Correspondence

On the Performance of Continuum Solvation Models for the Solvation Energy of Small Anions

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Sir: In a recent theoretical investigation on the role of anions in palladium-catalyzed cross-coupling reactions,[1] it was stated that the Poisson−Boltzmann self-consistent reaction field (PB-SCRF) method incorporated in the Jaguar 4.2 program package[2,3] is not reliable for calculations of free energy of solvation of anionic species, and therefore the investigation was conducted for reactions in the gas phase. Furthermore, it was suggested that at least 10 explicit THF molecules should be included in the calculations to yield physically relevant results for solvated species in THF. For the chloride ion in THF, a value of 569 kJ/mol (136 kcal/mol) was calculated for the free energy of solvation, which is far from that reported by Senn and Ziegler of 271 kJ/mol (calculated from the free energy of solvation in water + the free energy of transfer from water to THF of the ion).[4] This discrepancy is extremely large (298 kJ/mol) for any relevant chemical investigation, and surprising since earlier studies on solvation of anions using continuum models showed good agreement with experiments.[5] Since we are interested in the effect of chloride ions and other anionic species on metal-catalyzed reactions, we decided to investigate the performance of solvation models for anions further. As can be seen from Table 1, the results of our calculations differ considerably from the value reported earlier.[1]

Table 1. Calculated Free Energy of Solvation of Cl^-

basis set	free energy of solvation (kJ/mol)
6-31G*	296
6-31+G*	281
6-311++G**	283
ref	271

Our results strongly suggest that the PB-SCRF model is actually very good in predicting the free energy of solvation, with an error of 25 kJ/mol for the smaller basis set and merely 10−12 kJ/mol for the larger, converging rapidly with basis set size. It has now been verified that the original error came from reading the final reported energy in the output file or the only reported energy in the log file. In our version, the program displays the quantum mechanical energy in the reaction field, which is very different from the sought-after total energy in solvent. We therefore wish to advise users of the Jaguar software to use the “Solution phase energy” from the output file in calculations employing continuum solvation models. In newer versions of Jaguar, this is also reported as the final energy in the output file, but not in the log file.

Table 2. Calculated Free Energy of Solvation for Cl^- Including Explicit THF Molecules

basis set	THF molecules	free energy of solvation (kJ/mol)
6-31G*	1	292
	2	289
6-31+G*	1	268
	2	273
ref		271

To further investigate the reliability of the solvent model, we incorporated a few explicit THF molecules (Table 2). Inclusion of more solvent molecules would require equilibration of the orientations, for example by a molecular dynamics approach, a computationally very expensive approach.

For the smaller basis set only slight changes in the free energy of solvation result from the inclusion of explicit solvent molecules: 4 kJ/mol for the first THF molecule and another 3 kJ/mol when a second THF molecule is included. For the larger basis set the values were slightly higher, 13 kJ/mol for one THF molecule and 8 with two; yet these corrections are relatively small. The values obtained using the larger basis set, with both one and two explicit THF molecules, are strikingly close to the reference values reported by Senn and Ziegler.[4]

Having found that the PB-SCRF model in Jaguar 4.2 actually gives good results for free energies of solvation of chloride in THF, we decided to investigate its capability to describe other solvents and anions. A set of anions was chosen for which the experimental free energies of solvation were available for both H_2O and DMSO solutions.[6] The anions were selected to cover a broad spectrum of free energies of solvation as well as to include both small localized and larger and more delocalized charges. Three different basis sets were utilized to probe the dependence of the solvation energy on the size of the basis set (Table 3).

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(1) Kozuch, S.; Amatore, C.; Jutand, A.; Shaik, S. *Organometallics* **2005**, *24*, 2319.

(2) DFT calculations made with the Jaguar 4.2 program package from Schrödinger Inc., Portland, OR: http://www.schrodinger.com.

(3) Marten, B.; Kim, K.; Cortis, C.; Friesner, R. A.; Murphy, R. B.; Ringnalda, M. N.; Sitkoff, D.; Honig, B. *J. Phys. Chem.* **1996**, *100*, 11775.

(4) Senn, H. M.; Ziegler, T. *Organometallics* **2004**, *23*, 2980.

(5) (a) Chambers, C. C.; Hawkins, G. D.; Cramer, C. J.; Truhlar, D. G. *J. Phys. Chem.* **1996**, *100*, 16385. (b) Nielsen, P. A.; Jaroszewski, J. W.; Norrby, P.-O.; Liljefors, T. *J. Am. Chem. Soc.* **2001**, *123*, 2003. Selected publications for further reading on continuum solvation models: (c) Cramer, C. J.; Truhlar, D. G. *Chem. Rev.* **1999**, *99*, 2161. (d) Orozco, M.; Luque, F. J. *Chem. Rev.* **2000**, *100*, 4187. (e) Tomasi, J.; Mennucci, B.; Cammi, R. *Chem. Rev.* **2005**, *105*, 2999.

(6) Pliego, J. R.; Riveros, J. M. *Chem. Phys. Lett.* **2000**, *332*, 597.

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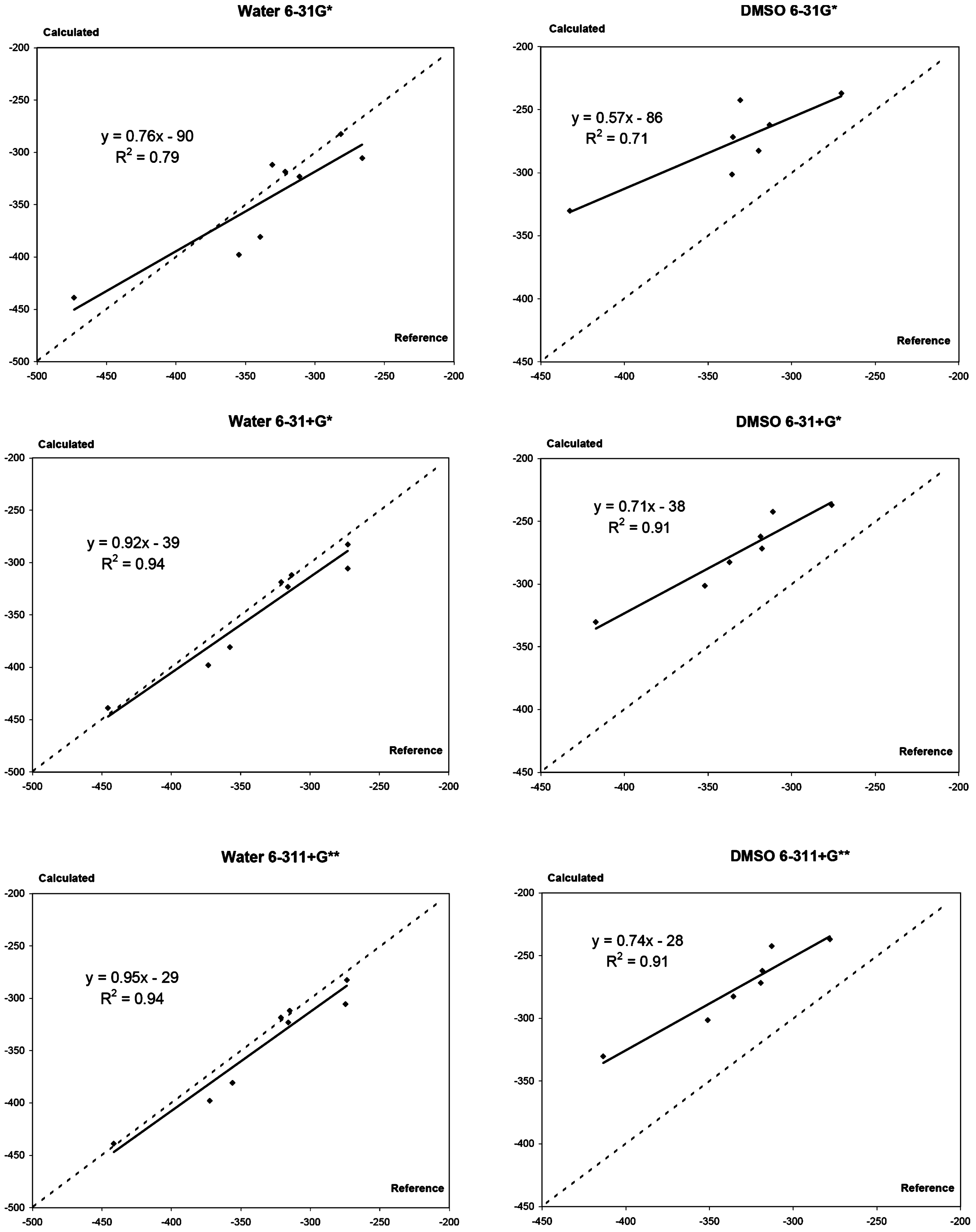

Figure 1. Calculated vs experimental solvation energies (data from Table 1).

For the water model the results are in good agreement with the experimental values reported by Pliego and Riveros,[6] especially so for the two larger basis sets, which both include diffuse functions for elements heavier than He. The best result is for the largest basis set, 6-311+G**, with $R^2 = 0.94$ and a slope of 0.95 (Figure 1). Similar results are obtained for the 6-31+G* basis set, while the results are poorer for 6-31G*. The poorer performance of the 6-31G* basis set, which does not include any diffuse functions, can be partly explained by its lesser ability to describe the anionic species in the gas phase,

Table 3. Solvation Energies in Water and DMSO with Different Basis Sets

	water				DMSO			
anion	6-31G*	6-31+G*	6-311+G**	ref	6-31G*	6-31+G*	6-311+G**	ref
Cl	−331	−313	−315	−312	−335	−318	−319	−272
CN	−281	−273	−274	−283	−331	−311	−313	−242
HCOO	−321	−321	−321	−319	−315	−315	−316	
MeCOO	−311	−316	−316	−323	−313	−319	−318	−262
OH	−473	−446	−442	−439	−433	−417	−414	−330
PhO	−266	−273	−275	−306	−270	−276	−278	−237
MeO	−355	−373	−372	−398	−336	−352	−351	−301
EtO	−339	−358	−356	−381	−320	−337	−336	−283

where it is known to be crucial to include diffuse functions in order to obtain physically relevant results.

The DMSO model does not show as good agreement with the reference values as the water model. As for the water model, the poorest results are yielded by the calculations where no diffuse functions are included in the basis set. However, the two sets of calculations utilizing basis sets that include diffuse functions both give satisfactory agreement with experimental values. A major difference between the water model and the DMSO model is that the latter systematically overestimates the free energy of solvation, whereas the former does not. We surmised that this is most likely due to the fact that the default water model in our version of Jaguar includes nonelectrostatic terms such as cavitation and dispersion, taken from an empirical model based on solvent accessible surface area (SASA), whereas explicitly defined models such as the DMSO model include only the electrostatic solvation terms. To test this hypothesis, we also performed calculations with an explicitly defined water model (without the nonelectrostatic terms) using the 6-311+G** basis set. The results are shown in Figure 2, from which it is clear that, when only electrostatic terms are included, the performance of the water model is similar to that of DMSO.

Conclusion

The full water model in Jaguar v 4.2, including also nonelectrostatic terms, *gives good correlation with* experimental values for energy of solvation. In the absence of nonelectrostatic terms, the correlation is somewhat poorer, but in cases where only relative solvation energies are important (such as for calculation of equilibria in a given solvent), the inclusion of a continuum model should still represent a vast improvement over calculations in the gas phase.

Computational Details

The Jaguar 4.2 build 77 program package was used throughout this study. DFT calculations were performed with the B3LYP hybrid functional as implemented in Jaguar 4.2. The basis sets utilized were 6-31G*, which includes polarization functions on all non-hydrogen atoms, and 6-31+G* with polarization functions and diffuse functions on all non-hydrogen atoms, and finally the highest basis set used was the valence triple-ξ basis set 6-311+G**, with polarization functions on all atoms and diffuse functions on all non-hydrogen atoms. To describe the solvent, the Poisson−Boltzmann self-consistent reaction field (PB-SCRF) in Jaguar 4.2 was applied. The parameters to describe THF were set to $\epsilon = 7.43$ and probe radius = radprb = 2.52372, for water $\epsilon = 80.37$ and probe radius = 1.40, and finally for DMSO $\epsilon = 46.7$ and probe radius = 2.41936. PB-SCRF is a continuum solvation model, where the molecule is put into a reaction field consisting of surface charges on a solvent accessible surface constructed using a hypothetical spherical solvent probe molecule with the indicated radius. The wave function and the reaction field charges are solved iteratively until self-consistency is reached. In our experience, a major role of this electrostatic model is to allow a separation of charges, something that incurs a substantially higher energy penalty in the gas phase.

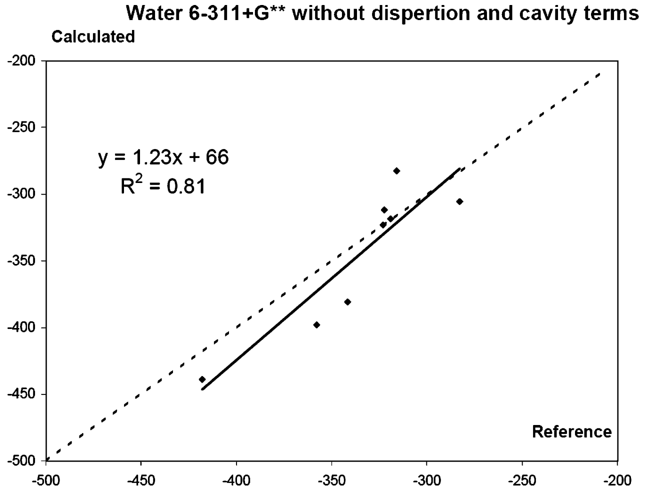

Figure 2. Performance of a water solvation model without nonelectrostatic terms.

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