Highly efficient *para*-selective bromination of simple aromatic substrates by means of bromine and a reusable zeolite

Keith Smith* and Dawoud Bahzad

Department of Chemistry, University of Wales Swansea,[†] Swansea, UK SA2 8PP

Reactions of mono-substituted aromatic substrates of moderate activity with bromine in the presence of stoichiometric amounts of zeolite NaY proceed in high yield and with high selectivity to the corresponding *para*-bromo products; the zeolite is easily regenerated by heating.

In recent years considerable emphasis has been placed on improvement in the environmental impact of industrial chemical processes.[1] It is well recognized that solids can play a significant role in the development of cleaner technologies through their abilities to act as catalysts, support reagents, entrain by-products, avoid aqueous work-ups and influence product selectivities, and a number of books on the applications of solids in organic synthesis have appeared.[2] Advances are particularly needed in the area of electrophilic aromatic substitutions,[3] where traditional Lewis acid catalysts are a cause of considerable concern and where reactions are frequently unselective. Bromination, which is of considerable industrial importance, is a case in point.

Some years ago we developed a highly *para*-selective method for chlorination of toluene and other simple aromatic compounds based on *tert*-butyl hypochlorite and a shape-selective zeolite catalyst.[4] We have also developed a selective bromination method for activated heterocycles based on *N*-bromosuccinimide and silica.[5,6] However, an adaptation of the former method involving expensive *tert*-butyl hypobromite would not be suitable for large scale application. Also, the latter method is not successful for bromination of aromatic compounds of moderate activity. We have therefore sought to develop a highly *para*-selective method for bromination of such compounds based on the use of bromine as the reagent and a shape-selective zeolite as the controlling agent and now report success in this endeavour.

Early attempts to use zeolites to gain regioselective control over bromination of toluene had limited success.[7] Recently, however, Sasson and coworkers achieved significant improvements by use of a zeolite Y catalyst and an epoxide as a hydrogen bromide scavenger.[8–10] They were able to obtain excellent *para*-selectivity (98%) in low yield (*ca.* 10%) or higher yields with significantly poorer selectivity.

Based on our earlier experiences with aromatic halogenations[4,11] we first investigated the use of various large-port, proton-form zeolites as catalysts in the reaction of bromine with toluene. The results (Table 1) showed that all were capable of catalysing the reaction to give high yields and with *para*-selectivities typically in the region of 80%.

Table 1 Bromination reactions of toluene over different proton-form zeolite catalysts[a]

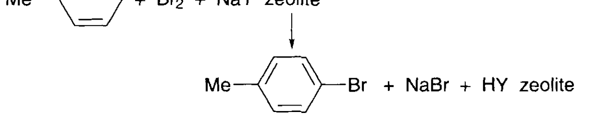
Catalyst	Toluene (%)[b]	*o*-Bromotoluene (%)[b]	*p*-Bromotoluene (%)[b]
HY	2	15	82
HX	19	20	61
Hβ	12	9	79
HMord	0.4	14	83

[a] Bromination of toluene (0.85 mmol) with bromine (0.94 mmol) over the catalyst (0.5 g) in CH_2Cl_2 (5 ml) at room temp. for 5 h. [b] Absolute yield determined by quantitative GC.

Sasson's best selectivities were achieved using NaY zeolite so we next investigated the sodium forms of a greater range of zeolites (Table 2). The yield of brominated product formed after one hour at room temperature was broadly a function of the size of the pores. To our surprise NaY and NaX produced high yields of almost entirely 4-bromotoluene, in contrast to the results of Sasson.[8–10]

The major difference between our experiments and corresponding ones carried out by Sasson was in the quantity of zeolite used. We therefore investigated the reaction as a function of the amount of zeolite NaY used (Table 3).

As the results show, there is a strong dependency of the yield on the quantity of NaY used and the reaction became quantitative when 0.55 g was employed. These results are consistent with the occurrence of a rapid and stoichiometric reaction involving the NaY zeolite [eqn. (1)] competing favourably with a slower and less selective catalytic reaction involving the HY zeolite (compare Table 1).



(1)

Although the best conditions allow the quantitative formation of 4-bromotoluene with very high selectivity, it is unattractive for large-scale use to require 3.8 g of NaY for every 1 g of product formed. This would be less of a problem if the solid could be easily regenerated following removal of the bromotoluene. It appears from eqn. (1) that the spent solid should have finely dispersed sodium bromide in the pores of HY zeolite. Simple heating of the solid might therefore cause expulsion of gaseous hydrogen bromide and regeneration of NaY [eqn. (2)].

$$\text{NaBr} + \text{HY zeolite} \longrightarrow \text{NaY zeolite} + \text{HBr} \qquad (2)$$

Table 2 Bromination reactions of toluene with different Na-form zeolite catalysts[a]

Catalyst	Toluene (%)[b]	*o*-Bromotoluene (%)[b]	*p*-Bromotoluene (%)[b]
NaY	5	1	93
NaX	8	1	91
Naβ	52	5	42
NaMord	75	3	20
NaA	98	0	1
NaZSM5	75	4	20

[a] Bromination of toluene (0.85 mmol) with bromine (0.94 mmol) over the catalyst (0.5 g) in CH_2Cl_2 (5 ml) at room temp. for 1 h. [b] Absolute yield determined by quantitative GC.

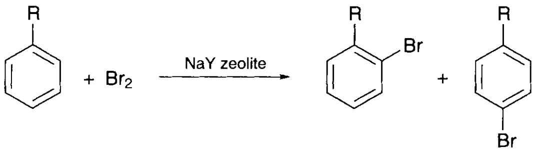
Table 3 Bromination of toluene over different amounts of Na+Y[a]

Quantity/ g	Toluene (%)[b]	*o*-Bromotoluene (%)[b]	*p*-Bromotoluene (%)[b]
0.05	75	1	20
0.1	44	4	51
0.25	13.5	2	82
0.5	5	1	93
0.55	0	1	98

[a] Bromination of toluene (0.85 mmol) with bromine (0.94 mmol) over NaY in CH_2Cl_2 (5 ml) at room temp. for 1 h. [b] Absolute yield determined by quantitative GC.

Indeed, calcination of the solid completely regenerated its reactivity. The regenerated material gave the same yield and selectivity as the original NaY. Therefore, in practice it becomes possible to produce much larger quantities of 4-bromotoluene from a particular batch of solid by repeated regeneration and reuse. The amount of solvent can also be reduced without detriment until there is insufficient to keep the system mobile. 4-Bromotoluene can also be used instead of dichloromethane if the avoidance of a separation step would be advantageous. Consequently, this approach now becomes commercially realistic for the synthesis of 4-bromotoluene.

In order to explore the scope of the reaction, similar conditions were applied to a range of substituted benzenes according to eqn. (3). The results are reported in Table 4.



1 2 3 (3)

As Table 4 shows, the reaction gives high yields and *para*-selectivities for a range of substituted benzenes of moderate activity, including alkyl and halogenobenzenes. The reaction of bromine with such compounds in the presence of sufficient NaY zeolite at room temperature therefore provides a convenient, high yielding and highly regioselective method for synthesis of *para*-brominated products. Furthermore, the zeolite is easily regenerated by heating.

We thank the Kuwaiti Institute for Scientific Research (KISR) for a studentship to D. B., The EPSRC for a grant which enabled purchase of the NMR equipment used in this study and the EPSRC mass spectrometry centre in Swansea for running mass spectra. We also thank PQ Zeolites for gifts of zeolites.

Table 4 Yields of brominated products according to eqn. (3)[a]

1	Residual **1** (%)[b]	Yield of **2** (%)[b]	Yield of **3** (%)[b]
Benzene	6	—	91[c]
Toluene	—	1	98
Ethylbenzene	—	1	97
Cumene	—	—	98
tert-Butylbenzene	2	—	97[d]
Chlorobenzene	22 (17)[e]	—	78 (82)[e]
Bromobenzene	44 (34)[e]	—	56 (66)[e]
Fluorobenzene	8 (6)[e]	—	92 (93)[e]
Anisole	—	—	85

[a] 0.55 g NaY, 0.84 mmol **1**, 0.93 mmol Br_2, 5 ml CH_2Cl_2, room temp., 5 h. [b] Absolute yield determined by quantitative GC. [c] 2% of dibromo product also obtained. [d] *Ca.* 1% of a side product also obtained. [e] Figures in parentheses are for similar reactions, but with 0.8 g of NaY.

Footnote

† Formerly known as the University College of Swansea.

References

1 *Chemistry of Waste Minimization*, ed. J. H. Clark, Chapman and Hall, London, 1995.
2 *Solid Supports and Catalysts in Organic Synthesis*, ed. K. Smith, Ellis Horwood, Chichester, 1992; *Preparative Chemistry Using Supported Reagents*, ed. P. Laszlo, Academic Press, London, 1987; H. Van Bekkum, E. M. Flanigen and J. C. Jansen, *Stud. Surf. Sci. Catal.*, 1991, **58**.
3 R. Taylor, *Electrophilic Aromatic Substitution*, John Wiley and Sons, Chichester, 1990.
4 K. Smith, M. Butters, W. E. Paget and B. Nay, *Synthesis*, 1985, 1155; K. Smith, M. Butters and B. Nay, *Synthesis*, 1985, 1157.
5 K. Smith, D. M. James, A. G. Mistry, M. R. Bye and D. J. Faulkner, *Tetrahedron*, 1992, **48**, 7479; A. G. Mistry, K. Smith and M. R. Bye, *Tetrahedron Lett.*, 1986, **27**, 1051.
6 K. Smith, D. M. James, I. Matthews and M. R. Bye, *J. Chem. Soc., Perkin Trans. 1*, 1992, 1877.
7 T. M. Wortel, D. Oudijn, C. J. Vleugel, D. P. Roelofsen and H. Van Bekkum, *J. Catal.*, 1979, **60**, 110.
8 J. Dakka and Y. Sasson, *J. Chem. Soc., Chem. Commun.*, 1987, 1421.
9 F. De La Vega and Y. Sasson, *J. Chem. Soc., Chem. Commun.*, 1989, 653.
10 F. De La Vega and Y. Sasson, *Zeolites*, 1989, **9**, 418; 1991, **11**, 617; 1991, **13**, 341.
11 L. Delaude, P. Laszlo and K. Smith, *Acc. Chem. Res.*, 1993, **26**, 607.

Received, 20th November 1995; Com. 5/07571H