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Facile and Convenient Synthesis of B-Amino-9-Borabicyclo[3.3.1]nonanes. Aminoboration of Isocyanates*

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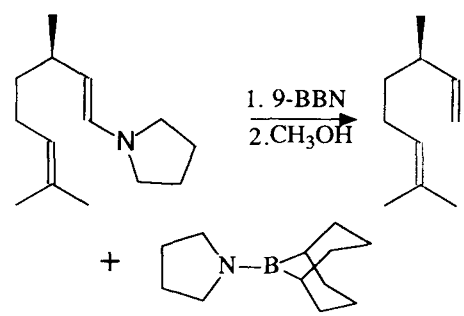
ABSTRACT

The reaction of 9-borabicyclo[3.3.1]nonane (9-BBN) with aliphatic and aromatic primary and secondary amines in tetrahydrofuran (THF) at 65°C proceeds rapidly and quantitatively with evolution of hydrogen and the formation of the corresponding B-amino-9-borabicyclo[3.3.1] nonane (B-amino-9-BBN). Simple evaporation of THF from the reaction mixture gives the B-amino-9-BBN derivatives in high yield and purity. These B-amino-9-BBN derivatives are reactive towards alkyl and aryl isocyanates. Consequently, the aminoboration of various isocyanates has been studied using B-phenylamino-9-BBN. Thus, two equivalents of isocyanates react with one equivalent of B-phenylamino-9-BBN to afford, following the hydrolysis of the intermediate with ethanolamine, N, N'-disubstituted-N -(phenylamido)-ureas in excellent yields. A plausible mechanism for this aminoboration reaction of isocyanates is also presented.

INTRODUCTION

We recently reported a novel method of converting aldehydes and ketones into the corresponding alkenes via hydroboration of their enamines [1]. Thus, hydroboration of aldehydes and ketone enamines by 9-borabicyclo[3.3.1]nonane (9-BBN), followed by methanolysis, affords the corresponding alkenes in very high yields. In this reaction, B-amino-9-BBN derivatives were speculated to be formed as by products (Equation 1).



(1)

In order to confirm the formation of B-amino-9-BBN derivatives in this elimination reaction by ^{11}B NMR spectral comparison, we needed authentic samples of B-amino-9-BBN derivatives. Existing syntheses of aminoboranes can be classified mainly into three groups (a) displacement of a substituent on boron by amine (Equation 2) [2];

$$R_2BX + HNR^1R^2 \xrightarrow[(X = Cl, OR, SR)]{} R_2BNR^1R^2 + HX \qquad (2)$$

(b) reaction of haloboranes with metal alkylamides (Equation 3) [3, 4]

$$R_2BX + MNR^1R^2 \xrightarrow[(X = F, Cl, OR;\ M = Li, Mg, Al)]{} R_2BNR^1R^2 + MX \qquad (3)$$

(c) reaction of metal alkyls with aminohaloboranes (Equation 4) [2].

$$R^1B(Cl)NR_2 + R^2M \xrightarrow[(M = Li, MgBr)]{} R^1R^2BNR_2 + MCl \qquad (4)$$

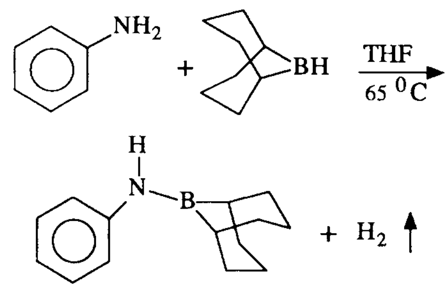
*Cordially dedicated to Professor Herbert. C. Brown on the occasion of his eightieth birthday.

Each of these methods possesses certain disadvantages, such as contamination of the products with inorganic materials, moderate yields and the use of air sensitive organometallic reagents. During the course of our study on the reaction of dialkylboranes (R_2BH) with diamines [5], we observed that ethylenediamine reacted slowly with R_2BH at 25°C liberating hydrogen to give the corresponding aminoboranes. Consequently, it appeared desirable to investigate the reaction between primary and secondary amines with 9-BBN as a potential route to B-amino-9-BBN derivatives. We report here the results of our study on the synthesis of B-amino-9-BBN derivatives and their reaction with isocyanates.

RESULTS AND DISCUSSION

Synthesis of B-Amino-9-BBN Derivatives

We first attempted the reaction of various primary and secondary amines with 9-BBN at 25°C. Unfortunately, no hydrogen evolution occurred at 25°C even after 24 hours. However, a facile reaction between the amines and 9-BBN occurred at 65 °C in THF leading to the formation of the corresponding B-amino-9-BBN. The reaction was carried out by a dropwise addition of an amine to a refluxing 9-BBN solution in THF. Hydrogen liberated during the reaction was measured using a gas-burette connected to the reaction flask. Except for the highly hindered diisopropylamine, all amines included in this study liberated hydrogen rapidly from 9-BBN and the hydrogen evolution was complete within 6 hours at 65°C. Both aromatic and aliphatic amines are readily accommodated in this reaction. After the evolution of hydrogen, no residual hydride was found upon hydrolysis of the reaction mixture indicating the completion of the reaction. Additionally, the ^{11}B NMR spectra of the reaction mixtures showed the clean formation of the respective B-amino-9-BBN derivatives. Simple evaporation of the solvent from the reaction mixture gives these aminoboranes in essentially quantitative yields (Table 1). The results summarized in Table 1 clearly indicate that the direct aminolysis of 9-BBN with primary and secondary amines provide a clean, convenient and general route to a wide variety of B-amino-9-BBN derivatives (Equations 5 and 6).



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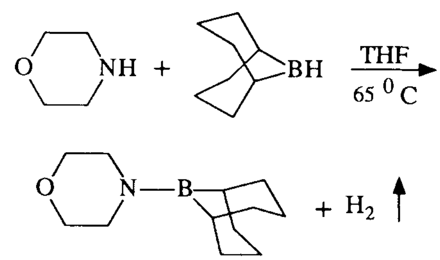

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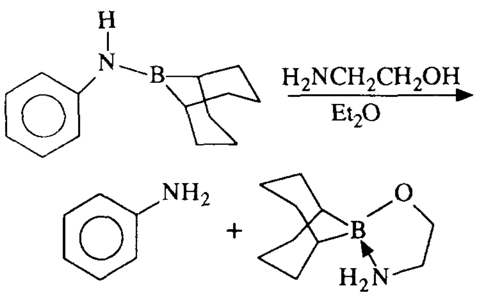
These B-amino-9-BBN derivatives were identical in all respects to those obtained from the hydroboration—elimination reaction of enamines [1]. Additionally, these aminoboranes react readily with

TABLE 1 Reaction of Amines with 9–BBN[a]

Amine	*Time, h*	*Hydrogen evolved, %*[b]	*B-Amino-9-BBN*[c] *Yield, %*[d]	*B-Amino-9-BBN*[c] *^{11}B NMR chem. shift, δ*[f]
Ethylamine	4	100	95	+48
n-Butylamine	4	98	97	+48
tert-Butylamine	2	98	95	+48
Diethylamine	1	100	95	+47
Di-n-butylamine	2	99	92	+48
Di-iso-butylamine	24	10	e	e
Pyrrolidine	6	97	95	+47
Piperidine	6	98	94	+46
N-Methylpiperazine	1	100	95	+46
Morpholine	2	99	95	+47
Aniline	2	100	97	+51
N-Methylaniline	2	100	97	+49

[a]Reaction was carried out in THF at 65°C.[b] Measured using a gas burette. [c]Isolated by evaporating the volatiles from the reaction mixture under reduced pressure (25°C , 12 Torr).
[d]Based on the weight of B-amino-9-BBN isolated. [e]Not formed in any significant amount.
[f]Relative to $Et_2O{\bullet}BF_3$ (δ, 0) with chemical shifts downfield from $Et_2O{\bullet}BF_3$ assigned positive.

monoethanolamine to liberate the free parent amine with concurrent precipitation of ethanolamine-9-BBN addition compound. This reaction was utilized to establish the composition and stoichiometry of these aminoborane derivatives. Thus, reaction of one molar equivalent of B-phenylamino-9-BBN with an equivalent of ethanolamine gave one equivalent of ethanolamine-9-BBN adduct. Gas chromatographic analysis of the supernatant solution using an internal standard showed the presence of an equimolar amount of aniline (Equation 7).



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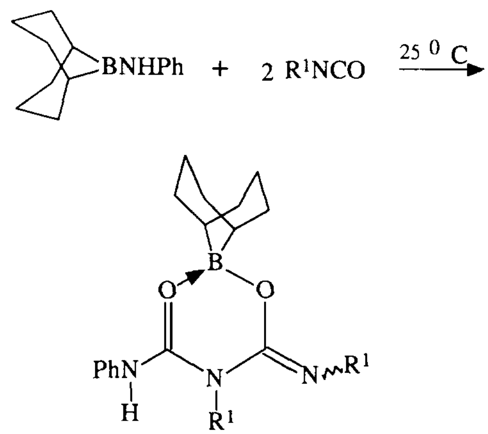
Aminoboration of Isocyanates

In recent years a number of aminoboranes have emerged as highly attractive reagents in organic synthesis. Numerous applications of this new class of compounds in organic synthetic transformations have already been reported [6–10]. Successful achievement of the simple synthesis of B-amino-9-BBN derivatives prompted us to explore their potential as synthetic reagents. Preliminary investigation revealed that these aminoboranes are reactive towards compounds with cumulative double bonds, such as isocyanates. We also noted that B-phenylamino-9-BBN was relatively more reactive than the other aminoboranes. Consequently, we undertook a systematic study of the aminoboration of isocyanates using B-phenylamino-9-BBN.

It has been known that the course of the reaction of organoboranes with isocyanates is critically dependent on the type of organoborane utilized. Thus, trialkylboranes do not react with isocyanates while triarylboranes [11], B-vinyl-9-BBN [12], and B-alkynyl-9-BBN [13] react with two equivalents of isocyanates. However, B-amino-diarylboranes are known to react with only an equivalent of isocyanate even in the presence of an excess of isocyanate [6, 14]. We have found that the course of the reaction of B-phenylamino-9-BBN with isocyanates is similar to that exhibited by B-alkenyl and B-alkynyl-9-BBN derivatives [13, 14]. Thus, the reaction of B-phenyamino-9-BBN with isocyanates proceeded with remarkable ease in *n*-pentane to provide excellent yields of the intermediate (**1**), which precipitated from the reaction mixture as a white solid (Equation 8).



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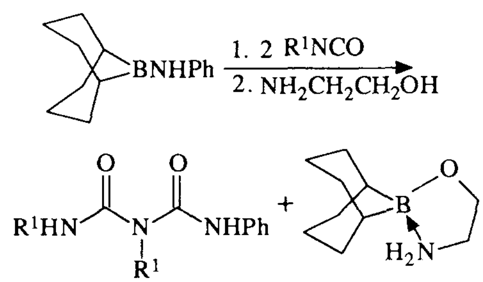
(8)

The intermediate was hydrolyzed with ethanolamine to give the ethanolamine-9-BBN adduct and the novel disubstituted urea derivatives (2) in excellent yields (Equation 9).



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(9)

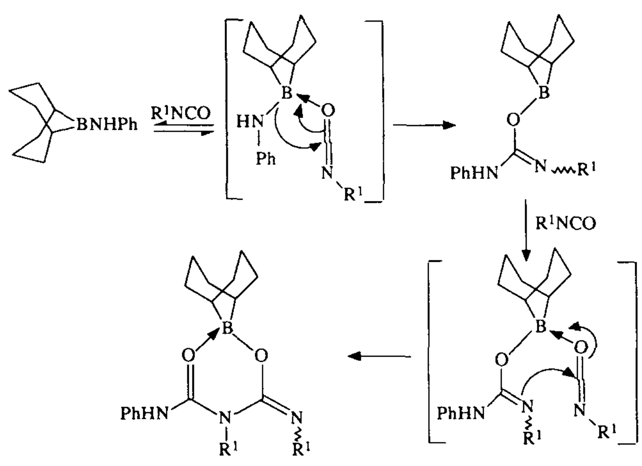
The [1]H NMR and [11]B NMR spectroscopic analyses of compounds (**1**) and [1]H NMR and the elemental analyses of compounds (**2**) clearly showed the 1: 2 stoichiometry. Reaction with both equivalents of isocyanate is essentially instantaneous. Thus, the reaction of B-phenylamino-9-BBN (10 mmol)with one equivalent of methyl isocyanate (10 mmol), followed by addition of ethanolamine, affords aniline (4.7 mmol, 47% , by GC analysis) , the urea derivative (**2**, R^1 = Me) and ethanolamine-9-BBN adduct as the only isolated products.

The mechanism of the reaction can be envisioned as an initial 1,-2-addition of B-phenylamino-9-BBN to the isocyanate, followed by rapid addition of a second equivalent of isocyanate through a six-membered transition state. Initial coordination of the boron atom with the oxygen is expected both on electronic and steric grounds [15]. The intermediate (**1**) immediately precipitates out of the solution preventing further reaction with isocyanate molecule (Scheme 1).

When methyl isocyanate was used, the intermediate (**1**, R^1 = Me) was obtained as a 1:1 mixture of the corresponding *syn* and *anti* isomers as evidenced by the two singlets of equal intensity for the imino methyl group in the [1]H NMR spectrum.

CONCLUSION

The present study describes a facile synthesis of B-amino-9-BBN from primary and secondary aliphatic and aromatic amines. Thus, simple addition of the primary and secondary amines to a THF solution of 9-BBN at 65°C affords the corresponding aminoboranes in essentially quantitative yields. The aminoboration of isocyanates using B-phenylamino-9-BBN and a possible mechanism to account for the observed stoichiometry are also presented.



SCHEME 1

EXPERIMENTAL

All operations were carried out under a nitrogen atmosphere. All glassware, syringes, and needles were oven-dried and cooled under a nitrogen atmosphere. Isocyanates, ethanolamine, 9-BBN , and *n*-pentane were commercial products and used without further purification. ¹H NMR spectra were recorded on a Perkin-Elmer R32 spectrometer. Chemical shifts are in δ units relative to internal Me_4Si. ¹¹B NMR spectra were obtained with a Varian FT8OA spectrometer and the chemical shifts are in δ units relative to $Et_2O{\cdot}BF_3$ with chemical shifts downfield from $Et_2O{\cdot}BF_3$ assigned positive. The infrared spectra were obtained with a Perkin-Elmer 1420 spectrometer. The microanalyses were performed by the Purdue Microanalytical Laboratory. Gas chromatographic analyses were carried out with a Hewlett-Packard 5750 chromatograph with a TC detector.

Reaction of 9-BBN with Amines

The following procedure for the synthesis of B-phenylamino-9-BBN is representative. A 100-ml flask, equipped with magnetic stirring bar and a reflux condenser was charged with a 0.5 M THF solution of 9-BBN (40 mL, 20 mmol). The flask was heated to 65°C and aniline (1.86 g, 20 mmol) was added dropwise. Hydrogen evolution began almost instantaneously and was essentially complete after 2 hours. The reaction mixture was cooled to 25°C and the solvent THF was evaporated under reduced pressure (12 Torr) to get B-phenylamino-9-BBN as a light yellow oil (4.0 g, 95 % yield) : ¹H NMR ($CDCl_3$) δ 1.2 (br s, 2 H), 1.8 (br s, 12 H), 7.0–7.3 (m, 5 H); ¹¹B NMR (THF) δ + 51 (s).

Reaction of B-Amino-9-BBN with Ethanolamine

The following procedure for the reaction between B-phenylamino-9-BBN and ethanolamine is representative. To a 1.0 M ether solution of B-phenylamino-9-BBN (10 mL, 10 mmol) and *n*-dodecane (4 mmol) in a 50-mL centrifuge vial, ethanolamine (0.6 g, 10 mmol) was added with stirring. The reaction mixture was stirred for 1 hour at 25°C and the ethanolamine-9-BBN precipitate was centrifuged down. The supernatant solution was analyzed by GC using a 10 % Carbowax 2OM–2% KOH column (6-ft x 0.25-in) and found to contain 9.8 mmol of aniline (98% yield).

Reaction of B-Phenylamino-9-BBN with Methyl Isocyanate in 1: 1 Molar Ratio

A 50-mL centrifuge tube was charged with a 1.0 M *n*-pentane solution of B-phenylamino-9-BBN (10 mL, 10 mmol), *n*-dodecane (4 mmol), and methyl isocyanate (10 mmol). The reaction mixture was stirred for 24 hours at 25°C and a white solid precipitated from the solution. ¹¹B NMR of the supernatant solution showed a signal at δ + 51 due to the presence of unreacted aminoborane. Ethanolamine (0.6 mL, 10 mmol) was then added and the ethanolamine adduct and the product urea derivative were centrifuged down. GC analysis of the supernatant solution showed the presence of 4.7 mmol of aniline.

Reaction of B-Phenylamino-9-BBN with Methyl Isocyanate in 1:2 Molar Ratio

A 50-mL centrifuge tube was charged with a 1.0 M *n*-pentane solution of B-phenylamino-9-BBN (10 mL, 10 mmol) and methyl isocyanate (25 mmol) was added dropwise with stirring. After stirring for 24 hours at 25°C , the white solid was separated by centrifugation, washed with *n*-pentane (2 × 10 mL) and dried to give the intermediate (**1**, R¹ = Me) (2.8

g, 90%) ; mp 130–132°C (acetone) : IR (KBr) ν_{max} 3240, 2840, 1680, 1595, and 1540 cm^{-1}; ^{1}H NMR (acetone-d_6) δ 0.9–2.0 (m, 14 H), 2.8, 2.9 (2s, 3H), 3.0 (s, 3 H), 7.2–7.7 (m, 5 H); ^{11}B NMR (THF) δ + 7.5 (br s).

The solid adduct (1.6 g, 5 mmol) was suspended in ether (25 mi) and reacted with ethanolamine (5 mmol) at 25°C for 3 hours. The product urea derivative co-precipitated with the ethanolamine-9-BBN adduct. Solvent ether was evaporated and the residue was purified by a plug-filtration through SiO_2-Gel 60 column (200–400 mesh, 6-in × 1-in) using ethyl acetate (40 mL) as the eluent. Evaporation of ethyl acetate afforded an analytical sample of N, N'-dimethyl-N'-phenylamido-urea (**2**, R^1 = Me, 0.9 g, 85 % yield); mp 146–148°C: ^{1}H NMR ($CDCl_3$) δ 2.6 (s, 3 H), 2.7 (s, 3 H), 7.1–7.7 (m , 5 H).

Anal. Calcd. for $C_{10}H_{13}N_3O_2$: C, 58.0; H, 6.3; N, 20.3. Found: C, 58.1; H, 6.1; N, 20.1.

Reaction of B-Phenylamino-9-BBN with n-Butyl Isocyanate in 1:2 Molar Ratio

With the usual experimental setup, the aminoborane (10 mmol) was reacted with *n*-butyl isocyanate (25 mmol) for 24 hours at 25°C as described above. The white solid was separated, washed with *n*-pentane (2 × 10 mL) and dried to give the intermediate (**1**, R^1 = *n*-Bu) (3.7 g, 95%); mp 88–90°C (ether): IR (KBr)ν_{max} 3240, 2260, 1670, 1595, and 1540 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 0.63–2.1 (m, 28 H), 3.2 (q, 3 H), 7.2–7.7 (m, 5 H); ^{11}B NMR (THF) δ + 7.4 (br s).

The solid adduct (2.0 g, 5 mmol) was suspended in ether (25 mL) and reacted with ethanolamine (5 mmol) at 25°C for 3 hours. Solvent ether was evaporated and the residue was purified by a plug-filtration through SiO_2-Gel 60 column (200–400 mesh, 6-in × 1-in) using ethyl acetate (40 mL) as the eluent. Evaporation of ethyl acetate afforded an analytical sample of N, N'-di-*n*-butyl-N'-phenylamido-urea as a viscous liquid (**2**, R^1 = *n* − Bu, 0.9 g, 85 % yield): ^{1}H NMR ($CDCl_3$) δ 0.85(t, 6 H), 1.0–1.6 (m, 8 H), 6.9 (br s, 2 H), 7.1–7.7 (m , 5 H).

Anal. Calcd. for $C_{16}H_{25}N_3O_2$: C, 66.0; H, 8.6; N, 14.4. Found: C, 66.1; H, 8.6; N, 14.2.

Reaction of B-Phenylamino-9-BBN with Phenyl Isocyanate in 1:2 Molar Ratio

This reaction was carried out, as described above, using phenyl isocyanate (25 mmol) and the aminoborane (10 mmol). The solid adduct was collected by centrifugation, washed with *n*-pentane (2 × 10 mL), and dried to afford the intermediate (**1**, R^1 = Ph) (4.0g, 90 %) ; mp 123–125°C (acetone) : IR (KBr) ν_{max} 3200, 2840, 1680, 1595, and 1560 cm^{-1}; ^{1}H NMR (acetone-d_6) δ 1.0 − 1.9 (m, 14 H), 3.2 (q, 3 H), 7.3 (s , 5 H), 7.4 (s, 5 H), 7.6 (s, 5 H); ^{11}B NMR (THF) δ + 11.6 (br s).

The solid adduct (2.3 g, 5 mmol) was suspended in ether (25 mL) and reacted with ethanolamine (5 mmol) at 2°C for 3 hours. Solvent ether was evaporated and the residue was purified by a plug-filtration through SiO_2-Gel 60 column (200–400 mesh, 6-in × 1-in) using ethyl acetate (40 mL) as the eluent. Evaporation of ethyl acetate afforded an analytical sample of N, N'-diphenyl-N'-phenylamido-urea as crystalline solid (**2**, R^1 = Ph, 1.2 g, 75% yield): ^{1}H NMR ($CDCl_3$) δ 6.9–7.7 (m, 15H), 11.2 (br s, 2H).

Anal. Calcd. for $C_{20}H_{17}N_3O_2$: C, 72.5; H, 5.2; N, 12.7. Found: C, 72.7; H, 5.3; N, 12.5.

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