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Selective Nuclear Halogenation of Polymethylbenzenes with Alumina-Supported Copper(II) Halides

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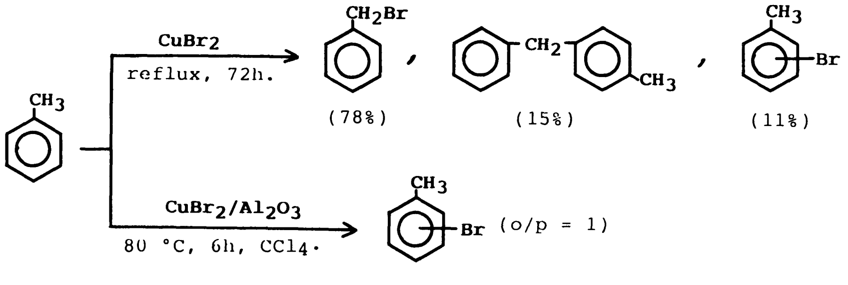
Synopsis. The halogenation of polymethylbenzenes with alumina-supported copper(II) halides under heterogeneous conditions in nonpolar solvents gave nuclear-halogenated compounds selectively in high yields; no side-chain-halogenated compounds were formed.

Although copper(II) halides have been used to halogenate aromatic hydrocarbons under heterogenous conditions in nonpolar solvents,[1] aromatic hydrocarbons with ionization potential (IP) higher than approximately 7.55 eV are entirely unreactive toward chlorination with copper(II) chloride.[2] For example, chlorination of naphthalene (IP=8.10[3]) or phenanthrene (IP=8.03[3]) does not occur, even under reflux, with copper(II) chloride in high-boiling solvents, such as chlorobenzene and nitrobenzene.[1,4] Previously, we reported that copper(II) halides can be activated remarkably by supporting onto neutral alumina,[5] and polycyclic aromatic hydrocarbons or alkoxybenzenes are halogenated selectively to give corresponding halides by use of copper(II) halides supported onto neutral alumina.[6,7] In reactions of alkylbenzenes with metal halides, side-chain-halogenation and polymerization in addition to nuclear-halogenation occur.[8] In contrast, we found that similar reactions with alumina-supported copper(II) halides gave selectively nuclear-halogenated products in high yields. In this paper, we report on a convenient method of selective nuclear halogenation of polymethylbenzenes with alumina-supported copper(II) halides.

Results and Discussion

The halogenation of polymethylbenzenes with alumina-supported copper(II) halides in nonpolar solvents in which copper(II) halides were not soluble, occurred as a heterogeneous reaction on the surface and gave only nuclear-halogenated compounds in high yields; no side-chain-halogenated compounds were obtained. The reaction of copper(II) bromide with mesitylene in carbon tetrachloride at reflux yielded no detectable products after 5 h. In contrast, in a similar reaction using alumina-supported copper(II) bromide, bromomesitylene in 97% yield from a reaction run at 50 °C for 1 h and dibromomesitylene in 99% yield from the reaction run at 80 °C for 5 h were obtained. The results of chlorination and bromination of polymethylbenzenes are summarized in Tables 1 and 2. The reactivity of polymethylbenzenes toward copper(II) halides increased with increasing the number of methyl groups. For instance, bromination of toluene in carbon tetrachloride did not proceed at reflux, even though pentamethylbenzene was brominated at 30 °C to give bromopentamethylbenzene quantitatively. Toluene and copper(II) bromide reacted at reflux for 72 h to give benzyl bromide as the main product. In a similar reaction with alumina-supported copper(II) bromide, bromotoluene (*o*/*p*=1) was obtained in good yield and no side-chain-brominated compounds were detected.

The reaction of alkylbenzene with copper(II) bromide is critically influenced by the presence of water in small quantities.[9] With toluene, nuclear bromination predominates in a rigorously anhydrous system. When small amounts of water are added, phenyl(*p*-tolyl)methane is the main product, in addition to benzyl bromide. In contrast, in a reaction with alumina-supported copper(II) bromide in the presence of water in small quantities, only nuclear bromination occurred and no products resulting from side-chain-bromination were formed. It seems that alumina not only activates copper(II) halides but also acts as a dehydrating agent in this system. Copper(II) chloride was less reactive than copper(II) bromide toward the polymethylbenzenes. The chlorination of the polymethylbenzenes required more severe conditions than that of bromination. The chlorination of xylene did not occur under the same conditions, even though the bromination proceeded at 80 °C in carbon tetrachloride. With polymethylbenzenes containing more than three methyl groups. The corresponding nuclear-monochlorinated compounds were obtained selectively in high yield. A reaction of pentamethylbenzene, even at 80 °C for 5 h gave chloropentamethylbenzene in 98% yield (isolated).



Scheme 1.

Table 1. Bromination of Polymethylbenzenes with $CuBr_2/Al_2O_3$[a]

Polymethylbenzene	Reaction temp/°C	Reaction time/h	Product	Yield/%[b]
a Methyl-	80	6	2- and 4-Br	85[c]
b 1,3-Dimethyl-	80	2	4-Br	98(85)
c 1,2,3-Trimethyl-	80	1	4-Br	97(87)
d 1,3,5-Trimethyl-	50	1	2-Br	97(86)
	80	5	2,4-Br	99(97)
e 1,2,3,5-Tetramethyl-	50	1	4-Br	92(90)
	80	5	4,6-Br	99(98)
f 1,2,3,4,5-Pentamethyl-	30	1	6-Br	(99)

a) All the reaction was carried out in carbon tetrachloride. The molar ratio of CuBr/polymethylbenzene was 5. b) Determined by GLC; figures in parentheses show the yield of isolated product. c) $o/p=1$.

Table 2. Chlorination of Polymethylbenzenes with $CuCl_2/Al_2O_3$[a]

Polymethylbenzene	Reaction temp/°C	Reaction time/h	Product	Yield/%[b]
c	110	4	4-Cl	95(80)
d	110	5	2-Cl	90(78)
e	130	3	4-Cl	91(82)
f	80[c]	5	6-Cl	(98)

a) Reactions were carried out in chlorobenzene. The molar ratio of $CuCl_2$/polymethylbenzene was 5. b) Determined by GLC; figures in parentheses show the yield of isolated product. c) The reaction was carried out in carbon tetrachloride.

The advantages of this procedure are simple workups, mild reaction conditions and higher selectivities. Products can be isolated by simple filtration and solvent evaporation, and no extraction steps are required.

Experimental

Preparation of Copper(II) Bromide Supported on Alumina: To a solution of copper(II) bromide (10 g) in distilled water (30 ml) was added neutral alumina (20 g, Woelm N-Super 1) at room temperature. The water was evaporated by using a rotary evaporator at 80 °C under reduced pressure. The resulting reagent was then dried under vacuum (4 Torr; 1 Torr≈133.322 Pa) at 100 °C for 15 h. The preparation of alumina-supported copper(II) chloride was similar to that described above.

4-Bromo-*m*-xylene: General Procedure for Bromination of Polymethylbenzenes. A mixture of *m*-xylene (2.4 g, 22.6 mmol), alumina-supported copper(II) bromide (50.5 g), and carbon tetrachloride (60 ml) was placed in a 100 ml round-bottom flask and stirred with a Teflon-coated magetic stirring bar at 80 °C for 1 h. The products mixture was filtered, and the spent and unused reagent were washed with carbon tetrachloride (30 ml). The solvent was evaporated from the combined filtrate under reduced pressure, and the residue was distilled under vacuum to give 3.6 g (86%) of 4-bromo-*m*-xylene. Bp 89—91 °C/14 Torr (lit,[10] 203 °C). The ^1H NMR and IR spectra was identical with those of an authentic sample.

6-Chloro-1,2,3,4,5-Pentamethylbenzene: General Procedure for Chlorination of Polymethylbenzenes. A mixture of pentamethylbenzene (2.0 g, 13.5 mmol), alumina-supported copper(II) chloride (28 g) and carbon tetrachloride (40 ml) was stirred at 80 °C for 5 h. The product mixture was filtered, and the spent and unused reagents were washed with carbon tetrachloride (30 ml). Evaporation of the solvent from the combined filtrate under reduced pressure yielded 2.42 g (98%) of 6-chloro-1,2,3,4,5-pentamethylbenzene as a white solid having mp 152—153 °C (lit,[11] mp 154.5—155 °C). The ^1H NMR and IR spectra was identical with those of an authentic sample.

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