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Construction of 3-aryl-1,2,4-benzotriazines via unprecedented rearrangement of bis(benzotriazol-1-yl)methylarenes

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ABSTRACT

3-Aryl-1,2,4-benzotriazines were formed unexpectedly by the treatment of 1,l-bis(benzotriazol-1-yl) methylarenes with allylsamarium bromide. A radical pathway was proposed involving steps, such as fragmentation, ring-opening, and cyclization.

Bifunctional derivatives bearing two leaving groups on one carbon, such as L–CH–L′ (L and L′ are leaving groups), constitute a class of useful substrates for the installation of multi-functionalities through proper transformations.[1] Cleavage of the bond of C–L or C–L′ and deprotonation depend on the leaving ability of L and L′ groups and the acidity of the α-H under specific conditions. For example, the cleavage of the C–halogen bond occurred preferentially over the C–H bond when (benzotriazol-1-yl)-1-chloroalkanes were treated with phenol in the presence of sodium hydroxide.[2] Deprotonation proceeded to give carbanions when (benzotriazol-1-yl)-1-ethoxylalkanes,[3] (benzotriazol-1-yl)methyl thioether,[4a] and (benzotriazol-1-yl)-1-carbazolylalkanes[4b] were treated with butyllithium. With the following addition of appropriate electrophiles (e.g., alkyl halides, aldehydes, ketones, and imines), a variety of ketone derivatives can be synthesized.

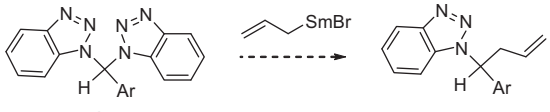
As a good leaving group and activating moiety, benzotriazolyl (Bt) plays an important role in the preparation of a variety of compounds.[5] The *gem*-Bt compounds (Bt–CH–Bt) already showed interesting applications in organic synthesis. For example, bis(benzotrizaol-1-yl)methylarenes could form carbanions at 0 °C with the treatment of LDA[6] or potassium *tert*-butoxide.[7] Reactions of the carbanions with alkyl, benzyl, or allyl halides gave the corresponding alkylated products in good yields, while reactions with acid halides and cyclohexenone led to the masked 1,2- and 1,4-diketones.[7]

In continuation of our research on the application of benzotriazole in organic synthesis, we attempt to synthesize homoallylic benzotriazoles. In our previous study, allylsamarium bromide was found to smoothly substitute one of the acyloxy group in 1,1′-diacetates to afford homoallylic esters.[8] We envisioned that allylsamarium reagent would undergo a Barbier-type reaction with bis(benzotriazol-1-yl)methylarenes **1** to form homoallylic amine derivatives (Scheme 1).[9] Interestingly, an unprecedented rearrangement of **1** was observed. Herein, we wish to report our preliminary results.

Bis(benzotriazolyl)arylmethanes **1** were previously synthesized from substituted benzaldehydes,[10a] α,α-dichlorotoluenes,[6] or benzaldehyde dimethylacetal.[10b] However, only limited examples were disclosed. A referential preparation of alkylidenebisamides, which contained an N–CH–N building block, was conducted by the condensation of aldehydes with amides.[11] It is apparent that the condensation of 1 equiv of aldehyde with 2 equiv of benzotriazole may provide a direct method for the synthesis of the desired bis(benzotriazolyl) methylarenes (Scheme 2).

To our delight, with PTSA as a catalyst, the reaction of benzotriazole with aromatic aldehyde in refluxing toluene proceeded smoothly to generate bis(benzotriazolyl) methylarenes **1** and **2** in moderate to good combined yields. In all the cases, two isomers, namely, 1,l-bis(benzotriazol-1-yl)methylarenes **1** and 1-(benzotriazol-1-yl)-l-(benzotriazol-2-yl)methylarenes **2** (Table 1) were obtained.[12] The 1,l-adduct **1** was isolated as the major product. Aromatic aldehydes with an electron-withdrawing group were found to afford slightly better yields of **1** than those bearing an electron-donating group.

When bis(benzotriazolyl)methyl arenes **1a** was subjected to the freshly prepared allylsamarium bromide in THF, the characteristic violet color of allylsamarium bromide faded gradually and disappeared within 1 h. After completion of the reaction, no considerable amount of substitution product was isolated. To our surprise, 3-phenyl-1,2,4-benzotriazine **3a** was isolated instead along with a debenzotriazolyl compound **4a** (Scheme 3).



1

Scheme 1.

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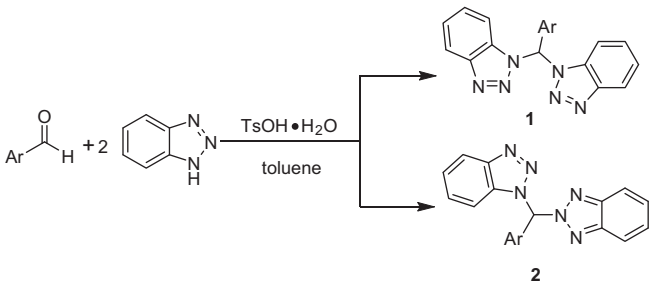
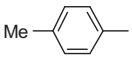
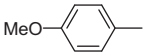
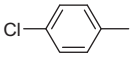
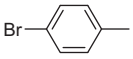
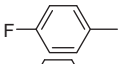
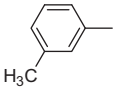
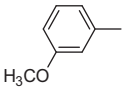
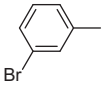
3-Aryl-1,2,4-benzotriazines **3** have been prepared by the oxidation of *N*-phenylsulfonyl-*N*′-arylbenzamidrazones with mercury(II) oxide through a diazonium intermediate.[13] It was also reported that, when treated by 3 equiv of *n*-butyllithium in the presence of TMEDA, two specific α-(benzotriazol-1-yl)hydrazones rearranged to 3-phenyl- and 3-*p*-tolyl-1,2,4-benzotriazines, respectively, by opening the benzotriazole ring.[14a] The formation of **3a** and **4a** (the structures were ascertained by NMR and by comparison with literature data) under the mild conditions from readily available materials intrigued us to develop an alternative useful method for the synthesis of 3-aryl-1,2,4-benzotriazines.



Scheme 2.

Table 1
Synthesis of bis(benzotriazolyl)arylmethanes from the condensation of aromatic aldehydes and benzotriazole

Entry	Ar	Products	Mp (lit. °C)	Yields[a] (%)
1		**1a**	143–145 (lit.[10a] 144–146)	46
		2a	134–135 (lit.[10a] 134–135)	16
2		**1b**	180–182 (lit.[10a] 183–185)	40
		2b	122–124 (lit.[10a] 123–125)	13
3		**1c**	158–160	29
		2c	106–108	8
4		**1d**	120–121	57
		2d	104–105	19
5		**1e**	138–140	55
		2e	128–129	19
6		**1f**	117–119	59
		2f	102–103	19
7		**1g**	161–163	41
		2g	118–120	13
8		**1h**	145–147	44
		2h	107–109	16
9		**1i**	129–131	50
		2i	113–114	18
10		**1j**	125–127	49
		2j	116–117	10

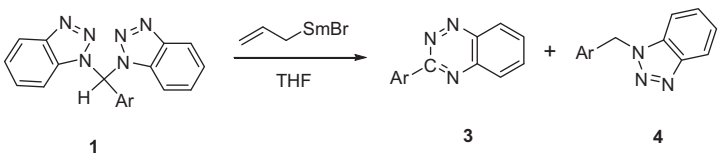
[a] The reaction time was 36 h; Isolated yields based on aldehydes.

Thus, a variety of bis(benzotriazol-1-yl)methylarenes were subsequently investigated under the same reaction conditions.[15] As dictated in Table 2, the reaction has general applicability and delivers moderate to good yields of product **3**. The electron-donating or withdrawing group on the aryl did not have a distinct influence on the yield of the 3-aryl-1,2,4-benzotriazines (Table 2, entries 1–10). It remains unclear why **1d** afforded **3d** in a relatively lower yields. It should also be mentioned that **1i** failed to produce the desired product **3i** and only **4i** was isolated in 68% yield under the optimized conditions.

The formation of **3** obviously resulted from a rearrangement of **1** through a ring-opening of benzotriazole. The benzotriazole ring usually is stable to acids and bases, oxidation and reduction, and heat. Nevertheless, opening of the benzotriazole ring in certain benzotriazole derivatives has been observed. Photolysis- and pyrolysis-induced ring opening of benzotriazole were usually accompanied by the extrusion of N_2.[16a] Grignard reagent induced specific benzotriazoles to undergo the ring-opening via the nucleophilic attack.[16b,c] Base-catalyzed or amine-promoted ring-opening of benzotriazoles with electron-withdrawing substituents were also reported.[16d–f] We previously reported a reductive ring-opening of *N*-acylbenzotriazoles, where a cascade of ring-opening and ring-closure resulted in 1-acylamidobenzimidazoles.[16g] Since the ring-opening of *gem*-Bt compounds was previously unknown, several conditions were examined to get insights into the reaction mechanism.

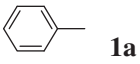
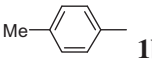
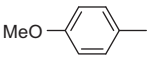
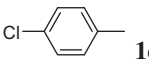
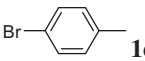
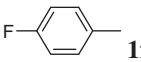
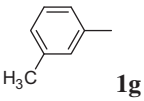
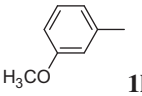
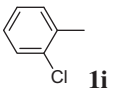
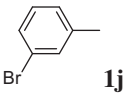
In the presence of a base, such as *n*-butyllithium and potassium *tert*-butoxide, the ring-opening reaction of bis(benzotriazol-1-yl)methylarenes **1a** did not take place. When allylmagnesium bromide was used as an alternative reagent of allylsamarium bromide, the ring-opening reaction failed to occur either. These results apparently did not support a carbanion intermediate.

In light of the good reducing ability of divalent samarium reagent, such as SmI_2, a probable single electron transfer (SET) mechanism is proposed as shown in Scheme 4. First, allylsamarium bromide reacts with one of the benzotriazoles of **1a** through a fragmentation process to form a benzyl radical **A** along with a benzotrizolyl Sm(III) complex. The radical species **A** may abstract a hydrogen atom from the solvent to form benzyl benzotriazoles **4a** as a by-product. And meanwhile, it may induce a ring-opening of triazole to form intermediate **B**, which subsequently reassembles to form a new ring system like 3-phenyl-1,2,4-benzotriazine radical (**C**). After expelling the hydrogen, benzotriazines **3a** was generated. On the other hand, the Sm(III) complex can be quenched by the solvent to give benzotriazole. The formation of benzotriazole was closely related to the amount of **3a** and **4a** (determined by the crude ^{1}H NMR analysis of the reaction mixture), which indicates the intermediate **A** was indeed a precursor to **3a** and **4a** as shown in the proposed mechanism. To further verify this free radical process, bis(benzotriazol-1-yl)arylmethane **1a**

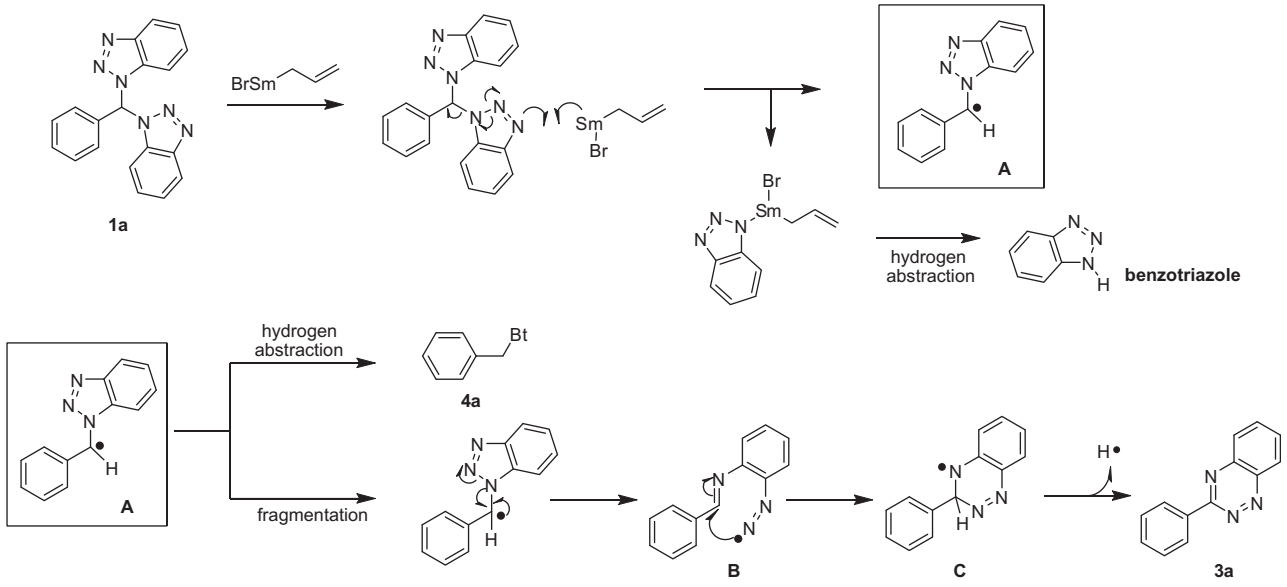


Scheme 3.

Table 2
Formation of 3-aryl-1,2,4-benzotriazines via ring-scissions of 1,l-bis(benzotriazol-1-yl)methylarenes

Entry	Ar	Products	Mp (lit. °C)	Yields[a] (%)
1	 **1a**	**3a** **4a**	123–124 (lit.[13] 124–126) 114–115 (lit.[14b] 114–115)	40 49
2	 **1b**	**3b** **4b**	116–118 (lit.[13] 119–120) 104–106 (lit.[14b] 108–109)	43 45
3	 **1c**	**3c** **4c**	140–142 (lit.[13] 143–144) —	65 Trace[b]
4	 **1d**	**3d** **4d**	148–150 (lit.[13] 150–152) 92–94 (lit.[14c] 101–102)	29 60
5	 **1e**	**3e** **4e**	134–136 120–122 (lit.[14d] 118–119)	56 39
6	 **1f**	**3f** **4f**	144–146 71–72 (lit.[14d] 68–69)	44 45
7	 **1g**	**3g** **4g**	105–106 116–117 (lit.[14d] 116–117)	51 42
8	 **1h**	**3h** **4h**	102–103 51–52 (lit.[14e] 54–55)	55 37
9	 **1i**	**3i** **4i**	— 57–58 (lit.[14b])	Trace[b] 68
10	 **1j**	**3j** **4j**	164–166 —	54 Trace[b]

[a] The reaction time was 1 h; isolated yields based on 1,l-bis(benzotriazol-1-yl)methylarenes.
[b] Detected by GC–MS.



Scheme 4.

was treated with SmI_2, a typical SET reagent. It was gratifying to find that both **3a** and **4a** were obtained at room temperature over 8 h in comparable isolated yields (**3a**, 52%; **4a**, 19%).

In conclusion, an improved preparation of bis(benzotriazol-1-yl)metylarenes has been developed by the direct condensation of benzotriazole with arylaldehydes. In addition, allylsamarium bromide was found to be a single-electron transfer agent for the first time, which induced an unprecedented and novel radical rearrangement of the bis(benzotriazol-1-yl)metylarenes to give benzotriazines in moderate to good yields. The alternative approach to the synthesis of 3-aryl-1,2,4-benzotriazines was thus established.

Acknowledgments

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Supplementary data

Supplementary data (the spectral data of compounds **1**–**4**, and the ^{1}H NMR, ^{13}C NMR spectra of compounds **1**–**3** can be found in the online version) associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2010.10.093.

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12. *General procedure*: To a solution of aromatic aldehyde (10 mmol) and benzotriazole (20 mmol) in toluene (50 mL) was added PTSA (20 mol %). The mixture was then refluxed for 36 h (monitored by TLC). The resulting brown reaction mixture was cooled to room temperature and extracted with ethyl acetate (3 × 20 mL). The combined extracts were washed successively with saturated sodium bicarbonate and brine, dried over anhydrous sodium sulfate, and concentrated under reduced pressure. The residue was subjected to purification on silica gel chromatography (PE:EA = 4:1) to give 1,l-bis(benzotriazol-yl)alkanes (**1a**–**j**) and 1-(benzotriazol-1-yl)-l-(benzotriazol-2-yl)methylarenes (**2a**–**j**).
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15. *Procedure for the rearrangement of* **1a**: To a two-necked flask, samarium (0.33 g, 2.2 mmol) and allyl bromide (0.30 g, 2.5 mmol) in THF (20 mL) were added at room temperature under nitrogen. When the color of the mixture turned purple, stirring was continued for an additional 1 h until the samarium powder disappeared. 1,l-Bis(benzotriazol-yl)alkanes **1a** (1.0 mmol) were added to the solution, and the resulting mixture was stirred at room temperature for 1 h. A saturated solution of sodium potassium tartrate (5 mL) was added to quench the reaction and the corresponding mixture was extracted with ethyl acetate (3 × 10 mL). The combined organic layers were washed with brine (2 × 10 mL) and dried over anhydrous $MgSO_4$. The solvent was removed by evaporation under reduced pressure. The crude product was purified by column chromatography on silica gel (PE:EA = 6:1) to afford 3-aryl-1,2,4-benzotriazines **3a** (82.8 mg, 40% yield) as yellow solid and benzyl benzotriazoles **4a** (102.4 mg, 49% yield) as light brown solid.
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