Tetrahedron, 1963, Vol. 19, pp. 1969 to 1979. Pergamon Press Ltd. Printed in Northern Ireland

MECHANISM OF THE REACTION OF STYRENE OXIDE WITH PHOSPHONATE-CARBANIONS

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(*Received* 29 *April* 1963)

Abstract—Assignment of absolute configuration to the *trans*-2-phenylcyclopropane-carboxylic acid reveals that the reaction between optically active styrene oxide and phosphonate-carbanions proceeds with inversion at the asymmetric centre.

As part of a research programme[1,2] concerning the mechanism and stereochemistry of the Wittig reaction, the reaction between optically active styrene oxide (I) and alkoxycarbonylmethylphosphonatecarbanion (II) was investigated. Just as the experiments were complete, Denney *et al.*[3] reported on the same subject and this prompted immediate publication.

In a previous paper Denney and Boskin[4] reported that reaction under forced conditions between styrene oxide and triphenylethoxycarbonylmethylenephosphorane (III) gave ethyl *trans*-2-phenylcyclopropanecarboxylate (IVa) in low yield (21%). The same compound was obtained by Wadsworth and Emmons[5] under much milder conditions by using II instead of III; the yield of IVa, however, was double of that given by Denney and Boskin. Since in Wittig's view[6] alteration of substituents in $RR'R''P{-}\overset{\ominus}{C}(H){-}H$ (e.g. $R = R' = R'' = Ar$; $R = R' = OR$, $R'' = O$, etc.) does not appreciably change the course of the reaction, phosphonate-carbanions (II) were preferentially chosen for study.

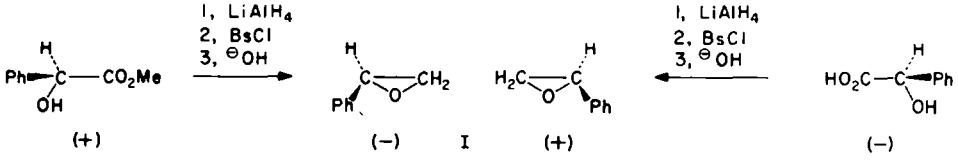

FIG. 1.

RESULTS

(+) and (−) Styrene oxide (I) were prepared by a slight modification of the method described by Eliel and Delmonte.[7] (+) and (−)Mandelic acid afforded (+) and (−)-1-phenylethane-1,2-diols which were then selectively esterfied on the primary hydroxyl group with *p*-bromobenzenesulphonyl chloride in pyridine solution.[8] Brosylation has

[1] I. Tömösközi and G. Janzsó, *Chem. & Ind.* 2085 (1962).
[2] I. Tömösközi, *Angew. Chem.* (1963). In press.
[3] D. B. Denney, J. J. Will. and M. J. Boskin, *J. Amer. Chem. Soc.* **84**, 3944 (1962)
[4] D. B. Denney and M. J. Boskin, *J. Amer. Chem. Soc.* **81**, 6330 (1959).
[5] W. S. Wadsworth and W. D. Emmons, *J. Amer. Chem. Soc.* **83**, 1738 (1961).
[6] G. Wittig, W. Böll, and K. H. Krück, *Chem. Ber.* **95**, 2514 (1962).
[7] E. L. Eliel and D. W. Delmonte, *J. Org. Chem.* **21**, 596 (1956).
[8] R. B. Clayton, H. B. Henbest and M. Smith, *J. Chem. Soc.* 1982 (1957).

some advantage over the method of tosylation[9] since brosylates can be readily purified by recrystallization from benzene–light petroleum. Closure of the epoxide ring was readily achieved in comparable yields either by ethanolic sodium ethoxide or methanolic potassium hydroxide solution. Both (+) and (−)I react with IIa (derived from the corresponding phosphonate by treatment with sodium hydride in 1,2-dimethoxyethane[5]) to give (+) and (−) IVa, resp., in yields of 30–40% comparable with those reported by Wadsworth and Emmons for the inactive compound. Alkaline saponification liberated the free acids (IVd) in optically active form, the sign of rotation being the same as that of the esters. The reproducibility of the results is reflected by the X_i/X_j values. The mean deviation from the theoretical value is about 3·6%.

TABLE 1

Compound	Series *a* $[\alpha]_D$	Optical purity, %	Series *b* $[\alpha]_D$	Optical purity, %
Mandelic acid	—	—	−104	66
Methyl mandelate	+82·5	47·3	—	—
Phenylethanediol	+26·5	ca. 47	−41·3	ca. 70
Diol monobrosylate	+17·65	—	−22·2	—
Styrene oxide	−15·53	ca. 47	+21·1	ca. 64
Ethyl *trans*-2-phenylcyclopropanecarboxylate	−62·2	—	—	—
	−61·5	—	—	—
trans-2-Phenylcyclopropanecarboxylic acid	−127	X_1	+164·9	X_3
	−118	X_2	+157·9	X_4

X_1/X_2	X_3/X_4	theoretical 47/47 or 64/64	X_1/X_3	X_1/X_4	X_2/X_3	X_2/X_4	theoretical 47/64
1·07	1·04	1·00	0·77	0·805	0·715	0·75	0·76

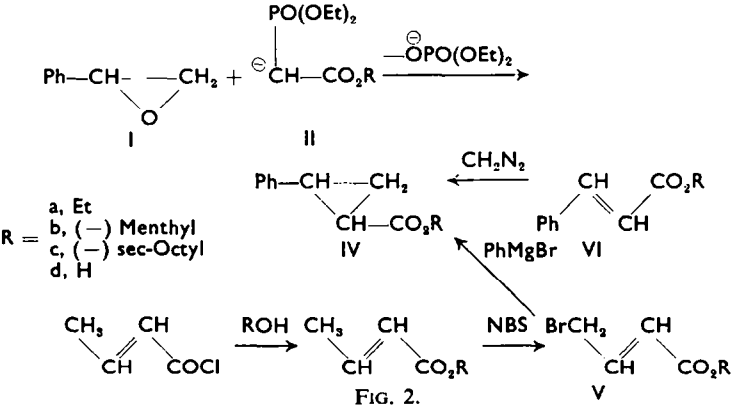

FIG. 2.

The absolute configurations of the *trans*-2-phenylcyclopropane-carboxylic acids being unknown (*cf.* ref. 3), a suitable method for their determination was selected, which was based on the easy availability of the materials involved, and because

[9] Other independent methods are under investigation.

similar experiments described in the literature[10,11,24,27,30] are known to lead to a reliable correlation of configurations. (−)Menthyl 4-bromo-crotonate (Vb) and (−)*sec*-octyl 4-bromocrotonate (Vc) were prepared as shown in Fig. 2. Bromination with elementary bromine in dilute CCl_4 solution gave Vb and Vc in rather unsatisfactory yields. Treatment of an ethereal solution of Vb and Vc with ethereal phenylmagnesium bromide at room temperature[12] gave the esters (+)IVb and (+)IVc, respectively, saponification of which by boiling for 8 hours with aqueous ethanolic potassium hydroxide afforded (+)IVd in both cases.

TABLE 2

	b.p. °C/mm or m.p. °C	$[\alpha]_D$	Optical purity, %
Menthyl crotonate	82–3°/1	−85·3	100
Menthyl bromocrotonate Vb	140–2/0·5	−62·1	100
Phenylcyclopropanecarboxylic acid	89–92	+42·1	15·6*
	89–92	+36·2	13·4*
sec-Octyl crotonate	75–8/1·5–2	−9·78	100
sec-Octyl bromocrotonate	128–132/0·5	−7·12	100
Phenylcyclopropanecarboxylic acid	89–91	+22·1	8·2*
	89–92	+28·4	10·4*

* Maximum value calculated on the assumption that the reaction (I + II → IV) proceeds with full retention of optical purity.

In order to avoid any error introduced by partial resolution due to incomplete saponification, (−)menthyl and (−)*sec*-octyl(±)*trans*-2-phenylcyclopropanecarboxylates were prepared by boiling (±)*trans*-2-phenylcyclopropanecarbonyl chloride[13] with (−)menthol and (−)sec-octanol in chloroform for 6 hours, and the resulting products, were saponified under the conditions mentioned above to give (±)IVd.

An independent determination of the absolute configuration of IVb depended on the addition of methylene (prepared by the photochemical decomposition of diazomethane[14]) to the olefinic bond of (−)menthyl cinnamate (VIb) to give IVb which was then saponified under standard conditions to yield (−)IVd, $[\alpha]_D$ −5·4°. In order to determine whether a reaction can be asymmetrically influenced[1,10,11,15,27] by an optically active group in the $—CO_2R$ moiety, the reactions between (±)I and diethyl (−)menthoxycarbonylmethylphosphonate (IIb) and diethyl (−)sec-octyloxycarbonylmethylphosphonate (IIc), respectively[2] were investigated. In both cases (+)IVd was obtained as the final product of the reaction and alkaline saponification.

[10] Y. Inouye, S. Inamasu, M. Ohno, T. Sugita, and H. M. Walborsky, *J. Amer. Chem. Soc.* **83,** 2962 (1961); H. M. Walborsky, T. Sugita, M. Ohno, and Y. Inouye, *Ibid.* **82,** 5255 (1960); Y. Inouye and H. M. Walborsky, *J. Org. Chem.* **27,** 2707 (1962).

[11] V. Prelog and H. Scherrer, *Helv. Chim. Acta* **42,** 2227 (1959); J. A. Berson and M. A. Greenbaum, *J. Amer. Chem. Soc.* **81,** 6456 (1959).

[12] R. S. Ratney and J. English, *J. Org. Chem.*, **25,** 2213 (1960).

[13] A. Burger and W. L. Yost, *J. Amer. Chem. Soc.* **70,** 2198 (1948).

[14] For references, see W. Kirmse, *Angew. Chem.* (1962) **73,** 161 (1961).

[15] R. J. D. Evans and S. L. Landor, *Proc. Chem. Soc.* 182 (1962); M. M. J. Kubitschek and W. A. Bonner, *J. Org. Chem.* **26,** 2194 (1961); K. Sisido, K. Kumazawa, and H. Nozaki, *J. Amer. Chem. Soc.* **82,** 125 (1960); V. E. Althouse, E. Kaufmann, P. Loefler, K. Ueda, and H. S. Mosher, *Ibid.* **83,** 3138 (1961); M. H. Palmer and J. A. Reid, *J. Chem. Soc.* 931, 1762 (1960); Herbrandson and Cusano, *J. Amer. Chem. Soc.* **83,** 2124 (1961); for earlier references, see ref. 24 and 27.

TABLE 3

Compound	$[\alpha]_D$	b.p. °C/mm or m.p. °C	Optical purity %	Compound	$[\alpha]_D$	b.p. °C/mm or m.p. °C	Optical purity %
IIb	−51·3°	149°/1		IIc	−6·66	145–7°/2	
IVb	−47·5°	155–168°/0·5					
IVd	+17·5°	89–92°	6·5*	IVd	+12·0	91–93°	4·45*
	+16·5[b]	90–92°	6·1*		+15·2	91·5–93°	5·07*
IVd-amide	9·2°						

* Maximum value calculated on the assumption that the reaction (I + II → IV) proceeds with full retention of optical activity.

DISCUSSION

The mechanism of the reaction of epoxides with alkoxycarbonylmethylenephosphoranes,[3,4] phosphonate-carbanions,[5] phosphinate-carbanions,[16] and phosphinoxide-carbanions[16] is assumed to involve essentially the same elementary processes[6] although some differences in the transient electronic distributions, for which allowances must be made, could reasonably cause appreciable alterations. These differences may be foreshadowed in the pronounced difference in reactivity.[5,16,17]

The first step of the reaction is considered[3,4,18,19] to be an S_N2 displacement of the oxide bridge by a nucleophilic P—CH—CO_2R carbanion (hereafter P means either Ph_3P, $(RO)_2PO$, (RO)RPO, or R_2PO). This mechanism supported by the observations of McEwen *et al.*[18] in the case of the reaction of styrene oxide with ^{14}C-labelled methylethylphenylbenzylidenephosphorane. Methylethylphenylphosphine oxide was shown to be an *inversion* product[19] which is a difference worthy of note in reactions between epoxides and carbonyl compounds with P—CH—R, as in the last case *retention* of configuration of phosphorus has been found.[20] Since retention excludes the alternative mechanism in which the phosphorus is *first coordinated* with the oxygen,[21] inversion may tentatively be considered to predict it in the case of epoxides although the stereochemistry is somewhat complicated by the intervention of an additional methylene group.[19] On this basis it may reasonably be assumed that the opening of the epoxide ring can take place in two parallel ways.[22] Path A should produce mainly the cyclopropane and phosphine oxide of inverted configuration whereas path B should mainly give benzylacetophenone and phosphine.[18,19] Path A may be particularly important in the case of phosphoranes in which the high oxygen affinity of phosphorus is buttressed by the partial positive charge carried on the phosphorus. This view has some logical support in the fact that phosphoranes do not readily behave as nucleophilic reagents toward electrophilic carbon in cases where

[16] L. Horner, H. Hoffman, W. Klink, H. Ertel, and V. G. Toscano, *Chem. Ber.* **95**, 581 (1962) and references therein cited.

[17a] H. J. Bestmann and B. Arnason, *Chem. Ber.* **95**, 1513 (1962); H. J. Bestmann and O. Kratzer, *Ibid.* **95**, 1894 (1962).

[b] G. Fodor and I. Tömösközi, *Tetrahedron Letters* No 16, 579 (1961).

[18] W. E. McEwen and A. P. Wolf, *J. Amer. Chem. Soc.* **84**, 676 (1962).

[19] W. E. McEwen, A. Bladé-Front, and C. A. Vander Werf, *J. Amer. Chem. Soc.* **84**, 677 (1962).

[20] A. Bladé-Front, C. A. Vander Werf, and W. E. McEwen, *J. Amer. Chem. Soc.* **82**, 2396 (1960).

[21] A. J. Speziale and K. W. Ratts, *J. Amer. Chem. Soc.* **84**, 854 (1962).

[22] R. E. Parker and N. S. Isaacs, *Chem. Rev.* **59**, 737 (1959).

the phosphorus cannot coordinate with oxygen.[17b] It is felt that at present no results are available to make a rigorous distinction between the two pathways.

The further course of the reaction may comprise rotation to the required conformation, formation of a cyclic intermediary product, cleavage of the P—C bond, etc., depending upon the path along which it proceeds. Elucidation of this part of the mechanism depends on whether: (1) the cyclopropane derivative maintains the activity of an optically active epoxide or (ii) the cyclopropane derivative maintains the configuration of the epoxide, i.e., whether it is produced with retention or inversion.

From the results which are listed above the first question can unequivocally be answered in the affirmative (although the extent to which activity is maintained is not known at present). Denney *et al.* have reached the same result, but the retention of optical activity is markedly lower in their case than is reported in this paper. This may partly be due to the rather high temperature and long reaction period

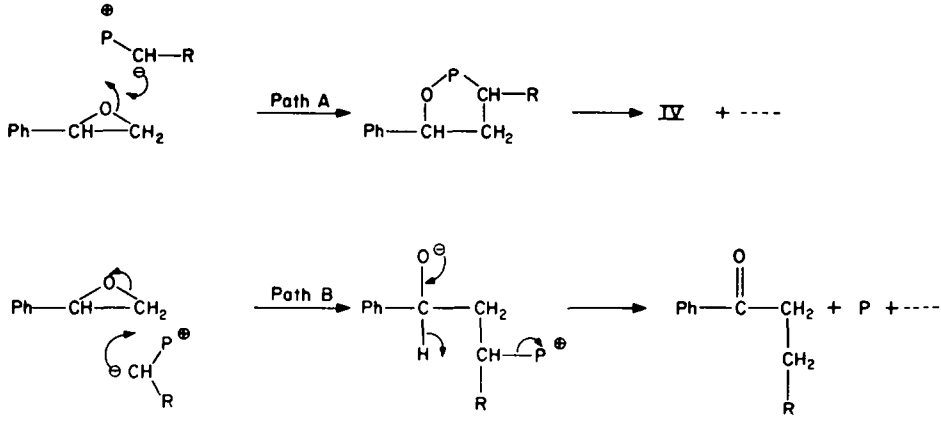

FIG. 3

required to decompose[18,19] the betaine (or cyclic compound) formed. The high rotation of IVd obtained in our experiments should correspond to a considerable preservation optical activity. Although, assumption of complete (i.e. 100%) preservation seems to be violated by the results of asymmetric induction, a probable explanation of this virtual contradiction is that the asymmetric group changes the product distribution[18,19] without any other appreciable effect upon the stereochemistry of the reaction. On this basis the diastereomer betain should largely give rise to a cyclopropane derivative thus involving the less hindered intermediary state (see below). Denney *et al.* interpreted the reaction between cyclohexene oxide and triphenylethoxycarbonylmethylenephosphorane leading to ethyl norcaranecarboxylate in terms of a mechanism implying inversion on both carbon atoms of the epoxide moiety. Actually the mechanism involving retention on both carbons seems to have the same *a priori* probability, even the relative high yield 63% appears to be compatible rather with path A than with path B which requires intensive conformational changes.[23] Assuming that both path A and B contribute to some extent to the whole reaction, one may expect that the ratio extent of path B:extent of path A should be smaller

[23] Experiment with 4-t-butylcyclohexene oxide which is assumed to be unable to undergo conformational changes are in progress in our laboratory.

in the case of phosphoranes (see above) than in the case of phosphonate carbanions which is virtually reflected in the difference of preservation of optical activity. Furthermore, decomposition of VII may involve serious racemization.[24]

Phosphonate carbanions are strongly nucleophilic[5,15,17] thus path B should not to any extent compete with path A. On the basis of Denny's mechanism, thus, it is expected that IV is formed by inversion from I, although in open chain series the

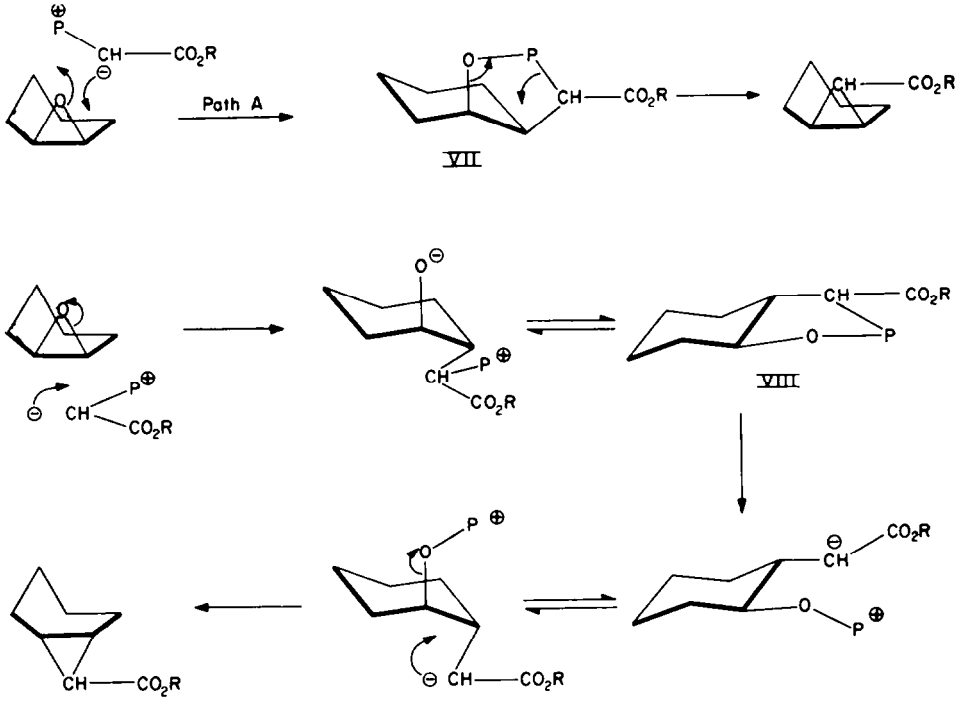

FIG. 4

compound corresponding to VIII may conceivably decompose with retention of the configuration *via* an electronic displacement similar to VII. Establishment of the absolute configuration of IVd confirms Denny's mechanism[3,19] for the case investigated i.e., IV is formed with inversion *via* an intramolecular S_Ni process.

Assignment of configuration to IVd was based on the fact[25] that the addition product of Grignard reagents to optically active α,β-unsaturated esters can configurationally be related to that of the alcohol component of the ester group; the R group in RMgX enters from the less hindered side. Since the spacial arrangement of the L,M,S groups[26] has the same pattern in (−)menthol[26] as in (−)sec-octanol,[27] the most favoured conformation of IVb and IVc is represented by IX.[11,28]

[24] Th. V. Van Auken and K. L. Rinehart, *J. Amer. Chem. Soc.* **84,** 3736 (1962).

[25] J. A. Mills and W. Klyne in *Progress in stereochemistry* (Edited by W. Klyne) Vol. 1, p. 198. Butterworth, London (1954).

[26] ref. 25, p. 189

[27] ref. 25, p. 195

[28] H. M. Walborsky, L. Barash, A. E. Young, and F. J. Impastato, *J. Amer. Chem. Soc.* **83,** 2517 (1961).

The same consideration holds true for the addition of methylene to double bonds influenced by an asymmetric centre.[10] Since in both series the less hindered side is that shown by the dotted arrow, the results are in excellent agreement with the assignment of absolute configuration. A further corroboration is afforded by the results of the reaction of (±)I with IIb and IIc, respectively, with a few reasonable assumptions. If the preferred conformation of IIb and IIc is considered[29,30] to be the one shown in Fig. 6, the S_N2 displacement may take place most readily through a transition state in which the groups are oriented so as to have minimum interaction (S means styrene oxide).

It is readily seen that XI can more easily follow the path toward the cyclopropane formation than does X which should considerably be hindered by the *cis* 1:3 interaction.[31] The by-products[18,19] are probably more readily formed from X than from XI, moreover partial racemization of X to XI may be possible.[18]

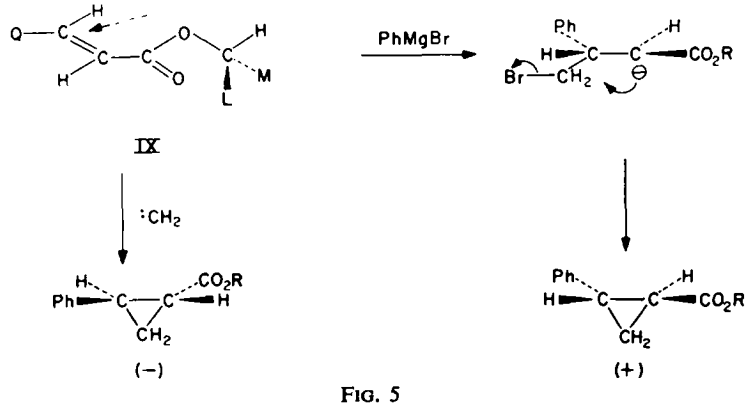

FIG. 5

EXPERIMENTAL

(+)Phenylethane-1,2-diol

To a suspension of 3·4 g (0·09 mole) $LiAlH_4$ in 100 ml dry ether, 14·5 g (0·0875 mole) of methyl (−)mandelate $[\alpha]_D$ +82·5° (*c* 3·01 in benzene), optical purity[32] 47·3%] in 50 ml ether was added with stirring, at such a rate as to maintain gentle boiling (ca. 1 hr). The mixture was stirred for 5 hr at room temp and then for 1 hr at reflux temp. Excess of the hydride was destroyed by the careful addition of 25 ml moist ether (during 15 min) followed by 65 ml dil. H_2SO_4 (10%) with cooling and stirring. The layers were separated, the aqueous layer extracted with two 25 ml portions ether and the combined extracts after drying (Na_2SO_4) evaporated to dryness to give 11 g of a white crystalline compound which was then recrystallized from 50 ml benzene–light petroleum mixture (3:2). The crystals which separated after standing in the refrigerator overnight, were filtered with suction, washed with cold light petroleum and dried in a vacuum desiccator. The yield was 10·3 g, m.p. 58–62°, $[\alpha]_D$ +26·5° (*c*, 2·95 in EtOH) (repd.[33] m.p. 67–68° for the racemic compound) (Found: C, 69·85; H, 7·52. Calc. for $C_8H_{10}O_2$: C, 69·54; H, 7·30%).

[29] This is considered to be the most probable on the basis of steric and dipole interactions (cf. D. J. Cram and F. A. A. Elhafez, *J. Amer. Chem. Soc.* **74**, 5828 (1952); V. Prelog, *Helv. Chem. Acta* **36**, 308 (1953)

[30] Planar configuration of the carbanion carbon is required by the [sp^2] hybridization (cf. W. E. Doering and L. K. Levy, *J. Amer. Chem. Soc.* **77**, 509 (1955); D. J. Cram, W. D. Nielsen and B. Rickborn, *Ibid.* **82**, 6415 (1960).

[31] D. H. R. Barton and R. C. Cookson, *Quart. Rev.* **10**, 44 (1956).

[32] P. Walden, *Chem. Ber.* **38**, 372 (1908); H. Erlenmeyer and H. Schenkel, *Helv. Chem. Acta* **21**, 114 (1938).

[33] H. H. Lewis, M. Nierenstein, and E. M. Rich, *J. Amer. Chem. Soc.* **47**, 1728 (1925).

(−)*Phenylethane-1,2-diol* was prepared from (−)mandelic acid [$[\alpha]_D$ −104° (*c*, 2·07 *in* EtOH), optical purity 66%] by means of $LiAlH_4$ in a similar manner as described above. The product was, however, an oil at room temp, which partially crystallized after long standing, $[\alpha]_D$ −41·3° (*c*, 3·043 in EtOH). (Found: C, 69·78; H, 7·61. Calc. for $C_8H_{10}O_2$: C, 69·54; H, 7·30%).

(+)2-(p-*Bromobenzenesulphonyloxy*)-1-*phenylethanol*

To a solution of 17·6 g (0·065 mole) brosyl chloride in 50 ml dry pyridine, 9 g (0·065 mole) (+)phenylethane-1,2-diol dissolved in 50 ml pyridine was added in portions with shaking at −3°. The mixture was let stand in the refrigerator for the week-end and then at room temp for 1·5 hr. The mixture was poured into ice-cold dil. HCl (600 g ice + 100 ml conc. HCl) and the gummy solid which deposited was dissolved in ether (300 ml), washed subsequently with dil. HCl, water and dried. Evaporation yielded a viscous oil which was dissolved in 70 ml benzene–pet ether mixture (5:2) with gentle warming and cooled in an ice-bath. The crystals deposited were filtered and washed with 20 ml pet ether, yield 17·1 g (70%), m.p. 76·2–88·8°, $[\alpha]_D$ +17·65° (*c*, 2·603 in EtOH).

(−)2-(p-*Bromobenzenesulphonyloxy*)-1-*phenylethanol* was prepared as described above from (−)phenylethane-1,2-diol ($[\alpha]_D$ −41·3°), yield 82%, m.p. 51–62·3°, $[\alpha]_D$ −22·2° (*c*, 2·164 in EtOH).

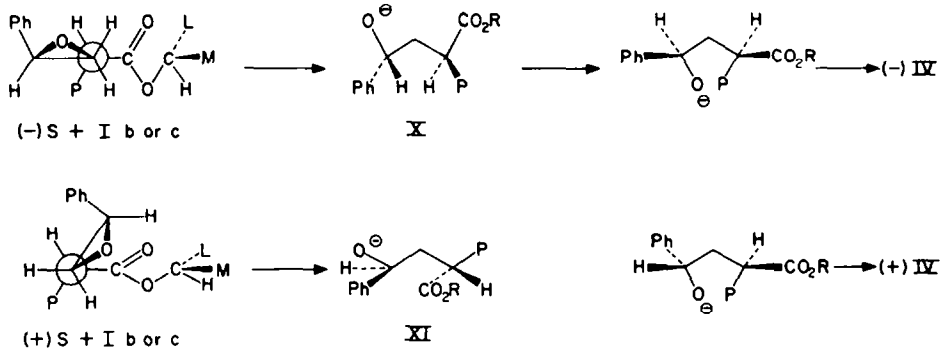

FIG. 6.

(−)*Styrene oxide*

(+)2-Brosyloxy-1-phenylethanol (9·5 g) was dissolved in 50 ml methanol, cooled to 5° and treated with a solution of 2 g potassium hydroxide in 20 ml methanol. After several min a voluminous white precipitate separated. Water (150 ml) was added and the mixture extracted with ether, washed with water and dried over freshly ignited potassium carbonate. Evaporation of the solvent at red. press. (150–200 mm) and removal of traces of water by azeotropic distillation (alcohol–benzene) left a pale yellow liquid (3·2 g) which was then fractionally distilled. The fraction boiling at 90–92°/20 mm was collected (repd. b.p. 62–63°/4·5 mm,[7] 188-192°/atm[84]), yield 2·65 g (85%), n_D^{20} 1·5353 (repd. n_D^{20} 1·5354[7]), $[\alpha]_D$ −15·53 (neat).

(+)*Styrene oxide* was obtained in a similar manner from (−)2-brosyloxy-1-phenylethanol ($[\alpha]_D$ −22·2°) in 79% yield, n_D^{20} 1·5358, $[\alpha]_D$ +21·1° (neat).

(−)2-*Phenylcyclopropanecarboxylic acid*

The solution of 2·9089 g (0·013 mole) diethyl ethoxycarbonylmethylphosphonate[85] in 20 ml dry 1,2-dimethoxyethane was allowed to drop (15 min) with stirring into a suspension of 0·687 g (0.0139 mole) 50% sodium hydride in 20 ml 1,2-dimethoxyethane. Hydrogen evolution practically ceased after about 15 min, and a clear solution resulted to which 1·5622 g (0·013 mole) (−)styrene oxide ($[\alpha]_D$ −15·53°) dissolved in 10 ml dimethoxyethane was added. The mixture was stirred for a further 5 hr at 70° and allowed to stand for overnight. Most of the solvent was removed under red. press. (150–200 mm), the residue treated with 150 ml water, extracted with three 50 ml portions ether, dried ($MgSO_4$) and after removal of the solvent distilled to give 1·2 g (48·5%) colorless liquid,

[84] H. Hibbert and P. Burt, *Organic Syntheses* Coll. Vol. 1, p. 494. Wiley, New-York (1947).
[85] G. Kosolapoff, *Organophosphorous Compounds* p. 160. Wiley, New York (1950).

b.p. 102–112°/2 mm (repd. 99–106°/4 mm,[12] 105–110°/1–2 mm[13]), $[\alpha]_D$ −62·2° (*c* 2·537 in EtOH); in a subsequent experiment the ester of $[\alpha]_D$ −61·5° (*c* 6·362 in EtOH) was obtained. The esters were saponified without further purification by boiling with aqueous alcoholic potassium hydroxide for 8 hr, evaporated to dryness on the water bath at red. press., taken up in water, extracted with ether to remove nonacidic materials, acidified by the careful addition of conc. HCl and extracted with ether. The ethereal extracts were dried (Na_2SO_4) and evaporated to dryness to give *trans*-2-phenylcyclopropanecarboxylic acids in yields of 63 and 71 % (calcd. on the amount of ester saponified), $[\alpha]_D$ −127° (*c* 0·863 in EtOH), m.p. 87·5–91° (obtained from the ester of $[\alpha]_D$ −62·2°) and $[\alpha]_D$ −118° (*c* 2·443 in EtOH), m.p. 87–91° (obtained from the ester of $[\alpha]_D$ −61·5°) (repd. m.p. 97–98·5°[12], 93°[13] for the racemic compound). (Found: C, 74·15; H, 6·35. Calc. for $C_{10}H_{10}O_2$ ($[\alpha]_D$ −127°): C, 74·05; H, 6·22%).

(±)2-*Phenylcyclopropanecarboxylic acid* was similarly obtained from (+)styrene oxide of $[\alpha]_D$ +41·3° in 40 and 41 % overall yield in two subsequent experiments, $[\alpha]_D$ +164·9° (*c* 0·825 in EtOH) and +157·9° (*c* 2·185 in EtOH), respectively.

(−)*Menthyl crotonate*

To a solution of 47 g (0·3 mole) (−)menthol and 51 g (0·342 mole) N,N-diethylaniline in 100 ml pet ether (b.p. 40–60°), 36·3 g (0·345 mole) crotyl chloride[36] (b.p. 123–126°) dissolved in 100 ml pet ether was added with stirring at room temp. The clear solution was refluxed on the water bath for 26 hr with interruption during the night. The crystals which began to separate several min after reflux had started were filtered off with suction and washed with the solvent. The combined filtrates were washed with dil. HCl, water, saturated aqueous sodium hydrogen carbonate and water, and dried (Na_2SO_4). After removal of the solvent, the residue distilled at 82–83°/1 mm to yield the product, 53·9 g, 80%, $[\alpha]_D$ −85·3° (*c* 2·115 in EtOH), (repd.[37] b.p. 124–125°/9·5 mm, 72°/2 mm, $[\alpha]_D$ −84·5°, −85·5°).

(−)*sec-Octyl crotonate* was similarly prepared from (−)*sec*-octanol [$[\alpha]_D$ −9·78° (*c* 4 in EtOH)] and crotyl chloride in 78% yield, b.p. 75–78°/1·5–2 mm, $[\alpha]_D$ −8·92° (*c* 3·15 in EtOH).

(−)*Menthyl* trans-4-*bromocrotonate*

(−)Menthyl crotonate (31·1 g, 0·139 mole) obtained in a foregoing experiment was refluxed for 16 hr with 24·8 g (0·138 mole) freshly prepared and thoroughly dried N-bromosuccinimide in 50 ml carbon tetrachloride containing benzoyl peroxide in catalytic amounts. The mixture was cooled, the succinimide filtered off with suction, and washed with carbon tetrachloride (20 ml). The residual succinimide in the filtrate was removed by washing with four 60 ml portions of water. After drying with $MgSO_4$, the solvent was evaporated and the dark red, viscous residual liquid fractionated at red. press. through a small column, the following fractions being collected: *A*, b.p. 82–110°/2 mm, 12·2 g; *B*, b.p. 110–132°/2 mm, 2·3 g; *C*, 126–146°/0·5 mm, 15·3 g. Fraction *C* was redistilled to give 12·5 g (30%) pure bromo ester, b.p. 140–142°/0·5 mm, $[\alpha]_D$ −62·1° (*c* 2·28 in $CHCl_3$). (Found: C, 55·18; H, 7·08; Br, 26·47. Calc. for $C_{14}H_{23}BrO_2$: C, 55·47; H, 7·65; Br 26·36%).

(−)*sec-Octyl* trans-4-*bromocrotonate* was similarly obtained in 26% yield from the (−)sec-octyl crotonate with b.p. 128–132°/0·5 mm, $[\alpha]_D$ −7·12 (*c* 3·12 in $CHCl_3$). (Found: Br, 29·01. Calc. for $C_{13}H_{21}BrO_2$: Br, 28·83%).

Addition of PhMgBr *to* (−)*menthyl* trans-4-*bromocrotonate*

An ethereal solution of phenylmagnesium bromide (prepared from 0·85 g Mg and 5·3 g bromobenzene in 50 ml ether) was added with stirring to a solution of 10 g of the bromoester at room temp. After addition was complete (ca. 25 min) the mixture was stirred for 1·5 hr; occasionally a heavy viscous liquid deposited at the bottom of the flask. The mixture was cooled in an ice-bath and hydrolysed with aqueous ammonium chloride solution. The ethereal layer was separated, washed with water and dried. Evaporation of the solvent left a yellow liquid which was refluxed with 5 g potassium hydroxide in 130 ml water–alcohol mixture (3:10) for 10 hr. The alcohol was removed *in vacuo*, the residue was diluted with water (20 ml) and thoroughly extracted with ether to eliminate nonacidic materials (extract A). The alkaline mother liquor was then carefully acidified with

[36] H. C. Brown, *J. Amer. Chem. Soc.* **60**, 1325 (1938).

[37] B. Dasannacharya, *J. Amer. Chem. Soc.* **46**, 1629 (1924); W. A. Pavelich and R. W. Taft, *Ibid.* **79**, 4935 (1957).

conc. HCl, extracted with ether (extract B). From extract A, 4·5 g (−)menthol (86%) was recovered by evaporation of the solvent. Similar working up of extract B resulted in an oil 3·12 g, $[\alpha]_D$ +12·2°. The oil in 10 ml CCl_4 was boiled with water (20 ml) and the water still warm decanted. This procedure was repeated several times the last portion having been carefully separated in a small separatory funnel. The carbon tetrachloride solution was then extracted with aqueous dil. KOH solution which was acidified, extracted with ether, dried, and evaporated to give 1·12 g of viscous oil which did not crystallize even after long standing in the refrigerator or at room temp. Vacuum sublimation (90°, 2 mm) afforded a colourless crystalline material, 0·61 g (11·4%), m.p. 89–92°, $[\alpha]_D$ +42·1° (*c* 2·112 in EtOH); in a subsequent experiment an acid of m.p. 88–92° and $[\alpha]_D$ +36·2° (*c* 1·892 in EtOH) was obtained.

To see whether the alkaline saponification of (−)menthyl *trans*-(±)2-phenylcyclopropanecarboxylate might led to partial resolution under the conditions described above, this compound was prepared by boiling a solution of (−)menthol with *trans*-2-phenylcyclopropanecarbonyl chloride[18] in chloroform for 3 hr. The solvent was evaporated *in vacuo* and the resulting oil saponified and worked up as above to give the racemic acid, m.p. 95–96·5°, mixed m.p. with the active acid of $[\alpha]_D$ +42·1°: 90–94°.

Addition of PhMgBr to (−)sec-*octyl* trans-4-*bromocrotonate*

The experiments were carried out as described above for the (−)menthyl ester, and gave the acid of $[\alpha]_D$ +22·1° and +28·4° in 12 and 10% yields, respectively.

Addition of methylene to (−)menthyl trans-*cinnamate*

An ethereal solution of 180 ml diazomethane[38] (4·1 g) was cooled to 0° and treated with 14·3 g (−)menthyl *trans*-cinnamate,[39] [$[\alpha]_D$ −75·7° (*c* 2·15 in benzene)], dissolved in ether (30 ml). The solution after standing for 4 hr at room temp was irradiated with a mercury vapour lamp (500 w) for 8 hr. A few drops of glacial acetic acid were added and the mixture stirred for 40 min. The ethereal solution was washed with saturated aqueous $NaHCO_3$ then with water and dried. After the removal of the solvent *in vacuo* (100 mm) on the water bath, a red viscous oil remained which was saponified by boiling with aqueous alcoholic potassium hydroxide for 10 hr and worked up in the usual way (see above) to give a syrup, 9·3 g, $[\alpha]_D$ +5·2° (*c* 5·012 in EtOH). Pure material was obtained by several recrystallizations from aqueous alcohol, m.p. 93–95°, $[\alpha]_D$ +5·4° (*c* 4·51 in EtOH). (Found: C, 73·87; H, 6·38. Calc for $C_{10}H_{10}O_2$: C, 74·05; H, 6·22%).

Diethyl (−)menthyloxycarbonylmethylphosphonate

A mixture of 50·1 g (018 mole) (−)menthyl bromoacetate (b.p. 144–145°/12 mm, $[\alpha]_D$ − 62·1°) and 33 g (0·2 mole) triethyl phosphite was slowly warmed in an oil-bath. The ethyl bromide formed was allowed to distil out through a short column. At 100–120° a vigorous exothermic reaction set in and the temp rose rapidly, temporary cooling was necessary to maintain at 140–150°. After the vigorous reaction subsided the mixture was heated at 140–150° for further 3 hr. Excess of triethyl phosphite distilled off at 10–12 mm and the residue fractionated. After a small forerun the product distilled as a colourless liquid at 149°/1 mm, 52·3 g (87%), $[\alpha]_D$ −51·3° (*c* 2·25 in EtOH). (Found: C, 57·60; H, 9·43. Calc for $C_{16}H_{31}O_5P$: C, 57·47; H, 9·34%).

Diethyl (−)sec-octyloxycarbonylmethylphosphonate was prepared in a similar way (93%). The ester had b.p. 145–147°/2 mm, $[\alpha]_D$ −6·66° (*c* 5 in EtOH). (Found: C, 54·41, H, 9·27; Calc. for $C_{14}H_{29}O_5P$: C, 54·53; H, 9·48%).

Reaction of diethyl (−)menthyloxycarbonylmethylphosphonate with (±)styrene oxide

To a stirred slurry of 2·5 g 50% sodium hydride (0·052 mole) in 80 ml dry 1,2-dimethoxyethane, 16·7 g (0·05 mole) of the phosphonate ester was added dropwise and the mixture washed with 10 ml of the solvent. After about 1 hr at 30–40° the hydrogen evolution ceased and 6 g (0·05 mole) (±)styrene oxide dissolved in 10 ml dimethoxyethane was added at once. The mixture was kept at 65–70° for 4 hr. Most of the solvent was distilled off at red. press. (150–200 mm) on the water-bath, the residue diluted with 200 ml water and thoroughly extracted with ether. The combined ethereal

[38] Th. J. DeBoer and H. J. Backer, *Organic Syntheses* **36**, 16 (1956).
[39] H. Rupe, *Liebigs Ann.* **369**, 311 (1909).

extracts were dried (Na_2SO_4) and the ether distilled off on the water-bath. A light orange liquid was obtained, 13·7 g, $[\alpha]_D$ −37·61° (*c* 2·063 in $CHCl_3$), a part of which (4·3 g) was subjected to alkaline saponification to yield 0·85 g *trans*-2-phenylcyclopropanecarboxylic acid, m.p. 89–91°, $[\alpha]_D$ +16° (*c* 1·67 in EtOH), as the result of the standard procedure (see above). The remainder of the liquid (12 g) was fractionated yielding a pale yellow liquid, 8·45 g, b.p. 155–168°/0·5 mm, $[\alpha]_D$ −47·5° (*c* 2·335 in $CHCl_3$), which was similarly saponified to give *trans*-2-phenylcyclopropanecarboxylic acid, 1·97 g, m.p. 89–92°, $[\alpha]_D$ +17·5° (*c* 2·049 in EtOH).

In a subsequent experiment acid of $[\alpha]_D$ +16·5° (*c* 2·108 in EtOH), m.p. 90–92°, was obtained in 44% yield.

The amide prepared from the acid of $[\alpha]_D$ +17·5° *via* acyl chloride had $[\alpha]_D$ +9·2° (*c* 1·582 in EtOH, 2 dm).

Reaction of diethyl (−)sec-octyloxycarbonylmethylphosphonate with (±)styrene oxide was similarly accomplished and gave *trans*-2-phenylcyclopropanecarboxylic acid, m.p. 91–93°, $[\alpha]_D$ +12·0 (*c* 3·185 in EtOH) in 38% yield, and acid, m.p. 91·5–93°, $[\alpha]_D$ +15·2° (*c* 3·215 in EtOH) in 42% yield, respectively, in two subsequent experiments.

Acknowledgement—The author thanks Professor G. Fodor for valuable discussions, Mr. I. Koczor, Director of the Institute for Organic Chemical Industry, for supporting this work, and Mrs. M. Gyulay for technical assistance.