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ABSOLUTE ASYMMETRIC SYNTHESIS

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ABSOLUTE ASYMMETRIC SYNTHESIS

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ABSTRACT

Absolute asymmetric synthesis of helicenes with circularly polarized light was observed. Irradiation in the long wavelength region of the diarylolefin precursors with left circularly polarized light always gave helicenes of positive long wavelength optical activity, and vice versa. The optical yield of the helicene was found to be strongly dependent on the wavelength of irradiation and the structure of the precursor. These data indicate a mechanism involving selective excitation of the enantiomeric conformations of the precursors, and also provide information about aryl-ethylene bond rotation in the excited state. This hypothesis suggests a general model which may be extended to other examples of absolute asymmetric synthesis with circularly polarized light, should they be found.

Absolute asymmetric synthesis by irradiation of the diarylolefins under high magnetic field was sought, but not found.

The differential radiolysis of amino acid enantiomers with ^{14}C beta radiation was also unsuccessful.

CHAPTER 1

HISTORICAL ASPECTS OF "ABSOLUTE" ASYMMETRIC SYNTHESIS

HISTORICAL ASPECTS OF "ABSOLUTE" ASYMMETRIC SYNTHESIS

In 1874 le Bel stated that any synthesis of chiral molecules,¹ starting from either achiral or racemic reactants, would always produce equal amounts of the enantiomers of the product provided that no optically active reagents, catalysts, or other asymmetric influences are employed.

For instance, cis-3-hexene may be converted into 3-hexanol by the following procedure:

In accordance with le Bel's rule, the 3-hexanol formed consists of equal amounts of its enantiomers and is thus not optically active.

However, the B_2H_6 can first be complexed with (+)- α -pinene.^{2,3}

When reacted with cis-3-hexene this complex has been shown to produce the levorotatory isomer of 3-hexanol in 91% optical purity.

$$\text{optical purity} = |\%D - \%L| = \frac{[\alpha]_{\text{observed}}}{[\alpha]_{\text{pure enantiomer}}} \times 100\%$$

Such a synthesis of a chiral material in optically active form using optically active reagents is known as an induced asymmetric synthesis. This thesis is concerned with the production of optically active material without the aid of optically active reagents, i.e., absolute asymmetric synthesis.

Thus, according to le Bel's rule it is necessary to use some asymmetric physical influence to accomplish this.

In 1845 Michael Faraday discovered that materials which ordinarily did not exhibit optical activity would do so under the influence of a magnetic field.⁴ For instance such classically symmetric compounds such as CoCl_6 ⁵ and benzene⁶ exhibit optical activity when placed in a magnetic field. It thus might seem reasonable to expect that if a magnetic field can cause dissymmetry in optical processes, it might also produce dissymmetry in the product distribution of photolyses carried out in a magnetic field.

This was attempted several times: In 1926 Read and McMath⁷ used plane as well as circularly polarized light of wavelength 5161 Å in the presence of a strong magnetic field to disturb the equilibrium between the salts of 1-hydroxyhydrindamine and racemizing DL-chlorobromomethanesulphonic acid. No optical activity was observed. In 1939 Radulescu and Moga⁸ reported that irradiation of 2-ethoxy-2-allyl-1,3-indandione with bromine in chloroform under the influence of a high magnetic field resulted in a slight optical activity. However, the resultant optical activity was small enough to cast considerable doubt on the claim of absolute asymmetric synthesis.

Another physical influence that might be expected to produce optical activity is photolysis with circularly polarized light (CPL). This was first suggested by van't Hoff in 1894.¹

One such principle that has met with complete success involves the asymmetric destruction of racemic mixtures with CPL.^{9,10} Just as enantiomers exhibit equal and opposite optical rotations, so do they exhibit equal and opposite circular dichroisms. Thus, we see that if one enantiomer absorbs RCPL (right circularly polarized light) more than LCPL (left circularly polarized light) the other enantiomer will absorb more LCPL than RCPL, to the same extent (see Chapter 2 for more thorough discussion). If such a compound is destroyed by light of the appropriate wavelength it is clear that irradiation with one chirality of light will destroy one of the enantiomers faster than the other, resulting in optical activity in the remaining mixture. If, however, the reaction is carried to completion, no optical activity remains. Successful "asymmetric photodestructions" have been carried out on racemic mixtures of e.g., α -azidopropionic acid dimethylamide,⁹ 2-chloro-2-nitroso-1,4-diphenylbutane,¹⁰ humulene nitroside,¹¹ and 3-acetyl-2,6-dimethyl-5-methoxycarbonyl-4-(2'-nitrophenyl)-1,4-dihydropyridine.¹² This can be explained more easily in the following way: Let us assume that a compound possesses a circular dichroism at a certain wavelength, $\Delta\epsilon = \epsilon_L - \epsilon_R$, where ϵ_L is the absorption coefficient of one enantiomer for LCPL, and ϵ_R its absorption coefficient for RCPL. Let us further designate the enantiomers (+) and (-). Since, as mentioned above, enantiomers have equal and opposite circular dichroism:

$$\Delta\epsilon = \epsilon_L^{(+)} - \epsilon_R^{(+)} = \epsilon_R^{(-)} - \epsilon_L^{(-)} \quad (1)$$

$$\frac{\epsilon_L^{(+)} + \epsilon_R^{(+)}}{2} = \frac{\epsilon_L^{(-)} + \epsilon_R^{(-)}}{2} = \epsilon \quad (2)$$

where ϵ is the absorption coefficient for unpolarized light. From (1) and (2),

$$\epsilon_L^{(+)} = \epsilon_R^{(-)} = \epsilon + \frac{\Delta\epsilon}{2} \text{ and } \epsilon_R^{(+)} = \epsilon_L^{(-)} = \epsilon - \frac{\Delta\epsilon}{2} \quad (3)$$

For example, $\epsilon_L^{(+)}$ is the absorption coefficient for LCPL of the (+) enantiomer. Assuming that the compound in question is destroyed by light the resultant optical activity, α is expressed by

$$\alpha = (C^{(+)} - C^{(-)})M \quad (4)$$

where M is the appropriate specific or molar rotational value, and $C^{(+)}$ and $C^{(-)}$ are the concentrations of the (+)- and (-)-enantiomers, respectively.

If RCPL is employed,

$$\frac{dC^{(+)}}{dt} = -\epsilon_R^{(+)}t = -\left(\epsilon - \frac{\Delta\epsilon}{2}\right)t \quad (5)$$

$$\frac{dC^{(-)}}{dt} = -\epsilon_R^{(-)}t = -\left(\epsilon + \frac{\Delta\epsilon}{2}\right)t \quad (6)$$

(In fact, $\frac{dC}{dt} = k\epsilon t$, however, the proportionality constant k , which is a function of light intensity,

concentration, and other experimental variables, can be ignored for the purpose of this discussion).

Integrating,

$$C^{(+)} = C_0^{(+)} e^{-(\epsilon - \frac{\Delta\epsilon}{2})t} \quad (7)$$

$$C^{(-)} = C_0^{(-)} e^{-(\epsilon + \frac{\Delta\epsilon}{2})t} \quad (8)$$

Since $C_0^{(+)} = C_0^{(-)}$ (i.e., the starting mixture is racemic)

$$\alpha = C_0^{(+)} [e^{-(\epsilon - \frac{\Delta\epsilon}{2})t} - e^{-(\epsilon + \frac{\Delta\epsilon}{2})t}]_M \quad (9)$$

$$= C_0^{(+)} e^{-\epsilon t} (e^{\Delta\epsilon t/2} - e^{-\Delta\epsilon t/2})_M \quad (10)$$

Now, the anisotropy factor "g" is defined as:

$$g = \frac{\Delta\epsilon}{\epsilon} \quad (11)$$

The anisotropy factor is the fraction of circular light differentially absorbed between the two enantiomers. Substituting (11) into (10) we get

$$\alpha = C_0^{(+)} e^{-\epsilon t} (e^{g\epsilon t/2} - e^{-g\epsilon t/2})_M \quad (12)$$

Since anisotropy factors are usually quite small (12) simplifies to

$$\alpha = C_0^{(+)} e^{-\epsilon t} [(1 + g\epsilon t/2) - (1 - g\epsilon t/2)] M \quad (13)$$

$$\alpha = C_0^{(+)} e^{-\epsilon t} g\epsilon t M \quad (14)$$

Now, $2C_0^{(+)} = C_0$, and since "g" is small,

$$C = C^{(+)} + C^{(-)} = 2C_0^{(+)} e^{-\epsilon t} \quad (15)$$

Thus, if the fraction of the reactant remaining is defined as " β ",

$$\beta = e^{-\epsilon t} \quad (16)$$

Substituting (16) into (14),

$$\alpha = C_0^{(+)} g M \beta \ln\left(\frac{1}{\beta}\right) \quad (17)$$

Setting $\frac{d\alpha}{d\beta} = 0$ we get $\beta = \frac{1}{e}$, that is, the rotation is greatest when there is $\frac{1}{e}$ ($\sim 36.8\%$) of the compound left.

Another quite successful principle is that of partial photoresolution. Stevenson and Verdick^{13,14} have studied several chromium complexes that are known to photoracemize, i.e. d-complex $\xrightarrow{h\nu}$ l-complex. Since the use of circular light in a CD band will excite one enantiomer to a greater extent than the other, an imbalance between the two enantiomers will result.

Starting with a racemic mixture, upon irradiation

one will observe optical activity increasing to a certain limiting value, at which a photostationary state has been reached. At this photostationary state,

$$\frac{dC^{(+)}}{dt} = \frac{dC^{(-)}}{dt} \quad (18)$$

If, as above, RCPL is used (18) transforms to:

$$\epsilon_R^{(+)} C^{(+)} = \epsilon_R^{(-)} C^{(-)} \quad (19)$$

For small g ,

$$\frac{C^{(+)}}{C^{(-)}} = \frac{\epsilon + \Delta\epsilon/2}{\epsilon - \Delta\epsilon/2} \approx g$$

In this way Stevenson and Verdick have obtained the CD and ORD curves of several chiral chromium complexes.^{13,14}

However, until the recent results in this laboratory¹⁵ and in the laboratory of H. Kagan,^{16,17,18} no clear cut case of absolute asymmetric synthesis with CPL has been observed.

The first recorded attempt at absolute asymmetric synthesis with circular light was that of Padoa,^{19,20} who added bromine to angelic acid in the presence of CPL. No optical activity resulted. In 1922 Pirak²¹ unsuccessfully attempted an asymmetric synthesis of lactic acid by the action of sodium bisulphite on

acetaldehyde under the influence of CPL. In 1925 Cherbuliez²² brominated cinnamic acid in the presence of CPL, but failed to detect any optical activity. However, in the 1930's Karagunis and Drikos^{23,24,25,26} irradiated triarylmethyl radicals (obtained from reaction of the triarylmethyl chlorides with mercury) with CPL in the presence of chlorine, and observed an optical activity that increased, reached a maximum, and then decreased to zero upon further irradiation. Similar irradiation of the chiral triarylmethyl chlorides (such as phenyl-4-tolyl-4-ethylphenyl-, and phenyl-4-biphenyl-1-naphthylmethyl chloride) failed to produce any rotations, thereby ruling out asymmetric destruction of the triarylmethyl chlorides. Opposite rotations resulted with RCPL and LCPL. The proposed asymmetric synthesis was explained in terms of the selective reaction of the enantiomers of tetrahedral triarylmethyl radicals. Since there are an equal amount of the triarylmethyl radicals formed, Karagunis and Drikos implied that the circular light was doing an asymmetric destruction of the presumably (sic) stable triarylmethyl radicals; the optical activity goes to zero at the end, just as described by Kuhn.⁹ However, much has been learned about such systems in recent years that casts doubt on the results of Karagunis and Drikos. First, although such radicals may exist in chiral (tetrahedral or propeller-like) conformations, they

almost certainly will interconvert rapidly enough so that there will always be a 50-50 mixture of the two enantiomers. We would thus not expect to see the optical activity disappear at the end of the experiment, since one is no longer doing a "classical" asymmetric destruction where the enantiomers cannot interconvert. Second, it is now known that triarylmethyl radicals dimerize into such forms as, for triphenylmethyl,²⁷

It is possible that Karagunis and Drikos may have been performing asymmetric destructions of such chiral compounds in their work.

Davis and Heggie^{28,29} observed slight rotations upon the bromination²⁸ or chlorination²⁹ of 2,4,6-trinitrostilbene with CPL. Attempts at asymmetric destruction of trinitrostilbenedibromide and dichloride failed. However, these rotations were at best marginal, and a recent attempt to reproduce this work has failed.³⁰ Davis and Ackerman³¹ attempted an asymmetric synthesis of tartaric acid by the photochemical addition of hydrogen peroxide to diethylfumarate:

Slight rotations were reported, and only RCPL was used. A recent attempt to reproduce this work has also failed.³² Betti and Lucchi³³ subjected propene, 2-butene, and 1,4-butadiene to CPL in the presence of chlorine, and observed slight optical activity. Again, a recent attempt to reproduce the result with propene³² has failed.

The above work, all performed before 1945, indicated that little, if any, absolute asymmetric synthesis results from irradiation with CPL. All of the recorded rotations (on D-line polarimeters) were marginal, and only in the work of Karagunis and Drikos^{23,26} were opposite rotations obtained with RCPL and LCPL.

Due to recent availability of commercial spectropolarimeters there has recently been renewed interest in the problem of absolute asymmetric synthesis. These machines are much more sensitive than the

old-fashioned polarimeters and can measure optical activity over a very wide range of wavelength, not just at a few visible spectral lines.

Most recently Boldt et al.³² attempted to synthesize non-racemic 1,1,2-trimethylcyclopropane from 2-methyl-2-butene and carbene, generated from diazomethane with CPL.

No rotations were found. The analytical method was sensitive enough to detect less than $10^{-4}\%$ optical yield. They also attempted the asymmetric dimerization of cyclopentenone with CPL.³²

Significant rotations were found. However, they were shown to result from asymmetric destruction of the product dimers.

Scott and Rasmussen³⁰ have tested two other systems with CPL:

In neither case was any optical activity detected. Scott and Rasmussen³⁰ are continuing work in this field with other systems. The failure of Boldt³² et al. to observe asymmetric synthesis with circular light prompted them to hypothesize the impossibility of "transfer of chirality" from the photon to the product molecule.

Recently, the work described herein¹⁵ and work

in the laboratory of H. Kagan^{16,17,18} have unequivocally demonstrated absolute asymmetric synthesis with circular light, using reactions such as:

In this reaction a highly optically active molecule, e.g., hexahelicene, is synthesized with CPL from a classically symmetric starting material. The induced optical activity is very reproducible and quite large in some cases. A model has been proposed^{15,17,18} explaining this specific example of absolute asymmetric synthesis. This model, described in a later chapter, can easily be extended to other examples, if found.

In 1965 Hammond and Cole³⁴ studied the photo-equilibrium between cis- and trans-1,2-diphenylcyclopropane.

If an asymmetric sensitizer such as

was used, the trans compound isolated showed high optical activity. Hammond estimated the optical yield at 10-20%.³⁵ This uneven distribution of enantiomers is presumably due to their unequal (diastereomeric) interaction with the chiral sensitizer. Thus, the trans isomer enantiomers isomerize to the cis isomer at different rates, resulting in an unequal mixture. Strictly speaking, this is an induced, not absolute, asymmetric synthesis. However, it is the first such asymmetric sensitizer-induced reaction reported, and

offers an attractive alternative to circular light for photochemical asymmetric synthesis, the latter giving at best optical yields of a few percent.^{16,17,18,15}

Lastly, it has been observed that β - and α -radiation from nuclear decay is longitudinally and circularly polarized, respectively.³⁶ This is a consequence of the non-conservation of parity postulated by Yang and Lee.³⁷ It thus might be expected that this chiral radiation ("bremsstrahlung" or "brake radiation", i.e., radiation resulting from collisional energy loss from ejected nuclear particles) may synthesize or destroy enantiomers unequally. An attempt to asymmetrically synthesize 1-chloroethylethyl ether with bremsstrahlung from ^{32}P , ^{90}Y , ^{90}Sr , and ^{152}Eu proved unsuccessful.^{38,39} However, most of this kind of work has centered upon searching for asymmetric destruction of amino acids in an attempt to explain the almost universal predominance of L-amino acids in living organisms. In 1968 A. S. Garay⁴⁰ reported that ^{90}Sr β -particle "bremsstrahlung" decomposes D-tyrosine faster than L-tyrosine in alkaline (but not acid) solution. However, his evidence consisted solely of comparative UV spectroscopy. Work is underway in this and other laboratories on the problem.

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CHAPTER 2

POLARIZED LIGHT: ITS PROPERTIES, INTERCONVERSION, AND INTERACTION WITH CHIRAL MATTER

POLARIZED LIGHT: ITS PROPERTIES, INTERCONVERSION, AND INTERACTION WITH CHIRAL MATTER

Since this thesis is concerned mainly with the use of polarized light for the irradiation and subsequent measuring of the optical activity of chemical systems, the production, interconversion, and measurement of the various forms of polarized light will be considered here.

The term "light," of course, means "electromagnetic radiation," usually referring to the infrared, visible, and ultraviolet portions of the electromagnetic spectrum.

Light has properties of wavelength and frequency, their relationship being $\lambda = \frac{c}{\nu}$, where λ is wavelength, ν frequency, and c the speed of light, a constant.¹ Thus, plane polarized light may be visualized as below:

Note that the electric vector remains in one plane.

Circularly polarized light may be visualized as below:

Note that the $\vec{E}$ vector may be thought of as rotating either clockwise or counterclockwise while moving in the direction of propagation. Hence, circularly polarized light can be described as a helix. Although conventions vary, in this work right circularly polarized light (RCPL) so propagates a left-handed helix and left circularly polarized light (LCPL) propagates a right-handed helix.² In other words, as the light approaches the observer, LCPL moves counterclockwise, RCPL clockwise.

Linearly polarized light may be shown to result from the addition of two colinear beams of RCPL and LCPL of equal magnitude and wavelength,^{3,4} as shown in figure 1.

Circularly polarized light may similarly be shown to be the sum of two colinear, perpendicular, linearly polarized components, which are 90° (a quarter of a wavelength) out of phase with each other.²

For example, let us consider two linearly polarized beams propagating in the z direction, one

A

B

C

D

E

Figure 1 Linear light as the vector sum of two circular components.

with its $\vec{E}$ vector vibrating in the x direction, the other in the y direction. If the two beams are 90° out of phase with each other, their motion may be plotted out as shown in figure 2, part a.

If the two vectors are now added, we see that they trace out a circular path,² as shown in figure 2, part b.

In practice, circularly polarized light is produced from linearly polarized light, utilizing the above principle. For instance, many crystals have two or more optical axes, i.e., linearly polarized light of different orientations move through the crystal at different speeds.²

Consider a biaxial crystal, shown below:

Figure 2 Circular light as the vector sum
of two linear components
C- Fresnel Rhomb-Show linear
light entering

Linear light entering the crystal with its $\vec{E}$ vector moving parallel to the y axis will exit the crystal before a similar beam polarized parallel to the x axis. If a linearly polarized beam enters 45° to the two axes, it can be separated into two equal components along these axes. The component moving along the x axis will be retarded with respect to the component along the y axis.

If the properties of the crystal and of the wavelength of light are such that the x component is retarded exactly a quarter of a wavelength behind the y component, circular light will result, as shown above.² Thus we see that such biaxial crystals ("quarter wave plates") will produce the $\lambda/4$ retardance necessary for circular light at only one wavelength. At other nearby wavelengths the light becomes elliptical. In practice, such plates are cleaved from mica, and are actually $3/4\lambda$, $5/4\lambda$ or $7/4\lambda$ retardance plates.

Other optical devices, however, will produce a quarter wavelength retardance over a large range of wavelengths. For instance, a fused silica Fresnel rhomb,⁵ according to the principle of internal reflection, may be made to produce nearly circularly polarized light from 2900 Å to 5000 Å (see figure 2, part c).

Let us now consider the properties of elliptical light, that is, light whose $\vec{E}$ vector traces out an

ellipse perpendicular to the axis of propagation.

Such light may be considered to be the contribution of two colinear beams of LCPL and RCPL of different amplitudes⁶ (see figure 3a), or of two colinear beams of linearly and circularly polarized light⁷ (see figure 3b).

The ellipticity, "e," in the above case is defined as

$$e = \frac{\vec{E}_{\text{circular}}}{\vec{E}_{\text{circular}} + \vec{E}_{\text{linear}}}$$

(The ellipticity may also be the inverse of the above expression.)

If the intensity of such an elliptical beam is analyzed with a linear polarizer, the square of the denominator of the above expression is obtained when the axis of the polarizer is parallel to the $\vec{E}_{\text{linear}}$ vector, and the square of the numerator when the polarizer is perpendicular to it. Thus, if one observes the intensity, I , of a beam of elliptical light passed through a rotating linear polarizer,

$$e = \sqrt{\frac{I_{\text{minimum}}}{I_{\text{maximum}}}} = \sqrt{\text{"percent circularity"}}$$

Asymmetric compounds exhibit two intimately related properties. The first is circular birefringence: i.e., the possession of different indices of refraction

Figure 3 Elliptical light as the vector sum of 2 unequal circular components(a) and of linear and circular components(b).

for RCPL and LCPL. Consider the above example of a beam of linearly polarized light composed of equal components of LCPL and RCPL. After such a beam has passed through a circularly birefringent substance, the phase of the LCPL component will be either retarded or advanced with respect to that of the RCPL component, with the net result being a rotation of the plane of polarization of the light⁸ (see figure 4).

The amount of rotation α , is given by the expression

$$\alpha = \frac{\pi l}{\lambda} (n_L - n_R)$$

where n_L and n_R are the indices of refraction for LCPL and RCPL, and l is the path length of the birefringent substance.

A more common unit is specific rotation $[\alpha]$ where

$$[\alpha] = \frac{\alpha}{c} \times \frac{1800}{\pi},$$

$$\text{or } = \frac{\alpha^\circ}{cl} \text{ where } l \text{ is in decimeters,}$$

c in gm/cc, and α° is the observed rotation in degrees.

The molar rotation, Φ , is defined as

$$\Phi = \frac{[\alpha]M}{100}$$

The second optical property of asymmetric substances is circular dichroism (CD), i.e., the

Figure 4 Linear light, treated as the sum of two circular components, before (a) and after (b) entering a circularly birefringent medium.

differential absorption of LCPL and RCPL by an asymmetric substance.⁹

Again, using the above example of linearly polarized light composed of RCPL and LCPL, we see that these components will no longer be of equal magnitude. Upon passing through a circularly dichroic substance in an absorption band, the light becomes elliptically polarized.

Circular dichroism, then, may be experimentally determined by measuring the ellipticity (as described above) induced in a beam of linearly polarized light, or by directly measuring the different absorptions of RCPL and LCPL. The quantity most often used is molar ellipticity $[\theta]$,

$$[\theta] = \frac{e \times 100}{cl} = 3300 (\epsilon_L - \epsilon_R)$$

where e is the observed ellipticity, c = the molar concentration, l = length in cm, and ϵ_L and ϵ_R are the extinction coefficients for LCPL and RCPL.

Circular dichroism and circular birefringence are both strongly wavelength dependent, and for any single electronic transition located at λ_0 , will exhibit the behavior shown in figure 5. Case (a) demonstrates a so-called positive Cotton effect, (b) a negative Cotton effect. Since there are usually many overlapping electronic transitions in the spectra of most substances, circular dichroism spectra and circular birefringence

Figure 5

(optical rotary dispersion i.e., ORD) spectra may be much more complex than shown in figure 5.

CD and ORD are related by the Keonig-Kramers equations, the simplified expression of which is shown below:

$$[\phi_{\lambda}] = \frac{2}{\pi} \int_0^{\infty} [\theta_{\lambda_0}] \frac{\lambda}{\lambda_0^2 - \lambda^2} d\lambda$$

$$[\theta_{\lambda}] = \frac{2}{\pi \lambda} \int_0^{\infty} [\phi_{\lambda_0}] \frac{\lambda_0^2}{\lambda_0^2 - \lambda^2} d\lambda$$

It has been determined experimentally that the ratio of the CD to absorption

$$("g" = \text{anisotropy factor} = \frac{(\epsilon_L - \epsilon_R)}{(\epsilon_L + \epsilon_R)/2})$$

is constant with wavelength within strong transitions. Thus, this constancy of "g" is often observable in the long wavelength region of many compounds,¹⁰ where only one strong transition is present.

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CHAPTER 3

THE PHOTOLYSIS OF NITRONES UNDER HIGH MAGNETIC FIELD AND WITH CIRCULARLY POLARIZED LIGHT

THE PHOTOLYSIS OF NITRONES UNDER HIGH MAGNETIC
FIELD AND WITH CIRCULARLY POLARIZED LIGHT

Asymmetric synthesis was first attempted using the photoconversion of nitrones to oxaziridines. Since 1958¹ it has been known that nitrones (I) rearrange upon irradiation to oxaziridines* (II).

This reaction involves the conversion of a planar, achiral molecule into a molecule with an asymmetric center on the ring carbon. The ring nitrogen may also be an optical center if there is an alkyl group

* Oxaziridines had previously been synthesized by the peroxidation of imines:^{2,3,4}

attached to it,^{2,5,6} but is not if it is aryl substituted.⁷ (Aryl groups lower the barrier to inversion sufficiently to allow rapid epimerization at room temperature).

An apparatus was set up for the irradiation of samples within the 66,000 Gauss magnet used in the magnetic circular dichroism apparatus in the Laboratory of Chemical Biodynamics. The magnet could be revolved on its vertical axis 90° in order to allow for irradiation.

Irradiation was effected by a PEK 100 Watt medium pressure mercury lamp focused through a quartz lens into a 3/8" diameter quartz light pipe of length 24". The far end of the light pipe was placed in the cell compartment (see figure 1). A NiSO₄ solution filter was placed immediately after the focusing lens, to avoid overheating of the sample. A CuSO₄ solution filter⁸ was employed to exclude all light below 3500 Å. A round, stainless quartz cell of capacity ca. 3 ml contained the sample.

Samples of α -cyano- α ,N-diphenylnitrone, (R_1 = -CN, R_2 = R_3 = C₆H₅), α -styryl-N-phenylnitrone and α -phenyl-N-p-nitrophenylnitrone, synthesized by Dr. Janet Splitter, were irradiated at a concentration of ca. 2×10^{-4} M in 90% cyclohexane-10% methylene chloride for 10 minutes. (The complete conversion to the oxaziridine was indicated by the disappearance of absorption above 320 nm).⁷

figure 1

The samples were then transferred to a 2 cm quartz lollipop cell for analysis in the CD mode of the Cary 60. In none of the samples was any significant optical activity present.

Irradiations were also carried out with CPL using procedure A (see Chapter 4, part C). The three solutions described above were irradiated to completion (~ 1 hr) with both RCPL and LCPL in a quartz cell of 5 ml capacity at 270 nm. The paired samples were then run together in the CD mode of the Cary 60, no baseline being required. None of the sample curves showed any difference between the samples irradiated with RCPL and LCPL.

It was decided to abandon the nitron - oxaziridine system for two reasons:

First, no specific rotational values for these oxaziridines are known. Thus if they are quite low, significant optical yields of oxaziridine might go undetected.

Second, the oxaziridines are both thermally and photochemically unstable,⁷ which are obvious experimental disadvantages. The photochemical reactivity further complicates matters by introducing the possibility of asymmetric destruction of the oxaziridine with circular light. Thus, it might be nearly impossible to determine whether any resultant optical activity resulted from the asymmetric destruction or asymmetric synthesis of the oxaziridines with circularly polarized light.

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CHAPTER 4

THE ABSOLUTE ASYMMETRIC SYNTHESIS OF HELICENES WITH CIRCULARLY POLARIZED LIGHT

A. INTRODUCTION: THE SYNTHESIS AND PROPERTIES OF HELICENES

The classical definition of chirality states that the geometric structure of a chiral molecule must be such that it is nonsuperimposable on its mirror image.¹

The most common type of chirality involves a carbon atom bonded to four different atoms or groups, as shown above. However, there are other types of molecular chirality, among which are optically active allenes,

optically active biphenyls,

and optically active alkenes.

(trans-cyclooctene)

Still another type of asymmetry involves helicenes, such as hexahelicene²

in which the terminal rings of the system are so crowded together that they are forced to overlap so that the system forms a helix which can exist in right and left handed forms. These molecules are highly optically

active, since the entire electronic structure is chiral. In most chiral molecules the optical activity is due to smaller, secondary effects. For instance, in 2-methylcyclohexanone

the ORD and CD from the long-wavelength $n \rightarrow \pi^*$ transition of the carbonyl function are due to the asymmetric perturbation of the α -carbon on the inherently symmetric carbonyl chromophore.

The first synthesis of hexahelicene by Newman, outlined in figure 1, was a tedious, low yield series of reactions. The hexahelicene was resolved by complexing with (+) and (-) 2-(2,4,5,7)-tetranitro-9-fluorenylidene-aminoxy)-propionic acid (TAPA).³

figure 1

A new route to the helicenes was opened by the discovery that stilbenes give, upon irradiation, 4a,4b-dihydrophenanthrenes which are immediately oxidized to the fully aromatic structures at even quite low concentrations of oxidants.^{4,10}

The ring-closure of stilbenes to dihydrophenanthrenes is believed to proceed through the S_1 state,⁴⁻⁸ whereas the photochemical cis-trans isomerization is believed to take place from the lowest triplet state (T_1).⁶ NMR spectroscopy and theoretical calculations strongly suggest that the 4a,4b hydrogens of compound C are situated trans to each other.⁹

This reaction series has been shown to take place for stilbenes with substituents such as CH_3 , $(CH_3)_3C$, C_6H_5 , CN , CO_2H , CO_2R , CF_3 , CH_3O , F , Cl , and Br , but not NO_2 , I , CHO or $COCH_3$.¹⁰ In addition, this reaction was

shown to take place for larger diaryl ethylenes, e.g.

It will be noted that although the latter reaction has two possible photoproducts from a stilbene-type photoclosure only one is formed as the major product.

Shortly thereafter Martin *et al.*¹² synthesized heptahelicene by the following photoclosure:

It will be noted that in this case there are three possible photoproducts. However, heptahelicene is the major product, but is isolated in only 12% yield.¹² Other helicenes were soon made by stilbene-type photoclosures (see figure 2).

figure 2

Again, there are several possible photoproducts in all of the above reactions. However, in all cases, except for synthesis of heptahelicene from IIa, the helicene is the major product, and in all cases the helicene is easily isolated by chromatography.¹³⁻¹⁷

The stilbenes used as precursors are all readily available, e.g., by the Wittig synthesis. Thus it clearly is seen that the above described syntheses provide a method for preparing helicenes which is far superior to the method of Newman.² (Indeed compound IIb was synthesized as early as 1941.¹⁸)

Recently, a new synthesis for 1,2-diarylethylenes was reported¹⁹ which is superior in some respects to the Wittig synthesis in that it requires less complex starting materials, often proceeds in higher yields and affords only the trans isomer, thereby making purification a simpler process. This synthesis involves an appropriately substituted aldehyde-anil (easily available from the aldehyde) and an arylmethyl compound:

These diarylolefin $\rightarrow$ helicene reactions provide ideal subjects for asymmetric synthesis with circular light. The helicenes possess enormous optical activities which make optical yields as low as 0.02% observable with less than a milligram of the easily isolable helicene.

Unfortunately, thus far none of the higher helicenes have been fully resolved, although their CD and ORD curves have been obtained from samples partially resolved by slow crystallization from benzene and selective crystal picking,^{13,17,20} but it seems reasonable to expect their CD and ORD curves to be of similar magnitude as those of hexahelicene. (However, it is expected that the $[\alpha]^D$ values of helicenes increase rapidly with the increasing number of rings in the helicene, due to the displacement of the ORD curve to longer wavelength).

**B. EXPERIMENTAL: THE SYNTHESIS OF HEXA-,
HEPTA-, OCTA-, AND NONANELICENE AND THEIR
CORRESPONDING 1,2-DIARYLOLEFINS**

1 N LiOMe in MeOH. 7 g reagent grade lithium was dissolved in 1 l anhydrous methanol with stirring, and the mixture allowed to reflux. The solution could be stored indefinitely.

1-(2-Naphthyl)-2-(4-tolyl)ethylene. 50 g 2-(bromomethyl)naphthalene and 60 g triphenylphosphine was dissolved in 1 l xylene and stirred at reflux. The solution first turned yellow, then a white precipitate appeared. Eventually the precipitate interrupted stirring, after which the solution was filtered and the reflux continued. After 2 hours the precipitate was filtered, and washed with 200 ml xylene and 200 ml petroleum ether. The precipitate, which consisted of 109 g (99.5%) 2-naphthylmethyltriphenylphosphonium bromide, mp $>300^{\circ}$, was collected by filtration. 40 g of the salt was dissolved in 120 ml 1 N LiOMe in MeOH, and 10 g 4-tolualdehyde was slowly added, with stirring. The solution was stirred vigorously for 10-20 minutes, allowed to stand for 2 hours, and the precipitate isolated by filtration. Crystallization from EtOH-C₆H₆ gave 8 g 1-(2-naphthyl)-2-(4-tolyl)ethylene, mp $186-8^{\circ}$ (39%). (This is the pure trans isomer, as shown by tlc).

2-Methylbenzo[*a*]phenanthrene. 4 g 1-(2-naphthyl)-

2-(4-tolyl)ethylene was dissolved in 4 l cyclohexane in a large pyrex plask, a few crystals of I_2 were added, and the solution was irradiated for 18 hr with stirring in a Rayonet reactor (3500 Å). The reaction was followed by tlc (Eastman Chromogram Sheet, 6060 silica gel with fluorescent indicator) using petroleum ether as eluent. The trans-olefin appeared at short R_f as a brightly fluorescing spot; the cis-olefin as a dark spot at longer R_f , and the product as a dark spot at slightly shorter R_f than the cis-olefin. The solution was reduced in volume to 10 ml, and applied to a 10 cm column of neutral aluminum oxide, and chromatographed with cyclohexane. The chromatography was followed by UV spectrophotometry at 300 nm. After evaporation of the fraction a clear oil remained, which was dissolved in 10 ml acetone, and then added to 50 ml ethanol. H_2O was added to the point of turbidity. The solution was then allowed to stand for 1 hour, and was then cooled to -40° overnight. 1.5 g white crystals (30%) mp $81-2^\circ$ (lit.²¹ $80-1^\circ$) was collected by filtration. 0.5 g (13%) further (mp $77-81^\circ$) was obtained by warming the mother liquor to room temperature and adding additional H_2O .

An alternate procedure involved completely removing the solvent from the irradiation mixture, and dissolving the residue in 30 ml boiling ethanol. 2 g picric acid, dissolved in 20 ml boiling ethanol, was

then added. The combined solution immediately turned red, and was allowed to stand for 2 hr. 3.2 g of the picrate (mp 118-9°, lit.²¹ 118-8.5°) was collected by filtration. The picrate was cleaved either by boiling for a few minutes in aqueous potash and extracting the cooled mixture with petroleum ether, or by taking up the picrate in warm acetone and applying it to a 20 cm of neutral aluminum oxide, eluting with cyclohexane. With either method, the final solution was evaporated, and the oil remaining induced to crystallization by seeding, scratching, or praying. Yield = 1.6 g (40%) mp 80-1°.

Caution - 2-methylbenzo[c]phenanthrene is suspected of having potent carcinogenic activity. Handle with care. If spilled on skin, wash with copious soap and water, not organic solvents.

2-Benzo[c]phenanthrylmethyltriphenylphosphonium bromide. 2.3 g 2-methylbenzo[c]phenanthrene was mixed in 20 ml anhydrous CCl₄ with 1.6 g N-bromosuccinimide (crystallized from 12 times its weight of water). A trace of dibenzoyl peroxide was added, and the mixture was stirred at reflux for 8 hr. The reaction was followed by tlc as described above, using petroleum ether as eluent. The brominated compound appeared at shorter *rf* than the unbrominated compound. The solution was evaporated, dissolved in 10 ml benzene, and chromatographed on a 15 cm column of silica gel with benzene

as eluent. The residue from the first fraction was then dissolved in 20 ml xylene, to which 3 g triphenylphosphine was added. The solution was refluxed with vigorous stirring for 1 hr and filtered. The precipitate was washed with xylene and then petroleum ether. 5 g (90%) of a nearly colorless powder, mp $>300^{\circ}$ was collected by filtration.

2-Benzo[c]phenanthraldehyde.²² 0.6 g crude 2-(bromomethyl)benzo[c]phenanthrene, obtained in the previous experiment, was refluxed with stirring in 1.5 ml glacial acetic acid, 1.5 ml distilled H_2O , and 0.8 g hexamethylenetetramine. The diphasic mixture first turned homogeneous and clear, and then an oil appeared. After 2 hrs 1.5 ml conc. HCl was added, and the mixture stirred for 15 minutes more. The mixture was then extracted with 5 ml ether, and washed successively with 3 x 1 ml H_2O , 1 ml 10% $NaHCO_3$, and 3 ml H_2O . The ether fraction was then added to 20 ml benzene, which was reduced in volume to 5 ml and then evaporated with an N_2 stream yielding 0.45 g (90%) of the crude aldehyde (mp $72-6^{\circ}$).

4-Methylstilbene. 50 g p-xylyl chloride was refluxed with stirring with 94 g triphenylphosphine in 1 l xylene. When stirring became hindered by the precipitate the solution was filtered and reflux continued. After 6 hr the combined precipitate was washed with 200 ml xylene, and then 200 ml petroleum ether. Yield

= 135 g (93%) p-xylyltriphenylphosphonium chloride. 40 g of this salt was dissolved in 150 ml 1 N LiOMe in MeOH, and 11 g benzaldehyde was then added. The solution was allowed to stand overnight. 9 g 4-Methyl stilbene (47%) mp 118-9° (lit.²³ 120°) was collected by filtration.

3-Methylphenanthrene. 2 g 4-methylstilbene was dissolved in 2 l cyclohexane to which a few crystals of I₂ had been added, and irradiated in a quartz vessel with stirring in a Rayonet reactor 24 hr (3000 Å). The solution was distilled down to 10 ml, and applied to a 15 cm column of neutral aluminum oxide. The column was eluted with cyclohexane, the first 200 ml being collected (the chromatography was followed by UV spectrophotometry). The solvent was removed, and the residue crystallized from ethanol-H₂O, keeping the temperature below 60°. 1 g (51%) 3-methylphenanthrene, mp 62.5-3.5° (lit.²⁴ 65°) was collected by filtration. Alternatively, a procedure utilizing the picrate (mp 139°),²⁴ similar to that employed above for 2-methylbenzo[c]phenanthrene, was also employed, giving a product of similar yield and purity.

3-Phenanthrylmethyltriphenylphosphonium bromide. 1 g 3-methylphenanthrene was refluxed with 1 g N-bromosuccinimide (crystallized from 12 times its weight of water) for 8 hrs in 10 ml dry CCl₄ with stirring. The bromination was followed by tlc as in the bromination

of 2-methylbenzo[c]phenanthrene. The solution was filtered and evaporated, yielding 1.5 g of crystalline residue (105%). (A small sample was crystallized from ethanol-H₂O yielding 70% 3-bromomethylphenanthrene, mp 113-5°). 75 g of the crude compound was dissolved with 1 g triphenylphosphine in 10 ml xylene and refluxed for 1 hr, the precipitate filtered, and washed with xylene and petroleum ether. 1.7 g (95%) 3-phenanthrylmethyltriphenylphosphonium bromide, mp >300° was collected by filtration.

3-Phenanthraldehyde.²² 0.6 g crude 3-bromomethylphenanthrene, from above, was refluxed in 1.5 ml glacial acetic acid, 1.5 ml H₂O and 0.8 g hexamethylenetetramine for 2 hrs with stirring. The diphasic mixture first turned homogeneous, and then an oil appeared. 1.5 ml concentrated HCl was added, and reflux continued for 15 minutes more. The cooled solution was extracted with 5 ml ether, which was washed successively with 3 x 1 ml H₂O, 1 ml 10% NaHCO₃, and 3 ml H₂O. 20 ml benzene was added, the solution boiled down to 5 ml, which was then evaporated with a stream of N₂. 0.4 g crude 3-phenanthraldehyde (85%) mp 72-6° (lit.²⁵ 80°) was obtained.

4,4'-Dimethylstilbene. 40.2 g p-Xylyltriphenylphosphonium chloride (see above) and 12.1 g p-tolualdehyde were mixed in 120 ml 1 N LiOMe in MeOH and allowed to stand 1 hr. The precipitate was collected by filtra-

tion, and crystallized from benzene-ethanol yielding 7.5 g (36%) 4,4'-dimethylstilbene, mp 180° (lit.²⁶ $179-180^{\circ}$).

3,6-Dimethylphenanthrene. 2 g 4,4'-dimethylstilbene was stirred into a 2 l vessel containing cyclohexane with a trace of I_2 and irradiated with stirring for 24 hr in a Rayonet reactor (3500 Å). The solvent was distilled down to 50 ml, which was chromatographed on a short neutral aluminum oxide column with cyclohexane as eluent. The first fraction was evaporated and crystallized from EtOH-H₂O yielding 1.6 g (81%) 3,6-dimethylphenanthrene, mp $142.5-3^{\circ}$ (lit.²⁷ 141°).

1-(2-Benzo[c]phenanthryl)-2-phenylethylene (Ia).
Method A. 1 g 2-benzo[c]phenanthrylmethyltriphenylphosphonium bromide was mixed with 0.5 g benzaldehyde in 10 ml 1 N LiOMe in MeOH. An oil quickly separated, which was dissolved in 5 ml benzene and chromatographed on a 20 cm column of neutral aluminum oxide with benzene as eluent. The fractions were analyzed by UV spectrophotometry. Two fractions were collected, the first yielding 178 mg (32%), mp $76-8^{\circ}$, from petroleum ether, the second yielding 300 mg (53%), mp $145-6^{\circ}$, from benzene-ethanol. The compounds gave separate spots by tlc. Upon irradiation of degassed solutions, both compounds showed the same ratio of spots by tlc, and prolonged irradiation of both undegassed solutions gave

a spot corresponding to hexahelicene. Finally, the UV spectra of both compounds were strongly suggestive of cis- and trans-stilbene, respectively.²⁸ On this basis the compounds were designated cis-Ia and trans-Ia, respectively.

Method B. 5 g benzaldehyde and 7 ml aniline were dissolved in 100 ml ethanol and allowed to stand overnight. The crystals were collected and recrystallized from warm ethanol, yielding benzalanil, mp 52-3°. 200 mg 2-methylbenzo[c]phenanthrene, 200 mg of the above benzalanil and 200 mg potassium tert.-butoxide were heated with stirring in 5 ml DMF at 90° for 1 hr. The reaction mixture was added to 100 ml benzene, washed twice with 100 ml H₂O, reduced volume to a few ml, and chromatographed with benzene as eluent on a 10 cm column of neutral aluminum oxide. The first fraction was crystallized from benzene-EtOH giving 98 mg (36%) trans-Ia, mp 145-6° (lit.¹³ 144-5°).

1-(3-Phenanthryl)-2-(2-naphthyl)ethylene (Ib).

0.9 g 3-phenanthrylmethyltriphenylphosphonium bromide and 0.3 g 2-naphthaldehyde were added to 4 ml 1 N LiOMe in MeOH and allowed to stand overnight. The precipitate was chromatographed as with Ia, yielding 171 mg (25%) cis-Ib, mp 134-5°, from petroleum ether, and 173 mg (25%) trans-Ib, mp 209-10°, from EtOH-benzene. Both isomers exhibited behavior similar to those of Ia.

1-(2-Benzo[c]phenanthryl)-2-(2-naphthyl)ethylene

(IIa). Method A. 0.5 g 2-benzo[c]phenanthrylmethyltriphenylphosphonium bromide was added to 0.25 g 2-naphthaldehyde in 5 ml 1 N LiOMe in MeOH, and was left standing overnight. The precipitate was chromatographed as with Ia, yielding 59 mg (18%) cis-IIa, mp 116-7°, from EtOH-H₂O, and 150 mg (46%) trans-IIa, mp 202-3°, from EtOH-benzene. Both isomers exhibited behavior similar to those of Ia.

Method B. 2-Naphthaldehyde was combined with an excess of aniline as with benzaldehyde (see above) to give 2-naphthaldehyde anil, mp 112-4°. 200 mg of this compound was combined with 200 mg 2-methylbenzo[c]phenanthrene, and 200 mg KOt-Bu in 5 ml DMF and heated with stirring at 90° for 1 hr. The reaction mixture was worked up as with Ia (Method B), yielding (from benzene-ethanol) 134 mg (43%) trans-IIa (mp 203-4°), and 93 mg more from the mother liquor (30%) mp 199-200° (lit.¹³ 199-200°).

1,2-Bis-(3-phenanthryl)ethylene (IIb). Method A.

522 mg 3-phenanthrylmethyltriphenylphosphonium bromide and 200 mg crude 3-phenanthraldehyde were combined in 4 ml 1 N LiOMe. The crude product was filtered, and dissolved in 50 ml warm benzene which was chromatographed with benzene on a short neutral aluminum oxide column. Two fractions were collected. The first was crystallized twice from benzene-ethanol yielding 75 mg, mp 255-75°,

the second from benzene yielding 25 mg, mp 289-91^o (lit.¹⁸ 287-9^o) (total yield = 100 mg = 24%). The first crop was shown by tlc to be a cis-trans mixture, the second pure trans.

Method B. 150 mg crude 3-phenanthraldehyde was combined with 200 mg aniline in 5 ml ethanol, and allowed to evaporate overnight in a 100 ml beaker, which was then placed under vacuum for 2 hr. The yellow crystalline residue was combined with 150 mg 3-methylphenanthrene and 150 mg KOt-Bu and heated 1 hr at 90^o in 5 ml DMF. The reaction mixture was worked up as above for IIb (Method B) yielding 50 mg (17%) IIa, mp 291-4^o (lit.¹⁸ 287-9^o).

1-(2-Benzo[c]phenanthryl)-2-(3-phenanthryl)ethylene (III). 1 g 2-benzo[c]phenanthrylmethyltriphenylphosphonium bromide and 0.4 g crude 3-phenanthraldehyde were added to 4 ml 1 N LiOMe in MeOH and allowed to stand overnight. The precipitate was dissolved in 5 ml warm benzene and chromatographed as with Ia, yielding 220 mg (30%) cis-III, mp 200-1^o, from EtOH-H₂O, and 220 mg (30%) trans-III, mp 200-2^o, from EtOH-benzene. Both isomers exhibited behavior similar to those of Ia.

1,2-Bis-(2-benzo[c]phenanthryl)ethylene (IVa). 0.45 g crude 2-benzo[c]phenanthraldehyde was combined with 1 g 2-benzo[c]phenanthrylmethyltriphenylphosphonium bromide in 4 ml 1 N LiOMe in MeOH. The precipitate was

filtered, and recrystallized from benzene-ethanol giving 500 mg (68%) IVa, mp 229-30° (lit.¹³ 229-30°).

3,6-Bis-(2-naphthstyryl)phenanthrene (IVb). 100 mg 3,6-dimethylphenanthrene, 200 mg 2-naphthaldehyde anil, and 500 mg KOt-Bu were stirred at 90° for 1 hr. The precipitate was filtered, and 4 ml H₂O and 4 ml conc. HCl added to the filtrate, which was allowed to stand. The precipitate was collected. The combined precipitate was crystallized from xylene, yielding 220 mg (94%) IVb, mp 239-41°.

Hexahelicene (VI). Method A. 100 mg trans-Ia was dissolved in 100 ml benzene, a few crystals of I₂ added, and irradiated in a stirred pyrex flask with an SP-200 super high pressure mercury lamp for 2 hr. The solution was evaporated and applied to a short (~ 10 cm) column of neutral aluminum oxide, eluted with benzene. The first fraction was crystallized from EtOH yielding 60 mg (61%) hexahelicene, mp 230-1° (lit.² 230°).

Method B. 100 mg trans-Ib was dissolved in 300 ml benzene to which a few crystals of I₂ had been added and irradiated in a stirred pyrex vessel for 5 hr with an SP-200 super high pressure mercury lamp. The solution was then chromatographed and crystallized as in Method A, yielding 22 mg (22%) hexahelicene, mp 230-1° (lit.² 230°).

The products from both Methods A and B gave a

picrate from chlorobenzene, mp $194-6^{\circ}$ (lit.² $196-7^{\circ}$).

Heptahelicene (VII). Method A. 80 mg trans-IIa was dissolved in 100 ml benzene to which a few crystals of I_2 had been added and irradiated in a stirred pyrex vessel with an SP-200 super high pressure mercury lamp for 2 hr. The solution was reduced in volume to a few ml and chromatographed on a long (>25 cm) column of neutral aluminum oxide with benzene as eluent. The first fraction was heptahelicene, which was crystallized from EtOH-benzene, giving 11.2 mg (13%) mp $256-7^{\circ}$ (lit.¹³ $254-5^{\circ}$). The second fraction was dinaphtha[1,2-a; 1'2'-h]anthracene,

This fraction was crystallized from EtOH-benzene, giving 45 mg (57%), mp $230-1^{\circ}$ (lit.¹³ $230-1^{\circ}$). The chromatography was followed by UV spectrophotometry of the diluted fractions at 328 nm. The latter compound has an extremely intense ($\epsilon >100,000$) transition centered at this wavelength, and the second fraction was collected when high absorption at 328 nm appeared.

Method B. 20 g 4-xylene-bis-(triphenylphosphonium bromide), obtained after Campbell and McDonald,²⁹ was added to 5 g 2-naphthaldehyde in 100 ml LiOMe in MeOH. The precipitate was crystallized from xylene, giving 4.6 g (50%), β,β' -bis-(2-naphthyl)-4-distyrylbenzene, mp 326°. A similar yield could be obtained from 2-naphthylmethyl-triphenylphosphonium bromide and terephthalaldehyde. 100 mg of the above compound was irradiated in 1 l benzene-I₂ with stirring in a Rayonet reactor (3500 Å) in a pyrex vessel for 2 days. The mixture was chromatographed and crystallized as in Method A, giving a similar yield.

Method C. 50 mg IIb was dissolved in 200 ml benzene with a trace of I₂ added and irradiated with stirring 10 hr with an SP-200 super high pressure mercury lamp in a pyrex vessel. The mixture was evaporated and chromatographed on a short (~10 cm) neutral aluminum oxide column with benzene as eluent. The first fraction was crystallized from benzene-EtOH, giving 5 mg (10%) heptahelicene, mp 230-1° (lit.¹³ 230-1°).

Octahelicene (VIII) 60 mg trans-III was dissolved in 150 ml benzene, to which a few crystals of I₂ had been added, and irradiated 8 hr in a Rayonet reactor (3500 Å) with stirring. The mixture was evaporated and chromatographed with benzene as eluent on a short column of neutral aluminum oxide. The first fraction was crystallized from benzene-EtOH, giving 25 mg (43%), mp 322-6°

(lit.¹³ 330-1°).

Nonahelicene (IX) Method A. 100 mg IVa was dissolved in 300 ml benzene with a trace of I₂ added, and irradiated with stirring 8 hr with an SP-200 super high pressure mercury lamp in a pyrex vessel. The mixture was then evaporated and chromatographed on a short (~10 cm) neutral aluminum oxide column with benzene as eluent. Crystallization of the first fraction from benzene-ethanol yielded 35 mg (35%) nonahelicene, mp 357-60° (lit.¹³ 360°).

Method B. 160 mg IVb was photolyzed overnight with stirring in a Rayonet reactor (3500 Å) in 400 ml benzene, with a trace of I₂ added. The mixture was evaporated and chromatographed on a short aluminum oxide column with benzene as eluent. By tlc, the first fraction showed 2 spots. One was identified as nonahelicene, the other formed a less intense spot at shorter rf. Crystallization from benzene-EtOH gave 20 mg (13%) nonahelicene, mp 345-50° (lit.¹³ 360°).

Para- and ortho-substituted derivatives of Ia.

Three methods were used for the synthesis of the para- and ortho-substituted derivatives of Ia. The method used, yield, and mp of product, and other synthetic data are given in Table 1. Double focussing mass spectral and UV data are given in Table 2.

Method A. 500 mg 2-benzo[c]phenanthrylmethyltri-

Table 1

Product olefin	Method used	Wt and aldehyde used	Plc, solvent system	Recrystallization solvent	Yield	Mp.
<u>trans-p</u> -Br-Ia	A	159 mg 4-bromobenzaldehyde		C ₆ H ₆ -pet.ether	84 mg (24%)	160-160.5°
<u>trans-o</u> -Br-Ia	B	159 mg 2-bromobenzaldehyde	7 times, pet.ether	2 times, EtOH-H ₂ O	60 mg (17%)	108-10°
<u>trans-p</u> -Cl-Ia	B	120 mg 4-chlorobenzaldehyde	5 times, 9:1 pet. ether:benzene	EtOH-H ₂ O	65 mg (21%)	143-4°
<u>trans-o</u> -Cl-Ia	B	120 mg, 2-chlorobenzaldehyde	5 times pet. ether	EtOH-H ₂ O	49 mg (16%)	102-4°
<u>trans-p</u> -F-Ia	C	4-fluorobenzaldehyde	3 times, 9:1 pet. ether:benzene	EtOH-H ₂ O	88 mg (31%)	136-7°
<u>trans-p</u> -F-Ia	C	2-fluorobenzaldehyde	3 times, 9:1 pet. ether:benzene	EtOH-H ₂ O	85 mg (30%)	101-2°

(continued)

Table 1 (continued)

<u>cis-o-</u> F-Ia	A	106 mg 2-fluoro- benzaldehyde		pet.ether	43 mg 75-6° (14%)
<u>trans-o-</u> F-Ia	A			EtOH-H ₂ O	60 mg 101-2° (20%)
<u>trans-p-</u> Me-Ia	B	103 mg. 4-methyl- benzaldehyde	5 times, pet. ether	EtOH-H ₂ O	52 mg 114-6° (18%)
<u>trans-o-</u> Me-Ia	B	103 mg 2-methyl- benzaldehyde	12 times, pet. ether	EtOH-H ₂ O	55 mg 86.5-88° (19%)

Table 2

Olefin	m/e, parent molecular ion (by double focus MS).		UV λ_{max} , log ϵ (HCCl ₃)
	found	calculated	
<u>trans-p-Br-Ia</u>	408.0522 410.0475	408.0514 410.0494	365 nm, 4.42; 350 nm, 4.50; 315 nm, 4.60; 275 nm, 4.54.
<u>trans-o-Br-Ia</u>	408.0522 410.0556	408.0514 410.0494	349 nm, 4.35; 312 nm, 4.53; 273 nm, 4.44.
<u>trans-p-Cl-Ia</u>	364.1008 366.0991	364.1029 366.0989	363 nm, 4.41; 348 nm, 4.49; 313 nm, 4.60; 274 nm, 4.54.
<u>trans-o-Cl-Ia</u>	364.1008 366.0991	364.1029 366.0989	349 nm, 4.40; 313 nm, 4.58; 273 nm, 4.49.
<u>trans-p-F-Ia</u>	348.1250	348.1236	360 nm, 4.36; 344 nm, 4.41; 312 nm, 4.58; 271 nm, 4.48.
<u>trans-o-F-Ia</u>	348.1250	348.1236	359 nm, 4.35; 345 nm, 4.42; 314 nm, 4.57; 271 nm, 4.48.
<u>cis-o-F-Ia</u>	348.1250	348.1236	299 nm, 4.58.
<u>trans-p-Me-Ia</u>	344.1580	344.1565	364 nm, 4.39; 348 nm, 4.47; 315 nm, 4.58; 274 nm, 4.48.

(continued)

Table 2 (continued)

<u>trans-o-Me-Ia</u>	344.1571	344.1565	348 nm, 4.30; 312 nm, 4.70; 273 nm, 4.59.
<u>trans-Ia</u>			360 nm, 4.56; 344 nm, 4.63; 312 nm, 4.78; 272 nm, 4.70.
<u>cis-Ia</u>			299 nm, 4.39.

phenylphosphonium bromide and a stoichiometric amount of the appropriately substituted benzaldehyde was mixed in 4 ml 1 N LiOMe in MeOH, and left overnight. The solution was decanted from the residue, which was dissolved in 5 ml benzene and applied to a short column of neutral aluminum oxide. Elution was performed with petroleum ether until all of the 2-methylbenzo[c]-phenanthrene appeared. (The fractions were analyzed by UV spectrophotometry). The cis-olefin was then eluted by the gradual addition of benzene to the solvent. The trans-olefin appeared immediately afterward.

Method B. Same as Method A, except that the residue was dissolved in 3 ml benzene, which was applied to a preparative layer chromatography (plc) plate of 20 cm height and 100 cm width with a 1.5-2.0 mm layer of silica gel. The plc plate was developed as given in Table 1. A dark band, probably consisting of the cis-olefin and 2-methylbenzo[c]phenanthrene, and a brightly blue fluorescing band at shorter r_f (trans-olefin) appeared. This latter band was removed and extracted with a Soxhlet device using benzene.

Method C. The appropriately substituted aldehyde was combined with excess aniline in EtOH and left standing for 2 hr. The solvent was then evaporated, and the residue placed under vacuum for 2 hr. 200 mg of the residue, 200 mg 2-methylbenzo[c]phenanthrene, and 200 mg fresh potassium-*t*-butoxide were stirred at 90° for

1 hr. The mixture was then added to 100 ml benzene, washed twice with 100 ml dilute HCl, reduced to a few ml, and chromatographed as in Method B.

2- and 4-substituted hexahelicene. 2- and 4-substituted hexahelicene result from the photolysis of para- and ortho-substituted derivatives of Ia, respectively:

In each case 15 mg of the Ia derivative was irradiated with stirring in 60 ml toluene with a trace of I_2 added for 8 hr in a Rayonet reactor (3500 Å). The reaction mixture was then reduced in volume to a few ml, and chromatographed on a short column of neutral aluminum oxide with benzene. The helicene was then crystallized from petroleum ether at -40° . Mass spectral, absorption, yield, and mp data are presented in Tables 3 and 4.

Table 3

Parent olefin	Hexahelice- ne formed	Yield	m/e parent molecu- lar ion (by double focus MS).		Mp.
			observed	calculated	
<u>p</u> -Br-Ia	2-bromo-	3.5 mg	408.0331	408.0338	246-8°
<u>o</u> -Br-Ia	4-bromo-	2.5 mg	408.0372	408.0338	330-2°
<u>p</u> -Cl-Ia	2-chloro-	5.4 mg	364.0826	364.0833	245-6°
<u>o</u> -Cl-Ia	4-chloro-	3.8 mg	364.0826	364.0833	218-20°
<u>p</u> -F-Ia	2-fluoro-	3.8 mg	346.1101	346.1158	235-7°
<u>o</u> -F-Ia	4-fluoro-	2.5 mg	346.1101	346.1158	209.5-10°
<u>p</u> -Me-Ia	2-methyl-	4.0 mg	342.1411	342.1408	194-6°
<u>o</u> -Me-Ia	4-methyl-	3.0 mg	342.1377	342.1408	286-7°
Ia	unsubs.	4.5 mg			

Table 4

Parent olefin	Hexahelicene formed	UV; λ_{max} , log ϵ (HCCl ₃)
<u>p</u> -Br-Ia	2-bromo-	414 nm, 2.66; 392 nm, 2.79; 352 nm, 4.01; 330 nm, 4.32; 318 nm, 4.36; 268 nm, 4.70; 260 nm, 4.69.
<u>o</u> -Br-Ia	4-bromo-	414 nm, 2.45; 392 nm, 2.66; 350 nm, 4.00; 330 nm, 4.29; 318 nm, 4.29; 270 nm, 4.59; 257 nm, 4.59.
<u>p</u> -Cl-Ia	2-chloro-	414 nm, 2.71; 392 nm, 2.82; 351 nm, 4.05; 330 nm, 4.36; 318 nm, 4.39; 266 nm, 4.72.
<u>o</u> -Cl-Ia	4-chloro-	414 nm, 2.51; 392 nm, 2.73; 351 nm, 4.09; 330 nm, 4.38; 318 nm, 4.38; 270 nm, 4.67; 258 nm, 4.67.
<u>p</u> -F-Ia	2-fluoro-	414 nm, 2.85; 392 nm, 2.92; 349 nm, 4.07; 328 nm, 4.39; 317 nm, 4.42; 259 nm, 4.69.
<u>o</u> -F-Ia	4-fluoro-	414 nm, 2.54; 392 nm, 2.73; 348 nm, 4.09; 329 nm, 4.39; 317 nm, 4.40; 267 nm, 4.65; 252 nm, 4.67.
<u>p</u> -Me-Ia	2-methyl-	414 nm, 2.62; 392 nm, 2.77; 350 nm, 4.08; 330 nm, 4.35; 318 nm, 4.40; 265 nm, 4.69; 258 nm, 4.70.

(continued)

Table 4 (continued)

<u>o</u> -Me-Ia	4-methyl-	414 nm, 1.46; 392 nm, 2.70; 350 nm, 4.12; 330 nm, 4.40; 318 nm, 4.42; 270 nm, 1.68; 258 nm, 4.64.
Ia	unsubs.	413 nm, 2.52; 391 nm, 2.73; 349 nm, 4.11; 328 nm, 4.44; 317 nm, 4.45; 265 nm, 4.74; 258 nm, 4.73.

C. EXPERIMENTAL: PROCEDURES FOR IRRADIATION WITH CIRCULARLY POLARIZED LIGHT

Throughout the course of this work, different procedures and different apparatus for irradiation with circularly polarized light were employed. The described experimental "setups" reflect the chronological states of development of the experimental work. Three different sets of apparatus were used, which are described below, in the chronological order of their use.

In all cases the percent circularity of the light was measured as the ratio of the minimum to the maximum intensity readings of a beam passed through a rotating polaroid linear polarizing plate.

Procedure A (see figure 1). This apparatus consisted of a xenon-mercury high pressure lamp (1000 W), filtered by a quartz-encased cooling jacket, NiSO_4 filter, interference filter, polaroid plate, and $\lambda/4$ plate.

Interference filters centered at wavelength 370 nm, 350 nm, 310 nm, 290 nm and 270 nm were employed. Two $\lambda/4$ plates were used, centered at 270 nm (origin unknown) and 450 nm (Gaertner Inc.). Both were set in square mounts, with the fast and slow axes along the diagonal, so that the chirality of light could be determined by which edge the mounting was laid on (see Chapter 2).

figure 1

The following % circularities of light were measured:

Filter	$\lambda/4$ plate used	Measured % circularity
370 nm	450 nm	72%
350 nm	450 nm	62%
310 nm	270 nm	80%
290 nm	270 nm	87%
270 nm	270 nm	100%

Procedure B (see figure 2). This apparatus consisted of an SP-200 super high pressure mercury lamp, the beam of which was collimated by a fused silica lens and passed through a chemical filter³⁰ (a 5 cm wide cell with quartz windows, containing 50 g/l CuSO_4 and 0.1 g/l 2,7-dimethyl-3,6-diazocyclohepta-1,6-diene perchlorate, which allows light from 340 nm to 550 nm through. Since none of the helicene precursors irradiated absorbed significantly above 420 nm, all the light absorbed by the sample was between 340 nm and 420 nm.) This beam was then passed through an ultraviolet polarizing filter (Polacoat Inc., PL-40) followed by a $\lambda/4$ plate (Gaertner Inc.) centered at 390 nm, followed by the sample. This $\lambda/4$ plate was also set in a square frame with its optical axes along the diagonals, so that LCPL or RCPL could be produced by setting the frame on the appropriate edge. The percent circularity of the light could not be determined due to the fact that

figure 2

elliptically polarized light produced at the frontiers of a wavelength band passed through a $\lambda/4$ plate centered in the middle of that band is oriented along different axes. This makes the light appear more circular than it actually is using the above described method, rendering determinations by this method meaningless.

Procedure C (see figure 3). This apparatus consisted of an SP-200 super high pressure mercury lamp coupled to a monochromator (Bausch and Lomb, 36-85-25) with either visible, UV, or visible-UV gratings (33-86-25-02, 33-86-25-01, and 33-86-25-07, respectively). The beam was collimated by a fused silica lens, passed through a polaroid linear polarizing plate (Polacoat Inc., PL-40), and a fused silica Fresnel rhomb (Karl Lambrecht Inc.) followed by the sample.

figure 3

D. RESULTS AND DISCUSSION³¹

Compounds I-IX were synthesized as described in the first portion of the experimental section. The irradiation procedures A, B, and C are described in the second portion of the experimental section.

Solutions of 0.01 mg/ml Ia in cyclohexane were irradiated using method A in a 5 ml, 1 cm quartz cell for ten minutes at 370 nm, 350 nm, 310 nm, 290 nm, and 270 nm; both RCPL and LCPL were used. The degree of completion was determined by UV spectrophotometry by following the decline in absorption at 368 nm, and was determined as 60% for the 370 nm samples, 50% at 350 nm, 100% at 310 nm, 100% at 290 nm, and 70% at 270 nm. The samples were then transferred to a 2 cm round quartz cell and analyzed in the CD mode of the Cary 60. Since the cell has a volume of 6.5 ml, an increase in observable absorption by a factor of 1.6 occurs on changing cells.

The samples were run in pairs without a baseline. At none of the irradiated wavelengths did the CD scans of the paired LCPL and RCPL samples differ observably (i.e., no significant optical activity was generated). This method was sensitive enough to detect optical yields as low as 0.02%. (A sample of optically pure hexahelicene, generously donated by Dr. Lin Tsai, NIH, Bethesda, Md., was used for the

calibration of the above determination of sensitivity).

There are many disadvantages inherent in this procedure. The helicene is not purified, and its concentration cannot be accurately determined.

The problem of increasing the sensitivity in measurement of optical yields is of paramount importance to this work. Since increasing the sensitivity of instrumentation is generally a time-consuming and costly process, an alternate solution is to increase the amount of optical activity by increasing the amount of compound present. If optical activity is measured as Circular Dichroism, however, two factors immediately limit the sensitivity. First, measurement of CD and ORD becomes very difficult, due to high machine noise, at high absorption. With current instrumentation, a meaningful CD or ORD measurement cannot be made above an optical density of 2 or 3, in which case almost none of the incident light reaches the photodetector. Second, as mentioned in Chapter 2, at long wavelengths the g value ($g = \Delta\epsilon/\epsilon = \Delta A/A$) remains fairly constant for most asymmetric substances over a fairly wide wavelength range. Thus, the maximum CD that can be measured in the long wavelength region occurs in the wavelength region where the optical density reaches 2 or 3, since the observable CD is proportional to the absorption. Furthermore, it can be seen that once the concentration

is reached at which the optical density in the long wavelength region becomes 2 or 3, no increase in observable CD occurs with increasing concentration. By increasing the concentration, one merely moves the high absorption "cutoff" to longer wavelengths without increasing the observable CD. Even worse, increasing the concentration increases the slope of the absorption as it approaches the "cutoff," resulting in instrumental difficulties peculiar to CD instruments using Poockel-cell apparatus.^{32,33}

On the other hand, the character of an ORD curve is such that the ratio of the ORD value to the optical density approaches infinity as one goes to longer and longer wavelengths. This becomes obvious when it is noted that almost all asymmetric substances exhibit significant ORD values in regions of little or no absorption. E.g. even asymmetric alkanes exhibit significant D-line (yellow) rotations. Hence, the amount of observable rotation, and thus the sensitivity of measurements of optical yields, is increased by increasing the concentration. (The increase in sensitivity, however, is not quite proportional to the increase in concentration, as increasing the concentration moves the "cutoff" to longer wavelengths, where the ORD has a smaller value).

It was thus decided to irradiate several milligrams of helicene precursor and observe the

resultant optical activity by ORD. Solutions (6.5 ml) of 1.239 mg/ml (3.75×10^{-3} M) Ia in benzene/I₂ were irradiated after method A to varying degrees of completion. Samples were irradiated in a 2 cm round quartz cell of capacity of 6.5 ml, transferred to an identical cell, and analyzed by ORD.

As just mentioned, the ORD of an asymmetric substance never quite disappears as one goes away from the absorption region. However, the baseline of a highly sensitive spectropolarimeter such as the Cary 60 is highly unstable upon changing samples,³² and we thus set the pen at the same point at the long wavelength start of the scan for both of the paired samples irradiated with RCPL and LCPL, even though their rotations might be different at that wavelength.

Thus, all ORD measurements in this work taken with the Cary 60 are described by a) the amount of rotational difference between the LCPL and RCPL sample curves at the end of the scan (i.e., the wavelength at which the optical density reaches 2 or 3), and, b) the wavelength at which the scan was begun, where the ORD values for the two samples were set equal. It was found that a scan of ca. 100 nm is of sufficient length. Longer scanning increases the observable optical activity only a few percent.

The following results were obtained:

Table 1

Wavelength of irradiation	Time irradiated	Percent completion (by tlc)	Observed optical rotation	Scan start and finish
270 nm	1 hr.	5%	$+0.0003^{\circ} \pm 0.0004^{\circ}$	550 nm- 400 nm
270 nm	13.5 hr.	40%	$-0.0001^{\circ} \pm 0.0004^{\circ}$	"
290 nm	0.75 hr.	10%	$+0.0004^{\circ} \pm 0.0004^{\circ}$	"
290 nm	5.5 hr.	60%	$+0.0002^{\circ} \pm 0.0004^{\circ}$	"
310 nm	4 hr.	50%	$-0.0001^{\circ} \pm 0.0004^{\circ}$	"
350 nm	3 hr.	20%	$+0.0001^{\circ} \pm 0.0004^{\circ}$	"
350 nm	6.5 hr.	35%	$+0.0005^{\circ} \pm 0.0004^{\circ}$	"
370 nm	5 hr.	5%	$+0.0002^{\circ} \pm 0.0004^{\circ}$	"

The above Table shows that the rotations observed were at best marginal. Thus, at this time it was decided that a more powerful light source was needed for the photolysis of such "large" amounts of compound. The amount of circular light available for photolysis is usually quite small: if a $\lambda/4$ plate is employed the light used must be fairly monochromatic; if a Fresnel-type device is employed the light must be well collimated into a beam of small diameter and of high parallel character. The light is further attenuated if the linear polarizer employed is of the Polaroid type. Furthermore, the photoclosures of

compounds I-IV to the respective helicenes usually proceed in quite low quantum yields ($\phi < 10^{-3}$).⁹ Thus, the rate at which these reactions may be carried to completion is small.

Method B was therefore employed to irradiate the hexa-, hepta-, octa-, and nonahelicene precursors (I-IV), since it produces a relatively intense, albeit broad-band, beam of CPL. Samples (1.0 mg/ml in toluene/I₂, unless otherwise noted) were irradiated with RCPL and LCPL in a 2 cm quartz cell of 6.5 ml capacity to varying degrees of completion, as judged by tlc ($\pm 10\%$), and chromatographed as described in the experimental section. The samples were then analyzed in pairs by ORD. The results obtained are presented in Table 2.

Table 2

Starting material	Rotation observed	Limits of scan	Time irradiated	Percent ^c completion
Ia ^a	.0011° ± .0004°	470nm-400nm	30 min.	50%
Ib	.0086° ± .0004°	500nm-370nm	30 min.	20%
IIa	.0044° ± .0004°	520nm-385nm	20 min.	30%
IIa	.0100° ± .0004°	520nm-385nm	45 min.	60%
IIa	.0140° ± .0004°	520nm-385nm	90 min.	80%
III	.0174° ± .0004°	500nm-410nm	60 min.	30%
III ^b	.0320° ± .0004°	500nm-410nm	120 min.	30%
IV	.0144° ± .0004°	500nm-415nm	120 min.	15%

- a. Performed in benzene/I₂, not chromatographed.
- b. Performed at 2.0 mg/ml in toluene/I₂.
- c. In all cases it was observed that the cis-olefins chromatograph together with their helicenes, both by tlc and on column. This is easily understandable since the compounds have nearly the same molecular "shape." Thus, in following such reactions one should be careful not to mistake the cis-olefin on the tlc plate for the helicene.

In the cases of IIa, III, and IV, the solutions were diluted so that the first maximum in the ORD curve could be observed at 385 nm, 400 nm, and 415 nm, respectively. These wavelengths correspond to the observed first maxima for heptahelicene, octahelicene, and nonahelicene, respectively; these samples were resolved by spontaneous crystallization.²⁰

For the last four entries in Table 2, a "baseline" from a sample irradiated to approximately the same degree of completion with unpolarized light was used. In all four cases this "baseline" was found midway between the RCPL and LCPL curves, within the experimental error of 0.0004°. This indicates that equal and opposite rotations are produced by irradiation with RCPL and LCPL.

Substantial optical activity is generated

by photolysis of Ia-IV with circularly polarized light. It was impossible, however, to obtain either absolute or relative optical yields for any of these systems, as the presence of the cis-olefin in the chromatographed mixtures prevented an accurate determination of the helicene concentration. Samples could not be irradiated to completion in these cases, thereby eliminating this problem, since extended irradiation damaged the PL-40 polaroid plates used for linear polarization. Furthermore, hepta-, octa-, and nonahelicene have not yet been fully resolved, allowing only the determination of relative optical yields in these cases. However, the optical yields represented in Table 2 are estimated to be in the region of 0.2%-0.4%.

A priori, four mechanisms could be invoked to explain the observed induced optical activity:

1. Primary formation of racemic helicenes with subsequent asymmetric destruction of the helicene with circularly polarized light. (See Chapter 1).

2. Like the photoclosure of simple stilbene itself,⁹ the photoclosures of compounds I-IV proceed through chiral, dihydrohelicenes which are oxidized to the helicenes. Inspection of molecular

models indicates that this oxidation is stereospecific. Studies of simple stilbenes in carefully degassed solutions⁹ indicate that the dihydro compound may photochemically revert to the cis-olefin, establishing a photoequilibrium, e.g.,

If circular light is employed, it can be seen that a nonracemic mixture of dihydrohelicene can result, analogously to the partial photoresolutions of Stevenson and Verdick.³⁴ (See Chapter 1). The inequality between the enantiomers of the dihydrohelicenes would result in a similar inequality in the helicenes if the oxidation is stereospecific.

3. Molecular models show all cis-stilbenes to exist in chiral conformations. It is possible that these chiral conformations are resolvable at room temperature, in which case irradiation with circular light would asymmetrically destroy the racemic mixture, leaving the remaining olefin optically active.

Molecular models also indicate that the cis-diarylolefins I-IV should stereospecifically close to the helicene, as the enantiomeric diarylolefin conformations very strongly resemble the corresponding enantiomeric helicenes. Thus at partial conversions, the helicene formed in such circumstances will be optically active (see Chapter 1).

4. The enantiomeric cis-diarylolefins are not optically stable at room temperature. However, if racemization does not occur in the excited state before closure occurs, irradiation with circular light will result in unequal excitation of the cis-diarylolefin enantiomeric conformations, which will thus result in unequal product mixtures of the helicenes.

Mechanism 1 may be eliminated without further experimentation. Since irradiation was performed primarily in the long wavelength absorption region of the product helicene, asymmetric destruction with, for example, LCPL, would have destroyed the (+) isomer at a faster rate (A positive circular dichroism indicates that $\epsilon_L > \epsilon_R$) than the (-) isomer, resulting in negative optical activity (ORD and CD) in the long wavelength region. The

opposite is observed. To be certain, samples of heptahelicene (0.42 mg/ml and 0.12 mg/ml) and octahelicene (0.57 mg/ml) in toluene were irradiated with LCPL and RCPL for 30 and 60 minutes, respectively. No optical activity at all was observed in these attempts. (Indeed, studies by Moradpour et al.,¹⁴ and studies described later in this chapter indicate that asymmetric destruction of helicenes by prolonged irradiation with circularly polarized light does produce optical activity in the opposite direction of that induced in the formation of the helicenes).

Mechanism 2 involves the establishment of a $\text{III} \rightleftharpoons \text{V}$ photostationary state with an unequal distribution of the enantiomers of V resulting from their unequal absorption of circular light (see above figure). Nonracemic yields of helicenes would reflect this "partial photoresolution"³⁴ of V. Muszkat and Fischer⁹ have shown for a group of substituted stilbene-dihydrophenanthrene systems that the rates of the forward (cis-III $\rightarrow$ V) and reverse (V $\rightarrow$ cis-III) photolyses are comparable, and that the dihydrophenanthrenes aromatize quite rapidly, even at low concentrations of oxidant (V $\rightarrow$ VIII). Since many of the above-described photolyses required hours, in the presence of a relatively powerful oxidant (molecular iodine with atmospheric exposure), the rate of the forward reaction to the

helicene must be slow from the cis-olefin. (The trans-olefin + cis-olefin conversion is fast compared to succeeding steps). Since the reverse reaction is of comparable rate,³⁴ no dihydrohelicene can accumulate for its photoreversal back to the cis-diarylolefin to occur. Thus, if the results of Muszcat and Fischer may be applied here, it appears that mechanism 2 is highly unlikely.

In order to clarify the above mechanistic possibilities it was decided to irradiate some of the above helicene precursors to completion, and to undertake a wavelength dependence study on the relative optical yield of one selected precursor.

Accurate determinations of even "relative" optical yields, i.e., assigning an arbitrary optical purity to one sample as a reference, at many wavelengths presents special problems. First, the sample must be completely irradiated so that the helicene fraction from chromatography contains no cis-diarylolefin, which would prohibit an accurate determination of the helicene concentration. Second, since the monochromatic circular light produced by procedure C, the apparatus employed for these studies, was of low intensity, relatively little compound could be irradiated; especially if photolysis was to be complete. Thus, the concentration of the helicene precursor was reduced to 0.1 mg/ml (using the 2 cm, 6.5 ml quartz cell for irradiation and

measurement of optical activity). This concentration was barely high enough to allow for determination of completion of reaction by tlc, and low enough so that in most cases analysis could be determined by CD as well as by ORD. Since the Cary 60 was shared by many other users, all of whom used the CD mode, use of the CD mode in this work avoided the high machine wear caused by frequent changing of modes.

Compound III was chosen for the wavelength dependence study, as the III $\rightarrow$ VIII photoconversion proceeds relatively quickly in high yield with the production of high amounts of optical activity (see table II). Compound III, at a concentration of 0.10 mg/ml in toluene/I₂, was irradiated to completion at seven different wavelengths by procedure C with LCPL only. The samples were chromatographed and analyzed by CD, using an identical sample produced by irradiation of III in a Rayonet (3500 Å) for the baseline, in order to eliminate absorption anomalies. The results are tabulated in Table 3, and plotted in figure 1. Note that the sign of the induced optical activity at 290 nm is in the opposite direction of what is normally observed.

From separate ORD measurements, the sample irradiated at 410 nm was found to be 2.7% resolved with reference to the previously mentioned sample

Table 3

Wavelength irradiated	% Circularity of light	Time irrad.	Grating/slit- width/dispersion	θ° at 385 nm	Helicene conc. $\times 10^{-4} M$	Relative optical yield
410 nm	75	48 hr	vis/2 mm/12.8 nm	+0.0247	2.38	2.00%
390 nm	75	36 hr	vis/2 mm/12.8 nm	+0.0236	2.34	1.96%
370 nm	75	12 hr	vis/2 mm/12.8 nm	+0.0231	2.53	1.77%
350 nm	75	195 hr	UV/4 mm/12.8 nm	+0.0156	2.22	1.37%
330 nm	75	94 hr	UV/4 mm/12.8 nm	+0.0138	2.36	1.14%
310 nm	75	48 hr	UV/4 mm/12.8 nm	+0.0030	2.48	0.21%
290 nm	75	86 hr	UV/4 mm/12.8 nm	-0.0054	2.51 (-)	0.42%

figure 1

of octahelicene partially resolved by spontaneous crystallization by Professor R. H. Martin.²⁰ Since the actual optical purity of the crystallized sample is not known, the true optical yield of the 410 nm sample may be significantly lower than 2.7%. This, taken together with an assumed g value for optically pure octahelicene in the long wavelength region of 0.01 (the g of our sample of optically pure hexahelicene was 0.009) led us to assume a relative optical yield of 2.0% for the 410 nm sample.

From the optically active solutions of octahelicene, its previously unrecorded CD was obtained, assuming a 2.0% resolution for the sample irradiated at 410 nm (see figure 2).

Samples of Ia and Ib (0.1 mg/ml in toluene/ I_2 ; $3.0 \times 10^{-4} M$) were similarly irradiated at 370 nm for 12 hr with both RCPL and LCPL, chromatographed, and analyzed by CD. Ia and Ib gave hexahelicene of $0.04\% \pm 0.04\%$ and $0.50\% \pm 0.04\%$ optical yield, respectively.

The wavelength dependence data are completely inconsistent with mechanism 1, as optical activity generated by asymmetric destruction should follow the g value of octahelicene as a function of wavelength. The g value of octahelicene is also plotted on figure 1. Clearly, this does not agree with the actual wavelength dependence curve.

figure 2

Mechanism 3 is also eliminated by the above data, as asymmetric destruction of resolvable cis-diarylolefins would result in zero optical activity at the completion of the photo-reaction.

However, Moradpour et al.¹⁴ suggest that the photochemical cis-trans isomerization may maintain a racemic mixture of rigidly asymmetric cis-olefin, thus allowing for uniform asymmetric synthesis of the helicene throughout the course of the reaction, as shown below:

Muszcak and Fischer⁹ have shown, and cursory examination of the initial progress of helicenic reaction mixtures by tlc reveals, that the cis-trans equilibrium is established at a much higher rate than that for the dihydrohelicene formation. Thus, for the above scheme, the ratio (D-cis-olefin)/(L-cis-olefin) = $k_4 k_2 / k_1 k_3$. In the case of irradiation with unpolarized light, $k_1 = k_4$, $k_2 = k_3$, and

$k_5 = k_6$. Thus, the above ratio of the enantiomeric cis-diarylolefin conformers is unity. However, for circularly polarized light, $k_1 \neq k_4$, so this ratio now equals k_4/k_1 . Now,

$$\frac{d(\text{D-helicene})/dt}{d(\text{L-helicene})/dt} = k_5(\text{D-cis-olefin})/k_6(\text{L-cis-olefin}) \\ = k_5 k_4 / k_6 k_1.$$

The ratio of the rate of excited cis-olefin giving the dihydrohelicene to that giving the trans-olefin is not dependent on the chirality of the radiation or the chirality of the molecule, i.e., $k_5/k_2 = k_6/k_4$. This rearranges to $k_4/k_1 = k_6/k_5$. Thus,

$$\frac{d(\text{D-helicene})/dt}{d(\text{L-helicene})/dt} = 1:$$

there can be no asymmetric induction by this mechanism. Thus, mechanism 3, even allowing photochemical equilibration of the enantiomeric cis-diarylolefins, is eliminated.

It is thus left to choose between mechanisms 2 and 4. If mechanism 4 were valid, the wavelength dependence data would be a plot of the g value of cis-III. Cis-III was isolated from the synthesized cis-trans mixture by chromatography, and its absorption spectrum determined (see figure 3). This spectrum is quite consistent with the wavelength dependence data. (The optical yield remains fairly

figure 3

constant down to ca. 380 nm, where there appears to be only one transition in cis-III. The induced optical yield changes sign and becomes negative in the region of the 295 nm UV-maximum in the spectrum of cis-III). Compound V, on the other hand, would probably have transitions well out into the visible, if studies of the absorption of 4a,4b-dihydrophenanthrenes are applicable here.⁹ Thus, if mechanism 2 were valid, one would expect a change in sign of the induced optical activity, reflecting a change in sign in the CD of compound V, well above 305 nm, where it actually occurs.

A final result which is inconsistent with mechanism 2 is the observation above (and by Moradpour et al.¹⁴) that Ib gives about ten times the optical yield of hexahelicene as Ia does. Ia and Ib should form related dihydrohexahelicenes, and it seems reasonable to expect them to have similar capacities for partial photoresolution with circular light.

However, mechanism 4 can account for this difference. Hammond has noted³⁵ that in the lowest excited singlet state (S_1) of "electronically" unsymmetrical stilbenes, the state from which all stilbene photoclosures presumably take place, the excitation is "localized" in the aryl group with the lower S_1 energy. Thus, in the S_1 state of cis-Ib,

we would expect rotation up to 180° about the naphthyl-ethylene bond to be nearly free, the excitation being localized on the larger phenanthryl group. Similarly, we would expect rotation about the phenyl-ethylene bond in S_1 cis-Ia to be nearly free. Due to the symmetry of the phenyl group, rotation about the phenyl-ethylene bond ($\sim 180^\circ$) in cis-Ia results in interchange of its enantiomeric conformations, whereas the corresponding rotation about the naphthyl-ethylene bond in cis-Ib does not, due to the dissymmetry of the 2-naphthyl group, with respect to the bond. (see figure 3a).

Thus, if mechanism 4 is operative, it can be seen that although irradiation of cis-Ia with circular light excites its enantiomeric conformations unequally, this imbalance of the D- and L-excited forms is reduced through the above described bond rotation. Unequally excited cis-Ib, on the other hand, cannot similarly racemize in the excited state, and thus produces a higher optical yield of dihydrohexahelicene, which forms nonracemic hexahelicene. The same is true for the III-V-VIII system, and all of the other systems studied above.

However, the different optical yields of VI from Ia and Ib may also be due to differences in the CD spectra between cis-Ia and cis-Ib in the wavelength region employed for irradiation.

figure 3a

Since the above evidence completely eliminates mechanisms 1 and 3, and strongly argues against mechanism 2, we believe that absolute asymmetric synthesis with circularly polarized light is best explained by mechanism 4. It now remains to examine the two possible explanations for the difference between the optical yields of VI from Ia and Ib offered by mechanism 4.

The first hypothesis may be tested by the irradiation of ortho- and para-substituted derivatives of Ia. With o-substituted compounds, rotation of $\sim 180^\circ$ about the phenyl-ethylene bond no longer racemizes the conformers, because these compounds exist in two separate sets of enantiomeric conformations, i.e., exo- and endo-.

Several things immediately become apparent upon examination of such a system:

1. Closure to the helicene may occur only when the compound is in the exo configuration.

2. Rotation of $\sim 180^\circ$ of the phenyl-ethylene bond interchanges the D-endo form with the L-exo form, and the L-endo form with the D-exo form.

3. Assuming that the X group does not contribute significantly to the electronic structure of the molecule, i.e., it is nonchromophoric, the endo and exo forms will have nearly the same CD and absorption spectra.

4. The relative abundances of the exo and endo conformations will depend upon the substituent, the temperature, and the solvent.

Let us assume that conditions are such that the o-substituted cis-olefin under consideration exists only in the exo conformation in the ground state. It can be seen that upon excitation, free rotation about the phenyl-ethylene bond up to $\sim 180^\circ$ will equilibrate the D-exo/L-endo and L-exo/D-endo pairs, as mentioned above. However, since the excited molecules may close only in the exo conformation, irradiation with circular light will produce nonracemic yields of helicenes, and in the same direction as found for compounds I-IV, i.e., LCPL inducing positive optical activity, RCPL, negative optical

activity at long wavelength.

On the other hand, if conditions are such that the o-substituted cis-olefin exists only in the endo conformation, it can be seen that the excited molecule must rotate into the exo conformation of the opposite chirality before closure can occur. Thus, irradiation with circular light in this case will induce long wavelength optical activity in the opposite direction of that observed for compounds I-IV.

Applying the same argument, it is predicted that a 50-50 mixture of the endo and exo forms upon irradiation with CPL will result in a racemic mixture of the D- and L-helicene. (In fact, compound Ia presents such a situation, where the o-substituent is hydrogen, and the "exo" and "endo" conformations are present in equal amounts).

The p-substituted compounds provide a control for such experiments, revealing the the electronic factors associated with such substitution. Otherwise, they should behave identically to Ia.

Thus it appears that discovery of significantly greater optical yields for o-substituted derivatives of Ia than those found for their p-substituted derivatives or for Ia would provide good evidence for the hypothesis of bond-rotation.

The possibility that the difference in yield between Ia and Ib was due to a difference in their

CD, and thus their g-factors, might be tested by obtaining relative optical yields for the production of heptahelicene from IIa and IIb. The electronic relationship between IIa and IIb is the same as between Ia and Ib. In other words, IIb is more symmetric than IIa, just as Ib is more symmetric than Ia. Using the above hypothesis, one might expect a more symmetrically substituted cis-stilbene to have a higher circular dichroism, due to excitation interaction. (The chirally oriented aryl groups in a cis-stilbene will interact to a greater extent in the excited state if their energies are more similar, resulting in a more "asymmetric" transition from the ground state to the excited state, which will produce a higher CD.³⁶) For example, the S_1 energies of the naphthyl and phenanthryl groups in Ib are almost the same, whereas the S_1 energies of the phenyl and benzo[c]phenanthryl groups in Ia are quite different. Thus, if the large difference in optical yields of VI from Ia and Ib is due to this effect, one would expect to see the same order of magnitude of difference in IIa and IIb.

Derivatives of Ia substituted with F, Cl, Br, and methyl in the para position of the phenyl ring, and substituted with the same groups in the ortho position, were irradiated after procedure C.

Samples of either 6.0 mg or 7.5 mg were irradiated at 370 nm (total dispersion = 12.2 nm) in 27 ml toluene/ I_2

in a 10 cm quartz cell with both RCPL and LCPL. Due to their slow rates of reaction, o-F-Ia, o-Cl-Ia, and o-Br-Ia were irradiated to only approximately 80% completion. The helicene was then separated from the remaining cis-olefin by chromatography on neutral aluminum oxide, using graded mixtures of benzene-petroleum ether as eluent. The other five compounds were irradiated to completion, and chromatographed on neutral aluminum oxide using benzene as eluent. In all cases the helicene fractions were evaporated to dryness and dissolved in 1 ml chloroform, and analyzed for optical activity in a 10 cm cell in a Perkin-Elmer 141 polarimeter. The samples were then diluted, and their concentrations determined by UV spectrophotometry. The results are presented in Table 4.

From Table 4 it is seen that all of the ortho-substituted Ia derivatives give optical yields ca. five times larger than the unsubstituted Ia precursor. It is also seen that as the size of the para-phenyl substituent increases, an increasing optical yield is observed, indicating an increased hindrance to rotation about the phenyl-ethylene bond in the excited state. Examination of molecular models of para-substituted Ia shows steric interaction between the hydrogen atom in the 11-position of the benzo[c]phenanthryl group and the para-substituent of the phenyl group in the transition state for racemization (see figure 4).

Table 4

Starting material ^a	Product hexa-helicene	[α] ₄₃₆ ^{20°} in CHCl ₃ with				Irradiation period	% Circularity of light
		LCL (conc.) ^b	RCL (conc.) ^b	(0.566)	(0.591)		
7.5 mg Ia	unsubs.	7.6°±0.9°	-8.0°±0.8°	(0.566)	(0.591)	24 hr	89%
7.5 mg p-F-Ia	2-fluoro-	10.7°±0.9°	-10.5°±0.9°	(0.535)	(0.554)	24 hr	89%
7.5 mg p-Cl-Ia	2-chloro-	15.8°±0.8°	-16.4°±0.8°	(0.653)	(0.660)	24 hr	89%
6.0 mg p-Br-Ia	2-bromo-	23.2°±0.9°	-23.8°±0.9°	(0.590)	(0.585)	24 hr	89%
7.5 mg p-Me-Ia	2-methyl-	37.5°±1.1°	-36.4°±1.0°	(0.468)	(0.503)	36 hr	89%
7.5 mg o-F-Ia	4-fluoro-	34.0°±1.3°	-31.5°±1.2°	(0.382)	(0.410)	36 hr	89%
7.5 mg o-Cl-Ia	4-chloro-	46.9°±2.0°	-45.8°±1.4°	(0.255)	(0.367)	72 hr	89%
6.0 mg o-Br-Ia	4-bromo-	34.2°±2.4°	-38.7°±1.4°	(0.211)	(0.349)	68 hr	89%
7.5 mg o-Me-Ia	4-methyl-	35.9°±1.1°	-35.6°±1.0°	(0.442)	(0.508)	24 hr	89%

a. The starting material in each case consisted of the pure trans-olefin.

b. gm/100 ml.

figure 4

None of the new hexahelicenes except 2-bromohexahelicene has yet been totally resolved. However it was, a priori, expected that they would have nearly the same UV, ORD, and CD spectra as hexahelicene itself. Substituents such as those employed should effect the electronic structures of the ground state and the low lying excited states to a small extent as seen from their almost identical UV spectra (see experimental section, Table 4). Since the asymmetry is almost entirely due to the inherently dissymmetric helicene chromophore, it is similarly reasonable to expect a likeness in ORD and CD. Indeed Lightner et al. have found that partially resolved 2-bromohexahelicene with $[\alpha]_{589}^{20} = -444^{\circ}$ is converted to hexahelicene with $[\alpha]_{589}^{20} = -420^{\circ}$, by reduction with butyl lithium in hexane.³⁷

The data in Table 4 agree quite well with the bond rotation hypothesis. The alternative (CD) hypothesis was tested by the irradiation of IIa and IIb.

Unfortunately, unlike VI, VIII, and IX, compound VII has a relatively high rate of photodestruction,^{16,20} so that complete irradiation of IIa, and especially IIb, whose photoconversion to VII is quite slow, results in a significant degree of asymmetric destruction of the VII produced.¹⁶ This will generate optical activity of opposite sign to that generated by the asymmetric synthesis, making it very difficult to determine the relative optical yield due to asymmetric synthesis alone.

Compounds IIa and IIb are irradiated to low conversion (approximately 50% for IIa, 20% for IIb) after procedure C. The irradiations were performed at 1.0 mg/ml in a 2 cm quartz cell of capacity 6 ml in toluene/I₂ with both RCPL and LCPL. Compound IIa was irradiated at 310 nm, 335 nm, 370 nm, and 400 nm, and IIb at 370 nm. The samples were evaporated to dryness and refluxed for 2 hr in 10 ml chloroform with 10 mg 3-chloroperbenzoic acid, which was then shaken with 100 ml aqueous 1 N NaOH. The solvent was evaporated and taken up in 2 ml warm benzene, and chromatographed on neutral aluminum oxide with benzene as eluent. This procedure eliminated all of the remaining olefin, allowing for accurate determination of the helicene concentration.

The helicene fraction was reduced in volume to 6 ml, and analyzed by CD and UV spectrophotometry. The results are presented in Table 5 and figure 5. The UV spectrum of cis-IIa is presented in figure 6.

From the Table it is seen that the optical yield from IIb is smaller than that from IIa at 370 nm. Thus a more symmetric precursor does not necessarily give the corresponding helicene in higher optical yield than a less symmetrical one. It may be argued that the optical yield from IIb could be much larger at different wavelengths. However, the wavelength studies on both IIa and III show that the highest optical yields are obtained with light in the long wavelength region of the

Table 5

Starting material	Time irradiated	Wavelength irradiated	Relative optical yield ^a of heptahelicene with		% Circularity of light
			LCL	RCL	
IIa	24 hr	400 nm	1.26% ± 0.06%	-1.29% ± 0.06%	89%
IIa	4 hr	370 nm	0.76% ± 0.06%	-0.74% ± 0.06%	89%
IIa	24 hr	335 nm	0.47% ± 0.06%	-0.47% ± 0.06%	89%
IIa	12 hr	310 nm	0.11% ± 0.06%	-0.11% ± 0.06%	89%
IIb	24 hr	370 nm	0.62% ± 0.06%	-0.57% ± 0.06%	89%

a. Based on $g = \Delta\epsilon/\epsilon = 0.01$ in the long wavelength ($\lambda > 370$ nm) region for fully-resolved heptahelicene.

figure 5

figure 6

absorption spectra of the cis-diarylethylenes (figures 5 and 6). Since IIb, like IIa and III, could not be converted to the helicene at wavelengths longer than 400 nm, it would be expected to show the same wavelength dependence. Unfortunately, the excessively slow rate of photoclosure of IIb prevented wavelength studies of this compound with procedure C.

Thus, it may be concluded that rotation of the phenyl-ethylene bond in the S_1 state of Ia leads to the low optical yield of hexahelicene from irradiation of Ia with CPL.

E. CONCLUSION

The first concrete example of absolute asymmetric synthesis has been observed in the production of various helicenes from diarylolefins with circular light.³¹ Experimental evidence involving wavelength dependence and structural studies, as well as theoretical considerations, indicate a mechanism involving differential excitation of the chiral conformations of the cis-diarylolefins from which the reactions take place.

The cis-diarylolefins exist in enantiomeric conformations similar to the enantiomers of the helicenes, except that they are in rapid equilibrium at room temperature, and therefore unresolvable. If irradiated with circular light, they will be unequally excited, due to the Cotton effect.³⁸ Furthermore, if the cis-olefin reacts in the excited state before it racemizes, an unequal amount of helicene enantiomers will result.

This suggests a model for all asymmetric synthesis with circular light, in which unequal amounts of enantiomers of a chiral product are formed from what would normally be regarded as an achiral reactant.

All "achiral" compounds are achiral only in the average sense. For example, even methane exists in asymmetric vibrational states, and ethanol exists in chiral conformations. Normally, these chiral states are in rapid equilibrium with their enantiomers.

If such a "time-averaged" achiral compound photolyzes to a chiral product, and if the transformation from one enantiomeric state of the reactant to one of the product enantiomers is stereospecific, then asymmetric synthesis with circular light is possible.

Circular light will unequally excite the enantiomeric states of the reactant. If the product forming step is faster than equilibration of the enantiomeric states, then unequal amounts of the product enantiomers will result.

However, if the overall reaction rate is faster than the equilibration of the reactant enantiomeric states, an asymmetric destruction of the reactant enantiomers results (see chapter 1).

For example, octahelicene (VIII) may be synthesized from III and IIIa. The enantiomeric conformations of compound III will equilibrate much faster than the overall rate of ring-closure. Thus, asymmetric synthesis of VIII occurs upon irradiation with CPL. On the other hand,

the enantiomeric conformations of compound IIIa are optically stable at room temperature. Thus, although the initial rate of formation of one of the enantiomers of VIII from IIIa will be faster, the complete reaction with circular light will result in no net optical activity, just as in an asymmetric destruction.¹⁵ (Indeed, such a situation describes an asymmetric destruction of compound IIIa).

Thus, three conditions must be satisfied for an asymmetric synthesis with circular light:

- 1) The reactant should exist in chiral states which differentially absorb the circular light employed, and which stereospecifically convert to product enantiomers.
- 2) The transformation of reactant to product resulting from the excited state should be faster than the equilibration of the enantiomeric states of the reactant.
- 3) The equilibration of the reactant enantiomeric states should be faster than the overall rate of reaction.

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CHAPTER 5

THE ATTEMPTED ASYMMETRIC SYNTHESIS OF HELICENES BY PHOTOLYSIS UNDER HIGH MAGNETIC FIELD

THE ATTEMPTED ASYMMETRIC SYNTHESIS OF HELICENES
BY PHOTOLYSIS UNDER HIGH MAGNETIC FIELD

The helicene-diarylolefin series discussed in the previous chapter also provided an excellent system with which to attempt absolute asymmetric synthesis by irradiation under high magnetic field.

Two irradiation procedures were employed. Procedure I used an SP-200 super high pressure mercury lamp with an 0-52 pyrex filter (Corning), cutting off all light below 340 nm, placed directly in front of the lamp aperture. The beam was focused with a quartz lens into one end of a quartz light pipe of 3/8" diameter and 18" length. The other end of the pipe was placed into the aperture of an 11,000 Gauss magnet which had been modified for use in MCD spectroscopy. The sample was placed in a 2 cm quartz cell with a capacity of 6.5 ml, between the two magnet poles. Although the magnet was water-cooled, it could not be used for more than a few hours due to overheating. The direction of the magnetic field could be reversed by a switch on the magnet's control panel.

Procedure II, shown in figure 1, consisted of the same SP-200 lamp, 0-52 filter, and quartz lens as above. The photocell compartment of the MCD apparatus in the Laboratory of Chemical Biodynamics was removed, and the lamp setup secured firmly in its place. The beam was

figure 1

focused directly into the aperture of the 65,000 Gauss super-cooled magnet. This magnet could be rotated 180° to allow for irradiation in both directions relative to the magnetic field. The sample was placed in a specially designed stemless 1 cm quartz cell of capacity 3 ml.

0.1 mg/ml III in toluene/ I_2 was irradiated to completion (45 minutes) with procedure I in both directions relative to the field. The solutions were chromatographed (see experimental section) and analyzed together by CD. No detectable difference appeared between the two curves, placing an upper limit on the relative optical yield, defined in the previous chapter, of 0.02% on the octahelicene formed.

1.0 mg/ml Ia in toluene/ I_2 was irradiated to completion (60 minutes) with procedure I in both directions relative to the field. The solutions were chromatographed and analyzed by ORD from 500 nm to 375 nm. No detectable difference appeared between the two curves, placing an upper limit of 0.01% optical yield on the samples.

0.2 mg/ml In toluene/ I_2 was irradiated to completion (30 minutes) with procedure II in both directions relative to the magnetic field. Chromatography and analysis by CD showed no detectable optical activity, placing an upper limit of 0.02% relative optical yield on the octahelicene formed.

1.0 mg/ml Ia in toluene/ I_2 was irradiated to completion (30 minutes) with procedure II in both directions

relative to the magnetic field. Again, chromatography and analysis by ORD from 500 nm to 370 nm showed no detectable optical activity, placing an upper limit of 0.01% optical yield on the hexahelicene formed.

Since these experiments were performed on a nearly ideal chemical system with the most powerful magnets experimentally available for such work, the failure to detect any optical activity places grave doubt on the possibility of absolute asymmetric synthesis by irradiation under high magnetic field.

However, this failure is perhaps not surprising. Faraday¹ was the first to note that magnetically-induced optical activity is additive to the natural rotation. In fact, the two are almost independent of each other, with enantiomers exhibiting nearly identical MORD and MCD spectra, of the same sign.² (There is, however, a small coupling factor between natural and magnetic optical activity.³) Downie states that "... magnetically-induced optical activity is quite different from natural optical activity in the type of information that it provides. Specifically, magnetically-induced optical activity measures quantities pertinent to the electronic structure of molecules while natural optical activity reveals subtleties regarding molecular stereochemistry."⁴

It is thus not surprising⁵ that application of a magnetic field to an irradiation mixture does not affect the outcome of its stereochemistry.

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CHAPTER 6

AN INVESTIGATION OF THE POSSIBLE DIFFERENTIAL RADIOLYSIS
OF AMINO ACID OPTICAL ISOMERS BY ^{14}C BETAS

AN INVESTIGATION OF THE POSSIBLE DIFFERENTIAL RADIOLYSIS
OF AMINO ACID OPTICAL ISOMERS BY ^{14}C BETAS

A recent report by Garay presents evidence that, in alkaline solution, ^{90}Sr β particles and/or their associated bremsstrahlung (γ -rays) cause a more rapid radiolysis of D-tyrosine than of L-tyrosine.¹ The differential effect on the tyrosines was sought, but not found, in acidic solutions. The possible existence of this differential radiolysis was not tested on the crystalline tyrosine enantiomers.

A difference in the radiation susceptibility of amino acid enantiomers might provide the explanation of why modern proteins are constructed almost exclusively of L-amino acids. (The exceptions are a few percent of D-amino acids reported in the proteins of some bacteria and molds.²) However, the Garay alkaline-solution results with tyrosine present certain theoretical difficulties. Although the circular polarization of the ^{90}Sr bremsstrahlung has been demonstrated,³ it is difficult to see how this could lead to any selective radiolysis in dilute aqueous solution. The radiolysis of organic molecules in such solutions is due to the initial production (from the water) of such active species as H atoms, OH radicals, and hydrated electrons, followed by attack of these species on the solute molecules.^{4,5} It is difficult to see how any chirality of the β -rays

or the bremsstrahlung could be induced in the water-derived species. However, the direct action of polarized bremsstrahlung on amino acid molecules in the solid state, in contrast to the necessarily indirect action in dilute aqueous solution, still provides an attractive hypothesis for the existence of the overwhelming predominance of L-amino acids in living systems. If it could be securely demonstrated that, under any plausible prebiotic conditions, D-amino acids were less stable than L-, we could understand the prevalence of the latter in proteins. With one exception, other theories about chirality in living systems ascribe to some chance event in the primitive Earth's history the present prevalence of one enantiomer over the other. The exception is the idea based on a minute fraction of right-circularly polarized light in sunshine.⁶ However, considering the very limited rotations found in the products of laboratory syntheses and/or photolyses carried out under strong sources of polarized light, the idea has gained little favor (see Chapter 1).

Earlier workers have unsuccessfully attempted to induce optical rotatory power in crystalline DL-alanine that was irradiated with the bremsstrahlung from ^{108}Ag and ^{110}Ag .⁷ However, in these experiments the DL-alanine was subjected to reactor neutrons and γ -radiation, as well as to the γ -radiation from the silver isotopes themselves. These additional forms of ionizing radiation

may have masked any possible differential radiolysis induced by the bremsstrahlung.

This laboratory has a considerable stock of ^{14}C -labeled, crystalline DL-amino acids that were synthesized here 12-24 years ago. During the ensuing years these amino acids have been subjected to the radiolytic effects of their own longitudinally polarized β particles. Carbon-14 is a pure β emitter; thus, the amino acids were subjected to no nuclear γ -rays. The β particles have a low kinetic energy (maximum = 156 KeV) and most of them are stopped in the sample itself. Consequently, the samples are well irradiated by both the β particles and their associated bremsstrahlung, each of which are polarized and present the possibility of a differential interaction with the two optical isomers.

The amount of beta-particle radiation that each sample received was calculated on the basis that all beta particles were absorbed by the sample - a reasonable assumption since the average range of ^{14}C betas (av. energy = 5.0×10^4 eV) in organic material is only about 0.1 mm.⁸ For example, the total radiation absorbed by our DL-norvaline sample, synthesized 15.0 years ago, and having a specific activity of 5.0 $\mu\text{Ci/mg}$ (= 5.0 mCi/gram) is:

$$\begin{aligned} & (5.0 \text{ mCi/gram}) (2.2 \times 10^9 \text{ dis/min/mCi}) (5.0 \times 10^4 \text{ eV/dis}) \\ & \times (5.25 \times 10^{-7} \text{ min/year}) (15.0 \text{ year}) \\ & = 4.34 \times 10^{21} \text{ eV/gram} \end{aligned}$$

The rad (100 ergs/gram) is equivalent to the absorption of 6.2×10^{13} eV/gram. Therefore, the DL-valine's radiation dose was 7.0×10^7 rads.

In Table 1 are summarized the data on our ^{14}C -labeled amino acids.

Table 1
Amino acid ^{14}C -exposure data

	Sp. Act.	Date	Radiation dose, %	
<u>DL-amino acid</u>	<u>mCi/gram</u>	<u>Syn.</u>	<u>Rads ($\times 10^{-7}$)</u>	<u>decomp.</u>
Norvaline	5.0	5/56	7.0	3
Alanine	3.2	9/59	3.5	26
Dopa	1.1	6/47	2.5	3
Aspartic acid	2.4	7/52	4.2	75-80
Methionine	7.3	2/56	10.4	59

The percentages of decomposition were measured on a Beckman Model 120C amino acid analyzer, and by the counting of radioactive spots on paper chromatograms of the radiation-decomposed material. The two methods were in essential agreement in all cases. The apparent small amounts of decomposition of the norvaline and dopa (dihydroxyphenylalanine) are surprising. However, there may have been considerably more radiolysis. If the radiolysis products were volatile, both the amino acid analyzer and the radioactive-spot counting would show less

decomposition than that which had actually taken place.

The analyses for possible differential radiolysis of the optical isomers was carried out by a search for measurable optical activity in each sample. The following amounts of sample were used: norvaline (100 mg), alanine (268 mg), dopa (5.1 mg), aspartic acid (1.093 g), and methionine (185 mg). Each sample was dissolved in 10 ml H_2O and placed in a 7-ml (2-cm) "lollipop" cell and analyzed in the ORD mode of a Cary 60 spectropolarimeter. The sample of aspartic acid was crystallized from ethanol-water yielding 20% of the pure amino acid. This allowed the ORD observation to be extended further into the UV region. (In all cases the impurities resulting from radiolysis gave the samples significant absorption well into the visible). In addition, it provided the possibility of concentrating, in the crystals, the enantiomer that might be in excess in the impure material. It is known that the aspartic acid enantiomers are less soluble in water than is the racemate,⁹ and there is no reason to believe that the L- (or D-) crystals are thermodynamically less stable than the DL-crystals.¹⁰

No rotations were found within the sensitivity of the spectropolarimeter (0.002°). Using the equation of Kuhn and Knopf,¹¹ then, an upper limit to the degree of differential decomposition could be found for each sample. (Differential decomposition = $(k_D - k_L)/(k_D + k_L)/2$,

where k_D and k_L are the rates of decomposition of the D and L enantiomers, respectively). These were: norvaline, 4.0; alanine, 0.08; dopa, 17.0; aspartic acid, 0.007; methionine, 0.5. The upper limit values for norvaline and dopa were very high due to the low degree of decomposition of these samples, and the low specific rotation for methionine also resulted in a high upper limit. However, the results for alanine and aspartic acid clearly rule out any significant differential radiolyses in these cases.

The failure to detect any differential radiolysis may be rationalized in one of two ways. First, of course, the enantiomers may react equally to polarized β and γ -rays. Second, ^{14}C betas have a low kinetic energy (156 KeV maximum), and the degree of polarization is known to be directly proportional to that energy.¹² Thus, β particles from ^{14}C may not have sufficient polarization to cause experimentally observable amounts of differential radiolysis of amino acid enantiomers.

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