Rules on chiral and achiral molecular transformations

Paul G. Mezey

Mathematical Chemistry Research Unit,
Department of Chemistry and Department of Mathematics and Statistics,
University of Saskatchewan, 110 Science Place, Saskatoon, SK, Canada S7N 5C9

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The properties of chiral and achiral transformations between mirror images of n-dimensional point sets are investigated. Several rules are proven, relevant to chirality-preserving and chirality-abandoning molecular transformations.

1. Introduction and preliminaries

Molecular transformations which interconvert chiral mirror images yet avoid achiral intermediate nuclear configurations have been reported long ago [1], but still are considered oddities by many chemists. In this study we shall consider this problem in a more general setting: the transformation of chiral point sets in an n-dimensional Euclidean space.

Chirality of point sets in various dimensions, specifically, chirality in the ordinary, three-dimensional space and two-dimensional chirality along planar surfaces are of importance in chemistry. In recent years the interest in mathematical-chemical aspects of chirality in general, n-dimensional spaces has increased. Detailed background information on several newer results can be found in refs. [2–43], whereas some of the earlier developments are reviewed in refs. [44,45].

In this study we are interested in various nuclear motions of molecules and their influence on molecular chirality. Usually, the chirality of nuclear arrangements is studied in a three-dimensional space; however, some motions can be restricted to two dimensions, for example, some molecular motions along surfaces of metallic catalysts can be approximated by motions along a plane. In rare instances, for example, within channels of zeolites or within nanotubes, one-dimensional chirality of chain molecules may be relevant. Chirality problems of dimensions higher than three also occur in studies of potential energy hypersurfaces and multidimensional configuration spaces [46]. In this study we shall investigate the problem of chirality preserving and violating properties of motions of point sets in a general, n-dimensional Euclidean space E^n.

Chirality will be considered in the following sense: a set S embedded in an n-dimensional space E^n is chiral, if no rigid motion of S can bring it into superposition with its mirror image within E^n. Otherwise, S is achiral. The definition of chirality is precise only if the space is specified. Chirality of point sets is dimension-dependent; a point set can be chiral when embedded in one Euclidean space, while the same point set embedded in a Euclidean space of different dimension can be achiral. In general, we use the terms *n-chiral* or *n-achiral* for a point set S if it is chiral or achiral, respectively, when embedded in the n-dimensional Euclidean space E^n.

The following important restriction applies: any n-chiral object S is $(n+1)$-achiral. More precisely, the following restrictions hold:

THEOREM 1

An object S that is chiral in n-dimensions is achiral in $(n+1)$-dimensions and in any higher dimensions. Chirality may occur only in the lowest dimension where S is embeddable.

A simple proof and some implications of this theorem have been given in refs. [31,45].

A similarly simple but important property is proven below. Consider an n-chiral arrangement S of m points in E^n, where m is finite:

$$S = \{a_1, a_2, a_3, \ldots a_n, a_{n+1}, \ldots a_{m-1}, a_m\}\,. \tag{1}$$

THEOREM 2

For an n-chiral arrangement S of m points, each point $a_j \in S$ can be moved in any direction by some small enough distance without S becoming n-achiral.

Proof

Take any point $a_j \in S$. Let $d(a_j, a_k)$ denote the distance between any two points a_j, a_k of set S. Note that $d(a_j, a_k) \neq 0$ and positive for each $k \neq j$, since all points of S are different. Let $\alpha(S, a_j))$ denote the set of all possible locations for a displaced point a_j which turn the set S into n-achiral. This set $\alpha(S, a_j))$ may be empty. Let $d(a_j, \alpha(S, a_j))$ denote the distance between point $a_j \in S$ and set $\alpha(S, a_j))$, that is, the nearest new position for a_j that turns the set S into n-achiral. If $\alpha(S, a_j))$ is empty, then set $d(a_j, \alpha(S, a_j)) = \infty$. Note that the distance $d(a_j, \alpha(S, a_j)) \neq 0$ and positive for each $a_j \in S$, since S is an n-chiral set. Define a distance $d(a_j)$ as

$$d(a_j) = (1/2)\min\{d(a_j, a_k), d(a_j, \alpha(S, a_j))\}_{k=1,\ldots,m,k\neq j}\,. \tag{2}$$

Evidently, $d(a_j) > 0$ for each point $a_j \in S$, and each point a_j can be moved in any direction by the distance $d(a_j)$ while the point set retains its n-chiral property. □

In other words, n-chiral configurations S of finite point sets form an open set in the corresponding configuration space. This can be regarded as the consequence of the fact that any non-trivial symmetry in E^n can be destroyed by some infinitesimal change of position of some points.

Of course, some n-chiral point sets S cannot be turned into an n-achiral set by any motion restricted to a limited number of points. We say that such sets S can *tolerate* the arbitrary motion of some number of points without becoming n-achiral. We shall return to this problem after a discussion of some relevant concepts.

We shall need the concept of *maximum n-achiral subset A* of a finite, n-chiral point set S [31,45].

Take a set S of m points, and the mirror image $S^\diamond$ of S in E^n. A set $S^{\diamond\prime}$ obtained from $S^\diamond$ by translation and rotation is called a *version* of $S^\diamond$. In a finite number of steps we can determine the maximum number $c(S)$ of point coincidences possible between S and a version of $S^\diamond$. The collection of points of S participating in such an arrangement of maximum number of coincidences is a *maximum n-achiral subset A* of S, where the cardinality of A is $c(S)$. As it has been pointed out [31,45], set A is not necessarily unique, however, for any finite point set S there are only a finite number of maximum n-achiral subsets, all with $c = c(S)$ elements. The number of different pointwise partial superpositions between S and the versions $S^{\diamond\prime}$ of $S^\diamond$ is bounded by the number $m!$ of permutations of the points of set S, hence, indeed, a finite number of trials is sufficient to find $c(S)$ and a maximum n-achiral subset A of S.

The value $c = c(S)$ is at least n, the dimension of the space, since any n points define a hyperplane that is at most $(n-1)$-dimensional, and any $(n-1)$-dimensional hyperplane can be taken as a reflection plane. Such a reflection plane contains the selected n points common to both the original point set S and its mirror image $S^\diamond$ generated by this reflection plane, hence at least n point pairs can be made coincident, $c \geqslant n$. Evidently, for an n-chiral set S of m points c is bounded by the relation $c < m$, otherwise, if c were equal to m, then the set S would be n-achiral, a contradiction. Note that a symmetry operator implying the n-achirality of a maximum n-achiral subset A of S is not necessarily a reflection hyperplane; for example, if $n = 3$, then the presence of the familiar 3D rotation-reflection symmetry elements of even fold are sufficient for achirality in 3D, where the corresponding operators S_{2k} are used to diagnose achirality of A. In general, we shall denote a symmetry operator implying the n-achirality of a maximum n-achiral subset A by R.

2. Chirality-preserving and chirality-abandoning motions of point sets in n-dimensions

Most of the general results derived in this section will be based on the relations between point symmetry operators and motions of individual points of a finite point set.

We recall a rather self-evident property of point symmetry operations: a single application of any symmetry operator R of a finite point set A has one of the following two actions on a single point a_j of set A:

(i) R assigns a_j to itself (if a_j is a fixed point of R),

(ii) R assigns a_j to a specific other point, denoted by $a_j^{\diamond}$.

Motions of a single point of a finite, n-chiral point set S of m points in E^n can affect the maximum achiral subsets. Consider a maximum n-achiral subset A of S. If all points of S are fixed, except a single point a_j which does not belong to A, and if a_j is allowed to move without constraints, then for any new position a_j' of a_j and for the resulting new set S' the following three cases cover all possibilities:

(i) the maximum n-achiral subset A of S preserves its maximum n-achiral subset status in the new arrangement S', $c(S) = c(S') = c$, or

(ii) the cardinality $c'(S')$ of a new maximum n-achiral subset A' is one greater than c, $c' = c + 1$, or

(iii) the cardinality $c'(S')$ of a new maximum n-achiral subset A' of S' is at least $c + 2$, $c'(S') \geqslant c(S) + 2$.

Clearly, if $c = n$, then in case (i), the new point set S' is still n-chiral.

Similarly, if $m > n + 1$ and $c = n$, then in case (ii), the cardinality of any maximum n-achiral subset A' of the new point set S' is $c' = n + 1$, hence the new set S' of $m > n + 1$ points is still n-chiral.

Case (iii) can occur only by moving a_j to isolated locations of the space E^n, that is, there is no continuum within E^n where case (iii) would occur. This will be proven after the establishment of some important properties of maximum n-achiral subsets.

The set of the isolated points of case (iii) is denoted by W. Since points of W are isolated, within a space E^n of dimensions $n \geqslant 2$, any point x not in W, $x \notin W$, can be reached from point a_j by a path $p_j(u)$ avoiding set W:

$$p_j(u): \quad [0,1] \to E^n, \quad \text{where} \quad p_j(0) = a_j, \quad p_j(1) = x \notin W, \tag{3}$$

$$p_j(u) \cap W = \emptyset, \quad \forall u. \tag{4}$$

This fact will be exploited in proving a chirality-preserving interconversion property of chemical transformations.

We recall the intuitive concept of tolerance, mentioned in the introduction: a finite n-chiral point set S may tolerate arbitrary motions of some number of points without becoming achiral. Here we shall use a precise definition.

DEFINITION

A finite point set S in E^n is *f-intolerant* n-chiral, if no motion of any $f - 1$ points can turn S into an n-achiral set, but some motions of some f points can.

Such a set S is said to be f'-tolerant n-chiral for any $f' < f$.

For any finite point set S in E^n the f value can be determined as follows. Each maximum achiral subset of the n-chiral set S of m points contains c points. Hence, for a maximum n-achiral subset A of S, there are $m - c$ points of S not in A. If $m - c$ is even, then half of these points can be moved to become R-images of the other half of these points; if $m - c$ is odd, then $(m - c - 1)/2$ points can be moved to become R-images of another $(m - c - 1)/2$ points, and one additional point can be moved to a fixed point of R, for example, if R is a reflection hyperplane, then this single point can be moved to the reflection hyperplane. In either case, the new configuration S' of m points becomes n-achiral, and no motion of fewer points can accomplish this. Consequently,

$$f = \mathrm{ent}[(m - c + 1)/2]. \tag{5}$$

Since chiral configurations form an open set, by some small deformation of any S the value of f can be increased to the maximum possible value of

$$f = \mathrm{ent}[(m - n + 1)/2], \tag{6}$$

while preserving n-chirality.

The next result is specific for the case of n-chiral simplex arrangements of $m = n + 1$ points.

THEOREM 3

No n-chiral simplex

$$S = \{a_1, a_2, a_3, \dots a_n, a_{n+1}\} \tag{7}$$

can be transformed continuously within E^n into its mirror image

$$S^\diamond = \{a_1^\diamond, a_2^\diamond, a_3^\diamond, \dots a_n^\diamond, a_{n+1}^\diamond\} \tag{8}$$

without passing through an n-achiral intermediate.

Proof

Consider general paths moving each point a_i to its new position $a_i^\diamond$,

$$p_i(u): \quad [0,1] \to E^n, \quad \text{where} \quad p_i(0) = a_i, \quad p_i(1) = a_i^\diamond, \tag{9}$$

for each i, $1 \leqslant i \leqslant n + 1$. These paths are continuous mappings of the parameter interval $[0,1]$ into the n-dimensional Euclidean space E^n.

We prove that for *any* such family $\{p_i(u)\}_{(i=1,n+1)}$ of $n + 1$ paths, that is, for any interconversion between the mirror images, there must exist a parameter value u' such that the corresponding configuration of points, $\{p_i(u')\}_{(i=1,n+1)}$ is n-achiral.

Consider first the first n paths, $\{p_i(u)\}_{(i=1,n)}$. There are the following two possibilities, (i) and (ii):

(i) If there is a parameter value u'' for which the n points $\{p_i(u'')\}_{(i=1,n)}$ fall within an $(n - 2)$-dimensional hyperplane Q, then by adding the point $p_{n+1}(u'')$ to this set, the entire collection $\{p_i(u'')\}_{(i=1,n+1)}$ of points is necessarily contained in an

$(n-1)$-dimensional hyperplane $P(u'')$. This hyperplane can then be taken as a reflection plane within the n-dimensional Euclidean space E^n, reflecting the point configuration $\{p_i(u'')\}_{(i=1,n+1)}$ onto itself, hence this configuration is n-achiral, and u'' can be taken as u'.

(ii) If for the given family of paths $\{p_i(u)\}_{(i=1,n+1)}$ there is no such parameter value u'' for which the n points $\{p_i(u'')\}_{(i=1,n)}$ fall within an $(n-2)$-dimensional hyperplane Q, then the first n points $\{p_i(u)\}_{(i=1,n)}$ define an $(n-1)$-dimensional hyperplane $P(u)$ for each parameter value u. For each hyperplane $P(u)$, a (not necessarily orthogonal) coordinate system is defined by the $n-1$ linearly independent vectors

$$\{p_i(u) - p_1(u)\}_{(i=2,n)} \tag{10}$$

with origin at $p_1(u)$.

Choose a normal vector $v(0)$ orthogonal to the $P(0)$ hyperplane defined by the initial points $\{p_i(0)\}_{(i=1,n)}$. Since the paths $\{p_i(u)\}_{(i=1,n)}$ are continuous, the $P(0)$ plane changes continuously through intermediate planes $P(u)$ to the final plane $P(1)$, and similarly, the normal vector $v(0)$ changes continuously through intermediate vectors $v(u)$ to the final normal vector $v(1)$. The entire transformation can be viewed within a reference frame attached to the moving hyperplane $P(u)$ and normal vector $v(u)$, where the motion of the first n points is confined to the moving hyperplane. *With respect to this moving frame*, the plane $P(u)$ is a stationary, constant plane P, and normal vector $v(u)$ is also a stationary, constant vector v. Recall that $\{p_i(1)\}_{(i=1,n+1)}$ is the n-dimensional mirror image of $\{p_i(0)\}_{(i=1,n+1)}$, and the fact that any set of n points in an n-dimensional space is n-achiral. Consequently, at $u=1$, after completing their paths within P, the first n points $\{p_i(u)\}_{(i=1,n)}$ return to their initial relative positions $(u=0)$. Since $\{p_i(0)\}_{(i=1,n+1)}$ and $\{p_i(1)\}_{(i=1,n+1)}$ are chiral, point

$$a^{\diamond}_{n+1} = p_{n+1}(1) \tag{11}$$

becomes the reflected image of point $a_{n+1} = p_{n+1}(0)$, with reference to the plane P as reflection plane. Without loss of generality, we may assume that point

$$a_{n+1} = p_{n+1}(0) \tag{12}$$

is within the half-space with positive components along the normal vector $v(0)$, then point $a^{\diamond}_{n+1} = p_{n+1}(1)$ must fall within the half-space with negative components along the normal vector $v(1)$. The path $p_{n+1}(u)$ interconnecting a_{n+1} and $a^{\diamond}_{n+1}$ is continuous, consequently, at some parameter value u', path $p_{n+1}(u)$ must pass through the $(n-1)$-dimensional hyperplane P separating a_{n+1} and $a^{\diamond}_{n+1}$. For this parameter value u', all points $\{p_i(u')\}_{(i=1,n+1)}$ fall within the $(n-1)$-dimensional hyperplane P, hence the point configuration $\{p_i(u')\}_{(i=1,n+1)}$ is achiral in n dimensions. □

How special n-chiral simplex arrangements are is fully appreciated only if they are compared to n-chiral point sets with more than $n+1$ points. Some of the following results refer to this case. In order to derive these results we first establish some rather evident and some more subtle properties of maximum n-achiral subsets and their changes induced by the motions of a single point of finite n-chiral point set S.

THEOREM 4

The lowest dimension of a hyperplane P where a maximum n-achiral subset A of an n-chiral finite point set S of E^n is embeddable is $n-1$.

Proof

We show that A cannot be embedded in a hyperplane Q of dimension $(n-2)$. Contrary to this, let us assume that all points of A are in Q, then S must have points not falling within Q, otherwise S could not be n-chiral, since any point set of hyperplane Q is necessarily n-achiral. Consequently, we can choose a point $a_j \in S$, $a_j \notin Q$. The set $Q \cup a_j$ defines a unique hyperplane P of dimension $n-1$. Taking this hyperplane P as a plane of reflection in E^n, the set

$$A'' = A \cup a_j \tag{13}$$

is its own mirror image, hence A'' is an n-achiral subset of S with more elements than A. Hence A cannot be a maximum n-achiral subset of S, a contradiction. Hence A cannot be embedded in a hyperplane Q of dimension $(n-2)$. □

THEOREM 5

If A is a maximum n-achiral subset of a finite point set S in E^n, where the cardinality of A is c, then by moving any point a_j of A to a new location a_j' that generates a new achiral point set A' of cardinality $c' \geqslant c+2$, while keeping all other points of S fixed, no point symmetry operator R of a symmetry element implying n-achirality of A' can map point a_j' to itself.

Proof

Pick one location for a_j' where c increases by more than one,

$$c' \geqslant c+2\,, \tag{14}$$

for a new n-achiral set A'. Take any point symmetry operator R that implies the n-achirality of the new set A'. Contrary to the proposition, let us assume that the R image of point a_j' is itself, then R must map the subset $A' \setminus a_j'$ of all remaining points of A' to the same subset $A' \setminus a_j'$ of A'. That is, R is an n-achirality implying symmetry operator for $A' \setminus a_j'$, consequently, $A' \setminus a_j'$ is n-achiral. But A' contains at least $c+2$ points, hence $A' \setminus a_j'$ contains at least $c+1$ points, all at their original locations. Hence $A' \setminus a_j'$ is an n-achiral subset of the original set S. But $A' \setminus a_j'$ has more points than A, hence A could not be a maximum n-achiral subset of S, a contradiction. Hence, a_j' cannot be its own R image for any R implying the achirality of the new set A'. □

THEOREM 6

If the conditions of theorem 5 are fulfilled, then A' cannot be embedded in a hyperplane P of dimension $n-1$.

Proof

We know from theorem 5 that any point symmetry operator R implying n-achirality of the new set A' must map a_j' to another point

$$Ra_j' = a_j'^{\diamond} = a_k \tag{15}$$

of A'. Consequently, no R can be an n-achirality implying point symmetry operator of A' that has an effect equivalent to the trivial permutation $\pi(1,2,\ldots,c')$ of points in A'. This implies that A' cannot be contained within a hyperplane P of dimension $n-1$, since such a hyperplane P, as a reflection plane, would correspond to an n-achirality implying point symmetry operation R mapping each point of A' to itself, with an effect equivalent to the trivial permutation of points of A', a contradiction. Consequently, A' cannot be embedded in a hyperplane P of dimension $n-1$. □

THEOREM 7

Motion of a single point a_j of an n-chiral finite point set S of E^n, where a_j is not in a maximum n-achiral subset A of cardinality c, cannot generate any new maximum n-achiral subset A' of cardinality c' less than c.

Proof

Since $a_j \in S$, and $a_j \notin A$, the motion of a_j does not influence the symmetry of set A, hence A can lose its status as a maximum n-achiral subset only if another maximum n-achiral subset of more points is generated by the motion of a_j. Hence, c' of any new maximum n-achiral subset A' of the new point set S' cannot be less than c, $c' \geqslant c$. □

THEOREM 8

Consider an n-chiral finite point set S of E^n, where c is the cardinality of the maximum n-achiral subsets A_t of S. Assume that some motion of a single point a_j of S to a new position a_j' generates a new set S' of a maximum n-achiral subset A' of cardinality $c' \geqslant c+2$, while keeping all other points fixed. Denote a point symmetry operator implying the n-achirality of A' by R and denote the minimum distance between any two points of A' by d_{min}. Define an open ball $B(a_j', d_{min})$ of radius d_{min} about point a_j'. Within the open ball $B(a_j', d_{min})$ it is *not* possible to move point a_j' to any new location $a_j'' \neq a_j'$ where the *same* point symmetry operator R would imply n-achirality of a new subset A'' of cardinality $c'' \geqslant c+2$.

Proof

Since R is a point symmetry operator of the n-achiral set A', and $a_j' \in A'$, the relation $Ra'_j \in A'$ must hold. Since the cardinality of A' is $c' \geqslant c+2$, we know from theorem 5 that $Ra'_j \neq a'_j$. For any point $a_i \in S'$, $a_i \neq Ra'_j$, the following distance constraint holds:

$$d_{min} \leqslant d(Ra'_j, a_i)\,. \tag{16}$$

Since point symmetry operators are linear and leave distance invariant, by applying the inverse operator R^{-1}, one obtains

$$d_{min} \leqslant d(R^{-1}Ra'_j, R^{-1}a_i) = d(a'_j, R^{-1}a_i)\,. \tag{17}$$

That is, for any potential location $R^{-1}a_i$ where a new position

$$a'''_j = R^{-1}a_i \tag{18}$$

for a'_j could produce an R image $Ra'''_j = RR^{-1}a_i = a_i$ within the set of the remaining, fixed points of S, the distance

$$d(a'_j, a'''_j) = d(a'_j, R^{-1}a_i) \tag{19}$$

from a_j is greater than d_{min}. That is, point a'_j cannot be moved to any new location $a''_j \neq a'_j$ within the open ball $B(a'_j, d_{min})$ where the same point symmetry operator R would imply n-achirality of a new subset A'' of cardinality $c'' \geqslant c+2$. □

Our goal is to show that any a'_j location where the cardinality of the induced new maximal n-achiral set A' is greater by two or more than that of A (that is, $c' \geqslant c+2$), must be an isolated point. From theorem 8 we know that all a'_j locations where the *same* point symmetry operator R implies achirality for an induced new A' maximal n-achiral set with cardinality increased by two or more, must be isolated. The only possibility not yet excluded for non-isolated a'_j locations involves *different* R point symmetry operators implying n-achirality. Theorem 9 below will show that even if the point symmetry operators R, implying n-achirality, are assumed to have the freedom to change along a continuum, this freedom cannot be realized if $c' \geqslant c+2$, and no continuum of such a'_j locations exists.

THEOREM 9

Consider an n-chiral finite point set S of E^n, where c is the cardinality of the maximum n-achiral subsets A_t of S. Assume that some motion of a single point a_j of S to a new position a'_j generates a new set S' of a maximum n-achiral subset A' of cardinality $c' \geqslant c+2$, while keeping all other points fixed. There can exist *no continuous path* $p(u)$ for the motion of point a_j, with parametrization $0 \leqslant u \leqslant 1$, starting at $p(0) = a'_j$, and terminating at $p(1) = a''_j$, $a'_j \neq a''_j$, where for each location $p(u)$ of point a_j along this path the cardinality $c'(u)$ of the induced maximal n-achiral set $A'(u)$ is greater by two or more than the cardinality of A_t, that is, where for each location $p(u)$ of point a_j along this path $c'(u) \geqslant c+2$.

Proof

We know from theorem 8 that no such path can exist if the point symmetry operator R implying n-achirality of $A'(u)$ is the *same* along the path; if such path would exist, this path would have to pass through a part of an open ball $B(a_j', d_{min})$ where within $B(a_j', d_{min})$ only at point a_j' does R imply n-achirality of any corresponding maximal n-achiral subset A, a contradiction.

Consequently, all we have to prove is that no such path $p(u)$ is possible with *continuously varying* point symmetry operators $R(u)$ along the path, implying n-achirality of some $A'(u)$ of $c'(u) \geqslant c+2$.

Contrary to the proposition, assume that such path $p(u)$ and family of point symmetry operators $\{R(u)\}$ exist. Since path $p(u)$ is continuous, the associated point symmetry operators $R(u)$ must also change at least piecewise continuously along $p(u)$. (An example for such continuously changing point symmetry operators is a continuously turning mirror plane, kept turning on an axis by the motion of an off-axis point of the plane.) Without loss of generality, we assume that the entire path $p(u)$ is such a piece, that is, $R(u)$ changes continuously along $p(u)$. To each of these point symmetry operators $R(u)$ we assign a permutation operator $\pi(u)$ of the point set within $A'(u)$ that reproduces the effect of $R(u)$ on $A'(u)$. However, for a point set $A'(u)$ of distinct points, no permutation operator $\pi(u)$ can change into another one continuously, hence

$$\pi(u) = \pi\,, \tag{20}$$

a constant permutation, common for all values of u. Furthermore, these properties of permutations also imply that each set $A'(u)$ must include the actual moving point $p(u) = a_j'(u)$ and the *same* set of additional points, since no permutation can continuously switch between distinct points. Consequently, the cardinality of $A'(u)$ must also be a constant,

$$c'(u) = c' \geqslant c + 2\,. \tag{21}$$

The detailed description of the constant permutation π is given as

$$\pi = \pi(k_1, k_2, \ldots k_i, \ldots k_{c'})\,. \tag{22}$$

We know from theorem 6 that this permutation π cannot be the trivial permutation $\pi(1, 2, \ldots c')$ of points in $A'(u)$, since $c' \geqslant c+2$, and the n-achiral point set $A'(u)$ cannot be embedded in a hyperplane P of dimension $n-1$.

Since π is constant, and only point $a_j'(u)$ moves, the $R(u)$ image of point $p(u) = a_j'(u)$ is the same, fixed point

$$R(u)a_j'(u) = a_{k_j}' \tag{23}$$

for all u values. Denote by B the set

$$B = A'(u) \setminus [a_j'(u) \cup a_{k_j}']\,, \tag{24}$$

that is, the fixed set obtained by removing $a'_j(u)$ and its $R(u)$ image a'_{k_j} from $A'(u)$. Since B is the same set for all u values, its baricenter (center of mass, if we associate a formal mass with each point) is fixed at some point $x \in E^n$. For each, instantaneous position of $a'_j(u)$, the baricenter (center of mass) $y(u)$ of the entire set $A'(u)$ is found within a 2D plane $T(u)$ containing the three points x, a'_{k_j}, and $a'_j(u)$. Unless x, a'_{k_j}, and $a'_j(u)$ are colinear, they define a triangle and the plane $T(u)$ is unique; the proof is equally applicable for colinear and non-colinear cases. Since $R(u)$ is a point symmetry operator of $A'(u)$, this implies that the distances of a'_{k_j} and $a'_j(u)$ from the center of mass $y(u)$ must be the same, and since a'_{k_j} and $a'_j(u)$ are related by $R(u)$ [eq. (23)], their formal "masses" must also be equal even if not all "masses" are uniform. Consequently, both $y(u)$ and x must fall on the bisector hyperplane $H(u)$ of the $[a'_{k_j}, a'_j(u)]$ linear segment. Also note that any displacement of $a'_j(u)$ and the displacement of $y(u)$ induced by a displacement of $a'_j(u)$ must be parallel, as follows from the properties of the center of mass.

Since the distance $d(x, a'_{k_j})$ is constant, the distance $d(x, a'_j(u))$ must be the same constant, for any displacement of $a'_j(u)$, that is, for all values of u. Consequently, all motions of $a'_j(u)$ that are not rotations about an axis containing x are excluded.

We shall explore what further restrictions apply for rotations.

By applying the point symmetry operator $R(u)$ on set $A'(u) = \{a'_i\}$, the same set of points is obtained,

$$A'(u) = \{R(u)a'_i\} = \{a'_{k_i}\}\,. \tag{25}$$

Using the notation for points with permuted indices, set B can be specified as

$$B = \{a'_{k_i}\}_{(k_i \neq j, k_i \neq k_j)}\,. \tag{26}$$

For each of the $c' - 2$ points a'_{k_i} of B, the distance from a'_{k_j} is constant,

$$d(a'_{k_i}, a'_{k_j}) = \text{const.}\,, \quad \forall a'_{k_i} \in B\,. \tag{27}$$

When applying the inverse operator $R^{-1}(u)$ on all these points, then these $c' - 2$ constant distances are mapped to $c' - 2$ constant distances of the same magnitude, involving the moving point $a'_j(u)$:

$$\begin{aligned} d(a'_i, a'_j(u)) &= d(R^{-1}(u)a'_{k_i}, R^{-1}(u)a'_{k_j}) = d(a'_{k_i}, a'_{k_j}) \\ &= \text{const.}\,, \quad \forall a'_{k_i} \in B\,. \end{aligned} \tag{28}$$

That is, each of the $c' - 2$ distances $d(a'_i, a'_j(u))$ with the constraint $a'_{k_i} \in B$ for index i must also be constant, independent of the value of u, that is, independent of the location of point $a'_j(u)$.

Depending on the nature of point symmetry operator $R(u)$, there are two possibilities.

(i) If

$$R^2(u)a'_j(u) \neq a'_j(u)\,, \tag{29}$$

that is, if

$$R^2(u)a'_j(u) = R(u)a'_{k_j} = a'_{k_{k_j}} \in B\,, \tag{30}$$

then the following distance between two fixed points $a'_{k_{k_j}}$ and a'_{k_j} must be a constant,

$$d(a'_{k_{k_j}}, a'_{k_j}) = \text{const.} \tag{31}$$

The distance between the $R^{-1}(u)$ images of these points must be the same constant,

$$d(a'_{k_j}, a'_j(u)) = d(R^{-1}(u)a'_{k_{k_j}}, R^{-1}(u)a'_{k_j}) = d(a'_{k_{k_j}}, a'_{k_j}) = \text{const.}\,, \tag{32}$$

that is, the motion of point $a'_j(u)$ must preserve its distance from a'_{k_j}. We know already that point $a'_j(u)$ must preserve its distance from x, hence, the motion of point $a'_j(u)$ must follow a rotation about an axis P that contains both fixed points x and a'_{k_j}.

We show that all but one of the points of B must fall on this axis P.

Precisely one of the $c' - 2$ constant distances $d(a'_i, a'_j(u))$ with the constraint $a'_{k_i} \in B$ for index i (eq. 28) involves the specific point $a'_{k_{k_j}} \in B$. For all other $c' - 3$ points $a'_{k_i} \in B$, the relation

$$R^{-1}(u)a'_{k_i} = a'_i \in B \quad (a'_{k_i} \notin a'_{k_{k_j}}) \tag{33}$$

must hold, consequently, there must be $c' - 3$ constant distances

$$d(a'_i, a'_j(u)) = \text{const.}\,, \quad \forall a'_i \in B \setminus a'_{k_{k_j}}\,, \tag{34}$$

involving points of B and the moving point $a'_j(u)$. These distances can stay constant for all values of u only if all these $c' - 3$ points of $B \setminus a'_{k_{k_j}}$ fall within an $(n-2)$-dimensional rotation axis P of the motion of point $a'_j(u)$. But we also know that the additional point a'_{k_j} must also fall within P, consequently, P must contain $c' - 2$ points from the original set S. Since P, as an axis of rotation in E^n, is at most $(n-2)$-dimensional, the dimension of a set Q obtained as

$$Q = P \cup a'_{k_{k_j}}\,, \tag{35}$$

where point $a'_{k_{k_j}} \in B$ is also a fixed point of the original set S, is at most $n - 1$. The $c' - 1$ points in the $(n-1)$-dimensional set Q necessarily form an n-achiral set, a subset present in the original set S. Consequently, the cardinality of any of the maximum n-achiral subsets of S must be at least $c' - 1$, but we know that for the cardinality c of any of the original A_t maximum n-achiral subsets of S $c' \geqslant c + 2$ holds, a contradiction. Consequently, if $R^2(u)a'_j(u) \neq a'_j(u)$ holds, no continuous path $p(u)$ of properties specified in the conditions exists.

(ii) If the alternative relation,

$$R^2(u)a'_j(u) = a'_j(u) \tag{36}$$

holds, then the effect of $R(u)$ in B must be equivalent to permuting the elements of B within B, that is, for each of the $c' - 2$ elements of B, if

$$a'_{k_i} \in B\,, \tag{37}$$

then

$$R^{-1}(u)a'_{k_i} = a'_i \in B\,. \tag{38}$$

Consequently, for each of the $c' - 2$ constant distances

$$\begin{aligned} d(a'_i, a'_j(u)) &= d(R^{-1}(u)a'_{k_i}, R^{-1}(u)a'_{k_j}) = d(a'_{k_i}, a'_{k_j}) \\ &= \text{const.}\,, \quad \forall a'_{k_i} \in B\,, \end{aligned} \tag{39}$$

the $d(a'_i, a'_j(u))$ distance is between a point of B and the moving point $a'_j(u)$. These $c' - 2$ distances can remain constant for all values of u, that is, for all positions of point $a'_j(u)$, only if all $c' - 2$ points of B fall within a $(n-2)$-dimensional axis P of rotation for the motion of point $a'_j(u)$.

We follow similar steps as in case (i). Since P, as an axis of rotation in E^n, is at most $(n-2)$-dimensional, the dimension of a new set Q obtained as

$$Q = B \cup a'_{k_j}\,, \tag{40}$$

where point a'_{k_j} is also a fixed point of the original set S, is at most $n-1$. The $c' - 1$ points in the $(n-1)$-dimensional set Q necessarily form an n-achiral set, a subset present in the original set S. We conclude that the cardinality of any of the maximum n-achiral subsets of S must be at least $c' - 1$. But we also know that for the cardinality c of any of the original A_t maximum n-achiral subsets of S, the relation $c' \geqslant c + 2$ holds, a contradiction. Consequently, if $R^2(u)a'_j(u) = a'_j(u)$ holds, no continuous path $p(u)$ of properties specified in the conditions exists.

Cases (i) and (ii) cover all possibilities, consequently, no continuous path $p(u)$ of nonzero length exists for the motion of a single point a_j of S where throughout this motion the cardinality of maximum n-achiral subsets $A'(u)$ is $c' \geqslant c + 2$. □

After these preparations, we can easily prove the next result.

THEOREM 10

Any n-chiral point set

$$S = \{a_1, a_2, a_3, \dots, a_n, a_{n+1}, \dots, a_{m-1}, a_m\} \tag{41}$$

of $m \geqslant n + 2$ points can be transformed continuously within E^n, $n \geqslant 2$, into its mirror image

$$S^\diamond = \{a_1^\diamond, a_2^\diamond, a_3^\diamond, \dots, a_n^\diamond, a_{n+1}^\diamond, \dots, a_{m-1}^\diamond, a_m^\diamond\} \tag{42}$$

without passing through any n-achiral arrangement.

Proof

First determine the cardinality c of a maximum n-achiral subset A of S. The c value is the same for the corresponding mirror image $S^{\diamond}$. If $c>n$, then reduce c to $c^{\circ}=n$ by applying a chirality-preserving transformation T on S, turning it into S°:

$$TS = S^{\circ}, \tag{43}$$

$$S^{\circ} = \{a_1^{\circ}, a_2^{\circ}, a_3^{\circ}, \ldots, a_n^{\circ}, a_{n+1}^{\circ}, \ldots, a_{m-1}^{\circ}, a_m^{\circ}\} \tag{44}$$

We know from theorem 2 that such transformation T exists.

Since any point set A° of n points within E^n must fall within an $(n-1)$-dimensional hyperplane, each maximum n-achiral subsets A° of S° defines a reflection plane P°. Using a specific n-achiral subset A° of S°, defining a reflection plane, this plane P° generates the mirror image $S^{\circ\diamond}$ of S°,

$$S^{\circ\diamond} = \{a_1^{\circ\diamond}, a_2^{\circ\diamond}, a_3^{\circ\diamond}, \ldots, a_n^{\circ\diamond}, a_{n+1}^{\circ\diamond}, \ldots, a_{m-1}^{\circ\diamond}, a_m^{\circ\diamond}\}. \tag{45}$$

This reflection plane P° contains $c^{\circ}=n$ pairwise coincident points from S° and $S^{\circ\diamond}$, where without loss of generality, we can assign indices $1, 2, \ldots, n$ to the points within P°:

$$a_1^{\circ}, a_2^{\circ}, a_3^{\circ}, \ldots, a_n^{\circ} \in P^{\circ}, \tag{46}$$

where

$$a_k^{\circ\diamond} = a_k^{\circ}, \quad 1 \leqslant k \leqslant n. \tag{47}$$

Define transformation $T^{\diamond}$ as the mirror image of transformation T, one that transforms $S^{\diamond}$ to the mirror image $S^{\circ\diamond}$ of S°,

$$T^{\diamond}S^{\diamond} = S^{\circ\diamond}. \tag{48}$$

Since T exists, a transformation $T^{\diamond}$ carrying out the mirror image of the transformation T on the mirror image $S^{\diamond}$ of S, must also exist. Clearly, $T^{\diamond}$ is also n-chirality preserving.

Since

$$m \geqslant n+2 = c^{\circ}+2, \tag{49}$$

we find that for the chirality intolerance of S°

$$f \geqslant 1. \tag{50}$$

Denote the subset of S° not within hyperplane P° by Q°. Select a path p_j for each point a_j° of Q° that converts a_j° to its mirror image $a_j^{\circ\diamond}$ by the reflection hyperplane P°:

$$p_j(u): \quad [0,1] \to E^n, \quad \text{where} \quad p_j(0) = a_j^{\circ}, \quad p_j(1) = a_j^{\circ\diamond}, \tag{51}$$

where

$$P^{\circ} a_j^{\circ} = a_j^{\circ\diamond} , \quad j = n+1, \ldots, m , \tag{52}$$

and where the same notations are used for the reflection hyperplane P° as a geometrical object and P° as a symmetry operator. In addition, we require that each path p_j fulfills the following conditions:

(i) each path $p_j(u)$ avoids all points $a_{j'}^{\circ}$ and their mirror images $a_{j'}^{\circ\diamond}$ for all $j' \neq j$,

(ii) each path $p_j(u)$ avoids all points where the cardinality c' of a maximum n-achiral subset $A(u)$ of the actual set $S(u)$ is greater than $c^{\circ} + 1$, $c' \geqslant c^{\circ} + 2$. We know from theorem 9 that no such points can form continua, that is, all such points are isolated.

Since there are only isolated points to be avoided, such paths $p_j(u)$ exist within E^n for any $n \geqslant 2$ and for all $j = n+1, \ldots m$.

If these motions of points of subset Q along paths $p_j(u)$ are applied sequentially, then chirality is maintained in all stages of these motions. The actual motion of point a_j° along the path p_j to its new position $a_j^{\circ\diamond}$ is regarded as an operation P_j on the actual point set. Then, the sequence of transformations

$$T, P_{n+1}, \ldots, P_j, \ldots, P_m, (T^{\diamond})^{-1} \tag{53}$$

converts the original chiral point set S into its mirror image $S^{\diamond}$ by a series of motions preserving chirality:

$$(T^{\diamond})^{-1} P_m \ldots P_j \ldots P_{n+1} T S = S^{\diamond} . \tag{54}$$

□

The fact that there are only isolated points to be avoided by transformations $P_{n+1}, \ldots P_j, \ldots P_m$ is of special significance, implying that according to most of the "natural" choices of geometrical probability measures of paths, the family of chirality-preserving interconversion paths has a probability measure of 1, whenever $n \geqslant 2$.

Hence, the above proof also demonstrates that for any dimension $n \geqslant 2$, chirality preservation is more the rule than the exception, whenever the number of points exceeds the dimension by two or more.

3. Conclusions and closing remarks

Interconvention paths between different molecular nuclear arrangements can be characterized and classified using chirality properties, more specifically, chirality changes along these paths. Chirality is a shape property, hence such a classification is based on relations between molecular shape properties and the shape properties of the interconversion paths. The rules described in this study can be viewed within the framework of a global approach to molecular chirality [26], where some of the general properties of chirality and achirality preserving reaction paths have been discussed.

By theorems 3 and 10, the n-dimensional generalization of a special, chemical question is addressed: what are the conditions and probabilities for the occurrence of chiral and achiral nuclear configurations along interconversion paths between enantiomers? Most chemical visualization approaches assume that interconversion between enantiomers usually occurs *via* some achiral intermediate structure. A molecule with a single formal chiral center, such as the trisubstituted methane CHDFCl, can be visualized to convert to its mirror image by forcing the bonding pattern through an achiral planar arrangement. However, the interconversion of the mirror images of CHDFCl, a five-nucleus molecule, does not require an achiral intermediate structure. Such possibilities are well known; an early example of transformations between enantiomers by reaction paths along which *all* nuclear arrangements are chiral has been described by Mislow and Bolstad [1]. The proof of theorem 10 implies that this example is typical, representing a property of the majority of chemical reactions.

Theorems 3 and 10 provide direct proof of the following chirality properties of three-dimensional molecular transformations:

(i) Any chiral molecular arrangement S of four nuclei must encounter an achiral arrangement in every process transforming S into its mirror image $S^{\diamond}$.

(ii) Any chiral molecular arrangement S of five nuclei or more can always be transformed to its mirror image $S^{\diamond}$ without ever encountering an achiral intermediate arrangement.

Note that the theorems do not involve energy considerations, and the energy required to follow a chirality preserving path (to pass through its maximum point) may be excessively high to be of practical importance. However, reaction paths involving only chiral nuclear configurations and interconnecting two mirror images always exist for molecules of five or more nuclei. In fact, for any chiral molecular structure of five nuclei or more, almost all interconversion paths between enantiomers have the property that no achiral nuclear arrangement is found along them; within a formal, geometrical probability framework, paths with achiral arrangements of five nuclei or more form a set of measure zero. Paths with some achiral nuclear arrangements, for example, those which involve planar nuclear arrangements, are exceptional.

The results are applicable to dimensions different from 3, for example, to the two-dimensional problems of nuclear arrangements along a planar catalytic surface [47], or to dimensions $n \geqslant 4$, if one is interested in the interrelations and shapes of *sets* of configurations in a multidimensional nuclear configuration space M [46]. Note that the dimension $n = 1$ is special. *In* E^1, all interconversion paths must occur along a single line, that in the case of $m = 3$ implies either a formal "collision" between some points, or the occurrence of 1-achiral structures in all rearrangements interconverting enantiomers.

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