Molar Ellipticity of the Pure Enantiomer by Partial Photoresolution. Photoreaction of 4,4,4',4'-Tetramethyl-2,2',3,3'-tetraazaspiro-[4.4]nona-2,2'-diene

Rüdiger Blume, Hermann Rau,* and Otto Schuster

Contribution from the Fachgebiet Physikalische Chemie, Institut für Chemie, Universität Hohenheim, D-7000 Stuttgart 70, West Germany. Received July 16, 1975

Abstract: The molar ellipticity, $[\theta]$ = 178 000 deg cm^2 $dmol^{-1}$ (345 nm), of one pure enantiomer of 4,4,4',4'-tetramethyl-2,-2',3,3'-tetraazaspiro[4.4]nona-2,2'-diene is determined by photolysis with circularly polarized light (cpl). $[\theta]$ is calculated from the maximum value of circular dichroism (CD) during irradiation and the value of optical density (OD) at the same time. By introducing a new variable representing the number of photons absorbed, which replaces the irradiation time, kinetic equations are obtained which can be integrated and linearized. In this way all data from the whle irradiation experiment are used for the graphical evaluation of $[\theta]$. As the degree of circular polarization of the irradiating light enters the equations, they can be used for cpl actinometry.

Molar ellipticity, $[\theta]$, of the pure enantiomer is an important constant for characterization of optically active molecules. The knowledge of this value is necessary for the spectroscopic determination of the optical purity of an enantiomeric mixture.[1] $[\theta]$ is easily obtained if a pure enantiomer is available.[2] There are methods, too, that do not require total resolution of the enantiomers; it is sufficient to determine the ratio of the concentrations of the diasteriomeric derivatives, e.g., with NMR,[3,4] gas chromatography,[5] or isotopic dilution techniques.[6] If the optically active molecules are fluorescent the circular polariation of the emission can be used for determination of optical purity.[7,8]

Partial resolution is achieved by kinetic resolutions,[9] e.g., by photolysis with circularly polarized light (cpl).[1,10-15]

If photoracemization is the only photoreaction, the kinetic evaluation of the photostationary state gives access to $[\theta]$.[13,14] If photodestruction dominates photoracemization $[\theta]$ may be obtained from the initial slopes of plots which contain combined information of CD and OD measurements.[15]

In this paper we present the photodestruction version of a general method of determination of $[\theta]$ by partial kinetic resolution. We analyze the whole CD and OD curves in detail and find numerical and graphical procedures to determine $[\theta]$ either from the information given by the maximum and inflection points of the CD curves or from linearized plots.

The methods are demonstrated using the pyrazoline system. This photolysis is an unequivocal photoreaction because photoracemization cannot be expected for molecules like the pyrazoline I, where a cleavage of bonds leads to nitrogen elimi-

I   II   III
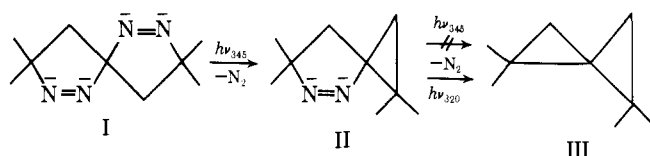
nation. Therefore, irradiation of pyrazolines is an experimentally well developed procedure for the production of cyclic systems.[16] M. Schneider, e.g., used the spiro compound 4,4,4',4'-tetramethyl-2,2',3,3'-tetraazaspiro[4.4]nona-2,2'-diene (I) to produce 2,2,2',2'-tetramethylsppiro[2.2]pentane (III).[17]

General Equations

When a racemic mixture of photoreactive molecules is irradiated with circularly polarized light (cpl)[12] both enantiomeric R and S forms are photolyzed, one of them, however,

faster than the other because of their slightly different absorption coefficients for cpl. So one of the enantiomers is accumulated. We assume that the S form is photolyzed faster than the R form.[1]

This can be used to determine the molar ellipticity, $[\theta]$, of a pure enantiomer if one succeeds in transforming the differential equations of the photochemical reaction to functions of the same type as those of pseudo-first-order dark reactions. For photochemical reactions the true rate-determining quantity is the number of photons asorbed and this number changes with irradiation time t as the absorbance of the solution changes. The parameter τ, which takes the place of the irradiation time t, is defined as

$$\tau \equiv \int_0^t \frac{1 - 10^{-A_\alpha(t)}}{A_\alpha(t)} dt \equiv \int_0^t G(A_\alpha) dt \qquad (1)^{18}$$

where A_α is the optical density at the irradiation wavelength α.

The differing absorption coefficients of the enantiomers for, e.g., right cpl

$$\epsilon_{\alpha S}(+cpl) = \epsilon_\alpha(npl) + (\delta_\alpha/2) \qquad (2a)$$

$$\epsilon_{\alpha R}(+cpl) = \epsilon_\alpha(npl) - (\delta_\alpha/2) \qquad (2b)$$

make the optical density $A_\alpha{}^*(t)$ measured by cpl different from $A_\alpha(t)$ measured by nonpolarized light (npl). Therefore a reaction parameeter for cpl analogous to τ ought to be defined; however as $A_\alpha{}^*(t) \approx A_\alpha(t)$, τ may be retained.

Irradiation with Pure Cpl. During cpl irradiation there are the two independent parallel reactions

$$R \text{ form} \rightarrow \text{Products} \qquad (3a)$$

$$S \text{ form} \rightarrow \text{Products} \qquad (3b)$$

If there are no other reactions (as, e.g., photoracemization), the velocity of photolysis by cpl of the two enantiomers is

$$dc_S(t)/dt = -1000I_0{}^{cpl}\Phi_\alpha\epsilon_{\alpha S}c_S(t)G(A_\alpha)$$

$$dc_S(\tau)/d\tau = -B\epsilon_{\alpha S}c_S(\tau) = -k_2c_S(\tau) \qquad (4a)$$

and:

$$dc_R(t)/dt = -1000I_0{}^{cpl}\Phi_\alpha\epsilon_{\alpha R}c_R(t)G(A_\alpha)$$

$$dc_R(\tau)/d\tau = -B\epsilon_{\alpha R}c_R(\tau) = -k_1c_R(\tau) \qquad (4b)$$

where c_i = concentration of i)mol l.$^{-1}$), $I_0{}^{cpl}$ = constant intensity of the source for cpl (einstein cm^{-2} min^{-1}), and Φ_α =
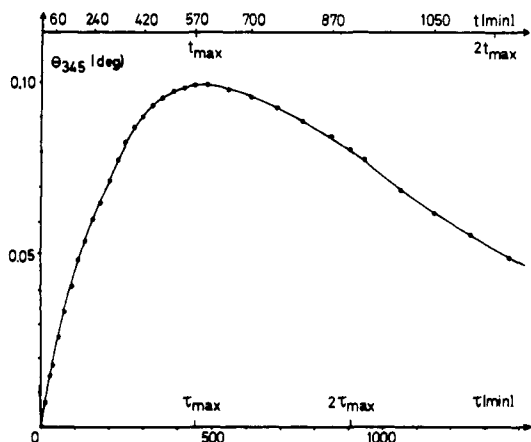
Figure 1. $\theta_{345}-\tau$ diagram of the evaluated experiment. The t axis is incorporated to demonstrate the distortion.
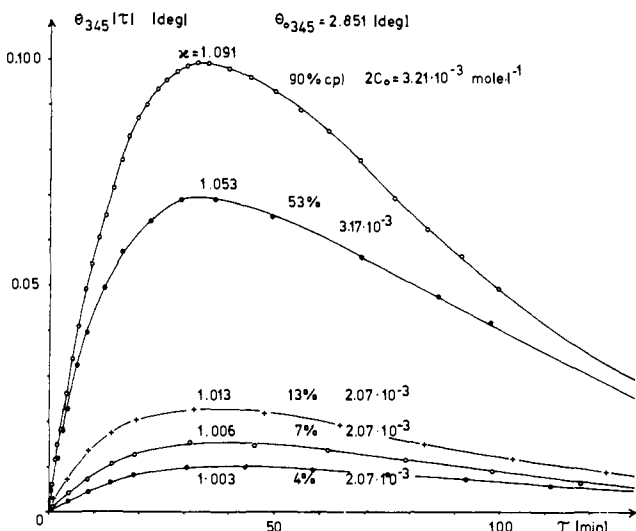

Figure 2. $\theta_{345}-\tau$ diagram of irradiation of spiropyrazoline 1 with varying cpl part. The curves are normalized to equal lamp intensity.

constant quantum yield. Equations 4a,b define the coefficient B (mol cm^{-2} min^{-1}) and the velocity constants k_1 and k_2. The starting concentration of each enantiomer in the racemic mixture is C_0.

Integration of eq 4a,b yields the $c_R-\tau$ and $c_S-\tau$ functions, respectively, which are of the form of those of pseudo-first-order reactions. The concentrations of each enantiomer cannot be determined separately, whereas the sum of these concentrations is given by any nonchirospecific measurement as, for example, absorbance at an arbitrary wavelength λ. The reduced concentration sum is proportional to the reduced absorbance difference R_λ:

$$\frac{c_R(\tau) + c_S(\tau)}{2C_0} = \frac{A_\lambda(\tau) - A_\lambda(\tau \to \infty)}{A_\lambda(\tau = 0) - A_\lambda(\tau \to \infty)} \equiv R_\lambda(\tau) \quad (5)$$

The concentration difference can be obtained from the ellipticity θ_λ at arbitrary wavelength λ:

$$\frac{c_R(\tau) - c_S(\tau)}{C_0} = \frac{\theta_\lambda(\tau)}{\theta_{0\lambda}} \quad (6)$$

$\theta_{0\Lambda}$ (deg) is related to the molar ellipticity $[\theta]_\Lambda$ (deg cm^2 dmol^{-1}) by

$$[\theta]_\Lambda = (100/C_0)\theta_{0\Lambda} \quad (7a)$$

and to the difference $\delta_\Lambda{}^{1,12}$ by

$$\delta_\Lambda = \Delta\epsilon_\Lambda = (\epsilon_{\Lambda R} - \epsilon_{\Lambda S}) = [\theta]_\Lambda/3300 = \theta_{0\Lambda}/33C_0 \quad (7b)$$
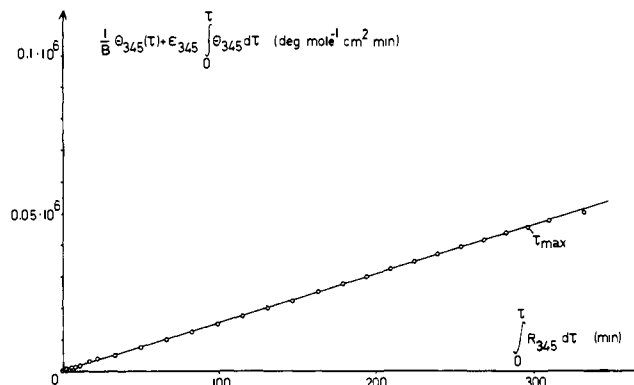

Figure 3. Plot according to eq 13 for the evaluation of $\theta_{0,345}$.

Experimental $\theta_\Lambda-\tau$ curves[11] are plotted in Figures 1 and 2. A maximum exists at the value of the reaction parameter τ

$$\tau_{max} = \int_0^{t_{max}} G(A_\alpha)dt = \frac{\ln \varkappa}{B\delta\Lambda} \quad (8)$$

where $\varkappa = k_2/k_1 = \epsilon_{\alpha S}/\epsilon_{\alpha R} = (\epsilon_\alpha + (\delta_\alpha/2))/(\epsilon_\alpha - (\delta_\alpha/2))$
The ratio of the concentrations is at τ_{max}

$$c_R(\tau_{max})/c_S(\tau_{max}) = \varkappa \quad (9)$$

The inflection point of the $\theta_\Lambda-\tau$ curve is at $\tau_{IP} = 2\tau_{max}$, i.e., at double the value of the integral (eq 8), which is by no means the value of the integral (eq 1) in the limits of $t = 0$ and $t = 2t_{max}$ (see Figure 3). At $2\tau_{max}$ we obtain

$$c_R(2\tau_{max})/c_S(2\tau_{max}) = \varkappa^2 \quad (10)$$

Further important relations are

$$(\varkappa - 1)/(\varkappa + 1) = \tfrac{1}{2}(\delta_\alpha/\epsilon_\alpha), \quad (11a)$$

and with $\delta_\alpha{}^2 \ll \epsilon_\alpha{}^2$

$$(\varkappa^2 - 1/\varkappa^2 + 1) = \delta_\alpha/\epsilon_\alpha \quad (11b)$$

$\delta_\alpha/\epsilon_\alpha$ is Kuhn's anisotropy factor g_α.[12]

By use of eq 11 the determination of $\varkappa$ is unnecessary if θ_Λ is measured at the irradiation wavelength α. From eq 9, 10, 5, 6, and 11 we obtain

$$\theta_\alpha{}^2(\tau_{max}) = \tfrac{1}{2}\theta_{0\alpha}{}^2(1/33C_0)(1/\epsilon_\alpha)\theta_\alpha(2\tau_{max}) \quad (12a)$$

$$\theta_\alpha(\tau_{max}) = \theta_{0\alpha}{}^2(1/33C_0)(1/\epsilon_\alpha)R_\lambda(\tau_{max}) \quad (12b)$$

$$\theta_\alpha(2\tau_{max}) = 2\theta_{0\alpha}{}^2(1/33C_0)(1/\epsilon_\alpha)R_\lambda(2\tau_{max}) \quad (12c)$$

$2C_0\epsilon_\alpha$ can be replaced by $A_\alpha(t = 0)$. With eq 12b it is possible to calculate $\theta_{0\alpha}$ and from it $[\theta]_\alpha$, using only the values of θ_α and R_λ at the time of maximum CD. So we avoid the calculation of the integral (eq 1). Accuracy will be determined by the errors in recognizing the exact time of maximal CD. A help in finding τ_{max} gives $R_\lambda(\tau)$, which decreases essentially exponentially: $R_\lambda(\tau_{max}) \approx 1/e$; $R_\lambda(2\tau_{max}) \approx 1/e^2$.

Equation 12b is sufficient for normal practical requirements; eq 12a and 12c require calculation of the integrals (eq 1).

For eq 12a–c only some prominent points of the experimental data have been used. The following procedure makes use of all experimental points available. From eq 6 and 4a,b we derive with $\Lambda = \alpha$

$$(C_0/\theta_{0\alpha})(d\theta_\alpha/d\tau) = -B[\epsilon_{\alpha R}c_R(\tau) - \epsilon_{\alpha S}c_S(\tau)]$$

Introducing eq 5, 6, 2a,b, and 7 we arrive after integration at

$$(1/B)\theta_\alpha(\tau) + \epsilon_\alpha \int_0^\tau \theta_\alpha(\tau)d\tau = (1/33C_0)\theta_{0\alpha}{}^2 \int_0^\tau R_\lambda(\tau)d\tau \quad (13)$$
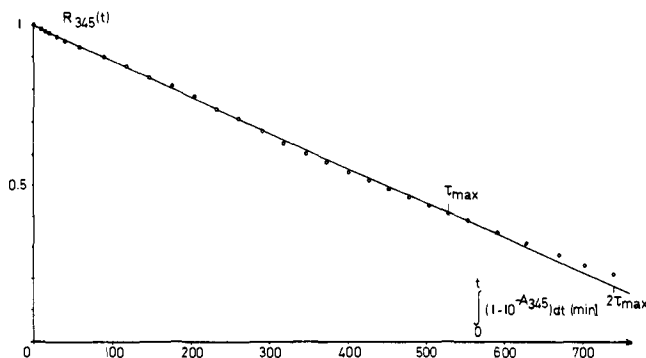
Figure 4. Plot according to eq 15 for the evaluation of B.

A plot of the left side vs. the integral of the right side gives $\theta_{0\alpha}$ from the slope of the straight line through the origin (Figure 3).

However, up to now the constant B is not known. It can be found from the evaluation of the following equations, which are derived from eq 5 and 4a,b:

$$2C_0(dR_\lambda/d\tau) = -B[\epsilon_{\alpha R}c_R(\tau) + \epsilon_{\alpha S}c_S(\tau)]$$

$$1/B[R_\lambda(\tau) - 1] + \epsilon_\alpha \int_0^\tau R_\lambda(\tau)d\tau$$

$$= (1/4.33C_0) \int_0^\tau \theta_\alpha(\tau)d\tau \quad (14a)$$

which can be brought in a form suited for graphical determination of B:

$$R_\lambda(\tau) = 1 - B\left[\epsilon_\alpha \int_0^\tau R_\lambda(\tau)d\tau\right.$$

$$\left. - (1/4.33C_0) \int_0^\tau \theta_\alpha(\tau)d\tau\right] \quad (14b)$$

Numerical calculations show that the term containing $\theta_\alpha(\tau)$ is negligible compared with $\epsilon_\alpha\int_0^\tau R_\lambda(\tau)d\tau$, which is a consequence of $\Delta\epsilon_\alpha \ll \epsilon_\alpha$. Then eq 14b can be transformed to the equation also valid for irradiation with npl:

$$\ln R_\lambda(\tau) = -B\epsilon_\alpha\tau \quad (14c)$$

A straight line results if $\varkappa \approx 1$. If, furthermore, the reaction products do not absorb at the irradiation wavelength, as is the case with the spiropyrazoline I, eq 14b can be simplified

$$R_\lambda(t) = 1 - (B/2C_0) \int_0^t (1 - 10^{-A_\alpha(t)})dt \quad (15)$$

So B can be taken from the slopes of the graphs according to eq 14c and/or 15 (Figure 4).

Variation of the Cpl Part in the Irradiation Light. If the irradiation source does not give pure cpl the differential equations have to be modified, e.g., for $c_R(t)$:

$$dc_R/dt = -1000 \, \Phi_\alpha[I_0^{npl}\epsilon_\alpha G(A_\alpha) + I_0^{cpl}\epsilon_{\alpha R}G(A_\alpha^*)]c_R(t)$$

We define a cpl part γ of total intensity I_0

$$I_0^{cpl} = \gamma I_0 \quad \text{and} \quad I_0^{npl} = (1 - \gamma)I_0$$

With $G(A_\alpha^*) \approx G(A_\alpha)$ we obtain

$$dc_R = -B[\epsilon_\alpha - \gamma(\delta_\alpha/2)]c_R(\tau)d\tau$$

$$dc_S = -B[\epsilon_\alpha + \gamma(\delta_\alpha/2)]c_S(\tau)d\tau$$

By variation of γ the value of $\varkappa$ can be varied, too (see Figure 2).

The integrated R_λ-τ and θ_Λ-τ functions give equations like 13 and 14a, the right-hand side being multiplied by γ. If eq 12a-c are used, γ enters $\varkappa = (\epsilon_\alpha + \gamma(\delta_\alpha/2))/(\epsilon_\alpha - \gamma(\delta_\alpha/2))$ and the right sides of (eq 12a-c) are multiplied by γ. So γ
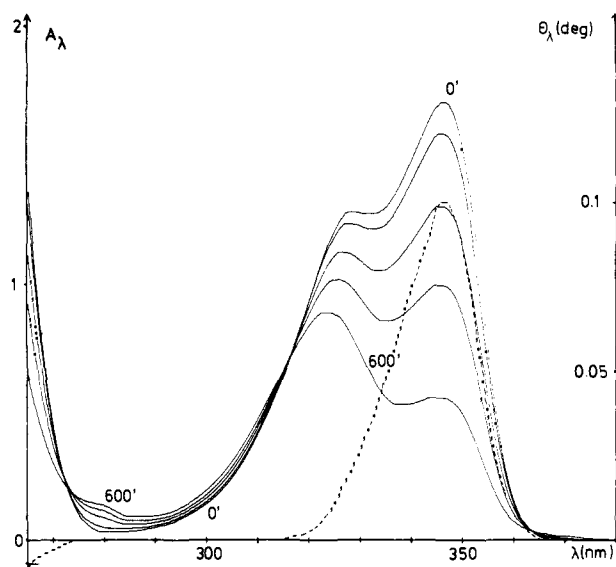

Figure 5. OD and CD spectra (dotted line) of the spiropyrazoline I ($2C_0$ = 3.1×10^{-3} mol l.$^{-1}$).

enters the results as $\sqrt{\gamma}$, which makes small deviations of pure cpl uncritical.

Experimental Section

Materials, Spectra, Irradiation. The spiropyrazoline I was synthesized by Schneider.[17] Solvent was n-hexane (Merck-Uvasol).

OD spectra have been taken with a ZEISS DMR 10 spectrophotometer, CD spectra with a Cary 60 spectropolarimeter with CD attachment 6002. The OD measurements at fixed wavelengths were taken with a ZEISS PM QII spectrophotometer.

The irradiation set-up consisted of a XBO 450-W Xenon high-pressure source (OSRAM), a grating monochromator (Bausch & Lomb 33-86-79), a linear polarizer (Halle), a Fresnel parallelepiped (Karl Lambert), and a 10-mm ORD cuvette.

The irradiation wavelength was at 345 (±7) nm (maximum of the n $\rightarrow$ π^* band), the cpl part γ of the radiation was 90%, which was determined by an additional rotable linear polarizer of the same make as the linear polarizer (Halle), combined with a semiconductor photoelement (Siemens BPY 11).

This combination was placed in the irradiation set-up instead of the cuvette. The maximal and minimal reading of a galvanometer due to rotation of the second linear polarizer gives the circularity

$$\gamma = \frac{\text{minimal intensity}}{\text{maximal intensity}}$$

We also used a cutoff filter and a $\lambda/4$ device (365 nm) for polarizing the irradiating light. The polarizing effect of the $\lambda/4$ plate is strongly wavelength dependent and the one we have is rather inefficient at the wavelength of the n $\rightarrow$ π^* band, so accumulation is small. Moreover with broad band irradiation and a $\lambda/4$ device, circularity changes over the absorption band. Mean circularities have to be calculated, which are not too reliable. The curves for 13, 7, and 4% cpl in Figure 2 are of this sort. A Fresnel parallelepiped is strongly recommended.

Results and Evaluation

A cpl photolysis experiment (α = 345 nm) with the total concentration of racemic spiropyrazoline I of $2C_0$ = 3.20 $\times$ 10^{-3} mol l.$^{-1}$ has been evaluated; ϵ_{345} 555 mol^{-1} cm^2. Typical OD spectra during irradiation with cpl and the CD spectrum of maximal amplitude of a cpl-irradiated solution are presented in Figure 5.[19] Isosbestic points[20] as well as the linear absorbance diagrams[21] (Figure 6) indicate a simple photoreaction. Comparison of CD and OD spectra reveal that the photoproduct II, which has an n $\rightarrow$ π^* band with maximum at 321 nm, is not optically active on the scale of I.

To determine $[\theta]_{345}$ we used the θ_{345} values and the A_{345}, A_{350}, and A_{355} values at identical irradiation times. The ab-

Table I.

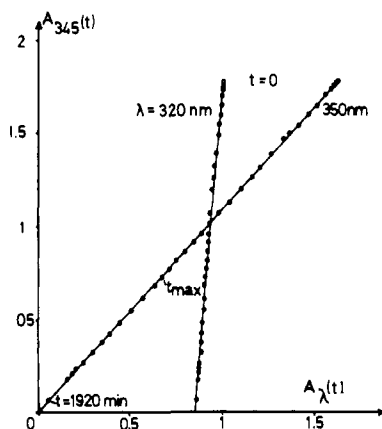| Equation	$\theta_{0,345}$, deg	$[\theta]_{345}$, deg cm^2 dmol^{-1}	$\Delta\epsilon_{345} = \delta_{345}$ mol^{-1} cm^2	g_{345}	x
12a	2.822	176 000	53.33	0.096	1.090
12b	2.806	175 000	53.03	0.096	1.090
12c	2.788	174 000	53.73	0.095	1.090
Average (12a–c)	2.805	175 000	53.03	0.096	1.090
13	2.989	186 000	56.36	0.102	1.096
Total average	2.851	178 000	53.86	0.097	1.091

Figure 6. Absorbance diagram of the photoreaction.

sorbance diagram shows that the photoproducts do not absorb at $\alpha = 345$ nm and $\lambda = 350$ nm, since $A_\lambda(\tau \rightarrow \infty) = 0$. So eq 15 can be evaluated to determine B.

Integration of the $G(A_{345})$-t function (eq 1b) using the trapezoid approximation gives the τ coordinate of the other figures. In Figure 1, which shows the θ_{345} values as a function of τ, the axis of irradiation time t is given for comparison and demonstration of the large difference between $2t_{max}$ and $2\tau_{max}$. Figure 4 is a plot of eq 15 for the determination of B. This constant has been determined also from plots of eq 14b and c. The average value is $B = (3.59 \pm 0.06) \times 10^{-6}$ mol cm^{-2} min^{-1}. With this value the data of the straight line of Figure 3 are calculated. From the slope we obtain $\theta_{0,345}\sqrt{\gamma} = 2.836°$ and with $\gamma = 0.90$ we calculate $\theta_{0,345} = 2.989°$.

The simpler evaluation according to eq 12b gives with $\theta_{345}(t_{max}) = 0.0994°$ and $R_{345}(t_{max}) = 0.412$ the value of $\theta_{0,345} = 2.806°$. By use of eq 12a with $\theta_{345}(2\tau_{max}) = 0.081°$, the value of $\theta_{0,345} = 2.822°$. From eq 12c we calculate with the measured value $R_{345}(2\tau_{max}) = 0.215$ $\theta_{0,345} = 2.479°$. This value is considerably at variance from the others. The reason is that the measured data of R_λ in Figure 4 deviate systematically from the straight line for long irradiation times ($\gtrsim 10$ h). This can be attributed to solvent evaporation as a major factor (CD cuvettes have to have a pressure release). Correction of the $R_\lambda(2\tau_{max})$ to the straight line gives $R_\lambda(2\tau_{max}) = 0.17$ and with this value $\theta_{0,345} = 2.788°$.

The accuracy of the $\theta_{0\lambda}$ values from eq 12a–c depends on the quality of determination of t_{max}. Variation of t_{max} between 570 ± 30 min gives changes in $\theta_{0,345}$ of $\pm 3\%$ (eq 12a,b) and $\pm 5.6\%$ (eq 12c).

The results for different evaluation procedures are accumulated and averaged in Table I.

The values of $[\theta]_{345}$ according to eq 12 and 13 differ $\pm 5\%$ from the total average. The evaluation procedures and, accordingly, the errors are quite different. Whereas eq 12 uses the prominent points and the errors depend on the accuracy of the experimental determination of t_{max}, the errors in eq 13 produced by the double integration, which is performed graphically, add to the experimental errors.

As the anisotropy factor is high ($g_\alpha = 0.1$), the accumulation at t_{max} is 1.7% of the starting material. The optical purity is: at $t_{max} = 4.3\%$ and at $2\tau_{max} = 8.4\%$. At t_{max} the destruction of the spirane I is $[1 - R_\lambda(t_{max})]100 = 59\%$,[1] at $2\tau_{max}$ 83%.

The spiropyrazoline I has a very high optical activity. This is probably due to the n–π orbital overlap of the two cis-azo groups. A spectroscopic investigation is under way.

In many laboratories where the referred polarizing unit we employed is not available, circularly polarizing sheets are used. These usually have a γ well below unity. γ can be determined if the sheet is transparent at 345 nm by use of I as a cpl actinometer. As the alignment of a polarizing unit as ours is somewhat critical, the calibration of a cpl irradiation set up by an actinometer is advisable, too.

References and Notes

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