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ROTATORY DISPERSION AND THE VIBRATING MOMENTUM OF OPTICALLY ACTIVE ABSORPTION BANDS

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OPTICAL rotatory power is a phenomenon which has from the time when it was discovered excited the curiosity of many scientists. Optical rotation itself is at first sight a problem of theoretical physics; but its dependence on chemical structure makes it an important object of research in both inorganic and organic chemistry and the occurrence of pure optical antipodes in living organisms gives it a fundamental importance in biochemistry and biology[1] and the question of the origin of optically active substances in nature even touches the problem of the origin of life. The occurrence of the "wrong" antipode in antibiotics and also in small quantities in natural proteins, together with their necessary formation for kinetic and thermodynamic reasons, in the organisms makes it probable that the decrease of the optically active purity of some fundamental substances in the organism will be one of the main reasons of aging and limitation of the lifetime of the individual organisms.

It is not possible in a limited time to follow all the aspects in detail; but it is possible to mention them and to state that they form a unity in spite of the specialization which is characteristic for great parts of todays scientific research.

As the subject of the symposium is optical rotation and rotatory dispersion, we will, in this introductory note, deal with these phenomena; we will see that there is in fact only *one phenomenon*, rotation and rotatory dispersion being intrinsically the same.

I wish, before entering into the main subject to thank the organizing committee, in particular Dr. Levedahl for the invitation to come here and for the great honour which has come to me by being asked to open the symposium. I appreciate the fact that the symposium is dedicated to the memory of Doctors Kirkwood and Moffit who have both made such outstanding contributions in the field which is covered by this conference. The last congress in which optical activity was being the main subject was, as far as I remember, a symposium held by the Faraday[2] Society in 1930. The field has developed in many respects since that date.[3] I believe that the most important progress which was made is the establishment of absolute configuration of the asymmetric carbon atom on one hand (Kuhn, Bijvoet) and the development of the one electron theory (Condon, Eyring, Kauzmann) on the other hand. I also mention the recent investigations on stereoids and experimental development (Djerassi, Klyne).

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[1] For a recent review see e.g. W. Kuhn, *Advanc. Enzymol.* **20**, 1 (1958).

[2] *Trans. Faraday Soc.* **26**, 266–461 (1930); with contributions by: P. C. Austin, Belaiew, M. Betti, B. Bhaduri, E. Bretscher, G. Bruhat, A. Cotton, E. Darmois, R. Descamps, C. Drucker, P. P. Ewald, J. Kenyon, W. Kuhn, J. Liquier-Milward, T. M. Lowry, R. Lucas, R. de Mallemann, W. H. Mills, Gl. Owen. H. Phillips, J. Read, H. G. Rule, B. K. Singh, C. P. Snow, G. Temple and K. L. Wolf.

[3] For a recent review see *Ann. Rev. Phys. Chem.* **9**, 417 (1958).

As far as rotatory dispersion is concerned, this property is connected and will always be connected with the fundamental discovery made by Cotton[4] in 1896. He found that optical rotatory power as a function of the wavelength often shows, in the region where the substances show ordinary optical absorption, a characteristic *anomaly* which is associated with a *circular dichroism* in the absorption region and which after the name of its discoverer is called a *Cotton-effect.*

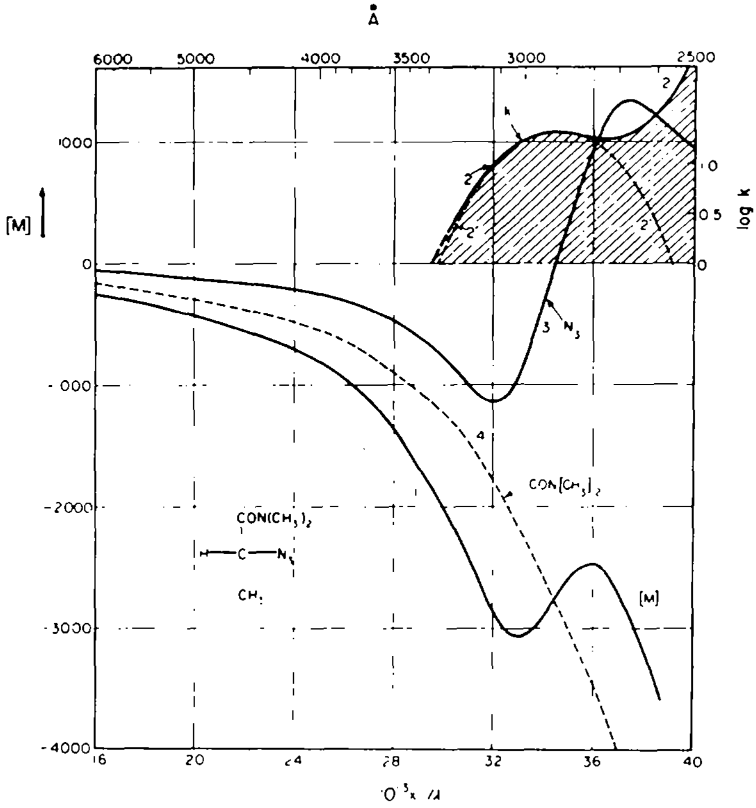

FIG. 1. Azidopropionic-dimethylamide [$CH_3CHN_3CON(CH_3)_2$] in ether.

Curve 1: Molecular rotatory power (M) observed.
Curve 2: Molecular absorption coefficient observed.
Curve 2': Absorption band (with Gaussian error curve shape), which is used as basis for computing curve 3.
Curve 3: Rotatory contribution of the absorption band (curve 2 or 2') due to the azido-group.
Curve 4: Difference of curve 1 and 3; significance: rotatory contribution from the remaining absorption bands of the molecule; i.e. essentially the rotatory contribution of the $CON(CH_3)_2$-group.

The first figure[5] shows the situation with respect to rotatory power and optical absorption in the case of D-α-azido propionic dimethylamide. It is the antipode whose Emil Fischer projection formula is indicated in the same figure and whose actual shape, i.e. the absolute configuration[6] is obtained by moving the substituents H and N_3 from the plane of the paper towards the observer. Curve 1 of Fig. 1 is the observed

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[4] A. Cotton, *Ann. Chim. Phys.* **8**, 347 (1896).
[5] Taken from W. Kuhn and E. Braun, *Z. Phys. Chem.* (B) **8**, 281 (1930).
[6] W. Kuhn, *Z. Phys. Chem.* (B) **31**, 23 (1935); J. M. Bijvoet, A. F. Peerdeman and A. J. van Bommel, *Nature, Lond.* **168**, 271 (1951); J. Trommel and J. M. Bijvoet, *Acta Cryst.* **7**, 703 (1954).

molecular rotation which shows the Cotton-effect. Curve 2 is the ordinary absorption, a very weak absorption in fact; the f-value or number of dispersion electrons corresponding to about $5 . 10^{-4}$. Fig. 2 gives the ordinary absorption and the circular dichroism[7] of the same molecule in the region of the N_3-absorption band near 2900 Å. It is seen in this figure that the maximum of the circular dichroism practically coincides with the maximum of the ordinary absorption and that the anisotropy factor g, i.e. the relative difference of the absorption coefficients for right and left hand circular light, remains roughly constant in the main region of the absorption band.

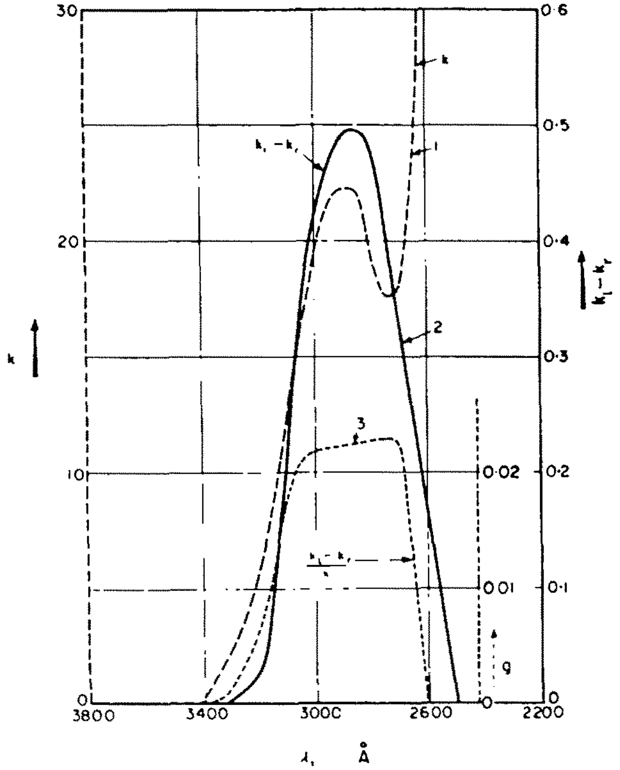


FIG. 2. Azidopropionic-dimethylamide $[CH_3CHN_3CON(CH_3)_2]$ in hexane.
Curve 1: Ordinary absorption (k)
Curve 2: Circular dichroism $(k_l - k_r)$
Curve 3: The anisotropy factor $g = (k_l - k_r)/k$.

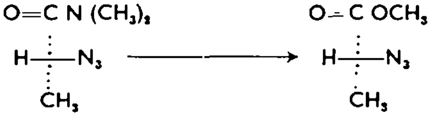
The further analysis has shown[5] that the rotatory anomaly observed both inside and outside the region of absorption is quantitatively connected with the circular dichroism and thereby with the existence of the absorption band. It can in this way be stated in the case of the azidopropionic dimethylamide that curve 3 of Fig. 1 is the contribution of the N_3-absorption band near 2900 Å and that in the visible, e.g. near 6000 Å about 25 per cent of the observed value of the rotatory power are contributed by said absorption band. The *generalization of this statement* is that each absorption band gives a well defined contribution to the molecular rotatory power

[7] W. Kuhn and E. Braun, *Z. Phys. Chem.* (B) 8, 445 (1930).

not only inside but also outside the absorption region and moreover that the rotatory power of the substance at a given wavelength is the algebraic sum of the rotatory contributions made by the various absorption bands of the molecule.

This is an important statement telling us *that any understanding of the dependence of optical rotatory power on chemical constitution must necessarily proceed through a description or understanding of the Cotton-effect,* i.e. rotatory contributions of the absorption bands exhibited by the substances considered. If we want to understand the influence on optical rotation of a chemical change made in a given molecule we must necessarily ask for the effect produced by the chemical change on the Cotton-effect of the absorption bands. We will in the following consider some of the results obtained on this basis. The azido-compounds have played a particular part in these investigations which we have carried out some years ago in following a proposition of and in close collaboration with Freudenberg[8]. As far as the theory is concerned, I mention the fundamental work which has been done by Oseen[9], Born[10] and later by Condon, Eyring[11] and Kirkwood[12].

It is seen, that we can in a simple way and without changing the arrangement of the substituents attached to the asymmetric carbon atom pass from the azidopropionic dimethylamide to the azidopropionic methylester



$$\begin{matrix} O{=}C\,N\,(CH_3)_2 \\ H\!-\!\!\!\vdots\!\!\!-\!N_3 \\ CH_3 \end{matrix} \xrightarrow{\qquad\qquad} \begin{matrix} O{=}C\,OCH_3 \\ H\!-\!\!\!\vdots\!\!\!-\!N_3 \\ CH_3 \end{matrix}$$

D (−)Azidopropionic dimethylamide D (+)Azidopropionic methylester

Both compounds contain in particular the N_3-group which has an absorption band near 2900 Å and we can, by measuring the rotatory dispersion in the absorption region, or also by measuring the circular dichroism in the absorption band, determine the rotatory contribution of the N_3 absorption band in the ester. The result is shown in Fig. 3. Having made this analysis as well in the dimethylamide (Fig. 1) as in the ester (Fig. 3) we are thus in a position to compare besides the total rotation the effect of the chemical change on the rotatory contribution of a specific absorption band of a specific group (the N_3-group) which remained unaltered by the chemical change. The comparison shows that the rotatory contribution of the N_3-group is negative on the long wavelength side of the N_3-absorption band; we call this a negative Cotton-effect of the N_3-band, both in the ester and in the corresponding dimethylamide. There is a change in the absolute magnitude but, roughly speaking, *a conservation of the rotatory contribution of the N_3-absorption band when going from the ester to the corresponding dimethylamide.*

In contrast to the moderate change produced in the optically active behaviour

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[8] For a summary see: W. Kuhn und K. Freudenberg in *Hand und Jahrbuch der Chemischen Physik* Bd. 8/III (1932) and K. Freudenberg, *Stereochemie* pp. 662-720. Wien (1933).

[9] C. W. Oseen, *Ann. Phys.* **48**, 1 (1915).

[10] M. Born, *Phys. Z.* **16**, 251 (1915); *Ann. Phys.* **55**, 177 (1918).

[11] E. U. Condon. W. Altar and H. Eyring, *J. Chem. Phys.* **5**, 753 (1937); E. U. Condon, *Rev. Mod. Phys.* **9**, 432 (1937); E. Gorin, J. Walter and H. Eyring, *J. Chem. Phys.* **6**, 824 (1938); W. J. Kauzmann, J. E. Walter and H. Eyring, *Chem. Rev.* **26**, 339 (1940).

[12] J. Kirkwood, *J. Chem. Phys.* **5**, 479 (1937); **7**, 139 (1939); E. Hückel, *Z. Elektrochem.* **50**, 13, (1944). [The arguments developed in these papers (polarizability theory of optical rotatory power) are formally different but physically about the same as those described by W. Kuhn.]

of the N_3-absorption band, the effect of the chemical change on the total rotation of the molecule is enormous. For the mercury yellow-line 5780 Å a change of the molecular rotation from +24° in the ester to −259° in the dimethylamide is registered. This enormous change is, as we see *not* due to a change of the N_3-contribution; the analysis of the dispersion curves proves that the change is due to the optically active contribution of the next absorption band which has to be attributed to the $COOCH_3$-group and to the $CON(CH_3)_2$-group of the ester and the dimethylamide. It is noted that the $COOCH_3$ and $CON(CH_3)_2$-group which shows the enormous change in the rotatory contribution (Fig. 4) is the group in the molecule which so to say *personally* undergoes the big change when going from the one to the other of the two molecules compared.

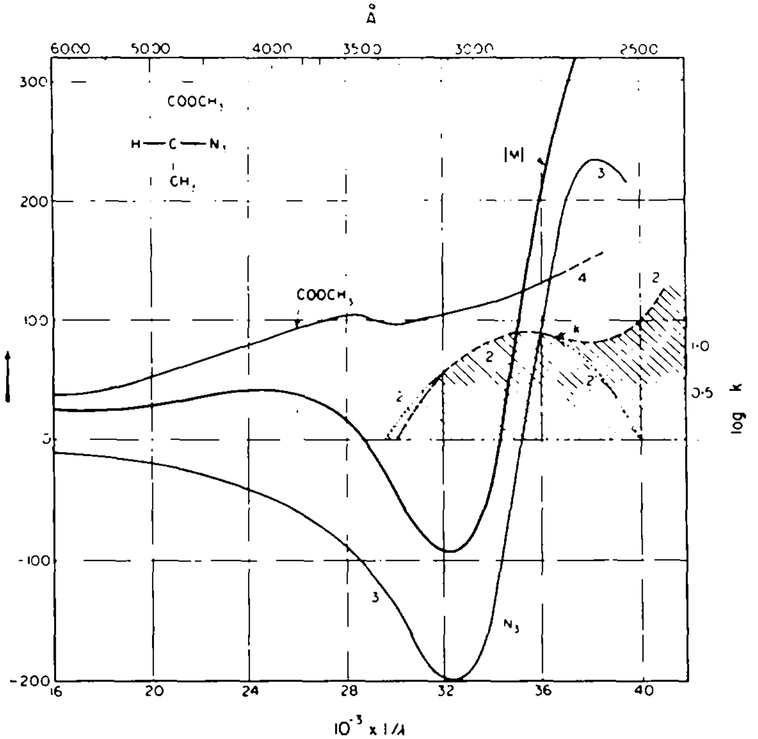

FIG. 3. D(+)-azidopropionic methyl ester in alcohol.

Curve 1: Molecular rotatory power (M) observed.
Curve 2: Molecular absorption coefficient observed.
Curve 2′: N_3-absorption band (with Gaussian error curve shape), used as basis for computing curve 3.
Curve 3: Rotatory contribution of the N_3-absorption band (curve 2 or 2′).
Curve 4: Difference of curve 1 and 3; significance: rotatory contribution from the remaining absorption bands of the molecule, i.e. essentially rotatory contribution of the $COOCH_3$-absorption band.

Statements similar to those made for the N_3-absorption band and the $COOCH_3$- and $CON(CH_3)_2$-absorption bands in the azidopropionic ester and dimethylamides have been made experimentally in a number of further more or less analogous cases, e.g. for the halogen absorption bands in α-halogenated acids,[5,8] the phenyl absorption band in mandelic acid and its derivatives, the O-NO absorption bands of nitrites, etc.

We are now going to *transform these findings concerning the Cotton-effects or the rotatory dispersion into findings concerning the vibrating momentum of the absorption bands* and to interpret the regularities by physical considerations concerning the vibrating moment. This is possible because we can state that the origin of the Cotton-effect of a given absorption band is substantially a description of the vibrating electrical momentum associated with the absorption band considered. The main point may again be elucidated in the case of the N_3-absorption band near 2900 Å which gives the pronounced Cotton-effect in azidopropionic acid and dimethylamide, shown in Fig. 1 and 3. An absorption band whose vibrating momentum is isotropic or unidirectionally orientated in the molecule will not be circularly dichroitic. This is the reason why the N_3-absorption band near 2900 Å present in ethyl azide is not optically active though situated at the same wavelength as the N_3-absorption band in azidopropionic acid and dimethylamide. For the N_3-absorption band to become optically active, it is necessary that its vibrating moment will have components non parallel and non complanar relative to each other in distant parts of the molecule.[8-10,13] According to this the vibrating moment of the N_3-absorption band of azidopropionic dimethylamide (point 1 of Fig. 5a) will have some component in the region of the OCN$(CH_3)_2$-group (point 2 of Fig. 5a) non parallel and non complanar to the main vibrating moment located in the N_3 group itself (point 1 of Fig. 5a). It is indeed seen that a system with the mode of vibration shown in Fig. 6 will respond differently to a beam of right hand or left hand circular light, i.e. that it will show circular dichroism and optical rotation.

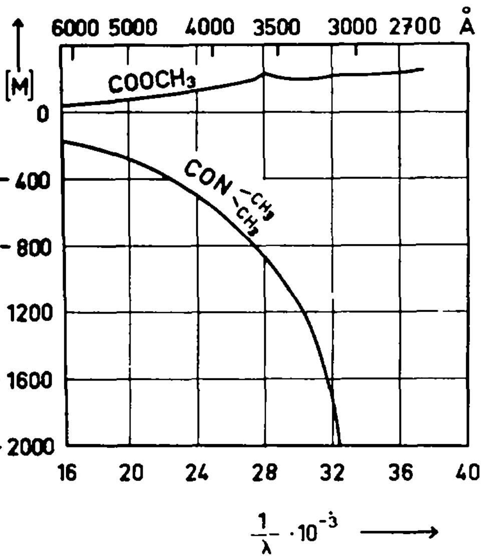

FIG. 4. Approximate rotatory contribution of $COOCH_3$- and $CON(CH_3)_2$-absorption band of of D-configurated azidopropionic ester and dimethylamide (i.e. curves 4 from Fig. 4 and 1).

Mode of vibration of optically active absorption bands.

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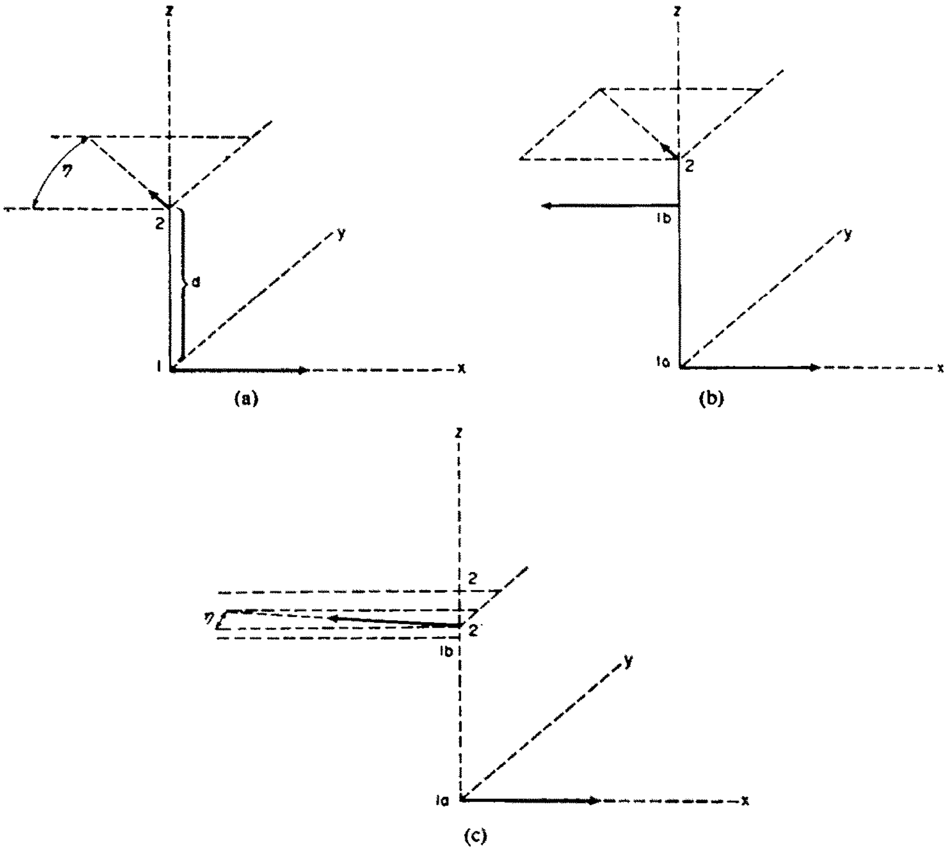
[13] For a discussion of the vibrating moment in the case of weak absorption bands where the anisotropy factor is, as a rule, much higher than in the case of strong absorption bands (a discussion not contained in ref. 8) see W. Kuhn and K. Bein, *Z. Phys. Chem.* (B) **22**, 406 (1933); see also W. Kuhn, *Angew. Chem.* **68**, 93 (1956); *An. Rev. Phys. Chem.* **9**, 417 (1958).

As far as the participation of the $CON(CH_3)_2$-group in the mode of vibration of the N_3-absorption band is concerned, this participation is mainly produced by the electronic polarizability and the orientation of the polarizability of the group. A vibrating moment existing in the N_3-group (point 1 of Fig. 5) will indeed, due to the existence of a polarizable oriented group in point 2, produce an induced momentum in the latter. A less important[14] second effect is according to the one-electron theory of optical activity[11] based on the electric field produced by the $CON(CH_3)_2$-group in the region of the N_3-group.

We have called *vicinal action* the participation of a neighbouring group e.g. the



(a) (b)

(c)

Fig. 5a. A vibrating momentum localized (in a first approximation) in point 1 produces in a polarizable suitably oriented substituent located in point 2 a (small) induced momentum (vibrating with the frequency characteristic for the vibration in point 1). The resulting vibration, having components at angles in various parts of the molecule is optically active. Figs. 5b and c. Vibrating momentum of *weak* optically active absorption bands. The vibrating moment localized (in a first approximation) in point 1 consists of two nearly equal and nearly antiparallel components in point 1a and 1b (quadrupole moment). The vibration in 1a and 1b produces in a polarizable group in point 2 a (small) induced momentum. The resultant of the components in points 1b and 2 (represented by the arrow in point 2′ in Fig. 6c) together with the component 1a in Fig. 6c is a quadrupole moment with nearly antiparallel components of nearly equal magnitude, the angle y in Fig. 6c being very small. Vibrating momenta of this type are shown to give particularly high values of the anisotropy factor[13] (much higher than vibrating momenta of type Fig. 6a). They are however sensitive to small disturbances of y (solvent influence etc.).

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[14] W. Kuhn, *Z. Elektrochem.* **56**, 506 (1952).

$CON(CH_3)_2$-group in the vibrating moment of a chromophoric group (e.g. the N_3-group) of the same molecule. As this vicinal action is mainly based on the polarizability and its orientation inside the molecule it is plausible that this action is not extremely sensitive to a small chemical change of the group, say of the $CON(CH_3)_2$-group as long as the general character of the group is maintained. This is exactly what has been observed in the example considered: the transition from the dimethylamide to the methyl ester has left the vicinal action, i.e. the participation of the $CON(CH_3)_2$- or $COOCH_3$-group in the vibrating moment of the N_3-group and thereby the Cotton-effect of the N_3-absorption band nearly unchanged.

The generalization of these statements and findings can be summarized roughly in the following way:

Each substituent of a chemical compound contributes in two ways to the rotatory power.

1° by being a chromophoric group, i.e. possessing absorption bands which become optically active through the vicinal action of the rest of the substituents.

2° by its vicinal action, i.e. by taking part through the electronic polarizability in the mode of vibrations of neighbouring chromophoric groups. (Helping to make those vibrations optically active.)

The mode of vibration of a given absorption band is, in particular in the case of weak absorption bands where the vibrating moment in a quadrupole moment (Figs. 5b and c) very sensitive to a chemical change produced on the chromophoric group directly because it touches the very origin, the first approximation of the vibrating moment of the individual absorption band. This first approximation is an individual property of an individual absorption band of an individual group, a property which varies from one absorption band of the same group to another and very often even varies inside the absorption region of an individual apparently simple absorption band.[15]

The *vicinal action* on the other hand is less sensitive to a chemical change because it is due to the polarizability *which is an average manifestation of the group.*

Two simple cases where the application of these rules is particularly effective may shortly be mentioned.

(a) *Isolated absorption band*

If one isolated absorption band belonging to a specific group is found in the molecule, the Cotton-effect of the absorption band considered can be measured and rules concerning the vicinal action of the surrounding groups be found. Basing on such rules it will be possible to determine the relative configuration of related compounds basing on the fact that similar substituents with similar vicinal function in a similar arrangement will give to the absorption band considered a similar Cotton-effect.

This method which has been illustrated in the case of the N_3-absorption band in azidopropionic dimethylamide and methylester has recently been applied successfully by Djerassi and Klyne to the Cotton-effect of the CO-absorption band of steroids.[16]

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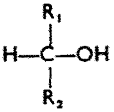
[15] E.g. in many of the absorption bands of inorganic complexes, for example in trioxalato-potassium-cobaltiate [W. Kuhn and K. Bein, *Z. Phys. Chem.* (B) **24**, 335 (1934) or in triethylenediaminecobaltibromide J. Mathieu, *J. Chim. Phys.* **33**, 78 (1936)].

[16] C. Djerassi and W. Klyne, *Chem. & Ind.* 988 (1956); *J. Amer. Chem. Soc.* **79**, 1506 (1957).

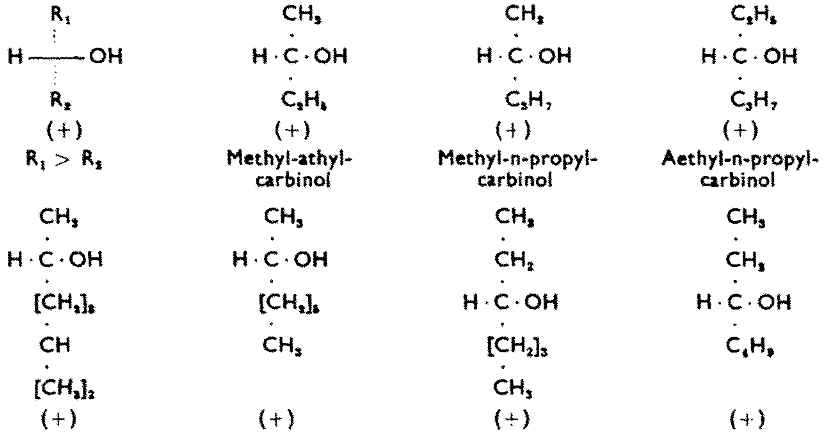
If the molecules compared, e.g. aliphatic alcohols, are containing *one* absorption band (in the example the OH-absorption band) in the *near* ultra-violet, the absorption of the rest of the substituents being located in the very far ultra-violet exclusively, the rotatory contribution of the one absorption band (the OH-band) in the near ultra-violet will be so predominant that it determines the sign and the approximate magnitude of the rotatory power in the visible. In this case the vicinal rule explains[8] the fact that aliphatic alcohols of the formula R_1



$$\begin{array}{c} R_1 \\ | \\ H—C—OH \\ | \\ R_2 \end{array}$$

where R_1 and R_2 are aliphatic alkyl groups and where $R_2 > R_1$ have the same sign of rotatory power in the visible. This is illustrated by the following examples:[8]

Relative configuration and sign of optical rotation of secondary alcohols



(b) *Several groups giving rotatory contributions of comparable magnitude*

In the majority of cases the molecules will contain several groups giving absorption bands with Cotton-effects in the near ultraviolet in such a way that the rotatory power in the visible cannot be said to be dictated by one specific group or one specific absorption band alone. In the case of D-azido-propionic dimethylamide the contribution of the $OCN(CH_3)_2$-group was seen to be strongly negative, the contribution of the OC-OCH_3-group in the corresponding ester however strongly positive (Fig. 4) with an absolute value which was in the visible greater than the N_3-contribution. This is the reason for a strong shift of the rotatory power in the visible when going from the dimethylamide to the ester in the D-azidopropionic compound. If we compare the D-bromopropionic dimethylamides and esters instead of the azido-compounds, we will expect that the $COOCH_3$-contribution is still positive and the $CON(CH_3)_2$-contribution negative if the vicinal actions of Br and N_3 are similar. In this case the shift when going from the ester to the dimethylamide will again be a shift towards negative values of rotation. A shift is indeed observed in the mercury yellow line from $+92$ to -159 when going from the ester to the dimethylamide of D-α-bromopropionic acid (Fig. 6, curve 6). An analogous shift is observed in going from the ester to the dimethylamide in the case of further D-configurated α-substituted acids (Fig. 6). The vicinal rule thus predicts or explains the existence of a shift of the molecular rotation of a specific sign and comparable magnitude when making analogous chemical changes in equally configurated analogous optically active molecules. These rules of shift, first found by Freudenberg[17] and then explained and corroborated by the vicinal rule brought the complete resolution of contradictions which were brought about by earlier tentative rules for amides and lactones established by C. A. Hudson.[19] They were of great importance for the establishment of the relative configuration especially in the series of the biologically important α-substituted aliphatic acids. The first consistent answer to the question, in which cases Walden inversion takes place and in which cases it does not, resulted from the relative configuration determinations thus obtained.[8,19]

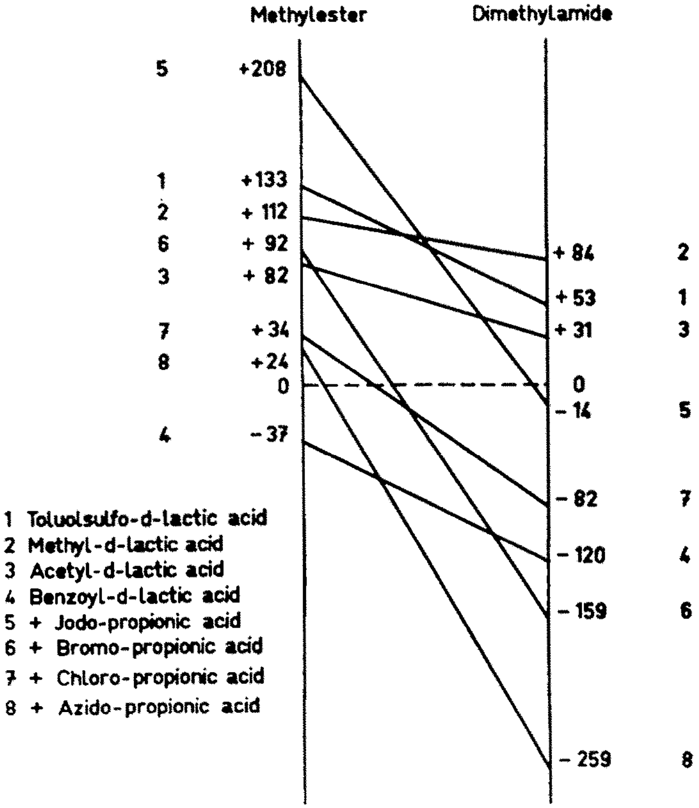


FIG. 6. Rules of shift: A strong shift towards negative values of the molecular rotatory power (for $\lambda = 5780$ Å) is observed in the case of D-configurated α-substituted acids when going from the methylester to the dimethylamide. The data represented in this figure are taken from a table given by K. Freudenberg (ref. 8).

The optical *superposition* and the limitation of its validity[18] are another example

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[17] K. Freudenberg, Fr. Brauns and H. Siegel, *Ber. Dtsch. Chem. Ges.* **56**, 193 (1923). K. Freudenberg und L. Markert, *Ibid.* **60**, 2447 (1927); K. Freudenberg and A. Luchs, *Ibid.* **61**, 1083 (1928).

[18] K. Freudenberg and W. Kuhn, *Ber. Dtsch. Chem. Ges.* **64**, 703 (1931).

[19] K. Freudenberg, *Stereochemie* p. 709. Wien (1933); *Heidelb. Akad. Wiss.* No. 14 (1930); *Ber. Dtsch. Chem. Ges.* **66**, 177 (1933); *Monatsh. Chem.* **85**, 537 (1954).

of the application of the vicinal rule to chemical problems and to the description of the relations between optical rotatory power and chemical constitution.

Our insight into all these phenomena is, therefore, a result of the studies of rotatory dispersion, an insight which had and has to be expressed in terms of the vibrating moment of optically active absorption bands. There is no doubt that still more information will be gained through further analysis of the Cotton-effect.

SUMMATION RULE AND RELATIVE IMPORTANCE OF WEAK ABSORPTION BANDS

There is one more point which should be mentioned when discussing optical rotation as a sum of contributions made by various absorption bands of an optically active substance. It is the fact that the sign of the Cotton-effect is necessarily changing when considering the various absorption bands of a given antipode of an optically active substance. The quantitative treatment shows that the integral

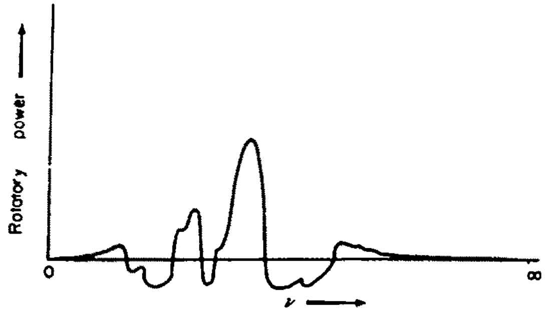

FIG. 7. Optical rotation is a property which, for a given substance, disappears both in the limit of low and high frequencies.

$$\int_0^\infty \frac{\varepsilon_l - \varepsilon_r}{\nu} d\nu = 0 \qquad \text{or} \qquad \sum f_i g_i \frac{1}{\nu_i} = 0$$

i.e. that the circular dichroism of a given substance, taken over the entire absorption spectrum is zero.[20] For the optical rotation in the visible of a substance possessing absorption bands in the near and far ultra-violet this means that the rotatory contributions are of partly opposite sign; a far-going cancellation of the contributions therefore takes place. The cancellation would be complete if frequency factors were disregarded. The situation is different from the case of ordinary light refraction where the contributions in the visible of the U.V. absorption bands are *all* of the same sign. The peculiar situation in optical activity is also described correctly by the statement that rotatory power is a phenomenon which exactly disappears when going to the limit of both high and low frequencies (Fig. 7).

The existence of this summation rule does by no means impair the validity of the vicinal rules and the validity of the explanations given for the sign of the rotatory power of some groups of substances or the correctness of the rules of shift. Leaving these explanations unchanged it explains however in conjunction with the behaviour of weak absorption bands mentioned the well known sensitivity of the optical rotatory power towards physical and chemical changes. If the rotatory contributions are

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[20] W. Kuhn, *Z. Phys. Chem.* (B) 4, 14 (1929).

nearby cancelling it is obvious indeed that even a minor change, e.g. of the contribution of one weak band may even produce a renewal of the sign of the resulting optical rotation.

It is for this reason in many instances an advantage to base any considerations concerning optical activity as far as possible on the rotatory contributions of single isolated absorption bands.

However the procedure chosen in discussing optical rotatory may be, it will in all cases be essential to be clear about the one point that the investigation of optical rotatory power means the investigation of the vibrating momentum of one or several absorption bands of the molecules, a property which has to be described and defined and investigated in addition to the absorption frequency and intensity and which is of interest to the physicist as well as to the chemist.