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9-BORABICYCLO[3.3.1]NONANE INDUCED FRAGMENTATION OF 2-AZANORBORNENES: A FORMAL BORA-AZA RETRO ENE REACTION

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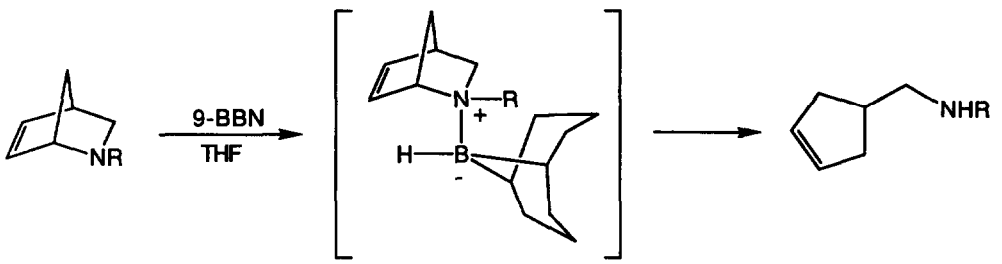
Abstract: N-Substituted 2-azanorbornenes undergo a 9-borabicyclo[3.3.1]nonane induced fragmentation in tetrahydrofuran giving rise to cyclopentenylmethyl amines (cf **3** and **5**).

It has been demonstrated that 2-azanorbornenes undergo facile acid-catalyzed retro Diels-Alder reaction under a variety of conditions giving rise to primary amines[2] or N-methylated amines.[3] We wish to report that the retro Diels-Alder process can be interrupted leading to the formation of cyclopentenylmethyl amines of the type illustrated in Equation 1 by complexation of 2-azanorbornenes with 9-borabicyclo[3.3.1]nonane(9-BBN).



(1)

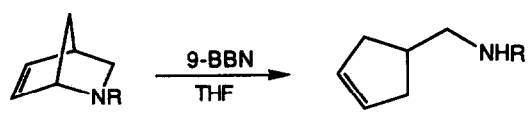
1 2 3

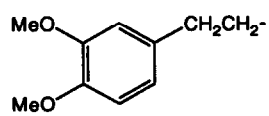
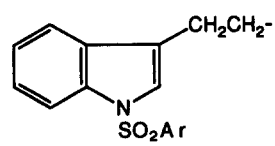
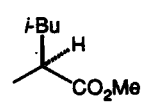
The 9-BBN mediated fragmentation of azanorbornenes, which constitutes a formal bora-aza retro ene reaction, was first observed during an attempt to hydroborate N-benzyl-2-azanorbornene **1** (R = $CH_2C_6H_5$). Exposure of **1** (R = $CH_2C_6H_5$) to an equivalent of 9-BBN at ambient temperature provided less than 10% of the anticipated hydroboration products. The major product (44%) was cyclopentenylmethyl amine **3** (R = $CH_2C_6H_5$). Approximately 25% of **1** (R = $CH_2C_6H_5$) was recovered. No reaction was observed at 0°C. The formation of **3** is best performed in tetrahydrofuran at reflux. For example, exposure of a 0.1 M solution of N-benzyl-2-azanorbornene in tetrahydrofuran to 1.0 equiv of 9-BBN at reflux over 17 h provides the corresponding cyclopentenylmethyl amine **3** (R = $CH_2C_6H_5$) in 54% yield along with 20% of recovered

starting material. Use of 1.2 equiv of 9-BBN did not improve the yield. After the fact, the formation of **3** (R = $CH_2C_6H_5$) is not unreasonable in view of the well-documented[4] affinity of boron for amines and our observation that protonation[2,3] of the nitrogen atom in 2-azanorbornenes dramatically weakens the C(1), N(2) carbon nitrogen bond.

The boron mediated ring opening detailed above has been applied to a number of N-substituted 2-azanorbornenes (Table I). All reactions were performed in tetrahydrofuran at elevated temperatures employing 1.0 equiv of 9-BBN. Yields are modest in the range of 50-60%. Efforts to improve yields by employing diborane or disiamylborane failed to give any ring cleaved product. Use of diborane provided only hydroboration products. Attempts to extend this chemistry to N-benzyl-2-azabicyclo[2.2.2]octene resulted in complete recovery of starting material with no trace of ring opened product.

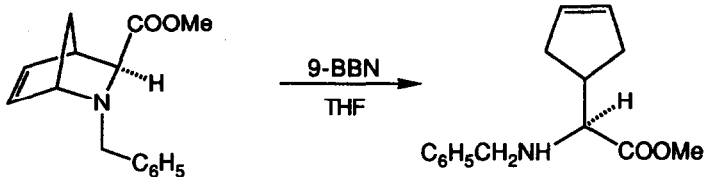
Table I. 9-BBN Mediated Ring Openings of Azanorbornenes[a]



entry	R	time (h)	% yield[b]
1		20	56
2[c]		18	50
3[d]		13	51

[a]All reactions were carried out 1.0 M tetrahydrofuran with 1.0 equiv of 9-BBN at reflux unless stated otherwise. [b]Isolated yields. [c]Ar=4-$MeOC_6H_4$. [d]Reaction performed at 55°C.

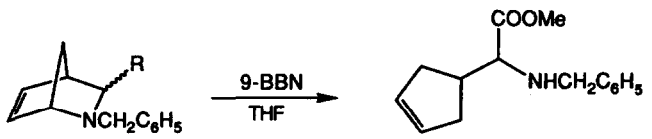
The moderate success achieved above with unsubstituted 1-azanorbornenes led us to investigate more functionalized azanorbornenes. In this regard a number of 3-substituted 2-azanorbornenes were prepared[5] and examined. In a preliminary study, azanorbornene **4** was exposed to 1.0 equiv of 9-BBN in tetrahydrofuran at 50°C. After 22 h, only a 12% yield of **5** was obtained. The yield of **5** could be improved by



4 5

employing 2.0 equiv of 9-BBN in tetrahydrofuran at 50°C. After 1 h, the starting material was completely consumed giving rise to a 44% yield of **5**. The above conditions were applied to a number of 3-substituted azanorbornenes (Table II). Inspection of the data reveals that the exo-substituted azanorbornenes provided

Table II. Reaction of 3-Substituted Azanorbornenes with 9-BBN[a]

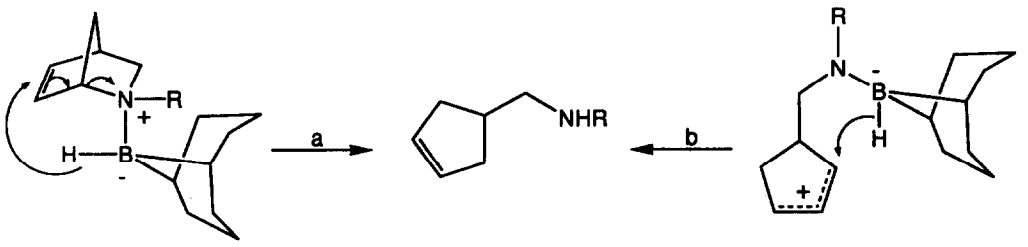


entry	R	time (h)	% yield[b]
1	-COOMe (exo)	0.5	44
2	-COOMe (endo)	1	16
3	$-CH_2OTBDMS$ (exo)	0.5	59
4	$-CH_2OMOM$ (exo)	0.5	55
5[c]	$-CH_2OTBDMS$ (endo)	24	22

[a]All reactions were performed 0.1 M in azanorbornene with 2.0 equiv of 9-BBN at 50°C unless stated otherwise. [b]Isolated yields. [c]1.0 equivalent of 9-BBN used at 40°C.

modest yields (44-59%) of the corresponding cyclopentenylamines whereas the endo-substituted azanorbornenes gave rise to poor yields of rearranged products. The low yields associated with the 3-endo substituted substrates may be due to severe steric crowding on the endo face of the azanorbornene which inhibits complexation. As a consequence one observes hydroboration of the olefin.

The rearrangement of 2-azanorbornenes with 9-BBN reported above can be derived from zwitterionic intermediate **2** via two different pathways: (a) a concerted shift of hydride from boron to C(5) or (b) initial bond cleavage of the C(1), N(2) bond leading to allyl cation **6** which subsequently is trapped by transfer of hydride from boron.



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