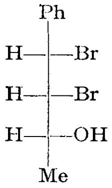
# 277. *The Addition of Acyl Hypobromites to Styrene.*

By D. C. Abbott and C. L. Arcus.

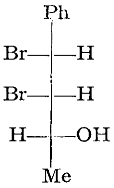
Acyl hypobromites, prepared by the reaction of bromine with silver (+)- and (—)-2-ethylhexanoates, add to styrene to form (+)- and (—)-2-bromo-1-phenylethyl 2-ethylhexanoates,* hydrolysis of which yields optically inactive phenylglycol; it is concluded that racemisation does not occur during hydrolysis and, therefore, that the two configurations at the new asymmetric centre are formed in equal quantities.

Acetyl hypobromite by addition to styrene forms 2-bromo-1-phenylethyl acetate.

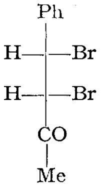
By the addition of bromine to (+)-4-phenylbut-3-en-2-ol, Kenyon and Partridge (*J.*, **1936**, 1313) obtained a mixture of unequal quantities of the dibromo-alcohols (I) and (II). Only two of the four possible isomers were formed and they are here represented as the products of *trans*-addition to the *trans*-alcohol. Oxidation of the mixed dibromo-alcohols gave an optically-active mixture of the enantiomeric ketones (III) and (IV). These reactions, in which two new centres of asymmetry are formed with one configuration preponderating and the original centre is subsequently rendered symmetrical, constitute a (partial) asymmetric synthesis.



(I)



(II)



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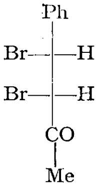

(IV)

The asymmetric synthesis just described was effected by the addition of a symmetrical reagent to an optically active compound containing a double bond, and it was decided to attempt an asymmetric synthesis in the reverse way, by adding an optically active reagent to a symmetrical olefin. Several examples of the addition of acyl hypobromites (formed by the reaction of two equivalents of bromine with the silver salt of the acid) to *cyclo*hexene have been recorded (Bockemüller and Hoffmann, *Annalen*, 1935, **519**, 165; Uschakow and Tschistow, *Ber.*, 1935, **68**, 824)—they give the 2-bromo*cyclo*hexyl esters—and the acyl hypobromite derived from an optically active acid appeared to be a possible reagent for an asymmetric synthesis. Styrene used was because only one new asymmetric centre is formed and, after removal of the acyl group, diastereoisomerism cannot occur.

Silver (+)-2-ethylhexanoate * and bromine were allowed to react in carbon tetrachloride at —15°; the colour disappeared after 10 minutes; reaction of styrene with the solution

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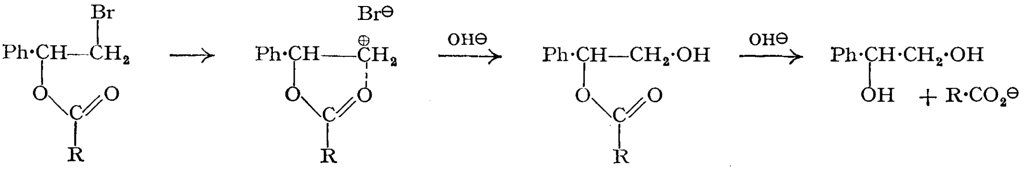
* Geneva numbering, $CO_2H=1$.

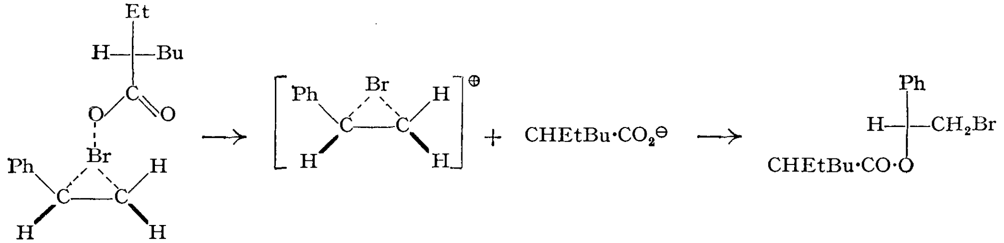
then gave (+)-2-bromo-1-phenylethyl 2-ethylhexanoate. Alkaline hydrolysis of this ester yielded (±)-phenylglycol. Silver (—)-2-ethylhexanoate similarly gave the (—)-ester and then (±)-phenylglycol.

The most probable course for the hydrolysis is considered, from the results of Winstein and Buckles for the reaction of 2-acetoxy-3-bromobutanes with silver acetate (*J. Amer. Chem. Soc.*, 1942, **64**, 2780), to be :

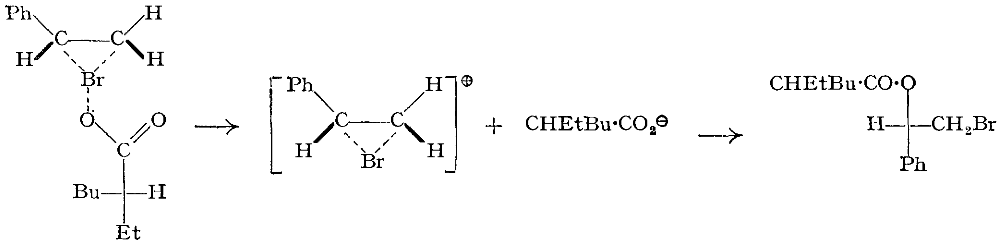


the last stage occurring by normal alkaline hydrolysis with acyl–oxygen fission. The bonding of the new asymmetric centre remains unchanged on this mechanism. It is possible, in the second stage of reaction, for the hydroxyl ion to attach itself to this centre, yielding 2-hydroxy-2-phenylethyl 2-ethylhexanoate; this would result in inversion but not in racemisation.

It is concluded that racemisation did not occur during the hydrolysis of the bromo-ester to phenylglycol and, therefore, that addition occurred symmetrically yielding the intermediates (VII) and (VIII) in equal quantities. The result implies that there is no appreci-



(V) (VII)

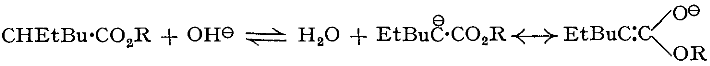


(VI) (VIII)

able difference in the rates of formation of the diastereoisomeric critical complexes (V) and (VI).

Acetyl hypobromite, prepared from silver acetate and bromine, gave with styrene an ester, the physical constants of which agreed closely with those of the 2-bromo-1-phenylethyl acetate prepared by Marvel and Moon (*J. Amer. Chem. Soc.*, 1940, **62**, 40) by the acetylation of styrene bromohydrin, and it is inferred that the 2-ethylhexanoates above are also 2-bromo-1-phenylethyl esters.

The (+)- and (—)-2-ethylhexanoic acid recovered from the hydrolyses were respectively 36 and 40% racemised. Racemisation is probably due to the removal of a proton from $C_{(\alpha)}$ during hydrolysis :



$$\mathrm{CHEtBu{\cdot}CO_2R + OH^{\ominus} \rightleftharpoons H_2O + EtBu\overset{\ominus}{C}{\cdot}CO_2R \longleftrightarrow EtBuC{:}C\begin{cases}O^{\ominus}\\ OR\end{cases}}$$

Kenyon and Young (*J.*, 1940, 216) found that (−)-ethyl 2-ethylhexanoate, when heated with one equivalent of sodium ethoxide in alcohol for 20 minutes at 80°, was completely racemised.

## EXPERIMENTAL

Carbon tetrachloride was kept over calcium chloride and distilled, then dried with, and distilled from, phosphoric oxide; it was kept over the latter.

Bromine was twice shaken with an equal volume of concentrated sulphuric acid and distilled from phosphoric oxide.

Styrene was kept over sodium sulphate and was distilled, a little quinol having been added, immediately before use.

2-Ethylhexanoic acid was prepared and resolved by the method of Kenyon and Platt (*J.*, 1939, 633).

(+)-2-Ethylhexanoic acid (19·8 g.) was added to warm N-sodium hydroxide (130 ml.) and the solution titrated with further aqueous sodium hydroxide until just alkaline to phenolphthalein. This solution was added dropwise with stirring to a warm solution of silver nitrate (23·4 g.) in water (100 ml.); the precipitated silver (+)-2-ethylhexanoate was washed with water, acetone, and ether. It was dried ($CaCl_2$) in a vacuum, finely ground, and dried again ($P_2O_5$) in a vacuum; the yield was 34·2 g. (99%). Silver (−)-2-ethylhexanoate and silver acetate were prepared similarly.

*Addition Reactions.*—A suspension of the silver salt (15·2 g.) of (+)-2-ethylhexanoic acid (b. p. 118—121°/15 mm., $\alpha_{5893}^{22}$ +15·07°, *l* 2·0; 93% optically pure) in carbon tetrachloride (150 ml.) was cooled, in ice–salt at between −20° and −10°, and vigorously stirred while a solution of bromine (9·5 g.) in carbon tetrachloride (25 ml.) was added. After 10 minutes all colour of bromine had disappeared, and styrene (6·3 g.) in carbon tetrachloride (25 ml.) was added; stirring and cooling were continued for 30 minutes. The reaction mixture was allowed to attain room temperature and filtered through sintered-glass. The filtrate was twice washed with aqueous sodium hydrogen carbonate (25 ml., 20%) and dried ($Na_2SO_4$). The carbon tetrachloride was distilled and unchanged styrene removed at 100°/15 mm. The residue on distillation yielded two fractions: (i), b. p. 110—120°/1 mm., which solidified and, after recrystallisation from aqueous alcohol, gave styrene dibromide (0·9 g.), plates, m. p. 73° alone and when mixed with an authentic specimen of m. p. 73°; and (ii), (+)-2-*bromo*-1-*phenylethyl* 2-*ethylhexanoate* (12·0 g., 60%), b. p. 152—156°/1·5 mm., $n_D^{25}$ 1·5081, $\alpha_{5893}^{18}$ +0·88° (*l* 0·5) (Found: C, 58·9; H, 7·0; Br, 24·7. $C_{16}H_{23}O_2Br$ requires C, 58·7; H, 7·1; Br, 24·4%).

A similar experiment with the silver salt (14·8 g.) of (−)-2-ethylhexanoic acid (b. p. 122—125°/17 mm.; $\alpha_{5893}^{15}$ −2·95°, *l* 0·5; 75% optically pure) gave styrene dibromide (1·9 g.), m. p. 69—71°, m. p. 73° after recrystallisation, and (−)-2-bromo-1-phenylethyl 2-ethylhexanoate (6·6 g., 35%), b. p. 150—154°/1 mm., $n_D^{25}$ 1·5080, $\alpha_{5893}^{17}$ −0·61° (*l* 0·5) (Found: C, 58·8; H, 7·3; Br, 24·8%).

A similar experiment with silver acetate (33·4 g.) yielded 2-bromo-1-phenylethyl acetate (29·1 g., 60%) having b. p. 100—104°/0·6 mm., $n_D^{25}$ 1·5391 and, after redistillation, b. p. 98—100°/0·3 mm., $n_D^{25}$ 1·5389 (Found: C, 49·2; H, 4·6; Br, 33·3. Calc. for $C_{10}H_{11}O_2Br$: C, 49·4; H, 4·6; Br, 32·8%). Marvel and Moon (*loc. cit.*) record b. p. 105—107°/3 mm., $n_D^{20}$ 1·5380.

*Hydrolyses.*—2-Bromo-1-phenylethyl acetate (1·8 g.) was heated under reflux for 3 hours with N-sodium hydroxide (20 ml.). The cooled solution was saturated with potassium carbonate and extracted with ether. The extract was dried ($Na_2SO_4$) and ligroin (b. p. 100—120°) added, whereupon there separated phenylglycol (0·6 g., 60%), m. p. 64—65° Found: C, 69·4; H, 7·4. Calc. for $C_8H_{10}O_2$: C, 69·5; H, 7·3%); its dibenzoate had m. p. 93—94°. Milas and Sussman (*J. Amer. Chem. Soc.*, 1937, **59**, 2346) record m. p. 65—66° and m. p. 92—93° for phenylglycol and the dibenzoate.

(+)-2-Bromo-1-phenylethyl 2-ethylhexanoate (3·3 g.) was similarly hydrolysed for 10 hours with 3N-sodium hydroxide (40 ml.). The ethereal extract (dried with $K_2CO_3$) was optically inactive (*c* 5, *l* 2·0) and yielded phenylglycol (0·9 g., 65%), m. p. 63—65° and, after recrystallisation from ether–ligroin, m. p. 64·5—65·5°. The aqueous solution was acidified with hydrochloric acid and extracted with ether. The extract was dried ($Na_2SO_4$) and distilled, and yielded (+)-2-ethylhexanoic acid (1·2 g., 80%), b. p. 223—225°, $\alpha_{5893}^{17}$ +2·40° (*l* 0·5), whence the acid had undergone 36% racemisation.

From a similar hydrolysis of (−)-2-bromo-1-phenylethyl 2-ethylhexanoate (3·3 g.) there was obtained an ethereal extract having $\alpha_{5893}^{14}$ −0·02° (*c* 5·9, *l* 2·0) which gave phenylglycol (1·0 g., 74%), m. p. 60—62°, m. p. 64—65° and optically inactive in ether (*c* 3·7, *l* 2·0) after recrystallisation. From the aqueous solution there was recovered (−)-2-ethylhexanoic acid (1·25 g., 83%), b. p. 223°, $\alpha_{5893}^{15}$ −1·80° (*l* 0·5), whence the acid had undergone 40% racemisation.

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