ChemInform Abstract: Gold-Catalyzed Cycloisomerization of 1,7-Enyne Esters to Structurally Diverse cis-1,2,3,6-Tetrahydropyridin-4-yl Ketones.

ARTICLE *in* THE JOURNAL OF ORGANIC CHEMISTRY · MARCH 2013

Impact Factor: 4.72 · DOI: 10.1021/jo400121j · Source: PubMed

4 AUTHORS, INCLUDING:

Weidong Rao
Nanjing Forestry University
44 PUBLICATIONS **714** CITATIONS
SEE PROFILE

Sally Sally
Nanyang Technological University
4 PUBLICATIONS **59** CITATIONS
SEE PROFILE

Ming Joo Koh
Boston College, USA
8 PUBLICATIONS **169** CITATIONS
SEE PROFILE

JOC The Journal of Organic Chemistry

Article

pubs.acs.org/joc

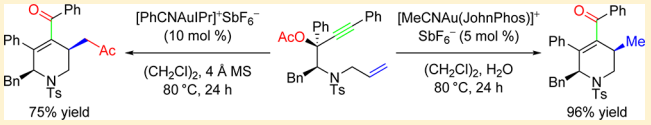
Gold-Catalyzed Cycloisomerization of 1,7-Enyne Esters to Structurally Diverse *cis*-1,2,3,6-Tetrahydropyridin-4-yl Ketones

Weidong Rao, Sally, Ming Joo Koh, and Philip Wai Hong Chan*

Division of Chemistry and Biological Chemistry, School of Physical and Mathematical Sciences, Nanyang Technological University, Singapore 637371, Singapore

Supporting Information

ABSTRACT: A synthetic method that relies on gold(I)-catalyzed cycloisomerization of 1,7-enyne esters to prepare highly functionalized *cis*-1,2,3,6-tetrahydropyridin-4-yl ketone derivatives in good to excellent yields and as a single regio-, diastereo-, and enantiomer is described. By taking advantage of the distinctive differences in the electronic and steric properties between an NHC (NHC = *N*-heterocyclic carbene) and phosphine ligand in the respective gold(I) complexes, a divergence in product selectivity was observed. In the presence of $[PhCNAuIPr]^+SbF_6^-$ (IPr = 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidine) as the catalyst, tandem 1,3-acyloxy migration/6-*exo-trig* cyclization/1,5-acyl migration of the substrate was found to selectively occur to give the *δ*-diketone-substituted 1,2,3,6-tetrahydropyridine adduct. In contrast, reactions with the gold(I) phosphine complex $[MeCNAu(JohnPhos)]^+SbF_6^-$ (JohnPhos = (1,1′-biphenyl-2-yl)-di-*tert*-butylphosphine) as the catalyst was discovered to result in preferential 1,3-acyloxy migration/6-*exo-trig* cyclization/hydrolysis of the 1,7-enyne ester and formation of the *cis*-1,2,3,6-tetrahydropyridin-4-yl ketone derivative. The utility of this piperidine forming strategy as a synthetic tool that makes use of 1,7-enyne esters was exemplified by its application to the synthesis of an enantiopure analogue of the bioactive 2,3,4,4a,5,9b-hexahydroindeno[1,2-*c*]pyridine family of compounds.



INTRODUCTION

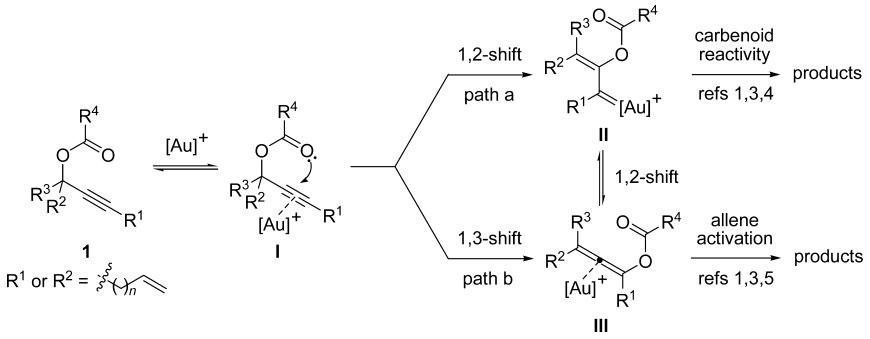
1,*n*-Enyne cycloisomerizations mediated by a gold(I) or gold(III) catalyst represent one of the most powerful and versatile methods for the efficient and atom-economical synthesis of complex molecules in a single step.[1−7] Included in this have been synthetic strategies that have made use of readily accessible 1,*n*-enyne esters **1** (Scheme 1).[1,3−7] From a mechanistic point of view, the reaction relies on the susceptibility of the acyloxy moiety of the Au(I)-activated adduct **I** to undergo either the respective 1,2- or 1,3-acyloxy migration pathways a and b shown in Scheme 1. This is followed by further functionalization of the corresponding gold carbenoid and allene species **II** and **III** by a remaining pendant functional group. In the case of the latter, which density functional theory (DFT) calculations show could also be due to two consecutive 1,2-acyloxy shifts;[5f,6] strategies that allow for selective alkene activation of the resulting 1,*n*-allenene **III** by the Au(I) catalyst, in contrast, have been less widely investigated.[7,8]

Recently, we delineated the first example that provided azabicyclo[4.2.0]oct-5-enes from tandem 1,3-migration/[2 + 2] cycloaddition of 1,7-enyne benzoates of the type **1** as a result of this novel mode of activation by the gold catalyst (Scheme 2, path a).[7] Building on the mechanistic premise put forward in this earlier work, we reasoned that a new cycloisomerization pathway might ensue on fine-tuning the steric and electronic interactions between the R groups in the substrate. In doing so, we discovered that when $R^2 \neq Ph = R^3$ in 1,7-enyne ester **1** and in the presence of an NHC−gold(I) complex, the resultant in situ formed organogold species **V** was susceptible to a 1,5-acyl migration process to give the *cis*-1,2,3,6-tetrahydropyridin-4-yl *δ*-diketone ring system (Scheme 2, path b). This unique type of reactivity has only been described once before where a vinyl gold species, generated from Au(I)-catalyzed tandem 1,3-acyloxy migration/5-*exo-dig* cyclization of 1,6-diyne acetates, was trapped by the acylium moiety to give *δ*-diketone substituted cyclopentenes (Scheme 2, eq 2).[9] In contrast, 1,5-acyl migrations to a Au−C(sp^3) moiety of an alkyl gold species that results in the construction of a C−C bond are not known.[10] The use of a gold(I) phosphine catalyst, on the other hand, was found to lead to the substrate undergoing a more rapid 1,3-acyloxy migration/6-*exo-trig* cyclization/hydrolysis pathway to deliver *cis*-1,2,3,6-tetrahydropyridin-4-yl ketone derivatives (Scheme 2, path c). As part of ongoing efforts to examine the utility of gold catalysis in heterocyclic synthesis,[11] we present in this paper the details of this chemistry that offers an expedient and chemoselective route to these two potentially useful nitrogen-containing heterocycles in good to excellent yields. The *cis*-1,2,3,6-tetrahydropyridines, of which the nitrogen-containing heterocycle is a common structural motif in a wide variety of bioactive natural products and pharmaceutically interesting compounds, were additionally obtained as a single regio-, diastereo- and enantiomer. The application of this catalytic piperidine formation process to the synthesis of an enantiopure analogue of the 2,3,4,4a,5,9b-hexahydroindeno-[1,2-*c*]pyridines, a family of compounds known to exhibit

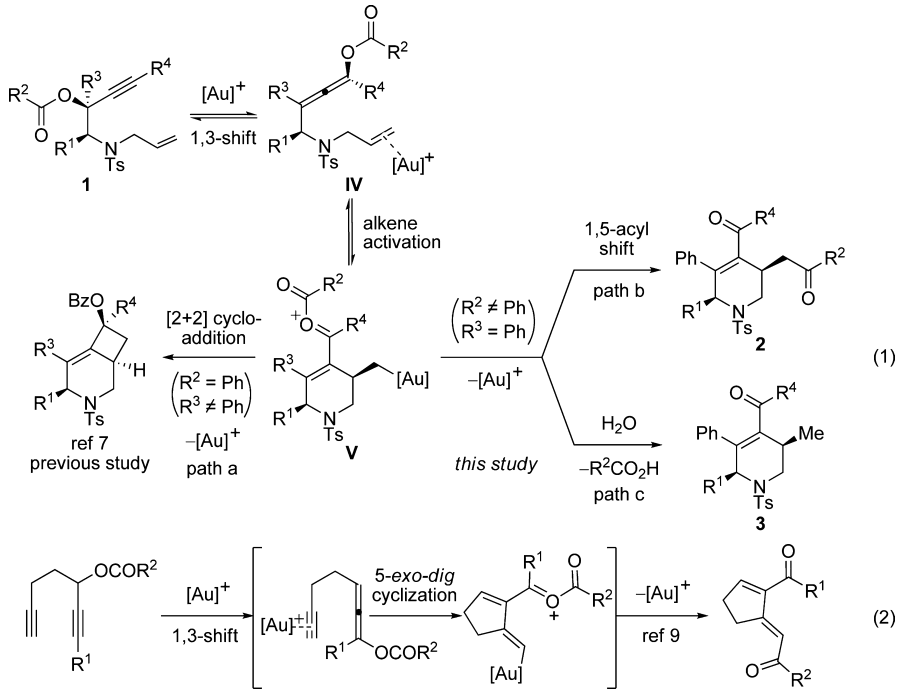
Received: January 19, 2013
Published: March 4, 2013

   dx.doi.org/10.1021/jo400121j | J. Org. Chem. 2013, 78, 3183−3195

Scheme 1. Gold-Catalyzed Reactivities of 1,*n*-Enyne Esters



Scheme 2. Gold(I)-Catalyzed Cycloisomerization of 1,6-Diyne and 1,7-Enyne Esters Involving 1,5-Acyl Migration



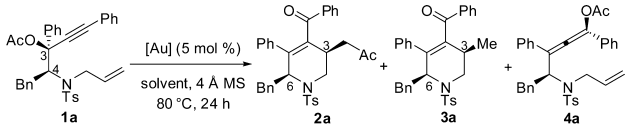
bioactivities ranging from antispermatogenic to antidepressant to antiintegrin activity, in three steps is also presented.[12]

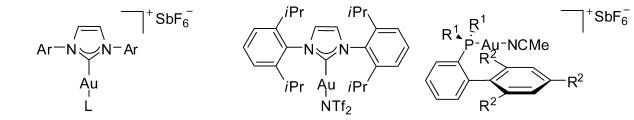
RESULTS AND DISCUSSION

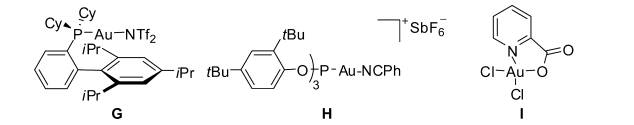
Our studies commenced with the gold-catalyzed reactions of the enantiopure *syn*-1,7-enyne acetate **1a**, prepared from L-phenylalanine following literature procedures, to establish the reaction conditions (Table 1).[13] The (3*S*,4*S*) absolute configuration of the starting material was determined by X-ray structure analysis.[14] This study initially revealed that treating **1a** with 5 mol % of NHC–gold(I) complex **A** in 1,2-dichloroethane at 80 °C for 24 h gave **2a** and **3a** in 60 and 16% yield, respectively, and, in both instances, as a single regio-, diastereo-, and enantiomer (entry 1). The *cis* diastereoselectivity and (3*R*,6*S*) absolute configuration of the two nitrogen-containing ring products were established by X-ray crystallographic analysis.[14] Our studies subsequently showed that the introduction of 4 Å molecular sieves (MS) led to the same product yield and formation of **4a** in 12% yield (entry 2).[15] By increasing the catalyst loading from 5 to 10 mol %, the generation of the 1,6-allenene could be suppressed to give **2a** as the only product in 75% yield (entry 3). In contrast, an inspection of entries 4–18 shows that repeating the reaction with other gold(I) and gold(III) complexes in place of **A** as the catalyst or in other solvents was markedly less effective. Changing the solvent from 1,2-dichloroethane to toluene, MeCN, or THF in the presence of 10 mol % of **A** as the catalyst was found to result in only formation of the 1,6-allenene in 35–81% yield (entries 4–6). The reaction with toluene as the solvent additionally afforded the ketone **3a** in 23% yield (entry 4). A similar outcome was observed when the reaction was repeated with 5 mol % of NHC–gold(I) complex **B** and **C**, AuCl, and gold(III) complex **I** in place of **A** (entries 7, 8 and 17, 18). Moreover, the analogous transformation with NHC–gold(I) complex **D** as the catalyst afforded a mixture of all three compounds in yields of 28, 11, and 23%, as shown in entry 9. Likewise, replacing catalyst **A** with 5 mol % of the gold(I) phosphine catalysts **E**–**G** and $Ph_3PAuNTf_2$, and gold(I) phosphite complex **H** was found to result in a mixture of **2a** and/or **3a** and/or **4a** (entries 10 and 13–16). Further inspection with the gold(I) phosphine complex **E** as the catalyst and in the absence of 4 Å MS showed that **3a** could be obtained as the sole product in 84% yield (entry 11). The addition of 2 equiv of water to these latter conditions was then found to increase the yield of the ketone product by 12% (entry 12). On the basis of the above results, reaction of **1a** in the

dx.doi.org/10.1021/jo400121j | J. Org. Chem. 2013, 78, 3183–3195

Table 1. Optimization of the Reaction Conditions[a]







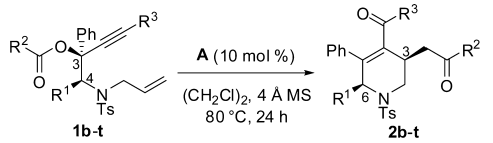
			yield (%)		
entry	catalyst	solvent	2a	3a	4a
1[b]	**A**	$(CH_2Cl)_2$	60	16	
2	**A**	$(CH_2Cl)_2$	60		12
3[c]	**A**	$(CH_2Cl)_2$	75		
4[c]	**A**	toluene		23	35
5[c]	**A**	MeCN			67
6[c]	**A**	THF			81
7	**B**	$(CH_2Cl)_2$			86
8	**C**	$(CH_2Cl)_2$			81
9	**D**	$(CH_2Cl)_2$	28	11	23
10	**E**	$(CH_2Cl)_2$	14	69	
11[b]	**E**	$(CH_2Cl)_2$		84	
12[b,d]	**E**	$(CH_2Cl)_2$		96	
13	**F**	$(CH_2Cl)_2$	12	71	
14	**G**	$(CH_2Cl)_2$	31	48	
15	$Ph_3PAuNTf_2$	$(CH_2Cl)_2$	10	70	
16	**H**	$(CH_2Cl)_2$		53	15
17	AuCl	$(CH_2Cl)_2$			67
18	**I**	$(CH_2Cl)_2$			85

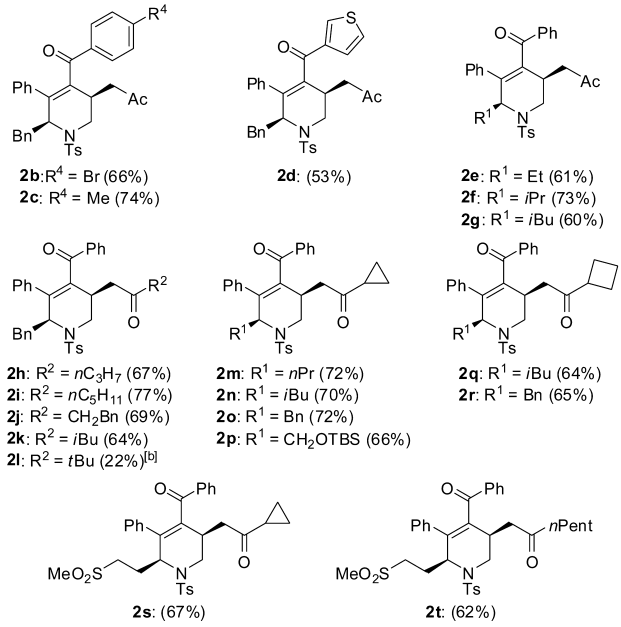
[a]All reactions were performed on a 0.2 mmol scale with catalyst/**1a** ratio = 1:20 and 4 Å MS (100 mg) at 80 °C for 24 h. Cy = cyclohexyl. [b]Reaction conducted in the absence of 4 Å MS. [c]Reaction conducted with 10 mol % of catalyst. [d]Reaction conducted in the presence of 2 equiv of H_2O.

presence of 10 mol % of NHC−gold(I) complex **A** and 4 Å MS in 1,2-dichloroethane at 80 °C for 24 h provided the optimum conditions to the δ-diketone-substituted 1,2,3,6-tetrahydropyridine derivative. On the other hand, reaction of **1a** with 5 mol % of gold(I) phosphine catalyst **E** and 2 equiv of H_2O in 1,2-dichloroethane at 80 °C for 24 h gave the best conditions for the *cis*-1,2,3,6-tetrahydropyridin-4-yl ketone product.

With the two optimized conditions to access the ketone and δ-diketone substituted *cis*-1,2,3,6-tetrahydropyridines in hand, we first sought to assess the generality of the latter for a series of 1,7-enyne carboxylates prepared from the corresponding L-α-amino acids.[13] The results, summarized in Table 2, reveal that with the NHC−gold(I) complex **A** as the catalyst, the conditions proved to be broad, furnishing a diverse set of δ-diketone-substituted *cis*-1,2,3,6-tetrahydropyridines in 22−77% yield from the corresponding substrates **1b−t**. Starting materials **1b** and **1c**, in which the alkynyl carbon center is occupied by an aryl substituent with an electron-withdrawing or electron-donating group at the *para* position, were found to

Table 2. Cycloisomerization of 1,7-Enyne Esters 1b−t Catalyzed by A[a]





[a]Unless otherwise stated, all reactions were performed on a 0.2 mmol scale with **A**/**1** ratio = 1:10 and 4 Å MS (100 mg) in $(CH_2Cl)_2$ at 80 °C for 24 h. Values in parentheses denote product yields. [b]Reaction carried out with 20 mol % of **A** for 48 h and furnished **3a** in 45% yield.

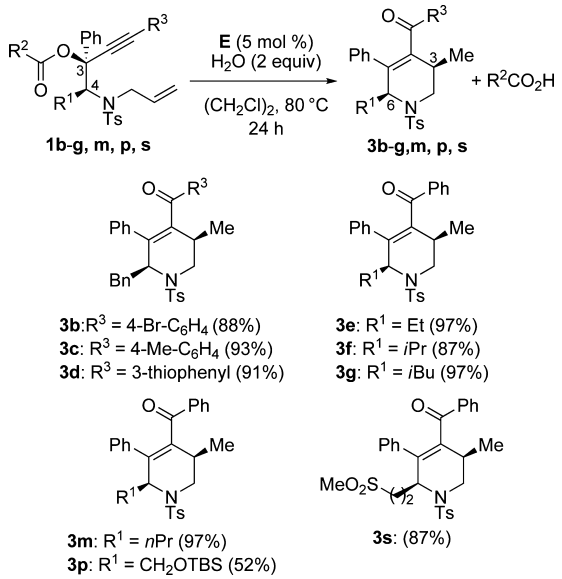
proceed to give the corresponding δ-diketones **2b** and **2c** in 66 and 74% yield. Similarly, reactions of substrates possessing a thiophene moiety at the same position (**1d**) or other linear (**1e**) and branched chain (**1f** and **1g**) alkyl groups at the amino carbon center were found to be well-tolerated under the reaction conditions. In these transformations, the corresponding piperidine products were afforded in yields of 53−73%. The presence of other alkyl- or cycloalkyl-substituted carboxylic esters was generally found to have no influence on the course of the reaction with **2h−k** and **2m−t** furnished in good to excellent yields. Pleasingly, this included 1,7-enyne esters with a pendant OTBS (**1p**) or MeO_2S (**1s** and **1t**) moiety which gave the corresponding δ-diketones **2p**, **2s**, and **2t** in 62−67% yield. The only exception was that of **1l**, containing a sterically bulky pivalate group, which was found to require a catalyst loading of 20 mol % and a reaction time of 48 h to furnish **2l** along with **3a** in respective yields of 22 and 45%. More notably, all the cycloisomerizations examined demonstrate that the piperidine forming process is highly selective. In contrast to our recent findings for the analogous reactions of 1,7-enyne benzoates[7] and those of 1,6-allenenes,[16,17] ^1H NMR analysis of the crude mixtures did not detect any cyclization products arising from Au(I)-mediated [2 + 2] cycloaddition. Furthermore, the δ-diketone ring adducts were obtained as a single diastero- and enantiomer with the *cis* stereochemistry and (3*R*,6*S*) absolute configurations for **2l**, **2p**, and **2q** determined by X-ray single-crystal structure analysis.[14]

We next sought to define the scope of the 1,3-acyloxy migration/6-*exo*-*trig* cyclization/hydrolysis reaction with 1,7-

dx.doi.org/10.1021/jo400121j | J. Org. Chem. 2013, 78, 3183−3195

enyne ester compounds **1b–g,m,p,s** as representative examples (Table 3). Overall, this led us to find the cyclization reactions

Table 3. Cycloisomerization of 1,7-Enyne Esters 1b–g,m,ps Catalyzed by E[a]

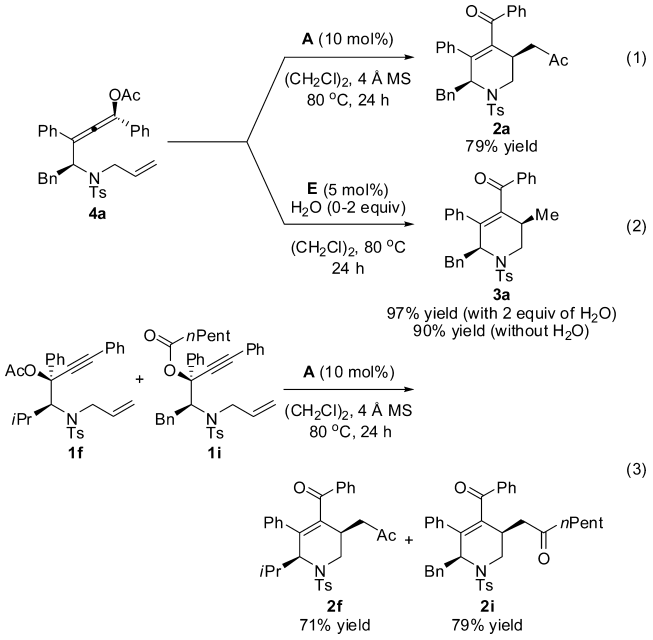


[a]Unless otherwise stated, all reactions were performed on a 0.2 mmol scale with **E**/**1** ratio = 1:20 and 2 equiv of H_2O in 1,2-dichloroethane at 80 °C for 24 h. Values in parentheses denote product yields.

to proceed well on applying the gold(I) complex **E**-catalyzed conditions described in Table 1, entry 12. Under these conditions, the corresponding *cis*-1,2,3,6-tetrahydropyridin-4-yl ketones **3b–g,m,p,s** were afforded in 52–97% yield. The nitrogen-containing ring adducts were also furnished as a single diastereo- and enantiomer on the basis of ^{1}H NMR measurements. While not listed in Table 3, it is worth noting that **3g** could also be prepared in 94 and 96% yield from the analogous reactions of **1n** and **1q** catalyzed by Au(I) complex **E** under similar conditions. Likewise, subjecting **1t** to 5 mol % of Au(I) complex **E** under these same conditions gave the corresponding ketone adduct **3s** in 83% yield.

The mechanistic posit put forward in Scheme 2 and based on our previous works[7] predicts that the Au(I)-catalyzed formation of the two nitrogen-containing ring products will occur through a pathway involving a common 1,6-allenene adduct. While unanticipated, the competitive formation of **4a** for the cycloisomerization of **1a** under certain conditions shown in Table 1 lends weight to its involvement in the Au(I)-mediated tandem process. This premise is further supported by the observation that when a solution of **4a** in 1,2-dichloroethane was treated with 10 mol % of **A** under the conditions shown in Scheme 3, eq 1, the expected *δ*-diketone **2a** was obtained as the sole product in 79% yield. Likewise, repeating this experiment under similar conditions but with 5 mol % of **E** in place of **A** as the catalyst in the absence or presence 2 equiv of H_2O gave **3a** in 90 and 97% yield, respectively (Scheme 3, eq 2). The subsequent role of the Au(I) complex in selectively activating the alkene moiety of this intermediate is also corroborated by our findings when the reaction was repeated for a third time in the absence of the Lewis acidic catalyst. In this latter control experiment, the substrate was recovered in near quantitative yield, consistent with previous studies demonstrating 1,6-allenenes with a pendant unactivated alkene group being

Scheme 3. Control Experiments with 1f,i and 4a Catalyzed by Au(I) Complexes A or E

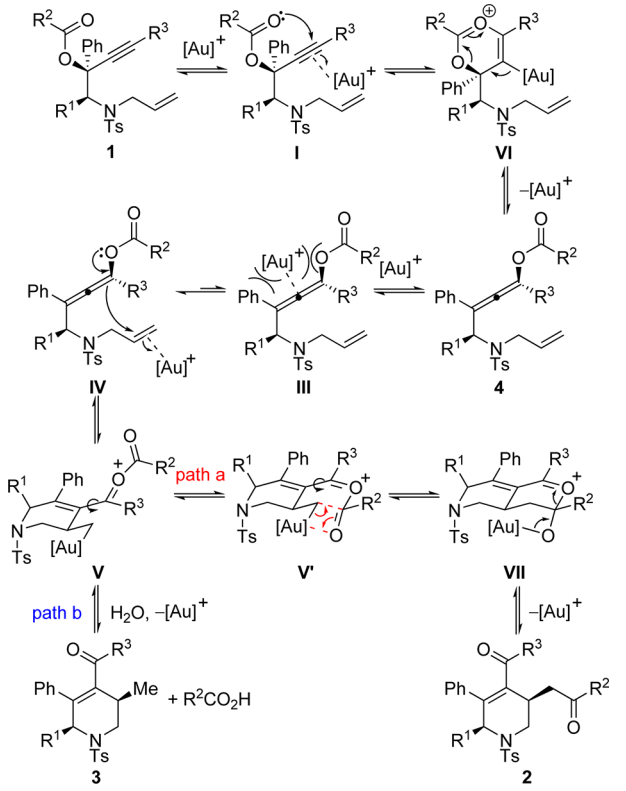


resistant to a thermally driven cyclization process.[7,17] For reactions mediated by **A**, the likely involvement of a 1,5-acyl shift was also supported by our findings when we investigated the cyclization of a 1:1 mixture of **1f** and **1i** in the presence of the NHC-gold(I) complex **A** under the conditions shown in Scheme 3, eq 3. This revealed the production of the corresponding *δ*-diketones **3f** and **3i** as the only products in 71 and 79% yield, respectively, with ^{1}H NMR analysis of the crude reaction mixture detecting the presence of no other cyclization products.

A tentative mechanism for the present gold(I)-catalyzed cycloisomerization reactions to form the *cis*-1,2,3,6-tetrahydropyridin-4-yl ketones is presented in Scheme 4. In a manner similar to that reported in our previous work,[7] this might initially involve selective activation of the alkyne moiety of the 1,7-enyne ester substrate by the metal catalyst to give the gold(I)-coordinated complex **I**. This could result in a *syn* 1,3-shift of the carboxylate functionality via the 1,3-dioxin-1-ium intermediate **VI** to generate 1,6-allenene **4**. Preferential coordination to the remaining alkene group by the Lewis acidic catalyst to form the gold(I)-activated adduct **IV** over that of **III** might then occur to avoid unfavorable steric interactions between the metal complex and the substituents on the allene moiety in the latter. Subsequent 6-*exo*-*trig* cyclization involving *anti* addition through the more nucleophilic distal 2*π* component of the allenic moiety to the Au(I)-activated alkene bond of this newly formed species would then afford the putative alkyl gold adduct **V**.[18] A divergence in reactivity mode is thought to proceed at this point in the pathway depending on the nature of the gold(I) catalyst employed. It is possible that the oxocarbenium complex **V** derived from the reactions of **1** catalyzed by **A** could be more resistant to a hydrolysis process involving protodeauration than its counterpart generated from the substrate mediated by **E**. As a result, rotation of the oxonium C–C bond in the former piperidine intermediate can now take place to give conformer **V′** so as to minimize any unfavorable steric interactions between the acylium moiety and the aryl group (path a in Scheme 4). In doing so, this might

dx.doi.org/10.1021/jo400121j | J. Org. Chem. 2013, 78, 3183–3195

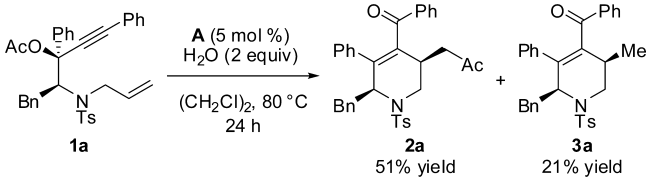
Scheme 4. Proposed Mechanism for the Cycloisomerization of 1 Catalyzed by A or E



trigger the 1,5-acyl migration process involving nucleophilic addition of the Au–C(sp^3) bond to the acyl carbonyl carbon center of the acyloxy moiety via a 4-membered cyclic transition state.[19,20] The resultant bicyclic gold intermediate **VII** obtained then delivers **2** on release of the gold(I) catalyst. The postulated change in conformation from **V** to **V′** that initiates the 1,5-acyl shift involving nucleophilic attack of the Au–C(sp^3) bond to the acyl carbonyl carbon center would be consistent with our earlier findings showing **3a** and not **2l** obtained as the major product for the reaction of **1l** catalyzed by **A**. This might be anticipated as such a pathway may not be expected to be as efficient in substrates containing a sterically bulky carboxylic ester. In contrast and as mentioned, reactions mediated by **E**, presumably the corresponding alkyl gold **V** is more prone to a simultaneous or stepwise hydrolysis process involving protodeauration (path b in Scheme 4). Aided by the presence of water, this leads to the formation of **3** and the carboxylic acid byproduct.

Although also speculative, we surmise that the obtained product chemoselectivities could be presumably due to the difference in the electronic and steric properties of the ligands in the two metal catalysts **A** and **E**. In a recent study, the rate of protodeauration of a vinyl gold species derived from various Au(I) complexes was demonstrated to be fastest with those containing a JohnPhos ligand.[21] A reason for this was thought to be due to a η2-interaction provided by the *o*-Ph substituent in combination with the two electron-rich *t*-Bu groups on the phosphine center in the ligand stabilizing the generated cationic gold complex. It would not be inconceivable that a similar ligand effect is being observed in the present study, with the rate of protodeauration in **V** increasing on changing the catalyst from the NHC–gold(I) complex **A** to the Au(I) phosphine complex **E**. Indeed, this possible rationale based on ligand effects was further supported by our findings when we investigated the NHC–gold(I) complex **A**-catalyzed reaction of **1a** in the presence of 2 equiv of H_2O under the conditions described in Scheme 5. In this control experiment, the *δ*-

Scheme 5. NHC–Gold(I) Complex A Catalyzed Reaction of 1a in the Presence H_2O



diketone derivative **2a** and not the ketone adduct **3a** (yields of 51 and 21%, respectively) was afforded as the major product despite the presence of the proton source. The origin of the *cis* diastereoselectivity could be due to the gold(I)-activated alkene moiety in **IV** preferentially occupying the conformation shown in Scheme 4 prior to the cyclization event. In this manner, the potential for any unfavorable transannular steric interactions between the substituents on formation of the nitrogen ring intermediate **V** can be kept to a minimum. What is evident, on the other hand, is the formation of both nitrogen-containing ring compounds as a single enantiomer from an enantiopure substrate implying that neither the starting material nor any of the putative intermediates are prone to racemization. Consequently, this leads to the enantioselectivity observed at the newly formed stereogenic C3 position in the product. The possibility that the origin of the stereoselectivity could be due to thermodynamic control of the reaction was considered but thought to be less likely based on density functional theory (DFT) calculations of the two possible isomers of **2a**. For each case, a conformational search was performed in the gas phase, using the Monte Carlo Multiple Minimum (MCMM) method as implemented in the MacroModel 9.9 program along with the use of the OPLS2005 force field.[22,23] The top 20 lowest-energy conformers for each isomer were then subjected to refined geometry optimizations at the B3LYP/6-31G* level.[24,25] Gaussian 09 was used for the DFT calculations and UCSF Chimera was used to draw the molecules.[26,27] As shown in Figure 1, this gave the most stable conformers of *cis*-**2a** and *trans*-**2a** and relative energies that were similar, with the latter

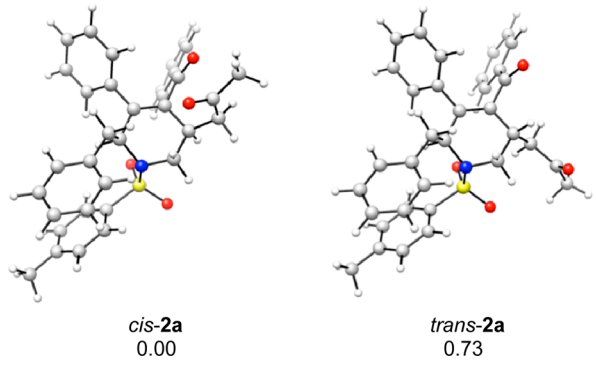


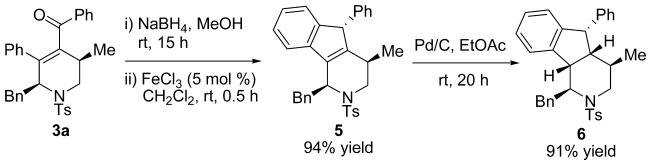
Figure 1. Most stable conformers of *cis*-**2a** and *trans*-**2a** (in kcal/mol) as obtained at the B3LYP/6-31G* level.

dx.doi.org/10.1021/jo400121j | J. Org. Chem. 2013, 78, 3183–3195

being is slightly less stable by 0.73 kcal/mol, that indicated the two isomers to be of almost equal stability.

Having established an efficient route to *cis*-1,2,3,6-tetrahydropyridines, we applied this new strategy to the synthesis of an enantiopure 2,3,4,4*a*,5,9*b*-hexahydroindeno[1,2-*c*]pyridine analogue (Scheme 6). The tricyclic *N*-heterocycles are a class of

Scheme 6. Synthesis of an Enantiopure 2,3,4,4a,5,9b-Hexahydroindeno[1,2-*c*]pyridine Analogue 6 from 3a



compounds reported to exhibit bioactivities ranging from antispermatogenic to antidepressant to antiintegrin activity.[12] At room temperature, reduction of the ketone functional group in **3a** was achieved with $NaBH_4$ in MeOH. This was then followed by treatment of the resultant crude mixture with 5 mol % of $FeCl_3$ in dichloromethane to furnish the chiral 2,3,4,5-tetrahydro-1*H*-indeno[1,2-*c*]pyridine **5** in 94% yield over two steps.[28] Subsequent Pd/C-mediated hydrogenation of the newly formed tricyclic adduct in EtOAc then gave the desired *N*-tosylated indenopiperidine **6** in 91% yield and as a single diastereo- and enantiomer. The three-step conversion from **3a** to **6** proceeded in a stereoselective manner from the *cis*-1,2,3,6-tetrahydropyridine substrate to the product with the stereochemistry of both **5** and **6** being assigned on the basis of NMR spectroscopic measurements.

CONCLUSION

In summary, we have described an efficient synthetic method for the preparation of a wide variety of *cis*-1,2,3,6-tetrahydropyridin-4-yl ketones and *δ*-diketones from Au(I)-catalyzed cycloisomerization of 1,7-enyne esters. In the case of the latter product, the new cycloisomerization pathway was thought to involve an unprecedented 1,5-migration of the acyl moiety to the Au−C(sp^3) bond of the in situ formed alkyl gold intermediate. The synthetic approaches were shown to tolerate a diverse set of 1,7-enyne esters and provide stereochemically well-defined *cis*-1,2,3,6-tetrahydropyridines for application in natural products synthesis and as versatile privileged scaffolds in medicinal chemistry. Our studies showed that effective control of product selectivity was found to be possible by exploiting the differences in the electronic and steric properties between a NHC-gold(I) complex and phoshine-based gold(I) catalyst. The synthetic utility of the present method to these two classes of nitrogen-containing heterocycles was also demonstrated by further modifying one adduct obtained to the preparation of an enantiopure analogue of the bioactive 2,3,4,4a,5,9b-hexahydroindeno[1,2-*c*]pyridine family of compounds. Efforts to expand the scope and synthetic applications of the present reactions are currently being pursued and will be reported in due course.

EXPERIMENTAL SECTION

General Considerations. Unless otherwise stated, all reactions were performed in oven-dried glassware under an argon atmosphere. All reagents and starting materials along with gold complex **E**, **G**, **I** were purchased from commercial sources and used as received unless otherwise specified. Gold complexes **A**−**D**, **F**, and **H** were prepared following literature procedures.[13] Solvents were purified following standard literature procedures. Analytical thin layer chromatography (TLC) was performed using precoated silica gel plate. Visualization was achieved by UV light (254 nm). Flash chromatography was performed using silica gel and gradient solvent system (EtOAc/*n*-hexane as eluent). ^1H and ^{13}C NMR spectra were recorded on a 300, 400, or 500 MHz NMR spectrometer. Chemical shifts (ppm) were recorded with tetramethylsilane (TMS) as the internal reference standard. Multiplicities are given as: s (singlet), br s (broad singlet), d (doublet), t (triplet), dd (doublet of doublets) or m (multiplet). The number of protons (*n*) for a given resonance is indicated by *n*H and coupling constants are reported as a *J* value in Hz. Infrared spectra were recorded on a FTIR spectrometer. Solid samples were examined as a thin film between NaCl salt plates. Low resolution mass spectra were determined on a mass spectrometer and reported in units of mass to charge (*m*/*z*). High resolution mass spectra (HRMS) were obtained on a LC/HRMS TOF spectrometer using simultaneous electrospray (ESI). Optical rotations were measured in $CHCl_3$ on a polarimeter with a sodium vapor lamp at 589 nm and 10 cm cell (*c* given in g/100 mL).

General Procedure for the Preparation of 1,7-Enyne Esters 1a−t. To a solution of the appropriate *N*-((3*S*,4*S*)-3-hydroxy-1,3,5-substituted-alk-4-yn-2-yl)-4-methylbenzenesulfonamide[7,11a] (1 mmol) in THF (5 mL) was added LiHMDS (2.1 mL, 2.1 mmol, 1.0 M in THF) at 0 °C. The reaction solution was stirred at this temperature for a further 20 min, and then the appropriate acyl chloride (1.5 mmol) was added. The resulting reaction mixture was stirred at 0 °C for 30 min. Upon completion (indicated by TLC), the reaction mixture was quenched by addition of saturated NH_4Cl (10 mL), and the organic layer was extracted with EtOAc (3 × 15 mL). The combined organic layers were washed with brine (10 mL), dried over $MgSO_4$, concentrated under reduced pressure, and purified by flash column chromatography on silica gel (eluent: *n*-hexane/EtOAc = 7:1 → 4:1) to yield the intermediate. To a solution of the intermediate was added NaH (60% dispersion in mineral oil, 1.5 equiv) in DMF (5 mL) followed by allyl bromide (1.5 equiv) at 0 °C. The reaction mixture was warmed up to room temperature and stirred for 5−10 h. Upon completion (indicated by TLC), the reaction mixture was quenched with H_2O (10 mL) and the organic layer was extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with brine (10 mL), dried over $MgSO_4$, concentrated under reduced pressure and purified by flash column chromatography on silica gel (eluent: *n*-hexane/EtOAc = 9:1 → 6:1) to give the title compound.

General Experimental Procedure for NHC−Gold(I) Complex A Catalyzed Cycloisomerization of 1,7-Enyne Esters 1 to *cis*-1,2,3,6-Tetrahydropyridin-4-yl *δ*-Diketone Derivatives 2. To a solution of the 1,7-enyne ester 1 (0.2 mmol) and 4 Å MS (100 mg) in 1,2-dichloroethane (2 mL) was added gold(I) complex A (20 *μ*mol). The reaction mixture was stirred at 80 °C for 24 h. The reaction mixture was then cooled to room temperature, filtered through Celite, washed with CH_2Cl_2, and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (*n*-hexane/EtOAc = 7:1 → 3:1 as eluent) gave the title compound.

General Experimental Procedure for Au(I) Complex E Catalyzed Cycloisomerization of 1,7-Enyne Esters 1 to *cis*-1,2,3,6-Tetrahydropyridin-4-yl Ketone Derivatives 4. To a solution of 1,7-enyne ester 1 (0.2 mmol) and H_2O (0.4 mmol) in 1,2-dichloroethane (2 mL) was added gold(I) complex **E** (10 *μ*mol). The reaction mixture was stirred at 80 °C for 24 h. The reaction mixture was then cooled to room temperature and the solvent was removed under reduced pressure. Purification by flash column chromatography on silica gel (*n*hexane/EtOAc = 9:1 → 6:1 as eluent) gave the title compound.

Experimental Procedure for the Preparation of (1*S*,4*R*,5*S*)-1-Benzyl-4-methyl-5-phenyl-2-tosyl-2,3,4,5-tetrahydro-1*H*-indeno[1,2-*c*]pyridine (5). To a solution of **3a** (0.3 mmol) in MeOH (3 mL) was added $NaBH_4$ (9 mmol) at room temperature for 1 h. The reaction mixture was stirred for 24 h. Upon completion, the reaction mixture was quenched with H_2O (10 mL) and extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with

dx.doi.org/10.1021/jo400121j | J. Org. Chem. 2013, 78, 3183−3195

brine (20 mL), dried over $MgSO_4$,and concentrated under reduced pressure. The crude residue was dissolved in CH_2Cl_2 (3 mL) and anhydrous $FeCl_3$ (15 μmol) was added. The reaction mixture was stirred at room temperature for 30 min. Removal of the solvent under reduced pressure and purification by flash column chromatography on silica gel (*n*-hexane/EtOAc = 9:1 as eluent) gave the title compound in 94% yield.

Experimental Procedure for the Preparation of (1*S*,4*R*,4*aR*,5*S*,9*bS*)-1-Benzyl-4-methyl-5-phenyl-2-tosyl-2,3,4,4a,5,9b-hexahydro-1*H*-indeno[1,2-*c*]pyridine (6). To a solution of **5** (0.2 mmol) in EtOAc (5 mL) was added 10% Pd/C (22 mg) under a H_2(g) atmosphere. The reaction mixture was stirred at room temperature for 20 h. The reaction mixture was then filtered through Celite and washed with EtOAc (20 mL) and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (*n*hexane/EtOAc = 9:1 as eluent) gave the title compound in 91% yield.

*(3S,4S)-4-(N-Allyl-4-methylphenylsulfonamido)-1,3,5-triphenylpent-1-yn-3-yl Acetate (**1a**):* yield 75%, 0.423 g; colorless solid; mp = 185−186 °C; $[\alpha]^{23}_D$ −4.5 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.04 (s, 3H), 2.27 (s, 3H), 3.08 (dd, 1H, *J* = 14.5, 9.6 Hz), 3.37 (dd, 1H, *J* = 14.7, 3.9 Hz), 4.02 (dd, 1H, *J* = 16.8, 7.2 Hz), 4.12 (dd, 1H, *J* = 16.8, 7.2 Hz), 4.91 (d, 1H, *J* = 10.2 Hz), 5.01 (d, 1H, *J* = 17.3 Hz), 5.17 (d, 1H, *J* = 5.8 Hz), 5.61−5.63 (m, 1H), 6.79 (d, 2H, *J* = 7.8 Hz), 6.85 (d, 2H, *J* = 8.2 Hz), 7.11−7.24 (m, 5H), 7.31−7.43 (m, 6H), 7.60−7.63 (m, 2H), 7.67 (d, 1H, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.4, 21.8, 34.7, 46.9, 68.6, 82.5, 86.4, 90.8, 116.3, 122.2, 126.5, 126.5, 127.9, 128.3, 128.4, 128.6, 129.0, 129.0, 129.6, 132.2, 136.1, 137.3, 138.6, 139.2, 142.5, 167.5; IR (NaCl, neat) ν 3019, 2232, 1755, 1215 cm^{-1}; HRMS (ESI) calcd for $C_{35}H_{33}NO_4SNa$ (M^+ + Na) 586.2028, found 586.2035.

*(3S,4S)-4-(N-Allyl-4-methylphenylsulfonamido)-1-(4-bromophenyl)-3,5-diphenylpent-1-yn-3-yl acetate (**1b**):* yield 72%, 0.463 g; colorless solid; mp = 181−183 °C; $[\alpha]^{23}_D$ +8.3 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.14 (s, 3H), 2.29 (s, 3H), 3.03 (dd, 1H, *J* = 14.5, 10.2 Hz), 3.25 (dd, 1H, *J* = 14.7, 3.0 Hz), 4.00 (dd, 1H, *J* = 16.9, 6.9 Hz), 4.21 (dd, 1H, *J* = 16.9, 4.5 Hz), 4.98 (d, 1H, *J* = 10.2 Hz), 5.08 (d, 1H, *J* = 17.3 Hz), 5.15 (dd, 1H, *J* = 9.6, 2.8 Hz), 5.69−5.78 (m, 1H), 6.81 (d, 2H, *J* = 8.1 Hz), 6.87 (d, 2H, *J* = 8.1 Hz), 7.01 (d, 2H, *J* = 6.7 Hz), 7.19−7.25 (m, 3H), 7.37−7.49 (m, 5H), 7.53 (d, 2H, *J* = 8.6 Hz), 7.65 (d, 2H, *J* = 7.4 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.5, 21.8, 33.7, 46.9, 69.4, 82.8, 87.8, 89.4, 116.2, 121.3, 123.3, 126.3, 126.5, 127.7, 128.4, 128.5, 128.7, 129.0, 129.4, 131.6, 133.7, 136.3, 137.2, 138.4, 139.1, 142.4, 167.6; IR (NaCl, neat) ν 3447, 3019, 2234, 1753, 1215 cm^{-1}; HRMS (ESI) calcd for $C_{35}H_{32}NO_4S^{79}BrNa$ (M^+ + Na) 664.1133, found 664.1140.

*(3S,4S)-4-(N-Allyl-4-methylphenylsulfonamido)-3,5-diphenyl-1-(p-tolyl)pent-1-yn-3-yl acetate (**1c**):* yield 73%; 0.422 g; colorless solid; mp =153−154 °C; $[\alpha]^{23}_D$ −2.3 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.02 (s, 3H), 2.28 (s, 3H), 2.35 (s, 3H), 3.09 (dd, 1H, *J* = 14.4, 9.5 Hz), 3.40 (dd, 1H, *J* = 14.6, 4.1 Hz), 4.02 (dd, 1H, *J* = 16.7, 7.2 Hz), 4.13 (dd, 1H, *J* = 14.0, 6.9 Hz), 4.90 (d, 1H, *J* = 10.2 Hz), 5.00 (d, 1H, *J* = 17.2 Hz), 5.17−5.18 (m, 1H), 5.54−5.60 (m, 1H), 6.78 (d, 1H, *J* = 7.9 Hz), 6.86 (d, 2H, *J* = 8.2 Hz), 7.13−7.15 (m, 4H), 7.23−7.25 (m, 3H), 7.34−7.43 (m, 3H), 7.50 (d, 2H, *J* = 8.0 Hz), 7.67 (d, 2H, *J* = 7.3 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.4, 21.6, 21.8, 34.9, 46.9, 68.5, 82.5, 85.8, 91.1, 116.4, 119.1, 126.5, 126.6, 127.9, 128.3, 128.4, 128.6, 129.0, 129.1, 129.6, 132.1, 136.1, 137.4, 138.7, 139.2, 139.3, 142.5, 167.5; IR (NaCl, neat) ν 3019, 2232, 1753, 1215 cm^{-1}; HRMS (ESI) calcd for $C_{36}H_{35}NO_4SNa$ (M^+ + Na) 600.2185, found 600.2186.

*(3S,4S)-4-(N-Allyl-4-methylphenylsulfonamido)-3,5-diphenyl-1-(thiophene-3-yl)pent-1-yn-3-yl acetate (**1d**):* yield 82%; 0.467 g; colorless solid; mp = 192−194 °C; $[\alpha]^{23}_D$ +1.9 (*c* 0.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.07 (s, 3H), 2.28 (s, 3H), 3.03 (dd, 1H, *J* = 14.2, 10.0 Hz), 3.29 (dd, 1H, *J* = 14.7, 3.4 Hz), 4.00 (dd, 1H, *J* = 16.8, 7.0 Hz), 4.15 (d, 1H, *J* = 16.5 Hz), 4.94 (d, 1H, *J* = 10.2 Hz), 5.04 (d, 1H, *J* = 17.3 Hz), 5.13 (d, 1H, *J* = 7.4 Hz), 5.67−5.68 (m, 1H), 6.78−6.87 (m, 4H), 7.04−7.29 (m, 7H), 7.33−7.43 (m, 3H), 7.63−7.70 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.4, 21.8, 34.2, 46.9, 69.0, 82.8, 86.0, 86.1, 116.2, 121.3, 125.2, 126.4, 126.5, 127.8, 128.3, 128.5, 128.6, 129.0, 129.5, 130.3, 130.5, 136.3, 137.3, 138.6, 139.2, 142.4, 167.6; IR (NaCl, neat) ν 3026, 2232, 1755, 1217 cm^{-1}; HRMS (ESI) calcd for $C_{33}H_{31}NO_4S_2Na$ (M^+ + Na) 592.1592, found 592.1595.

*(3S,4S)-4-(N-Allyl-4-methylphenylsulfonamido)-1,3-diphenylhex-1-yn-3-yl acetate (**1e**):* yield 66%; 0.397 g; colorless solid; mp = 141−142 °C; $[\alpha]^{23}_D$ −34.0 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.88 (t, 3H, *J* = 7.4 Hz), 1.92−2.05 (m, 2H), 2.12 (s, 3H), 2.32 (s, 3H), 4.01−4.05 (m, 2H), 4.65 (dd, 1H, *J* = 9.8, 3.1 Hz), 4.89−5.00 (m, 1H), 5.04 (d, 2H, *J* = 1.2 Hz), 5.72−5.82 (m, 1H), 7.04 (d, 2H, *J* = 8.1 Hz), 7.21 (d, 2H, *J* = 8.0 Hz), 7.29−7.43 (m, 6H), 7.52−7.64 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 11.7, 20.6, 21.5, 22.0, 46.7, 68.0, 82.2, 86.6, 90.2, 116.3, 122.2, 126.5, 128.1, 128.2, 128.3, 128.4, 128.8, 129.1, 132.0, 135.9, 137.4, 139.7, 142.9, 167.6; IR (NaCl, neat) ν 3018, 2232, 1753, 1217 cm^{-1}; HRMS (ESI) calcd for $C_{30}H_{31}NO_4SNa$ (M^+ + Na) 524.1872, found 524.1877.

*(3S,4S)-4-(N-Allyl-4-methylphenylsulfonamido)-5-methyl-1,3-diphenylhex-1-yn-3-yl acetate (**1f**):* yield 70%; 0.361 g; colorless solid; mp = 147−149 °C; $[\alpha]^{23}_D$ −32.1 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.08 (d, 3H, *J* = 6.7 Hz), 1.24 (d, 3H, *J* = 6.6 Hz), 2.06 (s, 3H), 2.33 (s, 4H), 2.48−2.58 (m, 1H), 3.90 (dd, 1H, *J* = 16.8, 5.1 Hz), 4.19 (dd, 1H, *J* = 16.8, 7.6 Hz), 4.61 (d, 1H, *J* = 9.3 Hz), 4.85 (dd, 1H, *J* = 10.1, 0.9 Hz), 4.97 (dd, 1H, *J* = 17.2, 1.2 Hz), 5.56−5.66 (m, 1H), 7.03 (d, 2H, *J* = 8.2 Hz), 7.16 (d, 2H, *J* = 8.2 Hz), 7.31−7.39 (m, 6H), 7.48−7.51 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.4, 22.0, 22.1, 22.6, 30.4, 47.7, 71.2, 81.8, 86.3, 91.3, 116.7, 122.1, 126.8, 128.2, 128.3, 128.4, 128.4, 128.9, 129.0, 131.8, 135.4, 137.2, 140.1, 142.8, 167.2; IR (NaCl, neat) ν 2230, 1755, 1217 cm^{-1}; HRMS (ESI) calcd for $C_{31}H_{33}NO_4SNa$ (M^+ + Na) 538.2028, found 538.2029.

*(3S,4S)-4-(N-Allyl-4-methylphenylsulfonamido)-6-methyl-1,3-diphenylhept-1-yn-3-yl acetate (**1g**):* yield 79%; 0.418 g; colorless solid; mp = 169−170 °C; $[\alpha]^{23}_D$ −38.1 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.91−0.95 (m, 6H), 1.63−1.71 (m, 2H), 1.92−1.98 (t, 3H), 2.13 (s, 3H), 2.33 (s, 3H), 3.91−4.04 (m,2H), 4.86 (d, 2H, *J* = 10.3 Hz), 4.95 (d, 1H, *J* = 17.2 Hz), 5.57−5.67 (m, 1H), 7.04 (d, 2H, *J* = 8.1 Hz), 7.16 (d, 2H, *J* = 8.0 Hz), 7.32−7.42 (m, 6H), 7.51−7.53 (m, 2H); 7.63 (d, 2H, *J* = 6.7 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.5, 21.9, 23.6, 24.1, 37.2, 46.8, 64.1, 82.1, 86.6, 90.3, 116.3, 122.2, 126.6, 128.2, 128.3, 128.4, 129.0, 132.0, 135.9, 137.3, 139.6, 143.0, 167.6; IR (NaCl, neat) ν 2957, 2232, 1757, 1219 cm^{-1}; HRMS (ESI) calcd for $C_{32}H_{35}NO_4SNa$ (M^+ + Na) 552.2185, found 552.2185.

*(3S,4S)-4-(N-Allyl-4-methylphenylsulfonamido)-1,3,5-triphenylpent-1-yn-3-yl butyrate (**1h**):* yield 70%, 0.414 g; colorless solid; mp = 88−90 °C; $[\alpha]^{23}_D$ −14.1 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.94 (t, 3H, *J* = 7.4 Hz), 1.57−1.69 (m, 2H), 2.26−2.29 (m, 5H), 3.10 (dd, 1H, *J* = 14.2, 9.8 Hz), 3.41 (dd, 1H, *J* = 14.7, 3.6 Hz), 4.05 (dd, 1H, *J* = 14.7, 7.2 Hz), 4.15 (d, 1H, *J* = 14.2 Hz), 4.90 (d, 1H, *J* = 10.2 Hz), 5.00 (d, 1H, *J* = 17.2 Hz), 5.20 (d, 1H, *J* = 6.4 Hz), 5.56−5.58 (m, 1H), 6.76 (d, 2H, *J* = 7.7 Hz), 6.84 (d, 2H, *J* = 8.0 Hz), 7.14−7.25 (m, 5H), 7.33−7.43 (m, 6H), 7.59−7.61 (m, 2H), 7.68 (d, 2H, *J* = 7.4 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 13.7, 18.4, 21.4, 34.9, 36.8, 46.9, 68.6, 82.2, 86.5, 90.7, 116.4, 122.3, 126.5, 126.6, 127.9, 128.3, 128.4, 128.4, 128.6, 128.9, 129.0, 129.6, 132.1, 136.0, 137.4, 138.7, 139.3, 142.5, 170.1; IR (NaCl, neat) ν 3318, 2235, 1749, 1215 cm^{-1}; HRMS (ESI) calcd for $C_{37}H_{37}NO_4SNa$ (M^+ + Na) 614.2341, found 614.2356.

*(3S,4S)-4-(N-Allyl-4-methylphenylsulfonamido)-1,3,5-triphenylpent-1-yn-3-yl hexanoate (**1i**):* yield 70%; 0.434 g; yellow oil; $[\alpha]^{23}_D$ −12.5 (*c* 1.2, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.88 (t, 3H, *J* = 6.5 Hz), 1.30−1.32 (m, 4H), 1.56−1.63 (m, 2H), 2.26−2.30 (m, 5H), 3.11 (dd, 1H, *J* = 14.2, 9.8 Hz), 3.11 (dd, 1H, *J* = 14.6, 3.6 Hz), 4.05 (dd, 1H, *J* = 16.7, 7.2 Hz), 4.15 (d, 1H, *J* = 15.6 Hz), 4.90 (d, 1H, *J* = 10.2 Hz), 5.00 (d, 1H, *J* = 17.2 Hz), 5.20 (d, 1H, *J* = 6.4 Hz), 6.76 (d, 2H, *J* = 7.6 Hz), 6.85 (d, 2H, *J* = 8.0 Hz), 7.15−7.43 (m, 11H), 7.59−7.69 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.0, 21.4, 22.4, 24.5, 31.3, 34.9, 46.9, 68.5, 82.2, 86.5, 90.8, 116.4, 122.3, 126.5, 126.6, 127.9, 128.3, 128.4, 128.6, 128.9, 129.0, 129.6, 132.1, 136.0, 137.4, 138.7, 139.3, 142.4; IR (NaCl, neat) ν 3019, 2231, 1751, 1215, 1155 cm^{-1};

dx.doi.org/10.1021/jo400121j | *J. Org. Chem.* 2013, 78, 3183−3195

HRMS (ESI) calcd for $C_{39}H_{41}NO_4SNa$ (M^+ + Na) 642.2654, found 642.2647.

*(3S,4S)-4-(N-Allyl-4-methylphenylsulfonamido)-1,3,5-triphenylpent-1-yn-3-yl 3-phenylpropanoate (**1j**):* yield 58%; 0.379 g; colorless solid; mp =66−67 °C; $[\alpha]^{23}_D$ −15.5 (*c* 0.6, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ 2.27 (s, 3H), 2.60−2.64 (m, 2H), 2.92 (t, 2H, *J* = 7.5 Hz), 3.02 (dd, 1H, *J* = 14.2, 9.7 Hz), 3.29 (dd, 1H, *J* = 14.7, 3.8 Hz), 3.99 (dd, 1H, *J* = 16.8, 7.2 Hz), 4.10 (d, 1H, *J* = 16.0 Hz), 4.89 (d, 1H, *J* = 10.2 Hz), 4.99 (d, 1H, *J* = 17.2 Hz), 5.13−5.15 (m, 1H), 5.57−5.59 (m, 1H), 6.77 (d, 2H, *J* = 7.7 Hz), 6.84 (d, 2H, *J* = 8.0 Hz), 7.08−7.35 (m, 16H), 7.53−7.61 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.4, 30.7, 34.7, 36.4, 46.9, 68.6, 82.6, 86.4, 90.8, 116.3, 122.2, 126.3, 126.5, 126.5, 127.9, 128.3, 128.3, 128.4, 128.4, 128.4, 128.6, 128.6, 129.0, 129.5, 132.2, 136.1, 137.3, 138.7, 139.1, 140.3, 142.4, 169.4; IR (NaCl, neat) ν 3026, 2234, 1753, 1155 cm^{-1}; HRMS (ESI) calcd for $C_{42}H_{39}NO_4SNa$ (M^+ + Na) 676.2498, found 676.2491.

*(3S,4S)-4-(N-Allyl-4-methylphenylsulfonamido)-1,3,5-triphenylpent-1-yn-3-yl 3-methylbutanoate (**1k**):* yield 72%; 0.436 g; colorless solid; mp =102−104 °C; $[\alpha]^{23}_D$ −24.8 (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ 0.94−0.96 (m, 6H), 2.04−2.21 (m, 3H), 2.27 (s, 3H), 3.12 (dd, 1H, *J* = 14.2, 9.9 Hz), 3.44 (dd, 1H, *J* = 14.6, 3.6 Hz), 4.05 (dd, 1H, *J* = 16.7, 7.2 Hz), 4.14 (d, 1H, *J* = 14.4 Hz), 4.89 (d, 1H, *J* = 10.2 Hz), 4.99 (d, 1H, *J* = 17.2 Hz), 5.21−5.23 (m, 1H), 5.52−5.54 (m, 1H), 6.74 (d, 2H, *J* = 7.6 Hz), 6.85 (d, 2H, *J* = 8.0 Hz), 7.16−7.43 (m, 11H), 7.58−7.60 (m, 2H), 7.70 (d, 4H, *J* = 7.3 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.4, 22.4, 25.7, 35.0, 43.9, 46.9, 68.3, 82.2, 86.4, 90.8, 116.4, 122.2, 126.5, 126.7, 127.9, 128.4, 128.6, 128.9, 129.6, 132.0, 135.9, 137.4, 138.7, 139.3, 142.4, 169.6; IR (NaCl, neat) ν 3020, 1749, 1215, 1157 cm^{-1}; HRMS (ESI) calcd for $C_{38}H_{39}NO_4SNa$ (M^+ + Na) 628.2498, found 628.2496.

*(3S,4S)-4-(N-Allyl-4-methylphenylsulfonamido)-1,3,5-triphenylpent-1-yn-3-yl pivalate (**1l**):* yield 62%; 0.376 g; colorless solid; mp = 172−173 °C; $[\alpha]^{23}_D$ −45.2 (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 1.31 (s, 9H), 2.28 (s, 3H), 3.20 (dd, 1H, *J* = 12.6, 10.7 Hz), 3.52 (d, 1H, *J* = 13.1 Hz), 4.09−4.24 (m, 2H), 4.91 (d, 1H, *J* = 10.1 Hz), 5.02 (d, 1H, *J* = 17.2 Hz), 5.33 (d, 1H, *J* = 8.7 Hz), 5.50−5.47 (m, 1H), 6.69 (d, 2H, *J* = 7.9 Hz), 6.85 (d, 2H, *J* = 7.9 Hz), 7.23−7.50 (m, 11H), 7.63 (d, 2H, *J* = 3.5 Hz), 7.77 (d, 2H, *J* = 7.1 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.4, 27.1, 34.9, 39.3, 46.8, 68.7, 81.9, 86.3, 90.6, 116.6, 122.3, 126.6, 127.9, 128.4, 128.8, 128.9, 129.0, 129.7, 132.1, 135.7, 137.6, 138.5, 139.3, 142.4, 174.5; IR (NaCl, neat) ν 3019, 2234, 1746, 1630, 1215 cm^{-1}; HRMS (ESI) calcd for $C_{38}H_{39}NO_4SNa$ (M^+ + Na) 628.2498, found 628.2493.

*(3S,4S)-4-(N-Allyl-4-methylphenylsulfonamido)-1,3-diphenylhept-1-yn-3-yl cyclopropanecarboxylate (**1m**):* yield 71%; 0.385 g; colorless solid; mp = 158−160 °C; $[\alpha]^{23}_D$ −35.4 (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ 0.88−0.96 (m, 6H), 1.03−1.07 (m, 1H), 1.22−1.43 (m, 2H), 1.68−1.74 (m, 1H), 1.92−1.97 (m, 2H), 2.32 (s, 3H), 4.00−4.10 (m, 2H), 4.76 (t, 1H, *J* = 6.3 Hz), 4.90 (d, 1H, *J* = 10.2 Hz), 5.02 (d, 1H, *J* = 17.2 Hz), 5.69−5.77 (m, 1H), 7.04 (d, 2H, *J* = 8.1 Hz), 7.19 (d, 2H, *J* = 7.9 Hz), 7.29−7.42 (m, 6H), 7.51−7.53 (m, 2H), 7.63 (d, 2H, *J* = 6.9 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 8.3, 8.5, 13.7, 14.0, 20.0, 21.5, 30.0, 46.9, 66.2, 81.9, 86.8, 90.1, 116.4, 122.3, 126.5, 128.1, 128.2, 128.3, 128.4, 128.8, 129.0, 132.0, 135.9, 137.4, 139.9, 142.9, 171.2; IR (NaCl, neat) ν 2961, 2232, 1742, 1217 cm^{-1}; HRMS (ESI) calcd for $C_{33}H_{35}NO_4SNa$ (M^+ + Na) 564.2185, found 564.2188.

*(3S,4S)-4-(N-Allyl-4-methylphenylsulfonamido)-6-methyl-1,3-diphenylhept-1-yn-3-yl cyclopropanecarboxylate (**1n**):* yield 78%; 0.434 g; colorless solid; mp = 167−168 °C; $[\alpha]^{23}_D$ −35.5 (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ 0.89−1.08 (m, 10H), 1.68−1.76 (m, 3H), 2.04 (t, 1H, *J* = 11.4 Hz), 2.33 (s, 3H), 4.01 (dd, 1H *J* = 12.7, 4.1 Hz), 4.11 (dd, 1H, *J* = 16.9, 7.5 Hz), 4.89 (d, 2H, *J* = 10.5 Hz), 4.99 (d, 1H, *J* = 17.2 Hz), 5.62−5.72 (m, 1H), 7.05 (d, 2H, *J* = 8.0 Hz), 7.17 (d, 2H, *J* = 8.0 Hz), 7.32−7.43 (m, 6H), 7.52−7.54 (m, 2H), 7.66 (d, 2H, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 8.3, 8.5, 13.7, 21.5, 21.5, 23.7, 24.1, 37.3, 46.9, 81.9, 86.8, 90.2, 116.3, 122.3, 126.5, 128.1, 128.3, 128.3, 128.4, 128.9, 129.1, 132.0, 135.9, 137.4, 139.9, 143.0, 171.2; IR (NaCl, neat) ν 3019, 2231, 1742, 1215 cm^{-1}; HRMS (ESI) calcd for $C_{34}H_{37}NO_4SNa$ (M^+ + Na) 578.2341, found 578.2350.

*(3S,4S)-4-(N-Allyl-4-methylphenylsulfonamido)-1,3,5-triphenylpent-1-yn-3-yl cyclopropanecarboxylate (**1o**):* yield 79%; 0.466 g; colorless solid; mp = 179−181 °C; $[\alpha]^{23}_D$ −1.5 (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ 0.86−0.95 (m, 3H), 1.03−1.07 (m, 1H), 1.58−1.63 (m, 1H), 2.27 (s, 3H), 3.11 (dd, 1H, *J* = 14.2, 10.3 Hz), 3.41 (dd, 1H, *J* = 14.6, 3.0 Hz), 4.05 (dd, 1H, *J* = 16.7, 7.2 Hz), 4.16 (d, 1H, *J* = 13.8 Hz), 4.91 (d, 1H, *J* = 10.2 Hz), 5.01 (d, 1H, *J* = 17.2 Hz), 5.19 (d, 1H, *J* = 7.7 Hz), 5.58−5.60 (m, 1H), 6.76 (d, 2H, *J* = 7.6 Hz), 6.85 (d, 2H, *J* = 8.0 Hz), 7.12−7.43 (m, 11H), 7.60−7.69 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 8.4, 8.6, 21.4, 34.6, 47.0, 68.9, 82.4, 86.6, 90.6, 116.4, 122.3, 126.5, 127.9, 128.3, 128.3, 128.4, 128.7, 128.9, 129.0, 129.6, 132.2, 136.1, 137.5, 138.7, 139.4, 142.4, 171.3; IR (NaCl, neat) ν 3019, 2234, 1742, 1215 cm^{-1}; HRMS (ESI) calcd for $C_{37}H_{35}NO_4SNa$ (M^+ + Na) 612.2185, found 612.2184.

*(3S,4S)-4-(N-Allyl-4-methylphenylsulfonamido)-5-((tert-butyldimethylsilyl)oxy)-1,3-diphenylpent-1-yn-3-yl cyclopropanecarboxylate (**1p**):* yield 67%; 0.431 g; colorless solid; mp = 120−122 °C; $[\alpha]^{23}_D$ +3.7 (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ 0.02 (s, 3H), 0.09 (s, 3H), 0.86−1.08 (m, 13H), 1.66−1.70 (m, 1H), 2.34 (s, 3H), 4.16−4.20 (m, 4H), 4.82 (d, 1H, *J* = 10.3 Hz), 4.92−4.97 (m, 2H), 5.65−5.75 (m, 1H), 7.07 (d, 2H, *J* = 8.0 Hz), 7.33−7.56 (m, 10H), 7.91 (d, 2H, *J* = 7.4 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ −5.8, −5.6, 8.4, 8.6, 13.6, 18.6, 21.5, 26.0, 47.0, 59.7, 67.9, 80.7, 86.1, 90.3, 115.7, 122.2, 126.3, 128.2, 128.3, 128.4, 128.5, 128.9, 128.9, 132.1, 136.0, 138.2, 139.2, 142.6, 171.1; IR (NaCl, neat) ν 2953, 2232, 1748, 1157 cm^{-1}; HRMS (ESI) calcd for $C_{37}H_{45}NO_5SSiNa$ (M^+ + Na) 666.2685, found 666.2688.

*(3S,4S)-4-(N-Allyl-4-methylphenylsulfonamido)-6-methyl-1,3-diphenylhept-1-yn-3-yl cyclobutanecarboxylate (**1q**):* yield 52%; 0.296 g; colorless solid; mp =143−144 °C; $[\alpha]^{23}_D$ −49.1 (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ 0.95 (d, 3H, *J* = 5.8 Hz), 0.98 (d, 3H, *J* = 5.4 Hz), 1.67−1.76 (m, 2H), 1.87−2.06 (m, 3H), 2.18−2.39 (m, 7H), 3.19−3.27 (m, 1H), 3.99 (dd, 1H, *J* = 12.6, 4.2 Hz), 4.10 (dd, 1H, *J* = 16.9, 7.6 Hz), 4.85−4.98 (m, 3H), 5.58−5.67 (m, 1H), 7.03 (d, 2H, *J* = 8.2 Hz), 7.11 (d, 2H, *J* = 8.2 Hz), 7.30−7.44 (m, 6H), 7.52−7.54 (m, 2H), 7.66 (d, 2H, *J* = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 18.4, 21.5, 21.6, 23.7, 24.1, 24.9, 25.0, 37.5, 38.6, 46.9, 64.1, 81.6, 86.6, 90.3, 116.3, 122.2, 126.6, 128.1, 128.3, 128.3, 128.4, 128.9, 129.0, 132.0, 135.8, 137.3, 139.9, 143.0, 171.7; IR (NaCl, neat) ν 2955, 2232, 1749, 1155 cm^{-1}; HRMS (ESI) calcd for $C_{35}H_{39}NO_4SNa$ (M^+ + Na) 592.2498, found 592.2495.

*(3S,4S)-4-(N-Allyl-4-methylphenylsulfonamido)-1,3,5-triphenylpent-1-yn-3-yl cyclobutanecarboxylate (**1r**):* yield 66%; 0.398 g; colorless solid; mp = 74−76 °C; $[\alpha]^{23}_D$ −16.2 (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ 1.87−2.04 (m, 2H), 2.14−2.34 (m, 7H), 3.06−3.18 (m, 2H), 3.40 (dd, 1H, *J* = 14.7, 3.4 Hz), 4.05 (dd, 1H, *J* = 16.6, 7.4 Hz), 4.15 (d, 1H, *J* = 16.6 Hz), 4.89 (d, 1H, *J* = 10.2 Hz), 5.00 (d, 1H, *J* = 17.2 Hz), 5.20 (d, 1H, *J* = 7.2 Hz), 5.52−5.54 (m, 1H), 6.73 (d, 2H, *J* = 7.8 Hz), 6.84 (d, 2H, *J* = 8.1 Hz), 7.13−7.26 (m, 5H), 7.32−7.44 (m, 6H), 7.59−7.62 (m, 2H), 7.69 (d, 2H, *J* = 7.4 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 18.4, 21.4, 24.8, 25.1, 34.8, 38.5, 46.9, 68.6, 86.5, 90.6, 116.4, 122.3, 126.5, 126.5, 127.9, 128.3, 128.4, 128.6, 128.9, 129.6, 132.1, 135.9, 137.5, 138.6, 139.4, 142.4, 171.7; IR (NaCl, neat) ν 3020, 2236, 1746, 1638, 1215 cm^{-1}; HRMS (ESI) calcd for $C_{38}H_{37}NO_4SNa$ (M^+ + Na) 626.2341, found 626.2335.

*(3S,4S)-4-(N-Allyl-4-methylphenylsulfonamido)-6-(methylsulfonyl)-1,3-diphenylhex-1-yn-3-yl cyclopropanecarboxylate (**1s**):* yield 52%; 0.315 g; colorless solid; mp = 71−73 °C; $[\alpha]^{23}_D$ −51.7 (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ 0.87−1.01 (m, 4H), 1.66−1.71 (m, 1H), 2.27 (s, 3H), 2.63−2.72 (m, 2H), 2.90 (s, 3H), 3.06−3.13 (m, 1H), 3.19−3.27 (m, 1H), 4.00 (d, 1H, *J* = 15.6 Hz), 4.19 (dd, 1H, *J* = 16.5, 8.0 Hz), 4.80 (s, 1H), 4.98 (d, 1H, *J* = 10.1 Hz), 5.08 (d, 1H, *J* = 17.2 Hz), 5.73−5.83 (m, 1H), 6.96−7.02 (m, 4H), 7.27−7.43 (m, 8H), 7.58 (d, 2H, *J* = 5.3 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 8.6, 8.8, 13.5, 20.6, 21.5, 41.3, 47.0, 52.1, 64.8, 81.2, 85.5, 91.1, 118.0, 121.6, 126.2, 128.1, 128.3, 128.4, 128.7, 129.1, 129.3, 131.9, 134.8, 136.3, 139.3, 143.5, 171.0; IR (NaCl, neat) ν 3022, 2232, 1746, 1152

dx.doi.org/10.1021/jo400121j | J. Org. Chem. 2013, 78, 3183−3195

cm^{-1}; HRMS (ESI) calcd for $C_{33}H_{35}NO_6S_2Na$ (M^+ + Na) 628.1804, found 628.1815.

*(3S,4S)-4-(N-Allyl-4-methylphenylsulfonamido)-6-(methylsulfonyl)-1,3-diphenylhex-1-yn-3-yl hexanoate (**1t**):* yield 55%; 0.350 g; yellow oil; $[\alpha]^{23}_D$ −74.0 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.87 (t, 3H, *J* = 6.8 Hz), 1.28−1.33 (m, 4H), 1.58−1.65 (m, 2H), 2.28 (s, 3H), 2.37 (td, 2H, *J* = 7.5, 2.3 Hz), 2.61−2.67 (m, 2H), 2.91 (s, 3H), 3.07−3.15 (m, 1H), 3.21−3.29 (m, 1H), 3.98 (d, 1H, *J* = 15.6 Hz), 4.17 (d, 1H, *J* = 16.6, 8.2 Hz), 4.80 (s, 1H), 4.96 (d, 1H, *J* = 10.2 Hz), 5.06 (d, 1H, *J* = 17.2 Hz), 5.70−5.76 (m, 1H), 6.98 (s, 4H), 7.28−7.44 (m, 8H), 7.59−7.60 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 13.9, 20.6, 21.5, 22.3, 24.4, 31.2, 34.8, 41.3, 47.0, 52.1, 64.5, 81.1, 85.3, 91.3, 118.1, 121.6, 126.4, 128.1, 128.4, 128.5, 128.7, 129.2, 129.3, 131.9, 134.7, 136.2, 139.3, 143.6, 170.0; IR (NaCl, neat) ν 3024, 2229, 1755, 1317, 1217, 1153 cm^{-1}; HRMS (ESI) calcd for $C_{35}H_{41}NO_6S_2Na$ (M^+ + Na) 658.2273, found 658.2266.

*1-((3R,6S)-4-Benzoyl-6-benzyl-5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-3-yl)propan-2-one (**2a**):* yield 75%; 0.085 g; colorless solid; mp = 143−145 °C; $[\alpha]^{23}_D$ +103.4 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.13 (s, 3H), 2.41 (s, 3H), 2.48 (dd, 1H, *J* = 18.2, 7.1 Hz), 2.74 (dd, 1H, *J* = 18.2, 4.6 Hz), 2.85−2.87 (m, 2H), 3.08 (dd, 1H, *J* = 14.4, 11.0 Hz), 3.19−3.26 (m, 1H), 3.92 (dd, 1H, *J* = 14.4, 6.2 Hz), 4.99 (t, 1H, *J* = 6.5 Hz), 6.98−7.01 (m, 2H), 7.07−7.20 (m, 12H), 7.33−7.48 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.6, 30.4, 30.8, 38.1, 42.5, 44.0, 58.1, 126.4, 127.6, 128.0, 128.2, 128.3, 129.0, 129.2, 129.4, 129.6, 133.1, 136.1, 136.4, 136.9, 137.6, 137.7, 139.6, 143.2, 198.3, 206.0; IR (NaCl, neat) ν 3021, 1717, 1659, 1597, 1215 cm^{-1}; HRMS (ESI) calcd for $C_{35}H_{34}NO_4S$ (M^+ + H) 564.2209, found 564.2218.

*1-((3R,6S)-6-Benzyl-4-(4-bromobenzoyl)-5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-3-yl)propan-2-one (**2b**):* yield 66%; 0.085 g; yellow solid; mp =74−76 °C; $[\alpha]^{23}_D$ +62.7 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.13 (s, 3H), 2.41 (s, 3H), 2.48 (dd, 1H, *J* = 18.2, 6.4 Hz), 2.72−2.89 (m, 3H), 3.10 (dd, 1H, *J* = 14.2, 11.0 Hz), 3.20−3.26 (m, 1H), 3.91 (dd, 1H, *J* = 14.4, 6.2 Hz), 4.93−4.96 (m, 1H), 6.95−6.97 (m, 2H), 7.09−7.17 (m, 10H), 7.31−7.37 (m, 4H), 7.43 (d, 2H, *J* = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.6, 30.4, 30.7, 38.0, 42.5, 43.9, 58.1, 126.4, 127.6, 128.3, 128.3, 128.5, 128.9, 129.3, 129.6, 130.6, 131.6, 134.9, 136.0, 136.6, 137.5, 137.5, 139.9, 143.3, 197.4, 206.0; IR (NaCl, neat) ν 1717, 1663 cm^{-1}; HRMS (ESI) calcd for $C_{35}H_{33}NO_4S^{79}Br$ (M^+ + H) 642.1314, found 642.1323.

*1-((3R,6S)-6-Benzyl-4-(4-methylbenzoyl)-5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-3-yl)propan-2-one (**2c**):* yield 74%; 0.086 g; pale yellow solid; mp = 80−82 °C; $[\alpha]^{23}_D$ +91.5 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.10 (s, 3H), 2.27 (s, 3H), 2.40−2.46 (m, 4H), 2.72 (dd, 1H, *J* = 18.2, 4.6 Hz), 2.82−2.90 (m, 2H), 3.04 (dd, 1H, *J* = 14.4, 11.0 Hz), 3.16−3.23 (m, 2H), 3.93 (dd, 1H, *J* = 14.4, 6.3 Hz), 4.99 (t, 1H, *J* = 6.6 Hz), 6.98−7.01 (m, 4H), 7.08−7.21 (m, 10H), 7.40 (d, 2H, *J* = 8.0 Hz), 7.47 (d, 2H, *J* = 8.1 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.6, 21.7, 30.4, 30.8, 38.1, 42.5, 44.1, 58.0, 126.4, 127.6, 128.0, 128.3, 129.0, 129.1, 129.4, 129.5, 129.6, 133.5, 136.6, 136.9, 137.6, 137.8, 138.9, 143.2, 144.1, 197.8, 206.0; IR (NaCl, neat) ν 1717, 1603 cm^{-1}; HRMS (ESI) calcd for $C_{36}H_{36}NO_4S$ (M^+ + H) 578.2365, found 578.2375.

*1-((3R,6S)-6-Benzyl-5-phenyl-4-(thiophene-3-carbonyl)-1-tosyl-1,2,3,6-tetrahydropyridin-3-yl)propan-2-one (**2d**):* yield 53%; 0.061 g; yellow oil; $[\alpha]^{23}_D$ +71.4 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.15 (s, 3H), 2.40 (s, 3H), 2.51 (dd, 1H, *J* = 18.2, 7.2 Hz), 2.73−2.90 (m, 3H), 3.12 (dd, 1H, *J* = 14.0, 11.4 Hz), 3.26−3.27 (m, 1H), 3.97 (dd, 1H, *J* = 14.5, 6.4 Hz), 4.93 (t, 1H, *J* = 5.3 Hz), 6.95−7.03 (m, 3H), 7.14−7.21 (m, 11H), 7.44 (d, 2H, *J* = 7.8 Hz), 7.59 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.6, 30.4, 30.8, 37.9, 42.4, 44.1, 58.1, 126.1, 126.3, 126.7, 127.6, 128.1, 128.3, 128.4, 128.9, 129.3, 129.7, 135.9, 136.7, 137.2, 137.6, 137.8, 139.2, 141.4, 143.4, 191.8, 206.1; IR (NaCl, neat) ν 1717, 1651 cm^{-1}; HRMS (ESI) calcd for $C_{33}H_{32}NO_4S_2$ (M^+ + H) 570.1773, found 570.1774.

*1-((3R,6S)-4-Benzoyl-6-ethyl-5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-3-yl)propan-2-one (**2e**):* yield 61%; 0.061 g; colorless oil; $[\alpha]^{23}_D$ +198.9 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.86 (t, 30H, *J* = 7.3 Hz), 1.48−1.62 (m, 1H), 2.10 (s, 3H), 2.42−2.49 (m, 4H), 2.75 (dd, 1H, *J* = 18.2, 4.8 Hz), 3.01−3.17 (m, 2H), 4.20 (dd, 1H, *J* = 14.0, 5.6 Hz), 4.50 (d, 1H, *J* = 7.0 Hz), 6.97−7.15 (m, 9H), 7.30 (t, 1H, *J* = 7.2 Hz), 7.44 (m, 2H, *J* = 8.0 Hz), 7.99 (d, 2H, *J* = 8.1 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 11.0, 21.7, 25.3, 30.3, 30.3, 42.7, 44.1, 58.3, 127.5, 127.8, 128.0, 128.1, 128.8, 128.9, 130.0, 133.0, 135.4, 136.2, 137.8, 138.3, 140.3, 143.5, 198.2, 205.9; IR (NaCl, neat) ν 1717, 1657 cm^{-1}; HRMS (ESI) calcd for $C_{30}H_{32}NO_4S$ (M^+ + H) 502.2052, found 502.2047.

*1-((3R,6S)-4-Benzoyl-6-isopropyl-5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-3-yl)propan-2-one (**2f**):* yield 73%; 0.075 g; colorless solid; mp = 101−102 °C; $[\alpha]^{23}_D$ +187.5 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.88 (d, 3H, *J* = 6.7 Hz), 0.92 (d, 3H, *J* = 7.0 Hz), 1.80−1.88 (m, 1H), 2.09 (s, 3H), 2.42 (dd, 1H, *J* = 18.3, 7.4 Hz), 2.49 (s, 3H), 2.81 (dd, 1H, *J* = 18.3, 4.8 Hz), 2.99 (m, 1H), 3.15 (dd, 1H, *J* = 14.8, 11.0 Hz), 4.26 (dd, 1H, *J* = 14.7, 6.4 Hz), 4.59 (d, 1H, *J* = 4.6 Hz), 7.00−7.16 (m, 9H), 7.30 (t, 1H, *J* = 7.2 Hz), 7.44 (m, 2H, *J* = 8.0 Hz), 8.00 (d, 2H, *J* = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 19.3, 20.6, 21.7, 29.8, 30.3, 31.9, 44.7, 44.9, 61.0, 127.7, 127.7, 128.0, 128.1, 128.8, 128.9, 130.0, 132.9, 136.0, 137.0, 138.1, 138.6, 139.0, 143.5, 198.4, 205.8; IR (NaCl, neat) ν 1719, 1655 cm^{-1}; HRMS (ESI) calcd for $C_{31}H_{34}NO_4S$ (M^+ + H) 516.2209, found 516.2200.

*1-((3R,6S)-4-Benzoyl-6-isobutyl-5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-3-yl)propan-2-one (**2g**):* yield 60%; 0.064 g; colorless solid; mp = 137−138 °C; $[\alpha]^{23}_D$ +174.4 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.70 (d, 3H, *J* = 6.4 Hz), 0.81 (d, 3H, *J* = 6.6 Hz), 1.05−1.12 (m, 1H), 1.61−1.75 (m, 2H), 2.10 (s, 3H), 2.43−2.48 (m, 4H), 2.77 (dd, 1H, *J* = 18.2, 4.6 Hz), 3.07−3.20 (m, 2H), 4.11−4.17 (m, 1H), 4.67 (d, 1H, *J* = 10.3 Hz), 6.98−7.10 (m, 7H), 7.17 (d, 2H, *J* = 7.4 Hz), 7.29 (t, 1H, *J* = 7.3 Hz), 7.44 (m, 2H, *J* = 8.1 Hz), 7.99 (d, 2H, *J* = 8.1 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 20.9, 21.7, 23.6, 24.4, 30.1, 30.3, 41.3, 42.5, 44.2, 127.7, 127.8, 128.0, 128.1, 128.8, 129.0, 130.0, 132.9, 135.2, 136.2, 137.8, 138.0, 140.6, 143.6, 198.3, 205.9; IR (NaCl, neat) ν 1717, 1657 cm^{-1}; HRMS (ESI) calcd for $C_{32}H_{36}NO_4S$ (M^+ + H) 530.2365, found 530.2358.

*1-((3R,6S)-4-Benzoyl-6-benzyl-5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-3-yl)pentan-2-one (**2h**):* yield 67%; 0.079 g; colorless solid; mp = 147−148 °C; $[\alpha]^{23}_D$ +112.4 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.88 (t, 3H, *J* = 7.4 Hz), 1.50−1.59 (m, 2H), 2.31−2.43 (m, 6H), 2.70 (dd, 1H, *J* = 18.0, 4.7 Hz), 2.83−2.90 (m, 2H), 3.04 (dd, 1H, *J* = 14.4, 11.0 Hz), 3.19−3.25 (m, 1H), 3.93 (dd, 1H, *J* = 14.5, 6.2 Hz), 4.98 (t, 1H, *J* = 6.5 Hz), 7.00−7.19 (m, 13H), 7.25−7.35 (m, 2H), 7.43−7.49 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 13.7, 17.1, 21.6, 30.8, 38.2, 42.7, 43.3, 45.0, 58.1, 126.4, 127.6, 128.0, 128.2, 128.3, 129.1, 129.2, 129.5, 129.6, 133.1, 136.1, 136.6, 137.0, 137.6, 137.7, 139.4, 143.2, 198.2, 208.3; IR (NaCl, neat) ν 3022, 1713, 1661, 1217 cm^{-1}; HRMS (ESI) calcd for $C_{37}H_{38}NO_4S$ (M^+ + H) 592.2522, found 592.2528.

*1-((3R,6S)-4-Benzoyl-6-benzyl-5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-3-yl)heptan-2-one (**2i**):* yield 77%; 0.096 g; yellow oil; $[\alpha]^{23}_D$ +89.5 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.88 (t, 3H, *J* = 7.2 Hz), 1.19−1.32 (m, 4H), 1.48−1.55 (m, 2H), 2.34−2.43 (m, 6H), 2.70 (dd, 1H, *J* = 18.0, 4.6 Hz), 2.85−2.90 (m, 2H), 3.03 (dd, 1H, *J* = 14.3, 11.0 Hz), 3.21−3.23 (m, 1H), 3.93 (dd, 1H, *J* = 14.6, 6.2 Hz), 4.98 (d, 1H, *J* = 6.4 Hz), 7.00−7.19 (m, 14H), 7.32−7.35 (m, 1H), 7.43−7.49 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 13.9, 21.6, 22.4, 23.3, 30.8, 31.3, 38.2, 42.7, 43.1, 43.3, 58.1, 126.4, 127.6, 128.0, 128.2, 128.3, 129.1, 129.2, 129.5, 129.6, 129.6, 133.1, 136.1, 136.6, 137.0, 137.6, 137.7, 139.4, 143.2, 198.2, 208.4; IR (NaCl, neat) ν 1713, 1661 cm^{-1}; HRMS (ESI) calcd for $C_{39}H_{42}NO_4S$ (M^+ + H) 620.2835, found 620.2825.

*1-((3R,6S)-4-Benzoyl-6-benzyl-5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-3-yl)-4-phenylbutan-2-one (**2j**):* yield 69%; 0.090 g; colorless oil; $[\alpha]^{23}_D$ +93.5 (*c* 0.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.36−2.42 (m, 4H), 2.65−2.73 (m, 3H), 2.79−2.88 (m, 4H), 3.02 (dd, 1H, *J* = 14.5, 11.0 Hz), 3.20−3.25 (m, 1H), 3.89 (dd, 1H, *J* = 14.5, 6.3 Hz), 4.97 (t, 1H, *J* = 6.6 Hz), 6.97−7.29 (m, 19H), 7.32−7.35 (m, 1H), 7.44−7.47 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.6, 29.7, 30.8, 38.1, 42.6, 43.5, 44.6, 58.1, 126.1, 126.4, 127.6, 128.1, 128.2, 128.3, 128.5, 129.0, 129.2, 129.5, 129.6, 133.2, 136.1, 136.4, 136.9, 137.6, 137.7, 139.6, 140.9, 143.2, 198.2, 207.3; IR (NaCl, neat)

dx.doi.org/10.1021/jo400121j | J. Org. Chem. 2013, 78, 3183−3195

ν 1717, 1653 cm^{-1}; HRMS (ESI) calcd for $C_{42}H_{40}NO_4S$ (M^+ + H) 654.2678, found 654.2680.

1-((3R,6S)-4-Benzoyl-6-benzyl-5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-3-yl)-4-methylpentan-2-one (**2k**): yield 64%; 0.078 g; colorless solid; mp = 161−162 °C; $[\alpha]^{23}_D$ +110.8 (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ 0.86−0.90 (m, 6H), 2.02−2.12 (m, 1H), 2.24−2.26 (m, 2H), 2.34−2.41 (m, 4H), 2.69 (dd, 1H, *J* = 18.1, 4.7 Hz), 2.85 (d, 2H, *J* = 6.6 Hz), 3.01 (dd, 1H, *J* = 14.5, 11.0 Hz), 3.19−3.25 (m, 1H), 3.94 (dd, 1H, *J* = 14.5, 6.3 Hz), 4.98 (t, 1H, *J* = 6.6 Hz), 7.01−7.20 (m, 14H), 7.34 (t, 1H, *J* = 7.3 Hz), 7.44 (d, 2H, *J* = 7.6 Hz), 7.49 (d, 2H, *J* = 8.1 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.6, 22.5, 22.6, 24.4, 30.7, 38.2, 42.7, 43.9, 52.1, 58.0, 126.4, 127.6, 128.0, 128.2, 128.3, 129.1, 129.2, 129.5, 129.6, 133.1, 136.1, 136.7, 137.0, 137.6, 137.7, 139.4, 143.2, 198.2, 207.9; IR (NaCl, neat) ν 2957, 1713, 1661, 1155 cm^{-1}; HRMS (ESI) calcd for $C_{38}H_{40}NO_4S$ (M^+ + H) 606.2678, found 606.2678.

1-((3R,6S)-4-Benzoyl-6-benzyl-5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-3-yl)-3,3-dimethylbutan-2-one (**2l**): yield 22%; 0.027 g; colorless solid; mp = 187−188 °C; $[\alpha]^{23}_D$ +110.7 (*c* 0.75, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ 1.08 (s, 9H), 2.43−2.50 (m, 4H), 2.71−2.91 (m, 4H), 3.17−3.19 (m, 1H), 3.96 (dd, 1H, *J* = 14.6, 6.3 Hz), 4.98 (t, 1H, *J* = 6.0 Hz), 7.02−7.26 (m, 14H), 7.32−7.38 (m, 3H), 7.57 (d, 2H, *J* = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.3, 26.5, 30.4, 38.1, 38.4, 42.8, 44.1, 58.0, 126.5, 127.5, 128.0, 128.2, 128.3, 129.1, 129.6, 129.7, 133.1, 136.0, 137.2, 137.3, 137.5, 137.7, 139.0, 143.2, 197.9, 213.2; IR (NaCl, neat) ν 3021, 1703, 1661, 1157 cm^{-1}; HRMS (ESI) calcd for $C_{38}H_{40}NO_4S$ (M^+ + H) 606.2678, found 606.2668.

2-((3R,6S)-4-Benzoyl-5-phenyl-6-propyl-1-tosyl-1,2,3,6-tetrahydropyridin-3-yl)-1-cyclopropylethanone (**2m**): yield 72%; 0.078 g; yellow oil; $[\alpha]^{23}_D$ +162.3 (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ 0.77−1.02 (m, 7H), 1.21−1.60 (m, 4H), 1.83−1.89 (m, 1H), 2.48 (s, 3H), 2.60 (dd, 1H, *J* = 18.1, 6.9 Hz), 2.88 (dd, 1H, *J* = 18.1, 4.0 Hz), 3.10 (dd, 2H, *J* = 19.3, 10.6 Hz), 4.23 (dd, 1H, *J* = 19.8, 11.4 Hz), 4.59 (d, 2H, *J* = 9.2 Hz), 6.98−7.14 (m, 9H), 7.30 (t, 1H, *J* = 7.2 Hz), 7.43 (d, 2H, *J* = 8.1 Hz), 7.99 (d, 2H, *J* = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 10.8, 11.0, 13.6, 19.6, 20.8, 21.7, 30.0, 34.4, 42.8, 44.5, 56.8, 127.5, 127.8, 128.0, 128.1, 128.9, 128.9, 130.0, 133.0, 135.6, 136.1, 137.8, 138.3, 140.1, 143.4, 197.8, 207.9; IR (NaCl, neat) ν 1697, 1661 cm^{-1}; HRMS (ESI) calcd for $C_{33}H_{36}NO_4S$ (M^+ + H) 542.2365, found 542.2366.

2-((3R,6S)-4-Benzoyl-6-isobutyl-5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-3-yl)-1-cyclopropylethanone (**2n**): yield 70%; 0.078 g; colorless solid; mp = 173−174 °C; $[\alpha]^{23}_D$ +163.6 (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ 0.71 (d, 3H, *J* = 6.4 Hz), 0.81−0.94 (m, 6H), 0.98−1.01 (m, 1H), 1.07−1.14 (m, 1H), 1.58−1.65 (m, 1H), 1.71−1.77 (m, 1H), 1.84−1.90 (m, 1H), 2.48 (s, 3H), 2.59 (dd, 1H *J* = 17.9, 7.6 Hz), 2.91 (dd, 1H *J* = 17.9, 4.3 Hz), 3.05−3.11 (m, 2H), 4.19 (d, 1H, *J* = 8.8 Hz), 4.68 (d, 1H, *J* = 10.4 Hz), 6.99−7.10 (m, 7H), 7.17 (d, 2H, *J* = 7.2 Hz), 7.30 (t, 2H, *J* = 7.3 Hz), 7.42 (m, 2H, *J* = 8.1 Hz), 7.99 (d, 2H, *J* = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 10.8, 11.0, 20.8, 20.9, 21.7, 23.7, 24.4, 30.0, 41.4, 42.6, 44.6, 55.1, 127.6, 127.8, 128.0, 128.1, 128.8, 129.0, 130.0, 132.9, 135.5, 136.1, 137.8, 138.1, 140.4, 143.5, 197.9, 208.0; IR (NaCl, neat) ν 1697, 1659 cm^{-1}; HRMS (ESI) calcd for $C_{34}H_{38}NO_4S$ (M^+ + H) 556.2522, found 556.2522.

2-((3R,6S)-4-Benzoyl-6-benzyl-5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-3-yl)-1-cyclopropylethanone (**2o**): yield 72%; 0.085 g; colorless solid, mp = 177−178 °C; $[\alpha]^{23}_D$ +111.0 (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ 0.85−0.95 (m, 3H), 1.00−1.03 (m, 1H), 1.85−1.91 (m, 1H), 2.40 (s, 3H), 2.58 (dd, 1H, *J* = 17.8, 8.0 Hz), 2.80−3.01 (m, 4H), 3.24−3.28 (m, 1H), 3.98 (dd, 1H, *J* = 14.7, 6.3 Hz), 4.99 (t, 1H, *J* = 7.2 Hz), 7.00−7.20 (m, 14H), 7.35 (t, 1H, *J* = 7.2 Hz), 7.48 (d, 4H, *J* = 8.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 10.8, 11.1, 20.8, 21.6, 30.7, 38.2, 42.7, 44.4, 126.4, 127.6, 128.0, 128.2, 128.3, 129.1, 129.2, 129.5, 129.6, 133.2, 136.0, 136.8, 137.0, 137.6, 137.7, 139.4, 143.2, 197.9, 208.0; IR (NaCl, neat) ν 1697, 1663 cm^{-1}; HRMS (ESI) calcd for $C_{37}H_{36}NO_4S$ (M^+ + H) 590.2365, found 590.2359.

2-((3R,6R)-4-Benzoyl-6-(((tert-butyldimethylsilyl)oxy)methyl)-5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-3-yl)-1-cyclopropylethanone (**2p**): yield 66%; 0.085 g; colorless solid; mp = 125−126 °C; $[\alpha]^{23}_D$ +121.0 (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ −0.07 (s, 3H), −0.02 (s, 3H), 0.81−0.90 (m, 12H), 0.95−0.90 (m, 1H), 1.80−1.87 (m, 1H), 2.48−2.56 (m, 4H), 2.87 (dd, 1H, *J* = 17.8, 5.2 Hz), 3.06−3.10 (m, 1H), 3.46 (dd, 1H, *J* = 14.1, 10.9 Hz), 3.58 (dd, 1H, *J* = 10.5, 3.8 Hz), 3.79 (dd, 1H, *J* = 10.6, 2.4 Hz), 4.20 (dd, 1H, *J* = 14.1, 6.0 Hz), 4.65 (s, 1H), 6.98−7.34 (m, 10H), 7.42 (d, 2H, *J* = 8.1 Hz), 7.96 (d, 2H, *J* = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ −5.7, −5.6, 18.2, 20.8, 21.7, 25.9, 30.3, 44.3, 45.1, 58.1, 64.9, 127.3, 127.9, 128.0, 128.9, 129.1, 130.0, 133.0, 136.1, 136.3, 137.2, 138.3, 138.6, 143.4, 197.8, 207.9; IR (NaCl, neat) ν 1697, 1661 cm^{-1}; HRMS (ESI) calcd for $C_{37}H_{46}NO_5SSi$ (M^+ + H) 644.2866, found 644.2861.

2-((3R,6S)-4-Benzoyl-6-isobutyl-5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-3-yl)-1-cyclobutylethanone (**2q**): yield 64%; 0.073 g; colorless solid; mp = 189−191 °C; $[\alpha]^{23}_D$ +172.0 (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ 0.71 (d, 3H, *J* = 6.4 Hz), 0.82 (d, 3H, *J* = 6.7 Hz), 1.07−1.13 (m, 1H), 1.63−1.66 (m, 1H), 1.73−1.78 (m, 2H), 1.82−1.99 (m, 1H), 2.04−2.21 (m, 4H), 2.38 (dd, 1H *J* = 18.2, 6.6 Hz), 2.49 (s, 3H), 2.66 (dd, 1H *J* = 18.3, 3.7 Hz), 3.06−3.23 (m, 3H), 3.05−3.11 (m, 2H), 4.18 (dd, 1H, *J* = 19.8, 11.6 Hz), 4.68 (d, 1H, *J* = 10.1 Hz), 6.98−7.15 (m, 9H), 7.30 (t, 1H, *J* = 7.2 Hz), 7.44 (m, 2H, *J* = 8.0 Hz), 8.02 (d, 2H, *J* = 8.1 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 17.7, 20.9, 21.8, 23.7, 24.1, 24.4, 24.7, 29.7, 40.9, 41.4, 42.7, 45.5, 55.2, 127.6, 127.8, 128.0, 128.1, 128.8, 129.0, 130.0, 132.9, 135.5, 136.1, 137.8, 138.2, 140.4, 143.5, 198.0, 209.1; IR (NaCl, neat) ν 1707, 1659 cm^{-1}; HRMS (ESI) calcd for $C_{35}H_{40}NO_4S$ (M^+ + H) 570.2678, found 570.2677.

2-((3R,6S)-4-Benzoyl-6-benzyl-5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-3-yl)-1-cyclobutylethanone (**2r**): yield 65%; 0.079 g; colorless solid; mp = 173−175 °C; $[\alpha]^{23}_D$ +117.1 (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ 1.74−1.83 (m, 1H), 1.88−2.00 (m, 1H), 2.07−2.25 (m, 4H), 2.31−2.41 (m, 4H), 2.62 (dd, 1H, *J* = 18.2, 4.4 Hz), 2.86 (d, 2H, *J* = 6.6 Hz), 3.00 (dd, 1H, *J* = 14.4, 11.0 Hz), 3.15−3.24 (m, 2H), 3.95 (dd, 1H, *J* = 14.5, 6.3 Hz), 4.99 (t, 1H, *J* = 6.5 Hz), 7.01−7.21 (m, 14H), 7.34 (t, 1H, *J* = 7.3 Hz), 7.44 (d, 2H, *J* = 7.6 Hz), 7.50 (d, 2H, *J* = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 17.7, 21.6, 24.2, 24.6, 30.5, 38.2, 40.7, 42.7, 45.5, 58.1, 126.4, 127.6, 128.0, 128.2, 128.3, 129.1, 129.1, 129.5, 129.7, 133.1, 136.1, 136.8, 137.0, 137.6, 137.7, 139.4, 143.2, 198.0, 209.2; IR (NaCl, neat) ν 1705, 1659 cm^{-1}; HRMS (ESI) calcd for $C_{38}H_{38}NO_4S$ (M^+ + H) 604.2522, found 604.2526.

2-((3R,6S)-4-Benzoyl-6-(2-(methylsulfonyl)ethyl)-5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-3-yl)-1-cyclopropylethanone (**2s**): yield 67%; 0.081 g; colorless solid; mp = 195−197 °C; $[\alpha]^{23}_D$ +183.2 (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ 0.84−1.01 (m, 4H), 1.83−1.89 (m, 1H), 1.99−2.04 (m, 1H), 2.11−2.17 (m, 1H), 2.52 (s, 3H), 2.61 (dd, 1H, *J* = 18.1, 7.5 Hz), 2.80−2.87 (m, 4H), 3.01−3.17 (m, 3H), 3.23−3.31(m, 3H), 4.32 (dd, 1H, *J* = 17.8, 4.8 Hz), 4.66 (dd, 1H, *J* = 10.5 Hz), 6.91−6.95 (m, 4H), 7.01−7.10 (m, 5H), 7.29 (t, 1H, *J* = 7.3 Hz), 7.49 (d, 2H, *J* = 8.0 Hz), 8.01 (d, 2H, *J* = 8.1 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 11.0, 11.1, 20.9, 21.8, 23.7, 29.7, 41.4, 42.8, 43.9, 51.7, 55.6, 127.4, 128.0, 128.3, 128.4, 128.7, 128.8, 130.3, 133.1, 135.8, 136.6, 137.1, 137.8, 137.9, 144.0, 197.0, 207.7; IR (NaCl, neat) ν 1697, 1661 cm^{-1}; HRMS (ESI) calcd for $C_{33}H_{36}NO_6S_2$ (M^+ + H) 606.1984, found 606.1980.

1-((3R,6S)-4-Benzoyl-6-(2-(methylsulfonyl)ethyl)-5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-3-yl)heptan-2-one (**2t**): yield 62%; 0.079 g; colorless solid; mp = 105−107 °C; $[\alpha]^{23}_D$ +179.7 (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ 0.87 (t, 3H, *J* = 7.2 Hz), 1.19−1.31 (m, 5H), 1.46−1.53 (m, 2H), 1.96−2.02 (m, 1H), 2.11−2.20 (m, 1H), 2.32−2.44 (m, 3H), 2.53 (s, 3H), 2.69 (dd, 1H, *J* = 18.2, 4.8 Hz), 2.87 (s, 3H), 3.01−3.17 (m, 3H), 3.27 (td, 1H, *J* = 10.7, 4.2 Hz), 4.29 (dd, 1H, *J* = 14.3, 5.4 Hz), 4.68 (d, 1H, *J* = 10.2 Hz), 6.90−6.93 (m, 4H), 7.00−7.09 (m, 5H), 7.29 (t, 1H, *J* = 7.4 Hz), 7.50 (d, 2H, *J* = 8.2 Hz), 8.02 (d, 2H, *J* = 8.1 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 13.9, 21.8, 22.4, 23.3, 23.7, 29.7, 31.3, 41.4, 42.8, 43.0, 43.1, 51.7, 55.6, 127.5, 128.0, 128.4, 128.5, 128.7, 130.3, 133.1, 135.8, 136.6, 137.0, 137.8, 137.9, 144.1, 197.3, 208.1; IR (NaCl, neat) ν 2930, 1711, 1659, 1313, 1161 cm^{-1}; HRMS (ESI) calcd for $C_{35}H_{42}NO_6S_2$ (M^+ + H) 636.2454, found 636.2457.

dx.doi.org/10.1021/jo400121j | J. Org. Chem. 2013, 78, 3183−3195

*((3R,6S)-6-Benzyl-3-methyl-5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-4-yl)(phenyl)methanone (**3a**):* yield 96%; 0.100 g; colorless solid; mp = 146−148 °C; $[\alpha]^{23}_{D}$ +47.7 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.96 (d, 3H, *J* = 6.5 Hz), 2.40 (s, 3H), 2.75 (dd, 1H, *J* = 14.2, 9.5 Hz), 2.82−2.93 (m, 3H), 3.80−3.89 (m, 1H), 4.91 (dd, 1H, *J* = 9.4, 3.8 Hz), 6.93−6.95 (m, 2H), 7.12−7.28 (m, 12H), 7.38−7.42 (m, 3H), 7.63 (d, 1H, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 16.5, 21.6, 30.1, 38.3, 44.8, 58.4, 126.3, 127.5, 127.8, 128.2, 128.3, 128.4, 129.2, 129.3, 129.3, 129.6, 133.2, 135.9, 136.9, 137.5, 137.8, 138.1, 139.4, 143.1, 197.3; IR (NaCl, neat) ν 3019, 1665, 1215 cm^{-1}; HRMS (ESI) calcd for $C_{33}H_{32}NO_3S$ (M^+ + H) 522.2103, found 522.2095.

*((3R,6S)-6-Benzyl-3-methyl-5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-4-yl)(4-bromophenyl)methanone (**3b**):* yield 88%; 0.106 g; pale yellow solid; mp = 146−148 °C; $[\alpha]^{23}_{D}$ +5.9 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.98 (d, 3H, *J* = 6.6 Hz), 2.40 (s, 3H), 2.71−2.95 (m, 4H), 3.86 (dd, 1H, *J* = 14.0, 5.3 Hz), 4.87 (dd, 1H, *J* = 9.5, 3.8 Hz), 6.92 (d, 2H, *J* = 7.8 Hz), 7.10−7.28 (m, 10H), 7.37 (d, 2H, *J* = 8.2 Hz), 7.41 (d, 2H, *J* = 8.6 Hz), 7.52 (d, 2H, *J* = 8.6 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 16.5, 21.6, 30.1, 38.2, 44.7, 58.4, 126.4, 127.6, 128.1, 128.3, 128.4, 128.6, 129.1, 129.3, 129.6, 130.8, 131.8, 134.6, 136.6, 137.4, 137.6, 138.6, 138.9, 143.2, 196.3; IR (NaCl, neat) ν 3021, 1667, 1215, 1153 cm^{-1}; HRMS (ESI) calcd for $C_{33}H_{31}NO_3S^{79}Br$ (M^+ + H) 600.1208, found 600.1208.

*((3R,6S)-6-Benzyl-3-methyl-5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-4-yl)(p-tolyl)methanone (**3c**):* yield 93%; 0.1 g; yellow oil; $[\alpha]^{23}_{D}$ +28.3 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.96 (d, 3H, *J* = 6.3 Hz), 2.31 (s, 3H), 2.41 (s, 3H), 2.73−2.93 (m, 4H), 3.86 (dd, 1H, *J* = 13.6, 4.9 Hz), 4.93 (dd, 1H, *J* = 8.9, 3.1 Hz), 6.96 (d, 2H, *J* = 5.9 Hz), 7.06−7.31 (m, 12H), 7.41 (d, 2H, *J* = 8.0 Hz), 7.54 (d, 2H, *J* = 7.9 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 16.5, 21.6, 21.7, 30.2, 38.3, 44.8, 58.4, 126.3, 127.5, 127.8, 128.2, 128.3, 129.2, 129.4, 129.5, 129.6, 133.4, 137.0, 137.6, 137.6, 137.9, 139.5, 143.1, 144.1, 196.9; IR (NaCl, neat) ν 3026, 1663, 1217 cm^{-1}; HRMS (ESI) calcd for $C_{34}H_{34}NO_3S$ (M^+ + H) 536.2259, found 536.2261.

*((3R,6S)-6-Benzyl-3-methyl-5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-4-yl)(thiophene-3-yl)methanone (**3d**):* yield 91%; 0.096 g; colorless solid; mp = 155−157 °C; $[\alpha]^{23}_{D}$ +16.0 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.02 (d, 3H, *J* = 6.2 Hz), 2.40 (s, 3H), 2.73 (dd, 1H, *J* = 14.2, 9.6 Hz), 2.83 (dd, 1H, *J* = 14.2, 3.9 Hz), 2.89−2.97 (m, 2H), 3.91 (dd, 1H, *J* = 20.2, 11.5 Hz), 4.83 (dd, 1H, *J* = 9.5, 3.8 Hz), 6.91 (d, 2H, *J* = 6.4 Hz), 7.06−7.29 (m, 12H), 7.40 (d, 2H, *J* = 8.2 Hz), 7.70 (d, 1H, *J* = 2.4 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 16.6, 21.6, 30.2, 38.2, 44.7, 58.5, 126.2, 126.3, 126.8, 127.6, 127.9, 128.3, 128.3, 129.1, 129.2, 129.6, 135.6, 136.7, 137.5, 137.6, 137.8, 140.1, 141.3, 143.3, 191.0; IR (NaCl, neat) ν 3025, 1655, 1153 cm^{-1}; HRMS (ESI) calcd for $C_{31}H_{30}NO_3S_2$ (M^+ + H) 528.1667, found 528.1667.

*((3R,6S)-6-Ethyl-3-methyl-5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-4-yl)(phenyl)methanone (**3e**):* yield 97%; 0.089 g; yellow oil; $[\alpha]^{23}_{D}$ +105.8 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.82 (t, 3H, *J* = 7.3 Hz), 0.92 (d, 3H, *J* = 6.9 Hz), 1.54−1.59 (m, 2H), 2.43 (s, 3H), 2.50−2.66 (m, 1H), 3.02 (dd, 1H, *J* = 14.7, 11.3 Hz), 4.10 (dd, 1H, *J* = 14.8, 6.1 Hz), 4.42−4.45 (m, 1H), 7.07−7.42 (m, 12H), 7.93 (d, 2H, *J* = 8.1 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 11.1, 16.4, 21.7, 25.4, 29.7, 44.9, 58.6, 127.5, 127.6, 128.0, 128.2, 129.0, 129.0, 129.9, 133.0, 136.0, 137.9, 138.3, 138.3, 138.8, 143.4, 197.3; IR (NaCl, neat) ν 3019, 1663, 1157 cm^{-1}; HRMS (ESI) calcd for $C_{28}H_{30}NO_3S$ (M^+ + H) 460.1946, found 460.1942.

*((3R,6S)-6-Isopropyl-3-methyl-5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-4-yl)(phenyl)methanone (**3f**):* yield 87%; 0.082 g; yellow oil; $[\alpha]^{23}_{D}$ +172.0 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.87−0.95 (m,9H), 1.81−1.87 (m, 1H), 2.50 (s, 3H), 3.10 (dd, 1H, *J* = 15.0, 11.2 Hz), 4.11 (dd, 1H, *J* = 15.0, 6.5 Hz), 4.56 (d, 1H, *J* = 4.3 Hz), 7.03−7.17 (m, 7H), 7.29−7.37 (m, 3H), 7.42 (d, 2H, *J* = 8.1 Hz), 7.93 (d, 2H, *J* = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 16.7, 19.2, 20.6, 21.7, 29.1, 31.8, 47.1, 61.3, 127.6, 128.0, 128.2, 128.9, 129.0, 130.0, 133.0, 135.8, 137.4, 138.3, 138.5, 139.7, 143.4, 197.4; IR (NaCl, neat) ν 3021, 1665, 1161 cm^{-1}; HRMS (ESI) calcd for $C_{29}H_{32}NO_3S$ (M^+ + H) 474.2103, found 474.2116.

*((3R,6S)-6-Isobutyl-3-methyl-5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-4-yl)(phenyl)methanone (**3g**):* yield 97%; 0.095 g; colorless oil; $[\alpha]^{23}_{D}$ +100.4 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.64 (d, 3H, *J* = 6.4 Hz), 0.81 (d, 3H, *J* = 6.7 Hz), 0.94 (d, 3H, *J* = 6.9 Hz), 1.14−1.27 (m, 1H), 1.57−1.72 (m, 2H), 2.50 (s, 3H), 2.62−2.68 (m, 1H). 3.02−3.08 (m,1H), 4.04 (dd, 1H, *J* = 14.9, 6.1 Hz), 4.95 (d, 1H, *J* = 10.5 Hz), 7.06−7.18 (m, 7H), 7.33−7.42 (m, 5H), 7.93 (d, 2H, *J* = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 16.5, 20.8, 21.7, 23.7, 24.4, 29.5, 41.6, 44.7, 55.4, 127.6, 128.0, 128.2, 129.0, 129.1, 129.9, 133.0, 136.0, 137.9, 138.1, 139.1, 143.5, 197.3; IR (NaCl, neat) ν 3019, 1663, 1217 cm^{-1}; HRMS (ESI) calcd for $C_{30}H_{34}NO_3S$ (M^+ + H) 488.2259, found 488.2267.

*((3R,6S)-3-Methyl-5-phenyl-6-propyl-1-tosyl-1,2,3,6-tetrahydropyridin-4-yl)(phenyl)methanone (**3m**):* yield 97%; 0.092 g; colorless solid, mp = 143−144 °C; $[\alpha]^{23}_{D}$ +128.4 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.75 (t, 3H, *J* = 7.2 Hz), 0.92 (d, 3H, *J* = 6.9 Hz), 1.11−1.21 (m, 1H), 1.38−1.61 (m, 3H), 2.50 (s, 3H), 2.57−2.66 (m, 1H), 3.04 (dd, 1H, *J* = 14.8, 11.3 Hz), 4.09 (dd, 1H, *J* = 14.8, 6.2 Hz), 4.52 (d, 1H, *J* = 9.6 Hz), 7.07−7.18 (m, 7H), 7.31−7.42 (m, 5H), 7.92 (d, 2H, *J* = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 13.6, 16.4, 19.6, 21.7, 29.6, 34.5, 44.9, 57.1, 127.5, 127.6, 129.0, 128.2, 129.0, 129.0, 129.9, 133.0, 136.0, 137.9, 138.2, 138.3, 138.9, 143.4, 197.3; IR (NaCl, neat) ν 3019, 2399, 1663, 1159 cm^{-1}; HRMS (ESI) calcd for $C_{29}H_{32}NO_3S$ (M^+ + H) 474.2103, found 474.2105.

*((3R,6R)-6-(((tert-Butyldimethylsilyl)oxy)methyl)-3-methyl-5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-4-yl)(phenyl)methanone (**3p**):* yield 52%; 0.06 g; yellow solid; mp = 96−98 °C; $[\alpha]^{23}_{D}$ +91.1 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ −0.04 (s, 3H), −0.03 (s, 3H), 0.90 (s, 12H), 2.50 (s, 3H), 2.61−2.62 (m, 1H), 3.46 (dd, 1H, *J* = 14.0, 11.2 Hz), 3.64 (dd, 1H, *J* = 10.6, 3.6 Hz), 3.76 (d, 1H, *J* = 10.6 Hz), 4.07 (dd, 1H, *J* = 14.2, 6.0 Hz), 4.60 (s, 1H), 7.05−7.10 (m, 5H), 7.19 (t, 2H, *J* = 7.6 Hz), 7.36−7.43 (m, 5H), 7.88 (t, 2H, *J* = 8.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ −5.7, −5.6, 16.1, 18.2, 21.7, 25.9, 30.1, 47.1, 58.4, 64.6, 127.2, 127.7, 127.9, 128.2, 129.0, 129.2, 129.9, 133.0, 134.9, 136.4, 137.3, 138.4, 140.9, 143.3, 197.3; IR (NaCl, neat) ν 1665 cm^{-1}; HRMS (ESI) calcd for $C_{33}H_{42}NO_4SSi$ (M^+ + H) 576.2604, found 576.2593.

*((3R,6S)-3-Methyl-6-(2-(methylsulfonyl)ethyl)-5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-4-yl)(phenyl)methanone (**3s**):* yield 87%; 0.094 g; colorless solid; mp = 93−95 °C; $[\alpha]^{23}_{D}$ +159.1 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.92 (d, 3H, *J* = 6.9 Hz), 2.04−2.17 (m, 2H), 2.48−2.55 (m, 4H), 1.96−2.02 (m, 1H), 2.11−2.20 (m, 1H), 2.32−2.44 (m, 3H), 2.99 (s, 3H), 3.02−3.12 (m, 2H), 3.21−3.27 (m, 1H), 4.18 (dd, 1H, *J* = 15.1, 6.0 Hz), 4.62 (d, 1H, *J* = 7.2 Hz), 6.98−7.00 (m, 2H), 7.09−7.15 (m, 7H), 7.34−7.38 (m, 1H), 7.48 (d, 2H, *J* = 8.2 Hz), 7.93 (d, 2H, *J* = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 16.2, 21.8, 23.8, 29.3, 41.3, 44.8, 51.7, 55.9, 127.3, 128.2, 128.4, 128.8, 128.9, 130.3, 133.2, 135.7, 136.6, 136.8, 137.8, 139.6, 144.1, 196.4; IR (NaCl, neat) ν 3019, 1661 cm^{-1}; HRMS (ESI) calcd for $C_{29}H_{32}NO_5S_2$ (M^+ + H) 538.1722, found 538.1721.

*(2R,4S)-4-(N-Allyl-4-methylphenylsulfonamido)-1,3,5-triphenylpenta-1,2-dienyl acetate (**4a**):* yield 87%; 0.094 g; colorless oil; $[\alpha]^{23}_{D}$ −18.0 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.14 (s, 3H), 2.36 (s, 3H), 3.04 (dd, 1H, *J* = 14.0, 4.7 Hz), 3.19 (dd, 1H, *J* = 14.0, 9.8 Hz), 3.82−3.95 (m, 2H), 4.89−4.93 (m, 2H), 5.56−5.66 (m, 1H), 5.73 (dd, 1H, *J* = 9.8, 4.7 Hz), 7.09−7.38 (m, 15H), 7.46−7.52 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 20.7, 21.5, 39.6, 46.5, 59.5, 116.8, 118.9, 124.8, 126.4, 127.3, 127.5, 127.8, 128.4, 128.5, 128.6, 128.7, 128.8, 129.3, 129.4, 132.1, 134.4, 135.6, 137.4, 137.8, 143.2, 167.9, 200.4; IR (NaCl, neat) ν 3019, 2399, 1755, 1215, 1157 cm^{-1}; HRMS (ESI) calcd for $C_{35}H_{34}NO_4S$ (M^+ + H) 564.2209, found 564.2196.

*(1S,4R,5S)-1-Benzyl-4-methyl-5-phenyl-2-tosyl-2,3,4,5-tetrahydro-1H-indeno[1,2-c]pyridine (**5**):* yield 94%; 0.143 g; colorless solid; mp = 85−87 °C; $[\alpha]^{23}_{D}$ +107.4 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.74 (d, 3H, *J* = 6.8 Hz), 2.13−2.22 (m, 1H), 2.37 (s, 3H), 2.49 (dd, 1H, *J* = 14.6, 11.0 Hz), 3.19 (dd, 1H, *J* = 14.0, 7.0 Hz), 3.35 (dd, 1H, *J* = 13.9, 4.5 Hz), 3.82 (dd, 1H, *J* = 14.7, 6.2 Hz), 4.42 (s, 1H), 5.30 (s, 1H), 6.62 (d, 2H, *J* = 6.3 Hz), 7.10−7.17 (m, 2H), 7.24−7.31 (m, 5H), 7.51 (d, 2H, *J* = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz)

dx.doi.org/10.1021/jo400121j | *J. Org. Chem.* 2013, 78, 3183−3195

δ 17.0, 21.6, 27.0, 40.2, 46.1, 54.2, 55.4, 118.8, 123.9, 125.3, 126.7, 126.8, 126.9, 127.9, 128.3, 128.7, 129.7, 130.0, 136.1, 137.5, 138.3, 138.5, 141.6, 142.7, 148.2, 148.2; IR (NaCl, neat) ν 3019, 1599, 1337, 1215, 1159 cm^{-1}; HRMS (ESI) calcd for $C_{33}H_{32}NO_2S$ (M^+ + H) 506.2154, found 506.2159.

*(1S,4R,4aR,5S,9bS)-1-Benzyl-4-methyl-5-phenyl-2-tosyl-2,3,4,4a,5,9b-hexahydro-1H-indeno[1,2-c]pyridine (**6**):* yield 91%; 0.092 g; colorless oil; $[\alpha]^{23}_D$ −127.3 (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ 0.12 (d, 3H, *J* = 6.2 Hz), 1.62−1.69 (m, 1H), 2.52 (s, 3H), 2.68−2.75 (m, 2H), 2.93 (dd, 1H, *J* = 13.2, 3.9 Hz), 3.08 (t, 1H, *J* = 12.1 Hz), 3.27 (d, 1H, *J* = 5.8 Hz), 3.46 (dd, 1H, *J* = 13.2, 5.6 Hz), 4.56 (d, 1H, *J* = 5.8 Hz), 5.09 (dd, 1H, *J* = 10.8, 3.6 Hz), 7.23−7.48 (m, 16H), 7.72 (d, 2H, *J* = 8.1 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 18.2, 21.5, 26.7, 36.7, 45.4, 45.7, 50.2, 53.5, 54.7, 123.0, 125.1, 126.6, 126.7, 127.1, 127.3, 128.5, 128.8, 129.2, 129.6, 129.9, 137.8, 138.4, 139.6, 143.0, 143.6, 144.0; IR (NaCl, neat) ν 3019, 2399, 1601, 1497, 1341, 1215, 1157 cm^{-1}; HRMS (ESI) calcd for $C_{33}H_{34}NO_2S$ (M^+ + H) 508.2310, found 508.2313.

■ ASSOCIATED CONTENT

Supporting Information

Copies of ^1H and ^{13}C NMR spectra for all starting materials and products, as well as X-ray structures of compounds **1a,n**, **2a,l,p,q**, and **3p**. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: waihong@ntu.edu.sg.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was supported by a College of Science Start-Up Grant from Nanyang Technological University (NTU) and a Science and Engineering Research Council Grant (092 101 0053) from A*STAR, Singapore. A Yousef Jameel Graduate Scholarship (to S.) and an Undergraduate Research Experience on Campus stipend (to M.J.K.) from NTU is also acknowledged. We thank Drs. Yongxin Li and Rakesh Ganguly and Prof. Hajime Hirao of this Division for providing the respective X-ray crystallographic data and DFT calculations reported in this work.

■ REFERENCES

(1) For selected recent general reviews on homogeneous gold catalysis, see: (a) Rudolph, M.; Hashmi, A. S. K. *Chem. Soc. Rev.* **2012**, *41*, 2448. (b) Garayalde, D.; Nevado, C. *ACS Catal.* **2012**, *2*, 1462. (c) Krause, N.; Winter, C. *Chem. Rev.* **2011**, *111*, 1994. (d) Corma, A.; Leyva-Pérez, A.; Sabater, M. J. *Chem. Rev.* **2011**, *111*, 1657. (e) Hashmi, A. S. K.; Rudolph, M. *Chem. Soc. Rev.* **2008**, *37*, 1766. (f) Lipshutz, B. H.; Yamamoto, Y. *Chem. Rev.* **2008**, *108*, 2793. (g) Gorin, D. J.; Sherry, B. D.; Toste, F. D. *Chem. Rev.* **2008**, *108*, 3351. (h) Hashmi, A. S. K. *Chem. Rev.* **2007**, *107*, 3180. (i) Jiménez-Núñez, E.; Echavarren, A. M. *Chem. Commun.* **2007**, 333.

(2) For selected reviews on gold-catalyzed 1,*n*-enyne cycloisomerizations, see: (a) Hashmi, A. S. K. *Angew. Chem., Int. Ed.* **2010**, *49*, 5232. (b) Fürstner, A. *Chem. Soc. Rev.* **2009**, *38*, 3208. (c) Jiménez-Núñez, E.; Echavarren, A. M. *Chem. Rev.* **2008**, *108*, 3326. (d) Zhang, L.; Sun, J.; Kozmin, S. A. *Adv. Synth. Catal.* **2006**, *348*, 2271.

(3) For reviews on gold-catalyzed cycloisomerizations of 1,*n*-enyne carboxylic esters, see: (a) Marion, N.; Nolan, S. P. *Angew. Chem., Int. Ed.* **2007**, *46*, 275. (b) Marco-Contelles, J.; Soriano, E. *Chem.—Eur. J.* **2007**, *13*, 1350. (c) Ma, S.; Yu, S.; Gu, Z. *Angew. Chem., Int. Ed.* **2006**, *45*, 200.

(4) For selected examples of gold-catalyzed reactions of 1,*n*-enyne esters via a gold carbene species, see: (a) Watson, I. D. G.; Ritter, S.; Toste, F. D. *J. Am. Chem. Soc.* **2009**, *131*, 2056. (b) Uemura, M.; Watson, I. D. G.; Katsukawa, M.; Toste, F. D. *J. Am. Chem. Soc.* **2009**, *131*, 3464. (c) Zou, Y.; Garayalde, D.; Wang, Q.; Nevado, C.; Goeke, A. *Angew. Chem., Int. Ed.* **2008**, *47*, 10110. (d) Boyer, F.-D.; Le Goff, X.; Hanna, I. *J. Org. Chem.* **2008**, *73*, 5163. (e) Moreau, X.; Goddard, J.-P.; Bernard, M.; Lemière, G.; López-Romero, J. M.; Mainetti, E.; Marion, N.; Mouriès, V.; Thorimbert, S.; Fensterbank, L.; Malacria, M. *Adv. Synth. Catal.* **2008**, *350*, 43. (f) Marion, N.; de Frémont, P.; Stevens, E. D.; Fensterbank, L.; Malacria, M.; Nolan, S. P. *Chem. Commun.* **2006**, 2048.

(5) For examples of gold-mediated reactions of 1,*n*-enyne and propargylic esters via the metal-activated allene species, see: (a) Hashmi, A. S. K.; Yang, W.; Yu, Y.; Hansmann, M. M.; Rudolph, M.; Rominger, F. *Angew. Chem., Int. Ed.* **2013**, *51*, 1329. (b) Teng, T.-M.; Liu, R.-S. *J. Am. Chem. Soc.* **2010**, *132*, 9298. (c) Garayalde, D.; Gómez-Bengoa, E.; Huang, X.; Goeke, A.; Nevado, C. *J. Am. Chem. Soc.* **2010**, *132*, 4720. (d) Peng, Y.; Cui, L.; Zhang, G.; Zhang, L. *J. Am. Chem. Soc.* **2009**, *131*, 5062. (e) Mauleón, P.; Krinsky, J. L; Toste, F. D. *J. Am. Chem. Soc.* **2009**, *131*, 4513. (f) Marion, N.; Lemière, G.; Correa, A.; Costabile, C.; Ramón, R. S.; Moreau, X.; De Frémont, P.; Dahmane, R.; Hours, A.; Lesage, D.; Tabet, J.-C.; Goddard, J.-P.; Gandon, V.; Cavallo, L.; Fensterbank, L.; Malacria, M.; Nolan, S. P. *Chem.—Eur. J.* **2009**, *15*, 3243. (g) Zhang, G.; Peng, Y.; Cui, L.; Zhang, L. *Angew. Chem., Int. Ed.* **2009**, *48*, 3112. (h) Lemière, G.; Gandon, V.; Cariou, K.; Fukuyama, T.; Dhimane, A.-L.; Fensterbank, L.; Malacria, M. *Org. Lett.* **2007**, *9*, 2207. (i) Yu, M.; Zhang, G.; Zhang, L. *Org. Lett.* **2007**, *9*, 2147. (j) Buzas, A.; Gagosz, F. *J. Am. Chem. Soc.* **2006**, *128*, 12614. (k) Wang, S.; Zhang, L. *J. Am. Chem. Soc.* **2006**, *128*, 8414. (l) Zhao, J.; Hughes, C. O.; Toste, F. D. *J. Am. Chem. Soc.* **2006**, *128*, 7436. (m) Wang, S.; Zhang, L. *Org. Lett.* **2006**, *8*, 4585. (n) Buzas, A.; Istrate, F.; Gagosz, F. *Org. Lett.* **2006**, *8*, 1957. (o) Zhang, L.; Wang, S. *J. Am. Chem. Soc.* **2006**, *128*, 1442. (p) Zhang, L. *J. Am. Chem. Soc.* **2005**, *127*, 16804.

(6) Correa, A.; Marion, N.; Fensterbank, L.; Malacria, M.; Nolan, S. P.; Cavallo, L. *Angew. Chem., Int. Ed.* **2008**, *47*, 718.

(7) Rao, W.; Susanti, D.; Chan, P. W. H. *J. Am. Chem. Soc.* **2011**, *133*, 15248.

(8) For the only other example showing 1,6-enyne esters generated from dipropargylic amides to be resistant to this type of cyclization, see: Hashmi, A. S. K.; Molinari, L.; Rominger, F.; Oeser, T. *Eur. J. Org. Chem.* **2011**, 2256.

(9) Leboeuf, D.; Simonneau, A.; Aubert, C.; Malacria, M.; Gandon, V.; Fensterbank, L. *Angew. Chem., Int. Ed.* **2011**, *50*, 6868.

(10) The only other known example prior to this work is a 1,3-acyl shift proposed in Au(I)-catalyzed dimerization of propiolic acids to 4-hydroxy-α-pyrones; see: Luo, T.; Dai, M.; Zheng, S.-L.; Schreiber, S. L. *Org. Lett.* **2011**, *13*, 2834.

(11) For selected recent examples by us, refer to ref 7 and: (a) Rao, W.; Koh, M. J.; Kothandaraman, P.; Chan, P. W. H. *J. Am. Chem. Soc.* **2012**, *134*, 10811. (b) Kothandaraman, P.; Huang, C.; Susanti, D.; Rao, W.; Chan, P. W. H. *Chem.—Eur. J.* **2011**, *17*, 10081. (c) Sze, E. M. L.; Rao, W.; Koh, M. J.; Chan, P. W. H. *Chem.—Eur. J.* **2011**, *17*, 1437. (d) Kothandaraman, P.; Rao, W.; Foo, S. J.; Chan, P. W. H. *Angew. Chem., Int. Ed.* **2010**, *49*, 4619. (e) Rao, W.; Chan, P. W. H. *Chem.—Eur. J.* **2008**, *14*, 10486.

(12) For selected examples, see: (a) Eckhardt, M.; Peters, S.; Nar, H.; Himmelsbach, F.; Zhuang, L. PCT Int. Appl. WO 2011057054 A1 20110512, 2011. (b) Cook, C. E.; Tallent, C. R.; Thomas, B. F.; Navarro, H. A. PCT Int. Appl. WO 2007124353 A2 20071101, 2007. (c) Chen, W.; Lee, T. U.S. Pat. Appl. Publ. US 20070049613 A1 20070301, 2007. (d) Kinney, W. A.; Luci, D. K.; Maryanoff, B. E. U.S. Pat. Appl. Publ. US 20050026917 A1 20050203, 2005. (e) Fail, P. A.; Anderson, S. A.; Cook, C. E. *Reprod. Toxicol.* **2000**, *14*, 265.

(13) For the synthesis of compound **1**, see the Experimental Section and refs 7 and 11a. For the synthesis of gold complexes **A**−**I**, see ref 7 and: (a) López-Carrillo, V.; Echavarren, A. M. *J. Am. Chem. Soc.* **2010**, *132*, 9292. (b) Amijs, C. H. M.; López-Carrillo, V.; Raducan, M.;

Pérez-Galán, P.; Ferrer, C.; Echavarren, A. M. *J. Org. Chem.* **2008**, *73*, 7721. (c) Ricard, L.; Gagosz, F. *Organometallics* **2007**, *26*, 4704. (d) Herreo-Gómez, E.; Nieto-Oberhuber, C.; López, S.; Benet-Buchholz, J.; Echavarren, A. M. *Angew. Chem., Int. Ed.* **2006**, *45*, 5455. (e) Hashmi, A. S. K.; Weyrauch, J. P.; Rudolph, M.; Kurpejović, E. *Angew. Chem., Int. Ed.* **2004**, *43*, 6545.

(14) See Figures S57−63 in the Supporting Information for the ORTEP drawings of the crystal structures of **1a**,**n**, **2a**,**l**,**p**,**q**, and **3a** reported in this work. CCDC 892352 (**1a**), CCDC 892355 (**1n**), CCDC 892353 (**2a**), CCDC 892354 (**2l**), CCDC 892357 (**2p**), CCDC 892356 (**2q**), and CCDC 892351 (**3a**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Center via www.ccdc.cam.ac.uk/data_request/cif.

(15) For examples of allene synthesis in gold catalysis, see: (a) Wang, D.; Gautam, L. N. S.; Bollinger, C.; Harris, A.; Li, M.; Shi, X. *Org. Lett.* **2011**, *13*, 2618. (b) Nun, P.; Gaillard, S.; Slawin, A. M. Z.; Nolan, S. P. *Chem. Commun.* **2010**, *46*, 9113. (c) Bolte, B.; Odabachian, Y.; Gagosz, F. *J. Am. Chem. Soc.* **2010**, *132*, 7294. (d) Lo, V. K.-Y.; Wong, M.-K.; Che, C.-M. *Org. Lett.* **2008**, *10*, 517. (e) Sherry, B. D.; Toste, D. *J. Am. Chem. Soc.* **2004**, *126*, 15978.

(16) For examples of [2 + 2] cycloadditions of 1,6-allenenes in gold catalysis, see: (a) Teller, H.; Corbet, M.; Mantilli, L.; Gopakumar, G.; Goddard, R.; Thiel, W.; Fürstner, A. *J. Am. Chem. Soc.* **2012**, *134*, 15331. (b) González, A. Z.; Benitez, D.; Tkatchouk, E.; Goddard, W. A., III; Toste, F. D. *J. Am. Chem. Soc.* **2011**, *133*, 5500. (c) Teller, H.; Flügge, S.; Goddard, R.; Fürstner, A. *Angew. Chem., Int. Ed.* **2010**, *49*, 1949. (d) Luzung, M. R.; Mauleón, P.; Toste, F. D. *J. Am. Chem. Soc.* **2007**, *129*, 12402.

(17) (a) Ohno, H.; Mizutani, T.; Kadoh, Y.; Aso, A.; Miyamura, K.; Fujii, N.; Tanaka, T. *J. Org. Chem.* **2007**, *72*, 4378. (b) Ohno, H.; Mizutani, T.; Kadoh, Y.; Aso, A.; Miyamura, K.; Fujii, N.; Tanaka, T. *Angew. Chem., Int. Ed.* **2005**, *44*, 5113.

(18) For examples proposing the involvement of a putative alkyl gold species, see refs 7 and 10 and: (a) Xiao, Y.-P.; Liu, X.-Y.; Che, C.-M. *Angew. Chem., Int. Ed.* **2011**, *50*, 4937. (b) LaLonde, R. L.; Brenzovich, W. E., Jr.; Benitez, D.; Tkatchouk, E.; Kelley, K.; Goddard, W. A., III; Toste, F. D. *Chem. Sci* **2010**, *1*, 226. (c) Brown, T. J.; Dickens, M. G.; Widenhoefer, R. A. *J. Am. Chem. Soc.* **2009**, *131*, 6350. (d) Brown, T. J.; Dickens, M. G.; Widenhoefer, R. A. *Chem. Commun.* **2009**, 6451. (e) Hooper, T. N.; Butts, C. P.; Green, M.; Haddow, M. F.; McGrady, J. E.; Russell, C. A. *Chem.—Eur. J.* **2009**, *15*, 12196. (f) Hooper, T. N.; Green, M.; McGrady, J. E.; Patel, J. R.; Russell, C. A. *Chem. Commun.* **2009**, 3877. (g) Shapiro, N. D.; Toste, F. D. *Proc. Natl. Acad. Sci. U.S.A.* **2008**, *105*, 2779.

(19) A 1,5-acyl migration step initiated by rotation of the acyloxy group of a vinyl gold intermediate has also been proposed and supported by DFT calculations in Au(I)-catalyzed cycloisomerization of 1,6-diyne acetates to δ-diketone substituted cyclopentenes, see ref 9.

(20) See refs 7 and 10 for examples of nucleophilic addition of a Au−C(sp^3) bond to a carbonyl carbon center. Also, for the proposed intermediacy of a four-membered cyclic transition state, see refs 5k and 10.

(21) Wang, W.; Hammond, G. B.; Xu, B. *J. Am. Chem. Soc.* **2012**, *134*, 5697.

(22) MacroModel, version 9.9; Schrödinger, LLC: New York, 2011.

(23) Jorgensen, W. L.; Tirado-Rives, J. *Proc. Natl. Acad. Sci. U.S.A.* **2005**, *102*, 6665.

(24) (a) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648. (b) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785. (c) Vosko, S. H.; Wilk, L.; Nusair, M. *Can. J. Phys.* **1980**, *58*, 1200.

(25) Hehre, W.; Radom, L.; Schleyer, P. v. R.; Pople, J. *Ab Initio Molecular Orbital Theory*; John Wiley & Sons: New York, 1986.

(26) Gaussian 09, revision B.01; Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A., Jr.; Vreven, T.; Kudin, K.; Burant, J. C.; Millam, J. M.; Iyengay, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Adamo, C.; Jaramillo, J.; Comperts, R.; Startmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenbuerg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chem, W.; Wong, M. W., Gonzalez, C.; Pople, J. A.; Gaussian, Inc.: Wallingford, CT, 2010.

(27) Pettersen, E. F.; Goddard, T. D.; Huang, C. C.; Couch, G. S.; Greenblatt, D. M.; Meng, E. C.; Ferrin, T. E. *J. Comput. Chem.* **2004**, *25*, 1605.

(28) (a) Wang, J.; Zhang, L.; Jing, Y.; Huang, W.; Zhu, X. *Tetrahedron Lett.* **2009**, *50*, 4978. (b) Bandini, M.; Tragni, M.; Umani-Ronchi, A. *Adv. Synth. Catal.* **2009**, *351*, 2521.

NOTE ADDED AFTER ASAP PUBLICATION

This paper was published ASAP on March 22, 2013. Table 2 was updated. The revised paper was reposted on March 26, 2013.