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# Density functional complexation study of metal ions with amino polycarboxylic acid ligands: EDDHA and HBED in comparison to EDTA, EDDS, ODS, and ISA

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## Abstract

Metal complexes of amino polycarboxylic acid ligands have been studied using density functional methods and a continuum solvation model (COSMO). Complexation energies for complexes of  $\text{Mg}^{2+}$ ,  $\text{Ca}^{2+}$ ,  $\text{Mn}^{2+}$ ,  $\text{Fe}^{3+}$ , and  $\text{Zn}^{2+}$  have been determined. The studied ligands include ethylenediaminedi-(*o*-hydroxyphenylacetic)acid (EDDHA) (including its *ortho,ortho*, *ortho,para*, and *para,para*-isomers), *N,N'*-bis(2-hydroxybenzyl)ethylenediamine-*N,N'*-diacetic acid (HBED), ethylenediamine tetraacetic acid (EDTA), ethylenediiminodibutanedioic acid (EDDS), meso-oxybis(butanedioic acid) (ODS), and 2,2'-bis(carboxymethyl)iminodiacetic acid (ISA). New, more accurate parameterisation is introduced to correct the neglected contributions in energetics. For *o,o*-EDDHA, the method is tested also for partly deprotonated forms of ligand. The results indicate that *o,o*-EDDHA<sup>4−</sup> and HBED<sup>4−</sup> are clearly the most effective ligands for all the metals.

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**Keywords:** EDDHA; HBED; Complexation; Metal ion; DFT; *Ab initio*

## 1. Introduction

Amino polycarboxylic acids are well-known and effective chelators for metal ions. Their excellent binding capacity is widely used especially for the complexation of transition metals. In agricultural applications, iron is added in soils as a ethylenediaminedi-(*o*-hydroxyphenylacetic)acid (EDDHA) complex to control iron chlorosis. [1] The most efficient isomer of EDDHA is the *o,o*-EDDHA which has two hydroxyl groups in *ortho*-positions in the phenol ring and it is able to form extremely stable 6-coordinated complexes with metal ions. Metal complexes of EDDHA have been widely studied for decades [2], mostly by experimental methods. In medical applications, EDDHA is used as a simplified model for the transferrin complexes [3]. Very

similar ligand to EDDHA is *N,N'*-bis(2-hydroxybenzyl)ethylenediamine-*N,N'*-diacetic acid (HBED) [4] which is also known for its capacity as a transition metal binder.

The chelation of transition metal ions is not important only in the nature but also in some industrial processes. One of these is the pulp bleaching process where the pulp is bleached with the hydrogen peroxide or peracids. Traces of transition metal ions in pulp, specially  $\text{Fe}^{3+}$  and  $\text{Mn}^{2+}$ , participate in the decomposition of these substances and thus, the effect of bleaching agents is reduced. In addition to  $\text{Fe}^{3+}$  and  $\text{Mn}^{2+}$ , pulp contains also other metals, e.g. magnesium and calcium. The former has been found to be beneficial to the bleaching process and the latter one only consumes the used chelating agent. [5] During the last decades, the non-biodegradability of the commonly used chelating agents, such as EDTA and DTPA, has lead to intensive research for more environmentally friendly chelators. Usually this means lower nitrogen content of a ligand and as a result, lower nitrogen content in wastewaters. In

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addition to traditional experimental methods, the wide variety of theoretical and computational methods can be applied to support the experimental research.

In a previous study [6], we studied complexation of metal ions with amino polycarboxylic acid ligands using DFT-COSMO and Car-Parrinello *ab initio* molecular dynamics. As a result, a fast and straightforward computational method for evaluating the performance of complexing agents was developed. The DFT-COSMO method was further tested with oligomeric ligands [7,8] and the results (obtained binding degrees and complexation geometries) were promising compared to the available experimental data. The use of implicit solvation model is rather approximate choice as strong hydrogen bonding between the charged complex and solvent is expected. However, classical molecular dynamics, which would be the most obvious choice when the large systems including solvent are studied, requires force field parameterisation. Partly because of the missing parameterisation, we have chosen to use DFT together with to implicit solvent description.

The aim of the present study was to further test and develop the method built previously and, on the other hand, to study the geometries and binding properties of different isomers of EDDHA in comparison to other amino polycarboxylic acid ligands. Despite of the large amount of the experimental data, to our knowledge this the first *ab initio* level study related to the metal complexes of EDDHA and HBED. The density functional theory together with the solvation model produces reliable and realistic results (both geometrically and energetically) and is thus appropriate for this kind of investigation, where the local metal ligand interaction is studied. If needed, the method can be easily applied to higher level *ab initio* methods, such as CCSD and MP2. Furthermore, the solvent description can be improved by treating a part of solvent explicitly. Fig. 1 shows the structures of all ligands and Table 1 the abbreviations used in this study for different ligands.

## 2. Computational details

All DFT calculations have been performed using the program TURBOMOLE 5.6 [9]. We have employed the TZVP basis set for all atoms and the BP86-functional [10] throughout the study. The RI-approximation [11] has been used to speed up the calculations. All geometries have been optimized using the COSMO-solvation model [12]. As the COSMO do not have optimized radii for metal ions, they were determined using hexaaquo metal complexes. Determination of COSMO-radii for metal ions is described and discussed in detail in our previous studies, so we refer reader to Refs. 6–8. Table 2 shows the used COSMO-radii for different metals. For all the other atoms the default options in the program TURBOMOLE have been used. In geometry optimizations, for the transition metal complexes (except those of  $\text{Zn}^{2+}$ ), the spin unrestricted formalism have been employed and for the earth alkaline metal

complexes (and those of  $\text{Zn}^{2+}$ ) the spin restricted formalism. The  $\text{Fe}^{3+}$  and  $\text{Mn}^{2+}$  complexes have been taken to be in the high spin state. In general, we have begun with  $\text{Mg}^{2+}$  complexes, and then used the optimized geometry of  $\text{Mg}^{2+}$  complex as a starting configuration for other metals.

## 3. Results

We will first focus on the metal complexes of EDDHA and HBED. As they were not included in our previous study [6] it is necessary to study their complexation properties before the more specific analysis and comparison to other ligands. The actually most used synthesis route of EDDHA produces different isomers [13] so we have included in the present study the isomers, which have the hydroxyl groups in *ortho* or *para*-position in the phenyl rings (see Fig. 1). After the results for metal complexes of EDDHA and HBED, we will make some comparison to previously studied amino polycarboxylic acids, mainly concentrating on the energetics of the complexation for different metal ions. The results for reoptimization of correction parameters are presented in the end of the chapter.

### 3.1. Metal complexes of EDDHA and HBED

#### 3.1.1. Geometries

One of the most important factors effecting on ligand's metal ion binding ability is its structure and the position of possible metal-coordinating atoms in the ligand's backbone. In addition to two chiral carbon atoms (those next to two  $\text{COO}^-$ -groups, respectively), EDDHA contains also two *prochiral* nitrogen atoms, which become chiral when they bind to the metal. Thus, the total number of chiral atoms in M-EDDHA-complexes is 4 and the number of possible configurations 16. However, it has been predicted earlier [14] that for the  $\text{NCH}_2\text{CH}_2\text{N}$ -group, the *gauche*-conformation is dominating in metal complexes and thus the number of possible configurations reduces to 8. The *cis*-conformation, which would also be possible, has never been observed under experimental conditions. Fig. 2 shows the racemic and mesomeric configurations of M-*o,o*-EDDHA-complexes. For the other isomers of EDDHA (*o,p*-EDDHA and *p,p*-EDDHA, respectively) the geometries are expected to be similar with the exception of one or two hydroxyl groups that do not coordinate to the metal ion (those in *para*-positions in the phenyl rings, respectively).

The racemic geometries (A) and (B) differ from each other with respect to the position of metal-coordinating oxygen atoms. In the geometry (A), phenolate oxygens are in axial positions of plane defined by  $\text{NCH}_2\text{CH}_2\text{N}$ -ring of EDDHA and in the geometry (B) carboxylate oxygen atoms occupy axial positions. However, it has been shown [15] that the complex is more stable when the carboxylate oxygens are in the axial positions and thus, the complex (B) should be energetically more

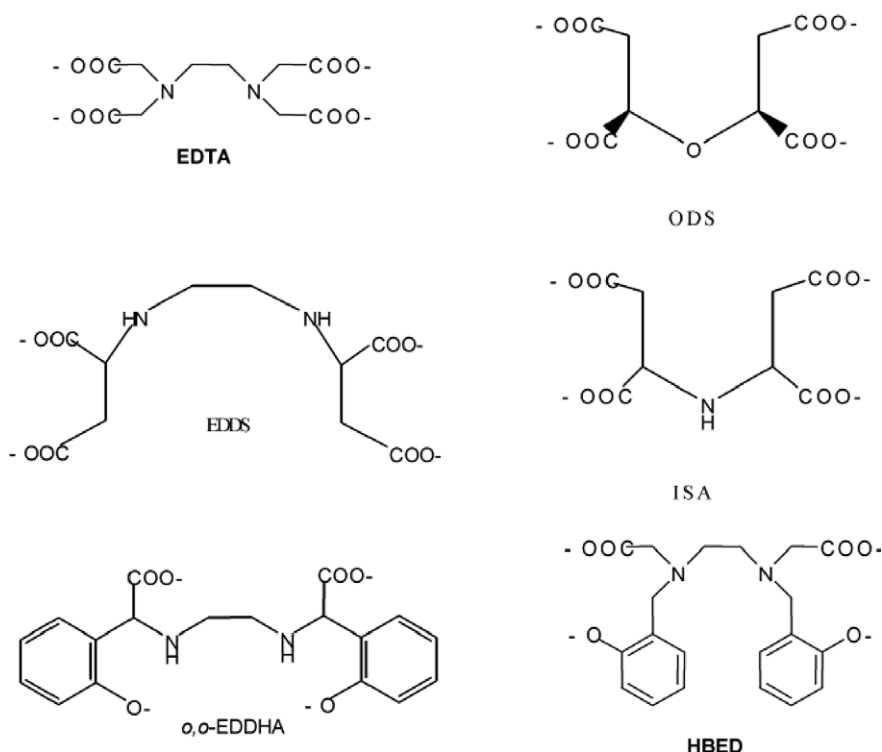


Fig. 1. Chemical structures indicating the deprotonation state of all studied ligands. Refer to Table 1 for the names of the ligands. *o,p*- and *p,p*-isomers of EDDHA have the same structure with the difference of the position of oxygen atoms attached to phenol rings.

Table 1  
Abbreviations and names of studied ligands

Abbreviation	Name
EDDHA*	Ethylenediaminedi-( <i>o</i> -hydroxyphenylacetic) acid
EDDS	Ethylenediiminodibutanedioic acid
EDTA	Ethylenediamine tetraacetic acid
EHPG*	<i>N,N'</i> -Ethylenebis[2-( <i>o</i> -hydroxyphenyl)glycine]
HBED	<i>N,N'</i> -Bis(2-hydroxybenzyl)ethylenediamine- <i>N,N'</i> -diacetic acid
ISA	2,2'-Bis(carboxymethyl)iminodiacetic acid
ODS	Meso-oxybis(butanedioic acid)

Refer to Fig. 1 for structures. For different isomers of EDDHA, we use through this study abbreviations *o,o*-EDDHA, *o,p*-EDDHA, and *p,p*-EDDHA.

\*Both names are used for the compound, throughout the study we have used the name EDDHA.

favourable. In the *meso* conformation two chiral carbon atoms have different stereochemistry. In HBED, the COOH-groups are attached to the nitrogen atoms (via carbon atom, respectively) and therefore, conformational isomerism is less present.

These above described experimental observations in mind we optimized metal complexes of EDDHA and HBED with different coordination modes. For EDDHA, the *ortho,ortho*, *ortho,para*, and *para,para*-isomers were studied. For HBED, only the isomers with OH-group in *ortho*-position were included. Where possible, the crystal structures were used as a starting structures for geometry optimizations. Fig. 3 shows the optimized geometries for

Table 2  
COSMO-radii (in Ångströms) for metal ions

Metal ion	$r_{\text{CSM}}$
Mg <sup>2+</sup>	1.456
Ca <sup>2+</sup>	1.825
Mn <sup>2+</sup>	1.467
Fe <sup>3+</sup>	1.391
Zn <sup>2+</sup>	1.342

Fe<sup>3+</sup> with *o,o*-EDDHA<sup>4-</sup>, *o,p*-EDDHA<sup>4-</sup>, *p,p*-EDDHA<sup>4-</sup>, and HBED<sup>4-</sup>. Stereochemically irrelevant hydrogen atoms are removed for the clarity. In addition to totally deprotonated ligands, also the protonation states of 3- and 2- were studied for *o,o*-EDDHA. As these geometries for different deprotonation states do not considerably differ from each other, only the energetics is reported (see Section 3.1.2 Energetic).

For all the metal ions, the 6-coordinated structure was found to be the most stable one with *o,o*-EDDHA and HBED ligands. As the experimental studies have predicted, in the most stable structure of metal-*o,o*-EDDHA-complexes, two nitrogen atoms have the same stereochemistry, as well as the two carbon atoms, and the carboxylate oxygens occupy the axial positions of plane defined by NCH<sub>2</sub>CH<sub>2</sub>N ring. Fig. 4 shows the minimum energy structure of [Fe-*o,o*-EDDHA]<sup>-1</sup> compared to the other *racemic* isomer and the *mesomeric* isomer of the complex together with their relative energies (see Fig. 2 for 2-dimensional structures). The calculated energy difference between the *racemic* (B) and the *mesomeric* isomer (12 kJ mol<sup>-1</sup>)

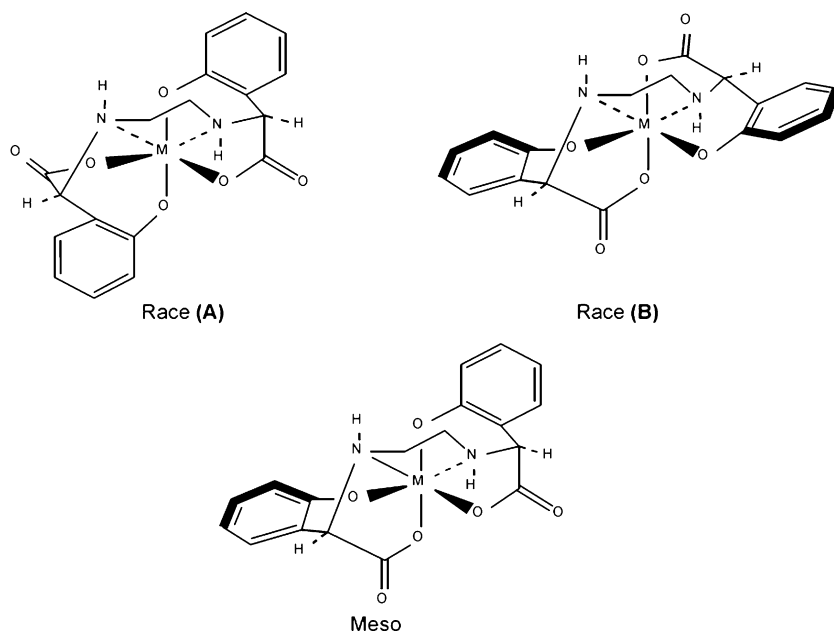


Fig. 2. Schematic representation of octahedral M-*o,o*-EDDHA -isomers. Only the stereochemically relevant hydrogen atoms are shown.

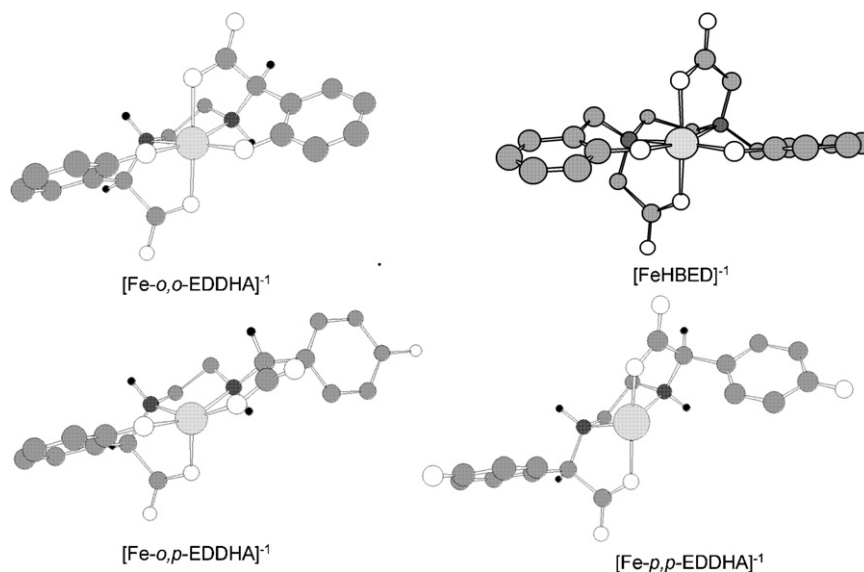


Fig. 3. The most stable structures for Fe<sup>3+</sup>-complexes with EDDHA<sup>4-</sup> and HBED<sup>4-</sup> ligands. White spheres depict oxygen atoms, black spheres hydrogens, and dark gray carbon atoms. Only stereochemically important hydrogen atoms are shown. The geometries for all other metals are similar with only minor differences in bond lengths and angles.

corresponds very well the experimentally determined value ( $-13 \text{ kJ mol}^{-1}$ ) [16]. In Fig. 5, the [Fe-*o,o*-EDDHA]<sup>-1</sup> complex is presented in comparison to the crystal structure [17].

Also the most stable structure of HBED complex (Fig. 3) has carboxylate oxygens in axial positions. For the *o,p*-isomer of EDDHA, the complexation geometry changes during the optimization in a way that one carboxylate group ends up to occupy position that is closer to equatorial site of plane defined by NCH<sub>2</sub>CH<sub>2</sub>N-ring. In the *p,p*-EDDHA-complex the carboxylate oxygen move back to axial position. Obviously, the complexes of *o,p*-

and *p,p*-EDDHA are more open to the solvent due to lower coordination number. Table 3 shows some selected geometrical parameters for the complexes [Fe-*o,o*-EDDHA]<sup>-1</sup>, [Fe-*o,p*-EDDHA]<sup>-1</sup>, [Fe-*p,p*-EDDHA]<sup>-1</sup> and [Fe-HBED]<sup>-1</sup>. As our main interest is in the Fe<sup>3+</sup> complexes, we do not report in detail the geometrical parameters for the complexes of the other metals.

As seen in Table 3, the distances in the COSMO-optimized structure of *o,o*-EDDHA-complex are slightly larger than in the crystal structure. This is logical as the effect of the solvent is taken into account in our procedure and the ligand interacts with the continuum solvent. The angles

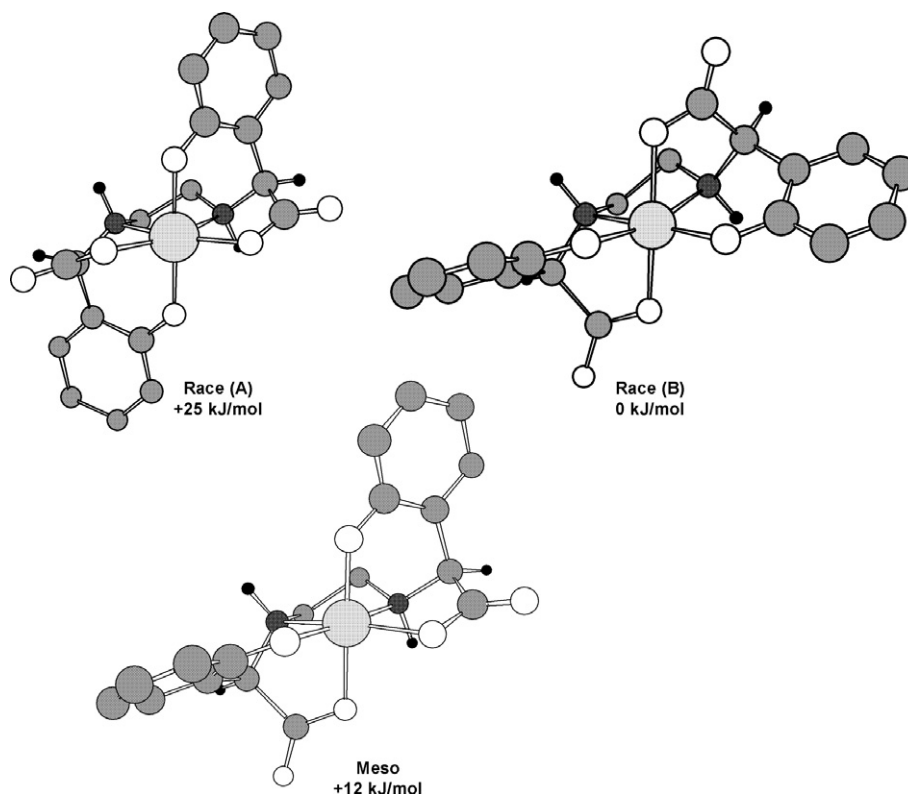


Fig. 4. Stereochemically different  $[\text{Fe}^{3+}\text{-}o,o\text{-EDDHA}]^{-1}$ -complexes and their relative energies. Stereochemically irrelevant hydrogen atoms are removed. (see Fig. 2 for 2-dimensional representation of the structures).

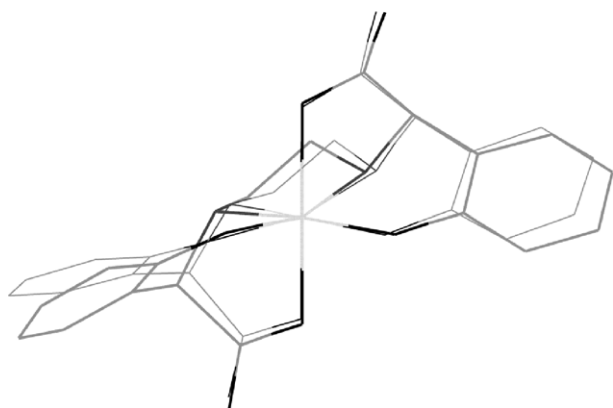


Fig. 5. COSMO-optimized  $[\text{Fe-}o,o\text{-EDDHA}]^{-1}$  complex and its crystal structure [17]. The COSMO-optimized structure is presented with thinner line.

have similar values with the exception of  $\text{O}_{\text{carb}}\text{-M-O}_{\text{carb}}$  angle which is noticeably smaller in the COSMO-optimized geometry and thus, the octahedral geometry is more distorted. This means also that the complex optimized with COSMO is more open to the solvent and consequently the geometry might be 7-coordinated with one explicit solvent molecule (water). The distances and the angles in  $[\text{Fe-}o,p\text{-EDDHA}]^{-1}$ -complex have quite the same values than in  $o,o\text{-EDDHA}$ -complex with the clear exception of  $\text{O}_{\text{carb}}\text{-M-O}_{\text{carb}}$  angle which is more than  $45^\circ$  smaller than in  $o,o\text{-EDDHA}$ -complex. This is caused by one of the met-

al-coordinating carboxylate group moving in equatorial position during the optimization (Fig. 3). In  $p,p\text{-EDDHA}$ -complex the  $\text{M-N}$  and  $\text{M-O}_{\text{carb}}$  distances are slightly smaller than in the complexes of other isomers. This is expectable as the coordination number is lower and thus the repulsion between the metal-coordinating atoms is also smaller. The distances and the  $(\text{N-M-O}_{\text{hyd}})$  angle in  $[\text{FeHBED}]^{-1}$ -complex are close to the values of  $\text{EDDHA}$ -complex. Two other angles, however, are clearly smaller.

### 3.1.2. Energetics

Complexation energies were determined according to Eq. (1):

$$\begin{aligned}\Delta E_{\text{CO}} &= \Delta E_{\text{CSM}} \\ &= E_{\text{CSM}}(\text{ML}^{n-m}) + 6E_{\text{CSM}}(\text{H}_2\text{O}) - E_{\text{CSM}}(\text{L}^{m-}) \\ &\quad - E_{\text{CSM}}(\text{M}(\text{H}_2\text{O})_6^{n+})\end{aligned}\quad (1)$$

where  $E_{\text{CSM}}(X)$  is the COSMO-corrected total energy of species (X). M and L refer to metal and ligand, respectively. The corrected complexation energies are then determined according to Eq. (2):

$$\Delta G_{\text{C}}(\text{M}_i, \text{L}_j) = \Delta E_{\text{CO}}(\text{M}_i, \text{L}_j) + \text{GML}_i \quad (2)$$

where the  $\text{GML}_i$  is an empirical metal specific correction parameter (see Table 4 for the values for different metal ions and Ref.[6] for the details). In the appendix of



Table 3

Selected geometrical parameters for Fe<sup>3+</sup>-complexes of EDDHA and HBED (distances in Ångströms and angles in degrees)

	<i>d</i> (M–N)	<i>d</i> (M–O <sub>hyd</sub> )	<i>d</i> (M–O <sub>carb</sub> )	∠(N–M–O <sub>hyd</sub> )	∠(O <sub>hyd</sub> –M–O <sub>hyd</sub> )	∠(O <sub>carb</sub> –M–O <sub>carb</sub> )
<i>o,o</i> -EDDHA	2.237	1.937	2.097	87.4	108.4	165.9
<i>o,o</i> -EDDHA <sub>cr</sub>	2.151	1.904	2.028	87.3	107.2	172.1
<i>o,p</i> -EDDHA	2.183	1.911	1.974	87.8	—	119.6
<i>p,p</i> -EDDHA	2.162	—	1.887	—	—	162.8
HBED	2.281	1.927	2.085	87.9	104.5	160.9

EDDHA<sub>cr</sub> refers to corresponding values in the crystal structure of [FeEDDHA]<sup>−1</sup>-complex [17].

Table 4

Correction parameters for metal ions (in kJ mol<sup>−1</sup>), see Ref [6] for details

Metal ion	Mg <sup>2+</sup>	Ca <sup>2+</sup>	Mn <sup>2+</sup>	Fe <sup>3+</sup>	Zn <sup>2+</sup>
GML <sub>i</sub>	91	77	115	284	116

Ref. [6] we examined in detail several of the possible errors for the complexation energies. These include the BSSE, thermal corrections, etc. Even together these corrections could not explain the GML<sub>i</sub> parameters and we have not repeated here the very tedious error analysis. The correction parameters were recalculated using the results obtained with the previously developed ones. The new, more accurate (but still, they should be considered empirical) correction parameters are introduced and discussed after the comparison to other ligands. At this point, however, we have used the old parameters to calculate the corrected complexation energy for new ligands.

Table 5 shows the calculated and experimental free energies of complexation for the metal complexes of *o,o*-EDDHA, *o,p*-EDDHA, *p,p*-EDDHA, and HBED. For *o,o*-EDDHA table includes also the deprotonation states −3 and −2, for all the other ligands only the −4 form is included. The calculated experimental values refer to ionic strength of  $\mu = 0.1 \text{ mol dm}^{-3}$  and temperature of 298 K, and they do not include any additional corrections. In Fig. 6, the calculated complexation energies are plotted against the experimental values.

Table 5 shows that for the *o,o*-EDDHA<sup>4−</sup> and HBED<sup>4−</sup> ligands (with the exception of [Fe-HBED]<sup>−1</sup> complex), the corrected complexation energies are visibly overestimated with respect to the experimental values. The energies for partially deprotonated forms of *o,o*-EDDHA, on the other hand, are clearly underestimated with respect to the experimental values. For the other isomers of EDDHA, the calculated values are underestimated (with the exception of [Ca-*o,p*-EDDHA]<sup>2−</sup> complex for which the  $\Delta G_{C2}$  is overestimated by 7 kJ mol<sup>−1</sup>), specially in the case of *p,p*-isomer. The used correction do not depend on the coordination number or mode of the ligand, it depends only on the metal. The results clearly show that the correction needed should be smaller for the complexes with the coordination number lower than 6. The fully coordinated EDDHA and HBED, on the other hand, need a larger correction than the smaller ligands (EDTA, EDDS etc.) used in parameterisation.

Table 5

Calculated and experimental complexation free energies (in kJ mol<sup>−1</sup>)

Ligand		Metal				
		Mg <sup>2+</sup>	Ca <sup>2+</sup>	Mn <sup>2+</sup>	Fe <sup>3+</sup>	Zn <sup>2+</sup>
<i>o,o</i> -EDDHA <sup>4−</sup>	$\Delta E_{CO}$	−207	−160	−260	−520	−265
	$\Delta G_{C2}$	−116	−83	−145	−236	−149
	$\Delta G_{exptl}$	−56	−42	N/A	−200	−107
<i>o,o</i> -EDDHA <sup>3−</sup>	$\Delta E_{CO}$	−160	−124	−201	−447	−224
	$\Delta G_{C2}$	−69	−47	−86	−163	−108
	$\Delta G_{exptl}$	−36	−28	N/A	−142	N/A
<i>o,o</i> -EDDHA <sup>2−</sup>	$\Delta E_{CO}$	−103	−84	−147	−358	−169
	$\Delta G_{C2}$	−12	−7	−32	−74	−53
	$\Delta G_{exptl}$	−15	−19	N/A	N/A	N/A
<i>o,p</i> -EDDHA <sup>4−</sup>	$\Delta E_{CO}$	−133	−122	−196	−411	−222
	$\Delta G_{C2}$	−42	−45	−81	−127	−106
	$\Delta G_{exptl}$	−53	−38	N/A	−164	N/A
<i>p,p</i> -EDDHA <sup>4−</sup>	$\Delta E_{CO}$	−46	−53	−120	−269	−147
	$\Delta G_{C2}$	17	24	−5	15	−31
	$\Delta G_{exptl}$	−21	−20	N/A	N/A	N/A
HBED <sup>4−</sup>	$\Delta E_{CO}$	−192	−151	−230	−507	−249
	$\Delta G_{C2}$	−101	−74	−115	−223	−133
	$\Delta G_{exptl}$	−60	−53	−84	−227	−105

The first value  $\Delta E_{CO}$  is the uncorrected complexation energy (in kJ mol<sup>−1</sup>) obtained using Eq. (1). The second is the corrected complexation energy obtained using Eq. (2) and the last line gives the experimental complexation energy  $\Delta G_{exptl}$ , where available [18–20].  $\Delta G_{exptl}$  have been derived from log  $K_1$ -values for complexation at 0.1 ionic strength and temperature of 298 K using equation  $\Delta G_{exptl} = -RT \ln 10 \log K_1$ .

Fig. 6 shows that there is an excellent correlation between calculated and experimental complexation free energies for both EDDHA (including *o,o*- and *o,p*-isomers at the deprotonation state of −4) and HBED. However, as seen in linear regression fit in Fig. 6, the energies of *o,o*-EDDHA-complexes are overestimated by ca. −55 kJ mol<sup>−1</sup>. This can be considered significant and could partly be explained by the size and the composition of the new ligands. The sources of error, e.g. BSSE, are expected to be larger for bigger ligands and the new ligands with two phenyl rings are clearly larger than the corresponding ligands without the rings (EDTA and EDDS, respectively). Even though, as all the neglected contributions to solvation energies are assumed to be included in the correction parameters [6], the quite large deviation from the experimental energies remains to be studied in future.

The corrected complexation energies indicate that both ligands, *o,o*-EDDHA<sup>4−</sup> and HBED<sup>4−</sup>, are clearly best chelators for Fe<sup>3+</sup> ion. The manganese (II) and zinc (II) bind to *o,o*-EDDHA<sup>4−</sup> ligand with the similar strength with the

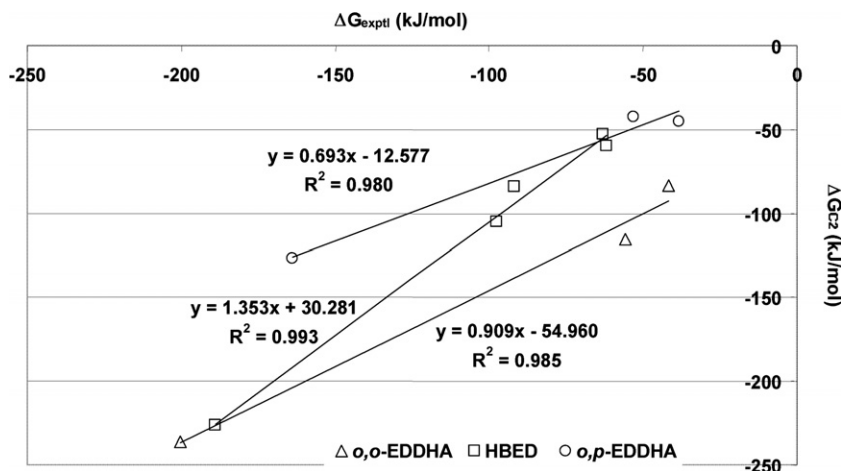


Fig. 6. The calculated complexation energies plotted against the experimental values. See Table 5. for the exact values. *p,p*-EDDHA is excluded due to the lack of experimental data.

energy difference less than  $5 \text{ kJ mol}^{-1}$ . With the other isomers of EDDHA and with HBED,  $\text{Zn}^{2+}$  binds noticeably more strongly than  $\text{Mn}^{2+}$ . Both *o,o*-EDDHA and HBED are better chelators for  $\text{Mg}^{2+}$  than for the other alkaline earth metal ion,  $\text{Ca}^{2+}$ . With *o,p*- and *p,p*-isomers of EDDHA both  $\text{Mg}^{2+}$  and  $\text{Ca}^{2+}$  show similar binding strength even if the experimental results slightly favour the binding of  $\text{Mg}^{2+}$ .

### 3.2. Comparison to other ligands

As the complexes in the previous study [6] were not optimized using the solvation model, we reoptimized all the complexes of EDTA, EDDS, ISA, and ODS in order to make some comparison to EDDHA and HBED. Another reason for this was simply to further study the energy differences caused by these two approaches (gas phase optimization + COSMO singlepoint energy calculation vs. direct COSMO-optimization) that we have used in our studies. With DTPA and AES ligands, metal ions can adopt different complexation geometries, so these ligands are excluded in the present study. Table 6 shows the calculated uncorrected and corrected complexation energies for these COSMO-optimized structures and as references values, experimental  $\Delta G$ -values and the energies calculated previously [6].

As seen in Table 6, the uncorrected complexation energies obtained by COSMO-optimization and reference values obtained by gas phase optimization followed by COSMO-singlepoint energy calculation do not differ a lot from each other. In general, the energies obtained by COSMO-optimization are slightly higher (less negative) than the ones obtained with gas phase optimization. The correlation between corrected complexation energies ( $\Delta G_{C2}$ ) and experimental complexation free energies ( $\Delta G_{\text{exptl}}$ ) is good with the  $R^2$ -value of 0.91 and the slope of 1.00. This was predictable as three of these ligands (EDTA, EDDS, and ISA) were used in the parameterisation of the correction

Table 6

Calculated and experimental complexation free energies (in  $\text{kJ mol}^{-1}$ ) for the complexes of EDTA, EDDS, ISA, and ODS

Ligand		Metal				
		$\text{Mg}^{2+}$	$\text{Ca}^{2+}$	$\text{Mn}^{2+}$	$\text{Fe}^{3+}$	$\text{Zn}^{2+}$
EDTA	$\Delta E_{\text{CO}}$	-150	-131	-190	-413	-217
	$\Delta E_{\text{CO}}(\text{ref})$	-148	-132	-202	-426	-220
	$\Delta G_{C2}$	-59	-54	-75	-129	-101
	$\Delta G_{\text{exptl}}$	-51	-61	-79	-143	-94
EDDS	$\Delta E_{\text{CO}}$	-111	-93	-150	-378	-170
	$\Delta E_{\text{CO}}(\text{ref})$	-112	-102	-151	-393	-168
	$\Delta G_{C2}$	-20	-16	-35	-94	-54
	$\Delta G_{\text{exptl}}$	-33	-24	-50	-116	N/A
ISA	$\Delta E_{\text{CO}}$	-98	-91	-136	-345	-146
	$\Delta E_{\text{CO}}(\text{ref})$	-113	-86	-154	-370	-166
	$\Delta G_{C2}$	-7	-14	-21	-61	-30
	$\Delta G_{\text{exptl}}$	-31	-25	-42	-80	-58
ODS	$\Delta E_{\text{CO}}$	-105	-104	-135	-323	-139
	$\Delta E_{\text{CO}}(\text{ref})$	-106	-87	-143	-333	-146
	$\Delta G_{C2}$	-14	-27	-20	-39	-23
	$\Delta G_{\text{exptl}}$	-29	-33	-32	-69	-43

Complexes have been reoptimized with continuum solvation model and the reference values ( $\Delta E_{\text{CO}}(\text{ref})$ ), taken from Ref. [6]) have been obtained with gas phase optimization and COSMO singlepoint energy calculation. Reference  $\Delta E_{\text{CO}}$ -values have been taken from Ref. [6].  $\Delta G_{\text{exptl}}$  have been derived from  $\log K_1$ -values (Ref [21]) for complexation at 0.1 ionic strength and temperature of 298 K using equation  $\Delta G_{\text{exptl}} = -RT \ln 10 \log K_1$ .

parameters and the COSMO-optimization was not considered to change neither energetics nor geometries significantly.

Fig. 7 shows the uncorrected complexation energies for  $\text{Mg}^{2+}$ ,  $\text{Ca}^{2+}$ ,  $\text{Mn}^{2+}$ , and  $\text{Fe}^{3+}$  with different ligands. The results show that clearly the best chelator for all the metal ions is *o,o*-EDDHA, and the second effective HBED. For transition metals, the poorest chelator is nitrogen-free ODS. For  $\text{Mg}^{2+}$  and  $\text{Ca}^{2+}$ , on the other hand, ODS performs as potential chelating agent as are ISA and EDDS. However, it is interesting to notice that the general trend for complexation is the same for different metals. That means that the ligands are not very metal specific, and,



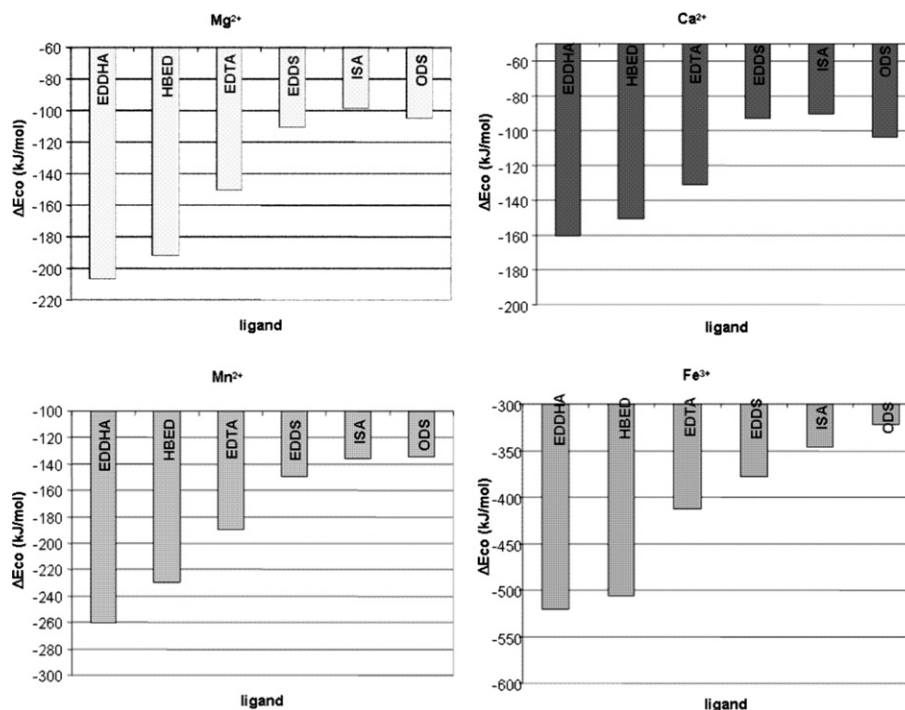


Fig. 7. Complexation energies (in  $\text{kJ mol}^{-1}$ ) for  $\text{Mg}^{2+}$ ,  $\text{Ca}^{2+}$ ,  $\text{Mn}^{2+}$ , and  $\text{Fe}^{3+}$  with studied ligands.

furthermore, the general complexation trend for ligands could be predicted modelling only one metal with different ligands. However, as seen in our previous studies [6–8], the metal ions can prefer different complexation geometries with the same ligand, and thus, it is necessary to study behaviour of all metal ions before making any conclusions about complexation properties of the specific chelator.

In Fig. 8 are shown more in detail the calculated and experimental complexation energies for  $\text{Fe}^{3+}$ -complexes of different ligands. In addition to Fig. 7, also the different isomers of EDDHA are included as well as the previously studied [8] ligand PESA (poly(epoxy succinic acid)) which showed complexation behaviour comparable to (amino) polycarboxylic acid ligands. Fig. 8 shows clearly that *o,o*-

and *o,p*-EDDHA are very effective chelators for  $\text{Fe}^{3+}$  even if the latter is not able to shield the metal ion completely and thus, it is expected to be still catalytically active.

### 3.3. Correction parameters

The use of correction parameters is necessary as the uncorrected complexation energies correlate poorly with the experimental free energies of solvation. However, as shown previously [6], uncorrected complexation energies ( $\Delta E_{\text{CO}}$ ) cannot be improved only taking into account the contribution of thermal effects. Instead of using several different parameters for each type of source of error, we have decided to include all the neglected contributions in one

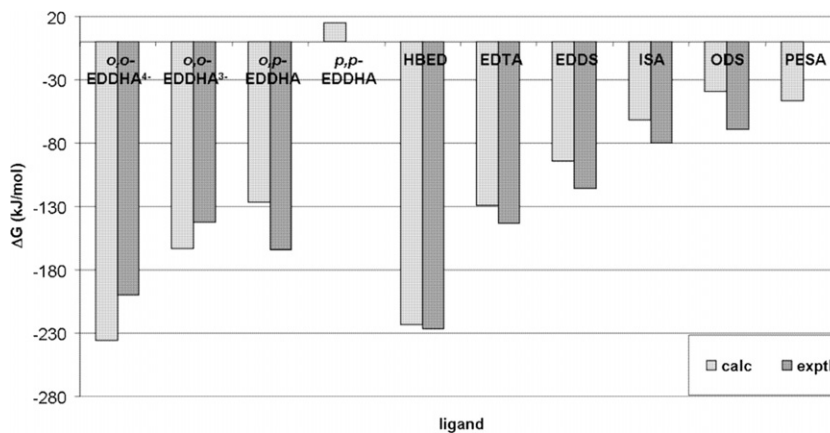


Fig. 8. Complexation energies (in  $\text{kJ mol}^{-1}$ ) for  $\text{Fe}^{3+}$  with the studied ligands. The different isomers of EDDHA and previously studied [8] poly(epoxy succinic acid) (PESA) are included.

Table 7

Reoptimized correction parameters for metal ions (in kJ mol<sup>-1</sup>)

Metal ion	Mg <sup>2+</sup>	Ca <sup>2+</sup>	Mn <sup>2+</sup>	Fe <sup>3+</sup>	Zn <sup>2+</sup>
GML <sub>i</sub>	101	82	111	275	117

correction parameter. The parameters we have used are three, one for each metal  $GM_i$ , one for each ligand  $GL_j$ , and finally, one metal-specific parameter  $GML_i$  which is used separately while the previous ones are used together. The parameters are obtained minimising the difference between the complexation energies  $\Delta E_{CO}$  and the experimental values.

$$\min \sum_{i,j} (\Delta E_{CO}(M_i, L_j) - \Delta G_{\text{exptl}}(M_i, L_j) + GML_i)^2 \quad (3)$$

In order to further improve the set of previously determined correction parameters, we re-optimized metal-specific parameter  $GML_i$  including into set of ligands also the new ligands *o,o*-EDDHA and HBED. The new correction parameters are shown in Table 7. Only the totally deprotonated forms of ligands are included in the reoptimization.

Compared to the old values (shown in Table 4), the reoptimized correction parameters are well at the same level. The change in the values is for all the metals less than 10 %. For transition metal ions (Fe<sup>3+</sup> and Mn<sup>2+</sup>) the new values are smaller and for alkaline earth metal ions (and for Zn<sup>2+</sup>), the new values are slightly larger. However, it should be remembered that we did not include all the ligands used in the previous optimization in this new optimization and, on the other hand, the new set of ligands include also two completely new ligands (*o,o*-EDDHA and HBED, respectively). If only the four old ligands (EDTA, EDDS, ISA, and ODS) are included in reoptimization, the new parameters are smaller (in average 12 %) than the previously optimized ones for all the metal ions. This confirms the assumption that COSMO-optimization produces geometries which are energetically closer to the experimental values than the gas phase optimized structures.

#### 4. Discussion

For almost all the ligands (the only exception is *o,o*-EDDHA), only the totally deprotonated forms have been included in the study. As the conditions in pulp bleaching process are very alkaline, this assumption is reasonable. Nevertheless, experimental studies [18] have demonstrated that when pH is 11.5 (or higher), the complex form  $[\text{FeLOH}]^{2-}$  of Fe<sup>3+</sup>-EDDHA is present and, in fact, this could compete with the dominating  $[\text{FeL}]^-$  form of complex. Calculation of OH<sup>-</sup> ion is rather complicated and thus we limit our study in the conditions where all the metal ions form 1:1-complex with the ligand without any additional metal-coordinating species.

In general, the corrected complexation energies are very satisfactory. For *o,o*-EDDHA<sup>4-</sup> and HBED (with the exception of Fe<sup>3+</sup>) the calculated  $\Delta G_{C2}$ -values are overesti-

mated. One very important reason for this is the used correction parameters, which were determined for smaller ligands. EDDHA and HBED, being significantly larger than previously studied ligands (EDTA, EDDS, etc.), need a larger correction. For the other isomers (*ortho,para* and *para,para*, respectively) of EDDHA, the coordination numbers are lower due to the positions of hydroxyl groups and thus, the complexation is not as favourable as in the case of *o,o*-isomer. However, as seen in the case of ISA and ODS, the relative “error” (deviation from the experimental value) is clearly larger if the complex is “undercoordinated” and optimized with COSMO and thus, the conclusions may be at least a bit misleading. In fact, the gas phase optimization (followed by a singlepoint energy calculation using the solvation model) seems to produce in these cases (metal–ligand coordination number lower than 6) more reliable results than the direct COSMO-optimization.

Depending on the application, there are some requirements or preferences for the ligand. From the ecological point of view, an ideal iron chelator would be nitrogen free. However, comparing two very similar ligands, ISA and ODS, for only Fe<sup>3+</sup> ion nitrogen free ODS is clearly poorer chelator than ISA. Alkaline earth metal ions, Mg<sup>2+</sup> and Ca<sup>2+</sup>, slightly favour the chelation with ODS over the ISA, and for the Mn<sup>2+</sup>, these two ligands show similar complexation capacity. This was also seen in our previous study [8] with poly(epoxy succinic acid) (PESA), which for the other metals (Mg<sup>2+</sup>, Ca<sup>2+</sup>, Mn<sup>2+</sup>, and Zn<sup>2+</sup>) showed well comparable (or in fact, better) complexation capacity compared to ISA.

An ideal iron chelator is able to shield the metal completely from the solvent and other molecules. In the pulp bleaching process, the most essential molecule may be hydrogen peroxide, which can be decomposed in the presence of Fe<sup>3+</sup> ions. Being quite effective chelator, *o,p*-isomer of EDDHA compete with the *o,o*-EDDHA in complexation if it is present in chelating material. The effectiveness of *o,p*-EDDHA as a chelator for Fe<sup>3+</sup> and Mn<sup>2+</sup> ions is well comparable to EDTA but its 5-coordinated complex structure is almost certainly still catalytically active and the results is not desirable from the point of view of the bleaching process.

Based on the new geometry optimization, all the correction parameters have been reoptimized. With the direct COSMO-optimization the uncorrected complexation energies are closer to experimental complexation free energies and thus, the correction needed is smaller in comparison to previously used procedure (gas phase optimization together with the continuum singlepoint energy calculation). Even though the exact origin of the correction parameters remains to be studied in future, the present study confirms that they are applicable for the evaluation of binding capacity of new ligands. Furthermore, if necessary, the parameters can be easily recalculated to include also the new set of ligands and as a results, they become more accurate.

The use of only metal-specific parameter is somewhat rough approximation as the original study [6] already

showed that variation between ligands in the needed correction is from 80 kJ mol<sup>-1</sup> for ODS up to 107 kJ mol<sup>-1</sup> for DTPA. Even so, as the aim is to keep the procedure as simple as possible, we have decided to concentrate on using only one parameter which include all the neglected contributions, also the variation between the ligands. However, if the method is applied for clearly larger or smaller ligands, the ligand-specific variation should be considered as a source of error and so taken into account when the results are being analysed.

## 5. Conclusions

We have studied the complexation properties of amino polycarboxylic acids using the density functional methods and a continuum solvation model (COSMO). Complexation energies for the metal complexes of EDDHA and HBED have been determined and they have been corrected with previously determined empirical correction parameters. The correlation with the experimental free energies of complexation is excellent for both ligands (including the different isomers of EDDHA) even if the calculated complexation energies are overestimated with respect to the experimental values. This fact leads us to a conclusion that the previously developed method can successfully be used for the evaluation of the complexation properties of new ligands.

In addition to the determination of complexation energies for the metal complexes of these two ligands, we have reoptimized the previously studied complexes of EDTA, EDDS, ISA, and ODS, and compared the results to the new ligands. Complexation energies, as well as the geometries, obtained by COSMO-optimization are in good agreement with the previously used procedure where the complexes were first optimized in gas phase and then the singlepoint energies were calculated using the COSMO-model. Direct optimization using a continuum solvation model is undoubtedly more straightforward procedure even if the computational cost is slightly higher.

The comparison between the ligands show that the most effective chelator for all the metal ions is *o,o*-EDDHA. Also HBED and EDTA perform quite well while the smaller ligands ISA and ODS do not show considerable complexation capacity. Transition metals, especially trivalent iron, seem to be able to form extremely stable complexes with the studied ligands while the complexes of alkaline earth metals, Mg<sup>2+</sup> and Ca<sup>2+</sup> are clearly less stable.

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