VIII and IX were further purified by steam distillation, dried over calcium chloride and finally distilled under a vacuum. Treatment with bromine in chloroform solution indicated complete saturation in each case.

Summary

Cyclohexanone has been condensed with *p*-toluic aldehyde, 2,4-dimethyl- and *p*-bromobenzaldehyde. 2,6-Dibenzyl-, dianisyl-, dipiperonyl-, di-*p*-tolylyl-, di(2,4,-dimethyl)benzyl- and di-*p*-chlorobenzyl-cyclohexanones have been obtained by hydrogenating the corresponding unsaturated ketones.

Tertiary alcohols have been prepared by the action of the Grignard reagent on cyclohexylidene-cyclohexanone. These have been hydrogenated. The saturated and the unsaturated tertiary alcohols have been dehydrated and the unsaturated hydrocarbons have been hydrogenated.

BALTIMORE, MARYLAND

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF ORGANIC CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

STUDIES ON THE DIRECTIVE INFLUENCE OF SUBSTITUENTS IN THE BENZENE RING. III. THE ACTIVE AGENT IN AQUEOUS BROMINATION[1]

BY A. W. FRANCIS[2]

RECEIVED APRIL 14, 1925 PUBLISHED SEPTEMBER 5, 1925

Bromination in aqueous solution is usually considered to be due to the presence of hypobromous acid,[3,4] since it is very much faster than bromination in anhydrous media. The idea is further favored and even considered proved[4] by the fact that aqueous bromination is markedly slower in the presence of large amounts of acid, especially hydrobromic acid, these being the conditions for extremely low concentrations of hypobromous acid. Furthermore, saturation of ethylenic bonds with bromine water frequently gives considerable amounts of bromohydrin compounds.[5]

There are, however, certain considerations which throw doubt upon the assumption that hypobromous acid is the only, or even the principal active agent in aqueous bromination. Some of these appeared in connection with the work described in Part II.[6]

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[1] Presented in part at the Sixty-ninth Meeting of the American Chemical Society, Baltimore, April, 1925.

[2] National Research Fellow in Chemistry.

[3] Stark, *Ber.*, **43**, 670 (1910).

[4] Baines, *J. Chem. Soc.*, **121**, 2810 (1922).

[5] Read and others, *J. Chem. Soc.*, **101**, 760 (1912); **111**, 240 (1917); **117**, 359, 1214 (1920); **119**, 1774 (1921); **121**, 2550 (1922); *J. Proc. Roy. Soc. N. S. Wales*, **51**, 558 (1917).

[6] Francis, Hill and Johnston, THIS JOURNAL, **47**, 2211 (1925).

The enormous velocities of bromination of certain aromatic compounds estimated in that paper, which seem to have velocity constants as high as 10^{12} with respect to the total bromine concentration, make one hesitate to postulate constants several thousand times higher still in order to correspond with the concentration of hypobromous acid. Furthermore, if the latter were the active agent, it might be expected that some small amount of phenolic compound would be formed, especially if Holleman's mechanism[7] of preliminary addition to the double bonds of the ring were followed, the hydroxyl instead of bromine remaining in the ring. No one has found this to be the case.

More definite evidence against hypobromous acid is provided by the fact that basic compounds such as aniline and the toluidines, upon bromination by solutions of hypobromous acid (prepared in various ways as described below), give precipitates which are invariably grayish, or even dark brown or black and partly colloidal, while with bromine water, if slightly acidified, the same compounds give white crystalline precipitates. The dark color is due, presumably, to partial oxidation, and appears even when the solution is strongly acid, or ice cold, or extremely dilute, or when the hypobromous acid is being generated, as by the addition of bromine water to a mixture of aniline and silver sulfate in water solution. With bromine water itself, if it is not acidified, the precipitate is usually slightly darkened, probably because of traces of hypobromous acid.

A comparison of the relative rates of bromination with bromine water and with hypobromous acid solution should be decisive. If the latter compound were the active agent in both cases, the velocity should be several thousand times greater in the latter case than in the former.

The chief difficulty is the tremendous velocity in all cases. Competition experiments[6] would show nothing because the products from the two brominating agents upon the same compound would be identical. *m*-Nitrophenol was chosen for most of the experiments because, of the compounds so far tried, it is brominated most slowly.[6]

There was also considerable difficulty in preparing satisfactory solutions of hypobromous acid. A brief consideration of the bromine equilibria will make the reason clear.

Bromine is hydrolyzed by water in two ways,

$$Br_2 + H_2O \rightleftharpoons HBr + HOBr \qquad (1)$$

$$3Br_2 + 3H_2O \rightleftharpoons HBrO_3 + 5HBr \qquad (2)$$

In acid solution the hydrolysis is very slight as shown by the constants,

$$K_1 = \frac{(H^+)\ (Br^-)\ (HOBr)}{(Br_2)} = 5.2 \times 10^{-9} \qquad (3)^8$$

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[7] Holleman, "Die direkte Einführung von Substituenten in den Benzolkern," Veit and Co., Leipzig, **1910**.

[8] Bray and others, THIS JOURNAL, **32**, 932 (1910); **33**, 1487 (1911).

$$K_2 = \frac{(H^+)^6 (Br^-)^5 (BrO_3^-)}{(Br_2)^3} = 10^{-33} \qquad (4)^9$$

The first equilibrium is established with extreme speed and may be considered instantaneous. The second is of moderate speed, and it is only because of the sluggishness of this reaction that hypobromous acid can be obtained in solution in appreciable quantities, since it oxidizes itself to bromic acid.

$$3HOBr \longrightarrow HBrO_3 + 2HBr \qquad (5)$$

Hypobromous acid is commonly prepared by adding mercuric oxide to bromine water and, if necessary, distilling in a vacuum to remove it from the mercuric bromide. The product is not at all satisfactory for rate comparisons, because it still contains considerable amounts of free bromine. This was evidenced by the color and strong odor of bromine, both of which were completely absent from a solution to be described later. This free bromine, if it could cause direct substitutions, would produce hydrobromic acid which, with hypobromous acid, would regenerate bromine. The results would, therefore, be ambiguous. In fact, it was not possible to ascertain whether this solution or free bromine water was the more reactive because of the high rate in both cases. It is necessary, therefore, to have a solution practically free from bromine. From the equilibria, this is possible only when the bromide ion is reduced to an extremely low concentration. Lead carbonate is not capable of doing this, though solutions prepared with this substance, as well as those employing mercuric oxide, caused the partial oxidation of aniline referred to above. Silver oxide gives a good solution of hypobromous acid, but because of Reaction 5 the bromide ion reappears quickly, causing also the return of the yellow color of bromine. Silver sulfate, which prevents this by providing an excess of silver ions, is more satisfactory. In the remaining experiments the hypobromous acid used was prepared by saturating bromine water with solid silver sulfate and separating the silver bromide and excess of silver sulfate. The solution becomes turbid quickly because of precipitation of the bromide ion. It was always used within a few minutes, being standardized before and afterwards with fair agreement by titrations with thiosulfate solution after the addition of potassium iodide. Silver iodide is precipitated in the standardizations, but does not interfere. The absence of appreciable amounts of bromic acid (formed according to Reaction 5) was shown by adding an excess of phenol to react with the hypobromous acid, and then potassium iodide; only a trace of iodine was obtained.

Bromination of *m*-nitrophenol by means of free bromine water was found to be nearly one thousand times as rapid as that under similar conditions with hypobromous acid from which the bromine had been removed completely by silver sulfate. This is quite the reverse of what would be ex-

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[9] Sammet, *Z. physik. Chem.*, **53**, 641 (1905).

pected if hypobromous acid were the principal active brominating agent. The ratio is approximately that of the relative concentrations of free bromine as calculated from Equation 3 and the solubilities of silver sulfate and silver bromide. There is still the possibility that the relatively slower rate may be due to some negative catalytic effect of the silver or the sulfate ion, but this is discounted by the fact that other sulfates, such as that of copper, seem to have no effect upon the rate with bromine water.

It is possible that an impurity of iodine in the bromine would be catalytically active. In order to test for this, a 1g. sample of the bromine was dissolved in water and reduced, except for a trace, by sodium bisulfite. A few drops of carbon disulfide, which were added, acquired a light brown color because of the residual bromine, but no violet color from dissolved iodine.

That the active agent is probably the same, whichever brominating solution is used, is shown by a series of competition experiments between potassium iodide and certain organic compounds for hypobromous acid and for free bromine water. These gave in each case ratios of rates, agreeing closely for the two forms of bromine. Since the reactions with potassium iodide,

$$Br_2 + 2KI \longrightarrow I_2 + 2KBr \tag{6}$$

$$2HOBr + 4KI + H_2SO_4 \longrightarrow 2I_2 + 2KBr + K_2SO_4 + 2H_2O \tag{7}$$

are quite different from those with the organic compounds, and somewhat different from each other, the agreement seems to indicate that the same agent is effective in every case, and that the ratios observed are actually the ratios of reactivities of the competitors. This idea is further supported by the fact that competitions between titanous chloride and an organic compound for the two forms of bromine likewise give good agreement.

Saturation of double bonds with bromine water gives principally the bromohydrin derivatives. The relative amount of this reaction in several cases was estimated by a subsequent titration with silver nitrate (Volhard's method), since hydrobromic acid is formed in equivalent amounts with the bromohydrin compound, while direct addition of bromine to a double bond produces no bromine ion in solution. Only 10–15% of dibromo derivative was formed in the cases of cinnamyl alcohol and cinnamic, maleic and fumaric acids. In spite of this, however, these compounds seemed to be saturated more quickly with bromine water than with hypobromous acid. It is probable that the formation of bromohydrin compound does not necessarily involve the addition of hypobromous acid as a whole, and that the preferential addition of its parts is due merely to some inherent influence in the organic compound, such as negativity or steric influence. This view is favored by the fact that the relative amount of dibromide formation is just as small with bromine water in strong (4 *N*) sulfuric acid, in which the concentration of hypobromous acid is negligible; though the rate of saturation is less than one one-thousandth as great. It is unlikely that this retarding effect of the acid should be precisely the same for addition of hypobromous acid and of bromine, especially as no reason is apparent why there should be any effect upon the latter. It is more reasonable to suppose that only one active agent is present, whose concentration or reactivity is decreased by the acid. In order to account for the dual product, it is necessary only to assume that this active agent consists of bromine atoms, probably with positive charges,[10] which add to one side of the double bond, and that the free positive radicals thus produced unite with negative bromine or hydroxyl ions, mostly the latter, according to their own peculiar properties.

Recently Terry and Eichelberger[11] have shown that bromohydrin formation can be prevented in the case of sodium maleate and sodium fumarate by a high concentration of sodium bromide. This is not inconsistent with the above observation where sulfuric acid was employed, because the high bromide-ion concentration might overcome the natural preference of the free radical, $(\mathrm{RCBr{-}\underset{|}{C}R})^{+}$, for hydroxyl ions. Strong support for this view is furnished by the observation of these authors that the action of bromine and potassium chloride upon sodium maleate produces the chloride-bromide compound, but no dichloride, a fact which they were unable to explain. The corresponding formation of α-chloro-β-bromo-ethane from ethylene and bromine in neutral sodium chloride solution has been confirmed by the present author. No trace of ethylene dichloride was found, making the intermediate formation of free chlorine improbable. The action of bromine chloride is at once suggested, but there is good evidence[12] against the existence of such a compound. Moreover, if it did exist, its formation under the above conditions would seem to require a positive bromine ion. Additional mixed derivatives made in a similar manner were α-chloro-β-iodo-ethane and β-bromo-ethyl nitrate. The hypothetical intermediate bromine nitrate in the last case seems even less probable than bromine chloride.

Nascent or monatomic bromine could be quite reasonably the intermediate product in the dynamic equilibrium of Equation 1, and might well be decreased to a very low concentration if the equilibrium is shifted too far in *either* direction, as in the case of hypobromous acid in the presence of silver sulfate, or in the case of bromine water with strong acid, or still more with non-aqueous solvents, thus corresponding with all the evidence previously offered for hypobromous acid. In any intermediate stage of

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[10] The existence of positive halogen ion has been suggested previously. Noyes, THIS JOURNAL, **23**, 460 (1901). Stieglitz, *ibid.*, **23**, 796 (1901).

[11] Terry and Eichelberger, *ibid.*, **47**, 1067 (1925).

[12] Lebeau, *Compt. rend.*, **143**, 589 (1906). Karsten, *Z. anorg. Chem.*, **53**, 365 (1907).

the equilibrium, such as with ordinary bromine water, or with the hypobromous acid solution made with mercuric oxide, the concentration of the nascent bromine may be sufficient to produce almost instantaneous reactions. It is not unlikely that the conditions of maximum concentration of nascent bromine and maximum reactivity would be at some stage of the equilibrium intermediate between those of the latter two solutions.

The hypothesis of nascent bromine would be very difficult to prove experimentally because nothing is known about its equilibria; but consistent with the idea is the fact that gold leaf is dissolved readily in bromine water, while it is entirely unattacked by hypobromous acid solution, and only very slowly by a solution of bromine in carbon tetrachloride. The "purple of Cassius" test with stannous chloride was negative in the case of hypobromous acid after 24 hours' contact with gold, while it gave a deep purple when bromine water had been used, the solution having taken place in less than a minute. Three or four hours were required for the solution of a similar amount of gold in the carbon tetrachloride solution.

The suggestion has been made that the solution of the gold is due to the formation of complex ions, for example, $AuBr_4^-$. This is quite possibly formed, but it does not seem to the author to affect the above reasoning in regard to nascent bromine.

Experimental Part

Several qualitative experiments which were made are already described.

Rates of reaction between *m*-nitrophenol and freshly prepared (within five minutes) hypobromous acid solution saturated with silver sulfate were studied at several different concentrations. In each experiment equivalent amounts of the reacting substances were used. Aliquot portions were pipetted out and the reaction was stopped at suitable intervals by the addition of potassium iodide. Titrations were made with 0.1 *N* sodium thiosulfate solution. At the higher concentrations, the second-order "con-

RATE OF REACTION, HYPOBROMOUS ACID AND *m*-NITROPHENOL

TABLE I

Temperature, 25° Concentration, 0.004 *N*

Time, min.	Titration Cc. of thiosulfate	*K*
0	12.00 (calcd.)	...
0.33	9.21	227
1.0	5.95	254
1.67	4.66	236
3.0	3.23	226
5.0	2.11	234
10.0	1.07	255
	Mean	239

TABLE II

Temperature, 25°

Concn., *N*	Mean *K*
0.001	375
.001	337
.002	428
.004	239
.0083	184
.0167	250
.018	196
.033	358
Mean	296

stant" decreased slightly with time, as might be expected from the fact that the reaction occurs in three stages instead of one. At very low concentrations, the constant increased, possibly because sufficient time was allowed for a little more free bromine to accumulate. One experiment is shown in Table I, and a summary of the others in Table II. The constants are of the same order of magnitude and show no general trend either up or down, confirming the expectation of a bimolecular reaction.

With free bromine water the rates were so high that only one point was determinable in each experiment. These are summarized in Table III. The constants are very approximate, and are probably minimum values.

TABLE III

RATE OF REACTION, BROMINE WATER AND *m*-NITROPHENOL

Temperature, 25°

Concentration	Time, min.	% Reacted		K
0.00005	0.25	67		160,000
.00010	.17	85		340,000
.00025	.25	93		220,000
.00025	.25	96		380,000
			Mean	275,000

Competition experiments between organic and inorganic compounds for bromine are shown in Table IV. Equivalent amounts of the two competitors were mixed and bromine solution sufficient for only one of them was added. When potassium iodide was a competitor, the iodine liberated was titrated with thiosulfate solution. When titanous chloride was a competitor, after the reaction, the solution was heated to boiling (properly protected with carbon dioxide), and the excess of titanous chloride was titrated with ferric alum, using methylene blue as an indicator; x_A is the fraction of Competitor A which has reacted with bromine, and x_B that of Competitor B (in these experiments $x_B = 1 - x_A$), and K_A/K_B is the ratio of rates from the equation,[6]

$$\frac{K_A}{K_B} = \frac{\log (1 - x_A)}{\log (1 - x_B)} \qquad (8)$$

TABLE IV

COMPETITION EXPERIMENTS

Competitor A	Competitor B	Bromine solution	x_A	K_A/K_B
KI	Dibromoresorcinol	HOBr	0.814	8.2
KI	Dibromoresorcinol	Br_2	.817	8.4
KI	Dibromoresorcinol	Br_2	.777	6.0
KI	*m*-Aminophenol	HOBr	.513	1.08
KI	*m*-Aminophenol	Br_2	.537	1.24
$TiCl_3$	Dibromophenol	HOBr	.495	0.97
$TiCl_3$	Dibromophenol	Br_2	.479	.89
$TiCl_3$	Dibromophenol	Br_2	.484	.91

Mixed halogen addition products of ethylene were made in the following way.

A 1-liter pressure bottle was filled two-thirds full with a saturated salt solution, and sufficient halogen was added to saturate it. The bottle was closed with a cap containing a bicycle valve, and a moderate pressure (4 or 5 atmospheres) of ethylene was added from a cylinder. The bottle was well shaken for one minute or until the pressure had become practically atmospheric, and more ethylene was added. When the solution had become colorless, more halogen and ethylene were introduced. The process was continued until a sufficient amount of oil had been accumulated. This was separated from the aqueous solution, washed with water, dried with calcium chloride and examined by determination of density, refractive index or boiling point. In each case a mixture was obtained, some of the halogen having added directly to the ethylene. A partial separation was made by fractional distillation.

α-Chloro-β-bromo-ethane was prepared from ethylene, bromine and sodium chloride solution. The oil contained about 46% of C_2H_4ClBr as estimated from the index of refraction, 1.513 (the value for $C_2H_4Br_2$ in the literature is 1.534; for $C_2H_4Cl_2$, 1.442). A portion was separated by fractional distillation with the following properties: *n*, 1.4864; b. p., 106–8°; d, 1.701 (the values for C_2H_4ClBr in the literature are as follows: b. p., 106°; d., 1.69; for $C_2H_4Br_2$; b. p., 131°; d., 2.189).

α-Chloro-β-iodo-ethane was prepared from ethylene, iodine and sodium chloride solution. The oil contained considerable ethylene iodide, part of which crystallized, and readily decomposed, giving up iodine. It was partly purified by being washed with sodium thiosulfate solution and by steam distillation; d., 2.173 (the value in the literature is 2.12) showing the probable presence of some $C_2H_4I_2$. A sample was reduced with zinc and sulfuric acid and both halogens were determined by the addition of an excess of standard silver nitrate solution, collection of the precipitate in a Gooch crucible and titration of the excess of silver.

Anal. Calcd. for C_2H_4ClI: Cl, 18.65; I, 66.7. Found: Cl, 16.5; I, 68.7.
Calcd. for C_2H_4ClI containing 11% of $C_2H_4I_2$: Cl, 16.6; I, 69.2.

β-Bromo-ethyl Nitrate was prepared from ethylene, bromine and sodium nitrate solution. Before distillation the oil was washed with sodium bicarbonate solution to remove any trace of nitric acid. The oil began to boil at 132° ($C_2H_4Br_2$) but a portion boiled at 163–5°; d., 1.78 (the values in the literature for $C_2H_4BrNO_3$ are as follows: b. p., 164°; d., 1.73). A sample analyzed with titanous chloride required about 80% of the calculated amount, while pure ethylene bromide failed to oxidize titanous chloride. In the distillation the last trace exploded with evolution of brown nitrous fumes, recognized also by their odor.

The author is indebted for many helpful suggestions to Professor James F. Norris of the Massachusetts Institute of Technology, and to Professor A. J. Hill of Yale University.

Summary

Evidence has been presented against the view that aqueous bromination is due to the presence of hypobromous acid. This is based upon (1) the much greater tendency of this compound than that of bromine water to oxidize aniline and other amines; (2) its much slower reactions with organic compounds than with those of bromine water; (3) its inactivity towards gold and (4) the formation, in salt solutions, of mixed halogen addition products of unsaturated compounds. The suggestion has been made that

the reactivity of bromine water is due to nascent bromine, and a mechanism for the addition of halogens to double bonds has been proposed.

CAMBRIDGE 39, MASSACHUSETTS

[CONTRIBUTION FROM THE KENT CHEMICAL LABORATORY OF THE UNIVERSITY OF CHICAGO]

3-NITROPHTHALIC ANHYDRIDE AS A REAGENT FOR ALCOHOLS

BY BEN H. NICOLET AND JACOB SACKS[1]

RECEIVED MAY 5, 1925 PUBLISHED SEPTEMBER 5, 1925

The reagent most commonly recommended for the identification of the lower monohydric alcohols is 3,5-dinitrobenzoyl chloride.[2] It is common practice to prepare a fresh sample of this chloride for each test, making its use somewhat unpleasant and tedious. The present paper reports a study of the use for identification of such alcohols of 3-nitrophthalic anhydride. This substance is easily prepared and keeps well. It readily gives crystalline derivatives of definite melting point with the alcohols in question, and these have solubilities that make hot water a suitable solvent for recrystallizing small quantities, thus avoiding any questoin of the possibility of alkyl interchange with the solvent. Furthermore, the mono-esters thus obtained still have one free carboxyl group, so that the equivalent weight of unknown alkyl radicals can readily be determined by titration.

3-Nitrophthalic acid was prepared by the method of Miller.[3] Nitric acid, d. 1.45, was as effective as that of d. 1.50, and caused less fuming. The yield was uniformly 28–30%, as also reported by Cohen, Woodroffe and Anderson.[4] The anhydride was readily made by heating the acid with acetic anhydride.[5]

The mono-esters were best prepared by treating the anhydride with about half its weight of the alcohol, and heating on a water-bath for five to ten minutes after the mixture became liquid. The products were then dissolved in hot water and allowed to crystallize. One or two recrystallizations usually gave products of constant melting points. The substances so obtained are 2-mono-alkyl esters of 3-nitrophthalic acid (I).[6] McKen-

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[1] The material here presented was used by Jacob Sacks in partial fulfilment of the requirements for the degree of Master of Science in the University of Chicago.

[2] (a) Mulliken, "The Identification of Pure Organic Compounds," John Wiley and Sons, **1904**, vol. 1, p. 168. (b) Kamm, "Qualitative Organic Analysis," John Wiley and Sons, **1923**, p. 150.

[3] Miller, *Ann.*, **208**, 233 (1881). E. R. Littman [THIS JOURNAL, **47**, 1980 (1925)] has since published what appears to be a much improved method for the preparation of this acid.

[4] (a) Cohen, Woodroffe and Anderson, *J. Chem. Soc.*, **109**, 233 (1916). (b) Miller's statement that the yield is 40% apparently refers to percentage by weight of original phthalic anhydride.

[5] McKenzie, *J. Chem. Soc.*, **79**, 1157 (1901).

[6] (a) Wegscheider and Lipschitz, *Monatsh.*, **21**, 787 (1900). (b) Marckwald and McKenzie, *Ber.*, **34**, 486 (1901).