

## 2-Benzothiazolyhydrazones with Cation Radicals in Nitrile Solvents. Formations of 1,2,4-Triazoles and Triazolo[3,4-*b*]benzothiazoles

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Arenealdehyde 2-benzothiazolyhydrazone in thianthrene cation radical afforded triazolo[3,4-*b*]benzothiazoles and 1,2,4-triazoles as major and minor product, respectively. On the contrary the similar reaction in tris(2,4-dibromophenyl)aminium hexachloroantimonate gave 1,2,4-triazoles and triazolo[3,4-*b*]benzothiazoles as major and minor product, respectively.

### Introduction

Thianthrene cation radical (Th<sup>•+</sup>) has been extensively investigated and its diverse reactivities with organic substrates are well documented.<sup>1,2</sup> In reacting with nucleophiles, reaction sites of the Th<sup>•+</sup> are sulfur atom and ring carbon depending on the substrates. Reactions of the Th<sup>•+</sup> with arylhydrazones of benzaldehyde,<sup>3</sup> chalcone and benzalacetone<sup>4</sup> have been reported to make oxidative cycloaddition products to nitrile solvents to give 1,2,4-triazoles and oxidative intramolecular cyclization to pyrazoles, respectively. Recently we reported that the major product was switched when arenealdehyde 2-pyridylhydrazones (**1**) were reacted with Th<sup>•+</sup> and tris(2,4-dibromophenyl)aminium hexachloroantimonate (TDBPA<sup>+</sup>) in nitrile solvent.<sup>5</sup> That is, *s*-triazolo[4,3-*a*]pyridines (**2**), an intramolecular cyclization product, and 1-(2-pyridyl)-1,2,4-triazole (**3**), an intermolecular cycloaddition product, were obtained as major products in reacting with Th<sup>•+</sup> and TDBPA<sup>+</sup>, respectively.

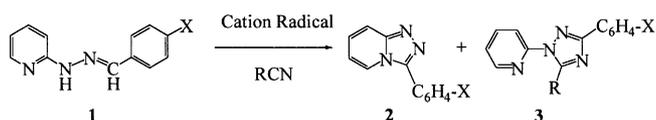
This result prompted us to study further the reactions of cation radicals with **4a-e** whose structures are similar with **1**.

### Experimental Section

Nitrile solvents (Aldrich HPLC grade) were purified by distillation over phosphorus pentoxide under argon prior to use. Thianthrene (Aldrich) was recrystallized twice from acetone. Aldehydes, hydrazines, acid chlorides, and inorganic chemicals were used without further purification. Thianthrene cation radical perchlorate,<sup>6</sup> thianthrene 5-oxide,<sup>7</sup> and tris(2,4-dibromophenyl)aminium hexachloroantimonate<sup>8</sup> were prepared according to the known procedure.

#### Preparation of Hydrazones

**Benzaldehyde 2-benzothiazolyhydrazone (4a).** A solu-



X=H, Me, NO<sub>2</sub>, Br

Scheme 1

tion of benzaldehyde (1.59 g, 15.0 mmol) and 2-hydrazinobenzothiazole (3.00 g, 18.2 mmol) in ethanol (20 mL) containing acetic acid (5% by wt. to the amount of the aldehyde) was refluxed for 3 h. Upon cooling, the hydrazone precipitated as a pale yellow solid. Recrystallization from ethanol gave pale yellow crystals (2.40 g, 9.49 mmol, 63.3%). mp 225-226 °C (lit.<sup>9</sup> mp 230-231 °C).

#### 4-Methoxybenzaldehyde 2-benzothiazolyhydrazone (4b).

By following the similar procedure as described above for **4a**, pale yellow crystals (3.00 g, 10.6 mmol, 70.7%) were obtained from 4-methoxybenzaldehyde (2.04 g, 15.0 mmol) and 2-hydrazinobenzothiazole (3.00 g, 18.2 mmol). mp 193.5-194.5 °C (lit.<sup>10</sup> mp 194-195 °C).

#### 4-Bromobenzaldehyde 2-benzothiazolyhydrazone (4c).

By following the similar procedure as described above for **4a**, pale yellow crystals (5.03 g, 15.7 mmol, 83.6%) were obtained from 4-bromobenzaldehyde (3.80 g, 18.8 mmol) and 2-hydrazinobenzothiazole (3.51 g, 21.2 mmol). mp 274-276 °C (lit.<sup>9</sup> mp 280-281 °C).

#### 4-Methylbenzaldehyde 2-benzothiazolyhydrazone (4d).

By following the similar procedure as described above for **4a**, pale yellow crystals (3.40 g, 12.3 mmol, 71.1%) were obtained from 4-methylbenzaldehyde (2.08 g, 17.3 mmol) and 2-hydrazinobenzothiazole (3.00 g, 18.2 mmol). mp 231-233 °C (lit.<sup>9</sup> mp 232-233 °C).

#### 4-Dimethylaminobenzaldehyde 2-benzothiazolyhydrazone (4e).

By following the similar procedure as described above for **4a**, pale yellow crystals (4.10 g, 13.9 mmol, 76.5%) were obtained from 4-dimethylaminobenzaldehyde (2.70 g, 18.1 mmol) and 2-hydrazinobenzothiazole (3.00 g, 18.2 mmol). mp 236-238 °C (lit.<sup>10</sup> mp 243-244.5 °C).

#### General reactions of thianthrene cation radical (Th<sup>•+</sup>) with heterocyclic hydrazones in nitrile solvents

Hydrazone (0.5 mmol) and Th<sup>•+</sup> (1.0 mmol) were placed in a septum-capped flask which was evacuated, filled with argon. After nitrile solvent (20 mL) was added to the flask with a syringe, the mixture was stirred for 24 h at room temperature. Water (10 mL) was then added and the reaction mixture was neutralized with dilute sodium bicarbonate solution. The organic products were extracted with methylene chloride (5×30 mL) and the solvent was dried over anhydrous

sodium sulfate. Filtration and evaporation afforded solid residue which was dissolved in methylene chloride (50 mL) and was used for identification of products by GC and GC-MS and for quantitative analysis by GC. Authentic samples were used as controls. The products were separated by preparative TLC using methylene chloride/methanol (20/1, v/v) as developing solvents, removed from the plate and extracted with methylene chloride. The separated products were identified by GC-MS,  $^1\text{H}$  NMR, melting points, elemental analysis, HRMS and comparison with authentic samples. Each reaction was carried out twice. The results of products and yields are listed in Table 1.

#### General reactions of tris(2,4-dibromophenyl)aminium hexachloroantimonate (TDBPA $^{+}$ ) with heterocyclic hydrazones in nitrile solvents

Hydrazone (0.5 mmol) and TDBPA $^{+}$  (1.0 mmol) were placed in a septum-capped flask, which was evacuated, filled with argon. After nitrile solvent (20 mL) was added to the flask with a syringe, the mixture was stirred for 12 h at room temperature. When water (5 mL) was added to the reaction mixture, TDBPA was precipitated out. The filtrate was then neutralized with aqueous sodium carbonate and precipitate of antimony oxide was removed. Work-up of the organic products and analysis procedure were the same as those described in general reactions of Th $^{+}$ .

#### Preparation of authentic compounds

The known triazolobenzothiazoles **5a-d** were prepared according to the previous procedure.<sup>11</sup> The new compounds **5e** and **6a-e** were obtained from the corresponding reactions of **4** with cation radicals, and were used as authentic compounds after purification. Physical properties of the new compounds **5e** and **6a-e** are as follows.

**3-(4-Dimethylaminophenyl)-s-triazolo[3,4-b]benzothiazole (5e)**. mp 204-206 °C (ethanol).  $^1\text{H}$  NMR (300 MHz, DMSO- $d_6$ ):  $\delta$  3.02 (s, 6H), 6.90 (d, 2H,  $J$  = 8.8), 7.43-7.52 (m, 3H), 7.60 (d, 2H,  $J$  = 8.8), 8.03-8.06 (m, 1H); GC/MS: (relative intensity) 294 ( $M^+$ , 100), 145 (27.2). Found: C, 65.00; H, 4.75; N, 18.91; S, 10.96%. Calculated for  $\text{C}_{16}\text{H}_{14}\text{N}_4\text{S}$ : C, 65.30; H, 4.76; N, 19.04; S, 10.88%.

**1-(2-Benzothiazolyl)-3-phenyl-5-methyl-1,2,4-triazole (6a)**. mp 191-192 °C (ethanol).  $^1\text{H}$  NMR (300 MHz, pyridine- $d_5$ ):  $\delta$  2.97 (s, 3H), 7.36-7.51 (m, 5H), 7.99 (d, 1H,  $J$  = 8.1), 8.09 (d, 1H,  $J$  = 8.1), 8.41 (dd, 2H,  $J$  = 8.0, 1.6); GC/MS: (relative intensity) 292 ( $M^+$ , 100), 251 (29.2). Found: C, 65.53; H, 3.95; N, 18.76; S, 11.08%. Calculated for  $\text{C}_{16}\text{H}_{12}\text{N}_4\text{S}$ : C, 65.75; H, 4.10; N, 19.18; S, 10.96%.

**1-(2-Benzothiazolyl)-3-(4-methoxyphenyl)-5-methyl-1,2,4-triazole (6b)**. mp 183-185 °C (ethanol).  $^1\text{H}$  NMR (300 MHz, DMSO- $d_6$ ):  $\delta$  3.02 (s, 3H), 3.86 (s, 3H), 7.02 (d, 2H,  $J$  = 9.0), 7.41 (td, 1H,  $J$  = 7.6, 1.3), 7.54 (td, 1H,  $J$  = 7.7, 1.3), 7.94-8.03 (m, 2H), 8.05 (d, 2H,  $J$  = 9.0); GC/MS: (relative intensity) 322 ( $M^+$ , 8.1), 281 (100), 148 (33.6), 133 (16.7), 103 (10.7), 90 (12.5), 78 (10.9), 63 (9.4). HRMS. Found: 322.0887. Calculated for  $\text{C}_{17}\text{H}_{14}\text{N}_4\text{OS}$ : 322.0887.

**1-(2-Benzothiazolyl)-3-(4-bromophenyl)-5-methyl-1,2,4-triazole (6c)**. mp 221-223 °C (ethanol).  $^1\text{H}$  NMR (300 MHz, DMSO- $d_6$ ):  $\delta$  3.03 (s, 3H), 7.47 (t, 1H,  $J$  = 7.6), 7.56 (td, 1H,

$J$  = 7.7, 1.2), 7.69 (d, 2H,  $J$  = 8.5), 7.98 (d, 1H,  $J$  = 7.6), 8.06 (m, 3H); GC/MS: (relative intensity) 372 ( $M^+$ , 100), 370 ( $M^+$ , 98.3), 331 (54.9), 329 (67.7), 148 (31.9), 122 (12.1), 102 (16.4), 78 (10.7). HRMS. Found: 369.9923. Calculated for  $\text{C}_{16}\text{H}_{11}\text{N}_4\text{Br}$ : 369.9920.

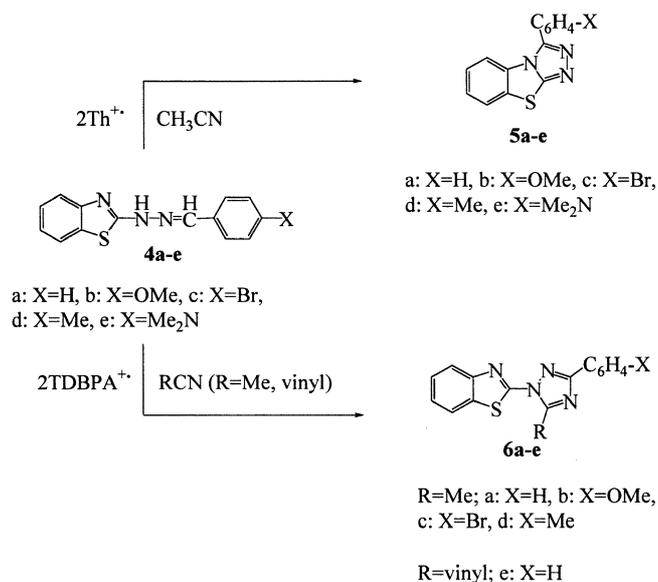
**1-(2-Benzothiazolyl)-3-(4-methylphenyl)-5-methyl-1,2,4-triazole (6d)**. mp 191-193 °C (ethanol).  $^1\text{H}$  NMR (300 MHz, DMSO- $d_6$ ):  $\delta$  2.40 (s, 3H), 3.00 (s, 3H), 7.33 (d, 2H,  $J$  = 8.1), 7.47 (d, 1H,  $J$  = 7.6), 7.56 (td, 1H,  $J$  = 7.7, 1.3), 7.97-8.00 (m, 3H), 8.10 (d, 1H,  $J$  = 8.0); GC/MS: (relative intensity) 306 ( $M^+$ , 100), 265 (60.1). HRMS. Found: 306.0965. Calculated for  $\text{C}_{17}\text{H}_{14}\text{N}_4\text{S}$ : 306.0963.

**1-(2-Benzothiazolyl)-3-phenyl-5-vinyl-1,2,4-triazole (6e)**. mp 179-183 °C (ethanol).  $^1\text{H}$  NMR (300 MHz, chloroform- $d$ ):  $\delta$  5.91 (d, 1H,  $J$  = 11.0), 6.75 (d, 1H,  $J$  = 17.3), 7.37-7.52 (m, 5H), 7.87 (d, 1H,  $J$  = 7.7), 7.96-8.05 (m, 2H), 8.21-8.22 (m, 2H); GC/MS: (relative intensity) 304 ( $M^+$ , 68.3), 303 ( $M^+$ , 100). HRMS. Found: 304.0798. Calculated for  $\text{C}_{17}\text{H}_{12}\text{N}_4\text{S}$ : 304.0797.

## Results and Discussions

Reactions of **4a-e** with Th $^{+}$  and TDBPA $^{+}$  proceeded to give oxidative intramolecular cyclization and cycloaddition products as shown in Scheme 2 and the results are listed in Table 1. As can be seen in Table 1, reactions of **4a, c, d** with Th $^{+}$  in acetonitrile gave products **5** and **6** in a ratio of 2 : 1. On the other hand, each of **4b** and **4e** gave **5** as a sole product. The other products observed in our reactions were Th as a redox partner product and ThO. Formation of ThO is not related to the main reaction but stems from the hydrolysis of Th $^{+}$  due to either adventitious water or water added in the work-up procedure.

To make it clear whether the acid-catalyzed reaction might be undergoing in our reaction conditions or not, **4a** was treated with aqueous perchloric acid in a 1 : 2 molar ratio



Scheme 2

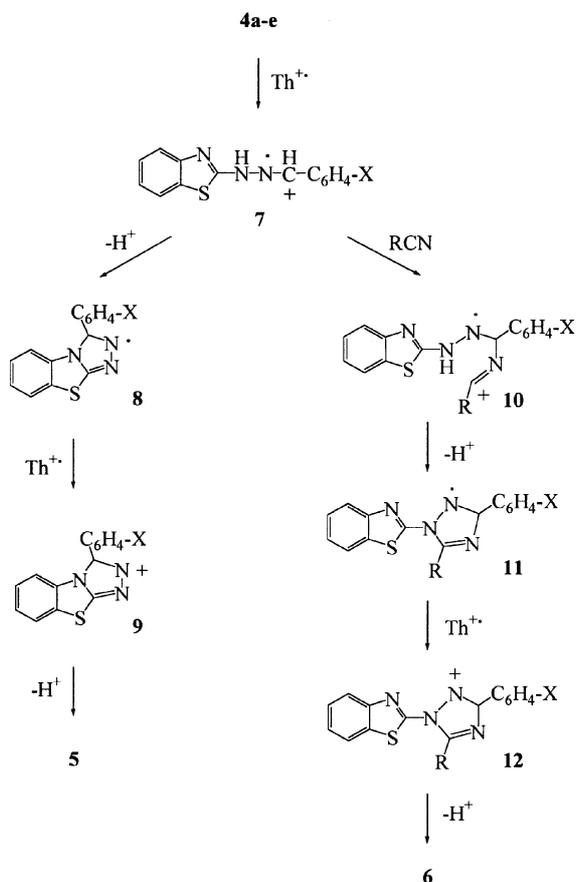
**Table 1.** Quantitative analysis of products in the reactions of **4** with cation radicals in nitrile solvents

4(X)	Solvent (RCN) R	Cation Radical <sup>a</sup>	Products, Yield% <sup>b</sup>					
			Th <sup>+</sup>	ThO <sup>+</sup>	TDBPA	5 <sup>c</sup>	6 <sup>c</sup>	ArClIO <sup>d</sup>
4a(H)	Me	A	98.9	1.0		49.2	25.0	
4b(MeO)	Me	A	93.3	1.0		98.2		
4b(MeO)	Me	A	93.3	1.0		98.2		
4b(MeO)	Me	A	93.3	1.0		98.2		
4c(Br)	Me	A	96.4	2.7		59.2	24.6	
4d(Me)	Me	A	97.6	1.2		46.8	28.6	
4e(Me;N)	Me	A	97.4	2.4		51.6		
4a(H)	Me	B			87.9	6.2	63.6	2.0
4a(H)	Vinyl	B			90.3	13.0	26.4	3.0
4b(MeO)	Me	B			89.0	55.4	28.2	2.0
4c(Br)	Me	B			92.7	4.2	51.6	2.0
4d(Me)	Me	B			98.7	4.0	65.4	1.0

<sup>a</sup>A=Th<sup>+</sup> ClO<sub>4</sub><sup>-</sup>; B=TDBPA<sup>+</sup> SbCl<sub>6</sub><sup>-</sup>. <sup>b</sup>Determined by GC. <sup>c</sup>Based on the amount of Th<sup>+</sup>. <sup>d</sup>Characterized by <sup>1</sup>H NMR, GC/MS, IRMS, and mp, and by comparing those of authentic samples. <sup>e</sup>Characterized by <sup>1</sup>H NMR, GC/MS, HRMS, and/or elemental analysis.

(**4a** : 70% HClO<sub>4</sub>) in acetonitrile. And we found out that no reaction proceeded under these conditions. This observation indicated that the products formed in reactions of Th<sup>+</sup> were not derived from the liberated acid during the reaction.

The results obtained from reactions of **4a-d** with TDBPA<sup>+</sup>

**Scheme 3**

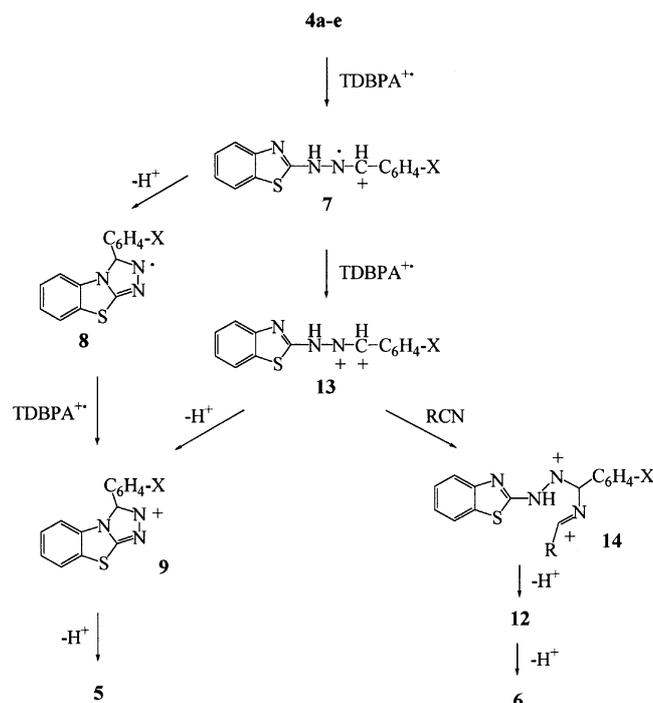
are collected in Table 1.

Those reactions proceeded rapidly and gave **6** as a major product together with **5** and aldehyde in most cases. Oxidation with TDBPA<sup>+</sup> led to the formation of TDBPA as a redox partner product. To clarify the acid-catalyzed reaction by SbCl<sub>5</sub>, the reaction was carried out in a 1 : 2 molar ratio (**4a** : SbCl<sub>5</sub>) in acetonitrile, from which the products were **5a** (2.0%), benzaldehyde (9.4%), unreacted **4a** (11.8%) and some unidentified products (76.8%).

Therefore, it was not obvious whether **5** was formed by cation radical induced reaction or acid catalyzed reaction. To distinguish between nucleophilic and pericyclic routes to **5** and **6**, the reaction of TDBPA<sup>+</sup> with **4a** was carried out in acrylonitrile. Product **6e** (26.4%) was obtained along with **5a** (13.0%) and benzaldehyde (3.0%). As reported previously,<sup>12,13</sup> pericyclic cycloaddition by nitrilimine intermediate with acrylonitrile occurred at the vinyl rather than at the cyano group. Accordingly, it is clear that cation radical reactions do not go through the nitrilimine intermediate. In addition to this, when the reaction of **4a** in the presence of triethylamine was carried out in acrylonitrile, 5-cyanopyrazoline was not detected. The formation of 5-vinyl-1,2,4-triazole rather than 5-cyanopyrazoline provided an evidence that a cation radical induced cycloaddition does not go through a nitriliminium ion intermediate either. From these results, two plausible pathways for the formation of **5** and **6** would be considered as shown in Scheme 3 and Scheme 4.

In the reaction of **4** with Th<sup>+</sup>, the formation of product **5** and **6** is suggested in Scheme 3.

The intermediate **7** which was formed by one electron oxidation of **4** gave both **5** by an intramolecular cyclization and **6** by an intermolecular cyclization with solvent nitrile.

**Scheme 4**

As can be seen in Table 1, formation of **5** is favored by the substrate having electron donating group such as methoxy (**4b**) and dimethylamino (**4e**) which would stabilize the radical cation **7**.

In contrast with  $\text{Th}^{1+}$ , the reaction of  $\text{TDBPA}^{1+}$  gave **6** as a major product along with **5** and aldehyde as a minor product except **4b**.

As shown in Scheme 4, a dication **13** would be easily formed from the intermediate **7** by more stronger oxidant  $\text{TDBPA}^{1+}$  than  $\text{Th}^{1+}$  ( $\text{Th}^{1+}$ : 1.3V vs SCE,<sup>1</sup>  $\text{TDBPA}^{1+}$ : 1.5V vs SCE<sup>14</sup>), which react with nitrile solvent and the successive deprotonation to yield **6**.

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