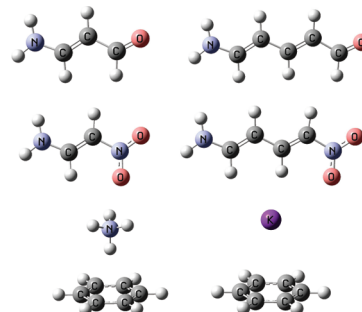# Coupled Cluster Calculations in Solution with the Polarizable Continuum Model of Solvation

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ABSTRACT Coupled cluster theory (CC) provides very accurate estimates of energies and molecular properties. Such calculations are often limited to gas-phase species due to the large computational cost of this level of theory; however, most of the chemical phenomena take place in solution. We propose an efficient implementation of the polarizable continuum model of solvation (PCM) with the coupled cluster singles and doubles method (CCSD) to take into account the solvent effects on the ground-state energy and geometry. Differently from atomistic representations, the PCM approach does not require conformational sampling of the solvent molecules and naturally describes mutual polarization effects between solute and solvent. Applications of the CCSD-PCM method to representative molecules are presented.

SECTION Molecular Structure, Quantum Chemistry, General Theory

Although most of the chemical phenomena are studied in solution, the representation of the solvent in accurate quantum chemistry calculations such as those at the coupled cluster level (CC)[1] is still very challenging. In fact, a large set of solvent molecules should be included in the calculation, and many configurations should be considered. This is not possible with the current computational resources, and some approximations must be introduced. These can be classified under two common approaches. One makes use of a discrete solvent representation at a lower level of theory compared to that of the solute, usually at the molecular mechanics (MM) level.[2−9] The other approach describes the solvent as a polarizable medium represented by the solvent dielectric constant ε, thus implicitly averaging over the various solvent conformations and reducing the computational cost.[10,11] A widely used method in the latter category is the polarizable continuum model (PCM), developed by Tomasi and co-workers.[12−15]

In this Letter, we present the first implementation of PCM with coupled cluster singles and doubles (CCSD) for energy and analytical gradients in a development version of Gaussian[16] following the work of Cammi.[17,18] We do not repeat the details of the equations here, but we summarize some important aspects.[17−20] The reference function is obtained through a self-consistent reaction field (SCRF)[15] calculation in which the solvent polarization mutually equilibrates with the density of the reference function (in this case, the Hartree−Fock wave function, HF-PCM). The CCSD wave function is then computed in the presence of the frozen reference reaction field and of a CCSD reaction field which is mutually equilibrated with the CCSD reduced one-particle density matrix (1PDM).[21,22] This model is referred to as PTED[17,23] since it was first developed in the context of perturbation theory where the energy (E) and density (D)

are considered for the computation of the reaction field. In gas-phase calculations, the CCSD energy is obtained by solving a set of equations that provides the wave function expansion coefficients (T amplitude equations).[1] When the CCSD density is needed for the calculation of properties or geometry optimizations, another set of equations must be solved that provides the so-called Λ amplitudes.[21,22] The CCSD-PCM-PTED approach couples the CCSD equations for the T and Λ amplitudes since the CCSD reaction field depends on the 1PDM. Thus, it is computationally more expensive than a CCSD energy calculation in the gas phase. Alternatively, in the PTE approximation,[17] the CCSD reaction field is neglected, and only the frozen reference reaction field is used, and thus, the Λ amplitude equations need not be solved. CCSD-PCM-PTE is thus computationally equivalent to a CCSD gas-phase calculation since the extra time spent in the SCRF to account for the solvent polarization is negligible compared to that for the solution of the T amplitude equations.

Calculations on a variety of molecular systems are reported in this Letter. We compare results obtained at HF-PCM, CCSD-PCM-PTE, and CCSD-PCM-PTED levels (in the following, we refer to the last two schemes simply as PTE and PTED, respectively). Although our implementation can handle open-shell systems through the unrestricted HF and CCSD wave functions, we only report calculations on closed-shell systems here. All calculations utilize the 6-31+G(d,p) basis set.[24] We use the integral equation formalism version of PCM (IEF-PCM)[13,14] since it properly describes the electrostatics of low polar solvents. However, the conductor-like version of

Table 1. Solvation Free Energy (kcal/mol)

	Cyc/IEF[a]	Dce/IEF[a]	H$_2$O/IEF[a]	Cyc/SMD[a]	Dce/SMD[a]	H$_2$O/SMD[a]
Pyridine						
exp[b]	−4.30	−5.53	−4.70	−4.30	−5.53	−4.70
HF	−1.99	−4.58	−5.35	−4.79	−7.43	−5.71
PTE[c]	−1.76	−4.04	−4.73	−4.43	−6.70	−4.89
PTED[c]	−1.78	−4.11	−4.80	−4.46	−6.77	−4.97
Aniline						
exp[b]	−5.52	−7.39	−5.49	−5.52	−7.39	−5.49
HF	−2.21	−5.22	−6.15	−5.51	−9.09	−5.82
PTE[c]	−1.92	−4.51	−5.32	−5.12	−8.18	−4.70
PTED[c]	−1.94	−4.57	−5.38	−5.15	−8.25	−4.78
Phenol						
exp[b]	−5.57	−7.48	−6.62	−5.57	−7.48	−6.62
HF	−2.43	−5.61	−6.58	−5.71	−8.85	−7.20
PTE[c]	−2.14	−4.94	−5.79	−5.35	−8.06	−6.18
PTED[c]	−2.16	−4.99	−5.85	−5.37	−8.12	−6.27
***p*-Bromophenol**						
exp[b]	−7.14	−9.10	−7.13	−7.14	−9.10	−7.13
HF	−2.72	−6.13	−7.14	−6.99	−10.15	−7.89
PTE[c]	−2.39	−5.40	−6.29	−6.68	−9.48	−7.01
PTED[c]	−2.42	−5.46	−6.36	−6.70	−9.52	−7.08
Chlorobenzene						
exp[b]	−5.10		−1.12	−5.10		−1.12
HF	−1.26	−2.84	−3.31	−5.55	−7.11	−2.06
PTE[c]	−0.95	−2.15	−2.50	−5.18	−6.27	−1.05
PTED[c]	−0.98	−2.20	−2.57	−5.20	−6.33	−1.12

[a] Cyc: cyclohexane; Dce: dichloroethane; IEF: electrostatic-only UFF radii; SMD: SMD nonelectrostatic and radii. [b] Reference 30. [c] PTE: CCSD-PCM-PTE; PTED: CCSD-PCM-PTED.

PCM (C-PCM)[25,26] is also available in our code with both the PTE and PTED approximations. A detailed description of our implementation of PCM can be found elsewhere[27] and is based on the work of York and Karplus.[28] We consider only the electrostatic solvent effect and the UFF radii[29] for all of the calculations unless explicitly specified. All of the geometries are optimized at the corresponding level of theory and in the corresponding medium (gas phase or solution).

The first series of data consists of solvation free energies, ΔG, of five aromatic compounds: pyridine, aniline, phenol, *p*-bromophenol, and chlorobenzene, in three solvents of increasing polarity: cyclohexane ($\varepsilon = 2.02$), dichloroethane ($\varepsilon = 10.13$), and water ($\varepsilon = 78.36$). The results are reported in Table 1. The table also reports the data computed with the SMD model of Truhlar and co-workers,[30] which includes nonelectrostatic terms in addition to the IEF-PCM treatment of electrostatics and uses its own set of radii. The reference data is taken from the SMD data set.[30] These results show a significant change in ΔG when passing from HF to CCSD, with differences of about 1 kcal/mol. CCSD always provides smaller absolute values of ΔG. On the other hand, the difference between PTE and PTED is very small, usually less than 0.1 kcal/mol. The trend of ΔG with the solvent polarity is not well reproduced when only the electrostatic effect is

considered, even when a high level of theory such as CCSD is used. Even though the SMD parameters were not fitted for these levels of theory, the agreement with the reference data is remarkable. For the cases where the HF-PCM absolute errors are on the order of 1−1.5 kcal/mol, as for all of the molecules in dichloroethane, CCSD with either PTE or PTED approximations significantly improves the agreement with experiment. Two larger basis sets, namely, aug-cc-pVDZ and 6-311++g(2d,2p), are tested to access basis set effects, and the results are reported in the Supporting Information. The geometries were not reoptimized since these are fairly rigid molecules. The differences with respect to the small basis set are usually less than 0.5 kcal/mol, except for phenol and *p*-bromophenol, where they are around 0.7 kcal/mol. The larger basis sets provide larger ΔG, except for chlorobenzene with the aug-cc-pVDZ basis. The agreement with the reference data is not always improved, depending on whether the value computed with the 6-31+G(d,p) basis set overestimates (or underestimates) the corresponding reference. The trend between the different methods described above is however maintained with all of the basis sets.

The next test case is the stabilization energy of the zwitterionic form of glycine in comparison to the neutral form in water.[8,9,31−33] The results are reported in Table 2. The

Table 2. Stabilization Free Energy (kcal/mol) of the Zwitterionic Form of Glycine Compared to the Neutral Form in Water

exp[a]	HF	PTE[b]	PTED[b]
−7.2	−0.86	−2.22	−2.21

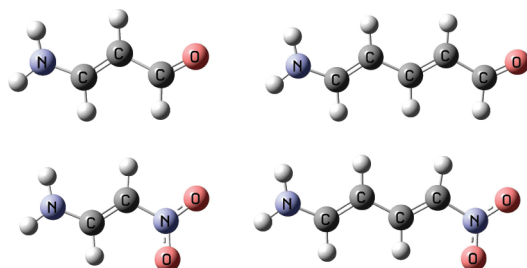[a] Reference 33. [b] PTE: CCSD-PCM-PTE; PTED: CCSD-PCM-PTED.

Figure 1. Push−pull polyenes.

difference between HF and CCSD is about 1.4 kcal/mol, whereas the difference between PTE and PTED is again negligible. The disagreement with the experiment is probably due to the simplistic representation of the solvation in water of such a polar solute by a continuum-only model. A more detailed analysis would require the description of specific interactions between the solute and the solvent by considering some explicit water molecules. However, such analysis is beyond the scope of this report and will be the subject of future research.

Another example is the solvent effect on the geometry of push−pull polyenes with electron donor and acceptor groups at the opposite ends of the conjugated chain. These systems are important for their nonlinear optical activity.[34−36] The presence of a polar solvent like water deforms their electronic π structure, pushing the neutral gas-phase structure toward a zwitterionic one. We consider chains with one and two C=C double bonds, NH_2 as the donor group, and CHO and NO_2 as the acceptor groups; see Figure 1. The geometry is forced to be planar; thus, a C_s symmetry is maintained. Table 3 reports the C=C bond length and the dipole moment for the two smallest systems and the bond length alternation (BLA, defined as the difference between the average lengths of the C−C and C=C bonds) and the dipole moment for the largest systems. The solvent increases the length of the C=C bond and decreases the BLA in comparison to that in the gas phase, and the dipoles are much larger in solution, confirming a charge separation effect in water. The difference between HF and CCSD is still significant, especially for the largest systems (see Table 3), with a variation in the dipoles in solution larger than 1 D. The PTE-PTED comparison shows small difference also in this case with a separation of at most 0.2 D in the largest polyene with the nitro group.

The final example is the cation−π interaction between a benzene ring and two cations, NH_4^+ and K^+; see Figure 2. These model systems are used to represent this kind of interaction in proteins.[37,38] NH_4^+ has one of the hydrogen atoms pointing toward the ring. The geometry optimizations were carried out without constraints. The results for NH_4^+ and K^+ are reported in Table 4. The interaction energies, E_{int} (free

Table 3. C=C Bond Length (Å), Bond Length Alternation (Å), and Dipole Moment (D) for the Polyenes $NH_2-(CH=CH)_n$-X in the Gas Phase and in Water

$n = 1$	X = CHO				X = NO_2			
	$R_{C=C}$		dipole		$R_{C=C}$		dipole	
	gas	H_2O	gas	H_2O	gas	H_2O	gas	H_2O
HF	1.341	1.361	6.519	9.758	1.339	1.364	7.394	10.901
PTE[a]	1.356[b]	1.370	6.055[b]	9.322	1.351[b]	1.370	6.845[b]	10.615
PTED[a]		1.370		9.283		1.370		10.548

$n = 1$	X = CHO				X = NO_2			
	BLA		dipole		BLA		dipole	
	gas	H_2O	gas	H_2O	gas	H_2O	gas	H_2O
HF	0.108	0.072	7.912	12.483	0.103	0.044	9.178	14.945
PTE[a]	0.092[b]	0.070	7.130[b]	11.128	0.092[b]	0.054	8.194[b]	13.454
PTED[a]		0.069		11.073		0.054		13.253

[a] PTE: CCSD-PCM-PTE; PTED: CCSD-PCM-PTED. [b] CCSD in the gas phase.
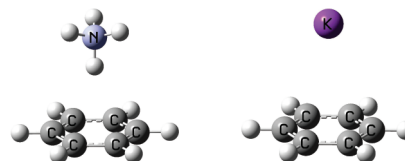
Figure 2. Cation−π systems.

Table 4. Cation−Ring Distance (Å) and Interaction Free Energy (kcal/mol) for the Cation−π Systems

	NH_4^+				K^+			
	R_{N-ring}		G_{int}		R_{K-ring}		G_{int}	
	gs	H_2O	gas	H_2O	gas	H_2O	gas	H_2O
HF	3.242	3.753	−13.435	−0.090	2.982	3.578	−14.775	0.015
PTE[a]	3.082[b]	3.341	−14.019[b]	−0.658	2.911[b]	3.493	−14.661[b]	−0.620
PTED[a]		3.339		−0.649		3.493		−0.619

[a] PTE: CCSD-PCM-PTE; PTED: CCSD-PCM-PTED. [b] CCSD in the gas phase.

energies in solution, G_{int}), are corrected for the basis set superposition error (BSSE) using the counterpoise method.[39,40] The BSSE correction for the species in solution is computed in the gas phase at the geometry optimized in solution since the procedure for the BSSE correction is not well-established with continuum solvation models. The distances are from the cation heavy atom to the center of the aromatic ring. The CCSD gas-phase distances are in very good agreement with those computed by Sherrill and co-workers at the CCSD(T)/6-311++G-(2d,2p) level.[37] E_{int} differs by about 2 kcal/mol, which is reasonable considering the difference in the level of theory. G_{int} for NH_4^+ is also in reasonable agreement with ref 37, whereas this is not the case for K^+, for which we found $G_{int} = -0.6$ kcal/mol compared to −8.5 kcal/mol in ref 37. This discrepancy is

probably due to a variety of factors since in ref 37, the solvent effect is introduced at the B3LYP level at the same geometry of the gas phase and with different PCM radii. Our calculations show that the equilibrium distance in solution is about 0.5 and 0.25 Å longer than that in the gas phase for NH_4^+ with HF and CCSD, respectively; the equilibrium distance is 0.6 Å longer for K^+ for both HF and CCSD. The solvent basically cancels the attraction between the cation and the π electronic cloud with $G_{int} < -1$ kcal/mol (K^+ at the HF level shows a very small positive value for G_{int}). Also in this case, the difference between PTE and PTED is negligible both for energy and geometry.

The convergence of the PCM iterations in the PTED model varies with the molecular system and the solvent polarity, and it is in the range of 5–10 iterations. We used very tight convergence criteria for the examples in this work (root-mean-square variation of the 1PDM $< 10^{-6}$, which corresponds to a convergence of the free energy within 10^{-9} au). Convergence of the free energy within 10^{-7} au was reached in 3–5 iterations. The root-mean-square variation for the T and Λ amplitudes was set to be $<10^{-6}$. We note that in later iterations, the effort to compute the T and Λ amplitudes was greatly reduced since the converged amplitudes from the previous PCM iteration could be used as a starting guess. An example of the convergence of the PTED equations is reported in the Supporting Information for pyridine in cyclohexane, dichloroethane, and water with the aug-cc-pVDZ basis.

The results reported in this Letter show that calculations in solution at a highly accurate computational level such as CCSD are feasible and effective for systems of medium size. However, the presence of the solvent introduces further complexity, and a high level of theory for the solute is not enough to account for the proper solute–solvent interaction in some cases. The examples for ΔG show that nonelectrostatic effects are necessary to obtain good agreement with experimental data, and the glycine example shows that a continuum-only model may not be sufficient when a specific solute–solvent interaction is present. The solvent may have a large effect on the solute structure, as shown by the polyenes and the cation–π systems; hence, the geometry should be optimized in solution. Finally, CCSD-PCM-PTE appears to be a very effective approximation for CCSD-PCM-PTED, at least for the cases studied, which are all closed-shell systems close to their equilibrium geometry. Indeed, the two schemes provide basically the same results.

SUPPORTING INFORMATION AVAILABLE Tables of ΔG with the aug-cc-pVDZ and the 6-311++G(2d,2p) basis sets. Figures for the CCSD-PCM-PTED free energy and the T and Λ amplitude convergence for pyridine with the aug-cc-pVDZ basis set in cyclohexane, dichloroethane, and water. This material is available free of charge via the Internet at http://pubs.acs.org.

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