JACS
JOURNAL OF THE AMERICAN CHEMICAL SOCIETY

Subscriber access provided by ISTANBUL TEKNIK UNIV

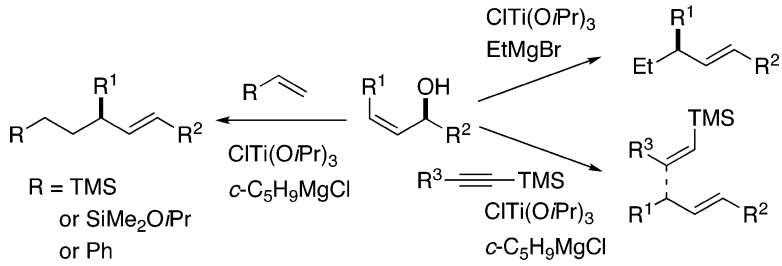
Article

Low-Valent Titanium-Mediated Stereoselective Alkylation of Allylic Alcohols

Ivan L. Lysenko, Keunho Kim, Hyung Goo Lee, and Jin Kun Cha

J. Am. Chem. Soc., **2008**, 130 (47), 15997-16002 • DOI: 10.1021/ja806440m • Publication Date (Web): 06 November 2008

Downloaded from http://pubs.acs.org on February 8, 2009



More About This Article

Additional resources and features associated with this article are available within the HTML version:

- Supporting Information
- Access to high resolution figures
- Links to articles and content related to this article
- Copyright permission to reproduce figures and/or text from this article

View the Full Text HTML

ACS Publications
High quality. High impact.

Journal of the American Chemical Society is published by the American Chemical Society. 1155 Sixteenth Street N.W., Washington, DC 20036

J|A|C|S
ARTICLES

Published on Web 11/06/2008

Low-Valent Titanium-Mediated Stereoselective Alkylation of Allylic Alcohols

Ivan L. Lysenko, Keunho Kim, Hyung Goo Lee, and Jin Kun Cha*

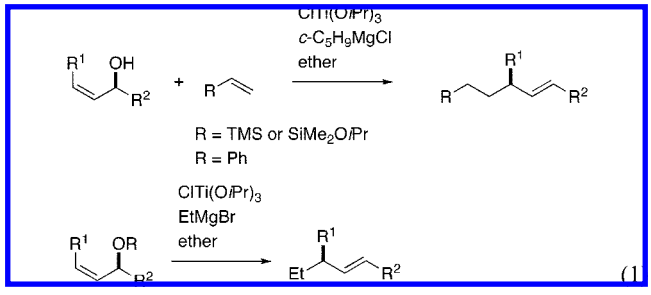
Department of Chemistry, Wayne State University, 5101 Cass Avenue, Detroit, Michigan 48202

Received July 8, 2008; E-mail: jcha@chem.wayne.edu

Abstract: We have developed low-valent titanium-mediated 1,3-transpositive cross-coupling reactions of acyclic and cyclic allylic alcohols for the stereoselective introduction of ethyl, 2-silylethyl, 2-phenethyl, and alkenyl groups. Cross-coupling of an allylic alcohol with a vinylsilane or styrene derivative is particularly noteworthy, as an efficient cross-selective coupling of two alkenes has been elusive. The stereochemistry of the cross-coupling alkylation is consistent with syn addition/β-elimination.

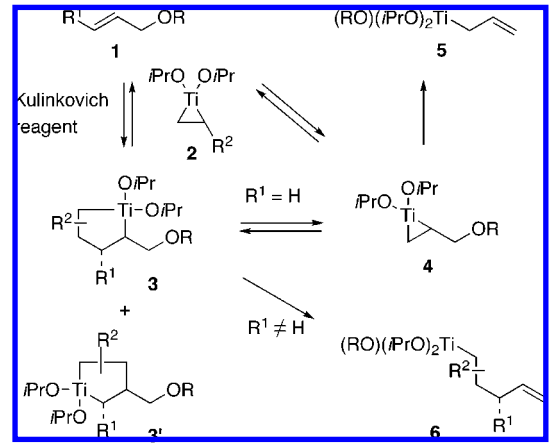
Introduction

Direct carbometalation of unactivated alkenes enables versatile C−C bond forming reactions and has been typically catalyzed by late-transition-metal complexes.[1] Group IVA metals have received less attention, but the Negishi reagent is particularly effective for cyclic carbozirconation of dienes, enynes, and diynes.[2] The use of a titanacyclopropane intermediate (Kulinkovich reagent) has been directed primarily at alkynes.[3] Alkenes containing heteroatoms at allylic positions undergo synthetically useful transformations by the action of the Negishi or Kulinkovich reagent.[2−4] Despite many elegant applications in transition-metal-catalyzed transformations; however, an intermolecular cross-selective coupling of two alkenes stands as a challenging goal.[5] As part of research programs on synthetic applications of the Kulinkovich reagent, we have developed cross-coupling of an allylic alcohol with a vinylsilane or styrene derivative (eq 1). Also included are stereoselective ethyl- and alkenylation reactions of allylic alcohols with the ethyl Grignard reagent and alkynes, respectively, along with stereochemical studies.



Previous Work and Mechanistic Hypothesis. Treatment of (monosubstituted) allylic alcohol derivatives **1** ($R^1 = H$) with the Kulinkovich reagent **2** was previously shown to provide a convenient method for generating allyltitanium reagents **5** in situ via β-elimination of the presumed intermediate **4** (Scheme 1).[3] The initial titanacyclopentane intermediates **3** and **3′** were believed to be in equilibrium with **4**, and steric effects (e.g., the degree of substitution in alkenes) appeared to be the dominant factor in controlling the position of equilibria.[6] In the

Scheme 1

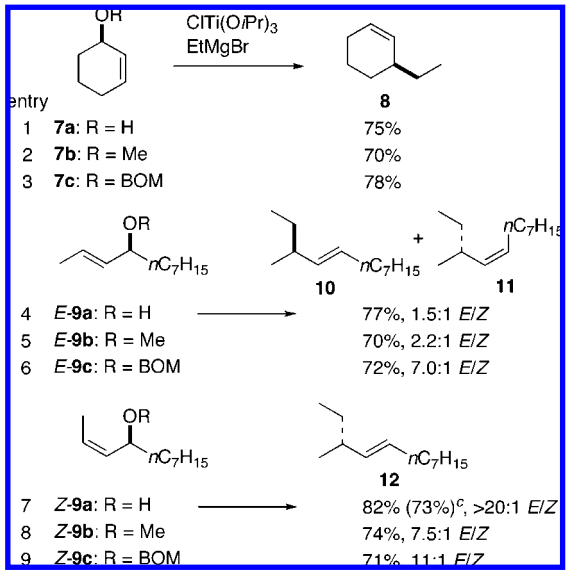


case of di- or trisubstituted olefins (i.e., $R^1 \neq H$), formation of the corresponding titanacyclopropane was believed to be unfavorable due to steric effects. This structural hypothesis on ligand exchange led to the development of an olefin exchange-mediated variant of the Kulinkovich cyclopropanation of carboxylic acid derivatives.[7,8] When $R^1 \neq H$, it was further hypothesized that a different reaction pathway of converting **3** (and **3′**) to **6** by β-elimination could become dominant. Additionally, a judicious choice of R^2 was deemed to be a critical element of successful implementation and regiocontrol.

The Kulinkovich group first reported a formal S_N2' ethylation reaction by the ethyl Grignard reagent ($R^2 = H$),[9] but no stereochemical studies have been reported to date. In situ formation of a Ti−O tether from an allylic alcohol, which had been exploited in the directed Kulinkovich cyclopropanation of homoallylic alcohol,[8c,10] could be presumed to direct syn addition/β-elimination. The stereochemical outcome was uncertain for allylic ethers, however, as the β-elimination step might require an ate complex by addition of a Grignard reagent. The cognate zirconocyclopentane intermediates were reported to prefer anti elimination, but geometrical constraints appeared

 © 2008 American Chemical Society

Table 1. Ethylation of Allylic Alcohols and Ethers[a,b]



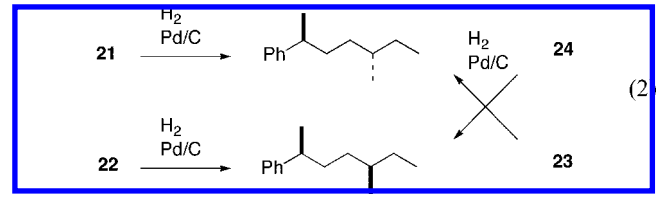
[a] Stereochemistry assigned by analogy to Table 2 (see text). [b] Reaction conditions: $ClTi(OiPr)_3$ (1 equiv), EtMgBr (3 equiv), ether, rt. [c] Reaction temperature: −78 °C to rt.

to be the overriding stereocontrol element.[11] As no unequivocal stereochemical information was available on these reactions, we decided to determine the stereochemistry of the 1,3-transpositive ethylation reaction of both allylic alcohols and ethers. Also included were related alkylation and alkenylation reactions of allylic alcohols.

Results and Discussion

Stereochemistry of Ethylation. In view of the different conformational preferences of *E*- and *Z*-olefins, both cyclic and acyclic substrates **7** and **9** were selected for allylic ethylation by the action of the Kulinkovich reagent (Table 1). At the oustet significant solvent effects were noted that THF afforded poor yields. Thus, diethyl ether was used as the solvent both for the reaction solvent and the Grignard reagent in subsequent studies. Several trends were apparent from Table 1. The protecting groups R of the allylic alcohol exerted little influence on yields. Ethylation of acyclic *Z*-allylic alcohol derivatives proceeded with good selectivity for the *E*-double bond geometry, but that of *E*-substrates was nonselective (entries 4−6 vs 7−9). Interestingly, *E*-selectivity was increased for the BOM ethers (entries 6 and 9), and this observation was in accord with Kulinkovich's earlier report on the THP protecting group.[9a]

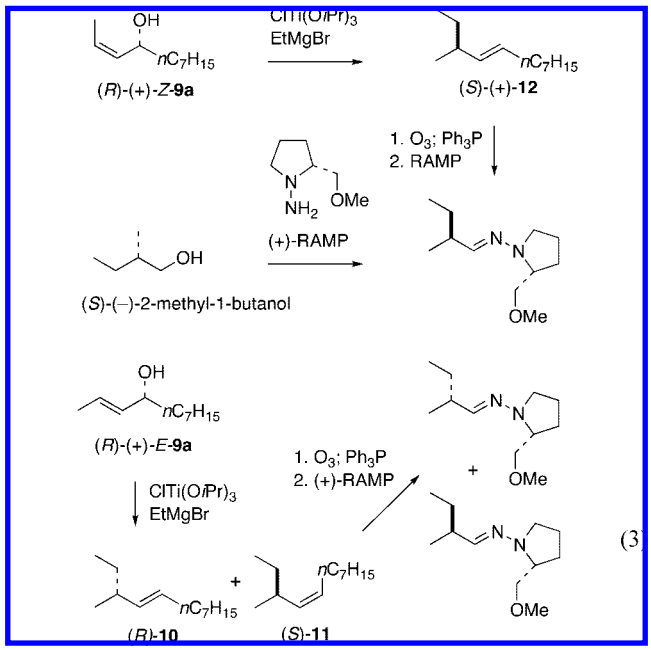
The stereochemical course of the ethylation reaction could be probed by employing nonracemic allylic alcohol derivatives and measuring the degree of chirality transfer. One drawback of this customary method stems from the fact that *E*- and *Z*-olefin products (e.g., **10** and **11**) are typically inseparable. Additionally, accurate measurements of ee's of both major and minor products were deemed to be nontrivial according to our mechanistic conjecture that the configuration of the major ethylation product **10** from an *E*-olefin substrate would be enantiomeric to that of the minor isomer **11**. An alternate method was thus chosen to exploit the diastereomeric nature of the two products (e.g., **10** and **11**). Directed (syn) addition/syn elimination at the double bond was first established by 2-cyclohexen-1-ol derivatives (entries 1−4 in Table 2). Thus, the ethylation reaction of allylic ethers (entries 2 and 4) was unequivocally ascertained to proceed with the identical stereochemistry as that of the respective allylic alcohols (entries 1 and 3). Comparative evaluation of diastereomeric substrates **17**−**20** was next undertaken (entries 5−12). Diastereomers **21** and **22** were obtained selectively from *Z*-anti- and *Z*-syn-isomers **17** and **19**, respectively, and their stereochemical assignment was made initially on the basis of syn addition/syn elimination. The corresponding *E*-anti substrates **18** afforded a mixture of two diastereomers **22** and **23** (entries 7 and 8), which were different from a mixture of **21** and **24** obtained from *E*-syn-compounds **20** (entries 11 and 12). Hydrogenation of **21** and **22** was carried out individually in addition to that of separate mixtures of **22/23** and **21/24** to reveal their stereochemical relationship (eq 2). The ^1H NMR spectra of the resulting two alkane products were unmistakably distinguishable so as to firmly establish the configurations of **21**−**24**.



As indicated, the stereochemistry of the acyclic products in Table 1 was initially assigned by analogy and subsequently

(1) For reviews, see: *Transition Metals for Organic Synthesis*; Beller, M., Bolm, C., Eds.; Wiley-VCH: Weinheim, 1998; Vols. *1* and 2.
(2) (a) For reviews, see: Negishi, E. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; Wiley-VCH: New York, 2000; pp 165−189. (b) Negishi, E. In *Titanium and Zirconium in Organic Synthesis*; Marek, I., Ed.; Wiley-VCH: New York, 2002; pp 1−49. (c) Hoveyda, A. H.; Heron, N. In *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer: Berlin, 1999; pp 431−454. (d) Hoveyda, A. H. In *Titanium and Zirconium in Organic Synthesis*; Marek, I., Ed.; Wiley-VCH: New York, 2002; pp 180−229.
(3) For reviews, see: (a) Sato, F.; Urabe, H.; Okamoto, S. *Chem. Rev.* **2000**, *100*, 2835. (b) Sato, F.; Urabe, H. In *Titanium and Zirconium in Organic Synthesis*; Marek, I., Ed.; Wiley-VCH: New York, 2002; pp 319−354.
(4) (a) Ito, H.; Motoki, Y.; Taguchi, T.; Hanzawa, Y. *J. Am. Chem. Soc.* **1993**, *115*, 8835. (b) Hanzawa, Y.; Kiyono, H.; Taguchi, T. *Heterocycles* **2004**, *62*, 297.
(5) For recent advances in transition-metal-catalyzed couplings of 2π components, see, inter alia: (a) RajanBabu, T. V. *Chem. Rev.* **2003**, *103*, 2845. (b) Montgomery, J. *Angew. Chem., Int. Ed.* **2004**, *43*, 3890. (c) Iida, H.; Krische, M. J. *Top. Curr. Chem.* **2007**, *279*, 77. (d) Ng, S.-S.; Ho, C.-Y.; Schleicher, K. D.; Jamison, T. F. *Pure Appl. Chem.* **2008**, *80*, 929.
(6) Lee, J.; Cha, J. K. *Tetrahedron Lett.* **1996**, *37*, 3663.
(7) For reviews, see: (a) Kulinkovich, O. G.; de Meijere, A. *Chem. Rev.* **2000**, *100*, 2789. (b) Kulinkovich, O. G. *Russ. Chem. Bull., Int. Ed.* **2004**, *53*, 1065.
(8) (a) Lee, J.; Kang, C. H.; Kim, H.; Cha, J. K. *J. Am. Chem. Soc.* **1996**, *118*, 291. (b) Lee, J.; Kim, H.; Cha, J. K. *J. Am. Chem. Soc.* **1996**, *118*, 4198. (c) Quan, L. G.; Kim, S.-H.; Lee, J. C.; Cha, J. K. *Angew. Chem., Int. Ed.* **2002**, *41*, 2160.
(9) (a) Kulinkovich, O. G.; Epstein, O. L.; Isakov, V. E.; Khmel'nitskaya, E. A. *Synlett* **2001**, 49. (b) Matyushenkov, E. A.; Churikov, D. G.; Sokolov, N. A.; Kulinkovich, O. G. *Russ. J. Org. Chem.* **2003**, *39*, 478. (c) Kulinkovich, O. G.; Shevchuk, T. A.; Isakov, V. E.; Prokhorevich, K. N. *Russ. J. Org. Chem.* **2006**, *42*, 659. (d) Kulinkovich, O. G. *Pure Appl. Chem.* **2000**, *72*, 1715.
(10) (a) Savchenko, A. I.; Kulinkovich, O. G. *Russ. J. Org. Chem.* **1997**, *33*, 846. (b) Isakov, V. E.; Kulinkovich, O. G. *Synlett* **2003**, 967.
(11) (a) See, inter alia: Owen, D. R.; Whitby, R. J. *Synthesis* **2005**, 2061. (b) Barluenga, J.; Álvarez-Rodrigo, L.; Rodríguez, F.; Fañanás, F. J. *Angew. Chem., Int. Ed.* **2004**, *43*, 3932.
(12) (a) Marshall, J. A.; Yu, R. H.; Perkins, J. F. *J. Org. Chem.* **1995**, *60*, 5550. (b) Enders, D.; Kipphardt, H.; Fey, P. *Org. Synth.* **1987**, *65*, 183. (c) Enders, D.; Eichenauer, H. *Chem. Ber.* **1979**, *112*, 2933.

confirmed by the following chirality transfer experiment employing enantiomerically enriched (95% ee) *E*-(+)- and *Z*-(+)-**9a**, which were prepared from the corresponding known propargyl alcohol[12a] by LAH reduction and hydrogenation with the Lindlar catalyst (eq 3). Thus, (*S*)-**12** was obtained from (*R*)-(+)-*Z*-**9a** as a single isomer and its *S* configuration was unequivocally established by straightforward derivatization with (+)-RAMP[12b] and comparison with an authentic sample[12c] prepared from commercially available (*S*)-2-methyl-1-butanol. The cognate experiment with (*R*)-(+)-*E*-**9a** gave a mixture of (*R*)-**10** and (*S*)-**11**, and their configurations were determined by the formation of two diastereomeric chiral hydrazones. The minor hydrazone product derived from (S)-**11** was identical to that obtained from (S)-**12**.



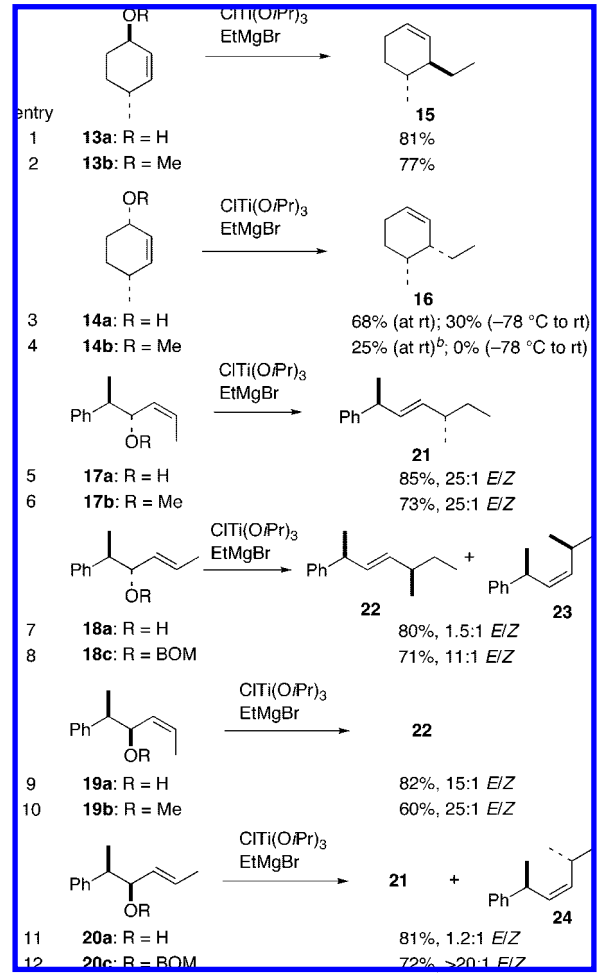
Additional examples were obtained to show a broad scope with respect to allylic alcohols (Table 3). The use of a trisubstituted olefin allows convenient construction of a quaternary center (entry 1). A tertiary alcohol is also a suitable substrate (entry 2). Selective ethylation of an allylic alcohol is achieved in competition with an allylic ether (entry 4). As expected, enantioselective ethylation is readily available by using nonracemic allylic alcohols (entries 4 and 5).[13]

Alkylation and Alkenylation. A broad scope for installing functionalized groups other than the ethyl moiety at an allylic position is highly desirable and synthetically valuable. When a homologous Grignard reagent (e.g., *n*-BuMgBr) was employed in place of EtMgBr, a ca. 1:1 mixture of regioisomeric allylation products (including both C1 and C2 positional isomers: R^2 = Et in Scheme 1) was obtained in modest (ca. 40−50%) yields from allylic alcohols. In sharp contrast to the aforementioned ethylation, however, allylic ethers failed to undergo alkylation. The directing effects by a temporary alkoxide-Ti tether were clearly necessary to override unfavorable steric effects engendered by a homologous Grignard reagent.

Cross-coupling between allylic alcohols and olefins (or alkynes) by means of a sacrificial Grignard reagent is more

(13) This allylic ethylation was reminiscent of Dzhemilev's carbomagnesation, which was elegantly developed by Hoveyda as a powerful tool in asymmetric synthesis.[2c,d]

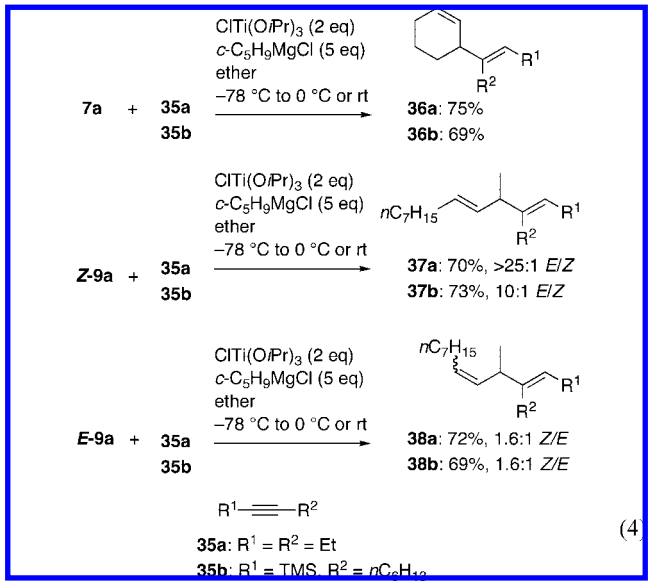
Table 2. Stereochemical Studies on Ethylation of Allylic Alcohols and Ethers[a]



[a] Reaction conditions: $ClTi(OiPr)_3$ (1 equiv), EtMgBr (3 equiv), ether, rt (entries 1, 2, 3, 4, 6, 8, 10, and 12) or −78 °C to rt (entries 3, 4, 5, 7, 9, and 11). [b] 4-Methylcyclohexene was also isolated in 40% yield.

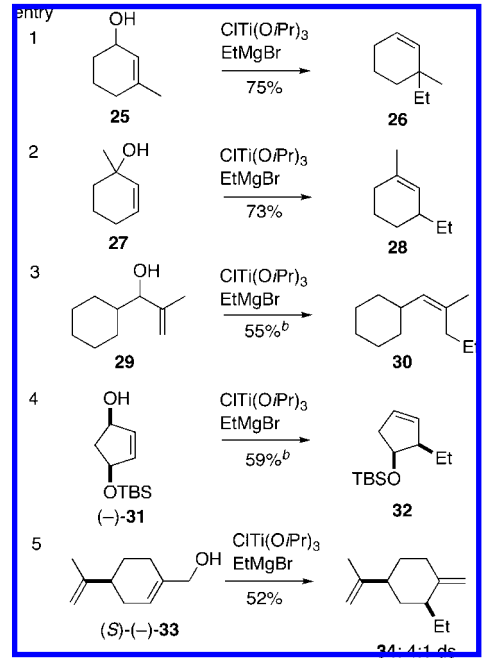
attractive conceptually and operationally. Our attention was thus focused on the development of such cross-coupling reactions instead of optimizing the alkylation with *n*BuMgBr. In view of the well-documented facile preparation (even at low temperature) and utility of titanium−alkyne complexes,[3] coupling of **7a** and an alkyne was first examined toward this end. Efficient alkenylation products were isolated in satisfactory yields from allylic alcohols (eq 4). As was the case with the aforementioned ethylation, the alkenylation of *Z*-**9a** proceeded with high diastereoselectivity, but the respective reaction with *E*-**9a** was stereorandom to give a 1.6:1 mixture of *Z*- and *E*-double bond isomers. Allylic ethers gave only trace amounts of the coupling products. Only internal alkynes were amenable to the coupling reaction, and regiocontrol was expected to be problematic with unsymmetrical alkynes. Because similar alkenylation examples appeared in the literature,[14] no additional studies were pursued.

(14) Recently, Micalizio reported this coupling reaction of alkynes, which affords enantio- and diastereoselective alkenylation: (a) Kolundzic, F.; Micalizio, G. C. *J. Am. Chem. Soc.* **2007**, *129*, 15112. (b) Shimp, H. L.; Hare, A.; McLaughlin, M.; Micalizio, G. C. *Tetrahedron* **2008**, *64*, 3437.



Cross-Coupling of Two Alkenes. The respective coupling reaction of allylic alcohols with alkenes, which was one of our two main objectives, proved to be challenging. Reductive dimerization of homoallylic alcohols was achieved by the Kulinkovich group by harnessing preassociation of a homoallylic alkoxide to a titanacyclopropane intermediate.[9] However, a cross-coupling reaction between two alkenes has been elusive and undoubtedly hinges on a judicious choice of two reactants. As a key prerequisite, alkene substrates should display a strong affinity for the Kulinkovich intermediate **2** to readily form the requisite titanacyclopentane **3**. The positional preference of R^2 in **3** (Scheme 1) would also be crucial to regioselective cross-coupling in conjunction with the formation of a temporary alkoxide linker to the titanacyclopropane intermediate and the thermodynamically favorable β-elimination step. The aforementioned alkylation reaction with *n*BuMgBr clearly indicated that an alkyl group would exert little positional preference. After considerable experimentation, vinylsilane and styrene were selected for allylic alkylation. Our choice was guided by notable observations made in the olefin exchange-mediated cyclopropanation of esters: treatment with a mixture of methyl 6-heptenoate and trimethyl(vinyl)silane with the Kulinkovich reagent (derived from *i*PrMgCl) gave the intermolecular cyclopropanation product at the expense of the intramolecular counterpart.[15] The olefin exchange-mediated cyclopropanation of an ester with styrene was achieved by the ethyl Grignard reagent,[16] whereas other terminal ω-alkenes require cyclohexyl or cyclopentyl Grignard reagents for successful Kulinkovich cyclopropanation reactions.[7,8] These previous observations hinted at the distinctive yet unexplored utility of vinylsilane (or vinylsiloxane) and styrene in forming the requisite titanacyclopropane and titanacyclopentane intermediates (i.e., **2** and **3** in Scheme 1). Moreover, high positional selectivity was noted for silyl and phenyl substituents in the low-valent titanium-mediated transformations of the respective alkyne derivatives, as illustrated by eq 4.[3]

Table 3. Additional Examples of Ethylation of Allylic Alcohols[a]



[a] Reaction conditions: $ClTi(OiPr)_3$ (1 equiv), EtMgBr (3 equiv), ether, rt. [b] Reaction conditions: $ClTi(OiPr)_3$ (1 equiv), EtMgBr (4 equiv), ether, rt.

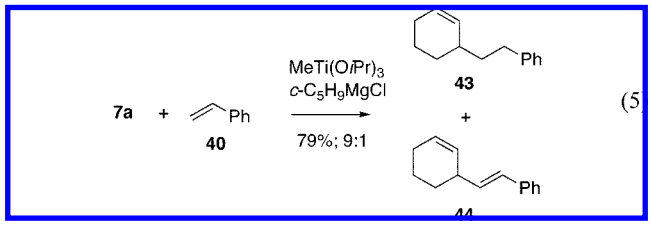
Ultimately, trimethyl(vinyl)silane (**39a**), vinylsiloxanes **39b**, and styrene (**40**) were found to be well suited for reductive cross-coupling reactions with allylic alcohols (Table 4). Under typical reaction conditions, a 1:1 mixture of an allylic alcohol and **39a** or **39b** in ether was treated sequentially with commercially available $ClTi(OiPr)_3$ and an ether solution of cyclopentylmagnesium chloride at −78 °C, followed by allowing the resulting mixture to slowly warm to 0 °C or rt. To ensure complete conversion of the allylic alcohol substrate, 2 equiv of $ClTi(OiPr)_3$ and 5 equiv of the cyclopentyl Grignard reagent were satisfactory. Alternatively, $MeTi(OiPr)_3$ (1 equiv) and the cyclopentyl Grignard reagent (2 equiv) were also used.[17] Coupling between **7a** and styrene (**40**) was subsequently studied by employing $MeTi(OiPr)_3$ to give a 9:1 mixture of the coupling product **43** and its dehydrostyrene derivative **44** in 79% yield (eq 5). The minor byproducts are not shown in Table 4 for convenience. As was the case with the ethylation reaction, the scope was broad regarding allylic alcohols to allow a convenient, stereoselective preparation of quaternary centers (entries 11 and 12) and an enantioselective synthesis of coupling products (entries 15 and 16). Comparable reactivity was noted for **39a** and **40** on the basis of their competition experiment. A similar competition experiment between the two styrenes **40** and **41** indicated the considerably lower reactivity of the latter compared to the former (cf. entries 3 and 4).[18]

(15) For the Kulinkovich cyclopropanation of vinylsilanes, see: (a) Lee, K.; Kim, S.-I.; Cha, J. K. *J. Org. Chem.* **1998**, *63*, 9135. (b) Mizojiri, R.; Urabe, H.; Sato, F. *Tetrahedron Lett.* **1999**, *40*, 2557. (c) Mizojiri, R.; Urabe, H.; Sato, F. *J. Org. Chem.* **2000**, *65*, 6217.

(16) Kulinkovich, O. G.; Savchenko, A. I.; Sviridov, S. V.; Vasilevskii, D. A. *J. Chem. Soc., Mendeleev Commun.* **1993**, 230.

(17) Subsequent to the publication of the trans-dialkyl selective cyclopropanation of esters with homoallylic alcohols,[8c] the use of $MeTi(OiPr)_3$ was also found to be convenient and effective.

(18) (a) Electronic effects of other substituents on the benzene ring will be examined in due course. (b) Interestingly, Z-disubstituted alkenylsilanes also undergo stereoselective coupling, albeit in moderate (40−53%) yields, and optimization is currently in progress.



(5)

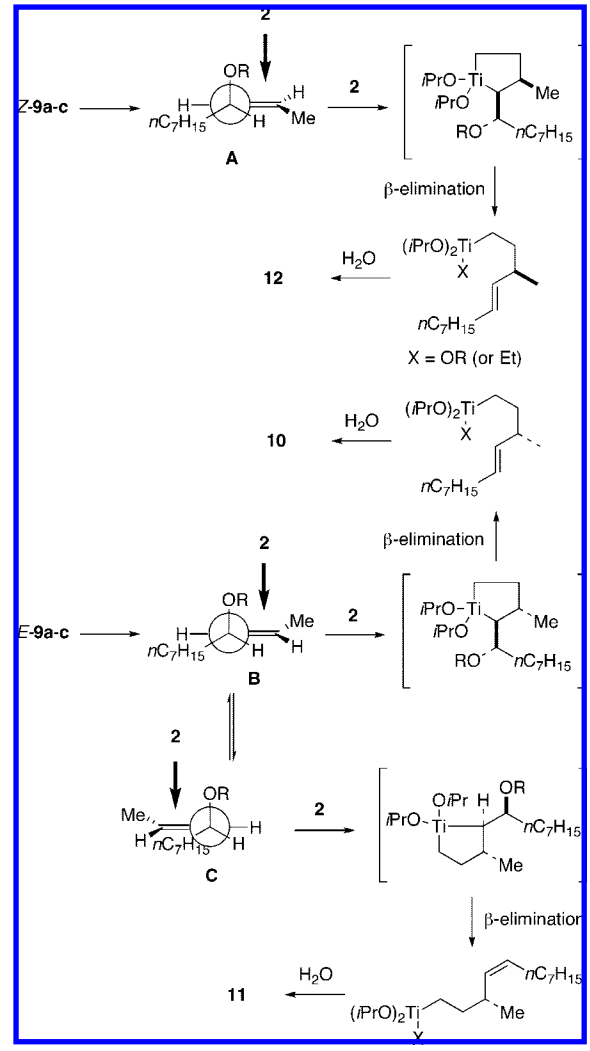
The siloxane functionality of the coupling products was readily converted by Woerpel's protocol to the hydroxyl group (eq 6),[19] which should be useful for subsequent elaboration.

Table 4. Cross-Coupling between Allylic Alcohols and Vinylsilanes[a] or Styrenes[b]

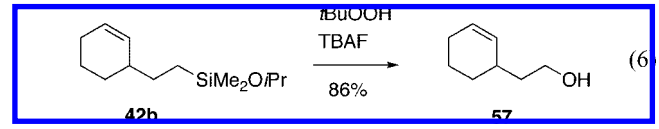
entry			
1	**7a** +	**39a**: R^3 = TMS	**42a**: 69%
2		**39b**: R^3 = $SiMe_2OiPr$	**42b**: 72%
3		**40**: R^3 = Ph	**43** (+**44**): 79%; 9:1[c]
4		**41**: R^3 = C_6H_4-*p*OMe	**45**: 38% (66% brsm); 18:1[c]
5	***Z*-9a** +	**39a**	**46a**: 70%, >20:1 *E*/*Z*
6		**39b**	**46b**: 74%, >20:1 *E*/*Z*
7	**13a** +	**39b**	**47b**: 70%
8		**40**	**48**: 78%; 10:1[c]
9	**14a** +	**39b**	**49b**: 32%
10		**40**	**50**: 75%; 10:1[c]
11	+	**39b**	**51b**: 74%
12		**40**	**52**: 75%; 11:1[c]
13	+	**39b**	**53b**: 31%
14		**40**	**54**: 35%; 10:1[c]
15	+	**39b**	**55b**: 52%
16		**40**	**56**: 30% (52% brsm)

[a] Reaction conditions: allylic alcohol (1 equiv), **39a** or **39b** (1 equiv), $ClTi(OiPr)_3$ (2 equiv), c-C_5H_9MgCl (5 equiv), ether, −78 to 0 °C or rt. [b] Reaction conditions: allylic alcohol (1 equiv), **40** or **41** (1 equiv), $MeTi(OiPr)_3$ (1 equiv), *c*-C_5H_9MgCl (2.2 equiv), ether, −78 to 0 °C. [c] Minor products are not shown; see eq 5.

Scheme 2



Thus, this 1,3-transpositive cross-coupling and the Tamao−Fleming oxidation complement the conventional Claisen rearrangement approach.



(6)

Stereochemical Model. The high diastereoselectivity displayed by *Z*-allylic alcohols can be rationalized by the involvement of conformer **A**, where the allylic strain is minimized (Scheme 2).[20] The lack of selectivity for *E*-allylic alcohols and the attendant formation of both *E*- and *Z*-olefins suggest the coinvolvement of both conformers **B** and **C**. The identical stereochemical models also account for the stereochemistry of cross-coupling reactions of allylic alcohols with vinylsilanes, styrenes, and alkynes.

A priori, an alternate stereochemical pathway of anti addition/antiperiplanar elimination could be considered for the ethylation reaction of allylic ethers. However, formation of the identical

(19) Smitrovich, J. H.; Woerpel, K. A. *J. Org. Chem.* **1996**, *61*, 6044.
(20) Note added in proof: The stereochemical study of the ethylation just appeared. Isakov, V. E.; Kulinkovich, O. G. *Tetrahedron Lett.* **2008**, *49*, 6959.

product **15** from alcohol **13a** and methyl ether **13b** (and **16** from **14a** and **14b**) in a cyclic system (entries 1−4 in Table 2), as well as a noticeable difference in alkylation yields between cis and trans isomers (entries 2 vs 4 in Table 2), precludes this scenario. In the case of the cross-coupling between allylic alcohols **13a**/**14a** and vinylsilane **39b**, a similar divergence in yields was also noted (entries 7 vs 9 in Table 4). Interestingly, the corresponding coupling reactions of styrene (**40**) showed little variation between cis and trans isomers (entries 8 vs 10 in Table 4). At present, the origin for high *E*-selectivity exhibited by BOM allylic ethers is not clear.

Conclusion

In conclusion, we have developed convenient 1,3-transpositive cross-coupling reactions of acyclic and cyclic allylic alcohols to allow the stereoselective introduction of ethyl, 2-silylethyl, 2-phenethyl, and alkenyl groups. The stereochemistry of the cross-coupling alkylation is consistent with syn addition/β-elimination. New cross-coupling reactions between an allylic alcohol and a vinylsilane or styrene derivative are particularly noteworthy and demonstrate the unexplored utility of vinylsilanes and styrenes in low-valent titanium-mediated transformations.

Acknowledgment. Dedicated to Professor Sir Jack E. Baldwin, FRS, on the occasion of his 70th birthday. We thank the NIH (GM35956) and NSF (CHE-0615604) for generous financial support.

Supporting Information Available: Experimental details and spectroscopic data for key intermediates. This material is available free of charge via the Internet at http://pubs.acs.org.

JA806440M