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Increasing the Selectivity of Bromination of Aromatic Compounds Using Br_2/SiO_2

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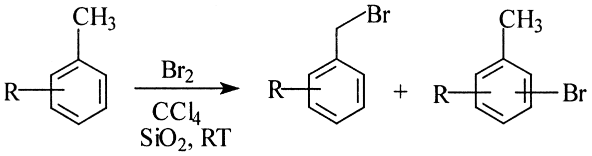
In the presence of silica, a number of aromatic hydrocarbons such as toluene, *o*-, *m*-, and *p*-xylene, anthracene and phenol are brominated by Br_2 under mild conditions; for example Br_2/SiO_2 brominates naphthalene readily at 25 °C to 1-bromonaphthalene. For comparison, we have also brominated all of the substrates in Table 1 with bromine in the absence of silica gel.

The synthetic utility of supported reagents is readily demonstrable. Many reactions can be carried out cleanly, rapidly, and in high yields under mild conditions using supported reagents.[1] Smith and Bye[2] have reported the use of NBS/SiO_2 for aromatic bromination. We now report that silica gel has a profound effect on the rate and the mechanism of bromination of aromatic hydrocarbons. It is worthwhile noting that, in comparison to other methods,[3–11] this procedure has the advantage of simple reaction conditions, especially a lower temperature and shorter reaction time. In this work we have also shown that the selectivity of the bromination can be altered in the presence of silica gel [Fluka, particle size 0.063–0.2 nm (70–230 mesh)]. The nature of silica gel is important for success of the reactions. Optimal results are obtained with silica gel which has been dried at 250 °C for 1 h.

To increase the rate of halogenation (in this particular case, the bromination of the aromatic compounds), we searched for an additive that would effectively remove hydrobromic acid from the reaction mixture without the formation of water or solid salt. In this regard, we examined the effect of silica gel.

In carbon tetrachloride as solvent, and in the presence of this



Scheme 1.

Table 1. Bromination of Aromatic Hydrocarbons Using Br_2/SiO_2 in CCl_4

Entry	Substrate	Subst : Br_2 on SiO_2	Time	Products[a)]	mp (°C)	Yield/%
1	Toluene	1 : 1	10 min	Benzyl bromide	—	95
2	*o*-Xylene	1 : 1	2 h	4-Bromo-1,2-dimethylbenzene (54%) 3-Bromo-1,2-dimethyl benzene (29%)	—	88
3	*m*-Xylene	1 : 1	Instantly	4-Bromo-*m*-xylene	—	94
4	*p*-Xylene	1 : 1	10 min	2-Bromo-1,4-dimethylbenzene	—	90
5	*p*-Chlorotoluene	1 : 1	8 h	*p*-Chlorobenzyl bromide	49–50	70
6	*p*-Bromotoluene	1 : 1	5 h	*p*-Bromobenzyl bromide	—	65
7	*o*-Cresol	1 : 1	Instantly	4-Bromo-2-methylphenol	52	96
8	*p*-Cresol	1 : 1	Instantly	2-Bromo-4-methylphenol	—	95
9	*m*-Toluidine	1 : 1	Instantly	2-Bromo-4-methylaniline	48	85
10	Mesitylene	1 : 1	Instantly	2,6-Dibromomesitylene (70%) 2-Bromomesitylene (13%)		83
11	2-Methylpyridine	1 : 1	24 h	2-Bromomethylpyridine		< 5
12	3-Methylpyridine	1 : 1	24 h	3-Bromomethylpyridine		< 5
13	Pyridine	1 : 1	24 h	Pyridinium hydrobromide		—
14	Acetophenone	1 : 1	20 min	2,2-Dibromo-1-phenylethanone		69
15	1-*p*-Tolylethanone	1 : 1	20 min	2,2-Dibromo-1-*p*-tolylethanone	97	61
16	Ethylbenzene	1 : 1	24 h	Mixture of products		
17	Naphthalene	1 : 1	25 min	1-Bromonaphthalene	Liq. Crystal	84
18	Anthracene	1 : 1	5 min	9,10-Dibromoanthracene	226	86
19	Fluorene	1 : 1	20 min	2,6-Dibromofluorene	102	85
20	Diphenyl sulfone	1 : 1	24 h	No reaction		
21	Aniline	1 : 1	Instantly	*p*-Bromoaniline	64–65	80
22	Phenol	1 : 1	Instantly	*p*-Bromophenol	62–64	81

a) All yields and products distributions were determined by GLC using an added standard, products were compared directly with authentic materials.

additive, toluene reacts with bromine instantly. But the interesting result was that we separated benzyl bromide as the only product. The reaction was applied to a range of aromatic hydrocarbons (scheme 1). Benzene does not react significantly with this reagent. By placing the toluene on the borderline, one finds a great difference between the electron-withdrawing and the electron-donating groups. In compounds containing electron-withdrawing substituents, the corresponding benzyl derivative was obtained in good yield (entries 5 and 6) (Table 1).

We have realized that acetophenone under this condition was dibrominated[12] adjacent to the carbonyl group in acceptable yield (entry 14) (69%). 1-*p*-Tolylethanone was also dibrominated adjacent to the carbonyl group with a trace of the corresponding benzyl derivative. Phenyl *p*-tolyl sulfone and *p*-nitrotoluene were unreactive under these conditions, and were recovered virtually unchanged after treating with bromine.

Compounds containing electron-donating substituents show mainly bromination on the rings. The behaviour of *o*-, *m*- and *p*-xylene show predominant substitution on the ring (entries 2, 3 and 4). *p*-Bromination of phenol has previously been achieved by the use of Amberlyst-A26,[13] and other reagents.[14,15] In this work we have brominated phenol to *p*-bromophenol in good yield (81%) (entry 22). Mesitylene, with its three activating groups, is so reactive that it undergoes bromination instantly (entry 10). These simple observations demonstrate that SiO_2 has the potential to alter reaction selectivity markedly. It may be able to switch a mechanism from radical to polar, or to influence the regioselectivity of the products formed. In this respect, one can compare the product distribution of bromination of aromatic hydrocarbon in the presence of silica gel and in the absence of it. In the absence of silica gel, we lose the selectivity and obtain a mixture of products by substitution of bromine atom on the ring and on the side chain without any preferability.

Evidently, the Lewis and Brønsted acid sites on silica gel help the bromine to produce Br^+ and $Br^\bullet$, here Br^+ can be stabilized more by the Lewis bases of the silica gel surface. Then, for an aromatic hydrocarbon with a withdrawing substituent, the side chain bromination would occur. But in the case of aromatic hydrocarbons with more than one donating substituents, the substitution on the ring would be preferential.

In order to explore the scope of the reaction, similar conditions were applied to naphthalene and anthracene. Here, naphthalene was monobrominated to 1-bromonaphthalene in good yield (84%) in less than 3 min (entry 17), and anthracene was dibrominated to 9,10-dibromoanthracene in 86% yield in less than 5 min (entry 18). Fluorene is dibrominated to 2,6-dibromofluorene in 85% yield in 20 min (entry 19).

The results reported here demonstrate that Br_2/SiO_2 possesses considerable practical advantages over traditional reagents for bromination of aromatic hydrocarbons. The reactions are clean and good-yielding and work-up is simple.

Experimental

All melting points are uncorrected. ^1H NMR spectra were recorded on an EM-390 and ^{13}C NMR spectra were recorded on a Bruker Advance 500. Mass spectra were recorded on a Solid Probe Mass Spectrometer Fisons model Trio 1000.

***p*-Chlorobenzyl Bromide; Typical Procedure:** 2 g (15.8 mmol, 1.87 mL) *p*-chlorotoluene in tetrachloromethane (20 mL) was mixed with 4 g of dried silica gel (250 °C, 1 h). While keeping the mixture at 25 °C, 2.52 g (15.8 mmol, 0.87 mL) of bromine was added. Mixing was continued for 8 h, then the catalyst was removed by filtration and washed well with chloroform. The filtrate and washings were treated with aqueous thiosulfate solution (10 mL). The organic phase was separated and dried over $MgSO_4$, and concentrated under reduced pressure to give 2.27 g, (70%) of *p*-cholrobenzyl bromide as colorless crystals, mp 49–50 °C (Ref. 16 mp. 51 °C).

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References

1 a) A. Mckillop and D.W. Young, *Synthesis*, **1979**, 401. b) J. H. Clark, A. P. Kybett, and D. J. Macquarrie, "Supported Reagents: Preparation, Analysis, and Application," VCH, New York (1992). c) "Solid Supports and Catalysts in Organic Synthesis," ed by K. Smith, Ellis Harwood, Chichester (1992). d) J. H. Clark, "Catalysis of Organic Reactions by Supported Inorganic Reagents," VCH, New York (1994).

2 K. Smith and M. R. Bye, *Tetrahedron Lett.*, **27**, 1051, (1986).

3 G. A. Olah and W. John, *Synth. Commun.*, **1974**, 653.

4 A. Mckillop and D. Bromley, *J. Org. Chem.*, **37**, 88, (1972).

5 P. R. Brian and C. Wilson, *J. Chem. Soc., Chem. Commun.*, **1978**, 752.

6 S. D. Saraf and Z. A. Malik, *Chem. Abstr.,* **80**, 36784*z,* (1974).

7 S. Lee Irvin, *Org. Syn., Coll. Vol. 2*, 95.

8 V. P. Kravets, *Zh. Org. Khim.*, **2**, 1244, (1966).

9 G. A. Olah, *Synthesis*, **12**, 895, (1974).

10 F. A. Vingiello, T. J. Delia, P. Polss, and D. Farrier, *J. Chem. Educ.*, **40**, 544, (1963).

11 I. M. Herlborn and J. S. Heaton, *Org. Syn., Coll. Vol. 1*, 207.

12 S. Kajigaeshi, M. Noguchi, and S. Fujisaki, *Bull. Chem. Soc. Jpn.,* **60**, 2667, (1987).

13 K. Smith, D. M. James, I. Mattews, and M. R. Bye, *J. Chem. Soc., Perkin. Trans. 1*, **1992**, 1877.

14 J. Berthelot, C. Gutte, M. Ouchefoune, P. L. Desbene, and J. J. Basselier, *J. Chem. Res. Synop.,* **1986**, 381.

15 C. Venkatachalapathy and K. Pitchumani, *Tetrahedron*, **53**, 7, 2581, (1997).

16 M. S. Kharasch, E. Margolis, P. C. White, and F. R. Mayo, *J. Am. Chem. Soc.,* **59**, 1405, (1937).