Selective Syntheses of *N*-Monoalkyl and *N,N′*-Dialkyl Derivatives of 1,8-Diaminonaphthalene−9-BBN as an Activating and Directing Group

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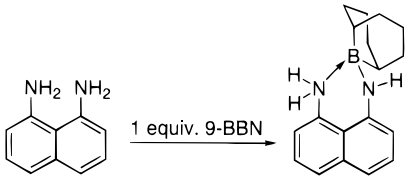
N-Alkylated derivatives of 1,8-diaminonaphthalene have attracted considerable attention because of their unique stereoelectronic characteristics. The prototype member of this family, *N,N,N′N′*-tetramethyl-1,8-diaminonaphthalene was named "proton sponge" because of its enhanced basicity toward a single proton.[1] The synthesis of proton sponge and other symmetrical tetra alkyl derivatives is straightforward, based on reacting 4 equiv of an alkylating agent with 1,8-diaminonaphthalene in the presence of a base. However, the selective synthesis of *N,N′*-dialkyl derivatives, which may find use as starting materials for more elaborate proton sponges or as ligands for metals, is not that simple. Particularly revealing is the report by Alder *et al.* describing various unsuccessful attempts for the synthesis of *N,N′*-dimethyl-1,8-diaminonaphthalene.[2] To this day, there is only one general method for the preparation of *N,N′*-dialkyl derivatives of 1,8-diaminonaphthalene, which relies on stepwise alkylation of the appropriate perimidones.[3] However, this method suffers from the inconvenience of having to eliminate the μ-carbonyl of the dialkylated perimidone, by fusing it with anhydrous potassium hydroxide at 200−220 °C. Herein we present a selective method for the preparation of symmetrical and nonsymmetrical *N,N′*-dialkyl derivatives (as well as *N*-monoalkyl derivatives) of 1,8-diaminonaphthalene, under ambient conditions, relying on 9-BBN as an activating and directing group.

Recently we described the use of a bridging amine−aminoborane, **1**, obtained in high yield by reacting 1,8-diaminonaphthalene and 1 equiv of 9-BBN (eq 1), as a precursor for a novel diaminoborate ligand for transition metals.[4]

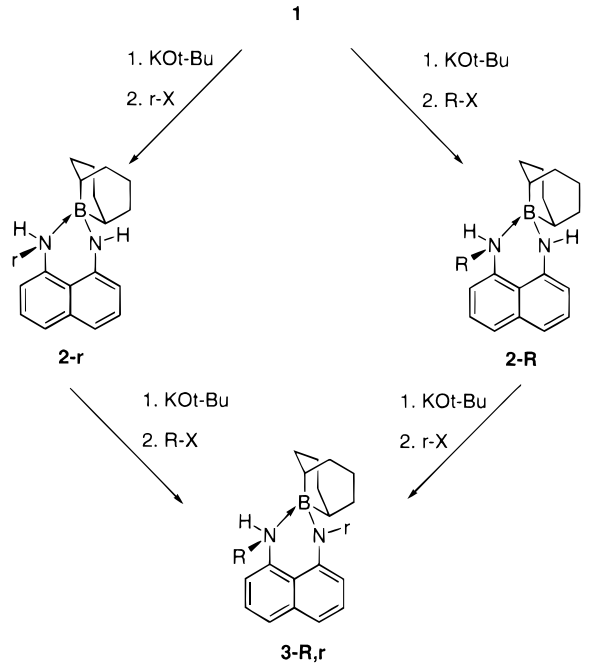


(1)

1

Our need for *N*-alkyl derivatives of this ligand, and the obvious difficulties in performing the procedure described above, prompted us to attempt a direct alkylation of the parent amine−aminoborane, **1**. Indeed, this methodology works efficiently and allows the preparation of *N*-alkyl derivatives of 1,8-diaminonaphthalene, **2-R** (or **2-r**), by a deprotonation/alkylation reaction sequence. Repeating this alkylation sequence affords the selective preparation of *N,N′*-dialkyl derivatives **3-R,r**. The *N,N′*-dialkyl derivatives can be produced in multigram scale in higher than 90% yield, without any contamination of an *N,N*-dialkyl derivative, or scrambling of the alkyl substituents in the case that **R** ≠ **r**. Of the variety of strong bases that can be employed for the deprotonation steps, the mild potassium *tert*-butoxide proved most convenient (Scheme 1).

Scheme 1[a]



[a] Key: R ≥ r; RX, rX = MeI, EtI, BnCl.

There seem to be several factors that contribute to the selective alkylation of the nitrogen atoms in this system: (a) The unique stereoelectronic effects operating in 1,8-diaminonaphthalene favor the formation of the bridging amine−aminoborane **1**, in which one of the three NH protons is acidic enough to be eliminated by the relatively mild base KOt-Bu. (b) In the second alkylation step, the preferred formation of the *N,N′*-dialkyl **3-R,r** over an *N,N*-dialkyl regioisomer is apparently due to steric interactions.

One peculiar aspect of the dialkylation reaction is that in the case that R is not equal to r in **3-R,r**, the larger of the two alkyl groups is always bound to the quarternary nitrogen atom, and the smaller alkyl group is bound to the tertiary nitrogen atom, no matter what the alkylation sequence was. The origin of this regioselectivity, which may take place by a proton migration following the second alkylation step, is the high steric congestion of this system: by binding to the NH group, the larger R avoids both the 9-BBN group and the ortho protons of the naphthalene system. This explanation is supported by molecular mechanics calculations as well as by preliminary X-ray crystal structure of the *N*-monomethyl derivative **2-Me** (Figure 1) in which the methyl group is seen to be pointing away from the 9-BBN group by occupying an "axial" position.[5]

All that is required for completing the synthesis of the *N*-monoalkyl or the *N,N′*-dialkyl-1,8-diaminonaphthalene

(1) (a) Alder, R. W. *Chem. Rev.* **1989**, *89*, 1215. (b) Alder, R. W. *Tetrahedron* **1990**, *46*, 683. (c) Staab, H. A.; Saupe, T. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 865.

(2) Alder, R. W.; Bryce, M. R.; Goode, N. C.; Miller, N.; Owen, J. *J. Chem. Soc. Perkin 1 Trans.*, **1981**, 2840.

(3) Konstantinchenko, A. A.; Pozharskii, A. A.; Stepanova, V. N. *Zh. Org. Khim.* **1993**, *29*, 1437 and references cited therein.

(4) Bar-Haim, G.; Shach, R.; Kol, M. *Chem. Commun.* **1997**, 229.

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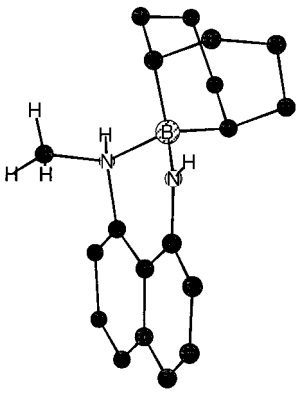
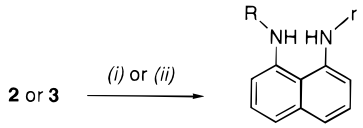


Figure 1. Molecular view of **2-Me** as obtained from a preliminary X-ray structure (H atoms of 9-BBN and naphthalene units are omitted for clarity).

Scheme 2[a]



[a] Key: R = Me, Et, Bn; r = H, Me, Et. (i) 1 N HCl, rt, 2 d. (ii) 1 N NaOH, rt, 2 d.

derivatives **4** is hydrolysis of the bridging 9-BBN group. This is performed by either mild acidic conditions or mild basic conditions at room temperature (Scheme 2).

An even milder hydrolysis procedure, which works efficiently, however, only for the *N*-monoalkyl naphthalene diamines, is reacting **2-R** with a slight excess of ethanolamine in ether at rt for 30 min and filtering off the precipitated ethanolamine−9-BBN adduct.[6]

Compared to the published synthesis, the method we present here is carried out under mild conditions, and we hope it will enable the preparation of hydrolysis-sensitive symmetrical and nonsymmetrical derivatives of 1,8-diaminonaphthalene. In this synthesis, 9-BBN serves in the unorthodox roles of enhancing the acidity of the NH protons and directing of the incoming alkyl groups. We are currently investigating the stereoelectronic effects in the boron-bridged system and their applications.

Experimental Section

1 was prepared from 1,8-diaminonaphthalene and 9-BBN as described elsewhere.[4] All the operations leading to the *N*-alkyl derivatives **2-R**, and *N,N′*-dialkyl derivatives **3-R,r**, were done under a dry nitrogen atmosphere. THF was distilled from sodium benzophenone ketyl. Pentane was distilled from sodium benzophenone ketyl and tetraglyme. All other reagents were of commercial source and used as received.

Preparation of *N*-Alkyl Derivatives (2-R) and *N,N′*-Dialkyl Derivatives (3-R,r) of the Amine−Aminoborane 1. 2-Me. A 1.1 equiv amount of KOt-Bu was added to a solution of **1** (2.5 g) in THF under nitrogen, and the mixture was stirred for 30 min. A 1.1 equiv amount of methyl iodide was added, and the reaction mixture was stirred for another 30 min. Filtration, removal of the solvent under reduced pressure, and precipitation with pentane gave pure **2-Me** in ca. 95% yield. ^{1}H NMR (200 MHz, C_6D_6) δ 0.58 (1H, br s), 0.78 (1H, br s), 1.23−2.21 (12H, m), 2.03 (3H, d, J = 5.8 Hz, HNCH_3), 4.14 (1H, br s, N*H*), 4.51 (1H, br s, N*H*), 5.91 (1H, d), 6.49 (1H, d), 6.94 (1H, t), 7.01 (1H, d), 7.33 (1H, t), 7.49 (1H, d). Anal. Calcd for $C_{19}H_{25}BN_2$: C 78.09, H 8.62, N 9.58; found: C 77.62, H 8.55, N 9.02.

2-Et was prepared as above by reacting **1** with ethyl iodide in ca. 95% yield. ^{1}H NMR (200 MHz, C_6D_6) δ 0.33 (3H, t, J = 7 Hz), 0.56 (1H, br s), 0.90 (1H, br s), 1.57−2.13 (12H, m), 2.55 (1H, m), 2.80 (1H, m), 4.13 (1H, br s, N*H*), 4.31 (1H, br s, N*H*), 6.05 (1H, d), 6.48 (1H, d), 6.90 (1H, t), 6.94 (1H, d), 7.31 (1H, t), 7.50 (1H, d). Anal. Calcd for $C_{20}H_{27}BN_2$: C 78.44, H 8.89, N 9.15; found: C 78.17, H 9.01, N 8.98.

2-Bn was prepared as above by reacting **1** with benzyl chloride in ca. 90% yield. ^{1}H NMR (200 MHz, C_6D_6) δ 0.66 (1H, br s), 1.12 (1H, br s), 1.81−2.26 (12H, m), 2.8−2.95 (2H, m), 3.70 (1H, m), 4.20 (1H, m), 4.30 (1H, br s, N*H*), 4.86 (1H, br s, N*H*), 5.51 (1H, d), 6.37 (2H, d), 6.56 (1H, d), 6.60 (1H, t), 6.86 (2H, t), 6.92 (1H, t), 7.03 (1H, d), 7.36 (1H, t), 7.42 (1H, d). Anal. Calcd for $C_{25}H_{29}BN_2$: C 81.52, H 7.94, N 7.61; found: C 81.18, H 7.93, N 7.26.

3-Me,Me was prepared as above by reacting **2-Me** with methyl iodide in ca. 95% yield. ^{1}H NMR (200 MHz, C_6D_6) δ 0.48 (1H, br s), 0.97 (1H, br s), 1.23−2.43 (12H, m), 1.89 (3H, d, J = 5.8 Hz, HNCH_3), 3.18 (3H, s, NCH_3), 4.50 (1H, br s, N*H*), 5.90 (1H, d), 6.72 (1H, d), 6.96 (1H, t), 7.08 (1H, d), 7.47 (1H, t), 7.53 (1H, d). Anal. Calcd for $C_{20}H_{27}BN_2$: C 78.44, H 8.89, N 9.15; found: C 78.15, H 8.85, N 9.18.

3-Et,Et was prepared as above by reacting **2-Et** with ethyl iodide in ca. 90% yield. ^{1}H NMR (200 MHz, C_6D_6) δ 0.39 (3H, t, J = 7 Hz), 0.50 (1H, br s), 1.08 (1H, br s), 1.31 (3H, t, J = 7 Hz), 1.40−2.40 (13H, m), 2.75 (1H, m), 3.66 (2H, m), 4.35 (1H, m, N*H*), 6.02 (1H, d), 6.84 (1H, d), 6.93 (1H, t), 7.08 (1H, d), 7.43 (1H, t), 7.53 (1H, d). Anal. Calcd for $C_{22}H_{31}BN_2$: C 79.04, H 9.35, N 8.38; found: C 78.78, H 9.36, N 8.36.

3-Et,Me was prepared as above either by reacting **2-Et** with methyl iodide or by reacting **2-Me** with ethyl iodide in ca. 90% yield. ^{1}H NMR (200 MHz, C_6D_6) δ 0.39 (3H, t, J = 7 Hz), 0.51 (1H, br s), 0.87 (1H, br s), 1.59−2.46 (13H, m), 2.75 (1H, m), 3.18 (3H, s, NCH_3), 4.36 (1H, m, N*H*), 6.06 (1H, d), 6.72 (1H, d), 6.94 (1H, t), 7.08 (1H, d), 7.47 (1H, t), 7.54 (1H, d). Anal. Calcd. for $C_{21}H_{29}BN_2$: C 78.75, H 9.13, N 8.75; found: C 78.46, H 9.10, N 8.77.

3-Bn,Me was prepared as above either by reacting **2-Bn** with methyl iodide or by reacting **2-Me** with benzyl chloride in ca. 90% yield. ^{1}H NMR (200 MHz, C_6D_6) δ 0.55 (1H, br s), 1.23 (1H, br s), 1.45−2.55 (12H, m), 3.24 (3H, s, NCH_3), 3.40 (1H, m), 4.16 (1H, m), 4.86 (1H, m, N*H*), 5.49 (1H, d), 6.38 (2H, d), 6.63 (1H, d), 6.78 (1H, t), 6.83 (2H, t), 6.94 (1H, t), 7.10 (1H, d), 7.46 (1H, t), 7.49 (1H, d). Anal. Calcd for $C_{26}H_{31}BN_2$: C 81.67, H 8.17, N 7.33; found: C 81.47, H 8.24, N 7.31.

General Hydrolysis Procedures. In a typical acidic hydrolysis, 15 mL of 1 N aqueous HCl were added to **3-Me,Me** (1 g) dissolved in THF, and the reaction mixture was stirred at rt for two days. Neutralization, extraction with methylene chloride, and purification by chromatography over alumina with ethyl acetate/hexane as eluent gave 1,8-bis(methylamino)naphthalene as a light yellow crystalline solid in 95% yield. In a typical basic hydrolysis, 1 N NaOH was added to **3-Me,Me** dissolved in THF, and the reaction mixture was stirred at rt for two days. After neutralization, 1,8-bis(methylamino)naphthalene was isolated in a similar yield following the same workup.

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Supporting Information Available: ^{1}H NMR spectra and ^{13}C NMR peak lists for several compounds of the type **2-4** (10 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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(5) A suitable crystal of **2-Me** was grown from THF/pentane and mounted on a CAD4 diffractometer under a stream of nitrogen at ca. 100 K. The data collected afforded unequivocal determination of the X-ray structure of **2-Me**. The correctness of the structure was confirmed by a clean difference Fourier map. However, due to poor quality of the crystal, the structure could not be refined beyond an *R* factor of 9.4.

(6) Singaram, B. *Heteroat. Chem.* **1992**, *3*, 245.