J. Org. Chem. **2000,** *65,* 2192−2194

Polar Bromination of Cyclopropane: A DFT Study

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Received November 30, 1999

Hitherto the polar addition of bromine to cyclopropane has been considered as a two-step process. Current calculations have established the energetics for the proposed cation−anion pairs required by these mechanisms. An energetically lower pathway is proposed here in the form of a *syn*-cycloaddition process. Compared to the two-step process, a significantly lower activation enthalpy for this process has been found. The stereochemical consequences of the cyclic mechanism are retention−retention for the two adding moieties. This result is consistent with published experimental data on the bromination of a deuterated cyclpropane.

Introduction

The polar addition of bromine to cyclopropane forming 1,3-dibromopropane has elicited a number of mechanistic studies concerned with questions regarding the nature of the reaction intermediates, if any, and the stereochemistry of the addition.[1] According to a computer search of the literature the last word on this subject appears to be the paper by Lambert et al.[2] The preparation of cyclopropane-*cis*-1,2,3-*d* was described along with its subsequent reaction with bromine and iron in the dark at room temperature. The variation with temperature of the $^{1,3}J_{HH}$ coupling constant (AX_2 spectrum) for the deuterated 1,3-dibromopropane product was analyzed and used to support a mechanistic proposal. The three mechanisms considered by the Lambert group are shown in Scheme 1.

The three major conformers of 1,3-dibromopropane are given in Figure 1. The conformational analysis of 1,3-dibromopropane was based on "the gauche−gauche conformer has been found to be the only conformer present in the solid and the dominant conformer in the gas"[2] phases. They predicted from this analysis a dependence of $^{1,3}J_{HH}$ with temperature for the product(s) of retention−inversion, inversion−inversion, and retention−retention. Their experimental observation indicated a monotonic decrease of the $^{1,3}J_{HH}$ coupling with temperature.

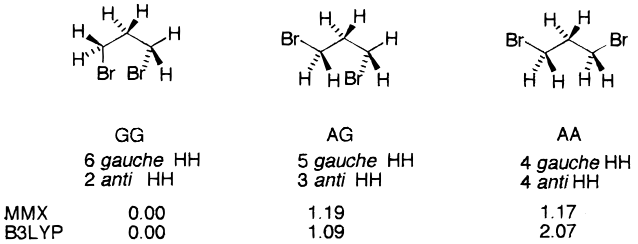
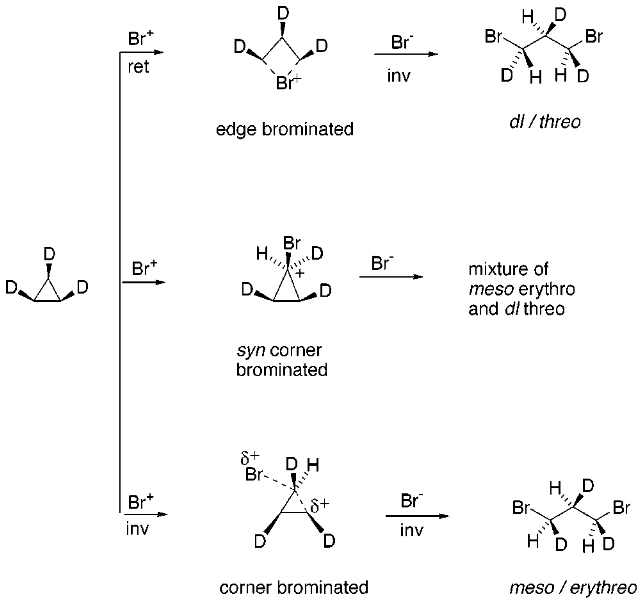


Figure 1. Principle conformers of 1,3-dibrompropane. The given energy differences are in kcal/mol.

Scheme 1



The inversion−inversion mechanism was disposed of as requiring an inverse relation between temperature and the magnitude of $^{1,3}J_{HH}$. The experimental data was considered to be most consistent with a retention−inversion mechanism that predicts a decrease in the coupling constant with a decrease in temperature. They acknowledged the retention−retention mechanism would also exhibit this behavior but argued that "a double retention mechanism would have required an unknown retention stereochemistry for the nucleophilic attack"[2] and that the "relatively small decrease (in coupling constant) as the temperature is lowered is better explained by the retention−inversion mechanism, but these data do not logically exclude the double retention mechanism mode".[2] Restrained to the chloro and fluoro analogues by basis set limitations, they calculated (MP2/6-31G*//HF/3-21 G*) the edge-halogenated cation intermediates to be more stable than the corner-halogenated cations. A similar conclusion had been previously published by Yamabe et al.[3] (MP2/MIDI-1) on chloro and bromo cations. A further argument was presented that the percentage of *gauche* interactions in the GG, AG, and

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(1) (a) Lambert, J. B.; Schulz, W. J.; Mueller, P. H.; Kobayashi, K. *J. Am. Chem. Soc.* **1984**, *106*, 792. (b) Battiste, M. A.; Coxon, J. M. *Tetrahedron Lett.* **1986**, *27*, 517−518 and references therein.

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10.1021/jo991831u CCC: $19.00

Table 1. ZPE-Corrected Energies (hartrees) for Structures of Interest in This Study (Becke3LYP/631G*)

structure	energy
cyclopropane	−117.894 518
bromine	−5143.306 594
corner bromocation **3-A**	−2689.182 741
edge bromocation **3-B**	−2689.216 806
syn cyclic TS	−5261.154 172
1,3-dibromopropane (GG)	−5261.247 636

AA conformers (Figure 1) for a product of retention−inversion is the same as for the undeuterated 1,3-dibromopropane. So “for this and only this mechanism, the magnitude of the coupling constant should be identical in the unlabeled and labeled materials. Indeed, at 30 °C, both the unlabeled and labeled materials showed a *J* of about 6.2 Hz at 30 °C and 5.9 Hz at −40 °C”.[2]

Currently available quantum mechanical technology now offers the opportunity to examine the mechanism of the cyclopropane bromination in greater detail and accuracy. The results of such a study are reported herein.

Computational Methods

All energy and geometry calculations were carried out at the B3LYP/6-31G* level.[4] This level of theory has been demonstrated to be adequate where either bridged or nonclassical ions are to be expected as stationary structures.[5] Frequency calculations were carried out on all prospective transition structures to verify a single imaginary frequency. Gaussview verified vibrations corresponding to the reaction coordinate.[6]

For the determination of the geometry of cyclic transition states an increase in the criteria for energy convergence was required, using the keyword “tight” in the transition state optimization procedure. This requirement is consistent with a relatively flat potential energy surface in the region of the transition state. The frequency calculation and zero point energy (ZPE) of the *syn* transition structure were carried out at the B3LYP/6-31G* level. Other ZPEs were calculated at the HF/3-21G* level and scaled by 1.06. All energies discussed below are corrected for ZPE. A summary of all ZPE corrected energies is given in Table 1.

Results and Discussion

Before considering the mechanism of cyclopropane bromination, some observations on the influence of the iron are appropriate. While it is well recognized that the presence of iron materially enhances the rate of bromination, no meaningful discussion of the role it plays has been forthcoming. For example, during the iron-catalyzed halogenations of aromatic hydrocarbons it has long been assumed that an iron species with a positive bromine has been formed and this is usually represented as $FeBr_5^+$. Given the size of this system, current ab initio methods are either unavailable or prohibitive in time requirements to compute such species. The program SPARTAN (version 5.0)[7] offers a semiempirical PM3-tm method parametrized for transition metals.

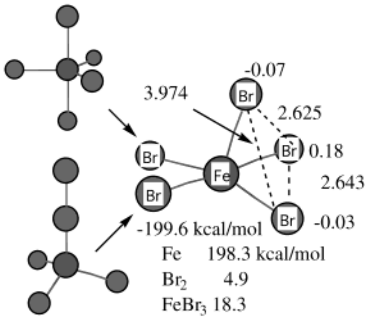

Figure 2. The PM3-tm structure and heats of formation for $FeBr_5^+$ and related molecules.

Two potential $FeBr_5^+$ structures were generated, and each was optimized (Figure 2) to a species with a unique bromine bearing a charge of 0.18 units while the two adjacent bromines each carry a slight negative charge. The distances between these three bromine atoms in the complex are shown**.** The positive charge on one of the bromine atoms will enhance the electrophilic character of the reactant relative to the reactivity of elemental bromine. Moreover, the difference in Br−Br distances between bromine (2.44 Å) and the complex suggests that the use of elemental bromine in further calculations is a reasonable assumption.

In an attempt to examine the potential energy surface of the 1-propyl-3-bromo-cation, two different conformations (planar zigzag and planar U-shaped) were optimized, giving the corner-bromocation (**3-A**, Figure 3**)** and edge-bromocation (**3-B**, Figure 3), respectively. In keeping with earlier low level calculations,[2,3] **3-B** is the more stable at the B3LYP/6-31G* level by 22.9 kcal/mol. The transition structure **3-C** between **3-A** to **3-B** exhibited an activation enthalpy (**3-A** to **3-B)** of 3.2 kcal/mol.

In low polarity media these species will be formed as tight ion pairs with the bromide ion, and the enthalpy of formation for the species must be corrected for the change in potential energy in bringing the two ions together from infinity. The Coulomb’s Law correction for this effect is given by the equation ΔPE (hartrees) $= 0.529q_1q_2(1/X)$ where the ion separation X is given in Å and the 0.529 is a factor for the conversion of distance to Bohrs. The separation of the cation−bromide ion pairs was approximated as the sum of the van der Waals radii for two bromines, and the ions were considered to be of unit charge throughout. When this correction is applied to the enthalpies of formation of **3-A**,$\mathbf{Br}^-$ and **3-B**,$\mathbf{Br}^-$, the enthalpy is reduced from 161.3 to 75.1 and 139.9 to 53.7 kcal/mol, respectively. The correction for bringing a negative bromide into a positive unit charge is exactly the same for A, B, and C.

The low energy conformers pertinent to 1,3-dibromopropane are given in Figure 1 along with the number of *anti* and *gauche* proton couplings. The energies for these structures were determined by two methods.

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(6) Gaussian, Inc., Pittsburgh, PA.

(7) Wavefunction Inc., Irvine, CA.

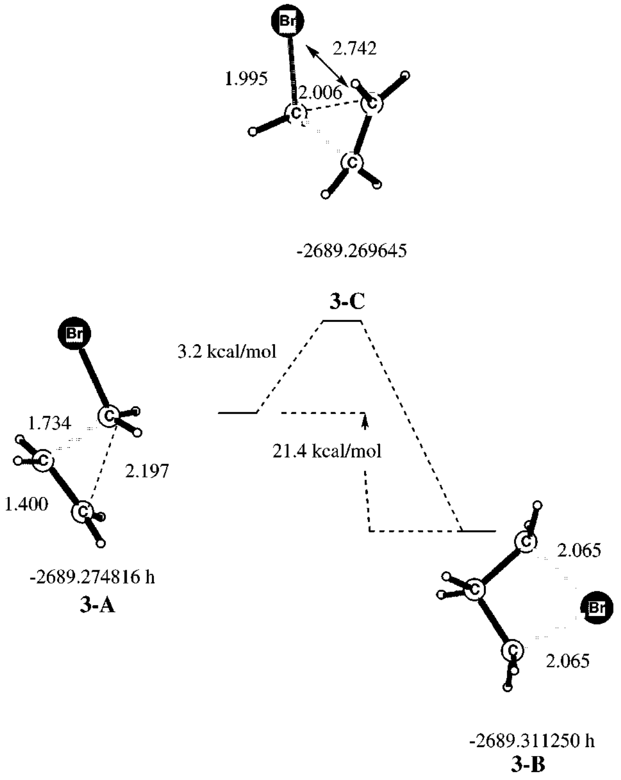

Figure 3. The results of optimizing the corner and edge bromcyclopropyl cations and the TS for rearranging A to B.

The molecular mechanics values were determined by PCMODEL,[8] which employs the MMX force field. The B3LYP/6-31G* values are corrected for ZPE. While the calculations agree that the GG conformer is the most stable conformer and the AA conformer is a minor contributor only to the conformer mix, it is clear that the calculation is dependent on the method employed. It is generally considered that MM, single ab initio, and DFT methods produce energies that are not better than ±2 kcal/mol.[9] Attempts to quantitate the exact conformer contributions are not possible by standard computational methods. While the decrease in $^{1,3}J_{HH}$ with temperature is an experimental fact, mechanistic arguments based on the magnitude of the decrease (0.8 Hz) may be questioned.

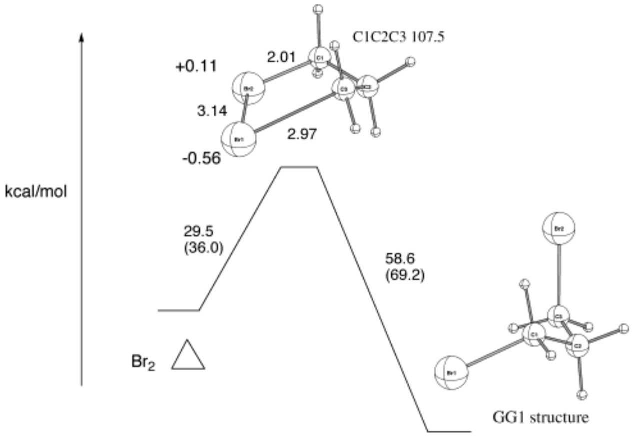

Figure 4. The TS structure and the energetics for the bromination of cyclopropane by a concerted cyclic mechanism. The charges shown for the TS are from the Mulliken population analysis.

Earlier workers have considered only two-step mechanisms for the bromination. The concept of cyclic mechanisms in addition and rearrangement reactions has recently provided useful insights of stereochemistry and energetic considerations in selected reactions.[10] For example, by utilizing the QST3 method of Ayala and Schlegel,[11] it was possible to find a valid transition structure for the cyclic concerted addition of bromine to cyclopropane. The structure and calculated activation enthalpy are shown in Figure 4. The imaginary motions associated with the transition structure were appropriate for the cyclic structure, showing bond making and breaking. The activation enthalpy was calculated as 29.5 kcal/mol. Processes requiring cyclic TSs often exhibit activation entropy changes of the order of −10 to −30 eu corresponding to increases in activation free energy of 3−9 kcal/mol. Since the minimum activation enthalpy for forming the *syn* ion pair **3-B** would be 53.7 kcal/mol, the cyclic mechanism proposed here is not prohibited by the entropy consideration. The stereochemistry of the addition is an unequivocal act of retention at both carbons 1 and 3.

In summary, the polar addition of bromine to cyclopropane is best accommodated by a concerted cyclic transition structure possessing aspects of a tight ion pair. The calculated energetics favors this mechanism over the substantially higher activation enthalpy for any two-step process. The stereochemistry of the product of such a cyclic process is not inconsistent with the NMR data of Lambert et al.[2] It should be pointed out that these calculations provide energies calculated in the gas phase at 0° K. Two-step mechanisms may occur for the reaction in a polar solvent. Since the experimental results were obtained in neat cyclopropane, the considerations above should apply.

Acknowledgment. J.M.C. wishes to acknowledge grants from the New Zealand Lotteries Board and the New Zealand Government Marsden Fund.

Supporting Information Available: Data on the DFT computations. This material is free of charge via the Internet at http://pubs.acs.org.

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