

Aromatic Displacements. III. The Cleavage of Benzhydrols. The Mechanism in 50% Aqueous Acetic Acid¹

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Received July 13, 1964

Variation of bromide ion concentration at constant ionic strength changes the cleavage rates for 4,4'-dimethoxybenzhydrol and 4-methoxy-4'-nitrobenzhydrol in a way that demands (by steady-state analysis) an unstable intermediate from attack of bromine on the carbinol. The intermediate can then return to starting materials or go on to product. We have prepared the hypobromite of 4,4'-dimethoxybenzhydrol and shown that it probably is not the intermediate, thereby supporting its assignment as a σ -complex. The data are used to consider some limiting values for the effects of substitution on the three rate constants in the kinetic scheme which are presented in terms of free-energy diagrams. This analysis shows that the leaving group under these conditions does not resemble a protonated aldehyde at the moment of departure. Although the effect of leaving group substitution in the benzhydrol series is small from every viewpoint, the presence of an oxygenated function at the cleavage site seems to be important. In dichloromethane at low temperatures red solids precipitate quickly from mixtures of bromine and activated arylcarbinols. It is shown that these are probably not σ -complexes but instead carbonium tribromide salts. Trianisylcarbonium tribromide is a very stable salt, its shelf life in the open laboratory being at least 1 year.

Introduction

The evidence which has been presented in the previous two papers^{2,3} supports completely the conclusion of Kohler and Patch⁴ that the cleavage of activated arylcarbinols by bromine is an example of electrophilic displacement.



In 50 to 80% aqueous acetic acid the over-all bromination rates for a number of arylmethyl compounds cleanly follow the simple integrated second-order rate expression to several half-lives. In one case chosen for intensive analysis³ it was possible to show first-order dependence of rate on the concentrations of bromine and of aromatic substrate. The rates may be dissected by yield data² into those for cleavage and the competing reactions: bromodeprotonation on the activated ring and oxidation to the benzophenone. Linear free-energy correlations are found for the effect of sub-

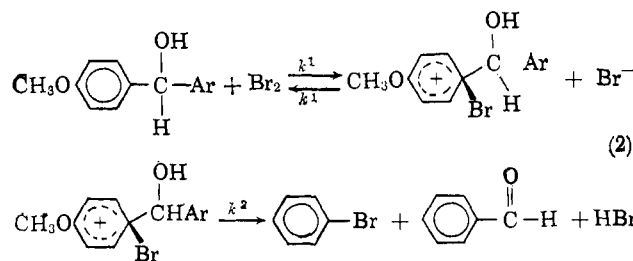
stituents in the ring being attacked and in the leaving group ring for the cleavage reaction and the ring bromination. Since the competing reactions are known to be polar under these conditions and since the over-all rate of bromine consumption is kinetically clean and unaffected by light, the case for calling the cleavage reaction an electrophilic displacement is strong. Perhaps the most compelling evidence is to be found below in the demonstration of an unstable intermediate through variation of bromide ion concentration, behavior that would be difficult to explain by a radical mechanism.

These facts and the detailed elaboration of them in the previous two papers make it safe to assume an electrophilic displacement mechanism. In the following discussion we shall be concerned with developing some finer points of the reaction sequence rather than justification for placing the reaction in this class.

Results and Discussion

1. Kinetic Detection of an Unstable Intermediate.

The mechanism of the cleavage reaction may be symbolized as follows, in conformity with the general theory of electrophilic aromatic displacements. An



important test of the reality of this scheme would be provided by demonstrating that our second-order kinetics in a given medium are a particular solution to the more general and complex expression for this mechanism when the bromide ion is varied at constant ionic strength. If a quasi-equilibrium is established one might either observe the intermediate directly through its ultraviolet spectrum, if it is stable enough, or observe the effect of varying common ion bromide on the over-all bromination rate through reversal of the first step.

It must be emphasized that although evidence of this kind contributes to our over-all knowledge of the process it is neither necessary nor sufficient for proving the reality of the above scheme. It is not necessary because the intermediate may be so unstable as to elude detection by the mass law treatment (as in the case of the *t*-butyl cation in *t*-butyl

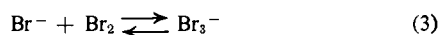
(1) This research was supported by a grant from the Petroleum Research Fund of the American Chemical Society. Grateful acknowledgement is hereby made to the donors of this fund. The work described here is taken from the Ph.D. Thesis of G. B. K., University of Pittsburgh, 1963.

(2) E. M. Arnett and G. B. Klingensmith, *J. Am. Chem. Soc.*, **87**, 1023 (1965).

(3) E. M. Arnett and G. B. Klingensmith, *ibid.*, **87**, 1032 (1965).

(4) E. P. Kohler and R. H. Patch, *ibid.*, **38**, 1205 (1916).

chloride solvolysis).⁵ It is not sufficient because, as we shall see below, from the viewpoint of kinetic formalism, some other kind of intermediate might equally well play the role of the σ -complex. Finally, the direct observation of a species (such as a σ -complex in this case) under the reaction conditions is only mediocre evidence for its being a genuine intermediate along the reaction coordinate. The fact that a molecular entity is isolable or directly observable in the reaction medium suggests that it be so stable as to be far removed in energy and geometry from the transition states for its formation or destruction under these conditions.^{6,7} We searched for direct spectral evidence⁸ of σ -complexes in the aqueous acetic acid systems that gave cleavage products but found none, and therefore turned to common ion variation as a test for intermediates. The steady-state treatment for brominative displacements has been applied with success by Cannell⁹ and Grovenstein¹⁰ to situations very similar to this involving desulfonation and decarboxylation of activated aromatic systems. The main complication is that allowance must be made for the fact that variation of bromide ion influences the reaction by altering the concentration of free bromine through the following equilibrium, as well as by consuming the intermediate. Therefore,



for which the concentration equilibrium constant is

$$K = \frac{(\text{Br}_3^-)}{(\text{Br}^-)(\text{Br}_2)_f} = 27.6^{11} \quad (4)$$

where $(\text{Br}_2)_f$ is the concentration of free bromine. If $(\text{Br}_2)_T$ is the total stoichiometric concentration of bromine in a solution, it follows that

$$(\text{Br}_2)_f = \frac{(\text{Br}_2)_T}{1 + K(\text{Br}^-)} \quad (5)$$

and for the simple case of bimolecular reaction of bromine with the aromatic substrate (Ar) and no intermediate

$$\frac{-d(\text{Br}_2)_T}{dt} = \frac{k}{1 + K(\text{Br}^-)} (\text{Br}_2)_T (\text{Ar}) \quad (6)$$

and

$$k_{\text{obsd}} = \frac{k}{1 + K(\text{Br}^-)} \quad (7)$$

where k is the actual specific second-order rate constant of the brominative cleavage under the conditions and k_{obsd} is the observed second-order rate constant for cleavage at a given bromide ion concentration. At constant ionic strength in 50% aqueous acetic acid this treatment would predict reduction of the rate constant by a factor of 3.94 on going from $(\text{Br}^-) = 0.1$ to $0.5 M$ if the only effect of bromide addition is

(5) A. Streitwieser, Jr., "Solvolytic Displacement Reactions," McGraw-Hill Book Co., Inc., New York, N. Y., 1962.

(6) G. Hammond, *J. Am. Chem. Soc.*, **77**, 6087 (1955).

(7) R. Breslow, *Tetrahedron Letters*, 399 (1964).

(8) G. Olah and S. Kuhn, *J. Am. Chem. Soc.*, **80**, 6541 (1958).

(9) L. G. Cannell, *ibid.*, **79**, 2927, 2932 (1957).

(10) E. Grovenstein, Jr., and U. V. Henderson, Jr., *ibid.*, **78**, 569 (1956).

(11) T. W. Nakagawa, L. J. Andrews, and R. M. Keefer, *J. Phys. Chem.*, **61**, 1007 (1957).

to complex molecular bromine and there is no detectable intermediate.^{9,12}

In order to examine the effect of substitution on intermediate stability we have used two similar benzhydrols varying only by *para* substitution in the leaving group: 4,4'-dimethoxybenzhydrol and 4-methoxy-4'-nitrobenzhydrol. When these were subjected to the above variation of bromide ion their cleavage rates changed by factors of 7.6 and 15.1, respectively, instead of 3.94, showing that the simple effect of the tribromide ion equilibrium could not account for the rate decrease; some other equilibrium was also being reversed and this most likely was the formation of an intermediate.

To take account of the intermediate, which we shall write (I^+), a steady-state treatment of reaction 2 gives

$$\frac{d(\text{I}^+)}{dt} = 0 = k_1(\text{Ar}_2\text{CHOH})(\text{Br}_2)_f - k_{-1}(\text{I}^+)(\text{Br}^-) - k_2(\text{I}^+) \quad (8)$$

$$(\text{I}^+) = \frac{k_1(\text{Ar}_2\text{CHOH})(\text{Br}_2)_f}{k_2 + k_{-1}(\text{Br}^-)} \quad (9)$$

$$\frac{-d(\text{Br}_2)_T}{dt} = k_2(\text{I}^+) = \frac{k_2 k_1 (\text{Ar}_2\text{CHOH})(\text{Br}_2)_f}{k_2 + k_{-1}(\text{Br}^-)} \quad (10)$$

Incorporating the tribromide ion equilibrium (eq. 5)

$$\frac{-d(\text{Br}_2)_T}{dt} = \frac{k_2 k_1 (\text{Ar}_2\text{CHOH})(\text{Br}_2)_T}{[1 + K(\text{Br}^-)][k_2 + k_{-1}(\text{Br}^-)]} \quad (11)$$

thus

$$k_{\text{obsd}} = \frac{k_2 k_1}{[1 + K(\text{Br}^-)][k_2 + k_{-1}(\text{Br}^-)]} \quad (12)$$

and

$$\frac{1}{k_{\text{obsd}}[1 + K(\text{Br}^-)]} = \frac{k_2 + k_{-1}(\text{Br}^-)}{k_2 k_1} = \frac{1}{k_1} \left[\frac{k_{-1}}{k_2} (\text{Br}^-) + 1 \right] \quad (13)$$

Equation 13 predicts a straight line when $1/(k_{\text{obsd}}[1 + K(\text{Br}^-)])$ is plotted against (Br^-) . Such a linear relationship was found to hold for the bromination of 4,4'-dimethoxybenzhydrol (Tables I and II and Figure 1) and

Table I. The Effect of Changing the Bromide Ion Concentration on the Rates of Bromination of 4,4'-Dimethoxybenzhydrol and 4-Methoxy-4'-nitrobenzhydrol in 50% Aqueous Acetic Acid at Constant Ionic Strength^a

Added salts	4,4'-Dimethoxybenzhydrol		4-Methoxy-4'-nitrobenzhydrol	
	k_{obsd} (over-all)	k_{obsd} (cleavage)	k_{obsd} (over-all)	k_{obsd} (cleavage)
0.1 M NaBr	24.45	17.63	1.44	0.748
0.4 M NaClO ₄				
0.2 M NaBr	11.86	8.49	0.572	0.248
0.3 M NaClO ₄				
0.3 M NaBr	6.95	4.94	0.337	0.128
0.2 M NaClO ₄				
0.4 M NaBr	4.52	3.19	0.212	0.0735
0.1 M NaClO ₄				
0.5 M NaBr	3.31	2.32	0.154	0.0496

^a At 25.05°.

(12) E. Berliner and M. C. Beckett, *J. Am. Chem. Soc.*, **79**, 1425 (1957).

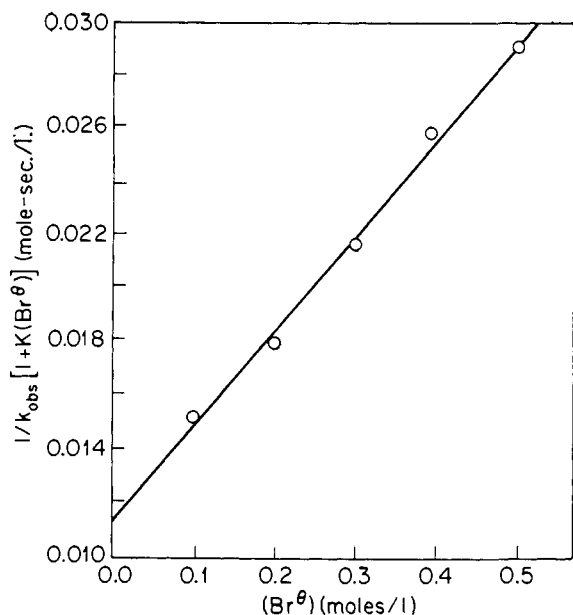


Figure 1. $1/(k_{\text{obs}}[1 + K(\text{Br}^-)])$ vs. (Br^-) from the rate of bromination of 4,4'-dimethoxybenzhydrol in 50% aqueous acetic acid as a function of bromide ion concentration.

4-methoxy-4'-nitrobenzhydrol (Tables I and II and Figure 2), supporting the mechanistic scheme presented by eq. 2. According to this relationship the intercept

Table II. Data Obtained through the Steady-State Treatment of Reaction 2^a

(NaBr), moles/l.	(NaClO ₄), moles/l.	$\frac{1}{k_{\text{obs}}[1 + K(\text{Br}^-)]}$, mole-sec./l.
a. 4,4'-Dimethoxybenzhydrol		
0.1	0.4	0.0151
0.2	0.3	0.0181
0.3	0.2	0.0218
0.4	0.1	0.0260
0.5	0.0	0.0291
$k_1 = 89.8$ l./mole sec.; $k_{-1}/k_2 = 3.25$ l./mole		
b. 4-Methoxy-4'-nitrobenzhydrol		
0.1	0.4	0.356
0.2	0.3	0.617
0.3	0.2	0.840
0.4	0.1	1.130
0.5	0.0	1.362
$k_1 = 9.90$ l./mole-sec.; $k_{-1}/k_2 = 24.9$ l./mole		

^a k_{obs} is the second-order rate constant for cleavage.

at $(\text{Br}^-) = 0$ is equal to $1/k_1$ and the slope of the straight line is k_{-1}/k_1k_2 . From these values the ratio k_{-1}/k_2 can be determined and is found to be 3.25 l./mole for 4,4'-dimethoxybenzhydrol and 24.9 l./mole for 4-methoxy-4'-nitrobenzhydrol. From this ratio the extent of reversibility at a particular bromide ion concentration can be estimated since (rate reverse)/(rate forward) is equal to $K_{-1}(\text{Br}^-)/k_2$. When the bromide ion concentration is 0.5 M, the intermediate from 4,4'-dimethoxybenzhydrol and bromine reverts to starting materials 1.6 times for every time it goes on to cleavage products and the intermediate from 4-methoxy-4'-nitrobenzhydrol and bromine reverts to starting materials 12.4 times for each successful cleavage.

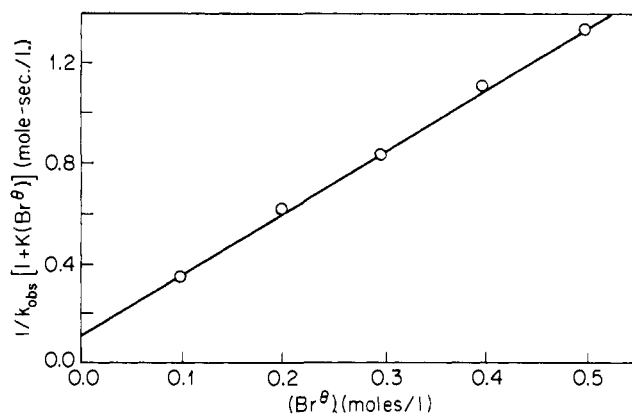
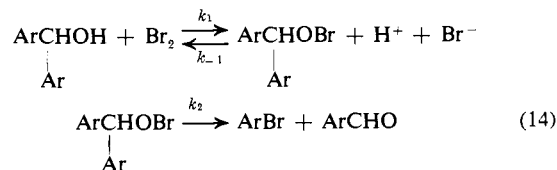


Figure 2. $1/(k_{\text{obs}}[1 + K(\text{Br}^-)])$ vs. (Br^-) from the rate of bromination of 4-methoxy-4'-nitrobenzhydrol in 50% aqueous acetic acid as a function of bromide ion concentration.

Further support for the validity of the reaction scheme as applied to the cleavage of arylcarbinols by bromine comes from the demonstrated dependence of the cleavage yield on the bromide ion concentration. It follows from eq. 13 that when k_{-1}/k_2 is small the bromination step is rate determining regardless of the bromide ion concentration; i.e., eq. 13 reduces to eq. 7 and bromide dependence is simply a function of the tribromide equilibrium. The bromination of arylcarbinols in aqueous acetic acid is then a competition between the parallel mixed second-order reactions: bromodeprotonation *ortho* to the activating substituent and *para* fragmentation. Although both reactions will experience the same rate retardation from the tribromide equilibrium, only the latter^{9,10,12} will show additional bromide dependence due to reversal of intermediate formation. Thus if the postulated reaction scheme holds for the carbinol cleavage, the cleavage yield will decrease as the bromide ion concentration is increased since the bromodeprotonation will be able to compete more effectively for the available bromine. The dependence of the cleavage yield on bromide ion concentration was examined for the brominations of 4,4'-dimethoxybenzhydrol and 4-methoxy-4'-nitrobenzhydrol. The decreases in cleavage yield for the two benzhydrols were 2.1 and 19.7%, respectively.² The ratio of these two values, 19.7/2.1 = 9.4, is close to that of their relative reversibility ratios in 0.5 M sodium bromide, 12.4/1.6 = 7.8.

2. Evidence That the Intermediate Is Not a Hypobromite. The treatment used above shows that the data are consistent with mechanism 2 which was arrived at by analogy to many other well established cases of electrophilic substitution. It is also consistent with the reversible formation of any other intermediate and bromide ion followed by conversion of the intermediate to products by simple first-order kinetics. The following alternative path must therefore be eliminated before we can accept mechanism 2.



Until recently it would have been necessary to leave the choice between these mechanism to speculation. However, by applying the procedure of Walling and Padwa¹³ it has been possible to prepare a sample of 4,4'-dimethoxydiphenylmethyl hypobromite and subject it to the reaction conditions. When this was done almost all of the material that had been converted into hypobromite was recovered as dimethoxybenzhydrol and its acetate. A small amount of anisaldehyde was also found, but this could be accounted for as an impurity from direct attack of hypobromous acid on the carbinol in the original preparation of the hypobromite. To our knowledge this is the first report of a secondary hypobromite, a fact which may reflect their instability. Details of preparation and justification of the assigned structure are given in the Experimental section. In view of these results it seems quite unlikely that a hypobromite intermediate occurs in the cleavage reaction.

3. Free-Energy Profiles of the Cleavage Reaction.

The most reasonable interpretation of the facts so far is that cleavage of the methoxybenzhydrols occurs by mechanism 2. The effect of the leaving group on the reaction then is felt on all three of the rate constants that determine the rate of product formation from reactants. We shall now consider in quantitative terms of Hammett reaction parameters how this influence may be exerted. The ρ -value for k_1 is obtained easily from the data in Table I and is found on the basis of these two points alone to be -0.63 . This is of the same order of magnitude as the ρ -value for bromodeprotonation on the activated carbon *meta* to the cleavage position.³ However, the fact that the latter is, if anything, slightly larger despite the greater distance of its site from the substituent suggests that there may be some extra leveling effect on the attacking step in the cleavage reaction which is absent in the ring bromination reaction. The ratio of k_{-1} and k_2 in eq. 13 cannot be separated for evaluation of the effect of substitution in the leaving group on these two steps. However, by making extra assumptions reasonable limits may be put on the reaction parameters ρ_{-1} and ρ_2 for the two steps.

We may use the k_{-1}/k_2 ratio along with substituent parameters for the nitro and methoxy groups to obtain ρ^+ values for k_2 from assumed values for k_{-1} as shown in eq. 15 and 16. If the leaving group were actually

$$\log k_{-1}^{\text{OCH}_3}/k_2^{\text{OCH}_3} - \log k_{-1}^{\text{NO}_2}/k_2^{\text{NO}_2} = \log k_{-1}^{\text{OCH}_3}/k_{-1}^{\text{NO}_2} - \log k_2^{\text{OCH}_3}/k_2^{\text{NO}_2} = \rho_{-1}(\sigma_{\text{OCH}_3} - \sigma_{\text{NO}_2}) - \rho_2^+(\sigma_{\text{OCH}_3}^+ - \sigma_{\text{NO}_2}^+) \quad (15)$$

$$\rho_2^+ = \left\{ \rho_{-1}(\sigma_{\text{OCH}_3} - \sigma_{\text{NO}_2}) - (\log k_{-1}^{\text{OCH}_3}/k_{-1}^{\text{NO}_2} - \log k_2^{\text{OCH}_3}/k_2^{\text{NO}_2}) \right\} / (\sigma_{\text{OCH}_3}^+ - \sigma_{\text{NO}_2}^+) \quad (16)$$

similar to a protonated aldehyde it would be proper to use a ρ^+ parameter for the leaving step as shown in eq. 16. This would probably be an extreme statement of the situation. If the leaving group were behaving in a less electron-demanding way, ordinary Hammett σ - and ρ -values would be in order.

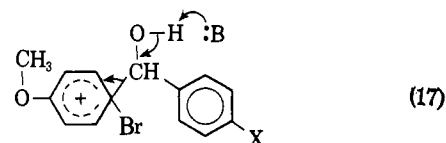
One limiting possibility for the effect of substitution on k_{-1} is that $\rho = 0.0$ (substitution has no effect on the reverse rate). If the intermediate were very unstable it should have nearly the same energy and geometry as transition states surrounding it.⁶ Then substitution

(13) C. Walling and A. Padwa, *J. Org. Chem.*, **27**, 2976 (1962).

would influence both intermediate and transition state in the same way and its influence on this step would not be observable. When eq. 16 is applied to this situation one obtains for the second step $\rho_2^+ = -0.56$ or $\rho_2 = -0.84$ using substituent parameters from the recent review of Stock and Brown.¹⁴ The other reasonable limit would be that the effect of substitution on k_{-1} would be equal and opposite to that on k_1 . For this case we find that $\rho_2^+ = -0.14$ or $\rho_2 = -0.22$.

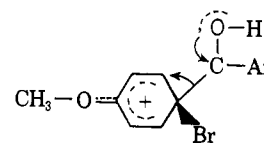
Although the actual positions of troughs and peaks cannot be placed exactly, Figures 3 and 4 give a rough estimate of the two limiting situations covered above. The upshot of this analysis is to confirm again what was anticipated from the cruder examination of over-all bromination rates and then from cleavage rates: *the influence of the leaving group in this carefully controlled case of electrophilic substitution is small.* Substitution of nitro for methoxy in the *para* position of the leaving ring discourages creation of positive charge in the second transition state, but not very much. If the leaving group had reached the configuration of a protonated aldehyde a much larger ρ -value would be expected. In aqueous sulfuric acid the protonation of benzaldehydes¹⁵ requires $\rho^+ = -1.85$.

The small effect of substitution on this step may be interpreted in several ways. If the intermediate were very unstable then again the second transition state, as well as the first, might look very much like it and there would be little influence from substituents. Another possibility is that the hydroxyl proton is removed synchronously by a general base as the carbon-carbon bond is being cleaved. This would greatly reduce the development of charge at the incipient carbonyl carbon and so prevent much electron demand.



Recent work by Mr. Charles Jeuell in our laboratory shows that the reaction is not catalyzed by added acetate ion at constant ionic strength, so this explanation is unlikely.

A third possibility (suggested to us by Professor Grovenstein) relates the small effect of the leaving group to participation by the electron pairs of the hydroxy group in the cleavage transition state.



In view of the number of other displacements^{9,10} where electron-rich groups are involved, there seems good precedent for this. However, as we have seen, the second transition state cannot involve enough carbon-carbon bond cleavage for the leaving group to resemble a protonated benzaldehyde. In this case the oxygen must be assisting the cleavage quite early in the

(14) L. M. Stock and H. C. Brown, *Advan. Phys. Org. Chem.*, **1**, 89 (1963).

(15) K. Yates and R. Stewart, *Can. J. Chem.*, **37**, 664 (1956).

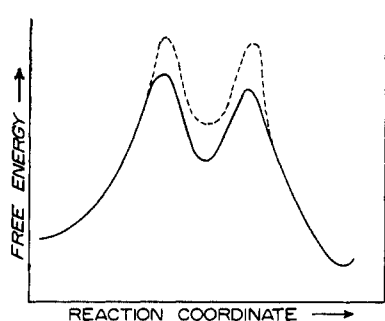


Figure 3.

second stage. At present, this seems to be the most reasonable picture. It suggests that a much larger substituent effect might be found for the leaving group if there were no assistance from neighboring oxygen but that without this aid the cleavage would be unable to compete with bromodeprotonation.

4. *Effect of Solvent Polarity on Rate.* Both dimethoxybenzhydrol and methoxynitrobenzhydrol show overall bromination rate acceleration as the ionic strength of the 50% aqueous acetic acid medium is increased from 0.2 to 0.5 mole/l. (Table III). We have

Table III. The Effect of Ionic Strength on the Rates of Bromination of 4,4'-Dimethoxybenzhydrol and 4-Methoxy-4'-nitrobenzhydrol in 50% Aqueous Acetic Acid

Compd.	(NaBr), moles/l.	(NaClO ₄), moles/l.	<i>k</i> _{obsd} (over-all)
4,4'-Dimethoxybenz- hydrol	0.2	...	7.02
	0.2	0.3	11.86
4-Methoxy-4'-nitro- benzhydrol	0.2	...	0.346
	0.2	0.3	0.572

also observed in a number of cases that the reaction rate increases considerably upon going from 80% acetic acid to 50% acetic acid. Both of these trends are in accordance with the previous experience^{12,16-20} of other workers and the Hughes-Ingold interpretation²¹ of solvent effects on reactions of nonpolar molecules through highly polar transition states. More than that cannot honestly be said since we are dealing with a complex reaction and have not obtained necessary yield data for showing the effect of changing ionic strength on cleavage rate or beyond that the effect of changing ionic strength on the various rate constants for the cleavage process. In view of the present state of ignorance about the details of solvent effects for simple reactions in binary mixtures it does not seem worthwhile developing these missing data.

5. *Effect of Temperature on Bromination of 4,4'-Dimethoxybenzhydrol.* In 50% aqueous acetic acid containing 0.2 M sodium bromide this compound exhibits over-all rates for bromine consumption of 1.30

(16) R. M. Keefer, A. Ottenberg, and L. J. Andrews, *J. Am. Chem. Soc.*, **78**, 255 (1956).

(17) H. G. Kuivila and E. K. Easterbrook, *ibid.*, **73**, 4629 (1951).

(18) I. K. Waler and P. W. Robertson, *J. Chem. Soc.*, 1515 (1939).

(19) E. D. Hughes, *Trans. Faraday Soc.*, **37**, 763 (1941).

(20) P. B. D. de la Mare and P. W. Robertson, *J. Chem. Soc.*, 279 (1943).

(21) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, Chapter VII.

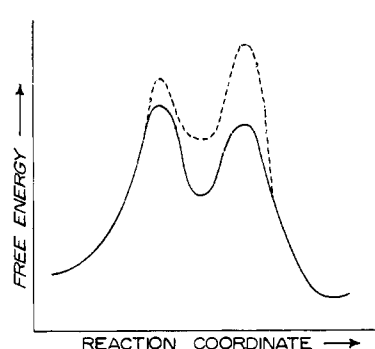


Figure 4.

l./mole sec. at 0° and 7.02 l./mole sec. at 25.30°. The effect of temperature on cleavage yield was not determined. After correction for ΔH (1.5 kcal./mole) and ΔS (-0.4 e.u.) for the tribromide equilibrium (in water) one may use these data to obtain apparent composite activation parameters for bromination under these conditions: $\Delta H^* = 8.1$ kcal./mole and $\Delta S^* = -27.7$ e.u. In view of the complexities of the situation it would be foolish to interpret these numbers. We simply note in passing that the difference between the corresponding values found by Berliner and Powers²² for the bromination of benzene are 18.1 kcal./mole and -28 e.u., suggesting a very large difference in energy of activation between the two systems.

6. *Cleavage in Nonaqueous Media. Formation of Isolable Ionic Species at Low Temperature.* The original investigators⁴ of the cleavage reaction used mostly chloroform or glacial acetic acid for their solvent. Our choice of 50% aqueous acetic acid was dictated by kinetic considerations and all of our mechanistic studies were done in that medium. As a postscript to the main body of our work on the mechanism we wish to add a few observations on the reaction in anhydrous media. Some of these are only preliminary but are still germane.

When 4,4'-dimethoxybenzhydrol was treated with bromine in dichloromethane at room temperature and the products were examined on a silicic acid-chloroform column some eleven fractions with different infrared spectra were found. The usual cleavage products, *p*-bromoanisole and anisaldehyde, were still the major components, amounting to a 50% yield, but oxidation to the corresponding dimethoxybenzophenone had now become measurable and amounted to 10% of the product. The other materials in the fractions were not identified but their presence and variety shows that our choice of solvent for the careful kinetic studies was a fortunate one.

Clarke and Esselen²³ observed the formation of a red oil when chloroform solutions of bromine and 4-N,N-dimethylaminobenzhydrol were mixed at -80°. When this oil was removed and allowed to warm to room temperature it decomposed to give products smelling strongly of benzaldehyde, indicating that some of the materials in the tar had undergone the cleavage reaction. When we noted similar precipitates in glacial acetic acid mixtures of bromine with 4-methoxytri-

(22) E. Berliner and J. C. Powers, *J. Am. Chem. Soc.*, **83**, 705 (1961).

(23) L. Clarke and G. J. Esselen, Jr., *ibid.*, **36**, 308 (1914).

phenylcarbinol at room temperature our suspicions were aroused that the red products might actually be σ -complex intermediates which were isolable under these conditions.²⁴

When equivalent amounts of bromine and 4,4'-dimethoxybenzhydrol were mixed at -80° in dichloromethane an orange-red precipitate deposited within 1 min. Isolated under nitrogen in a drybox the solid decomposed quickly on warming to room temperature yielding cleavage products, some of the corresponding ketone, and ring-brominated material. Cleavage yields obtained this way were nearly as high as in aqueous acetic acid. Other carbinols showed the same behavior. The rate of solid formation and apparent stability ran in the order 4-methoxybenzhydrol > 4-methoxy-4'-nitrobenzhydrol > 4-methoxybenzyl alcohol. 4,4'-Dimethylbenzhydrol, 4,4'-dimethoxydiphenylmethane, and *p*-methylanisole rapidly decolorized bromine under these conditions but gave no precipitates. Trianisylcarbinol quickly deposited large amounts of solid which could be recrystallized from dichloromethane-carbon tetrachloride. *This product has turned out to be stable at room temperature for several years.*

The above results show that a hydroxyl group is necessary but not sufficient for the red solid to form. At least one activated ring is needed, but stability of the solid product is increased greatly by the presence of more activated rings and is reduced by deactivating groups on other rings attached to the carbinol carbon. This is not what one would expect of a σ -complex but is quite consistent with formation of an ordinary di- or triarylcation ion salt. Careful examination of the precipitate from trianisylcarbinol by several methods shows that it is trianisylcarbonium tribromide. It is an extraordinarily stable carbonium ion salt and may be studied at leisure at room temperature in the open laboratory.

Although we were unable to examine the red solids from the other carbinols cited above, it was possible, with great care, to obtain an infrared spectrum in Nujol or Fluorolube mull of the cold precipitate from 4,4'-dimethoxybenzhydrol. This was quite similar to that found for trianisylcarbonium tribromide. The most striking feature of both spectra when compared to their starting carbinols was the dramatic decrease of intensity of the normal carbon-hydrogen stretching frequencies to the point where they could not be seen at all on the strip chart although they could be brought back to normal strength at once by quenching with water. In support of our assigning carbonium tribromide structures to the other red precipitates are the two observations: (a) 4,4'-Dimethoxybenzhydrol bromide gives a red oil product with bromine at low temperature in dichloromethane which is identical with that obtained from the carbinol in every way except that it gives no cleavage products when warmed to room temperature. (b) The acetate of 4,4'-dimethoxybenzhydrol gives the same solid and this does give cleavage products when warmed.

These results show that the cleavage reaction occurs well in quite diverse media provided the carbinol is sufficiently activated. The red precipitates are prob-

(24) (a) For a list of recent references see T. J. Katz and E. H. Gold, *ibid.*, **86**, 1600 (1964); (b) M. Christen and H. Zollinger, *Helv. Chim. Acta*, **45**, 2057, 2066 (1962).

ably carbonium ion salts and not reactive σ -complex intermediates. They may arise from interaction of the carbinol with hydrobromic acid produced by nuclear bromination or possibly by direct electrophilic attack of bromine on carbinol oxygen. The mode of formation is at present mysterious to us. It is very rapid even at -80° . Since the carbonium ion must be formed by loss of the carbinol hydroxyl group, water or some other hydroxylic entity must be present which then reacts with the carbonium ion as the temperature rises to regenerate the original carbinol for subsequent reaction with bromine from the tribromide ion, giving cleavage and completing the illusion that the red product is an intermediate.

Experimental

Purification of most of the carbinols and the solvent medium have been described previously.^{2,3} The sodium perchlorate used for adjustment of ionic strength was Fisher purified grade, recrystallized from water and dried at 130° for 24 hr. before use.

4,4',4''-Trimethoxytriphenylcarbinol was prepared by lead peroxide oxidation of 4,4',4''-trimethoxytriphenylmethane according to Baeyer and Villiger²⁵ and recrystallized from an ethyl ether-Skellysolve B mixture to give a 53% yield of material melting from $81-82.5^\circ$ (lit. $83.5-84^\circ$,²⁵ $81-82^\circ$).

4,4'-Dimethoxydiphenylmethyl bromide was prepared by passing dry hydrogen bromide through a solution of 3.5 g. of 4,4'-dimethoxybenzhydrol in 30 ml. of dry benzene over calcium chloride. The reaction was carried out in a drybox under nitrogen. After 5 min. the clear solution was filtered and 50 ml. of Skellysolve F was added. Cooling of this solution with a Dry Ice-acetone bath resulted in the formation of pink crystals. These were collected and washed with additional cold Skellysolve F. Unless kept under strictly dry conditions, the bromide rapidly became dark purple in color. The melting point (sealed tube) was $68-69^\circ$ (lit. 70°).

Kinetic Procedures. Rates were followed spectrophotometrically in the manner previously described.³ The relationship between total bromine concentration and optical density will naturally change as the bromide ion concentration is varied because of its effect on the tribromide ion equilibrium.

The equilibrium constant governing this system (bromine and bromide ion in 50% aqueous acetic acid) has been determined spectrophotometrically by Nakagawa, Andrews, and Keefer.¹¹ The above value (27.6) for the equilibrium constant has been used throughout this study. Although it was obtained at 0.1 *M* ionic strength whereas the system to which it is applied herein was 0.5 *M* in added salts, it is assumed that the change in ionic strength does not significantly alter *K*. The validity of this assumption is supported by the close agreement between the values of *K* obtained spectrophotometrically¹⁰ in 75% aqueous acetic acid at 0.3 *M* ionic strength and that determined at 0.01 to 0.02 *M* ionic strength in the same solvent by an

(25) A. Baeyer and V. Villiger, *Ber.*, **35**, 1198 (1902).

(26) N. C. Deno, J. J. Jaruzelski, and A. Schriesheim, *J. Am. Chem. Soc.*, **77**, 3044 (1955).

(27) J. Cyerman-Craig, K. U. Martin, and P. C. Wailes, *Australian J. Chem.*, **8**, 385 (1955).

aspiration technique (88 and 91 ± 3 l./mole, respectively).²⁸ Furthermore, K is not greatly affected by changes in ionic strength in the iodine, iodide-triiodide system.^{29,30}

Fortunately, the individual molar absorptivity indices for tribromide ion (ϵ 880) and bromine (ϵ 120) at 370 μ are nearly constant¹¹ so that the total bromine concentration $(Br)_T$ may be related at each bromide ion concentration to the optical density A_{370} in the following manner without going through the enormous labor of establishing a separate Beer's law plot at each bromide ion concentration through iodometric titrations.

$$A_{370} = \epsilon(Br_3^-) + \epsilon(Br_2)_f$$

$$A_{370} = 880(Br_3^-) + 120(Br_2)_f$$

since

$$K = \frac{(Br_3^-)}{(Br_2)_f(Br^-)}$$

$$(Br_3^-) = K(Br_2)_f(Br^-)$$

$$A_{370} = 880K(Br_2)_f(Br^-) + 120(Br_2)_f$$

and

$$(Br_2)_f = \frac{A_{370}}{880K(Br^-) + 120}$$

$$(Br_2)_T = (Br_2)_f + (Br_3^-) =$$

$$\frac{A_{370}}{880K(Br^-) + 120} + \frac{K(Br^-)A_{370}}{880K(Br^-) + 120}$$

and

$$(Br_2)_T = \frac{A_{370}[1 + K(Br^-)]}{880K(Br^-) + 120}$$

Preparations of 4,4'-dimethoxydiphenylmethyl hypobromite were carried out utilizing the procedure of Walling and Padwa¹³ except that the reaction was conducted at 0° . Silver sulfate was added in small portions to 0.01 mole of bromine in 100 ml. of distilled water until the bromine color was discharged. The resulting solution of hypobromous acid was cooled to 0° in an ice bath, decanted away from the precipitated silver bromide, and added to 0.01 mole of 4,4'-dimethoxybenzhydrol incompletely dissolved in 100 ml. of Freon 11 at 0° in a separatory funnel. The system was shaken vigorously for 10 min. (with cooling to keep the temperature near 0°) and the yellow Freon 11 layer was separated. The aqueous layer was extracted twice with small portions of ice-cold ether which were then added to the Freon 11 layer. The combined organic layers were dried over sodium sulfate and then Drierite. Solvent was removed in the cold with a rotary film evaporator. During evaporation the formation of crystals was noted; however, these dissolved in the yellow-brown sirup remaining after removal of the solvents.

The infrared spectrum of this yellow-brown sirup was similar to that of the starting 4,4'-dimethoxybenzhydrol except for the absence of O-H stretching

(28) A. E. Bradfield, G. I. Davies, and E. Long, *J. Chem. Soc.*, 3376 (1949).

(29) W. O. Bray and C. M. J. McKay, *J. Am. Chem. Soc.*, 32, 914 (1910).

(30) L. I. Katzin and E. Gilbert, *ibid.*, 77, 5814 (1955).

absorbance and the presence of weak aryl aldehyde and diaryl ketone carbonyl absorbance.

The aldehyde absorbance is considered to result from *p*-anisaldehyde formed by direct cleavage of the carbinol by weakly electrophilic hypobromous acid. Examination of the product by infrared spectrophotometry after 1, 2, and 3 days revealed no noticeable increase in the size of the aldehyde carbonyl band. On the other hand the size of the ketone carbonyl band increased with time. After 4 days (in the dark at 0°), the product sirup had set to a brown crystalline mass. Recrystallization of this mass from ether and hexane yielded *ca.* 2 g. of pale pink crystals which were recrystallized from CCl_4 to give nearly white crystals, melting at 143 – 144° . This compound was identified as 4,4'-dimethoxybenzophenone by comparison with an authentic sample.

A positive sodium fusion test for halogen was obtained on the product and it liberated iodine when shaken with aqueous potassium iodide. This latter behavior is consistent with the known oxidizing character of hypohalites. The molecular weight of this crude material was determined by vapor pressure osmometry. Two determinations gave 346 and 350, in reasonable agreement with predicted value, 323.19, considering that the measurements were made with the crude product. The preparation described above was repeated and the product, 3.02 g. (100% yield of hypobromite requires 3.23 g.), isolated at once and stored in the dark under nitrogen at 0° after a small amount (0.27 g.) of formed 4,4'-dimethoxybenzophenone was removed. Even with these precautions an infrared spectrum taken immediately shows diaryl ketone absorbance. In addition, an n.m.r. spectrum taken soon after was consistent with the product being a mixture of 4,4'-dimethoxybenzophenone and 4,4'-dimethoxydiphenylmethyl hypobromite.

We were unable to prepare a sample of sufficient purity to merit elemental analysis but consider that the evidence given above is overwhelmingly in support of our structural assignment.

Standing by itself the material quickly decomposes to the corresponding benzophenone. When added to excess 50% aqueous acetic acid and allowed to stand for 2 days in the dark, the residue left after sodium carbonate neutralization and ether extraction was shown by infrared spectrum to be a mixture of 4,4'-dimethoxybenzhydrol and the corresponding acetate. Careful examination of all fractions showed little or no cleavage products saving the original small amount of anisaldehyde noted above. To our knowledge no primary or secondary hypobromites have ever been reported. The primary and secondary hypochlorites that have been made³¹ are very unstable, decomposing spontaneously to hydrogen chloride and aldehyde or ketone.

Reactions of Arylcarbinyl Compounds with Bromine in Dichloromethane. 4,4',4''-Trimethoxytriphenylcarbinol (1.63 g., 0.0049 mole) in 15 ml. of carefully purified dichloromethane was mixed with 1 equiv. of bromine in 15 ml. of the same solvent at -70° . No precipitate was formed, but the color changed from red to yellow as hydrogen bromide was evolved. The solution could be warmed to room

(31) F. D. Chattaway and O. G. Backeberg, *J. Chem. Soc.*, 123, 2999 (1923).

temperature without further change and upon addition of carbon tetrachloride red needles came down which could be further recrystallized from carbon tetrachloride-dichloromethane mixture. Despite repeated attempts at complete purification, the infrared spectrum always showed the presence of traces of nuclear brominated material. We were also unsuccessful in getting a good analysis.

Anal. Calcd. for $C_{22}H_{21}Br_3O_3$: C, 46.10; H, 3.69; Br, 41.83; mol. wt., 573. Found: C, 46.53; H, 3.59; Br, 42.28; mol. wt. (vapor pressure osmometer), 566.

Ultraviolet and n.m.r. spectra were compatible with assignment to trianisylcarbonium tribromide as are the above data. The infrared spectrum showed no hydroxyl band but the original carbinol could be regenerated upon quenching with water.

4,4'-Dimethoxydiphenylcarbinol was mixed with bromine in dichloromethane in the same equivalent

quantities as in the above experiment. At -70 and -30° a dark red precipitate was formed rapidly which turned yellow-orange within about 10 min. The solution remained homogeneous at 0° . Cold filtration in a drybox yielded crystals which when warmed on a spatula to room temperature decomposed to products smelling of anisaldehyde and hydrogen bromide. Infrared spectra showed the presence of cleavage products and considerable nuclear brominated material.

4,4'-Dimethoxydiphenylcarbinyl bromide²⁹ was subjected to the treatment described above for the carbinol. The behavior at -70° was the same but upon warming to room temperature the only apparent products were hydrogen bromide and ring brominated material.

Acknowledgment. We are grateful to Mellon Institute for providing facilities for the preparation of this manuscript.

Isomerization and Isotopic Exchange of 4,4'-Dimethylbenzhydryl Thiocyanate in Acetonitrile. Partition of Electron-Deficient Intermediates between Thio- and Isothiocyanate^{1,2}

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Received October 3, 1964

In the isomerization and exchange of 4,4'-dimethylbenzhydryl thiocyanate in acetonitrile containing $NaS^{35}CN$, only a small fraction of the isothiocyanate formed appears to equilibrate its SCN group with the ionic thiocyanate in solution. Thus isomerization largely proceeds via an ionic path in which the organic moiety and the SCN group do not become separated. An intimate ion pair is postulated. Both isomerization and exchange reactions are subject to positive salt effect of the "normal" type. However, the exchange reaction is much more affected, indicating that it involves a more advanced stage of ionization of the substrate. By studying the relative initial rate of radioactivity intake by the two organic species, thiocyanate and isothiocyanate, it has been established that, in returning to covalent state, the ionic intermediate involved in exchange partitions between thio- and isothiocyanate in the ratio of about 5 to 1. Thus, in the assumption that the intimate ion pair is a precursor of the ionic species involved in exchange, the rate of ionization exceeds the rate of isomerization by a factor of six. From the ratio of the rate of

exchange to rate of ionization, the upper limit of the fraction of intimate ion pairs which dissociate is set to 5.4%. Thus, of 100 intimate ion pairs, about 5 undergo further ionization and 95 return to covalent state. Of the latter, about 79 return to thiocyanate and 16 to isothiocyanate.

Introduction

In recent papers evidence has been presented concerning the mechanism of isomerization of organic thiocyanates, $R-SCN \rightarrow R-NCS$.⁵ Solvent, salt, and structural effects indicated large charge separation in the transition state, consistent with an ionization mechanism.⁵ The knowledge of the ionization mechanism was further particularized by an experiment in which the isomerization of benzhydryl thiocyanate in acetonitrile solvent was allowed to occur in the presence of $NaS^{35}CN$.^{5c} The distribution of the label on the ionic thiocyanate, the organic thiocyanate, and isothiocyanate indicated that in the isomerization the "organic" SCN group did not equilibrate with the ionic thiocyanate in solution. As a consequence, for this

(1) Abstracted from the doctoral thesis of P. Koch, University of Padova, 1962.

(2) The financial support of Consiglio Nazionale delle Ricerche, Roma, and Shell Internationale Maatschappij, The Hague, Holland, is gratefully acknowledged.

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(4) Deceased.

(5) (a) A. Iliceto, A. Fava, and U. Mazzucato, *Tetrahedron Letters*, **11**, 27 (1960); (b) A. Iliceto, A. Fava, U. Mazzucato, and P. Radici, *Gazz. chim. ital.*, **99**, 919 (1960); (c) A. Iliceto, A. Fava, U. Mazzucato, and O. Rossetto, *J. Am. Chem. Soc.*, **83**, 2729 (1961); (d) P. A. S. Smith and D. W. Emerson, *ibid.*, **82**, 3076 (1960).