1,2-dichloroethane at the B3LYP/6-31G(d) level to further validate the transition state. To characterize the aromaticity of several transition structures, nucleus-independent chemical shift[31] (NICS) calculations have been employed using the gauge-independent atomic orbital (GIAO) perturbation method at the HF/6-311++G(d,p) level of theory with the B3LYP/6-311++G(d,p) optimized structures. The selection of Hartree−Fock instead of the gradient-corrected density functional method in the NICS calculations is due to the fact that the effect of electron correlation on the calculated magnetizabilities is small, and the density functional even yields results inferior to the Hartree−Fock.[32] A natural localized molecular orbitals (NLMO) analysis[33] was performed to obtain the bond order by using the built-in G98 NBO 3.1 package.[34]

Results and Discussion

Table 1 summarizes the reactants and their calculated activation energies with zero-point energy (ZPE) correction for a series of dyotropic rearrangements of chlorine migration.

In all cases studied, a transition state for which the schematic diagram is depicted in Figure 1b has been located. For the basic dyotropic rearrangement, the intramolecular isomerization of 1,2-dichloroethane (**1**), an IRC analysis shows clearly not only the transition structure connects smoothly the degenerate stationary point, but also the migrations of the two chlorines are perfectly synchronous. The transition state of **1** (Figure 2) has a D_{2h} symmetry; its C_2H_4 moiety resembles ethylene closely except for a longer C−C interatomic distance (1.41 vs 1.33 Å). Evidently, the $C^{\alpha}-C^{\beta}$ bond (throughout this paper, $C^{\alpha}-C^{\beta}$ bond refers to the bond linking the two carbons to which the halogen atoms are bonded) in the transition state is characteristic of the double bond, and the longer distance may well be ascribed to the repulsive interactions between the π-electrons in the $C^{\alpha}-C^{\beta}$ bond and the lone-pair electrons on the chlorines. For this reason, one would anticipate that a delocalization of the newly



(a) (b)

Figure 2. The transition states of the dyotropic migrations of (a) 1,2-dichloroethane and (b) 5,6-dichlorocyclohexa-1,3-diene. The structural parameters of ethylene are listed in the square brackets for comparison.

formed π-bond would facilitate the dyotropic rearrangement. Indeed, the activation energy ($\Delta E^{\ddagger}$) of 1,2-dichloropropane (**2**) is predicted to be 38.4 kcal/mol, lower than that of **1** by 3.5 kcal/mol; an incorporation of vinyl or phenyl in the basic system has been found to give an even lower $\Delta E^{\ddagger}$, 34.8 kcal/mol for 3,4-dichlorobut-1-ene (**3**) and 34.3 kcal/mol for (1,2-dichloroethyl)-benzene (**4**). The former can be ascribed to the hyperconjugation interaction between the methyl group and the elongated $C^{\alpha}-C^{\beta}$ double bond in the transition state, while the latter is attributed to the conjugation effects. Similarly, the dyotropic rearrangement of 2,3-dichloropropene (**5**) has been examined and predicted to be traceable, in principle, although the activation energy is somewhat high (52.3 kcal/mol) due to the fact that this rearrangement proceeds via an allenic transition state.

To further explore the structure−reactivity relationship, a number of cyclic systems have also been considered. The activation energy of dyotropic migration for 1,2-dichlorocyclopropane (**6**) is calculated to be 67.5 kcal/mol. Such a high-energy barrier may result from an increasing strain of angle in the transition state as compared to that in the reactant. The calculated results show that the endocyclic angle $\angle CC^{\alpha}C^{\beta}$ is 62.8°, very close to 60.3° in the reactant, whereas the exocyclic angle $\angle HC^{\alpha}C^{\beta}$ is 146.3°, deviating remarkably from a normal value of ~120°. With the enlargement of the ring, the energy barrier decreases markedly to 46.8 kcal/mol for 1,2-dichlorocyclobutane (**7**), and 35.0 kcal/mol for the five-membered ring system, 1,2-dichlorocyclopentane (**8**). No significant change of the activation energy has been found with further enlargement of the ring; cf. the $\Delta E^{\ddagger}$ values of 1,2-dichlorocyclohexane (**9**) and 1,2-dichlorocyclooctane (**11**) are nearly identical to that of **8**, and that of 1,2-dichlorocycloheptane (**10**) is slightly lower, 33.1 kcal/mol. This demonstrates that, for dichlorinated cycloalkane series, the ring strain is primarily responsible for the rate of dyotropic migrations.

In contrast to a relatively simple trend that the dyotropic rearrangement of dichlorinated cycloalkanes follows, the reaction of dichlorinated cycloalkenes exhibits some complexities. For 3,4-dichlorocyclohexene (**14**), 4,5-dichlorocyclohexene (**15**), 5,6-dichlorocyclohepta-1,3-diene (**17**), and 7,8-dichlorocycloocta-1,3,5-triene (**19**), we found that the incorporated double bonds merely lower the barrier heights of dyotropic chlorine migration by less than 2 kcal/mol. Particularly, the energy barrier of 3,4-dichlorocyclopentene (**13**) is almost identical to that of the corresponding dichlorinated cycloalkane, **8** (see Table 1). In this case, it seems that the conjugation effect and the strain effect achieve a certain subtle balance. As revealed by a longer $C^{\alpha}-C^{\beta}$ bond in the transition state, 1.433 Å for **13** versus 1.425 Å for **8**, the introduction of a double bond has led to the delocalization of the newly formed π electrons. On the other hand, the elongated bond has resulted in an increase of the angle strain of the planar five-membered ring and therefore destabilized the transition state.

For 5,6-dichlorocyclohexa-1,3-diene (**16**), our B3LYP/6-311++G(d,p) calculations reveal that the activation energy of dyotropic rearrangement is only 25.1 kcal/mol, lower than those of other six-membered cyclic analogues by as much as 10 kcal/mol. Similarly, we examined the dyotropic chlorine shift of 6,7-dichlorocyclohepta-1,4-diene (**18**) and found that its dyotropic barrier is 28.7 kcal/mol, lower than those of the other two seven-membered systems, **10** and **17**, by 4.4 and 2.9 kcal/mol, respectively. Although the two simultaneous allylic stabilizations involved may lower significantly the dyotropic barrier and indeed lead to a reduction in the barrier of **18** relative to **10** and **17**, they account only partly for the anomalously low barrier of **16**. Due to the fact that there are $4N + 2$ electrons in the cyclic moiety of the transition state, it is reasonable to propose that such a drastic change may, to a great extent, result from the aromaticity of the transition state of **16**. However, an examination of the structure of the transition state shows that the C_6H_6 moiety does not resemble a benzenoid structure, but presents a characteristic of bond alternation (Figure 2). The reason might be two-fold: the localized structure is not necessarily indicative of a lack of aromaticity as demonstrated in previous studies on the aromaticity in large annulenes[35a] and strained benzenes;[35b] on the other hand, there is no evidence that the criteria of aromaticity that the stable structures follow are always fully suitable for the transition state. Furthermore, a NICS calculation, which has proven very successful in characterizing the aromaticity,[36] has also been performed at the HF/6-311++G(d,p) level of theory with the B3LYP/6-311++G(d,p) geometry. At the center of the six-membered ring, the NICS value is calculated to be 1.0, deviating significantly from the normal values of aromatic systems; cf. the NICS value is −9.6 for benzene at the same level of theory. The migrating chlorine atoms affect the ring structure and the chemical shift remarkably, vide infra. Similarly, due to the antiaromaticity involved in the transition state, the energy barrier of 3,4-dichlorocyclobutene (**12**) is higher than that of dichlorocyclobutane by as much as 10.8 kcal/mol. An attempt to quantify the aromaticity of the transition state has been made, and it has proven to be marginally successful. A NICS value of 14.2 is obtained at the center of the four-membered ring. Again, because of the effect of the migrating groups, this value is remarkably smaller than those of typical antiaromatic systems such as cyclobutadiene, which has a NICS of 27.6 at the HF/6-311++G(d,p) level, despite being qualitatively consistent with what one would expect.

Interestingly, it has been found that the barrier height of the dyotropic rearrangement correlates well with the $C^{\alpha}-C^{\beta}$ bond length in the transition state, as shown in Figure 3. As readily seen from Figure 3, deviation of the data point corresponding to the dyotropic rearrangement of **12** where the antiaromatic transition state is present is remarkably serious. When this data point is excluded, a better linear relationship with a correlation coefficient of 0.92 and a standard error of 3.88 has been obtained. This linear relationship provides further support for the aforementioned statement that the delocalization of the newly formed π-bond would accelerate the dyotropic rearrangement. It is also noted that the C−Cl distances, another important structural parameter of the transition state, range from 2.29 to 2.47 Å. These values are significantly smaller than those in the 1,3-sigmatropic shifts, which are all greater than 2.78 Å, and the 1,5-sigmatropic shifts, which are all greater than 2.60 Å

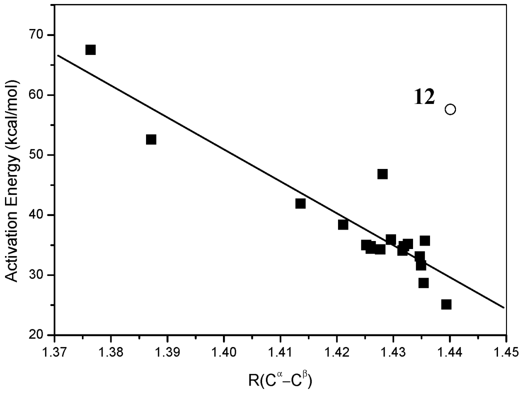


Figure 3. Plot of the activation energies versus the bond lengths of $C^{\alpha}-C^{\beta}$ in the transition states.

(refer to the transition structures of the 1,3-chlorine shift of systems **3**, **13**, **14**, **16**, and **17**, and the 1,5-chlorine shift of systems **16** and **17** in the Supporting Information). It implies that, in the transition structures, there still exists a relatively strong interaction between the migrating chlorine atoms (Cl^m) and the remaining C_mH_n moiety. To quantify the strength of the interaction, bond orders of $C^{\alpha}-Cl^m$ and $C^{\beta}-Cl^m$ in each transition state have been calculated by using the NLMO method, and the results show that they fall in a range of 0.17−0.35. Hence, it seems reasonable that the bond alternation instead of delocalized geometry in the C_6H_6 moiety of the transition state of system **16** is ascribed to the effect of the migrating chlorine atoms. Furthermore, we have examined the relationship between the average C^k-Cl^m ($k = \alpha$ and β) distance (Table 1) and the dyotropic barrier. Although no universal correlation is obtained, the result reveals that, excluding the singular behavior of system **12**, all of the systems with an average C^k-Cl^m distance of larger than 2.40 Å in the transition state have a relatively low dyotropic barrier of no more than 36 kcal/mol, whereas all of the systems having a $\Delta E^{\ddagger}$ value of greater than 40 kcal/mol possess an average C^k-Cl^m distance of less than 2.37 Å in the transition state; that is, there is an approximate trend that the longer the C^k-Cl^m distance in the transition state, the lower the dyotropic barrier. Particularly, system **16** with the lowest dyotropic barrier represents the largest average C^k-Cl^m distance (2.446 Å), indicating that the migrating chlorine atoms of **16** have the smallest effect upon the dyotropic barrier among all of the systems considered.

In addition to the structure−reactivity relationship, competition between the dyotropic rearrangement and other reaction paths needs to be taken into account to predict observable dyotropic processes. One of the possible interferences is the thermal eliminations of 1,2-dichlorohydrocarbons. A recent single pulse shock tube study[37] revealed that the activation energy of thermal elimination of 1,2-dichloroethane was 57.8 ± 2.0 kcal/mol, significantly higher than that of dyotropic rearrangement. Theoretical calculations were also considered in that study, and the B3LYP/6-311++G(d,p) result of 57.6 kcal/mol was found to reproduce well the experimental value.[37] In the present work, the eliminations of several representative systems (**2**−**4**, **8**, **9**, and **13**−**16**) were investigated at the B3LYP/6-311++G(d,p) level of theory, and their ZPE-corrected activation energies were collected in Table 1. As shown in the data, the activation energy of the thermal elimination follows the same trend as that of the dyotropic shift, manifesting that the hyperconjugation effect, conjugation effect, as well as aromatic stabilization also facilitate the stability of the transition structure of the elimination process. Moreover, it seems that these factors contribute even more to the thermal elimination reaction. For example, the activation energy of thermal elimination of **16** is predicted to be 26.3 kcal/mol, decreased by as much as 30 kcal/mol as compared to the basic elimination reaction of 1,2-dichlorohydrocarbon (**1**). A NICS calculation was also performed to characterize the aromaticity of the transition state of the thermal elimination of **16**. However, because of the aforementioned reason, no satisfactory result was obtained (the NICS value is 1.46). Nevertheless, the thermal elimination pathway does not interfere severely with the dyotropic rearrangement, judging from the fact that the elimination has a higher, or at most comparable, activation energy.

For systems containing a C−C double bond, the sigmatropic rearrangement needs to be examined. The activation energies of several selected sigmatropic 1,3- and 1,5-shifts are listed in Table 1. Calculations show that the $\Delta E^{\ddagger}$ values of the 1,3-sigmatropic shifts for systems **3**, **13**, and **14** are 40.66, 37.42, and 39.3 kcal/mol, respectively; all are higher than those of the corresponding dyotropic shifts. Thus, the dyotropic processes of these systems seem to be observable, in principle. For **16**, although the dyotropic migration has a relatively low barrier due to the aromaticity of the transition state, this process is not likely to be observed because a 1,5-sigmatropic shift of this system is energetically more favorable with $\Delta E^{\ddagger}$ being 22.7 kcal/mol. The preference of the 1,5-sigmatropic shift may be ascribed to two factors: (1) only one C−Cl bond needs to be ruptured, whereas for the dyotropic shift, the number of the rupturing C−Cl bond is two; and (2) aromatic stabilization is also thought to be involved in the transition structure. For the latter, despite no direct evidence, it has been reported recently that the transition state of its topologically identical 1,5-H shift is aromatic.[38] Our present HF/6-311++G**//B3LYP/6-311++G** calculations show that the NICS values at the ring center of the transition structures of the sigmatropic 1,5-hydrogen, methyl group, and chlorine shifts are −9.5, −7.5, and 2.6, respectively. While the NICS value for the transition state of hydrogen shift is very close to that for benzene and predicts the aromaticity, the NICS value of 2.6 for the chlorine shift does not mean that the transition state is antiaromatic because this process has a much lower activation energy than the analogous hydrogen migration (23.6 vs 41.7 kcal/mol). To minimize the paratropic effects of other σ bonds and provide a more reliable indication of aromaticity,[36e,39] the NICS values at the points of 0.6 Å (NICS(0.6)) and 1.0 Å (NICS(1.0)) above the center of the ring in the opposite direction to the migrating atom have been calculated on the above transition states. The NICS(0.6) values for the transition states corresponding to the hydrogen, methyl, and chlorine shifts are −8.42, −7.38, and −0.05, respectively, and the NICS(1.0) values are −8.11(H), −7.29(Me), and −2.36(Cl). Apparently, the migrating chlorine may seriously affect the magnetic shielding tensor of the ring center regardless of which value is used, and thus the use of NICS criterion to evaluate the aromaticity of the dyotropic transition states is, as presented above, no longer feasible. Nevertheless, taking into account that the occurrence of migrating chlorine leads to an overestimation of the NICS value of the sigmatropic transition state and that the dyotropic transition state of **16** with two migrating chlorine atoms represents a lower NICS value than the corresponding transition state of sigmatropic chlorine shift (1.0 vs 2.6), one would reasonably expect that the dyotropic transition state of **16** is, at least weakly, aromatic despite possessing a positive NICS value at the ring center.

The transition state of the 1,3-sigmatropic chlorine shift of **16** is also located and is found to lie 9 kcal/mol above the energy of the transition state of the dyotropic shift. Similarly, the dyotropic rearrangement of **17** should be difficult to observe experimentally because both 1,3- and 1,5-shifts are preferable with the latter being predominant. The activation energy is 31.0 kcal/mol for the 1,3-shift and 26.6 kcal/mol for the 1,5-shift. As mentioned above, to date, there have been only two examples of dyotropic halogen rearrangement detected experimentally, and both refer to the dyotropic bromine migration. It is therefore of interest to investigate the effect of the migrating group on this type of reaction. Little is known on this subject even for the well-documented sigmatropic halogen migrations. The basic dyotropic bromine migration of dibromoethane (**20**) is predicted to have an activation energy of 32.4 kcal/mol at the B3LYP/6-311++G(d,p) level of theory. This value is significantly lower than that of the basic dyotropic chlorine migration (41.9 kcal/mol), which can be reasonably ascribed to the smaller dissociation energy of the C−Br bond in comparison to the C−Cl bond; cf. experimentally determined bond dissociation energies[40] of CH_3-Cl and CH_3-Br are 83.2 and 70.9 kcal/mol, respectively. Similarly, several six-membered cyclic systems were examined. The calculated dyotropic migration barriers of 1,2-dibromocyclohexane (**21**), 3,4-dibromocyclohexene (**22**), and 4,5-dibromocyclohexene (**23**) are 27.3, 25.8, and 25.6 kcal/mol, respectively, lower than those of the corresponding dichlorinated analogues by more than 8 kcal/mol. For 5,6-dibromocyclohexa-1,3-diene (**24**), the activation energy is calculated to be 15.1 kcal/mol, a decrease of 10 kcal/mol as compared to the dyotropic rearrangement of chlorine migration of **16**. Moreover, this $\Delta E^{\ddagger}$ is even slightly lower than the corresponding value of the 1,5-sigmatropic shift, 15.6 kcal/mol, indicating that the dyotropic rearrangement of **24** seems to be an observable process. It is noteworthy that an attempt to locate the transition state of the 1,3-sigmatropic shift of **24** failed. In addition, the influence of the migrating atom upon the thermal elimination has been investigated. The activation energies of the eliminations of **20**, **21**, and **24** are 53.6, 44.6, and 23.4 kcal/mol, respectively. The fact that the activation energies for the corresponding dichlorinated species **1**, **9**, and **16** are 57.6, 48.4, and 26.3 kcal/mol, respectively, indicates that a replacement of chlorine atoms in the reactants by bromine atoms does not reduce significantly the elimination barrier. The reason is that the elimination of dihalogenated hydrocarbon to yield halogenated olefin hydrocarbon and hydrogen halide (HX) is associated with not only the breaking of the C−X bond, but also the rupture of the C−H bond.

Deyà et al.[22] reported an AM1 study on the dyotropic rearrangement of *trans*-2,3-dibromo-*tert*-butylcyclohexane (**25**) as described in Scheme 1. Although the transition state was located successfully, the energy barrier of this process was predicted to be as high as 62.2 kcal/mol. Obviously, the barrier was overestimated because this isomerization occurred under a reasonably mild condition. The present density functional theory calculation shows that the dyotropic migration barrier of 1,2-dibromocyclohexane (**21**) is merely 27.3 kcal/mol. To evaluate the influence of the vicinal bulky *tert*-butyl, the rearrangement of **25** has also been examined; no considerable alternation ($\Delta E^{\ddagger} = 26.7$ kcal/mol) has been found. Thus, a semiempirical method is thought to be incompetent for describing quantitatively this type of reaction. Furthermore, we predicted the diaxial isomer to be more stable than the diequatorial isomer by 6.0 kcal/mol, which is on the same order of the experimental value, 3.6 kcal/mol.

TABLE 2: Reactants with Their Calculated Activation Energies (in kcal/mol) of Dyotropic Migration $\Delta E^{\ddagger}$, Sigmatropic Migration $\Delta E_s^{\ddagger}$, and the Elimination Process ($\Delta E_{elim}^{\ddagger}$)

	reactant	$\Delta E^{\ddagger a}$	$\Delta E_s^{\ddagger a}$	$\Delta E_{elim}^{\ddagger a}$
20	1,2-dibromoethane	32.4		53.6
21	1,2-dibromocyclohexane	27.3		44.6
22	3,4-dibromocyclohexene	25.8	33.4[b]	
23	4,5-dibromocyclohexene	25.6		
24	5,6-dibromocyclohexa-1,3-diene	15.1	15.6[c]	23.4
25	2,3-dibromo-*tert*-butylcyclohexane	26.7		
26	1*a*,8*a*-dibromodecahydronaphthalene	24.8		
27	9,10-dichloro-9,10-dihydrophenanthrene	26.9		
28	1-bromo-2-chloroethane	37.2		
29	1-bromo-2-chlorocyclohexane	31.6		
30	5-bromo-6-chlorocyclohexa-1,3-diene	20.1		

[a] Zero-point vibrational energy is included. [b] Activation energy of the 1,3-shift. [c] Activation energy of the 1,5-shift.

Dyotropic rearrangement of 1*a*,8*a*-dibromodecahydronaphthalene (**26**), which can be regarded as a model of the known dyotropic reaction, that is, the isomerization of 5,6-dibromocholestane,[20] has been examined. Our calculation predicts the energy barrier of this reaction to be 24.8 kcal/mol, lower than that of the 1,2-dibromocyclohexane (**21**) by 2.5 kcal/mol. It suggests that a participation of the bridgehead halogen can promote the dyotropic isomerization process.

According to the above argument, it is reasonable to believe that the dyotropic rearrangement is most likely to occur in dibrominated systems, as the known examples presented. In contrast, because of a relatively high activation energy and the competition with the sigmatropic rearrangement, the dyotropic migration has difficulty taking place in dichlorinated systems. Nevertheless, several dyotropic chlorine migrations are predicted to be observable in mild conditions. For example, the dyotropic rearrangement of 9,10-dichloro-9,10-dihydrophenanthrene (**27**) is predicted to have a ZPE-corrected $\Delta E^{\ddagger}$ of 26.9 kcal/mol at the B3LYP/6-311++G(d,p) computational level, comparable to that of the known dyotropic bromine migration of **25**. The low barrier may result from the aromatic stabilization of the transition state; meanwhile, the possible sigmatropic shift pathways have been interrupted by the benzannulation.

Intriguingly, a mixed dyotropic rearrangement, that is, that the chlorine and the bromine interchange their positions, is also predicted to be feasible. The activation energy of the dyotropic rearrangement of 1-bromo-2-chloroethane (**28**) is calculated to be 37.2 kcal/mol, near the average of the activation energy of the dyotropic migrations of chlorine and of bromine. Similarly, the dyotropic rearrangements of 1-bromo-2-chlorocyclohexane (**29**) and 5-bromo-6-chlorocyclohexa-1,3-diene (**30**) have also been investigated, and the activation energy for each reaction has been found to lie between that of the dyotropic migration of the corresponding dichlorinated compound and the corresponding dibrominated compound, cf. the data displayed in Tables 1 and 2. These results provide further evidence for the close relationship between the dyotropically migratory aptitude of halogen atoms and the dissociation energy of C−X bonds.

Conclusion

Potential energy surfaces for a series of dihalogenated hydrocarbons have been investigated by using the B3LYP/6-311++G(d,p) method to provide insight into the dyotropic halogen migrations. It has been shown that this type of reaction proceeds via an ethylenic transition state. Conjugation and hyperconjugation effects that would lead to a delocalization of the newly formed π electrons in the transition state accelerate the rearrangement. In particular, due to the involvement of both aromatic and doubly allylic stabilizations in the transition state, the activation energy of 5,6-dichlorocyclohexa-1,3-diene has been found to decrease significantly as compared to those of other dichlorinated six-membered cyclic systems. For several systems, possible thermal elimination and sigmatropic migration have also been examined. The results suggest that the competitions with sigmatropic migration need to be scrutinized to predict observable dyotropic processes.

In contrast to the dyotropic chlorine migrations, the dyotropic bromine migrations are demonstrated to have much lower activation energies and are more likely to take place. The mixed dyotropic rearrangements, that is, the chlorine and the bromine interchange their positions, are also proven to be feasible with the energy barrier lying between that of the dyotropic chlorine migration and that of the dyotropic chlorine migration.

Acknowledgment. This work was supported by the National Science Council of the Republic of China through Grant No. NSC 92-2113-M-007-040. We are grateful to the reviewers for helpful suggestions.

Supporting Information Available: Optimized Cartesian coordinates and energies for all calculated structures. This material is available free of charge via the Internet at http://pubs.acs.org.

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