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The Liquid-phase Oxidation of Methylbenzenes by the Cobalt-Copper-Bromide System

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The liquid-phase oxidation of methylbenzenes catalyzed by a catalyst system composed of cobalt(II) and copper(II) acetates and sodium bromide was carried out in acetic acid at 150 °C. The corresponding benzyl acetates and benzaldehydes were obtained in high selectivities in most cases. A nuclear-brominated product, *i.e.*, 3-bromo-4-methoxytoluene was also obtained in the oxidation of *p*-methoxytoluene, which has two different reaction sites, *i.e.*, *o*-positions to the electron-donating methoxyl substituent and the benzyl position. However, the substitution of the bromide ion for the acetate ion in the catalyst system gave satisfactory selectivities for the side-chain oxidation products. In *p*-xylene oxidation, α,α'-diacetoxy-*p*-xylene and *p*-(acetoxymethyl)benzonic acid were also obtained, as well as *p*-methylbenzyl acetate, though their amounts were small. The oxidation of polymethylbenzenes was also carried out.

There have been many reports concerning liquid-phase oxidations catalyzed by transition metal ions.[1] In general, however, primary products (*e.g.*, aldehyde or alchhol) are more sensitive toward oxidation than the starting substrate, and the selective synthesis of alcohols with the liquid-phase oxidation has some limitations.[2] An improved method for the alcohol and glycol synthesis is to use the acetoxylation of them, by which the resulting primary products are restrained toward the secondary oxidation. In acetoxylation, many transition metals are employed as catalysts: palladium(II) acetate for a nuclear[3] and a side-chain acetoxylation of aromatic hydrocarbons,[4] silver(I) acetate for a side-chain acetoxylation,[5] and copper(II) acetate–lithium bromide,[6] and tellurium dioxide–hydrogen bromide[7] for olefens. In a previous report,[8] we have studied the liquid-phase oxidation of toluene catalyzed by a cobalt(II) acetate–sodium bromide catalyst in the presence of copper(II) acetate in acetic acid, we found that benzyl acetate, which is a useful organic intermediate for benzaldehyde and benzyl alcohol synthesis, can be synthesized in one pot.

In the oxidation of toluene catalyzed by the Co–Cu–Br system, the reaction can be considered to proceed through the abstraction of α-hydrogen by bromide atoms (from cobalt(III) bromide or copper(II) bromide), the ligand-transfer of the resulting benzil radical by copper(II) bromide to benzyl bromide, and the replacement of benzyl bromide with the acetate ion to give benzyl acetate.

Here, we wish to report on the liquid-phase oxidation of substituted toluenes and polymethylbenzenes catalyzed by the Co–Cu–Br system as an extension of the study of the oxidative side-chain acetoxylation of aromatic hydrocarbons.

Experimental

General. *p*-Methoxytoluene, *p*-xylene, *p*-chlorotoluene, *p*-*t*-butyltoluene, *p*-nitrotoluene, *etc.*, mesitylene, durene, and hexamethylbenzene were purified by usual methods. When a substrate easily oxidized to the hydroperoxides was used, the substrate was further treated with an active alumina.

Acetic acid, cobalt(II) acetate tetrahydrate, copper(II) acetate monohydrate, and sodium bromide of a reagent grade were used without further purification. The products were identified by means of IR (Shimadzu IR 420) ^{1}H-NMR (Varian EM 360A), and GC-MS (ANELVA TE 600S).

Oxidation Procedure. A 200-ml Ti-made autoclave equipped with a gas inlet, a magnetic-induced stirrer, and a pressure gauge was charged with *ca.* 50 mmol of a substrate, 4 mmol of cobalt(II) acetate, 4 mmol of copper(II) acetate, 28 mmol of sodium bromide, and 60 ml of acetic acid. Then, the autoclave, pressured with air to 40 kg/cm^2 was placed in an electric furnace and heated to 150 °C.

After 1.0 h, the autoclave was cooled with water and vented. Internal standards (chlorobenzene, *p*-bromoanisole, and 1-chloronaphthalene) were then added to the autoclave. The contents were poured into ice water and then extracted with ether.

The extract was washed with water and a saturated sodium carbonate solution, and subsequently dried (sodium sulfate), and the ether was removed on a rotary evaporator. The residue was submitted to GC analysis.

The substituted benzoic acids isolated by the acidification of the combined aqueous solution were determined by the weighing of their quantities or by ^{1}H-NMR analysis. The GC analysis was mainly conducted on a Shimadzu GC-3T gas chromatograph, using a 10% PEG 20 M on Uniport B column operated isothermally at 180 °C.

Results and Discussion

The liquid-phase oxidations of the substituted toluenes were carried out in acetic acid, using cobalt(II) and copper(II) acetates and a sodium bromide system with air. The results are summarized in Table 1. As may be seen from the Table, a corresponding substituted benzyl acetate was obtained as the main product, along with a significant amount of the substituted benzaldehyde. The increase in the electron-donating ability of the substituent on the ring caused the higher conversion, which is roughly accordant with the tendencies on the oxidation of substituted toluenes catalyzed by a cobalt–bromide system[9] and on the bromination with NBS.[10] As compared with the palladium-catalyzed side-chain acetoxylation of methylbenzenes, the Co–Cu–Br catalyzed reaction seems to be more useful because of the lower cost of the catalyst and because of the possibility of a wider application to the acetoxylation of many methylbenzenes (the palladium-catalyzed reactions of

Table 1. Oxidation of substituted toluenes catalyzed by the Co-Cu-Br system

Toluenes	Conversion	Products (mol%)$^{a)}$	
	%	$ArCH_2OAc$	ArCHO
O-Chlorotoluene	40	55	27
m-Chlorotoluene	39	63	30
p-Chlorotoluene	60	52	13
p-Nitrotoluene	20	62	22
Toluene	55	54	20
p-*t*-Butyltoluene	74	55	27
p-Methoxytoluene$^{b)}$	94	21	13
p-Toluic acid$^{c)}$	29	30	12
p-Tolualdehyde$^{d)}$	98	0	1
p-Methylbenzyl acetate$^{e)}$	82	44	17

Reaction conditions: $[Co(OAc)_2]=[Cu(OAc)_2]=5.7\times 10^{-2}$ M,† [NaBr]=0.4 M, [Substrate]=0.7 M, air pressure; 40 kg/cm^2, 1.0 h, 150 °C. a) Based on the substrate consumed. b) 3-Bromo-4-methoxytoluene (20%) was also obtained. c) The evolution of carbon dioxide was observed. d) The other product was *p*-toluic acid. e) *p*-Tolualdehyde (16%) and *p*-acetoxymethylbenzoic acid (8%) were also obtained, accompanied by *p*-toluic acid (10%).

toulenes bearing substituents such as chloro, nitro, and methyl groups more than two on the ring are very slow[4]). It is noteworthy that the benzaldehyde, as a by-product, can also be obtained in many cases. However, in the *p*-methoxytoluene oxidation, as will be described later in detail, a ring bromination occurred, because 3-bromo-4-methoxytoluene was detected. On the other hand, it is interesting that *p*-acetoxymethylbenzoic acid can be produced, though its yield is low in the oxidation of *p*-toluic acid. The oxidation of *p*-tolualdehyde gave *p*-toluic acid as the sole product, suggesting that the aldehyde group in the catalyst system is more sensitive toward the oxidation. On the other hand, the mechanism in the oxidation by the Co–Cu–Br system has been estimated on the basis of the results of an earlier variable study.[8]) It could be considered to proceed through the pathway of the bromination with copper(II) bromides of the benzyl radical, which can be produced from the hydrogen abstraction of benzylic hydrogen by cobalt(III) bromide and/or bromine atoms arising from the rapid reaction of cobalt(II) bromide and the peroxyl radical[9]) and from the decomposition of copper(II) bromide,[11]) *i.e.*,

$$ArCH_3 \xrightarrow[\text{and/or Br}\cdot]{\text{Co(III)Br}} ArCH_2\cdot \xrightarrow{\text{Cu(II) Br}} ArCH_2Br \xrightarrow{\text{OAc}^-} ArCH_2OAc.$$

Although aryl alkyl bromides can usually be detected under the given conditions because of the low substitution rate of aryl alkyl bromide with the acetate ion, aryl alkyl bromide could hardly be detected under the conditions employed here suggesting that the substitution is rapid. Furthermore, the rate of the ligand transfer by copper(II) halides is known to be diffusion-controlled according to the study by Kochi.[12]) Therefore, the substituents on the ring can be considered to influence the hydrogen abstraction of benzylic hydrogen.

Table 2. Oxidation of *p*-methoxytoluene catalyzed by the Co-Cu system

Sodium salt	*p*-Methoxytoluene conversion/%	Products (mol%)$^{a)}$		
		$ArCH_2OAc$	ArCHO	[A]$^{b)}$
None	0	—	—	—
NaBr$^{c)}$	26	47	1	49
NaBr$^{d)}$	94	21	13	20
NaOAc	44	51	42	—
NaOAc$^{e)}$	54	56	26	—

Reaction conditions: $[Co(OAc)_2]=[Cu(OAc)_2]=5.7\times 10^{-2}$ M, [Sodium salt]=0.4 M, [*p*-Methoxytoluene]=1.4 M, air pressure; 40 kg/cm^2, 1.0 h, 150 °C. a) Based on the *p*-methoxytoluene consumed. b) [A] represents 3-bromo-4-methoxy toluene. c) This run was carried out under the conditions: 100 °C, 20 h, air flow. e) Acetic anhydride (5 ml) was added. d) [*p*-Methoxytoluene]=0.7 M.

As has been mentioned above, 3-bromo-4-methoxytoluene and *p*-anisic acid were both obtained as by-products in the oxidation of *p*-methoxytoluene. In order to avoid the ring bromination, some experiments were carried out (Table 2). Many works have reported on the ring halogenation of aromatic hydrocarbons with copper(II) halides at high temperatures,[13]) and it is a useful method for the halogenation even now. On the other hand, a cobalt(III) acetate and halogen-ion system such as cobalt(III) chloride,[14]) has also the ability to effect ring halogenation as well as side-chain halogenation. Accordingly, it appears to be difficult to prevent the ring bromination in the Co–Cu–Br catalyzed oxidation of *p*-methoxytoluene, because the above two systems exist. Indeed, the ratio of the amount of the benzyl acetate to the ring-bromination product at a low conversion shows nearly the same value as at a high conversion (Table 2). The ^{1}H-NMR analysis of the reaction mixture (an ether residue) showed the formation of 3-bromo-4-methoxybenzyl acetate when the conversion of *p*-methoxytoluene was completely achieved. A ring bromination similar to the oxidation of *p*-methoxytoluene was observed in the oxidation of 1-methylnaphthalene, *m*-phenoxytoluene, and mesitylene (*e.g.*, in the oxidation of 1-methylnaphtalene, 4-bromo-1-methylnaphthalene(12%) was obtained, accompanied by 1-naphthaldehyde(18%) and 1-acetoxymethylnaphthalene(39%) at a 70% conversion of 1-methylnaphthalene). Since *p*-methoxytoluene, having a relatively lower ionization potential, could be supposed to react with cobalt(III) acetate even in the presence of copper(II) acetate, a run with no bromide ion was examined. However, the induction period was found to be very long in the cobalt(II) and copper(II) acetates system. The addition of the acetate ion to the system, however, caused a rapid oxidation, in which satisfactory selectivities for the benzyl acetate and the benzaldehyde were achieved. It is interesting that an unusual selectivity for *p*-anisaldehyde was obtained. Fur-

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† 1M=1 mol dm^{-3}.

Table 3. Oxidation of *p*-xylene catalyzed by the Co-Cu-Br system

Run	1	2
p-Xylene(mmol)	41	81
Conversion/%	90	59
Products(mol%)[a]		
p-Tolualdehyde	13	24
p-Methylbenzyl acetate	34	59
p-Acetoxymethylbenzaldehyde	2	5
p-Phthalaldehyde	Trace	0
α,α'-Diacetoxy-*p*-xylene	8	8
p-Toluic acid	28	—[b]
p-Formylbenzoic acid	0	—
Terephthalic acid	0	—
p-Acetoxymethylbenzoic acid	4	—

Reaction conditions: $[\mathrm{Co(OAc)_2}]=[\mathrm{Cu(OAc)_2}]=5.7\times10^{-2}$ M, $[\mathrm{NaBr}]=0.4$ M, air pressure: 40 kg/cm^2, 150 °C, 1.0 h. a) Based on the *p*-xylene consumed. b) No determination.

thermore, the addition of acetic anhydride accelerated the oxidation and caused a higher selectivity for the benzyl acetate. Recently, Imamura has reported in detail on the oxidation of *p*-methoxytoluene catalyzed by the addition of cobalt(II) acetate and a small amount of a bromide-ion system to *p*-anisaldehyde, he found that *p*-methoxybenzyl acetate was also obtained under the given conditions.[15] However, our results are somewhat better than their results in the selectivity for *p*-methoxybenzyl acetate. As it is now well established that cobalt(III) acetate can oxidize alkyl aromatics such as toluene by direct electron-transfer, even in the presence of oxygen,[16] the mechanism in the Co–Cu–OAc system can be estimated to be as follows:

$$\mathrm{Co(III)} + p\text{-}\mathrm{MeOC_6H_4CH_3} \rightleftharpoons \mathrm{Co(II)} + (p\text{-}\mathrm{MeOC_6H_4CH_3})^{+\cdot}$$

$$(p\text{-}\mathrm{MeOC_6H_4CH_3})^{+\cdot} \longrightarrow p\text{-}\mathrm{MeOC_6H_4CH_2}\cdot + \mathrm{H^+}$$

$$p\text{-}\mathrm{MeOC_6H_4CH_2}\cdot + \mathrm{Co(III)\ and/or\ Cu(II)} \longrightarrow p\text{-}\mathrm{MeOC_6H_4CH_2OAc}$$

$$p\text{-}\mathrm{MeOC_6H_4CH_2}\cdot + \mathrm{O_2} \longrightarrow p\text{-}\mathrm{MeOC_6H_4CH_2OO}\cdot \xrightarrow[\mathrm{Co(III)}]{} p\text{-}\mathrm{MeOC_6H_4CHO}.$$

However, as has previously been reported, it should be mentioned that the oxidizing activity of cobalt(III) acetate was lowered by the binuclear complex formation with copper(II) acetate.[17]

As has been described above, many important oxidation products of *p*-xylene are used as monomers in the polymer industry.[18] α,α'-*p*-Xylene-diol and *p*-hydroxymethylbenzoic acid as well as terephthalic acid are of particular interest.

Thus, we attemped the synthesis of these compounds in the oxidation of *p*-xylene by the Co–Cu–Br system. The results are presented in Table 3. At a low conversion of *p*-xylene, the products are *p*-methylbenzyl acetate and *p*-tolualdehyde, by analogy with the substituted toluene oxidations. On the other hand, at a high conversion, since *p*-xylene has two methyl groups, many products were obtained. It was found that *p*-xylene-α,α'-diol and *p*-acetoxymethylbenzoic acid are obtainable, though small amounts. Thus, the secondary oxidations of *p*-methylbenzyl acetate, *p*-toluic acid, and *p*-tolualdehyde were investigated. As has already been shown in Table 1, although no effort to seek out the optimum conditions for the selective oxidation was made, the expected compounds were obtained in considerable amounts. In the oxidation of *p*-methylbenzyl acetate, *p*-tolualdehyde was also obtained, even at a low conversion (for example, at a 44% conversion, 17% of *p*-tolualdehyde as well as 54% of α,α'-diacetoxy-*p*-xylene and 20% of *p*-acetoxymethylbenzaldehyde were obtained), indicating that the further oxidation of the benzyl acetate can not be ignored in these cases. Under these conditions, the oxidation of benzyl acetate gave benzaldehyde(14%) and benzoic acid(76%) at a 55% conversion of benzyl acetate. Therefore, there appears to be a limitation in the one-step synthesis of α,α'-diacetoxy-*p*-xylene with the oxidation of *p*-xylene. However, the results of the oxidation of *p*-tolualdehyde and *p*-toluic acid indicate that the formation of *p*-acetoxymethylbenzoic acid in the oxidation of *p*-xylene is through the pathway of the secondary oxidation of *p*-methylbenzyl acetate, because of the low rate of *p*-toluic acid oxidation and the high rate of *p*-tolualdehyde oxidation.

Table 4. Oxidation of polymethylbenzenes catalyzed by the Co-Cu-Br system

Substrate	Conversion	Products (mol%)[a]	
	%	$\mathrm{ArCH_2OAc}$	ArCHO
o-Xylene[b]	89	34	1
p-Xylene[b]	34	34	13
Mesitylene	89	49	11
Durene	98	63	10
Hexamethylbenzene	99	45	8

Reaction conditions: $[\mathrm{Co(OAc)_2}]=[\mathrm{Cu(OAc)_2}]=5.7\times10^{-2}$ M, $[\mathrm{NaBr}]=0.4$ M, $[\mathrm{Substrate}]=0.7$ M, air pressure; 20 kg/cm^2, 150 °C, 1.0 h. a) Based on the substrate consumed. b) Air pressure; 40 kg/cm^2.

Accordingly, it was concluded that two synthetically useful compounds, α,α'-diacetoxy-*p*-xylene and *p*-acetoxymethylbenzoic acid, were obtainable in the oxidation of *p*-methylbenzyl acetate, for the by-products are the precursors of *p*-acetoxymethylbenzoic acid.

$$p\text{-}\mathrm{CH_3C_6H_4CH_2OAc} \xrightarrow{\mathrm{Co\text{-}Cu\text{-}Br}} p\text{-}\mathrm{AcOCH_2C_6H_4CH_2OAc},\quad p\text{-}\mathrm{AcOCH_2C_6H_4COOH}$$

$$p\text{-}\mathrm{CH_3C_6H_4CHO} \qquad p\text{-}\mathrm{AcOCH_2C_6H_4CHO}$$

By-products

$$p\text{-}\mathrm{CH_3C_6H_4COOH} \qquad p\text{-}\mathrm{AcOCH_2C_6H_4COOH}$$

Finally, the Co–Cu–Br catalyzed oxidations of *o*- and *p*-xylenes, mesitylene, durene, and hexamethylbenzene were conducted. The results are summarized in Table 4. Since these compounds have more than two methyl groups and low ionization potentials, they were very reactive as compared with the palladium-catalyzed side-chain acetoxylation. In the oxidation of hexamethylbenzene, for example, the products which have more than two oxidized methyl groups were detected, though they could not be completely determined before the whole conversion.

Then, the reaction was controlled by the amount of oxygen charged. As may be seen from Table 4, the monoacetoxylated compounds can be synthesized in high selectivities, even if at a high conversion.

In the oxidation of mesitylene, as has been reported by many workers,[19] the ring bromination occurred, though its amount was not determined.

In conclusion, the Co–Cu–Br system previously reported in the oxidative side-chain acetoxylation of toluene was found to be applicable to the side-chain acetoxylation of substituted toluenes and polymethylbenzenes. In the oxidation of *p*-methoxytoluene, ring bromination also occurred, although the side reaction could be removed by replacing the bromide ion in the catalyst system with the acetate ion.

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