380. *The Dependence of Optical Rotatory Power on Chemical Constitution. Part XLI.*

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The use of rotation and dispersion data in the discussion of labile molecular configurations, as applied in the preceding communications, is briefly surveyed.

SINCE 1928, optically active alcohols have been prepared in this laboratory for use in the study of reaction mechanisms, rather than for the study of optical activity itself. In 1942 the derivation of a two-term Drude equation to fit the rotatory dispersion of 2-furylmethylcarbinol (Airs, Balfe, Irwin, and Kenyon, *J.*, 1942, 531) encouraged us to consider the rotatory dispersion of *cyclo*hexylphenylcarbinol, which was in preparation at that time, and to prepare three other optically active compounds with heterocyclic substituents, *viz.*, 2-thienylmethylcarbinol, 2-(2-hydroxy-*n*-propyl)pyridine, and glycide phenyl ether, for similar examination. In the preceding communications it is suggested, mainly on the basis of changes in rotatory dispersions, that molecular association occurs in the last two substances. The purpose of the present communication is to examine the basis for such suggestions: most of the matters involved are discussed fully by Lowry ("Optical Rotatory Power," London, 1935), Kuhn (*Trans. Faraday Soc.*, 1930, **26**, 293), Levene and Rothen (in Gilman's "Organic Chemistry," 1st Edn., New York, 1938), and Kauzmann, Walter, and Eyring (*Chem. Reviews*, 1940, **26**, 339).

A comparison of the magnitudes of the rotatory powers of different substances, under the same experimental conditions, can be related to differences in structure, notably in the observation that ring structures produce a much higher rotatory power than do isomeric open-chain structures (see, *e.g.*, the values recorded by Kauzmann, Walter, and Eyring, *loc. cit.*). For the present purpose, however, we are concerned with changes in structure on variation of the experimental conditions. These variations may alter the rotatory power, even if the structure of the optically active molecules remains substantially unchanged, and such effects must be eliminated if, as described later, it is desired to relate changes in optical rotation to changes in structure. We also suggest that changes in rotatory dispersion may be used as an indication of changes in structure, because rotatory dispersion is controlled by the optically active (or anisotropic) bands in the absorption spectrum, the frequencies of which are not, so far as is known, greatly altered by changes of, *e.g.*, temperature or solvent. If then such a change in conditions of observation causes a change in dispersion, it would appear that the dispersion becomes controlled by new absorpton frequencies, which must imply some change in the molecule.

It is assumed (following Lowry, and Levene and Rothen, *opp. cit.*) that, in regions of transparency, rotatory dispersion can be expressed by a Drude equation $\alpha_\lambda = \Sigma \frac{k_1}{\lambda^2 - \lambda_1^2}$, the constants λ_1, λ_2 . . . being frequencies of anisotropic absorption bands. " Simple " dispersion is expressed by a one-term equation and " complex " dispersion by a two-term equation (if the terms have opposite signs and $k_1 < k_2$, $\lambda_1 > \lambda_2$, the dispersion is " anomalous "); it is rarely that more than two terms are required to fit the dispersion in accessible wave-lengths. The most secure basis for comparison of rotatory dispersions is given by calculation of Drude equations from selected observations, to fit the dispersion curves observed under the different experimental conditions. It is, however, essential that the observations should be carried as far as possible into the ultra-violet, and unfortunately the facilities for so doing are not commonly available. Moreover, it is not always possible to derive a Drude equation to fit observations which extend into the ultra-violet. One possible reason for this is that the measurements may not be sufficiently delicate (the calculations can be very sensitive to small variations in rotatory powers).

Even when it is not possible to derive an equation from the observations of rotatory power alone, it is usually possible to calculate one or more which fit tolerably well the observations, by assuming values for the characteristic frequencies λ_1, λ_2, and adjusting the k constants by trial and error. The procedure is less elegant than direct calculation, but would appear to be applicable for the present purpose. Some reasonable basis is of course necessary for the assumed frequencies : for example, characteristic frequencies of optically active substances of similar structure, or absorption frequencies in the spectrum of the substance under examination. It may be found that several equations can be so derived to fit approximately the dispersion, but, if a change in experimental conditions causes changes in the constants of all of such several equations, then it would appear that the change in conditions has caused a change in the optically active molecules. Indications of changes in dispersion may also be obtained by the classification into simple dispersion (linear plot of $1/\alpha$ against λ^2) and complex dispersion (curvature of plot) : extrapolation of linear plots to the $1/\alpha$ axis gives the value of λ_0 of the one-term equation. In most cases this is composite, and of no exact physical significance, but notable changes in it must reflect changes in the constants of the dispersion equation, as shown by Hunter (*J.*, 1924, **125**, 1198) and Levene and Rothen (*op. cit.*). Similar comments apply to the use of the dispersion ratio, $\alpha_{4358}/\alpha_{5461}$ (Lowry, *op. cit.*, p. 132), which, if a one-term equation is applicable, is 1·61 for λ 1000 A., 1·65 for λ 1500 A., 1·73 for λ 2000 A., and 2·09 for λ 3000 A. Dispersion ratios below 1·57 indicate that the dispersion equation has two terms of opposite sign; ratios between 1·61 and 1·65 indicate that a one-term equation applies (particularly if the ratio does not change with solvents); ratios above 1·70, if constant in different solvents, indicate absorption in the near ultra-violet; if varying with solvent, they indicate that a two-term equation is required (Lowry, *op. cit.*).

The variables which we have used are temperature and solvent. Both may alter the optical rotation because they alter the refractive index of the medium. This effect can be eliminated, perhaps not completely (compare the results of Kenyon and Platt, *J.*, 1939, 633, with an optically active hydrocarbon), but probably sufficiently for the present purpose, by use of an expression such as Beckmann and Cohen's " rotivity " $\Omega\{= 3[\alpha]/(n^2 - 2)\}$ (*J. Chem. Physics*, 1936, **4**, 784 ; 1938, **6**, 183); this expression can be derived from quantum-mechanical concepts of the theory of optical rotatory power (Kauzmann *et al.*, *loc. cit.*). The temperature coefficient of density, which affects the number of molecules influencing the beam of polarised light, is eliminated in the calculation of specific rotatory power. Increase in temperature also reduces specific rotatory power because it gives increased freedom of rotation about single bonds (this decrease is not observed in the rotatory powers of substances which have a cyclic, and therefore rigid, structure). The total decrease in specific rotatory power caused by the temperature coefficients of refractive index and freedom of rotation is not more than 10—20% on 100° rise in temperature. If then a specific rotatory power is very greatly altered by change in temperature, it would seem reasonable to assume that there has been some alteration in molecular configuration, or in an equilibrium condition thereof, which is equivalent to an alteration in the optically active species.

When the rotatory powers (see, *e.g.*, Rule, Smith, and Harrower, *J.*, 1933, 386) or preferably the rotivities (Kauzmann, Walter, and Eyring, *loc. cit.*) of a given solute in a variety of solvents are plotted against the dielectric constants (or a function thereof), a fairly clear relation can sometimes be observed. This is ascribed to solvent–solute interactions, which are outside the scope of the present investigations. We therefore ascribe to changes in the solute, only those changes in rotatory powers in different solvents, which are not caused by changes in refractive index and do not show any relation to the dielectric constants of the solutions.

Kauzmann, Walter, and Eyring (*loc. cit.*) observed that the sensitivity of rotatory power to influences such as temperature, solvent, and small changes in structure make it a potentially powerful tool for investigating minor alterations which other molecular properties (*e.g.*, refractivity) are incapable of disclosing; Rule (*J.*, **1933**, 1217, and earlier papers, summarised by Lowry, *op. cit.*) had made a similar comment (the comparison is with other methods in which no chemical disturbance of structure occurs). The comment seems valid in principle. In its practical application, however, as outlined in the present communications, there remains a need for increased certainty of interpretation, which may come with further applications on similar lines. Bernstein and Pedersen (*J. Chem. Physics*, 1949, **17**, 885) have recently reported a somewhat similar application of rotivity data to discussion of the configurations of *sec.*-butyl alcohol; extension of the present investigations is not contemplated.

If the procedures here outlined do, in fact, lack precision, this is not due to fundamental deficiencies in the theoretical study of rotatory power, regarding which Kauzmann, Walter, and Eyring (*loc. cit.*) observe that " the problem of optical rotation can be said to be solved in principle." Nor does it seem that increased accuracy in observations of rotatory power in the visible or near ultra-violet regions would improve the discussions. So far as discussions based on dispersion data are concerned, the most useful advance would be an extension of the range of wave-lengths in which rotations can be measured. Even the range covered by visible and accessible ultra-violet frequencies is only a small part of the spectral region in which optical activity may be manifested (see Kuhn, *loc. cit.*). Comparisons of complete optical rotatory spectra would clearly be preferable to comparisons of calculated characteristics of inaccessible regions based on observations in the comparatively narrow accessible regions. There seems, however, to be no immediate prospect of extending optical rotatory spectra into the vacuum-ultra-violet; quantitative absorption spectra have not yet been extended into this region, though qualitative and some semi-quantitative observations have been made (see Platt and Klevens, *Rev. Mod. Physics*, 1944, **16**, 182). Such an extension of rotatory spectra would be of intrinsic interest, but whether it would be more rewarding, in the study of labile configurations, than the study of infra-red absorption, in which advances have already been made, is open to question.

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