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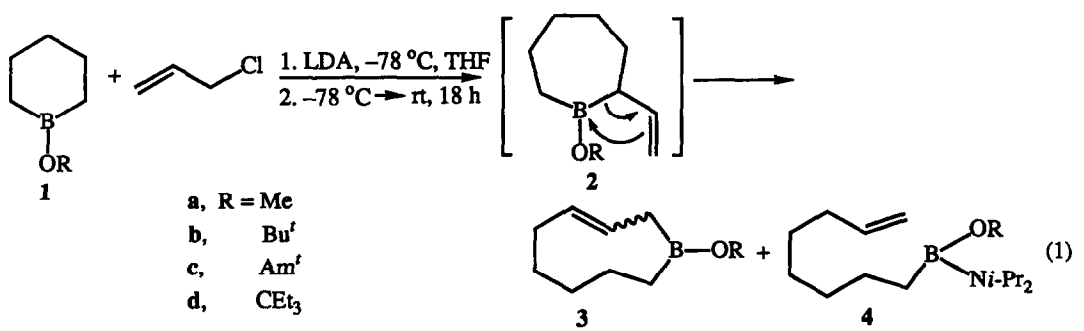
THREE-CARBON RING EXPANSION OF BORACYCLANES

Herbert C. Brown* and Seetharaman Jayaraman
H. C. Brown and R. B. Wetherill Laboratories of Chemistry
Purdue University, West Lafayette, Indiana 47907, U.S.A.

Abstract: (α-Chloroallyl)lithium, generated in situ from $LiNR_2$ and allyl chloride, reacts with cyclic borinates to furnish ring-expanded allylic boracyclenes. The undesired protonolysis by the amine generated during metalation has been overcome either by increasing the steric bulk of the alkoxy group on boron or by addition of $BF_3.OEt_2$ to deactivate the amine. The synthetic utility of the allylic B-alkoxy-3-boracyclenes has been demonstrated.

Allylic organometallic reagents have found extensive application in organic synthesis.[1] In particular, the allyl- and crotylboron reagents reported from our laboratory[2] have been utilized by many research groups to achieve acyclic stereoselection in the synthesis of many complex natural products.[3] While acyclic boron reagents are accessible by the reaction of an allyl Grignard/crotyl metal with suitable boron substrates or by the homologation route,[4] a general synthesis of cyclic allylboron compounds is lacking. We have reported[5a] recently that the alkylboronate esters react with (α-chloroallyl)lithium[5b] to furnish the homologated α-vinylboronate esters, thermally rearranged to the isomeric allylboronate esters. In this communication, we wish to report application of this protocol to the synthesis of allylic boracyclenes and an exploration of their applications in allylboration reactions.

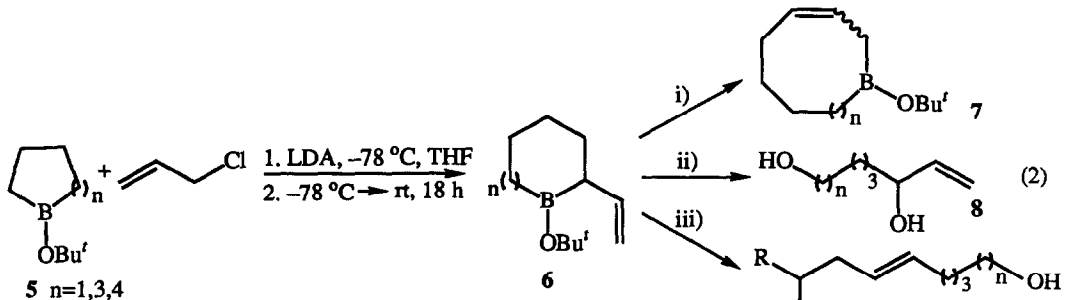
Earlier reports have shown that $LiCH_2Cl$, generated *in situ* from ICH_2Cl and *n*-BuLi,[6a] can be utilized for the one-carbon ring expansion of boracyclanes.[6b] Even though this linear method provided access to medium-size rings, it was felt that a convergent approach to boracyclanes is desirable. Reaction of (α-chloroallyl)lithium with *B*-methoxyborinane **1a**, furnishes two products **3a** and **4a** in a ratio of 3:7(eq 1).



The homologation proceeds with a concomitant allylic rearrangement to yield the three-carbon ring expanded allylic borinate **3a**. Unfortunately, **3a** is protonolyzed to compound **4a** by the *i*-Pr_2NH produced in

the reaction. It was thought that this undesired ring-opening might be overcome in two possible ways: i) increasing the steric bulk of the OR group on boron to resist coordination with the amine, and ii) by complexing the amine.

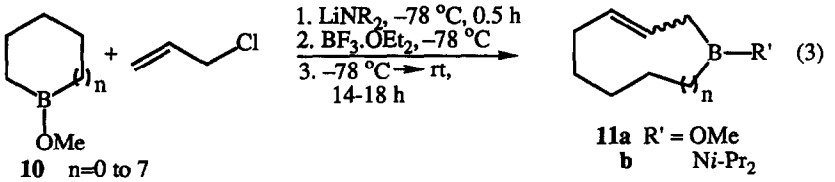
Increasing the bulkiness of R group has a remarkable effect in avoiding the protonolysis. Gratifyingly, a *tert*-alkyl group (R=*t*-Bu, *t*-Am, CEt_3)[7] prevents the undesired ring-opening, but also the rearrangement, **2**→**3**, so that the homologation furnishes the α-vinylborinate **2** in yields of 80-65%.[8] These alkoxy borinates **2b-c** can be thermally rearranged in refluxing toluene (18 h) to the isomeric borinates **3b-c** (*E*:*Z* ≈ 8:2; yield: 90-95%). However, **2d** is resistant to isomerization even after 50 h of reflux. Using this procedure, the *B*-OBu^t boracyclanes **5**[9] can be smoothly homologated to the α-vinylborinates **6** in 75-78% yield, which then undergo the thermal rearrangement[10] to yield **7** (*E*:*Z* ≈ 8:2, except for n=1 when *E*:*Z* ≈ 1:3). The utility of this protocol for the synthesis of the higher membered rings is limited because the rearrangement product contains 15-30% of ring-opened material.[11] However, the homologation reaction product **6** is useful for the preparation of allylic diols **8** (yield: 80-85%) and homoallylic diols **9** (yield: 76-78%) (eq 2).



5 n=1,3,4 **6**

i) $PhCH_3$, reflux, 0.5-24 h; ii) OH^-/H_2O_2; iii) RCHO, 0 °C, 24 h, then OH^-/H_2O_2

We tested the possibility that complexation of the amine would also overcome the ring-opening and would furnish the three-carbon homologated product directly. Indeed, addition of BF_3.EE circumvents the protonolysis. Unfortunately, the lower *B*-methoxyboracyclanes (n=0 to 3) yield a mixture of **11a** (^{11}B NMR δ 52) and the amine-incorporated product **11b** (^{11}B NMR δ 47),[12] when LDA is used as the base (eq 3).



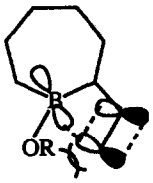
10 n=0 to 7

11a R' = OMe
b N*i*-Pr_2

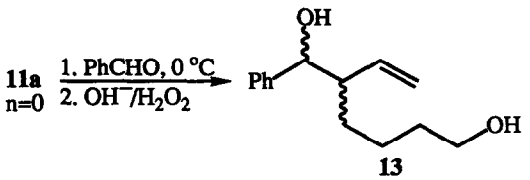
This difficulty was overcome by using lithium 2,2,6,6-tetramethylpiperidide (LiTMP) as base[13] and the desired compound **11a** was obtained exclusively in yields of 75-85%. However, the more economical LDA can be utilized[14] for the preparation of higher membered (less strained) *B*-methoxyboracyclenes (n=4 to 7).

The facile [1,3]-sigmatropic rearrangement of *B*-methoxy substrates and the thermal treatment for the *B*-*t*-butoxy substrates suggest the interaction of OR group in the transition state **12**. It is believed that the OR

group would sterically hinder the overlap of the vacant 'p' orbital at boron with the 'p' orbital of the terminal carbon atom which is necessary for the rearrangement. However, we are not ruling out possible conformational effects in this reaction.



12



13

(*anti* : *syn*, 3:1)

The above protocol provides access to allylic *B*-alkoxyboracyclenes stereoselectively, with predominant *E* or *Z* configuration depending upon the ring-size of the product. Allylboration followed by the oxidation of the 8-membered boracyclene **11a** (n=0; *Z*:*E* ≈ 3:1) gives the *anti* and *syn* diols **13** (ratio 3:1 by ^{1}H NMR analysis). This is in agreement with recent reports that allylic boracyclenes with cisoid configuration furnish the *anti* isomer on allylboration followed by oxidation.[15] The synthetic utility of these *B*-alkoxyboracyclenes for acyclic stereoselection is further enhanced by the ready availability of the precursors for the synthesis of substituted boracycles.[16]

General procedure for the three-carbon ring expansion of boracyclanes. The procedure for the preparation of *B*-methoxy-3-borocene (**11a**, n=0) is representative. To a stirred and cooled (–78 °C) solution of *B*-methoxyborolane (1.96 g, 20 mmol) in THF (20 mL) under argon, was added allyl chloride (2.1 mL, 26 mmol) through a syringe. After 10 min. LiTMP [prepared by reacting 2,2,6,6-tetramethylpiperidine (4.4 mL, 26 mmol) with *n*-BuLi (2.5 M; 10.4 mL, 26 mmol) in THF (25 mL) at 0 °C] was added through a cannula onto the surface of the reaction mixture. It was then stirred for 0.5 h and $BF_3.OEt_2$ (3.2 mL, 26 mmol) was added through a syringe. The reaction mixture was gradually allowed to warm to room temperature over a period of 15 h. After verifying the progress of the reaction by ^{11}B NMR, the solvents were removed *in vacuo*. The residue was extracted with anhydrous pentane (3 x 20 mL) and the pentane extracts were combined in a separate flask (pre-heated and cooled under Ar). Removal of solvent furnished a liquid which was distilled under reduced pressure (75-78 °C/0.3 mm; yield: 2.2 g, 80%). [17]

Allylboration and Oxidation. To a cooled (0 °C) solution of *B*-methoxy-3-borocene (1.38 g, 10 mmol) in anhydrous EE (10 mL) was added PhCHO (1.2 mL, 12 mmol). The progress of the reaction was monitored by ^{11}B NMR following the complete disappearance of the δ 53 peak and the appearance of the δ 29 peak. After stirring at room temperature for 20 h, the solvent was pumped off *in vacuo* and THF (10 mL) was added. Oxidation ($NaOH-H_2O_2$) followed by workup and column chromatography [elution with an ether-hexane mixture (1:1)] furnished the diols **13** (yield: 1.98 g, 90%).

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7. The *B*-alkoxyborinanes were prepared by the alcoholysis of borinane. For the preparation of borinane, see Brown, H.C.; Pai, G.G. *Heterocycles* **1982**, *17*, 77.
8. Increase in steric bulk of the OR group slightly decreases the yield of **2**.
9. *B-t*-Butoxyborolane and *B-t*-butoxyborepane were prepared by procedures similar to that reported for the respective *B*-methoxy compound. See reference 14.
10. With increase in size of the ring to less strained rings, the rearrangement becomes more facile.
11. As revealed by the ^{1}H NMR (300 MHz) and by the GC analysis of the oxidation product. The mechanism for this ring-opening is unclear.
12. Presumably, the *i*-$Pr_2NH.BF_3$ complex dissociates and the free amine attacks the boron in **11a** eliminating the BF_3.MeOH complex. The strain associated with the medium-rings is also a contributing factor.
13. In a separate study (unpublished results) we have shown that LiTMP and $LiNChx_2$ are also effective for the generation of (α-chloroallyl)lithium.
14. In all cases the *E:Z* ratio is ≈ 8:2 (by 300 MHz ^{1}H NMR analysis of the oxidation product), except for n=0 when it is ≈ 1:3. The starting *B*-methoxyboracyclanes **10** (n=3 to 7) were prepared by hydrogenating (using 5% Pd-C/H_2 in a Brown and Brown automatic gasimeter) the corresponding allylic *B*-alkoxy-3-boracyclene **11a** (n=0 to 4). For the preparation of **10** (n=0 to 2), see Brown, H.C.; Negishi, E.I. *Tetrahedron* **1977**, *33*, 2331 and references cited therein.
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17. All new compounds gave satisfactory spectroscopic data.

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