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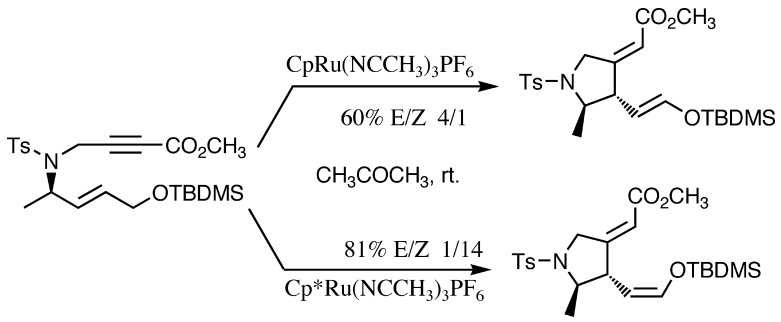

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Ruthenium-Catalyzed Enyne Cycloisomerizations. Effect of Allylic Silyl Ether on Regioselectivity

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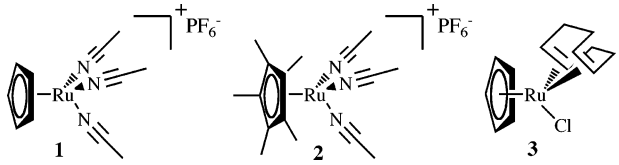
Abstract: The ruthenium-catalyzed cycloisomerization of 1,6- and 1,7-enynes substituted in the terminal allylic position with a *tert*-butyldimethylsilyl ether group emerges as an effective reaction to form unprecedented five- or six-membered rings possessing a geometrically defined enol silane. Straightforward synthetic access to a variety of achiral 1,6- and 1,7-enynes, as well as chiral ones, is presented. Ruthenium catalysts effect efficiently such single-step cycloisomerization at room temperature in acetone under neutral conditions. The cycloisomerization functions with (*E*) or (*Z*) 1,2-disubstituted alkenes. Parameters influencing the enol silane geometry are discussed. The level of selectivity depends on the alkyne substitution, the geometry of the double bond, and the nature of the catalyst. Furthermore, examples of stereoinduction are shown and lead to highly substituted carbo- and heterocycles with excellent diastereocontrol.

Introduction

The development of novel and effective cyclization methods constitutes a continuing challenge as five- and six-membered cycles are essential structural units widely found in biologically active molecules serving as pharmaceuticals or agrochemicals.[1] Besides the transition-metal-catalyzed ring-closing metathesis,[2] complementary intramolecular carbon−carbon bond-forming processes have recently emerged, offering new possibilities for the design and synthesis of cyclic templates. Among others, a number of cycloisomerizations of enynes have evolved, leading to a myriad of transition metal catalysts.[3] One of the main features of this reaction stems from the direct transformation of a linear precursor to a cyclic product without additional reactants and typically producing few byproducts. As such, the cycloisomerization process appears ideal in terms of synthetic efficiency and atom economy.[4] The nature of the catalyst determines the mechanistic pathway followed during the course of the process. Four mechanisms can be identified: (1) initial hydrometalation of the alkyne, followed by carbometalation of the olefin;[5] (2) initial formation of a metallacyclopentene, followed by β-hydrogen elimination;[6] (3) formation of a metallacyclopentene, followed by reductive elimination to form a cyclobutene that undergoes a conrotatory cycloreversion;[7] and (4) a metal alkylidene.[8]

During the past years, efforts in these laboratories have been focused on the discovery and development of new catalytic systems for the intermolecular coupling of alkenes and alkynes.[9] Through these studies we have shown that the alkene−alkyne coupling was greatly improved with the use of the cationic catalyst $CpRu(CH_3CN)_3^+PF_6^-$ (**1**)[10] (or $Cp^*Ru(CH_3CN)_3^+PF_6^-$, **2**), compared with the earlier complex **3**, which functioned only with monosubstituted alkenes.[11] The enhanced reactivity observed for complex **1** renders effective the intramolecular reaction between the alkene and alkyne partners (henceforth



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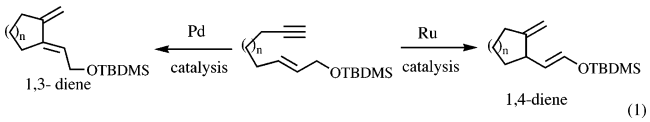
called cycloisomerization of 1,6- and 1,7-enynes) to form respectively five- and six-membered rings, through the intermediacy of a ruthenacyclopentene.[12] However, in the intriguing case of a 1,6-enynoate, the introduction of a quaternary center at the propargylic position completely changes the nature of the reaction and its mechanism. A seven-membered ring forms under equally mild conditions through a C−H insertion, generating a π-allylruthenium intermediate.[13]

Following this initial work, we considered the effect of heteroatom substituents, notably oxygen and nitrogen, at the allylic position to form enol and enamide derivatives in intermolecular reactions.[14] While the simple allyl system worked very well, extrapolating to more substituted allyl systems has proved difficult to date. As a result, we initiated studies involving an intramolecular process, namely one wherein the alkyne and the allyl silyl ether are tethered through various linkers. Such studies are important to provide a straightforward access to highly substituted carbo- and heterocycles and to extend further the scope of the ruthenium-catalyzed cycloisomerization of enynes.

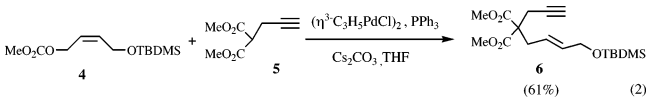
The formation of the cyclic template is accompanied with the concomitant formation of an enol silane. Because the geometry of the latter is crucial in influencing the stereochemical outcome of potential subsequent events, the gain of a geometrically defined enol silane remains of considerable importance. It is worth noting that the proposed ruthenium-catalyzed process allows only the formation of the 1,4-diene, whereas the related palladium-catalyzed cycloisomerization may produce both 1,3- and 1,4-dienes (eq 1).[15]



(1)

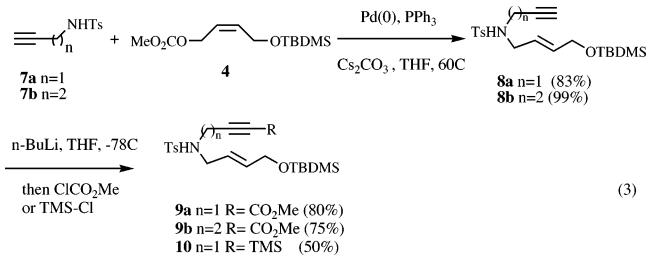
Preparation of Substrates

Different strategies were employed for the synthesis of enynes and enynoates featuring the required terminal allylic alcohol protected as a *tert*-butyldimethylsilyl ether. Palladium-catalyzed allylic alkylation[16] offers a rapid access to such entities. Thus, the carbonate **4**[17] was reacted with propargyl malonate **5** in the presence of 2.5 mol % of $(\eta^3\text{-}C_3H_5PdCl)_2$, 20 mol % of triphenylphosphine, and 2 equiv of cesium carbonate, to generate the enyne **6** in 61% isolated yield (eq 2).



(2)

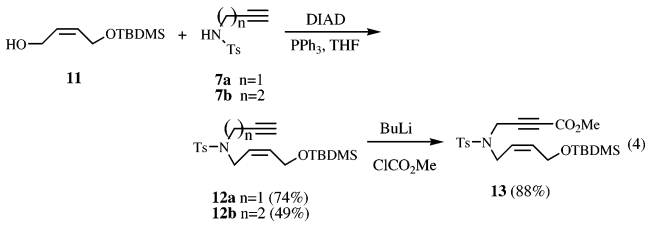
Subjection of propargyl and homopropargyl tosylamine **7a**[18] and **7b**[19] to similar reaction conditions afforded the corresponding 1,6- and 1,7-enynes **8a** and **8b** in high yield (eq 3).



(3)

The resulting products could be further derivatized. After deprotonation of the acetylide, the anion was trapped with methyl chloroformate (Cl-CO_2Me) or chlorotrimethylsilane (TMS-Cl) to give respectively enynoates **9a**, **9b** or TMS-alkyne **10**.[20]

The corresponding cis isomers were generated using a Mitsunobu-type reaction[21] to preserve the integrity of the alkene moiety. After monosilylation of *cis*-but-2-ene-1,4-diol,[22] the resulting alcohol **11** reacted with tosylamines **7a** or **7b** under typical Mitsunobu conditions (DIAD, PPh_3) to yield (*Z*)-olefins **12a** and **12b** in 74% and 49% yield.[23] Alkyne **12a** was subsequently transformed to its corresponding enynoate **13** using the aforementioned protocol (eq 4).



(4)

We then envisioned the preparation of enantiomerically pure enynes starting from (*S*)-ethyl lactate **14**. The chiral starting material was transformed to the corresponding α,β-unsaturated ester **15** using previously described procedures.[24] The protective group (TBDMS) was removed under acidic conditions (aqueous trifluoroacetic acid),[25] and the alcohol **16** was subsequently reacted in a Mitsunobu-type reaction (DIAD, PPh_3) using either tosylamine **7a** or **7b** to give the *R*-isomers **17a** and **17b**[26] in respectively 74% and 49% yield. Subjection of the resulting substances to an excess of DIBAL-H reduces the ester moiety

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(21) Mitsunobu, O. *Synthesis* **1981**, 1−28. Hughes, D. L. *Org. Prep. Proced. Int.* **1996**, *28*, 127−164.
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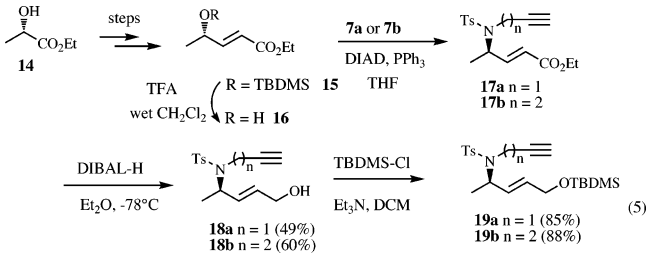
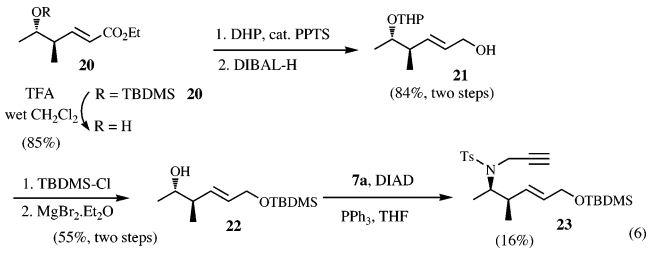
(23) The *Z*-stereochemistry was confirmed with the $J = 11$ Hz for the alkene protons and by direct comparison with the NMR data recorded for the corresponding *E*-isomers.
(24) Brandange, S.; Lindqvist, B. *Acta Chem. Scand.* **1985**, *B39*, 589592. Mulzer, J.; Funk, G. *Synthesis* **1995**, 101−112.
(25) For details on protective group manipulations, see: *Protective Groups in Organic Synthesis*, 3rd ed.; Greene, T. W., Wuts, P. G., Eds.; Wiley: New York, 1999.
(26) We assumed that the inversion of configuration normally proceeded without loss of the chiral information.

cleanly. The formed alcohols **18a** and **18b** were transformed to the enynes **19a** and **19b** in an acceptable overall yield (eq 5).



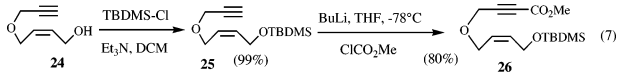
(5)

Enyne substrate **23** could also be obtained from the more elaborated α,β-unsaturated ester **20**.[27] The protecting group (TBDMS) was replaced by a tetrahydropyranyl ether (THP) in two steps, and the ester moiety was further reduced using DIBAL-H to provide the allylic alcohol **21**. The latter was reacted with TBDMS-Cl in the presence of triethylamine, and the chemoselective removal of the THP group ($MgBr_2$ in ether)[28] furnished the secondary alcohol **22**. A Mitsunobu-type reaction with tosylamine **7a** gave enyne **27** in an expected low 16% yield (due to the competing β-elimination of the intermediate phosphonium salt) (eq 6).



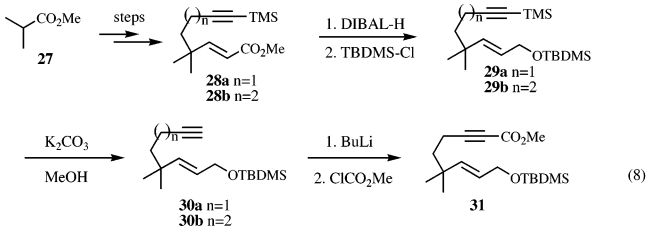
(6)

1,6-Enynes containing an oxygen atom in the linker were obtained using well-established chemistry. Mono-propargylation of *cis*-but-2-ene-1,4-diol gave allylic alcohol **24**,[29] which was subsequently protected as the silyl ether **25**. The terminal alkyne was then transformed to the corresponding methoxycarbonyl derivative **26** in standard fashion (eq 7).



(7)

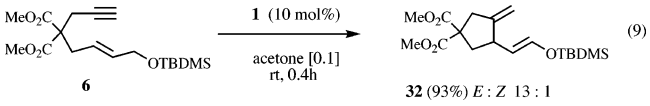
A *gem*-dialkyl-substituted substrate was constructed, starting by converting the ester **27** to the corresponding α,β-unsaturated esters **28a**,**b** in four steps.[30] The allylic silyl ethers **29a**,**b** were then obtained as already described (reduction and silylation). Finally, TMS-alkynes were treated with K_2CO_3 in methanol to yield enynes **30a**,**b**. Alkynoate **31** was also synthesized using the standard carboxymethylation protocol (eq 8).



(8)

Cycloisomerization

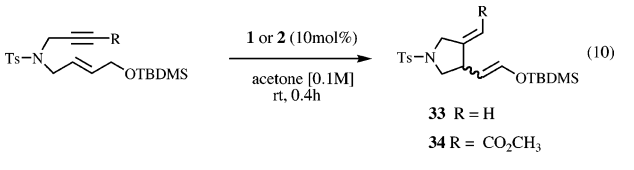
Our first attempt concerned the cycloisomerization of 1,6-enyne **6**. Reaction conditions that were successfully developed for the intermolecular version of this reaction, i.e., 10 mol % of catalyst **1** in acetone, but lowering the substrate concentration to 0.1 M, were used. After 20 min, the starting material was entirely consumed, and simple chromatography afforded the cyclic compound **32** in 93% yield as a 13:1 *E*:*Z* mixture of isomers. NMR analysis of the crude mixture revealed that 1,4-diene **32** was the only product formed. Indeed, no traces of 1,3-diene nor degradation products could be observed, demonstrating the mildness and the selectivity of the process. The *E*-geometry of the major silyl enol ether was characterized by $J = 12$ Hz for the vinyl hydrogens (compared to $J = 6$ Hz for the *Z*-geometry) (eq 9).[31] When a lower catalyst loading (5 mol % of **1)** was used, an incomplete conversion was observed after the same reaction time (20 min). Allowing the reaction to proceed for a longer time did not improve this result.



(9)

Using these conditions (10 mol % of catalyst in acetone [0.1 M]) as standard, linear precursors **8a**, **9a**, and **10** were cleanly converted to the five-membered-ring derivatives **33**, **34**, and **35** in good to excellent yields (eq 10, Table 1).

Table 1. Cycloisomerization to Pyrrolidine



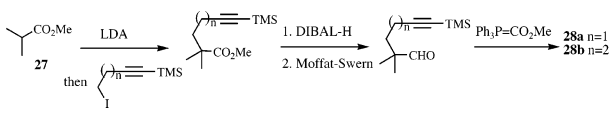
(10)

substrate	R	catalyst	yield	*E*:*Z*[a]
8a	H	**1**	**33**, 89%	>32:1
8a	H	**2**	**33**, 95%	12.5:1
9a	CO_2Me	**1**	**34**, 77%	2.4:1
9a	CO_2Me	**2**	**34**, 95%	1:5
10	TMS	**1**	**35**, 97%	32:1

[a] Measured by ^1H NMR.

Substrates **8a** and **10** afforded respectively the desired *N*-tosylpyrrolidines **33** and **35** with an excellent *E*:*Z* selectivity using the catalyst **1** (Cp ligand). On the other hand, compound **34** was obtained in a modest 2.4:1 ratio starting from enynoate

(27) Trost, B. M.; Metz, P.; Hane, J. T. *Tetrahedron Lett.* **1986**, *27*, 5691−5694.
(28) Kim, S.; Park, J. H. *Tetrahedron Lett.* **1987**, *28*, 439−442.
(29) Marco-Contelles, J. *Synth. Commun.* **1997**, *27*, 3163−3170.
(30) After alkylation of ester **27** with the corresponding iodide, esters moitey were transformed in two steps (reduction to the alcohol and then Moffat−Swern oxidation) to the aldehydes, which were subjected to an excess of carbomethoxytriphenylphosphorane to yield respectively **28a** or **28b**. See Supporting Information section for more details.

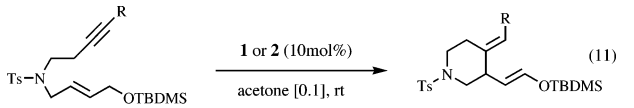


(31) These observations are consistent with the coupling constants we observed in the case of the intermolecular study; see ref 14.

9a. The same experiments were carried out with catalyst **2** (Cp* ligand). Unexpectedly, the use of the latter catalyst gave rise to significantly different results. The *E*:*Z* ratio for product **33** decreased somewhat, while an inversion of geometrical selectivity occurred in the case of **34**, wherein the Z-isomer predominated (*Z*:*E* 5:1).

Cyclization of **8b** and **9b** explores the effect of ring size as summarized in eq 11 and Table 2. The linear starting materials

Table 2. Cycloisomerization to Piperidine



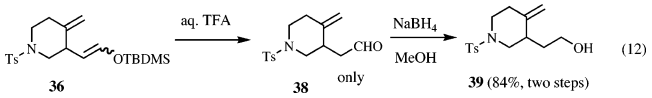
(11)

36 R = H
37 R = CO_2CH_3

substrate	R	catalyst	yield	*E*:*Z*[a]
8b	H	**1**	**36**, 99%	4:1
8b	H	**2**	**36**, –[c]	1:1
9b	CO_2Me	**1**	**37**, 94%	3:1[b]
9b	CO_2Me	**2**	**37**, 80%	1:5

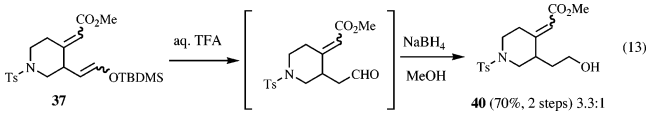
[a] Measured by ^{1}H NMR. [b] As a mixture with respect to the α,β-unsaturated ester that was obtained. [c] Low conversion.

were smoothly reacted at ambient temperature with the complex **1** as a catalyst to afford *N*-tosylpiperidine **36** and **37** in respectively 99% and 94% yield. In stark contrast with the selective formation of **33**, ^{1}H NMR showed a modest 4:1 selectivity in favor of the *E*-enol silane **36**, and the cyclic product **37** was recovered as a mixture of isomers. In the latter case, NMR data suggest that both the α,β-unsaturated ester and enol silane moieties were formed as geometrical mixtures (see Table 2). The estimated ratios were confirmed after hydrolysis of the silyl enol ethers in aqueous acid conditions (eqs 12 and 13). In the case of **36**, the hydrolysis led only to aldehyde **38**, which was reduced to the alcohol **39** (eq 12).[32] Performing the same



36 **38** **39** (84%, two steps) (12)

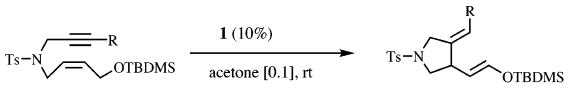
sequence with the cyclic compound **37** resulted in the formation of the alcohol **40** in a 3.3:1 ratio of isomers with respect to the α,β-unsaturated ester double bond (eq 13).



37 **40** (70%, 2 steps) 3.3:1 (13)

In contrast to the above results, using catalyst **2** to perform the cycloisomerization of the 1,7-enyne **8b** and enynoate **9b** provided a low conversion of derivative **36** in a poor yield and with no selectivity (1:1 ratio). On the other hand, precursor **9b** participated in the reaction to give the cyclic product **37** in a satisfying 80% yield. As observed in the case of the five-membered ring **9a**, the enol silane was formed mainly as the *Z*-isomer (5:1 ratio).

To study the influence of the alkene geometry of the substrate, *Z*-enynes **12a** and **13** were submitted to our standard conditions using 10 mol % of **1** in acetone at room temperature for 20 min. The corresponding five-membered-ring products **33** and **34** formed in respectively 96% and 63% yield (eq 14).[33] Even though enynes **8a** and **12a** gave rise to **33** in a similar selectivity, we noted that, in the case of the cyclic product **34**, the *E*:*Z* ratio jumped to 25:1 when *Z*-enyne **13** was used as a precursor.

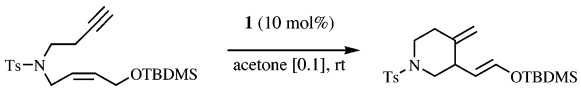


(14)

12a R = H
13 R = CO_2Me

33 (96%) only *E*
34 (63%) *E* : *Z* 25 : 1

Similarly, *Z*-enyne **8b**, when reacted in the presence of a catalytic amount of complex **1**, is transformed cleanly to the *N*-tosylpiperidine **36** with an improved 9:1 selectivity in favor of the *E*-enol silane (eq 15). The yield was slightly decreased in the latter case due to a lower conversion.

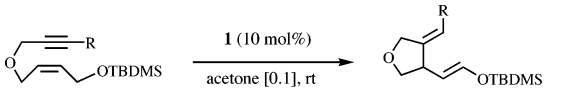


(15)

8b

36 (90% yield) *E* : *Z* 9 : 1

Other substrates characterized by a cis double bond also reacted cleanly to produce the corresponding cyclic products. Thus, enyne **25** and alkynoate **26** gave rise to the substituted tetrahydrofurans **41** and **42** respectively in good yield and excellent selectivity (eq 16).

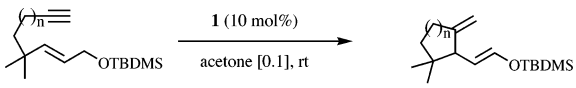


(16)

25 R = H
26 R = CO_2Me

41 R = H (80% yield) *E* : *Z* = 19 : 1
42 R = CO_2Me (83% yield) only *E*

Using the more sterically congested 1,6-enyne **30a**, the cycloisomerization took place accordingly to yield the substituted cyclopentane **43** in 93% yield as a single *E*-isomer (eq 17). Unexpectedly, the corresponding 1,7-enyne **30b** failed to



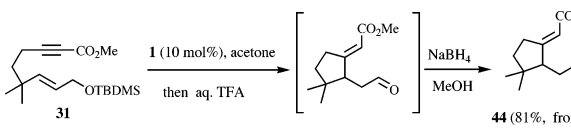
(17)

30a n = 1
30b n = 2

43 n = 1 (93% yield) only *E*
n = 2 no reaction

react under the same conditions, returning only the unchanged starting material. Raising the temperature to 60 °C did not lead to any reaction. Switching the solvent to DMF, still at 60 °C, gave rise to a mixture of compounds containing only a trace amount of a cyclic aldehyde, resulting from the hydrolysis of the enol silane.

Placing a carbomethoxy substituent on the alkyne terminus of **30a**, as in **31**, gave a mixture of products. An aqueous acidic treatment of the latter greatly simplified the mixture to deliver, after reduction of the resulting aldehyde with $NaBH_4$, the alcohol **44** in 81% yield for the three steps (eq 18).



31 **44** (81%, from **31**) (18)

(32) The aldehyde was further reduced to the alcohol to ensure the standard characterizations.

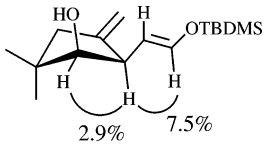
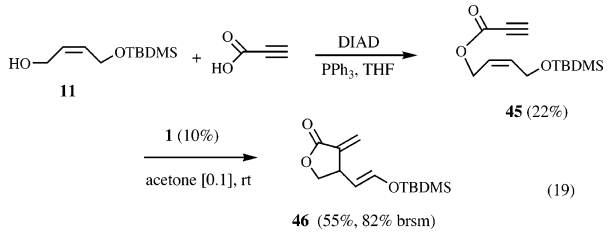


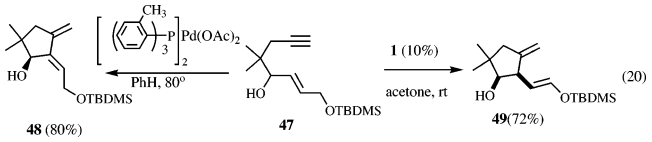
Figure 1. Relative stereochemistry as determined by NOE experiments.

The effect of reversing the polarity of the alkynoate as in ester **45**, readily obtained by a Mitsunobu process,[34] was examined (eq 19). The cycloisomerization was performed under our standard conditions (10 mol % **1** in acetone). Remarkably, the desired cyclic product **46** could be obtained in 55% yield (82% based on recovered starting material) as a single *E*-isomer. Thus, the effect of a highly activated terminal acetylenic hydrogen did not inhibit the reaction. This reaction serves as a convenient entry into α-methylene-*δ*-butyrolactones, important structural units of many bioactive natural products[35] such as anthecotuloide.[36]



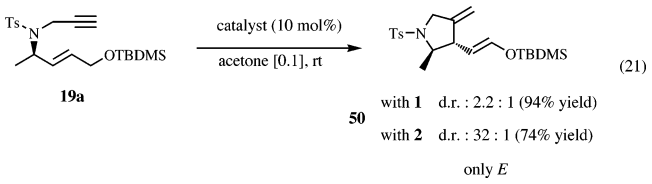
Diastereoselective Cycloisomerization

The diastereoselectivity of the cycloisomerization was also studied by employing substrates possessing stereogenic centers. To examine this point as well as to compare the selectivity between the Pd- and Ru-catalyzed cycloisomerizations, we initially employed enyne **47**, the substrate for our synthesis of sterepolide (eq 20), which produced the conjugated diene **48**



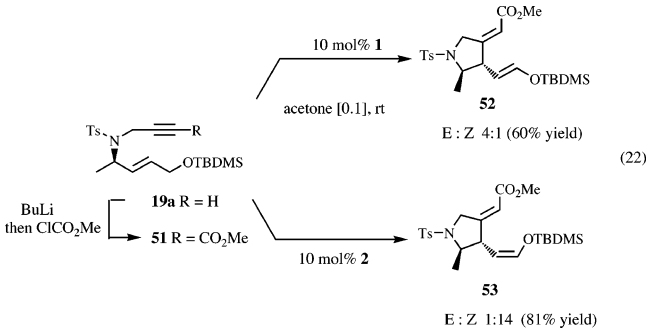
regioselectively with Pd catalysis.[37] In contrast, the Ru-catalyzed reaction affords the enol silane **49** in 72% yield as a single diastereomer (eq 20). The ability to form an enol silane in the presence of a free hydroxyl group was already demonstrated in the related intermolecular process. The cis relationship was ascertained by NOE experiments as illustrated in Figure 1.

The cycloisomerization of the enyne **19a** was carried out in our standard conditions, using both complexes **1** and **2** (eq 21). Using complex **1** as a catalyst gave rise to the trisubstituted *N*-tosylpyrrolidine **50** in 94% yield.

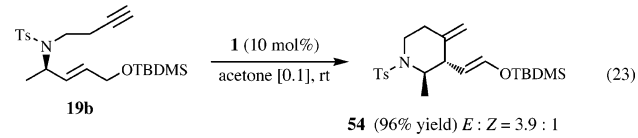


The enol silane moiety was formed as a unique *E*-isomer, but two diastereomers were observed by ^{1}H NMR (two doublets at 6.26 and 6.17 ppm exhibiting a $J = 11.9$ Hz), accounting for a 2.2:1 induction. Increasing the steric demands of the catalyts as in complex **2**, the product **50** was obtained in 74% yield,[34] almost as a single diastereomer. The minor isomer was detected only as a trace. The assignment of the trans relationship between the two groups was tentatively based on the observed coupling constant for the major diastereomer, $J_{2,3} = 8.5$ Hz. Further support comes from the chemical shift differences for the hydrogens of the terminal methylene group. Previous work established that the trans isomer had a smaller difference compared to the cis isomer.[38] The observation that the major isomer exhibited a $\Delta\delta$ of 0.07, whereas the minor had a $\Delta\delta$ of 0.14 ppm, is in good accord with the above assignment.

The effect of placing a substituent on the terminal alkyne was examined in the cycloisomerization of the alkynoate **51** (eq 22). Stereoinduction due to the methyl group was very high (>30:1) in both cases. Interestingly, the nature of the catalyst directly influenced the stereochemistry of the enol silane. Indeed, the enol silyl ether double bond processed mainly the *E* geometry as in **52** when complex **1** was used, but predominantly the Z geometry with complex **2**.



The cycloisomerization of the 1,7-enyne **19b** under our standard conditions gave rise to the expected *N*-tosylpiperidine **54** in 96% yield as a mixture of two isomeric enol silanes (*E*:*Z* 3.9:1) (eq 23). The 1,2 stereoinduction also turned out to be very high, only one diastereomer in each case being observed.



The impact of additional stereogenic centers was also examined. Treatment of the alkyne **23** under our standard conditions resulted in the consumption of the starting material within 5 min. Upon an acid treatment of the crude mixture, the aldehyde **55** was isolated in 65% yield after purification. For further characterization, the latter was reduced to the alcohol **56**. The selectivity with respect to the newly formed stereogenic center is excellent (only one isomer could be observed by ^{1}H

(33) The lower chemical yield is explained by a lower conversion.

(34) The purity of **45** is crucial for the success of the isomerization, since we have noticed that contaminants (presumably hydrazine derivatives due to the Mitsunobu reaction) poisoned the catalyst.

(35) For reviews, see: Hoffmann, H. M. R.; Rabe, J. *Angew. Chem., Int. Ed. Engl*. **1985**, *24*, 94−110.
(36) van Klink, J.; Becker, H.; Andersson, S.; Boland, W. *Org. Biomol. Chem.* **2003**, *1*, 1503−1508.
(37) Trost, B. M.; Chung, J. Y. L. *J. Am. Chem. Soc*. **1985**, *107*, 4586−4588.
(38) Cancho, Y.; Martin, J. M.; Martinez, M.; Llebaria, A.; Moreto, J. M.; Delgado, A. *Tetrahedron* **1998**, *54*, 1221−1232.

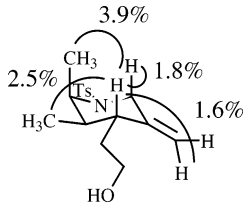
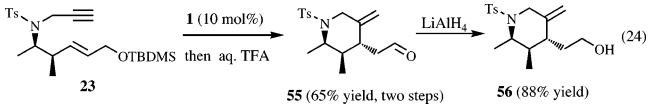


Figure 2. Assignment of the relative stereochemistry of substituted piperidine **56**.

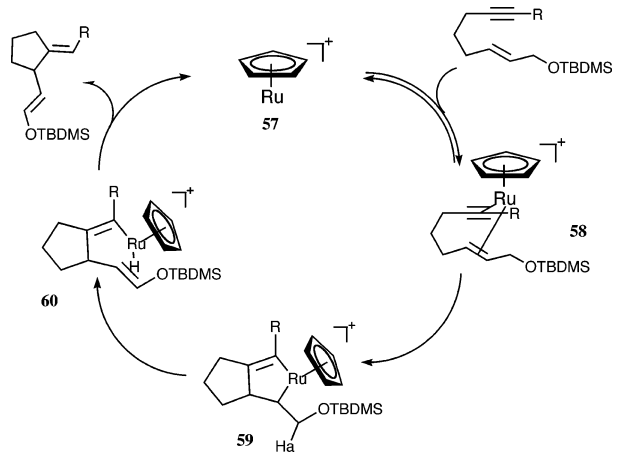
NMR) (eq 24). The trans relationship was established by NOE experiments (Figure 2).



Discussion

Studies on the ruthenium-catalyzed enyne cycloisomerization have demonstrated that the operative mechanism is directly dictated by the nature of the substrate. The 1,6- and 1,7-enynes normally react with ruthenium complexes to form a ruthenacyclopentene that evolves to form the corresponding five- or six-membered ring. On the other hand, a 1,6-enynoate containing a quaternary center next to the propargylic center gave rise to a seven-membered ring, presumably via a π-allyl ruthenium arising from a C−H insertion.[13] In our present study, substrate similarities suggest that the ruthenacyclopentene pathway should dominate. Thus, complexation of coordinatively unsaturated cyclopentadienylruthenium(2+) (**57**) to the enyne generates complex **58**. Tautomerization of the enyne provides the ruthenium(4+) metallacycle **59**, the product of an internal redox process. A β-hydrogen elimination of H_a forms the vinylruthenium(4+) hydride **60**, which subsequently undergoes a reductive elimination to regenerate the ruthenium(2+) catalyst and provides the 1,4-diene product (Scheme 1).

Scheme 1. Proposed Mechanism for the Ruthenium-Catalyzed Cycloisomerization of Enynes



To a large extent, the ruthenacycle mechanism accounts for the selectivity we have observed for the formation of the enol silane during the ruthenium-catalyzed cycloisomerization. In the case of enynoates **9a** and **13**, double-bond geometry isomers, a 10-fold increase of selectivity was observed for the formation of the major enol silane **34** (from 2.4 to 25:1 going from the *E*- to the *Z*-isomer). Starting from enyne **9a** (*E*-isomer), the intermediate ruthenacyclopentene **61** places the silyl ether group in a favorable pseudoequatorial position. On the other hand, starting from *Z*-enyne **13**, the same group orients in a pseudoaxial position in intermediate **62**. The following β-hydrogen elimination involves abstraction of that diastereotopic hydrogen (H_a or H_b) in a best position for overlap of the breaking C−H and C−Ru bond to form the new double bond.

The data suggest that conformer **61b** (leading to the *E*-enol silane) is slightly preferred over **61a** (*E*:*Z* ratio 2.4:1), whereas the differences are much larger in the case of **62b** vs **62a**. A possible explanation is illustrated in Figure 3, where a strong steric interaction between the silyl ether group and the pyrrolidine ring appears clearly in conformer **62a** compared to conformer **61a**.

Furthermore, increasing the size of the Cp group on the ruthenium to Cp* shifts the selectivity in favor of the Z-isomer (see Figure 4). The steric repulsion between the silyl ether group and the ruthenium ligand disfavors H_b abstraction and favors adoption of an orientation where H_a is proximal to the metal, leading in this case to the opposite olefin geometry. The same trend was observed to a somewhat smaller extent in the transformation of enynoate **9b** to the six-membered-ring derivative **37**.

Interestingly, the cycloisomerations of 1,6-enyne **8a** and 1,7-enyne **8b** using catalyst **1** returned contrasting results. The five-membered-ring **33** is obtained in an excellent *E*:*Z* >32:1 selectivity; meanwhile, the corresponding six-membered-ring **36** is recovered in a modest *E*:*Z* 4:1. Furthermore, increasing the size of the Cp fragment to Cp* results in a further loss of selectivity (*E*:*Z* 1:1 for **36**); meanwhile, using the 1,7-*Z*-enyne **8b** significantly improves the selectivity (*E*:*Z* 9:1). As we suggested in the case of the 1,6-enynoates (Figures 3 and 4), this difference of selectivity between the 1,6-enynes and the 1,7-enynes is likely due to minute changes in the balance of steric interactions between the Ru ligand and the silyl ether group.

A putative rationale for the diastereoselectivity we observed in the case of the formation of derivative **50** derives also from the intermediacy of a ruthenacyclopentene. The isomerization of 1,6-enyne **19a** produced pyrrolidine **50** as a 2.2:1 mixture of cis/trans isomers when complex **1** was used, while use of complex **2** enabled the formation of the unique trans isomer. Two diastereomeric ruthenacycles are accessible as depicted in Figure 5.

In intermediate **63a**, methyl group adopts an equatorial orientation, whereas the same group occupies an axial one in conformer **63b**. However, the slight preference observed for conformer **63a** is greatly improved by switching the ligand on the ruthenium to Cp*. Enhancement of the steric interaction between the Cp fragment and the pseudoaxial methyl group in **63b** by switching to Cp* favors conformer **64,** which leads to the trans isomer (Figure 5).

The presence of an electron-withdrawing group on the alkyne also has a dramatic impact on these basic models, as shown for the cycloisomerization of 1,6-enynoate **51**. The nature of the ligand no longer has an effect on the selectivity observed at the level of the pyrrolidine ring, but guides the geometry of the enol silane as we observed in the case of unbranched enynes.

Previous work with Pd catalysis suggested that the presence of an allylic oxygen substituent impacted the regioselectivity

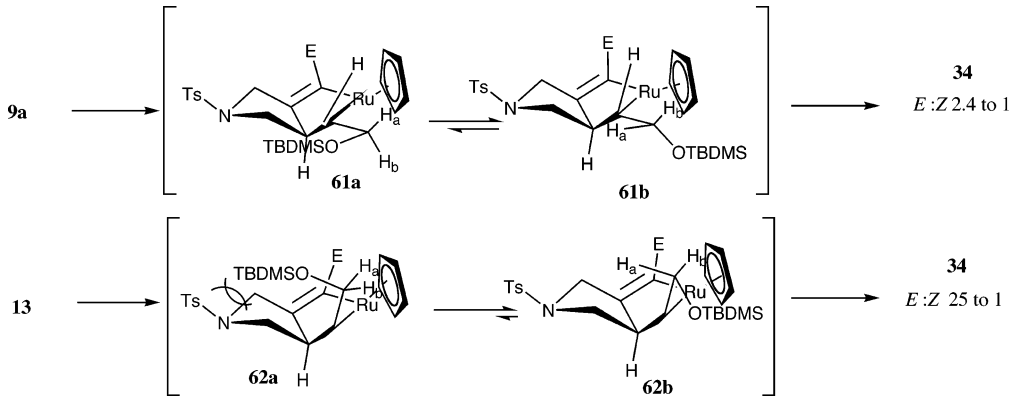


Figure 3. Comparison of Cp-ruthenium(4+) metallacycle intermediate conformers.

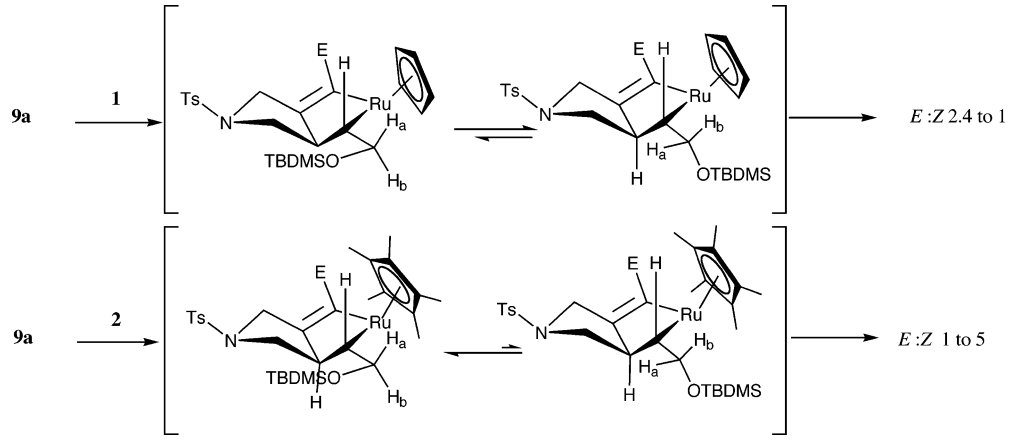


Figure 4. Comparison of Cp- and Cp*-ruthenium(4+) metallacycle intermediate conformers.

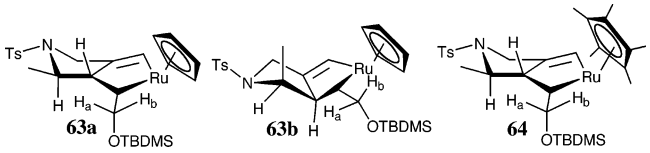
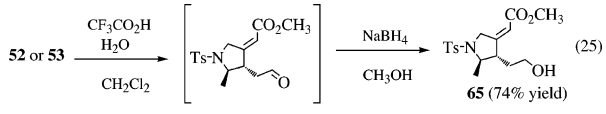
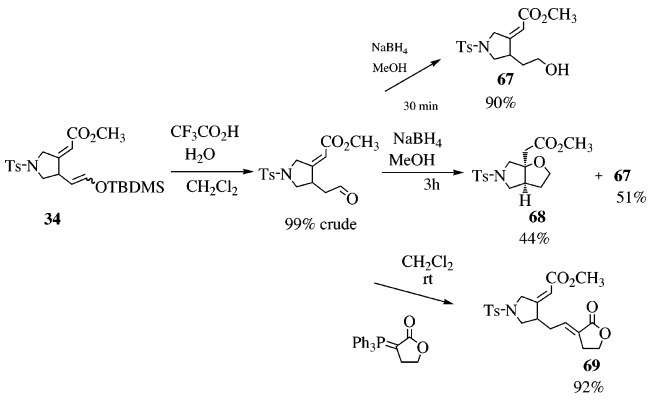


Figure 5. Comparison of intermediate conformers leading to **59**.

of the C−H abstraction observed in the cycloisomerization of 1,6- and 1,7-enynes to favor formation of the 1,3- rather than 1,4-dienes.[36,39] The current results indicate that the Ru-catalyzed process complements that of Pd and provides access to the synthetically very useful enol silyl ethers. As carbonyl surrogates, they can be easily hydrolyzed to unmask aldehydes. In addition to those examples wherein the further transformations were employed to facilitate characterization of the products (eq 12, 13, 18, and 24), hydrolysis followed by reduction of the enol silyl ethers **52**, **53**, and **54** (eq 25 and 26) provided single alcohols **65** and **66**—a fact that confirms the presence of mixtures derives from double bond rather than ring geometry. Scheme 2 illustrates a range of structural entities now readily available via this cycloisomerization process.



Scheme 2. Transformations of the Cycloisomerization Products



The observation that prolonged reaction times in the sodium borohydride reduction led to the bicyclic product **68** suggested that the basic medium might be responsible for the conjugate addition of the free alcohol. Support for this contention arises from the smooth cyclizations to the [6.5]- and [5.5]bicycles **70** and **71** (eq 27 and 28).

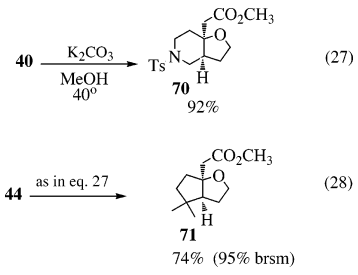


Table 3.

substrates (mg, mmol)	catalysts (mg, mmol)	products (mg, mmol)
8a; 118, 0.3	**1**; 13, 0.03	**33**; 105, 0.266
8a; 118, 0.3	**2**; 14, 0.03	**33**; 115, 0.292
9a; 135, 0.3	**1**; 13, 0.03	**34**; 105, 0.232
9a; 135, 0.3	**2**; 14, 0.03	**34**; 128, 0.283
10; 93; 0.2	**1**; 9, 0.02	**35**; 91, 0.195

Particularly intriguing is the ability in some cases to control the geometry of the resultant enol silyl ether. Since the geometry of the enol silyl ether can have subsequent consequences, such as transforming into alkene geometry after subsequent cross-coupling or into diastereomers after aldol additions or cycloadditions, this approach to enol silyl ethers has special merit. The ability to tune the geometry by modifying the steric demands of the catalyst is particularly noteworthy for the Ru catalyst. The diastereoselectivity of the reaction, which is exceptional, also derives from the steric demands of the catalyst and the ability to tune it. Thus, this reaction represents an attractive strategy for the diastereoselective formation of carbo- and heterocycles from available acyclic precursors.

Experimental Section

1,1-Bis(methoxycarbonyl)-3-[(*E*)-2-(*tert*-butyldimethylsilyloxy)-vinyl]-4-methylenecyclopentane (32). To an argon-flushed test tube containing $Cp(CH_3CN)_3PF_6$ (**1**) (0.021 g, 0.05 mmol) was added via a syringe a solution of enyne **6** (0.177 g, 0.5 mmol) in acetone (5 mL). The reaction was then stirred at room temperature during 20 min. After concentration in vacuo, the residue was directly chromatographed over silica gel, eluting with 6:1 petroleum ether−diethyl ether, to afford **32** (0.165 g, 0.466 mmol) as a nonseparable 13:1 mixture of diastereomers as a colorless oil. IR (film): 2955, 1737, 1661, 1259, 1167 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 6.32 (d, J = 5.8 Hz, 0.07H), 6.28 (d, J = 12 Hz, 0.93H), 4.95 (d, J = 2.2 Hz, 0.93H), 4.90 (m, 0.07H), 4.84 (d, J = 2.2 Hz, 1H), 4.81 (dd, J = 9.2, 12 Hz, 0.93H), 4.37 (dd, J = 5.8, 8.7 Hz, 0.07H), 3.75 (s, 3H), 3.73 (s, 3H), 3.14 (m, 0.07H), 3.08 (d, J = 17.1 Hz, 0.93H), 3.04 (m, 1H), 2.98 (dd, J = 2.4, 17.1 Hz, 1H), 2.58 (dd, J = 7.6, 12.8 Hz, 0.07H), 2.52 (dd, J = 7.6, 13.0 Hz, 0.93H), 1.92 (dd, J = 11.4, 12.9 Hz, 1H), 0.93 (s, 9H), 0.15 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): major diastereomer, δ 172.3, 172.0, 151.5, 142.0, 112.1, 107.6, 58.2, 52.8, 52.7, 42.3, 41.5, 40.0, 25.8 (3), 18.3, −5,2, −5.3. Anal. Calcd for $C_{18}H_{30}O_5Si$: C, 60.98; H, 8.52. Found: C, 61.02; H, 8.48.

Procedure for the Conversion of Alkynes 8a, 9a, and 10. To an argon-flushed test tube containing the Ru(I) catalyst (see Table 3) was added via a syringe a solution of enyne (see Table 3) in acetone (0.1 M, 2 or 3 mL). The reaction was then stirred at room temperature for 20 min. After concentration in vacuo, the residue was directly chromatographed over silica gel.

***N*-(4-Methylbenzenesulfonyl)-3-[(*E*)-2-(*tert*-butyldimethylsilyloxy)vinyl]-4-methylenepyrrolidine (33)** was isolated by flash chromatography, eluting with 2:1 petroleum ether−diethyl ether, as a >32:1 mixture of diastereomers as a colorless solid. Mp: 84−86 °C. IR (neat): 2929, 1661, 1348, 1162 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.72 (d, J = 8.3 Hz, 2H), 7.34 (d, J = 8.3 Hz, 2H), 6.30 (d, J = 11.9 Hz, 1H), 4.94 (s, 1H), 4.88 (s, 1H), 4.64 (dd, J = 9.3, 9.5 Hz, 1H), 4.05 (br d, J = 14.1 Hz, 1H), 3.65 (m, 2H), 3.14 (m, 1H), 2.67 (t, J = 9.8 Hz, 1H), 2.45 (s, 3H), 0.91 (s, 9H), 0.14 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 147.8, 143.6, 143.5, 132.6, 129.6 (2), 127.7 (2), 108.2, 107.7, 54.0, 51.7, 42.4, 25.5 (3), 21.5, 18.2, −5.3 (2). Anal. Calcd for $C_{20}H_{31}NO_3SSi$: C, 61.03; H, 7.94; N, 3.55; S, 8.14. Found: C, 61.20; H, 7.97; N, 3.52; S, 8.12.

Table 4.

substrates (mg, mmol)	catalysts (mg, mmol)	products (mg, mmol)
8b, 96, 0.235	**1**; 10, 0.0235	**36**; 95, 0.233
9b; 54, 0.116	**2**; 5, 0.0115	**37**; 0.051, 0.109
9b; 136, 0.3	**1**; 14, 0.03	**37**; 120[a]

[a] Contaminated with starting material (∼20%).

***N*-(4-Methylbenzenesulfonyl)-3-[(*E*) and (*Z*)-2-(*tert*-butyldimethylsilyloxy)vinyl]-4-methoxycarbonylmethylenepyrrolidine (34)** was isolated by flash chromatography, eluting with 2:1 petroleum ether−diethyl ether, as a nonseparable 2.5:1 mixture of diastereomers as a colorless oil. IR (film): 2953, 1716, 1662, 1351, 1164 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): major diastereomer, δ 7.74 (d, J = 8.3 Hz, 2H), 7.34 (d, J = 8.3 Hz, 2H), 6.35 (d, J = 11.7 Hz, 1H), 5.67 (m, 1H), 4.61 (dd, J = 9.2, 11.7 Hz, 1H), 4.54 (dd, J = 2.5, 18.3 Hz, 1H), 4.01 (dt, J = 2.5, 18.3 Hz, 1H), 3.71−3.69 (m, 1H), 3.70 (s overlapped, 3H), 3.32 (br q, J_{app} = 8 Hz, 1H), 2.59 (dd, J = 9.2, 10.3 Hz, 1H), 2.45 (s, 3H), 0.92 (s, 9H), 0.15 (s, 6H); minor diastereomer, δ 7.74 (d, J = 8.3 Hz, 2H), 7.34 (d, J = 8.3 Hz, 2H), 6.39 (d, J = 5.8 Hz, 1H), 5,67 (m, 1H), 4.61 (dd, J = 5.8, 8.5 Hz, 1H), 4.54 (dd, J = 2.5, 18.3 Hz, 1H), 4.01 (dt, J = 2.5, 18.3 Hz, 1H), 3.94 (app q, J = 8.5 Hz, 1H), 3.73 (dd, J = 8.3, 9.0 Hz, 1H), 3.69 (s, 3H), 2.63 (dd, J = 9.5, 10.2 Hz, 1H), 2.44 (s, 3H), 0.89 (s, 9H), 0.14 (s, 3H), 0.13 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): major diastereomer, δ 166.2, 161.7, 144.8, 143.8, 132.0, 129.7 (2), 127.2 (2), 113.7, 106.7, 52.8, 52.4, 51.4, 44.2, 25.3 (3), 21.5, 18.3, −5.2, −5.3; minor diastereomer, δ 166.1, 161.7, 143.7, 142.6, 132.2, 129.7 (2), 127.2 (2), 112.7, 105.4, 52.4, 52.0, 51.3, 40.1, 25.3 (3), 21.5, 18.3, −5.4. Anal. Calcd for $C_{22}H_{33}NO_5SSi$ (mixture of diastereomers): C, 58.50; H, 7.36; N, 3.10; S, 7.09. Found: C, 58.60; H, 7.41; N, 3.13; S, 6.89.

***N*-(4-Methylbenzenesulfonyl)-3-[(*E*)-2-(*tert*-butyldimethylsilyloxy)vinyl]-4-(trimethylsilylmethylene)pyrrolidine (35)** was isolated by flash chromatography, eluting with 4:1 petroleum ether−ether, as a 32:1 mixture of diastereomers as a white solid. Mp: 83−84 °C. IR (film): 2955, 1661, 1635, 1351, 1164 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.70 (d, J = 8.3 Hz, 2H), 7.34 (d, J = 8.3 Hz, 2H), 6.25 (d, J = 12 Hz, 1H), 5.35 (d, J = 2.4 Hz, 1H), 4.58 (dd, J = 9.5, 12 Hz, 1H), 4.04 (dd, J = 2.4, 14.0 Hz, 1H), 3.62 (m, 2H), 3.10 (dd, J = 8.6, 9.5 Hz, 1H), 2.59 (t, J = 9.5 Hz, 1H), 2.44 (s, 3H), 0.91 (s, 9H), 0.13 (s, 6H), 0.03 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.3, 143.8, 143.6, 132.5, 129.6 (2), 127.7 (2), 121.6, 108.8, 53.2, 51.3, 45.1, 25.6 (3), 21.5, 18.3, −0.7 (3), −5.3 (2). Anal. Calcd for $C_{23}H_{39}NO_3SSi_2$: C, 59.30; H, 8.44; N, 3.00; S, 6.88. Found: C, 59.20; H, 8.224; N, 2.94; S, 6.48.

Procedure for the Conversion of Alkynes 8b and 9b. To an argon-flushed test tube containing the catalyst (see Table 4) was added via a syringe a solution of substrate (see Table 4) in acetone (0.1 M). The reaction was then stirred at room temperature for 20 min. After concentration in vacuo, the residue was directly chromatographed over silica gel (see below for eluting system) to afford the corresponding product (see Table 4; see below for physical properties).

***N*-(4-Methylbenzenesulfonyl)-3-[(*E*)-2-(*tert*-butyldimethylsilyloxy)vinyl]-4-methylenepiperidine (36)** was isolated by flash chromatography, eluting with 4:1 petroleum ether−diethyl ether, as a nonseparable 4:1 mixture of diastereomers as a colorless oil. IR (neat): 2955, 2930, 1662, 1162 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): major diastereomer, δ 7.63 (d, J = 8.3 Hz, 2H), 7.32 (d, J = 8.3 Hz, 2H), 6.36 (d, J = 11.9 Hz, 1H), 4.89 (dd, J = 9.2, 11.9 Hz, 1H), 4.74 (s, 2H), 3.60 (m, 1H), 3.53 (ddd, J = 1.7, 4.9, 11.2 Hz, 1H), 2.88 (m, 1H), 2.46 (m, 1H), 2.43 (s, 3H), 2.41−2.34 (m, 2H), 2.25 (t, J = 10.8 Hz, 1H), 0.93 (s, 9H), 0.16 (s, 6H); minor diastereomer, δ 7.63 (d, J = 8.3 Hz, 2H), 7.32 (d, J = 8.3 Hz, 2H), 6.31 (d, J = 5.8 Hz, 1H), 4.74 (s, 1H), 4.70 (s, 1H), 4.45 (dd, J = 5.9, 9.1 Hz, 1H), 3.43 (m,

(39) In a recent report, monopropargyl ethers of 2-butene-1,4-diol have been reported to cycloisomerize to the 1,4-dienes with Pd catalysis, see: Kressierer, C. J.; Müller, T. J. J. *Tetrahedron Lett.* **2004**, *45*, 2155−2158.

Table 5.

substrates (mg, mmol)	alcohols (mg, mmol)
36; 155, 0.380	**39**; 94, 0.319
37; 101, 0.216	**40**; 55, 0.155

Table 6.

substrates (mg, mmol)	products (mg, mmol)
25; 72, 0.3	**41**; 58, 0.241
26; 90, 0.3	**42**; 75, 0.251

2H), 2.68 (td, J = 3.6, 10.5 Hz, 1H), others signals are overlapped with those from *E*-isomers. ^{13}C NMR (125 MHz, $CDCl_3$): major diastereomer, δ 146.7, 143.4, 142.8, 133.1, 129.5 (2), 127.5 (2), 109.6, 108.6, 52.7, 47.4, 40.9, 33.6, 25.6 (3), 21.4, 18.2, −5.2, −5.3 (1); minor diastereomer, δ 145.6, 143.2, 140.4, 133.1, 1129.5 (2), 127.5 (2), 108.8, 107.2, 51.9, 47.4, 37.3, 33.3, 25.5 (3), 18.1, −5.3, −5.4. Anal. Calcd for $C_{21}H_{33}NO_3SSi$ (mixture of diastereomers): C, 61.87; H, 8.15; N, 3.43; S, 7.86. Found: C, 62.03; H, 8.16; N, 3.43; S, 7.69.

***N*-(4-Methylbenzenesulfonyl)-3-[(*E*) and (*Z*)-2-(*tert*-butyldimethylsilyloxy)vinyl]-4-methoxycarbonylmethylenepiperidine (37)** was isolated as a colorless oil by flash chromatography, eluting with 4:1 petroleum ether−diethyl ether. IR (neat): 2953, 1716, 1655, 1353, 1253, 1165 cm^{-1}. First diastereomer—^{1}H NMR (500 MHz, $CDCl_3$): δ 7.64 (d, J = 8.3 Hz, 2H), 7.32 (d, J = 8.3 Hz, 2H), 6.35 (d, J = 5.6 Hz, 1H), 5.74 (s, 1H), 4.48 (t, J = 5.8, 8.5 Hz, 1H), 3.77 (br s, 1H), 3.65 (s, 3H), 3.58 (m, 1H), 3.42 (m, 1H), 3.32 (m, 1H), 2.91 (m, 1H), 2.79 (m, 1H), 2.71 (m, 1H), 2.44 (s, 3H), 0.91 (s, 9H), 0.16 (s, 3H), 0.11 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 167.0, 158.1, 141.4, 133.1, 129.4 (2), 127.7 (2), 114.3, 105.8, 78.6, 51.7, 51.0, 46.8, 39.3, 27.3, 25.6, 25.5 (3), 18.1, −5.1 (2). Second diastereomer—^{1}H NMR (500 MHz, $CDCl_3$): δ 7.64 (d, J = 8.3 Hz, 2H), 7.32 (d, J = 8.3 Hz, 2H), 6.36 (d, J = 11.9 Hz, 1H), 5.71 (s, 1H), 4.86 (dd, J = 9.3, 12.0 Hz, 1H), 3.64 (s, 3H), 3.63 (m, 1H), 3.55 (m, 1H), 2.98 (td, J = 4.9, 9.1 Hz, 1H), 2.58 (m, 2H), 2.39 (dd, J = 3.4, 11.5 Hz, 1H), 2.25 (dd, J = 2.9, 11.5 Hz, 1H), 2.43 (s, 3H), 0.93 (s, 9H), 0.16 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.7, 158.8, 143.8, 143.1, 132.7, 129.6 (2), 127.5 (2), 114.9, 109.7, 52.4, 51.0, 47.3, 42.7, 34.8, 27.7, 25.5 (3), 21.4, 18.2, −5.4 (2). Third diastereomer—^{1}H NMR (500 MHz, $CDCl_3$): δ 7.64 (d, J = 8.3 Hz, 2H), 7.32 (d, J = 8.3 Hz, 2H), 6.60 (d, J = 12.0 Hz, 1H), 5.55 (s, 1H), 5.32 (dd, J = 8.1, 12.0 Hz, 1H), 4.61 (d, J = 8.1 Hz, 1H), 3.93 (m, 1H), 3.65 (s, 3H), 3.55 (m, 1H), 3.32 (m, 1H), 2.86 (m, 1H), 2.81 (m, H), 2.43 (s, 3H), 2.09 (br d, J = 14 Hz, 1H), 0.90 (s, 9H), 0.15 (s, 3H), 0.12 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.1, 158.7, 143.6, 143.5, 132.7, 129.6 (2), 127.5 (2), 114.3, 107.1, 51.4, 51.0, 46.6, 32.3, 27.2, 25.6 (3), 21.4, 18.3, −5.2 (2). Anal. Calcd for $C_{23}H_{35}NO_5SSi$: C, 59.32; H, 7.57; N, 3.00; S, 6.88. Found: C, 59.09; H, 7.65; N, 3.12; S, 6.96.

Experimental Procedure for Preparation of Alcohols 39 and 40. To a solution of silyl enol ether (see Table 5) in CH_2Cl_2 (5 mL) were added water (0.1 mL) and trifluoroacetic acid (2 mL). The solution was stirred at room temperature for 15 min, and the volatiles were removed in vacuo. The residue was chromatographed, eluting with 3:1 diethyl ether−petroleum ether, to afford respectively the corresponding aldehyde (62 mg, 0.176 mmol, or 107 mg, 0.366 mmol). Each aldehyde was taken up in MeOH (5 mL) and treated with sodium borohydride (0.05 g, 1.35 mmol). The reaction was stirred at room temperature until completion (between 15 and 20 min). Water (5 mL) was added, and the volatiles were removed under reduced pressure. The residue was partitioned between water (5 mL) and CH_2Cl_2 (10 mL). The aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried over $MgSO_4$. After concentration in vacuo, the residue was chromatographed, eluting with diethyl ether, to afford alcohol **39** or **40** (see Table 5).

***N*-(4-Methylbenzenesulfonyl)-3-(2-hydroxyethyl)-4-methylenepiperidine (39)** was recovered as an oil. IR (neat): 3351, 3070, 2943, 1651, 1597 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.61 (d, J = 8.3 Hz, 2H), 7.31 (d, J = 8.3 Hz, 2H), 4.73 (s, 2H), 3.71 (td, J = 6.1, 10.7 Hz, 1H), 3.65 (td, J = 6.6, 10.7 Hz, 1H), 3.34 (td, J = 5.4, 11.0 Hz, 1H), 3.15 (dd, J = 4.4, 11.2 Hz, 1H), 2.84 (dd, J = 3.9, 11.2 Hz, 1H), 2.71 (td, J = 3.9, 10.1 Hz, 1H), 2.54−2.42 (m, 2H), 2.41 (s, 3H), 2.20 (ddd, J = 4.5, 4., 13.6 Hz, 1H), 2.10 (s, 1H), 1.91 (tq, J = 6.1, 7.6 Hz, 1H), 1.75 (tq, J = 7.0, 13.6 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 145.9, 143.4, 133.0, 129.5 (2), 127.4 (2), 109.7, 60.2, 51.6, 47.7, 38.9, 32.8, 31.8, 21.3. Anal. Calcd for $C_{15}H_{21}NO_3S$: C, 60.99; H, 7.16; N, 4.74; S, 10.85. Found: C, 61.17; H, 7.32; N, 4.71; S, 10.66.

***N*-(4-Methylbenzenesulfonyl)-3-(2-hydroxyethyl)-4-methoxycarbonylmethylenepiperidine (40)** was recovered as an oil. IR (neat): 3534, 2951, 1715, 1652, 1597, 1163 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.61 (d, J = 8.1 Hz, 2H), 7.31 (d, J = 8.1 Hz, 2H), 5.71 (s, 1H), 3.73 (dd, J = 5.9, 10.9 Hz, 1H), 3.64 (s, 3H), 3.65−3.59 (m, 2H), 3.50 (dd, J = 3.7, 11.5 Hz, 1H), 2.69 (m partially overlapped, 1H), 2.59 (m, 1H), 2.51 (dd, J = 3.4, 11.0 Hz, 1H), 2.41 (s, 3H), 2.03 (br s, 1H), 1.90 (q, J = 6.6 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.4, 158.3, 143.6, 132.7, 129.6, 127.4, 115.4, 59.7, 50.09, 50.06, 47.0, 40.8, 33.2, 25.8, 21.4. Anal. Calcd for $C_9H_{13}NO_4$: C, 57.77; H, 6.56; N, 3.96. Found: C, 57.65; H, 6.37; N, 3.81.

[5-(4-Methylbenzenesulfonyl)hexahydrofuro[3,2-*c*]pyridin-7a-yl]-acetic Acid Methyl Ester (70). To a solution of alcohol **40** (0.055 g, 0.155 mmol) in MeOH (3 mL) was added potassium carbonate (0.022 g, 0.155 mmol). The reaction mixture was stirred at room temperature for 3 h. The volatiles were removed under reduced pressure, and the residue was partitioned between 1 N $NaHSO_4$ (3 mL) and CH_2Cl_2 (4 × 5 mL). The combined organic layers were dried over $MgSO_4$. After concentration in vacuo, the residue was purified by chromatography, eluting with 1:4 petroleum ether−diethyl ether, to afford **70** (0.051 g, 0.144 mmol) as a colorless oil. IR (neat): 2952, 1734, 1598, 1338, 1167 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.64 (d, J = 8.0 Hz, 2H), 7.34 (d, J = 8.0 Hz, 2H), 3.87 (m, 2H), 3.68 (s, 3H), 3.30 (dd, J = 6.6, 11.9 Hz, 1H), 3.20 (td, J = 5.7, 11.9 Hz, 1H), 2.81 (ddd, J = 3.9, 9.7, 13.4 Hz, 1H), 2.55 (dd, J = 8.3, 11.9 Hz, 1H), 2.45 (s, 3H), 2.48−2.44 (m, 2H), 2.38 (m, 1H), 2.18 (m, 1H), 2.06 (ddd, J = 3.9, 5.1, 14.4 Hz, 1H), 2.00 (ddd, J = 4.6, 10.0, 14.4 Hz, 1H), 1.78 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.4, 143.5, 133.1, 129.7 (2), 127.5 (2), 79.2, 64.9, 51.7, 46.3, 42.4 (2), 40.5, 31.5, 28.4, 21.5. Anal. Calcd for $C_{17}H_{23}NO_5S$: C, 57.77; H, 6.56; N, 3.96. Found: C, 57.61; H, 6.72; N, 3.91.

Procedure for the Conversion of Alkynes 25 and 26. To an argon-flushed test tube containing **1** (13 mg, 0.03 mmol) was added via a syringe a solution of substrate (see Table 6) in acetone (3 mL). The reaction was then stirred at room temperature for 20 min. After concentration in vacuo, the residue was directly purified (see below for conditions) to afford the corresponding product (see Table 6).

2-[(*E*)-2-(*tert*-Butyldimethylsilyloxy)vinyl]-3-methylenetetrahydrofuran (41) was isolated by flash chromatography, eluting with 19:1 petroleum ether−ether, as a 19:1 mixture of diastereomers as a colorless oil. IR (neat): 2930, 1661, 1167 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): major diastereomer, δ 6.32 (d, J = 11.9 Hz, 1H), 4.95 (app q, J = 2.5 Hz, 1H), 4.90 (app q, J = 2.5 Hz, 1H), 4.78 (dd, J = 9.2, 11.9 Hz, 1H), 4.43 (br d, J = 13.4 Hz, 1H), 4.27 (dq, J = 2.2, 13.4 Hz, 1H), 4.04 (app t, J = 8.3 Hz, 1H), 3.15 (br q, J = 8.3 Hz, 1H), 0.92 (s, 9H), 0.15 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 151.8, 142.8, 109.0, 104.6, 74.1, 71.3, 43.5, 25.6 (3), 18.3, −5.2 (2). Anal. Calcd for $C_{13}H_{24}O_2Si$: C, 64.94; H, 10.06. Found: C, 65.14; H, 10.17.

2-[(*E*)-2-(*tert*-Butyldimethylsilyloxy)vinyl]-3-ethoxycarbonylmethylenetetrahydrofuran (42) was isolated as a colorless oil by flash chromatography, eluting with 9:1 petroleum ether−ether. IR (neat): 2954, 1716, 1663, 1350, 1168 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.38 (d, J = 11.9 Hz, 1H), 5.74 (app q, J = 2.4 Hz, 1H), 4.93 (dd, J = 2.4, 17.5 Hz, 1H), 4.76 (dd, J = 9.2, 11.9 Hz, 1H), 4.66 (td, J = 2.4, 17.5 Hz, 1H), 4.09 (t, J = 7.8 Hz, 1H), 3.72 (s, 3H), 3.37 (dd, J

= 8.5, 10.1 Hz, 1H), 3.30 (m, 1H), 0.94 (s, 9H), 0.17 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.68, 166.65, 144.1, 111.5, 107.0, 72.6, 72.0, 51.2, 45.2, 25.5 (3), 18.2, −5.23, −5.25. Anal. Calcd for $C_{21}H_{33}NO_3SSi$: C, 60.36; H, 8.78. Found: C, 60.18; H, 8.60.

1-[(*E*)-2-(*tert*-Butyldimethylsilyloxy)vinyl]-5,5-dimethyl-2-methylenecyclopentane (43) was obtained from alkyne **30a** (0.08 g, 0.3 mmol) and catalyst **1** (0.013 g, 0.03 mmol) in acetone (3 mL) and was isolated as a colorless oil by flash chromatography, eluting with 19:1 petroleum ether−diethyl ether. IR (neat): 2955, 1657, 1256, 1164 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.21 (d, J = 11.9 Hz, 1H), 4.88 (s, 1H), 4.81 (s, 1H), 4.78 (dd partially overlapped, J = 10.5, 11.9 Hz, 1H), 2.39 (m, 3H), 1.62−1.44 (m, 2H), 0.99 (s, 3H), 0.96 (s, 9H), 0.72 (s, 3H), 0.18 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 156.0, 142.3, 109.8, 106.3, 54.9, 41.8, 39.3, 29.3, 27.3, 25.7 (3), 21.3, 18.4, −5.1, −5.2. Anal. Calcd for $C_{16}H_{30}OSi$: C, 72.11; H, 11.34. Found: C, 72.09; H, 11.13.

1-[2-Hydroxyethyl]-5,5-dimethyl-2-methoxycarbonylmethylenecyclopentane (44). To an argon-flushed test tube containing **1** (0.013 g, 0.03 mmol) was added via a syringe a solution of alkynoate **31** (0.097 g, 0.3 mmol) in acetone (3 mL). The reaction was then stirred at room temperature for 20 min. After concentration in vacuo, the residue was filtered over silica gel, eluting with 1:1 petroleum ether−diethyl ether. After evaporation to dryness, the crude material was diluted with CH_2Cl_2 (5 mL). Trifluoroacetic acid (5 mL) and water (1 mL) were added, and the reaction was stirred for 15 min. After concentration in vacuo, the residue was chromatographed, eluting with 4:1 petroleum ether−diethyl ether, to afford the intermediate aldehyde. The latter substance was dissolved in MeOH (5 mL), and sodium borohydride (0.02 g, 0.5 mmol) was added. The reaction was stirred for 5 min. Water (5 mL) was added, and the volatiles were removed under reduced pressure. The residue was partitioned between water (5 mL) and Et_2O (10 mL). The aqueous layer was extracted with Et_2O (4 × 10 mL). The combined ethereal extracts were dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by chromatography, eluting with 1:1 petroleum ether−diethyl ether, to afford alcohol **44** (0.052 g, 0.245 mmol) as an oil. IR (neat): 3426, 2953, 1715, 1651, 1198 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.73 (q, J = 2.4 Hz, 1H), 3.78 (ddd, J = 6.0, 8.4, 10.9 Hz, 1H), 3.68 (s, 3H), 2.81 (m, 2H), 2.16 (m, 2H), 1.80−1.48 (m, 5H), 1.02 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 172.3, 167.2, 111.5, 61.7, 53.1, 50.8, 40.9, 38.4, 30.9, 29.9, 27.5, 21.4. Anal. Calcd for $C_{12}H_{20}O_3$: C, 67.89; H, 9.49. Found: C, 68.05; H, 9.60.

(4,4-Dimethylhexahydrocyclopenta[*b*]furan-6a-yl)acetic Acid Methyl Ester (71). To a solution of alcohol **44** (0.05 g, 0.234 mmol) in MeOH (2 mL) was added potassium carbonate (0.05 g, 0.36 mmol). The reaction mixture was heated at 40 °C for 2 h. After concentration in vacuo, the residue was chromatographed, eluting with 1:1 petroleum ether−diethyl ether, to afford first bicycle **71** (0.037 g, 0.174 mmol) as an oil and then remaining alcohol **44** (0.011 g, 0.051 mmol). IR (neat): 2953, 1738, 1436 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.84 (ddd, J = 5.4, 7.1, 8.6 Hz, 1H), 3.73 (ddd, J = 7.1, 8.5, 14.1 Hz, 1H), 3.70 (s, 3H), 2.68 (d, J = 13.9 Hz, 1H), 2.58 (d, J = 13.9 Hz, 1H), 2.11 (dd, J = 5.9, 8.6 Hz, 1H), 2.0−1.90 (m, 3H), 1.80 (ddd, J = 5.8, 7.0, 12.9 Hz, 1H), 1.61 (ddd, J = 8.3, 11.2, 12.2 Hz, 1H), 1.38 (m, 1H), 1.00 (s, 3H), 0.99 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 171.5, 92.7, 68.5, 58.1, 51.5, 44.6, 40.6, 38.7, 36.5, 29.6, 29.3, 24.7. HRMS: calcd for $C_{12}H_{20}O_3$, [M$^+$], 212.1412; found, 212.1400.

[(*Z*)-4-(*tert*-Butyldimethylsilyloxy)but-2-enyl] Propynoate (45). To an ice-cooled solution of alcohol **11** (1.0 g, 4.94 mmol) in THF (25 mL) were added triphenylphosphine (2.6 g, 9.91 mmol), propiolic acid (0.608 mL, 9.88 mmol), and diisopropyl azodicarboxylate (1.94 mL, 9.85 mmol). The reaction mixture was stirred at room temperature for 2 h. The volatiles were removed under vacuum. The residue was directly purified by chromatography, eluting with 15:1 petroleum ether−diethyl ether, to yield alkyne **45** (0.480 g, 1.88 mmol) as a colorless oil. IR (neat): 3265, 2956, 2122, 11719, 1362, 1220 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.80 (ttd, J = 1.4, 5.6, 11.2 Hz, 1H), 5.60 (ttd, J = 1.4, 6.8, 11.2 Hz), 4.80 (d, J = 6.8 Hz, 2H), 4.30 (d, J = 5.6 Hz, 2H), 2.91 (s, 1H), 0.91 (s, 9H), 0.09 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 152.44, 135.0, 122.7, 74.8, 74.4, 62.0, 59.5, 25.8 (3), 18.2, −5.3 (2). HRMS: calcd for $C_{13}H_{22}O_3Si$, [M$^+$], 254.1195; found, 254.1211.

Table 7.

substrate (mg, mmol)	catalysts (mg, mmol)	products (mg, mmol)
19a, 81, 0.2	**1**; 9, 0.02	**50**; 76, 0.186
19a; 81, 0.2	**2**; 9, 0.02	**50**; 61, 0.149

Table 8.

catalyst (mg, mmol)	substrate **51** (mg, mmol)	product (mg, mmol)
1; 8, 0.0184	81, 0.2	**52** 48, 0.103
2; 9, 0.02	85, 0.2	**53** 81, 0.174

4-[(*E*)-2-(*tert*-Butyldimethylsilyloxy)vinyl]-3-methylenedihydrofuran-2-one (46). The typical procedure was carried out with alkyne **45** (76 mg, 0.3 mmol). After chromatography, eluting with 20:1 petroleum ether−diethyl ether, remaining **45** (25 mg, 0.0983 mmol) and then lactone **46** (0.042 g, 0.165 mmol) were recovered as colorless oils. IR (neat): 2930, 1769, 1662, 1254, 1172, 838 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.44 (d, J = 12.0 Hz, 1H), 6.30 (d, J = 3.0 Hz, 1H), 5.62 (d, J = 3.0 Hz, 1H), 4.86 (dd, J = 12.0, 9.3 Hz, 1H), 4.50 (t, J = 9.0 Hz, 1H), 3.90 (t, J = 8.7 Hz, 1H), 3.58 (ddt, J = 3.0, 8.7, 9.0 Hz, 1H), 0.95 (s, 9H), 0.19 (s, 3H), 0.18 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.3, 144.4, 138.4, 122.8, 107.8, 71.0, 39.2, 25.5 (3), 18.3, −5.3, −5.32. HRMS: calcd for $C_9H_{13}O_3Si$, [M$^+$ − C_4H_9], 197.0637; measd, 197.0633.

***cis*-1-Hydroxy-2-[(*E*)-2-(*tert*-butyldimethylsilyloxy)vinyl]-3-methylene-5,5-dimethylcyclopentane (49)** was isolated as an oil. IR (neat): 3483, 3072, 2957, 2931, 2859, 1655, 1471, 1256, 1169, 1073 cm^{-1}. ^{1}H NMR (500 MHz, C_6D_6): δ 6.35 (dd, J = 12.1, 0.5 Hz, 1H), 5.23 (dd, J = 12.1, 9.4 Hz, 1H), 5.09 (s, 1H), 5.06 (s, 1H), 3.35 (t, J = 4.5 Hz, 1H), 3.18 (m, 1H), 2.43 (dd, J = 16.2, 6.5 Hz, 1H), 2.03 (dd, J = 16.2, 0.7 Hz, 1H), 1.16 (d, J = 4.5 Hz, 1H), 1.01 (s, 3H), 0.93 (s, 9H), 0.83 (s, 3H), 0.08 (s, 6H). ^{13}C NMR (125 MHz, C_6D_6): δ 154.4, 143.9, 110.2, 109.0, 83.5, 48.5, 44.9, 27.3, 26.2, 23.1, 18.8, −4.7, −4.8. HRMS: calcd for $C_{16}H_{30}O_2Si$, [M$^+$], 282.2015; found, 282.2013.

(2*S*,3*R*)-*N*-(4-Methylbenzenesulfonyl)-2-methyl-3-[(*E*)-2-(*tert*-butyldimethylsilyloxy)vinyl]-4-methylenepyrrolidine (50). To an argon-flushed test tube containing the catalyst (see Table 7) was added via a syringe a solution of substrate (see Table 7) in acetone (2 mL). The reaction was then stirred at room temperature for 20 min. After concentration in vacuo, the residue was directly chromatographed over silica gel, eluting with 9:1 petroleum ether−diethyl ether, to afford **50** (see Table 7) as a colorless oil. $[\alpha]_D$ = −28.7 (*c* 2.48, $CHCl_3$). IR (neat): 2930, 1661, 1463, 1349 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.70 (d, J = 8.3 Hz, 2H), 7.33 (d, J = 8.3 Hz, 2H), 6.26 (d, J = 111.9 Hz, 1H), 4.88 (q, J = 2.2 Hz, 1H), 4.82 (q, J = 2.2 Hz, 1H), 4.46 (dd, J = 9.5, 11.9 Hz, 1H), 4.17 (d, J = 14.4 Hz, 1H), 3.80 (qd, J = 2, 14.4 Hz, 1H), 2.90 (qd, J = 6.3, 8.5 Hz, 1H), 2.70 (br t, J = 9.5 Hz, 1H), 2.45 (s, 3H), 1.43 (d, J = 6.3 Hz, 3H), 0.92 (s, 9H), 0.14 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 146.2, 143.7, 143.4, 133.4, 129.6 (2), 127.7 (2), 108.6, 107.2, 61.9, 53.1, 51.4, 25.6 (3), 21.5, 19.8, 18.3, −5.3 (2). Anal. Calcd for $C_{21}H_{33}NO_3SSi$: C, 61.87; H, 8.15; S, 7.86; N, 3.43. Found: C, 61.67; H, 7.94; S, 7.41; N, 3.38.

(2*S*,3*R*)-*N*-(4-Methylbenzenesulfonyl)-2-methyl-3-[(*E*)-2-(*tert*-butyldimethylsilyloxy)vinyl]-4-methoxycarbonylmethylenepyrrolidine (52). The typical procedure, described previously, was employed using the amounts listed in Table 8. **52** and **53** were isolated as a colorless oil by flash chromatography, eluting with 9:1 petroleum ether−ether.

Data for 52. IR (neat): 2930, 1715, 1654, 1358, 1166 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) ((*E*)-enol silane): δ 7.73 (d, J = 8.3 Hz, 2H), 7.34

(d, J = 8.3 Hz, 2H), 6.31 (d, J = 11.8 Hz, 1H), 5.65 (app q, J = 2.5 Hz, 1H), 4.61 (dd, J = 2.5, 18.5 Hz, 1H), 4.46 (dd, J = 9.2, 11.8 Hz, 1H), 4.18 (br d, J = 18.5 Hz, 1H), 3.71 (s, 3H), 2.86 (tt, J = 2.2, 9.2 Hz, 1H), 2.78 (qd, J = 5.8, 9.2 Hz, 1H), 2.45 (9s, 3H), 1.48 (d, J = 5.8 Hz, 3H), 0.93 (s, 9H), 0.16 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) ((*E*)-enol silane): δ 166.2, 159.8, 145.1, 143.7, 132.4, 129.7 (2), 127.9 (2), 113.2, 107.0, 60.4, 53.6, 52.9, 51.3, 25.5 (3), 21.5, 19.0, 18.2, −5.29, −5.33.

Data for 53. IR (neat): 2930, 1715, 1654, 1358, 1166 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.73 (d, J = 8.3 Hz, 2H), 7.33 (d, J = 8.3 Hz, 2H), 6.40 (d, J = 5.6 Hz, 1H), 5.63 (q, J = 2.5 Hz, 1H), 4.62 (dd, J = 1.9, 18.5 Hz, 1H), 4.19 (dt, J = 2.5, 18.5 Hz, 1H), 4.03 (dd, J = 5.6, 8.7 Hz, 1H), 3.69 (s, 3H), 3.67 (br t partially overlapped, J = 8.7 Hz, 1H), 2.86 (qd, J = 6.1, 9.0 Hz, 1H), 2.43 (s, 3H), 1.46 (d, J = 6.1 Hz, 3H), 0.90 (s, 3H), 0.13 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.3, 159.9, 143.5, 142.8, 132.8, 129.6 (2), 127.8 (2), 112.3, 105.4, 60.7, 53.6, 51.2, 48.5, 25.4 (3), 21.5, 19.5, 18.0, −5.43, −5.48. Anal. Calcd (as mixture) for $C_{23}H_{35}NO_5SSi$: C, 59.32; H, 7.57; N, 3.00; S, 6.88. Found: C, 59.23; H, 7.47; N, 3.03; S, 6.71.

(2*S*,3*R*)-*N*-(4-Methylbenzenesulfonyl)-2-methyl-3-[2-hydroxyethyl]-4-methoxycarbonylmethylenepyrrolidine (65) was obtained using the procedure described for the obtention of derivative **40**. Alcohol **65** was then recovered in 74% yield as a colorless oil. $[\alpha]_D$ = +67.0 (*c* 2.75, $CHCl_3$). IR (neat): 3534, 2951, 1715, 1667, 1162 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.76 (d, J = 8.3 Hz, 2H), 7.32 (d, J = 8.3 Hz, 2H), 5.82 (td, J = 1.4, 2.7 Hz, 1H), 4.51 (dd, J = 2.2, 18.3 Hz, 1H), 4.33 (ddd, J = 2.0, 2.9, 18.3 Hz, 1H), 3.86 (dq, J = 1.7, 6.5 Hz, 1H), 3.71 (s, 3H), 3.57 (m, 2H), 2.63 (tq, J = 1.3, 7.3 Hz, 1H), 2.42 (s, 3H), 1.71 (br s, 1H), 1.45 (ddt, J = 5.6, 7.0, 12.7 Hz, 1H), 1.32 (m, 1H), 1.19 (d, J = 6.3 Hz, 3H).^{13}C NMR (125 MHz, $CDCl_3$): δ 166.0, 161.2, 143.4, 135.9, 129.6 (2), 127.1 (2), 1114.3, 59.7, 59.4, 51.4, 499.9, 49.4, 35.9, 21.4, 20.9. Anal. Calcd for $C_{17}H_{23}NO_5S$: C, 57.77; H, 6.56; N, 3.96; S, 9.07. Found: C, 57.88; H, 6.58; N, 3.91; S, 9.27.

(2*S*,3*R*)-*N*-(4-Methylbenzenesulfonyl)-2-methyl-3-[(*E*)-2-(*tert*-butyldimethylsilyloxy)vinyl]-4-methylenepiperidine (54) was obtained by carrying out the typical procedure from alkyne **19b** (0.085 g, 0.2 mmol). The crude product was directly chromatographed over silica gel, eluting with 9:1 petroleum ether−ether, to afford **54** (0.082 g, 0.194 mmol) as a colorless oil. IR (neat): 2930, 1654, 1340, 1163 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.66 (d, J = 8.3 Hz, 2H), 7.24 (d, J = 8.3 Hz, 2H), 6.29 (d, J = 11.9 Hz, 0.8H), 6.12 (d, J = 5.8 Hz, 0.2H), 5.14 (dd, J = 7.6, 11.9 Hz, 0.8H), 4.76 (br s, 1H), 4.74 (m overlapped, 0.2H), 4.71 (br s, 1H), 4.08 (q, J = 6.6 Hz, 0.8H), 4.05 (q, J = 7.0 Hz, 0.2H), 3.74 (dd, J = 5,8, 12.2 Hz, 0.2H), 3.70 (dd, J = 5.8, 12.2 Hz, 0.8H), 3.18 (br d, J = 8.8 Hz, 0.2H), 2.86 (td, J = 3.4, 12.4 Hz, 1H), 2.57 (d, J = 7.5 Hz, 0.8H), 2.41 (m overlapped, 1H), 2.38 (s, 3H), 2.01 (br d, J = 13.4 Hz, 1H), 0.89 (s, 9H), 0.11 (s, 3H), 0.10 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 144.2, 143.5, 142.88, 142.82, 141.7, 138.79, 137.9, 129.5, 129.4, 127.05, 127.02, 111.82, 111.7, 109.8, 54.6, 54.2, 48.0, 44.5, 40.71, 40.68, 30.89, 30.4, 25.65, 25.55, 21.4, 18.2, 18.1, 15.33, 15.0, −5.22, −5.4. Anal. Calcd for $C_{22}H_{35}NO_3SSi$: C, 62.66; H, 8.36; N, 3.32; S, 7.60. Found: C, 62.49; H, 8.31; N, 3.34; S, 7.44.

(2*S*,3*R*)-*N*-(4-Methylbenzenesulfonyl)-2-methyl-3-(2-hydroxyethyl)-4-methylenepiperidine (66). To a solution of silyl enol ether **54** (prepared from 0.127 g, 0.3 mmol of alkyne **19b**) in CH_2Cl_2 (5 mL) were added water (0.2 mL) and trifluoroacetic acid (2 mL). The reaction was stirred at room temperature for 15 min. The volatiles were removed under reduced pressure, and the residue was purified by chromatography, eluting with 1:9 petroleum ether−diethyl ether, to give the intermediate aldehyde. IR (neat): 2924, 1722, 1450, 1162 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.68 (s, 1H), 7.62 (d, J = 8.3 Hz, 2H), 7.26 (d, J = 8.3 Hz, 2H), 4.87 (s, 1H), 4.83 (s, 1H), 4.06 (dq, J = 6.6, 17.3 Hz, 1H), 3.77 (ddd, J = 5.8, 12.2, 22.2 Hz, 1H), 2.94 (dd, J = 7.5, 17.3 Hz, 1H), 2.84 (td, J = 3.4, 12.4 Hz, 1H), 2.66 (m, 1H), 2.56 (ddd, J = 1, 5.5, 22.2 Hz, 1H), 2.39 (s, 3H), 2.39 (m overlapped, 1H), 2.12 (br d, J = 13.9 Hz, 1H), 0.84 (d, J = 6.9 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 201.8, 143.3, 141.2, 137.3, 129.7 (2), 126.7 (2), 113.8, 52.7, 445.6, 42.7, 40.2, 30.4, 21.4, 14.7.

The latter substance was then taken up in ether (3 mL), and lithium aluminum hydride (0.025 g, 0.66 mmol) was added. The reaction was stirred at room temperature for 5 min. Technical Et_2O (3 mL) and a saturated solution of Na_2SO_4 (0.1 mL) were added. After 10 min, the heterogeneous mixture was filtered through a pad of silica (Et_2O) to afford pure **66** (0.060 g, 0.194 mmol) as a colorless oil. $[\alpha]_D$ = −44.0 (*c* 2.02, $CHCl_3$). IR (neat): 3521, 2942, 1651, 1336, 1160 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.68 (d, J = 8.3 Hz, 2H), 7.29 (d, J = 8.3 Hz, 2H), 4.89 (t, J = 2 Hz, 1H), 4.81 (t, J = 1.7 Hz, 1H), 4.14 (q, J = 6.8 Hz, 1H), 3.79 (dd, J = 6.1, 12.2 Hz, 1H), 3.68 (td, J = 5.6, 11.0 Hz, 1H), 3.60 (td, J = 6.6, 11.0 Hz, 1H), 2.87 (td, J = 3.1, 12.4 Hz, 1H), 2.42 (s, 3H), 2.42 (m overlapped, 1H), 2.25 (t, J = 7.5 Hz, 1H), 2.09 (d, J = 13.4 Hz, 1H), 1.86 (d, J = 6.3 Hz, 1H), 1.83 (d, J = 6.3 Hz, 1H), 1.63 (br s, 1H), 0.87 (d, J = 6.8 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.3, 142.9, 137.8, 129.6 (2), 126.8 (2), 113.0, 60.7, 53.3, 46.3, 40.5, 34.2, 30.2, 21.4, 15.0. Anal. Calcd for $C_{16}H_{23}NO_3S$: C, 62.10; H, 7.49; N, 4.52; S, 10.36. Found: C, 61.97; H, 7.26; N, 4.39; S, 10.19.

(2*S*,3*R*,4*R*)-*N*-(4-Methylbenzenesulfonyl)-2,3-dimethyl-4-(2-hydroxyethyl)-5-methylenepiperidine (56) was obtained starting from alkyne **23** (75 mg, 0.2 mmol) and using procedures reported before. **56** (0.031 g, 0.096 mmol) was recovered as a colorless oil. $[\alpha]_D$ = 11.2 (*c* 1.62, $CHCl_3$). IR (neat): 3510, 2935, 1338, 1154 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.69 (d, J = 8.3 Hz, 2H), 7.29 (d, J = 8.3 Hz, 2H), 5.04 (s, 1H), 4.82 (s, 1H), 3.92 (d, J = 13.4 Hz, 1H), 3.92 (m overlapped, 1H), 3.75 (d, J = 13.4 Hz, 1H), 3.66 (ddd, J = 4.8, 7.5, 10.5 Hz, 1H), 3.59 (dt, J = 7.3, 10.5 Hz, 1H), 2.43 (s, 3H), 2.11 (br t, J = 9.3 Hz, 1H), 1.75 (tdd, J = 2.9, 7.8, 13.9 Hz, 1H), 1.53 (m, 1H), 1.42 (m, 1H), 1.61 (br s, 1H), 1.12 (d, 7.1 Hz, 3H), 0.89 (d, J = 6.8 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.3, 143.0, 137.0, 129.5 (2) 127.0 (2), 111.8, 60.0, 54.0, 47.3, 38.8, 38.4, 32.3, 32.3, 21.4, 16.8, 13.1. Anal. Calcd for $C_{17}H_{25}NO_3S$: C, 63.12; H, 7.79; N, 4.33; S, 9.91. Found: C, 63.53; H, 7.39; N, 3.96; S, 9.56. HRMS: calcd for $C_{17}H_{25}NO_3S$, [M^+], 323.1555; found, 323.1551.

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Supporting Information Available: Experimental procedure for compounds **6**, **8a**, **8b**, **9a**, **9b**, **10**, **12a**, **12b**, **13**, **16**, **19a**, **19b**, **21**, **22**, **23**, **25**, **26**, **30a**, **30b**, **31**, **38**, **39**, **40**. This material is available free of charge via the Internet at http://pubs.acs.org.

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