

Stereochemical Studies

IX *. The Relationship between Optical Rotatory Dispersion and Configuration for Some Carboxylic Acids

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The optical rotatory dispersion of several series of arylsubstituted mono- and dicarboxylic acids, and acid derivatives, has been investigated. The utility of plain dispersion curves for establishing configurational relationships has been demonstrated. Attention is called to the high rotation and the steepness of the dispersion curves of anilides in these series. The advantage, and at times the necessity, of using dispersion curves instead of measurements at the D-line, when applying Freudenberg's displacement rule, has been demonstrated.

A knowledge of the configurational relationships between different types of optically active compounds is important in many branches of chemistry. Several chemical and physical methods have been developed for correlating relative configurations^{1,2}. From the X-ray crystallographic investigations on sodium rubidium tartrate by Bijvoet, Peerdeman and van Bommel³ it follows that for compounds with a configuration related to glyceraldehyde even the absolute configuration is known. Most of the methods referred to¹⁻³ are laborious and require a fairly large amount of optically active substance. Studies of the optical rotatory dispersion, (*i.e.* the change of optical rotation with wavelength), can be performed on as little as 0.1–2 mg of a compound, and with a modern spectropolarimeter a simple dispersion curve from 700 to 275 m μ can be produced in less than half an hour.

Measurements of optical rotatory dispersion have been made by various scientists since the phenomenon was discovered in 1817 by Biot⁴. These investigations have mainly been concerned with physico-chemical aspects of rotatory dispersion⁵⁻⁷, but some workers, (for instance Tschugaeff, Rupe, Freudenberg, Kuhn and Levene), also tried to relate the observed optical rotation to molecular structure, (for reviews and references see Refs.^{1,6,8-13}). It was not until Djerassi started in 1954 extensive studies of the optical rotatory

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dispersion of ketones and aldehydes that it was proved that spectropolarimetry was an extremely valuable tool for the chemist in solving structural and stereochemical problems. The work by Djerassi and collaborators has been published in the series "Optical Rotatory Dispersion Studies I¹⁴—XXXIV¹⁵", and has also been reviewed¹⁶⁻¹⁸.

In order to facilitate further discussion of the application of optical rotatory dispersion in this paper, a brief description will be given of some of the physical background and of the nomenclature used. A compound possesses optical rotatory power in an isotropic medium only when the mirror images of the molecule cannot be superimposed. When plane polarized light, (which is the superposition of right and left circularly polarized components), is transmitted through an optically active medium, the two components travel with unequal velocities. A phase difference between the right and the left circularly polarized components will thus arise, producing a rotation of the plane of polarization. The angle of rotation per unit length, α , is given by the expression,

$$\alpha = \frac{\pi}{\lambda_{\text{vac}}} (n_l - n_r) \quad (1)$$

where λ_{vac} is the wavelength of the light *in vacuo* and n_l and n_r are the refractive indices of the left and right circularly polarized waves, respectively.

Simultaneously with the optical activity produced by the difference in velocity of propagation of right and left circularly polarized waves, there is a second effect referred to as circular dichroism, arising from unequal absorption of the two waves. This is due to differential absorption of the two components of the incident linearly polarized wave so that they have different amplitudes after traversing the medium. They thus combine to give elliptically polarized light. The difference between the absorption coefficients for left and right circularly polarized light is only a small fraction of the mean absorption coefficient, and as a consequence the ellipse is very elongate. Any medium that exhibits circular birefringence will simultaneously show circular dichroism and the light will then not be plane polarized, but the effect is only apparent in the immediate vicinity of an absorption band. The variation of rotation and ellipticity in the neighbourhood of an absorption band has been called the *Cotton effect*.

Several physical theories have been developed which attempt quantitatively, to relate molecular structure to optical rotatory power, examples are those based on classical mechanics by Drude¹⁹, Born^{20,21} and Kuhn^{7,22,23}, and based on quantum-mechanical treatment of dispersion by Rosenfeld²⁴. Further theories employing quantum-mechanical considerations have been put forward by Kirkwood²⁵, Condon, Altar, Eyring^{26,27} and by Moffitt and Moscovitz²⁸⁻³⁰. A clear account of some of the theories of optical rotatory power has been given by Schellman³¹.

The system of nomenclature used in this context by organic chemists is outlined in Fig. 1^{32,33}. It is somewhat different from that used by physical chemists^{5,34}. The term *plain* curve is used if the curve shows no maximum, (peak), or minimum, (trough), directly related to a Cotton effect. They are

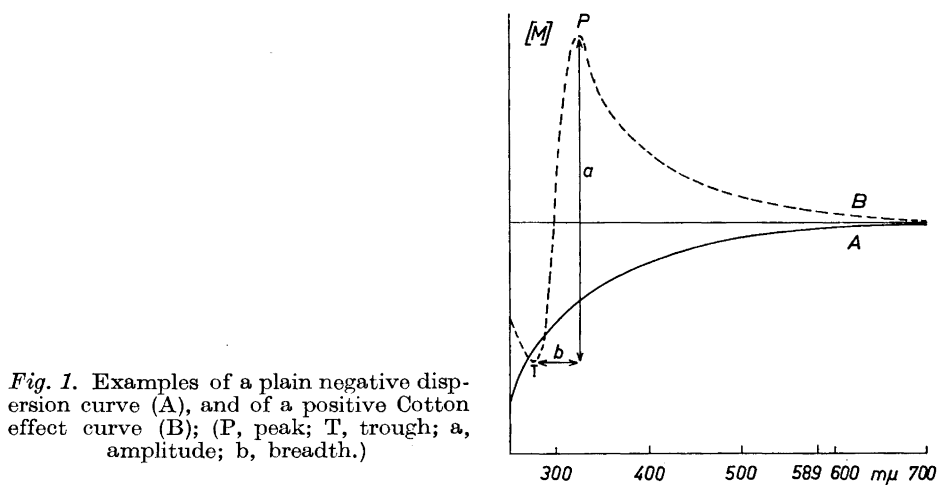


Fig. 1. Examples of a plain negative dispersion curve (A), and of a positive Cotton effect curve (B); (P, peak; T, trough; a, amplitude; b, breadth.)

called *positive* or *negative* respectively if they rise or fall towards shorter wavelengths. Other types of curves are called *anomalous* and in Fig. 1, this type is represented by a *positive single Cotton effect* curve. The Cotton effect is *positive* if the peak occurs at a longer wavelength than the corresponding absorption maximum, and the trough at a shorter wavelength.

The variation of the partial specific rotation $[\alpha]_{\text{px}}$ with wavelength outside the range of optically active absorption, can be expressed according to Drude¹⁹

$$[\alpha]_{\text{px}} = \frac{A_x}{\lambda^2 - \lambda_x^2} \quad (2)$$

where A_x is a molecular parameter, and λ_x is the centre of the single optically active absorption band. If more than one absorption band contributes to the rotation within the given spectral range, the general Drude equation¹⁹ must be used:

$$[\alpha] = \sum \frac{A_i}{\lambda^2 - \lambda_i^2} \quad (3)$$

A numerical evaluation of the unknown constants in eqn. 3 is extremely time-consuming even for its abbreviated forms³⁵.

The optical rotatory dispersion work performed recently by organic chemists has mainly been concerned with anomalous dispersion curves, and rotations have been measured in the regions of maximum absorption for the low intensity bands of, for example, ketones and aldehydes. With these compounds it is often unnecessary to calculate λ_i in the Drude equation because comparison of the rotatory dispersion curve and the electronic absorption spectrum of the substances, directly gives λ_i . It has been clearly shown that the sign, shape, and amplitude of these anomalous dispersion curves can be correlated empirically to certain structural and steric features of the compounds¹⁶⁻¹⁸. Only when more information is sought about the quantitative contributions of the

various optically active chromophores must the molecular parameters A_i , (which are related to the rotational strength³⁰), be calculated.

The present paper deals with the optical rotatory dispersion of some carboxylic acids. As the carboxyl group absorbs in a region which is at present inaccessible for rotatory dispersion measurements, it was expected that only the plain part of the curves could be experimentally determined. With the compounds investigated by Djerassi¹⁶⁻¹⁸ the useful information had been obtained mainly from the anomalous part of the dispersion curves. Thus two different problems arose: (a), What information can be obtained from plain dispersion curves, and (b), how can compounds with plain curves be transformed into derivatives possessing anomalous dispersion curves. Both problems are being investigated and some aspects of the second one have already been published³⁶; further studies will follow. The first problem will now be discussed in more detail.

GENERAL EXPERIMENTAL PROCEDURE

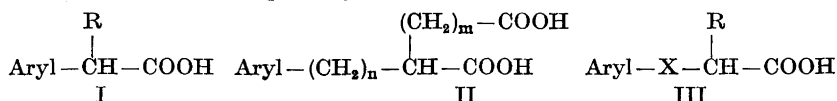
The optical rotatory dispersion curves in this paper have been obtained with a Rudolph photoelectric spectropolarimeter with the exception of a few cases (the measurements were made at Wayne State University, Detroit, Michigan, USA). A detailed description of the instrument as well of its operation, scope and limitations has been given elsewhere³⁷, and so will only be briefly mentioned here. The spectropolarimeter unit consisted of a light source, monochromator, polarimeter with photomultiplier tube, and photometer. The light source was a glass-jacketed concentrated-arc zirconium lamp in the spectral region 700–320 $m\mu$. For shorter wavelengths a quartz-jacketed xenon high pressure arc lamp was used. The monochromatic light was produced by means of a Beckman DU quartz monochromator. Readings were taken by the method of symmetrical angles^{37,38}, and the polarimeter equipped with a polarizer drive which automatically changed a chosen symmetrical angle from positive to negative to positive at four seconds periods. One photomultiplier tube was used over the spectral range covered.

The polarimeter tubes were of the centre-filling type with permanently fastened fused silica end windows. The length of the tubes was either 10 cm or 5 cm and the capacity 1.9 ml. The substance to be investigated, 1–4 mg, was weighed out in a 2.00 ml volumetric flask on a microbalance. Solutions were made up in spectro grade solvents, most measurements being made in methanol. Readings were usually performed at 700, 650, 589, 550, 525, 400–330 $m\mu$ at 10 $m\mu$ intervals, and below 330 $m\mu$ at 5 $m\mu$ intervals. Blank readings using pure solvent were taken daily. Temperatures were recorded (see experimental) for each run, but no special temperature control was used. The temperature fluctuations were those encountered in the isolated room employed only for polarimetric studies. The errors inherent in the present rotatory dispersion measurements are of such an order of magnitude, that ordinary variations of the room temperature are not significant.

The maximum error in the readings was of the order of $\pm 0.02^\circ$ which, for a concentration $c = 0.2$ g/100 ml, is equivalent to a specific rotation of $\pm 10^\circ$ (10 cm tube). This error could have been substantially decreased in the visible region by using a much higher concentration, but for the measurements at shorter wavelengths a concentration $c = 0.2$ g/100 ml, or even less, had to be used due to the increased absorption both by the optical system and the compounds. For the purpose of the present investigation, information about the dispersion curves in the ultraviolet region is more important than in the visible.

RESULTS AND DISCUSSION

A great number of optically active carboxylic acids of the following types,



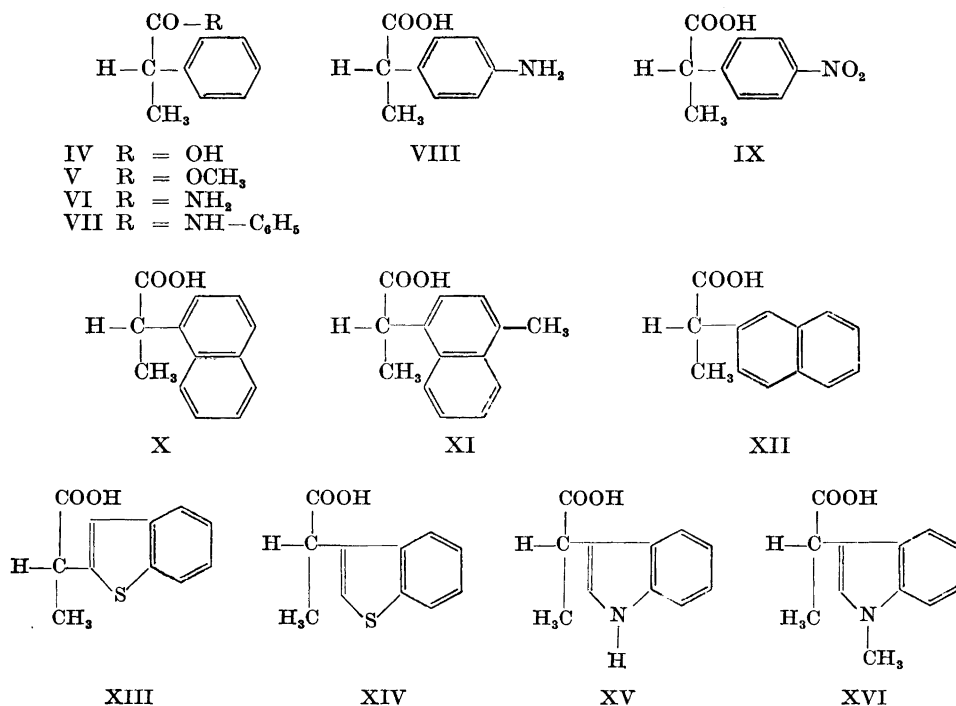
where X is CH₃, NH, O, S or Se, have previously been made in Uppsala ³⁹⁻⁴². The steric relationships have been established, usually by means of the Fredga quasi-racemate method ^{43,44}. The optical rotatory dispersion of some series of these compounds has now been studied to see if the relative configurations of compounds in special series could be derived from the dispersion curves. The investigations on compounds related to type III will be discussed in a separate paper ⁴⁵. Information about the position of the optically active absorption bands can be obtained from the Drude equation. However, it was thought likely that the same type of empirical approach as has been used by Djerassi ¹⁶⁻¹⁸ would be more successful, with a large number of compounds, than using a detailed analysis of the Drude equation. All the investigated compounds have only one asymmetric centre, and the problem of determining the configuration is thus simplified in distinguishing between the two possibilities. When the region of the Cotton effect can not be quite reached, it is of course not possible to observe all the features — sign, shape and amplitude — which have been used in the correlation of optical rotatory dispersion and molecular structure. Nevertheless, it seemed likely that for the simple compounds of types I—III, dispersion curves and configuration could be correlated if measurements were made close to the first anisotropic absorption band.

α -Aryl monocarboxylic acids and derivatives

The compounds in this series can all be derived from type I, and they may be divided into three sections. In the first, the alkyl group is methyl and the aryl group varies. Most of the dispersion curves have been produced on the D-enantiomers, and even when the actual measurements in some cases were made on the L-forms, the curves throughout this paper will refer to compounds of D-configuration.

According to the Kuhn-Freudenberg theory ^{1,6} each group attached to the asymmetric centre contributes to the total rotation in two ways — (a), by its own rotatory contribution and (b), by its vicinal action on the other substituents. Weak absorption bands located in the near ultraviolet region often furnish strong partial rotations. The rotation in the visible region will be particularly influenced by these absorption bands due to their proximity. The rotatory contribution from absorption bands in the far ultraviolet will not be so apparent in the visible wavelength range, even if these absorption bands have high anisotropy factors.

The compounds of type I have their aromatic nuclei directly attached to the asymmetric centre. The first absorption in the region 270 to 230 m μ will come from the aromatic group, and if any of these benzenoid absorption bands are anisotropic, the aromatic group will be dominant for the rotation in the visible and near ultraviolet region. Investigations by Kuhn and Biller ¹² clearly showed that the phenyl group is highly anisotropic in mandelic acid, atrolactic acid, and some derivatives of these acids, while the anisotropy of the phenyl bands was shown to be very small for phenyl substituted carbinols and halides ^{12,46}. Rothen and Levene ⁴⁷ studied the optical rotatory dispersion of some phenyl substituted carboxylic acids, and they found no anomaly in the 250 m μ region. Numerical evaluation of the unknown constants in the Drude



equation indicated that the first optically active absorption band should be somewhere between 205 and 235 $m\mu$, and so these authors concluded that the phenyl absorption in the 250 $m\mu$ region is not anisotropic for phenyl substituted fatty acids.

The rotatory dispersion curve of hydratropic acid (IV) is found in Fig. 2. The rotation rapidly increases towards the region of phenyl absorption. In this way the dispersion curve of hydratropic acid resembles that of mandelic acid¹². Measurements with a recording Rudolph spectropolarimeter could be extended further into the ultraviolet region (dotted curve), and a peak was found in the experimental dispersion curve at about 270 $m\mu$. An anomalous dispersion curve was also obtained with a Perkin-Elmer spectropolarimeter³⁷. This anomaly, however, which was found close to the limiting range of the instruments may not be real. When the direct monochromatic light is almost completely absorbed a small fraction of scattered light of higher wavelengths will result in an effectively higher wavelength than that read on the monochromator. This circumstance may have caused the decreased rotation in the experimental curve below 270 $m\mu$. Even though Rothen and Levene explicitly stated that no anomaly had been found in the 250 $m\mu$ region, it can be seen from their own measurements that the rotation of (+)-ethylphenylacetic acid was considerably less at 241 $m\mu$ than at 275 $m\mu$ (Ref.⁴⁶, Table II), *i.e.* the dispersion curve must have had a peak between 275 and 241 $m\mu$.

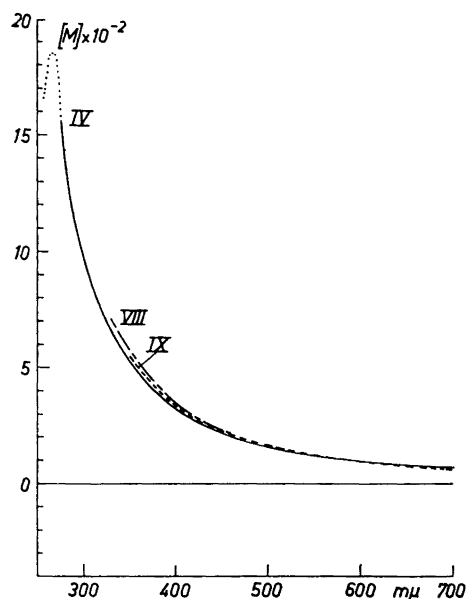


Fig. 2. Optical rotatory dispersion curves of (+)-hydratropic acid (IV), (+)-*p*-amino-hydratropic acid (VIII) and (+)-*p*-nitro-hydratropic acid (IX).

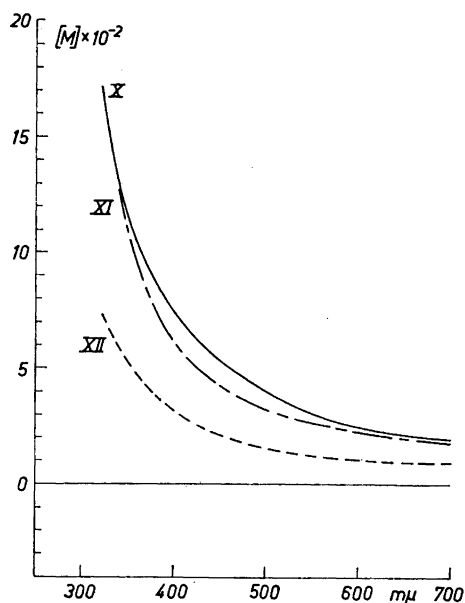


Fig. 3. Optical rotatory dispersion curves of (+)- α -(1-naphthyl)-propionic acid (X), (+)- α -(4-methyl-1-naphthyl)-propionic acid (XI) and (+)- α -(2-naphthyl)-propionic acid (XII).

The present author finds it likely that the phenyl absorption in the 250 $m\mu$ region is anisotropic and that the anisotropy factor of this absorption band has the same sign as that of the absorption at about 200 $m\mu$, which may be the second absorption region of the phenyl group, or the first absorption region of the carboxyl group. The values of λ_1 , found by Rothen and Levene may be unreliable. Heller³⁵ pointed out that it is easy to have a fortuitous agreement between calculated and observed $[\alpha]$ -values, and therefore unreliable constants in the two-term Drude equation. It is particularly difficult to calculate the constants, when two absorption bands with the same sign for the anisotropy factors are close together.

For the purpose of the present investigation it is not absolutely necessary to know if a certain absorption band is anisotropic, but it is important that the analogous compounds to be compared have similar groups which are dominant in the rotation. A certain group, for example an aromatic one, may have anisotropic bands or it may have strong vicinal action on the other groups.

The effects on the rotatory power of substitution in different aromatic systems have been studied by several investigators, by Betti⁴⁸, Nerdel *et al.*^{49,50} and Singh *et al.*^{51,52}. The optical rotatory dispersions of hydratropic acid (IV), *p*-aminohydratropic acid (VIII) and *p*-nitrohydratropic acid (IX) have previously been investigated by Nerdel and Würgau⁵³ in the visible region,

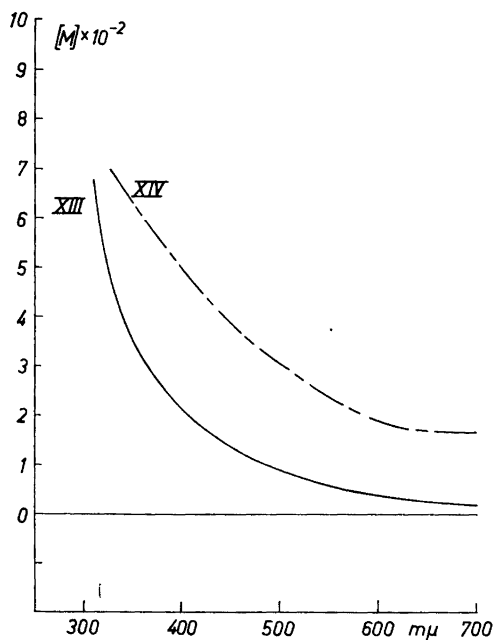


Fig. 4. Optical rotatory dispersion curves of (+)- α -(2-thianaphthenyl)-propionic acid (XIII) and (+)- α -(3-thianaphthenyl)-propionic acid (XIV).

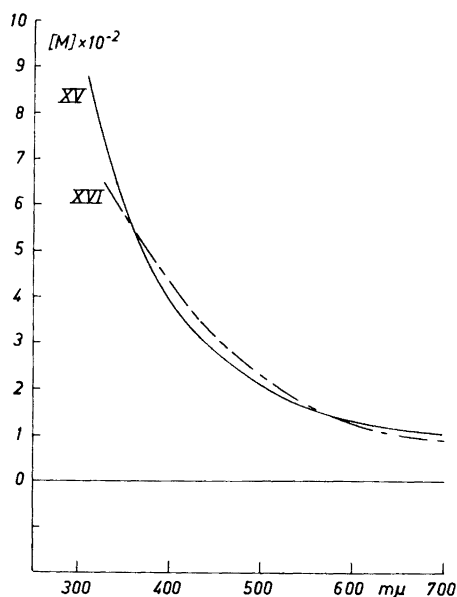


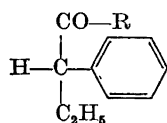
Fig. 5. Optical rotatory dispersion curves of (+)- α -(3-indolyl)-propionic acid (XV) and (+)- α -(1-methyl-3-indolyl)-propionic acid (XVI).

and now repeated and extended to the ultraviolet region, by the author. The curves are found in Fig. 2.

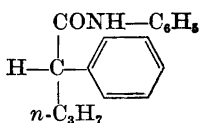
Introduction of an amino or a nitro group alters the benzenoid absorption bands considerably. The principal peak is displaced about 25 $m\mu$ towards longer wavelengths, and the intensity of this band is greatly increased⁵⁴. Hydratropic acid *p*-aminohydratropic acids have almost the same molecular rotation in ethanol at the D-line, while that of *p*-nitrohydratropic acid is somewhat lower⁵⁵. The dispersion curves are similar for the three acids; the amino and the nitro compounds having slightly higher molecular rotations towards shorter wavelengths. The dispersion curves of *p*-chlorohydratropic acid and *p*-hydroxyhydratropic acid seem also to be positive for the D-forms⁵³.

The dispersion curves of (+)- α -(1-naphthyl)-propionic acid (X), (+)- α -(4-methyl-1-naphthyl)-propionic acid (XI) and (+)- α -(2-naphthyl)-propionic acid (XII) are found in Fig. 3. The three curves are similar and correspond well with the dispersion curve of hydratropic acid. Other aromatic systems which have been studied are the thianaphthenyl and the indolyl (Figs. 4 and 5). Phenyl, naphthyl, thianaphthenyl and indolyl groups apparently have similar influences on the rotation with this type of compound.

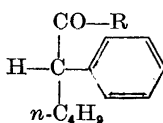
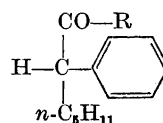
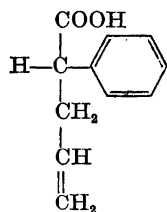
The second series derived from type I has been obtained by keeping the aryl group constant and varying the alkyl group. The following compounds have been investigated:



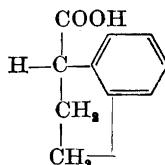
XVII R = OH

XVIII R = NH₂XIX R = NH-C₆H₅

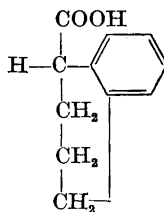
XX

XXI R = NH₂XXII R = NH-C₆H₅XXIII R = NH₂XXIV R = NH-C₆H₅

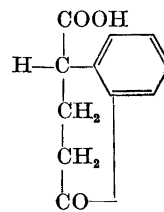
XXV



XXVI



XXVII



XXVIII

The configurational relationship between hydratropic acid (IV) and ethylphenylacetic acid (XVII) has been established by Levene *et al.* from optical rotatory measurements at the D-line⁵⁶, and also from rotatory dispersion measurements⁴⁷. Pettersson^{57,58} related the compounds XVII–XXIV by applying the quasi-racemate method to the amides. The relationship between hydratropic acid and glyceraldehyde has been established in several ways^{41,55,59} (for references to earlier work see Ref.⁵⁵). The configuration of allylphenylacetic acid (XXV) was established by Fredga and Westman⁶⁰.

The dispersion curves of (+)-ethylphenylacetic acid (XVII) and (+)-allylphenylacetic acid (XXV) are given in Fig. 6. These curves, are plain positive, and correspond well with the dispersion curve of hydratropic acid (Fig. 2). Changing the alkyl group from methyl to ethyl or allyl does not appreciably alter the rotatory dispersion of the acids in this series.

Fredga⁶¹ investigated 1-indanecarboxylic acid and proved that the (–)-form belongs to the D-series. It was concluded from the higher auxin activity that (–)-1-indanecarboxylic acid (XXVI) and (–)-1,2,3,4-tetrahydro-1-naphthoic acid (XXVII), (which also shows higher activity than its enantiomer⁶²), have the same configuration. More evidence was obtained from the similar shifts in rotation when the rotatory power of the acids was measured in different solvents⁶³. Levorotatory 1,2,3,4-tetrahydro-1-naphthoic acid was also shown to belong to the D-series by Westman⁶³, who synthesized it from (+)- α -phenylglutaric acid *cf.* formulas XXVII and XXXIX. The optical rotatory dispersion curves of (–)-1-indanecarboxylic acid and (–)-1,2,3,4-tetrahydro-1-naphthoic acid are to be found in Fig. 7; both curves being plain negative, and show the same order of rotation.

In the series of alkylphenylacetic acids, the compounds of D-configuration have plain positive dispersion curves in the region 700–275 m μ with high rotation at lower wavelengths. However, when the acids have the alkyl

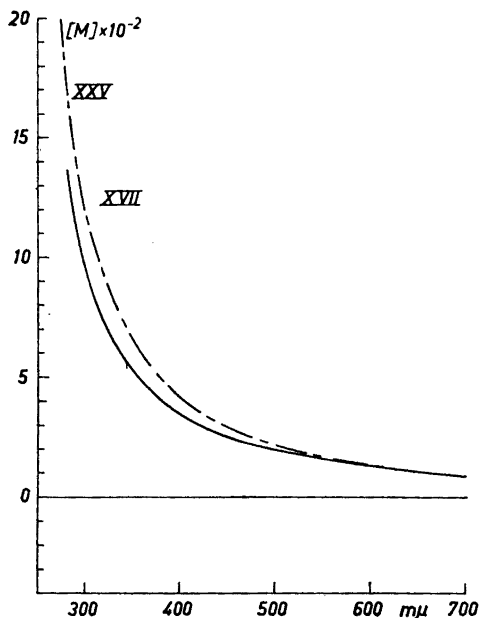


Fig. 6. Optical rotatory dispersion curves of (+)-ethylphenylacetic acid (XVII) and (+)-allylphenylacetic acid (XXV).

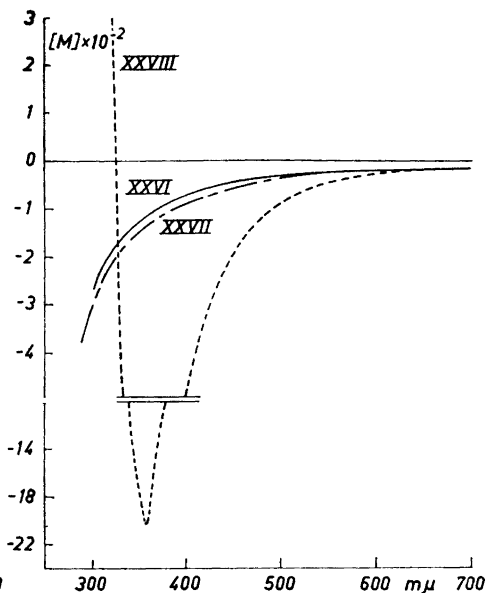
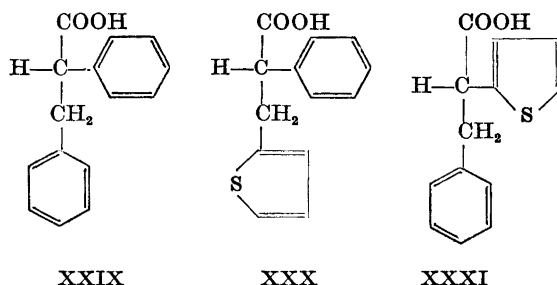


Fig. 7. Optical rotatory dispersion curves of (-)-1-indanecarboxylic acid (XXVI), (-)-1,2,3,4-tetrahydro-1-naphthoic acid (XXVII) and (-)-4-keto-1,2,3,4-tetrahydro-1-naphthoic acid (XXVIII).

group ring closed to the *ortho* position, so as to form a five or six membered ring, the D-compounds have plain negative dispersion curves of comparatively low rotation in the same wavelength region. The "ring closed forms" have only been investigated in two cases in this series; it is unlikely that the same relation between configuration and sign of the dispersion curve will be found for compounds with small, medium and large rings. Parallels to these "open and closed forms" have also been studied for phenoxy acids and phenylthio acids⁴⁵.

The third section of compounds derived from type I has been obtained by varying both the aryl and alkyl groups. The diarylpropionic acids, previously studied by Pettersson⁶⁴⁻⁶⁶, belong to this group. The optical rotatory dispersion curves of three of the acids (XXIX-XXXI) have been investigated. The curves of benzylphenylacetic acid (XXIX) and of 2-thenylphenylacetic acid (XXX) are almost identical throughout the investigated wavelength region, while benzyl-2-thienylacetic acid (XXXI), which has a thiophene nucleus attached to the asymmetric carbon instead of a benzene nucleus, has a lower rotation in the visible region, and a somewhat steeper curve below 300 $m\mu$ (Fig. 8).

Analogous benzene and thiophene compounds are closely similar in many respects⁴², and so it was expected that the three compounds XXIX-XXXI



of the same configuration should have the same type of dispersion curves. The first series of ultraviolet absorption bands of thiophene is displaced by about $20\text{ m}\mu$ towards shorter wavelengths compared to benzene⁶⁷. Pettersson⁴⁰ investigated the optical rotation at the D-line of some 2-thienyl substituted acids; he pointed out that it was not possible to decide from these measurements if the lower rotation of the 2-thienyl compounds compared to the phenyl analogs depends on the shorter wavelength of absorption, or on a lower anisotropy of the band. The greater steepness of the dispersion curve of benzyl-2-thienylacetic acid at lower wavelengths compared to the curve of benzylphenylacetic acid, suggests instead a higher anisotropy of the 2-thienyl absorption

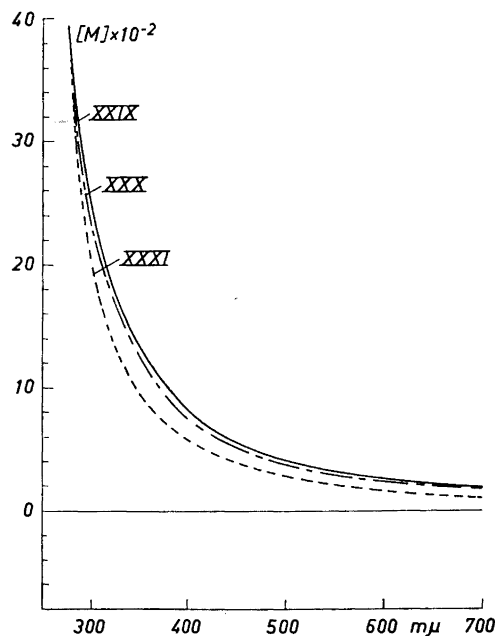


Fig. 8. Optical rotatory dispersion curves of (+)-benzylphenylacetic acid (XXIX), (+)-2-thienylphenylacetic acid (XXX) and (+)-benzyl-2-thienylacetic acid (XXXI).

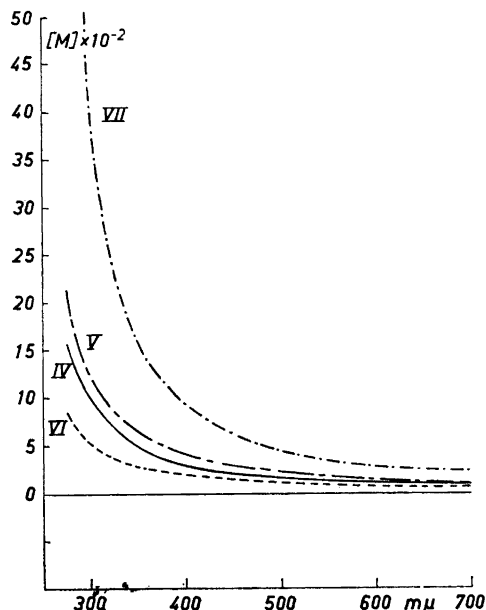


Fig. 9. Optical rotatory dispersion curves of (+)-hydratropic acid (IV), (+)-methyl hydratropate (V), (+)-hydratropamide (VI) and (+)-hydratropanilide (VII).

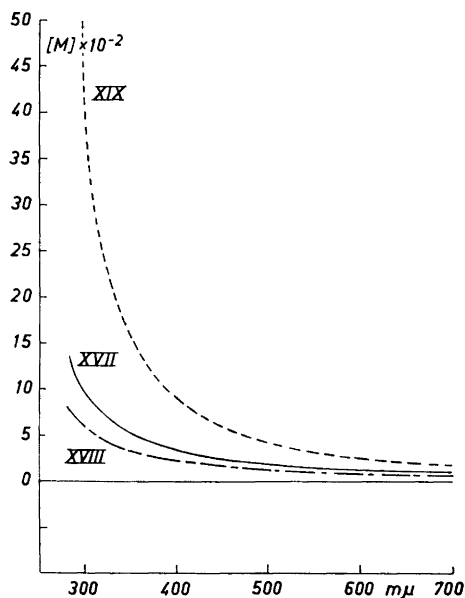


Fig. 10. Optical rotatory dispersion curves of (+)-ethylphenylacetic acid (XVII), (+)-ethylphenylacetamide (XVIII) and (+)-ethylphenylacetanilide (XIX).

band, and the lower rotation in the visible region should be due to the shorter wavelength of absorption. Definite answers regarding the anisotropy of an absorption band can only be obtained from careful calculation of the rotational strength³⁰, or experimentally from measurements of the circular dichroism^{5,7}.

The displacement rule

Optical rotation data from the sodium D-line has often been used for correlation of configurations within series of similar compounds; (for reviews see Mills and Klyne², and Klyne⁶⁸). This approach is based on the application of different rules, for instance the *rule of optical superposition* and the *distance rule*. Another qualitative rule which has been more generally used is *Freudenberg's displacement rule*¹¹, which can be formulated: "If two similar asymmetric molecules A and B are altered in the same way to give A' and B', then the differences in molecular rotation (A'—A) and (B'—B) are of the same sign"⁶⁸. The displacement rule follows from Kuhn's *vicinal rule*⁶ which says that when a small change is made in one of the groups attached to the asymmetric centre, the anisotropy of this group suffers the most change, while the vicinal action is less affected.

The displacement rule is best used when the shifts are large. As the rotational shifts at the sodium D-line for a given structural change are nearly

always less than in the ultraviolet region, it is better to apply Freudenberg's displacement rule on data obtained as far into the ultraviolet region as possible, but without losing accuracy in the measurements. Series of similar carboxylic acids are usually converted to esters, amides or anilides, and the shifts compared. The dispersion curves of hydratropic acid (IV), its methyl ester (V), amide (VI) and anilide (VII), are compared in Fig. 9, and those of ethylphenylacetic acid (XVII), its amide (XVIII) and anilide (XIX) are given in Fig. 10. The rotations of the amides at the D-line are slightly lower than those of the corresponding acids, while the rotations of the anilides are higher; the differences in molecular rotation are enhanced in the ultraviolet region. The calculated shifts for methylphenylacetic acid (hydratropic acid) and ethylphenylacetic acid at 589 $m\mu$ (sodium D-line) and 290 $m\mu$, are found in Table 1.

Table 1. Molecular rotational shifts for methylphenylacetic acid and ethylphenylacetic acid; Δ_1 for (amide-acid); Δ_2 for (anilide-acid).

Acid	589 $m\mu$		290 $m\mu$	
	Δ_1	Δ_2	Δ_1	Δ_2
Methylphenylacetic	- 30°	+ 190°	- 480°	+ 4 880°
Ethylphenylacetic	- 30°	+ 160°	- 450°	+ 4 660°

Just as the optical rotatory dispersion curves for a series of acids were compared above, the curves for (+)-methylphenylacetamide (VI), (+)-*n*-butylphenylacetamide (XXI) and for (+)-*n*-amylphenylacetamide (XXIII) are compared in Fig. 11. In Fig. 12 are the curves of (+)-*n*-propylphenylacetanilide (XX), (+)-*n*-butylphenylacetanilide (XXII) and (+)-*n*-amylphenylacetanilide (XXIV). The three amides in Fig. 11, have all plain positive dispersion curves with comparatively low rotations even in the ultraviolet region, while the anilides have very high rotations at lower wavelengths.

From the examples discussed above it can be concluded, that the configurational relationships between different members in the series of alkylphenylacetic acids can be obtained with certainty, directly from the rotatory dispersion curves of the acids, as well as from the dispersion curves of the anilides. The amides are not very suitable for comparison due to the lower rotation throughout the investigated wavelength region.

Solvent effects. The influences of external conditions, such as solvent, temperature and concentration, on optical activity has been observed, and its importance recognized, ever since Biot's early investigations on tartaric acid ^{69,70}. These factors produce complicated results since both chemical and physical changes may occur from the alteration in external conditions ⁷¹. It is quite obvious that the rotatory power will usually be greatly affected by changes in solvent or temperature, if the solute constitutes an equilibrium mixture of two or more distinct molecular species. The optical rotation is also very sensitive to conformational changes, and inversion of the Cotton effect has been observed ⁷² on altering the polarity of the solvent. The dipole-dipole interaction between solvent and solute will not only influence the conformation of

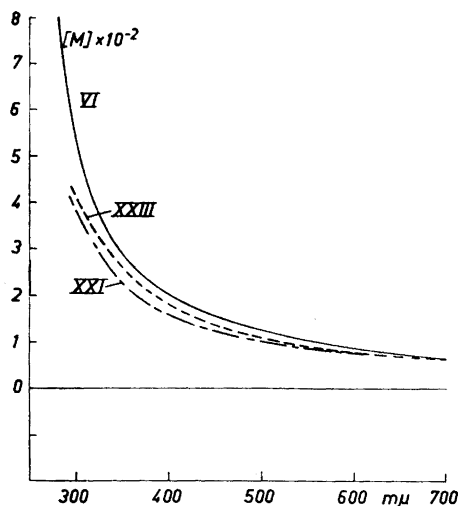


Fig. 11. Optical rotatory dispersion curves of (+)-methylphenylacetamide (VI), (+)-*n*-butylphenylacetamide (XXI) and (+)-*n*-amyphenylacetamide (XXIII).

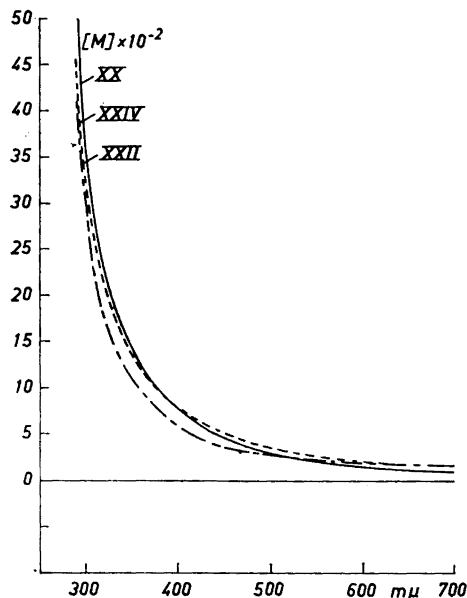


Fig. 12. Optical rotatory dispersion curves of (+)-*n*-propylphenylacetanilide (XX), (+)-*n*-butylphenylacetanilide (XXII) and (+)-*n*-amyphenylacetanilide (XXIV).

the molecules, but will also affect the local field, and in that way exert direct vicinal action on the chromophores of the optically active compounds. Furthermore, if strong bonds are formed between solvent and solute, the chromophores of the optically active molecule will change; sometimes even the solvent molecules can act as chromophoric groups.

Solvent influence on the rotation in the visible region was extensively studied by Pickard and Kenyon⁷³ and by Rule *et al.*^{74,75} The solvent effect is especially noticeable in rotatory dispersion work^{76,77}, and thus when the dispersion curves of different compounds are compared, they should be made with the same solvent and at about the same concentration and temperature. Nevertheless, the solvent effect can be utilized, and comparison of the effect on similar compounds may give information regarding their steric relationship. Such investigations at the sodium D-line have been made on several compounds^{39-41,78}. These studies of the rotational shifts can be considered as a special way of applying Freudenberg's displacement rule, and from the discussion above it is evident that information which is more reliable will be obtained if the rotatory dispersion curves are studied in different solvents, and not only the rotational shifts at the D-line in this way.

Pettersson⁴⁰ investigated the solvent effect on several α -arylcarboxylic acids at the D-line. Large negative shifts were observed for compounds of D-configuration when the rotation was measured in dilute sodium hydroxide solution. The rotatory dispersion curves in sodium hydroxide solution of some

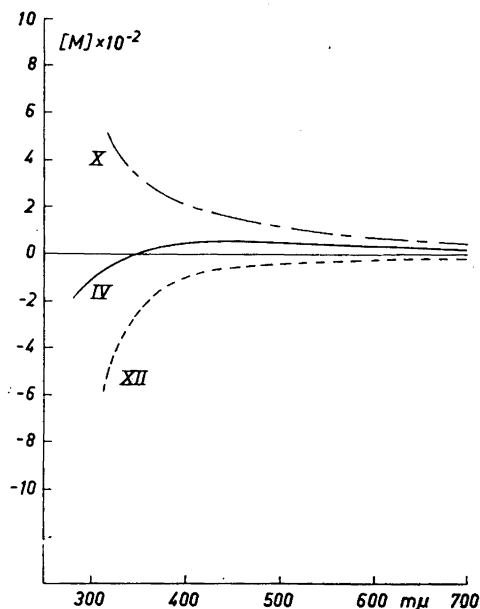


Fig. 13. Optical rotatory dispersion curves in 0.1 N sodium hydroxide of (+)-hydratropic acid (IV), (+)- α -(1-naphthyl)-propionic acid (X) and (+)- α -(2-naphthyl)-propionic acid (XII).

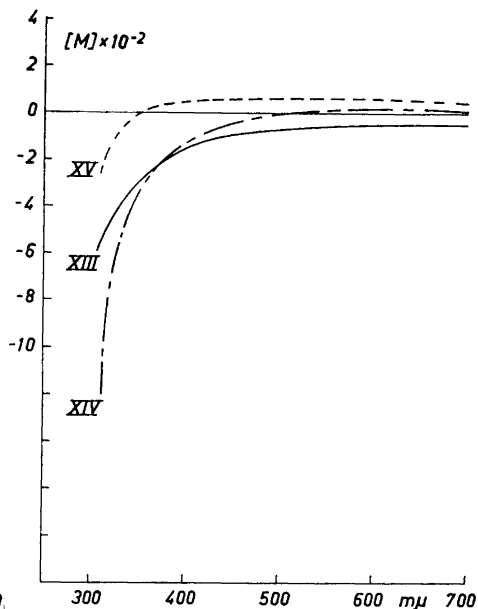


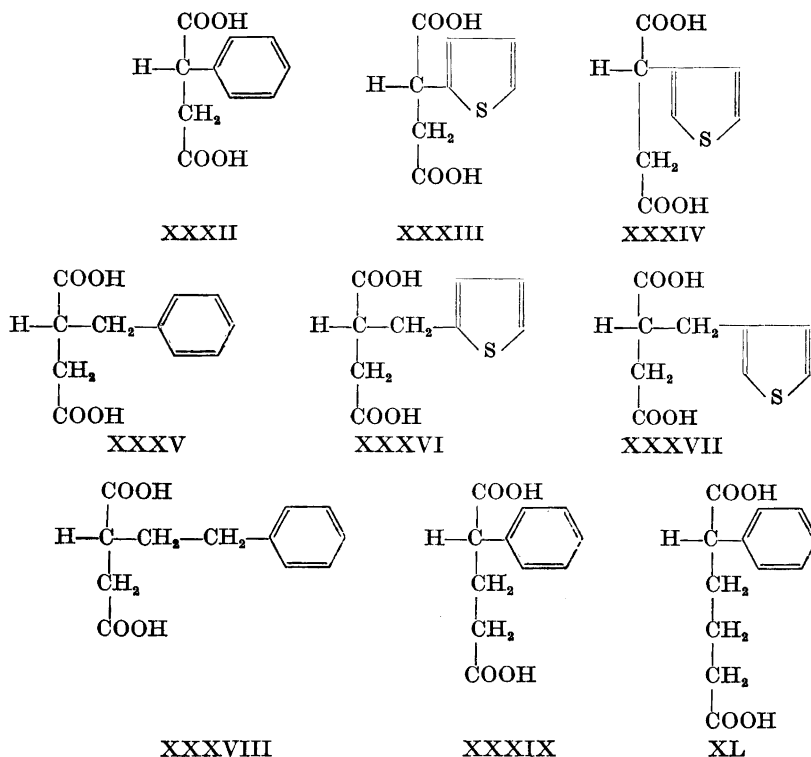
Fig. 14. Optical rotatory dispersion curves in 0.1 N sodium hydroxide of (+)- α -(2-thianaphthenyl)-propionic acid (XIII), (+)- α -(3-thianaphthenyl)-propionic acid (XIV), and (+)- α -(3-indolyl)-propionic acid (XV).

of these acids are given in Figs. 13 and 14. It can be seen that the negative shifts are very prominent in the ultraviolet region, and for all the compounds, except α -(1-naphthyl)-propionic acid (X), even the sign of the dispersion curves is reversed compared to that in methanol.

Aryl dicarboxylic acids

Oxidative degradation of natural products often yields alkyl substituted dicarboxylic acids; for example alkylsuccinic and alkylglutaric acids have been key substances in stereochemical studies on terpenes. Alkylsuccinic acids have also proved to be valuable substances in connecting aromatic compounds to the steric system of glyceraldehyde. Analogous benzene and thiophene derivatives can often be sterically related by the quasi-racemate method, and the thiophene compounds desulphurized with Raney nickel to the corresponding aliphatic compounds without racemisation ⁷⁹.

In order to see if the steric relationships between different dicarboxylic acids could be found directly from their optical rotatory dispersion curves, an investigation of a large number of dicarboxylic acids was undertaken. The results on the alkylsubstituted acids will be published in a separate paper ⁸⁰, and only the acids which are derived from type II will be discussed here.



The configurations of these acids have previously been determined and the dextrorotatory compounds all belong to the D-series, (references are given below). The optical rotatory dispersion curves of (+)-phenylsuccinic acid (XXXII)⁸¹, (+)-2-thienylsuccinic acid (XXXIII)⁸² and (+)-3-thienylsuccinic acid (XXXIV)⁸³ are shown in Fig. 15. The dispersion curves are very similar for all these compounds being plain and positive with high rotation at lower wavelengths. It is interesting to compare the dispersion curve of phenylsuccinic acid to that of hydratropic acid (Fig. 2). Substitution of a hydrogen atom in the methyl group of hydratropic acid with a carboxyl group, gives phenylsuccinic acid. It can be seen that such a substitution does not change the main character of the curve, but only causes a higher rotation. The higher rotation may either be due to the vicinal action of the carboxymethyl group on the phenyl and carboxyl groups attached to the asymmetric centre, or (and) to a positive rotatory contribution from the carboxymethyl group. It has been shown by Levene and Rothen^{47,48} that a carboxymethyl group has an opposite sign for its rotatory contribution to that of a carboxyl group in some series of compounds. For example, α -phenylpropionic acid, (hydratropic acid), of D-configuration is dextrorotatory, while β -phenylbutyric acid is levorotatory. Similarly a change in sign due to the partial rotation of the carboxyl group occurs when going from α -methylbutyric acid to β -methylvaleric acid. The

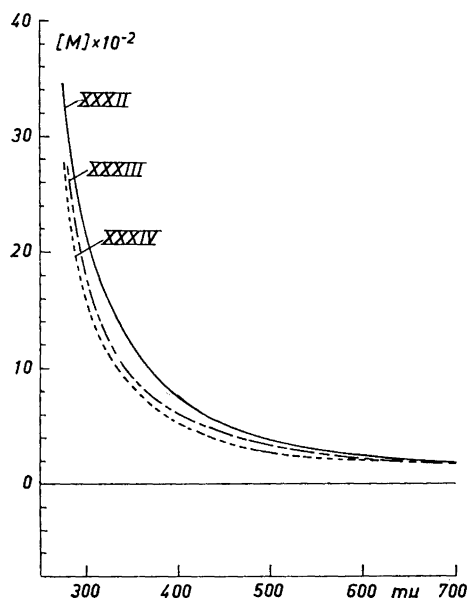


Fig. 15. Optical rotatory dispersion curves of (+)-phenylsuccinic acid (XXXII), (+)-2-thienylsuccinic acid (XXXIII) and (+)-3-thienylsuccinic acid (XXXIV).

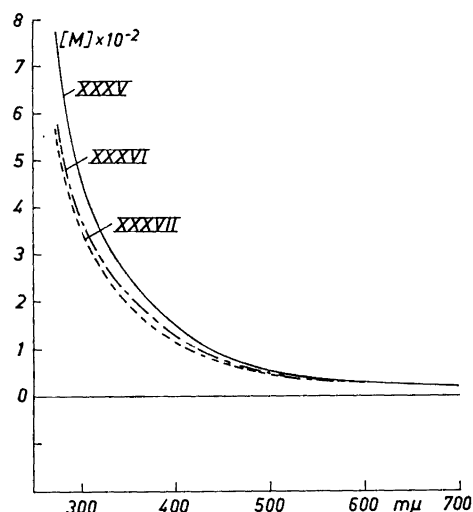


Fig. 16. Optical rotatory dispersion curves of (+)-benzylsuccinic acid (XXXV), (+)-2-thienylsuccinic acid (XXXVI) and (+)-3-thienylsuccinic acid (XXXVII).

reason that the same type of inversion is not found when going from hydrotropic acid to phenylsuccinic acid, must be connected with the mutual influence of a phenyl and a carboxyl group attached to the same asymmetric centre.

The variations in the rotatory dispersion curves of some compounds belonging to type II, when n increases from 0 to 1, can be seen from a comparison of Figs. 15 and 16. Benzylsuccinic acid (XXXV)⁷⁹, 2-thienylsuccinic acid (XXXVI)⁷⁹, and 3-thienylsuccinic acid (XXXVII)⁸⁵ of D-configuration have plain positive dispersion curves, but the rotation is considerably lower than for the corresponding compounds with the aryl group directly attached to the asymmetric centre.

According to the distance rule a smaller change in rotation will be expected when n increases from 1 to 2 compared to that for an increase of n from 0 to 1. That this is so can be seen from Fig. 17, where the dispersion curves of (+)-phenylsuccinic acid (XXXII), (+)-benzylsuccinic acid (XXXV) and (+)-phenylethylsuccinic acid (XXXVIII)⁸⁶ are reproduced.

The influence on the rotatory dispersion curves of compounds belonging to type II, when n is kept constant ($n = 0$) and m is varied from 1 to 3, has been studied on the series (+)-phenylsuccinic acid (XXXII), (+)- α -phenylglutaric acid (XXXIX)⁸⁷ and (+)- α -phenyladipic acid (XL)⁸⁸. The dispersion curves for these compounds, all of D-configuration, are found in Fig. 18;

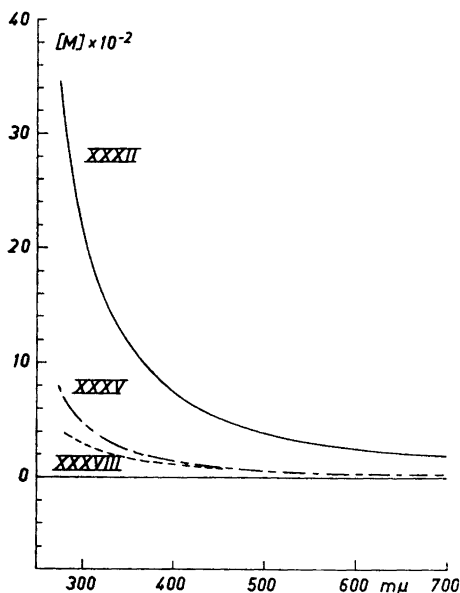


Fig. 17. Optical rotatory dispersion curves of (+)-phenylsuccinic acid (XXXII), (+)-benzylsuccinic acid (XXXV) and (+)-phenylethylsuccinic acid (XXXVIII).

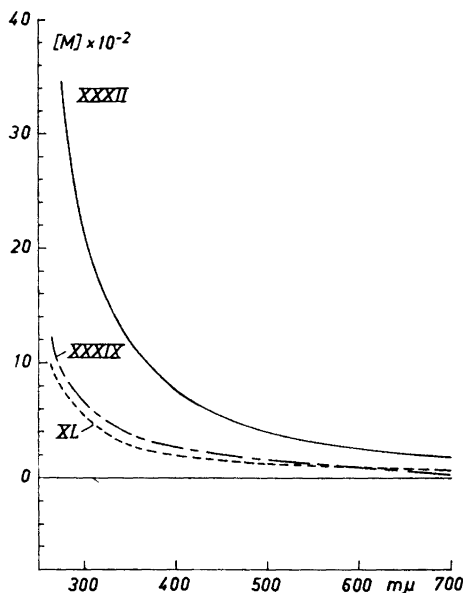


Fig. 18. Optical rotatory dispersion curves of (+)-phenylsuccinic acid (XXXII), (+)- α -phenylglutaric acid (XXXIX) and (+)- α -phenyladipic acid (XL).

the curves are all plain and positive. In the series of alkyl dicarboxylic acids the D-alkylsuccinic acids are dextrorotatory with plain positive dispersion curves, while D- α -alkylglutaric acids are levorotatory with plain negative dispersion curves⁸⁰.

In the present paper all dispersion curves refer to compounds of D-configuration. All the curves, except the three of the "ring closed" compounds XXVI, XXVII and XXVIII, are plain and positive in the investigated wavelength region. It may be fortuitous, of course, that such different compounds have the same type of rotatory dispersion curves for analogous configuration, but nevertheless, the relative configurations of compounds within some series of types I and II can be obtained with great certainty using these curves. In

R
|

the Aryl-CH-COOH series, where R is alkyl, an analogous configuration will give a similar dispersion curve if the aryl group is kept constant, and the alkyl group varies. If the alkyl is the same and the aryl group varies, the magnitude of the rotation may change considerably, but the dispersion curves are still of the same general type and especially sign. The last statement is probably not of unrestricted validity, as the aryl group has a dominant influence on the rotation, and very great variations in this group may be expected to reverse the sign of the dispersion curves. However, the following variations in the aryl group have not resulted in any major rotatory dispersion changes:

phenyl, *p*-aminophenyl, *p*-nitrophenyl, *p*-chlorophenyl, *p*-hydroxyphenyl, 1-naphthyl, 4-methyl-1-naphthyl, 2-naphthyl, 2-thianaphthenyl, 3-thianaphthenyl, 3-indolyl and 1-methyl-3-indolyl.



In the Aryl-(CH₂)_n-CH-COOH series, the relative configuration of compounds with different aryl groups can be obtained directly from the dispersion curves if *n* and *m* are kept constant, (*n* equal to 0). The aryl group can probably be varied in the same way as for compounds belonging to type I (see above). It may not always be safe to compare compounds belonging to the series with *m* = 1 to that with *m* = 2, even if phenylsuccinic and α -phenylglutaric acid of the same configuration have the same type of dispersion curves. However, a change of *m* from 2 to a higher integer will have a smaller influence on the rotation, and a comparison of different acids with *n* = 0, *m* = 2 with acids having *n* = 0, *m* = 3, 4 . . . is fairly sound. When *m* is constant (equal to 1), and *n* varies from 0 to 2, as with the investigated compounds phenylsuccinic, benzylsuccinic, phenylethylsuccinic acids, the dispersion curves are of the same type for analogous configuration. When *m* is greater than 1, these dicarboxylic acids are more similar to the series of α -alkyl- ω -phenylcarboxylic acids investigated by Levene and Rothen^{47,48}, which had an alternating change in the rotation at the D-line, but still had the same type of dispersion curves on movement of the phenyl group away from the asymmetric centre. The effect of separation distance of an aliphatic carbonyl function (ketone, aldehyde) on an asymmetric centre has been investigated by Djerassi and Geller⁸⁹, and they found that the sign of the Cotton effect curve is reversed when either one, or no carbon atoms are interposed.

The extensive investigations of the anomalous optical rotatory dispersion of ketones and aldehydes by Djerassi *et al.*¹⁶⁻¹⁸ have clearly shown the advantages of using dispersion curves instead of only sodium D-line rotations. Compounds, such as carboxylic acids, which have their ultraviolet absorption in a presently inaccessible region for rotatory dispersion measurements, give only plain dispersion curves, but nevertheless the configurational relationship between compounds belonging to certain series of simple compounds can be obtained directly from their dispersion curves. Occasionally the plain dispersion curves cross the zero rotation line somewhere below 589 m μ ^{18,45,47} and then configurational assignments based on a single measurement at the D-line may be impossible. The displacement rule applied using D-line rotations often gives valuable information about configurational relationships, but even when this rule is used it is more reliable to make a comparison of the dispersion curves of the different derivatives. Freudenberg and Biller⁹⁰ pointed out that when the displacement rule is used, the nature of the optical activity has to be considered. Comparisons should be made with great caution if the rotational shifts, when going from one derivative to another, are more dependent on changes in the vicinal action than on changes in the direct contribution from the altered group. For example the rotatory contribution of the phenyl group in the methyl ester of mandelic acid methyl ether is negative, but positive in the dimethylamide. On the other hand, the phenyl contribution is positive in

the corresponding derivatives of atrolactic acid (α -methylmandelic acid)^{12,90}. Similar changes in the rotatory contributions cannot be detected from measurements of only D-line rotations, but can at least qualitatively be observed directly in the optical rotatory dispersion curves.

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EXPERIMENTAL

The experimental results are recorded in the manner outlined in Ref. ³². If not otherwise stated the rotatory dispersion curves were taken in methanol. The samples were purified, usually by recrystallization, and the D-line rotations were checked to be in accordance with the literature values. As these measurements were taken in various solvents and at high concentrations, the rotations are not directly comparable with those obtained in the rotatory dispersion (R.D.) measurements, and the results are not reported. The molecular rotation values at the D-line and the previous configurational determinations can be found in the references given.

(+)-*Hydratropic acid (IV)* ⁵⁵ R.D. (Fig. 2) in methanol (c. 0.0905), temp. 29°: $[M]_{589} + 110^\circ$, $[M]_{400} + 320^\circ$, $[M]_{350} + 500^\circ$, $[M]_{300} + 960^\circ$, $[M]_{275} + 1560^\circ$.

R.D. (Fig. 13) in 0.1 N sodium hydroxide (c 0.100), temp. 27°: $[M]_{589} + 30^\circ$, $[M]_{400} + 40^\circ$, $[M]_{350} + 10^\circ$, $[M]_{300} - 100^\circ$, $[M]_{280} - 290^\circ$.

(+)-*Methyl hydratropate (V)* Prepared from (+)-hydratropic acid using diazomethane. R.D. (Fig. 9) in methanol (c 0.225), temp. 25°: $[M]_{589} + 170^\circ$, $[M]_{400} + 440^\circ$, $[M]_{350} + 650^\circ$, $[M]_{300} + 1200^\circ$, $[M]_{275} + 2120^\circ$.

(+)-*Hydratropamide (VI)* ⁵⁷ R.D. (Fig. 9) in methanol (c 0.120), temp. 27°: $[M]_{589} + 80^\circ$, $[M]_{400} + 200^\circ$, $[M]_{350} + 290^\circ$, $[M]_{300} + 530^\circ$, $[M]_{280} + 780^\circ$.

(+)-*Hydratropamide (VII)* ⁵⁷ R.D. (Fig. 9) in methanol (c 0.167), temp. 27°: $[M]_{589} + 300^\circ$, $[M]_{400} + 920^\circ$, $[M]_{350} + 1600^\circ$, $[M]_{300} + 4250^\circ$, $[M]_{290} + 5680^\circ$.

(+)-*p-Aminohydratropic acid (VIII)* ⁵⁵ R.D. (Fig. 2) in methanol (c 0.122), temp. 27°: $[M]_{589} + 110^\circ$, $[M]_{400} + 330^\circ$, $[M]_{350} + 540^\circ$, $[M]_{330} + 710^\circ$.

(+)-*p-Nitrohydratropic acid (IX)* ⁵⁵ R.D. (Fig. 2) in methanol (c 0.150), temp. 29°: $[M]_{589} + 130^\circ$, $[M]_{400} + 330^\circ$, $[M]_{390} + 340^\circ$.

(+)- α -(1-Naphthyl)-propionic acid (X) ⁹¹ R.D. (Fig. 3) in methanol (c 0.094), temp. 30°: $[M]_{589} + 260^\circ$, $[M]_{400} + 740^\circ$, $[M]_{350} + 1240^\circ$, $[M]_{320} + 1710^\circ$.

R.D. (Fig. 13) in 0.1 N sodium hydroxide (c 0.090) temp. 26°: $[M]_{589} + 60^\circ$, $[M]_{400} + 230^\circ$, $[M]_{350} + 360^\circ$, $[M]_{315} + 520^\circ$.

(+)- α -(4-Methyl-1-naphthyl)-propionic acid (XI) ⁹² R.D. (Fig. 3) in methanol (c 0.096), temp. 27°: $[M]_{589} + 210^\circ$, $[M]_{400} + 590^\circ$, $[M]_{350} + 1100^\circ$, $[M]_{340} + 1240^\circ$.

(+)- α -(2-Naphthyl)-propionic acid (XII) ⁹² R.D. (Fig. 3) in methanol (c 0.096), temp. 27°: $[M]_{589} + 110^\circ$, $[M]_{400} + 310^\circ$, $[M]_{350} + 510^\circ$, $[M]_{320} + 720^\circ$.

R.D. (Fig. 13) in 0.1 N sodium hydroxide (c 0.100), temp. 24°: $[M]_{589} - 30^\circ$, $[M]_{400} - 90^\circ$, $[M]_{350} - 260^\circ$, $[M]_{315} - 580^\circ$.

(+)- α -(2-Thianaphthenyl)-propionic acid (XIII) ⁹⁴ R.D. (Fig. 4) in methanol (c. 0.060), temp. 27°: $[M]_{589} + 40^\circ$, $[M]_{400} + 210^\circ$, $[M]_{350} + 340^\circ$, $[M]_{310} + 680^\circ$.

R.D. (Fig. 14) in 0.1 N sodium hydroxide (c 0.100), temp. 25°: $[M]_{589} - 60^\circ$, $[M]_{400} - 130^\circ$, $[M]_{350} - 330^\circ$, $[M]_{305} - 600^\circ$.

(+)- α -(3-Thianaphthenyl)-propionic acid (XIV) ⁹⁵ R.D. (Fig. 4) in methanol (c 0.092), temp. 28°: $[M]_{589} + 190^\circ$, $[M]_{400} + 480^\circ$, $[M]_{350} + 650^\circ$, $[M]_{320} + 710^\circ$.

R.D. (Fig. 14) in 0.1 N sodium hydroxide (c 0.105) temp. 25°: $[M]_{589} + 10^\circ$, $[M]_{400} - 80^\circ$, $[M]_{350} - 300^\circ$, $[M]_{310} - 1170^\circ$.

(+)- α -(3-Indolyl)-propionic acid (XV) ⁵⁶ R.D. (Fig. 5) in methanol (c 0.120), temp. 27°: [M]₅₈₉ + 130°, [M]₄₀₀ + 390°, [M]₃₅₀ + 600°, [M]₃₁₀ + 880°.

R.D. (Fig. 14) in 0.1 N sodium hydroxide (c 0.179), temp. 24°: [M]₅₈₉ + 50°, [M]₄₀₀ + 50°, [M]₃₅₀ - 10°, [M]₃₁₀ - 270°.

(+)- α -(1-Methyl-3-indolyl)-propionic acid (XVI) ^{57,58} R.D. (Fig. 5) in methanol (c 0.100), temp. 23°: [M]₅₈₉ + 140°, [M]₄₀₀ + 440°, [M]₃₅₀ + 580°, [M]₃₁₀ + 630°.

(+)-Ethylphenylacetic acid (XVII) ⁵⁷ R.D. (Fig. 6) in methanol (c 0.575), temp. 27°: [M]₅₈₉ + 130°, [M]₄₀₀ + 350°, [M]₃₅₀ + 530°, [M]₃₁₀ + 790°; (c 0.115): [M]₃₁₀ + 780°, [M]₃₀₀ + 970°, [M]₂₈₀ + 1 370°.

(+)-Ethylphenylacetamide (XVIII) ⁵⁷ R.D. (Fig. 10) in methanol (c 0.130), temp. 27°: [M]₅₈₉ + 100°, [M]₄₀₀ + 240°, [M]₃₅₀ + 330°, [M]₃₀₀ + 620°, [M]₂₈₀ + 810°.

(+)-Ethylphenylacetanilide (XIX) ⁵⁷ R.D. (Fig. 10) in methanol (c 0.170), temp. 27°: [M]₅₈₉ + 290°, [M]₄₀₀ + 890°, [M]₃₅₀ + 1 560°, [M]₃₀₀ + 4 170°, [M]₂₈₀ + 5 700°.

(+)-*n*-Propylphenylacetanilide (XX) ^{58,59} R.D. (Fig. 12) in methanol (c 0.140), temp. 27°: [M]₅₈₉ + 190°, [M]₄₀₀ + 780°, [M]₃₅₀ + 1 360°, [M]₃₀₀ + 3 010°; (c 0.028): [M]₃₀₀ + 3 100°, [M]₃₀₀ + 3 640°, [M]₂₉₀ + 5 200°.

(+)-*n*-Butylphenylacetamide (XXI) ^{58,59} R.D. (Fig. 11) in methanol (c 0.142), temp. 27°: [M]₅₈₉ + 80°, [M]₄₀₀ + 160°, [M]₃₅₀ + 200°, [M]₃₂₀ + 300°; (c 0.071): [M]₃₂₀ + 310°, [M]₃₀₀ + 380°, [M]₂₉₀ + 420°.

(+)-*n*-Butylphenylacetanilide (XXII) ^{58,59} (Fig. 12) in methanol (c 0.115), temp. 27°: [M]₅₈₉ + 220°, [M]₄₀₀ + 600°, [M]₃₅₀ + 1 020°, [M]₃₁₀ + 2 210°; (c 0.023): [M]₃₁₀ + 2 250°, [M]₃₀₀ + 3 060°, [M]₂₉₀ + 4 100°.

(+)-*n*-Amylphenylacetamide (XXIII) ^{58,59} R.D. (Fig. 11) in methanol (c 0.127), temp. 27°: [M]₅₈₉ + 80°, [M]₄₀₀ + 180°, [M]₃₅₀ + 270°, [M]₃₀₀ + 420°, [M]₂₉₀ + 450°.

(+)-*n*-Amylphenylacetanilide (XXIV) ^{58,59} R.D. (Fig. 12) in methanol (c 0.235), temp. 28°: [M]₅₈₉ + 220°, [M]₄₀₀ + 770°, [M]₃₅₀ + 1 320°, [M]₃₀₀ + 3 240°, [M]₂₉₀ + 4 570°.

(+)-Allylphenylacetic acid (XXV) ⁶⁰ R.D. (Fig. 6) in methanol (c 0.263), temp. 28°: [M]₅₈₉ + 150°, [M]₄₀₀ + 420°, [M]₃₅₀ + 660°, [M]₃₀₀ + 1 220°, [M]₂₇₅ + 1 980°.

(-)-1-Indanecarboxylic acid (XXVI) ⁶¹ R.D. (Fig. 7) in methanol (c 0.098), temp. 27°: [M]₅₈₉ - 20°, [M]₄₀₀ - 70°, [M]₃₅₀ - 120°, [M]₃₀₀ - 270°.

(-)-1,2,3,4-Tetrahydro-1-naphthoic acid (XXVII) ⁶² R.D. (Fig. 7) in methanol (c 0.257), temp. 28°: [M]₅₈₉ - 20°, [M]₄₀₀ - 90°, [M]₃₅₀ - 140°, [M]₃₁₀ - 270°; (c 0.0514): [M]₃₁₀ - 260°, [M]₃₀₀ - 330°, [M]₂₉₀ - 360°.

(-)-4-Keto-1,2,3,4-tetrahydro-1-naphthoic acid (XXVIII) ⁶³ R.D. (Fig. 7) in methanol (c 0.105), temp. 24°: [M]₅₈₉ - 30°, [M]₄₀₀ - 470°, [M]_{357.5} - 2 050° (T), [M]₃₂₇ ± 0°, [M]₃₀₅ + 1 770°.

(+)-Benzylphenylacetic acid (XXIX) ^{40,65} R.D. (Fig. 8) in methanol (c 0.125), temp. 28°: [M]₅₈₉ + 290°, [M]₄₀₀ + 800°, [M]₃₅₀ + 1 310°, [M]₃₁₀ + 2 040°; (c 0.0125): [M]₃₁₀ + 2 140°, [M]₃₀₀ + 2 600°, [M]₂₇₅ + 4 060°.

(+)-2-Thienylphenylacetic acid (XXX) ^{40,64} R.D. (Fig. 8) in methanol (c 0.133), temp. 27°: [M]₅₈₉ + 270°, [M]₄₀₀ + 770°, [M]₃₅₀ + 1 210°, [M]₃₁₀ + 2 020°; (c 0.0133): [M]₃₁₀ + 2 100°, [M]₃₀₀ + 2 440°, [M]₂₇₅ + 3 950°.

(+)-Benzyl-2-thienylacetic acid (XXXI) ^{40,64} R.D. (Fig. 8) in methanol (c 0.121), temp. 28°: [M]₅₈₉ + 190°, [M]₄₀₀ + 590°, [M]₃₅₀ + 940°, [M]₃₁₀ + 1 640°; (c 0.0242): [M]₃₁₀ + 1 800°, [M]₃₀₀ + 2 150°, [M]₂₇₅ + 4 000°.

(+)-Phenylsuccinic acid (XXXII) ^{81,89} R.D. (Fig. 15) in methanol (c 0.120), temp. 24°: [M]₅₈₉ + 250°, [M]₄₀₀ + 750°, [M]₃₅₀ + 1 170°, [M]₃₀₀ + 2 160°, [M]₂₇₅ + 3 460°.

(+)-2-Thienylsuccinic acid (XXXIII) ⁸² R.D. (Fig. 15) in methanol (c 0.130), temp. 24°: [M]₅₈₉ + 220°, [M]₄₀₀ + 610°, [M]₃₅₀ + 950°, [M]₃₀₀ + 1 750°, [M]₂₈₀ + 2 700°.

(+)-3-Thienylsuccinic acid (XXXIV) ⁸³ R.D. (Fig. 15) in methanol (c 0.143), temp. 25°: [M]₅₈₉ + 200°, [M]₄₀₀ + 530°, [M]₃₅₀ + 840°, [M]₃₀₀ + 1 560°, [M]₂₇₅ + 2 800°.

(+)-Benzylsuccinic acid (XXXV) ^{79,100} R.D. (Fig. 16) in methanol (c 0.163), temp. 24°: [M]₅₈₉ + 30°, [M]₄₀₀ + 160°, [M]₃₅₀ + 260°, [M]₃₀₀ + 440°, [M]₂₇₅ + 780°.

(+)-2-Thienylsuccinic acid (XXXVI) ^{79,100} R.D. (Fig. 16) in methanol (c 0.110), temp. 25°: [M]₅₈₉ + 20°, [M]₄₀₀ + 150°, [M]₃₅₀ + 230°, [M]₃₀₀ + 340°, [M]₂₇₅ + 570°.

(+)-3-Thienylsuccinic acid (XXXVII) ⁸⁵ R.D. (Fig. 16) in methanol (c 0.171), temp. 25°: [M]₅₈₉ + 30°, [M]₄₀₀ + 110°, [M]₃₅₀ + 190°, [M]₃₀₀ + 330°, [M]₂₇₅ + 580°.

(+)-Phenylethylsuccinic acid (XXXVIII) ^{86,101} (Fig. 17) in methanol (c 0.100), temp. 24°: [M]₅₈₉ + 30°, [M]₄₀₀ + 100°, [M]₃₅₀ + 180°, [M]₃₀₀ + 280°, [M]₂₇₀ + 450°.

(+)-*a*-Phenylglutaric acid (XXXIX) ** R.D. (Fig. 18) in methanol (*c* 0.100), temp. 21°: $[M]_{550} + 100^\circ$, $[M]_{400} + 230^\circ$, $[M]_{350} + 390^\circ$, $[M]_{300} + 650^\circ$, $[M]_{255} + 1220^\circ$.
 (+)-*a*-Phenyladipic acid (XL) ** R.D. (Fig. 18) in methanol (*c* 0.100), temp. 21°: $[M]_{550} + 90^\circ$, $[M]_{400} + 190^\circ$, $[M]_{350} + 320^\circ$, $[M]_{300} + 550^\circ$, $[M]_{255} + 1010^\circ$.

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