



# Poly(*N,N'*-dibromo-*N*-ethyl-benzene-1,3-disulfonamide), *N,N,N,N'*-tetrabromobenzene-1,3-disulfonamide and novel poly(*N,N'*-dibromo-*N*-phenylbenzene-1,3-disulfonamide) as powerful reagents for benzylic bromination

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## ABSTRACT

*N,N,N,N'*-Tetrabromobenzene-1,3-disulfonamide [**TBBDA**], poly(*N,N'*-dibromo-*N*-ethyl-benzene-1,3-disulfonamide) [**PBBS**], and novel poly(*N,N'*-dibromo-*N*-phenylbenzene-1,3-disulfonamide) [**PBPS**] can be used for bromination of benzylic positions in solvent.

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## 1. Introduction

Molecular bromine in preparative chemistry is a serious cause of concern due to its toxicity and corroding properties. Therefore, in 1942, Ziegler used NBS for benzylic bromination in solvent CCl<sub>4</sub>.<sup>1</sup> Eduardo I. Sanchez reported benzylic bromination with *N*-bromosaccharin in solvent CCl<sub>4</sub>.<sup>2</sup> These brominations are radical reactions, which are either photo-initiated or promoted by addition of benzoyl peroxide. Carbon tetrachloride has proven to be a useful solvent for the bromination of a wide range of compounds, and reports on its use still appear frequently.<sup>3,4</sup> A major drawback of carbon tetrachloride, however, is its toxicity and carcinogenicity and also its properties of ozone-layer damaging.<sup>5</sup> In particular, the effects on the global environment have led to international agreements restricting the use of carbon tetrachloride.<sup>6</sup> So far, research has focused on using NBS and non-chlorinated solvent,<sup>7</sup> ionic liquids<sup>8</sup>, and water.<sup>9</sup>

In 1977, Offermann and Vogtel reported benzylic bromination of several arenes with NBS in non-chlorinated solvents, for example, methyl acetate or methyl formate.<sup>10</sup> Recently, benzylic brominations have been developed by using the following brominium-donating reagents: Br<sub>2</sub>/H<sub>2</sub>O/*hν*,<sup>11</sup> NaBrO<sub>3</sub>–NaHSO<sub>3</sub>/EtOAc–H<sub>2</sub>O,<sup>12</sup> bromide/hydrogen peroxide,<sup>13</sup> NBS/MeOAc,<sup>7</sup> and H<sub>2</sub>O<sub>2</sub>–HBr/water.<sup>14</sup>

We now report a convenient method for the benzylic bromination of alkyl benzenes using reagents *N,N,N,N'*-tetrabromobenzene-1,3-disulfonamide [**TBBDA**], poly(*N,N'*-dibromo-*N*-ethyl-benzene-1,3-disulfonamide) [**PBBS**],<sup>15</sup> and novel reagent poly(*N,N'*-dibromo-*N*-phenyl-benzene-1,3-disulfonamide) [**PBPS**] (Fig. 1).

The advantages of **TBBDA**, **PBBS**, and **PBPS** are as follows:

1. The preparation of **TBBDA**, **PBBS**, and **PBPS** is easy and convenient.
2. The reagents are selective (benzylic position).
3. **TBBDA**, **PBBS**, and **PBPS** are stable from two to three months under normal conditions.
4. After the reaction of **TBBDA**, **PBBS**, or **PBPS** with a substrate, the sulfonamide is recovered and can be reused many times without decreasing the yield.
5. Gel permeation chromatography (GPC) was used to determine molecular weight average of PBPS ( $M_w = 5742$ ), and we found 15 monomeric units for the polymer.

The reaction of methyl benzene (**I**) with **TBBDA**, **PBBS**, and **PBPS** in EtOAc in presence benzyl peroxide under reflux conditions afforded benzyl bromide (**II**) with good to excellent yields (Scheme 1).

Thus, in order to test the generality and versatility of this procedure in the benzylic bromination, we examined a number of alkyl benzenes using the optimized conditions. As shown in Table 1, var-

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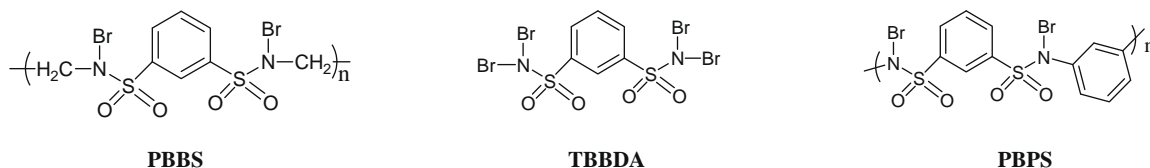
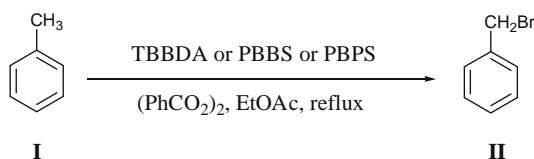


Figure 1.



Scheme 1.

ious alkyl benzenes were cleanly converted to the corresponding products with good to excellent yields (Table 1, compounds a–n).

In Table 1 (compound b), we showed that the benzylic bromination occurred in the benzylic position. From the peak of 5.08 ppm for brominated ethyl benzene it is obvious that there is no dibromination observed under this procedure. Also, Table 1 shows benzylic bromination of the 3-methylbenzaldehyde (compound i) without over oxidation.

In this reaction, we observed that by control of the reaction time, the bromination of *p*-xylene afforded mainly a product that is preferentially brominated at only one of the methyl groups. The major products were monobrominated with the best selectivity in 73% yields (Table 1, compound c). On prolonging the reaction time, we obtained two methyl groups that were monobrominated (Table 1, compound d). Similar results were obtained for compounds f and h listed in Table 1.

It seems interesting that 4-methylacetophenone (Table 1, compound I) was exclusively brominated by a free radical process at the benzyl position leading to benzyl bromide.

We used two solvents in this work, non-chlorinated and chlorinated solvents. We found (Table 1) that two solvents afforded approximately equal results. Therefore, we selected ethyl acetate as a green solvent instead of carbon tetrachloride because carbon tetrachloride is toxic and is not to be used as a green solvent due its effects on the environment.

The advantages of our reagents over common reagents in the benzylic bromination of toluene are listed in Table 2.

## 2. Experimental

### 2.1. Poly(*N*-phenylbenzene-1,3-disulfonamide)

$\text{PCl}_5$  (16.5 mmol), as chlorination agent, was added to the sodium salt of benzene-1,3-disulfonic acid (5.00 g, 18 mmol). To initiate the reaction, the vessel was heated (40–50 °C), then the reaction continued autonomously. After complete conversion (2 h), crushed ice (100 g) and  $\text{CHCl}_3$  (100 mL) were added. Removal of the solvent under reduced pressure gave benzene-1,3-disulfonylchloride (4.2 g 84%), which was placed in a beaker. The beaker was heated on an oil bath (80 °C) until the benzene-1,3-disulfonylchloride liquefied. The molten 1,3-phenylenediamine (9 mmol, 0.972 g) was added dropwise to the reactant, and the mixture was stirred with a glass rod. The mixture was heated (80 °C) and stirred for 20 min and then cooled, and water (50 ml) was added. The product was collected by vacuum filtration and washed with a little cold water (10 mL). Recrystallization from acetone gave the title compound.

Yield: (3.2 g, 85%), mp: 200 °C; IR (KBr):  $\nu$  3419 (NH), 1609 (aromatic), 1385 and 1170 ( $\text{SO}_2$ )  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (DMSO- $d_6$ , FT-

250 MHz):  $\delta$  8.21–7.55 (br, aromatic), 7.15 (s, NH); Anal. Calcd for  $[\text{C}_{12}\text{H}_{10}\text{N}_2\text{O}_4\text{S}_2: (310.22)_n]$ : C, 46.46; H, 3.22; N, 9.03; S, 20.67. Found: C, 46.18; H, 3.47; N, 8.34; S, 19.62.

### 2.2. Poly(*N,N'*-dibromo-*N*-phenylbenzene-1,3-disulfonamide)

Poly(*N*-phenylbenzene-1,3-disulfonamide) (1.00 g) was dissolved in chilled aq NaOH (2 mL, 3 M) at rt and the solution was transferred to a beaker.  $\text{Br}_2$  (58.4 mmol) was added to the solution with vigorous stirring and a precipitate formed immediately. The product was collected by vacuum filtration, washed with distilled cold water (30 ml), and then dried in a vacuum desiccator at rt for 5 h.

Yield: (1.2 g, 80%), mp: 180 °C; IR (KBr):  $\nu$  1609 (aromatic), 1380 and 1172 ( $\text{SO}_2$ )  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (DMSO- $d_6$ , FT-250 MHz):  $\delta$  8.20–7.50 (br, aromatic);  $^{13}\text{C}$  NMR (DMSO- $d_6$ , FT-400 MHz):  $\delta$  147.25, 140.70, 138.51, 133.28, 131.63, 131.12, 130.34, 129.52, 126.44, 123.81, 123.38, 119.03. Anal. Calcd for  $[\text{C}_{12}\text{H}_8\text{N}_2\text{O}_4\text{S}_2\text{Br}_2: (470.02)_n]$ : C, 30.66; H, 1.70; N, 5.96; S, 13.64. Found: C, 31.10; H, 1.17; N, 5.50; S, 13.73.

### 2.3. Typical procedure: benzylic bromination of toluene with TBBDA

*N,N,N',N'*-Tetrabromobenzene-1,3-disulfonamide (0.30 g, 0.54 mmol), benzoyl peroxide (0.1 g, 0.413 mmol), and EtOAc (10 mL) were placed in a 25 mL flask. The flask was cooled in ice-water and toluene (2 mmol) was added dropwise with stirring. The mixture was refluxed for 90 min. The reaction was monitored by TLC (*n*-hexane/acetone, 9:1). Then, the flask was cooled, the sulfonamide was filtered off under vacuum filtration, solvent was removed under reduced pressure, and benzyl bromide was collected as a single product; yield: 93%. For less volatile compounds, thin layer chromatography (4:1, *n*-hexane/acetone) was used for purification.

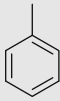
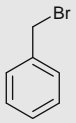
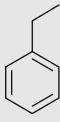
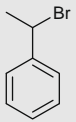
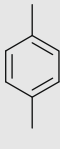
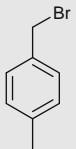
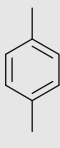
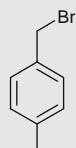
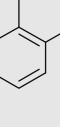
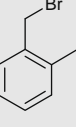
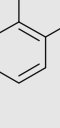
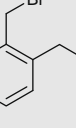
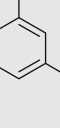
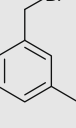
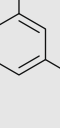
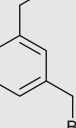
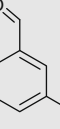
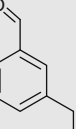
### 2.4. Typical procedure: benzylic bromination of toluene with PBBS

Poly(*N,N'*-dibromo-*N*-ethylbenzene-1,3-disulfonamide) (0.50 g), benzoyl peroxide (0.1 g, 0.413 mmol), and EtOAc (10 mL) were placed in a 25 mL flask. The flask was cooled in ice-water, and toluene (2 mmol) was added dropwise with stirring. The mixture was refluxed for 120 min. The reaction was monitored by TLC (*n*-hexane/acetone, 9:1). Then, the flask was cooled, the polysulfonamide was removed by vacuum filtration, solvent was removed under reduced pressure, and benzyl bromide was collected as a single product; yield: 90%. For less volatile compounds, thin layer chromatography (4:1, *n*-hexane/acetone) was used for purification.

### 2.5. Typical procedure: benzylic bromination of toluene with PBPS

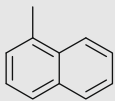
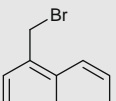
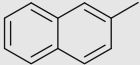
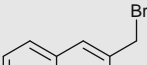
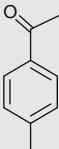
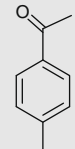
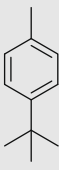
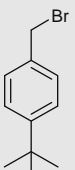
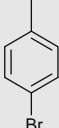
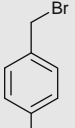
Poly(*N,N'*-dibromo-*N*-phenylbenzene-1,3-disulfonamide) (0.50 g), benzoyl peroxide (0.1 g, 0.413 mmol), and EtOAc (10 mL) were placed in a 25 mL flask. The flask was cooled in ice-water, and toluene (2 mmol) was added dropwise with stirring. The mixture was

**Table 1**  
Benzylic bromination of alkyl benzenes with **TBBDA**, **PBBS**, and **PBPS** in  $\text{CCl}_4$  and EtOAc solvents

Entry		Compound	Product	Solvent	Reagent	Time (h)	Yield <sup>a</sup> (%)
1	a			EtOAc	TBBDA	1.5	93
2				EtOAc	PBBS	2	90
3				EtOAc	PBPS	2	90
4				$\text{CCl}_4$	TBBDA	1.5	97
5				$\text{CCl}_4$	PBBS	1.5	94
6				$\text{CCl}_4$	TBPS	2	96
7	b			EtOAc	TBBDA	2	92
8				EtOAc	PBBS	3	93
9				EtOAc	PBPS	3	89
10				$\text{CCl}_4$	TBBDA	2	95
11				$\text{CCl}_4$	PBBS	2.5	91
12				$\text{CCl}_4$	TBPS	3	92
13	c			EtOAc	TBBDA	2.5	73
14				EtOAc	PBBS	3.5	70
15				EtOAc	PBPS	3.5	72
16				$\text{CCl}_4$	TBBDA	2	75
17				$\text{CCl}_4$	PBBS	3.5	70
18				$\text{CCl}_4$	TBPS	3.5	70
19	d <sup>b</sup>			EtOAc	TBBDA	5.5	75
20				EtOAc	PBBS	6.5	68
21				EtOAc	PBPS	6.5	70
22				$\text{CCl}_4$	TBBDA	5	75
23				$\text{CCl}_4$	PBBS	6.5	70
24				$\text{CCl}_4$	TBPS	6	70
25	e			EtOAc	TBBDA	4	70
26				EtOAc	PBBS	5	69
27e				EtOAc	PBPS	5	68
28				$\text{CCl}_4$	TBBDA	4	70
29				$\text{CCl}_4$	PBBS	4.5	66
30				$\text{CCl}_4$	TBPS	4.5	65
31	f <sup>b</sup>			EtOAc	TBBDA	8.5	72
32				EtOAc	PBBS	9	60
33				EtOAc	PBPS	9	60
34				$\text{CCl}_4$	TBBDA	8	70
35				$\text{CCl}_4$	PBBS	9	66
36				$\text{CCl}_4$	TBPS	9	65
37	g			EtOAc	TBBDA	2.5	70
38				EtOAc	PBBS	3.5	65
39				EtOAc	PBPS	3.5	75
40				$\text{CCl}_4$	TBBDA	2.5	72
41				$\text{CCl}_4$	PBBS	3.5	67
42				$\text{CCl}_4$	TBPS	3	72
43	h <sup>b</sup>			EtOAc	TBBDA	6	73
44				EtOAc	PBBS	7	65
45				EtOAc	PBPS	7	65
46				$\text{CCl}_4$	TBBDA	5.5	72
47				$\text{CCl}_4$	PBBS	7	67
48				$\text{CCl}_4$	TBPS	7	70
49	i			EtOAc	TBBDA	5.5	64
50				EtOAc	PBBS	6.5	65
51				EtOAc	PBPS	6.5	65
52				$\text{CCl}_4$	TBBDA	5	65
53				$\text{CCl}_4$	PBBS	6	63
54				$\text{CCl}_4$	TBPS	6	66

(continued on next page)

Table 1 (continued)

Entry	Compound	Product	Solvent	Reagent	Time (h)	Yield <sup>a</sup> (%)
55			EtOAc	TBBDA	4.5	90
56			EtOAc	PBBS	6.5	85
57			EtOAc	PBPS	6.5	85
58			CCl <sub>4</sub>	TBBDA	4.5	95
59			CCl <sub>4</sub>	PBBS	6.5	87
60			CCl <sub>4</sub>	TBPS	6	83
61			EtOAc	TBBDA	4.5	92
62			EtOAc	PBBS	6.5	85
63			EtOAc	PBPS	6.5	80
64			CCl <sub>4</sub>	TBBDA	4.5	95
65			CCl <sub>4</sub>	PBBS	6	85
66			CCl <sub>4</sub>	TBPS	6.5	84
67			EtOAc	TBBDA	5.5	65
68			EtOAc	PBBS	7	60
69			EtOAc	PBPS	7	60
70			CCl <sub>4</sub>	TBBDA	5	62
71			CCl <sub>4</sub>	PBBS	6	60
72			CCl <sub>4</sub>	TBPS	6	64
73			EtOAc	TBBDA	2.5	88
74			EtOAc	PBBS	3	87
75			EtOAc	PBPS	3	87
76			CCl <sub>4</sub>	TBBDA	2.5	86
77			CCl <sub>4</sub>	PBBS	3	85
78			CCl <sub>4</sub>	TBPS	3	85
79			EtOAc	TBBDA	3	87
80			EtOAc	PBBS	3.5	86
81			EtOAc	PBPS	3.5	85
82			CCl <sub>4</sub>	TBBDA	3	85
83			CCl <sub>4</sub>	PBBS	4	84
84			CCl <sub>4</sub>	TBPS	4	84

<sup>a</sup> Products were characterized by their physical properties, comparison with authentic samples, and by spectroscopic methods.

<sup>b</sup> Conditions of benzylic bromination for these compounds: Benzoyl peroxide (0.2 g, 0.83 mmol), TBBDA (0.6 g, 1.08 mmol) or PBBS (1.00 g) or PBPS (1.00 g), xylene (2 mmol).

Table 2

Reaction time and yield for previously published methods

Substrate	Condition	Time	Yield (%)	Reference
Toluene	NBS, H <sub>2</sub> O, visible light	25 h	77	9
Toluene	<i>N</i> -Bromosaccharin, reflux, (PhCO <sub>2</sub> ) <sub>2</sub> , CCl <sub>4</sub>	15 min	75	2
Toluene	NBS, (PhCO <sub>2</sub> ) <sub>2</sub> , reflux, CCl <sub>4</sub>	45 min	65	16
Toluene	BNBS, (PhCO <sub>2</sub> ) <sub>2</sub> , reflux, CCl <sub>4</sub> , 77 °C	1.5 h	61	17
Toluene	H <sub>2</sub> O <sub>2</sub> -HBr, H <sub>2</sub> O, rt, <i>hν</i>	10 h	86	14
<i>p</i> -Xylene	NaBrO <sub>3</sub> /NaHSO <sub>3</sub> , AcOEt/H <sub>2</sub> O, rt	4 h	59	12
<i>p</i> -Xylene	NBS, microwave, 3.5 bar, 200 W	4 min	50	18
4-Methylacetophenone	NBS, H <sub>2</sub> O, Visible light	25 min	81	9

refluxed for 120 min. The reaction was monitored by TLC (*n*-hexane/acetone, 9:1). Then, the flask was cooled, the polysulfonamide was removed by vacuum filtration, solvent was removed under reduced pressure, and benzyl bromide was collected as a single product; yield: 90%. For less volatile compounds, thin layer chromatography (4:1, *n*-hexane/acetone) was used for purification.

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