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Regioselective Bromination of Activated Aromatic Substrates with N-Bromosuccinimide over HZSM-5*

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Abstract: *The nuclear as well as side-chain bromination of activated aromatic substrates has been achieved in high yields and substantial regioselectivity with N-Bromosuccinimide (NBS) over HZSM-5.*

Brominated arenes are versatile intermediates in the synthesis of a wide variety of biologically active compounds.[1] Consequently, a variety of methods for the bromination of aromatics have been reported in the literature ranging from Br_2-Lewis acids[2], NBS-H_2SO_4[3], NBS-SiO_2[4], NBS-PTSA[5], Br_2-Zeolite[6], NBS-Amberlyst[7] to aqueous base catalysed NBS-NaOH[8].

Most recently, the brominations involving heterogeneous acid catalysts have attracted considerable attention due to obvious advantages over their homogeneous counterparts. However, these methods entail the problem of generation of acidic HBr rendering the zeolite catalyst inactive[6] or require inordinately long reaction time (~ 240 h) as in the case of amberlyst[7]. Hence there is a genuine need for an efficient and truly catalytic (heterogeneous) method for bromination of arenes using inexpensive and non-polluting reagents. As a part of our ongoing research programme on zeolite-mediated organic transformations[9], we wish to report, for the first time, a HZSM-5 catalysed regioselective bromination of activated aromatics in high yields using NBS.

$$\mathrm{Ar - H} \xrightarrow[\mathrm{CCl_4}]{\mathrm{NBS\ /\ HZSM\text{-}5\ (\ catalytic\ )}} \mathrm{Ar - Br}$$

HZSM-5 ($SiO_2/Al_2O_3 = 40$) was prepared following literature procedure[10]. The catalyst was calcined at 573K before use. In a typical reaction, a mixture of anisole (1.08 g; 0.01 mol), NBS (1.8 g; 0.01 mol) and HZSM-5 (100 mg) in carbon tetrachloride (30 ml) was refluxed for 5h. The succinimide separating out was recovered by filtration. The products were analysed by GLC, purified by flash chromatography and characterised[11]. The yields are summarised in **Table-1.**

Evidently, activated arenes underwent bromination efficiently and regioselectively. The efficiency of the catalytic system is clearly demonstrated as can be seen from **Table-1,** wherein the yield and selectivity of the catalysed reaction is generally higher as compared to the uncatalysed one. In spite of the presence of electron-withdrawing substituents such as a carbomethoxy and a nitro group [entries 6 and 7]; regiospecific brominations in excellent yields have been observed. Xylenes, unexpectedly, took a different course altogether to furnish the side-chain brominated bis(bromomethyl)benzenes in moderate to excellent yields. Benzene, toluene, naphthalene, thiophene, chlorobenzene and *o*-nitroaniline, however, failed to undergo bromination under the reaction conditions . The zeolite catalyst was recovered and reused several times with no loss of activity.

Table-1: HZSM-5 catalysed bromination of aromatic substrates with NBS.

Entry	Substrate	Product	(%)Yield (para:ortho)[a]	
			Catalyst	No Catalyst
1	Anisole	4-Bromoanisole	70	28
2	p-Cresol	2-Bromo-4-methylphenol	64	0
3	2,6-Dimethylphenol	4-Bromo-2,6-dimethylphenol	93	68
4	N,N-Dimethylaniline	4-Bromo-N,N-dimethylaniline	80	71 (4:1)
5	3-Aminophenol	2-Bromo-5-aminophenol	94 (30:1)	84 (6:1)
6	Methylanthranilate	2-Amino-5-bromomethylbenzoate	90	66
7	2-Nitro-4-chloroaniline	2-Bromo-4-chloro-6-nitroaniline	80	27
8	Nerolin	1-Bromonerolin	90	57
9	o-Xylene[b]	1,2-Bis(bromomethyl)benzene	90	41
10	m-Xylene[b]	1,3-Bis(bromomethyl)benzene	35	11
11	p-Xylene[b]	1,4-Bis(bromomethyl)benzene	68	04

[a] Isolated after chromatographic purification; para:ortho ratios have been determined by GLC; the rest is essentially starting material.

[b] 2 moles of NBS were used.

In conclusion, the present study demonstrates the novelty of HZSM-5 catalyst exercising a unique regioselectivity in the nuclear as well as side chain bromination of activated aromatics with NBS. The formation of bis(bromomethyl)arenes in excellent yields adds to the synthetic potential of the method since these are important precursors of aromatic dialdehydes and quinodimethanes.

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11 The bromoaromatics were characterised by IR, ^{1}H NMR and MS.

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