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# Perturbing the Structure of the 2-Norbornyl Cation through C−H···N and C−H···π Interactions

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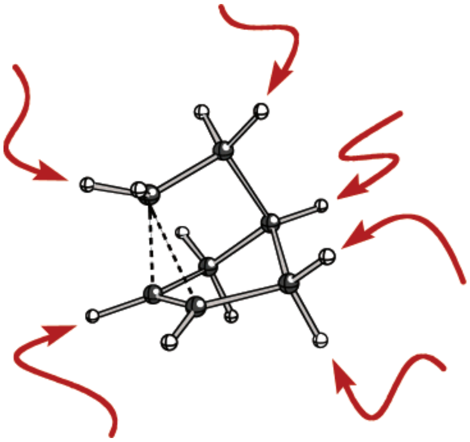

Quantum chemical studies on complexes of the 2-norbornyl cation with ammonia and benzene are described. These calculations demonstrate that the delocalized, bridged, nonclassical geometry that is usually favored for this carbocation can be perturbed significantly toward the normally less favorable classical geometry through appropriately oriented noncovalent interactions. Since such cations have been proposed as intermediates in enzyme and antibody catalyzed reactions, these results have implications for the nature of the cationic species that may be generated in the presence of electron-rich amino acid side chains of the sort that may be present in the active sites of biocatalysts.

## Introduction

Can the geometry of the 2-norbornyl cation (**1**) be manipulated through noncovalent interactions? The 2-norbornyl cation is arguably the most famous “nonclassical” carbocation (i.e., a carbonium ion, or carbocation containing a hypercoordinate carbon), having been at the crux of the vitriolic debates on the plausibility of bridged carbocation intermediates that enlivened the early days of physical organic chemistry.[1] It is now well-established that the equilibrium geometry of this carbocation does indeed involve a bridged hypercoordinate carbon,[1] but it is also well-established that the symmetry of this structure (i.e., the “degree of bridging”) is sensitive to substituents on the norbornyl framework—in particular, at the two carbons of the partial double bond.[2] On the basis of quantum chemical studies, the energy difference between the nonclassical 2-norbornyl cation (a $C_s$-symmetric minimum) and models of a classical 2-norbornyl cation has been estimated to be 10−15 kcal/mol both in the gas phase and in water.[1f−h] In this report, we address the issue of whether the classical structure can be selectively stabilized by specific *non*covalent interactions.

Besides their fundamental interest, complexes of the 2-norbornyl cation are also of relevance to several biological processes. Both substituted and unsubstituted norbornyl cations have been proposed as intermediates in biological reactions, the former having been postulated, for example, as intermediates

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[1] For leading references, see: (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. For key computational studies, see: (f) Schreiner, P. R.; Severance, D. L.; Jorgensen, W. L.; Schleyer, P. v. R.; Schaefer, H. F., III. *J. Am. Chem. Soc.* **1995**, *117*, 2663−2664. (g) Schreiner, P. R.; Schleyer, P. v. R.; Schaefer, H. F., III. *J. Org. Chem.* **1997**, *62*, 4216−4228. (h) Schleyer, P. v. R.; Sieber, S. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1606−1608. For X-ray crystal structures, see: (i) Laube, T. *Acc. Chem. Res.* **1995**, *28*, 399−405.

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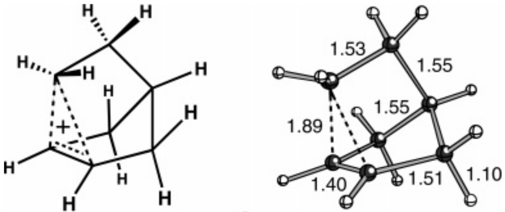

**1**

in the enzyme catalyzed formation of the terpene natural products camphene,[3a] santalene,[3b] and longifolene,[3c,d] and the latter having been invoked as a potential intermediate in the antibody catalyzed hydrolysis of *endo*-2-norbornyl mesylate.[4] The possibility was raised in the latter report that the inherent asymmetry of the antibody-combining site might favor the intermediacy of a classical rather than a nonclassical 2-norbornyl cation; alternatively, the asymmetric combining site might favor a particular trajectory for trapping of a symmetrical nonclassical 2-norbornyl cation. Herein we assess the viability of these possibilities, using quantum chemical methods to probe the susceptibility of the 2-norbornyl cation to structural perturbations induced by noncovalent interactions of the sort that might occur in the interiors of biocatalysts.

Our interest in biologically relevant carbocations—in particular, those with nonclassical structures—led us previously to examine the interaction of ammonia with classical and nonclassical $C_2H_5^+$, $C_3H_7^+$, and $C_4H_9^+$ species.[5] The structures of these carbocations were generally only very slightly perturbed upon participation in $C-H\cdots N$ interactions.[5,6] Herein we examine the interaction of the 2-norbornyl cation with both ammonia and benzene and show, in contrast, that its delocalized structure can be significantly perturbed through noncovalent interactions. The degree of structural distortion, however, strongly depends on the relative position of the carbocation and the species with which it interacts.

## Methods

All calculations were performed with GAUSSIAN03.[7a] Geometries were optimized without symmetry constraints using the hybrid Hartree−Fock/density functional theory (HF/DFT) B3LYP/6-31+G(d,p)[7b−e] method unless noted otherwise. Similar theoretical approaches have been advocated previously for modeling norbornyl cation structures; see, for example, ref 1g. It was recently recommended that diffuse functions be used regularly with density functional calculations.[7f] Tests with smaller basis sets can be found in the Supporting Information. All stationary points were characterized by frequency calculations, and reported energies include zero-point energy corrections (unscaled). Interaction energies ($E_{bind}$) for various structures were computed as the difference in zero-point-corrected energies for complexes and the sum of the energies for the separate components (entropies are not included). Corrections to these complexation energies for basis set superposition error were computed and are included in all reported interaction energies.[7g] These corrections were all $<1.2$ kcal/mol (and most considerably less) for our B3LYP/6-31+G(d,p) calculations. Herein negative interaction energies indicate exothermic complex formation. Structural drawings were produced using Ball & Stick.[7h] We demonstrated previously, through comparisons with MP2 calculations, that the B3LYP/6-31+G(d,p) method gives reasonable geometries and binding energies for carbocation−ammonia complexes, and that these favorable interaction energies appear to result primarily from electrostatic interactions.[5]

## Results and Discussion

The results of our B3LYP/6-31+G(d,p) computations[7] on complexation of the 2-norbornyl cation with ammonia are summarized in Chart 1 (the ability of each interaction to disrupt the symmetry of **1** is color coded from red to blue, with red interactions having the largest effects). Interaction of ammonia with $H_a$ had little effect on the geometry of the 2-norbornyl cation (here we define $\Delta r$ as the difference in the two C−C distances of the three-center bonding array in a given complex),

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(2) For leading references and seminal reports, see: (a) Prakash, G. K. S.; Iyer, P. S. *Rev. Chem. Intermed.* **1988**, *9*, 65−116. (b) Prakash, G. K. S. *J. Org. Chem.* **2006**, *71*, 3661−3676. (c) Farnum, D. G.; Wolf, A. D. *J. Am. Chem. Soc.* **1974**, *96*, 5166−5175. (d) Olah, G. A.; Prakash, G. K. S.; Liang, G. *J. Am. Chem. Soc.* **1977**, *99*, 5683−5687. (e) Olah, G. A.; Prakash, G. K. S.; Farnum, D. G.; Clausen, T. P. *J. Org. Chem.* **1983**, *48*, 2146−2151. (f) For crystallographically determined geometries of unsymmetrically substituted norbornyl cations, see, for example, ref 1i. (g) For computed geometries of unsymmetrically substituted norbornyl cations, see, for example, ref 1g.

(3) (a) Croteau, R. B.; Wheeler, C. J.; Cane, D. E.; Ebert, R.; Ha, H.-J. *Biochemistry* **1987**, *26*, 5383−5389. (b) Jones, C. G.; Ghisalberti, E. L.; Plummer, J. A.; Barbour, E. L. *Phyochemistry* **2006**, *67*, 2463−2468. (c) Cane, D. E. *Tetrahedron* **1980**, *36*, 1109−1159. (d) For a related biomimetic route to longifolene that involves nonclassical norbornenyl cations, see: Ho, G. A.; Nouri, D. H.; Tantillo, D. J. *J. Org. Chem.* **2005**, *70*, 5139−5143 and references therein.

(4) Ma, L.; Sweet, E. H.; Schultz, P. G. *J. Am. Chem. Soc.* **1999**, *121*, 10227−10228.

(5) Bojin, M. D.; Tantillo, D. J. *J. Phys. Chem. A* **2006**, *110*, 4810−4816. Related studies have also been reported by Morton and coworkers. See, for example: Audier, H. E.; Morton, T. H. *Org. Mass Spectrom.* **1993**, *28*, 1218−1224; Marinelli, W. J.; Morton, T. H. *J. Am. Chem. Soc.* **1978**, *100*, 3536−3539 (correction: *J. Am. Chem. Soc.* **1979**, *101*, 1908).

(6) X-ray crystal structures of carbocations with weakly associated counterions also have been described, and these show only very small geometric deviations from isolated gas phase carbocations.[1i]

(7) (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 *Gaussaina 03*, revision B.04; Pittsburgh, PA, 2003. (b) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648−5652. (c) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 1372−1377. (d) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785−789. (e) Stephens, P. J.; Devlin, F. J.; Chabalowski, C. F.; Frisch, M. J. *J. Phys. Chem.* **1994**, *98*, 11623−11627. (f) Lynch, B. J.; Zhao, Y.; Truhlar, D. G. *J. Phys. Chem. A* **2003**, *107*, 1384−1388. (g) Boys, S. F.; Bernardi, F. *Mol. Phys.* **1970**, *19*, 553−566. (h) Müller, N.; Falk, A. *Ball & Stick V.3.7.6*, molecular graphics application for MacOS computers; Johannes Kepler University: Linz, 2000. (i) Test calculations were performed on the complexes shown in Figures 1 and 2 with CPCM (Barone, V.; Cossi, M. *J. Phys. Chem. A* **1998**, *102*, 1995−2001; Barone, V.; Cossi, M.; Tomasi, J. *J. Comput. Chem.* **1998**, *19*, 404−417; UAKS radii were used; see: Takano, Y.; Houk, K. N. *J. Chem. Theor. Comput.* **2005**, *1*, 70−77) using both water (a very polar environment) and toluene (an environment not unrelated to an active site with many aromatic side chains) as solvents. For the left-hand complex in Figure 1, C−C distances of 1.88/1.88 Å and 1.87/1.87 Å were found in toluene and water, respectively. For the right-hand complex in Figure 1, only minima resembling **2** were found, suggesting that proton transfer is barrierless in these environments (at this level of theory). For the left-hand complex in Figure 2, C−C distances of 1.88/1.88 Å and 1.87/1.87 Å were found in toluene and water, respectively. For the right-hand complex in Figure 2, C−C distances of 1.69/2.16 Å ($\Delta r = 0.47$) and 1.71/2.08 ($\Delta r = 0.37$) Å were found in toluene and water, respectively. See Supporting Information for details.

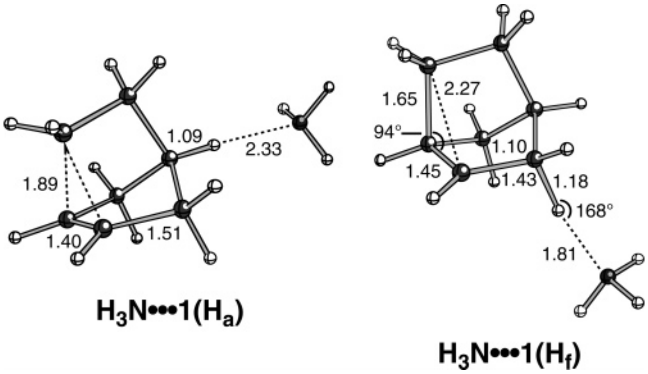
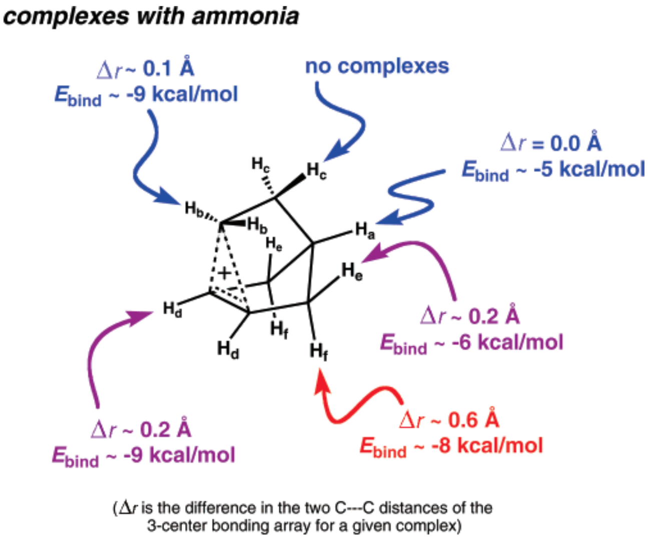


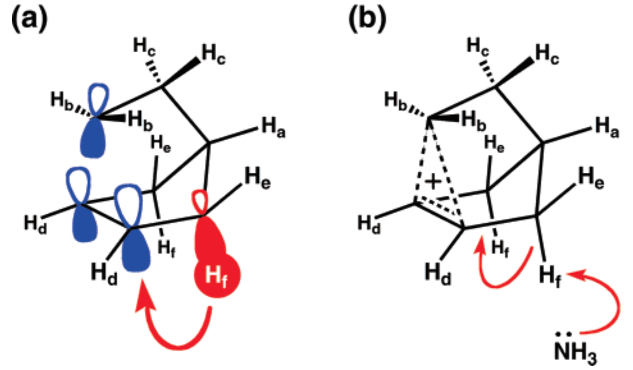
**FIGURE 1.** Computed (B3LYP/6-31+G(d,p)) geometries (distances in Å) of representative complexes of ammonia with the 2-norbornyl cation.[7i]

**CHART 1**



as expected given its distance from the bridging substructure and its position in the symmetry plane of the cation (geometries of representative complexes are shown in Figure 1). Interaction with $H_b$ led to only very small deviations from a $C_s$-symmetric cation structure even though these hydrogens are part of the bridging unit.[8] The greater positive charge on these hydrogens did, however, lead to stronger interactions (larger predicted binding energies, $E_{bind}$).[8] Starting geometries with ammonia near $H_c$ consistently led to complexes with $H_b$. Interaction with $H_d$ led to slightly larger $\Delta r$ values, as did interaction with $H_e$, with the former again having larger $E_{bind}$ values. The most significant distortions to the norbornyl structure were observed upon interaction with $H_f$, which led to a structure resembling a classical (but hyperconjugated) 2-norbornyl cation.[9,10] The different behavior of $H_e$ and $H_f$ is readily explained by a geometry dependent orbital interaction (i.e., a stereoelectronic effect). As shown in Chart 2a, each C−$H_f$ bond is roughly antiperiplanar to one partial C−C bond of the bridging unit, which allows the gain of electron density associated with complexation to be transmitted to the bridging unit in a manner analogous to the delocalization in a transition state structure for an E2 elimination reaction (Chart 2b).[11] Thus, the 2-norbornyl cation structure can indeed be perturbed by noncovalent interactions—even to the extreme of classicality—but these must be specifically oriented ones.

**CHART 2**



How sensitive are these results to the level of theory used? $H_3N\cdots\mathbf{1}(H_f)$ complexes held together by C−H⋯N bonds could not be located as minima when the BP86, mPW1PW91, and PW91 functionals (all with the 6-31+G(d,p) basis set) were used.[12a−c] Instead, all attempts at optimizing complexes, such as that shown at the right of Figure 1, yielded $NH_4^+$−norbornene complexes (**2**) that result (formally) from deprotonation of the norbornyl cation by $NH_3$. Moreover, at the B3LYP/6-31+G(d,p) level, the barrier for deprotonating the $H_3N\cdots\mathbf{1}(H_f)$ complex to form complex **2** is only 0.6 kcal/mol. Optimization using MP2/6-31+G(d,p),[12d] however, did lead to a norbornyl cation−$NH_3$ complex, but with a smaller $\Delta r$ of ~0.1 Å, consistent with the reported tendency of MP2 to favor more delocalized carbocations than does B3LYP.[5,7i]

Do these results then imply that strongly distorted $H_3N\cdots\mathbf{1}(H_f)$ complexes will generally not exist? All of these methods agree that interaction of ammonia with $H_f$ leads to a distortion of the nonclassical norbornyl cation structure toward a classical

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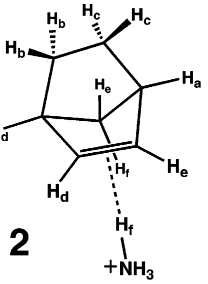
[8] (a) A complex of a water molecule with the $H_b$/$H_d$ face of the 2-norbornyl cation was previously computed at the MP4(fc)SDQ/6−31+G*//MP2(full)/6-31G* level.[1f] The geometry of the 2-norbornyl unit in this complex changed very little (e.g., the bridging bond lengths changed by ~0.01 Å) compared to the gas phase structure. The predicted interaction energy for this complex was −12.3 kcal/mol. We obtained a similar complex at the B3LYP/6-31+G(d,p) level (see Supporting Information). (b) Additional complexes of **1** and methyl-substituted derivatives of **1** with water can be found in the Supporting Information.

[9] (a) Note that the geometry of the 2-norbornyl unit in the ammonia and benzene complexes with $H_f$ resembles, somewhat, the model of the classical 2-norbornyl cation described by Schleyer and co-workers (a transition structure for the rearrangement of the nonclassical 2-norbornyl cation to the 2-norpinyl cation at both the MP2/6-31G*[1h] and B3LYP/6-31G*[1g] levels). (b) When we remove ammonia or benzene from complexes with $H_f$ and compute single point energies at the B3LYP/6-31+G(d,p) level, the remaining "classical" cation structures are ~5 and ~2 kcal/mol higher in energy, respectively, than the fully optimized nonclassical norbornyl cation. (c) No strong correlation was observed between C−H or H⋯N distances and $E_{bind}$. This likely reflects the complex interplay of structural distortion and charge redistribution in determining how tightly bound a given complex will be.

[10] Transition structures for loss of water from *endo* and *exo* 2-norbornyl-$OH_2^+$ are also discussed in detail in ref 1g; in the *endo* transition structure, weak interactions between the departing water and $H_f$ appear to be present.

[11] (a) Note that the C−$H_f$ bond elongates by 0.08 Å upon complexation. (b) For leading references on E2 transition state structures, see: Gronert, S. *Acc. Chem. Res.* **2003**, *36*, 848−857.

[12] (a) For leading references on BP86, see: van der Wijst, T.; Guerra, C. F.; Swart, M.; Bickelhaupt, F. M. *Chem. Phys. Lett.* **2006**, *426*, 415−421. (b) For leading references on mPW1PW91, see: Matsuda, S. P. T.; Wilson, W. K.; Xiong, Q. *Org. Biomol. Chem.* **2006**, *4*, 530−543; Gutta, P.; Tantillo, D. J. *J. Am. Chem. Soc.* **2006**, *128*, 6172−6179. (c) For leading references on PW91, see: Perdew, J. P.; Burke, K.; Wang, Y. *Phys. Rev. B* **1996**, *54*, 16533−16539. (d) For leading references on MP2, see ref 5.



**2**

structure—whether this distortion corresponds to a small or large $\Delta r$, or is expressed in the extreme through deprotonation—and this distortion is larger than when ammonia interacts with other hydrogens of the norbornyl cation. Although highly distorted structures will certainly exist at some point along the reaction coordinate for deprotonation, they may only exist as true minima in situations where their surroundings favor structures with more positive charge on the carbocation unit rather than on the amine (or where severe geometric constraints are imposed); this should be possible in the interiors of enzymes and antibodies. It is also important to point out that these simple models make use of a relatively strong base (an amine), while many other less basic groups may also participate in similar interactions with lesser proclivities for deprotonation.

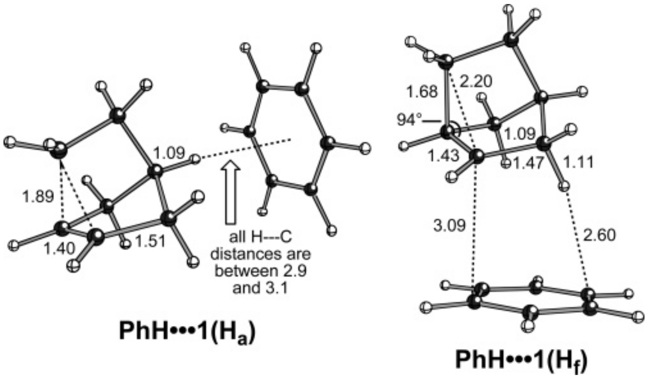
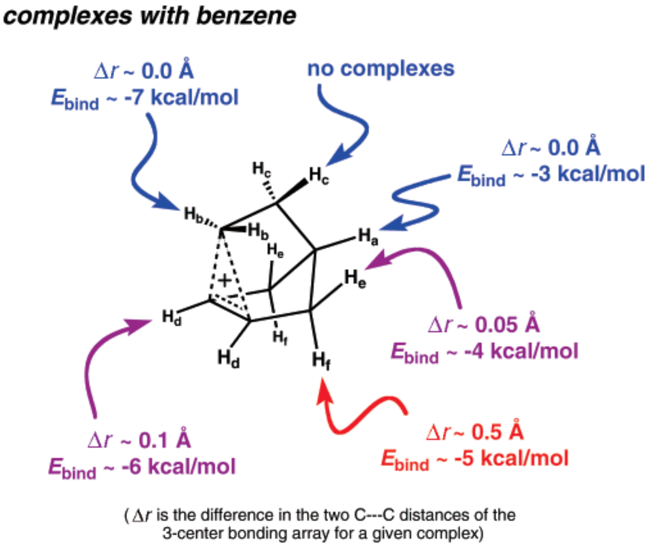


**FIGURE 2.** Computed (B3LYP/6-31+G(d,p)) geometries (distances in Å) of representative complexes of benzene with the 2-norbornyl cation.[7i]

**CHART 3**



Take, for example, aromatic rings. Can interactions with $\pi$-systems (C−H$\cdots\pi$ interactions[13]) such as benzene (which can be thought of as a simple model of phenylalanine, tyrosine, and tryptophan side chains) cause similar perturbations? Although computed binding energies (B3LYP/6-31+G(d,p)) for these interactions are somewhat smaller than for the C−H$\cdots$N interactions described above, the geometric changes to the 2-norbornyl structure upon complexation are quite similar (compare Chart 3 with Chart 1).[14] Geometries of representative complexes are shown in Figure 2 (here, complexes with benzene interacting simultaneously with more than one H of **1** and families of related complexes for each type of H with slightly different benzene positions were located, due to the larger electron-rich surface area of benzene as compared to the lone pair of ammonia; see Supporting Information for details). Again, interaction with $H_f$ has the most dramatic effect, consistent with a stereoelectronic effect analogous to that described in Chart 2, although an additional direct electrostatic interaction between the benzene $\pi$-system and the carbon bearing $H_d$ likely also contributes (see Figure 2). As for the ammonia complexes described above, calculations with MP2/6-31+G(d,p) led to less desymmetrized structures; a PhH$\cdots$**1**($H_f$) complex with $\Delta r$ = 0.14 Å was found at this level of theory. For the norbornyl−benzene system, however, very similar PhH$\cdots$**1**($H_f$) structures were obtained using all of the B3LYP, BP86, mPW1PW91, and PW91 functionals, consistent with the absence of a driving force for deprotonation when it is benzene that interacts with $H_f$. For example, at the B3LYP/6-31+G(d,p) level, the norbornene$\cdots$cyclohexadienyl cation complex that would result from deprotonation of **1** at $H_f$ by benzene is >19 kcal/mol *higher* in energy than the PhH$\cdots$**1**($H_f$) complex shown in Figure 2.

Thus, unlike the carbocations that we described previously,[5] the 2-norbornyl cation can show large distortions in structure upon complexation—for *specifically oriented* interactions with functionality in the outside environment. Appropriately oriented C−H$\cdots$X interactions can even overcome the substantial inherent preference for the nonclassical bridged geometry.[1f−h] Such environmentally induced desymmetrization could be used

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(13) (a) Nishio, M.; Hirota, M.; Umezawa, Y. *The CH/π Interaction. Evidence, Nature, and Consequences*; Wiley-VCH: New York, 1998. Computations on complexes of classical carbocations with $\pi$-systems: (b) Miklis, P. C.; Ditchfield, R.; Spencer, T. A. *J. Am. Chem. Soc.* **1998**, *120*, 10482−10489. (c) Filippi, A.; Roselli, G.; Renzi, G.; Grandinetti, F.; Speranza, M. *Chem.—Eur. J.* **2003**, *9*, 2072−2078. (d) Berthomieu, D.; Brenner, V.; Ohanessian, G.; Denbez, J. P.; Millié, P.; Audier, H. E. *J. Phys. Chem.* **1995**, *99*, 712−720. (e) Marcantoni, E.; Roselli, G.; Lucarelli, L.; Renzi, G.; Filippi, A.; Trionfetti, C.; Speranza, M. *J. Org. Chem.* **2005**, *70*, 4133−4141. (f) Chalk, A. J.; Radom, L. *Int. J. Mass Spectrom.* **2000**, *199*, 29−40. (g) Heidrich, D. *Angew. Chem., Int. Ed.* **2002**, *41*, 3208−3210. (h) Jenson, C.; Jorgensen, W. L. *J. Am. Chem. Soc.* **1997**, *119*, 10846−10854.

(14) Herein we treat norbornyl cation$\cdots$benzene complexes using the B3LYP/6-31+G(d,p) method. Recent studies on the appropriateness of various computational methods for treating C−H$\cdots\pi$ interactions include: (a) Ran, J.; Wong, M. W. *J. Phys. Chem. A* **2006**, *110*, 9702−9709. (b) Tsuzuki, S.; Honda, K.; Uchimaru, T.; Mikami, M.; Fujii, A. *J. Phys. Chem. A* **2006**, *110*, 10163−10168. (c) Tsuzuki, S.; Uchimaru, T. *Curr. Org. Chem.* **2006**, *10*, 745−762. (d) Zhao, Y.; Truhlar, D. G. *J. Chem. Theory Comput.* **2006**, *2*, 1009−1018. These papers (and references therein) note the problems that B3LYP and other density functional methods have with properly treating dispersion interactions. As a result, B3LYP tends to *under*estimate the C−H$\cdots\pi$ binding energies and *over*estimate the corresponding intermolecular distances, suggesting that the interactions we describe may be even stronger at "higher" levels of theory. However, the relative importance of dispersion interactions (as compared to electrostatic interactions) should be decreased for C−H$\cdots\pi$ interactions involving *cationic* C−H donors. B3LYP has also been used previously to examine C−H$\cdots\pi$ complexes of benzene with $CH_3^+$.[13b]

by a biocatalyst to push and pull otherwise noncommittal structures toward desired modes of reactivity.

## Conclusion

To our knowledge, our calculations are the first to demonstrate the viability of a means by which the symmetrical geometry of the *unsubstituted* 2-norbornyl cation can be significantly distorted toward that of a classical structure. On the basis of these calculations, we suggest that, in an enzyme active site or antibody-combining site, both symmetrical nonclassical and unsymmetrical classical structures can exist for 2-norbornyl cations (if such cations are generated as discrete intermediates), even in the absence of covalently attached substituents. This geometric changeability is reminiscent of the behavior of “mimic octopuses” (and other cephalopods), which change their shape (as well as body patterns and behavior) depending on the environment that surrounds them or the identities of the predators that challenge them.[15,16]

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

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(15) Norman, M. D.; Finn, J.; Tregenza, T. *Proc. R. Soc. London, Ser. B* **2001**, *268*, 1755−1758.

(16) So-called “chameleonic” behavior has also been described for transition structures for Cope rearrangements, but the structural variations in such cases were controlled by covalently attached substituents. See, for example: (a) Doering, W. v. E.; Wang, Y. *J. Am. Chem. Soc.* **1999**, *121*, 10112−10118. (b) Hayase, S.; Hrovat, D. A.; Borden, W. T. *J. Am. Chem. Soc.* **2004**, *126*, 10028−10034. (c) We have also investigated the potential for induction of chameleonic behavior in Cope reactions through intermolecular interactions; see: Wang, S. C.; Tantillo, D. J. *J. Phys. Chem. A* **2007**, *111*, 7149−7153.