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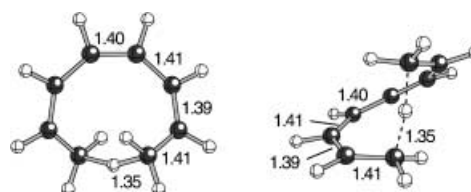**Hydrogen Shifts**

Breaking Down Barriers: The Liaison Between Sigmatropic Shifts, Electrocyclic Reactions, and Three-Center Cations**

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In a recent computational study we found that the antarafacial [1,8] hydrogen shift in the octatrienyl cation has a very low activation barrier (only 6.3 kcal mol^{-1}).[1–2] The transition structure for this rearrangement (Figure 1, two views) is

Figure 1. Two views of the transition structure for the antarafacial [1,8] hydrogen shift in the octatrienyl cation. Selected distances are shown in Å.

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DOI: 10.1002/ange.200352853 © 2003 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

remarkably delocalized; all bonds (carbon–carbon, and even carbon–hydrogen) are about equal in length. Herein we note an intriguing connection between different types of pericyclic transition structures and carbocations that emerged during our scrutiny of this rearrangement.
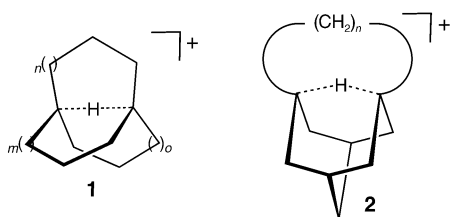
Three-Center Cations

From one perspective, the [1,8] transition structure is simply a cationic extension of a standard sigmatropic reaction (Figure 2, top). But there are other ways to look at this
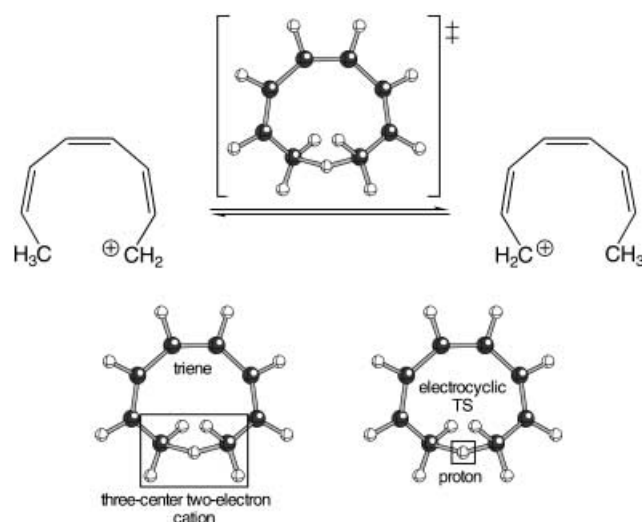
Figure 2. Different ways to view the transition structure for the antara-facial [1,8] hydrogen shift in the octatrienyl cation.

transition structure. For instance, this geometry may be viewed (Figure 2, bottom left) as the transition structure for a hydride transfer from an alkyl group to a carbocation center through a three-center two-electron cationic array, the two reaction partners linked by a triene.[3–4]

Let's examine this perspective a little further. With appropriate geometrical constraints, delocalized [C···H···C]+ arrays can even persist as ground-state molecules, for example, **1** and **2**.[3] Molecules such as **1** and **2** are therefore

sometimes described as "stable transition states"[5] for trans-annular hydride shifts. The [1,8] transition structure in Figure 1, however, is just that—a transition structure (albeit of low energy), rather than a minimum. Nonetheless, one can play games with that transition structure that lead to species which *are* minima and for which the distinction between [1,8]

transition structure and stable [C···H···C]+ cation is effectively lost. Consider, for example, the optimized[6–8] but still theoretical pinwheel cation shown in Figure 3, in which a central [C···H···C]+ array is supported by three hexatriene bridges.

Figure 3. Two views of a pinwheel cation:[8] a "side" view that empha-sizes the C···H···C unit and a "top" view that emphasizes the overall threefold symmetry of the structure. Selected distances are shown in Å.

Protonating Electrocyclic Reactions

There's more. Might one not describe the parent [1,8] transition structure as the product of protonation of another pericyclic transition structure, that for the conrotary electro-cyclic closure of an octatetraene to a cyclooctatriene (Figure 2, bottom right)? The calculated[6–7] transition struc-tures for the charged [1,8] sigmatropic hydrogen shift and the neutral 8π electrocyclic reaction are shown side-by-side in Figure 4. Note how similar these are!
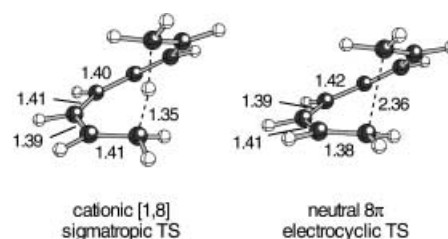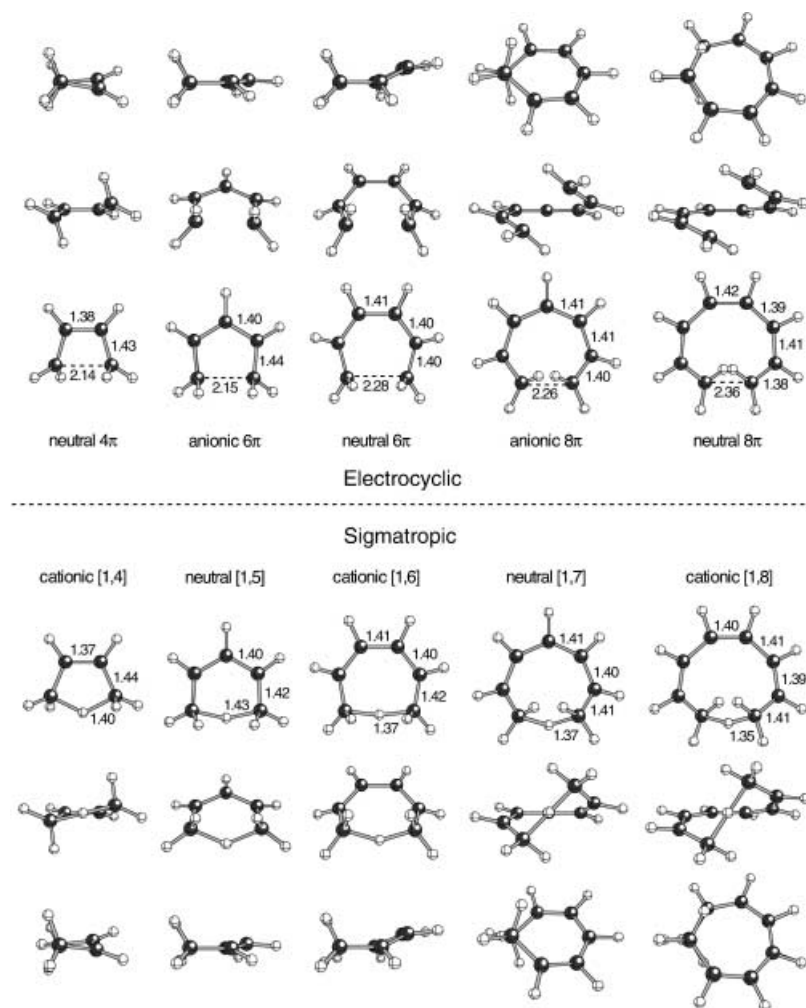

Figure 4. Transition structures for the antarafacial [1,8] hydrogen shift in the octatrienyl cation and the eight-electron electrocyclic ring closure of octatetraene. Selected distances are shown in Å.

This relationship—transition structures for sigmatropic hydrogen shifts resembling protonated electrocyclic transi-tion structures—is quite general.[9] Figure 5 shows the calcu-lated geometries of a series of sigmatropic and electrocyclic transition structures involving different charges, different numbers of electrons, and different topologies (antarafacial/suprafacial; conrotatory/disrotatory).[2, 10] In every case, the geometries of the corresponding electrocyclic and sigma-tropic transition structures are strikingly similar.[11]

This actually makes quite good sense. Imagine the transition structure for an allowed disrotatory (C_s symmetry) or conrotatory (C_2 symmetry) electrocyclic reaction. Such a transition structure, for an allowed reaction, is characterized by a substantial gap between filled and unfilled levels. Now bring in a proton in the mirror plane or along the C_2 axis. The empty proton 1s orbital is symmetric and it will interact

Figure 5. Optimized geometries of electrocyclic and sigmatropic transition structures. Three views of each are shown: a "top" view (closest to dividing line), a "side" view (middle row for each), and a view down the C···(H)···C axis. Selected distances are shown in Å.

(entirely in a one-electron method; mostly, in an all-electron approach) with the filled symmetric levels of the electrocyclic transition structure, stabilizing them (Figure 6 a). Perhaps accommodating that proton also "pushes" the ends of the polyene apart slightly, but the primary effect is simply stabilization of the system, without change of electron count or orbital topology. Of course, the proton will also interact with the reactant and product of the rearrangement, making it difficult to predict how the activation barrier will change (see below).

That the "aromaticity" of the transition structures shown in Figure 5, gauged by the delocalization of the bond lengths (and other criteria[12]), is so well-expressed, was not expected. The particularly impressive congruence between the geometries of the electrocyclic and sigmatropic transition structures is likely due, at least in part, to the metrical similarity of a "natural" $[C\cdots H\cdots C]^+$ separation in a hydride shift to a carbonium ion (around 2.5–2.7 Å for the sigmatropic transition structures in Figure 5)[13] to a typical C···C separation in the transition state for an electrocyclic reaction (around 2.1–2.4 Å).[11]

Transition-State Proton Affinities

If we view the transition structures for sigmatropic hydrogen shifts as protonated electrocyclic transition structures, then we can talk about *transition-state proton affinities*—in other words, the affinities of parti-
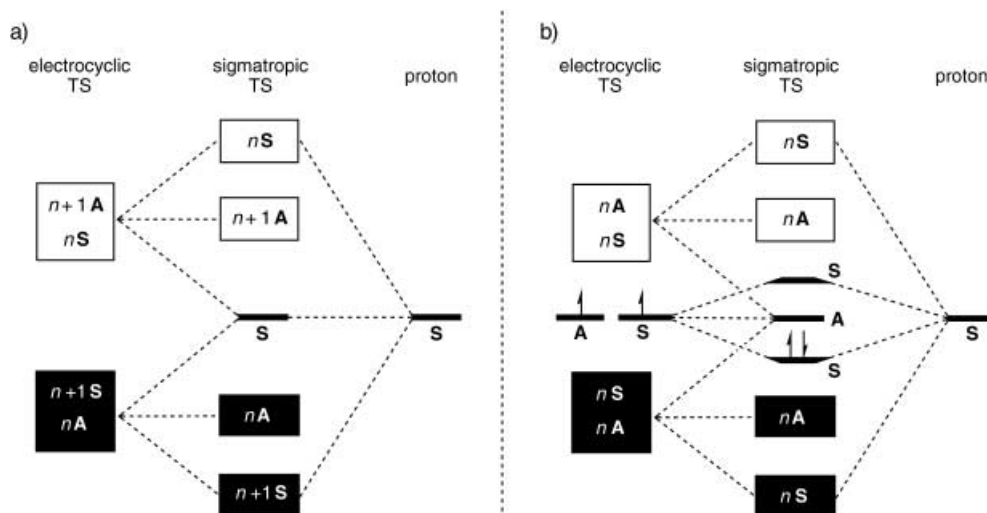
Figure 6. A schematic view of orbital interactions between the symmetric unfilled orbital of a proton with the symmetric filled (black) and unfilled (white) π orbitals of an allowed (a) and forbidden (b) transition structure for a generic electrocyclic reaction involving $4n+2$ orbitals and the same number of electrons. Only the numbers of filled and unfilled orbitals (and the reaction topology) change for $4n$ orbitals, or for different numbers of electrons or orbitals.

ally formed or broken carbon–carbon bonds in pericyclic transition structures for protons.[14]

The calculated proton affinities of the anionic electrocyclic transition structures shown in Figure 5 (i.e. the energy differences between the electrocyclic and corresponding sigmatropic transition structures) are 389 kcal mol^{-1} for the anionic 6π ring closure and 366 kcal mol^{-1} for the anionic 8π ring closure. For comparison, proton affinities for benzylic anions are typically ~380–395 kcal mol^{-1} and for alkyl anions are typically ~410–420 kcal mol^{-1}.[15a,b] The delocalized anionic electrocyclic transition structures thus appear to be of comparable basicity to other resonance-stabilized anions.

The calculated proton affinities for the neutral electrocyclic transition structures shown in Figure 5 are 203 kcal mol^{-1} for the 4π system and 216 kcal mol^{-1} for both the 6π and 8π systems. For comparison, the proton affinities of typical alkanes are generally ~130–145 kcal mol^{-1},[15a] of simple alkenes are ~165 kcal mol^{-1},[15a] and of conjugated alkenes are ~200–230.[15c] Again, the basicity of the delocalized electrocyclic transition structures appears to be comparable to that of stable delocalized π-systems.

Different Surfaces, but Similar Transition Structures

The potential energy surfaces for the electrocyclic reactions in Figure 5 are, of course, asymmetric (Figure 7 a). Whether the ring-closed or ring-opened form is favored in a given case is determined by many factors (strain, delocalization, charge). On protonation, however, symmetrical sigmatropic shift potential energy surfaces result (Figure 7 b). In one case, that of the neutral 6π electrocyclization/cationic suprafacial

[1,6] sigmatropic shift pair, the activation barrier for the sigmatropic reaction is lower than that for either electrocyclic ring opening or ring closure.

The surfaces we describe are curious, hundreds of kcal/mol apart on an absolute energy scale, yet gently shaped into unmistakable congruence at their transition states by the stringent demands of orbitals and electrons.

What Protonation Might Change

In general, it is difficult to locate true transition structures for orbital-symmetry-forbidden processes. Our searches (and those of others) for forbidden transition structures for electrocyclic reactions, for example, have not been fruitful.[16–17] Being unstable and with nothing good going for them, these transition states escape, so to speak. To put it another way, molecules, even quite constrained, find other ways to effect the transformation than by a forbidden process.

However, if protonation stabilizes an allowed transition state without altering its topology, what might it do to a forbidden reaction? A simple orbital argument (analogous to that used for analyzing the effects of protonating the transition structures for allowed reactions) indicates that the "pair of electrons in a degenerate level" problem of a potential forbidden electrocyclic transition structure is partially removed[18] upon protonation (see Figure 6 b). So we set out in search of protonated forbidden electrocyclic transition structures, with interesting results.
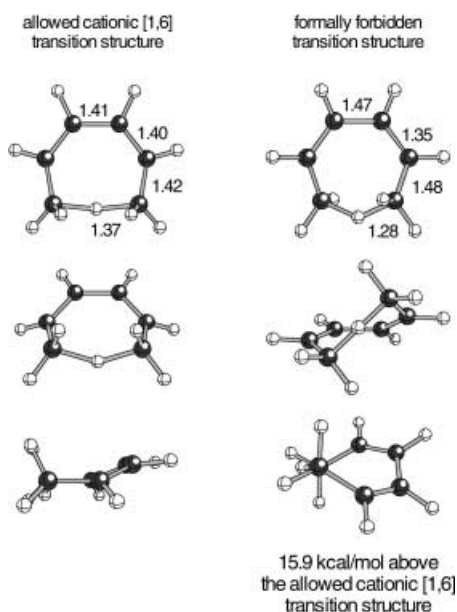
We were able to locate a C_2-symmetric transition structure for formally forbidden antarafacial interconversion of two hexadienyl cations (Figure 8).[19] Much higher in energy (by approximately 16 kcal mol^{-1}) than that for the orbital symmetry-allowed rearrangement,[20] the formally forbidden [1,6] transition structure now has lost the high degree of delocalization that characterizes all the allowed structures shown in Figure 5. Instead, it resembles a three-center [C···H···C]$^+$ cation, whose ends are tethered by a simple diene (notice the localized C=C and C–C bonds in the diene linker and the shortened C···H bonds in the [C···H···C]$^+$ array).

We've also looked at the cationic [1,4] case. Our preliminary results suggest that the potential energy surface in the vicinity of the allowed [1,4] transition structure is quite flat and may be populated by both antarafacial and suprafacial structures. More extensive calculations will be required, however, to pin down the nature of this system.

To summarize, the forbidden transition states are certainly stabilized. But they also escape, by localizing into a [C···H···C]$^+$ cation and a polyene. Thus, we have come full circle, returning again to our first analogy, that between sigmatropic shifts and three-center carbocations.
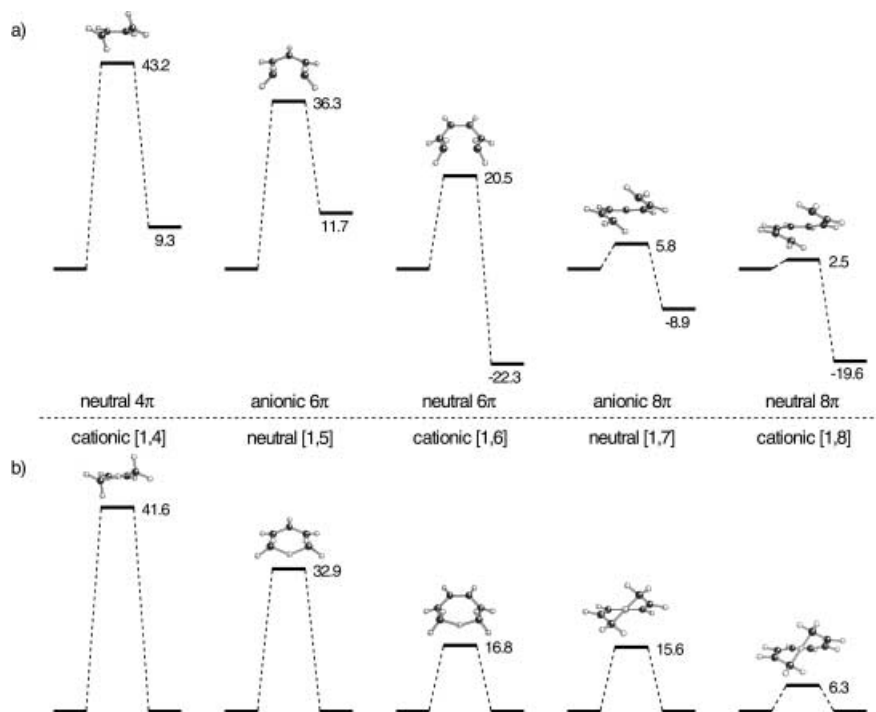
Figure 7. Calculated (B3LYP/6-31G(d)) barriers (in kcal mol^{-1}) for electrocyclic (a) and sigmatropic (b) reactions shown in Figure 5. These are from productive conformers, and for electrocyclic reactions, are shown in the ring-closing direction.

allowed cationic [1,6]
transition structure

formally forbidden
transition structure

1.41
1.40
1.42
1.37

1.47
1.35
1.48
1.28

15.9 kcal/mol above
the allowed cationic [1,6]
transition structure

Figure 8. Optimized geometries of allowed and formally forbidden transition structures for cationic [1,6] hydrogen shifts. Three views of each are shown: a "top" view, a "side" view, and a view down the C···(H)···C axis. Selected distances are shown in Å.

Forward to the Past

The remarkable similarities between electrocyclic and sigmatropic transition states reinforce what was just a plausible argument in early orbital-symmetry days[21]—that there is an underlying electronic unity to all pericyclic reactions. As we can see, now three-center cations are drawn into the game.

[1] From the *all-cisoid* reactant conformer; see: a) D. J. Tantillo, R. Hoffmann, *Helv. Chim. Acta*, in press; b) D. J. Tantillo, C. Ranjan, R. Hoffmann, unpublished results.

[2] For leading references on calculations and experiments on other related sigmatropic shifts, see: a) C. W. Spangler, *Chem. Rev.* **1976**, *76*, 187–217; b) D. J. Tantillo, R. Hoffmann, *J. Am. Chem. Soc.* **2002**, *124*, 6836–6837; c) I. V. Alabugin, M. Manoharan, B. Breiner, F. D. Lewis, *J. Am. Chem. Soc.* **2003**, *125*, 9329–9342; d) O. Dmitrenko, R. D. Bach, R. R. Sicinski, W. Reischl, *Theor. Chem. Acc.* **2003**, *109*, 170–175; e) B. A. Hess, Jr., *J. Org. Chem.* **2001**, *66*, 5897–5900; f) N. J. Saettel, O. Wiest, *J. Org. Chem.* **2000**, *65*, 2331–2336; g) reference [1a].

[3] Cationic three-center two-electron arrays have been studied extensively; for leading references, see: a) J. E. McMurry, T. Lectka, *Acc. Chem. Res.* **1992**, *25*, 47–53; b) M. Saunders, H. A. Jimenez-Vazquez, *Chem. Rev.* **1991**, *91*, 375–397; c) C. A. Grob, *Acc. Chem. Res.* **1983**, *16*, 426–431; d) H. C. Brown, *Acc. Chem. Res.* **1983**, *16*, 432–440.

[4] a) Other researchers have made similar analogies for neutral sigmatropic shifts. See, for example, K. N. Houk, Y. Li, J. D. Evanseck, *Angew. Chem.* **1992**, *104*, 711–739; *Angew. Chem. Int.*

Ed. Engl. **1992**, *31*, 682–708; and F. Jensen, *J. Am. Chem. Soc.* **1995**, *117*, 7487–7492; b) it has been proposed that the nature (protonic or hydridic) of the migrating hydrogen in sigmatropic shifts can vary considerably, depending on the nature of the hydrocarbon framework over which it migrates; see: S. D. Kahn, W. J. Hehre, N. G. Rondan, K. N. Houk, *J. Am. Chem. Soc.* **1985**, *107*, 8291–8292; see also: I. V. Alabugin, M. Manoharan, B. Breiner, F. D. Lewis, *J. Am. Chem. Soc.* **2003**, *125*, 9329–9342.

[5] For leading references, see: a) R. V. Williams, *Chem. Rev.* **2001**, *101*, 1185–1204; b) H. Quast, M. Seefelder, C. Becker, M. Heubes, E.-M. Peters, K. Peters, *Eur. J. Org. Chem.* **1999**, 2763–2779; c) R. V. Williams, *Eur. J. Org. Chem.* **2001**, 227–235.

[6] All calculations were performed with GAUSSIAN98 (Gaussian 98 (Revision A.9), M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, V. G. Zakrzewski, J. A. Montgomery, R. E. Stratmann, J. C. Burant, S. Dapprich, J. M. Millam, A. D. Daniels, K. N. Kudin, M. C. Strain, O. Farkas, J. Tomasi, V. Barone, M. Cossi, R. Cammi, B. Mennucci, C. Pomelli, C. Adamo, S. Clifford, J. Ochterski, G. A. Petersson, P. Y. Ayala, Q. Cui, K. Morokuma, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. Cioslowski, J. V. Ortiz, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. Gomperts, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, C. Gonzalez, M. Challacombe, P. M. W. Gill, B. G. Johnson, W. Chen, M. W. Wong, J. L. Andres, M. Head-Gordon, E. S. Replogle, J. A. Pople, Gaussian, Inc., Pittsburgh, PA, **1998**.

[7] Geometries were optimized (without symmetry constraints) at the B3LYP/6-31G(d) level (A. D. Becke, *J. Chem. Phys.* **1993**, *98*, 5648–5652; A. D. Becke, *J. Chem. Phys.* **1993**, *98*, 1372–1377; C. Lee, W. Yang, R. G. Parr, *Phys. Rev. B* **1988**, *37*, 785–789; P. J. Stephens, F. J. Devlin, C. F. Chabalowski, M. J. Frisch, *J. Phys. Chem.* **1994**, *98*, 11623–11627), whose effectiveness in describing structures and energetics for pericyclic reactions is well-documented (see, for example: O. Wiest, D. C. Montiel, K. N. Houk, *J. Phys. Chem. A* **1997**, *101*, 8378–8388; K. N. Houk, B. R. Beno, M. Nendel, K. Black, H. Y. Yoo, S. Wilsey, J. K. Lee, *J. Mol. Struct.* **1997**, *398–399*, 169–179; D. A. Hrovat, B. R. Beno, H. Lange, H.-Y. Yoo, K. N. Houk, W. T. Borden, *J. Am. Chem. Soc.* **2000**, *122*, 7456–7460); all structures were characterized by frequency calculations at the B3LYP/6-31G(d) level, and zero-point energy corrections (scaled by 0.9806 as recommended in A. P. Scott, L. Radom, *J. Phys. Chem.* **1996**, *100*, 16502–16513) from these calculations are included in the reported energies. Ball-and-stick drawings were produced with *Ball & Stick* (N. Müller, A. Falk, Ball & Stick V.3.7.6, molecular graphics application for MacOS computers, Johannes Kepler University Linz, **2000**).

[8] This optimized structure has one imaginary frequency, corresponding to displacement of the bridging H atom along the C···H···C axis; however, the barrier associated with the H shift is less than 1 kcalmol^{-1} in terms of electronic energies, and disappears when zero-point energy corrections are included.

[9] For a discussion of a different sort of connection between the properties of sigmatropic and electrocyclic transition structures (specifically in transition structures for certain rearrangments of α-lactams), see: D. J. Tantillo, K. N. Houk, R. V. Hoffman, J. Tao, *J. Org. Chem.* **1999**, *64*, 3830–3837.

[10] Only anionic and neutral electrocyclic transition structures and neutral and cationic sigmatropic transition structures are shown, since protonation of cationic electrocyclic transition structures would lead to dicationic sigmatropic transition structures and deprotonation of anionic sigmatropic transition structures would lead to dianionic electrocyclic transition structures.

[11] The similarities in forming and breaking bond lengths for different types of pericyclic transition structures have been discussed previously.[4a]

[12] Calculated nucleus-independent chemical-shift (NICS) values (GIAO-B3LYP/6-31G(d); for details on the NICS method, see: P. von R. Schleyer, C. Maerker, A. Dransfeld, H. J. Jiao, N. J. R. von E. Hommes, *J. Am. Chem. Soc.* **1996**, *118*, 6317–6318; P. von R. Schleyer, M. Manoharan, Z.-X. Wang, B. Kiran, H. Jiao, R. Puchta, N. J. R. von E. Hommes, *Org. Lett.* **2001**, *3*, 2465–2468) for all of these transition structures are negative (ranging from −13.6 to −7.2). For small systems, there is no clear connection between the NICS calculated for the electrocyclic and sigmatropic transition structures, but for larger systems, nearly identical NICS values were calculated for the electrocyclic and corresponding sigmatropic transition structures (−11.0 for the anionic 8π electrocyclic transition structure and −11.1 for the neutral [1,7] transition structure, and −9.6 for the neutral 8π electrocyclic transition structure and −9.9 for the cationic [1,8] transition structure). This reflects comparable degrees of delocalization in these structures, consistent with the similarities of their geometries. Deviations in the smaller systems may be due to differences in ring size for the electrocyclic and sigmatropic transition structures affecting the proximity of the points at which NICS values were calculated to the carbon–carbon bonds; such problems should be minimized in the larger systems.

[13] For the simple [H₃C···H···CH₃]⁺ model system, a bent structure with a C···C distance of 2.1 Å is preferred.

[14] "Transition-state acidity" has been discussed previously; for leading references, see: J. L. Kurz, *Acc. Chem. Res.* **1972**, *5*, 1–9 and A. B. Watts, H. Patel, *J. Theor. Biol.* **2001**, *209*, 417–429. This concept does deal with the differences in rate for reactions involving protonated and unprotonated transition states, but is often (although not always) cast in terms of the protonation state of a catalytic molecule, rather than that of a transition structure itself. To our knowledge, this concept has not previously been applied to the analysis of pericyclic reactions.

[15] a) F. A. Carroll, *Perspectives on Structure and Mechanism in Organic Chemistry*, Brooks/Cole, Pacific Grove, **1998**, and references therein; b) http://webbook.nist.gov/chemistry/; c) based on B3LYP6-31G(d) calculations on the reactants for the reactions corresponding to the transition structures in Figure 5.

[16] It was previously reported that the disrotatory "transition state" for the cyclobutene–butadiene interconversion is actually a second-order saddle point; see: J. Breulet, H. F. Schaefer III, *J. Am. Chem. Soc.* **1984**, *106*, 1221–1226.

[17] It was shown previously that formally forbidden electrocyclic transition structures can be stabilized significantly through complexation to certain transition metals; see: D. J. Tantillo, R. Hoffmann, *Helv. Chim. Acta* **2001**, *84*, 1396–1404; D. J. Tantillo, R. Hoffmann, *J. Am. Chem. Soc.* **2001**, *123*, 9855–9859, and references therein.

[18] We say "partially" because the Jahn–Teller-like situation in the forbidden transition structure is replaced upon protonation by a second-order Jahn–Teller system.

[19] High-energy, but real, transition structures for formally forbidden suprafacial [1,7] shifts over cycloheptatriene were previously described; see: T. Okajima, K. Imafuku, *J. Org. Chem.* **2002**, *67*, 625–632.

[20] The effects of substituents on the stereochemical preferences of sigmatropic shifts have been discussed previously; see: M. T. Zoeckler, B. K. Carpenter, *J. Am. Chem. Soc.* **1981**, *103*, 7661–7663 and N. D. Epiotis, *J. Am. Chem. Soc.* **1973**, *95*, 1206–1214.

[21] R. B. Woodward, R. Hoffmann, *The Conservation of Orbital Symmetry*, Verlag Chemie, Weinheim, Germany, **1970**.