

Two-Dimensional Rotational Dynamic Chirality and a Chirality Scale

Yaacov Hel-Or,[†] Shmuel Peleg,[†] and David Avnir^{*‡}

Department of Computer Science, The Hebrew University of Jerusalem, Jerusalem, 91904 Israel, and Department of Organic Chemistry, F. Haber Research Center for Molecular Dynamics, The Hebrew University of Jerusalem, Jerusalem, 91904 Israel

Received February 22, 1990

A scale for the quantitative assessment of the degree of shape chirality and for the absolute assignment of handedness is developed. The scale is based on a new definition of chirality, which, in turn, is based on the dynamic rotational properties of molecules. These concepts and their demonstration are carried out for the case of two-dimensional chirality, i.e., for chirality issues associated with adsorbate-surface interaction.

1. Introduction

Two aspects of chirality are developed in this report: rotational dynamic chirality (and diastereomerism) and a chirality scale. We develop these concepts in two dimensions (2D). It suffices in the sense that an extension to three-dimensional (3D) chirality does not require additional principle arguments. The 2D analysis has consequences to issues of chirality in surface science, and therefore we review briefly in section 2 some relevant concepts involved with 2D chirality. In section 3, we summarize some principle differences between the classical static isomerism and the dynamic approach we develop here. In section 4, we comment on the need to develop a scale of chirality. In section 5, we combine the various topics introduced in sections 2-4 and arrive at a 2D, dynamic chirality scale, which is then applied to the 2D chirality of (adsorbed) alkanes (sections 6 and 7).

2. Some Comments on Two-Dimensional Chirality

The set of rules which determine the chirality properties of an adsorbed molecule is quite different from the set which characterizes "normal" chirality in 3D. It is the reduction in the dimensionality of the system which makes all the difference: in 2D the conditions for chirality are significantly relaxed.¹ There is an interesting consequence to that situation which, we feel, may have escaped the attention of many surface scientists, which is that chirality is by far more common in the adsorbed state, compared to the bulk state. Consider, for example, *trans*-2-butene or the anti conformer of *n*-butane. These are, of course, not chiral molecules in 3D; yet when adsorbed, they become a racemic mixture of two enantiomers. Figure 1 shows the two enantiomers (2, 3), and the reader can easily be convinced that the two cannot be superimposed by any two-dimensional translation, i.e., that the 2D mirror images (the mirror being a line in this case) are two enantiomers.

In general, a planar molecule (or conformer) is chiral in 2D if it does not have a symmetry axis in the 2D plane (cf. *cis*-2-butene, which has this axis and is achiral in 2D). Such molecules are *prochiral for adsorption* and have two

enantiotopic faces:^{2b} i.e., adsorption induces chirality, and the two enantiomers are obtained by molecule-surface interaction with one or the other of the two enantiotopic molecular faces. The adsorption prochirality will show up in chiral 3D products, if there is interaction with a catalytic surface and an $sp^2 \rightarrow sp^3$ reaction occurs. This is well documented.^{2a} Relaxation of the requirements for chirality in 2D show up also for tetrahedral carbon molecules. Consider for instance the compound CX_2YZ . It is achiral in 3D but prochiral for adsorption: two enantiomers are possible if the molecule is adsorbed through XYZ (with the remaining X pointing away from the surface) depending on which of the two enantiotopic X's is adsorbed. Again, there is no symmetry axis in the plane formed by the triangle XYZ. Finally, we notice that the surface itself can be chiral in 2D; for instance, surfaces of crystals of chiral molecules (either 2D or 3D chiral molecules) may have a surface pattern of atom arrangement which is 2D chiral.³ An interesting situation evolves here, considering interaction of 2D chiral molecules with such a surface: 2D diastereometric interactions form, so that the chiral surface may be able to distinguish between the two prochiral faces of the adsorbate. In 3D chromatography, this is of course well-known.⁴

3. Rotational Dynamic Chirality and Diastereoisomerism

Although not stated explicitly, the concept of chirality is (in texts and in the mind of chemists) a static concept. A molecule or a conformer is judged chiral or not chiral based on its static shape: is it or is it not superimposable with its mirror image? However, this concept collapses if one substitutes the static picture with a dynamic one. This is in particular so because a moving object can be chiral even if its static shape is achiral. Perhaps the most basic movement which is capable of introducing chirality is rotation. Consider the simplest case of all—a rotating rod in 2D (and it does not matter where the axis of rotation is located): a clockwise rotating rod and a counterclockwise rotating rod are two dynamic enantiomers. They are enantiomers in the sense that the R_r (subscript r for rotation)

* Author to whom correspondence should be addressed.

[†] Department of Computer Science.

[‡] Department of Chemistry, F. Haber Research Center for Molecular Dynamics.

(1) Prelog, V. *Science* 1982, 193, 17. Helmchen, G.; Haas, G.; Prelog, V. *Helv. Chem. Acta* 1973, 56, 2255.

(2) (a) For example: Morrison, J. D.; Mosher, H. S. *Asymmetric Organic Reactions*; American Chemical Society: Washington, DC, 1976. (b) For a brief survey of these concepts, see: March J. *Advanced Organic Chemistry*, 3rd ed.; Wiley: New York, 1985; Chapter 4.

(3) Addadi, L.; Berkowitch-Yellin, Z.; Weissbuch, I.; Lahav, M.; Leiserowitz, L. *Top. Stereochem.* 1981, 16, 1.

(4) For example: Roumeliotis, P.; Unger, K. K.; Kurganov, A. A.; Davankov, V. *J. Chromatogr.* 1983, 225, 51.

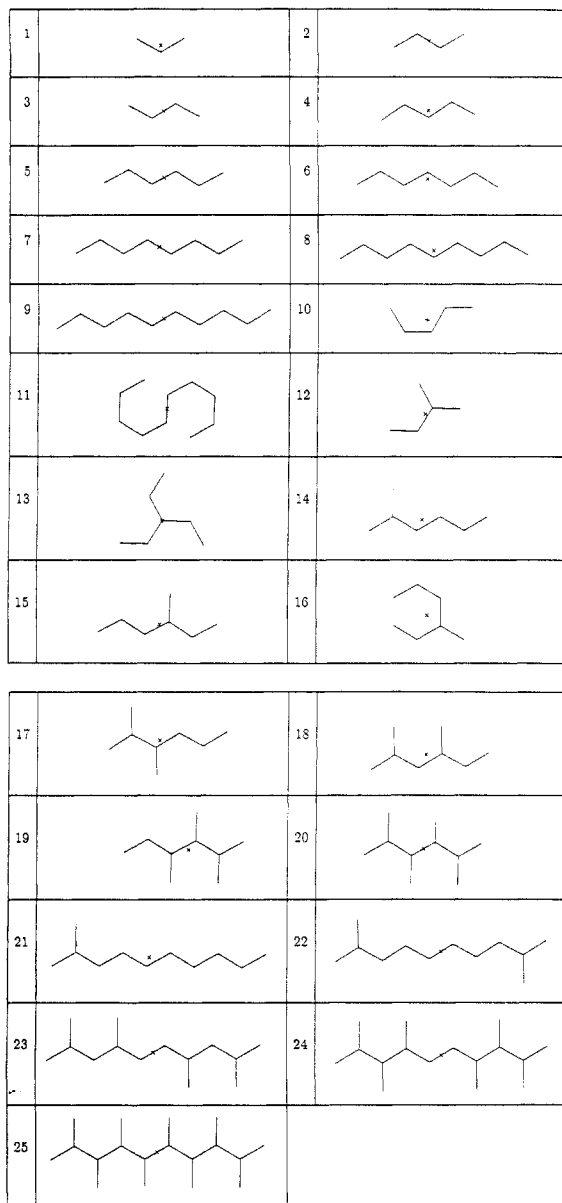


Figure 1. Alkane skeleton structures analyzed in this study (see Table I). The rotation centers are also indicated.

and the S_r enantiomers will interact diastereomerically with other chiral objects; they are *dynamic* enantiomers in the sense that only motion reveals this property. For instance, the activation energy for rotation on an R -chiral surface will be different for S_r and R_r enantiomers. An illustrative example could be acetylene, which rotates, in the adsorbed state, on the surface of crystalline E -styrene: clockwise and counterclockwise rotation should have, in principle, different activation energies. Not only a rod but other simple symmetrical shapes can become dynamically chiral. For instance, propane, which is *statically* achiral in 2D (and of course in 3D), becomes dynamically chiral if it rotates in 2D around a center of rotation which is located on it or near it.

A particularly interesting outcome of these rotation arguments emerges for the case of chiral objects. Imposing a clockwise (R_r) or counterclockwise (S_r) rotation on a molecule which is statically chiral (say R) creates *two* dynamical diastereoisomers: $R_r R_r$ and $R_r S_r$. The two are *not* superimposable upon reflection through a one-dimensional mirror axis. The other pair of dynamic stereoisomers would be $S_r R_r$ and $S_r S_r$, so that the dynamical enantiomeric pairs are $R_r R_r/S_r S_r$ and $R_r S_r/S_r R_r$. In other

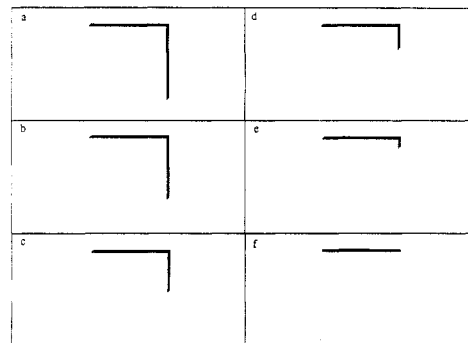


Figure 2. L-shapes with various degrees of chirality.

words, whereas for static adsorption molecules may have enantiotopic faces or substituents, when the adsorbates rotate the enantiotopic moieties become diastereotopic. Note that if a molecule is statically achiral (propane in 2D) then the rotational isomers are 2D reflection images of each other. Next we use the dynamical diastereomerism (or lack of it) for developing the chirality scale.

4. Measuring the Degree of Chirality

Being a symmetry property, chirality is treated in terms of chiral or not chiral. In a recent paper, we addressed ourselves to that issue⁵ and argued that important and useful structural information on the shape of molecules is lost by this "black or white" approach. Thus, classically, naphthalene is not chiral in 2D, but 2-deuterio-, 2-methyl-, and 2-phenylnaphthalene all are. Yet intuition tells us that 2-deuterionaphthalene, which is only barely different from naphthalene, is "less chiral" than 2-phenylnaphthalene, which has a significantly different shape. And so one could ask the question, by how much is the 2-deuterio derivative less chiral than the 2-phenyl derivative?

On a more abstract level, consider the L shapes in Figure 2. Shapes a and f are achiral in 2D: their 2D mirror images are superimposable. Shape b is slightly different than a but is already chiral, so are shapes c and d. Shape e is chiral too, although it is quite close in shape to f. Under the current convention, shapes b–e are simply chiral; we seek to say more than that: by how much is shape c more chiral than shape b?

Few suggestions for chirality scales have appeared in the literature. (The interested reader is referred to the most recent suggestions by Gilat⁶ and by us⁵ and to references cited therein.) The approach suggested here, though, is completely different: previous studies concentrated on the classical static picture of chirality, while here we use the dynamic approach, outlined in section 3.

Beyond the purely mathematical motivation to provide a more refined tool for the evaluation of chirality, there are practical aspects to a chirality scale, as already noted in previous quantitative molecular shape studies. These include guest–host interactions,⁷ molecular packing in crystals and in solid solutions,⁸ and, in our case, packing and phase transition of adsorbates on surfaces.

5. Chirality Scale Based on Molecular Rotation

We apply the ideas presented above for the development of a sensitive measure of chirality. The approach would

(5) Avnir, D.; Meyer, A. Y. *J. Mol. Struct. (THEODEM)*, in press.

(6) Gilat, G. *J. Phys. A: Math. Gen.* **1989**, *22*, L545 and earlier references.

(7) Hodgkin, E. E.; Richards, W. G. *J. Chem. Soc., Chem. Commun.* **1986**, 1342.

(8) Kitaigorodski, A. I. *Org. Chem. Crystallogr.*; Consultants Bureau: New York, 1961; Chapter 4. Compare with: Gavezzoti, A. *J. Am. Chem. Soc.* **1989**, *111*, 1835.

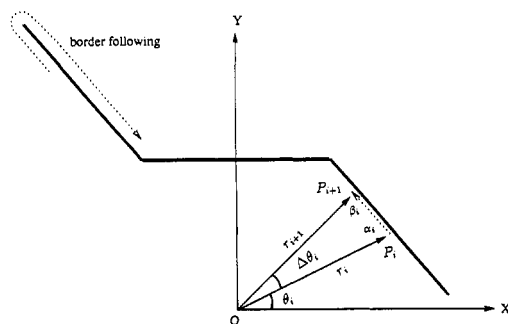


Figure 3. Computational method for determining the Z values and presentation of the variables described in the text.

be to compare the intensities of some rotational property of a dynamic R_r object to an S_r object: the difference will be zero for achiral molecules, it will be non-zero for the pair of diastereomers R_r/R_s , and this value can serve as a chirality measure (the larger it is, the more chiral the shape is defined to be). Two enantiomers will have the same difference value, but with opposite signs. This is done in practice as follows:

Imagine an object rotating in a medium of fine particles ("sand"). If the object is not statically chiral (a rod), then the amount of sand particles collected by the dynamically chiral object upon a clockwise rotation will be the same as collected by its dynamic enantiomer in a counterclockwise rotation. This, however, is not the case for a statically chiral object. Here, rotation in the two different directions will result in collection of a different amount of particles. The idea is to use this difference as a chirality measure. For the rod it will be zero; for a chiral object it is non-zero. The rotation may be formed around the centroid or around any other (nearby) point. This will be discussed later.

The mathematical formulation of this procedure follows. At some points it is tailored to the computerized image analysis technique we employed.⁹ Let K be a set of points (or pixels, in the image analysis) of a line presentation of the molecule. (For sake of simplicity, we employed here line presentation of molecules. However, the procedure is general and may be applied to any other desirable molecular presentation. The principles of our paper do not suffer from the minimalistic approach we chose.) We assume that K is simply connected. Let $\{P_{2i-1}\}^n$ be the ordered sequence of the boundary pixels of the line. They are counted by following the circumference of the object, so that the object is to the right ("right-following"), as shown in Figure 3. In order to make the technique general and applicable to closed structures, e.g., polycyclic hydrocarbons (not discussed in this report), we count the pixels by following the circumference of the object, even if it is an open line object. In such cases, each pixel is counted twice, but this does not affect the method. For a boundary pixel P_i of an object which is rotated around O , the axis of rotation, we also define the following (Figure 3): \tilde{r}_i , the vector from O to P_i ; d_i , the length of \tilde{r}_i ; θ_i , α_i , β_i , angles as defined in Figure 3; $\Delta d_i = d_{i+1} - d_i$ (Δd_i can be positive, negative, or zero); and $\Delta \theta_i = \theta_{i+1} - \theta_i$ ($-\pi \leq \Delta \theta_i \leq \pi$). A boundary segment between P_i and P_{i+1} will encounter particles upon clockwise rotation (see dashed line $[P_i, P_{i+1}]$ in Figure 3) only if $\Delta d_i < 0$. It will encounter

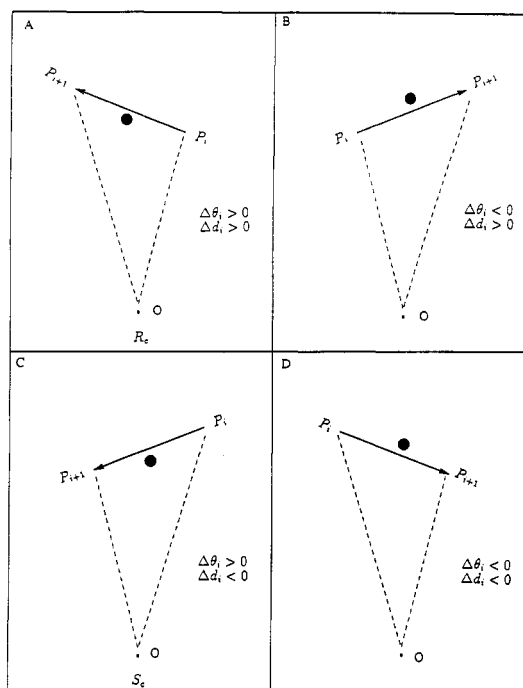


Figure 4. Four Δd_i , $\Delta \theta_i$ combinations. O denotes the center of rotation. \bullet marks the side where "particles are collected".

particles in counterclockwise rotation if $\Delta d_i > 0$. The collected particles will be thrown away by centrifugal force if $\Delta \theta_i < 0$; they will remain in place if $\Delta \theta_i > 0$. The four combinations of Δd_i and $\Delta \theta_i$ are shown in Figure 4.

Let us now denote with R_c and S_c the subsets of K that collect particles upon clockwise (right) and counterclockwise (left) rotations, respectively. The conditions for the existence of R_c or S_c are (Figure 4)

$$R_c = \{P_i | \Delta \theta_i > 0, \Delta d_i < 0\} \quad (1)$$

$$S_c = \{P_i | \Delta \theta_i > 0, \Delta d_i > 0\} \quad (2)$$

Notice that $R_c \cap S_c = 0$ and $R_c \cup S_c \in K$. In order to further refine the measurement, we give the d_i values the proper weight, by taking $d_i \sin \alpha_i$ and $d_i \sin \beta_i$ for left- and right-hand rotation, respectively. The sine function was chosen for this weighing procedure because it behaves properly in the sense that it maximizes the contribution of a 90° angle and minimizes the contribution of minor bends (zero, for $\alpha_i = 180^\circ$). So, as an approximate measure for the particle-collecting ability upon a left-hand rotation, we define

$$L = \frac{1}{d_{\max}} \sum_{i \in S_c} d_i \sin \alpha_i \quad (3)$$

and for the right-hand rotation

$$R = \frac{1}{d_{\max}} \sum_{i \in R_c} d_i \sin \beta_i \quad (4)$$

where d_{\max} , the maximal value of d_i , is taken as a normalization parameter, to avoid size effects. We are ready now for the final definition of our chirality measure, Z :

$$Z = \frac{L - R}{L + R} \quad (5)$$

Z has the following properties: (1) As Z increases, so does the degree of chirality of the analyzed object. (2) If left and right rotations behave equivalently, $Z = 0$ and the object is not chiral.¹⁰ (3) The absolute value of Z is an

(9) For a preliminary image-analysis technical report, see: Hel-Or, Y.; Peleg, S.; Zabrodsky, H. *Proc. IEEE Comput. Vision Pattern Recognition* 1988, 304.

(10) It should be noted that although $Z \neq 0$ always implies chirality, there may exist "pathological" chiral objects for which coincidentally $L = R$ (eqs 3 and 4).

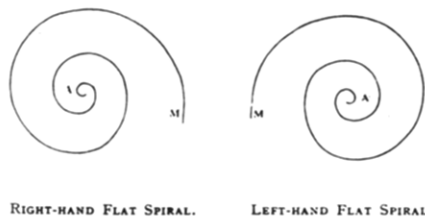


Figure 5. Reproduction of the absolute chirality assignment of Cook.¹¹

Table I. Two-Dimensional Chirality Z Values for Various Alkane Skeletons

structure ^a	alkane ^b	Z value ^c
1	propane	-1.8 ^d
2	(<i>R</i>)- <i>n</i> -butane	+142
3	(<i>S</i>)- <i>n</i> -butane	-142
4	<i>n</i> -pentane	-4
5	<i>n</i> -hexane	+26
6	<i>n</i> -heptane	-2
7	<i>n</i> -octane	+19
8	<i>n</i> -nonane	-1
9	<i>n</i> -decane	+9
10	<i>n</i> -pentane (c)	-81
11	<i>n</i> -decane (c) ^e	-11
12	2-methylbutane	-74
13	3-ethylpentane	-107
14	2-methylhexane	-9
15	3-methylhexane	+31
16	3-methylhexane (c)	+9
17	2,3-dimethylhexane	-5
18	2,4-dimethylhexane	0
19	2,3,4-trimethylhexane	+7
20	2,3,4,5-tetramethylhexane	-18
21	2-methyldecane	-6
22	2,9-dimethyldecane	-17
23	2,4,7,9-tetramethyldecane	-23
24	2,3,4,7,8,9-hexamethyldecane	-8
25	2,3,4,5,6,7,8,9-octamethyldecane	-5

^a The numbers refer to the structures in Figure 1. ^b Unless indicated, the most stable conformer is taken, usually the all-trans. "c" means at least one cis angle (see Figure 1). ^c The error bars decrease with the size of the object. Thus, for *n*-pentane (4) it is ± 4 , and for the decanes it is ± 1 . (Propane (1) was calculated from a larger object (Figure 1), hence the better accuracy). ^d See Figure 6. ^e This is the farnesol skeleton (a sesquiterpene).

indicator for the absolute configuration. $Z > 0$ is left-handed chirality (more particles are collected upon a left-hand rotation than upon a right-hand rotation). $Z < 0$ is right-handed chirality.

It is interesting to notice at this point that Cook, in his classical 1914 treatise on spirals in nature,¹¹ defined absolute handedness as shown in Figure 5. Our absolute chirality definition is in keeping with Cook's definition.

6. Results: Degree of Dynamic Chirality of Various Alkane Skeletons

In Table I, we have collected the Z values of the various alkanes shown in Figure 1, as determined by rotation around their center of mass (also shown in Figure 1). The negative or positive signs refer to the specific enantiomer and to the specific conformers shown in Figure 1. A detailed discussion follows in section 7.

In Figure 6, we show the effect of changing the location of the center of rotation: point b is the center of mass of the propane skeleton, and the chirality is practically zero. So is the chirality of point a, which is located on the symmetry axis of that shape. The object, however becomes dynamical chiral upon rotations around points c and d.

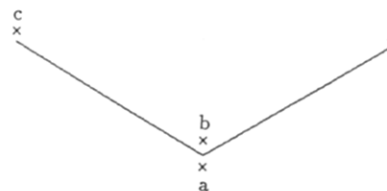


Figure 6. Effect of location of the rotation center on the degree of chirality. The Z values are (a) -1.8 ± 2.5 , (b) -1.1 ± 2.5 , (c) $+27 \pm 2.5$, and (d) -27 ± 2.5 .

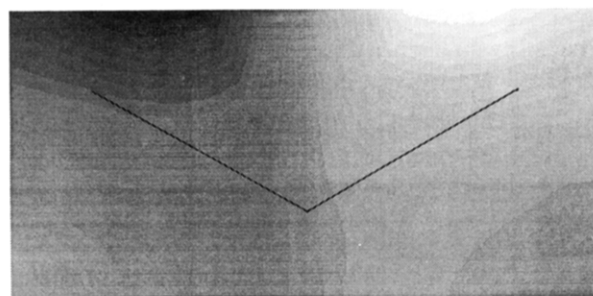


Figure 7. Gray-level map of the degree of chirality, Z , as a function of location of the rotational axis. White and black represent locations of the highest positive and negative Z values, respectively.

As shown in Figure 7, one can actually prepare a full map of the degree of chirality as a function of the location of the rotation center. This is represented here as a grey level map.

7. Discussion

We analyze and highlight here the properties of the Z value and the trends of its change with structure.

In the series of all-*trans*-*n*-alkanes, the odd-number carbon skeletons are not chiral in 2D. Thus, propane, pentane, heptane, and nonane (1, 4, 6, and 8 in Table I) have Z values around zero (see footnote c in Table I). The even-numbered alkanes (except ethane) are chiral: butane (2), hexane (5), octane (7), and decane (9) have Z values of 142, 26, 19, and 9, respectively. In other words, our first observation is that the degree of chirality drops with increase in chain length. This is understood by realizing that as the chain increases, the relative weight of cutting one methylene group and thus removing the chirality decreases. Removing one methylene from chiral *n*-decane in order to obtain the nonchiral *n*-nonane is a smaller structural change than removing it from butane. In other words, the deviation of butane from nonchiral symmetry is larger than that of decane.

Next we notice that the two 2D enantiomers of butanes 2 and 3 have the same Z value but with opposite signs. According to our absolute convention (and that of Cook), the positive Z value of 2 means that it has left-hand chirality (i.e., it will collect more particles by counterclockwise rotation). The reader can easily be convinced that this is the case by comparing 2 and 3. Notice that not only are 2 and 3 2D mirror images of each other, but so are 2 rotating in one direction with 3 rotating in the opposite direction.

The cisoid conformer of *n*-pentane (10) demonstrates an important property, namely, that molecular chirality must be defined per specific conformer. Thus, while all-*trans*-*n*-pentane (4) is not chiral, the cis-trans conformer 10 is highly chiral with a Z value of -81. But while *trans*-*n*-butane is chiral (2, 3), the cis conformer has an axis of symmetry and is not chiral (not shown). A third possibility is that the *n*-alkane is chiral and so is one of its conformers,

(11) Cook, A. T. *The Curves of Life*; Constable: London, 1914 (reprinted by Dover: New York, 1979); p 25.

as demonstrated for decane (9, 11). This pair of conformers shows another interesting aspect: notice that the transition from conformer 9 to conformer 11 (which was performed by rotation of the end groups) results in changing the absolute handedness of the object: 9 is a left-hand object while 11 is a right-hand object, and the ΔZ between the two is 20.

Next we consider the effects of substitution or branching. The 2-methylbutane (12) can be regarded either as resulting from *trans*-butane (3, $Z = -142$) or from *cis*-butane ($Z = 0$). So introducing an additional methyl is either inducing chirality into the *cis*-butane or diminishing the degree of chirality of the *trans*-butane. The fact that the $Z = -74$ value for 2-methylbutane (12) is exactly the average of the two Z values of the butane conformers may be coincidental, but it certainly reflects the fact that 12 contains moieties of both *cis*- and *trans*-butane. 3-Ethylpentane (13) is a highly chiral object with $Z = -107$. It should be compared to the unsubstituted pentane conformer 10, which has a lower Z value of -81 . The increase in chirality of 13 compared to 10 is a direct outcome of triplicating in 13 the structural shape of 10. Actually, the propeller shape of 13 belongs to a distinct family of chiral shapes, the properties of which will be the topic of further reports. Again, notice that we are capable now of answering questions of the type "how much chirality is induced in pentane if its 3-position is substituted with an ethyl?"

Structures 14–20 and 21–25 represent various substituted hexanes and decanes, respectively. The pattern of the shift from left chirality to right chirality (cf. also 5 and 9) and vice-versa follows the same type of arguments used above. Note structure 18, which demonstrates the sensitivity limit of our technique: the object is chiral, but its Z value apparently is very low.

Figure 6 demonstrates how rotational chirality is very much determined by the choice of rotational center: propane is a highly chiral object if it is rotated around axes

located near but outside the end methyls. The chirality map (Figure 7) has a mirror image symmetry: for each axis that gives a certain Z value, there is a symmetric opposite axis which gives the same Z value but with opposite sign.

8. Conclusions

We have shown that by replacing the static picture of chirality analysis with a dynamic-rotational one, chirality becomes a much richer phenomenon. In particular, we have shown that rotation properties can be used for the construction of a shape-chirality scale. Our study, which focused on two-dimensional (surface) chirality, bears on problems of 2D molecular packing,¹² ordering within islands of adsorbates, 2D phase transition in chiral adsorbates, 2D crystallization,¹³ rotational properties of adsorbates (as induced, e.g., by circularly polarized far-infrared irradiation¹⁴), the efficiency of chromatographic chiral separations, and selectivity in a chiral catalytic reaction. Some of these applications are the subject of current research in our laboratories.¹⁵

Acknowledgment. D.A. thanks Prof. A. Y. Meyer for helpful discussions on two-dimensional chirality. Y.H. was supported by the Leibniz Center for Research in Computer Science.

(12) (a) Arnett, E. M.; Harvey, N. G.; Rose, P. L. *Acc. Chem. Res.* **1989**, *22*, 131. (b) Gavezzoti, A.; Simoneta, M. *Comp. Math. Appl.* **1986**, *12B*, 465.

(13) Weiss, R. M.; McConnell, M. H. *Nature* **1984**, *310*, 47.

(14) Evans, M. W. *Phys. Scr.* **1989**, *39*, 689.

(15) **Note added in proof:** The concept of "level of prochirality" has been suggested (Mislow, K.; Siegal, J. *J. Am. Chem. Soc.* **1984**, *106*, 3319. Halevi, E. I. *J. Chem. Res. (S)* **1985**, 206). It is obtained by counting the number of steps needed for desymmetrization. We also note that although the analysis of molecular rotors is well-known (e.g., Mislow, K.; et al. *J. Am. Chem. Soc.* **1983**, *105*, 1427. Reference 5), these are treated in their "frozen" form, in contradistinction to the dynamic approach suggested here.