Molecular Gymnastics of Alkynes Orchestrated by Ruthenium Complexes

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Received May 15, 1996

Key Words: Vinylidene complexes / Allenylidene complexes / Ene type reactions / Atom economial reactions / Reconstitutive additions

Ruthenium complexes catalyze a variety of addition or isomerization reactions that are highly atom economical. Terminal alkynes react with allyl alcohols to form β,γ-unsaturated ketones that can be readily isomerized to α,β-unsaturated ketones via transient vinylidene complexes. A cyclization via a transient allenylidene complex concomitant with this addition represents a novel way to build heterocycles. Ancillary studies with these catalysts revealed an internal oxidation reduction whereby allyl alcohols are isomerized to saturated ketones and propargyl alcohols are isomerized to α,β-unsaturated carbonyl compounds. Consideration of the reaction mechanism led to a general Alder ene type reaction wherein alkynes serve as the enophile and alkenes serve as the ene component. These discoveries have led to a number of efficient total syntheses of biologically interesting targets. Mechanistic investigations into the activation of a ruthenium complex led to the discovery of a novel bis-homo-Diels-Alder reaction of 1,4-cyclooctadiene.

A major goal for synthetic chemistry is efficiency. In considering the nature of this issue, two main themes emerge: selectivity[1] and atom economy[2]. Almost all attention has focused on issues of selectivity without too much concern about the question, "How much of what you put into the pot ends up in the product"? For reasons of both maximal

Barry Trost was born in Philadelphia, Pennsylvania in 1941 where he began his university training at the University of Pennsylvania (BA, 1962). He obtained a Ph. D. degree in Chemistry just three years later at the Massachusetts Institute of Technology (1965). He moved directly to the University of Wisconsin where he was promoted to Professor of Chemistry in 1969 and subsequently became the Vilas Research Professor in 1982. He joined the faculty at Standford as Professor of Chemistry in 1987 and became Tamaki Professor of Humanities and Sciences in 1990. In addition, he has been Visiting Professor of Chemistry in Germany (Universities of Marburg, Hamburg and Munich), Denmark (University of Copenhagen), France (Universities of Paris VI and Paris-Sud), Italy (University of Pisa) and Spain (University of Barcelona). In 1994 he was presented with a Docteur honoris causa of the Université Claude-Bernard (Lyon I), France.

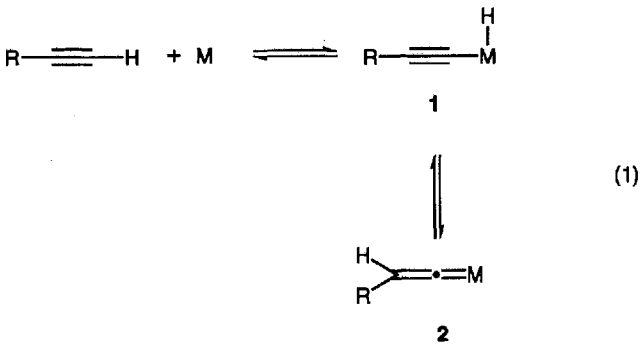
Professor Trost made a major contribution early in his career with the isolation, structure determination, and synthesis of the insect juvenile hormone which initiated the concept of insect growth regulants as an alternative to pesticides. Enhancing synthetic effectiveness has been a major goal. How can the ever increasing complex molecules needed to meet the needs of society in an economical and practical fashion be created? Developing the tools, i.e. the reactions and reagents, that enhance selectivity and impart "atom economy" is the first stage. He has pursued this goal in many ways with a major thrust being the rational design of selective catalysts which may make them the "chemists' enzymes". Inserting sulfur substituents to impart synthetic versatility has created the concept of organosulfones as chemical chameleons – i.e., serving as both nucleophiles and electrophiles depending upon the environment. Coordinating a set of reactions into a sequence that permits the construction of a complex target from readily available starting materials represents the second and final stage. Over one hundred total syntheses of divergent molecules ranging from antitumor agents to electrical conductors have been completed.

In recognition of his many contributions, Professor Trost has received a number of awards, including the ACS Award in Pure Chemistry (1977), the ACS Award for Creative Work in Synthetic Organic Chemistry (1981), the Baekeland Award (1981), the first Allan R. Day Award of the Philadelphia Organic Chemists' Club (1983), the Chemical Pioneer Award of the American Institute of Chemists (1983), the Alexander von Humboldt Stiftung Award (1984), MERIT Award of NIH (1988), Hamilton Award (1988), Arthur C. Cope Scholar Award (1989), Guenther Award in the Chemistry of Essential Oils and Related Products (1990), the Dr. Paul Janssen Prize (1990), the ASSU Graduate Teaching Award (1991), Pfizer Senior Faculty Award (1992), Bing Teaching Award (1993), and the ACS Roger Adams Award (1995). He has held a Sloan Fellowship, a Camille and Henry Dreyfus Teacher-Scholar grant and an American-Swiss Foundation Fellowship as well as having been the Julius Stieglitz Memorial Lecturer of the ACS-Chicago section (1980–81) and Centenary Lecturer of the Royal Society of Chemistry (1981–82). Professor Trost has been elected a Fellow of the American Academy of Sciences (1982) and a member of the National Academy of Sciences (1980). He has served as editor and on the editorial board of many books and journals, including being Associate Editor of the Journal of the American Chemical Society (1974–80). He has served as a member of many panels and scientific delegations, and served as Chairman of the NIH Medicinal Chemistry Study Section. He has held over 60 special university lectureships and presented over 160 lectures at national and international meetings. He has published two books and over 550 scientific articles. He edited a major compendium entitled Comprehensive Organic Synthesis consisting of nine volumes and serves as editor for ChemTracts/Organic Chemistry.

  0009–2940/96/1111–1313 $ 15.00+.25/0

use of raw materials and minimization of production of waste, the ideal reaction is a simple addition, if intermolecular, or an isomerization, if intramolecular, with anything else being required only catalytically. While most of the time, we will not achieve the ideal, we should try to approach it as much as possible. As a result, major opportunities exist to invent new addition reactions, to expand the scope of existing ones, and to develop other reactions that minimize the mass of any stoichiometric by-product.

In considering the utilization of transition metal catalyzed reactions, we became intrigued by the opportunities offered by the general process outlined in eq. 1. In one sense, a low valent metal may be viewed as a base that can remove the relatively acidic terminal alkyne hydrogen to produce **1**. The resultant complex represents the reactive intermediate for numerous carbon-carbon bond forming reactions illustrated by palladium catalyzed cross-coupling[3] and addition reactions[4]. A further equilibration generates a vinylidene complex **2** whose chemistry in catalytic cycles has been extremely sparse[5]. Since it forms so readily directly from the alkyne, we became intrigued with its synthetic potential. Our initial efforts considered palladium because we have been quite successful in a number of useful reactions involving **1**. Our lack of success encourated us to turn our attention to ruthenium because (1) formation of vinylidene complexes is well known and (2) there is a dearth of catalytic carbon-carbon bond forming reactions involving ruthenium in spite of its rich organometallic literature[6,7].

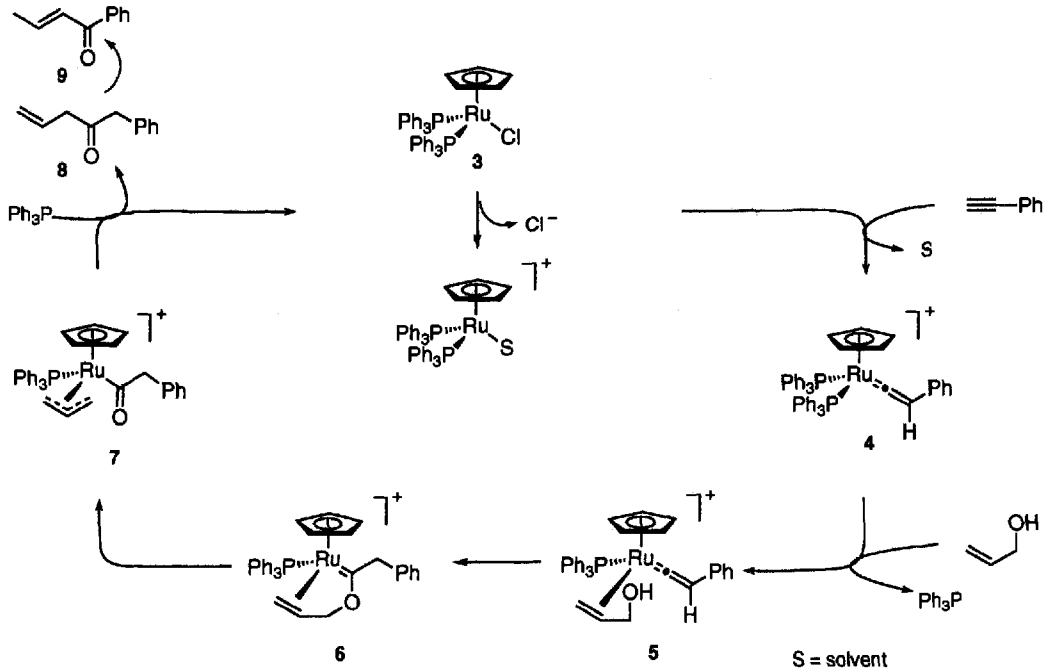


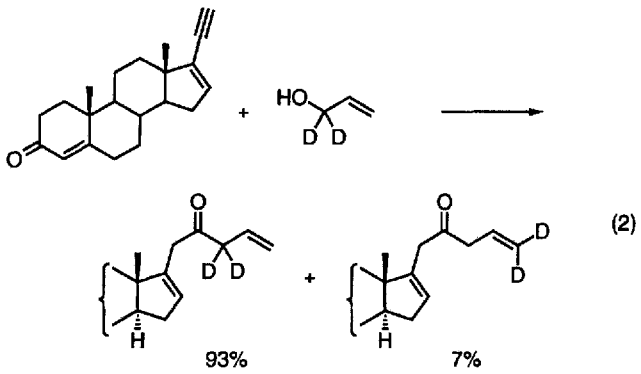
(1)

Reconstitutive Condensation of Alkynes and Allyl Alcohols

Initial attention focused on the known vinylidene complex **4**[8] whose formation derives from reaction of the ruthenium complex **3** and phenylethyne and whose low reactivity towards addition of nucleophiles suggested that precoordination as in **5** may overcome a kinetic barrier that may exist as depicted in Scheme 1. In contrast to its lack of reactivity with saturated alcohols higher than methanol[8b], **4** reacts readily with allyl alcohol to form **8** and its isomer wherein the double bond migrated to form the conjugated product **9**[9]. Transforming this stoichiometric reaction into a catalytic one involved simply heating the terminal alkyne in excess allyl alcohol as solvent with 6% **3** and 10% ammonium hexafluorophosphate. Completing the isomerization of the β,γ-isomer **8** into the α,β-isomer **7** by heating the mixture with catalytic rhodium trichloride in aqueous THF gave the pure enone **9** in 79% isolated overall yield. Mechanistic insight was revealed with two labelling studies as shown in eqs. 2 and 3[10]. The former indicates the carbon bearing the hydroxy group preferentially forms the new C–C bond to the terminal alkyne carbon. The latter indicates alkene geometry is largely retained. These studies support the intervention of a π-allyl species like **7** wherein rotation around the ruthenium-allyl axis is slow relative to the rate of reductive elimination and the absence of σ-allyl intermediates.

Scheme 1. A proposed catalytic cycle involving a vinylidene intermediate





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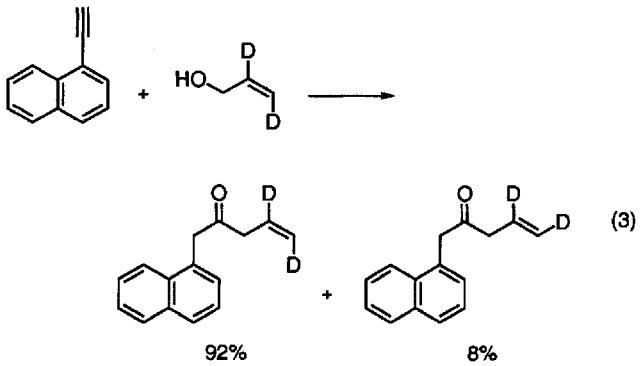
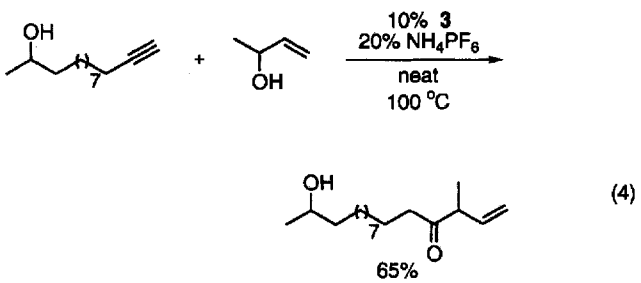


(3)

With a branched allyl alcohol like methallyl alcohol this regioselectivity was maintained (eq. 4). Because the rate of double bond migration is slowed considerably by the presence of the methyl substituent at the α-position, the β,γ-unsaturated ketone was readily isolated without impurities. However, labelling the double bond as in eq. 5 revealed a dramatic difference relative to allyl alcohol since alkene geometry was almost totally scrambled. Apparently, placing an alkyl group on the π-allyl carbon that participates in the new C–C bond formation sufficiently slows reductive elimination in the analogous complex to **7** that η^3 to η^1 isomerization now competes[11].



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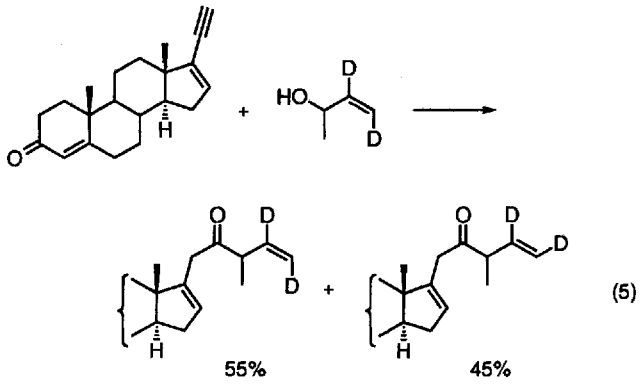
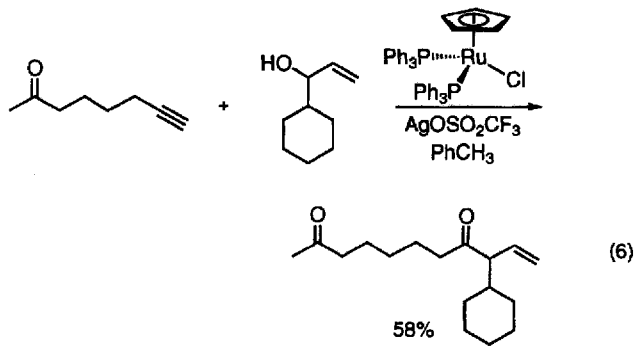


(5)

Although substituents on the double bond are not tolerated, substituents on the carbinol carbon may be quite large. For example 1-cyclohexyl-2-propenol participated in this reconstitutive addition as shown in eq. 6[12]. While this reaction does proceed with ruthenium complex **3** alone as the pre-catalyst, addition of silver triflate permits reaction to occur in toluene with as little as a 1:5 ratio of terminal alkyne to allyl alcohol.

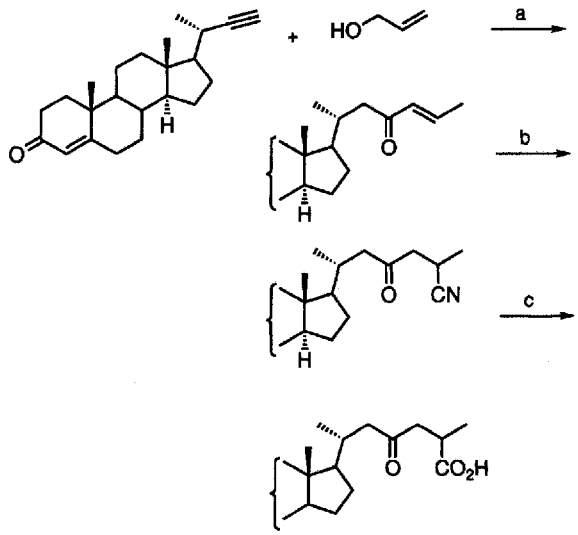


(6)

Synthetically, this reaction exhibits extraordinary chemoselectivity in which acetals, esters, saturated and conjugated ketones, internal alkynes, alcohols etc. are tolerated. On the other hand, it is highly sensitive to steric interactions, tolerating no substituents on the double bond.

Easy access to α,β-unsaturated ketones, when employing allyl alcohol itself as the reaction partner, permitted creation of an entry to the steroid side chain of the gonaderic acids, novel ACE inhibitors[13], as shown in Scheme 2[14]. In this case, the ruthenium catalyst was employed as catalyst for both the reconstitutive addition and the double bond isomerization. Access to β,γ-unsaturated ketones with

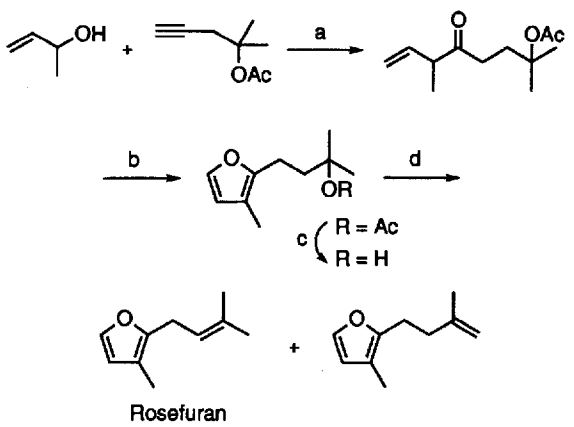
Scheme 2. Access to a steroid side chain



(a) 10% **3**, 20% NH_4PF_6, 100 °C, 68%. (b) LiCN, DMF, THF, r.t., 58%. (c) conc. HCl, 100 °C, 69%.

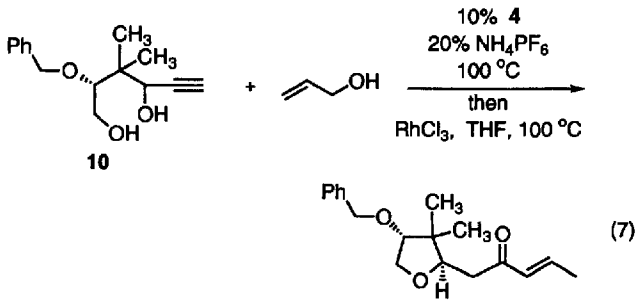
the α-substituted allyl alcohols led to development of a facile furan synthesis exemplified by a practical synthesis of the fragrance rosefuran[15] shown in Scheme 3[16]. The formation of furans follows from the ease of cyclodehydration of the diol resulting from dihydroxylation[17] of the β,γ-double bond.

Scheme 3. A practical synthesis of rosefuran



(a) 10% **3**, 20% NH_4PF_6, 100 °C, 69%. (b) cat. OsO_4, NMO, THF, t-C_4H_9OH, H_2O, r.t., then TsOH, r.t., 83%. (c) LiOH, H_2O, CH_3OH, r.t., 88%. (d) DMSO, 160 °C, 54% rosefuran, 13% isorosefuran.

Progargyl alcohols bearing a terminal alkyne represent a special class of substrates since the initial ruthenium acetylide intermediate may effect ionization of the hydroxyl group[5,18] rather than protonation of the alkyne as depicted in Scheme 4. Indeed, this behavior dominated in the reaction of the diol **10** with allyl alcohol as shown in eq. 7[19]. If the capture of the allenylidene complex **11** (Scheme 4) by the nucleophile is slow, then isomerization to a vinylvinylidene complex may compete. A substrate lacking substituents that favor cyclization as in the case of diol **12** (eq. 8), illustrates this competition. The product of tandem allenylidene cyclization-reconstitutive addition **13** and allenylidene isomerization-reconstitutive addition **14** are obtained in a nearly equimolar mixture in 69% yield.



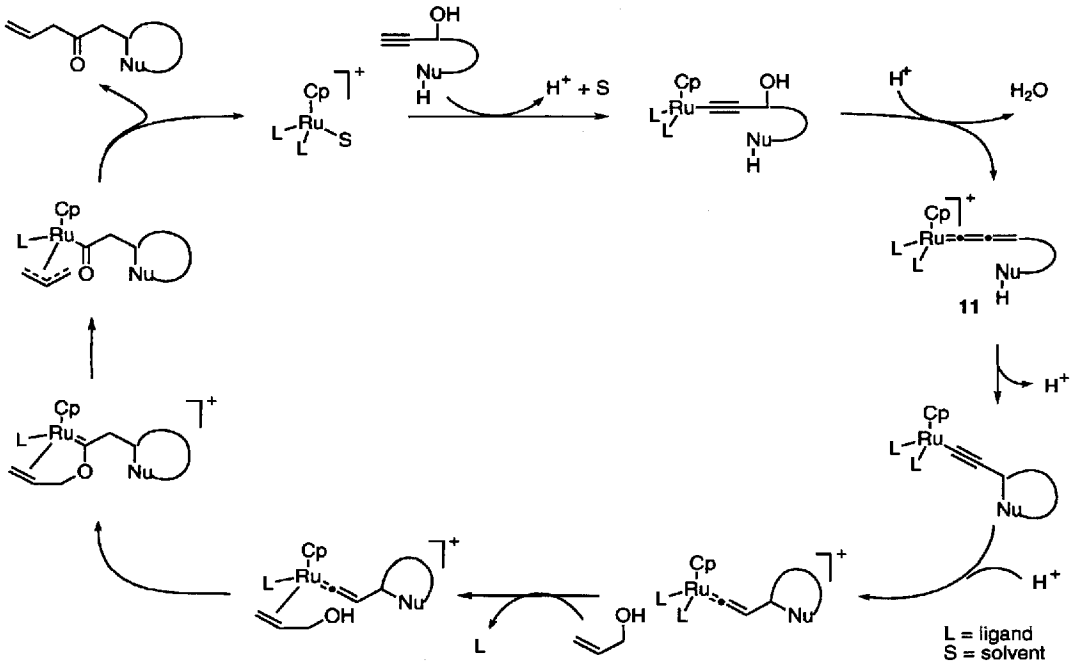
(7)

This atom-economical process, wherein the only stoichiometric by-product is water, served as a key to a strategy for the synthesis of the spiroketal core of the phosphatase inhibitor (−)-calyculin[20] (see Scheme 5)[21]. Formation of the substrate **15** occurred with no control of stereochemistry at the propargylic center. However, ruthenium catalyzed cyclization-reconstitutive addition formed a single diastereomer with respect to the tetrahydrofuran ring. Thus, the stereochemistry of the propargylic stereocenter of **15** was irrelevant to the stereochemical course of the reaction – an observation quite consistent with the proposed mechanism. Indeed, the examples of eq. 7 and Scheme 5 reveal the excellent diastereoselectivity of this reaction.

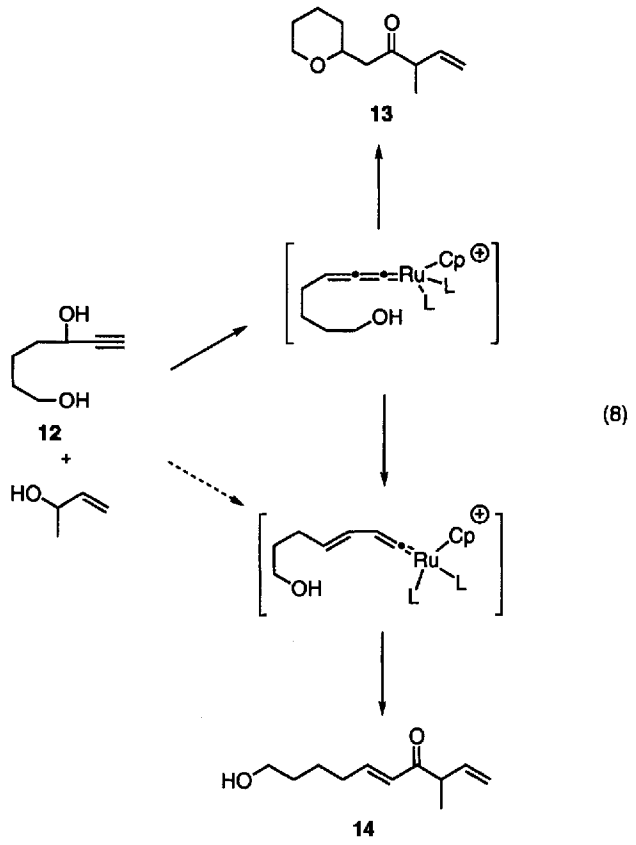
A Control Experiment

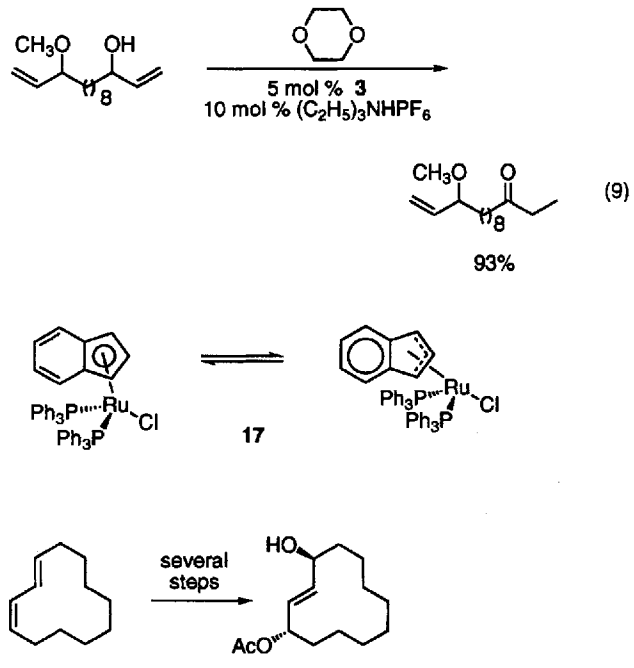
In the above reactions, an excess of allyl alcohol is required for completion of the reaction. Simply treating an

Scheme 4. A tandem process involving allenylidene-vinylidene ruthenium intermediates

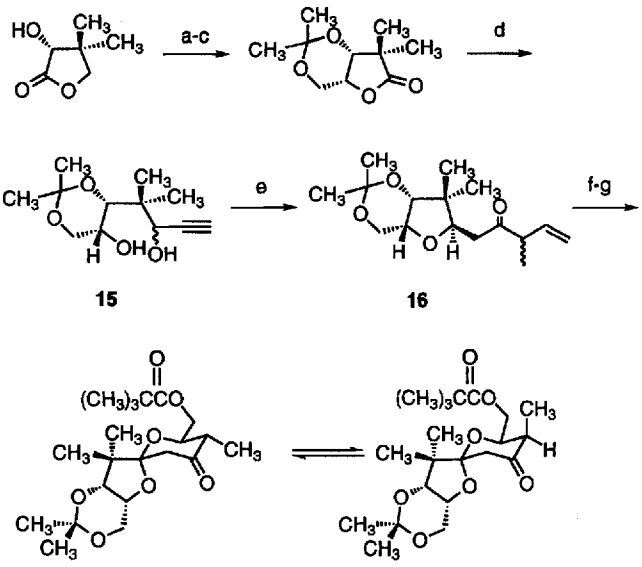


allyl alcohol with the ruthenium complex **3** in dioxane under similar conditions led to smooth and highly chemoselective isomerization of an allyl alcohol without affecting other alkenes as illustrated in eq. 9[22] – a type of chemoselectivity not normally observed with other catalysts capable of effecting a similar reaction[23]. Extending this reaction to allyl alcohols bearing substituents on the double bond requires use of the indenyl complex **17**[24]. The tautomerization depicted opens a valence thereby allowing the ruthenium to accept a sterically more congested substrate as illustrated in eq. 10.

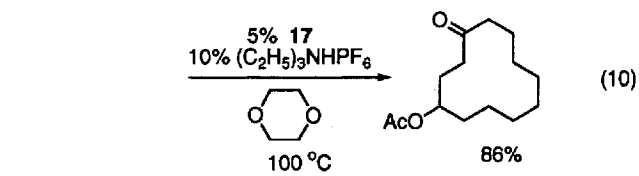




Scheme 5. Synthesis of (−)-calyculin spiroketal



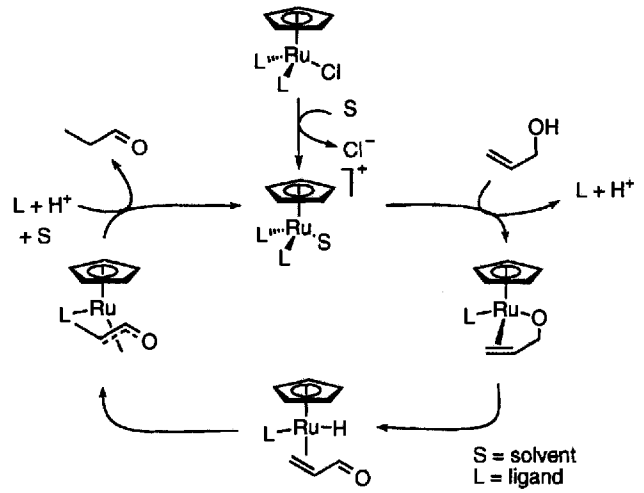
(a) DIBAL-H, CH_2Cl_2, −78 °C; CH_2=CHMgBr, THF, 0 °C; CH_3COCH_3, TsOH, r.t., 72%. (b) PDC, DMF, r.t.; CF_3CO_2H, r.t., 68%. (c) O_3, CH_2Cl_2, CH_3OH, −78 °C add $NaBH_4$ then CH_3COCH_3, TsOH, 90%. (d) DIBAL-H,CH_2Cl_2, −78 °C then LiC≡CH, THF, −78 °C, 92%. (e) 10% **4**, 20% NH_4PF_6, CH_2=CHCH(OH)CH_3, 100 °C, 66%. (f) DHQD-PHN, $K_3Fe(CN)_6$, K_2CO_3, *t*-C_4H_9OH, H_2O, 0 °C then *N*-pivaloylthiazolidin-2-thione, $PhCH_3$, reflux, 84%. (g) HgO, I_2, CCl_4, 70 °C, 67%.

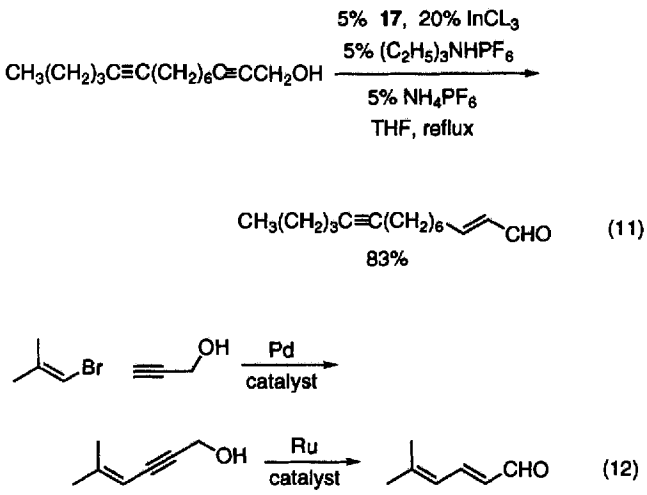


The selectivity stems from the mechanism as outlined in Scheme 6. Deuterium labeling studies support the intramolecular delivery of the proton adjacent to oxygen of the allyl alcohol to the allyl terminus as depicted. The ability of the allyl alcohol to function as the bidentate ligand depicted accounts for the requirement of a free allylic alcohol as a substrate.

Application of this reaction to a propargyl alcohol in order to form enals or enones proceeded poorly with indenyl complex **17** as did attempts to employ tris(triphenylphosphine) ruthenium dichloride[25]. On the other hand, addition of catalytic quantities of indium trichloride served to greatly facilitate reaction. An effective catalyst system consists of 5 mol% of indenyl complex **17**, 20 mol% of indium chloride, 5 mol% of triethylammonium hexafluorophosphate and 5 mol% of ammonium hexafluorophosphate[26]. As shown in eq. 11, a highly chemoselective redox isomerization resulted. Once again, isolated double and triple bonds are not affected by this catalyst.

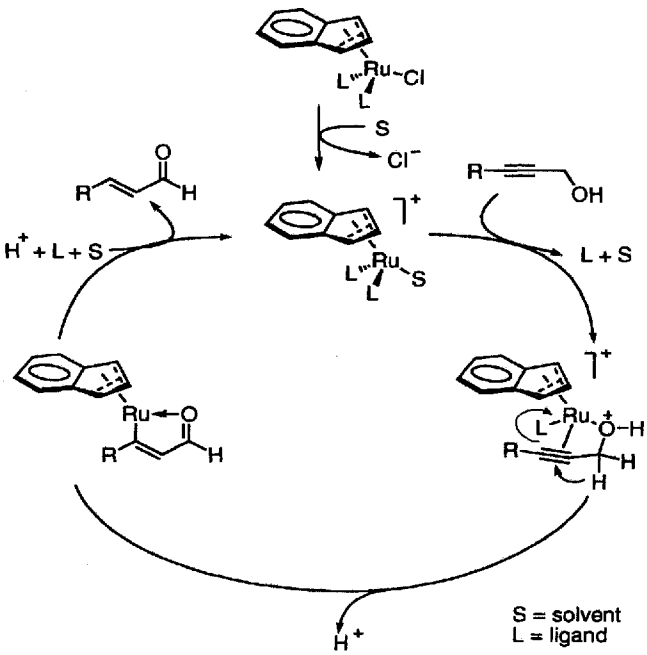
Scheme 6. A rationale for redox isomerization of allyl alcohols





Deuterium labelling studies provided insight into this mechanism and revealed that a quite different pathway was involved (see Scheme 7). In particular, the propargylic proton ends up on the adjacent alkynyl carbon via a 1,2-shift[27] to form a vinylruthenium complex which undergoes protonation at the distal alkyne carbon to liberate the enal. The synthetic utility of this sequence is illustrated by the sequential palladium catalyzed crosscoupling[3] – ruthenium catalyzed redox isomerization illustrated in eq. 12, the latter proceeding in 67% isolated yield. The ability to form such sensitive products in this ruthenium catalyzed reaction attests to the mildness of the reaction conditions.

Scheme 7. A rationale for redox isomerization of progargyl alcohols



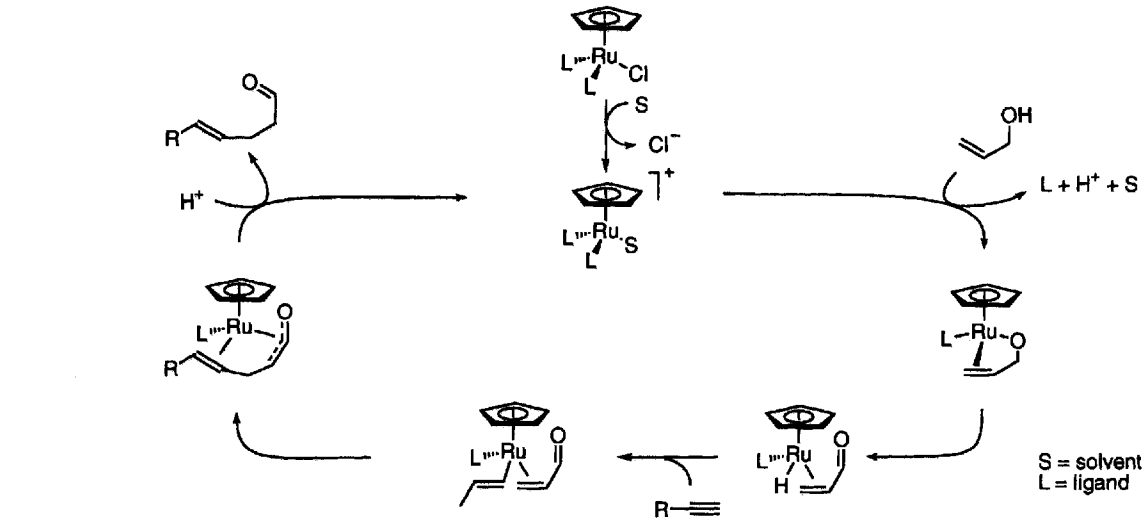
A Proposed Ene Type Reaction

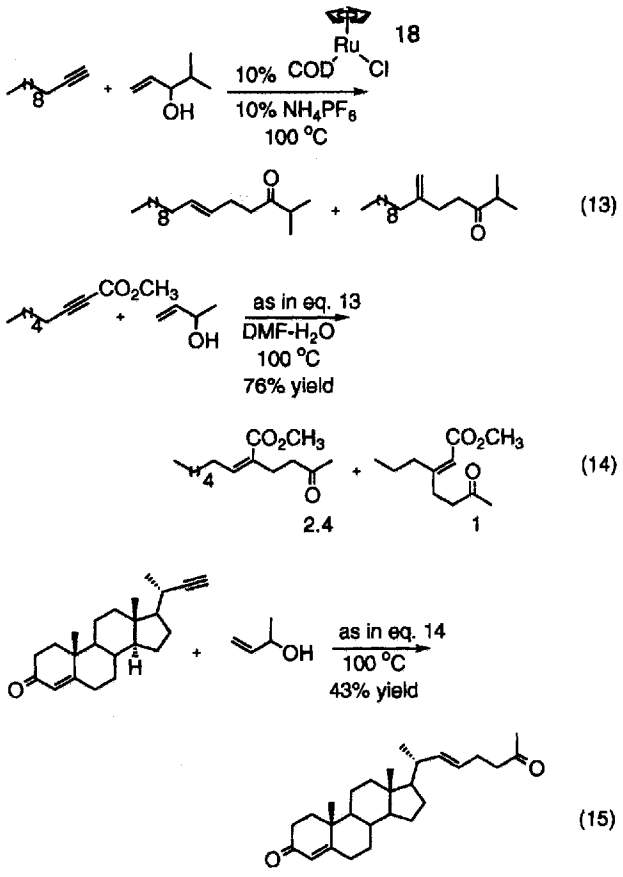
The intervention of an enone ruthenium hydride complex in the redox isomerization of allyl alcohols (Scheme 6) suggested a catalytic cycle as illustrated in Scheme 8. Capture of the ruthenium hydride by an external alkyne may provide a vinylruthenium complex that sets the stage for its conjugate addition. The net result becomes a synthesis of γ,δ-unsaturated ketones by the addition of allyl alcohols to alkynes. Since capture by the alkyne may require an open coordination site on the ruthenium (i.e., loss of the second L), the ruthenium complex **18**[28], which allows opening up to three coordination sites, was employed[29]. Heating a neat mixture of the allyl alcohol shown in eq. 13 and 1-dodecyne at 100°C with the ruthenium complex **18** gave a 73% yield of a nearly 1:1 mixture of a linear and branched product corresponding to the two regioisomeric hydrometallations of the alkyne[30]. Performing the reaction in DMF-water enhances the regioselectivity to favor the linear product. The regioselectivity of the reaction of methyl 2-nonynoate wherein the major product involves formation of the new C–C bond at the carbon α to the ester (eq. 14) seemed to support the proposed mechanism as did the absence of any homocoupling products. Steric hindrance also effects the regioselectivity of the addition to the alkyne. The steroid substrate of eq. 15 formed the linear product as the major one.

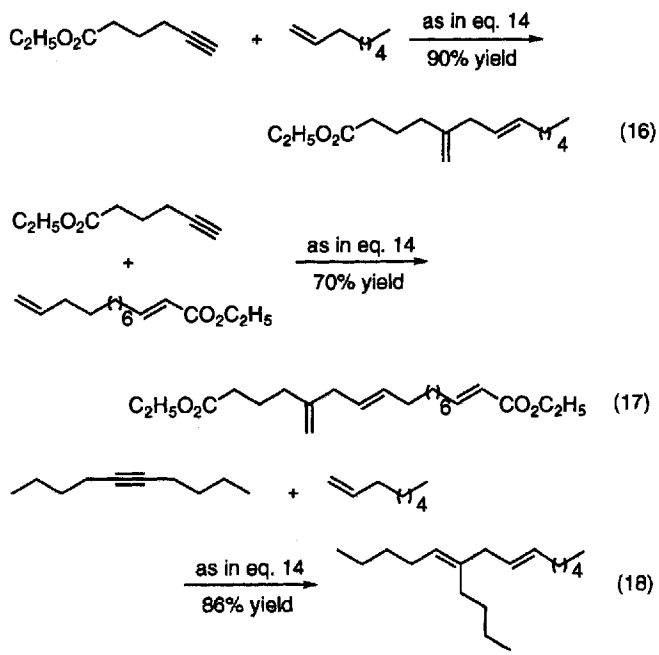
A General Ene Reaction

The mechanism of Scheme 8 invokes a special role for allyl alcohols as the ene component. If this proposal is correct, a simple alkene should not serve as the ene component. In contradistinction to this prediction, a simple alkene suffices as revealed by the example in eq. 16 in which a preference for formation of the branched product exists (5.6:1 branched to linear)[31]. Excellent chemoselectivity for reaction of terminal alkynes is observed in that even an an activated alkene failed to react (eq. 17). On the other hand, disubstituted alkynes are readily tolerated as illustrated in eq. 18.

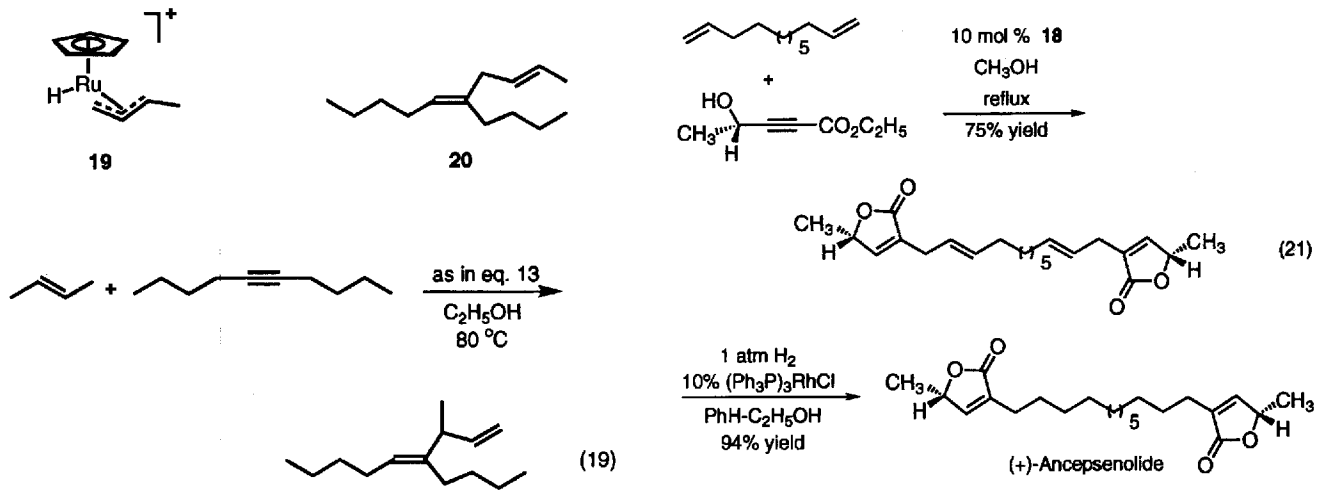
Scheme 8. A proposed ene type reaction



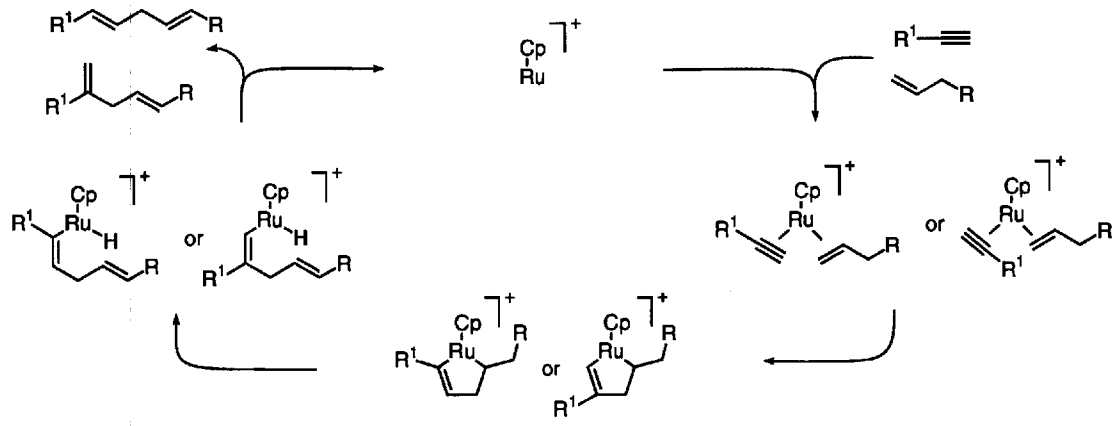




These reactions refuted the importance of an allyl alcohol as a substrate. One possible explanation consonant with Scheme 8 was the involvement of a simple η^3-allylruthenium hydride as in **19** which would function in a fashion similar to the corresponding enone complex of Scheme 8. If such was the case, use of a 2-alkene should give the same product(s) as a 1-alkene to the extent that the same monosubstituted η^3-allylruthenium species was involved. To minimize complexity, 2-butene was employed. A single regioisomeric product formed which involved clean allyl transposition (eq. 19)[32]. If an η^3-allyl complex were involved, then the same product that is obtained from a 1-alkene, namely **20**, would have been observed and was not. This observation invalidates Scheme 8 or a simple variation thereof, at least for the more general case. A metallacycle mechanism[33] as outlined in Scheme 9 is in accord with all current information. Considering such a mechanism, the absence of homocoupling products, especially of the alkyne partners, appears peculiar at first glance. Keeping in mind the intrinsically higher reactivity of alkynes compared to alkanes, the absence of a low energy reaction pathway for a ruthenacyclopentadiene to traverse may lead to its formation being reversible and account for the lack of alkyne homocoupling. On the other hand, the β-hydrogen elimination provides a ready path for reaction of a ruthenacyclopentene, thereby leading to the cross-coupling of an alkene and an alkyne to dominate.



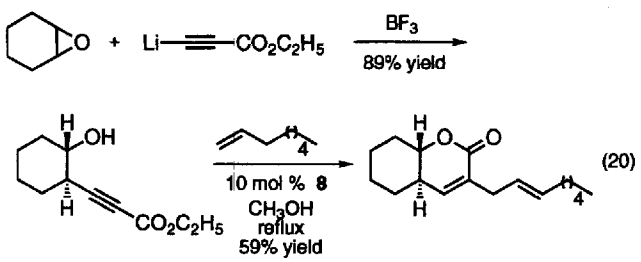
Scheme 9. Ruthenacycle mechanism of ene-yne addition



A Lactone Synthesis

Using a hydroxyalkynoate as an enophile sets the stage for a lactone synthesis. Ready access to δ-hydroxy-α-β-alkynoates by epoxide ring opening created a facile pentenolide synthesis (eq. 20)[34]. Interestingly, an excellent selectivity exists for formation of the new C–C bond at the carbon α to the carbonyl group – a type of behavior that is opposite that normally seen for alkynoates and especially in an Alder ene reaction.

Employing a γ-hydroxyalkynoate provides direct access to 2-substituted butenolides (eq. 21)[34,35]. In this example, the annulation occurs twice to form the simple acetogenin (+)-ancepsenolide. The lack of any racemization at the easily racemizable butenolide carbon attest to the mildness of the conditions. The chemoselectivity is clearly demonstrated by the annulations of eqs. 22 and 23 wherein internal alkenes,



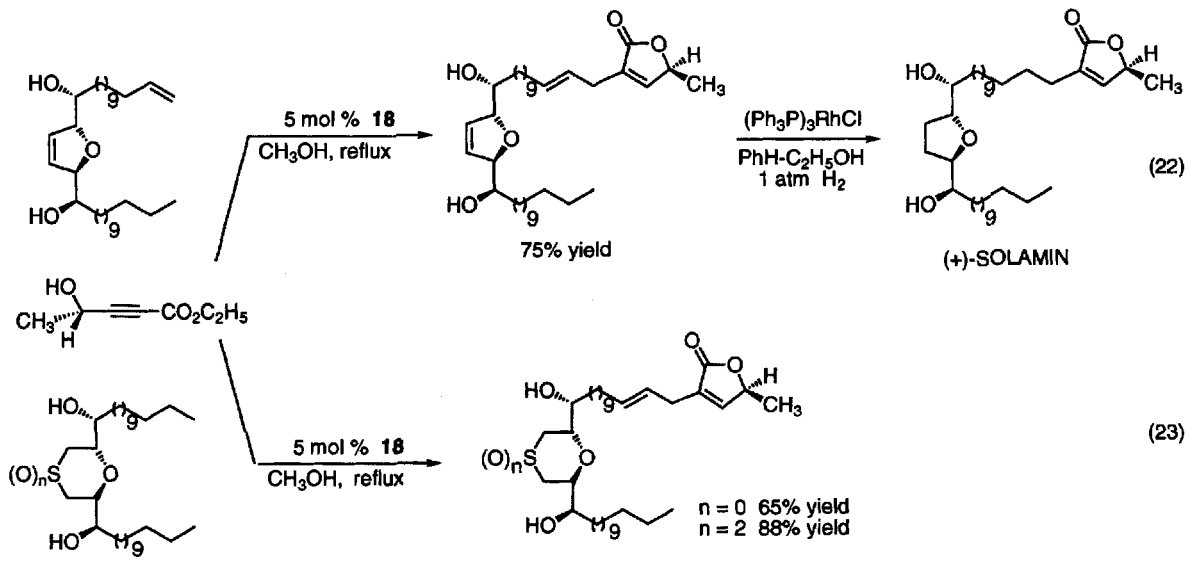
free alcohols, divalent sulfur, and β-alkoxysulfones were all compatible[36]. The former served as the end game of a very simple synthesis of the important acetogenin (+)-solamin.

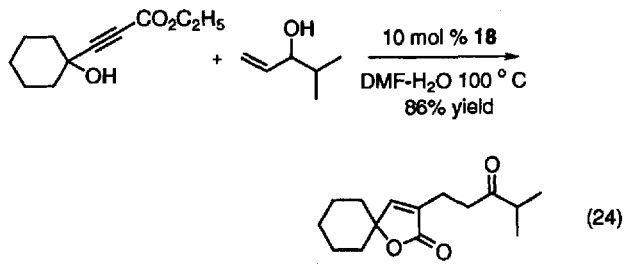
Allyl alcohols participate equally well in this lactone synthesis (eq. 24)[34]. Since the initial product of the ene process is an enol, tautomerization leads to formation of the ketone.

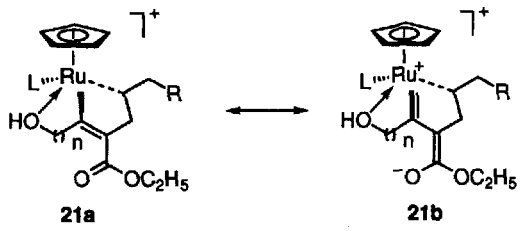
The regioselectivity may derive from stabilizing interactions in the ruthenacycle **21** compared to the alternative **22**. The internal coordination of the hydroxyl group may be enhanced by the delocalization represented by resonance structure **21b**. Furthermore, complex **22** may be destabilized by a non-bonded interaction of the ester with the remaining ligand. This contra-electronic addition of an alkene to an alkynoate constitutes a chemo-, regio-, and diastereoselective addition as well as being highly atom economical.

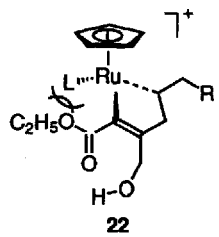
Discovery of a [2 + 2 + 2] Cycloaddition

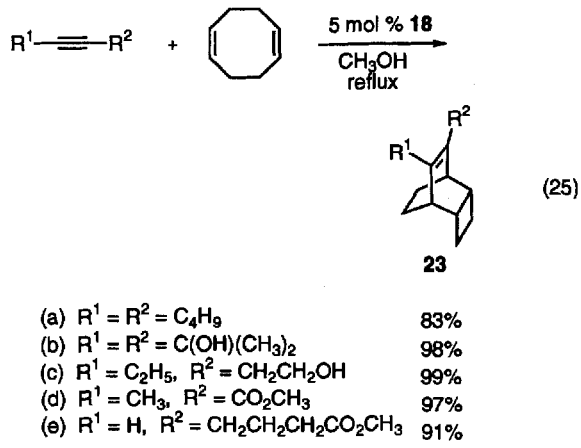
In the above reactions utilizing the COD (COD ≡ 1,5-cyclooctadiene) complex of ruthenium **18**, a very minor product invarient with alkene is always detected. The amount corresponds to the amount of catalyst. Concluding that a reaction occurs involving the catalyst precursor and the alkyne, a mixture of 5-decyne and a twofold excess of COD in methanol was heated in the presence of 5 mol% **18**. An 83% distilled yield of the adduct **23a** is obtained



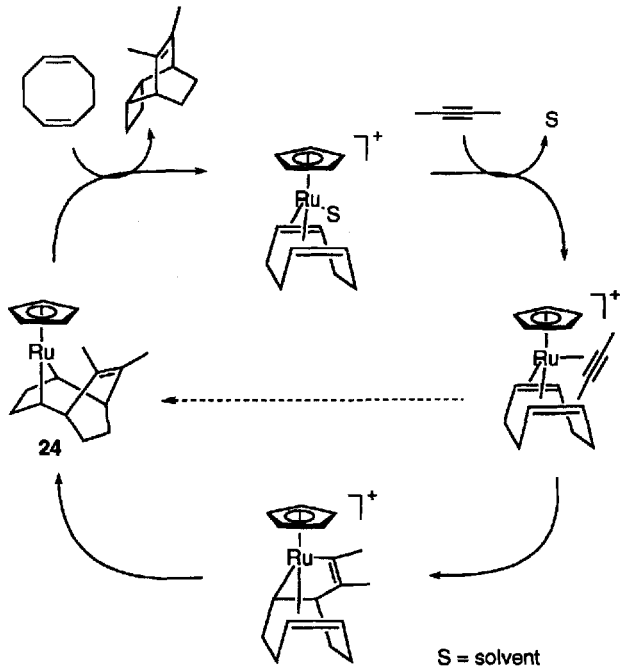








Scheme 10. A rationale for a Ru-catalyzed bis-homo-Diels-Alder reaction



(eq. 25) in what proves to be a very general process for both internal and terminal alkynes[29]. The novel bis-homo-Diels-Alder reaction is a highly atom economical approach to polycycles. Consider formation of the adduct **23b**. The starting alkyne stems from the simple addition of acetylene to acetone. The COD stems from the nickel catalyzed dimerization of 1,3-butadiene. Thus, the cycloadduct **23b** derived from just a series of metal catalyzed additions of one equivalent of acetylene, two equivalents of acetone, and two equivalents of 1,3-butadiene.

Scheme 10 represents a reasonable rationale for this unusual metal catalyzed Diels-Alder type reaction with a bis-homodiene. The importance of a cationic ruthenium species

was supported by the requirement for a polar solvent such as methanol or aqueous DMF. In a nonpolar solvent like 1,2-dichloroethane, no reaction occurred at 70°C. However, addition of silver triflate to this latter system to abstract chloride effected smooth cycloaddition. Using a COD rhodium complex, hexafluoro-2-butyne formed a metallacycle analogous to **24**, providing further support for the mechanism[37]. The uniqueness of the COD system is revealed by the absence of any cycloaddition by either inserting an additional carbon in one chain (i.e., 1,5-cyclononadiene) or taking one out (i.e., a 1,4-cycloheptadiene).

Conclusion

The special coordination properties of alkynes to metals make them excellent substrates for metal catalyzed processes. Insertion into the acetylenic C–H of a terminal alkyne provides a wealth of opportunity for numerous transformations, some of which involve novel intermediates like vinylidene and allenylidene complexes. The π-system constitutes an energy rich system to promote addition reactions. The result of such behavior is the ability to effect simple additions or, at most, loss of small harmless molecules like water. The ability to tune ruthenium whereby it can orchestrate whatever reaction mode desired represents a true adventure for the development of atom economical reactions.

My heartiest thanks go to my ruthenium team beginning with *Gerald Dyker* and extending to *Robert J. Kulawiec, Adriano Indolese, Katsuhara Imi, John Flygare, Jose A. Martinez, Thomas J. J. Müller, Zhongping Shi*, and *Robert C. Livingston*. We thank the *National Science Foundation* and the *National Institutes of Health, General Medicinal Sciences*, for their generous support of our programs.

[1] B. M. Trost, *Science* **1983**, *229*, 245.
[2] B. M. Trost, *Angew. Chem.* **1995**, *107*, 285; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 259; B. M. Trost, *Science* **1991**, *254*, 1471.
[3] For a leading reference, see: M. Alami, F. Ferri, G. Linstrumelle, *Tetrahedron Lett.* **1993**, *34*, 6403.
[4] B. M. Trost, C. Chan, G. Rühter, *J. Am. Chem. Soc.* **1987**, *109*, 3486; B. M. Trost, S. Matsubara, J. Caringi, *J. Am. Chem. Soc.* **1989**, *111*, 8745; B. M. Trost, M. McIntosh, *J. Am. Chem. Soc.* **1995**, *117*, 7255; B. M. Trost, G. Kottirsch, *J. Am. Chem. Soc.* **1990**, *112*, 2816.
[5] M. I. Bruce, *Chem. Rev.* **1991**, *91*, 197; M. I. Bruce, G. A. Swincer, *Adv. Organomet. Chem.* **1983**, *22*, 59; W. A. Nugent, J. M. Mayer in *Metal-Ligand Multiple Bonds*, Wiley & Sons, New York, **1988**.
[6] [6a] S. G. Davies, J. P. McNally, A. J. Smallridge, *Adv. Organomet. Chem.* **1990**, *30*, 1. – [6b] H. Le Bozec, D. Touchand, P. H. Dixneuf, *Adv. Organomet. Chem.* **1989**, *29*, 163.
[7] For some examples, see: G. Albertin, S. Antoniutti, E. Bordignon, F. Cazzaro, S. Ianelli, G. Pelizzi, *Organometallics* **1995**, *14*, 4114; Y. Wakatsuki, N. Koga, H. Yamazaki, K. Morokuma, *J. Am. Chem. Soc.* **1994**, *116*, 8105; R. LeLagadec, E. Roman, L. Toupet, U. Müller, P. H. Dixneuf, *Organometallics* **1994**, *13*, 5030; R. Maché, Y. Sasaki, C. Bruneau, P. H. Dixneuf, *J. Org. Chem.* **1989**, *54*, 1518 and earlier references; G. P. Chiusoli, G. Salerno, W. Girioldini, L. Pallini, *J. Organomet. Chem.* **1981**, *219*, C16.
[8] [8a] M. I. Bruce, F. J. Wong, B. W. Skeleton, A. H. White, *J. Chem. Soc. Dalton Trans.* **1982**, 2203. – [8b] M. I. Bruce, A. G. Swincer, *Aust. J. Chem.* **1980**, *33*, 1471.
[9] B. M. Trost, G. Dyker, R. J. Kulawiec, *J. Am. Chem.Soc.* **1990**, *112*, 7809.
[10] B. M. Trost, R. J. Kulawiec, *J. Am. Chem. Soc.* **1992**, *114*, 5579.
[11] Cf. T. Kondo, T. Mukai, Y. Watanabe, *J. Org. Chem.* **1991**, *56*, 487; Y. Tsuji, T. Mukai, T. Kondo, Y. Watanabe, *J. Organomet. Chem.* **1989**, *369*, C51.
[12] B. Treptow, unpublished work in these laboratories.
[13] A. Morigiwa, K. Kitabatake, Y. Fujimoto, N. Ikekawa, *Chem. Pharm. Bull.* **1986**, *34*, 3025.
[14] B. M. Trost, R. J. Kulawiec, A. Hammes, *Tetrahedron Lett.* **1993**, *34*, 587.
[15] E. Guenther in *The Essential Oils*, D. Van Nostrand Inc., New York, **1949**, Vol. 5, p. 1.
[16] B. M. Trost, J. A. Flygare, *J. Org. Chem.* **1994**, *59*, 1078.
[17] V. Van Rheenan, R. C. Kelley, D. Y. Cha, *Tetrahedron Lett.* **1976**, *23*, 1973.
[18] A. Wolinska, D. Touchard, P. H. Dixneuf, A. Romero, *J. Organomet. Chem.* **1991**, *420*, 217 and earlier references; J. P. Selegue, B. A. Young, S. L. Logan, *Organometallics* **1991**, *10*, 1972; D. Touchard, N. Pirio, P. H. Dixneuf, *Organometallics* **1995**, *14*, 4920; H. Werner, A. Stark, P. Steinert, C. Grünwald, J. Wolf, *Chem. Ber.* **1995**, *128*, 49.
[19] B. M. Trost, J. A. Flygare, *J. Am. Chem. Soc.* **1992**, *114*, 5476.
[20] S. Matsunaga, N. Fusetani, *Tetrahedron Lett.* **1991**, *32*, 5605. For a total synthesis, see: D. A. Evans, J. R. Gage, J. L. Leighton, *J. Am. Chem. Soc.* **1992**, *114*, 9434.
[21] B. M. Trost, J. A. Flygare, *Tetrahedron Lett.* **1994**, *35*, 4059.
[22] B. M. Trost, R. J. Kulawiec, *J. Am. Chem. Soc.* **1993**, *115*, 2027.
[23] For a few examples, see: J. E. Bäckvall, V. Andreasson, *Tetrahedron Lett.* **1993**, *34*, 5459; Y. Lin, X. Zhu, Y. Zhou, *J. Organomet. Chem.* **1992**, *429*, 269; T. Karlen, A. Ludi, *Helv. Chim. Acta* **1992**, *75*, 1604; D. V. McGrath, R. H. Grubbs, J. W. Ziller, *J. Am. Chem. Soc.* **1991**, *113*, 958; N. Iranpoor, E. Mottaghinejad, *J. Organomet. Chem.* **1992**, *423*, 399; C. Quian, D. Zhu, D. Li, *J. Organomet. Chem.* **1992**, *430*, 175; M. Sodeoka, H. Yamada, M. Shibasaki, *J. Am. Chem. Soc.* **1990**, *112*, 4906. However, see: Y. Lin, X. Lu, *J. Organomet. Chem.* **1983**, *251*, 321.
[24] L. A. Oro, M. A. Ciriano, M. Campo, C. Foces-Foces, F. H. Cano, *J. Organomet. Chem.* **1985**, *289*, 117. Also see: T. B. Marder, D. C. Roe, D. Milstein, *Organometallics* **1988**, *7*, 1451.
[25] D. Ma, X. Lu, *J. Chem. Soc. Chem. Commun.* **1989**, 890.
[26] B. M. Trost, R. C. Livingston, *J. Am. Chem. Soc.* **1995**, *117*, 9586.
[27] For a 1,2-aryl shift, see: D. Pilette, S. Moreau, H. Le Bozec, P. H. Dixneuf, J. F. Corrigan, A. J. Carty, *J. Chem. Soc. Chem. Commun.* **1994**, 409.
[28] M. O. Albers, D. J. Robinson, A. Shaver, E. Singleton, *Organometallics* **1986**, *5*, 2199.
[29] B. M. Trost, K. Imi, A. Indolese, *J. Am. Chem. Soc.* **1993**, *115*, 8831.
[30] B. M. Trost, J. A. Martinez, R. J. Kulawiec, *J. Am. Chem. Soc.* **1993**, *115*, 10402. Also see: S. Dérien, P. H. Dixneuf, *Chem. Commun.* **1994**, 2551.
[31] B. M. Trost, A. Indolese, *J. Am. Chem. Soc.* **1993**, *115*, 4361.
[32] B. M. Trost, A. F. Indolese, T. J. J. Müller, B. Treptow, *J. Am. Chem. Soc.* **1995**, *117*, 615.
[33] T. Mistudo, H. Naruse, T. Kondo, Y. Ozaki, Y. Watanabe, *Angew. Chem.* **1994**, *106*, 595; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 580 and earlier references cited therein.
[34] B. M. Trost, T. J. J. Müller, J. Martinez, *J. Am. Chem. Soc.* **1995**, *117*, 1888.
[35] B. M. Trost, T. J. J. Müller, *J. Am. Chem. Soc.* **1994**, *116*, 4985.
[36] B. M. Trost, Z. Shi, *J. Am. Chem. Soc.* **1994**, *116*, 7459.
[37] D. R. Russell, P. A. Tucker, *J. Chem. Soc. Dalton Trans.* **1976**, 841.

[96103]