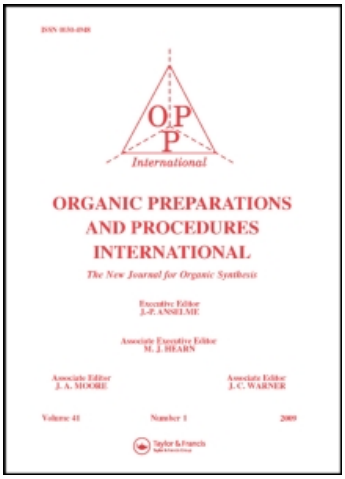

Organic Preparations and Procedures International
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

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To cite this Article Katritzky, Alan R. , Fang, Yunfeng and Belyakov, Sergei A.(1998) 'BORANE-(*N*-SUBSTITUTED)BENZOTRIAZOLE COMPLEXES AND THEIR ALKYLATION REACTIONS', Organic Preparations and Procedures International, 30: 3, 325 — 330
To link to this Article: DOI: 10.1080/00304949809355292
URL: http://dx.doi.org/10.1080/00304949809355292

ORGANIC PREPARATIONS AND PROCEDURES INT., 30 (3), 325-330 (1998)

BORANE-(*N*-SUBSTITUTED)BENZOTRIAZOLE COMPLEXES AND THEIR ALKYLATION REACTIONS

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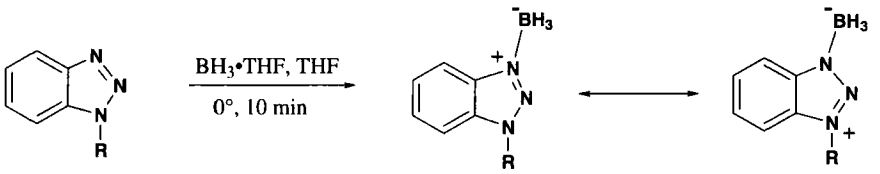
Activation towards electrophilic attack of the α-position of tertiary amines and related compounds, including heterocyclic systems with tertiary nitrogens, has been achieved *via* their complexation with various Lewis acids.[1] The positive charge created on the nitrogen by complexation facilitates the redistribution of electron density in a manner favorable for α-deprotonation. Boron trifluoride and particularly borane complexes of tertiary amines and nitrogen-containing heterocycles have provided such activation.[2a-d]



1a-e **2a-e**

Scheme 1

The activating and stabilizing ability of benzotriazole in α-deprotonation/electrophilic substitution reactions has become a useful synthetic tool.[3] *N*-Alkylbenzotriazoles are important intermediates in the preparation of several classes of organic compounds, including acetylenes,[4] cyclopropanes,[5] and 2-substituted phenols.[6,7] As recently demonstrated,[8] such benzotriazoles show high potential in the carbon insertion reactions. The general scope of the synthetic utility of the *N*-alkylbenzotriazoles is coveniently summarized in a recent review.[3] However, some benzotriazole derivatives are deprotonated with difficulty or not at all. We therefore decided to study the complexation of several N-substituted benzotriazoles with borane and their subsequent deprotonation/alkylation reactions.

Treatment of benzotriazole derivatives **1a-e** (Scheme 1) with BH_3•THF in THF at 0° led to the formation of the new borane-benzotriazole derivative complexes **2a-e** within a very short reaction time in high isolated yields (96-99%, Table 1). These easy-to-handle complexes are solids in most

cases (**2b-e**) and are stable to air and water at room temperature. They were purified by flash column chromatography for analytical purposes; however, as shown below, it is practical to use them *in situ*. Complexes **2a-e** were fully characterized by ^1H and ^{13}C NMR and elemental analyses. The physical characteristics and results of elemental analyses for complexes **2a-e** are shown in the Table 1 and Table 2.

TABLE 1. Preparation of Borane Complexes of Benzotriazole Derivatives **2a-e**

Complex 2	R	Yield (%)	mp. (°C)	Molecular Formula	Elemental Analysis Calcd. (Found) C	H	N
a	*n*-Bu	97	oil	$C_{10}H_{16}BN_3$	63.53 (63.17)	8.53 (8.96)	22.22 (22.33)
b	$PhCH_2$	99	150-152	$C_{13}H_{14}BN_3$	69.99 (69.55)	6.33 (6.56)	18.83 (18.78)
c	*i*-Pr	98	63-65	$C_9H_{14}BN_3$	61.76 (61.44)	8.05 (8.37)	24.01 (23.90)
d	$MeOCH_2$	99	75-77	$C_8H_{12}BN_3O$	54.29 (54.43)	6.83 (6.89)	23.74 (23.82)
e	$PhOCH_2$	96	89-90	$C_{13}H_{14}BN_3O$	65.31 (64.82)	5.90 (5.89)	17.58 (17.40)

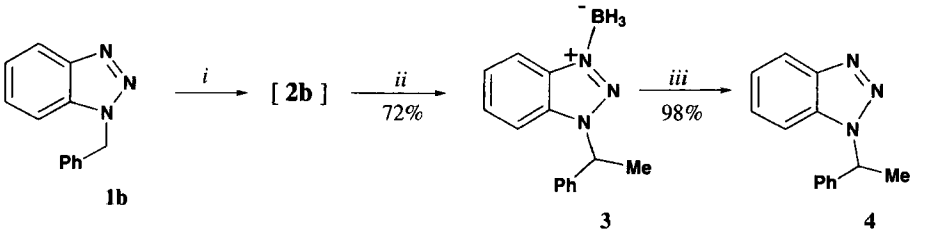
TABLE 2. Spectral Data of Compounds **2a-e**

Cmpd 2	^1H NMR [a] (δ, ppm; J, Hz)	^{13}C NMR (δ, ppm)
a	8.11 (d, 1H, J = 8.4 Hz), 7.76 (d, 1H, J = 8.4 Hz), 7.69-7.57 (m, 2H), 4.73 (t, 2H, J = 7.3 Hz), 2.08-1.98 (m, 2H), 1.44-1.36 (m, 2H), 0.96 (t, 3H, J = 7.2 Hz)	139.3, 133.3, 128.9, 127.0, 117.2, 110.5, 49.4, 31.0, 19.5, 13.1
b	8.19-8.16 (m, 1H), 7.60-7.52 (m, 2H), 7.50-7.43 (m, 1H), 7.42-7.30 (m, 5H), 5.87 (s, 2H)	140.1, 133.3, 132.5, 129.3, 129.2, 128.0, 127.2, 118.1, 110.8, 53.9
c	8.16 (d, 1H, J = 8.3 Hz), 7.75 (d, 1H, J = 8.3 Hz), 7.69-7.58 (m, 2H), 5.24-5.15 (m, 1H), 1.77 (d, 6H, J = 6.7 Hz)	139.7, 132.6, 128.8, 127.1, 117.7, 110.6, 53.6, 21.9
d	8.23 (d, 1H, J = 8.2 Hz), 7.81 (d, 1H, J = 8.2 Hz) 7.74-7.65 (m, 2H), 6.01 (s, 2H), 3.41 (s, 3H)	140.2, 133.2, 129.8, 127.6, 118.1, 111.0, 80.4, 57.7
e	8.19 (d, 1H, J = 8.3 Hz), 7.80 (d, 1H, J = 8.3 Hz), 7.71-7.61 (m, 2H), 7.29 (t, 2H, J = 7.9 Hz), 7.07 (t, 1H, J = 7.2 Hz), 7.03 (d, 2H, J = 8.2 Hz), 6.57 (s, 2H)	155.6, 140.2, 133.4, 130.1, 129.8, 128.2, 127.7, 124.0, 118.3, 116.2, 111.0

a) All compounds have 3.20-2.20 (br s, 3H).

Since the formation of complexes **2a-c** occurs smoothly and almost quantitatively, we studied their metallation reactions without isolation. Thus, treatment of benzyl benzotriazole (**1b**) with borane at -78° in THF afforded complex **2b**, which was treated *in situ* with *n*-BuLi at the same temperature (Scheme 2). Instant development of a deep-blue solution indicated the formation of the

carbanion, which was then trapped with methyl iodide to give the complex **3**. After isolation, complex **3** was subsequently hydrolyzed with ethanol to give the expected α-alkylated benzotriazole **4**. Compound **4** was characterized by ^{1}H and ^{13}C NMR and elemental analysis. Again, the whole reaction sequence can be performed without isolation of the intermediates **2** and **3**, in a one-pot fashion.



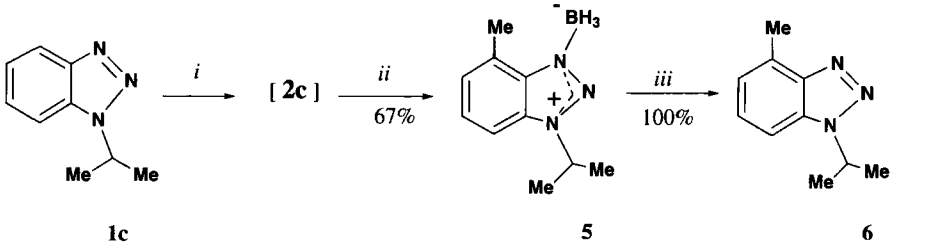
1b **3** **4**

i) BH_3•THF, THF, -78°, 10 min ii) BuLi, -78°, 15 min., then MeI, -78°, 2 h iii) Hydrolysis

Scheme 2

When the α-carbon atom in N-substituted benzotriazoles is sterically hindered, the direction of lithiation and subsequent alkylation is changed, as shown in the example of 1-(2-propyl)benzotriazole (**1c**) (Scheme 3). In this case, the formation of the carbanion in complex **1c**, which was prepared in the usual manner, took a much longer time (2 h), and occurred at the C(4) carbon (benzene moiety), which was established by quenching of the carbanion with methyl iodide. The corresponding methylated complex **5** was isolated in 67% yield and characterized by ^{1}H and ^{13}C NMR and elemental analysis. Hydrolysis of complex **5** gave pure **6** in quantitative yield. If necessary, this reaction can also be carried out in a one-pot reaction, without isolation of the intermediate complexes **2c** and **5**. Examples of metallation in the benzene ring of benzotriazoles are quite rare and usually give several isomers.[9]

Attempts to prepare the analogous complexes of borane with some other benzotriazole derivatives, *i.e.*, with Mannich type adducts of benzotriazole, formaldehyde, and *sec*-amines failed. Apparently, the highly labile >N-CH_2-N< fragment is prone to reduction with borane.



1c **5** **6**

i) BH_3•THF, THF, -78°, 10 min *ii*) BuLi, -78°, 15 min., then MeI, -78°, 30 min *iii*) Hydrolysis

Scheme 3

In summary, stable complexes of benzotriazole derivatives with borane (**2a-e**) were prepared and isolated in excellent yields. Depending on the type of substituent on the benzotriazole, metallation of the complex can occur selectively.

EXPERIMENTAL SECTION

Melting points were determined with a Kofler hot stage apparatus without correction. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ at 300 and 75 MHz respectively on a Varian VXR-300 NMR spectrometer with TMS ($\delta = 0.00$) as the internal reference for ^1H NMR and the central line of $CDCl_3$ ($\delta = 77.0$) as the reference for ^{13}C NMR. Chemical shifts (δ) are reported in ppm downfield from TMS. Microanalyses were performed on a Carlo Erba 1106 elemental analyzer. THF was distilled from sodium/benzophenone prior to use.

For general methods and preparations of the starting benzotriazole derivatives **1a-e**, see lit. refs.[10a-d]

Borane Complexes of 1-(Substituted) Benzotriazoles (2a-e).- Complex BH_3•THF (2.0 mL of a 1 M solution in THF, 2.0 mmol) was added dropwise to a stirred solution of 1-alkylbenzotriazole (**1a-e**, 2.0 mmol) in THF (10 mL) at 0°. After the solution was stirred for 10 min, the solvent was removed under reduced pressure, and the resulting white solid purified by flash column chromatography on silica gel (30% EtOAc in hexanes as eluent) to give pure product **2a-e**.

(±)1-(1-Benzotriazol-1-yl)phenylethane/Borane Complex (3).- Complex BH_3•THF (2.4 mL of a 1 M solution in THF, 2.4 mmol) was added dropwise to a stirred solution of 1-benzylbenzotriazole (500 mg, 2.4 mmol) in THF (10 mL) at -78°. The solution was stirred for 10 min, then *n*-butyl lithium (1.8 mL of a 1.6 M solution in hexanes, 2.9 mmol) was added dropwise to the solution at -78° under an atmosphere of N_2. The solution was stirred for 15 min at -78° and methyl iodide (341 mg, 2.4 mmol) was added in the same temperature. After 2 h the cooling bath was removed and the reaction mixture allowed to warm to room temperature for 2 h before addition of saturated aqueous $NaHCO_3$ solution (15 mL). The phases were separated and the aqueous layer extracted with EtOAc (2 x 20 mL). The combined organic extracts were then washed with water (10 mL) and saturated brine (20 mL), and then dried over Na_2SO_4. The solvent was removed under reduced pressure and under 25° to yield a white solid. The crude material was then purified by flash column chromatography on silica gel (25% EtOAc in hexanes as eluent) to give a white solid (410 mg, 72%), mp. 110-112°.

Anal. Calcd. for $C_{14}H_{16}BN_3$: C, 70.92; H, 6.80; N, 17.72. Found: C, 70.73; H, 6.99; N, 18.02

^1H NMR: δ 8.17 (d, 1H, J = 7.9 Hz), 7.55-7.46 (m, 2H), 7.35-7.33 (m, 6H), 6.10-6.07 (m, 1H), 3.20-2.20 (br s, 3H), 2.19 (d, 3H, J = 7.1 Hz); ^{13}C NMR: δ 140.2, 138.1, 133.0, 129.3, 129.0, 128.9, 127.1, 126.4, 118.0, 111.1, 53.9, 20.9.

1-Isopropyl-4-methylbenzotriazole/Borane Complex (5).- Complex BH_3·THF (2.0 mL of a 1M solution in THF, 2.0 mmol) was added dropwise to a stirred solution of 1-isopropylbenzotriazole (320 mg, 2.0 mmol) in THF (10 mL) at -78°. The solution was stirred for 10 min, then *n*-butyl-lithium (1.5 mL of a 1.6 M solution in hexanes, 2.4 mmol) was added dropwise to the solution at -78° under an atmosphere of N_2. The solution was stirred for 2 h at -78° and methyl iodide (284 mg, 2.0 mmol) was added in the same temperature. After 30 min, the reaction was quenched by addition of saturated aqueous $NaHCO_3$ solution (15 mL). The phases were separated and the aqueous layer extracted with EtOAc (2 x 20 mL). The combined organic extracts were then washed with water (10 mL) and saturated brine (20 mL), and then dried over Na_2SO_4. The solvent was removed under

reduced pressure and under 25° to yield a white solid. The crude material was then purified by flash column chromatography on silica gel (25% EtOAc in hexanes as eluent) to give a white solid (250 mg, 67%), mp. 118-120°.

Anal. Calcd. for $C_{10}H_{16}BN_3$: C, 63.53; H, 8.53; N, 22.22. Found: C, 63.49; H, 8.53; N, 22.19

^{1}H NMR: δ 8.03 (d, 1H, J = 8.3 Hz), 7.44 (t, 1H, J = 7.1 Hz), 7.35 (d, 1H, J = 7.1 Hz), 5.35 (hept, 1H, J = 6.6 Hz), 2.80 (s, 3H), 1.78 (d, 6H, J = 6.6 Hz); ^{13}C NMR: δ 139.9, 132.5, 130.4, 127.0, 121.7, 115.4, 54.3, 23.0, 18.6.

1-Isopropyl-4-methylbenzotriazole (6).- A solution of 1-isopropyl-4-methyl benzotriazole/borane complex (120 mg, 0.63 mmol) in EtOH (5 mL) was refluxed for 30 min, the solvent was removed under reduced pressure and the residue was dried to a constant mass to yield a white solid (110 mg, 100%), mp. 73-74°.

Anal. Calcd. for $C_{10}H_{13}N_3$: C, 68.54; H, 7.48; N, 23.98. Found: C, 68.75; H, 7.82; N, 24.19.

^{1}H NMR: δ 7.89 (d, 1H, J = 7.8 Hz), 7.24-7.16 (m, 2H), 5.30-5.22 (m, 1H), 2.74 (s, 3H), 1.75 (d, 2H, J = 6.6 Hz); ^{13}C NMR: δ 146.2, 131.9, 128.5, 123.7, 120.3, 117.7, 52.1, 23.4, 18.8.

(±)1-(Benzotriazol-1-yl)-1-phenylethane (4).- A solution of 1-(benzotriazol-1-yl)-1-phenylethane/ borane complex (60 mg, 0.25 mmol) in EtOH (5 mL) was refluxed for 30 min, the solvent was removed under reduced pressure and the residue was dried to a constant mass to yield a white solid (56 mg, 98%), mp. 64-65°, lit.[11] 64.5-65.5°.

^{1}H NMR: δ 8.05 (d, 1H, J = 7.0 Hz), 7.29 (br s, 8H), 6.05-6.01 (m, 1H), 2.17 (d, 3H, J = 6.9 Hz); ^{13}C NMR: δ 146.4, 140.1, 132.4, 128.9, 128.2, 127.0, 126.2, 123.8, 119.9, 110.1, 59.0, 21.1.

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(Received November 21, 1997; in final form March 31, 1998)