ELECTRONIC SUPPLEMENTARY INFORMATION (ESI)

Coordination polymers of paramagnetic bis(leucinato)copper(II) diastereomers: experimental and computational study of the stereoisomerism and conformations

Darko Vušak,^a Jelena Pejić,^b Mia Jurković,^a Gábor Szalontai^c and Jasmina Sabolović*^b

^a Department of Chemistry, Faculty of Science, University of Zagreb, Horvatovac 102a, HR-10000 Zagreb, Croatia

^b Institute for Medical Research and Occupational Health, Ksaverska cesta 2, HR-10000 Zagreb, Croatia

^c NMR laboratory, Institute of Chemistry, Faculty of Engineering, University of Pannonia, Egyetem utca 10, H-8201 Veszprém, Hungary

1. Powder X-ray diffraction (PXRD)



Figure S1. Powder patterns of the products of mechanochemical reactions of copper(II) acetate and L-Leu using neat grinding (NG) or liquid assisted grinding (LAG) with denoted different solvents. Powder patterns of the reactants {L-Leu and $[Cu(OAc)_2(H2O)]_2$ } and *trans*- $[Cu(L-Leu)_2]_n$ (1) were calculated from crystal structures. Powder patterns separated with a broken line are not on the same intensity scale.



Figure S2. Powder patterns of the products of mechanochemical reactions of copper(II) hydroxide and DL-Leu using neat grinding (NG) or liquid assisted grinding (LAG) with denoted different solvents. Powder patterns of the reactants [DL-Leu and Cu(OH)₂] and *trans*-[Cu(D-Leu)(L-Leu)]_n (2) were calculated from crystal structures. Powder patterns separated with a broken line are not on the same intensity scale.



Figure S3. Powder patterns of the products of solution based reactions with L-Leu using different denoted copper(II) compounds. Powder patterns of *trans*-[Cu(L-Leu)₂]_n (1) were calculated from the crystal structure. Powder patterns separated with a broken line are not on the same intensity scale.



Figure S4. Powder patterns of the products of solution based reactions with DL-Leu using different denoted copper(II) compounds. The powder pattern of *trans*-[Cu(D-Leu)(L-Leu)]_n (2) was calculated from the crystal structure. Powder patterns separated with a broken line are not on the same intensity scale.

2. Thermogravimetric analysis



Figure S5. Thermogravimetric analysis of 2.

3. Infrared spectroscopy



Figure S6. IR (ATR) spectrum of 2.

4. Hirshfeld surface analysis



Figure S7. Hirshfeld surface of the primary building unit of *trans*-[Cu(D-Leu)(L-Leu)]_n (2) was mapped over d_{norm} in the color range -0.4861 to 1.3134 a.u. Contacts shorter than the sum of the van der Waals radii are represented as red areas. Intermolecular close O···C contact is represented by an orange dashed line, and Cu···O by a red dashed line.

5. Defining the Cu(L-Leu)₂ and Cu(D-Leu)(L-Leu) conformer names

Each Leu ligand of Cu(Leu)₂ can have 18 conformations as follows: two conformations of the five-member chelate ring, with C^{β} (C3) in an axial or equatorial positions, and 9 conformations of the Leu residue defined by the torsions angles N–C2–C3–C4 and C2–C3–C4–H (Figure 1). The two torsion angles can have values approximately equal to 60° , -60° and 180° . The conformer names are composed of letters "a" and "e", which stand for the axial and equatorial, and the numbers from 1 to 9, which are defined in Table S1. For instance, if both Leu ligands have C3 in an axial position, and both N–C2–C3–C4 and C2–C3–C4–H are $\approx 60^{\circ}$, for Cu(L-Leu)₂ the conformer name is La2-La2, and for Cu(D-Leu)(L-Leu) the conformer name is Da6-La2. The D-Leu geometries in Cu(D-Leu)(L-Leu) were constructed from the L-Leu geometries by changing the C2 atom chirality from 2*S* (L-Leu) to 2*R* (D-Leu).

L-Leu conformation			D-Leu conformation				
name	NC2C3C4	С2С3С4Н	 name	N-C2-C3-C4	С2С3С4Н		
1	60°	180°	1	-60°	180°		
2	60°	60°	2	-60°	-60°		
3	60°	-60°	3	-60°	60°		
4	-60°	180°	4	60°	180°		
5	-60°	60°	5	60°	-60°		
6	-60°	-60°	6	60°	60°		
7	180°	180°	7	180°	180°		
8	180°	60°	8	180°	-60°		
9	180°	-60°	9	180°	60°		

Table S1. Defining the L-Leu and D-Leu ligand conformations from 1 to 9 in $Cu(Leu)_2$ by means of the combinations of three possible values of the N–C2–C3–C4 and C2–C3–C4–H torsion angles (in degrees; approximate values are given).

According to the name definitions, the $Cu(Leu)_2$ conformers in the X-ray crystal and molecular structures are as follows: *trans* Le5-La9^{10,11} (Figure 1) and *trans* Da9-La5 (Figure 2).

6. DFT conformational analyses of LL and DL Cu(Leu)₂ diastereomers in the gas phase and aqueous solution

We constructed 18 *trans*-Cu(Leu)₂ and 18 *cis*-Cu(Leu)₂ starting geometries with the same conformations of L-Leu ligands in Cu(L-Leu)₂. The corresponding 18 conformations of L-Leu and D-Leu ligands in Cu(D-Leu)(L-Leu) were constructed in a such manner that the D-Leu conformation was a mirror image of the L-Leu conformation with Cu as an inversion center.

The equilibrium geometries of the starting geometries were calculated in the gas phase and in implicitly modeled aqueous solution using the polarizable continuum model (PCM).^{56,57} Tables S2 and S3 list the characteristic torsion angles of the obtained conformers, and compare the relative DFT/B3LYP electronic and Gibbs free energies of the *trans-* and *cis-*conformers of Cu(L-Leu)₂ and Cu(D-Leu)(L-Leu) in aqueous solution.

Two combinations of N–C2–C3–C4 and C2–C3–C4–H angles, 5 and 9 (Table S1) yielded the lowest electronic and Gibbs free energies both in the equatorial and axial conformations (i.e., e5-e5, a5-a5, e9-e9, a9-a9, Tables S2 and S3). Figure S8 illustrates these conformers. The Gibbs free energies of these conformers in *trans*-configuration were very similar for the LL (Table S2) and DL (Table S3) diastereomers (that is, the energy differences were up to 1.4 kJ mol⁻¹). These

results agree with the experimental observation that no diastereoselectivity effect was detected in the formation of bis complexes of Cu(II) with either L-Leu or DL-Leu in aqueous solutions.^{5,6}

Table S2. Characteristic torsion angles for defining conformations of two L-Leu ligands in Cu(L-Leu)₂, relative electronic ΔE_{water} (kJ mol⁻¹) and Gibbs free energies ΔG_{water} (kJ mol⁻¹) of denoted DFT-calculated minimum structures (conformers) in implicitly modeled aqueous solution^{*a*}

Conformer	Cu-N-C2-C3	N-C2-C3-C4	С2-С3-С4-Н	$\Delta E_{\rm water}$	$\Delta G_{ m water}$	
trans-[Cu(L-Leu) ₂]						
Lal-Lal	-124.1, -128.8	63.8, 63.4	178.2, 176.6	40.0	44.5	
$La2-La2^{b}$	/	/	/	/	/	
La3-La3 ^b	/	/	/	/	/	
La4-La4	-101.5, -101.5	-84.0, -84.0	178.3, 178.3	21.9	24.6	
La5-La5	-100.1, -101.0	-67.6, -67.3	56.6, 56.8	4.3	3.7	
La6-La6	-100.0, -100.0	-87.1, -87.1	-59.1, -59.1	15.7	17.2	
La7-La7	-90.3, -90.4	-176.7, -176.4	162.4, 162.3	28.9	35.7	
La8-La8	-92.2, -92.2	179.8, -179.8	24.9, 24.0	22.9	24.5	
La9-La9	-92.3, -92.6	-179.9, -179.7	-59.7, 60.4	6.1	11.3	
Le1-Le1	-148.9, -149.1	60.0, 59.9	172.1, 171.9	40.0	46.6	
Le2-Le2	-150.3, -149.5	79.3, 79.5	61.5, 61.6	19.4	23.3	
Le3-Le3	-151.8, -151.6	51.0, 51.0	-61.9, -62.0	14.6	20.5	
Le4-Le4	-150.7, -150.3	-80.4, -80.2	179.9, 179.7	17.8	20.6	
Le5-Le5	-148.7, -148.7	-64.1, -63.9	55.1, 55.1	0.0	0.0	
Le6-Le6	-152.8, -152.3	-85.6, -85.7	-58.2, -58.3	12.3	14.8	
Le7-Le7	-151.8, -151.8	-163.2, -163.4	149.4, 149.4	42.4	49.1	
$Le8-Le8^b$	/	/	/	/	/	
Le9-Le9	-156.1, -155.9	-158.5, -158.1	-51.9, -51.5	9.5	9.9	
Le5-La9 ^c	-166.2, -87.8	-72.5, 176.6	61.8, -54.9	3.1	3.1	
		cis-[Cu(L-Leu	u) ₂]			
Lal-Lal	-122.1, -122.1	63.9, 63.9	178.1, 178.1	45.7	58.5	
La2-La2	-150.6, -150.3	79.5, 79.4	61.4, 61.7	24.5	31.3	
La3-La3	-116.3, -114.7	55.9, 56.5	-51.2, -49.8	25.4	28.8	
La4-La4	-100.4, -100.9	-84.2, -84.9	178.3, 178.0	27.4	30.0	
La5-La5	-99.1, -100.6	-68.2, -67.9	56.1, 56.4	9.8	12.4	
La6-La6	-100.0, -100.8	-87.2, -87.5	-59.1, -59.1	21.2	26.7	
La7-La7	-89.9, -89.9	-176.2, -176.5	163.3, 161.9	33.6	43.0	
La8-La8	-91.8, -91.2	-178.8, 179.4	25.9, 24.9	27.8	31.1	
La9-La9	-92.1, -92.4	-179.5, 179.9	-59.7, -60.4	11.0	16.1	
Le1-Le1	-153.3, -153.9	57.5, 56.4	168.5, 166.5	45.0	53.0	
Le2-Le2	-151.1, -147.6	79.5, 79.9	61.6, 61.9	24.6	30.0	
Le3-Le3	-152.8, -152.7	51.1, 50.3	-61.7, -62.7	19.7	23.9	
Le4-Le4	-151.0, -149.2	-79.9, -77.6	-179.8, -177.3	22.9	26.9	
Le5-Le5	-149.8, -150.8	-64.1, -64.9	55.4, 54.6	4.9	8.3	

Le6-Le6	-152.4, -152.5	-85.2, -85.6	-58.0, -58.1	17.3	18.9
Le7-Le7	-153.8, -153.3	-162.7, -162.3	148.9, 149.3	47.4	50.9
$Le8-Le8^b$	/	/	/	/	/
Le9-Le9	-155.7, -158.2	-159.3, -158.9	-52.4, -51.8	14.3	11.4

^{*a*} The conformer names are defined in Table S1. The electronic and Gibbs free energies of *trans* Le5-Le5 are used as reference values ($E_0 = -2522.94867722$ a.u.; $G_0 = -2522.636441$ a.u.). ^{*b*} The starting structures of *trans*-conformers La2-La2, La3-La3, Le8-Le8 and *cis* Le8-Le8 changed to *trans* Le2-Le2, Le3-Le3, Le5-Le5, and *cis* Le5-Le5, respectively, via the geometry optimization. ^{*c*} The X-ray crystal structure of Cu(L-Leu)₂¹⁰ (Figure 1) was the starting structure for the geometry optimization.

Table S3. Characteristic torsion angles for defining conformations of D-Leu and L-Leu in Cu(D-Leu)(L-Leu), relative electronic ΔE_{water} (kJ mol⁻¹) and Gibbs free energies ΔG_{water} (kJ mol⁻¹) of DFT-calculated minimum structures (conformers) in implicitly modeled aqueous solution^{*a*}

Conformer	Cu-N-C2-C3 (D, L)	N-C2-C3-C4 (D, L)	C2-C3-C4-H (D, L)	$\Delta E_{\rm water}$	$\Delta G_{ m water}$		
trans-[Cu(D-Leu)(L-Leu)]							
Dal-Lal	121.5, -121.5	-63.7, 63.7	-177.9, 177.9	39.7	47.5		
Da2-La2 ^b	/	/	/	/	/		
Da3-La3 ^b	/	/	/	/	/		
Da4-La4	102.7, -102.7	74.6, -83.9	-178.4,178.4	21.9	21.3		
Da5-La5	100.5, -100.5	67.1, -67.1	-57.6, 57.6	4.5	3.5		
Da6-La6	100.1, -100.1	86.9, -86.9	58.8, -59.8	15.6	18.6		
Da7-La7	90.7, -90.7	176.5, -176.5	-162.4, 162.4	28.8	35.9		
Da8-La8	92.5, -92.5	-179.9, 179.9	-24.5, 24.5	22.8	25.5		
Da9-La9	93.1, -93.1	179.6, -179.6	60.1, -60.1	6.0	11.4		
Del-Lel	146.3, -146.3	-60.5, 60.5	-172.3, 172 .3	40.1	44.6		
De2-Le2	147.6, -147.6	-79.4, 79.4	-61.6, 61.6	19.4	17.7		
De3-Le3	150.8, -150.8	-51.1, 51.1	62.1, -62.1	14.6	15.6		
De4-Le4	149.7, -149.7	81.1, -81.1	-179.2, 179.2	17.9	19.7		
De5-Le5	149.5, -149.5	63.5, -63.5	-55.2, 55.5	-0.1	1.4		
De6-Le6	150.9, -150.9	85.6, -85.6	58.6, -58.6	12.4	9.4		
De7-Le7	151.4, -151.4	163.5, -163.5	-149.4, 149.4	42.3	49.1		
De8-Le8	/	/	/	/	/		
De9-Le9	155.9, -155.9	159.1, -159.1	52.5, -52.5	9.5	8.9		
Da9-La5 ^c	92.7, -100.2	-179.6, -67.1	60.1, 57.3	5.3	7.5		
cis-[Cu(D-Leu)(L-Leu)]							
Dal-Lal	122.6, -151.7	-62.9, 59.9	-176.9, 171.7	45.6	55.2		
Da2-La2	149.8, -150.6	-79.3, 79.9	-61.3, 61.9	24.8	29.2		
Da3-La3 ^b	/	/	/	/	/		
Da4-La4	100.2, -101.7	84.9, -83.7	-178.2, 178.7	27.7	30.2		
Da5-La5	98.5, -100.4	68.1, -67.5	-56.8, 56.7	10.1	9.4		
Da6-La6	98.7, -100.1	87.7, -86.9	59.2, -58.9	21.5	25.9		
Da7-La7	89.5, -90.3	176.9, -175.8	-161.9, 162.3	33.9	41.5		
Da8-La8	91.5, -92.4	179.8, -179.1	-24.9, 24.1	28.0	29.7		

Da9-La9	92.1, -92.8	-179.9, -179.2	60.2, -60.3	11.2	15.5	
Del-Lel	154.7, -154.1	-56.7, 57.3	-166.9, 168.4	45.3	52.7	
De2-Le2	150.7, -150.2	-79.9, 79.4	-61.7, 61.4	24.9	28.7	
De3-Le3	153.1, -152.4	-50.9, 50.7	61.8, -62.1	19.8	25.2	
De4-Le4	152.3, -150.6	80.6, -80.6	-179.7, 179.7	23.2	26.1	
De5-Le5	151.5, -149.8	64.2, -64.7	-55.6, 54.6	5.1	9.0	
De6-Le6	153.4, -153.1	85.8, -85.5	58.1, -58.4	17.5	20.0	
$De7-Le7^b$	150.1, -154.3	162.9, -161.4	-149.8, 149.6	47.6	49.2	
De8-Le8	/	/	/	/	/	
De9-Le9	158.4, -157.8	161.1, -159.1	54.1, -52.4	14.5	13.4	
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 a^{a} The conformer names are defined in Table S1. The reference values of electronic and Gibbs free energy are given in Table S2.

^b The starting structures of conformers *trans* Da2-La2, Da3-La3, De8-Le8 and *cis* Da3-La3 and De8-Le8 changed to *trans* De2-Le2, De3-Le3, De5-Le5, and *cis* De3-Le3 and De5-Le5, respectively, via the geometry optimization.

^c The X-ray crystal structure (Figure 2) was the starting structure for the geometry optimization.



Figure S8. Illustrations of the $Cu(L-Leu)_2$ and Cu(D-Leu)(L-Leu) conformers with side-chain conformations 5 and 9 (their characteristic torsion angles and relative energies are given in Tables S2 and S3).

Figure S9 compares the energy landscapes of the Cu(Leu)₂ conformers in the gas phase and aqueous solutions. We assumed that the energies of the conformers with mixed Leu conformations can be expressed as a half value of the energies of the conformers with the same corresponding Leu conformations in Cu(Leu)₂ {e.g. E_{DFT} (De1-Le2) $\approx 1/2$ [E_{DFT} (De1-De1) + E_{DFT} (Le2-Le2)] $\approx 1/2$ [E_{DFT} (Le1-Le1) + E_{DFT} (Le2-Le2)], where E_{DFT} (De1-De1) = E_{DFT} (Le1-Le1)}. The assumption is approved by the calculated energy values for the Da9-Le5, La9-Le5, and Da9-La5 conformers (the latter transformed to Da9-Le5 in the gas phase) (Figure S9).



Figure S9. DFT/B3LYP minimum electronic (potential) energy values estimated for the Cu(L-Leu)₂ and Cu(D-Leu)(L-Leu) systems in the gas phase (red) and in implicitly modeled aqueous solution using PCM (blue) for denoted conformers with a *trans*- or *cis*-configuration. The energy values of corresponding LL and DL diastereomer conformers (e.g., La1-La1 and Da1-La1) differ up to 1 kJ mol⁻¹. The ΔE values were calculated relative to the *trans* e5-e5 conformers. An empty space means that the corresponding starting conformer changed to another conformer via geometry optimization (from axial to equatorial Leu conformations in the gas phase, and from e8-e8 to e5-e5 in aqueous solution).

The energies of *trans* Cu(Leu)₂ conformers are significantly lower than those of the *cis* conformers in the gas phase, while the energies of both *trans* and *cis* conformers adopted comparable values in aqueous solution. The same outcome was obtained for previously studied copper(II) amino acid complexes with glycinato-like coordination (that is, with Cu(II) coordinated with the amino N and carboxyalato O atoms).^{8,9,31,32} The lowering of the energy of the *cis* relative to the *trans* conformers in aqueous solution compared to the gas phase was explained by the molecular dynamics simulations to be due to more favorable intermolecular interaction with the solvent medium by *cis* than *trans* isomers.⁸

Two Leu conformations, 5 and 9 (Table S1), distinguished as the ones with the lowest energies, both in the gas phase and aqueous solution (Tables S2 and S3, Figure S9). These are

exactly the conformations whose combinations occurred in the observed crystal structures of LL and DL Cu(Leu)₂.(Le5-La9 and Da9-La5, respectively).

In the gas phase, the Leu side-chain conformations yielding the relative electronic energy of trans-[Cu(Leu)₂] lower than 10 kJ mol⁻¹ are: 3, 5, 6, and 9 (Figure S9). However, in aqueous solution, the conformations with $\Delta E_{\text{DFT}} < 10$ kJ mol⁻¹ are only 5 and 9 in the LL and DL *trans*-and *cis*-[Cu(Leu)₂] conformers.

7. MM reproduction of the X-Ray crystal and molecular structures of Cu(Leu)₂

The FFWa-SPCE reproduces well the experimental X-ray unit cell packing and the molecular geometries of *trans*-[Cu(L-Leu)₂] **1** and *trans*-[Cu(D-Leu)](L-Leu)] **2** as may be seen from the superposition of the MM and X-ray unit cell packings (Figure S10).

The root-mean-square (rms) deviations between experimental and MM bond lengths, valence and torsion angles are 0.032 Å, 3.1°, 6.1°, respectively, for **1**,³¹ and 0.016 Å, 2.2°, 4.2°, respectively, for **2**. The reproduction of the unit cell dimensions (given in Figures S11) was comparable to the values obtained previously for 25 bis(amino acidato)copper(II) crystal and molecular structures.³¹ Good overall reproduction of the experimental crystal and molecular structures using FFWa-SPCE (reported elsewhere)³¹ confirmed that the force field was reliable, that it accurately reproduced the crystal lattice effects, and that the van der Waals and hydrogenbonding intermolecular interactions were properly modeled.



Figure S10. Superposition of the X-ray (red) and MM crystal (blue) unit cells and packing of *trans*-[Cu(L-Leu)₂] and *trans*-[Cu(D-Leu)](L-Leu)]. The X-ray unit cell dimensions of the former complex are:¹⁰ a = 9.725(4) Å, b = 5.127(1) Å, c = 14.689(6) Å; $\beta = 105.79(3)^{\circ}$, V = 704.8 Å³, while the latter ones are given in Table 6. The MM unit cell dimensions are given in Table 5.

8. MM partial conformational analysis in crystal

The MM partial conformational analysis in crystal was performed for selected conformers of *trans*-[Cu(L-Leu)₂] and *trans*-[Cu(D-Ile)(L-Ile)] in the simulated $P2_1$ and C2 unit cell packings, respectively. The selected conformers of *trans*-[Cu(L-Leu)₂] were as follows: the combinations of La9 with nine possible L-Leu (e) conformations, the combinations of Le5 with nine possible L-Leu (a) conformations, and La5-Le9. For *trans*-[Cu(D-Ile)(L-Ile)], the selected conformers were the combinations of Da9 with nine possible L-Leu (a) conformations, the combinations, the combinations of La5 with nine possible D-Leu (a) conformations, and Da5-La9. Prior to the geometry optimization, the conformer position and orientation were constructed to be the same as in the respective experimental X-ray crystal structures.

During the energy minimization, some of the conformers could not preserve their geometries and "disintegrated" with bond breaking (e.g., La9-Le2 and Da9-Le1), and the C3-axial position transformed to the equatorial one in several conformers (Figure S11). The low intermolecular energy values, E_{lattice} , are in the range from –389.5 to –392.8 kJ mol⁻¹ for the conformers La9-Le5 and La9-Le9 in the *P*2₁ space group, and Da9-La5, Da5-La5, and Da5-La9 in space group *C*2. Six additional unit cell packing have E_{lattice} in the range from –382.0 to –392.8 kJ mol⁻¹ (Le2-Le5, La4-Le5, La5-Le5, La6,-Le5, Da9-La6 and Da9-La8).

Not only the intermolecular energy E_{lattice} , but also the intramolecular energy E_{strain} can have a considerable contribution to the total potential energy, E_{crystal} , of a specific conformer in the crystal lattice. To examine how reliable the FFWa-SPCE E_{strain} values are, we compared the gas phase DFT and MM intramolecular energies of the LL and DL Cu(Leu)₂ stereoisomers (Figure S12). In the comparison, we focused on the trans conformers only, as this chelation configuration was observed in the crystal structures. Both DFT and MM methods gave practically the same energy values (within 1 kJ mol⁻¹) for the same corresponding LL and DL conformers (e.g., Le1-Le1 and De1-Le1). The calculated MM relative energies of the conformers a9-Le5 and Da9-La5 can be consider as half of the energies of the a9-a9 and e5-e5 (a5-a5) conformers (Figure S11). The MM energy landscape profile reproduces qualitatively the DFT one for most conformers, except for a9-a9 and a8-a8, for which FFWa-SPCE yielded lower MM potential energy values than for the reference e5-e5 conformer (Figure S12). The MM prediction that the side-chain Leu conformations 5 and 9 are among the most stable ones in the gas phase agrees well with the DFT/B3LYP prediction, but yields conformation 9 more stable than conformation 5. Thus, FFWa-SPCE might overestimate the intramolecular E_{strain} contribution to E_{crystal} for the conformers having the a9 and e9 Leu conformations.



Figure S11. MM minimum energy values, $E_{crystal}$ (red) and $E_{lattice}$ (blue), estimated for denoted conformers of *trans*-[Cu(L-Leu)₂] and *trans*-[Cu(D-Leu)(L-Leu)] in the $P2_1$ and C2 unit cell packings, respectively. The deviations between the MM simulated and experimental unit cell dimensions expressed by the root-means-square (rms) errors in the *a*, *b*, and *c* unit cell lengths, differences in the unit cell angle β , and relative unit cell volume reproduction, are given under the graphs. The simulation results for the experimentally observed conformers are denoted in green.



Figure S12. Comparison of the potential DFT/B3LYP (E_{DFT}) and MM (E_{MM} or E_{strain}) relative energy values calculated in the gas phase for the denoted *trans* conformers of Cu(L-Leu)₂ and Cu(D-Leu)(L-Leu) (the relative energies between the same corresponding LL and DL conformers differ up to 1 kJ mol⁻¹). The corresponding energy values of the *trans* e5-e5 conformers are the reference values. Empty space means that the corresponding starting conformer changed to another conformer (usually to the equatorial counterpart) via geometry optimization.

The FFWa-SPCE intermolecular energy was established as an empirical criterion to predict conformation(s) occurring in the crystal lattice in our previous papers.^{8,32} Namely, the criterion was proven suitable by good match between the predicted conformers having the most favorable intermolecular interactions in aqueous solution (calculated using molecular dynamics) as well as in crystal (calculated using MM) and the experimental crystallization results of *trans*-[Cu(L-Val)₂],³² aqua *cis*-[Cu(L-Val)₂],³² and aqua *cis*-[Cu(L-Ile)₂].⁹ The same criterion proved valid for the unit-cell packings of Cu(Leu)₂ complexes. Specifically, the lowest *E*_{lattice} was calculated for the *P*2₁ unit-cell packing of the experimental conformer La9-Le5 (-392.8 kJ mol⁻¹). A slightly higher value was obtained for the *C*2 unit-cell packing of the observed conformer Da9-Da5 (-389.5 kJ mol⁻¹). *E*_{crystal} is slightly lower for the DL then LL stereoisomer (by 2.6 kJ mol⁻¹). These very similar energy values suggest that the reasons for the crystallization of only DL over LL and DD stereoisomers of Cu(Leu)₂ during the crystal growth should be sought for in the kinetic rather than the thermodynamic effects.