[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

# The Acid-catalyzed Rearrangement of the Stilbene Oxides

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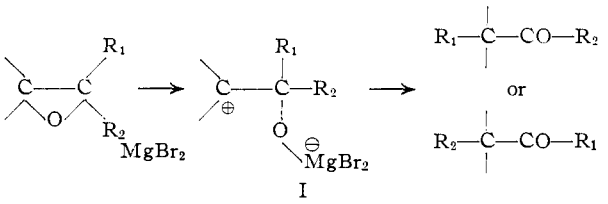
Both *cis*- and *trans*-stilbene oxides have been isomerized to diphenylacetaldehyde by treatment with boron trifluoride etherate. Although the *cis*-oxide was also converted to diphenylacetaldehyde in the presence of magnesium bromide, *trans*-stilbene oxide was isomerized to mixtures of diphenylacetaldehyde and desoxybenzoin under the same conditions. The existence of two reaction paths for epoxide isomerizations catalyzed by magnesium bromide has been supported by evidence gained from a study of the rearrangement of the *erythro*- and *threo*-2-bromo-1,2-diphenylethanol systems.

Although numerous examples have been reported[1,2] wherein either magnesium bromide or some magnesium salt derived from a Grignard reagent has catalyzed the rearrangement of substituted ethylene oxides, the interpretation to be placed on these experimental results is sometimes not clear. Winstein and Henderson[2] have noted that the products of such isomerizations may be predicted if the oxirane ring is cleaved to form the more stable ionic intermediate I. However, any prediction as to which group ($R_1$ or $R_2$) will migrate is more difficult. In certain cases the migratory aptitudes of the substituents ($R_1$ and $R_2$) suggested by the magnesium bromide-catalyzed rearrangement of epoxides disagree with the relative migratory abilities of the same groups as determined by pinacol-type rearrangements of related systems. For example, an ether solution of 1,2-diphenyl-1-methoxyethylene oxide, probably the *trans* isomer,[3] was isomerized to the methyl ether of desoxybenzoin in the presence of magnesium bromide[4]; such a rearrangement requires the migration or elimination of a hydrogen atom in preference to the migration of a phenyl group. However, the migration of a phenyl group rather than a hydrogen atom has been observed both in the acid-catalyzed rearrangement of each of the diastereoisomeric hydrobenzoins[5] and in the rearrangement of each of the diastereoisomeric 2-bromo-1,2-diphenylethanols catalyzed by silver ion (*vide infra*); the product was diphenylacetaldehyde in each case. Because of such discrepancies this investigation was initiated both to learn what effect the stereochemistry of the reactant exerted on the structure of the product[6] and to identify the compound which

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was actually undergoing rearrangement. Possible structures for the rearranging compound include the oxide, the bromoalcohol derived from the oxide and the bromomagnesium salt of the bromoalcohol.

The isomerization of *cis*- and *trans*-stilbene oxides was selected for an initial study. In a previous study Tiffeneau and Levy[7] pyrolyzed *trans*-stilbene oxide; the products isolated were *trans*-stilbene and benzaldehyde. Kayser[8] has reported that both *cis*- and *trans*-stilbene oxides react with the methyl, ethyl and benzyl Grignard reagents without rearrangement, the product being the expected alcohol in each case.

To study the acid-catalyzed rearrangement of the stilbene oxides under conditions which precluded the intervention of halohydrin intermediates, each of the isomeric oxides II and III was treated with boron trifluoride etherate[9] either in benzene or in ether (Table I). In every case the only product obtained was diphenylacetaldehyde (IV), isolated either as its methone derivative or as its 2,4-dinitrophenylhydrazone. The transient existence of the other possible rearrangement product, desoxybenzoin (V), in the reaction mixture was excluded since the ketone V was not isomerized under the conditions of the reaction.

The above lack of steric control, previously observed when the isomeric hydrobenzoins were heated with acid,[5] was also noted with the stilbene bromohydrins VI and VII. Each of these alcohols was converted to diphenylacetaldehyde (IV) by the action of alcoholic silver nitrate.[10] These data suggest the formation of an ionic intermediate VIIIa or VIIIc of sufficient stability to permit the migration of the group with the higher migratory aptitude.

In the presence of magnesium bromide a solution of *cis*-stilbene oxide (II), either in benzene or in a benzene–ether mixture, was isomerized to diphenyl acetaldehyde (IV) accompanied in some cases by 1–3% of desoxybenzoin (V) (Table II). *trans*-

(1) N. G. Gaylord and E. I. Becker, *Chem. Revs.*, **49**, 413 (1951).

(2) E. C. Elderfield, "Heterocyclic Compounds," Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1950, pp. 1–58.

(3) C. L. Stevens and J. H. Coffield, 126th Meeting of the American Chemical Society, New York, N. Y., Sept. 12–17, 1954, Abstracts of Papers, p. 63-O.

(4) C. L. Stevens, M. L. Weiner and R. C. Freeman, THIS JOURNAL, **75**, 3977 (1953); C. L. Stevens and S. J. Dykstra, *ibid.*, **76**, 4402 (1954).

(5) A. Breuer and T. Zincke, *Ann.*, **198**, 141 (1879).

(6) The influence of the stereochemistry of the reactant on the structure of the product from pinacol-type rearrangements has been summarized by D. Y. Curtin [*Rec. Chem. Progress*, **15**, 111 (1954)].

(7) M. Tiffeneau and J. Levy, *Bull. soc. chim. France*, [4] **39**, 768 (1926).

(8) F. Kayser, *Compt. rend.*, **196**, 1127 (1933); *ibid.*, **199**, 1424 (1934); *Ann. chim. (Paris)*, [11] **6**, 145 (1936).

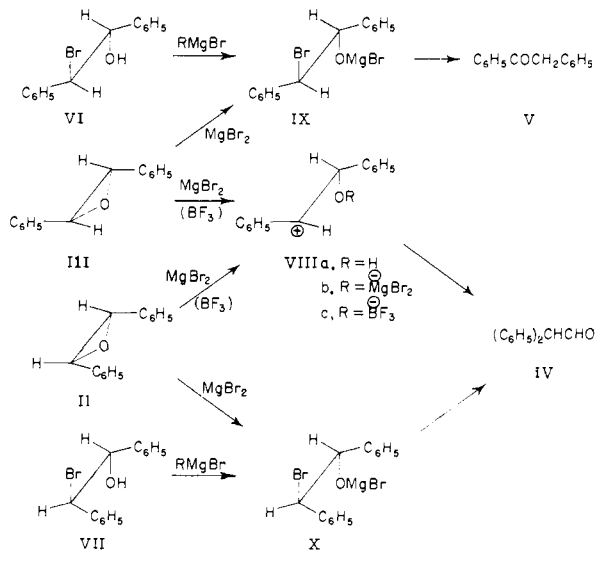
(9) Other reports of the use of this reagent to catalyze the isomerization of substituted ethylene oxides include: (a) H. Heusser, K. Eichenberger, P. Kurath, H. R. Dallenbach and O. Jeger, *Helv. Chim. Acta*, **34**, 2106 (1951); (b) K. Heusler and A. Wettstein, *ibid.*, **36**, 398 (1953); (c) P. Bladon and co-workers, *J. Chem. Soc.*, 2921 (1953); (d) H. B. Henbest and A. A. Wagland, *ibid.*, 728 (1954); (e) H. O. House, THIS JOURNAL, **76**, 1235 (1954).

(10) Reulos and Collin (ref. 35) reported the conversion of *threo*-2-iodo-1,2-diphenylethanol to diphenylacetaldehyde (IV) under similar conditions. However, Reulos (ref. 34) found that the same reaction conditions converted the corresponding *erythro*-iodohydrin to *trans*-stilbene.

Stilbene oxide (III) was converted to mixtures of the aldehyde IV and the ketone V under the same conditions (Table II). The amount of rearranged product obtained from each of the oxides was appreciably less when the isomerization was run at the boiling point of ether rather than at the boiling point of benzene. This observation may explain the lack of rearrangement reported by Kayser[8] although, with the exception of the reactions involving the benzyl Grignard reagent, a reagent often observed to react with the oxirane ring without attendant rearrangement,[1] the low yields obtained by Kayser do not exclude the possibility that an appreciable fraction of each of the stilbene oxides underwent rearrangement.

In the case of the *trans*-oxide III the initial presence of ether in the reaction mixture markedly increased the proportion of desoxybenzoin (V) in the product. This result suggested that the more polar ether–benzene mixture favored the formation of the bromomagnesium salt IX prior to rearrangement.[11] To test this hypothesis each of the 2-bromo-1,2-diphenylethanols VI and VII was treated with one equivalent of ethylmagnesium bromide; the resulting bromomagnesium salts were heated in boiling benzene. The *erythro*-bromohydrin VI yielded only desoxybenzoin (V) whereas the *threo*-isomer VII was converted to diphenylacetaldehyde (IV). That the salts IX and X rather than the free bromohydrins VI and VII were the rearranging species was indicated when a benzene solution of each of the bromohydrins was heated with magnesium bromide; no carbonyl compound could be isolated in either case.

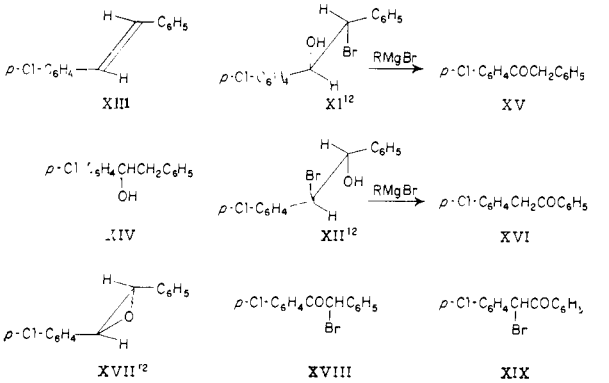
CHART I[12]




Additional evidence indicating that the *erythro*-bromohydrin bromomagnesium salt IX and not the *trans*-oxide III is the direct precursor of the desoxybenzoin (V) was gained from a study of the bromohydrins XI and XII derived from *trans*-*p*-chlorostilbene (XIII). The *trans*-configuration was assigned this olefin on the basis of evidence previously cited,[13] the method of preparation (dehydration of XIV), a comparison of the ultraviolet spectrum of the compound with the spectra of *cis*- and *trans*-stilbene and the presence in the infrared spectrum of a strong band at 965 cm.$^{-1}$, attributable to the carbon–hydrogen rocking vibration of a *trans*-olefin. When treated with one equivalent of ethylmagnesium bromide in boiling benzene each of the bromohydrins XI and XII was converted to the corresponding ketone XV and XVI. Thus the *trans*-oxide XVII cannot be an intermediate.

Although the above data do not exclude the possibility that the *threo*-bromohydrin VII is converted to *cis*-stilbene oxide (II) prior to rearrangement it does not seem unreasonable to suppose that the bromomagnesium salt X is converted directly to diphenylacetaldehyde (IV). In the stilbene halohydrin series the *threo*-isomer is converted to the *cis*-oxide by alkali more slowly than the *erythro*-isomer is converted to the *trans*-oxide both in the case of the chlorohydrins[14] and in the case of the bromohydrins.[15] The conclusion can be drawn that the magnesium bromide-catalyzed rearrangement of *trans*- and, probably, *cis*-epoxides can proceed by at least the two routes pictured in Chart I. Magnesium bromide can serve as a Lewis acid to promote a pinacol-type rearrangement involving an ionic intermediate such as VIIIb. Alternately, the initially formed oxirane–magnesium bromide complex may be attacked by bromide ion to produce the bromomagnesium salt of the bromohydrin (*e.g.*, IX) which then decomposes in a fashion quite unlike the pinacol-type rearrangement.

The preparation of the two *erythro*-bromohydrins XI and XII posed certain problems. The reaction of the *trans*-olefin XIII with hypobromous acid,[16] a reaction employed successfully with *trans*-stilbene, produced a viscous oil from which a series of fractional crystallizations served to separate a




(11) The conversion of the oxirane ring to an ethylene bromohydrin derivative by the action of magnesium bromide or a Grignard reagent is a well-known phenomenon (ref. 1). The effect of ether is interesting since most of the reported reactions (ref. 1) of Grignard reagents with epoxides involve the initial presence of ether in the reaction mixture.

(12) For simplicity only one of the enantiomorphic structures for each of the racemates employed has been pictured.

(13) F. Bergmann, J. Weizman and D. Shapiro, *J. Org. Chem.*, **9**, 408 (1944).

(14) H. Felkin, *Compt. rend.*, **231**, 1316 (1950).

(15) H. W. Holly, Ph.D. Dissertation, Rutgers University, 1952.

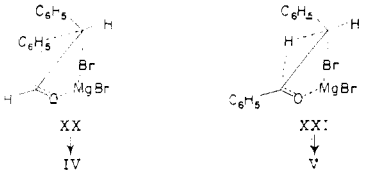
(16) The hypobromous acid was derived from N-bromoacetamide according to the procedure of C. Meystre and A. Wettstein [*Helv. Chim. Acta*, **32**, 1978 (1949)].

small amount of the higher melting *erythro*-bromohydrin, m.p. 85–86°. The product was subsequently shown to be *erythro*-2-bromo-2-[4-chlorophenyl]-1-phenylethanol (XII) both by consideration of its rearrangement product and by the preparation of the second *erythro*-isomer. Attempts to separate the remaining mixture by chromatography on neutral alumina met with failure, a portion of the product being converted to the *trans*-oxide XVII on the column. Chromatography on magnesium sulfate seemed not to effect appreciable separation. Studies with pure *erythro*-2-bromo-1,2-diphenylethanol (VI) suggested that this system would not survive chromatography on neutral alumina, acid-washed alumina or silica gel.

The reported[17] reduction of α-chloro- and α-bromodesoxybenzoin to the corresponding *erythro*-halohydrins in 76 and 10% yield, respectively, with lithium aluminum hydride suggested an alternate synthetic route based on the bromoketones XVIII and XIX. In an attempt to minimize replacement of the halogen atom sodium borohydride[18] was selected as the reducing agent. The reduction of α-bromobenzyl *p*-chlorophenyl ketone (XVIII) with one equivalent[19] of sodium borohydride produced a viscous oil from which no solid could be isolated by crystallization; chromatography on magnesium sulfate permitted the separation of the debrominated ketone XV and the desired *erythro*-bromohydrin XI, m.p. 57–58, from the mixture. The corresponding reduction of the isomeric bromoketone XIX produced a mixture from which the ketone XVI and a bromohydrin, m.p. 122–123.5°, were isolated. This bromoalcohol was converted to an oil by sodium hydroxide under conditions which converted the above bromohydrins XI and XII to the *trans*-oxide XVII; the reduction product is considered to be *threo*-2-bromo-2-[4-chlorophenyl]-1-phenylethanol. The presence of the *erythro*-isomer XII in the mother liquor from the fractional crystallization was indicated since the treatment of a portion of the residual oil with alcoholic sodium hydroxide produced *trans*-*p*-chlorostilbene oxide (XVII).[20]

The partial dehalogenation of an α-bromoketone during its reduction with sodium borohydride has been ascribed to isomerization during the isolation[18e]; this explanation cannot be reasonably applied to the cases reported here. Although the formation of a hemiacetal[18a] might account for these results, the attack of a hydride ion to displace the bromide ion at a rate comparable to the rate of attack at the carbonyl function would provide an equally rational explanation.

The stereochemical influence noted in the rearrangement of the bromomagnesium salts IX and X is of interest. Tiffeneau, Tchoubar and Le-Tellier[21] have noted the importance of stereochemistry in the rearrangement of the bromomagnesium salts of the 2-bromo-1-alkylcyclohexanols and related compounds. That the products of this type of rearrangement differ from those obtained in the pinacol-type rearrangement of certain diastereoisomeric bromohydrins was recently reported by Curtin and Meislich.[22] The reaction conditions[1,2] employed for this isomerization usually involve heating the bromomagnesium salt of the halohydrin either in the absence of a solvent or as a suspension in a non-polar solvent. Such conditions are more compatible with a cyclic intramolecular process than with an ionic process.[22,23] Possible transition states[22] for such a cyclic intramolecular rearrangement are pictured below (XX and XXI). If the solvated oxymagnesium bromide group is considered to be larger than the phenyl group then the least energetic transition state for the rearrangement process would be the one wherein the β-phenyl group and the oxymagnesium bromide group are *trans*.[6] The transition states formulated on this basis are in accord with the experimental facts both for the *threo*-isomer XX which rearranges with the migration of a phenyl group and for the *erythro*-isomer XXI which arranges with the migration (or elimination) of a hydrogen atom.




This investigation is being continued with certain aliphatic ethylene oxides and the halohydrins derived from them.

## Experimental[24]

*p*-**Chlorophenylbenzylcarbinol (XIV).**—To a solution of benzylmagnesium chloride, prepared from 63.5 g. (0.50 mole) of benzyl chloride and 48.6 g. (2.0 g. atoms) of magnesium, in 450 ml. of ether was added, dropwise and with stirring, a solution of 70.3 g. (0.50 mole) of *p*-chlorobenzaldehyde in 300 ml. of ether. After the mixture had been stirred for 30 minutes, it was poured into an aqueous solution of ammonium chloride and the resulting solution was extracted with ether. The ether solution was washed first with aqueous ammonium chloride and then with 5% aqueous sodium bicarbonate and dried over magnesium sulfate. The solvent was removed and the residue was distilled under reduced pressure. The carbinol, collected over the range

(17) R. E. Lutz, R. L. Wayland and H. G. France, THIS JOURNAL, **72**, 5511 (1950).

(18) Examples of the use of this reagent to reduce bromoketones include: (a) E. T. McBee and T. M. Burton, *ibid.*, **74**, 3022 (1952); (b) L. F. Fieser and R. Ettore, *ibid.*, **75**, 1700 (1953); (c) L. F. Fieser and X. A. Dominguez, *ibid.*, **75**, 1704 (1953); (d) L. F. Fieser and W. Huang, *ibid.*, **75**, 4837 (1953); (e) E. J. Corey, *ibid.*, **75**, 4832 (1953).

(19) Only the *trans*-oxide XVII was isolated when four equivalents of sodium borohydride and a longer reaction time were employed.

(20) The isolation of only the *erythro*-isomers from the desyl halides (ref. 17) is understandable when one considers that the *threo*-isomers have much lower melting points in each case (ref. 34 and 35). The formation of both isomeric halohydrins has been noted in other cases (ref. 18), including the reported (ref. 14) reduction of α-chlorodesoxybenzoin to an equal mixture of the *threo*- and *erythro*-chlorohydrins with lithium aluminum hydride.

(21) M. Tiffeneau and B. Tchoubar, *Compt. rend.*, **198**, 941 (1934); *ibid.*, **199**, 360 (1934); M. Tiffeneau, B. Tchoubar and S. LeTelliet, *ibid.*, **216**, 856 (1943).

(22) D. Y. Curtin and E. K. Meislich, THIS JOURNAL, **74**, 5905 (1952).

(23) F. Bergmann and A. Kalmus, *ibid.*, **76**, 4137 (1954).

(24) All melting points are corrected and all boiling points are uncorrected. The infrared spectra were determined with a Baird double beam infrared recording spectrophotometer, model B, fitted with a sodium chloride prism. The ultraviolet spectra were determined in 95% ethanol with a Cary recording spectrophotometer, model 11 MS. The microanalyses were performed by Dr. S. M. Nagy and his associates.

TABLE I

ISOMERIZATIONS CATALYZED BY BORON TRIFLUORIDE ETHERATE

| Reaction conditions | | | Yield of diphenylacetaldehyde derivative | |
|---|---|---|---|---|
| Solvent | Reaction time (min.) | Method of isolation | From *cis*-stilbene oxide | From *trans*-stilbene oxide |
| Benzene | 1 | 2,4-Dinitrophenylhydrazone | 0.63 g. (64%) M.p. 145–148.5° | 0.77 g. (79%) M.p. 147.5–149.5° |
| Benzene | 2 | 2,4-Dinitrophenylhydrazone | 0.39 g. (40%) M.p. 149.5–151° | 0.61 g. (62%) M.p. 147.5–149.5° |
| Benzene | 2 | Methone | 0.48 g. (41%) M.p. 207–209.5° | 0.57 g. (49%) M.p. 207.5–210° |
| Benzene | 5 | Methone | 0.36 g. (31%) M.p. 208–210° | 0.33 g. (28%) M.p. 207–210° |
| Benzene | 10 | 2,4-Dinitrophenylhydrazone | None | None |
| Ether | 15 | 2,4-Dinitrophenylhydrazone | 0.47 g. (48%) M.p. 149–151° | 0.58 g. (59%) M.p. 148–150.5° |

145–158° (0.07–0.1 mm.), amounted to 78.6 g. (67.5%) of a colorless oil which crystallized when cooled. A portion of the product was recrystallized from hexane to give white needles melting at 52.5–54°.

*Anal.* Calcd. for $C_{14}H_{13}ClO$: C, 72.24; H, 5.63; Cl, 15.24. Found: C, 72.34; H, 5.76; Cl, 15.21.

The infrared spectrum[25] of the product has a broad band at 3325 cm.$^{-1}$ (associated O–H stretching).

***trans*-*p*-Chlorostilbene (XIII).**—A solution of 23.3 g. (0.10 mole) of *p*-chlorophenylbenzylcarbinol in a mixture of 250 ml. of ethanol and 125 ml. of hydrochloric acid was heated on a steam-bath for 19 hours. Additional portions of ethanol were added from time to time to keep the mixture homogeneous. The resulting solution was chilled and the crystalline precipitate was collected on a filter. The stilbene crystallized from ethanol as white plates, m.p. 128–129° (lit.[13] 129°), yield 10.57 g. (49.2%). The ultraviolet spectrum of *trans*-*p*-chlorostilbene which exhibits maxima at 229 mμ ($\epsilon_{max.}$ 15,900), 300 mμ ($\epsilon_{max.}$ 33,900) and at 313 mμ ($\epsilon_{max.}$ 32,800) resembles closely the spectrum of *trans*-stilbene and differs from the spectrum of *cis*-stilbene. The infrared spectrum[25] of the material has a strong band at 965 cm.$^{-1}$ (C–H rocking of *trans*-olefin) and a weak band at 1630 cm.$^{-1}$ (C=C stretching).

***trans*-*p*-Chlorostilbene Oxide (XVII).**—A solution of 7.00 g. (0.0325 mole) of *trans*-*p*-chlorostilbene in 150 ml. of chloroform containing 5.0 g. of sodium acetate trihydrate was treated, dropwise and with stirring, with 3.8 g. (0.050 mole) of peracetic acid as a 43.1% solution in acetic acid.[26] The temperature of the reaction mixture was kept at 16° during the addition and was then allowed to rise to room temperature over a period of 4 hours. The mixture was stirred for a total of 48 hours and then was washed first with cold water, then with a saturated solution of sodium bicarbonate in water and, finally, with water. After the chloroform solution had been dried over magnesium sulfate, the solvent was removed on a steam-bath. The residue crystallized from methanol as white plates, m.p. 94–97°, yield 6.65 g. (88.7%). Two additional crystallizations from methanol afforded the pure oxide melting at 99–100°.

*Anal.* Calcd. for $C_{14}H_{11}ClO$: C, 72.86; H, 4.81; Cl, 15.37. Found: C, 72.99; H, 4.94; Cl, 15.03.

**The Stilbene Oxides.**—*cis*-Stilbene oxide (II), m.p. 38–40° (lit.[27] 37.0–37.5°), and *trans*-stilbene oxide (III), m.p. 69–70° (lit.[27] 69.0–69.5°), were prepared from the corresponding hydrocarbons by the method outlined above.

**Preparation of the 2,4-Dinitrophenylhydrazones.**—A mixture of 0.50 g. (0.0026 mole) of crude diphenylacetaldehyde, b.p. 104–109° (0.22 mm.), $n^{25}D$ 1.5882 [lit.[28] b.p. 170–175° (15 mm.)], 0.75 g. (0.0038 mole) of 2,4-dinitrophenylhydrazine and 100 ml. of ethanol was heated to boiling. After 3 ml. of concentrated hydrochloric acid had been added, the mixture was boiled for 5 minutes and allowed to cool. The dinitrophenylhydrazone separated as golden yellow needles, m.p. 146–149°, yield 0.79 g. (81%). Recrystallization from ethanol raised the melting point to 150–151°.

*Anal.* Calcd. for $C_{20}H_{16}N_4O_4$: C, 63.82; H, 4.29; N, 14.88. Found: C, 63.89; H, 4.30; N, 15.08.

In the same fashion *p*-chlorobenzyl phenyl ketone, m.p. 134.5–135.5° (lit.[29] 138°), was converted to its 2,4-dinitrophenylhydrazone which crystallized from an ethanol–ethyl acetate mixture as red prisms, m.p. 222–223.5°.

*Anal.* Calcd. for $C_{20}H_{15}ClN_4O_4$: C, 58.47; H, 3.68; Cl, 8.63; N, 13.64. Found: C, 58.54; H, 3.89; Cl, 8.79; N, 13.59.

Benzyl *p*-chlorophenyl ketone,[30] m.p. 104.5–106° (lit.[29] 107.5°), gave a 2,4-dinitrophenylhydrazone which crystallized from an ethanol–ethyl acetate mixture as orange plates melting at 209–210°.

*Anal.* Calcd. for $C_{20}H_{15}ClN_4O_4$: C, 58.47; H, 3.68; Cl, 8.63; N, 13.64. Found: C, 58.36; H, 3.97; Cl, 8.59; N, 13.67.

An approximately equal mixture of the two pure ketone dinitrophenylhydrazones melted at 189–198°.

**Rearrangement of the Stilbene Oxides with Boron Trifluoride Etherate.**—A solution of 0.50 g. (0.0026 mole) of the oxide in 25 ml. of the appropriate solvent was treated with 2.0 ml. of boron trifluoride etherate. After the mixture had been stirred for the specified time, it was diluted with ether and the resulting solution was washed with two portions of water. The solvents were removed on a steam-bath and the residue was treated with 0.75 g. of 2,4-dinitrophenylhydrazine in the manner described above.

Alternately, the diphenylacetaldehyde could be isolated from the above reaction mixture as its methone derivative. The material remaining after the evaporation of the solvents was dissolved in 20 ml. of a 1:1 ethanol–water mixture and treated with 1.00 g. (0.0071 mole) of dimedon and 5 drops of piperidine. The mixture was boiled for 10 minutes, diluted with sufficient boiling ethanol to give a clear solution and allowed to cool. The crude product was purified by recrystallization from ethanol. The methone derivative prepared from an authentic sample of diphenylacetaldehyde melted at 209.9–210.5°.[31]

The results of the rearrangements effected with boron trifluoride etherate are listed in Table I. In each case the product isolated from the reaction was identified by a mixed melting point with an authentic sample. When 0.50 g. (0.0026 mole) of desoxybenzoin in cyclohexane solution was treated with boron trifluoride etherate for a period of 2 minutes and then worked up as described above (dimedon method) none of the methone of diphenylacetaldehyde was isolated. However, 0.43 g. (86%) of the unchanged ketone, m.p. 54–56°, was recovered. A mixed melting point with an authentic sample was not depressed.

Each of the isomeric stilbene oxides was treated directly with 2,4-dinitrophenylhydrazine in the manner described above. In neither case could any dinitrophenylhydrazone be isolated.

**Rearrangement of the Stilbene Oxides with Magnesium Bromide Etherate.**—Magnesium bromide etherate[32] was

(25) Determined as a suspension in a potassium bromide pellet.

(26) Epoxidation procedure of A. C. Cope, S. W. Fenton and C. F. Spencer [THIS JOURNAL, **74**, 5884 (1952)].

(27) D. Y. Curtin and D. B. Kellom, *ibid.*, **75**, 6011 (1953).

(28) M. Tiffeneau, *Ann. chim.* (*Paris*), [8] **10**, 322 (1907).

(29) S. S. Jenkins and E. W. Richardson, THIS JOURNAL, **55**, 1618 (1933); S. S. Jenkins, *ibid.*, **56**, 682 (1934).

(30) N. G. Buu-Hoi and R. Rogers, *Rec. trav. chim.*, **65**, 251 (1946).

(31) A. C. Cope and P. Starke, to be published.

(32) H. H. Rowley, THIS JOURNAL, **72**, 3305 (1950).

TABLE II

ISOMERIZATIONS CATALYZED BY MAGNESIUM BROMIDE ETHERATE

| Reaction conditions | | Yield of diphenylacetaldehyde 2,4-dinitrophenylhydrazone | | Yield of desoxybenzoin 2,4-dinitrophenylhydrazone | |
|---|---|---|---|---|---|
| Solvent and temp. | Reaction time | From *cis*-stilbene oxide | From *trans*-stilbene oxide | From *cis*-stilbene oxide | From *trans*-stilbene oxide |
| Boiling benzene | 15 min. | 0.64 g. (65%) M.p. 146.5–150.5° | 0.34 g. (35%) M.p. 149.5–151° | 0.03 g. (3%) M.p. 197–200° | 0.12 g. (12%) M.p. 196–200° |
| Boiling benzene | 17.5 hr. | 0.54 g. (55%) M.p. 149.5–151° | 0.38 g. (39%) M.p. 149–151° | None | 0.10 g. (10%) M.p. 194–200° |
| Boiling mixture of 2:1 ether-benzene (by vol.) | 3 hr. | 0.24 g. (25%) M.p. 148.5–151° | 0.12 g. (12%) M.p. 150–151° | 0.01 g. (1%) M.p. 192–196° | 0.18 g. (18%) M.p. 195–199° |
| A 1:1 ether–benzene mixture (by vol.) was allowed to stand 100 min. Then the ether was distilled from the mixture and the benzene soln. was boiled for 20 min. | | 0.55 g. (56%) M.p. 146.5–149° | 0.14 g. (14%) M.p. 149.5–151° | None | 0.43 g. (44%) M.p. 197–201° |

prepared by the dropwise addition of 2.0 ml. (5.86 g., 0.0367 mole) of bromine to 3.00 g. (0.123 g.-atom) of magnesium covered with 150 ml. of anhydrous ether. The resulting suspension was decanted from the unchanged magnesium, chilled and the ethereal mother liquor was decanted from the crystalline etherate. The salt was dissolved in 100 ml. of either benzene or a benzene–ether mixture and used immediately.

A solution of 0.50 g. (0.0026 mole) of the oxide in ether or benzene was treated with 25 ml. (from 0.0092 mole of bromine) of the previously described magnesium bromide solution and subjected to the reaction conditions summarized in Table II. The resulting reaction mixture was diluted with ether and poured into an aqueous solution of ammonium chloride. After the organic layer had been separated and washed twice with water the solvents were removed on a steam-bath and the residue was treated with 0.75 g. of 2,4-dinitrophenylhydrazine in the fashion previously outlined.

The products of the isomerizations (Table II) were identified by mixed melting points with authentic samples. An authentic sample of desoxybenzoin was converted quantitatively to its 2,4-dinitrophenylhydrazone which crystallized from an ethanol–ethyl acetate mixture as orange plates, m.p. 201–202° (lit.[33] m.p. 204°). When mixtures of the dinitrophenylhydrazones of desoxybenzoin and diphenylacetaldehyde were encountered they were separated by extraction with 75 ml. of boiling ethanol. The less soluble ketone derivative was removed from the hot mixture by filtration. The crude aldehyde and ketone derivatives thus obtained were purified by recrystallization from the solvents indicated above.

A solution of 0.50 g. (0.0026 mole) of desoxybenzoin in 10 ml. of benzene was treated with 25 ml. of a benzene solution of magnesium bromide etherate. The resulting solution was boiled under reflux for 1.5 hours and worked up as described above. The desoxybenzoin, recovered as its dinitrophenylhydrazone melting at 197–201°, amounted to 0.93 g. (95% recovery). Recrystallization raised the melting point to 200–202°. A mixed melting point with an authentic sample was not depressed.

*erythro*-2-Bromo-1,2-diphenylethanol (VI).—A solution of 1.80 g. (0.010 mole) of *trans*-stilbene and 2.0 g. of sodium acetate trihydrate in 100 ml. of acetone, 25 ml. of water and 25 ml. of acetic acid was treated with 2.76 g. (0.020 mole) of N-bromoacetamide. After the resulting solution had been allowed to stand for 2 hours, it was concentrated to about 75 ml. under an air jet. The mixture was diluted with 300 ml. of water and extracted with ether. The extract was washed with water and then with two portions of 5% aqueous sodium bicarbonate and dried over magnesium sulfate. After the ether had been removed, the residue was dissolved in a boiling petroleum ether (b.p. 90–100°)–hexane mixture and cooled. The bromohydrin separated as flat, white needles, m.p. 83.5–85°, yield 1.72 g. (62.2%). An additional recrystallization raised the melting point to 84.5–85.5° (lit.[34] 86°). The infrared spectrum[25] has a band at 3350 cm.$^{-1}$ (associated O–H stretching); no band is present which can be ascribed to a carbon–oxygen double bond stretching vibration.

*threo*-2-Bromo-1,2-diphenylethanol (VII).—A solution of 1.00 g. (0.0051 mole) of *cis*-stilbene oxide in 25 ml. of anhydrous ether was saturated with hydrogen bromide. After the resulting solution had been allowed to stand for 24 hours, it was washed with two portions of water and dried over magnesium sulfate. The ether was removed on a steam-bath and a solution of the residue in petroleum ether (b.p. 30–60°) was chilled in solid carbon dioxide. The bromohydrin separated as a white crystalline solid, m.p. 51–52° (lit.[35] 49°), in quantitative yield. The infrared spectrum[25] of the product exhibits a band at 3325 cm.$^{-1}$ (associated O–H stretching); the lack of absorption in the 6 $\mu$ region indicates the absence of the carbonyl function.

**Rearrangement of the 2-Bromo-1,2-diphenylethanols in the Presence of Silver Nitrate.**—Each of the isomeric bromohydrins was treated with 2,4-dinitrophenylhydrazine in the manner described earlier. In neither case was it possible to isolate a dinitrophenylhydrazone.

**The *threo*-Isomer.**—A solution of 277 mg. (0.001 mole) of *threo*-2-bromo-1,2-diphenylethanol in 15 ml. of ethanol was treated with a solution of 180 mg. (0.00106 mole) of silver nitrate in 6 ml. of water. The resulting mixture, which became turbid instantly, was warmed to about 50° for 5 minutes, diluted with 10 ml. of ethanol and filtered. The residual silver bromide was washed with an additional portion of ethanol. The alcoholic filtrate was treated with 0.30 g. of 2,4-dinitrophenylhydrazine in the usual manner. Only the 2,4-dinitrophenylhydrazone of diphenylacetaldehyde, identified by a mixed melting point with an authentic sample, could be isolated from the reaction mixture, yield 190 mg. (50.5%), m.p. 147.5–149.5°.

**The *erythro*-Isomer.**—In the same manner 277 mg. (0.001 mole) of *erythro*-2-bromo-1,2-diphenylethanol was converted to diphenylacetaldehyde 2,4-dinitrophenylhydrazone, yield 208 mg. (55.3%), m.p. 148.5–150.5°.

**Rearrangement of the 2-Bromo-1,2-diphenylethanols as their Bromomagnesium Salts. The *erythro*-Isomer.**—A solution of 0.25 g. (0.00090 mole) of the *erythro*-bromohydrin in 15 ml. of benzene was treated with 1.0 ml. (0.00090 mole) of a standard solution of ethylmagnesium bromide in a 1:1 mixture of ether and benzene. A white precipitate appeared soon after the Grignard reagent was added. The resulting mixture was refluxed for 30 minutes and then decomposed with an aqueous ammonium chloride solution. The product was taken up in ether, washed with water and the ether removed. The residue was treated with 0.35 g. of 2,4-dinitrophenylhydrazine in the fashion outlined above. The 2,4-dinitrophenylhydrazone of desoxybenzoin crystallized from the reaction mixture as orange plates, m.p. 197–200°, yield 0.29 g. (85%). The product was identified by a mixed melting point with an authentic sample.

**The *threo*-Isomer.**—Similarly, 0.25 g. (0.00090 mole) of *threo*-2-bromo-1,2-diphenylethanol was converted the 2,4-dinitrophenylhydrazone of diphenylacetaldehyde, m.p. 147.5–149.5°, yield 0.22 g. (65%). A mixed melting point with an authentic sample was not depressed.

**The Action of Magnesium Bromide on the 2-Bromo-1,2-diphenylethanols. The *threo*-Isomer.**—A solution of 0.71 g. (0.0026 mole) of the *threo*-bromohydrin in 10 ml. of benzene was treated with 25 ml. of a solution of magnesium bromide etherate in benzene, prepared as described previously. The mixture was refluxed for 30 minutes and

(33) C. F. H. Allen and J. R. Richmond, *J. Org. Chem.*, **2**, 222 (1937).

(34) D. Reulos, *Compt. rend.*, **216**, 774 (1943).

(35) D. Reulos and C. Collins, *ibid.*, **218**, 795 (1944).

worked up as described for the magnesium bromide-catalyzed oxide isomerizations. A hexane solution of the crude product deposited 70 mg. of *meso*-$\alpha,\alpha'$-dibromobibenzyl as white needles, m.p. 241–242° (lit. 237°,[34] 244°[36]). The mother liquor was concentrated and treated with 2,4-dinitrophenylhydrazine; no 2,4-dinitrophenylhydrazone could be isolated.

**The *erythro*-Isomer.**—In a similar manner 0.10 g. (0.0004 mole) of the *erythro*-bromoalcohol was treated with 5 ml. of a solution of magnesium bromide etherate in benzene. No 2,4-dinitrophenylhydrazone could be isolated.

**The Reaction of *trans*-*p*-Chlorostilbene (XIII) with N-Bromoacetamide.**—A solution of 2.15 g. (0.01 mole) of the *trans*-olefin and 2.00 g. of sodium acetate trihydrate in 125 ml. of acetone, 25 ml. of water and 25 ml. of acetic acid was treated with 2.76 g. (0.020 mole) of N-bromoacetamide and worked up in the manner outlined previously. When a solution of the crude product, a viscous oil, in pentane was chilled in Dry Ice a white solid melting over the range 60–75° was induced to separate. The combined solids from two runs were subjected to a series of fractional crystallizations from hexane; 517 mg. (8.3%) of flat, white needles, m.p. 83–85°, was separated. An additional crystallization afforded the pure *erythro*-2-bromo-2-[4-chlorophenyl]-1-phenylethanol (XII) melting at 85–86.5°.

*Anal.* Calcd. for $C_{14}H_{12}BrClO$: C, 53.95; H, 3.88. Found: C, 53.84; H, 3.94.

A 27.16-mg. sample of the material gave 28.56 mg. of mixed silver halides ($C_{14}H_{12}BrClO$ requires 28.86 mg.).

The infrared spectrum[25] of the bromoalcohol has a band at 3325 cm.$^{-1}$ (associated O–H stretching) and lacks absorption attributable to a carbonyl group.

The crude solid (312 mg., m.p. 71–82°) obtained from the mother liquors of the above fractional recrystallization was treated with 223 mg. of *p*-nitrobenzoyl chloride and 0.1 ml. of pyridine in 10 ml. of benzene. The *p*-nitrobenzoate of *erythro*-2-bromo-2-[4-chlorophenyl]-1-phenylethanol crystallized from ethanol as needles, m.p. 156–159°, yield 327 mg. (3.5% based on the *p*-chlorostilbene, 71% based on the crude bromohydrin employed). An additional crystallization sharpened the melting point to 157–159°.

*Anal.* Calcd. for $C_{21}H_{15}BrClNO_4$: C, 54.74; H, 3.28; N, 3.04. Found: C, 54.45; H, 3.24; N, 3.25.

The infrared spectrum[25] of the material exhibits a band at 1710 cm.$^{-1}$ attributable to the carbonyl group of a conjugated ester. The spectrum closely resembles the infrared spectrum[25] of the *p*-nitrobenzoate of *erythro*-2-bromo-1,2-diphenylethanol (needles from ethanol–water, m.p. 117.5–118.5°, lit.[34] 121–122°) which exhibits a band, attributable to the carbonyl function, at 1705 cm.$^{-1}$.

**Reduction of $\alpha$-Bromo-*p*-chlorobenzyl Phenyl Ketone (XIX).**—A solution of 3.10 g. (0.010 mole) of the bromoketone, m.p. 68.5–70° (lit.[29] 67.5–68.5°), infrared spectrum[37] 1685 cm.$^{-1}$ (conjugated C=O stretching), in 50 ml. of methanol was treated with a solution of 0.11 g. (0.0029 mole) of sodium borohydride in 15 ml. of methanol. After the solution had been stirred for 2 minutes, it was acidified to litmus with dilute hydrochloric acid and concentrated under a jet of air. *p*-Chlorobenzyl phenyl ketone (XVI) (232 mg., 10%) m.p. 134–135.5°, separated from the solution. A mixed melting point with an authentic sample showed no depression. The concentrated solution was poured into water and extracted with ether. After the extract had been washed with water and dried over magnesium sulfate the ether was removed and the residual oil was taken up in hexane. A series of fractional crystallizations separated 1.384 g. (44.5%) of *threo*-2-bromo-2-[4-chlorophenyl]-1-phenylethanol as colorless, diamond shaped crystals, m.p. 122–123.5°.

*Anal.* Calcd. for $C_{14}H_{12}BrClO$: C, 53.95; H, 3.88. Found: C, 53.66; H. 4.06.

A 30.30-mg. portion of the material gave 32.00 mg. of mixed silver halides ($C_{14}H_{12}BrClO$ requires 32.20 mg.).

The infrared spectrum[25] of the *threo*-bromohydrin exhibits a broad, intense band with its center of gravity at 3160 cm.$^{-1}$ attributable to an associated hydroxyl group; evidence for a carbonyl function is lacking. When sodium hydroxide was added to a methanolic solution of the product it was converted to an oil which could not be induced to crystallize.

Concentration of the mother liquor from the fractional crystallizations yielded only additional traces of *p*-chlorobenzyl phenyl ketone and a viscous oil. A portion of the oil when treated with a methanolic solution of sodium hydroxide was converted in part to *trans*-*p*-chlorostilbene oxide (XVII), m.p. 97.5–99.5°. A mixed melting point with an authentic sample showed no depression.

**Reduction of $\alpha$-Bromobenzyl *p*-Chlorophenyl Ketone (XVIII).**—A solution of 3.06 g. (0.0099 mole) of the bromoketone, m.p. 61–63° (lit.[29] 62–62.5°), infrared spectrum[37] 1690 cm.$^{-1}$ (conjugated C=O stretching), was treated with 0.11 g. (0.0029 mole) of sodium borohydride and worked up in the manner outlined above. Since no solid could be separated from the crude product it was chromatographed on 150 g. of a 1:5 mixture (by weight) of Celite and anhydrous magnesium sulfate. The adsorbent was heated to 160° for 2.5 hours prior to its use. Fraction 2, eluted with pentane, was recrystallized from pentane to give benzyl *p*-chlorophenyl ketone (XV), m.p. 104–106°, yield 91 mg. (4.0%). A mixed melting point with an authentic sample was not depressed. From fractions 3 to 6, eluted with pentane, was obtained a viscous oil which was not investigated further.

A solution in pentane of the oil obtained from fractions 7 to 17, eluted with pentane which contained increasing quantities of benzene, deposited 280 mg. (9%) of *erythro*-2-bromo-1-[4-chlorophenyl]-2-phenylethanol (XI) as white crystals, m.p. 56–58°. Recrystallization sharpened the melting point to 57–58°.

*Anal.* Calcd. for $C_{14}H_{12}BrClO$: C, 53.95; H, 3.88. Found: C, 53.96; H, 3.79.

A 31.88-mg. portion of material gave 33.70 mg. of mixed silver halides ($C_{14}H_{12}BrClO$ requires 33.80 mg.).

The infrared spectrum[37] of the product exhibits a band at 3450 cm.$^{-1}$ (O–H stretching) and has no band attributable to a carbonyl group. A 31 mg. (0.10 millimole) sample of the bromohydrin was treated with 0.2 ml. of 10% aqueous sodium hydroxide in 5 ml. of methanol. After 2 minutes the solution was concentrated and diluted with water. *trans*-*p*-Chlorostilbene oxide, identified by a mixed melting point with an authentic sample, was isolated as white plates, m.p. 99–100°, yield 13 mg. (57%).

**Rearrangement of *erythro*-2-Bromo-2-[4-chlorophenyl]-1-phenylethanol (XII).**—A solution of 280 mg. (0.00090 mole) of the bromohydrin (m.p. 83–85°) in 15 ml. of benzene was treated with ethylmagnesium bromide and then worked up as in the previous cases. The 2,4-dinitrophenylhydrazone of phenyl *p*-chlorobenzyl ketone was obtained as red prisms, m.p. 219–221.5°, yield 150 mg. (41%). No depression was observed in a mixed melting point determination with an authentic sample. Concentration of the mother liquor gave an additional crop of the crude dinitrophenylhydrazone (21 mg., 5.7%) as red prisms which melted over the range 205–218°.

**Rearrangement of *erythro*-2-Bromo-1-[4-chlorophenyl]-2-phenylethanol (XI).**—A solution of 140 mg. (0.00045 mole) of the bromohydrin (m.p. 57–58°) in 15 ml. of benzene was treated with 0.50 ml. (0.00045 mole) of a standard solution of ethylmagnesium bromide in the fashion described above. The crude product from this reaction was treated with 0.20 g. (0.001 mole) of 2,4-dinitrophenylhydrazine in the usual manner. The 2,4-dinitrophenylhydrazone of benzyl *p*-chlorophenyl ketone was isolated as orange plates, m.p. 208–210°, yield 43 mg. (22%). The melting point of a mixture of the product with an authentic sample was not depressed. No other crystalline product could be separated from the mother liquor.

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(36) C. F. van Duin, *Rec. trav. chim.*, **45**, 345 (1926).

(37) Determined in carbon tetrachloride solution.