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Selective *ortho*-chlorination of phenol using sulfuryl chloride in the presence of *t*-butylaminomethyl polystyrene as a heterogeneous amine catalyst

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Abstract—Reaction of phenol with sulfuryl chloride in the presence of a catalytic amount of the heterogeneous amine catalyst, *t*-butylaminomethyl polystyrene, in a nonpolar solvent, proceeds with high conversion (~98%) and with high selectivity (~89%) to *ortho*-chlorophenol. The catalyst is stable under the chlorination conditions, and can easily be regenerated by filtration and reused. This method could be applicable to other phenols.

Electrophilic aromatic halogenation[1,2] reactions are of considerable importance in the production of agrochemicals, pigments, drugs, pharmaceuticals and photographic materials.[3] Chlorination of phenol is a particularly important reaction, since many chlorophenols are useful intermediates for the manufacture of insecticides, dyestuffs, preservatives and disinfectants.[4,5] Traditional methods of aromatic chlorination involve the use of acidic reagents that can lead to separation difficulties and unacceptable levels of toxic and corrosive waste.[6] In addition, such reactions are subject to problems of both chemo- and regioselectivity, generally giving mixtures of mono-, di- and tri-chlorinated products.[7]

The available methods for direct *ortho*-chlorination of phenol involve the use of *t*-butyl hypochloride,[8–12] *N*,*N*-dichloro-*t*-butylamine,[13] *N*-chloroamines/silica gel,[14] and Cl_2 catalyzed by amines.[15] Recently,[16] we have reported the liquid phase *ortho*-chlorination of phenol using SO_2Cl_2 catalyzed by secondary amines. The reaction is fast, specific for monochlorination and highly regioselective for *ortho*-substitution.[17] Herein, we report an efficient and reusable amine-based catalyst, *t*-butylaminomethyl polystyrene, for the regioselective *ortho*-chlorination of phenol.

Several commercial solid amine materials, for example, amino silica gel, *n*-propylamino glass and methyl polystyrene–NH_4Cl resin, were tested in the chlorination of phenol using SO_2Cl_2 in toluene at 70 °C for 1 h. The results are summarized in Table 1. The *o*/*p* ratios obtained are low and very similar to those obtained with silica gel as a catalyst under identical conditions. An improvement in the selectivity of the reaction was achieved by using aminomethyl polystyrene (amino-MPS) catalyst (run 5), where the *o*/*p* ratio was increased about twofold compared to the control reaction (run 1).

Interestingly, the *o*/*p* ratio was increased from 2.02 to 2.20, by decreasing the amount of the amino-MPS catalyst from 0.50 g to 0.01 g (runs 5 and 6), and the *o*/*p* ratio was increased from 2.02 to 2.73, by decreasing the degree of divinylbenzene cross linked units from 2% to 1% (runs 5 and 7). Although, the cross linking in the catalyst reduces the *ortho* selectivity of the chlorination, nevertheless, a certain degree of cross linking in the polystyrene structure is an essential factor in order to enhance the stability of the catalyst, and to diminish its solubility in organic solvents, and therefore retain its heterogeneous properties.

When the chlorination of phenol was conducted homogeneously in the presence of a catalytic amount of

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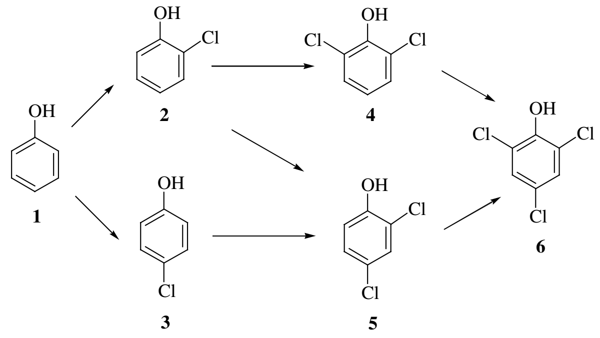
Table 1. Chlorination of phenol with sulfuryl chloride in the presence of various catalysts[a]



Run no.	Catalyst[b]	Amount of catalyst, g	Yield, mol%				
			1	**2**	**3**	**4 + 5 + 6**	*o*/*p* Ratio
1	None	—	92.8	3.8	3.4	Traces	1.12
2	Amino silica gel	0.50	7.5	43.4	47.0	2.1	0.92
3	Aminopropyl glass	0.50	4.5	45.0	47.8	2.7	0.94
4	Polystyrene methyl–NH_4Cl	0.50	19.5	37.7	40.7	2.1	0.93
5	Amino-MPS (2% DVB)	0.50	6.8	59.0	29.2	5.0	2.02
6	Amino-MPS (2% DVB)	0.01	10.5	59.1	26.9	3.5	2.20
7	Amino-MPS (1% DVB)	0.50	5.0	66.1	24.2	4.7	2.73
8	Chloro-MPS (2% DVB)	0.50	94.0	3.6	2.4	Traces	1.48
9	*N*-di(*s*-butyl)amino-MPS[c]	0.50	4.8	69.6	21.6	4.0	3.22
10	*N*-*s*-Butylamino-MPS	0.50	5.1	68.3	21.0	5.6	3.25
11	*N*-*n*-Butylamino-MPS	0.50	4.1	70.8	17.6	7.5	4.02
12	*N*-*t*-Butylamino-MPS	0.50	2.1	85.9	8.2	3.8	10.48
13	*N*-*t*-Butylamino-MPS	0.10	2.5	86.3	6.6	4.6	13.08
14	Recycled catalyst from run 13	0.10	3.0	85.4	6.6	5.0	12.94
15	Recycled catalyst from run 14	0.10	2.6	86.6	6.8	4.0	12.74
16	Recycled catalyst from run 15	0.10	2.9	85.1	6.5	5.5	13.09

[a] Chlorination of phenol: To a mixture of phenol (12.6mmol), toluene (87g) and the appropriate solid catalyst (0.01 or 0.1 or 0.5g) gently stirred in 250mL round bottom flask, was added SO_2Cl_2 (12.6mmol) dropwise at 70°C. The mixture was stirred at this temperature for 1h. The solid catalyst was filtered off, volatile solvents were removed under vacuum and the residue was analyzed by GLC. The GLC analyses were performed with a Hewlett Packard instrument equipped with a F.I.D. coupled to a Perkin–Elmer GP100 recorder. A glass column (50m, 0.53mm i.d.) was packed with CP sil 5 CB (2.0μm). Yields, given in mol percent, determined with 1,2-dichlorobenzene as an internal standard.

[b] Amino silica gel and *n*-propylamino glass were supplied by Macherey-Nagel Co. Aminomethyl polystyrene (amino-MPS) and chloromethyl polystyrene (chloro-MPS) were supplied by Fluka. Amino-MPS (2% DVB) and amino-MPS (1%) polymers contain 1.1 and 0.6mmol amine/1g, respectively. Chloro-MPS (2%) polymer contains 0.7mmol chlorine/1g.

[c] Preparation of *N*-alkylaminomethyl polystyrene catalyst: To a mixture of K_2CO_3 (1.0g), amine (1mL) and dry DMF (10mL), was added chloromethyl polystyrene (1g). The reaction mixture was heated overnight at 50°C. The solid was filtered, washed with 20mL portions of dichloromethane, acetone, water, 8% NaOH solution, water and finally with acetone. The resulting solid was dried overnight under vacuum.

benzylamine, an *o*/*p* ratio of 1.75 was obtained. Using a secondary amine, *N*-methylbenzylamine, a significant enhancement of the *ortho* selectivity was observed, that is, *o*/*p* ratio of 14.51. We found these results promising enough for further study, and therefore, further structural modification of the amino group in the solid amino-MPS catalyst has been investigated.

Preparation of secondary amine derivatives of the methyl polystyrene resin can be achieved by reaction of amino-MPS with alkyl halides, or by reaction of chloromethyl polystyrene (chloro-MPS) with alkyl amine. We preferred the second approach for the following reasons: (i) the benzyl chloride group present in chloro-MPS is more reactive towards nucleophilic substitution than that of alkyl halides, (ii) one possible product can be formed according to the first approach, however, a mixture of products (secondary, tertiary and quaternary amines) may be formed by reaction of amino-MPS with alkyl halides and (iii) the commercial starting material chloro-MPS is 10 times less expensive than amino-MPS.

We have prepared several modified *N*-butylamino-MPS catalysts, for example, *n*-butyl-, *s*-butyl-, di-*s*-butyl- and *t*-butylamino-MPS by reaction of the appropriate amine with chloro-MPS in a K_2CO_3/DMF suspension. The chlorination results using these modified catalysts are presented in Table 1. The observed *o*/*p* ratios for *n*-butyl-, *s*-butyl-, di-*s*-butyl- and *t*-butylamino-MPS are 4.02, 3.25, 3.22 and 10.48, respectively.

By conducting the reaction with a reduced amount of the *t*-butylamino-MPS catalyst, a further improvement in the *o*/*p* ratio was achieved, that is, *o*/*p* ratio of 13.08 (run 13). The heterogeneous *t*-butylamino-MPS catalyst was recycled three times, without any special treatment, and the chlorination results showed clearly that the catalyst is very stable under SO_2Cl_2 chlorination conditions, and retained its catalytic activity (runs 14–16).

The results with *t*-butylamino-MPS are similar to those obtained with homogeneous amine catalysts, and confirm our previous observation [16] that, secondary amines with bulky substituents are excellent catalysts for regioselective *ortho*-chlorination of phenol in a nonpolar medium. Preliminary results show that this method could be applicable to other phenolic compounds. Under similar conditions using *N*-bromosuccinimide (NBS) in the presence of *t*-butylamino-MPS catalyst, selective *ortho*-bromination of phenol was achieved.[18] Therefore, it will be of great interest to test this catalyst in other amine catalyzed reactions.

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