

calculations were carried out using a PDP8/I computer. Resonance integrals were taken to be β for adjacent atoms, 0 for nonadjacent atoms, 1.5β for a strong bonding interaction, and 0.5β for a weak bonding interaction. The result of Jacobi diagonalization of the resulting H-matrix afforded a list of eigenvalues, eigenfunctions, and a bond-order matrix.

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Preparation of Chiral Compounds with High Optical Purity by Irradiation with Circularly Polarized Light, a Model Reaction for the Prebiotic Generation of Optical Activity¹

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Abstract: The partial photodecomposition of racemic α -azido-*N,N*-dimethylpropionamide and of camphor with circularly polarized light was investigated. The evolution of the enantiomeric yield during the course of the photolysis is reported. The experimental results are in good agreement with theoretical values obtained from a computer simulation of the chemical system. The highest enantiomeric yield achieved yet in an asymmetric transformation induced by circularly polarized light is reported; namely, by carrying the photodecomposition of racemic camphor to 99% completion, the residual starting material had an enantiomeric purity of $19.9 \pm 2\%$. Calculations show that by carrying the reaction to 99.99% completion the residual camphor would be 35.5% enantiomerically pure. It is shown that the obtention of very high optical purity is therefore possible by this way. The relationship between the significance of these results and the prebiotic generation of optical activity is discussed.

The way by which optical activity was generated and propagated on Earth is not yet fully understood and several processes could be postulated. This is a fascinating problem which is closely related to the origin of life, and Pasteur³ regarded the generation of optical activity as having a cosmic origin, as a consequence of the dissymmetry of the Universe.

Discussions and speculations about the appearance and propagation of optical activity can be found very early in the literature. For example, Le Bel^{4a} and Van't Hoff^{4b} considered circularly polarized light as a way to create the optical activity found in living systems. The propagation and increase of a small optical activity in living systems has been discussed by Mills.⁵ Prebiotic chemistry has recently received much attention and optical activity remains one of the points to be clarified. Several recent articles have reviewed the different theories and the experimental evidence.⁶⁻¹² A

part of this material was recently reinvestigated^{13,14} and the review by Vigneron¹⁵ seems to be the most complete to date.

To achieve the synthesis of a living system in one enantiomeric form two questions need in general to be considered: (a) the initial creation of a racemic mixture slightly enriched in one antipode and (b) the chemical evolution giving rise to the optically pure material. Chemical evolution which does not need the help of a new chiral auxiliary was recently discussed from a theoretical point of view and some models were proposed¹⁶⁻¹⁸ involving autocatalysis.

Several ways to initiate optical activity were suggested, such as spontaneous resolution¹⁰ and preferred crystallization of either one enantiomer¹⁹ or a labile chiral compound.^{20,21} Photochemistry with circularly polarized light²²⁻²⁵ was also considered for achieving the partial destruction or the optical activation²⁶ of a race-

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mic mixture as well as asymmetric syntheses.²⁷⁻³⁰ The maximum enantiomeric excesses of the compounds prepared by these photochemical methods were of the order of 0.5%.³¹

We wish to report evidence that *circularly polarized light can be used to prepare chiral compounds of very high enantiomeric purity*, thereby avoiding the complicated evolution processes necessary to increase a small initial optical activity to its maximum value.

Prebiotic Significance of Circularly Polarized Light.

Since the initial suggestion of Le Bel^{4a} to use circularly polarized light as a "chiral reagent," several experimental observations have shown that light which was in contact with the Earth in prebiotic times could have been circularly polarized. Thus the light diffused by Jupiter and other planets was observed by Kemp to be circularly polarized.³⁶ Mortberg³⁷ has discussed the possible relationship between the asymmetry of a planetary system and molecular asymmetry whereby linearly polarized light falling on a planet is subjected to a magnetic field, and successive refractions in the atmosphere could eliminate one of the circularly polarized components of the light. This interesting theory is similar to ideas put forth by Pasteur.³

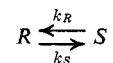
The diffusion of light below the surface of the sea is another natural source of circularly polarized light which can reach an ellipticity of 0.3.^{38,39} The origin of this circularly polarized light comes from an initial diffusion in the sea producing a linear polarization. This light can then be rediffused toward the surface at an angle greater than 48°, giving a reflected light which is now elliptical by polarization. This phenomenon could be of importance in initiating a local predominance of one enantiomer over the other in the prebiotic soup.

In conclusion, enough experimental data exist to support the assumption that circularly polarized light could be one chiral factor involved in the creation of optical activity. This is why chemical models are of interest in evaluating the ability of circularly polarized light to produce compounds enriched in one enantiomer.

Characteristic Features of Asymmetric Reactions Performed with Circularly Polarized Light. The evolution of optical activity in a reaction medium, or of enantiomeric purity of the reactants as a function of either time or extent of reaction, depends on the nature of the asymmetric transformation effected by the circularly polarized light. We classify these transformations in three categories, a-c, namely (a) optical

activation of a racemic mixture, (b) partial decomposition of a racemic mixture, and (c) asymmetric synthesis, respectively.

The reaction described by Stevenson and Verdieck²⁶ as a partial photoresolution may be considered as a particular example of the optical activation of a racemic mixture (category a). In fact, this reaction is a photoequilibration between the two enantiomers, *R* and *S*, of a trioxalatochromate(III) complex



The rate constants, k_R and k_S , are proportional to the molecular absorption coefficients (ϵ_R and ϵ_S , respectively) for polarized light. The enantiomeric purity of the irradiated compound increases progressively to reach a value corresponding to a steady state, such that $C_R/C_S = \epsilon_S/\epsilon_R$. The maximum value of the enantiomeric purity y is attained when the photoequilibration is established and depends solely on the anisotropy factor g , defined by

$$g = \Delta\epsilon/\epsilon$$

where $\Delta\epsilon = \epsilon_R - \epsilon_S$ and $\epsilon = 1/2(\epsilon_R + \epsilon_S)$. Thus

$$y = \frac{C_R - C_S}{C_R + C_S} = \frac{|\epsilon_S - \epsilon_R|}{\epsilon_S + \epsilon_R} = \frac{\Delta\epsilon}{\epsilon} = g/2$$

In the case of an asymmetric synthesis (category c) the enantiomeric purity of the product formed is constant whatever the extent of the reaction as was shown in the synthesis of [8]- and [9]helicenes by circularly polarized light.¹ In this type of reaction, the maximum enantiomeric excess attained was always very small. For example, in the synthesis of helicenes^{26,29} the enantiomeric yields were below 1%.

The variation of optical activity (category b) as a function of time, obtained by the *photodestruction of a racemic mixture* with circularly polarized light, has been studied by Mitchell.²⁴ A solution of *N*-nitrosohumulene was irradiated and its rotatory power monitored. The optical activity was initially zero but it increased, went through a maximum, and reached zero at the end of the reaction, the optically active product having then been totally destroyed. The curve given by Mitchell concerns the variation of the optical activity of the irradiated solution but does not show the evolution of the enantiomeric excess of the chiral substance. The asymmetric destruction of a racemic mixture (*R,S*) by circularly polarized light is a slightly asymmetric transformation which can be represented by two competitive, pseudo-first-order reactions with unequal rate constants, k_R and k_S for *R* and *S*, respectively. In this discussion the nature of the products is immaterial.

The rate constants are proportional to the molecular absorption coefficients (ϵ_R and ϵ_S , respectively) of the two antipodes *R* and *S*, and the efficiency of a partial asymmetric destruction depends on the ratio k_R/k_S or, in this case as Kuhn has already outlined,²³ on the anisotropy factor g

$$g = 2 \frac{\epsilon_R - \epsilon_S}{\epsilon_R + \epsilon_S} = 2 \frac{k_R - k_S}{k_R + k_S} = 2 \frac{k_R/k_S - 1}{k_R/k_S + 1}$$

Putting $K = k_R/k_S$, we have $K = (1 + g/2)/(1 - g/2)$.

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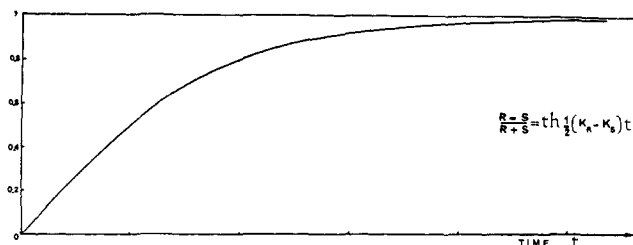


Figure 1. Evolution of enantiomeric purity $(R - S)/(R + S)$ in a kinetic resolution as a function of reaction time for given k_R and k_S rate constants.

Starting from the equations for first-order kinetics

$$d[R]/dt = -k_R[R]$$

$$d[S]/dt = -k_S[S]$$

we obtain

$$[R] = [R_0]e^{-k_R t}$$

$$[S] = [R_0]e^{-k_S t}$$

where $[R]$ and $[S]$ represent the concentration of the antipodes at time t .

Enantiomeric excess y as a function of time is therefore given by

$$y = \frac{[R] - [S]}{[R] + [S]} = \frac{R_0 e^{-k_R t} - S_0 e^{-k_S t}}{R_0 e^{-k_R t} + S_0 e^{-k_S t}}$$

If one starts with a racemic mixture, $R_0 = S_0$ at time $t = 0$ (Figure 1). Thus

$$y = \frac{e^{(k_S - k_R)t} - 1}{e^{(k_S - k_R)t} + 1}$$

i.e.

$$y = \tanh \frac{1}{2}(k_S - k_R)t \quad (1)$$

The hyperbolic tangent function is one which increases continuously with time and thus the enantiomeric purity in a photoreaction tends to unity as the time tends to infinity. This remarkable fact means that photodecomposition should lead to a product with *enantiomeric purity approaching unity even if the reaction is only weakly stereoselective*, as is always the case in reactions induced by circularly polarized light. Of course, as the optical yield approaches unity the chemical yield approaches zero. This point will be discussed later on quantitative basis.

Equations similar to eq 1 were developed by pioneering workers thinking about asymmetric destruction by enzymes.^{40,41} The theoretical aspects of asymmetric photodecomposition were first considered by Kuhn and Knopf²³ and it is surprising to find that although the relationship stated in eq 1, as well as the consequences derived from it, was clearly expressed by them in 1930, they seem to have remained completely unnoticed by all those later authors who proposed models to explain the appearance and propagation of optical activity. Actually, it does not seem necessary to consider complicated systems to obtain optical enrichment starting from a weak optical activity. In the case of asymmetric

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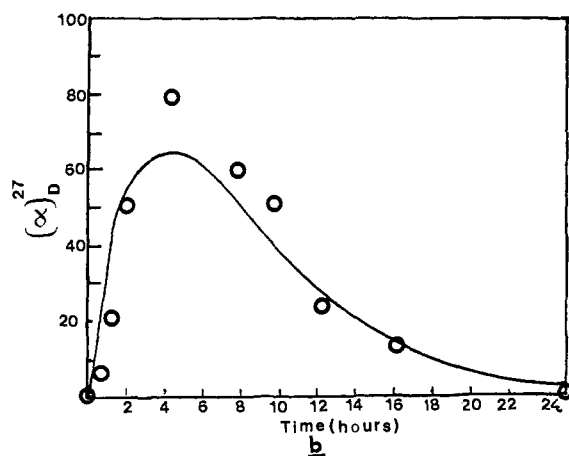
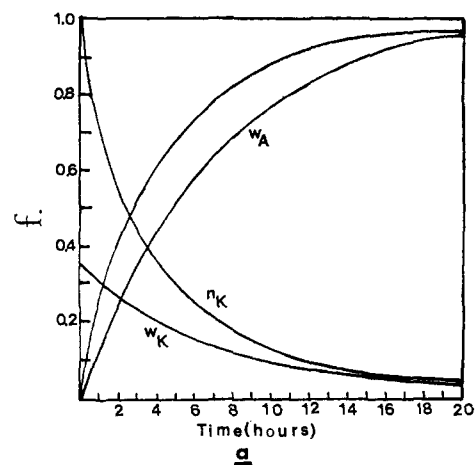


Figure 2.⁴² (a) Calculated fractional (f) enantiomeric purities (W_A and W_B) and mole fractions (n_A and n_K) in a kinetic resolution of pseudo first order. A and K represent the product and the starting racemic material, respectively. (b) Curve of calculated specific rotation of the mixture (A + K) as a function of time for $k_R/k_S = 2.2$. Circles are experimental points.

photodecomposition, an antipode of very high enantiomeric purity should be isolated readily provided that the reaction be allowed to proceed far enough, *i.e.*, to destroy a sufficient proportion of the starting material. As far as we are aware a simple rigorous experimental verification of the relationship represented by eq 1 has never been published. The result reported by Kuhn and Knopf²³ in 1930 concerned only a 40% extent of reaction, allowing the isolation of α -azido-*N,N*-dimethylpropionamide (1) with enantiomeric purity of the order of 0.5%.

The variation of the enantiomeric purity with time in a resolution had also been discussed by Mislow and co-workers⁴² in their study of the asymmetric reduction of a racemic ketone, 1',4'-dinitrodibenzo-1,2,3,4-cycloheptadi-1,3-en-6-one (DNDBCH-6-one), by chiral alcohols in the presence of aluminium *tert*-butoxide (the Meerwein-Ponndorf-Verley reaction). In the presence of a large excess of the chiral alcohol the reduction was a pseudo-first-order reaction. The theoretical treatment of this system is thus identical with that of the asymmetric photodecomposition and allowed Mislow and coworkers to obtain the curves shown in Figure 2. Their experimental verification only concerned the

(42) P. Newman, M. Rutkin, and K. Mislow, *J. Amer. Chem. Soc.*, **80**, 455 (1958).

evolution of the optical activity of the constituents. It therefore appeared important to reinvestigate this question both on a formal mathematical basis and also experimentally, in the specific case of a partial photodecomposition.

Equation 1 represents the variation of the enantiomeric purity with time and the extent of reaction x can be defined by

$$x = 1 - \frac{[R] + [S]}{[R_0] + [S_0]}$$

where $[R]$ and $[S]$ represent the amount of the antipodes left and $[R_0]$ and $[S_0]$ the initial amounts of each antipode at time $t = 0$. For a racemic mixture $[R_0] = [S_0]$, which leads to

$$x = 1 - (e^{-k_R t} + e^{-k_S t})/2 \quad (2)$$

In order to know how the enantiomeric purity y varies with the extent of reaction x , one must either eliminate the time t to obtain

$$y = f(x)$$

or else calculate values of x and y for identical values of t and plot the results graphically. The former method leads to eq 3. The values of Table I and the curves of

$$x = 1 - \frac{1}{2} \left[\left(\frac{1+y}{1-y} \right)^{1/2 - 1/g} + \left(\frac{1+y}{1-y} \right)^{-1/2 - 1/g} \right] \quad (3)$$

Table I

Extent of rxn, %	Enantiomeric purity, %					
	$g = 0.02$	$g = 0.08$	$g = 0.24$	$g = 0.80$	$g = 1.00$	$g = 1.50$
10	0.11	0.42	1.27	4.25	5.33	8.14
20	0.22	0.89	2.68	9.07	11.44	17.75
30	0.36	1.43	4.29	14.59	18.49	29.24
40	0.51	2.04	6.15	21.02	26.73	43.00
50	0.69	2.77	8.34	28.61	36.47	53.31
60	0.92	3.67	11.02	37.76	48.07	77.37
70	1.20	4.82	14.47	49.04	61.85	92.79
80	1.61	6.44	19.30	63.28	77.60	99.20
90	2.30	9.20	27.38	81.38	92.83	99.99
95	3.00	11.95	35.17	91.60	98.06	>99.99
99	4.60	18.28	51.63	98.93	99.92	>99.99
99.9	6.90	27.09	70.12	99.95	99.99	>99.99
99.99	9.20	35.50	82.59	99.99	>99.99	>99.99

Figure 3 represent the variation of the enantiomeric purity as a function of the extent of reaction for different values of the anisotropy factor g and were calculated by computer (see Experimental Section). These curves confirm that very high enantiomeric purities should be attained by photodecomposition and the curves corresponding to high values of g show that an almost optically pure starting material should be isolated before its decomposition has gone to completion. This conclusion is not apparent when time is taken as the variable.

Experimental Verification. In order to confirm experimentally the calculated values (Table I, Figure 3) we first reinvestigated the photodecomposition of the racemic compound **1**, previously studied by Kuhn.²³ The curve of variation of the anisotropy factor g with

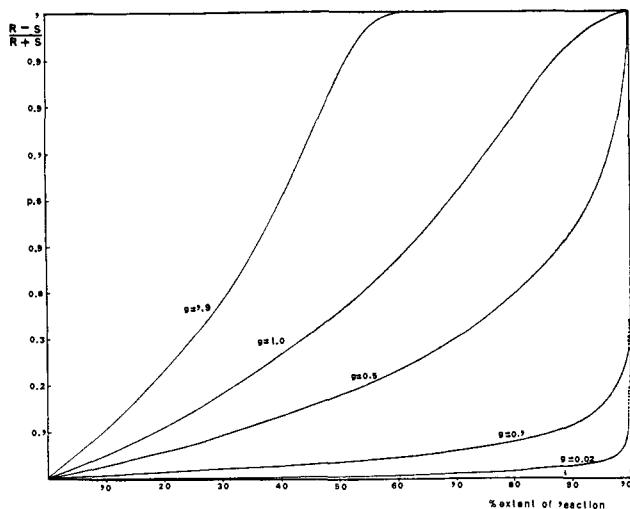
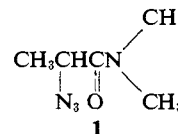


Figure 3. Evolution of enantiomeric purity in a photoresolution as a function of g factor and extent of reaction.

the wavelength of the circularly polarized light⁴³ shows a maximum $g = 0.024$ for λ 280 nm, and for λ 310 nm the value of g is 0.02, corresponding to a value of 1.02 for K (the ratio of the rate constants). As we have stated above, Kuhn's experiments were conducted up to a 40% extent of the reaction and the remaining starting material had $[\alpha]_D$ 1.04° (neat), corresponding to an optical purity of 0.5%. In our hands the photodecomposition of **1** was followed over the range 25–



50% extent of reaction, irradiating a solution of 10 g of the racemic compound in hexane in each run. The extent of reaction was estimated by the amount of gas evolved and the remaining azidoamide was isolated by distillation and its specific rotation measured. Our results show that the experimental values of the enantiomeric purity correspond quite well with the predicted, theoretical values (Table II).

Table II

Extent of rxn, %	Enantiomeric purity of 1 , %	
	Calcd $g = 0.02$	Obsd
20	0.22	0.17
35	0.43	0.34
40	0.51	0.4, 0.5 ^a
50	0.69	0.50, 0.60

^a From ref 23.

The discrepancies arise from a variation of g in the irradiation band used. Beyond a certain degree of irradiation, secondary reactions, previously noted by Kuhn, led to a deposit on the walls of the reaction vessel and prevented us from obtaining an extent of reaction greater than 50%. Nevertheless, these experiments conclusively showed the increasing optical purity of **1** in the course of its asymmetric photodestruction.

(43) W. Kuhn and H. L. Lehmann, *Z. Elektrochem.*, 37, 549 (1939).

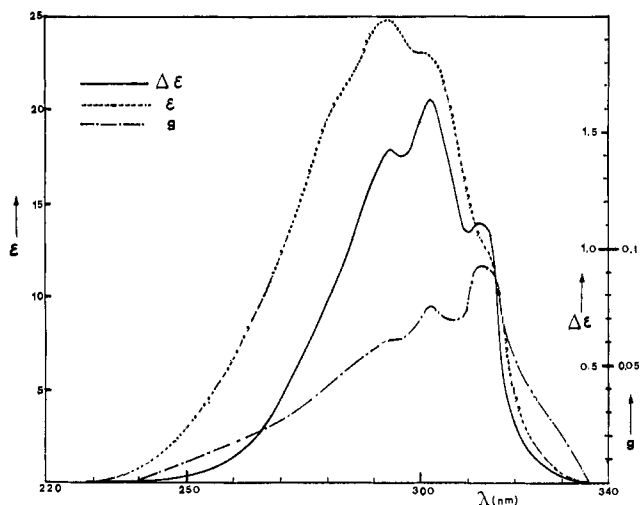
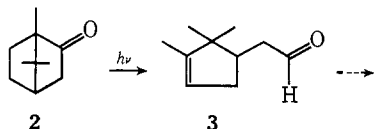


Figure 4. Absorption (ϵ), circular dichroism ($\Delta\epsilon$), and anisotropy factor (g) of camphor in hexane.

In order to obtain further quantitative results to test the theoretical conclusions another system was investigated. A study of the asymmetric decomposition of racemic camphor **2** was undertaken because of its



high g factor (0.09 at 310 nm, as shown in Figure 4) and because the photochemistry of camphor is well known, the primary photoproducts being the α -campholenic aldehyde **3** resulting from a Norrish I cleavage (see ref 44 and 45). Since the products of photolysis can be identified by gas-liquid-phase chromatography (glc) the extent of the reaction can be easily followed. The reverse reaction of closure has not been reported.

Each photolysis was performed on a solution of camphor in hexane and the extent of reaction was determined by glc (see Experimental Section). The camphor was isolated from the reaction mixture by preparative glc and its specific rotation was determined.

Figure 5 shows that the observed values of the enantiomeric purity fall on the theoretical curve corresponding to a g value of 0.08. One reason for the small divergence of this value from $g = 0.09$, which applies only to a quite narrow wavelength band (315–330 nm) is that the radiation employed had a slightly larger wavelength spread (290–370 nm), requiring that an average g factor for this band be used in the calculations.

Discussion and Conclusion

A good agreement between predicted and observed values for the enantiomeric purity during different stages of a partial photodecomposition has been found. We have been able to carry the photodecomposition of racemic camphor far enough to recover camphor with an enantiomeric purity of 20%. *At present this is the greatest enantiomeric purity brought about by using circularly polarized light as the sole chiral agent.*

(44) J. Meinwald and R. A. Chapman, *J. Amer. Chem. Soc.*, **90**, 3218 (1968).

(45) W. C. Agosta and D. K. Heron, *J. Amer. Chem. Soc.*, **90**, 7025 (1968).

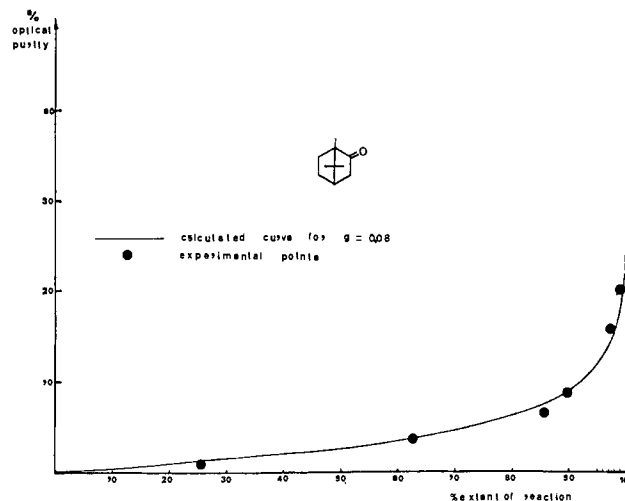


Figure 5. Photodestruction of racemic camphor by left circularly polarized light.

Calculations show that it should be possible to easily obtain even greater enantiomeric purities if a compound with a suitable g factor is available. *trans*-Hydrindan-2-one has the highest known value of g (0.24),^{46,47} and Table I shows that an enantiomeric purity of 52% ought to be attainable if the photodecomposition is stopped at the same stage (99%) as was adopted for camphor.

The ideas put forward by Kuhn in 1930 concerning a prebiotic intervention by circularly polarized light were relatively hypothetical at the time they were postulated. Taking into account the progress made toward understanding the possible origins of circularly polarized light and also toward obtaining significant optical purities experimentally, it is no longer possible to ignore Kuhn's hypotheses.

The process has necessarily been slow on the evolutionary time scale because of the need to bring large quantities of material into play. A continuing photolytic process induced by circularly polarized light can be imagined, finally giving rise to by-products which would be eliminated while a small amount of chiral substance would be retained as a catalyst for propagating optical activity. One can also envisage a series of photolytic steps occurring at different periods with the elimination of by-products at some intermediate time, but the final result remains the same.

We have not discussed the case where the products from the photolyses are themselves chiral. The enantiomeric purity of the products decreases throughout the course of the photolysis, from an initial value of $(K - 1)/(K + 1)$. It is therefore less interesting to consider reaction models where the optical activity is concentrated more in the products than in the remaining starting material. However, it is possible to overcome this difficulty by means of consecutive reactions; the beneficial effect of a chain of weakly asymmetric reactions starting with a racemic mixture was foreseen by Yamagata,⁴⁸ and we are working in this direction.

Our calculations allow us to discuss on a quantita-

(46) C. A. Emeis, L. J. Oosterhoff, and G. De Vries, *Proc. Roy. Soc., Ser. A*, **297**, 54 (1967).

(47) There has been no recent tabulation of g factors since that of S. F. M. Mason, *Quart. Rev., Chem. Soc.*, **17**, 20 (1963).

(48) Y. Yamagata, *J. Theor. Biol.*, **11**, 495 (1966).

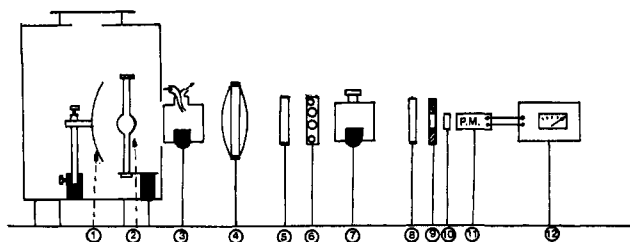


Figure 6. Schematic diagram of the irradiation apparatus.

tive basis the attempts to demonstrate the possibility of inducing optical activity by the bremsstrahlung from β radioactivity.³¹⁻³³ It was recently demonstrated by Bonner³⁵ that racemic leucine can be partially destroyed without any stereoselectivity at up to 80% of decomposition (at 0.5% precision on enantiomeric purity). To see 0.5% of enantiomeric excess in the decomposition of a racemic amino acid it would be necessary to achieve 99.99% of destruction if $k_R/k_S = 1.001$.

Apart from the fact that a clarification of the quantitative effects of the use of circularly polarized light can be hoped for, our calculations (Table I) indicate a possible application of kinetic photodecomposition, namely the determination of the maximum rotatory power and g factor (and thus $\Delta\epsilon$) of the enantiomers in a racemic mixture. It should be only necessary to perform two separate photodecompositions to known extents of reaction, x_1 and x_2 , with isolation of the material remaining in each case, allowing the determination of the specific rotations $[\alpha_1]$ and $[\alpha_2]$. The corresponding enantiomeric purities, y_1 and y_2 , are unknown but related by

$$y_1/y_2 = [\alpha_1]/[\alpha_2]$$

and it becomes possible to find g from the results of eq 3. Once g is known y can be determined and thence $[\alpha]$ for the enantiomerically pure compound. Experiments to study the validity of this method are in progress.

Experimental Section

Instrumentation. Glc analyses were performed with a Perkin-Elmer F.11 chromatograph. Column A was a 10 ft \times 0.125 in., 15% Carbowax 20M on 60-80 mesh support Gas Chrom Q.

Glc preparative scale separations were achieved using a Carlo Erba fractovap, Model G.V., Serie 200. Column B was a 10 ft \times 0.4 in., 15% D.E.G.S. on 45-60 mesh Chromosorb W. Determination of peak areas was performed with an OTT planimeter.

Optical rotations were obtained from a Perkin-Elmer polarimeter Model 141. Circular dichroism spectra (Figure 4) were obtained from a Roussel-Jouan dichrograph and a Cary spectrometer Model 14 was used to obtain ultraviolet measurements (Figure 4).

Apparatus. Irradiation with circularly polarized light was performed using the apparatus shown in Figure 6, which was the same as that used in our early work and previously described very briefly.²⁶

A 500-W OSRAM (HBO-500) very high pressure mercury lamp was used as the light source (2) behind which placed the elliptical mirror (1). The beam was passed through the cell (d, diameter 100 mm, length 100 mm) containing a circulating solution which was externally cooled and a filter to isolate radiation in the band 290-370 nm was employed. Then the beam was collimated with a fused silica lens 4, diameter 150 mm, focus 150 mm), linearly polarized by a PL 40 polarizing filter (5, Polacoat, Inc.), and, finally, circularly polarized by passing it through a fused silica plate (6) which was made birefractive by compression. The circularity of the light was checked by using the following optical train: a polarizing filter PL 40 (8) similar to the polarizer (5) but used here as an

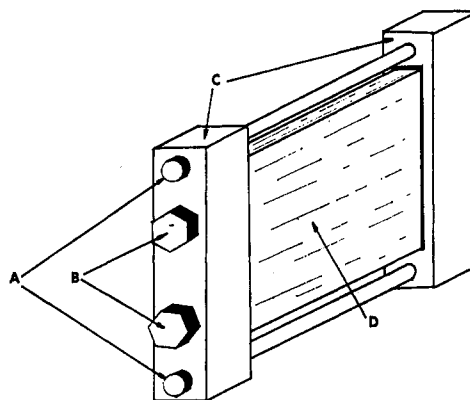


Figure 7. Quarer wave plate system: A and B, adjusting screw; C, metallic holder; D, fused silica plate.

analyser; a diaphragm (9); an interference filter (10, U.V. Pil Schott); and a photomultiplier (11, XP 1118, RTC) coupled with a galvanometer (12, G 323, A.O.I.P.). When circularly polarized light of a given wavelength was desired the filter (10) was used to isolate this wavelength and therefore the intensity of the beam reaching the photomultiplier should have remained constant on rotating the analyser (8) through 360°; if this was not the case the necessary adjustment was obtained by modifying the compression of the silica plate with the adjusting screws A and B (Figure 7). In this work, all the irradiations were carried out with the light circularly polarized for the wavelength λ 313 nm. Therefore, the ellipticity, *i.e.*, the square root of the ratio of minimum to maximum intensity of the beam transmitted by the rotating analyzer (8), was 1.16 for 290 nm and 0.79 for 370 nm.

The solution to be photolyzed was placed in an irradiation cell (7, diameter 100 mm) and therefore the available circularly polarized beam had a diameter of about 100 mm.

Filter. The filter used to isolate the band 290-370 nm has been described by Wladimiroff⁴⁹ and was prepared by dissolving $\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$ (20 g) and $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (10 g) in 550 ml of DMF and 84 ml of HCl (12 N) and then diluting this solution to 1 l. with distilled water.

Actinometry. The light energy available in the irradiation cell was measured by the ferrioxalate method of Hatchard and Parker⁵⁰ and also by the decafluorobenzophenone method.⁵¹ The energy found was about 200 mW for λ 313 nm.

Materials. The solvent used for all the photolyses was Merck Uvasol spectrograde *n*-hexane.

α -Azido-*N,N*-dimethylpropionamide (1). This compound was obtained in a four-step synthesis by the following sequence as described in the literature:^{52,53} ethyl α -azidopropionate from α -bromopropionate, then α -azidopropionic acid, α -azidopropionyl chloride, and α -azido-*N,N*-dimethylpropionamide. The last compound was obtained as a colorless liquid, bp 84-85° (1 mm).

Partial Kinetic Photoresolution of α -Azido-*N,N*-dimethylpropionamide [(±)-1]. A solution of (+)-1 (12.6 g, 0.89 mol) in 660 ml of *n*-hexane was placed in an irradiation cell (volume 660 ml, diameter 100 mm). The photolysis was conducted with the apparatus described in Figure 6. The nitrogen evolved during the irradiation was determined volumetrically and gave the extent of the reaction x . When the required extent x_1 was achieved, the irradiation was stopped, the solvent was removed under reduced pressure, and careful distillation gave optically active α -azido-*N,N*-dimethylpropionamide. The optical rotatory power $[\alpha_1]$ was measured on a neat sample.

Note. For high values of x the accumulation of the degradation products was inconvenient (deposit on the face of the cell, ...). For the purposes of kinetic resolution we were concerned only with the relationship between the extent of reaction and the enantiomeric purity. Therefore, in order to achieve an extent of reaction

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x_2 greater than x_1 , it was possible to submit the isolated product 1 (with $[\alpha]_D$) obtained from the experiment with an extent of reaction of x_1 to a further photolysis under the same conditions. In this way, if a photolysis of reaction extent x' is achieved from this already optically active product 1 ($[\alpha]_D$) the remaining product has a new optical rotatory power ($[\alpha]_D$). The corresponding extent of reaction x_2 of the photolysis starting with (\pm)-1 is given by

$$x_2 = 1 - (1 - x_1)(1 - x') = x_1 + x'(1 - x_1)$$

This procedure was also used by Mitchell.²⁵

We checked that the enantiomeric purity of the remaining compound in the partial photoresolution was the same either by achieving directly the reaction extent x_2 , or by achieving x_1 and then x' , separately. This procedure was used in the photolysis of both α -azido-*N,N*-dimethylpropionamide and camphor.

(\pm)-Camphor. Racemic camphor provided by the Delaire Co. (France) was recrystallized twice from hexane and then sublimed. Its glc analysis showed a purity greater than 99% and the optical activity was $[\alpha]^{25}_D -0.14^\circ$ (*c* 6, hexane).

This racemic camphor was obtained by a synthesis starting from naturally occurring optically active α -pinene and since one of the steps of this synthesis was a racemization, the slight residual optical activity observed in the final product was probably due to incomplete racemization.

A sample of camphor ($[\alpha]_D -0.14^\circ$) purified by the above procedure was submitted to preparative glc, and there was no difference in the specific rotation of the highly purified camphor collected. The presence of an optically active impurity was therefore ruled out, so that the slight optical activity observed was due to an enantiomeric excess of 0.25% in the camphor. For our experiments requiring completely racemic material, we adjusted the rotatory power of the nearly racemic compound to $[\alpha]_D 0.005 \pm 0.005^\circ$ by the addition of optically pure (+)-camphor ($[\alpha]^{25}_D +52.9^\circ$ (*c* 2.5, hexane)).

Partial Kinetic Photoresolution of Racemic Camphor. A solution

of 6 g of racemic camphor in 360 ml of *n*-hexane was placed in the irradiation cell (diameter 100 mm, volume 360 ml) which was closed with a glass stopper and magnetic stirring was maintained during the course of the irradiation. For the determination of the extent of the photodecomposition, 1-ml samples were taken, a known weight of a standard (*n*-hexadecane) was added, and the mixture was analyzed by glc (column A temperature 120°, carrier N₂ 25 ml/min); thus, the disappearance of camphor was determined by measurement of the peak areas of camphor and the standard. When the desired extent of reaction had been achieved the irradiation was stopped. The solvent then was carefully removed avoiding sublimation of remaining camphor which was separated from the mixture of photoproducts by preparative glc (column B temperature 145°, carrier N₂ 100 ml/min). Two such purifications by glc were necessary and the purified camphor was used for the determination of the optical purity. The optical rotatory power was measured in *n*-hexane. We checked that there was no change in the specific activity of a known sample of camphor under these chromatographic conditions. The experimental results are: $x = 25\%$, $y = 0.69 \pm 0.07\%$; $x = 62\%$, $y = 3.7 \pm 0.4\%$; $x = 85\%$, $y = 6.5 \pm 0.7\%$; $x = 90\%$, $y = 9.0 \pm 1\%$; $x = 97\%$, $y = 15.8 \pm 1.5\%$; $x = 99\%$, $y = 19.9 \pm 2\%$.

Computation. The program allowing the simulation of the chemical systems involved in this work was written in FORTRAN IV and used the classical method of numerical integration Runge-Kutta order 4. The computation was performed on Univac 1108 and 1110 computers of the Centre de Calcul de l'Université, Paris-Sud.

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cis-Azoxyalkanes. IV. Preparation and Nuclear Magnetic Resonance Spectra¹

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Abstract: A three-step high-yield procedure for the generation of a series of polycyclic *cis*-azoxyalkanes is described. ¹³C and shift reagent nmr studies confirm the unsymmetrical nature of the NNO unit, while anisotropy calculations provide a basis for understanding the anomalous proton nmr spectra of the title compounds. The effect of both conformation and configuration is assessed and applied to a variety of acyclic azoxyalkanes.

Although azoxyalkanes have surfaced in the chemical literature from time to time³ they first attracted serious attention with the discovery that two naturally occurring pretoxins, macrozamin^{4a,b} and cycasin,^{4c} contain glycosylated methylazoxymethanol. The aglycone portion has since been established as the trigger substance for a series of detrimental biological events.⁵

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(5) Enzymes (β -glycosidases) in the tissues of mammalian systems cleave the sugar residue from the aglycone fragment releasing methyl-

It is of some historical interest that Captain James Cook's crew apparently fell victim to these plant-bound

azoxymethanol (MAM),^{6a} a powerful mutagen and carcinogen.^{6b} The latter has been implicated in the methylation of liver RNA and DNA at the 7 position of guanine.^{7a} Similarly inhibition of DNA synthesis and degradation of cellular DNA occur upon exposure of bacteria (*e.g.*, mutant strains of *E. coli*) to MAM.^{7b} Certain insect larvae, on the other hand, thrive on MAM by performing an *in vivo* synthesis of the relatively nontoxic cycasin from its components.^{7c}

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