

Commercially Important Chlorinated Phenols

Subjects: **Others**

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Phenols are compounds having a hydroxyl group attached to an aromatic ring such as a benzene or naphthalene ring. Several phenols that also possess one or more chlorine substituents attached to the aromatic ring have significant commercial importance, and these are the subject of this entry.

selective chlorination

phenols

sulphuryl chloride

sulphur-containing catalysts

aromatic electrophilic substitution reactions

monochlorination

double chlorination

para/ortho-isomer ratio

1. Commercial Applications of Chlorinated Phenols

As a class of compounds, chlorinated phenols are of substantial commercial interest. Already by 1936, 2,3,4,5,6-pentachlorophenol was being used as a wood preservative in the US; in addition, it was involved in the preparation of paints, adhesives, ropes, and insulation ^[1]. 2,4-Dichlorophenoxyacetic acid (2,4-D), manufacture of which involves 2,4-dichlorophenol, was first synthesized in 1941 and has been commercially produced in many parts of the world since the 1950s^[2]. Subsequently, the range of applications of chlorinated phenols has expanded and they are currently useful both as synthetic intermediates for more complicated products and as end products themselves. The range of areas of application includes antiseptics, herbicides, pesticides, and dyes^[3]. For example, 2,4-D and 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) were the first herbicides produced commercially for weed control^[4] and 2,4-D is still in widespread use in 2021^[5]. In addition, 2,4,5-trichlorophenol acts as a leather and wood fungicide^[6], 2,3,4,5,6-pentachlorophenol is used as an insecticide^[7], 4-chloro-3,5-dimethylphenol is used as a household and hospital disinfectant, 4-chloro-2-methylphenol is used as a herbicide, and 4-chloro-3-methylphenol is used as an antiseptic and preservative ^{[8][9][10]}. Figure 1 shows some of the most common industrial products containing chlorinated phenolic components.

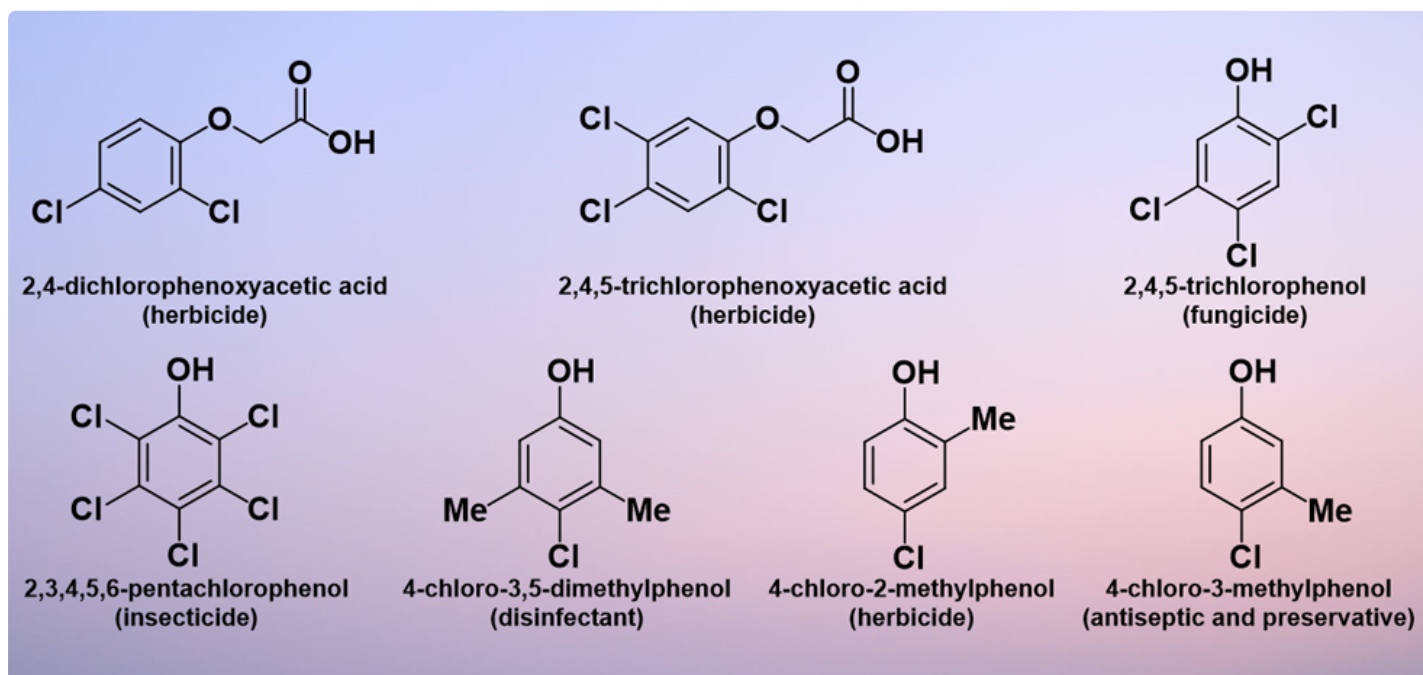


Figure 1. Common industrial products containing chlorinated phenol components.

2. Synthesis of Chlorinated Phenols

Chlorinated phenols are almost always manufactured by direct chlorination of the parent phenols. Many approaches have been attempted for such chlorinations^{[12][13][14][15][17][16][18][19][20][21][22][23]}, including use of a range of different chlorinating agents, but either chlorine gas or sulfuryl chloride is usually used in commercial processes. Chlorination using chlorine is not very regioselective for many phenols, and several important products require a pure *para*-chloro derivative. A review in 2021^[24] has reported on the development of various sulfur-containing catalysts and in particular poly(alkylene sulfide)s that render chlorination reactions of several simple phenols (Figure 2) highly selective with sulfuryl chloride as the reagent.

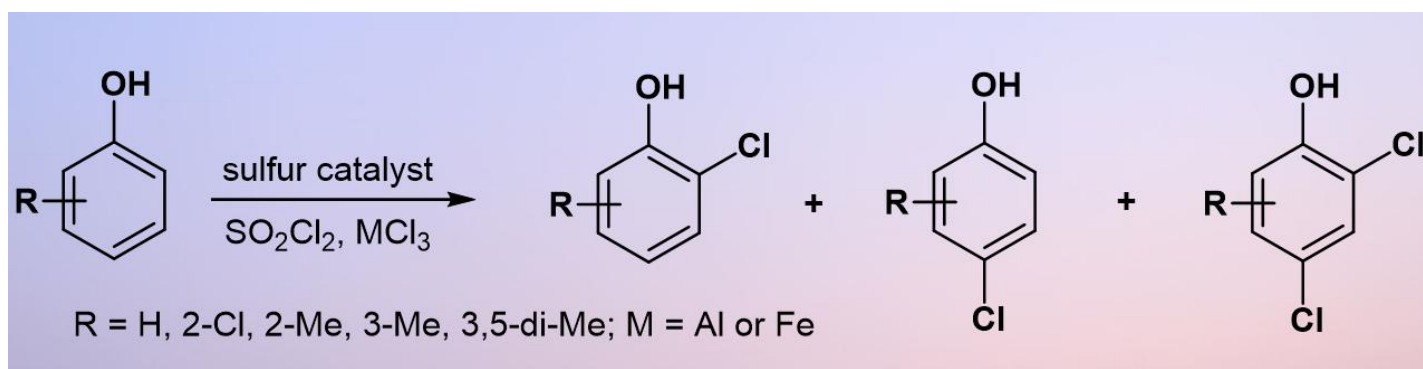


Figure 2. Chlorination of phenols using sulfuryl chloride (SO_2Cl_2) in the presence of sulfur-containing catalysts.

3. *Para*-Selective Chlorination of Phenols

Figure 3 shows some of the sulfur containing catalysts used recently for the *para*-selective chlorination of phenols^{[25][26][27][28][29][30][32][31][33][34]}.

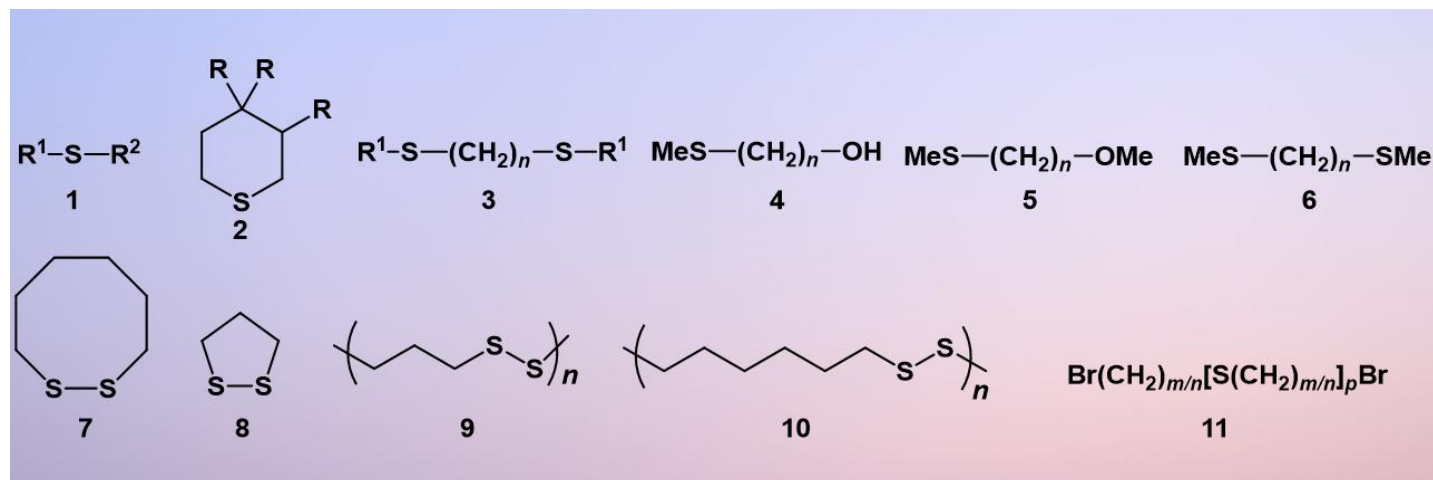


Figure 3. Some sulfur-containing catalysts for the *para*-selective chlorination of phenols.

Chlorination of phenols in the presence of dialkyl sulfides **1** was very selective towards 4-chloro-*m*-cresol. For example, the use of **1** ($R^1 = n\text{-Bu}$, $R^2 = n\text{-Bu}$, *iso*-Bu, *sec*-Bu) in chlorination of *m*-cresol led to a *para/ortho* ratio of 17.1–17.3^[26]. Cyclic sulfides **2** showed high *para*-selectivity in chlorination of phenols. For example, the use of unsubstituted tetrahydrothiopyran (**2**; $R = \text{H}$) in chlorination of *o*-cresol led to the production of 4-chloro-*o*-cresol in 96% yield with a *para/ortho* ratio of 45.7^[30]. Dithiaalkanes **3** and in particular 5,18-dithiadocosane (**3**; $m = 4$, $n = 12$) have shown high *para*-selectivity in chlorination of *m*-cresol^{[28][29]}. ω -Hydroxy-1-(methylthio)alkanes **4**, ω -methoxy-1-(methylthio)alkanes **5**, and 1, ω -bis(methylthio)alkanes **6** show somewhat similar trends as a function of the length of the spacer group in chlorination of phenols. For *o*-cresol, the highest *para*-selectivity was obtained with the shorter spacer groups ($n = 2$ or 3), while the longer spacer groups ($n = 6$ or 9) showed the highest *para*-selectivity in chlorination of *m*-cresol and *m*-xylenol, regardless of the substituent at the ω -position of the catalyst^[30]. Cyclic and polymeric disulfides **7–10** were compared as catalysts in chlorination of phenols. For phenol, the longer spacers showed better *para*-selectivity than the smaller ones and the cyclic compounds were better than the polymers at delivering *para*-selectivity. For *m*-xylenol, the opposite was seen. For *m*-cresol, the spacer length seems to make no difference, but the cyclic compounds appear to be better than the polymers, while for *o*-cresol, the longer spacers were favored for the cyclic compounds and the shorter ones were better for the polymers^[31]. Poly(alkylene sulfide)s **11** containing longer spacers led to a high *para*-selectivity in chlorination of *m*-cresol and *m*-xylenol, while the ones with shorter spacers were *para*-selective in chlorination of phenol, 2-chlorophenol, and *o*-cresol^{[33][34]}. The use of catalysts **11** led to the highest yield and *para*-selectivity ever reported in chlorination of phenols and in particular *m*-xylenol. Indeed, catalysts **11** have been used commercially to produce 4-chloro-3,5-dimethylphenol.

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