

VBSM: A Solvation Model Based on Valence Bond Theory<sup>†</sup>Peifeng Su,<sup>‡</sup> Wei Wu,<sup>\*,‡</sup> Casey P. Kelly,<sup>§</sup> Christopher J. Cramer,<sup>§</sup> and Donald G. Truhlar<sup>\*,§</sup>

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A new solvation model, called VBSM, is presented. The model combines valence bond (VB) theory with parameters determined for the SM6 solvation model (Kelly, C. P.; Cramer, C. J.; Truhlar, D. G. *J. Chem. Theo. Comp.* **2005**, *1*, 1133–1152). VBSM, like SM6, is based on the generalized Born (GB) approximation for bulk electrostatics and atomic surface tensions to account for cavitation, dispersion, and solvent structure (CDS). The solvation free energy of VBSM includes (i) a self-consistent polarization term obtained by using VB atomic charges in a GB reaction field with a VB self-consistent field procedure that minimizes the total energy of the system with respect to the valence bond orbitals and (ii) a geometry-dependent CDS term to account for deviations from bulk-electrostatic solvation. Test calculations for a few systems show that the liquid-phase partial atomic charges obtained by VBSM are in good agreement with liquid-phase charges obtained by charge model CM4 (Kelly, C. P.; Cramer, C. J.; Truhlar, D. G. *J. Chem. Theo. Comp.* **2005**, *1*, 1133–1152). Free energies of solvation are calculated for two prototype test cases, namely, for the degenerate S<sub>N</sub>2 reaction of Cl<sup>-</sup> with CH<sub>3</sub>Cl in water and for a Menshutkin reaction in water. These calculations show that the VBSM method provides a practical alternative to single-configuration self-consistent field theory for solvent effects in molecules and chemical reactions.

## 1. Introduction

One of the major triumphs of modern physical chemistry has been elucidating the role of solvation effects in chemical structure and reactivity.<sup>1–14</sup> Reaction rate theory and dynamical simulations have elucidated such effects both with explicit<sup>3,5–8,10,12</sup> solvent and with implicit<sup>4,9,11,14</sup> solvent, often coupled to molecular orbital calculations. Valence bond (VB) theory, because it provides a natural way to describe chemical reactions, is very well suited to elucidating solvent effects on reactivity, and it has been employed by a number of workers for this purpose.<sup>6,15–21</sup> In the present article, we describe the incorporation of an implicit universal solvation model, SM6,<sup>22</sup> in the Xiamen Valence Bond (XMVB) package.

The XMVB package<sup>23</sup> is an ab initio nonorthogonal VB program. It employs both the spin-free approach<sup>24</sup> and the conventional Slater determinant approach<sup>25</sup> to VB theory and has a variety of capabilities, including VB self-consistent-field<sup>26</sup> (VBSCF), breathing orbitals VB<sup>27,28</sup> (BOVB), the bond-distorted-orbitals (BDO) method,<sup>29</sup> and VB configuration interaction<sup>30</sup> (VBCI). The orbitals used to construct VB configuration-state functions, which are called VB structures, may be localized to a single center or partially (or fully) delocalized. The present article illustrates the new solvation capability of XMVB by calculations that employ the VBSCF and BOVB methods with localized orbitals, which are also called hybrid atomic orbitals, and that employ BDO calculations with partially delocalized orbitals.

SM6 treats the electrostatics due to bulk solvent by the generalized Born (GB)<sup>31–37</sup> approximation with self-consistent partial atomic charges.<sup>37,38</sup> The electrostatic free energy of

solvation is augmented by terms proportional to the solvent-accessible surface areas<sup>39</sup> of the solute's atoms times empirical geometry-dependent atomic surface tensions; these terms account for cavitation, dispersion, and solvent-structure effects, where the solvent structure effects include short-range deviations of the electrostatics from the bulk electrostatic model. The empirical nature of the atomic surface tensions results in their also including all other effects not accounted for by the GB treatment of the bulk-solvent electrostatic free energy. The free-energy term associated with the sum of the negative electric polarization term ( $G_P$ ) and the positive electronic energy term ( $\Delta E_E$ ) is called the bulk electrostatic free energy of solvation,  $\Delta G_{EP}$ , and the free-energy term associated with the atomic surface tensions is called  $G_{CDS}$  (cavitation, dispersion, and solvent structure).

We will consider two reactions as examples in this paper. First, we consider the Menshutkin reaction of ammonia with chloromethane in aqueous solution. Then, we consider the degenerate S<sub>N</sub>2 reaction of chloride with chloromethane in aqueous solution. Section 2 presents the method, Section 3 presents the applications, and Section 4 presents the discussion. Concluding remarks are in Section 5.

## 2. Methods

In the present paper, we make the assumption (which is usually quite reasonable) that the free energy of solvation may be calculated by using the gas-phase geometry in both the gas phase and solution. In the context of kinetics, this has been called the separable-equilibrium-solvation approximation. The standard-state solvation energy when the standard-state concentration is the same (e.g., 1 mol/L) in the gas phase and in the solution is then approximated as

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$$\Delta G_S^* = \Delta G_{EP} + G_{CDS} \quad (1)$$

For the more common choice of standard states, namely, 1 atm ideal gas in the gas phase and 1 mol/L ideal solution in the liquid, the standard-state free energy of solvation is (at 298 K)

$$\Delta G_S^0 = \Delta G_S^* + 1.89 \text{ kcal/mol} \quad (2)$$

The free energy term  $G_{EP}$  can be decomposed into two contributions. If we let  $E$  denote the expectation value of the internal electronic and nuclear Hamiltonian of the solute and let  $G_P$  denote the free energy due to the solute polarizing the solvent, where the latter includes both the favorable free energy of solute–solvent interaction and the positive cost of polarizing the solvent within the linear response approximation, then

$$\Delta G_{EP} = \Delta E_E + G_P \quad (3)$$

where

$$\Delta E_E = E(\text{liq}) - E(\text{gas}) \quad (4)$$

In the above equation, liq denotes the evaluation of the expectation value of the gas-phase Hamiltonian with the solute's liquid-phase wave function (for the special case of aqueous solution, liq is replaced by aq), and gas denotes the evaluation of the same expectation value with the solute's gas-phase wave function. The calculation of  $G_P$  is discussed below (step B).

The present model can also be used to calculate the statistical mechanical potential of mean force<sup>40–44</sup>  $W(\mathbf{R})$ , where  $\mathbf{R}$  denotes a set of  $3N - 6$  solute internal coordinates. For any geometry  $\mathbf{R}$ , we have

$$W(\mathbf{R}) = V(\mathbf{R}) + \Delta G_S^0(\mathbf{R}) \quad (5)$$

where  $V(\mathbf{R})$  is the gas-phase Born–Oppenheimer potential energy surface<sup>45</sup> and  $\Delta G_S^0(\mathbf{R})$  is computed as in eq 1 but for the geometry  $\mathbf{R}$ . Note that by our approximation of using a rigid gas-phase geometry for computing the thermodynamic free energy of solvation, one has

$$\Delta G_S^0 \equiv \Delta G_S^0(\mathbf{R}_e) \quad (6)$$

where  $\mathbf{R}_e$  is the gas-phase equilibrium geometry.

For a chemical reaction, the free energy of reaction in liquid solution is given by

$$\Delta G^0 \equiv G^0(\text{P, liq}) - G^0(\text{R, liq}) \quad (7)$$

where P and R denote the product and reactant, respectively. The free energy of a given species X (where X may be a reagent R or P, or it may be a transition state) is given by

$$G^0(\text{X, liq}) = E(l) + G_{EVR}(\text{liq}) + \Delta G_S^0 \quad (8)$$

where  $G_{EVR}$  denotes the standard-state electronic vibrational–rotational contribution to the Gibbs free energy, including the vibrational zero-point contribution. In practice,  $G_{EVR}$  is usually approximated as the electronic vibrational–rotational free energy in the gas phase. However, for some of the molecules considered in this work, no stationary point corresponding to a gas-phase minimum geometry can be found; therefore,  $G_{EVR}$  is obtained on the basis of liquid-phase optimized geometries. Four different approximations to  $G_{EVR}$  will be considered in this article. The first, called the zero-order approximation, completely omits the  $G_{EVR}$  term in eq 8. The first-order approximation to  $G_{EVR}$  considers only the zero-point correction to the vibrational energy, and the second-order approximation considers the electronic vibrational–

rotational enthalpy (which also includes the zero-point correction to the vibrational energy). Finally, we also calculate  $G^0(\text{X,l})$  by using the full contribution from  $G_{EVR}$  in eq 8.

In VB theory, a many-electron wave function is expressed in terms of VB configuration-state functions  $\Phi_K$ :

$$\Psi = \sum_{K=1}^N C_K \Phi_K \quad (9)$$

where  $\Phi_K$  corresponds to a conventional VB structure and is defined by a Heitler–London–Slater–Pauling function. There are several computational approaches for VB theory at the ab initio level, where the most commonly used methods are VBSCF,<sup>26</sup> BOVB,<sup>27,28</sup> and VBCI.<sup>30</sup> The VBSCF and BOVB methods involve VB orbital optimization, whereas the VBCI method is a post-VBSCF approach that uses optimized VBSCF orbitals for configuration interaction. In the VBSCF method, the structure coefficients  $C_K$  and the VB orbital coefficients  $\mathbf{c}$  are simultaneously optimized, and the inclusion of more than one  $C_K$  accounts for static correlation. The BOVB method uses different orbitals for different VB structures so that the BOVB method also accounts for part of the dynamic correlation. In the VBSCF and BOVB methods, the forms of VB orbitals may be strictly localized or delocalized, and the choice between those options may depend on the application. To describe a Lewis bond concisely, one can delocalize orbitals between the two atoms (fragments) that are bonded as an electron-pair bond. Such orbitals are called BDOs. Thus, a VB structure that uses BDOs corresponds to Lewis bonding, including a covalent and two charge-transferred structures. (Note that charge-transferred structures are usually called ionic structures, but this is ambiguous when the whole system or its fragments are overall ionic, as in the applications of this article).

To perform a VB calculation with orbital optimization, the following steps are involved in the current version of XMVB:

1. Compute basis-set integrals or read integral files from other quantum chemistry packages.
2. Initialize the orbital coefficients  $\mathbf{c}$  or read an initial guess of  $\mathbf{c}$ .
3. Calculate the VB energy and energy gradients for the current set of orbital coefficients as follows:
  - 3.1 Evaluate the  $N \times N$  Hamiltonian ( $\mathbf{H}$ ) and overlap ( $\mathbf{S}$ ) matrices.
  - 3.2 Solve the secular equation

$$\mathbf{HC} = \mathbf{ESC}$$

for the structure coefficients  $C_K$  and VB energy  $E$ .

3.3 Successively vary each element of  $\mathbf{c}$  by a small amount  $\Delta$  (forward differences) or by  $\pm\Delta$  (central differences) and repeat steps 3.1 and 3.2 for the evaluation of numerical energy gradients.

4. Take an optimization step by a Davidson–Fletcher–Powell algorithm<sup>46</sup> to optimize the orbital coefficients  $\mathbf{c}$ .

5. Repeat steps 3 and 4 until the VB energy is converged to within a convergence criterion for energy gradients.

To incorporate the SM6 model into VB calculations, we added the following steps:

A. Before step 1, we calculate (i) the Coulomb integrals<sup>37,47–50</sup>  $\gamma_{kk}(\mathbf{R})$  that enter the GB calculation, where  $k$  and  $k'$  label atoms, (ii) the solvent-accessible surface areas<sup>51</sup>  $A_k(\mathbf{R})$ , and (iii) the geometry-dependent factors<sup>49</sup> that enter the  $G_{CDS}$  calculation.

B. After step 3.2, we calculate the current partial atomic charges  $q_k(\mathbf{R})$  by Mulliken<sup>52</sup> or Löwdin<sup>53</sup> population analysis. This is carried out as follows. First, the VB electron density corresponding to the current VB wave function is calculated. Second, population analysis is carried out by

$$q^{\text{Mulliken}}(\mathbf{R}) = Z_k - \sum_{\alpha \in k} (\hat{P}\hat{S})_{\alpha\alpha} \quad (11)$$

or

$$q_k^{\text{Löwdin}}(\mathbf{R}) = Z_k - \sum_{\alpha \in k} (\hat{S}^{1/2}\hat{P}\hat{S}^{1/2})_{\alpha\alpha} \quad (12)$$

where  $Z_k$  is the nuclear charge of atom  $k$ ,  $\alpha$  is a basis function on atom  $k$ , and  $\mathbf{P}$  and  $\mathbf{S}$  are the one-electron density and overlap matrices, respectively. Then, the GB polarization energy is calculated by

$$G_p = -\frac{1}{2} \left( 1 - \frac{1}{\epsilon} \right) \sum_k \sum_{k'} q_k(\mathbf{R}) q_{k'}(\mathbf{R}) \gamma_{kk'}(\mathbf{R}) \quad (13)$$

where  $\epsilon$  is the bulk dielectric constant of the liquid solvent.

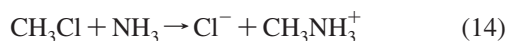
C. After the iterations converge, the total solvation energy is calculated by using eqs 1, 3, and 4.

In the present article, VBSM solvation free energies are calculated by using partial atomic charges obtained from Löwdin population analysis (eq 12; SM6 calculations<sup>22</sup> use CM4 partial atomic charges mapped from Löwdin partial charges, but such a mapping is omitted in VBSM).

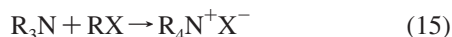
### 3. Examples

All calculations in this paper are at 298 K.

First, we consider the partial atomic charges in some small molecules. Then, we consider a particular case<sup>40</sup>



of the Menshutkin reaction:<sup>12,40,54–72</sup>



and compare it to an earlier study<sup>40</sup> by employing the SM5.2R<sup>51,73</sup> and SM5.4<sup>50,73</sup> solvation models in aqueous solution. Finally, we consider an aqueous S<sub>N</sub>2 reaction in solution.<sup>10,18,19b,74–79</sup>



**3.1. Partial Atomic Charges of Small Molecules.** Table 1 lists VBSM Mulliken partial atomic charges and Löwdin partial atomic charges, defined by eqs 11 and 12, respectively, for each symmetrically unique atom in NH<sub>3</sub>, CH<sub>3</sub>Cl, and NH<sub>2</sub>Cl in the gas phase and in the aqueous phase, where the 6-31G(d) basis set was used for VBSM calculations. For comparison, Table 1 also lists the Mulliken,<sup>52</sup> Löwdin,<sup>53</sup> and CM4<sup>22</sup> partial atomic charges calculated at the *m*PW1PW/6-31G(d) (gas) and SM6/*m*PW1PW/6-31G(d) (aqueous solution) levels. It can be seen that the VBSM values of partial atomic charges match semiquantitatively with the Löwdin charges of the SM6 model. The largest deviation is 0.21 for the Löwdin charge of the N atom of NH<sub>3</sub> in the aqueous phase. For both the VBSM and SM6 methods, the absolute values of Löwdin charges are smaller than those of the Mulliken charges. For the further test calculations, the Löwdin charges are used because the Mulliken charges are sometimes much too polar, with a maximum absolute deviation from CM4/SM6 charges of 0.55, but the Löwdin charges agrees with the CM4/SM6 charges with a median absolute deviation of 0.12 and a maximum absolute deviation of 0.30.

**3.2. Reactions in Aqueous Solution.** Next, we used VBSM and SM6 to study the Menshutkin reaction between NH<sub>3</sub> and CH<sub>3</sub>Cl, which is an example of type II<sup>57,79</sup> S<sub>N</sub>2 reactions. For both reactions 14 and 16, one nonbonding lone pair (a lone pair of N for reaction 14 and of Cl<sup>-</sup> for reaction 16) and the H<sub>3</sub>C–Cl bond are directly involved in the reaction process. We use the same six structures as in ref 19b. These structures encompass all the possible ways of distributing the four electrons of the lone pair and the H<sub>3</sub>C–Cl bond among the three fragments, as specified in Table 2. Note that we use the same numbering as that in ref 19b. Structures **1–3** are the VB structures that describe the electronic structure of the reactants, and structures **3**, **4**, and **6** correspond to the products. Besides the four active electrons, the other 18 valence-shell electrons are also involved in the VB calculation and are arranged in doubly occupied orbitals. The six VB structures with localized  $\sigma$  orbitals are used in the VBSCF and BOVB calculation, except that the BOVB calculations are based on the VB structures that have weights larger than 0.001 in VBSCF calculations. For the BDO calculation, only structures **1** and **4** are taken because the structures differing by a charge transfer are effectively created by using BDOs, each of the two VB structures uses its own BDOs.

The aqueous-phase free energy of activation and free energy of reaction were calculated by using four different approximations to  $\Delta G_{\text{EVR}}$ :

$$\Delta G^{\circ}(0) = \Delta E(\text{gas}) + \Delta \Delta G_{\text{S}}^{\circ} \quad (17)$$

$$\Delta G^{\circ}(1) = \Delta E(\text{gas}) + \Delta \Delta G_{\text{S}}^{\circ} + \Delta E_{\text{ZPE}} \quad (18)$$

$$\Delta G^{\circ}(2) = \Delta E(\text{gas}) + \Delta \Delta G_{\text{S}}^{\circ} + \Delta H_{\text{EVR}} \quad (19)$$

$$\Delta G^{\circ}(\text{full}) = \Delta E(\text{gas}) + \Delta \Delta G_{\text{S}}^{\circ} + \Delta G_{\text{EVR}} \quad (20)$$

where  $\Delta G^{\circ}$  is either the free energy of activation, which is the free-energy difference between the transition state (TS) and the reactants, or the free energy of reaction ( $r$ ), which is the free-energy difference between the products and the reactants, and  $\Delta \Delta G_{\text{S}}^{\circ}$  denotes the difference between  $\Delta G_{\text{S}}^{\circ}$  at TS or P minus that at R. The SM6 calculations use the *m*PW1PW/6-31G(d) level of theory. We compute  $\Delta E_{\text{ZPE}}$ ,  $\Delta H_{\text{EVR}}$ , and  $\Delta G_{\text{EVR}}$  at the SM6/*m*PW1PW/6-31G(d) level of theory for both the VBSM and the SM6 methods.

**3.2.1. Menshutkin Reaction.** Table 3 shows the VBSM and SM6 energies and free energies in the gas phase and the aqueous phase. It can be seen that the  $\Delta E_{\text{E}}$ ,  $G_{\text{P}}$ , and  $\Delta G_{\text{S}}^{\circ}$  values of reactant and product calculated by VBSM are very close to the SM6 results, except that VBSM  $G_{\text{P}}$  and  $\Delta G_{\text{S}}^{\circ}$  of the reactant are smaller than those computed by SM6 by about 3.0 kcal/mol. This good agreement is due in part to the partial atomic charges in the two methods being similar; however, one must recognize that similar charges would not necessarily yield similar free energies of solvation if different atomic radii and electrostatic formulations were used—as discussed further in Section 4. Although VBSM and SM6 use the same atomic radii and the same electrostatic formalism, at the TS, the VBSM values of  $\Delta G_{\text{S}}^{\circ}$  are smaller than those computed by SM6 by about 6.0 kcal/mol.

Table 4 lists the free energies of activation and the free energies of reaction with the four approximations described above and compares them to values from VBPCM studies.<sup>72</sup> Also listed in Table 4 is an experimental value for the free energy of reaction. This value was obtained from a thermodynamic cycle by using an experimental value of  $110 \pm 5^56$  kcal/mol for the gas-phase free energy of reaction and experimental

**TABLE 1: Computed Partial Atomic Charges by Using the VBSCF and SM6 Solvation Models<sup>a</sup>**

atom	VBSCF <sup>b</sup>		SM6 <sup>c</sup>		
	Mulliken	Löwdin	Mulliken	Löwdin	CM4
NH <sub>3</sub>					
N	-0.80, -0.79	-0.62, -0.62	-0.94, -1.02	-0.80, -0.83	-0.89, -0.92
H	0.27, 0.26	0.21, 0.21	0.32, 0.34	0.26, 0.28	0.30, 0.31
NH <sub>2</sub> Cl					
N	-0.88, -0.70	-0.51, -0.49	-0.77, -0.81	-0.61, -0.63	-0.67, -0.68
Cl	0.02, 0.04	0.02, 0.04	0.04, 0.02	0.04, 0.03	0.04, 0.3
H	0.43, 0.33	0.24, 0.23	0.36, 0.39	0.28, 0.3	0.31, 0.33
CH <sub>3</sub> Cl					
C	-0.68, -0.55	-0.39, -0.37	-0.60, -0.60	-0.50, -0.49	-0.13, -0.13
Cl	-0.22, -0.10	-0.08, -0.07	-0.08, -0.14	-0.05, -0.09	-0.15, -0.19
H	0.30, 0.21	0.15, 0.15	0.23, 0.25	0.18, 0.19	0.09, 0.1

<sup>a</sup> Values listed first are for the gas phase, and those listed second are for the aqueous solution. <sup>b</sup> The 6-31G(d) basis set was used. <sup>c</sup> SM6/mPW1PW/6-31G(d).

**TABLE 2: VB Structures<sup>a</sup>**

number	structure
1	(X:)(M·-·Y)
2	(X:)(M:)
3	(X:)(Y:)
4	(X·-·Y)(Y:)
5	(X·)(M:)(Y·)
6	(M:)(Y:)

<sup>a</sup> X, chloride ion or ammonia; M, methyl; and Y, chlorine atom.

values of  $-0.6 \pm 0.2$ ,<sup>22</sup>  $-4.3 \pm 0.2$ ,<sup>22</sup>  $-76.4 \pm 3.0$ ,<sup>81</sup> and  $-74.5 \pm 2.0$ ,<sup>81</sup> kcal/mol for the aqueous solvation free energies of CH<sub>3</sub>Cl, NH<sub>3</sub>, CH<sub>3</sub>NH<sub>3</sub><sup>+</sup>, and Cl<sup>-</sup>, respectively.

As expected, the VBSCF free energy of activation is inaccurate because of the lack of dynamic correlation. However, table 3 shows that the activation free energies computed by BDO and BOVB methods are in good agreement with the SM6 calculation. Also, the VBSCF computed reaction free energies are lower than the SM6 ones by about 10 kcal/mol. However, the values of  $\Delta G_{\text{r}}^{\ddagger}(\text{full})$  for all four levels of calculation, from  $-31$  to  $-40.5$  kcal/mol, are in the range of experimental data,  $-36 \pm 6$  kcal/mol. By comparing these values with the VBPCM results, it can be found that the free energies of activation by VBSCF and BOVB are both close to the VBPCM one; however, the free energies of reaction by VBPCM are higher than those obtained by VBSCF by about 11 kcal/mol.

Table 5 lists the computed weights of the VB structures at each of the VBSCF and BOVB levels. It can be seen that the wave function of the TS is dominated by structures 1 and 3. The weight of structure 4, which is much smaller than that of structure 1, shows that the N-C bond is almost unformed at the TS. This is consistent with the TS in aqueous phase being early. The weights of structures 2, 5, and 6 in TS are very small because of their unfavorable chemical bonding pattern. For comparison, the weights computed by VBPCM<sup>72</sup> at the VBSCF and BOVB levels are also shown in Table 5. In the reactant (R) and product (P), the VBPCM weights are similar to the VBSCF ones; but at the TS, the weight of structure 1 is larger in VBSCF than in VBPCM/VBSCF by 0.134, and the weight of structure 3 is smaller in VBSCF than in VBPCM/VBSCF by 0.093. For the weight of structure 4, the value from VBSCF is smaller than that from VBPCM/VBSCF by 0.046. For the BOVB level, the situation is basically the same as with VBSCF.

**3.2.2. Degenerate S<sub>N</sub>2 Reaction: Cl<sup>-</sup> + CH<sub>3</sub>Cl → CH<sub>3</sub>Cl + Cl<sup>-</sup>.** By using the same procedures as in the Menshutkin example, free energies of activation were calculated for the S<sub>N</sub>2 degenerate rearrangement between Cl<sup>-</sup> and CH<sub>3</sub>Cl. For this reaction, one lone pair of Cl<sup>-</sup> and the H<sub>3</sub>C-Cl bond are directly involved in the reaction process. For the VBSCF and VBSCF/BOVB calculations, six VB structures (see Table 2) were considered. In a similar fashion to the Menshutkin reaction, only structures 1 and 4 are considered in the VBSCF/BDO calculation. The 6-31+G(d) basis set was used for this example. All of the orbitals that are involved in the bond forming or breaking processes are localized. This strategy was followed because it decreases the computation time significantly. The SM6 calculations are for the mPW1PW/6-31G(d) level of theory.

The gas-phase and aqueous-phase energies and free energies that were calculated by using VBSCF and SM6 are shown in Table 6. The values of  $G_{\text{P}}$  and  $\Delta G_{\text{r}}^{\ddagger}$  computed by the three levels of VBSCF are the same as those from the SM6 calculation. Table 7 gives free energies of activation with each of the four levels for  $\Delta G_{\text{EV}}^{\ddagger}$  as specified in eqs 17–20 (including eq 17, which neglects this term) for both VBSCF and SM6. The BOVB calculations yield the lowest free energy of activation among the three levels of VB methods, but even the BOVB barrier is larger than the SM6 results by about 10 kcal/mol. For comparison, the corresponding results computed by VBPCM<sup>19b</sup> are also shown in Table 8. It can be found that the values of VBSCF activation energy match those of VBPCM calculations. However, the SM6 results are closer to the experimental free energy of activation, which is<sup>82</sup> 26.5 kcal/mol.

Table 8 lists the computed weights of the VB structures with VBSCF and BOVB. The table shows that the wave function of the TS is dominated by structures 1, 3, and 4. The weights of 2, 5, and 6 are very small in both the VBSCF and the BOVB calculations. It can be seen that the BOVB weight of structure 3 is smaller than that of VBSCF by about 0.1, whereas the BOVB weights of 1 and 4 are larger than those of VBSCF by 0.034. This is because in the BOVB method, the orbitals are optimized so as to lower the energy of each individual structure and simultaneously minimize the configuration interaction energy; thus, the weights of the less important structures increase. For comparison, the VBPCM/BOVB weights<sup>77</sup> are also shown in Table 8. All VBSCF/BOVB weights that are greater than 0.039 agree with the corresponding VBPCM/BOVB weights within 15%, which is very encouraging for both VBSCF and VBPCM.

**TABLE 3: Energies for Reactants (R), Transition State (TS), and Products (P) in the Menshutkin Reaction in the Gaseous and Aqueous Phases**

	VBSM <sup>a</sup>									SM6 <sup>b</sup>		
	VBSCF			BDO			BOVB			R <sup>e</sup>	TS	P <sup>d</sup>
	R <sup>c</sup>	TS	P <sup>d</sup>	R <sup>c</sup>	TS	P <sup>d</sup>	R <sup>c</sup>	TS	P <sup>d</sup>			
$E(\text{g})^f$	-0.2897	-0.2431	-0.1098	-0.2908	-0.2540	-0.1125	-0.3045	-0.2693	-0.1266	-1.6340	-1.6020	-1.4469
$E(\text{aq})^f$	-0.2894	-0.2416	-0.1090	-0.2902	-0.2461	-0.1112	-0.3042	-0.2682	-0.1259	-1.6331	-1.5963	-1.4456
ZPE <sup>g,h</sup>	46.4	47.6	50.9	46.4	47.6	50.9	46.4	47.6	50.9	46.4	47.6	50.9
$\Delta H_{\text{EVR}}^{\text{g,h}}$	51.3	51.8	55.1	51.3	51.8	55.1	51.3	51.8	55.1	51.3	51.8	55.1
$\Delta G_{\text{EVR}}^{\text{g,h}}$	20.2	29.9	26.9	20.2	29.9	26.9	20.2	29.9	26.9	20.2	29.9	26.9
$\Delta E_{\text{E}}^{\text{g}}$	0.2	1.0	0.5	0.3	5.0	0.8	0.2	0.7	0.4	0.6	3.5	0.8
$G_{\text{P}}^{\text{g}}$	-4.2	-11.6	-162.6	-4.3	-16.3	-162.8	-4.1	-12.6	-162.5	-7.4	-20.9	-162.1
$G_{\text{CDS}}^{\text{g}}$	0.8	0.2	0.1	0.8	0.2	0.1	0.8	0.2	0.1	0.8	0.2	0.1
$\Delta G_{\text{S}}^{\text{g}}$	-3.1	-10.5	-162.0	-3.2	-11.2	-161.9	-3.1	-11.8	-162.0	-6.0	-17.2	-161.2

<sup>a</sup> The 6-31G(d) as is set was used. <sup>b</sup> SM6/mPW1PW/6-31G(d). <sup>c</sup> This species was modeled as a supermolecule with an intermolecular distance of 10 Å. <sup>d</sup> This species was modeled as a supermolecule with an intermolecular distance of 5000 Å. <sup>e</sup> Modeled as two infinitely separated molecules. <sup>f</sup> These energies are in hartrees (1 hartree = 1 E<sub>h</sub> = 627.51 kcal/mol); for ease of tabulation, -555.0000 hartree must be added to each tabulated value to obtain the absolute energy. <sup>g</sup> Energies are in kcal/mol. <sup>h</sup> Calculated at the SM6/mPW1PW/6-31G(d) level of theory.

**TABLE 4: Calculated Free Energies of Activation and Reaction (kcal/mol) for the Menshutkin Reaction in the Aqueous Phase**

	VBSM			SM6	VBPCM <sup>f</sup>	
	VBSCF	BDO	BOVB		VBSCF	BOVB
$\Delta G^{\ddagger}(0)^a$	21.9	15.1	13.4	11.9		
$\Delta G^{\ddagger}(1)^b$	23.1	16.3	14.6	13.1		
$\Delta G^{\ddagger}(2)^c$	22.4	15.6	13.9	12.4		
$\Delta G^{\ddagger}(\text{full})^d$	31.6	24.8	23.1	21.6	31.0	21.8
$\Delta G_{\text{r}}^*(0)^a$	-46.0	-46.9	-47.2	-37.5		
$\Delta G_{\text{r}}^*(1)^b$	-41.5	-42.4	-42.7	-33.0		
$\Delta G_{\text{r}}^*(2)^c$	-42.2	-43.1	-43.4	-33.7		
$\Delta G_{\text{r}}^*(\text{full})^d$	-39.3	-40.2	-40.5	-30.8	-28.2	-29.2
$\Delta G_{\text{r}}^*(\text{expt})^e$			-36 ± 6			

<sup>a</sup> Zero-order approximation; changes in the electronic vibrational-rotational contribution to the free energy are neglected. <sup>b</sup> First-order approximation; changes in the zero-point vibrational energy are included. <sup>c</sup> Second-order approximation; changes in the electronic vibrational-rotational contribution to the enthalpy are included. <sup>d</sup> Full calculation; changes in the electronic vibrational-rotational contribution to the free energy are included. <sup>e</sup> This value was obtained from a thermodynamic cycle by using experimental values for the gas-phase free energy of reaction and aqueous solvation free energies of the reactants and products (see text). <sup>f</sup> VBPCM/6-31G(d) results at the HF/IEFPCM optimized geometry from ref 72.

#### 4. Discussion

The methodological and physical reasons for the differences of the present VBSM results from previous SM6 and VBPCM results are found both in the differences in the construction of the electronic wave function and in the differences in the treatment of the solute-solvent interactions. VBSM differs from previous SM6 methods in the former respect and from VBPCM in the latter. Most of this section is concerned with elaborating on this topic and with discussing the advantages and limitations of the two methods.

Previous applications<sup>22</sup> of SM6 were based on density functional theory, whereas VBSM and VBPCM are based on VB theory. The correlation energy is defined as the difference between the true electronic energy and that calculated by the Hartree-Fock approximation, and contributions to the correlation energy may be sorted into two types: dynamical and static. Density functional theory contains dynamical correlation energy explicitly via the correlation functional, and it contains some static correlation energy in an uncontrolled way in the exchange functional. VB theory contains little or no dynamical correlation

**TABLE 5: Weights of VB Structures Obtained by VBSM/VBSCF and VBSM/BOVB Computations for the Menshutkin Reaction in Aqueous Phase<sup>a</sup>**

	species					
	1	2	3	4	5	6
	VBSCF					
R	0.662	0.093	0.245	0.000	0.000	0.000
R <sup>b</sup>	0.654	0.091	0.255	0.000	0.000	0.000
TS	0.488	0.007	0.437	0.054	0.015	0.000
TS <sup>b</sup>	0.354	0.000	0.530	0.100	0.017	0.000
P	0.000	0.000	0.353	0.607	0.000	0.040
P <sup>a</sup>	0.000	0.000	0.348	0.612	0.000	0.040
	BOVB					
R	0.612	0.112	0.276	0.000	0.000	0.000
R <sup>b</sup>	0.604	0.110	0.287	0.000	0.000	0.000
TS	0.449	0.014	0.415	0.088	0.033	0.000
TS <sup>b</sup>	0.320	0.000	0.484	0.162	0.034	0.000
P	0.000	0.000	0.386	0.546	0.000	0.068
P <sup>a</sup>	0.000	0.000	0.381	0.548	0.000	0.071

<sup>a</sup> VB structures are defined in Table 2. <sup>b</sup> Weights of VB structures obtained by VBPCM/VBSCF and VBPCM/BOVB with 6-31G(d) basis set in ref 72.

energy, but it contains static correlation energy in a way that can be specifically controlled through the choice of configuration-state functions.

SM6 and VBSM treat solvation effects with the GB approximation<sup>31-37</sup> for bulk electrostatics, augmented by surface tension terms<sup>22,37,47,49,50,73</sup> that account for cavitation, dispersion, and solvent structure (CDS), whereas VBPCM treats electrostatic contributions to solvation by using an integral equation formalism<sup>83,84</sup> (IEF) to solve a nonhomogeneous Poisson equation<sup>85</sup> (NPE), and in principle (see below), it augments the IEF-NPE calculation by terms that account for cavitation,<sup>86,87</sup> dispersion,<sup>88</sup> and repulsion<sup>15</sup> (CDR). (Although only dispersion and repulsion are mentioned in ref 19a,b, the standard nonelectrostatic term of the PCM model includes all three terms.) The improvement in the treatment of solvation is the reason for the creation of VBSM. There is a major difference in philosophy between the GB-CDS methods (sometimes called SMx methods) and the philosophy behind IEF-NPE-CDR in that the CDR terms are defined independently of the treatment of electrostatics, whereas the CDS terms are parametrized to be consistent with a given formulation of the bulk electrostatics, as described in the next paragraph.

**TABLE 6: Gas-Phase and Aqueous-Phase Energies for Reactants (R) and Transition State (TS) in the Degenerate S<sub>N</sub>2 Reaction of CH<sub>3</sub>Cl with Cl<sup>-</sup>**

	VBSM <sup>a</sup>						SM6 <sup>b</sup>	
	VBSCF		BDO		BOVB		R <sup>d</sup>	TS
	R <sup>c</sup>	TS	R <sup>c</sup>	TS	R <sup>c</sup>	TS		
<i>E</i> (g) <sup>e</sup>	-0.6484	-0.6250	-0.6540	-0.6345	-0.6632	-0.6555		
<i>E</i> (aq) <sup>e</sup>	-0.6483	-0.6246	-0.6538	-0.6332	-0.6631	-0.6552		
ZPVE <sup>f,g</sup>	24.1	23.6	24.1	23.6	24.1	23.6	24.1	23.6
Δ <i>H</i> <sub>EVR</sub> <sup>f,g</sup>	28.1	27.1	28.1	27.1	28.1	27.1	28.1	27.1
Δ <i>G</i> <sub>EVR</sub> <sup>f,g</sup>	-0.2	5.9	-0.2	5.9	-0.2	5.9	-0.2	5.9
Δ <i>E</i> <sub>E</sub> <sup>f</sup>	0.1	0.2	0.1	0.8	0.0	0.2	0.4	0.5
<i>G</i> <sub>p</sub> <sup>f</sup>	-81.8	-58.4	-82.0	-59.6	-81.8	-56.9	-83.5	-58.8
<i>G</i> <sub>CDS</sub> <sup>f</sup>	1.5	1.0	1.5	1.0	1.5	1.0	1.2	0.8
Δ <i>G</i> <sub>S</sub> <sup>f</sup>	-80.3	-57.1	-80.3	-57.8	-80.2	-55.7	-81.9	-57.5

<sup>a</sup> The 6-31+G(d) basis set was used. <sup>b</sup> SM6/mPW1PW/6-31G(d). <sup>c</sup> This species was modeled as a supermolecule with an intermolecular distance of 10 Å. <sup>d</sup> Modeled as two infinitely separated molecules. <sup>e</sup> These energies units are in hartrees; the reader must add -958.0000 to each number. <sup>f</sup> Energies are in kcal/mol. <sup>g</sup> Calculated at the SM6/mPW1PW/6-31G(d) level of theory.

**TABLE 7: Calculated Free Energies of Activation (kcal/mol) for the CH<sub>3</sub>Cl/Cl<sup>-</sup> Degenerate S<sub>N</sub>2 Reaction in the Aqueous Phase**

	VBSM			SM6	VBPCM <sup>e</sup>	
	VBSCF	BDO	BOVB		VBSCF	BOVB
Δ <i>G</i> <sup>‡</sup> (0) <sup>a</sup>	37.8	34.8	29.4	19.7	34.7	26.1
Δ <i>G</i> <sup>‡</sup> (1) <sup>b</sup>	37.3	34.3	28.9	19.2		
Δ <i>G</i> <sup>‡</sup> (2) <sup>c</sup>	36.8	33.8	28.4	18.8		
Δ <i>G</i> <sup>‡</sup> (full) <sup>d</sup>	43.9	40.9	35.5	25.8		

<sup>a</sup> Zero-order approximation; changes in the electronic vibrational-rotational contribution to the free energy are neglected. <sup>b</sup> First-order approximation; changes in the zero-point vibrational energy are included. <sup>c</sup> Second-order approximation; changes in the electronic vibrational-rotational contribution to the enthalpy are included. <sup>d</sup> Full calculation; changes in the electronic vibrational-rotational contribution to the free energy are included. <sup>e</sup> VBPCM results with the same basis set at the HF/IEFPCM optimized geometry as that in ref 19b.

**TABLE 8: Weights of VB Structures Obtained by VBSM/VBSCF and VBSM/BOVB Computations for the CH<sub>3</sub>Cl/Cl<sup>-</sup> Degenerate S<sub>N</sub>2 Reaction in the Aqueous Phase<sup>a</sup>**

	species					
	1	2	3	4	5	6
	VBSCF					
R	0.662	0.093	0.245	0.000	0.000	0.000
TS	0.227	0.000	0.527	0.227	0.000	0.000
	BOVB					
R	0.612	0.112	0.276	0.000	0.000	0.000
R <sup>b</sup>	0.640	0.097	0.263	0.000	0.000	0.000
TS	0.261	0.005	0.429	0.261	0.039	0.005
TS <sup>b</sup>	0.239	0.003	0.488	0.239	0.029	0.003

<sup>a</sup> VB structures are defined in Table 2. <sup>b</sup> Weights of VB structures obtained by VBPCM/BOVB with 6-31G(d) basis set as in ref 19b.

The bulk electrostatics are intrinsically uncertain because of arbitrariness in the definition, size, and shape of the solute cavity and the way that the gas-phase permittivity inside the solute cavity is joined to the solvent permittivity outside it. This arbitrariness is intrinsic because the concept of a permittivity is a macroscopic one, and it does not strictly apply on the atomistic scale (or even the nanoscale). A further uncertainty in practical applications is the treatment of the tails of electronic charge distributions that extend outside the solute cavity; the charge in these outlying tails is especially significant for anions, which are involved in the applications in the present article. In

recognition of these uncertainties, the structural component of the CDS terms is designed to complement a given formulation of the bulk electrostatics and to account for the atomistic structure of the first solvation shell. Furthermore, the structural component (which also includes repulsion and hydrogen-bonding effects) is not adjusted separately from the electrostatics, cavitation, and dispersion terms; instead the entire CDS term is parametrized simultaneously, which also allows it to compensate for any systematic errors in partial charges and in the way the various terms are combined.

In both the PCM electrostatic model and the SM<sub>x</sub> electrostatic model, the boundary between the solute and the solvent is based on effective atomic radii that will be called intrinsic Coulomb radii. The intrinsic Coulomb radii used in VBSM are those optimized in SM6; they are constants depending only on atomic number. In the VBPCM calculations of ref 19b, using constant radii grossly elevated the energies of the ionic fragments and certain structures along the reaction path; therefore, the radii were specifically adjusted for that application so that different values were used for the reactant and the TS, based on gas-phase charges computed by Mulliken population analysis at the Hartree-Fock level. In the present VBSM calculations of the reaction profiles in solution, no gas-phase charges or Hartree-Fock calculations are used; instead, the entire bulk-electrostatic calculation (i.e., the GB calculation) is based on self-consistent liquid-phase charges obtained by Löwdin population analysis of VB calculations (Löwdin population analysis is generally more basis-set-independent than Mulliken population analysis).<sup>89</sup> Furthermore, in the VBSM calculations presented here, no parameters are adjusted or readjusted for the specific applications under consideration; all parameters are taken from the general SM6 aqueous solvation model.

In the calculations presented in ref 19a,b, all nonelectrostatic terms (the CDR terms of PCM) were omitted, but they could be included in future PCM calculations. In the calculations in the present paper, all CDS contributions were included with the standard SM6 parameters.

The advantage of VBSM over previously available solvation methods is in its unique combination of the GB-CDS approach with the VB theory. The GB-CDS approach has been shown to be capable of much greater accuracy than the NPE-CDR approach (at least in presently available parametrizations) for predicting quantitative free energies of solvation.<sup>22,90,91</sup> The VB theory, on the other hand, has well-known interpretative advantages for discussing chemical reactivity in many contexts.<sup>20,21,92-96</sup>

A final word of caution is in order. Although VBSM can be expected to profit from the high quantitative accuracy of the SM6 approach, the present formulation still omits the CM4 charge mapping,<sup>22</sup> and this will lead to some degradation of accuracy. In future work, it would be worthwhile to add a class-IV charge mapping step.

In the future, it would also be worthwhile to apply VBSM with SM8 parameters. The SM8 model<sup>91</sup> is almost identical to SM6 for aqueous solutions but has also been parametrized to give high accuracy for both neutral and charged solutes in nonaqueous solvents. Because SM8 and SM6 have the same functional forms, no extension is required; only the parameters will be different.

## 5. Conclusion

This paper presents a VB method, called VBSM, that combines VB with the SM6 solvation model to calculate equilibrium free energies of solvation or potentials of mean force. In the examples presented, VB atomic charges at VBSM liquid-phase geometries are used along with SM6 universal solvation parameters. The VBSM method takes the polarization free energy into account in a self-consistent field procedure, and it also includes first-solvation-shell effects. Thus, the VBSM method enables us to study the solvent effects in both aqueous and nonaqueous solution by ab initio VB computation.

The partial atomic charges of some small molecules computed by the VBSCF method indicate that the Löwdin charges of the VBSCF method are more suitable for the VBSM calculation than those obtained by Mulliken population analysis.

The VBSM method is applied to the Menshutkin reaction and the degenerate S<sub>N</sub>2 reaction of CH<sub>3</sub>Cl with Cl<sup>-</sup> at the VBSCF, BDO, and BOVB levels. We find that the VBSCF level of VBSM does not give accurate free energies of activation for the two S<sub>N</sub>2 reactions because of its lack of dynamic correlation. However, the BOVB and BDO levels of VBSM give reasonable results, and the VBSM results for both S<sub>N</sub>2 reactions with general SM6 parameters are in reasonably good agreement with the previous VBPCM study that involved atomic radii parametrized for the specific reaction.<sup>72</sup>

In summary, VBSM is validated as a tool for the study of chemical reactions in solution. The VBSM method shares some of the advantages of the SM6 model for quantitative predictions, and in addition, it provides insights into chemical bonding and bond rearrangement that can only be obtained by using VB wave functions. In addition, the VB formulation, because it involves an interacting state picture, can serve as a useful starting point for treating nonequilibrium solvation.<sup>97-99</sup>

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