Thole's interacting polarizability model in computational chemistry practice

4 AUTHORS:

Alex H de Vries
University of Groningen
60 PUBLICATIONS   **4,907** CITATIONS

SEE PROFILE

Piet Th. van Duijnen
University of Groningen
110 PUBLICATIONS   **3,479** CITATIONS

SEE PROFILE

R.W.J. Zijlstra
University of Groningen
27 PUBLICATIONS   **943** CITATIONS

SEE PROFILE

Marcel Swart
Catalan Institution for Research and …
155 PUBLICATIONS   **3,434** CITATIONS

SEE PROFILE

ELSEVIER

Thole's interacting polarizability model in computational chemistry practice

Alex H. de Vries[a],[*], Piet Th. van Duijnen[b], Rob W. J. Zijlstra[b], Marcel Swart[b]

[a]*Department for Computation and Information, Daresbury Laboratory, Daresbury, Warrington WA4 4AD, UK*
[b]*Department of Chemistry (OMAC), University of Groningen, Nijenborgh 4, 9747 AG Groningen, The Netherlands*

Abstract

Thole's interacting polarizability model to calculate molecular polarizabilities from interacting atomic polarizabilities is reviewed and its major applications in computational chemistry are illustrated. The applications include prediction of molecular polarizabilities, use in classical expressions for intermolecular interactions for the computation of binding energies of molecular dimers, solvation (free) energies, and solvent effects in combined quantum-chemical-classical (QM-MM) calculations.

The examples demonstrate the wide applicability of the model, which is due to its firm foundation in the perturbation theory of intermolecular interactions, from which the polarizability emerges as one of the material properties determining the interaction between species. The true power of the model is its generality, rendering transferability to all sorts of chemical problems almost a non-issue. © 1997 Elsevier Science B.V.

Keywords: Classical modelling of molecular polarizability; Intermolecular interactions; Hybrid QM-MM methods

1. Introduction

Computational approaches to probe nature's secrets have always looked for ways to escape brute-force methods. Two obvious reasons for this are the limitations computational resources put on the feasibility of brute-force methods and the fact that these methods do not provide us with anything we regard as 'insight': a simple, appealing concept valid in a wider setting than the particular system under study.

Brute-force methods cannot be avoided, however, because one encounters the limitations of simpler material models in representing nature as it appears to us: there is a hierarchy of detail which is required to explain certain phenomena. More specifically, in

* Corresponding author. Tel. +44 1925 603362; fax: +44 1925 603634; e-mail: ahv@dl.ac.uk

physical chemistry virial coefficients may be calculated quite successfully by accounting for interactions between molecules, and infrared spectra may be simulated from an atomic interaction model, but, for example, bond-breaking/bond-making reactions and electronic spectra require a quantum-mechanical description at the level of interactions between nuclei and electrons, including the consequences of the Pauli principle. Also, the more detailed descriptions provide the underlying rationale for coarse-grained methods and may be used to obtain numerical input (the parameters) for them.

In chemistry, the entities of interest span a range of length-scales. There is a need to know about electronic motions for spectroscopy, atomic movement for reactions, and molecular behaviour for material properties. This diversity of interest explains the multitude of concepts current in chemistry. Initial

approaches to explaining phenomena focus on a particular scale in isolation, as it were, but a second look obviates the need to consider other levels as well and the simple concepts need to be modified and expanded. A well-defined hierarchy is an asset to combine different levels sensibly, preserving the simple picture whilst accounting for subtle perturbative effects in a general, unforced way.

Thole's interacting polarizability model is one such sensible approach in computational chemistry, enabling the description of the effects of material directly surrounding a region of particular chemical interest (be it a reaction or a chromophore) which requires a quantum-chemical description (at the level of nuclei and electrons) *without including the same level of detail of the surroundings*. Rather it expresses the electronic response of the surroundings (the polarizability, which is a collective property) to an applied field in terms of the classical quantity. The power of the model lies in its simplicity and generality. In this short review, we will discuss the ideas underlying the model, and demonstrate its generality by recalling a selection of applications in computational chemical studies.

2. Concepts

Thole developed the interacting polarizability model as part of a scheme to perform meaningful calculations on processes of interest in biochemistry [1,2]. The idea was to model the region of interest by a quantum-chemical treatment, accounting for the attenuating effects of the surroundings via classical models. The parameterization of the classical models should be such that a maximum amount of physical content should be preserved.

Arguing from the perturbation theory of intermolecular interactions, the natural properties of the surroundings to be represented in an interaction model are the charge distribution and the polarizability. These entities are properties of the molecules by themselves and can be used to predict the behaviour of molecules when thrown together. Both the measurement [3,4] and computations [5] of these properties is quite difficult, especially for larger molecules, higher electrostatic moments, and polarizabilities. A simple, empirical scheme for obtaining reliable

polarizabilities is therefore an enormous asset to both experimental and theoretical approaches to intermolecular interactions.

For the theoretical approaches, a reliable polarizability representation is paramount to obtaining conceptually straightforward, general force fields. It was this vision of constructing a general approach for the inclusion of the electrostatic field and electronic response of material surrounding an active site described in quantum-chemical detail that instigated the search for a reliable polarizability model [1].

Earlier work by Appleqvist [6] and Birge [7] (following original work by Silberstein [8]) provided the starting point for Thole's model. The basis of the idea is that molecular polarizabilities may be expressed as the result of interacting atomic polarizabilities.

The dipole–dipole polarizability (the first response function resulting from the perturbation expansion and the only one we will be concerned with here) expresses how a charge distribution will deform due to an applied electric field E^0 in terms of an induced dipole moment

$$\mu_{mol} = \alpha_{mol} E^0 \tag{1}$$

Following what is called 'chemical intuition', it is quite conceivable that a molecular induced dipole moment may be built up from induced dipole moments on atoms, where the underlying atomic polarizabilities show a high degree of transferability between different molecules, just as quantum chemists successully use the same Gaussian basis sets for atoms through a range of molecules

$$\mu_{mol} = \sum_i \mu_i = \sum_i \alpha_i E \tag{2}$$

The obstacle to this approach is that the atomic polarizabilities must interact within the molecule in order to be able to distinguish between molecules of the same composition but different geometry, e.g. through different connectivity. If E in Eq. (2) is just the applied field, the molecular dipole moment will be the sum of the atomic dipole moments, which are independent of geometry because the applied field is homogeneous. The actual field at the atomic positions will be inhomogeneous, however, through distortions of the charge distribution inside the molecule. By allowing the polarizabilities to interact, geometrical

information may be built into the model

$$\mu_{mol} = \sum_i \mu_i = \sum_i \alpha_i \left\{ \mathbf{E}^0 - \sum_{j \neq i} T_{ij} \mu_j \right\} = \alpha_{mol} \mathbf{E}^0 \qquad (3)$$

Now, the resulting molecular polarizability is obtained by solving the coupled equations implied in Eq. (3), by contracting the $3N \times 3N$ coupling matrix which sums the atomic polarizabilities and their interactions, and diagonalizing the resulting matrix

$$\alpha_{mol} = \sum_i \sum_j \left\{ \alpha_i^{-1} + T_{ij} \right\}^{-1} \qquad (4)$$

The earlier models used the full dipole–dipole interaction tensor T_{ij} in Eq. (3), thus assuming point-polarizabilities. The parameterization was then made in representing the behaviour of the components of the atomic polarizability tensors α_i. Thole's contribution to the model was the realization that in reality the classical entities do not represent point properties, but collective properties and therefore have an extension in space. In casu, the electrons circling a nucleus to make up an atom fill a certain region in space. When two atoms come close, the extended charge distributions overlap, giving rise to an *interaction* that is *modified* with respect to what they would be if the atoms were truly point-like. Thus, Thole investigated a number of realistic shapes for the atomic charge distributions and calculated a modified dipole–dipole interaction tensor for them, keeping the atomic polarizabilities isotropic. The atomic and resulting molecular polarizabilities are still assumed to be point-like; it is their effect on other atoms that is modified through the shape-function. The success of this approach compared to the earlier work was the enormous reduction in parameters needed to get a good or even better agreement between calculated and observed molecular polarizabilities. All that was required was one atomic polarizability for each atom type, irrespective of its type of chemical binding, and one scaling parameter for the shape-function itself.

With this model in place, in combination with the Dipole Preserving Charge (DPC) analysis [9] for the representation of the charge distribution from ab initio calculations, the ingredients for performing fully classical and combined QM-MM calculations were prepared. Scrutiny of the expectation values of

the reaction-field operator

$$H_{DRF} = \mathbf{F}^\dagger \alpha \mathbf{F} \qquad (5)$$

where $\mathbf{F}$ is the field operator, revealed that both induction and dispersion interactions between a quantum-chemically treated subsystem A and a classically modelled subsystem S are evaluated [2]. Although the dispersion as treated in this Direct Reaction Field (DRF) approach is approximate [2,10], the method is extremely powerful as distinction can be made between electronic states in their dispersion interaction with the surroundings.

The success and wide applicability of this model is demonstrated in the next section, ranging from purely classical calculations of intermolecular interactions between dimers to state-of-the-art combined quantum-chemical-classical approaches to solvated molecules.

3. Applications

3.1. Molecular polarizabilities

The earliest application of Thole's interacting polarizability model was the prediction of molecular polarizabilities from interacting atomic polarizabilities as part of the fitting procedure to obtain parameters for the model [1]. Fig. 1 shows the correlation between the polarizabilities from experiment and Thole's model for both the learning set used by Thole, and for a number of molecules outside the learning set, using the so-called linear shape function. The agreement is remarkably good considering the wide range of compound types.

Note the compounds marked with the diamonds in Fig. 1 which have chemical binding types outside those in the learning set. Even these compounds are catered for very well. Most of these compounds have aromatic rings, and the defect of the polarizability is in the out-of-plane component. Attempts to correct for this default have been made for benzene in a classical treatment of the benzene–benzene interaction (see also Section 3.2) [11]. The atomic polarizabilities and the scaling parameter for the so-called exponential and linear shape-functions have recently been refitted in the context of the combined QM-MM DRF model [12]. The refitting
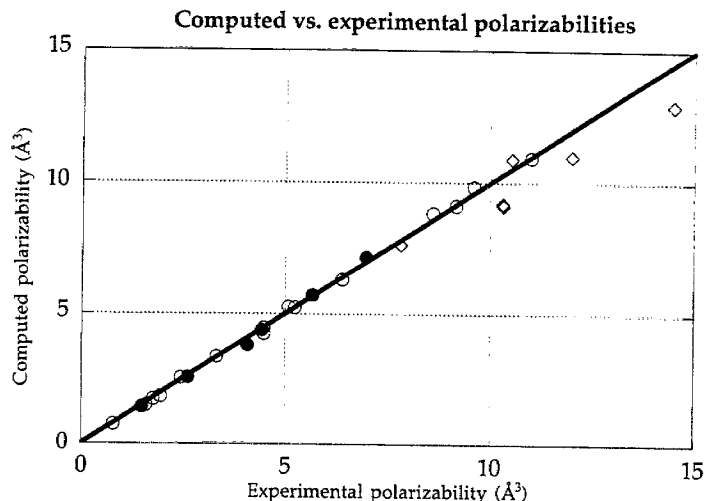
Computed vs. experimental polarizabilities

Fig. 1. Comparison between observed and computed molecular polarizabilities: O, compounds in learning set; ●, compounds outside learning set; ◇, compounds with binding types outside learning set.

included the halogens and was done to both experimental and computed molecular polarizabilities. The latter has the advantage that the molecular geometries are well-defined and that a consistent QM-MM model may be built up from ab initio building blocks.

3.2. Classical treatment of intermolecular interactions

The dipole polarizability is involved in the induction and dispersion terms that appear from the second-order perturbation treatment of intermolecular interactions, as explained above. The magnitude of
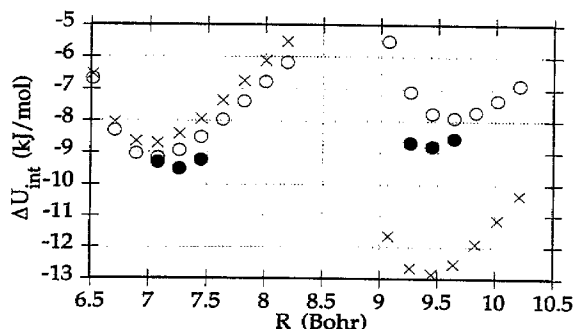

Fig. 2. Benzene dimer interaction energy as a function of intermolecular distance. Left, parallel-displaced orientation; right, perpendicular orientation; O, standard parameters; ×, scaled parameters; ●, Hobza et al. (ab initio results).

these terms as they come out of Thole's model has been validated against quantum-chemical reference calculations for the water dimer, showing satisfactory agreement for both the linear and exponential shape functions [11,13,14]. The polarizabilities have also been applied to the interaction between (mixed) dimers of substituted arenes [11], which require very expensive quantum-chemical calculations. Fig. 2 shows interaction curves for two orientations of benzene molecules in the dimer.

As noted in Section 3.1, the standard model fails to fully reproduce the molecular polarizability of benzene, due to the fact that the model used atomic centres only, and much of the charge distribution of benzene is out of the molecular plane. Nevertheless, Fig. 2 shows that the standard parameters reproduce the ab initio quantum-chemical results of Hobza et al. [15,16] very well. Scaling the atomic polarizabilities to reproduce the molecular polarizability causes the perpendicular arrangement to be more stable. This simple scaling of the parameters is probably not the best way to improve the parameters in these compounds, as it does not lead to the experimental anisotropy. Interestingly, the standard model does excellently for a number of substituted benzenes in comparison to experiment. Further studies into these types of dimer complexes with the refitted parameters (see Section 3.1) confirm the delicate balance between the parallel-displaced and perpendicular arrangements

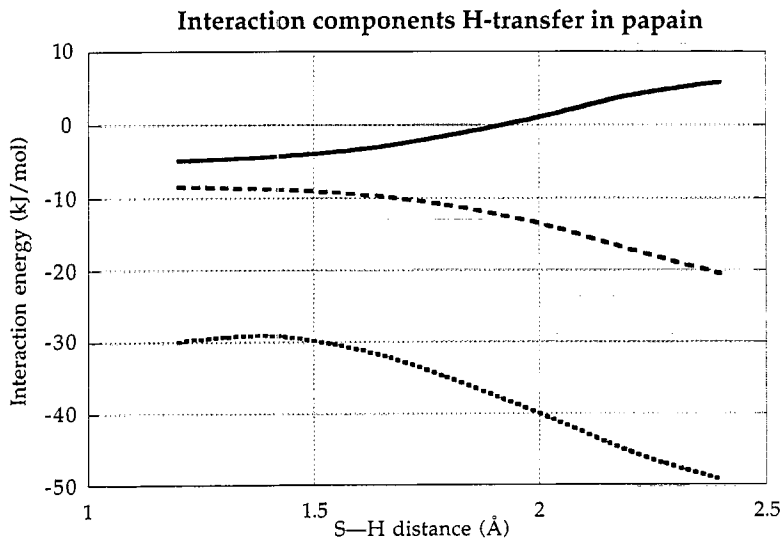**Interaction components H-transfer in papain**

Fig. 3. Interaction components between active site and surroundings in QM-MM study of papain as a function of S–H distance. ——————, screening; - - -, induction; · · ·, Coulomb interaction.

and the shifting of the preferred conformation with different substitution patterns [17].

Further application has been in the calculation of solvation energies of different solutes in water [11,14,18] by Monte Carlo sampling methods. These values have been compared to dielectric continuum models for aqueous solvation. The general conclusion is that the explicit solvent model is much more generally applicable and reliable than dielectric continuum models, be it at a much higher cost.

Other groups have developed similar approaches to dealing explicitly with polarizable solvent molecules [19–26]. Most studies with these approaches have concentrated on water as a solvent. In combined QM-MM calculations (see Section 3.3), our group has treated other solvent molecules on the same basis as water without the need for reparameterization, opening the way for a very simple 'universal' force field for the simulation of solvated systems.

3.3. Combined QM-MM treatment of intermolecular interactions

Thole started a series of investigations into the mechanism of proteolytic enzymes, more specifically, the roles of the α-helix and of specific residues in the active site in stabilizing the ionic form, which is clearly unstable when the active site is modelled without the surrounding material present [27]. He found the electrostatic field of the α-helix to be the major attenuating influence, but there was clearly some extra stabilization of the ionic form due to the polarizability of the surroundings. Rullmann [28] and Dijkman [29] extended these initial investigations, using more accurate X-ray data and adding the solvent effect by explicit modelling of solvent molecules and a surrounding dielectric to model bulk solvent. They largely confirmed Thole's initial findings.

It is interesting to note one observation made by Rullmann, however, concerning the effect of polarizable material at a microscopic level. He noted first of all that the effect of the polarizable surroundings was not quite as large as anticipated: the ionic form is expected to be much more stabilized due to its large dipole moment interacting favourably with the surroundings (induction). This is found to be true, but a destabilization due to the attenuation of the electrostatic interactions through the polarizable environment (screening) counteracts the induction.

Fig. 3 shows the screening and induction contributions to the total energy for the H-transfer curve in papain, as well as the Coulomb interaction for comparison. The screening and induction terms counteract each other as the active site becomes more ionic (larger S–H distance). The screening just happens to be destabilizing in this case. Rullmann noted this

Table 1

Analysis of the contributions to the excitation energy shifts (in cm^{-1}) of acetone in H_2O, MeCN, and CCl_4 for the explicit solvent model

Contribution	Solvent					
	H_2O		CH_3CN		CCl_4	
	Ref.[a]	MC[b]	Ref.[a]	MC[b]	Ref.[a]	MC[b]
Polarization	− 608	− 611	− 518	− 298	− 48	− 75
Induction	+ 888	+ 903	+ 974	+ 512	+ 96	+ 151
Electrostatic	+ 2509	+ 2726	+ 1141	+ 1,673	+ 9	+ 18
Dispersion	− 1149	− 1197	− 978	− 965	− 273	− 475
Total	+ 1639	+ 1821	+ 620	+ 922	− 216	− 381
Experimental	+ 1700 ± 200		+ 400 ± 200		− 350 ± 200	

[a] Reference geometry, obtained after equilibrating solvent molecules to classically described acetone.
[b] Monte Carlo average: 7000 steps for water; 7500 for MeCN; and 15 000 for CCl_4.

phenomenon, which cannot be modelled by a dielectric continuum model. The microscopic behaviour of polarizable material is not the same as the macroscopic behaviour, where the charge–charge interaction is always diminished by the intervening polarizable material. At a microscopic level, like charges may repel each other more than in a vacuum, depending on the amount of polarizable material present in their neighbourhood, as was reconfirmed by again using Thole's model to fill space with interacting polarizabilities to model a polarizable material at the microscopic level [30].

For various reasons, the interests of the group at Groningen diverted to solvation effects. The DRF QM-MM method for modelling these effects with explicit, polarizable solvent molecules was shown to be superior to the ubiquitous dielectric continuum self-consistent reaction-field (SCRF) models [11,18]. Apart from offering a natural extension from aqueous solutions to treating any type of solvent, the explicit polarizability model provides a handle to distinguishing between ground- and excited states as concerns the dispersion interactions between solute and solvent. This distinction proves to be essential for both qualitative and quantitative calculation of solvent-induced shifts on electronic spectra. Table 1 shows results for the $\pi^* \leftarrow n$ transition of acetone in three different solvents [31].

The dispersion contribution to the shift is negative in all cases due to the larger polarizability of the excited state with respect to that of the ground state. It is this contribution which is essential to reproducing the red-shift in non-polar solvents, such as CCl_4.

Further application of the model is currently the solvent effect on the potential energy surface (PES) and electronic coupling of the V and S states of ethylene as a function of the twist-angle around the C–C bond. These studies are helping to relate the experimental observations concerning the observed dipole moment after excitation and the life-times of the states in different solvents [32]. The polarizability does not seem to be all-important in these systems in directing the electronic state, but once a dipolar state of the substrate has been occupied, the polarization of the solvent helps in stabilizing this state. Furthermore, the ease of accounting for the dispersion interaction with the different electronic states proves an asset to describing these systems reliably. Also, the solvent effect on the S_N1 dissociation step for t-butylchloride is being studied, with a potential of the mean force solvent effect on the vacuum potential energy surface in excellent agreement with experimental data [33]. From all of these studies, Thole's polarizability model emerges as being particularly powerful in treating polar and non-polar solvents on an equal basis in an entirely general way.

Apart from our group, Thole's model has been implemented in two other QM-MM packages [34,35].

4. Conclusion

It has been shown in this review that Thole's model of interacting polarizabilities for describing inter- as well as intramolecular interactions has a wide range of applicability with a minimum of effort. It can be

used to predict molecular polarizabilities from a knowledge of structure. It can be used to provide induction and dispersion terms in a classical force field. In combined QM-MM methods, polarization of the surroundings at a microscopic level may be described for many types of material (protein matrix, solvents), with an ease of deriving force-field parameters that is unparallelled by the more widespread force-fields. It may be concluded from these studies that Thole's polarizability model in conjunction with Thole and van Duijnen's dipole preserving charges (DPCs) offer a straightforward approach to obtaining reliable force fields for solvated systems across a wide range of solutes and solvents. The realization that accounting for electronic polarizability explicitly in classical descriptions of molecules is essential in modelling solvent effects has recently grown to such an extent that all major packages now provide these options or promise to do so shortly.

Acknowledgements

References

[1] B.T. Thole, Chem. Phys. 59 (1981) 341.
[2] B.T. Thole, P.Th. van Duijnen, Theor. Chim. Acta 55 (1980) 307.
[3] J. Bentley, in P. Pulitzer, D.G. Truhlar (Eds.), Chemical Applications of Atomic and Molecular Electrostatic Potentials, Academic Press, New York, 1981.
[4] A.D. Buckingham, in B. Pullman (Ed.), Intermolecular Interactions: From Diatomics to Biopolymers, John Wiley and Sons, Chichester, 1978.
[5] C.E. Dykstra, S.-Y. Liu, D.J. Malik, in I. Prigogine, S.A. Rice (Eds.), Advances in Chemical Physics, J. Wiley and Sons, Inc., New York, 1989.
[6] J. Appleqvist, J.R. Carl, K.K. Fung, J. Am. Chem. Soc. 94 (1972) 2952.
[7] R.R. Birge, J. Chem. Phys. 72 (1980) 5312.
[8] L. Silberstein, Philos. Mag. 33 (1917) 92, 215, 521.
[9] B.T. Thole, P. Th. van Duijnen, Theor. Chim. Acta 63 (1983) 209.
[10] J.G. Ángyán, G. Jansen, Chem. Phys. Lett. 175 (1990) 313.
[11] P.Th. van Duijnen, A.H. de Vries, Int. J. Quant. Chem. (1996) in press.
[12] M. Swart, P.Th. van Duijnen, to be published (1997).
[13] B.T. Thole, P.Th. van Duijnen, Chem. Phys. 71 (1982) 211.
[14] J.A.C. Rullmann, P.Th. van Duijnen, Mol. Phys. 63 (1988) 451.
[15] P. Hobza, H.L. Selzle, E.W. Schlag, J. Am. Chem. Soc. 116 (1994) 3500.
[16] P. Hobza, H.L. Selzle, E.W. Schlag, Chem. Rev. 94 (1994) 1767.
[17] M. Swart, P.Th. van Duijnen, to be published (1997).
[18] A.H. de Vries, P.Th. van Duijnen, A.H. Juffer, Int. J. Quant. Chem., Quant. Chem. Symp. 27 (1993) 451.
[19] A. Warshel, M. Levitt, J. Mol. Biol. 103 (1976) 227.
[20] A. Wallqvist, G. Karlström, Chem. Scr. 29A (1989) 131.
[21] P. Ahlström, A. Wallqvist, S. Engström, B. Jönsson, Mol. Phys. 68 (1989) 563.
[22] F.S. Lee, A. Warshel, J. Chem. Phys. 97 (1992) 3100,
[23] E.C. Meng, P. Cieplak, J.W. Caldwell, P.A. Kollman, J. Am. Chem. Soc. 116 (1994) 12 061.
[24] A.J. Stone, Mol. Phys. 56 (1985) 1065.
[25] G. Karlström, Theor. Chim. Acta 60 (1982) 535.
[26] G. Karlström, P. Linse, A. Wallqvist, B. Jönsson, J. Am. Chem. Soc. 105 (1983) 3777.
[27] B.T. Thole, P.Th. van Duijnen, Biophys, Chem. 18 (1983) 53–59.
[28] J.A.C. Rullmann, M.N. Bellido, P.Th. van Duijnen, J. Mol. Biol. 206 (1989) 101.
[29] J.P. Dijkman, P.Th. van Duijnen, Int. J. Quant. Chem. Quant. Biol. Symp., 18 (1991) 49.
[30] P.Th. van Duijnen, A.H. de Vries, Int. J. Quant. Chem. Quant. Chem. Symp., 29 (1995) 523.
[31] A.H. de Vries, P.Th. van Duijnen, Int. J. Quant. Chem. 57 (1996) 1067.
[32] R.W.J. Zijlstra, P.Th. van Duijnen, A.H. de Vries, Chem. Phys. 204 (1995) 439.
[33] M. Swart, P.Th. van Duijnen, to be published (1997).
[34] D. Bakowies, W. Thiel, J. Phys. Chem. 100 (1996) 10580.
[35] M. Vinkers, J.H. van Lenthe, A.H. de Vries, to be published (1997).