

Environmentally friendly catalysis using supported reagents: the fast and selective bromination of aromatic substrates using supported zinc bromide¹

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Zinc bromide supported on mesoporous silica or acid-activated montmorillonite is a fast, efficient, selective and reusable catalyst for the *para*-bromination of activated and moderately deactivated aromatic substrates.

Bromoaromatics are widely used as intermediates in the manufacture of pharmaceuticals, agrochemicals and other speciality chemical products. Traditional methods of aromatic bromination involve the use of non-selective hazardous acidic reagents such as mineral acids and metal halides, which can lead to separation difficulties and unacceptable levels of toxic and corrosive waste. The replacement of such reagents by non-toxic and more selective solid catalysts is very desirable and represents an important goal in the context of Clean Synthesis.^{2,3} While some progress has been made in this area, notably through the use of microporous zeolites, improvements in reaction selectivity are at the expense of poor reaction rates or the need for large quantities of catalyst.^{4,5} We have discovered that good regioselectivity and excellent reaction rates in the bromination of activated and moderately deactivated aromatics can be achieved through the use of supported zinc bromide catalysts.⁶

Bromination of bromobenzene using elemental bromine in CCl₄ in the dark proceeds slowly in the absence of an added catalyst. At 25 °C only 10% conversion of substrate is achieved after 24 h with a selectivity (*p/o* isomer ratio) of 4.1. Rates improve at higher temperatures but at the expense of selectivity and complete conversion of substrate within 24 h is only achieved at 76 °C when the formation of tribromobenzene further complicates the reaction. In the presence of 0.067 equiv. of zinc bromide supported on the acid-activated montmorillonite K10 (1.0 mmol g⁻¹; catalyst prepared from methanol in the same way as 'clayzic'⁷ and dried at 200 °C before use), complete substrate conversion is achieved at 25 °C within 8 h and with a much improved selectivity of 9.6. At higher temperatures, the reaction rate increases but the selectivity falls (Table 1). We then screened a range of commonly used support materials as supports for zinc bromide (Table 1). Of these, mesoporous silica gel gives the best selectivity, along with a good rate of reaction. It is interesting to note that the same type of support proved to be the most effective in developing the Friedel–Crafts catalyst clayzic.⁷

While CCl₄ has commonly been used as a solvent in many halogenation reactions, environmental legislation will preclude its use in the future. We next tested likely non-polar and low-polarity alternative solvents (Table 1) and have found that of the non-halogenated solvents, hexane gives a good reaction rate and a reasonable selectivity.

As part of the catalyst optimisation studies we have examined the effect of loading of zinc bromide (Fig. 1). Loading clearly has a major effect on catalyst activity. The optimum loading for the K10 analogue is significantly lower than that for the higher surface area⁷ silica gel. Catalyst activity on reuse is also an important variable and we have found that the silica-based catalyst only suffers a relatively gradual decrease in activity and selectivity on use (with an apparent increase in selectivity after the first use). It is important that the catalyst is kept solvent

damp in between reactions to avoid deactivation of the catalytic sites (by decantation of the reaction liquors followed by recharging with fresh substrate solution). Total turnover efficiencies (total mole substrate converted per mole equivalent

Table 1 Comparison of catalytic systems for the bromination of bromobenzene^a

Catalyst	Solvent	T/°C	t/min	Conversion of bromobenzene (GC %)	Selectivity (<i>p/o</i> ratio)
None	CCl ₄	25	24	10	4.1
None	CCl ₄	50	24	30	3.4
Clayzib ^b	CCl ₄	25	8	100	9.6
Clayzib	CCl ₄	50	6	100	8.6
Clayzib	CCl ₄	76	1.5	100	6.6
ZnBr ₂	CCl ₄	25	7	3.1	3.0
Clayzib	CCl ₄	25	7	85.6	8.8
ZnBr ₂ -silica ^c	CCl ₄	25	7	93.6	9.7
ZnBr ₂ -alumina ^d	CCl ₄	25	7	93.3	8.2
ZnBr ₂ -alumina ^e	CCl ₄	25	7	98.5	9.3
Clayzib	CHCl ₃	25	7	91.5	9.1
Clayzib	CH ₂ Cl ₂	25	7	93.5	11.0
Clayzib	<i>n</i> -C ₆ H ₁₄	25	7	99.6	8.5
Clayzib	<i>c</i> -C ₆ H ₁₂	25	7	98.3	7.4
ZnBr ₂ -silica ^{c,f}	<i>n</i> -C ₆ H ₁₄	25	7	100	8.7
(1st use)					
ZnBr ₂ -silica ^{c,f}	<i>n</i> -C ₆ H ₁₄	25	7	97.9	9.2
(1st reuse)					
ZnBr ₂ -silica ^{c,f}	<i>n</i> -C ₆ H ₁₄	25	7	88.1	9.0
(2nd reuse)					
ZnBr ₂ -silica ^{c,f}	<i>n</i> -C ₆ H ₁₄	25	7	81.4	8.6
(3rd reuse)					
ZnBr ₂ -silica ^{c,f}	<i>n</i> -C ₆ H ₁₄	25	7	68.6	8.0

^a Reactions carried out using 1.0 mmol g⁻¹ ZnBr₂ loaded on the dried support from methanol unless stated otherwise. ^b ZnBr₂ supported on K10. ^c 100 Å. ^d Neutral. ^e Acidic. ^f 1.75 mmol g⁻¹.

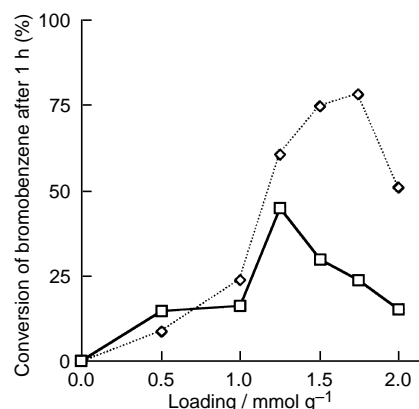


Fig. 1 Effect of loading of ZnBr₂ on (◇) silica (100 Å) and (□) K10 on activity in the bromination of bromobenzene at 25 °C

Table 2 Bromination of aromatic substrates using ZnBr₂-silica (100 Å)^a

Substrate	Catalyst	Solvent	T/°C	t/min	Conversion of substrate (GC %)	Selectivity (p/o ratio)
PhMe	None	n-C ₆ H ₁₄	25	2	0.8	2.0
PhMe	ZnBr ₂ -silica	n-C ₆ H ₁₄	25	2	100	2.7
PhEt	None	n-C ₆ H ₁₄	25	5	0.0	—
PhEt	ZnBr ₂ -silica	n-C ₆ H ₁₄	25	5	68.5	2.4
Bu ^t Ph	None	n-C ₆ H ₁₄	25	2	0.0	—
Bu ^t Ph	ZnBr ₂ -silica	n-C ₆ H ₁₄	25	2	100	∞
PhCl	None	n-C ₆ H ₁₄	25	80	0.0	—
PhCl	ZnBr ₂ -silica	n-C ₆ H ₁₄	25	80	92.9	10.0

^a Reactions carried out using 1.75 mmol g⁻¹ ZnBr₂ supported on silica (100 Å).

zinc bromide) of >40 over 5 runs can be achieved for 1 h room temperature reactions giving selectivities of >8.

The supported zinc bromide catalysts can be effectively used in the room temperature bromination of other aromatic substrates (Table 2). The bromination of toluene is very slow in the absence of an added catalyst and gives a p/o ratio (selectivity) of 2.0. On addition of the catalyst [1.75 mmol g⁻¹ on silica (100 Å)] there is complete conversion of the substrate within 2 min and an increase in the selectivity to 2.7. The bromination of ethylbenzene is extremely slow in the absence of a catalyst but once the silica-ZnBr₂ is added the reaction is complete within 5 min with a selectivity of 2.4. Bromination of *tert*-butylbenzene in the presence of the catalyst is complete within 2 min and has 100% selectivity to the *para*-isomer. For all reactions using alkylbenzene substrates we did not observe any α -brominated products. Chlorobenzene, which is mildly deactivated towards electrophiles, is unaffected by bromine at room temperature but reacts in the presence of the catalyst to give 92.9% conversion to monobrominated products within 80 min with a remarkable selectivity value of 10.

We thank Contract Chemicals Ltd, the EPSRC and the Royal Academy of Engineering (for a Clean Technology Fellowship to J. H. C.) and the Royal Society (for a Research Fellowship to D. J. M.) for financial support and other members of the EnvirocatsTM and York Clean Synthesis Groups for helpful discussions.

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Received in Cambridge, UK, 8th April 1997; Com. 7/02399E