Brominations of Aliphatic Ketones by Copper(II) Bromide in Organic Solvents. II. The Reaction of Acetone with Copper(II) Bromide in *N*,*N*-Dimethylformamide

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Because of a long induction period, the reaction between acetone and copper(II) bromide does not occur readily in pure DMF. However, in the presence of an acid, it proceeds readily. The initial rate is proportional to the product of the concentration of acetone and perchloric acid, but independent of the concentration of copper(II) bromide. The acid-catalyzed bromination of acetone by bromine has also been studied in DMF and found to obey the same second-order rate law as that in water. Both bromination reactions of acetone in DMF by copper(II) bromide and bromine were interpreted to be controlled by the enolization process of acetone.

In a previous paper[1] we reported on the reaction of copper(II) bromide with acetone in methanol. In the presence of copper(II) bromide, the reaction of acetone with methanol to form acetone dimethylacetal attained equilibrium quickly even at 0°C, making the reaction system complicated. Water produced in the acetal formation made the acid-catalyzed reaction so complicated that the observed dependence of the rate upon the acetone concentration could not be explained quantitatively.

To avoid such troubles the reaction between copper(II) bromide and acetone has been studied in *N*,*N*-dimethylformamide (DMF) and found not to proceed at room temperature unless assisted by an acid catalyst. The acid-catalyzed reaction is reported in this paper.

Experimental

Materials. DMF was boiled with benzene (5 vol%) to eliminate water as an azeotrope and distilled twice under reduced pressure (bp 27—29°C/5mmHg). Contamination with the free amine was examined by means of a saturated ethanol solution of 2,4-dinitrofluorobenzene.[2] Bromine was washed with water repeatedly to eliminate chlorine and iodine, and then dissolved in a solution of pure potassium bromide and distilled over zinc oxide. The distillate was again distilled over calcium oxide and finally dried with phosphorus pentoxide. Acetone was purified by a standard method.[3] Purity of organic solvents was checked by vapor phase chromatography.

Identification and Determination of Reaction Products. After the reaction mixture was kept standing at room temperature for a few days, volatile substances were distilled under reduced pressure. In one experiment to determine the amount of copper(I) bromide, the residue was dissolved in a sulfuric acid solution containing iron(III) ammonium sulfate, and iron(II) produced was titrated with an aqueous solution of cerium(IV) ammonium sulfate.[4] In another experiment, the residue was dissolved in aqueous ammonia, and total copper was determined by electrolysis, and bromine gravimetrically as silver bromide.

Monobromoacetone in the distillate was identified by comparing the infrared spectrum and gas-chromatogram with those of the authentic specimen. A 3 m column (4 mm in diameter) containing Diglycerol (5%) and Silicone Grease (5%) on Neosorb NCS was used at 63°C with hydrogen as a carrier gas at a flow rate of 20 cc/min. Content of monobromoacetone in the distillate was determined by iodometry, and that of hydrogen bromide by titration with an aqueous solution of sodium hydroxide.

Kinetics. Acetone and perchloric acid were added to a DMF solution of copper(II) bromide in a three-necked flask equipped with a stirrer, a nitrogen gas inlet tube and an outlet tube containing calcium chloride. At appropriate time intervals, aliquots were withdrawn from the flask and quenched in cold sulfuric acid solutions of iron(III) ammonium sulfate and titrated with cerium(IV) solutions as described above.

The reaction of acetone with bromine in DMF was also followed in a similar fashion without the nitrogen flow. Each aliquot was quenched in a potassium bromide solution buffered with acetic acid and sodium acetate, and the liberated iodine was titrated with a thiosulfate solution.[5] Monobromoacetone does not liberate iodine under these conditions.

In spite of careful purification of DMF, fluctuation in the reaction rate with the change of solvent was inevitable. Hence the dependence of the reaction rate on concentration was examined with DMF in the same bottle.

Results

Stoichiometry of the Reaction. Acetone was allowed to react with copper(II) bromide at room temperature for several days, and then the mixture was analyzed by the methods described in the Experimental Section. As shown in Table 1, the mole ratio of copper(I) bromide to monobromoacetone in the first experiment was close to 2 : 1 in conformity with the following equation.

$$CH_3COCH_3 + 2CuBr_2 = CH_3COCH_2Br + 2CuBr + HBr \tag{1}$$

The very low acid content in the distillate is due to the formation of a non-volatile adduct $(CH_3)_2NCHO \cdot HBr$.[6] This was proved by the second set of data in Table 1 which shows that sum of bromine gram-atoms in the residue and in the distillate is colse to twice moles of copper(II) bromide employed.

Kinetics. When acetone was mixed with a DMF solution of copper(II) bromide at 30°C, an in-

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[1] Y. Kojima and S. Kawaguchi, This Bulletin, **45**, 1293 (1972).

[2] S. Buffagni and T. M. Dunn, *J. Chem. Soc.*, **1961**, 5105

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

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

[5] R. P. Bell and K. Yates, *J. Chem. Soc.*, **1962**, 1927.

[6] S. J. Kuhn and J. S. McIntyre, *Can. J. Chem.*, **43**, 995 (1965).

TABLE 1. PRODUCTS OF THE REACTION BETWEEN ACETONE AND COPPER(II) BROMIDE IN DMF AT ROOM TEMPERATURE FOR SEVERAL DAYS

$CuBr_2$ used mmol	Residue			Distillate	
	Total Cu mg·atom	Total Br mg·atom	Cu(I) mg·atom	H^+ mmol	CH_3COCH_2Br mmol
			10.87	0.35	4.92
10.13	10.00	15.17		0.41	4.18

duction period longer than 100 min was observed before the reaction started (curve 1, Fig. 1). This result suggests that copper(II) bromide does not react with acetone in pure DMF and the reaction after the induction period might be caused by the catalytic effect of hydrogen bromide produced by side reactions. In fact when perchloric acid was added to the system, the reaction started without the induction period (curve 2, Fig. 1). However, the disturbing influences of reaction products made the kinetic run too difficult to analyze, and the effects of various factors were investigated by the initial rate method.

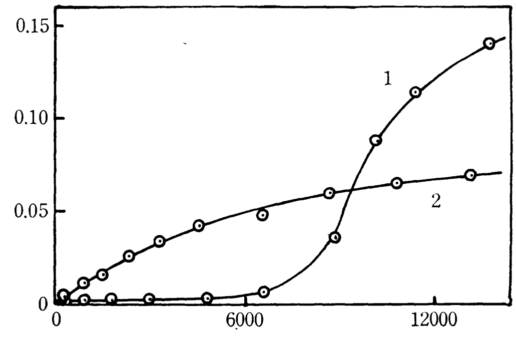

Fig. 1. Rates of reactions between acetone and copper (II) bromide in the absence (Curve 1) and presence (Curve 2) of perchloric acid. Curve 1: $[CuBr_2]=0.310$ M, [acetone] $=3.45$ M, 30°C. Curve 2: $[CuBr_2]=0.227$ M, [acetone] $=1.73$ M, $[HClO_4]=0.115$ M, 25°C.

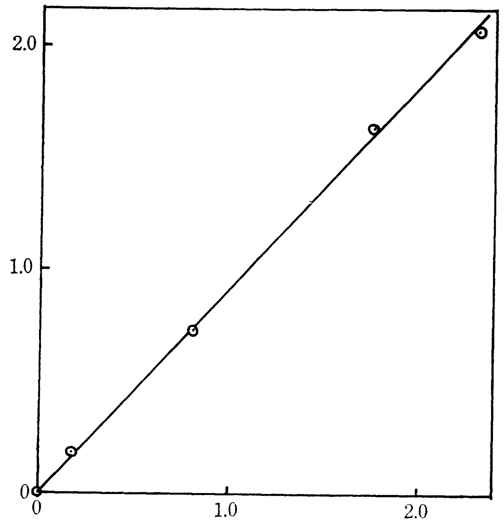

Fig. 2. The dependence of the reaction rate on the perchloric acid concentration at 23.2°C. $[CuBr_2]=0.284$ M, [acetone] $=1.73$ M.

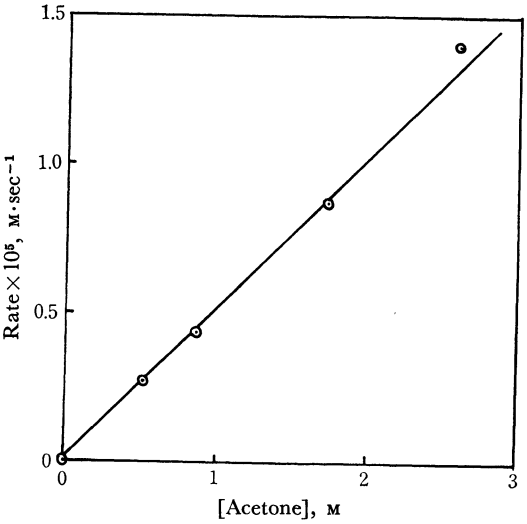

Fig. 3. The dependence of the reaction rate on the acetone concentration at 23.2°C. $[CuBr_2]=0.284$ M, $[HClO_4]=0.0115$ M.

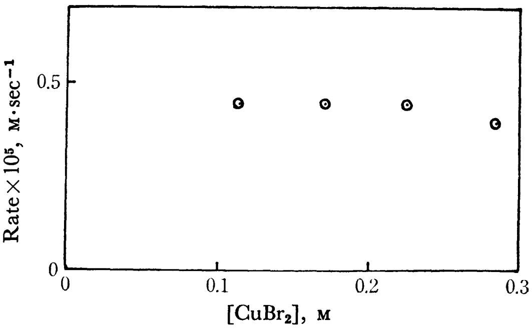

Fig. 4. The independence of the reaction rate from the copper(II) bromide concentration at 23.2°C. [acetone] $=0.875$ M, $[HClO_4]=0.0115$ M.

As shown in Figs. 2, 3, and 4 the initial rates of the reaction of acetone with copper(II) bromide in DMF at 23.2°C are proportional to the products of perchloric acid and acetone concentrations and independent of the copper(II) bromide concentration, providing the following equation.

$$d[CuBr]/dt = k[\text{acetone}][HClO_4] \qquad (2)$$

The second order rate constant was obtained as $k=4.60\times10^{-4}M^{-1}sec^{-1}$ at 23.2°C. In these experiments perchloric acid was added as a 60% aqueous solution. The effect of water on the reaction rate was confirmed in advance to be negligible.

At 0°C, however, the rate of the acid-catalyzed reaction of acetone with copper(II) bromide was not independent of the latter concentration. As shown in Table 2 the pseudo second-order rate constant k in-

Table 2. Rate data of the acid-catalyzed reaction between acetone and copper(II) bromide in DMF at 0°C

$[CuBr_2]$, M	[acetone], M	$[HClO_4]$, M	Initial rate $\times 10^6$ M·sec^{-1}	Pseudo 2nd-order rate const. $\times 10^5$ M^{-1} sec^{-1}
0.038	1.75	0.046	0.88	1.1
0.075	1.75	0.046	1.18	1.5
0.113	1.75	0.046	1.75	2.2
0.200	1.75	0.046	2.27	2.8
0.225	0.87	0.023	0.52	2.9

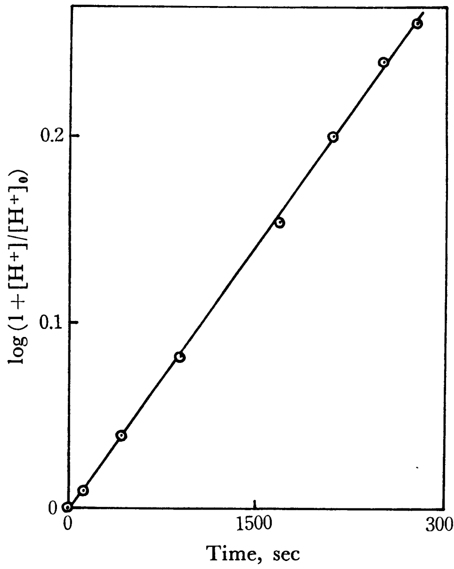

Fig. 5. The pseudo first-order plot of a kinetic run of the reaction of acetone with bromine in DMF at 23.2°C. [acetone] = 1.144 M, $[Br_2]$ = 0.189 M, $[HClO_4]$ = 0.096 M.

creased with the concentration of copper(II) bromide, but no simple relationship between them could be found.

The Acid-catalyzed Bromination of Acetone by Bromine. For the sake of comparison, the acid-catalyzed bromination of acetone by bromine was followed in DMF solutions. With a large excess of acetone the reaction proceeded according to the pseudo first-order rate law as evidenced by the linear plot of $\log(1+[H^+]/[H^+]_0)$ *vs.* time in Fig. 5. Values of the second-order rate constant k_{Br} in the equation

$$-d[Br_2]/dt = d[H^+]/dt$$
$$= k_{Br}[\text{acetone}]([H^+]_0 + [H^+]) \quad (3)$$

were 2.2×10^{-5}, 6.1×10^{-5}, and 19.0×10^{-5} M^{-1}sec^{-1} at 0.0, 11.0, and 23.2°C, respectively. From these data kinetic parameters were calculated as $E_a = 14.8$ kcal·mol^{-1} and $A = 1.65\times10^7$ M^{-1}sec^{-1}.

Although the reaction of acetone with copper(II) bromide was followed by measuring the copper(I) bromide concentration according to Eq. (1), that with elemental bromine was followed by measuring the bromine concentration according to the following equation.

$$CH_3COCH_3 + Br_2 \rightarrow CH_3COCH_2Br + HBr$$

Thus k_{Br} defined by Eq. (3) should be compared with one half of k in Eq. (2). The value of k_{Br}, 19.0×10^{-5} M^{-1}sec^{-1} at 23.2°C is close to one half of k at the same temperature.

Discussion

Kosower *et al.*[7] reported reactions of various ketones with copper(II) chloride or copper(II) bromide at temperatures higher than 80°C. However, the present investigation revealed that copper(II) bromide does not react readily with acetone in pure DMF at room temperature, a long induction period being observed before the reaction starts. Dissolution of copper(II) bromide in DMF is very exothermic and the solutions were usually prepared with cooling in an ice-bath. If a copper(II) bromide solution in DMF prepared without cooling and heated spontaneously is allowed to react with acetone, the induction period almost disappears. On heating, DMF tends to decompose to dimethylamine and carbon monoxide,[8] and dialkylamine is known to react with copper(II) halides.[9] In fact it was confirmed that copper(II) bromide reacts with dimethylamine much faster than with acetone in DMF. Thus the following reactions may occur during the induction period of the reaction between copper(II) bromide and acetone in DMF, and hydrogen bromide produced may catalyze the latter reaction.

$$(CH_3)_2NCHO \rightarrow (CH_3)_2NH + CO \quad (4)$$

$$CuBr_2 + (CH_3)_2NH \rightarrow CuBr + HBr$$
$$+ \text{ oxidation products of the amine} \quad (5)$$

Ichikawa *et al.*[10] noticed that about 20% of copper(II) chloride was consumed when heated with DMF at 80—90°C for 10 hr. These results are also interpreted to be caused by reactions similar to (4) and (5).

Copper(II) bromide reacts with acetone in methanol, playing dual roles as the catalyst which activates acetone and also as the brominating agent.[1] On the contrary the same reaction does not occur in DMF possibly because DMF is a stronger ligand to copper(II) than acetone, and the following ligand substitution equilibrium is very unfavorable to the latter.

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

[8] A. B. Thomas and E. G. Rochow, *J. Amer. Chem. Soc.*, **79**, 1843 (1957).

[9] For instance, J. R. Clifton and J. T. Yoke, III, *Inorg. Chem.*, **7**, 39 (1968).

[10] K. Ichikawa, S. Uemura, T. Hiramoto, and Y. Takagaki, *Kogyo Kagaku Zasshi*, **71**, 1657 (1968).

$$CuBr_2(DMF)_n + n\ \text{acetone} \rightleftharpoons CuBr_2(\text{acetone})_n + n\ DMF \quad (6)$$

However, copper(II) bromide still retains brominating ability and reacts with acetone even in DMF if an acid is added to catalyze the enolization of acetone.

It has been well established that the rate of acid-catalyzed halogenation of acetone by elemental halogen in an aqueous solution is controlled by the enolization step.⁵⁾ The bromination of acetone in DMF proceeds according to the same rate law (3) as that in water, and is represented by the following steps.

$$HA + DMF \rightarrow DMFH^+ + A^- \quad (7)$$

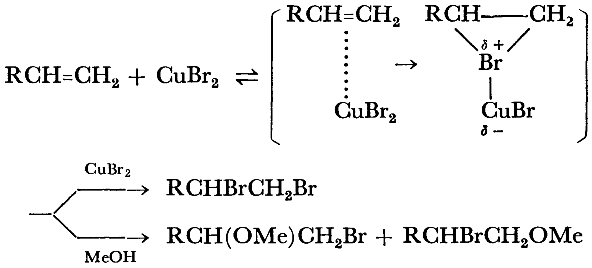
$$(CH_3)_2CO + DMFH^+ \rightleftharpoons (CH_3)_2COH^+ + DMF \quad (8)$$

$$(CH_3)_2COH^+ + DMF \xrightarrow{\text{slow}} CH_3C(OH){=}CH + DMFH^+ \quad (9)$$

$$CH_3C(OH){=}CH_2 + Br_2 \xrightarrow{\text{fast}} CH_3COCH_2Br + HBr \quad (10)$$

The second order rate constant k_{Br} at 25°C obtained by extrapolation of data at three temperatures is $2.2 \times 10^{-4}\ \text{M}^{-1}\text{sec}^{-1}$ which is several times larger than $2.8 \times 10^{-5}\ \text{M}^{-1}\text{sec}^{-1}$ in water.⁵⁾ This seems to reflect the higher basicity of DMF than that of water which functions as the proton acceptor in the rate-determining step (9).

By analogy the reaction of acetone with copper(II) bromide at around room temperature is also considered to be controlled by the enolization step (9). It is not certain, however, whether copper(II) bromide or bromine liberated therefrom brominates enolic molecules of acetone in the succeeding step (10). Castro *et al.*¹¹⁾ found the formula rate$=k[CuBr_2]^2$ for the reaction between allyl alcohol and copper(II) bromide at 64°C and attributed the rate law to the rate determining dissociation of the latter followed by bromination of the unsaturated alcohol by bromine. Barnes and Hume¹²⁾ also reported that elemental bromine was distilled from a boiling solution of copper(II) bromide in acetonitrile. On the other hand, Koyano¹³⁾ has recently reported that the bromination of olefins with copper(II) bromide in methanol at 40°C may be represented by the following polar mechanism.



At such lower temperatures as employed in the present investigation, the following equilibrium concentration of elemental bromine produced by the dissociation of copper(II) bromide may not be enough to explain the observed overall rates.

$$2CuBr_2 \rightleftharpoons 2CuBr + Br_2 \quad (11)$$

It might be preferable to consider that copper(II) bromide plays a role of the brominating agent.

At 0°C the initial rate shows some dependence on the copper(II) bromide concentration. This may indicate that the brominating step is slower than the preceding enolization steps (7)—(9) at 0°C. The detailed mechansim is not clear.

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11) C. E. Castro, E. J. Gaugham, and O. C. Owsley, *J. Org. Chem.*, **30**, 587 (1965).

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

13) T. Koyano, This Bulletin, **44**, 1158 (1971).