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Some Comments on the Possibility of Achieving Asymmetric Synthesis from Achiral Reactants in a Rotating Vessel

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Abstract: Recent attempts to achieve asymmetric synthesis from achiral reactants contained in a rapidly rotating vessel are examined theoretically. It is concluded that such attempts must fail.

In a recent pair of communications,[1,2] Dougherty and co-workers claim to have achieved asymmetric synthesis from achiral reactants by carrying out the reactions in a rapidly rotating vessel. They report a positive optical rotation when the vessel is rotated clockwise (as viewed from above) with axis of rotation perpendicular to the earth's surface and a smaller negative rotation when the vessel is rotated counterclockwise; they report no optical rotation when the vessel is spun about an axis parallel to the earth's surface. They also present some theoretical considerations purporting to account for these results in terms of interactions among the rotating vessel, the earth's gravitational field, and the coriolis force. The purpose of the present paper is to point out that all of the theoretical points made by Dougherty and co-workers are without merit and that short of a drastic break with well-established theoretical principles, it is impossible to account for their results in terms of any such interactions.

In collaboration with Wynberg and Meuwese, we recently showed[3] that asymmetric synthesis at thermal equilibrium cannot be brought about by any combination of uniform, static electric and magnetic fields. Earlier, de Gennes[4] had proved the theorem for the special case of parallel fields. Since the proof depends only on the symmetry properties of the fields under reflection and time reversal, it is easily generalized to cover other analogous cases, where the environment is also characterized by polar and axial vectors. The situation posed by Dougherty is of this sort.

We suppose that a reaction is carried out with achiral starting materials which can produce either a product molecule M or its enantiomer M*. The environment is characterized by two vectors, $\vec{P}$ and $\vec{A}$. $\vec{P}$ is a polar vector which is unchanged by time reversal, while $\vec{A}$ is an axial vector which changes direction under time reversal. For example, $\vec{P}$ could be an electric field or equally well a gravitational field, while $\vec{A}$ could be a magnetic field or vorticity (angular momentum). The concentrations of M and M* at equilibrium will be the same if their molecular partition functions are equal, and this in turn will be true if there is a one-one correspondence between states of M in the given environment and states of M* with the same energy in the same environment. We show such a correspondence by making use of the fact that the energy of the entire system (including environment) is unchanged under both spatial reflection and time reversal. The proof proceeds exactly as in ref 3. Starting with molecule M in the fields $\vec{P}$ and $\vec{A}$, we first apply $\hat{\sigma}$, the reflection in the plane containing $\vec{P}$ and $\vec{A}$. (If $\vec{P}$ and $\vec{A}$ are parallel, there are an infinite number of such planes, any one of which may be used to define $\hat{\sigma}$.) This will leave the energy and $\vec{P}$ unchanged, reverse the direction of $\vec{A}$, and transform M into M*. We now apply the time reversal operator $\hat{T}$, which reverses $\vec{A}$ again, leaving everything else unchanged. We can summarize the effect of the two operators $\hat{\sigma}$ and $\hat{T}$ symbolically as in eq 1.

$$(\mathrm{M},\vec{P},\vec{A}) \xrightarrow{\hat{\sigma}} (\mathrm{M}^*,\vec{P},-\vec{A}) \xrightarrow{\hat{T}} (\mathrm{M}^*,\vec{P},\vec{A}) \quad (1)$$

Equation 1 shows that, for every state of M in the given environment, there exists a state of M* in the same environment with the same energy. It follows that the two enantiomers have the same partition functions, and hence the same equilibrium concentrations in the given environment. In ref 3, the vectors $\vec{P}$ and $\vec{A}$ were assumed to be the applied external electric and magnetic fields. But the argument is unchanged if $\vec{P}$ and $\vec{A}$ are assumed to be, respectively, gravitational field and vorticity, so the result applies equally well to the experimental situation of ref 2.

Dougherty[1] attempts a similar procedure by using inversion $\hat{I}$ instead of $\hat{\sigma}$. Application of $\hat{I}$ followed by $\hat{T}$ gives *in our notation* eq 2.

$$(\mathrm{M},\vec{P},\vec{A}) \xrightarrow{\hat{I}} (\mathrm{M}^*,-\vec{P},\vec{A}) \xrightarrow{\hat{T}} (\mathrm{M}^*,-\vec{P},-\vec{A}) \quad (2)$$

This result differs from the one given by Dougherty[1] in his eq 2. Aside from notational differences (his $\vec{G}$ and $\vec{B}$ correspond to our $\vec{P}$ and $\vec{A}$, respectively) the discrepancy between our result and his arises because Dougherty incorrectly assumes that the gravitational field changes sign under time reversal. In any case, contrary to Dougherty's assertions, eq 2 gives no information one way or the other about the possibility of asymmetric synthesis since it does not relate states of M and M* in the *same* environment.

If overall reflection and time reversal invariance hold, therefore, the setup of ref 2 cannot lead to any enantiomeric excess at equilibrium. We will consider the possibility of a kinetic effect later. Before leaving the equilibrium case, however, it is worthwhile to consider the order of magnitude of a hypothetical as-yet-undiscovered, symmetry-violating term that would be necessary to produce the claimed effects at equilibrium.

If the concentrations of the enantiomers are to be in the ratio $(1 + \alpha)/1$, where α is small, their energy difference, as is well known, must be approximately $\epsilon = \alpha kT$ per molecule. Thus, at 255 K, the temperature considered by Dougherty,[1] for which $kT = 3.5 \times 10^{-14}$ erg, one needs $\epsilon \approx 3.5 \times 10^{-20}$ erg for $\alpha = 10^{-6}$ (1 ppm) or $\epsilon \approx 3.5 \times 10^{-18}$ erg for $\alpha = 10^{-4}$ (100 ppm). Dougherty[1] incorrectly finds 3.5×10^{-26} erg and 3.5×10^{-22} erg for $\alpha = 10^{-6}$ and 10^{-4}, respectively.

Suppose our reacting system to be in a gravitational field $\vec{G}$ and in a vessel rotating with (vector) angular frequency $\vec{\omega}$. Within the vessel, there will be a velocity field $\vec{v} = \vec{\omega} \times \vec{r}$, where $\vec{r}$ is measured relative to an origin on the axis of rotation, and a corresponding vorticity $\vec{\Omega}$:

$$\vec{\Omega} = \nabla \times \vec{v} = 2\vec{\omega} \quad (3)$$

If we are willing to suspend time reversal invariance, we could imagine a term in the molecular hamiltonian of the form of (4),

$$H_{\mathrm{as}} = \chi\vec{\Omega}\cdot\vec{G} \quad (4)$$

where χ is proportional to some pseudoscalar property of the molecule, leading to different signs for H_{as} in the two enantiomers. Of course, a term such as (4) would be forbidden by time-reversal invariance, so we are being extremely unorthodox to consider it at all.

The units of $\vec{\Omega}$ are in s^{-1}; those of $\vec{G}$ are in cm/s^2. Thus, if H_{as} is to have units of erg = g cm^2/s^2, χ must have units g cm s and

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(1) R. C. Dougherty, *J. Am. Chem. Soc.* **102**, 380 (1980).

(2) D. Edwards, K. Cooper, and R. C. Dougherty, *J. Am. Chem. Soc.*, **102**, 381 (1980).

(3) C. A. Mead, A. Moscowitz, H. Wynberg, and F. Meuwese, *Tetrahedron Lett.*, 1063 (1977).

(4) P. G. deGennes, *C. R. Hebd. Seances Acad. Sci., Ser. B*, *270*, 891 (1970).

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be made up of *molecular* properties. To maximize χ, we assume it to be built up from the largest mass, distance, and time associated with the molecule: the total mass (say 200 amu = 3×10^{-22} g), a molecular diameter (say 10^{-7} cm), and a rotational time (say 10^{-8} s). We do not pretend that any of this is really plausible; we are just trying to make H_{as} as large as possible consistent with *dimensional* correctness. At the surface of the earth, the acceleration of gravity is 980 cm/s^2, and the largest angular frequencies used in ref 2 are 14 000 rpm, leading to $\Omega = 2.9 \times 10^3$ s^{-1}. Putting all this together, our estimate for H_{as} is about 9×10^{-31} erg. At 255 K, the temperature considered by Dougherty,[1] this leads to $\alpha \approx 2 \times 10^{-17}$. This is to be regarded as a high upper limit, since quite implausible assumptions were needed to obtain it. Thus, to produce an enantiomeric excess of even 1 ppm, there would have to be a dimensionless multiplicative factor in expression 4 at least of order 10^{10}; i.e., the supposed time-reversal-violating interaction would have to be overwhelmingly stronger than the known interactions involving gravitation and would be readily recognizable on the macroscopic level.

As pointed out by Rhodes and Dougherty,[5] the above theorem applies to an equilibrium situation and thus does not, strictly speaking, rule out the possibility of a kinetic effect. To see how such an effect might come about, consider an activated complex X, which is the precursor of product M and which has associated with it a current or velocity vector $\vec{\mathbf{j}}$, indicating that it is moving away from reactant(s) R in the direction of M. Applying $\hat{\sigma}$ and $\hat{T}$ successively to this species, we obtain eq 5 in place of eq 2. Thus,

$$(\mathrm{X},\vec{\mathbf{j}},\vec{\mathbf{P}},\vec{\mathbf{A}}) \xrightarrow{\hat{\sigma}} (\mathrm{X}^*,\vec{\mathbf{j}}^*,\vec{\mathbf{P}},-\vec{\mathbf{A}}) \xrightarrow{\hat{T}} (\mathrm{X}^*,-\vec{\mathbf{j}}^*,\vec{\mathbf{P}},\vec{\mathbf{A}}) \qquad (5)$$

the species required to be present in equal concentration with $(\mathrm{X},\vec{\mathbf{j}})$ is $(\mathrm{X}^*,-\vec{\mathbf{j}}^*)$, which is moving in the opposite direction, from product M* back to R. The species $(\mathrm{X}^*,\vec{\mathbf{j}}^*)$, moving toward product M*, could possibly be present in a different concentration, leading in a pseudoequilibrium theory to a difference in the rate constants for formation of M and M*.

An imaginable interaction which might bring this about would be the presence, in the hamiltonian of the precursor, of two terms: $H_g = b\vec{\mathbf{G}}\cdot\vec{\mathbf{L}}$ (b a constant and $\vec{\mathbf{L}}$ a polar vector associated with the molecule) and $H_c = \chi\vec{\Omega}\cdot\vec{\mathbf{j}}$ (χ a pseudoscalar associated with the molecule). Both H_g and H_c are invariant under both reflection and time reversal.

For simplicity in estimating the effect, we assume that there are only two orientations, so that H_g has eigenvalues $\pm u$, while H_c has $\pm w$. Of the precursors on the way to products, $(\mathrm{X},\vec{\mathbf{j}})$ and $(\mathrm{X}^*,\vec{\mathbf{j}}^*)$, one will have eigenvalues $\pm(u + w)$ and the other $\pm(u - w)$. The ratio of their concentrations will be that of their partition functions

$$\frac{q}{q^*} = \frac{e^{(u+w)/kT} + e^{-(u+w)/kT}}{e^{(u-w)/kT} + e^{-(u-w)/kT}} \approx 1 + 2uw/(kT)^2 \qquad (6)$$

if both u and w are small compared to kT. The enantiomeric excess parameter α in this case is thus of order of magnitude $uw/(kT)^2$. Again, we try to make this as large as imaginable consistent with dimensional correctness.

Since G has dimensions of cm/s^2, bL must have dimensions of g cm, the dimensions of a "mass dipole moment". According to well-established theory, the mass dipole moment is zero because of the positive definiteness of mass; nevertheless, we will maximize the effect by assuming that it is of order of magitude of molecular mass times the diameter of a molecule, leading to eq 7.

$$u \approx (980\ \mathrm{cm/s^2})(3 \times 10^{-22}\ \mathrm{g})(10^{-7}\ \mathrm{cm}) \approx 3 \times 10^{-26}\ \mathrm{erg} \qquad (7)$$

As for H_c, Ω has dimensions of s^{-1}, so $\chi\mathrm{j}$ must have units of g cm^{-} s^{-1}. Again, we choose these as large as possible: (total mass of molecule)(diameter)^2(vibrational frequency), the last assumed of the order of 10^{14} s^{-1}. With these assumptions, one obtains eq 8.

$$w \approx (3 \times 10^3\ \mathrm{s^{-1}})(10^{-7}\ \mathrm{cm})^2(3 \times 10^{-22}\mathrm{g})(10^{14}\ \mathrm{s^{-1}}) \approx 9 \times 10^{-19}\ \mathrm{erg} \qquad (8)$$

Putting the numbers from (7) and (8) into (6), one finds eq 9.

$$\alpha \approx 4 \times 10^{-17} \qquad (9)$$

For both kinetic and equilibrium effects, therefore, we conclude that even the most radically implausible assumptions lead to enantiomeric excesses of no more than a few parts in 10^{17}. Even to get this high a value, one must assume either a large mass dipole moment or large terms violating time reversal invariance.

In connection with the kinetic effect just discussed, we note that the condition of detailed balancing actually requires that it be zero. If we write

$$\mathrm{R} \underset{k_b}{\overset{k_f}{\rightleftharpoons}} \mathrm{M}$$

and

$$\mathrm{R} \underset{k_b^*}{\overset{k_f^*}{\rightleftharpoons}} \mathrm{M}^*$$

then detailed balancing gives at equilibrium

$$[\mathrm{R}]k_f = [\mathrm{M}]k_b \qquad (10)$$

$$[\mathrm{R}]k_f^* = [\mathrm{M}^*]k_b^* \qquad (11)$$

In light of eq 1, we also have at equilibrium

$$[\mathrm{M}] = [\mathrm{M}^*] \qquad (12)$$

Applying $\hat{\sigma}$ and $\hat{T}$ to the precursor of M, whose equilibrium concentration is proportional to $[\mathrm{R}]k_f$, and using (12), we find

$$[\mathrm{R}]k_f = [\mathrm{M}^*]k_b^* = [\mathrm{M}]k_b^* \qquad (13)$$

Comparison of (10), (11), and (13) then yields $k_f = k_f^*$ and $k_b = k_b^*$.

Dougherty and co-workers[2] report a positive rotation when the reaction vessel, as viewed from above, has been rotated clockwise and a smaller negative one when the rotation has been counterclockwise. This they attribute to the coriolis force due to the earth's rotation about its axis and suggest that opposite results might be obtained in the southern hemisphere. If this were correct, of course, it would mean that the coriolis force accounts for nearly half the effect under their experimental conditions, so that one should observe a sizable effect with the coriolis force alone, without the need of spinning the reaction vessel. Actually, however, the coriolis force is much too small and in the wrong direction to account for the reported results.

The effect of the earth's rotation in a setup of this type is to give the vessel an additional effective angular velocity (relative to an inertial system) of $\vec{\omega}_e = 7.3 \times 10^{-5}$ s^{-1}, the angular velocity of the earth's motion about its axis. The effective vorticity is thus $\vec{\Omega} = 2(\vec{\omega} + \vec{\omega}_e)$. This is the only effect; it is clear that $\vec{\omega}_e$ is much too small to account for nearly 50% of the total, as claimed. Also, $\vec{\omega}_e$ in the northern hemisphere is counterclockwise from above, so whatever effect there is should be enhanced when the rotation is counterclockwise and diminished when the rotation is clockwise, in contradiction to what Dougherty and co-workers[2] report.

We conclude that the theory of ref 1 and 2 is entirely without foundation and cannot possibly be taken seriously as an explanation for the data reported. We feel that the most likely explanation by far is that they are due to some artifact.

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[5] W. Rhodes and R. C. Dougherty, *J. Am. Chem. Soc.*, **100**, 6257 (1978).