The Electrophilic Addition of Bromine to Arylcyclopropanes. Kinetics and Mechanistic Implications

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The kinetics of the electrophilic addition of bromine to phenylcyclopropane in chlorinated solvents have been examined. The rate of bromination was observed to be first order in both bromine and phenylcyclopropane at 20° in chloroform ($k = 2.0 \times 10^{-3}$ l. M^{-1} sec^{-1}) and methylene chloride ($k = 7.3 \times 10^{-3}$ l. M^{-1} sec^{-1}). The resulting ring-opened products are 1,2,3-tribromo-1-phenylpropane and 1,3-dibromo-1-phenylpropane. Addition of bromine to *trans*-1,2-diphenylcyclopropane resulted in 1,3-dibromo-1,3-diphenylpropane with a *dl*/meso ratio of 1.0 as the major product. Bromine addition to *cis*-1,2-diphenylcyclopropane resulted in dibromide with a *dl*/meso ratio of 0.82. A mechanism is presented which involves electrophilic attack of bromine on the cyclopropane ring to give a free benzyl carbonium ion as the major intermediate.

Previously reported results[1] from this laboratory on the addition of bromine to phenylcyclopropane and 1,2-diphenylcyclopropane showed that changes in temperature, concentration, light, and solvent have drastic effects on the rate of reaction and on product distribution. These results were rationalized in terms of three major competing types of reactions. Type A was one which could be initiated either photolytically or thermally, results in addition of bromine to yield 1,3-dibromo-1-phenylpropane as the only product, and was favored in less polar solvents. This reaction type had some of the characteristics usually attributed to free-radical bromine addition. Reaction type B had characteristics of an electrophilic bromine addition which resulted in cyclopropane ring cleavage and was favored by more polar solvents. Reaction type C involved aromatic substitution resulting in the formation of *p*-bromoarylcyclopropane and was favored at low temperatures and in polar solvents.

Our recent efforts have been devoted to searching for conditions under which each of the three reaction types could be isolated and studied individually. This report presents results of our investigation of the reaction type B, the addition reaction having characteristics of an ionic process. An interpretation of the results in terms of a reaction mechanism is included.

Results

The conditions which were found favorable for isolating the ionic addition reaction were as follows: the use of chloroform and methylene chloride as solvents at concentrations between 0.1 and 0.5 M, temperatures between 5 and 30°, and the presence of isoamyl nitrite, a free-radical inhibitor.[2,3] Within the temperature and concentration range employed, aromatic substitution does not occur in carbon tetrachloride and occurs to only a minor extent in chloroform and methylene chloride. The results of our kinetic studies of the bromination of phenylcyclopropane under these conditions are presented in Table I.

Kinetics.—The two products resulting from the addition of bromine to phenylcyclopropane are 1,3-dibromo-1-phenylpropane and 1,2,3-tribromo-1-phenylpropane. One mole of bromine is required to convert 1 mol of phenylcyclopropane to dibromide and 2 mol are required in the conversion to tribromide and hydrogen bromide. The tribromide–dibromide ratio remains constant throughout the course of the reaction. The relation between the phenylcyclopropane concentration, P, and the bromine concentration, B, is given in eq 1. Symbols, ρ, P_0, and B_0 refer, respectively, to

$$P = P_0 - \frac{B_0 - B}{\rho + 1} \qquad (1)$$

the ratio of tribromide to total bromides, initial phenylcyclopropane concentration, and initial bromine concentration. Equation 2 represents the second-order

$$\frac{\mathrm{d}B}{\mathrm{d}t} = kBP \qquad (2)$$

rate expression for a reaction which is first order with respect to both P and B. Equation 3 is the integrated

$$kt = \frac{1}{P_0 - B_0/(1 + \rho)} \ln \frac{B_0}{P_0(1 + \rho)} + \left[\frac{P_0(1 + \rho) - (B_0 - B)}{B}\right] \qquad (3)$$

form of eq 2 in which P was substituted by the quantity given in eq 1. Substituting P back into eq 3 yields the rate expression 4.

$$kt = \frac{1}{P_0 - B_0/(1 - \rho)} \ln (PB_0/BP_0) \qquad (4)$$

Straight-line plots are obtained for more than 70% of the reaction in chloroform and methylene chloride when $\ln (PB_0/BP_0)$ is plotted against time. Derived second-order rate constants are given in Table I. Slight deviations from linearity appearing in some cases are attributed to competing aromatic substitution, which occurs to less than 10% when $B_0/P_0 \leq 1$. The extent of these deviations is represented by the coefficient of linear regression, R (Table I), determined for each kinetic run. Examination of the R values in Table I shows that the plots tend to deviate least from linearity for the smaller values of B_0/P_0. Coincidentally, the amount of competing aromatic substitution increases with increasing B_0/P_0.

The second-order rate constant for the bromination of phenylcyclopropane in ethanol-free chloroform is invariable for B_0/P_0 values of 0.25, 0.50, and 1.00 (runs 18–21, 31–34, and 28–30). Over 20% para substitution occurs in competition with ring opening when B_0/P_0 is 2.00 (runs 16–17). Consequently, the second-order rate constant was not determined. The presence

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[1] R. T. LaLonde, P. Ferrara, and A. Debboli, Jr., *J. Org. Chem.*, **37**, 1094 (1972).

[2] M. S. Karasch, P. White, and F. Mayo, *J. Org. Chem.*, **3**, 33 (1938).

[3] D. Applequist and R. Searle, *J. Amer. Chem. Soc.*, **86**, 1389 (1964).

TABLE I[a]

KINETICS OF THE ADDITION OF BROMINE TO PHENYLCYCLOPROPANE

Solvent	Run no.	B_0[b]	P_0[b]	Temp, °C	k,[c] 10^3 l. M^{-1} sec^{-1}	R[d]	ρ[e]
$CHCl_2$	1–2	0.25	0.125	20.1			0.36 ± 0.02
	3–6	0.125	0.125	20.1	7.83 ± 0.25	0.995	0.36 ± 0.02
	7–8	0.125	0.250	20.1	7.82 ± 0.08	0.995	0.36 ± 0.02
	9–10	0.09	0.36	20.1	7.46 ± 0.05	0.998	0.36 ± 0.02
	11–13[f]	0.125	0.250	20.1	7.30 ± 0.30	0.997	0.38 ± 0.02
	14–15[f]	0.125	0.250	5.0	2.97 ± 0.03	0.989	0.38 ± 0.02
$CHCl_3$	16–17[f]	0.50	0.25	20.1			0.50 ± 0.02
	18–21[f]	0.10	0.40	20.1	1.87 ± 0.06	0.997	0.50 ± 0.02
	22–23	0.10	0.40	20.1	2.31 ± 0.01	0.997	0.38 ± 0.02
	24–25[f]	0.10	0.40	5.0	0.825 ± 0.015	0.998	0.50 ± 0.02
	26–27[f]	0.10	0.40	30.0	3.11 ± 0.17	0.997	0.50 ± 0.02
	28–30[f]	0.25	0.25	20.1	2.08 ± 0.06	0.993	0.50 ± 0.02
	31–34[f]	0.25	0.50	20.1	2.08 ± 0.06	0.995	0.50 ± 0.02
CCl_4	35–36	0.25	0.25	20.1	0.384 ± 0.013	0.999	0
	37–38[f]	0.25	0.25	20.1	0.0202 ± 0.0002	0.997	0.57 ± 0.02
	39[f,g]	0.25	0.25	20.1	0.0199	0.999	0.57 ± 0.02

[a] All experiments except run 39 were performed in the dark. [b] Initial concentration of bromine, B, and phenylcyclopropane, P, in moles per liter. [c] Rate constant reported with average deviation for multiple runs. [d] R = average coefficient of linear regression for multiple runs. [e] Mole ratio of tribromide product to total ring-opening products. [f] Contains 5 mol % isoamyl nitrite with respect to bromine. [g] In room light.

of isoamyl nitrite has the effect of decreasing k by 20% in chloroform (runs 18–21 and 22–23).

Likewise, the second-order rate constant remains invariable for the reactions carried out in methylene chloride solutions when B_0/P_0 is varied from 0.25 to 0.50 to 1.00 (runs 9–10, 7–8, and 3–6). However, when B_0/P_0 was 2.00, the second-order rate constant was not determined because of the nearly 30% para substitution occurring in competition with the addition reaction (runs 1–2). Added isoamyl nitrite in methylene chloride decreases the rate constant by approximately 7% (runs 11–13 and 7–8).

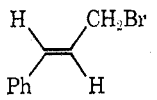
Using data from Table I the enthalpy of activation, $\Delta H^{\ddagger}$, and entropy of activation, $\Delta S^{\ddagger}$, were calculated according to the absolute rate equation.[4] The activation parameters for the reactions carried out in chloroform were $\Delta H^{\ddagger} = 8.3 \pm 0.8$ kcal mol^{-1} and $\Delta S_{293}{}^{\ddagger} = -43 \pm 3$ cal mol^{-1} °K^{-1} (runs 18–21, 24–27). The activation parameters for the reaction carried out in methylene chloride were $\Delta H^{\ddagger} = 9.3 \pm 0.8$ kcal mole^{-1} and $\Delta S_{293}{}^{\ddagger} = -36 \pm 3$ cal mol^{-1} °K^{-1} (runs 11–13, 14–15).

Straight-line plots are not observed when eq 4 is applied to the addition of bromine to phenylcyclopropane in carbon tetrachloride. However, plots of the reciprocal of the bromine concentration against time are linear. Rate constants in carbon tetrachloride were determined using the rate expression $kt = 1/B - 1/B_0$, which is derived from the rate equation $dB/dt - kB^2$. It is obvious that major kinetic differences exist between the bromine addition to phenylcyclopropane in carbon tetrachloride and in the other chlorinated solvents studied. We are not able at this time to rationalize this difference. Nevertheless, the rate constants for the carbon tetrachloride system are presented for comparative purposes.

The rate constant for the bromination of phenylcyclopropane in carbon tetrachloride in the dark is decreased by 95% when isoamyl nitrite is present (runs 35–38, Table I). Room light does not affect the rate when isoamyl nitrite is present (runs 37–39). However, without the added inhibitor room light has a drastic catalytic effect.[1]

Some interesting comparisons can be drawn from Table I concerning the effect of solvent on the rate of bromination. The second-order rate constants measured at 20° for the dark reaction increase with increasing solvent dielectric constants in the order $CCl_4 < CHCl_3 < CH_2Cl_2$ (runs 3-6, 22-23, and 35-36). Added isoamyl nitrite decreases the rate of bromination in each solvent without changing the overall order of the solvent effect (runs 37–38, 28–30, and 11–13). The ability of isoamyl nitrite to retard the rate of bromination is more pronounced in the solvents of lower dielectric constant. Added isoamyl nitrite decreases the rate constant by 95% in carbon tetrachloride, 20% in chloroform, and only 7% in methylene chloride.

Since cinnamyl bromide (**1**) appeared to be a probable precursor of the tribromide formed in the addition of bromine to phenylcyclopropane, the rate of bromine addition to **1** in chloroform at 22° in the dark was measured. The addition is observed to follow the third-order kinetic expression $kt = 1/B^2 - 1/B_0^2$ when the initial concentration of **1** and bromine are equal. These results are consistent with reported third-order kinetics for the bromine addition to simple olefins in carbon tetrachloride.[5] A straight line is obtained when $1/B^2$ is plotted against time through 80% completion for runs where B_0 and the initial cinnamyl bromide concentration are 0.025 M. The rate constant is 8.25 l.$^2/M^2$ sec and the coefficient of linear regression, R, for the plot is 1.00.



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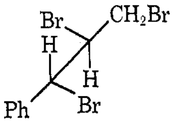

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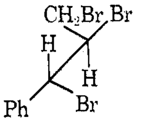

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cis- and *trans*-1,2-diphenylcyclopropane were brominated in the dark in chloroform at 20.1° with the initial bromine and hydrocarbon concentrations equal to 0.25 M. The time required for consumption of one

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(4) K. B. Wiberg, "Physical Organic Chemistry," Wiley, New York, N. Y., 1964, pp 377–379.

(5) C. G. Gebelein and G. D. Frederick, *J. Org. Chem.*, **37**, 2211 (1972).

half of the bromine is 37 min for the trans and 12.5 min for the cis isomers. The bromine half-life for the addition to the trans and cis isomers is 25 and 16 min, respectively, when isoamyl nitrite was present.

Product Analysis.—The analysis and structure characterization of *dl*- and *meso*-1,2,3-tribromo-1,3-diphenylpropane, *p*-bromophenylcyclopropane, 1,3-dibromo-1-phenylpropane, and *dl*- and *meso*-1,3-dibromo-1,3-diphenylpropane have been presented in a previous paper.[1]

The erythro tribromide, **2**, isolated from the phenylcyclopropane bromination product, has identical physical and spectral properties with those of the erythro tribromide from the bromination of cinnamyl bromide, **1**. The dark addition of bromine to **1** in carbon tetrachloride gives a mixture of two tribromides, **2** and **3**. Since trans addition predominates under these conditions, the predominant diastereomer must be the erythro tribromide, **2**. Therefore the predominant downfield doublet (τ 4.69) in the nmr of the cinnamyl bromide product mixture is assigned to the erythro benzyl proton. Moreover, the doublet coupling constant for the erythro isomer is larger than the coupling constant for the threo isomer. This observation is consistent with the results from earlier nmr studies of erythro–threo dibromide pairs.[6]

The threo tribromide could not be separated from the phenylcyclopropane–bromine addition mixture. However, the spectral and chromatographic properties of the mixture are consistent with the presence of threo tribromide.

The tribromide–dibromide product ratio is affected by both solvent and the presence of isoamyl nitrite. Isoamyl nitrite increases the amount of tribromide in the product by 57% in carbon tetrachloride (runs 35–36 and 37–38), 12% in chloroform (runs 18–21 and 22–23), and 2% in methylene chloride (runs 11–13 and 7–8). The tribromide–dibromide ratio is the same for each of the three solvents at 50 and 100% completion and remains unchanged by temperature in the range 5–30° (runs 11–13, 14–15, 24–25, and 26–27).

Bromination of *trans*-1,2-diphenylcyclopropane in chloroform in the dark results in 100% conversion to 1,3-dibromo-1,3-diphenylpropane. The *dl*/meso ratio is 1.0. Under the same conditions with 5 mol % of isoamyl nitrite added the resulting product consists of 50% of 1,3-dibromo-1,3-diphenylpropane (*dl*/meso = 1.0), approximately 20% of 1,2,3-tribromo-1,3-diphenylpropane, and 30% of aromatic substitution products. Bromination of *cis*-1,2-diphenylcyclopropane in chloroform results in approximately 70% dibromide (*dl*/meso = 45/55) and 30% tribromide. Added isoamyl nitrite has no appreciable effect on the product composition.

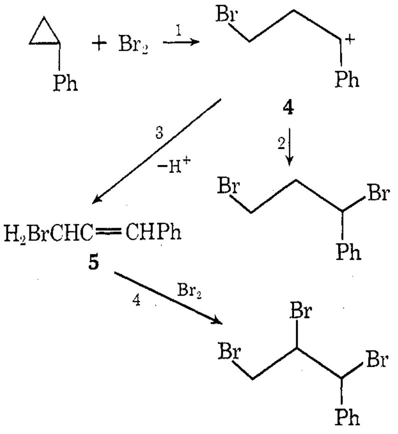
Pure 1,3-dibromo-1-phenylpropane and *erythro*-1,-2,3-tribromo-1-phenylpropane were stable under the conditions employed for the addition of bromine. The stability of *dl*- and *meso*-1,3-dibromo-1,3-diphenylpropane under reaction conditions had been determined previously.[1]

Discussion

The results reported above for the dark bromination of arylcyclopropanes in chlorinated solvents in the presence of isoamyl nitrite show the following characteristics: (1) the formation of 1,3-dibromo-1-phenylpropane and 1,2,3-tribromo-1-phenylpropane as the main products from phenylcyclopropane; (2) the second-order kinetics, which are first order in both phenylcyclopropane and bromine concentration; (3) the increasing rate of bromine addition with increasing solvent dielectric constant, (4) the complete lack of stereospecificity in the addition to *trans*-1,2-diphenylcyclopropane and near lack of stereospecificity in the addition to the cis isomer.

These characteristics are consistent with addition occurring by electrophilic attack of bromine on arylcyclopropane and product formation involving intermediate ion **4**. The sequence of steps is summarized in Scheme I. The rate-determining step, step 1, is the cleavage of the carbon–carbon single bond with accompanying carbonium ion formation.

Scheme I



Since bromine addition to cinnamyl bromide is fast relative to bromine addition to phenylcyclopropane, the ratio of tribromide to dibromide in the final product will depend on the relative rates of steps 2 and 3 and the extent to which the fast radical addition, reaction type A, competes with the much slower ionic reaction, reaction type B. Our earlier results coupled with those reported here demonstrate that reaction type A occurs photolytically or thermally and converts phenylcyclopropane completely to 1,3-dibromo-1-phenylpropane but is effectively retarded by isoamyl nitrite.

That the tribromide and dibromide products came from a common intermediate is consistent with the observations that the tribromide to dibromide ratio remains constant throughout the course of the reaction and is not effected by a change in the initial bromine–phenylcyclopropane ratio. Moreover, the dibromide was found to be stable to reaction conditions. Since the tribromide–dibromide product ratio is inversely related to the solvent dielectric constant, the amount of reaction proceeding by step 3 relative to step 2 decreases with increasing dielectric constant.

The complete lack of stereospecificity in the bromination of *trans*-1,2-diphenylcyclopropane would suggest that the carbonium ion intermediate, **4**, formed from phenylcyclopropane is symmetrical. Bromine atom participation such as in the bridged ring bromonium ion, **6**, would require a preference for trans stereo-

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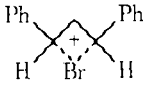
[6] R. C. Fahey and J. J. Schneider, *J. Amer. Chem. Soc.*, **90**, 4429 (1968).



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specific addition and therefore can be eliminated as a plausible intermediate.

1,2-Dibromo-1-phenylpropane, an expected product of 1,2-cyclopropane addition, was undetected in product mixtures resulting from bromine addition to phenylcyclopropane. Yet as much as 2% of this dibromide could be detected by nmr in synthetic mixtures. 1,2-Cyclopropane addition is observed in additions to some alkylcyclopropanes.[7,8] The absence of such addition in the case of the arylcyclopropanes is undoubtedly the result of the increased stability of benzyl carbonium ions relative to the bridge ion species of the type offered as intermediates in 1,2 addition to alkylcyclopropanes.

Differences in product composition and the effects of light and isoamyl nitrite connected with the carbon tetrachloride reactions seem best explained as follows. The photochemically or thermally initiated reaction (type A) is the only effective one in carbon tetrachloride solution, the ionic reaction competing only very slowly. However, when isoamyl nitrite is added, reaction type A is strongly retarded and the decreased rate of bromine consumption and appearance of tribromide reflects the occurrence of the ionic pathway given in Scheme I. In contrast to the carbon tetrachloride reactions, type A reaction in chloroform and methylene chloride amounts to only 20 and 7%, respectively, since the reaction rates are decreased by 20 and 7% when isoamyl nitrite is present. The tribromide–dibromide product compositions of the chloroform reaction support this view. The observed tribromide–dibromide ratios in the absence of isoamyl nitrite is 0.61 ± 0.04. The expected ratio is 0.66 based on 20% reaction type A, which yields only dibromide, and 80% type B, which yields tribromide and dibromide in a 1:1 ratio when isoamyl nitrite is present.

Experimental Section

Spectra were obtained as follows: nmr in $CDCl_3$ solution (unless otherwise indicated), 1% TMS (τ 10.00), Varian A-60A, symbols s, d, t, q, and m refer to singlet, doublet, triplet, quartet, and multiplet, respectively; ir in CCl_4 solution (unless otherwise indicated) Perkin-Elmer 137, 0.05-mm sample and reference cells, symbols s, m, w, sh, and br refer to strong, medium, weak, sharp, and broad, respectively; mass spectrum at 70 eV and 160–165° with an all-glass heated inlet, Hitachi Perkin-Elmer RMU-6E.

Melting points were determined on a Köfler micro hot stage and are uncorrected. Vpc was performed on a Varian Aerograph Model 200 and high-speed liquid chromatography was performed on a Waters Associates ALC/GPC Model 502 using conditions as indicated. The elemental analyses were performed by Galbraith Laboratories, Knoxville, Tenn. Evaporation of solvent or concentration of solution was done at the flash evaporator at reduced pressures.

Materials.—All solvents were distilled over P_2O_5 through a 12-in. Vigreux column. Chloroform was washed successively with concentrated H_2SO_4, water, and 10% aqueous Na_2CO_3 followed by preliminary drying ($CaCl_2$) prior to distillation.

Bromine (reagent grade, Fisher) was used without further purification.

Phenylcyclopropane was purchased from Chemical Samples Co. and found to be at least 99% pure by vpc on both a Carbowax and a SE-30 column. 1,2-Diphenylcyclopropane was purchased from Chemical Samples Co. and separated on a spinning band column to obtain cis [bp 116° (0.2 mm)] and trans [bp 125° (0.2 mm)] isomers. The cis isomer was further purified by recrystallization from *n*-pentane. *cis*- and *trans*-1,2-Diphenylcyclopropane were found to be greater than 99% pure by vpc (0.25 in. × 8 ft, 5% SE-30 on Chromosorb W, 200°, flow rate of 1.4 ml/sec). Retention times of 5.2 min for the cis isomer and 6.4 min for the trans isomers were observed. Cinnamyl bromide was purchased from Aldrich Chemical Co. and distilled [bp 76° (0.3 mm)] immediately before its use.

Stock Solutions.—Stock solutions of approximately 0.5 *M* Br_2 in CCl_4, $CHCl_3$, and CH_2Cl_2 were prepared by pipeting 1.3 ml of Br_2 into 49 ml of the solvent in a ground glass stoppered volumetric flask. The concentration of the solution was determined by titration with 0.1 *N* $Na_2S_2O_3$ solution in the presence of excess KI.[9] These stock solutions were then diluted to the desired concentration.

Kinetic Procedure.—The reaction rates for the arylcyclopropane brominations were followed by determining the Br_2 concentration spectrophotometrically with a Cary 15 spectrophotometer. The absorbance of the reaction solution was determined in a 2-mm quartz cell with a 1.9-mm spacer in the solvent indicated at the following wavelengths: CCl_4, 415 nm; $CHCl_3$, 413 nm; CH_2Cl_2, 411 nm. The diluted Br_2 and arylcyclopropane solutions were allowed to equilibrate thermally in a thermostated water bath in a darkened room, and then mixed in a blackened glass stoppered reaction flask. Aliquots were removed periodically and the Br_2 absorbance was determined. The first reaction measurement was always made within 1 min of mixing. A fresh aliquot was removed for each measurement. The reaction product mixtures were isolated by flash evaporation of the solvent and excess bromine in the dark.

The rate constants for the $CHCl_3$ and CH_2Cl_2 systems were calculated using the expression $kt = 1/K \ln (B_0P/P_0B)$, where P and B are the arylcyclopropane and Br_2 concentrations, respectively, P_0 and B_0 refer to initial concentrations, t is the time, and $K = P_0 - B_0/(1 - \rho)$. The ratio of tribromide product to total ring opening products is ρ. The rate constants for the CCl_4 system were calculated using the expression $kt = 1/B + 1/B_0$. All reported rate constants are the average of multiple runs followed through at least 70% completion, and were determined using a least squares method.

Product Analysis.—The ratio of erythro and threo tribromides to dibromide was determined from the benzyl proton resonances in the nmr spectra of the crude product mixtures. The dibromide benzyl proton resonance appeared at τ 4.89 (d of d, J = 7.8 Hz). The benzyl proton of the erythro tribromide appeared at τ 4.69 (d, J = 9 Hz). The benzyl proton of the threo tribromide appeared at τ 4.47 (d, J = 4 Hz). Synthetic mixtures of tri- and dibromides of various ratios were prepared from the pure tri- and dibromides. The percentage compositions of these synthetic mixtures determined by nmr agreed within 3% with the compositions determined by weight.

***erythro*- (2) and *threo*-1,2,3-Tribromo-1-phenylpropane (3).**—To 0.62 g of cinnamyl bromide in 6.6 ml of $CHCl_3$ was added 6.1 ml of a 0.52 *M* Br_2 in $CHCl_3$ solution. After decolorization (15 min) the solution was flash evaporated to yield 1.15 g (100% yield) of a white solid. Nmr analysis revealed the product to contain a 1:1 mixture of **2** and **3**. When the bromination was carried out in CCl_4, the resulting product contained 85% of **2** and 15% of **3**.

Recrystallization from pentane of the mixture containing 85% of **2** gave pure **2**: mp 123–124°;[10] white needles; nmr ($CDCl_3$) τ 2.65 (s, 5 H, ArH), 4.69 (d, 1 H, J = 9.0 Hz, ArCHBr), 5.28 (quintet, 1 H, J = 9.0, 4.5, and 4.5 Hz, C-2 H), 5.80 (q, 1 H, J = 11.5 and 4.5 Hz, C-3 H), 6.09 (q, 1 H, J = 11.5 and 4.5 Hz, C-3 H); ir (1% KBr pellet) 690 cm^{-1} (s, sh), 760 (m, sh), 825 (m, sh), 880 (m, sh), 1130 (m, sh), 1250 (m, sh), and 1410 (m, sh); mass spectrum m/e 354 (M^+), 356 ($M^+ + 2$), 358 ($M^+ + 4$), 350 ($M^+ + 6$), 375, 377, and 379 ($C_9H_8Br_2^+$), 169 and 171 ($C_6H_5CHBr^+$), 117 (base peak, $M^+ - Br_3$).

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[7] R. T. LaLonde, *J. Amer. Chem. Soc.*, **87**, 4217 (1965).

[8] N. C. Deno and D. N. Lincoln, *J. Amer. Chem. Soc.*, **88**, 5357 (1966).

[9] H. H. Furan, "Scott's Standard Methods of Chemical Analysis," Vol. I, Van Nostrand, Princeton, N. J., 1959.

[10] T. Taguchi, M. Tomoeda, and I. Aratani, *J. Amer. Chem. Soc.*, **78**, 1468 (1956).

threo-1,2,3-Tribromo-1-phenylpropane (**3**) was purified by preparative liquid–solid chromatography employing a 0.0125 in. × 2 ft Corasil II column at a flow rate of 1.0 ml/min. The eluting solvent was *n*-hexane. The retention times for **2** and **3** were 2.6 and 2.1 min, respectively. In this manner pure **3** was obtained as a clear oil: nmr ($CDCl_3$) τ 2.68 (s, 5 H, ArH), 4.47 (d, 1 H, J = 4 Hz, ArCHBr), 5.65 (m, 1 H, C-2 H), 6.20 (m, 2 H, C-3 H); ir 695 (s, sh), 1220 (m, sh), 1435 (m, sh), 1450 (m, sh), 1495 cm^{-1} (m, sh); mass spectrum m/e 354 (M^+), 356 ($M^+ + 2$), 358 ($M^+ + 4$), 360 ($M^+ + 6$), 375, 377, and 379 ($C_9H_9Br_2^+$), 169 and 171 ($C_6H_5CHBr^+$), 117 (base peak, $M^+ - Br_3$). *Anal.* Calcd for $C_9H_9Br_3$: C, 30.28; H, 2.54; Br, 67.17. Found: C, 30.58; H, 2.57; Br, 67.06.

Stability of Ring-Opening Products to Reaction Conditions.—1,3-Dibromo-1-phenylpropane (200 mg) in 5 ml of a 0.25 M Br_2–$CHCl_3$ solution was allowed to stand at room temperature in the dark for 40 hr. Flash evaporation of the solvent and Br_2 yielded a clear oil which was determined to be the starting 1,3-dibromophenylpropane by comparative nmr and ir analysis.

2 (200 mg) in 5 ml of a 0.25 M Br_2–$CHCl_3$ solution was allowed to stand for 40 hr in the dark at room temperature. Flash evaporation of the solvent yielded a white, crystalline solid, mp 122–125°, which was determined to be the starting **2** by comparative nmr analysis.

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Registry No.—**1**, 4392-24-9; **2**, 42334-76-9; **3**, 42334-77-0; phenylcyclopropane, 873-49-4.

Stereochemistry of Reduction of Substituted Cyclohexanones with Triisobutylaluminum and Diisobutylaluminum Hydride

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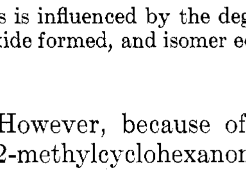
The reduction of 3,3,5-trimethylcyclohexanone and 4-*tert*-butylcyclohexanone with diisobutylaluminum hydride (DIBAH) and with triisobutylaluminum (TIBA) has been examined in ether and in benzene. Reduction of these ketones with DIBAH in 1:1 stoichiometry produces the epimeric alcohols in quantitative yield. The isomer ratio of the product mixture is essentially independent of solvent and reactant stoichiometry. On the other hand, reduction of these ketones with TIBA is more selective and is accompanied by some (~5%) formation of aluminum enolate. The isomer ratio of the product mixture is essentially independent of solvent, but dependent on the reactant stoichiometry and the initial concentration of TIBA. Evidence is presented which indicates that the epimeric ratio of alcohol products is influenced by the degree of association of TIBA, complex formation between TIBA and the aluminum alkoxide formed, and isomer equilibration by a Meerwein–Ponndorf–Verley pathway.

Since the reduction of chloral to 2,2,2-trichloroethanol by treatment with triethylaluminum etherate was first noted,[1] organoaluminum compounds have been investigated in considerable detail as reducing agents for a wide variety of organic functional groups. Although the reaction of organoaluminum reagents with carbonyl compounds can afford mixtures of alkylated and reduced products, the primary mode of reaction is that of reduction when the organometallic reagent has an available hydrogen at a branched β position,[2] or contains aluminum–hydrogen bonds.[3] Despite intensive investigation over a period of several decades, surprisingly little is presently known about the factors influencing the stereochemistry of reduction. The present study was undertaken with a twofold purpose in mind: (1) to systematically examine triisobutylaluminum (TIBA) and diisobutylaluminum hydride (DIBAH) as potential stereoselective reagents for the reduction of carbonyl compounds, and (2) to delineate the experimental parameters affecting the stereochemistry of reduction, particularly the effect of reactant stoichiometry on stereochemistry in hydrocarbon solvent.

Reduction of 2-methylcyclohexanone with DIBAH leads to predominant formation of *cis*-2-methylcyclohexanol, the least stable of the two expected alcohols.[4] However, because of the conformational mobility of 2-methylcyclohexanone, stereochemical interpretation of this result is at best uncertain. Furthermore, the isomer ratio of the product mixture was determined by measurement of density, a technique considerably less accurate than modern gas chromatographic methods. Haubenstock and Davidson[5] found that the composition of the product mixture obtained by reduction of 3,3,5-trimethylcyclohexanone with TIBA in benzene at 42° was dependent on the ratio of reactants. When TIBA was present in excess, the product mixture contained 96% of the least stable alcohol, *trans*-3,3,5-trimethylcyclohexanol. In the presence of excess ketone the isomeric ratio of the product mixture changed with time, approaching pure *cis*-3,3,5-trimethylcyclohexanol after 31 hr at 42°. This was attributed to thermodynamically controlled isomer equilibration *via* a Meerwein–Ponndorf–Verley type reduction involving

$$R_2CHOAl\text{-}i\text{-}Bu_2 + R'_2C{=}O \longrightarrow$$



$$\longrightarrow R'_2CHOAl\text{-}i\text{-}Bu_2 + R_2C{=}O \quad (1)$$

a six-center transition state. The authors concluded that hydride transfer in a kinetically controlled process occurs predominantly from the least hindered side of

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