Evaluation of Magnetic Properties as a Criterion for the Elucidation of the Pseudopericyclic Character of 1,5-Electrocyclizations in Nitrile Ylides

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Received: March 6, 2003; In Final Form: April 24, 2003

A comprehensive B3LYP/6-31+G* study of various 1,5-electrocyclizations in nitrile ylides was performed. The complete reaction pathway for each reaction was determined, and changes in magnetic susceptibility and its anisotropy were monitored during the process. This allowed us to examine aromaticity changes and classify the reactions into two distinct groups. In one, the reaction involves a marked increase in aromaticity in the vicinity of the transition state, which can be ascribed to a typical pericyclic behavior; in the other, no such aromatization is observed, so the underlying mechanism must be one of the pseudopericyclic type involving an in-plane attack of the lone pair in the heteroatom.

Introduction

According to the original definition of Lemal, a pseudopericyclic reaction is a concerted transformation whose primary changes in bonding encompass a cyclic array of atoms, of which one (or more) nonbonding and bonding atomic orbitals interchange roles.[1] The role interchange means a "disconnection" in the cyclic array of overlapping orbitals because the atomic orbitals switching functions are mutually orthogonal. Hence, pseudopericyclic reactions cannot be orbital symmetry forbidden.

Following this definition by Lemal, pseudopericyclic reactions fell into oblivion until Birney[2−8] first and several other authors[9−13] later revived interest in them by showing that a number of organic syntheses involve this type of process. On the basis of his results, Birney concluded that pseudopericyclic reactions share three essential features, namely, very low or zero activation energies, planar transition states; and the fact that none can be symmetry forbidden.

Although Lemal's definition is seemingly quite clear, there is some ambiguity in it as the orbital description is not unique; thus, any unit transformation of canonical molecular orbitals can be used to reproduce molecular properties. The studies on pseudopericyclic reactions conducted so far generally support Lemal's conclusions on a specific type of orbitals, viz. the natural bonding orbitals (NBOs).[14−16] This type of localized orbital provides a "chemical picture" of the process concerned, so its analysis can be of a high interest. However, it imposes some restrictions such as the need to choose a specific localization scheme, which introduces some arbitrariness. Also, most of the studies on the topic have so far focused virtually exclusively on the properties of the transition state when it would have been more advisable to monitor the whole reaction.

Therefore, no clear-cut, absolute criterion for distinguishing a pseudopericyclic reaction from a normal pericyclic reaction appears to exists. This has raised some controversy in classifying some reactions. Thus, Lera et al. claim that the electrocyclizations of (2*Z*)-2,4,5-hexatrien-1-imine and (2*Z*)-2,4,5-hexatrienal involve a nucleophilic addition that is pseudopericyclic in nature;[17] on the other hand, our own results not only challenge their conclusions,[18] but also seem to support an essentially pericyclic mechanism for both reactions.[19] To further support this conclusion, in addition to using structural criteria and NBOs, we examined magnetic properties with a view to assessing aromatization during the process. This relies on the fact that the cyclic loop of a pericyclic reaction yields an aromatic transition state,[20] as quantitatively confirmed for various reactions.[21−24] Thus, Herges et al. showed that, in the vicinity of the transition state in the Diels−Alder reaction, the magnetic susceptibility (χ) and its anisotropy (χ_{anis}) exhibit well-defined minima with respect to the reactant and product.[21] On the other hand, the typical disconnection of pseudopericyclic reactions would have prevented this aromatization, as shown by our group for the unequivocally pseudopericyclic cyclization of 5-oxo-2,4-pentadienal to pyran-2-one.[19] This reaction involves the in-plane attack of the lone electron pair on the carbonyl oxygen to the electrophilic allene carbon; there is a lack of overlap between σ and π orbitals, and no barrier to ring closure. The way χ and, especially, χ_{anis} change along the reaction coordinate reveals that the process involves no appreciable aromatization. This clearly departs from the typical aromatization of pericyclic processes. Using this criterion in combination with other considerations allowed us to identify an essentially pericyclic character in the electrocyclizations of (2*Z*)-2,4,5-hexatrien-1-imine and (2Z)-2,4,5-hexatrienal.

In any case, we believe the study of magnetic properties should be extended to other series of pericyclic or pseudopericyclic reactions to confirm its universality and usefulness. For this reason, in this work we examined the 1,5-electrocyclizations of nitrile ylides recently studied by Fabian et al. (see Figure 1).[11] By using energetic and structural criteria in combination

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10.1021/jp034579+ CCC: $25.00 © 2003 American Chemical Society
Published on Web 05/28/2003

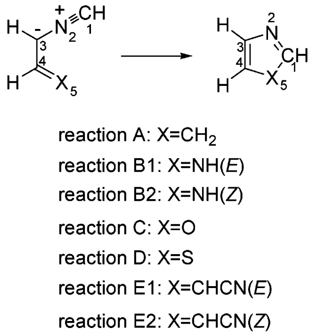

Figure 1. Reaction scheme for the electrocyclizations studied.

with natural orbitals, these authors developed the following classification: B1, C, and D reactions take place via pseudopericyclic mechanisms that involve a nucleophilic attack of the lone pair in the heteroatom (N, O, and S, respectively); on the other hand, A and E1 reactions follow the classical pericyclic mechanism. These authors provided Supporting Information consisting of magnetic anisotropy calculations, but failed to analyze or discuss their results. Also, these results must be completed and extended since, as shown in this paper, studies should encompass the whole reaction pathway rather than singular points alone if one is to derive comprehensive, reliable information about any potential aromatization occurring in these reactions.

Moreover, in this work we extended the study to B2 and E2 reactions involving the *Z* configuration of the imine. Comparing the behavior of B1 and B2 reactions allowed us to carefully examine the influence of the orientation of the lone pair in the N atom on the reaction mechanism.

Computational Methods

The geometry of each stationary point was fully optimized using the Gaussian98 software package[25] with the 6-31+G* basis set and the density functional theory (specifically, the Becke3LYP functional).[26,27] All points were characterized as minima or transition structures by calculating the harmonic vibrational frequencies, using analytical second derivatives. Also, the whole pathway for each reaction was obtained by using the intrinsic reaction coordinate (IRC) with mass-weighted Cartesian coordinates.[28−30] Although the evaluation of the absolute aromaticity of a compound remains a controversial, relatively obscure issue,[31] we were primarily interested in its variation during the reaction and the evaluation of magnetic properties can be a useful tool for this purpose. Changes in magnetic properties along the IRC were monitored at different points for which the magnetic susceptibility (χ) and its anisotropy (χ_{anis}) were calculated. Magnetic susceptibility values were calculated by computing the NMR shielding tensors at the B3LYP/6-311+G(2d,p) level using the individual gauges for atoms in molecules (IGAIM) method,[32,33] which is a slight variation of the continuous set of gauge transformations (CSGT) method.[32−34]

Results and Discussion

Reaction Paths and Vibrational Analysis. It should be noted that the need to obtain the whole IRC for each reaction precluded the use of a high computational level. In any case, our results suggest that the chosen level (B3LYP/6-31+G*) provided more than acceptable results (see Table 1, which compares our energies of reaction and activation with those previously obtained by Fabian et al.).[11] The energies of activation listed in Table 1 are not true activation energies since calculating them accurately would have entailed using the most stable conformation of the reactant rather than simply that giving rise to the cyclization. Basically, this entails optimizing trans conformations with respect to the C3−C4 bond, which are generally—D reaction excepted—more stable. Under these considerations, we obtained an energy of activation of 14.5, 4.9, 16.9, 5.2, 0.2, 17.9, and 15.3 kcal/mol for A, B1, B2, C, D, E1, and E2 reactions, respectively. The same arguments apply to the energies of reaction, which are in fact somewhat less exothermic than those listed in Table 1; as with those of activation, however, the differences were minimal. Just like Table 1 confirms the validity of our energy calculations, Table 2 confirms that of our geometric results (in terms of the distance of the bond being formed in the transition state, which is probably the most interesting geometric parameter in this context). As can be seen, there are no appreciable discrepancies.

TABLE 1: Reaction and Activation Energies (including ZPVE) at the B3LYP/6-31+G* Level (kcal/mol)[a]

	E_r	E_a
A	−39.1 (−37.9) [−46.5]	13.3 (13.1) [9.6]
B1	−55.8 (−58.3) [−60.6]	3.7 (3.4) [2.7]
B2	−56.5	16.2
C	−38.4 (−36.9) [−43.6]	4.8 (4.4) [3.2]
D	−48.2 (−47.3) [−56.6]	0.3 (0.0) [−0.1]
E1	−30.0 (−28.0) [−39.5]	15.7 (14.2) [9.4]
E2	−29.0	14.3

[a] The values obtained for Fabian et al. (ref 11) are in brackets {(B3LYP/6-311+G**) and [MP4(SDTQ)/6-311+G**//MP2/6-311+G**] levels}.

TABLE 2: B3LYP/6-31+G* C1-X5 Bond Lengths (Å) at the Transition States[a]

	R
A	2.427 [2.512]
B1	2.555 [2.542]
B2	2.290
C	2.460 [2.436]
D	3.263 [3.298]
E1	2.421 [2.525]
E2	2.450

[a] The values obtained for Fabian et al. (ref 11) are in brackets [MP2/6-311+G** level].

The energies of activation and the whole energy curves for the calculated IRCs (see Figure 2) clearly reveal two different types of behavior. Thus, A, B2, E1, and E2 reactions exhibit intermediate energy barriers (13−16 kcal/mol) and quite long reaction pathways. On the other hand, B1, C, and D reactions exhibit minimal energy barriers (especially D reaction, with a virtually zero energy) and short reaction pathways. As noted earlier, a low energy barrier is one of the essential features of a pseudopericyclic reaction, so this criterion can in principle be quite useful with a view to classifying the studied reactions.

One other interesting variable is the normal vibrational frequency corresponding to the imaginary frequency in the transition state. Figure 3—which would be even clearer if modes were animated—allows one to draw the following conclusions in this respect: A, B2, E1, and E2 reactions involve rotation about the C4−X5 double bond, which is disrotatory with respect to the other end of the transition structure. On the other hand, B1 reaction seemingly involves no such rotation about the C4−N5 bond. The differential behavior of B1 and B2 is clearly apparent from Figures 4 and 5. Figure 4 compares the variation of the C3C4N5H dihedral angle along the B2 reaction pathway with that of the C3C4C5H dihedral angle along the A pathway

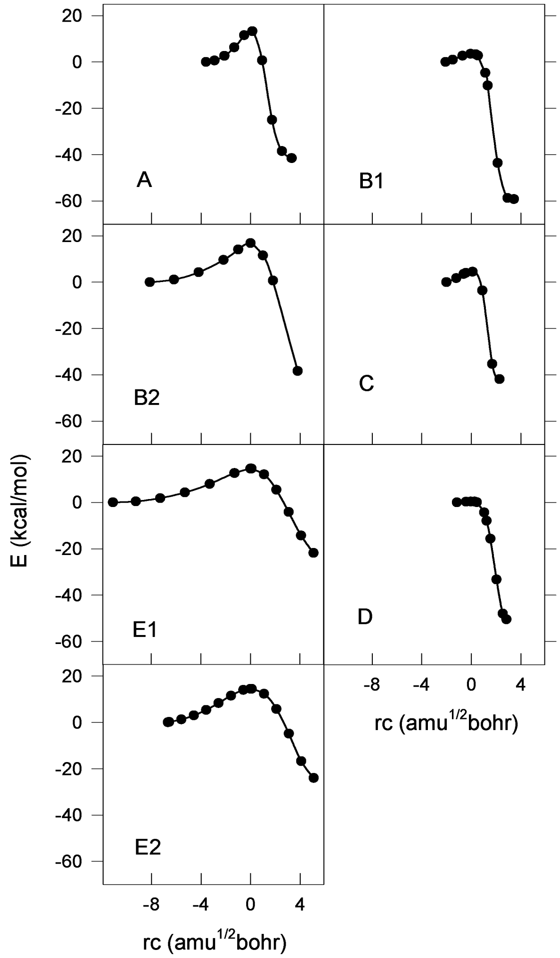

Figure 2. Energy profile for the reactions.

(in terms of the inner hydrogen atom on C5). As can be seen, the two reactions evolve identically, with the same type of rotation. Therefore, the rotations about the C4−X5 bond in A and B2 are equivalent. Figure 5 shows the variation of the same dihedral angle but for the B1 reaction and in terms of the outer hydrogen atom for the A reaction pathway. In this case, the rotation observed in A is not paralleled in B1: the hydrogen atom bonded to N5 remains in trans with respect to the C3−C4 bond virtually throughout (the dihedral angle in the transition state is −175.0°). Therefore, no appreciable rotation about the C4N5 bond occurs in B1, so the reaction must take place in a pseudopericyclic manner, with a nucleophilic attack of the lone electron pair in N5 on the nitrile ylide group. E1 and E2 behave similarly to A. On the other hand, the absence of a hydrogen atom bonded to the heteroatom in C and D precludes the confirmation of a potential rotation.

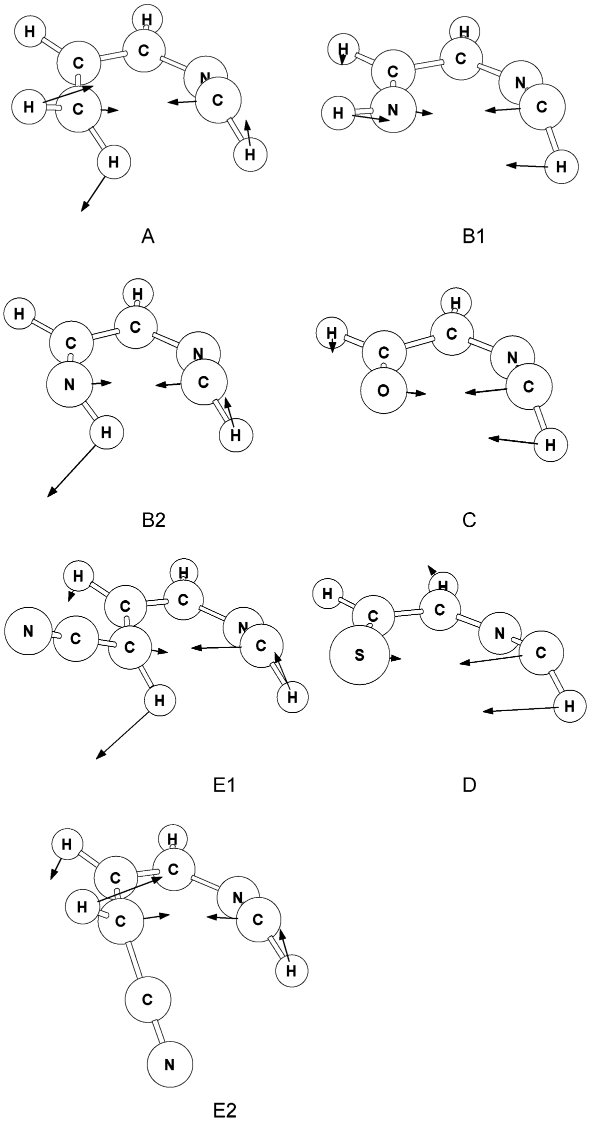

Figure 3. Transition structures and normal mode eigenvectors for the coordinate frequency.

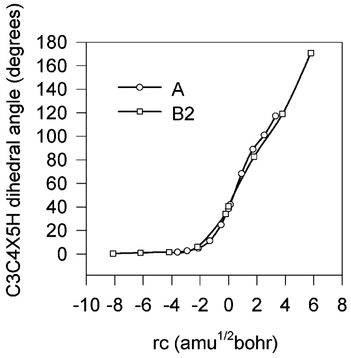

Figure 4. Change of the C3C4X5H dihedral angle along the A and B2 reactions. For reaction A, hydrogen atom refers to the inner one on C5.

Variation of Magnetic Properties. Table 3 shows the magnetic susceptibilities and their anisotropies for the singular points of each reaction. This table provides very useful information regarding the presence or absence of aromatization in the transition state relative to the reactant and product. However, some data are unclear and can lead to spurious conclusions. Thus, while χ for B2 appears to decrease steadily from reactant to product, χ_{anis} exhibits a minimum in the transition state. Also, E1 seemingly involves aromatization but exhibits a very small minimum (χ_{anis} is very similar for the transition state and the product). It is also unclear whether E2 involves any aromatization as χ and χ_{anis} behave disparately. All these uncertainties, which preclude ascertaining whether some reactions involve aromatization, disappear when one examines the behavior of these magnetic properties throughout the IRC. To this end, Figures 6 and 7 show the variation of χ and χ_{anis} with respect to the reactant. These two figures expose two clearly distinct behavior patterns reflected in two completely different variations for χ and χ_{anis}. Thus, both quantities exhibit a well-defined minimum with its center virtually coinciding with the transition state in A, B2, E1, and E2. Beyond the transition point, further decreases are observed that suggest a high

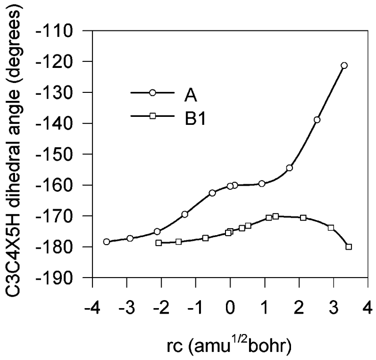

Figure 5. Change of the C3C4X5H dihedral angle along the A and B1 reactions. For reaction A, hydrogen atom refers to the outer one on C5.

TABLE 3: Isotropic Magnetic Susceptibilities (χ) and Anisotropies (χ_{anis}) at the Singular Points of Reactions

		χ (cgs-ppm)	χ_{anis} (cgs-ppm)
reaction A	reactant	−36.43	−12.45
	ts	−41.88	−40.90
	product	−38.85	−36.08
reaction B1	reactant	−32.02	−13.21
	ts	−35.56	−30.17
	product	−42.81	−44.35
reaction B2	reactant	−32.09	−14.67
	ts	−38.91	−45.10
	product	−39.96	−40.28
reaction C	reactant	−28.36	−13.83
	ts	−31.83	−30.95
	product	−38.24	−39.37
reaction D	reactant	−37.98	−26.17
	ts	−40.77	−37.66
	product	−50.87	−51.60
reaction E1	reactant	−46.91	−6.67
	ts	−51.35	−32.33
	product	−48.77	−30.61
reaction E2	reactant	−48.60	−10.26
	ts	−55.22	−36.15
	product	−48.40	−36.28

aromaticity in the products. This is particularly outstanding in the variation of χ for B2 and was the origin of the apparent sustained decrease in this quantity in Table 3. However, Figure 6 shows that B2 exhibits an unequivocal relative minimum in the vicinity of the transition state. In summary, the variation of the two magnetic properties in A, B2, E1, and E2 reactions is consistent with increased aromatization near the transition state, which is a typical feature of classical pericyclic reactions. On the other hand, B1, C, and D reactions exhibit a radically different behavior. Thus, both χ and χ_{anis} decrease monotonically throughout the reaction pathway, with the sole, slight exception of the variation of χ_{anis} in B1 and D, where it appears to increase at the end of the process. However, this apparent discrepancy is negligible; in fact, χ_{anis} exhibits a very strong decrease near the transition state (r.c. = 0.0) and the above-mentioned increase occurs when the reaction has virtually finished. Thus, in D (where the effect is the most marked), the anisotropy increase occurs at an S5−C1 bond distance shorter than 2.4 Å (such a distance is 3.710 Å in the reactant, 3.263 Å in the transition state and 1.715 Å in the product), i.e., the variation of both magnetic properties in B1, C, and D is consistent with the absence of increased aromatization in the vicinity of the transition state, which must be related to a pseudopericyclic character in these three reactions.

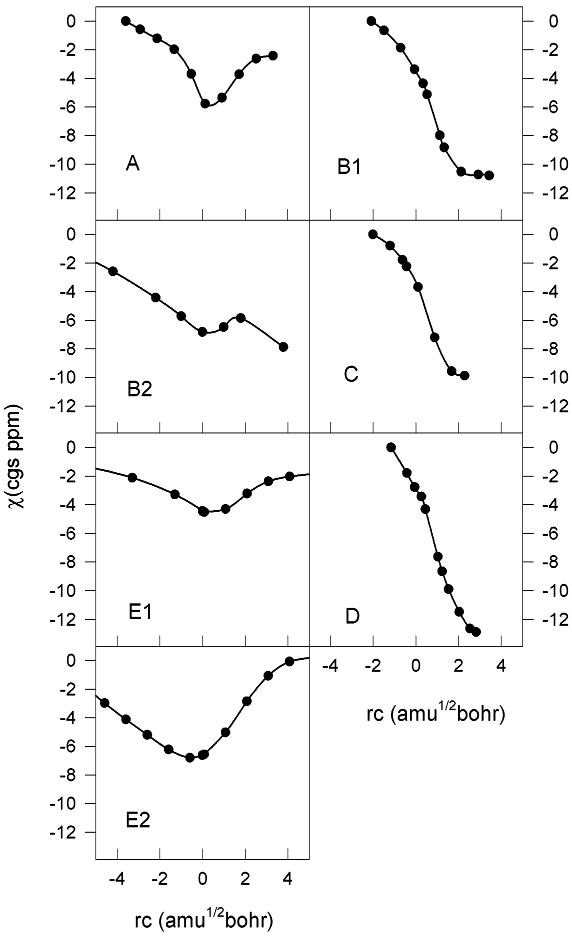

Figure 6. Variation of magnetic susceptibility relative to the reactant.

It should be noted that the assignation of A, B1, C, D, and E1 reactions as pericyclic or pseudopericyclic coincides with that made by Fabian et al. from a structural analysis of natural orbitals.[11] On the basis of our results, B2 and E2 reactions, which had not been examined in this respect before, must be deemed classical pericyclic reactions. We should emphasize the differential behavior of B1 and B2, which results from the favorable orientation of the lone pair for a pseudopericyclic behavior in the former case. This clearly departs from the cyclization of (2*Z*)-2,4,5-hexatrien-1-imine previously studied by our group,[19] where both the *E* and the *Z* configuration of the imine give pericyclic reactions: the participation of the lone pair oriented toward the inside of the ring and hence involved in the cyclization does not seem to suffice to suppress the essential features of pericyclic reactions (the increased aromatization in the transition state included).

Conclusions

The variation of the magnetic properties used to quantify aromaticity (χ and χ_{anis}) along the reaction pathway allows pericyclic and pseudopericyclic mechanisms in the 1,5-electrocyclizations of nitrile ylides to be clearly distinguished. Our results suggest the presence of two typical variation patterns. Thus, the pericyclic reactions exhibit markedly increased aromaticity in the vicinity of the transition state as a result of the cyclic loop involved in the process. In clear contrast, no such aromaticity increase occurs in the pseudopericyclic mechanism owing the “disconnection” of the atoms involved. The driving force in B1, C, and D reactions, of the pseudopericyclic type, is the nucleophilic attack of the lone pair in the heteroatom.

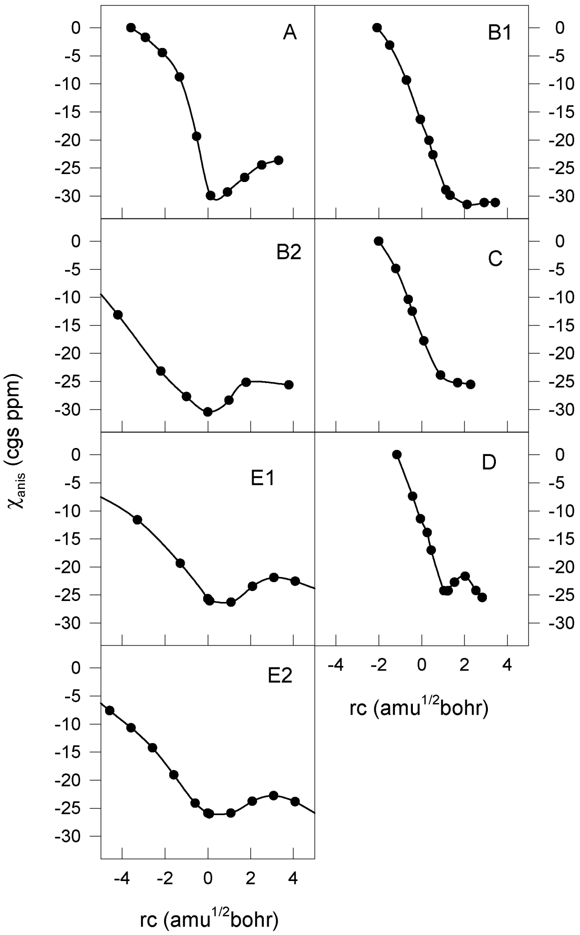

Figure 7. Variation of anisotropy of the magnetic susceptibility relative to the reactant.

This clearly reflects in the fact that the unfavorable orientation of the lone pair in B2 reactions precludes the attack and gives rise to a pericyclic rotation similar to that in A reaction. The occurrence of such a rotation is clearly apparent from the variation of the C3C4X5H dihedral angle along the A and B2 reaction pathways.

The results obtained in this work, together with those reported in a previous paper by our group,[19] appear to confirm that monitoring the variation of magnetic properties along the reaction pathway is a useful method for the unambiguous discrimination of pericyclic and pseudopericyclic mechanisms.

Acknowledgment. The authors thank the Xunta de Galicia (Project PGIDIT02PXIA20901PR) for financial support.

References and Notes

(1) Ross, J. A.; Seiders, R. P.; Lemal, D. M. *J. Am. Chem. Soc.* **1976**, *98*, 4325−7.

(2) Birney, D. M.; Wagenseller, P. E. *J. Am. Chem. Soc.* **1994**, *116*, 6262−70.

(3) Birney, D. M. *J. Org. Chem.* **1996**, *61*, 243−51.

(4) Birney, D. M.; Ham, S.; Unruh, G. R. *J. Am. Chem. Soc.* **1997**, *119*, 4509−4517.

(5) Birney, D. M. *J. Am. Chem. Soc.* **2000**, *122*, 10917−10925.

(6) Shumway, W.; Ham, S.; Moer, J.; Whittlesey, B. R.; Birney, D. M. *J. Org. Chem.* **2000**, *65*, 7731−7739.

(7) Shumway, W. W.; Dalley, N. K.; Birney, D. M. *J. Org. Chem.* **2001**, *66*, 5832−5839.

(8) Zhou, C.; Birney, D. M. *J. Am. Chem. Soc.* **2002**, *124*, 5231−5241.

(9) Luo, L.; Bartberger, M. D.; Dolbier, W. R. J. *J. Am. Chem. Soc.* **1997**, *119*, 12366−12367.

(10) Fabian, W. M. F.; Bakulev, V. A.; Kappe, C. O. *J. Org. Chem.* **1998**, *63*, 5801−5805.

(11) Fabian, W. M. F.; Kappe, C. O.; Bakulev, V. A. *J. Org. Chem.* **2000**, *65*, 47−53.

(12) Alajarin, M.; Vidal, A.; Sanchez-Andrada, P.; Tovar, F.; Ochoa, G. *Org. Lett.* **2000**, *2*, 965−968.

(13) Rauhut, G. *J. Org. Chem.* **2001**, *66*, 5444−5448.

(14) Foster, J. P.; Weinhold, F. *J. Am. Chem. Soc.* **1980**, *102*, 7211.

(15) Reed, A. D.; Curtiss, L. A.; Weinhold, F. *Chem. Rew.* **1988**, *88*, 899.

(16) Glendening, E. D.; Reed, A. E.; Carpenter, J. E.; Weinhold, F. *NBO 3.1 Program Manual*, 1988.

(17) (a) De Lera, A. R.; Alvarez, R.; Lecea, B.; Torrado, A.; Cossio, F. P. *Angew. Chem., Int. Ed.* **2001**, *40*, 557−561. (b) De Lera, A. R.; Cossio, F. P. *Angew. Chem., Int. Ed.* **2002**, *41*, 1150−1152.

(18) Rodríguez-Otero, J.; Cabaleiro-Lago, E. M. *Angew. Chem., Int. Ed.* **2002**, *41*, 1147−1150.

(19) Rodríguez-Otero, J.; Cabaleiro-Lago, E. M. *Chem. Eur. J.* **2003**, *9*, 1837−1843.

(20) Zimmermann, H. E. *Acc. Chem. Res.* **1971**, *4*, 272.

(21) Herges, R.; Jiao, H.; Schleyer, P. v. R. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1376.

(22) Jiao, H.; Schleyer, P. v. R. *J. Org. Phys. Chem.* **1998**, *11*, 655−662.

(23) Manoharan, M.; De Proft, F.; Geerlings, P. *J. Org. Chem.* **2000**, *65*, 7971−7976.

(24) Manoharan, M.; De Proft, F.; Geerlings, P. *J. Chem. Soc., Perkin Trans. 2* **2000**, 1767−1773.

(25) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A., Jr.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B. G.; Chen, W.; Wong, M. W.; Andres, J. L.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian 98*, revision A.9; Gaussian, Inc.: Pittsburgh, PA, 1998.

(26) Lee, C.; Yang, W.; Parr, R. J. *Phys. Rev. B* **1988**, *37*, 785−789.

(27) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648−5652.

(28) Fukui, K. *Acc. Chem. Res.* **1981**, *14*, 363.

(29) Gonzalez, C.; Schlegel, H. B. *J. Chem. Phys.* **1989**, *90*, 2154.

(30) Gonzalez, C.; Schlegel, H. B. *J. Phys. Chem.* **1990**, *94*, 5223.

(31) See Special Issue 5 entirely dedicated to aromaticity, *Chem. Rev.* **2001**, 101.

(32) Keith, T. A.; Bader, R. F. W. *Chem. Phys. Lett.* **1992**, *194*, 1.

(33) Keith, T. A.; Bader, R. F. W. *Chem. Phys. Lett.* **1993**, *210*, 223.

(34) Cheeseman, J. R.; Frisch, M. J.; Trucks, G. W.; Keith, T. A. *J. Chem. Phys.* **1996**, *104*, 5497.