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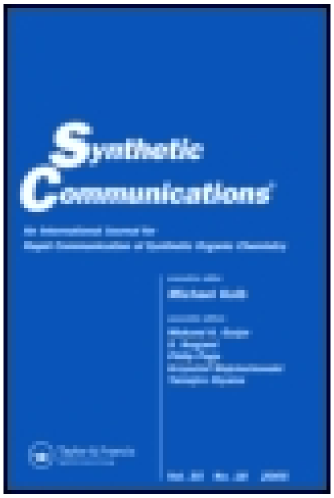

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Rapid and Total Bromination of Aromatic Compounds Using $TsNBr_2$ Without Any Catalyst

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RAPID AND TOTAL BROMINATION OF AROMATIC COMPOUNDS USING $TsNBr_2$ WITHOUT ANY CATALYST

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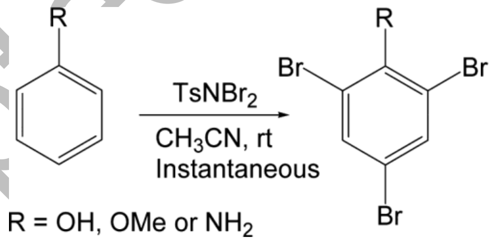
Abstract

N,*N*-dibromo-*p*-toluenesulfonamide ($TsNBr_2$) has been found to be a new reagent for bromination of aromatic compounds. The reaction is extremely fast which goes into completion instantaneously at ambient temperature to produce exclusively the corresponding polybrominated product. This procedure is applicable to various phenols, anisole and anilines to give corresponding polybrominated compound as single product in excellent yield.



KEYWORDS: Bromination; $TsNBr_2$; Phenol; Aniline; Anisole; Tribromophenol.

INTRODUCTION

In recent years, bromoaromatics are finding extensive applications in organic synthesis as versatile precursors for construction of carbon-carbon bond via transition metal mediated coupling reactions [1]. They are also used as important synthetic intermediates for the manufacture of pharmaceuticals, agrochemicals and specialty chemicals [2]. Polybrominated phenols such as tribrmophenol (TBP) is used as an intermediate in the preparation of flame retardants such as brominated epoxy resins [2]. Moreover, many bromo compounds exhibit antitumor, antibacterial, antifungal, antineoplastic, antiviral, antioxidizing property [3]. Sodium salt of tribromophenol (TBPNa) is used as fungicide and wood preservative [3]. In nature, TBP has been found in ocean sediments as a metabolite of marine fauna [4]. Although bromination with elemental bromine is a well known reaction [5], due to the hazardous effect of bromine several brominating agent were utilized which includes examples such as NBS [6], tetraalkylammonium tribromides [7], DBUH.Br_3 [8], cetyltrimethylammonium tribromide [9], pyridinium tribromide [10], LiBr/ceric ammonium nitrate [11], HBr [12], dioxanedibromide [13], pyridium hydrobromide perbromide [14], DBU hydrobromide perbromide [15], tetrabromocyclohexadienone [16], tetraalkylammonium bromides [17], hexamethylenetetramine tribromide [18], 1-butyl-3-methylpyridinium tribromide [19], $ZrBr_4$/diazene mixture [20], metal bromides/oxidants [21], $AlBr_3$ in presence of NH_4VO_3 [22], bromochromates [23] etc. However, in many cases, the products contain a mixture of ortho & para products or a mixture of mono & poly brominated compounds Moreover, it is difficult to achieve exclusive formation of polybrominated products. Even use of an excess reagent results in a mixture of mono and polybrominated compounds. Very recently, Liu et. al. reported a method for mono and di bromination of arenes using a combination of I_2O_5 and KBr . [24]

A most popular brominating agent NBS brominates in the aromatic nucleus when no radical initiator is present [6a,b]. Generally, acidic catalysts such as H_2SO_4 [6c-e], TsOH [6f], silica gel [6g], HZSM-5 [6h], are used with NBS for the bromination of activated aromatic substrate. Other activators such as microwave or ultrasound [6i], UV radiation [6j] or ionic liquid [6k] have also been reported for NBS assisted bromination of activated aromatics. Bromination with NBS favoured by polar solvents like propylene carbonate [6l], DMF [6m, n], CH_3CN [6o] etc. However, in case of bromination of phenol in CH_3CN, NBS gives mixture of substrate, monobrominated phenol and corresponding dibrominated phenol with longer time period [6p].

RESULT AND DISCUSSION

We have recently reported few efficient protocols for various transformations using *N*,*N*-dibromo-*p*-toluenesulfonamide ($TsNBr_2$) [25]. As a continuation of our work on $TsNBr_2$, we report herein a rapid procedure for bromination of phenols and anilines (Scheme 1).

Initial experiments to study the feasibility of the reagent for bromination reaction were carried out by taking phenol as a model substrate. The reaction was carried out by adding $TsNBr_2$ to the organic solution of phenol (1mmol) in acetonitrile (2mL) at room temperature. The reaction was found to complete instantaneously to produce corresponding bromo products. After 10 minutes exposure, the reaction mixture was treated with sodium thiosulfate and subjected to usual work-up procedure. When 0.5 mmol of $TsNBr_2$ was added the reaction produced a mixture of 4-bromophenol (40%)

and 2,4,6-tribrophenol (10%) along with unreacted phenol (Table 1). When 1 mmol of phenol was used, the reaction produced a mixture of 4-bromo and tribromophenol. No unreacted phenol was found. Further increment of the amount of $TsNBr_2$ to 1.5 mmol led to the formation of 2,4,6-tribromo phenol exclusively with 87 % isolated yield (Table 1). The reaction was also carried out at low temperature (0 ^{o}C). In both cases 2,4,6-tribromo phenol was obtained with similar yield in an instantaneous reaction.

After obtaining an acceptable reaction condition from the initial experiments, we extended the procedure to varieties of substituted phenols (Table 2). However, total bromination of substituted phenols could be achieved using 1 mmol of $TsNBr_2$ per mole of the substrate. It can be seen from Table 2 that different kinds of phenolic substrates undergo total bromination reaction instantaneously at room temperature. 2-Naphthol produced the corresponding 1,3-dibromo product in 76% yield. However, in case of 2-aminophenol, the yield of corresponding brominated product is relatively low (Table 2, entry 9). When, the reaction was extended to anisol, 77% of corresponding tribrmoanisole has been obtained.

The success of the method with phenols encouraged us to extend the reaction to anilines (Table 3). Initial reaction with aniline was encouraging. The reaction was completed instantaneously with 90% yield of the desired tribromo aniline in presence of 1.5 equivalent of $TsNBr_2$. In this case, however, the addition of $TsNBr_2$ should be done at 0 °C for better yield. It is necessary to add the brominating agent at low temperature to subsidize the exothermicity. Then the process was extended to variety of anilines and the results are summarized in Table 3.

It can be seen from Table 3 that different kind of anilines could be converted to corresponding polybrominated product in excellent yield.

EXPERIMENTAL

To a solution of the aromatic compound (1 mmol) in acetonitrile (2 ml) $TsNBr_2$ (1 mmol) was added at 0 °C. After 10 min of stirring at room temperature, sodium thiosulphate (200mg approx.) was added and stirred for 10 minutes. The reaction was taken up in ethyl acetate, dried over $NaSO_4$ and concentrated. Crude product was purified by flash chromatography or silica gel (230-400 mesh) with a mixture of petroleum ether and ethyl acetate as eluent.

2, 6-Dibromo-4-chloro-5-methylphenol: IR (KBr, cm^{-1}) ν: 3430, 1595, 1442, 1380, 1308, 1219, 1171, 1028, 969, 854, 771, 707, 646; ^{1}HNMR ($CDCl_3$, 400 MHz) δ: 7.32 (s, 1H), 5.73 (s, 1H), 2.3 (s, 3H); ^{13}CNMR ($CDCl_3$, 100 MHz) δ: 148.4, 136.2, 131.2, 126.1, 113.4, 106.4, 21.0; GCMS (M/Z %) : 302 (M^++2, 75), 300 (M^+, 98), 265 (58), 221 (63), 139 (21), 111 (100), 75 (83), 38 (24). Elemental Analysis: C 27.56%, H 1.89%, O 6.29%

CONCLUSION

In conclusion, we have developed an efficient method for bromination of phenol and anilines. The reaction completes instantaneously to produce corresponding polybrominated product in excellent yield.

SUPPLEMENTAL MATERIAL

Supplemental data for this article can be accessed on the publisher’s website.

ACKNOWLEDGMENTS

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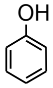
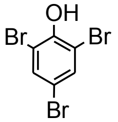
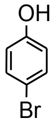
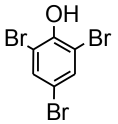
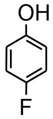
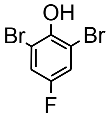
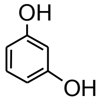
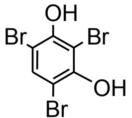
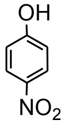
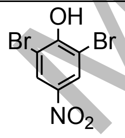
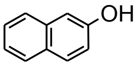
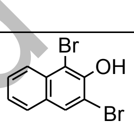
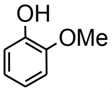
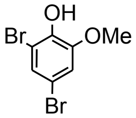
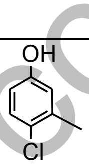
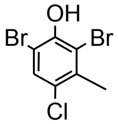
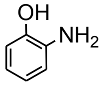
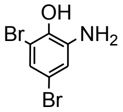
Table 1 Bromination of phenol using $TsNBr_2$[a]

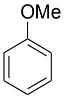
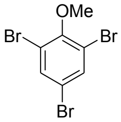
Entry	Phenol (mmol)	$TsNBr_2$ (mmol)	Products	Yield[b]
1	1	0.5	4-bromophenol +	40
			2,4,6-tribromophenol	10
2	1	1	4-bromo phenol +	30
			2,4,6-tribromophenol	50
3	1	1.5	2, 4,6 tribromophenol	87

[a]Reaction condition: acetonitrile, 2mL, rt;

[b]isolated yield.

Table 2 Bromination of phenols using $TsNBr_2$

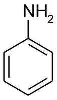
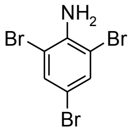
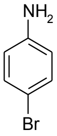
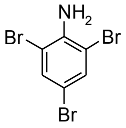
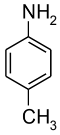
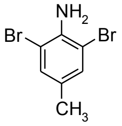
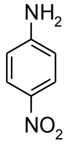
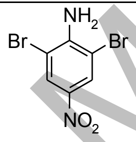
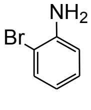
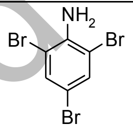
Entry	Substrate(a)	$TsNBr_2$(equiv)	Product(b)	Yield[a](%)
1		1.5		87
2		1		85
3		1		78
4		1.5		84
5		1		82
6		1		76
7		1		87
8		1		95
9		1		69

10[b]		1.5		77

[a] isolated yield after chromatographic purification

[b] reaction time is 2 hours

Table 3 Bromination of anilines using $TsNBr_2$

Entry	Substrate(a)	$TsNBr_2$(equiv)	Product(b)	Yield[a](%)
11		1.5		90
12		1		92
13		1		90
14		1		88
15		1		90

[a]Isolated yield after chromatographic purification.

Scheme 1 Bromination of aromatics using $TsNBr_2$