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Energy Difference between the Classical and the Nonclassical 2-Norbornyl Cation in Solution. A Combined *ab Initio*−Monte Carlo Aqueous Solution Study

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While theory and experiment agree on the nonclassical, symmetrically bridged minimum energy structure (C_s, **1**) for the 2-norbornyl cation,[2] it is not always straightforward to compare experimental data obtained mostly in solution with computed gas phase values. The classical 2-norbornyl cation (**2**) is a transition structure[2] which can only be structurally characterized by computation. To close the gap between theory and experiment with respect to the 2-norbornyl cation problem, we report our study on the effects of solvation on the classical (**2**) and nonclassical ion (**1**) by employing *ab initio* MO methods and statistical Monte Carlo (MC) solution simulations.

Cation **1** is more stable than **2** by 13.6 kcal mol^{-1} [MP4(fc)SDQ/6-31G**/MP2(full)/6-31G* + ZPVE], but the difference in the transition state energies for the 2-*exo* and 2-*endo* norbornyl solvolyses[3] is reduced to less than half of this value (4−7 kcal mol^{-1} from experiment,[4] 6 kcal mol^{-1} from theory).[5] We will show in another place[5] that bridging does lag behind ionization,[6] and that this effect should be mainly responsible for the aforementioned differences in activation energies. The hypothesis that the relative energies of anchimerically assisted solvolysis reactions are very similar in the gas phase and in solution, implying that relative carbocation stabilities are the same in both media, is probed in the present work by including solvent effects in the energy computations.

We chose water as our solvent since we expect the difference in solvation energies to be large in highly polar media. To obtain the differences in free energies of hydration ($\Delta\Delta G_{\text{hyd}}$, Figure 1), we perturbed[7] between the MP2(full)/6-31G* optimized[8] cation structures **1** and **2** using statistical perturbation theory[9] as implemented in the BOSS program.[10] The intermolecular interactions are represented by Coulomb and Lennard-Jones terms with all atoms explicit.[11] For water, the TIP4P model was adopted,[12] while standard OPLS Lennard-Jones parameters were used for the solute.[11] Charges were obtained from MP2(full)/6-31G* − CHELPG[13] calculations. The simulations were performed in the NPT ensemble at 25 °C and 1 atm with Metropolis and preferential sampling.[9] The system consisted of 506 water molecules and the solute in a periodic cell, ca. 25 Å on a side. Each of the six simulations for the mutation entailed 10^6 configurations of equilibration and 2×10^6 configurations of averaging. Solute−water interactions were included for water molecules with an oxygen within 10 Å of any solute atom, and the water−water cutoff was set at 10 Å on the basis of the O−O distance.

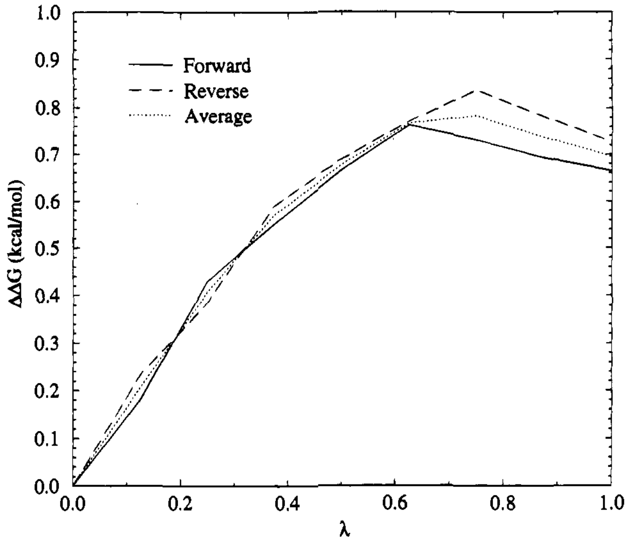
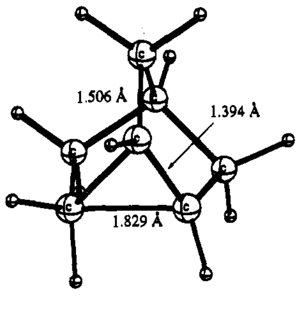


Figure 1. Free energy of solvation ($\Delta\Delta G$) vs coupling parameter λ (λ = 0 corresponds to **2**, λ = 1 to **1**).[7]



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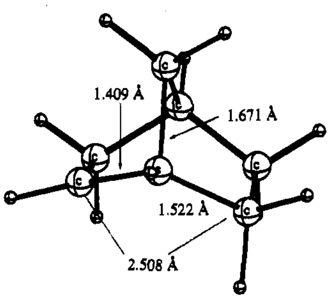

2

First, we established a reference point between the *ab initio* and BOSS force field results by optimizing the structures and energies of the nonclassical ion−water complex.[14] Both methods yield remarkably similar structures (**3** and **4**, both C_s)

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(7) A linear interpolation of the internal coordinates for the conversion of **1** into **2** was performed as a function of the coupling parameter λ.

(8) We used the *ab initio* program Gaussian 92: Frisch, M. J.; Trucks, G. W.; Head-Gordon, M.; Gill, P. M. W.; Wong, M. W.; Foresman, J. B.; Johnson, B. G.; Schlegel, H. B.; Robb, M. A.; Replogle, E. S.; Gomperts, R.; Andres, J. L.; Raghavachari, K.; Binkley, J. S.; Gonzales, G.; Martin, R. L.; Fox, D. J.; Defrees, D. J.; Baker, J.; Stewart, J. J. P.; Pople, J. A. *GAUSSIAN 92*; Gaussian, Inc.: Pittsburgh, PA, 1992. Foresman, J. B.; Frisch, Æ. *Exploring Chemistry with Electronic Structure Methods: A Guide to Using Gaussian*; Gaussian Inc.: Pittsburgh, PA, 1993. For a general review, see: Hehre, W. J.; Radom, L.; Pople, J. A.; Schleyer, P. v. R. *Ab Initio Molecular Orbital Theory*; John Wiley & Sons, Inc.: New York, 1986.

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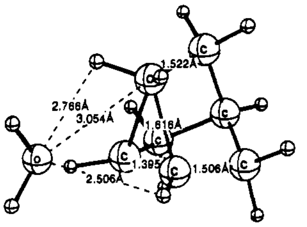
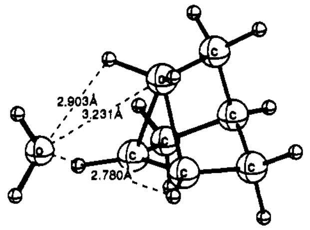
and complexation energies[15] [MP4(fc)SDQ/6-31+G*//MP2(full)/6-31G* = 12.3 kcal mol^{-1}; BOSS = 10.4 kcal mol^{-1}], although the computational approaches are entirely different.



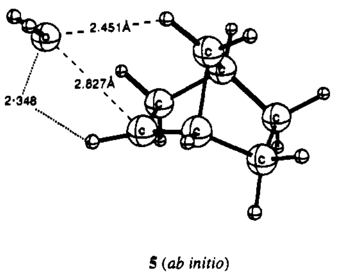
3 (*ab initio*)



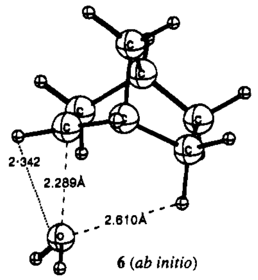
4 (BOSS Optimization)

The $\Delta\Delta G_{hyd}$ (Figure 1) profile summarizes the present MC solution simulations. To our surprise, the classical cation (**2**) is *not* considerably more stabilized by hydration than the nonclassical cation (**1**), as the $\Delta\Delta G_{hyd}$ is only 0.7 kcal mol^{-1} in favor of **2**. Partial (allowing only the water molecule to be optimized while keeping the cation moiety fixed) *ab initio* (**5** and **6**) and BOSS force field optimizations (**7** and **8**) of the possible complexes of **2** with a water molecule yield a similar result.

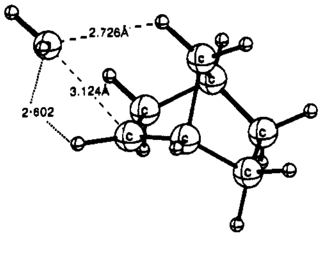
While the complexation energy of **3** is 12.3 kcal mol^{-1}, we find an interaction energy of 12.8 kcal mol^{-1} for **5** and 8.5 kcal mol^{-1} for **6** at MP4(fc)SDQ/6-31+G*//MP2(full)/6-31G*. Thus, the preferentially more favored *exo* complex of **2** with water is only 0.5 kcal mol^{-1} more stabilized than the water complex of **1**. One might have speculated that **2** has a more localized positive charge and would therefore benefit more from solvation than the delocalized **1**. This assumption does not hold as the MP2(full)/6-31G* − CHELPG[11] charges show very similar partial charges (+0.10 to +0.15) on the hydrogens close to the cationic centers. Moreover, the sums of all hydrogen charges are comparable (+1.2 for **2**; +1.1 for **1**). The sp^2 carbon in **2** does not have a full positive charge (+0.36). Since the water–cation binding appears to feature interactions with the cation's hydrogens, the energies are quite similar.



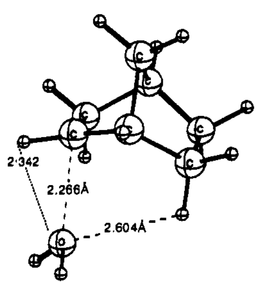
5 (*ab initio*)



6 (*ab initio*)



7 (BOSS force field)



8 (BOSS force field)

In conclusion, the classical 2-norbornyl cation (**2**) is not significantly more stabilized in aqueous solution than the nonclassical ion (**1**). Thus both the gas phase *ab initio* computations and Monte Carlo solution simulation come to the same result. In less polar solvents, the solvation energies are expected to be even more similar. Our results confirm that the nonclassical form **1** of the 2-norbornyl cation is the only stable form in the gas phase and in solution. The classical form **2** is unlikely to be involved in solvolysis reactions. As a consequence, the differences in rates of solvolysis for 2-*exo* and 2-*endo* norbornyl derivatives can only be explained in terms of the differences in the *exo* vs *endo* transition states.[5]

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Supplementary Material Available: Cartesian coordinates, charges, and values for ϵ for the Lennard-Jones potentials for **1** and **2** (4 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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(14) We used the MP2(full)/6-31G* optimized geometry for the MC simulation, i.e., only the position and energy of the water molecule were optimized. One may expect geometrical changes upon relaxation of the cation geometries in the solvent which would probably be more important for the less stable classical ion. However, *ab initio* optimizations within the MC simulation are currently not feasible, and the relative stabilities are not expected to change much upon reoptimization in solution.

(15) In a more rigorous treatment, one should include entropic effects and ZPVE corrections in the *ab initio* complexation energy, but frequency calculations were computationally not feasible for **3**. Although we have used diffuse functions for our energy evaluations to overcome (see: Feller, D. *J. Chem. Phys.* **1992**, *96*, 6104) most of the basis set superposition error (BSSE), the stability of **3** may still be somewhat overestimated. In short, 12.3 kcal mol^{-1} seems to be an upper limit for the complexation energy.