

STEREOSPECIFIC OLEFIN SYNTHESIS VIA BORONIC ESTERS.
STUDIES RELATED TO PROSTAGLANDIN SYNTHESIS

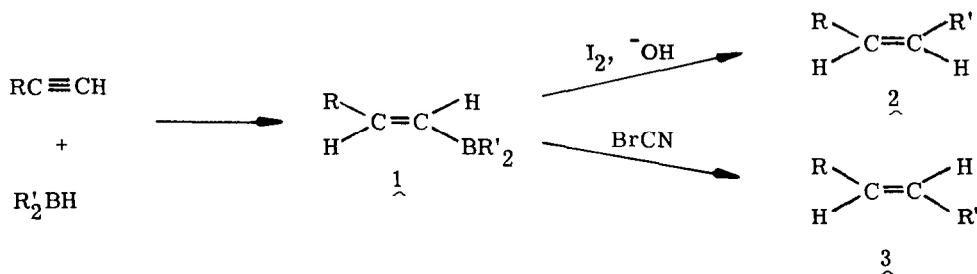
D. A. Evans,¹ R. C. Thomas, and J. A. Walker

Contribution No. 5268 from the Laboratories of Chemistry
California Institute of Technology, Pasadena, California 91125

(Received in USA 13 February 1976; received in UK for publication 23 March 1976)

The utility of organoboranes in stereospecific olefin synthesis is now well recognized.² Of particular interest to us for synthetic studies currently in progress has been the boron-mediated cross-coupling reactions shown below (Scheme I) which result in the stereospecific

Scheme I

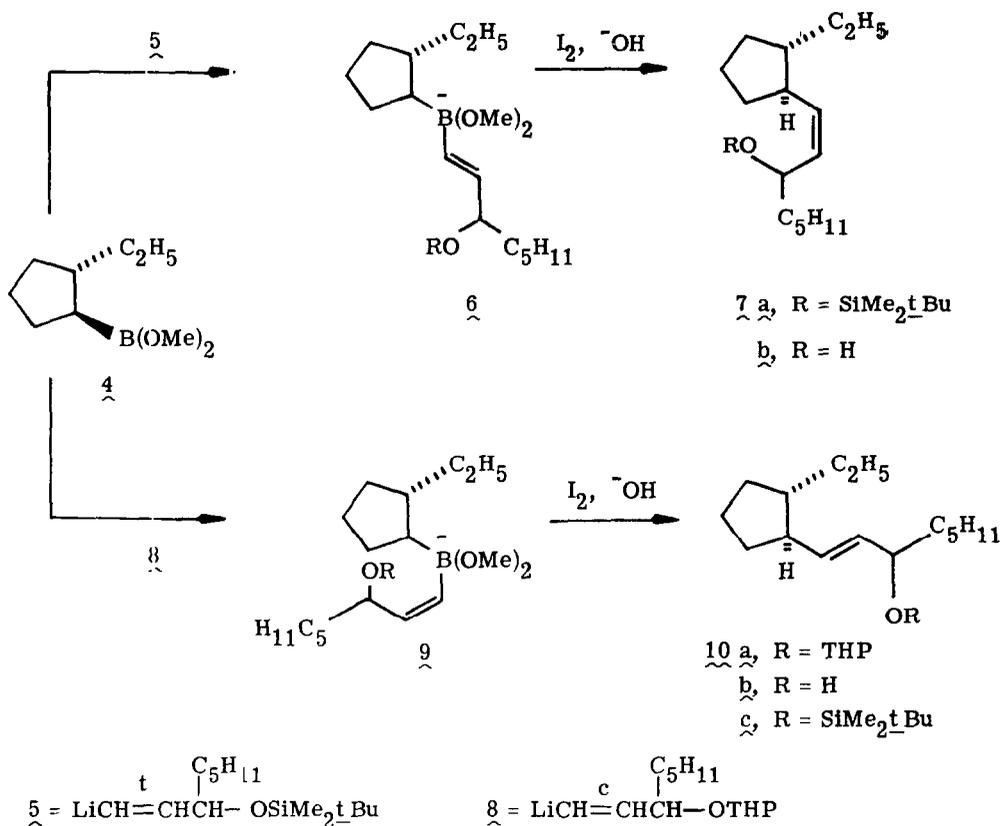


synthesis of either E or Z-1,2-disubstituted olefins.³ Although the decomposition of vinylborane 1 with the indicated reagents affords olefins 2 and 3 with ca 95% stereospecificity, the overall reaction sequence is flawed by the fact that only one of the carbon ligands attached to boron is utilized in the cross-coupling process. One solution to this general problem has been to employ "mixed" dialkylboranes where one of the boron-bound carbon ligands (e.g., thexyl) demonstrates a low migratory aptitude.⁴ However, it is now becoming clear that the definition of a hierarchy of migratory aptitudes is both reaction specific and substrate dependent.⁵ A case in point is the observation that thexyl and alkenyl ligands show comparable migratory capabilities in the vinylborane iodination process 1 → 2.^{5a} This present study (vide infra) provides further support to the preceding contention.

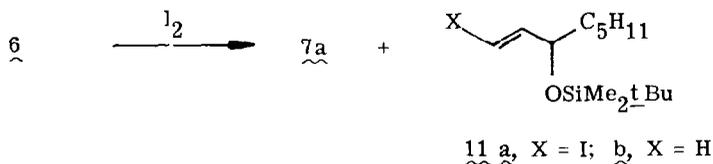
In conjunction with our interest in developing efficient stereospecific olefination reactions for projected prostaglandin syntheses, we have investigated the boron-mediated cross-coupling process outlined in Scheme II. Since oxygen ligands do not compete with carbon in the

rearrangements of boron π -complexes,⁶ we were interested in ascertaining whether intermediates 6 and 9 could be induced to couple to give the Z and E-olefins 7 and 10 respectively.⁷ Accordingly, boronic ester 4 (bp, 40°/1 mm) was prepared in direct analogy to the procedure reported by Brown,⁸ while the E and Z-vinyl lithium reagents 5 and 8 were prepared from the corresponding vinyl iodide:^{9,10} via metal-halogen exchange (s-butyllithium, -78°).

Scheme II



Addition of boronic ester 4 (1 equiv) to a solution of 5 (1 equiv) in tetrahydrofuran (THF) at -45° followed by the addition of iodine (1 equiv) and subsequent stirring at 25° (3 hr) afforded the desired Z-olefin 7a (22%) as well as vinyl iodide 11a (22%) and olefin 11b (11%). Control



olefination sequence (Scheme II) which afforded 7a in 75% yield. Furthermore, attempts to obtain the E-olefin 10c via acetylene monohydroboration with either 12a or 12b followed by cyanohalogenation^{3b} (c.f. 1 → 3) failed to yield any of the desired product. The major olefinic material obtained in this reaction showed nitrile incorporation and loss of silyl ether

To date, the use of boronic esters in carbon-carbon bond constructions has been quite limited.^{6,7} However, these organofunctional species offer a general solution to some of the problems of stoichiometry in the organoborane area of organic synthesis. Applications of this versatile olefin synthesis will be reported in due course.

Acknowledgement: Support from the National Science Foundation, the National Institutes of Health and the Upjohn Company are gratefully acknowledged.

REFERENCES

1. Camille and Henry Dreyfus Teacher-Scholar recipient, 1971-76.
2. G.M.L. Cragg, "Organoboranes in Organic Synthesis," Marcel Dekker, Inc., New York, N.Y., 1973.
3. (a) G. Zweifel, R.P. Fisher, J.T. Snow, and C.C. Whitney, J. Amer. Chem. Soc., 93, 6309 (1971); (b) G. Zweifel, R.P. Fisher, J.T. Snow, and C.C. Whitney, ibid., 94, 6560 (1972).
4. E. Negishi and H.C. Brown, Synthesis, 77 (1974).
5. (a) G. Zweifel, N.L. Polston, and C.C. Whitney, J. Amer. Chem. Soc., 90, 6243 (1968); (b) N. Miyaara, T. Yoshinari, M. Itoh, and A. Suzuki, Tetrahedron Lett., 2961 (1974); (c) M. Naruse, K. Utimoto, and N. Nozaki, Tetrahedron, 30, 2159 (1974).
6. D.S. Matteson and R.W.H. Mah, J. Org. Chem., 28, 2171 (1963).
7. D.S. Matteson has briefly mentioned a similar cross-coupling process; c.f., Synthesis, 147 (1975).
8. H.C. Brown, E. Negishi, and J. Katz, J. Amer. Chem. Soc., 97, 2791 (1975).
9. E.J. Corey, D.J. Beames, ibid., 94, 7210 (1972).
10. A.F. Kluge, K.G. Untch, and J.H. Fried, ibid., 94, 9256 (1972); 8 must be prepared in ether or hexane.
11. Satisfactory spectral and elemental analyses have been obtained on all new compounds reported herein.
12. Yields determined by glc using internal standards.
13. Both 7a and 10a were obtained as a mixture of alcohol-protected diastereoisomers.