Contrasteric Regiocontrol in Rhodium-Catalyzed Hydrogenative Couplings of Nonsymmetric 1,3-Diynes to Ethyl Glyoxalate

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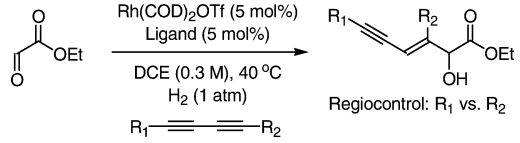
To probe the origins of regioselection in rhodium-catalyzed hydrogenative couplings of 1,3-diynes to ethyl glyoxalate, a series of structurally related nonsymmetric 1,3-diynes, **1a**−**14a**, were prepared and surveyed. Nonsymmetric 1,3-diynes **1a**−**8a** possess different degrees of alkyl substitution at the propargylic carbons. Unusual contrasteric regioselectivity is observed, often with a complete preference for coupling at the diyne terminus proximal to the more substituted propargylic center. Couplings to diynes **9a**−**14a** are meant to probe the effects of heteroatom substitution at the propargylic position *vis-à-vis* partitioning of regioisomeric coupling manifolds. Heteroatom substitution exerts only a modest influence on the regiochemistry of coupling, except in the case of (trimethylsilyl)methyl-substituted diynes **13a** and **14a**. The observed trends suggest that substituents at the diyne termini compete for stabilization of intermediate regioisomeric rhodium−alkyne π-complexes via hyperconjugative interactions, with regio-determining oxarhodacycle formation occurring from the more stable π-complex.

Introduction

The Fischer−Tropsch[1] reaction and alkene hydroformylation[2] are practiced on enormous scale and may be regarded as the prototypical hydrogen-mediated C−C bond formations. Despite the impact of these processes, systematic efforts toward hydrogenative C−C bond formations beyond carbon monoxide coupling only recently have begun to emerge.[3−8] Through the use of cationic rhodium and iridium precatalysts, the hydrogenative coupling of conjugated enones,[4] conjugated alkenes,[5] and conjugated[6a−g] and nonconjugated alkynes[6h,i] to carbonyl and imine[6c] partners have been devised. Additionally, hydrogenation of 1,6-diynes, 1,6-enynes, and 1,6-alkynals is found to provide products of reductive carbocyclization.[7]

Earlier studies from our laboratory on the hydrogen-mediated coupling of nonsymmetric 1,3-diynes to glyoxals,[6a] glyoxalates,[6f] and iminoacetates[6c] reveal unusual contrasteric regiocontrol. To probe the origins of regioselection, a survey of structurally related nonsymmetric 1,3-diynes **1a**−**14a** in hydrogenative couplings to ethyl glyoxalate was performed, as disclosed herein. These studies enable correlation of various substructures in terms of their relative ability to direct partitioning of regioisomeric coupling manifolds. It is found that the degree of substitution at the propargylic position of the diyne terminus plays a significant role in directing regiochemistry. Potential interactions that dictate partitioning of regioisomeric coupling modes are discussed.



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† University of Texas at Austin.
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(1) For a review, see: Cornils, Boy; Herrmann, A.; Rasch, Manfred. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 2144.

(2) For recent reviews on alkene hydroformylation, see: (a) Cornils, B.; Herrmann, W. A.; Kohlpaintner, C. W. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 2144. (b) Beller, M.; Cornils, B.; Frohning, C. D.; Kohlpaintner, C. W. *J. Mol. Catal.* **1995**, *104*, 17. (c) Eilbracht, P.; Barfacker, L.; Buss, C.; Hollmann, C.; Kitsos-Rzychon, B. E.; Kranemann, C. L.; Rische, T.; Roggenbuck, R.; Schmidt, A. *Chem. Rev.* **1999**, *99*, 3329. (d) Nozaki, K. In *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds. Springer-Verlag: Berlin, 1999; Vol. 1, p 381. (e) Breit, B. *Acc. Chem. Res.* **2003,** *36*, 264.

(3) For a review, see: (a) Ngai, M.-Y.; Kong, J.-R.; Krische, M. J. *J. Org. Chem.* **2007**, *72*, 1063. (b) Iida, H.; Krische, M. J. *Top. Curr. Chem.* **2007**, in press.

(4) For hydrogen-mediated reductive aldol couplings, see: (a) Jang, H.-Y.; Huddleston, R. R.; Krische, M. J. *J. Am. Chem. Soc.* **2002**, *124*, 15156. (b) Huddleston, R. R.; Krische, M. J. *Org. Lett.* **2003**, *5*, 1143. (c) Koech, P. K.; Krische, M. J. *Org. Lett.* **2004**, *6*, 691. (d) Marriner, G. A.; Garner, S. A.; Jang, H.-Y.; Krische, M. J. *J. Org. Chem.* **2004**, *69*, 1380. (e) Jung, C.-K.; Garner, S. A.; Krische, M. J. *Org. Lett.* **2006**, *8*, 519. (f) Han, S. B.; Krische, M. J. *Org. Lett.* **2006**, *8*, 5657. (g) Jung, C.-K.; Krische, M. J. *J. Am. Chem. Soc.* **2006**, *128*, 17051.

(5) For hydrogen-mediated couplings of conjugated alkenes to carbonyl compounds, see: (a) Jang, H.-Y.; Huddleston, R. R.; Krische, M. *Angew. Chem., Int. Ed.* **2003**, *42*, 4074. (b) Hong, Y.-T.; Barchuk, A.; Krische, M. J. *Angew. Chem., Int. Ed.* **2006**, *128*, 6885.

(6) For hydrogen-mediated couplings of conjugated alkynes to carbonyl compounds and imines, see: (a) Huddleston, R. R.; Jang, H.-Y. Krische, M. J. *J. Am. Chem. Soc.* **2003**, *125*, 11488. (b) Jang, H.-Y.; Huddleston, R. R.; Krische, M. J. *J. Am. Chem. Soc.* **2004**, *126*, 4664. (c) Kong, J.-R.; Cho, C.-W.; Krische, M. J. *J. Am. Chem. Soc.* **2005**, *127*, 11269. (d) Cho, C.-W.; Krische, M. J. *Org. Lett.* **2006**, *8*, 891. (e) Kong, J.-R.; Ngai, M.-Y.; Krische, M. J. *J. Am. Chem. Soc.* **2006**, *128*, 718. (f) Cho, C.-W.; Krische, M. J. *Org. Lett.* **2006**, *8*, 3873. (g) Komanduri, V.; Krische, M. J. *J. Am. Chem. Soc.* **2006**, *128*, 16448. (h) Kong, J.-R.; Krische, M. J. *J. Am. Chem. Soc.* **2006**, *128*, 16040. (i) Ngai, M.-Y.; Barchuk, A.; Krische, M. J. *J. Am. Chem. Soc.* **2007**, *129*, 280.

(7) For hydrogen-mediated carbocyclizations, see: (a) Jang, H.-Y.; Krische, M. J. *J. Am. Chem. Soc.* **2004**, *126*, 7875. (b) Jang, H.-Y.; Hughes, F. W.; Gong, H.; Zhang, J.; Brodbelt, J. S.; Krische, M. *J. Am. Chem. Soc.* **2005**, *127*, 6174. (c) Rhee, J.-U.; Krische, M. J. *J. Am. Chem. Soc.* **2006**, *128*, 10674.

(8) Prior to our work, two isolated examples of hydrogen-mediated C−C bond formations not involving couplings to carbon monoxide were reported: (a) Molander, G. A.; Hoberg, J. O *J. Am. Chem. Soc.* **1992**, *114*, 3123. (b) Kokubo, K.; Miura, M.; Nomura, M. *Organometallics* **1995**, *14*, 4521.

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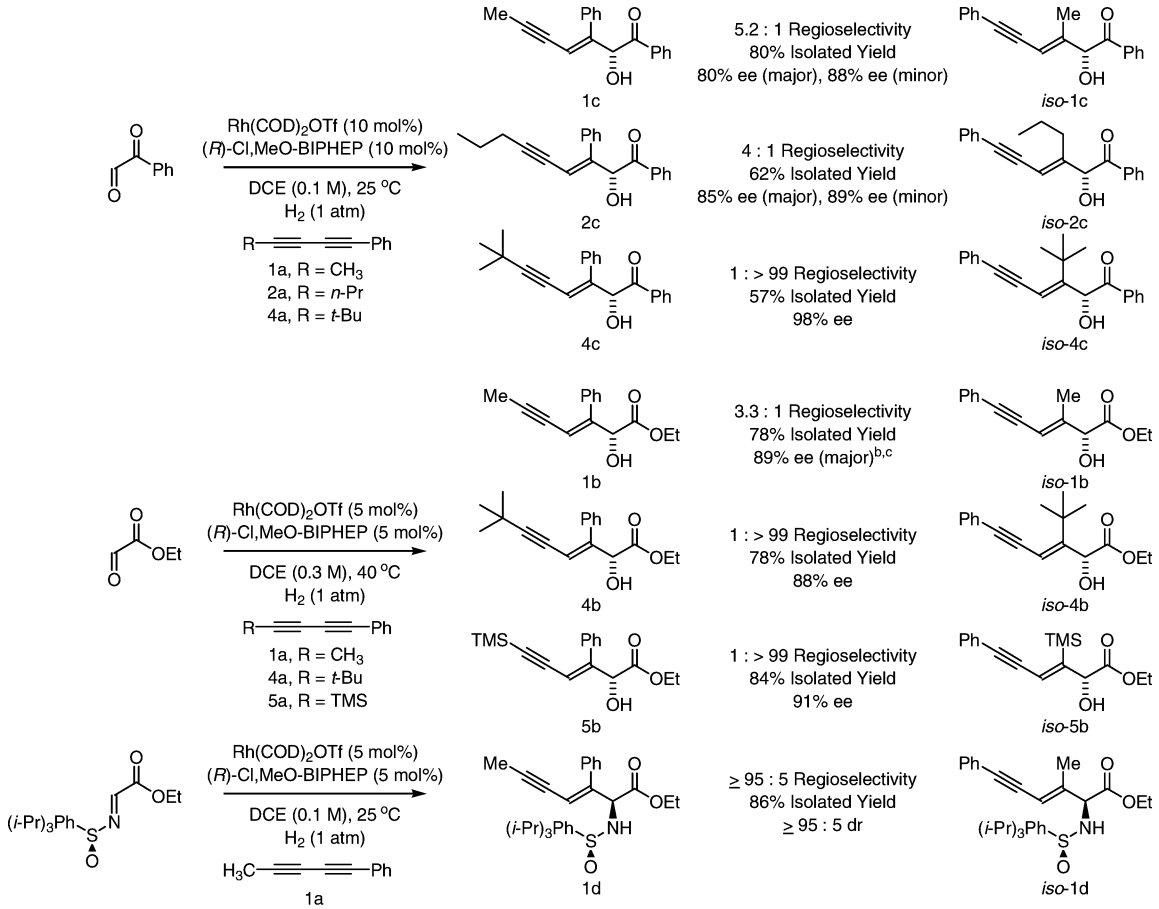
Scheme 1. Selected Results Obtained Previously in the Hydrogen-Mediated Coupling of 1,3-Diynes to Glyoxals,[6a] Glyoxalates,[6f] and Iminoacetates[6c] with Contrasteric Regiocontrol[a]



[a] The regiochemical assignment of the major isomer is made on the basis of ^{13}C NMR data. Specifically, acetylenic carbon atoms bearing a phenyl moiety possess a characteristic ^{13}C NMR chemical shift at δ 122 − 123. [b]Enantiomeric excess of the minor isomer was not determined. [c]Reaction was performed at ambient temperature.

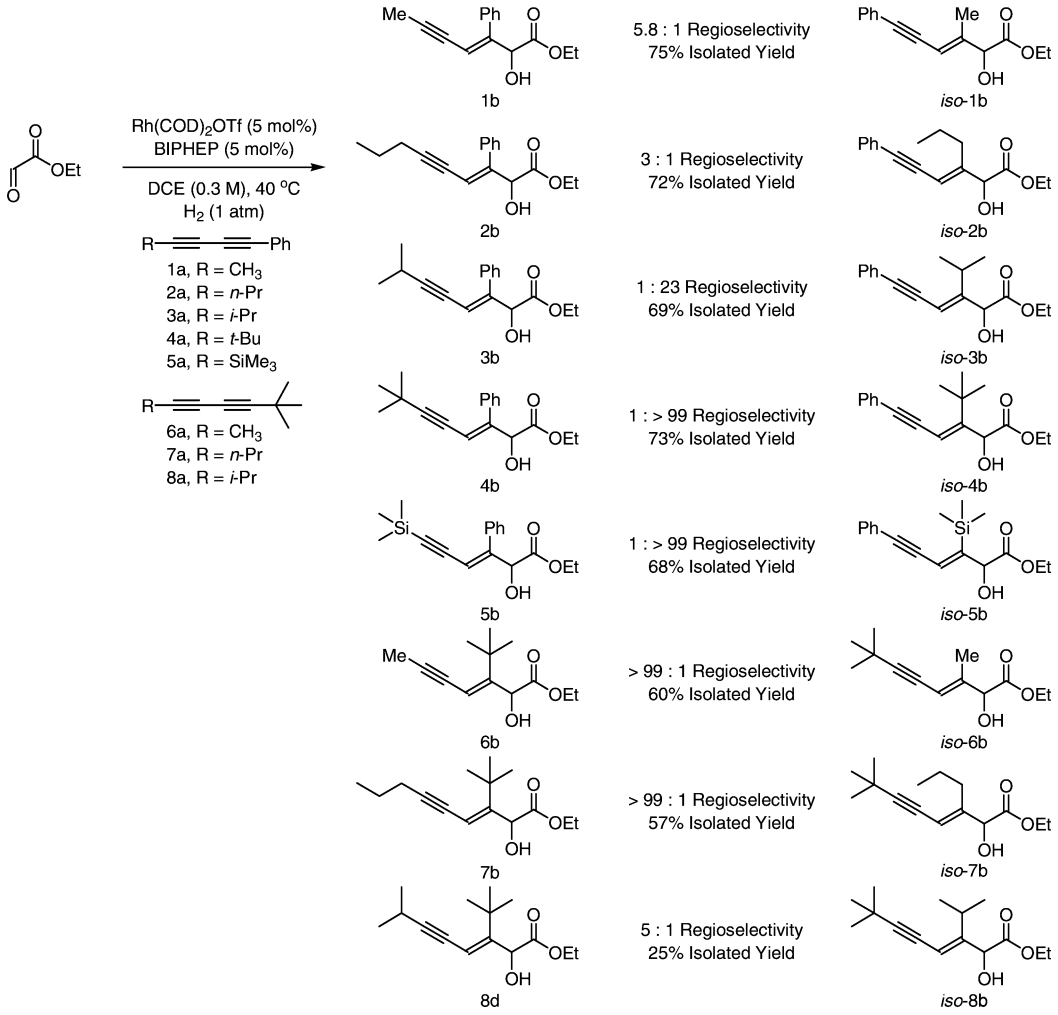
Results and Discussion

In previously disclosed studies, the hydrogenative couplings of nonsymmetric 1,3-diynes **1a**, **2a**, **4a**, and **5a** to glyoxals,[6a] glyoxalates,[6f] and iminoacetates[6c] was examined. Specifically, 1-phenylpenta-1,3-diyne **1a** was found to engage in reductive couplings to phenyl glyoxal, ethyl glyoxalate, and ethyl (*N*-2,4,6-triisopropylbenzenesulfinyl)iminoacetate proximal to the phenyl-substituted terminus of the diyne to furnish adducts **1c**, **1b**, and **1d**, respectively, with partial (**1c**, **1b**) or complete (**1d**) levels of regiocontrol. It was initially hypothesized that electronic effects associated with the phenyl moiety direct the regiochemistry of coupling. However, the coupling of 5,5-dimethyl-1-phenylhexa-1,3-diyne **4a** occurs proximal to the *tert*-butyl moiety to provide *iso*-**4c** with complete levels of regiocontrol.[9] Analogous regiochemistry is observed in the coupling of the trimethylsilyl-substituted diyne **5a** to furnish adduct *iso*-**5b**. The latter two results suggest that the degree of substitution at the propargylic carbon atoms plays a significant role in directing regiochemistry (Scheme 1).

These data provoked a more systematic investigation into how the degree of alkyl substitution at the propargylic carbon atoms of the 1,3-diyne termini influences partitioning of regioisomeric coupling manifolds. Toward this end, nonsymmetric 1,3-diynes **1a**−**8a** were prepared and coupled to ethyl glyoxalate under a standard set of conditions: the diyne (200 mol %) was hydrogenated at ambient pressure in the presence of ethyl glyoxalate (100 mol %) using $Rh(COD)_2OTf$ (5 mol %) as precatalyst and BIPHEP (5 mol %) as ligand in dichloroethane solvent (0.3 M) at 40 °C. For phenyl substituent diynes **1a**−**5a**, the degree of alkyl substitution at the alternate diyne terminus is varied from primary (Me, **1a**) to secondary (*n*-Pr, **2a**) to tertiary (*i*-Pr, **3a**) to quaternary (*t*-Bu and $SiMe_3$, **4a** and **5a**, respectively). Upon exposure to standard conditions for hydrogenative coupling, a gradual inversion in regiochemistry is observed as the degree of alkyl substitution at the propargylic position is successively increased. Specifically, whereas the methyl-substituted diyne **1a** exhibits a 5.8:1 regiochemical preference for coupling proximal to the phenyl moiety, the corresponding *n*-propyl diyne **2a** exhibits a 3:1 regiochemical preference. Notably, for the constitutionally isomeric isopropyl diyne **3a**, an inversion in regiochemistry is observed. Coupling now occurs preferentially at the diyne terminus distal to the phenyl moiety to provide adducts **3b** and *iso*-**3b** in a 1:23 ratio, respectively. Upon further increase in the degree of alkyl substitution at the propargylic position, as for *tert*-butyl diyne **4a**, complete levels of regioselection are observed. The adduct *iso*-**4b** is produced as a single regioisomer. Similarly, coupling adjacent to the quaternary propargylic center is observed for the *iso*-structural diyne **5a**, wherein the central carbon atom of

(9) In refs 6a and 6f, regiochemistry of the *tert*-butyl-substituted diyne coupling products were incorrectly assigned. Coupling takes place proximal to the *tert*-butyl moiety of the nonsymmetric diyne possessing *tert*-butyl and phenyl termini. An "Addition and Correction" has been published.

Scheme 2. Effect of Alkyl Substitution at the Propargylic Termini of 1,3-Diynes with Respect to Partitioning of Regioisomeric Coupling Manifolds[a]



[a] The regiochemical assignment of the major isomer is made on the basis of ^{13}C NMR data. Specifically, acetylenic carbon atoms bearing a phenyl moiety possess a characteristic ^{13}C NMR chemical shift at δ 122−123.

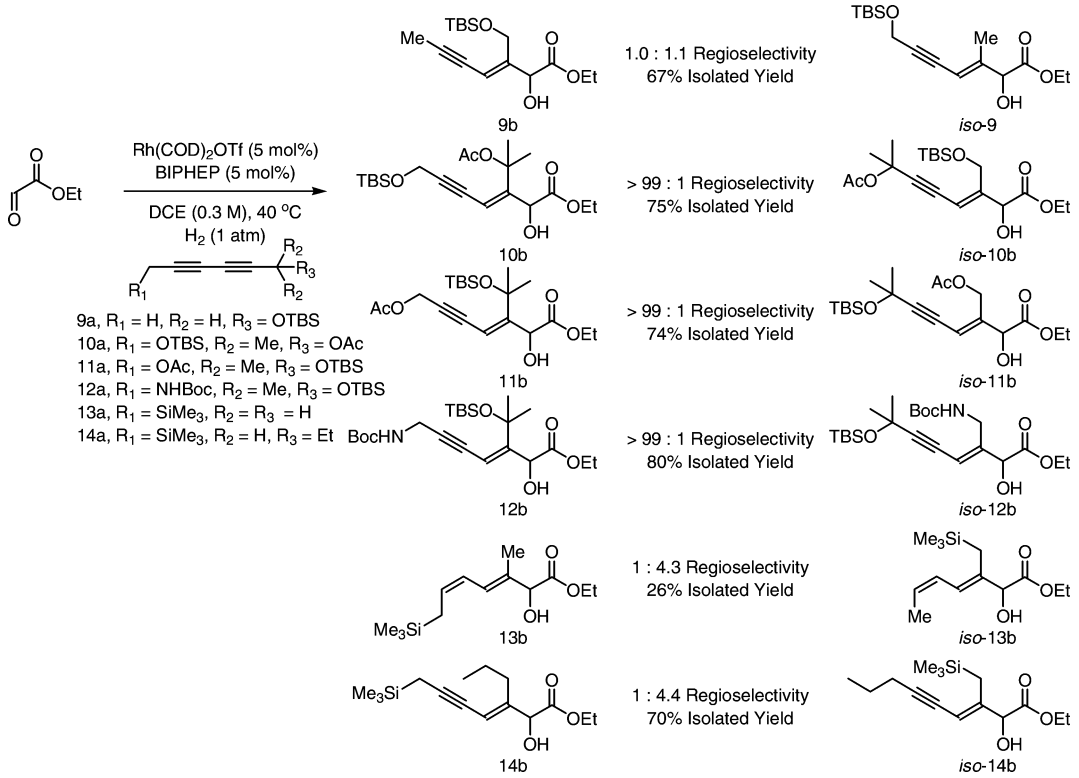
the *tert*-butyl moiety is substituted for silicon. The ethyl glyoxalate adduct *iso*-**5b** is obtained as a single regioisomer (Scheme 2).

To further challenge the hypothesis that the degree of alkyl substitution directs partitioning of regioisomeric coupling manifolds, 1,3-diynes **6a**−**8a** were prepared and coupled to ethyl glyoxalate under standard conditions. For diynes **6a**−**8a**, a *tert*-butyl moiety at one terminus of the diyne is held constant as the degree of alkyl substitution at the alternate diyne terminus is successively increased. In the coupling of diyne **6a**, which incorporates methyl and *tert*-butyl groups at the diyne termini, coupling occurs adjacent to the *tert*-butyl moiety to provide **6b** as a single regioisomer. Complete levels of regiocontrol are also observed using diyne **7a**, which incorporates *n*-propyl and *tert*-butyl groups at the diyne termini. Again, coupling occurs at the diyne terminus proximal to the *tert*-butyl moiety to provide **7b**. For the corresponding isopropyl diyne **8a**, tertiary and quaternary propargylic termini compete as regiocontrol elements. In the event, hydrogenative coupling of **8a** to ethyl glyoxalate delivers adducts **8b** and *iso*-**8b** in a 5:1 ratio, respectively. This result underscores remarkable sensitivity to the degree of alkyl substitution at the propargylic center in terms of contrasteric regiocontrol (Scheme 2).

The effect of heteroatom substitution at the propargylic position *vis-à-vis* partitioning of regioisomeric coupling manifolds is probed through the coupling of 1,3-diynes **9a**−**13a** to ethyl glyoxalate under the aforementioned standard set of conditions. For 1,3-diyne **9a**, which incorporates methyl and silyloxymethyl substituents at the diyne termini, roughly equimolar quantities of regioisomeric coupling products **9b** and *iso*-**9b** are obtained. The 1,3-diyne **10a** embodies primary and tertiary propargylic alcohols protected as the silyl ether and acetate, respectively. For the related diyne **11a**, the position of the protecting groups is inverted. For both diynes **10a** and **11a**, coupling occurs at the more highly substituted propargylic terminus to provide **10b** and **11b**, respectively, with complete regiocontrol regardless of the protecting group. Analogous regioselectivity is observed in the coupling of diyne **12a**, which incorporates a primary propargyl amine protected as the Boc-carbamate and a tertiary propargylic alcohol protected as the silyl ether. The regiochemistry observed in the coupling of the (trimethylsilyl)methyl-substituted diynes **13a** and **14a** is especially noteworthy. A significant preference for coupling at the diyne termini proximal to the (trimethylsilyl)methyl moiety is observed. This preference persists even when the degree of alkyl substitution at the diyne termini is identical, as in the case of diyne **14a** (Scheme 3).

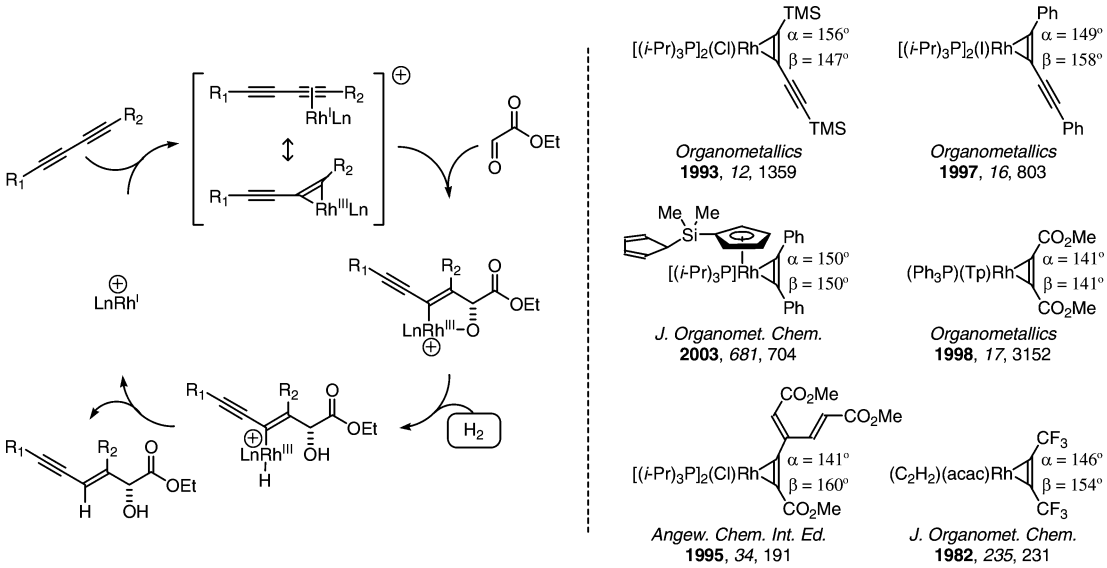
The observed regiochemistry may be reconciled with a catalytic mechanism involving alkyne−carbonyl oxidative coupling followed by hydrogenolytic cleavage of the resulting

Scheme 3. Probing the Effects of Heteroatom Substitution and the Degree of Alkyl Substitution at the Propargylic Position of 1,3-Diyne with Respect to Partitioning of Regioisomeric Reductive Coupling Manifolds[a]



[a] The regiochemical assignment of the major isomer is made on the basis of ^{13}C NMR data. Specifically, acetylenic carbon atoms bearing a phenyl moiety possess a characteristic ^{13}C NMR chemical shift at δ 122−123. As described in the Supporting Information, for adducts **10b**−**12b**, regiochemical assignment was corroborated via ^{1}H NMR of the corresponding Lindlar reduction products. For couplings involving diyne **13a**, over-reduction of the enyne-containing product occurs under the coupling conditions. Hence, the resulting dienes **13b** and *iso*-**13b** were isolated.

Scheme 4. Plausible Catalytic Cycle Involving Alkyne π-Complex Formation (left) and Alkyne Complexes of Rhodium Characterized by Single-Crystal X-ray Diffraction (right)



oxarhodacyclopentene (Scheme 4, left). Alternative catalytic mechanisms initiated by alkyne hydrometalation cannot be disqualified on the basis of available data. The proposed mechanism is consistent with the results of deuterium labeling[6a] and ESI mass spectrometric analysis of reaction mixtures.[10] In the latter case, the molecular ion corresponding to the mass of the putative oxarhodacyclopentene is the most abundant ion in the spectrum, suggesting that the oxarhodacyclopentene is the catalyst resting state.[11] Regio-determining oxarhodacyclopentene formation should be preceded by alkyne coordination in accordance with the Dewar−Chatt−Duncanson model.[12] Prior

(10) Jang, H.-Y. Development of Hydrogen-Mediated Carbon-Carbon Bond Formations. Ph.D. Thesis, University of Texas at Austin, Austin, TX, August 2006.

(11) For reviews covering the use of ESI mass spectrometric analysis as applied to the characterization of catalytic reaction mechanisms, see: (a) Plattner, D. *Int. J. Mass Specrom.* **2001**, *207*, 125. (b) Chen, P. *Angew. Chem., Int. Ed.* **2003**, *42*, 2832.

to the work described herein, we had speculated that alkyne coordination by low-valent rhodium should be driven by π-back-bonding and, hence, should occur at the most π-acidic position of the conjugated diyne.[6f] Single-crystal X-ray diffraction analysis of rhodium(I)−alkyne complexes does in fact reveal significant distortion of alkyne geometry by virtue of π-back-bonding (Scheme 4, right).[13] Additionally, theoretical treatments of metallacycle formation predict that nonsymmetric olefins oxidatively couple to furnish metallacycles with the largest lobe of the olefin π^* β to the metal.[14] The present studies suggest that π-complex stabilization via hyperconjugation with vicinal σ-bonds may play an even more important role in directing the regiochemistry of π-complexation and subsequent oxametallacycle formation. However, while the response to the degree of substitution at the propargylic position, as borne out by the regiochemistry of coupling, is unambiguous, invocation of hyperconjugation presupposes that coupling occurs from the more stable π-complex. The experiments herein cannot exclude a Curtin−Hammet type scenario, wherein coupling occurs from the less stable π-complex. Further, should hyperconjugative interactions be responsible for partitioning of regioisomeric coupling manifolds, it remains unclear whether the vicinal σ-bond serves as a donor or acceptor of electron density, and the relative hyperconjugative abilities of C−C and C−H σ-bonds is itself an issue that is still widely debated.[15,16] More detailed insight into the origins of regioselection in these couplings will be obtained through computational studies aimed at assessing the relative stabilities of regioisomeric alkyne π-complexes akin to those proposed in this account.

In summary, we report a survey of structurally related nonsymmetric 1,3-diynes **1a**−**14a** in hydrogenative couplings to ethyl glyoxalate. This study reveals unusual contrasteric regiocontrol, often with a complete preference for coupling at the diyne terminus proximal to the more substituted propargylic center. For diyne **14a**, where the degree of alkyl substitution at the diyne termini is identical, coupling proximal to the (trimethylsilyl)methyl moiety is observed, suggesting that electronic effects can also direct partitioning of regioisomeric coupling pathways. While the experiments herein cannot exclude a Curtin−Hammet type scenario, wherein coupling occurs from the less stable π-complex, the collective data suggest that hyperconjugation of vicinal bonds to the rhodium alkyne π-complex may play a key role in directing regioselectivity. Further insight into the origins of regioselection in these couplings will be obtained through computational studies involving modeling of regioisomeric alkyne π-complexes.

Experimental Section

General Procedures. Anhydrous solvents were transferred by an oven-dried syringe. Flasks were flame-dried and cooled under a stream of nitrogen. Dichloromethane (DCM) was distilled from calcium hydride. BIPHEP was used as received from Strem Chemicals. $[Rh(COD)_2]OTf$ was used as received from Umicore. Analytical thin-layer chromatography (TLC) was carried out using 0.2 mm commercial silica gel plates (DC-Fertigplatten Kieselgel 60 F_{254}). Preparative column chromatography employing silica gel was performed according to the method of Still. ^{1}H NMR spectra were recorded with a Varian Mercury 400 (400 MHz) or Unity+ 300 (300 MHz) spectrometer. Chemical shifts are reported in delta (δ) units, parts per million (ppm) downfield from trimethylsilane. Coupling constants are reported in hertz (Hz). Carbon-13 nuclear magnetic resonance (^{13}C NMR) spectra were recorded with a Varian Mercury 400 (100 MHz) or Unity+ 300 (75 MHz) spectrometer. Chemical shifts are reported in delta (δ) units, ppm relative to the center of the triplet at 77.0 ppm for deuteriochloroform. ^{13}C NMR spectra were routinely run with broadband decoupling. High-resolution mass spectra were obtained on a Micromass ZAB-E spectrometer. FT-IR spectra were obtained using a Nicolet Impact 410 spectrometer. Melting points were obtained on a Thomas-Hoover Unimelt apparatus and are uncorrected. Diynes **1a**,[6a] **2a**,[6a] **3a**,[17] **4a**,[6a] **5a**,[6f] and **6a**[18] were synthesized according to the previously reported procedures. Compounds **1b**, *iso*-**1b, 4b**, *iso*-**4b**, **7b**, and *iso*-**7b** were previously characterized in the reported literature.[6f]

General Procedure A: 1,3-Diyne Synthesis. To a reaction vessel containing H_2O (1.6 M with respect to substrate) and *n*-$BuNH_2$ (270 mol %) was added CuCl (2 mol %) at ambient temperature followed by addition of $NH_2OH\cdot HCl$ (2 mol %). The terminal alkyne (120 mol %) was added to the solution at ambient temperature. The resulting suspension was cooled with an ice bath. The bromoalkyne (100 mol %) was introduced to the reaction mixture in one portion. After all starting material was consumed as indicated by TLC, water was added. The reaction mixture was extracted repeatedly with Et_2O (3 × 10 mL), and the combined organic extracts were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography to provide the conjugated diyne.

General Procedure B: 1,3-Diyne Synthesis. To a reaction vessel containing 1-methyl-2-pyrrolidinone (0.2 M with respect to substrate) was added H_2O (1500 mol %) and *n*-$BuNH_2$ (280 mol %) at ambient temperature followed by the addition of CuCl (10 mol %) and $NH_2OH\cdot HCl$ (10 mol %). The reaction mixture was cooled with an ice bath and saturated with propyne gas over a period of 5 min. The corresponding bromoalkyne (100 mol %) was introduced in one portion. The reaction mixture was allowed to stir for 5 h under 1 atm of propyne. The product was extracted with Et_2O (3 × 10 mL), and the combined organic extracts were dried over Mg_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography to provide the conjugated diyne.

2,2-Dimethylnona-3,5-diyne (7a). The title compound was prepared in accordance with general procedure A in 78% yield as a clear oil. Column chromatography (SiO_2: neat hexane). ^{1}H NMR (400 MHz, $CDCl_3$): 2.23 (t, J = 7.0 Hz, 2H), 1.54 (q, J = 7.4, 7.0 Hz, 2H), 1.23 (s, 9H), 0.98 (t, J = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): 85.1, 78.6, 65.1, 63.8, 30.6, 27.9, 27.9, 21.8, 21.2, 13.5. HRMS: calcd for $C_{11}H_{17}$ [M + 1] 149.1330, found 149.1336. FTIR (neat): 2968, 2360, 1456, 1362, 1281, 913, 744 cm^{-1}.

2,2,7-Trimethylocta-3,5-diyne (8a). The title compound was prepared in accordance with general procedure A in 71% yield as

(12) (a) Dewar, M. J. S. *Bull. Soc. Chim. Fr.* **1951**, *18*, C71. (b) Chatt, J.; Duncanson, L. A. *J. Chem. Soc.* **1953**, 2939. (c) Dewar, M. J. S.; Ford, G. P. *J. Am. Chem. Soc.* **1979**, *101*, 783.

(13) (a) Barlow, H. J.; Curl, G. M.; Russell, R. D.; Clark, R. G. *J. Organomet. Chem.* **1982**, *235*, 231. (b) Rappert, D.; Nurnberg, O.; Werner, H. *Organometallics* **1993**, *12*, 1359. (c) Werner, H.; Schafer, M.; Wolf, J.; Peters, K.; Georg Von Schnering, H. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 191. (d) Werner, H.; Gevert, O.; Haquette, P. *Organometallics* **1997**, *16*, 803. (e) Hill, F. A.; White, J. P. A.; Williams, J. D.; Wilton-Ely, D. E. T. J. *Organometallics* **1998**, *17*, 3152. (f) Stemfe, B.; Gevert, O.; Werner, H. *J. Organomet. Chem.* **2003**, *681*, 704. (g) Adams, J. C.; Connelly, G. N.; Emslie, J. H. D.; Hayward, D. O.; Manson, T.; Orpen, G.; Rieger, P. *Dalton Trans.* **2003**, 2835.

(14) Stockis, A.; Hoffman, R. *J. Am. Chem. Soc.* **1980**, *102*, 2952.

(15) For leading references that encompass discussion of the relative abilities of C−C and C−H σ-bonds to stabilize positive charge via hyperconjugation, see: (a) Apeloig, Y.; Arad, D. *J. Am. Chem. Soc.* **1985**, *107*, 5285. (b) Spinello, M.; White, J. M. *Org. Biomol. Chem.* **2003**, *1*, 3094. (c) Alabugin, I. V.; Manoharan, M. *J. Org. Chem.* **2004**, *69*, 9011.

(16) Dewar, M. J. S. *Hyperconjugation*; Ronald Press Co.: New York, 1962.

(17) Egan, W.; Tang, R.; Zon, G.; Mislow, K. *J. Am. Chem. Soc.* **1971**, *93*, 6205.

(18) Chwang, T. L.; West, R. *J. Am. Chem. Soc.* **1973**, *95*, 3324.

a clear oil. Column chromatography (SiO_2: neat hexane). ^1H NMR (400 MHz, $CDCl_3$): δ 2.66−2.56 (m, 1H), 1.23 (s, 9H), 1.18 (d, $J = 6.8$ Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 85.7, 83.6, 64.2, 63.7, 30.5, 27.8, 22.5, 20.9. HRMS: calcd for $C_{11}H_{17}$ [M + 1] 149.1330, found 149.1333. FTIR (neat): 2970, 2929, 1455, 1362, 1278, 1189, 908 cm^{-1}.

***tert*-Butyl(hexa-2,4-diynoxy)dimethylsilane (9a).** The title compound was prepared in accordance with general procedure B in 57% yield as a clear oil. Column chromatography (SiO_2: neat hexane). ^1H NMR (400 MHz, $CDCl_3$): δ 4.32 (s, 2H), 1.90 (s, 3H), 0.87 (s, 9H), 0.09 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 76.4, 73.5, 69.9, 63.8, 52.0, 25.7, 18.2, 4.2, −5.2. HRMS: calcd for $C_{12}H_{21}OSi$ [M + 1] 209.1362, found 209.1362. FTIR (neat): 2929, 2857, 2260, 1470, 1362, 1256, 1088, 837, 778 cm^{-1}.

6-Methylhepta-2,4-diyn-1-oxy-(*tert*-butyl)dimethylsilane-6-acetate (10a). The title compound was prepared in accordance with general procedure A in 66% yield as a clear oil. Column chromatography (SiO_2: EtOAc/hexanes, 5:95). ^1H NMR (400 MHz, $CDCl_3$): δ 4.36 (s, 2H), 2.02 (s, 3H), 1.66 (s, 6H), 0.89 (s, 9H), 0.11 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.9, 79.0, 78.7, 71.5, 68.6, 68.4, 51.9, 28.5, 25.6, 21.6, 18.1, −5.3. HRMS: calcd for $C_{16}H_{26}O_3Si$ [M + 1] 294.1651, found 294.1654. FTIR (neat): 2954, 2931, 2858, 2254, 2162, 1747, 1367, 1240, 1129, 1089, 1015, 838, 781 cm^{-1}.

6-Methylhepta-2,4-diynylacetate-6-oxy-(*tert*-butyl)dimethylsilane (11a). The title compound was prepared in accordance with general procedure A in 69% yield as a clear oil. Column chromatography (SiO_2, EtOAc/hexanes, 5:95). ^1H NMR (400 MHz, $CDCl_3$): δ 4.67 (s, 2H), 2.03 (s, 3H), 1.40 (s, 6H), 0.79 (s, 9H), 0.09 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.8, 84.7, 72.9, 70.5, 66.7, 66.4, 52.2, 32.4, 25.5, 20.5, 17.7, −3.1. HRMS: calcd for $C_{16}H_{27}O_3Si$ [M + 1] 295.1729, found 295.1732. FTIR (neat): 2931, 2857, 2255, 2160, 1754, 1472, 1371, 1360, 1219, 1170, 1039, 838, 777 cm^{-1}.

***tert*-Butyl 6-methylhepta-2,4-diynylcarbamate-6-oxy-(*tert*-butyl)dimethylsilane (12a).** The title compound was prepared in accordance with general procedure A in 78% yield as a light yellow oil. Column chromatography (SiO_2, EtOAc/hexanes, 1:9). ^1H NMR (400 MHz, $CDCl_3$): δ 4.70 (br s, 1H), 4.02 (d, $J = 4.0$ Hz, 2H), 1.46 (s, 9H), 1.45 (s, 6H), 0.85 (s, 9H), 0.16 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.0, 83.1, 80.1, 75.7, 67.2, 67.1, 66.5, 32.5, 31.0, 28.2, 25.6,17.8, −3.1. HRMS: calcd for $C_{19}H_{33}NO_3Si$ [M + 1] 352.23079, found 352.23025. FTIR (neat): 3340, 2981, 2930, 2857, 1694, 1519, 1367, 1252, 1168, 1041, 936, 838, 777 cm^{-1}.

Hexa-2,4-diynyltrimethylsilane (13a). The title compound was prepared in accordance with general procedure B in 17% yield as a clear oil. Column chromatography (SiO_2: neat pentane). ^1H NMR (400 MHz, $CDCl_3$): δ 1.88 (s, 3H), 1.53 (s, 2H), 0.1 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 76.7, 75.3, 65.1, 63.9, 7.8, 4.2, −2.0. HRMS: calcd for $C_9H_{14}Si$ [M + 1] 150.0886, found 150.0869. FTIR (neat): 2987, 2360, 913, 744 cm^{-1}.

Trimethyl(octa-2,4-diynyl)silane (14a). The title compound was prepared in accordance with general procedure B in 52% yield as a clear oil. Column chromatography (SiO_2: neat hexane). ^1H NMR (400 MHz, $CDCl_3$): δ 2.22 (t, $J = 7.2$ Hz, 2H), 1.59−1.49 (m, 4H), 0.98 (t, $J = 7.2$ Hz, 3H), 0.12 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 76.0, 75.8, 65.9, 63.9, 21.9, 21.2, 13.4, 7.8, −2.0. HRMS: calcd for $C_{11}H_{19}Si$ [M + 1] 179.1256, found 179.1250. FTIR (neat): 2961, 2934, 2875, 2248, 2142, 1457, 1339, 1250, 1137, 851, 699 cm^{-1}.

General Procedure C: Reductive Coupling. To a reaction vessel containing ethyl glyoxylate (100 mol %) and 1,3-diyne (200 mol %) in dichloroethane (0.3 M) at ambient temperature was added $Rh(COD)_2OTf$ (5 mol %) and BIPHEP (5 mol %). The system was purged with argon gas and then purged with hydrogen gas, and the reaction mixture was allowed to stir at 40 °C under 1 atm of hydrogen. Once complete consumption of starting material was observed, the reaction mixture was evaporated onto silica gel and the coupling product was isolated by flash column chromatography.

(*E*)-Ethyl-2-hydroxy-3-phenylnon-3-en-5-ynoate (2b). The title compound was prepared in accordance with general procedure C in 72% yield as a clear oil. Column chromatography (SiO_2: EtOAc/hexane, 1:9). ^1H NMR (400 MHz, $CDCl_3$): δ 7.47−7.41 (m, 2H), 7.34−7.28 (m, 3H), 5.93 and 5.90 (major: t, $J = 2.4$ Hz, minor: s, 1H), 4.91 and 4.64 (major: d, $J = 5.6$ Hz, minor: d, $J = 5.6$ Hz, 1H), 4.26 and 4.12 (major: m, minor: m, 2H), 3.29 and 3.24 (major: d, $J = 5.2$ Hz, minor: d, $J = 5.2$ Hz, 1H), 2.43 and 2.18 (major: dt, $J = 6.8$, 2.4 Hz, minor: m, 2H), 1.57 and 1.43 (major: m, minor: m, 2H), 1.31 and 1.10 (major: t, $J = 7.2$ Hz, minor: t, $J = 7.2$ Hz, 3H), 0.98 and 0.84 (major: t, $J = 7.2$ Hz, minor: t, $J = 7.2$ Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): major: δ 172.8, 146.9, 136.5, 131.3, 128.5, 127.8, 111.6, 96.1, 77.7, 74.5, 62.1, 21.8, 21.5, 13.8, 13.3; minor: δ 173.2, 150.9, 128.3, 128.1, 127.8, 123.4, 109.5, 94.8, 86.2, 73.7, 62.3, 32.2, 21.7, 14.2, 14.0. HRMS: calcd for $C_{17}H_{20}O_3$ [M + 1] 272.1412, found 272.1412. FTIR (neat): 3470, 2922, 2850, 1730, 1463, 1204, 1093, 1020, 756, 697 cm^{-1}.

(*E*)-Ethyl-2-hydroxy-3-isopropyl-6-phenylhex-3-en-5-yonate (*iso*-3b). The title compound was prepared in accordance with general procedure C in 69% yield as a clear oil. Column chromatography (SiO_2: EtOAc/hexane, 1:9). ^1H NMR (400 MHz, $CDCl_3$): δ 7.44−7.42 (m, 2H), 7.33−7.30 (m, 3H), 5.80 (s, 1H), 4.62 (d, $J = 6.0$ Hz, 1H), 4.26 (q, $J = 7.2$ Hz, 2H), 3.24 (d, $J = 6.0$ Hz, 1H), 3.01−2.90 (m, 1H), 1.32−1.24 (m, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.5, 156.2, 131.1, 128.3, 128.2, 123.4, 108.5, 96.3, 86.1, 72.9, 62.2, 30.8, 21.0, 20.5, 14.0. HRMS: calcd for $C_{17}H_{21}O_3$ [M + 1] 273.1491, found 273.1494. FTIR (neat): 3480, 2965, 1732, 1490, 1252, 1209, 1103, 1021, 862, 756, 690 cm^{-1}.

(*E*)-Ethyl *tert*-butyl-2-hydroxyhept-3-en-5-ynoate (6b). The title compound was prepared in accordance with general procedure C in 60% yield as a clear oil. Column chromatography (SiO_2: EtOAc/hexane, 1:9). ^1H NMR (400 MHz, $CDCl_3$): δ 5.54 (q, $J = 2.6$ Hz, 1H), 4.46 (s, 1H), 4.21 (q, $J = 7.2$ Hz, 2H), 3.02 (s, 1H), 1.97 (d, $J = 2.6$ Hz, 3H), 1.30 (s, 9H), 1.26 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.2, 156.1, 110.1, 95.6, 77.4, 72.9, 62.0, 36.3, 29.5, 14.0, 4.6. HRMS calcd for $C_{13}H_{21}O_3$ [M + 1] 225.1491, found 225.1492. FTIR (neat): 3477, 2958, 2915, 1731, 1480, 1363, 1214, 1108, 1065, 862 cm^{-1}.

(*E*)-Ethyl 3-*tert*-butyl-2-hydroxynon-3-enynoate (7b). The title compound was prepared in accordance with general procedure C in 57% yield as a clear oil. Column chromatography (SiO_2: EtOAc/hexane, 1:9). ^1H NMR (400 MHz, $CDCl_3$): 5.57 (s, 1H), 4.65 (d, $J = 5.5$ Hz, 1H), 4.22 (q, $J = 7$ Hz, 2H), 3.00 (d, $J = 5.5$ Hz, 1H), 2.31 (t, $J = 6.85$ Hz, 2H), 1.55 (q, $J = 7.2$ Hz, 2H), 1.31 (s, 9H), 1.27 (t, $J = 7.2$ Hz, 3H), 0.97 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): 174.2, 156.0, 110.3, 100.2, 78.5, 76.7, 73.0, 62.0, 36.3, 29.5, 21.9, 21.8, 14.1, 13.6. HRMS: calcd for $C_{15}H_{25}O_3$ [M + 1] 253.1802, found 253.1804. FTIR (neat): 3476, 2961, 2871, 1733, 1463, 1362, 1214, 1055, 1026, 861 cm^{-1}.

(*E*)-Ethyl 3-*tert*-butyl-2-hydroxy-7-methyloct-3-en-5-ynoate (8b). The title compound was prepared in accordance with general procedure C in 57% yield as a clear oil. Column chromatography (SiO_2: EtOAc/hexane, 1:9). ^1H NMR (400 MHz, $CDCl_3$): δ 5.58 and 5.54 (major: d, $J = 2.4$ Hz, minor: s, 1H), 4.68 and 4.53 (major: d, $J = 5.6$ Hz, minor: d, $J = 5.6$ Hz, 1H), 4.27−4.21 (m, 2H), 3.05 and 3.01 (major: d, $J = 5.2$ Hz, minor: d, $J = 6.0$ Hz, 1H), 2.81 and 2.72 (major: m, minor: m, 1H), 1.33 and 1.25 (major: s, minor: s, 9H), 1.29 and 1.20 (major: t, $J = 7.2$ Hz, minor: t, $J = 6.8$ Hz, 3H), 1.19 and 1.05 (major: d, $J = 6.8$ Hz, minor: d, $J = 11.2$ Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): major: δ 174.2, 156.1, 110.2, 105.3, 77.7, 72.9, 62.0, 36.3, 29.4, 22.5, 21.5, 14.0; minor: δ 173.7, 154.2, 109.2, 105.9, 77.3, 73.2,

62.1, 30.7, 30.3, 20.6, 20.4, 14.0. HRMS: calcd for $C_{15}H_{25}O_3$ [M + 1] 253.1804, found 253.1808. FTIR (neat): 3477, 2963, 2922, 2850, 1732, 1463, 1362, 1213, 1059, 863 cm^{-1}.

(*E*)-Ethyl 2-hydroxy-3-methylhept-3-en-5-ynoate-7-hydroxy-(*tert*-butyl)dimethylsilane (*iso*-9b). The title compound was prepared in accordance with general procedure C in 67% yield as a clear oil. The regioisomers were chromatographically separated (SiO_2: EtOAc/hexane, 1:9). ^1H NMR (400 MHz, $CDCl_3$): δ 5.68 (s, 1H), 4.52 (d, J = 5.3 Hz, 1H), 4.45 (s, 2H), 4.23 (q, J = 7.2 Hz, 2H), 3.17 (d, J = 5.3 Hz, 1H), 1.85 (s, 3H), 1.27 (t, J = 7.2 Hz, 3H), 0.90 (s, 9H), 0.10 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.9, 146.3, 109.2, 93.3, 81.3, 74.7, 62.4, 52.2, 25.8, 18.3, 15.0, 14.0, −5.1. HRMS: calcd for $C_{16}H_{29}O_4Si$ [M + 1] 313.1835, found 313.1837. FTIR (neat): 3498, 2930, 2857, 1732, 1472, 1368, 1255, 1082, 837, 778 cm^{-1}. Minor (**9b**). ^1H NMR (400 MHz, $CDCl_3$): δ 5.59 (s, 1H), 4.61 (d, J = 6.8 Hz, 1H), 4.53 (s, 2H), 4.23 (q, J = 12.0 Hz, 1H), 4.46 (d, J = 12.0 Hz, 1H), 4.24 (dq, J = 10.6, 7.2 Hz, 1H), 4.14 (dq, J = 10.6, 7.2 Hz, 1H), 3.56 (d, J = 6.8 Hz, 1H), 1.97 (s, 3H), 1.25 (t, J = 7.2 Hz, 3H), 0.88 (s, 9H), 0.06 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.8, 146.9, 110.7, 92.9, 75.3, 73.2, 61.7, 61.2, 25.8, 18.3, 14.1, 4.4, −5.5. HRMS: calcd for $C_{16}H_{29}O_4Si$ [M + 1] 313.1835, found 313.1837. FTIR (neat): 3505, 2930, 2857, 1737, 1471, 1252, 1076, 838, 778 cm^{-1}.

(*Z*)-Ethyl 3-(2-acetoxypropan-2-yl)-2-hydroxyhept-3-en-5-ynoate-7-hydroxy-(*tert*-butyl)dimethylsilane (10b). The title compound was prepared in accordance with general procedure C in 75% yield as a clear oil. Column chromatography (SiO_2: EtOAc/hexane, 1:9). ^1H NMR (400 MHz, $CDCl_3$): δ 5.71 (t, J = 2.0 Hz, 1H), 4.66 (d, J = 4.8 Hz, 1H), 4.47 (d, J = 2.0 Hz, 2H), 4.28−4.22 (m, 2H), 3.42 (d, J = 5.2 Hz, 1H), 2.00 (s, 3H), 1.81 (s, 3H), 1.78 (s, 3H), 1.30 (t, J = 7.2 Hz, 3H), 0.90 (s, 9H), 0.11 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.6, 169.8, 153.2, 110.3, 98.1, 82.3, 80.6, 73.9, 61.8, 52.1, 26.3, 26.0, 25.7, 21.5, 18.2, 14.1, −5.2. HRMS: calcd for $C_{20}H_{34}O_6Si$ [M + 1] 398.2125, found 398.2127. FTIR (neat): 3466, 2954, 2857, 1740, 1472, 1368, 1254, 1147, 1081, 837, 778 cm^{-1}.

(*Z*)-Ethyl 7-acetoxy-2-hydroxy-(*tert*-butyl)dimethylsilanepropan-2-yl-hept-3-en-5-ynoate (11b). The title compound was prepared in accordance with general procedure C in 74% yield as a clear oil. Column chromatography (SiO_2: EtOAc/hexane, 1:9). ^1H NMR (400 MHz, $CDCl_3$): δ 5.56 (t, J = 2.0 Hz, 1H), 4.83 (d, J = 2.0 Hz, 2H), 4.69 (d, J = 8.8 Hz, 1H), 4.21 (q, J = 7.2 Hz, 2H), 3.67 (d, J = 8.8 Hz, 1H), 2.10 (s, 3H), 1.71 (s, 3H), 1.69 (s, 3H), 1.29 (t, J = 7.2 Hz, 3H), 0.91 (s, 9H), 0.19 (s, 3H), 0.12 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.3, 170.1, 159.7, 106.5, 91.9, 83.0, 78.3, 74.6, 61.4, 52.6, 30.0, 29.3, 25.9, 20.5, 18.0, 14.0, −1.7, −2.0. HRMS: calcd for $C_{20}H_{34}O_6Si$ [M + 1] 398.2125, found 398.2126. FTIR (neat): 3479, 2933, 2857, 1748, 1361, 1221, 1162, 1025, 830, 775 cm^{-1}.

***tert*-Butyl (*Z*)-6-(ethoxycarbonyl)-6-hydroxy-5-(2-hydroxy-(*tert*-butyl)dimethylsilanepropan-2-yl)hex-4-2-ynylcarbamate (12b).** The title compound was prepared in accordance with general procedure C in 80% yield as a light yellow oil. Column chromatography (SiO_2: EtOAc/hexane, 1:9). ^1H NMR (400 MHz, $CDCl_3$): δ 5.51 (t, J = 2.0 Hz, 1H), 4.70 (s, 1H), 4.66 (d, J = 8.4 Hz, 1H), 4.21 (q, J = 7.2 Hz, 2H), 4.07 (d, J = 3.6 Hz, 2H), 3.68 (d, J = 8.8 Hz, 1H), 1.71 (s, 3H), 1.69 (s, 3H), 1.45 (s, 9H), 1.28 (t, J = 7.2 Hz, 3H), 0.91 (s, 9H), 0.19 (s, 3H), 0.12 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.5, 158.5, 155.2, 107.1, 94.7, 79.9, 79.2, 78.4, 74.9, 61.3, 30.1, 29.3, 28.2, 26.0, 18.0, 14.0, −1.7, −2.0. HRMS: calcd for $C_{23}H_{40}NO_6Si$ [M − 1] 454.2625, found 454.2626. FTIR (neat): 3365, 2977, 2931, 2857, 1721, 1698, 1506, 1365, 1252, 1162, 1028, 835, 775 cm^{-1}.

(3*Z*,5*Z*)-Ethyl 2-hydroxy-3-((trimethylsilyl)methyl)hepta-3,5-dienoate) (*iso*-13b). The title compound was prepared in accordance with general procedure C in 20% yield as a clear oil. The regioisomers were chromatographically separated (SiO_2: EtOAc/hexane, 1:9). ^1H NMR (400 MHz, $CDCl_3$): δ 6.29 (d, J = 11.5 Hz, 1H), 6.05 (t, J = 10.9 Hz, 1H), 5.51 (dt, J = 10.9, 7 Hz, 1H), 4.46 (d, J = 6.3 Hz, 1H), 4.27−4.17 (m, 2H), 3.04 (d, J = 6 Hz, 1H), 1.72 (m, 4H), 1.63 (d, J = 14 HZ, 1H), 1.27 (t, J = 7 Hz, 3H), 0.03 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.9, 136.8, 126.3, 125.4, 119.7, 76.7, 75.7, 61.9, 19.5, 14.1, 13.4, −0.6. HRMS calcd for $C_{13}H_{25}O_3Si$ [M + 1] 257.1573, found 257.1569. FTIR (neat): 3509, 2954, 2360, 1729, 1248, 1207, 1097, 853, 725 cm^{-1}. Minor (**13b**). ^1H NMR (400 MHz, $CDCl_3$): 6.38 (d, J = 10.7 Hz, 1H), 6.12 (t, J = 11.2 Hz, 1H), 5.68 (q, J = 10.7 Hz, 1H), 5.57 (d, J = 6.2 Hz, 1H), 4.24 (q, J = 7.2 Hz, 2H), 3.17 (d, J = 6.4 Hz, 1H), 1.72 (m, 2H), 1.36 (t, J = 7.2 Hz, 3H), 1.31 (s, 3H), 0.02 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.9, 131.8, 130.6, 124.6, 121.5, 62.0, 29.4, 19.7, 14.1, −1.75. HRMS: calcd for $C_{13}H_{25}O_3Si$ [M + 1] 257.1573, found 257.1569. FTIR (neat): 3512, 2948, 2360, 1737, 1232, 1075, 864, 725 cm^{-1}.

(*Z*)-Ethyl 2-hydroxy-3-((trimethylsilyl)methyl)non-3-en-5-ynoate (*iso*-14b). The title compound was prepared in accordance with general procedure C in 70% yield as a clear oil. The regioisomers were chromatographically separated (SiO_2: EtOAc/hexane, 1:9). ^1H NMR (400 MHz, $CDCl_3$): δ 5.47 (s, 1H), 4.46 (d, J = 6.0 Hz, 1H), 4.28−4.18 (m, 2H), 3.07 (d, J = 6.0 Hz, 1H), 2.31 (dt, J = 7.2, 2.4 Hz, 2H), 1.88 (dd, J = 41.6, 12.8 Hz, 2H), 1.59−1.50 (m, 2H), 1.28 (t, J = 7.2 Hz, 3H), 0.99 (t, J = 7.2 Hz, 3H), 0.08 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.2, 148.4, 105.4, 95.8, 78.4, 74.4, 62.2, 22.2, 22.0, 21.6, 14.0, 13.5, −0.5. HRMS: calcd for $C_{15}H_{27}O_3Si$ [M + 1] 283.1729, found 283.1730. FTIR (neat): 3504, 2960, 1732, 1248, 1202, 1105, 1019, 857 cm^{-1}. Minor (**14b**). ^1H NMR (400 MHz, $CDCl_3$): δ 5.66−5.65 (m, 1H), 4.55 (d, J = 5.6 Hz, 1H), 4.30−4.17 (m, 2H), 3.10 (d, J = 5.6 Hz, 1H), 2.31−2.27 (m, 2H), 1.66 (d, J = 2.4 Hz, 2H), 1.51−1.45 (m, 2H), 1.29 (t, J = 7.2 Hz, 3H), 0.92 (t, J = 7.2 Hz, 3H), 0.12 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.6, 147.8, 110.8, 94.2, 76.0, 73.9, 62.1, 31.9, 21.7, 14.1, 14.0, 8.3, −2.0. HRMS: calcd for $C_{15}H_{27}O_3Si$ [M + 1] 283.1729, found 283.1729. FTIR (neat): 3500, 2959, 2203, 1731, 1464, 1249, 1205, 1094, 851 cm^{-1}.

General Procedure D: Hydrogenation Using Lindlar's Catalyst. Quinoline (50 mol %) and the desired enyne (100 mol %) were dissolved in dry dichloromethane (0.07 M). Lindlar's catalyst (5 wt %, 20 mol %) was added, and the resulting suspension was stirred at ambient temperature under 1 atm of hydrogen gas until complete consumption of substrate was observed by TLC analysis. The reaction mixture was filtered through a pad of Celite with the aid of dichloromethane. The filtrate was evaporated under reduced pressure. The residue was subjected to flash column chromatography to provide the product of hydrogenation.

(3*Z*,5*Z*)-Ethyl 3-(2-acetoxypropan-2-yl)-2,7-dihydroxy-7-(*tert*-butyl)dimethylsilane-3,5-dienoate (Lindlar reduction of 10b). The title compound was prepared in accordance with general procedure D in 90% yield as a clear oil. Column chromatography (SiO_2: EtOAc/hexane, 1:9). ^1H NMR (400 MHz, $CDCl_3$): δ 6.50 (tt, J = 11.2, 1.6 Hz, 1H), 6.30 (d, J = 13.2 Hz, 1H), 5.69 (ddt, J = 11.2, 6.4, 1.2 Hz, 1H), 4.79 (d, J = 4.0 Hz, 1H), 4.35 (dd, J = 6.4, 1.6 Hz, 2H), 4.26 (q, J = 7.2 Hz, 2H), 3.68 (d, J = 4.0 Hz, 1H), 1.98 (s, 3H), 1.68 (s, 3H), 1.65 (s, 3H), 1.30 (t, J = 7.2 Hz, 3H), 0.89 (s, 9H), 0.07 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.8, 170.1, 141.5, 135.3, 125.4, 123.4, 81.2, 74.0, 61.5, 59.0, 27.7, 27.6, 25.8, 21.4, 18.2, 14.1, −5.2. HRMS: calcd for $C_{20}H_{37}O_6Si$ [M + 1] 401.2359, found 401.2363. FTIR (neat): 3445, 2930, 2857, 1739, 1367, 1253, 1133, 1096, 1018, 838, 779 cm^{-1}.

(3*Z*,5*Z*)-Ethyl 7-acetoxy-2-hydroxy-(*tert*-butyl)dimethylsilane-3-(2-hydroxypropan-2-yl)hepta-3,5-dienoate (Lindlar reduction of 11b). The title compound was prepared in accordance with general procedure D in 96% yield as a clear oil. Column chromatography (SiO_2: EtOAc/hexane, 1:9). ^1H NMR (400 MHz, $CDCl_3$): δ 6.62 (dt, J = 11.2, 0.8 Hz, 1H), 6.19 (d, J = 12.0 Hz, 1H), 5.64 (ddt, J = 11.2, 6.8, 0.8 Hz, 1H), 4.75 (dd, J = 6.8, 1.2

Hz, 2H), 4.71 (d, $J = 7.6$ Hz, 1H), 4.23 (q, $J = 7.2$ Hz, 2H), 3.54 (d, $J = 7.6$ Hz, 1H), 2.07 (s, 3H), 1.60 (s, 3H), 1.58 (s, 3H), 1.29 (t, $J = 7.2$ Hz, 3H), 0.90 (s, 9H), 0.18 (s, 3H), 0.11 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.2, 170.7, 148.1, 127.8, 126.5, 122.3, 75.7, 61.4, 59.7, 31.8, 31.2, 26.0, 20.8, 18.1, 14.0, −1.6, −1.9. HRMS: calcd for $C_{20}H_{37}O_6Si$ [M + 1] 401.2359, found 401.2360. FTIR (neat): 3489, 2955, 2856, 1741, 1478, 1365, 1229, 1162, 1028, 835, 774 cm^{-1}.

***tert*-Butyl (2*Z*,4*Z*)-6-(ethoxycarbonyl)-6-hydroxy-5-(2-hydroxypropan-2-yl)hexa-2,4-dienylcarbamate (Lindlar reduction of 12b).** The title compound was prepared in accordance with general procedure D in 83% yield as a light yellow oil. Column chromatography (SiO_2: EtOAc/hexane, 1:9). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.50 (t, $J = 11.6$ Hz, 1H), 6.18 (d, $J = 12.0$ Hz, 1H), 5.57−5.51 (m, 1H), 4.69 (d, $J = 7.2$ Hz, 1H), 4.58 (br s, 1H), 4.23 (q, $J = 7.2$ Hz, 2H), 3.93−3.87 (m, 2H), 3.58 (d, $J = 8.0$ Hz, 1H), 1.59 (s, 3H), 1.57 (s, 3H), 1.44 (s, 9H), 1.29 (t, $J = 7.2$ Hz, 3H), 0.90 (s, 9H), 0.18 (s, 3H), 0.11 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.3, 155.7, 147.3, 129.8, 126.3, 122.4, 79.4, 77.5, 75.9, 61.4, 37.2, 31.8, 31.1, 28.3, 26.0, 18.1, 14.1, −1.6, −1.9. HRMS: calcd for $C_{23}H_{43}NO_6Si$ [M + 1] 457.2860, found 457.2863. FTIR (neat): 3369, 2977, 2930, 2857, 1719, 1515, 1366, 1253, 1164, 1029, 835, 775 cm^{-1}.

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Supporting Information Available: Spectral data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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