A REVIEW OF ABSOLUTE ASYMMETRIC SYNTHESES BY CIRCULARLY POLARIZED LIGHT

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ABSTRACT. — The paper discusses the use of circularly polarized light for the purpose of absolute asymmetric syntheses. A theoretical section includes mechanistic requirements as well as a quantitative description of the process. Pertinent experiments involving both asymmetric photolysis and asymmetric photosyntheses are reviewed.

An absolute asymmetric synthesis is the production of optically active materials without the intervention of any dissymmetric chemicals. Such a synthesis requires the influence of some dissymmetric physical agent. By convention, and perhaps unfortunately, the phenomenon of fortuitous spontaneous crystallization from a supersaturated racemic modification has also been classified as an absolute asymmetric synthesis. This paper will be confined to a discussion of the use of circularly polarized light as the influencing physical element. Some of the theoretical aspects of this kind of synthesis will be discussed as well as the more significant experiments of this area.

THE BASIS OF ASYMMETRIC PHOTOCHEMISTRY

Haidinger (1847) discovered that in certain spectral regions circularly polarized light of opposite sign is unequally absorbed by quartz crystals (circular dichroism). Later, Cotton (1895) demonstrated circular dichroism in the region of optically active absorption bands. Van't Hoff (1894) predicted that conversely, if circularly polarized light of a given sign is unequally absorbed by the (+) and (—) forms of an optically active material, and if the material is photochemically active, asymmetric photolysis should give rise to unequal decomposition of the enantiomers. For example, if left circular light is more strongly absorbed by (+) isomers, then the right circular light is preferentially absorbed at the same wavelength by the (—) isomers. Hence right circular incident light is more strongly absorbed by the (—) components of a racemate. If these molecules are decomposed by the light, then the (+) isomer should predominate in the product mixture.

Likewise, one might expect that under the dissymmetric influence of circularly polarized light, asymmetric photosynthesis might be achieved as well as asymmetric photodecompositions.

In order for a dissymmetric physical element, such as circularly polarized light, to modify a product ratio successfully, it is necessary that the

agent be essential to the reaction rather than play an inactive environmental role. Some of the early investigations, subsequent to Van't Hoff's suggestion to use circular light were doomed to failure, for although this physical agent is indeed dissymmetric, it is not in any way involved in many of the chemical reactions investigated, (For example, the experiments by Guye and Drouginine (1909)). A mechanistic requirement for observable asymmetric synthesis is that products must arise directly from the primary photochemical process, since the probability of asymmetry persisting through a chain reaction of any appreciable length is vanishingly small.

The above conditions were not fulfilled in the experiments by Cotton (1896) with alkaline copper tartrate solutions. This material exhibits strong circular dichroism in the red region of the spectrum. It also undergoes decomposition in sunlight. However, Byk (1904) demonstrated that the decomposition is caused by ultraviolet light (350-400 mu) and that alkaline solutions of copper tartrate are not acted on by red light as Cotton had thought. Furthermore, Mitchell (1930) could not detect any cirular dichroism in the ultraviolet region. Thus upon irradiation with circular light of any wavelength, both enantiomers are affected to the same extent.

Quantitative Considerations

The magnitude of the expected activation is dependent upon the length of the photochemical influence and is always proportional to the relative difference of the extinction coefficients of the enantiomers. The latter parameter has been defined by Kuhn (1930) as the anisotropy factor:

$$g = \frac{\varepsilon^{+} - \varepsilon^{-}}{\varepsilon}$$

where ε^{+} and ε^{-} are the extinction coefficients of the (+) and (—) isomers, respectively, for light circularly polarized in a given sense. E is the extinction coefficient of the racemate. Kuhn shows that the anisotropy factor must also be equal to:

$$g = \frac{n_l - n_r}{n - 1}$$

where n_l and n_r are the different indices of refraction for left and right circularly polarized light respectively. Since it has been shown, Djerassi, (1960) that the rotatory power of an optically active medium is:

$$\phi = \frac{\pi}{\lambda}(n_l - n_r)$$

where ϕ is the rotation per centimeter for light of vacuum wavelength, it follows that:

$$g = \frac{\phi\,\lambda}{\pi\,(n - 1)}$$

Thus the anisotropy factor and subsequently the asymmetric efficiency may be evaluated either by rotation or absorption measurements. In some cases where optically pure enantiomers are not available, and consequently g is experimentally inaccessible, the asymmetric efficiency may be approximated from the anisotropy factor which is inversely proportional to f, the oscillator strength of the photochemically active absorption band (Kuhn, 1930). The oscillator strength is a constant times the integrated intensity of the band:

$$f = \frac{mc}{\pi e^2}\,\frac{1}{L}\int u\,d\nu$$

where c = velocity of light, e and m are the charge and mass of an electron, L = Loschmidt number (number of molecules per unit volume) and $\int u\,d\nu$ represents the area of the absorption band, u being defined by:

$$I/I_0 = e^{-ud}$$

It is unfortunate that Kuhn, in all his papers, used the symbol ε for absorption coefficient instead of molecular extinction coefficient; thus the ε has been changed to u in this paper to avoid discrepancy with the convention in common use in absorption spectroscopy as defined in the International Critical Tables.

To a first approximation

$$g = 10^{-5}/f$$

Note that only weak absorption bands can exhibit strong circular dichroism or have a high anisotropy factor. Hence, it is necessary to use materials which, in addition to possessing a high rotatory power in their optically pure state, exhibit photochemically and optically active absorption bands of low extinction in order to attain an observable activation of the racemate photochemically.

The magnitude of rotation expected after irradiation with circular light has been related to the anisotropy factor by Kuhn and Knopf (1930). The basic assumption involved in this relationship is the Einstein equivalent law: one and only one absorbing molecule will decompose after absorbing a light quantum hv. This assumption is of utmost importance in the quantitative evaluation of the rate of dissymmetric transformation, and thus the expected activation. If the mechanism of a photodecomposition involves a chain reaction, it is apparent that the asymmetric efficiency will be less than expected. The rates of change of concentration of (+) and (—) isomers due to asymmetric photolysis are:

$$-\frac{dc^+}{dt^+} = I_r^+ \frac{1}{h\nu v} \quad \& \quad \frac{dc^-}{dt^+} = I_r^- \frac{1}{h\nu v}$$

where I_r^+ & I_r^- are the relative amounts of energy absorbed from right circular light (I_r) per unit time by the (+) and (—) isomers, respectively, and v is the total volume of the sample. But since

$$I_r^+ = I_r \frac{\varepsilon_r^+ C^+}{\varepsilon_r^+ C^+ + \varepsilon_r^- C^-}$$

and

$$I_r^- = I_r \frac{\varepsilon_r^- C^-}{\varepsilon_r^+ C^+ + \varepsilon_r^- C^-}$$

where ε_r^+ is the extinction coefficient of (+) isomers for right circular light:

$$-\frac{dc^+}{dt^+} = I_r \frac{\varepsilon_r^+ C^+}{\varepsilon_r^+ C^+ + \varepsilon_r^+ C^+} \frac{1}{h\nu v}$$

and

$$-\frac{dc^-}{dt^+} = I_r \frac{\varepsilon_r^- C^-}{\varepsilon_r^+ C^+ + \varepsilon_r^+ C^+} \frac{1}{h\nu v}$$

Upon integrating the above equations, one obtains an expression for C^+ and C^-. It can then be shown that:

$$C^+ - C^- = 2\, C_0\, g/2\ (1-\delta)\ \ln \frac{1}{1-\delta}$$

where δ is the fractional part of material decomposed and $2\, C_0$ is the initial concentration of the racemate. A more useful form of this equation relates the degree of photolysis with the optical rotation.

$$\alpha = G\ g/2\ (1-\delta)\ \ln \frac{1}{1-\delta}$$

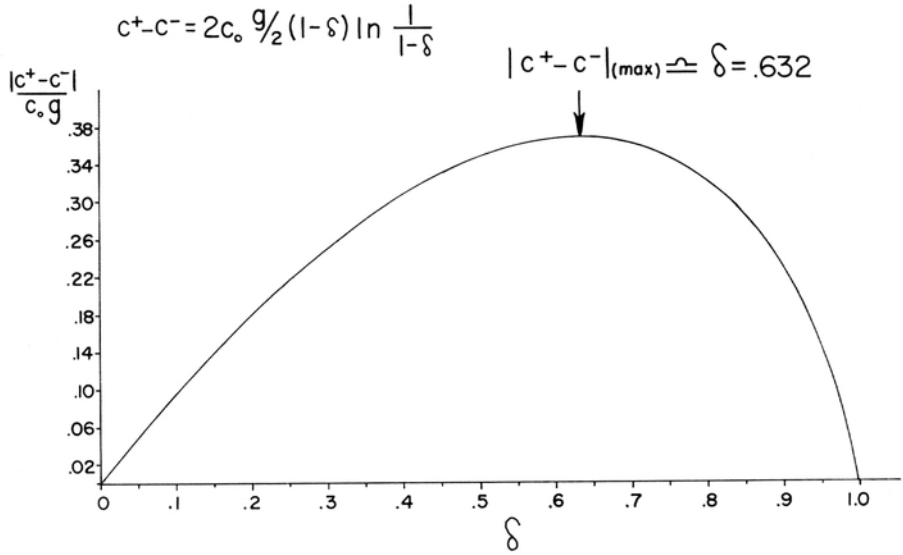

FIGURE 1.—A plot of optical activation as a function of the degree of dissymmetric photodecomposition.

where G represents the rotation that would be observed in an equivalent optically pure sample. Note that α is maximum when $\delta = 0.632$ (63.2% decomposition). This can easily be shown by setting $\frac{d\alpha}{d\delta} = 0$ and solving for δ. Figure 1 shows how the activation $(C^+ - C^-)$ depends on the degree of decomposition (δ). Note that maximum activation corresponds to .368 $C_0g = (1-\delta)\ C_0g$; ($(1-\delta)\ C_0$ is the quantity of non-reacted material). It is apparent that only low yields are possible by this method. At the onset of the experiment (in the region of positive slope) one enantiomer is decomposed more rapidly than the other due to its higher extinction coefficient for circular polarized light of a given sign. When a concentration difference between the enantiomers exists the solution is optically active. However, this relative difference in photolysis rate can only persist for a limited time (until 63.2% of the material is decomposed). Eventually the difference in concentration of the enantiomers is such that both are decomposed at the same rate. Ultimately all of the material is decomposed and the activation $(C^+ - C^-)$ is diminished to zero. Hence it is only possible to attain a partial dissymmetric transformation of the racemate by an asymmetric photolysis. For typical systems where $g = 10^{-2}$ the maximum percentage of activation is

$$\frac{1C^+ - C^-1}{C_0} \times 100 = 0.4\%$$

Figure 2 illustrates experimental data obtained by Mitchell (1930) on the decomposition of humulene nitrosite with right and left circularly polarized light. It should be kept in mind that δ will not be linear with time and hence, a plot of α (which is proportional to $C^+ - C^-$) vs δ will not be expected to have the same shape as α vs time.

At best this method of producing optically active materials is very inefficient and is primarily of academic significance.

Absolute Asymmetric Synthesis Via Asymmetric Photolysis

After several investigators (Cotton (1896), Freundler (1907), Guye and Drouginine (1909), Henle and Haakh (1908) and Bredig (1923)) failed to verify Van't Hoff's prediction, Zocher (1925) made a very encouraging and significant observation. He noted that sheets of silver halides became temporarily optically active after they had been irradiated with circularly polarized light. No activity was observed if the same substance was irradiated with plane polarized or non-polarized light. Although this experiment cannot be considered a true absolute asymmetric synthesis, since silver halides have neither an inherent "molecular" asymmetry nor lattice dissymmetry, it did indicate the need of utilizing a photochemical reaction in which the light plays an active and essential role. In this unique experiment, the silver halide lattice was rendered temporarily dissymmetric by the nature of the photoactivation.

Kuhn and Braun (1929) were apparently the first to succeed in an absolute asymmetric photolysis. In 1929 they investigated the photodecomposition of the ethyl ester of α-bromopropionic acid. This material has an ultraviolet absorption band and a corresponding Cotton effect around 245 mu. When a racemic mixture of the ester (5% in ethanol) was sealed in a quartz cuvette and exposed to circular polarized light (Mg line - 280 mu), an activation was achieved. The extent of decomposition was determined by simultaneous exposure of a control sample to non-polarized light from the same source. The largest activity observed was around 0.05° after 50% decomposition.

Later Kuhn and Knoph (1929, 1930) effected a successful asymmetric photolysis of the dimethylamide of α-azido-propionic acid,

$CH_3CHN_3CON(CH_3)_2$, with circularly polarized light of wavelength 280-310 mu. The azido compound has a photochemically active absorption band in the ultraviolet spectrum at 290 mu. The extent of photodecomposition may be conveniently determined by measuring the amount of N_2 evolved. In this experiment $G = 340°$, $g = 0.024$, $\delta = 0.40$ (40%). On the theoretical grounds previously cited, the expected activation was: $\alpha = 1.25°$. The observed rotations were $\alpha_D = -1.04$ and $\alpha_D = +0.78$ after irradiation with left and right circular light respectively. Since the light was not exactly, but only approximately circularly polarized and furthermore, since the Einstein equivalent law (which was assumed) represents an idealized system, the theoretical treatment previously described and the understanding of the activation process may be considered as being confirmed.

Similar experiments utilizing the same technique have been carried out by Mitchell (1930) with humulene nitrosite and more recently by Berson and Brown (1955) with 4-(2′-nitrophenyl) -1,4-dihydropyridine. Tsuchida, Nakamura and Kobayashi (1935) have reported success with an asymmetric photolysis of K_3 [Co (oxylate)$_3$]. Apparently this has been the only successful attempt to carry out such an experiment with a metallic complex. K_3 [Co (oxylate)$_3$] possesses an absorption band at 605 mu with an anisotropy factor in the order of 10^{-2} in magnitude. Asymmetric photolysis was carried out with D-line radiation. Rotation measurements were made at 499 mu to avoid any accidental photolysis during the measuring periods. Maximum activation ($\alpha = .16°$) was observed after 8.5 hours of illumination.

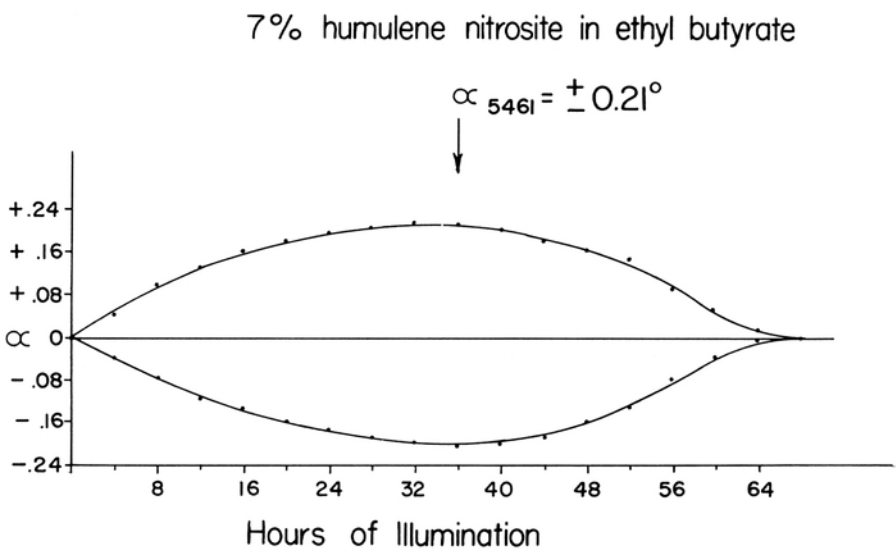

FIGURE 2.—Optical rotation of humulene nitrosite irradiated with right and left circularly polarized light (Mitchell (1930)).

Absolute Asymmetric Synthesis Via Asymmetric Photosynthesis

Whereas the particular experiments cited invoke asymmetric destruction, cases of absolute asymmetric synthesis under the influence of circularly polarized light have also been reported, although the observed rotations of the products were very small (less than 0.2°). Davis and Heggie (1935) reported the asymmetric photochemical addition of bromine to 2,4,6-trinitrostilbene under the influence of circularly polarized light of wave length 360-450 mu. Trinitrostilbene would seem to be particularly suited to the purpose of asymmetric synthesis since dark reaction is negligible, it possesses an absorption band in the visible spectrum, and since the phenyl and trinitrophenyl group differ markedly from one another in their electrical character, the ethylenic linkage has a polar character. They were successful in producing optically active trinitrostilbene dibromide by the photochemical addition of reagents under the influence of circularly polarized light in carbon tetrachloride and in nitrobenzene. Betti and Lucchi (1938) carried out a similar experiment in which the asymmetric photochemical addition of chlorine to an ethlylenic linkage was attained with both gaseous reactants and products. Karagunis and Drikos (1933, 1934) synthesized optically active triarylmethylchlorides from triarylmethyl radicals and chlorine. They have suggested that the three valencies of the carbon atom of the radical do not lie on a plane. Thus the radical itself, although racemic, is asymmetric. They propose that circularly polarized light activates one of the enantiomers so that by the addition of chlorine, optical activity appears.

It is of interest to note that Souty (1934) has reported the rate of mutarotation of certain carbohydrates is different in right and in left circularly polarized light of wave length 546 mu, but is the same in right and in left circularly polarized light of wavelength 589 mu.

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