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The Application of a Shapiro Reaction - Suzuki Coupling Sequence to the Stereoselective Synthesis of *E*-Trisubstituted Olefins

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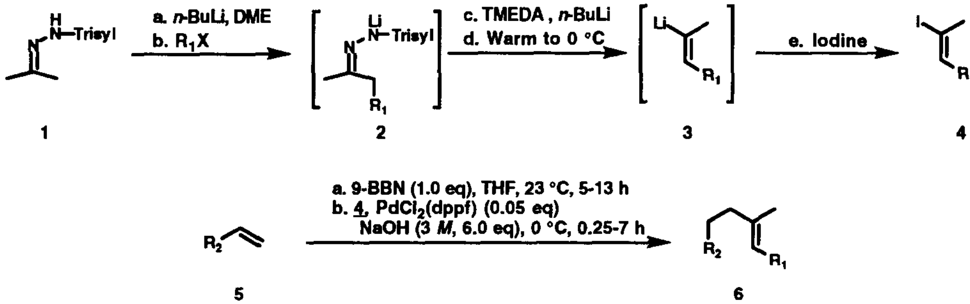
Abstract: *A three-component coupling process is described for the rapid, stereoselective synthesis of a wide variety of E-trisubstituted olefins.* © 1997 Elsevier Science Ltd.

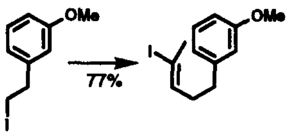
The preceding paper describes a modification of the Shapiro reaction which resulted in a versatile and stereoselective three-component coupling to produce *E*-trisubstituted olefins.[1] This methodology is well suited to the construction of a variety of chiral polyolefins and therefore has particular applicability in the efficient production of substrates for cation-olefin cyclization. The present paper describes a complementary extension of this approach to the rapid assembly of trisubstituted olefinic substrates which is based on sequential Shapiro and Suzuki coupling reactions.[2]

The sequence of steps involved in the present route to trisubstituted olefins is shown in Scheme 1. The details of the Shapiro reaction are similar to those presented in the preceding paper. Double deprotonation of acetone trisylhydrazone (**1**) followed by alkylation with R_1X produces unsymmetrical hydrazone **2**. Subsequent deprotonation followed by warming of the resulting dianion to 0 °C provides *Z*-vinyllithium reagent **3**. Treatment of **3** with iodine affords *E*-trisubstituted vinyl iodide **4** which can be purified by silica gel chromatography. Suzuki cross-coupling ($PdCl_2$(dppf),[3] NaOH) of vinyl iodide **4** and the alkyl borane derived from 9-BBN hydroboration[4] of terminal olefin **5** produces trisubstituted olefin **6**.

Scheme 1. Reaction sequence summary



The coupling products **7**, **8**, and **9** were prepared in the yields shown from reaction of the appropriate alkyl iodides with acetone trisylhydrazone (**1**) and iodine. Table 1 describes the elaboration of such vinyl iodides via Suzuki coupling to generate trisubstituted olefins, as shown. Suzuki coupling of both simple and functionalized olefins proceeds well, as is indicated in Table 1.[5] The reaction sequence described herein provides an alternative method for trisubstituted olefin synthesis which should be advantageous for couplings in which the olefinic starting material is more readily accessible than the corresponding alkyl iodide.[6]



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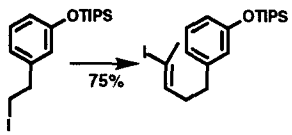

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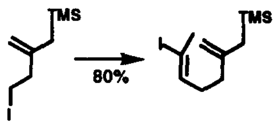

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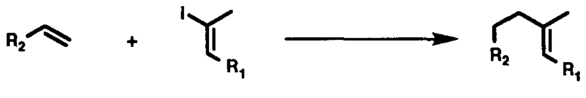
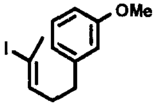
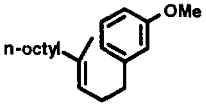
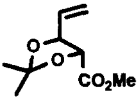
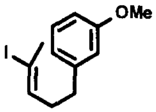
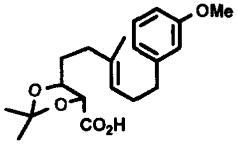
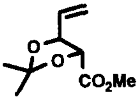
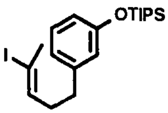
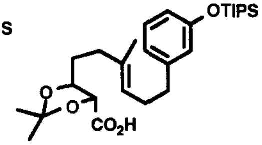
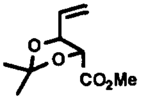
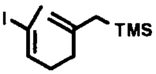
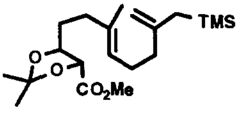
Table 1. Trisubstituted olefin synthesis by Suzuki coupling of vinyl iodides



5 4 6

Entry	Olefin	Vinyl Iodide	Product	Yield
A	1-octene	 	 	99%
B	 	 	 	80%
C	 	 	 	76%
D	 	 	 	75%

References and Notes:

1. Corey, E. J.; Lee, J.; Roberts, B. E. *Tetrahedron Lett.* preceding paper in this issue.
2. For a review of Suzuki coupling methodology see: Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457.
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4. Brown, H. C.; Knights, E. F.; Scouten, C. G. *J. Am. Chem. Soc.* **1974**, *96*, 7765.
5. For Table 1, entries B, C and D, Suzuki reaction to form the coupled methyl ester was generally complete within 15 min at 0 °C, however conversion of the methyl ester to the carboxylic acid can be effected over an additional 5-7 h under these reaction conditions.
6. This research was supported by the National Science Foundation and the National Institutes of Health.

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