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A Comparison of Crystallographically Independent Iminodiacetic Acid Residues

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The dimensions of the iminodiacetic acid residues in six different crystal structures, which have been determined by X-ray crystallography, are compared by the method of half-normal probability plots. The bond distances (except C–O) within the organic molecule are independent of the crystallographic environment, with N–C and C–C distances of 1.488(3) and 1.505(3) Å, respectively. Bond angles are more dependent on the crystallographic environment and have different values in different crystal structures. The molecular residue $N-C-C\langle_{O}^{O}$ is shown to have a preferred planar conformation in the solid state. The double bond character in the C–OH bond is estimated to be in the range 10–20 %.

General information about the conformations of chemical groups can be of value in the interpretation of physical observations and for predicting the most probable spatial arrangements in larger molecules. For example the knowledge of the geometry of the peptide group was of great importance in deducing the stable conformations of polypeptide chains.[1] A determination of the geometry of a molecule in the solid state using X-ray diffraction methods cannot give any detailed information about the energy of different conformations. However, if one particular conformation is observed in a number of crystal structures with different packing arrangements, one may conclude that the intermolecular forces here are of less importance than the intramolecular ones and hence the conformation observed is the one with the lowest energy.[2] One aim of the present investigation is to search for preferred conformations in the solid state of the iminodiacetic acid group (Fig. 1).

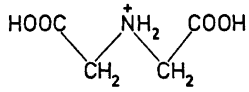


Fig. 1. The positively charged iminodiacetic acid ion.

A prerequisite for a quantitative conformational analysis based on classical mechanical principles is the access to accurate, strain free bond distances and angles. No compound is really "strain free" but if the same bond distances and angles for a molecule are observed in several crystal structures, one may conclude that the strain factors involved in these quantities are quite small. The set of "normal" structural parameters given in this paper are calculated from six different crystal structures.[3–7]

HALF-NORMAL PROBABILITY PLOT ANALYSIS

De Camp [8] and Albertsson and Schultheiss [9] have shown that the use of normal probability plot analysis [10] can be extended to the comparison of independently determined molecular geometries. This method is convenient in detecting minor differences in the residues compared. In the present paper half-normal probability plots are used. Observed ranked values

$$\delta d_i = |d(1)_i - d(2)_i| / [\sigma^2 d(1)_i + \sigma^2 d(2)_i]^{1/2}$$

are plotted *versus* the quantiles ζ_i expected for a normal distribution of errors.[11] The quantities $d(1)_i$ and $d(2)_i$ are the corresponding intramolecular distances with estimated stand-

ard deviations $\sigma d(1)_i$ and $\sigma d(2)_i$ in the structures 1 and 2. To make the analysis cover a comparison of all bond distances, bond angles and conformational angles in an organic molecule, all independent intramolecular distances up to about 4.65 Å should be included in the calculation of δd_i. A cut-off at about 2.55 Å is equivalent to a comparison of bond distances and bond angles only. Besides information about differences in the compared molecular geometries these plots also give information about the reliability of the standard deviations assigned to the interatomic distances, as discussed by Abrahams and Keve [10] in their original paper on the method. A correct match between the measured and assumed error distributions in two equal molecules will result in a linear plot with a slope of unity and zero

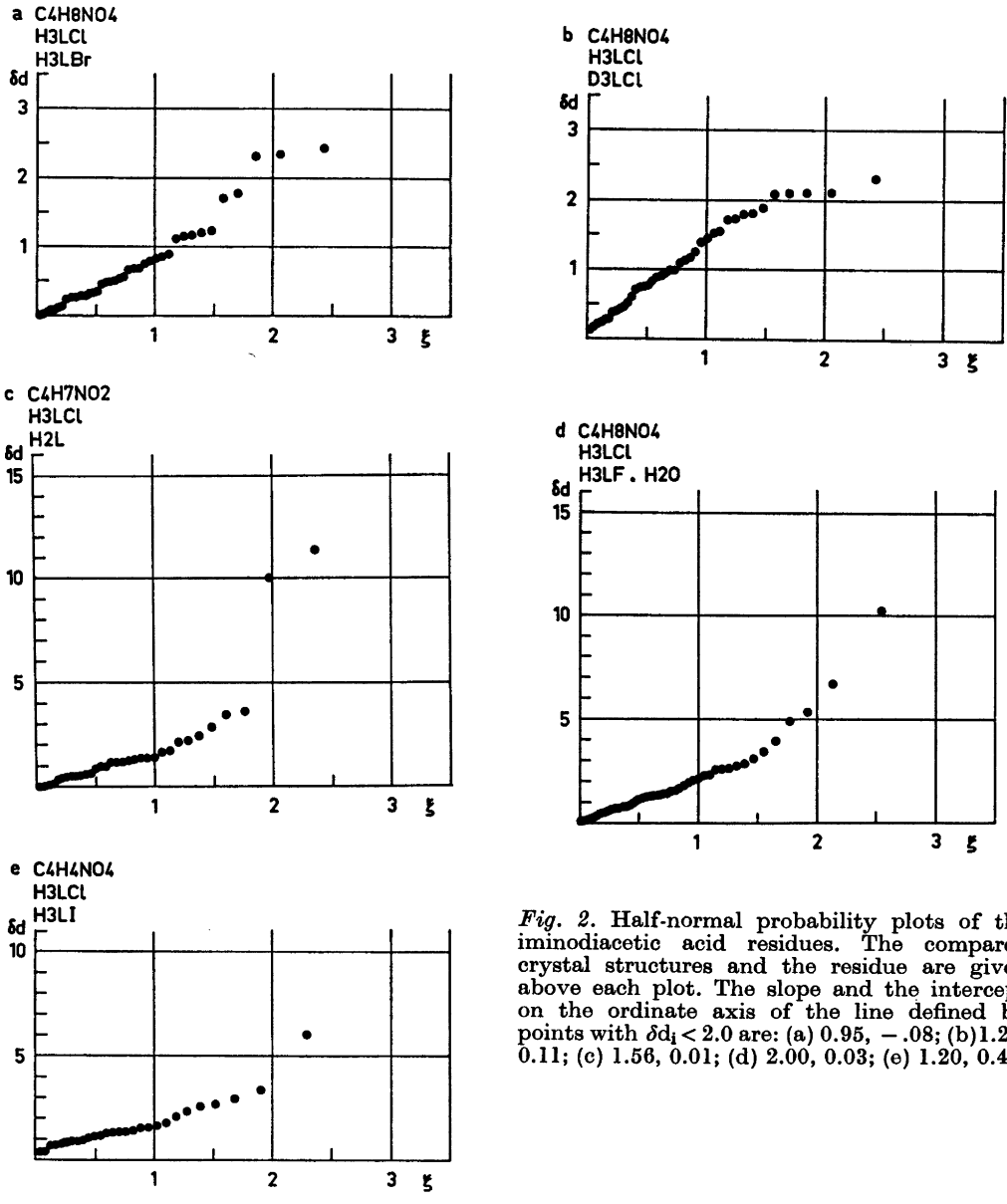


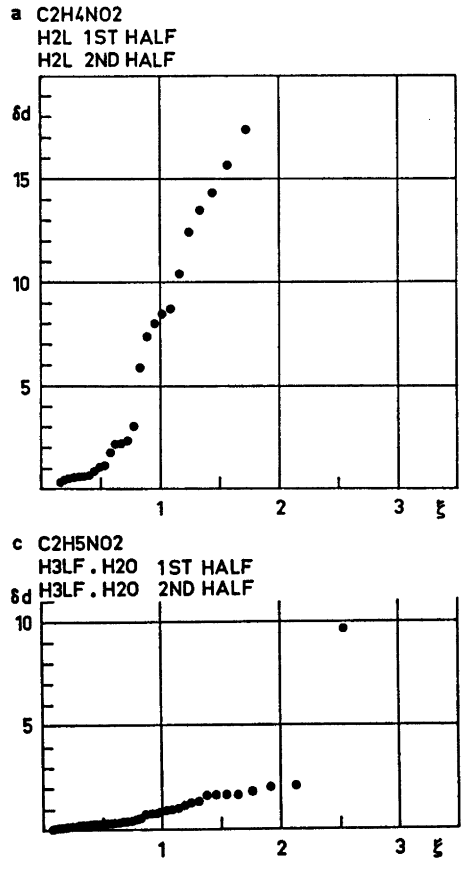
Fig. 2. Half-normal probability plots of the iminodiacetic acid residues. The compared crystal structures and the residue are given above each plot. The slope and the intercept on the ordinate axis of the line defined by points with $\delta d_i < 2.0$ are: (a) 0.95, −.08; (b)1.28, 0.11; (c) 1.56, 0.01; (d) 2.00, 0.03; (e) 1.20, 0.46.

intercept. Systematic differences in the two compared geometries normally give rise to a curved plot but can also show up as a non-zero intercept. A linear plot with a slope s different from unity, may be an indication of uniform under or overestimation in $\sigma d_i = [\sigma^2 d(1)_i + \sigma^2 d(2)_i]^{1/2}$ by a constant factor s. The plots discussed below were obtained by the program PPCMOL.[12]

The structures of H_3LCl ($L^{2-} = HN(CH_2COO^-)_2$, H_3LBr and D_3LCl are closely isostructural.[4-5] A comparison of the ion $H_2\overset{+}{N}(CH_2COOH)_2$ in the chloride and bromide salts using interatomic distances less than 4.65 Å gave a linear plot (Fig. 2a) with an intercept close to zero and a slope of 0.95 suggesting that in these two structures the errors may have been correctly estimated. Therefore the structure of H_3LCl was chosen as a reference structure for checking the presence of systematic differences between the iminodiacetic acid geometries and the reliability of the standard deviations in the other structures.

Only distances less than 2.55 Å were included in the comparisons with the other structures, since the conformation of the organic molecule in these structures is different from that of H_3LCl. The results are given in Figs. 2c–e. The plots are only linear up to about $\delta d = 2$ and with slopes in the range 1.2–2.0. In Fig. 2c the eight points with $\delta d > 2$ represent two C–C distances, two C–O distances and four bond angles. The two C–C distances are the points closest to $\delta d = 2$. In Fig. 2d, the twelve points with $\delta d > 2.5$ represent three C–O distances and nine bond angles. In Fig. 2e, the seven points with $\delta d > 2$ represent two O–H distances and five bond angles. The intercepts are close to zero except for H_3LI (0.4). This deviation is probably caused by a systematic underestimation of the standard deviations in that structure.

The two halves of the iminodiacetic acid group are crystallographically independent in H_2L, $H_3LF.H_2O$ and H_3LI and can therefore be compared using this method. Since the half-normal probability plots in these cases are not based upon two independent sets of data the original obtained standard deviations were



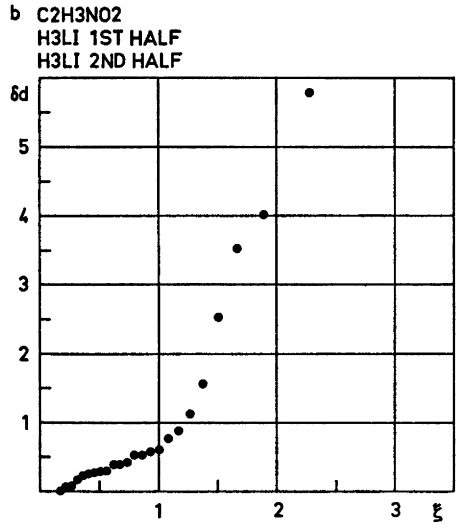


Fig. 3. Half-normal probability plots of the independent halves of the iminodiacetic acid residues in H_2L, $H_3LF.H_2O$ and H_3LI.

multiplied by the factor s obtained by the comparison with H_3LCl for this particular structure (Fig. 2). Interatomic distances less than 4.65 Å have been used. The results are shown in Fig. 3. For H_2L a non-linear plot is expected because of the different states of protonation of the carboxylic groups. In H_3LI the points falling off the straight line represent a bond angle, the conformation across the C–C bonds and the conformation involving a hydrogen atom in the methylene group. In $H_3LF.H_2O$ the plot is judged as linear.

A detailed study of the half-normal probability plots clearly shows that the differences in the bond distances (except C–O) are normally distributed and that such a conclusion is untrue for the bond angles.

BOND DISTANCES AND ANGLES

The N–C and C–C bonds. From the half-normal probability plots it was concluded that the N–C and C–C distances are independent of the crystallographic environment. The values of these distances in $H_3LF.H_2O$ are not significantly different from the values obtained in the other structures, in spite of the fact that the data set was collected at −100 °C for this compound. Therefore it seems reasonable to assume that differences in the iminodiacetic acid residue in $H_3LF.H_2O$ as compared to the other structures should not primarily be attributed to the temperature difference.

The average values of the bond distances and angles are collected in Table 1. Only the N–C and C–C distances are assumed to be of general validity in different types of iminodiacetic acid structures. The N–C distance is the same as the average value [1.488(2) Å] calculated from 13 neutron structure determinations of α-amino acids.[13] The C–C distance is not significantly different from the average value found in oxydiacetates [1.515(3) Å].[14] Several authors have pointed out that bond lengths should vary with hybridization.[15–17] The carbon atoms in the C–C bond are sp^3 and sp^2 hybridized in the iminodiacetates and oxydiacetates, so that a C–C distance slightly smaller than the pure aliphatic C–C single bond length found in gas phase (1.533 Å)[18] is to be expected in these compounds.

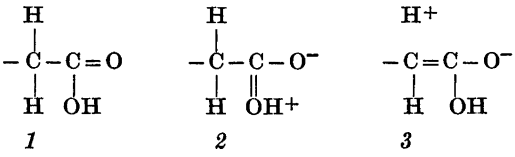
Table 1. Bond distances and angles in the iminodiacetic acid residue. Only the N–C and C–C distances are assumed to be of general validity.

	Distance/Å		Angle/°
N–C	1.488(3)[a]	C–N–C	114.0
C–C	1.505(3)	N–C–C	109.6
C–OH	1.315	C–C–O	110.8
C=O	1.200	C–C=O	123.5
		O–C=O	125.7

[a] Figures within parentheses represent standard deviations in the least significant digit.

Bond angles. A majority of the points falling off the straight lines in the half-normal probability plots represent bond angles. Therefore these quantities are dependent on the environment and cannot be assigned same values in different structures. The same situation was found for the oxydiacetates.[14] This is not surprising since angular deformation constants are much smaller than those for bond lengths and hence the variation of bond angles will be greater than the range of values for bond lengths.

The carboxylic groups. The dimensions of the carboxylic group are dependent on the environment, why the distances given in Table 1 cannot be used uncorrected in other structures. In terms of valence bond theory the following structures can be used to describe the unionized carboxyl group:



1 *2* *3*

Bond length – bond number curves were derived with the use of the relation

$$r_x = r_1 - (r_1 - r_2) \times 1.84(x-1)/(0.84x + 0.16)$$

where x is the bond number, r_x is the actual bond length and r_1 and r_2 are the pure single and double bond lengths, respectively.[19] For the C–O bond Hahn has proposed the value 1.185 Å for r_2 and the value 1.395 Å as an upper limit for r_1.[20] A value of r_1 was found by holding r_2 constant at 1.185 Å and calculat-

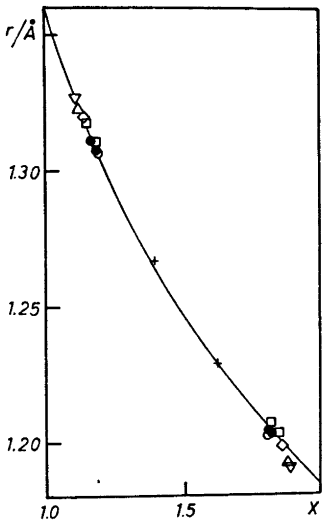


Fig. 4. A Bond length-bond number curve for C–O bonds calculated with $r_1 = 1.360$ Å and $r_2 = 1.185$ Å. The symbols are experimental points and refer to H_2L, carboxylic group (○), H_2L, carboxylate group (+), $H_3LF.H_2O$ (□), H_3LCl (△), D_3LCl (▽), H_3LBr (◇) and H_3LI (●).

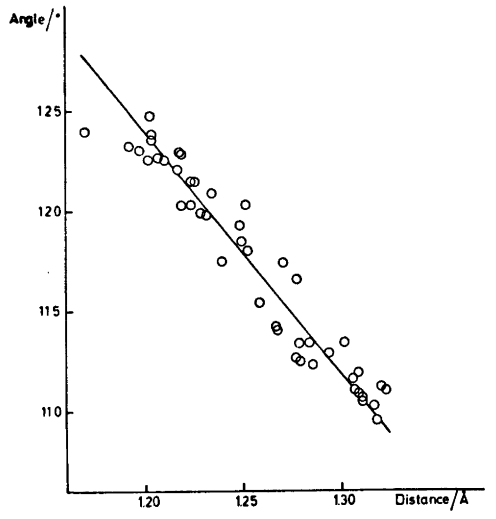


Fig. 5. The graph illustrates the C–C–O angle as a function of the corresponding C–O distance in some compounds containing the C–C(=O) group. The data are taken from Refs. 3–7, 28–31, Thomas, J. O.: *Acta Crystallogr. B 28* (1972) 2073, *B 29* (1973) 1767, Nahringbauer, I.: *Acta Crystallogr. 23* (1967) 956, *Acta Chem. Scand. 23* (1969) 1653, and Abdel Hady, S., Nahringbauer, I. and Olovsson, I. *Acta Chem. Scand. 23* (1969) 2764.

ing x for different values of r_1. The initial value was 1.395 Å and this was decreased in steps of 0.005 Å. If there is no hyperconjugation (structure *3*) the total bond number in C=O should be three. A pure single bond length of 1.360 Å results in an average bond number close to three in the investigated compounds and was therefore accepted as the value for r_1. Fig. 4 shows a bond length bond number curve calculated with $r_1 = 1.360$ Å and $r_2 = 1.185$ Å and it is seen that the contribution of form *2* is only about 10–20 %. The points from the carboxylate group in H_2L have been included in Fig. 4 and it would seem that the same relation is valid for the ionized carboxylate group as for the un-ionized carboxylic group. Hahn [20] has suggested that there is a linear relationship between bond-number and bond-angles C–C–O in carboxylic acids, with end points 109.5 and 125.25° for C–C–O and C–C=O, respectively. This is not found in the present investigation and it is not to be expected according to the previous statement that bond angles are more sensitive to packing forces than bond distances. However, there is roughly a linear relationship between the bond angle C–C–O and the bond distance C–O (Fig. 5), but the spread of the points is so large that the error in the bond angle may be as large as 4° if that curve is used for predicting bond angles from bond lengths. Although the C–O and C=O bond lengths depend upon the environment a χ^2 test shows, with a probability of 0.95, that their sum does not. The average value of the sum, 2.515(1) Å, is not significantly different from the value 2.52 Å found by Speakman *et al.*[21]

A contribution of structure *3* would imply a shorter C–C bond, a longer C–O^- bond and a smaller O–C–O angle compared to compounds where form *3* has zero weight. All these three criteria must be fullfilled if structure *3* is of any importance. The average value of the O–C–O angle is 125.7° in the investigated compounds, which is larger than the expected value 125.25°. The short C–C bond length found is in agreement with the different state

Table 2. Dihedral angles (°) about the C–C bond. The angle is defined as positive, if going from C–O to Cα–N one describes a right-handed screw.

Compound	N–Cα–C–O″	N–Cα–C=O′
H_3L	−169.5	17.3
	−177.1[a]	4.7[a]
$H_3LF.H_2O$	−173.1	6.7
	179.5	0.0
$[Pr_2(H_2O)_4(HL)_2L]Cl_2.3H_2O$	178[a]	−2[a]
	175[a]	−5[a]
	−162[a]	12[a]
Compound	N–Cα–C–O″	N–Cα–C=O′
H_3LCl	180.0	0.0
D_3LCl	180.0	0.0
H_3LBr	180.0	0.0
H_3LI	−177.4	2.6
	180.0	0.0
$[NdL(H_2O)_3]Cl$	158[a]	−36[a]
	153[a]	−24[a]

[a] Carboxylate group.

Table 3. Deviations (Å) from the least-squares plane through the group N–Cα–C(=O′)–O″. This group is situated in a mirror plane in H_3LCl, D_3LCl and H_3LBr.

Compound	N	C	C	O′	O″
H_3L	−.112	0.165	0.027	0.035	−.081
	−.024	0.036	−.004[a]	0.011[a]	−.015[a]
$H_3LF.H_2O$	0.043	−.060	−.011	−0.016	0.040
	−.003	0.003	0.003	0.000	−.003
H_3LI	0.000	0.007	−.002	−.003	−.002
	0.025	−.032	−.004	−.009	0.020
$[NdL(H_2O)_3]Cl$	0.193	−.261	0.034[a]	0.134[a]	−.101[a]
	−.181	0.218	0.055[a]	−.156[a]	0.064[a]
$[Pr_2(H_2O)_4(HL)_2L].$	0.035	−.040	−.018[a]	−.010[a]	0.033[a]
$Cl_2.3H_2O$	0.030	0.002	−.039[a]	0.023[a]	−.016[a]
	−.124	0.055	0.136[a]	0.046[a]	−.113[a]

[a] Carboxylate group.

of hybridization of the carbon atoms. Therefore it is concluded that form *3* does not contribute to the resonance energy of the carboxylic group.

CONFORMATION

The dihedral angles about the Cα–C bond is a suitable parameter if one wants to describe the relative positions of N and O in N–Cα–C(=O′)–O″–H″. The atoms are designated according to IUPAC recommendations.[22] Dihedral angles collected from the previously discussed structures and from two rare earth compounds [23,24] are given in Table 2. It is evident that the group N–Cα–C(=O)–O has a

preferred planar arrangement in the solid state, independent of the state of protonation of the carboxylic group. The largest deviation from planarity (Table 3) is found in $[NdL(H_2O)_3]Cl$, where this group forms a chelate with the metal ion. The shape of the coordination polyhedron in this compound is determined by three factors (if one disregards restrictions imposed by the packing arrangement of the polyhedra): (a) the C_{4v} or D_{3h} configuration, adopted by nine identical monodentate ligands; (b) a preferred planar arrangement of the group $N-C\alpha-C(=O)-O$; (c) a strong coordination bond between the nitrogen and the metal ion. The resulting polyhedron might be a compromise between the influence from these factors. Therefore the chelates in $[NdL(H_2O)_3]Cl$ are formed at the expence of an energetically more stable conformation of the organic ligand.

The double-bonded oxygen in the carboxylic group is in a position *cis* to the nitrogen in all studied structures. The two carbon-oxygen distances in the carboxylate group in H_2L are significantly different, with the oxygen participating in the shortest C–O bond *cis* to the nitrogen.

The group $C\beta-C\alpha-C(=O')-O''-H''$ has also been found to have a preferred planar arrangement in the solid state.[25–27] This feature has often been ascribed to non-bonded interactions $C\beta\cdots O$. Non-bonded distances $N\cdots O'$ and $(N-)H\cdots O'$ obtained in this study are given in Table 4. The average value of the $N\cdots O'$ distance, 2.69(4) Å, may be compared with the calculated non-bonded distances for the two planar structures. The parameters in Table 1 imply a $N\cdots O$ distance of 2.70 Å with O′ in a position *cis* to the nitrogen and 2.47 Å with O″ in this position. On the assumption that the planar conformation is stabilized by non-bonded interactions the potential energy curve describing the interactions $NH_2\cdots O$ should have a minimum around 2.7 Å. This relatively small value is not surprising since it is well known that intramolecular non-bonded distances may be smaller than the sum of the corresponding van der Waals radii. In one case (H_2L: $H\cdots O'$ = 2.16 Å) there might be a contribution to the potential well from an intramolecular hydrogen bond. However, the group $R-C\alpha-C(=O)-O$, where R = O or S, is also planar with O′ in a position *cis* to R.[28–33] Since these residues cannot be stabilized by intramolecular hydrogen bonding, one may assume that the contribution of this factor is of minor importance in stabilizing the planar iminodiacetic acid residue.

From the preceding discussion it may be concluded that a planar arrangement of the group $-R-C-C(=O)-O$, seems to be a general feature for a great variety of R. Furthermore, if the C–O bonds have different lengths, the arrangement with O′ *cis* to R is the preferred one.

I am indebted to Dr. Jörgen Albertsson for useful discussions and many valuable suggestions. This work is part of a research project supported by the Swedish Natural Science Research Council.

Table 4. Non-bonded distances (Å) $N\cdots O'$ and $(N-)H\cdots O'$ in the studied structures. H is the hydrogen atom in the NH_2 group, which is closest to O′.

Compound	N···O′	(N–)H···O′	Compound	N···O′	H···O′
H_2L	2.660(3)	2.55(2)	H_3LI	2.75(1)	2.4(1)
	2.675(2)	2.16(2)		2.68(1)	2.3(1)
$H_3LF.H_2O$	2.744(3)	2.60(2)	$[NdL(H_2O)_3]Cl$	2.74(3)	
	2.693(2)	2.60(3)		2.72(4)	
H_3LCl	2.660(3)	2.55(2)	$[Pr_2(H_2O)_4(HL)_2L]Cl_2.$	2.73(3)	
D_3LCl	2.651(8)	2.49(3)		2.65(3)	
H_3LBr	2.666(4)	2.60(3)	$3H_2O$	2.60(3)	

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