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Regioselective bromination of aromatic compounds with Br_2/SO_2Cl_2 over microporous catalysts

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Abstract—A new selective brominating system Br_2/SO_2Cl_2/zeolite, has been discovered. Partially cation-exchanged Ca^{2+}-Y zeolite efficiently catalyzes the selective *para*-bromination of neat chlorobenzene (CB) by Br_2/SO_2Cl_2 affording a CB conversion of ~89% and a *para*-selectivity of ~97%. During the bromination reaction, SO_2Cl_2 oxidizes HBr, prevents its accumulation within the zeolite pores and yields a more active brominating species. The Ca^{2+}-Y catalyst was found to be stable under the bromination conditions, and can easily be regenerated by calcination. The $Br_2/SO_2Cl_2/Ca^{2+}$-Y brominating system could be applicable to other activated aromatic compounds such as *o*-xylene, toluene and fluorobenzene.

The manufacture of many bulk and fine chemicals involves bromination of aromatics.[1] Various methods have been developed and reported for the bromination of aromatic systems using a variety of brominating agents under various reaction conditions.[2] Some of these methods involve the use of Br_2/Lewis acids,[3] $Br_2/SbF_3/HF$,[4] NBS/H_2SO_4/CF_3CO_2H,[5] NBS/PTSA,[6] NBS/NaOH,[7] NBS in ionic liquids,[8] HBr/*tert*-BuOOH, HBr/H_2O_2,[9] HBr/DMSO,[10] $NH_4Br/H_2O_2/CH_3COOH$,[11] quaternary ammonium tribromide,[12] $KBrO_3$,[13] KBr/sodium tungstate/H_2O_2,[14] hexamethylene tetramine tribromide,[15] pyridinium hydrobromide perbromide,[16] NaBr/Oxone, KBr/Oxone, KBr/H_2O_2/Oxone,[17] $CuBr_2$/*t*-BuONO,[18] sodium monobromoisocyanurate[19] and the catalytic oxidation of bromide ions.[20]

Numerous methods have also been proposed to increase the yield and the selectivity of the *para*-bromo isomer, which has greater commercial significance.[21–27] In particular, zeolites have attracted much attention of organic chemists over the last two decades. Due to their regular microporous structure they proved to be useful as a tool for reaction control in organic synthesis.[28] The zeolite-catalyzed bromination of aromatics is highly selective at low conversions, however, a decrease in selectivity and reaction rate were observed with the progress of the reaction.[29] The main factor responsible for decreasing the selectivity of the bromination was the effect of HBr, which was liberated during the reaction, on the structure of the zeolite catalyst.[30] One way to increase both the activity and the selectivity of the zeolite-catalyzed bromination is to remove the HBr by using various scavengers and oxidants such as inorganic salts,[31,32] organic bases, alcohols and carboxylic acids,[33] oxiranes[34] and oxygen.[35] In this communication, we report an efficient procedure for the *para*-bromination of halo- and alkyl-benzenes using a new brominating system Br_2/SO_2Cl_2, with the aid of microporous catalysts.

In the absence of catalyst, neat chlorobenzene (CB) was very slowly monobrominated with Br_2 with a molar ratio of 2:1 at 25 °C and at 100 °C, giving after 24 h, CB conversions of ~0.2% and ~16%, respectively (Table 1, runs 1 and 2). The rate and the isomer distribution obtained in the bromination varied significantly when the reaction was conducted in the presence of a catalytic amount of Lewis acid catalysts, such as $AlCl_3$ and $FeCl_3$ (runs 3 and 4). The relatively high conversions and selectivities were attributed to the effect of polarizing the bromine molecule and consequently enhancing its electrophilicity.[1,2]

Keywords: Bromination; Catalysis; Aromatics; Chlorobenzene; Bromine; Sulfuryl chloride; Regioselectivity; Heterogeneous catalyst; Zeolites; Clays; Cation-exchange.

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Table 1. Bromination of chlorobenzene (CB) with Br_2 in the presence of various catalysts[a]

Run no.	Catalyst	CB Conversion (mol %)	Selectivity (mol %)		
			p-BCB[b]	*o*-BCB[b]	*p*/*o* Ratio
1	None	Traces	—	—	—
2	None	15.6[c]	89.1	10.9	8.2
3	$AlCl_3$[d]	49.5	93.6	6.4	14.6
4	$FeCl_3$[d]	50.0	89.9	10.1	8.9
5	Zeolite X	13.5	98.4	1.6	61.5
6	LZ-Y82	35.8	93.7	6.3	14.9
7	Ca^{2+}-Y[e]	45.3	89.6	10.4	8.6
8	Ce^{3+}-Y	46.0	96.1	3.9	24.6
9	Fe^{3+}-Y	46.5	84.0	16.0	5.3
10	Zn^{2+}-Y	47.3	87.5	12.5	7.0
11	Ni^{2+}-Y	47.4	89.5	10.5	8.5
12	Cu^{2+}-Y	48.1	90.3	9.7	9.3
13	Cu^{2+}-X	50.0	90.6	9.4	9.6

[a] See note 35 for conditions.
[b] *p*-BCB: *para*-bromochlorobenzene; *o*-BCB: *ortho*-bromochlorobenzene.
[c] The reaction was carried out at 100 °C.
[d] The amounts of $AlCl_3$ and $FeCl_3$ catalyst used were 0.7 and 0.8 g, respectively.
[e] See note 36.

The combination of high Brønsted acidity and interlamellar spaces present in aluminosilicate structures make them good candidates as chemo- and regio-selective catalysts in electrophilic substitution of aromatics. Therefore, we tested several types of microporous catalysts such as SiO_2, Al_2O_3, zeolite 3A, 4A, Y, mordenite, X, LZ-Y82, KSF clay and K10 clay, in the bromination of CB with Br_2. The results show that CB conversions and *para*-selectivities were improved compared to those of the control reaction. For example, the large-pore size zeolite X and zeolite LZ-Y82 catalyze the bromination of CB with Br_2, affording CB conversions of ~14% and ~36%, and *para*-selectivities of ~98% and ~94%, respectively (runs 5 and 6). These results also indicate that larger-pore size zeolites are superior catalysts to the smaller ones. This is probably due to the inability of the reactants to diffuse through the channels of the small-pore size zeolites and/or the small space available in these structures may not be able to accommodate the bulky transition state of the bromine-CB reaction.

A large number of clays and zeolites supported with metal cations such as Na^+, K^+, Cs^+, Ca^{2+}, Ba^{2+}, Cu^{2+}, Co^{2+}, Ce^{3+}, Al^{3+}, Fe^{3+}, Zn^{2+}, Mg^{2+} and Ni^{2+}, were prepared[37] and their catalytic properties were examined in the bromination of CB. The following observations can be made: (1) great improvements of the CB conversions were observed, for example by using Cu^{2+}-X catalyst, a 50% CB conversion was achieved at 25 °C (run 13); (2) the catalytic performance of the various partially cation-exchanged zeolites are strongly dependent on the type of the zeolite and the charge and size of the cation used; (3) the most active and *para*-selective of the cation-exchanged catalysts studied was Ce^{3+}-Y, which afforded a CB conversion of ~46% and a *para*-selectivity of ~96%, that is a *para*/*ortho* ratio of ~25 (run 8) and (4) the selectivity of the bromination was higher at low conversions and slightly decreased with the progress of the reaction.

Table 2. Bromination of CB with Br_2/SO_2Cl_2 in the presence of various catalysts[a]

Run no.	Catalyst[b]	CB Conversion (mol %)	Selectivity (mol %)		
			p-BCB	*o*-BCB	*p*/*o* Ratio
1	Co^{2+}-X	63.0	89.1	10.9	8.2
2	Ni^{2+}-Y	63.0	93.0	7.0	13.3
3	Mg^{2+}-Y	68.1	94.2	5.8	16.2
4	Cu^{2+}-Y	73.6	93.8	6.2	15.1
5	Co^{2+}-Y	82.8	92.8	7.2	12.9
6	Ce^{3+}-Y	86.0	96.9	3.1	31.3
7	Zn^{2+}-Y	86.5	92.7	7.3	12.7
8	Cu^{2+}-X	88.7	93.1	6.9	13.5
9	Ca^{2+}-Y	89.2	96.7	3.3	29.3

[a] See note 38 for conditions.
[b] See note 36.

Next we turned our attention to the bromination of CB with SO_2Cl_2/Br_2 in the presence of the cation-exchanged zeolites X and Y. The results are shown in Table 2. The observed reaction rates, CB conversions and *para*-selectivities were substantially improved in comparison with the corresponding values obtained using only Br_2 under the same conditions. With Ca^{2+}-Y and Ce^{3+}-Y catalysts, ~89% and ~86% CB conversions, and ~97% and ~97% *para*-selectivities were achieved, respectively (runs 6 and 9). These observations suggest that probably the mechanism of the Br_2/SO_2Cl_2-reaction is different from that of the Br_2-reaction. Despite the presence of SO_2Cl_2 in the reaction mixture, no chlorination products were observed.

In a continuous bromination experiment, a mixture of CB, Br_2 and SO_2Cl_2 with a 2:1:1 molar ratio was passed through a glass column containing solid Ca^{2+}-Y catalyst at 25 °C for a contact period of 2 h. The resulting reaction mixture was analyzed and showed an ~85% CB conversion and a ~96% *para*-selectivity. Interestingly, by decreasing the amount of the Ca^{2+}-Y catalyst 10-fold under the same reaction conditions, the *para*-selectivity of the bromination was almost unchanged, that is, ~97% and ~96%, respectively. The [catalyst (g)/substrate (mmol)] ratio in our present study (0.2 g catalyst per 40 mmol substrate) is less than 0.005 g/ mmol, which is lower than those (0.1–1.5 g/mmol) of previous work.[30,31,33,34,41]

A typical reaction profile of the bromination of CB using Br_2/SO_2Cl_2 and Ca^{2+}-Y zeolite indicates that the *para*/*ortho* ratio is almost constant during the course of the reaction. The effect of the calcination temperature of the Ca^{2+}-Y zeolite on the bromination of CB was also examined. The optimum activity of the catalyst, which corresponded with the maximum Brønsted acidity, was obtained after calcination at about 400 °C. Preliminary results showed that the Ca^{2+}-Y zeolite catalyst, which was regenerated by washing with deionized water, drying at 110 °C and then reactivation at 400 °C, retained its catalytic activity.

The cation-exchanged reaction of Na^+-Y with an aqueous solution of $CaCl_2$ yielded the corresponding Ca^{2+}-Y zeolite (~3.6 mass% of Ca, which is ~0.9 mmol of Ca in

1.0 g zeolite, i.e., ~52% of the Na content was exchanged with Ca) without affecting the original Si/Al ratio (~2.7), that is, no dealumination of the zeolite had occurred. A comparison of the Na/Si ratio, Na/Al ratio and the amount of Ca in the original Ca^{2+}-Y zeolite (0.11, 0.28 and 0.90 mass %, respectively) with that of the recovered Ca^{2+}-Y zeolite (0.11, 0.32 and 0.90 mass %, respectively) indicates that there are only very slight structural variations. The stability of the Ca^{2+}-Y zeolite under the bromination conditions was also confirmed by analyzing the IR spectra and the X-ray diffractograms of the Na^{+}-Y, Ca^{2+}-Y and the recovered Ca^{2+}-Y zeolites.

SO_2Cl_2[39–41] may react with Br_2 in the presence of zeolite to give BrCl and SO_2 (Eq. 1), in a similar way to the reaction of Cl_2 with Br_2 (Eq. 2). On the other hand, SO_2Cl_2 may also react with HBr to afford Br_2, HCl and SO_2 as shown in Eq. 3. In both cases a new brominating agent is formed, that is BrCl or Br_2, as a result of redox reactions, and regeneration of the Br atoms.

$$SO_2Cl_2\ (l) + Br_2\ (l) \rightarrow 2BrCl\ (l) + SO_2\ (g) \tag{1}$$

$$Cl_2\ (g) + Br_2\ (l) \rightarrow 2BrCl\ (l) \tag{2}$$

$$SO_2Cl_2\ (l) + 2HBr\ (g) \rightarrow Br_2\ (l) + 2HCl\ (g) + SO_2\ (g) \tag{3}$$

The $Br_2/SO_2Cl_2/Ca^{2+}$-Y catalytic system was applied in the bromination of other aromatic compounds. Under optimum conditions, *o*-xylene or toluene or fluorobenzene were brominated using Br_2/SO_2Cl_2 with a 2:1:1 molar ratio in the presence of a catalytic amount of Ca^{2+}-Y catalyst at 25 °C for 3 h. Bromo-*o*-xylenes, bromotoluenes and bromofluorobenzenes were produced with ~99%, ~83 % and ~90% substrate conversions and ~92%, ~85% and ~99% *para*-selectivities, respectively. These preliminary results clearly demonstrate the generality of our heterogeneous catalytic system in the regioselective *para*-bromination of activated aromatic compounds, and they are sufficiently promising to encourage further study such as poisoning the outer active acidic sites of the Ca^{2+}-Y zeolite by bulky and hydrophobic substituents, in order to enhance further the selectivity of the catalyst.

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35. Bromination of chlorobenzene with Br_2: To a mixture of chlorobenzene (11.3 g, 100 mmol) and the appropriate solid catalyst (2.0 g) gently stirred in a 100 mL round bottom flask, was added Br_2 (20 mmol) at 25 °C. The mixture was stirred at rt for 24 h in a system protected from atmospheric moisture. The solid catalyst was filtered off and washed with CCl_4 (25 mL). The combined organic solution was treated with 30% aqueous solution of $NaHSO_3$ (25 mL) to neutralize excess Br_2. The organic layer was washed with water, separated and dried over anhydrous $MgSO_4$. The total volume of the solution was made up to 100 mL, and nitrobenzene (2.46 g, 20 mmol) as an internal standard, was added. A sample of the resultant solution was then drawn out and analyzed by GLC using a Packard instrument Model 417, equipped with F.I.D. coupled to an SP4290 integrator. The glass column (6 ft, 1.5 mm) was packed with 10% SP2401 on Supelcoport 100/120. The operating conditions were: detector temp 250 °C, injector temp 250 °C, carrier gas argon, oven temp 70 °C, ramp rate 5 °C/min, final temp 220 °C and sample size 0.2 μL. Products were identified by comparing retention times with those of authentic samples. Nitrobenzene was used as the internal standard. The compound were eluted in the following order: CB, nitrobenzene, *p*-BCB and *o*-BCB.
36. Preparation of cation-exchanged clays and zeolites: The sodium form of the clay or the zeolite (10 g), was suspended in an aqueous solution (100 mL, 1.0 M) of the metal salt. The mixture was stirred at 25 °C for 24 h. The solid was separated by centrifugation and washed several times with deionized water. The resulting solid was dried overnight at 110 °C and calcined at 400 °C for 12 h.
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38. Bromination of chlorobenzene with Br_2/SO_2Cl_2: To a mixture of chlorobenzene (11.3 g, 100 mmol) and the appropriate solid catalyst (2.0 g), was added a mixture of Br_2 (20 mmol) and SO_2Cl_2 (20 mmol) at 25 °C. The mixture was stirred at this temperature for 24 h. Workup of the reaction mixture and GLC analysis were performed as described in note 35.
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