the orbitals most strongly involved in the reactions. As can be seen, the position of the p orbitals (99.99 % p character) are identical in **TSa**, **TSb**, and **TSc**: the X1−C6 and C2−C3 π bonds are rotated in a disrotatory manner, which is consistent with the Woodward–Hoffmann rules. Clearly, a difference exists in the involvement of the electron lone pair on the heteroatom. However, the most salient conclusion is that this lone pair does not attack C2 directly, but rather takes part in an extremely lateral overlap as the X1−C6 bond is already slightly rotated (in **TSa** the Lp-N1-C6-C5 dihedral angle is −22.9°). Thus, in **TSa** the lone pair deviates by 57° from the plane formed by the N1-C2-C3 atoms. If reaction A were pseudopericyclic, the lone pair—which would be in the N1-C2-C3 plane or very close to it—would perform a more direct attack on C2. In **TSb**, the deviation is even greater: the lone pair lies virtually normal (89°) to the O1-C2-C3 plane. Nevertheless, the role of the lone pair in **TSa** and **TSb** is very important, as judged from the energy results shown in Table 1. However, this contribution—which allows the process to take place with a reduced energy investment—does not exclude a prominent role of π orbitals in the reaction.

In conclusion, we believe that the evidence reported by Cossio and co-workers is not conclusive enough to state that reactions A and B are pseudopericyclic. Rather, the results suggest that both are essentially pericyclic even though they are favored (or assisted) by the electron lone pair on the heteroatom. As shown in a previous paper on the electrocyclization of hexatriene and its derivatives,[11] the lone pair provides a reaction path with a decreased energy investment, but the essential features of the process are typical of a disrotatory electrocyclization.

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Reply

Angel R. de Lera* and Fernando P. Cossio*

Rodriguez-Otero et al. have questioned our results on the pseudopericyclic nature of the cyclization of (2*Z*)-hexa-2,4,5-trienals and their Schiff bases. Since the electrocyclic nature of the all-carbon reaction reported in our paper (**6c** → **7c** transformation) has not been questioned by these authors, we will focus our discussion on the cyclization of compound **6a** of our article[1] to form the cyclic structure **7a**, and we shall demonstrate that the analysis of Rodriguez-Otero is incorrect.

First, we must emphasize that the nature of the imaginary vibration of **TSa** corresponds to the attack of the electron lone pair of the nitrogen atom on the terminal double bond of **6a**. Animation of this imaginary frequency (for instance, by means of the MOLDEN program[2]) clearly shows that the attack of the NH group does not involve any significant rotation around the N=C bond, although in-plane motion of the imine hydrogen atom clearly participates in the imaginary frequency. Moreover, the geometries of the points along the intrinsic reaction coordinate (IRC) pathway at the B3LYP/6-31 + G* level shows only marginal variations of the H-N1=C6-H dihedral angle, denoted as ω in Figure 1, motivated by small conformational variations of the cycle being formed.

Concerning the observation of Rodriguez-Otero and Cabaleiro-Lago on the magnitude of the NBO charge of the exocyclic atom, the value of about −0.2 e included in our article has been obtained by integration of the charges on the hydrogen atoms bonded to the exocyclic carbon atom, a common practice in computational chemistry since the charge on the isolated carbon atom has no chemical meaning. The values of about −0.5 e reported by these authors correspond to the isolated C7 atom and are not relevant from a chemical standpoint.

Rodriguez-Otero and Cabaleiro-Lago also report an analysis of the bond length between the C2−C7 atoms. The authors do not take into account that, according to Scheme 3 of our paper,[1] the electronic reorganization in structure **TS′** does not necessarily imply any significant variation of the length of the C2−C7 bond. Therefore, the long discussion on this topic reported by these authors does not contribute to the elucidation of the nature of the mechanism of the cyclization.

The NBO analysis of **TSa** reported by Rodriguez-Otero and Cabaleiro-Lago is also erroneous. The most convenient tool to elucidate the nature of the reaction mechanism is to examine

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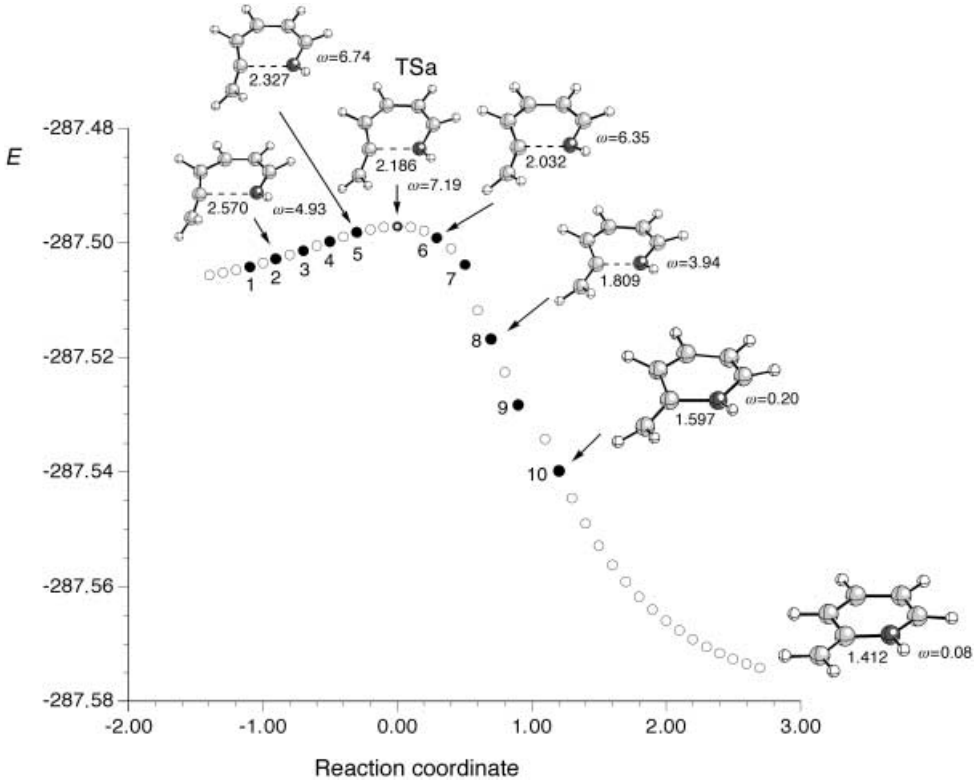

Figure 1. B3LYP/6-31 + G* IRC plot for the **6a** → **7a** transformation (see Scheme 2 in ref. [1]). Energies are given in atomic units; ω is the H-N1=C6-H dihedral angle.

the magnitude of the two-electron interactions in **TSa**. Given the limitations of space we did not include this analysis in our paper, but we can report our results here. As can be seen from Figure 2C, the importance of the donation from the sp^2-hybridized lone pair of electrons on N1 (38.56 and 61.34% of s and p character, respectively) on the π*(C2=C7) localized orbital increases along the reaction coordinate, to reach a value of about -17 kcal mol^{-1} at **TSa**. In addition, there is another two-electron donation from the lone pair of electrons on N1 on the π*(C2=C3) localized orbital, whose associated second-order perturbation energy is approximately -8 kcal mol^{-1}. In sharp contrast, the interactions between the π(C2=C3) and π(N1=C6) localized orbitals, which would be associated with the disrotatory process, are only about -3 kcal mol^{-1} (Figure 2A and B). Certainly, these results do *not* correspond to a mere *assistance* of the lone pair! Instead, our results demonstrate that the formation of the N1–C2 bond stems from the attack of the nitrogen lone pair on the sp-hybridized carbon atom of the cumulene system. This interaction is what we represented in the abstract of our article.[1] If we consider the delocalized Kohn–Sham orbitals, we can also appreciate the N1 ··· C2-C7 interaction in the highest occupied molecular orbital (HOMO)-1 of **TSa**, as evident in Figure 2E.

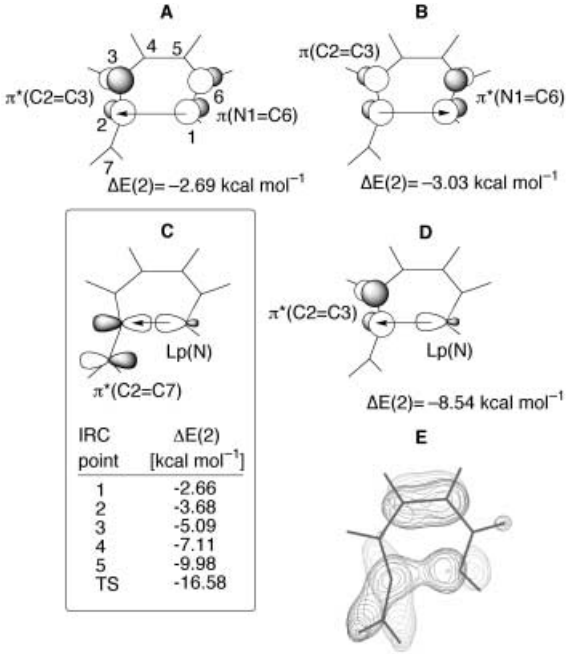

Figure 2. A)–D) Second-order perturbation analysis of the main two-electron interactions found in **TSa** by means of the natural bond orbital (NBO) method. E) HOMO-1 Kohn–Sham orbital of **TSa** showing the interaction between the lone pair of N1 and the C2=C7 moiety.

The considerations about the aromaticity of **TSa**–**c** reported by Rodriguez-Otero and Cabaleiro-Lago are also inadequate, since they refer to different types of aromaticity (transition structures and stable molecules), different ring sizes (four- and six-membered rings), and different methods (χ_{anis}, nucleus-independent chemical shift (NICS), computed at different levels). Instead, in our article we applied the NICS method,[3] which is relatively ring-size insensitive to similar structures such as **TSa**–**c**. We can extend this analysis to structure **TSd**, which is diastereomeric with **TSa**. In our paper, we did not discuss the features of **TSd** since this transition structure corresponds to the cyclization of a *Z* imine, and our experimental data correspond to *E* imines .[1] The main geometric features of **TSd**, a transition structure less planar than **TSa**, are shown in Figure 3. The *Z* geometry of the imine moiety of **TSd** prevents the attack of the nitrogen atom lone pair on the C2=C7 bond. As a consequence, the MOLDEN animation of the imaginary frequency of **TSd** shows clearly a rotation around N1=C2, which corresponds to a disrotatory reaction. The largely negative NICS value of **TSd** obtained at the ring point (R_p) of electron density[4] attests to the aromatic character of this disrotatory transition structure, and emphasizes the different nature of **TSa** (pseudopericyclic) and **TSd** (pericyclic), thus confirming the utility of this magnetic criterium to distinguish between both mechanistic proposals, which is the main finding reported in our paper.

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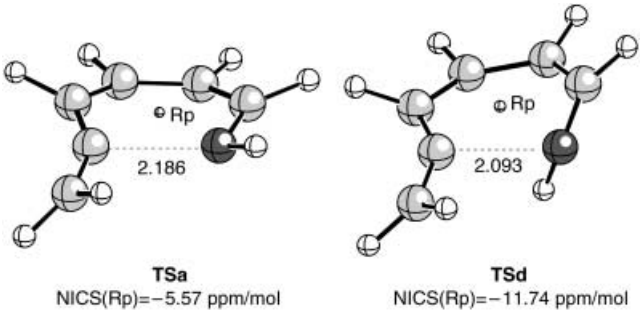

Figure 3. B3LYP/6-31 + G* ball and stick representation of transition structures **TSa** and **TSd**. Bond lengths are given in Å. Rp denotes the ring point of electron density. The nucleus-independent chemical shifts have been calculated at the GIAO-B3LYP/6-31 + G* level.

In summary, we further reinforce our conclusion that geometric, electronic, orbital, and magnetic criteria indicate that thermal cyclization of (2*Z*)-hexa-2,4,5-trienals and related imines takes place by a pseudopericyclic mechanism, whereas the all-carbon equivalent corresponds to a disrotatory (aromatic) electrocyclization.

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