A Convenient Synthesis of 2,2-Diallylated Nitrogen Heterocycles by Allylboration of Lactams

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Lactams containing an N–H bond are smoothly transformed into 2,2-diallylated nitrogen heterocycles on heating with allylic boranes in THF followed by deboronation

Introduction

Carboxylic acids,[1–3] esters,[1,2,4] acid anhydrides[4] and *N*,*N*-dimethylbenzamide[4] undergo reductive diallylation on treatment with allylic boranes to give (after deboronation with base or ethanolamine) the corresponding alkyl- or aryldiallylcarbinols. Attempts to stop the above allylboration reactions at the monoaddition stage were unsuccessful. To the best of our knowledge, transformations of lactams and primary amides under the action of allylboranes have not been studied yet. It is known that: (i) reaction of RMgX with 5–8-membered lactams leads to the corresponding 1-methyl-1-aza-2-cyclenes **A** or to a mixture of **A** and 2,2-dialkylated (arylated) heterocycles **B** (Figure 1);[5–7] (ii) the compound $C_{14}H_{23}N$ of unknown structure has been isolated from the reaction of 2-piperidone with allylmagnesium bromide;[8] (iii) ω-lactams containing an N–H bond dealkylate (20–115°C) trialkylboranes R_3B (R = Et, *i*Pr), to give RH and *O*-borylated lactims having various degree of association.[9,10]

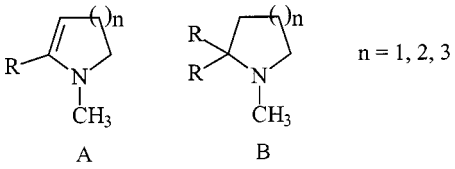

Figure 1. 1-Azacycloalkenes and 2,2-disubstituted 1-azacycloalkanes

As a part of our ongoing research program on the reductive allylboration of nitrogen heterocycles[11,12] we have investigated the reactions of lactams with allylic boranes.

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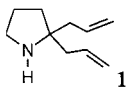
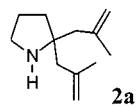
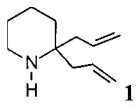
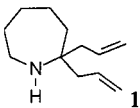
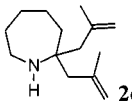
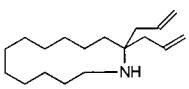
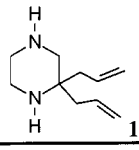
Results and Discussion

Lactams containing an N–H bond are transformed into the corresponding 2,2-diallylated nitrogen heterocycles **1** and **2** (Table 1) on heating under reflux with triallyl- or tri-

Table 1. 2,2-Diallylated nitrogen heterocycles

Compound	Yield, %	B. p., °C (torr)
 **1a**	90	86-88 (13)
 **2a**	91	65-66 (0.5)
 **1b**	79	66-67 (1)
 **1c**	50	76-77 (1)
 **2c**	84	80-81 (0.5)
 **1d**	83	Picrate, m. p. 151-153°C (EtOAc -MeOH)
 **1e**	95	55-56 (0.2)

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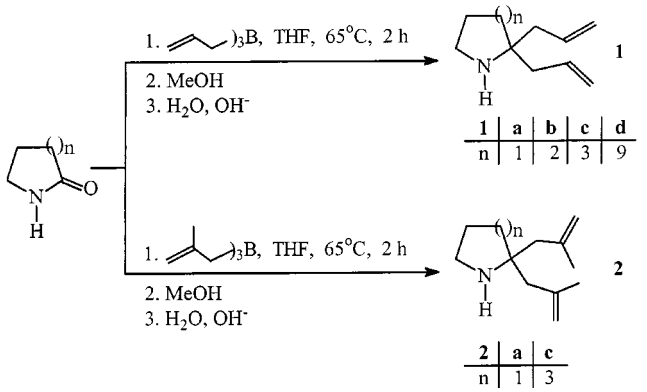
methallylborane in THF followed by deboronation with methanol and base (Scheme 1).



Scheme 1. Reductive allylation of lactams with allylic boranes

Allylboration reactions are completed within two hours. The lactam and allylborane were used in a ratio of 1:1.3. The following lactams were used in the reaction: 2-pyrrolidinone, 2-piperidone, caprolactam, laurolactam and piperazinone. N.B. 2,2-Diallylpyrrolidine[14] and 2,2-diallylpiperidine[8] have been synthesized previously by the reaction of allylmagnesium bromide with 2-ethoxypyrroline and *O*-methylvalerolactim, respectively. With only one exception (reaction of All_3B with caprolactam) the 2,2-diallylated heterocycles **1** and **2** were obtained in 80–95% yields (Table 1).

A possible mechanism of reductive allylboration of lactams is shown in Scheme 2. In the first step, deprotonation of the lactam proceeds (propene is eliminated) to give the *N*-borylated lactam **3a** and/or the *O*-borylated lactim **3b**. Amide **3a** seems to rearrange into lactim **3b** because the B–O bond is stronger than the B–N bond.[13] Both **3a** and **3b** undergo allylboration leading to the intermediates **4a** and **4b**, which eliminate the >B–O–$BAll_2$ fragment to produce the lactim **5**. This compound immediately undergoes allylboration to form aminoborane **6**, deboronation of which gives the corresponding 2,2-diallylated heterocycle **1a**.

It should be mentioned here that acyclic amides containing an N–H bond also react with All_3B to give the analogous diallylated amines. This work is now in progress.

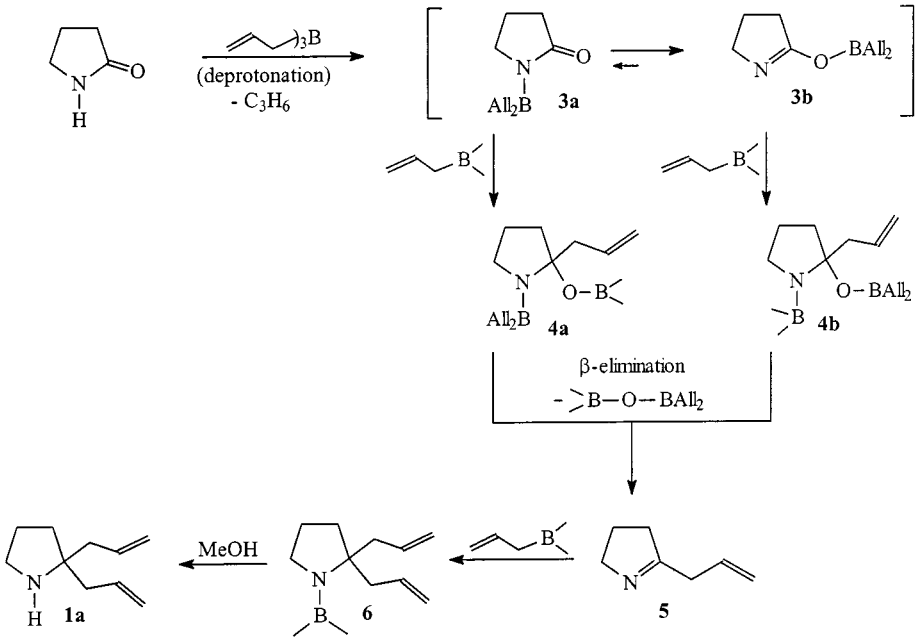
Conclusion

The reductive diallylation of lactams containing an N–H bond presents a novel convenient approach to the 2,2-diallylated nitrogen heterocycles. The method developed possesses obvious advantages over the previously known methodology.[8,14] The reactions of allylic boranes with lactams proceed under mild conditions to give the target products in good to excellent yields. 2,2-Diallylated nitrogen heterocycles contain two double bonds and an NH function and can be used for the preparation of various derivatives, such as bicyclic compounds and spiro-compounds.

Experimental Section

General Remarks: All operations with organoboron compounds were carried out in a dry argon atmosphere. Absolute THF was used. ^1H and ^{13}C NMR spectra were recorded with Bruker AC-200P and AMX-400 instruments. Mass spectra were obtained with a VARIAN-MAT instrument.

Synthesis of 2,2-Diallylpyrrolidine (1a). – General Procedure: Triallylborane (7.0 mL, 40 mmol) was added dropwise with stirring to a solution of 2-pyrrolidinone (2.55 g, 30 mmol) in 10 mL THF. The mixture was refluxed for 1.5 h, then worked up with 5 mL of methanol at room temperature and refluxed for 1 h. Then 5 M NaOH (25 mL) was added and the mixture was vigorously stirred until complete deboronation (no green coloration of flame) of the or-



Scheme 2. Possible mechanism of the reductive diallylation of lactams with allylboranes

ganic layer (≈ 30 min). The organic layer was separated and the aqueous layer extracted with diethyl ether (3 × 10 mL). Combined organic layers were dried with K_2CO_3 and concentrated. Distillation gave **1a** (4.1 g, 90%), b.p. 86–88°C (13 Torr), n_D^{18} = 1.4780. – $C_{10}H_{17}N$ (151.3): calcd. C 79.41, H 11.33, N 9.26; found C 79.47, H 11.29, N 9.69. – ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.50–1.77 (m, 5 H, 2 H_3 + 2 H_4 + NH), 2.15 (d, ^3J = 7.28 Hz, 4 H, CH_2 allylic), 2.9 (t, ^3J = 6.77 Hz, 2 H, CH_2–N), 5.05 (m, 4 H, CH_2 vinylic), 5.8 (m, 2 H, CH vinylic). – ^{13}C NMR ($CDCl_3$): δ = 25.6, 35.0 (C_3, C_4 cyclic), 43.6 (CH_2 allylic), 45.9 (CH_2N), 63.2 ($NC_{quat.}$), 117.6 (CH_2 vinylic), 134.9 (CH vinylic). – MS (EI, 70 eV): *m/z* (%) = 110 (100) [$M^+ - C_3H_5$]. Semmelhack et al. reported b.p. 75–80°C (10 Torr) and identical ^{1}H NMR spectroscopic data.[14]

2,2-Diallylpiperidine (1b): Yield 5.8 g (79%), b.p. 66–67 °C (1 Torr), n_D^{18} = 1.4862. – ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.35–1.55 (m, 7 H, 3 CH_2 cyclic + NH), 2.15 (d, 4 H, CH_2 allylic), 2.75 (t, 2 H, CH_2N), 5.05 (m, 4 H, CH_2 vinylic), 5.8 (m, 2 H, CH vinylic). – ^{13}C NMR ($CDCl_3$): δ = 20.16, 26.2, 34.1 (3 CH_2 cyclic), 40.8 (CH_2N), 41.0 (2 CH_2 allylic), 53.5 (NC_{quat}), 117.9 (CH_2 vinylic), 134.0 (CH vinylic). Lukeš and Černy reported b.p. 83 °C (10 Torr), n_D^{20} = 1.4882.[8]

2,2-Diallylazepane (1c): Yield 3.1 g (50%), b.p. 76–77 °C (1 Torr), n_D^{18} = 1.4881. – ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.4–1.7 (9 H, 4 CH_2 cyclic + NH), 2.05 (d, 4 H, 2 CH_2 allylic), 2.65 (br. s, 2 H, CH_2N), 5.0 (m, 4 H, 2 CH_2 vinylic), 5.75 (m, 2 H, 2CH vinylic). – ^{13}C NMR ($CDCl_3$): δ = 22.33, 30.28, 33.22, 38.41 (4 CH_2 cyclic), 41.80 (CH_2N), 43.40 (2 CH_2 allylic), 57.37 (NC_{quat}), 117.59 (2 CH_2 vinylic), 134.70 (2 CH vinylic).

Picrate of 2,2-Diallyl-1-azacyclotridecane (1d): The oily compound **1d** was obtained analogously to **1a** and transformed into picrate, m.p. 151–153 °C (from methanol/ethyl acetate). Yield 10.3 g (83%). – $C_{24}H_{36}N_4O_7$ (492.6): calcd. C 58.52, H 7.37, N 11.37; found C 58.18, H 7.43, N 11.52. – ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.3–1.9 (20 H, 10 CH_2 cyclic), 2.50 (ABX, ^{AB}J = 14.41 Hz, ^{AX}J = 6.82 Hz, 2 H + 2 H, 2 CH_2 allylic), 3.1 (br. s, 2 H, $CH_2NH_2^+$ cyclic), 5.3 (m, 4 H, 2CH_2 vinylic), 5.81 (m, 2 H, 2 CH vinylic), 7.25 (br. s, 2 H, NH_2^+), 8.9 (s, 2 H, aromatic). – ^{13}C NMR ($CDCl_3$): δ = 18.4, 23.2, 24.1, 24.8, 25.3, 25.8, 26.0, 26.5 (8 CH_2 cyclic), 31.8 (CH_2NH cyclic), 37.9 (2 CH_2 allylic), 63.1 ($C_{quat}NH_2^+$), 120.3 (2 CH_2 vinylic), 124.2, 125.1, 141.7, 160.7 (aromatic); 130.8 (2 CH vinylic).

2,2-Diallylpiperazine (1e): Two equivalents of All_3B with respect to piperazinone were used. Yield 4.5 g (95%), b.p. 55–56 °C (0.2 Torr), n_D^{18} = 1.5054. – $C_{10}H_{18}N_2$ (166.3): calcd. C 72.24, H 10.91, N 16.83; found C 72.35, H 10.89, N 16.71. – ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.5 (s, 2 H, 2 NH), 2.15 (ddd, 4 H, CH_2 allylic), 2.5 (s, 2 H, 3 CH_2N), 2.65 (s, 4 H, CH_2CH_2), 5.0 (dd, 4 H, CH_2 vinylic), 5.7 (m, 2 H, CH vinylic). – ^{13}C NMR ($CDCl_3$): δ = 39.1 (CH_2 allylic), 41.1, 46.4 (C_5, C_6 cyclic), 52.7 (NC_{quat}), 53.9 (NC_3), 118.0 (CH_2 vinylic), 133.5 (CH vinylic).

2,2-Bis(2-methylallyl)pyrrolidine (2a): Yield 4.8 g (91%), b.p. 65–66 °C (0.5 Torr), n_D^{18} = 1.4848. – $C_{12}H_{21}N$ (179.3): calcd. C 80.38, H 11.80, N 7.81; found C 80.13, H 11.72, N 8.08. – ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.51–1.65 (m, 5 H, 2 H_3 + 2 H_4 + NH), 1.72 (s, 6 H, 2 CH_3), 2.11 (s, 4 H, 2 CH_2 allylic), 2.8 (t, 2 H, ^3J = 6.54 Hz), 4.61, 4.80 (s + s, 2 H + 2 H, 2 CH_2 vinylic). – ^{13}C NMR ($CDCl_3$): δ = 24.8 (CH_3), 25.6, 35.9 (C_3, C_4 cyclic), 45.4 (CH_2N), 46.8 (2 CH_2 allylic), 63.9 (NC_{quat}), 114.4 (2 CH_2 vinylic), 143.3 (C_{quat} vinylic). – EI-MS (70 eV): *m/z* (%) = 124 (100) [$M^+ - C_4H_7$].

2,2-Bis(2-methylallyl)azepane (2c): Yield 9.2 g (84%), b.p. 80–81 °C (0.5 Torr), n_D^{18} = 1.4955. – $C_{14}H_{25}N$ (207.4): calcd. C 81.09, H 12.15, N 6.75; found C 80.80, H 12.10, N 7.10. – ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.35 (br. s, 1 H, NH), 1.50 (br. s, 6 H, 3 CH_2 cyclic), 1.65 (2 H, CH_2 cyclic), 1.85 (s, 6 H, 2 CH_3), 2.10 (AB, ^2J = 13.31 Hz, 4 H, 2 CH_2 allylic), 2.68 (m, 2 H, CH_2N), 4.70, 4.88 (s, 4 H, 2 CH_2 vinylic). – ^{13}C NMR ($CDCl_3$): δ = 23.5, 30.8, 33.6, 39.4 (4 CH_2 cyclic), 42.5 (CH_2N cyclic), 25.5 (2 CH_3), 48.5 (2 CH_2 allylic), 58.4 (NC_{quat}), 114.4 (2 CH_2 vinylic), 143.6 (2 $C_{quat.}$ vinylic). – EI-MS (70 eV): *m/z* (%) = 152 (100) [$M^+ - C_4H_7$], 96 (92) [$M^+ - C_4H_7 - C_4H_8$].

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