Development of New Biarylphosphane Coinage Metal Complexes for the Regioselective Synthesis of Fused Carbocycles

by
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À mes parents, Jocelyne et Normand…

Abstract

In the last century, no less than five nobel prizes have been awarded for the construction of carbon-carbon bonds : The Grignard reaction (1912), the Diels-Alder reaction (1950), the Wittig reaction (1979), Olefin metathesis (2005) and palladium cross-coupling reactions (2011). The latter two are transition metal catalyzed transformations and their impact on the synthesis of pharmaceutically active compounds, bulk chemicals, fine chemicals, high tech materials as well as agricultural chemicals has been phenomenal. These reactions have changed the way the scientific community views the science of synthesis.

Unlike palladium, gold has long been considered to be an expensive and inert metal and therefore, research on Au catalysis was scarse until the begining of the new millenium. Once the scientific community realized the treasure trove of reactivity that gold had to offer, the number of chemical transformations as well as total syntheses involving Au(I)/Au(III) catalysis has sky rocketed. A methodology initially developped by Toste and coworkers has shown that intramolecular addition of a silyl enol ether on alkynes proceeds via a *5-exo-dig* process. In the first part of this thesis, we will discuss how the ancilary ligand on Au(I) species can influence pathway selectivity for these cyclizations, therefore opening the door to selective *6-endo-dig* cyclizations to generate fused carbocycles.

With biological processes as well as other competing processes becoming ever more efficient, the future of chemical synthesis is threatened. If it is to survive, the focus of new chemical transformations will have to be on the cost and the greeness of the process. In the second part of this thesis, we will demonstrate how Ag(I) and Cu(I) complexes can offer even better *6-endo-dig* selectivity than analogous Au(I) complexes. Silver is about 56 times less expensive than gold, and copper is about 453 times less expensive than gold. Due to the greatly increased selectivity as well as the diminished cost of the catalysts, we have provided access to an attractive *6-endo-dig* cyclization process.

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Mes premiers remerciements vont à celui qui m'a donné la chance de travailler dans un labo de chimie pour la première fois il y a un peu plus de quatre ans. Son enthousiasme contagieuse pour la chimie et ses conseils ont été d'une valeur innestimable. Par-dessus tout, je suis reconnaissant pour la confiance qu'il m'a accordé; j'ai eu la chance de suivre mes instincs, de prendre des risques et des directions comme bon me semblait, et je crois sincèrement que c'est ce qui a fait de ma maitrise une expérience d'apprentissage si enrichissante. Merci Louis.

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Chapter 1

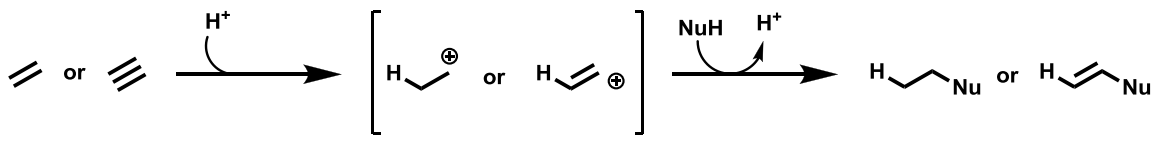
Introduction

Gold, silver, copper, mercury and platinum are metals that even non-chemists are aware of. Whether it is because their watch is made of gold and silver, or the copper wires in their homes, or the mercury thermometer indicating the outside temperature, or because their favorite album has gone "platinum", they are aware that these metals exist. Oddly, the most well known metal, gold, had received little attention from the organic chemistry community until the end of the 1990's. Silver on the other hand, has not yet received broad attention.

Addition reactions to C-C multiple bonds

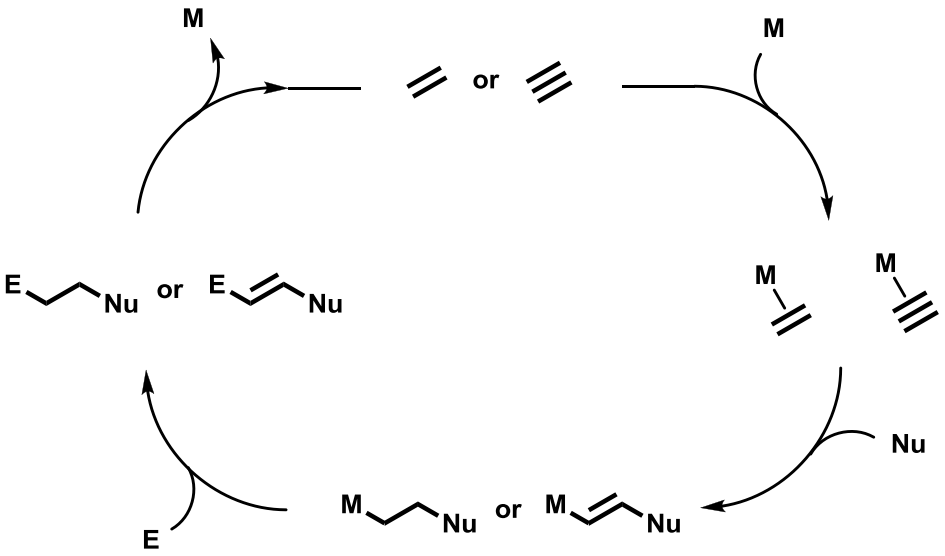
Additions of nucleophiles onto C-C multiple bonds by Brønsted acid catalysis (Scheme 1) generally requires harsh reaction conditions. Furthermore, the generation of the carbocation intermediate engenders the possibility for a number of side reactions giving rise to undesired side products.[1] Replacement of H^+ with an isolobal "soft" Hg^{2+} ion was once a classical way of solving some of these problems.[2] However, the toxic nature of mercury salts, which are often produced in stoichiometric quantities, due to the kinetically stable (sp^3)carbon-mercury bond, is a major handicap.[2,3]

Scheme 1.1 Brønsted Acid Catalyzed Addition on to C-C multiple bonds



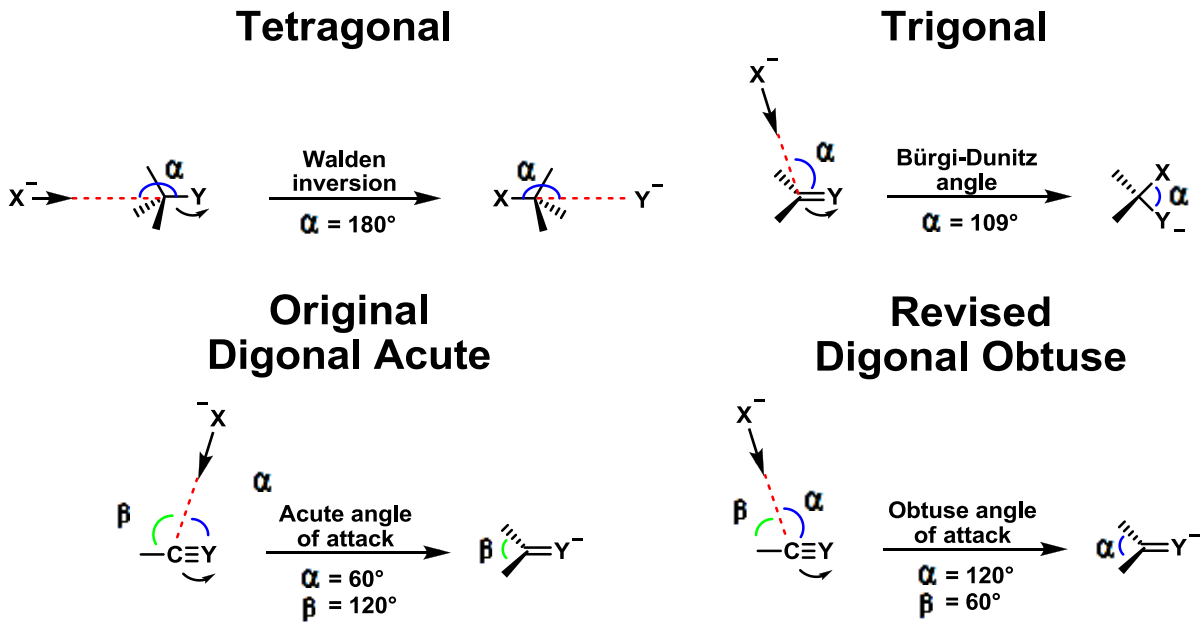
The logical alternative is to use a "soft" Lewis acid that has high affinity for C-C multiple bonds and a labile metal-carbon bond to insure turnover in a catalytic cycle (Figure 1.1). Such metals include, but are not limited to, Au, Ag, Cu, W, In, Pd, Zn and Pt.

Figure 1.1 General Catalytic Cycle of Nucleophilic Additions to Alkynes



Additions of various nucleophiles onto C-C multiple bonds can occur intermolecularily as well as intramolecularily. In the case of intramolecular nucleophilic additions, a cyclization occurs. It was Jack E. Baldwin who first proposed, in 1976, a set of rules to guide synthetic chemists in planning syntheses. Baldwin's rules for ring closure are based on the ring size being formed and on the geometry of the carbon undergoing the ring closing reaction (Figure 1.2).[4] At the time, nucleophilic additions onto tetrahedral carbons were known to occur according to Walden's inversion of the S_N2 reaction, meaning that the nucleophilic attack occurred at an angle of 180° from the leaving group.[5] Bürgi and Dunitz had only just published their findings on the ideal angle of 109° for carbonyl additions.[6] However, the ideal angle of 120° for additions onto digonal carbons was postulated according to limited information available at the time.[7]

Figure 1.2 Baldwin's Original and Revised Geometry of Nucleophilic Additions



In 2011, Alabugin and Gilmore decided it was time to reconsider Baldwin's rules for ring closure pertaining to alkyne cyclizations.[8] Baldwin's assumptions of an acute angle of attack, when α = 60°, was based on his conception of a general predominance of endo ring closures for digonal systems as well as some x-ray studies.[7] However, the acute angle of attack does not comply with molecular orbital predictions, which suggest an obtuse angle of attack in order for the attack trajectory to be directed at the alkyne π* orbital. According to higher level calculations, the obtuse is indeed the preferred angle, although it varies according to the nuclophile and whether the transition state (TS) is considered as and early TS (α = ~115°) or a late TS (α = ~130°).[9,10] These findings corroborate stereoelectronic considerations, as the obtuse approach minimizes interaction of the incoming nucleophile with the nodal plane of π*-orbital. When these considerations are put in the context of an intramolecular digonal cyclization, the obtuse angle of attack would imply stereoelectronic preference for the *exo* trajectory over the *endo* trajectory (Table 1.1).[10]

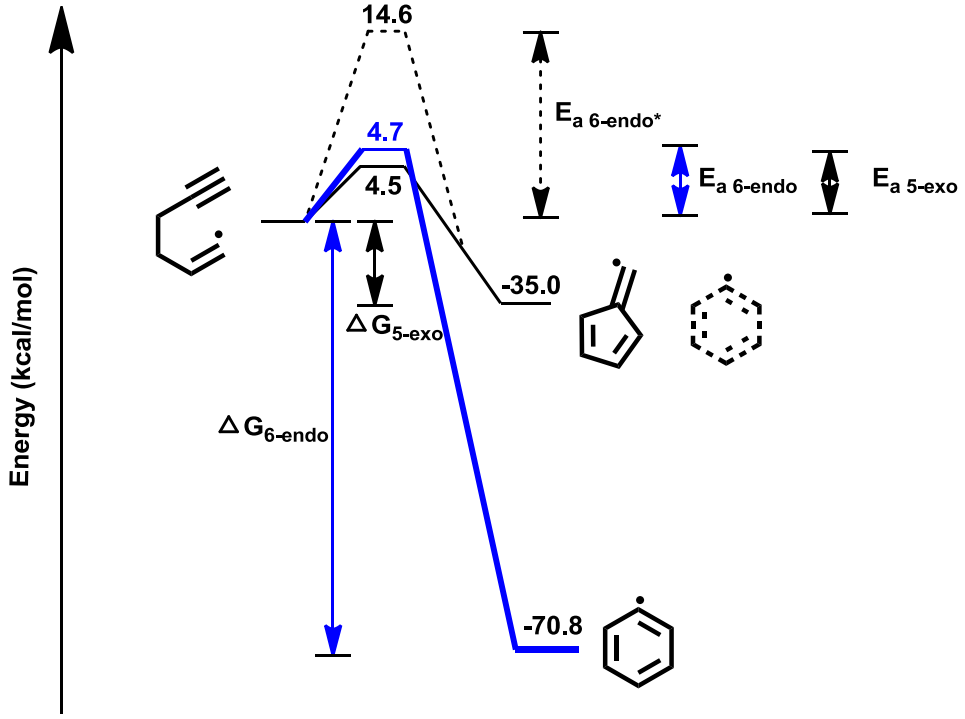
Table 1.1 Obtuse angle of attack on alkynes determined from Alabugin and coworkers' DTF calculations

Cyclization mode	Obtuse angle of attack
3-*exo*	140°
4-*endo*	76°
4-*exo*	133°
5-*endo*	82°
5-*exo*	116°
6-*endo*	99°

If one considers the ideal obtuse angle to be 115-130°, then the ideal angle of attack should favor *3-exo-dig* and *4-exo-dig* cyclizations. However, according to Baldwin's rules, *3-exo-dig* and *4-exo-dig* cyclizations are disfavored. Although no example of *3-exo* and *4-exo-dig* cyclizations were known at the time Baldwin proposed his rules for ring closure, a few examples of *3-exo* cationic and anionic ring closures have since surfaced in the literature.[8] To reconcile the ideal obtuse angle of attack postulate with the predominance of *4-endo* and *5-endo* cyclizations, Gilmore and Alabugin have proposed that in the case of small (3-4-membered) ring systems, the intrinsic stereoelectronic preference for the *exo* cyclizations can be *masked by the greater thermodynamic stability of the less strained endo-products.* As the ring size increases, the obtuse angle of attack in *endo*-type cyclizations becomes more favorable and starts to compete with *exo*-type cyclizations; this is the case for *6-endo-dig* processes although *5-exo-dig* cyclizations are typically preferred. The later remark brings into context the thermodynamic aspects of these cyclizations. In the case of thermodynamic processes, the nature of the bonds being formed needs to be considered especially in the case of heterocycles.[11] One also needs to consider that thermodynamic contributions are not negligible even when reactions proceed under kinetic control since thermodynamic factors may *relax stereoelectronic requirements (optimal trajectories)* therefore modifying kinetic predispositions of the Baldwin rules.[8] Furthermore, exothermic processes are known to have earlier, reactant-like transition states,[12] which require less distortion of the initial geometry of the reactants and therefore, if these conditions are met, the decreased distortions permit optimal obtuse angle of attack. Also, based on Marcus' theory, favorable thermodynamic

contributions can effectively reduce the activation energy of a process, it is therefore inappropriate to compare the favorability of the nucleophile's trajectories of two processes (*exo vs endo*) when their exothermicities are different.[13] The generation of an aromatic product is a great example of how thermodynamic bias (large negative ΔG) can have a large impact on the activation energy (E_a). The theoretical activation energy of the *6-endo-dig* TS, based on assumed identical exothermicities of both the *5-exo* and *6-endo* processes, is much higher than the TS energy of the *5-exo-dig* process. However, the large ΔG effectively reduces the E_a of the *6-endo-dig* process and thereby makes it kinetically competitive (Figure 1.3).[8]

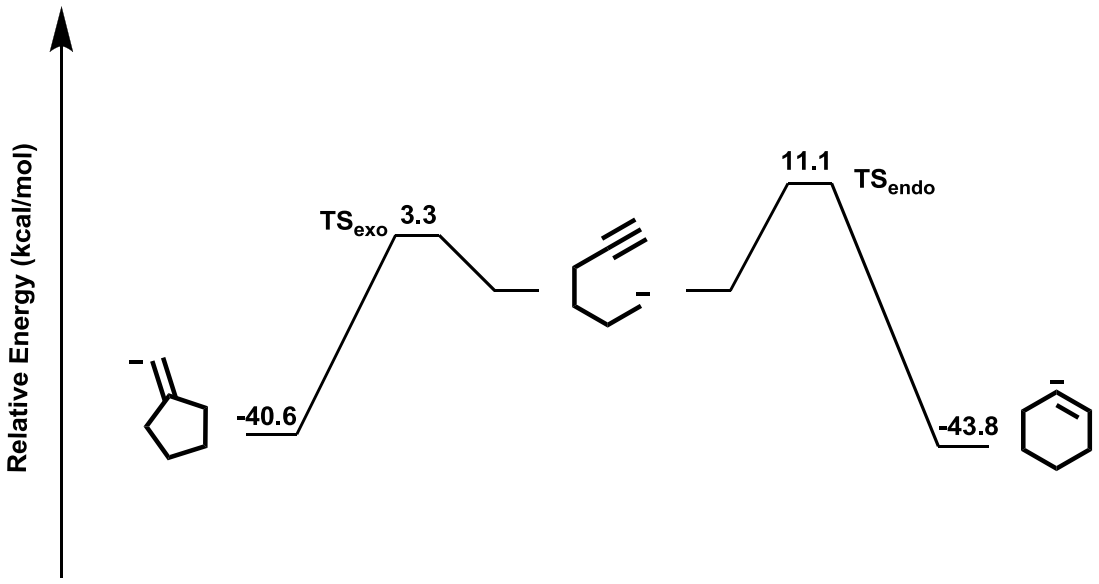
Figure 1.3 Effect of Thermodynamic Bias on the Kinetic Competition between 5-exo and 6-endo-dig processes in fully conjugated systems (Modified figure from Alabugin et al. [8])



The cyclizations discussed hereafter will concern cyclizations of the *5-exo-dig* and *6-endo-dig* type as these are the ones that we have studied. As stated, *6-endo-dig* cyclizations have a more favorable obtuse angle of attack than analogous *endo* cyclizations of smaller ring sizes. Therefore, the *6-endo-dig* process becomes competitive with the *5-exo-dig* process. However, the *5-exo-dig* TS is still favored by 7.8 kcal/mol in simplified systems (Figure

1.4)[10], which implies that only the *5-exo* product would be observed as it is generally the case.

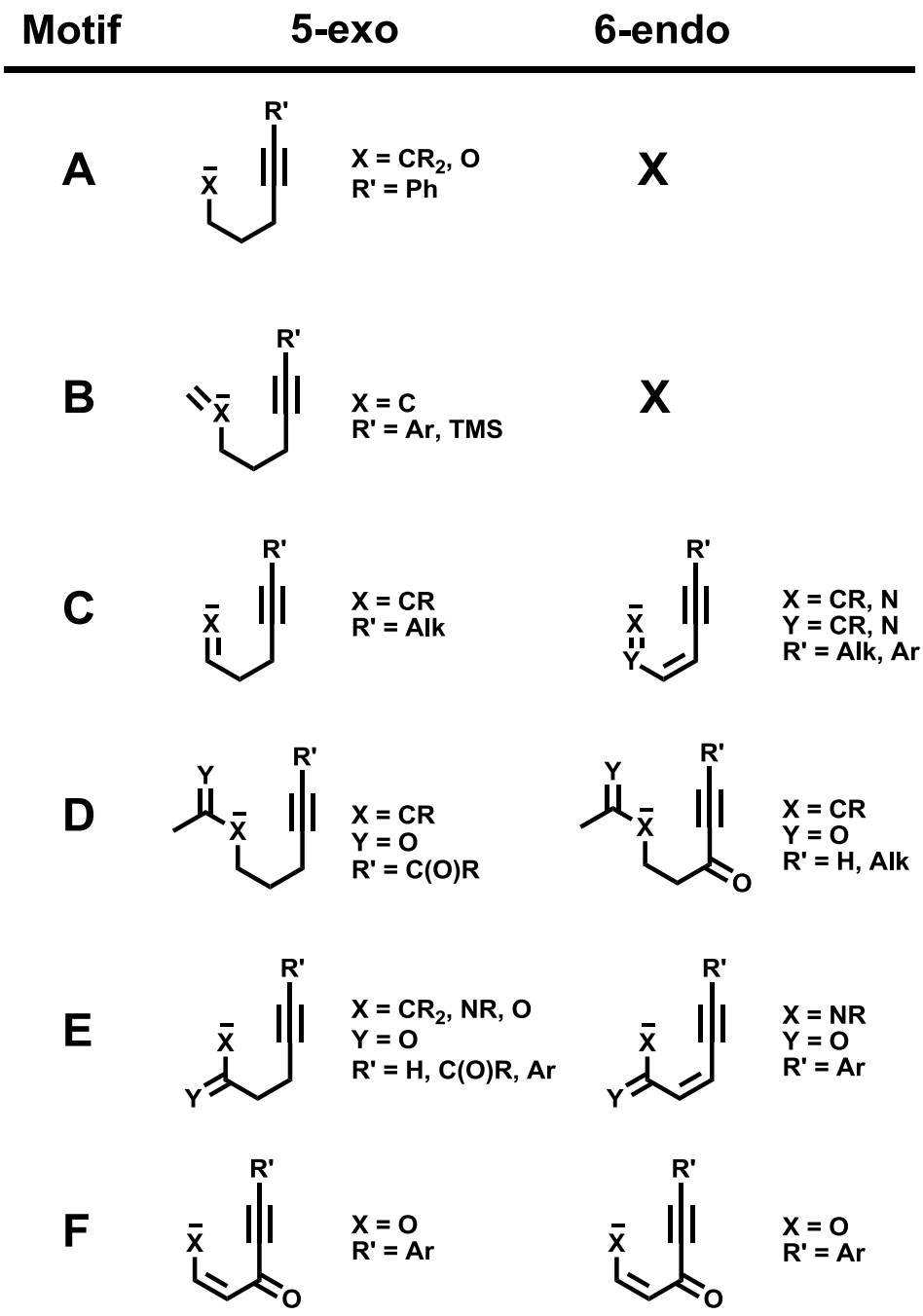
Figure 1.4 Relative TS and Product Energies for 5-exo and 6-endo-dig Cyclizations in a Simplified System according to DFT calculations by Alabugin et al.[10]



Structural aspects have a tremendous impact on the predisposition of a molecule to undergo *5-exo* or *6-endo-dig* cyclizations. As seen in Figure 1.5,[8] certain motifs are less predisposed to undergo *6-endo-dig* cyclizations, as in the case of motifs A and B. In the case of motifs C and E, if one omits unsaturations in the linker, these motifs are also ill-disposed to undergo *6-endo-dig* cyclizations. One can therefore deduce that the addition of an unsaturation in the linker between the nucleophile and the alkyne induces more selectivity for the *6-endo-dig* pathway. It is worth noting that one of the determining factors for selectivity is the polarization of the alkyne, as seen for motif D. These biaised motifs generally favor a Michael-type conjugate addition, although if one can produce thermodynamic conditions, both products can sometimes be accessed, as was the case for Miranda and coworkers[14], as represented in the F motif. It is also noteworthy that the *6-endo-dig* cyclization will generally be preferred when the cyclization product contains internal strain, as in the case of bridged rings.[15,16] Internal strain also plays an important role in the case of fused ring systems with different annulated ring sizes (Scheme 1.2)[8,17], although one might ague that in this

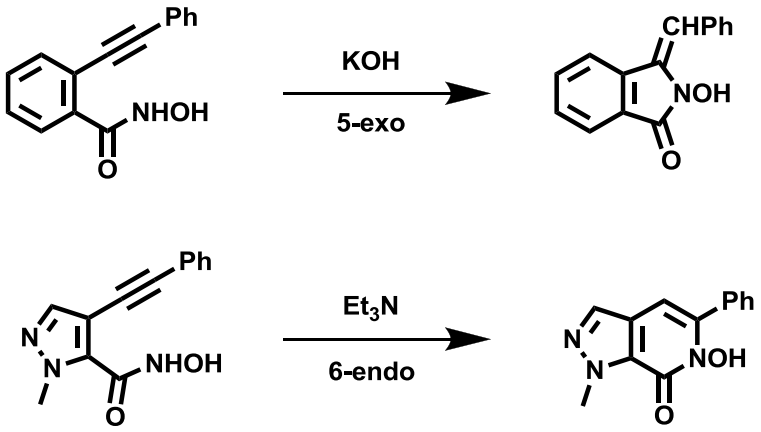
particular case the electronic properties or the heterocycle compared to the phenyl ring might also have had an impact on the selectivity.

Figure 1.5 Literature examples of 5-exo and 6-endo-dig cyclizations that proceed via anionic closure[a] (modified figure from Alabugin et al.)[8]



[a] **X** marks gaps in the literature.

Scheme 1.2 Effect of annealed ring size on 5-exo-dig vs 6-endo-dig selectivity



In strictly anionic cyclizations, alkyl substituents have a higher activation barrier for both *endo* and *exo* cyclization pathways when compared to their analogous terminal alkyne counterparts. The cyclization of phenyl substituted alkynes however, appears to be a barrierless process. This implies that a phenyl substituent instead of a methyl substituent accelerates the reaction by a factor of 10^6.[18] According to DFT calculations, a phenyl substituent also renders the 5-exo-dig cyclization >12 kcal/mol more exothermic than other *5-exo-dig* ring closures (Figure 1.5).[8,10] TMS substituents typically induce *exo*-selectivity with relatively low activation energies when compared to methyl substituents.[8,19]

Previously discussed cyclizations have, for the most part, been anionic, uncatalyzed cyclizations. Contrary to uncatalyzed cyclizations, Lewis Acid (LA) promoted ring formations tend to form *6-endo* products more easily, but this is predominantly the case when an aromatic product is formed or when the newly formed ring contains more than one unsaturation.[20] The same principles for anionic *5-exo-dig* and *6-endo-dig* cyclizations apply to LA-catalyzed cyclizations. It is worth noting however, that the metal itself may have unique influence on the reactivity and selectivity. As these properties are metal and ligand specific, we will only discuss cases relevant to our work on Au(I)-catalysis, and by extention to Ag(I) and Cu(I) systems, in the following sections.[21]

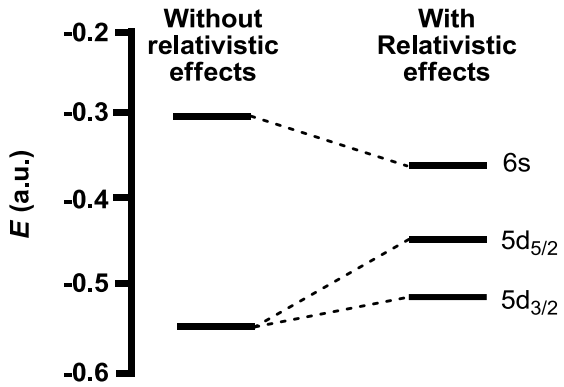
Gold-catalyzed cyclizations

Gold is a metal that is as old as history; gold chemistry however, is fairly young when compared to other transition metals. Au(I)/(III) complexes show distinctive reactivity[21] and catalysis by Au(I) has now blossomed into a very wide and competitive field. The unique reactivity of gold can be attributed, in part, to relativistic effects.[22,23] It is not the objective of this work to explain the fundamental and theoretical aspects of relativism but to explain the consequences of relativism on the properties of gold as a metal catalyst.

Relativism causes contraction of the atomic s and p orbitals, which results in an increased shielding effect which induces an expansion of the atomic d and f orbitals. In the case of Au, it implies the contraction of the 6s atomic orbital and expansion of the 5d orbital (Figure 1.6).[23,24,25] One of the direct consequences of relativism for gold is the increase in M-L bond strength, where M is the metal and L is any ligand. However, these types of bond contractions are sensitive to the nature and electronegativity of the ligands.[26] For example, the bond contractions are more significant for Au-phosphine bonds than for Au-halogen bonds.

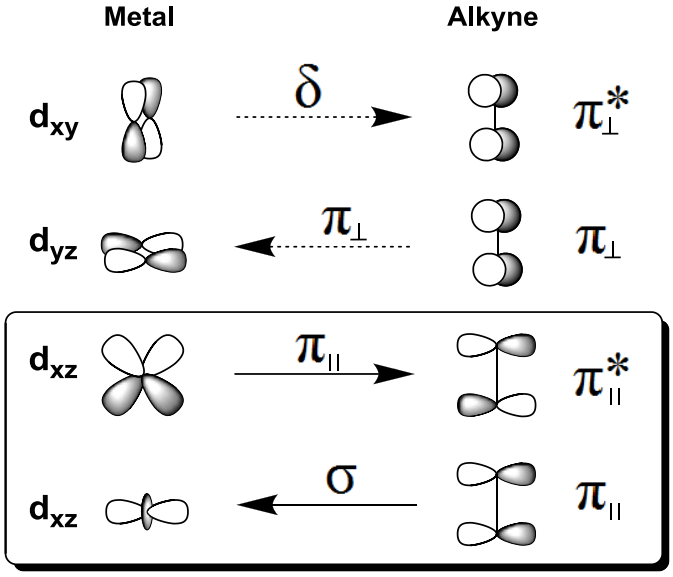
Theoretical calculations suggest that the 5d electrons of Au are located at a lower energy than the 3d electrons of Cu because of decreased electron repulsion of the more diffuse 5d electrons of Au. The consequence of this is that Au species tend to be both less nucleophilic and less prone to oxidative additions.[27] More calculations have indicated that reductive elimination from Au(III) species is disfavored.[28] Therefore, one may expect that Au does not generally cycle between oxidation states, although it should be noted that progress in this field has been made and it is possible under certain condition for this type of reactivity to occur.[29,30] It is the reluctance of Au to oxidize that makes most Au species stable to air, therefore rendering futile the need for inert atmosphere during reactions. One of the other consequences of relativism is the “soft” nature of Au, which is attributed to the diffuse d orbitals. Au(I) is also the least predisposed of the Group 11 metals to increase its coordination number to more than two.[31]

Figure 1.6 Calculated (Hartree Fock) Bond Energies of AuH With and Without Relativistic Effects (Modified figure from Toste el al.)[23]



One of the last consequences of relativism is the ability of the metal to back-donate. If one considers the bonding of an alkyne onto Au, there are four major bonding components to consider (Figure 1.7).[32] In the case of $Au(C_2H_2)^+$, the major bonding contribution (~65%) is the σ-donation of the in-plane π orbitals of acetylene, followed by back-donation (~27%) of Au d orbitals into the in-plane π* orbitals of acetylene. Bonding contributions from the orthogonal π orbitals of acetylene (~7%) and back-donation from Au d orbitals into the orthogonal π* orbitals of acetylene (~1%) are minor contributions.[33]

Figure 1.7 Orbital Diagram Illustrating the Major Bonding components between a Transition Metal and an Alkyne Ligand



Calculations show that in the case of $Au(CH_2)^+$, there should be double bond character associated with back-donation and further calculations have shown that relativistic effects would contribute up to 70% of the total bond energy for Au in that system.[34] Evidence supporting back-donation from Au came with reports of enyne cycloisomerizations by the groups of Toste, Fürstner and Echavarren and a debate on the existence of such intermediates followed suit (Figure 1.8). Although the [1,2]-migration of the deuterium suggested that the proposed mechanism was correct, a debate on the actual nature of resonance stabilized intermediate **1** erupted. This resulted in a series of experiments that fashioned the field of gold catalysis to what it is today.[35] Particularly strong evidence supporting carbene-like behavior came in a 2004 report by Fürstner and coworkers, in which vinylidene intermediate **3** was thought to be generated in order to furnish halophenanthrene **4** due to the migration of the bromine substituent on the alkyne (Figure 1.9).[36] It is noteworthy that $InCl_3$ did not furnish **4**, but the isomer **5**, which suggests that the In(III)-catalyzed reaction occurs through another mechanism.

Figure 1.8 Initial Experimental Evidence of Carbene-like Behavior

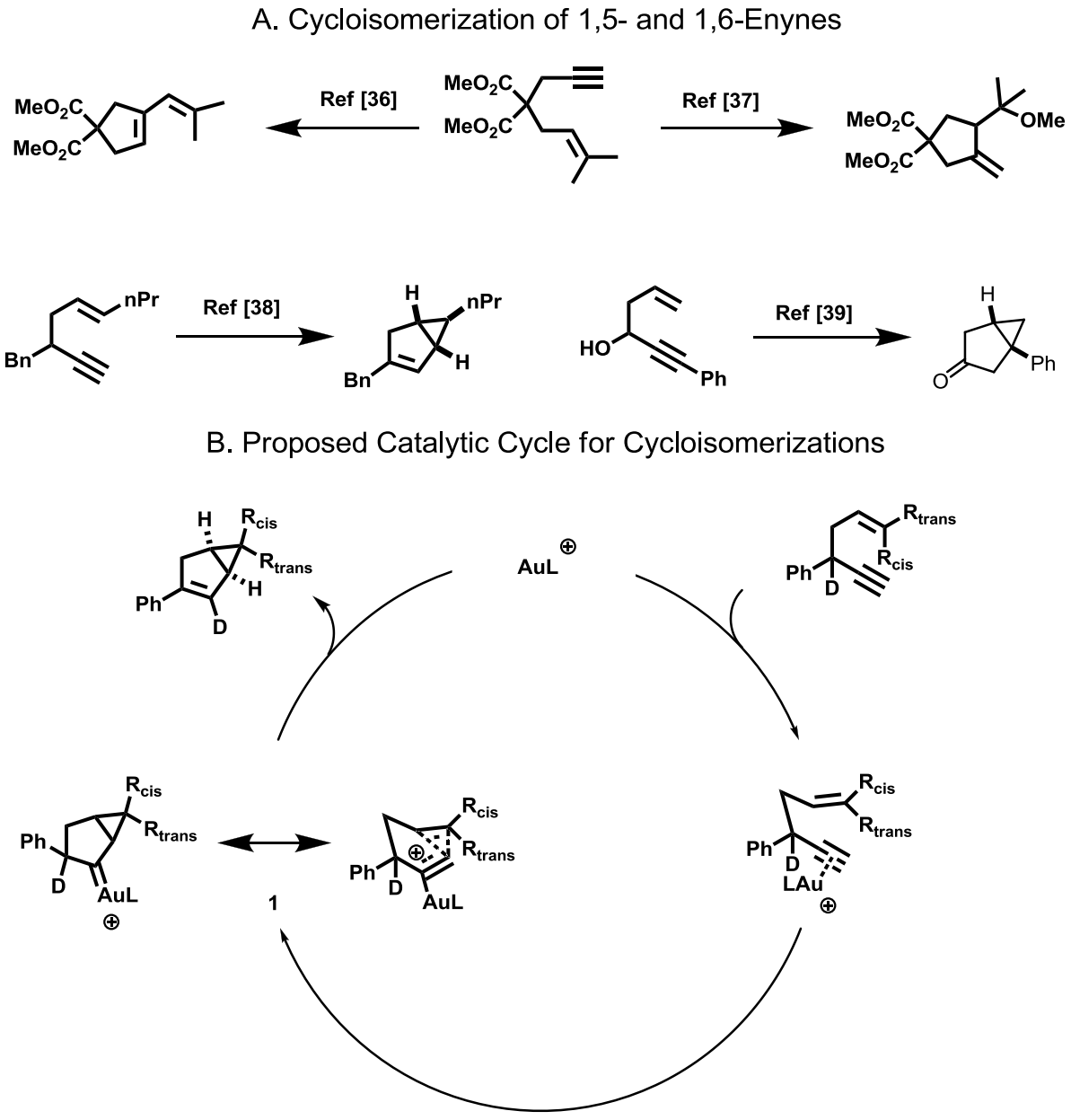
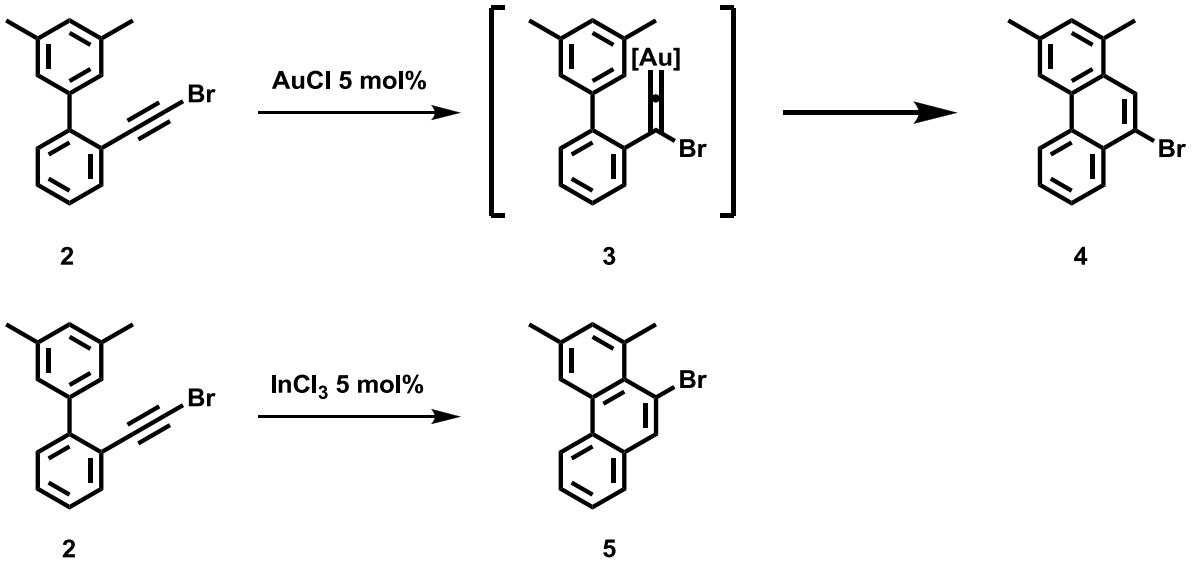


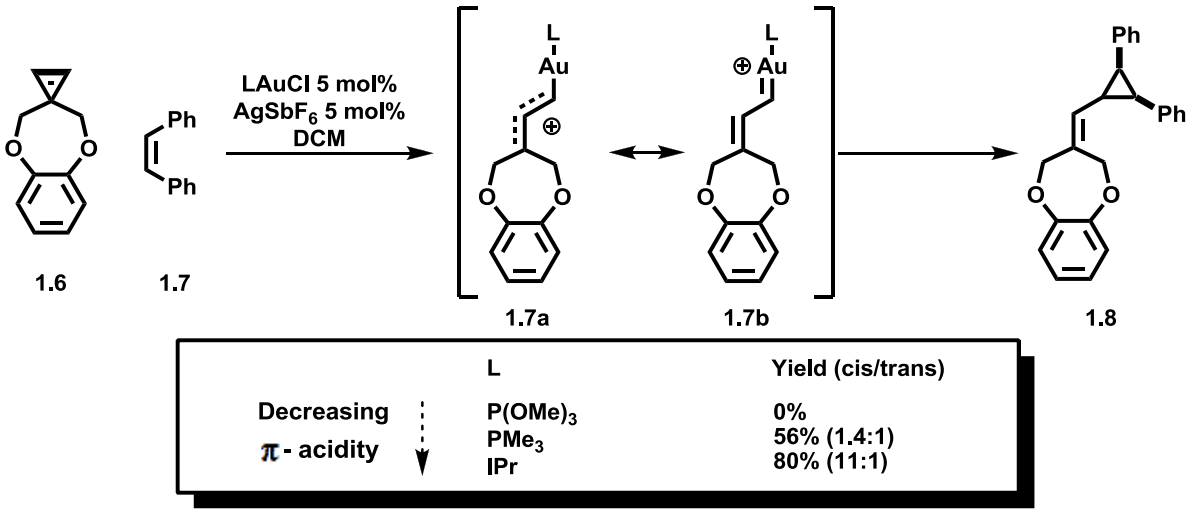
Figure 1.9 Comparison of Reactivity between AuCl and $InCl_3$ in the Metal-Catalyzed Synthesis of Halophenanthrenes



By 2009, the carbene vs carbocation debate, with regards to Au-catalysis, was pretty much settled even if no carbene species with sufficient double bond character had been isolated to support the existence of such species. Due to the carbene-like reactivity shown by Au, the intermediates exploiting this type of reactivity were coined as carbenoids.[32] The logical question that followed suite was: now that we know that carbenoid and carbocationic pathways are both possible, can we use ligand effects to modulate the reactivity of Au complexes in order to favor one pathway over the other?

This question was answered shortly thereafter by the group of Toste, who discussed the nature of bonding in gold(I)-carbene complexes and suggested that the dominant contributing factor in pathway selectivity in terms of ligand is π-acidity.[37] It is evident that π-acidic ligands draw electron density from the metal and one can assume that the σ-bonding of the ligand-gold bond is thus diminished, therefore making this bond longer and through a trans-effect, shortening the gold-carbon bond length. The overall result is an increase of electrophilicity of the carbene, which generally means favoring carbocationic reaction pathways. In the case of the Au(I)-catalyzed cyclopropanation of propene **1.6**, the π-acidic ligand triphenylphosphite seems to favor the formation of resonance intermediate **1.7a** over **1.7b**. This could explain why no desired product is formed.

Figure 1.10 Effect of π-acidity of the ancillary ligand on the reactivity of Au(I)-carbene complexes

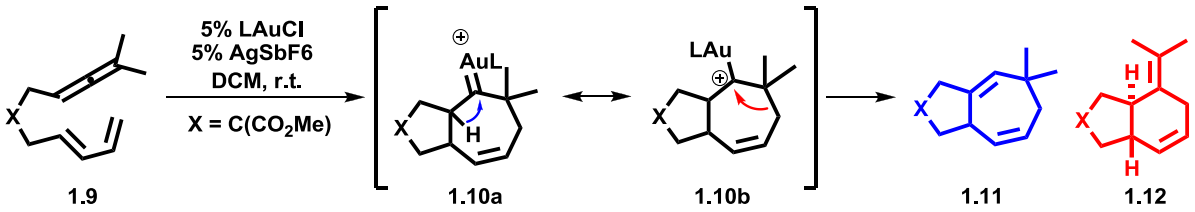


In the case of poor π-acidic or strong σ-donor ligands, there is more donation of electron density from the ligand to the metal. Since the metal is richer in electron density, its back-donation to the carbon will increase, and if we assume that increasing the π-component of the gold-carbon bond will automatically diminish its σ-bonding component, then we would expect that the gold-carbon bond become longer and through a trans-effect, the ligand-gold bond would become shorter. This would result in an increase in electron density of the gold-carbon bond, therefore making the carbon less electrophilic, which should favor carbene-like reactivity in reaction pathways. As shown in Figure 1.10, the Au(I)-catalyzed cyclopropanation of **1.6** occurs only when the ligand on gold has sufficiently low π-adidity. As the general π-acidity of the ligands decreases, there is an increase of yield. This increase of yield suggests the stabilization of carbene **1.7b** over carbocation **1.7a.**

Toste and coworkers also showed that these ligand effects are important in systems where both cationic and carbenoid-like pathways are possible.[38] Upon complexation of allene-diene **1.9** with various Au(I) complexes comprised of ligands varying in π-acidity, a [4+3] cycloaddition occurs to generate resonance structures **1.10a** and **1.10b**. When ligands of low π-acidity are used, carbenoid **1.10** becomes electron rich and a [1,2]-hydride shift occurs to furnish **1.11**. On the other hand, when π-acidic ligand $P(OPh)_3$ is utilized, carbenoid **1.10** becomes more electrophilic and we observe a [1,2]-alkyl shift, typical of carbocationic pathways, to yield **1.12**. According to the Toste group, Buchwald-type ligands

tend to distort the ligand-gold-carbon bonds, which allows for the preferential formation of **1.11** over **1.12**.

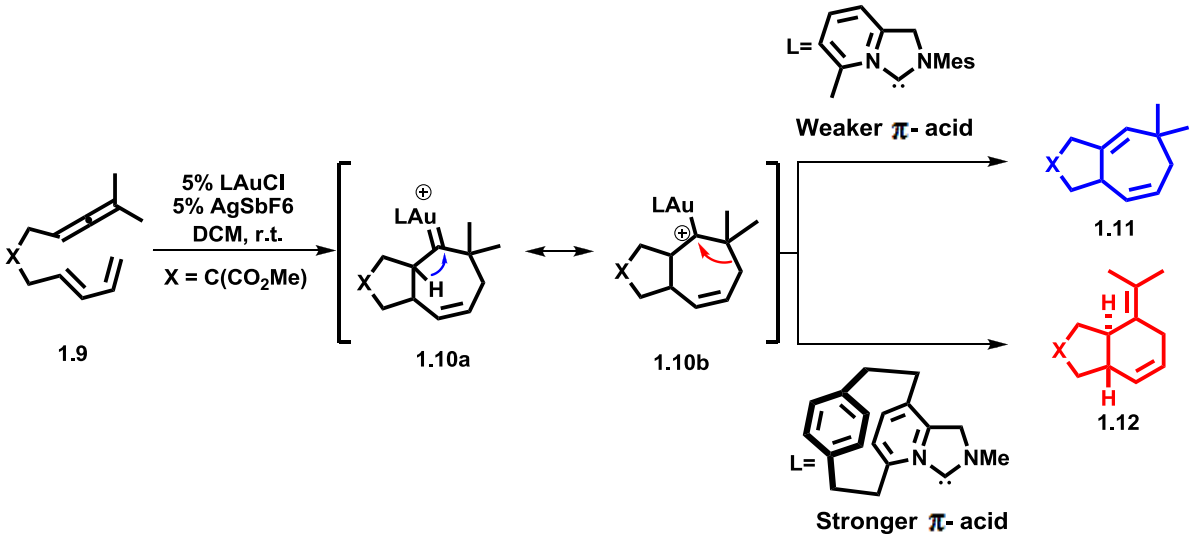
Figure 1.11 Effect of π-acidity of the ancillary phosphine ligand on pathway selectivity



L	Ratio (1.11:1.12)
$P(_tBu)_2$(o-biphenyl)	96:4
PPh_3	33:67
$P(OPh)_3$	0:100

Fürstner and coworkers also described similar results with N-Heterocyclic Carbene (NHC) ligands. They discovered that modulating the π-acidity of N-heterocyclic carbene ligands enables the same steering of selectivity between reaction pathways (Figure 1.12) as Toste and coworkers.[39] The π-acidity of NHC ligands is often considered to be negligible, but in the case of allene-diene **1.9**, when two NHC ligands of different π-acidity but of similar σ-donating properties are compared, more π-acidic ligands retain their tendency to favor carbocationic pathways.

Figure 1.12 Effect of π-acidity of the ancillary NHC ligand on pathway selectivity



The pioneering works of the Toste and Furstner groups showed that modulating the ancillary ligand on Au(I) species was the key solution to modulate pathway selectivity. By that time, our group was wondering whether this statement would hold true for pathway divergence at the first bond formation or, in other words; could *exo* vs *endo* selectivity be also modulated via proper choice of ligand?

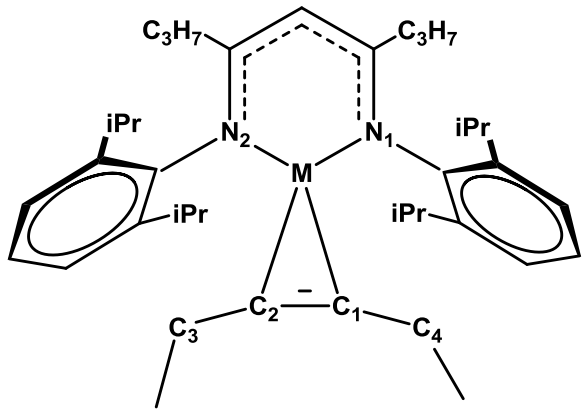
Silver & Copper-catalyzed cyclizations

Silver and copper are also part of the group 11 elements, as is gold, and yet, there are notable differences between each metal that makes each unique. Silver, because of decreased relativistic effects and the lack of lanthanide contraction effect, has a slightly larger atomic volume than gold. On the other hand, copper has a smaller molecular volume than gold and constitutes a much harder Lewis acid due to the diminished relativistic effects.

Kroll and coworkers have investigated monomeric Au(I), Ag(I) and Cu(I) alkyne complexes and have determined trends within the coinage metal family. Silver generally has longer metal-ligand bond lengths than gold and copper. As for copper, the metal-ligand bond lengths are typically similar to those of gold. A noteworthy remark is that contrary to Au(I), which prefers a quasi-linear two coordinate system, there is a prevalence for tricoordinate or

tetracoordinate Ag(I) and Cu(I) systems. Also, organocuprates are generally more nucleophilic because of the electron-electron repulsion of Cu 3d electrons, which implies that copper will be more likely to undergo oxidative additions. Cu(I) species are also generally more prone to oxidation than their Au(I) counterparts. Ag(II) complexes are rare and are generally bridging complexes containing a Ag(I) and a Ag(III) atom, giving the effective oxidation state of Ag(II). Ag(III) complexes are known but are much less common than Ag(I) species. Ag(I) and Cu(I) species are generally considered to be less Lewis acidic than Au(I) species due to the low-lying LUMO of gold. Typically, reactions catalyzed by Ag(I) or Cu(I) complexes are known to be much slower than when catalyzed by Au(I). Often, longer reaction times are required if not higher reaction temperatures. Interestingly, the lengths of the metal-alkyne bonds and shorter for Cu(I) than for Au(I) than for Ag(I) (Figure 1.13).[40] Furthermore, the bending of the alkyne is more pronounced for Au(I) species than it is for Cu(I) species. Ag(I) has the least impact of the bending of the alkyne, according to X-ray studies.

Figure 1.13 Bond lengths and angles of monomolecular coinage metal alkyne complexes obtained by Kroll and coworkers



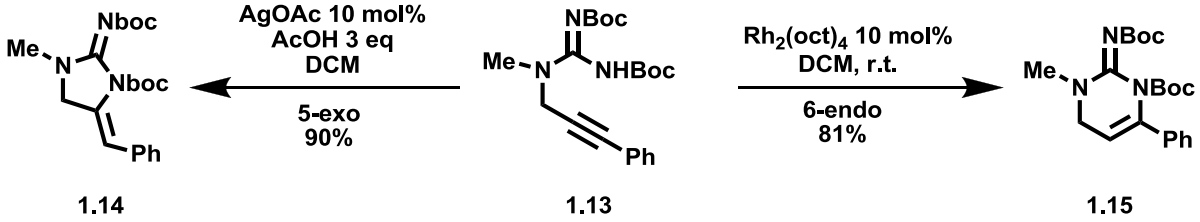
	M-C_1 (Å)	M-C_1-C_4 (°)
M= Au	2.069	155.0
= Ag	2.233	164.7
= Cu	1.983	156.5

DFT calculations from the same publication indicate that Au(I) complexes form stronger metal-alkyne bonds and offer more metal-alkyne backdonation, followed by Cu(I) and then Ag(I) as the weakest bonding and least back-donating metal.

Nucleophilic additions to alkynes catalyzed by Ag or Cu complexes are well-known in the literature, but precedence for carbon nucleophile additions is scarce. However, heteroatom nucleophiles are well known to undergo addition reactions on alkynes. Such reactions include popular 5-endo dig cyclizations to form indoles, benzofurans, furo[2,3-*d*]pyrimidinones, furans and pyrole derivatives via Cu(I)[41] and Ag(I)[42] catalysis. The selectivity of 5-exo versus 6-endo dig cyclizations catalyzed by Ag(I) or Cu(I) complexes is in accordance with the trends introduced previously (p.1-8). Ag-catalyzed nucleophilic addition of heteroatoms on alkynes in a selective 5-exo-dig fashion has enabled the synthesis of various heterocycles[43] such as furans, oxazolines and oxazolidinones and imidazolidin-2-imines[44].

Interestingly, both imidazolidin-2-imines and 3,4-dihydropyrimidin-2(1H)-iminewere synthesized in a regioselective manner by Looper and coworkers (Scheme 1.3). A regioselective 5-exo-dig cyclization of **1.13** occurred to generate **1.14** when silver acetate was utilized in catalytic quantities in the presence of acetic acid. When conditions were modified and a rhodium dimmer was used instead of AgOAc, exclusive formation of 6-endo-dig product **1.15** occurred. To our knowledge, this is one of only two[45] publications illustrating metal-catalyzed inversion of selectivity between 5-exo and 6-endo-dig processes. Numerous examples of selective 6-endo-dig additions of heteroatomic nucleophiles catalyzed by Ag(I) and Cu(I) appear in the literature. Notable accessed motifs include isoquinolines, isochromenones, pyranones, furans and others.

Scheme 1.3 Looper's regioselective hydroamination of propargylguanidines

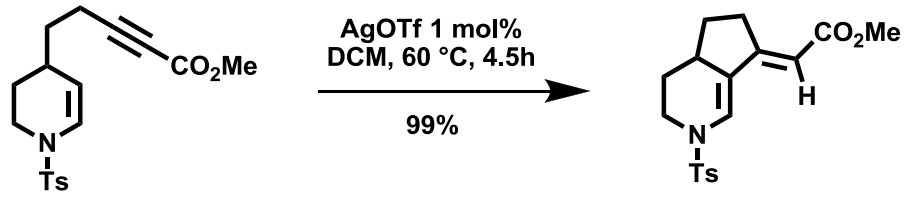


1.14 **1.13** **1.15**

Only a few examples of cyclizations utilizing carbon nucleophiles using Ag(I) or Cu(I) catalysis have been reported. Dake and coworkers have demonstrated that a 5-exo-dig

cyclization of an enamine nucleophile onto an ynone is possible using silver triflate and heat.[46] It is worth noting that an ynone type substrate such as **1.16** is likely to act as a Michael acceptor rather than an typical alkyne. Indeed, an ester/ketone/nitrile functionality on the alkyne appears to be necessary for the reaction to proceed and the geometry of enone **1.17** suggests a syn addition, which is contrary to the well-accepted trans-mechanism.[47] Of course, one cannot discard the potential post cyclization isomerization of enone **1.17**.

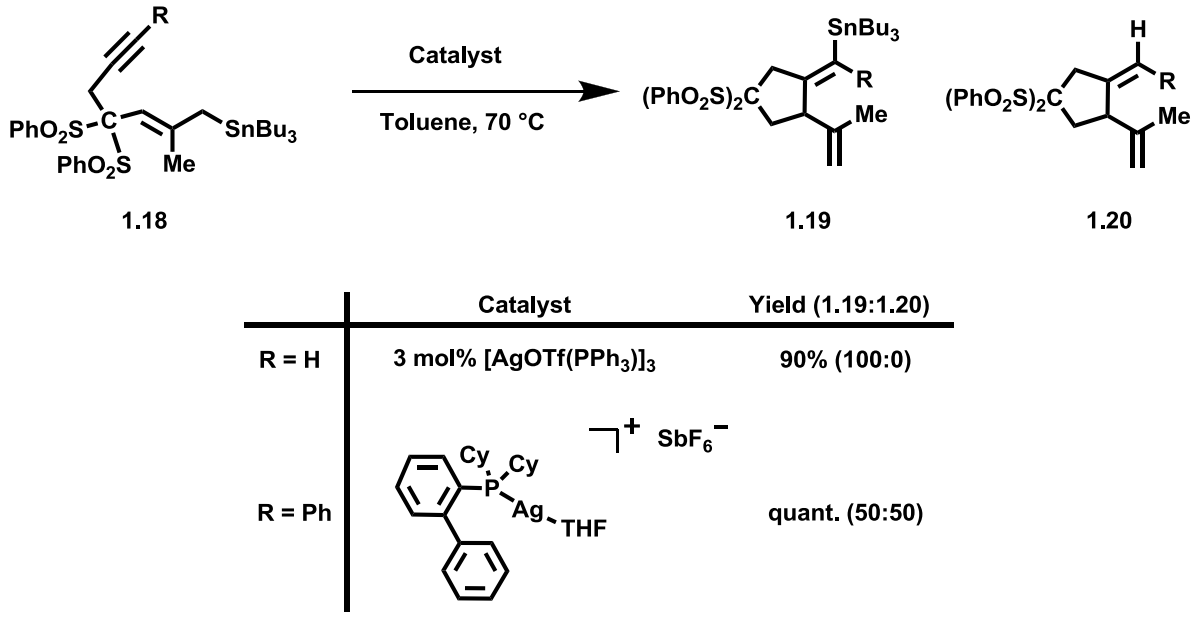
*Scheme 1.4 Dake Ag(I)-Catalyzed Cycloisomerization of Enamine **1.16***



1.16 **1.17**

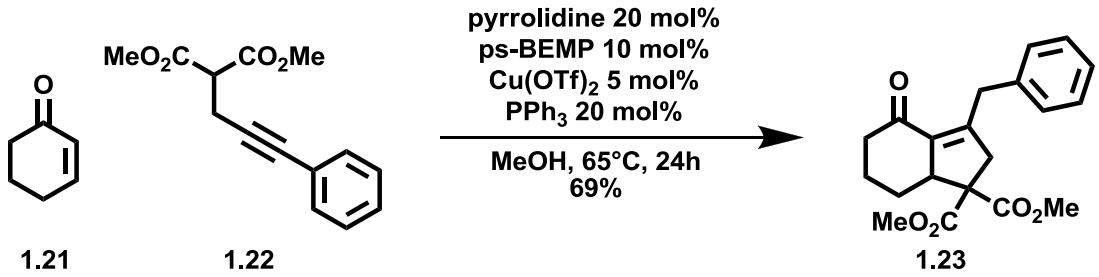
Another unique example is the work of Echavarren and Porcel, who demonstrated that allylstannanes may undergo additions on alkynes.[48] This work showed that **1.18** may undergo cyclization on a terminal alkyne using only 3 mol% of a trimer of silver triflate following which a transmetalation occurs to furnish the vinyl stannane **1.19**. Interestingly, when attempting to synthesize larger ring sizes as well as non-terminal alkynes, a $P(Cy)_2$(o-biphenyl) cationic Ag(I) complex proved to be ideal as it was a more active catalyst. A noticeable amount of proto-destannylation ensues when the later complex is utilized, furnishing a 1:1 mixture of **1.19** and **1.20.**

Figure 1.14 Echavarren Ag(I)-Catalyzed Carbostannylation of Alkynes



One of the few examples[49] of *5-exo* or *6-endo-dig* cyclization using a carbon nucleophile catalyzed by an Cu(I) catalyst is the work of Dixon and coworkers (|Scheme 1.5).[50] With an *in situ* formation of the iminium of **1.21** followed by 1,4-addition of **1.22** which generates the enamine that is predisposed to undergo a *5-exo-dig* addition on the alkyne to generate **1.24**. It is noteworthy that $Cu(OTf)_2$ readily undergoes a reduction to Cu(I) in the presence of triphenylphosphine.[51]

Scheme 1.5 Dixon and coworker's Cu(I)-catalyzed Iminium/Enamine/Carboanulation cascade



Without a doubt, the fundamental differences between each coinage metal bring into light the possibilities for catalyst discovery and optimization for organic transformations. One can

imagine that the combination of the proper ligand, the optimal reaction conditions (temperature, solvent, etc.), as well as the choice of coinage metal may allow a chemist to tune the metal complex's back-donation ability, nucleophilicity, binding ability, functional group tolerance and much more. Furthermore, as discussed during the reconsideration of the Baldwin rules, proper catalyst choice may indeed favor kinetic product or thermodynamic product pathways. Herein, we will discuss the unique properties and selectivities offered by gold, copper and silver complexes in the context of carbocyclizations.

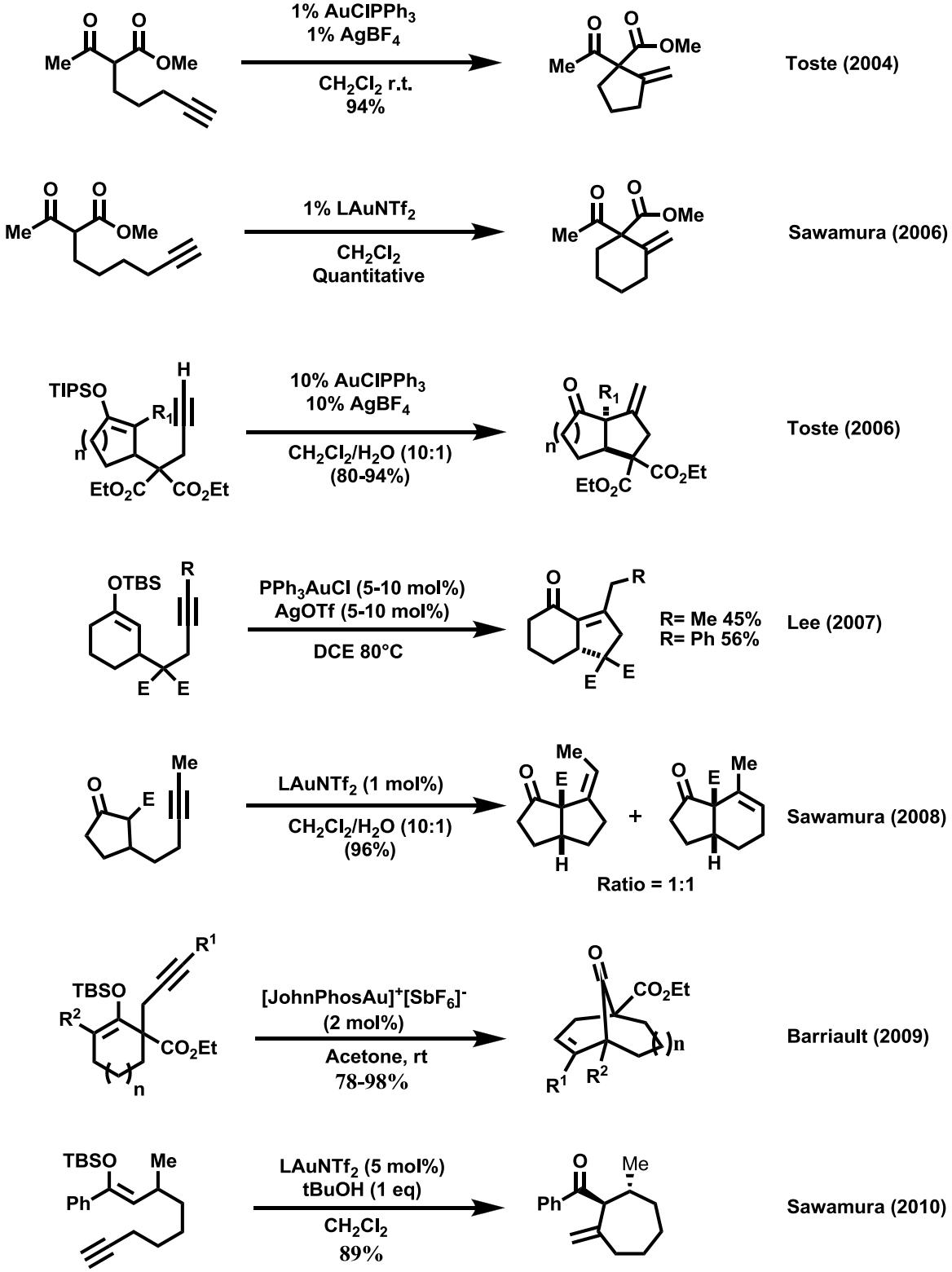
Chapter 2

Au(I)-Catalyzed Synthesis of Fused Carbocycles

Introduction

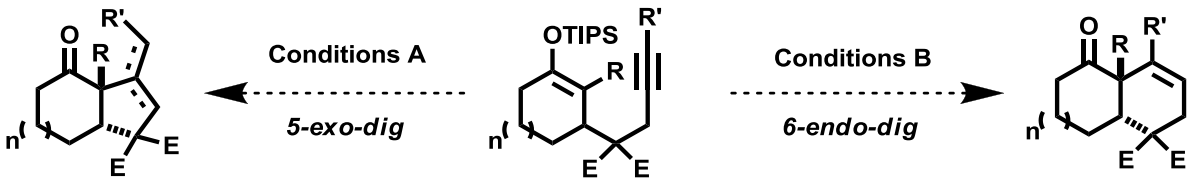
At the start of the new millennium, Au-catalysis was becoming one of the fastest growing fields. Pioneering work by Teles and coworkers had revealed that nucleophilic addition of alcohols on to alkynes was enabled by cationic Au(I) complexes.[52] This resulted in a wide investigation of alternative nucleophiles for addition on to alkynes.[21] In 2004, Toste and coworkers published a *5-exo-dig* conia-ene type reaction catalyzed by *in situ* formation of a cationic Au(I) species (Figure 2.1).[53] Following this initial contribution, the group of Sawamura published an analogous *6-exo-dig* cyclization.[54] The group of Toste then showed that instead of *in situ* generated enols, silyl enol ethers could be used instead as nucleophiles for additions on to alkynes via *5-endo*, *5-exo* and *6-exo-dig* processes.[55] The following year, Lee and coworkers demonstrated that Toste's cyclization of silyl enol ethers was also possible on non-terminal alkynes via a *5-exo-dig* process, albeit in low yields and few examples.[56] In 2008, Sawamura's group gave evidence that the selectivity between *5-exo* and *6-endo-dig* processes was mediocre (ca. 1:1 ratios) on analogous systems to the ones of the Toste group from 2006.[15] The following year, our group showed that *6-endo-dig* Au(I)-catalyzed cyclizations were favoured over the *5-exo-dig* process on systems where there is sufficient internal strain in the final products in order to generate bicycle[m.3.1]alkenones (m= 2-5).[16] In 2010, Sawamura's group demonstrated that increased yields could be obtained when using a tri-ethynylphosphine ligand (L)[57] in order to perform *7-exo dig* cyclizations of silyl enol ethers on alkynes.[58]

Figure 2.1 Literature examples of Conia-Ene type cyclizations catalyzed by Au(I)



Our group directed our attention to the selectivity problem encountered with internal alkynes. We wondered whether we could favour the 6-endo-dig pathway over the prevailing 5-exo-dig pathway in Toste's 2006 publication[55] and Lee's 2007 publication[56] by varying the ancillary ligand on the Au(I) species as well as the reaction conditions (Figure 2.2).

Figure 2.2 Proposed Selective Syntheses of Fused Carbocycles Enabled by Selective Conditions for 5-exo-dig and 6-endo-dig Cyclizations

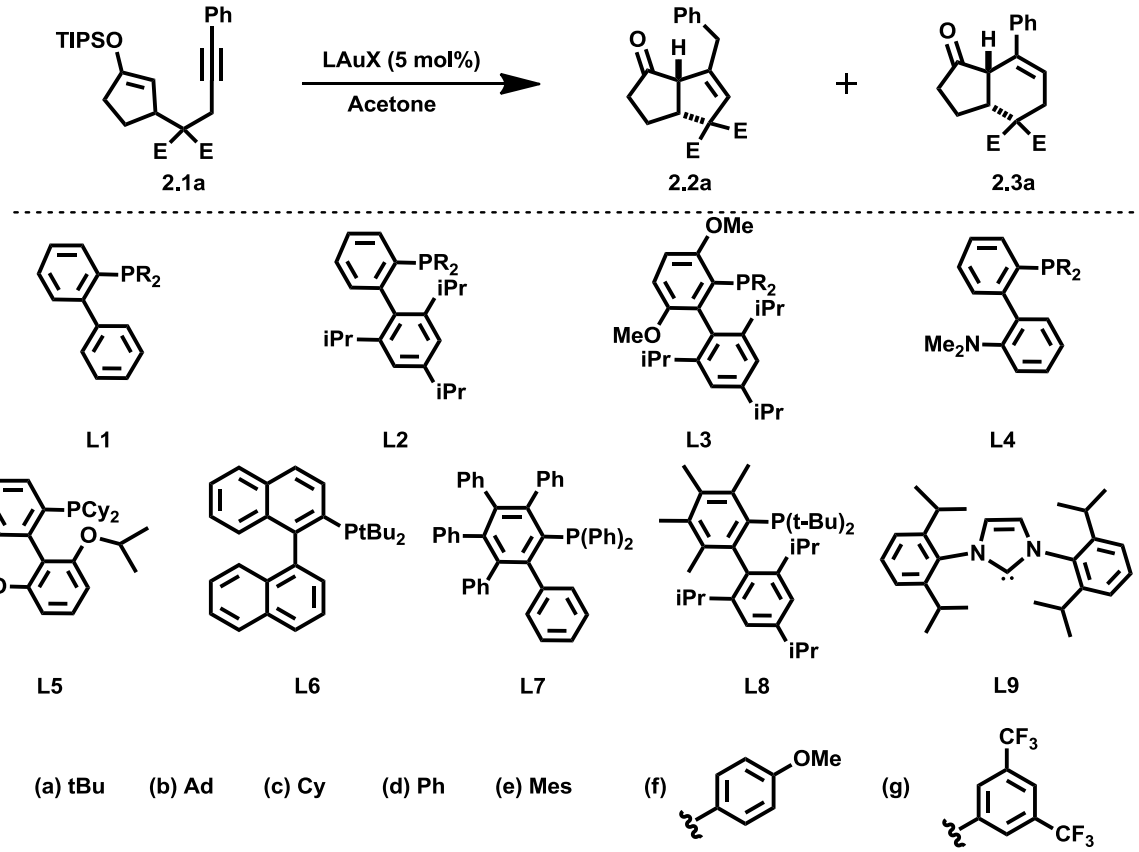


These studied were conducted by Francis Barabé, a Ph.D. candidate, and I. Francis was the one who performed the initial optimization for non-enyne substrates as well as all the cyclization reactions for these specific substrates. After the initial optimization, new ligands were synthesized and investigated and it would, therefore, be impossible not to discuss the importance of Francis' work in this thesis because it is too intimately linked to my own studies.

Reaction Optimization

Our investigation started with the cyclization of **2.1a**, which was a substrate that had previously shown to undergo *5-exo-dig* cyclizations.[56] As seen in *entry 1*, triphenyl phosphine was a poor ligand choice for both yield and *endo*-selectivity. Changing the counterion, *entry 2*, improved both the yield and the ratio but unfortunately, because the yield of *entry 1* was so low, it is difficult to assume that this is the optimal counterion, especially since reactions were generally slower when BF_4 was used instead of SbF_6. *Entries 3-5* show that alkyl substituents and electron poor aryls on the phosphine ligand do not influence the *exo*:*endo* ratio although they do increase the yield.

*Table 2.1 Optimization of the Au(I)-Catalyzed Cyclization of **2.1***



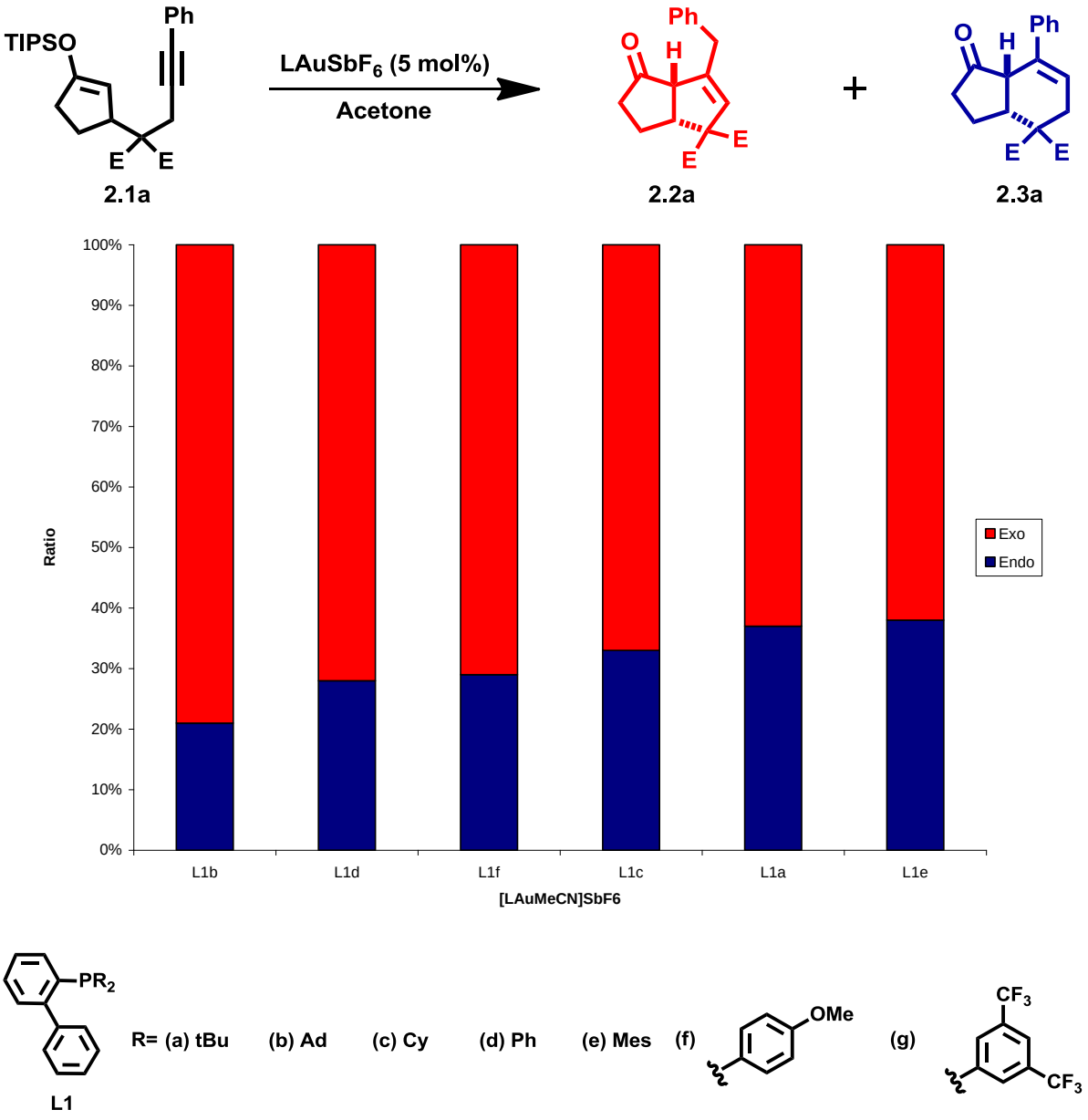
Entry	LAuX	Ratio (2.2a:2.3a)	Yield (%)
1	PPh_3AuSbF_6	88:12	22
2	PPh_3AuBF_4	74:26	39

3	$Et_3PAuSbF_6$	86:14	70
4	$(4\text{-}CF_3C_6H_4)_3AuSbF_6$	77:23	60
5	[tri-(2,4-diterbutylphenyl)phosphiteAu]NTf_2	85:15	46
6	[$\mathbf{L_{1a}}$AuMeCN]SbF_6	64:36	87
7	[$\mathbf{L_{1b}}$AuMeCN]SbF_6	79:21	85
8	[$\mathbf{L_{1c}}$AuMeCN]SbF_6	67:33	60
9	[$\mathbf{L_{1d}}$AuMeCN]SbF_6	72:28	73 (83 brsm)
10	[$\mathbf{L_{1e}}$AuMeCN]SbF_6	63:37	87
11	[$\mathbf{L_{1f}}$Au(RCN]SbF_6^x	71:29	37
12	[$\mathbf{L_{2a}}$AuMeCN]SbF_6	35:65	87
13	[$\mathbf{L_{2c}}$AuMeCN]SbF_6	37:63	89
14	[$\mathbf{L_{3c}}$AuMeCN]SbF_6	38:62	86
15	[$\mathbf{L_{3g}}$AuMeCN]SbF_6	54:46	72
16	[$\mathbf{L_{4c}}$AuMeCN]SbF_6	58:42	84
17	[$\mathbf{L_{4d}}$AuMeCN]SbF_6	62:38	90
18	[$\mathbf{L_5}$AuMeCN]SbF_6	71:29	78
19	[$\mathbf{L_6}$AuMeCN]SbF_6	41:59	75
20	[$\mathbf{L_7}$AuMeCN]SbF_6	82:18	56
21	**[$\mathbf{L_8}$AuMeCN]$\mathbf{SbF_6}$**	**29:71**	**82**
22	[$\mathbf{L_9}$AuMeCN]SbF_6	>95:5	91

Looking at Buchwald-type phosphines such as JohnPhos ($\mathbf{L_{1a}}$) improved the *endo*:*exo* ratio. With the intention of increasing steric bulk, an adamantyl analogue of JohnPhos ($\mathbf{L_{1b}}$) was tested and to our great surprise, the *endo*:*exo* ratio was very low. One could assume that if adamantyls are not bulkier than tert-butyls then, certainly, they would at least offer similar steric bulk. This made us consider that perhaps not only steric factors could influence the *endo*:exo ratio but also the electronic properties of the ligand. With this idea in mind, we investigated $\mathbf{L_1}$ ligands and varied the R groups. From the ratios, we were able to demonstrate (Figure 2.3) that R=adamantyl is in fact the least favorable ligand amongst all the Buchwald-type phosphines. Interestingly, R=mesityl offers similar selectivity to tert-

butyls. In short, adamantyls are the least selective, followed by aryl groups that do not provide steric bulk (**L_{1d}** and **L_{1f}**), followed by cyclohexyls and then mesityls/tert-butyls.

*Figure 2.3 Effect of **L_1** Ligands on the endo:exo Ratio for the cyclization of **2.1a***



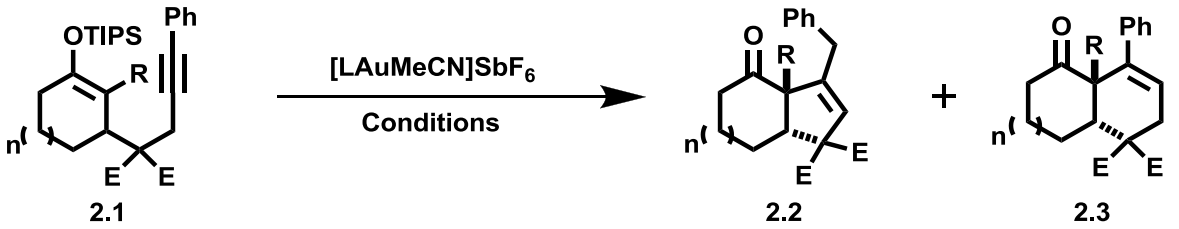
We then investigated other commercially available Buchwald ligands. Xphos (**L_{2c}**) and tBuXPhos (**L_{2a}**) showed the same trend as their **L_1** analogues. At this point, **L_{2a}** was the most selective ligand with a good yield and a ratio of 35:65, favouring the endo product **2.3a**. We

looked at both BrettPhos (**L_{3c}**) and JackiePhos (**L_{3g}**), but those ligands gave inferior ratios when compared to tBuXPhos (**L_{2a}**). DavePhos (**L_{4c}**), **L_{4d}**, as well as RuPhos (**L_5**) gave ratios similar to the **L_1** analogues. TrixiePhos (**L_6**) gave a surprisingly respectable ratio of 41:59 favoring **2.3a**, even though **L_{2a}** was still a superior ligand. **L_7** gave a low yield and a ratio comparable to the non-Buchwald-type phosphines. Finally, we had our best hit to date using Me-tBuXPhos (**L_8**) with a ratio of 29:71 favoring *endo* product **2.3a**, altogether with a good yield of 82%. We also looked at IPr as an N-heterocyclic carbene (NHC) ligand and were pleased to discover that this very σ-donating ligand is very selective for the *5-exo-dig* cyclization pathway, furnishing **2.2a** in exclusive selectivity. With these results in hand, we we explored other substrates aimed at extending the scope of this reaction.

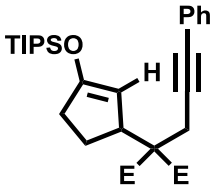
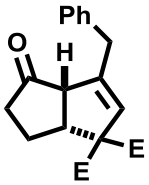
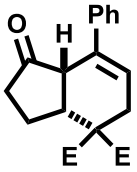
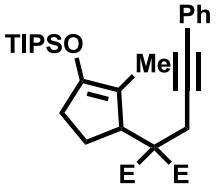
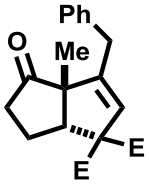
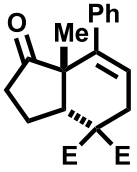
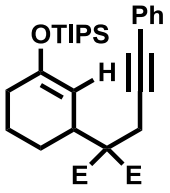
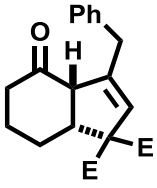
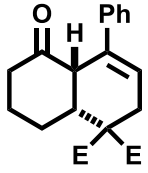
Cyclization of Aryl Substituted Substrates

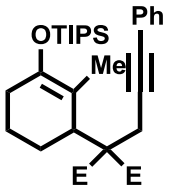
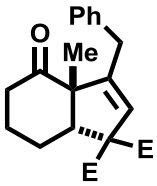
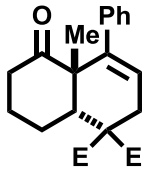
We began our investigation using phenyl substituted alkynes **2.1** and varied the ring size as well as the **R** substituents (Table 2.2). Cyclization of **2.1a** using *exo*-selective conditions A provided **2.2a** in 95% yield as the sole isomer (Table 2.2, *entry 1*). When the cyclization of **2.2a** was performed using the *endo*-selective conditions B, a ratio of 32:68 favoring **2.3a** was obtained (*entry 2*). Interestingly, an increase of the *6-endo-dig* cyclized product was obtained when R=Me (*entry 4*). Unfortunately, **2.1b** gave a poor ratio (~1:1) using *exo*-conditions A (*entry 3*). The cyclization of 6-membered ring silyl enol ether **2.1c** using conditions A gave **2.2c** and **2.3c** in 86% yield and in a ratio of 40:60 (*entry 5*). However, using conditions B and C afforded **2.3c** as the major product in excellent ratios (*entries 6-7*). While conditions B gave **2.3c** as the sole product, the yield was diminished (*entry 6*), but simply using **L_{1a}** as the ligand instead of **L_8** (*entry 7*) allowed for an increased yield and only a slight erosion of selectivity. The *5*-exo-selective conditions A gave **2.2d** and **2.3d** in 87% yield with a ratio of 86:14. On the other hand, conditions B furnished **2.3d** as the major product in 91% yield.

Table 2.2 Cyclization of Phenyl Substituted Alkynes ***2.1***



2.1 2.2 2.3

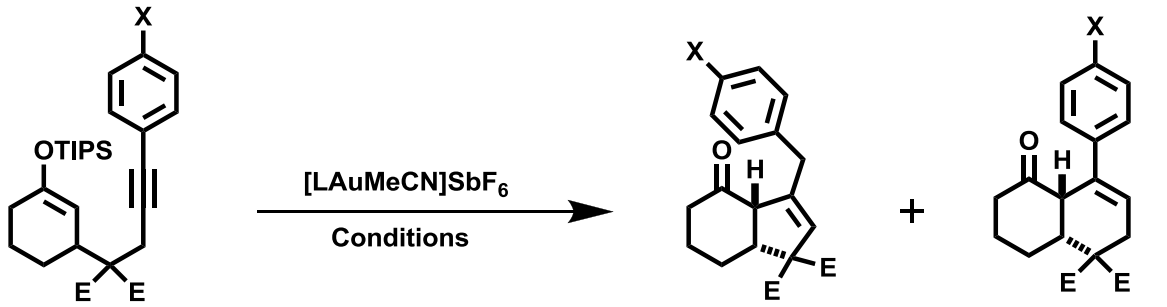
Entry	Substrate	Conditions[a]	Products	Yield (2.2 : 2.3)[b]
1		A		95% (95:5)
2	**2.1a**	B	**2.2a**  **2.3a**	82% (32:68)
3		A		88% (48:52)
4	**2.1b**	B	**2.2b**  **2.3c**	86% (13:87)
5		A		86% (40:60)
6	 **2.1c**	B	 **2.2c**  **2.3c**	60% (<5:95)
7		C		88% (10:90)

8		A			87% (86:14)
9	**2.1d**	B	**2.2d**	**2.3d**	91% (29:71)

[a] *Conditions A:* To a solution of **2.1 (**100mg) in acetone (2 mL), is added [$\mathbf{L_9}$AuMeCN][SbF_6] 5 mol% and the reaction is stirred O/N. *Conditions B:* To a solution of **2.1 (**100mg) in acetone (2 mL), is added [$\mathbf{L_8}$AuMeCN][SbF_6] 5 mol% and the reaction is stirred O/N. *Conditions C:* To a solution of **2.1 (**100mg) in acetone (2 mL), is added [$\mathbf{L_{1a}}$AuMeCN][SbF_6] 5 mol% and the reaction is stirred O/N.
[b] Isolated yields. Ratio of products determined by crude ^{1}H NMR.

One of the key concepts associated with *5-exo-dig vs 6-endo-dig* discussed previously, is the polarization of the alkyne.[8] We decided to investigate if electronic bias would have a big impact on our systems with respect to *5-exo*/*6-endo* selectivity. We explored the cyclization of para-substitued aryl groups on alkyne substrates **2.1** using both *exo*-selective conditions A and *endo*-selective conditions B (Table 2.3). When methoxy substituted substrate **2.1e** was subjected to conditions A, a poor ratio of 24:76 disfavoring *5-exo-dig* product **2.2e** was obtained (*entry 1*). On the other hand, **2.3e** could easily be furnished from **2.1e** using conditions B in exclusive selectivity. Replacing group **X** for a methyl substituent still made the *5-exo-dig* cyclization of **2.1f** difficult, furnishing **2.2f** as the minor product in a 46:54 ratio (*entry 2*). Cyclization of **2.1f** using conditions B furnished **2.3f** in 78% yield and exquisite selectivity. When a slightly electron-withdrawing group (EWG) such as a methyl ketone was used, we were able to obtain a 84:16 ratio favoring **2.2g** using conditions A and a 29:71 ratio favoring **2.3g** using conditions B (*entry 4*). When the cyclization of CF_3, cyano and nitro substituted substrates **2.1h-j** was performed using conditions A, **2.2h-j** were all obtained in good selectivity and ratio (*entries 5-7*). However, progressive erosion of 6-*endo-dig* selectivity was observed for **2.1h-j** when these were submitted to conditions B. Compounds **2.3h-j** were obtained as the major products, albeit in low yields and poor *exo*:*endo* ratios (*entries 5-7*).

*Table 2.3 Effect of Polarization on Au(I)-catalyzed cyclization of Aryl substituted alkynes **2.1***



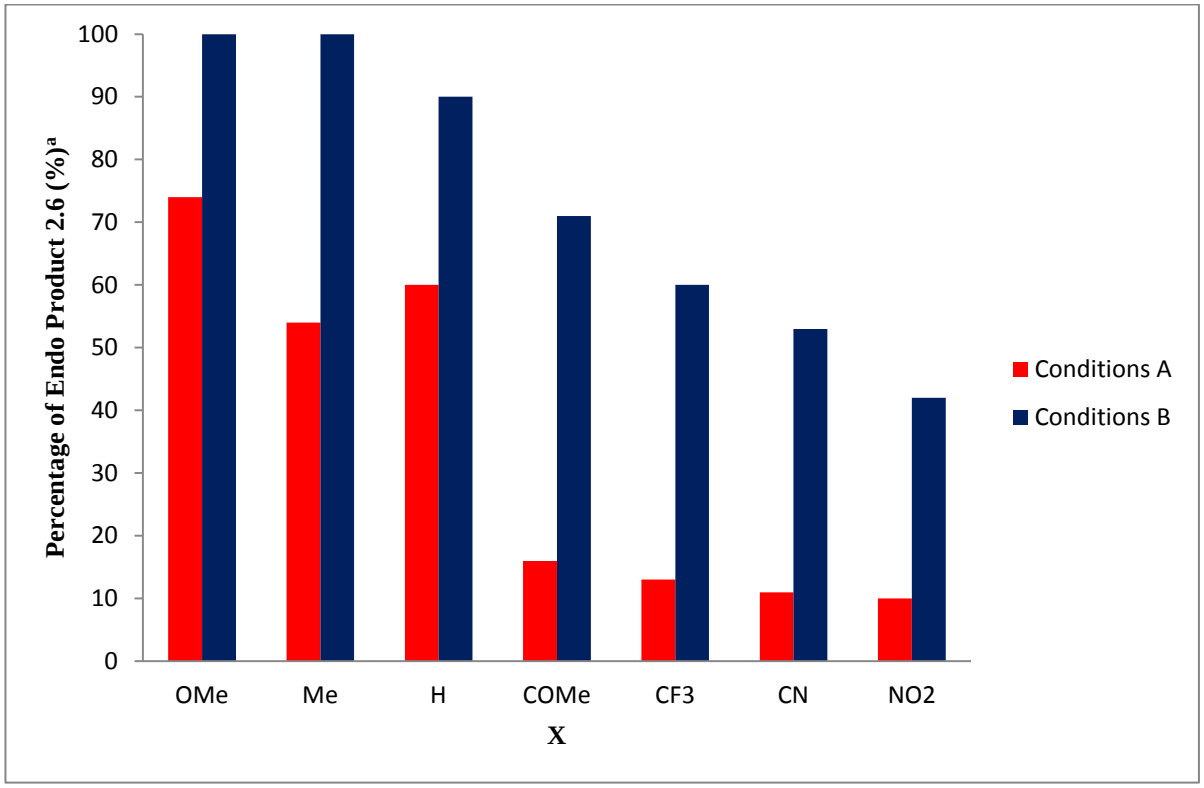
2.1 **2.2** **2.3**

			Conditions Yield (2.2 : 2.3)[a]	
Entry	**Substrate**	**X**	**A**	**B**
1	**2.1e**	OMe	90% (26:74)	72% (<5:95)
2	**2.1f**	Me	93% (46:54)	78% (<5:95)
3	**2.1c**	H	86% (40:60)	90% (10:90)
4	**2.1g**	COMe	91% (84:16)	75% (29:71)
5	**2.1h**	CF_3	89% (87:13)	75% (40:60)
6	**2.1i**	CN	88% (89:11)	67% (47:53)
7	**2.1j**	NO_2	80% (90:10)	65% (58:42)

[a] Isolated yields. Ratio of products determined by crude ^{1}H NMR.
[b] *Conditions A:* To a solution of **2.1 (**100mg) in acetone (2 mL), is added [**L$_9$**AuMeCN][SbF_6] 5 mol% and the reaction is stirred O/N.
[c] *Conditions B:* To a solution of **2.1 (**100mg) in acetone (2 mL), is added [**L$_8$**AuMeCN][SbF_6] 5 mol% at -10°C and the reaction let to warm up to r.t. O/N.

Our investigation on alkyne polarization led us to establish a trend between various **X** substitutions on aryl alkynes **2.1** (Figure 2.4). As expected, electron donating groups (EDGs) favors the *6-endo-dig* cyclization while EWGs generally provide greater selectivity for the 5-exo-dig pathway, regardless of the reaction conditions used. Conditions A, which make use of NHC ligand **L$_9$**, show greater dependence on alkyne polarization than conditions B which utilize Buchwald phosphine ligand **L$_8$**. While exclusive selectivity could not be achieved with some susbstrates, one can see that even in the case of nitro substituted **2.1j**, a substantial amount of *6-endo* product **2.3j** was obtained.

Figure 2.4 Percentage of Endo Product Generated Following the Cyclization of Substrates ***2.4c,e-j***

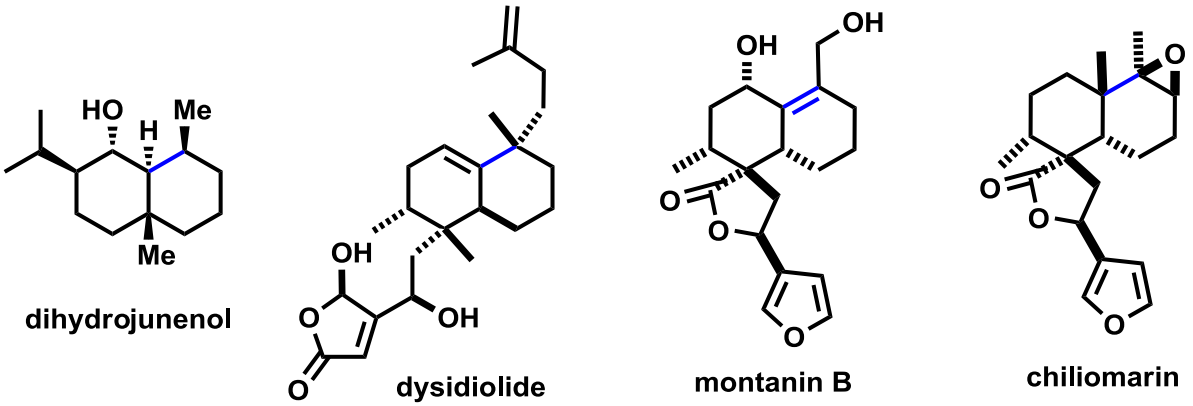


[a] The percentage of the *endo* product **2.6** was determined directly from the ratio of **2.5** and **2.6** of the crude ^{1}H NMR mixture.
[b] *Conditions A:* To a solution of **2.1 (**100mg) in acetone (2 mL), is added [$\mathbf{L_9}$AuMeCN][SbF_6] 5 mol% and the reaction is stirred O/N.
[c] *Conditions B:* To a solution of **2.1 (**100mg) in acetone (2 mL), is added [$\mathbf{L_8}$AuMeCN][SbF_6] 5 mol% at -10°C and the reaction let to warm up to r.t. O/N.

Cyclization of Methyl Substituted Substrates

Next, we investigated the cyclization of methyl substituted alkynes (Table 2.4). These are substrates known to cyclize only in a *5-exo-dig* fashion. One can easily recognize that the cyclization via a *6-endo-dig* pathway could potentially provide access to numerous diterpenoid natural products (Figure 2.5).

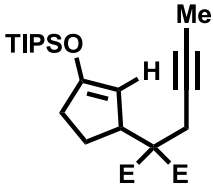
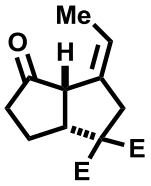
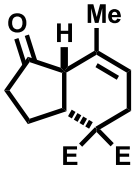
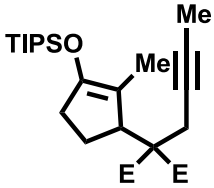
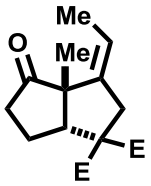
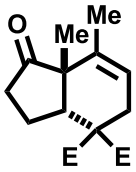
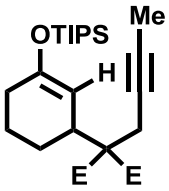
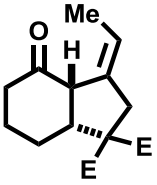
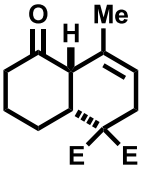
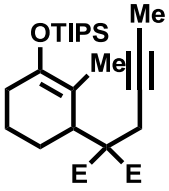
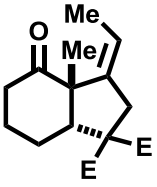
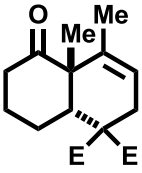
Figure 2.5 Natural Products Potentially Accessible via Selective 6-endo-dig Cyclizations (Newly-formed Bond Illustrated in Blue)



Cyclization of **2.4a** using conditions A gave exclusive selectivity for the 5-exo product **2.5a** in excellent yield (Table 2.4, *entry 1)*. A 45:55 ratio favouring **2.6a** was obtained using conditions B2 (*entry 2*). In the case of **2.4b**, the methyl substituent enabled the synthesis of **2.5b** in excellent selectivity using conditions A (*entry 3*). On the other hand, conditions B3 using dry DCM enabled the formation of **2.6b** in a ratio of 7:93 ratio (*entry 4*). The cyclization of **2.4c** (conditions A) afforded **2.5c** with good selectivity (*entry 5*). However, the use of conditions B1 provided **2.6c** in a modest ratio of 43:57 (*entry 6*). In an attempt to improve this ratio, dry conditions B3 were used, but it appears that the dry conditions generated an appreciable 18% of allene **2.7c** (*entry 7*). Cyclization of **2.4d** using conditions A gave exclusive formation of **2.5d**, and when conditions B1 were used, **2.6d** was obtained as the minor product in an 87:13 ratio (*entries 8-9*). Again, the use of conditions B3 generated allene **2.7d** as the major compound in 58% yield (*entry 10*). One can propose that allenes **2.7c** and **2.7d** are the result of a [1,5]-hydride shift as depicted in (Scheme 2.1) In the absence of water, the protodeauration and the carboxonium hydrolysis cannot occur. Therefore, a competitive [1,5]-hydride shift takes place forming the allene **2.7** and regenerating the Au(I) catalyst.

*Table 2.4 Cyclization of Methyl Substituted Alkynes **2.4***

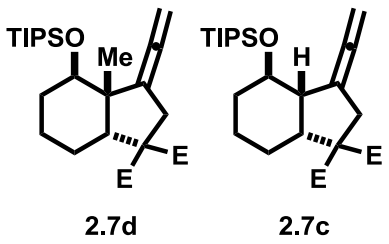
2.4 **2.5** **2.6**

Entry	Substrate	Conditions[a]	Product	Yield (2.5 : 2.6)[b]
1		A		86% (>95:5)
2	**2.4a**	B2	**2.5a**  **2.6a**	77% (45:55)
3		A		94% (92:8)
4	**2.4b**	B3	**2.5b**  **2.6b**	83% (7:93)
5		A		88% (83:17)
6		B1		79% (43:57)
7	**2.4c**	B3	**2.5c**  **2.6c**	60% (23:77)+ 18% allene[c]
8		A		86% (>95:5)
9		B1		82% (87:13)
10	**2.4d**	B3	**2.5d**  **2.6d**	28% (62:38) + 58% allene[c]

[a] *Conditions A:* To a solution of **2.1 (**100mg) in acetone (2 mL), is added [**L$_9$**AuMeCN][SbF_6] 5 mol% and the reaction is stirred O/N. *Conditions B1:* To a solution of **2.1 (**100mg) in acetone (2 mL), is added [**L$_8$**AuMeCN][SbF_6] 5 mol% at -10°C and the reaction let to warm up to r.t. O/N. *Conditions B2:* To a solution of **2.1 (**100mg) in DCM/acetone (2 mL/ 25 μL), is added [**L$_8$**AuMeCN][SbF_6] 5 mol% at -10°C and the reaction let to warm up to r.t. O/N. *Conditions B3:* To a solution of **2.1 (**100mg) in DCM (2 mL), is added [**L$_8$**AuMeCN][SbF_6] 5 mol% at -10°C and the reaction let to warm up to r.t. O/N.

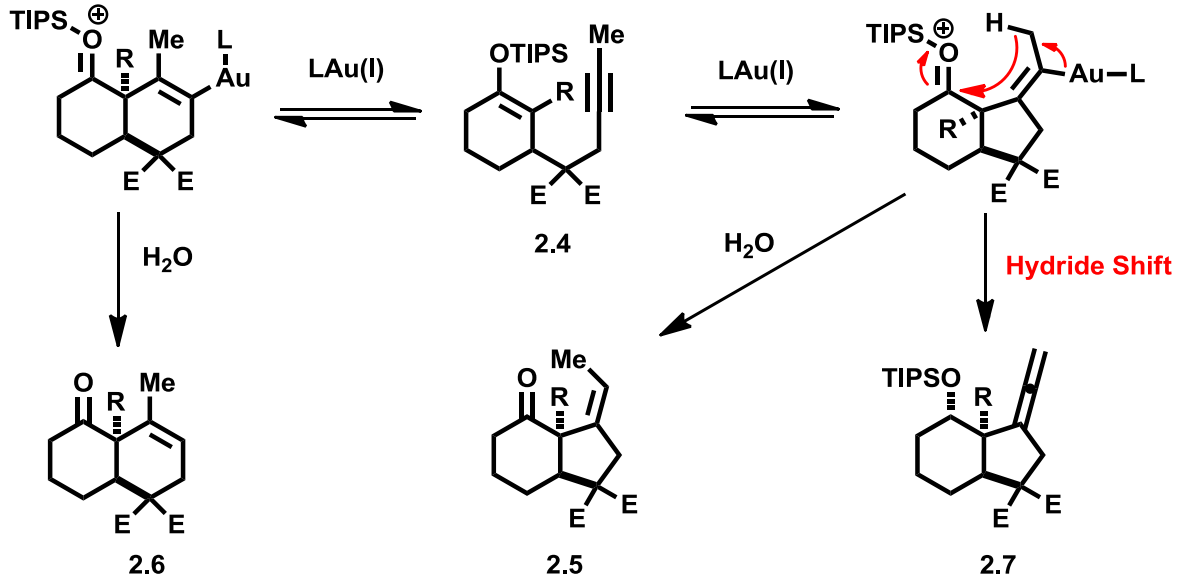
[b] Isolated yields. Ratio of products determined by crude ^{1}H NMR.

[c] Isolated from the reaction mixture in 18% yield for **2.7c** and 58% yield for **2.7d**.



2.7d 2.7c

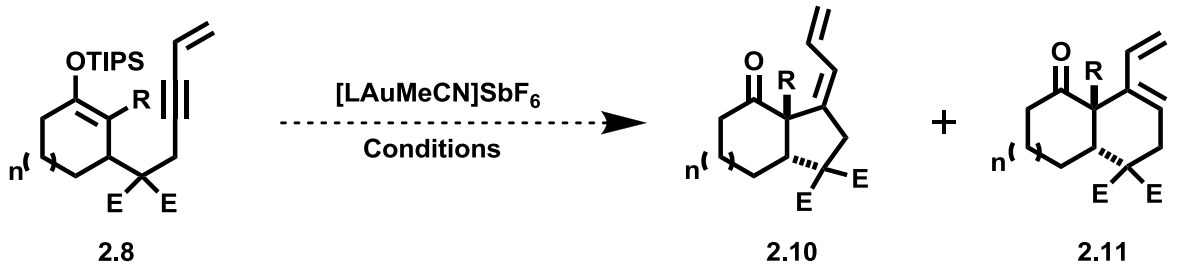
Scheme 2.1 Mechanism for the formation of allenes ***2.7c-d***



Cyclization of Vinyl Substituted Substrates

With the possibility of selective *6-endo-dig* cyclization of silyl enol ethers within reach, this opened up new possibilities in terms of potential syntheses. We wondered whether this reaction would be tolerant of enynes (Scheme 2.2) and whether we could achieve good selectivity for the *6-endo-dig* pathway with these types of substrates.

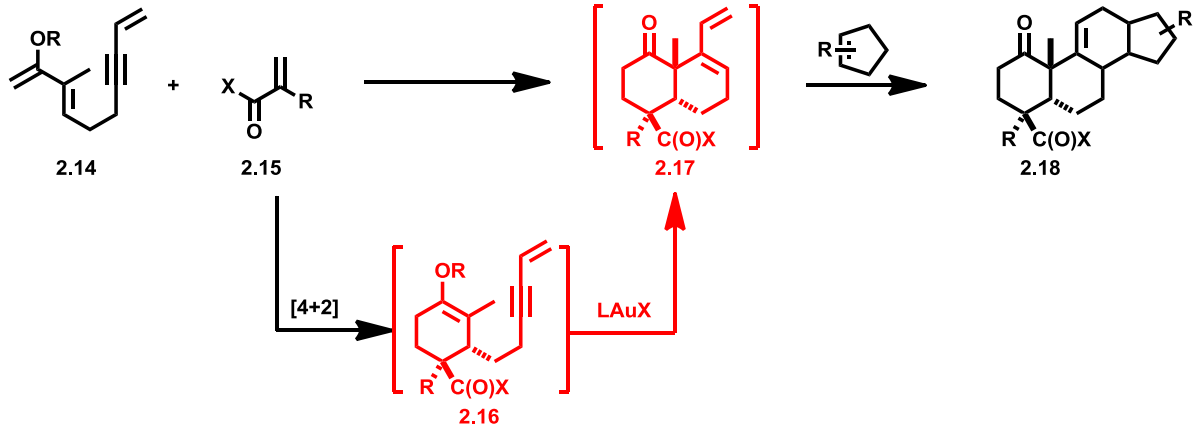
Scheme 2.2 Proposed Au(I)-Catalyzed Cyclization of Enynes



2.8 **2.10** **2.11**

If it is the case, this could enable quick syntheses of diterpenes and steroids via the proposed one-pot synthetic pathway shown below (Figure 2.6). Complex steroids as well as related diterpenes could be synthesized from a Diels-Alder reaction between diene **2.14** and dienophile **2.15** to furnish the enol ether intermediate **2.16**. The latter is poised to undergo a selective *6-endo-dig* Au(I)-catalyzed cyclization to provide diene **2.17**. The latter, in turn, would undergo a second intermolecular Diels-Alder reaction to provide polycyclic compounds **2.18**. Of course, the initial question was: can we perform selectively and in good yield the step shown in red?

Figure 2.6 Proposed One-pot Synthetic Procedure for the Synthesis of Steroids and Terpenes

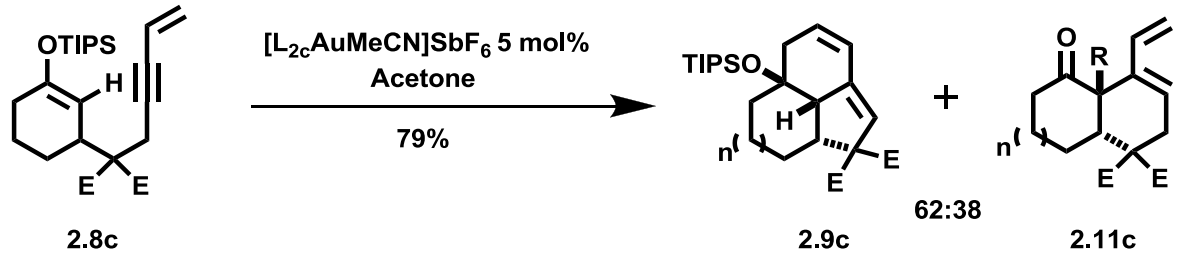


2.14 **2.15** **2.17** **2.18** **2.16**

When the cyclization of **2.8c** using various Au(I) catalysts was attempted in acetone, we obtained a mixture of two products: the minor one (**2.11c**) was the result of a *6-endo-dig* cyclization while the major product (**2.9c**) was the result of a *5-exo-dig* cyclization followed by a Prins cyclization. This formal [4+2] reaction catalyzed by Au(I) had previously been

reported by Echavarren and coworkers,[59] but whether our reaction is a stepwise process or a concerted one, remains uncertain.

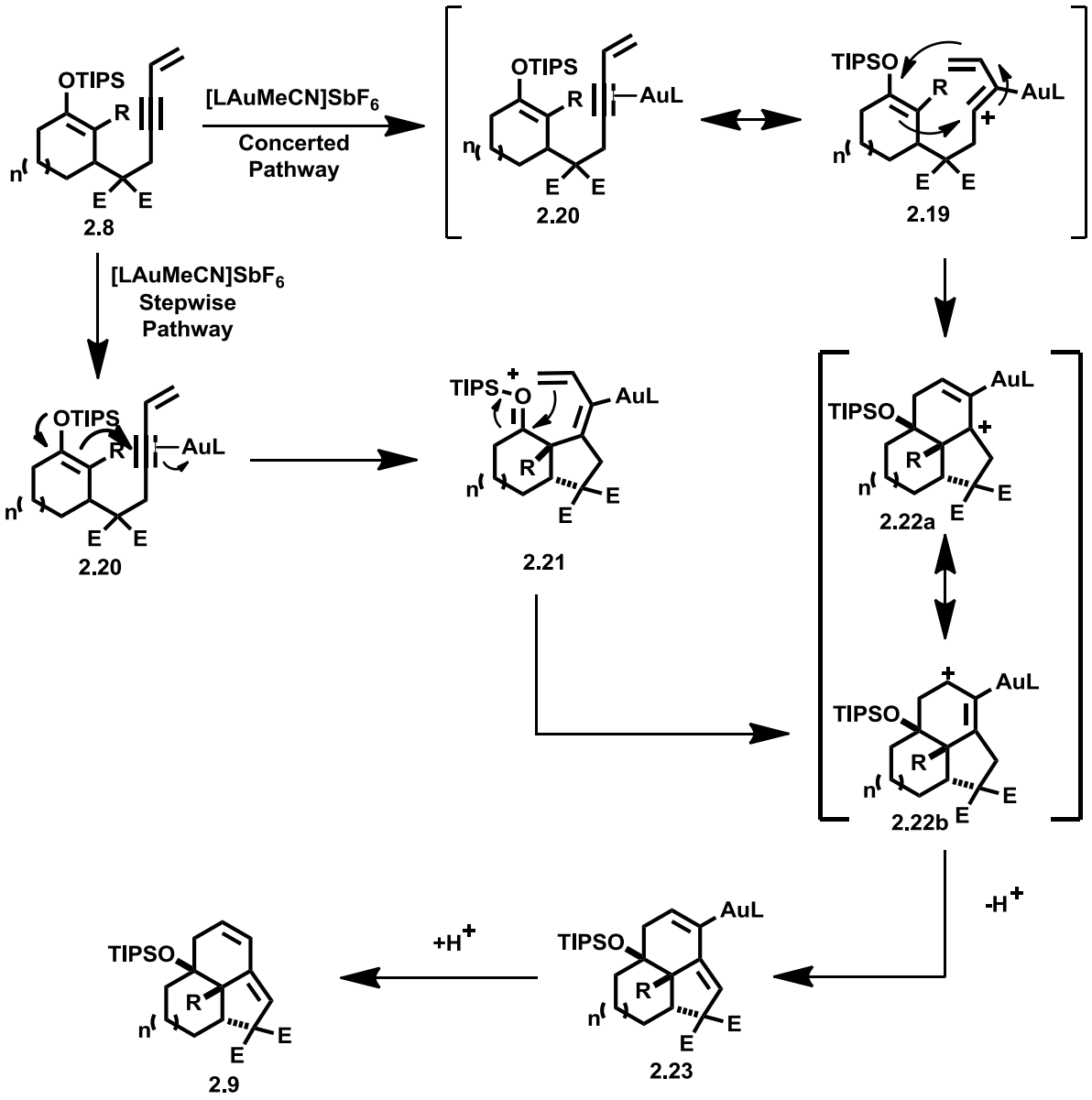
*Scheme 2.3 Initial Cyclization Attempt of **2.8c***



2.8c **2.9c** **2.11c**

We propose that upon complexation of the Au(I) species with the alkyne, two possibilities arise (Scheme 2.4). The first is a concerted mechanism in which the alkyne binds to the Au(I) to form a vinyl gold(I) species with a formal positive charge. This intermediate can then undergo a [4+2] cycloaddition to generate tertiary carbocation **2.22a**. The other alternative is that Au(I) coordinates to the alkyne, following which there is a nucleophilic addition of the silyl enol ether on the latter to generate carboxonium **2.21**. This carboxonium can then undergo a Prins cyclization to generate secondary carbocation **2.22b**, which in turn, through resonance, generates the more stable tertiary carbocation **2.22a**. A proton abstraction will follow to generate vinyl Au(I) species **2.23** and the final proto-deauration will furnish the final product **2.24**.

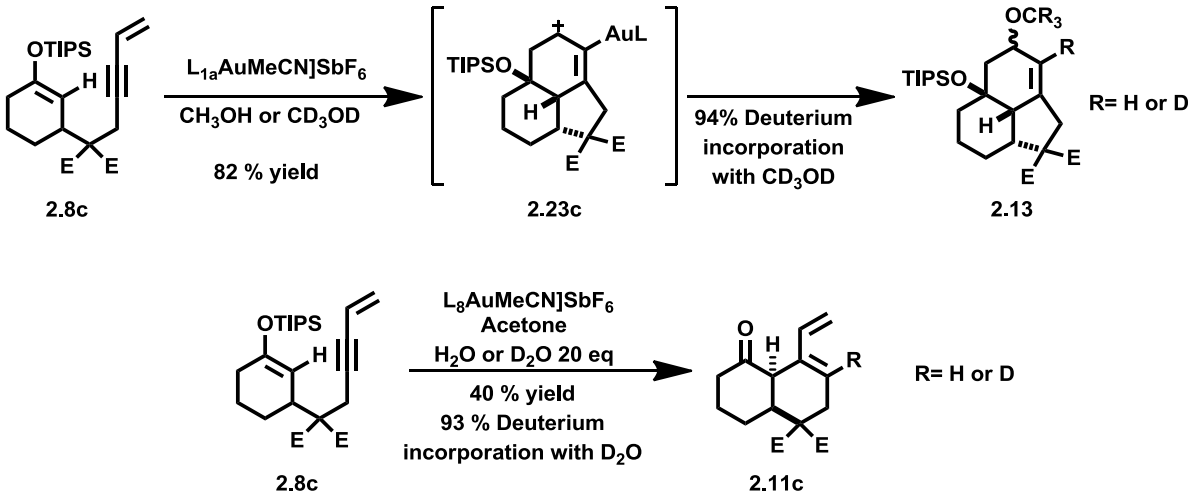
Scheme 2.4 Proposed Mechanism for the Formation of Tricyclic Compounds



In order to gain further insight into the reaction mechanism, the reaction was performed in methanol-d_4 and in acetone containing D_2O (Scheme 2.5). These experiments showed that when reactions are run in methanol-d_4 (CD_3OD), there is deuterium incorporation at the positions where the proto-deauration is suspected to occur (Scheme 2.5). Interestingly, when the same reactions are run in acetone-d_6 without any added water or deuterated water, very

little deuteration occurs. This suggests that the α-protons of acetone-d_6 are not sufficiently acidic to affect proto-deauration.

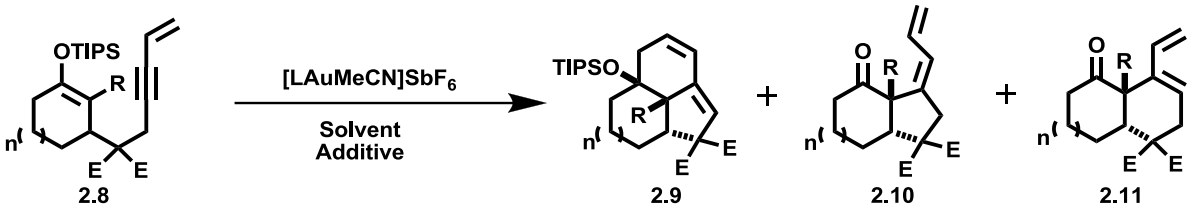
*Scheme 2.5 Trapping and Deuteration Experiments for the Cyclization of Enyne **2.8c***

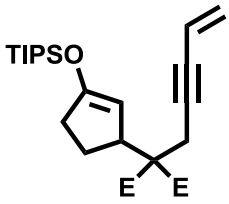
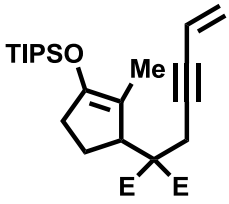
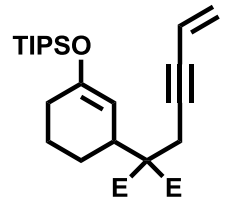
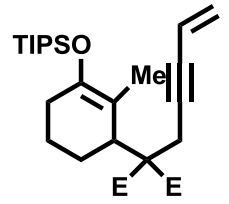


If sufficient water is present in the reaction mixture, one may reduce or completely eliminate the Prins cyclization (Table 2.5, *entry 14*). Furthermore, in the case of five-membered ring substrates such as **2.8a-b**, the Prins cyclization is not as efficient and the result is a mixture of the *5-exo-dig* product **2.10a-b** and its Prins cyclization product **2.9a-b**. To achieve exclusive Prins cyclization, nitromethane is the best option as the reaction solvent (*entry 9*).

All cyclizations of **2.8a-d** were attempted with at least four different Au(I)-catalysts (**L_9**, **L_{1a}**, **L_{2c}**, **L_8**) and as observed (*entries 1,5,10 & 15*) **L_9** is always the most selective for *5-exo-dig* cyclizations and generally furnishes the exo product in exclusive selectivity. **L_{1a}**, **L_{2c}** and **L_8** have an increasing favorability for the *6-endo* cyclization. However, **2.11** was never obtained as the major product in any of the cyclizations of unsubstituted enynes **2.8a-d**.

*Table 2.5 Cyclization of Vinyl Substituted Alkynes **2**.8a-d*



Entry	Substrate	L	Solvent	Additive	Ratio			Yield(%)[a]
					2.9	2.10	2.11	
1		L_9	MeOH	-	0	100	0	88
2		L_{1a}	Acetone	-	36	64	0	51
3		L_{2c}	Acetone	-	12	88	0	81
4		L_8	Acetone	-	86	0	14	35
5		L_9	MeOH	-	0	100	0	94
6		L_{1a}	MeOH	-	0	100	0	67
7		L_{2c}	MeOH	-	4	91	5	65
8		L_8	Acetone	-	62	0	38	69
9		L_9	NO_2Me	-	100	0	0	85
10		L_9	Acetone	-	100	0	0	83
11		L_{1a}	Acetone	-	66	0	34	89
12		L_{2c}	Acetone	-	62	0	38	79
13		L_8	MeOH	-	0	58	42	98
14		L_{1a}	Acetone	H_2O	0	66	34	79
15		L_9	Acetone	-	100	0	0	65
16		L_{1a}	Acetone	-	100	0	0	83
17		L_{2c}	MeOH	-	66	34	0	67
18		L_8	Acetone	-	48	23	29	68

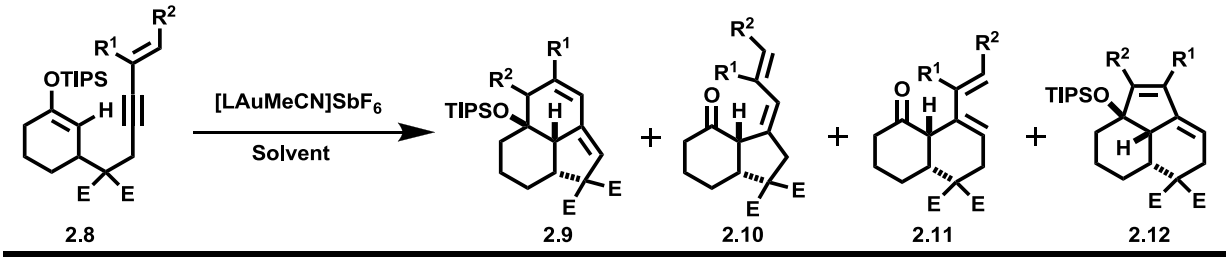
2.8a 2.8b 2.8c 2.8d

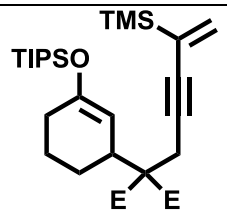
[a] Isolated yields. Ratio of products determined by crude ^{1}H NMR.

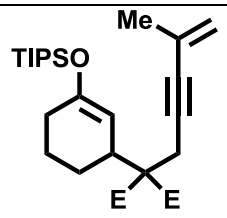
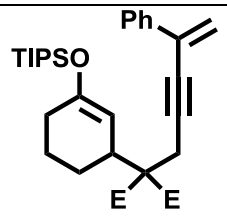
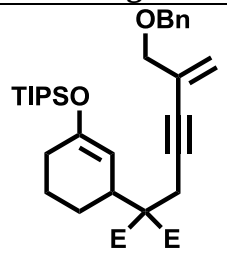
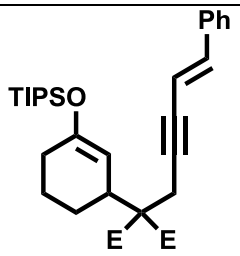
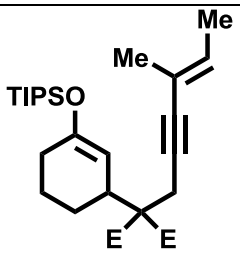
Although we had been unable to obtain the *6-endo-dig* product as the major product for enynes **2.8a-d**, we decided to explore the scope of these reactions further by adding substitution on the vinyl group of our enynes.

We first looked at varying R^1 substitution on **2.8** and discovered that when a TMS group is present (Table 2.6, *entry 1*), **2.11e** is obtained in 74% yield with a modest ratio of 38:62. In this particular case, only $\mathbf{L_{1a}}$ proved to be an adequate ligand because any other would give complex mixtures of products including the loss of the TMS group to furnish **2.11c** as well as hydrolyzed starting material and other unknown products. On the other hand, when R^1=Me, compound **2.11f** is obtained as the major product (*entry 5*). However, it appears that the more electron donating nature of the methyl group allows for a *6-endo-dig*/Prins cyclization to furnish **2.12f** in small quantities. In the case of R^1=Ph, **2.11g** is obtained as the major product in 70% yield and in a ratio of 15:85 (*entry 6*). When R^1=CH_2OBn, exquisite formation of **2.11h** is obtained using XPhos ($\mathbf{L_{2c}}$) as the ligand, albeit in 48% yield (*entry 7*). It is noteworthy that in the case of the cyclization of enyne **2.8h**, other conditions and ligands gave complex mixtures of products. A phenyl substituent at the R^2 position furnished **2.11i** in 84% yield with a ratio of 13:87 (*entry 11*). Interestingly, if IPr ($\mathbf{L_9}$) is used as the ligand, the selectivity is completely reversed and a 97:3 selectivity favouring **2.10i** is achieved. Not surprisingly, enyne **2.8j** with substitution at both R^1 and R^2 gave exclusive selectivity towards **2.11j** altogether with an 86% isolated yield.

Table 2.6 Cyclization of Substituted Enynes ***2*****.8 d-k**



Entry	Substrate	L	Solvent	Ratio				Yield(%)
				2.9	2.10	2.11	2.12	
1	 **2.8e**	$\mathbf{L_{1a}}$	Acetone	38	0	62	0	74

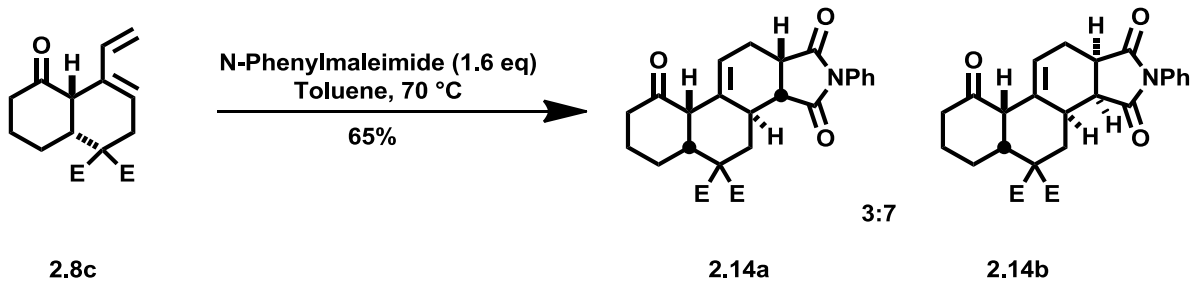
2	 **2.8f**	$\mathbf{L_9}$	MeOH	33	0	51	16	61
3		$\mathbf{L_{1a}}$	MeOH	68	0	68	14	77
4		$\mathbf{L_{2c}}$	MeOH	17	0	76	7	86
5		$\mathbf{L_8}$	MeOH	19	0	70	11	63
6	 **2.8g**	$\mathbf{L_8}$	Acetone	15	0	85	0	71
7	 **2.8h**	$\mathbf{L_{2c}}$	Acetone	0	0	100	0	48
8	 **2.8i**	$\mathbf{L_9}$	Acetone	0	97	3	0	97
9		$\mathbf{L_{1a}}$	Acetone	0	46	54	0	74
10		$\mathbf{L_{2c}}$	Acetone	0	28	72	0	82
11		$\mathbf{L_8}$	Acetone	0	13	87	0	84
12	 **2.8j**	$\mathbf{L_8}$	Acetone	0	0	100	0*	86

[a] Isolated yields. Ratio of products determined by crude ^{1}H NMR.

As seen in Table 2.6, we were able to obtain dienes such as **2.11** from enynes **2.8**. Although the selectivity is poor for vinyl substituted alkynes **2.8a-d**, cyclizations of substituted enynes **2.8e-j** provided the desired *6-endo-dig* product in high selectivity. As a proof of concept,

diene **2.8c** was converted to diterpene **14** using N-phenylmaleimide under thermal conditions in 65% yield.

*Scheme 2.6 Diels-Alder reaction of **2.8c** with N-Phenylmaleimide*

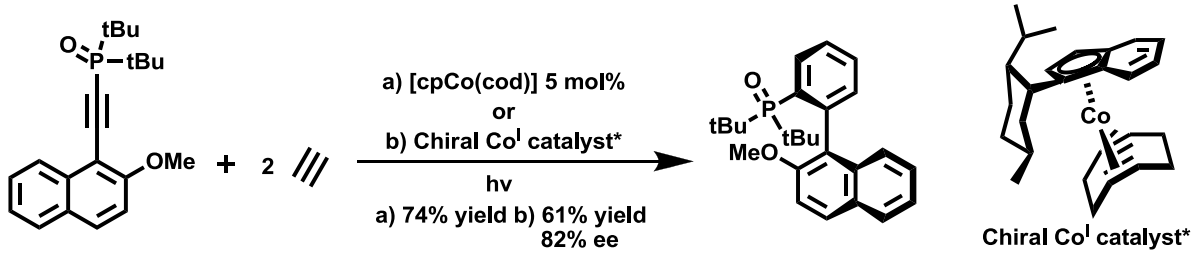


Ligand Synthesis

Two main types of ligands are used in Au(I)-catalysis: phosphines and N-heterocyclic carbenes (NHC's). Most of the ligands which were not commercially available were synthesized according to literature methods and herein, we will discuss a few of these and their relative usefulness.

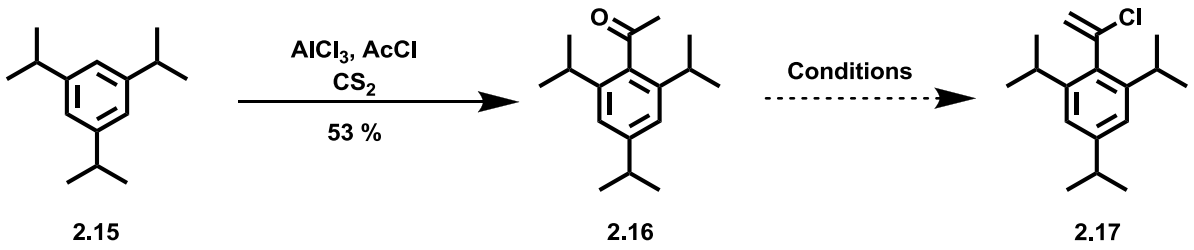
One of the most original methods investigated for the generation of new Buchwald-type phosphines was a method developed by Heller and coworkers and utilizes a cobalt(I)-catalyzed trimerization of alkynes.[60] This method (Scheme 2.7) seemed practical for two reasons: firstly, the trimerization may be done with achiral or chiral catalysts and secondly, it is tolerant of a very broad range of functionality.

Scheme 2.7 Representative Example of Heller's Co(I)-Catalyzed Cross-Cyclotrimerization



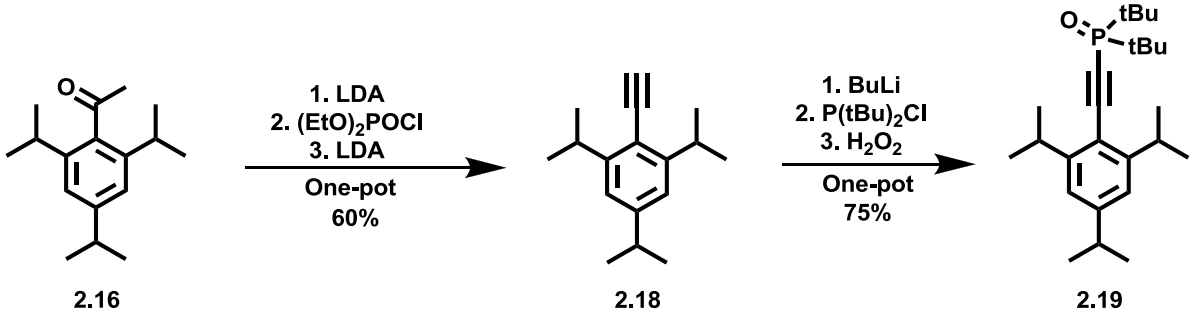
We proceeded to synthesize the appropriate Co(I) catalyst, [cpCo(cod)], as it is not commercially available.[61] With this catalyst in hand, we synthesized **2.16** (Scheme 2.8) via a Friedel-Crafts reaction from commercially available **2.15**. Several attempts at converting acetophenone **2.16** to the corresponding vinyl chloride **2.17** by the use of PCl_5 and PCl_3 were unsuccessful.

*Scheme 2.8 Friedel-Crafts acylation and attempts at the formation of vinyl chloride **2.17***



We turned our attention to a one-pot generation of a phosphonate ester followed by an elimination to generate aryl-acetylene **2.18**. A one-pot deprotonation of **2.18**, addition of a phosphine chloride followed by oxidation of the phosphine afforded phosphine oxide **2.19** (Scheme 2.9).

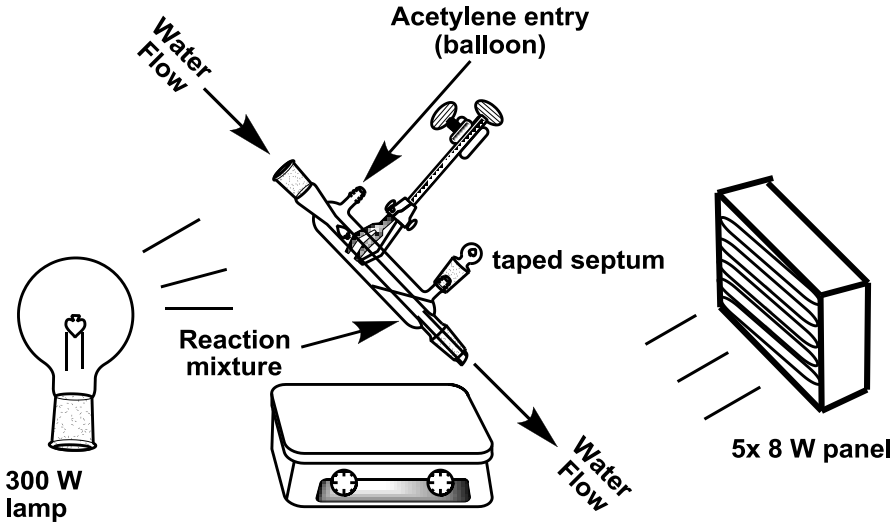
*Scheme 2.9 Conversion of acetophenone **2.16** to phosphine oxide **2.19** via arylacetylene **2.18***



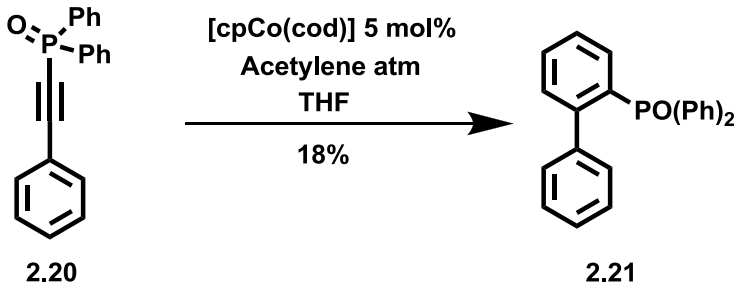
Before any cross-trimerization attempts were performed on phosphine oxide **2.19**, we tested the trimerization reaction on model **2.20**, which was synthesized from phenylacetylene using the same method depicted in Scheme 2.9 in 92% yield. We encountered several problems with the manipulations required in these procedures. We did not have the two 400 Watt 420 nm wavelength lamps and the proper set-up required. Our set-up was comprised of a lighting panel containing five 8 Watt 420 nm wavelength lamps and a 300 Watt regular light bulb. The reactions are supposed to be run at room temperature but this was also an issue because the heat generated by our 300 Watt lamp was causing the solvent to reflux. An ingenious set-up (Figure 2.7) was improvised, utilizing a glass reflux condenser (where the water flow usually is located) as the reaction vessel. This allowed for a cold water flow to go through the inside of the condenser (where the reflux usually occurs) in order to cool the reaction

mixture as the reaction proceeds under intense light. Strictly air-free and water-free conditions had to be used. Only under these strict reaction conditions and set-up would the conversion of **2.20** to **2.21** occur (Scheme 2.10), albeit in low yield. The low yield could surely have been improved by increasing the catalyst loading but since this was a probe to test the Co(I)-catalyzed trimerization, we decided to see if it would work, as reported, with 3-hexyne instead of acetylene. When the trimerization of **2.19** with 3-hexyne was attempted (Scheme 2.11), only starting material was recovered. After the realization that these cyclizations were temperamental and required a lot of optimization, we decided to discard this route.

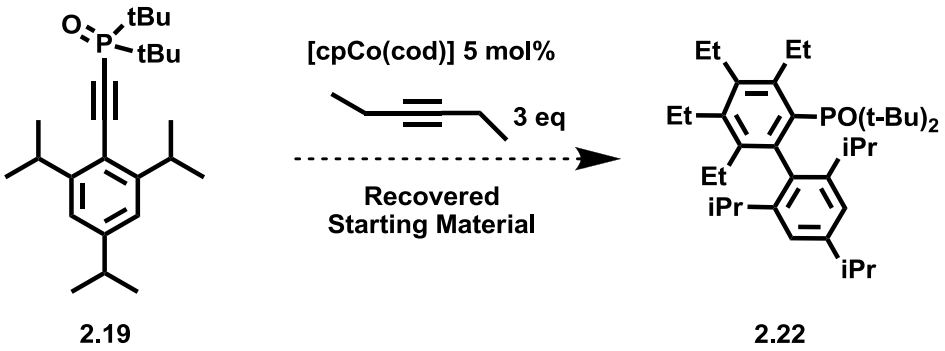
Figure 2.7 Set-up for Cross-trimerization reactions



*Scheme 2.10 Cross-trimerization of phosphine oxide **2.20** with acetylene*



*Scheme 2.11 Cross-trimerization attempt of **2.19** with 3-hexyne*



In order to develop bulkier ligands, another method developed by the Heller group seemed to be ideal for this purpose. With **2.20** already on hand, we performed a Diels-Alder reaction with tetraphenylcyclopentadienone, which generated phosphine oxide **2.23** (Scheme 2.12). This phosphine oxide was then reduced to generate phosphine $\mathbf{L_7}$. From this phosphine ligand, we were able to make the $\mathbf{L_7}$AuCl complex following this and an x-ray structure was obtained (Figure 2.8). A second Diels-Alder reaction was attempted using **2.19** as a substrate but no product was isolated. This failure was not surprising as Heller and coworkers stated that these reactions only work with bis(aryl)-phosphine oxides. The synthesis of **2.26**-**2.28** have yet to be synthesized, but it should be noted that this would be an ideal way of making Buchwald type ligands with aryl substituents on the phosphorous and a highly functionalized biaryl (Scheme 2.14).

Scheme 2.12 Synthesis of Phosphine $\boldsymbol{L_7}$

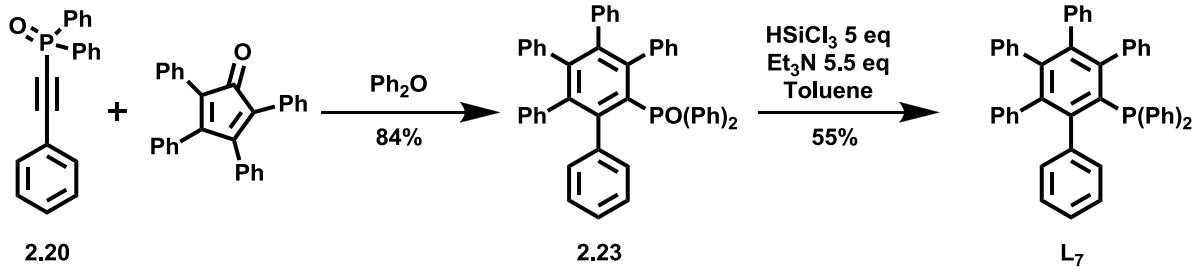
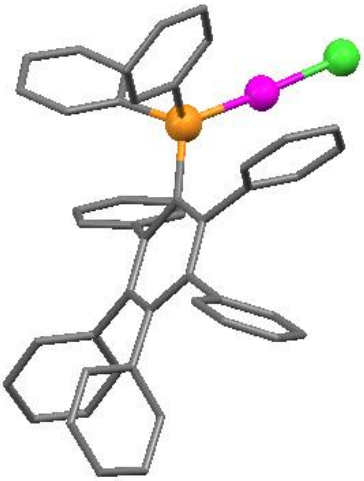
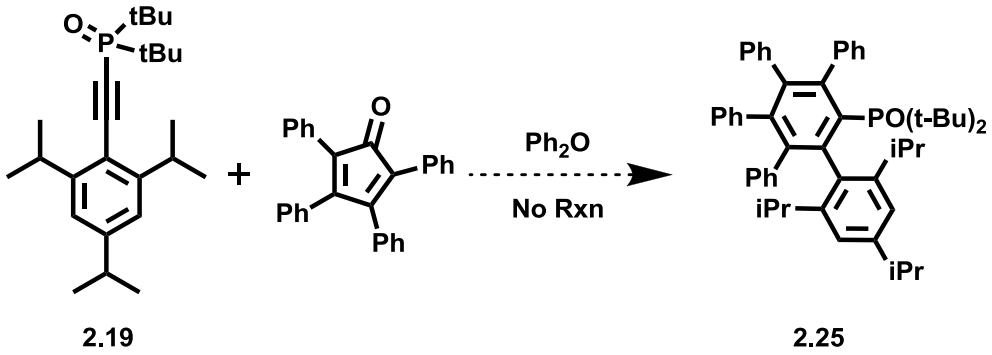


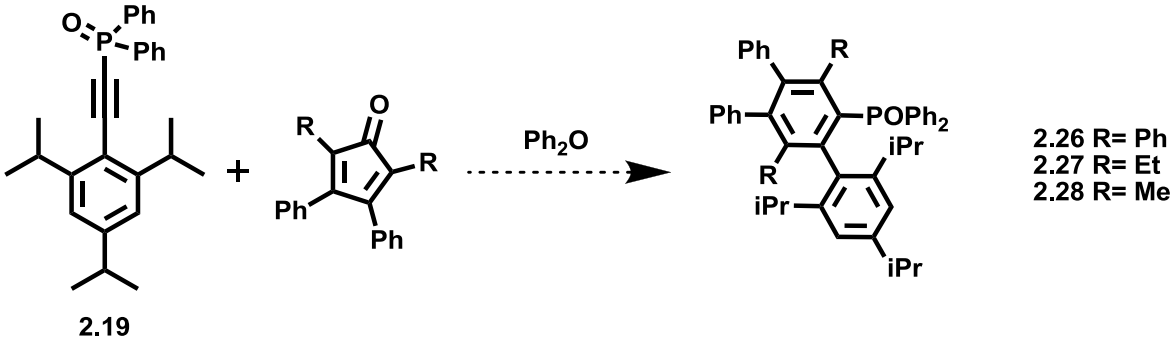
Figure 2.8 X-ray structure of ***L_7AuCl***



Scheme 2.13 Attempt at the Synthesis of Phosphine Oxide ***2.25***



Scheme 2.14 Proposed Synthesis of Highly Functionalized biaryl phosphines ***2.26-2.28***

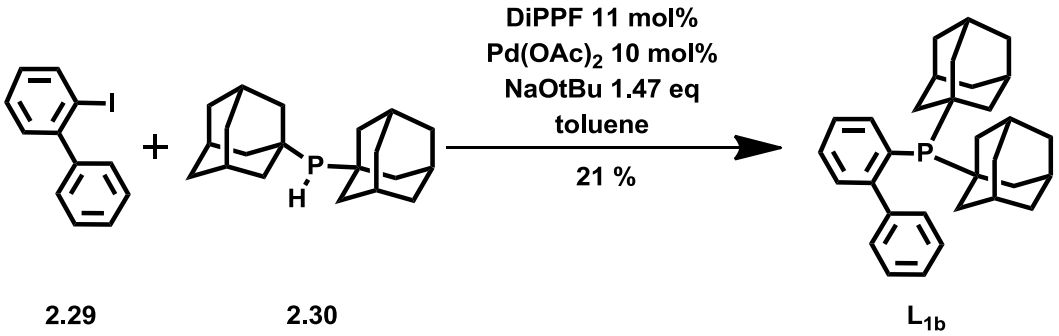


In order to synthesize most Buchwald-type ligands (**$L_{1a,c-g}$**, **L_{3a}**), we first synthesized the various substituted 2-iodobiaryls **2.29** using benzyne chemistry developed by the Buchwald group.[62] With these 2-iodobiaryls in hand, we were able to generate the desired phosphines by the use of two distinct methods: a palladium coupling reaction using bis-

(alkyl)phosphines (Scheme 2.15) or an alkylation reaction on to bis(alkyl)chlorophosphines or bis(aryl)chlorophosphines (Scheme 2.16).

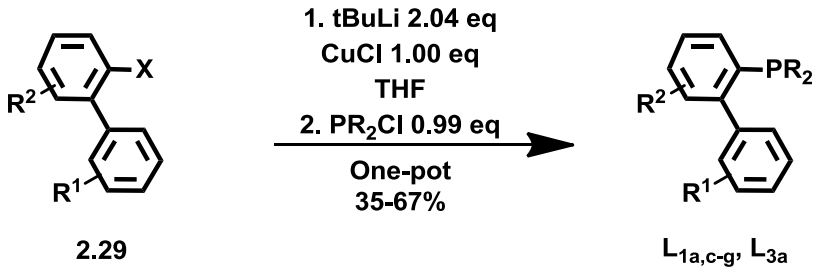
In order to increase the steric bulk of various Buchwald-type ligands, we envisaged adamantyls as R groups. Rather than using the Buchwald group's procedures, we used a simple coupling procedure from the Stradiotto Group.[63] Coupling of **2.29** with **2.30** proceeded cleanly to afford $\mathbf{L_{1b}}$ in 21% yield (Scheme 2.15).

Scheme 2.15 Synthesis of $\boldsymbol{L_{1b}}$ *by Pd-Coupling*



For all other Buchwald-type phosphines (R≠Adamantyl), an alkylation procedure was used and this afforded phosphines $\mathbf{L_{1a,c-g}}$ and $\mathbf{L_{3a}}$ (Scheme 2.16).

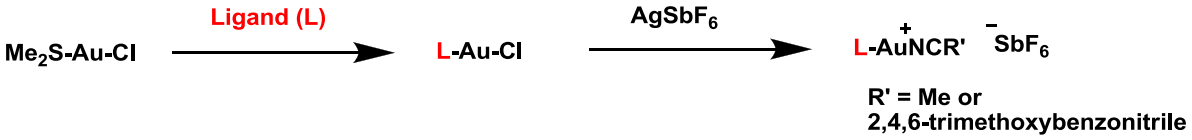
Scheme 2.16 Alkylation Method for the Synthesis of Buchwald-Type Phosphines



The cationic Au(I)-catalysts were readily prepared from DMS-AuCl (Scheme 2.17).). First, a ligand exchange reaction with DMS-AuCl generates the phosphine-AuCl species. Secondly, the treatment with a Ag(I) salt produces the cationic gold catalyst with the desired counter-ion (typically $[SbF_6]^-$). In all cases but one, the addition of the Au(I) salt generated

stable catalysts. However, in the case of $\mathbf{L_{1f}}$, the use of 2,4,6-trimethoxybenzonitrile instead of acetonitrile was required in order to generate a stable catalyst.

Scheme 2.17 Synthesis of Cationic Au(I)-Complexes



Chapter 3

Silver(I) / Copper(I)-Catalyzed Synthesis of Fused Carbocycles

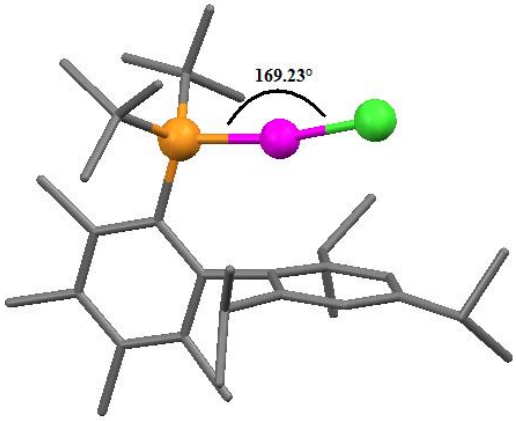
Introduction

"Our scientific theories do not, as a rule, spring full-armed from the brow of their creator. They are subject to slow and gradual growth…"

Professor Gilbert N. Lewis

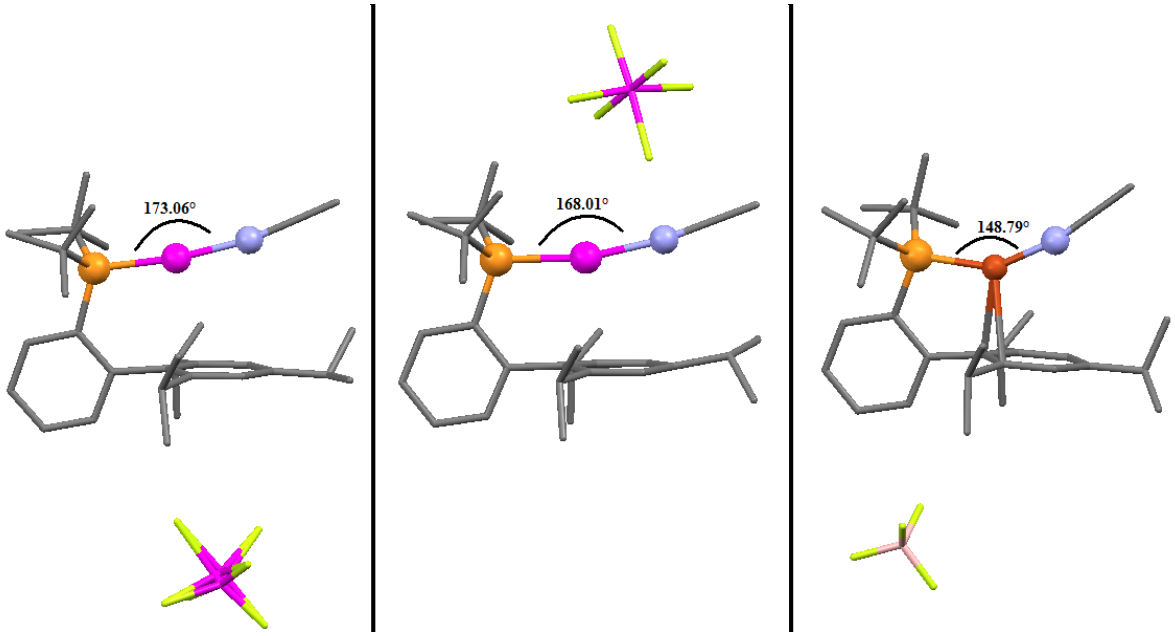
In our previous Au(I)-catalyzed synthesis of fused carbocycles, much optimization was needed in order to achieve respectable *6-endo-dig* selectivity. However, these Au(I)-catalyzed cyclizations remained very substrate dependent. Having obtained X-ray structures for most of the Au(I)-catalysts used in this optimization, we had noticed that our most selective ligand for *6-endo-dig* cyclizations was Me-tBuXPhos (**L_8**). The Au(I) chloride complex of **L_8** (Figure 3.1) had an interesting P-Au-Cl angle of 169.2° which was, at the time, the largest bend of all Au(I) chloride complexes synthesized by our group and in the literature.

Figure 3.1 X-Ray Structure of ***L*** *AuCl*



In 2010, Echavarren and coworkers investigated *metal-arene interactions in dialkylbiaryphosphane complexes of copper, silver and gold* and showed that the phosphine-metal-acetonitrile ligand bond (Figure 3.2) shows an increasingly larger bend with metal complexes of tBuXphos (**L**$_{2a}$) as one varies the metal from Au(I) to Ag(I) to Cu(I).[64] It is worth noting that, in the case of the Cu(I) complex, BF_4 instead of SbF_6 was used as the counteranion and therefore it is difficult to say what impact the SbF_6 counteranion would have had on the phosphine-metal-acetonitrile angle of the Cu(I) complex.

Figure 3.2 Cationic Au(I), Ag(I) and Cu(I) Complexes with ***L*** *and MeCN ligands*



[**L**$_{2a}$AuMeCN]SbF_6 [**L**$_{2a}$AgMeCN]SbF_6 [**L**$_{2a}$CuMeCN]BF_4

From our perspective, these were thrilling results. As we suspected that the bending of certain phosphine-metal complexes might have a direct influence on the *exo*:*endo* selectivity of our carbocyclizations, we wondered whether Ag(I) and Cu(I) complexes would be sufficiently active catalysts to achieve good conversion. We therefore set out to investigate these assumptions.

Reaction optimization – Aryl Substituted Alkynes

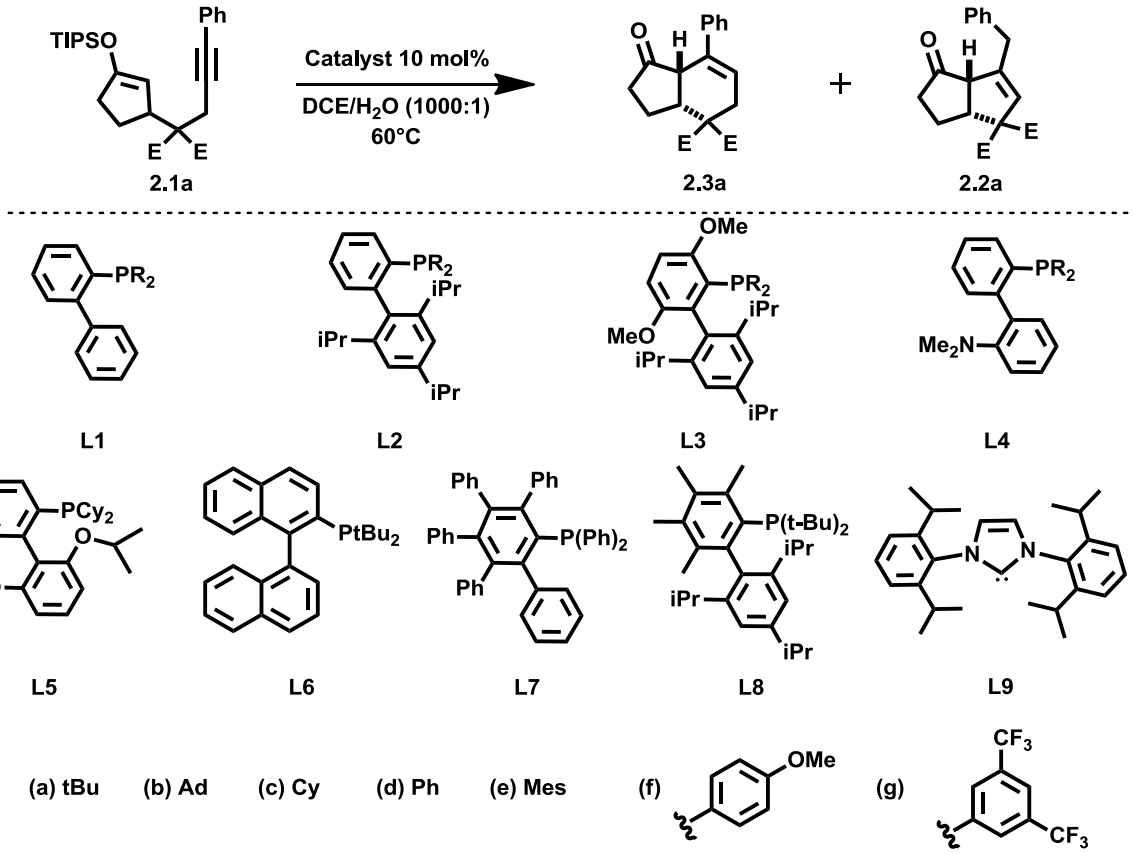
Our initial optimization started with **2.1a**, as the optimal conditions for the cyclization of this substrate using [$\mathbf{L_8}$AuMeCN]SbF_6 had furnished **2.2a** and **2.3a** in 82% yield and an 29:71 ratio in favor of **2.3a**.

When the reaction was run with [$\mathbf{L_{1a}}$AgTHF]SbF_6 (Table 3.1, *entry 4*), we were surprised to see that **2.3a** could be obtained in 84% yield with a 95:5 ratio. This result surpassed Au(I)-catalyzed cyclizations attempted on these substrates (*entries 1-3*). Encouraged by this result, we changed the JohnPhos ($\mathbf{L_{1a}}$) to tBuXPhos ($\mathbf{L_{2a}}$) and obtained **2.3a** exclusively in 82% yield. Increasing the quantity of water present during the cyclization from 1000:1 to 20:1 DCE/H_2O was useful, as the yield was increased to 89% (*entry 6*). However, increasing the quantity of water to 10:1 started decreasing the yield slightly (*entry 7*). It is logical that increasing the water content from 5% to 10% did not generate much change in yield since both give biphasic mixtures due to the low solubility of water in DCE. Increasing the temperature to 100°C gave mostly hydrolysis of the starting material, along with 11% of **2.3a** (*entry 8*). When the reaction was performed at room temperature with [$\mathbf{L_{2a}}$AgTHF]SbF_6, we were surprised to observe that the reaction proceeded smoothly in exquisite selectivity and in 86% yield (*entry 9*).

Control experiments were performed with $AgSbF_6$ or $\mathbf{L_{2a}}$ as the catalyst and in each case, no product was observed (*entries 10-11*). In the absence of catalyst, only starting material and some hydrolysis of the starting material were observed (*entry 12*). We were surprised to see that even [$\mathbf{L_{1a}}$CuMeCN]BF_4 is an active catalyst, albeit in a 41% yield (*entry 13*). We were hoping to obtain better *exo*-selectivity with triphenylphosphine as a ligand but unfortunately,

the catalyst was not sufficiently active. Depending on the reaction time, either starting material or hydrolysis of the starting material was observed with traces of **2.3a** (*entry 14*). It is noteworthy that we did not try [$\mathbf{L_8}$AgMeCN]SbF_6 as a catalyst during this optimization as the selectivity with $\mathbf{L_{2a}}$ was remarkable and we suspected that $\mathbf{L_8}$ might induce longer reaction times.

*Table 3.1 Optimization of the cyclization of **2.1a** using coinage metal catalysts*



Entry	Catalyst	Ratio (2.3a : 2.2a)	Yield (%)[f]
1	[$\mathbf{L_{1a}}$AuMeCN]SbF_6[a]	36:64	87
2	[$\mathbf{L_{2a}}$AuMeCN]SbF_6[a]	65:35	87
3	[$\mathbf{L_8}$AuMeCN]SbF_6	71:29	82
4	[$\mathbf{L_{1a}}$AgTHF]SbF_6	95:5	84
5	[$\mathbf{L_{2a}}$AgTHF]SbF_6	> 95:5	82
6	**[$\mathbf{L_{2a}}$AgTHF]SbF_6[b]**	**> 95:5**	**89**
7	[$\mathbf{L_{2a}}$AgTHF]SbF_6[c]	> 95:5	86
8	[$\mathbf{L_{2a}}$AgTHF]SbF_6[d]	> 95:5	11

9	[$\mathbf{L_{2a}}$AgTHF]SbF_6[e]	> 95:5	87
10	$AgSbF_6$	-	0
11	$\mathbf{L_{2a}}$	-	0
12	-	-	0
13	[$\mathbf{L_{1a}}$CuMeCN]BF_4	89:11	41
14	[$\mathbf{PPh_3}$AgMeCN]SbF_6	-[g]	<5

[a] Reaction was run in acetone with 5 mol% catalyst loading. [b] Reaction was run in DCE/H_2O (20:1). [c] Reaction was run in DCE/H_2O (10:1). [d] Reaction was run at 100°C. [e] Reaction was run at room temperature. [f] NMR yields . [g] Reaction was sluggish.

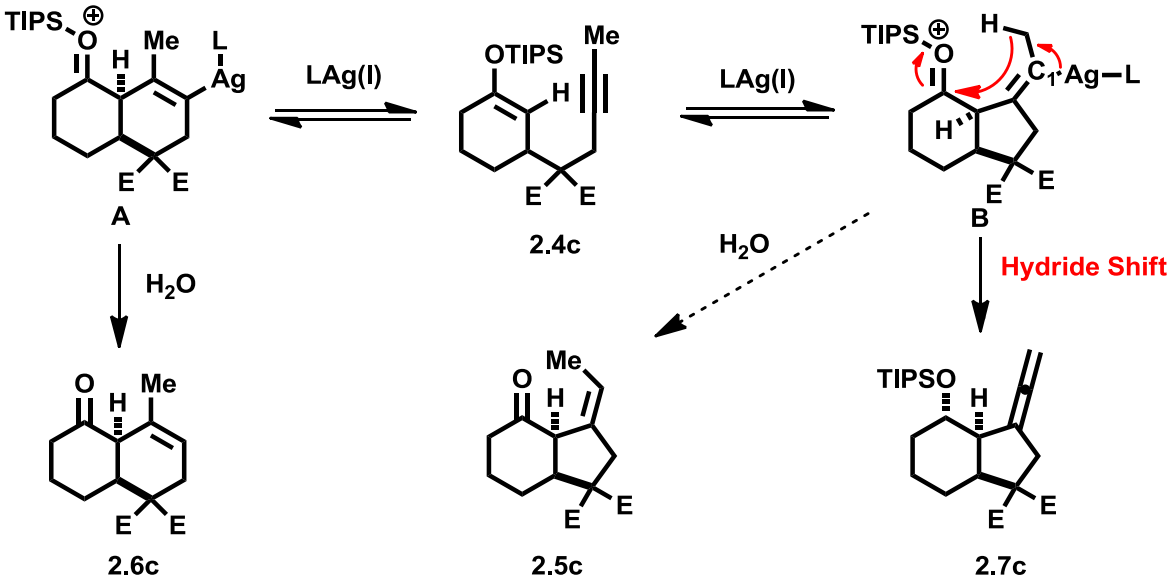
Reaction optimization – Methyl Substituted Alkynes

Following the optimization of aryl substituted alkynes, we explored the scope of the reaction in order to measure the effectiveness of [$\mathbf{L_{2a}}$AgTHF]SbF_6 on other more challenging substrates such as **2.4c**. However, when **2.4c** was submitted to typical conditions (Table 3.2, *entry 5*) using [$\mathbf{L_{2a}}$AgTHF]SbF_6, it was with utter disappointment that we observed only a 25:75 ratio favoring **2.5c** over **2.7c**. It was clear that methyl substituted alkynes require different conditions.

The formation of **2.7c** caught our attention because it is a product that is typically only formed when there is a lack of water in the reaction medium (Figure *3.3*). However, with 5% v/v of water in DCE, the solvent is saturated with water and therefore, we did not expect the formation of **2.7c**. One may recall that when Au(I) catalysts are utilized (*entries 1-2*), we observe formation of 5-exo-dig product **2.5c** instead of allene **2.7c**. Nonetheless, we performed analogous experiments to entry 5 with less and more water content. When a very small volume of water (0.1% v/v) was used, exclusive formation of allene **2.7c** is observed (*entry 4*). Interestingly, when the reaction is ran in 10% v/v of water in DCE, only a slight increase in the **2.6c**:**2.7c** ratio is observed (*entry 6*). The less than dramatic increase is most likely due to the fact that DCE is saturated in water with both 5% and 10% v/v H_2O in DCE. We suspected the formation of allene **2.7c** was due to a more difficult protodeargentation which resulted in a displacement in the equilibrium towards intermediate **B** (*Figure 3.3*); because of the lower energy barrier for the hydride shift, we decided to use a more acidic

source of protons to lower the protodeargentation barrier. Unfortunately, this resulted in the hydrolysis of the starting material (*entry 7*). However, it is noteworthy that this hypothesis could still hold true if **2.4c** was more resistant to hydrolysis.

*Figure 3.3 Mechanism for the formation of **2.6c*** and **2.7c** using Ag(I) catalysts



Our second hypothesis was that perhaps steric properties of $\mathbf{L_{2a}}$ were preventing proto-deargentation. In order to verify this assumption, we used less bulky, but also less electron donating, JohnPhos ($\mathbf{L_{1a}}$) as a ligand and we were pleased to see that we increased the ratio of **2.6c** over **2.7c** to almost 1:1 (*entry 3*). It was difficult to say whether this increase in *endo*:*exo* ratio was due to steric or electronic effects or a combination of both.

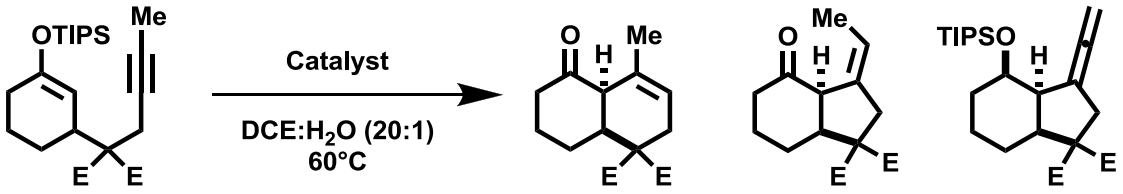
To verify whether electronic properties of the ligand might be able to prevent the hydride shift by making the C_1 carbon less nucleophilic, JackiePhos ($\mathbf{L_{3g}}$) was considered as a ligand due to its very electron withdrawing aryl groups which should make the metal center of the the catalyst more electrophilic. We therefore synthesized its Ag(I) complex, [$\mathbf{L_{3g}}$AgTHF]SbF_6, and to our great pleasure, we observed a ratio of 85:15 favoring **2.6c** in 98% yield (*entry 8*). Lowering the temperature to room temperature provided **2.6c** in a slightly improved ratio of 87:13, albeit in 75% yield (*entry 9*).

On the basis that a more electron withdrawing phosphine ligand would induce better selectivity, we decided to synthesize phosphine $\mathbf{L_{2g}}$ which lacked the methoxy groups of JackiePhos ($\mathbf{L_{3g}}$). The Ag(I) complex gave a similar ratio as the $\mathbf{L_{3g}}$ complex, however the conversion was low and the reproducibility of this result was difficult (*entry 10*).

Because JohnPhos ($\mathbf{L_{1a}}$) had proved to be a better ligand than tBuXPhos ($\mathbf{L_{2a}}$), we synthesized a hybrid between $\mathbf{L_{1a}}$ and $\mathbf{L_{3g}}$, which had proved to be our optimal ligand yet. The Ag(I) complex of this electron withdrawing ligand ($\mathbf{L_{1g}}$) was therefore synthesized and, to our displeasure, offered a lower ratio and yield than $\mathbf{L_{3g}}$ and $\mathbf{L_{2g}}$ complexes when submitted to the typical reaction conditions (*entry 11*). Therefore, one may assume that the initial observation that $\mathbf{L_{1a}}$ was more *endo*-selective ligand than $\mathbf{L_{2a}}$ is mostly the result of the poorer electron donating nature of $\mathbf{L_{1a}}$ and that sterics, in this particular case, play a less important role.

Other Ag(I) complexes were tested in order to increase both yield and ratio for this reaction and unfortunately, all other catalyst were deemed not sufficiently active (*entries 12-14*). $\mathbf{L_{3g}}$ and $\mathbf{L_8}$ Cu(I) complexes were synthesized but found to be inactive at room temperature (*entries 15-16*). When [$\mathbf{L_{3g}}$CuMeCN]SbF_6 was used as the catalyst at 60°C however, low conversion and was observed (*entry 17*).

*Table 3.2 Optimization of the cyclization of **2.4c** using coinage metal catalysts*



2.4c **2.6c** **2.5c** **2.7c**

Entry	Catalyst	Ratio (2.6c : 2.5c : 2.7c)	Yield (%)[f]
1	[$\mathbf{L_{1a}}$AuMeCN]SbF_6[a]	43:57:0	85
2	[$\mathbf{L_8}$AuMeCN]SbF_6[a]	57:43:0	79
3	[$\mathbf{L_{1a}}$AgTHF]SbF_6	46:0:54	76
4	[$\mathbf{L_{2a}}$AgTHF]SbF_6[b]	0:0:100	90
5	[$\mathbf{L_{2a}}$AgTHF]SbF_6	25:0:75	98

6	[$\mathbf{L_{2a}}$AgTHF]SbF_6 [c]	31:0:69	99
7	[$\mathbf{L_{2a}}$AgTHF]SbF_6 [d]	-	- [g]
8	[$\mathbf{L_{3g}}$AgTHF]SbF_6	85:0:15	98
9	**[$\mathbf{L_{3g}}$AgTHF]SbF_6** [e]	**87:0:13**	**75**
10	[$\mathbf{L_{2g}}$AgTHF]SbF_6	88:0:12	42 (52 brsm)
11	[$\mathbf{L_{1g}}$AgTHF]SbF_6	82:0:18	24
12	[**Tris(2,4-di-*tert*-butylphenyl) phosphite**AgTHF]SbF_6	-	- [g]
13	[**(3,5-bis(CF_3)C_6H_3)$_3$P**AgMeCN]SbF_6	-	- [g]
14	[**(DPPF)**Ag_2][SbF_6]$_2$	-	- [g]
15	[$\mathbf{L_{3g}}$CuMeCN]SbF_6 [e]	-	- [h]
16	[$\mathbf{L_8}$CuMeCN]SbF_6 [e]	-	- [h]
17	[$\mathbf{L_{3g}}$CuMeCN]SbF_6	77:0:23	23 (40 brsm)

[a] reaction was run in acetone with 5 mol% catalyst loading. [b] DCE:H_2O ratio 1000:1. [c] DCE:H_2O ratio 10:1. [d] DCE:AcOH ratio 1000:1 with no water. [e] Reaction was run at r.t. [f] NMR yields. [g] Only hydrolysis of the starting material occurred. [h] No reaction occurred with minimal degradation of the starting material.

Reaction optimization – Terminal Alkynes

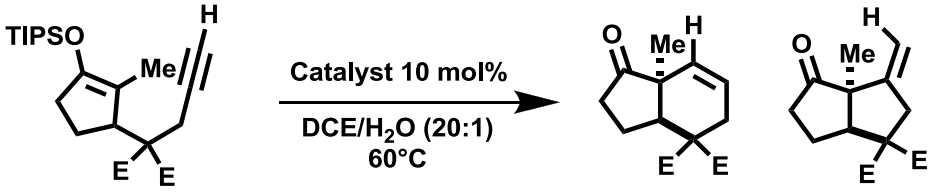
Upon exploring the scope of the Ag(I)-catalyzed cyclizations, we attempted the cyclization of terminal alkyne **3.1**. Terminal alkynes of this nature are well known to undergo *5-exo-dig* cyclizations exclusively when Au(I) catalysts are used (Table 3.3, *entry 1*). It is therefore with great surprise that we observed a ratio of 34:66, albeit favoring the *5-exo-dig* product **3.3** over **3.2** (*entry 2*). Reducing the water content to 0.1% v/v slightly increased the ratio and yield (*entry 3*). $\mathbf{L_{1a}}$ and $\mathbf{L_{3g}}$ proved to be even less satisfactory ligands than $\mathbf{L_{2a}}$ (*entries 4-5*). Because the electron withdrawing but still fairly bulky phosphine $\mathbf{L_{3g}}$ seemed to be the least selective ligand for the *6-endo-dig* cyclization of **3.1**, we assumed that, in this case, bulky and electron rich Me-tBuXPhos ($\mathbf{L_8}$) would be ideal to achieve increased selectivity. Indeed, this is the case as we obtained **3.2** in 91% yield with a ratio of 48:52 (*entry 6*). When the reaction is performed at room temperature, an increase of selectivity to 51:49 favouring **3.2** is obtained, thus achieving, for the first time, a ratio favouring the *endo* product on terminal alkynes.

Because $\mathbf{L_8}$ is one of the most sterically demanding and electron rich Buchwald ligands, we considered other ways by which we could improve the selectivity towards the *endo* product **3.2** by varying the ligand on the Ag(I) metal center. We first used BrettPhos ($\mathbf{L_{3c}}$), which has two methoxy groups on its biaryl, which we thought would make the metal center more electron rich. Encouraged by the identical ratio BrettPhos ($\mathbf{L_{3c}}$) had to tBu-XPhos ($\mathbf{L_{2a}}$) (*entry 8*), we set our sights on tBu-BrettPhos ($\mathbf{L_{3a}}$), which we thought would be a even more selective ligand than Me-tBuXPhos ($\mathbf{L_8}$). Unfortunately, $\mathbf{L_{3a}}$ turned out to be less selective than $\mathbf{L_8}$ (*entry 9-10*). However it is noteworthy that $\mathbf{L_{3a}}$ was slightly more selective than $\mathbf{L_{2a}}$.

Because we were unable to find a better ligand than Me-tBuXPhos ($\mathbf{L_8}$), we directed our attention towards analogous Cu(I) complexes. We synthesized [$\mathbf{L_8}$CuMeCN]SbF_6 and we were pleased to observe that at 60°C, we increased the ratio favouring **3.3** to 61:39 while altogether with 90% yield (*entry 11*). Lowering the temperature to r.t. allowed for both an increased ratio of 63:39 and yield of 92%.

We wondered whether exchanging the SbF_6 counteranion for a bulky and extremely non-coordinating BArF anion would induce further selectivity towards *6-endo-dig* product **3.3**. Unfortunately our efforts, thus far, have been unsuccessful at synthesizing such Cu(I) complexes.

*Table 3.3 Optimization of the cyclization of **3.1** using coinage metal catalysts*



3.1 3.2 3.3

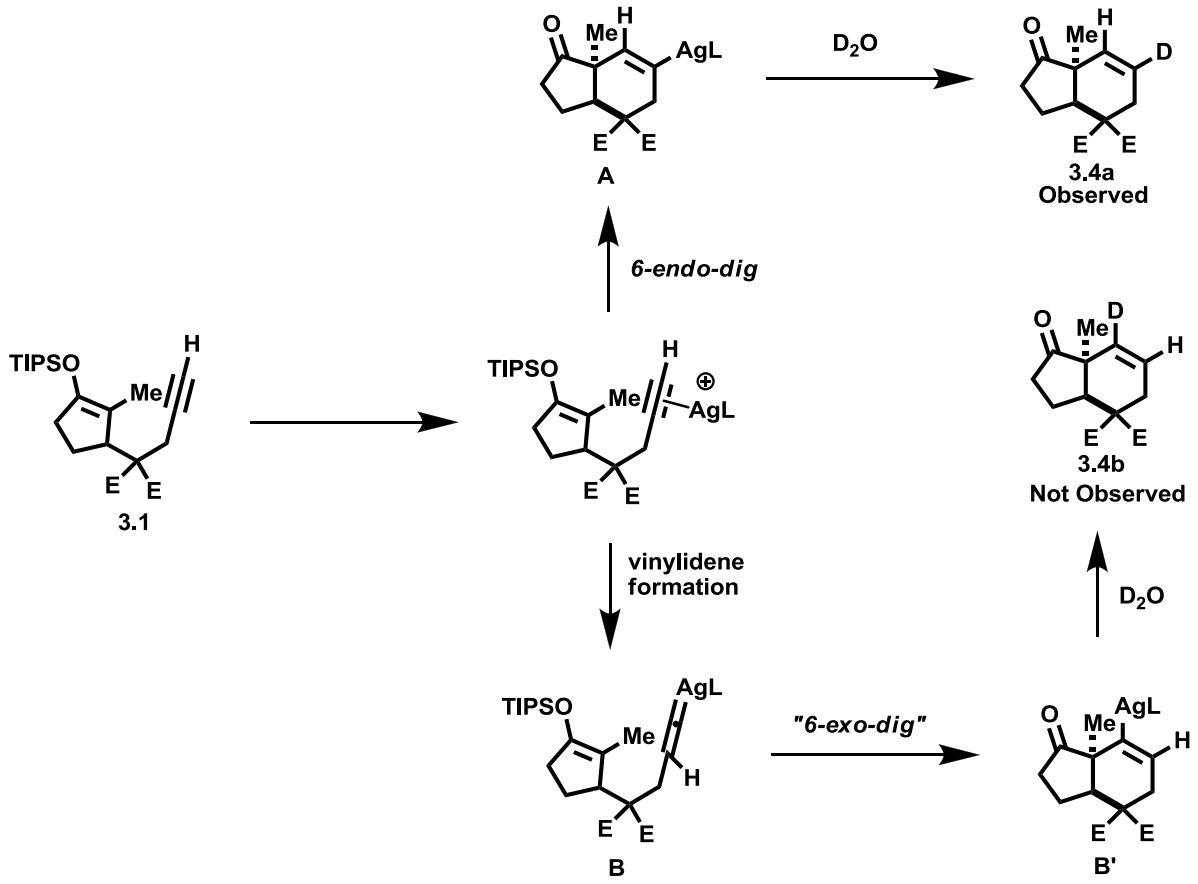
Entry	Catalyst	Ratio (3.2 : 3.3)	Yield (%)[d]
1	[$\mathbf{L_8}$AuMeCN]SbF_6[a]	0:100	100
2	[$\mathbf{L_{2a}}$AgTHF]SbF_6	34:66	98
3	[$\mathbf{L_{2a}}$AgTHF]SbF_6[b]	38:61	99
4	[$\mathbf{L_{1a}}$AgTHF]SbF_6	21:79	43
5	[$\mathbf{L_{3g}}$AgTHF]SbF_6	11:89	64
6	[$\mathbf{L_8}$AgMeCN]SbF_6	48:52	91

7	[$\mathbf{L_8}$AgMeCN]SbF_6[c]	51:49	93
8	[$\mathbf{L_{3c}}$AgMeCN]SbF_6	34:66	97
9	[$\mathbf{L_{3a}}$AgMeCN]SbF_6	43:57	97
10	[$\mathbf{L_{3a}}$AgMeCN]SbF_6[c]	43:57	94
11	[$\mathbf{L_8}$CuMeCN]SbF_6	61:39	90
12	**[$\mathbf{L_8}$CuMeCN]$\mathbf{SbF_6}$[c]**	**63:37**	**92**

[a] reaction was run in acetone with 5 mol% catalyst loading. [b] DCE:H_2O ratio 1000:1. [c] Reaction was run at r.t. [d] NMR yields.

Previous reports have shown that the 6-endo-dig cyclization of terminal alkynes may occur via two different mechanisms.[36] We wanted to gain further insight into the mechanism utilized by our Ag(I) and Cu(I) complexes in order to potentially develop even more selective catalysts. Because the proto-demetalation would not occur at the same carbon in each mechanism, a simple deuteration experiment showed that the cyclization of terminal alkynes proceeds via the same mechanism as non terminal alkynes when our Ag(I) or Cu(I) catalysts are utilized (Figure 3.3).

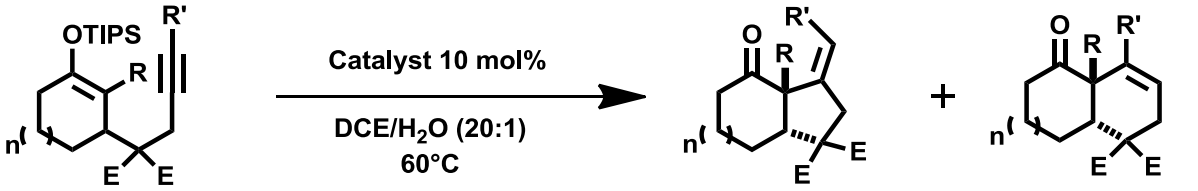
*Figure 3.4 Determination of the Mechanism of Ag(I)-catalyzed Cyclizations of Terminal Alkynes **3.3** using D_2O*



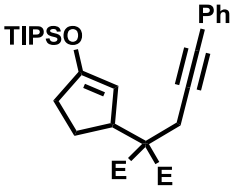
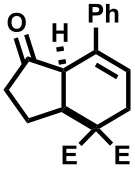
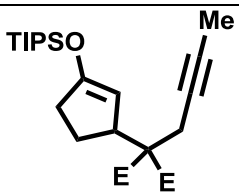
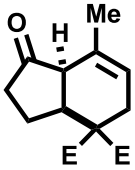
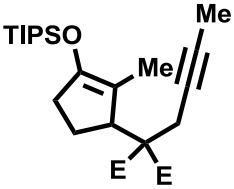
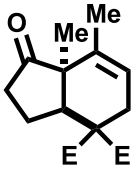
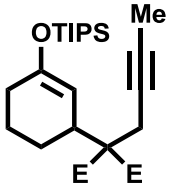
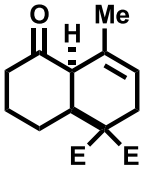
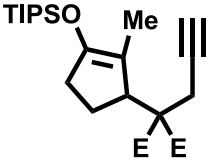
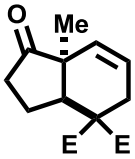
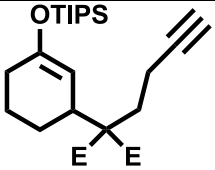
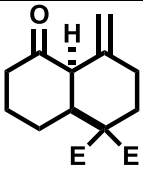
Reaction Scope

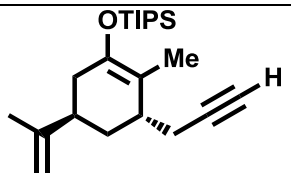
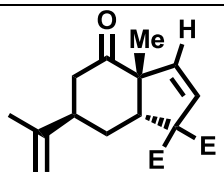
With the optimization of three different types of substrates in hand, we explored the scope of these reactions further (Table 3.4). With the optimal reaction conditions, **2.3a** could be synthesized exclusively and in 89% yield. Methyl substituted substrate **2.4a** did not require electron poor $\mathbf{L_{3g}}$ in order to obtain exquisite selectivity, $\mathbf{L_{2a}}$ sufficed to furnish **2.6a** exclusively (*entry 2*). Silyl enol ether **2.4b** could also be cyclized in exquisite *6-endo* selectivity and in 80% yield to furnish **2.6b** (*entry 3*). Decalin **2.6c** was obtained in 75 % yield with a ratio of 87:13 at room temperature (*entry 4*). It is noteworthy that decalin **2.6c** can also be obtained in a greatly improved yield by performing the reaction at 60°C with minimal decrease of selectivity towards the *6-endo-dig* product (*entry 5*).

Table 3.4 Substrate Scope of Selective 6-endo-dig Ag(I) or Cu(I)-Catalyzed Cyclizations



2.4 2.5 2.6

Entry	Substrate	Catalyst	Product	Endo:Exo Ratio	Yield (%)[b]
1	 **2.1a**	[$\mathbf{L_{2a}}$AgTHF]SbF_6	 **2.3c**	>95:5	89
2	 **2.4a**	[$\mathbf{L_{2a}}$AgTHF]SbF_6	 **2.6a**	>95:5	87
3	 **2.4b**	[$\mathbf{L_{3g}}$AgTHF]SbF_6	 **2.6b**	>95:5	80
4 5	 **2.4c**	[$\mathbf{L_{3g}}$AgTHF]SbF_6 [$\mathbf{L_{3g}}$AgTHF]SbF_6	 **2.6c**	87:13 85:15	75[a] 95
6	 **3.1**	[$\mathbf{L_8}$CuMeCN]SbF_6	 **3.3**	63:37	92
7	 **3.7**	[$\mathbf{L_{2a}}$AgTHF]SbF_6	 **3.8**	*6-exo* only	96

8	 **3.9**	[$\mathbf{L_{1a}}$AgTHF]SbF_6	 **3.10**	*5-endo* only	97

[a] Reaction was run at r.t. [b] Isolated yields.

Terminal alkyne **3.1** could also be cyclized to furnish **3.3** in a 63:37 ratio (*entry 6*), only this time the use of a Cu(I) species proved to be the ideal catalyst.

We also wanted to show that Ag(I) catalysts are fairly versatile and can catalyze other types of cyclizations which are known to proceed via Au(I) catalysis. For example, the *6-exo-dig* cyclization of terminal alkyne **3.7** proceeds in excellent yield using the Ag(I) complex of $\mathbf{L_{2a}}$ (*entry 7).* The *5-endo-dig* cyclization of terminal alkyne **3.9** also proceeds smoothly using less expensive JohnPhos ($\mathbf{L_{1a}}$) as the ligand on a Ag(I) cationic complex (*entry 8*).

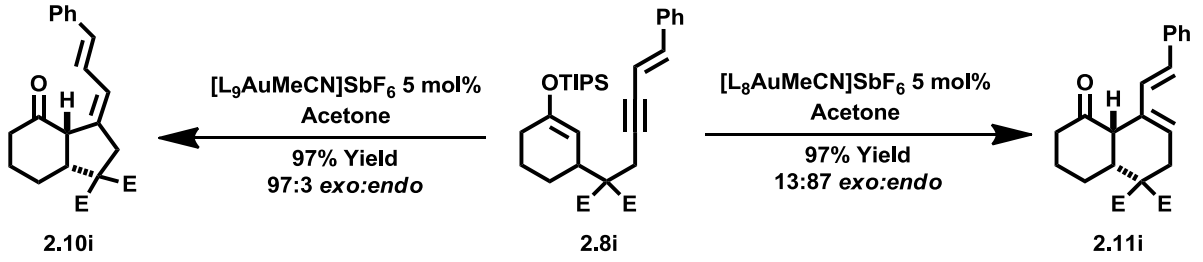
Chapter 4

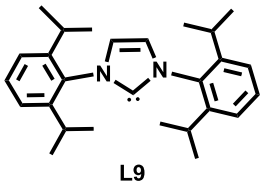
Summary and Outlook

Summary

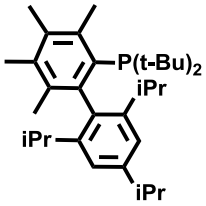
We have demonstrated that the *6-endo-dig* pathway is accessible and not limited to sterically or electronically biased substrates. Pathway selectivity may be modulated by the proper choice of ancillary ligand on the metal species. It seems the ancillary ligand can affect pathway selectivity at the first bond formation rather than through a common intermediate generated after an initial bond formation.

*Scheme 4.1 Selected Example of Ligand Effect on the cylization of **2.8i***





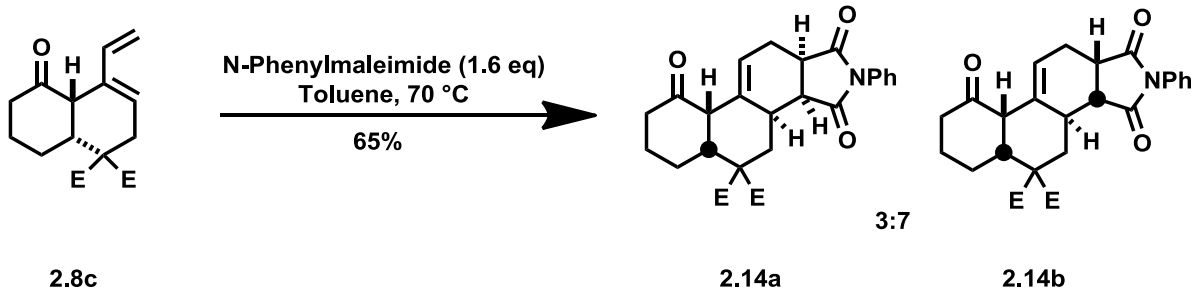
L9



L8

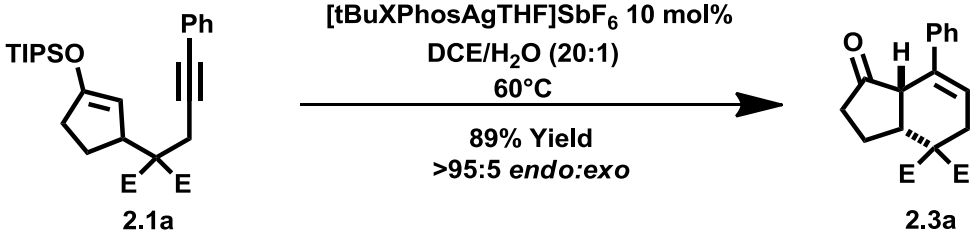
In the case of Au(I) complexex, we discovered that [IPrAuMeCN]SbF_6 was the ideal catalyst for *5-exo-dig* cyclizations whereas [Me-tBuXPhosAuMeCN]SbF_6 proved to be the most selective catalyst towards *6-endo-dig* cyclizations (Scheme 4.1). This allows for the formation of a variety of fused bicycles. As a proof of concept, a Diels-Alder reaction was performed on **2.8c** in order to generate steroid analogue **2.14** (Scheme 4.2).

*Scheme 4.2 Diels-Alder reaction of **2.8c** with phenylmaleiimide*



X-ray analysis of LAuCl species bearing a Buchwald-type phosphine (L) showed a nice correlation between the L-Au-Cl angle and the general selectivity of Au(I) catalysts towards *6-endo-dig* cyclizations. Inspired by the x-ray studies conducted by Echavarren and coworkers, which demonstrated that the L-M-NCMe angle increased when the metal was replaced from Au(I) to Ag(I) to Cu(I), we set out to re-explore the cyclization of silyl enol ether **2.1a**. Our assumptions were confirmed when [tBuXPhosAgTHF]SbF_6 gave exquisite formation of *6-endo-dig* product **2.3a** in 89% yield (Scheme 4.3).

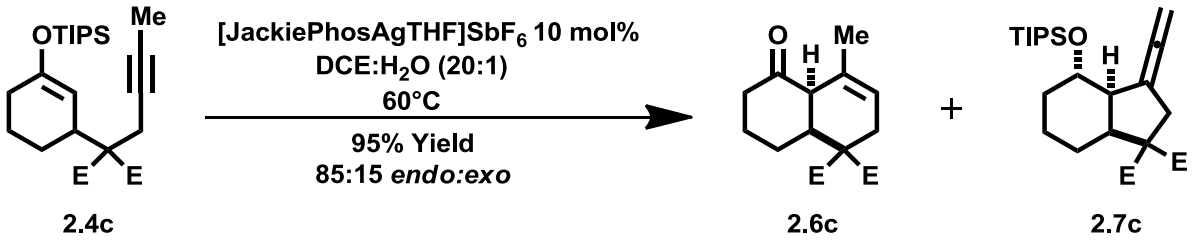
*Scheme 4.3 Ag(I)-Catalyzed 6-endo-dig Cyclization of **2.1a***



It soon became clear that not all substrates were going to cyclize as selectively as **2.1a**, when we attempted the cyclization of **2.4c**. Due to the formation of allene **2.7c**, electron withdrawing JackiePhos ligand was used in order to form *6-endo-dig* product **2.6c** in 95%

yield with a good **2.6c** to **2.7c** ratio (Scheme 4.4). [JackiePhosAgTHF]SbF_6 proved to be the ideal catalyst for the cyclization of methyl substituted alkynes.

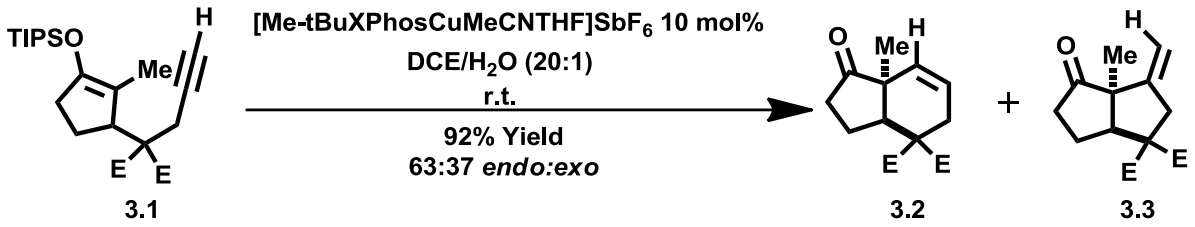
*Scheme 4.4 Ag(I)-Catalyzed 6-endo-dig Cyclization of **2.4c***



2.4c **2.6c** **2.7c**

Finally, because terminal alkyne **3.1** had always cyclized in a *5-exo-dig* fashion with even our most *6-endo-dig* selective Au(I)-catalyst, our hopes of accessing the *6-endo-dig* pathway with Ag(I) or even Cu(I) catalysts were low. However, we were happy to see that [Me-tBuXPhosCuMeCN]SbF_6 offered decent selectivity at room temperature, furnishing the *6-endo-dig* product **3.2** as the major isomer. While the selectivity towards **3.2** is certainly not ideal, only we were able to access the *6-endo-dig* pathway on a substrate that was previously known to only cyclize *via* the *5-exo-dig* pathway when coinage metal catalysts were utilized.

*Scheme 4.5 Cu(I)-Catalyzed Cyclization of **3.1***



3.1 **3.2** **3.3**

Outlook

Our investigations into coinage metal catalyzed cyclizations of silyl enol ethers have brought many questions. For instance, where does the selectivity originate? It is our belief that NMR spectroscopy studies using stoichiometric quantities of metal catalyst may reveil crucial information.

A second question one might ask is, what is the exact mechanism of these reactions and how does it impact pathway selectivity? Are we under kinetically controlled conditions or are thermodynamics more important?

A recent publication by Hammond and coworkers has, for the first time, shone light on the proto-deauration step of typical Au(I)-catalyzed reactions.[65] These authors state that two rate-limiting steps (RLS) are possible for Au(I)-catalyzed reactions. In some cases, the RLS is the alkyne activation and in other, it is the proto-deauration. In the case of difficult alkyne activations, the ideal ligand is an electron-poor one, which renders the metal more lewis acidic. Therefore, one should expect a faster reaction rate with electron-poor ligands on systems where the RLS is the alkyne activation. On the other hand, electron-rich ligands tend to favor proto-deauration. Therefore, if the RLS is the protodeauration, electron-rich ligands would offer a faster reaction rate while electron poor ligands would slow down the reaction considerably.

It is our view that similar experiments could be conducted using electron poor and electron rich ligands in order to determine whether the RLS varies according to which metal is used. Also, if the RLS is the proto-demetalation for all coinage metal catalyzed cyclizations, this might suggest that the relative rate of proto-demetalation between metals is at the origin of the *6-endo-dig* selectivity if the latent proto-demetalation offers a thermodynamic equilibrium.

Chapter 5

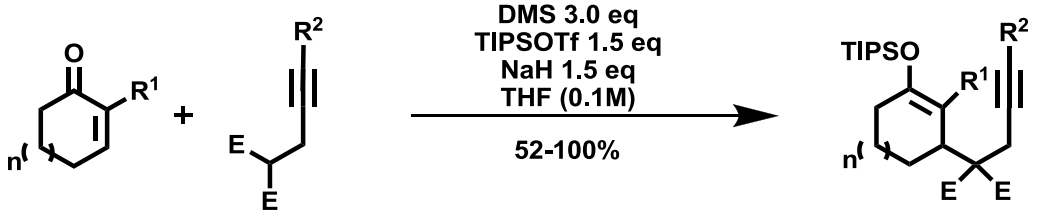
Experimental

General Information

All reactions were performed under nitrogen or argon atmosphere in flame-dried glassware equipped with a magnetic stir bar and a rubber septum, unless otherwise indicated. Most solvents were freshly distilled prior to use; diethyl ether and THF over sodium and benzophenone; toluene, triethylamine, and DCM over calcium hydride. All other commercial reagents were used without further purification, unless otherwise noted. The acetonitrile[(2-biphenyl)di-*tert*-butylphosphine]gold(I) complex was purchased from Sigma-Aldrich® and kept on bench without any further precaution or made as reported in the litterature[1]. Chloro[1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene]gold(I) and Chloro[2-dicyclohexyl(2′,4′,6′-trisopropylbiphenyl)phosphine]gold(I) were purchased from Sigma-Aldrich® but used as its acetonitrile cationic form with hexafluroantimonate as counterion.[1] Reactions were monitored by thin layer chromatography (TLC) analysis of aliquots using glass sheets pre-coated (0.2 mm layer thickness) with silica gel 60 F_{254} (E. Merck). Thin layer chromatography plates were viewed under UV light and stained with phosphomolybdic acid or *p*-anisaldehyde staining solution. Column chromatographies were carried out with silica gel 60 (230-400 mesh, Merck). Preparative HPLC was performed on a waters LC 4000 system equipped with a PDA detector and a 21.2 mm - 2.5 mm reverse phase columm. Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded on Bruker AMX 300 MHz, Bruker AMX 400 MHz and Bruker AMX 500 MHz spectrometers. NMR samples were dissolved in chloroform-*d* (unless specified otherwise) and chemical shifts are reported in ppm from ppm relative to the residual undeuterated solvent. Data are reported as follows:

chemical shift, integration, multiplicity (s = singlet, d = doublet, dd = doublet of doublets, ddd = doublet of doublets of doublets, dddd = doublet of doublets of doublets of doublets, br = broad signal, t = triplet, q = quartet, quint = quintet, sex = sextet, sept = septuplet, m = multiplet, or otherwise noted), coupling constant. Carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on a 75.5 MHz, 100.7 MHz, or 125.7 MHz spectrometer. NMR samples were dissolved in chloroform-*d* (unless specified otherwise) and chemical shifts are reported in ppm relative to the solvent. IR spectra were recorded with a Bomem Michaelson 100 FTIR spectrometer. HRMS were obtained on a Kratos Analytical Concept instrument (University of Ottawa Mass Spectrum Centre). The crystals were mounted on thin glass fibers using paraffin oil and cooled to 200.15 °K. Data were collected on a Bruker AXS SMART single crystal diffractometer equipped with a sealed Mo tube source (wavelength 0.71073 Å) APEX II CCD detector. Raw data collection and processing were performed with APEX II software package from BRUKER AXS.

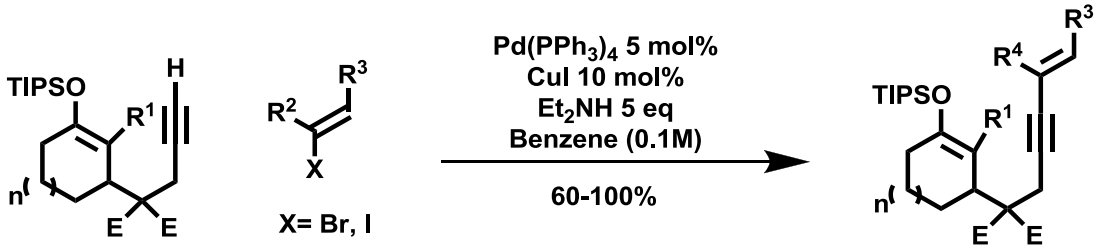
General Procedure A – Synthesis of Silyl Enol Ethers



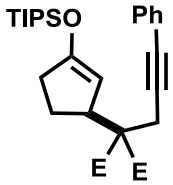
To a flame-dried flask equipped with a magnetic stir bar and under argon atmosphere was added cycloalkenone (1.0 mmol) and THF (5 mL). The solution was cooled to -78 °C and TIPSOTf (1.5 mmol) was added followed by the dropwise addition of Me_2S (3.0 mmol). The reaction was stirred 30 min at -78 °C. During this time, in a separate flame-dried flask equipped with a magnetic stir bar and under argon atmosphere, a THF solution of a mono alkylated diethyl propargylmalonate (1.5 mmol) was added to a THF (5 mL) suspension of NaH 60% w/w in oil (2.0 mmol) at r.t. The mixture was stirred 30 min and added dropwise to the first flask at –78°C. The reaction mixture was stirred at -78 °C for 1h and quenched with a saturated solution of $NaHCO_{3(aq)}$. The aqueous layer was extracted three times with

EtOAc. The organics layers were combined, dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude residue was purified by flash column chromatography on silica gel (eluted with hexane/AcOEt (98:2 to 90:10)) to give silyl enol ether as clear oils. (52-100% yield).

General Procedure B – Synthesis of Silyl Enol Ethers with Alkene Substituted Alkynes



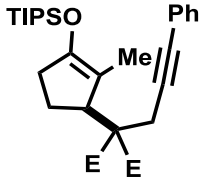
A flame-dried flask equipped with a magnetic stir bar was charged with $Pd(PPh_3)_4$ (0.05 mmol) followed by CuI (0.1 mmol). Benzene (10.0 mL) was then added and the solution was degassed with argon for 15 minutes. During the degassing, the terminal alkyne (1.0 mmol) was added followed by vinyl halide or aryl halide (1.5-3.0 mmol). Once the degassing was completed, diethyl amine (5.0 mmol) was added to the solution and the mixture was stirred overnight. Silica was added directly to the mixture and the solvent was evaporated off under reduced pressure. The residue was then purified by flash column chromatography on silica gel (eluted with hexane/AcOEt (98:2 to 95:5)) to give the desired compound as a clear yellow oil (60-100% yield). Vinyl halides for the synthesis of compounds 8k-p were synthesized according to the literature procedures.3, 4



Silyl enol ether 2.1a

Silyl enol ether was prepared according to the general procedure A and isolated as a colorless oil.

IR (neat, cm^{-1}) ν max 2944-2867, 1733, 1645, 1252; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.38-7.33 (m, 2H), 7.29-7.26 (m,3H), 4.75 (ddd, J = 1.9 Hz, 1.6 Hz, 1.6 Hz, 1H), 4.36,-4.13 (m, 4H), 3.69-3.64 (m,1H), 3.04 (d, J = 17.1 Hz, 1H), 2.98 (d, J = 17.1 Hz, 1H), 2.32-2.27 (m, 2H), 2.15-2.05 (m, 1H), 1.97-1.88 (m, 1H), 1.28 (t, J = 7.1 Hz,, 3H), 1.26 (t, J = 7.1 Hz, 3H), 1.21-1.13 (m, 3H), 1.06 (d, J =7.0 Hz, 18H) ; **^{13}C NMR (100 MHz, $CDCl_3$)** δ 170.4 (C), 170.2 (C), 157.2 (C), 131.7 (CHx2), 128.3 (CHx2), 127.9 (CH), 123.7 (C), 102.7 (CH), 85.8 (C), 82.9 (C), 61.4 (CH_2x2), 61.0 (C), 45.8 (CH), 33.1 (CH_2), 23.8 (CH_2), 23.3 (CH_2), 18.0 (CH_3x6), 14.2 (CH_3x2), 12.5 (CHx3); **HRMS (EI)** m/z calcd for $C_{30}H_{44}O_5Si$ [M^+] 512.2958, found 512.2958.

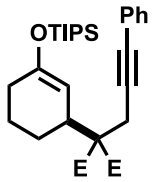


Silyl enol ether 2.1b

Silyl enol ether was prepared according to the general procedure A and isolated as colorless oil.

IR (neat, cm^{-1}) ν max 3057, 2980-2874, 1734, 1492, 1297, 1027; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.38-7.34 (m,2H), 7.29-7.26 (m, 3H), 4.26-4.16 (m, 4H), 3.66-3.61 (m, 1H), 3.15 (d J =17.3 Hz, 1H), 2.99 (d, J = 17.3 Hz, 1H), 2.47-2.38 (m, 1H), 2.26-2.13 (m, 2H), 2.09-2.01 (m, 1H), 1.59 (s, 3H), 1.29 (dd, J = 7.1 Hz, 7.1 Hz, 3H), 1.27 (dd, J = 7.1 Hz, 7.1 Hz, 3H), 1.16-1.11 (m, 3H), 1.10-1.06 (m, 18H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 170.5 (C), 170.2 (C), 150.9 (C), 131.6 (CHx2), 128.2 (CHx2), 127.8 (CH), 123.8 (C), 111.8 (C), 86.4

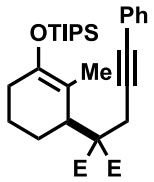
(C), 82,6 (C), 61.5 (CH_2), 61.4 (CH_2), 61.2 (C), 49.1 (CH), 32.4 (CH_2), 23.8 (CH_2), 23.3 (CH_2), 18.0 (CH_3x6), 14.2 (CH_3), 14.1 (CH_3), 13.0 (CHx3), 11.9 (CH_3); **HRMS (EI)** m/z calcd for [M^+] $C_{31}H_{46}O_5Si$ 526.3115, found 526.3105.



Silyl enol ether 2.1c

Silyl enol ether was prepared according to the general procedure A and isolated as colorless oil.

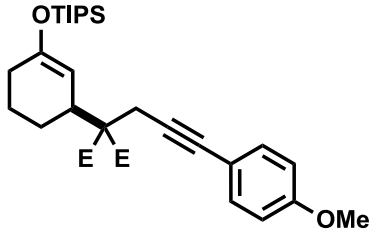
IR (neat, cm^{-1}) ν max 2944, 2867, 1730, 1653, 1188, 883; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.40-7.32 (m, 2H), 7.28-7.25 (m, 3H), 4.94-4.92 (m, 1H), 4.21 (dddd, J = 10.9 Hz, 7.2 Hz, 7.2 Hz, 7.2 Hz, 2H), 4.21 (dddd, J = 10.9 Hz, 7.2 Hz, 7.2 Hz, 7.2 Hz, 2H), 3.29-3.22 (m, 1H), 3.04 (s, 2H), 2.15-1.98 (m, 2H), 1.97-1.82 (m, 2H), 1.66-1.58 (m, 1H), 1.49-1.39 (m, 1H), 1.27 (dd, J = 7.1 Hz, 7.1 Hz, 3H), 1.27 (dd, J = 7.1 Hz, 7.1 Hz, 3H), 1.17-1.10 (m, 3H), 1.07 (d, J =7.3 Hz, 18H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 170.2 (C), 170.0 (C), 131.9 (CHx2), 128.3 (CHx2), 127.9 (CH), 123.7 (C), 104.0 (CH), 85.9 (C), 83.1 (C), 61.5 (C), 61.4 (CH_2), 60.9 (CH_2), 39.1 (CH), 29.8 (CH_2), 24.4 (CH_2), 23.2 (CH_2), 22.7 (CH_2), 18.1 (C), 17.9 (CH_3x6), 14.2 (CH_3), 14.2 (CH_3), 12.7 (CHx3); **HRMS (EI**) m/z calcd for $C_{31}H_{46}O_5Si$ [M^+] 526. 3115, found 326. 3118.



Silyl enol ether 2.1d

Silyl enol ether was prepared according to the general procedure A and isolated as colorless oil.

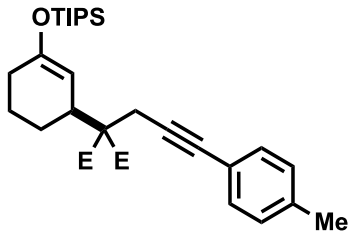
IR (neat, cm^{-1}) ν max 2944, 2867, 1730, 1653, 1188, 883; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.37-7.33 (m, 2H), 7.28-7.23 (m, 3H), 4.21 (ddd, J = 13.1 Hz, 7.2 Hz, 7.2Hz, 4H), 3.39-3.34 (br, 1H), 3.07 (d, J = 16.9 Hz, 1H), 3.01 (d, J = 16.9 Hz, 1H), 2.12-2.01 (m, 2H), 1.80-1.74 (m, 2H), 1.67 (s, 3H), 1.60-1.53 (m, 2H), 1.28 (t, J = 7.2 Hz, 3H), 1.25 (t, J =7.2 Hz, 3H), 1.15-1.10 (m, 3H), 1.07 (d, J =7.3 Hz, 18H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 170.8 (C), 170.7 (C), 131.7 (CHx2), 128.3 (CHx2), 127.7 (CH), 124.0 (C), 110.8 (C),, 87.0 (C), 82.7 (C), 61.5 (C), 61.5 (CH_2), 61.4 (CH_2), 43.2 (CH), 30.3 (CH_2), 25.8 (CH_2), 24.7 (CH_2), 21.4 (CH_2), 18.4 (CH_3x6), 18.3 (C), 15.5 (CH_3), 14.2 (CH_3), 14.1 (CH_3), 13.4 (CHx3); **HRMS (EI)** m/z calcd for [M^+] $C_{32}H_{48}O_5Si$ 540.3271, found 540.3284.



Silyl enol ether 2.1e

Silyl enol ether was prepared according to the general procedure A and isolated as a colorless oil.

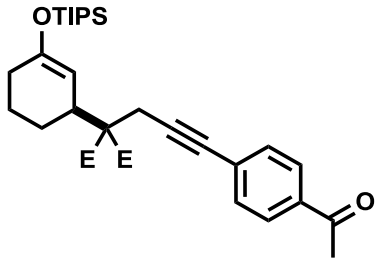
IR (neat, cm^{-1}) ν max 2943, 2867, 1730, 1511, 1248, 1195, 1035; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.29-7.26 (m, 2H), 6.81-6.77 (m, 2H), 4.94-2.92 (m, 1H), 4.21 (dddd, J = 11.1 Hz,, 7.2 Hz,, 7.2 Hz, 7.2 Hz, 2H), 4.21 (dddd, J = 11.1 Hz,, 7.2 Hz,, 7.2 Hz, 7.2 Hz, 2H), 3.79 (s, 3H), 3.28-3.22 (m, 1H), 3.02 (s, 2H), 2.12-1.80 (m, 4H), 1.67-1.55 (m, 1H), 1.48-1.38 (m, 1H), 1.26 (dd, J = 7.1 Hz, 7.1 Hz, 3H), 1.26 (dd, J = 7.1 Hz, 7.1 Hz, 3H), 1.19-1.10 (m, 3H), 1.06 (d, J =7.2 Hz, 18H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 170.3 (C), 170.1 (C), 159.3 (C), 152.8 (C), 133.1 (CHx2), 116.0 (C), 113.9 (CHx2), 104.1 (CH), 84.2 (C), 82.9 (C), 61.4 (CH_2), 61.4 (CH_2), 61.0 (C), 55.4 (CH_3), 39.0 (CH), 29.8 (CH_2), 24.4 (CH_2), 23.4 (CH_2), 22.7 (CH_2), 18.1 (CH_3x6), 14.2 (CH_3), 14.1 (CH_3), 12.7 (CHx3); **HRMS (EI)** m/z calcd for [M^+] $C_{32}H_{48}O_6Si_1$ 556.3220, found 556.3237.



Silyl enol ether 2.1f

Silyl enol ether was prepared according to the general procedure A and isolated as a colorless oil.

IR (neat, cm^{-1}) ν max 3028, 2942, 2865, 1733, 1662, 1511, 1196 1036; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.23 (d, J = 8.0 Hz, 2H), 7.06 (d, J = 7.9 Hz, 2H), 4.93 (s, 1H), 4.20 (m, J = 11.1 Hz, 7.2 Hz, 4H), 3.28-3.22 (m, 1H), 3.02 (s, 2H), 2.32 (s, 3H), 2.16-2.05 (m, 1H), 2.01-1.80 (m, 3H), 1.66-1.54 (m, 1H), 1.48-1.39 (m, 1H), 1.26 (dd, J = 7.1 Hz, 7.1 Hz, 3H), 1.24 (dd, J = 7.1 Hz, 7.1 Hz, 3H), 1.19-.109 (m, 3H), 1.06 (d, J = 6.0 Hz, 18H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 170.2 (C), 170.0(C), 152.7(C), 137.8(C),, 131.5 (CHx2), 129.0 (CHx2), 120.6 (C), 104.0 (CH), 84.9 (C), 83.1(C), 61.4 (CH_2), 61.3 (CH_2), 60.9 (C), 39.0 (CH), 29.8 (CH_2), 24.3 (CH_2), 23.2 (CH_2), 22.6 (CH_2), 21.5 (CH_3), 18.1 (CH_3x6), 14.2 (CH_3), 14.2 (CH_3), 12.6 (CHx3); **HRMS (EI)** m/z calcd for $C_{32}H_{48}O_5Si$ $[(M-C_5H_{10}O_2)^+]$ 497.2723, found

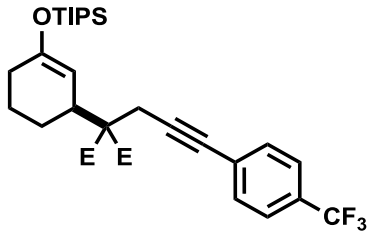


Silyl enol ether 2.1g

Silyl enol ether was prepared according to the general procedure A and isolated as a yellow oil.

IR (neat, cm^{-1}) ν max 2943, 2867, 1735, 1685, 1367, 1263, 1195, 1073; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.84 (d, J = 8.2 Hz, 2H), 7.40 (d, J = 8.5 Hz, 2H), 4.89 (s, 1H), 4.27-4.13 (m, 4H), 3.26-3.20 (m, 1H), 3.03 (s, 2H), 2.56 (s, 3H), 2.15-2.04 (m, 1H), 2.01-1.92 (m, 1H),

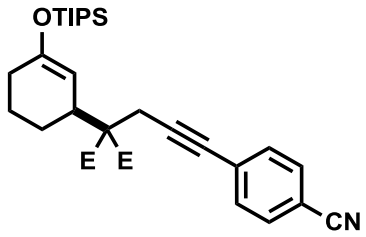
1.90-1.81 (m, 2H), 1.65-1.53 (m, 1H), 1.45-1.36 (m, 1H), 1.25 (dd, J = 7.1 Hz, 7.1 Hz, 3H), 1.24 (dd, J = 7.1 Hz, 7.1 Hz, 3H), 1.16-1.08 (m, 3H), 1.03 (d, J = 6.5 Hz, 18H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 197.4 (C), 170.0 (C), 169.8 (C), 153.0 (C), 136.0 (C), 131.8 (CHx2), 128.6 (C), 128.2 (CHx2), 103.7 (CH), 89.9 (C), 82.5 (C), 61.5 (CH_2), 61.4 (CH_2), 60.8 (C), 39.1 (CH), 29.7 (CH_2), 26.7 (CH_3), 24.4 (CH_2), 23.2 (CH_2), 22.5 (CH_2), 18.0 (CH_3x6), 14.2 (CH_3), 14.1 (CH_3) 12.6 (CHx3); **HRMS (EI)** m/z calcd for $C_{33}H_{48}O_6Si$ [M^+] 568.3220, found 568.3247.



Silyl enol ether 2.1h

Silyl enol ether was prepared according to the general procedure A and isolated as a yellow-orange oil.

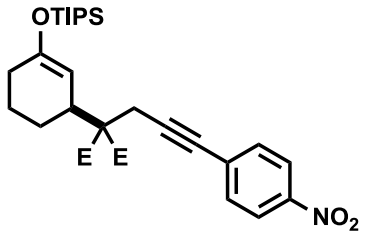
IR (neat, cm^{-1}) ν max 2944, 2868, 1734, 1663, 1465, 1324, 1168, 1068; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.51 (d, J = 8.2 Hz, 2H), 7.43 (d, J = 8.1 Hz, 2H), 4.90 (s, 1H), 4.30-4.15 (m, 4H), 3.27-3.20 (m, 1H), 3.04 (s, 2H), 2.16-2.05 (m, 1H), 2.01-1.94 (m, 1H), 1.91-1.82 (m, 2H), 1.64-1.54 (m, 1H), 1.46-1.35 (m, 1H), 1.26 (dd, J = 7.1 Hz, 7.1 Hz, 3H), 1.25 (dd, J = 7.1 Hz, 7.1 Hz, 3H), 1.17-1.08 (m, 3H), 1.05 (d, J =6.4 Hz, 18H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 170.0 (C), 169.9 (C), 153.0 (C), 131.9 (CHx2), 130.2 (CH), 125.4 (C), 125.2 (q, J_{C-F} = 3.9 Hz) (CHx2), 124.9 (q, J_{C-F} = 3.9 Hz) (C), 103.8 (CH), 88.9 (C), 81.9 (C), 61.5 (CH_2), 61.5 (CH_2), 60.9 (C), 39.2 (CH), 29.8 (CH_2), 24.4 (CH_2), 23.1 (CH_2), 22.6 (CH_2), 18.1 (CH_3x6), 14.2 (CH_3), 14.2 (CH_3) 12.7 (CHx3); **HRMS (EI)** m/z calcd for $C_{32}H_{45}F_3O_5Si_1$ [M^+] 594.2988, found 594.3012.



Sillyl enol ether

Sillyl enol ether was prepared according to the general procedure 1,4-addition of propargyl malonate B and isolated as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, J = 8.6 Hz, 2H), 7.40 (d, 8.6 Hz, 2H), 4.88 (s, 1H), 4.26-4.15 (m, 4H), 3.21 (d, J = 9.2 Hz, 1H), 3.03 (s, 2H), 2.14-2.04 (m, 1H), 2.00-1.92 (m, 1H), 1.85 (dd, J = 10.4 Hz, 4.0 Hz, 2H), 1.63-1.52 (m, 1H), 1.44-1.33 (m, 1H), 1.25 (t, J = 7.1 Hz, 7.1 Hz, 3H), 1.23 (t, J = 7.1 Hz, 7.1 Hz, 3H), 1.17-1.07 (m, 3H), 1.02 (d, J =7.2 Hz, 18H) **; ^{13}C NMR (100 MHz, $CDCl_3$)** δ 169.9 (C_{quat}), 169.7 (C_{quat}), 153.1 (C_{quat}), 132.2 (CHx2), 131.9 (CHx2), 128.6 (C_{quat}), 118.6 (C_{quat}), 111.2 (C_{quat}), 103.6 (CH), 91.3 (C_{quat}), 81.7 (C_{quat}), 61.6 (CH_2), 61.5 (CH_2), 60.8 (C_{quat}), 39.2 (CH), 29.8 (CH_2), 24.4 (CH_2), 23.1 (CH_2), 22.6 (CH_2), 18.1 (CH_3x6), 14.3 (CH_3), 14.2 (CH_3) 12.7 (CHx3); **HRMS (EI)** m/z calcd for $C_{32}H_{45}NO_5Si_1$ 551.3027, found 571.3054

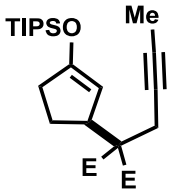


Silyl enol ether 2.1j

Silyl enol ether was prepared according to the general procedure A and isolated as a yellow oil.

IR (neat, cm^{-1}) ν max 2943, 2866, 1733, 1662, 1594, 1520, 1464m 1343, 1195; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.11 (dd, J = 8.9 Hz, 2.2 Hz, 2H), 7.45 (dd, 8.9 Hz, 2.2 Hz, 2H), 4.98-

4.87 (m, 1H), 4.24-4.15 (m, 4H), 3.25-3.19 (m, 1H), 3.04 (s, 2H), 2.15-2.04 (m, 1H), 2.00-1.92 (m, 1H), 1.88-1.81 (m, 2H), 1.63-1.52 (m, 1H), 1.43-1.33 (m, 1H), 1.24 (dd, J = 7.1 Hz, 7.1 Hz, 3H), 1.24 (dd, J = 7.1 Hz, 7.1 Hz, 3H), 1.14-1.07 (m, 3H), 1,03 (d, J =7.3 Hz, 18H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 169.9 (C), 169.7 (C), 153.1 (C), 146.9 (C), 132.4 (CHx2), 130.6 (C), 123.5 (CHx2), 103.6 (CH), 92.4 (C), 81.6 (C), 61.6 (CH_2), 61.5 (CH_2), 60.8 (C), 39.3 (CH), 29.8 (CH_2), 24.4 (CH_2), 23.2 (CH_2), 22.6 (CH_2), 18.0 (CH_3x6), 14.2 (CH_3), 14.2 (CH_3) 12.7 (CHx3); **HRMS (EI)** m/z calcd for [M^+] $C_{31}H_{45}NO_7Si$ 571.2965, found 571.2980.



Silyl enol ether 2.4a

Silyl enol ether was prepared according to the general procedure A and isolated as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.77(dd, J = 3.4 Hz, 1,7 Hz, 1H), 4.24-4.07 (m, 4H), 3.59-3.52 (m, 1H), 2.73 (dq, J = 16.9 Hz, 2.6 Hz, 1H), 2.69 (dq, J= 16.9 Hz, 2.6 Hz, 1H), 2.32-2.21 (m, 2H), 2.04 (dddd, J = 13.2 Hz, 8.8 Hz, 8.8 Hz, 4.5 Hz, 1H), 1.88-1.79 (m, 1H), 1.73 (dd, J = 2.6 Hz, 3H), 1.25 (dd, J = 7.1 Hz, 7.1 Hz, 3H), 1.23 (dd, J = 7.1 Hz, 7.1 Hz, 3H), 1.18-1.13 (m, 3H), 1.06 (d, J= 7.2 Hz, 18H) ; **^{13}C NMR (100 MHz, $CDCl_3$)** δ 170.5 (C_{quat}x2), 156.8 (C_{quat}), 102.9 (CH), 78.2 (C_{quat}), 74.5 (C_{quat}), 61.2 (CH_2x2), 60.8 (C_{quat}), 45.5 (CH), 33.1 (CH_2), 23.7 (CH_2), 23.0 (CH_2), 18.0 (CH_3x6), 17.8 (CH_3), 14.2 (CH_3), 12.5 (CH), 12.0 (CHx3); **HRMS (EI)** m/z calcd for $C_{25}H_{42}O_5Si$ 450.2802, found 450.2790

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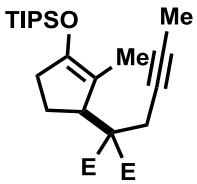
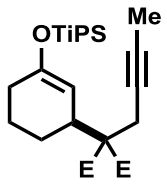


Silyl enol ether 2.4b

Silyl enol ether was prepared according to the general procedure A and isolated as a colorless oil.

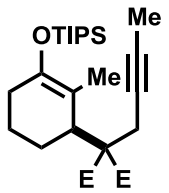
IR (neat, cm^{-1}) ν max 2944, 2867, 1734, 1465, 1225, 883; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 4.22-4.10 (m, 4H), 3.52-3.47 (m, 1H), 2.84 (dq, J = 17.0 Hz, 2.6 Hz, 1H), 2,68 (dq, J = 17.0 Hz, 2,6 Hz, 1H), 2.37-2.27 (m, 1H), 2.23-2.13 (m, 1H), 2.12-2.05 (m, 1H), 1.91 (dddd, J = 13.5 Hz, 9.2 Hz, 4,6 Hz, 4.6 Hz, 1H), 1.73 (dd, J = 2.6 Hz, 2.6 Hz, 3H), 1.54 (d, J = 0.9 Hz, 3H), 1.25 (dd, J = 7.1 Hz, 7.1 Hz, 3H), 1.23 (dd, J = 7.1 Hz, 7.1 Hz, 3H), 1.19-1.10 (m, 3H), 1.07-1.03 (m, 18H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 170.7 (C), 170.5 (C), 150.5 (C), 112.0 (CH), 78.0 (C), 75.0 (C), 61.3 (CH_2), 61.2 (CH_2), 61.1 (C), 48.9 (CH), 32.3 (CH_2), 23.7 (CH_2), 23.3 (CH_2), 18.0 (CH_3x6), 17.8 (CH_3), 14.2 (CH_3), 14.1 (CH_3), 13.0 (CHx3); **HRMS (EI)** m/z calcd for [M^+] $C_{26}H_{44}O_5Si$ 464.2958, found 464.2936.



Silyl enol ether 2.4c

Silyl enol ether was prepared according to the general procedure A and isolated as a clear oil.

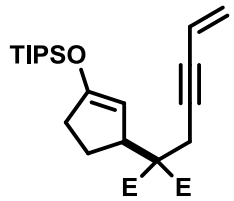
IR (neat, cm^{-1}) ν max 3056, 2943-2867, 1734, 1665, 1464, 1327, 1190; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 4.94-4.89 (m, 1H), 4.18 (dq, J = 15. 5 Hz, 7.1 Hz, 2H), 4.18 (dq, J = 15. 5 Hz, 7.1 Hz, 2H), 3.17-3.11 (m, 1H), 2.75 (dd, J = 5.8 Hz, 2.6 Hz, 2H), 2.13-1.90 (m, 2H), 1.87-1.78 (m, 2H), 1.72 (t, J = 2.5 Hz, 3H), 1.59-1.54 (m, 1H), 1.29-1.18 (m, 1H), 1.24 (t, J = 7.1 Hz, 3H), 1.24 (t, J = 7.1 Hz, 3H), 1.15-1.10 (m, 3H), 1.06 (d, J =7.1 Hz, 18H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 170.3 (C), 170.2 (C), 152.5 (C), 104.2 (CH), 78.3 (C), 74. 5 (C), 61.2 (CH_2), 61.2 (CH_2), 60.8 (C), 38.7 (CH), 29.7 (CH_2), 24.2 (CH_2), 23.0 (CH_2), 22.6 (CH_2), 18.1 (CH_3x6), 14.2 (CH_3x2), 12.7 (CH_3), 12.6 (CHx3); **HRMS (EI)** m/z calcd for $C_{26}H_{44}O_5Si$ [M^+] 464.2958 found 464.2948.



Silyl enol ether 2.4d

Silyl enol ether was prepared according to the general procedure A and isolated as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.21-4.11 (m, 4H), 4.23 (t, J = 5.9 Hz, 1H), 2.75 (dq, J = 16.8 Hz, 2.5 Hz, 1H), 2.71 (dq, J = 16.8 Hz, 2.5 Hz, 1H), 2.06-1.99 (m, 2H), 1.73 (t, J = 2.5 Hz, 3H), 1.71-1.65 (m, 3H), 1.63 (s, 3H), 1.55-1.46 (m, 1H), 1.25 (t, J = 7.2 Hz, 3H), 1.23 (t, J = 7.2 Hz, 3H), 1.13-1.08 (m, 3H), 1.06 (d, J =7.1 Hz, 18H) ; **^{13}C NMR (100 MHz, $CDCl_3$)** δ 171.0 (C_{quat}), 170.9 (C_{quat}), 147.2 (C_{quat}), 111.2 (CH), 77.9 (C_{quat}), 75.4 (C_{quat}), 61.4 (C_{quat}), 61.2 (CH_2), 61.2 (CH_2), 42.9 (CH), 30.3 (CH_2), 25.6 (CH_2), 24.6 (CH_2), 21.2 (CH_2), 18.2 (CH_3x6), 15.5 (CH_3), 14.0 (CH_3x2), 13.7 (CH_3), 12.6 (CHx3), **HRMS (EI)** m/z calcd for $C_{27}H_{46}O_5Si$ 478.3115 found 478.3119.

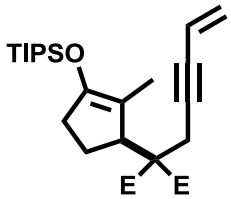


Enyne 2.8a

Silyl enol ether was prepared according to the general procedure A and isolated as a colorless oil in 76% yield.

IR (neat, cm-1)) ν max 1737; **^{1}H NMR (500MHz, $CDCl_3$)** δ = 5.71 (tdd, *J* = 2.2, 11.1, 17.5 Hz, 1 H), 5.52 (dd, *J* = 2.2, 17.5 Hz, 1 H), 5.38 (dd, *J* = 2.2, 11.1 Hz, 1 H), 4.68 (q, *J* = 1.8 Hz, 1 H), 4.25 - 4.10 (m, 4 H), 2.89 (dq, *J* = 2.1, 17.5 Hz, 2 H), 2.32 - 2.20 (m, *J* = 1.9, 9.2 Hz, 2 H), 2.05 (dtd, *J* = 4.6, 8.8, 13.3 Hz, 1 H), 1.89 - 1.79 (m, 1 H), 1.24 (t, *J* = 7.1 Hz, 3 H), 1.25 (t, *J* = 7.2 Hz, 3 H), 1.20 - 1.10 (m, 3 H), 1.08 - 1.02 (m, 18 H); ^{13}C NMR **(126MHz, $CDCl_3$)** δ = 170.3 (C_{quat}), 170.3 (C_{quat}), 157.1 (C_{quat}), 126.3 (CH_2), 117.4 (CH), 102.7 (CH), 86.4 (C_{quat}), 81.6 (C_{quat}), 61.4 (2xCH_2), 60.9 (C_{quat}), 45.7 (CH), 33.1 (CH_2), 23.7

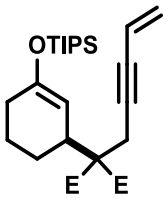
(CH_2), 23.3 (CH_2), 18.0 (9xCH_3), 14.2 (CH_3), 14.2 (CH_3), 12.5 (3xCH); **HRMS (EI)** m/z calcd for $C_{26}H_{42}O_5Si$ [M^+] 462.2802, found 462.2802.



Enyne 2.8b

Silyl enol ether was prepared according to the general procedure A and isolated as a colorless oil in 76% yield.

IR (neat, cm-1)) ν max 2943, 2868, 1738; **^{1}H NMR (400MHz, $CDCl_3$)** δ = 5.72 (tdd, *J* = 2.3, 11.0, 17.5 Hz, 1 H), 5.51 (dd, *J* = 2.3, 17.5 Hz, 2 H), 5.37 (dd, *J* = 2.3, 11.0 Hz, 2 H), 4.26 - 4.10 (m, 4 H), 3.58 - 3.50 (m, 1 H), 3.03 (dd, *J* = 2.2, 17.3 Hz, 1 H), 2.85 (dd, *J* = 2.1, 17.3 Hz, 1 H), 1.54 (s, 3 H), 1.26 (dt, *J* = 3.5, 7.1 Hz, 16 H), 1.07 (s, 12 H), 1.06 (s, 6 H); **^{13}C NMR (101MHz, $CDCl_3$)** δ = 170.4 (C_{quat}), 170.1 (C_{quat}), 150.7 (C_{quat}), 126.0 (CH2), 117.4 (CH), 111.6 (C_{quat}), 86.9 (C_{quat}), 81.3 (C_{quat}), 61.3 (CH_2), 61.3 (CH_2), 61.0 (C_{quat}), 49.0 (CH), 32.2 (CH_2), 23.6 (CH_2), 23.3 (CH_2), 17.9 (CH_3x3), 17.9 (CH_3x3), 14.1 (CH_3), 14.0 (CH_3), 12.8 (CHx3), 11.8 (CH_3); **HRMS (EI)** m/z calcd for $C_{27}H_{44}O_5Si$ [M^+] 476.2958, found 476.2959.

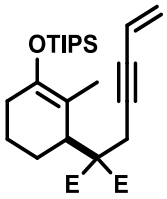


Enyne 2.8c

Silyl enol ether was prepared according to the general procedure A and isolated as a colorless oil in quantitative yield.

IR (neat, cm-1) ν max 2943, 2867, 1734, 1663, 1465, 1368, 1195, 916, 883, 684; **^{1}H NMR (300MHz , $CDCl_3$)** δ = 5.72 (tdd, *J* = 2.0, 11.0, 17.5 Hz, 1 H), 5.51 (dd, *J* = 2.3, 17.6 Hz, 1

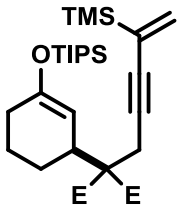
H), 5.37 (dd, *J* = 2.3, 10.9 Hz, 1 H), 4.88 (s, 1 H), 4.24 - 4.12 (m, 4 H), 3.23 - 3.10 (m, 1 H), 2.92 (d, *J* = 2.0 Hz, 2 H), 2.17 - 1.77 (m, 4 H), 1.66 - 1.50 (m, 1 H), 1.43 - 1.02 (m, 4 H), 1.25 (dt, *J* = 5.0, 7.1 Hz, 6 H), 1.07 (s, 12 H), 1.05 (s, 6 H); **^{13}C NMR (75MHz, $CDCl_3$)** δ = 170.1 (C_{quat}), 170.0 (C_{quat}), 152.8 (C_{quat}), 126.3 (CH_2), 117.4 (CH), 103.9 (CH), 86.4 (C_{quat}), 81.8 (C_{quat}), 61.4 (CH_2), 61.3 (CH_2), 60.8 (C_{quat}), 38.9 (CH), 29.7 (CH_2), 24.3 (CH_2), 23.2 (CH_2), 22.6 (CH_2), 18.1 (CHx3), 14.2 (CH_3), 14.2 (CH_3), 12.6 (CH_3x6); **HRMS (EI)** m/z calcd for $C_{27}H_{44}O_5Si$ [M^+] 476.2958, found 476.2982.



Enyne 2.8d

Prepared according to the general procedure 1,4-addition of propargyl malonate B from the corresponding cycloalkenone and isolated in 75% yield as a clear oil.

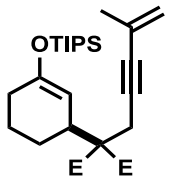
IR (neat, cm-1) ν max 2944, 2867, 1732, 1465, 1188, 924, 883, 681; **^{1}H NMR (300MHz, $CDCl_3$)** δ = 5.73 (tdd, *J* = 2.0, 10.9, 17.6 Hz, 1 H), 5.50 (dd, *J* = 2.4, 17.6 Hz, 1 H), 5.35 (dd, *J* = 2.4, 11.0 Hz, 1 H), 4.18 (qd, *J* = 7.1, 9.9 Hz, 4 H), 3.29 (t, *J* = 5.7 Hz, 1 H), 2.91 (dd, *J* = 2.0, 9.4 Hz, 2 H), 2.18 - 1.93 (m, 2 H), 1.63 (s, 3 H), 1.85 - 1.45 (m, 3 H), 1.26 (dt, *J* = 5.0, 7.1 Hz, 6 H), 1.18 - 0.94 (m, 22 H); **^{13}C NMR (75MHz, $CDCl_3$)** δ = 170.8 (C_{quat}), 170.7 (C_{quat}), 147.6 (C_{quat}), 126.0 (CH_2), 117.7 (CH), 110.8 (C_{quat}), 87.6 (C_{quat}), 81.4 (C_{quat}), 61.5 (CH_2), 61.5 (CH_2), 61.3 (CH), 43.2 (CH), 30.3 (CH_2), 25.8 (CH_2), 24.7 (CH_2), 21.4 (CH_2), 18.2 (CHx3), 15.4 (CH_3), 14.2 (CH_3), 14.0 (CH_3), 13.4 (CH_3x6); **HRMS (EI)** m/z calcd for $C_{28}H_{46}O_5Si$ [M^+] 490.3115, found 490.3126.



Enyne 2.8e

Prepared according to general procedure B from the corresponding terminal alkyne and (1-bromovinyl)trimethylsilane in 55% yield as a clear oil.

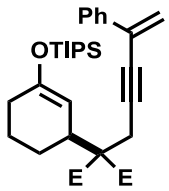
IR (neat, cm-1) 2945, 2866, 1734, 1249, 1197, 841; **^{1}H NMR (400MHz ,$CDCl_3$)** δ = 5.97 (d, *J* = 3.4 Hz, 1 H), 5.61 (d, *J* = 3.5 Hz, 1 H), 4.90 (s, 1 H), 4.22 - 4.11 (m, 4 H), 3.24 - 3.14 (m, 1 H), 3.00 (d, *J* = 5.4 Hz, 2 H), 2.14 - 1.78 (m, 4 H), 1.63 - 1.50 (m, 1 H), 1.44 - 1.32 (m, 1 H), 1.24 (q, *J* = 7.2 Hz, 6 H), 1.20 - 1.09 (m, 3 H), 1.07 (s, 12 H), 1.05 (s, 6 H), 0.12 (s, 9 H); **^{13}C NMR (101MHz, $CDCl_3$)** δ = 170.1 (C_{quat}), 169.9 (C_{quat}), 152.4 (C_{quat}), 134.7 (C_{quat}), 133.4 (CH2), 104.1 (CH), 89.0 (C_{quat}), 84.3 (C_{quat}), 61.2 (CH_2), 61.1 (CH_2), 60.7 (C_{quat}), 38.5 (CH), 29.6 (CH_2), 24.1 (CH_2), 23.9 (CH_2), 22.5 (CH_2), 18.0 (CH3x6), 14.1 (CH_3), 14.1 (CH_3), 12.5 (CHx3), -2.2 (CH_3x3); **HRMS (EI)** m/z calcd for $C_{25}H_{39}O_5Si$ [M^+] 548.3353, found 548.3350.



Enyne 2.8f

Prepared according to general procedure B from the corresponding terminal alkyne and 2-bromoprop-1-ene in 78% yield as a clear oil.

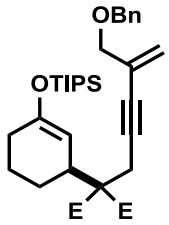
IR (neat, cm-1) ν max 2943, 2867, 1734, 1664, 1464, 1371, 1195, 883, 685; **^{1}H NMR (400MHz, $CDCl_3$)** δ = 5.17 - 5.14 (m, 1 H), 5.12 (dq, *J* = 1.7 Hz, 1 H), 4.87 (s, 1 H), 4.26 - 4.10 (m, 4 H), 3.20 - 3.13 (m, 1 H), 2.91 (d, *J* = 1.7 Hz, 2 H), 2.15 - 2.02 (m, 1 H), 2.01 - 1.91 (m, 1 H), 1.90 - 1.79 (m, 2 H), 1.83 - 1.79 (m, 3 H), 1.67-1.50 (m, 1 H), 1.44 - 1.31 (m, 1 H), 1.25 (q, *J* = 7.2 Hz, 6 H), 1.19 - 1.09 (m, 3 H), 1.07 (s, 12 H), 1.05 (s, 6 H); **^{13}C NMR (101MHz, $CDCl_3$)** δ = 170.0 (C), 169.9 (C), 152.7 (C), 126.9 (C), 120.8 (CH2), 103.8 (CH), 84.7 (C), 84.2 (C), 61.3 (CH_2), 61.2 (CH_2), 60.7 (C), 38.8 (CH), 29.6 (CH_2), 24.2 (CH_2), 23.5 (CH_3), 23.0 (CH_2), 22.5 (CH_2), 18.0 (CH_3x6), 14.1 (CH_3), 14.0 (CH_3), 12.5 (CHx3); **HRMS (EI)** m/z calcd for $C_{28}H_{46}O_5Si$ [M_+] 490.3115, found 490.3134.



Enyne 2.8g

Prepared according to general procedure B from the corresponding terminal alkyne and α-bromostyrene in 53% yield as a clear oil.

IR (neat, cm-1) ν max 2443, 2866, 1731, 1195, 880, 675; **^{1}H NMR (400MHz ,$CDCl_3$)** δ = 7.62 - 7.58 (m, 2 H), 7.35 - 7.27 (m, 3 H), 5.84 (d, *J* = 1.0 Hz, 1 H), 5.55 (d, *J* = 0.7 Hz, 1 H), 4.91 (s, 1 H), 4.24 - 4.14 (m, 6 H), 3.28 - 3.19 (m, 1 H), 3.04 (d, *J* = 2.2 Hz, 2 H), 2.17 - 2.03 (m, 1 H), 2.01 - 1.78 (m, 3 H), 1.55 (s, 1 H), 1.42 (ddt, *J* = 2.4, 10.2, 12.5 Hz, 1 H), 1.24 (dt, *J* = 4.0, 7.1 Hz, 6 H), 1.19 - 1.09 (m, 3 H), 1.08 - 1.06 (m, 12 H), 1.06 - 1.04 (m, 6 H); **^{13}C NMR (101MHz, $CDCl_3$)** δ = 170.0 (C), 169.9 (C), 152.7 (C), 137.4 (C), 130.6 (C), 128.2 (CHx2), 128.1 (CH), 126.0 (CHx2), 119.9 (CH_2), 103.8 (CH), 87.2 (C), 82.1 (C), 61.4 (CH_2), 61.3 (CH_2), 60.8 (C), 39.0 (CH), 29.6 (CH_2), 24.3 (CH_2), 23.3 (CH_2), 22.5 (CH_2), 18.0 (CHx3), 14.0 (CH_3), 14.0 (CH_3), 12.5 (CH_3x6); **HRMS (EI)** m/z calcd for $C_{33}H_{48}O_5Si$ [M^+] 552.3271, found 552.3245.

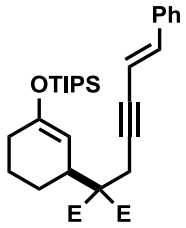


Enyne 2.8h

Prepared according to general procedure B from the corresponding terminal alkyne and ((2-bromoallyloxy)methyl)benzene in 57% yield as a clear oil.

IR (neat, cm-1) ν max 2943, 2866, 1734, 1662, 1368 1221, 1194, 1096, 881, 752, 681; **^{1}H NMR (400MHz, $CDCl_3$)** δ = 7.40 - 7.24 (m, 5 H), 5.49 (q, *J* = 1.7 Hz, 1 H), 5.43 - 5.40 (m, 1 H), 4.86 (s, 1 H), 4.53 (s, 2 H), 4.30 - 4.09 (m, 4 H), 3.96 (t, *J* = 1.3 Hz, 2 H), 3.22 - 3.10 (m, 1 H), 2.94 (d, *J* = 3.5 Hz, 2 H), 2.14 - 2.02 (m, 1 H), 1.95 (td, *J* = 2.8, 17.0 Hz, 1 H),

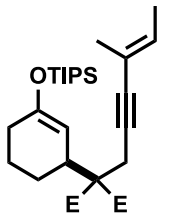
1.91 - 1.77 (m, 2 H), 1.61 - 1.49 (m, 1 H), 1.45 - 1.30 (m, 1 H), 1.23 (dt, *J* = 4.5, 7.1 Hz, 6 H), 1.19 - 1.09 (m, 3 H), 1.07 (s, 12 H), 1.06 (s, 6 H); **^{13}C NMR (101MHz, $CDCl_3$)** δ = 170.0 (C), 169.8 (C), 152.7 (C), 138.1 (C), 128.4 (C), 128.4 (CHx2), 127.7 (CHx2), 127.6 (CH), 121.0 (CH_2), 103.7 (CH), 86.7 (C), 81.3 (C), 72.2 (CH_2), 72.1 (CH_2), 61.3 (CH), 61.2 (CH_2), 60.7 (C), 38.9 (CH), 29.6 (CH_2), 24.2 (CH_2), 23.1 (CH_2), 22.5 (CH_2), 18.0 (CHx3), 14.1 (CH_3), 14.0 (CH_3), 12.5 (CH_3x6); **HRMS (EI)** m/z calcd for $C_{35}H_{42}O_6Si$ [$(M-CH_2Ph)^+$] 505.2985, found 505.2977.



Enyne 2.8i

Prepared according to general procedure B from the corresponding terminal alkyne and (E)-(2-iodovinyl)benzene in 89% yield as a clear oil.

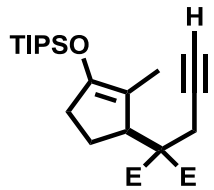
IR (neat, cm-1) ν max 2943, 2866, 1731, 1661, 1463, 1367, 1195, 748, 690; **^{1}H NMR (400MHz, $CDCl_3$)** δ = 7.36 - 7.23 (m, 5 H), 6.82 (d, *J* = 16.3 Hz, 1 H), 6.09 (td, *J* = 1.9, 16.2 Hz, 1 H), 4.91 (s, 1 H), 4.27 - 4.14 (m, 4 H), 3.21 (d, *J* = 9.2 Hz, 1 H), 2.99 (d, *J* = 1.7 Hz, 2 H), 2.18 - 1.79 (m, 4 H), 1.68 - 1.49 (m, 1 H), 1.45 - 1.33 (m, *J* = 11.9 Hz, 1 H), 1.26 (q, *J* = 7.3 Hz, 6 H), 1.23 - 1.10 (m, 3 H), 1.08 (s, 12 H), 1.06 (s, 6 H); **^{13}C NMR (101MHz, $CDCl_3$)** δ = 170.0 (C), 169.9 (C), 152.7 (C), 140.6 (CH), 136.4 (C), 128.6 (CHx2), 128.3 (CH), 126.1 (CHx2), 108.5 (CH), 103.8 (CH), 88.0 (C), 82.1 (C), 61.3 (CH_2), 61.3 (CH_2), 60.8 (C), 38.9 (CH), 29.7 (CH_2), 24.2 (CH_2), 23.4 (CH_2), 22.5 (CH_2), 18.0 (CHx3), 14.1 (CH_3), 14.1 (CH_3), 12.5 (CH_3x6); **HRMS (EI)** m/z calcd for $C_{33}H_{48}O_5Si$ [M^+] 552.3271, found 552.3260.



Enyne 2.8j

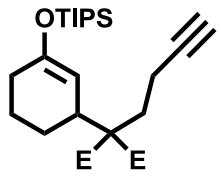
Prepared according to general procedure B from the corresponding terminal alkyne and (E)-2-bromobut-2-ene in 52% yield as a clear oil.

IR (neat, cm-1) ν max 2943, 2867, 1734, 1663, 1465, 1366, 1223, 1194, 884, 680; **^{1}H NMR (300MHz, $CDCl_3$)** δ = 5.75 (qq, *J* = 1.3, 7.0 Hz, 1 H), 4.86 (s, 1 H), 4.22 - 4.08 (m, 4 H), 3.19 - 3.10 (m, 1 H), 2.87 (s, 2 H), 2.12 - 1.98 (m, 1 H), 1.98 - 1.92 (m, 1 H), 1.92 - 1.74 (m, *J* = 4.8 Hz, 2 H), 1.67 (t, *J* = 1.3 Hz, 3 H), 1.60 (dd, *J* = 0.9, 7.0 Hz, 3 H), 1.65 - 1.27 (m, 2 H), 1.22 (dt, *J* = 5.5, 7.1 Hz, 6 H), 1.04 (s, 12 H), 1.02 (s, 6 H), 1.16 - 1.00 (m, 3 H); **^{13}C NMR (75MHz, $CDCl_3$)** δ = 170.0 (C), 169.9 (C), 152.4 (C), 131.2 (CH), 118.4 (C), 103.9 (CH), 86.0 (C), 81.3 (C), 61.1 (CH_2), 61.0 (CH_2), 60.7 (C), 38.6 (CH), 29.6 (CH_2), 24.1 (CH_2), 23.0 (CH_2), 22.4 (CH_2), 17.9 (CHx3), 16.9 (CH_3), 14.0 (CH_3), 14.0 (CH_3), 13.8 (CH_3), 12.5 (CH_3x6); **HRMS (EI)** m/z calcd for $C_{29}H_{48}O_5Si$ [M^+] 504.3271, found 552.3256.



Enyne 3.1

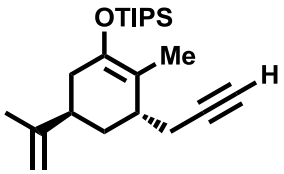
Prepared according to general procedure A in 80% yield as a colorless oil. Exhibited spectral data in accordance with previous report.[66]



Enyne 3.7

Silyl enol ether was prepared according to the general procedure A and isolated as a colorless oil in 74% yield.

IR (neat, cm-1) ν max 3312, 2943, 2867, 1722; **^{1}H NMR (500MHz, $CDCl_3$)** δ = 4.86 (br. s, 1 H), 4.23 - 4.13 (m, 4 H), 3.00 - 2.93 (m, 1 H), 2.33 - 1.99 (m, 7 H), 1.93 (t, *J* = 2.6 Hz, 1 H), 1.87 - 1.76 (m, 1 H), 1.74 - 1.65 (m, 1 H), 1.60 - 1.48 (m, 1 H), 1.30 - 1.20 (m, 6 H), 1.18 - 1.09 (m, 3 H), 1.06 (s, 9 H); **^{13}C NMR (126MHz, $CDCl_3$)** δ = 170.6 (C_{quat}), 170.6 (C_{quat}), 152.4 (C_{quat}), 104.0 (CH), 84.0 (C_{quat}), 68.4 (CH), 61.2 (CH_2), 61.1 (CH_2), 60.6 (C_{quat}), 40.1 (CH), 31.6 (CH_2), 29.7 (CH_2), 24.4 (CH_2), 22.6 (CH_2), 18.1 (9xCH_3), 14.9 (CH_2), 14.2 (2xCH_3), 12.6 (3xCH); **HRMS (EI)** m/z calcd for $C_{26}H_{44}O_5Si$ [M^+] 464.2958, found 464.2944.



Silyl enol ether 3.9

Prepared according to literature procedure and exhibited spectral data in accordance with previous report.[67]

General Procedure C – Au(I)-Catalyzed cyclizations

The flask was charged with silyl enol ether (0.175 mmol), solvent (2 mL) and the cationic gold(I) complex (0.0087 mmol, 5 mol%). The mixture was stirred for 1 to 42 hours at room temperature. The reaction was monitored by TLC. Upon completion, the solvent was removed under reduced pressure and the residue was purified by flash column chromatography on silica gel eluted with hexane/AcOEt (9:1 to 6:1) to give the cyclization products.

Note 1: When hydrolysis of the starting material was an issue, flasks uses were kept in a base bath prior to performing the reaction. (Base Bath preparation: KOH pellets (70 g) were dissolved in iPrOH (1L) and distilled water (200 mL)). The flasks from the base bath were washed with water, rinsed with acetone prior usage and dry in the oven (60 °C) for a couple of hours.

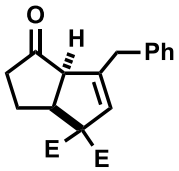
Note 2: When DCM was used as the solvent, dry conditions were necessary for reproducibility of these results. The round bottom flask was flame-dried and the solvent distilled over CaH_2.

General Procedure D – Ag(I)–Catalyzed cyclizations

A reaction vessel was charged with a magnetic stirrer and purged with argon. A solution of the silyl enol ether (0.100 mmol), solvent (1.5 ml), water (75 μL) and the appropriate Ag(I) catalyst (0.010 mmol) is added via seringe. The reaction mixture is stirred at r.t. or 60°C for 1.5 days. Upon completion, the solvent was removed under reduced pressure and the residue was purified by flash column chromatography on silica gel eluted with hexane/AcOEt (9:1 to 6:1) to give the cyclization products.

General Procedure E – Cu(I)–Catalyzed cyclizations

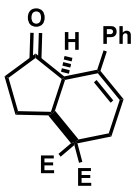
A reaction vessel was charged with a magnetic stirrer and the appropriate Cu(I) catalyst (0.010 mmol). This vessel is then purged with argon and a solution of the silyl enol ether (0.100 mmol), solvent (1.5 ml) and water (75 μL) is added via seringe. The reaction mixture is stirred at r.t. or 60°C for 1.5 days. Upon completion, the solvent was removed under reduced pressure and the residue was purified by flash column chromatography on silica gel eluted with hexane/AcOEt (9:1 to 6:1) to give the cyclization products.



Bicyclo[3,3,0]alkenone 2.2a

Isolated as a colorless oil.

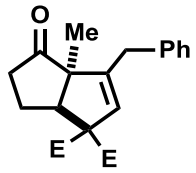
IR (neat, cm^{-1}) ν max 2980-2891, 1703, 1368, 1259, 1067; **mp (°C)** 85.3-88.7; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.62-7.57 (m, 2H), 7.34-7.22(m, 3H), 6.54-6.52 (m, 1H), 4.26 (dddd, J = 10.7 Hz, 7.2 Hz, 7.2 Hz, 7.2 Hz, 2H), 4.18 (q, J =7.1 Hz, 2H), 3.78-3.67 (m, 2H), 3.16 (ddd, J =15.6 Hz, 1.9 Hz, 1,9 Hz, 1H), 2.82 (d, J = 15.9 Hz, 1H), 2.51-2.33 (m, 2H), 2.16-2.07 (m, 1H), 1.64-1.54 (m, 1H), 1.29 (t, J = 7,2 Hz, 3H), 1.23 (t, J = 7.2 Hz, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 215.8 (C), 170.9 (C), 169.6 (C), 136.4 (C), 135.7 (C), 128.4 (C_H), 128.0 (CHx2), 128.0 (CH), 127.5 (CHx2), 62.2 (C), 61.9 (CH_2), 61.8 (CH_2), 53.2 (CH), 45.6 (CH), 42.3 (CH_2), 39.7 (CH_2), 23.0 (CH_2), 14.3 (CH_3), 14.2(CH_3); **HRMS (EI)** m/z calcd for $C_{21}H_{24}O_5$ [M^+] 356.1623, found 356.1609.



Bicyclo[4,3,0]alkenone 2.3a

Isolated as a colorless oil.

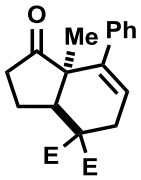
IR (neat, cm^{-1}) ν max 2994-2855, 1729, 1236, 1097; **mp (°C)** 69.6- 72.5; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.32-7.19 (m, 5H), 5.86 (ddd, J =4.4 Hz, 4.4 Hz, 2.2 Hz, 1H), 4.30-4.07 (m, 4H), 3.88 (dd, J = 7.8 Hz, 1.5 Hz, 1H), 3.34 (ddd, J = 12.0 Hz, 7.5 Hz, 7.5 Hz, 1H), 2.86 (dd, J = 4.2 Hz, 2.9 Hz, 2H), 2.33-2.12 (m, 2H), 1.92-1.84 (m, 1H), 1.75 (ddd, J = 12.2 Hz, 9.2 Hz, 2.8 Hz, 1H), 1.27 (t, J = 7.1 Hz, 3H), 1.19 (t, J = 7.2 Hz, 3H) ; **^{13}C NMR (100 MHz, $CDCl_3$)** δ 214.0 (C), 170.7 (C), 170.3 (C), 140.1 (C), 134.3 (C), 128.1 (CHx2), 127.4 (CH), 126.9 (CHx2), 123.4 (CH), 61.9 (CH_2), 61.8 (CH_2), 55.1 (C), 50.0 (CH), 39.7 (CH), 36.8 (CH_2), 26.7 (CH_2), 22.6 (CH_2), 14.3 (CH_3), 14.1 (CH_3); **HRMS (EI)** m/z calcd for $C_{21}H_{24}O_5$ [M^+] 356.1623, found 356.1635.



Bicyclo[3.3.0]alkenone 2.2b

Isolated as a white powder.

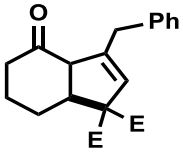
IR (neat, cm^{-1}) ν max 2983, 1734, 1469, 1257, 1153; **mp (°C)** 68.6-70.4; **^{1}H NMR (400 MHz, $CDCl_3$)** δ ppm 7.43 (dd, J = 6.9 Hz, 0.6 Hz, 1H) 7.33-7.12 (m, 4 H) , 6.62 (s, 1H), 4.32-4.15 (m, 4H), 3.35 (dd, J=16.4, 2.4 Hz, 1H), 3.28 (dd, J = 7.9 Hz, 7.9 Hz, 1H), 3.02 (ddd, J=16.5 Hz, 1.3 Hz, 1.3 Hz, 1H), 2.32 (dd, J=16.6 Hz, 2.3 Hz, 1H), 2.32 (s, 1H), 2.04 (dddd, J=13.7 Hz, 8.4 Hz, 8.4 Hz, 6.7 Hz, 1H), 1.67-1.49 (m, 1H) 1.28 (ddd, J = 7.1Hz, 7.1 Hz, 4.0 Hz, 6H), 1.16 (s, 3H) ; **^{13}C NMR (100 MHz, $CDCl_3$)** δ 216.6 (C), 171.1 (C), 169.7 (C), 140.7 (C), 136.3 (C), 129.3(CHx2), 127.7 (CHx2), 127.6 (CH), 127.1 (CH), 62.0 (C), 61.9 (CH_2), 61.8(CH_2), 59.5 (C), 54.7 (CH), 43.3 (CH_2), 37.1 (CH_2), 21.9 (CH_2), 21.8 (CH_3), 14.3(CH_3), 14.2 (CH_3); **HRMS (EI)** m/z calcd for [M^+] $C_{22}H_{27}O_5$ 371.1859, found 371.1887.



Bicyclo[4.3.0]alkenone 2.3b

Isolated as a colorless oil.

IR (neat, cm^{-1}) ν max 2976, 2941, 2904, 1734, 1492, 1444, 1257; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.24-7.21 (m, 3H), 6.94-6.91 (m, 2H), 5.67 (dd, J = 5.7 Hz, 2.5 Hz, 1H), 4.32-4.21 (m, 2H), 4.21-4.12 (m, 2H), 3.11 (dd, J = 18.4 Hz, 6.1 Hz, 1H), 3.05 (dd, J = 11.1 Hz, 7.0 Hz, 1H), 2.57 (dd, J = 18.7 Hz, 2.3 Hz, 1H), 2,50 (dt, J = 9.5 Hz, 2.3 Hz, 1H), 2.41-2.34 (m, 1H), 2.30-2.20 (m, 1H), 1.87-1.76 (m, 1H), 1.29 (t, J = 7.1 Hz, 6H), 1.13 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 216.1 (C), 170.3 (C), 170.2 (C), 140.5 (C), 137.9 (C), 129.4 (CHx2), 127.5 (CH), 127.2 (CHx2), 126.3 (CH), 61.9 (CH_2x2), 54.3 (C), 54.3 (C), 46.8 (CH), 35.2 (CH_2), 27.2 (CH_2), 22.0 (CH_2), 21.7 (CH_3), 14.2 (CH_3), 14.1 (CH_3); **HRMS (EI)** m/z calcd for [M^+] $C_{22}H_{26}O_5$ 370.1780, found 370. 1777.

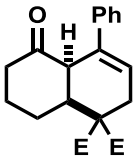


Bicyclo[4.3.0]alkenone 2.2c

Isolated as a white powder.

IR (neat, cm^{-1}) ν max 2987, 2932, 1736, 1454, 1254, 1238, 1153; **mp (°C)** 116.9-118.7 ; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.27-7.22 (m, 2H), 7.20-7.16 (m, 1H), 7.13-7.10 (m, 2H), 6.60 (d, J = 1.8Hz, 1H), 4.29-4.12 (m, 4H), 3.80 (d, J= 7.5 Hz, 1H), 3.54 (ddd, J = 17.4 Hz, 2.3 Hz, 2.3 Hz, 1H), 3.34 (ddd, J = 12.3 Hz, 6.1 Hz, 6.1 Hz, 1H), 3.02 (d, J = 17.4 Hz, 1H), 2.21-2.13 (m, 1H), 2.07-2.02 (m,1H), 1.95-1.87(m, 1H), 1.74-1.61 (m, 2H), 1.43 (ddd, J = 12.6, 12.6 Hz, 3.8Hz, 1H), 1.26 (t, J = 7.2 Hz, 6H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 210.2 (C), 171.1 (C), 169.5 (C), 137.9 (C), 136.2 (C), 128.9 (CHx2), 128.1 (CHx2), 127.2 (CH), 126.8 (CH), 62.0 (C), 61.9 (CH_2), 56.9 (CH), 49.2 (CH), 40.5 (CH_2), 39.0 (CH_2), 24.9

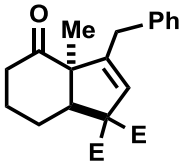
(CH_2), 24.1 (CH_2), 14.2 (CH_3), 14.1 (CH_3); **HRMS (EI)** m/z calcd for $C_{22}H_{26}O_5$ [M^+] 370.1780, found 370.1792.



Bicyclo[4.4.0]alkenone 2.3c

Isolated as a colorless oil.

IR (neat, cm^{-1}) ν max 2980, 2941, 2867, 1732, 1444, 1254, 1180, 1044; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.26-7.16 (m, 5H), 5.94 (ddd, J = 5.4 Hz, 2.7 Hz, 2.7 Hz, 1H), 4.27-4.15 (m, 4H), 3.94 (br, 1H), 3.08-3.00 (m, 1H), 3.04-3.00 (m, 1H), 2.82 (ddd, J = 19.3 Hz, 4.3 Hz, 2.5 Hz, 1H), 2.10-1.96 (m, 3H), 1.71-1.59 (m, 3H), 1.26 (t, J = 7.1 Hz, 3H), 1.26 (t, J = 7.1 Hz, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 211.7 (C), 170.0 (C), 169.7 (C), 140.0 (C), 134.4 (C), 128.3 (CHx2), 127.5 (CH), 127.2 (CHx2), 124.6 (CH), 62.0 (CH_2), 61.9 (CH_2), 56.2 (C), 53.0 (CH), 40.9 (CH), 39.9 (CH_2), 27.5 (CH_2), 26.1 (CH_2), 23.6 (CH_2), 14.1 (CH_3), 14.1 (CH_3); **HRMS (EI)** m/z calcd for $C_{22}H_{26}O_5$ [M^+] 370.1780, found 370.1778.

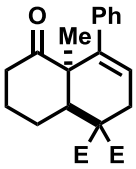


Bicyclo[4.3.0]alkenone 2.2d

Isolated as a white powder.

IR (neat, cm^{-1}) ν max 2982, 2940, 2867, 1732, 1711, 1445, 1256, 1178, 1049; **mp (°C)** 79.7 - 82.3; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.24-7.12 (m, 4H), 7.04 (dd, J = 7.3 Hz, 0.9 Hz, 1H), 6.55 (s, 1H), 4,28-4.10 (m, 4H), 3.63 (dd, J = 18.0 Hz, 1.9 Hz, 1H), 3.31 (dd, J = 17.9 Hz, 1.4 Hz, 1H), 3.12 (dd, J = 11.4 Hz, 5.1 Hz, 1H), 2.08-2.02 (m, 1H), 1.94-1.81 (m, 2H), 1.57-1.44 (m, 3H), 1.31-1.24 (m, 6H), 1.27 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 211.8

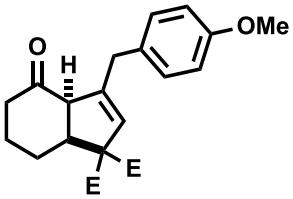
(C), 171.8 (C), 169.7 (C), 144.5 (C), 136.4 (C), 129.0 (CHx2), 127.9 (CHx2), 127.2 (CH), 124.9 (CH), 62.5 (C), 62.1 (CH_2), 60.3(C), 57.1 (CH), 40.3 (CH_2), 39.2 (CH_2), 25.8 (CH_2), 25.4 (CH_2), 23.1 (CH_3), 14.2 (CH_3), 14.1 (CH_3); **HRMS (EI)** m/z calcd for [M^+] $C_{23}H_{28}O_5$ 384.1937, found 384.1927.



Bicyclo[4.4.0]alkenone 2.3d

Isolated as a colorless oil.

IR (neat, cm^{-1}) ν max 3062**,** 2981, 2941 1731, 1297, 1232, 1096; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.24-7.12 (5H), 5.92 (dd, J = 4.8 Hz, 2.2 Hz, 1H), 4.30-4.10 (m,4H), 3.29 (dd, J = 19.6 Hz, 4.9 Hz, 2H), 2,94 (dd, J = 11.7 Hz, 7.9 Hz, 1H), 2.76 (dd, J = 19.6 Hz, 3.2 Hz, 1H), 2.28-2.15 (m, 1H), 2.01-1.81 (m, 2H), 1.75-1.62 (m, 2H), 1.42 (s, 3H), 1.31-1.24 (m, 6H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 212.1 (C), 170.9 (C), 170.4 (C), 140.6 (C), 139.6 (C), 128.3 (CHx2), 127.8 (CH), 127.3 (CHx2), 125.6 (CH), 62.0 (CH_2), 62.0 (CH_2), 56.4 (C), 55.4 (C), 49.1 (CH), 40.9 (CH_2), 27.5 (CH_2), 26.2 (CH_2), 25.9 (CH_2), 23.0 (CH_3), 14.1 (CH_3), 13.9 (CH_3); **HRMS (EI)** m/z calcd for [M^+] $C_{23}H_{28}O_5$ 384.1937, found 384.1932.

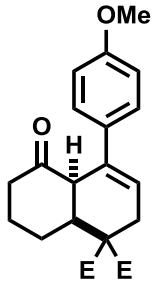


Bicyclo[4.3.0]alkenone 2.2e

Isolated as a colorless oil.

IR (neat, cm^{-1}) ν max 2980, 2920, 1730, 1701, 1511, 1250, 1176; **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.04 (d, J = 8.7 Hz, 2H), 6.77 (d, J = 8.9 Hz, 2H), 6.51 (d, J = 2.1 Hz, 1H), 4.30-4.20 (m, 4H), 3.81-3.15 (m, 1H), 3.76 (s, 3H), 3.52 (ddd, J = 17.6 Hz, 2.4 Hz, 2.4 Hz, 1H),

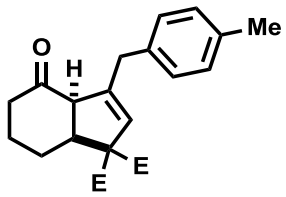
3.52 (ddd, J = 12.4 Hz, 6.5 Hz, 5.6 Hz, 1H), 3.02 (d, J = 17.6 Hz, 1H), 2.23-2.13 (m, 1H), 2.07-1.99 (m, 1H), 1.96-1.85 (m, 1H), 1.74-1.56 (m, 2H), 1.42 (qd, J = 13.2 Hz, 3.9 Hz, 1H), 1.25 (t, J = 7.1 Hz, 6H), 1.25 (t, J = 7.1 Hz, 6H); **^{13}C NMR (75 MHz, $CDCl_3$)** δ 210.6 (C), 171.1 (C), 169.5 (C), 158.7 (C), 136.2 (C), 130.1 (CHx2), 128.8 (C), 126.3 (CHx2), 113.4 (CH), 62.0 (C), 61.9 (CH_2), 61.8 (CH_2), 57.0 (CH), 55.2 (CH_3), 49.2 (CH), 40.3 (CH_2), 39.9 (CH_2), 24.9 (CH_2), 24.2 (CH_2), 14.2 (CH_3), 14.1 (CH_3); **HRMS (EI)** m/z calcd for [M^+] $C_{23}H_{28}O_6$ 400.1886, found 400.1855.



Bicyclo[4.4.0]alkenone 2.3e

Isolated as a colorless oil.

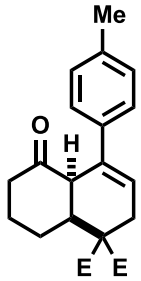
IR (neat, cm^{-1}) ν max 2982, 2940, 1733, 1714, 1609, 1512, 1245, 1181; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.16-7.13 (m, 2H), 6.80-6.76 (m, 2H), 5.87 (ddd, J = 5.4 Hz, 2.6 Hz, 2.6 Hz, 1H), 4.21 (dq, J = 16.4 Hz, 7.1 Hz, 2H), 4.21 (dq, J = 16.4 Hz, 7.1 Hz, 2H), 3.91 (br, 1H), 3.76 (s, 3H), 3.06-2.98 (m, 1H), 3.03-2.98 (m, 1H), 2.81 (ddd, J = 4.6 Hz, 2.5 Hz, 2.5 Hz, 1H), 2.10-1.97 (m, 3H), 1.71-1.59 (m, 3H), 1.26 (dd, J = 7.1 Hz, 7.1 Hz, 3H), 1.24 (dd, J = 7.1 Hz, 7.1 Hz, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 212.0 (C), 170.1 (C), 169.8 (C), 133.8 (C), 132.6 (C), 128.4 (CHx2), 123.3 (CHx2), 113.6 (CH), 62.0 (CH_2), 61.9 (CH_2), 56.2 (C), 55.3 (CH), 53.0 (CH_3), 40.9 (CH), 39.9 (CH_2), 27.5 (CH_2), 26.1 (CH_2), 23.6 (CH_2), 14.2 (CH_3), 14.1 (CH_3); **HRMS (EI)** m/z calcd for $C_{23}H_{28}O_6$ [M^+] 400.1886, found 400.1874.



Bicyclo[4.3.0]alkenone 2.2f

Isolated as a colorless oil.

IR (neat, cm^{-1}) ν max 2975-2865, 1738, 1714, 1260, 1235, 1182; **mp (°C)** 69.0 –75.3; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.08-6.98 (m, 4H), 6.55 (d, J = 1.5 Hz, 1H), 4.28-4.11 (m, 4H), 3.79 (d, J = 7.4 Hz, 1H), 3.52 (ddd, J = 17.4 Hz, 2.3 Hz, 2.3 Hz, 1H), 3.32 (ddd, J = 12.3 Hz, 6.2 Hz, 6.2 Hz, 1H), 3.01 (d, J = 17.4 Hz, 1H), 2.28 (s, 3H), 2.21-2.13 (m, 1H), 2.07-1.97 (m, 1H), 1.94-1.86 (m, 1H), 1.71-1.57 (m, 2H), 1.47-1.37 (m, 1H), 1.26 (t, J = 7.1 Hz, 3H) , 1.23 (t, J = 7.1 Hz, 3H) ; **^{13}C NMR (100 MHz, $CDCl_3$)** δ 210.4 (C), 171.1 (C), 169.5 (C), 137.0 (C), 136.9 (C), 133.3 (C), 128.7 (CHx2), 128.7 (CH), 126.6 (CHx2), 61.9 (C), 61.9 (CH_2x2), 56.9 (CH), 49.2 (CH), 40.4 (CH_2), 38.9 (CH_2), 24.9 (CH_2), 24.1 (CH_2), 21.3 (CH_3) 14.2 (CH_3), 14.1 (CH_3);

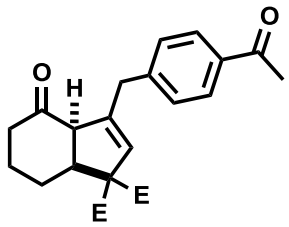


Bicyclo[4.4.0]alkenone 2.3f

Isolated as a colorless oil.

IR (neat, cm^{-1}) ν max 2979, 2941, 2866, 1733, 1714, 1445, 1234, 1180,1044; **mp (°C)** 89.5-91.6 ; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.12-7.03 (m, 4H), 5.91 (ddd, J = 5.4 Hz, 2.6 Hz, 2.6 Hz, 1H), 4.27-4.15 (m, 4H), 3.91 (br, 1H), 3.07-2.99 (m, 2H), 2.81 (ddd, J = 19.2 Hz, 2.5 Hz, 1.7 Hz, 1H), 2.27 (s, 3H), 2.07-1.98 (m, 3H), 1.70-1.62 (m, 3H), 1.26 (t, J = 7.1 Hz, 3H), 1.24 (t, J = 7.1 Hz, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 211.9 (C), 170.0 (C), 169.7 (C), 137.2 (C), 137.1 (C), 134.3 (C), 129.0 (CHx2), 127.0 (CHx2), 123.9 (CH), 62.0 (CH_2), 61.9

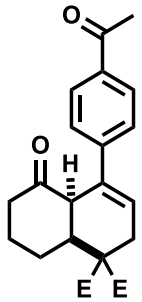
(CH_2), 56.2 (C), 53.0 (CH), 40.9 (CH), 39.9 (CH_2), 27.5 (CH_2), 26.1 (CH_2), 23.6 (CH_2), 21.2 (CH_3), 14.2 (CH_3), 14.1 (CH_3); **HRMS (EI)** m/z calcd for $C_{23}H_{28}O_5$ [M^+] 384.1937, found 384.1928



Bicyclo[3,4,0]alkenone 2.2g

Isolated as a colorless oil.

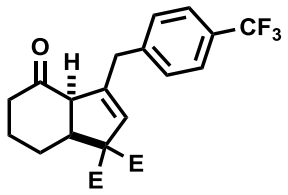
IR (neat, cm^{-1}) ν max 2973, 2947, 1730, 1698, 1256, 1233, 1043; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.84 (d, J = 8.3 Hz, 2H), 7.21 (d, J = 8.2 Hz, 2H), 6.61 (d, J = 1.8 Hz, 1H), 4.29-4.12 (m, 4H), 3.84 (d, J = 7.6 Hz, 1H), 3.55 (ddd, J = 17.6 Hz, 2.4 Hz, 2.4 Hz, 1H), 3.37 (ddd, J = 11.6 Hz, 7.2 Hz, 5.6 Hz, 1H), 3.03 (d, J = 17.6 Hz, 1H), 2.56 (s, 3H), 2.20-2.04 (m, 2H), 1.96-1.87 (m, 1H), 1.76-1.62 (m, 2H), 1.48-1.38 (m, 1H), 1.26 (t, J = 7.1 Hz, 6H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 209.5 (C), 197.7 (C), 171.0 (C), 169.3 (C), 141.0 (C), 140.1 (C), 135.6 (C), 128.9 (CHx2), 128.2 (CHx2), 126.0 (CH), 62.0 (CH_2), 61.9 (CH_2), 61.8 (C), 56.8 (CH), 49.0 (CH), 40.9 (CH_2), 39.0 (CH_2), 26.7 (CH_3), 24.6 (CH_2), 24.1 (CH_2), 14.2 (CH_3), 14.1 (CH_3); **HRMS (EI)** m/z calcd for $C_{24}H_2O_6$ [M^+] 412.1886, found 412.1879.



Bicyclo[4,4,0]alkenone 2.3g

Isolated as a colorless oil.

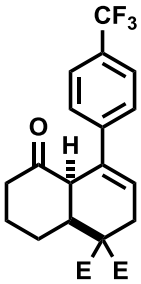
IR (neat, cm^{-1}) ν max 2977-2869, 1733, 1684, 1268, 1168, 1057; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.84 (d, J = 8.5 Hz, 2H), 7.31 (d, J = 8.4 Hz, 2H), 6.06 (ddd, J = 5.4 Hz, 2.7 Hz, 2.7 Hz, 1H), 4.28-4.16 (m, 4H), 3.96 (br, 1H), 3.10-3.02 (m, 2H), 2.85 (ddd, J = 19.5 Hz, 4.2 Hz, 2.6 Hz, 1H), 2.55 (s, 3H), 2.03-1.98 (m, 3H), 1.70-1.62 (m, 3H), 1.26 (dd, J = 7.1 Hz, 7.1 Hz 3H), 1.26 (dd, J = 7.1 Hz, 7.1 Hz, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 211.2 (C), 197.7 (C), 169.8 (C), 169.6 (C), 144.6 (C), 136.0 (C), 133.7 (C), 128.5 (CHx2), 127.4 (CHx2), 126.6 (CH), 62.1 (CH_2), 62.0 (CH_2), 56.1 (C), 52.8 (CH), 40.8 (CH), 39.8 (CH_2), 27.6 (CH_2), 26.7 (CH_3), 25.9 (CH_2), 23.6 (CH_2), 14.2 (CH_3), 14.1 (CH_3); **HRMS (EI)** m/z calcd for [M^+] $C_{24}H_{28}O_6$ 412.1886, found 412.1881.



Bicyclo[4.3.0]alkenone 2.2h

Isolated as a white solid.

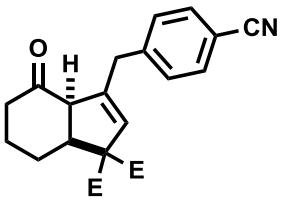
IR (neat, cm^{-1}) ν max 2983-2877, 1732, 1616, 1263, 1122, 1067; **mp (°C)** 73.8-76.6; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.48 (d, J = 8.1 Hz, 2H), 7.23 (d, J = 8.2 Hz, 2H), 6.60 (s, 1H), 4.29-4.11 (m, 4H), 3.81 (d, J = 7.7 Hz, 1H), 3.53 (ddd, J = 17.5 Hz, 2.2 Hz, 2.2 Hz, 1H), 3.38 (ddd, J = 11.5 Hz, 7.4 Hz, 5.8 Hz, 1H), 3.01 (d, J = 17.5 Hz, 1H), 2.20-2.06 (m, 2H), 1.95-1.87 (m, 1H), 1.71-1.62 (m, 2H), 1.48-1.37 (m, 1H), 1.26 (t, J = 6.9 Hz, 3H), 1.26 (t, J = 6.9 Hz, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 209.6 (C), 171.0 (C), 169.5 (C), 140.1 (C), 139.8 (C), 139.8 (C), 129.0 (CHx2), 127.5 (q, J_{C-F} = 266.0 Hz) (C), 125.7 (CH), 125.1 (q, J_{C-F} = 3.8 Hz) (CHx2), 62.0 (CH_2), 62.0 (CH_2), 61.8 (C), 56.7 (CH), 48.9 (CH), 40.9 (CH_2), 39.0 (CH_2), 24.4 (CH_2), 24.1 (CH_2), 14.2 (CH_3), 14.2 (CH_3); **HRMS (EI)** m/z calcd for $C_{23}H_{25}F_3O_5$ [M^+] 438.1654, found 438.1684.



Bicyclo[4.4.0]alkenone 2.3h

Isolated as a white solid.

IR (neat, cm^{-1}) ν max 2981-2875, 1734, 1326, 1236, 1122, 1069; **mp (°C)** 59.5-61.9; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.50 (d, J = 8.2 Hz, 2H), 7.33 (d, J = 8.0 Hz, 2H), 7.33, 6.03 (ddd, J = 5.4 Hz, 2.6 Hz, 2.6 Hz, 1H), 4.29-4.10 (m, 4H), 3.96 (br, 1H), 3.10-3.03 (m, 2H), 2.85 (ddd, J = 19.5 Hz, 4.2 Hz, 2.5 Hz, 1H), 2.06-1.96 (m, 3H), 1.71-1.62 (m, 3H), 1.27 (t, J = 7.1 Hz, 3H), 1.25 (t, J = 7.1 Hz, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 211.1 (C), 169.8 (C), 169.4 (C), 143.5 (C), 133.6 (C), 129.6 (C), 129.0 (CHx2), 127.4 (q, J_{C-F} = 271.8) (C), 126.7 (CH), 125.3 (q, J_{C-F} = 3.7 Hz) (CHx2), 62.1 (CH_2), 62.0 (CH_2), 61.9 (C), 52.7 (CH), 40.8 (CH), 39.0 (CH_2), 27.6 (CH_2), 25.8 (CH_2), 23.7 (CH_2), 14.2 (CH_3), 14.1 (CH_3); **HRMS (EI)** m/z calcd for $C_{23}H_{25}O_5F_3$ [M^+] 438.1654, found 438.1688.

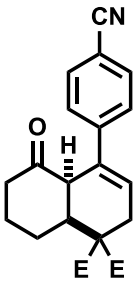


Bicyclo[3,4,0]alkenone 2.2i

Isolated as a white solid.

IR (neat, cm^{-1}) ν max 2987-2871**,** 2227, 1733, 1723, 1240, 1040 ; **mp (°C)** 118.1-121.3 **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.51 (d, J = 8.3 Hz, 2H), 7.21 (d, J = 8.1 Hz, 2H), 6.57 (d, J = 1.6 Hz, 1H), 4.28-4.11 (m, 4H), 3.80 (d, J = 7.7 Hz, 1H), 3.52 (ddd, J = 17.6 Hz, 2.4 Hz, 2.4 Hz, 1H), 3.37 (ddd, J = 11.4 Hz, 7.4 Hz, 5.9 Hz, 1H), 3.00 (d, J = 17.7 Hz, 1H), 2.15-2.09 (m, 2H), 1.95-1.87 (m, 1H), 1.74-1.63 (m, 2H), 1.46-1.35 (m, 1H), 1.25 (t, J = 6.9 Hz, 3H), 1.25 (t, J = 6.9 Hz, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 209.1 (C_{quat}), 170.9 (C_{quat}), 169.3

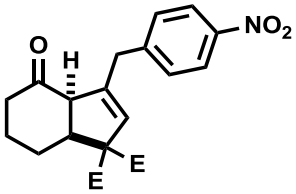
(C_{quat}), 141.3 (C_{quat}), 140.8 (C_{quat}), 131.9 (CHx2), 129.3 (CHx2), 125.4 (CH), 119.0 (C_{quat}), 62.0 (CH_2), 61.9 (CH_2), 61.7 (C_{quat}), 56.5 (CH), 48.7 (CH), 41.0 (CH_2), 39.0 (CH_2), 24.3 (CH_2), 24.0 (CH_2), 14.1 (CH_3), 14.1 (CH_3) ;**HRMS (EI)** m/z calcd for $C_{23}H_{25}NO_5$ 395.17327, found 395.1747



Bicyclo[4,4,0]alkenone 2.3i

Isolated as a white solid.

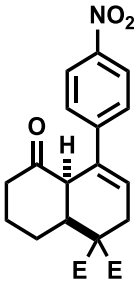
IR (neat, cm^{-1}) ν max 2981, 2941, 2227, 1750, 1731, 1605, 1255, 1181 ; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.54 (d, J = 8.6 Hz, 2H), 7.32 (d, J = 8.6 Hz, 2H), 6.05 (ddd, J = 5.4 Hz, 2.6 Hz, 2.6 Hz, 1H), 4.28-4.12 (m, 4H), 3.94 (br, 1H), 3.10-3.02 (m, 2H), 2.85 (ddd, J = 19.6 Hz, 4.2 Hz, 2.6 Hz, 1H), 2.06-1.88 (m, 3H), 1..76-1.59 (m, 3H), 1.26 (t, J = 7.1 Hz, 3H), 1.24 (t, J = 7.1 Hz, 3H) ; **^{13}C NMR (100 MHz, $CDCl_3$)** δ 210.8 (C_{quat}), 170.9 (C_{quat}), 169.6 (C_{quat}), 144.5 (C_{quat}), 133.3 (C_{quat}), 132.2 (CHx2), 127.8 (CH), 127.7 (CHx2), 118.8 (C_{quat}), 111.2 (C_{quat}), 62.1 (CH_2), 62.1 (CH_2), 56.0 (C_{quat}), 52.6 (CH), 40.6 (CH), 39.9 (CH_2), 27.7 (CH_2), 25.7 (CH_2), 23.5 (CH_2), 14.2 (CH_3), 14.1 (CH_3) ; **HRMS (EI)** m/z calcd for $C_{23}H_{25}NO_5$ 395.17327, found 395.1722



Bicyclo[4.3.0]alkenone 2.2j

Isolated as a yellow oil.

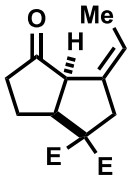
IR (neat, cm^{-1}) ν max 2943, 2867, 1733, 1662, 1521, 1343, 1195; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.10 (d, J = 8.8 Hz, 2H), 7.28 (d, J = 8.6 Hz, 2H), 6.63 (d, J = 1.6 Hz, 1H), 4.40-4.09 (m, 4H), 3.85 (d, J = 7.8 Hz, 1H), 3.54 (ddd, J = 17.6 Hz, 2.4 Hz, 2.4 Hz, 1H), 3.39 (ddd, J = 11.3 Hz, 7.5 Hz, 6.0 Hz, 1H), 3.03 (d, J = 17.7 Hz, 1H), 2.25-2.12 (m, 2H), 1.97-1.89 (m, 1H), 1.79-1.66 (m, 2H), 1.49-1.38 (m, 1H), 1.26 (t, J = 6.9 Hz, 6H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 209.0 (C), 170.9 (C), 169.4 (C), 146.6 (C), 142.9 (C), 142.0 (C), 129.6 (CHx2), 125.1 (CH), 123.5 (CHx2), 62.1 (C), 62.0 (CH_2), 61.8 (CH_2), 56.6 (CH), 48.7 (CH), 41.2 (CH_2), 39.1 (CH_2), 24.3 (CH_2), 24.0 (CH_2), 14.2 (CH_3x2); **HRMS (EI)** m/z calcd for $C_{22}H_{25}NO_7$ [M^+] 415.1631, found 415.1651.



Bicyclo[4.4.0]alkenone 2.3j

Isolated as a yellow oil.

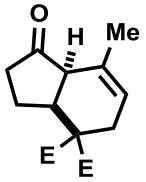
IR (neat, cm^{-1}) ν max 2981, 2942, 1729, 1596, 1345, 1262, 1181; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.11-8.06 (m, 2H), 7.37 (d, J = 8.9 Hz, 2H), 6.11 (ddd, J = 5.4 Hz, 2.6 Hz, 2.6 Hz, 1H), 4.28-4.12 (m, 4H), 3.96 (br, 1H), 3.12-3.09 (m, 2H), 2.87 (ddd, J = 19.6 Hz, 4.2 Hz, 2.6 Hz, 1H), 2.06-1.88 (m, 3H), 1..77-1.61 (m, 3H), 1.26 (t, J = 7.1 Hz, 3H), 1.24 (t, J = 7.1 Hz, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 210.7 (C), 169.6 (C), 169.3 (C), 147.0 (C), 146.4 (C), 133.0 (C), 128.3 (CHx2), 127.8 (CH), 123.6 (CHx2), 62.1 (CH_2), 62.0 (CH_2), 55.9 (C), 52.6 (CH), 40.6 (CH), 39.9 (CH_2), 27.6 (CH_2), 25.7 (CH_2), 23.5 (CH_2), 14.1 (CH_3), 14.1 (CH_3); **HRMS (EI)** m/z calcd for $C_{22}H_{25}NO_7$ [M^+] 415.1631, found 415.1650.



Bicyclo[3,3,0]alkenone 2.5a

Isolated as a white powder.

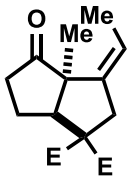
IR (neat, cm^{-1}) ν max 2980, 2937, 1734, 1464, 1256, 1191 ; **mp (°C)** 60.4-62.6 ; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 5.58 (qdd, J= 7.0 Hz, 1.7 Hz, 1.7 Hz, 1H), 4.28-4.20 (m, 4H), 3.55-3.49 (m, 2H), 3.06 (ddd, J = 16.0 Hz, 2.7 Hz, 2.7 Hz, 1H), 2.66 (d, J = 16.0 Hz, 1H), 2.34-2.28 (m, 2H), 2.07-1.98 (m, 1H), 1.79 (dd, J = 6.4 Hz, 2.5 Hz, 3H), 1.52-1.45 (m, 1H), 1.27 (dd, J = 7.1 Hz, 7.1 Hz, 3H), 1.23 (dd, J = 7.1 Hz, 7.1 Hz, 3H),; **^{13}C NMR (100 MHz, $CDCl_3$)** δ 216.1 (C_{quat}), 171.3 (C_{quat}), 169.5 (C_{quat}), 134.2 (C_{quat}), 123.1 (CH), 62.8 (C_{quat}), 61.7 (CH_2), 61.6 (CH_2), 53.6 (CH), 46.2 (CH), 39.4 (CH_2), 39.0 (CH_2), 23.0 (CH_2), 15.2 (CH_3), 14.3 (CH_3), 14.2 (CH_3),**; HRMS (EI)** m/z calcd for $C_{16}H_{22}O_5$ 294.1467 found 294.1452.



Bicyclo[4,3,0]alkenone 2.6a

Isolated as a colorless oil.

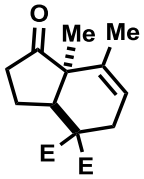
IR (neat, cm^{-1}) ν max 2982, 2940, 2867, 1746, 1733, 1464, 1256 ; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 5.40 (ddt, J = 3.6 Hz, 2.3 Hz, 1.4 Hz, 1H), 4.25-.4.05 (m, 4H), 3.15 (dt, J = 12.1 Hz, 7.3 Hz, 1H), 3.07-2.99 (m, 1H), 2.67-2.58 (m, 2H), 2.22-2.11 (m, 2H), 1.85-1.78 (m, 1H), 1.74 (dd, J = 7.0 Hz, 2.8 Hz, 3H), 1.50-1.41 (m, 1H), 1.23 (t, J = 7.2 Hz, 3H), 1.18 (t, J = 7.2 Hz, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 215.8 (C_{quat}), 170.8 (C_{quat}), 170.4 (C_{quat}), 128.8 (C_{quat}), 120.0 (CH), 61.5 (CH_2), 61.5 (CH_2), 54.9 (C_{quat}), 52.8 (CH), 39.9 (CH), 36.9 (CH_2), 26.1 (CH_2), 22.9 (CH_2), 21.0 (CH_3), 14.1 (CH_3), 14.0 (CH_3)**; HRMS (EI)** m/z calcd for $C_{16}H_{22}O_5$ 294.1467 found 294.1463.



Bicyclo[3.3.0]alkenone 2.5b

Isolated as a colorless oil.

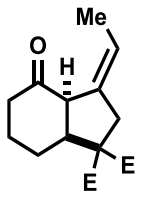
IR (neat, cm^{-1}) ν max 2980, 2937, 2890, 1734, 1464, 1256, 1097; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 5.48 (qdd, J= 7.4 Hz, 1.8 Hz, 1.8 Hz, 1H), 4.23-4.22 (m, 4H), 3.19-3.16 (m, 1H), 3.14-3.11 (m, 1H), 2.97 (dq, J = 17.1 Hz, 1.3 Hz, 1H), 2.36 (dd, J = 9.3 Hz, 3.7 Hz, 1H), 2.34 (dd, J = 9.3 Hz, 3.7 Hz, 0.5H), 2.26-2.12 (m, 1H), 1.99 (ddddd, J = 13.3 Hz, 9.4 Hz, 3.7 Hz,0.9 Hz, 1H), 1.68 (ddd, J = 7.4 Hz, 2.7 Hz, 1.3 Hz, 3H), 1.55-1.44 (m, 1H), 1.29 (s, 3H), 1.22 (t, J = 7.1 Hz, 7.1 Hz, 3H), 1.22 (t, J = 7.1 Hz, 7.1 Hz, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 217.6 (C), 171.0 (C), 169.6 (C), 138.6 (C), 123.0 (CH), 62.1 (C), 61.8 (CH_2), 61.6 (CH_2), 59.1 (C), 55.6 (CH), 39.9 (CH_2), 37.0 (CH_2), 22.1(CH_3), 22.0 (CH_2), 14.2 (CH_3), 14.0 (CH_3), 13.7 (CH_3); **HRMS (EI)** m/z calcd for [M^+] $C_{17}H_{24}O_5$ 308.1624 found 308.16345.



Bicyclo[4.3.0]alkenone 2.6b

Isolated as a colorless oil.

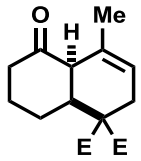
IR (neat, cm^{-1}) ν max 2984, 2941, 2866, 1743, 1733, 1464 1256; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 5.51 (ddd, J = 5.4 Hz, 1.9 Hz, 1.9 Hz, 1H), 4.26-4.06 (m, 4H), 2.97 (dd, J = 11.5 Hz, 6.7 Hz, 1H), 2.91 (dddd, J = 18.4 Hz, 5.8 Hz, 1.1 Hz, 1.1 Hz, 1H), 2.45-2.21 (m, 4H), 1.68-1.59 (m, 1H), 1.58 (ddd, J = 2.6 Hz, 1.4 Hz, 1.4 Hz, 3H), 1.25 (t, J = 7.2 Hz, 3H), 1.24 (t, J = 7.2 Hz, 3H), 1.13 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 217.5 (C), 170.3 (C), 170.1 (C), 131.2 (C), 121.9 (CH), 61.5 (CH_2x2), 54.4 (C), 53.5 (C), 46.8 (CH), 35.2 (CH_2), 26.8 (CH_2), 21.9 (CH_2), 21.6 (CH_3), 18.3 (CH_3), 14.0 (CH_3), 13.8 (CH_3); **HRMS (EI)** m/z calcd for $C_{17}H_{24}O_5$ [M^+] 308.1624 found 308.1633.



Bicyclo[3,4,0]alkenone 2.5c

Isolated as a colorless oil.

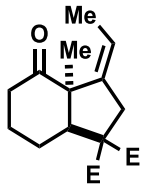
IR (neat, cm^{-1}) ν max 2980- 2941, 1733, 1725, 1240, 1178 ; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 5.54-5.50 (m, 1H), 4.24-4.06 (m, 4H), 3.56 (br, 1H), 3.27 (ddd, J = 16.9 Hz, 2.6 Hz, 2.6 Hz, 1H), 3.18 (ddd, J = 12.4 Hz, 6.3 Hz, 6.3 Hz, 1H), 2.78 (d, J = 16.9 Hz, 1H), 2.31-2.27 (m, 2H), 2.01-1.93 (m, 1H), 1.70-1.52 (m, 2H), 1.48-1.66 (m, 3H), 1.33 (dq, J= 12.8 Hz, 3.8 Hz, 1H), 1.20 (t, J = 7.3 Hz, 3H), 1.17 (t, J = 7.3 Hz, 3H) ; **^{13}C NMR (100 MHz, $CDCl_3$)** δ 211.2 (C_{quat}), 170.8 (C_{quat}), 169.3 (C_{quat}), 134.7 (C_{quat}), 122.1 (CH), 62.7 (C_{quat}), 61.7 (CH_2), 61.7 (CH_2), 55.6 (CH), 48.1 (CH), 39.3 (CH_2), 26.7 (CH_2), 24.5 (CH_2), 24.3 (CH_2), 14.1 (CH_3), 14.0 (CH_3), 13.8 (CH_3); **HRMS (EI)** m/z calcd for $C_{17}H_{24}O_5$ 308.1624 found 308.1624.



Bicyclo[4.4.0]alkenone 2.6c

Isolated as a colorless oil.

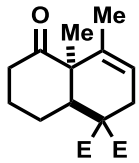
IR (neat, cm^{-1}) ν max 2984, 2940, 2870, 1733, 1445, 1239, 1179; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 5.50 (d, J = 2.7Hz, 1H), 4.22-4.10 (m, 4H), 3.25 (br, 1H), 2.88-2.83 (m, 1H), 2.80-2.73 (m, 1H), 2.62 (dddd J = 18.6 Hz, 4.2 Hz, 2.3 Hz, 2.3 Hz, 1H), 2.32-2.26 (m, 1H), 2.24-2.15 (m, 1H), 2.04-1.97 (m, 1H), 1.67-1.54 (m, 3H), 1.50 (d, J = 1.2 Hz, 3H), 1.22 (dd, J = 7.1 Hz, 7.1 Hz, 3H), 1.20 (dd, J = 7.1 Hz, 7.1 Hz, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 212.0 (C), 170.2 (C), 169.8 (C), 128.3 (C), 121.0 (CH), 61.8 (CH_2), 61.7 (CH_2), 56.4 (C), 54.4 (CH), 40.0 (CH), 39.8 (CH_2), 26.8 (CH_2), 25.0 (CH_2), 23.6 (CH_2), 14.1 (CH_3), 14.0 (CH_3); **HRMS (EI)** m/z calcd for $C_{17}H_{24}O_5$ [M^+] 308.1624 found 308.1629.



Bicyclo[3,4,0]alkenone 2.5d

Isolated as a colorless oil.

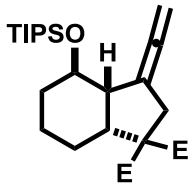
IR (neat, cm^{-1}) ν max 2981, 2939, 2867, 1733, 1707, 1447, 1256, 1051 ; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 5.41 (qdd, J= 7.3 Hz, 2.0 Hz, 2.0 Hz, 1H), 4.25-4.08 (m, 4H), 3.40 (ddd, J = 17.7 Hz, 2.2 Hz, 2.2 Hz, 1H), 3.12 (dddd, J = 17.7 Hz, 1.8 Hz, 1.8 Hz, 1.0 Hz, 1H), 3.10-3.05 (m, 1H), 2.57-2.36 (m, 2H), 2.02-1.93 (m, 1H), 1.72-1.60 (m, 2H), 1.48 (ddd, J = 3.5 Hz, 1.8 Hz, 1.8 Hz, 1H), 1.45 (dt, J = 7.3 Hz, 2.1 Hz, 3H), 1.28 (dd, J= 7.1 Hz, 7.1 Hz, 3H), 1.28 (dd, J= 7.1 Hz, 7.1 Hz, 3H), 1.20 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 213.1 (C_{quat}), 171.7 (C_{quat}), 169.7 (C_{quat}), 141.8 (C_{quat}), 119.5 (CH), 63.4 (C_{quat}), 61.9 (CH_2), 61.8 (CH_2), 59.2(C_{quat}), 56.4 (CH), 39.3 (CH_2), 39.0 (CH_2), 26.0 (CH_2), 24.8 (CH_2), 22.5 (CH_3), 14.1 (CH_3), 14.1 (CH_3), 13.3 (CH_3); **HRMS (EI)** m/z calcd for $C_{18}H_{26}O_5$ 322.1780, found 322.1767.



Bicyclo[4,4,0]alkenone 2.6d

Isolated as a colorless oil.

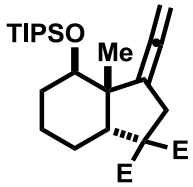
IR (neat, cm^{-1}) ν max 2981, 2940, 2867, 1735, 1722, 1447, 1233, 1095 ; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 5.52 (ddq, J = 5.3 Hz, 2.6 Hz, 1.4 Hz, 1H), 4.25-4.01 (m, 4H), 2.84-2.80 (m, 1H), 2.53-2.37 (m, 2H), 2.32-2.26 (m, 2H), 2.02-1.94 (m, 2H), 1.68-1.59 (m, 2H), 1.46-1.43 (m, 3H), 1.26 (t, J = 7.2 Hz, 6H), 1.11 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 212.8 (C_{quat}), 170.9 (C_{quat}), 170.5 (C_{quat}), 133.2 (CH), 120.9 (C_{quat}), 61.9 (CH_2), 61.9 (CH_2), 56.5 (C_{quat}), 55.0(C_{quat}), 47.4 (CH), 40.3 (CH_2), 26.9 (CH_2), 26.2 (CH_2), 25.2 (CH_2), 21.3 (CH_3), 19.3 (CH_3), 14.2/(CH_3), 14.1 (CH_3); **HRMS (EI)** m/z calcd for $C_{18}H_{26}O_5$ 322.1780, found 322.1793.



Allene 2.7c

Isolated as a white solid.

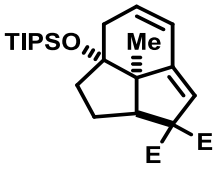
IR (neat, cm^{-1}) ν max 1735; **^{1}H NMR (300MHz, $CDCl_3$)** δ = 4.83 - 4.66 (m, 2 H), 4.28 - 4.03 (m, 5 H), 3.37 (dtd, *J* = 2.6, 5.1, 17.6 Hz, 1 H), 3.06 (q, *J* = 6.5 Hz, 1 H), 3.00 - 2.87 (m, 2 H), 1.73 (s, 2 H), 1.66 - 1.51 (m, 1 H), 1.24 (t, *J* = 7.1 Hz, 3 H), 1.23 (t, *J* = 7.1 Hz, 3 H), 1.06 (s, 18 H), 1.48 - 0.84 (m, 6 H); **^{13}C NMR (75MHz, $CDCl_3$)** δ = 201.3 (C_{quat}), 170.5 (C_{quat}), 160.7 (C_{quat}), 99.8 (C_{quat}), 77.4 (CH_2), 66.3 (CH), 62.0 (CH), 60.6 (CH_2), 60.5 (CH_2), 47.4 (CH), 40.5 (CH), 33.7 (CH_2), 28.2 (CH_2), 23.1 (CH_2), 17.3 (6xCH_3), 13.3 (CH_3), 13.1 (CH_3), 11.5 (3xCH); **HRMS (EI)** m/z calcd for $C_{23}H_{35}O_5Si$ [(M-iPr)$^+$] 421.2410, found 421.2427.



Allene 2.7d

Isolated as a white solid.

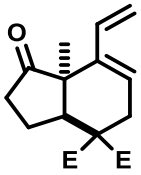
IR (neat, cm^{-1}) ν max 1734; **^{1}H NMR (400MHz, $CDCl_3$)** δ = 4.76 (ddd, *J* = 3.2, 5.1, 9.4 Hz, 1 H), 4.68 (ddd, *J* = 3.4, 5.4, 9.2 Hz, 1 H), 4.29 - 4.04 (m, 4 H), 3.87 (dd, *J* = 3.4, 9.0 Hz, 1 H), 3.65 (td, *J* = 5.2, 17.2 Hz, 1 H), 2.90 - 2.85 (m, 1 H), 2.83 (td, *J* = 3.2, 17.2 Hz, 1 H), 1.65 - 1.43 (m, 5 H), 1.23 (t, *J* = 7.1 Hz, 3 H), 1.22 (t, *J* = 7.2 Hz, 3 H), 1.14 - 0.98 (m, 25 H); **^{13}C NMR (75MHz, $CDCl_3$)** δ = 202.8 (C_{quat}), 172.6 (C_{quat}), 171.8 (C_{quat}), 107.4 (C_{quat}), 77.9 (CH_2), 71.2 (CH), 61.9 (CH_2), 61.7 (CH_2), 61.1 (C_{quat}), 50.9 (C_{quat}), 50.7 (CH), 36.2 (CH_2), 30.4 (CH_2), 22.7 (CH_2), 20.3 (CH_2), 18.4 (3xCH_3), 18.2 (3xCH_3), 17.8 (CH_3), 14.0 (CH_3), 14.0 (CH_3), 13.1 (3xCH); **HRMS (EI)** m/z calcd for $C_{24}H_{39}O_5Si$ [(M-iPr)$^+$] 435.2567, found 435.2563.



Tricycle 2.9b

Prepared according to the general procedure Gold-Catalyzed Carbocyclization from **enyne 17a** using [**L3**AuMeCN]SbF_6 as the catalyst, **acetone** as the solvent and isolated as white powder.

IR (neat, cm-1) ν max 2945, 2867, 1734, 1325, 1210, 1140, 1056, 916; **mp (°C)** 63.4-64.8; **^{1}H NMR (400MHz ,$CDCl_3$) ^{1}H NMR (400MHz, $CDCl_3$)** δ = 6.16 (dd, *J* = 1.5, 9.8 Hz, 1 H), 5.70 (ddd, *J* = 2.7, 5.2, 9.8 Hz, 1 H), 5.55 (s, 1 H), 4.28 - 4.08 (m, 4 H), 3.22 (dd, *J* = 2.7, 10.8 Hz, 1 H), 2.50 (ddd, *J* = 1.5, 5.2, 18.5 Hz, 1 H), 2.39 (dtd, *J* = 0.6, 2.7, 18.7 Hz, 1 H), 2.22 - 2.06 (m, 1 H), 1.59 (s, 2 H), 1.28 (s, 6 H), 1.08 (s, 18 H), 1.23 - 1.05 (m, 7 H); **^{13}C NMR (101MHz , $CDCl_3$)** δ = 170.9 (C_{quat}), 170.2 (C_{quat}), 151.1 (C_{quat}), 129.5 (CH), 121.1 (CH), 120.4 (CH), 83.7 (C_{quat}), 69.7 (C_{quat}), 61.5 (C_{quat}), 61.4 (CH_2), 61.2 (CH_2), 51.7 (CH), 37.0 (CH_2), 35.6 (CH_2), 25.8 (CH_2), 18.4 (CHx3), 17.7 (CH_3), 14.2 (CH_3), 14.1 (CH_3), 13.5 (CH_3x6); **HRMS (EI)** m/z calcd for $C_{24}H_{37}O_5Si$ [$(M-{}_iPr)^+$] 433.2410, found 433.2423.

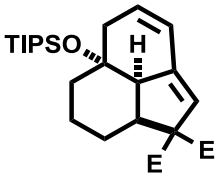


Diene 2.11b

Isolated as a colorless oil.

IR (neat, cm-1) ν max 2983, 2934, 1735, 1241, 1174, 1095, 1059; **^{1}H NMR (300MHz ,$CDCl_3$)** δ = 6.26 (dd, *J* = 10.8, 17.0 Hz, 1 H), 5.95 (dd, *J* = 2.3, 5.8 Hz, 1 H), 5.33 (d, *J* = 17.2 Hz, 1 H), 4.96 (d, *J* = 11.2 Hz, 1 H), 4.30 - 4.04 (m, 4 H), 3.11 - 2.94 (m, 2 H), 2.53 (d, *J* = 19.3 Hz, 1 H), 2.46 - 2.12 (m, 3 H), 1.72 - 1.54 (m, 1 H), 1.26 (dt, *J* = 5.9, 7.1 Hz, 6 H), 1.14 (s, 3 H); **^{13}C NMR (75MHz ,$CDCl_3$)** δ = 217.0 (C_{quat}), 170.1 (C_{quat}), 169.8 (C_{quat}), 134.5 (CH), 134.2 (C_{quat}), 121.9 (CH), 114.7 (CH_2), 61.6 (CH_2x2), 54.0 (C_{quat}), 52.5 (C_{quat}),

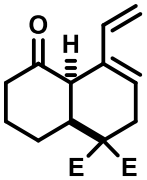
46.5 (CH), 35.0 (CH_2), 26.9 (CH_2), 22.2 (CH_3), 21.8 (CH_2), 14.0 (CH_3), 13.9 (CH_3); **HRMS (EI)** m/z calcd for $C_{18}H_{24}O_5$ [M^+] 320.1624, found 320.1623.



Tricycle 2.9c

Isolated as a white powder.

IR (neat, cm-1) ν max 2940, 2865, 1733, 1461, 1221, 1058, 882, 675; **mp (°C)** 100.4-102.1; **^{1}H NMR (300MHz, C_6D_6)** δ = 6.11 (dd, *J* = 3.0, 9.7 Hz, 1 H), 6.04 (d, *J* = 3.0 Hz, 1 H), 5.55 (ddd, *J* = 2.2, 6.1, 9.7 Hz, 1 H), 4.15 - 3.90 (m, 3 H), 3.80 (m, 2 H), 3.60 (br. s., 1 H), 2.44 (d, *J* = 17.4 Hz, 1 H), 2.06 (dd, *J* = 6.1, 17.2 Hz, 1 H), 2.14 - 1.91 (m, 1 H), 1.75 - 1.63 (m, 1 H), 1.53 - 1.32 (m, 4 H), 1.22 - 1.00 (m, 21 H), 0.90 (td, *J* = 7.1, 20.0 Hz, 6 H); **^{13}C NMR (75MHz, C_6D_6)** δ = 169.4 (C_{quat}), 168.6 (C_{quat}), 144.2 (C_{quat}), 131.0 (CH), 122.6 (CH), 122.4 (CH), 72.0 (C_{quat}), 69.4 (C_{quat}), 60.8 (CH_2), 60.5 (CH_2), 52.2 (CH), 43.1 (CH), 41.2 (CH_2), 34.4 (CH_2), 23.4 (CH_2), 19.4 (CH_2), 18.4 (CHx3), 13.8 (CH_3), 13.6 (CH_3), 13.6 (CH_3x6); **HRMS (EI)** m/z calcd for $C_{24}H_{37}O_5Si$ [$(M-{}_iPr)^+$] 433.2410, found 433.2416.

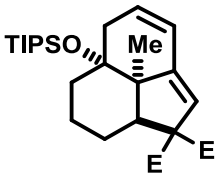


Diene 2.11c

Isolated as a colorless oil.

IR (neat, cm-1) 2927, 2849, 1733, 1463, 1444, 1236, 1180, 1051, 862, 736; **^{1}H NMR (400MHz ,$CDCl_3$)** δ = 6.12 (dd, *J* = 11.3, 17.7 Hz, 1 H), 5.85 (td, *J* = 2.4, 5.2 Hz, 1 H), 5.14 (d, *J* = 17.7 Hz, 1 H), 4.90 (d, *J* = 11.3 Hz, 1 H), 4.26 - 4.08 (m, 4 H), 3.49 (br. s., 1 H), 2.97 - 2.87 (m, 2 H), 2.74 (d, *J* = 20.0 Hz, 1 H), 2.34 - 2.16 (m, 2 H), 2.05 - 1.97 (m, 1 H), 1.70 - 1.48 (m, 3 H), 1.22 (q, *J* = 7.1 Hz, 6 H); **^{13}C NMR (101MHz ,$CDCl_3$)** δ = 213.0 (C_{quat}),

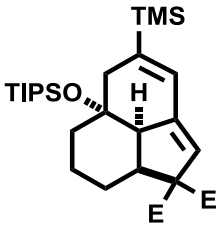
169.8 (C_{quat}), 169.4 (C_{quat}), 136.8 (CH), 131.8 (C_{quat}), 125.6 (CH), 114.5 (CH_2), 61.9 (CH_2), 61.8 (CH_2), 56.2 (C_{quat}), 52.0 (CH), 41.0 (CH), 39.5 (CH_2), 27.3 (CH_2), 26.0 (CH_2), 23.5 (CH_2), 14.0 (CH_3), 14.0 (CH_3); **HRMS (EI)** m/z calcd for $C_{18}H_{24}O_5$ [M^+] 320.1624, found 320.1604.



Tricycle 2.9d

Isolated as a white powder.

IR (neat, cm-1) ν max 2943, 2867, 1733, 1456, 1188, 1095, 1058, 882, 715, 672; **mp (°C)** 71.8-73.2; **^{1}H NMR (300MHz, $CDCl_3$)** δ = 6.21 (dd, *J* = 2.7, 9.7 Hz, 1 H), 5.75 (ddd, *J* = 2.4, 5.9, 9.7 Hz, 1 H), 5.64 (s, 1 H), 4.31 - 4.05 (m, 4 H), 3.07 (dd, *J* = 6.5, 10.8 Hz, 1 H), 2.59 (td, *J* = 2.2, 17.8 Hz, 1 H), 2.08 (dd, *J* = 6.1, 18.1 Hz, 1 H), 1.83 - 1.55 (m, 2 H), 1.44 (dd, *J* = 3.7, 8.0 Hz, 2 H), 1.25 (dt, *J* = 6.0, 7.1 Hz, 6 H), 1.35 - 1.02 (m, 26 H); **^{13}C NMR (75MHz, $CDCl_3$)** δ = 171.3 (C_{quat}), 170.5 (C_{quat}), 149.6 (C_{quat}), 129.9 (CH), 122.2 (CH), 120.7 (CH), 75.5 (C_{quat}), 70.2 (C_{quat}), 61.7 (CH_2), 61.6 (CH_2), 52.9 (C_{quat}), 48.5 (CH), 39.7 (CH_2), 35.1 (CH_2), 25.7 (CH_2), 24.3 (CH_3), 18.8 (CHx1), 18.7 (CH_2), 18.7 (CHx2), 14.3 (CH_3), 14.1 (CH_3), 13.9 (CH_3x6); **HRMS (EI)** m/z calcd for $C_{28}H_{46}O_5Si$ [M^+] 490.3115, found 490.3147.

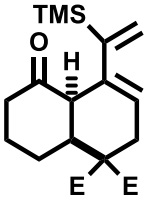


Tricycle 2.9e

Isolated as a colorless oil.

Compound aromatizes readily in $CDCl_3$. Use of deactivated silica (washed with 1% Et_3N in hexanes) was necessary for flash chromatography purification.

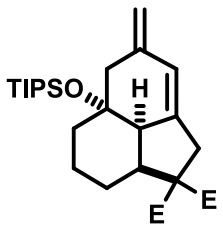
IR (neat, cm-1) ν max 2943, 2866, 1733, 1464, 1242, 1221, 1118, 1059, 835, 679; **^{1}H NMR (300MHz, C_6D_6)** δ = 6.48 (d, *J* = 2.8 Hz, 1 H), 6.06 (d, *J* = 2.8 Hz, 1 H), 4.20 - 3.68 (m, 5 H), 3.65 - 3.59 (m, 1 H), 2.59 (dd, *J* = 3.3, 16.6 Hz, 1 H), 2.41 (d, *J* = 16.6 Hz, 1 H), 2.15 - 1.95 (m, 1 H), 1.78 - 1.60 (m, 1 H), 1.55 - 1.31 (m, 4 H), 1.27 - 1.07 (m, 21 H), 0.93 (td, *J* = 7.1, 16.5 Hz, 6 H), 0.07 (s, 9 H); **^{13}C NMR (75MHz, C_6D_6)** δ = 169.4 (C_{quat}), 168.6 (C_{quat}), 144.9 (C_{quat}), 144.9 (C_{quat}), 129.6 (CH), 123.0 (CH), 72.4 (C_{quat}), 69.4 (C_{quat}), 60.8 (CH_2), 60.6 (CH_2), 52.1 (CH), 43.3 (CH_2), 43.3 (CH), 34.0 (CH_2), 23.3 (CH_2), 19.3 (CH_2), 18.5 (CHx3), 13.8 (CH_3), 13.7 (CH_3x6), 13.7 (CH_3), -2.9 (CH_3x3); **HRMS (EI)** m/z calcd for $C_{27}H_{45}O_5Si_2$ [$(M-{}^{i}Pr)^+$] 505.2806, found 505.2809.



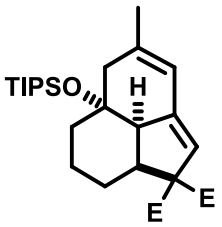
Bicyclo[4.4.0]decenone 2.11e

Isolated as a colorless oil.

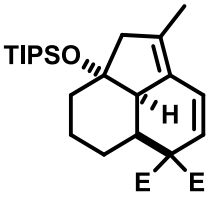
IR (neat, cm-1) ν max 2954, 1733, 1714, 1249, 1179, 841, 760; **^{1}H NMR (300MHz, $CDCl_3$)** δ = 5.52 (d, *J* = 2.7 Hz, 1 H), 5.47 (td, *J* = 2.5, 5.4 Hz, 1 H), 5.31 (d, *J* = 2.7 Hz, 1 H), 4.31 - 4.08 (m, 4 H), 3.59 (br. s., 1 H), 3.01 - 2.81 (m, 2 H), 2.71 (ddd, *J* = 2.5, 3.9, 19.0 Hz, 1 H), 2.35 - 1.92 (m, 3 H), 1.71 - 1.53 (m, 3 H), 1.24 (t, *J* = 7.1 Hz, 6 H), 0.08 (s, 9 H); **^{13}C NMR (75MHz, $CDCl_3$)** δ = 211.1 (C_{quat}), 169.9 (C_{quat}), 169.6 (C_{quat}), 152.9 (C_{quat}), 137.3 (C_{quat}), 126.7 (CH_2), 120.7 (CH), 61.7 (CH_2), 61.6 (CH_2), 56.1 (C_{quat}), 53.2 (CH), 40.4 (CH), 40.3 (CH_2), 26.8 (CH_2), 25.5 (CH_2), 23.6 (CH_2), 14.0 (CH_3), 14.0 (CH_3), -0.8 (CH_3x3); **HRMS (EI)** m/z calcd for $C_{21}H_{32}O_5Si$ [M^+] 392.2019, found 392.2023.



Major (65%)



Minor (31%)



Trace (4%)

Tricyclic Compound mixture of 2.9f & 2.12f

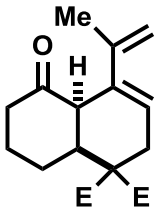
Isolated as an inseparable clear oil mixture. Characterized as a mixture.

Mixture: IR (neat, cm-1) ν max 2940, 2866, 1739, 1733, 1460, 1242, 1058, 882, 680; **HRMS (EI)** m/z calcd for $C_{25}H_{39}O_5Si$ [(M-$_i$Pr)$^+$] 447.2567, found 447.2572.

Major: ^{1}H NMR (500MHz, $CDCl_3$) δ = 5.96 (d, *J* = 1.8 Hz, 1 H), 4.80 - 4.68 (br. s., 2 H), 4.33 - 4.02 (m, 4 H), 3.31 (d, *J* = 19.5 Hz, 1 H), 3.02 (td, *J* = 5.7, 13.0 Hz, 1 H), 2.93 (d, *J* = 19.6 Hz, 1 H), 2.87 (br. s., 1 H), 2.49 (d, *J* = 13.7 Hz, 1 H), 2.34 (d, *J* = 13.7 Hz, 1 H), 1.24 (s, 6 H), 1.11 - 1.08 (m, 18 H), 1.85 - 0.68 (m, 9 H); ^{13}C **NMR (126MHz, $CDCl_3$)** δ = 171.6 (C_{quat}), 169.8 (C_{quat}), 143.6 (C_{quat}), 143.1 (C_{quat}), 122.2 (CH), 110.4 (CH_2), 73.2 (C_{quat}), 62.5 (C_{quat}), 61.4 (CH_2), 61.3 (CH_2), 52.2 (CH), 45.4 (CH_2), 42.1 (CH), 35.6 (CH_2), 32.2 (CH_2), 23.2 (CH_2), 19.6 (CH_2), 18.5 (CHx2), 18.4 (CH), 14.1 (CH_3), 14.1 (CH_3), 13.6 (CH_3x6).

Minor: ^{1}H NMR (500MHz, $CDCl_3$) δ = 6.44 (d, *J* = 9.8 Hz, 1 H), 5.89 (d, *J* = 9.8 Hz, 1 H), 4.31 - 4.03 (m, 4 H), 3.28 - 3.21 (m, 0 H), 2.76 (dtd, *J* = 0.9, 4.8, 12.9 Hz, 1 H), 2.65 (d, *J* = 15.2 Hz, 1 H), 2.09 (d, *J* = 15.2 Hz, 1 H), 1.71 (s, 3 H), 1.29 - 1.17 (m, 6 H), 1.13 - 1.04 (m, 18 H), 1.83 - 0.68 (m, 9 H); **^{13}C NMR (126MHz, $CDCl_3$)** δ = 170.8 (C_{quat}), 169.3 (C_{quat}), 133.9 (C_{quat}), 129.8 (C_{quat}), 122.6 (CH), 122.5 (CH), 80.3 (C_{quat}), 61.3 (CH_2), 61.2 (CH_2), 59.5 (C_{quat}), 52.2 (CH_2), 49.3 (CH), 36.2 (CH_2), 34.1 (CH), 24.4 (CH_2), 21.0 (CH_2), 18.4 (CHx_3), 14.1 (CH_3), 14.1 (CH_3), 14.0 (CH_3), 13.2 (CH_3x6).

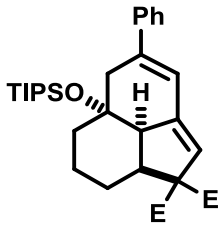
Trace: ^{1}H NMR (500MHz ,$CDCl_3$) δ = 6.00 (s, 1 H), 5.49 (d, *J* = 2.8 Hz, 1 H), 4.30 - 4.04 (m, 4 H), 3.27 - 3.22 (m, 1 H), 3.16 - 3.12 (m, 1 H), 2.49 (d, *J* = 16.9 Hz, 1 H), 2.04 (d, *J* = 16.9 Hz, 1 H), 1.79 (s, 3 H), 1.29 - 1.18 (m, 6 H), 1.12 - 1.07 (m, 18 H), 1.83 - 0.68 (m, 9 H); **^{13}C NMR (126MHz, $CDCl_3$)** δ = 170.4 (C_{quat}), 169.3 (C_{quat}), 145.0 (C_{quat}), 140.9 (C_{quat}), 118.6 (CH), 118.2 (CH), 72.2 (C_{quat}), 69.4 (C_{quat}), 61.0 (CH_2), 60.9 (CH_2), 51.4 (CH), 46.5 (CH_2), 42.4 (CH), 34.4 (CH_2), 23.9 (CH_3), 23.2 (CH_2), 19.1 (CH_2), 18.5 (CHx3), 14.1 (CH_3), 14.1 (CH_3), 13.7 (CH_3x6).



Bicyclo[4.4.0]decenone 2.11f

Isolated as a colorless oil.

IR (neat, cm-1) ν max 2979, 2942, 2870, 1733, 1714, 1445, 1367, 1255, 1180, 898; **^{1}H NMR (300MHz, $CDCl_3$)** δ = 5.80 (td, *J* = 2.6, 5.3 Hz, 1 H), 4.80 (s, 2 H), 4.22 - 4.10 (m, 4 H), 3.61 - 3.51 (m, *J* = 1.5 Hz, 1 H), 2.95 - 2.84 (m, 2 H), 2.71 (td, *J* = 3.3, 19.5 Hz, 1 H), 2.31 - 2.07 (m, 2 H), 2.07 - 1.88 (m, 1 H), 1.79 (s, 3 H), 1.70 - 1.49 (m, 3 H), 1.21 (dt, *J* = 3.4, 7.1 Hz, 6 H); **^{13}C NMR (75MHz, $CDCl_3$)** δ = 212.8 (C), 169.8 (C), 169.5 (C), 143.4 (C), 135.2 (C), 122.4 (CH), 114.0 (CH_2), 61.8 (CH_2), 61.7 (CH_2), 56.1 (C), 52.4 (CH), 41.0 (CH), 39.4 (CH_2), 27.1 (CH_2), 26.2 (CH_2), 23.5 (CH_2), 21.6 (CH_3), 14.0 (CH_3), 13.9 (CH_3); **HRMS (EI)** m/z calcd for $C_{19}H_{26}O_5$ [M^+] 334.1780, found 334.1781.

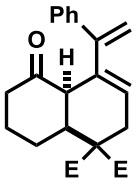


Tricycle 2.9g

Isolated as a colorless oil.

IR (neat, cm-1) ν max 2942, 2865, 1732, 1241, 1217, 1060, 883, 761, 674; **^{1}H NMR (300MHz, $CDCl_3$)** δ = 7.46 - 7.21 (m, 5 H), 6.64 (d, *J* = 2.8 Hz, 1 H), 5.76 (d, *J* = 2.8 Hz, 1 H), 4.30 - 4.06 (m, 4 H), 3.37 - 3.25 (m, 2 H), 2.87 (dd, *J* = 2.7, 16.9 Hz, 1 H), 2.65 (d, *J* = 16.3 Hz, 1 H), 1.95 - 1.73 (m, 1 H), 1.25 (td, *J* = 7.1, 18.4 Hz, 6 H), 1.13 (s, 18 H), 1.52 - 0.84 (m, 8 H); **^{13}C NMR (75MHz, $CDCl_3$)** δ = 170.2 (C_{quat}), 169.0 (C_{quat}), 145.1 (C_{quat}), 141.0 (C_{quat}), 140.7 (C_{quat}), 128.5 (CHx2), 127.8 (CH), 125.4 (CHx2), 122.3 (CH), 119.2 (CH), 72.3 (C_{quat}), 69.6 (C_{quat}), 61.2 (CH_2), 61.1 (CH_2), 51.7 (CH), 43.6 (CH_2), 42.6 (CH),

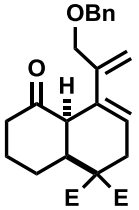
34.1(CH_2), 23.1 (CH_2), 19.1 (CH_2), 18.5 (CHx3), 14.2 (CH_3), 14.0 (CH_3), 13.7 (CH_3x6); **HRMS (EI)** m/z calcd for $C_{33}H_{48}O_5Si$ [M^+] 552.3271, found 552.3275.



Bicyclo[4.4.0]decenone 2.11g

Isolated as a colorless oil.

IR (neat, cm-1) ν max 2980, 2940, 1733, 1717, 1180, 780, 701; **^{1}H NMR (300MHz, $CDCl_3$)** δ = 7.33 - 7.20 (m, 5 H), 5.85 (td, *J* = 2.6, 5.4 Hz, 1 H), 5.19 (d, *J* = 1.2 Hz, 1 H), 5.09 (d, *J* = 1.2 Hz, 1 H), 4.27 - 4.15 (m, 4 H), 3.52 (br. s., 1 H), 3.04 - 2.90 (m, 2 H), 2.75 (ddd, *J* = 2.5, 4.1, 19.3 Hz, 1 H), 2.42 - 2.29 (m, 1 H), 2.26 - 2.17 (d, *J* = 12.6 Hz, 1 H), 2.13 - 2.00 (m, 1 H), 1.79 - 1.59 (m, 3 H), 1.25 (dt, *J* = 1.5, 7.1 Hz, 6 H); **^{13}C NMR (75MHz ,$CDCl_3$)** δ = 210.6 (C), 169.8 (C), 169.6 (C), 149.2 (C), 140.1 (C), 134.2 (C), 128.2 (CHx2), 127.8 (CH), 127.4 (CHx2), 126.6 (CH), 114.6 (CH_2), 61.9 (CH_2), 61.7 (CH_2), 56.2 (C), 52.4 (CH), 40.6 (CH), 39.7 (CH_2), 27.2 (CH_2), 25.6 (CH_2), 23.6 (CH_2), 14.0 (CH_3), 14.0 (CH_3); **HRMS (EI)** m/z calcd for $C_{24}H_{28}O_5$ [M^+] 396.1937, found 396.1918.

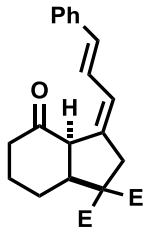


Bicyclo[4.4.0]decenone 2.11h

Isolated as a colorless oil.

IR (neat, cm-1) ν max 2979, 2942, 2866, 1732, 1366, 1217, 1180, 1094, 913, 738, 699; **^{1}H NMR (400MHz ,$CDCl_3$)** δ = 7.37 - 7.23 (m, 5 H), 5.89 (td, *J* = 2.6, 5.5 Hz, 1 H), 5.11 (d, *J* = 0.9 Hz, 1 H), 5.06 (s, 1 H), 4.46 (dd, *J* = 11.9, 27.3 Hz, 2 H), 4.31 - 4.06 (m, 5 H), 3.99 (d, *J* = 12.7 Hz, 1 H), 3.66 (s, 1 H), 3.02 - 2.84 (m, 2 H), 2.75 (ddd, *J* = 2.8, 3.9, 19.4 Hz, 1 H), 2.42 - 2.23 (m, 1 H), 2.18 (d, *J* = 12.6 Hz, 1 H), 2.06 - 1.96 (m, 1 H), 1.71 - 1.53 (m, 3 H),

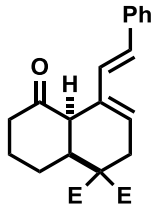
1.21 (td, *J* = 7.1, 19.0 Hz, 6 H); **^{13}C NMR (101MHz , CDCl$_3$)** δ = 212.3 (C), 169.9 (C), 169.4 (C), 144.6 (C), 138.3 (C), 132.7 (C), 128.3 (CHx2), 127.7 (CHx2), 127.5 (CH), 123.7 (CH), 115.4 (CH_2), 72.1 (CH_2), 71.7 (CH_2), 61.8 (CH_2), 61.8 (CH_2), 56.1 (C), 52.4 (CH), 40.7 (CH), 39.5 (CH_2), 27.1 (CH_2), 25.9 (CH_2), 23.5 (CH_2), 14.0 (CH_3), 14.0 (CH_3); **HRMS (EI)** m/z calcd for $C_{26}H_{32}O_6$ [M^+] 440.2199, found 440.2204.



Bicyclo[4.3.0]decenone 2.9i

Isolated as a colorless oil.

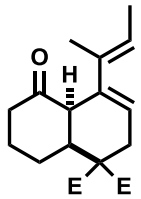
IR (neat, cm-1) ν max 2980, 2869, 1735, 1447, 1243; **^{1}H NMR (300MHz, CDCl$_3$)** δ = 7.37 - 7.15 (m, 5 H), 6.94 (dd, *J* = 11.3, 15.4 Hz, 1 H), 6.39 (d, *J* = 15.5 Hz, 1 H), 6.27 (d, *J* = 11.2 Hz, 1 H), 4.32 - 4.09 (m, 4 H), 3.87 - 3.77 (m, 1 H), 3.51 (d, *J* = 18.0 Hz, 1 H), 3.28 (td, *J* = 6.3, 12.3 Hz, 1 H), 2.96 (d, *J* = 18.1 Hz, 1 H), 2.40 - 2.31 (m, 2 H), 2.04 (td, *J* = 4.2, 13.5 Hz, 1 H), 1.78 - 1.58 (m, 2 H), 1.49 - 1.36 (m, 1 H), 1.25 (td, *J* = 7.1, 10.0 Hz, 6 H); **^{13}C NMR (75MHz, CDCl$_3$)** δ = 211.3 (C), 170.5 (C), 169.0 (C), 137.3 (C), 136.6 (C), 133.0 (CHx2), 128.6 (CH), 127.5 (CH), 127.2 (CH), 126.4 (CHx2), 124.2 (CH), 62.7 (C), 61.8 (CH_2), 61.7 (CH_2), 56.5 (CH), 48.3 (CH), 39.6 (CH_2), 39.5 (CH_2), 24.6 (CH_2), 24.3 (CH_2), 14.1 (CH_3), 14.0 (CH_3); **HRMS (EI)** m/z calcd for $C_{24}H_{28}O_5$ [M^+] 396.1937, found 396.1940.



Bicyclo[4.4.0]decenone 2.11i

Isolated as a colorless oil.

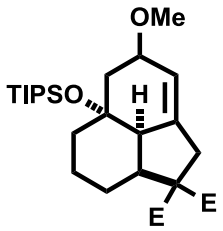
IR (neat, cm-1) ν max 2939, 1733, 1711, 1450, 1235, 1178, 694; **^{1}H NMR (300MHz, $CDCl_3$)** δ = 7.37 - 7.15 (m, 5 H), 6.56 (s, 2 H), 6.02 (td, *J* = 2.7, 5.5 Hz, 1 H), 4.26 - 4.15 (m, 4 H), 3.63 (br. s., 1 H), 3.06 - 2.94 (m, 2 H), 2.83 (td, *J* = 3.3, 20.0 Hz, 1 H), 2.39 - 2.20 (m, 2 H), 2.10 - 2.01 (m, 1 H), 1.77 - 1.53 (m, 3 H), 1.25 (dt, *J* = 5.5, 7.1 Hz, 6 H); **^{13}C NMR (101MHz ,$CDCl_3$)** δ = 213.0 (C), 169.8 (C), 169.4 (C), 137.2 (C), 131.4 (C), 128.9 (CH), 128.7 (CH), 128.5 (CHx2), 127.5 (CH), 126.4 (CHx2), 125.8 (CH), 61.9 (CH_2), 61.8 (CH_2), 56.3 (C), 52.3 (CH), 41.1 (CH), 39.6 (CH_2), 27.5(CH_2), 26.1 (CH_2), 23.6 (CH_2), 14.0 (CH_3), 14.0 (CH_3); **HRMS (EI)** m/z calcd for $C_{24}H_{28}O_5$ [M^+] 396.1936, found 396.1942.



Bicyclo[4.4.0]decenone 2.11j

Isolated as a colorless oil.

IR (neat, cm-1) ν max 2981, 2940, 2866, 1733, 1713, 1445, 1235, 1180, 1049, 916, 733; **^{1}H NMR (300MHz, $CDCl_3$)** δ = 5.64 (td, *J* = 2.4, 5.1 Hz, 1 H), 5.35 (q, *J* = 6.7 Hz, 1 H), 4.22 - 4.10 (m, 4 H), 3.57 (br. s., 1 H), 2.92 - 2.81 (m, 2 H), 2.67 (td, *J* = 2.8, 19.2 Hz, 1 H), 2.27 - 2.07 (m, 2 H), 2.05 - 1.90 (m, 1 H), 1.63 (d, *J* = 0.7 Hz, 3 H), 1.54 (d, *J* = 6.7 Hz, 3 H), 1.66 - 1.50 (m, 3 H), 1.21 (ddt, *J* = 0.7, 2.4, 7.1 Hz, 6 H); **^{13}C NMR (75MHz ,$CDCl_3$)** δ = 212.4 (C), 169.9 (C), 169.6 (C), 137.3 (C), 135.9 (C), 122.8 (CH), 120.5 (CH), 61.7 (CH_2), 61.6 (CH_2), 56.1 (C), 52.3 (CH), 40.7 (CH), 39.5 (CH_2), 26.9 (CH_2), 26.0 (CH_2), 23.5 (CH_2), 15.0 (CH_3), 14.0 (CH_3), 13.9 (CH_3), 13.6 (CH_3); **HRMS (EI)** m/z calcd for $C_{20}H_{28}O_5$ [M^+] 348.1937, found 348.1905.

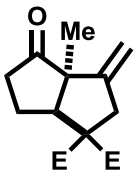


Tricycle 2.13

Isolated as a 7:13 mixture of diasterioisomers as clear oils. Stereochemistry could not be determined by 2D-NMR.

Major: IR (neat, cm-1) 2942, 2866, 1734, 1462, 1247, 1152, 1093, 883, 676; **^{1}H NMR (400MHz, $CDCl_3$)** δ = 5.62 (br. s., 1 H), 4.31 - 4.05 (m, 4 H), 3.85 (ddd, *J* = 2.0, 3.7 Hz, 1 H), 3.33 (s, 3 H), 3.28 (ddd, *J* = 2.1 Hz, 1 H), 3.03 (ddd, *J* = 5.8, 13.0 Hz, 1 H), 2.88 (d, *J* = 18.7 Hz, 1 H), 2.66 (br. s., 1 H), 2.11 (d, *J* = 13.8 Hz, 1 H), 1.91 - 1.77 (m, 1 H), 1.76 - 1.63 (m, 2 H), 1.44 - 1.29 (m, 3 H), 1.24 (dt, *J* = 7.1 Hz, 6 H), 1.13 - 1.06 (m, 21 H), 0.80 (dddd, *J* = 2.7, 13.0 Hz, 1 H); **^{13}C NMR (101MHz, $CDCl_3$)** δ = 171.8 (C_{quat}), 169.8 (C_{quat}), 142.9 (C_{quat}), 117.6 (CH), 76.4 (CH), 72.3 (C_{quat}), 62.3(C_{quat}), 61.4 (CH_2), 61.4 (CH_2), 56.6 (CH), 52.1 (CH), 42.4 (CH), 40.3 (CH_2), 35.6 (CH_2), 32.9 (CH_2), 23.4 (CH_2), 20.0 (CH_2), 18.5 (CHx3), 14.1 (CH_3), 14.0 (CH_3), 13.7 (CH_3x6); **HRMS (EI)** m/z calcd for $C_{25}H_{41}O_6Si$ [(M-$_i$Pr)$^+$] 465.2672, found 465.2716.

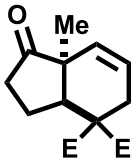
Minor: IR (neat, cm-1) 2941, 2866, 1735, 1465, 1366, 1248, 1085, 883, 679; **^{1}H NMR (300MHz, $CDCl_3$)** δ = 5.56 (br. s., 1 H), 4.32 - 4.05 (m, 4 H), 3.91 (br. s., 1 H), 3.36 (s, 3 H), 3.34 - 3.23 (m, 1 H), 3.00 (ddd, *J* = 6.0, 12.3 Hz, 1 H), 2.89 (d, *J* = 18.9 Hz, 1 H), 2.81 (br. s**.**, 1 H), 2.18 (dd, *J* = 6.2, 11.8 Hz, 1 H), 1.85 - 1.59 (m, 2 H), 1.23 (dt, *J* = 7.1 Hz, 6 H), 1.51 - 1.02 (m, 7 H), 1.09 (s, 18 H), 0.73 (dddd, *J* = 3.2, 13.1 Hz, 1 H); **^{13}C NMR (75MHz, $CDCl_3$)** δ = 171.6 (C_{quat}), 169.9 (C_{quat}), 142.7 (C_{quat}), 117.8 (CH), 77.6 (CH), 73.8 (C_{quat}), 62.2 (C_{quat}), 61.4 (CH_2x2), 55.6 (CH_3), 51.8 (CH), 42.6 (CH_2), 41.7 (CH), 35.4 (CH_2), 32.8 (CH_2), 23.2 (CH_2), 19.5 (CH_2), 18.5 (CHx3), 14.1 (CH_3), 14.0 (CH_3), 13.6 (CH_3x6); **HRMS (EI) m/z calcd for** $C_{25}H_{41}O_6Si$ [(M-$_i$Pr)$^+$] 465.2672, found 465.2696.



Bicyclo[4.3.0]decenone 3.2

Isolated as a colorless oil.

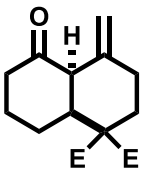
IR (neat, cm-1) ν max 1742, 1730; **^{1}H NMR (400MHz, $CDCl_3$)** δ = 5.05 - 5.00 (m, 2 H), 4.26 - 4.12 (m, 4 H), 3.30 - 3.18 (m, 2 H), 3.05 - 2.98 (m, 1 H), 2.40 - 2.23 (m, 2 H), 2.09 - 2.00 (m, 1 H), 1.55 - 1.42 (m, 1 H), 1.23 (s, 3 H), 1.25 (dt, *J* = 4.0, 7.1 Hz, 6 H); **^{13}C NMR (101MHz, $CDCl_3$)** δ = 217.8 (C_{quat}), 171.1 (C_{quat}), 169.6 (C_{quat}), 149.3 (C_{quat}), 110.2 (CH_2), 62.3 (C_{quat}), 61.9 (CH_2), 61.8 (CH_2), 59.7 (C_{quat}), 53.3 (CH), 38.8 (CH_2), 37.3 (CH_2), 24.0 (CH_3), 22.4 (CH_2), 14.2 (CH_3), 14.1 (CH_3); **HRMS (EI)** m/z calcd for $C_{16}H_{22}O_5$ [$(M)^+$] 294.1467, found 294.1467.



Bicyclo[4.3.0]decenone 3.3

Isolated as a colorless oil. Characterized as an inseperable mixture of **3.2** and **3.3**.

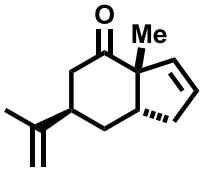
IR (neat, cm-1) ν max 1738, 1733; **^{1}H NMR (400MHz, $CDCl_3$)** δ = 5.74 (ddd, *J* = 2.2, 5.7, 10.0 Hz, 1 H), 5.26 (td, *J* = 1.4, 10.0 Hz, 1 H), 4.27 - 4.07 (m, 4 H), 3.05 - 2.98 (m, 2 H), 2.43 - 2.16 (m, 4 H), 1.61 - 1.40 (m, 1 H), 1.25 (dt, *J* = 4.0, 7.0 Hz, 6 H), 1.11 (s, 3 H); **^{13}C NMR (101MHz, $CDCl_3$)** δ = 218.8 (C_{quat}), 170.3 (C_{quat}), 170.2 (C_{quat}), 127.3 (CH), 125.1 (CH), 61.8 (2xCH_2), 54.7 (C_{quat}), 51.3 (C_{quat}), 45.5 (CH), 35.8 (CH_2), 26.2 (CH_2), 23.3 (CH_3), 22.4 (CH_2), 14.2 (CH_3), 14.1 (CH_3); **HRMS (EI)** m/z calcd for $C_{16}H_{22}O_5$ [$(M)^+$] 294.1467, found 294.1471.



Bicyclo[4.4.0]alkenone 3.8

Isolated as a colorless oil.

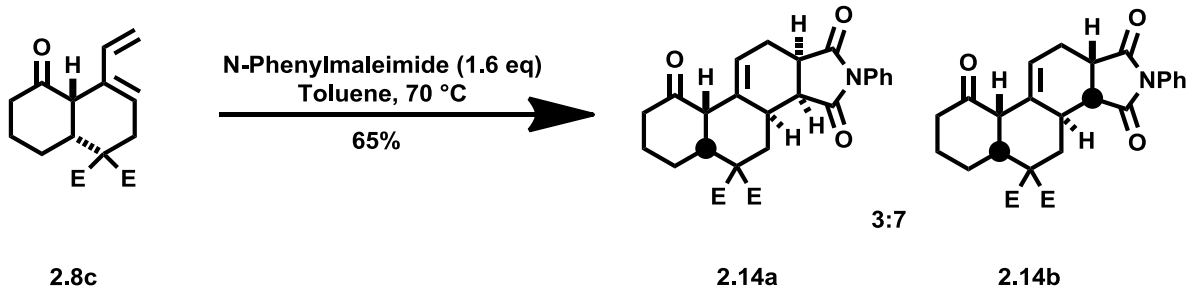
IR (neat, cm-1) ν max 1732, 1709; **^{1}H NMR (400MHz, $CDCl_3$)** δ = 4.94 (s, 1 H), 4.38 (s, 1 H), 4.25 - 4.09 (m, 4 H), 3.56 (br. s., 1 H), 2.90 - 2.81 (m, 1 H), 2.56 - 2.44 (m, 1 H), 2.42 - 2.27 (m, 3 H), 2.07 (dq, *J* = 3.8, 14.2 Hz, 1 H), 2.07 - 1.87 (m, 2 H), 1.70 - 1.55 (m, 2 H), 1.24 (q, *J* = 6.9 Hz, 6 H), 1.32 - 1.19 (m, 1 H); **^{13}C NMR (101MHz, $CDCl_3$)** δ = 211.2 (C_{quat}), 170.2 (C_{quat}), 170.1 (C_{quat}), 142.8 (C_{quat}), 111.6 (CH_2), 61.8 (CH_2), 61.7 (CH_2), 58.1 (C_{quat}), 55.4 (CH), 41.9 (CH), 39.8 (CH_2), 32.0 (CH2), 26.7 (CH_2), 25.0 (CH_2), 23.0 (CH_2), 14.2 (CH_3), 14.2 (CH_3); **HRMS (EI)** m/z calcd for $C_{17}H_{24}O_5$ [$(M)^+$] 308.1624, found 308.1606.



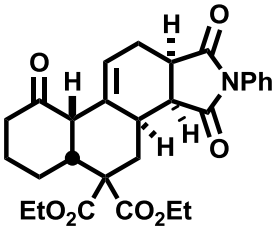
Bicyclo[4.3.0]alkenone 3.10

Prepared according to literature procedure and exhibited spectral data in accordance with previous report.[68]

Synthesis of Steroid-analogues 2.14a and 2.14b



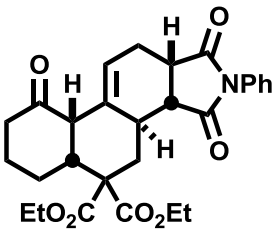
N-phenylmaleimide (16.8 mg, 0.0963 mmol) was canulated with toluene (0.24 mL) to a solution of the diene **2.8c** (19.3 mg, 0.0602 mmol) in toluene (0.40 mL) at room temperature in a sealed tube. The reaction mixture was then stirred for 3 day at 70°C. Once the reaction was completed, the solvent was evaporated and the residue was purified by flash column chromatography (40% EtOAc : Hexane) to yield 5.8 mg of **2.14a** and 13.4 mg of **2.14b** as colorless oils in a total 65% yield.



Diterpene 2.14a

Isolated as a white solid.

IR (neat, cm-1)) ν max 1713; **^{1}H NMR (500MHz, $CDCl_3$)** δ = 7.50 - 7.43 (m, 2 H), 7.41 - 7.36 (m, 1 H), 7.35 - 7.31 (m, 2 H), 5.54 (qd, *J* = 2.7, 6.4 Hz, 1 H), 4.28 - 4.09 (m, 4 H), 3.35 - 3.30 (m, 1 H), 3.13 - 3.02 (m, 3 H), 2.79 - 2.64 (m, 2 H), 2.53 (ddd, *J* = 6.7, 13.0, 15.4 Hz, 1 H), 2.34 - 2.21 (m, 2 H), 2.03 - 1.93 (m, 1 H), 1.79 - 1.57 (m, 4 H), 1.47 (dq, *J* = 3.7, 13.0 Hz, 1 H), 1.24 (t, *J* = 7.2 Hz, 3 H), 1.25 (t, *J* = 7.1 Hz, 3 H); **^{13}C NMR (126MHz, $CDCl_3$)** δ = 209.9 (C_{quat}), 178.0 (C_{quat}), 177.4 (C_{quat}), 171.5 (C_{quat}), 170.5 (C_{quat}), 135.9 (C_{quat}), 131.9 (C_{quat}), 129.2 (2xCH), 128.6 (CH), 126.5 (2xCH), 123.4 (CH), 62.0 (CH_2), 61.5 (CH_2), 55.7 (C_{quat}), 53.3 (CH), 45.5 (CH), 39.5 (CH), 38.8 (CH), 37.8 (CH_2), 33.7 (CH_2), 31.8 (CH), 25.0 (CH_2), 24.6 (CH_2), 23.7 (CH_2), 14.2 (CH_3), 14.2 (CH_3); **HRMS (EI)** m/z calcd for $C_{28}H_{31}NO_7$ [$(M)^+$] 493.2101, found 493.2021.

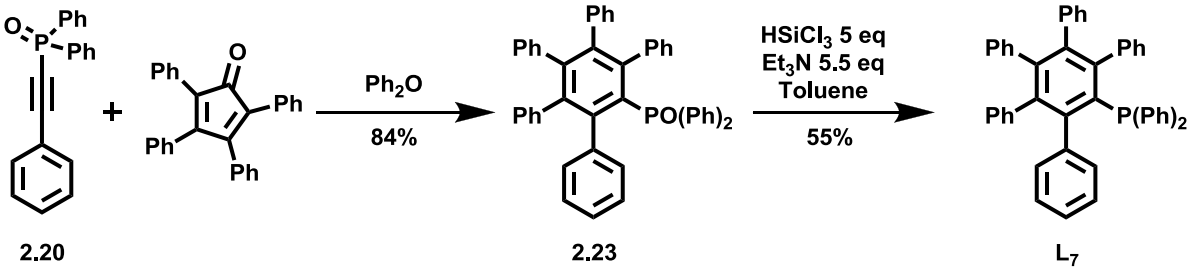


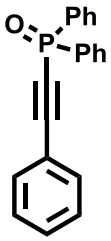
Diterpene 2.14b

Isolated as a white solid.

IR (neat, cm-1)) ν max 1710; **^{1}H NMR (500MHz, $CDCl_3$)** δ = 7.53 - 7.40 (m, 2 H), 7.39 - 7.34 (m, 1 H), 7.17 - 7.13 (m, 2 H), 5.45 (qd, *J* = 2.8, 7.2 Hz, 1 H), 4.33 - 4.18 (m, *J* = 7.1, 7.1, 7.1, 10.6, 10.6 Hz, 2 H), 4.12 (qt, *J* = 7.1, 10.6 Hz, 2 H), 3.34 - 3.26 (m, 2 H), 3.19 (ddd, *J* = 3.4, 4.8, 13.0 Hz, 1 H), 3.09 - 2.98 (m, 1 H), 2.83 (dd, *J* = 7.1, 15.6 Hz, 1 H), 2.64 (dd, *J* = 4.5, 14.9 Hz, 1 H), 2.57 - 2.43 (m, 2 H), 2.38 - 2.25 (m, 2 H), 1.98 (ddd, *J* = 2.6, 7.1, 13.4 Hz, 1 H), 1.72 - 1.59 (m, *J* = 4.5, 4.5, 4.5, 8.7, 13.1 Hz, 2 H), 1.59 - 1.50 (m, 1 H), 1.36 (dq, *J* = 3.7, 12.8 Hz, 1 H), 1.26 (t, *J* = 7.2 Hz, 3 H), 1.24 (t, *J* = 7.2 Hz, 3 H); **^{13}C NMR (126MHz, $CDCl_3$)** δ = 209.6 (C_{quat}), 178.4 (C_{quat}), 176.5 (C_{quat}), 171.4 (C_{quat}), 171.2 (C_{quat}), 138.6 (C_{quat}), 131.6 (C_{quat}), 129.1 (2xCH), 128.7 (CH), 126.6 (2xCH), 122.0 (CH), 61.9 (CH_2), 61.2 (CH_2), 55.3 (C_{quat}), 53.1 (CH), 43.1 (CH), 39.6 (CH), 39.0 (CH), 37.8 (CH_2), 32.0 (CH), 29.6 (CH_2), 24.8 (CH_2), 24.7 (CH_2), 24.3 (CH_2), 14.0 (CH_3), 13.9 (CH_3); **HRMS (EI)** m/z calcd for $C_{28}H_{31}NO_7$ [$(M)^+$] 493.2101, found 493.2087.

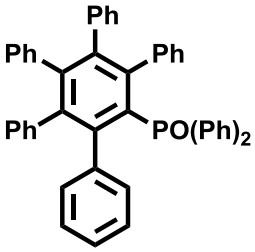
Synthesis of L_7





Phosphine oxide 2.20

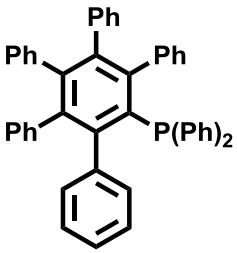
Prepared according to literature procedure.[60] Exhibited spectral data in accordance with previous report.[69]



Phosphine oxide 2.23

Isolated as a white solid.

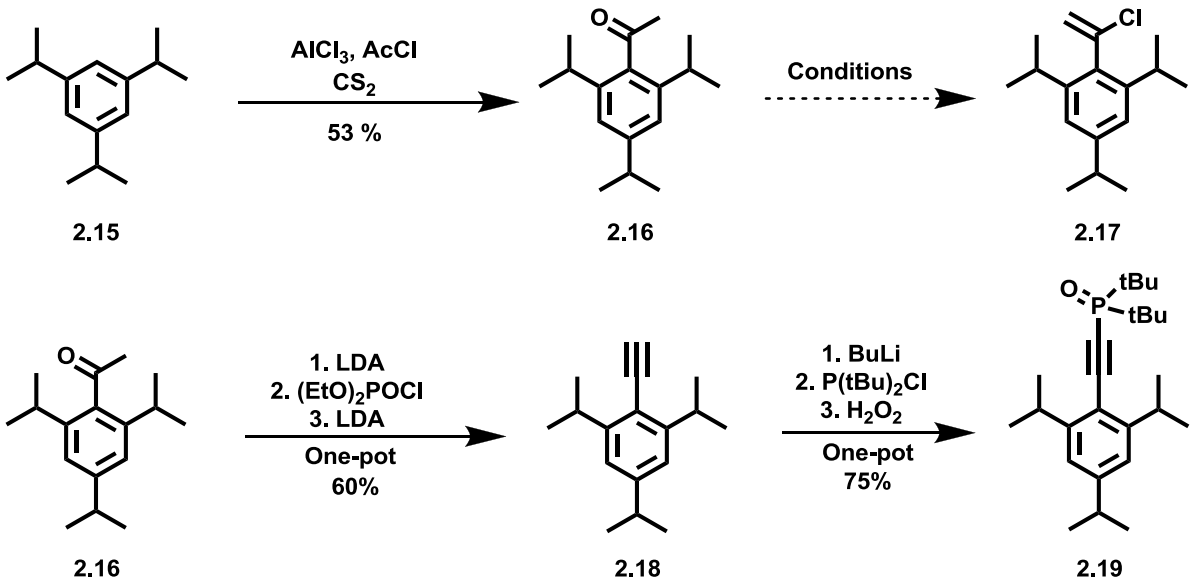
^{1}H NMR (500MHz, $CDCl_3$) δ = 7.35 (dd, *J* = 8.3, 10.4 Hz, 4 H), 7.04 - 6.72 (m, 26 H), 6.66 (t, *J* = 7.3 Hz, 12 H); **^{13}C NMR (126MHz, $CDCl_3$)** δ = 147.3 (d, J= 10.5 Hz, C_{quat}), 145.1 (d, J= 2.5 Hz, C_{quat}), 141.8 (d, J= 10.5 Hz, C_{quat}), 140.0 (s, C_{quat}), 139.3 (s, C_{quat}), 139.0 (d, J= 5.5 Hz, C_{quat}), 137.1 (d, J= 104.2 Hz, C_{quat}), 133.0 (s, CH), 132.3 (d, J = 103.7 Hz, C_{quat}), 131.2 (s, CH), 130.6 (s, CH), 130.2 (d, J= 8.5 Hz, CH), 129.2 (d, J= 2.5 Hz, CH), 127.6 (d, J= 12.0 Hz, CH), 126.6 (s, CH), 126.4 (d, J= 41.9 Hz, CH), 126.3 (s, CH), 125.7 (s, CH), 125.6 (s, CH); **HRMS (ESI)** m/z calcd for $C_{48}H_{35}PO$ [$(M)^+$] 658.2426, found 568.2427.

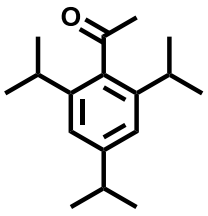


L_7

^{1}H NMR (300MHz, $CDCl_3$) δ = 7.16 - 7.02 (m, 10 H), 6.92 - 6.62 (m, 25 H); **^{13}C NMR (75MHz, $CDCl_3$)** Observed complexity due to ^{13}C-^{31}P coupling δ = 148.1 (C_{quat}), 147.8 (C_{quat}), 142.8 (C_{quat}), 141.8 (C_{quat}), 141.8 (C_{quat}), 140.6 (C_{quat}), 140.5 (C_{quat}), 140.3 (C_{quat}), 137.2 (C_{quat}), 137.0 (C_{quat}), 132.3 (CH), 132.1 (CH), 131.1 (CH), 130.9 (CH), 130.8 (CH), 130.8 (CH), 127.6 (CH), 127.5 (CH), 126.8 (CH), 126.4 (CH), 126.3 (CH), 126.3 (CH), 125.6 (CH), 125.3 (CH), 125.1 (CH);); **^{31}P NMR (121MHz, $CDCl_3$)** δ = -4.2; **HRMS (ESI)** m/z calcd for $C_{48}H_{35}P$ [$(M)^+$] 642.2476, found 642.2460.

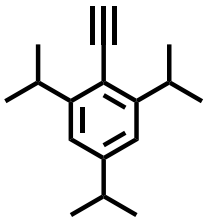
Synthesis of Phosphine oxide 2.19





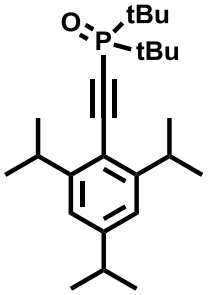
Ketone 2.16

Prepared according to literature procedure and exhibited spectral data in accordance with previous report.[70]



Aryl acetylene 2.18

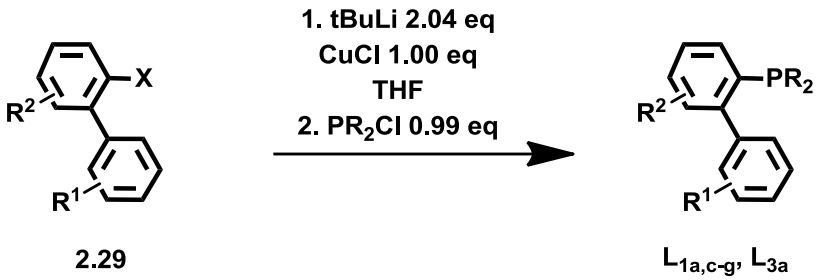
Prepared according to literature procedure in 60% yield an isolated as a clear oil.[71] Exhibited spectral data in accordance with previous report.[72]



Phosphine oxide 2.19

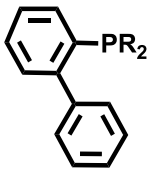
Prepared according to literature procedure in 75% yield and isolated as a pale yellow solid.[60] **^{1}H NMR (400MHz, $CDCl_3$)** δ = 6.98 (s, 2 H), 3.51 (spt, *J* = 6.8 Hz, 2 H), 2.87 (spt, *J* = 6.8 Hz, 1 H), 1.37 (d, *J* = 15.2 Hz, 18 H), 1.24 (d, *J* = 7.2 Hz, 12 H), 1.22 (d, *J* = 7.7 Hz, 6 H); **^{13}C NMR (101MHz, $CDCl_3$)** δ = 152.4 (d, J= 1.1 Hz, 2xC_{quat}), 151.3 (s, C_{quat}), 120.6 (s, 2xCH), 116.0 (d, J= 3.3 Hz, C_{quat}), 100.8 (d, J= 19.1 Hz, C_{quat}), 88.9 (d, J= 129.8 Hz, C_{quat}), 36.3 (d, J= 72.6 Hz, 2xC_{quat}), 34.7 (s, CH), 31.9 (s, 2xCH), 26.5 (s, 6xCH_3), 23.8 (s, 2xCH_3), 23.6 (s, 4xCH_3); **HRMS (EI)** m/z calcd for $C_{25}H_{41}OP$ [$(M)^+$] 388.2895, found 388.2897.

General procedure F – Synthesis of Buchwald-type phosphines via alkylation



2.29 **$L_{1a,c-g}$, L_{3a}**

To a shlenk containing a -78°C solution of 2-iodobiphenyl (1.81 mmol) in THF (7.4 mL) was added a 1.5 M solution of tBuLi in pentane (3.69 mmol) dropwise. The reaction is stirred for 1 hour at -78°C and CuCl is added. The reaction mixture is allowed to warm up to room temperature before PR_2Cl (1.78 mmol) is added as a THF solution (2 mL) via seringe. The shlenk is sealed and the mixture is heated to 70°C for 18 hours. The reaction mixture is cooled to room temperature, diluted with EtOAc and washed with NH_4OH until the aqueous phase remains colorless. The organic phase is then washed with $NaHCO_3$(aq), brine and dried over sodium sulfate before being filtered and concentrated by rotary evaporation. The resulting crude phosphine is then recrystallized.



L_1 ligands

L_{1d} (R= Ph)

Prepared according to general procedure literature procedure F in 67% yield and crystalized from methanol. Exhibited spectral data in accordance with previous report.[73]

L_{1e} (R= Mes)

Prepared according to general procedure literature procedure F in 40% yield and crystalized from methanol.

^{1}H NMR (400MHz, $CDCl_3$) δ = 7.33 - 7.25 (m, 2 H), 7.23 - 7.12 (m, 7 H), 6.74 (d, *J* = 2.5 Hz, 4 H), 2.24 (s, 6 H), 2.01 (t, *J* = 0.5 Hz, 12 H); **^{13}C NMR (101MHz, $CDCl_3$)** Two CH signals appear to have the same chemical shift, however, we are unsure which ones. δ = 147.8 (d, J= 31.2 Hz, C_{quat}), 143.2 (d, J= 16.5 Hz, 4xC_{quat}), 142.2 (d, J= 5.9 Hz, C_{quat}), 137.9 (s, 2xC_{quat}), 136.7 (d, J= 16.1 Hz, C_{quat}), 133.9 (s, CH), 131.0 (d, J= 21.3 Hz, 2xC_{quat}), 130.2 (d, J= 4.8 Hz, CH), 129.9 (d, J= 2.9, 4xCH), 129.3 (d, J= 4.4 Hz, CH), 128.0 (s, CH), 127.4 (s, 2xCH), 126.8 (s, 2xCH), 23.2 (d, J= 16.5 Hz, 4xCH_3), 21.0 (s, 2xCH_3); **^{31}P NMR (121MHz, $CDCl_3$)** δ = -27.1; **HRMS (EI)** m/z calcd for $C_{30}H_{31}P$ [$(M-H)^+$] 422.2163, found 422.2175.

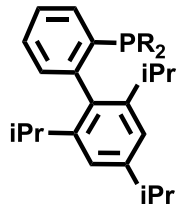
L_{1f} (R = (4-OMe)C_6H_4)

Prepared according to general procedure literature procedure F in 35% yield and crystalized from methanol. Exhibited spectral data in accordance with previous report.[74]

L_{1g} (R = (3,5-bis(CF_3))C_6H_3)

Prepared according to general procedure literature procedure F in 65% yield and crystalized from methanol.

^{1}H NMR (300MHz, $CDCl_3$) δ = 7.86 (s, 2 H), 7.62 (d, *J* = 6.6 Hz, 4 H), 7.53 (dt, *J* = 1.3, 7.6 Hz, 1 H), 7.44 - 7.33 (m, 2 H), 7.31 - 7.21 (m, 3 H), 7.19 - 7.11 (m, 2 H), 6.95 - 6.89 (m, 1 H); **^{13}C NMR (101MHz, $CDCl_3$)** δ = 148.3 (d, J= 27.1 Hz, C_{quat}) , 140.8 (d, J= 5.9 Hz, C_{quat}), 139.7 (d, J= 19.4 Hz, 2xC_{quat}), 133.7 (dd, J= 21.6, 2.6 Hz, 2xCH), 132.9 (s, CH), 132.3 (d, J= 12.1 Hz, C_{quat}), 132.2 (qd, J= 33.7, 6.6 Hz, 4xC_{quat}), 131.0 (d, J= 4.4 Hz, CH), 130.5 (s, CH), 129.6 (d, J= 3.7 Hz, CH), 128.5 (s, CH), 128.2 (s, 2xCH), 128.0 (s, 2xCH), 123.4 (dt, J= 7.3, 3.7 Hz, 4xCH), 123.1 (q, 274.4 Hz, 4xC_{quat}); **^{31}P NMR (121MHz, $CDCl_3$)** δ = -9.1; **HRMS (EI)** m/z calcd for $C_{28}H_{15}PF_{12}$ [$(M-H)^+$] 609.0642, found 609.0616.

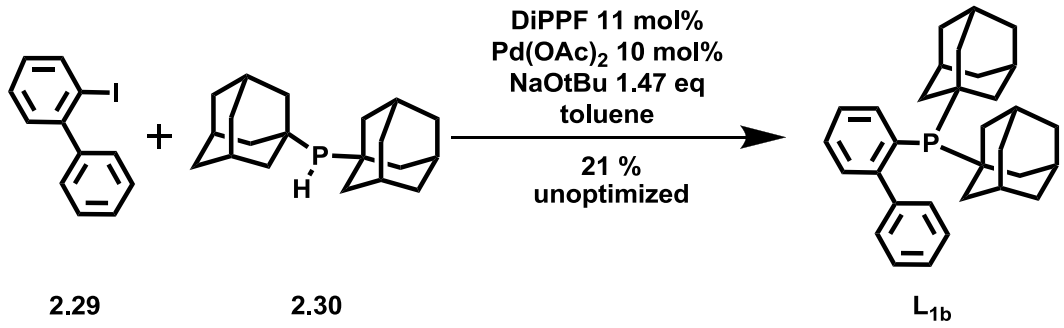


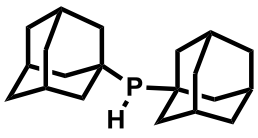
L_2 ligands

L_{2g} (R = (3,5-bis(CF_3))C_6H_3)

Prepared according to general procedure literature procedure F in 35% yield and crystalized from methanol. Exhibited spectral data in accordance with previous report.[75]

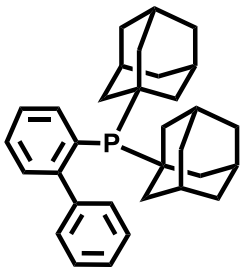
Synthesis of L_{1b} via Pd-Coupling





Phosphine 2.30

Prepared according to literature procedure and exhibited spectral data in accordance with previous report.[76]



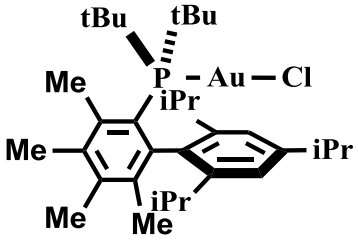
L_{1b} (R= adamantyl)

Prepared according to a modified literature procedure.[77] Exhibited spectral data in accordance with previous report.[78]

In a glovebox, $Pd(OAc)_2$ (30.5 mg, 0.136 mmol) and DiPPF (1,1'-bis(diisopropylphosphino)ferrocene; 58.6 mg, 0.140 mmol) were combined. Toluene (2 mL) was then added and the reaction mixture was stirred for 10 min. This solution was added to a via containing di(1-adamantyl)phophine **2.30** (which in this case contained 50 mol% of the corresponding phosphine oxide; 411.3 mg, 0.770 mmol) and NaOtBu (192.2 mg, 2.00 mmol), followed by the addition of the 2-bromobiphenyl (241.4 μL, 1.40 mmol). The vial was then heated at 110°C for 20 hours. The reaction mixture was filtered on silica (10% EtOAc : Hexane) and concentrated *in vacuo* before being purified by flash chromatography (3% EtOAc: Hexane). The residue was then triturated with cold pentane to yield 72.3 mg of $\mathbf{L_{1b}}$ in 21% yield.

General procedure G - Synthesis of Au(I) catalysts

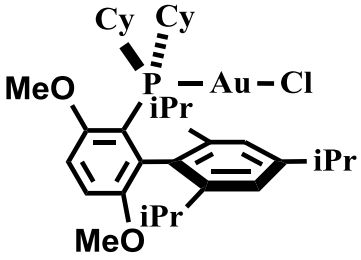
To suspension of a phosphine (0.208 mmol) in DCM (2 mL) was added chloro(dimethylsulfide)gold(I) (61 mg, 0.208 mmol). The mixture was stirred for 4h at room temperature. The solvent was evaporated off under reduced pressure and the residue was triturated with pentane to give $\mathbf{L_8}$AuCl (125 mg, 83%) as a grey powder.



L_8AuCl

Prepared according to general procedure G in 83% yield as a grey powder.

^{1}H NMR (400 MHz, C_6D_6) δ 7.37 (s, 2H), 3.21 (sept, J =6.9 Hz, 1H), 2.57 (sept, J = 6.7 Hz, 2H), 2.16 (s, 3H), 189 (s, 3H), 1.85 (s, 3H), 1.64 (d , J = 6.9 Hz, 6H), 1.60 (s, 3H), 1.52 (d, J= 6.7 Hz, 6H), 1.31 (s, 9H), 1,28 (s, 9H), 0.98 (d, J = 6.7 Hz, 6H) ;**^{13}C NMR (100 MHz, C_6D_6)** δ 151.0 (C_{quat}), 146.9 (C_{quat}), 146.6 (C_{quat}), 146.0 (C_{quat}), 140.2 (C_{quat}) (d, J_{C-P} = 2.6 Hz),, 138.3 (C_{quat}) (d, J_{C-P} = 3.3 Hz), 138.2 (C_{quat}), 137.8 (C_{quat}) (d, J_{C-P} = 9.2 Hz), 135.9 (C_{quat}) (d, J_{C-P} = 7.0 Hz),, 129.1 (C_{quat}), 128.8 (CH), 123.3 (CH), 41.5 (C_{quat}x2) (d, J_{C-P} = 20.2 Hz),, 35.0 (CH), 33.3 (CH_3x3) (d, J_{C-P} = 8.4 Hz), 31.2 (CHx2), 27.9 (CH_3), 27.9 (CH_3), 25.4 (CH_3x3), (d, J_{C-P} = 7.7 Hz) 25.1 (CH_3x2), 22.6 (CH_3), 22.6 (CH_3), 17.6 (CH_3x2), 17.1 (CH_3x2) ; **^{31}P NMR (162 MHz, C_6D_6)** δ 76.51; **HRMS (EI)** m/z calcd for $C_{33}H_{54}PAuCl$ $[(M-Cl)^+]$ = 677.3550, found 6755.3548

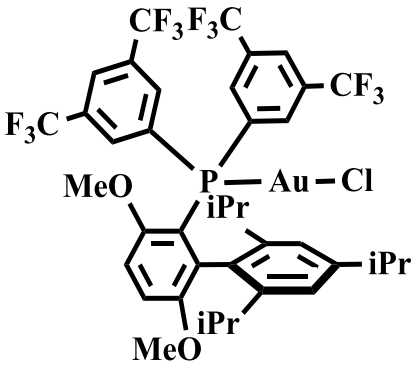


$L_{3c}AuCl$

Prepared according to general procedure G in 78% yield as a white powder.

^{1}H NMR (400 MHz, C_6D_6) δ; **^{13}C NMR (100 MHz, C_6D_6)** δ 7.44 (s, 2H), 6.47 (d, J = 9.0 Hz, 1H), 6.32 (dd, J = 9.0 Hz, 3.4 Hz, 1H), 3.23 (sept, J = 7.0 Hz, 1H), 3.18 (s, 3H), 2.94 (s, 3H), 2.58 (sept, J = 6.8 Hz, 2H), 2.47 (qdd, J = 12.3 Hz, 2.8 Hz, 2.8 Hz, 2H), 2.11 (s, 1H), 1.96-1.87 (m, 2H), 1.77-1.44 (m, 10H), 1.56 (d, J = 6.9 Hz, 12H), 1.41-1.27 (m, 2H), 1.14 (d, J = 6.8 Hz, 6H), 1.10-0.99 (m, 5H); **^{13}C NMR (75 MHz, C_6D_6)** δ 155.6 (C_{quat}), 154.0

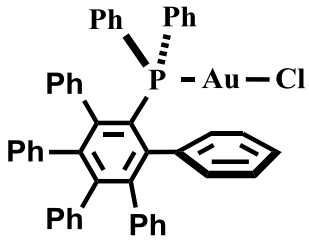
(C_{quat}) (d, J_{C-P} = 11.4 Hz), 151.1 (C_{quat}), 146.5 (C_{quat}), 139.5 (C_{quat}) (d, J_{C-P} = 14.7 Hz), 131.6 (C_{quat}) (d, J_{C-P} = 7.4 Hz), 128.9 (CH), 122.9 (CH), 119.1 (C_{quat}), 118.6 (C_{quat}), 113.9 (CH) (d, J = 2.2 Hz), 110.4 (CH) (d, J = 5.5 Hz), 55.5 (CH_3), 54.6 (CH_3), 39.6 (CHx2) (d, J_{C-P} =34.5 Hz), 35.3 (CHx2), 35.0 (CH_2x2), 34.9 (CH_2x2), 31.6 (CH), 30.6 (CH_2), 28.0 (CH_2x2) (d, J_{C-P} = 12.8 Hz), 27.4 (CH_2x2) (d, J_{C-P} = 16.1 Hz), 26.3 (CH_2), 25.9 (CH_3x2), 25.2 (CH_3x2), 24.8 (CH_3x2); **^{31}P NMR (121 MHz, C_6D_6)** δ 40.43; **HRMS (EI)** m/z calcd for $C_{35}H_{53}AuClO_2P$ [$(M-Cl)^+$] 733.3449, found 733.3512.



L_{3g}AuCl

Prepared according to general procedure G in 89% yield as a white powder.

^{1}H NMR (300 MHz, C_6D_6) δ 7.65 (d, J = 11.3 Hz, 4H), 7.65 (s, 2H), 7.38 (s, 2H), 6.44 (d, J = 6.4 Hz, 1H), 6.11 (dd, J = 9.1 Hz, 4.5 Hz, 1H), 3.12 (sept, J = 6.9 Hz, 1H), 2.90 (s, 3H), 2.64 (s, 3H), 2.56 (dt, J = 13.6 Hz, 6.7 Hz, 2H), 1.48 (d, J = 6.9 Hz, 6H), 1.32 (d, J = 7.0 Hz, 6H), 1.14 (d, J = 6.7 Hz, 6H); **^{13}C NMR (75 MHz, C_6D_6)** δ 154,5 (C_{quat}) , 153,9 (C_{quat}) (d, J_{C-P} = 14.3 Hz), 151.8 (C_{quat}), 146.3 (C_{quat}), 139.3 (C_{quat}), 139.0 (C_{quat}), 134.7 (C_{quat}), 133.9 (C_{quat}), 133.0-132.9 (C_{quat}) (m), 132.8-132.7 (C_{quat}) (m), 132.6 (C_{quat}), 132.9 (CH), 132.6 (CH), 132.4 (C_{quat}), 132.1 (C_{quat}), 131.8 (C_{quat}) (d, J_{C-P} = 11.5 Hz), 130.1 (C_{quat}) (d, J_{C-P} = 9.0 Hz), 128.3 (CHx4), 125.0 (C_{quat}), 124.7-124.6 (C_{quat}) (m), 124.6 (CH), 123.1 (CH), 121.4 (C_{quat}), 117.0 (CH), 111.3 (CH) (d, J_{C-P} = 5.5 Hz), 54.7 (CH_3), 54.2 (CH_3), 34.9 (CH), 32.1 (CHx2), 25.1 (CH_3x2), 24.6 (CH_3x2), 23.8 (CH_3x2) ; **^{31}P NMR (121 MHz, C_6D_6)** δ 16.00; **HRMS (EI)** m/z calcd for $C_{39}H_{37}O_2PF_{12}AuCl$ 1028.1692, found 1028.1646.

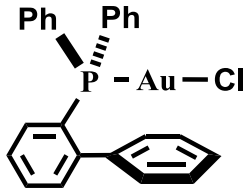


L_7AuCl

Prepared according to general procedure G in 89% yield as a white powder.

^{1}H NMR (500MHz, $CDCl_3$) δ = 7.49 (dd, *J* = 7.7, 13.1 Hz, 4 H), 7.17 - 6.99 (m, 6 H), 6.93 (d, *J* = 7.2 Hz, 4 H), 6.89 - 6.65 (m, 21 H); **^{13}C NMR (126MHz, $CDCl_3$)*** δ = 146.7 (d, J= 9.0 Hz, C_{quat}), 144.9 (d, J= 2.0 Hz, C_{quat}), 142.7 (d, J=7.5 Hz, C_{quat}), 139.5 (s, C_{quat}), 138.9 (d, J= 1.0 Hz, C_{quat}), 138.5 (d, J= 5.0 Hz, C_{quat}), 134.1 (d, J= 15.0 Hz, CH), 132.7 (d, J= 63.8 Hz, C_{quat}), 132.0 (s, CH), 131.0 (s, CH), 130.6 (s, CH), 130.3 (d, J= 2.5 Hz, CH), 128.3 (d, J= 12.0 Hz, CH), 127.3 (s, CH), 127.2 (d, J= 59.3 Hz, C_{quat}), 126.7 (d, J= 7.5 Hz, CH), 126.6 (s, CH), 125.9 (s, CH), 125.8 (s, CH); **^{31}P NMR (202MHz, $CDCl_3$)** δ = 37.8; **HRMS (EI) m/z calcd for** $C_{48}H_{35}AuClP$ [$(M)^+$] 874.1830, found 874.1816.

**Due to the high number of similar carbons, we were not able to attribute which ^{13}C signal belonged to which carbon.*

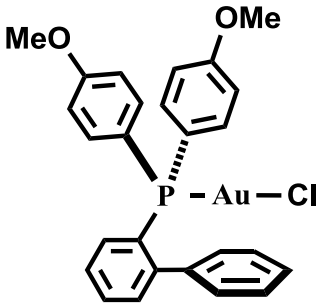


$L_{1d}AuCl$

Prepared according to general procedure G in 89% yield as a white powder.

^{1}H NMR (400MHz, $CDCl_3$) δ = 7.59 - 7.35 (m, 15 H), 7.29 - 7.23 (m, 1 H), 7.04 (ddd, *J* = 1.0, 7.8, 11.6 Hz, 1 H), 6.99 (dd, *J* = 1.0, 8.1 Hz, 2 H); **^{13}C NMR (101MHz, $CDCl_3$)** δ = 148.2 (d, J= 15.0 Hz, C_{quat}), 140.1 (d, J= 7.0 Hz, C_{quat}), 134.6 (d, J= 13.9 Hz, 4xCH), 133.8 (d, J= 6.6 Hz, CH), 132.1 (d, J= 8.4 Hz, CH), 131.9 (d, J= 2.2 Hz, 2xCH), 131.5 (d, J= 2.2 Hz, CH), 129.9 (d, J= 62.0 Hz, C_{quat}), 129.8 (s, 2xCH), 129.3 (d, J= 11.7, 4xCH), 128.6 (s, CH), 128.6 (s, 2xCH), 127.7 (d, J= 8.8 Hz, CH), 127.6 (d, J= 61.6 Hz, C_{quat}); **^{31}P NMR**

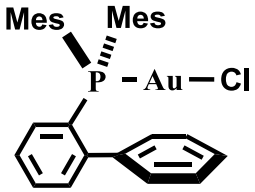
(121MHz, $CDCl_3$) δ = 26.8; **HRMS (EI) m/z calcd for** $C_{24}H_{19}PAuCl$ $[(M)^+]$ 570.0578, found 570.0561.



$L_{1f}AuCl$

Prepared according to general procedure G in 81% yield as a white powder.

^{1}H NMR (400MHz, $CDCl_3$) δ = 7.54 (tt, *J* = 1.2, 7.5 Hz, 1 H), 7.45 - 7.33 (m, 7 H), 7.27 (t, *J* = 7.6 Hz, 2 H), 7.08 - 6.91 (m, 7 H), 3.85 (s, 6 H); **^{13}C NMR (101MHz, $CDCl_3$)** δ = 162.3 (d, J= 2.2 Hz, C_{quat}), 147.8 (d, J= 15.0 Hz, C_{quat}), 140.0 (d, J= 6.6 Hz, C_{quat}), 136.0 (d, J= 15.4, 4xCH), 133.4 (d, J= 7.0 Hz, CH), 131.9 (d, J= 8.1 Hz, CH), 131.1 (d, J= 2.2 Hz, CH), 129.7 (s, 2xCH), 128.7 (s, C_{quat}), 128.4 (s, CH), 128.3 (s, 2xCH), 127.4 (d, J= 9.2 Hz, CH), 120.8 (d, J= 68.2 Hz, C_{quat}), 114.7 (d, J= 13.2 Hz, 4xCH), 55.5 (s, 2xCH_3); **HRMS (EI) m/z calcd for** $C_{26}H_{23}O_2PAuCl$ $[(M)^+]$ 630.0790, found 630.0791.



$L_{1e}AuCl$

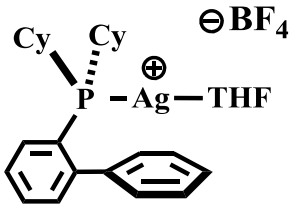
Prepared according to general procedure G in 93% yield as a white powder.

^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.54 (tt, *J* = 1.5, 7.5 Hz, 1 H), 7.48 - 7.42 (m, *J* = 7.0 Hz, 2 H), 7.40 (dd, *J* = 7.9, 12.1 Hz, 1 H), 7.35 - 7.25 (m, 3 H), 7.16 (d, *J* = 7.5 Hz, 2 H), 6.88 (d, *J* = 3.9 Hz, 4 H), 2.31 (s, 6 H), 2.24 (s, 12 H); **^{13}C NMR (126MHz, $CDCl_3$)** δ = 148.4 (d, J= 16.5 Hz, C_{quat}), 142.5 (d, J= 10.5 Hz, 4xC_{quat}), 141.3 (d, J= 2.0 Hz, C_{quat}), 141.0 (d, J= 7.0 Hz, C_{quat}), 135.1 (d, J= 6.5 Hz, CH), 132.9 (d, J= 8.5 Hz, CH), 132.0 (d, J= 9.5 Hz, 4xCH),

131.3 (d, J= 3.0 Hz, CH), 129.5 (d, J= 56.8 Hz, C_{quat}), 129.4 (s, 2xCH), 128.8 (s, CH), 128.7 (s, 2xCH), 127.6 (d, J= 9.0 Hz, CH), 125.8 (d, J= 56.9 Hz, C_{quat}), 25.1 (d, J= 11.0 Hz, 4xCH_3), 21.1 (d, J= 1.0 Hz, 2xCH_3); **^{31}P NMR (202MHz, $CDCl_3$)** δ = 1.3; **HRMS (EI) m/z calcd for** $C_{30}H_{31}PAuCl$ [$(M)^+$] 654.1517, found 654.1511.

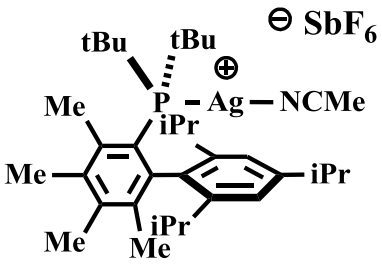
General procedure H - Synthesis of Ag(I) catalysts

The phosphane ligand (300 mmol) dissolved in acetonitrile (5 mL) was added to a suspension of $AgSbF_6$ (300 mmol) in acetonitrile or THF (5 mL) under Ar. The reaction mixture was stirred for 2 h in the dark at RT, then the solvent was reduced to 3 mL and the solution was filtered through a Celite pad. The solvent was then evaporated to form a white solid which was triturated 2-3 times with pentane and then dried under vacuum. Crystals were obtained by slow evaporation of DCM or $CDCl_3$ at r.t.[64]



[L_{1c}AgTHF]BF_4

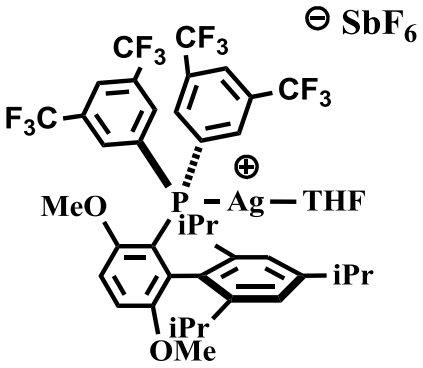
Prepared according to literature procedure and exhibited spectral data in accordance with previous report.[48]



[L_8AgMeCN]SbF_6

Prepared according to general procedure H in 93% yield as a white powder.

^{1}H NMR (400MHz, $CDCl_3$) δ = 7.24 (s, 2 H), 2.98 (spt, *J* = 6.9 Hz, 1 H), 2.62 (s, 3 H), 2.41 (spt, *J* = 6.7 Hz, 2 H), 2.31 (s, 3 H), 2.22 (s, 3 H), 2.21 (s, 3 H), 1.46 (s, 3 H), 1.42 (s, 9 H), 1.37 (s, 9 H), 1.32 (d, *J* = 6.9 Hz, 6 H), 1.28 (d, *J* = 6.8 Hz, 6 H), 0.89 (d, *J* = 6.6 Hz, 6 H); **^{13}C NMR (101MHz, $CDCl_3$)** δ = 150.1 (s, C_{quat}), 146.8 (dd, J= 1.7, 1.7 Hz, 2xC_{quat}), 144.0 (dd, J= 27.9, 1.1 Hz, C_{quat}), 140.9 (d, J= 2.6 Hz, C_{quat}), 139.3 (d, J= 7.7 Hz, C_{quat}), 136.7 (d, J= 5.1 Hz, C_{quat}), 136.5 (d, J= 8.1 Hz, C_{quat}), 135.2 (dd, J= 12.1, 1.1 Hz, C_{quat}) , 127.2 (dd, J= 19.1, 6.2 Hz, C_{quat}), 123.8 (s, 2xCH), 119.3 (s, C_{quat}), 38.4 (dd, J= 5.9, 4.0 Hz, 2xC_{quat}), 34.0 (s, CH), 33.3 (dd, J= 11.9, 1.7 Hz, 6xCH_3), 30.8 (s, 2xCH), 27.7 (s, CH_3), 26.0 (s, 2xCH_3), 25.0 (s, 2xCH_3), 24.0 (s, 2xCH_3), 22.4 (d, J= 3.7 Hz, CH_3), 17.7 (s, CH_3), 17.4 (s, CH_3), 2.1 (s, CH_3); **^{31}P NMR (121MHz, $CDCl_3$)** δ = 63.1 (d, J(^{31}P-^{109}Ag) = 721.2 Hz), J(^{31}P-^{107}Ag) = 625.4 Hz); **HRMS (ESI) m/z calcd for** $C_{35}H_{56}AgNP$ [(M-SbF_6)$^+$] 628.3201, 628.3205.

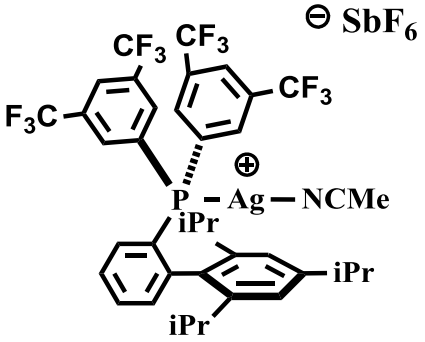


[L_{3g}AgTHF]SbF_6

Prepared according to general procedure H in 89% yield as a white powder.

^{1}H NMR (500MHz, $CDCl_3$) δ = 7.94 (s, 2 H), 7.76 (d, *J* = 11.7 Hz, 4 H), 7.32 (d, *J* = 9.2 Hz, 1 H), 7.25 (s, 2 H), 7.05 (dd, *J* = 3.0, 9.1 Hz, 1 H), 3.71 - 3.68 (m, 3 H), 3.78 - 3.58 (m, 4 H), 3.38 (s, 3 H), 3.00 (spt, *J* = 6.9 Hz, 1 H), 2.39 (spt, *J* = 6.8 Hz, 2 H), 1.84 (td, *J* = 3.2, 6.7 Hz, 4 H), 1.31 (s, 6 H), 1.29 (s, 6 H), 1.03 (d, *J* = 6.8 Hz, 6 H), 0.99 (d, *J* = 6.7 Hz, 6 H); **^{13}C NMR (126MHz, $CDCl_3$)** δ = 155.1 (dd, J= 5.2, 2.7, C_{quat}), 153.1 (d, J= 12.5 Hz, C_{quat}), 151.0 (s, C_{quat}), 147.1 (s, 2xC_{quat}), 137.0 (d, J= 26.4 Hz, C_{quat}), 132.6 (dq, J=18.5, 3.4 Hz, 4xCH), 132.4 (qd, J= 33.9, 10.5 Hz, 4xC_{quat}), 132.1 (d, J= 36.9 Hz, 2xC_{quat}), 129.5 (dd, J= 14.0, 1.5 Hz, C_{quat}), 124.7 (br. s., 2xCH), 122.8 (q, J= 272.8 Hz, 4xC_{quat}), 122.5(s, C_{quat}), 117.6 (s, CH), 113.2 (dd, J= 44.9, 7.0 Hz, C_{quat}), 112.4 (d, J= 4.0 Hz, CH), 68.5 (s, 2xCH_2),

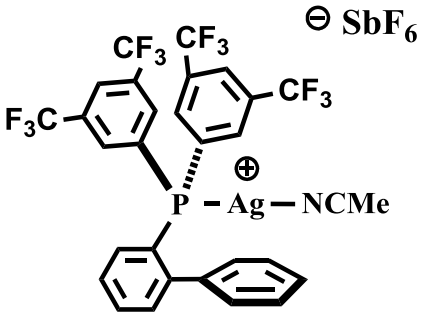
55.5 (s, CH_3), 55.2 (s, CH_3), 34.0 (s, CH), 31.5 (s, 2xCH), 25.7 (s, 2xCH_2), 24.6 (s, 2xCH_3), 23.8 (s, 2xCH_3), 23.8 (s, 2xCH_3); **^{31}P NMR (202MHz, $CDCl_3$)** δ = -4.9 (d, J(^{31}P-^{109}Ag) = 807.3 Hz), J(^{31}P-^{107}Ag) = 700.1 Hz); **HRMS (ESI) m/z calcd for** $C_{43}H_{45}AgF_{12}O_3P$ [(M-SbF_6)$^+$] 975.1965, found 975.1920.



[L_{2g}AgMeCN]SbF_6

Prepared according to general procedure H in 75% yield as a white powder.

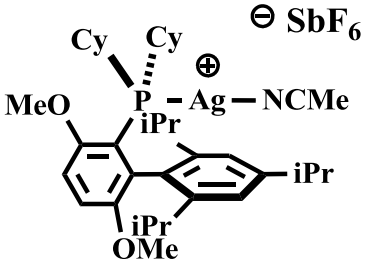
^{1}H NMR (500MHz, $CDCl_3$) δ = 8.02 (s, 2 H), 7.75 - 7.72 (m, 4 H), 7.75 (d, *J* = 11.6 Hz, 1 H), 7.63 (tt, *J* = 1.0, 7.7 Hz, 1 H), 7.41 (tt, *J* = 1.0, 7.0 Hz, 0 H), 7.35 (dt, *J* = 1.0, 8.0 Hz, 1 H), 7.24 (s, 2 H), 3.00 (spt, *J* = 7.0 Hz, 1 H), 2.24 (spt, *J* = 6.8 Hz, 2 H), 2.18 (s, 3 H), 1.32 (d, *J* = 7.0 Hz, 6 H), 1.01 (d, *J* = 7.0 Hz, 6 H), 1.00 (d, *J* = 6.7 Hz, 6 H); **^{13}C NMR (126MHz, $CDCl_3$)** δ = 151.2 (s, C_{quat}), 147.4 (d, J= 26.4 Hz, C_{quat}) , 146.7 (d, J= 1.0Hz, 2xC_{quat}), 134.9 (dd, J= 2.0, 20. Hz, CH), 133.3 (d, J= 1.5 Hz, CH), 133.0 (qd, J= 34.3, 10.5 Hz, 4xC_{quat}), 133.0 (dd, J= 16.1, 2.5 Hz, 4xCH), 133.3 (d, J= 12.0 Hz, C_{quat}), 132.8 (d, J= 7.5 Hz, CH), 132.5 (dd, J= 35.5, 2.8 Hz, C_{quat}) , 129.9 (s, CH), 129.7 (d, J= 5.5 Hz, CH), 128.0 (s, CH), 126.5 (s, CH), 125.7 (s. br., 2xCH) , 124.7 (d, J= 44.4 Hz, 2xC_{quat}), 122.9 (s, 2xCH), 122.6 (q, J= 274.3 Hz, 4xC_{quat}), 120.6 (s, CH), 119.9 (s, C_{quat}), 34.3 (s, CH), 31.4 (s, 2xCH), 25.2 (s, 2xCH_3), 23.8 (s, 2xCH_3), 23.3 (s, 2xCH_3), 2.2 (s, CH_3); **^{31}P NMR (202MHz, $CDCl_3$)** δ = -3.7 (d, J(^{31}P-^{109}Ag) = 785.1 Hz), J(^{31}P-^{107}Ag) = 681.6 Hz); **HRMS (ESI) m/z calcd for** $C_{39}H_{36}NF_{12}PAg$ [(M-SbF_6)$^+$] 884.1445, found 884.1455.



[L_{1g}AgMeCN]SbF_6

Prepared according to general procedure H in 45% yield as a white powder.

^{1}H NMR (300MHz, $CDCl_3$) δ = 8.05 (s, 2 H), 7.90 - 7.31 (m, 10 H), 7.19 - 6.93 (m, 3 H), 2.20 (s, 3 H); **HRMS (ESI) m/z calcd for** $C_{30}H_{18}AgF_{12}NP$ $[(M\text{-}SbF_6)^+]$ 758.0036, found 758.0028.

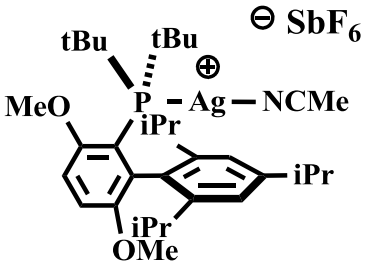


[L_{3c}AgMeCN]SbF_6

Prepared according to general procedure H in 85% yield as a white powder.

^{1}H NMR (400MHz, $CDCl_3$) δ = 7.18 (s, 2 H), 7.08 (d, *J* = 9.0 Hz, 1 H), 7.01 (dd, *J* = 2.1, 9.1 Hz, 1 H), 3.91 (s, 3 H), 3.55 (s, 3 H), 2.96 (spt, *J* = 6.9 Hz, 1 H), 2.54 - 2.37 (m, 2 H), 2.27 (s, 3 H), 2.31 (spt, *J* = 6.8 Hz, 2 H), 1.97 - 1.84 (m, 2 H), 1.80 (d, *J* = 12.2 Hz, 2 H), 1.69 (t, *J* = 14.5 Hz, 4 H), 1.52 - 1.40 (m, 2 H), 1.33 (d, *J* = 7.0 Hz, 6 H), 1.26 (d, *J* = 6.9 Hz, 6 H), 1.39 - 0.99 (m, 8 H), 0.99 - 0.78 (m, 6 H); **^{13}C NMR (126MHz, $CDCl_3$)** δ = 155.3 (dd, J= 6.2, 2.2 Hz, C_{quat}), 152.6 (d, J= 10.5 Hz, C_{quat}), 149.6 (s, C_{quat}), 146.9 (s, 2xC_{quat}), 136.2 (d, J= 20.0 Hz, C_{quat}), 130.4 (dd, J= 11.4, 1.5 Hz, C_{quat}), 122.4 (s, 2xCH), 119.3 (s, C_{quat}), 116.2 (d, J= 35.4, 6.7 Hz, C_{quat}), 114.7 (d, J= 2.0, CH), 110.8 (d, J= 4.0 Hz, CH), 56.0 (s, CH_3), 54.9 (s, CH_3), 36.3 (dd, J= 21.4, 4.5 Hz, 2xCH) , 34.7 (d, J= 13.0, 2.0 Hz, 2xCH_2),

33.9 (s, CH), 30.8 (2xCH), 30.5 (d, J= 1.5 Hz, 2xCH_2), 27.2 (d, J= 12.5 Hz, 2xCH_2), 26.8 (d, J= 17.5 Hz, 2xCH_2), 25.7 (d, J= 1.1 Hz, 2xCH_2), 24.8 (s, 2xCH_3), 24.6 (s, 2xCH_3), 23.8 (s, 2xCH_3), 2.2 (s, CH_3); **^{31}P NMR (202MHz, $CDCl_3$)** δ = 24.8 (d, J(^{31}P-^{109}Ag) = 750.7 Hz), J(^{31}P-^{107}Ag) = 651.0 Hz); **HRMS (ESI) m/z calcd for** $C_{37}H_{56}AgNO_2P$ [(M-SbF_6)$^+$] 684.3099, found 684.3106.



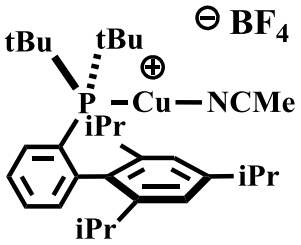
[L_{3a}AgMeCN]SbF_6

Prepared according to general procedure H in 88% yield as a white powder.

^{1}H NMR (500MHz, $CDCl_3$) δ = 7.22 (s, 2 H), 7.12 (d, *J* = 9.0 Hz, 1 H), 7.07 (d, *J* = 9.0 Hz, 1 H), 3.87 (s, 3 H), 3.75 (t, *J* = 6.4 Hz, 4 H), 3.55 (s, 3 H), 2.97 (spt, *J* = 6.8 Hz, 1 H), 2.40 (spt, *J* = 6.6 Hz, 2 H), 1.90 (quin, *J* = 3.2 Hz, 4 H), 1.32 (d, *J* = 7.2 Hz, 6 H), 1.29 (d, J= 17.0 Hz, 18 H), 1.27 (d, *J* = 6.8 Hz, 6 H), 0.90 (d, *J* = 6.6 Hz, 6 H); **^{13}C NMR (126MHz, $CDCl_3$)** δ = 155.1 (d, J= 5.0 Hz, C_{quat}), 152.6 (d, J= 10.5 Hz, C_{quat}), 150.0 (s, C_{quat}), 147.0 (s, 2xC_{quat}), 136.5 (dd, J= 21.9, 1.5 Hz, C_{quat}), 130.3 (dd, J= 11.5, 2.0 Hz, C_{quat}), 122.2 (s, 2xCH), 118.4 (dd, J= 20.9, 6.5 Hz, C_{quat}), 114.9 (d, J= 2.0 Hz, CH), 110.8 (d, J= 4.0 Hz, CH), 70.6 (s, 2xCH_2), 54.7 (s, CH_3), 54.7 (s, CH_3), 37.1 (dd, J= 10.5, 5.0 Hz, 2xC_{quat}), 33.8 (s, CH), 32.1 (dd, J= 11.0, 2.0 Hz, 6xCH_3), 31.2 (s, 2xCH), 25.5 (s, 2xCH_2), 25.2 (s, 2xCH_3, 24.4 (2xCH_3), 23.7 (2xCH_3); **^{31}P NMR (202MHz, $CDCl_3$)** δ = 57.1 (d, J(^{31}P-^{109}Ag) = 789.8 Hz), J(^{31}P-^{107}Ag) = 683.4 Hz); **HRMS (ESI) m/z calcd for** $C_{33}H_{52}AgNO_2P$ [(M-SbF_6)$^+$] 632.2787, found 632.2784.

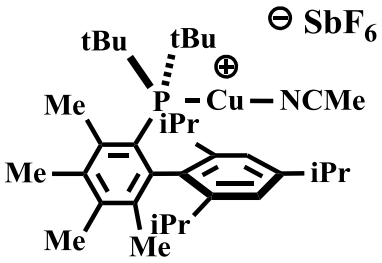
General procedure I - Synthesis of Cu(I) catalysts

In a typical reaction, a flame-dried Schlenck flask (50 mL) was charged with $Cu(CH_3CN)_4][X]$ (0.318 mmol) in DCM (2 mL) and the mixture was stirred under Ar at r.t. The desired phosphane ligand (0.318 mmol) was added, the mixture was stirred for 30 min, and then the solvent was evaporated to yield the corresponding copper(I) complex as a white solid. Crystals were obtained by slow evaporation (hexane/DCM, 10:1 v/v). (X= BF_4 or SbF_6)



$[L_{2a}CuMeCN]BF_4$

Prepared according to literature procedure and exhibited spectral data in accordance with previous report.[64]

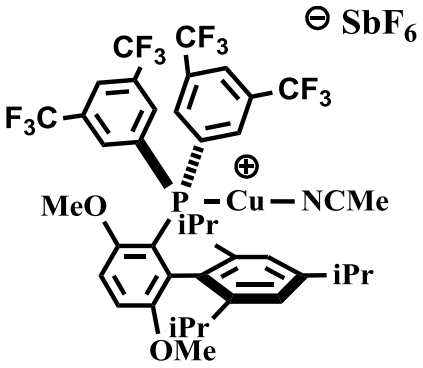


$[L_{2a}CuMeCN]SbF_6$

Prepared according to general procedure I as a white powder.

^{1}H NMR (400MHz, $CDCl_3$) δ = 7.31 (s, 2 H), 3.00 (spt, *J* = 6.9 Hz, 1 H), 2.60 (s, 3 H), 2.40 (spt, *J* = 6.7 Hz, 2 H), 2.31 (s, 3 H), 2.28 (s, 3 H), 2.23 (s, 3 H), 1.62 (s, 1 H), 1.46 (s, 3 H), 1.38 (d, J= 15.7 Hz, 18 H), 1.33 (d, *J* = 7.0 Hz, 6 H), 1.29 (d, *J* = 6.8 Hz, 6 H), 0.90 (d, *J* = 6.6 Hz, 6 H). **^{13}C NMR (101MHz, $CDCl_3$)** δ = 151.0 (d, J= 2.2 Hz, C_{quat}), 145.5 (d, J= 2.2 Hz, 2xC_{quat}), 144.5 (d, J= 32.6 Hz, C_{quat}), 140.8 (d, J= 2.2 Hz, C_{quat}), 139.1 (s, C_{quat}), 136.9 (d, J= 5.5 Hz, C_{quat}), 136.1 (d, J= 9.5 Hz, C_{quat}), 130.0 (d, J= 21.6 Hz, C_{quat}), 129.8 (s, C_{quat}),

125.8 (d, J= 1.8 Hz, 2xCH), 119.3 (s, C_{quat}), 37.9 (d, J= 9.5 Hz, 2xC_{quat}), 34.1 (s, CH), 32.8 (d, J= 9.5 Hz, 6xCH_3), 31.1 (s, 2xCH), 27.0 (s, CH_3), 25.6 (s, 2xCH_3), 25.3 (s, 2xCH_3), 24.2 (s, 2xCH_3), 22.1 (d, J= 3.3 Hz, CH_3), 17.6 (s, CH_3), 17.3 (s, CH_3), 2.6 (s, CH_3); **^{31}P NMR (121MHz, $CDCl_3$)** δ = 48.7; **HRMS (ESI) m/z calcd for** $C_{35}H_{56}CuNP$ [$(M\text{-}SbF_6)^+$] 584.3446, found 584.3434.



[L_{3g}CuMeCN]SbF_6

Prepared according to general procedure I as a white powder.

^{1}H NMR (400MHz, $CDCl_3$) δ = 7.95 (s, 2 H), 7.77 (d, *J* = 10.9 Hz, 4 H), 7.31 (d, *J* = 9.1 Hz, 1 H), 7.24 (s, 2 H), 7.08 (dd, *J* = 2.9, 9.1 Hz, 1 H), 3.69 (s, 3 H), 3.49 (s, 3 H), 3.00 (spt, *J* = 6.9 Hz, 1 H), 2.35 (spt, *J* = 6.7 Hz, 2 H), 2.13 (s, 3 H), 1.33 (s, 3 H), 1.31 (s, 3 H), 0.99 (d, *J* = 7.2 Hz, 6 H), 0.96 (d, *J* = 6.9 Hz, 6 H); **^{13}C NMR (101MHz, $CDCl_3$)** δ = 155.1 (d, J= 2.2 Hz, C_{quat}), 152.8 (d, J= 13.2 Hz, C_{quat}), 150.4 (s, C_{quat}), 145.4 (d, J= 1.5 Hz, 2xC_{quat}), 136.6 (d, J= 29.3 Hz, C_{quat}), 133.1 (d, J= 36.7 Hz, 2xC_{quat}), 133.0 (dd, J= 16.9, 2.2 Hz, 4xCH), 132.2 (qd, J= 33.7, 10.3 Hz, 4xC_{quat}), 128.8 (d, J= 12.5 Hz, C_{quat}), 124.2 (m, 2xCH), 123.4 (s, 2xCH), 122.9 (q, J= 273.3 Hz, 4xC_{quat}) , 118.1 (s, C_{quat}), 117.4 (d, J= 1.5 Hz, CH), 114.8 (d, J= 44.0 Hz, C_{quat}), 112.4 (d, J= 4.0 Hz, CH), 55.4 (s, CH_3), 55.1 (s, CH_3), 34.3 (s, CH), 31.6 (s, 2xCH), 24.7 (s, 2xCH_3), 23.8 (s, 2xCH_3), 22.8 (s, 2xCH_3), 2.0 (s, CH_3); **^{31}P NMR (121MHz ,$CDCl_3$)** δ = -11.5; **^{19}F NMR (377MHz, $CDCl_3$)** δ = -63.1; **HRMS (ESI) m/z calcd for** $C_{41}H_{40}CuF_{12}NO_2P$ [$(M\text{-}SbF_6)^+$] 900.1901, found 900.1905.

Glossary of Abbreviations

Ac	acetate
Ad	Adamantyl
BArF	tetrakis[3,5-bis(trifluoromethyl)phenyl] borate
Bn	benzyl
Bu	butyl
BuLi	n-butyllithium
Cy	Cyclohexyl
DCE	dichloroethane
DCM	dichloromethane
DMS	dimethylsulfide
DMSO	dimethylsulfoxide
E_a	activation energy
EDG	electron donating group
equiv	equivalents
Et	ethyl
EWG	electron withdrawing group
ΔG	Gibbs free energy
GC	gas chromatography
GC/MS	gas chromatography coupled to mass spectrometry
HMPA	hexamethylphosphoramide
HMQC	heteronuclear multiple quantum coherence
HPLC	high-performance liquid chromatography
HRMS	high resolution mass spectrum
L	ligand
LA	Lewis Acid
M	metal
Me	methyl

Mes	Mesityl
NHC	N-heterocyclic carbene
NMR	nuclear magnetic resonance
OTf	trifluoromethylsulfonate
P	phosphine ligand
Ph	phenyl
ppm	parts per million
quant.	quantitative yield (i.e. >98%)
RLS	rate limiting step
r.t.	room temperature
t-Bu	*tert*-butyl
TBS	*tert*-butyldimethyl silyl
t-BuLi	*tert* butyllithium
TBS	*Tert*-butyldimethylsilyl
THF	tetrahydrofuran
TIPS	triisopropylsilyl
TIPSOTf	triisopropylsilyl trifluoromethylsufonate
TLC	thin layer chromatography
TMS	trimethylsilyl
TS	transition state
UV	Ultraviolet
v/v	volume/volume

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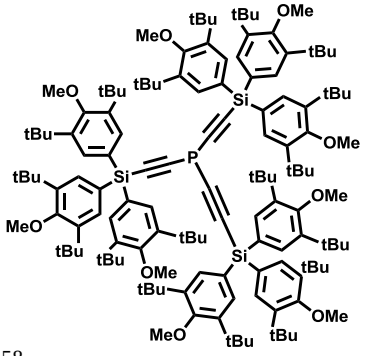

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