

A New Pathway into [*b*]-Annulated Indole Derivatives through Trialkyl(1-methyl-2-indolyl)borates

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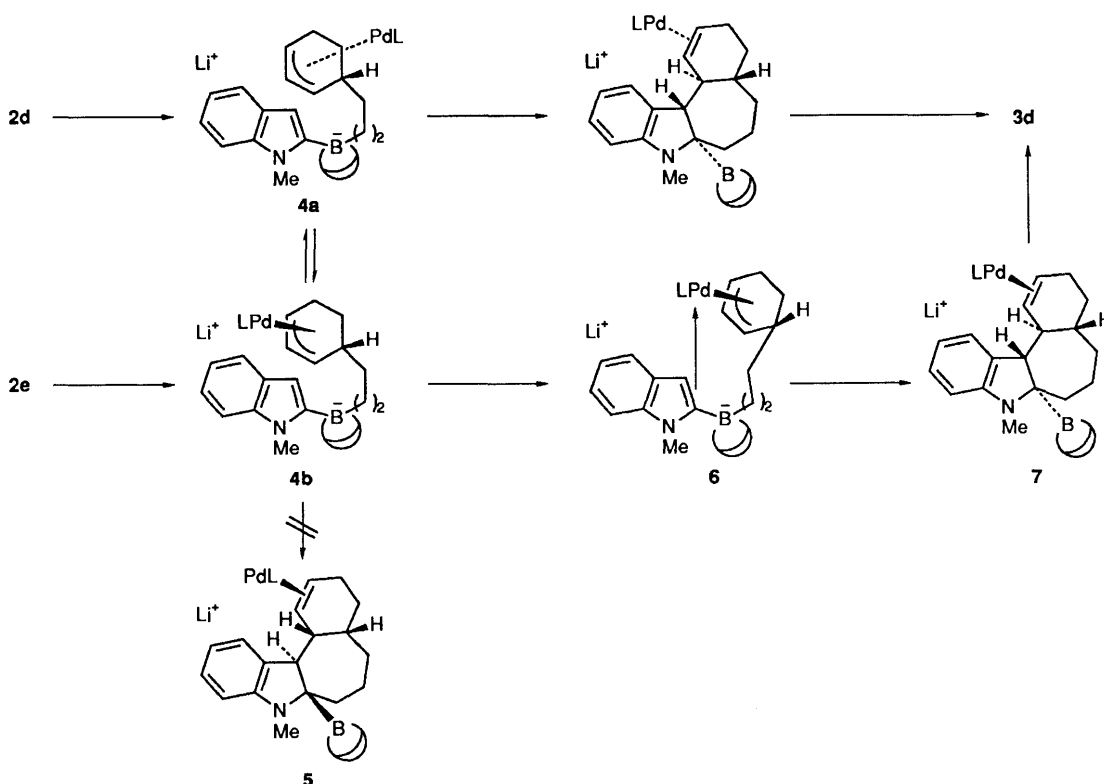
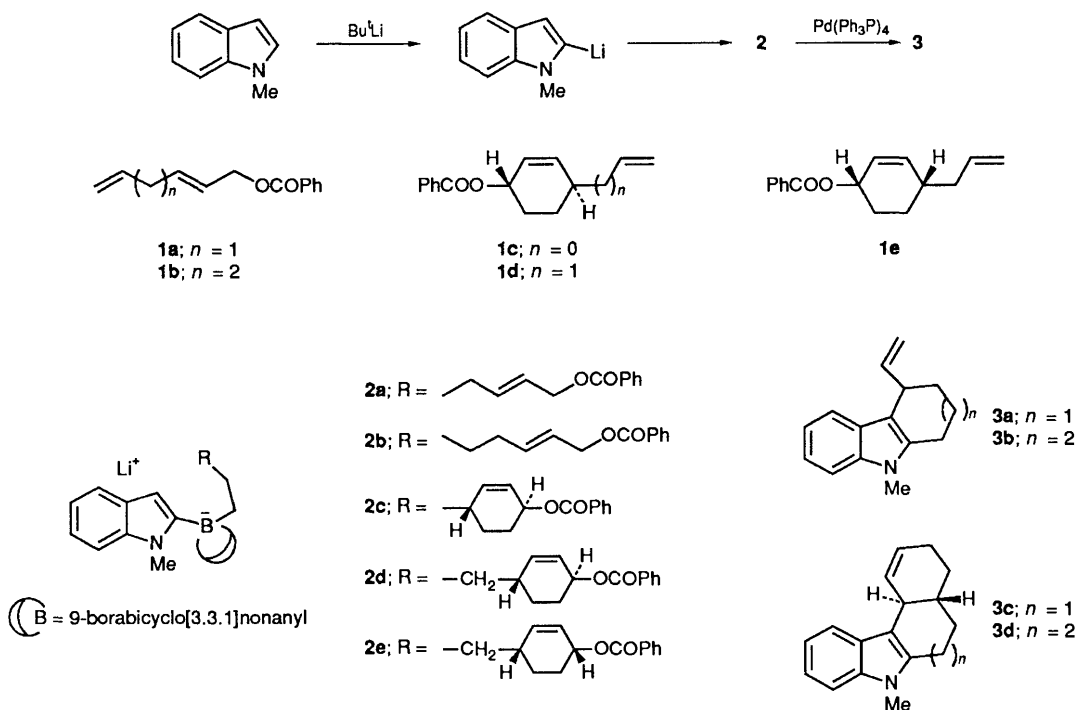
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A new one-pot cyclization procedure for [*b*]-annulated indoles through an intramolecular reaction of trialkyl-(1-methyl-2-indolyl)borates with an allylpalladium complex is reported.

Trialkylalkenylborates are well-defined synthetic intermediates, the synthetic versatilities of which mainly arise from the fact that the electrophile intermolecularly reacts with the alkenylborate accompanied by an intramolecular 1,2-alkyl migration from boron to carbon.¹ However, there has been no report, to our knowledge, on an intramolecular cyclization through the 1,2-alkyl migration promoted by an intramolecular electrophilic reaction of the alkenylborate. In

connection with our efforts directed toward a potential synthetic utilization of trialkylindolylborates,² further studies have revealed that treatment of indolylborates **2** having an allylic ester function in the presence of palladium catalyst allowed the catalysed intramolecular cyclization leading to [*b*]-annulated indole derivatives **3**³ via the known 1,2-alkyl migration path.⁴

The reaction was simply carried out as follows: trialkyl-



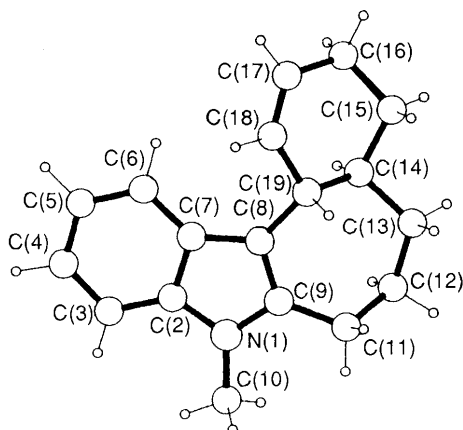
indolylborate **2** was generated *in situ* from hydroboration of diene **1**† with 2-lithio-1-methylindole.‡ The THF solution of borate **2** containing 10 mol% of Pd(Ph₃P)₄ was heated under reflux for 1 to 3 hours to give [b]-annulated indole **3** (Scheme 1).

† Dienes **1** were prepared as follows. **1a** and **b**: from 4-bromobut-1-ene and 5-bromopent-1-ene, respectively according to the modified procedure of the literature.⁸ **1c**: from *cis*-3-acetoxy-6-chlorocyclohexene⁹ according to the sequence (i) vinylmagnesium bromide-CuCN in THF; (ii) 10% NaOH; (iii) PhCOCl-Et₃N in CH₂Cl₂. **1d** and **e**: from 4-allylcyclohex-2-en-1-one¹⁰ according to the sequence (i) NaBH₄-CeCl₃·6H₂O; (ii) PhCOCl-Et₃N in CH₂Cl₂; (iii) separation by column chromatography (SiO₂-hexane: AcOEt 100:1).

‡ Generation of 2-lithio-1-methylindole was performed by treatment of 1-methylindole with Bu^tLi in THF under an argon atmosphere at room temp. for 1 h. Yield of indole **3** was based on 1-methylindole.

Indoles **3a** and **b** were obtained in 56 and 40% yields through borates **2a** and **b**, respectively. An attempted cyclization of borate **2c** provided a very small amount of indole

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Fig. 1 Structure of **3d**

3c (~10% yield) with a variety of unidentified products. Exposure of borate **2d** to the cyclization reaction afforded indole **3d** in 40% yield as a sole product, whose structure was unambiguously established to be that shown in Fig. 1 by single crystal X-ray analysis. § The pathway leading to indole **3d** contains initial generation of allylpalladium complex **4a**, and a subsequent intramolecular nucleophilic attack of indole on the allylpalladium intermediate from the opposite side of the palladium⁵ with a simultaneous 1,2-alkyl migration from boron to carbon⁴ (Scheme 2). Indole **3d** was also formed solely in 32% yield through borate **2e** possessing a *cis*-1,4-disubsti-

§ *Crystal data for 3d*: C₁₈H₂₁N, *M* = 251.373, monoclinic, space group *P*2₁/*a*, *a* = 15.285(2), *b* = 9.680(2), *c* = 14.157(2) Å, β = 138.74(1)°, *U* = 1381.4(5) Å³, *D*_c = 1.209 g cm⁻³, *Z* = 4, graphite-monochromated Cu-Kα radiation, crystal dimensions 0.6 × 0.4 × 0.3 mm³, μ(Cu-Kα) = 5.334 cm⁻¹. AFC-5R (RIGAKU) diffractometer, ω/2θ scan mode with 2θ in the range 0–120°, 2044 unique reflections measured, no absorption correction applied. The structure was solved by direct method (MULTAN) and refined by full-matrix least-squares with all non-hydrogen atoms anisotropic and hydrogen isotropic (8 hydrogens in calculated positions and fixed). The weighting scheme; *w* = 1/σ²(*F*_o). The final *R*(*R*_w) values are 0.0470 (0.0490). Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.

tuted cyclohexene ring under a similar cyclization condition. Inspection of a molecular model showed that serious steric repulsion between indole and cyclohexene rings prevented the cyclization to indole **5** with *cis* ring fusion. Either the isomerization of allylpalladium intermediates **4a** → **b**,⁶ or the coordination of indole to palladium accompanied by a migration of indole from palladium to allylic carbon **4b** → **6** → **7**⁷ could be assumed in the transformation of borate **2e** to indole **3d**.

Although this investigation is still in its preliminary stages, these results show that the use of intramolecular reaction between indolylborate and allylpalladium intermediate with a simultaneous 1,2-alkyl migration from boron to carbon provides a novel pathway into [*b*]-annulated indole derivatives. Further work on the present cyclization reaction is in progress.

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