N-Bromosuccinimide-Silica Gel: A Selective Monobromination Reagent for Aromatic Amines and Phenols

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Summary: *N*-Bromosuccinimide catalysed by silica gel in carbon tetrachloride has been found to be a mild, effective and selective monobrominating agent for aromatic amines and phenols.

Introduction

A number of methods [1] for the selective nuclear bromination of reactive aromatic rings have been developed in view of the synthetic and commercial importance of the brominated compounds. Bromination of aromatic amines and phenols have been reported by a number of workers but the results are highly variable in terms of both products and yields. Bromination of aromatic amines or phenols with molecular bromine commonly results in polybromination and oxidation of the substrates. Bromine in acetic acid [2] gives *p*-bromoderivative with aniline while the β-naphthylamine [3] and diphenylamine in acetic acid [4] only polybromination have been observed. Dioxane perbromide is a good monobrominating agent for 1,3-dimethoxybenzene [5] and *N,N*-dialkylaniline [6] but gives a poor yield with aniline and *N*-alkylaniline [6]. Another disadvantage of dioxane perbromide complex is its thermal unstability at room temperature and hygroscopic nature. Bromination of aniline with NBS is accompanied by decomposition [7] while phenols are susceptible to oxidation [8]. The alkylbromide in DMSO results in *N*-alkylated products with aniline and *N*-alkylaniline [9,10].

Selective monobromination of amines [11] and phenols [12] have been reported with 2,4,4,6-tetrabromocyclohexa-2,5-dienone in dichloro methane at very low temperature (-20 to -50°C) but the results with phenols have been observed to modify the orientation of bromination with the change of solvent [12]. Selective monobromination of phenols has also been carried out with potassium bromide-sodium nitrate mixture but method fails with aromatic amines [13].

Recently silica gel catalysed chlorination of aromatic compounds has been a subject of much interest due to its selectivity and simplicity [14-17]. Analogous bromination method using NBS-silica gel has been reported for the selective monobromination of indoles, benzimidazoles [18] and alkoxybenzenes [19]. These studies provided us the impetus to carry out the silica gel catalysed nuclear bromination of aromatic amines and phenols using *N*-bromosuccinimide. The results obtained are described in this paper.

A mixture of appropriate substrate and NBS in equimolar quantities in the presence of silica gel

Table: Bromination of phenol and aromatic amine using NBS-silica gel in carbon tetrachloride at room temeprature.

	Substrate	Product	Stirring Time (hrs)	Yield (%)	m.p.(°C)	b.p.(°C)/760 mm of Hg
1.	Phenol	4-Bromophenol	5.0	60.0	66.0 (lit. [8] 67.0)	-
2.	Resorcinol	4-Bromoresorcinol	6.0	70.0	101.0 (lit. [21] 102.0)	-
3.	Catechol	4-Bromocatechol	6.0	60.0	86.0 (lit. [21] 87.0)	-
4.	*p*-Cresol	2-Bromo-*p*-cresol	5.0	50.0	-	243.0 (lit. [21] 243-245.0)
5.	*m*-Cresol	4-Bromo-*m*-cresol	6.0	65.0	58.0 (lit. [8] 57-58.0)	-
6.	Anisole	4-Bromoanisole	5.0	70.0	-	214.0 (lit. [21] 214-215)
7.	Aniline	4-Bromoaniline	6.0	70.0	67.0 (lit. [8] 66.0)	-
8.	*N*-,*N*-Dimethyl aniline	4-Bromo-*N*,*N*-dimethylaniline	7.0	70.0	54.0 (lit. [21] 55.00)	-
9.	*N*,*N*-Diethyl aniline	4-Bromo-*N*,*N*-diethyl aniline	6.5	72.0	35.0 (lit. [21] 33.00)	-
10.	*p*-Toluidine	2-Bromo-*p*-toluidine	6.0	70.00	-	238.00 (lit. [21] 240.00)

in carbon tetrachloride on stirring at room temperature gave the corresponding monobromo derivatives. The results obtained are summarised in the Table. All reactions proceeded smoothly and gave good yields of the products (50-72%). The identity of the products was established on the basis of comparison of their melting points, boiling points and spectral properties with that of literature data or with authentic samples. The purity of the product was checked by TLC.

Method is superior than the previously reported procedures for the selective monobromination of phenol or aromatic amines using NBS-DMF or NBS-water where some phenols and amines have been reported [8] to undergo oxidation.

The role of silica gel in the reaction appears to be significant because, no bromination was observed in the absence of silica gel, rate of the reaction was also dependent on the amount of silica gel and the stirring period. The bromination, presumably involves the polarization of the NBS on silica gel surface to produce a brominating species of soft character. The regioselectivity in the electrophilic aromatic substitution by soft electrophiles is determined by the frontier electron density [19,20], therefore the attack of electrophile is expected to occur predominantly at the para-position of the substrate. The other contributing factor for the para-selectivity in these reactions could be the steric hindrance. However, if the *para*-position is occupied then the attack occurs at the *ortho*-position. These observations are substantiated by the fact that all the substrates used in present investigation yielded the corresponding *p*-bromoderivatives, however, when the *p*-position is occupied by substituent then the *ortho* bromoderivatives (table) are formed.

The mild reaction conditions, easy availability of reagents, no evolution of hydrogen bromide, its general applicability, selectivity and good yields of monobromoderivatives makes the method of synthetic values.

Experimental

N-Bromosuccinimide was dried over phosphorus pentoxide silica gel used was from Merck. Bromination was conducted in the dark.

General method for the bromination of aromatic amines and phenols

A mixture of appropriate substrate (0.01 mole), *N*-bromosuccinimide (0.01 mole) and silica gel (2.0 g) in carbon tetrachloride (25.0 ml) was vigorously stirred in the dark at room temperature for 5-7 hours. The reaction mixture was filtered, residue washed with more carbon tetrachloride. The filtrate was washed with aqueous solution of sodium thiosulphate, dried over sodium sulphate and filtered. The removal of solvent gave the monobromoderivatives which were further purified by crystallization or distillation. The results are given in the table.

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