A New Highly Stereoselective Rearrangement of Acyclic Tertiary Organoboranes: An Example of Highly Stereoselective Remote C−H Activation

Hamid Laaziri, Lars O. Bromm, Frédéric Lhermitte, Ruth M. Gschwind, and Paul Knochel*

Fachbereich Chemie der Philipps-Universität Marburg Hans-Meerwein Strasse, D-35032 Marburg, Germany

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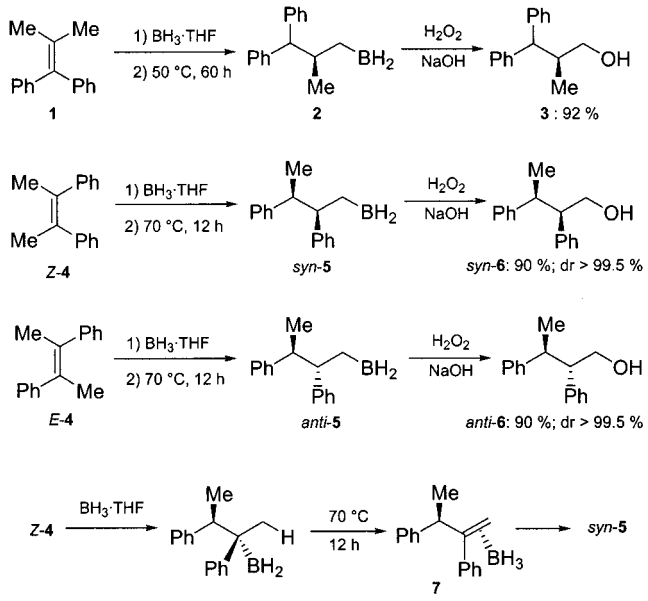
The activation of allylic C−H bonds is an important reaction, which has attracted much attention. Most results have been obtained with cyclic systems.[1] Recently, we have shown that an efficient allylic C−H activation can be formally realized by the hydroboration of tetrasubstituted cycloalkenes with BH_3 in THF followed by a smooth thermal rearrangement.[2,3] We are pleased to report that this rearrangement can be performed with acyclic tetrasubstituted olefins and that it is opening a new way for the acyclic control of two adjacent carbon centers. In the course of this study, we have also found a new remote C−H activation allowing a unique functionalization at a carbon center in position 6.

Preliminary results have shown that the hydroboration of 1,1-diphenyl-2-methylpropene (**1**) with BH_3 in THF furnishes an intermediate tertiary organoborane, which rearranges at 50 °C within 60 h, providing the primary organoborane **2**. After oxidative workup (30% H_2O_2, NaOH), 3,3-diphenyl-2-methylpropanol (**3**) can be isolated in 92% yield showing that mild thermic conditions are sufficient to induce a complete rearrangement (Scheme 1).

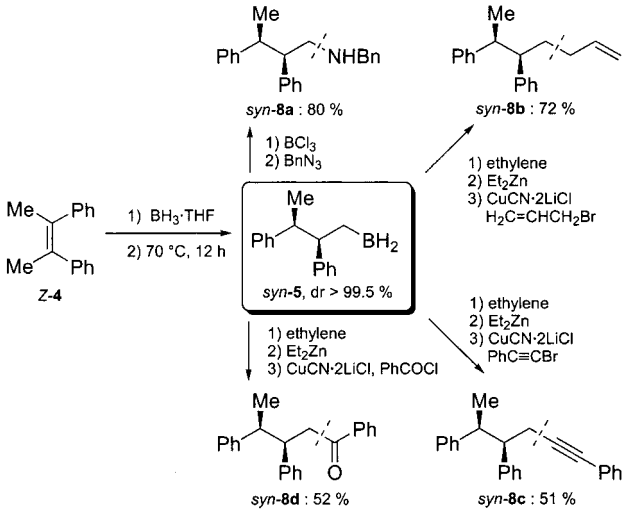
Next, we have examined the hydroboration of *Z*- and *E*-2,3-dimethylstilbene **(4)**.[4] The treatment of *E*-**4** and *Z*-**4** with BH_3·THF and subsequent heating at 70 °C for 12 h furnishes stereoselectively the *syn*- and *anti*-organoboranes **5**, which after oxidative workup provide the corresponding alcohols *syn*-**6** and *anti*-**6** in 90% yield and dr > 99.5% (Scheme 1). This high diastereoselectivity can be explained by assuming a dehydroboration−rehydroboration mechanism, in which the intermediate borane−olefin complex of type **7** never dissociates (Scheme 1). The resulting organoboranes *syn*-**5** and *anti*-**5** can be converted to various organic products (Scheme 2).

Thus, the reaction of *syn*-**5** with BCl_3 (4 equiv) in CH_2Cl_2 followed by the reaction with benzyl azide[5] furnishes the amine *syn*-**8a** in 80% yield.[6] The organoborane *syn*-**5** is converted to the corresponding diethylborane derivative by bubbling ethylene (excess) through the reaction mixture. This compound undergoes a smooth transmetalation[7] to the corresponding zinc derivative by reaction with diethylzinc (10 equiv, 0 °C, 3 h). This mixed diorganozinc can be further converted to the corresponding zinc−copper derivative by the addition of CuCN·2LiCl[8] and reacted with allyl bromide, leading to the desired allylated product *syn*-**8b** in 72% yield.[9] Its reaction with 2-bromo-1-phenylacetylene

Scheme 1



Scheme 2



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(6) Typical procedure for the amination. To a solution of (*Z*)-2,3-diphenyl-2-butene (*Z*-**4**) (230 mg, 1.1 mmol) in THF (5 mL) at room temperature was added BH_3·THF (2.2 mL, 2.2 mmol, 1 M). The resulting solution was heated at reflux for 16 h. After cooling to room temperature, the solvent and excess of borane were removed under vacuum (rt, 0.1 mmHg, 45 min). The residue was dissolved in CH_2Cl_2 (5 mL). BCl_3 (4.4 mL, 4.4 mmol, 1 M) was added at 0 °C. The mixture was warmed to room temperature and was stirred for 2 h. The solvent and excess of BCl_3 were removed under vacuum (rt, 0.1 mmHg, 45 min) The resulting residue was dissolved in CH_2Cl_2 (5 mL), and benzyl azide (160 mg, 1.2 equiv) was added at 0 °C. The mixture was warmed to room temperature and was stirred for 1 h. The resulting mixture was quenched with an aqueous 3 M NaOH solution and was extracted with Et_2O. The combined organic layers were dried ($MgSO_4$) and concentrated. Flash-chromatographical purification of the residue (*n*-pentane: ether 7:3) afforded the desired product *syn*-**8a** (280 mg, 80%) as a clear oil.

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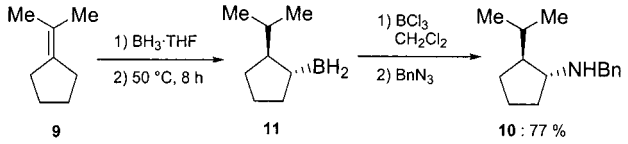
Scheme 3



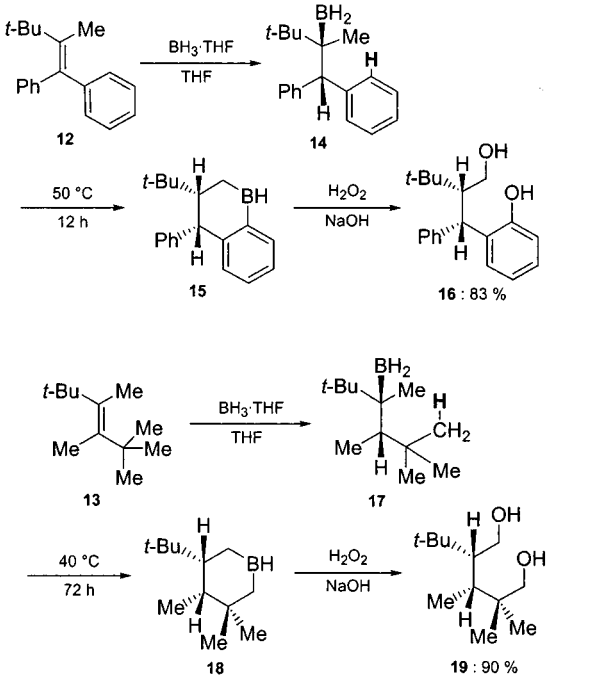
provides the cross-coupling product *syn*-**8c** in 51% yield, and its benzoylation with PhCOCl furnishes as sole product the diastereomerically pure ketone *syn*-**8d** in 52% yield. Similarly, the organoborane *anti*-**5** furnished under the same reaction conditions *anti*-**8a** (78%), *anti*-**8b** (68%), and *anti*-**8d** (52%).

By using exocyclic tetrasubstituted olefins such as the cyclopentene derivative **9** the migration in the five-membered ring is the only observed reaction pathway leading exclusively to the *trans*-benzylamine **10** after treatment of the intermediate organoborane **11** with BCl_3 followed by benzyl azide (Scheme 3).[5,10]

Finally, we have observed a remarkable intramolecular C−H activation,[11] which occurred with the sterically hindered tetrasubstituted olefins **12** and **13**. The initial hydroboration of **12** is leading to **14**. Then, a diastereoselective insertion into the *ortho*-C−H bond of a phenyl ring occurs at 50 °C, affording the borane **15**, which is oxidized with H_2O_2/NaOH providing the hydroxyphenol **16** as only one diastereoisomer.[12]

Similarly, the *tert*-butyl-substituted olefin **13** furnishes after initial hydroboration the organoborane **17**, which gives the six-membered intermediate organoborane via regio- and stereoselective C−H insertion reaction (40 °C, 72 h). After oxidation, the diol **19** is obtained in 90% yield as only one diastereoisomer (Scheme 4).[13]

Scheme 4



In summary, we have shown that the thermic rearrangement of tertiary organoboranes readily obtained by the hydroboration of tetrasubstituted olefins affords a variety of primary organoboranes corresponding formally to an allylic functionalization of the starting olefin. The high stereoselectivity of the migration should make this reaction very useful for the stereoselective synthesis of open-chain products. Applications of these organoborane rearrangements are currently being actively investigated in our laboratories.

Acknowledgment. This work was supported by the Deutsche Forschungsgemeinschaft (SFB 260, Leibniz program). We thank the BASF AG (Ludwigshafen), Chemetall (Frankfurt), and Degussa AG (Hanau) for the generous gift of chemicals.

Supporting Information Available: Spectral data for compounds **3**, *syn*-**6**, *anti*-**6**, **8**, **10**, **16**, **19**, and **A**[12] (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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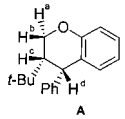
(9) Typical procedure for a transmetalation to the zinc organometallic and allylation. To a solution of (*Z*)-1,3-diphenyl-2-butene (*Z*-**4**) (416 mg, 2.0 mmol) in THF (10 mL) at room temperature was added BH_3·THF (4 mL, 4 mmol, 1 M). The resulting solution was heated at reflux for 16 h. After cooling to room temperature, the solvent and excess of borane were removed under vacuum (rt, 0.1 mmHg, 1 h). The residue was taken up in THF (10 mL) and treated with ethylene for 0.5 h. After the solvent was removed under vacuum, Et_2Zn (1 mL) was added at 0 °C, and stirring was continued for 3 h. The excess of Et_2Zn was removed under vacuum, and the residue was diluted with THF (10 mL). The resulting mixture was cooled to −78 °C, and a solution of CuCN·2LiCl (0.4 mL, 0.2 equiv, 1 M) was slowly added. The mixture was allowed to warm to −60 °C, and allyl bromide (2 mL) was added. The resulting mixture was warmed to room temperature, stirred for 1 h, and quenched with a 5% aqueous HCl solution. After extraction with Et_2O, the combined organic phases were dried ($MgSO_4$), and the solvents were evaporated. Flash-chromatographical purification of the residue (*n*-pentane) afforded the desired product *syn*-**8b** (361 mg, 72%) as a clear oil.

(10) The relative stereochemistry of **11** and **10** has been proven by performing an oxidation (H_2O_2/NaOH) of **11**, leading to the corresponding *trans*-2-isopropylcyclopentanol as shown by comparison with the literature spectra: Schneider, H.-J.; Nguyen-Ba, N.; Thomas, F. *Tetrahedron* **1982**, *38*, 2327.

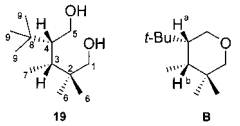
(11) Some remote C−H activations of organoboranes have been described: (a) Köster, R.; Larbig, W.; Rotermund, G. W. *Liebigs Ann.* **1965**, *682*, 21. (b) Köster, R.; Rotermund, G. *Angew. Chem.* **1960**, *72*, 563. (c) Köster, R.; Benedikt, G.; Fenzl, W.; Reinert, K. *Liebigs Ann.* **1967**, *702*, 197.

(12) The relative stereochemistry of **16** is obtained by converting it to the cyclic ether **A** (1.3 equiv DEAD, 1.0 equiv Ph_3P, THF, 12 h, rt, 79%). The observed long-range coupling constant $^4J(H^b,H^d) = 1.3$ Hz shows a W conformation of H^b and H^d, the large coupling constant $^3J = (H^a,H^c) = 11.2$ Hz, the diaxial combination of H^a and H^c.



A

(13) The regioselectivity of the C−H activation has been determined by NMR analysis. The complete proton and carbon assignment was done by a combination of COSY, HMQC, and HMBC spectra (Croasmun, W. R.; Carlson, R. M. K. *Two-Dimensional NMR Spectroscopy*; VCH Publishers Inc.: New York, 1994). The HMBC experiment can be used to connect proton spin systems that are interrupted by nonprotonated atoms. Owing to the observed HMBC cross-peaks (e.g., H^9/C^4, H^3/C^1, H^4/C^9, and H^3/C^6) the linkage positions of the substituents of **19** could be identified. Again, the relative stereochemistry of **19** is obtained after conversion to the cyclic ether **B** (1.3 equiv DEAD, 1.0 equiv Ph_3P, THF, 3 h, rt, 75%). The absence of an observable coupling constant between H^a and H^b indicates a very rigid conformation in the substituted part of **B** with an axial/equatorial combination of H^a/H^b.



19 B