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para-Selective chlorination of cresols and *m*-xylenol using sulfuryl chloride in the presence of poly(alkylene sulfide)s

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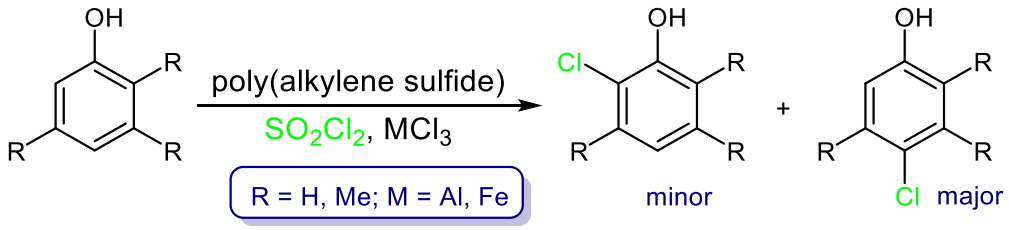
ABSTRACT

Chlorination of *o*-cresol, *m*-cresol, and *m*-xylenol using sulfuryl chloride in the presence of a range of poly(alkylene sulfide)s and a Lewis acid (aluminium or ferric chloride) has been studied. The sulfur containing catalysts used led to the production of *para*-chlorophenols in high yields and higher *para/ortho* ratios than for reactions in the absence of such poly(alkylene sulfide)s. The effectiveness of the polymers was found to be dependent on the length of the spacer groups between the sulfur atoms. For example, polymers with shorter spacers provided high yields of 4-chloro-*o*-cresol (*ca.* 97%), while polymers with at least one longer spacer provided high yields of both 4-chloro-*m*-cresol (up to 94.6%) and 4-chloro-*m*-xylenol (up to 97.6%).



KEYWORDS

Poly(alkylene sulfide)s; *o*-cresol; *m*-cresol; *m*-xylenol; *para*-selective chlorination; sulfuryl chloride; Lewis acid

1. Introduction

Chlorinated phenols belong to an important class of organic compounds with wide utility. They are produced on industrial scale and are involved in the production of pharmaceuticals, dyes, herbicides, pesticides, and antiseptics [1]. For example, 4-chloro-*m*-xylenol (4-CMX) is used as a disinfectant in households and hospitals [2–4]. It is effective against Gram-positive bacteria through inhibition of their cell wall biosynthesis [5]. Also, 4-chloro-*o*-cresol (4-COC) is used in the production of fungicides [6]. Chlorination of phenols has traditionally been conducted in the liquid phase using molecular chlorine as the chlorinating reagent and in the presence of a Lewis acid, but such processes lead to mixtures of isomers with low selectivity towards the more desirable *para*-isomers [7]. For industrial applications nowadays, chlorophenols need to be produced more selectively in high yields without generation of the large quantities of waste associated with the

traditional chlorination processes [8–10]. Recently, various chlorinating systems for phenols have been developed, but most were selective towards the synthesis of *ortho*-chlorophenols [11–15].

Zeolites and other acidic solids have been used as catalysts in *para*-selective halogenation of organic compounds [16–21], but only a little success has been achieved in this way with phenols [10]. Chlorination of *o*-cresol (OC) using sulfuryl chloride (SO_2Cl_2) in the presence of aluminium-pillared montmorillonite in 2,2,4-trimethylpentane led to a *para/ortho* ratio of only 6.1 with a conversion of 98% [10]. The use of the acidic solid catalyst eliminated the need for a Lewis acid, but the need for a long reaction time and an excessive amount of solvent and the modest yield of *para*-isomer render the process unattractive for commercial application.

Several other processes have been developed for the *para*-selective chlorination of phenols. For example, chlorination of OC bound to Merrifield resin using SO_2Cl_2 in dichloromethane (DCM) at 25°C gave a *para/ortho* of 50 according to analysis of the ^{1}H-NMR spectrum of the mixture of chloro-*ortho*-cresols formed [22]. However, the process is not practical since it involves coupling of OC to the resin, and then decoupling steps to free the chlorinated products after chlorination. In addition, the reaction time was long (more than 48 h), various solvents (dimethylformamide and DCM) and reagents (caesium carbonate, sodium iodide and trifluoroacetic acid) were used in the process, and the reaction was conducted on only a very small scale (0.33 mmol).

Selective chlorinating systems involving use of sulfur-containing catalysts and SO_2Cl_2 have been developed [23–27]. For example, the SO_2Cl_2/diphenyl sulfide (Ph_2S)/aluminium chloride ($AlCl_3$) system was efficient in chlorination of OC and *m*-cresol (MC) to give the *para*-isomers in 94% yield (*para/ortho* ratio = 19) and 83% yield (*para/ortho* ratio = 7.5), respectively [23,24]. Similarly, chlorination of *m*-xylenol (MX) using the SO_2Cl_2/Ph_2S/ferric chloride ($FeCl_3$) system gave the corresponding 4-CMX and 2-chloro-*m*-xylenol (2-CMX) in 89.9 and 2.4% yields, respectively [25]. Chlorination of MC using the SO_2Cl_2/dibutyl sulfide (Bu_2S)/$AlCl_3$ system gave 4-chloro-*m*-cresol (4-CMC) in 89.9% yield with a *para/ortho* ratio of 17.3 [26], but an even better yield of 4-CMC (95.5%) with a *para/ortho* ratio of 20.7 was achieved when 5,18-dithiadocosane was used as the catalyst instead of Bu_2S [27].

Cyclic and polymeric disulfides have also been used as selective catalysts for the production *para*-chlorophenols [28]. For example, chlorination of OC using the SO_2Cl_2/1,2-dithiocane/$AlCl_3$ system led to the production of 4-COC in a yield of up to 95% with a *para/ortho*

ratio of 20.6, while 1,2-dithiolane or polyalkylene disulfides under similar reaction conditions led to formation of 4-COC in yields of up to 93.2% (*para/ortho* = 16.6) or 93.7% (*para/ortho* = 18.7), respectively [28]. With MC under similar reaction conditions 4-CMC was produced in a yield up to 93% with a *para/ortho* ratio of 15.5 [28]. Chlorination of MX using cyclic or polymeric disulfides in the presence of $FeCl_3$ in DCM as solvent gave 4-CMX in a yield up to 91.8% (*para/ortho* = 19.1) or 93% (*para/ortho* = 23.8), respectively [28].

Methylthioalkanes containing a second functional group (OH, OMe, or SMe) have also been used as selective catalysts for the chlorination of phenols using SO_2Cl_2 and a Lewis acid [29]. The catalysts with smaller numbers of spacer methylene groups (2 or 3) between the SMe group and the second functionality provided better *para*-selectivity in chlorination of MC and MX, but those with longer spacers (6 or 9 methylene units) provided higher *para*-selectivity in chlorination of OC [29].

Recently, we have synthesised a range of poly(alkylene sulfide)s [30,31] and shown that they act as *para*-selective catalysts for the production of 2,4-dichlorophenol in up to 97.1% yield from either chlorination of 2-chloropheneol or double chlorination of phenol [31]. *para*-Chlorinated products of OC, MC, and MX are commercially important and it was therefore, of interest to test the poly(alkylene sulfide) catalysts in chlorination of these phenols under similar reaction conditions. Now, we report an efficient procedure for the production of the corresponding 4-COC, 4-CMC, and 4-CMX in high yield and selectivity.

2. Results and discussion

Poly(alkylene sulfide)s **1–26** (Figure 1) were available from previous work [31]. They varied in the method of synthesis, involving the use of either organolithium reagents (polymers **1**–**19**) or sodium sulfide (polymers **20**–**29**), the length of the spacer groups between the sulfur atoms (n, m = 2–12), the nature of the terminal groups (nominally Br or Bu, depending on the method of synthesis), and their symmetry (whether or not n = m).

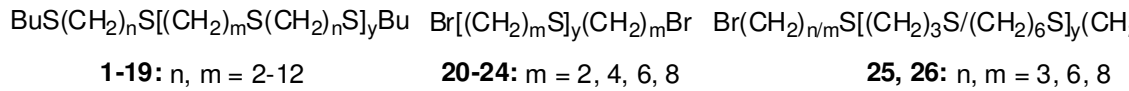
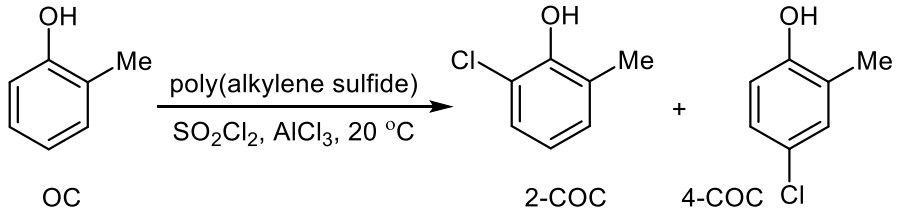


Figure 1. Poly(alkylene sulfide)s **1–26**.

Chlorination of melted OC (100 mmol) using freshly distilled SO_2Cl_2 (110 mmol) in the presence of poly(alkylene sulfide)s **1–26** (0.2 g) and $AlCl_3$ (0.2 g) was attempted at 20°C (Scheme 1). For comparison, the reaction was performed in the absence of any catalyst to provide the baseline result. The yields of 2-chloro-*o*-cresol (2-COC) and 4-COC are shown in Table 1.



Scheme 1. Chlorination of *o*-cresol using sulfuryl chloride and poly(alkylene sulfide)s **1–26**.

Table 1. Chlorination of *o*-cresol using sulfuryl chloride and poly(alkylene sulfide)s **1–26** as catalysts in the presence of $AlCl_3$ at 20 °C according to Scheme 1.[a]

Polymer	Repeating unit		Terminal group	Yield (%)[b]			*p*/*o* ratio	Mass balance (%)[c]
	n	m		OC	2-COC	4-COC		
—	—	—	—	11.2	11.3	76.3	6.8	98.8
1	2	2	Bu	—	3.3	94.9	28.7	98.2
2	3	3	Bu	—	2.3	96.0	41.7	98.3
3	3	4	Bu	0.7	3.0	96.1	32.0	99.8
4	3	6	Bu	—	1.8	96.0	53.3	97.8
5	3	9	Bu	—	1.9	97.1	51.1	99.0
6	3	12	Bu	—	2.0	96.2	48.1	98.2
7	4	4	Bu	2.4	1.7	95.5	56.2	99.6
8	4	6	Bu	—	2.6	95.7	36.8	98.3
9	4	8	Bu	5.2	3.1	91.0	29.3	99.3
10	4	10	Bu	3.3	2.6	93.3	35.9	99.2
11	4	12	Bu	1.2	3.1	94.9	30.6	99.2
12	5	5	Bu	0.6	2.8	96.2	34.4	99.6
13	6	6	Bu	5.5	2.2	91.6	41.6	99.3
14	6	8	Bu	—	2.2	96.4	43.8	98.6
15	6	10	Bu	—	2.9	95.4	32.9	98.3
16	6	12	Bu	—	2.8	96.4	34.4	99.2
17	8	8	Bu	4.6	3.4	91.3	26.9	99.3
18	8	10	Bu	2.8	3.6	92.9	25.8	99.3
19	8	12	Bu	1.0	3.5	94.7	27.1	99.2
20	—	2	Br	—	4.4	95.4	21.7	99.8
21	—	3	Br	0.6	3.4	95.8	28.2	99.8

22	—	4	Br	—	1.8	96.2	53.4	98.0
23	—	6	Br	0.3	3.6	95.6	26.6	99.5
24	—	8	Br	1.3	5.3	92.8	17.5	99.4
25	3	6	Br	0.5	3.2	95.8	29.9	99.5
26	6	8	Br	2.1	3.4	94.1	27.7	99.6

[a] $SOCl_2$ (8.9 ml, 110 mmol) was slowly added to a mixture of OC (10.8 g, 100 mmol), $AlCl_3$ (0.5 g) and **1–26** (0.2 g) at 20°C over 2 h.
[b] Quantitative GC was used to calculate the yield (%) of all identified components of the product mixture.
[c] The sum of the yields (%) of the identified products, to check whether significant quantities of materials were unaccounted for.

Table 1 shows that all polymers benefitted both the yield of 4-COC and the *para/ortho* ratio, and the differences in performance were not huge. In general, polymers with at least one shorter chain (three or four methylene groups between the sulfur atoms) seemed to produce somewhat better *para/ortho* ratios than those with only longer chains, and those that were produced by the organolithium method (*i.e*. polymers **1–19**) in general gave somewhat better results than those produced by the sodium sulfide method (*i.e*. polymers **20–26**). Similar observations have been made in chlorination of phenol and 2-chlorophenol in the presence of these catalysts [31].

Next, a range of polymers (**5**, **7**, **12**, **14**, **21**, **23**, **25**, and **26**) that provided high yields of 4-COC and high *para/ortho* ratios were chosen to see whether they are equally effective with smaller quantities of polymer. The *para/ortho* ratios recorded with three different quantities (200, 100, and 50 mg) of these polymers are shown in Figure 2. Clearly, the *para/ortho* ratio declined in most cases when the quantity of polymer was reduced, but polymer **21** was exceptional in showing virtually no change in *para/ortho* ratio as the quantity was reduced from 200 mg to 50 mg.

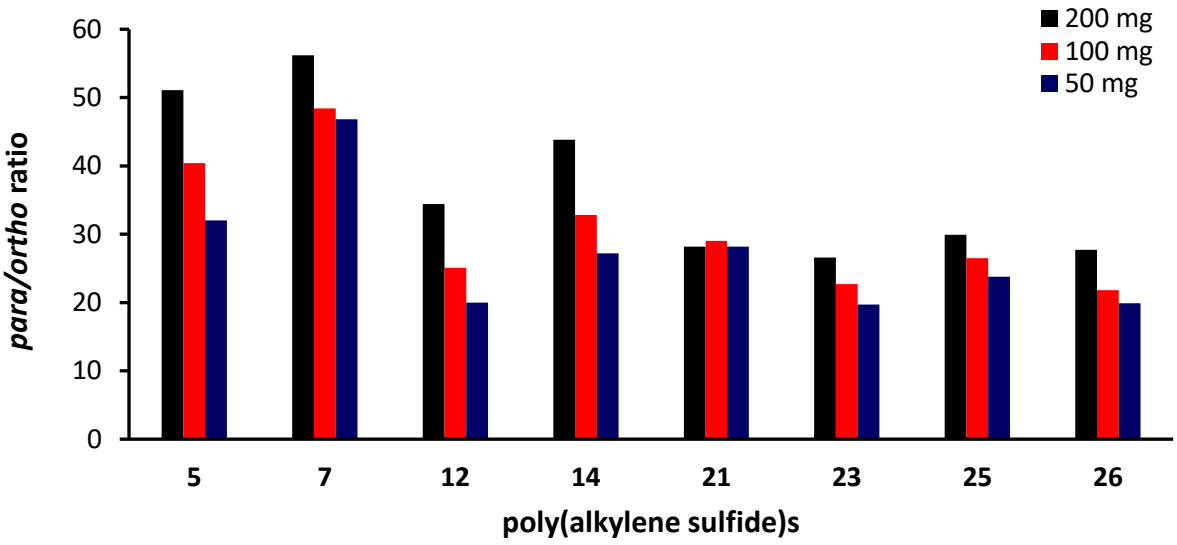


Figure 2. Effect of quantity of polymers on *p/o* ratio in chlorination of *o*-cresol.

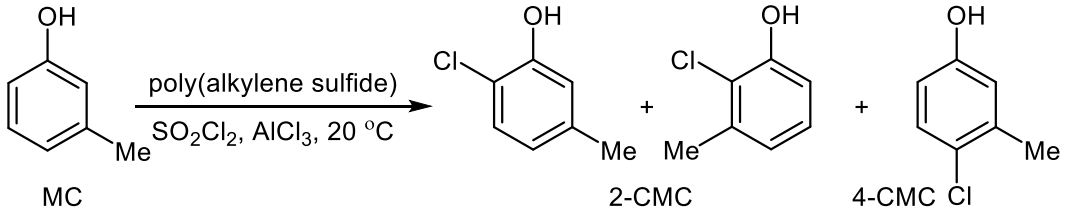
Polymer **21** provided a consistent *para/ortho* ratio and did not give much poorer results as the quantity was decreased. Therefore, a more extensive study of the effect of the amount of polymer **21** used was conducted (Table 2). It should be noted that polymer **21** is also easy to make and has a higher sulfur content than most of the other polymers. Clearly, the yield of 4-COC was still high (95.5%) even when a very small quantity of polymer **21** was used (only 2 mg).

Table 2. Chlorination of *o*-cresol using sulfuryl chloride and polymer **21** as a catalyst in the presence of $AlCl_3$ at 20°C according to Scheme 1.[a]

21 (mg)	$AlCl_3$ (mg)	Yield (%)[b]			*p*/*o* ratio	Mass balance (%)[c]
		OC	2-COC	4-COC		
—	500	11.2	11.3	76.3	6.8	98.8
200	500	0.6	3.4	95.8	28.2	99.8
200	300	0.6	3.5	95.6	27.3	99.7
100	500	0.7	3.3	95.8	29.0	99.8
100	300	0.6	3.2	96.0	30.0	99.8
50	500	0.4	3.4	95.9	28.2	99.7
50	300	—	3.5	96.1	27.5	99.6
50	100	0.4	3.6	95.9	26.6	99.9
50	50	0.2	3.7	95.9	25.9	99.8
40	100	—	3.6	96.3	26.7	99.9
40	50	—	3.5	96.3	27.5	99.8
30	50	0.2	3.6	96.1	26.7	99.9
20	50	—	3.5	96.4	27.5	99.9
10	50	0.2	3.7	96.0	25.9	99.9
10	30	0.2	3.9	95.8	24.6	99.9
10	20	—	3.7	95.9	25.9	99.6
5	20	—	3.7	95.7	25.8	99.4
5	15	—	3.9	95.6	24.5	99.5
3	15	0.2	3.8	95.7	25.2	99.7
2	20	—	4.1	95.6	23.3	99.7
2	15	—	4.2	95.5	22.7	99.7
2	10	—	4.3	95.5	22.2	99.8

[a] $SOCl_2$ (8.9 ml, 110 mmol) was slowly added to a mixture of OC (10.8 g, 100 mmol), $AlCl_3$ and **21** at 20°C for 2 h.
[b] Quantitative GC was used to calculate the yields (%).
[c] Sum of the yields (%) of the identified products.

Next, chlorination of MC was investigated under conditions similar to those used in the chlorination of OC (Scheme 2). The yields of 2-chloro-*m*-cresol (2-CMC) and 4-CMC are shown in Table 3. Some improvement in the yield of 4-CMX and *para/ortho* ratio was seen when any of the catalysts were used, and in the best cases the yield of 4-CMC increased to 94.6% (polymers **7** and **14**), from 87.4% in the absence of any catalyst, or the *para/ortho* ratio increased to 26.0-27.9 (polymers **17** and **18**) from 8.3 in the absence of any catalyst. Generally, catalysts with shorter spacers (n, m = 2–4) provided lower yields (88.2–91.9%) than the ones with longer spacers (n, m = 6–12; 90.5–94.6%), but differences in yield of 4-CMC or in selectivity ratio were not dramatic.



Scheme 2. Chlorination of *m*-cresol using sulfuryl chloride and poly(alkylene sulfide)s **1–26**.

Table 3. Chlorination of *m*-cresol using sulfuryl chloride and poly(alkylene sulfide)s **1–26** as catalysts in the presence of $AlCl_3$ at 20°C according to Scheme 2.[a]

Polymer	Repeating unit		Terminal group	Yield (%)[b]			*p*/*o* ratio	Mass balance (%)[c]
	n	m		MC	2-CMC	4-CMC		
—	—	—	—	1.6	10.5	87.4	8.3	99.5
1	2	2	Bu	0.6	8.6	88.8	10.3	98.0
2	3	3	Bu	2.9	7.4	88.2	11.9	98.5
3	3	4	Bu	0.5	9.0	89.7	10.0	99.2
4	3	6	Bu	1.6	3.8	93.2	24.5	98.6
5	3	9	Bu	3.5	5.1	90.5	17.7	99.1
6	3	12	Bu	1.6	4.7	93.2	19.8	99.5
7	4	4	Bu	0.6	4.1	94.6	23.1	99.3
8	4	6	Bu	2.4	4.5	92.4	20.5	99.3
9	4	8	Bu	1.9	3.9	92.3	23.7	98.1
10	4	10	Bu	2.9	4.4	92.1	20.9	99.4
11	4	12	Bu	2.4	4.5	92.0	20.4	98.9
12	5	5	Bu	0.3	5.3	94.2	17.8	99.8
13	6	6	Bu	0.6	6.7	92.3	13.8	99.6
14	6	8	Bu	0.5	4.6	94.6	20.6	99.7
15	6	10	Bu	0.6	3.9	93.6	24.0	98.1
16	6	12	Bu	3.5	3.6	92.2	25.6	99.3
17	8	8	Bu	2.0	3.6	93.7	26.0	99.3
18	8	10	Bu	3.9	3.3	92.1	27.9	99.3
19	8	12	Bu	1.7	3.7	93.6	25.3	99.0
20	—	2	Br	1.5	8.2	89.3	10.9	99.0
21	—	3	Br	0.4	9.0	90.1	10.0	99.5
22	—	4	Br	0.5	7.1	91.9	12.9	99.5
23	—	6	Br	0.5	6.7	92.4	13.8	99.6
24	—	8	Br	0.4	4.1	94.0	22.9	98.5
25	3	6	Br	0.6	6.7	92.3	13.8	99.6
26	6	8	Br	0.9	4.7	93.6	19.9	99.2

[a] $SOCl_2$ (8.9 ml, 110 mmol) was slowly added to a mixture of MC (10.8 g, 100 mmol), $AlCl_3$ (0.5 g) and **1–26** (0.2 g) at 20°C over 2 h.
[b] Quantitative GC was used to calculate the yields (%).
[c] The sum of the yields (%) of the identified products.

In view of the lack of clear trends in selectivity, a range of different polymers (**4**, **5**, **6**, **14**, and **25**) was selected to test the effect of their quantities on the *para/ortho* ratios. The *para/ortho* ratios recorded using 200, 100, and 50 mg of these polymers are shown in Figure 3. Clearly, the *para/ortho* ratio generally declined when the quantity of polymer was reduced, but the degree of reduction with polymers **14** and **25** was exceptionally small. Polymer **25** was even used in a very low amount (5 mg) to provide 4-CMC in 92.1% yield with a *p/o* of 13.2, values that are only marginally lower than with 200 mg of that polymer. It may be possible to identify a polymer that gives even higher values with a very small amount of catalyst, but further studies were not justified at this stage. Instead, attention was turned to chlorination of *meta*-xylenol.

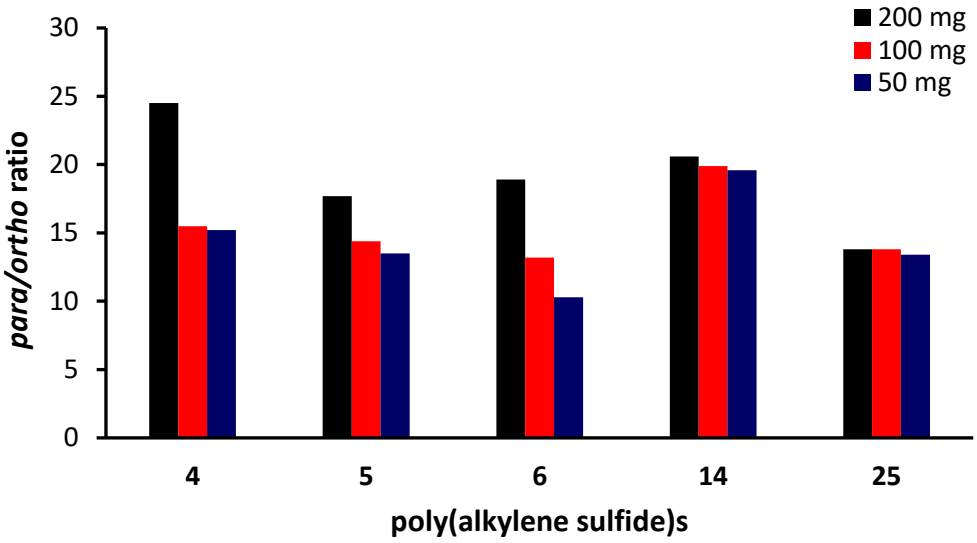
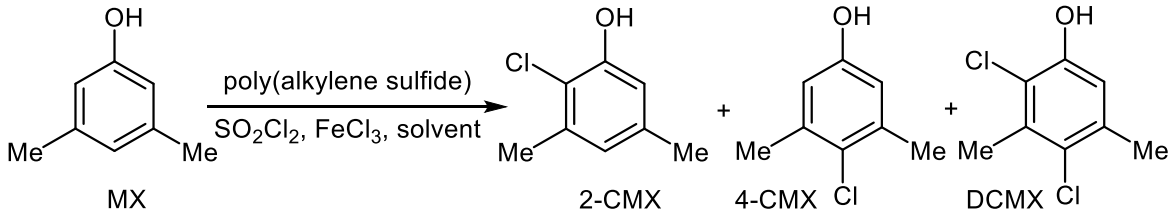


Figure 3. Effect of quantity of polymers on *para/ortho* ratio in chlorination of *m*-cresol.

Since MX does not melt at a low enough temperature, a solvent is needed for its reactions with sulfuryl chloride in the presence of a polymer catalyst. Furthermore, commercial 4-CMX has a specification limiting the amount of aluminium permitted. Chlorination of MX was attempted in the presence of $FeCl_3$ rather than $AlCl_3$ and in DCM, since $FeCl_3$ was previously used in chlorination of MX using cyclic and polymeric disulfides as catalysts in DCM [28]. In view of the

fact that smaller quantities than 200 mg of some catalysts had proved very successful with OC and MC, the chlorination of MX (Scheme 3) was initially attempted at 20°C using only 100 mg of poly(alkylene sulfide)s **1–26** as catalysts. The results obtained are recorded in Table 4.



Scheme 3. Chlorination of *m*-xylenol using sulfuryl chloride and poly(alkylene sulfide)s **1–26**.

Table 4. Chlorination of *m*-xylenol using sulfuryl chloride and poly(alkylene sulfide)s **1–26** as catalysts in the presence of $FeCl_3$ in DCM at 20°C according to Scheme 3.[a]

Polymer	Repeating unit		Terminal group	Yield (%)[b]				*p*/*o* ratio	Mass balance (%)[c]
	m	n		MX	2-CMX	4-CMX	DCMX		
—	—	—	—	13.0	8.7	78.3	—	9.03	100.0
1	2	2	Bu	0.8	7.8	88.4	2.8	11.3	99.8
2	3	3	Bu	2.2	6.6	88.1	2.8	13.3	99.7
3	3	4	Bu	2.0	6.8	90.5	0.6	13.3	99.9
4	3	6	Bu	0.5	5.6	92.7	1.0	16.6	99.8
5	3	9	Bu	1.1	4.9	91.8	1.8	18.7	99.6
6	3	12	Bu	3.2	6.7	89.8	—	13.4	99.7
7	4	4	Bu	1.8	7.4	90.3	0.4	12.2	99.9
8	4	6	Bu	3.1	10.1	86.1	0.5	8.5	99.8
9	4	8	Bu	4.8	9.3	85.7	—	9.2	99.8
10	4	10	Bu	1.4	10.0	87.7	0.6	8.8	99.7
11	4	12	Bu	1.4	7.4	89.0	2.0	12.0	99.8
12	5	5	Bu	0.3	4.7	94.1	0.8	20.0	99.9
13	6	6	Bu	1.4	3.8	94.4	0.2	24.8	99.8
14	6	8	Bu	1.0	3.5	92.5	2.7	26.4	99.7
14[d]	6	8	Bu	1.9	4.0	93.8	—	23.5	99.7
15	6	10	Bu	2.2	5.1	92.4	—	18.1	99.7
16	6	12	Bu	2.4	4.6	92.8	—	20.2	99.8
17	8	8	Bu	1.2	4.1	94.4	—	23.0	99.7
17[e]	8	8	Bu	1.0	3.5	94.2	1.1	26.9	99.8
18	8	10	Bu	3.8	4.6	91.2	—	19.8	99.6
19	8	12	Bu	2.5	4.0	93.3	—	23.3	99.8
20	—	2	Br	0.7	11.2	86.3	1.7	7.70	99.9
21	—	3	Br	1.8	8.7	88.7	0.7	10.2	99.9

22	—	4	Br	3.0	7.1	89.3	0.5	12.6	99.9
23	—	6	Br	1.4	6.8	90.8	0.9	13.3	99.9
24	—	8	Br	0.8	5.2	93.6	—	18.0	99.6
25	3	6	Br	1.4	6.8	90.8	0.9	13.3	99.9
26	6	8	Br	0.6	4.9	93.6	0.8	19.1	99.9

[a] $SOCl_2$ (8.9 ml, 110 mmol) was slowly added to a mixture of MX (12.2 g, 100 mmol), $FeCl_3$ (0.1 g) and **1–26** (0.1 g) in DCM (50 ml) at 20°C over 2 h.
[b] Quantitative GC was used to calculate the yields (%).
[c] The sum of the yields (%) of the identified products.
[d] Polymer **14** (50 mg) was used.
[e] Polymer **17** (50 mg) was used.

The results showed that polymers with longer spacer units (at least five methylene units, but especially when one of the spacer units was eight methylene groups long) gave higher yields of 4-CMX and higher *para/ortho* ratios than those with short spacer units, and that polymers made using the lithiation method (recorded as having Bu terminal groups; *i.e*. polymers **1**–**19**) generally gave higher ratios than those made using the sodium sulfide method (Br terminal groups; *i.e*. polymers **20**–**26**), although the latter types have the advantage that they are simpler and cheaper to make. In consequence, we selected several of the polymer sulfides (namely **14**, **17**, **23**, **24** and **26**) for more detailed study. It should be noted that 2,4-dichloro-*m*-xylenol was produced in most reactions, but in low yield (0–2.8%, See Table 4).

Several other solvents such as diethyl ether, acetonitrile, 1,2-dichloroethane, chloroform and toluene were tested as media for the chlorination of *m*-xylenol, but most of these solvents did not provide high enough yields of 4-CMX or high enough *para/ortho* selectivity. However, chlorination of MX in tetrachloroethylene (TCE) provided high yields of 4-CMX when using the selected catalysts, even with smaller quantities of catalyst. Therefore, the standard 100 mmol reaction was conducted in TCE in the presence of 30 mg or less of the selected catalysts, at 20°C. The results obtained are shown in Table 5. Excellent yields of 4-CMX (*ca*. 97%) were obtained in most cases. Lowering the quantity of catalyst to only 5 mg with polymer **23** still produced 94.9% of the *para*-product.

Table 5. Chlorination of *m*-xylenol using sulfuryl chloride and poly(alkylene sulfide)s **14**, **17**, **23**, **24**, or **26** as catalysts in the presence of $FeCl_3$ in TCE at 20°C according to Scheme 3.[a]

Polymer	(mg)	Yield (%)[b]

		$FeCl_3$ (mg)	MX	2-CMX	4-CMX	DCMX	*p*/*o* ratio	Mass balance (%)[c]
—	—	100	3.2	9.4	87.0	0.3	9.2	99.9
14	30	50	0.7	1.4	97.4	0.3	69.6	99.8
17	30	50	0.3	1.3	97.6	0.4	74.9	99.6
23	5	50	1.5	2.8	94.9	0.7	33.9	99.9
24	30	50	0.7	1.1	96.7	1.4	87.9	99.9
26	30	50	0.5	3.1	96.0	0.3	31.0	99.9
26	10	25	0.5	3.9	95.2	0.3	24.4	99.9

[a] $SOCl_2$ (8.9 ml, 110 mmol) was slowly added to a mixture of MX (12.2 g, 100 mmol), $FeCl_3$ and appropriate catalyst in TCE (50 ml) at 20°C over 2 h.
[b] Quantitative GC was used to calculate the yields (%).
[c] The sum of the yields (%) of the identified products.

A further advantage of TCE is that it can be used at higher temperatures than DCM, which is preferable for maintaining a concentrated solution during reaction, as would be desirable for commercial scale application. Therefore, reactions were conducted at 2.5 times higher concentration and at various temperatures (30–60 °C), and in some cases the amount of catalyst was further reduced. The results are shown in Table 6. High yields (93.5–95.3%) of 4-CMX could still be obtained under the conditions attempted. The results demonstrate that the temperature, solvent and quantity of both $FeCl_3$ and catalyst can be manipulated without a large drop in the yield of 4-CMX. This could therefore provide a useful commercial process and to reinforce that point a reaction was scaled up to 0.5 mole scale. Chlorination of MX (61 g, 500 mmol) using SO_2Cl_2 (525 mmol) in TCE (100 ml) at 40°C in the presence of polymer **23** (25 mg) and $FeCl_3$ (75 mg) gave 4-CMX in 94% yield and 2-CMX in only 4.3% yield (a *para*/*ortho* ratio of 21.9).

Table 6. Chlorination of *m*-xylenol using sulfuryl chloride and poly(alkylene sulfide)s **14**, **17**, **23**, **24**, or **26** as catalysts in the presence of $FeCl_3$ in TCE at different temperatures according to Scheme 3.[a]

Polymer	(mg)	$FeCl_3$ (mg)	T (°C)	Yield (%)[b]				*p*/*o* ratio	Mass balance (%)[c]
				MX	2-CMX	4-CMX	DCMX		
14	30	50	50	0.7	4.0	94.9	0.3	23.7	99.9
14	30	50	60	0.4	4.3	95.2	—	22.1	99.9
17	30	50	30	0.5	2.4	94.9	1.9	39.5	99.7
17	30	50	40	0.3	3.9	95.3	0.3	24.4	99.8
17	30	50	50	0.8	4.0	95.1	—	23.7	99.9
17	30	50	60	0.3	5.2	94.4	—	18.2	99.9

23	5	20	40	1.6	3.5	94.2	0.6	26.9	99.9
23	10	50	50	0.5	5.0	94.4	—	18.9	99.9
24	30	50	40	1.2	2.4	94.6	1.3	39.4	99.5
24	20	50	50	0.6	4.9	94.3	0.1	19.2	99.9
24	30	50	60	0.8	5.2	93.5	0.3	18.0	99.8
26	30	50	30	0.6	3.9	95.1	0.3	24.4	99.9
26	30	50	40	0.5	4.2	94.8	0.3	22.6	99.8
26	15	25	50	0.7	4.3	94.3	0.6	21.9	99.9

[a] $SOCl_2$ (8.9 ml, 110 mmol) was slowly added to a mixture of MX (12.2 g, 100 mmol), $FeCl_3$ and the appropriate catalyst in TCE (20 ml) over 2 h.
[b] Quantitative GC was used to calculate the yields (%).
[c] The sum of the yields (%) of the identified products.

3. Conclusion

Chlorination of *o*-cresol, *m*-cresol, and *m*-xylenol using sulfuryl chloride in the presence of poly(alkylene sulfide)s and a Lewis acid provides high yields of the corresponding 4-chlorophenols with high *para/ortho* ratios. For *o*-cresol, poly(alkylene sulfide)s with at least one shorter chain (three or four methylene groups between sulfur atoms) led to somewhat better *para/ortho* ratios than those obtained with polymers containing only longer chains (at least six methylene groups between the sulfur atoms). On the other hand, high yields of both 4-chloro-*m*-cresol and 4-chloro-*m*-xyelenol were obtained when chlorination of *m*-cresol and *m*-xylenol was carried out in the presence of poly(alkylene sulfide)s containing at least one longer spacer group (six methylene groups or more), whereas the *para*-selectivity was typically somewhat lower with catalysts having shorter spacers (four methylene groups and less). The chlorination processes reported are highly selective towards *para*-chlorophenols and have the potential to be applied commercially.

4. Experimental Section

4.1. General

Reagents and solvents were obtained from Sigma-Aldrich Chemical Company. Sulfuryl chloride was distilled under an inert atmosphere and used freshly. A Shimadzu GC-2014 Gas Chromatograph using a capillary ZB Carbowax column (30 m, 0.32 mm ID) was used to analyse components of chlorination reaction mixtures quantitatively using tetradecane as a standard. The

temperature of the column started at 40°C for 3 min, ramped to 220°C (10°C/min) and held for 10 min. The detector and injector temperatures were 250 and 300°C, respectively.

4.2 General procedure of the chlorination of cresols

To a mixture of melted *o*-cresol or *m*-cresol (10.8 g, 100.0 mmol), $AlCl_3$ (0.5 g) and the appropriate poly(alkylene sulfide) (**1–26**, 0.2 g), freshly distilled SO_2Cl_2 (8.9 ml, 110.0 mmol) was slowly added over 2 h. The reaction mixture was stirred for 2 h longer and then quenched with water (30 ml) and the products were extracted with Et_2O (3 × 30 ml). The organic layers were dried over $MgSO_4$, filtered, and the solvent was removed under vacuum. The crude product was weighed and analyzed quantitatively by GC. Some reactions had different amounts of polymer catalyst and/or aluminium chloride (see results section), but were otherwise conducted in the same manner.

4.3 General procedure for the chlorination of m-xylenol

To a stirred mixture of *m*-xylenol (12.2 g, 100.0 mmol), $FeCl_3$ (0.1 g), and the appropriate poly(alkylene sulfide) (**1–26**, 0.1 g) in DCM (50 ml), freshly distilled SO_2Cl_2 (8.9 ml, 110.0 mmol) was slowly added over 2 h and the mixture was stirred for another 2 h. The mixture was worked up as described for the chlorination of cresols and the product mixture was analyzed by GC. Some reactions were conducted in different solvents, and/or with different quantities of solvent, polymer and/or ferric chloride (see results section), but were otherwise conducted in the same manner.

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Disclosure statement

No potential conflict of interest was reported by the authors.

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