179. *Experiments on the Walden Inversion. Part XII.* The Displacement of Hydroxyl by Chlorine in the Optically Active Ethyl α-Naphthylglycollates.*
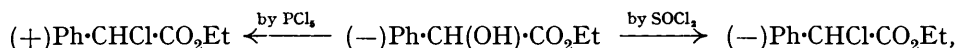
By ALEX. MCKENZIE and EVELYN R. L. GOW.

FROM earlier work it had emerged that the rotatory power undergoes a reversal of sign when phosphorus pentachloride acts on an optically active compound containing a hydroxy-group directly attached to an asymmetric carbon atom. But there is no such

uniformity when the chlorinating agent is thionyl chloride, the sign being reversed with (—)malic acid, ethyl (—)malate, ethyl (+)lactate, ethyl (—)α-hydroxy-β-phenylpropionate, but not with (—)mandelic acid, methyl (—)mandelate, (—)atrolactinic acid, ethyl (+)atrolactinate, (+)β-hydroxy-β-phenylpropionic acid, and (+)phenylmethylcarbinol. In every one of the last six compounds it is noteworthy that a phenyl group is directly attached to an asymmetric carbon atom, a striking uniformity which is perhaps not unconnected with the electron-attracting nature of the hydrocarbon radical. Again, halogenation with phosphorus pentachloride is often accompanied with very pronounced displacement racemisation, whereas the tendency for this type of racemisation to occur is very much less pronounced with thionyl chloride.

The contrast between phosphorus pentachloride and thionyl chloride in their behaviour towards ethyl (—)mandelate was detected by McKenzie and Barrow (J., 1911, **99**, 1910) :

$$(+)\text{Ph·CHCl·CO}_2\text{Et} \xleftarrow{\text{by PCl}_5} (-)\text{Ph·CH(OH)·CO}_2\text{Et} \xrightarrow{\text{by SOCl}_2} (-)\text{Ph·CHCl·CO}_2\text{Et},$$
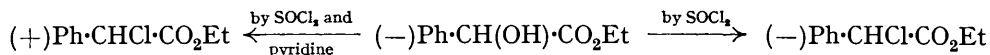
and a similar difference towards the optically active mandelic acids enabled the interconversion of these acids to be accomplished (McKenzie and Clough) in two different ways.

According to Frankland and Garner (J., 1914, **105**, 1101) a change of sign of rotation takes place when ethyl (+)lactate is acted on by thionyl chloride, both in the presence and in the absence of pyridine :

$$(+)\text{Me·CH(OH)·CO}_2\text{Et} \longrightarrow (-)\text{Me·CHCl·CO}_2\text{Et}$$

Belonging to the same category is (—)β-octanol, which gives (+)β-chloro-octane with thionyl chloride both in the absence (Levene and Mikeska, *J. Biol. Chem.*, 1924, **59**, 45) and in the presence of pyridine (McKenzie and Tudhope, *ibid.*, 1924, **62**, 551).

More recently, the halogenation of methyl (+)mandelate by the agency of phosphorus oxychloride in the presence of pyridine was investigated by Wagner-Jauregg (*Helv. Chim. Acta*, 1929, **12**, 61), who found that the reversal of sign was much more pronounced than that observed with phosphorus pentachloride, the prediction being made that the action of thionyl chloride in the presence of pyridine would lead to a chloro-ester of almost complete optical purity. Soon afterwards, Kenyon, Lipscomb, and Phillips (J., 1930, 415) made the remarkable discovery that ethyl (+)phenylchloroacetate is obtained, but not its (—)isomeride, if ethyl (—)mandelate is first dissolved in a tertiary base (pyridine, quinoline, or *iso*quinoline), and then heated with thionyl chloride, thus :
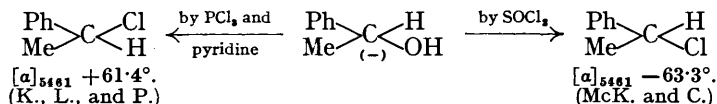
$$(+)\text{Ph·CHCl·CO}_2\text{Et} \xleftarrow[\text{pyridine}]{\text{by SOCl}_2 \text{ and}} (-)\text{Ph·CH(OH)·CO}_2\text{Et} \xrightarrow{\text{by SOCl}_2} (-)\text{Ph·CHCl·CO}_2\text{Et}$$

The chloro-ester of highest rotation observed by Kenyon, Lipscomb, and Phillips had $\alpha_{5461} + 122°$ ($l = 1$), whilst the corresponding value for the chloro-ester obtained by McKenzie and Barrow, using thionyl chloride alone, was $- 91·3°$ (calculated from the observed α_D by the dispersion ratio determined by K., L., and P.).

The contrast between ethyl (—)mandelate on the one hand and ethyl (+)lactate and (—)β-octanol on the other shows the striking difference between the influence exerted by the aryl and alkyl groups respectively, a difference which also is apparent in another field, *viz.*, that of catalytic racemisation by alcoholic alkali.

By the halogenation of the optically pure (+)phenylmethylcarbinol with $[\alpha]_{5893} + 43·4°$ or $[\alpha]_{5461} + 51·7°$ by means of thionyl chloride alone, McKenzie and Clough (J., 1913, **103**, 687) obtained (+)α-chloroethylbenzene with $[\alpha]_{5893} + 50·6°$ or $[\alpha]_{5461} + 63·3°$, an observation which enabled the interconversion of optically active alcohols to be realised for the first time. Kenyon, Phillips, and Taylor (J., 1931, 382) studied the action of thionyl chloride in the presence of pyridine on an alcohol with $[\alpha]_{5461} - 49·8°$, and found a change of sign, but their products fell far short of optical purity. Thus, the behaviour of thionyl chloride in the presence of pyridine differs markedly from the corresponding action with ethyl (—)mandelate.

From the constancy of the magnitude of the rotation observed by McKenzie and Clough

for their chloro-compound in different preparations (cf. Ott, *Ber.*, 1928, **61**, 2124) the conclusion was drawn that this product contained very little, if indeed any, of the *dl*-form. But there was pronounced racemisation when phosphorus trichloride acted on (+)phenyl-methylcarbinol, the product having only $[a]_{5893}$ — 8·1°. All the more important, therefore, was the observation of Kenyon, Lipscomb, and Phillips that the action of phosphorus trichloride in the presence of pyridine occurred without any appreciable racemisation, thus :

$$\begin{array}{ccc} \underset{\text{Me}}{\overset{\text{Ph}}{>}}C\underset{\text{H}}{\overset{\text{Cl}}{<}} & \xleftarrow[\text{pyridine}]{\text{by PCl}_3 \text{ and}} \underset{\text{Me}}{\overset{\text{Ph}}{>}}C\underset{(-)}{\overset{\text{H}}{<}}\text{OH} & \xrightarrow{\text{by SOCl}_2} \underset{\text{Me}}{\overset{\text{Ph}}{>}}C\underset{\text{Cl}}{\overset{\text{H}}{<}} \\ [a]_{5461} +61\cdot4°. & & [a]_{5461} -63\cdot3°. \\ (\text{K., L., and P.}) & & (\text{McK. and C.}) \end{array}$$

According to Kenyon and his colleagues, the interaction of thionyl chloride and hydroxyl compounds with a phenyl group directly attached to the asymmetric carbon atom is unaccompanied by configurational change. On this view a complete Walden inversion must have occurred in the interaction of phosphorus trichloride and the (—)alcohol in the presence of pyridine.

The present authors (this vol., p. 32) have already contrasted the displacement of hydroxyl by chlorine in the isomeric (—)menthyl α-naphthylglycollates with that in the corresponding mandelates, and certain points of difference emerged. Incidentally, the action of thionyl chloride (alone and in the presence of pyridine) and also of phosphorus pentachloride on the optically active ethyl α-naphthylglycollates has been investigated, and the results are now described.

Unexpected difficulties were encountered, as the preparation of the (+)ethyl ester by the use of mineral acid gave products of different rotatory powers. This was not due to the action of heat (cf. " Experimental "). It was recognised, however, that racemisation can be induced by mineral acids (cf., *inter alia*, Fitger, " Racemisierungserscheinungen," Lund, 1924; McKenzie and Dennler, *Ber.*, 1927, **60**, 220; Roger and McKenzie, *Ber.*, 1929, **62**, 272; Wagner-Jauregg, *Monatsh.*, 1929, **53** and **54**, 791), and, accordingly, the dextrorotatory ethyl ester was refluxed for several hours in the presence of a small amount of sulphuric acid; its rotatory power then fell. This behaviour is exceptional, and must be attributed to the presence of the α-naphthyl group. Accordingly, recourse was had to the method of ester formation through the silver salt, and the rotations of various samples of the ethyl ester were then concordant. This procedure was, however, adopted with some misgivings. In the light of Purdie's results on the interaction of silver lactates, etc., and alkyl halides the possibility of the formation of small amounts of ethoxy-ester, $C_{10}H_7 \cdot CH(OEt) \cdot CO_2Et$, was not excluded, but we were unable to detect the presence of any of this in our products.

Table I gives a summary of the rotatory powers of the ethyl α-naphthylchloroacetates and of their mixtures with unattacked ethyl (+)α-naphthylglycollate. The percentages of chloro-ester in the mixtures were calculated from the percentages of chlorine which they contained.

TABLE I.

*The Specific Rotatory Powers (in Acetone) of Ethyl α-Naphthylchloroacetates obtained by the Halogenation of Ethyl (+)α-Naphthylglycollate.**

| Halogenating agent.	Pyridine.	$[a]_{5893}$ of hydroxy-ester.	$[a]_{5893}$ of chloro-ester.	% Chloro-ester in the product.
SOCl$_2$, 6 mols.	None	+132·9°	+60°	100
SOCl$_2$, 6 mols.	None	+129	+57	100
SOCl$_2$, 6 mols.	2 mols.	+132·9	+ 1	100
SOCl$_2$, 2 mols.	2 mols.	+132·9	+79	41
SOCl$_2$, 6 mols.	3 mols.	+129	+27	92
SOCl$_2$, 4 mols.·	12 mols.	+129	+32	69
PCl$_5$, 1·5 mols.	None	+129	− 6	93

* Some of the experiments were performed with the (—)ester, but for uniformity the results of those are expressed in the table as if the (+) ester were used.

On contrasting these results with those obtained from ethyl (—)mandelate, we find, first,

that phosphorus pentachloride causes reversal of the sign of rotation, but to a much less extent than with the mandelate. The action of thionyl chloride alone gives a chloro-ester of the same sign as the original hydroxy-ester, the behaviour being thus similar to that of the mandelate. In the presence of pyridine the behaviour of the α-naphthylglycollate and the mandelate is, however, different, the sign of rotation of the former not even being reversed, although nearly so when the chlorination is complete. A perusal of the results in Table I suggests that pyridine, so far from acting as an accelerating agent, actually retards the velocity of the halogenation, since with the excess of pyridine the product contains some unattacked hydroxy-ester; possibly the swing round of sign might actually have occurred if 1 mol. of pyridine only had been used. That pyridine may act as a retarding agent receives some support from our observation that it forms an additive *compound* with thionyl chloride, $(C_5H_5N)_2,SOCl_2$. A similar complex with carbonyl chloride is known (Morel, *Bull. Soc. chim.*, 1899, **21**, 823).

Ethyl (+)α-naphthylchloroacetate undergoes partial racemisation when distilled under diminished pressure, as also does ethyl (−)α-naphthylglycollate under the influence of alcoholic alkali.

The formation of (+)amyl chloride from (−)amyl alcohol and thionyl chloride takes place through the intermediate formation of (+)amyl chlorosulphinate, which loses sulphur dioxide when heated at 120° under ordinary pressure (McKenzie and Clough, J., 1913, **103**, 687) :
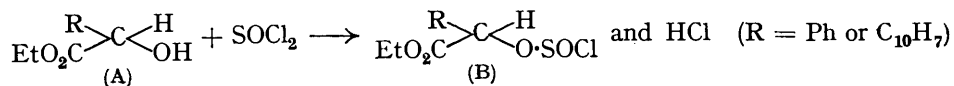
$$(-)C_5H_{11}\cdot OH \longrightarrow (+)C_5H_{11}\cdot O\cdot SOCl \longrightarrow (+)C_5H_{11}Cl$$
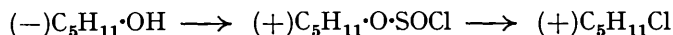
Unfortunately, the analogous compounds could not be isolated by the action of thionyl chloride either on ethyl (−)mandelate or on ethyl (−)α-naphthylglycollate, but it seems certain that they are actually formed as intermediate phases in each of those actions, and the interpretation advanced by Kenyon, Lipscomb, and Phillips (*loc. cit.*) is based on this assumption in the case of the mandelate (cf. also Kenyon and Phillips, J., 1930, 1676; *Trans. Faraday Soc.*, 1930, **26**, 451; Kenyon, Phillips, and Taylor, J., 1931, 382; Kenyon, Lipscomb, and Phillips, J., 1931, 2275; Houssa and Phillips, J., 1932, 108). When the halogenation was conducted in the presence of pyridine, an unstable pyridinium chloride (I) was supposed to be formed. During the decomposition of this complex, the carbinyl group separates as a positive carbonium ion, and the entering chloro-group exists as a negative ion, a Walden inversion occurring when the chlorine has become attached (cf. Meer and Polanyi, *Z. physikal. Chem.*, 1932, *B*, **19**, 182). On the other hand, in the absence of pyridine the chlorosulphinate (II) loses sulphur dioxide, and the electron-

(I.) $\begin{array}{c} Ph \\ EtO_2C \end{array}\!\!>\!\!C\!\!<\!\!\begin{array}{c} H \\ O \end{array}\!\!-\!\!\overset{\bar{O}}{\underset{+}{S}}\!\!-\!\!\overset{+}{N}\cdot C_5H_5 \\ \underset{Cl}{\overset{-}{|}}$

(II.) $\begin{array}{c} Ph \\ EtO_2C \end{array}\!\!>\!\!C\!\!<\!\!\begin{array}{c} H \\ O\cdot SOCl \end{array}$
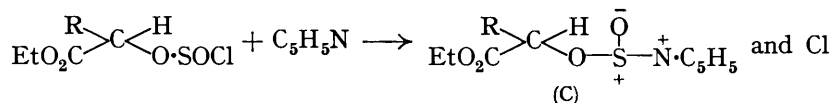
attracting phenyl group enables the mandelyl radical to separate as an anion and subsequently to combine with a chlorine kation. Under these conditions there is no Walden inversion. Kenyon and his colleagues thus reach the conclusion that ethyl (−)phenyl-chloroacetate has the same configuration as ethyl (−)mandelate, and that there is no configurational change in the action examined by McKenzie and Barrow. The identical conclusion had previously been arrived at by Clough (*loc. cit.*) from an entirely different standpoint.

We prefer the following interpretation to that advanced above, and base it on the following considerations.

(1) *Addition precedes substitution*, e.g., in the action of thionyl chloride alone on ethyl (−)mandelate or on ethyl (−)α-naphthylglycollate :

$$\begin{array}{c} R \\ EtO_2C \end{array}\!\!>\!\!C\!\!<\!\!\begin{array}{c} H \\ OH \end{array} + SOCl_2 \longrightarrow \begin{array}{c} R \\ EtO_2C \end{array}\!\!>\!\!C\!\!<\!\!\begin{array}{c} H \\ O\cdot SOCl \end{array} \text{ and HCl} \quad (R = Ph \text{ or } C_{10}H_7)$$
$$(A)(B)$$

and in the presence of pyridine,

$$\underset{EtO_2C}{\overset{R}{>}}C\underset{O\cdot SOCl}{\overset{H}{<}} + C_5H_5N \longrightarrow \underset{EtO_2C}{\overset{R}{>}}C\underset{O-S-\overset{+}{N}\cdot C_5H_5}{\overset{H}{<}}\overset{\bar{O}}{\underset{+}{|}} \text{ and Cl}$$

(C)

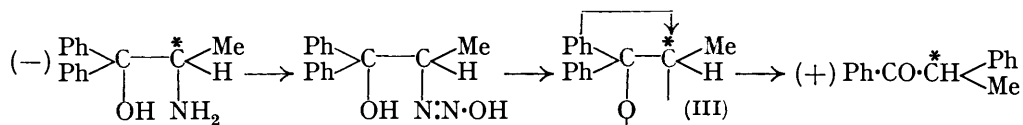(or, in place of C, some other complex with pyridine).

(2) *An optically active structure containing a tervalent carbon atom can possess a transient existence without losing its optical activity.* This hypothesis was suggested by Biilmann (*Annalen*, 1912, **388**, 330), and at the time was criticised adversely by McKenzie and Clough (*loc. cit.*). In order to visualise a " Zwitterion " of the nature postulated by Biilmann, the suggestion was made by McKenzie and Clough that the carbon atom is situated at the apex of a tetrahedron and the three other groups at the corners (cf. Ebel in Freudenberg's " Stereochemie," 1932, 661). There was no experimental evidence in 1912 that an optically active compound could be depicted in this manner.

The idea that an optically active complex with a tervalent carbon atom is capable of a transient existence must now, however, be taken seriously in the light of the evidence which has gradually been accumulating in its favour. Thus, McKenzie, Drew, and Martin (J., 1915, **107**, 26) found that (−)phenylchloroacetic acid could be converted into (+)diphenylsuccinic acid by the action of phenylmagnesium bromide,

$$(-)C_6H_5\cdot CHCl\cdot CO_2H \longrightarrow (+)\overset{C_6H_5\cdot CH\cdot CO_2H}{\underset{CO_2H\cdot CH\cdot C_6H_5}{}},$$
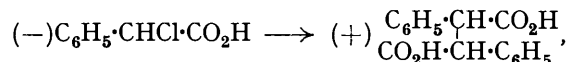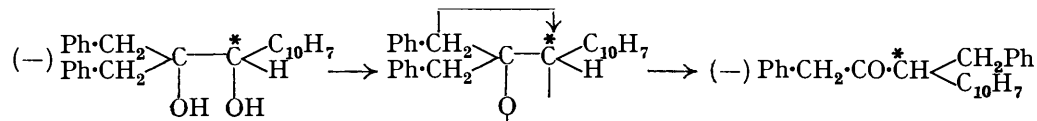
an example of the coupling action of the Grignard reagent (cf. Fuson and Ross, *J. Amer. Chem. Soc.*, 1933, **55**, 720 and previous papers). It is possible that the withdrawal of the halogen is associated with the intermediate formation of the optically active phenylcarboxymethyl.

The first example of the retention of optical activity during the semipinacolinic deamination of certain amino-alcohols was depicted on the lines : †

$$(-)\underset{Ph}{\overset{Ph}{>}}C-\overset{*}{\underset{|}{C}}\underset{H}{\overset{Me}{<}} \longrightarrow \underset{Ph}{\overset{Ph}{>}}C-\underset{|}{C}\underset{H}{\overset{Me}{<}} \longrightarrow \underset{Ph}{\overset{Ph}{>}}C-\overset{*}{\underset{|}{C}}\underset{H}{\overset{Me}{<}} \longrightarrow (+)\,Ph\cdot CO\cdot\overset{*}{C}H\underset{Me}{\overset{Ph}{<}}$$
$$\underset{OH\quad NH_2}{}\qquad\underset{OH\quad N{:}N\cdot OH}{}\qquad\underset{O\quad (III)}{}$$

This implies that an optically active carbonium ion can exist in the free state, and that an intramolecular Walden inversion can take place, since the (+)methyldeoxybenzoin may not have the same configuration as the (−)amino-alcohol from which it is derived. The C* atom in (III) has three dissimilar groups attached to it. In the same paper (McKenzie, Roger, and Wills, J., 1926, 779) it is suggested that the optically active methylethylthetine ion (Pope and Peachey, J., 1900, **77**, 1072) and the optically active ethyl *p*-toluenesulphinate (Phillips, J., 1925, **127**, 2552) have each an electric charge which plays the part of a group. The retention of optical activity in semipinacolinic transformation has been observed not only with amino-alcohols but also with glycols (McKenzie and Dennler, *Ber.*, 1927, **60**, 220; Roger and McKenzie, *Ber.*, 1929, **62**, 272), thus :

$$(-)\underset{Ph\cdot CH_2}{\overset{Ph\cdot CH_2}{>}}C-\overset{*}{\underset{|}{C}}\underset{H}{\overset{C_{10}H_7}{<}} \longrightarrow \underset{Ph\cdot CH_2}{\overset{Ph\cdot CH_2}{>}}C-\overset{*}{\underset{|}{C}}\underset{H}{\overset{C_{10}H_7}{<}} \longrightarrow (-)\,Ph\cdot CH_2\cdot CO\cdot\overset{*}{C}H\underset{C_{10}H_7}{\overset{CH_2Ph}{<}}$$
$$\underset{OH\quad OH}{}\qquad\underset{O}{}$$

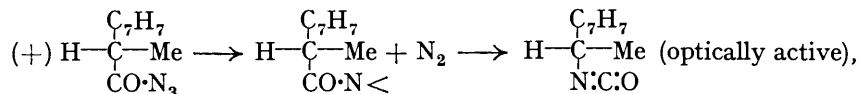In the same category as the latter reaction might also be included the conversion of tetra-

† Other interpretations have been submitted by Freudenberg (*Sitzungsber. Heidelberger Akad. Wissenschaft.*, 1927, *A*, p. 1), and by Kenyon, Lipscomb, and Phillips (*loc. cit.*).

methyl (+)catechin into an optically active chloride (Freudenberg, Carrara, and Cohn, *Annalen*, 1925, **446**, 87) by a sort of pinacolin transformation :
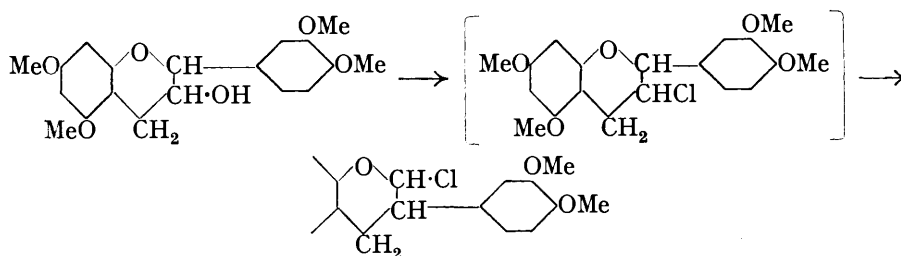
Again, R. Kuhn and Albrecht (*Ber.*, 1927, **60**, 1297) showed that the rotation of (+)2-nitro-butane, $\underset{Et}{\overset{Me}{>}}C\underset{NO_2}{\overset{H}{<}}$, did not disappear when the hydrocarbon was converted into the sodium salt, the ion of *aci*-2-nitrobutane being represented as $\underset{Et}{\overset{Me}{>}}\overset{-}{C}\!\!=\!\!\overset{+}{N}\underset{O}{\overset{O}{<}}$ (cf. Shriner and Young, *J. Amer. Chem. Soc.*, 1930, **52**, 3332; Shriner and Parker, *ibid.*, 1933, **55**, 766). More speculative is the remark of Levene (*Science*, 1927, **66**, 561) that optically active propylene oxide undergoes Walden inversion on hydrolysis with acids, when the free radical O—CH_2—CH—CH_3 has an independent existence for a finite, even though infinitesimal, interval of time.

Notable contributions on the experimental side are provided by other American workers. Thus, Jones and Wallis (*J. Amer. Chem. Soc.*, 1926, **48**, 169) describe the ready transformation of (+)benzylmethylacetazide into an optically active *iso*cyanate,

$$(+)\ H—\underset{CO\cdot N_3}{\overset{C_7H_7}{\underset{|}{\overset{|}{C}}}}—Me \longrightarrow H—\underset{CO\cdot N<}{\overset{C_7H_7}{\underset{|}{\overset{|}{C}}}}—Me + N_2 \longrightarrow H—\underset{N\!\!:\!\!C\!\!:\!\!O}{\overset{C_7H_7}{\underset{|}{\overset{|}{C}}}}—Me \text{ (optically active),}$$

where it was considered that the optically active complex $CHMe\cdot C_7H_7$ existed momentarily as a positive radical, which is of the nature of a carbonium ion, and which maintained a configuration required to preserve optical activity in migrating from carbon to nitrogen when it leaves behind the electron it shared with the carbon atom. It is also suggested by the same authors that, in the change $(+)\underset{Me}{\overset{Ph}{>}}C\underset{OH}{\overset{H}{<}}\overset{\text{by }SOCl_2}{\longrightarrow}(+)\underset{Me}{\overset{Ph}{>}}C\underset{Cl}{\overset{H}{<}}$ (McKenzie and Clough, *loc. cit.*), the complex CHMePh exists as a free positive carbonium ion (cf. Wallis, *J. Amer. Chem. Soc.*, 1929, **51**, 2982; 1931, **53**, 2253).

(+)α-Benzylpropionamide (Wallis and Nagel, *J. Amer. Chem. Soc.*, 1931, **53**, 2787) also undergoes the Hofmann rearrangement, and the resulting amine hydrochloride is optically active : *

$$(+)H—\underset{CO\cdot NH_2}{\overset{C_7H_7}{\underset{|}{\overset{|}{C}}}}—Me \longrightarrow (+)H—\underset{NH_2,HCl}{\overset{C_7H_7}{\underset{|}{\overset{|}{C}}}}—Me$$
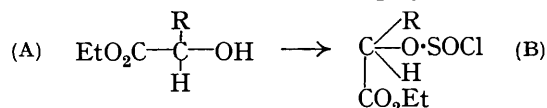
Finally, in the recent work of one of us with Drs. Mitchell and Ritchie (*Biochem Z.*, 1929, **208**, 456 and subsequent papers) on the connexion between asymmetric synthesis and asymmetric induction it is suggested with reserve that the α-carbonyl group in (—)menthyl benzoylformate, *e.g.*, may assume a dissymmetrical environment, although in such cases there is no possibility of the actual separation of a carbonium ion.

(3) *The stereochemical environment of the group* $\underset{EtO_2C}{\overset{R}{>}}C\!\!\diagup^{\!H}$ *is different in* (*A*), (*B*), *and* (*C*). In the course of his interpretation of the Walden inversion, Gadamer (*J. pr.*

* After the present paper was submitted for publication, Wallis and Dripps (*J. Amer. Chem. Soc.*, 1933, **55**, 1701) showed that the Lossen rearrangement of an optically active hydroxamic acid yields an optically active rearrangement product.

Chem., 1913, **87**, 344) discusses the displacement of chlorine by hydroxyl by means of silver oxide. The chlorine is not at once liberated by the influence of the kation, but is first *drawn away* from the asymmetric carbon atom, the position of the three remaining groups relatively to this atom being altered. On this idea, as well as on that of Werner, is based Meisenheimer's interpretation of the Walden inversion (*Annalen*, 1927, **456**, 126; cf. Freudenberg and Lux, *Ber.*, 1928, **61**, 1085) where the distortion of the tetrahedral environment is altered when a group is displaced.

(4) When the $-O \cdot SOCl$ group is substituted for the hydroxyl group in (A), the forces of attraction or repulsion of the three remaining groups attached to the asymmetric carbon atom are altered, and distortion takes place as postulated by Meisenheimer (cf. W. Kuhn and Freudenberg, "Drehung der Polarisationsebene des Lichtes," 1932, p. 9). The distance from the asymmetric carbon atom of the $-O \cdot SOCl$ group in (B) is different from that of the hydroxyl in (A). It may be nearer or it may be further away, and on the latter assumption we have this " distance factor " displayed in the structures,

$$\text{(A)} \quad EtO_2C-\underset{\underset{H}{|}}{\overset{\overset{R}{|}}{C}}-OH \quad \longrightarrow \quad \underset{CO_2Et}{\overset{R}{\underset{|}{C}}} \diagdown^{O \cdot SOCl} \quad \text{(B)}$$
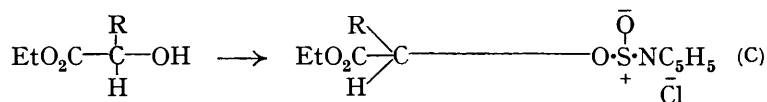
It must be emphasised, however, that (1) in (A) the groups are not arranged as if they were attached at the corners of a *regular* tetrahedron, and (2) the structure of (B) is not pyramidal, *the tetrahedral environment being retained in the formation of the chloride*. The chlorine takes the place of the hydroxyl, the configuration of the original ester is maintained, and there is no Walden inversion.

In the case of the ethyl $(-)$mandelate this interpretation would account for the main trend of the reaction which gives the $(-)$chloro-ester. But McKenzie and Barrow did not obtain an optically pure product, the amount of antimeride present being, however, small. There are valid grounds for drawing the conclusion that the presence of a small amount of $(+)$chloro-ester in the product is to be attributed to the racemising effect on the $(-)$mandelate of the hydrogen chloride present during the action with thionyl chloride, and especially so since mineral acids cause partial racemisation of ethyl $(+)\alpha$-naphthylglycollate, and Ott (*Annalen*, 1931, **488**, 186) has shown that profound racemisation takes place when $(+)$phenylmethylcarbinol is acted on by hydrogen chloride. In this connexion it is significant that a perusal of the recorded optical data for ethyl $(-)$mandelate prepared by the Fischer–Speier method shows that figures are quoted which are by no means uniform. It is conceivable, therefore, that ethyl $(-)$mandelate may undergo slight racemisation under the influence of hydrogen chloride, and we propose to examine this experimentally later. Meanwhile, attention may be directed to the fact that some optically active esters are known to undergo partial racemisation under the influence of halogen ions, and the mechanism of such actions has been discussed by Holmberg (*J. pr. Chem.*, 1913, **88**, 553) and by Wagner-Jauregg (*Monatsh., loc. cit.*).*

With regard to the action of thionyl chloride both on $(+)$phenylmethylcarbinol and on ethyl $(+)\alpha$-naphthylglycollate we have no experimental evidence that any racemisation had taken place.

(5) The distortion of the tetrahedral environment is different in (B) and (C) and the groups R, CO_2Et, and H in (C) have now taken up a configuration antimeric to that in (A) and (B). Owing to the greater pull exerted by the pyridine complex as compared with that of the $-O \cdot SOCl$, the molecule is turned inside out, a mechanism which does not appear to us as incongruous. Such a transformation can readily be pictured without the groups R, CO_2Et, and H having become coplanar at any stage of the transition.

$$EtO_2C-\underset{\underset{H}{|}}{\overset{\overset{R}{|}}{C}}-OH \quad \longrightarrow \quad EtO_2C\diagdown\underset{H\diagup}{\overset{R\diagdown}{C}}\!-\!\!-\!\!-\!\!-\!\!-O \cdot \overset{\bar{O}}{\underset{+}{S}} \cdot NC_5H_5 \quad \text{(C)}$$
$$\overset{}{\underset{\bar{Cl}}{}}$$

* Meisenheimer's suggestion on the mechanism of halogenation by thionyl chloride implies that the free hydrogen chloride adds on to the sulphinate (*Annalen*, 1930, **479**, 238).

In (C) the linking between the asymmetric carbon atom and oxygen is then severed, and the tervalent complex is then antimeric to that obtained from (B). A complete Walden inversion may have occurred when ethyl (—)mandelate was acted on by thionyl chloride and pyridine. As already mentioned, however, the behaviour of ethyl (+)α-naphthylglycollate is very different, because on complete chlorination approximately equal amounts of the (+) and (—)chloro-esters are formed, and we interpret this result as follows. Two separate reactions are involved, the pyridinium complex not being the sole product present before the sulphur dioxide is eliminated, but the sulphinate is also present. On elimination of sulphur dioxide, a mixture of (+) and (—)chloro-compounds is therefore formed. The proportion of (+) and (—)chloro-esters formed from ethyl (+)α-naphthylglycollate by thionyl chloride in the presence of pyridine clearly depends on the velocity of the reaction, which will be modified by changes in concentration and temperature (cf. Ott, *loc. cit.*).

The above hypothesis differs from those of Meisenheimer (*loc. cit.*) and of Holmberg (*Ber.*, 1926, **59**, 125; *Svensk Kem. Tidskr.*, 1927, **39**, 1), which are also based on " distance " effects. It also differs from that of Rördam (J., 1928, 2447; 1929, 1282; 1930, 2017; 1932, 2931), who assumes that, after one group has been split off from the optically active molecule, the remaining complex oscillates between the two possible extremes corresponding with the *d*- and *l*-configurations, each of which will produce only one of the two possible antimerides by the addition of a new radical.

EXPERIMENTAL.

Racemisation Phenomena during the Esterification of (+)α-*Naphthylglycollic Acid by the Fischer–Speier Method.*—The first observation in this connexion was made when we esterified (+)α-naphthylglycollic acid (McKenzie and Dennler, *Ber.*, 1927, **60**, 220; McKenzie and Gow, this vol., p. 32) with MeOH in the presence of conc. H_2SO_4. The resulting methyl ester boiled sharply at 215°/24 mm., and gave $[\alpha]_{5893}^{18°} + 106.2°$ ($c = 1.088$) in acetone, a value which is considerably lower than that of McK. and D., who also used H_2SO_4 as the catalyst, and record $[\alpha]_{5893}^{16°} + 146°$ ($c = 1.5816$) in acetone.

Discrepant values for the rotation in acetone were also noted when the ethyl ester (b. p. 203—204°/18 mm.) of the (+)acid was prepared on two occasions in the presence of conc. H_2SO_4; the first specimen gave $[\alpha]_{5893}^{20.5°} + 114.3°$ ($c = 3.1355$), and the second $[\alpha]_{5893}^{20.5°} + 57.3°$ ($c = 2.5224$). Since the latter ester did not change in rotation after distillation under diminished press., the low value could not be attributed to racemisation by heat. 1.2 G. of this ester were accordingly dissolved in EtOH (6 c.c.) and conc. H_2SO_4 (0.4 g.), and refluxed for 4 hr., the recovered ester having only $[\alpha]_{5893} + 28.2°$ ($c = 1.0788$) in acetone. Apparently the mineral acid caused the partial racemisation.

When the ethyl ester was prepared by the hydrogen chloride method, it had a slightly higher rotation than that observed on any occasion when H_2SO_4 was used, the values for two separate preparations being $[\alpha]_{5893}^{20°} + 120.4°$ ($c = 1.1965$) and $+ 122.2°$ ($c = 1.289$) in acetone. The ester (1.5 g.) with $[\alpha]_{5893} + 120.4°$ was refluxed with a mixture of EtOH (8 c.c.) and conc. H_2SO_4 (0.8 g.), and the recovered ester was found to have only $[\alpha]_{5893}^{20°} + 99°$ ($c = 1.077$).

Preparation of the Ethyl Esters by the Silver Salt Method.—Ethyl (+)α-naphthylglycollate, prepared by the interaction of silver (+)α-naphthylglycollate (15 g.) and EtI (45 g.), is an oil, b. p. 203°/18 mm. Yield, 8 g. (Found : C, 73.3; H, 6.3. $C_{14}H_{14}O_3$ requires C, 73.1; H, 6.1%). In acetone ($l = 2$, $c = 3.0425$, $t = 20°$) :

λ	6708	6563	6162	5893	5461	5106	4861
α	+ 5.93°	+ 6.32°	+ 7.25°	+ 8.09°	+ 9.63°	+ 11.47°	+ 12.96°
[α]	+97.5°	+103.9°	+119.1°	+132.9°	+158.3°	+188.5°	+213.0°

Two other prepns. gave yields of 75% of the theoretical, and the rotations were $[\alpha]_{5893}^{20°} + 132.7°$ ($c = 2.57$) and $[\alpha]_{5893}^{20°} + 132.2°$ ($c = 1.286$) in acetone. The enantiomorphous ethyl (—)α-naphthylglycollate, also prepared by the silver salt method, had $[\alpha]_{5893} - 129°$ ($c = 1.05$) in acetone, and was thus approximately optically pure.

Action of Thionyl Chloride on the Optically Active Ethyl Esters.—12 G. of $SOCl_2$ (6 mols.) were added to a solution of 3.9 g. of ethyl (+)α-naphthylglycollate (1 mol.) in 3 c.c. of Et_2O, and the mixture heated on the steam-bath for ½ hr. The excess of $SOCl_2$ was removed under

diminished press. at room temp., the Et_2O solution of the product washed with H_2O and dried, and the oil obtained from it kept in vac. until const. in wt.

Ethyl (+)α-naphthylchloroacetate is a mobile oil (Found : Cl, 14·3. $C_{14}H_{13}O_2Cl$ requires Cl, 14·3%). In acetone : $l = 2$, $c = 1·959$, $\alpha_{5893}^{20·7°} + 2·35°$, $[\alpha]_{5893}^{20·7°} + 60·0°$. It has b. p. 180—182°/7 mm., and, when distilled twice at 7 mm., it underwent partial racemisation (Found : Cl, 14·2%) ; in acetone, $l = 2$, $c = 1·7095$, $\alpha_{5893}^{20·5°} + 0·56°$, $[\alpha]_{5893}^{20·5°} + 16·4°$. The rotation dropped further after a third distillation, when the product (b. p. 170—172°/3 mm.) gave in acetone : $l = 2$, $c = 2·232$, $\alpha_{5893}^{21·5°} + 0·19°$, $[\alpha]_{5893}^{21·5°} + 4·3°$.

A similar behaviour was exhibited with the chloro-ester obtained by keeping a solution of ethyl (—)α-naphthylglycollate (with $[\alpha]_{5893} - 129°$ in acetone) in $SOCl_2$ at room temp. for 10 days, and then refluxing it for 5 min. The resulting chloro-ester (Found : Cl, 14·2%) gave $[\alpha]_{5893}^{20·5°}$ in acetone $- 57·3°$ ($c = 1·9465$).

Action of Thionyl Chloride on the Optically Active Ethyl Esters in the Presence of Pyridine.—*Expt.* 1. 12 G. of $SOCl_2$ (6 mols.) were added gradually to a solution of 3·9 g. of ethyl (+)α-naphthylglycollate (1 mol.) in a mixture of 2·7 g. of pyridine (2 mols.) and Et_2O (25 c.c.). A white solid separated immediately, but it was converted into an orange-coloured oil when the mixture was heated for 1 hr., the solution becoming dark red. H_2O was added, and the Et_2O extract washed with dil. HCl, then with H_2O, and dried. The resulting oil was kept in vac. until const. in wt. (Found : Cl, 14·3. Calc., 14·3%). Its solution in acetone was practically inactive : $l = 2$, $c = 1·6495$, $\alpha_{5893}^{16°} + 0·04°$.

Expt. 2. 4·2 G. of ethyl (+)α-naphthylglycollate (1 mol.), 2·9 g. of pyridine (2 mols.), 4·3 g. of $SOCl_2$ (2 mols.), Et_2O (20 c.c.). Heating, 30 min. The Et_2O solution was decanted from the orange-coloured oil, and gave an oil with $[\alpha]_{5893}^{20°} + 79·2°$ ($c = 1·761$). The oil underwent partial racemisation when distilled at 185—190°/18 mm., giving only $[\alpha]_{5893}^{20°} + 29·0°$ ($c = 1·674$) in acetone, and containing only 41% of the chloro-ester.

When the orange-coloured oil was mixed with Et_2O and cooled to $- 15°$, it solidified in cryst. plates [Found : Cl, 26·0. $(C_5H_5N)_2,SOCl_2$ requires Cl, 25·6%]. This *compound* also separated from a solution of 11·4 g. of pyridine and 9·4 g. of $SOCl_2$ to which an excess of Et_2O had been added. When an attempt to chlorinate ethyl (+)α-naphthylglycollate by means of this complex was made in $CHCl_3$ solution, the ester was recovered unchanged.

Expt. 3. 3·5 G. of ethyl (—)α-naphthylglycollate (1 mol.), 2·4 g. of pyridine (2 mols.), 10 g. of $SOCl_2$ (6 mols.), Et_2O (20 c.c.). A white solid was deposited. The mixture was kept at room temp. for 10 min., then at 30° for 15 min., and boiled for 5 min. After 24 hr., 1·2 g. more of pyridine were added. Two days later, the mixture was heated for 15 min., and H_2O added. The product gave in acetone $[\alpha]_{5893}^{20°} - 27·2°$ ($c = 2·3165$), and after distillation in vac. $[\alpha]_{5893} - 9·9°$ ($c = 1·7655$). The latter oil both before and after distillation contained 92% of the chloro-ester.

Expt. 4. 2·2 G. of ethyl (—)α-naphthylglycollate (1 mol.), 9·2 g. of pyridine (12 mols.), 4·6 g. of $SOCl_2$ (4 mols.), Et_2O (25 c.c.). As before, a white solid separated. Room temp. 24 hr. ; on steam-bath for 15 min. The ethereal solution decanted from the oil gave, after washing with dil. HCl, an ester mixture (not distilled) with $[\alpha]_{5893}^{20°} - 32·2°$ ($c = 1·9715$) in acetone. This contained 69% of chloro-ester.

The ethyl (+)hydroxy-ester (1·7 g.) was refluxed with pyridine (7 g.) for 4 hr., and was recovered with no fall in its rotatory power.

Action of Phosphorus Pentachloride on Ethyl (—)α-Naphthylglycollate.—5·2 G. of PCl_5 (1·5 mols.) were added gradually to a solution of 3·9 g. of the ester (1 mol.) in 15 c.c. of $CHCl_3$. After heating on the water-bath for 2 hr., the solution was washed with H_2O and dried, the resulting oil being kept in vac. until const. in wt. (Found : Cl, 13·3%). In acetone : $l = 2$, $c = 2·4965$, $\alpha_{5893}^{21·5°} + 0·31°$, $[\alpha]_{5893}^{21·5°} + 6·2°$. After distillation in vac., the oil (Found : Cl, 13·5. Calc., 14·3%) gave in acetone : $l = 2$, $c = 2·6375$, $\alpha_{5893}^{20°} + 0·21°$, $[\alpha]_{5893}^{20°} + 4·0°$.

Racemisation of Ethyl (+)α-Naphthylglycollate.—The ester used had $[\alpha]_{5893} + 114·3°$ ($c = 3·1358$) in acetone. 6 Drops of alc. KOH ($0·89N$) were added to an alc. solution of the ester with $l = 2$, $c = 4·21$, $\alpha_{5461}^{20°} + 14·35°$, $[\alpha]_{5461}^{20°} + 170·4°$. The dextrorotation gradually fell so long as the solution was alkaline.

Time	20 min.	40 min.	1 hr.	4 hr.	5 hr.
$\alpha_{5461}^{20°}$	+14·19°	+14·11°	+14·07°	+13·91°	+13·83° (solution neutral)

After 24 hr. the addition of 6 drops of alc. KOH caused a further fall to + 13·39° during 5 hr. and the solution had then again become neutral. The further addition of a few drops of alc. KOH caused the rotation to fall still further. The catalytic racemisation of ethyl (—)man-

delate with $l = 2$, $c = 3.68$, $\alpha_{5461}^{20^\circ} - 9.54°$ in EtOH was examined under comparable conditions. Apparently this ester undergoes saponification more quickly than does the α-naphthyl homologue, since the solution was neutral after 25 min., the rotation falling to $- 9.43°$ after 10 min. and remaining const. On the addition of 6 drops more alc. KOH, the solution was neutral after 45 min., the rotation then being $- 9.22°$.

As was anticipated, the complete saponification of ethyl $(+)\alpha$-naphthylglycollate (0.5 g.) with excess of alc. KOH (4 c.c. of $0.89N$; calc., 2.4 c.c.) gave a partially racemised α-naphthylglycollic acid with $[\alpha]_{5893}^{20^\circ} + 158°$ ($c = 0.766$), whereas the optically pure acid has $[\alpha]_{5893}^{20^\circ} + 187°$.