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In-Plane Aromaticity in Double Group Transfer Reactions

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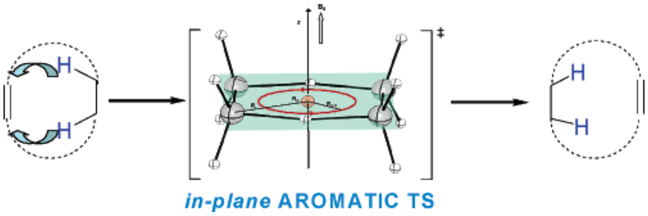

The main features of double group transfer reactions have been studied under the density-functional theory framework. It is found that a wide range of structure-types and processes including type II-dyotropic reactions and the Meerwein−Ponndorf−Verley reduction take place via highly synchronous in-plane aromatic transition structures. Actually, the orbital topology of these saddle points is equivalent to that which corresponds to a D_{2h}-symmetric aromatic molecule such as pyrazine.

In-plane aromaticity is a general feature of transition states associated with pericyclic reactions.[1] This type of aromaticity exhibits a maximum diamagnetic shielding at the molecular plane and decays above and below such a plane. If the concept of aromaticity is not free of ambiguities, the idea of in-plane aromaticity is even more difficult to quantify.[2] However, we proposed[1b,3] that the evaluation of the nuclear-independent chemical shifts (NICS) of the cyclic saddle point at the (3,+1) ring critical point of the electron density and its variation along the axis perpendicular to the molecular plane reflects the in-plane aromatic character of the transition states involved in pericyclic reactions.

On the other hand, double group transfer reactions (DGTR) are a general class of chemical transformations. These reactions occur usually through the simultaneous migration of two atoms/groups from one compound to another in a concerted pathway. The archetypical DGTR process is the thermally allowed concerted transfer of two hydrogen atoms from ethane to ethylene (reaction 1, Table 1). Less frequent is the concomitant transfer of a hydrogen and a metal atom. This definition includes textbook reactions like the diimide reduction of double or triple bonds, some type II-dyotropic reactions, and the Meerwein−Ponndorf−Verley reduction (MPV) of carbonyl groups. The common feature of these transformations is a cyclic six-membered transition state. Therefore, they are good examples to quantify the in-plane aromaticity of the different transition states. Reported here is the study of model DGTR based on this criterion.

The calculated DGTRs (B3LYP/def2-TZVPP level)[4] are gathered in Table 1. First, we consider the parent reaction between ethane and ethene (eq 1), the diimide reduction of ethene and ethyne (eqs 2, 3), and the uncatalyzed MPV reduction of formaldehyde (eq 4).[5] These examples include a wide range of structure-types and processes. In all cases, the reactions involve the concerted transfer of two hydrogen atoms in a process suprafacial on both reaction sites. Therefore, these transformations may be considered as a thermally allowed pericyclic reaction according to the Woodward and Hofmann rules.[6]

The C−C bonds and C−X bonds involved in the transition states have a partial double-bond character (NBO bond order ranging from 1.30 in eq 4 to 1.63 in eq 2), which means that π-orbitals are involved in the migration of the two σ_{XH} bonds. It is also noteworthy that the four reactions studied are found to be close to the perfect synchronicity ($S_y = 0.87-0.93$).[7] Thus, if we assume that the bonding equalization criterion for aromaticity[8] is related to the synchronicity associated with a cyclic transition structure, the four highly symmetric saddle

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(1) (a) Jiao, H.; Schleyer, P. v. R. *J. Phys. Org. Chem.* **1998**, *11*, 655. (b) Cossío, F. P.; Morao, I.; Jiao, H.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1999**, *121*, 6737.

(2) (a) Chandrasekhar, J.; Jemmis, E. D.; Schleyer, P. v. R. *Tetrahedron Lett.* **1979**, 3707. (b) Dewar, M. J. S. *J. Am. Chem. Soc.* **1984**, *106*, 669.

(3) (a) Morao, I.; Lecea, B.; Cossío, F. P. *J. Org. Chem.* **1997**, *62*, 7033. (b) Fernández, I.; Sierra, M. A.; Cossío, F. P. *J. Org. Chem.* **2006**, *71*, 6178.

(4) All calculations were carried out with the Gaussian 03, rev. C02, suite of programs. (a) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A., Jr.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A. *Gaussian 03*, revision C.02; Gaussian, Inc.: Wallingford, CT, 2004. All calculations were carried out at the B3LYP level of theory: (b) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648. (c) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1998**, *37*, 785. We used the triple-ζ basis set denoted by def2-TZVPP, which is supposed to be close to the DFT basis set limit. See: (d) Weigend, F.; Alhrichs, R. *Phys. Chem. Chem. Phys.* **2005**, *7*, 3297.

(5) This latter process was recently proposed to evolve through a cyclic six-membered transition state at elevated temperatures. See: Sominsky, L.; Rozental, E.; Gottlieg, H.; Geganken, A.; Hoz, S. *J. Org. Chem.* **2004**, *69*, 1492.

(6) Woodward, R. B.; Hoffmann, R. *The Conservation of Orbital Symmetry*; Verlag, Chemie, GmbH: Weinheim, 1970; p 141.

(7) For a perfectly synchronous reaction, $S_y = 1$. See refs 1b and 3.

(8) Schleyer, P. v. R.; Jiao, H. *Pure Appl. Chem.* **1996**, *68*, 209 and references therein.

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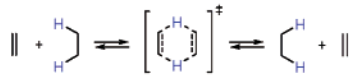
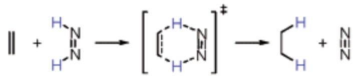
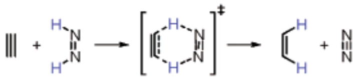
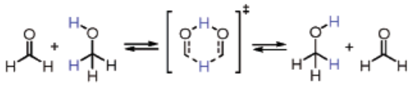
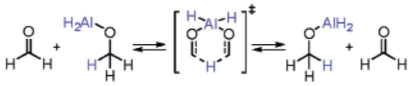
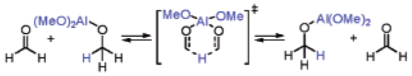
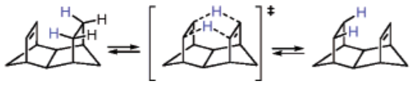
TABLE 1. Free Activation Energies[a] (at 298 K, in kcal mol^{-1}), Synchronicities[a] (S_y), and NICS Values[b] (in ppm) of Double Group Transfer Reactions

Eq.	Reaction	$\Delta G^{\ddagger}_{298}$	S_y	NICS
1		58.2	0.92	-27.4
2		10.4	0.87	-22.1
3		9.8	0.87	-18.7
4		36.3	0.93	-24.8
5		7.6	0.89	-14.9
6		6.5	0.88	-14.8
7		40.1	0.92	-26.4

[a] Computed at the B3LYP/def2-TZVPP level. [b] Computed at the GIAO-B3LYP/def2-TZVPP level.

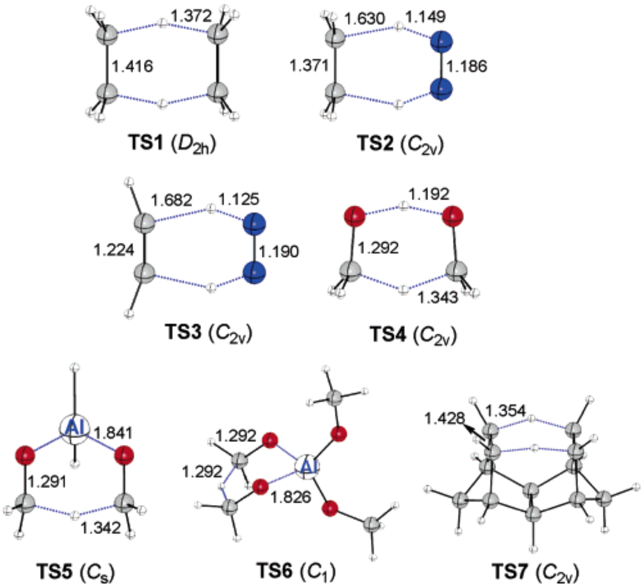


FIGURE 1. Ball and stick representations of the transition states **TS1**−**7** corresponding to the double group transfer reactions. All structures correspond to fully optimized B3LYP/def2-TZVPP geometries. Bond distances are given in angstroms. Unless otherwise stated, white, gray, red, and blue colors denote hydrogen, carbon, oxygen, and nitrogen atoms, respectively.

points (Figure 1) fulfill reasonably well this geometric requisite of aromaticity. Therefore, it is very likely that these [$_{\sigma}2_s+_{\sigma}2_s+_{\pi}2_s$] transformations evolve through highly aromatic transition states.

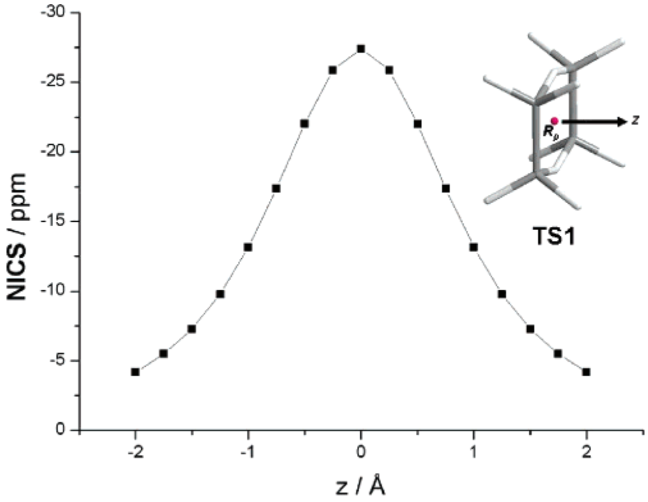


FIGURE 2. Plot of the computed NICS values along the *z*-axis perpendicular to the molecular plane for **TS1**.

To get a better understanding of the hypothetical aromatic character of these processes, we calculated the NICS[9] inside the transient cyclic atomic array at the (3,+1) ring critical point of the electron density, as defined by Bader,[10] due to its high sensitivity to diamagnetic effects and its unambiguous character.

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[9] Chen, Z.; Wannere, C. S.; Corminboeuf, C.; Puchta, R.; Schleyer, P. v. R. *Chem. Rev.* **2005**, *105*, 3842.

[10] Bader, R. F. W. *Atoms in Molecules -A Quantum Theory*; Clarendon Press: Oxford, 1990.

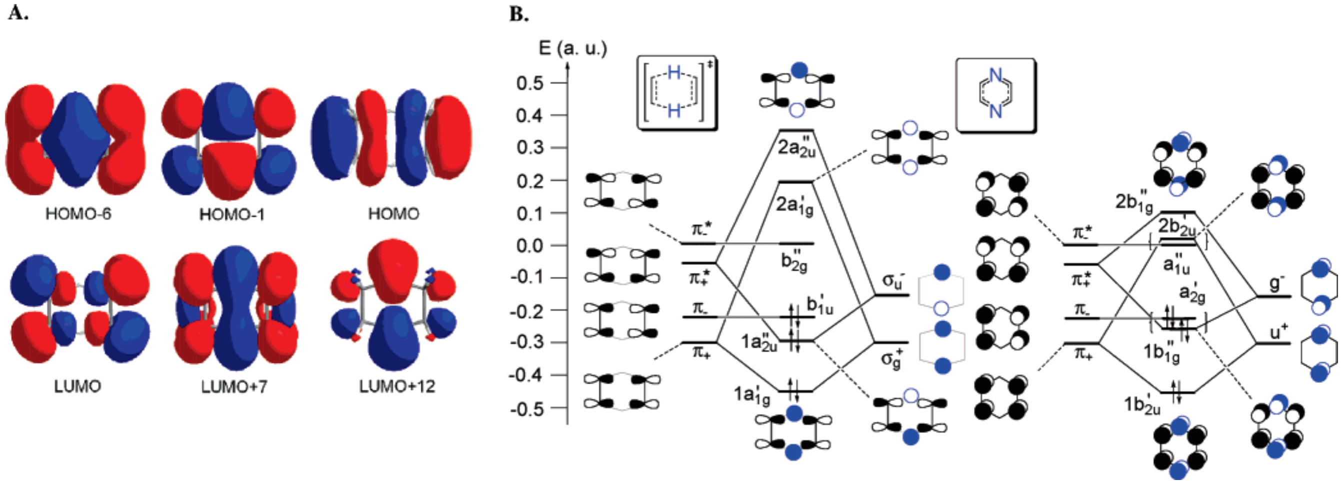

FIGURE 3. (A) Molecular orbitals of **TS1**, associated with in-plane aromaticity. (B) Generation of the in-plane molecular orbitals of **TS1** (left) and pyrazine (right) within the D_{2h} symmetry group. The main symmetry axis is that which contains both migrating hydrogen atoms. The molecular orbitals within brackets are degenerate in D_{6h} benzene.

From the data in Table 1, it becomes obvious that the different transition states exhibit strong in-plane aromaticity. We propose that the six electrons involved in the double hydrogen atom transfers lie approximately in the molecular plane and give rise to an appreciable ring current. In turn, this ring current promotes a strong diamagnetic shielding at the ring critical point, leading to the observed high NICS values. We also computed the variation of NICS values for the transition state (**TS1**) involved in the parent reaction 1 along the *z*-axis perpendicular to the molecular plane. As expected for an in-plane aromatic transition state, we found the maximum NICS value at $z = 0$ (Figure 2).

To understand the origins of the high aromaticity of the above saddle points, we also analyzed in detail the electronic features of **TS1**. The connection between the FMO's and the aromaticity models is evident if one takes into account that the Woodward–Hoffmann rule for pericyclic reactions is similar to the Hückel rule. Interestingly, the FMO's of this D_{2h}-**TS1** do not include any contribution from the migrating hydrogen atoms (vide supra). The MO's can be generated by mixing an ensemble of two D_{2h}-symmetric ethylene subunits and an elongated $D_{\infty h}$-symmetric combination of two hydrogen atoms (Figure 3B, left). The π_+ combination of bonding MO's of ethylene can therefore interact with the $\sigma_g{}^+$ subunit to yield two $a_{1g}{}'$ MO's within the D_{2h} symmetry group, which are the HOMO−6 and LUMO+7 MO's of **TS1**, respectively. Similarly, the interaction between $\pi_+{}^*$ and $\sigma_u{}^-$ results in two $a_{2u}{}''$ MO's, which correspond to the HOMO−1 and LUMO+12 of **TS1**, respectively. In contrast, neither π_- nor $\pi_-{}^*$ can interact with the 1s AO's of the hydrogen atoms and therefore remain unchanged in **TS1**, becoming the $b_{1u}{}'$ and $b_{2g}{}''$ MO's, which correspond to the HOMO and LUMO of **TS1**, respectively (Figure 3B, left). As a consequence of these symmetry restrictions, the contributions of the hydrogen atoms are not present in the FMO's of these transition structures.

It is noteworthy that the previously discussed MO pattern of **TS1** constitutes the in-plane equivalent of π^2-aromatic six-electron molecules.[11] This conclusion can be readily understood if we apply the previously discussed treatment to a D_{2h}-symmetric six-electron aromatic molecule such as pyrazine (Figure 3B, right). In this case, the u_+ and g_- combinations of two p_z AO's of the nitrogen atoms yield $b_{2u}{}'$ and $b_{1g}{}''$ MO's, whereas the π_- and $\pi_-{}^*$ ethylene subunits cannot interact with either u_+ and g_-, thus remaining unchanged and becoming the corresponding $a_{2g}{}'$ and $a_{1u}{}''$ MO's.[12]

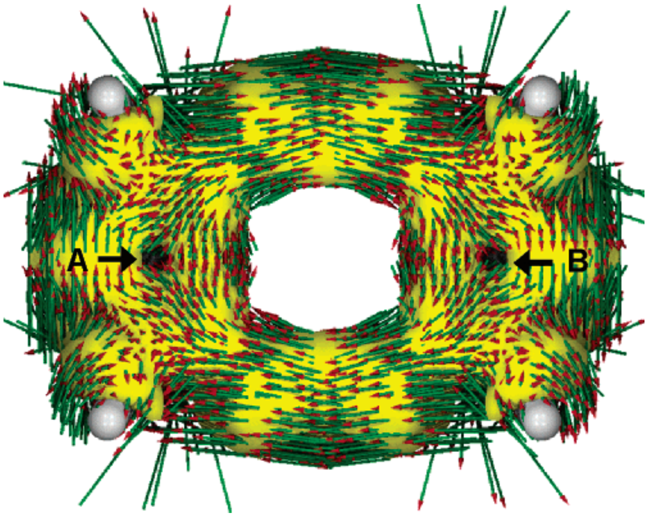

FIGURE 4. ACID isosurface plot of **TS1** (isosurface value of 0.05).

Finally, we also applied the Anisotropy of the Induced Current Density (ACID) method developed by Herges[13] to visualize the delocalization of the electrons in **TS1**, which produces the observed in-plane aromaticity. We found that the in-plane aromaticity is represented by a toroid interrupted at points A and B by the nodal planes of the in-plane p-AOs of the four carbon atoms (Figure 4).

This model is also applicable to the highly synchronous aluminum-catalyzed MPV reductions (Table 1, eqs 5, 6), which

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(11) de Lera, A. R.; Álvarez, R.; Lecea, B.; Torrado, A.; Cossío, F. P. *Angew. Chem., Int. Ed.* **2001**, *40*, 557.

(12) It is interesting to note that in D_{6h} benzene the equivalents of $b_{1g}{}''$ and $a_{2g}{}'$ are degenerate to each other, as well as $b_{2u}{}'$ and $a_{1u}{}''$, whereas in D_{2h}-symmetric pyrazine, they are very close in energy.

(13) (a) Herges, R.; Geuenich, D. *J. Phys. Chem. A* **2001**, *105*, 3214. (b) Geuenich, D.; Hess, K.; Köhler, F.; Herges, R. *Chem. Rev.* **2005**, *105*, 3758.

were proposed to evolve through a six-membered cyclic transition state.[14] However, in these cases, the lack of planarity imposed by the Al-atom leads to lower NICS values. In addition, the change from the D_{2h} symmetry group to a C_s or C_1 symmetry supposes the involvement of Al-orbitals in the FMO's of the respective transition states corresponding to the processes depicted in eqs 5 and 6 in clear contrast to the processes depicted in eqs 1−4. More interestingly, we can also apply this model to the type II-dyotropic process depicted in eq 7 (Table 1).[15] This process is the intramolecular analogue of eq 1, and the FMO's of the corresponding cyclic transition state share with **TS1** the common feature of not including any contribution from the migrating hydrogen atoms.

In summary, we conclude that transition structures associated with two group migrations are in-plane analogues of six-membered hetero-aromatic rings. In addition, this model is applicable to different reactions that share common electronic features along the corresponding reaction paths.

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Supporting Information Available: Cartesian coordinates (in Å) and total energies (in au, noncorrected zero-point vibrational energies included) of all of the saddle points discussed in the text. This material is available free of charge via the Internet at http://pubs.acs.org.

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[14] (a) Shiner, V. J.; Whittaker, D. *J. Am. Chem. Soc.* **1963**, *85*, 2337. (b) Warnhoff, E. W.; Reynolds-Warnhoff, P.; Wong, M. Y. H. *J. Am. Chem. Soc.* **1980**, *102*, 5956.

[15] (a) Reetz, M. T. *Angew. Chem., Int. Ed. Engl.* **1972**, *11*, 129. (b) Reetz, M. T. *Angew. Chem., Int. Ed. Engl.* **1972**, *11*, 130. (c) Reetz, M. T. *Tetrahedron* **1973**, *29*, 2189. (d) Reetz, M. T. *Adv. Organomet. Chem.* **1977**, *16*, 33.