Volume 1 | Number 1 | Jan 2013 | Pages 1–100

ChemComm

Chemical Communications
www.rsc.org/chemcomm

ROYAL SOCIETY OF CHEMISTRY

This is an *Accepted Manuscript*, which has been through the Royal Society of Chemistry peer review process and has been accepted for publication.

Accepted Manuscripts are published online shortly after acceptance, before technical editing, formatting and proof reading. Using this free service, authors can make their results available to the community, in citable form, before we publish the edited article. We will replace this *Accepted Manuscript* with the edited and formatted *Advance Article* as soon as it is available.

You can find more information about *Accepted Manuscripts* in the **Information for Authors**.

Please note that technical editing may introduce minor changes to the text and/or graphics, which may alter content. The journal's standard **Terms & Conditions** and the **Ethical guidelines** still apply. In no event shall the Royal Society of Chemistry be held responsible for any errors or omissions in this *Accepted Manuscript* or any consequences arising from the use of any information it contains.

www.rsc.org/chemcomm

Journal Name

COMMUNICATION

The 9-Homocubyl Cation Rearrangement Revisited

Said Jalife,[a] Judy I-Chia Wu,[b] Gerardo Martínez-Guajardo,[a,c] Paul von Ragué Schleyer,[b*] María A. Fernandez-Herrera,[a*] and Gabriel Merino.[a*]

Abstract. Complexity of the potential energy surface of 9-homocubyl cation is revealed by Born-Oppenheimer Molecular Dynamics simulations and high *ab initio* levels. The stereospecific automerizations observed experimentally involve bridged ions, which have either aromatic or anti-aromatic character. New pathways leading to more stable isomers are unveiled.

Carbonium ions are prone to intriguing rearrangements; scrambling can even lead to complete degeneracy.[1-4] The stable 2-norbornyl cation is the best-known example. Its single ^{1}H NMR documents the equivalence of all 11 hydrogen atoms in super acid media.[5-7] Further carbocation rearrangements in the gas phase are more extensive; complex cage-opening isomerization results in the 1,3-dimethylcyclopentenyl cation.[8]

Degenerate rearrangements of the nine CH groups of the 9-homocubyl cation were sought in 1967 first by Schleyer, et al. [9] and a few months later by Barborak and Pettit.[10] Both groups reported that solvolysis of deuterated 9-homocubyl precursors led to different degrees of automerization, depending on the reaction conditions. The more facile stereoselective mechanism (via 1,2-C-C shifts) equilibrated only five of the nine CH groups, was considered to involve rotation of the five-membered ring (5MR) relative to the four-membered ring (4MR). Schleyer et al. proposed that "because of the symmetry of the homocubyl system, this enhanced rate suggests that the 9-homocubyl cation may have a bridged structure".[9]

The observed preservation of the steric distribution is explained via the nonclassical structure (**1** in our numbering scheme), first proposed by Jorgensen.[11] Furthermore, completely degenerate scrambling might involve a classical C_{2v} symmetrical transition state (**TS$_{1-1}$'**, see Figure 1), in which all four equivalent adjacent bonds can migrate and allow the nine CH groups to interchange. Since the formolysis product of 9-deuterohomocubyl tosylate gave only 10% deuterium at C9, Schleyer et al. concluded that complete scrambling can occur under such more favorable conditions.[9] However, subsequent experiments on 9-homocubyl triflate by Spitz (1993)[12]

and by Spitz and Eaton (1995)[13] only found evidence for partial scrambling.

Jorgensen's seminal MINDO/3 computations identified a bridged transition state (**TS$_{1-1}$**) described as being "bis-homoaromatic". **TS$_{1-1}$** explains the observed partial isomerization as well as the stereochemistry. However, **TS$_{1-1}$** was only 2.7 kcal/mol lower in energy than the classical C_{2v} transition state **TS$_{1-1}$'** (inconsistent with the observed difficulty in achieving degeneracy).

Interestingly, Schleyer et al. noted that during acetolysis of 9-homocubyl tosylate the solution darkens at longer reaction times.[9] Spitz reported that "for reasons not understood, the solvolysis in neat hexafluoro-2-propanol even at 0 °C led to a complex mixture of cage-opened compounds".[12] But such products have never been identified explicitly. Herein, we analyse a series of rearrangement pathways of the 9-homocubyl cation, based on *ab-initio* computations and Born-Oppenheimer Molecular Dynamics (BOMD) simulations. Our results indicate that parallel to the automerization process, the 9-homocubyl cation also can undergo other types of rearrangements involving cage-opening.

a)

1.846
C9 — 1.391

1
C_s
0.0

TS$_{1-1}$
C_s
3.9

TS$_{1-1}'$
C_{2v}
11.1

b)

1.448
1.615

TS$_{1-2}$
C_s
9.3

2
C_{2v}
-1.0

Figure 1. Stationary points involved in a) the automerization of the 9-homocubyl cation (**1**) and b) isomerization of **1** into **2**. The computed relative free energies (vs. **1** in kcal/mol at CCSD(T)/def2-TZVP//MP2/def2-TZVP with MP2/def2-TZVP zero point energy corrections) are given for each structure. Bond lengths are in Angstroms.

Full geometry optimizations were carried out at the MP2[14] level with the def2-TZVP[15] basis set using the Gaussian 09 program.[16] Harmonic frequency analyses (at the same computational level) established the nature of the stationary points as minima or transition states. The total electronic energies were computed at CCSD(T)[17]/def2-TZVP//MP2/def2-TZVP and included the MP2/def2-TZVP zero point energy corrections. Intrinsic reaction coordinate computations at MP2/def2-TZVP validated the transition state connections. Born-Oppenheimer Molecular-Dynamics simulations were carried out using the deMon2k program[18] at the PBE/DZVP level,[19] with Hoover chain thermostat temperature control. All systems were sampled using a 1 fs step size. The simulations started from the equilibrium geometry of **1**, with random velocities assigned to each of the atoms.

Figure 1 shows the C_s bridged 9-homocubyl cation minimum (**1**); a cationic carbon atom of the 4MR interacts with a double bond of the 5MR via three-center two-electron (3c-2e) bonding involving two C-C bonds of 1.846 Å. **TS$_{1-1}$** (3.9 kcal/mol higher in energy than **1**), the transition state for the automerization of **1**, governs the "rotation" of the 5MR, which equilibrates its five CH-group protons.

1
NICS(0)$_{MOzz}$ = –28.7 ppm

3c-2e **"aromatic"**

TS$_{1-1}$
NICS(0)$_{MOzz}$ = +42.9 ppm

5c-4e **"anti-aromatic"**

TS$_{1-1}$' (C_{2v})
NICS(0)$_{MOzz}$ = +11.8 ppm
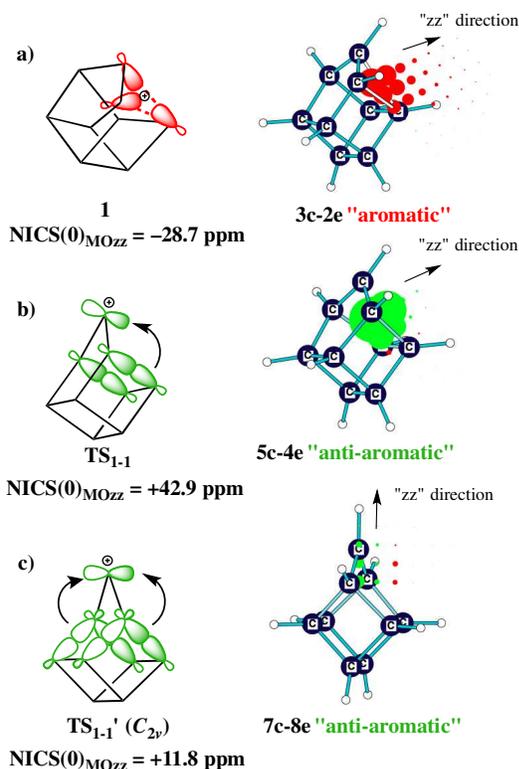
7c-8e **"anti-aromatic"**

Figure 2. Computed dissected NICS$_{MOzz}$ for a) **1** (3c-2e aromatic) b) **TS$_{1-1}$** (5c-4e antiaromatic), and c) **TS$_{1-1}$'** (7c-8e antiaromatic) at PW91/IGLO-III level (in ppm). Negative NICS values indicate aromaticity (diatropic, in red); positive NICS values indicate antiaromaticity (paratropic, in green).

Although both **1** and **TS$_{1-1}$** have non-classical structures, their modes of electron delocalization are very different. This is revealed in Figure 2 by the computed dissected nucleus independent chemical shifts (NICS$_{MOzz}$),[20-22] which is equal to the B^{ind}_{z-MO},[23-25] these include only the "zz" tensor component of the selected localized molecular orbitals (LMO's). In **1** (Figure 2a), the 3c-2e interaction responsible for delocalized bonding has "aromatic" character, and "negative" (diatropic, aromatic) computed LMO-NICS(0)$_{MOzz}$ (–28.7 ppm). The magnetic descriptor is computed at the geometrical center of the three participating carbon atoms, and the external field is applied perpendicular to the plane defined by these three atoms. In **TS$_{1-1}$** (Figure 2b), the five-center-four-σ-electron (5c-4e) delocalization involving two σ-C–C bonds and the formally empty p-orbital at C9 is "antiaromatic." Thus, the LMO-NICS(0)$_{MOzz}$ for **TS$_{1-1}$** (+42.9 ppm, which is computed at the center of the five participating carbon atoms) is "positive" and indicates antiaromatic character. For comparison, in the classical **TS$_{1-1}$'** (C_{2v} form, Figure 2c), the seven-center-eight-σ-electron (7c-8e) delocalization involving four σ-C–C bonds (two sets on each side of the C9 bridge) and the formally empty p-orbital at C9 displays reduced antiaromatic character (LMO-NICS(0)$_{MOzz}$ = +11.8 ppm, computed at the geometric center of the seven participating carbons).

Based on MINDO/3 computations, Jorgensen reported that the "nonclassical" C_{2v} structure, **2** (see Figure 1) is also competitive,[11] and 3.7 kcal/mol lower in energy than **1**. However, at the CCSD(T)/def2-TZVP//MP2/def2-TZVP level, this energy difference reduces to only 1.0 kcal/mol, but the reaction barrier connecting **1** and **2** via **TS$_{1-2}$** (ΔG_{1-2} = 9.3 kcal/mol) is 5.4 kcal/mol higher than that of the automerization process. Cation **2** bears a pentacoordinate carbon atom with four equivalent C-C bond distances of 1.615 Å.

At 300 K, BOMD simulations (see movie 1 in the supplementary information) reveal only the automerization of **1**. But at 600 K (See movie 2-SI), the situation changes drastically, and an unanticipated "open" structure (**3**, see Figure 3) for the 9-homocubyl cation appears. Cation **1** is transformed into **3** via **TS$_{1-3}$**, with only a 4.2 kcal/mol barrier. In **TS$_{1-3}$**, the C-C bond distances involved in delocalized bonding (2.248 Å) are elongated by 0.512 Å compared to **1** (see Figure 3). The single C–C bond (1.577 Å) connecting the 4MR and 5MR also is lengthened in **3**. Since such changes relieve some of the geometric strain of the 9-homocubyl cation, **3** is 30.5 kcal/mol lower in energy than **1**. Natural population analysis (NPA)[26] reveals that the positive charge in **3** is distributed to both rings (0.6 |e| in the 4MR and 0.4 |e| in the 5MR).
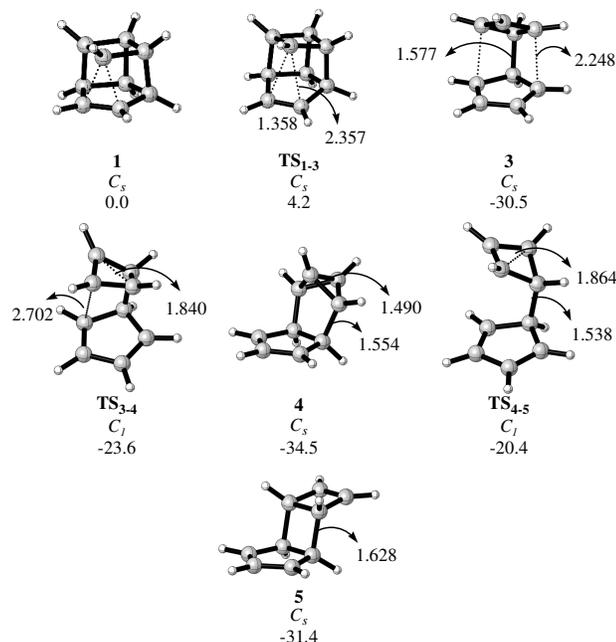
Figure 3. The 9-homocubyl cation cage-opening mechanism. The computed relative free energies (in kcal/mol at CCSD(T)/def2-TZVP//MP2/def2-TZVP with MP2/def2-TZVP zero point energy corrections for each structures (cf. **1**) are labelled. Bond lengths are in Angstroms.

Following its formation, **3** also undergoes a degenerate rearrangement (see Figure 4) with a very low barrier (ΔG_{3-3} = 1.3 kcal/mol), in which the 4MR transits over the cyclopentadienyl fragment. In **TS$_{3-3}$**, the two C-C bond distances (1.741 Å) are longer than a typical single bond length (see Figure 4). Repetitive extension of this process results in eventual equilibration of five of the nine methine units in **3**.
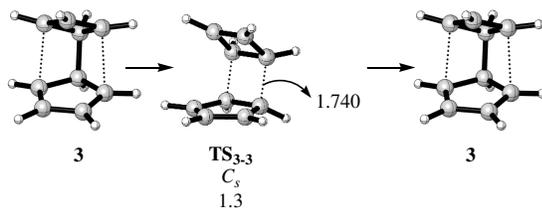
Figure 4. Automerization of **3** and the computed free energy (in kcal/mol at CCSD(T)/def2-TZVP//MP2/def2-TZVP with MP2/def2-TZVP zero point energy corrections) for this process. Bond lengths are in Angstroms.

Another interesting transformation of **3** takes place at 900 K (see movie 2-SI). Rotation of its 4MR leads to **4** via **TS$_{3-4}$** (ΔG_{3-4} = 6.9 kcal/mol), and a short C–C bond (1.490 Å) across the 4MR forms. Despite having a highly strained bicyclobutadienyl fragment, cation **4** is the most stable isomer found in the cage-opening pathway and is 4.0 kcal/mol lower in energy than **3**. Alternatively, BOMD simulations reveal the formation of cation **5**, in which the 4MR is connected to the 5MR via two single C-C bonds in a *trans* orientation. However, the **4** to **5** transformation (via **TS$_{4-5}$**) is endergonic (ΔG = 3.1 kcal/mol) with a computed barrier of 14.1 kcal/mol.

Schleyer reported 80-90% yields of 9-homocubyl acetate upon acetolysis (with partial scrambling). The formolysis yield only 30-40%, but no isomers were detected by capillary gas chromatography. Spitz reported "a complex mixture of cage-opened compounds" from HFIP solvolysis. But such products have never been identified explicitly. He found only partial scrambling under such conditions. Evidently, the transition state energies both for completely degenerate rearrangement (automerization, via **TS$_{1-1'}$**) and for cage opening (via **TS$_{1-3}$**) are significantly higher than that (**TS$_{1-1}$**) for partial scrambling. Although, the 9-homocubyl cation prefers a non-classical structure and undergoes a counter-rotation of a 4MR and 5MR ring, cage-opened structures are accessible via low computed barriers. Indeed, there are hints that this occurs experimentally. So, our work shows that the chemistry of homocubyl cation is more exciting that previously thought.

Notes and references

[a] Departamento de Física Aplicada, Centro de Investigación y de Estudios Avanzados, Unidad Mérida. Km 6 Antigua Carretera a Progreso. Apdo. Postal 73, Cordemex, 97310, Mérida, Yuc., México. gmerino@mda.cinvestav.mx, mfernandez@mda.cinvestav.mx
[b] Center for Computational Quantum Chemistry, Department of Chemistry, University of Georgia, Athens, Georgia 30602, USA. schleyer@uga.edu
[c] Unidad Académica de Ciencias Químicas, Área de Ciencias de la Salud, Universidad Autónoma de Zacatecas, Km. 6 carretera Zacatecas-Guadalajara s/n, Ejido La Escondida C. P. 98160, Zacatecas, Zac., México.

Electronic Supplementary Information (ESI) available: Cartesian coordinates for all the stationary points. See DOI: 10.1039/c000000x/

1 H. C. Brown, *The Nonclassical Ion Problem (with comments of P. v. R. Schleyer)*, Plenum, New York, 1977.
2 G. A. Olah, *J. Org. Chem.*, 2001, **66**, 5943.
3 P. Ahlberg, G. Jonsall and C. Engdahl, *Adv. Phys. Org. Chem.*, 1983, **19**, 223.
4 R. E. Leone and P. v. R. Schleyer, *Angew. Chem., Int. Ed.*, 1970, **9**, 860.
5 R. A. Moss, *J. Phys. Org. Chem.*, 2014, **27**, 374.
6 G. A. Olah, G. K. S. Prakash and M. Saunders, *Acc. Chem. Res.*, 1983, **16**, 440.
7 P. v. R. Schleyer, W. E. Watts, R. C. Fort, M. B. Comisarow and G. A. Olah, *J. Am. Chem. Soc.*, 1964, **86**, 5679.
8 S. Jalife, G. Martínez-Guajardo, C. Zavala-Oseguera, M. A. Fernandez-Herrera, P. v. R. Schleyer and G. Merino, *Eur. J. Org. Chem.*, 2014, **Accepted**.
9 P. v. R. Schleyer, J. J. Harper, G. L. Dunn, V. J. Dipasquo and J. R. E. Hoover, *J. Am. Chem. Soc.*, 1967, **89**, 698.
10 J. C. Barborak and R. Pettit, *J. Am. Chem. Soc.*, 1967, **89**, 3080.
11 W. L. Jorgensen, *J. Am. Chem. Soc.*, 1977, **99**, 4272.
12 U. P. Spitz, *J. Am. Chem. Soc.*, 1993, **115**, 10174.
13 U. P. Spitz and P. E. Eaton, *Angew. Chem., Int. Ed.*, 1995, **34**, 2030.
14 C. Moller and M. S. Plesset, *Phys. Rev.*, 1934, **46**, 0618.
15 F. Weigend and R. Ahlrichs, *Phys. Chem. Chem. Phys.*, 2005, **7**, 3297.
16 M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. Montgomery, J. A., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, N. J. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg,

S. Dapprich, A. D. Daniels, Ö. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski and D. J. Fox, Wallingford CT, 2009.

17 J. A. Pople, M. Headgordon and K. Raghavachari, *J. Chem. Phys.*, 1987, **87**, 5968.

18 A. M. Koster, G. Geudtner, P. Calaminici, M. E. Casida, V. D. Dominguez, R. Flores-Moreno, G. U. Gamboa, A. Goursot, T. Heine, A. Ipatov, F. Janetzko, J. M. d. Campo, J. U. Reveles, A. Vela, B. Zuniga-Gutierrez and D. R. Salahub, The deMon developers, Cinvestav, Mexico City 2011.

19 J. P. Perdew, K. Burke and M. Ernzerhof, *Phys. Rev. Lett.*, 1996, **77**, 3865.

20 P. v. R. Schleyer, C. Maerker, A. Dransfeld, H. J. Jiao and N. Hommes, *J. Am. Chem. Soc.*, 1996, **118**, 6317.

21 P. v. R. Schleyer, M. Manoharan, Z. X. Wang, B. Kiran, H. J. Jiao, R. Puchta and N. Hommes, *Org. Lett.*, 2001, **3**, 2465.

22 Z. F. Chen, C. S. Wannere, C. Corminboeuf, R. Puchta and P. v. R. Schleyer, *Chem. Rev.*, 2005, **105**, 3842.

23 G. Merino, T. Heine and G. Seifert, *Chem. Eur. J.*, 2004, **10**, 4367.

24 T. Heine, R. Islas and G. Merino, *J. Comput. Chem.*, 2007, **28**, 302.

25 R. Islas, T. Heine and G. Merino, *Acc. Chem. Res.*, 2012, **45**, 215.

26 A. E. Reed, R. B. Weinstock and F. Weinhold, *J. Chem. Phys.*, 1985, **83**, 735.

TOC
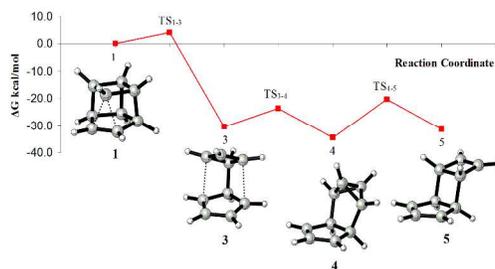
High ab initio computations indicate that parallel to the automerization process, the 9-homocubyl cation also can undergo other types of rearrangements involving cage-opening.