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Mild bromination of unreactive aromatic compounds

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ABSTRACT

N,*N*,*N*′,*N*′-Tetrabromobenzene-1,3-disulfonamide and poly(*N*,*N*′-dibromo-*N*-ethylene-benzene-1,3-disulfonamide) in concentrated H_2SO_4 can be used as efficient reagents for the mild bromination of unreactive arenes at room temperature, under solvent-free conditions, in yields.

Halogenated aromatic compounds are a useful class of intermediates as they are precursors to a number of organometallic species for the synthesis of natural products and pharmaceutically important compounds.[1] There are many known methods for the preparation of haloarenes from aromatic compounds, especially from electron-rich systems.[2] However, few methods are known for the halogenations of deactivated aromatics as harsh experimental conditions are required for their preparation.[3]

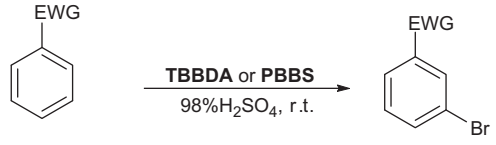
N-Halo compounds have been studied extensively as electrophilic halogenating agents for the halogenation of activated aromatic rings. The low reactivity of *N*-halo compounds with deactivated arenes requires the addition of activating agents and direct bromination methods have been recently developed using the following bromonium donating reagents: TBCA/H_2SO_4,[2r] NXS/BF_3-H_2O[3d] and NBS/H_2SO_4.[3e]

N,*N*,*N*′,*N*′-Tetrabromobenzene-1,3-disulfonamide [**TBBDA**] and poly(*N*,*N*′-dibromo-*N*-ethylene-benzene-1,3-disulfonamide) [**PBBS**] are halogenating agents,[2s] and are effective catalysts for various organic transformations.[4]

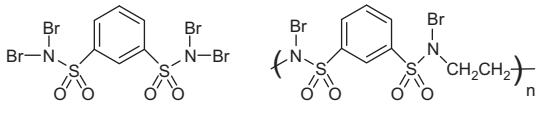
In continuation of our interest in the application of *N*,*N*,*N*′,*N*′-tetrabromobenzene-1,3-disulfonamide [**TBBDA**] and poly(*N*,*N*′-dibromo-*N*-ethylene-benzene-1,3-disulfonamide) [**PBBS**], in organic synthesis,[4] herein we report a simple and improved protocol for the preparation of haloarene from unreactive aromatic compounds. The reactions proceed in the presence of **TBBDA** and **PBBS** in strong acid (98% H_2SO_4), at room temperature, under solvent-free conditions (Scheme 1).

This reaction does not proceed in the absence of sulfuric acid, and therefore the following mechanism is suggested (Scheme 2). Acid catalysis plays an important role in the reaction of TBBDA with deactivated arenes via O-protonation generating a cation, a resonance contributor which makes it clear that this is an agent which can act as an efficient bromonium-transfer agent. This superelectrophilic agent is able to attack even relatively unreactive arenes.

The results of the bromination of some deactivated arenes are presented in Table 1. 1,3-Dinitrobenzene, nitrobenzene, and pentafluorobenzene were successfully brominated under these conditions (Table 1, entries 1–4). Our attempts to brominate benzonitrile over 4 hours failed.



EWG= Electron-withdrawing group



TBBDA **PBBS**

Scheme 1. Bromination of unreactive aromatic compounds.

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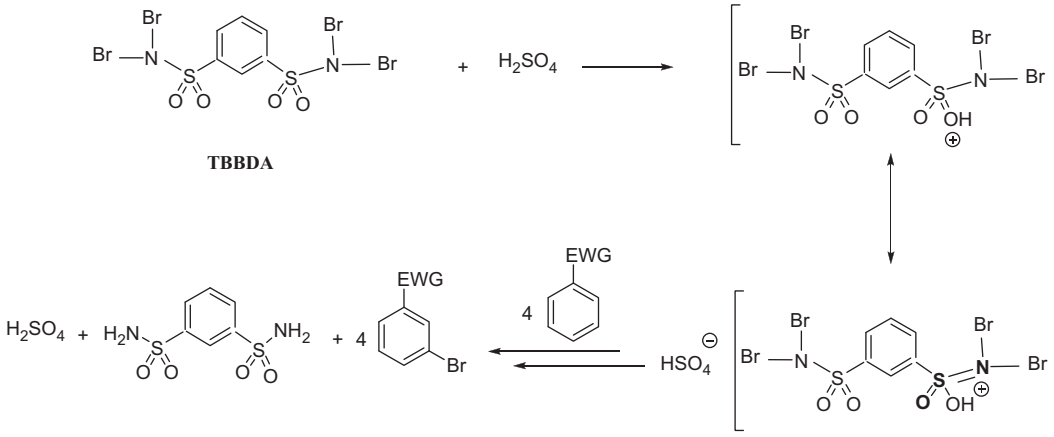
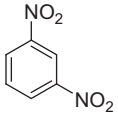
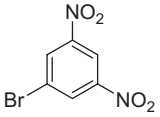
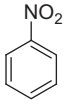
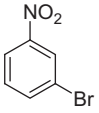
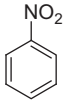
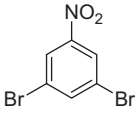
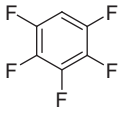
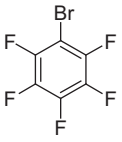
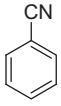


Scheme 2. Suggested mechanism for bromination of unreactive aromatic compounds.

Table 1
Bromination of various unreactive arenes using **TBBDA** or **PBBS** at room temperature

Entry	Substrate	Product[a]	TBBDA		PBBS		Ref.
			Time (h)	Yield (%)	Time (h)	Yield (%)	
1			4	88	8	71	2r
2			4	63	8	55	2r
3			6	73	10	64	5
4			1	76	2	70	2r
5		No reaction	4	–	4	–	–

[a] Products were characterized from their physical properties, by comparison with authentic samples, and by spectroscopic methods.

N,*N*,*N*′,*N*′-Tetrabromobenzene-1,3-disulfonamide [**TBBDA**] and poly(*N*,*N*′-dibromo-*N*-ethylene-benzene-1,3-disulfonamide) [**PBBS**] are stable, non-volatile, inexpensive, and safe reagents.

In conclusion, we have described the application of **TBBDA** and **PBBS** in 98% H_2SO_4 for the bromination of deactivated aromatic compounds under solvent-free conditions.

Typical procedure for the preparation of 1-bromo-3,5-dinitrobenzene

98% H_2SO_4 (4 mL) was added to a mixture of 1,3-dinitrobenzene (2 mmol) and **TBBDA** (0.25 g, 0.45 mmol) or **PBBS** (0.45 g) in a 25 mL flask. The flask was closed, and the mixture was stirred at room temperature for the specified period of time (Table 1). The progress of the reaction was monitored by TLC (*n*-hexane/acetone, 10:2). The mixture was poured onto crushed ice (30 g), neutralized with 5% NaOH and extracted with cold CH_2Cl_2 (2 × 30 mL). The organic layer, was dried, evaporated, and the product was collected and recrystallized from hexane [yellow solid, 88% (using **TBBDA**), mp 74–76 °C]. IR (KBr): 3098, 2925, 1808, 1747, 1616, 1595, 1534, 1344, 1309, 1162, 1075, 915, 897, 741, 726, 638, 517, 488; ^{1}H NMR [DMSO-d_6, 500 MHz]: δ_H (ppm) 8.80 (1H, s), 8.83 (2H, s), ^{13}C NMR [DMSO-d_6, 125 MHz]: δ_C (ppm) 118.7, 123.7, 132.9, 149.5; MS [*m*/*z*] 246 [M^+], 248 [M+2]$^+$.

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