BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 45, 1293—1299(1972)

Bromination of Aliphatic Ketones with Copper(II) Bromide in Organic Solvents. I. The Reaction of Acetone with Copper(II) Bromide in Methanol

Yoshitane Kojima and Shinichi Kawaguchi
Department of Chemistry, Faculty of Science, Osaka City University, Osaka, 558

(Received August 16, 1971)

The reaction between acetone and methanol to form acetone dimethylacetal attains equilibrium quickly under the influence of copper(II) bromide. Reaction of both acetone and acetone dimethylacetal with copper(II) bromide thus proceed simultaneously to produce copper(I) bromide, hydrogen bromide, and brominated substrates. The mass balances of these reactions were established. On account of the retarding effect of copper(I) bromide and the enhancing effect of hydrogen bromide, the time course of reaction is too complicated to be analyzed, and the initial rate formula was determined. Two reaction pathways were suggested and copper(II) bromide was considered to play dual roles as a catalyst and a brominating agent in either case. The acid-catalyzed reactions were also found to follow a two-term rate law, one being independent of and the other first-order with respect to copper(II) bromide.

Copper(II) bromide is highly soluble in acetone and reacts with the solvent resulting in copper(I) bromide. Kosower, *et al.* reported halogenation reactions of various ketones with copper(II) chloride and bromide in dimethylformamide.[1] Castro and his coworkers also described halogenations of unsaturated compounds with copper(II) halides in boiling alcohols.[2] Kinetic studies of copper(II) chloride reactions were performed by Kochi[3] with acetone in aqueous solutions and by Lorenzini and Walling[4] with butylaldehyde and isobutylaldehyde in aqueous isopropyl alcohol. However, detailed kinetic studies of reactions between anhydrous copper(II) bromide and ketones in inert organic solvents have not been reported.

Reactivities of various organic solvents with copper(II) bromide have been examined, and methanol and dimethylformamide were found to be most suitable as unreactive solvents. Thus, we started the kinetic study of the reaction between copper(II) bromide and acetone in methanol. Unfortunately, however, this system has turned out to be complicated on account of the rapid acetal formation in the presence of copper(II) bromide.

Experimental

Materials. Organic solvents were purified by standard methods,[5] and their purities were checked by the vapor phase chromatography. The water contents of methanol and acetone were measured by the Karl-Fischer method to be 3.8×10^{-3} and 2.2×10^{-2}M, respectively. Anhydrous copper(II) bromide was supplied by Kishida Chemical Co. Ltd. The contaminant copper(I) bromide was checked by titration with a cerium(IV) ammonium sulfate solution. Found for two

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[1] (a) E. M. Kosower, W. J. Cole, G.-S. Wu, D. E. Cardy, and G. Meisters, *J. Org. Chem.*, **28**, 630 (1963); (b) E. M. Kosower and G.-S. Wu, *ibid.*, **28**, 633 (1963).

[2] C. E. Castro, E. J. Gaughan, and D. C. Owsley, *ibid.*, **30**, 587 (1965).

[3] J. K. Kochi, *J. Amer. Chem. Soc.*, **77**, 5274 (1955).

[4] A. Lorenzini and C. Walling, *J. Org. Chem.*, **32**, 4008 (1967).

[5] J. A. Riddick and E. E. Toops, Jr., "Organic Solvents", Vol. 7 of "Technique of Organic Chemistry" edited by A. Weissberger and E. S. Proskauer, 2nd ed., Interscience Publishers, New York (1955).

specimens: Cu, 28.60; Br, 71.38% and Cu, 28.34; Br, 71.58%. Calcd for $CuBr_2$: Cu, 28.45; Br, 71.55%.

Copper(I) bromide was prepared by reduction of copper(II) sulfate with sodium sulfite in an aqueous solution containing potassium bromide.[6] Sodium acetylacetonate was prepared by adding an aqueous solution of sodium hydroxide to a methanol solution of acetylacetone, and recrystallized from methanol. Commercial tetraethylammonium bromide was used without further purification. Dry methanol solutions of perchloric acid were prepared by passing dry methanol solutions of sodium perchlorate through a column of dried acid form cation exchange resin Dowex 50WX8 (100—200 mesh).[7] A stream of nitrogen was bubbled through boiling deionized water prior to use for quenching of the reaction mixture.

Identification and Determination of Reaction Products. After the desired period of reaction, volatile substances were distilled under reduced pressure. The residue was a mixture of copper(I) bromide and copper(II) bromide. To determine the copper(I) content, the whole residue was dissolved in a sulfuric acid solution containing iron(III) ammonium sulfate and iron(II) ions produced were titrated with an aqueous solution of cerium(IV) ammonium sulfate.[3] For the determination of total copper and bromine, the residue was dissolved in aqueous ammonia. Bromine was determined gravimetrically as silver bromide and copper by electrolysis.

The distillate was composed of methanol, acetone, and brominated substrates. Each component was identified by comparison of the gas-chromatogram with that of the authentic specimen and also by IR and NMR assays when possible. The combined quantity of hydrogen bromide and methyl bromide was measured by titration with an aqueous solution of sodium hydroxide using methyl red as an indicator. The amount of brominated substrates was determined by iodometry.[8]

Kinetics. A methanol solution of copper(II) bromide was thermostated (±0.02°C) in a three-necked flask equipped with a stirrer, a nitrogen gas inlet tube, and an outlet tube containing calcium chloride. The reaction started when thermostated acetone was added to this solution. At appropriate time intervals aliquots were withdrawn from the reacting mixture and quenched in cold sulfuric acid solutions of iron(III) ammonium sulfate. Iron(II) produced was determined by titration with a standardized sulfuric acid (0.5N) solution of cerium(IV) ammonium sulfate (0.01—0.05N).[3] The initial concentration of copper(II) bromide was determined in advance by the EDTA titration with murexide as an indicator.[9]

Equilibrium Determination of the Reaction between Acetone and Methanol. The reaction between acetone and methanol forming acetone dimethylacetal is quite slow, but it attains equilibrium fairly rapidly, within 5 min at the latest, in the presence of copper(II) bromide. The reaction mixture was poured into a methanol solution of sodium acetylacetonate cooled in a dry ice-methanol bath. The equilibrium was thus frozen by chelation of copper and neutralization of acid produced. The solution was then submitted to the gas-chromatographic separation through a column (3 m×4 mm in diameter) containing diglycerol (5%) and silicone grease (5%) carried on Neosorb NCS (63°C, hydrogen gas flow: 20 cc/min), and the equilibrium contents of acetone and acetone dimethylacetal were determined.

Results

Stoichiometry of Reactions of Copper(II) Bromide with Acetone and Acetone Dimethylacetal in Methanol. About 2 g of copper(II) bromide was dissolved in 20 m*l* of methanol, to which 4—5 m*l* of acetone or acetone dimethylacetal was added and allowed to react at room temperature for about 2 hr. The reaction mixtures were then analyzed by the method described in Experimental and the results are summarized in Table 1.

The distillation residue was composed of copper(I) bromide and copper(II) bromide, and the composition is given by the following equations:

$$CuBr = 2(\text{Total Cu}) - Br$$

$$CuBr_2 = Br - \text{Total Cu}$$

The mass balance is accounted for in the accuracy better than 95% in the case of acetone, but only around 90% for the acetal. Reactions occurring in the earlier stage of this system can thus be represented by the following equations:

$$(CH_3)_2CO + 2CH_3OH \overset{\text{fast}}{\rightleftharpoons} (CH_3)_2C(OCH_3)_2 + H_2O \quad (1)$$

$$(CH_3)_2CO + 2CuBr_2 \longrightarrow CH_3COCH_2Br + 2CuBr + HBr \quad (2)$$

$$(CH_3)_2C(OCH_3)_2 + 2CuBr_2 \longrightarrow CH_3(CH_2Br)C(OCH_3)_2 + 2CuBr + HBr \quad (3)$$

$$HBr + CH_3OH \overset{\text{fast}}{\rightleftharpoons} CH_3Br + H_2O \quad (4)$$

Monobromoacetone dimethylacetal was identified not only by IR and NMR assays but also by isolation as

TABLE 1. PRODUCTS OF REACTIONS BETWEEN COPPER(II) BROMIDE AND ACETONE OR ACETONE DIMETHYLACETAL

Starting material			Residue			Distillate		
Acetone m*l*	Acetal m*l*	$CuBr_2$ mmol	Total Cu mmol	Br meq	Cu(I) mmol	HBr meq	Monobrominated substrate[a] meq	Dibrominated substrate[b] meq
4	0	6.90	6.83	10.83		1.42	1.46	
5	0	6.62	6.53	7.50		2.80	2.84	
0	5	7.19	7.17	8.60		2.66	1.65	0.92
0	5				4.41	2.05	1.70	0.28

a) Sum of monobromoacetone and monobromoacetone dimethylacetal

b) α, α′-dibromoacetone dimethylacetal

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[6] G. Brauer, "Handbuch der Preparativen Anorganischen Chemie," 2nd ed., Ferdinand Enke Verlag, Stuttgart (1962), Vol. 2, p. 888.

[7] C. D. Ritchie and P. D. Heffley, *J. Amer. Chem. Soc.*, **87**, 5402 (1965).

[8] F. P. Treadwell and W. T. Hall, "Analytical Chemistry," Vol. 2, 9th ed., J. Wiley, New York (1942), p. 583.

[9] K. Ueno, "Chelate Tekiteiho (Methods of Chelate Titration)," Nankodo, Tokyo (1962), p. 254.

neat liquid. Found: C, 33.10; H, 5.98; Br (by iodometry), 45.2%. Calcd for $C_5H_{11}O_2Br$: C, 32.81; H, 6.06; Br, 43.2%. In the course of vacuum distillation of the reaction mixture from copper(II) bromide and acetone dimethylacetal, white needles separated out. Found: C, 23.08; H, 3.90%. Calcd for $C_5H_{10}O_2Br_2$: C, 22.93; H, 3.85%. NMR spectrum of this compound in CCl_4 shows CH_2Br signal at 3.72 τ and OCH_3 peak at 3.46 τ with the intensity ratio of 2: 3, but has no absorption assignable to CH_3. Thus the compound was identified as α,α'-dibromoacetone dimethylacetal, mp 61—63°C (lit. 63.5°C). The usual iodometric determination of bromine at room temperature was not useful for this compound, but disclosed about 90% of the theoretical value at around 50°C.

By means of the gas chromatographic measurements described earlier, the equilibrium constant of the acetal formation reaction (1), $K=[(CH_3)_2C(OCH_3)_2][H_2O]/[(CH_3)_2CO][CH_3OH]^2$, was determined to be $6.6\times10^{-4}\text{M}^{-1}$ at 0°C and $5.5\times10^{-4}\text{M}^{-1}$ at 8.15°C. These values are close to $6.5\times10^{-4}\text{M}^{-1}$ at 10°C and $4.0\times10^{-4}\text{M}^{-1}$ at 25°C obtained spectrophotometrically by Bell, *et al.*[10]

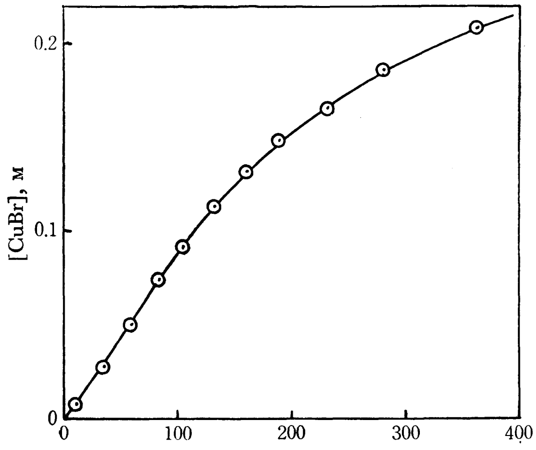

Fig. 1. A kinetic run of the reaction between copper(II) bromide and acetone in methanol at 0°C. Initial concentrations: $[CuBr_2]=0.234\text{M}$, $[\text{acetone}]=1.78\text{M}$.

The Rate Equation for the Reaction of Copper(II) Bromide with Acetone and Acetone dimethylacetal. A kinetic run of the title reaction shows complicated feature as illustrated by the curve in Fig. 1. The rate of decrease of copper(II) bromide can't be formulated by a simple rate law concerning the concentration of copper(II) bromide. Complicating factors involve the retarding effect of copper(I) bromide and the accelerating effect of hydrogen bromide, both accumulating with the progress of reaction. Thus the complete analysis of each kinetic run was difficult and effects of various factors were examined on the initial rate (R_0) which was defined by the initial linear portion of the [CuBr] *vs.* time curve.

Plots of R_0/[acetone] *vs.* [acetal]/[acetone] gave straight lines at constant $[CuBr_2]$ as illustrated in Fig. 2. Both of the intercept and the slope of these straight lines increase with the concentration of copper(II) bromide, conforming to the rate Eq. (5),

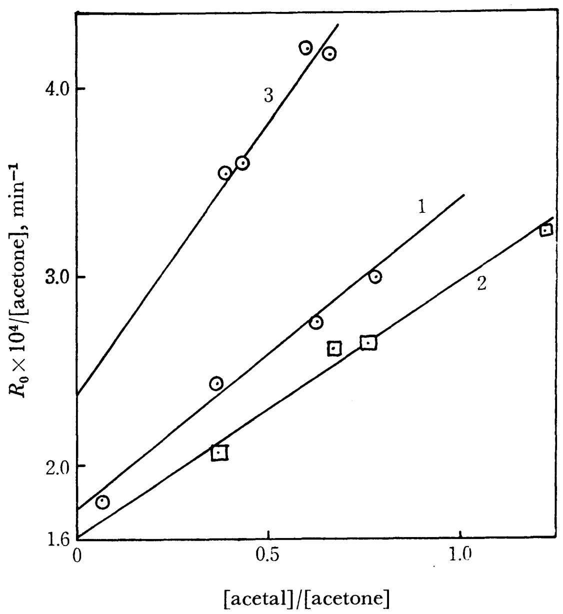

Fig. 2. Linear plots of initial rate data. Line 1: $[CuBr_2]=0.658\text{ M}$, 0°C; line 2: $[CuBr_2]=0.368\text{M}$. 8.15°C; line 3: $[CuBr_2]=0.142\text{M}$, 22.05°C.

$$R_0 = (k_1'+k_2'[CuBr_2])[CuBr_2][\text{acetone}] + (k_1''+k_2''[CuBr_2])[CuBr_2][\text{acetal}] \qquad (5)$$

where acetal stands for acetone dimethylacetal. The concentrations of acetone and acetal in the reaction mixture were measured at several time intervals and confirmed to be unchanged from the initial equilibrium value governed by the mixing ratio of acetone and methanol.

Table 2. Rate constants referring to the rate equation (5) for reactions of copper(II) bromide with acetone and acetone dimethylacetal

Temp. °C	$k_1'\times10^5$ $\text{M}^{-1}\text{sec}^{-1}$	$k_2'\times10^5$ $\text{M}^{-2}\text{sec}^{-1}$	$k_1''\times10^5$ $\text{M}^{-1}\text{sec}^{-1}$	$k_2''\times10^5$ $\text{M}^{-2}\text{sec}^{-1}$
0	~0	0.68	~0	0.62
8.15	0.12	1.73	0.04	1.52
22.05	1.10	13.5	1.19	12.4

Observed values of rate constants are summarized in Table 2. Activation energies referring to the third-order rate constants k_2' and k_2'' are both 22.0 kcal/mol, and frequency factors are 2.46×10^{12} and $2.29\times10^{12}\text{M}^{-2}\text{sec}^{-1}$, respectively. It is worth noting that the second-order rate constant is smaller than one tenth of the third-order rate constant in either case, vanishing at 0°C. Furthermore, the corresponding constants for acetone and acetone dimethylacetal lie quite close together. Taking into account the poor accuracy in gas chromatographic determinations of these two substrates, it might be allowed to presume that $k_1'=k_1''$ and $k_2'=k_2''$, that is, acetone and the acetal are brominated at equal rates. Then Eq. (5) is simplified as (6). In fact straight lines are obtained by plotting

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[10] J. M. Bell, D. G. Kubler, P. Sartwell, and R. G. Zepp, *J. Org. Chem.*, **30**, 4284 (1965).

$$R_0 = (k_1+k_2[\text{CuBr}_2])([\text{acetone}]+[\text{acetal}])[\text{CuBr}_2] \qquad (6)$$

$R_0/([\text{acetone}]+[\text{acetal}])[\text{CuBr}_2]$ against $[\text{CuBr}_2]$ as illustrated in Fig. 3, resulting in the rate constants as listed in Table 3.

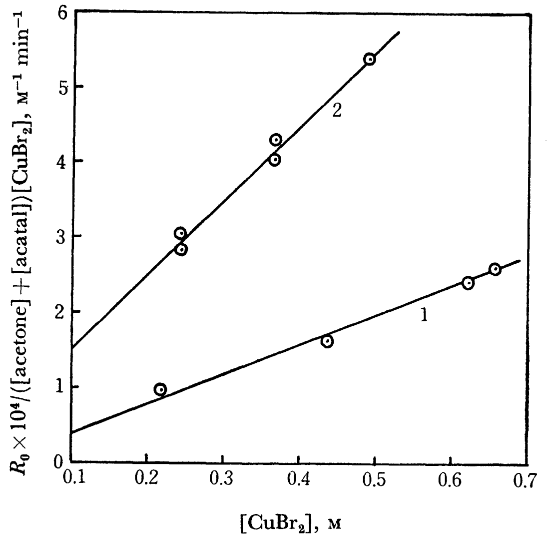

Fig. 3. Linear plots of initial rate data at 0° (line 1) and 8.15°C (line 2) referring to Eq. (6).

TABLE 3. RATE CONSTANTS REFERRING TO THE RATE EQUATION (6) FOR REACTIONS OF COPPER(II) BROMIDE WITH ACETONE AND ACETONE DIMETHYLACETAL

Temp. °C	$k_1\times10^5$M^{-1}sec^{-1}	$k_2\times10^5$M^{-1}sec^{-1}
0	~0	0.66
8.15	0.08	1.67
22.05	1.13	13.0

Retardation Effect of Copper(I) Bromide. Copper(I) bromide is insoluble in methanol and acetone, but it is dissolved appreciably in the solvents with the coexistence of copper(II) bromide. The solubilization of copper(I) halide is well known to be effected by halide ions forming complex ions. Similar effect may be brought about by the addition of copper(II) halide. McConnell and Davidson, for example, suggested the existence of Cu_2Cl_3 to interpret the interaction absorption of solutions containing copper(I), copper(II), and low concentrations of chloride ion.[11] In the present system, copper(I) bromide may also be considered to be solubilized by the interaction with copper(II) bromide as represented by Eq. (7),

$$\text{CuBr} + n\text{CuBr}_2 = \text{CuBr}\cdot n\text{CuBr}_2 \qquad (7)$$

Addition of copper(I) bromide to the reaction mixture lowers the initial rate remarkably. If the retarding effect of copper(I) bromide is caused by the partial deactivation of copper(II) bromide according to Eq. (7), the reduced rate at 0°C may be represented by Eq. (8) since k_1 in Eq. (6) is zero at 0°C.

$$R_0 = k_2([\text{acetone}]+[\text{acetal}])([\text{CuBr}_2]-n[\text{CuBr}])^2 \qquad (8)$$

If much less quantity of copper(I) bromide is added to copper(II) bromide, Eq. (8) can be approximated by Eq. (9). In Fig. 4 are plotted the initial rates measured at constant concentrations of copper(II) bromide and acetone against the concentration of copper(I) bromide added. From the slope and the intercept of this straight line n was obtained as 1.6.

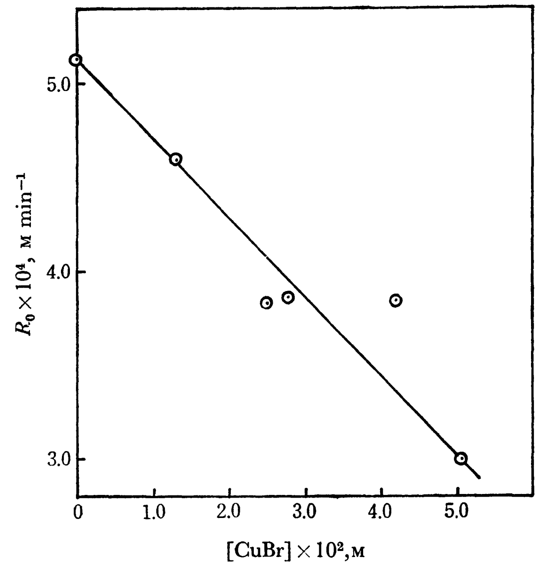

Fig. 4. The retarding effect of copper(I) bromide at 0°C. $[\text{CuBr}_2]=0.401$M, $[\text{acetone}]+[\text{acetal}]=7.47$M.

$$R_0 = k_2([\text{acetone}]+[\text{acetal}]) \times ([\text{CuBr}_2]-2n[\text{CuBr}])[\text{CuBr}_2] \qquad (9)$$

Addition of tetraethylammonium bromide also suppressed the bromination reaction of copper(II) bromide as shown in Table 4. This is probably caused by coordination of bromide ions to copper(II) forming complex anions such as $CuBr_3^-$ and $CuBr_4^{2-}$.

TABLE 4. RETARDATION EFFECT OF TETRAETHYLAMMONIUM BROMIDE ON THE REACTION OF COPPER(II) BROMIDE WITH ACETONE AND ACETONE DIMETHYLACETAL AT 0°C

$[\text{CuBr}_2]=0.0713$M, $[\text{acetone}]+[\text{acetal}]=2.38$M

Et_4NBr added, M	Initial rate$\times10^6$, M sec^{-1}
0	5.25
0	4.72
0.020	4.72
0.059	4.20
0.079	4.20
0.136	1.83
0.194	1.27
0.291	0.65
0.933 (heterogeneous system)	0.00

Acid-catalyzed Reactions of Copper(II) Bromide with Acetone and Acetone Dimethylacetal. If dry acids such as hydrogen bromide, perchloric acid, and *p*-toluenesulfonic acid are added in advance, the initial rate of the reaction is increased linearly with the acid concentration. The initial rate of the acid-catalyzed reaction ΔR_0 was calculated as the difference between the initial rates in the presence and absence of an acid. Figure

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[11] H. McConnell and N. Davidson, *J. Amer. Chem. Soc.*, **72**, 3168 (1950).

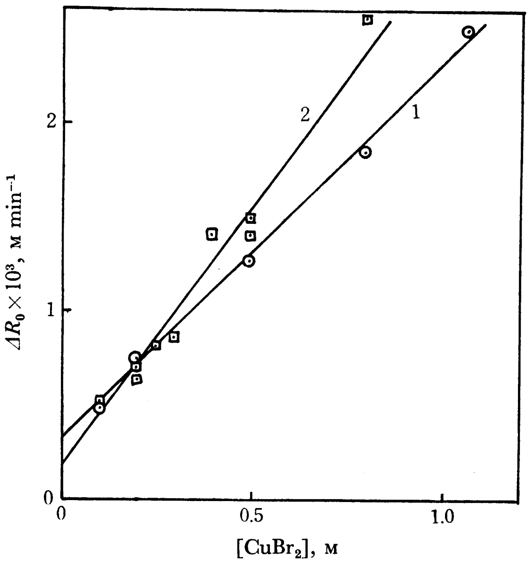


Fig. 5. The initial rate of acid-catalyzed reaction of copper(II) bromide with acetone and acetone dimethylacetal as a funtion of the concentration of copper(II) bromide at 0°C. Line 1: [HClO$_4$]=0.0318M, [acetone]+[acetal]=4.56M: Line 2: [*p*-toluenesulfonic acid]=0.0406M, [acetone]+[acetal]= 4.56M.

5 shows the dependence of ΔR_0 upon the concentration of copper(II) bromide at constant concentrations of perchloric acid or *p*-toluenesulfonic acid and acetone. The linear relationship between ΔR_0 and [CuBr$_2$] reveals that there exist two reaction pathways, one being independent of and the other first-order with respect to copper(II) bromide. At constant concentrations of copper(II) bromide and perchloric acid ΔR_0 increased with the concentration of acetone. However, the interrelation was not linear but represented by a Langmuir-type curve as illustrated in Fig. 6.

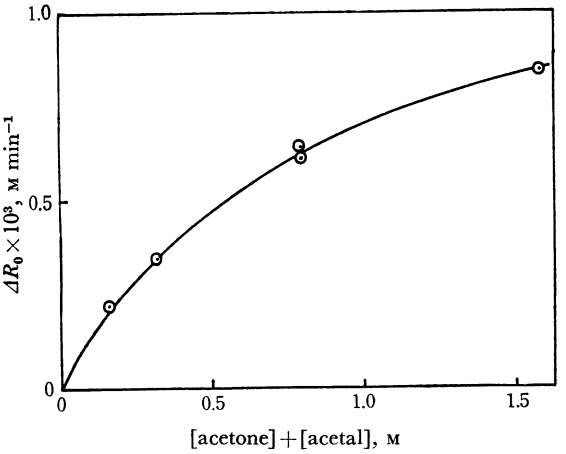
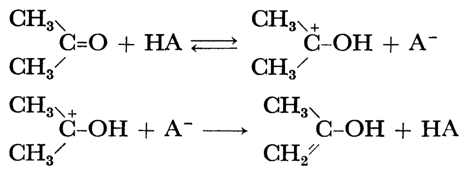


Fig. 6. The initial rate of acid-catalyzed reaction of copper(II) bromide with acetone and acetone dimethylacetal as a function of the combined concentration of acetone and the acetal at 0°C. [HClO$_4$]=0.034M, [CuBr$_2$]=0.659M.

Discussion

The reaction between acetone and methanol seemed troublesome for study of the reaction of copper(II) bromide with acetone, but fortunately the equilibria of acetal formation reactions are established so quickly in the presence of copper(II) bromide and the amount of hemiacetal is known to be so minute[10] that a single equilibrium (1) needs to be considered. Furthermore approximately equal rates of reactions of acetone and acetone dimethylacetal towards copper(II) bromide simplified the analysis of rate data.

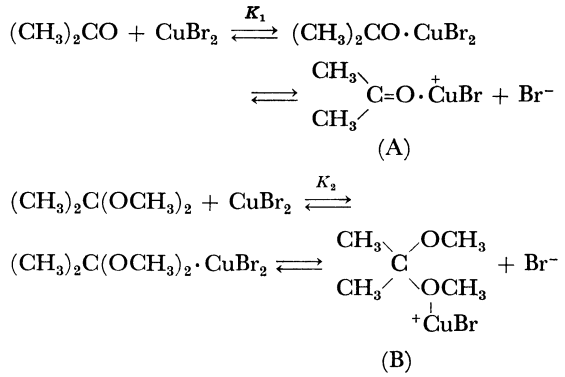
It has been well established that the acid catalyzed halogenation of acetone in aqueous solutions is preceded by the rate-controlling enolization steps:[12]



$$\begin{array}{l}\mathrm{CH_3}\diagdown\\ \quad\mathrm{C{=}O}\\ \mathrm{CH_3}\diagup\end{array} + \mathrm{HA} \rightleftharpoons \begin{array}{l}\mathrm{CH_3}\diagdown_{+}\\ \quad\mathrm{C{-}OH}\\ \mathrm{CH_3}\diagup\end{array} + \mathrm{A^-} \tag{10}$$

$$\begin{array}{l}\mathrm{CH_3}\diagdown_{+}\\ \quad\mathrm{C{-}OH}\\ \mathrm{CH_3}\diagup\end{array} + \mathrm{A^-} \longrightarrow \begin{array}{l}\mathrm{CH_3}\diagdown\\ \quad\mathrm{C{-}OH}\\ \mathrm{CH_2}/\!\!/\end{array} + \mathrm{HA} \tag{11}$$

By analogy, the first steps in reactions of copper(II) bromide with acetone and the acetal may be coordination of substrate molecules to copper atoms (Eqs. (12) and (13)). Partial ionizations of copper(II) bromide itself and of substrate complexes will be at rapid equilibrium, and both the neutral and charged complexes are conceivable to be equally effective in succeeding reactions.



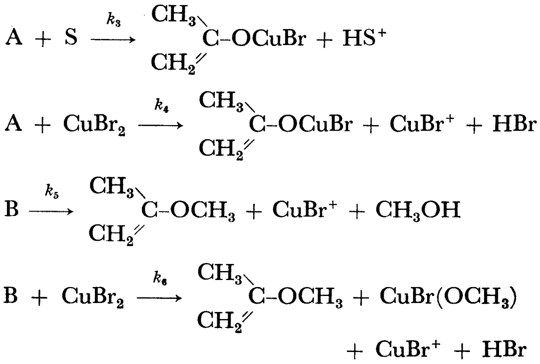
$$\mathrm{(CH_3)_2CO + CuBr_2} \overset{K_1}{\rightleftharpoons} \mathrm{(CH_3)_2CO\cdot CuBr_2} \rightleftharpoons \begin{array}{l}\mathrm{CH_3}\diagdown\\ \quad\mathrm{C{=}O\cdot \overset{+}{C}uBr}\\ \mathrm{CH_3}\diagup\end{array} + \mathrm{Br^-} \tag{12}$$

(A)

$$\mathrm{(CH_3)_2C(OCH_3)_2 + CuBr_2} \overset{K_2}{\rightleftharpoons} \mathrm{(CH_3)_2C(OCH_3)_2\cdot CuBr_2} \rightleftharpoons \begin{array}{l}\mathrm{CH_3}\diagdown\ \diagup\mathrm{OCH_3}\\ \qquad\mathrm{C}\\ \mathrm{CH_3}\diagup\ \diagdown\mathrm{OCH_3}\\ \qquad\quad\ |\\ \qquad\ \ \mathrm{^{+}CuBr}\end{array} + \mathrm{Br^-} \tag{13}$$

(B)

Although Kochi[3] reported that the initial rate of the reaction between acetone and copper(II) chloride in water was one-half order in gross copper(II), the observed initial rate Eq. (5) or (6) in the present study reflects the existence of two kinds of transition states for each substrate, one containing another copper(II) bromide and the other not. Thus steps (14) through (17) are presumed to be rate-controlling.



$$\mathrm{A + S} \xrightarrow{k_3} \begin{array}{l}\mathrm{CH_3}\diagdown\\ \quad\mathrm{C{-}OCuBr}\\ \mathrm{CH_2}/\!\!/\end{array} + \mathrm{HS^+} \tag{14}$$

$$\mathrm{A + CuBr_2} \xrightarrow{k_4} \begin{array}{l}\mathrm{CH_3}\diagdown\\ \quad\mathrm{C{-}OCuBr}\\ \mathrm{CH_2}/\!\!/\end{array} + \mathrm{CuBr^+ + HBr} \tag{15}$$

$$\mathrm{B} \xrightarrow{k_5} \begin{array}{l}\mathrm{CH_3}\diagdown\\ \quad\mathrm{C{-}OCH_3}\\ \mathrm{CH_2}/\!\!/\end{array} + \mathrm{CuBr^+ + CH_3OH} \tag{16}$$

$$\mathrm{B + CuBr_2} \xrightarrow{k_6} \begin{array}{l}\mathrm{CH_3}\diagdown\\ \quad\mathrm{C{-}OCH_3}\\ \mathrm{CH_2}/\!\!/\end{array} + \mathrm{CuBr(OCH_3)} + \mathrm{CuBr^+ + HBr} \tag{17}$$

Here S stands for a proton acceptor which may be a methanol molecule. The detailed scheme for bromina-

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[12] R. P. Bell and Y. Yates, *J. Chem. Soc.*, **1962**, 1927.

tion of acetone dimethylacetal is very difficult to envisage, but is just assumed to involve an enolic ether as visualized in Eq. (16). In steps (15) and (17) copper(II) bromide is supposed to act as a proton acceptor in accordance with the second term with respect to copper(II) bromide in Eq. (5). Succeeding steps in which enolate intermediates are brominated by copper(II) bromide should be fast. Then the overall reaction rate is represented by Eq. (18),

$$\text{rate} = (k_3+k_4[\text{CuBr}_2])[\text{A}] + (k_5+k_6[\text{CuBr}_2])[\text{B}]. \qquad (18)$$

Substituting equilibrium values of [A] and [B] derived from Eqs. (12) and (13) to Eq. (18),

$$\begin{aligned}\text{rate} = \{&(k_3+k_4[\text{CuBr}_2])K_1[\text{CuBr}_2][\text{acetone}] \\ &+ (k_5+k_6[\text{CuBr}_2])K_2[\text{CuBr}_2][\text{acetal}]\}/ \\ &(1+K_1[\text{acetone}]+K_2[\text{acetal}]). \qquad (19)\end{aligned}$$

If $1 \gg (K_1[\text{acetone}]+K_2[\text{acetal}])$, the rate Eq. (19) reduces to the observed rate law (5) with $k_1'=k_3K_1$, $k_2'=k_4K_1$, $k_1''=k_5K_2$, and $k_2''=k_6K_2$.

Mechanisms of bromination of enolic molecules by copper(II) bromide in succeeding steps are not clear at all. Castro, *et al.*[2)] obtained a rate equation independent of allyl alcohol, $\text{rate}=k[\text{CuBr}_2]^2$, for bromination of allyl alcohol by copper(II) bromide in refluxing methanol and attributed the rate expression to the reversible dissociation of copper(II) bromide to molecular bromine.

$$2\text{CuBr}_2 \rightleftharpoons 2\text{CuBr} + \text{Br}_2$$

Similar possibility may not be denied for the present system although it seems less probable since the equilibrium concentration of bromine will be very low at 0°C. Alternatively copper(II) bromide itself might brominate an enolate molecule.

The retardation by copper(I) bromide was attributed to the association with copper(II) bromide invalidating 1.6 times as many molecules of the latter. Similar retarding effect of copper(I) chloride was also observed by Lorenzini and Walling[4)] in reactions of copper(II) chloride with butyraldehydes in aqueous isopropyl alcohol and by Kochi[3)] in the reaction of copper(II) chloride with acetone in water.

Bromide ions were found to act as a retarder in the present system. On the contrary, chloride ions were reported to stimulate reactions both by the Walling group and Kochi. This discrepancy is due to the difference in the reaction media. As discussed above copper(II) halide plays a dual function. The activity of copper(II) halide as a catalyst would be $\text{CuX}^+ > \text{CuX}_2 > \text{CuX}_3^-$, while effectiveness as a halogenating agent should be $\text{CuX}^+ < \text{CuX}_2 < \text{CuX}_3^-$. In aqueous solutions ionization of copper(II) halide (Eq. (20)) is extensive, and the halogenating capacity is rather

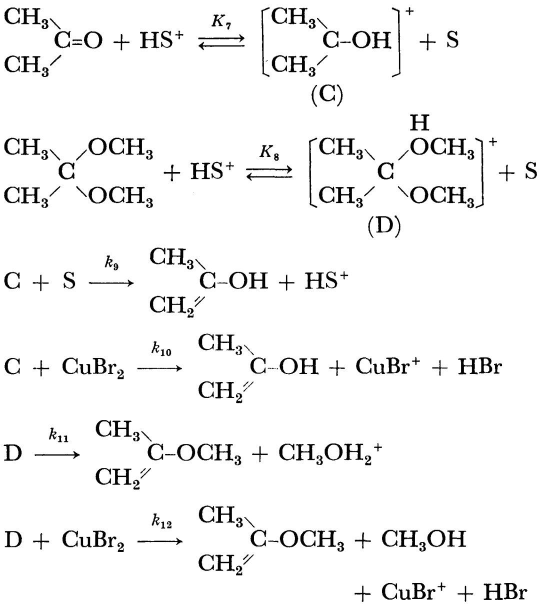
$$\text{CuX}_2 \rightleftharpoons \text{CuX}^+ + \text{X}^- \qquad (20)$$

poor. Addition of chloride ions reverts the equilibrium (20) to the left, increasing the chlorinating efficiency. On the other hand in methanol the ionization (20) is less significant and excess bromide ions added will enhance the addition equilibrium (21),[13)]

$$\text{CuX}_2 + \text{X}^- \rightleftharpoons \text{CuX}_3^- \qquad (21)$$

thus diminishing the catalytic ability of copper(II). In reaction systems containing some acid the coordinative activation of an acetone molecule is effected by a proton, and copper(II) bromide only needs to function as a brominating agent. In such a case addition of bromide ions should increase the reaction rate. In fact, although the initial rate of reaction between copper(II) bromide (0.073M) and acetone (1.30M) in methanol containing perchloric acid (0.026M) was 9.7×10^{-7}M/sec at 0°C, addition of tetraethylammonium bromide in excess (0.27M) raised the rate to 5.8×10^{-6}M/sec. A methanol solution of copper(II) bromide at such a concentration shows a brown color, but changes to purple by addition of excess bromide ions[14)] suggesting formations of CuBr_3^- and CuBr_4^{2-}.

In analogy to Eqs. (10) and (11) for the reaction with bromine, the following scheme is presumed for the acid catalyzed reactions of copper(II) bromide with acetone and acetal. The concentration of acids employed was usually less than 0.15M and the complete



$$(\text{CH}_3)_2\text{C=O} + \text{HS}^+ \underset{}{\overset{K_7}{\rightleftharpoons}} \left[(\text{CH}_3)_2\text{C-OH}\right]^+ (\text{C}) + \text{S} \qquad (22)$$

$$(\text{CH}_3)_2\text{C}(\text{OCH}_3)_2 + \text{HS}^+ \overset{K_8}{\rightleftharpoons} \left[(\text{CH}_3)_2\text{C}(\text{OCH}_3)(\overset{\text{H}}{\text{O}}\text{CH}_3)\right]^+ (\text{D}) + \text{S} \qquad (23)$$

$$\text{C} + \text{S} \xrightarrow{k_9} \text{CH}_2\text{=C(CH}_3\text{)-OH} + \text{HS}^+ \qquad (24)$$

$$\text{C} + \text{CuBr}_2 \xrightarrow{k_{10}} \text{CH}_2\text{=C(CH}_3\text{)-OH} + \text{CuBr}^+ + \text{HBr} \qquad (25)$$

$$\text{D} \xrightarrow{k_{11}} \text{CH}_2\text{=C(CH}_3\text{)-OCH}_3 + \text{CH}_3\text{OH}_2^+ \qquad (26)$$

$$\text{D} + \text{CuBr}_2 \xrightarrow{k_{12}} \text{CH}_2\text{=C(CH}_3\text{)-OCH}_3 + \text{CH}_3\text{OH} + \text{CuBr}^+ + \text{HBr} \qquad (27)$$

dissociation could be assumed, HS^+ then standing for the protonated methanol molecule. From Eqs. (22) and (23) concentrations of protonated substrates C and D are represented by

$$[\text{C}] = K_7[\text{HA}]_0[\text{acetone}]/([\text{MeOH}]+K_7[\text{acetone}]+K_8[\text{acetal}])$$

$$[\text{D}] = K_8[\text{HA}]_0[\text{acetal}]/([\text{MeOH}]+K_7[\text{acetone}]+K_8[\text{acetal}])$$

where $[\text{HA}]_0$ stands for the total concentration of the acid employed. Then the rate of the acid-catalyzed reaction, namely the difference between rates in the presence and absence of an acid, can be written as

$$\begin{aligned}\Delta(\text{rate}) = \{&(k_9+k_{10}[\text{CuBr}_2])K_7[\text{acetone}] \\ &+ (k_{11}+k_{12}[\text{CuBr}_2])K_8[\text{acetal}]\}[\text{HA}]_0/ \\ &([\text{MeOH}]+K_7[\text{acetone}]+K_8[\text{acetal}]) \qquad (28)\end{aligned}$$

If it is presumed that $k_9=k_{11}=k_a$, $k_{10}=k_{12}=k_b$, and $K_7=K_8=K$, Eq. (28) reduces to Eq. (29):

[13)] J. C. Barnes and D. N. Hume, *Inorg. Chem.*, **2**, 444 (1963).

[14)] S. Matsuo, *Nippon Kagaku Zasshi*, **83**, 1229 (1962).

$$\Delta(\text{rate}) = (k_a + k_b[\text{CuBr}_2])[\text{HA}]_0 K([\text{acetone}] + [\text{acetal}])/\{[\text{MeOH}] + K([\text{acetone}] + [\text{acetal}])\} \quad (29)$$

Braude[15] determined the equilibrium constants $K_B{}^s$ of the proton-transfer reactions $SH^+ + B \rightleftarrows BH^+ + S$ between the solvated proton SH^+ and the proton-accepting indicator (B), *p*-nitroaniline. The value of $K_B{}^s$ was 9, 20, 31, and 53 for water, dioxane, ethanol, and acetone, respectively, indicating that the basicity decreases in the order, water > dioxane > ethanol > acetone. The relative basic strengths of water, methanol, and ethanol were also reported[16] to be 1 : 0.13 : 0.33 or 1 : 0.13 : 0.22. These two sets of data indicate that the basicity of acetone is very similar to that of methanol, namely the equilibrium constant K_7 of the proton-transfer equilibrium (22) is close to one. K_8 will not be larger than K_7. Then, in the denominator of Eq. (29), [MeOH] is much larger than the second term in the concentration region of acetone employed (Fig. 5). Equation (29) may thus be approximated by Eq. (30),

$$\Delta(\text{rate}) = (k_a + k_b[\text{CuBr}_2])[\text{HA}]_0 K([\text{acetone}] + [\text{acetal}])/[\text{MeOH}] \quad (30)$$

The rate equation (30) for the acid-catalyzed reaction well conforms with observed dependences of the initial rate on the concentrations of acid (first order) and copper(II) bromide (Fig. 5), but contradicts the observed acetone dependence (Fig. 6). Equation (30) requires a straight line relationship as observed in Fig. 3, but actual data gave such a Langmuir-type curve. This discrepancy could be attributed to water formation in the reaction (1). As described in Experimental, the equilibrium constant of the acetal formation reaction (1) was determined to be $6.6 \times 10^{-4}\text{M}^{-1}$ at 0°C. If it is put that $[H_2O] = [\text{acetal}]$, $[H_2O] = [\text{MeOH}](K[\text{acetone}])^{1/2}$ and takes rather large values as 0.2M when [acetone] = 0.1 and [MeOH] = 25M, and 0.6M when [acetone] = 1 and [MeOH] = 23M. Under such circumstances appreciable portions of protons are trapped by water molecules and the proton transfer equilibria to be taken into account are intractably complex. Qualitatively speaking, however, with the increase in the acetone concentration employed, the concentration of water is increased and the fraction of protons transferred to acetone moleculs is decreased. This might be concluded as the reason why the rate of the acid-catalyzed reaction is not enhanced in proportion to the acetone concentration (Fig. 6).

The authors are grateful to Dr. T. Ogura for his valuable discussion. Thanks are also due to Mr. J. Gohda for elemental analysis and IR measurements, and to Mr. K. Noda of the Osaka Municipal Technical Research Institute for NMR measurements.

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[15] E. A. Braude, *J. Chem. Soc.*, **1948**, 1971.

[16] R. P. Bell, "The Proton in Chemistry," Cornell University Press, Ithaca, N. Y. (1959), p. 43.