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THE REGIOSELECTIVE <u>PARA</u> CHLORINATION OF 2-METHYLPHENOL

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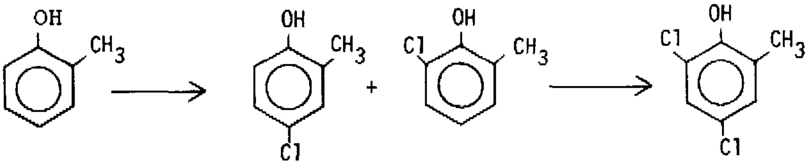
This paper reports a new and novel catalyst system that has been developed for the sulfuryl chloride chlorination of 2-methylphenol. This technique is very regioselective[1] for para chlorination and is also specific toward monochlorination. The system consists of chlorinating 2-methylphenol containing catalytic amounts of aluminum chloride and diphenyl sulfide with a stoichiometric amount of sulfuryl chloride at approximately 15°C. The reaction is also characterized by being very fast compared to either the noncatalyzed or the Friedel Crafts catalyzed reaction.

4-Chloro-2-methylphenol, 1, is a commerically important intermediate that is used in the manufacture of (4-chloro-2-methylphenoxy) acetic acid, MCPA, a major phenoxy herbicide used to control weeds in small grains.

The chlorination of 2-methylphenol produces three chlorination products as shown below.



1 2 3

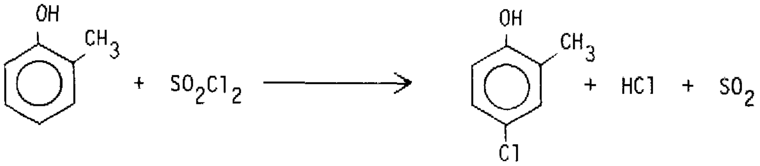
Various chlorination techniques have been used to maximize the yield of 1. However, one must take into consideration the physical properties of the components. Table I shows that to obtain high yields of 1, 2-methylphenol cannot be underchlorinated or over chlorinated. Since distillation and recrystallization are usually the most efficient and economical separation processes, underchlorination causes a yield loss because 2-methylphenol and 2 cannot readily be separated. If the reaction is overchlorinated it is extremely difficult to separate 1 and 3.

TABLE I

PHYSICAL PROPERTIES[2]

Compound	Boiling Point °C, 760 mm	Melting Point °C
2-methylphenol	191.0	30.5
4-chloro-2-methylphenol, 1	232.6	51.2
2-chloro-6-methylphenol, 2	189.8	0.0
2,4-dichloro-6-methylphenol, 3	232.5	53.0

Although chlorine[3] and cupric chloride[4] have been used, the most common chlorinating agent used to produce **1** is sulfuryl chloride[5].



The advantage of using sulfuryl chloride is that it produces only small amounts of polychlorinated compounds and tars since it is a relatively weak electrophile[6]. The disadvantage of using sulfuryl chloride is that since it is such a weak electrophile the rate of reaction is slow. It should also be noted that the sulfur dioxide generated in the above reaction can be reacted with chlorine over activated carbon to regenerate sulfuryl chloride[7].

Table II shows the advantages of using the diphenyl sulfide-aluminum chloride co-catalyst system. All the results were obtained by glpc and are listed in weight %. No meta substitution was observed. Distillation of various samples produced only 1-2% non-distillable tars.

TABLE II

CHLORINATION OF 2-METHYLPHENOL

Chlorinating Agent	Catalyst[a]	Temp. °C	Time hr.	2-Methyl phenol	**1**	**2**	**3**	Ratio 4-Chloro/2-Chloro
Cl_2	None	35	1.5	14.2	57.0	23.2	5.6	2.45
Cl_2	$Ph_2S,AlCl_3$	35	1.5	11.1	70.6	12.3	6.0	5.73
SO_2Cl_2	None[b]	25	27.5	3.0	83.2	13.4	.4	6.21
SO_2Cl_2	$AlCl_3$[b]	25	25.5	2.3	90.0	7.2	.5	12.5
SO_2Cl_2	Ph_2S	15	2.0	4.7	79.0	12.4	3.9	6.35
SO_2Cl_2	$Ph_2S,AlCl_3$	15	2.5	.4	94.1	5.0	.5	18.8

a) 1g of each catalyst was used per mole of 2-methylphenol.
b) 1.10 Moles of SO_2Cl_2 used.

The chlorination of 2-methylphenol with chlorine produces a 4-chloro/2-chloro ratio of 2.45 in good agreement with previous work[3]. The addition of diphenyl sulfide and aluminum chloride[8] as catalyst increase the 4-chloro/2-chloro ratio to 5.73 but only gives an approximate 71% maximum yield of **1**.

The reaction of sulfuryl chloride with 2-methylphenol non-catalyzed and with aluminum chloride gives a 4-chloro/2-chloro ratio of 6.21 and 12.5, respectively, also agreeing with previous work[5]. However, to obtain these product distributions, an excess of sulfuryl chloride is needed as well as an approximate twenty-four hours reaction time at room temperature. When diphenyl sulfide is used as a catalyst the reaction is complete in only two hours, but the 4-chloro/2-chloro ratio is only 6.35. However, when the co-catalyst system of diphenyl sulfide and aluminum chloride is used the reaction is not only fast, but the 4-chloro/2-chloro ratio is 18.8 and the maximum yield of **1** is 94.1%! Thus the reaction is regioselective toward para chlorination and is highly specific since it produces 99.1% monochloro product. Thus one can readily see the advantages of the above described system over the prior art in the preparation of **1** on either the laboratory or commercial scale.

The data in Table II shows that the sulfuryl chloride is not simply decomposing to sulfur dioxide and chlorine since the co-catalyzed chlorine chlorination differs from the sulfuryl chloride chlorination by having significant amounts of **3** and a lower 4-chloro/2-chloro ratio. This conclusion is supported by previous work comparing chlorine and sulfuryl chloride chlorinations[6].

The rate of reaction is greatly enhanced by the presence of diphenyl sulfide. It is therefore proposed that the first step is the reaction of sulfuryl chloride with diphenyl sulfide to form diphenyl sulfide dichloride. Diphenyl sulfide is a known catalyst in the decomposition of sulfuryl chloride[9]. Diphenyl sulfide dichloride and related compounds[10-13] are known to be reactive intermediates in the preparation of sulfoxides[13], sulfuranes[14], and other reactive intermediates[15]. The aluminum chloride interacts with the diphenyl sulfide dichloride to form a bulky reagent that accounts for the regioselective *para* substitution. It has been determined by glpc that the diphenyl sulfide is recovered unreacted after the reaction. Based on the above discussion and the data in Table II the following reactions account for both a fast reaction and high *para* regioselectivity.

$$\mathrm{Ph_2S + SO_2Cl_2 \longrightarrow Ph_2SCl_2 + SO_2}$$

$$\mathrm{Ph_2SCl_2 + AlCl_3 \longrightarrow Ph_2\overset{+}{S}Cl{-}{-}{-}AlCl_4^-}$$

$$\mathrm{Ph_2\overset{+}{S}Cl{-}{-}{-}AlCl_4^- + 2\text{-}Methylphenol \longrightarrow \mathbf{1} + HCl + Ph_2S + AlCl_3}$$

The use of the co-catalyst system is, of course, also useful in the *para* chlorination of other phenols. Phenols as well as other aromatic systems are currently under investigation in our laboratory.

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