THEORIES OF OPTICAL ROTATORY POWER

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I. INTRODUCTION

In an optically active molecule there are always two influences at work which render the molecule capable of rotating the plane of polarization of plane polarized light. The first of these is the purely structural one which permits the molecule to exist in non-superimposable mirror image forms (enantiomorphs); the second is that which makes possible the interaction of a given enantiomorphic form of the molecule with a plane polarized light wave so as to rotate its plane of polarization.

The structural influences which make possible the existence of enantiomorphic forms are simple and diverse. The first to be recognized was the asymmetric carbon atom, but there are many other factors besides the occurrence of such an atom in a molecule which may operate to give rise to non-superimposable mirror image forms. Thus, it is conceivable for such a highly symmetrical molecule as ethane to occur in conformations which, if they could be isolated, would undoubtedly be found to be optically active (e.g., a conformation resulting from a rotation of one methyl group relative to the other from either the staggered or opposed form). The only feature which distinguishes those mechanisms for the production of enantiomorphs which the chemist has been able to uncover from those which are theoretically possible but which have not yet been proven operative is the fact that some enantiomorphs racemize much more readily than others. As the technique of the chemist becomes more and more refined, it will undoubtedly be found possible to resolve an ever-widening variety of types of substances into enantiomorphic forms.

In contrast to the simplicity of the structural conditions leading to optical activity in a substance, the mechanism of the interaction of such a substance with a light wave causing the plane of polarization to be rotated has resisted such complete interpretation. Thus, although it is easy to see why secondary butyl alcohol exists in two optically active forms, it is quite another matter to explain why it should have a molecular rotation of 10.3° in sodium D light at 20°C. in the absence of a solvent, and why this rotation should be different in different solvents and at different temperatures and wave lengths.

The structural conditions leading to optically active molecules have been adequately treated elsewhere, so need concern us no further here. It is the purpose of this paper to consider the mechanism of the interaction of an optically active molecule with a light wave from the standpoint of recent quantum-mechanical theories of rotatory power. It will be shown that these theories are capable of accounting for the observed orders of magnitude of optical rotations, and that, by showing how the rotatory power depends on molecular structure, they provide a powerful means of studying such structures under a wide variety of experimental conditions. They will also be found to be capable of supplying information concerning the nature of forces which act between molecules.

II. The Physical Basis of Optical Rotatory Power

A. SOURCE OF OPTICAL ROTATION; THE MOLECULAR ROTATORY PARAMETER; ROTATORY STRENGTHS

The general theory of optical rotatory power has been presented in complete detail in the review article by Condon (8). We here summarize briefly the essential steps in the derivation of the fundamental equations, referring the mathematically inclined reader to Condon's paper for the justification of certain statements here given without proof.

The electromagnetic field in a region free from real charges or real currents is completely specified by Maxwell's equations:

$$\operatorname{div} \mathbf{D} = 0 \qquad \operatorname{div} \mathbf{B} = 0 \tag{1}$$

$$\operatorname{curl} \mathbf{E} = -\frac{1}{c}\frac{\partial}{\partial t}\mathbf{B} \qquad \operatorname{curl} \mathbf{H} = \frac{1}{c}\frac{\partial}{\partial t}\mathbf{D}$$

$$\mathbf{D} = \mathbf{E} + 4\pi\mathbf{P} \qquad \mathbf{B} = \mathbf{H} + 4\pi\mathbf{M}$$

(Heavy type indicates vector quantities.) For an isotropic medium which is not optically active, we may write

$$\mathbf{D} = \epsilon\mathbf{E} \qquad \mathbf{B} = \mu\mathbf{H} \tag{2}$$

where ϵ is the dielectric constant and μ is the magnetic permeability. The solution of equations 1 then represents electromagnetic waves propagated with a velocity

$$v = \frac{c}{\sqrt{\epsilon\mu}}$$

where c is the velocity of light. For all cases in which we shall be interested, μ is very nearly unity, therefore $v = c/\sqrt{\epsilon}$. If n is the index of refraction of the medium, we have the familiar result $n^2 = \left(\frac{c}{v}\right)^2 = \epsilon$. For media which are optically active, equations 2 are no longer complete. If N_1 is the number of molecules per cubic centimeter, we have $\mathbf{P} = N_1\mathbf{p}$, $M = N_1\mathbf{m}$, where $\mathbf{p}$ and $\mathbf{m}$ are the induced electric and magnetic moments per molecule. A theory which enables us to calculate $\mathbf{p}$ and $\mathbf{m}$ in terms of the structure of the individual molecule will thus give us the correct expressions of the form 2, and hence a complete theory of the propagation of electromagnetic waves through the medium in question. The quantum-mechanical calculations of Rosenfeld (34) showed that the electric and magnetic moments induced in a molecule by the perturbing electromagnetic field are given by the equations:

$$\mathbf{p}_a = \alpha_a\mathbf{E}' - \frac{\beta_a}{c}\frac{\partial}{\partial t}\mathbf{H}' + \gamma_a\mathbf{H}' \tag{3}$$

$$\mathbf{m}_a = \frac{\beta_a}{c}\frac{\partial}{\partial t}\mathbf{E}' + \gamma_a\mathbf{E}'$$

where $\mathbf{E}'$ is the effective electric field on the molecule,
$\mathbf{H}'$ is the effective magnetic field on the molecule,

$$\alpha_a = \frac{2}{3h}\sum_b \frac{\nu_{ab}\,|(a/p/b)|^2}{\nu_{ab}^2 - \nu^2}$$

$$\beta_a = \frac{c}{3\pi h}\sum_b \frac{\operatorname{Im}\{(a/\mathbf{p}/b)\cdot(b/\mathbf{m}/a)\}}{\nu_{ab}^2 - \nu^2}$$

$$\gamma_a = \frac{2}{3h}\sum_b \frac{\nu_{ab}\operatorname{Re}\{(a/\mathbf{p}/b)\cdot(b/\mathbf{m}/a)\}}{\nu_{ab}^2 - \nu^2}$$

The expressions for α_a, β_a, γ_a have been averaged over all orientations of the molecule with respect to the field, assuming all orientations to be equally probable. $\mathbf{p}_a$, $\mathbf{m}_a$, α_a, β_a, γ_a refer to the molecule in the state a; $(a/\mathbf{p}/b)$ and $(b/\mathbf{m}/a)$ are the matrix components of the electric and magnetic moments connecting states a and b; ν_{ab} is the frequency of the transition between states a and b; Im and Re mean that we are to take the imaginary or real part of the scalar product $(a/\mathbf{p}/a)\cdot(b/\mathbf{m}/a)$, which will be in general complex.

The terms in γ_a will produce only a very small second-order effect on the optical rotation (8), and are neglected in the following discussion. For an isotropic medium, we use the Lorentz field

$$\mathbf{E}' = \mathbf{E} + \frac{4\pi N_1}{3}\mathbf{p}$$

This relation seems to hold quite well even for liquids in which the molecular distribution would not necessarily be random. Since the intensity of magnetization M is quite small for non-magnetic media, we set $\mathbf{H}' = \mathbf{H}$. We shall need to consider only those states a which are available to the molecule at ordinary temperatures. The molecule may exist in various rotational-vibrational levels, or various configurations due to free rotation of the groups of the molecule. The average induced moments may then be written

$$\mathbf{p} = \alpha\left(\mathbf{E} + \frac{4\pi N_1}{3}\mathbf{p}\right) - \frac{\beta}{c}\frac{\partial}{\partial t}\mathbf{H} \tag{4}$$

$$\mathbf{m} = \frac{\beta}{c}\frac{\partial}{\partial t}\left(\mathbf{E} + \frac{4\pi N_1}{3}\mathbf{p}\right)$$

where $\alpha = \sum_a \rho_a\alpha_a$, $\beta = \sum_a \rho_a\beta_a$, and ρ_a is the probability that the molecule be in the state a of a certain conformation. α is the polarizability and β the molecular rotatory parameter of the molecule.

Use of equations 4 gives for **D** and **B** the relations

$$\mathbf{D} = \mathbf{E} + 4\pi\mathbf{P} = \mathbf{E} + 4\pi N_1\mathbf{p}$$

$$= \left(\frac{3 + 8\pi N_1\alpha}{3 - 4\pi N_1\alpha}\right)\mathbf{E} - \frac{12\pi N_1\beta/c}{3 - 4\pi N_1\alpha}\frac{\partial}{\partial t}\mathbf{H} \tag{5}$$

$$\mathbf{B} = \mathbf{H} + 4\pi\mathbf{M} = \mathbf{H} + 4\pi N_1\mathbf{m}$$

$$= \mathbf{H} + \frac{12\pi N_1\beta/c}{(3 - 4\pi N_1\alpha)}\frac{\partial}{\partial t}\mathbf{E} \qquad \text{(to the first order in } \beta\text{)}$$

By identifying the coefficient of **E** in equations 2 and 5 and indicating the coefficient of $\frac{\partial}{\partial t}$ **H** by g we have

$$\frac{\epsilon - 1}{\epsilon + 2} = \frac{4\pi N_1\alpha}{3} \tag{6}$$

$$g = 4\pi N_1\beta/c\,\frac{\epsilon + 2}{3} \tag{7}$$

Introducing ϵ and g, the equations 5 take the form:

$$\mathbf{D} = \epsilon\mathbf{E} - g\frac{\partial}{\partial t}\mathbf{H} \qquad \mathbf{B} = \mathbf{H} + g\frac{\partial}{\partial t}\mathbf{E} \tag{8}$$

Equation 6 is the familiar relation between dielectric constant and the molecular polarizability. The optical rotatory power of the medium will be found to be a function of g.

For a plane wave moving along the z-axis, the general solution for **D** may be written in the form

$$\mathbf{D} = \mathbf{D}_0 e^{i\psi} \tag{9}$$

where

$$\psi = 2\pi\nu\left(t - \frac{z}{v}\right) = 2\pi\nu\left(t - \frac{nz}{c}\right)$$

with similar expressions for **B**, **E**, and **H**. We shall be interested only in the real part of **D** in equation 9, and in the following equations **D** refers only to the real part of the general solution (equation 9).

D can be proved from equation 1 to be perpendicular to the direction of propagation, and so may be written in terms of its components as $\mathbf{D} = \mathbf{i}D_x + \mathbf{j}D_y$.

D for right circularly polarized light (i.e., **D** rotating clockwise as viewed by an observer looking along the $-z$-axis) must be of the form

$$\mathbf{D}_r = D(\mathbf{i}\cos\psi_r - \mathbf{j}\sin\psi_r)$$

Similarly for left circularly polarized light

$$\mathbf{D}_l = D(\mathrm{i} \cos \psi_l + \mathbf{j} \sin \psi_l)$$

Now we see that equation 9 will reduce to the above equations if we take the correct expression for the vector amplitude, i.e., if we take

$$\mathbf{D}_r = \mathrm{Re}\{D(\mathrm{i} + i\mathbf{j})e^{i\psi_r}\}$$

$$\mathbf{D}_l = \mathrm{Re}\{D(\mathrm{i} - i\mathbf{j})e^{i\psi_l}\} \qquad (10)$$

where D is the scalar amplitude. The solution of Maxwell's equations subject to the conditions 8 shows that the indices of refraction are different for the two types of circular polarization (8). The results are

$$n_r = \epsilon^{1/2} - 2\pi\nu g \qquad (11)$$

$$n_l = \epsilon^{1/2} + 2\pi\nu g$$

We therefore write

$$\psi_r = \psi_0 + \delta \qquad \psi_l = \psi_0 - \delta \qquad (12)$$

where

$$\psi_0 \left(= 2\pi\nu \left(t - \frac{nz}{c} \right) \right)$$

is the phase of a wave propagated with the mean index of refraction $n = \epsilon^{1/2}$ and

$$\delta = 4\pi^2 \nu^2 g \frac{z}{c}$$

The superposition of the right and left circularly polarized waves leads to a plane polarized wave. If we substitute equations 12 in 10 and add, we have

$$\mathbf{D} = \mathbf{D}_r + \mathbf{D}_l = 2\mathrm{D} \cos \psi_0 \, (\mathrm{i} \cos \delta - \mathbf{j} \sin \delta)$$

For $\delta = 0$, we have a plane polarized wave, with the electric induction vector in the x direction. For $\delta > 0$, the plane of polarization has been rotated through an angle δ in the clockwise sense as viewed in the z direction. The rotation of the plane of polarization in radians per centimeter is therefore

$$\varphi' = \frac{\delta}{z} = \frac{4\pi^2\nu^2}{c} g = \left(\frac{2\pi}{\lambda}\right)^2 cg \qquad (13)$$

By comparison with equation 11, we may also write

$$\varphi' = \frac{\pi}{\lambda} (n_l - n_r) \qquad (14)$$

i.e., a medium is dextrorotatory if the refractive index for left circularly polarized light is greater than that for right circularly polarized light. Experimentally, the rotation φ is usually expressed in degrees per decimeter, or

$$\varphi = \frac{1800}{\pi} \varphi'$$

The specific rotation, $[\alpha]$, is defined as $[\alpha] = \varphi/\rho$, where ρ is the density of the active material. The molecular rotation, $[M]$, is usually defined as

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

where M is the molecular weight of the active material. Using the above relations, and expressing g in terms of the molecular rotatory parameter β by equation 7, we have

$$[M] = \frac{288\pi^2 N}{\lambda^2} \frac{n^2 + 2}{3} \beta \tag{15}$$

$$[M]_{\mathrm{D}} = 4.93 \times 10^{35} \frac{n^2 + 2}{3} \beta_{\mathrm{D}} \text{ for sodium D light}$$

Substituting for β

$$[M] = \frac{96\pi N}{hc} \frac{n^2 + 2}{3} \sum_{a_i} \rho_{ai} \sum_{b_i} \frac{R_{b_i a_i} \nu^2}{\nu^2_{b_i a_i} - \nu^2} \tag{15a}$$

where

$$R_{b_i a_i} = \mathrm{Im}\ \{(a_i/\mathbf{p}/b_i) \cdot (b_i/\mathbf{m}/a_i)\}$$

$R_{b_i a_i}$ is called the rotatory strength of the transition $a_i \rightarrow b_i$. ρ_{a_i} is the probability that the molecule lies in a particular electronic state with definite relative positions for the atoms. Any particular relative position of the atoms in a molecule we call a *conformation.* The electronic state a_i includes all those corresponding translational, vibrational, and rotational states which have no appreciable influence on the optical rotation, so that a_i is actually made up of a set of states. If only one electronic level is accessible to the molecules in thermal equilibrium, as is usually the case, we may speak of the set of states a_i as making up a conformation i, so that ρ_{a_i} is now equal to the probability of the molecule's occurring in a conformation i.

In order to obtain some idea of the orders of magnitude of the quantities involved in equation 15, we may substitute values for a typical active substance, *sec*-butyl alcohol. Here $[M]_{\mathrm{D}} = 10.3°$ and $n_{\mathrm{D}} = 1.397$, so that we find $\beta = 1.59 \times 10^{-35}$.

Equation 15a corresponds to the dispersion formula in general use in expressing the variation of rotation with wave length:

$$[M] = \sum_i \frac{A_i}{\lambda^2 - \lambda_i^2} \tag{15b}$$

In going from equation 15a to equation 15b, however, the effect of variation of refractive index with wave length has been neglected. The factor $(n^2 + 2)/3$ remains nearly constant throughout the visible for most substances, but in careful work and in work extending into the ultraviolet its variation should be taken into account.

B. SYMMETRY PROPERTIES OF ROTATORY STRENGTHS

The operators **p** and **m** expressed in cartesian coördinates are

$$\mathbf{p} = e(\mathbf{i}x + \mathbf{j}y + \mathbf{k}z)$$

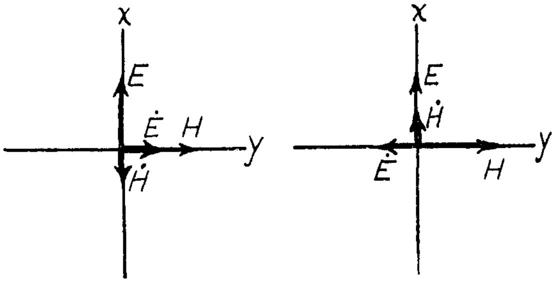
$$\mathbf{m} = \frac{eh}{4\pi mci}\left\{\mathbf{i}\left(y\frac{\partial}{\partial z} - z\frac{\partial}{\partial y}\right) + \mathbf{j}\left(z\frac{\partial}{\partial x} - x\frac{\partial}{\partial z}\right) + \mathbf{k}\left(x\frac{\partial}{\partial y} - y\frac{\partial}{\partial x}\right)\right\} \tag{16}$$

If the molecule has a center of symmetry, we may classify the states of the molecule as odd or even, according as the wave function for a given state changes sign or retains the same sign when we reflect the function through the center of symmetry, i.e., replace each coördinate by its negative. Since the operator **p** changes sign upon reflection, we have a non-vanishing value of $(a/p/b)$ only between odd and even states. The operator **m** does not change sign upon reflection, hence we have a non-vanishing value of $(b/\mathbf{m}/a)$ only between two odd or two even states. The scalar product $(a/\mathbf{p}/b)\cdot(b/\mathbf{m}/a)$ will therefore be identically zero for all states a and b, and the optical rotation will vanish. If the molecule has a plane of symmetry, we may again classify the wave functions as even or odd with respect to reflection in this plane. Thus when there is a plane of symmetry there is no pair of states a and b for which the x components of $(a/\mathbf{p}/b)$ and of $(b/\mathbf{m}/a)$ are both different from zero. The same is true of the y and z components. A fundamental requirement for optical activity is thus that the molecule possess neither a plane nor a center of symmetry.

We now consider the values of $(a/\mathbf{p}/b)\cdot(b/\mathbf{m}/a)$ for a given molecule and its mirror image. A molecule may be transformed into its mirror image by reflection of its coördinates in any plane, which is equivalent to changing from a right-handed to a left-handed coördinate system. If we reflect a molecule in the x-y plane, the new value of $(a/\mathbf{p}/b)\cdot(b/\mathbf{m}/a)$ for the molecule is obtained if we replace z by $-z$ in the wave functions a and b in the corresponding expression for the old molecule. If we change z to $-z$ in both eigenfunctions and operators, the product of the matrix components will remain unchanged, as the values of the integrals involved, being pure numbers, are independent of the particular coördinate system in which they are evaluated. As we see from equation 16, $\mathbf{p}\cdot\mathbf{m}$ changes sign upon replacing z by $-z$; therefore $(a/\mathbf{p}/b)\cdot(b/\mathbf{m}/a)$ must change sign if we replace z by $-z$ in the eigenfunctions only. An unsymmetrical molecule and its mirror image must therefore have equal and opposite optical rotations. If a molecule is the same as its mirror image, its optical rotation must vanish.

C. A QUALITATIVE DISCUSSION OF THE ORIGIN OF OPTICAL ROTATION

The preceding discussion can be made more explicit by giving a simple physical picture of the meaning of certain of the equations. Equation 4 states that there is a contribution to the induced electric moment **p** proportional to the time rate of change of the magnetic field, and a contribution to the induced magnetic moment **m** proportional to the time rate of change of the electric field. We may visualize how such contributions could arise if we assume that the potential field in an unsymmetrical molecule is such that the electrons are not free to move in the direction of applied forces, but are constrained to move along a spiral path with a component of motion normal to the impressed force. If we have a circularly polarized wave moving along the z-axis (z-axis pointing below the plane of the paper), the electric and magnetic vectors and their time derivatives will at some instant have the configuration shown in figure 1 (the xz-plane being the plane of polarization):



I Right circular polarization II Left circular polarization

FIG. 1. Electric and magnetic vectors and their time derivatives

Let us focus our attention on configuration I, and assume that the electron is forced to move along a right-handed spiral about the $+ x$-axis. The electric dipole moment will arise largely from the displacement of the electron in the $-x$ direction under the influence of the field E. But by

Lenz's law, the changing magnetic field will tend to move the electron in the right-handed direction about the $+x$-axis around a circle in the plane perpendicular to $\dot{H}$. Since the electron is forced to move along the spiral path, it will be displaced in the $+x$ direction, and thus we will have a contribution to the electric moment in the direction of E, and proportional to $\dot{H}$. This proportionality constant is related to β in equation 4; and, as we see from our simple example, it depends upon the pitch of the spiral and hence upon the degree to which the potential field is unsymmetric. The changing electric field will tend to move the electron along the $-y$-axis. The spiral forces the electron to move in a circular path, thus producing a magnetic moment proportional to $\dot{E}$. Considering the induced electric moment only, we have for configuration I, $p_{x_{\text{I}}} = aE - b\dot{H}$. For configuration II, since E is in the same direction as before but $\dot{H}$ is in the opposite direction, we have $p_{x_{\text{II}}} = aE + b\dot{H}$, where the constants a and b will be the same in the two cases. The amplitude of the vibration of the electron will thus be greater for left than for right circularly polarized light; the former therefore loses more energy to the molecule than does the latter. This means that $n_l > n_r$ and a medium composed of such "molecules" would be dextrorotatory.

We shall now consider equation 15 in terms of the above model. The only quantities in this equation whose magnitudes depend upon the nature of the model are ν_{ba} and $\mathbf{p}_{ba} \cdot \mathbf{m}_{ba}$. ν_{ba} is the frequency of a certain type of motion executed by the model. Classically, $\mathbf{p}_{ab} \cdot \mathbf{m}_{ba}$ is $\mathbf{P} \cdot \mathbf{M}$, where $\mathbf{P}$ and $\mathbf{M}$ are the vector amplitudes of the variable electric and magnetic moments associated with this type of motion. For an electron moving periodically back and forth along a spiral, $\mathbf{M}$ is directed essentially along the axis of the spiral, while $\mathbf{P}$ has a component along this direction, so that $\mathbf{P} \cdot \mathbf{M}$ will not vanish and there is a non-vanishing β. The greater the pitch of the spiral, the greater will be the component of $\mathbf{P}$ in the direction of $\mathbf{M}$, hence the greater will be the optical rotatory power of the model. If, on the other hand, the pitch of the spiral is zero, so that the electron moves in a circle, then $\mathbf{P}$ and $\mathbf{M}$ will be perpendicular, and the model will possess no optical activity. Thus we see that there is a direct relationship between the magnitude of $\mathbf{P} \cdot \mathbf{M}$ and b in the relation $p_x = aE \pm b\dot{H}$ given above.

D. ROTATORY STRENGTHS, LINE STRENGTHS, AND ANISOTROPY FACTORS

It can be shown (8) that for each state a

$$\sum_b R_{ba} = 0$$

Therefore all the quantities R_{ba} cannot have the same sign. We see from equation 15 that for $\nu = \infty$

$$[M] = \text{const.} \sum_b R_{ba} = 0$$

also for $\nu = 0$, $[M] = 0$. Optical rotatory power is thus a property that tends to zero for very large and for very small frequencies.

The polarizability can be written as

$$\alpha = \frac{2}{3h} \sum_b \frac{\nu_{ba} S_{ba}}{\nu_{ba}^2 - \nu^2} \tag{17}$$

where $S_{ba} = |(a/\mathbf{p}/b)|^2$ = line strength of the transition $a \rightarrow b$ or

$$\alpha = \frac{e^2}{4\pi^2 m} \sum_b \frac{f_{ba}}{\nu_{ba}^2 - \nu^2} \tag{18}$$

$$f_{ba} = \frac{8\pi^2 m}{3e^2 h} \nu_{ba} S_{ba} = \text{oscillator strength of the transition}$$

For the oscillator strengths, we have the relation that for each state a,

$$\sum_b f_{ba} = n$$

where n is the number of electrons in the molecule (17, 40). Since S_{ba} is always positive, while R_{ba} may be positive or negative, we see that optical rotatory power is a small effect in comparison to ordinary refraction.

Kuhn (19) defines the anisotropy factor g_{ab} for the transition $a \rightarrow b$. For gases ($n \approx 1$) the definition leads to the expression

$$\frac{(n_l - n_r)_{a \rightarrow b}}{(n - 1)_{a \rightarrow b}} = \frac{\nu}{\nu_{ba}} g_{ba} \tag{19}$$

In terms of the quantum-mechanical quantities defined above,

$$g_{ba} = 4 \frac{R_{ba}}{S_{ba}}$$

which is valid for condensed phases as well as for gases. The anisotropy factor is thus the number by which the contribution of a given transition to the polarizability must be multiplied to obtain the contribution to the optical rotatory power. In most cases, the wave functions of a molecule will be approximately either even or odd, hence for a given transition either $(a/\mathbf{p}/b)$ or $(b/\mathbf{m}/a)$ may be large, but in general both will not be large. Therefore strong absorption bands will have small anisotropy factors, and weak bands may have large anisotropy factors, with the result that the rotational strengths of both strong and weak absorption bands may be of the same order of magnitude.

E. CIRCULAR DICHROISM

An optically active medium also has different absorption coefficients for right and left circularly polarized light. The quantum-mechanical treatment has been presented in detail by Condon, Altar, and Eyring (9). For a given transition, it is found that

$$\frac{\epsilon_l - \epsilon_r}{\epsilon} = 4\frac{\nu}{\nu_{ba}}\frac{R_{ba}}{S_{ba}} = \frac{\nu}{\nu_{ba}}g_{ba} \tag{20}$$

where ϵ is the mean absorption transition probability, and ϵ_r and ϵ_l are the absorption transition probabilities for right and left circularly polarized light. This unequal absorption of left and right circularly polarized light is known as circular dichroism, and is experimentally measured by determining the ellipticity of an originally plane polarized beam, the ellipticity per unit length being

$$\theta = \frac{\pi}{\lambda}(\epsilon_l - \epsilon_r)$$

Measurements of the absorption and ellipticity for a given band will give us the anisotropy factor g_{ba} for this band, and thus enable us to determine rotatory strengths from line strengths.

The ellipticity is a maximum where the absorption is a maximum, i.e., in the absorption band. Taking

$$\epsilon = \frac{8\pi^3}{3h^2c}S_{ba}$$

and using equation 15 for R_{ba} in equation 20 we obtain:

$$[M]_{ba} = \frac{3hN}{\pi^2}\frac{\nu\nu_{ba}(\epsilon_l - \epsilon_r)(n^2 + 2)}{\nu_{ba}^2 - \nu^2}$$

This gives Natanson's rule that if a medium absorbs left circularly polarized light more strongly than right, then the partial rotation of the given transition is positive for $\nu < \nu_{ab}$.

The expressions given above for α and β are of course not correct for $\nu = \nu_{ab}$. In this case, as Condon points out, analogy with the quantum-mechanical theory of dispersion gives for the molecular rotation:

$$[M] = \frac{96\pi N}{hc}\frac{n^2 + 2}{3}\sum_a \rho_a \sum_b \frac{\nu^2(\nu_{ba}^2 - \nu^2)R_{ba}}{[(\nu_{ba}^2 - \nu^2)^2 + \nu^2\Gamma_{0ba}^2]}$$

The ellipticity per unit length then has the form:

$$\theta = \frac{\pi}{\lambda}(\epsilon_l - \epsilon_r) = \frac{16\pi^2 N_1}{3hc}\sum_a \rho_a \sum_b \frac{\nu^3\Gamma_{0ba}R_{ba}}{[(\nu_{ba}^2 - \nu^2)^2 + \nu^2\Gamma_{0ba}]}$$

Here Γ_0 (the half-width of the line) measures the strength of the damping factor. The change of sign of the partial contribution, plus the ellipticity produced in the band, is known as the Cotton effect; the general behavior of these quantities in the neighborhood of a band is shown diagrammatically in figure 2.

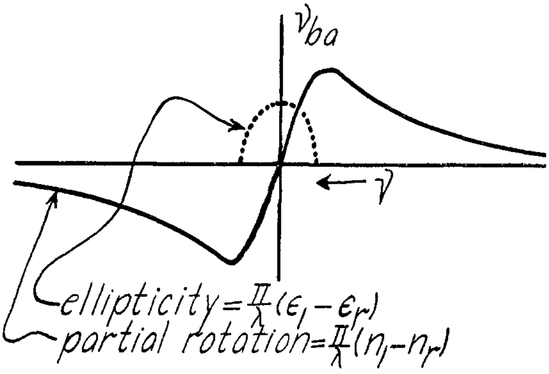


FIG. 2. General behavior of the ellipticity and the partial rotation in the neighborhood of a band

F. PARTIAL ROTATIONS, CHROMOPHORIC GROUPS, AND VICINAL ACTION

We have seen that the molecular rotatory power may be expressed as

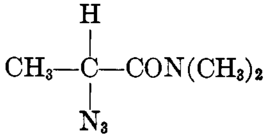
$$[M] = \text{const} \sum_b \frac{R_{ba}\nu^2}{\nu_{ba}^2 - \nu^2}$$

where each term in the sum represents the contribution of a single transition. Only electronic transitions will be of importance in producing optical rotation, as we see from the manner in which the mass enters into the expressions for magnetic moment in equations 16. Thus transitions involving changes in nuclear vibrations or rotations will be less effective than electronic transitions in contributing to optical activity by a factor of the order of the ratio of nuclear to electronic masses. For transparent substances, the electronic transitions with which we will be concerned will lie in the ultraviolet. Because of the factor ν_{ba}^2 in the denominator, transitions in the far ultraviolet will be of less importance than transitions of comparable rotatory strengths in the near ultraviolet, and in addition the contributions from the far ultraviolet absorption lines will tend to cancel out, since the several values for R_{ba} will not all be of the same sign. In many cases, therefore, the resultant optical rotation will be due largely to the one or two absorption bands nearest the visible. If the dispersion data are accurate enough, and especially if the dispersion has been measured through the band, the constants for the bands nearest the visible may be fairly accurately determined, any residual rotation being expressed by a term representing the resultant of the remaining bands. It must be emphasized that in the cases where the empirical dispersion data are expressed by a single term, the constants R_{ba} and ν_{ba} determined by this data will in general represent some sort of average of the constants of several bands.

If the partial rotation of a single transition can be separated from the residual rotation, it is frequently found that this transition is localized in a particular group of the molecule, called the chromophoric group. The remaining groups of the molecule affect this partial rotation only through their vicinal effect on the chromophoric group, that is, they produce the dissymmetry necessary to make the transition in the chromophoric group optically active.

The general discussion given above may be made more specific by several examples given by Kuhn (19, 20, 22).

In



$$CH_3\text{—}\overset{\displaystyle H}{\underset{\displaystyle N_3}{C}}\text{—}CON(CH_3)_2$$

there is an absorption band at 2900 Å. which can be associated with a transition in the N_3 group. The oscillator strength of this band can be determined by integrating the absorption over the band.

$$\int \epsilon_\nu \, d\nu = N_1 f \frac{\pi e^2}{mc} \left(\frac{n^2 + 2}{3} \right)^2$$

The value found for this band is $f = 5 \times 10^{-4}$. Since $\Sigma f \sim 50$, we see that the N_3 band at 2900 Å. accounts for about 10^{-5} of the total absorption and polarizability. The anisotropy factor for this band is $g = 2 \times 10^{-2}$, and the band contributes about 20 per cent of the observed rotation in the visible.

In camphor, the band at 3000 Å. can be associated with a transition in the C=O group, as this band appears in all aldehydes and ketones. Measurements of circular dichroism and absorption show that this band is actually two superposed electronic bands, the one nearest the visible being optically active, the other inactive. The active band has an f value of 2×10^{-4}, the inactive band an f value several times greater. This active band represents only about the 3×10^{-5} part of the total absorption, but its partial rotation accounts for the greater part of the observed optical rotation.

III. THEORIES OF OPTICAL ROTATORY POWER

A. THE COUPLED-OSCILLATOR THEORY

With the derivation of equation 15 by means of quantum mechanics, the problem of optical activity can be said to be solved in principle. Any modern theory seeking to relate observed optical rotations to molecular structure should have this equation as its starting point. Two such theories have been proposed in recent years,—the polarizability theory of Kirkwood and the one-electron theory of Condon, Altar, and Eyring. Considerable success has been obtained, however, in the interpretation of experimental data, at least in a qualitative sense, by the use of the coupled-oscillator theory of Born (5), Oseen (31), and Kuhn (18), especially in the form developed and applied by Kuhn. Although this theory was originally formulated in classical terms, it has since been derived from equation 15 for Kuhn's simple model by Condon (8).

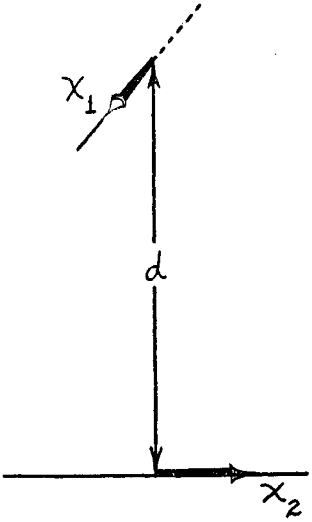


FIG. 3. Simplest system of coupled oscillators which gives optical activity

For this simplest system of coupled oscillators (see figure 3) which gives optical activity, we consider that there are in the molecule two oscillators of charge e_1, e_2, and mass m_1, m_2, which in the absence of interactions will vibrate at right angles to one another with frequencies ν_1', ν_2', the positions of equilibrium being separated by a distance d.

If now there is a coupling between the oscillators, that is, if the potential energy has the form $V = 1/2\, k_1x_1^2 + 1/2\, k_1x_2^2 + k_{12}x_1x_2$, the resulting motion can be resolved into two normal vibrations by a transformation to a new set of axes which are related to the old set by a rotation through an angle α, which will be small if the coupling constant k_{12} is small. The normal frequencies, ν_1, ν_2, will be nearly equal to the original frequencies ν_1', ν_2' in the case of small coupling. In the classical treatment it is shown that the energy transferred to these normal vibrations is different for right and left circularly polarized light, resulting in differing indices of refraction for the two types of circular polarization, and thus in optical rotation. In the quantum-mechanical treatment, the rotatory strength, R_{ba}, is calculated by the use of harmonic oscillator wave functions. Either treatment of this model leads to the result, for N_1 molecules per unit volume, oriented at random:

$$\alpha = \frac{2\pi N_1}{3} \frac{n^2 + 2}{3} \frac{d}{\lambda^2} \sin \alpha \cos \alpha \frac{e_1 e_2}{(m_1 m_2)^{1/2}} \left\{ \frac{1}{\nu_1^2 - \nu^2} - \frac{1}{\nu_2^2 - \nu^2} \right\} \quad (21)$$

The presence of two non-parallel oscillators in a molecule will thus give rise to an optical rotation. Since the coupling forces between these oscillators may be expected to be small, both oscillators will maintain their characteristic frequencies, but by their mutual interaction they will become optically active. Oscillator No. 1 is said by its *vicinal action* to cause an *induced anisotropy* in oscillator No. 2 and *vice versa.* It is in this way that Kuhn is able to account for the optical rotation associated with an absorption band of a symmetrical group such as the carbonyl in an unsymmetrical molecule such as camphor.

Inspection of equation 21 shows immediately that the sum rule is obeyed, since the rotatory strength associated with ν_1 is the negative of that associated with ν_2.

Since the details of this important theory and especially its application in interpreting experimental data have been thoroughly covered in a review article by Kuhn (21), we shall not devote so much space to it in the following pages as to the more recent theories.

B. POLARIZABILITY THEORY OF KIRKWOOD

Equation 15a has been applied to the calculation of optical rotations by Kirkwood (15), who was able to transform it into an expression for rotatory power in terms of the polarizabilities and anisotropies of the groups in the molecule. The underlying principle is that the electrons of a molecule may be considered as assignable to definite groups between which there is no exchange. (This is nearly true of all electrons in lower states except the small fraction involved in the bonding of one group to another.) Furthermore, each transition which a molecule can undergo is to a first approximation localized in a distinct group. (This is justified by the fact that, for instance, the presence of a carbonyl group in a molecule is always accompanied by an absorption band in the neighborhood of 2900 Å., and similarly for other groups.)

The first of these assumptions is introduced by breaking up the electric moment and magnetic moment terms in equation 15a into sums over groups:

$$\mathbf{p}_{ab} = \sum_k \mathbf{p}_{ab}^{(k)}$$

$$\mathbf{m}_{ba} = \sum_k \left(\mathbf{R}_k \times \mathbf{P}_{ba}^{(k)} + \frac{2mc}{e} \mathbf{m}_{ba}^{(k)} \right)$$

where the superscript k refers to the k^{th} group, $\mathbf{R}_k$ is the radius vector of the center of gravity of the k^{th} group relative to some fixed point in the molecule, $\mathbf{P}^{(k)}$ is the total electronic momentum operator of group k, $\mathbf{p}^{(k)}$ is the electric moment operator of group k, and $\mathbf{m}^{(k)}$ is the magnetic moment operator of the k^{th} group relative to its center of gravity. Substituting in equation 15a,

$$\beta = \frac{c}{3\pi h} \sum_{a,b} \left\{ e^{-\frac{\epsilon_a}{kT}} \frac{\operatorname{Im}\,(\mathbf{p}_{ab} \cdot \mathbf{m}_{ba})}{\nu_{ba}^2 - \nu^2} \right\} = \beta^{(0)} + \beta^{(1)} + \sum_k \beta_k \tag{22}$$

where

$$\beta^{(0)} = \frac{1}{3h} \sum_{i>k} \sum_a e^{\frac{-\epsilon_a}{kT}} \sum_{b>a} \frac{\nu_{ba}}{\nu_{ba}^2 - \nu^2} \operatorname{Re}(\mathbf{R}_{ik} \cdot (\mathbf{p}_{ab}^{(i)} \times \mathbf{p}_{ba}^{(k)})) \tag{22a}$$

$$\beta^{(1)} = \frac{c}{3\pi h} \sum_{i>k} \sum_a e^{\frac{-\epsilon_a}{kT}} \sum_{b>a} \frac{\operatorname{Im}\,(\mathbf{p}_{ab}^{(k)} \cdot \mathbf{m}_{ba}^{(i)})}{\nu_{ba}^2 - \nu^2} \tag{22b}$$

$$\beta_k = \frac{c}{3\pi h} \sum_k \sum_a e^{\frac{-\epsilon_a}{kT}} \sum_{b>a} \frac{\operatorname{Im}\,(\mathbf{p}_{ab}^{(k)} \cdot \mathbf{m}_{ba}^{(k)})}{\nu_{ba}^2 - \nu^2} \tag{22c}$$

$\mathbf{R}_{ik} = \mathbf{R}_k - \mathbf{R}_i =$ vector from center of gravity of i to that of k. β_k is assumed negligible to the approximation considered here for symmetrical groups, it being the contribution of the k^{th} group alone to the optical rotation parameter. $\beta^{(1)}$, the contribution due to coupling of magnetic moment on one group with an electric moment on another, is neglected as probably small, although it deserves further consideration. $\beta^{(0)}$ therefore remains as the major source of the rotatory power; it is similar in origin to the coupling of oscillators in the theories of Born and Kuhn.

The second approximation (that of localization of transitions within definite groups) is now introduced in order to calculate $\beta^{(0)}$. A set of zero-order eigenfunctions is set up, characterized by quantum numbers assignable to each of the groups of the molecule. First-order perturbation theory is applied, using as the perturbing potential, V, the expression for thei nteraction of two dipoles, $\mathbf{p}_i$ and $\mathbf{p}_j$, at a distance $\mathbf{R}_{ij}$ apart, where this distance is large compared with the separation of charge in the dipoles:

$$V = \frac{p_i p_j}{R_{ij}^3}(\cos\theta - 3\cos\chi\cos\psi) \tag{23}$$

where χ is the angle between $\mathbf{p}_i$ and $\mathbf{R}_{ij}$, ψ is the angle between $\mathbf{p}_j$ and $\mathbf{R}_{ij}$, and θ is the angle between $\mathbf{p}_i$ and $\mathbf{p}_j$.

The perturbed eigenfunctions are now used to calculate the $\mathbf{p}_{ba}^{(k)}$, and it is found that by a series of transformations it is possible to replace the product

$$\mathbf{R}_{ik}\cdot(\mathbf{p}_{ab}^{(i)} \times \mathbf{p}_{ba}^{(k)})$$

by an expression involving the polarizabilities, anisotropies, and relative orientations of the principal axes of the groups i and k.

The de Mallemann theory of optical rotatory power results from an application of second-order perturbation theory, while the Boys theory would come out of a third-order calculation. Whereas the first-order calculation results in an expression involving simultaneous interactions of pairs of groups, the second- and third-order calculations result in expressions involving simultaneous interactions of three and four groups, respectively.

The final expression obtained by Kirkwood is:

$$\beta^{(0)} = -\tfrac{1}{6}\sum_{i>k}\sum_{r,s}\alpha_{rr}^{(i)}\alpha_{ss}^{(k)}(\mathbf{b}_r^{(i)}\cdot\mathbf{T}_{ik}\cdot\mathbf{b}_s^{(k)})\mathbf{R}_{ik}\cdot(\mathbf{b}_r^{(i)} \times \mathbf{b}_s^{(k)}) \tag{24}$$

where

$$\mathbf{T}_{ik} = \frac{1}{R_{ik}^3}\left(1 - 3\,\frac{\mathbf{R}_{ik}\mathbf{R}_{ik}}{R_{ik}^2}\right)$$

$\alpha_{rr}^{(i)}$ are the three polarizabilities along the principal axes $\mathbf{b}_r^{(i)}$ of group i, and similarly for $\alpha_{ss}^{(k)}$ and $\mathbf{b}_s^{(k)}$.

If the groups in the molecule are cylindrically symmetrical (two of the $\alpha_{rr}^{(i)}$ equal), this may be simplified to:

$$\beta^{(0)} = -\tfrac{1}{6}\sum_{i>k}\alpha_i\alpha_k\delta_i\delta_k(\mathbf{b}_i\cdot\mathbf{T}_{ik}\cdot\mathbf{b}_k)(\mathbf{R}_{ik}\cdot\mathbf{b}_i \times \mathbf{b}_k) \tag{25}$$

where α_i and α_k are the mean polarizabilities of the interacting groups i and k, and δ_i and δ_k are their anisotropies:

$$\delta_i = \frac{\alpha_{11}^{(i)} - \alpha_{22}^{(i)}}{\alpha_i}$$

where $\alpha_{11}^{(i)}$ is the polarizability along axis of cylindrical symmetry, $\mathbf{b}_i$, and similarly for δ_k. The values of the polarizabilities α_i involved here can be found from the molecular refractions of the groups present. The anisotropies δ_i may be estimated from the depolarization of light by simple derivatives containing the group in question, and also from the Kerr constant of such substances. The other quantities, $\mathbf{b}_i$, $\mathbf{R}_{ik}$, etc., are determined by a knowledge of the structure of the molecule in question. The vectors $\mathbf{b}_i$ are, of course, of unit length. Unfortunately there may sometimes be some doubt as to the direction of some of the **b**'s due to our inadequate knowledge of the origin of optical anisotropy.

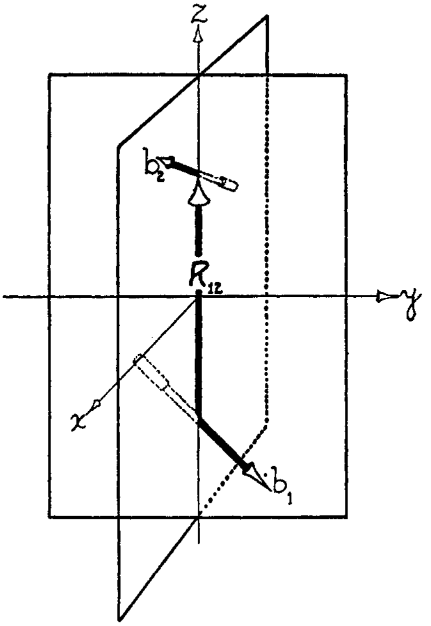


FIG. 4

The above treatment bears a very close resemblance to the calculation of van der Waals forces, and indeed it may be said that the interactions which are taken into account are those which give rise to those forces.

There are some indications that this theory is not able to deal adequately with all factors observed in connection with optical rotatory power. This is particularly true of the rotations associated with weak absorption bands and this is a typical defect of all polarizability theories, as was pointed out by Lowry and Allsopp (26). Thus, in camphor, for example, it is known that a major portion of the observed rotation is associated with the transition at 2950 Å. in the carbonyl group (20). Yet this band is known to contribute very little to the polarizability of a carbonyl-containing molecule (26). This fact can only be brought into conformity with the theory if the anistropy ratio, δ, were to change markedly with wave length without altering the polarizability, which is unlikely. It seems probable that in this theory the optical activity associated with weak bands is contained in the terms $\beta^{(1)}$ and $\beta^{(k)}$, since such bands probably obtain the large values of their anisotropy factors from a large value for the magnetic moment of their transitions (see later).

A further limitation to the theory is found in the inadequacy of the potential, V, of equation 23. This expression is only true for dipoles which are separated by distances large compared with the separation of charge within the dipoles. In the case under consideration, however, this condition is far from being met, especially when perturbations involving excited states are involved, since the eigenfunctions for these extend out over a considerable region of space and even overlap considerably most of the nearby groups. Of the similar calculation of the van der Waals forces between helium atoms, it is known (29) that the term in the potential given by equation 23 becomes seriously inadequate at a distance of 3 Å. This distance would be increased when interactions between excited states are concerned. Therefore, it would seem that the theory cannot be expected to give good results for more compact molecules where interactions between groups closer than, say, 4 or 5 Å. give rise to the optical activity.

It is instructive to calculate the optical rotation of a very simple model (figure 4) on this theory. Let there be two cylindrically symmetric groups whose principal axes have the following directions:

$$\mathbf{b}_1 = \frac{1}{\sqrt{2}}(\mathbf{j} - \mathbf{k})$$

$$\mathbf{b}_2 = \frac{1}{\sqrt{2}}(\mathrm{i} + \mathbf{k})$$

The vector from the center of group No. 1 to the center of group No. 2 is

$$\mathbf{R}_{12} = d\mathbf{k}$$

so that d is the distance between them. Using these quantities in equation 25 we find that

$$\mathbf{b}_1 \cdot \mathbf{T}_{12} \cdot \mathbf{b}_2 = \frac{1}{d^3}$$

$$R_{12} \cdot (b_1 \times b_2) = \frac{1}{2}(\mathrm{i} - \mathbf{j} - \mathbf{k}) \cdot d\mathbf{k} = -\frac{d}{2}$$

$$\beta^{(0)} = +\frac{\alpha_1 \alpha_2 \delta_1 \delta_2}{12 d^2}$$

If the principal axes of the hydroxyl groups of hydrogen peroxide have the orientations postulated here (and they are probably not far from it (33)), we may calculate the optical rotation of one of the optically active forms of this substance. Taking $\alpha = 10.3 \times 10^{-25}$ cc., $\delta = 0.35$, $d = 1.25$ Å., and refractive index = 1.414, we find that

$$\beta^{(0)} = +6.8 \times 10^{-35}$$

and

$$[M]_{\mathrm{D}} = +45^{\circ}$$

on this model.

If $\delta_1 = \delta_2 = 1$ we have the groups acting as linear oscillators, and the model takes on the aspect of that of Kuhn, except that more explicit account is taken here of the physical nature of the coupling of the oscillators.

Since on this theory the optical rotation depends on the products of two polarizabilities, and since the polarizability depends upon the frequency, as follows,

$$\alpha = \sum_i \frac{k_i}{\nu_i^2 - \nu^2}$$

the effect on the optical rotation of changing the frequency of the light should be given by

$$[M] = \sum_{i>j} \frac{k_{ij}\nu^2}{(\nu_i^2 - \nu^2)(\nu_j^2 - \nu^2)} = \sum_{i>j} \nu^2 k'_{ij} \left\{ \frac{1}{\nu_i^2 - \nu^2} - \frac{1}{\nu_j^2 - \nu^2} \right\} \tag{26}$$

A test of this relationship to find if it agrees with the observed behavior of rotatory dispersion is at present beyond the ability of experimental technique.

C. THE ONE-ELECTRON THEORY OF OPTICAL ACTIVITY

In applying equation 15 to actual molecules, the problem is to select a model which has the twin properties of tractability and accuracy in essential features. In a mathematical sense the problem is completely solved, but this is not a particularly interesting remark to one interested in obtaining numbers to compare with experiment. An inspection of experimental dispersion curves for optical rotatory power reveals, as equation 15 already suggests, a striking correlation between absorption and optical rotation. The absorption by a molecule in the visible and ultraviolet is due to electronic transitions, so that electronic transitions must be the central feature of any model that is to treat the dispersion satisfactorily.

Atomic spectra have been successfully interpreted as arising principally from one-electron transitions (10). The same procedure is usually adopted in interpreting most molecular transitions.[1] We thus expect that rotatory power can be treated by the same procedure. Our next problem is, therefore, to find the intial and final states of these one-electron transitions. We note that the transitions which a molecule can undergo are generally each characteristic of one of the groups in the molecule. Thus hydroxyl-containing compounds have an absorption band at ~ 1800 Å., while compounds with an unconjugated C═C bond absorb at ~ 2150 Å. In speaking of the optical activity associated with these transitions, we refer to the group primarily involved in the transition as the *chromophoric group* and the forces which act on it to make its transition optically active as *vicinal actions*. Therefore, in calculating the optical rotation we must first find out the natures of the electronic states of these groups. Insofar as previous descriptions of transitions define these states for the important chromophoric groups, the procedure here is straightforward. The perturbation of these electronic states by neighboring radicals leads to altered states which give transitions which are optically active provided the system as a whole has no plane or center of symmetry.

The general procedure is as follows: The eigenfunctions for two non-degenerate states of a chromophore which are acted on by a perturbation V can, using the usual perturbation theory, be expressed as:

$$\begin{aligned} \psi_a &= \psi_a^0 + \sum_{i \neq a} c_{ia}\psi_i^0 \\ \psi_b &= \psi_b^0 + \sum_{j \neq b} c_{jb}\psi_j^0 \end{aligned} \tag{27}$$

where

$$c_{ia} = \frac{\int \psi_i^0 V \psi_a^0 \mathrm{d}\tau}{E_a^0 - E_i^0} \qquad c_{jb} = \frac{\int \psi_j^0 V \psi_b^0 \mathrm{d}\tau}{E_b^0 - E_j^0}$$

Using these new functions in calculating R_{ba} in equation 15, we find

$$\begin{aligned} R_{ba} = \mathbf{p}_{ab}\cdot\mathbf{m}_{ba} &+ \sum_i c_{ia}(\mathbf{p}_{ib}\cdot\mathbf{m}_{ba} + \mathbf{p}_{ab}\cdot\mathbf{m}_{bi}) + \sum_j c_{jb}(\mathbf{p}_{aj}\cdot\mathbf{m}_{ba} + \mathbf{p}_{ab}\cdot\mathbf{m}_{ja}) \\ &+ \sum \text{(terms involving products of two } c\text{'s)} \\ &+ \sum \text{(terms involving products of three } c\text{'s)} + \cdots \end{aligned} \tag{28}$$

where

$$\mathbf{p}_{ab} = \int \psi_a^0 \mathbf{p} \psi_b^0 \mathrm{d}\tau; \quad \mathbf{p}_{ai} = \int \psi_a^0 \mathbf{p} \psi_i^0 \mathrm{d}\tau; \quad \mathbf{m}_{ab} = \int \psi_a^0 \mathbf{m} \psi_b^0 \mathrm{d}\tau; \text{ etc.}$$

For the unperturbed states ψ_a^0 and ψ_b^0 which are usually taken there is no optically active transition, so that $\mathbf{p}_{ab}\cdot\mathbf{m}_{ba}$ is zero. Furthermore, a

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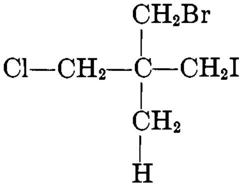
[1] See, for example, papers by R. S. Mulliken.

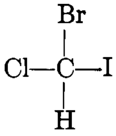
good many of the products **p**·**m** are either zero or very small, so that in practice only a few of the coefficients c_{ia} and c_{ib} need be calculated.

We shall see that the coefficients, c, are made up of sums of contributions from the interactions of individual groups with each chromophore. Therefore, the optical rotation can be regarded as made up of the sums of interactions between groups taken two at a time, plus the sums over products of two of these interactions (i.e., sums over interactions involving three groups at a time), and so on. The first sum gives what we shall call the first-order contributions to the optical activity, the second sum gives the second-order contributions, etc. Since the interactions are always small (all c's < 1) the first-order effects will be the largest in general, while the second-order effects will be next largest, etc. And, since, as we shall see, vicinal actions fall off with increasing distance, the interactions involving the groups which are farther off will show a greater tendency to give rise primarily to first-order contributions. Thus the second-order contribution in



$$\begin{array}{ccc} & \mathrm{CH_2Br} & \\ & | & \\ \mathrm{Cl{-}CH_2{-}} & \mathrm{C} & \mathrm{{-}CH_2I} \\ & | & \\ & \mathrm{CH_2} & \\ & | & \\ & \mathrm{H} & \end{array}$$

will be much less than that in



$$\begin{array}{ccc} & \mathrm{Br} & \\ & | & \\ \mathrm{Cl{-}} & \mathrm{C} & \mathrm{{-}I} \\ & | & \\ & \mathrm{H} & \end{array}$$

If we are to use equation 28 in calculating the optical activity of a given substance, we must decide (*a*) what eigenfunctions are to be used in describing the unperturbed states of the electrons in the chromophoric group and (*b*) what forces from the surrounding radicals perturb these states.

(*a*) Whether we choose to describe a state of the chromophoric electron in terms of a linear combination of eigenfunctions for the three-dimensional oscillator, or in terms of the hydrogen-like functions, or in terms of any other complete orthogonal set is entirely a matter of convenience. This is true whether the electron spends its time moving about one center or moving about many centers. Only the two types of function mentioned, however, have been applied to the problem of calculating optical rotations on the one-electron model, and of these the hydrogen-like functions are the closer to reality, that is, they require fewer terms to give a good picture of the true state of affairs.

(*b*) The perturbing field V can usually be treated as being made up of a number of central force fields, V_j, arising from the various groups and atoms surrounding the given chromophore, the subscript j referring to the j^{th} such atom or group. The contribution to any c_{ia} by a V_j involves the calculation of the two-center integral

$$\int \psi_i^0 V_j \psi_a^0 \, d\tau$$

For hydrogen-like eigenfunctions which are not spherically symmetrical, this integral will depend upon the direction of the center j from the center of the eigenfunction with respect to a set of axes defined by the eigenfunction. Now it is generally true that a transformation can be applied

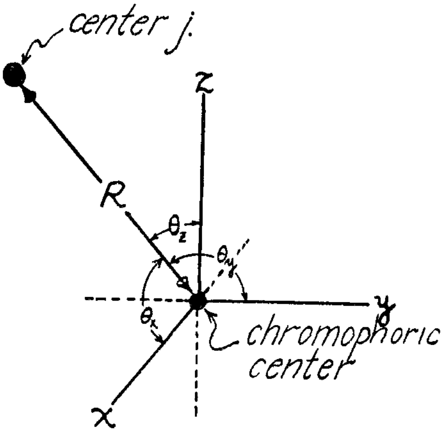


FIG. 5

which will permit the integral to be expressed as a sum of the products of two types of functions (13); one of the types depends upon the distance, R, between the perturbing center and the center of the chromophoric group under consideration, while the other type depends upon the angles which the line **R** joining the two groups makes with the chosen coördinate axes of the eigenfunction of the chromophoric group. This may be represented as follows (the angles θ are as given in figure 5):

$$\int \psi_i^0 V_j \psi_a^0 \, d\tau = F(R) f(\theta_x \theta_y \theta_z) + G(R) g(\theta_x \theta_y \theta_z) + \cdots \tag{29}$$

where the sum usually contains a small number of terms, and where the forms of the functions F, f, G, g, $\cdots$ depend upon the nature of ψ_a^0, ψ_i^0, and V_j.

In the event that the potential V_j is not spherically symmetric about the center j but depends upon the angles φ_x, φ_y, φ_z, which the line R

makes with a set of coördinate axes in the center j, the integral may be expressed as

$$\int \psi_i^0 V_j \psi_a^0 \, \mathrm{d}\tau = F(R) f(\theta_x \theta_y \theta_z) \Phi(\varphi_x \varphi_y \varphi_z) + G(R) g(\theta_x \theta_y \theta_z) \Gamma(\varphi_x \varphi_y \varphi_z) \tag{30}$$

The functions f, g, $\cdots$ are the angular dependence functions of the chromophoric group; Φ, Γ, $\cdots$ are the angular dependence functions of the vicinal group. These functions are usually relatively simple expressions involving products of sines and cosines of angles. The functions F, G, $\cdots$ are the radial dependence functions of the vicinal action between the vicinal and chromophoric groups and are usually complicated functions of R best expressed by a graphical plot.

When the perturbing fields V_j are sufficiently small to make the second-order effects mentioned before negligible, the optical rotation is given in terms of these functions by:

$$[M] = \frac{96\pi N}{hc} \frac{n^2 + 2}{3} \sum_a \rho_a \sum_b R_{ba} \nu^2 / \nu_{ba}^2 - \nu^2 \tag{31}$$

$$R_{ba} = \sum_{j.k} \frac{(Ff\Phi + Gg\Gamma + \cdots)_{jk}}{E_a^0 - E_k^0} (\mathbf{p}_{kb} \cdot \mathbf{m}_{ba} + \mathbf{p}_{ab} \cdot \mathbf{m}_{bk})$$
$$+ \sum_{j.l} \frac{(F'f'\Phi' + G'g'\Gamma' + \cdots)_{jl}}{E_b^0 - E_l^0} (\mathbf{P}_{al} \cdot \mathbf{m}_{ba} + \mathbf{P}_{ab} \cdot \mathbf{m}_{la})$$

The first sum in R_{ba} refers to the effect of perturbations on the lower state, while the second sum refers to the effect on the upper state of the given transition. The primes and subscripts on F, g, Φ, etc., refer to the fact that these must be calculated for each perturbation j and for each perturbing level k and l acting on each of the levels a and b of the transition.

It is seen from equation 31 that insofar as the first-order contribution to the optical rotation is concerned, the rotation is additive in the vicinal actions of the perturbing groups in the sense that the introduction of a new vicinal group adds a quantity to the partial rotation of a given chromophore which is independent of the number, nature, and arrangement of the other vicinal groups.

The problem of calculating optical rotations by the one-electron theory therefore resolves itself into a calculation of the radial and angular dependence functions for the various types of fields and states which we find in a given problem.

An example of these functions and their use in calculating the optical rotation will be given later. Meanwhile, we must investigate the forces which can be expected to act as perturbations in giving rise to optical rotatory power.

Perturbations which can act as vicinal forces

(*1*) *Dipole forces* may be treated in two ways: they may be considered as arising from a separation of charges, the effect of each charge being calculated as a separate spherically symmetrical perturbation, or we may use the expression for the potential of an electron in the field of a dipole of moment μ, the axis of which makes an angle θ with the line of length R to the point at which the potential is calculated:

$$V = \frac{\mu e}{R^2} \cos \theta \tag{32}$$

Here the angular dependence function of the perturbing field is cos θ if the distance between dipole and chromophore is large.

That the fields from dipoles in a dissymmetric molecule may give rise to appreciable optical rotations was shown by Condon, Altar, and Eyring (9), who were able to account for the order of magnitude of the partial rotation of the nitrite band in phenylmethylcarbinol nitrite by using harmonic oscillator eigenfunctions and the accepted values for the bond moments occurring in the molecule. A further indication that dipole fields may affect the optical rotation in an important way is found in the work of Betti, Rule, and Beckmann and Cohen (see later). The latter workers, however, interpret the dipole effect as being due to a distortion of the molecular framework.

That dipoles are not sufficient to account for the observed rotations in all cases, however, is shown by the work of Condon, Altar, and Eyring on *sec*-butyl alcohol. Following the same procedure here as for phenylmethylcarbinol nitrite a rotation too small by two powers of ten was obtained.

(*2*) *The fields of ions and ionic charges* in the neighborhood of a dissymmetric molecule should produce a marked effect on the rotation, since they are more intense than dipole fields. These have the form

$$V = \frac{Ze^2}{DR} \tag{33}$$

where D is the dielectric constant and Ze the ionic charge. Here, of course, the angular dependence function of the perturbing group is independent of angle, hence is equal to unity.

Linear fields should also be capable of producing optical activity. Here

$$V = -zeF \tag{34}$$

where z is the distance measured in the direction of the field F.

(*3*) Since the electronic clouds about a nucleus are spread out over a finite region, the potential in the neighborhood of even a neutral atom is not zero. Therefore, if the electron cloud of the chromophoric group overlaps those of the surrounding atoms, a perturbation from this source will result. This is especially likely to occur when the chromophoric electron is in an excited state. An example is the potential at a distance r from a neutral hydrogen atom in its lowest state:

$$V_{\mathrm{H}} = -\frac{e^2}{a_0}\, e^{-\frac{2r}{a_0}}\left(1 + \frac{a_0}{r}\right) \tag{35}$$

where a_0, the Bohr radius of a hydrogen atom, equals 0.529 Å. These potentials are usually spherically symmetric or nearly so about the perturbing atom.

Calculations by Gorin, Walter, and Eyring have shown that these forces are adequate to account for the observed rotations of *sec*-butyl alcohol and some of the sugars (12, 13).

(*4*) When there is any overlapping of the electronic orbits, it follows that the Pauli principle must be considered; this gives rise to the so-called "*exclusion forces*" or "*exchange repulsions*" similar in origin to the exchange forces in a valence bond. In order to evaluate the relative importance of these forces and the classical coulombic forces which were considered directly above and with which they will always be associated, we can compare their values in a molecule such as hydrogen for which they are well known. In making the comparison, however, we must remember that the coulombic repulsion between the hydrogen nuclei is included in the energy of a hydrogen molecule, and that this interaction is of no importance in determining the optical rotation arising from the interaction of two groups, since here only those interactions which involve electrons are important. This internuclear repulsion amounts to 440 kg-cal. for a nuclear separation of 0.76 Å. The energy of H_2 is 103 kg-cal., of which about 10 per cent, or 10 kg-cal., is the net coulombic energy (including nuclear repulsions) and 90 per cent, or 90 kg-cal., is exchange energy. Now, if the energy of repulsion of nuclei is 440 kg-cal. and the net coulombic energy is 10 kg-cal., the attractive energy of the electrons interacting with the nuclei less the repulsive energy of the electrons interacting with each other must be 450 kg-cal., or five times the exchange energy. (Of course, in this calculation our point of zero energy was taken as the two separated hydrogen atoms.) Furthermore, in bonds between atoms other than hydrogens the exchange energy usually makes up a smaller proportion of the bond energy than in the case of H_2, so that the importance of exchange forces relative to coulombic forces in causing optical activity may be even less.

It is also observed that in the excited states of hydrogen, triplet states (i.e., those in which exchange forces oppose molecule formation) are very nearly as stable as the corresponding singlet states (i.e., those in which the exchange forces favor molecule formation). For example:

INTER-NUCLEAR DISTANCE	STATE	CONFIGURATION	ENERGY ABOVE NORMAL H_2	DIFFERENCE	ENERGY OF DISSOCIATION
1.08 Å.	$^1\Sigma_g^+$ $^3\Sigma_g$	1*s* 3*d*	111810 cm.$^{-1}$ = 319.665 kg-cal. 111860 cm.$^{-1}$ = 319.808	0.143 kg-cal.	About 60 kg-cal. for all
~1.06 Å.	$^1\Sigma_g^+$ $^3\Sigma_g^+$	1*s* 4*d*	117404 cm.$^{-1}$ = 335.658 117522 cm.$^{-1}$ = 335.996	0.338 kg-cal.	
~1.07 Å.	$^1\Pi_g$ $^3\Pi_g$	1*s* 4*d*	117574 cm.$^{-1}$ = 336.144 117656 cm.$^{-1}$ = 336.379	0.235 kg-cal.	

The data are from reference 39.

This would indicate that where excited states are involved, exclusion forces are still less important than they are between atoms in normal states. This is the more significant because the overlapping of orbits is greatest where excited states are involved.

It is noted that in general the ratio of exchange to coulombic energies is approximately equal to the square of the overlap integral, and this is usually a small quantity.

(*5*) *van der Waals forces.* It is only valid to speak of van der Waals forces between groups when the groups are rather far apart so that their electronic clouds do not overlap, since otherwise the assumptions underlying the quantum-mechanical calculation leading to their formulation break down. Therefore, in small compact molecules like *sec*-butyl alcohol, and more especially in considering the perturbations on excited states, care must be exercised in applying this concept.

In the one-electron theory, explicit account is not taken of the van der Waals forces between groups. This neglect is probably not serious, especially for more compact molecules, since in the calculation of the effects of the forces due to incomplete screening of atoms, a procedure is automatically adopted similar to that which Hartree has used so successfully in studying atomic energies; here the chromophoric electron is assumed to be moving in a static field due to the other electrons and protons of the system. From the success of the Hartree method in giving wave functions which in turn give good values for energy levels and charge distributions in atoms, we can assume that the same method will give the correct wave functions for optical activity, especially as the molecules being considered become more and more compact and also when the wave functions of excited states are calculated. From the failure of the method to account for van der Waals forces at larger separations, it evidently tends to become less true at greater distances between chromophoric and vicinal groups. But because of the breakdown of the assumptions underlying the study of van der Waals forces at intermediate distances, it is probably the best available approximation to the true state of affairs in these regions.

It is to be noted again that the forces considered by Kirkwood when he formulated his theory (see elsewhere) are essentially van der Waals forces, so that the formula for optical rotation which he obtains should tend to be more valid as groups are more widely separated from one another.

The large optical rotations associated with weak absorption bands are understandable in the one-electron theory, since weak bands (i.e., transitions with small electric moment) may have large magnetic moments. Thus, the carbonyl band at 2950 Å. is believed (30) to be due to a transition of a non-bonding $2p_y$ electron on the oxygen to either a (Z_C-Z_O) or an (X_C-X_O) antibonding orbital. The situation may be roughly approximated by description of the transition in terms of hydrogen-like orbitals located on the oxygen atom. Then the transition is between a $2p_y$ state and a $2p_x$ or $2p_z$ state, either of which would give rise to a large magnetic moment, which could then couple with the small electric moment associated with the band to give rise to optical rotation.

In general, in the one-electron theory, although the sum rule, $\sum_b R_{ba} = 0$, still holds true, it does not hold true because of pairwise cancellations such as occur in the Kuhn and Kirkwood theories. Therefore, it will not be possible to write the dispersion in the form of equation 26.

Owing to the inadequacy of the eigenfunctions used in practice in calculating the optical rotation by the one-electron theory, one is restricted to giving at most signs of the partial rotations associated with given transitions and their relative orders of magnitude. The theory, however, allows us to form a new and broader concept of vicinal action which we shall find to be very useful in interpreting some of the experimental results concerning optical rotation.

Calculation of optical rotation on the one-electron model

In order to show that the one-electron theory can account for the observed order of magnitude of optical rotations in general, and also to illustrate the type of procedure which is followed in calculating a rotation on this theory, we now consider an explicit example. A simple transition for our purpose, as expressed in atomic, hydrogen-like orbitals, is one between a $2p_y$ state and a $2p_z$ state. Such a transition bears some resemblance to the transition which gives rise to the 2950 Å. absorption band of the carbonyl group, which according to Mulliken (30) is between a $2p_y$ nonbonding electron on the carbonyl oxygen and a (Z_C-Z_O) antibonding orbital between the carbon and the oxygen[2] (the coördinate axes referred to here are as given in figure 6). Therefore, we shall assume that a transition, $2p_y \rightarrow 2p_z$, is occurring on the oxygen atom of a carbonyl group, and that this transition will give approximately, so far as the optical rotation is concerned, the behavior of an electron actually located in the carbonyl group.[3]

The simplest optically active carbonyl-containing compound is 3-methylcyclopentanone; because of its simplicity we shall calculate the partial rotation of its 2950 Å. absorption band on the above model. Since there are no appreciable dipoles or charges in the molecule which can perturb the carbonyl group, the major portion of this rotation probably comes from the incomplete screening of the nuclei of atoms surrounding the carbonyl by their electrons, so that this type of vicinal action alone will be considered here.

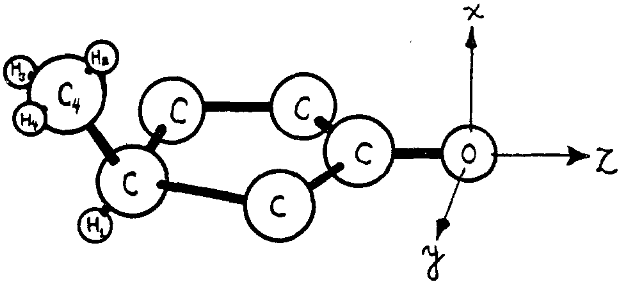


FIG. 6. Model of 3-methylcyclopentanone

When we apply equation 28, with $\psi_a^0 = 2p_y$ and $\psi_b^0 = 2p_z$, and employ only the approximation which gives the lowest-order contribution to the optical rotation, we must recognize that since the electron cloud of the excited state is more spread out in space than that of the lower state, the upper state will be perturbed to a greater degree by the incomplete screening of neighboring nuclei, and hence will give a larger contribution to the optical rotation arising from this source. (At the distances involved in the present example, the upper state overlaps the perturbing atoms to an extent about fifteen times greater than does the lower state for the eigenfunctions actually used.) Secondly, it is to be noted that the transi-

[2] It is possible that X_C-X_O is the upper state. This corresponds to a transition $2p_y \rightarrow 2p_x$ here, and an actual calculation shows that it would give a rotation which is equal but opposite in direction to that found for $2p_y \rightarrow 2p_z$.

[3] A more adequate treatment of the carbonyl will be made at a later date.

tion $2p_y \longrightarrow 2p_z$ gives rise to a large magnetic moment in the x direction and no electric moment in any direction, while the only perturbing function with a principal quantum number of 3 or less with which $2p_y$ will give an electric moment component in this direction is $3d_{x+y}$. Although some of the possible perturbing functions with principal quantum numbers larger than 3 will also give an electric moment component in this direction, this component will be very small, since the matrix element $(2p_y/x/nd_{x+y})$ decreases rapidly with increasing n.

Thus we find that as far as the first-order and major contribution of the transition to the rotation is concerned, the transition is

$$a = \psi_{2p_y} \longrightarrow b = (\psi_{2p_z'} + C\psi_{3d_{x+y}})$$

The rotatory strength for the transition is, from equation 31,

$$\begin{aligned} R_{ba} &= \text{Im}\left\{[\psi_{2p_y}/\mathbf{p}/(\psi_{2p_z'} + C\psi_{3d_{x+y}})]\cdot[(\psi_{2p_z'} + C\psi_{3d_{x+y}})/\mathbf{m}/\psi_{2p_y}]\right\} \\ &= C\ \text{Im}\left\{(\psi_{2p_y}/ex/\psi_{3d_{x+y}})(\psi_{2p_z'}/m_x/\psi_{2p_y})\right\} \\ &= -\frac{e^2h}{4\pi mc}(\psi_{2p_y}/x/\psi_{3d_{x+y}})(\psi_{2p_z'}/1/\psi_{2p_z})C \end{aligned}$$

since

$$m_x = \frac{eh}{4\pi mci}\left(y\frac{\partial}{\partial z} - z\frac{\partial}{\partial y}\right)$$

Now

$$\beta' = \frac{c}{3\pi h}\frac{R_{ba}}{\nu_{ba}^2 - \nu^2}$$

where β' is the contribution of the absorption band in question to the rotation of the plane of light of frequency ν. Taking the D line of sodium as the light employed ($\lambda = 5890$ Å., $\nu = 0.507 \times 10^{15}$ sec.$^{-1}$) and taking the absorption band at 2950 Å. ($\nu = 1.02 \times 10^{15}$ sec.$^{-1}$), it is found that

$$\beta' = -2.89 \times 10^{-24}(\psi_{2p_y}/x/\psi_{3d_{x+y}}))\psi_{2p_z'}/1/\psi_{2p_z})C$$

Using the usual hydrogen-like eigenfunctions:

$$\psi_{2p_y} = \frac{1}{4\sqrt{2\pi}}\left(\frac{Z_1}{a_0}\right)^{5/2}\left(e^{-\frac{Z_1r}{2a_0}}\right)y$$

$$\psi_{2p_z'} = \frac{1}{4\sqrt{2\pi}}\left(\frac{Z_2}{a_0}\right)^{5/2}\left(e^{-\frac{Z_2r}{2a_0}}\right)z$$

$$\psi_{3d_{x+y}} = \frac{\sqrt{2}}{81\sqrt{\pi}}\left(\frac{Z_2}{a_0}\right)\left(e^{-\frac{Z_2r}{3a_0}}\right)xy$$

and setting $Z_1 = 1.8$ and $Z_2 = 1.5$ from the observed values of the ionization potential of a $2p_y$ electron in the carbonyl and the energy of the transition under consideration, it is found that

$$(\psi_{2p_y}/x/\psi_{3d_{x+y}}) = 1.077 \times 10^{-8} \text{ cm.}$$

$$(\psi_{2p_z'}/1/\psi_{2p_z}) = 0.98$$

Substituting these values in the expression for β', we find that

$$\beta' = -3.04 \times 10^{-32}\, C$$

It remains, therefore, to find C. Now,

$$C = \frac{\int \psi_{2p_z'} V \psi_{3d_{x+y}} \mathrm{d}\tau}{E_{2p_z'} - E_{3d_{x+y}}}$$

and

$$E_{2p_z'} - E_{3d_{x+y}} = -\frac{e^2}{2a_0} 1.5^2 \left(\frac{1}{2^2} - \frac{1}{3^2}\right) = -\frac{5}{32}\frac{e^2}{a_0}$$

V is here the sum of the potentials due to the surrounding atoms. We are concerned only with potentials due to incomplete screening of the nuclei for hydrogen atoms and carbon atoms, for which, at a distance r from the respective nuclei,

$$V_{\mathrm{H}} = -\frac{e^2}{a_0} e^{-\frac{2r}{a_0}} \left(1 + \frac{a_0}{r}\right) \tag{35}$$

$$V_{\mathrm{C}} = -\frac{4e^2}{a_0} e^{-\frac{2.95r}{a_0}} \left(1.07 \left(\frac{r}{a_0}\right)^2 + 2.175 \left(\frac{r}{a_0}\right) + 2.213 + \frac{a_0}{r}\right) \tag{36}$$

The integrals $\int \psi_{2p_z'} V \psi_{3d_{x+y}} \mathrm{d}\tau$ are best evaluated using elliptical coördinates, with the foci at the centers of the perturbing atom and the oxygen atom. A rotation of axes must be performed, however, which will bring the Z-axis into line with the line joining the centers of the two atoms. Because of the cylindrical symmetry about the new Z-axis of the potentials V_{H} and V_{C} and of the radial parts, ψ_{2p} and ψ_{3d}, of the eigenfunctions, the integrals of odd powers of x and y vanish. And again, because of this symmetry, it is possible to arrange the x- and y-axes so that an integral over any power of y is the same as that over the same power of x. Then the rotation of axes will be found to transform the product xyz (which arises from the angular factors z and xy of $\psi_{2p_z'}$ and $\psi_{3d_{x+y}}$) into $\gamma_x\gamma_y\gamma_z(Z'^3 - X'^2Z')$, where γ_x, γ_y, and γ_z are the direction cosines of the line joining the two atomic centers in the odd coördinate system, and where z' and x' are the new coördinates. Since the overlapping of the functions in the integral $\int \psi_{2p_z'} V \psi_{3d_{x+y}} \mathrm{d}\tau$ will be greatest where z' is rather large and

x' rather small, we may neglect the term x'^2z' as compared with z'^3. Thus we have that

$$C = \gamma_x\gamma_y\gamma_z D$$

where

$$D = -\frac{32}{5}\frac{a_0}{e^2}\int \psi_{2p'} V\psi_{3d} z'^3 \, d\tau$$

and where $\psi_{2p'}$ and ψ_{3d} refer to the eigenfunctions without the angular factors z and xy.

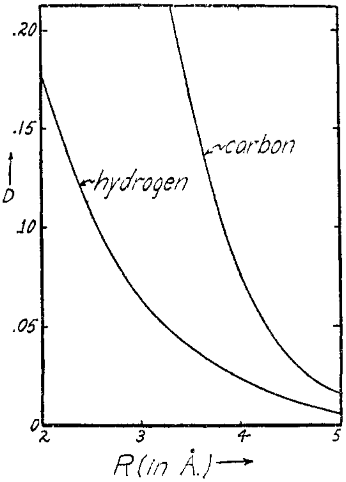


FIG. 7. Vicinal action of carbon and hydrogen atoms

For β' and $[M]'_D$, the contribution to the molecular rotation, we find

$$\beta' = -3.04 \times 10^{-32}\gamma_x\gamma_y\gamma_z D$$

$$[M]'_D = -15.1 \times 10^3 \frac{n^2+2}{3} \gamma_x\gamma_y\gamma_z D \tag{37}$$

Naturally, the value of D will depend upon the distance between the perturbing group and the chromophore. This dependence for V_H and V_C is given in figure 7. Referring to the terminology in a previous section (page 363), $\gamma_x\gamma_y\gamma_z$ is the angular dependence function of the carbonyl, while D, aside from the factor $-\frac{32}{5}\frac{a_0}{e^2}$, is the radial dependence function.

We now possess all the information necessary to calculate the partial rotation of the present approximation to the carbonyl group in 3-methylcyclopentanone from a knowledge of the structure of the molecule. The refractive index here is 1.434. The other necessary quantities appearing in equation 37 are given in table 1. R in this table is the distance from the oxygen to the atom in question. All distances are in Ångström units. The calculated value of the partial molecular rotation measured in D light for the pseudocarbonyl transition in methylcyclopentanone is +59.2° for the configuration given in figure 6. The observed total molecular rotation of methylcyclopentanone is 130°. (The two values are not directly comparable.) Thus it is seen that the observed order of magnitude of the rotation can be accounted for sufficiently well on this model with only the incomplete shielding of nuclei by their electrons as the vicinal action which operates.

TABLE 1

Coördinates of atoms in 3-methylcyclopentanone

	O	C_4	H_1	H_2	H_3	H_4
x	0	1.258	−0.889	2.148	1.258	1.258
y	0	1.293	1.140	0.923	0.943	2.325
z	0	−4.339	−4.130	−3.830	−5.071	−3.989
R		4.699	4.377	4.487	5.300	4.785
$\gamma_x = \frac{x}{R}$		+0.268	−0.203	+0.479	+0.237	+0.263
$\gamma_y = \frac{y}{R}$		+0.275	+0.261	+0.206	+0.178	+0.486
$\gamma_z = \frac{z}{R}$		−0.923	−0.944	−0.854	−0.957	−0.834
$\gamma_x\gamma_y\gamma_z$		−0.0662	+0.0480	−0.0841	−0.0404	−0.1065
D		+0.025	+0.016	+0.013	+0.002	+0.008
Contribution to $[M]'_D$		+33.8°	−15.7°	+22.2°	+1.6°	+17.3°

IV. Interpretation of Experimental Facts concerning Optical Rotation

There is a great mass of experimental data concerning optical rotatory power and the many factors which can affect it. We shall now seek to interpret some of the more important of these in the light of the theories mentioned on the previous pages.

Before studying the individual factors which may operate to alter the optical rotation of a molecule, it will be instructive to point out just where in equation 15a we might expect variable factors to occur.

$$[M] = \frac{96\pi N}{hc}\frac{n^2+2}{3}\sum_i \rho_i \sum_{b_i} \mathrm{Im}\,[(a_i/\mathbf{p}/b_i)\cdot(b_i/\mathbf{m}/a_i)]\,\frac{\nu^2}{\nu^2_{a_ib_i}-\nu^2} \tag{15a}$$

The effect of changing the frequency, ν, of the light used has already been mentioned. Relationships of the form of equation 15a are known experimentally to give the dependence of rotation on frequency with very high accuracy (25). The other factors which can alter the rotation include the refractive index, n, of the medium, the relative probabilities, ρ_i, of the different conformations, i, and the natures of the electronic states, a_i and b_i. There are thus these three ways in which the optical rotation at a given wave length can be altered, and all of the different factors which are known to be capable of varying the optical rotation must operate through them.

The sensitivity of the rotation to influences such as temperature, solvent action, and small changes in structure is annoying to one interested in forming a complete and accurate theory, but this same sensitivity makes it a potentially powerful tool in investigating the more or less minor alterations which other molecular properties (such as the refractivity) are incapable of disclosing.

A. EFFECT OF TEMPERATURE

In the liquid or solid as distinguished from the gaseous state we must include in the specifications of the conformations, **i**, not only the different possible orientations of the groups within the molecule, but the different possible orientations of the neighboring molecules as well, since these latter may also influence the optical rotation. Then if the conformation, i, of the entire complex has a free energy, F_i, per mole, from statistical mechanics we know that

$$\rho_i = \frac{e^{-F_i/RT}}{\sum_j e^{-F_j/RT}} \tag{38}$$

so that we obtain for the rotation of the actual mixture of conformations

$$\begin{aligned}[M] &= \frac{96\pi N}{hc}\frac{n^2+2}{3}\frac{1}{\sum_j e^{-F_j/RT}}\sum_i\left[e^{-F_i/RT}\sum_{b_i}\frac{\nu^2\mathrm{Im}[(a_i/\mathbf{p}/b_i)\cdot(b_i/\mathbf{m}/a_i)]}{\nu^2_{b_ia_i}-\nu^2}\right]\\ &= \frac{\sum_i [M]_i e^{-F_i/RT}}{\sum_j e^{-F_j/RT}}\end{aligned} \tag{39}$$

where $[M]_i$ is the molecular rotation corresponding to the pure complex i.

It was long considered that the unusual variations of the rotations of such substances as tartaric acid when temperature or even other factors were changed was due to the presence of several distinct molecular species in equilibrium. We see from the above and from the theoretical considerations of the earlier pages that as a result of the sensitivity of the optical rotation to molecular conformation, no very drastically different molecular species are necessary to account for these effects. A slightly different internal orientation or an altered amount of solvent effect may be sufficient to cause a marked change in the rotatory power.

As an example of how the temperature variation of optical rotation may be treated to obtain interesting information, we here consider the data of Winther (44) on the optical activity of the dimethyl, diethyl, and dipropyl esters of tartaric acid. The variation of the optical rotations of these esters with temperature may be interpreted roughly by assuming a simple reaction

$$\text{B (low-temperature form)} \rightleftarrows \text{A (high-temperature form)}$$

to be the one chiefly responsible for the observed effects. The equilibrium constant for this reaction may be written:

$$\frac{b_\lambda - [\alpha]_\lambda^T}{[\alpha]_\lambda^T - a_\lambda} = e^{\frac{\Delta S}{R}} e^{-\frac{\Delta H}{RT}} \tag{40}$$

where a_λ is the rotation of pure liquid A, b_λ is that of pure B, and $[\alpha]_\lambda^T$ is the observed rotation of the equilibrium mixture at a temperature T; all rotations are measured using light of wave length λ.

Values of the unknown constants of equation 40 were obtained which would give a fair agreement between observed and calculated rotations at various wave lengths. The values of ΔH are probably good to about ±400 cal.; ΔS may be in error by ±2 units. The values of a_λ and especially of b_λ are strongly dependent on the values of ΔS and ΔH taken, but the relative values at different wave lengths for a particular choice of ΔS and ΔH are probably more reliable. The results are summarized in table 2. Since ΔS and ΔH were chosen to give a good fit at one particular wave length and the same values were used at other wave lengths with values of a_λ and b_λ which give good agreement at but two temperatures, the agreement is better at some points than at others. Slightly different values of the constants would have given more even agreement, but the values used are sufficiently accurate for our purpose, which is that of obtaining an estimate of the heat and entropy changes involved.

The close similarity between the constants for the three esters leaves little doubt as to the essential correctness of the above interpretation of Winther's results. The large change in entropy between the two forms

TABLE 2

Variation of rotation of tartaric acid esters with temperature: values of constants in equation 40

ESTER	ΔS	ΔH	SPECIFIC ROTATIONS OF FORMS A AND B			
	E. U.	*calories*				
Dimethyl tartrate	10.6	2280	λ = 5890 Å.	λ = 4703 Å.	λ = 4445 Å.	
			$a = +10.2°$ $b = -30°$	$a = +10.94°$ $b = -61.4°$	$a = +11.1°$ $b = -81°$	
Diethyl tartrate	9.8	2530	λ = 5890 Å.	λ = 5335 Å.	λ = 4655 Å.	λ = 4435 Å.
			$a = +18.9°$ $b = -13.6°$	$a = +22.1°$ $b = -19.1°$	$a = +26.5°$ $b = -34.9°$	$a = +27.4°$ $b = -41.8°$
Dipropyl tartrate	8.4	2300	λ = 5890 Å.	λ = 4445 Å.		
			$a = +24.01°$ $b = -4.60°$	$a = +37.9°$ $b = -22.68°$		

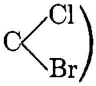
	λ = 5890 Å.			λ = 4703 Å.			λ = 4445 Å.					
	T	$[\alpha]_{\mathrm{calcd.}}$	$[\alpha]_{\mathrm{obsd.}}$	*T*	$[\alpha]_{\mathrm{calcd.}}$	$[\alpha]_{\mathrm{obsd.}}$	*T*	$[\alpha]_{\mathrm{calcd.}}$	$[\alpha]_{\mathrm{obsd.}}$			
Dimethyl tartrate	°*K.*			°*K.*			°*K.*					
	325.3	4.22	4.22	323.8	0.02	0.02	324.9	−2.64	−2.62			
	334.2	4.69	4.68	335.1	1.11	1.11	335.1	−1.43	−1.14			
	344.9	5.17	5.16	344.3	1.85	1.74	344.9	−0.06	−0.50			
	354.8	5.57	5.56	355.6	2.62	2.62	356.0	+0.58	+0.53			
	365.7	5.96	5.96	364.3	3.22	3.23	364.8	+1.27	+1.31			
	λ = 5890 Å.			λ = 5335 Å.			λ = 4655 Å.			λ = 4435 Å.		
	T	$[\alpha]_{\mathrm{calcd.}}$	$[\alpha]_{\mathrm{obsd.}}$	*T*	$[\alpha]_{\mathrm{calcd.}}$	$[\alpha]_{\mathrm{obsd.}}$	*T*	$[\alpha]_{\mathrm{calcd.}}$	$[\alpha]_{\mathrm{obsd.}}$	*T*	$[\alpha]_{\mathrm{calcd.}}$	$[\alpha]_{\mathrm{obsd.}}$
Diethyl tartrate	°*K.*			°*K.*			°*K.*			°*K.*		
	292.1	7.30	7.31	292.1	7.16	7.16	292.2	4.57	4.57	292.2	2.70	2.70
	301.2	8.27	8.26	303.9	8.80	8.71	302.7	6.64	6.61	303.2	5.12	5.04
	313.1	9.37	9.38	311.2	9.68	9.59	312.5	8.37	8.21	314.1	7.27	7.20
	325.0	10.33	10.35	321.4	10.73	10.69	322.8	9.98	9.89	324.7	9.14	8.89
	336.4	11.13	11.15	334.5	11.99	11.93	336.3	11.75	11.64	335.6	10.73	10.63
	344.3	11.63	11.65	343.6	12.75	12.76	345.2	12.84	12.78	344.4	11.93	11.87
	352.9	12.13	12.15	354.8	13.56	13.57	354.6	13.86	13.86	354.3	13.18	13.14
	λ = 5890 Å.			λ = 4445 Å.								
	T	$[\alpha]_{\mathrm{calcd.}}$	$[\alpha]_{\mathrm{obsd.}}$	*T*	$[\alpha]_{\mathrm{calcd.}}$	$[\alpha]_{\mathrm{obsd.}}$						
Dipropyl tartrate	°*K.*			°*K.*								
	289.1	11.36	11.39	289.1	11.14	11.14						
	301.1	12.48	12.58	302.6	13.73	13.65						
	312.1	13.40	13.41	312.4	15.45	15.56						
	321.8	14.15	14.22	322.4	17.04	17.18						
	335.4	15.05	15.10	335.4	18.90	18.99						
	343.9	15.56	15.57	346.1	20.25	20.26						

leads us to suspect that they differ in amounts of solvation or, more probably, of free rotation, rather than merely in static configuration.

Lucas (27) has pointed out that a maximum in the temperature *versus* rotation curve indicates the presence of at least three distinct substances in equilibrium. Such maxima are known to occur in the curves for the tartaric acid esters, so Lucas suggests that there must be three forms of these esters. On examining the actual data (32), however, it is found that the "maxima" are readily accounted for by the indirect effect of the density acting through the refractive index (see page 385), and that when account is taken of this, the maxima usually disappear.

B. EFFECTS OF ROTATION ABOUT BONDS AND SYMMETRY OF GROUPS

In discussing the modern theories of optical activity it was noticed that the theories of Kuhn and Kirkwood, as well as the one-electron theory when only first-order effects are considered, all assume that vicinal effects are additive; that is, the addition of a third group does not affect the interactions already existing between two other groups. We shall now examine some of the consequences of this assumption.

First, consider the interactions between atoms or groups A and B both attached to the same atom C, where the lines AC and BC are axes of symmetry of groups A and C, respectively (e.g.,  $\mathrm{C}\begin{smallmatrix}\diagup\mathrm{Cl}\\ \diagdown\mathrm{Br}\end{smallmatrix}$). Since such an arrangement of groups has a plane of symmetry, no interaction between A and B can alone give rise to optical activity.

Next consider four atoms arranged as shown in figure 8. (A plane passes through B, C, and D.) The interaction of AB with D when A is above the plane (position A′) is equal and opposite in sign to that when A is below the plane (in position A″, which is the reflection of A′ in the plane). Therefore, if positions A′ and A″ are equally probable, these interactions will cancel off. And if all other possible positions of A above the plane are matched by equally probable positions below the plane, the interactions of AB and D will not influence the optical activity.

The argument can be extended to groups of any size, as long as these groups can be split up into interacting units having planes of symmetry. It also holds true if there is restricted rotation in which the positions of minimum potential energy are equally probable on either side of a plane which passes through the asymmetric center and the group with which the given group is interacting, this being the situation in the figure accompanying the last paragraph.

The following are some of the consequences of the above: (*a*) Factors which decrease the freedom of rotation of groups about bonds will cause an increase in the first-order contribution to the optical activity. (*b*) Insofar as an increase in temperature causes an increase in the amount of rotation of groups about bonds in such molecules as *sec*-butyl chloride, their rotations should tend toward a value corresponding to the second-order contributions as the temperature rises. (*c*) Any optical rotation possessed by such compounds as $CHClBrI$ must be due to second-order effects.

Now we have seen (page 361) that second-order effects are in general smaller than first-order effects, especially as the groups which interact to give rise to optical activity become more and more widely separated. It will, then, be interesting to see if the conclusions which we can draw from this with *a*, *b*, and *c* above, agree with those found experimentally.

(*a*) A powerful factor in reducing the possibility of rotation about single bonds is the formation of ring compounds from open chains, and it should, from the above, be accompanied by an increase in optical rotation. The fact that ring formation greatly increases the optical rotation has long been known experimentally (42).

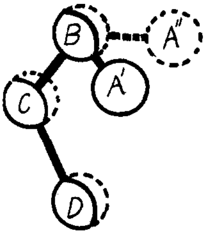
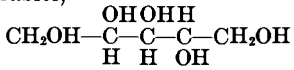
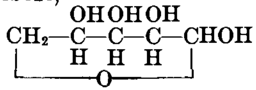
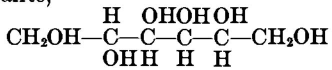
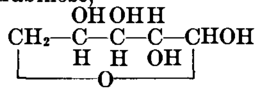
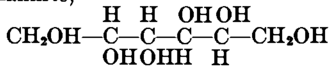
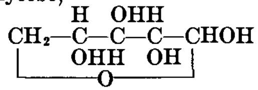
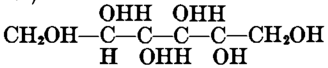
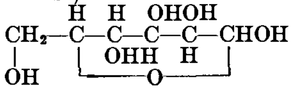
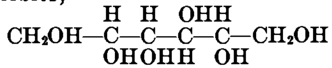
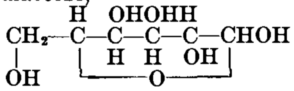
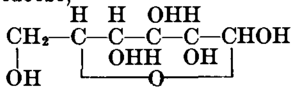


FIG. 8

In table 3 are given the rotations of compounds chosen at random which are similar in all respects save that some have open chains while others have closed rings. The influence of ring formation is found generally to be as predicted. Furthermore, the effect is the most pronounced in those compounds in which there is the most reason to believe that there is the greatest freedom of rotation in the open-chain form. Thus the introduction of the bulky acetyl in place of a hydrogen on a hydroxyl raises the rotation somewhat. (Even here, however, some of the increase is due to the fact that the acetyl has an absorption band nearer to the visible than does hydroxyl or the hydrocarbon residue.) A methyl group has a similar but less marked effect. The very low rotations of the polyhydroxy alcohols make it apparent that here there must be either very nearly free rotation or near-equivalence of the three equilibrium positions about each C—C and C—O bond.

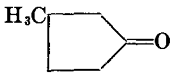
TABLE 3

Comparison of rotations of open-chain compounds and ring compounds of similar constitution

OPEN-CHAINS	$[M]_D$	RINGS		$[M]_D$
Arabite,  $CH_2OH-\underset{H}{\overset{OH}{C}}-\underset{H}{\overset{OH}{C}}-\underset{OH}{\overset{H}{C}}-CH_2OH$	8.4°	Ribose, 		32.3°
Talite,  $CH_2OH-\underset{OH}{\overset{H}{C}}-\underset{H}{\overset{OH}{C}}-\underset{H}{\overset{OH}{C}}-\underset{H}{\overset{OH}{C}}-CH_2OH$	5.5°	Arabinose, 	α-form	263°
			β-form	75°
Mannite,  $CH_2OH-\underset{OH}{\overset{H}{C}}-\underset{OH}{\overset{H}{C}}-\underset{H}{\overset{OH}{C}}-\underset{H}{\overset{OH}{C}}-CH_2OH$	0.9°	Xylose, 	α-form	138°
Idite,  $CH_2OH-\underset{H}{\overset{OH}{C}}-\underset{OH}{\overset{H}{C}}-\underset{H}{\overset{OH}{C}}-\underset{OH}{\overset{H}{C}}-CH_2OH$	6.4°	Mannose, 	α-form	54°
			β-form	24.5°
Sorbite,  $CH_2OH-\underset{OH}{\overset{H}{C}}-\underset{OH}{\overset{H}{C}}-\underset{H}{\overset{OH}{C}}-\underset{OH}{\overset{H}{C}}-CH_2OH$	3.6°	Galactose, 	α-form	260°
			β-form	93.5°
		Glucose, 	α-form	203°
			β-form	34°

			α-form	β-form
Mannose dimethylacetal	1.3°	Methyl mannopyranoside	159°	
(pentaacetate	69°)	(tetraacetate		170°)
Galactose dimethylacetal	34°	Methyl galactopyranoside	307°	62°
(pentaacetate	?)	(tetraacetate	474°	65°)
Glucose dimethylacetal	34°	Methyl glucopyranoside	345°	1.0°
(pentaacetate	52°)	(tetraacetate	478°	50°

Arabonic acid	$[\alpha]_{\mathrm{D}} = 18^\circ \rightarrow \gamma$-Lactone, $[\alpha]_{\mathrm{D}} = 74^\circ$
2,3,4-Trimethylarabonic acid	$[\alpha]_{\mathrm{D}} = 16^\circ \rightarrow \gamma$-Lactone, $[\alpha]_{\mathrm{D}} = 178^\circ$
2,3,5-Trimethylarabonic acid	$[\alpha]_{\mathrm{D}} = 2^\circ \rightarrow \gamma$-Lactone, $[\alpha]_{\mathrm{D}} = 44^\circ$
2,3,4-Trimethyllyxonic acid	$[\alpha]_{\mathrm{D}} = 1.3^\circ \rightarrow \gamma$-Lactone, $[\alpha]_{\mathrm{D}} = 35^\circ$
2,3,5-Trimethyllyxonic acid	$[\alpha]_{\mathrm{D}} = 21^\circ \rightarrow \gamma$-Lactone, $[\alpha]_{\mathrm{D}} = 82^\circ$
3,4-Dimethylrhamnonic acid	$[\alpha]_{\mathrm{D}} = 16^\circ \rightarrow \gamma$-Lactone, $[\alpha]_{\mathrm{D}} = 153^\circ$
Rhamnonic acid	$[\alpha]_{\mathrm{D}} = 7.7^\circ \rightarrow \gamma$-Lactone, $[\alpha]_{\mathrm{D}} = 40^\circ \rightarrow \delta$-Lactone, $[\alpha]_{\mathrm{D}} = 98^\circ$
Gluconic acid	$[\alpha]_{\mathrm{D}} = 7^\circ \rightarrow \gamma$-Lactone, $[\alpha]_{\mathrm{D}} = 68^\circ \rightarrow \delta$-Lactone, $[\alpha]_{\mathrm{D}} = 62^\circ$
Mannonic acid	$[\alpha]_{\mathrm{D}} = 10^\circ \rightarrow \gamma$-Lactone, $[\alpha]_{\mathrm{D}} = 52^\circ \rightarrow \delta$-Lactone, $[\alpha]_{\mathrm{D}} = 112^\circ$
Galactonic acid	$[\alpha]_{\mathrm{D}} = 13^\circ \rightarrow \gamma$-Lactone, $[\alpha]_{\mathrm{D}} = 77^\circ$
2,3,5,6-Tetramethylgluconic acid	$[\alpha]_{\mathrm{D}} = 34^\circ \rightarrow \gamma$-Lactone, $[\alpha]_{\mathrm{D}} = 72^\circ$
2,3,4,6-Tetramethylgluconic acid	$[\alpha]_{\mathrm{D}} = 22^\circ \rightarrow \gamma$-Lactone, $[\alpha]_{\mathrm{D}} = 101^\circ$

$CH_3CH_2CH(CH_3)CH_2CHO$	$[M]_{\mathrm{D}} = 8.7^\circ$		$[M]_{\mathrm{D}} = 120^\circ$

If we say that, on the average, ring formation causes a tenfold increase in optical rotation, and that this represents the difference in order of magnitude between first- and second-order effects, then this corresponds to values of the coefficients c in equation 28 of about 0.1,—a reasonable value such as has been found in actual calculations.

Another factor besides ring formation which acts to hinder the movement of one part of a molecule relative to another is the formation of the crystalline state. Therefore we expect that solidification will cause an increase in optical rotation. Thus for quartz, sodium perchlorate, etc., the optical rotation goes from zero for the melt to exceedingly high values for the crystal. For tartaric acid, the amorphous acid at room temperature has a specific rotation of +0.76° at λ = 5920 Å. and +15.9° at 180°C. for λ = 5880 Å., while the crystalline acid at room temperature has a specific rotation of −636° for λ = 5780 Å.

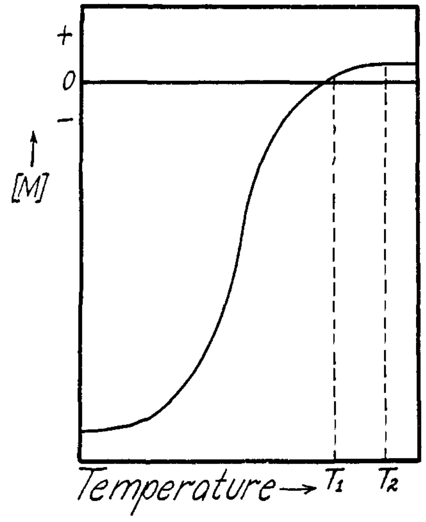


FIG. 9. Effect of temperature on rotatory power

(b) If we restrict ourselves to substances whose second-order contribution to the optical rotation should be small (as in $CH_3CH_2CHClCH_3$, where the groups responsible for the asymmetry,—namely, the CH_3 of the ethyl, the H of the methyl, and the H and Cl directly attached to the asymmetric center,—are considerably farther apart than the corresponding ones in, say, tartaric acid) then we must conclude that an increase in temperature will generally cause a considerable decrease in the numerical value of the rotation. Since the sign of the second-order contribution to the optical rotation need not be the same as that of the first-order contribution, this is not to say that over a small range of temperatures an increase in the rotatory power with increasing temperature will not be observed. Thus, in figure 9, although there is a change in rotation from a large to a small value, measurements in the interval T_1 to T_2 would show an increase in rotatory power with increasing temperature.

Now it has been noted in the past that the optical rotations of simple substances generally seem to decrease with increasing temperatures. Guye and Aston (14) found that for every one of thirty substances which meet the requirement given above, a temperature increase lowers the rotation. Several other substances noted by Walden (43) show the same effect. The magnitude of the decrease with temperature is, however, usually rather small, so that one wonders whether in many of the cases cited, at least, the decrease is not caused largely by a decrease in the refractive index consequent on the lower density at higher temperatures (see later). If this is the case, we are forced to the interesting conclusion that in these substances the molecules already possess freedom of rotation and that an adequate test of the principle is only possible with those substances having groups sufficiently bulky so that freedom of rotation only occurs at higher temperatures. A study of substances of this type is now being made, and preliminary findings tend to confirm expectations from the above.

(*c*) Recently, Berry and Sturtevant (2) have prepared $CH_3CHBrCN$ in optically active form. This substance was found to have a molecular rotation in sodium D light of at least 20.5°, and since the bonds joining the groups to the center of asymmetry all lie along axes of symmetry of the respective groups, this must be entirely a result of contributions of second order and higher. The proximity of the groups, along with the nearness of the absorption bands of Br and CN to the visible, makes this value quite reasonable. (In the polyhydroxy alcohols and the substances studied by Guye and Aston the value seems generally to be of the order of 10° or less.) It is worth noting that the value 20.5° is still very much smaller than the rotation of 120° by the even simpler methylcyclopentanone; in this compound there is a first-order contribution to the optical rotation (see later), and the comparison is the more striking when it is learned that this large rotation arises from an interaction over the very considerable distance of 4.5 Å., whereas in $CH_3CHBrCN$ the distances are of the order of 2.5 to 3 Å.

C. SOLVENT EFFECTS

In this discussion the solvent is considered as being made up of all those molecules which surround a given optically active molecule. These neighboring molecules may or may not be of the same species as the active molecule. There is obviously no distinction in principle between solvent effects of, for example, water on *sec*-butyl alcohol and the effects of one *sec*-butyl alcohol on another. Thus solvent effects will occur in all states except the dilute vapor.

It will be convenient to divide the effects which may act here into two types according to origin; the first will be the effect of refractive index, and the second the effects of alterations of β, which are more deep-seated, hence more interesting.

1. Effect of refractive index

The refractive index, n, enters into the expression for optical activity as a factor $(n^2 + 2)$, or better as $(n^2 + 2)/3$, since this reduces to unity for the vapor. Therefore, if β in equation 15 is a constant, the quantity $[M]/(n^2 + 2)$ should be a constant, in going from one solvent to another. Wolf and Volkmann (45) conclude that where non-polar solutes are involved, this quantity actually is a constant. Beckmann and Cohen (1) conclude the same and suggest that in investigating solvent effects on optical activity the variation of

$$\Omega = \frac{[\alpha]}{n^2 + 2} \tag{41}$$

should be studied. (For the reason mentioned above, it might be better to use three times this quantity, it having a value more nearly related to that of the conventional $[\alpha]$.) They call Ω the *rotivity* in analogy to the relation between the refractive index and the refractivity. The reasoning behind the use of Ω instead of $[\alpha]$ is sound, since Ω is proportional to the more fundamental molecular quantity β and its variation is of greater significance than the variation of $[\alpha]$.

The factor $(n^2 + 2)$ in the optical rotation, as in the theory of dipole moments, corrects the local field around a molecule for the polarization of neighboring molecules.

That β itself may in some way depend upon the refractive index is indicated by the results of Rule and Chambers (37) on the effect of refractive index on the rotation of the saturated hydrocarbon pinane in various solutions. In table 4 and figure 10 are given the dependence of $[M]_D^{20}$ of pinane solutions on n_D^{20}, the refractive index of the solution, on $(n^2 + 2)/3$, and on $[(n^2 + 2)/3]^2$. Although all of the variable factors have not been accounted for, the most important one in this case is clearly the refractive index. The major portion of this dependence appears to be eliminated when account is taken of the factors $(n^2 + 2)/3$ or $[(n^2 + 2)/3]^2$. Both of these factors give some residual dependence on the refractive index, but when account is taken of the fact that p-fold division by $(n^2 + 2)/3$ tends of itself to give a smaller slope to any plot of

TABLE 4

Refractive indices and rotations of solutions of pinane (reference 37)

SOLVENT	n_D^{20} OF SOLUTION	$[M]_D^{20}$	$[M]_D^{20} \div \left(\frac{n^2+2}{3}\right)$	$[M]_D^{20} \div \left(\frac{n^2+2}{3}\right)^2$
Methyl cyanide	1.3441	25.8	20.4	16.1
Methyl alcohol	1.3266	26.4	21.1	16.8
Acetic acid	1.3718	26.9	20.8	16.1
Nitromethane	1.3864	27.3	20.9	16.0
Pentane	1.3640	27.4	21.3	16.6
Acetaldehyde	1.3316	27.7	22.0	17.5
Hexane	1.3835	27.8	21.3	16.3
Acetone	1.3653	28.9	22.5	17.5
Methylene chloride	1.4245	29.0	21.6	16.1
Chloroform	1.4489	30.2	22.1	16.2
Phenyl cyanide	1.5255	30.8	21.3	14.7
Methylene bromide	1.5385	31.4	22.2	15.2
(Homogeneous)	1.4630	31.5	22.8	16.5
Carbon tetrachloride	1.4616	31.6	22.9	16.6
Pyridine	1.5088	32.3	22.6	15.9
Mesitylene	1.4944	32.5	23.1	16.4
Nitrobenzene	1.5468	32.5	22.2	15.2
Methyl iodide	1.5291	32.6	22.5	15.6
Benzene	1.4992	32.9	23.0	16.2
Acetophenone	1.5310	33.2	23.0	15.9
Benzaldehyde	1.5431	33.2	22.8	15.6
Toluene	1.4930	33.7	24.0	17.0
Anisole	1.5141	34.5	24.1	16.8
Chlorobenzene	1.5229	34.7	24.1	16.7
o-Dichlorbenzene	1.5466	34.7	23.7	16.2
α-Chloronaphthalene	1.6332	34.9	22.4	14.4
Bromobenzene	1.5580	35.1	23.8	16.1
α-Bromonaphthalene	1.6558	35.1	22.2	14.1
Ethylene dibromide	1.6303	35.3	22.7	14.6
Iodobenzene	1.6162	35.6	23.2	15.1
α-Methoxynaphthalene	1.6201	35.6	23.1	15.0
Aniline	1.5842	36.4	24.2	16.1
Methylene iodide	1.7341	36.6	22.0	13.2
Quinoline	1.6246	38.6	25.0	16.2
Carbon bisulfide	1.6246	38.7	25.0	16.2
α-Iodonaphthalene	1.7054	39.7	24.8	15.2

$[M] \div \left(\frac{n^2+2}{3}\right)^p$ *versus n*, it is found that the rotation[4] is more nearly proportional to $(n^2 + 2)$ than to $(n^2 + 2)^2$.

---

[4] Rule and Chambers find that for solvents with zero dipole moment the rotation is more nearly proportional to $(n^2 + 2)^2$ than to $(n^2 + 2)$. The dipole moment, however, does not appear to be related to those factors which, besides the refractive

Often data concerning refractive indices are not available, so that the rotivity cannot be found. In case the dependence of rotation on temperature is being investigated, however, the following method may prove satisfactory: We know that the Lorenz–Lorentz equation,

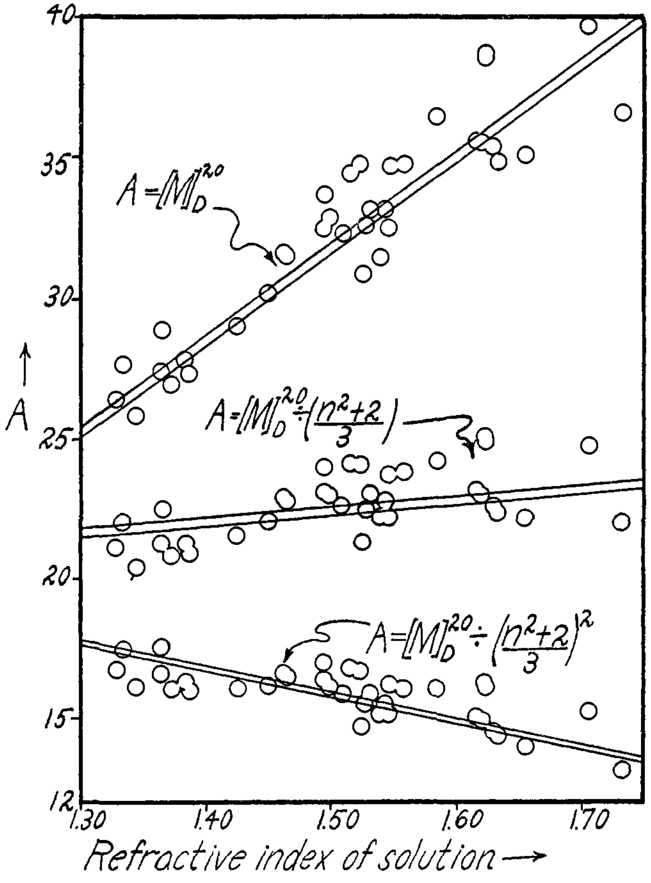


FIG. 10. Dependence of rotation of *d*-pinane on refractive index of its solutions. Distance between parallel straight lines indicates magnitude of probable experimental error.

$$\frac{n^2 - 1}{n^2 + 2}\frac{M}{d} = P$$

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index, can alter the rotation of pinane, so that the basis of the criterion upon which they base their conclusion is not valid. A dependence of V in equations 23, 32, and 33 on the dielectric constant, hence on the refractive index, might, however, cause a trend such as is observed in the rotivity *versus* refractive index plot.

where P is a constant, is accurately obeyed by most substances under varying conditions. For solutions, M and P may be calculated in the same way as any colligative property, or P/M may be found if the refractive index and density are known at any temperature. Now, from the Lorenz–Lorentz equation it is found that

$$\frac{n^2 + 1}{3} = \frac{1}{1 - (P/M)d} \tag{42}$$

so that once P/M is known, the rotivity of a given solution may be found at any temperature from a knowledge of the density variation alone. An example is given in table 5. Here a maximum in the rotation as the temperature increases does not appear in the rotivity.

TABLE 5

Effect of refractive index changes on rotation of ethyl tartrate at different temperatures

$P = 45.70$ from atomic refractions; $M = 206$; $P/M = 0.222$

t	d	$[M]^t_{5761}$	$(1 - 0.222d)[M]^t_{5761}$
°C.			
−22.0	1.2472	3.84	2.78
0.0	1.2254	11.03	8.03
15.5	1.2097	15.09	11.04
59.5	1.1656	23.77	17.62
114.9	1.1095	29.60	22.31
190.0	1.0345	31.99	24.64
223.5	1.0003	31.75	24.70

Data from reference 32.

2. Solvent effects which act through β

Changes in the rotivity must all result from alterations in the states a_i and b_i of the molecule. These alterations must in turn arise from compound formation of one sort or another, that is, there must be formed some kind of bonds, be they loose dipole–dipole bonds, or strong "chemical" bonds, between the solvent molecules and the active molecule. We shall here distinguish between the following mechanisms by which such compound formation alters the rotation: (*a*) action of a group or groups in the solvent molecule as chromophores; (*b*) direct vicinal action of the solvent molecule on the chromophores of the active molecule; and (*c*) distortion of the molecular framework of the active molecule by the solvent and consequent effect on the optical rotation.

(*a*) *Action of groups of the solvent molecule as chromophores* will certainly always occur to a considerable extent when a covalent bond between the solvent and the solute is formed. An example might be found in the fact that on addition of chromium ions to tartaric acid solutions, the absorption bands of chromium show anomalous dispersion of the optical rotation due to the formation of a chromi-tartrate complex. But of the very great and irregular effects of solvents which undergo a chemical reaction with the optically active molecule we need only remark that they are entirely understandable as compared with the more obscure and smaller variations caused by solvents which certainly undergo no ordinary chemical reaction with optically active molecules upon which they can act. It is therefore the latter which will interest us here.

Unless there is a very strong bond between the solvent molecule and the optically active molecule, it is questionable if the solvent will act appreciably as a chromophore. First of all, the many possible orientations of nearly the same energy which the solvent molecules could take on about an optically active molecule with which they form no complex of definite structure would tend to cause the contributions from this source to cancel out. Secondly, vicinal actions capable of causing the solvent to act as a chromophore fall off rapidly with distance, and two neighboring molecules in a solution are usually relatively farther apart than those groups in the molecule whose interactions determine the optical rotation.

Experimental evidence for the deduction that a solvent may have an effect on the optical rotation without itself acting as a chromophore is found in the work of Lifschitz (24). Lifschitz finds that several metal ions which have an appreciable effect on the rotation of oxymethylenecamphor and which have absorption lines in the visible show no anomalous dispersion in the neighborhood of these lines.

(b) and (c). Alteration of β both by direct vicinal action of the solvent molecule on the chromophores of the active molecule and by distortion of the molecular framework of the active molecule may occur and both will be considered together in the following treatment. Here the theory of Beckmann and Cohen (1) finds its application.

These writers begin by assuming that the rotivity of a molecule is linearly proportional to the electrostatic field acting on the active molecule. That is,

$$\Omega = \Omega_0 + \Omega' F \qquad (43)$$

where Ω' is the change in rotivity per unit field acting along a certain chosen direction. We shall see later that we need only be concerned with fields which act along the direction of the resultant dipole of the optically active molecule, so that Ω' will be defined here with respect to that direction.

It is instructive to ask if the theories of optical activity which we have outlined lead us to expect such a linear relationship. In the first place, we note again that since the development is made in terms of the rotivity, we are directly concerned with effects involving β, the molecular rotatory parameter. (Beckmann and Cohen, however, regarded the rotivity as a measure of the third-rank Darwin scattering factor, which they treat as a molecular constant.) We must therefore ask how β will be expected to depend on the field. The following mechanisms suggest themselves: first, the applied field might distort the structural framework of the molecule. Such distortions would affect the optical rotation, since this is so sensitive to the positions of atoms and groups with respect to the various chromophoric groups of the molecule. If the force resisting distortion obeys Hooke's law and if the force acting to cause distortion is proportional to the field (both assumptions are reasonable), there should be a linear relationship between the field and the amount of displacement of the groups of the molecule, even for quite large displacements. Now over a sufficiently small range of displacements it is possible to say that the effect on the optical rotation will be proportional to the amount of displacement. Therefore we have that the change in rotivity will be proportional to the field.

A second mechanism whereby a field might influence the optical rotation is illustrated by the following example: Suppose that there are two positions, A and B, in which a group is predominantly found with respect to rotation about a bond. Then the optical rotivity will be given by $\Omega = n_A\Omega_A + n_B\Omega_B$ where n_A and n_B are the fractions of molecules having the group in question in positions A and B, respectively, while Ω_A and Ω_B are the rotivities corresponding to each position. Now, in a field F position A may become more stable by an energy $\mathrm{d}_A F$, while position B may become less stable by an energy $\mathrm{d}_B F$, due to interaction of dipoles or polarizability ellipsoids with the field. n_A will then be increased by an amount proportional to $e^{\mathrm{d}_A F/kT}$, while n_B will be decreased by an amount proportional to $e^{\mathrm{d}_B F/kT}$. If the energies $\mathrm{d}_A F$ and $\mathrm{d}_B F$ are small relative to kT, the exponentials may be expressed as $(1 + \mathrm{d}_A F/kT)$ and $(1 + \mathrm{d}_B F/kT)$. Introducing these into our expression for Ω in terms of n_A and n_B, we see that the rotivity will depend linearly upon the field.

A third mechanism, distinct from the above, suggests itself when we inspect the experimental data concerning the relative orders of magnitude of the effects of solvents on rigid and non-rigid molecules. If the mechanisms proposed above were the only ones operating, we should expect the rotations of such molecules as camphor and fenchone, which possess cross-braced, rigid structures, to show very much less susceptibility to solvents than non-rigid substances such as menthylmethyl naphthoate. This is often found not to be the case; some rigid molecules show large solvent influences, while some non-rigid molecules show small ones. This would indicate that the solvent field is exerting some direct vicinal action on the chromophores of the active molecule. Such actions would be expected from the one-electron theory and have been shown in section III C to have a linear effect on the rotation to a first and probably good approximation. It is to be noted that arguments of symmetry similar to those of IV B lead to the expectation that such vicinal actions will be greatest when they do not lie along the axes of the more strongly chromophoric groups. That is, the direction of the resultant dipole moment of the active molecule must lie in a different direction from those of the axes of the important chromophoric groups. It is of interest that those molecules whose rotations show the greatest susceptibility to solvent action generally appear to conform to this requirement.

In order to calculate the rotivity for an actual system of molecules, using equation 43, it is necessary to weight the rotivity corresponding to each configuration of the active molecule and its neighbors by the probability of occurrence of the configuration. For the term in the rotivity proportional to the field, the same result is obtained by simply averaging the field over all configurations and introducing the resultant value of the field directly into equation 43. This is accomplished as follows: If the active molecule has a dipole moment μ_α, it will induce a moment in the surrounding molecules and it will also interact with their permanent moments. Each configuration of the system gives an electric field acting on the optically active molecule due to this polarization of the surrounding molecules, and each configuration has a probability of occurring which is proportional to $e^{-\epsilon/kT}$, where ϵ is the energy of the configuration. An average field is obtainable by the usual statistical mechanical methods. Assuming the molecules to be hard spheres with dipoles at their centers, and assuming the interaction energies to be small relative to kT, the average field will be in the direction of the dipole of the active molecule (whence the form of our definition of Ω' at the start) and has the value,

$$F_{av.} = \frac{2\mu_\alpha}{d^3_{\alpha\alpha}} \frac{n_\alpha}{N} P_\alpha + \frac{2\mu_\alpha}{d^3_{\alpha\beta}} \frac{n_\beta}{N} P_\beta + \cdots \tag{44}$$

where n_α = number of optically active molecules per unit volume,
n_β = number of solvent molecules of type β per unit volume,
N = Avogadro's number,
$d_{\alpha\alpha}$ = distance of closest approach of two active molecules, taken as hard spheres,
$d_{\alpha\beta}$ = distance of closest approach of an active molecule and a solvent molecule of type β,
$P_\alpha = \frac{4\pi N}{3}\left[A + \frac{\mu_\alpha^2}{3kT}\right]$, where A = mean polarizability of an active molecule,

$P_\beta = \frac{4\pi N}{3}\left[B + \frac{\mu_\beta^2}{3kT}\right]$, where B = mean polarizability of a solvent molecule of type β, and

μ_α, μ_β = dipole moments of active and solvent molecules.

It is to be noted that A and B are independent of the concentrations of the molecules in the solution to a very good approximation (38). Owing to the association of molecules, however, μ_α and μ_β may depend upon the concentration, but as long as the result of this association is the same for the microscopic field about an active molecule as for the microscopic field used in measuring dielectric constants, P_α and P_β may be found from the relation

$$\frac{\epsilon - 1}{\epsilon + 2} = \frac{1}{N}(n_\alpha P_\alpha + n_\beta P_\beta + \cdots) \tag{45}$$

where ϵ is the dielectric constant of the solution.

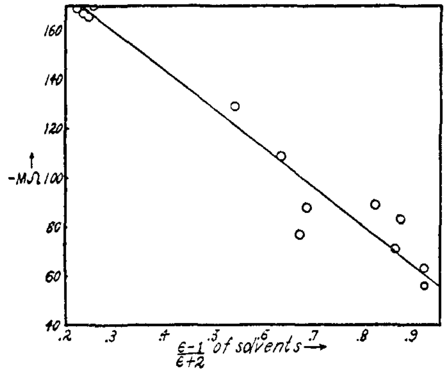


FIG. 11. Plot of Ω against $(\epsilon - 1)/(\epsilon + 2)$ for *l*-menthylmethyl naphthoate in aliphatic solvents

Substituting equations 44 and 45 in equation 43 and taking dilute solutions of the optically active molecule of a definite concentration, we find

$$\Omega = \Omega_0 + \Omega' \cdot \frac{2\mu_\alpha}{d^3} \frac{\epsilon - 1}{\epsilon + 2} \tag{46}$$

where d is approximately constant for solvents of similar structures. Taking ϵ for the pure solvent, Beckmann and Cohen find that Ω plotted against $\frac{\epsilon - 1}{\epsilon + 2}$ gives a fairly good straight line (see figures 11, 12, and 13) for several substances investigated by Rule.

The deviations from linearity and the fact that a distinction must be made between aromatic and aliphatic solvents show that other effects must be active but that the main effect is probably due to the action of dipoles in the manner pictured above. Furthermore, the independence of $\frac{\epsilon - 1}{\epsilon + 2}$ and the rotivity of pinane, whose dipole moment is zero, follows from equation 46.

The connection between the dipole moment of solvent molecules and their effect on the rotation had been demonstrated previously by Rule and his coworkers (35). This is now understandable, since the major contribution to the polarization of polar substances occurs through their dipole moments.

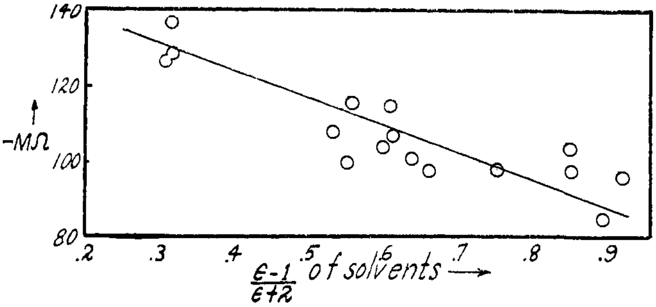


FIG. 12. Plot of Ω against $(\epsilon - 1)/(\epsilon + 2)$ for *l*-menthylmethyl naphthoate in aromatic solvents

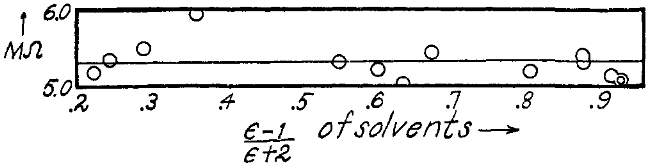


FIG. 13. Plot of Ω against $(\epsilon - 1)/(\epsilon + 2)$ for *d*-pinane

Beckmann and Cohen performed experiments in which they measured the optical rotations of active substances having a fixed concentration in mixtures of polar and non-polar solvents of different concentrations. They verified that there is a linear relation between the change in rotivity per unit amount of polar solvent and the polarization of the polar solvent at a given concentration. That is, as can readily be shown from their theory,

$$\frac{\Omega - \Omega_0}{n} = G + KP \tag{47}$$

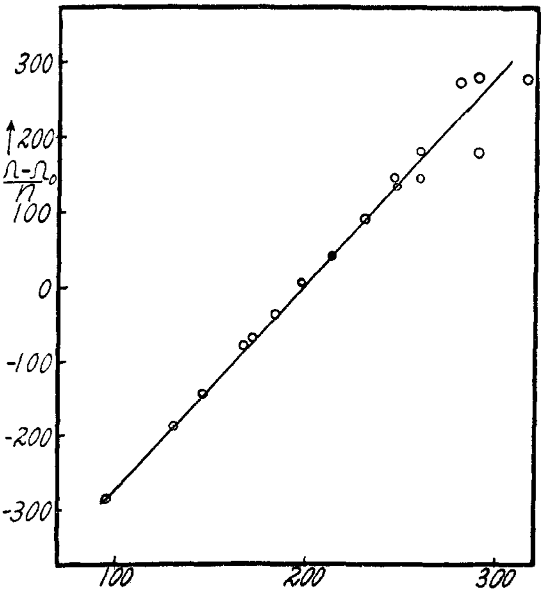
where n = concentration of polar substance in moles per cubic centimeter,

Ω = rotivity of a fixed concentration of active substance in the mixed solvent,

Ω_0 = rotivity of active substance at the same concentration in pure non-polar solvent,

G and K are constants depending on the nature of the polar substance, among other things, and

P = molecular polarization of polar substance as found from equation 45 for each value of n.



Polarization of nitrobenzene in solution (in cubic centimeters)

FIG. 14

G measures, at least in part, the difference in the rotivity when polar molecules replace non-polar ones owing to other than polarization forces. The linearity of the relation, equation 47, does not, however, prove that this difference is really independent of the polarization, since any linear dependence is included in K. A selective crowding out of non-polar molecules by polar ones in the neighborhood of the active molecule due to differences in polarization might be expected to introduce such a linear dependence on P.

The excellence of the relationship in equation 47 is shown by the curve in figure 14 for diethyl diacetyl-*d*-tartrate in mixtures of benzene and nitrobenzene, varying from 2 g. of nitrobenzene per 50 cc. of solution to 100 per cent nitrobenzene as solvent, with 5 g. of tartrate per 50 cc.

throughout. Neither P nor Ω varies linearly with the concentration of nitrobenzene, yet the two are themselves related linearly. For further deductions from the theory, the reader is referred to the original articles (1).

D. EFFECTS OF POLAR GROUPS WITHIN THE ACTIVE MOLECULE

We have just seen that a field applied along a certain direction of an optically active molecule causes a linear change in the rotivity. If such a field is produced directly by introducing a dipole into the molecule itself, a similar result both as to origin and magnitude is to be anticipated. Rule and Betti have indeed sought to establish a relationship between the polarity of a group substituted at some point in an optically active molecule and the optical rotation of the molecule.

Unfortunately there are a number of factors which complicate the problem. In the first place, the various groups which are introduced may themselves act as chromophores and the resultant contribution to the optical rotation may bear no relation to the polarity of the group. Secondly, no account is usually taken of the "solvent effect" of the dipoles in one active molecule on the rotation of another molecule of the same species. This action is the same as that discussed in the previous section and is certain to occur unless rotations are measured in dilute solution. It would lead to an apparent relationship between the polarity of the group and the optical rotation which is actually no different from the question of solvent action discussed before. Thirdly, even if the above factors were eliminated, although a definite relationship between the optical rotation and the magnitude of the dipoles in a molecule is to be expected from the one-electron theory, the directness of this relationship would be reduced by the fact that not only the magnitude of the moment but its orientation in space as well must be considered.

In the light of these considerations, then, the results obtained by Rule (36) and Betti (3), some of which are given in table 6, are understandable both in the regularities and in the discrepancies which they exhibit. Since Betti's measurements were made in benzene solution, the "solvent effects" of the molecules on one another are reduced and more regularity is exhibited than in the results of Rule, whose measurements were made using the undiluted material. Furthermore, the strikingly large changes in rotation which are obtained by Betti indicate that something more than simple solvent action must be acting here.

The key to the understanding of the unmistakable relationship found by Betti between the rotation of $RCH{=}NCH(C_6H_5)C_{10}H_6OH$ and the strength of the acid RCOOH is probably to be found in the work of Bjerrum, and Kirkwood, Westheimer, and Shookhoff (4, 16) on the effects of electrostatic fields resulting from dipoles and charges in an acid on the strength of the acid. These workers are able to account rather well for the values of the dissociation constants of acids in which there are dipoles and free charges by assuming that these, through their electrostatic fields, alter the potential energy of a proton on the carboxyl group. They thus find that

TABLE 6

(*A*) $[M]_D^{20}$ *of homogeneous esters of* XCH_2COOH (*reference 36*)

X	DIPOLE MOMENT	k OF ACID DISSOCIATION	$[M]_D^{20}$ OF l-MENTHYL ESTER	$[M]_D^{20}$ OF l-OCTYL ESTER
$N(CH_3)_2$	+1.4	1.3×10^{-10} (?)	−156.9°	
H		1.8×10^{-5}	−157.3°	−11.8°
CH_3	+0.4	1.4	−160.2°	−13.0°
COOH	−0.9	160	−160.2°	
OC_2H_5		23	−160.6°	
OCH_3	−1.2	33	−165°	−16.3°
OH	−1.7	15	−165° (94°C.)	
Br	−1.5	138	−169°	−28.8°
Cl	−1.5	155	−171°	−17.9°
CN	−3.8	370	−174°	

(*B*) $[M]_D$ *of benzene solutions of* $RCH{=}NCH(C_6H_5)C_{10}H_6OH$ *derivatives* (*reference 3*)

ALDEHYDE USED TO FORM =CHR	$[M]_D$	$k \times 10^5$ (25°C.) OF CORRESPONDING ACIDS	LOG ($k \times 10^6$)
p-Dimethylaminobenzoic	+2676.0	0.94	0.974
p-Oxybenzoic	+1049.5	2.9	1.463
3-Bromo-*p*-oxybenzoic	+648.0		
Protocatechuic	+588.8	3.3	1.519
3-Nitroanisic	+559.6		
m-Toluic	+504.5	5.6	1.749
Benzoic	+373.1	6.6	1.820
m-Oxybenzoic	+362.6	8.33	1.920
p-Chlorobenzoic	+311.8	9.3	1.969
m-Bromobenzoic	+280.9	13.7	2.137
m-Chlorobenzoic	+255.9	15.5	2.190
m-Nitrobenzoic	+167.6	34.8	2.541
Salicylic	−85.7	106	3.025
o-Chlorobenzoic	−128.4	132	3.121
o-Bromobenzoic	−308.2	145	3.161
o-Nitrobenzoic	−990.7	657	3.826

$$\log k' = \frac{e\mu \cos \theta}{2.303kTDR^2} + \text{const.} \tag{48}$$

where k' is the dissociation constant of the acid under consideration, μ is the dipole moment of a substituent in the molecule, D is the effective dielectric constant of the medium between the dipole and the carboxyl (D depends on the shape of the molecule and the point of attachment of the dipole as well as on the nature of the molecule and its surrounding solvent), R is the distance from the dipole to the carboxyl, θ is the angle between the axis of the dipole and the direction of the carboxyl from the dipole, e is the charge of the proton, k is the Boltzmann constant, and T is the temperature.

Now the factor $\frac{\mu \cos \theta}{DR^2}$ in equation 48 gives the potential due to a dipole; in section III C we have seen that such a potential can influence the optical rotation caused by a given chromophore by an amount proportional to $\frac{\mu}{D} \cos \theta \, f(R)$, where D is assumed constant for points in the neighborhood of the chromophoric group, where R is large enough that $\cos \theta$ is the angular dependence function, and where $f(R)$ is the radial dependence function of the perturbation acting on the group. Therefore, we may write

$$\Omega = \Omega_0 + \frac{e\mu}{D} \cos \theta f(R) \tag{49}$$

For any given value of R (that is, for any series of ortho-, meta-, or para-derivatives, in the example under consideration) we may combine equations 48 and 49 to obtain

$$\Omega = \Omega_0 + 2.303kTR^2 f(R)(\log k' - \text{const.})$$

or

$$\Omega = \Omega_0' + 2.303kTR^2 f(R) \log k' \tag{50}$$

That is, there should be a linear relationship between the logarithm of the dissociation constant of all derivatives of an acid having substituents in the same position and the rotivities of derivatives of the acid. Furthermore, the plots of Ω *versus* $\log k'$ for all sets of derivatives must intersect at the point given by the derivative for which all $\mu = 0$ (in this case for the benzoic acid derivative).

In figure 15 are given plots of the rotation (which is here very nearly proportional to the rotivity, since dilute solutions of benzene were used for all measurements, so that the refractive index is nearly constant) against the logarithms of the dissociation constants of the acids related to the active molecules. The agreement is satisfactory throughout, considering the approximations made. It is interesting that the orthoderivatives give the poorest agreement, and it is just these for which we should expect the largest disturbance by the substituents acting as chromophores and also by their exerting vicinal actions different in nature from those pictured here, on account of their relative closeness to the asymmetric center of the molecule.

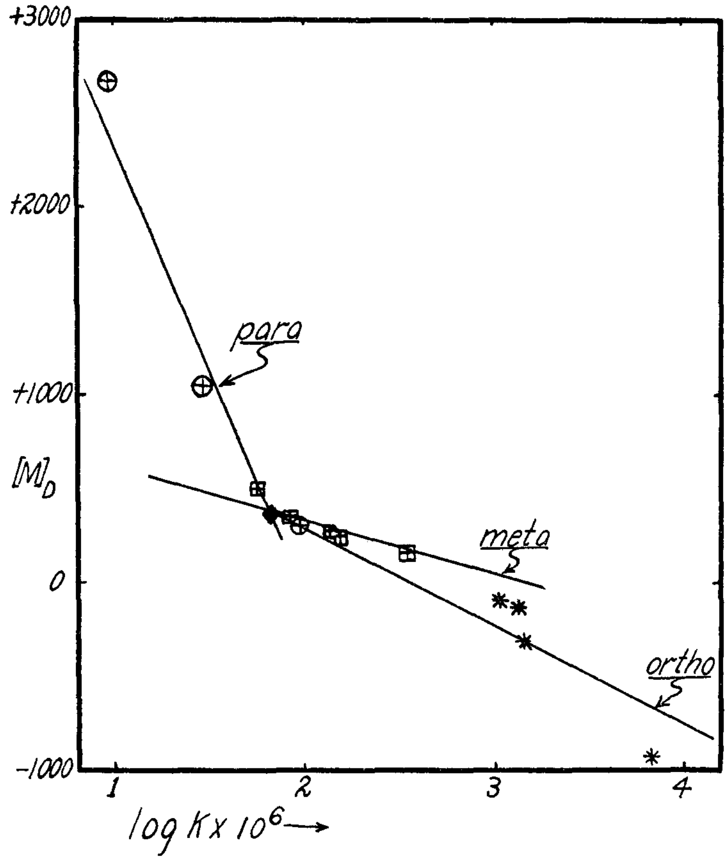


FIG. 15. Relation between optical rotation of $RCH{=}NCH(C_6H_5)C_{10}H_6OH$ and strengths of the acids RCOOH (data by Betti). ⊕, *p*-benzoic acid derivatives; ⊞, *m*-benzoic acid derivatives; *, *o*-benzoic acid derivatives; ◆, benzoic acid.

The data of Rule are also plotted (figures 16 and 17). Here the distances R are very nearly equal, while the angles θ probably are not too widely different, so that a plot both of dipole moment *versus* the rotation and of acid strength *versus* the rotation should give fairly straight lines. The other complicating factors mentioned above, however, make any agreement which might exist obscure. In addition, the effects which are produced are not very large as compared with those obtained by Betti.

If the values for X = COOH and OH are neglected (these are marked with circles in the figures), the agreement becomes better. This may be caused by auxiliary disturbances from hydrogen-bonding between two active molecules, which are only possible in these compounds. Furthermore, the rotation of the OH derivative was not taken at the same temperature as the others. On the whole, therefore, it may be said that these data tend to verify the ideas presented here.

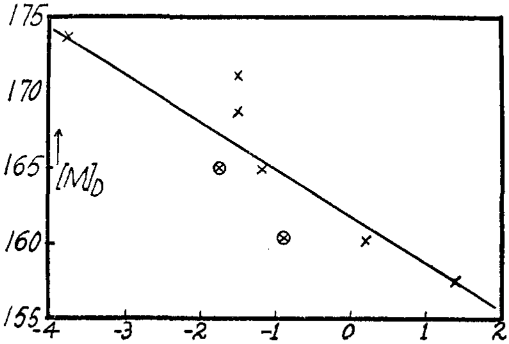


FIG. 16. Effect of bond moment of substituent on rotations of *l*-menthyl esters of XCH_2COOH

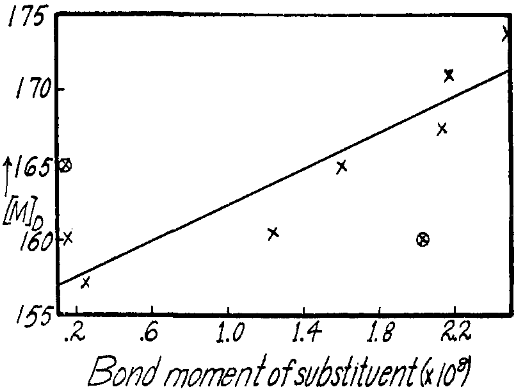


FIG. 17. Effect of acidity of XCH_2COOH on rotation of its *l*-menthyl ester

E. OPTICAL SUPERPOSITION

van't Hoff's theory of the asymmetric carbon atom as a structural condition giving rise to the ability to rotate the plane of polarized light led him to propose an additivity relationship known as the principle of optical superposition. According to this, in a molecule containing several asymmetric centers, each center contributes to the optical rotation independently of the others. Such a principle would be expected to be valid whenever the centers involved are widely enough separated; let us, however, examine a sugar, in which the centers are close to one another.

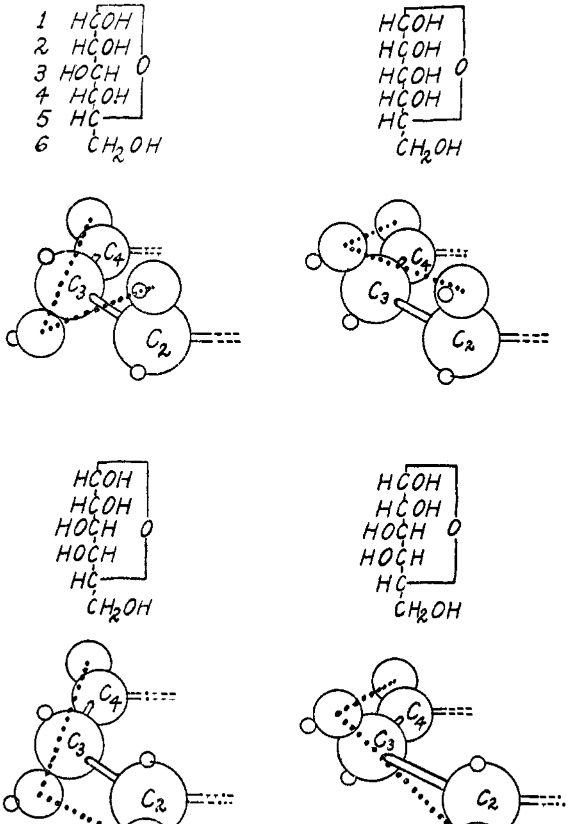


FIG. 18

It is readily seen from figure 18 that when the configuration about one center is changed, the changes occurring in the various inter-group distances and directions (these being indicated by the heavy dotted lines) depend very much on the configurations of the neighboring asymmetric carbon atoms. This is the more marked if the ring is puckered rather than planar.

For open-chain sugar derivatives a change of configuration about one center may not only bring about changes such as the above, but may also cause the chain to tend to assume a new conformation in order to adjust itself to the altered steric forces which are involved. Thus (see figure 19) if hydroxyl groups are assumed to repel each other very strongly, the chain will be found to be forced to assume different shapes for each diastereoisomer. This means that the rotation of a given isomer will depend on the configurations about all centers taken as a whole in contradiction to van't Hoff's principle of superposition. Therefore, it is not surprising that open-chain sugar derivatives fail to obey the principle of superposition. For instance, we consider the case of four sugar-acids cited by Freudenberg and Kuhn (11):

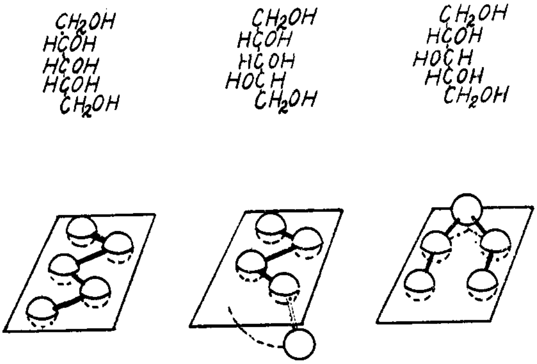
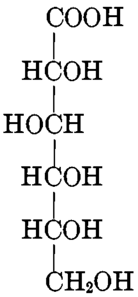
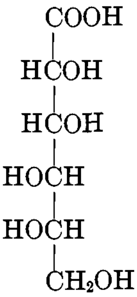


FIG. 19. Form of carbon chains if hydroxyls on neighboring atoms repel one another very strongly



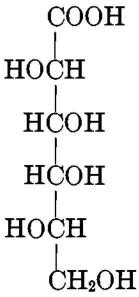
$$\begin{array}{c}\mathrm{COOH}\\|\\\mathrm{HCOH}\\|\\\mathrm{HOCH}\\|\\\mathrm{HCOH}\\|\\\mathrm{HCOH}\\|\\\mathrm{CH_2OH}\end{array}$$

d-Gluconic acid
$[M]_D = -13°$



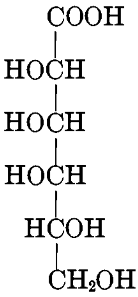
$$\begin{array}{c}\mathrm{COOH}\\|\\\mathrm{HCOH}\\|\\\mathrm{HCOH}\\|\\\mathrm{HOCH}\\|\\\mathrm{HOCH}\\|\\\mathrm{CH_2OH}\end{array}$$

l-Mannonic acid
$[M]_D = +1°$



$$\begin{array}{c}\mathrm{COOH}\\|\\\mathrm{HOCH}\\|\\\mathrm{HCOH}\\|\\\mathrm{HCOH}\\|\\\mathrm{HOCH}\\|\\\mathrm{CH_2OH}\end{array}$$

l-Galactonic acid
$[M]_D = +24°$



$$\begin{array}{c}\mathrm{COOH}\\|\\\mathrm{HOCH}\\|\\\mathrm{HOCH}\\|\\\mathrm{HOCH}\\|\\\mathrm{HCOH}\\|\\\mathrm{CH_2OH}\end{array}$$

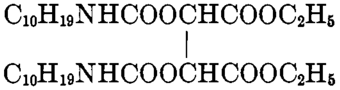
d-Talonic acid
$[M]_D = +33°$

The rotations of these acids, according to the principle of superposition, should be made up of the following contributions by each asymmetric atom:

+A	+A	−A	−A
−B	+B	+B	−B
+C	−C	+C	−C
+D	−D	−D	+D

Now it is apparent that the principle of superposition would predict the sum of the rotations of these compounds to be zero. It is actually +45°,—even larger than any of the individual rotations.

An instance in which the principle of superposition is probably obeyed because of the large distance between asymmetric centers is found in the dimenthylurethans of the diethyl tartrates (41):



$$\begin{array}{c} C_{10}H_{19}NHCOOCHCOOC_2H_5 \\ | \\ C_{10}H_{19}NHCOOCHCOOC_2H_5 \end{array}$$

l-Menthylurethan of diethyl *d*-tartrate: $[\alpha]_D = -74.34°$

l-Menthylurethan of diethyl *l*-tartrate: $[\alpha]_D = -38.76°$

$-57.78°$ (mean)

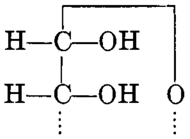
l-Menthylurethan of diethyl mesotartrate: $[\alpha]_D = -56.55°$

Similar results are found for the D-*l*-fenchyl urethans of the tartaric acids.

In these substances it would appear that the distance between the asymmetric centers in the menthyl radicals and those in the tartrate portion of the molecule is so great that the interaction is negligible. In taking the mean of the *d*- and *l*-esters, the effect of the tartrate portion cancels out, while in the meso compound the contribution is nil, so that the same residual rotations remain in both cases.

It might be surprising in the light of what has been said above that superposition appears to hold very well for many of the closed-ring sugars and their derivatives. This has led to the formulation of the so-called Hudson's rules of isorotation, whereby constant differences are found between the rotations of isomers which differ only in the configuration about a given asymmetric center. There are exceptions to these rules, particularly in the mannose, talose, and ketose series.

Freudenberg and Kuhn (11) explain both the occurrence of and the exceptions to Hudson's rules by assuming that groups attached to atoms twice removed from a given center are too far distant to be able to act appreciably in contributing to the rotation by the groups directly attached to the given center. Then the differences in the rotations of sugars containing the configurations



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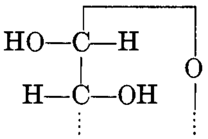
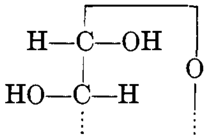


should be constant, regardless of the nature of the rest of the molecule. Furthermore, the value of this constant will not be the same as that obtained in the series



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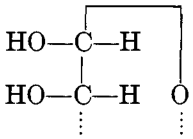


Since mannose and talose are of the second type, while the other sugars which are known to obey Hudson's rules belong to the first, this explanation is convincing.

The explanation becomes less convincing, however, when actual models of the sugars are made. If tetrahedral angles are maintained, it is seen that the groups on an atom twice removed from a given atom are in very close proximity to one or the other of the groups on the given atom. Besides, a large number of conformations of the ring are possible, and the stabilities of these would be expected to depend on the orientations of each and every group in the molecule, and so in turn affect the optical rotation to a marked degree. Furthermore, although vicinal actions fall off with distance, they probably do not fall off so rapidly as to have no more noticeable effect than they do on the validity of Hudson's rules. Therefore, it would appear that the problem deserves further consideration.

No final answer can be said to have been given, but some more general conditions under which Hudson's rules or superposition in general would hold have been developed (12). These are as follows: (1) that the vicinal actions of groups on a chromophore be additive (that is that the effect of one group on a chromophore is independent of the presence of other groups), and (2) that the structure to which the various groups whose configurations are changed are connected be symmetrical on the average (that is, that simultaneous change of configuration about two centers shall result merely in a change of sign of the vicinal actions between the groups involved in the change). If these conditions are satisfied, then regardless of how rapidly vicinal actions decrease with distance, there will appear to be superposition in the van't Hoff sense.

If it is these conditions which control the validity of Hudson's rules in the sugars, then some interesting conclusions can be drawn as to the structure of the rings involved. Thus, either the ring is flat, or else, if puckered in any way, it must exist in equal amounts in two conformations for each type of puckering which it can exhibit, so that the condition of the existence of the requisite effective symmetry in the ring is met. Presumably deviations from superposition occur whenever this is not true, and also when the additivity condition is violated (which is possible whenever there can be restricted rotation about the bonds of the attached groups, since a third group can then influence the vicinal actions between two other groups by influencing the position of maximum stability of one or the other of these groups about its axis).

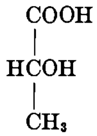
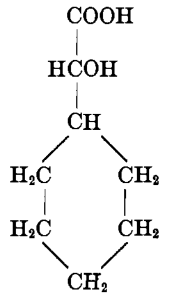
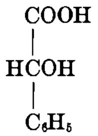
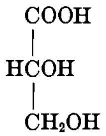
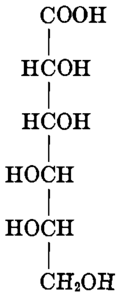
F. OPTICAL DISPLACEMENT

Consider the differences between the rotations of configurationally related α-hydroxy acids, RCHOHCOOH, and their amides, $RCHOHCONH_2$, where R may be any group (CH_3, C_2H_5, C_6H_5, etc.). The interactions which we must consider in calculating these differences are as follows:

(*a*) Interactions involving R and OH as chromophores and $CONH_2$ and COOH as vicinal groups. Since the COOH and $CONH_2$ groups are not very different, we would not expect them to act very differently as vicinal groups. (Thus, on the Kuhn theory and the Kirkwood theory, the similarity is expressible by similar orientations of the axes of the oscillators in the groups and similar values of the force constants and polarizabilities, while in the one-electron theory the charge distributions and dipole fields around the two groups are about the same, both groups having the same number of electrons and similar structures.) Therefore, if the substitution of $CONH_2$ for COOH produces no marked effect on the spatial structure of the group R (especially with respect to rotation about bonds, etc.), we should expect these interactions to remain about the same when we replace COOH by $CONH_2$, regardless of the nature of R.

(*b*) Interactions involving COOH and $CONH_2$ as chromophores and R and OH as vicinal groups. Since these groups are likely to show some difference when they act as chromophores, it is here that we would expect the major effect on the optical activity to show itself. Furthermore, the direction of the change in rotation when we pass from the acid to the amide should be the same for all R groups which are sufficiently similar. Just what is meant by "sufficiently similar" depends upon the theoretical approach that is taken. The Kuhn and Kirkwood theories require that the orientations of the axes of the oscillators in the different groups be similar. The one-electron theory requires that, insofar as dipoles are important, the dipoles possess about the same directions in space, and that.

insofar as incomplete screening of atoms is important, the atoms merely lie in the same direction in space with respect to the group being changed. In actual practice, such groups as methyl, phenyl, and cyclohexyl appear to meet well enough whichever of these criteria are actually operative, so that they may be called similar in the present sense of that word; this, along with a general experimental proof of what has been presented above, is indicated by the data (11) given below. All of the substances shown are, of course, configurationally related.

				
$COOH-HCOH-CH_3$		$COOH-HCOH-C_6H_5$	$COOH-HCOH-CH_2OH$	$COOH-HCOH-HCOH-HOCH-HOCH-CH_2OH$
$[M]_D$ of: lactic acid −3 } +23 amide +20	hexahydromandelic −42 } +107 +65	mandelic −233 } +97 −146	glyceric −2 } +72 +70	*l*-mannonic +1 } +33 +34

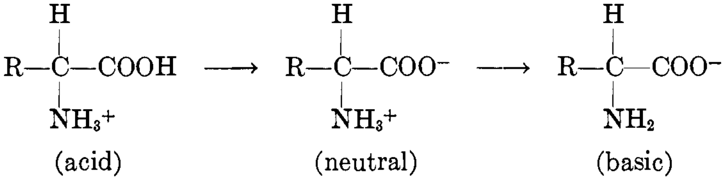
The ten other known cases in which one can convert an *α*-*d*-hydroxy acid to its amide all show a change of sign in the same direction as the above.

The reasoning which has been carried out for this more or less specific set of substances may be generalized to give the *displacement rule* (which was first[5] proposed by Freudenberg and later explained by Freudenberg and Kuhn in essentially the same terms which we have used here): Differences in rotation between analogous derivatives of analogously constructed compounds are approximately the same in magnitude and direction (21).

This rule is of great importance in explaining many of the qualitative relationships found in the data on optical rotation. Freudenberg proposed it as a basis for finding the relative configurations of similar substances which could not be related in any other way. The manner in which lactic acid and alanine were thus related to one another is illustrated in figure 20. The parallelism in the trend of the rotations of derivatives of (+) lactic acid and (+) alanine shows them to be configurationally similar. The method has also been employed in establishing other configurational relationships, but care must obviously be exercised in order to avoid its application to too widely different sets of compounds.

[5] Clough (7) in 1918 put forward a rule nearly identical with this.

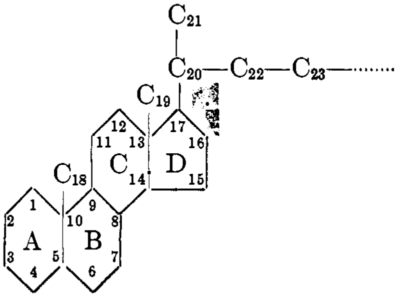
In going from acid to neutral to basic solution, all amino acids probably undergo the following sequence of changes:



$$\underset{\text{(acid)}}{\mathrm{R{-}\overset{H}{\underset{NH_3^+}{C}}{-}COOH}} \longrightarrow \underset{\text{(neutral)}}{\mathrm{R{-}\overset{H}{\underset{NH_3^+}{C}}{-}COO^-}} \longrightarrow \underset{\text{(basic)}}{\mathrm{R{-}\overset{H}{\underset{NH_2}{C}}{-}COO^-}}$$

Since the groups R are all fairly similar (in our sense of the word), we should expect to observe some regularity in the rotations which accompany these changes, provided all amino acids possess the same configuration. Lutz and Jergensons (28) have found such a regularity for natural amino acids, and their results are shown in figure 21. We may count this as the best sort of evidence that these naturally occurring amino acids possess the same configuration about their alpha carbon atoms. It is to be especially noted that in the details of the data shown there is considerable dependence on the nature of R, but that the general shapes of the curves are similar. This illustrates well the type of approximation which is embodied in the displacement rule.

Callow and Young (6) have pointed out some regularities in the rotations of the sterols which warrant attention here. The fundamental requirements which make these regularities possible seem to be (*1*) that vicinal actions are negligible beyond a certain distance, (*2*) that the steroid framework is spread out in space over a considerable area (so that any changes about position 17, for instance, have little effect on position 3), (*3*) that introduction of double bonds or a change in the *cis–trans* relationship of rings A and B does not result in any major movement of the atoms of the framework to new positions with respect to their more immediate neighbors, and (*4*) that when the effect of a given change at a certain point in the molecule is being examined, the changes which are allowed to occur at other points in the molecule are located at a sufficient distance from the given point as not to be able to exert any vicinal action on it.



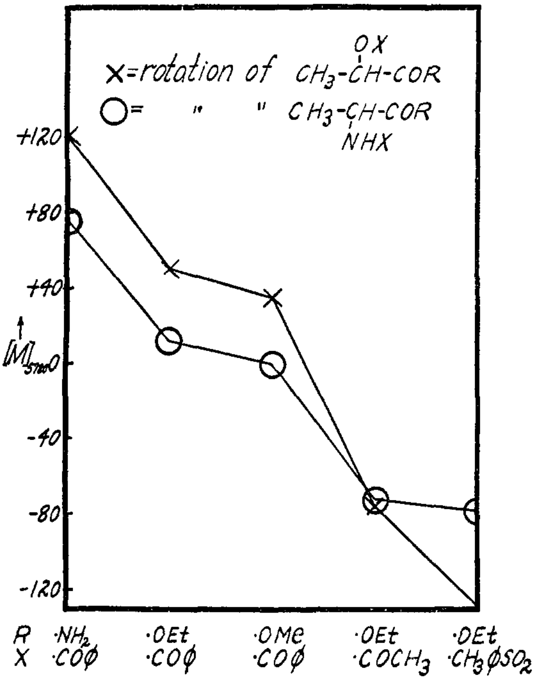


FIG. 20. Comparison of rotation of $CH_3CHOXCOR$ and $CH_3CH(NHX)COR$

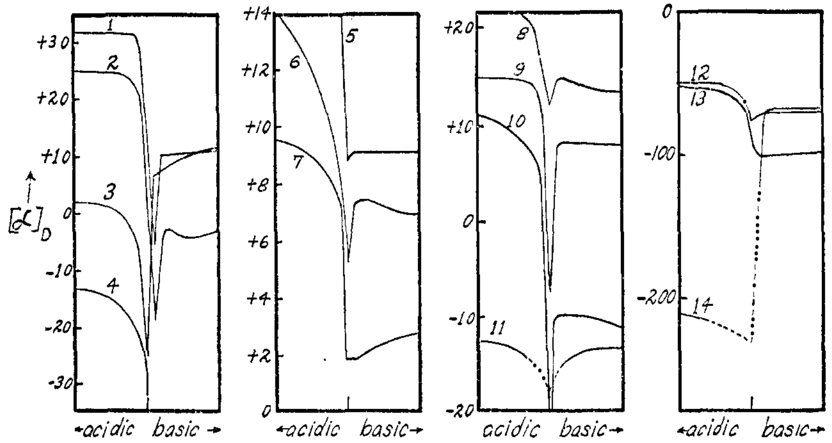


FIG. 21. Rotation of natural amino acids and acidity of their solutions. 1, glutamic acid; 2, aspartic acid; 3, tryptophan; 4, dihydroxyphenylalanine; 5, lysine; 6, ornithine; 7, alanine; 8, arginine; 9, leucine; 10, histidine; 11, tyrosine; 12, hydroxyproline; 13, proline; 14, cystine.

The observed regularities are of interest both in themselves and with regard to the exceptions which occur. They are therefore summarized below:

(*a*) A given change in configuration of a hydroxyl at position 3 for most epimers results in a change of optical rotation in the same direction. The magnitude of the change depends on the compound: for saturated sterols the change in molecular rotation is around 20°, while in the presence of a double bond the change[6] is larger, ranging from 50° to 400° depending on the proximity of the double bond to position 3.

(*b*) Introduction of a double bond at 4:5 increases the *d*-rotation by 150–200°. There are two exceptions, both involving the presence of a hydroxyl at 3: when this hydroxyl is *cis* to the methyl group, C_{18}, there is a decrease in *d*-rotation by 72° when the double bond is introduced, while when it is *trans* to C_{18} there is an increase in *d*-rotation by 373°. This discrepancy is readily explained: the 3-hydroxyl is very close to the position at which the double bond is introduced. Furthermore, in going from the *cis*-position to the *trans*, something close to reflection in one of the planes of symmetry of the double bond will be found to take place if a model is constructed. Therefore, the interaction of hydroxyl will be very large (say around 250°), and for the hydroxyl in the *cis*-position it depresses the normal change of +150° or 200° down to −50° or −100°, while for the *trans*-position it increases the normal change up to around +400°.

(*c*) Introduction of a double bond at 5:6 decreases the *d*-rotation by 200° or 300°. In one case in which there is already a double bond at 7:8, so that conjugation occurs when the new double bond is introduced, the decrease amounts to 436°. The bigger effect probably has largely to do with the movement of the absorption band nearer to the visible.

(*d*) Introduction of a double bond at 7:8 lowers the *d*-rotation by 62° in one case in which there is no conjugation, by 250–300° in two cases in which there is conjugation with a double bond at 5:6, and by 476° in one case in which there is conjugation with a double bond at 14:15. In two cases in which ring A is benzenoid (double bonds at 1:2, 3:4, 5:10) the introduction of a double bond at 7:8 results in an increase in *d*-rotation by 381° and 392°. Since the methyl at position 10 is no longer present, and since the benzene ring will act in an entirely different way as a chromophoric group, some such discrepancy is readily understandable.

(*e*) Introduction of a double bond at 8:14 is anomalous in its results on the optical rotation. This may be because in all cases the effect is small so that minor factors are able to throw the direction of change one way or the other.

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[6] The fact that in the presence of double bonds at different positions the direction of change of rotation remains the same must be counted a matter of chance.

(*f*) Introduction of a double bond at 14:15 results in a small increase in *d*-rotation.

(*g*) Introduction of a double bond at 22:23 results in a decrease in *d*-rotation by 36° to 174°.

(*h*) Reduction of a carbonyl in position 17 to hydroxyl results in a decrease in *d*-rotation by about 200°.

(*i*) A few other operations on the sterol molecule appear to exert a regular effect on the rotation but too few data are available to draw safely any conclusions about them.

It should be clear from the discussion above that these regularities ought to be considered as illustrating the displacement rule rather than optical superposition, since they are then given a wider scope and the mediocre quantitative agreement which is found becomes less objectionable.

We take this opportunity to thank Dr. E. Gorin for many helpful discussions on the subject of optical rotatory power, and Dr. J. M. Sturtevant and Mr. K. L. Berry for sending us some of the results of their experimental researches bearing on section IV B in advance of publication.

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