Comparing the Spatial Structure of Molecules by Minimizing a Comparison Function

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Abstract—A method for the quantitative comparison of the spatial geometric structure of two molecules is proposed. It is based on the minimization of a comparison function using the rotation of molecules when their centers of mass are brought into coincidence. The minimizing angles are found using the Rosenbrock method.

1. INTRODUCTION

This paper is devoted to the theoretical and numerical investigation of the mathematical model of comparing two molecules in a problem of structural chemistry. This model is reduced to comparing two objects consisting of N ordered points of fixed geometry that behave as rigid bodies in R^3. The comparison principle in this model is based on optimizing the superposition of these two objects by translations and rotations. The optimal superposition is achieved by finding the translations and rotations minimizing a function that compares the geometry of two objects. This function is the sum of distances between the points of the two objects with identical indexes. To minimize the comparison function (see [1, 2]), the zero-order Rosenbrock method is used (see [3, 4]). The results are used to compare the geometry of real-life molecules.

The molecules of many substances can exist in the form of conformers (conformation is the spatial arrangement of atoms in a molecule; there are various manifestations of this phenomenon in chemistry [5])—the conformers have the same structural formula but different spatial configuration. Hence, the problem of comparing the geometry of conformers in space arises because the conventional characteristics, such as bond lengths (interatomic distances) and valence angles, do not always show the differences of the molecular geometry. Moreover, there is need in comparing fragments of chemically different molecules, the close neighborhood of atoms (coordination polyhedra), or other large or small complexes of atoms. For this purpose, a method for the quantitative comparison of molecular geometry based on the minimization of a comparison functions by translating and rotating molecules is proposed. It is proved that the minimum with respect to translations is achieved by bringing certain characteristic points, which are arbitrary called the molecular centers of mass, into coincidence. Minimization with respect to rotation angles is performed using the zero-order Rosenbrock method.

2. DESCRIPTION OF THE MATHEMATICAL MODEL

In this section and in the next one, we present some definitions and theorems.

Definition 1. The geometric structure (or briefly structure) is a rigid geometric construct consisting of N ordered points in R^3 with the coordinates (x_i, y_i, z_i) $(i = 1, ..., N)$ that moves in R^3 as a rigid body.

We assume that each ith point of this structure is assigned a weighting coefficient $w_i \geq 0$ such that $\sum_{i=1}^{N} w_i = W > 0$. Let i_k, $k = 1, \ldots, K$, be the indexes of nonzero weighting coefficients w_i. Then,

$$W = \sum_{i=1}^{N} w_i = \sum_{k=1}^{K} w_{i_k} > 0. \tag{1}$$

Let two geometric structures consisting of N points each with the coordinates $(x_{1,i}, y_{1,i}, z_{1,i})$ and $(x_{2,i}, y_{2,i}, z_{2,i})$ $(i = 1, \ldots, N)$ be given. For each fixed index i, the point with the coordinates $(x_{1,i}, y_{1,i}, z_{1,i})$ of the first structure corresponds to the point $(x_{2,i}, y_{2,i}, z_{2,i})$ of the second structure.

Let the geometries of both structures be identical. Consider two arbitrary points specified by the vectors $\mathbf{r}_{1,0}$ and $\mathbf{r}_{2,0}$ that are identically positioned relative to the corresponding geometric structure (in particular, we may choose two points of these structures with the same indexes as $\mathbf{r}_{1,0}$ and $\mathbf{r}_{2,0}$). Then, by rotating one structure relative to the other, we can bring all points with identical indexes into coincidence thus achieving the complete coincidence of the two structures. If the two structures have different geometries, then it is natural to pose the problem of bringing them into optimal "coincidence" by various translations and rotations of one structure relative to the other considered as rigid bodies.

The optimality criterion of coincidence of two geometric structures is formulated in terms of the minimum of the comparison function

$$U(\mathbf{r}_{1,0}, \mathbf{r}_{2,0}, \varphi, \theta, \psi) = \sum_{i=1}^{N} w_i \left| \mathbf{r}_{1,i} - \mathbf{r}_{1,0} - Q(\mathbf{r}_{2,i} - \mathbf{r}_{2,0}) \right|^2, \tag{2}$$

with respect to translations and rotation (Euler) angles (see [6]), where the vectors $\mathbf{r}_{1,i}$ and $\mathbf{r}_{2,i}$ determine the position of points in the first and the second structures, respectively; the vectors $\mathbf{r}_{1,0}$ and $\mathbf{r}_{2,0}$ determine the displacement of the first and the second structures to the corresponding points; and $Q = Q(\varphi, \theta, \psi)$ are the rotation matrices through the Euler angles (ψ is the precession angle, θ is the nutation angle, and φ is the intrinsic rotation angle):

$$Q = \begin{pmatrix} \cos\psi\cos\varphi - \sin\psi\sin\varphi\cos\theta & -\cos\psi\sin\varphi - \sin\psi\cos\varphi\cos\theta & \sin\psi\sin\theta \\ \sin\psi\cos\varphi + \cos\psi\sin\varphi\cos\theta & -\sin\psi\sin\varphi + \cos\psi\cos\varphi\cos\theta & -\cos\psi\sin\theta \\ \sin\varphi\sin\theta & \cos\varphi\sin\theta & \cos\theta \end{pmatrix}. \tag{3}$$

Thus, the function U defined by (2) is the sum of distances between the corresponding points of two geometric structures with the weights w_i after bringing the points determined by the vectors $\mathbf{r}_{1,0}$ and $\mathbf{r}_{2,0}$ into coincidence and rotating the second structure relative to the first one. Let us examine problems emerging in the process of minimizing the comparison function (2).

3. MINIMIZING THE COMPARISON FUNCTION OF TWO GEOMETRIC STRUCTURES

We show that, by bringing certain characteristic points of two geometric structures into coincidence, the comparison function minimization problem with respect to the entire set of variables can be reduced to the minimization of the function U with respect to the rotation angles φ, θ, and ψ.

In this paper, we give more complete and rigorous formulation and proof of the idea proposed in [7].

Theorem 1. *The minimum of the function U is attained at the point corresponding to the "center of mass" of the two geometric structures determined by the vectors*

$$\mathbf{r}_{j,0} = \frac{1}{W} \sum_{i=1}^{N} w_i \mathbf{r}_{j,i}, \quad j = 1, 2. \tag{4}$$

Proof. In function (2), we fix the angles φ, θ, and ψ and, therefore, the matrix Q. Hence, we will consider (2) as a function of the variables $\mathbf{r}_{1,0}$ and $\mathbf{r}_{2,0}$. This function is convex and quadratic with respect to these two variables; therefore, its minimum with respect to $\mathbf{r}_{1,0}$ and $\mathbf{r}_{2,0}$ is attained at the points at which the derivative with respect to these variables vanishes. Thus, we obtain the equations

$$\frac{\partial U}{\partial \mathbf{r}_{1,0}} = 0, \quad \frac{\partial U}{\partial \mathbf{r}_{2,0}} = 0. \tag{5}$$

By differentiating, we obtain

$$-2\sum_{i=1}^{N} w_i(\mathbf{r}_{1,i} - \mathbf{r}_{1,0} - Q(\mathbf{r}_{2,i} - \mathbf{r}_{2,0})) = 0. \tag{6}$$

$$2Q^T\sum_{i=1}^{N} w_i(\mathbf{r}_{1,i} - \mathbf{r}_{1,0} - Q(\mathbf{r}_{2,i} - \mathbf{r}_{2,0})) = 0. \tag{7}$$

Since the matrix Q^T is nonsingular, Eq. (7) is equivalent to Eq. (6). By solving Eq. (6) for $\mathbf{r}_{1,0}$, we obtain

$$\mathbf{r}_{1,0} = \frac{1}{W}\sum_{i=1}^{N} w_i\mathbf{r}_{1,i} - Q\left(\frac{1}{W}\sum_{i=1}^{N} w_i\mathbf{r}_{2,i} - \mathbf{r}_{2,0}\right). \tag{8}$$

To make the expression in parentheses in (8) equal to zero, we choose $\mathbf{r}_{2,0}$ from the condition

$$\mathbf{r}_{2,0} = \frac{1}{W}\sum_{i=1}^{N} w_i\mathbf{r}_{2,i}. \tag{9}$$

Then, (8) implies

$$\mathbf{r}_{1,0} = \frac{1}{W}\sum_{i=1}^{N} w_i\mathbf{r}_{1,i}. \tag{10}$$

We have already mentioned above that Eqs. (6) and (7) are equivalent; therefore, points (9) and (10) satisfy Eqs. (5). Hence, the vectors $\mathbf{r}_{1,0}$ and $\mathbf{r}_{2,0}$ provide the minimum to function (2) at fixed rotation angles φ, θ, and ψ. This completes the proof of Theorem 1.

Thus, the minimum of function (2) corresponds to translating the centers of mass of the geometric structures determined by formulas (10) and (9) to the origin. Now, function (2) can be considered as a function of the rotation angles:

$$U(\varphi, \theta, \psi) = \sum_{i=1}^{N} w_i\left|\mathbf{r}_{1,i} - \mathbf{r}_{1,0} - Q(\varphi, \theta, \psi)(\mathbf{r}_{2,i} - \mathbf{r}_{2,0})\right|^2, \tag{11}$$

where $\mathbf{r}_{1,i}$ and $\mathbf{r}_{2,i}$ are the given coordinates of the geometric structures and the centers of mass $\mathbf{r}_{1,0}$ and $\mathbf{r}_{2,0}$ are found by formulas (10) and (9). Function (11) is minimized with respect to the angles φ, θ, and ψ.

Suppose that the minimum of the function $U = U(\varphi, \theta, \psi)$ defined by (11) is attained at the point $(\varphi_0, \theta_0, \psi_0)$. The proximity measure between two geometric structures is defined by

$$s = \left(\frac{U(\varphi_0, \theta_0, \psi_0)}{W}\right)^{1/2}. \tag{12}$$

This quantity can be considered as a quantitative characteristic of the proximity measure between two geometric structures because it is the averaged distance between the points with identical indexes in the two structures after they have been brought into "coincidence."

Two structures are said to be approximately equal if

$$s = \left(\frac{1}{W}\min_{\varphi, \theta, \psi} U(\varphi, \theta, \psi)\right)^{1/2} = \left(\frac{U(\varphi_0, \theta_0, \psi_0)}{W}\right)^{1/2} \leq s_0, \tag{13}$$

where s_0 is a given quantity (in applications, it is determined by the specific practical situations). The inequality $s \leq s_0$ is called the proximity criterion of two structures. In numerical computations, s can have a computational error.

Note that if the minimizer is not unique and there exists a point $(\varphi_1, \theta_1, \psi_1)$ such that $U(\varphi_1, \theta_1, \psi_1) = U(\varphi_0, \theta_0, \psi_0)$, then the quantity s remains unchanged and the nonuniqueness of the minimizer does not affect the proximity criterion of geometric structures.

Now, the test for comparing the geometry of two geometric structures can be subdivided into three phases: (1) translate the center of mass of each geometric structure to the origin; (2) minimize function (11) with respect to the Euler angles; (3) calculate the quantity s by formula (13) and draw a conclusion on the proximity of these structures.

Two geometric structures are called equal if their points with identical indexes can be brought into coincidence by moving this structures as rigid bodies. It is well known (see [8]) that such a movement can be made by a translation and orthogonal rotation.

Test (1)−(3) for comparing two geometric structures is valid if two equal structures with different coordinates $\mathbf{r}_{1,i}$ and $\mathbf{r}_{2,i}$ are brought into coincidence at the minimizer of function (11), i.e., if the proximity measure between two equal structures is $s = 0$.

Theorem 2. *The minimum of the nonnegative function* (11) *is zero if and only if two geometric structures are equal.*

Proof. Let two equal structures be given. This means that they can be brought into coincidence at the points with identical indexes and their centers of mass can be moved to the origin. In this case, the points of these structures with identical indexes have identical coordinates determined by the vectors $\mathbf{R}_i$, $i = 1, \dots, N$. Equal structures in which the points with identical indexes have different coordinates can be obtained by moving these structures apart, i.e., by rotating the second structure relative to the first one and displacing each structure. More precisely, rotate the second structure relative to the first one through the angles $\bar{\varphi}$, $\bar{\theta}$, and $\bar{\psi}$; and then move the center of mass of the first structure to the point determined by the vector $\mathbf{R}_{1,0}$ and the center of mass of the second structure to the point determined by the vector $\mathbf{R}_{2,0}$. Then, the coordinates of the points of the first and the second structures will be

$$\mathbf{r}_{1,i} = \mathbf{R}_i + \mathbf{R}_{1,0}, \quad \mathbf{r}_{2,i} = Q_0(\bar{\varphi}, \bar{\theta}, \bar{\psi})\mathbf{R}_i + \mathbf{R}_{2,0}, \quad i = 1, \dots, N, \tag{14}$$

where $Q_0(\bar{\varphi}, \bar{\theta}, \bar{\psi})$ is a matrix of form (3). It is clear that the coordinates $\mathbf{r}_{1,i}$, $\mathbf{r}_{2,i}$ in (14) can specify an arbitrary position of two equal structures in R^3.

Now assume that the coordinates of two equal structures with, generally, different coordinates (14) of points with identical indexes are given, i.e., $\sum_{i=1}^{N} w_i |\mathbf{r}_{1,i} - \mathbf{r}_{2,i}|^2 \geq 0$. Taking into account that the coordinates of two equal structures can be represented in form (14), we apply to these two structures algorithm (1)−(3).

(1) Calculate the centers of mass of two equal structures. According to (10) and (14), we have for the center of mass of the first structure

$$\mathbf{r}_{1,0} = \frac{1}{W} \sum_{i=1}^{N} w_i \mathbf{r}_{1,i} = \frac{1}{W} \sum_{i=1}^{N} w_i (\mathbf{R}_i + \mathbf{R}_{1,0}) = \mathbf{R}_{1,0}, \tag{15}$$

because $\mathbf{R}_i$ are the coordinates of the structure points relative to the center of mass and, therefore, $\sum_{i=1}^{N} w_i \mathbf{R}_i = 0$. Similarly, for the center of mass of the second structure, we obtain from (9) and (14) that

$$\mathbf{r}_{2,0} = \frac{1}{W} \sum_{i=1}^{N} w_i \mathbf{r}_{2,i} = \frac{1}{W} \sum_{i=1}^{N} w_i (Q_0 \mathbf{R}_i + \mathbf{R}_{2,0}) = \frac{1}{W} \left(Q_0 \sum_{i=1}^{N} w_i \mathbf{R}_i + \left(\sum_{i=1}^{N} w_i \right) \mathbf{R}_{2,0} \right) = \mathbf{R}_{2,0}. \tag{16}$$

(2) Taking into account (14), (15), and (16), the comparison function (11) takes the form

$$U(\varphi, \theta, \psi) = \sum_{i=1}^{N} w_i |\mathbf{r}_{1,i} - \mathbf{r}_{1,0} - Q(\varphi, \theta, \psi)(\mathbf{r}_{2,i} - \mathbf{r}_{2,0})|^2$$

$$= \sum_{i=1}^{N} w_i |\mathbf{R}_i + \mathbf{R}_{1,0} - \mathbf{R}_{1,0} - Q(Q_0 \mathbf{R}_i + \mathbf{R}_{2,0} - \mathbf{R}_{2,0})|^2 = \sum_{i=1}^{N} w_i |\mathbf{R}_i - QQ_0 \mathbf{R}_i|^2. \tag{17}$$

It is clear that the minimum of the function U, which is equal to zero, is attained, according to (1), at

$$\mathbf{R}_{i_k} - Q(\varphi, \theta, \psi) Q_0(\bar{\varphi}, \bar{\theta}, \bar{\psi}) \mathbf{R}_{i_k} = 0, \quad k = 1, \dots, K.$$

This implies that $QQ_0 = E$ and $Q = Q_0^{-1}$. Since the rotation matrix Q_0 is orthogonal, its inverse matrix coincides with the transpose matrix $Q_0^{-1} = Q_0^T$; hence, we obtain the rotation matrix Q that minimizes the minimum of the function U of form $Q(\varphi, \theta, \psi) = Q_0^T(\bar{\varphi}, \bar{\theta}, \bar{\psi})$. Since the matrices Q and Q_0 can be represented in form (3), it is easy to verify that $Q_0^T(\bar{\varphi}, \bar{\theta}, \bar{\psi}) = Q(\pi - \bar{\psi}, \bar{\theta}, \pi - \bar{\varphi})$ and, therefore,

$$Q(\varphi, \theta, \psi) = Q_0^T(\bar{\varphi}, \bar{\theta}, \bar{\psi}) = Q(\pi - \bar{\psi}, \bar{\theta}, \pi - \bar{\varphi}). \tag{18}$$
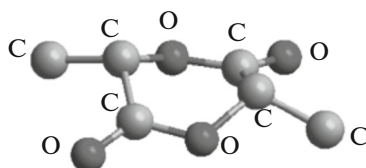
Fig. 1. Positions of the atoms C and O in the lactide molecule $C_6H_8O_4$.

This implies that, for two equal structures, the minimum of the function U, which equals zero, is attained at the point $(\varphi, \theta, \psi) = (\pi - \overline{\psi}, \overline{\theta}, \pi - \overline{\varphi})$. These structures can be brought into coincidence using translations (15), (16), and rotation (18).

The converse assertion of the theorem is obvious because $U = 0$ implies that the coordinates of each point i of the first structure with the weight $w_i \neq 0$ in (11) coincide with the coordinates of the second structure; i.e., the points and the structures as a whole are brought into coincidence by displacing the first structure by $\mathbf{r}_{1,0}$, the second structure by $\mathbf{r}_{2,0}$, and the rotation of the second structure through the angles φ, θ, and ψ determined by the matrix Q. This completes the proof of Theorem 2.

Thus, according to Theorem 2, the comparison algorithm (1)–(3), which minimizes the comparison function, identifies equal structures and, therefore, provides an objective estimate of the difference of geometry of two "close" structures.

While applying algorithm (1)–(3) for comparing two structures, we will numerically minimize the comparison function $U(\varphi, \theta, \psi)$ with respect to the Euler angles after bringing the centers of mass into coincidence.

4. NUMERICAL SOLUTION OF THE OPTIMIZATION PROBLEM

In this section, we present numerical results of comparing geometric structures by minimizing the comparison function (11). Since (11) is not a convex function, we used the zero-order Rosenbrock method [3, 4], which proved to be effective in structural chemistry [7]. In the computer program implementing algorithm (1)–(3) designed for the minimization of the comparison function (11) using the Rosenbrock method, we used the optimization library [9].

We demonstrate the effectiveness of algorithm (1)–(3) described and justified above using structural chemistry applications as examples. We will consider molecules with ordered arrangement of the point atoms as geometric structures. When comparing molecules with the same structural formula, we are interested in the difference in their spatial structure.

In the examples discussed below, we present the results of comparing lactide molecules $C_6H_8O_4$ studied in [10]; these molecules consist of $N = 10$ main atoms (four oxygen atoms and six carbon atoms). The coordinates of the hydrogen atoms were not involved in the computations because the accuracy of their determination is lower than that of other atoms, and they are irrelevant for the problem under examination. The geometry of these molecules is shown in Fig. 1. The coordinates of the molecules were obtained by X-ray structural analysis. In our experiments, the atoms to be brought into coincidence were assigned the weights $w_i = 1$.

Example 1. To check the validity of the comparison algorithm (1)–(3) and the effectiveness of the program, we consider the example of bringing two identical lactide molecules into coincidence. The initial coordinates $\mathbf{r}_{1,i}$, $\mathbf{r}_{2,i}$ ($i = 1,...,10$) of the atoms of two molecules were obtained using formulas (14) and (3). The coordinates of the first molecule atoms were obtained by displacing the coordinates of the original molecule atoms; the coordinates of the second molecule atoms were obtained from the coordinates of the original molecule atoms by displacing them and rotating through the angles $(\overline{\varphi}, \overline{\theta}, \overline{\psi}) = (\pi/3, \pi/6, \pi/2)$. Table 1 shows the values of coordinates of the first and the second molecules in ångströms. The minimizer of the function U is found by the Rosenbrock method to be $(\varphi_0, \theta_0, \psi_0) = (90.00°, 30.00°, 120.00°)$, which agrees with (18). The measure of proximity (which is called proximity characteristic in chemistry) calcu-

Table 1. Coordinates of atoms (in Å) of two identical lactide molecules

i	$x_{1,i}$	$y_{1,i}$	$z_{1,i}$	$x_{2,i}$	$y_{2,i}$	$z_{2,i}$	w_i
1	0.31077	0.90281	−0.76944	−0.25873	−0.12647	−0.73910	1
2	1.49955	−0.96244	0.84211	0.46314	2.08327	0.70499	1
3	1.41879	0.44535	2.51758	0.75186	0.82371	2.47297	1
4	0.06663	−0.60437	−2.34230	−0.20942	1.05671	−2.58374	1
5	0.61125	−0.28306	−1.31952	−0.24562	1.05076	−1.38183	1
6	1.63476	−1.11629	−0.59785	−0.29163	2.28412	−0.52197	1
7	1.36152	0.26291	1.32995	0.27999	0.95307	1.37404	1
8	1.13991	1.37253	0.32736	−0.53558	−0.11869	0.68722	1
9	0.43472	2.55976	0.89930	−0.23480	−1.49946	1.17398	1
10	1.52208	−2.57718	−0.88719	0.28080	3.49294	−1.18656	1

Table 2. Coordinates of atoms (in Å) of three lactide molecules $C_6H_8O_4$

i		$x_{1,i}$	$y_{1,i}$	$z_{1,i}$	$x_{2,i}$	$y_{2,i}$	$z_{2,i}$	$x_{3,i}$	$y_{3,i}$	$z_{3,i}$
1	O_1	1.7662	4.2832	0.3852	0.2009	−0.5132	−2.1717	6.8162	1.8230	4.0036
2	O_2	2.9550	2.9550	1.9967	2.4489	−2.0531	−2.1448	9.0275	3.2430	3.2601
3	O_3	2.8742	3.8258	3.6722	3.3503	−0.6698	−3.5931	9.1045	2.0885	1.3878
4	O_4	1.5221	2.7761	−1.1876	−0.4000	−1.4894	−0.2977	6.4668	3.2853	5.6067
5	C_1	2.0667	3.0974	−0.1648	0.2544	−1.5276	−1.3087	7.2331	2.8019	4.8144
6	C_2	3.0902	2.2641	0.5568	1.1859	−2.6453	−1.6872	8.6829	3.2022	4.6782
7	C_3	2.8170	3.6433	2.4846	2.3522	−1.1069	−3.0902	8.6970	2.1824	2.5132
8	C_4	2.5954	4.7530	1.4820	0.9474	−0.6508	−3.4148	7.8199	1.1668	3.1793
9	C_5	1.8902	5.9402	2.0539	0.9258	0.6793	−4.0860	7.0875	0.2831	2.2070
10	C_6	2.9775	0.8032	0.2674	1.5108	−3.5712	−0.5484	9.0453	4.5161	5.2636

lated by formula (12) was $s = 8.19 \times 10^{-8}$ Å. The ratio to the minimum distance $R_{\min}$ between the atoms in the molecules

$$R_{\min} = \min_{i>j} \left| \mathbf{r}_{1,i} - \mathbf{r}_{1,j} \right| = 1.20 \text{ Å}$$

is $s/R_{\min} = 6.83 \times 10^{-8}$, which is practically equal to zero. Thus, algorithm (1)−(3) perfectly brings identical molecules into coincidence.

Example 2. Comparison of three lactide molecules. Table 2 shows the coordinates of the oxygen O_j, $j = 1, \ldots, 4$ and carbon C_j, $j = 1, \ldots, 6$ atoms in ångströms in three symmetrically independent (within the same crystal) lactide molecules $C_6H_8O_4$, one of which is shown in Fig. 1.

Application of algorithm (1)−(3) for comparing molecules 1 and 2, 1 and 3, and 2 and 3 gives the results presented in Table 3. The minimizing angles produced by these computations are also presented in Table 3. Practical experience of examining conformation of molecules based on results of comparing a large number of structures [11] yielded the following arbitrary classification: $s \leq s_0 = 0.1$ Å indicates that the molecules are almost identical, 0.1 Å $< s \leq 0.2$ Å indicates that the molecules are close to each other, and $s > 0.2$ Å indicates that the molecules are different.

The analysis of residuals $\Delta r_i = \left| \mathbf{r}_{1,i} - \mathbf{r}_{2,i} \right|$, $i = 1, \ldots, 10$, i.e., the distances between the atoms with identical indexes after the molecules are brought into coincidence (at the minimizer of U) and of the quantity s for $s_0 = 0.1$ Å suggests that the first and the third molecules, as well as the second and the third molecules have almost identical geometries because in both cases $s < s_0$. The greatest differences are observed

Table 3. The residuals Δr_i, the characteristic s, and the Euler angles φ, θ, ψ for the minimizer of the comparison function

Atom		Δr_i for molecules 1 and 2, all $w_i = 1$	Δr_i when the rings of molecules 1 and 2 are brought into coincidence	Δr_i for molecules 1 and 3, all $w_i = 1$	Δr_i for molecules 2 and 3, all $w_i = 1$
1	O_1	0.020	0.009	0.011	0.015
2	O_2	0.040	0.021	0.044	0.004
3	O_3	0.156	0.138 $w = 0$	0.076	0.081
4	O_4	0.188	0.210 $w = 0$	0.098	0.090
5	C_1	0.040	0.051	0.039	0.011
6	C_2	0.056	0.064	0.016	0.043
7	C_3	0.046	0.036	0.038	0.009
8	C_4	0.059	0.049	0.029	0.038
9	C_5	0.149	0.127 $w = 0$	0.113	0.041
10	C_6	0.176	0.196 $w = 0$	0.139	0.049
s		0.111	0.043	0.073	0.047
φ, θ, ψ at the minimizer		$\varphi = 73.9°$ $\theta = 111.0°$ $\psi = -42.0°$	$\varphi = 253.6°$ $\theta = 249.4°$ $\psi = 138.6°$	$\varphi = 80.4°$ $\theta = 157.5°$ $\psi = 59.0°$	$\varphi = 27.8°$ $\theta = 74.8°$ $\psi = -51.0°$

between the first and the second molecules ($s = 0.11$ Å $> s_0$); these molecules can be considered close to each other. It is seen from Table 3 that the maximum residuals are characteristic of substituent atoms (atoms outside the ring). To demonstrate these differences more clearly, we performed an additional computation by assigning the zero weight $w_i = 0$ to the substituents. In this case, we obtained $s < 0.04$ Å. This indicates that the rings in the molecules are practically identical. The detected differences in the position of the atoms in the first and the second molecules when the rings are brought into coincidence are seen in Fig. 2, which was produced using the coordinates of molecules at the minimizer of the comparison function U.

Example 3. Checking the intrinsic symmetry of a molecule.

Using the comparison algorithm (1)–(3), we checked the intrinsic symmetry of the lactide molecule depicted in Fig. 1. The assumed second-order symmetry axis passes vertically through the ring center. To apply algorithm (1)–(3), we formed the "second" molecule by changing the indexing of the atoms. It is seen in Fig. 1 that, due to the assumed symmetry, atom 1 in the second molecule must correspond to
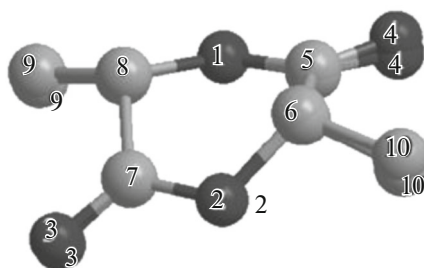

Fig. 2. The result of bringing the rings of molecules 1 and 2 into coincidence corresponding to the minimizer of the comparison function.

Table 4. The residuals Δr_i, the characteristic s, and the Euler angles φ, θ, ψ for the minimizer of the comparison function when checking the intrinsic symmetry of molecule 1

Atoms		Permutation of atoms		Δr_i for molecule 1 and for molecule 1 with pernutation
1	O_1	2	O_2	0.008
2	O_2	1	O_3	0.008
3	O_3	4	O_4	0.012
4	O_4	3	O_3	0.012
5	C_1	7	C_3	0.011
6	C_2	8	C_4	0.008
7	C_3	5	C_1	0.011
8	C_4	6	C_2	0.008
9	C_5	10	C_6	0.006
10	C_6	9	C_5	0.006
s		0.009		
φ, θ, ψ at the minimizer		$\varphi = 71.6°$ $\theta = 216.8°$ $\psi = 108.4°$		

atom 2 in the first molecule, atom 5 must correspond to atom 7, and so on. The reindexing of atoms in the second molecule is shown in Table 4. The results of comparing the "two" molecules are also shown in Table 4. The comparison characteristic in this case is $s = 0.009$ Å $< s_0 = 0.1$ Å; hence, the molecules can be considered identical and, therefore, the original molecule has second-order symmetry with a high degree of accuracy.

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