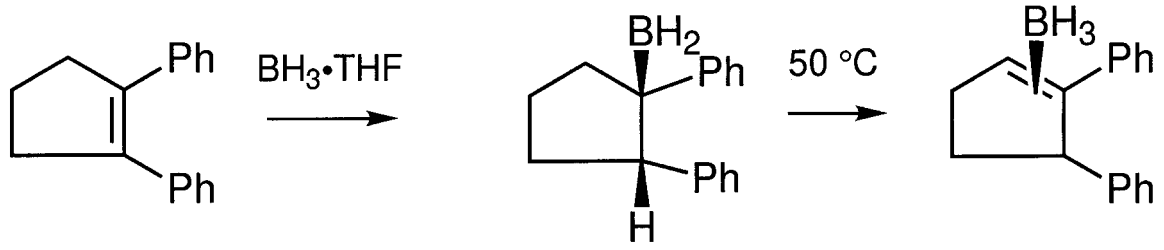
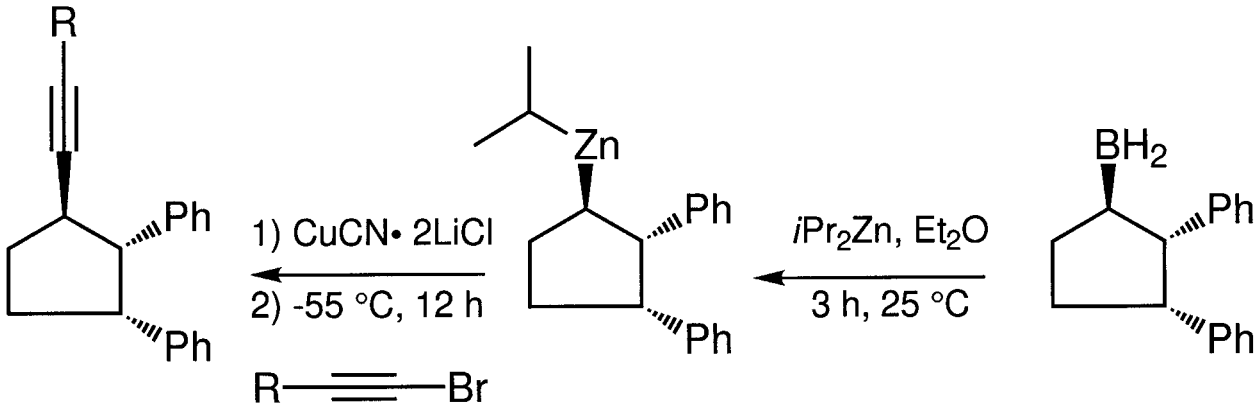


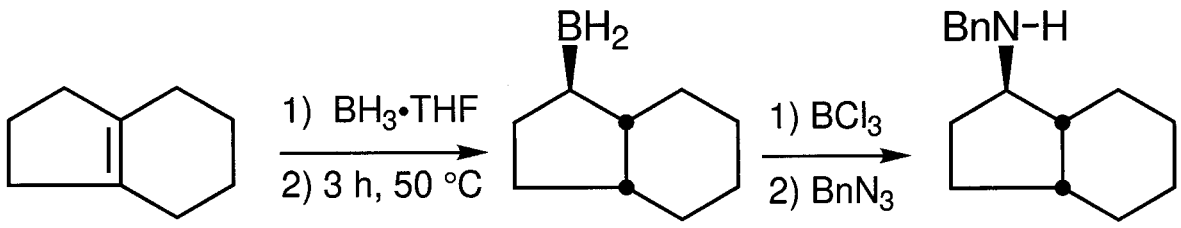
The hydroboration of tetrasubstituted cyclic alkenes produces tertiary organoboranes, which undergo a stereoselective rearrangement to furnish organoboranes bearing three adjacent stereocenters. These species can be converted into a variety of products.



1 diastereoisomer

With bicyclic systems, a preferential migration in the direction of the five-membered ring is observed.

Further details are given on the following pages.



69 %; *dr* > 99.5 %

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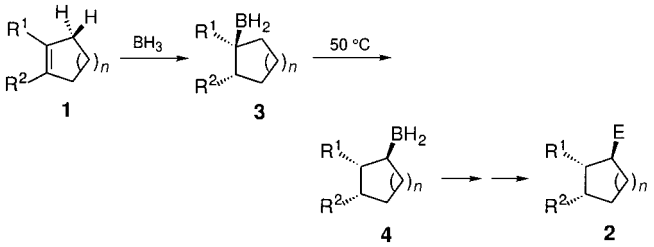
Stereoselective Allylic C–H Activation with Tertiary Alkylboranes: A New Method for Preparing Cycloalkyl Derivatives with Three Adjacent Stereocenters**

Frédéric Lhermitte and Paul Knochel*

Dedicated to Professor Gernot Boche on the occasion of his 60th birthday

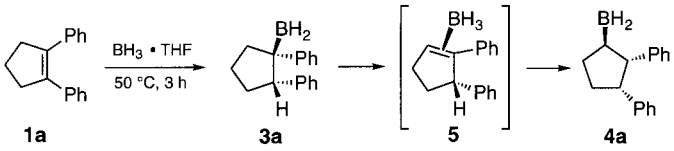
The functionalization of unreactive carbon–hydrogen bonds is an active field of investigation.[1] Transition metal complexes have been used with great success for selectively activating C–H bonds,[1, 2] and a few examples involving main group organometallic compounds have been described.[3] Herein, we report a highly stereoselective C–H activation of an allylic position that allows the construction of three adjacent stereocarbon centers by making use of a rearrangement of a tertiary alkylborane. Whereas most organoboranes undergo rearrangements at elevated temperature,[4] it was noticed by Rickborn and Wood[5] and Field and Galagher[6] that cyclic tetrasubstituted alkenes undergo such a dyotropic rearrangement[7] under much milder conditions. We found that this approach allows a highly stereoselective conversion of various cyclic or acyclic tetrasubstituted alkenes of type **1** into polyfunctional products of type **2** in a one-pot reaction via the intermediate organoboranes **3** and **4** (Scheme 1).



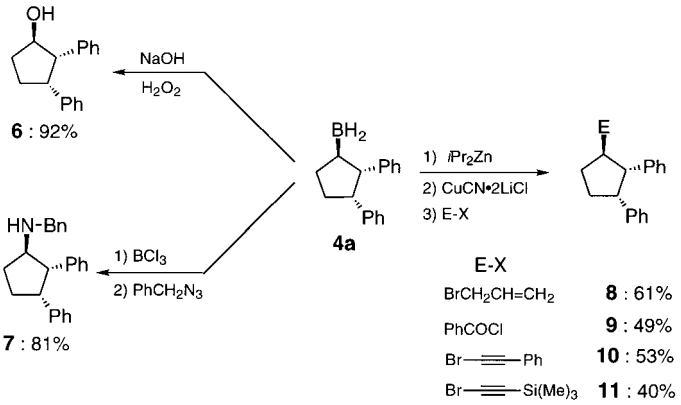
Scheme 1. Synthesis of **2** from **1** by hydroboration (→**3**) and migration (→**4**). $n = 1, 2$.

Thus, 1,2-diphenylcyclopentene (**1a**) was smoothly hydroborated with $BH_3 \cdot THF$ (THF, 50 °C, 3 h) to provide the tertiary alkylborane **3a**, which undergoes a stereoselective *syn* migration leading to the less sterically hindered secondary organoborane **4a** (Scheme 2). The high stereochemical control is explained by assuming a dehydroboration of **3a** to form the alkene–borane complex **5**, which undergoes a second hydroboration. Here, there can be no dissociation from the alkene, as this would result in a decrease in stereoselectivity.[5, 6]

The alkylborane **4a** was trapped with several electrophiles with retention of stereochemistry (Scheme 3). Thus, oxidation



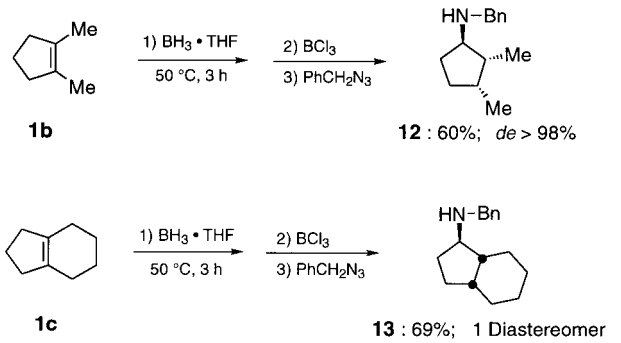
Scheme 2. Synthesis of **4a**.



Scheme 3. Synthesis of **6**–**11**.

of **4a** with 30% H_2O_2 affords the cyclopentanol **6** in 92% overall yield as a single stereoisomer. Treatment of **4a** with boron trichloride followed by benzyl azide[8] (25 °C, 1 h) provides the amine **7** as one stereoisomer in 81% overall yield. Transmetalation of **4a** to the corresponding organozinc compound[9] by treatment with iPr_2Zn (2 equiv) and subsequent transformation to the zinc–copper reagent[10] by addition of $CuCN \cdot 2\,LiCl$ furnishes—after reaction with electrophiles such as allyl bromide, benzoyl chloride, 2-phenylethynyl bromide, or 1-bromo-2-trimethylsilylacetylene—the expected products **8**–**11** with diastereomeric excesses of greater than 97% and in 40–61% overall yield.

Extention of this rearrangement to other tetrasubstituted alkenes has been examined (Scheme 4). Both 1,2-dimethylcyclopentene (**1b**) and the bicyclic alkene **1c** undergo the



Scheme 4. Synthesis of **12** and **13**.

stereoselective rearrangement. Amination of **1b** and **1c** (1. $BH_3 \cdot THF$, 50 °C, 3 h; 2. BCl_3, 25 °C, 3 h; 3. $PhCH_2N_3$, 25 °C, 1 h)[8] led to the desired stereoisomers **12** and **13** in 60–69% overall yield.[11]

Interestingly, in the case of **1c** the migration takes place almost exclusively in the direction of the five-membered ring.

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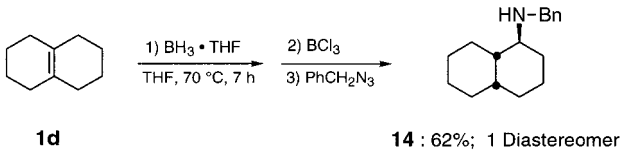
This may be due to the proper alignment of the adjacent C–H bond with the C–B bond in the five-membered ring facilitating the dehydroboration. In a six-membered ring, there would be an angle of about 60° between the C–H and C–B bonds; this alignment would require a higher energy of activation.

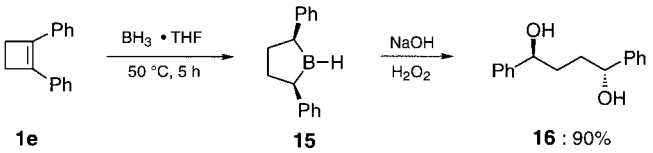
With bicyclo[4.4.0]dec-1(6)-ene (**1d**) the hydroboration must be carried out, as expected, at 70 °C in refluxing THF (Scheme 5). In this case also, a highly stereoselective migration takes place despite the elevated temperature. After



Scheme 5. Synthesis of **14**.

amination (1. $BH_3 \cdot THF$, 70 °C, 7 h; 2. BCl_3, 25 °C, 3 h; 3. $PhCH_2N_3$, 25 °C, 1 h)[8] the bicyclic amine **14** was obtained in 62 % yield as a single stereoisomer.

A novel stereoselective borane rearrangement was found upon use of 1,2-diphenylcyclobut-1-ene (**1e**; Scheme 6). After initial hydroboration, cleavage of the cyclobutene ring



Scheme 6. Synthesis of **16**.

occured to provide the intermediate boracyclopentane **15**. After oxidation with H_2O_2 the *meso*-diol **16** was isolated in 90 % yield as a pure diastereoisomer.

In summary, we have shown that the migration of tertiary boranes constitutes a novel stereoselective method for preparing cyclic and bicyclic rings. The rection corresponds formally to an stereoselective activation of allylic C–H bonds.

Experiment Section

Typical procedure for the amination: Preparation of (1*R**,2*R**,3*R**)-*N*-benzyl-2,3-dimethylcyclopentylamine (**12**): A $BH_3 \cdot THF$ solution (3 mL, 1.5 equiv, 3 mmol, 1.0 M) was slowly added to 1,2-dimethylcyclopentene (**1b**; 192 mg, 2 mmol) in THF (10 mL) at 25 °C. After 10 min the resulting solution was heated at 50 °C for 3 h. The solvent and excess of borane were removed under vacuum, and the residue was diluted with CH_2Cl_2 (10 mL), treated at 0 °C with a solution of BCl_3 (8 mL, 4 equiv, 8 mmol, 1.0 M) in CH_2Cl_2, and stirred for 3 h at 25 °C. After removal of the solvent and excess of BCl_3 under vacuum, the residue was diluted with CH_2Cl_2 (10 mL) and treated at 0 °C with a solution of benzyl azide (2.4 mL, 1.2 equiv, 1.0 M) in CH_2Cl_2. After 1 h at 25 °C the reaction was quenched with aq NaOH (10 mL, 3.0 M), extracted with ether, and dried ($MgSO_4$). The crude residue was purified as the hydrochloride by addition of a solution of dry HCl in ether. Analytically pure **12** · HCl was obtained after filtration (287 mg, 1.2 mmol, 60 % yield).

Typical procedure for the allylation: Preparation of (1*S**,2*S**,3*S**)-1-allyl-2,3-diphenylcyclopentane (**8**): A $BH_3 \cdot THF$ solution (3 mL, 1.5 equiv, 3 mmol, 1.0 M) was slowly added to 1,2-diphenylcyclopentene (**1a**; 440 mg, 2 mmol) in THF (10 mL) at 25 °C. After 10 min the resulting solution was heated at 50 °C for 3 h. The solvent and excess borane were removed under vacuum, and the residue was treated with a solution of iPr_2Zn (0.8 mL, 2 equiv, 4 mmol, 5.0 M) in ether at 25 °C for 4 h. After removal of the solvent and excess of iPr_2Zn under vacuum, the residue was diluted with THF (10 mL). The black precipitate of zinc was removed by filtration, and the filtrate was slowly treated at −90 °C with a solution of $CuCN \cdot 2LiCl$ in THF (0.4 mL, 0.2 equiv, 1.0 M) and after 15 min with allyl bromide (6 mL, 3 equiv, 6 mmol, 1.0 M) in THF. The reaction was allowed to warm up to 25 °C and was quenched after 1 h with aq HCl (10 mL, 3.0 M) and extracted with ether. The crude product obtained after evaporation of the solvent was purified by chromatography (pentane) to provide analytically pure **8** (320 mg, 1.2 mmol, 61 % yield).

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[1] J. C. W. Lohrenz, H. Jacobsen, *Angew. Chem.* **1996**, *108*, 1403; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1305, and references therein.
[2] B. A. Arndtsen, R. G. Bergmann, *Science* **1995**, *270*, 1970; L. D. Field, A. V. George, B. A. Messerle, *J. Chem. Soc. Chem. Commun.* **1991**, 1339; N. A. Williams, Y. Uchimaru, M. Tanaka, *J. Chem. Soc. Chem. Commun.* **1995**, 1129; F. Kakiuchi, S. Sekine, Y. Tanaka, A. Kamatani, M. Sonoda, N. Chatani, S. Murai, *Bull. Chem. Soc. Jpn.* **1995**, *68*, 62; Y.-G. Lim, Y. H. Kim, J.-B. Kang, *J. Chem. Soc. Chem. Commun.* **1994**, 2267; P. J. Alaimo, B. A. Arndtsen, R. G. Bergman, *J. Am. Chem. Soc.* **1997**, *119*, 5269.
[3] L. Weber in *Advances in Organometallic Chemistry*, *Vol. 41* (Eds.: F. G. A. Stone, R. West), Academic Press, New York, **1997**, pp. 1–125.
[4] R. Köster, W. Siebert, *Methoden Org. Chem. (Houben-Weyl), 4. ed., 1952–, Vol. 13, part 3a*, **1982**, pp. 1–908.
[5] S. E. Wood, B. Rickborn, *J. Org. Chem*. **1983**, *48*, 555.
[6] L. D. Field, S. P. Galagher, *Tetrahedron Lett.* **1985**, *26*, 6125.
[7] M. T. Reetz in *Advances in Organometallic Chemistry, Vol. 16* (Eds.: F. G. A. Stone, R. West), Academic Press, New York, **1977**, pp. 1–30.
[8] A. Suzuki, S. Ono, H. C. Brown, M. M. Midland, *J. Am. Chem. Soc.* **1971**, *93*, 4329; P.-Y. Chavant, F. Lhermitte, M. Vaultier, *Synlett* **1993**, 519.
[9] L. Micouin, M. Oestreich, P. Knochel, *Angew. Chem.* **1997**, *109*, 274; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 245; C. Darcel. F. Flachsmann, P. Knochel, *Chem. Commun.* **1998**, 205.
[10] P. Knochel, R. Singer, *Chem. Rev.* **1993**, *93*, 2117.
[11] The hydroboration of **1b** provides, after oxidation with 30 % H_2O_2, the expected alcohol (80 %) accompanied by the epimer at the hydroxyl position (1–2 %) as well as tertiary alcohol (18 %) that did not undergo migration. However, by the amination procedure, only the product resulting from the major isomer could be detected. The boron–zinc exchange of **4b** obtained by the hydroboration of **1b** provides, after copper-catalyzed allylation, two epimeric allylated products in the ratio 92:8 and in 51 % yield upond isolation. This shows that in this case the secondary cyclopentylzinc intermediate is less configurationally stable.[9]

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