CLXXX.—*Optical Activity and the Polarity of Substituent Groups. Part VIII. Growing-chain Effects and the* ortho-*Effect in Benzoic Esters.*

By H. Gordon Rule, William Hay, and Jack Paul.

In earlier communications of this series (J., 1926, 553; this vol., p. 178) it has been established that a group which is *m*-directive in benzene substitution raises the rotatory power of menthyl or *sec.*-β-octyl benzoate when introduced into the ortho-position to the carboxylic complex, and that an *o,p*-directive substituent in this position lowers the rotation. The magnitude of the resulting change has also been shown to be related directly to the magnitude of the directive power of the group on benzene substitution.

An effect of this kind must be transmitted to the asymmetric centre either through the chain of intervening atoms or directly through space. The former supposition is favoured by the similarity in the influence of the substituents on rotatory power and on benzene substitution, since orientation effects in benzene substitution are commonly explained by electronic rearrangements which are assumed to be transmitted through the nucleus (Robinson, *J. Soc. Chem. Ind.*, 1925, **44**, 456; J., 1926, 401; Ingold and Ingold, *ibid.*, p. 1310. Compare also Højendahl, J., 1924, 1381, on alternation in an aliphatic chain). On the other hand, the fact that substituents in the *m*- and *p*-positions do not produce the same type of change in rotatory power (this vol., p. 178) is strongly against this view. There remains the possibility that the influence in question is propagated directly through space. In this case a similar effect on the rotatory power should be evident in other compounds the stereochemical configuration of which is such as to bring the substituent into close proximity to the asymmetric group. Numbered among such compounds are the *o*- and *peri*-derivatives of naphthoic esters (to be dealt with in a subsequent communication) and the homologous series of esters of aliphatic acids containing the substituent as a terminal group in the alkyl radical. In the latter compounds the terminal group returns on itself at regular intervals as the chain increases in length, often giving rise to characteristic maxima or minima at intervals of about 5 carbon atoms. If, therefore, the *o*-effect in the benzoic esters is transmitted through space, it would be anticipated that similar differences would be exhibited in the behaviour of growing chains possessing terminal groups of different types.

An attempt has now been made to obtain further evidence bearing on this point by the investigation of two series of optically active esters, the menthyl *n*-alkyloxyacetates and the menthyl hydrogen esters of *n*-dicarboxylic acids. Of these, the former has a terminal group which is *o*-*p*-directive in type, and the latter has one which is *m*-directive. The values obtained for the rotatory powers of these esters in the homogeneous state and in solution are summarised in Tables I and II. Values observed for other temperatures and wave-lengths are given in the experimental section. All the following rotations are negative in sign.

I. l-*Menthyl* n-*Alkyloxyacetates,* $C_{10}H_{19}O{\cdot}CO{\cdot}CH_2{\cdot}OR$.

R.	Me.*	Et.*	Pr.	C_4H_9.	C_5H_{11}.	C_6H_{13}.	C_7H_{15}.	C_8H_{17}.
$[M]^{20°}_{5461}$	195·3°	189·6°	187·4°	189·2°	189·0°	186·8°	186·1°	186·2°
$[M]^{90°}_{5461}$	193·6°	193·1°	191·3°	192·3°	191·0°	188·6°	188·1°	188·7°
$\frac{\alpha_{4358}}{\alpha_{5893}}$ (20°) ...	1·968	1·962	1·967	1·964	1·963	1·964	1·964	1·963

* Rule and Smith, J., 1925, **127**, 2188.

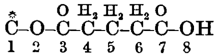
II. *Values of* $[M]_{5461}$ *for the* l-*Menthyl Hydrogen Dicarboxylates in the Homogeneous State and in Solution* (*approx.* 5%).

						Sodium salt in	
n.	Homog., 20°.	Homog., 60°.	In C_6H_6.	In EtOH.	In $CHCl_3$.	water.	alcohol.
6	189·9°	188·3°	183·8°	195·1°	203·3°	195·4°	—
7	—	—	180·4*	—	199·7*	193·6	—
8	191·9	191·1	198·4	200·2	203·2	189·5	198·3°
9	185·6	184·9	193·1	195·4	199·0	186·4	197·1
10	186·6	185·3	192·1	198·8	198·3	183·5	197·1
11	183·0	181·7	188·5	194·1	196·3	176·4	198·2
12	192·6	—	197·6	200·1	—	181·0	198·9
13	187·8	—	195·3	199·4	—	179·7	196·9

* Kenyon and Pickard, J., 1915, **107**, 54.

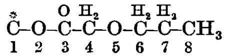
Except in a few instances the rotatory powers were measured over the range λ_{4358} to λ_{6708}, and in every case the values of $1/\alpha$ plotted against λ^2 gave a straight line. The esters therefore exhibit normal and simple dispersion under the conditions of experiment. The dispersion ratios $\alpha_{4358}/\alpha_{5893}$ for both series of compounds approximate closely to 1·96. As may be seen from the tables, a change of temperature has little effect on the rotatory power. The values for the alkyloxy-esters rise slightly with increase in temperature, whereas those for the dicarboxylates fall somewhat.

Comparison of the Rotation Curves.—The influence of the growing chains on the rotatory powers of the esters is illustrated in Fig. 1, in which the length of the chain, *n*, is measured from and including the asymmetric atom (terminal hydrogen being omitted). As will be seen from the following formulæ, the growing chain of each series resembles that of menthyl hydrogen phthalate in containing two oxygen atoms.



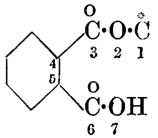
$$\underset{1}{\overset{*}{C}}-\underset{2}{O}-\underset{3}{\overset{O}{C}}-\underset{4}{\overset{H_2}{C}}-\underset{5}{\overset{H_2}{C}}-\underset{6}{\overset{H_2}{C}}-\underset{7}{\overset{O}{C}}-\underset{8}{OH}$$

Menthyl hydrogen glutarate.



$$\underset{1}{\overset{*}{C}}-\underset{2}{O}-\underset{3}{\overset{O}{C}}-\underset{4}{\overset{H_2}{C}}-\underset{5}{O}-\underset{6}{\overset{H_2}{C}}-\underset{7}{\overset{H_2}{C}}-\underset{8}{CH_3}$$

Menthyl propoxyacetate.

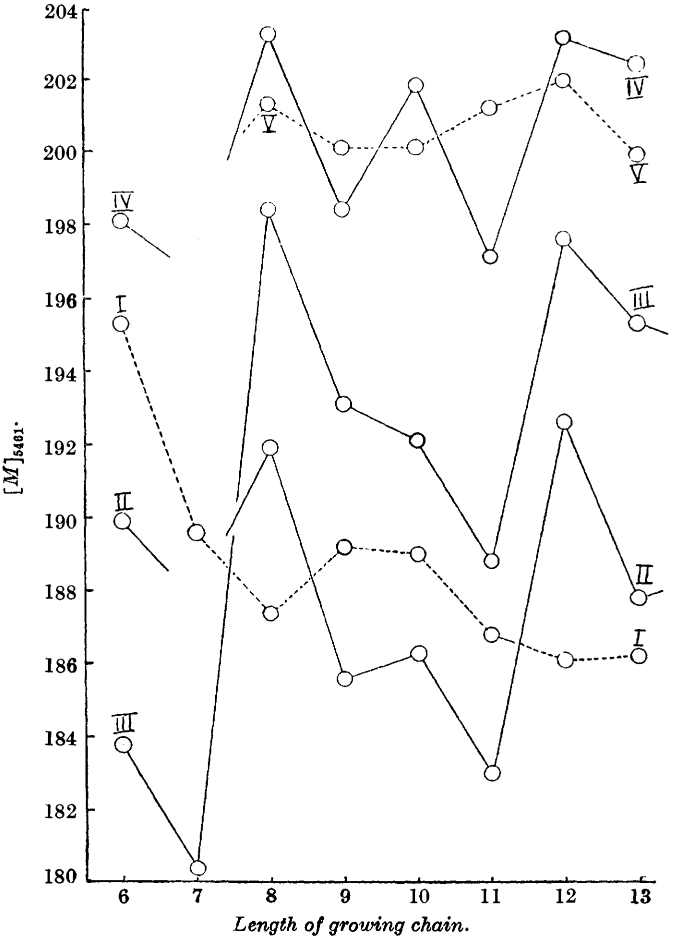


A striking difference between the two curves, which leaps at once to the eye, is the regular and pronounced alternation of the carboxy-compounds. Apart from this, however, the visible portions of the two sets of diagrams stand in the strongest possible contrast with one another. The values for the alkyloxyacetic esters fall steeply to a minimum at $n = 8$, rise rapidly to a maximum at $n = 9,10$, and then fall again to a minimum at $n = 12,13$. The values for the menthyl hydrogen carboxylates, on the contrary, rise to a maximum at $n = 8$, descend to minimum values at $n = (9),10,11$, and finally rise towards a maximum in the neighbourhood of $n = 12$. Except for a slight lack of exact correspondence in the central portion of the diagrams, due to the strongly alternating character of one of them, the maxima for the one series coincide with minima for the other, and *vice versa.*

Reference to the numbering diagram given above for the *o*-benzoic ester shows that the high value of the phthalate and the low value of the *o*-methoxy-ester occur at chain length $n = 7$, whereas the corresponding maximum and minimum points in Fig. 1 occur at $n = 8$. The discrepancy may possibly be explained by the fact that the interior angle between the valency bonds of the benzene ring is greater than that existing in a strainless compound; this brings the *o*-groups closer together than would be the case with the normal bending of an aliphatic chain and thus tends to accelerate the occurrence of the characteristic maximum or minimum values.

As might be expected, the magnitude of the *o*-effect in the benzoic esters is large compared with the deviations in the curves for the aliphatic esters. In the benzene derivatives the configuration of the molecule is such that the substituent group is permanently maintained at the most effective distance from the asymmetric atom.

FIG. 1.



I *Menthyl alkyloxyacetates* (*homog.* 20°). II *Menthyl hydrogen dicarboxylates* (*homog.* 20°). III *Menthyl hydrogen dicarboxylates* (*in* C_6H_6). IV *Dicarboxylates* (*in* EtOH). V *Dicarboxylates* (*sodium salt in* EtOH).

For rotations in alcohol subtract 3° *from scale value.*

In the aliphatic compounds the chain is probably in a state of constant motion, and the particular formation in which the end of the chain is so twisted as to be in spatial proximity to the asymmetric atom is only one of many arrangements assumed by the molecule. In this case, therefore, the spatial influence of the terminal group is very much weaker. Another factor which tends further to diminish the spatial influence in the alkyloxy-series is that the polarity of the terminal substituent becomes weaker as the chain lengthens. Indeed, in the longer chain compounds of this type under examination, the spatial effect of the terminal group is in all probability scarcely influenced by the presence of the oxygen atom.*

The above interpretation of the variations in the rotatory powers of the alkyloxyacetic esters is based on the assumption that these are caused by the end of the chain returning to the neighbourhood of the asymmetric atom or the adjacent oxygen atoms. But the possibility cannot be excluded that some of the observed changes are secondary effects due to the chain returning on the oxygen atom of the alkyloxyl group. The maximum at $n = 9,10$, for example, in so far as the length of the chain is considered, might equally well be due to either of these causes. The probabilities, however, point to the original assumption being correct. If the effect were a secondary one it would be expected to be small, since such an influence must necessarily be weakened by subsequent transmission through the chain from the O-atom to the asymmetric centre. On the contrary, the maximum shown in the diagram, although much less than the corresponding changes in the dicarboxylic esters, is scarcely smaller than would have been anticipated considering that we are comparing the influence of a comparatively inactive alkyl group with that of the highly active oxygen of the carboxyl group.

Further evidence on this point may be drawn from the dissociation constants of acids of the type of crotonic acid. As is well known, the commoner substituents with the exception of alkyl and amino-groups lead to an increase in acidic strength when introduced into an organic acid. Superimposed on this *general effect*, however, a secondary effect may sometimes be observed. This appears to be similar to that present in the above optically active compounds, in which the carboxyl group produces a change in the opposite sense

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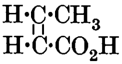
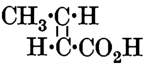
* The menthyl esters of n-aliphatic acids unfortunately give a rotation-curve in which the changes produced by the growing chain are small and irregular. A series of esters of ω-methoxy-aliphatic acids would have offered the ideal contrast with the above menthyl hydrogen dicarboxylates, but as their preparation presented too many difficulties the alkyloxyacetic esters were selected in the expectation of obtaining a series with well-defined maxima and minima.

to that given by CH_3, OH, or Cl, and is illustrated by the following dissociation constants taken from Landolt–Börnstein's "Tabellen." In these geometrical isomerides, and also in the phenyloximinoacetic acids, the spatial proximity of a CH_3, OH, or Cl to the carboxyl group lowers the acidic strength. In maleic and fumaric acids, and similar compounds, the juxtaposition of a second carboxyl group raises the acid strength.



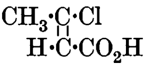
$$\begin{array}{c}\mathrm{H{\cdot}C{\cdot}CH_3}\\ \|\\ \mathrm{H{\cdot}C{\cdot}CO_2H}\end{array}$$

Crotonic acid, $0{\cdot}22 \times 10^{-4}$.



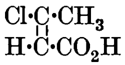
$$\begin{array}{c}\mathrm{CH_3{\cdot}C{\cdot}H}\\ \|\\ \mathrm{H{\cdot}C{\cdot}CO_2H}\end{array}$$

*iso*Crotonic acid, $0{\cdot}36 \times 10^{-4}$.



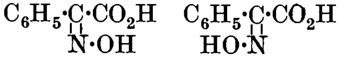
$$\begin{array}{c}\mathrm{CH_3{\cdot}C{\cdot}Cl}\\ \|\\ \mathrm{H{\cdot}C{\cdot}CO_2H}\end{array}$$

β-Chloro*iso*crotonic acid, $0{\cdot}95 \times 10^{-4}$.



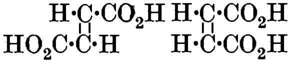
$$\begin{array}{c}\mathrm{Cl{\cdot}C{\cdot}CH_3}\\ \|\\ \mathrm{H{\cdot}C{\cdot}CO_2H}\end{array}$$

β-Chlorocrotonic acid, $1{\cdot}44 \times 10^{-4}$.



$$\begin{array}{c}\mathrm{C_6H_5{\cdot}C{\cdot}CO_2H}\\ \|\\ \mathrm{N{\cdot}OH}\end{array}\qquad\begin{array}{c}\mathrm{C_6H_5{\cdot}C{\cdot}CO_2H}\\ \|\\ \mathrm{HO{\cdot}N}\end{array}$$

Phenyloximinoacetic acids, 18×10^{-4}. 155×10^{-4}.



$$\begin{array}{c}\mathrm{H{\cdot}C{\cdot}CO_2H}\\ \|\\ \mathrm{HO_2C{\cdot}C{\cdot}H}\end{array}\qquad\begin{array}{c}\mathrm{H{\cdot}C{\cdot}CO_2H}\\ \|\\ \mathrm{H{\cdot}C{\cdot}CO_2H}\end{array}$$

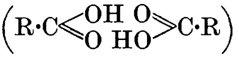
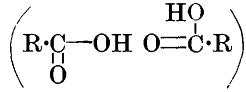
Fumaric and maleic acids, 10×10^{-4}. 150×10^{-4}.

On the whole, the available evidence supports the view expressed above that the opposite character of the two sets of diagrams in Fig. 1 is due to the dissimilar spatial influences exerted on the asymmetric atoms by the terminal groups of the growing chains.

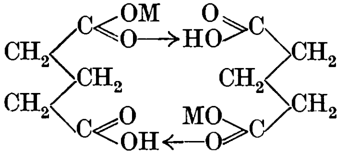
The irregular nature of these influences suggests one reason for the failure which has attended so many attempts to establish constitutional regularities in the domain of optical activity, and also explains some of the minor discrepancies observed in cases where such regularities have been successfully traced. In the sequence of groups representing the *general polar effect* of substituents on the rotatory powers of the menthyl esters, $XCH_2{\cdot}CO{\cdot}O{\cdot}C_{10}H_{19}$, *viz.*, $CN > Cl > Br > OH > OMe > Me > CO_2H > H$, the carboxyl was found to take an unexpectedly low place (Rule and Smith, J., 1925, **127**, 2188). This is now readily understood on reference to the diagram, in which menthyl hydrogen malonate, $n = 6$, is seen to occupy a minimum with the methoxyacetate, $n = 6$, on a corresponding maximum.

Alternation in the Menthyl Hydrogen Dicarboxylates.—The menthyl hydrogen dicarboxylates exhibit marked alternation in rotatory powers, both in the homogeneous state and when dissolved in benzene or chloroform. In alcoholic solution, in which the maxima at $n = 8$ and 12 are much less marked, the alternation becomes exceptionally prominent. This behaviour is in strong contrast with that of the dimenthyl esters, which show no alternation (Hall, J., 1923, **123**, 109). Similarly, no alternation has been observed for the corresponding dioctyl esters in the homogeneous state or in alcoholic solution, although it becomes feebly evident in carbon disulphide solution (Hall, *ibid.*, p. 32). In each of the above cases where alternation is present, the compounds derived from acids having an odd number of carbon atoms possess a higher rotation than those derived from even acids.

The rhythmic deviations in the rotation curve of a homologous series have been explained as space effects due to the spiral twisting of the growing chain. A regular alternation from member to member, on the other hand, may be caused by the zig-zag conformation of the chain leading to an alternate *cis*- and *trans*-structure of the molecule. Odd members of the above ester series, on this assumption, would have the terminal carboxyls in the *cis*-position to one another. As has already been seen in the cases of menthyl hydrogen glutarate and azelate, and of the analogous menthyl and *sec.*-β-octyl hydrogen phthalates, this spatial proximity would lead to an enhanced rotatory power and thus be in agreement with the experimental facts. Although it seems quite possible that structural changes of this kind may serve to explain the minor alternations visible under special conditions in the above-mentioned dioctyl esters, the magnitude of the alternation in the menthyl hydrogen carboxylates is greater than would be anticipated on this score. Moreover, these considerations do not appear to offer any reason for the complete disappearance of alternation when the ester-acids are examined in the form of their sodium salts. In aqueous solution, the values for the salts fall steadily, giving practically a straight line except for a minimum at the suberate ($n = 11$). At first it was thought that this unexpected result might be connected with the use of water as solvent, and as many as possible of the rotatory powers were therefore repeated with alcohol as solvent, in which both the ester-acids and their salts are soluble. It was then found that the salts gave a smooth curve following the mean trend of the strongly alternating values of the free acids (see Fig. 1) with corresponding, although not very marked, maxima at the glutarate ($n = 8$) and azelate ($n = 12$). In menthyl phthalate the presence of the free $\cdot CO_2H$ group raises the rotatory power, whereas that of the ionised $\cdot CO \cdot O'$ group lowers the activity. These groups also produce opposite types of orientation effects in benzene substitution. Hence it was expected that the salts of the menthyl hydrogen dicarboxylates would yield a curve with minima at $n = 8$ and 12, in contrast with the maxima given by the parent acids. Although the general form of the curve in the non-dissociating solvent benzene (III) becomes progressively flatter as it passes through chloroform to the homogeneous state (II) and the strongly ionising solvent alcohol (IV), the maxima still remain evident, even when the compounds are examined in the form of their salts (V).

The disappearance of alternation in the ionised compounds, coupled with the persistence of the maxima, is not readily explained by the simple *cis*- and *trans*-variation in structure outlined above. These facts suggest that the diagrams for the dicarboxylic esters represent the summation of two main disturbances, and that superimposed on the influence of the returning chain is a second effect caused by molecular association through the medium of the carboxyl groups. It is known from the *X*-ray analysis of the solid higher fatty acids that they are associated into double crystal cells (Müller and Shearer, J., 1923, **123**, 3156), and in order to explain the alternation in the molecular heats of these compounds Garner and Randall (J., 1924, **125**, 881) conclude that this association may take place in two ways, according as the acids contain an even  $\left(\mathrm{R{\cdot}C}\genfrac{<}{}{0pt}{}{\mathrm{OH}}{\mathrm{O}}\;\genfrac{}{>}{0pt}{}{\mathrm{O}}{\mathrm{HO}}\mathrm{C{\cdot}R}\right)$ or an odd number  $\left(\mathrm{R{\cdot}}\underset{\underset{\mathrm{O}}{\|}}{\mathrm{C}}\mathrm{{-}OH\;\;O{=}}\overset{\overset{\mathrm{HO}}{|}}{\mathrm{C}}\mathrm{{\cdot}R}\right)$ of carbon atoms. Now if reference be made to the figures recorded by these authors it will be seen that the odd acids, which have the higher specific heats in the solid state, have also the higher values in the liquid condition, although the alternation from odd to even in the liquids is much less pronounced. If, therefore, the alternation in the solid state is due to the two different forms of association suggested, the same difference of structure must exist to a lesser extent in the liquid phase. In this case it is possible to explain not only the alternation in the optical activity of the menthyl esters but also the disappearance of alternation in solutions of the sodium salts, because in the ionised condition the electrically charged terminal groups would mutually repel one another, thus preventing association.

A second form of association may be deduced from the success of Kendall and Booge (*J. Amer. Chem. Soc.*, 1916, **38**, 1712) in isolating a large number of bimolecular addition compounds resulting from the union of acids and esters, as a consequence of which the authors conclude that complex formation of this type is a general phenomenon in systems ester–acid. The menthyl esters under discussion, being both acids and esters, may therefore exist partly in a bimolecular state due to the carboxyl of one molecule linking up with the ester group of a second. Association may also take the more complete form shown in the annexed formula, in which co-ordination is represented by the symbol adopted by Sidgwick. In the latter case, the zig-zag arrangement of the carbon chain would be expected to facilitate combination in the odd, as compared with the even series, since the odd members have a natural tendency to occur in the *cis*-structure. This would then lead to an alternation in properties. It might even be anticipated that the odd members, existing in the cyclic bimolecular form to a greater degree than the even members, would on this account exhibit a higher rotation.



As there is no evidence pointing to an association of this type with ionised carboxyl groups, the alternation would probably not be found in the sodium salts.

Although the available data do not permit of an unequivocal decision as to the actual nature of the addition compounds formed, the assumption that the ester-acids are partly associated accounts for the observed influence of the growing chain. The alternating curves would then represent alternation due to the two types of association superimposed on the normal effect of the spiral chain.

EXPERIMENTAL.

l-*Menthyl Esters of Alkyloxyacetic Acids.*—The menthol used in the following preparations had a rotation of $[\alpha]_D^{15^\circ} = -49{\cdot}73^\circ$ in alcohol ($c = 9{\cdot}87$).

l-*Menthyl* n-*propoxyacetate.* To a boiling solution of sodium (25 g.) in *n*-propyl alcohol (240 g.), chloroacetic acid (46 g.) was gradually added with continuous shaking. A vigorous reaction occurred and sodium chloride was deposited from the solution. After 2 hours' further heating, the yellowish product was cooled, water added, and any excess of propyl alcohol extracted from the solution with ether. The aqueous layer, evaporated to a convenient bulk, was treated with the theoretical quantity of 25% sulphuric acid; ether then extracted the propoxyacetic acid which, after being dried, was distilled in a vacuum (yield, 37 g.); b. p. 108°/10 mm. (Gautier, *Ann. Chim.*, 1909, **16**, 309, quotes 213—214°/724 mm.) (Found : *M*, by titration, 117·5. Calc. : *M*, 118·1).

21 G. of *n*-propoxyacetyl chloride (b. p. 87—88°/101 mm.; obtained by use of thionyl chloride) were heated with menthol (24 g.), benzene (50 g.), and pyridine (2 mols.) for 4 hours on the water-bath, and the mixture was then worked up in the usual way, any unchanged menthol being distilled in steam. The l-*menthyl propoxyacetate* boiled at 161°/14 mm. and showed a constant rotatory power after one fractionation (Found : C, 70·2; H, 11·1. $C_{15}H_{28}O_3$ requires C, 70·3; H, 10·9%).

In preparing the remaining esters of this series a modification of the above procedure was adopted, anhydrous sodium chloroacetate (Kastle and Keiser, *Amer. Chem. J.*, 1893, **15**, 472) being used in place of chloroacetic acid. This had the advantage of requiring only half the amount of metallic sodium, thus reducing the volume of the alcohol necessary for its solution as alkyloxide.

n-*Butoxyacetic acid* was prepared from *n*-butyl alcohol (75 g.), sodium (8 g.), and sodium monochloroacetate (36 g.). Yield, 36 g. (84% theory), b. p. 115—116°/10 mm. (Found: C, 54·4; H, 9·2. $C_6H_{12}O_3$ requires C, 54·5; H, 9·15%).

l-*Menthyl* n-*butoxyacetate.* The above acid was converted into the acid chloride, and the fraction (29 g.) of this having b. p. 108—110°/108 mm. was brought into reaction with menthol in the manner described under the propoxy-ester, giving 42·5 g. of pure menthyl butoxyacetate, b. p. 172·5°/14 mm. (Found: C, 70·9; H, 11·3. $C_{16}H_{30}O_3$ requires C, 71·1; H, 11·2%).

n-*Amyloxyacetic acid.* *n*-Amyl alcohol was prepared from *n*-butyl alcohol, by converting the latter first into the bromide and thence by way of the cyanide into ethyl *n*-valerate. The latter was then reduced to *n*-amyl alcohol by means of anhydrous alcohol and sodium (Adams and Marvel, *J. Amer. Chem. Soc.*, 1920, **42**, 310). Amyl alcohol, b. p. 138—139°, was obtained in 63% yield. This was converted into n-*amyloxyacetic acid* by interaction with sodium and sodium chloroacetate (see above), the temperature of the oil bath not being allowed to exceed 130°. Reaction was complete in 3 hours. The acid boiled at 134°/12 mm. Yield, 77% (calculated on amyl alcohol) (Found: C, 57·4; H, 9·8. $C_7H_{14}O_3$ requires C, 57·5; H, 9·65%).

n-*Amyloxyacetyl chloride,* b. p. 103°/64 mm., was esterified in the usual manner to give l-*menthyl* n-*amyloxyacetate,* b. p. 148°/14 mm., the rotation of which remained constant after a second fractionation (Found: C, 71·6; H, 11·4. $C_{17}H_{32}O_3$ requires C, 71·7; H, 11·4%).

n-*Hexyloxyacetic acid,* b. p. 143—144°/10 mm., was prepared in a similar manner to the previous acids, from *n*-hexyl alcohol (Kahlbaum, b. p. 157°) (Found: C, 59·9; H, 10·1. $C_8H_{16}O_3$ requires C, 60·0; H, 10·1%).

n-*Hexyloxyacetyl chloride,* b. p. 106—108°/22 mm., was converted into l-*menthyl* n-*hexyloxyacetate,* b. p. 187°/10 mm., the rotation of which remained constant after the second fractionation (Found: C, 72·3; H, 11·6. $C_{18}H_{34}O_3$ requires C, 72·4; H, 11·5%).

n-*Heptyloxyacetic acid* (from Kahlbaum's *n*-heptyl alcohol, b. p. 175°) was a colourless liquid, b. p. 156°/10 mm., which solidified (m. p. 7·5—8·5°) in a freezing mixture (Found: C, 61·9; H, 10·5. $C_9H_{18}O_3$ requires C, 62·0; H, 10·4%).

n-*Heptyloxyacetyl chloride,* b. p. 116°/16 mm., was converted into l-*menthyl* n-*heptyloxyacetate* in the usual way. The ester was obtained as a colourless, odourless liquid, b. p. 200°/11 mm. The rotatory power was unaltered after the second fractionation and was not affected by refluxing the ester in an air stream under diminished pressure for 30 minutes (Found: C, 73·0; H, 11·8. $C_{19}H_{36}O_3$ requires C, 73·0; H, 11·6%).

n-*Octyloxyacetic acid* was prepared from a fraction of *n*-octyl alcohol (Kahlbaum) boiling at 195·5—196°, which was optically inactive. The procedure was the same as that adopted in the case of the foregoing acids, but special care was taken to keep the temperature below 130° during the addition of the sodium chloroacetate to the sodium octyloxide dissolved in octyl alcohol. At higher temperatures, the yield of crude acid diminished and the pure product could only be obtained after wasteful fractionation. From *n*-octyl alcohol (75 g.), sodium (8 g.), and sodium chloroacetate (39 g.) there was obtained a 68% yield of n-*octyloxyacetic acid* (43 g.), b. p. 166°/10 mm. The acid solidified on standing and then melted at 12·5—13·5° (Found: C, 63·7; H, 10·7. $C_{10}H_{20}O_3$ requires C, 63·8; H, 10·7%).

n-*Octyloxyacetyl chloride*, b. p. 125—126°/12 mm., was converted into l-*menthyl* n-*octyloxyacetate*, b. p. 183°/2 mm. The rotatory power was constant after a third fractionation (Found: C, 73·5; H, 11·9. $C_{20}H_{38}O_3$ requires C, 73·6; H, 11·7%).

l-*Menthyl Hydrogen Esters of the Saturated Dicarboxylic Acids.*—In most cases the dicarboxylic acids, purified by repeated recrystallisation from a suitable solvent, were first converted into the dimenthyl esters by the method of Hilditch (J., 1909, **95**, 1571; see also Hall, J., 1923, **123**, 109). The di-ester was then submitted to half-hydrolysis at room temperature by treatment with the requisite amount of sodium dissolved in 95% alcohol. The crude acid ester was dissolved in a slight excess of dilute sodium carbonate solution and extracted repeatedly (10 times) with an equal bulk of ether, to remove menthol and di-ester. The aqueous layer was then acidified, the liberated ester-acid extracted with ether, and the extract washed (10 times) with large volumes of water to remove any dicarboxylic acid or ethyl hydrogen carboxylate which might have been formed during the half-hydrolysis. The ethereal solution, after drying over calcium chloride, gave the menthyl hydrogen ester, which was further dried in a vacuum desiccator at 55° over calcium chloride. After 16—20 hours' drying, the rotation of the ester underwent no further change. The whole of the above treatment was repeated until the rotation was unaffected by continued washings.

l-*Menthyl hydrogen glutarate* was obtained from dimethyl glutarate having a rotatory power $[\alpha]_{5461} = -84·15°$ in chloroform solution ($c = 5$). Hall (*loc. cit.*) records $[\alpha]_{5461} = -84·12°$. The rotation of the homogeneous half-ester prepared by half-hydrolysis and washed as above was increased by 0·09° ($l = 0{\cdot}5$) by a repetition of the process. Further washings led to no change in rotatory power. The colourless, odourless syrup gave C, 66·7; H, 9·8 ($C_{15}H_{26}O_4$ requires C, 66·6; H, 9·7%).

l-*Menthyl hydrogen adipate* was prepared from dimethyl adipate (m. p. 62·5—63·5°; $[\alpha]_{5461} = -81{\cdot}63°$ in chloroform, $c = 5$. Hall, *loc. cit.*, records $[\alpha]_{5461} = -81{\cdot}75°$). Two separate preparations of the half-ester gave crude products which exhibited the same constant rotatory power after four treatments as above. The colourless, odourless syrup gave C, 67·4; H, 10·0 ($C_{16}H_{28}O_4$ requires C, 67·6; H, 9·9%).

l-*Menthyl hydrogen pimelate.* Pimelic acid, m. p. 101—103°, prepared by Perkin's method (J., 1887, **51**, 240; 1891, **59**, 822) by way of ethyl pentanetetracarboxylate was used without further purification. It gave crude dimenthyl pimelate, which was distilled in a high vacuum (b. p. 230°/0·07 mm.) and recrystallised from alcohol. The di-ester had the rotatory power $[\alpha]_{5461} = -93{\cdot}20°$ in chloroform ($c = 5$). Hall (*loc. cit.*) records $[\alpha]_{5461} = -92{\cdot}10°$. l-*Menthyl hydrogen pimelate* was obtained from the di-ester in the usual manner, as a slightly yellow syrup (Found: C, 68·2; H, 10·2. $C_{17}H_{30}O_4$ requires C, 68·4; H, 10·1%).

l-*Menthyl hydrogen suberate.* Suberic acid, purified by repeated recrystallisation from ethyl acetate, was converted into dimenthyl suberate. The crude di-ester was distilled in a high vacuum (b. p. 233°/0·07 mm.) and then recrystallised from alcohol. The pure ester melted at 36·5—37·5° and gave $[\alpha]_{5461} = -90{\cdot}20°$ in chloroform ($c = 5$). Hall (*loc. cit.*) records m. p. 36—37° and $[\alpha]_{5461} = -89{\cdot}33°$. l-*Menthyl hydrogen suberate,* as obtained from the di-ester, was a faintly yellow syrup (Found: C, 69·0; H, 10·6. $C_{18}H_{32}O_4$ requires C, 69·2; H, 10·3%).

l-*Menthyl hydrogen azelate.* Purified azelaic acid (m. p. 107—108°, corr.) was converted into the dimenthyl ester, which on repeated fractionation under 2 mm. pressure (b. p. 265°) had a low rotatory power. It was purified by solution in warm methyl alcohol and precipitation at $-14°$. $\alpha_{5461} = -76{\cdot}42°$ ($l = 1$) for the homogeneous ester. Hall (*loc. cit.*) records $\alpha_{5461} = -76{\cdot}24°$. l-*Menthyl hydrogen azelate* was obtained as a colourless syrup (Found: C, 69·7; H, 10·7. $C_{19}H_{34}O_4$ requires C, 69·9; H, 10·5%).

l-*Menthyl hydrogen sebacate,* from sebacic acid (m. p. 132·8—133·4°, corr.) was fractionated under 0·25 mm. pressure (b. p. 273°). The ester was finally purified from methyl alcohol (see azelate). $\alpha_{5461} = -72{\cdot}68°$ ($l = 1$). Hall (*loc. cit.*) records $\alpha_{5461} = -73{\cdot}12°$ (Found: C, 70·4; H, 10·8. $C_{20}H_{36}O_4$ requires C, 70·5; H, 10·7%).

l-Menthyl hydrogen succinate (Arth, *Ann. Chim. Phys.*, 1886, **7**, 483) and *l*-menthyl hydrogen malonate (Rule and Smith, J., 1925, **127**, 2188) were also prepared in order to obtain comparative rotations for the sodium salts in water and alcohol and for the esters in certain solvents. The succinate gave $[\alpha]_D = -70·2^\circ$ in benzene ($c = 5$). Pickard and Kenyon (J., 1915, **107**, 52) record $[\alpha]_D = -70·5^\circ$.

Observed Rotations and Densities of the Homogeneous Esters.

The sign of all the following *l*-menthyl esters is negative. Density determinations were made in a pyknometer holding about 3 c.c.

l-*Menthyl* n-*propoxyacetate* ($l = 1$).

$D_{4^\circ}^{t^\circ}$ 0·9448 at 24°; 0·9286 at 44·2°; 0·9151 at 61·05°; 0·8999 at 79·5°.
α_{6708} 44·42° at 18°; 44·04° at 37·5°; 43·36° at 65·1°; 42·64° at 93·1°.
α_{5893} 58·69° at 18°; 58·16° at 39·1°; 57·08° at 71·9°; 56·37° at 92·0°.
α_{5780} 61·31° at 18°; 60·63° at 39·1°; 59·49° at 71·9°; 58·73° at 92·0°.
α_{5461} 69·44° at 18°; 68·62° at 39·1°; 67·36° at 71·9°; 66·51° at 92·0°.
α_{4358} 115·49° at 18°; 114·26° at 39·1°; 111·95° at 71·9°; 110·49° at 92·0°.

l-*Menthyl* n-*butoxyacetate* ($l = 1$).

$D_{4^\circ}^{t^\circ}$ 0·9397 at 20·6°; 0·9228 at 42·2°; 0·9094 at 59·4°; 0·8932 at 80·1°.
α_{6708} 42·34° at 20·5°; 41·82° at 40·6°; 41·07° at 66·2°; 40·29° at 91·5°.
α_{5893} 55·74° at 20·5°; 55·08° at 40·6°; 54·17° at 66·2°; 53·15° at 91·5°.
α_{5780} 58·14° at 20·5°; 57·51° at 40·6°; 56·54° at 66·2°; 55·50° at 91·5°.
α_{5461} 65·83° at 20·5°; 65·13° at 40·6°; 64·08° at 66·2°; 62·91° at 91·5°.
α_{4358} 109·43° at 20·5°; 108·28° at 40·6°; 106·51° at 66·2°; 104·58° at 91·5°.

l-*Menthyl* n-*amyloxyacetate* ($l = 1$).

$D_{4^\circ}^{t^\circ}$ 0·9340 at 20·5°; 0·9174 at 42·5°; 0·9055 at 58·3°; 0·8864 at 83·5°.
α_{6708} 39·83° at 21·5°; 39·41° at 39°; 38·65° at 67°; 37·93° at 89·7°.
α_{5893} 52·52° at 21·5°; 51·93° at 39°; 51·0° at 67°; 50·11° at 89·7°.
α_{5780} 54·80° at 21·5°; 54·25° at 39°; 53·18° at 67°; 52·32° at 89·7°.
α_{5461} 61·99° at 21·5°; 61·44° at 39°; 60·26° at 67°; 59·28° at 89·7°.
α_{4358} 103·12° at 21·5°; 102·0° at 39°; 100·3° at 67°; 98·61° at 89·7°.

l-*Menthyl* n-*hexyloxyacetate* ($l = 1$).

$D_{4^\circ}^{t^\circ}$ 0·9270 at 24·3°; 0·9125 at 43·9°; 0·8985 at 62·7°; 0·8865 at 79·3°.
α_{6708} 37·31° at 21°; 36·96° at 38·1°; 36·19° at 65°; 35·40° at 94·5°.
α_{5893} 49·29° at 21°; 48·77° at 38·1°; 47·88° at 65°; 46·78° at 94·5°.
α_{5780} 51·33° at 21°; 50·84° at 38·1°; 49·90° at 65°; 48·83° at 94·5°.
α_{5461} 58·25° at 21°; 57·62° at 38·1°; 56·57° at 65°; 55·32° at 94·5°.
α_{4358} 96·82° at 21°; 95·74° at 38·1°; 94·18° at 65°; 92·05° at 94·5°.

l-*Menthyl* n-*heptyloxyacetate* ($l = 1$).

$D_{4^\circ}^{t^\circ}$ 0·9221 at 24·5°; 0·9101 at 40·9°; 0·8962 at 59·9°; 0·8818 at 79·7°.
α_{6708} 35·29° at 22°; 35·05° at 39·5°; 34·47° at 64·3°; 33·88° at 87·1°.
α_{5893} 46·74° at 22°; 46·24° at 39·5°; 45·50° at 64·3°; 44·74° at 87·1°.
α_{5780} 48·66° at 22°; 48·20° at 39·5°; 47·52° at 64·3°; 46·73° at 87·1°.
α_{5461} 55·11° at 22°; 54·54° at 39·5°; 53·61° at 64·3°; 52·89° at 87·1°.
α_{4358} 91·76° at 22°; 90·86° at 39·5°; 89·41° at 64·3°; 87·95° at 87·1°.

l-*Menthyl* n-*octyloxyacetate* ($l = 1$).

$D_{4^\circ}^{t^\circ}$ 0·9214 at 20·8°; 0·9072 at 40·1°; 0·8932 at 59·1°; 0·8779 at 79·9°.
α_{6708} 33·86° at 17·8°; 33·44° at 39°; 32·78° at 70·2°; 32·30° at 91·2°.
α_{5893} 44·64° at 17·8°; 44·07° at 39°; 43·23° at 70·2°; 42·57° at 91·2°.
α_{5780} 46·54° at 17·8°; 46·05° at 39°; 45·02° at 70·2°; 44·42° at 91·2°.
α_{5461} 52·69° at 17·8°; 52·08° at 39°; 51·03° at 70·2°; 50·28° at 91·2°.
α_{4358} 87·64° at 17·8°; 86·49° at 39°; 84·82° at 70·2°; 83·65° at 91·2°.

l-*Menthyl hydrogen malonate.*

Solvent.	*l.*	*t.*	G. ester/ 20 c.c.	α_{6708}.	α_{5893}.	α_{5780}.	α_{5461}.	α_{4358}.
EtOH	200	20°	0·8127	—	—	—	6·55°	10·87°
$CHCl_3$	200	20·4	1·0146	5·49°	7·22°	7·52°	8·52	14·16
Sod. salt H_2O...	200	20·2	1·0007	5·16	6·84	7·16	8·07	13·44
			l-*Menthyl hydrogen succinate.*					
Sod. salt H_2O...	200	15	0·9302	—	—	—	7·04	—
			l-*Menthyl hydrogen glutarate.*					
Homog. ...	50	21·0	(*d* 1·0318)	23·49	31·02	32·34	36·63	60·79
Homog. ...	50	60·2	(*d* 1·0046)	22·81	30·05	31·35	35·52	58·93
$CHCl_3$	200	18·9	1·0278	5·00	6·58	6·85	7·73	12·84
EtOH	200	19·5	1·0098	4·82	6·33	6·64	7·48	12·47
C_6H_6	200	19·5	1·0246	4·86	6·38	6·65	7·52	12·52
Sod. salt H_2O...	200	18·0	*1·0389	4·71	6·17	6·45	7·29	12·12
EtOH	200	15·0	*0·8697	—	—	—	6·38	—
			l-*Menthyl hydrogen adipate.*					
Homog. ...	50	20·0	(*d* 1·0252)	21·50	28·36	29·52	33·47	55·54
Homog. ...	50	60·0	(*d* 0·9959)	20·75	27·38	28·58	32·40	53·67
$CHCl_3$	200	18·4	1·0383	4·64	6·17	6·44	7·27	12·06
EtOH	200	19·2	1·0539	4·65	6·15	6·39	7·25	12·02
C_6H_6	200	18·3	1·0793	4·70	6·22	6·47	7·33	12·13
Sod. salt H_2O...	200	19·5	1·0125	4·27	5·61	5·88	6·64	11·06
EtOH	200	16·0	0·7544	—	—	—	5·23	—
			l-*Menthyl hydrogen pimelate.*					
Homog. ...	50	19·0	(*d* 1·0141)	20·45	26·89	28·00	31·73	—
Homog. ...	50	59·0	(*d* 0·9858)	19·65	25·93	27·03	30·63	—
$CHCl_3$	200	18·5	0·9835	4·21	5·56	5·80	6·54	10·89
EtOH	200	19·0	1·0320	4·37	5·78	6·05	6·88	11·36
C_6H_6	200	18·0	1·0418	4·35	5·70	5·94	6·71	11·10
Sod. salt H_2O...	200	19·0	1·0060	3·98	5·24	5·48	6·19	10·21
EtOH	100	15·0	0·7590	—	—	—	2·51	—
			l-*Menthyl hydrogen suberate.*					
Homog. ...	50	19·2	(*d* 1·0049)	18·83	24·86	25·98	29·45	—
Homog. ...	50	60·3	(*d* 0·9760)	18·18	24·04	25·03	28·38	—
$CHCl_3$	200	19·0	0·9828	3·95	5·21	5·46	6·18	10·26
EtOH	200	18·8	0·9668	3·85	5·07	5·31	6·01	9·96
C_6H_6	200	20·0	1·0306	3·97	5·27	5·50	6·22	10·36
Sod. salt H_2O...	200	19·0	1·0672	3·89	5·14	5·35	6·03	10·02
EtOH	200	16·0	0·8707	—	—	—	5·53	—

l-*Menthyl hydrogen azelate.*

Solvent.	*l.*	*t.*	G. ester/ 10 c.c.	α_{5893}.	α_{5461}.	α_{4358}.
Homog.	50	20°	(*d* 0·9952)	23·64°	28·63°	47·69°
C_6H_6	100	20	0·5733	2·98	3·47	5·60
EtOH	100	20	0·5368	2·81	3·29	5·37
Sod. salt H_2O......	100	20	0·4596	—	2·39	3·93
EtOH ...	100	20	0·4667	—	2·85	—
			l-*Menthyl hydrogen sebacate.*			
Homog.	50	20	(*d* 0·9923)	23·13	27·37	45·28
C_6H_6	100	20	0·5275	2·51	3·03	4·89
EtOH	100	20	0·4457	2·12	2·61	4·24
Sod. salt H_2O......	100	20	0·4309	—	2·27	3·62
EtOH ...	100	20	0·3894	—	2·12	—

* Rotations with the sodium salts were made by dissolving a weighed amount of ester in water or alcohol, and adding the calculated quantity of alkali dissolved in the same solvent.

Summary.

1. The rotatory powers of a number of the homologous menthy alkyloxyacetic esters and menthyl hydrogen dicarboxylic esters have been investigated. It is found that the maxima in the rotation curves of the one series correspond to minima in the other. This indicates that the terminal alkyloxyl and carboxyl groups of the growing chains produce opposite changes in rotatory power when they return to the neighbourhood of the asymmetric atom. Similar effects are noted in the influence of substituents on the acidity of geometrically isomeric acids. Hence it is concluded that the characteristic influence of *o*-substituents in the optically active benzoic esters (Rule, Hay, Numbers, and Paterson, this vol., p. 178) is propagated through space.

2. The rotatory powers of the menthyl hydrogen dicarboxylates exhibit pronounced alternation, both in the homogeneous state and in solution. This alternation disappears in the sodium salts. It is suggested that the alternation is a superimposed secondary effect due to association of the ester-acids through the medium of the carboxyl groups.

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