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

The Rearrangement of α,β-Epoxy Ketones. III. The Intramolecular Nature of the Rearrangement

BY HERBERT O. HOUSE

RECEIVED OCTOBER 3, 1955

A study of the rearrangement of 1,3-diphenyl-2,3-epoxy-1-propanone-2-C^{14} has shown that the isomerization of *trans*-benzalacetophenone oxide to α-formyldesoxybenzoin involves the migration of a benzoyl group. The isolation of only desoxybenzoin and *p,p'*-dichlorodesoxybenzoin from the isomerization and subsequent deformylation of a mixture of *trans*-benzalacetophenone oxide and *trans-p,p'*-dichlorobenzalacetophenone oxide has been interpreted to mean that the acid-catalyzed isomerization of the above and related α,β-epoxy ketones is an intramolecular process.

We have previously suggested that the acid-catalyzed isomerization of *trans*-benzalacetophenone oxide (I) to yield α-formyldesoxybenzoin (II) involved the migration of a benzoyl group.[1] This suggestion, based on the behavior of substituted analogs of I, has been verified by a study of the rearrangement of an isotopically labeled sample of the oxide I, namely, 1,3-diphenyl-2,3-epoxy-1-propanone-2-C^{14}. The synthesis of the labeled oxide I and the degradation of its isomerization product II are shown in Fig. 1.[2] The formation of 98% of 2,3-diphenyl-1,3-propanedione-1-C^{14} (IIa) and only 2% of IIb by rearrangement of the labeled oxide I is consistent with a major reaction path of the type IIIa (migration of a benzoyl group) rather than IIIb (migration of a phenyl group).

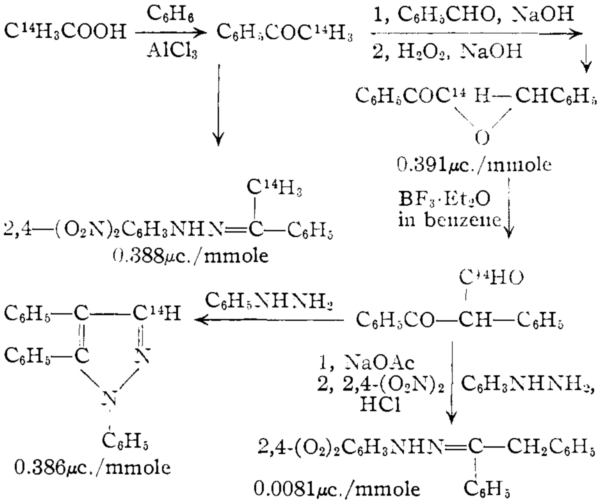
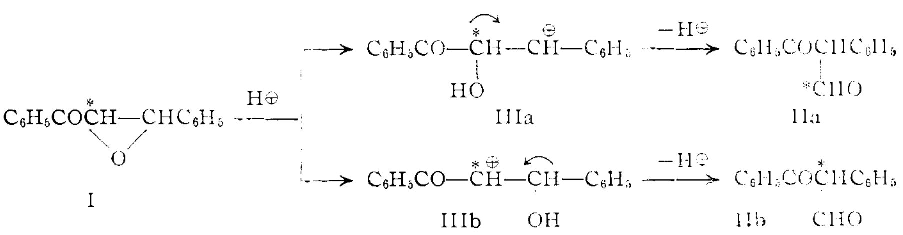


Fig. 1.



Although the over-all result of most of the acid-catalyzed isomerizations of α,β-epoxy ketones which we have studied[1,3] has been the migration of an acyl group, the interpretation to be placed on these results is less clear. Among the possible reaction paths, the intermediate formation of an enol ester (Fig. 2, reaction path A) might be considered since such esters are known to be converted to β-dicarbonyl compounds by acid catalysts.[4] However, in at least three instances[3] the appropriate enol esters have been found to be stable under the reaction conditions required for rearrangement of the corresponding epoxy ketones and, therefore, cannot be reaction intermediates.

Alternatively, the keto oxide might be cleaved to yield an acyl carbonium ion and the enol of a carbonyl compound (Fig. 2, reaction path B); subsequent acylation of the enol would yield the observed product. To test this hypothesis an equimolar mixture of *trans*-benzalacetophenone oxide (I) and *trans-p,p'*-dichlorobenzalacetophenone oxide (IV) was isomerized. The crude mixture of β-keto aldehydes II and V was deformylated to yield desoxybenzoin (VI) and *p,p'*-dichlorodesoxybenzoin (VII). Neither *p*-chlorobenzyl phenyl ketone (VIII) nor benzyl *p*-chlorophenyl ketone (IX), the products which would be expected to accompany VI and VII if the acyl group was transferred by an intermolecular process such as path B in Fig. 2, could be isolated from the reaction mixture. From these data it would not be valid to conclude that the isomerizations are intramolecular if the relative rates of rearrangement of the oxides I and IV differ by a large factor. However, the following considerations have led us to believe that the rates of isomerization of the two oxides are similar. The rate-determining step in the isomerization of an epoxy ketone such as I by either reaction path B or C (Fig. 1) would be expected to involve the formation of at least a partial positive charge at one or both of the carbon atoms adjacent to the benzene rings. An estimate

---

(1) H. O. House, THIS JOURNAL, **76**, 1235 (1954).

(2) Similar synthetic procedures have been employed in a study of the base-catalyzed isomerizations of 1,3-diphenyl-2,3-epoxy-1-propanone-1-C^{14} [C. J. Collins and O. K. Neville, *ibid.*, **73**, 2471 (1951)] and 2,3-epoxy-3-(4-methoxyphenyl)-1-phenyl-1-propanone-1-C^{14} [E. C. Hendley and O. K. Neville, *ibid.*, **75**, 1995 (1953)]. A discussion of the alkaline cleavage of α-formyldesoxybenzoin has been presented by J. G. Burr, Jr. [*ibid.*, **73**, 5170 (1951)].

(3) H. O. House and D. J. Reif, *ibid.*, **77**, 6525 (1955).

(4) C. R. Hauser, F. W. Swamer and J. T. Adams in R. Adams, "Organic Reactions," Vol. VIII, John Wiley and Sons, Inc., New York, N. Y., 1954, pp. 59-196.

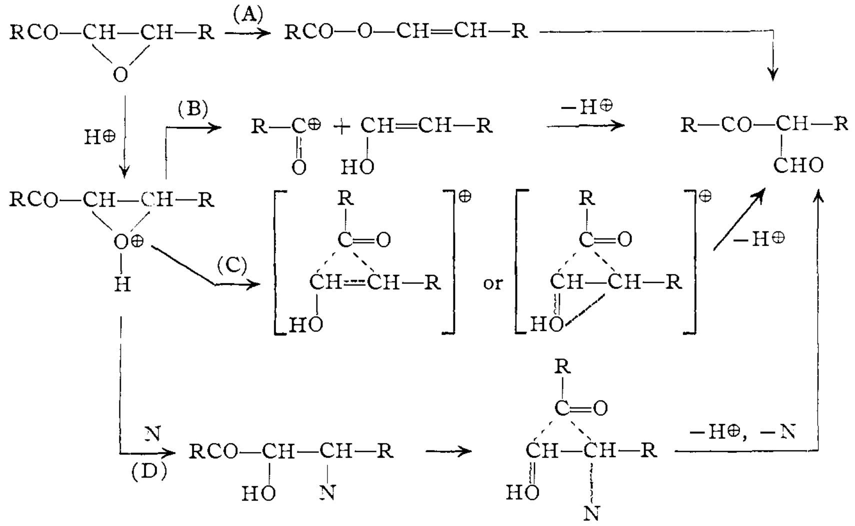
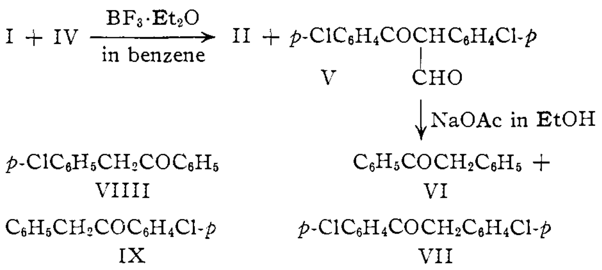


Fig. 2.[5]

of the effect of a p-chloro substituent on the rate of this reaction may be obtained by use of the Hammett equation.[6] The value of the substituent constant, sigma, for a p-chloro substituent is 0.227. The value of the reaction constant, rho, for the isomerization may be estimated by consideration of the values of rho for other reactions which involve the formation of a partial positive charge at a carbon atom adjacent to a benzene ring. Reactions of this type for which data are available include the solvolyses of benzyl halides and benzyl tosylate[6]; the value of rho for these reactions is approximately minus two which corresponds to a value of about three for the ratio of the rate of reaction of the unsubstituted compounds to the rate of reaction of the p-chloro substituted compounds. A difference in the relative rates of isomerization of the oxides I and IV might be expected if the stereochemistry of the epoxy ketones was not the same. Therefore, it was desirable to establish that the p,p'-dichlorobenzalacetophenone oxide (IV), like the benzalacetophenone oxide (I) employed, had the *trans* configuration. The precursor of IV, the unsaturated ketone X, was assigned the *trans* configuration since the ultraviolet spectrum of X resembles closely the spectrum of *trans*-benzalacetophenone and differs markedly from the spectrum of *cis*-benzalacetophenone. In addition the infrared spectrum of X has a strong band at 980 cm.$^{-1}$ attributable to the rocking vibration of a *trans*-1,2-disubstituted olefin. The stereochemistry of the oxide IV was established by the scheme of Wasserman and Aubrey[7] as is shown in the accompanying equations. Epoxidation of the unsaturated alcohol XI with peracetic acid yielded the crystalline epoxy alcohol XIII accompanied by a second impure product whose infrared spectrum resembles closely the spectrum of XIII. The two products are judged to be the two *trans* diastereoisomeric modifications of structure XIII since both alcohols yielded only the *trans*-epoxy ketone IV on oxidation with chromium trioxide in pyridine.

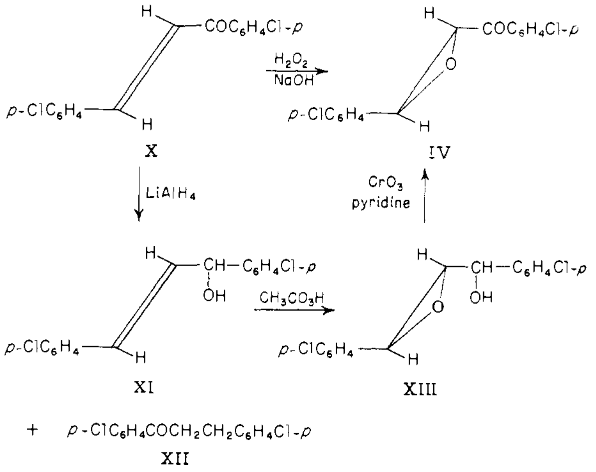


$$\mathrm{I} + \mathrm{IV} \xrightarrow[\text{in benzene}]{BF_3\cdot Et_2O} \underset{\mathrm{V}}{\mathrm{II}} + p\text{-}ClC_6H_4CO\underset{CHO}{\underset{|}{C}}HC_6H_4Cl\text{-}p$$

$$\downarrow \text{NaOAc in EtOH}$$

$$\underset{\mathrm{VIIII}}{p\text{-}ClC_6H_5CH_2COC_6H_5} \qquad \underset{\mathrm{VI}}{C_6H_5COCH_2C_6H_5} +$$

$$\underset{\mathrm{IX}}{C_6H_5CH_2COC_6H_4Cl\text{-}p} \qquad \underset{\mathrm{VII}}{p\text{-}ClC_6H_4COCH_2C_6H_4Cl\text{-}p}$$



Among the intramolecular mechanisms which might be operative in the rearrangement of α,β-epoxy ketones to yield β-dicarbonyl compounds is the ionic cleavage of the conjugate acid of the oxirane ring with simultaneous or subsequent migration of the acyl group (Fig. 2, reaction path C). The isomerizations which we have studied thus far have not provided information as to whether or not the migration of an acyl group is a concerted process, the only stereochemical effect observed having been a complete change in the nature of the rearrangement.[3] The recent demonstration[8] that the acid-catalyzed hydrolysis of aliphatic ethylene oxides involves the formation of a carbonium ion in the rate-determining step suggests that the rearrangements we have studied may involve carbonium ion formation prior to rearrangement. All of the cases which we have reported would form a carbonium ion of the relatively stable benzyl type.

A second intramolecular process which must be

---

(5) For simplicity the acidic catalyst, boron trifluoride, employed in our studies has been replaced by a proton.

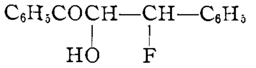
(6) (a) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, pp. 186–193; (b) H. H. Jaffe, *Chem. Revs.*, **53**, 191 (1953).

(7) H. H. Wasserman and N. E. Aubrey, THIS JOURNAL, **77**, 590 (1955).

(8) F. A. Long and J. G. Pritchard, 128th Meeting of the American Chemical Society, Minneapolis, Minn., Sept. 11–16, 1955, Abstracts of Papers, p. 32-O.

considered involves attack of the conjugate acid of the epoxide by some nucleophilic species N present in the reaction mixture (Fig. 2, reaction path D). In the case of rearrangements catalyzed by boron trifluoride etherate the most probable nucleophilic reactants are ethyl ether and fluoride ion. Subsequent migration of an acyl group preceded or accompanied by loss of the nucleophilic reagent would then lead to the rearranged product.

Since our previous studies of the isomerization of epoxy ketones catalyzed by boron trifluoride etherate have all employed amounts of catalyst in excess of quantities equimolar with the amount of oxide used, it was of interest to study the effect of varying the proportion of catalyst added. The results obtained when an ethereal solution of the oxide I was treated with various amounts of boron trifluoride are summarized in Table I. When equimolar quantities, or less, of the catalyst were employed the major constituent of the reaction mixture was not the isomerized product II but rather the fluorohydrin XIV. As the amount of catalyst was increased the yield of XIV dropped with the formation of increased amounts of the β-keto aldehyde II. Treatment of the fluorohydrin XIV with excess boron trifluoride in ether solution yielded II. Since the relative rates of isomerization of I and XIV have not yet been determined, it is not known whether the formation of the fluorohydrin XIV represents a side reaction or the first step in the major reaction path of the type D (Fig. 2) discussed earlier.

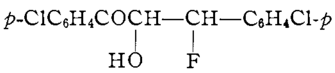


$C_6H_5COCH(OH)-CH(F)-C_6H_5$

XIV

$C_6H_5COCOCH_2C_6H_5$

XV



$p\text{-}ClC_6H_4COCH(OH)-CH(F)-C_6H_4Cl\text{-}p$

XVI

Conversion of XIV to the diketone XV in the manner previously described[1] for the corresponding chlorohydrin established the structure of the fluorohydrin. An analogous fluorohydrin XVI was obtained from the oxide IV.[9]

When the above isomerization was studied in benzene solution (Table I) none of the fluorohydrin XIV could be isolated, the isomerization product II being obtained in 68–100% yield when one-half of an equivalent or more of boron trifluoride etherate was employed.

Experimental[10]

1,3-Diphenyl-2,3-epoxy-1-propanone-2-C^{14} (I).—Acetic acid-2-C^{14}[11] was converted to methyl-labeled acetophenone, b.p. 198–201°, in 66.5% yield by the procedure of Neville.[12] A sample of the ketone was converted to its 2,4-dinitrophenylhydrazone, m.p. 248–250° (lit.[13] 249–250°); the specific activity of the 2,4-dinitrophenylhydrazone was 0.388 μc./mmole.[14] The acetophenone was converted to 1,3-diphenyl-2,3-epoxy-1-propanone-2-C^{14}, m.p. 89–90°, specific activity 0.391 μc./mmole, in an over-all yield of 74.8%.

Rearrangement of 1,3-Diphenyl-2,3-epoxy-1-propanone-2-C^{14} (I).—A solution of 1.79 g. (0.008 mole) of the oxide in 15 ml. of benzene was treated with 2.0 ml. (0.016 mole) of boron trifluoride etherate and the mixture allowed to stand for 20 minutes. The mixture was diluted with ether, washed with water and then diluted with ethanol to a volume of 100 ml. A 50-ml. aliquot of the solution was converted to 1,4,5-triphenylpyrazole, m.p. 209–211°, yield 1.04 g. (88.2%). Recrystallization from an ethanol–ethyl acetate mixture sharpened the melting point of the pyrazole to 210–211° (lit.[15] 210–211°). The specific activity of the pyrazole was 0.386 μc./mmole. The second 50-ml. aliquot of the reaction mixture was boiled with a solution of sodium acetate in aqueous ethanol for 45 minutes and then treated with 2,4-dinitrophenylhydrazine and hydrochloric acid. The 2,4-dinitrophenylhydrazone of desoxybenzoin crystallized from an ethanol–ethyl acetate mixture as orange plates, m.p. 198–201°; yield 0.902 g. (60%). Recrystallization raised the melting point of the dinitrophenylhydrazone to 200–202°; the specific activity was 0.0081 μc./mmole.

***trans-p,p'*-Dichlorobenzalacetophenone (X).**—This unsaturated ketone, prepared by the method of Straus and Ackermann,[16] crystallized from an ethanol–benzene mixture as yellow needles, m.p. 155–157° (lit.[16] 156–157°). The ultraviolet spectrum of the product, which has maxima at 228 mμ (ε 13,200) and 318 mμ (ε 29,000), resembles the spectrum of *trans*-benzalacetophenone [λ_{max} 227.5 mμ (ε 9,800) and 307.5 mμ (ε 24,300)][17] and differs from the spectrum of *cis*-benzalacetophenone [λ_{max} 250 mμ (ε 13,700) and 292.5 mμ (ε 8,800)].[17] The infrared spectrum[18] of *trans-p,p'*-dichlorobenzalacetophenone has bands at 1660 (conjugated C=O), 1610 (C=C) and 980 cm.$^{-1}$ (*trans* CH=CH); the corresponding bands in the spectrum[18] of *trans*-benzalacetophenone are found at 1650, 1600 and 975 cm.$^{-1}$.

***trans-p,p'*-Dichlorobenzalacetophenone Oxide (IV).**—A solution of 27.7 g. (0.1 mole) of *trans-p,p'*-dichlorobenzalacetophenone, 23 ml. (0.2 mole) of 30% aqueous hydrogen peroxide and 5 ml. (0.013 mole) of 10% aqueous sodium hydroxide in 400 ml. of acetone was stirred for 1 hour, diluted with an equal volume of water and filtered. The residue was washed with water and recrystallized from ethanol. The oxide crystallized as white needles, m.p. 120–121°; yield 20.7 g. (70.7%). The infrared spectrum[18] of the oxide has a band at 1675 cm.$^{-1}$ (conjugated C=O) but lacks the absorption at 980 cm.$^{-1}$ which was present in the corresponding olefin. The ultraviolet spectrum of the oxide has a maximum at 261 mμ (ε 21,800).

Anal. Calcd. for $C_{15}H_{10}Cl_2O_2$: C, 61.46; H, 3.44; Cl, 24.19. Found: C, 61.25; H, 3.67; Cl, 24.12.

Reduction of *trans-p,p'*-Dichlorobenzalacetophenone (X).—A slurry of 1.14 g. (0.03 mole) of lithium aluminum hydride in ether was added to 27.7 g. (0.1 mole) of the unsaturated ketone in 200 ml. of ether. After the addition was complete the mixture was stirred for 5 minutes and then treated with ethyl acetate to destroy the excess lithium aluminum hydride. The resulting ether solution was washed with water and the aqueous washings were acidified and extracted with ether. The combined ether solutions were dried over magnesium sulfate, the solvent was removed and the residual oil taken up in an ether–hexane mixture. When the solution was chilled in Dry Ice, the ***trans*-1,3-di-(4-chlorophenyl)-2-propen-1-ol** (XI) separated as white crystals, m.p. 68–70°; yield 14.6 g. When a solution of the residual oil from the mother liquors was chromatographed on Merck acid-washed alumina an additional 2.5 g. (total yield 17.1 g. or 61.4%) of the unsaturated alcohol was isolated from

---

(9) In a study of oxides derived from benzylidenecycloalkanones, to be reported later, the corresponding fluorohydrins were the only products which could be isolated when isomerization was attempted in ether solution.

(10) 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.

(11) Obtained as sodium acetate-2-C^{14} from Tracerlab, Inc., Boston 10 Mass.

(12) O. K. Neville, This Journal, **70**, 3499 (1948).

(13) N. R. Campbell, *Analyst*, **61**, 391 (1936).

(14) The radioactive samples were assayed by the procedure of Neville (ref. 12), the carbon dioxide activity in the ionization chamber being measured with a vibrating reed electrometer. The activities reported are the average values obtained from two determinations.

(15) W. Wislicenus and A. Ruthing, *Ann.*, **379**, 229 (1911).

(16) F. Straus and A. Ackermann, *Ber.*, **42**, 1804 (1909).

(17) W. B. Black and R. E. Lutz, This Journal, **75**, 5990 (1953).

(18) Determined in chloroform solution.

the later fractions. Recrystallization from hexane afforded the pure unsaturated alcohol melting at 70.5–71°. The infrared spectrum[18] of the alcohol has bands at 3400 (unassociated O–H), 3280 (associated O–H) and 965 cm.$^{-1}$ (*trans* CH=CH) but no absorption in the 6 μ region attributable to a carbonyl function. The ultraviolet spectrum has a maximum at 259 mμ (ϵ 28,600) attributable to the *p*-chlorostyrene chromophore.

Anal. Calcd. for $C_{15}H_{12}Cl_2O$: C, 64.52; H, 4.33; Cl, 25.40. Found: C, 64.46; H, 4.66; Cl, 25.33.

The first fractions obtained from the chromatogram afforded **1,3-di-(4-chlorophenyl)-1-propanone (XII)** which separated from methanol as white needles, m.p. 82–83.5°; yield 0.63 g. (2.3%). An additional recrystallization sharpened the melting point to 82.5–83.5°. The infrared spectrum[19] of the ketone has a band at 1670 cm.$^{-1}$ (conjugated C=O) but no absorption in the 3 μ region attributable to a hydroxyl group. The ultraviolet spectrum of the ketone, which has a maximum at 251 mμ (ϵ 18,200) attributable to the *p*-chlorophenyl ketone chromophore, resembles closely the spectrum of *p,p'*-dichlorodesoxybenzoin described below.

Anal. Calcd. for $C_{15}H_{12}Cl_2O$: C, 64.52; H, 4.33. Found: C, 64.70; H, 4.46.

***trans*-1,3-Di-(4-chlorophenyl)-2,3-epoxy-1-propanol (XIII).**—To a mixture of 13.95 g. (0.05 mole) of *trans*-1,3-di-(4-chlorophenyl)-2-propen-1-ol, 10 g. of sodium acetate trihydrate and 200 ml. of chloroform, cooled to 8°, was added, dropwise and with stirring, 30 ml. of 40% peracetic acid in acetic acid. After the cold mixture had been stirred for 2 hours, it was allowed to warm to room temperature, stirring being continued for a total of 65 hours. The resulting mixture was washed with two portions of water followed by two portions of 5% aqueous sodium bicarbonate and then dried over magnesium sulfate. After the solvents had been removed under reduced pressure the residue was recrystallized from a hexane–benzene mixture. The crude epoxy alcohol separated as white needles, m.p. 120–122°; yield 7.64 g. A solution of the residual oil from the mother liquor in methylene chloride was chromatographed on Merck acid-washed alumina. The later fractions from the chromatogram afforded an additional 0.44 g. (total yield 8.08 g. or 54.7%) of the epoxy alcohol. Recrystallization from hexane containing a few drops of benzene gave the pure *trans*-1,3-di-(4-chlorophenyl)-2,3-epoxy-1-propanol, m.p. 125–126°. The infrared spectrum[18] of the epoxy alcohol has bands at 3400 and 3200 cm.$^{-1}$ (unassociated and associated O–H) but lacks absorption in the 6 μ region attributable to a carbonyl function. In addition the band present at 965 cm.$^{-1}$ in the spectrum of the unsaturated alcohol is missing in the spectrum of the epoxy alcohol. The ultraviolet spectrum of the product has maxima at 227 mμ (ϵ 25,100) and 267 mμ (ϵ 640).

Anal. Calcd. for $C_{15}H_{12}Cl_2O_2$: C, 61.03; H, 4.10; Cl, 24.02. Found: C, 61.21; H, 4.38; Cl, 24.33.

The earlier fractions from the above chromatogram yielded a second impure compound (3.47 g., m.p. 63–70°) whose melting point was depressed when it was mixed with the starting material. Repeated crystallization from hexane failed to separate a single, pure compound, the melting range being slowly raised to 72–80°. The infrared spectrum[18] of the partially purified material has a broad band at 3300 cm.$^{-1}$ (associated O–H) but lacks absorption in the 6 μ region attributable to a carbonyl function. A 145-mg. sample of the crude product, when oxidized with chromium trioxide in pyridine as described below, yielded 76 mg. (53%) of *trans-p,p'*-dichlorobenzalacetophenone oxide, m.p. 119–121°, whose identity with the sample previously described was confirmed by a mixed melting point determination and by comparison of the infrared spectra[18] of the two samples.

Oxidation of *trans*-1,3-Di-(4-chlorophenyl)-2,3-epoxy-1-propanol (XIII).—A solution of 1.45 g. (0.0049 mole) of the epoxy alcohol, m.p. 125–126°, in 11 ml. of pyridine was oxidized with 1.23 g. of chromium trioxide in 10 ml. of pyridine as described by Wasserman and Aubrey.[7] The product, *trans-p,p'*-dichlorobenzalacetophenone oxide, crystallized from ethanol as white needles, m.p. 120–121°; yield 1.23 g. (85.6%). The melting point of a mixture of this product with a sample obtained by the base-catalyzed epoxidation of the unsaturated ketone was not depressed. The infrared spectra[18] of the two samples are identical.

Isomerization of *trans*-Benzalacetophenone Oxide (I) (Table I) A. In Ether Solution.—In a typical experiment a solution of 3.58 g. (0.016 mole) of the oxide in 100 ml. of anhydrous ether was treated with 2.0 ml. (0.016 mole) of freshly distilled boron trifluoride etherate. After the resulting mixture had been boiled under reflux for 30 minutes, it was washed with water and shaken with a saturated, aqueous solution of cupric acetate. The copper complex of α-formyldesoxybenzoin, m.p. 218–222° dec. (lit.[15] 220–221° dec.), yield 1.31 g. (32.2%). was removed by filtration [alternatively, the α-formyldesoxybenzoin could be isolated as 1,4,5-triphenylpyrazole, m.p. 210–211° (lit.[15] 210–211°)] and the solvent was removed from the filtrate. Recrystallization of the residue from hexane afforded 1.92 g. (49.2%) of **1,3-diphenyl-3-fluoro-2-hydroxy-1-propanone (XIV)**, m.p. 110–113°. The pure fluorohydrin crystallized from ethanol–water as white needles, m.p. 113–114°. The infrared spectrum[18] of the fluorohydrin has bands at 3350 cm.$^{-1}$ (O–H) and 1680 cm.$^{-1}$ (conjugated C=O).

Anal. Calcd. for $C_{15}H_{13}FO_2$: C, 73.74; H, 5.63; F, 7.78. Found: C, 73.52; H, 5.63; F, 8.04.

TABLE I

ISOMERIZATION OF *trans*-BENZALACETOPHENONE OXIDE (I)

Molar equiv. of boron trifluoride	Solvent	Yield of fluorohydrin XIV, %	Yield of α-formyldesoxybenzoin, % As copper complex	 As 1,4,5-triphenylpyrazole
0.5	Ether	58.8	3.2	..
1.0	Ether	49.2	32.2	..
2.0	Ether	38.4	45.3	..
5.0	Ether	7.2	64.8	..
10.0	Ether	None	80.8	..
0.5	Benzene	None	56.1[a]	16.9[a]
1.0	Benzene	None	67.8	..
2.0	Benzene	None	83.3	..
			..	99.7
4.0	Benzene	None	77.5	..
			..	66.5

[a] The total yield was 73.0%.

A 200-mg. (0.00082 mole) sample of the fluorohydrin, when heated on a steam-bath with 0.50 g. of sodium acetate and 10 ml. of acetic acid for 1 hour and then treated with *o*-phenylenediamine, was converted to 3-benzyl-2-phenylquinoxaline, m.p. 96.5–98° (lit.[20] 97–98°); yield 195 mg. (84%). When a sample of the fluorohydrin was treated with phenylhydrazine in the manner used for the preparation of 1,4,5-triphenylpyrazole no crystalline product could be isolated. Treatment of an ether solution of 0.49 g. (0.002 mole) of the fluorohydrin with 5.0 ml. (0.04 mole) of boron trifluoride etherate produced 0.40 g. (78.5%) of the copper complex of α-formyldesoxybenzoin.

A sample of the enol of α-formyldesoxybenzoin, isolated from the copper salt described above, crystallized from aqueous ethanol as white prisms, m.p. 111–113° (lit.[15] 112–113°). The infrared spectrum[21] of the enol form of the keto aldehyde has a broad, intense band with its center of maximum absorption at 1540 cm.$^{-1}$. A similar spectrum was obtained in chloroform solution, the position of maximum absorption in the 6 μ region being located at 1600 cm.$^{-1}$. As a control experiment an ether solution of the keto aldehyde was shaken with aqueous cupric acetate as described above; the copper complex of α-formyldesoxybenzoin was isolated in quantitative yield. A solution of 224 mg. (0.001 mole) of the keto aldehyde and 410 mg. (0.005 mole) of sodium acetate in 20 ml. of a 3:1 (by volume) mixture of ethanol and water was boiled under reflux for 30 minutes and then treated with 2,4-dinitrophenylhydrazine in the usual manner. The cold solution deposited 368 mg. (98%) of the 2,4-dinitrophenylhydrazone of desoxybenzoin, m.p. 198–200°, whose identity was confirmed by a mixed melting point determination with an authentic sample.

B. In Benzene Solution.—Solutions of 1.79 g. (0.008 mole) of the oxide in 15 ml. of benzene were allowed to react

---

(19) Determined in carbon tetrachloride solution.

(20) T. L. Jacobs, THIS JOURNAL, **58**, 2272 (1936).

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

with various amounts of boron trifluoride etherate for 20 minutes and the product isolated as described earlier. In one experiment, employing 1.0 equivalent of boron trifluoride etherate, a decrease in the reaction time to 5 minutes lowered the yield only slightly (to 64.2%). In no case could any of the fluorohydrin XIV be isolated. In another experiment (4.0 equivalents of boron trifluoride etherate being employed) the reaction mixture was washed rapidly with water, dried over magnesium sulfate and the solvents were removed. A solution of the residue in hexane deposited the **borofluoride complex of α-formyldesoxybenzoin** as yellow needles, m.p. 97–99°; yield 1.14 g. (52.4%). The infrared spectrum[18] of the complex has strong bands at 1600 and 1565 cm.$^{-1}$ in the 6 μ region; no band attributable to a hydroxyl function is present in the 3 μ region of the spectrum.

Anal. Calcd. for $C_{15}H_{11}O_2BF_2$: C, 66.23; H, 4.08; B, 3.98; F, 13.97. Found: C, 66.58; H, 4.19; B, 4.22; F, 13.98.

The mother liquors from the recrystallization, when boiled with an ethanolic solution of phenylhydrazine, yielded 0.45 g. (19%) of 1,4,5-triphenylpyrazole.

Isomerization of *trans-p,p'*-Dichlorobenzalacetophenone Oxide (IV).—A solution of 2.35 g. (0.008 mole) of the oxide in 25 ml. of benzene was treated with 4.0 ml. (0.0032 mole) of boron trifluoride etherate in the usual manner and the crude reaction product was crystallized from a hexane-benzene mixture. The **borofluoride complex of α-formyl-*p,p'*-dichlorodesoxybenzoin** separated as yellow plates, m.p. 209–211°; yield 0.98 g. (36%). An additional recrystallization sharpened the melting point to 209.5–211°. The infrared spectrum[18] of the complex has no bands in the 6 μ region with wave lengths shorter than at 1575 cm.$^{-1}$; the ultraviolet spectrum has a maximum at 254 mμ (ε 19,200).

Anal. Calcd. for $C_{15}H_9Cl_2BF_2O_2$: C, 52.84; H, 2.66; Cl, 20.80. Found: C, 52.82; H, 2.87; Cl, 20.75.

The mother liquor from the above recrystallization was concentrated and treated with a boiling, ethanolic solution of phenylhydrazine. The resulting cold solution deposited 1.0 g. (34.3%) of **1-phenyl-4,5-di-(4-chlorophenyl)-pyrazole** as tan needles, m.p. 181.5–183°. The pure pyrazole crystallized from ethanol as white needles, m.p. 182–183°; λ_{max} 243 mμ (ε 23,900) and 268 mμ (ε 18,700).

Anal. Calcd. for $C_{21}H_{14}Cl_2N_2$: C, 69.04; H, 3.86; Cl, 19.41; N, 7.67. Found: C, 68.90; H, 3.89; Cl, 19.40; N, 7.97.

In a second experiment the isomerization product, α-formyl-*p,p'*-dichlorodesoxybenzoin, was isolated as its copper complex, m.p. 264–265° dec.; yield 2.33 g. (94.8%). Treatment with 6 *N* hydrochloric acid converted a portion of the copper complex to the enol form of **α-formyl-*p,p'*-dichlorodesoxybenzoin (V)** which crystallized from hexane as yellow prisms, m.p. 92–93.5°. An ethanolic solution of the material gives an immediate violet color when treated with ferric chloride. The infrared spectrum[21] of the enol has a broad band at 1590 cm.$^{-1}$.

Anal. Calcd. for $C_{15}H_{10}Cl_2O_2$: C, 61.46; H, 3.44; Cl, 24.19. Found: C, 61.60; H, 3.14; Cl, 23.98.

A sample of the keto aldehyde, when treated with a boiling solution of sodium acetate in aqueous ethanol, was converted to ***p,p'*-dichlorodesoxybenzoin (VII)** which crystallized from hexane as white needles, m.p. 112.5–113.5° (lit.[22] 114°). The infrared spectrum[18] of the ketone has a band at 1675 cm.$^{-1}$ (conjugated C=O); the ultraviolet spectrum has a maximum at 253 mμ (ε 18,500). The **2,4-dinitrophenylhydrazone of *p,p'*-dichlorodesoxybenzoin** crystallized from acetic acid as red-orange prisms, m.p. 252–253° dec.

Anal. Calcd. for $C_{20}H_{14}Cl_2N_4O_4$: C, 53.94; H, 3.17; N, 12.58. Found: C, 54.08; H, 3.43; N, 12.38.

A solution of 2.35 g. (0.008 mole) of the epoxy ketone in 100 ml. of ether was treated with 5.0 ml. (0.04 mole) of boron trifluoride ethereate in the usual fashion. The copper complex of α-formyl-*p,p'*-dichlorodesoxybenzoin (1.16 g., 47.1%) was isolated, accompanied by **1,3-di-(4-chlorophenyl)-3-fluoro-2-hydroxy-1-propanone (XVI)** which crystallized from aqueous ethanol as white needles, m.p. 117–119°; yield 0.22 g. (8.8%). Recrystallization from hexane afforded the pure fluorohydrin, m.p. 119–120°, whose infrared spectrum[18] has bands at 3250 cm.$^{-1}$ (O-H) and 1670 cm.$^{-1}$ (conjugated C=O).

Anal. Calcd. for $C_{15}H_{11}Cl_2FO_2$: C, 57.52; H, 3.54; F, 6.07. Found: C, 57.47; H, 3.81; F, 5.89.

Isomerization of a Mixture of the Oxides I and IV.—A mixture of 1.18 g. (0.004 mole) of *trans-p,p'*-dichlorobenzalacetophenone oxide and 0.90 g. (0.004 mole) of *trans*-benzalacetophenone oxide in 20 ml. of benzene was treated with 2.0 ml. (0.016 mole) of boron trifluoride etherate as previously described. The crude reaction mixture was boiled with a solution of sodium acetate in aqueous ethanol, diluted with water and extracted with three portions of ether. The combined extracts were dried over magnesium sulfate, the solvents removed and a petroleum ether solution of the residue was chromatographed on Merck acid-washed alumina. Since no appreciable separation of the mixture of ketones was achieved by this procedure, the mixture was separated by fractional crystallization from aqueous ethanol. In this way 0.547 g. (51.6%) of *p,p'*-dichlorodesoxybenzoin, m.p. 111–113°, was isolated (the 2,4-dinitrophenylhydrazone derived from this sample crystallized from the reaction mixture as red-orange crystals, m.p. 252–253° dec). One recrystallization from hexane raised the melting point of the ketone to 112.5–113.5°. The infrared spectrum[18] of a 0.22 g. (28% of the theoretical amount) sample of crude desoxybenzoin, m.p. 49–52°, isolated from the mother liquors of the above fractional crystallization lacks absorption at 1085 cm.$^{-1}$; the spectra[18] of *p,p'*-dichlorodesoxybenzoin, *p*-chlorobenzyl phenyl ketone, m.p. 134.5–135.5° (lit.[22] 138°), and benzyl *p*-chlorophenyl ketone, m.p. 104.5–106° (lit.[22] 107.5°), all have a very strong band at this position. All of the desoxybenzoin in the reaction mixture was subsequently isolated as its 2,4-dinitrophenylhydrazone, m.p. 197–201°; yield 0.683 g. (45.5%). The melting points of the 2,4-dinitrophenylhydrazones of both desoxybenzoin and *p,p'*-dichlorodesoxybenzoin were depressed when mixed with each other or with the 2,4-dinitrophenylhydrazones[23] derived from *p*-chlorobenzyl phenyl ketone or benzyl *p*-chlorophenyl ketone. Since both *p*-chlorobenzyl phenyl ketone and benzyl *p*-chlorophenyl ketone are much less soluble in the recrystallizing solvents employed than is desoxybenzoin, we regard the possibility that appreciable quantities of either of these ketones would have escaped detection as highly improbable.

In a subsequent experiment the crude reaction mixture obtained from isomerization followed by deformylation was treated directly with 2,4-dinitrophenylhydrazine and the resulting mixture of 2,4-dinitrophenylhydrazones was separated by fractional crystallization. As before only two products could be isolated, *p,p'*-dichlorodesoxybenzoin 2,4-dinitrophenylhydrazone (1.036 g. (58.2%), m.p. 250–252°) and desoxybenzoin 2,4-dinitrophenylhydrazone (0.22 g. (15%), m.p. 196–199°).

CAMBRIDGE 39, MASSACHUSETTS

---

[22] S. S. Jenkins and E. M. Richardson, THIS JOURNAL, **55**, 1618 (1933).

[23] H. O. House, *ibid.*, **77**, 3070 (1955).