Is There a "Most Chiral Tetrahedron"?

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Abstract: A degree of chirality is a function that purports to measure the amount of chirality of an object: it is equal for enantiomers, vanishes only for achiral or degenerate objects and is similarity invariant, dimensionless and normalisable to the interval [0,1]. For a tetrahedron of non-zero three-dimensional volume, achirality is synonymous with the presence of a mirror plane containing one edge and bisecting its opposite, and hence it is easy to design degree-of-chirality functions based on edge length that incorporate all constraints. It is shown that such functions can have largest maxima at widely different points in the tetrahedral shape space, and by incorporation of appropriate factors, the maxima can be pushed to any point in the space. Thus the phrase "most chiral tetrahedron" has no general meaning: any chiral tetrahedron is the most chiral for some legitimate choice of degree of chirality.

Keywords: chirality · degree of chirality · quantitative chirality · symmetry · tetrahedron

Introduction

It would be difficult to overestimate the importance of chiral structures in chemistry and biology.[1–4] The original statement by Lord Kelvin[5] allows no degrees of chirality, as an object is either exactly superimposable on its mirror image (enantiomorph), or it is not. However, the continuous nature of properties such as rotational strength[6] or helical twisting power[7] has encouraged many to think that one molecule may be "more chiral" than another.[8,9]

For molecules, any one of the measurable pseudoscalar spectroscopic properties gives a ready-made scale of chirality. Such a scale may suffer from false zeroes,[6b,8b] dependence on the choice of property and lack of obvious extension to general geometric objects. The tetrahedron, a model for the asymmetric carbon atom, is the simplest motif capable of exhibiting chirality in three dimensions, and there has been discussion in the theoretical literature of the identity of the "most chiral tetrahedron".[8b,e,f] Herein we point out that no absolute meaning can be attached to this term: it has long been recognised that different criteria yield different results,[8b] here we demonstrate that criteria can be found that make *any* chiral tetrahedron the most chiral one. This result is an extension of a conjecture made by Dunitz[10] for the two-dimensional (2D) chirality of the scalene triangle.

Functions proposed for the quantification of chirality fall into two main types. A *degree of chirality*[8c] (χ) is a quantity that purports to measure the "amount of chirality" of a given object, without regard to its absolute configuration; thus the two mirror images of an object have the same value of χ. A *chirality index*[6a,11] (ψ) is a quantity that takes into account both "amount of chirality" and absolute configuration, so that a chiral object and its mirror image have equal and opposite values of ψ. Whereas χ is a scalar quantity, ψ is a pseudoscalar quantity, preserved under all proper and reversed under all improper transformations of the object.

In general, the definition of a chirality index as a continuous function presents difficulties caused by the *chiral connectness* of three-dimensional objects. Consider the formal interconversion of the two enantiomers of a chiral object by some continuous deformation: if it is possible to find a deformation pathway that consists entirely of chiral configurations, then the object is said to be chirally connected.[12] Famously, potatoes are chirally connected,[12] as are chiral tetrahedra considered as sets of *unlabelled* vertices.[8b,13] If labels are attached to the vertices, chiral tetrahedra lose this property, since a set of labelled vertices must contain at least five points if it is to be chirally connected.[14] In particular, a centred tetrahedral molecule such as the pentaatomic substituted methane C(XYZW) is chirally connected, whereas the empty tetrahedral cage XYZW is not. Our subject here is the chiral tetrahedron, free of labels.

Some pathways from a tetrahedron to its enantiomer may happen to pass, en route, through achiral configurations,

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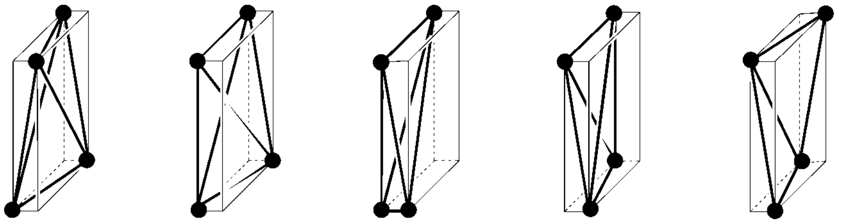

Figure 1. Snapshots of a continuous chiral connection between the two enantiomers an *unlabelled* D_2-symmetric tetrahedron. At no stage on the path **1**→**2**→**3**→**4**→**5** does the object become achiral. Note that if the tetrahedron were *labelled*, **1** and **5** would no longer be an enantiomeric pair.

but, crucially, it will always be possible to devise pathways that consist entirely of chiral configurations (see Figure 1 for an example). As a consequence, a smooth connection between the enantiomer with positive ψ and the partner with negative ψ then demands the existence of a "false zero", that is, a value of $\psi=0$ at a *chiral* configuration.[6b,8b] This problem with ψ does not arise with the degree of chirality, χ which can be constructed to have no chiral zero.

It is useful to compare features of the chirality of simplexes in two and three dimensions. In two dimensions, the scalene triangle exhibits (2D) chirality. Unlike tetrahedra, triangles are not chirally connected:[8b,13,14] interconversion of a chiral triangle and its enantiomer *necessarily* involves passage through an achiral intermediate structure. Degrees χ and indices ψ of 2D chirality can therefore both be defined consistently for triangles. However, this does not lead to a unique definition of the most chiral triangle. We have recently confirmed the conjecture of Dunitz that it is possible for *any* chiral triangle to appear as the most chiral for some legitimate function χ.[15] Hence the term "most chiral triangle" has no meaning independent of a definition of the criterion for quantification.

Our purpose here is to consider the equivalent problem in 3D chirality. We first review the requirements for a function to be a candidate for a degree of chirality. The search for the "most chiral tetrahedron" is the problem of maximising a suitable scalar function χ over the space of possible tetrahedra. It is shown that an infinity of purely geometrically defined functions, all equally legitimate, have the properties demanded of χ. By exploiting the available flexibility it is possible to design χ in such a way as to push its extrema to any chiral configuration. In other words, an extension of the 2D result holds: for some acceptable definition of degree of chirality, any chiral tetrahedron is the most chiral tetrahedron.

Degree of chirality: The objects whose chirality we wish to investigate are all possible tetrahedra, considered as arrays of four points linked by six edges. If a function is to serve as a degree of chirality for a set of 3D geometric objects, it should have the following basic properties:[8b]

1. It should be a real, continuous function of geometrical parameters (internal coordinates) and hence independent of any labelling scheme.
2. It should take equal values for an object and its enantiomorph.
3. It should vanish for all 3D achiral objects in the set, and only for the 3D achiral objects. (A necessary consequence,[15] sometimes forgotten,[8b] is that it should vanish for all degenerate (i.e. 2D and 1D) objects in the set.)
4. It should be similarity invariant, dimensionless and normalisable to the interval [0,1].

As the function is intended for comparison and assignment of extremal tetrahedra, another desirable property is that it should have a highest maximum that is unique up to isomorphism within the set of all tetrahedra. It is evident that many, indeed infinitely many,[16] functions could satisfy these basic requirements. In order to construct one of them, it is necessary to define the "shape space" of tetrahedra, within which we will work.

Representation of tetrahedral shape space: The four vertices of a tetrahedron in 3D space have 12 degrees of freedom, of which six represent rigid-body translations and rotations, and one accounts for the breathing mode that interconverts similarity-equivalent tetrahedra. There are many ways to describe the remaining five-dimensional space.[8b,e,f] One that has some advantages, in particular for visualisation, is to realise each tetrahedron on the circumsphere. This can be done as follows: the radius R and origin of the circumsphere are computed from a set of vertex coordinates (x_i, y_i, z_i) by solution of a set of linear equations; the coordinates are shifted and scaled onto the unit sphere centred at the origin; the tetrahedron is then rotated on that sphere so that one edge AB is symmetrically placed on the "Greenwich meridian": that is, with polar coordinates $\theta_A=\pi-\theta_B$, $\phi_A=\phi_B=0$ for this edge and (θ_C, ϕ_C) and (θ_D, ϕ_D) for the vertices of the opposite edge CD. Other conventions are possible. Moreau[8f] uses a related five-angle description of tetrahedral vertices on the circumsphere, in which two vertices are constrained to lie on the equator.

The set of five angles {θ_A, θ_C, ϕ_C, θ_D, ϕ_D} together span (redundantly) the five-dimensional space of freedoms of the tetrahedron: as the labels ABCD are disposable, any one of the six edges can be chosen as AB, and either end chosen as vertex A; thus, each enantiomer of a chiral tetrahedron ABCD has up to 12 distinct presentations on the sphere, up to 24 when the pair of enantiomers is taken together. It would also be possible to define a single canonical setting for each pair, perhaps based on a hierarchical choice of AB by length, positioning C in a preferred octant, and so on.

A natural way to display the tetrahedra on the unit sphere is with the second projection of Apianus.[17] The spherical surface is transformed into an ellipse with linear scaling of θ on the vertical axis, from $\theta=0$ at the North Pole

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to $\theta=\pi$ at the South, and linear scaling of the chord of the ellipse from $\phi=-\pi$ to $+\pi$. A shortcoming of such a projection, inherent to the use of spherical polar co-ordinates, is that the values of the ϕ coordinates of C and D may suffer a discontinuity when the route of a distortion takes a vertex over a pole.

Whatever the internal coordinates used to define the degree of chirality, its maximisation can be performed by making a search in the space of θ_A, θ_C, ϕ_C, θ_D, ϕ_D, computing the relevant internal coordinates of the implied tetrahedron and using them to calculate the given objective function χ. All distinct presentations of the solution tetrahedron defined by this process are calculated and can be visualised on a single map, which represents the solutions of this five-dimensional problem in two dimensions.

Symmetry considerations: We are looking for functions that vanish for all achiral tetrahedra and that are functions of internal coordinates only. To retain similarity invariance, all tetrahedra are taken to have unit circumradius. We use functions of side lengths and incorporate the constraints imposed by the symmetries of achiral tetrahedra as conditions for vanishing of these functions.

The tetrahedron has maximum point group symmetry T_d, attained when all edge lengths are equal. Distorted 3D configurations with at least one mirror plane belong to one of the achiral C_{3v}, D_{2d}, C_{2v} or C_s groups. In degenerate planar, linear or point configurations, all 3D achiral, various other symmetry groups are possible, but are not relevant here. Distorted 3D configurations without a mirror plane belong to one of the chiral D_2, C_2 or C_1 groups. The other subgroups of T_d, that is, T and C_3 (chiral) and S_4 (achiral), are not available to systems of only four points. Since S_4 is not available, achirality in a tetrahedron arises only from the presence of at least one mirror plane: there are six such in T_d, three in C_{3v}, two in C_{2v} and one in C_s.

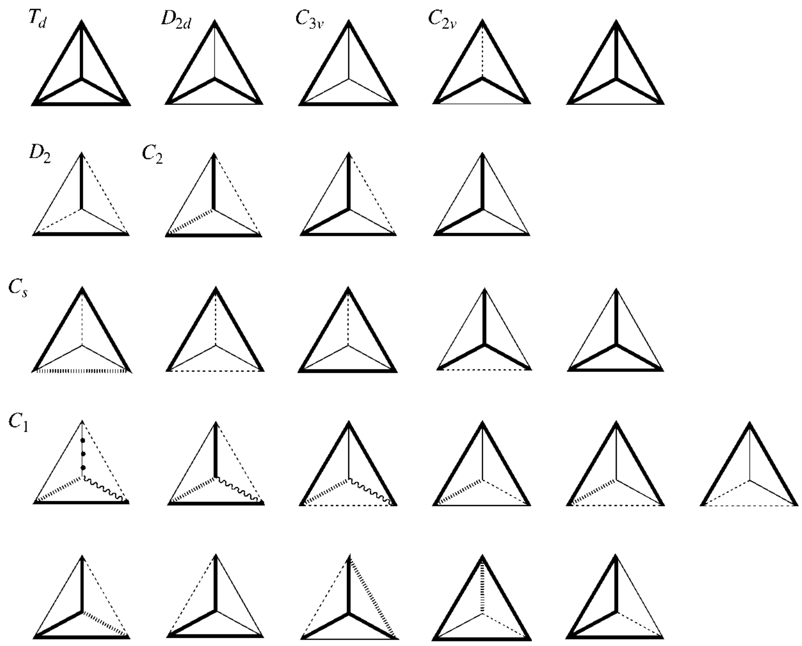

Figure 2. The twenty-five classes of tetrahedra, arranged by maximum point group symmetry and side-length pattern. Bold, feint, dashed, hatched, wavy and circle-decorated lines indicate distinct side lengths. The first entry for each point group corresponds to the maximally disparate set of side lengths, thus illustrating the distribution and sizes of the different orbits of edges. For instance, C_{2v} has one orbit of size 4 and two of size 1. Second and following entries then correspond to the cases of side-length degeneracy compatible with the given point group.

Each point group limits the number of degrees of freedom within the set of edge lengths. As for any deltahedron,[18] the reducible representation of the vibrations is identical with that of the edge lengths, and the number of totally symmetric components in this representation is the maximum number of distinct edge lengths, that is, in the available groups: 1 (T_d), 2 (D_{2d}, C_{3v}), 3 (D_2, C_{2v}), 4 (C_2, C_s), 6 (C_1). Additional equalities between non-equivalent edges can occur, giving rise to the 25 cases shown in Figure 2, one for T_d, D_{2d}, C_{3v}, D_2, two for C_{2v}, three for C_2, five for C_s, and eleven for C_1.

For each edge, there is a group of symmetry operations that leave this edge unshifted. These *site symmetries* of the edges determine the numbers of distinct settings in our cartographic representation of a given achiral tetrahedron or enantiomeric *pair* of chiral tetrahedra. From the partition of the set of edges of a tetrahedron of symmetry G into orbits, and the contributions of edges in the different site symmetries, the numbers of distinct settings are found as in Table 1. The edge orbits are indicated in Figure 2, in the first entry for each point group G, by the use of different line styles.

Design of a degree of chirality: Inspection of the different cases in Figure 2 immediately suggests plausible forms of χ. As shown above, if the tetrahedron is achiral, it has a mirror plane. Hence, in an achiral tetrahedron, there is a pair of opposite edges such that one edge lies in that plane and the other is normal to and bisected by the plane. Suppose the pair is AB, CD, with CD lying in the mirror plane. Then, both $AC=BC$ and $AD=BD$ (AB is the length of edge AB) and a function such as f_{CD} is zero.

$$f_{CD}=(AC-BC)^2+(AD-BD)^2$$

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Table 1. Number of different settings in the cartographic representation as a function of the orbit structure of the set of edges. An orbit is denoted $O_n(H)$, where n is the number of equivalent edges in the set (see Figure 2) and H is the site symmetry of an individual edge (i.e., the group of symmetry operations that leave this edge unshifted). Orbit signatures $\Sigma m O_n(H)$ list the numbers of copies (m) of the orbits of each type. Edges in sites of C_{2v}, C_2, C_s and C_1 symmetries contribute respectively 1, 2, 2, 4 settings per group of equivalent edges to the total count. For chiral tetrahedra, the count of settings includes an equal number for each enantiomer.

G	Edge orbits	Settings
T_d	$O_6(C_{2v})$	1
D_{2d}	$O_2(C_{2v}) + O_4(C_2)$	3
C_{3v}	$2O_3(C_s)$	4
C_{2v}	$2O_1(C_{2v}) + O_4(C_1)$	6
D_2	$3O_2(C_2)$	6
C_s	$2O_1(C_s) + 2O_2(C_1)$	12
C_2	$2O_1(C_2) + 2O_2(C_1)$	12
C_1	$6O_1(C_1)$	24

If alternatively, the edge in the mirror plane is AB, the function f_{AB} vanishes.

$$f_{AB} = (AC-AD)^2 + (BC-BD)^2$$

As there are three pairs of opposite edges, and two different choices of in-plane edge, a function that vanishes for any setting if and only if there is at least one mirror plane in the tetrahedron is the symmetrised product F.

$$F = f_{AB}\, f_{AC}\, f_{AD}\, f_{BC}\, f_{BD}\, f_{CD}$$

As all degenerate tetrahedra have zero volume, V, multiplication of F by V ensures that all conditions 1 to 4 are met. V is itself a function of edge lengths, through $6\,VR = \Delta$, where R is the circumradius (here equal to 1) and $\Delta = \sqrt{S(S-S_1)(S-S_2)(S-S_3)}$, with $S_1 = AB{\cdot}CD$; $S_2 = AB{\cdot}BD$; $S_3 = AD{\cdot}BC$ and $2S = S_1+S_2+S_3$.[19] Thus, χ_1 is a legitimate candidate for a degree-of-chirality function, whereas V and F by themselves are not.

$$\chi_1 = V f_{AB}\, f_{AC}\, f_{AD}\, f_{BC}\, f_{BD}\, f_{CD}$$

The most chiral tetrahedron, as obtained by maximising the function χ_1, has C_2 symmetry, with relative side-lengths given in entry T(1) of Table 2. One setting of this tetrahedron is represented in Figure 3a on the cartographic projection, and Figure 3b shows the 12 distinct settings of the enantiomeric pair defined by this set of side lengths.

However, it would be equally valid to take any one of many other functions related to χ_1, such as χ_m with any positive real number m, which also possess all the attributes of a degree of chirality. This simple modification, allowing varia-

$$\chi_m = V^m f_{AB}\, f_{AC}\, f_{AD}\, f_{BC}\, f_{BD}\, f_{CD}$$

tion of the balance between 3D achirality and geometric degeneracy conditions, leads to a continuum of "most chiral tetrahedra", T(m). Figure 4 shows (in the setting of Figure 3a) the trajectories of vertices under the variation of m.

Table 2. Predictions of the most chiral tetrahedron for different volume exponent m in the family of degree-of-chirality functions χ_m. Entries denote, for selected values of m, solutions T(m), given as sets of side lengths $AB \cdots CD$, here normalised to unity on the shortest side. All chiral T(m) have C_2 symmetry, with the C_2 axis passing through opposite edges AB and CD. The limiting achiral solutions [T(0)] (degenerate, trapezoidal) and [T(8)] (regular tetrahedron) are also listed. For comparison, data for the predictions from three functions taken from the literature are also listed: side lengths for T(a)[8e] and T(b)[8f] are given by Moreau[8f] and those for T(c) were calculated from the five independent internal angles.[8b]

Tetrahedron	AB	AC	AD	BC	BD	CD
[T(0)]	2.366	1	2.996	2.996	1	3.362
T(1/16)	2.324	1	2.936	2.946	1	3.314
T(1/8)	2.284	1	2.899	2.899	1	3.261
T(1/4)	2.210	1	2.813	2.813	1	3.165
T(1/2)	2.086	1	2.665	2.665	1	3.010
T(1)	1.899	1	2.441	2.441	1	2.743
T(2)	1.667	1	2.153	2.153	1	2.412
T(5)	1.371	1	1.765	1.765	1	1.950
T(10)	1.226	1	1.529	1.529	1	1.659
T(20)	1.109	1	1.360	1.360	1	1.442
T(80)	1.027	1	1.169	1.169	1	1.194
T(320)	1.006	1	1.082	1.082	1	1.089
[T(∞)]	1	1	1	1	1	1
T(a)	1	1	1.6	1.6	1	2.3
T(b)	1.504	1	1.361	1.361	1	1.504
T(c)	1.396	1	1.385	1.385	1	1.614

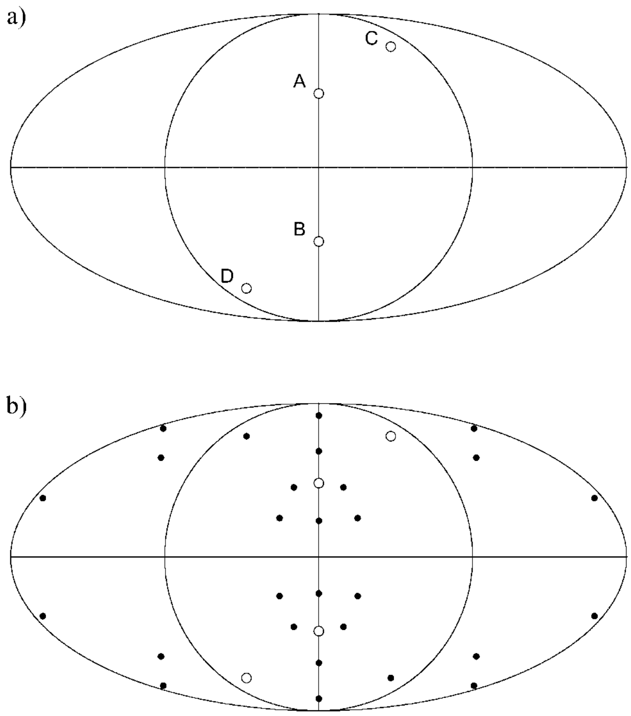

Figure 3. Cartographic representation of the C_2-symmetric most chiral tetrahedron as predicted by χ_1, the simplest product function that satisfies all conditions for a degree of chirality. a) A single setting of one enantiomer of this tetrahedron, and b) the 12 different settings of the enantiomeric pair. Labels ABCD in (a) are not attached to the tetrahedron, but denote the vertices with polar coordinates (θ_A, ϕ_A)… as defined in the text.

As can be seen from the side lengths (Table 2), the tetrahedra T(m) span a range of different shapes, from extremely flattened to near isotropic, and all different from the various

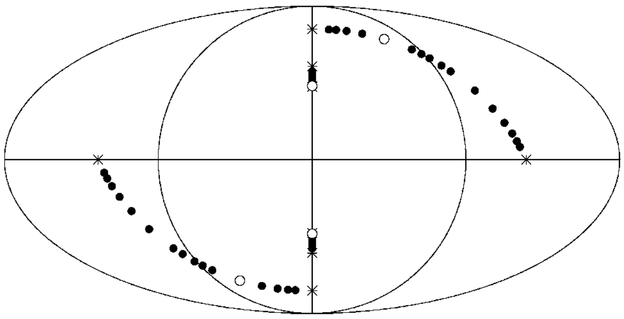

Figure 4. Trajectory of the most chiral tetrahedron under variation of the volume exponent m in the family of degree-of-chirality functions χ_m. The white-filled circles denote the C_2-symmetric solution tetrahedron T(1) in the setting of Figure 3a, and black-filled circles correspond to successive solutions T(m), for different values of m. Moving from T(1) towards the vertical axis, the points correspond to T(1/2), T(1/4), T(1/8), T(1/16); moving from T(1) towards the horizontal axis, the points correspond to T(2), T(2.5), T(3), T(4), T(5), T(10), T(20), T(40), T(80), T(160), T(320). The limiting solutions T(0) (degenerate, trapezoidal) and T(8) (regular tetrahedron) are denoted by stars. The side lengths of the different resulting tetrahedra are given in Table 2.

$$f_{AB,npq} = [|AC^n - AD^n|^p + |BC^n - BD^n|^p]^q$$

$$\chi_{mnpq} = V^m f_{AB,npq} f_{AC,npq} f_{AD,npq} f_{BC,npq} f_{BD,npq} f_{CD,npq}$$

Functions of this form produce different solution tetrahedra. Multiplication of any one χ_{mnpq} by a well behaved function that is symmetric in side lengths and positive for all physical tetrahedra will also yield a new and legitimate degree of chirality.

Combination of any legitimate degree-of-chirality function with a "pushing function"[15] P also yields a legitimate candidate, and hence it should be possible to reproduce any target chiral tetrahedron as the "most chiral" by suitable choice of P. For instance, multiplication of χ_1 by a function such as P_{T*} with ε set to a sufficiently small tolerance, will send the maximum of the product $P_{T*}\chi_1$ to a point arbitrarily close, to a precision determined by ε, to the tetrahedron T^* defined by the target side lengths AB^*, AC^*, AD^*, BC^*, BD^* and CD^*.

$$P_{T*} = \frac{1}{(AB-AB^*)^2 + (AC-AC^*)^2 + (AD-AD^*)^2 + (BC-BC^*)^2 + (BD-BD^*)^2 + (CD-CD^*)^2 + \varepsilon}$$

published "most chiral tetrahedra" found with other criteria.[8b,e,f] As m increases from 1 towards large positive values, the C_2-symmetric solution tetrahedron T(m) tends to T_d symmetry, all six side lengths equalising, and the vertices A, B, C, D tending to the T_d special positions on the projection, that is, $\theta_A = (\pi - \alpha)/2$, $\theta_B = (\pi + \alpha)/2$, $\phi_A = \phi_B = 0$, $\theta_C = \theta_D = \pi/2$, $\phi_C = \pi - (\alpha/2)$, $\phi_D = \pi + (\alpha/2)$, where α is the tetrahedral angle, $\cos^{-1}(-1/3) \approx 109.47°$. As m decreases from 1 towards zero, T(m) degenerates to a trapezium on the great circle at $\phi = 0$. Both limiting forms are understandable, as the function in the first case increasingly emphasises the volume factor (maximised by the regular tetrahedron), and in the second case progressively de-emphasises this factor, reducing its ability to protect against geometric degeneracy. At all points on the path that fall short of the limits $m = 0$ and $m = \infty$, the solution is an acceptable "most chiral tetrahedron" for some well defined choice of functional form for degree of chirality. All these chiral intermediate tetrahedra have C_2 symmetry. It may at first seem paradoxical that chirality is lost at both limits, but this is a straightforward consequence of the fact that at each limit the function is no longer constrained to obey both parts of condition 3, as one factor or the other becomes overwhelmingly dominant. A related "paradox" is encountered when incomplete functions that do not exclude degeneracy are used for 2D-chirality of triangles.[8b,15] Had we not included the "safety" factor V to protect from degenerate cases, we would have obtained the paradoxical result that the most chiral tetrahedron is infinitesimally separated from a planar and degenerate trapezoid.

Further freedom can be introduced by generalising the factors f_{AB}, f_{AC},$\cdots$ that were included in χ to detect mirror planes, for example, to the multi-parameter form $f_{AB,npq}$ (n, p, q real and positive), to create degrees of chirality:

In particular, this functional form allows the target and thus the "most chiral tetrahedron" to have any of the chiral symmetries, D_2, C_2, C_1, allowed for a tetrahedron. Moreover, we may take the target to be an achiral or even a degenerate tetrahedron, such as a planar quadrangle, a triangle or a "flat triangle". A convenient choice of ε can then make a most chiral tetrahedron that is arbitrarily close to the non-chiral target. The product $P_{T*}\chi_{mnpq}$ can be renormalised to bring it into the desired range [0,1]. Trial calculations indicate that $\varepsilon \approx 10^{-9}$ is generally sufficient to send the maximum to the target, whereas $\varepsilon \approx 10^{+9}$ leaves the maximum unchanged at the starting position T(1); variation of ε between the two limits produces a variety of intermediate "most chiral tetrahedra". The infinity of choices of T*, m, n, p and q give infinities of starting, intermediate and target positions.

Conclusion

It is not unexpected that the "most chiral tetrahedra" depend on the measure of chirality, but we see here that they do not even cluster in any particular region of the shape space. The present results demonstrate the correctness of the extension of Dunitz's conjecture to the tetrahedron: it is the case that, with an appropriate choice of degree of chirality, any chiral tetrahedron, no matter how close to an achiral limit, can be found to be the "most chiral tetrahedron", thus robbing the term of absolute significance.

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