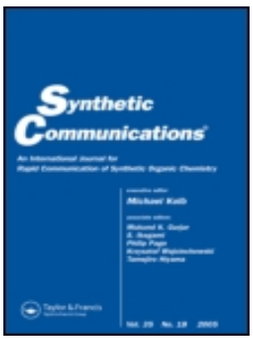

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Convenient sulfonylation of benzotriazoles with the in situ–generated sulfonyl bromides

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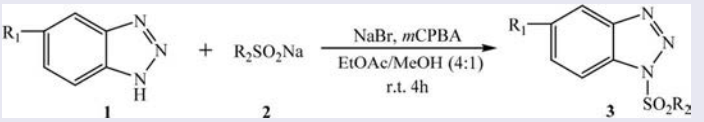
ABSTRACT

A convenient procedure is developed for the preparation of *N*-sulfonylbenzotriazoles from sodium sulfinates, benzotriazoles, and sodium bromide in the present of *m*-chloroperbenzoic acid as oxidant. This radical sulfonylation proceeds efficiently at room temperature under neutral conditions, affording the corresponding *N*-sulfonylbenzotriazoles in moderate to good yields in a short time.

GRAPHICAL ABSTRACT



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KEYWORDS
Benzotriazole; radical reaction; sodium bromide; sodium sulfonate; sulfonylation

Introduction

N-Sulfonylbenzotriazoles are important intermediates in organic synthesis. As advantageous sulfonylation reagents, they can react smoothly with amines and phenols to afford the corresponding sulfonamides and sulfonates, respectively.[1] They also easily convert carboxylic acids into *N*-acylbenzotriazoles, which are especially useful when the corresponding acid chlorides are difficult to obtain.[2,3] They have wide applicability in *C*-sulfonylation and a series of α-cyanoalkyl sulfones, sulfonylheteroaromatics, α-(sulfonylalkyl)heterocycles, α-sulfonylalkyl sulfones, and esters of α-sulfonyl acids have been prepared in excellent yields.[4] As stabilizers, *N*-sulfonylbenzotriazoles are often used in manufacturing the photosensitive materials.[5–10] They are also useful as herbicides, mutagens, insecticides, fungicides, and antibacterials.[11–15] The universal methods for the preparation of *N*-sulfonylbenzotriazole include the reaction of sulfonyl chloride with benzotriazole in the presence of bases[2,16] or with 1-(trimethylsilyl)benzotriazole[15] for alkyl- and arylsulfonylbenzotriazoles, and the reaction of organolithium reagents with sulfur dioxide at low temperature to obtain sulfinic acid salts, followed by the addition of *N*-chlorobenzotriazole for heteroarylsulfonylbenzotriazoles.[16] However, these methods have some limitations such as the availability of sulfonyl chlorides, some of which are hard to prepare and difficult to store or handle. Therefore, development of a general, practical, and efficient method for the construction of *N*-sulfonylbenzotriazoles under mild

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Supplemental data (Full experimental detail) can be accessed on the publisher's website.

conditions is still desirable. Herein, we report a convenient sulfonylation of benzotriazoles with sodium sulfinates and sodium bromide in the present of *m*-chloroperbenzoic acid. This radical sulfonylation proceeds efficiently at room temperature under neutral conditions, affording the corresponding *N*-sulfonylbenzotriazoles in moderate to good yields in short time.

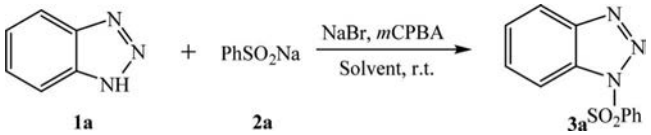
Results and discussion

Similar to the sulfonylation of sulfonyl chloride with benzotriazole, we initially investigated the reaction of sulfonyl bromide with benzotriazole and obtained a good result. Because sulfonyl bromides can be prepared by bromination of sulfinic acids or their salts,[17,18] and to develop a simpler route for preparation of *N*-sulfonylbenzotriazoles, we then tried the one-pot reaction of benzotriazole (**1a**), sodium benzenesulfinate (**2a**), sodium bromide, and *m*-chloroperbenzoic acid (*m*CPBA). It was found that when the mixture of 1.0 equiv of **1a**, sodium bromide, and *m*CPBA with 2.0 equiv of **2a** was stirred in ethyl acetate (EtOAc) for 12 h at room temperature, the expected product 1-phenylsulfonylbenzotriazole (**3a**) was obtained in 32% yield (Table 1, entry 1). In light of the successful formation of **3a**, the reaction conditions were optimized and the results are summarized in Table 1. The reaction was first evaluated in many solvents, giving poor yields (Table 1, entries 1–6). To improve the reaction, several mixed solvents were checked and EtOAc/MeOH (4:1) had the best effect, in which the yield of **3a** increased greatly to 78% (entries 7–13). Similar to NaBr, other bromides such as KBr, NH_4Br, and $(C_4H_9)_4NBr$ can promote the reaction, but provide the desired product in yields ranging from 32% to 62% (entries 14–16). Other oxidants such as THBP, H_2O_2, and $K_2S_2O_8$ were not active in the reaction and normally resulted in very poor yields (entries 17–19). The amounts of *m*CPBA and NaBr were also evaluated. As a result, 1.3 equiv and 1.2 equiv were found to be the suitable amounts for *m*CPBA and NaBr, respectively (entries 11 and 20–26). Finally, a suitable amount of **2a** was determined and 1.8 was the best choice (entries 24 and 27–29). Under the optimized conditions, the reaction processed smoothly and completed in 4 h (entries 28 and 30–32). However, in the absence of NaBr or *m*CPBA, no product was detected (entries 33 and 34).

Based on the extensive screening process, we arrived at the optimal reaction conditions (Scheme 1). Next, the one-pot sulfonylation of 1.0 equiv of benzotriazoles (**1**) with 1.8 equiv of sodium sulfinates (**2**), 1.2 equiv of NaBr, and 1.3 equiv of *m*CPBA in EtOAc/MeOH (4:1) at room temperature for 4 h was investigated. As a consequence, a series of corresponding *N*-sulfonylbenzotriazoles (**3**) were obtained. The results are summarized in Table 2.

As shown in Table 2, the sulfonylation was compatible with the studied benzotriazoles **1**, affording the corresponding sulfonylbenzotriazoles **3** in moderate to good yields (Table 2, entries 1–12). It was obvious that sodium benzenesulfinate **2a** had the best effect in the reaction compared with other two sodium sulfinates, and sodium methylsulfinate **2c** usually resulted in moderate yields. When 5-methylbenzotriazole **1b** and 5-chlorobenzotriazole **1c** were used in the reaction, these monosubstituted benzotriazoles typically gave 5-substituted and 6-substituted mixture products. Because the mixtures were difficult to isolate, the ratios of 5-substituted products to 6-substituted products were finally determined to be nearly 1:1 by ^1H NMR analysis (entries 4–9). Under the same reaction conditions, 1,2,4-triazole **1e** was also treated with **2a**, but the product **3m** was obtained with

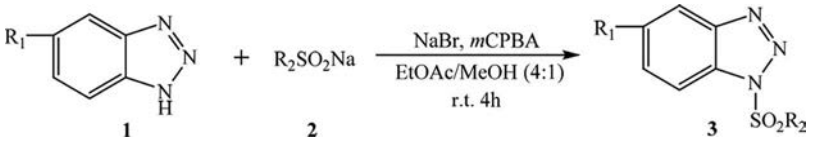
Table 1. Optimization of the sulfonylation of benzotriazole.



Entry	Sodium benzenesulfinate (equiv.)	*m*CPBA (equiv.)	NaBr (equiv.)	Solvent	Time (h)	Yield (%)[a]
1	2.0	1.0	1.0	EtOAc	12	32
2	2.0	1.0	1.0	CH_2Cl_2	12	5
3	2.0	1.0	1.0	MeCN	12	28
4	2.0	1.0	1.0	H_2O	12	0
5	2.0	1.0	1.0	CF_3CH_2OH	12	8
6	2.0	1.0	1.0	MeOH	12	12
7	2.0	1.0	1.0	EtOAc/MeOH(5:1)	12	72
8	2.0	1.0	1.0	CH_3CN/MeOH(5:1)	12	53
9	2.0	1.0	1.0	EtOAc/H_2O(5:1)	12	15
10	2.0	1.0	1.0	EtOAc/MeOH(10:1)	12	38
11	2.0	1.0	1.0	EtOAc/MeOH(4:1)	12	78
12	2.0	1.0	1.0	EtOAc/MeOH(10:3)	12	55
13	2.0	1.0	1.0	EtOAc/MeOH(5:2)	12	39
14	2.0	1.0	KBr (1.0)	EtOAc/MeOH(4:1)	12	32
15	2.0	1.0	NH_4Br (1.0)	EtOAc/MeOH(4:1)	12	45
16	2.0	1.0	$(C_4H_9)_4NBr$ (1.0)	EtOAc/MeOH(4:1)	12	62
17	2.0	THBP(1.0)	1.0	EtOAc/MeOH(4:1)	12	0
18	2.0	H_2O_2(1.0)	1.0	EtOAc/MeOH(4:1)	12	8
19	2.0	$K_2S_2O_8$(1.0)	1.0	EtOAc/MeOH(4:1)	12	10
20	2.0	1.2	1.0	EtOAc/MeOH(4:1)	12	82
21	2.0	1.3	1.0	EtOAc/MeOH(4:1)	12	84
22	2.0	1.4	1.0	EtOAc/MeOH(4:1)	12	78
23	2.0	1.5	1.0	EtOAc/MeOH(4:1)	12	72
24	2.0	1.3	1.2	EtOAc/MeOH(4:1)	12	90
25	2.0	1.3	1.3	EtOAc/MeOH(4:1)	12	90
26	2.0	1.3	1.5	EtOAc/MeOH(4:1)	12	90
27	1.5	1.3	1.2	EtOAc/MeOH(4:1)	12	80
28	1.8	1.3	1.2	EtOAc/MeOH(4:1)	12	90
29	2.5	1.3	1.2	EtOAc/MeOH(4:1)	12	90
30	1.8	1.3	1.2	EtOAc/MeOH(4:1)	6	90
31	1.8	1.3	1.2	EtOAc/MeOH(4:1)	4	90
32	1.8	1.3	1.2	EtOAc/MeOH(4:1)	3	85
33	1.8	1.3	—	EtOAc/MeOH(4:1)	12	0
34	1.8	—	1.2	EtOAc/MeOH(4:1)	12	0

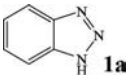
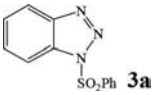
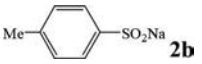
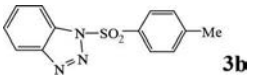
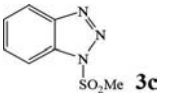
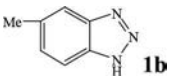
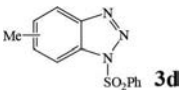
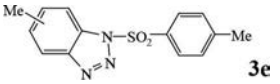
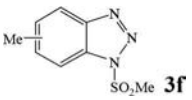
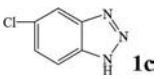
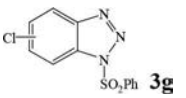
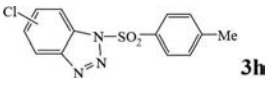
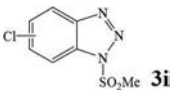
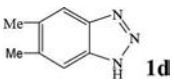
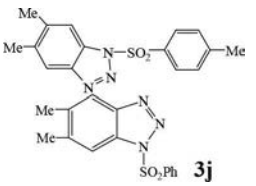
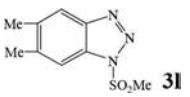
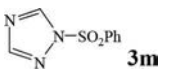
[a]Isolated yield.

a somewhat lower yield 38% (entry 13). To explore the efficiency and generally of our methodology, indole was treated under the same reaction conditions. However, the reaction resulted in 2-sulfonylated product via a radical addition and then elimination process.[19] 5-Nitroindazole and tetrazole, which have two or four nitrogen atom

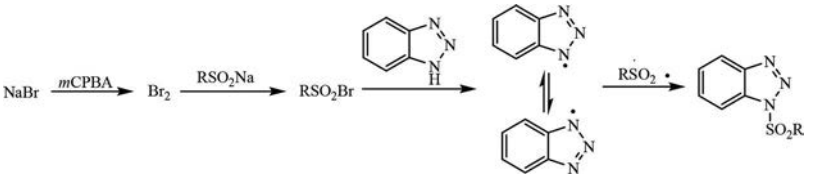


Scheme 1. Sulfonylation of benzotriazoles.

Table 2. Preparation of *N*-sulfonylbenzotriazoles **3**.

r	Benzotriazole 1	Sodiumsulfinate 2	Product 3	Yield (%)[a]
1	 **1a**	$PhSO_2Na$ **2a**	 **3a**	90
2	**1a**	 **2b**	 **3b**	70
3	**1a**	$MeSO_2Na$ **2c**	 **3c**	50
4	 **1b**	**2a**	 **3d**	70
5	**1b**	**2b**	 **3e**	62
6	**1b**	**2c**	 **3f**	40
7	 **1c**	**2a**	 **3g**	78
8	**1c**	**2b**	 **3h**	72
9	**1c**	**2c**	 **3i**	48
10	 **1d**	**2a**	 **3j**	82
11	**1d**	**2b**	**3k**	68
12	**1d**	**2c**	 **3l**	45
13	 **1e**	**2a**	 **3m**	38

[a]Isolated yields.



Scheme 2. Proposed mechanism for the sulfonylation of benzotriazoles.

heterocycles, respectively, were also checked, but the desired *N*-sulfonylated products were not obtained. Therefore, the new and convenient *N*-sulfonylation was suitable for triazoles.

A proposed mechanism for the sulfonylation of benzotriazoles is shown in Scheme 2. Initially, NaBr is oxidized by *m*CPBA into bromine, which reacts with sodium sulfinate easily to form sulfonyl bromide. The in situ–generated sulfonyl bromide, similar to sulfonyl iodide, is then subjected to homolysis to give sulfonyl and bromine radicals as a result of its instability.[19–21] Finally, the bromine radical or sulfonyl radical attacks the hydrogen of benzotriazole to produce the benzotriazole radical, which reacts with sulfonyl radical to afford the *N*-sulfonylbenzotriazole. To identify the mechanism, a radical scavenger, 2,2,6,6-tetramethylpiperidine1-oxyl (TEMPO) was added in the reaction and no sulfonylbenzotriazole was detected, demonstrating that a radical mechanism was involved. That 5-methylbenzotriazole **1b** and 5-chlorobenzotriazole **1c** resulted in the mixture products, also indicating the benzotriazole radical was formed during the reaction.

Conclusions

In summary, we have developed a new and convenient procedure for the preparation of sulfonylbenzotriazoles from benzotriazoles with sodium sulfinates, sodium bromide, and *m*CPBA at room temperature. This sulfonylation of benzotriazoles has some advantages such as mild reaction conditions, simple procedure, and good yields.

Experimental

Infrared (IR) spectra were recorded on a Thermo-Nicolet 6700 instrument, ^{1}H NMR and ^{13}C NMR spectra were measured on a Bruker-AVANCE III (500 MHz) spectrometer, and mass spectra were determined on Waters-GCT Premier, Thermo-DECAX-60000 LCQ Deca XP, and Thermo-ITQ 1100 mass spectrometers. Benzotriazoles, sodium sulfinates, sodium bromide, *m*CPBA, and solvents were commercially available.

General procedure for the sulfonylation of benzotriazoles with the in situ–generated sulfonyl bromides

In EtOAc/MeOH (4:1) mixed solvent (2 mL), benzotriazole **1a** (0.3 mmol), sodium benzenesulfinate **2a** (0.54 mmol), NaBr (0.36 mmol), and *m*CPBA (0.39 mmol) were added successively. The suspension mixture was vigorously stirred at room temperature for 4 h. Upon completion, the reaction was quenched by addition of saturated aqueous $Na_2S_2O_3$ (2 mL), saturated aqueous Na_2CO_3 (8 mL), and H_2O (5 mL). The mixture was extracted with CH_2Cl_2 (3 × 5 mL) and the combined organic phase was dried over anhydrous

Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was then purified by thin-layer chromatography (TLC; 3:1 (v/v) petroleum ether/ethyl acetate) to furnish 1-phenylsulfonylbenzotriazole **3a** (70 mg, 90%).

Pale yellow solid; mp 122–123 °C (lit.[11] 123–125 °C). IR (KBr): 3094.1, 3068.9, 1586.0, 1479.9, 1385.9, 1194.3, 954.8, 726.2, 589.2 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): $\delta = 8.15–8.11$ (m, 3H), 8.09 (d, $J = 8.4$ Hz, 1H), 7.70–7.64 (m, 2H), 7.57–7.53 (m, 2H), 7.52–7.47 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 145.4$, 137.0, 135.2, 131.6, 130.3, 129.6, 127.8, 125.9, 120.5, 111.9. MS (ESI): *m/z* (%) 260 ($[M+H]^+$, 100).

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