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Are Electrocyclization Reactions of (3*Z*)-1,3,5-Hexatrienone and Nitrogen Derivatives Pseudopericyclic? A DFT Study

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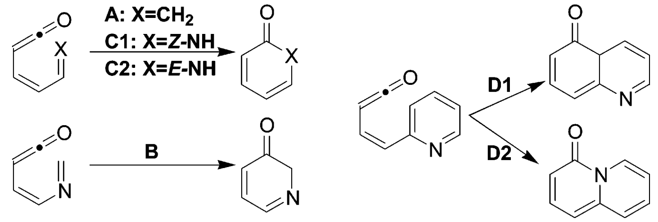

Electrocyclization reactions of (3*Z*)-1,3,5-hexatrienone and nitrogen derivatives were studied by performing density functional theory (DFT) calculations together with the 6-31+G* basis set. Reactants, products, and transition states for each reaction were localized and the IRC connecting reactants and products was also obtained. Magnetic properties were evaluated along the reaction path to elucidate the characteristics of the reactions studied. As obtained from the calculations, electrocyclization of (3*Z*)-1,3,5-hexatrienone is a pericyclic process, as indicated by a variety of indexes, such as Nucleus Independent Chemical Shift (NICS), anisotropy of the magnetic susceptibility, or anisotropy of the current-induced density (ACID). This reaction presents characteristics of pericyclic reactions despite the activation energy lowering relative to the electrocyclization of (4*Z*)-1,2,4,6-heptatetraene, and the relatively small NICS values observed in the transition state. Magnetic properties indicate that an enhancement of the aromaticity relative to reactants and products occurs revealing the absence of orbital disconnections on the cyclic loop of interacting orbitals. Only two reactions among those studied exhibit pseudopericyclic character due to the in-plane attack of the lone pair on nitrogen. In these cases, the reactions showed no barrier for the electrocyclization process, and no aromaticity enhancement was observed.

1. Introduction

In 1976, Lemal and co-workers found that the reaction of automerization of a sulfoxide by means of a sigmatropic displacement proceeded with ease.[1] The authors argued that the process was not typically pericyclic as it presented different characteristics. As a consequence, the term *pseudopericyclic reaction* was proposed to denote such reactions, characterized by a concerted transformation whose primary changes in bonding encompass a cyclic array of atoms, at one (or more) of which nonbonding and bonding atomic orbital interchange roles. The role interchanging implies a disconnection in the cyclic array of overlapping orbitals because the atomic orbital switching functions are mutually orthogonal. Hence, pseudopericyclic reactions cannot be orbital symmetry forbidden. Birney first[2−10] and several other authors[11−19] revived

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

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

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

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

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

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

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

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interest in them by showing that a number of organic syntheses involve this type of process. As a result of Birney's works,[2−10] a series of characteristics have been attributed to pseudopericyclic reactions: planar transition states, low activation energies, disconnections in orbital overlap, and impossibility of being forbidden. Though Lemal's definition seems clear, the orbital description is not unique and therefore the transformation between bonding and nonbonding orbitals is not clearly defined. As a consequence, some controversy was aroused about how several reactions must be classified.[20−23]

One of the recognized properties of pericyclic reactions is that they present aromatic transition states. In this context, the study of magnetic properties and their relation with aromaticity has appeared as one of the most useful criteria to distinguish between both types of mechanism. It is known that aromatization affects magnetic properties such as magnetic susceptibility and its anisotropy, leading to especially negative values for such properties.[24−26] Herges et al. showed that, for the Diels−Alder reaction, an important decrease in these magnitudes occurs in the transition state with respect to reactants or products.[25] On the other hand, the typical disconnection of pseudopericyclic reactions would have prevented this aromatization enhancement, as shown by our group in previous work, allowing both types of reactions to be distinguished.[21,23,27−30]

The previously mentioned magnitudes are global properties, which can be affected by parts of the molecule not directly implicated in the aromatization process. To avoid this problem, an useful property is the Nucleus Independent Chemical Shift proposed by Schleyer et al. and defined as the negative of the magnetic shielding.[31] This property can be evaluated at any point of the molecule, and exhibits very negative values in the center of aromatic rings.

Another method that uses magnetic properties is ACID (anisotropy of the current-induced density), recently developed by Herges and Geuenich.[32] It has been proved that this method is very useful for the quantitative study of delocalization in molecules.[33,34] The method allows the visualization of the ring current formed when a magnetic field is applied and permits us to decide whether there is a disconnection on the cyclic array of orbitals.[23,28,30]

In this work, a comprehensive density functional study about electrocyclization reactions of (3*Z*)-1,3,5-hexatrienone and nitrogen derivatives is presented. In a recent work, Zora presented results for cyclization reactions of several dienylketenes and concluded that they proceed by means of a pseudopericyclic pathway.[17,35] To support this affirmation, Zora argued the lowering of activation energy with respect to the totally carbonated compound ((4*Z*)-1,3,5,6-heptatetraene) and also the not so negative NICS values obtained in the transition states.[17]

However, we believe that a deeper study about the characteristics of the process is necessary to decide about the plausibility of the pseudopericyclic path. In fact, in our group we have carried out calculations which demonstrate that magnetic properties, together with other criteria are a valuable tool in deciding about the pericyclic/pseudopericyclic character of a reaction.[21,23,27−30] In previous works we have shown that a decrease of the energy barrier does not imply a pseudopericyclic reaction,[23] because the energy lowering does not necessarily indicate the presence of a disconnection in the overlapping orbitals. Furthermore, magnetic properties calculated only on the transition state can lead to misleading results, and more founded conclusions can be obtained by analyzing the variations along the reaction path.[27,28]

We have selected in our study cyclization reactions of (3*Z*)-1,3,5-hexatrienone and derivatives where one carbon atom has been substituted by nitrogen. The reactions studied and the numbering scheme followed in this work are shown in Figure 1. As noted by other authors, the presence of an oxygen atom in (2*Z*)-2,4,5-trienal allows the reaction to proceed by a pseudopericyclic, barrierless process.[3,23] In consequence, we have performed nitrogen substitutions in positions 5 and 6 and also included a nitrogen atom embedded into a pyridine ring.

2. Computational Details

The geometry of each stationary point was fully optimized by using the Gaussian98[36] software package with the 6-31+G* basis set and the density functional theory (specifically, the Becke3LYP functional).[37,38] All points were characterized as minima or transition structures by calculating the harmonic vibrational frequencies, using analytical second derivatives. Also, the pathway for each reaction was obtained by using the intrinsic reaction coordinate (IRC) with mass-weighted coordinates. Although the evaluation of the absolute aromaticity of a compound remains a controversial issue,[39] we were primarily interested in its variation during the reaction, and

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(8) Zhou, C.; Birney, D. M. *J. Am. Chem. Soc.* **2002**, *124*, 5231.
(9) Wei, H.-X.; Zhou, C.; Ham, S.; White, J. M.; Birney, D. M. *Org. Lett.* **2004**, *6*, 4289.
(10) Zhou, C.; Birney, D. M. *J. Org. Chem.* **2004**, *69*, 86.
(11) Luo, L.; Bartberger, M. D.; Dolbier, W. R., Jr. *J. Am. Chem. Soc.* **1997**, *119*, 12366.
(12) Fabian, W. M. F.; Bakulev, V. A.; Kappe, C. O. *J. Org. Chem.* **1998**, *63*, 5801.
(13) Fabian, W. M. F.; Kappe, C. O.; Bakulev, V. A. *J. Org. Chem.* **2000**, *65*, 47.
(14) Alajarin, M.; Vidal, A.; Sanchez-Andrada, P.; Tovar, F.; Ochoa, G. *Org. Lett.* **2000**, *2*, 965.
(15) Chamorro, E. E.; Notario, R. *J. Phys. Chem. A* **2004**, *108*, 4099.
(16) Finnerty, J. J.; Wentrup, C. *J. Org. Chem.* **2004**, *69*, 1909.
(17) Zora, M. *J. Org. Chem.* **2004**, *69*, 1940.
(18) Kalcher, J.; Fabian, W. M. F. *Theor. Chem. Acc.* **2003**, *109*, 195.
(19) Chamorro, E. *J. Chem. Phys.* **2003**, *118*, 8687.
(20) De Lera, A. R.; Alvarez, R.; Lecea, B.; Torrado, A.; Cossio, F. P. *Angew. Chem., Int. Ed.* **2001**, *40*, 557.
(21) Rodriguez-Otero, J.; Cabaleiro-Lago, E. M. *Angew. Chem., Int. Ed.* **2002**, *41*, 1147.
(22) De Lera, A. R.; Cossio, F. P. *Angew. Chem., Int. Ed.* **2002**, *41*, 1150.
(23) Rodriguez-Otero, J.; Cabaleiro-Lago, E. M. *Chem. Eur. J.* **2003**, *9*, 1837.
(24) Zimmermann, H. E. *Acc. Chem. Res.* **1971**, *4*, 272.
(25) Herges, R.; Jiao, H.; Schleyer, P. v. R. *Angew. Chem., Int. Ed.* **1994**, *33*, 1376.
(26) Jiao, H.; Schleyer, P. v. R. *J. Org. Phys. Chem.* **1998**, *11*, 655.
(27) Cabaleiro-Lago, E. M.; Rodriguez-Otero, J.; Hermida-Ramon, J. M. *J. Phys. Chem. A* **2003**, *107*, 4962.
(28) Pena-Gallego, A.; Rodriguez-Otero, J.; Cabaleiro-Lago, E. M. *J. Org. Chem.* **2004**, *69*, 7013.
(29) Montero-Campillo, M. M.; Rodriguez-Otero, J.; Cabaleiro-Lago, E. M. *J. Phys. Chem. A* **2004**, *108*, 8373.
(30) Rodríguez Otero, J.; Cabaleiro Lago, E. M.; Hermida-Ramón, J. M.; Peña-Gallego, A. *J. Org. Chem.* **2003**, *68*, 8823.
(31) von R Schleyer, P.; Maerker, C.; Dransfeld, A.; Jiao, H.; van Eikema Hommes, N. J. R. *J. Am. Chem. Soc.* **1996**, *118*, 6317.
(32) Herges, R.; Geuenich, D. *J. Phys. Chem. A* **2001**, *105*, 3214.
(33) Herges, R.; Papafilippopoulos, A. *Angew. Chem., Int. Ed.* **2001**, *40*, 4671.
(34) Kimball, D. B.; Weakley, T. J. R.; Herges, R.; Haley, M. M. *J. Am. Chem. Soc.* **2002**, *124*, 13463.
(35) Zora, M.; Sahpaz, F.; Ozarslan, E. *J. Mol. Struct.* (*THEOCHEM*) **2002**, *589−590*, 111.

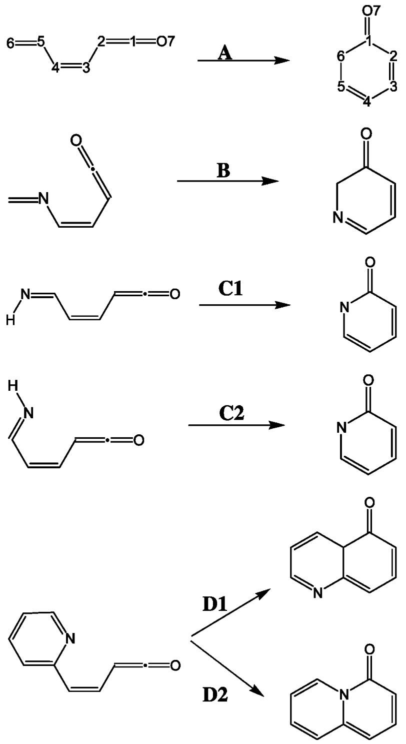

FIGURE 1. Reactions studied and numbering scheme. The most stable conformation of the reactant is represented.

the evaluation of magnetic properties can be a useful tool for this purpose.[39] Changes in magnetic properties along the IRC were monitored at different points for which the mean magnetic susceptibility (χ), its anisotropy (χ_{anis}), and NICS were calculated. Magnetic susceptibility values were calculated by computing the NMR shielding tensors with the IGAIM (individual gauges for atoms in molecules) method,[40,41] which is a slight variation of the CSGT (continuous set of gauge transformations) method.[42] NICS was calculated with the GIAO (Gauge-Independent Atomic Orbital) method.[43] We have also carried out some ACID calculations (anisotropy of the current-induced density) with the program supplied by Herges.[32]

3. Results

3.1. Energies. Table 1 summarizes the energies of the different species involved in the reactions studied. It should be noted that reactants can present different conformations. For reactions A and C1 the most stable structure corresponds to the *all-trans tZt* conformation, whereas for the other molecules the most stable reactant corresponds to other conformations such as *cZt* (reaction B) or *tZc* (reactions C2 and D). It should be remembered that only the *cZc* conformation is able to give way to the electrocyclization reaction. In any case, we should always refer to the most stable of these conformers when discussing activation energies.

TABLE 1. Energies (ZPE included) and Enthalpies (298 K) for the Species Participating in the Reactions Studied (kcal/mol) Relative to the Most Stable Conformer of the Reactant[a]

		tZt	*cZt*	*tZc*	*cZc*	TS	product
energies	A	0.00	2.05	3.56	6.15	13.22	−22.6
	B	0.03	0.00	6.27	7.90	17.22	−18.9
	C1	0.00	2.44	3.29	6.21	16.82	−43.7
	C2	1.58	3.69	0.00			−41.64
	D1	4.33	6.92	0.00		21.28	6.23
	D2						−26.57
enthalpies	A	0.00	2.06	3.47	6.09	12.32	−23.64
	B	0.08	0.00	6.39	8.12	16.47	−19.78
	C1	0.00	2.44	3.20	6.17	15.94	−44.97
	C2	1.76	3.90	0.00			−42.64
	D1	4.40	7.00	0.00		20.57	5.48
	D2						−27.52

[a] t and c refer to the conformation *s-cis* or *s-trans* of 2−3 and 4−5 bonds.

As noted in Table 1, the activation energy for reaction A amounts to 13.2 kcal/mol (activation enthalpy is 12.3 kcal/mol at 298 K), which agrees well with results from previous calculations found in the literature, which give values between 12 and 14 kcal/mol approximately.[17,35] Also, the reaction enthalpy amounts to −23.6 kcal/mol, again in good agreement with previous results. As argued by Zora, this barrier is about 7 kcal/mol smaller than that obtained for the cyclization of (4*Z*)-1,2,3,6-heptatetraene.[17] That is, the presence of the ketene promotes a decrease in the energy of activation for this electrocyclization reaction. However, such a reduction does not necessarily imply a change to a pseudopericyclic path. In fact, in previous work, our group has shown that very similar reactions with similar energy barriers (reactions A and B in ref 23) are in fact pericyclic reactions, despite the energy lowering observed with respect to the prototypical pericyclic case. In any case, the barrier is still large enough compared with the clearly pseudopericyclic reaction of (3*Z*)-1,3,5-trienone, which proceeds without any barrier as predicted by several calculations.[3,23]

Reactions B and C1 present energy barriers slightly larger that that obtained for reaction A, reaching 17 kcal/mol. All these reactions are exothermic, but reaction C1 presents a reaction enthalpy of about −44 kcal/mol, roughly twice that for reactions A and B.

Let us focus now on reaction C2. As shown in Table 1, no transition state was located for this reaction, which proceeds without energy barrier. That is, the only energy barrier the reactant must overcome is that corresponding to the conformational change from the most stable *tZc* conformation to the *cZc* conformation, which cycles without barrier. This behavior is similar to that observed for (3*Z*)-1,3,5-trienone, as expected, because the configuration of the imine in C2 allows the in-plane lone pair of nitrogen to attack the ketene C=O double bond located

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(36) 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.

(37) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648.

(38) Lee, C.; Yang, W.; Parr, R. G. *J. Phys. Rev. B* **1988**, *37*, 785.

(39) See special issue 5 entirely dedicated to aromaticity: *Chem. Rev.* **2001**, *101*.

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

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

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

(43) Wolinski, K.; Hilton, J. F.; Pulay, P. *J. Am. Chem. Soc.* **1990**, *112*, 8251.

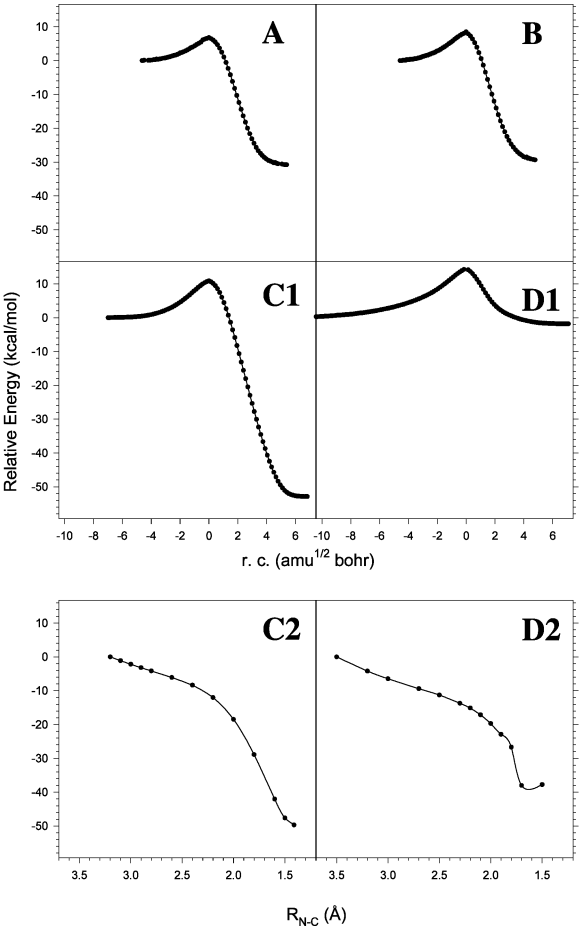

FIGURE 2. Variation of energy along the reaction path. For reactions C2 and D2 the energy profile was obtained by performing partial optimizations at fixed C−N distances.

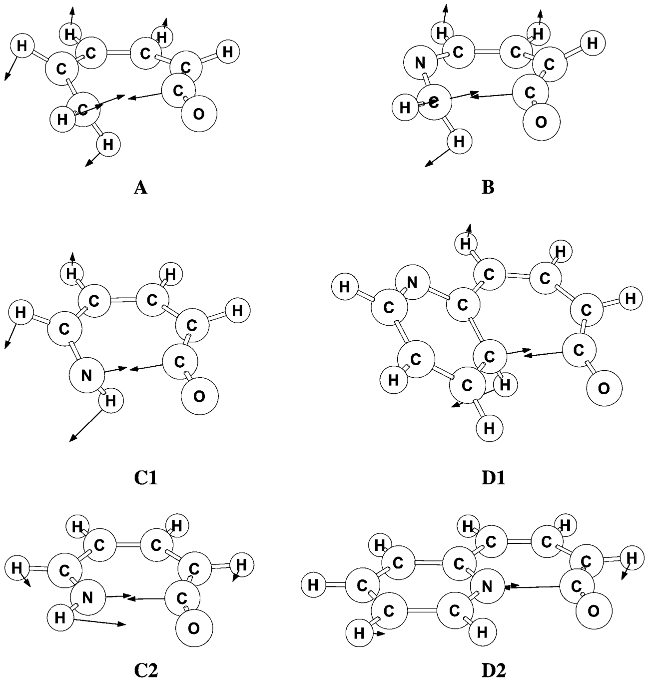

FIGURE 3. Transition states for the reactions studied. For reactions C2 and D2 structures obtained at AM1 level are shown for comparison.

TABLE 2. Selected Geometrical Parameters for the Transition State of the Reactions Studied

	A	B	C1	D1	C2	D2^{b}	HEP
R_{1-6}	2.243	2.199	2.089	2.045	2.000	2.000	2.274
θ_{123}	122.0	118.2	125.0	119.4	120.5	122.4	120.9
θ_{234}	120.9	123.0	119.2	120.6	120.7	128.6	122.1
θ_{345}	128.2	127.2	127.2	128.1	128.2	126.9	126.0
θ_{456}	128.1	126.5	126.3	127.0	127.3	102.8	129.2
θ_{561}	101.9	100.5	104.8	104.4	102.0	121.9	101.2
θ_{612}	106.2	111.4	108.9	111.6	121.3	121.2	105.8
θ_{567}	150.1	150.0	147.2	143.6	145.4	147.9	148.6
φ_{1234}	−30.8	34.7	−25.9	25.2	0.0	0.0	−30.6
φ_{2345}	−0.4	−2.0	0.4	−1.3	0.0	0.0	−0.2
φ_{3456}	6.1	−14.6	4.7	−4.7	0.0	0.0	20.0
φ_{4561}	8.3	2.7	6.6	−7.4	0.0	0.0	−1.5
φ_{5612}	−30.2	24.3	−24.7	26.3	0.0	0.0	−27.7
φ_{6123}	41.0	−41.5	34.8	−35.1	0.0	0.0	42.5
φ_{5617}	170.9	−171.6	172.7	−171.5	0.0	0.0	168.8

[a] Values for the electrocyclization of (4*Z*)-1,2,4,6-heptatetraene (HEP) are also included for comparison. For reactions C2 and D2 values are obtained at a distance C−N of 2 Å. Distances in Å, angles in deg. [b] For this reaction atom 6 corresponds to the nitrogen atom.

in the plane.[3,23] Therefore, for this reaction a disconnection occurs and it must be pseudopericyclic.

Something similar happens for reactions D. For the reactant molecule, two plausible electrocyclizations may occur. In one of these reactions a new C−C bond is formed, breaking the aromaticity of the pyridine moiety. The other possibility is to form a new N−C bond, leading to an aromatic product. As listed in Table 1, the first process (D1) presents a barrier of about 21 kcal/mol, the largest among the reactions studied in this work, as a consequence of the loss of aromaticity of the pyridine moiety in the transition state. In the second reaction (D2), no barrier is observed, and an in-plane attack of the lone pair in nitrogen is possible as in reaction C2, leading to a pseudopericyclic reaction. Reaction D1 is slightly endothermic, whereas reaction D2 is neatly exothermic, due to the aromaticity of the product.

Figure 2 shows the change in energy along the reaction path taking the *cZc* reactant as reference. It can be appreciated that the profiles for reactions C2 and D2 are totally different from the rest of the reactions studied. In reactions C2 and D2, the absence of transition state prevents the IRC from being calculated. Instead we have calculated the energy for a full relaxed geometry, but at fixed C−N distances, leading to graphs for reactions C2 and D2. All reactions present significant barriers except C2 and D2 which proceed without barrier, with the energy decreasing steadily from and open to a closed disposition. In summary, though activation energies for reactions A, B, C1, and D1 are smaller than those for the electrocyclization of (4*Z*)-1,2,4,6-heptatetraene,[3,17,23] the values are still significant, suggesting that there is no reason to conclude that they proceed through a pseudopericyclic mechanism.

3.2. Geometries. As noted by several authors, pseudopericyclic reactions exhibit planar or almost planar transition states.[2,4,6,23] Figure 3 shows the structures of the transition states of the reactions studied, and selected geometric parameters are listed in Table 2. Note that transition states for reactions C2 and D2 were included in Figure 3 as obtained from AM1 calculations for

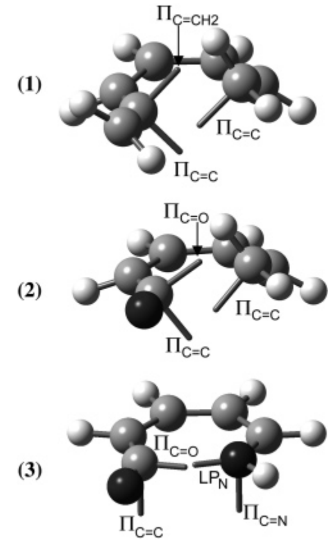

FIGURE 4. Representation of the orientation of selected natural bond orbitals on atoms 1 and 6 in the transition state of three different reactions: (1) pericyclic cyclization of (4*Z*)-1,2,4,6-heptatetraene; (2) reaction A; and (3) pseudopericyclic cyclization of (3Z,5*E*)-5-iminopenta-1,3-dienone (reaction C2, calculated at a C−N distance of 2.0 Å)

comparison, because no transition state for electrocyclization was located at either the B3LYP or the HF level. These structures are totally planar, which corresponds to typical pseudopericyclic reactions.

It can be seen from Table 2 that reactions A, B, C1, and D1 present similar structures in the transition states, with intermolecular distances ranging from 2.05 to 2.24 Å, typical values for pericyclic electrocyclizations. All transition states are nonplanar, though the deviation from planarity is not so strong as that observed for cyclization of hexatriene.[17,44] However, the structure of the transition state for these reactions is pretty similar to that obtained for (4*Z*)-1,2,4,6-heptatetraene. As revealed by dihedral angles, deviations from planarity are similar in all cases, though the ketene group is less distorted than the allene in the (4*Z*)-1,2,4,6-heptatetraenene cyclization. Therefore, it seems that no argument favoring the pseudopericyclic mechanism could be extracted from geometries, which in all cases are very similar to that of the transition state of the typically pericyclic cyclization of (4*Z*)-1,2,4,6-heptatetraene.

Zora indicates that no disrotatory process takes place for reaction A, contrary to what happens in typical pericyclic electrocyclizations.[17] However, it is not possible to confirm that point in the ketene group, due to the absence of out-of-line atoms. Nevertheless, this effect can be estimated by means of natural bond orbital analysis (NBO),[45−47] which gives us the direction of the natural orbitals. Figure 4 represents the orientation of Π interacting orbitals on atoms 1 and 6 in three different electocyclizations: (4*Z*)-1,2,4,6-heptatetraene (pericyclic), (3*Z*)-1,3,5-hexatrienone (reaction A), and (3*Z*,5*E*)-5-iminopenta-1,3-dienone (pseudopericyclic, reaction C2). The orientation of the orbitals thus represented corresponds to Π_{12} and Π_{17} (exocyclic) orbitals on the ketene or allene group and Π_{56} on the other side of the molecule. It should be noted that some rotation has occurred for cases 1 and 2 in Figure 4. Therefore, the interaction is more feasible with the C=C bond perpendicular to the molecular plane, as in the normal pericyclic reaction, than with the C=O bond as suggested by Zora. For case 3 in Figure 4, no rotation is observed as the reaction proceeds by an in-plane attack of the lone pair in nitrogen.

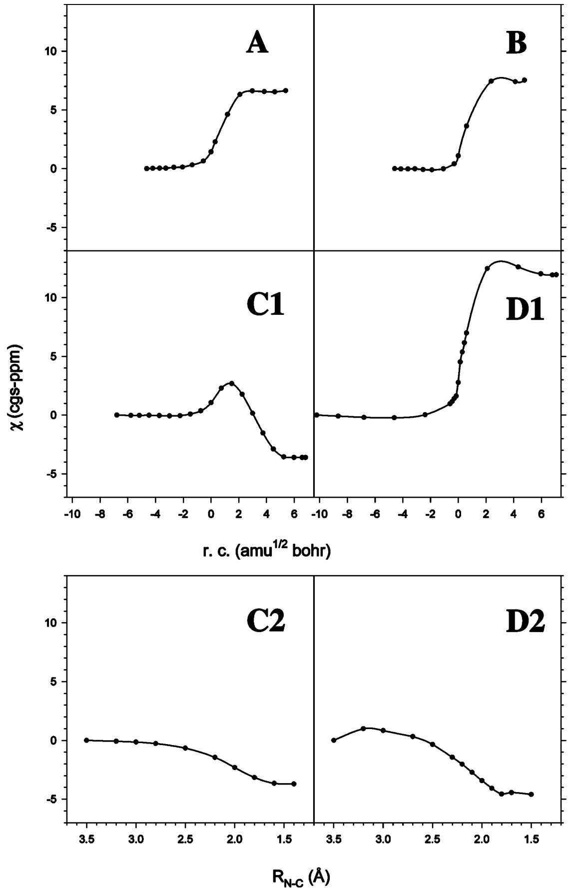

FIGURE 5. Variation of mean magnetic susceptibility along the reaction path. For reactions C2 and D2 the profile is obtained from totally relaxed geometries at fixed C−N distances.

3.3. Magnetic Susceptibility. Figure 5 shows the variation of mean magnetic susceptibility along the reaction path of the reactions studied. It should be remembered here that for a pericyclic reaction, an enhancement of the aromaticity is observed in the transition state, resulting in minimum values of the magnetic susceptibility.[25,26] Though there is not any a priori fundamental principle concerning the conditions which global properties others than energy have to fulfill in stationary points, previous works have shown that the evolution of magnetic properties along the IRC of pericyclic reactions exhibits enhanced values in the vicinity of the transition state.[21,23,27−30]

As observed in Figure 5, no minimum is observed near the transition state for any of the reactions studied. Instead, there is a sigmoid variation for reactions A, B, and D1, with the susceptibility increasing from reactants

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(44) Rodríguez-Otero, J. *J. Org. Chem.* **1999**, *64*, 6842.

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

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

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

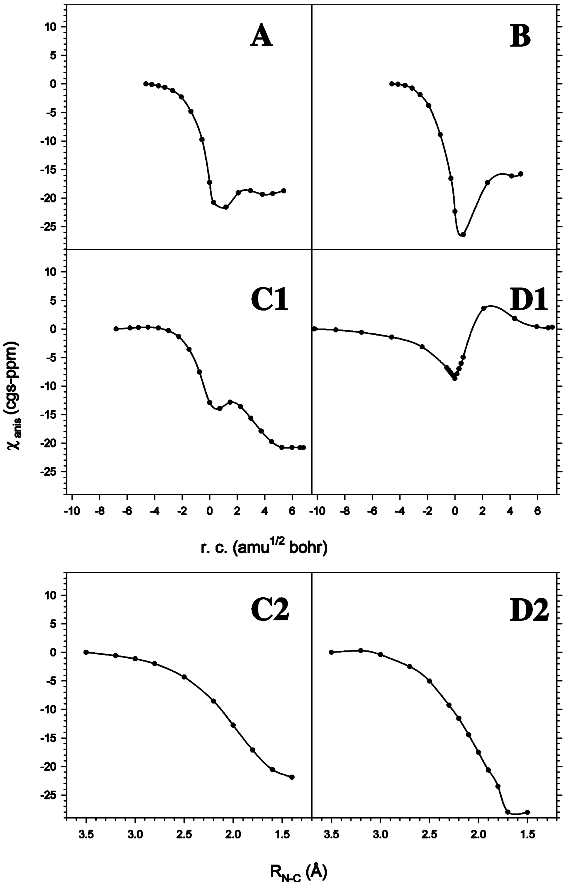

FIGURE 6. Variation of the anisotropy of the magnetic susceptibility along the reaction path. For reactions C2 and D2 the profile is obtained from totally relaxed geometries at fixed C−N distances.

to products without any sign of aromatization. For reaction C1, the situation is even more strange, and a maximum appears just passing the transition state. In fact, this behavior is similar to that of the other three reactions; the susceptibility increases steadily but, in this case, it must decrease after the transition state to reach negative values since the product is aromatic.

Therefore, as regarding susceptibility, there is no aromatization enhancement in the transition state, agreeing with a nonpericyclic behavior. However, it has been noted that magnetic susceptibility does not always clearly reflect aromaticity.[27,30] Moreover, changes for reactions C2 and D2, typically pseudopericyclic, are quite different, showing a continuous decrease of magnetic susceptibility.

Figure 6 shows the variation of anisotropy along the reaction path, which should in principle behave similarly to mean magnetic susceptibility. In this case, however, the behavior is totally different. More or less marked minima appear near the transition state for reactions A, B, C1, and D1. Such minima indicate that an aromaticity enhancement occurs near the transition state, thus indicating the pericyclic nature of the process. This is especially evident for reaction B, with the most defined minimum. The behavior for reactions A and D1 is not so evident, but a minimum is clearly distinguished in both cases. Again, reaction C1 exhibits a different pattern. In this case, a decrease of anisotropy occurs from reactants to transition state. Once the transition state is surpassed, the anisotropy increases, but at r.c. = 1.5 decreases again reaching the value for the product. As noted in a previous work, this is a consequence of the product being aromatic.[27] Near the transition state there is an aromaticity enhancement, compatible with pericyclic reactions, but the product being aromatic, anisotropy must decrease even more after the transition state. It should be noted here that at r.c. = 1.5 the H atom in N6 is almost perpendicular to the plane of heavy atoms, thus hindering the possibility of delocalization and, therefore, aromaticity. Finally, reactions C2 and D2 show a continuous decrease of anisotropy from reactants to products, without showing any increase of aromaticity near the transition state, in agreement with a pseudopericyclic behavior. In summary, anisotropy of the magnetic susceptibility clearly indicates that the reactions are pericyclic except reactions C2 and D2, in conflict with results from mean magnetic susceptibility. This contradicting behavior between mean magnetic susceptibility and anisotropy can be a consequence of the different role the *zz* component of the magnetic susceptibility tensor plays in both properties. The shielding associated with aromatization is mainly due to the *zz* (perpendicular to the molecular plane) component of magnetic susceptibility. The anisotropy responds more readily to changes in zz component than mean magnetic susceptibility does, probably leading to the differences thus noted.

In any case, it should be remembered that some caution must be present when analyzing results from magnetic susceptibility, since they correspond to global properties, and effects not directly involved in aromatization could distort the observed behavior.

3.4. NICS. Another way of measuring aromaticity is by means of the NICS index proposed by Schleyer, and defined as the negative of the magnetic shielding.[31] The advantage of NICS over susceptibility is that the former can be calculated at a single point thus avoiding some of the problems related to global properties. Figure 7 shows the variation of NICS along the reaction path in three different points of the molecule. These points correspond to the ring critical point as defined by Bader[48,49] and to points 1 Å above and below the critical plane. It should be remembered that Schleyer cautioned against the use of NICS(0) as it should include spurious effects associated to σ bonds.[50]

In his paper,[17] Zora argued that the relatively small NICS(0) values observed for the transition states of the reactions studied indicated their pseudopericyclic character. However, it has been indicated that not only values on the transition state but also those along the reaction path, and how these values change, should be analyzed.[27,28] As shown in Figure 7, two different behaviors can be observed. For reactions A, B, C1, and D1 a minimum appears near the transition state, indicating aromatization. This minimum is not so deep, especially for the critical point, located in the plane. However, for points placed above the plane, the NICS are more

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(48) Bader, R. F. W. *Atoms in Molecules*: *A Quantum Theory*; Clarendon Press: Oxford, UK, 1990.

(49) Bader, R. F. W. and co-workers. *AIMPAC*: A suite of programs for the Theory of Atoms in Molecules; contact bader@mcmail.cis.mcmaster-ca, Hamilton, Ontario, Canada.

(50) Schleyer, P. v. R.; Manoharan, M.; Wang, Z.-X.; Kiran, B.; Jiao, H.; Puchta, R.; van Eikema Hommes, N. J. R. *Org. Lett.* **2001**, *3*, 2465.

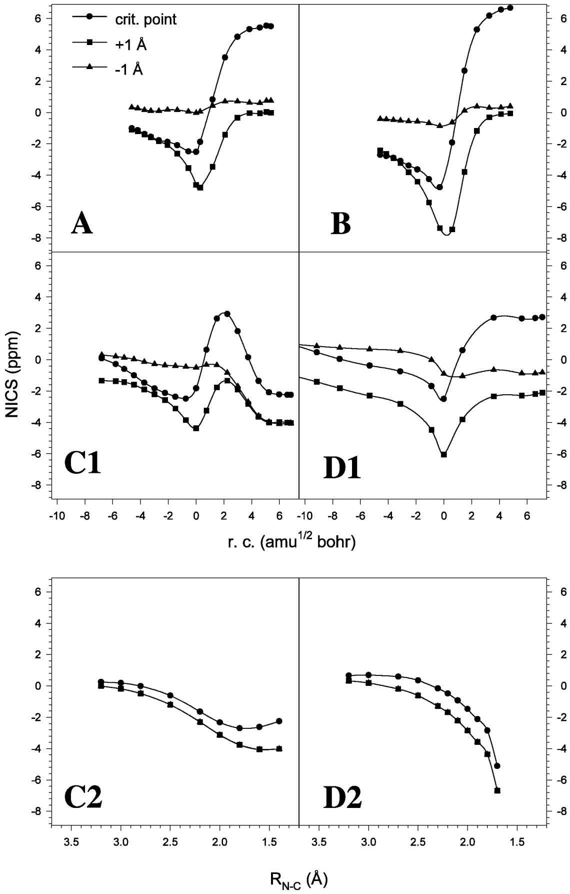

FIGURE 7. Variation of NICS along the reaction path. For reactions C2 and D2 the profile is obtained from totally relaxed geometries at fixed C−N distances.

negative indicating substantial aromatization. Again, reaction C1 shows a different pattern due to the aromaticity of the product, but still shows a clear minimum near the transition state. On the other side, reactions C2 and D2 do not exhibit any minimum in any of the points considered, but a continuous decrease of NICS as the reaction proceeds. Therefore, we can conclude that, as obtained from NICS, only reactions C2 and D2 are pseudopericyclic, whereas the rest exhibit aromatization enhancement to some extent and therefore pericyclic character.

3.5. ACID. Another method to evaluate aromaticity is ACID developed by Herges and Geuenich.[32] This method allows the induced current density vectors to be represented to visualize current flows due to applied magnetic field. The method proved to be useful to evaluate the extent of delocalization and aromaticity. Briefly, a cyclic topology with diatropic ring current implies aromaticity, cyclic topology with paratropic current antiaromaticity, and noncyclic topology nonaromaticity. Also, the presence of disconnections can be tested by means of the critical isosurface value (CIV), which indicates the isosurface value at which the topology changes from cyclic to noncyclic. Large CIV's indicate aromaticity or antiaromaticity and small CIV's indicate disconnection.

The values obtained for the CIV in the transition state of the reactions studied are 0.044, 0.049, 0.057, 0.061, 0.016, and 0.016 for reactions A, B, C1, D1, C2, and D2, respectively. For reactions C2 and D2 where no transition state was located CIV was evaluated at a C···N distance of 2.0 Å, a value similar to those of other transition states. The small CIV's of reactions C2 and D2 indicate the presence of a disconnection. It should be noted, however, that since the products for these reactions are aromatic, CIV's increase when C−N distance shortens reaching values typical of aromatic substances, but no enhancement is observed near the transition state. On the other hand, reactions A, B, C1, and D1 exhibit considerably large CIV's indicating the absence of disconnection and, therefore, the absence of pseudopericyclic character in the sense of Lemal.

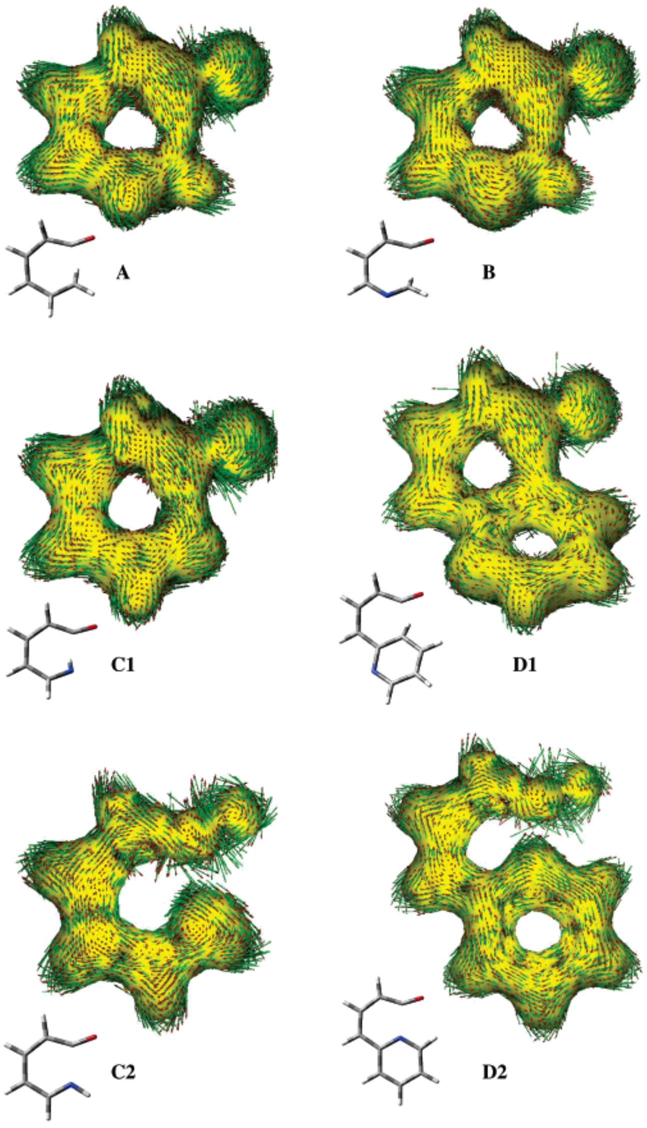

FIGURE 8. ACID plots for the transition state of the reactions studied (reactions C2 and D2 at a C−N distance of 2.0 Å). The isosurface value is 0.03 and the magnetic field points from the paper to the reader.

Though CIV's help us to distinguish between pericyclic and pseudopericyclic reactions, in fact a large CIV can be associated to an antiaromatic character. Therefore, one must corroborate aromaticity displaying the ring current, as shown in Figure 8. For reactions A, B, C1, and D1, a diatropic ring current is observed in the transition state, indicating aromatization and leading to a shielding effect. On the other hand, reactions C2 and D2 show a disconnection and no ring current is possible. However, for these reactions, a trend to establish a diatropic ring current as the C−N distance shortens can be appreciated as a consequence of the aromatic nature of the products.

Therefore, ACID confirms the pericyclic character of reaction A. Though it is not the purpose of the present work, reaction A is closely related to the electrocyclization of 1-isocyanato-2-vynilbenzene proposed by Dolbier et al. as pseudopericyclic.[11] Our ACID results suggest that this reaction is not a truly pseudopericyclic process, as indicated by the large CIV (0.049) of the transition state and the ACID map (see the Supporting Information) of the analogous electrocyclization of (*Z*)-1-isocyanato-1,3-butadiene.

4. Conclusions

A comprehensive study at the B3LYP/6-31+G* level of calculation has been carried out for the electrocyclization reactions of (3*Z*)-1,3,5-hexatrienone and nitrogen derivatives. Reactants, products, and transition states were located for the reactions studied and characterized by means of a vibrational analysis. Also, intrinsic reaction coordinate calculations have been performed to study changes on magnetic properties along the reaction path.

All reactions are clearly exothermic, except reaction D1, which is slightly endothermic. No transition state was found for reactions C2 and D2, which evolve to products without any barrier other than that corresponding to the conformational change of the reactant.

Contrary to what is supported by other authors, our calculations indicate that electrocyclization of (3*Z*)-1,3,5-hexatrienone is a pericyclic process, as revealed by magnetic properties. Though a significant decrease of energy barrier is observed with respect to (4*Z*)-1,2,3,6-heptatetraene, analysis of magnetic properties such as anisotropy of the magnetic susceptibility, NICS, and ACID shows that aromatization enhancement is present in the transition state. In this respect, it should be mentioned that mean magnetic susceptibility does not allow a conclusive assignment to be done.

The presence of nitrogen in position 5 (reaction B) does not affect significantly the characteristics of the reaction, which exhibits similar patterns to those observed for reaction A for all properties studied. In any case, the aromatization enhancement is larger in this case, as revealed by all magnetic properties.

Nitrogen in position 6 gives two different patterns depending on the configuration of the imine. In reaction C1, the lone pair cannot interact with the ketene group and the reaction is typically pericyclic as is shown by the properties studied. However, when the lone pair can interact with the ketene group, no barrier for electrocyclization is observed. Moreover, magnetic properties exhibit a completely different behavior, showing smooth variations from reactants to products without any sign of aromaticity enhancement for intermediate stages of the reaction. In any case, aromaticity must be developed as the cyclization progresses because the product is aromatic.

When the terminal nitrogen atom is embedded in a pyridine moiety, two reactions are possible, depending on whether a new C−C or C−N bond is formed. In the first case (D1), the reaction is clearly pericyclic, with an increase of aromaticity near the transition state; in the second case (D2), the reaction proceeds without barrier as in reaction C2.

As regards properties employed in this work to evaluate aromaticity it must be said that no single criterion should be employed, it being safer to use several different properties to contrast the results obtained. In the present case, mean magnetic susceptibility seems not to be able to distinguish between the pericyclic/pseudopericyclic character of the reactions. All other properties, that is, anisotropy of the magnetic susceptibility, NICS, and ACID, clearly indicate two different patterns which allow an unambiguous classification of the reactions studied.

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Supporting Information Available: Listings of optimized geometries for transition states and energies for all species participating in the reactions; ACID plot for the transition state of (*Z*)-1-isocyanato-1,3-butadiene. This material is available free of charge via the Internet at http://pubs.acs.org.

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