ORGANIC LETTERS

2013
Vol. 15, No. 7
1725–1727

Nonamethylcyclopentyl Cation Rearrangement Mysteries Solved

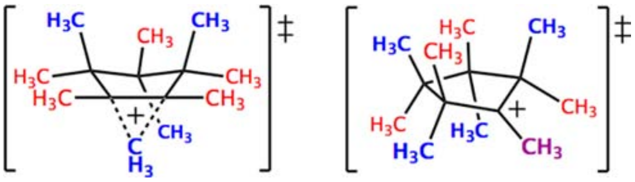
Dean J. Tantillo*,† **and Paul von Ragué Schleyer***,‡

Department of Chemistry, University of California—Davis, 1 Shields Avenue, Davis, California 95616, United States, and Department of Chemistry, University of Georgia, Athens, Georgia 30602, United States

djtantillo@ucdavis.edu; schleyer@uga.edu

Received February 24, 2013

ABSTRACT



The C_1 nonamethylcyclopentyl cation minimum undergoes complete methyl scrambling in SbF_5 with a 7 kcal/mol barrier. This corresponds to the rate-limiting conformational interconversion of enantiomeric hyperconjomers via a C_s transition structure (above right). A remarkable, more rapid, second process only exchanges methyls within sets of four and five (blue and red, see above), as has been observed experimentally at low temperatures. The computed ~2 kcal/mol barrier involves a C_s [1s,2s] sigmatropic methyl shift transition structure (above left).

Carbocations are proficient at undergoing cascades of sequential rearrangements. Degenerate isomerizations are among the most intriguing of these transformations, especially when they lead back to the original structure after a large number of intervening steps.[1] Indeed, complete proton and methyl substituent scrambling is known to occur for carbocations in five-membered rings.[1c−e]

The puzzling rearrangement mechanisms of the nonamethylcyclopentyl cation (Figure 1) are elucidated here. Mayr, Saunders, and co-workers showed decades ago that two different methyl group scrambling processes were involved.[1c−e] Full equilibration of all nine CH_3's had a 7 kcal/mol barrier, but a remarkable, more rapid process (barrier $\leq$2.5 kcal/mol) only allowed *partial* methyl group interchange. Separate ^1H and ^{13}C NMR signals of sets of five and four methyl groups were observed. The detailed nature of both of these processes has remained a mystery, although the possibility of sequential concerted up−down back-side *trans* displacements of one methyl by another has been suggested.[2]

The behavior of the parent cyclopentyl cation is different. Although it undergoes complete proton scrambling, partial interchange was not detected. Olah et al. only observed single ^1H and ^{13}C NMR peaks, but neither broadened at the lowest feasible temperatures in solution.[3a] Moreover, Myhre, Yannoni, et al.'s 70 K solid-state MAS NMR spectra[3b] and ab initio computations[3c] agreed that the classical (but hyperconjugatively stabilized) C_2 symmetry structure of the cyclopentyl cation was preferred over a hydrogen-bridged alternative. The flatness of the computed potential energy surface (PES)[3c] appears to preclude experimental elucidation of its scrambling mechanism.

However, Sorensen and Whitworth[1e] provided evidence for the preferred *trans* stereochemistry of sequential 1,2-hydride transfers by showing that these took place ~40 times more rapidly in the all-*trans* than the all-*cis* 1,2,3,4,5-pentamethyl cyclopentyl cation. This finding suggested that the mechanism of partial methyl exchange reported for the nonamethylcyclopentyl cation (**1**) by Mayr et al. might well be similar.[1c,d]

[†] University of California—Davis.

[‡] University of Georgia.

(1) (a) Saunders, M.; Schleyer, P. v. R.; Olah, G. A. *J. Am. Chem. Soc.* **1964**, *86*, 5679–5680. (b) Leone, R. E.; Barborak, J. C.; Schleyer, P. v. R. Degenerate Carbonium Ions. In *Carbonium Ions*; Olah, G. A., Schleyer, P. v. R., Eds.; Wiley-Interscience: New York, 1972; Vol. IV, Chapter 33, pp 1837−1939. (c) Mayr, H.; Koschinsky, R. *J. Am. Chem. Soc.* **1989**, *111*, 2305–2306. (d) Kronja, O.; Köhli, T.-P.; Mayr, H.; Saunders, M. *J. Am. Chem. Soc.* **2000**, *122*, 8067–8070. (e) Cf.: Sorensen, T. S.; Whitworth, S. M. *J. Am. Chem. Soc.* **1990**, *112*, 6647–6651.

(2) As noted in the Acknowledgements of ref 1c, one of the present authors first proposed this possibility. It also was suggested by Sorensen and Whitworth (ref 1e), who emphasized the relative rapidity of sequential 1,2-shifts of *trans* (over *cis)* oriented groups in substituted cyclopentyl cation systems.

10.1021/ol4005189

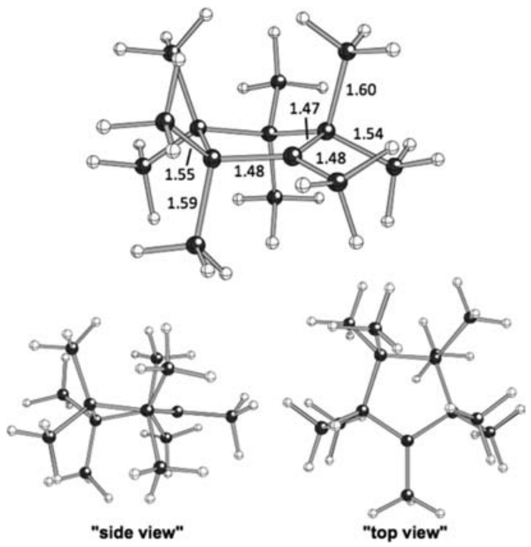


Figure 1. C_1 nonamethylcyclopentyl cation (**1**) minimum at B3LYP/6-31+G(d,p) (distances in angstroms).

We now describe our computed PES for **1**, which identifies rearrangement transition structures with barriers consistent with those determined experimentally for the different degrees of scrambling.

An asymmetric (C_1 point group) minimum for the nonamethylcyclopentyl cation was computed at the B3LYP/6-31G(d) density functional theory (DFT) level in 2000.[1d] We have located analogous C_1 minima for **1** at the B3LYP/6-31+G(d,p) (Figure 1), B3LYP/6-311+G**, M06-2X/6-31+G(d,p), mPW1PW91/6-31+G(d,p), and MP2/6-31+G(d,p) levels.[4] Unlike the parent cyclopentyl cation,[3] the PES of the nonamethyl derivative (**1**) cannot have C_{2v} or even C_2 symmetry since the formal cationic carbon bears a methyl group (a 3-fold rather than a 2-fold rotor; the tilting of the 5-carbon ring is apparent in the "side view" shown in Figure 1). Nevertheless, all the DFT minima have two quasi-axial methyl groups hyperconjugated to the carbocation center. Their C–C distances, 1.59 and 1.60 Å (Figure 1), are both ~0.05 Å longer than those of their more weakly hyperconjugated quasi-equatorial geminal methyl group counterparts (1.55 and 1.54 Å, Figure 1).[5] The computed ca. 100° DFT $H_3C{-}C{-}C^+$ angles for both of the more strongly hyperconjugated methyl groups (also reported in ref 1d) indicate substantial hyperconjugation[6] rather than bridging. While MP2/6-31+G(d,p) predicts one of these angles to be 84°, MP2 levels are known to overestimate such 3-center 2-electron delocalization.[7] Hence, the structure of the C_1 nonamethylcyclopentyl cation minimum (**1**) is best described as a classical, hyperconjugatively deformed tertiary carbocation.

As expected, a bridged [1s,2s] sigmatropic methyl shift *transition structure*[8] was found at all levels of theory employed. The nonclassical, delocalized, cyclic 3-center 2-electron carbocation character of its C_s B3LYP/6-31+G(d,p) geometry (Figure 2) is apparent.[5,9,10] As represented in the left side of Figure 3, the corresponding methyl shift process results in eventual equilibration of the set of four "blue" quasi-axial methyl groups as well as the set of five "red" quasi-equatorial methyl groups (which includes the methyl group attached to the carbocation center). While the five ring carbons also become equivalent, this process does not allow for crossover between the "red" and "blue" methyl sets. Hence, this transition structure is consistent with the experimentally determined ≤2.5 kcal/mol barrier.[1] The barrier for this process computed at various levels (Table 1) show the expected MP2 underestimation and B3LYP overestimation.[7] The other DFT levels in Table 1 predict barriers in line with experiment. We note that Saunders and Kates found similar experimental barriers for 1,2-methyl shifts in acyclic polymethylated carbocations.[11]

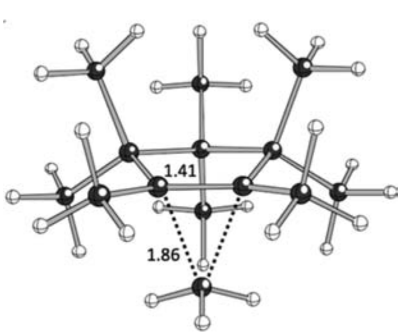


Figure 2. B3LYP/6-31+G(d,p)-optimized structure (C_s symmetry, distances in angstroms) for the [1s,2s] sigmatropic methyl shift transition structure (see Figure 3, left side, middle).

A transition structure for "twisting" interconverts two mirror image C_1 minima (see Figure 3, right side) by interchanging the sets of quasi-axial and quasi-equatorial

---

(3) (a) Olah, G. A.. *Acc. Chem. Res.* **1976**, *9*, 41–52. (b) Myhre, P. C.; Kruger, J. D.; Hammond, B. L.; Lok, S. M.; Yannoni, C. S.; Mcho, V.; Limbach, H. M.; Vieth, H. M. *J. Am. Chem. Soc.* **1984**, *106*, 6079–6080. (c) Schleyer, P. v. R.; Carneiro, J. W. d. M.; Koch, W.; Raghavachari, K. *J. Am. Chem. Soc.* **1989**, *111*, 5475–5477.

(4) (a) All calculations were carried out with Gaussian09 (Frisch, M. J. et al., Gaussian, Inc., Wallingford CT, 2004; full reference in the Supporting Information). (b) B3LYP: Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 1372–1377. Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648–5652. Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785–789. Stephens, P. J.; Devlin, F. J.; Chabalowski, C. F.; Frisch, M. J. *J. Phys. Chem.* **1994**, *98*, 11623–11627. Tirado-Rives, J.; Jorgensen, W. L. *J. Chem. Theory Comput.* **2008**, *4*, 297–306. (c) B2PLYP: Grimme, S. *J. Chem. Phys.* **2006**, *124*, 034108. (d) M06-2X: Zhao, Y.; Truhlar, D. G. *Theor. Chem. Acc.* **2008**, *120*, 215–241. (e) mPW1PW91: Adamo, C.; Barone, V. *J. Chem. Phys.* **1998**, *108*, 664–675. Matsuda, S. P. T.; Wilson, W. K.; Xiong, Q. *Org. Biomol. Chem.* **2006**, *4*, 530–543. (f) MP2: Møller, C.; Plesset, M. S. *Phys. Rev.* **1934**, *46*, 618–622. (g) Structural drawings were created with Ball&Stick: Müller, N.; Falk, A.; Gsaller, G. *Ball & Stick V.4.0a12*, molecular graphics application for MacOS computers, Johannes Kepler University, Linz, 2004.

(5) All DFT levels employed here gave similar geometries.

(6) Alabugin, I. V.; Gilmore, K. M.; Peterson, P. W. Hyperconjugation. *Wiley Interdiscip. Rev.: Comput. Mol. Sci.* **2011**, *1*, 109.

(7) Leading references: Tantillo, D. J. *Nat. Prod. Rep.* **2011**, *28*, 1035–1053.

(8) Seminal papers: (a) Wagner, G. *J. Russ. Phys. Chem. Soc.* **1899**, *31*, 690. (b) Meerwein, H. *Just. Lieb. Ann. Chem.* **1914**, *405*, 129–175. (c) Whitmore, F. C. *J. Am. Chem. Soc.* **1932**, *54*, 3274–3283. (d) A recent review: Gutierrez, O.; Tantillo, D. J. *J. Org. Chem.* **2012**, *77*, 8845–8850.

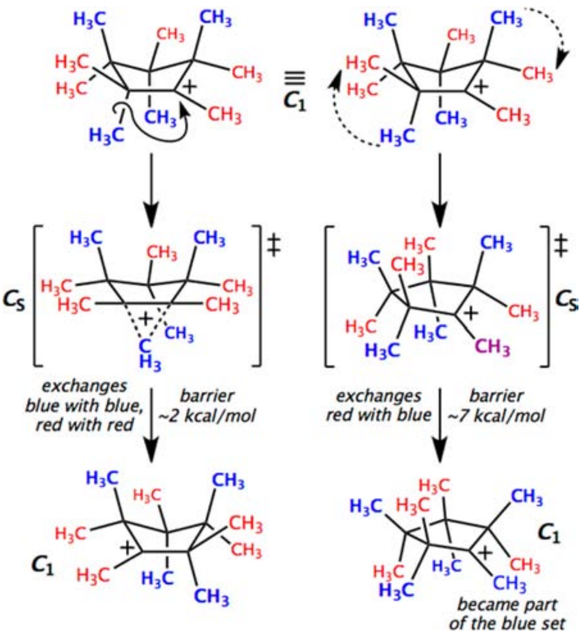


Figure 3. Computed nonamethylcyclopentyl cation rearrangement mechanisms. The methyl shift process on the left side repeats sequentially around the ring but only results in partial methyl scrambling. The "twisting" enantiomerization process on the right side (top) also is needed to enable complete "red−blue" methyl exchange.

Table 1. Computed Barriers (E + ZPE; kcal/mol)

method	1,2-shift	twisting
B3LYP/6-31+G(d,p)	4.3	6.0
B3LYP/6-311+G**	4.2	6.6
B2PLYP/6-311+G**[a]	2.9	6.8
M06-2X/6-31+G(d,p)	1.5	7.3
mPW1PW91/6-31+G(d,p)	2.5	6.7
MP2/6-31+G(d,p)	0.3	9.0

[a] Single point on B3LYP/6-31+G(d,p) geometry; no ZPE correction.

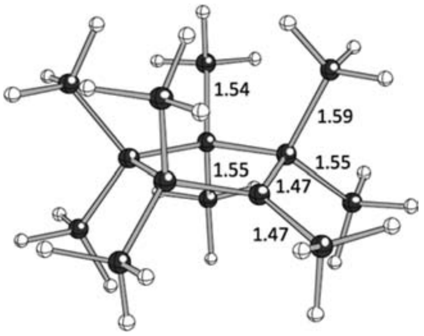


Figure 4. B3LYP/6-31+G(d,p) optimized structure (C_s symmetry, distances in angstroms) for the "twisting" transition structure (see Figure 3, right side, middle). The eclipsing of the distal pairs of geminal methyl groups is responsible for the higher (7 kcal/mol) barrier of this TS. Also note the "envelope" conformation of the five-membered ring and the orientation of the CH_3C^+ methyl group. Other C_s-symmetry rotational orientations of this methyl group and other five-membered ring conformtions are possible, but these result in higher order saddle points with higher energies.

"blue" and "red" geminal methyl groups. The B3LYP/6-31+G(d,p) transition structure (shown in Figure 4) has C_s symmetry and resembles a classical tertiary carbocation. The C_1 enantiomers (**1**) also can be considered to be hyperconjomers,[12] since different $C-CH_3$ bonds in each of the two sets of *gem*-dimethyl groups adjacent to the carbocation center participate in hyperconjugation. Twisting also interchanges the individual methyl groups of the distal geminal pairs, but their enforced eclipsing in the transition structure raises the barrier to the experimentally determined 7.0 kcal/mol value.[1c,d] All of the DFT-computed barriers (6.0−7.3 kcal/mol, Table 1) agree well with this value. The small MP2 overestimation may be attributed to the reduced delocalization in the twisting transition structure.[7]

When both the enantiomerization (twisting) and 1,2-methyl shift processes are operative, all the methyl groups in the nonamethylcyclopentyl cation scramble completely (Figure 3). The three principal stationary points involved in these rearrangements illustrate the classical-to-bridging continuum of carbocation structure types.[7,13] The C_s twisting transition structure is largely classical, the 1,2-shift transition structure is obviously bridged, and the C_1-symmetry minimum involves considerable hyperconjugation: the three sorts of species at the center of many debates on carbocation structure.[9]

Acknowledgment. We thank the National Science Foundation for support (CHE-0957416 and CHE-030089 to D.J.T.; CHE 1057466 to P.v.R.S.) and Martin Saunders (Yale) for discussions. Dedicated to the memory of Saul Winstein (UCLA) on the occasion of his 100th birthday.

Supporting Information Available. Coordinates and energies for computed structures and full Gaussian citation. This material is available free of charge via the Internet at http://pubs.acs.org.

The authors declare no competing financial interest.

(9) Leading references on nonclassical carbocations: (a) Grob, C. A. *Acc. Chem. Res.* **1983**, *16*, 426–431. (b) Brown, H. C. *Acc. Chem. Res.* **1983**, *16*, 432–440. (c) Olah, G. A.; Prakash, G. K. S.; Saunders, M. *Acc. Chem. Res.* **1983**, *16*, 440–448. (d) Walling, C. *Acc. Chem. Res.* **1983**, *16*, 448–454. (e) Brown, H. C. (with comments by P. v. R. Schleyer) *The Nonclassical Ion Problem*; Plenum: New York, 1977.

(10) A chairlike C_s stationary point also was found, but it is ~5 kcal/mol higher in energy than the boat-like TS shown in Figures 2 and 3.

(11) Saunders, M.; Kates, M. R. *J. Am. Chem. Soc.* **1978**, *100*, 7082.

(12) Rauk, A.; Sorensen, T. S.; Schleyer, P. v. R. *J. Chem. Soc., Perkin Trans. 2* **2001**, *6*, 869–874.

(13) (a) Tantillo, D. J. *Chem. Soc. Rev.* **2010**, *39*, 2847–2854. (b) Schleyer, P. v. R.; Lenoir, D.; Mison, P.; Liang, G.; Prakash, G. K.; Olah, G. A. *J. Am. Chem. Soc.* **1980**, *102*, 683–691.