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Regioselective Para Chlorination of Alkoxybenzenes by Use of Alumina Supported Copper(II) Chloride

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Alkoxybenzenes were highly regioselectively chlorinated by use of copper(II) chloride supported on neutral alumina in chlorobenzene to give p-alkoxychlorobenzenes in high yield. The p/o ratios were more than 30.

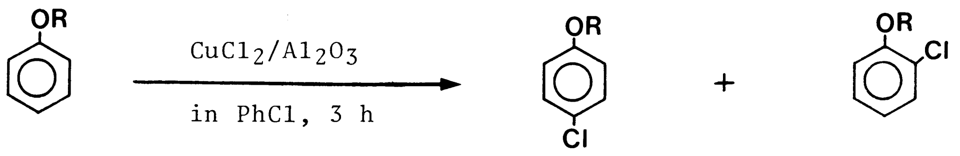
The chlorination of alkoxybenzenes can be performed with a variety of chlorinating agents such as sodium hypochlorite,1) t-butylhypochlorite,1,2) sulfuryl chloride-metal chlorides3) and chlorine,4) and gives a mixture of o- and p-chloroisomer in the p/o ratio of 4 or less. Copper(II) chloride has been used for the chlorination of a variety of active hydrogen compounds.5) In non-polar solvents, copper(II) chloride is not soluble and chlorination occurs as a heterogenous reaction on the surface.6) We have found that copper(II) chloride can be activated remarkably by support onto neutral alumina.7)

In this communication, we report a convenient method for chlorination of alkoxybenzenes with alumina supported copper(II) chloride. This method proceeds with high regioselectivity and requires only filtration and solvent evaporation for product isolation.

Attempted reaction of $CuCl_2$ with anisole in chlorobenzene at 100 °C yielded no detectable product after 5 h. In contrast, a similar reaction carried out in which $CuCl_2$ was supported onto neutral alumina produced a quantitative conversion.

Alumina supported copper(II) chloride ($CuCl_2/Al_2O_3$) was prepared as follows: Copper(II) chloride dihydrate (5.18 g) was dissolved in methanol (30 ml), and then neutral alumina (10 g, Woelm N-Super 1) was added to it in one portion. Methanol was removed by use of rotary evaporator, and the resulting reagent was dried under vacuum (5 Torr) at 100 °C for 5 h.

Typical procedure for chlorination of alkoxybenzenes is as follows: $CuCl_2/Al_2O_3$ (9.3 g) was added into a solution of anisole (0.433 g, 4 mmol) in chlorobenzene (30 ml), and the mixture was stirred vigorusly at 100 °C for 3 h. Analysis of the reaction mixture by GLC indicated the complete disapearance of anisole. The product mixture was filtered, and the spent and unused reagents were washed with chlorobenzene (15 ml). Removal of solvent from the combined filtrate under reduced pressure yielded 0.56 g (98%) of chloroanisole (p/o = 32.3). The purity was $>$ 96% (GLC).



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	Yeild/%$^{a)}$	
	2	3
R = Methyl:	93	3
Ethyl :$^{b)}$	94	<0.5
Propyl:	95	<0.5
Butyl :	92	3
Pentyl:$^{b)}$	95	2

a) By GLC. b) React. time; 2 h.

The loading of too much $CuCl_2$ resulted in decreased efficiency. The yield increased with increaseing the ratio of $CuCl_2/Al_2O_3$ to alkoxybenzene. The size of alkoxy group did not influence significantly the yield and the ratio of p/o. Alumina could be easily recovered from the spent and unused reagents, and used repeatedly for preparing the supported reagent.8) Silica gel and active carbon were also effective as a support, but the yield of p-alkoxychlorobenzene in the reaction with use of these supports was lower than that in the case of alumina. Molecular sieves (MS-5A, MS-13X) were not effective.

References

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8) The spent and unused reagents were washed with methanol, 10% hydrochloric acid, water, and methanol. The recovered alumina was dried by rotary evaporator at 60 °C under reduced pressure and used for reloading of $CuCl_2$ without further drying.

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