J. Am. Chem. Soc. 1987, 109, 2887-2894

of ionic crystals,[28] and the experimental results are extrapolated to the unperturbed free ion. The excellent agreement of the vibrational frequency obtained in this manner (1976 ± 4 cm^{-1}) with the frequency obtained in these gas-phase experiments seems to indicate a good understanding of lattice perturbations of this negative ion; however, a more extensive set of gas-phase data is clearly needed to show that the agreement is as good for other molecular anions.

While theoretical and low-resolution spectroscopic predictions guided the search for the ν_3 vibrational spectrum, previous chemical studies helped determine optimum chemistry for N_3^- production. In their flowing afterglow apparatus, Bierbaum et al.[10] have observed that the gas-phase reaction

$$NH_2^- + N_2O \rightarrow N_3^- + H_2O$$

occurs with an efficiency of 72% and a second-order rate constant of 2.9×10^{-10} cm^3 $molecule^{-1}$ s^{-1}. Interestingly, this is the gas phase analogues of the reaction

$$NaNH_2(s) + N_2O(g) \rightarrow NaN_3(l) + H_2O(l)$$

which is used extensively in large scale industrial production of azides.[3] Since Tack et al.[15] observed large concentrations (4×10^{11} molecules/cm^3) of the amide ion in pure ammonia discharges, it was predicted that adding N_2O to an ammonia discharge would result in formation of azide. As predicted, N_3^- was formed in a 1.7 torr NH_3/300 mtorr N_2O discharge. As in the NH_2^- study, enhancement of negative ion production by the presence of a metal coating on the discharge cell walls was found, as was a preference for low discharge power. Furthermore, all discharges found to produce detectable amounts of N_3^- contained both NH_3 and N_2O. This clearly indicates that the most likely mechanism for azide formation is the NH_2^-/N_2O reaction. Because of the strong basicity[10] and relatively low electron binding energy (0.744 eV)[29] of the amide ion, ammonia discharges may prove useful in the gas-phase production of other negative ions as well.

As mentioned previously, 25 lines have been tentatively assigned to the (011)-(010) hot band of N_3^-. Complete analysis awaits an improvement of our diode laser coverage in the region of the P-branch. In addition, we will search for the (101)-(000) combination band, which is predicted[7] to be quite strong (Γ_1 = 1512 cm^2/mol) and to be located at 3211 cm^{-1}. This combination of data should lead to the first experimental determination of the equilibrium structure of a polyatomic negative ion.

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Chirality Forces

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Abstract: The differential interaction energy between two chiral tetrahedral molecules, first with the same chirality (homochiral, $R \leftrightarrow R'$) and second with opposite chirality (heterochiral, $R \leftrightarrow S'$), is analyzed in the limit of free relative molecular rotation (high-temperature limit, interactions small relative to kT). This differential energy measures the degree of "chiral recognition" or "chiral discrimination". It is shown that, if the energy of interaction is expressed as a sum of interactions between atomic centers on the two molecules, *six-center* forces, occurring simultaneously between triplets of atoms, one triplet in each molecule, are responsible for the discrimination. Since this is the first natural phenomenon where six-center forces are found to play an important role we call these forces *chirality forces*. Models which are based on two-center forces alone (charges on the four atoms) or four-center forces (dipoles on the tetrahedron edges) fail to give any chiral discrimination in the freely rotating limit. A model based on the *simultaneous* overlap-exchange interaction between three pairs of centers on the two molecules does yield a discrimination after averaging freely over all relative orientations. The energy preference is found to be 0.5 10^{-2}–10^{-4} times the total rotationally averaged interaction energy at a distance of 5 Å. Two pyramidal chiral ammonia molecules (hydrogens with different exponents) interacting face-to-face at 4 Å also have an average SCF discrimination of 9.2 small J/mol for their eclipsed configurations. Comparison is made with the Boltzmann-weighted discrimination due to direct two-center net charge–net charge interactions. Third-order dispersion forces, which also contribute to the chiral discrimination between interacting tetrahedra, are discussed and compared with the six-center chirality forces.

1. Introduction

Surprising as it may seem, the asymmetric nature of tetrahedral carbon has been recognized for more than a century,[2] and yet no attempt has been made to evaluate the interaction energy between two asymmetric tetrahedral molecules. In several important papers[3a-c] and in an exhaustive review[3d] Craig and co-workers have examined the discriminating interactions between chiral molecules.

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(2) (a) Le Bel, J. A. *Bull. Soc. Chim. Fr.* **1874**, *22*, 337. (b) van't Hoff, J. H. *Arch. Neerland. Sci. Exact. Nat.* **1874**, *9*, 445.

(3) (a) Craig, D. P.; Power, E. A.; Thirunamachandran, T. *Proc. Roy. Soc. London* **1971**, *A322*, 165. (b) Craig, D. P.; Schipper, P. E. *Proc. Roy. Soc. London* **1975**, *A342*, 19. (c) Craig, D. P.; Radom, L.; Stiles, P. J. *Proc. Roy. Soc. London* **1975**, *A343*, 11. (d) Craig, D. P.; Mellor, D. P. *Topic Curr. Chem.* **1976**, *63*, 1. (e) Craig, D. P. In *Optical Activity and Chiral Discrimination*; Mason, S. F., Ed.; Reidel: Dordrecht, 1979; p 310.

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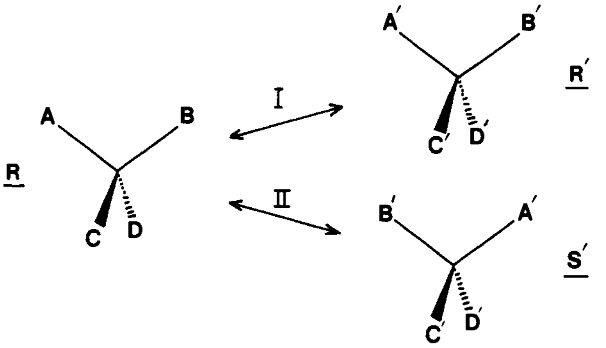

Figure 1. The differential energy due to chiral recognition is given by interaction I minus interaction II.

Other important contributions have been made by Schipper.[4]

Generally the multipole expansion method, in which a superposition of multipoles with a common center represents each molecule, has been used. It is particularly suited for distances of separation larger than the overlap distance. Discrimination may or may not arise according to the nature of the forces involved and to the size of the interaction relative to kT (small kT, large interactions; large kT, small interactions and free rotation). The most striking results are as follows:[5] Purely Coulombic dipole–dipole interactions fail to give any discrimination between $R \leftrightarrow R'$ and $R \leftrightarrow S'$ pairs,[3a] whether from electrostatic forces, induction (polarization) forces, or dispersion forces up to second order in the perturbation energy. More elaborate electrostatic forces, involving quadrupoles and octopoles, give a discriminatory force, on Boltzmann averaging, proportional to $(\mathrm{kT})^{-3}$ and varying as the inverse 17th power of the distance.[3b] Third-order dispersion forces give a temperature-independent discrimination term varying as the inverse ninth power of the distance.[4,3e] Mixed electric-magnetic forces give a similar term, proportional to the inverse sixth power of the distance, already to second order.[3a] We will return to third-order dispersion forces in section 10.

At shorter distances, ab initio calculations[3c,d] lead to large discriminations, of the order of the thermal energy. For instance calculations on *d*-, *l*-, and *meso*-2,3-dicyanobutane, where the discrimination is intramolecular, lead to a 3.1 KJ/mol stabilization of the meso form.

Here we use an atom–atom approach, particular suited for short intermolecular distances, to calculate the differential energy, averaged over all orientations, between two chiral tetrahedral molecules; this differential energy measures the degree of "chiral recognition" (Figure 1). The resulting discrimination is easily interpreted in terms of specific atom–atom interactions. In view of the previously quoted results, however, we insist on the outset that our approach does not provide an *exclusive* description of chiral discrimination between tetrahedral systems. The forces which we describe, even if important at short distances, are not the only ones to contribute to chiral discrimination. We do believe, however, that these forces are particularly meaningful in the overlap region and that they are particularly easy to visualize.

Our basic assumptions are as follows: The molecules are free to rotate relative to one another (interactions small relative to *kT*; the Boltzmann-weighted average energy reduces to a simple average over all orientations). The forces between the molecules are sums of the interactions between atomic centers at the substituents. The angles at the carbon centers are the regular tetrahedral angles; chirality is ensured by the different nature (charges, electronegativity, orbital exponents etc.) of the four substituents.

2. Coordinate Axes for the Interacting Tetrahedra

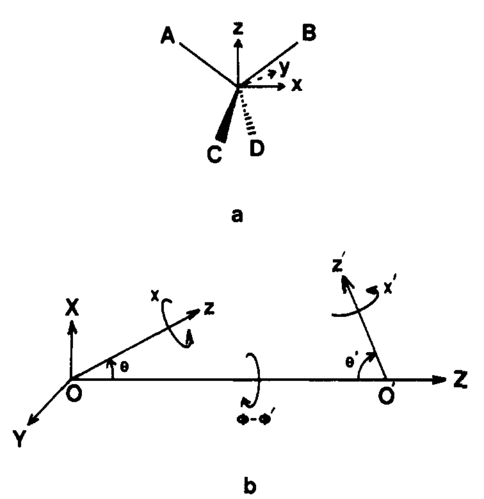

Figure 2. Representation of the two tetrahedra in (a) body-fixed and (b) external fixed axes systems. In part (b) we show only the *z* axis of each tetrahedron.

We first define the position of the four substituent atoms A, B, C, and D in a system of body-fixed axes *x*, *y*, *z* centered at the central atom O (the same thing is repeated for the second tetrahedron with primed coordinates). Figure 2a shows this axis system. The local coordinates of the four substituent atoms are given straightforwardly by

$$\begin{array}{lll} x_A = -\sqrt{2/3}r_A & y_A = 0 & z_A = \sqrt{1/3}r_A \\ x_B = \sqrt{2/3}r_B & y_B = 0 & z_B = \sqrt{1/3}r_B \\ x_C = 0 & y_C = -\sqrt{2/3}r_C & z_C = -\sqrt{1/3}r_C \\ x_D = 0 & y_D = \sqrt{2/3}r_D & z_D = -\sqrt{1/3}r_D \end{array} \tag{1}$$

We must now define the position of the two molecules in a fixed external axis system.[3a,6] This is illustrated in Figure 2b, where each tetrahedron is simply symbolized by its *z* axis. The external axes are *Z* (carried by the center–center line OO′*Z*), *X*, and *Y* for both molecules.

The three angles which define the position of a molecule in the external fixed axes *X*, *Y*, and *Z* are the Eulerian angles χ, θ, and φ.[7] The angle χ rotates OABCD around its own *z* axis, and for $\chi \rightarrow \chi + \pi$ bonds OA and OB exchange positions, as do OC and OD. The angles θ and φ are the familiar polar coordinates which define the position of the molecular *z* axis in the *XYZ* system (for the 2 molecules taken together, we need only consider the difference $\phi - \phi'$).

The external coordinates of A, B, C, and D are then given in terms of the local coordinates by the transformation

$$\begin{pmatrix} X_A \\ Y_A \\ Z_A \end{pmatrix} = (\mathrm{U}) \begin{pmatrix} x_A \\ y_A \\ z_A \end{pmatrix} \tag{2}$$

where (U) is the Eulerian matrix[7]

$$(\mathrm{U}) = \begin{pmatrix} \cos\theta\cos\varphi\cos\chi - \sin\varphi\sin\chi & -\cos\theta\cos\varphi\sin\chi - \sin\varphi\cos\chi & \sin\theta\cos\varphi \\ \cos\theta\sin\varphi\cos\chi + \cos\varphi\sin\chi & -\cos\theta\sin\varphi\sin\chi + \cos\varphi\cos\chi & \sin\theta\sin\varphi \\ -\sin\theta\cos\chi & \sin\theta\sin\chi & \cos\theta \end{pmatrix} \tag{3}$$

Apart from this transformation, the mathematics of the problem remains utterly simple.

3. Symmetry Properties of the Interacting System

It is essential to distinguish two processes: the "enantiomerization" in which we replace a chiral tetrahedron by its enantiomer, corresponding to a diastereoisomerization for the pair, and the overall rotation of a given tetrahedron.

For the first process, we assume *arbitrarily* that the enantiomers are mirror images in the OCD (or O′C′D′) plane, so that the enantiomer of OABCD is obtained by *exchanging* A and B.[8] This

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[4] (a) Schipper, P. E. *Chem. Phys.* **1977**, *26*, 29. (b) Schipper, P. E. *Chem. Phys.* **1979**, *44*, 261. (c) Schipper, P. E. *Aust. J. Chem.* **1982**, *35*, 1513.

[5] For the chiral selectivity between helical molecules, see: Kerdye, A.; Galatry, L. *Mol. Phys.* **1985**, *55*, 1383.

[6] Compare, for example, with Nauts, A.; Chapuisat, X. *Chem. Phys.* **1983**, *76*, 349, Figure 1.

[7] Wilson, E. B.; Decius, J. C.; Cross, P. C. *Molecular Vibrations*; McGraw Hill: New York, 1955; p 285.

assumption allows us to relate the positions of the four substituents in the two enantiomers R′ and S′ via the single variable χ'

$$\begin{array}{ll} R' \text{ enantiomer} & S' \text{ enantiomer} \\ \mathrm{A}' (\chi') & \mathrm{A}' (\chi' + \pi) \\ \mathrm{B}' (\chi') & \mathrm{B}' (\chi' + \pi) \\ \mathrm{C}' (\chi') & \mathrm{C}' (\chi') \\ \mathrm{D}' (\chi') & \mathrm{D}' (\chi') \end{array} \tag{4}$$

and simillary for the unprimed tetrahedon. Hence, in discriminating between $R \leftrightarrow R'$ and $R \leftrightarrow S'$ interactions, atoms A′ and B′, on the one hand, and C′ and D′, on the other, play a different role.

For the second process—the overall rotation—the coordinates of all four atoms change. For instance the changes $\chi' \rightarrow \chi' + \chi'_0$; $\varphi' \rightarrow \varphi' + \varphi'_0$; $\theta' \rightarrow \theta' + \theta'_0$ give

$$\begin{array}{ll} R' \text{ enantiomer} & R' \text{ rotamer} \\ \mathrm{A}' (\chi', \varphi', \theta') & \mathrm{A}' (\chi' + \chi'_0, \varphi' + \varphi'_0, \theta' + \theta'_0) \\ \mathrm{B}' (\chi', \varphi', \theta') & \mathrm{B}' (\chi' + \chi'_0, \varphi' + \varphi'_0, \theta' + \theta'_0) \\ \mathrm{C}' (\chi', \varphi', \theta') & \mathrm{C}' (\chi' + \chi'_0, \varphi' + \varphi'_0, \theta' + \theta'_0) \\ \mathrm{D}' (\chi', \varphi', \theta') & \mathrm{D}' (\chi' + \chi'_0, \varphi' + \varphi'_0, \theta' + \theta'_0) \end{array} \tag{5}$$

Of course, if $\chi'_0 = \pi$, $\varphi'_0 = 0$ and $\theta'_0 = 0$, the rotation is strictly equivalent for atoms A′ and B′ to an enantiomerization.

We note a final important property concerning the total energy difference $\overline{\Delta E}$, averaged over all orientations, between two interacting enantiomers and two interacting antipodes. By definition

$$\overline{\Delta E} = \bar{E}_{R \leftrightarrow R'} - \bar{E}_{R \leftrightarrow S'} \tag{6}$$

where the bar symbolizes an average over all orientations of the molecular pair. Since the left-hand molecule and right-hand molecule have identical substituents

$$\bar{E}_{R \leftrightarrow S'} = \bar{E}_{S \leftrightarrow R'} \tag{7}$$

and

$$\overline{\Delta E} = \bar{E}_{R \leftrightarrow R'} - \bar{E}_{S \leftrightarrow R'} \tag{8}$$

But intermolecular forces do not depend on the ordering of the centers involved, so

$$\overline{\Delta E} = \bar{E}_{R' \leftrightarrow R} - \bar{E}_{R' \leftrightarrow S} \tag{9}$$

Comparison of (6) and (9) shows that the required *energy difference is symmetrical with respect to the exchange of primed and unprimed indices.*

4. The Energy Difference Due to Chiral Recognition

We express the total interaction energy between the two tetrahedra as a sum of interactions between the substituent atomic centers on both molecules. We start with two-center interactions and include all terms up to simultaneous eight-center interactions

$$\begin{aligned} E = \sum_{\substack{\text{all centers,} \\ X,Y,Z,W}} \Bigl\{ & \sum_{\substack{\text{all single} \\ \text{centers } X'}} (E_{X,X'} + E_{XY,X'} + E_{XYZ,X'} + E_{XYZW,X'}) + \\ & \sum_{\substack{\text{all edges} \\ X'Y'}} (E_{X,X'Y'} + E_{XY,X'Y'} + E_{XYZ,X'Y'} + E_{XYZW,X'Y'}) + \\ & \sum_{\substack{\text{all faces} \\ X'Y'Z'}} (E_{X,X'Y'Z'} + E_{XY,X'Y'Z'} + E_{XYZ,X'Y'Z'} + E_{XYZW,X'Y'Z'}) + \\ & (E_{X,X'Y'Z'W'} + E_{XY,X'Y'Z'W'} + E_{XYZ,X'Y'Z'W'} + E_{XYZW,X'Y'Z'W'}) \Bigr\} \end{aligned} \tag{10}$$

(we justify later the exclusion of the tetrahedron centers).

We proceed to show that, in the averaged energy difference $\overline{\Delta E}$, all terms involving a single atom X' or a pair $X'Y'$ vanish.

Consider first the interaction between enantiomer R and single atoms on R' and S' (Figure 3). If the atom considered is C′ or D′ (atom inscribed in a square in the figure) its position is the *same* in R' and S' so the differential energy vanishes immediately. If the atom considered is A′ or B′ (atom in a circle in the figure) a rotation $\chi' \rightarrow \chi' + \pi$ of S' puts these atoms back in the original positions they had in R' (compare upper and lower figures on the right). This time the energy difference will vanish in the integration over angles: for each rotational configuration of R' there is a rotational configuration of S' which gives the same interaction term.

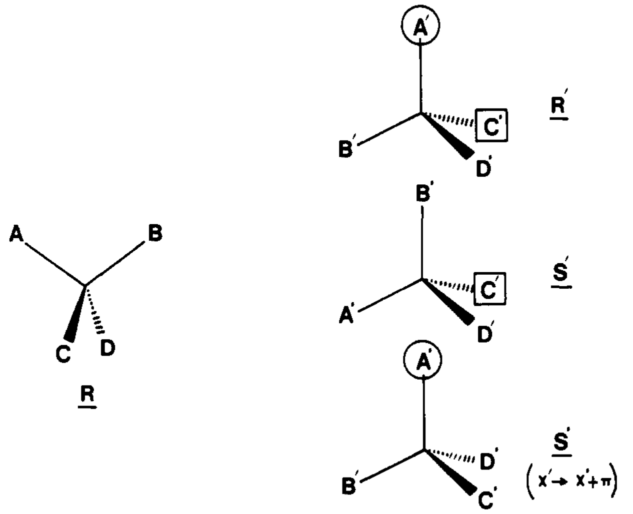

Figure 3. Differential interactions involving a single center on rh tetrahedron.

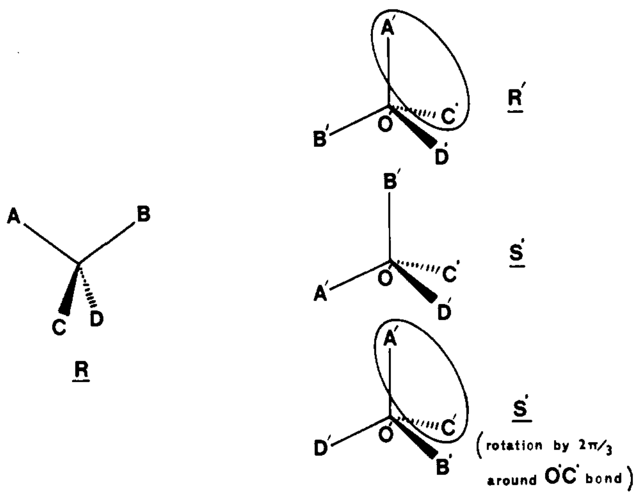

Figure 4. Differential interactions involving two atoms (on edge) on rh tetrahedron.

Consider next the interaction between enantiomer R and pairs of atoms (edges) on R' and S' (Figure 4). Three different types of edges may be considered: C′D′ involving the two atoms which are intact under enantiomerization, A′B′ involving the two atoms which are interchanged by enantiomerization, and A′C′ (or A′D′, B′C′, B′D′) involving one atom of each kind. For C′D′, as in the single atom case, the differential energy vanishes immediately since the position of C′D′ is the same in S' as in R'. For A′B′, a rotation $\chi' \rightarrow \chi' + \pi$ in S' places the edge A′B′ in the position it had originally in R'; hence $\overline{\Delta E}$ vanishes in the integration over angles. For A′C′ finally, a rotation by $2\pi/3$ around bond OC′ in S' brings the A′C′ edge in S' in concidence with the same edge in R', as shown by the two encapsuling ovals in the figure. Here again the differential energy vanishes when the integration over angles is performed.

Thus in $\overline{\Delta E}$ all the terms involving one center (X') or two centers ($X'Y'$) on the right-hand enantiomer vanish. Because of the symmetry demonstrated in the previous section this is also true of the terms involving X or XY on the l.h. molecule. The overall energy difference is simply

$$\Delta E = \sum_{\substack{XYZ \\ X'Y'Z'}} (E_{XYZ,X'Y'Z'} + E_{XYZ,X'Y'Z'W'} + E_{XYZW,X'Y'Z'} + E_{XYZW,X'Y'Z'W'}) \tag{11}$$

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(8) This is somewhat loose language since we have allowed for the possibility $r_A \neq r_B$. More precisely the axes OA and OB are exchanged.

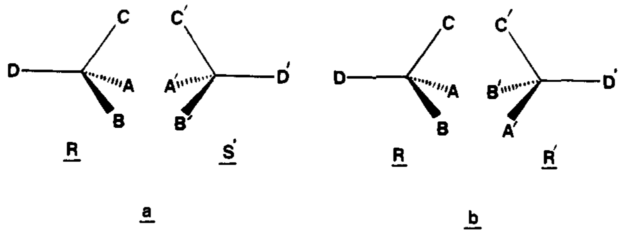

Figure 5. The six-center interaction on the left is unique and cannot be recovered on the right.

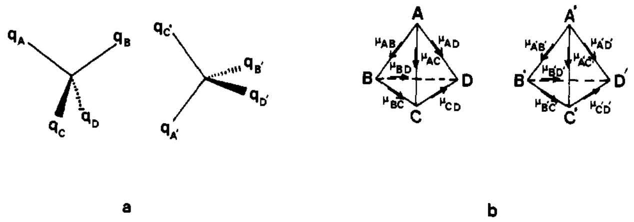

Figure 6. Erroneous models for chirality forces in the freely rotating limit (these models do, however, give discrimination in the Boltzmann-weighted limit: section 9).

The leading term is the six-center force term $E_{XYZ,X'Y'Z'}$ summed over all pairs of faces ($4 \times 4 = 16$) on each tetrahedron. The nonvanishing nature of this term becomes obvious when, by using models, one notices that it is not possible to put into coincidence a face of S' with that of R' by any rotation or combination of rotations. A typical unique situation in $R \leftrightarrow S'$ has interacting faces with three pairs of identical atoms opposite each other (Figure 5a); such a situation cannot be brought about in $R \leftrightarrow R'$ (Figure 5b). *The total interactions will be different* as long as the *simultaneous interactions between all three pairs are considered.*

Hence chiral discrimination depends on six-center forces alone and is purely a *"face-to-face"* phenomenon for the two tetrahedra. Although four-center forces are not new in chemistry,[9] this is, to the best of our knowledge, the first phenomenon where six-center forces play an important role. We call these forces *"chirality forces"*. We speak of chirality forces and not of "chiral" forces since these forces do not have any intrinsic sense of direction. Like all chemical forces, chirality forces find their origin in the electronic Hamiltonian. Their specificity is that they involve six-center atomic terms in the total energy.

As mentioned previously, we have left out all interactions involving the tetrahedron centers O and O′. Indeed, bonds such as OA, OB, etc. do not play any role in the overall interaction because the corresponding energy terms are always of the form $E_{X,X'}$ (for the interaction of two bonds OX and OX′) or $E_{X,X'Y'}$ (for the interaction of a bond OX with a nonbonded region $X'Y'$). As shown above, the contribution of such terms to $\overline{\Delta E}$ vanishes.

5. Two Fallacious Physical Models for Chiral Discrimination

Equation 11 for the differential energy due to chiral discrimination must be used with care. Certain simplifying assumptions lead to erroneous results. For instance expansion of the six-center energy in terms of two-center energies

$$E_{XYZ,X'Y'Z'} \approx E_{XX'} + E_{XY'} + \ldots + E_{ZZ'} \qquad (12)$$

would apparently allow the problem to be handled by a simple model with a net charge on each substituent (Figure 6a). Equation 12 would then be simply evaluated from the charge-charge interactions between the two molecules. But the end result is zero! Indeed Coulomb interactions between point charges are two-center forces, and we know that, in the free rotation limit, the contribution of two-center forces to chiral discrimination must vanish.

A similar catastrophy awaits an expansion in terms of four-center energies

$$E_{XYZ,X'Y'Z'} \approx E_{XY,X'Y'} + \ldots + E_{YZ,Y'Z'} \qquad (13)$$

corresponding to a model with interacting edges. Each edge, for instance, could contain a dipole moment (Figure 6b). Again, since four-center forces give no chiral discrimination, the differential energy will vanish. We have numerically verified the failure of the models of Figure 6a and b by the integration process of section 6.

The appropriate model must therefore include forces which are truly six-center, i.e., in which three pairs of atoms interact *simultaneously*. The difficulty is to find a mathematical translation for the word "simultaneous". Clearly, when two faces interact, they must do so in their *entirety*.

At the outset we can rule out certain types of forces. First of all any model built on simultaneously interacting permanent multipoles on six atoms, three on each tetrahedron, will fail. Indeed these multipoles can all be expanded in terms of a multipolar series at the *center* of each tetrahedron. But Craig and Schipper have shown[3b] that the average, over all configurations, of the interaction $R \leftrightarrow R'$ *or* $R \leftrightarrow S'$ for such centered multipoles is zero. Not only does the discrimination vanish, but the $R \leftrightarrow R'$ and $R \leftrightarrow S'$ interaction energies vanish separately! Craig explains[10a] the absence of discrimination by pointing out that each molecule feels only the *average* field of the other molecule and that the average fields of enantiomers R' and S' are identical.

What is true for purely electrostatic forces also holds for purely electric induction (polarization) forces[4,10b] to all orders of perturbation (this is no longer true for magnetic induction forces, which are extremely small). Although here the separate energies for $R \leftrightarrow R'$ and $R \leftrightarrow S'$ do not vanish, their difference is still zero. We have numerically verified (see next section for the procedure) that this is indeed the case for second-order induction forces in the free rotation limit, by using a model with local dipoles and local polarizabilities on the tetrahedron edges.

The case of dispersion forces deserves special attention and is considered in section 10.

We turn then to overlap and exchange forces for which, in the words of Craig,[10a] each face tends to "sense the detailed shape of the opposite interacting face".

6. A Crude Physical Model Based on Six-Center Forces

We now return to our interacting chiral tetrahedra. A very crude model force which would discriminate between the homochiral ($R \leftrightarrow R'$) and heterochiral ($R \leftrightarrow S'$) situations of Figure 5 is one in which, arbitrarily, all forces between *different* atoms would be set equal to zero. Then the situation of Figure 5a, in which there are three nonvanishing atom-atom interactions at short distances (directly opposed atoms) should be highly favored over that of Figure 5b, in which two of the interactions (AA′ and BB′) involve a longer distance. Mathematically we write the total energy as the *six-center* expression

$$E = -\sum_{\substack{\text{all faces}\\ I<J<K}} \sum_{\substack{\text{all faces}\\ I'=I,J'=J,K'=K}} S_{II'}S_{JJ'}S_{KK'} \qquad (14)$$

where the "overlap exchange" function S is assumed to have the simple empirical form

$$S_{IJ'} = \exp(-(\zeta_I + \zeta_{J'})R_{IJ'}/n) \qquad (15)$$

In (15) ζ_I is an exponent ascribed to atom I, $R_{IJ'}$ is the interatomic distance between atoms I and J′, and n is an arbitrary scale factor. The negative sign in eq 14 assumes that the simultaneous six-center force between pairs of like atoms is attractive.

Equation 14 was evaluated, by using double-precision mathematics, over the volume element $d\chi d\chi' d\varphi \sin\theta d\theta \sin\theta' d\theta'$. The overall integration over space (rotational averaging) is performed

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[9] For an excellent review, see: Margenau, H.; Kestner, N. R. *Theory of Intermolecular Forces*; Pergamon: Oxford, 1969; sections 5.3. and 7.2.

[10] (a) Craig, D. P., private communication to the authors, 1986. (b) Thirunamachandran, T., private communication to the authors, 1986. (c) Craig, D. P.; Thirunamachandran, T., unpublished results, 1986.

Table I. Energies Given by Eq 14[a]

	$N = 10$			$N = 20$		
R (Å)	$\bar{E}_{R\leftrightarrow R'}$	$\bar{E}_{R\leftrightarrow S'}$	$\overline{\Delta E}$	$\bar{E}_{R\leftrightarrow R'}$	$\bar{E}_{R\leftrightarrow S'}$	$\overline{\Delta E}$
5	−2.859 569 2	−2.873 240 7	+0.013 671	−2.791 364 3	−2.804 752 3	+0.013 388
6	−0.647 542 2	−0.649 790 3	+0.002 248	−0.632 178 8	−0.634 381 7	+0.002 203
7	−0.144 960 6	−0.145 336 3	+0.003 376	−0.141 538 3	−0.141 906 8	+0.000 368

[a] Energies are in KJ/mol.

Table II. Chiral Discrimination for the General Six-Center Expression (20) and the Parameters of Eq 21[a]

	$N = 10$			$N = 20$		
R (Å)	$\bar{E}_{R\leftrightarrow R'}$	$\bar{E}_{R\leftrightarrow S'}$	$\overline{\Delta E}$	$\bar{E}_{R\leftrightarrow R'}$	$\bar{E}_{R\leftrightarrow S'}$	$\overline{\Delta E}$
5	−36.785 402 9	−36.788 137 1	+0.002 734	−35.894 684 9	−35.897 362 4	+0.002 677
6	−8.073 424 2	−8.073 873 8	+0.000 450	−7.878 135 2	−7.878 575 8	+0.000 441
7	−1.743 427 3	−1.742 502 4	+0.000 075	−1.701 311 1	−1.701 384 8	+0.000 074

[a] Energies are in KJ/mol.

by dividing the angle 2π spanned by χ, χ', and φ into N equal intervals, and the angle π spanned by θ and θ' into $N/2$ equal intervals of same size. Grid points are chosen in the middle of the intervals, according to the usual method of rectangles.[11] The integral is then replaced by a simple summation over $N^5/4$ grid points. Convergence generally requires at least $N = 10$, but sometimes values as high as $N = 22$ (1.3 million points!) fail to converge (section 9). For the energy expression (14) convergence on the discrimination energy is obtained already for $N = 10$ (Table I).

It should be noted that, in making our rotational averages, we use as the origin in each molecule the position of the central atom. Furthermore we have assumed implicitly that the substituents have equal masses throughout, and we will even use equal bonds lengths to the substituents—see below. A more elaborate model would include different substituent masses and perform the overall rotation about the center of mass, which will not in general coincide with the position of the central atom.

Throughout this and the following three sections we chose all bond lengths equal to 1.5 Å. Asymmetry is introduced into each tetrahedron solely via different orbital exponents (sections 6, 7, and 8) or different charges (section 9).

In the present calculation we chose $\zeta(\mathrm{A}) = 1.5$, $\zeta(\mathrm{B}) = 1.2$, $\zeta(\mathrm{C}) = 1.0$, and $\zeta(\mathrm{D}) = 0.9$. The scale factor n was put arbitrarily equal to 8. Table I then shows the results for the homochiral ($R \leftrightarrow R'$), heterochiral ($R \leftrightarrow S'$), and differential energy of chiral recognition as a function of intermolecular distance R ($R = \mathrm{OO}'$).

The individual interaction energies are of the order of 2.8 KJ/mol at $R = 5$ Å, 0.65 KJ/mol at $R = 6$ Å, and 0.14 KJ/mol at $R = 7$ Å. These are all small relative to kT for a temperature of the order of 800 K. Furthermore these energies could all be reduced by a uniform factor (and the $\overline{\Delta E}$'s accordingly) by putting a small proportionality constant in front of the energy expression (or by decreasing the value of n) without any bearing on the qualitative results. For $R = 5$ Å, the total interaction energy for one separate pair is 2.8 KJ/mol, while a chiral discrimination of 13 small J/mol is obtained. The $R \leftrightarrow S'$ interaction is favored, as expected from the assumed attractive form of the simultaneous interaction energy between like atoms (Figure 5a). The chiral discrimination calculated from (14) varies roughly in an exponential manner ($\overline{\Delta E} \approx \exp(-0.98R_{\text{Å}})$). More importantly its size is roughly *one-half of 1%* of the total (homochiral or heterochiral) interaction energies.

Finally we have verified that a function similar to (14) but involving only four centers simultaneously

$$E = -\sum_{\substack{\text{all edges}\\ \mathrm{I<J}}}\ \sum_{\substack{\text{all edges}\\ \mathrm{I'=I,J'=J}}} S_{\mathrm{II'}}S_{\mathrm{JJ'}} \qquad (16)$$

fails to give any discrimination, in agreement with the theory of section 4.

7. A More Refined Physical Model

An obvious generalization of (14) includes all possible triple products of overlap integrals, involving both like *and* unlike atoms in a fully symmetrized manner

$$E = -\sum_{\substack{\text{all faces}\\ \mathrm{I<J<K}}}\ \sum_{\substack{\text{all faces}\\ \mathrm{I'J'K'}}} S_{\mathrm{II'}}S_{\mathrm{JJ'}}S_{\mathrm{KK'}} \qquad (17)$$

A six-center expression resembling (17) would be expected to appear as a minute *nonadditive* correction in the total energy; similar four-center nonadditive terms were found in the theory of repulsive forces many years ago.[12] More generally, eq 17 can be seen to arise from third-order perturbation interaction terms such as

$$W_3 = -{\sum_{\mathrm{p}}}'{\sum_{\mathrm{q}}}'\frac{\langle 0|H'|\mathrm{p}\rangle\langle \mathrm{p}|\mathrm{H}'|\mathrm{q}\rangle\langle \mathrm{q}|\mathrm{H}'|0\rangle}{(E_{\mathrm{p}} - E_{\mathrm{o}})(E_{\mathrm{q}} - E_{\mathrm{o}})} \qquad (18)$$

where $|0\rangle$ is the ground state of the supersystem for the noninteracting molecules, $|\mathrm{p}\rangle$ and $|\mathrm{q}\rangle$ are the excited states, and H′ is the intermolecular interaction between the two chiral tetrahedra. (See also, further, the application of (18) to eq 30).

However, given the general "symmetrized" energy (17) *no* discrimination is found, either for the overlap function (15) or for similar functions

$$S_{\mathrm{IJ'}} = \exp\left(-(\zeta_{\mathrm{I}}\zeta_{\mathrm{J'}})^{1/2}R_{\mathrm{IJ'}}/n\right)$$

$$S_{\mathrm{IJ'}} = (\zeta_{\mathrm{I}} + \zeta_{\mathrm{J'}})/R_{\mathrm{IJ'}}$$

$$S_{\mathrm{IJ'}} = (\zeta_{\mathrm{I}} + \zeta_{\mathrm{J'}})\mathrm{R}_{\mathrm{IJ'}},\ \text{etc.} \qquad (19)$$

The reason can probably be found in the permutation properties of (17). More precisely we suspect that (17) is some complicated invariant of the permutation–rotation group of two tetrahedra. Yet we have not been able to find a water-tight proof that (17) cannot discriminate. Suffice it to say that the absence of discrimination has been checked by innumerable numerical calculations by using functions such as (19), *including* the exact overlap expression between a $1s(\zeta_{\mathrm{I}})$ and a $1s(\zeta_{\mathrm{J'}})$ orbitals.

In practice, however, the total energy must weight *differently* the overlaps between like atoms and those between unlike atoms

$$\begin{aligned} E = &-\alpha_1 \sum_{\mathrm{I<J<K}}\ \sum_{\mathrm{I'=I,J'=J,K'=K}} S_{\mathrm{II'}}S_{\mathrm{JJ'}}S_{\mathrm{KK'}} \\ &-\alpha_2 \sum_{\mathrm{I<J<K}}\Big(\sum_{\mathrm{I'=I,J'=J,K'\neq K}} S_{\mathrm{II'}}S_{\mathrm{JJ'}}S_{\mathrm{KK'}} + \text{two permutations thereof}\Big) \\ &-\alpha_3 \sum_{\mathrm{I<J<K}}\Big(\sum_{\mathrm{I'=I,J'\neq J,K'\neq K}} S_{\mathrm{II'}}S_{\mathrm{JJ'}}S_{\mathrm{KK'}} + \text{two permutations thereof}\Big) \\ &-\alpha_4 \sum_{\mathrm{I<J<K}}\ \sum_{\mathrm{I'\neq I,J'\neq J,K'\neq K}} S_{\mathrm{II'}}S_{\mathrm{JJ'}}S_{\mathrm{KK'}} \end{aligned} \qquad (20)$$

where $\alpha_1 \neq \alpha_2 \neq \alpha_3 \neq \alpha_4$.

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(11) An attempt at integration by Monte-Carlo sampling gave much poorer convergence for comparable cpu times.

(12) Salem, L. *Proc. Roy. Soc. London, A* **1961**, *264*, 379 (sections 4 and 5).

Table II then shows the discrimination due to chiral recognition, by using

$$\begin{aligned} \alpha_1 &= 1.0 & \zeta(\mathrm{A}) &= 1.5 \\ \alpha_2 &= 0.7 & \zeta(\mathrm{B}) &= 1.2 \\ \alpha_3 &= 0.6 & \zeta(\mathrm{C}) &= 1.0 \\ \alpha_4 &= 0.5 & \zeta(\mathrm{D}) &= 0.9 \end{aligned} \tag{21}$$

and the empirical form (15) for the "overlap-exchange" function S (a more elaborate form of S is not justified since we do not know the exact form of (20)). The discrimination at 5 Å is of the order of 10^{-4} times (energies in KJ/mol) the total rotationally averaged interaction energy. The variation of $\overline{\Delta E}$ is, again, not surprisingly exponential with R.

The extent of chiral discrimination is extremely sensitive to the choice of α's. For instance, for

$$\alpha_1 = 1.0 \quad \alpha_2 = 0.8 \quad \alpha_3 = 0.6 \quad \alpha_4 = 0.4 \tag{22}$$

the chiral discrimination is less than 3.10^{-7} KJ/mol at 5 Å, while for

$$\alpha_1 = 1.0 \quad \alpha_2 = 0.8 \quad \alpha_3 = 0.64 \quad \alpha_4 = 0.512 \tag{23}$$

the chiral discrimination in nonzero but still 20 times smaller than for set (21); in KJ/mol 0.0001294 at 5 Å, 0.0000265 at 6 Å and 0.0000056 at 7 Å (for total energies of the same order of magnitude as Table II).

The reason is as follows. We can evaluate the energy differences $\overline{\Delta E}$ for each of the four sums of (20) taken separately. For the ζ values of (21), at $R = 5$ Å

$$\begin{aligned} &\sum_{1<J<K} \sum_{1'=1,J'=J,K'=K} S_{11'}S_{JJ'}S_{KK'} \rightarrow \Delta E_1 = 0.0136715 \\ &\sum_{1<J<K} \Big(\sum_{1'=1,J'=J,K'\neq K} S_{11'}S_{JJ'}S_{KK'} \text{etc.}\Big) \rightarrow \Delta E_2 = -0.0403818 \\ &\sum_{1<J<K} \Big(\sum_{1'=1,J'\neq J,K'\neq K} S_{11'}S_{JJ'}S_{KK'} \text{etc.}\Big) \rightarrow \Delta E_3 = 0.0397478 \\ &\sum_{1<J<K} \sum_{J'\neq 1,J'\neq J,K'\neq K} S_{11'}S_{11'}S_{KK'} \rightarrow \Delta E_4 = -0.0130375 \end{aligned} \tag{24}$$

(for $N = 20$ the converged values are respectively 0.013388, 0.039500, 0.038775, and 0.012693). Note that by "zero discrimination" we mean that $\overline{\Delta E}$ vanishes with 10^{-7} precision (i.e., 10^{-9} times the total energies).

There are an infinite set of α's (including $\alpha_1 = \alpha_2 = \alpha_3 = \alpha_4 = 1$) for which

$$\alpha_1 \Delta E_1 + \alpha_2 \Delta E_2 + \alpha_3 \Delta E_3 + \alpha_4 \Delta E_4 = 0 \tag{25}$$

This happens, *per chance*, to be also the case for the set (22). However these zeros are very sharp, and it is easy, by looking at the numbers in (24), to find a set, such as (21), for which the chiral discrimination

$$\alpha_1 \Delta E_1 + \alpha_2 \Delta E_2 + \alpha_3 \Delta \mathrm{E}_3 + \alpha_4 \Delta E_4$$

is insignificant.

Note that the α's have a very simple physical interpretation. Let us expand the energy as a Taylor series in powers of the interatomic overlap

$$E = E_0 + \sum_{1}\sum_{J'} \left(\frac{\partial E}{\partial S_{1J'}} \right)_0 + \frac{1}{2!} \sum_{11'JJ'} \left(\frac{\partial^2 E}{\partial S_{11'} \partial S_{JJ'}} \right)_0 S_{11'}S_{JJ'} + \frac{1}{3!} \sum_{11'JJ'KK'} \left(\frac{\partial^3 \mathrm{E}}{\partial S_{11'} \partial S_{JJ'} \partial S_{KK'}} \right)_0 S_{11'}S_{JJ'}S_{KK'} + \ldots \tag{26}$$

We define the "super-polarizability" $\alpha_{11'JJ'KK'}$ as

$$\alpha_{11'JJ'KK'} = -\frac{1}{3!} \left(\frac{\partial^3 E}{S_{11'}S_{JJ'}S_{KK'}} \right)_0 \tag{27}$$

There are *96 such terms* so that, as written, eq 20 for the energy is already an approximation in which each of the coefficients α_1, α_2, α_3, and α_4 is an *average* of respectively 4, 12, 36, and 44 third differentials. An attempt to evaluate the α's by a simple model is given in the Appendix.

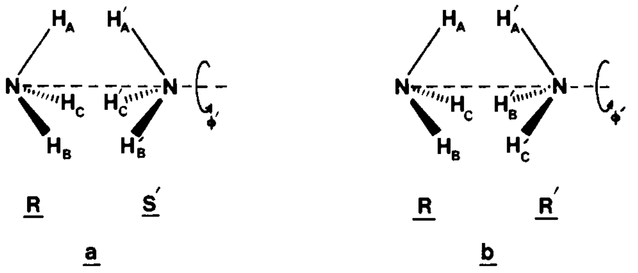

Figure 7. Geometry of the $(NH'H''H''')_2$ singlet state in the (a) heterochiral and (b) homochiral situations.

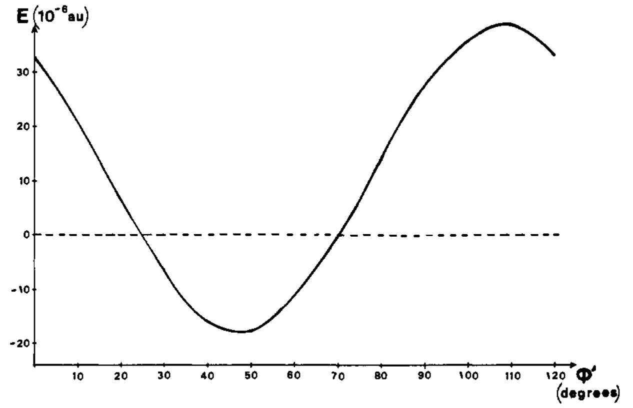

Figure 8. Energy difference $\sum(E_{R\leftrightarrow R'} - E_{R\leftrightarrow S'})$ for $(NH'H''H''')_2$ summed over the three points (ϕ', $\phi' + 120°$, $\phi' + 240°$).

Table III. Total Energy of the $(NH'H''H''')_2$ Singlet State[a]

ϕ' (deg)	$E_{R\leftrightarrow R'}$	$E_{R\leftrightarrow S'}$	$\overline{\Delta E}$
0	−110.335 623	−110.335 805	+0.000 182
120	−110.331 878	−110.332 185	+0.000 307
240	−110.332 641	−110.332 185	−0.000 456
av	−110.333 381	−110.333 392	+0.000 011

[a] The NN distance is 4 Å. Energies in au (integral precision: 10^{-7} au).

8. A Simple SCF Calculation

In the two previous sections we dealt with *models*, in the sense that we do not know whether the real six-center forces are represented by an equation such as 20 or have vastly different forms. In order to obtain further confirmation that our calculated discrimination is real, we decided to perform a simple SCF calculation on a six-center system. We then evaluated the total SCF energy of interaction between two NH'H''H''' molecules, face-to-face and eclipsed, in which each hydrogen is described by a 1s orbital. The three exponents $\zeta(\mathrm{A})$, $\zeta(\mathrm{B})$, and $\zeta(\mathrm{C})$ of H_A, H_B, and H_C are different with values 0.4, 0.8, and 1 (Figure 7).

We used the ab-initio MONSTERGAUSS program[13] and a minimal STO-3G orbital basis set. The results are given in Table III for $\phi' = 0°$ (H'_A opposite to H_A), $\phi' = 120°$, and $\phi' = 240°$. For the three configurations we obtain an average discrimination[14] of 1.1×10^{-5} au, i.e., 0.029 KJ/mol in favor of the heterochiral situation. (The total energies are enormous relative to any reasonable value of kT, but the actual *variations* in energy do not exceed 0.0038 au, i.e., 10 KJ/mol or 2.5 Kcal/mol. The average discrimination is 0.3×10^{-2} times this maximum variation.) We next extended the calculation to 10-deg intervals for ϕ'. The discrimination keeps the same sign but becomes on average 0.0092

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[13] Peterson, M.; Poirier, R. MONSTERGAUSS, Department of Chemistry, University of Toronto, Canada, 1981.

[14] The extent of discrimination depends in a very sensitive manner on the choice of ζ's: large for the set 0.4, 2.5, 6.0 but very small for the set 1, 1.2, 1.5.

Table IV. Boltzmann-Weighted Chiral Discrimination at Room Temperature (kT = 0.6 Kcal/mol) for Net Charge Model of Figure 6a[b]

	$N = 20$			$N = 22$		
R (Å)	$E_{R\leftrightarrow R'}$	$E_{R\leftrightarrow S'}$	$\overline{\Delta E}$	$E_{R\leftrightarrow R'}$	$E_{R\leftrightarrow S'}$	$\overline{\Delta E}$
4	−34.058 583[a]	−34.074 259[a]	0.016 666[a]	−34.581 735[a]	−34.626 995[a]	0.045 260[a]
5	−5.241 468	−5.241 930	0.000 462	−5.242 717	−5.243 179	0.000 463
6	−1.530 319 78	−1.530 328 25	0.000 008 47	−1.529 886 85	−1.529 895 27	0.000 008 42

[a] Not converged. [b] Energies in KJ/mol.

KJ/mol. Figure 8, however, shows that the discrimination will persist even for smaller angular intervals (compare the surfaces above and below 0 energy).

The SCF calculation shows only an extremely slight charge transfer of 4×10^{-4} electrons from one ammonia molecule to the other, so that the discrimination does not arise from extraneous charge–charge interactions (order of 10^{-7} au). However, this calculation is not immune to the criticism that, by choosing a *single* family of relative geometries (only face-to-face configurations), we may have *unwillingly favored*, per chance, a particularly strong discriminatory relative geometry.

9. Comparison with Boltzmann-Weighted Discrimination

It is instructive to compare the chiral discrimination for free relative rotation with that which occurs when certain interactions are larger and become weighted by kT. The appropriate Boltzmann-weighted average interaction energy is then given by

$$\bar{E} = \frac{\int\int E e^{-E/kT}\, d\omega\, d\omega'}{\int\int e^{-E/kT}\, d\omega\, d\omega'} \tag{28}$$

where $d\omega = d\chi\, d\phi\, d\theta \sin\theta$.

We have evaluated the thermally weighted rotationally averaged energy $\bar{E}$ for the net charge model of Figure 6a ($q_A = 0.2$, $q_B = 0.1$, $q_C = -0.05$, $q_D = -0.25$). The convergence was found to be very slow and to require large values of N: apparently, for small R, the energy oscillates fast relatively to the interval size between grid points. The results are given in Table IV. The total chiral discrimination varies roughly as the inverse 22nd power of the distance (compared with the R^{-17} leading term found by Craig[3b]).[15] At 5 Å, its size is roughly one-half of a small J/mol. The heterochiral $R \leftrightarrow S'$ interaction is favored over the homochiral $R \leftrightarrow R'$ interaction, as in all previous calculations.

10. Third-order Dispersion Forces: Another Discriminating Term[4,3e]

The Boltzmann-averaged dispersion forces are given to second order by the familiar London formula[4a]

$$E^{(2)}_{R\leftrightarrow R'} = -\frac{2}{3R^6}\sum_{s>0}\sum_{t>0}\frac{\mu_R^{0s}\mu_R^{s0}\mu_{R'}^{0u}\mu_{R'}^{u0}}{\epsilon_s^R + \epsilon_u^{R'}} \tag{29}$$

where $\epsilon_s^R + \epsilon_u^{R'}$ is the transition energy of the state $|\Psi_s^R\Psi_u^{R'}\rangle$ relative to the unperturbed ground state and μ_R is the transition moment from ground state $|\Psi_0^R\rangle$ to excited $|\Psi_s^R\rangle$.

Schipper was first to give the expression[4a] for the Boltzmann-weighted *third*-order dispersion energy

$$E^{(3)}_{R\leftrightarrow R'} = -\frac{2}{3R^9} \sum_{s>0}\sum_{u>0}\sum_{t>s}\sum_{v>u}\frac{(\epsilon_t^R - \epsilon_s^R)(\epsilon_v^{R'} - \epsilon_u^{R'})}{(\epsilon_s^R + \epsilon_u^{R'})(\epsilon_s^R + \epsilon_v^{R'})(\epsilon_t^R + \epsilon_u^{R'})(\epsilon_t^R + \epsilon_v^{R'})} \times (\mu_R^{0s} \times \mu_R^{st}\cdot\mu_R^{t0})(\mu_{R'}^{0u} \times \mu_{R'}^{uv}\cdot\mu_{R'}^{v0}) \tag{30}$$

Equations 29 and 30 are obtained by a triple expansion:[4b] (1) a multipolar expansion of the intermolecular potential between R and R', (2) a perturbation expansion to evaluate the quantum mechanical energy observable to be calculated, and (3) an expansion in inverse powers of kT. For the latter expansion, expressions (29) and (30) correspond to the leading, zeroth-order term, i.e., to free rotation.

To see whether $E^{(2)}$ or $E^{(3)}$ are discriminating terms, it suffices to change all the dipoles μ_R on one molecule into $-\mu_R$, thus creating the enantiomer S. A change in sign in the energy expression implies discrimination. Since $E^{(2)}$ does not change sign, it does not discriminate. In fact this is true for *all* multipolar contributions to the dispersion energy within the framework of second-order perturbation theory. The proof goes essentially as follows.[10c] In the leading term of the perturbation expansion and in a multipole expansion of the two-center electrostatic interaction between the coupled molecules, chiral properties appear only in combinations of multipoles at each center of which the sum of the multipole orders is odd. The rotational averages of such combinations all vanish.

The third-order energy $E^{(3)}$, however, changes sign for $\mu_R \rightarrow -\mu_R$. *Hence third-order dispersion forces yield chiral discrimination in the free rotation limit.* Although eq 30, with its two triple products, is difficult to visualize, it bears a certain resemblance to our own six-center term. Indeed (30) involves three ordered vectors on one molecule; six-center forces, on the other hand, involve two planes with three centers on each molecule. A further analogy is that both types of forces originate from the third-order perturbation energy (18) and would both be included in a full expansion of the latter.

We can finally give a very crude numerical estimate of the third-order dispersion contribution (30). We replace the quadruple sum by a single term and we evaluate the transition dipoles in this term by assuming that they have the *same* average value $\bar{\mu}$ as that required so that a single term in (29) would yield the correct second-order dispersion energy. For two methane molecules, the coefficient of R^{-6} is

$$\frac{2}{3}\frac{\bar{\mu}^4}{2\bar{\epsilon}} \tag{31}$$

and has an experimental value of roughly 265 atomic units.[17] For an average molecular transition energy $\bar{\epsilon} \approx 0.5$ au (the molecule is a saturated hydrocarbon) this gives $\bar{\mu}^4 = 400$ and $\bar{\mu} = 4.47$ au. The third-order chiral discrimination then becomes

$$\Delta E^{(3)} = -\frac{4}{3R^9}\frac{(\overline{\Delta E})^2}{16\bar{E}}\bar{\mu}^6 \tag{32}$$

For a *differential* transition energy $\overline{\Delta E}$ estimated as 0.2 au, we get, at $R = 5$ Å

$$\Delta E^{(3)} = -0.22 \text{ J/mol} \tag{33}$$

This is perhaps 10 times smaller than the corresponding numbers of Table II but, in view of the uncertainties in all the numbers, we can consider these forces to have the same order of magnitude as the six-center overlap–exchange forces (in any case, they should decay more slowly than the latter). A full numerical comparison would have to include the electric-magnetic R^{-6} second-order discrimination energy.[3a]

11. Conclusion

We have demonstrated that six-center forces are responsible for chiral discrimination between two freely rotating chiral tetrahedral molecules. These six-center forces imply *simultaneous* interaction between three pairs of atoms or two interacting faces.

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(15) Craig and Schipper's leading term[2b] corresponds to a squared quadrupole–quadrupole interaction ($\Theta^2\Theta'^2/R^{10}$) multiplied by an octopole–octopole interaction ($\Omega\Omega'/R^7$). In our model, with the coordinate system defined in (1), the octopole moment (see ref 16 for its definition) vanishes.

(16) Buckingham, A. D. *Quart. Revs. London* **1959**, *13*, 189 (eq 9). Buckingham, A. D. *Adv. Chem. Phys.* **1967**, *12*, 107 (section VB).

(17) Salem, L. *Mol. Phys.* **1960**, *3*, 441 (Table 2).

(Other forces, involving two centers, come into play only if the two molecules are partially locked into a preferred relative configuration). Unfortunately we are not able to give absolute magnitudes for the discrimination since we have had to assume model six-center forces involving empirical "overlap–exchange" functions. However, the chiral discrimination due to overlap–exchange is found to range between 0.5×10^{-2} and 10^{-4} times the total rotationally averaged interaction energy of the same kind between tetrahedra.

Our qualitative conclusion, which singles out the role of six-center forces, would appear in a different physical form in other models *not* based on atom–atom interactions but for instance on single-center expansions, provided that either (1) the expansion is not prematurely truncated or (2) the perturbation expansion is not prematurely truncated if one is working in the perturbative limit.

The six-center model bears some analogy with the three-center attachment theory of Ogston[18] who pointed out that a chiral substrate needs three points to fix in a unique fashion to a chiral support. Whether our model also has implications for chiral selectivity[19,20] or for homochiral preferences in natural selection[21] remains open to question.

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Appendix

Evaluation of the α Coefficients in the General Force Expansion (20). The simplest model for such an evaluation is a Hückel model in which each $CH_AH_BH_CH_D$ tetrahedron is represented by an eight-orbital, five-atom system. There are four atomic orbitals on carbon (one 2s, three 2p), whose hybrids are linked to four hydrogen atoms with different energies by a common resonance integral β. The nonbonded atoms between tetrahedra are linked by 16 different $\beta_{II'}$'s, and we also introduce $\beta_{II'}$'s for the interaction between nonbonded atoms within each tetrahedron. Discrimination occurs *without* these internal β's, but its numerical value increases when they are introduced.

We choose

$$\zeta(\mathrm{A}) = 0.2 \qquad \zeta(\mathrm{B}) = 0.4 \qquad \zeta(\mathrm{C}) = 0.8 \qquad \zeta(\mathrm{D}) = 1.0 \tag{A-1}$$

The corresponding hydrogen Coulomb energies are given by

$$H_{II} = -13.6\zeta^2{}_I\ (\mathrm{eV}) \tag{A-2}$$

while H_{2s2s} (carbon) = −21.4 eV and H_{2p2p} (carbon) = −11.4 eV. The off-diagonal matrix element

$$\beta_{IJ} = H_{IJ} = (\mathrm{CON}/2)(H_{II} + H_{JJ})S_{IJ} \tag{A-3}$$

where "CON" is a weighted expression[22] depending on $(H^2{}_{II}-H^2{}_{JJ})/(H^2{}_{II} + H^2{}_{JJ})$, and where the overlap integral is exactly the same expression used previously in (15). The carbon exponent is chosen equal to 1.625.

For the calculation of each $\alpha_{II'JJ'KK'}$ the appropriate geometry of Figure 5a is chosen, with the three pairs of atoms involved in the cubic differential eclipsing each other: I opposite to I′, J to J′, K to K′. So the actual overall geometry varies from one α to the next, but the atoms involved in each α are always in the *same* geometric relationship. Thus any difference in the α's will come exclusively from the overlaps and not from different geometrical relationships.

For a carbon–carbon distance of 4.73 Å, the results are (in units of 6.10^{-6}) (here α is the triple differential with respect to variations of the resonance integrals, not the overlap integrals):

$$\begin{gathered}\alpha_{AA'BB'CC'} = 2.44;\ \alpha_{AA'BB'DD'} = 0.44;\ \alpha_{AA'CC'DD'} = 0.82;\ \alpha_{BB'CC'DD'} = 1.70 \\ \alpha_{AA'BB'CD'} = 1.60;\ \text{etc. (12 parameters)} \\ \alpha_{AA'BC'CD'} = 0.82;\ \text{etc. (36 parameters)} \\ \alpha_{AB'BC'CD'} = 1.06;\ \text{etc (44 parameters)}\end{gathered} \tag{A-4}$$

Overall the highest is 2.75 ($\alpha_{AC'BB'CA'}$) and the lowest is 0.44 ($\alpha_{AA'BB'DD'}$). As surmized earlier they do indeed vary significantly.

The *average* values, corresponding to eq 20 are

$$\bar{\alpha}_1 = 1.35; \qquad \bar{\alpha}_2 = 1.07; \qquad \bar{\alpha}_3 = 1.32; \qquad \bar{\alpha}_4 = 1.55 \tag{A-5}$$

To calculate the chiral discrimination, we diagonalized directly the Hückel determinant, restricting ourselves to all 96 *eclipsed* configurations of the tetrahedra (48 of which are $R \leftrightarrow R'$ and 48 are $R \leftrightarrow S'$). We find

$$\Delta E = 0.000373\ \mathrm{eV} = 0.0360\ \mathrm{KJ/mol} \tag{A-6}$$

The order of magnitude is very similar to those (0.029 and 0.0092 KJ/mol) obtained in the SCF calculation on the chiral ammonia molecules. Without the internal $\beta_{II'}$s between nonbonded atoms, the discrimination falls to 0.0044 KJ/mol.

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[18] Ogston, A. G. *Nature*, **1948**, *162*, 963.

[19] For an elegant discussion of chirality, see: Kagan H. *C. R. Acad. Sci.* Série Générale (La Vie des Sciences), **1985**, *2*, 141 and references therein.

[20] For the "rule of reversal" in which a chiral solute is poisoned by a homochiral solvent, see: Addadi, L.; Berkovitch-Yellin, Z.; Weissbuch, I.; v. Mill, J.; Shimon, L. J. W.; Lahav, M.; Leiserowitz, L. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 466 and references therein.

[21] For recent attempts to explain the natural selection of L enantiomers, see: (a) Kondepundi, D. K.; Nelson, G. W. *Phys. Rev. Lett.* **1983**, *50*, 1023. (b) Mason, S. F. *Nature (London)* **1984**, *311*, 5981. (c) Tranter, G. E. *Chem. Phys. Lett.* **1985**, *120*, 93. (d) Gilat, G.; Schulman, L. S. *Ibid.* **1985**, *121*, 13. (e) Dunne L. J. *Ibid.* **1985**, *121*, 17.

[22] Hoffmann, R.; Hofmann, P. *J. Am. Chem. Soc.* **1976**, *98*, 589. Ammeter, J. H.; Bürgi, H.-B.; Hoffmann, R. *Ibid.* **1978**, *100*, 3686.