

Summary

1. The acid-catalyzed hydrolysis of urea has been investigated, using 0.5 *N* hydrochloric acid in aqueous solution. The activation energy was 24.6 kcal. and the entropy of activation -14.0 e. u.

2. The urease-catalyzed hydrolysis of urea was investigated in phosphate-buffered solutions over a range of urea concentrations and temperatures. At low urea concentrations the activation energy was 12.5 kcal. and the entropy of activation 7.5 e. u. The activation energy decreases markedly with increasing urea concentration.

3. The results are interpreted quantitatively on the basis of an enzyme model involving the formation of a urea-urease-water complex, the urease being assumed to displace the water reversibly at high concentrations. The heat and the

entropy of reaction for complex formation are 3.25 kcal. and 14.9 e. u. at *pH* 6.6, while the heat and the entropy of activation for complex decomposition into the products of reaction are 9.25 kcal. and -7.0 e. u.

4. It is suggested, in order to account for the positive value of the entropy of formation of the complex, and the increase in entropy in forming the activated state from the initial reactants, that a reversible structural change in the enzyme occurs, the molecule opening out, as in a deactivation, during complex formation.

5. The results are shown to be consistent with a decrease in activation energy with increasing temperature, the change being a gradual one and not a sharp one as had been suggested on the basis of certain previous experiments.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE STATE UNIVERSITY OF IOWA]

The Action of Bromine Vapor on Solid Aromatic Compounds¹

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The reaction of solid aryl olefins with bromine vapor has been reported² as a method of synthesis of the corresponding olefin dibromides. It has been found in the present investigation that the action of bromine vapor on solid aromatic compounds leads to results similar to those expected from bromination in solution by an ionic mechanism.³ Not only was the bromine often added to the double bond of an aryl olefin, but also bromination in the *p*-positions of unsubstituted phenyl groups took place. Aromatic compounds with no olefinic double bonds also underwent bromination by bromine vapor. The results are given in Table I.

A number of compounds with more highly substituted double bonds did not add bromine but underwent substitution of bromine for hydrogen in the *p*-positions of the phenyl groups and on the double bonds. Especially interesting is the case of the tetrakis-(*p*-bromophenyl)-ethylene obtained in the bromination of tetraphenylethylene. This tetrabromide exhibited a great affinity for bromine and adsorbed a good deal of bromine to give a powdery, green solid. This solid lost bromine on standing and regenerated the tetrabromide. The amount of bromine adsorbed depended qualitatively on the concentration of the bromine vapor. This behavior is reminiscent of the

reactions of halogens with highly arylated ethylenes having groups in the *p*-positions capable of supplying electrons to the aromatic rings, *i. e.*, the so-called positive ethylenes.⁴

In most cases the aromatic compounds remained in the solid state throughout the reactions with bromine vapor. At the end of the reactions more or less sticky solid products were obtained. In a few experiments so much excess bromine was taken up that the products were partially dissolved in it. The reaction with bromine evidently took place in an adsorbed phase on the surface of the crystals, in a film of solution formed by the aromatic compound dissolved in liquid bromine, or in a combination of both. In either event the reaction must be similar to the ionic reactions of bromine in solution.³ Both the addition of bromine to the double bond and the aromatic bromination are best explained by ionic mechanisms in which the double bond, the aromatic system, or a combination of the two exhibit basic character and complex with the bromine to form intermediates of the type, ABr^+Br^- . Such complexes have recently been studied by Benesi and Hildebrand⁵ in the case of iodine and aromatic compounds. It would be expected that the more complex electronic systems of highly arylated double bonds might associate with more than one halogen molecule as has been reported by Witzinger^{4b} in the case of the positive ethylenes. Such an ionic intermediate could then by the addition of bromide ion give olefin dibromide, by the loss of hydrogen bromide give a brominated

(1) Abstracted in part from two theses presented to the Graduate College of the State University of Iowa by Eugene A. Hausman and by Norris G. Wheeler in partial fulfillment of the requirements of the M.S. degree.

(2) (a) Baeyer, *Ber.*, **13**, 2254 (1880); (b) Elbs and Bauer, *J. prakt. Chem.*, [2] **34**, 243 (1886); (c) Sudborough and Thompson, *J. Chem. Soc.*, **83**, 666 (1903); (d) Wohrling, *Ber.*, **47**, 108 (1914).

(3) Price, "Reactions at Carbon-Carbon Double Bonds," Interscience Publishers, Inc., New York, N. Y., 1946, Chap. 2.

(4) (a) Witzinger, *J. prakt. Chem.*, [2] **154**, 1 (1939); (b) Witzinger and Fontaine, *Ber.*, **60**, 1377 (1929).

(5) Benesi and Hildebrand, *THIS JOURNAL*, **71**, 2703 (1949).

TABLE I
 THE ACTION OF BROMINE VAPOR ON AROMATIC COMPOUNDS

Reactant	Amt., g.	Time, days	Product	M. p., ^a °C.	Yield, %
$(C_6H_5)_2C=C(C_6H_5)_2^b$	3.3	17 hr.	$(p-BrC_6H_4)_2C=C(p-BrC_6H_4)_2^{c,d}$	258–259 (252 ^e)	70
$(C_6H_5)_2C=C(C_6H_5)_2$	1.0	14 ^f	$(p-BrC_6H_4)_2C=C(p-BrC_6H_4)_2$	258–259	51
$(C_6H_5)_2C=CHC_6H_5$	2.6	17 hr.	$(p-BrC_6H_4)_2C=CBr(p-BrC_6H_4)^{c,g}$	182–184	77
$(C_6H_5)_2C=CHC_6H_5$	1.0	14 ^f	$(p-BrC_6H_4)_2C=CBr(p-BrC_6H_4)$	176–179	44
$(C_6H_5)_2C=CBrC_6H_5$	3.4	17 hr.	$(p-BrC_6H_4)_2C=CBr(p-BrC_6H_4)$	184–185	70
$(C_6H_5)_2C=CH_2$	1.8	10	$(p-BrC_6H_4)_2C=CBr_2^{c,h}$	114–116 ⁱ	67
$(C_6H_5)_2C=CBr_2$	3.4	3	$(p-BrC_6H_4)_2C=CBr_2$	115–117	63
$C_6H_5C\equiv CC_6H_5$	3.0	10	$p-BrC_6H_4CBr=CBr(p-BrC_6H_4)^{c,j}$	236–238 (243 ^e)	53
$C_6H_5C\equiv CC_6H_5$	1.0	14 ^f	$p-BrC_6H_4CBr=CBr(p-BrC_6H_4)$	241 ^e	35
$C_6H_5CBr=CBrC_6H_5$	3.4	10	$p-BrC_6H_4CBr=CBr(p-BrC_6H_4)$	234–236	57
<i>trans</i> - $C_6H_5CH=CHC_6H_5$	4.0	14	$p-BrC_6H_4CHBr-CHBr(p-BrC_6H_4)^{c,k}$	235–327 (dec.) (260 ^e)	71
<i>meso</i> - $C_6H_5CHBrCHBrC_6H_5$	3.0	10	$p-BrC_6H_4CHBr-CHBr(p-BrC_6H_4)$	233–235 (dec.)	59
<i>trans</i> - $p-NO_2C_6H_4CH=CHC_6H_5^l$	2.3	24 hr.	$p-NO_2C_6H_4CHBr-CHBr(p-BrC_6H_4)^{c,m}$	247–248 (dec.) (280 ^e)	43
<i>trans</i> - $p-NO_2C_6H_4CH=CH(p-NO_2C_6H_4)^i$	1.0	24 hr.	$p-NO_2C_6H_4CHBrCHBr(p-NO_2C_6H_4)^n$	258–270 (dec.) (305 ^e)	57
<i>trans</i> - $C_6H_5CH=CHCOOH$	1.5	5 hr.	$C_6H_5CHBrCHBrCOOH$	197–199	59
<i>trans</i> - $C_6H_5CH=CHCOOH$ $C_6H_5BrCHBrCOOH$ }	1.5	10	$p-BrC_6H_4CHBrCHBrCOOH^o$	170–185	..
<i>o</i> - $NO_2C_6H_4CH=CHCOOH$	2.5	14	<i>o</i> - $NO_2C_6H_4CHBrCHBrCOOH^p$	184–185	66
<i>m</i> - $NO_2C_6H_4CH=CHCOOH$	3.0	14	<i>m</i> - $NO_2C_6H_4CHBrCHBrCOOH$	176	73
$C_6H_5CH=C(C_6H_5)COOH$	1.0	18 hr.	Mixture ^q	163	..
<i>p</i> - $NO_2C_6H_4CH=C(C_6H_5)COOH^r$	1.0	2	<i>p</i> - $NO_2C_6H_4CHBrCBr(p-BrC_6H_4)COOH^{c,s}$	163 (dec.)	53
<i>p</i> - $NO_2C_6H_4CH=C(p-NO_2C_6H_4)COOH^t$	2.1	24 hr.	<i>p</i> - $NO_2C_6H_4CHBrCBr(p-NO_2C_6H_4)COOH^u$	206 (dec.)	79
$C_6H_5CH_2CH_2C_6H_5$	1.8	4 ^f	$p-BrC_6H_4CH_2CH_2(p-BrC_6H_4)^v$	113–114 ^w	50
$C_6H_5CH_2CH_2C_6H_5$	1.8	2 hr.	<i>meso</i> - $C_6H_5CHBrCHBrC_6H_5$	236–238	44
$C_6H_5C_6H_5$	2.0	6 hr.	$p-BrC_6H_4(p-BrC_6H_4)^z$	162–164	94

^a All m. p.'s taken in a sealed capillary and corrected unless otherwise stated. ^b Schlenk and Bergmann, *Ann.*, **463**, 1 (1928). ^c Position of bromine on ring established by oxidation. ^d Footnote 6. ^e M. p. determined on the Maquenne block. ^f Reaction carried out in complete darkness. ^g *Anal.* Calcd. for $C_{20}H_{12}Br_4$: C, 42.0; H, 2.12. Found: C, 41.9; H, 2.21. ^h Cristol and Haller, *THIS JOURNAL*, **68**, 140 (1946). ⁱ Three crystallizations raised this m. p. to 119–120°. ^j *Anal.* Calcd. for $C_{14}H_8Br_4$: C, 33.9; H, 1.63. Found: C, 34.1; H, 1.95. ^k Wislicenus and Elvert, *Ber.*, **41**, 4121 (1908). ^l Calvin and Buckles, *THIS JOURNAL*, **62**, 3324 (1940). ^m *Anal.* Calcd. for $C_{14}H_{10}NO_2Br_3$: C, 36.3; H, 2.18. Found: C, 36.5; H, 2.07. ⁿ Pfeiffer and Eistert, *J. prakt. Chem.*, [2] **124**, 168 (1930). ^o Reimer and Tobin, *THIS JOURNAL*, **63**, 2490 (1941), report m. p. 192°. This impure preparation was treated with zinc dust in glacial acetic acid to give a 51% yield of *p*-bromocinnamic acid, m. p. 251–252°. ^p Schofield and Simpson, *J. Chem. Soc.*, 512 (1945). ^q Analysis showed this product to be a mixture of the dibromide with higher bromides. ^r Buckles and Hausman, *THIS JOURNAL*, **70**, 415 (1948). ^s *Anal.* Calcd. for $C_{15}H_{10}NO_4Br_3$: C, 35.5; H, 1.98. Found: C, 35.3; H, 2.13. ^t Ruggli and Lang, *Helv. Chim. Acta*, **21**, 38 (1938). ^u *Anal.* Calcd. for $C_{15}H_{10}N_2O_6Br_2$: C, 38.0; H, 2.12. Found: C, 41.5; H, 2.72. ^v None of this product could be obtained from the bromination of bibenzyl in water, as reported by Stelling and Fittig, *Ann.*, **137**, 257 (1866), or in carbon tetrachloride in the presence of iron. See also Bance, Barber and Wollman, *J. Chem. Soc.*, 1 (1943). An authentic sample was prepared by the action of zinc dust on *p*-bromobenzyl bromide in 95% ethanol, a modification of the method of Errera, *Gazz. chim. ital.*, **18**, 236 (1888). ^w Two crystallizations raised this m. p. to 115.5–116°. ^x The bromination of biphenyl in boiling glacial acetic acid was carried out in 90% yield. Scholl and Neovius, *Ber.*, **44**, 1075 (1911), report 71%. When carried out at room temperature no pure dibromide could be isolated from the bromination.

product, or, failing to stabilize itself in either of these two ways, revert to the original compound with evolution of bromine. This latter course is evidently that followed by solid tetrakis(*p*-bromophenyl)-ethylene which has adsorbed large amounts of bromine.

The only experiments in which photobromination played any part were those in which bromine vapor reacted with bibenzyl in diffuse light to give *meso*- α,α' -dibromobibenzyl. In all other cases tried the reactions in the absence of light were substantially the same as those carried out in diffuse daylight.

Experimental

General Procedure for the Reactions of the Solid Compounds with Bromine Vapor.—An open vessel containing liquid bromine was placed in the lower part of a desiccator. A beaker or evaporating dish containing the finely divided solid compound was placed on the rack above the bromine. The lid of the desiccator was not closed tightly since a good deal of hydrogen bromide was often given off. At the end of the reaction time the product was removed from the desiccator and allowed to stand until constant weight was reached. The crude products were dissolved in chloroform, ethanol or a mixture of the two and crystallized. The results of these experiments are presented in Table I.

Oxidation of the Brominated Products.—A number of the brominated products indicated in Table I were oxidized

by excess chromic acid in glacial acetic acid as described by Bilz.⁶ Olefin dibromides were first heated with zinc dust in glacial acetic acid. The zinc and zinc bromide were removed by filtration of the cooled solution before the chromic acid was added. The product of oxidation isolated was either 4,4'-dibromobenzophenone, m. p. 173-174°, or *p*-bromobenzoic acid, m. p. 254-255°, in yields of 50% or higher. Direct oxidation of $\alpha,\alpha',4,4'$ -tetrabromobenzyl gave a 91% yield of 4,4'-dibromobenzyl,⁷ m. p. 228°.

The Reaction of Bromine with Tetrakis-(*p*-bromophenyl)-ethylene.—A 1.00-g. sample of the tetrabromide was placed in a desiccator in which the atmosphere was saturated with bromine vapor. The green, powdery product weighed 1.32 g. After standing for several hours the solid product was nearly white and weighed 0.99 g. When this sample was left several days in an atmosphere containing bromine vapor at a much lower concentration than that of air saturated with bromine vapor, the solid product was slightly green and weighed only 1.05 g. Again standing yielded a white product. After crystallization from chloroform-ethanol the m. p. was 258-259°.

1,1-Dibromo-2,2-diphenylethylene.—A solution of 3.6 g. (0.020 mole) of 1,1-diphenylethylene in 20 ml. of glacial acetic acid was treated with 2.2 ml. (0.043 mole) of bromine. The solution became warm and the color rapidly faded. Heating the mixture partially restored the bro-

mine color and caused a rapid evolution of hydrogen bromide. The color faded again during the heating process. When hydrogen bromide was no longer evolved, about 40 g. of ice and water was added to the reaction mixture. The 6.5-g. yield of crude product was crystallized from 95% ethanol to yield 4.1 g. (61%) of 1,1-diphenyl-2,2-dibromoethylene, m. p. 83-84° which is the m. p. reported.⁸

Summary

1. Twenty solid aromatic compounds reacted with bromine vapor to yield products in which the *p*-positions of unsubstituted phenyl groups had brominated and in which olefinic double bonds, not highly substituted, had added bromine.

2. These reactions of bromine vapor with solid aromatic compounds have been explained as involving ionic intermediates in which a molecule of the aromatic compound and one or more bromine molecules are combined in either an absorbed phase or in a film of solution on the surface of the solid. Subsequent reactions of the intermediates explain the products which have been observed.

(8) Harris and Frankforter, *THIS JOURNAL*, **48**, 3144 (1926).

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(6) Bilz, *Ann.*, **296**, 219 (1897).

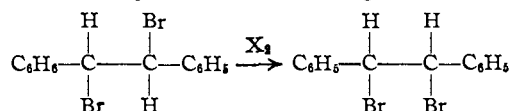
(7) Bilz, *Ber.*, **41**, 1761 (1908).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE STATE UNIVERSITY OF IOWA]

The Reactions of the α,α' -Dibromobibenzyls and the α,α' -Dichlorobibenzyls with Halogens¹

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The *cis-trans* isomerization of olefins by the action of halogen atoms is well known.³ A similar isomerization has now been observed in the conversion of *dl*- α,α' -dibromobibenzyl to the *meso*-isomer by the action of halogens.



The isomerization took place in good yield when solid *dl*-dibromide was left in contact with bromine vapor for two weeks or when a carbon tetrachloride solution of the *dl*-dibromide was treated with bromine or iodine for several days at room temperature. A carbon tetrachloride solution of the *dl*-dibromide containing chlorine gave the *meso*-dibromide, but only in 20% yield. The reaction of chlorine with either *dl*- or *meso*-dibromobibenzyl in sunlight gave α -bromo- α' -chlorobibenzyl plus other dihalides and trihalides.

(1) Abstracted in part from two theses presented to the Graduate College of the State University of Iowa by Walter E. Steinmetz in partial fulfillment of the requirements for the Ph.D. degree and by Norris G. Wheeler in partial fulfillment of the requirements of the M.S. degree. Part of this paper was presented before the Organic Division of the American Chemical Society, San Francisco, March 30, 1949.

(2) Allied Chemical and Dye Fellow, 1946-1947.

(3) Price, "Reactions at Carbon-Carbon Double Bonds," Interscience Publishing Co., New York, N. Y., Chap. 3, 1946.

These reactions were not observed when the reactions were carried out in absolute darkness except when bromine vapor reacted with the solid dibromide.

A similar isomerization of *dl*- α,α' -dichlorobibenzyl was brought about in sunlight by the action of chlorine or bromine in carbon tetrachloride, but it was impossible to ascertain to what extent this reaction took place. Both the *meso*- and *dl*-dichlorides reacted with chlorine or bromine to give mixtures of halogenated products. Only a small amount of *meso*-dichlorobibenzyl could be isolated from either the chlorination or bromination of the *dl*-isomer. The *dl*-dichloride was recovered in high yield from the reaction with iodine in sunlight. The reaction of either *meso*- or *dl*- α,α' -dichlorobibenzyl with chlorine gave rise to a number of chlorination products: α,α,α' -trichlorobibenzyl, $\alpha,\alpha,\alpha',\alpha'$ -tetrachlorobibenzyl and benzotrichloride. No evidence of ring chlorination could be found. Bromine reacted with *dl*-dichlorobibenzyl to give trihalides as well as dihalides while the *meso*-isomer gave mostly starting material.

The results all indicate that halogen replaces bromine from the *dl*-dibromide probably by way of halogen atoms. When the displacing halogen is not bromine, the bromine atom which is removed could effect a displacement of the new