The CO_2 was collected, transferred to gas counters, and then assayed by the method of Christman, *et al.*[26] The amines produced were assayed as their phenylthioureas or chloroplatinates. The 1-position was determined by difference.

Control Ethylbenzene-1-C^{14}.—Unreacted ethylbenzene-1-C^{14} was degraded as described above and shown to have almost all of its activity in the 1-position (see Table III).

The Disproportionation of Ethylbenzene at Short Contact Times.—The reactions were carried out in a flow system according to the procedure of Brown and Jungk.[16] The benzene–catalyst mixture (35 ml) and ethylbenzene (50 ml) were allowed to react for about 0.005 sec, quenched, and analyzed on a Carbowax capillary vpc column. The ratio of *m*-:*p*-diethylbenzene was 1.8:1.0 when 3% of the ethylbenzene had reacted. The peaks were calibrated with an authentic mixture of pure isomers.

The Preparation of *p*-Diethylbenzene-1-C^{14}.—The method of Mowry, *et al.*,[27] was used to prepare *p*-ethylacetophenone-4-C^{14} from ethylbenzene-1-C^{14}. The semicarbazone, mp 190° (lit.[28] mp 191°), was prepared and reduced as above to give *p*-diethylbenzene-1-C^{14} containing 0.5% of the *meta* isomer.

The Disproportionation of Ethylbenzene with Added *p*-Diethylbenzene-1-C^{14}.—Ethylbenzene (33 ml) containing 2 wt % of *p*-diethylbenzene-1-C^{14} was disproportionated as above at $+10 \pm 5°$ and quenched immediately after the proper amount of hydrogen bromide was added (1.5 min). The mixture was analyzed at 125° by vpc on a 0.25-in. column packed with 12% by weight of Bentone 34 on firebrick.[29] The *m*- and *p*-diethylbenzenes were completely separated in 7 min on this column. The *meta*:*para* ratio was 5.3:1.0 and 30% of the ethylbenzene had disproportionated. To collect samples for radioassay, a 0.5-in. column was used (see Figure 2).

Acknowledgment.—The authors wish to thank Miss C. S. Redvanly for her help in carrying out most of the Schmidt degradations. We also are indebted to Dr. D. R. Christman and Mrs. C. T. Paul for the carbon-14 radioassays. A generous supply of Bentone 34 was provided by the National Lead Company.

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The Mechanism of the Prins Reaction. V. The Prins Reaction of Styrenes[1]

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The stereochemistry of the products from the Prins reaction with *cis*- and *trans*-1-phenylpropene, *cis*- and *trans*-β-bromostyrene, and *cis*- and *trans*-β-chlorostyrene is reported. In no case was the reaction stereospecific, in contrast to previous reports. The Prins reaction of *cis*- and *trans*-1-phenylpropene appears to proceed predominantly *via* a simple symmetrically solvated carbonium ion intermediate. However, the Prins reaction with the β-halostyrenes is more complex.

The acid-catalyzed condensation of formaldehyde with various styrenes has been the subject of several investigations.[3–7] These studies have been concentrated on the stereochemistry of the reaction. One fact emerges from these studies; *cis* addition accounts for a large fraction of the products, whereas *trans* addition is the normal result with acyclic and aliphatic compounds.[8–12] Since most of the previous studies were carried out on cyclic styrenes or styrenes which would yield very stable intermediate carbonium ions, it seemed desirable to study a simple case, *cis*- and *trans*-1-phenylpropene. The Prins reaction of the *cis*- and *trans*-β-bromostyrenes was also of interest since it has been examined three times previously with various results. Bernardi and Leone[6] report only the formation of *trans*-5-bromo-4-phenyl-1,3-dioxane from both *cis*- and *trans*-β-bromostyrene, whereas Terada[4] reports the formation of both stereoisomeric 5-bromo-4-phenyl-1,3-dioxanes, and Hsing and co-workers[3] report two products, both liquids, although pure *cis*-4-phenyl-5-bromo-1,3-dioxane is crystalline.

In the present study we have determined the stereochemistry of the Prins reaction with three pairs of isomeric substituted styrenes; *cis*- and *trans*-β-bromostyrene, *cis*- and *trans*-β-chlorostyrene, and *cis*- and *trans*-1-phenylpropene. We find that the Prins reaction is not stereospecific with any of these olefins. The results of our study are summarized in Table I.

The olefins used in the study were pure isomers as shown by their spectroscopic and chromatographic behavior. *cis*-β-Chlorostyrene was the most difficult of the styrenes to prepare in pure form. The mixture of *cis*- and *trans*-β-chlorostyrenes obtained by the method of Biltz[13] was partially separated by fractional distillation, and pure *cis*-β-chlorostyrene was obtained by chromatography over alumina. Pure *trans*-β-chlorostyrene was obtained from mixtures of *cis* and *trans* material by destroying the *cis* isomer with sodium hydroxide in dimethyl sulfoxide. *cis*-β-Bromostyrene was prepared by the method of Cristol and Norris,[14] and *trans*-β-bromostyrene was obtained from mixtures of the *cis* and *trans* isomers by destroying the *cis* material with sodium hydroxide in 2-propanol. Pure *cis*-

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[1] Supported by a grant from the Petroleum Research Fund of the American Chemical Society, Grant No. 915-A4.

[2] Alfred P. Sloan Research Fellow.

[3] C. Hsing, C. Ta, and L. Hsueh, *Hua Hsueh Hsueh Pao*, **23**, 19 (1957).

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Table I

Stereochemistry of the Products from the Prins Reaction of β-Substituted Styrenes

Compd	Solvent	% yield	Temp, °C (±5°)	Ratio of *cis: trans* 5-substituted 4-phenyl-1,3-dioxane
cis-β-Bromostyrene	Dioxane	15	110	0.83
		20	110	0.87
		34	110	1.03
	HOAc	18[a]	100	0.83
trans-β-Bromostyrene	Dioxane	66	110	0.11
		95	110	0.13
		64	110	0.21
		87[b]	85	0.09
		64[b]	85	0.09
	HOAc	28[a]	100	0.24
cis-β-Chlorostyrene	Dioxane	12	100	0.10
trans-β-Chlorostyrene	Dioxane	51	110	0.22
		76	100	0.17
cis-1-Phenylpropene	Dioxane	74	25	1.00
		48	25	0.87
trans-1-Phenylpropene	Dioxane	15	25	0.82
		19	25	0.89
	Water	43	100	1.00
		28	90	1.00
		51	70	1.62
		46	70	1.71
	HOAc	24[c]	25	0.60

[a] *cis*-5-Bromo-4-phenyl-1,3-dioxane was converted to a mixture containing 25% of the *trans* isomer under the reaction conditions. [b] The recovered olefin contained 10% of *cis*-β-bromostyrene. [c] *cis*-5-Methyl-4-phenyl-1,3-dioxane isomerizes to a mixture containing 5% of the *trans* isomer under the reaction conditions.

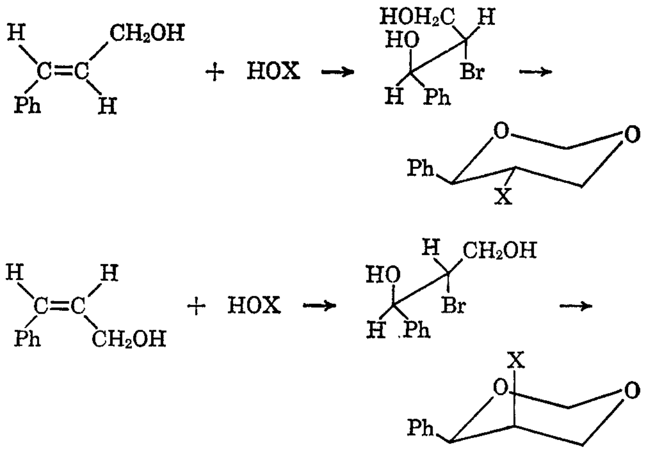
and *trans*-1-phenylpropene were prepared by the method of Dewar and Fahey.[15]

All of the possible 5-substituted 4-phenyl-1,3-dioxanes obtained as products from the Prins reaction with the several systems were prepared by independent synthesis except *cis*-5-methyl-4-phenyl-1,3-dioxane. The *cis*- and *trans*-5-halo-4-phenyl-1,3-dioxanes were obtained by the action of hypobromous and hypochlorous acid on *cis*- and *trans*-cinnamyl alcohol followed by treatment with formaldehyde and acid (Scheme I).

In accord with previous results, *cis*- and *trans*-cinnamyl alcohol gave isomeric bromohydrins.[16,17] The bromohydrin of *trans*-cinnamyl alcohol had previously been converted to the corresponding 1,3-dioxane and elimination studies provided evidence that this dioxane is *trans*-5-bromo-4-phenyl-1,3-dioxane.[6] The bromohydrin of *trans*-cinnamyl alcohol is thus *erythro*-2-bromo-3-phenyl-1,3-propanediol which corresponds to the expected *trans* addition of hypobromous acid to *trans*-cinnamyl alcohol. The isomeric bromohydrin from *cis*-cinnamyl alcohol must be *threo*-2-bromo-3-phenyl-1,3-propanediol which gives *cis*-5-bromo-4-phenyl-1,3-dioxane upon treatment with formaldehyde and acid.

The chlorohydrins of *cis*- and *trans*-cinnamyl alcohol were obtained as unmanageable oils. However, these chlorohydrins gave isomeric 1,3-dioxanes upon treatment with formaldehyde and acid, and the stereochemistry of the 5-chloro-4-phenyl-1,3-dioxanes is assigned by analogy to the corresponding bromo compounds. Some of the physical properties of the *cis*-5-halo-4-phenyl-1,3-dioxanes were surprisingly different from those of the *trans* isomers. The *cis* isomers were easily crystallized solids, whereas the *trans* isomers were liquid. More importantly, the retention times of the *cis* isomers on vapor phase chromatography were considerably longer than the retention times of the corresponding *trans* isomers. However, molecular weight measurements on the *cis*-bromo isomer gave the expected value, and the 5-bromo-4-phenyl-1,3-dioxanes and *cis*-5-chloro-4-phenyl-1,3-dioxane were hydrogenolyzed to 4-phenyl-1,3-dioxane which was identical with authentic material prepared by the Prins reaction with styrene.

Scheme I



Authentic *trans*-5-methyl-4-phenyl-1,3-dioxane was prepared from *threo*-2-methyl-3-phenyl-1,3-propanediol and dimethoxymethane in the presence of a trace of acid. A single pure compound was obtained which indicates that the reaction conditions could not have caused epimerization. Crude equilibration experiments were carried out which indicate that the equilibrium mixture contains about 20% of the *cis* isomer which would have been easily detected. The required *threo*-2-methyl-3-phenyl-1,3-propanediol was obtained by the lithium aluminum hydride reduction of *threo*-β-hydroxy-α-methyl-β-phenylpropionic acid which was prepared as previously described.[18] Pure *cis*-5-methyl-4-phenyl-1,3-dioxane was separated by chromatography on alumina from the mixture of 5-methyl-4-phenyl-1,3-dioxanes obtained from the Prins reaction of the 1-phenylpropenes. The properties of the *cis*-5-methyl-4-phenyl-1,3-dioxane prepared in this manner were in good agreement with those recently reported for this material by Smissman, Schnettler, and Portoghese.[7] The present work confirms the earlier assignment of configuration to *cis*-5-methyl-4-phenyl-1,3-dioxane which was based on nmr measurements. The studies just described and the previous work on these compounds provide good evidence for the stereochemistry of the products of the Prins reaction with the several

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[15] M. J. S. Dewar and R. Fahey, *J. Am. Chem. Soc.*, **85**, 3645 (1963).

[16] H. Berger and E. Haack, German Patent 1,059,409 (1959); *Chem. Abstr.*, **55**, 6442 (1961).

[17] I. Levi, U. S. Patent 2,951,876 (1960), *Chem. Abstr.*, **55**, 1533e (1961).

[18] H. E. Zimmerman and J. English, Jr., *J. Am. Chem. Soc.*, **76**, 2291 (1954). The authors are indebted to Professor D. S. Noyce for a sample of pure *threo*-β-hydroxy-α-methyl-β-phenylpropionic acid and for the results of nmr studies which further support the stereochemical assignment of this material.

styrenes studied. However, it is difficult to obtain accurate quantitative data on these reactions because some tar is produced and the material balances are not good.

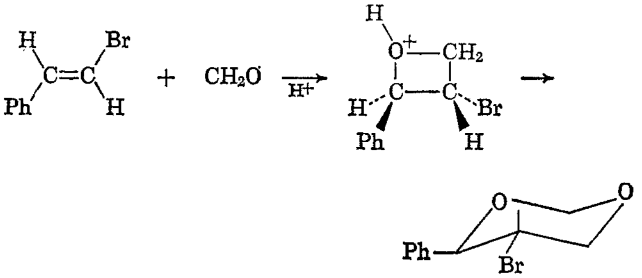
The products from the halostyrenes were analyzed by vapor phase chromatography using an internal standard and correcting for differences in thermal response. We did not find conditions for separating the isomeric 5-methyl-4-phenyl-1,3-dioxanes by vapor phase chromatography, but the total yield of the mixed dioxanes was determined as for the 5-halo-4-phenyl-1,3-dioxanes and the mixture of 5-methyl-4-phenyl-1,3-dioxanes was isolated by vapor phase chromatography and analyzed by nmr. In each case the unreacted styrene was analyzed to determine if any isomerization had taken place during the reaction.

The results of the stereochemical studies are sufficiently reproducible to allow some conclusions to be drawn. However, there are several difficulties encountered in making any mechanistic conclusions from a study of this type. It is important to consider solvent effects, temperature effects, and the stability of both the starting material and all of the products to the reaction conditions. In all of the experiments reported in Table I, except for the few noted, the unchanged starting olefin was recovered in part. Independent control experiments were carried out to determine if the products were stable to the reaction conditions. It was not possible to carry out the reactions in acetic acid without any isomerization of either the starting material or the products. The data for a few experiments in acetic acid are included since the amount of isomerization which would have taken place would not drastically change the product composition.

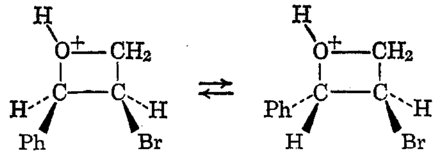
That the solvent can affect the stereochemistry of the Prins reaction is shown by the fact that noticeably more *trans* addition occurs in the Prins reaction of *trans*-1-phenylpropene in water at 70° than in dioxane at 25°. We have also noted a solvent effect on the stereochemistry of the Prins reaction with cyclohexene. Whereas the Prins reaction of cyclohexene in acetic acid yields 2-hydroxymethylcyclohexanol derivatives containing 97% of the *trans* addition products and 3% of the *cis* materials, this stereoselectivity is much less when the reaction is carried out in dioxane.[19] The fraction of *cis* materials increases to 15–20% in dioxane solution. A solvent effect may be responsible for the results of LeBel, Liesemer, and Mehemedbasich[11] who report that the Prins reaction with *cis*- and *trans*-4-octene in dioxane is not stereospecific, although the two geometrical isomers give different ratios of *trans*:*cis* addition. In contrast to this finding is the recent report that the Prins reaction in aqueous solutions with *cis*- and *trans*-2-butene gives stereospecific *trans* addition.[12] It appears that the Prins reaction in dioxane is generally less stereoselective than in other solvents such as water or acetic acid. It may be that dioxane intercepts carbonium ion intermediates to give unstable oxonium ion intermediates which subsequently suffer displacement to give the expected product. However, if the addition of the conjugate acid of formaldehyde and dioxane occurs in a *trans* manner, this process would result in net *cis* addition for the Prins reaction. This suggestion is supported by the observation that solvolysis reactions in dioxane show an unusually large fraction of retention of configuration.[20]

The data in Table I clearly show that the Prins reaction is not a stereospecific process. The results for the 1-phenylpropenes are perhaps the most informative since the reaction could be studied in aqueous media as well as in dioxane. Nearly equal amounts of *cis* and *trans* addition were observed for both 1-phenylpropenes, and we find no support for the recent generalization that *trans*-styrenes show stereospecific *cis* addition in the Prins reaction.[7] The lack of stereoselectivity in the Prins reaction of the 1-phenylpropenes suggest that the reaction proceeds predominantly through a symmetrically solvated benzylic cation.

However, a simple symmetrically solvated carbonium ion intermediate does not account for the stereochemistry of the Prins reaction with the β-halostyrenes. The *cis-trans* pairs do not give the same product mixture although we find that none of the reactions is stereospecific in contrast to the report of Bernardi and Leone[6] who studied the Prins reaction with *cis*- and *trans*-β-bromostyrene. It is conceivable but unlikely that differences in reaction conditions could account for this discrepancy. We find that when the products from the Prins reactions of the β-bromostyrenes are distilled we could not isolate any of the *cis*-5-bromo-4-phenyl-1,3-dioxane. However, the fact that the Prins reaction of *trans*-β-bromostyrene gives predominantly the product of *cis* addition requires further comment. Bernardi and Leone[6] postulate a four-membered ring oxonium ion intermediate to account for this result.



However, intermediates of this type have been criticized because solvolysis studies have yielded no evidence for their formation.[21] It is interesting to note that the addition of hypobromous acid to the cinnamyl alcohols could produce the same intermediates that are involved in the Prins reaction of the β-bromostyrenes. Bernardi and Leone postulate an equilibrium between the two isomeric four-membered oxonium ions which might be formed in the Prins reaction of the β-bromostyrenes as shown below.[6] They



conclude that the product distribution is determined by the stabilities of the isomeric four-membered oxonium ions. This hypothesis leads to the conclusion that the four-membered oxonium ion intermediate is more stable

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[19] M. Schwarz, unpublished results.

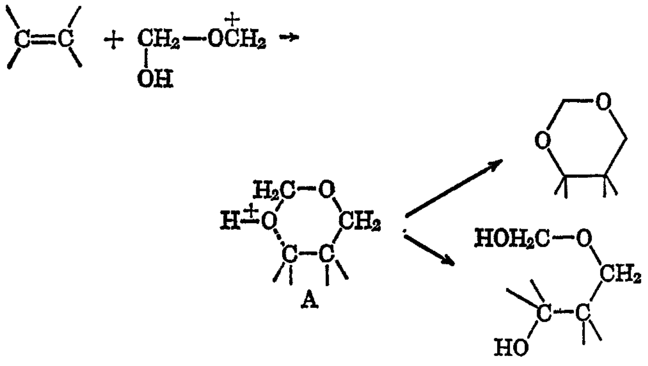
[20] A. Streitwieser, Jr., and S. Andreades, *J. Am. Chem. Soc.*, **80**, 6553 (1958); A. Streitwieser, Jr., and W. D. Schaeffer, *ibid.*, **79**, 6233 (1957); H. Weiner and R. Sneen, *ibid.*, **84**, 3599 (1962).

[21] L. J. Dolby, *J. Org. Chem.*, **27**, 2971 (1962).

than the corresponding bromonium ion intermediate. This follows because, when the benzylic carbon bond is broken and rotation about the C-1–C-2 bond takes place, there is opportunity for bromonium ion formation. If it is postulated that bromonium ion formation does not take place, it can only be because the bromonium ion is much less stable than the four-membered oxonium ion. If this were actually the case, one might expect to obtain the same bromohydrin from both *cis*- and *trans*-cinnamyl alcohol. This is not the situation since the cinnamyl alcohols give different bromohydrins, formed in each case by *trans* addition. This result also establishes that the bromonium ion intermediates do not equilibrate.

We originally thought that a neighboring bromine effect might be responsible for the large fraction of *cis* addition in the Prins reaction with *trans*-β-bromostyrene. However, a neighboring bromine effect might also be expected to result in *cis* addition with *cis*-β-bromostyrene which was not observed. Also, chlorine is not as effective as bromine as a neighboring group but both *trans*-β-halostyrenes show about the same fraction of *cis* addition and *cis*-β-chlorostyrene yields predominantly the product of *trans* addition in the Prins reaction. It is extremely difficult to rationalize all of the results on the stereochemistry of the Prins reaction, but it appears that the halogen has perturbing effects. Another complicating feature is that we were not able to find conditions to examine the reaction other than in dioxane solution. These reactions may be quite complex with several product-determining processes taking place at comparable rates.

It is of interest to examine the results of the present study with regard to the recent mechanistic proposal of Smissman and co-workers.[7] This proposal suggests an attacking species (A) derived from two molecules of formaldehyde.



This mechanism was suggested by the stereospecific *cis* addition observed in the Prins reaction of several styrenes. This proposal is open to question on several grounds. The experimental evidence is tenuous. Smissman reports no experiments showing that all of the possible products would be stable to the reaction conditions.[7] In the present study we find that product stability is a serious problem and the Prins reaction with the several styrenes we examined is clearly not a stereospecific process. Moreover, *trans* addition in the Prins reaction proceeding by way of intermediate A requires that a carbon–oxygen bond be broken rather than a proton loss. The application of this mechanism to *trans*-1-phenylpropene requires that carbon–oxygen bond breaking proceed about as fast as loss of a proton from oxygen. Such behavior is contrary to experience[22] and makes this mechanism unlikely as a route for *trans* addition.

Experimental Section[23]

***trans*-β-Chlorostyrene.**—A mixture of *cis*- and *trans*-β-chlorostyrenes (*ca.* 1:1), prepared by the method of Biltz,[13] was distilled through a 150-cm spinning-band column at atmospheric pressure. The first fraction (collected up to 197°) was enriched in *cis*-β-chlorostyrene (*ca.* 80% *cis*); thereafter the fractions were found to contain greater than 70% of the *trans* isomer. The mixture which was rich in *trans*-β-chlorostyrene (30 g, 0.22 mole) was added to a mixture of sodium hydroxide (17 g, 0.42 mole) and 100 ml of dry dimethyl sulfoxide. The reaction mixture was heated on a steam bath for 32 hr and at the end of that time, 500 ml of water was added and the mixture was extracted with ether. The ether layer was dried, the ether was removed, and the product was distilled to yield pure *trans*-β-chlorostyrene (6.0 g, 29% yield): bp 83–86° (19 mm); $n^{21}\text{D}$ 1.5782; nmr, carbon tetrachloride solution, AB quartet with the outer pairs centered at 6.63 and 6.78 ppm ($J = 14.0$ cps), acetone solution, two lines centered at 6.80 ppm, separated by 1.0 cps, acetone solution (higher dilution), one line at 6.80 ppm.

Anal. Calcd for C_8H_7Cl: C, 69.29; H, 5.13; Cl, 25.58. Found: C, 68.87; H, 5.05; Cl, 25.37.

***cis*-β-Chlorostyrene.**—The mixture (8.5 g, 0.061 mole) from the distillation fraction which was rich in the *cis* isomer (*ca.* 80% *cis*) was added to a column of 500 g of activity I neutral Woelm alumina. Elution was begun with pentane with 75-ml fractions being collected after a 100-ml forerun. Fractions 9–12 contained pure *cis*-β-chlorostyrene (1.16 g, 17% yield): nmr, carbon tetrachloride solution, AB quartet with the outer pairs centered at 6.08 and 6.33 ppm ($J = 8.0$ cps), acetone solution, AB quartet with the outer pairs centered at 6.25 and 6.88 ppm ($J = 8.0$ cps).

Anal. Calcd for C_8H_7Cl: C, 69.29; H, 5.13; Cl, 25.58. Found: C, 68.88; H, 5.10; Cl, 26.14.

***erythro*-2-Chloro-3-phenyl-1,3-propanediol.**—*trans*-Cinnamyl alcohol (5.0 g, 0.0373 mole) was dissolved in 75 ml of diethyl ether. N-Chlorosuccinimide (5.35 g, 0.0373 mole), 50 ml of water, and 3 drops of 70% perchloric acid were added. The mixture was shaken at room temperature for 4 days. Solid potassium carbonate was added, the water layer was separated, and the water was extracted with three more 25-ml portions of ether. The combined ether extracts were washed with 5% potassium carbonate solution, dried, and evaporated to give 6.31 g (*ca.* 90%) of a pale yellow oil. Some of the oil was distilled at reduced pressure to give a colorless oil, bp 150–151° (5 mm), $n^{25}\text{D}$ 1.5615.

***threo*-2-Chloro-3-phenyl-1,3-propanediol.**—*cis*-Cinnamyl alcohol was treated with N-chlorosuccinimide as previously described. The yield was *ca.* 90% of a pale yellow oil, which, when chromatographed on Florisil (30 g of adsorbent/g of oil), yielded the diol as a viscous colorless oil.

Anal. Calcd for $C_9H_{11}ClO_2$: C, 57.91; H, 5.94; Cl, 19.00. Found: C, 57.40; H, 5.90; Cl, 18.51.

***trans-erythro*-5-Chloro-4-phenyl-1,3-dioxane.**—*erythro*-2-Chloro-3-phenyl-1,3-propanediol (2.5 g, 0.0134 mole) was added to a mixture of paraformaldehyde (2.0 g, 0.0670 mole, as formaldehyde), *p*-toluenesulfonic acid monohydrate (1.27 g, 0.0067 mole), and 10 g of *p*-dioxane. The mixture was heated for 9 hr at 110–115° after which it was cooled, poured into 100 ml of 5% sodium bicarbonate solution, and extracted with ether. The combined ether extracts were washed with 5% sodium bicarbonate solution and dried over sodium sulfate. The ether

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[22] A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," John Wiley and Sons, Inc., New York, N. Y., 1961, p 209.

[23] All melting points and boiling points are uncorrected; unless otherwise specified, distillations were carried out with a 100-cm modified Podbielniak tantalum-spiral column. Infrared spectra were determined with a Beckman IR-7 infrared spectrophotometer. Proton magnetic resonance spectra were measured in either carbon tetrachloride or acetone solution, using tetramethylsilane as internal standard with a Varian A-60 spectrometer. Refractive indices were measured with a Bausch and Lomb Abbe refractometer. Gas–liquid partition chromatography was carried out with Aerograph A-90 and Aerograph Autoprep A-700 gas chromatographs. Analyses are by Pascher and Pascher Laboratories, Bonn, Germany, and Berkeley Analytical Laboratories, Berkeley, Calif. Prins reaction yields are based on unrecovered starting material.

was removed to yield 2.30 g of crude product (*ca.* 86% yield). This oil was distilled at reduced pressure to give the pure dioxane, bp 93° (1 mm), $n^{24}\mathrm{D}$ 1.5372.

Anal. Calcd for $C_{10}H_{11}ClO_2$: C, 60.46; H, 5.58; Cl, 17.85. Found: C, 59.73; H, 5.22; Cl, 18.23.

cis-threo-5-Chloro-4-phenyl-1,3-dioxane.—*threo*-2-Chloro-3-phenyl-1,3-propanediol (7.35 g, 0.0334 mole) was converted to the formal as just described. The crude product was distilled at reduced pressure to give the *trans-erythro*-dioxane (0.94 g, 12%), bp 95–97 (2 mm), $n^{24}\mathrm{D}$ 1.5365. The pot residue from the distillation yielded 3.55 g (45%) of the crystalline *cis-threo*-dioxane, mp 90–91°.

Anal. Calcd for $C_{10}H_{11}ClO_2$: C, 60.46; H, 5.58; Cl, 17.85. Found: C, 60.23; H, 5.81; Cl, 17.76.

trans-β-Bromostyrene.—A mixture (*ca.* 70% *trans*) of *cis*- and *trans*-β-bromostyrenes was prepared by the method of Biltz.[13] This mixture (20 g, 0.109 mole) was added to sodium hydroxide (3.2 g, 0.08 mole) in 200 ml of 2-propanol. The solution was heated under reflux for 2 hr. The reaction mixture was then cooled, 200 ml of water was added, and the mixture was extracted with petroleum ether (bp 30–60°). The ether was dried and evaporated to give 14.0 g (97%) of *trans*-β-bromostyrene: bp 45–50° (1.75 mm); $n^{25}\mathrm{D}$ 1.6048 (lit.[24] $n^{25}\mathrm{D}$ 1.6071); nmr, carbon tetrachloride solution, AB quartet with the outer pairs centered at 6.53 and 6.98 ppm (J = 14.0 cps), acetone solution, AB quartet with the outer pairs centered at 6.88 and 7.18 ppm (J = 14.0 cps).

cis-β-Bromostyrene.—*cis*-β-Bromostyrene was prepared by the method of Cristol and Norris.[14] It had $n^{25}\mathrm{D}$ 1.5980 and bp 55–58° (2 mm) [lit. $n^{25}\mathrm{D}$ 1.5980,[24] bp 55–56° (2 mm)[14]]; nmr, carbon tetrachloride solution, AB quartet with the outer pairs centered at 6.30 and 6.92 ppm (J = 8.0 cps).

threo-2-Bromo-3-phenyl-1,3-propanediol.—*cis*-Cinnamyl alcohol (6.25 g, 0.0467 mole) was dissolved in 75 ml of ether. N-Bromosuccinimide (8.35 g, 0.0467 mole), 50 ml of water, and 3 drops of 70% perchloric acid were added. The mixture was shaken at room temperature for 5 days. Solid potassium carbonate was added until the water layer became basic. The organic layer was separated and the water layer was extracted with three 25-ml portions of ether. The combined ether extracts were washed with 5% potassium carbonate solution, dried, and evaporated to give an oil which crystallized upon standing. The product was recrystallized from trichloroethylene. The yield was 7.5 g (71%) of white crystals, mp 84.5–85.5° (lit.[16] mp 86°).

trans-erythro-5-Bromo-4-phenyl-1,3-dioxane.—*erythro*-2-Bromo-3-phenyl-1,3-propanediol (3.86 g, 0.0167 mole) was added to mixture of 5 g of dioxane, paraformaldehyde (2.5 g, 0.0835 mole, as formaldehyde), and *p*-toluenesulfonic acid monohydrate (1.67 g, 0.0088 mole). This mixture was heated in an oil bath (bath temperature 110–115°) for 6 hr. The reaction mixture was processed as previously described and the crude product was distilled to give the *trans*-dioxane (2.42 g, 60%), bp 107° (1.55 mm), $n^{24}\mathrm{D}$ 1.5573 [lit.[4] bp 120° (3 mm), $n^{19}\mathrm{D}$ 1.5598].

erythro-2-Bromo-3-phenyl-1,3-propanediol.—*trans*-Cinnamyl alcohol (5.0 g, 0.0373 mole) was treated in the same manner as the *cis* isomer and gave 8.3 g (97%) of *erythro*-2-bromo-3-phenyl-1,3-propanediol as white crystals, which when recrystallized had mp 63–64° (lit.[17] mp 63–64°).

cis-threo-5-Bromo-4-phenyl-1,3-dioxane.—The *threo*-diol was treated in the same way as the *erythro* isomer and gave the desired *cis*-dioxane (2.0 g, 50%), bp 129° (1 mm), $n^{24}\mathrm{D}$ 1.5751. After recrystallization from ethanol, followed by sublimation, it had mp 69.5–70.0° (lit.[4] mp 75–76°).

Anal. Calcd for $C_{10}H_{11}BrO_2$: C, 49.40; H, 4.65; Br, 32.87; mol wt, 243.1. Found: C, 49.65; H, 4.64; Br, 32.72; mol wt (ebulliometric), 243.

Hydrogenolysis of 5-Halo-4-phenyl-1,3-dioxanes.—*cis*-5-Bromo-4-phenyl-1,3-dioxane (1.0 g, 0.0041 mole) was dissolved in 20 ml of absolute ethanol and added to a mixture of triethylamine (0.060 g, 0.006 mole), 20 ml of ethanol, and 5% palladium-on-carbon catalyst (0.300 g) under hydrogen. When the theoretical amount of hydrogen had been absorbed, the catalyst was filtered and ether was added. The ether solution was then extracted with 10% hydrochloric acid, dried, and evaporated. The product (0.61 g, 90%) was identical in every way with authentic 4-phenyl-1,3-dioxane.[25]

trans-5-Bromo-4-phenyl-1,3-dioxane was treated in the same way to give 4-phenyl-1,3-dioxane in 50% yield (based on unrecovered starting material).

cis-5-Chloro-4-phenyl-1,3-dioxane was also hydrogenolyzed in this way to give 4-phenyl-1,3-dioxane in 82% yield.

Analysis of Chlorostyrene Mixtures.—*cis*- and *trans*-β-chlorostyrene were found to be separable in analytical amounts by glpc on a 5 ft × 0.25 in. column of 5% Bentone 34–10% didecyl phthalate on 60–80 mesh firebrick. The optimum conditions were a column temperature of 130° and a flow rate of 50 cc/min of helium.

Analysis of Bromostyrene Mixtures.—*cis*- and *trans*-β-bromostyrene were analytically separable with a 5 ft × 0.25 in. column of 20% 1,2,3-tris(2-cyanoethoxy)propane on 60–80 mesh firebrick. The optimum conditions were a temperature of 135° and a flow rate of 50 cc/min of helium.

Analysis of Bromo- and Chloro-4-phenyl-1,3-dioxane Mixtures.—*cis*- and *trans*-5-chloro-1,3-dioxane were found to be easily separable with a 5 ft × 0.25 in. column of 5% Dow 710 silicone oil on 60–80 mesh firebrick. The corresponding bromo compounds were also easily separable on the same column. Quantitative analysis of the reaction mixtures was made possible through the use of 4-phenyl-1,3-dioxane as an internal standard. Relative thermal response of all compounds was obtained by the analysis of known mixtures. Optimum conditions were a temperature of 190° and a flow rate of 50 cc/min of helium.

Prins Reaction of _trans_-β-Chlorostyrene.—*trans*-β-Chlorostyrene (2.96 g, 0.0214 mole) was added to 12 g of dioxane, paraformaldehyde (1.25 g, 0.0417 mole, as formaldehyde), and 1.75 g of concentrated sulfuric acid. The reaction mixture was then heated at 110–115° for 12 hr after which the reaction mixture was cooled and poured into water, then extracted with ether. The ether was washed with 5% sodium bicarbonate solution, dried, and evaporated to give 2.4 g of oil. Glpc analysis showed the composition of this oil to be *trans*-5-chloro-4-phenyl-1,3-dioxane (1.18 g, 41%), *cis*-5-chloro-4-phenyl-1,3-dioxane (0.29 g, 10%), and β-chlorostyrene (0.96 g). No *cis*-β-chlorostyrene was detected in the recovered chlorostyrene.

In another reaction, *trans*-β-chlorostyrene (0.194 g, 0.0014 mole) was added to dioxane (3.0 g), paraformaldehyde (0.378 g, 0.0126 mole, as formaldehyde), and 0.125 g of concentrated sulfuric acid. The reaction mixture was then heated at 100–105° for 20 hr after which it was processed as before to give 0.173 g of oil. Glpc showed this oil to contain *trans*-5-chloro-4-phenyl-1,3-dioxane (0.0334 g, 65%), *cis*-5-chloro-4-phenyl-1,3-dioxane (0.0055 g, 11%), and *trans*-β-chlorostyrene (0.158 g). No *cis*-β-chlorostyrene was detected in the recovered chlorostyrene.

Prins Reaction of _cis_-β-Chlorostyrene.—*cis*-β-Chlorostyrene (0.300 g, 0.0022 mole) was added to 1.2 g of dioxane, paraformaldehyde (0.125 g, 0.0042 mole, as formaldehyde), and 0.175 g of concentrated sulfuric acid. The mixture was heated at 110–115° for 12 hr. At the end of that time the reaction mixture was cooled and worked up as in the *trans* case. The oily product weighed 0.370 g. Glpc analysis showed that it contained *trans*-5-chloro-4-phenyl-1,3-dioxane (0.097 g, 28%), *cis*-5-chloro-4-phenyl-1,3-dioxane (0.029 g, 8%), and 0.059 g of β-chlorostyrene. The recovered chlorostyrene was now *ca.* 30% *trans*-β-chlorostyrene.

In another reaction, *cis*-β-chlorostyrene (87.2 mg, 0.6 mmole), was added to 1.5 ml of dioxane, paraformaldehyde (170 mg, 5.7 mmoles), and concentrated sulfuric acid (65 mg). The solution was heated at 100–105° for 20 hr and worked up as before. Glpc showed that the 64.9 mg of oily product contained *trans*-5-chloro-4-phenyl-1,3-dioxane (7.1 mg, 11%), *cis*-5-chloro-4-phenyl-1,3-dioxane (0.7 mg, 1%), and β-chlorostyrene (42 mg). Glpc analysis of the recovered chlorostyrene showed that no isomerization had occurred.

Stability of 5-Chloro-4-phenyl-1,3-dioxanes.—*cis*-5-Chloro-4-phenyl-1,3-dioxane (150 mg, 0.0008 mole), was added to a mixture of paraformaldehyde (216 mg, 0.0072 mole), 2 ml of dioxane, and concentrated sulfuric acid (0.080 g). The solution was heated at 100–105° for 20 hr, then poured into excess 5% sodium carbonate solution and extracted with ether. The ether was dried and evaporated and the recovered material was analyzed by glpc. *trans*-5-Chloro-4-phenyl-1,3-dioxane was treated in exactly the same way. In both cases, less than 1% isomerization was found.

Prins Reaction of _trans_-β-Bromostyrene. A. In Dioxane.—*trans*-β-Bromostyrene (4.0 g, 0.0217 mole) was added to dioxane

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[24] E. Grovenstein, Jr., and D. E. Lee, *J. Am. Chem. Soc.*, **75**, 2639 (1953).

[25] R. L. Shriner and P. R. Ruby, "Organic Syntheses," Coll. Vol. IV, John Wiley and Sons, Inc., New York, N. Y., 1963, p 786.

(25 ml), paraformaldehyde (2.4 g, 0.0800 mole, as formaldehyde), and 1.87 g of concentrated sulfuric acid. The reaction mixture was heated at 110–115° for 9 hr. At the end of that time, the reaction mixture was cooled and poured into 50 ml of saturated sodium bicarbonate solution. This solution was then extracted with ether. The ether extract was dried and evaporated to give 4.71 g of crude product. This oil was analyzed by glpc and was found to contain *trans*-5-bromo-4-phenyl-1,3-dioxane (0.73 g, 53%), *cis*-5-bromo-4-phenyl-1,3-dioxane (0.16 g, 11%), and β-bromostyrene (2.97 g). Glpc analysis of the recovered bromostyrene showed that no isomerization had occurred.

In another experiment *trans*-β-bromostyrene (2.0 g, 0.0109 mole) was added to paraformaldehyde (1.2 g, 0.0400 mole, as formaldehyde), 12.5 ml of dioxane, and concentrated sulfuric acid (0.93 g). The mixture was heated at 85° for 48 hr. At the end of that time, the reaction was worked up in the usual manner and analyzed by glpc. The 2.5 g of crude product was found to contain *trans*-5-bromo-4-phenyl-1,3-dioxane (1.01 g, 80%), *cis*-5-bromo-4-phenyl-1,3-dioxane (0.09 g, 7%), and β-bromostyrene (1.05 g). Glpc analysis of the recovered bromostyrene showed that no isomerization had occurred. A duplicate reaction gave *trans*-5-bromo-4-phenyl-1,3-dioxane in 58% yield and the *cis* isomer in 6.4% yield.

B. In Acetic Acid.—Paraformaldehyde (2.7 g, 0.090 mole, as formaldehyde), 3.1 g of concentrated sulfuric acid, and 18 ml of glacial acetic acid were mixed well and warmed to 90°. *trans*-β-Bromostyrene (5.68 g, 0.031 mole) was then added and the mixture was heated, for 4.5 hr at 95–100°. At the end of that time, the reaction mixture was poured into 50 ml of water and extracted with ether. The ether extracts were dried and evaporated to give 7.16 g of oil. This oil was analyzed by glpc and was found to contain *trans*-5-bromo-4-phenyl-1,3-dioxane (1.67 g, 22%) and *cis*-5-bromo-4-phenyl-1,3-dioxane (0.41 g, 5%). The oil was distilled at reduced pressure and yielded pure *trans*-5-bromo-4-phenyl-1,3-dioxane (2.2 g, 29%), bp 100–103° (0.90 mm), $n^{24}\text{D}$ 1.5565.

Prins Reaction of *cis*-β-Bromostyrene. A. In Dioxane.—*cis*-β-Bromostyrene (4.0 g, 0.0217 mole) was added to 27 ml of dioxane, paraformaldehyde (2.4 g, 0.0800 mole, as formaldehyde), and 1.87 g of concentrated sulfuric acid. The reaction mixture was heated at 110–115° for 8 hr after which it was worked up as in the *trans* case to yield 2.75 g of oil. Glpc analysis showed that this oil contained *trans*-5-bromo-4-phenyl-1,3-dioxane (0.16 g, 8.5%), *cis*-5-bromo-4-phenyl-1,3-dioxane (0.13 g, 7%), and β-bromostyrene (2.5 g). Glpc analysis of the recovered bromostyrene showed no isomerization had occurred.

B. In Acetic Acid.—*cis*-β-Bromostyrene (20.0 g, 0.109 mole) was added to paraformaldehyde (9.5 g, 0.317 mole, as formaldehyde), 11.5 g of concentrated sulfuric acid, and 55 ml of glacial acetic acid. The reaction mixture was then heated at 95–100° for 8 hr. The mixture was then worked up as in the *trans* case. The yield was 29.23 g of oil. This oil was analyzed by glpc and found to contain *trans*-5-bromo-4-phenyl-1,3-dioxane (2.4 g, 10%) and *cis*-5-bromo-4-phenyl-1,3-dioxane (2.0 g, 8%). The oil was distilled to yield pure *trans*-5-bromo-4-phenyl-1,3-dioxane (4.2 g, 17%), bp 108–110° (1.35 mm), $n^{25}\text{D}$ 1.5570.

Stability of 5-Bromo-4-phenyl-1,3-dioxanes. A. Dioxane Solution.—*cis*-5-Bromo-4-phenyl-1,3-dioxane (34.1 mg, 0.145 mmole) was added to 2 ml of dioxane and 2 drops of concentrated sulfuric acid. The solution was refluxed for 9 hr, then poured into 6 ml of saturated sodium bicarbonate solution, and extracted with ether. The ether was evaporated, and the recovered material was analyzed by glpc. *trans*-5-Bromo-4-phenyl-1,3-dioxane (42.6 mg, 0.183 mmole) was treated in exactly the same way. In both cases, less than 1% isomerization was found.

B. Acetic Acid Conditions.—*cis*-5-Bromo-4-phenyl-1,3-dioxane (52.0 mg, 0.22 mmole) was added to paraformaldehyde (20 mg, 0.66 mmole as formaldehyde), concentrated sulfuric acid (30 mg), and 1 ml of glacial acetic acid. The solution was heated at 100–105° for 4.5 hr, then worked up as in the Prins reactions of the β-bromostyrenes. The recovered dioxane was analyzed by glpc and was now 74% *cis*-5-bromo-4-phenyl-1,3-dioxane and 26% *trans* isomer.

***cis*- and *trans*-1-phenylpropene** were prepared by the method of Dewar and Fahey.[15]

***threo*-2-Methyl-3-phenyl-1,3-propanediol.**—Ethyl β-hydroxy-α-methyl-β-phenylpropionate[18] was saponified and the acid thus obtained was recrystallized from chloroform–hexane six times. The acid had a melting point of 93–96° (lit.[18] mp 96.5–97.5°). β-Hydroxy-α-methyl-β-phenylpropionic acid (5.6 g, 0.031 mole) was dissolved in 10 ml of anhydrous ether. This solution was added dropwise, with stirring, to a mixture of lithium aluminum hydride (1.19 g, 0.031 mole) and 100 ml of anhydrous ether and the resulting mixture was refluxed overnight. The cooled reaction mixture was cautiously treated with 16 ml of 4% aqueous sodium hydroxide and the ether layer was separated and dried. Distillation of the crude product yielded 1.47 g (28%) of pure *threo*-2-methyl-3-phenyl-1,3-propanediol, bp 140–144° (2.4 mm), $n^{20}\text{D}$ 1.5352.

Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 72.24; H, 8.23.

***trans*-5-Methyl-4-phenyl-1,3-dioxane. A.**—*threo*-2-Methyl-3-phenyl-1,3-propanediol (0.56 g, 0.0034 mole) was dissolved in 62 ml of dimethoxymethane, and *p*-toluenesulfonic acid (0.060 g) was added. The solution was stirred at room temperature for 5 days. At the end of that time, the mixture was poured into an excess of 5% aqueous sodium bicarbonate solution and extracted with several portions of ether. The ether was evaporated (after drying) and 0.560 g of oil was obtained. The oil was then chromatographed on 25 g of E. Merck AG. activity I neutral alumina. Elution was begun with 10% ether in benzene. This yielded the *trans*-5-methyl-4-phenyl-1,3-dioxane (0.166 g, 27%) uncontaminated with *cis* isomer (determined by nmr and infrared spectra). Chloroform eluted 0.156 g of a mixture of the starting alcohol and the *trans*-dioxane. Using methanol as eluent, 0.146 g of the starting alcohol was recovered.

B.—*trans*-5-Methyl-4-phenyl-1,3-dioxane was also obtained by the chromatographic separation (described below, for the *cis* isomer) of the Prins reaction products of 1-phenylpropene. The *trans*-dioxane obtained in this way was identical with that obtained by method A and had $n^{20}\text{D}$ 1.5200 (after glpc on a 5% Dow 710 silicone oil on firebrick column at 190°, 50 cc/min of helium.

Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 73.68, 73.82; H, 7.79, 7.85.

***cis*-5-Methyl-4-phenyl-1,3-dioxane.**—A 1:1 mixture of *cis*- and *trans*-5-methyl-4-phenyl-1,3-dioxanes (1.31 g, 0.074 mole) obtained from the Prins reaction of 1-phenylpropene was added to a column of 50 g of E. Merck AG. activity I neutral alumina. Elution was begun with 1% ether in benzene. This eluent yielded 0.300 g of pure *cis*-5-methyl-4-phenyl-1,3-dioxane, $n^{20}\text{D}$ 1.5230 (after glpc) (lit.[7] $n^{20}\text{D}$ 1.5235). The nmr and infrared spectral properties of this compound corresponded to those previously reported.[7]

Further elution with 5% ether gave mixtures of the *cis*- and *trans*-dioxanes. Finally, elution with 10% ether in benzene yielded 180 mg of the pure *trans* isomer.

Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 74.12, 73.95; H, 8.44, 8.42.

Analysis of 1-Phenylpropene Mixtures.—*cis*- and *trans*-1-phenylpropene were separable by glpc on a 10 ft × 0.5 in. column of SE-30 on 60–80 mesh firebrick. The conditions used were a temperature of 150° and a flow rate of 200 cc/min of helium.

Analysis of Prins Reaction Products of 1-Phenylpropenes.—*cis*- and *trans*-5-methyl-4-phenyl-1,3-dioxane were not separated by a 5% Dow 710 silicone oil column (5 ft × 0.25 in.) at 170° and 50 cc/min of helium. Total yield of the isomeric dioxanes was therefore determined by the comparison of the area of the *cis*/*trans* dioxane peak with that of β-bromostyrene (which was used as an internal standard). The total amount of 1-phenylpropene could be simultaneously estimated, since under these conditions all three peaks were well separated. Relative thermal response of these compounds was obtained by analysis of known mixtures. Relative amounts of the *cis* and *trans* isomers were determined by comparing the areas of *cis*-methyl doublet (centered at 0.85 ppm in CCl_4 solution) and the *trans*-methyl doublet (centered at 0.53 ppm in CCl_4 solution) in the nmr spectra of mixtures.

Prins Reaction of *trans*-1-Phenylpropene. A. In Dioxane.—*trans*-1-phenylpropene (0.463 g, 0.004 mole) was added to 10 g of dioxane, paraformaldehyde (0.371 g, 0.0125 mole, as formaldehyde), and 0.376 g of concentrated sulfuric acid. The reaction mixture was stirred (protected from light) for 3 days at room temperature after which it was processed in the usual manner to give an oil (0.220 g). Glpc analysis showed that this oil contained 5-methyl-4-phenyl-1,3-dioxane (0.099 g, 15%) and 1-phenylpropene (0.025 g). Glpc analysis showed that no isomerization of the starting *trans*-1-phenylpropene had occurred. Nmr analysis showed that the product dioxanes were in the ratio, *cis*/*trans*, of 0.82.

In another experiment *trans*-1-phenylpropene (0.163 g, 0.0014 mole), paraformaldehyde (0.378 g, 0.0126 mole, as formaldehyde), 3 ml of dioxane, and concentrated sulfuric acid (0.125 g) were mixed and stirred, protected from light, at room temperature for 4 days. The reaction mixture was then worked up in the usual manner and analyzed by glpc. The yield of 5-methyl-4-phenyl-1,3-dioxanes was 45.3 mg (19%). *trans*-1-Phenylpropene (2.4 mg) was also found in the crude product. Nmr analysis showed that the product dioxanes were in the ratio, *cis/trans*, of 0.89.

B. In Water.—In one experiment the published procedure[25] was followed, using *trans*-1-phenylpropene (6.36 g, 0.054 mole), 37% formalin (11.2 g, 0.14 mole), and 1.0 g of concentrated sulfuric acid. The mixture was refluxed in the dark for 7 hr. Work-up gave 4.13 g of a mixture of *cis*- and *trans*-5-methyl-4-phenyl-1,3-dioxanes, bp 97–100° (2.5 mm), which was 1/1 *cis/trans* (determined by nmr). The yield was 43%. In another experiment the same relative amounts of reactants were used, but the reaction was carried out at 80–90° for 1.5 hr. A 1:1 mixture of the *cis*- and *trans*-dioxanes was obtained in 28% yield. Recovered *trans*-1-phenylpropene showed no isomerization.

In another experiment using the same relative amounts of reactants, the reaction was carried out at 70–75° for 22 hr. The reaction mixture was worked up and analyzed as before and gave 5-methyl-4-phenyl-1,3-dioxane in 46% yield. The ratio of *cis/trans* was 1.71. A duplicate reaction gave a 51% yield of the dioxanes with a *cis/trans* ratio of 1.62. Analysis of the recovered *trans*-1-phenylpropene showed no isomerization had occurred.

C. In Acetic Acid.—*trans*-1-Phenylpropene (0.163 g, 0.0014 mole), paraformaldehyde (0.378 g, 0.0126 mole, as formaldehyde), concentrated sulfuric acid (0.125 g), and 3 ml of glacial acetic acid were mixed and stirred in the dark for 4 days at room temperature. The reaction mixture was poured into an excess of 5% sodium carbonate solution and extracted with ether. The ether was dried and evaporated to yield 226.8 mg of oily product. The product was analyzed in the usual manner. 5-Methyl-4-phenyl-1,3-dioxane was found (59 mg, 24%). The ratio of the *cis/trans* isomers was 0.60. Glpc analysis of the recovered *trans*-1-phenylpropene showed less than 10% isomerization.

Prins Reaction of *cis*-1-Phenylpropene in Dioxane.—The same procedure was followed for this reaction as in the *trans*-1-phenylpropene case. The reaction yielded a mixture of the *cis*- and *trans*-5-methyl-4-phenyl-1,3-dioxanes (1:1) in 74% yield. Recovered *cis*-1-phenylpropene showed no isomerization.

In another experiment, *cis*-1-phenylpropene (0.163 g, 0.0014 mole) was added to paraformaldehyde (0.378 g, 0.0126 mole, as formaldehyde), 3 ml of dioxane, and concentrated sulfuric acid (0.125 g). The reaction mixture was stirred in the dark 4 days at room temperature and then worked up as before. The 5-methyl-4-phenyl-1,3-dioxanes were obtained in 48% yield. The ratio *cis-/trans*-5-methyl-4-phenyl-1,3-dioxane was 0.87. Analysis of recovered 1-phenylpropene showed that less than 5% isomerization had occurred.

Stability of 5-Methyl-4-phenyl-1,3-dioxanes. A. Dioxane Conditions.—*cis*-5-Methyl-4-phenyl-1,3-dioxane (0.110 g, 0.0006 mole) was added to paraformaldehyde (0.061 g, 0.0007 mole), 0.142 g of concentrated sulfuric acid, and 3 ml of dioxane. The mixture was stirred 3 days at room temperature and protected from light. At the end of that time the mixture was poured into an excess of 5% potassium carbonate solution and extracted with ether. The ether yielded 0.107 g of *cis*-5-methyl-4-phenyl-1,3-dioxane. Nmr showed that no detectable isomerization had occurred. The *trans* isomer was also found to be stable under these conditions.

B. Water Conditions.—*cis*-5-Methyl-4-phenyl-1,3-dioxane (0.135 g, 0.008 mole) was added to 0.06 g of concentrated sulfuric acid and 0.324 g of 37% formalin. Two drops of water were added. The mixture was heated at 80–90°, protected from light, for 3 hr after which the mixture was poured into an excess of 5% potassium carbonate solution and extracted with ether. The recovered dioxane (0.050 g) had isomerized about 15%. Pure *trans*-5-methyl-4-phenyl-1,3-dioxane was treated in exactly the same way. No isomerization was observed.

C. Acetic Acid Conditions.—A mixture of 5-methyl-4-phenyl-1,3-dioxanes (49% *cis*) (0.3041 g, 0.0017 mole) was added to paraformaldehyde (0.3058 g, 0.01 mole, as formaldehyde), concentrated sulfuric acid (0.125 g), and 3 ml of glacial acetic acid. The mixture was stirred in the dark at room temperature for 4 days and then worked up as in the Prins reaction. The recovered 5-methyl-4-phenyl-1,3-dioxane was analyzed by nmr and was now 45% *cis* and 55% *trans*.

Qualitative Equilibration Studies. A. 5-Methyl-4-phenyl-1,3-dioxane.—A 1:1 mixture of *cis*- and *trans*-5-methyl-4-phenyl-1,3-dioxanes (0.30 g, 0.0017 mole) was added to 5 ml of dioxane and concentrated sulfuric acid (0.40 g). This mixture was heated at 110° for 15 hr in the dark. At the end of this time the reaction mixture was worked up in the usual way and 0.26 g (87%) of the starting dioxanes was recovered. Nmr showed the composition was now 80% *trans*- and 20% *cis*-5-methyl-4-phenyl-1,3-dioxane.

B. 5-Chloro-4-phenyl-1,3-dioxane.—*cis*-5-Chloro-4-phenyl-1,3-dioxane (100 mg, 0.5 mmole) was added to paraformaldehyde (100 mg, 3.3 mmoles as formaldehyde), concentrated sulfuric acid (180 mg), and 1 ml of glacial acetic acid. This mixture was heated at 85° for 8 hr. The reaction mixture was then worked up in the usual way and 75 mg (75%) of starting dioxanes was recovered. Glpc showed that the mixture was 66% *trans*-5-chloro-4-phenyl-1,3-dioxane. *trans*-5-Chloro-4-phenyl-1,3-dioxane was treated in exactly the same way and yielded a mixture of the dioxanes which contained 75% *trans* isomer.

Nucleophilic Substitution in Halogenated Cyclobutenes[1]

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The reaction of 1,4,4-trichloro-3,3-difluorocyclobutene with ethoxide ion has been found to give the rearranged monoether, 1,2-dichloro-3-ethoxy-4,4-difluorocyclobutene, which undergoes further nucleophilic attack to yield 1-chloro-2,3-diethoxy-4,4-difluorocyclobutene. The results are interpreted on the basis of relative carbanion stabilities. A set of rules which predict the course of nucleophilic displacements in highly halogenated systems is presented.

The extensive studies during the past 20 years of the reactions of nucleophilic agents with fluoro olefins have given rise to numerous mechanistic interpretations. In 1948, Miller, Fager, and Griswold[3] explained the sodium-catalyzed addition of methanol to chlorofluoro olefins on the basis of rate-determining carbanion formation, followed by proton abstraction from solvent, and suggested that the fluorine atoms predisposed the system to polar activation by a resonance effect.

A paper[4] from our laboratory the following year suggested that the reaction of perfluorocyclobutene

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(1) This paper represents part of a thesis submitted by J. R. Dick to the Graduate School, University of Colorado, in partial fulfillment of the requirements for the Ph.D. degree, June 1964.

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(3) W. T. Miller, Jr., E. W. Fager, and P. H. Griswold, *J. Am. Chem. Soc.*, **70**, 431 (1948).

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