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ASSESSMENT OF LOPROP AND MPPROP MOLECULAR MECHANICS POTENTIALS FOR AMINO ACIDS

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Localized multipole moments up to the fifth moment as well as the dipole polarizabilities has been calculated with the MpProp and the newly developed LoProp methods for a total of twenty molecules, predominantly derived from amino acids. A comparison of electrostatic potentials calculated from the multipole expansion given by the two methods with *ab initio* results shows that both methods reproduce the electrostatic potentials with a rms error of less than 0.1 kJ/mol when terms up to the octupole moments are included. The polarizability is determined with the same accuracy. The MpProp method gives better multipole moments, whereas LoProp gives better polarizabilities.

Keywords: Multipole Moments, Polarizabilities, MOLCAS

1. Introduction

When an *ab initio* calculation is carried out, the resulting energies and properties describe the system as a whole. For a calculation on something like a single water molecule, it is indeed interesting to know the molecular energy, dipole moment, etc. However, this is not the case for large systems, since the chemical properties usually are confined to a single center in the molecule. For such systems, it is usually more informative to divide the molecular charge, multipole moments, and polarizabilities into local contributions, which give better insight into the actual chemical properties of the system. For example, it is be possible to estimate the electrostatic potential of the system from the localized charges and multipoles.

In order for such an approach to be useful, the method of localizing the properties must possess certain qualities: it should be computationally cheap, since we deal with large molecules; it should produce results that are physically meaningful; and the localized results should reproduce the global properties. A successful implementation of a localization scheme would make it possibile to determine the full intermolecular potentials from ab initio calculations. Such potentials have the great advantage over using empirical or semiempirical potentials in that they include more of the underlying physics and thus can be used to describe systems that have not been studied experimentally or have not been included in the parameterization of the potentials.

Several partitioning schemes have been proposed, e.g. the Mulliken[1] and the Löwdin[2] population analysis, the distributed multipole analysis (DMA) by Stone[3], the approach suggested by Williams based on the electrostatic potential[4], the Atoms in Molecules (AIM) scheme suggested by Bader[7,8] and similar methods by Cioslowski [9] and Lazzeretti and coworkers[10], as well as the Natural Atomic Orbitals (NAO) analysis developed by Weinhold *et al.*[11].

The partitioning of polarizabilities into local contributions is more tedious than for multipole moments[12]. As for the multipole moments, several schemes for distributing the polarizabilities have been suggested, e.g. the uncoupled Hartree–Fock approximation by Karlström[13] and more elaborate methods such as the one by Stone[14,15]. However neither of these schemes fulfill all the requirements listed above. For a more extensive discussion of the various methods see Gagliardi *et al.*[17].

However, recently the LoProp method[17] was proposed and implemented into the MOLCAS package[20]. By this approach, the local contributions of the charge, an arbitrary multipole moment, and the polarizability can be calculated at any level of theory in principle. It has been demonstrated[17] that the LoProp approach is computational cheap, gives transferable local properties, and that global properties can be reproduced from LoProp local properties.

In this paper we will investigate how well the newly developed LoProp method reproduces the electrostatic potential around a number of molecules. Its performance will be compared to the old methods for obtaining distributed multipoles and polarizabilities in MOLCAS[20], which are collectively denoted MpProp and are based on the Mulliken approach and the uncoupled Hartree–Fock approximation, respectively.

2. Methods

Here follows a short description of the LoProp and MpProp methods.

2.1. *LoProp*

Localization in LoProp is done by dividing the basis functions into "occupied" and "virtual" orbitals. The occupied orbitals are defined as the doubly occupied orbitals plus the valence orbitals for the atom in question. The rest of the orbitals are included in the virtual subspace.

This scheme requires that the basis functions are the atomic orbitals of each specie making it preferable to use basis sets of the ANO type, although other basis set types may be recontracted to give the desired properties.

The LoProp basis is obtained by a four-step diagonalization: First, it is ensured that each atomic block is orthonormal (in principal trivial for ANO type basis sets). Then, the basis in the occupied and virtual subspaces, respectively, are orthonormalized. In the third step, all components in the virtual-occupied and occupied-virtual blocks are projected out. Finally, the virtual subspace is orthonormalized. The total transformation matrix can be written as a product of the four individual matrices.

The static properties can with this transformation be found as:

$$\langle O_{AB} \rangle = \sum_{\mu \in A, \nu \in B} D_{\mu\nu}^{\text{LoProp}} \left\langle \mu \left| \hat{O} \right| \nu \right\rangle^{\text{LoProp}} \tag{1}$$

where $\hat{O}$ is the operator associated with the property; A and B are the indices of the atoms, i.e. $A = B$ specifies an atom center, otherwise it is a bond. D^{LoProp} is the 1-electron density matrix in the LoProp basis. It is worth noticing two things with this scheme. Since the LoProp basis is diagonal, charges from Eqn. 1 will be non-zero only if $A = B$, i.e. on an atom. Furthermore, one should be aware that the dipole moment and higher moments are origin dependent. In this work all results for atoms have been calculated at the atomic centers, and for the bond domains, the midpoint between the atoms has been chosen.

For the localized polarizabilities we have:

$$\begin{aligned} \alpha_{\kappa\lambda}^{AB} = & \frac{\mu_\kappa^{(AB)} (\mathbf{F} + \delta_\lambda) - \mu_\kappa^{(AB)} (\mathbf{F} - \delta_\kappa)}{2\delta_\kappa} \\ & + \frac{\left(\Delta Q^{(AB)} (\mathbf{F} + \delta_\lambda) - \Delta Q^{(AB)} (\mathbf{F} - \delta_\lambda)\right) \left(\mathbf{R}^{(A)} - \mathbf{R}^{(B)}\right)_\kappa}{2\delta_\kappa} \end{aligned} \tag{2}$$

Here κ, λ symbolizes the cartesian axes (x, y, z); $\mu_\kappa^{(AB)}$ is the localized dipole moment in the κ direction; $\mathbf{F}$ is the electric field; δ_κ is the perturbation in the field; $\Delta Q^{(AB)}$ is the charge transfer from center A to center B due to the change of the electric field; and $\mathbf{R}^{(A)}$ and $\mathbf{R}^{(B)}$ are the coordinates for centers A and B, respectively.

For a complete discussion of the LoProp method, see Gagliardi *et al.*[17].

2.2. *MpProp*

The MpProp method involves procedures for obtaining distributed multipoles and polarizabilities. The multipole procedure is based on the Mulliken approach[1] of obtaining atomic charges, generalized by Karlström[18] to provide higher multipole moments as well. The basic observation is that each pair of basis functions represents a charge distribution. That distribution is located at a site, which can be either an atom (if both basis functions belong to the same atom) or a bond (if they belong to different atoms). Here, a bond is defined between every pair of atoms in the molecule. It is then natural to define the charge for site K as

$$q_I = \sum_{(p,q)\in K} D_{pq}\langle\phi_p|\phi_q\rangle + Z_K \tag{3}$$

where D_{ij} is the density matrix element for basis functions ϕ_p and ϕ_q, and Z_K is the nuclear charge if K is an atom or zero otherwise. Higher multipoles are obtained by replacing the overlap integrals with the corresponding dipole integrals, quadrupole integrals, etc.

In contrast to the case for LoProp, charges in the bonds are not necessarily zero. Higher-order bond moments are generally nonzero in both methods. In order to obtain a representation with multipoles only on atoms, the bond multipoles have to be moved. In the original Mulliken approach, one-half of the contribution was moved to each atom. In the MpProp method, it is done with the scaling factor $r_{P,pq}/r_{PQ}$, where $r_{P,pq}$ is the distance between atom site P and the coordinate for the pair of basis functions $p \in P$ and $q \in Q$ and r_{PQ} is the bond distance between atoms P and Q. This strategy preserves the dipolar contribution from a charge.

The localized polarizabilities in the MpProp method are obtained in the uncoupled Hartree–Fock (HF) approximation[13]. The polarizability of a molecule is given in second-order perturbation theory by

$$\alpha_{\alpha\beta} = 2\sum_{n\neq 0} \frac{\langle 0|\, r_\alpha \,|n\rangle \, \langle n|\, r_\beta \,|0\rangle}{E_0 - E_n} \tag{4}$$

In the uncoupled HF approach, the states are taken to be singly excited HF determinants, formed from the unperturbed molecular orbitals. Thus, the polarizability reduces to

$$\alpha_{\alpha\beta} = 4\sum_{i}^{occ}\sum_{a}^{vir} \frac{\langle \psi_i|\, r_\alpha \,|\psi_a\rangle \, \langle \psi_a|\, r_\beta \,|\psi_i\rangle}{\epsilon_a - \epsilon_i} \tag{5}$$

Expanding the occupied molecular orbitals in the basis functions, $\psi_i = \sum_p c_{ip}\phi_p$, and using the same approach as for the distributed multipoles, it is possible to define the distributed polarizability for site K as[13]

$$\alpha^K_{\alpha\beta} = 4\sum_i^{occ}\sum_a^{vir}\sum_{(p,q)\in K} \frac{c_{ip}c_{iq}\left\langle\phi_p\right| r_\alpha - r^{ia}_\alpha \left|\psi_a\right\rangle \left\langle\psi_a\right| r_\alpha - r^{ia}_\alpha \left|\phi_q\right\rangle}{\epsilon_a - \epsilon_i} \tag{6}$$

where r^{ia} is the midpoint of the centers of charge for the molecular orbitals ψ_i and ψ_a.

In this study, the MpProp procedure was modified in order to obtain polarizabilities at the density functional level of theory. The optimized Kohn–Sham orbitals were first localized and the orbital energies were evaluated at the Hartree–Fock level, without letting the orbitals relax. We have not used DFT orbital energies in Eqn. 6 because such a use is not well tested and it seems to lead to a significant overestimation of the polarizabilities.

In general, the uncoupled Hartree–Fock approach does not reproduce the polarizability obtained in a perturbation calculation and the use of Kohn–Sham orbitals as well as the localization certainly introduces further discrepancy. Therefore, the MpProp polarizabilities were linearly scaled by three factors (x, y, and z direction) for each molecule, so that the total polarizability of the molecule attained the same value as in a perturbation calculation.

3. Details of Calculations

A total of 20 molecules have been investigated with both methods. A complete list of the molecules can be found in Table 1.

Molecule	Parent Amino Acid	Molecular formula
A	Glycine	$H(CH_2CONH)_2CH_3$
B	Valine	$CH(CH_3)_3$
C	Serine	CH_3CH_2OH
D	Cysteine	CH_3CH_2SH
E	Methionine	$CH_3CH_2SCH_3$
F	Aspartate	$[CH_3CH_2CO_2]^-$
G	Phenylalanine	$(C_6H_5)CH_3$
H	Lysine$^+$	$CH_3CH_2NH_3^+$
I	Arginine$^+$	$[CH_3NHC(NH_2)_2]^+$
J	Histidine ($H^{\epsilon 2}$)	$(C_3N_2H_3)CH_3$
K	Histidine$^+$	$[(C_3N_2H_4)CH_3]^+$
L	Histidine ($H^{\delta 1}$)	$(C_3N_2H_3)CH_3$
M	Tyrosine	$CH_3(C_6H_4)OH$
N	Glutamine	$CH_3CH_2CONH_2$
O	Tryptophan	$(C_6H_4)(C_2NH_2)CH_3$
P	Proline	$(C_4NH_8)COCH_3$
Q		CH_3OCH_3
R		CH_3COOCH_3
V		NH_3
W		H_2O

Table 1. The molecules investigated.

The conformations of the larger molecules were selected by cutting out the corresponding amino acid residues from some arbitrary proteins in the Protein Data Bank. The geometries of all molecules were optimized at the B3LYP/6-311+G(2d,2p) level.

All LoProp and MpProp calculations were performed at the DFT level of theory using the B3LYP functional and Dunning's cc-pVTZ basis set[19]. Since LoProp needs the basis set to be of an ANO type, all basis sets used for these calculations were recontracted to fulfill this requirement. This recontraction does not affect the molecular results.

The LoProp calculations have been done with the MOLCAS 6.5 software package[20], whereas the reference DFT calculations were performed with Turbomole 5.6 [21]. The MpProp calculations were performed with MOLCAS 6.5, but using wavefunctions optimized by Turbomole.

For testing the performance of the multipoles, the electrostatic potential from the ab initio density was computed at 10000 points around each molecule. Then, for each set of multipoles to test, the electrostatic potential generated by the multipoles was computed at the same points and the absolute deviation was recorded. The points were randomly located in the space P defined as

$$P = \{\mathbf{r} : \min(|\mathbf{r} - \mathbf{R_i}|/a_i) > 2 \text{ and } \min(|\mathbf{r} - \mathbf{R_i}|) < 8 \text{ Å}\} \tag{7}$$

where $\mathbf{R_i}$ and a_i are the position and van der Waals radius, respectively, of atom i. In that space, the charge penetration effect was negligible, as was shown by observing that the potential from the multipoles converged to the ab initio values when the multipole expansion was truncated at a sufficiently high level.

For testing the performance of the polarizabilities, the change in electrostatic potential when applying a homogeneous electric field of 0.01 atomic units in the x direction **xxx Not correct** (approximately corresponding to the field from an elementary charge at a distance of 5 Å) in the *ab initio* calculation was computed at the same points. When the same field was applied to the multipole/polarizability representation of the molecule, the induced dipole moments generate a potential change that can be point wise compared to the ab initio potential change in the same manner as for the static potential. Note that the multipoles do not influence this potential change. Thus, the tests of multipoles and polarizabilities are completely independent.

4. Results

In this paper, we compare the qualityoof multipole moments and plarizabilities calculated by the LoProp and MpProp approaches. The quality of the results has been estimated by calculating the electrostatic potential in 10,000 points from the MpProp and LoProp multipole moments (or induced dipole moments in the test of dynamic properties) and compared them to the results obtained by an *ab initio* calculation. To examine if there are any systematical errors, the slope is determined by linear regression. If the multipole expansion is exact, the points would form a straight line with a slope of one. The reported error is the root mean square deviation between the potential from the multipoles and from the *ab initio* calculation, converted to energy units by assuming interaction with an elementary charge.

The analysis has also been done with the smaller 6-31G* basis set. However, there was virtually no difference in the results, so only the cc-pVTZ results are discussed. **xxx Perhaps:** The results of with the 6-31G* basis set are shown in Tables S1 and S2 in the supplementary material.

4.1. *Static properties*

In Tables 2 and 3 we list the results of the calculations. The averages together with the standard deviations and the worst cases have been plotted in Figure 1 for both the slopes and errors. The trends are similar for the two methods.

Table 2. The static and polar properties using LoProp and the CC-pVTZ basis set.

Molecule	l = 1		l = 2		l = 3		l = 4		l = 5		Polar	
	Slope	Error $\frac{kJ}{mol}$	Slope	Error $\frac{kJ}{mol}$	Slope	Error $\frac{kJ}{mol}$	Slope	Error $\frac{kJ}{mol}$	Slope	Error $\frac{kJ}{mol}$	Slope	Error $\frac{kJ}{mol}$
A	1.1041	3.1926	1.0059	0.2515	1.0012	0.0613	0.9998	0.0356	1.0021	0.0266	0.9933	0.0811
B	−0.1207	0.6711	0.6853	0.2140	0.9826	0.0240	1.0093	0.0197	1.0009	0.0123	0.9999	0.0616
C	0.9527	0.7722	0.9998	0.1757	1.0016	0.0432	0.9990	0.0279	1.0014	0.0221	1.0001	0.0316
D	0.8537	1.9150	0.9923	0.2270	1.0093	0.0618	1.0075	0.0546	1.0078	0.0433	0.9969	0.0740
E	0.8179	1.5674	0.9713	0.2641	1.0045	0.0614	1.0094	0.0401	1.0044	0.0249	0.9941	0.0643
F	0.9991	2.0306	0.9998	0.3337	0.9999	0.0846	1.0001	0.0506	1.0000	0.0353	1.0124	0.0863
G	−1.0368	4.9727	1.0625	0.2057	0.9547	0.1071	0.9923	0.0357	1.0067	0.0175	0.9960	0.0503
H	1.0001	0.5041	1.0000	0.1363	1.0000	0.0281	1.0000	0.0253	1.0000	0.0177	0.9967	0.0335
I	1.0041	3.7702	1.0001	0.1974	1.0000	0.0593	1.0000	0.0342	1.0000	0.0239	0.9945	0.0568
J	0.8691	4.2218	0.9960	0.2282	0.9970	0.0877	0.9990	0.0308	1.0006	0.0243	0.9995	0.0650
K	1.0051	4.1168	1.0000	0.1807	1.0001	0.0856	1.0000	0.0322	1.0000	0.0181	0.9992	0.0595
L	0.8835	4.2402	0.9990	0.2225	0.9989	0.0875	1.0007	0.0285	1.0002	0.0204	0.9946	0.0728
M	0.2555	5.3744	1.0139	0.2361	0.9908	0.1042	0.9990	0.0410	1.0024	0.0222	0.9996	0.0636
N	1.0210	2.3934	0.9994	0.2449	0.9996	0.0666	1.0001	0.0442	1.0004	0.0333	0.9987	0.0538
O	0.0733	6.8158	1.0317	0.2618	0.9843	0.1272	0.9944	0.0437	1.0012	0.0238	0.9948	0.0984
P	1.0552	1.6123	1.0027	0.2272	0.9995	0.0553	1.0007	0.0358	1.0003	0.0229	0.9985	0.0712
Q	0.9225	0.8331	0.9653	0.2833	0.9973	0.0326	1.0001	0.0127	1.0011	0.0098	1.0010	0.0628
R	1.1021	1.5162	1.0020	0.2194	1.0015	0.0430	0.9989	0.0253	1.0041	0.0176	0.9939	0.0638
V	0.8871	1.6570	1.0035	0.1317	1.0011	0.0148	1.0003	0.0121	1.0009	0.0061	0.6648	0.0410
W	0.9514	1.4406	1.0019	0.0482	1.0004	0.0236	0.9999	0.0117	1.0004	0.0060	0.9997	0.0237
Average	0.7300	2.6809	0.9866	0.2145	0.9962	0.0629	1.0005	0.0321	1.0017	0.0214	0.9981	0.0608
Std. deviation	0.5241	1.7489	0.0717	0.0594	0.0113	0.0303	0.0040	0.0118	0.0022	0.0090	0.0041	0.0180
Worst agreement	−1.0368	6.8158	0.6853	0.3337	0.9547	0.1272	1.0094	0.0546	1.0078	0.0433	1.0124	0.0984

Table 3. The static and polar properties using MpProp and the CC-pVTZ basis set.

Molecule	l = 1		l = 2		l = 3		l = 4		l = 5		Polar	
	Slope	Error $\frac{kJ}{mol}$	Slope	Error $\frac{kJ}{mol}$	Slope	Error $\frac{kJ}{mol}$	Slope	Error $\frac{kJ}{mol}$	Slope	Error $\frac{kJ}{mol}$	Slope	Error $\frac{kJ}{mol}$
A	1.0223	2.1965	0.9978	0.0919	1.0010	0.0217	1.0006	0.0096	1.0005	0.0062	0.9946	0.2791
B	0.9909	0.0261	1.0356	0.0403	1.0026	0.0097	1.0011	0.0028	0.9996	0.0012	0.9994	0.0873
C	0.9281	1.0082	1.0023	0.0813	1.0007	0.0226	1.0001	0.0095	1.0006	0.0050	1.0020	0.0971
D	0.8859	1.6953	1.0050	0.0643	1.0078	0.0199	1.0077	0.0138	1.0074	0.0119	1.0026	0.1155
E	0.8521	1.4650	1.0032	0.0823	1.0057	0.0207	1.0058	0.0107	1.0057	0.0070	0.9949	0.1431
F	0.9999	1.3810	1.0001	0.2051	1.0001	0.0377	1.0000	0.0173	1.0000	0.0097	1.0185	0.2062
G	−0.6815	4.0380	1.0053	0.0333	1.0040	0.0133	1.0001	0.0063	1.0037	0.0034	0.9939	0.1742
H	1.0001	0.2487	1.0000	0.0303	1.0000	0.0089	1.0000	0.0036	1.0000	0.0022	0.9992	0.0546
I	1.0030	2.9143	0.9999	0.0431	1.0000	0.0114	1.0000	0.0055	1.0000	0.0039	0.9940	0.1027
J	0.8764	3.2241	0.9991	0.0855	1.0001	0.0223	1.0003	0.0082	1.0004	0.0035	1.0029	0.1922
K	1.0037	3.2425	1.0000	0.0488	1.0000	0.0136	1.0000	0.0051	1.0000	0.0024	1.0013	0.1267
L	0.9152	3.1585	1.0002	0.0652	1.0004	0.0231	1.0005	0.0086	1.0003	0.0039	0.9971	0.1925
M	0.3601	4.1955	1.0048	0.0822	1.0015	0.0191	1.0006	0.0102	1.0012	0.0061	0.9991	0.2020
N	0.9984	1.4910	0.9989	0.0881	1.0007	0.0222	1.0003	0.0123	1.0002	0.0080	1.0026	0.1335
O	0.2112	5.6606	1.0071	0.0584	1.0009	0.0168	0.9996	0.0098	1.0012	0.0050	0.9921	0.2858
P	1.0245	1.4516	0.9977	0.0899	1.0004	0.0203	1.0004	0.0075	1.0003	0.0041	1.0042	0.2729
Q	0.9961	0.5808	0.9938	0.0610	1.0034	0.0276	0.9999	0.0091	1.0006	0.0039	1.0004	0.0492
R	1.0070	1.0161	0.9983	0.0583	1.0009	0.0149	1.0009	0.0067	1.0008	0.0039	0.9977	0.1067
V	0.8933	1.4968	1.0004	0.0320	1.0009	0.0079	1.0008	0.0052	1.0008	0.0053	0.9998	0.0214
W	0.9494	1.2996	0.9999	0.0473	1.0005	0.0132	1.0004	0.0046	1.0005	0.0034	1.0023	0.0155
Average	0.8118	2.0895	1.0025	0.0694	1.0016	0.0183	1.0010	0.0083	1.0012	0.0050	0.9999	0.1429
Std. deviation	0.4018	1.4225	0.0082	0.0371	0.0021	0.0070	0.0020	0.0035	0.0020	0.0025	0.0055	0.0794
Worst agreement	−0.6815	5.6606	1.0356	0.2051	1.0078	0.0377	1.0077	0.0173	1.0074	0.0119	1.0185	0.2858

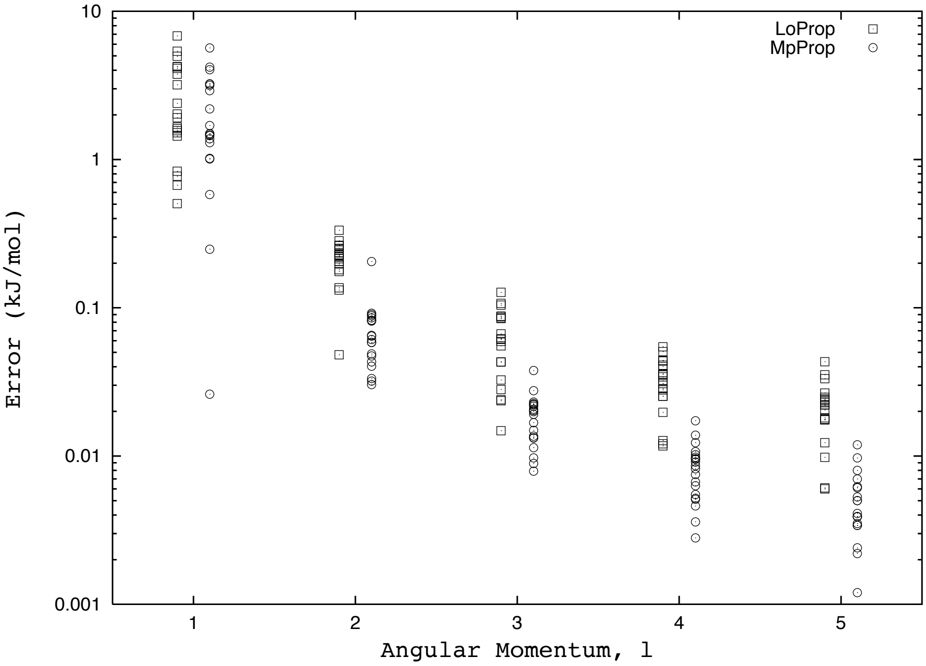

Fig. 1. A comparison of the errors from the predictions of the electrostatic potentials using LoProp and MpProp respectively.

The results show that the charges and dipoles reproduce the ab initio potentials quite poorly for both methods (average RMS errors of 2.1–2.7 kJ/mol). When quadrupole moments are included, the error is strongly reduced (to 0.07–0.21 kJ/mol). However, in order to obtain accurate results, it is necessary to include also the octupole moments (0.02-0.07 kJ/mol). Although the trend continues, the improvements when going to even higher multipole moments are minor, since the results using octupole moments are already of good quality.

In general, the errors arising from using the MpProp multipole expansion is a factor 3–4 smaller than the LoProp errors (but less with only dipole). The main reason for this is probably the better treatment of the expansion centers for the bonds in the MpProp method. Currently, the LoProp method simply places the expansion center in the midpoint. Another explanation is that the LoProp moments are somewhat more restricted, since it is required that the LoProp results have to be chemically intuitive, i.e. the properties are transferable.

4.2. *Dynamic properties*

The results of the calculations on the dynamic properties (polarizabilities) are also listed in Tables 2–3. As in the case of the static properties, the LoProp and MpProp results are similar. However, in contrast to the case of static properties, the error is in general smaller for the LoProp method, especially for the larger molecules (such as A, M, O, and P; average RMS error 0.06 compared to 0.14 kJ/mol). This was expected, because the LoProp method should give a more physical distribution of the polarizabilities throughout the molecule, which shows itself mainly for larger molecules. It should be noted that the MpProp definition of DFT polarizabilities to some extent is an *ad hoc* procedure, e.g. it is necessary to scale the polarizabilities.

5. Conclusions

The localized multipole moments and polarizabilities have been calculated using the LoProp and MpProp schemes for a total of twenty molecules. The local properties have been used to estimate the electrostatic potential in 10000 points for each molecule, and the result has been compared with the corresponding *ab initio* result. The two methods were able to reproduce the potentials (or energies, since interaction with an elementary charge was assumed) with an average accuracy of 0.0629 ± 0.0303 and 0.0183 ± 0.0070 kJ/mol respectively when a multipole expansion including the charge, dipole, quadrupole, and octupole terms were used. The errors are lower for the MpProp method, which is attributed to the better treatment of the multipoles in the bonds. The convergence to even higher multipole moments was also investigated, and it was concluded that including the 4th and 5th order terms improved the average accuracy to 0.0214 ± 0.0090 and 0.0050 ± 0.0025 kJ/mol respectively. It should be noted that the points were located sufficiently far from the molecule to make the charge penetration effect negligible.

In the case of polarizabilities, the results were reversed, i.e. the LoProp method showed best agreement with *ab initio* data. The change in electrostatic potential when applying a homogenous field of 0.01 atomic units was reproduced to an accuracy of 0.0608 ± 0.0180 kJ/mol for LoProp and 0.1429 ± 0.0794 kJ/mol for MpProp (again assuming interaction with an elementary charge). For LoProp, this accuracy corresponds to the static case truncated at the octupole moment, whereas for MpProp it corresponds to truncation at the quadrupole level. This suggests that, in combined electrostatic–induction models based on LoProp or MpProp, there is no need to include higher level of multipoles than octupoles or quadrupoles, respectively. However, it should be noted that the numbers regarding static properties and dynamic properties are not directly comparable, since the latter assume a specific field strength, which, although chosen to represent a typical high electric field in a molecular system, is not appropriate in all cases.

Because of the advantage of MpProp for the static properties and of LoProp for the dynamic properties, the best combined electrostatic–induction model would be to take multipole moments from MpProp and polarizabilities from LoProp. However, improvement of the LoProp method for static properties are underway.

By construction, the results of the LoProp method should be more transferable between different methods and basis sets. However, for the two basis sets tested here, 6-31G* and cc-pVTZ, no difference between the two methods is seen.

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