505. *Mechanism of Electrophilic Substitution at a Saturated Carbon Atom. Part I.* Scope and Plan. Optical Activity from a Single Asymmetric Carbon Atom bearing a Metal.*

By H. B. Charman, E. D. Hughes, and Sir Christopher Ingold.

The main habitat of this family of substitutions is in the field of organometal chemistry. The conditions inherent in the problem of mechanism are analysed sufficiently to explain the point and plan of attack. The attack is prepared by a necessary auxiliary research to secure, in a simple and typical alkyl compound, stable optical activity due to a single, asymmetric, metal-bearing carbon atom, in the absence of any other asymmetry. This object has been realised by the optical resolution of s-butylmercuric salts. The result determines that the first few studies of substitution mechanism will relate to mercury exchange in the s-butyl series. A classification is therefore presented of mercury exchanges by electrophilic substitution.

(1) *Object of the Series.*—Our concern will be to elucidate the mechanisms generally and normally available for the reactions of electrophilic substitution at saturated carbon. In such substitutions, the in-coming and out-going substituents must be groups which enter into or separate from neutral combination as cations. The available cations comprise hydrogen, and the metals generally, besides a few special non-metallic groups. To study typical aliphatic electrophilic substitution in its main central area, one has to enter the field of organometal chemistry. The metal substituent plays the same part in aliphatic electrophilic substitution as does the halogen substituent or the toluenesulphonate or other oxyester group in aliphatic nucleophilic substitution; the reactions of metal exchange among the metal alkyls correspond to those of halide exchange or similar anion-replacements of alkyl halides or esters; metal acidolysis similarly corresponds to halide or sulphonate hydrolysis or alcoholysis. We shall deal first with metal exchanges: we hope later to report on metal acidolysis.

(2) *Preconceptions as to Mechanism.*—In order to design such an investigation, it is essential to preconceive possible mechanisms of aliphatic electrophilic substitution, and their observable consequences. Our present preconceptions, which may be inadequate, are derived from analogy with aliphatic nucleophilic substitution. We thus expect three mechanisms of substitution, which should be distinguishable, at least partly, by their kinetics and stereochemistry, as follows.

First, with a readily ionisable metal bond in a suitably ionising medium, unimolecular electrophilic substitution (S_E1), a two-step mechanism, which can be formulated

$$\mathrm{R{-}M_1} \xrightarrow[\text{slow}]{} \mathrm{R^-} + \mathrm{M_1^+};\ \mathrm{R^-} + \mathrm{M_2^+} \xrightarrow[\text{fast}]{} \mathrm{R{-}M_2} \quad \ldots\ldots\ldots \quad (S_E1)$$

may be expected. It should exhibit a kinetic form reducible to first-order kinetics in the limit in which the first step is sufficiently little reversed. If RM_1 is optically active by

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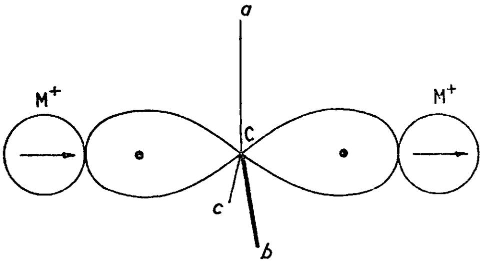
* For a preliminary account, see *Chem. and Ind.*, 1958, 1517. This and the following paper were summarised (by H. B. C.) before the Division of Organic Chemistry at the Amer. Chem. Soc. Meeting at Boston in April 1959.

virtue of asymmetry at the metal-bearing carbon atom, at least some racemisation should accompany substitution; whilst, as to rate, racemisation might either run ahead of, or lag behind substitution, in that limit which excludes both appreciable reversal of the first step and appreciable directive shielding by its products of the second, the two rates could coincide.

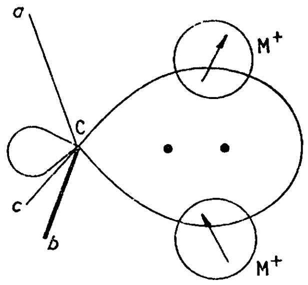
Secondly, with a less readily ionising metal bond, bimolecular electrophilic substitution (S_E2), whose one-step mechanism can be represented by

$$M_2^+ + R{-}M_1 \longrightarrow M_2{-}R + M_1^+ \quad . \; . \; . \; . \; . \; . \; . \; . \; . \quad (S_E2)$$

becomes possible. It should exhibit second-order kinetics if both reactants are in dilute solution. Unlike bimolecular nucleophilic substitution, which always inverts configuration, bimolecular electrophilic substitution might occur in two different stereochemical forms, according to the degree of ionicity developed during substitution. Bimolecular nucleophilic substitution is considered to have uniform stereochemistry because, in the transition state, four electrons compete for the same central orbital, and are best accommodated at that time, two on each side of the central atom. In bimolecular electrophilic substitution, on the other hand, only the two electrons of the original carbon–metal bond occupy the central orbital in the transition state, so more choice is available in their distribution. How they can best be distributed appears to depend on the degree of bond extension, and the correlated degree of bond ionicity, developed in the transition state. If so much bond extension, and such high ionicity, arise that the carbon orbital spreads comparably on both sides of the atom, substitution will take place with inversion, through a transition state such as S_E2(Inv.). If so little bond extension and ionicity arise in the transition state that the electrons of the original metal bond remain nearly where they were, then substitution will occur with retention of configuration, through a transition state such as S_E2(Ret).

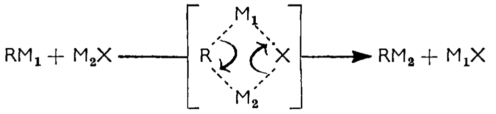


S_E2 (Inv.)



S_E2 (Ret.)

Thirdly, with a not-too-readily ionising bond in the substrate, and also a not-too-ionically-dissociable substituting agent, the internal mechanism of electrophilic substitution (S_Ei) might arise:



$$RM_1 + M_2X \longrightarrow \left[R \overset{M_1}{\underset{M_2}{\rightleftarrows}} X \right] \longrightarrow RM_2 + M_1X \quad . \; . \; . \; . \; . \; . \; . \quad (S_Ei)$$

This mechanism requires second-order kinetics if both reactants are in adequately dilute solution. As with the known internal mechanism of nucleophilic substitution (S_Ni), so with this analogue (S_Ei), it is not important to discuss how far the transition state is constituted covalently or by ion-pairs: what matters is that, however much or little electrostatic its bonds may be, they make it cyclic so that substitution by the internal mechanism retains configuration.

It is obviously possible that these mechanisms, graded as they are in the order in which they are discussed above, with respect to their requirements of ionisation, may shade into one another.

(3) *Optical Activity in Organometallic Compounds.*—With this approach to the problem of mechanism, the possibility of determining stereochemical course by observation of optical activity was too important to be foregone. However, among organometallic compounds optical activity is rare, and for most metals has never been claimed.

Claims have been made, which have been denied, for optical activity centred on carbon bearing an alkali-metal atom [1,2,3] and on carbon bearing magnesium.[4,5] Further studies have shown that optical activity at lithium-bearing carbon is quite unstable, disappearing too quickly to be detected in ordinary conditions,[3,6] although not necessarily too quickly at −70°.[7] It is an agreed conclusion that optical activity at magnesium-bearing carbon in Grignard reagents disappears too quickly to permit detection in any investigated conditions.[5,8]

It is consistent with this record of optical instability in carbon bearing lithium or magnesium, that both s-butyl-lithium and s-butylmagnesium chloride exist, as Wright showed by carbonating them,[9] in optically active forms in solutions in, or containing, (+)-2,3-dimethoxybutane. The interpretation is that the optically active ether co-ordinates with either metal, to form a complex solute molecule which contains asymmetric carbon atoms in permanently optically active form: the asymmetry confers a bias, by asymmetric induction, on the labile asymmetry at the metal-bearing centre. This asymmetric influence persists as long as the ether remains, but optical activity disappears as soon as it is removed. However, by conducting reactions of the metal alkyls in the presence of the ether, asymmetric syntheses have been effected.[10]

Optical activity dependent on a mercury substituent at asymmetric carbon is stable in several cases in which other sites of stable optical activity are simultaneously present in the molecule. Thus Marvel, and also Wright, using a mercuric salt in methyl alcohol as reagent, added the groups HgX and OMe one at each end of an ethylenic double bond, thus creating two new asymmetric carbon atoms; then, having provided further centres of asymmetry in optically active form, as in bornyl, menthyl, and lactate groups, separated diastereoisomers. Marvel and his co-workers used mercuric acetate in reaction with menthyl and bornyl cinnamates,[11] and Wright and his co-workers used mercuric lactate in reaction with cyclohexene.[12] Nesmeyanov, Reutov, and Poddubnaya showed that the direct mercuration, by metallic mercury, of a secondary alkyl halide, which was optically active by virtue only of the asymmetry of its secondary-halide group, led to complete loss of optical activity in the derived halogenomercuric compound.[13] However, when they provided a mercury-bearing asymmetric centre by similar mercuration of a secondary halide, which was optically active owing to independent centres of asymmetry,

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[1] Schlenk and Bergmann, *Annalen*, 1928, **463**, 98; Wright, *J. Amer. Chem. Soc.*, 1939, **61**, 2106.

[2] Wallis and Adams, *J. Amer. Chem. Soc.*, 1933, **55**, 3838.

[3] Wittig, Vidal, and Bohnert, *Ber.*, 1950, **83**, 359.

[4] Mousseron and Jacquier, *Bull. Soc. chim. France*, 1951, C 80.

[5] Goering and McCarron, *J. Amer. Chem. Soc.*, 1958, **80**, 2287.

[6] Tarbell and Weiss, *J. Amer. Chem. Soc.*, 1939, **61**, 1203; Ziegler and Wenz, *Ber.*, 1950, **83**, 354.

[7] Letsinger, *J. Amer. Chem. Soc.*, 1950, **72**, 4842.

[8] Pickard and Kenyon, *J.*, 1911, **99**, 45; Schwartz and Johnson, *J. Amer. Chem. Soc.*, 1931, **53**, 1063; Porter, *ibid.*, 1935, **57**, 1436; Marker, Oakwood, and Crookes, *ibid.*, 1936, **58**, 481; Roberts and Shoppee, *J.*, 1954, 3418.

[9] Cohen and Wright, *J. Org. Chem.*, 1953, **18**, 432; Brook, Cohen, and Wright, *ibid.*, p. 447.

[10] Bharucha, Cohen, and Wright, *J. Org. Chem.*, 1954, **19**, 1097; Alentoff and Wright, *ibid.*, 1957, **22**, 1; *Canad. J. Chem.*, 1957, **35**, 900.

[11] Sandborn and Marvel, *J. Amer. Chem. Soc.*, 1926, **48**, 1409; Griffin and Marvel, *ibid.*, 1931, **53**, 789.

[12] Romeyn and Wright, *J. Amer. Chem. Soc.*, 1947, **69**, 697; cf. Brook and Wright, *Acta Cryst.*, 1951, **4**, 50; Wright. *Ann. New York Acad. Sci.*, 1957, **65**, 436.

[13] Nesmeyanov, Reutov, and Poddubnaya, *Izvest. Akad. Nauk, S.S.S.R., Otdel. khim. Nauk*, 1953, 649.

they could separate diastereoisomers. The compounds thus mercurated and separated were (−)-menthyl α-bromophenylacetate[13] and (+)-α-bromocamphor.[14] In all these cases a permanent asymmetric influence affects the mercury-bearing centre.

(4) *Optical Activity from a Single Asymmetric Carbon Atom bearing a Metal Substituent.*—We know of no previous demonstration of stable optical activity which depends on a single asymmetric carbon atom bearing a metal substituent in the absence of an asymmetric environment (*i.e.*, another asymmetric carbon atom in the same or an associated molecule). However, it is to be inferred from the work of Marvel, Wright, Nesmeyanov, Reutov, and their colleagues that, with mercury as the metal substituent, it ought to be possible to demonstrate stable optical activity deriving from an isolated asymmetric centre involving a metal bond. And it was just such a demonstration, preferably involving as simple and typical an alkyl group as possible, that we required to start our investigations of the stereochemistry and mechanism of electrophilic substitutions which displace a metal from saturated carbon.

We obtained this pre-requisite by resolving the s-butylmercuric ion, $CHMeEtHg^+$: as the next several parts of this series will be concerned with its salts, we describe the resolution here. We have also resolved the 1-phenylethylmercuric ion, $CHMePhHg^+$, for later use.

The s-butylmercuric ion was resolved through the neutral (+)-tartrate, and, more conveniently and completely, through the (−)-mandelate. The rotation of the (+)-tartrate became negative in the less soluble fractions successively obtained by crystallisation from chloroform; its negative value was still increasing after sixteen such crystallisations, when conversion into bromide, $[\alpha]_D^{20}$ −17·7°, showed resolution of the cation to be about three-quarters complete. Resolution through the (−)-mandelate was effected by half-neutralising s-butylmercuric hydroxide with (−)-mandelic acid in acetone–methanol, and crystallising the separated mandelate from acetone. The negative rotation of the bromide, derived from the successive, less soluble crops of mandelate, at first rose rapidly, then more slowly, and then scarcely at all between the fifth and the sixth crystallisation; hence the highest observed rotation of bromide, $[\alpha]_D^{20}$ −24·0°, must be close to the limiting value. From that part of the original s-butylmercuric hydroxide which remained un-neutralised, bromide was regenerated, which had $[\alpha]_D^{20}$ +5·3°; from the more soluble fractions of mandelate, samples of bromide were obtained which had positive rotations up to $[\alpha]_D^{20}$ +18·8°. (All rotations of bromide were measured in acetone, $c \approx 5$ and $l = 1$.) No racemisation or mutarotation was observed in any of these salts.

(5) *Plan of Development of Studies of Mechanism.*—This demonstration of stable optical activity due to an isolated asymmetric centre containing a carbon–mercury bond caused our investigation of electrophilic substitution at saturated carbon to be begun with alkylmercury compounds, where the s-butyl derivatives were available to assist the stereochemical work. We knew that by requiring optical stability, we reduced our chance of observing the highly ionic S_E1 mechanism: we did so to allow a more thorough study of the less ionic S_E2 and the S_Ei mechanisms (cf. Section 2). However, it seemed to us that, if this study succeeded, we could increase the ionising tendency by moving along the alkyl series CHR_2, $CHRAr$, $CHAr_2$, $CH{<}(C{\vdots}C)_2$ (as we have begun to do) and if necessary, change the metal.

The general reactions of alkylmercury compounds on which we expect to report include those in which the original mercury substituent is replaced (*a*) by mercury (from a mercuric salt), and (*b*) by hydrogen (from an acid). Both are electrophilic substitutions. We shall deal with them in this order because the stereochemical study of exchange reactions involves no ancillary investigation to correlate optical rotation with configuration, such as is required when a different element is being introduced by substitution. Mercury exchange (*a*) between alkylmercury compounds and mercuric ions can play the same part in the stereochemical study of electrophilic substitution as iodine exchange between an

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[14] Reutov and Lu Tsin-Chen, *Doklady Akad. Nauk, S.S.S.R.*, 1956, **110**, 575.

alkyl iodide and iodide ions, and also bromine exchange between an alkyl bromide and bromide ions, played in the early stereochemical studies of nucleophilic substitution. The ancillary stereochemical investigation required for study of the acidolysis (*b*) is in hand.

All the exchange reactions (*a*) must be included among the " redistribution reactions " of alkylmercury compounds, which, as their name implies, are commonly pictured as transfers of alkyl groups between mercury atoms.[15] More of these seem to be possible than are known, and we can set down the apparent possibilities. The reactants are always two (repetition being allowed, provided that at least one alkyl group is included) selected from the three types, HgX_2, RHgX, and R_2Hg. The possible transfers are of R with R, and of R with X, that of X with X being trivial, since X is an actual or potential anion. Then there can be only one reaction, if the reactants have only one R between them, necessarily an interchange of R with X. There might be two reactions if the reactants carry two R's altogether, one reaction an interchange of R's, and the other an exchange of R with X. There might also be two reactions if three R's altogether are involved, an exchange of R's, and an exchange of R with X. There could be only one reaction involving four R's, necessarily an interchange of R's. The six possibilities are shown in Scheme 1.

SCHEME 1. *Possible redistribution of alkylmercury compounds.*

	Exchange	Labels			
1R	R *v* X	—	Hg	$\overset{*}{H}gX_2 + RHgX \rightleftharpoons R\overset{*}{H}gX + Hg_2X$	(*a*)
2R's	R's	R	Hg	$R'\overset{*}{H}gX + RHgX \rightleftharpoons R\overset{*}{H}gX + R'HgX$	(*b*)
	R *v* X	—	—	$RHgX + RHgX \rightleftharpoons R_2Hg + HgX_2$	(*c*)
3R's	R's	R	—	$R'HgX + R_2Hg \rightleftharpoons RHgX + RR'Hg$	(*d*)
	R *v* X	R or Hg		$R\overset{*}{H}gX + R_2Hg \rightleftharpoons R_2\overset{*}{H}g + RHgX$	(*e*)
4R's	R's	R	—	$R'_2Hg + R_2Hg \rightleftharpoons RR'Hg + RR'Hg$	(*f*)

Reaction (*c*) is unique in that its factors and products are always different. In reactions (*d*), (*e*), and (*f*) the factors and products are different if the alkyl groups are distinguished. In reactions (*a*) and (*e*) they are different if the mercury atoms are distinguished. In reaction (*b*) they are different if the alkyl groups and the mercury atoms are all distinguished. These conditions of distinction create the necessity for labels. A label distinguishing R can be chemical, stereochemical, or isotopic; a label distinguishing Hg has to be isotopic. The labels indicated in Scheme 1 are those required simply in order to observe that a reaction is occurring. A further label may be needed in order unambiguously to determine which reaction it is. For example, in order to be able to both observe and distinguish reactions (*d*) and (*e*), it is necessary to label both R and Hg.

Reactions (*a*), (*c*), and (*f*) have been described. We have observed a reaction interpretable as (*e*). However, it will now be argued that even these four reactions are not all independent, and certainly that the whole six are not.

The evidence against reaction (*f*) is that mixtures of Me_2Hg and Et_2Hg yield MeEtHg only when an impurity of the form RHgX is present.[16] The apparent redistribution of the dialkyls therefore goes by way of one of the other reactions, presumably, in view of other evidence, *via* (*e*). This other evidence is that we have observed a redistribution stoicheiometrically equivalent, under simple alkyl labelling, either to reaction (*d*) or to reaction (*e*); then, using the criterion of double-labelling as above, we have excluded interpretation in terms of reaction (*d*). These experiments will be included in Part III.[17] This is evidence against the existence of reaction (*d*), because the example was typical, the labels, enantiomeric and isotopic, could have had no kinetic effect, and the two conceivable paths go, as they always would, from the same factors to the same products: reaction (*d*) had every chance to occur, if it ever could, in the inevitable presence of reaction (*e*).

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[15] Gilman, " Organic Chemistry," John Wiley and Sons, New York, 1942, p. 1810.

[16] Calingaert, Beatty, and Soroos, *J. Amer. Chem. Soc.*, 1940, **62**, 1107.

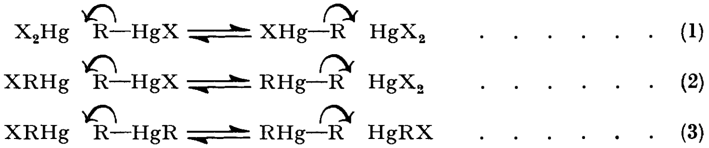
[17] Charman, Hughes, Ingold, and Thorpe, forthcoming paper; Charman, Ph.D. Thesis, London University, 1958.

This is as far as our criticism of the redistribution concept can be carried on the basis of already completed experiments, though we expect that it will be possible to prove that reaction (*b*) is not faster than is provided by the reversible reaction (*c*), which genuinely occurs, as can be shown without labelling, and automatically includes a switch of alkyl groups between labelled mercury atoms, as postulated in reaction (*b*).

It is largely our theoretical outlook which leads us firmly to abolish all three of the alkyl-exchanges (*b*), (*d*), and (*f*). For, when we replace the general redistribution idea by the sharper picture of electrophilic substitution, we obtain a less open choice of reactants. One must function as the substituting agent, which has to have potentially cationic mercury, and must therefore be either HgX_2 or RHgX; the other must be the substrate, which has to be an alkyl compound having mercury to lose, and therefore must be either RHgX or R_2Hg. The set of mercury-exchanges (*a*), (*c*), and (*e*) is necessary and sufficient to include these combinations, which are the only allowed combinations on these principles.

These are the three reactions which mercury exchange is conceived to comprise. They are rewritten as electrophilic substitutions in Scheme 2. We call them the one-alkyl, the two-alkyl, and the three-alkyl mercury-exchanges. They will be severally the subjects of the next three Parts of this series, though not in that order.

SCHEME 2. *Possible electrophilic mercury exchanges.*



$$X_2Hg\ \overset{\curvearrowleft}{R}\text{—}HgX \rightleftharpoons XHg\text{—}\overset{\curvearrowright}{R}\ HgX_2 \quad . . . . . . \quad (1)$$

$$XRHg\ \overset{\curvearrowleft}{R}\text{—}HgX \rightleftharpoons RHg\text{—}\overset{\curvearrowright}{R}\ HgX_2 \quad . . . . . . \quad (2)$$

$$XRHg\ \overset{\curvearrowleft}{R}\text{—}HgR \rightleftharpoons RHg\text{—}\overset{\curvearrowright}{R}\ HgRX \quad . . . . . . \quad (3)$$

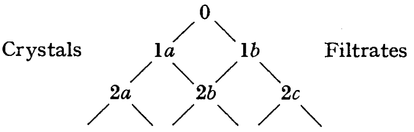
EXPERIMENTAL

(6) *Optical Resolution of s-Butylmercuric Salts.*—(6*a*) *s-Butylmercuric salts.*—The bromide was prepared, and converted into the hydroxide, and thence into the other salts required, as follows.

The Grignard reagent from s-butyl bromide (100 g.) in ether (300 ml.) was added to finely powdered mercuric bromide (300 g.) suspended in ether (250 ml.) at such a rate as to maintain boiling. The mixture thickened considerably, and was stirred strongly during, and for 2 hr. after, the addition. After decomposition of the product with added cold 0·5% aqueous sulphuric acid, the ether layer was separated, and the ether pumped off to leave a white solid, which was crystallised twice from ethanol; yield 197 g. (70%); m. p. 39°.

This bromide (10 g.) in acetone (40 ml.), on treatment with potassium hydroxide (2 g.) in methanol (25 ml.), gave immediately a precipitate, which, after 4 hr. at 0°, was filtered off. The filtrate, evaporated under reduced pressure, left a residue, whose filtered solution in ether (50 ml.) was evaporated under reduced pressure to give a residue of s-butylmercuric hydroxide, suitable for the preparation of other salts. Its solution in acetone, on neutralisation with 0·1N-aqueous hydrochloric acid, gave the chloride as an oil, which solidified at −20°, and, after being twice crystallised from ethanol, formed white crystals, m. p. 28°. The acetone solution of hydroxide, on treatment with 0·2N-aqueous potassium iodide, gave a solid precipitate of s-butylmercuric iodide, which, after being crystallised twice from ethanol, formed white crystals, m. p. 54°. The ***nitrate***, prepared from the acetone solution of hydroxide and 0·5N-aqueous nitric acid, separated on evaporation under reduced pressure as a dark oil, which subsequently solidified, and, on being crystallised twice from pentane, was obtained as white crystals m. p. 51° (Found: C, 15·4; H, 3·2. $C_4H_9O_3NHg$ requires C, 15·0; H, 2·8%). The ***tartrate***, prepared from the hydroxide (derived from 10 g. of bromide) by the slow addition with stirring to its solution in acetone, of tartaric acid (8 g.) in water (15 ml.), separated as a solid, and, after 1 hr. at 0°, was collected, and crystallised twice from ethanol, as white crystals (9 g.), decomposing at 158° (Found: C, 21·7; H, 3·4. $C_{12}H_{22}O_6Hg_2$ requires C, 21·7; H, 3·4%). The ***mandelate*** was prepared similarly, except that it was crystallised twice from acetone, as white crystals, m. p. 144° (Found: C, 35·3; H, 4·0. $C_{12}H_{16}O_3Hg$ requires C, 35·4; H, 3·7%).

(6*b*) *Resolution through the tartrate.* At room temperature, 1 g. of tartrate is soluble in about 30 ml. of chloroform, and in about 2 ml. of pyridine. Resolution proceeded in the same unhurried manner in either solvent. Fractionation was conducted according to the triangular scheme shown, the quantities of solvent being so adjusted that in each crystallisation the average recovery of crystals was about 67%. (The diagram means that, *e.g.*, specimen 2*b* is composed by combining the filtrate from the crystallisation of sample 1*a* with the crystals from the crystallisation of sample 1*b*.) The longest of the fractionations done (16 rows) was in chloroform, and, in the course of it, the rotations (taken in pyridine, $c \approx 5$ and $l = 1$) of the *na* samples of tartrate, *i.e.*, those designated down the left-hand edge of the triangular scheme, changed as follows:



n in *na*	1	2	3	4	5	6	7	8
$[\alpha]_D^{20}$	—	—	+5·6°	+4·9°	+3·5°	+2·5°	+1·8°	+1·1°
n in *na*	9	10	11	12	13	14	15	16
$[\alpha]_D^{20}$	0·0°	−1·0°	−1·5°	—	−2·9°	−3·5°	−4·0°	−4·4°

For conversion into the bromide, a solution of the tartrate (say 5 g.) in pyridine (10 ml.) was treated with concentrated hydrobromic acid (1·5 ml.; *d* 1·47), and then water was added, and, after 1 hr. at 0°, the bromide was collected, washed with water, and crystallised from methanol. The fraction 16*a* of tartrate, thus converted, gave bromide of $[\alpha]_D^{20}$ −17·7° in acetone (cf. Section 4).

(6*c*) *Resolution through the mandelate.* An acetone solution of the hydroxide, obtained from bromide (10 g.) as described in paragraph (6*a*), was added, slowly and with stirring, to a solution of (−)-mandelic acid (2·1 g.) in methanol (11 ml.). Towards the end of the addition, a precipitate appeared, which, after a day at 0°, was collected (sample 1*a*; 4·3 g.). The filtrate was evaporated off under reduced pressure to half its volume, when a further precipitate appeared, which, after being kept for some hours at 0°, was collected (sample 1*b*; 1·3 g.). The filtrate containing the excess of s-butylmercuric hydroxide was treated with concentrated hydrobromic acid (1·7 g.; *d*, 1·47), and the bromide which separated was collected some hours later (5·4 g.); after being crystallised from pentane, it had $[\alpha]_D^{20}$ +5·3° in acetone (cf. Section 4). The mandelate sample 1*a* was now crystallised from acetone (60 ml.), and sample 1*b* was added to the filtrate from that crystallisation. Then the fractionation was continued systematically from acetone, according to the general triangular scheme, for four more rows, *i.e.*, to a total of six rows, the solvent being employed in such quantity (about 14 ml. per g. of mandelate) that the recovery of crystals in each crystallisation was about 60%. Progress was followed (in this, our final, method of resolution, after it was known to be satisfactory), not through the rotation of the mandelate itself, but by converting most of the individual samples of mandelate into bromide, and observing the rotation of the latter (in acetone, $c \approx 5$, and $l = 1$), this procedure being adopted partly because the derived bromide samples all had rotations large enough to make them useful in experiments for which we wanted that substance optically active but not necessarily optically pure. The rotations of bromide derived from the successive *na* fractions of mandelate, *i.e.*, those on the left-hand edge of the triangular fractionation scheme, were as follows (cf. Section 4):

n in *na*	1	2	3	4	5	6
$[\alpha]_D^{20}$ of bromide	−12·5°	—	−19·8°	−22·4°	−23·7°	−24·0°

As to fractions belonging to the right-hand portion of the triangular diagram, fraction 3*c* gave bromide having $[\alpha]_D^{20}$ +11·9°, and the fractions designated below and to the right of it gave samples of bromide having various higher positive rotations up to $[\alpha]_D^{20}$ +17·8°. Conversions into bromide were effected by treating the mandelate (say, 5 g.) in dioxan (5 ml.) with hydrobromic acid (1 ml.; *d* 1·47) and water (5 ml.), and then, after 1 hr. at 0°, collecting the bromide, washing it with water, and crystallising it from methanol. The m. p. of the bromide appeared to be almost independent of its rotation. Crystallisation of the partly resolved bromide produced no marked further separation, but, with the solvents investigated, left slightly larger specific rotations in the filtrate, as the following experiments illustrate. In all of them, 1 g. of the bromide was crystallised from the quantities of solvents stated, and the specific rotations of the crystals, and of the solute in the filtrate, were measured in acetone:

30 ml. of	ligroin (b. p. 60—80°),	$[\alpha]_D^{20}$ of crystals	+14·1°;	of filtrate	+17·7°
10 ,,	nitromethane,	,, ,,	+15·1°,	,,	+16·9°
10 ,,	acetonitrile,	,, ,,	+15·4°,	,,	+18·8°

These quantities of solvent were adjusted to produce approximately equal divisions of the solute between the eventual crystals and filtrate.

William Ramsay and Ralph Forster Laboratories,
University College, Gower St., London, W.C.1.

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