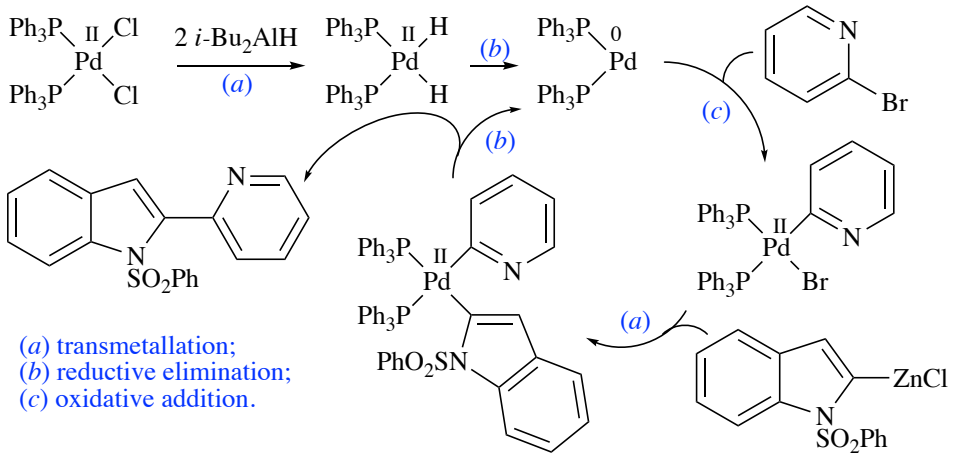
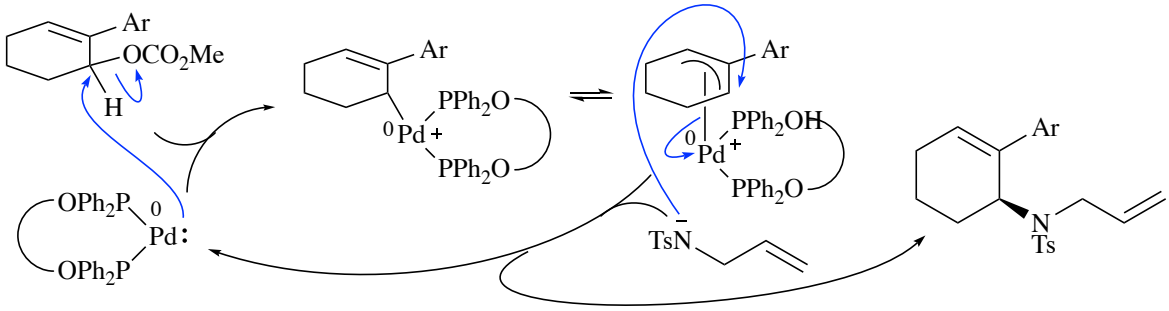
Answers to Chapter 6 Problems.

1. (a) A new C–C bond is formed between a nucleophilic C–Zn and an electrophilic C–Br. This Pd-catalyzed reaction proceeds through the standard oxidative addition, transmetallation, reductive elimination process characteristic of Pd-catalyzed cross-couplings. The oxidative addition requires Pd(0). The role of the DIBAL is to reduce the Pd(II) to Pd(0) by two transmetallations and reductive elimination of H_2.



(b) An allylic leaving group is replaced by a nucleophile. This reaction proceeds through the standard sequence for allylic substitutions catalyzed by Pd, i.e. two sequential backside displacements. The chiral ligand causes the nucleophile to attack only one of the two prochiral termini of the *meso* π allyl intermediate. The N may be deprotonated before or after it attacks the π allyl complex.

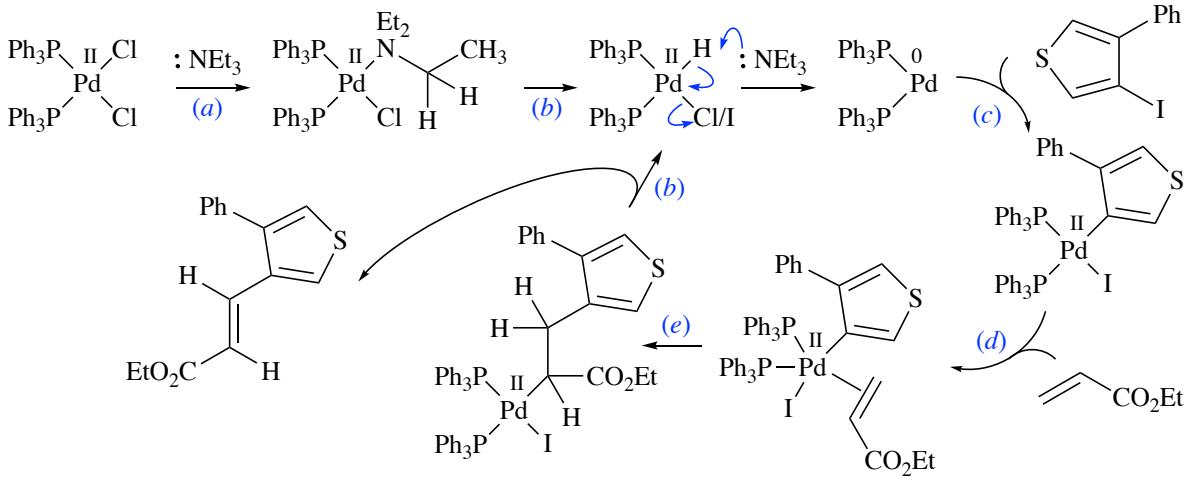


(c) A new C–C bond is formed between a nucleophilic terminal alkyne PhC≡CH and an electrophilic C–I. This Sonogashira reaction proceeds through the standard oxidative addition, transmetallation, reductive elimination process characteristic of Pd-catalyzed cross-couplings. The terminal alkyne is

converted to a Cu(I) acetylide before transmetallation to Pd occurs. The mechanism is discussed in the text.

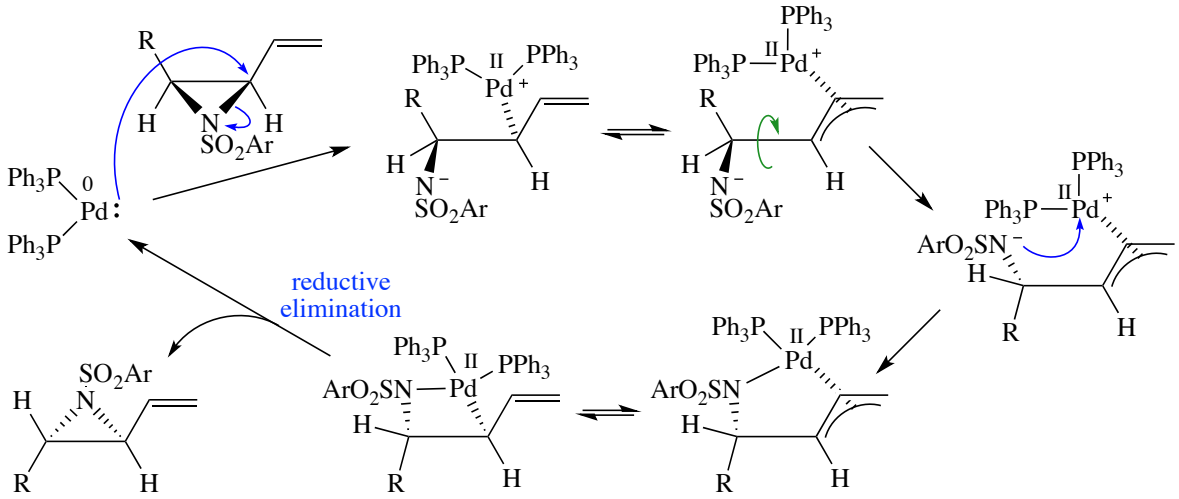
(d) A new C–C bond is formed between a nucleophilic C–B and an electrophilic C–I. This Suzuki coupling proceeds through the standard oxidative addition, transmetallation, reductive elimination process characteristic of Pd-catalyzed cross-couplings. The mechanism is discussed in the text.

(e) This is a Heck reaction. The first few steps use Et_3N to convert the Pd(II) complex that is added to the reaction mixture. The catalytic cycle is discussed in the text.

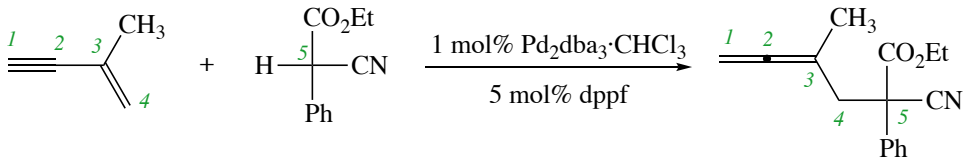


(*a*) ligand substitution; (*b*) *β*-hydride elimination; (*c*) oxidative addition; (*d*) coordination; (*e*) insertion.

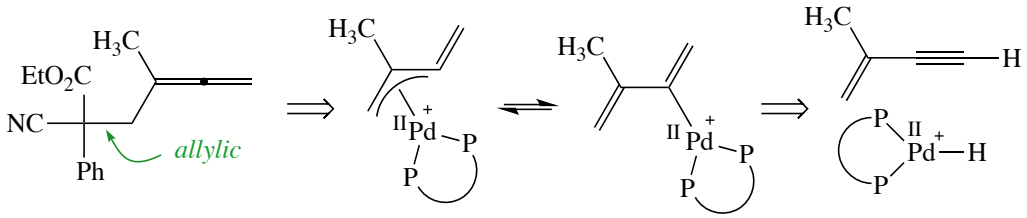
(f) An allylic C with a leaving group is being epimerized by the Pd(0) complex. One possible mechanism is simple displacement of N by Pd(0) to form the π allyl complex, then displacement of Pd(0) by N to reform the ring. The problem with this mechanism is that allylic substitution reactions catalyzed by Pd proceed with *retention* of configuration (two S_N2-type displacements), whereas this reaction proceeds with *inversion* of configuration. In this particular molecule, the anionic N can coordinate to the Pd π allyl intermediate in an intramolecular fashion; reductive elimination from this chelate would give the product with overall *inversion* of configuration.



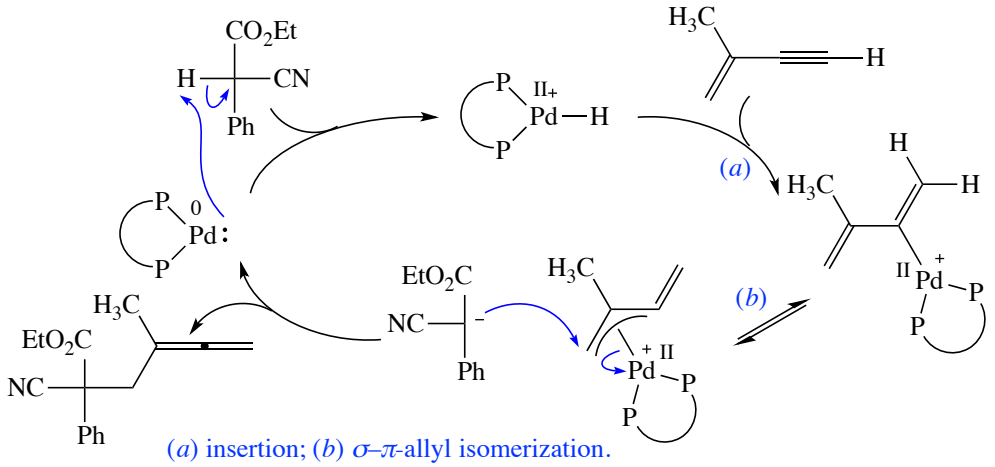
(g) Make: C4–C5, C1–H. Break: C5–H.



C5 is extremely acidic, and once deprotonated it is nucleophilic. C4, though, is not electrophilic, so we need to convert it to an electrophilic C. Looking at the product, one sees that the new C–C bond is allylic. This suggests attack of C5 on a π allyl complex. This complex could be made by insertion of one of the C1≡C2 π bonds into a Pd–H bond. This last could be made by protonation of Pd(0) by C5.

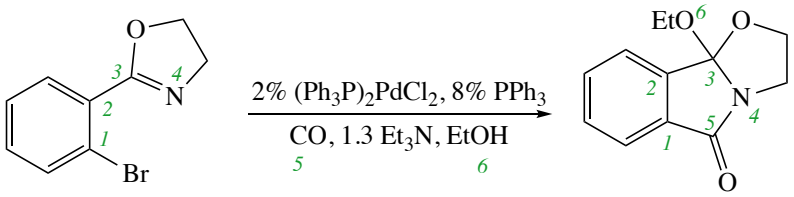


Protonation of Pd(0) gives [Pd(II)–H]$^+$. Coordination and insertion of the C1≡C2 π bond gives the Pd σ-allyl complex, which can isomerize to the π-allyl complex. Attack of the nucleophile on the less hindered terminus of the π-allyl complex gives the observed product.

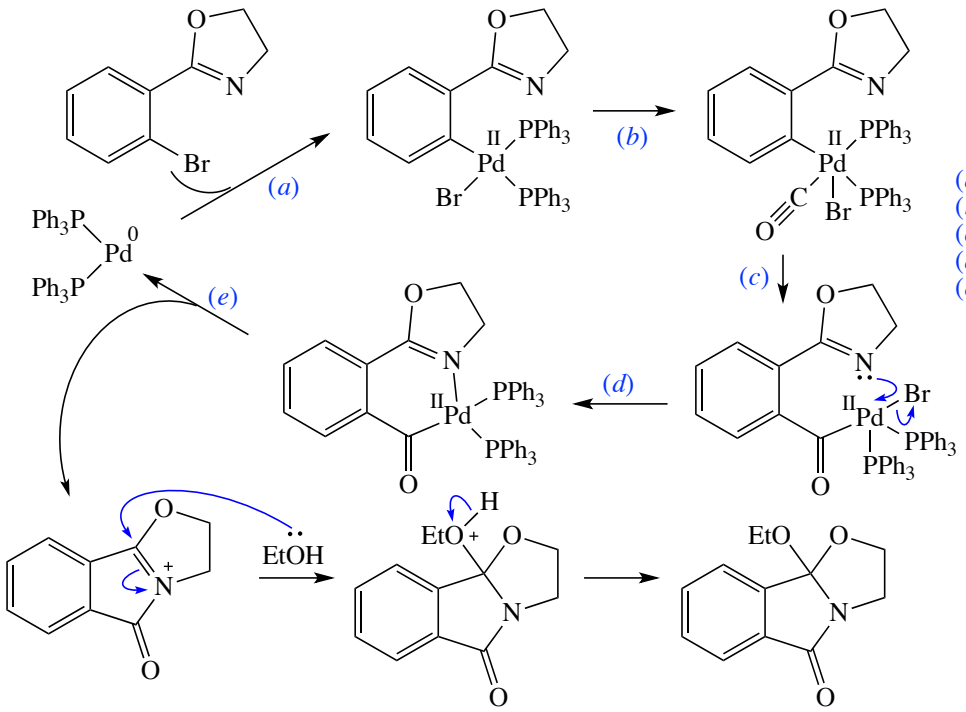


(h) This reaction is simply a Wacker oxidation. Its mechanism was discussed in the text. The key steps are attack of H_2O on an electrophilic Pd–alkene complex, then β-hydride elimination to give the enol.

(i) Make: C1–C5, N4–C5, C3–O6. Break: C1–Br.

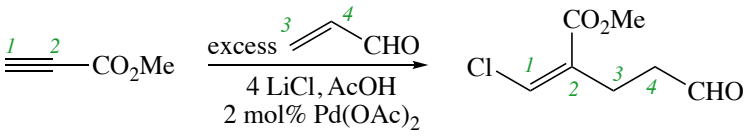


Incorporation of CO into an organic substrate usually occurs by insertion of CO into a C–metal bond. The requisite C1–metal bond is formed by oxidative addition of a Pd(0) species into the C1–Br bond, the normal first step upon combining a Pd(0) compound and an aryl halide. Coordination and insertion of CO follows. Substitution of Br with N on Pd(II) followed by reductive elimination gives an iminium ion, which is trapped by EtOH to give the product. The formation of the new N–C bond can also be written as nucleophilic addition of N to the carbonyl C followed by elimination of Pd to give the same iminium ion intermediate.

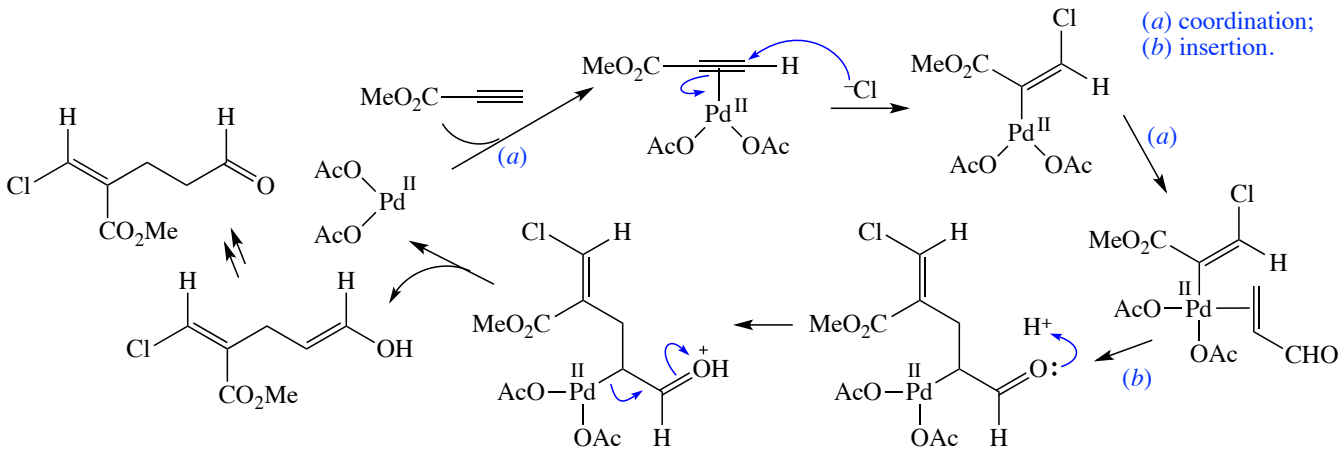


(j) This is another Heck reaction. After the insertion to give the σ-bound Pd(II), β-hydride elimination occurs in the direction of the OH to give an enol. The enol tautomerizes to the aldehyde.

(k) Make: C1–Cl, C2–C3. Break: none.

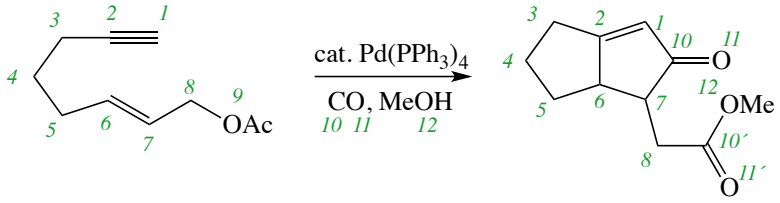


In fact, a mechanism for this reaction can be drawn that does not involve Pd at all, but let's assume that Pd is required for it to proceed. Cl^- must be nucleophilic. It can add to C1 of the alkyne if the alkyne is activated by coordination to Pd(II). (Compare Hg-catalyzed addition of water to alkynes.) Addition of Cl^- to an alkyne–Pd(II) complex gives a σ-bound Pd(II) complex. Coordination and insertion of acrolein into the C2–Pd bond gives a new σ-bound Pd(II) complex. In the Heck reaction, this complex would undergo β-hydride elimination, but in this case the Pd C-enolate simply is protonated to give the enol of the saturated aldehyde.



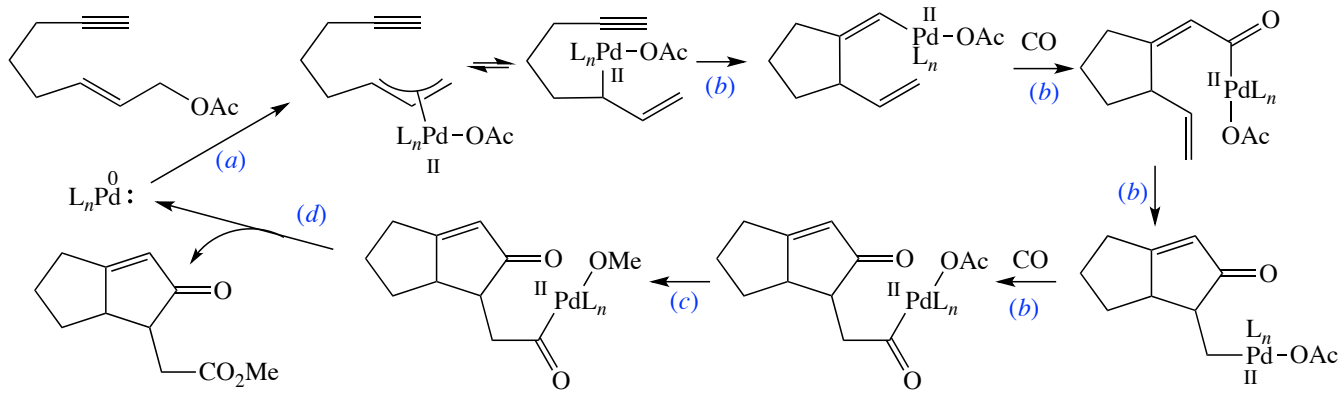
(l) A new C–C bond is formed between a nucleophilic C–Sn and an electrophilic C–Br. This Stille coupling proceeds through the standard oxidative addition, transmetallation, reductive elimination process characteristic of Pd-catalyzed cross-couplings. The mechanism was discussed in the text.

(m) There are two equivalents of CO incorporated into the product. Make: C1–C10, C2–C6, C7–C10, C8–C10´, C10´–O12. Break: C8–O9.



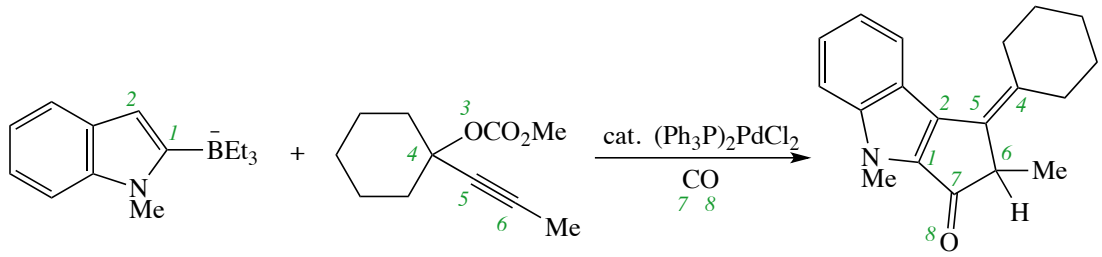
The first step is oxidative addition of Pd(0) to the C8–O9 bond to make a Pd π-allyl complex. Both C6 and C8 are rendered reactive by this step. At this point, we can either make the C8–C10´ bond by CO insertion, or we can make the C2–C6 bond by insertion of the C1=C2 π bond into the C6–Pd bond. The first alternative would be followed by displacement of Pd from C10´, requiring a new activation step to incorporate Pd into the substrate and allow the formation of the other bonds. After insertion of the C1=C2 π bond into the C6–Pd bond, though, we get a C1–Pd bond. This can insert CO to give the C1–C10 bond. The C8=C9 π bond can now insert into the C10–Pd bond, giving a C8–Pd bond. A second equivalent of CO then inserts. Ligand substitution of MeO for AcO is followed by reductive elimination to give the product. (Alternatively, acid-catalyzed displacement of Pd from C10´ by MeOH gives the

product. The Pd displacement proceeds is acid-promoted because the coproduct of the reaction is AcOH.)

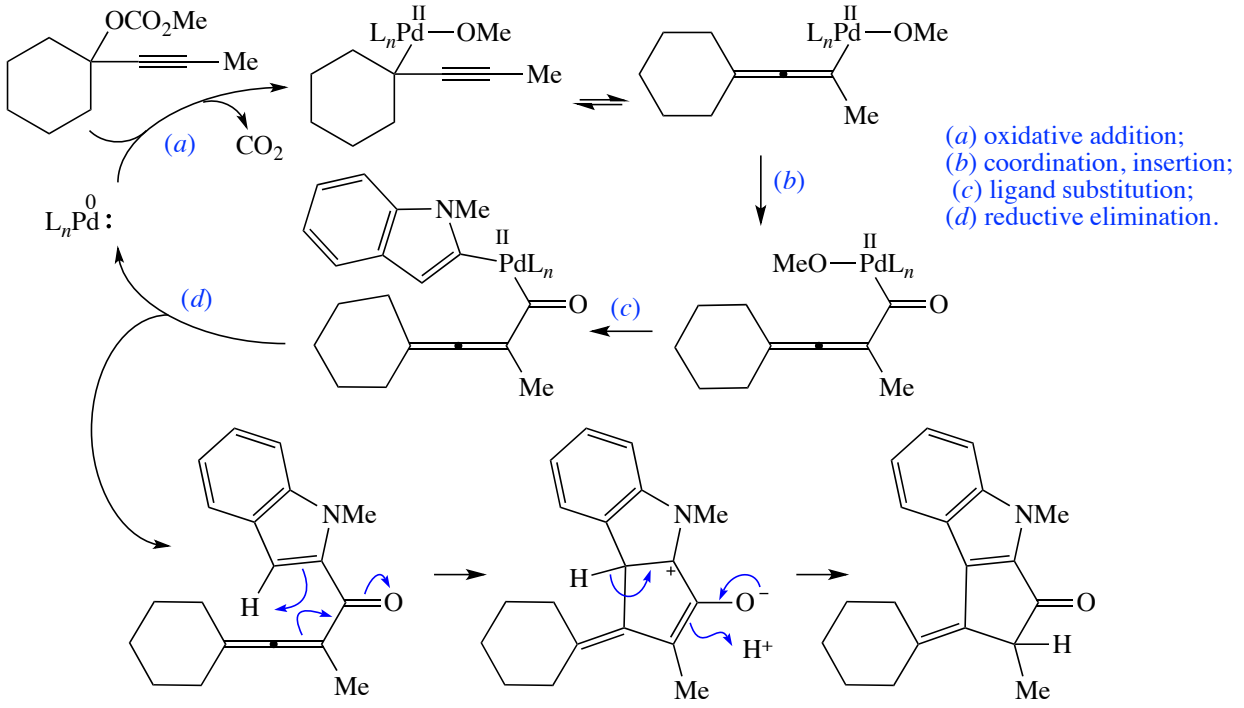


(*a*) oxidative addition; (*b*) coordination, insertion; (*c*) ligand substitution; (*d*) reductive elimination.

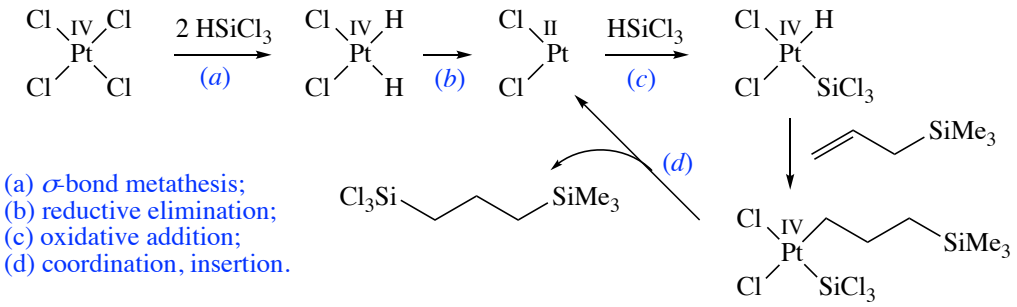
(n) Make: C1–C7, C2–C5, C6–C7. Break: C1–B, O3–C4. C1, with its bond to a negatively charged B, is nucleophilic.



A simple Suzuki-type coupling would form a bond between C1 and either C4 or C6. Obviously that isn't happening here. The O3–C4 bond is propargylic, so Pd(0) can undergo oxidative addition here to make a propargyl–Pd(II) complex. No new bonds are formed to C4, but the propargyl complex is in equilibrium with an allenyl complex with a C6–Pd bond. Insertion of CO into this bond gives the C7–C6 bond. Now transmetallation with the C1–B bond and reductive elimination gives the C1–C7 bond. At this point, the C2–C5 bond still needs to be formed. An electrocyclic ring-closing forms this bond and gives a zwitter-ionic oxyallyl. Proton transfer from C2 to C6 reestablishes indole aromaticity and completes the sequence.



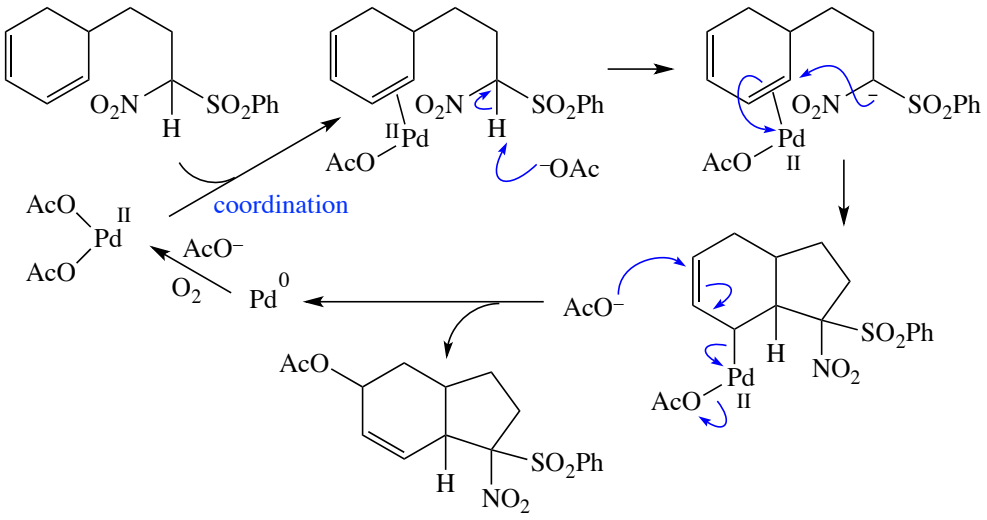
(o) The simplest mechanism that can be drawn for this reaction is as follows. First the Pt(IV) precatalyst needs to be reduced to Pt(II). This can be accomplished by σ bond metathesis of two Pt–Cl bonds with Cl_3Si–H to give a Pt(IV) dihydride, which can undergo reductive elimination to give a Pt(II) species. (The Pt species are shown as $PtCl_4$ and $PtCl_2$, but of course other ligands may be present.) The catalytic cycle then proceeds by oxidative addition of Cl_3Si–H to Pt(II), coordination and insertion of the alkene into the Pt–H bond, and reductive elimination of the product, just like a Pd-catalyzed hydrogenation.



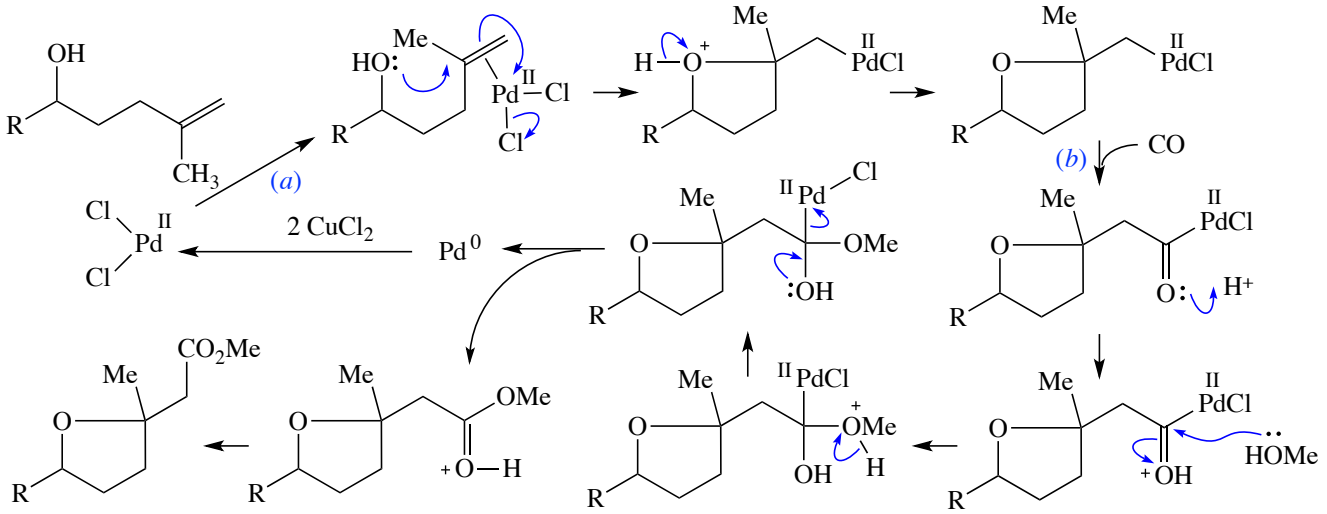
Experiments show that the actual mechanism of this reaction is considerably more complex than the one shown [radicals may be involved, especially in the reduction of Pt(IV) to Pt(II)], but the simple mechanism above provides a starting point for further investigation.

(p) The reaction is a carbonylative Stille coupling (twice). The mechanism is discussed in the text.

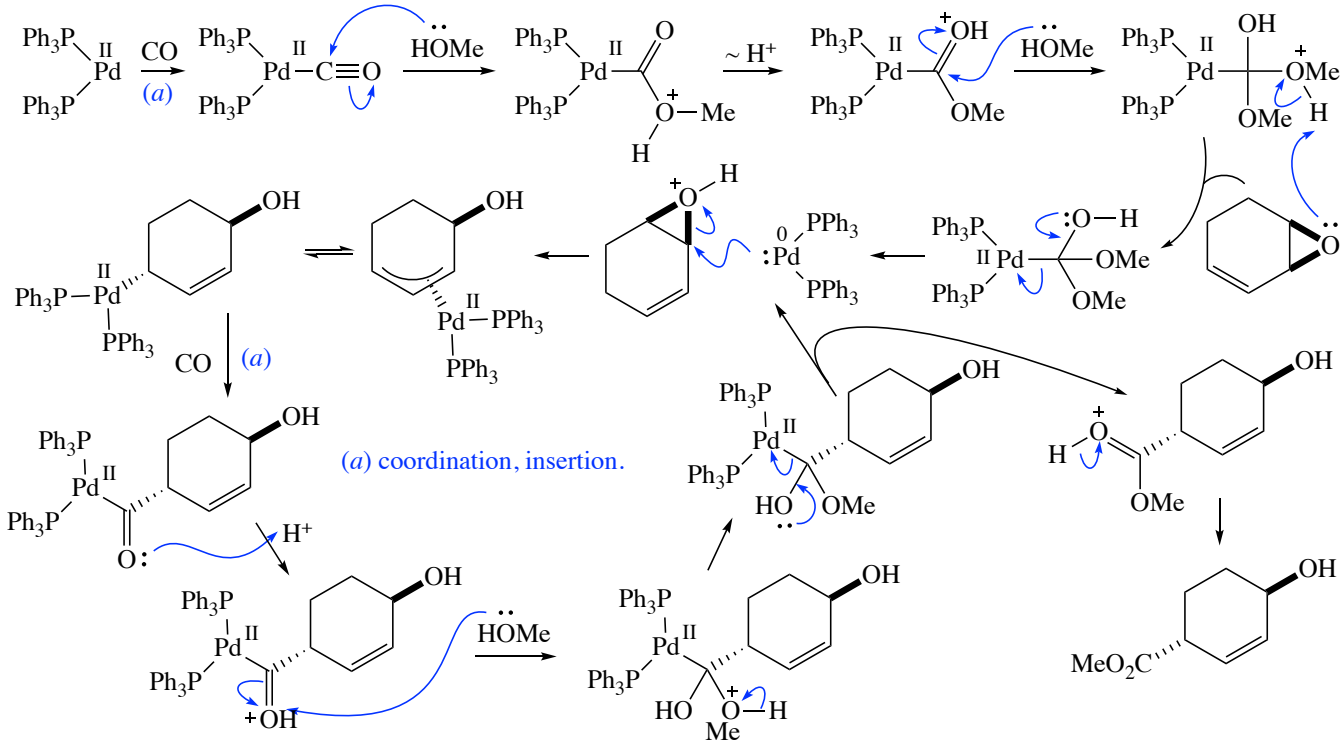
(q) Addition of a nucleophile to an alkene is catalyzed by Pd(II) salts. The Pd(II) coordinates to the alkene and makes it electrophilic, and the nucleophile attacks to give a C–Pd σ bond. In this case, because the substrate is a diene, the product is an allylpalladium(II) complex, a good electrophile. It is attacked by AcO^- to give the organic product plus Pd(0). O_2 then oxidizes the Pd(0) back to Pd(II).



(r) Addition of a nucleophile to an alkene is catalyzed by Pd(II) salts. The product, an alkylpalladium(II) compound, usually undergoes β-hydride elimination, but in this case insertion of CO occurs to give an acylpalladium(II) complex. Acid-catalyzed displacement of Pd(0) by MeOH gives the organic product and Pd(0). (An alternative is to have the last Pd(II) intermediate undergo β-hydride elimination to give the organic product and H–Pd–Cl, which, upon deprotonation, gives Pd(0).) Pd(0) is reoxidized to Pd(II) by $CuCl_2$.

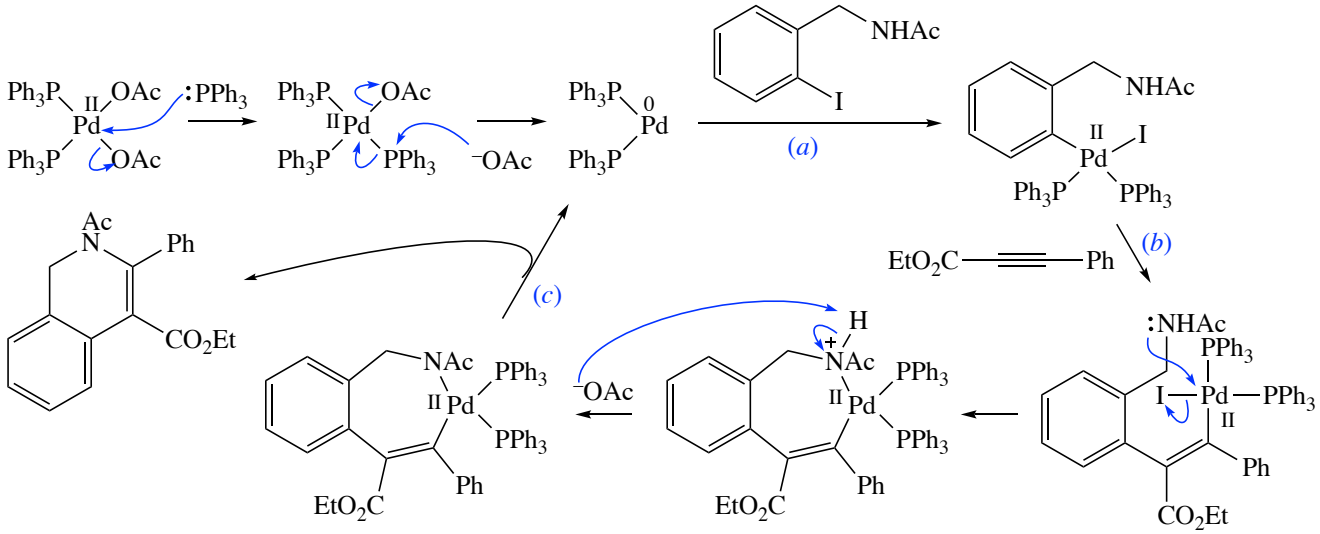


(s) This reaction combines allylic substitution with carbonylation. First, the Pd(II) must be reduced to Pd(0). The mechanism below shows one way that could happen. Once Pd(0) is generated, it opens the epoxide at the allylic position to give a Pd(II) π-allyl complex. Insertion of CO into the other allylic Pd–C bond is followed by displacement of Pd(0) to give the product and regenerate Pd(0). The Pd(II) salt is a weak Lewis acid, so the mechanism probably takes place under acidic conditions.



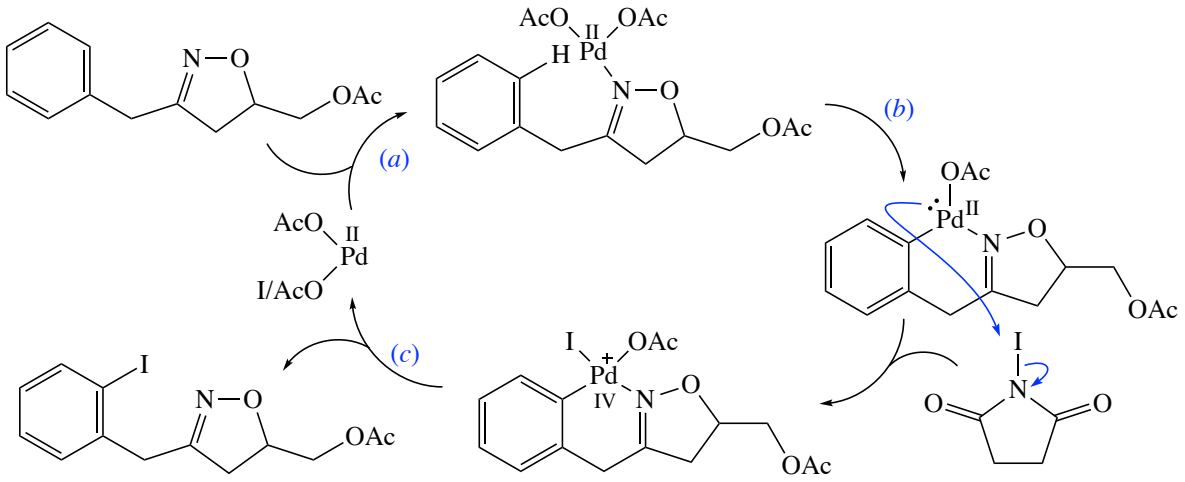
(t) This reaction is a Buchwald–Hartwig coupling. Its mechanism is discussed in the text.

(u) The mechanism starts by reduction of Pd(II) to Pd(0), here shown with the help of PPh_3. Oxidative addition to the aryl iodide gives an arylpalladium(II) complex. The alkyne inserts into the aryl–Pd bond to give a new Pd(II) complex. The pendant N displaces I from Pd, and deprotonation of the N triggers a reductive elimination to give the product and regenerate Pd(0). The role of the LiCl is unclear; Cl^- may substitute for AcO^- or I^- on Pd at one or more stages in the catalytic cycle.



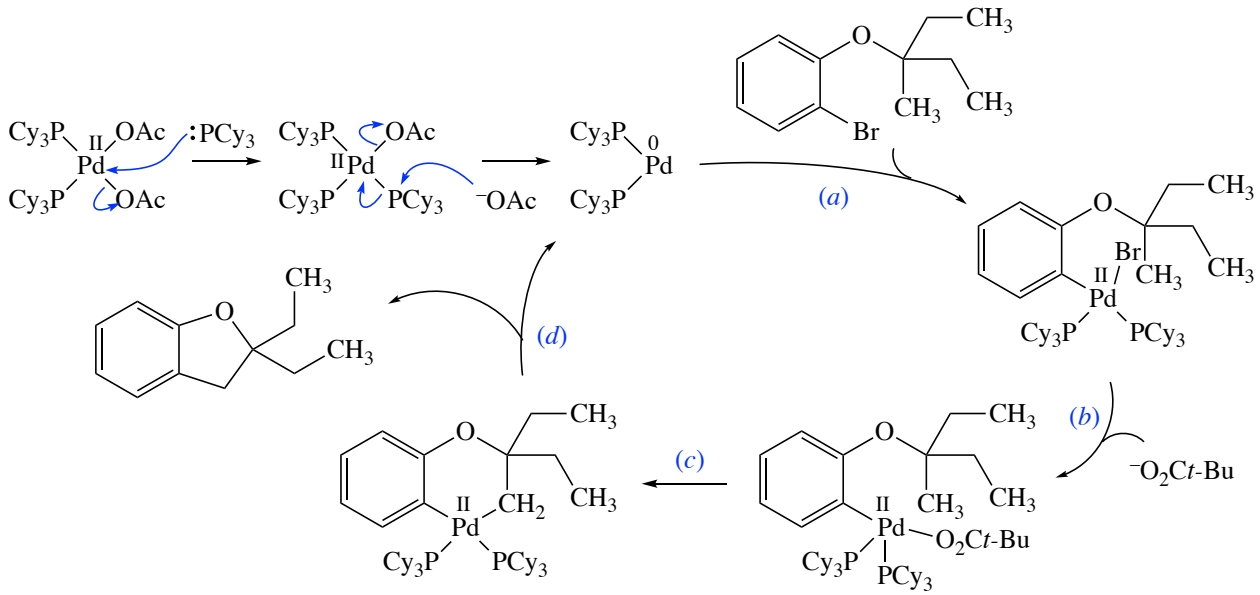
(*a*) oxidative addition; (*b*) coordination, insertion; (*c*) reductive elimination.

(v) This reaction is a Pd-catalyzed C–H activation. The mechanism starts with Pd(II) coordinating to the oxazoline N. Concerted metalation–deprotonation causes a Pd–aryl bond to form and an equivalent of AcOH to be lost to give a six-membered palladacycle with Pd still in the (II) oxidation state. Next, NIS transfers its I to Pd, oxidizing it to Pd(IV). Reductive elimination of the Ar–I bond and dissociation of N from Pd then gives the product and regenerates Pd(II).



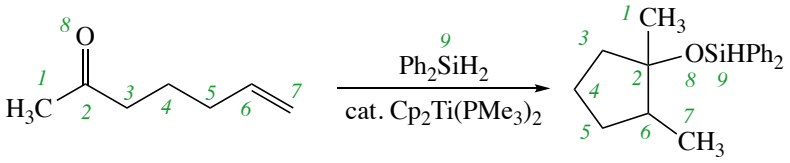
(*a*) coordination; (*b*) concerted metallation–deprotonation; (*c*) reductive elimination, dissociation.

(w) This reaction is a Pd-catalyzed C–H activation, but because the reaction involves substitution of an Ar–Br bond, the mechanism probably starts with Pd(0). It can be generated by reduction of the added Pd(II) salt with phosphine. Once Pd(0) forms, it can undergo oxidative addition to the Ar–Br bond to give a Pd(II) complex. After substitution of Br^- with *t*-$BuCO_2^-$, Pd(II) can undergo concerted metalation–deprotonation with the nearby C–H bond of the CH_3 group to give a six-membered palladacycle with Pd in an unchanged oxidation state. Reductive elimination gives the observed product and regenerates Pd(0).

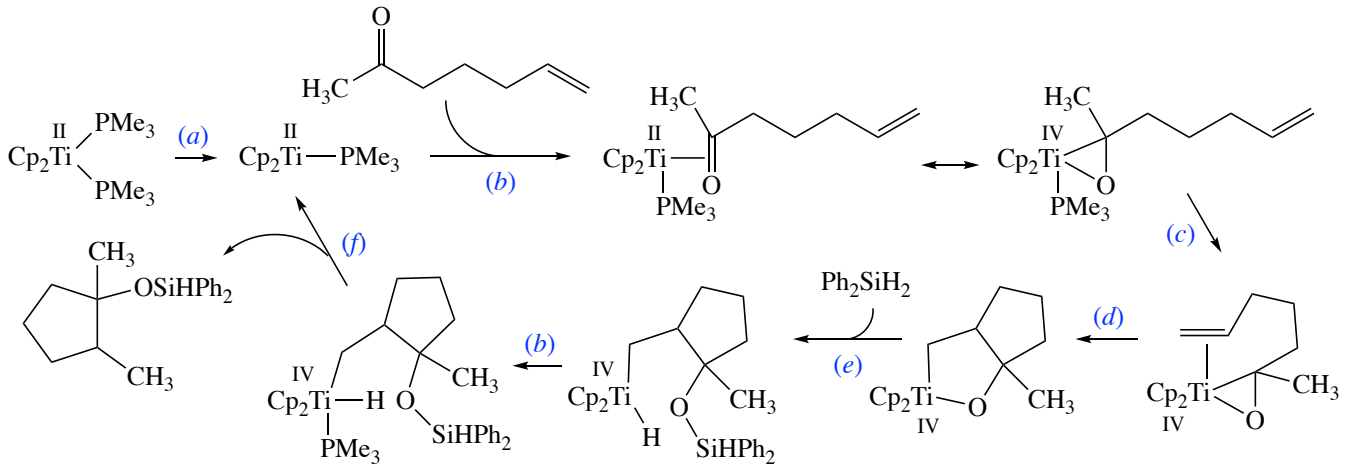


(*a*) coordination; (*b*) ligand substitution; (*c*) concerted metallation–deprotonation; (*d*) reductive elimination.

2. (a) Make: C2–C6, O8–Si9. We also remove one H from Si9 and add one to C7. Ti is in the (II) oxidation state. Low-valent Ti compounds are commonly used for reductive coupling reactions. We can form the C6–C2 bond by such a reductive coupling.



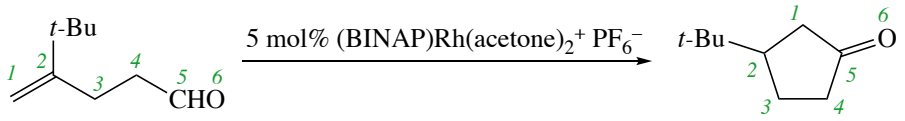
Dissociation of Me_3P from the 18-electron complex gives a 16-electron complex. Association of the carbonyl group gives a Ti(II) π complex that can also be described as a Ti(IV) metallaoxirane. Dissociation of the second Me_3P, association of the alkene, and migratory insertion of the alkene into the C2–Ti bond gives a five-membered metallacycle. A σ bond metathesis between the Si9–H and Ti–O8 bonds now occurs to give a very strong Si9–O8 bond and a Ti–H bond. No change in the Ti(IV) oxidation state occurs. Reductive elimination from Ti(IV) gives the product and regenerates Ti(II).



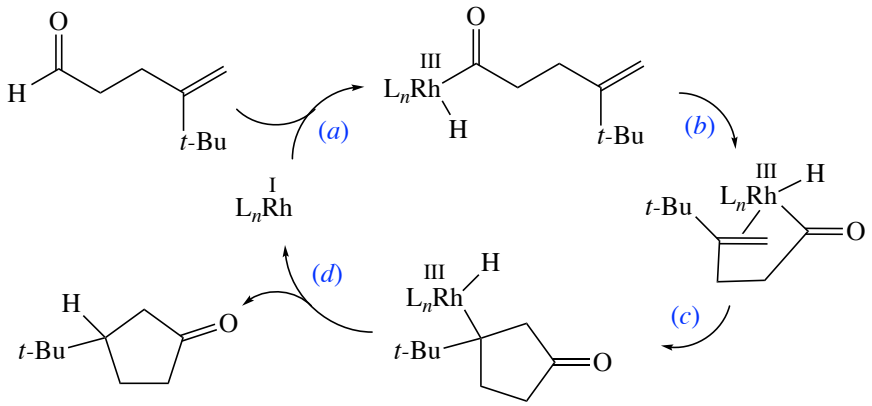
(a) ligand dissociation; (b) ligand association; (c) ligand substitution;
(d) insertion; (e) σ-bond metathesis; (f) reductive elimination.

(b) The mechanism of this alkene metathesis reaction (in ring-opening metathesis polymerization mode) is discussed in the text.

(c) Make: C1–C5, C2–H. Break: C5–H. Rh is in the (I) oxidation state, hence it is d^8; the two acetone molecules are counted as two-electron donors, so it is a 16-electron complex.

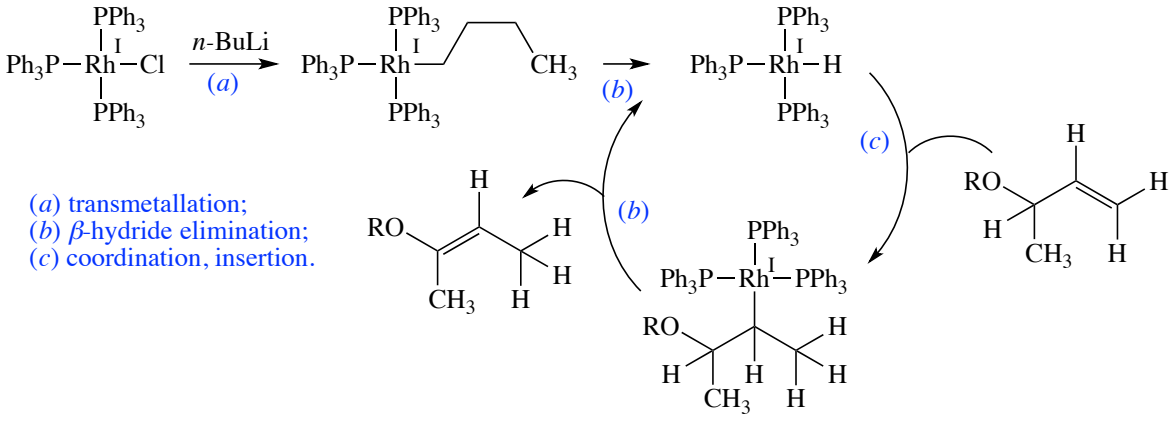


Essentially, the C1=C2 bond is inserted into the C5–H bond. This suggests that the Rh oxidatively adds across the C5–H bond. Rh can do this with aldehydes. After oxidative addition to the C5–H bond to give a Rh(III) complex, insertion and reductive elimination give the product and regenerate Rh(I). Solvent molecules may be associating or dissociating at any point in the sequence.



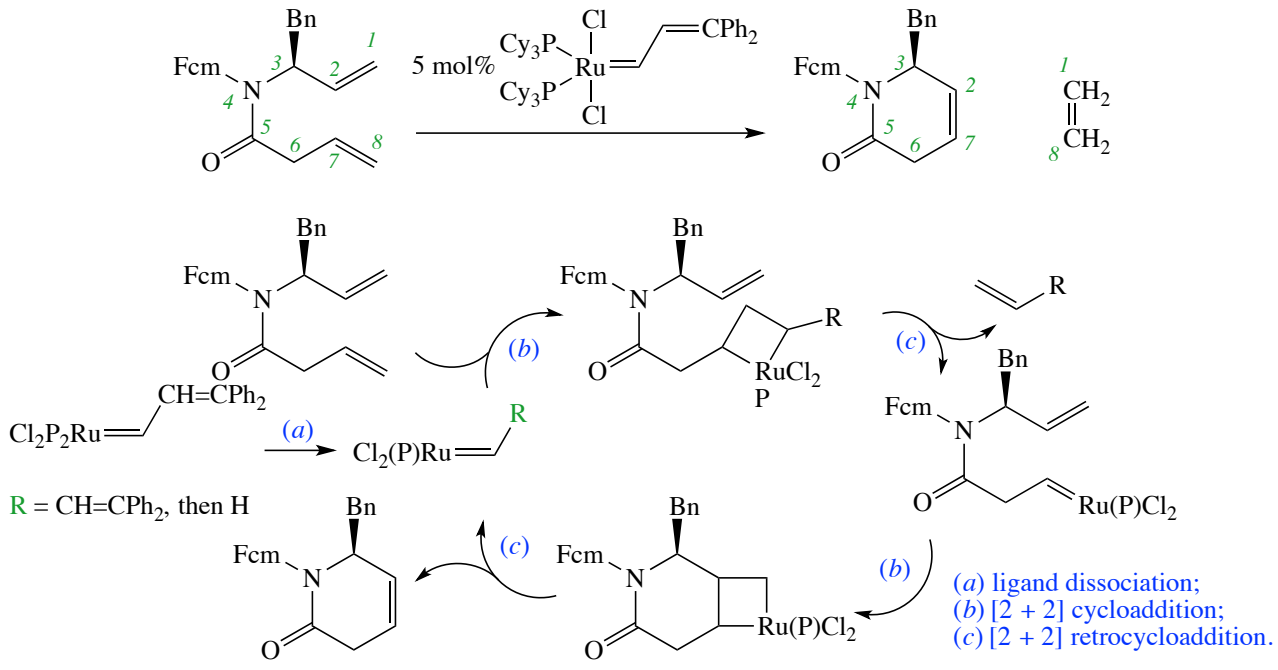
(a) oxidative addition;
(b) coordination;
(c) insertion;
(d) reductive elimination.

(d) Alkene isomerization can proceed by an oxidative addition (to the allylic C–H bond)/ reductive elimination sequence or by an insertion/ β-hydride elimination sequence. Wilkinson's catalyst normally isomerizes alkenes by the first mechanism. However, in this case BuLi is added to the catalyst first. This will give a Rh–alkyl bond, which can decompose by β-hydride elimination (as many metal alkyls do) to a Rh–H bond. Now the catalyst can carry out the insertion/ β-hydride elimination sequence to isomerize the alkene to a thermodynamic mixture of isomers. The most conjugated alkene is the lowest in energy and is obtained in greatest proportion.



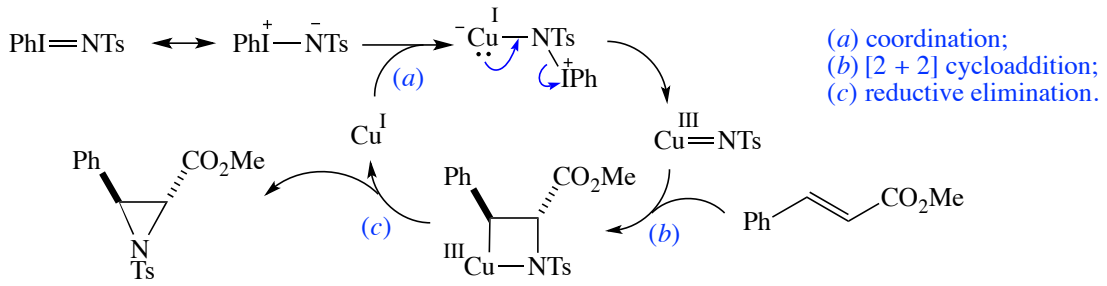
(e) The product is missing C1 and C8. They are lost as $H_2C{=}CH_2$. Make: C2=C7, C1=C8. Break: C1=C2, C7=C8. The Ru complex is 16-electron, d^2, Ru(IV). This is another olefin metathesis reaction, except this

time it is ring-*closing* metathesis. The mechanism begins by dissociation of one phosphine from the Ru center to open up a coordination site. proceeds by a series of [2+2] and retro [2+2] cycloadditions. The R group starts off as $CH{=}CPh_2$, but, after one cycle, it becomes H.

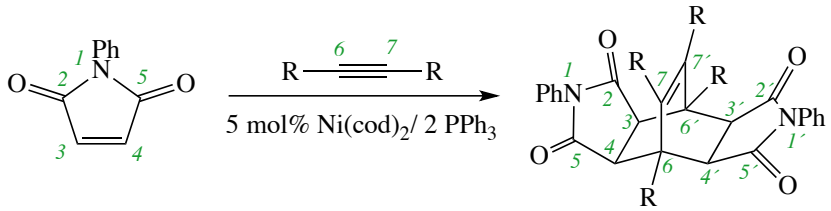


(f) The interaction of diazo compounds with Cu(I) complexes produces carbenoids, $L_nCu{=}CR_2$, with Cu in the (III) oxidation state. The carbenoids do typical reactions such as C–H insertion and [2 + 1]

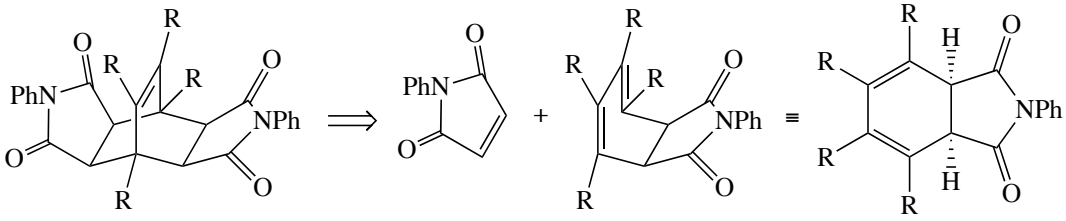
cycloaddition. The mechanism of the latter reaction involves [2 + 2] cycloaddition with the C=C π bond, followed by reductive elimination.



(g) Make: C3–C6′, C3′–C6′, C4–C6, C4′–C6, C7–C7′. Ni is in the (0) oxidation state. $Ni(cod)_2$ is an 18-electron complex. $(Ph_3P)_2Ni(cod)$ is also an 18-electron complex. The fact that we are making six-membered rings from isolated π bonds suggests a cyclotrimerization.

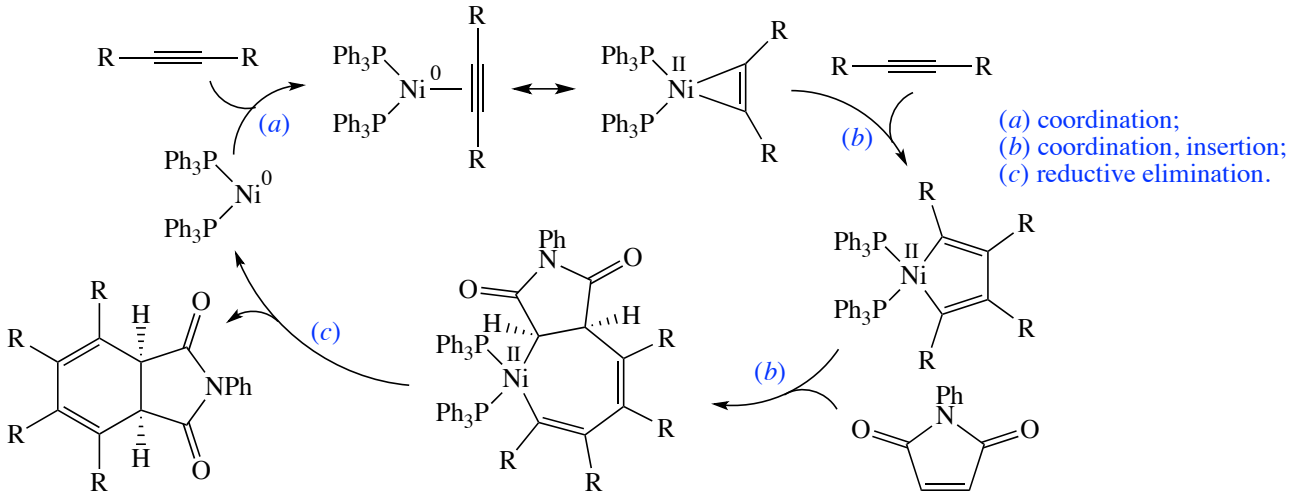


It seems clear that the product can be made by a Diels–Alder reaction of the maleimide with a cyclohexadiene. The Ni-catalyzed reaction, then, need only produce this diene.

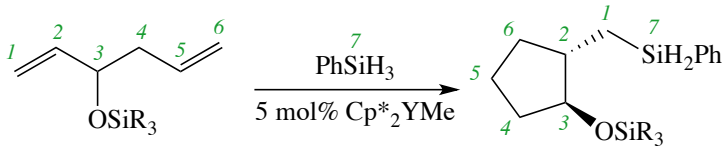


Coordination of Ni(0) to the alkyne gives a π complex, which can be written in its Ni(II) resonance form. Coordination and insertion of another alkyne forms the new C6–C7 bond and gives a nickelacyclopentadiene. Maleimide may react with the metallacycle by coordination, insertion, and reductive elimination to give a cyclohexadiene. Alternatively (not shown), [4 + 2] cycloaddition to the metallacycle followed by retro [4 + 1] cycloaddition to expel Ni(0) gives the same cyclohexadiene. The

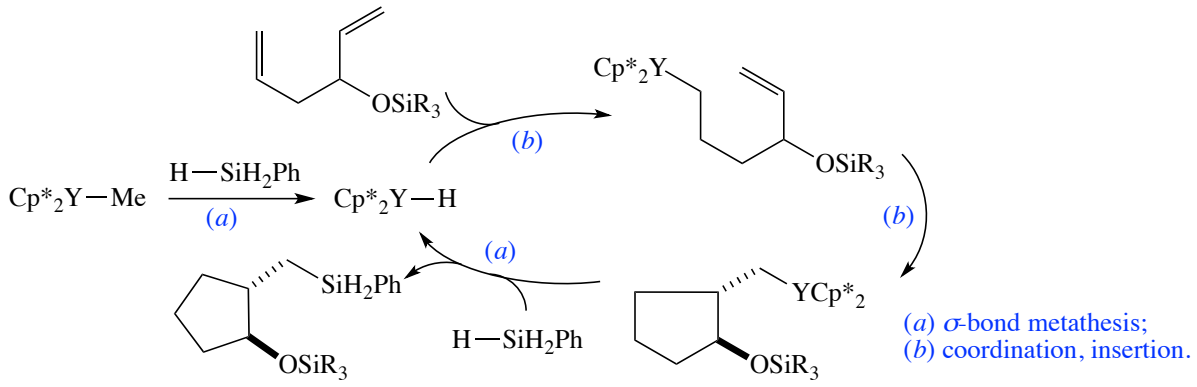
cyclohexadiene can then undergo a Diels–Alder reaction with another equivalent of maleimide to give the observed product.



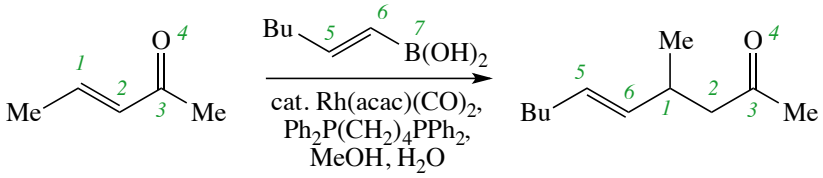
(h) Make: C1–Si7, C6–C2, C5–H. Break: Si7–H. Y is in the (III) oxidation state in the d^0, 14-electron complex.



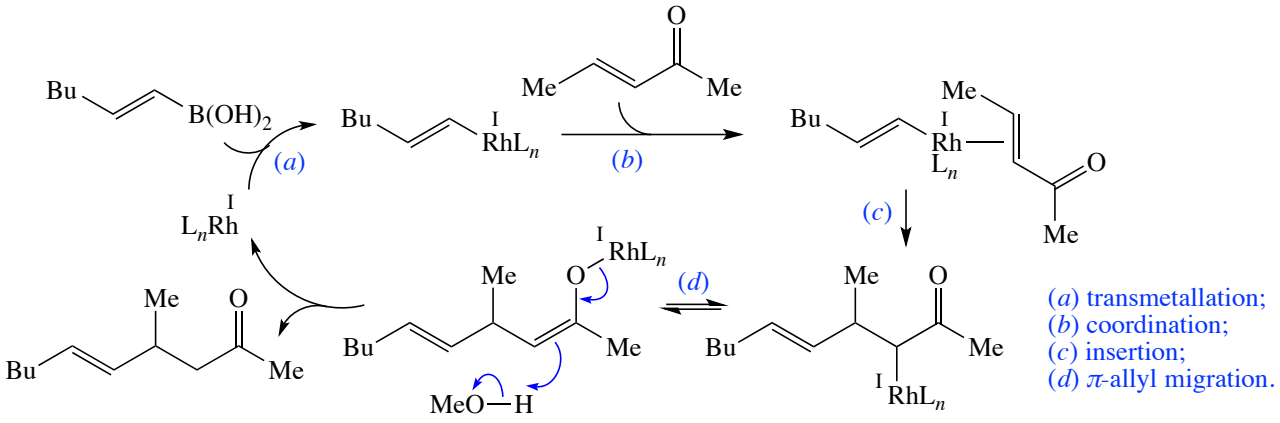
The overall transformation involves insertion of the C5=C6 and the C2=C1 π bonds into the Si7–H bond. An oxidative addition of Si–H to Y, insertion, insertion, reductive elimination sequence might occur. The problem with this is that the d^0 Y complex can't do oxidative addition. The alternative by which the Si–H bond is activated is a σ bond metathesis process. Cp^*_2Y–Me undergoes σ bond metathesis with the Si–H bond to give Cp^*_2Y–H. Coordination and insertion of the C5=C6 π bond into the Y–H bond gives the C5–H bond and a C6–Y bond. Coordination and insertion of the C1=C2 π bond into the C6–Y bond gives the key C6–C2 bond and a C1–Y bond. Finally, σ bond metathesis occurs once more to make the C1–Si bond and regenerate Cp^*_2Y–H.



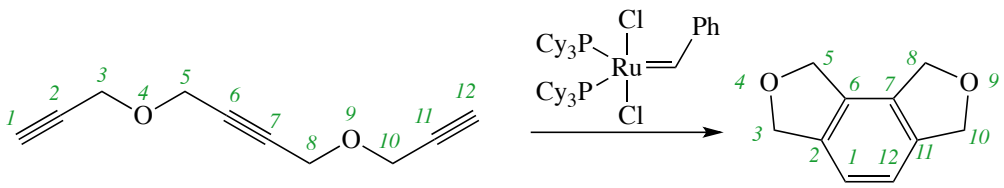
(i) Make: C6–C1. Break: C6–B7.



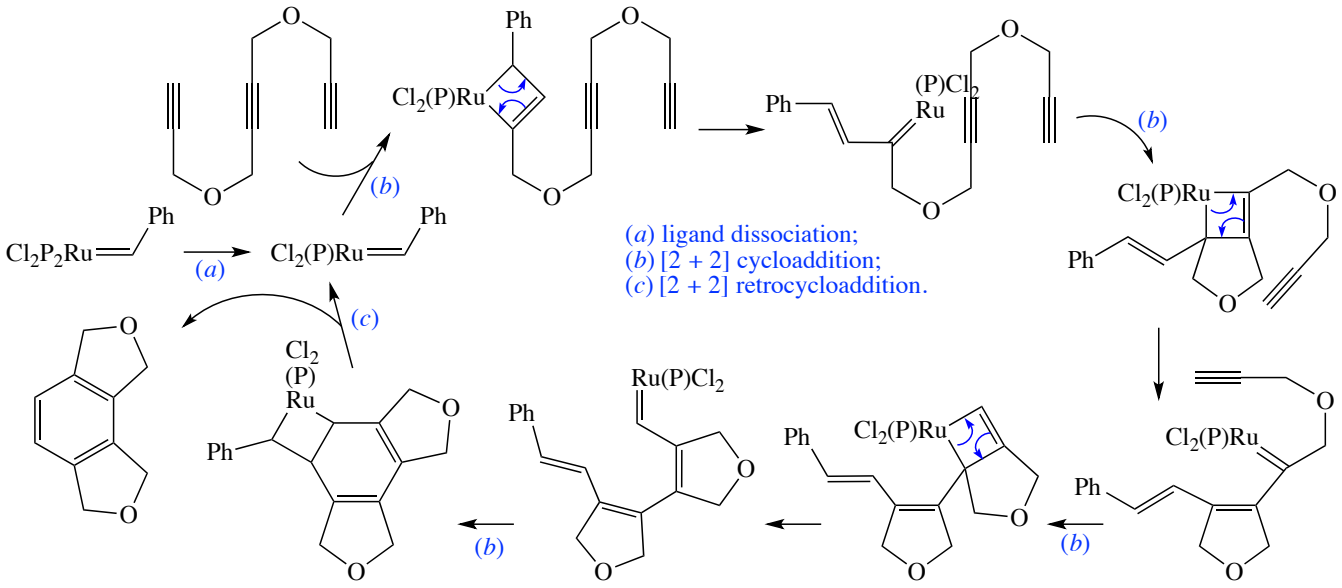
The reaction looks like a conjugate addition. A C6–Rh bond could insert into the C1=C2 π bond. The C6–Rh bond could be made by transmetallation. The transmetallation step is probably promoted by the coordination of MeO^- or HO^- generated in the previous catalytic cycle to the B.



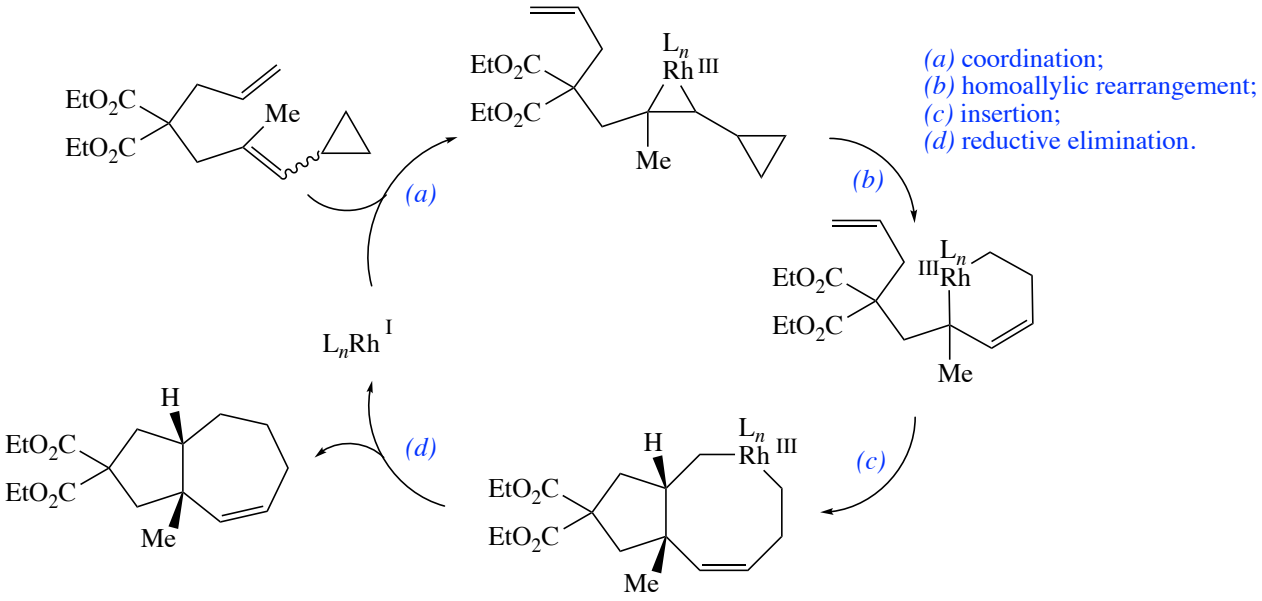
(j) Make: C1–C12, C2–C6, C7–C11.



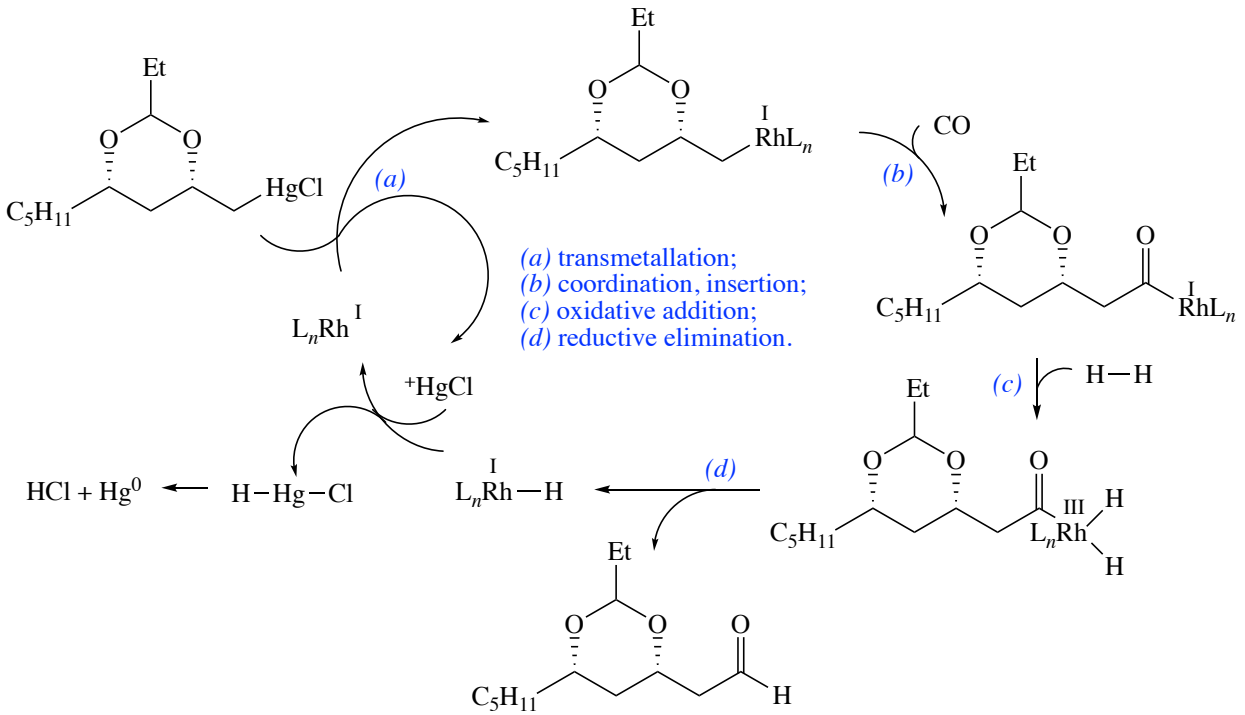
The overall reaction is a cyclotrimerization. Cyclotrimerizations are usually catalyzed by low-valent Co or Ni complexes by a reductive coupling mechanism, but the Ru=C complex lives to do [2+2] cycloadditions, so let it. Cycloaddition to the C1=C2 bond gives a ruthenacyclobutene, which can undergo electrocyclic ring opening to give a Ru=C2 π bond. This π bond can do a [2+2] cycloaddition to the C6=C7 π bond. Another ring opening, another [2+2] cycloaddition, another ring opening, another [2+2] cycloaddition, and a [2+2] retrocycloaddition give the product and regenerate the catalyst.



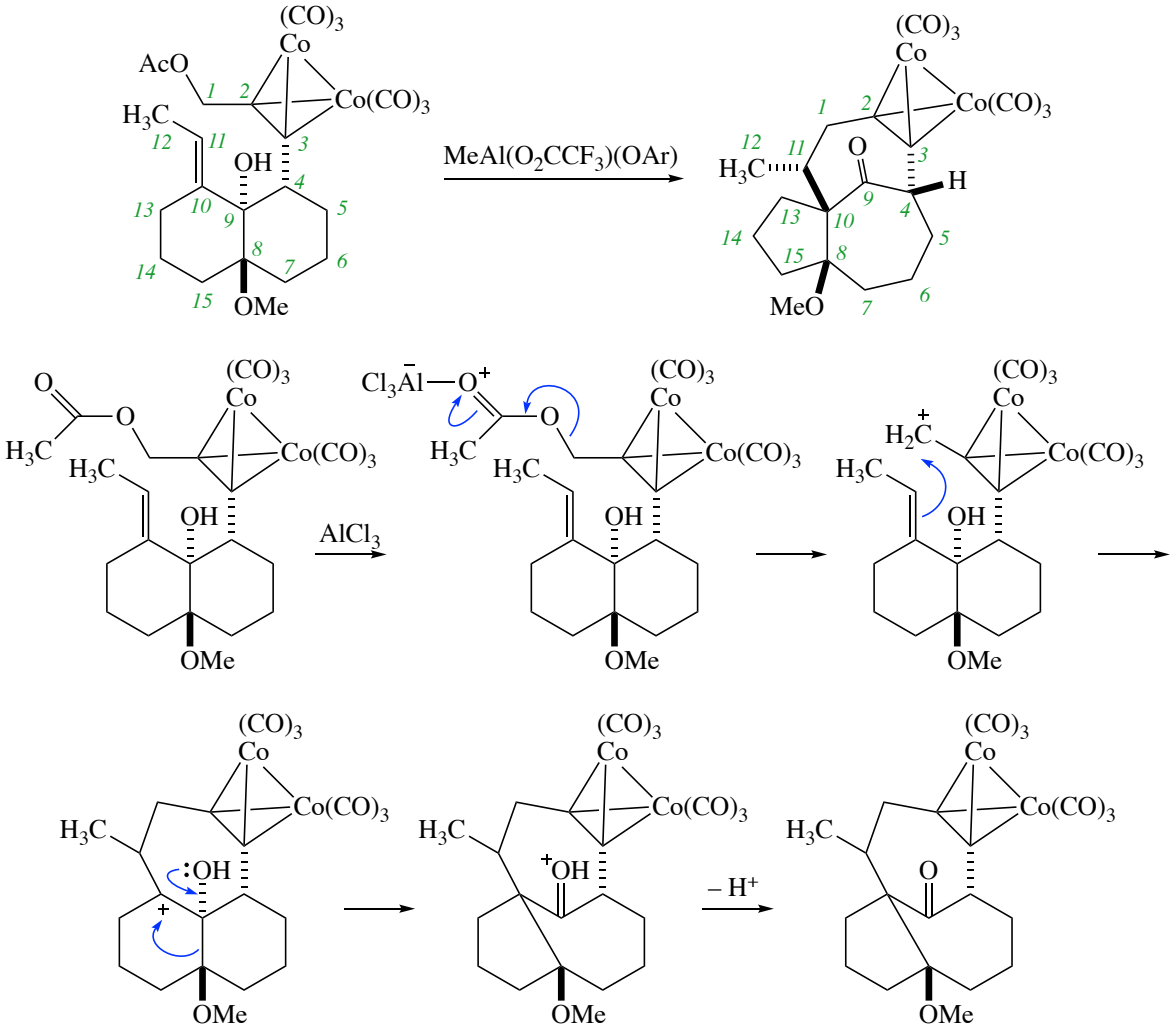
(k) As discussed in the text, two mechanisms are possible. In one, the Rh(I) first coordinates to the alkene next to the cyclopropane. The Rh(I)–alkene complex can also be drawn as a rhoda(III)cyclopropane complex. The cyclopropane ring can then open, with the C–Rh bond closer to the opening ring migrating to give a six-membered Rh(III) metallacycle. Coordination and insertion of the other alkene gives an eight-membered Rh(III) metallacycle, which undergoes reductive elimination to give the product and to regenerate Rh(I). Alternatively (not shown), the Rh(I) can first coordinate to the alkene distal to the cyclopropane ring. Insertion of the second alkene gives a five-membered Rh(III) metallacycle, which can then undergo the cyclopropane ring opening and migration of the C–Rh bond to give the same eight-membered Rh(III) metallacycle.



(l) Starting with Rh(I), transmetallation with RHgCl occurs to give an alkylrhodium(I) compound and $^{+}$HgCl. Carbon monoxide coordinates to Rh(I) and inserts into the C–Rh bond to give an acylrhodium(I) compound. Oxidative addition of H_2 is followed by reductive elimination of the aldehyde to give a new Rh(I) hydride complex. The question now is how to dispose of the hydride ligand on Rh. One possibility is that the Rh–H compound reacts with $^{+}$HgCl to give H–Hg–Cl, which decomposes to HCl and Hg(0).

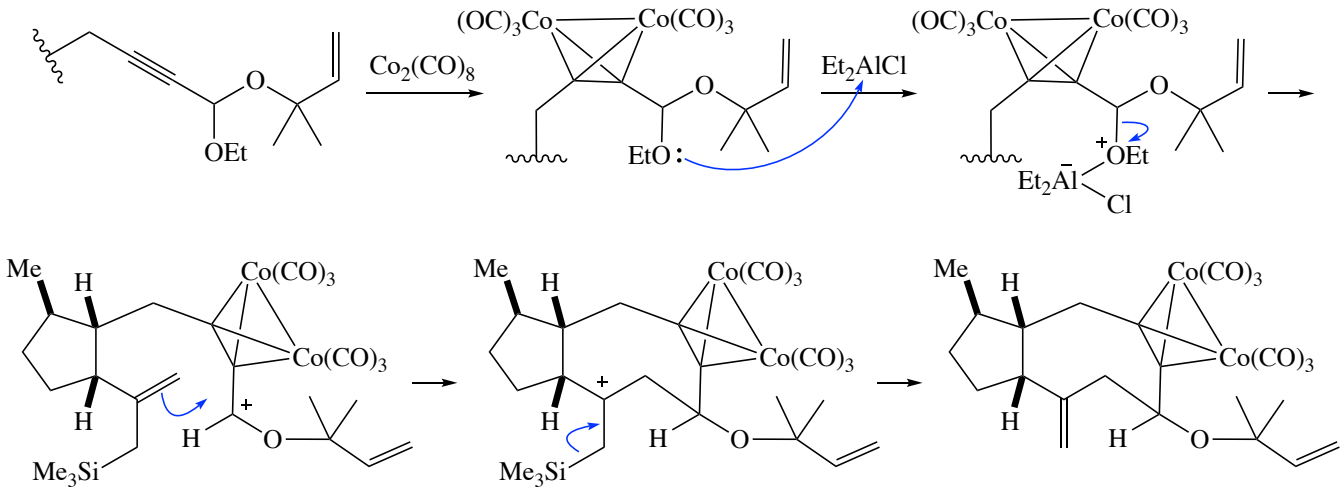


3. (a) Make: C1–C11, C8–C10. Break: C1–OAc, C8–C9. $Co_2(CO)_6$–alkyne complexes are prone to form cations at the propargylic position because the C–Co bonds hyperconjugatively stabilize the cation. The C10=C11 π bond can add to a C1 cation. Pinacol rearrangement (1,2-shift) then breaks the C8–C9 bond. Loss of H^+ from O completes the sequence.

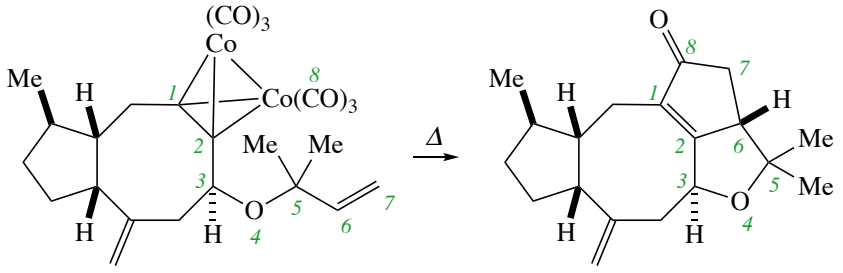


(b) Addition of $Co_2(CO)_8$ to an alkyne forms the $Co_2(CO)_6$–alkyne complex. Propargyl cation formation is thereby enhanced. The Lewis acid coordinates to the less hindered OEt group, converting it into a good leaving group. It leaves to give the propargyl cation, which is attacked by the alkene to form the eight-membered ring. Loss of Me_3Si^+ gives the product. Because of ring strain, the eight-membered ring could not form if the alkyne were not coordinated to $Co_2(CO)_6$. The $Co_2(CO)_6$ both reduces the

bond angles around the "alkyne" C's *and* reduces the entropic barrier to eight-membered ring formation by holding the two "alkyne" substituents near one another.



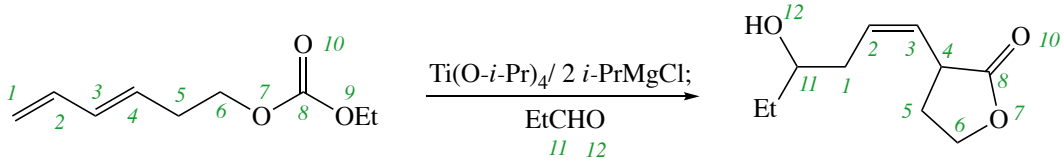
(c) Make: C1–C8, C2–C6, C7–C8. Break: Co–C1, Co–C2, Co–C8.



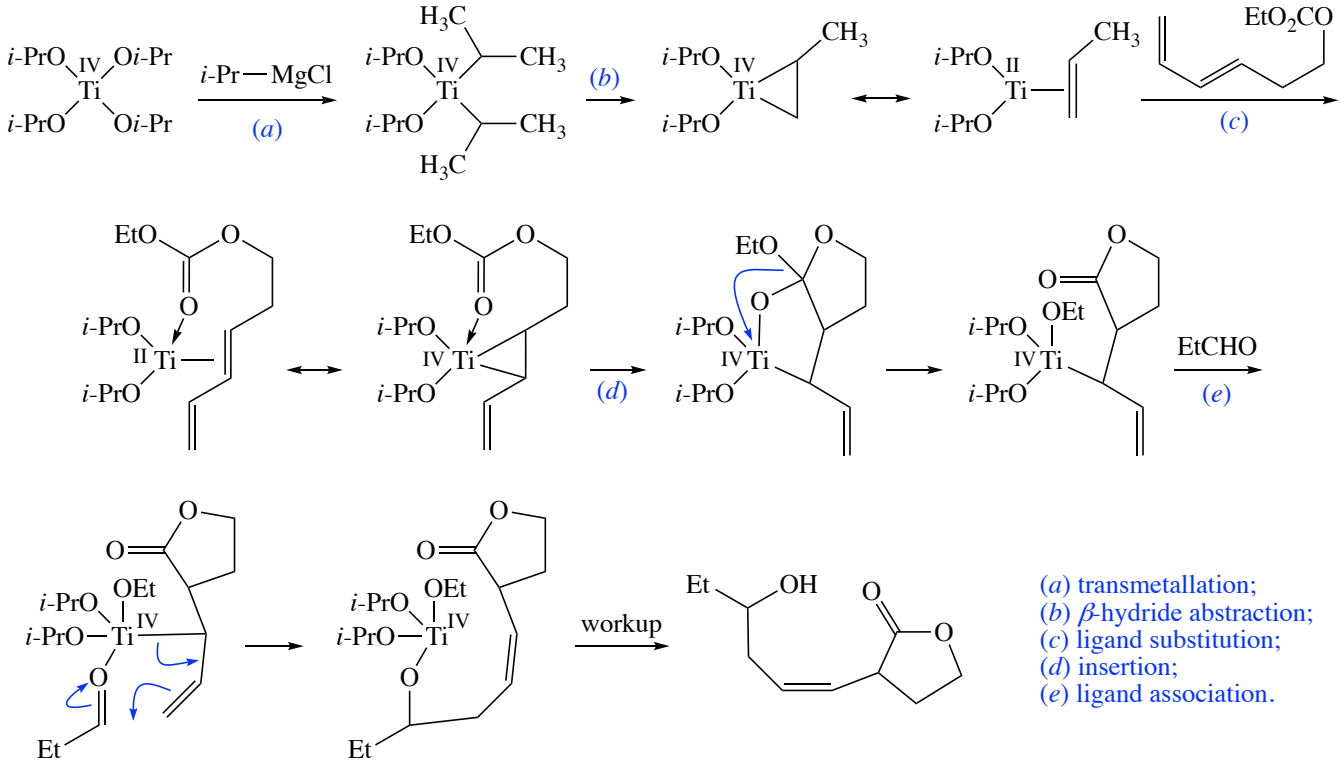
Conversion of a $Co_2(CO)_6$–alkyne complex into a cyclopentenone is the Pauson–Khand reaction. It proceeds by loss of CO from one Co to make a 16-electron complex, coordination and insertion of the C6=C7 π bond into the C2–Co bond to make the C2–C6 bond and a C7–Co bond, migratory insertion of CO into the C7–Co bond to make the C7–C8 bond, reductive elimination of the C1–C8 bond from Co, and decomplexation of the other Co from the C1=C2 π bond. The mechanism is discussed in the text.

(d) Make: C1–C11, C4–C8. Break: C8–C9. Ti is in the (IV) oxidation state, so it is d^0. Since we are forming new bonds from C4 to C8 and C1 to C11, and both C8 and C11 are electrophiles, both C1 and C4 must act as nucleophiles Normally in a diene one terminus acts as a nucleophile and one terminus

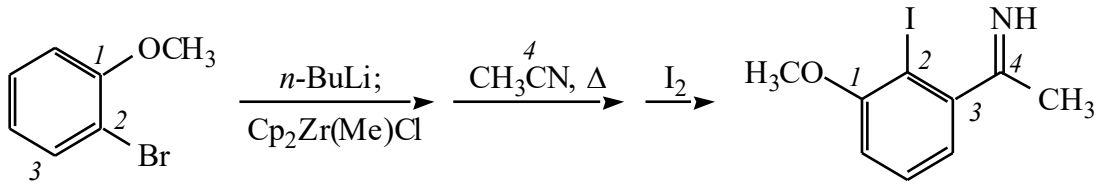
acts as an electrophile. The role of the Ti, then, is to supply the necessary electrons. But Ti(IV) is not a reducing agent, so the role of the Grignard reagent must be to reduce the Ti.



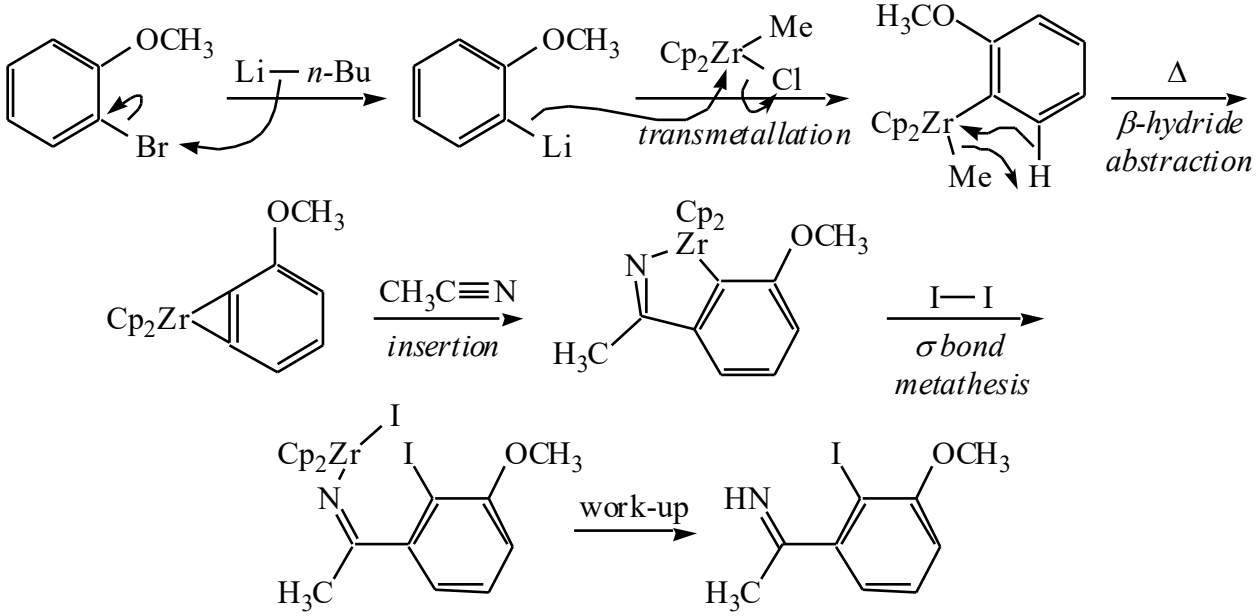
Addition of the Grignard to Ti(O-*i*-Pr)$_4$ will displace two *i*-PrO$^-$ groups and give (*i*-PrO)$_2$Ti(*i*-Pr)$_2$. β-Hydride abstraction (or β-hydride elimination followed by reductive elimination) then gives a Ti(II)–alkene complex ↔ titanacyclopropane. Coordination of the C3=C4 π bond and loss of propene gives a new titanacyclopropane; coordination of O10 promotes the formation of this particular titanacyclopropane. Insertion of the C8=C10 bond into the Ti–C4 bond forms the crucial C4–C8 bond. Expulsion of EtO$^-$ from C8 gives the lactone; the EtO$^-$ can coordinate to Ti(IV). There is still a Ti–C3 bond, so C3 is nucleophilic, as is C1 by vinylology. Nucleophilic addition of C1 to C11 and aqueous workup gives the product.



(e) Make: C2–I, C3–C4. Break: C2–Br. Since C4 is electrophilic, C3 must be made nucleophilic. This would be the role of the Zr complex.

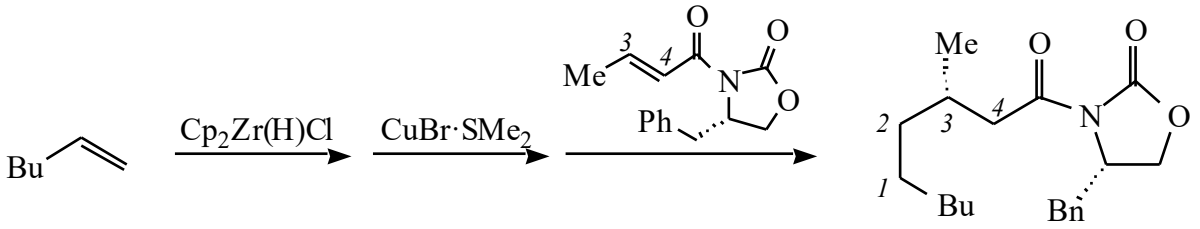


Addition of BuLi to ArBr results in halogen–metal exchange to give ArLi. Addition of $Cp_2Zr(Me)Cl$ to ArLi gives transmetallation to give $Cp_2Zr(Me)Ar$ and LiCl. We need to make a Zr–C3 bond in order to render C3 nucleophilic. This can be done by a β-hydride abstraction reaction to give a zirconacyclopropane. Insertion of the C4≡N bond into the C3–Zr bond gives the crucial C3–C4 bond. We still need to form the C2–I bond. Addition of I_2 cleaves the C2–Zr bond and gives the C2–I bond. Aqueous workup cleaves the N–Zr bond to give the observed product.

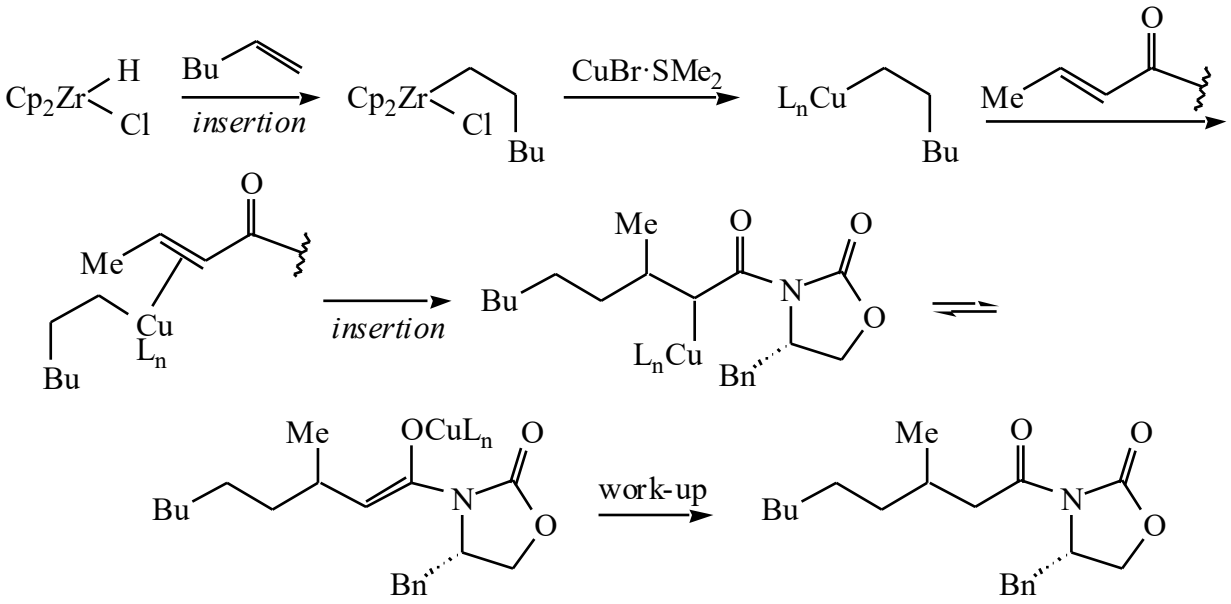


(f) This reaction proceeds via mechanisms similar to the previous two problems. The Grignard reagent reduces Ti(IV) to a Ti(II)–propene complex. Exchange of propene with the imine gives a titanaaziridine complex. Insertion of the alkyne into the C–Ti bond gives a titanapyrrolidine. Addition of I_2 cleaves the C–Ti bond in favor of a C–I bond. Aqueous workup then gives the product.

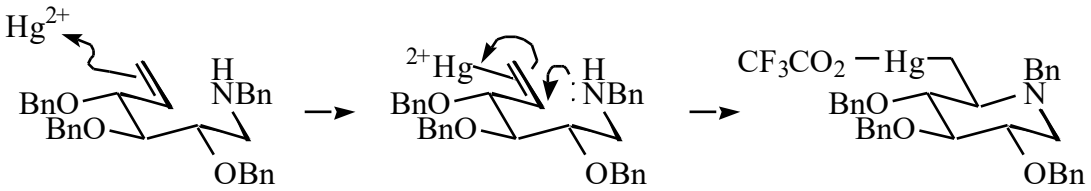
(g) Make: C2–C3. C3 is electrophilic, so C2 must be made nucleophilic.



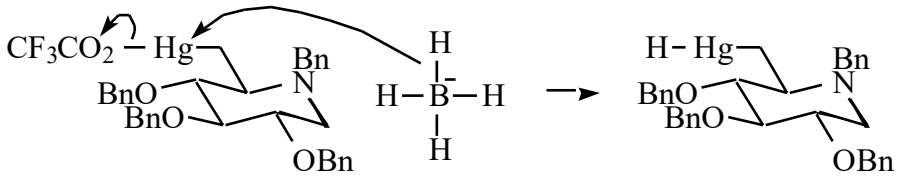
Addition of an alkene to a compound containing a metal–H bond usually results in insertion, and it does in this case, too, to give the stabler 1° alkylmetal. Addition of CuBr to this complex might result in transmetallation, to give a C2–Cu bond. Addition of the copper compound to the unsaturated imide gives conjugate addition, perhaps by coordination of the C3=C4 π bond and insertion into the C2–Cu bond. Workup gives the observed product.



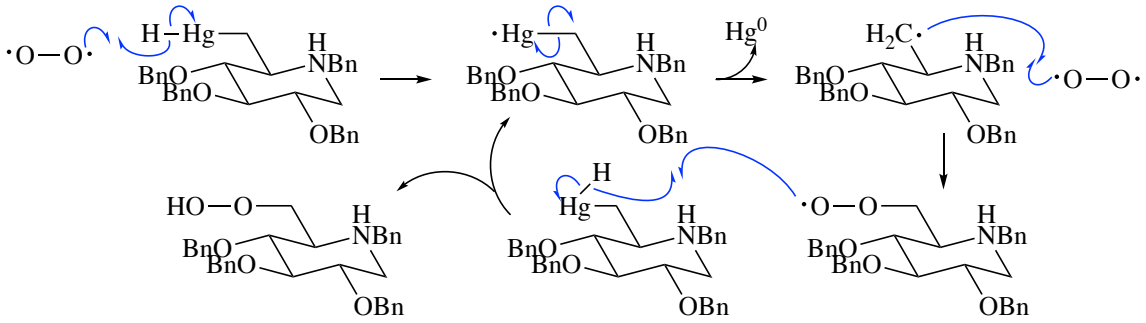
(h) Hg(II) salts coordinate to alkenes and make them more electrophilic. In this case, the N can attack the alkene–Hg complex, giving an alkylmercury intermediate.



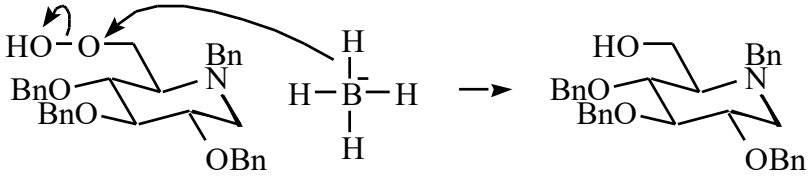
The $NaBH_4$ replaces the Hg–O_2CCF_3 bond with a Hg–H bond.



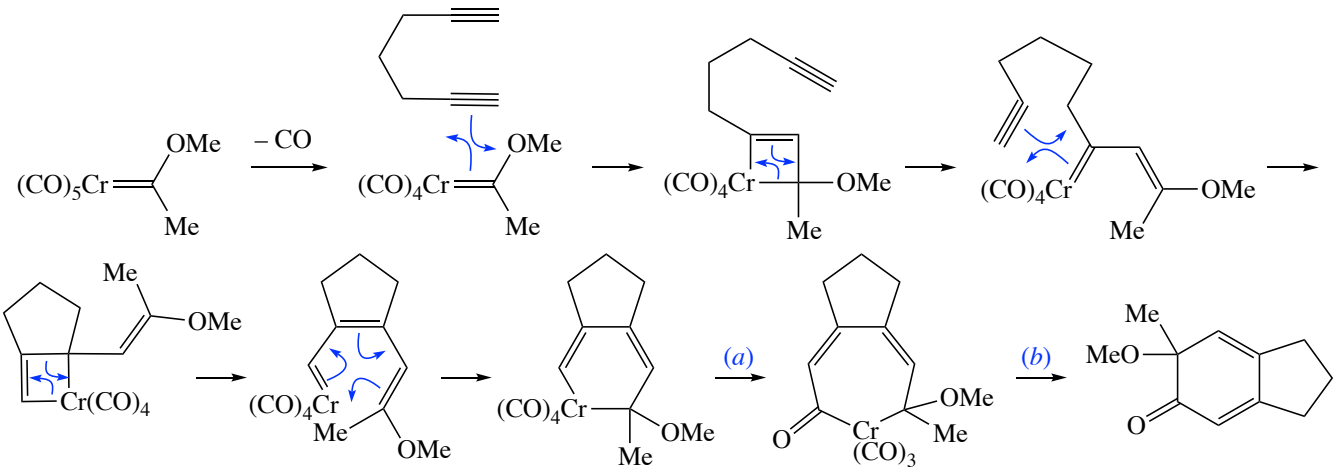
Free-radical decomposition of the alkylmercury hydride then occurs to replace the C–Hg bond with a C–O bond, with the O coming from O_2. The free-radical reaction gives a hydroperoxide C–OOH.



Finally, the hydroperoxide is reduced to the alcohol C–OH by excess $NaBH_4$.

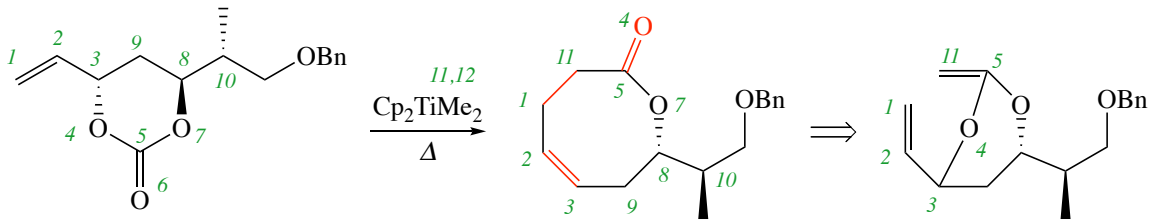


(i) Several reasonable mechanisms can be drawn for this reaction. One begins with loss of CO to make a more reactive 16-electron complex. The Cr=C π bond then undergoes [2 + 2] cycloaddition with an alkyne to give a chromacyclobutene, which can undergo four-electron electrocyclic ring opening to give a 1-chroma-1,3-butadiene. Another [2 + 2] cycloaddition, this time with the pendant alkyne, gives a new chromacyclobutene, and another four-electron electrocyclic ring opening occurs to give a 1-chroma-1,3,5-hexatriene. This compound undergoes six-electron electrocyclic ring closing to give a chromacyclohexadiene, and migratory insertion of a CO ligand from Cr into one of the Cr–C bonds is followed by reductive elimination to give the observed product.

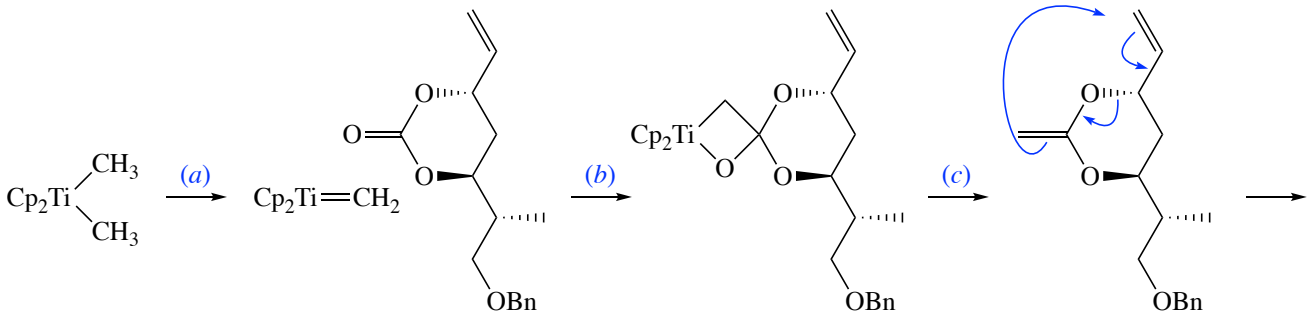


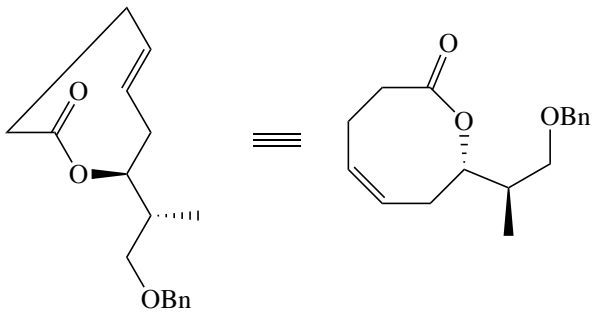
(*a*) migratory insertion; (*b*) reductive elimination.

(j) Make: C1–C11, C5–C11. Break: C3–O4, C5–O6. The product is a *γ,δ*-unsaturated carbonyl compound, also a 1,5-diene, with the new bond C1–C11 in the 3 and 4 positions of the 1,5-diene. This information hints that the product might be the product of a [3, 3] sigmatropic (Claisen) rearrangement. Working backwards from the product gives the intermediate shown, which differs from the starting material only in having C11 in place of O6. The role of the Cp_2TiMe_2 is to convert the C5=O6 π bond into a C5=C11 π bond.



α-Elimination of CH_4 from Cp_2TiMe_2 gives $Cp_2Ti{=}CH_2$, which undergoes [2 + 2] cycloaddition with the carbonate C=O π bond followed by [2 + 2] retrocycloaddition to give the alkene. A Claisen rearrangement follows to give the observed product.





(*a*) α-elimination;
(*b*) [2 + 2] cycloaddition;
(*c*) [2 + 2] retrocycloaddition.

4. Oxidative addition of Pd(0) to a *cis*-dihaloethylene gives an intermediate that can undergo β-halide elimination. The C–Br or C–I bond is more prone to undergo β-elimination than the much stronger C–Cl bond. The transmetallation and reductive elimination steps of the Sonogashira coupling have more time to occur when a C–Cl bond is β to Pd than when a C–Br or C–I bond is β to Pd.