Modular approach to trisubstituted alkenes

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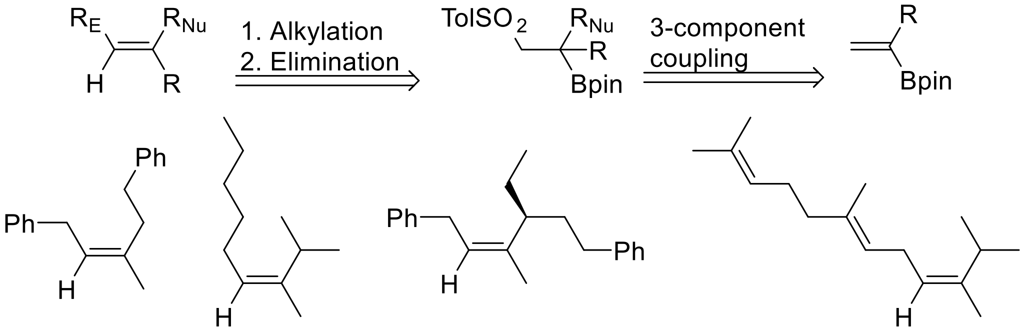
In this work, we present a new method for the preparation of trisubstituted alkenes. Starting from vinyl boronic acid pinacol esters various three-component coupling products[1] were prepared, which were used in a specially developed mild protocol to achieve alkylation. Previously, it has be reported that boronic ester can be employed as precursors in olefination reactions[2]. Similarly in this approach, the alkylation products were converted to the trisubstituted alkenes by a strictly *anti* elimination reaction. With the developed protocols, a wide range of electrophiles could be used for alkylation with yields of 40-80% and a dr of up to 1:9. The subsequent olefination reaction proceeded smoothly by addition of TBAF to yield the trisubstituted olefins in yields of 80% to quantitative.



50%
E/Z 35:65

47%
E/Z 15:85

45%
E/Z 45:55
%ee 99% & 96%

52%
E/Z 2:98
(only major dia used for elimination)

In addition to the wide variety of electrophiles, chiral nucleophiles in the form of enantioenriched boronic acid esters could also be used in the three-component coupling, whose chirality was preserved until olefination and was thus not altered. In addition to the stepwise protocol, a one-pot process was also developed that achieved the same yields but eliminated the time-consuming and tedious purification steps. As an application, the protocol has been successfully used for late-stage functionalization of natural products.

(1) Tappin, N. D. C.; Renaud, P. Radical Reactions of Boron-Ate Complexes Promoting a 1,2-Metallate Rearrangement. *CHIMIA International Journal for Chemistry* **2020**, *74* (1), 33–38. https://doi.org/10.2533/chimia.2020.33.

(2) Armstrong, R.; Aggarwal, V. 50 Years of Zweifel Olefination: A Transition-Metal-Free Coupling. *Synthesis* **2017**, *49* (15), 3323–3336. https://doi.org/10.1055/s-0036-1589046.