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The Use of Supported Zinc Bromide for the Fast and Selective Bromination of Aromatic Substrates

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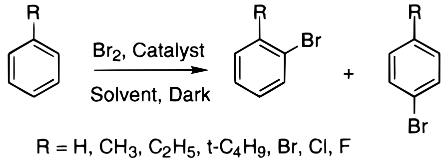
Abstract:

Zinc bromide supported on acid activated montmorillonite (K-10) or mesoporous silica (100 Å) is a fast, selective catalyst for the *para*-bromination of activated and mildly deactivated aromatic substrates. The optimum loading of zinc bromide on K-10 is 1.25 mmol/g and 1.75 mmol/g on the higher surface area silica (100 Å). Thermal activation of these catalysts at 200 °C results in optimum activity and selectivity. Also, system optimisation has allowed harmful chlorinated solvents to be replaced by less damaging hydrocarbon solvents.

Introduction

Bromoaromatics are widely used as intermediates in the manufacture of pharmaceuticals, agrochemicals, and other speciality chemical products. The bromination of aromatic compounds by electrophilic substitution has been extensively investigated in the past. Traditional methods use catalysts such as ferric and aluminium halides,[1,2] but there are many disadvantages with these processes such as difficulties in separation, the production of byproducts from side reactions, and the lack of regioselectivity. Clays have been established as solid acid catalysts for over 60 years, initially being used as catalysts for petroleum refining.[3] Improvements have been made to these catalysts with the development of the more robust pillared clays.[4] More recently, advances towards clean synthetic methods have been made with the introduction of silica,[5] alumina,[6] and microporous zeolites as catalysts.[7−13] These newer processes are a step towards waste minimisation but still have disadvantages with regards to cost efficiency and the large quantities of catalyst required for good regioselectivity.[12,13] Other alternatives to the traditional Lewis acids include the use of BrF.[14,15]

Scheme 1. **General bromination reaction**



Supported reagents have great potential as environmentally friendly alternatives to the more wasteful traditional catalysts. Supported reagents usually have large surface areas and are often layered or porous. These properties offer a large number of catalytic sites within a small quantity of catalyst, even if loadings are low. We have discovered a fast, effective method for the bromination of activated and moderately deactivated aromatic substrates by using supported zinc bromide as a catalyst (Scheme 1).[16] This paper discusses the optimisation of the system with regards to catalyst loading, thermal activation, support, and solvent effects.

Results and Discussion

To optimise the catalytic system, the bromination of bromobenzene was used as a model reaction. The catalytic activity and selectivity of supported zinc bromide can be influenced by various parameters such as zinc loading, solvent, support, and thermal activation.

Effect of Loading. Loading is known to have a major effect on catalyst activity; therefore, it is very important to ensure that the optimum loading is used. Underloading can result in the need for excess catalyst quantities thus decreasing the efficiency of the catalyst. Overloading increases the risk of leaching and the presence of unreactive, excess reagent can result in loss of catalyst activity.

For this study, various loadings of $ZnBr_2$ on silica (100 Å) (silizib) and K-10 (clayzib) were used in the bromination of bromobenzene. For the model reaction studies, carbon tetrachloride was used as the reaction solvent. The optimum loading for the K-10 analogue was found to be significantly

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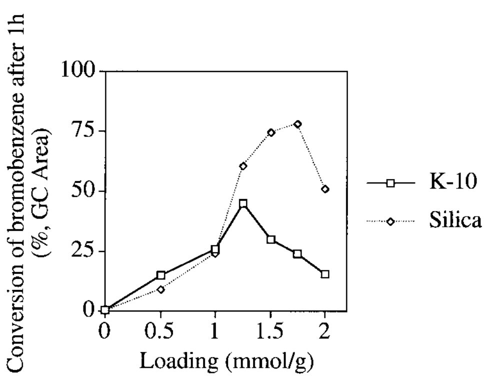

Figure 1. **Effect of loading on catalyst activity.**

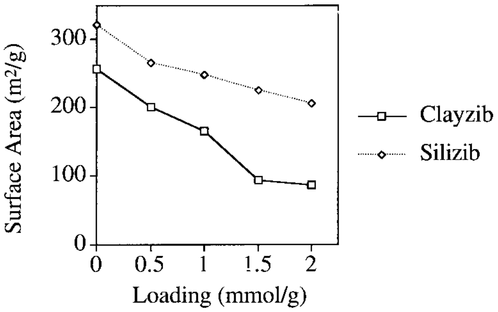

Figure 2. **Effect of loading on surface area.**

lower than that for the higher surface area[17] silica gel. K-10 has an optimum loading at 1.25 mmol/g, whereas the silica (100 Å) optimum loading is 1.75 mmol/g (Figure 1).

The high surface area of most supported reagents is generally considered to be one of their assets. Loading has been found to have an effect on the overall surface area of the catalyst. The surface area of the catalyst decreases with increasing loading (Figure 2). This is expected as the zinc bromide is filling up the pores of the support. For clayzib, the surface area levels off at loadings greater than 1.5 mmol/g, presumably because the excess zinc bromide is clustering on the external surface. Therefore, a maximum in activity and selectivity is achieved when there is an even distribution of the zinc bromide within the support resulting in the optimum number of active catalytic sites.

Effect of Support. Supports can be chosen for specific reactions depending on their surface area, acidity, and porosity. Particle size and crystallinity can also have a significant effect on reactivity. The actual molecular structure of the support is a very important factor as regular pore sizes and channel structures will often lead to shape selectivity in the reaction. This minimises the waste products that are often produced with more traditional catalysts.

The material used to support the zinc bromide has an effect on the relative rate and selectivity of the reaction (Table 1). In the absence of support, zinc bromide does not catalyse the reaction. The use of raw montmorillonite (i.e., before acid activation) as a support results in low conversions and poor selectivities. After acid activation of the montmorillonite support, the reaction results in good conversions and selectivities. Silica (100 Å) and acidic alumina are also suitable supports that give good selectivities and conversions. The use of hexagonal mesoporous silicas[18] gives reasonable conversions but surprisingly low selectivities. The regular pores and channels within the structure of the support must not be small enough to provide shape selectivity as found with microporous zeolites.[12] Using the nonporous silica Aerosil as a support results in reasonable but lower conversions and selectivities than the mesoporous silica (100 Å). This is evidence that the reaction can occur on the surface of the catalyst as well as in the mesopores.

Table 1. **Effect of Catalyst Support**

support[a]	conversion of bromobenzene[b] (GC %)	selectivity (p/o ratio)
$ZnBr_2$ only	0.0	
Tonsil 13	9.7	3.6
K-10	85.0	7.7
Peruvian montmorillonite	2.3	
acid-activated Peruvian montmorillonite	92.3	9.2
silica (100 Å)	88.8	7.8
silica (60 Å)	90.7	6.6
alumina (acidic)	87.1	7.3
alumina (neutral)	1.0	
HMS (16 Å)	77.0	5.4
HMS (21 Å)	91.7	5.3
HMS (24 Å)	88.1	5.0
HMS (35 Å)	49.7	5.8
Aerosil	45.6	6.4
zirconia	0.0	

[a] 25 °C, 4 h, hexane, 1.0 mmol/g $ZnBr_2$ loading. [b] Reaction without a catalyst results in only a 20% conversion of bromobenzene in 24 h with a p/o ratio of 4.1.

Effect of Solvent. While carbon tetrachloride has commonly been used as a solvent in many halogenation reactions, environmental legislation will preclude its use in industry. Furthermore, the role of solvent can be very significant in reactions catalysed by supported reagents.[19,20] Therefore, we have carried out a study on a variety of solvents.

For the chlorinated solvents (Table 2), there is a correlation between reaction rate and polarity (i.e., carbon tetrachloride is the least polar and, therefore, the fastest). This results in the expected inverse correlation with selectivity (i.e., the most polar is the most selective). For the alkane solvents (even less polar, so therefore even less selective), the reaction rates and selectivities are very similar and appear to be independent of chain length. It is also interesting to note that the reaction in neat bromobenzene is faster and therefore less selective. This is probably due to a concentration effect. From these results, it was decided that hexane would be the best solvent to use for all future studies.

Effect of Zinc Counterion. To study the effects of the zinc salt counterion, various zinc (II) salts were supported on silica (100 Å) (Table 3) and K-10 (Table 4) and used in the bromination of bromobenzene.

The best activity and selectivity for the bromination of bromobenzene is achieved when using either zinc(II) chloride

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Table 2. **Effect of Reaction Solvent**[21]

solvent[a]	conversion of bromobenzene (GC %)	selectivity (p/o ratio)
bromobenzene	100.0	9.2
CH_2Cl_2	32.8	13.3
$CHCl_3$	43.8	12.7
CCl_4	55.9	12.0
pentane	79.9	11.3
hexane	77.2	10.5
octane	78.9	10.6
decane	78.4	10.5

[a] 25 °C, 1 h, 1.75 mmol/g $ZnBr_2$ on silica (100 Å).

Table 3. **Silica (100 Å) as Support**

zinc salt[a]	time (h)	conversion of bromobenzene (GC %)	selectivity (p/o ratio)
$Zn(SO_4)\cdot 7H_2O$	7	7.3	3.6
$Zn(CH_3CO_2)\cdot 2H_2O$	7	11.1	6.5
$Zn(NO_3)_2\cdot 6H_2O$	7	44.9	8.3
$ZnBr_2$	2	97.8	9.9
$ZnCl_2$	3	90.4	10.7

[a] 25 °C, hexane, 1.75 mmol/g loading.

Table 4. **K-10 as Support**

zinc salt[a]	time (h)	conversion of bromobenzene (GC %)	selectivity (p/o ratio)
$Zn(SO_4)\cdot 7H_2O$	7	10.6	3.8
$Zn(CH_3CO_2)\cdot 2H_2O$	7	14.6	6.7
$Zn(NO_3)_2\cdot 6H_2O$	7	67.1	7.9
$ZnBr_2$	3	94.2	9.2
$ZnCl_2$	3	88.8	10.1

[a] 25 °C, hexane, 1.0 mmol/g loading.

or bromide. Of the other salts, zinc(II) nitrate is the best, but still has low conversion and selectivity even after 7 h. The zinc acetate and sulfate both result in very poor conversions and low selectivities. This effect might be related to poor dispersion of the zinc ions on the catalyst surface. These trends are independent of support and are very similar to previous results found for the alkylation of benzenes using clayzic.[22]

Effect of Thermal Activation. Pretreatment is an important step in the preparation of supported reagents. It has been shown on many occasions that a low level of water is beneficial to the activity of supported reagents. The most common form of treatment is thermal activation which controls the quantity of water present in the reagent although other, more profound changes cannot be precluded. The quantity of water required depends entirely on the reaction being carried out and can be modified accordingly.

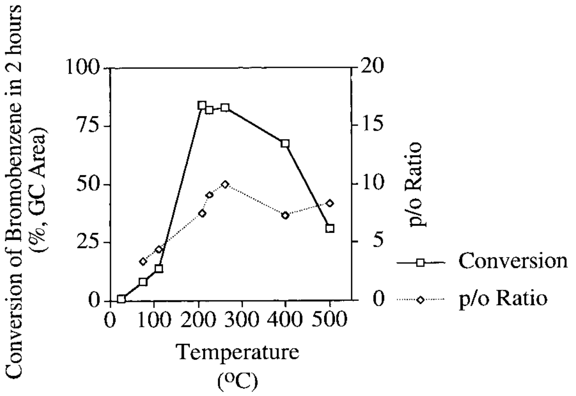

Figure 3. **Effect of thermal activation on activity of 1.0 mmol/g clayzib.**

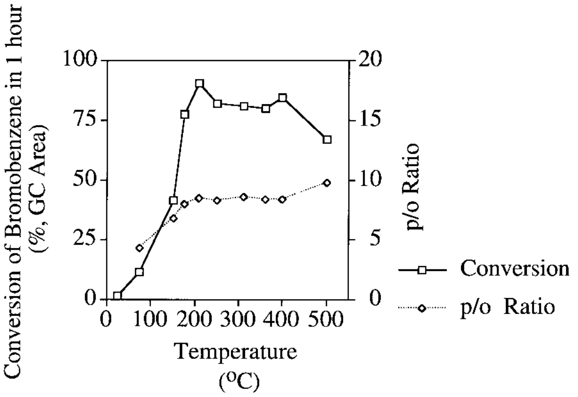

Figure 4. **Effect of thermal activation on activity of 1.75 mmol/g silizib.**

For this investigation, both silizib and clayzib were activated at a range of different temperatures (100−500 °C). They were then used in the bromobenzene model reaction system.

For clayzib, low temperatures of activation, result in a low conversion of bromobenzene (Figure 3). This is probably due to the presence of relatively large quantities of water in the catalyst. There is a maximum in the catalyst activity and selectivity at temperatures between 200 and 250 °C. Above these temperatures, the activity begins to decrease again and may be due to degradation of the clay structure at high temperatures. Similar behaviour has been seen in the cases of clayzic and claycuc.[23,24]

Silizib has a similar initial profile to clayzib with low conversions at low temperatures (Figure 4). Again there is a peak in activity and selectivity at about 200 °C. Above this temperature, the activity and selectivity remains fairly constant. It is not until activation temperatures reach 500 °C that a decrease in activity is observed. This is due to the greater thermal stability of silica with respect to clay.[25]

Thermal activation of the catalysts result in changes in surface area. The surface area of silica slightly increases

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(21) Cyclohexane and cyclooctane resulted in similar selectivities but lower activities than the straight chain alkanes. The reason for this is as yet unexplained.

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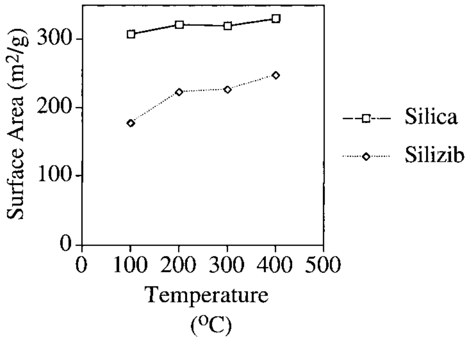

Figure 5. **Temperature vs surface area for silica and 1.75 mmol/g silizib.**

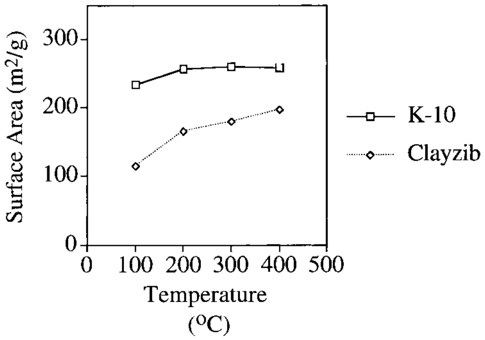

Figure 6. **Temperature vs surface area for K-10 and 1.0 mmol/g clayzib.**

with increasing activation temperature (Figure 5). The surface area of silizib follows the same pattern but at lower values. The low surface areas are probably due to, first, the zinc bromide blocking up the pores and, second, the presence of water within the pores (attracted by the zinc).

Again, the surface area of K-10 slightly increases up to 200 °C and then levels out (Figure 6). These results are indicative of an aged clay.[26] The surface area of clayzib, however, increases quite dramatically with increasing activation temperature. This is consistent with previous results found for clayzic, where the surface area increases linearly with the activation temperature.[17]

Other Substrates. This optimised system can be applied to the bromination of other substrates (Table 5). The catalytic system works best for activated and moderately deactivated substrates. Strongly deactivated substrates are not brominated with these systems.

For all of the substrates, the reaction rate is dramatically increased with the introduction of the catalyst. Chlorobenzene has similar selectivity to bromobenzene, whereas fluorobenzene and *tert*-butylbenzene give extremely high para/ortho ratios. The very selective nature of *tert*-butylbenzene is due to the steric hindrance of the *tert*-butyl functional group. However, for fluorobenzene, the fluorine group has high electronegativity which results in a powerful inductive effect and the enhanced deactivation of the *ortho*-position.

Table 5. **Bromination of Other Substrates**

substrate[a]	catalyst	time (min)	conversion of bromobenzene (GC %)	selectivity (p/o ratio)
t-BuPh	none	2	0.0	
t-BuPh	$ZnBr_2$−silica	2	100.0	∞
PhC_2H_5	none	5	0.0	
PhC_2H_5	$ZnBr_2$−silica	5	68.5	2.4
$PhCH_3$	none	2	0.8	2.0
$PhCH_3$	$ZnBr_2$−silica	2	100.0	2.7
C_6H_6	none	5	0.0	
C_6H_6	$ZnBr_2$−silica	5	75.0	
PhF	none	15	0.0	
PhF	$ZnBr_2$−silica	15	78.9	86.6
PhCl	none	80	0.0	
PhCl	$ZnBr_2$−silica	80	92.9	10.0

[a] 25 °C, hexane, 1.75 mmol/g loading.

Conclusions

Zinc bromide supported on either acid-activated montmorillonite or silica (100 Å) is a fast, selective catalyst for aromatic bromination. The optimum loading of zinc bromide is 1.75 mmol/g on silica (100 Å) and 1.25 mmol/g on the acid-activated montmorillonite. Dichloromethane, when used as a solvent, gives the highest selectivity but the lowest reaction rate. Thermal activation temperatures of 200 °C are also required for optimum catalyst activity and selectivity.

Experimental Section

General. Specific surface area data were determined by the adsorption of dinitrogen at 77 K (calculated by application of the Brunauer, Emmett, and Teller (BET) isotherm using a Coulter SA3100 analyser). Gas chromatography samples were recorded using a Hewlet Packard HP6890 gas chromatograph with HP5 capillary column. Mass spectra were obtained using a Varian 3400CX gas chromatograph with DB5 capillary column interfaced to a Finnigan Mat Magnum mass spectrometer.

Catalyst Preparation. Zinc bromide (10 mmol) was dissolved in methanol (150 mL). Support (10 g) was added, and the mixture was briefly stirred. The solvent was then slowly removed by rotary evaporation at 35 °C for 1 h. All catalysts were activated at 200 °C in a variable-temperature Gallenkamp oven unless otherwise stated.

General Bromination Procedure. The catalyst (0.6 g), solvent (15 mL), and substrate (10 mmol) were placed in a two-necked 25 mL round-bottomed flask (blacked out from light), and the mixture was magnetically stirred at 700 rpm. Bromine (10 mmol) was added, and the reaction was carried out at 25 °C. Samples (0.2 mL) were taken at regular intervals and quenched with a saturated solution of sodium thiosulfate (1 mL). The organic layer was then extracted with diethyl ether (3 mL) and analysed by GC.

Materials. Chromatography grade silica Keiselgel 100 was purchased from Merck, and the acid-activated montmorillonite, K-10, was obtained from Süd Chemie. Zinc bromide was purchased from Aldrich at 98% purity and stored under a dry atmosphere. The solvents hexane (HPLC grade), methanol (AR grade), diethyl ether (AR grade),

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dichloromethane (HPLC grade), chloroform (AR grade), cyclohexane (AR grade), and carbon tetrachloride (AR grade) were all from Fischer Scientific. All other reagents were from Aldrich.

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