Synthesis of Heterocyclic and Carbocyclic Compounds via Alkynyl, Allyl, and Propargyl Organometallics of Cyclopentadienyl Iron, Molybdenum, and Tungsten Complexes

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I. Introduction and Scope

Organometallics comprising an unsaturated hydrocarbyl group like an allyl, propargyl, allenyl, vinyl, or alkynyl group are very important reagents in organic synthesis. These organometallics can be classfied into two categories according to the elec-

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tronic properties of metals (1) main group, d^0 and d^{10} metals[1−13] including boranes, silanes, stannanes, titanium, zirconium, and zinc and (2) transition metals such as Mo(II), W(II), Mn(I), and Fe(II) species.[14−18] A common feature in chemical reactivities of these organometallics is that they can react with electrophiles to form carbonium intermediates, leading to carbon−carbon bond formation. There are some distinct features between the two classes of metals in their reactions with electrophiles. The carbonium intermediates generated by main group metal complexes are not isolable in most cases.[1−5] On the other hand, transition metal complexes can form stable carbonium species with participation of d-electrons.[19] Notably, several carbocations stabilized by transition metals such as carbenium or vinylidenium[19] still remain unknown to main group metals.

Despite interesting electronic features of transition metal complexes, synthetic application of organometallics of main group metals are more widespread and attractive to synthetic organic chemists. Considerable progress has been developed on the utilization of complexes of main group metals. The importance of these organometallics can be manifested by the increasing number of review articles.[1−13] Some of them focus on applications of these complexes directed toward total synthesis of natural products.[9−11] Marshall summarized the use of chiral allylic and allenic stannanes for enantiocontrolled synthesis of acyclic polyols and natural oxygenated compounds.[11] Weinreb also published a recent account on the use of imino ene reactions of allenyl silanes for total synthesis of papuamine and haliclonadiamine.[10] Schinzer and Langkopf recently published a review in a more broad scope to application of allyl-, propargyl-, and vinylsilanes to the synthesis of natural products.[9]

In addition to their chemical versatilities, the ease of purification and operation of organometallics of main group metals attract the interest of synthetic organic chemists. In contrast, many transition metal organometallics are rather sensitive to moist air and are often difficult to purify with conventional methods. These drawbacks discourage synthetic chemists to use these reagents. In some cases, reactive organometallics can be generated in situ without isolation. A well-known system is the allyl-, vinyl-, propargyl-, allenyl-, and alkynylchromium(III) species produced from CrX_2 and iodo derivatives. These reactions are now recognized as Nozaki−Hiyama−Kishi (NHK) reaction.[20] Furstner very recently published an account on these reactions. The article also shows numerous examples in which the NHK reaction is the key step in the synthesis of natural products. The Cr(III) center in the NHK reaction is considered to be electron-deficient, and many of the reactions with electrophiles resemble those of main group metals.

The organic chemistry of transition metal complexes having electron-rich properties was reported more than three decades ago.[14] These metal complexes are normally prepared with a cyclopentadienyl (Cp) or polypyrazolylborate (Tp)[21,22] ligand to enhance their stabilities toward moisture and air to allow routine handling. This review article deals with transition metal fragments such as $CpFe(CO)_2$, $CpMo(CO)_3$, and $CpW(CO)_3$ having a propargyl, allenyl, or alkynyl group. These three metal complexes have similar behaviors in various aspects of chemical reactions. Their cyclopentadienylmetal complexes can be prepared in a few steps and high yields from inexpensive $Fe(CO)_5$ and $M(CO)_6$ (M = Mo, W).[23] Since 1970, a large number of papers have focused on the organometallic chemistry of these complexes. These metal complexes are regarded as mild nucleophiles and form stable carboniums in the reaction with electrophiles.[14−18] Often products of reactions using these metals are very different from those of main group metals. However, many investigators have focused on fundamental organometallic reactions rather than on synthetic applications. The efficiency and easiness in manipulation of these reagents in organic synthesis are often ignored. In most cases, the electrophiles used in the reactions are very electron-deficient such as tetracyanoethylene, tetrafluoroethylene, and dimethylacetylene dicarboxylate. Although these organometallics are often involved in interesting carbon−carbon bond formation, many of the products are not demetalated. Removal of the metal fragment is critical to realize its synthetic use, and it does not proceed very easily. It is not surprising that many organometallic compounds fail to give good yields of products in demetalation reactions. Moreover, no investigators have extended their methodologies to the synthesis of natural products. The lack of examples of applications appears to be an obstacle in attracting synthetic organic chemists. NHK and Pauson−Khand reactions[24,25] are well appreciated by the organic chemistry community because their reliabilities are demonstrated by many examples in the synthesis of natural products.

Prior to this paper, several review articles have appeared on different aspects of these organometallics. Rosenblum published an account[14a] on his pioneering work on [3+2]-cycloadditions of iron−allyl complexes. This paper shows some instances where bicyclic carbocycles are constructed via iron−allyl complexes. This area was again reviewed by Welker and Ruck-Braun recently.[15] In the last two decades, intensive studies have centered on the use of π-allylmolybdenum complexes for stereocontrolled multifunctionalization, notably by the work of Pearson, Faller, and Liesbeskind.[16,18] Pearson and we also published separately review articles[16,18] on the use of molybdenum−π-allyl and −diene compounds in organic synthesis. These articles also disclose several methods for stereocontrolled synthesis of oxygen heterocyclic compounds. The most important contribution in this area is the work of Faller in early 1990 who developed reliable methods for demetalation of molybdenum−π-allyl complexes.[26−32] Faller's method is very significant in developing the synthetic utilities of allyl- and propargylmolybdenum and -tungsten complexes. These organometallics prove to be good reagents for efficient and stereocontrolled synthesis of various oxygen heterocycles.[33] They are also applicable to the synthesis of natural α-methylene butyrolactones (vide infra). Meanwhile, we also began

an independent work on functionalized alkynyltungsten complexes which appear to be more useful reagents in organic synthesis compared to their silane and stannane analogues.[34−35]

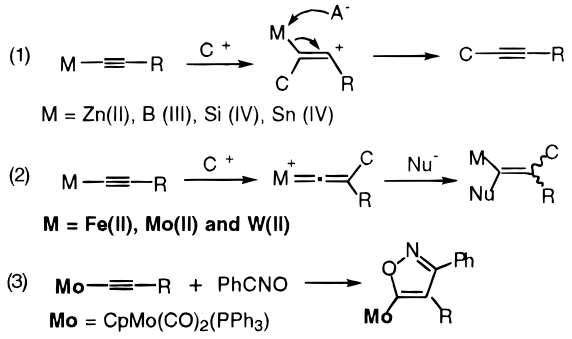
To attract the attention of the synthetic organic community, this article is written in such a way that the subject is focused on the use of allyl, propargyl, and alkynyl complexes of electron-rich Fe(II), Mo(II), and W(II) metals to construct useful carbocyclic and heterocyclic compounds. The scope of this article has minimum overlap with those of previous review articles in which the references were dated before 1993.[14−18] The work unrelated to the synthesis of these substances will not fall within the scope of this review even though they show interesting organometallic chemistry. The metal complexes having a polypyrazolylborate ligand (Tp) will be included here also if it is related to the subject. This article will exclude the reactions of vinylmetal complexes because they are still far from practical use. The allenyl and propargyl complexes are reported together because studies of allenyl complexes are less common.

II. η^1-Alkynyl Complexes

1. Preparation and Reaction with Electrophiles

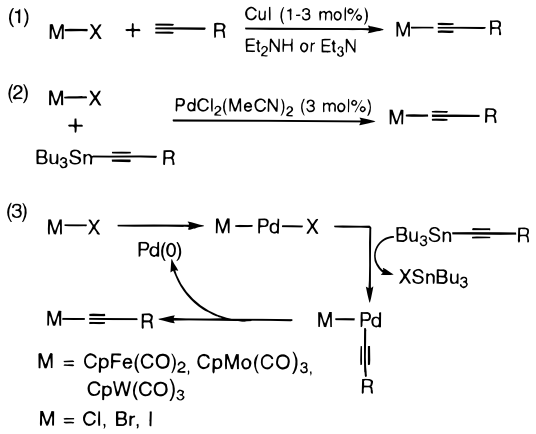
The reaction of alkynylmetal complexes with organic carbonyl compounds can lead to oxygenated molecules; the regioselectivities depend on the types of metals as shown in Scheme 1. Alkynyl organometallics of silanes, boranes, stannanes, and zinc are not as useful as their allyl, propargyl, and allenyl species because of their low reactivities.[34−36] These alkynyl organometallics undergo electrophilic addition at their C_α-carbons to generate an unstable vinyl cation that is easily captured by any basic species in solution to give the alkynyl derivative. Cyclopentadienyliron, -molybdenum, and -tungsten η^1-alkynyl compounds, however, show a distinct reaction pathway. These alkynyl organometallics react with electrophiles at their C_β-carbons to form a metal-η^1-vinylidenium intermediate which are fairly kinetically stable.[37] Nucleophilic attack at cations of these types proceeds regioselectively at the C_α-carbons to form a 1,2-addition product. An example is provided in Scheme 1 (eq 3), which shows a [3+2]-cycloaddition upon treatment of alkynylmolybdenum complex with nitrile oxide.[38−40] Similar to their main group metal analogues, the reaction of alkynyliron, -molybdenum, and -tungsten complexes with electrophiles has been investigated thoroughly. These organometallics, however, are far from practical use for two reasons: (i) the electrophiles are limited to very electron-deficient electrophiles such as tetracyanoethylene, isocyanates, and hexafluoroacetone[38−40] and (ii) the products cannot be demetalated.

Scheme 1. Electrophilic Additions of Alkynylmetal Species



There are two common and efficient methods to prepare alkynyliron, -molybdenum, and -tungsten compounds as shown in Scheme 2. These alkynyl compounds can be conveniently prepared from treatment of the metal halides with alkynes in the presence of CuI catalyst (1−3 mol %), but Et_2NH or Et_3N must be used as the solvent.[41] It is proposed that alkynylcuprate is formed as a reaction intermediate that subsequently undergoes transmetalation with metal halide to give the desired products. An alternative method for synthesis of these alkynylmetal complexes is based on a Pd-catalyzed transmetalation reaction (eq 2) with the mechanism proposed in eq 3.[42] In the presence of excess alkynylstannanes, Pd(II) is first reduced to an active Pd(0) species. Oxidative addition of Pd(0) to form the M−X bond affords a M−Pd(II)−X intermediate that then undergoes ligand exchange with alkynylstannane to give a M−Pd−alkynyl intermediate. Reductive elimination of this bimetallic species forms alkynylmetal complexes and the active Pd(0) species to complete a catalytic cycle.

Scheme 2

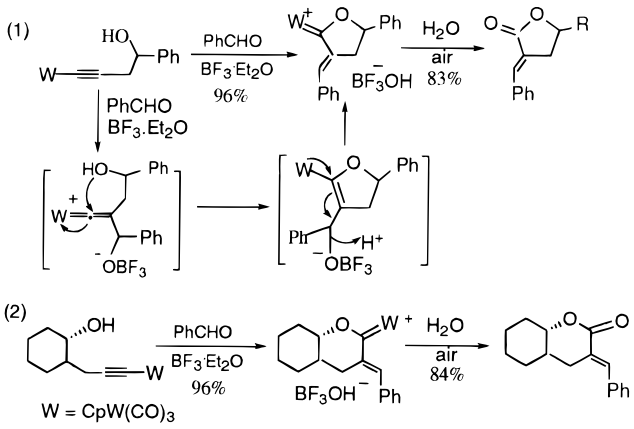


2. Synthesis of Oxygen Heterocycles

A. α-Alkylidene γ- and δ-Lactones

A variety of oxygen heterocycles can be synthesized with suitable modification of the alkynyl ligand. α-Alkylidene γ- and δ-lactones are important structural units in naturally occurring compounds.[43−45] These heterocycles are readily prepared from Lewis acid-promoted cycloalkenylation of tungsten−η^1-alkynol with aldehydes as shown in Scheme 3.[46] Treatment of tungsten−η^1-α,δ-alkynol with PhCHO in the presence of $BF_3{\cdot}Et_2O$ in cold diethyl ether forms a furylidenium salt quantitatively that has been characterized by X-ray diffraction (eq 1). The carbenium salts are air stable in solid form. Demetalation of this salt is readily achieved with H_2O/air in

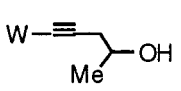
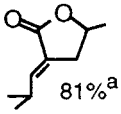
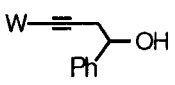
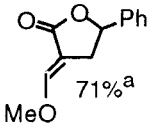
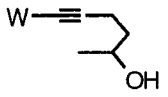
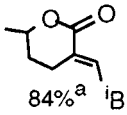
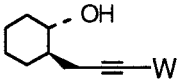
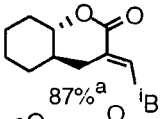
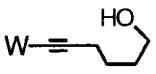
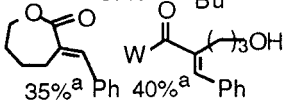
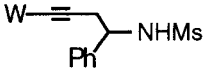
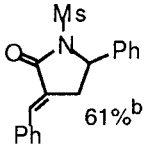
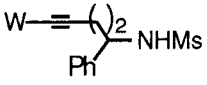
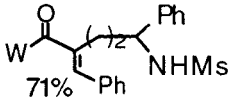
Scheme 3



CH_2Cl_2 to afford α-benzylidene-γ-lactone in 83% yield. This cyclization is extended to the synthesis of α-alkylidene-δ-lactones (Scheme 3, eq 2). Tungsten−η^1-α,ϵ-alkynol undergoes a similar cycloalkenylation reaction with PhCHO/BF_3·Et_2O in diethyl ether, leading to a pyrylidenium salt in 96% yield, and further giving bicyclic α-benzylidene δ-lactone in 84% yield after the demetalation reaction. The cycloalkenylations are both synthetically useful and also interesting in a mechanistic aspect. A plausible mechanism is proposed in eq 1 that involves two key intermediates: (1) a tungsten−η^1-allenylidenium species and (2) a tungsten−η^1-2,3-furanyl species.

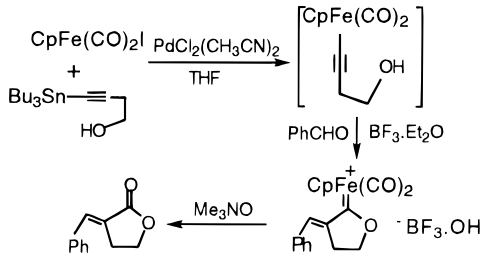
Table 1 shows examples of direct synthesis of α-alkylidene γ- and δ-lactones from tungsten−η^1-alkynols. The resulting oxacarbenium salts formed in diethyl ether solution were filtered from the mother solution and redissolved in CH_2Cl_2 for air-oxidation to liberate the desired products. The cycloalkenylation works for various aldehydes and trimethoxymethane but fails to proceed with ketones and unsaturated ketones. Good isolated yields (>70%) are obtained for α-alkylidene γ- and δ-lactones produced from aldehydes and trimethoxymethane. An attempt to extend this cyclization to the synthesis of α-alkylidene-ϵ-lactones was partially successful, and the desired ϵ-lactone is obtained in 35% yield together with an acyl compound as a byproduct (40%) as shown in entry 5. The cycloalkenylation reaction also works for tungsten−η^1-alkynylamine, but the corresponding azacarbenium salt is demetalated with m-CPBA-oxidation to give a 61% yield of α-benzylidene-γ-lactam. The reaction, however, fails to work for the synthesis of δ-lactam derivatives, and an acyl product is obtained in 71% yield in this case. The fact that tungsten−acyl compounds are found as byproducts may suggest that cyclization of the allenylidenium intermediate to form a larger lactone or lactam is difficult to achieve. The formation of C−O and C−N bonds in such cyclizations is envisaged to be reversible when a Lewis acid is present.

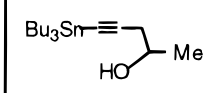
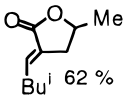
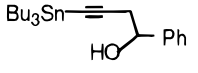
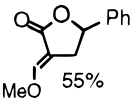
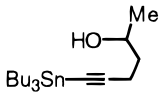
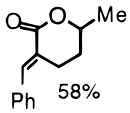
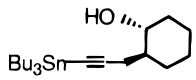
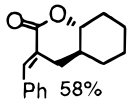
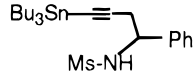
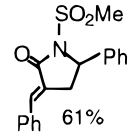
Table 1. Direct Synthesis of Lactones from η^1-Alkynols (W = CpW(CO)$_3$)

entry	η^1-alkynol	eletrophile	heterocycles
1		^{i}PrCHO/BF_3Et_2O	 81%[a]
2		$CH(OMe)_3$ /BF_3Et_2O	 71%[a]
3		^{i}BuCHO/BF_3Et_2O	 84%[a] ^{i}Bu
4		^{i}BuCHO/BF_3Et_2O	 87%[a] ^{i}Bu
5		PhCHO/BF_3Et_2O	 35%[a] 40%[a]
6		PhCHO/BF_3Et_2O	 61%[b]
7		PhCHO/BF_3Et_2O	 71%

[a] Demetalation of the carbenium salts with air/H_2O. [b] Demetalation of the carbenium salt with m-CPBA.

Scheme 4



entry	alkynyl stannanes	electrophiles	heterocycles
1		Bu^iCHO	 62 %
2		$CH(OMe)_3$	 55%
3		PhCHO	 58%
4		PhCHO	 58%
5		PhCHO	 61%

The preceding cyclizations are also operable for alkynyliron reagents.[47] Scheme 4 shows an example to employ a Pd-catalyzed transmetalation reaction to effect cycloalkenylation of alkynylstannanes with aldehydes/$BF_3{\cdot}Et_2O$. Utilization of this transmetalation reaction can add chemical versatility to alkynylstannanes. This synthesis also avoids the isolation of air-sensitive alkynyliron compounds that are generated and used in situ in this study. The preparation of alkynyliron compounds requires more caution compared to the molybdenum and tungsten analogues. The alkynyliron species generated in the reaction is treated with a mixture of aldehyde and $BF_3{\cdot}Et_2O$ to form iron−oxacarbenium salts following the same reaction pathway. The oxacarbenium is isolated for demetalation with Me_3NO, affording α-benzylidene γ-lactone in overall 64% yield based on alkynylstannanes. Scheme 4 shows several examples of this method for synthesis of α-alkylidene γ- and δ-lactones in good yields. The reaction is also extended to the synthesis of α-alkylidene-γ-lactam in 61% yield. Use of iron complexes does not enhance the scope of cycloalkenylation, and it fails to produce the ϵ-lactone and δ-lactam derivatives.

B. Nucleophilic Addition at Oxacarbenium Salts

(i) With CH_2N_2. The oxacarbenium salts generated in the cycloalkenylation reaction are very reactive, and their reactions with CH_2N_2[46] lead to cyclopropanation to give spirolactones in good yields after demetalation. The reaction pathway, however, depends on the types of alkylidene substituents in these salts as illustrated in Scheme 5. The α-benzylidene salt reacts with two molecules of CH_2N_2 to form a new oxacarbenium having a cyclopropane ring linked to a benzyl group. Demetalation of this salt with water affords the γ-lactone in 90% yield. In the case of ethylidene salt (eq 2), only one molecule of CH_2N_2 is uptaken to form a cyclopropane ring. Both reactions yield only one diastereomer. The reaction mechanism has been elucidated based on the results from isotopic ^{13}C- and ^2H-labeling experiments (eq 1). Spectroscopic analysis of the resulting γ-lactone concludes that one CH_2 unit forms a cyclopropane ring on the C−C double bond and the second CH_2 unit is inserted into the ^{13}C−Ph bond. The mechanism is proposed to involve a bridging phenonium intermediate,[46] which can account for insertion of the CH_2 unit into the C−Ph bond of the starting carbenium salt.

Scheme 5

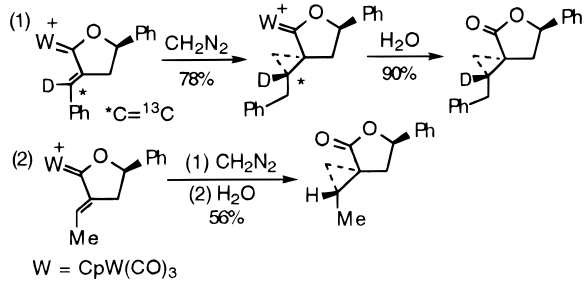
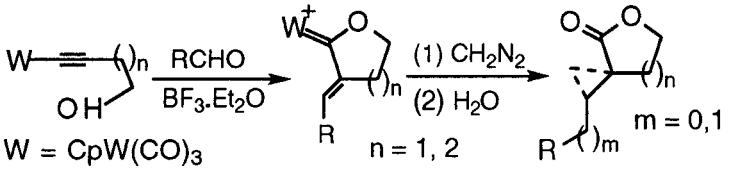
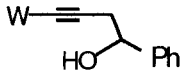
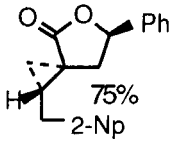
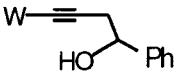
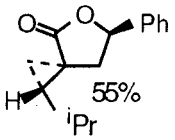
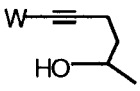
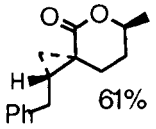
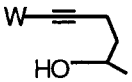
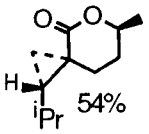


Table 2 shows the scope for direct transformation of tungsten−alkynol complexes into these spirolactone derivatives.[46] The oxacarbenium salts were filtered out of its diethyl ether solution and subsequently treated with excess dry CH_2N_2 in CH_2Cl_2 before demetalation with water. The cyclopropanation reaction was extended to pyrylidinium salts to yield spiro-δ-lactone in good yields. Like previous cases, only one diastereomer of the spirolactone was formed exclusively. A similar pattern was observed for 2-naphthyl and phenyl groups (entries 1 and 3) which uptook two molecules of CH_2N_2 to furnish a cyclopropane ring and inserted a CH_2 unit into the C−aryl bonds, affording the corresponding spirolactone products in 75% and 61%, respectively. Like the preceding ethylidene case, the isopropyl substituents in entries 2 and 4 effected a simple cyclopropane reaction to yield the corresponding lactones in 56% and 54% yields, respectively.

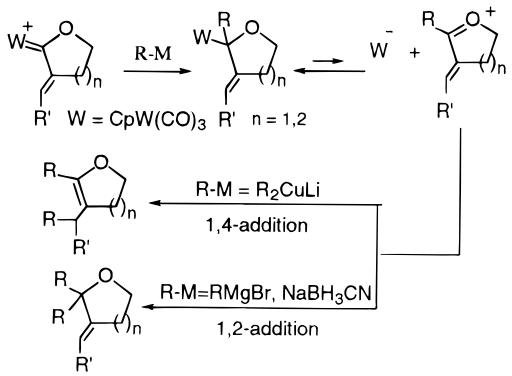
(ii) With Organometallic Nucleophiles. All acyclic oxacarbenium salts react with one molecule of nucleophile to give η^1-alkyl derivatives.[48] For example, $CpFe(CO)L[{=}C(OMe)Et]^+$ reacts at its carbene carbon facily with one molecule of organometallic nucleophile such as RMgBr or $LiAlH_4$. The preceding cyclic oxacarbeniums from the cycloalkenylation reaction, however, function as a dication synthon upon treatment with organometallic nucleophiles.[46] Their reaction pathways are shown in Scheme 6. Like other oxacarbeniums, RMgBr, R_2CuLi, and metal hydride first attack at the carbene carbon to give tungsten−η^1-furanyl and -pyranyl

Table 2. Synthesis of Spirolactones via Cyclopropanation with CH_2N_2



Entry	tungsten-alkynol	aldehyde	spiro lactone
1		2-NpCHO	
2		^{i}PrCHO	
3		PhCHO	
4		^{i}PrCHO	

Scheme 6

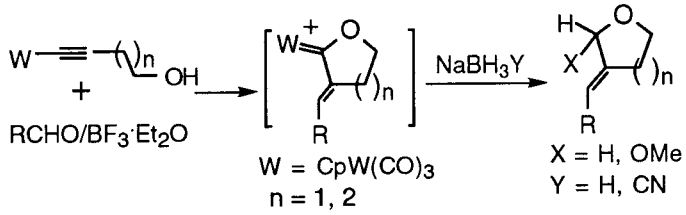


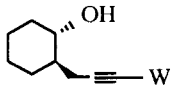
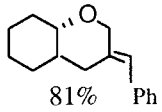
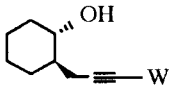
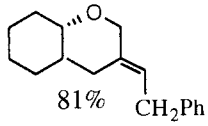
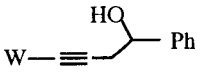
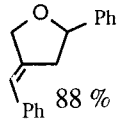
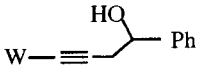
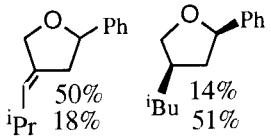
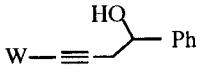
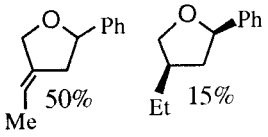
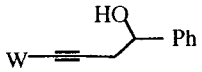
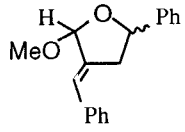
species. $CpW(CO)_3$ is considered to be sterically bulky and an electron-rich group. The oxygen atom forces $CpW(CO)_3$ to undergo dissociation from the η^1-oxacyclic complex. It is proposed that a small equilibrium exists between the η^1-oxacyclic and an enonium species. In this manner, RMgBr and boron-hydride undergo 1,2-addition reaction and R_2CuLi effects 1,4-addition reaction according to traditional enone chemistry.

Oxacyclic carbenium salts are readily separable from the reaction mixtures of alkynyltungsten and $RCHO/BF_3{\cdot}Et_2O$ species. Table 3 shows the examples for synthesis of oxygen heterocycles by reduction of the carbenium salts generated from tungsten−alkynols.[46] The double addition proceeds well with $NaBH_4$ reduction for both η^1-pyrylidinium and η^1-furylidinium salts to afford good yields (>81%) of β-alkylidene tetrahydrofuran and -pyran derivatives (entries 1−3). In the case of a furylidinium salt bearing an alkylidene group (entries 4−5), β-alkylidene tetrahydrofuran is formed together with 2,4-dialkyltetrahydrofuran. The latter is generated by reduction of the alkylidene group with $NaBH_3CN$, and its yields increase with increasing amount of $NaBH_3CN$. If a methanol solution of $NaBH_4$ is used, a lactol is formed exclusively (entry 6). In this case, one hydride and a methoxy group are involved in the double addition reaction.

Table 4 shows the results for 1,1-addition of RMgBr to the oxacarbenium salts, and the yields of oxygen heterocyclic products are calculated based on alkynols. This synthetic method is very effective for synthesis of 2,2-dialkyl-3-alkylidenefuran and pyran compounds derived from tungsten−η^1-α,δ tungsten and α,ϵ-alkynol and RCHO (R = alkyl, aryl).[46] Spirofuran and -pyran derivatives are also successfully prepared in high yields with the use of difunctionalized Grignard reagents $MgBr(CH_2)_nMgBr$ (n = 4, 5). The organocopper reagents R_2CuLi effect 1,3-addition to these salts to give 2,3-dialkyl-4,5-dihydrofuran and -pyran derivatives in moderate to goods yields,[46] provided that the alkylidene substituents are bulky, such as phenyl and isopropyl groups. The yields in Table 5 are calculated based on tungsten−η^1-alkynol species. 1,3-Addition products are obtained in good yields for oxacarbeniums bearing benzylidene substituents (entries 1, 2, 4). In the case of an ethylidene group (entry 5), the reaction of Me_2CuLi to this salt, however, affords a single addition product with regioselectivity at the ethylidene carbon; the yield is 72%.

Table 3. Examples for Demetalation with Boron Hydrides



entry	η^1-alkynols[a]	$BF_3.Et_2O$ /RCHO[b]	hydrides[c]	products isolated yield(%)[d,e]
1		PhCHO	$NaBH_3CN$ (1.0 equiv.)	 81%
2		$PhCH_2CHO$	$NaBH_3CN$ (1.0 equiv.)	 81%
3		PhCHO	$NaBH_3CN$ (1.0 equiv.)	 88 %
4		^{i}PrCHO	$NaBH_3CN$ (1.0 equiv.) (6.0 equiv.)	 50% 18% 14% 51%
5		MeCHO	$NaBH_4$ (2.0 equiv)	 50% 15%
6		PhCHO	$NaBH_4$(2.0 equiv)/MeOH	 *trans/cis*= 2/1, 88 %

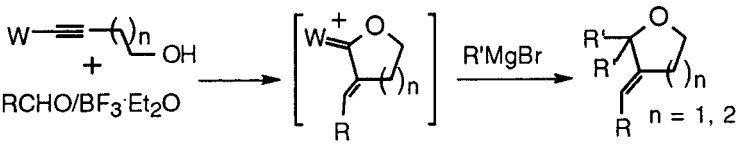
[a] W = $CpW(CO)_3$. [b] The amounts of BF_3·Et_2O and aldehyde were 1.0−1.1 and 2.0−5.0 equimolar proportions, respectively. [c] Solvent: CH_2Cl_2/CH_3CN (1/1 volume ration) for $NaBH_3CN$, −40 °C, 2 h. [d] Isolated yields were calculated based on tungsten−η^1-alkynol compunds. [e] The products were separated on a preparative silica TLC.

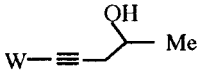
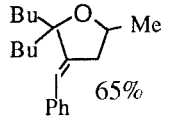
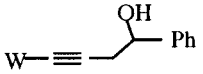
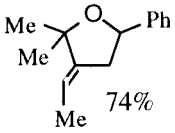
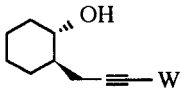
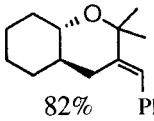
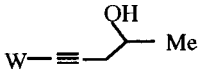
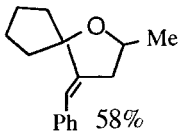
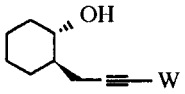
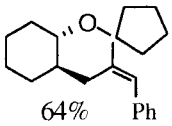
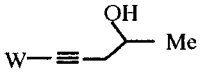
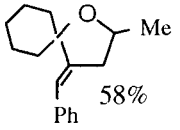
C. Intramolecular Cycloalkenation Reaction

Intramolecular cycloalkenylation of tungsten−η^1-alkynol reagents bearing an electrophile provides a short and efficient synthesis of unsaturated bicyclic lactones.[49] The synthetic protocol is shown in Scheme 7. The starting α-substituted alkynols are easily prepared from alkylation of the corresponding alkynols.[50] The reaction of tungsten−η^1-alkynol with BF_3·Et_2O in a 1:1 ratio leads to tungsten−η^1-oxacarbenium in 91% yield. The reaction mechanism is rationalized by formation of two key intermediates: (1) a tungsten−η^1-allenylidenium and (2) a tungsten−η^1-pyranyl species. Demetalation of the bicyclic carbenium salts is readily achieved by water/air oxidation to give a [3.4.0]-bicyclic lactone in 81% yield. Since oxacarbenium salts are isolated from the reaction solution, various bicyclic oxygen heterocycles can be obtained via treatment of the salt with a variety of nucleophiles including CH_2N_2, Et_3SiH, and MeMgBr to effect cyclopropanation, reduction of C=C bond, and α,α-dialkylation reaction, respectively. A summary of the products is given in eq 2. This synthetic method has also been applied to a short synthesis of natural bicyclic lactones such as mitsugashiwalactone and onikulactone. Addition of Me_2CuLi to the bicyclic oxacarbenium, followed by hydrolytic demetalation, affords mitsugashiwalactone and onikulactone in 56% and 13% yields, respectively, based on the tungsten−alkynol species.[49]

A variety of bicyclic lactones can be prepared from this intramolecular cycloalkenylation reaction with alternation of the electrophiles and the lengths of parent alkynols. Table 6 illustrates the scope of bicyclic lactones produced from this method. Entries 1−5 show the synthesis of δ- and ϵ-lactones fused to five-, six-, and seven-membered carbocyclic rings; the isolated yields were calculated based on starting tungsten−η^1-alkynols. The substrates in entries 1−5 have a tethered dimethoxymethane group; the yields are 54−81% depending on ring sizes of the products. The yields decrease for increasing ring sizes of bicyclic lactones. With this tethered dimethoxy-

Table 4. Isolated Yields for Demetalations with Grignard Reagents



entry	η^1-alkynyl complexes[a]	$BF_3.Et_2O$ / RCHO[b]	nucleophiles[c]	products isolated yield(%)[d]
1		PhCHO	n-BuMgBr (2.0 equiv.)	 65%
2		MeCHO	MeMgBr (2.0 equiv)	 74%
3		PhCHO	MeMgBr (2.0 equiv)	 82%
4		PhCHO	$MgBr(CH_2)_4MgBr$ (3.0 equiv)	 58%
5		PhCHO	$MgBr(CH_2)_4MgBr$ (3.0 equiv)	 64%
6		PhCHO	$MgBr(CH_2)_5MgBr$ (3.0 equiv)	 58%

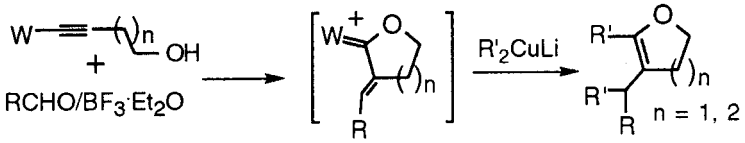
[a] W = $CpW(CO)_3$. [b] The amounts of $BF_3 \cdot Et_2O$ and aldehyde were 1.0−1.1 and 2.0−5.0 equimolar proportions, respectively. [c] Reaction condition: CH_2Cl_2−40 °C, 2 h. [d] Isolated yields were calculated based on tungsten−η^1-alkynol alkynols.

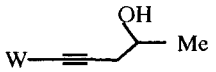
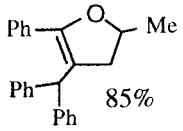
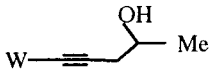
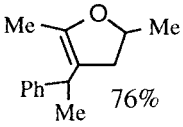
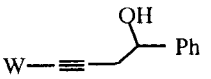
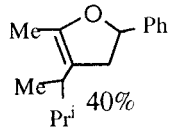
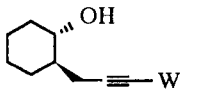
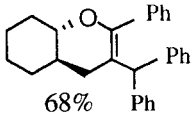
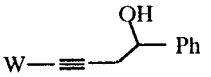
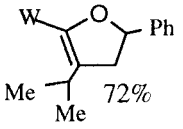
methane group, the ring size of product is up to a [5.5.0]-ϵ-lactone with a 54% yield (entry 5). Cyclization of tungsten−η^1-hept-1-yn-7-ol with $BF_3 \cdot Et_2O$ to form a [6.3.0]-bicyclic lactone is unsuccessful (entry 6). Entries 7 and 8 show two instances for annulations of tungsten−η^1-pent-1-yn-5-ols possessing a tethered ketone, affording the corresponding [4.3.0]- and [4.4.0]- δ-lactones in 58% and 61% yields, respectively. An attempt to form a larger [5.4.0]-lactone from η^1-hex-1-yn-6-ol with a tethered ketone was unsuccessful. The trimethoxymethane group is also effective in the cyclization reaction to yield [4.4.0]-β-ketolactone in 61% yield. There has been no attempt to perform the cyclizations with tungsten−alkynols tethered with electrophiles such as epoxides, unsaturated enones, and esters. The reaction should be also applicable to the synthesis of unsaturated bicyclic lactams since tungsten−η^1-alkynylamines form α-alkylidene γ-lactam in intermolecular cycloalkenylations (Scheme 4).

D. Reactivities of Tungsten–η^1-Oxacyclic Dienes

Tungsten−η^1-oxacyclic dienes are prepared directly from tungsten−η^1-alkynols by deprotonation of the oxacarbenium with Et_3N as shown in Scheme 8.[51] Cycloaddition of organic dienes with unactivated nitriles proceeds only with extreme difficulty upon prolonged heating at higher temperatures. The tungsten−η^1-furanyl diene, however, undergoes a smooth [4+2]-cycloaddition with acetonitrile to afford a 64% yield of furopyridine. The furopyridine derivatives have emerged as useful pharmacophores in several therapeutic areas. This cycloaddition is promoted by excess $Me_3NO \cdot 2H_2O$ or by photolysis to remove one carbonyl group of the tungsten complex. The tungsten−π-azaallyl intermediate can be successfully isolated under suitable conditions to establish the mechanism for this cyano-[4+2]-cycloaddition. A seven-membered tungsten−oxacarbenium is proposed to be the key intermediate.[51] This cycloaddition has been extensively studied, and the scope is shown in Scheme 8 (eq 2). The reaction works well for both aliphatic and aromatic nitriles which are used as the solvents to ensure good yields of furopyridines. Intramolecular cyano-[4+2]-cycloaddition[51] also works well (entries 6 and 7) for tungsten−η^1-furanyl diene despite the availability of one nitrile group. The reaction is not applicable to η^1-pyranyl diene, which leads to an undesired organometallic species.

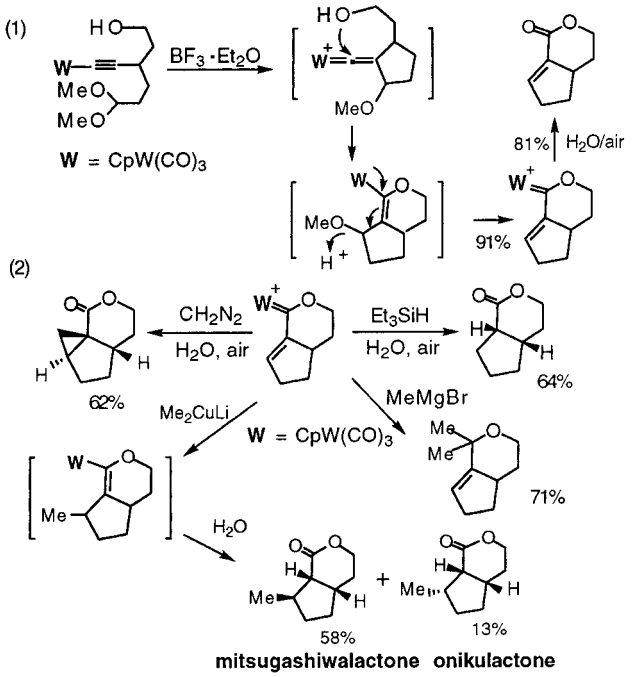
Table 5. Isolated Yields for Demetalations with Organocuprates



Entry	η^1-alkynyl complexes[a]	$BF_3.Et_2O$ / RCHO[b]	nucleophiles[c]	products isolated yield(%)[d]
1		PhCHO	Ph_2CuLi (2.0 equiv)	 85%
2		PhCHO	Me_2CuLi (2.0 equiv)	 76%
3		Pr^iCHO	Me_2CuLi (2.0 equiv)	 40%
4		PhCHO	Ph_2CuLi (2.0 equiv)	 68%
5		MeCHO	Me_2CuLi (2.0 equiv)	 72%

[a] W = $CpW(CO)_3$ [b] The amounts of $BF_3.Et_2O$ and aldehyde were 1.0 and 2.0−5.0 equimolar proportions, respectively. [c] Reaction conditions: CH_2Cl_2, − 40 °C, 2 h. [d] Isolated yields were estimated based on tungsten−η^1-alkynols

Scheme 7. Reaction Sequence of Bicyclic Oxacarbenium

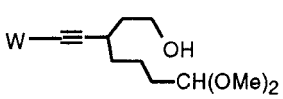
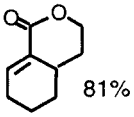
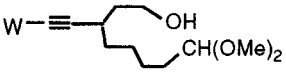
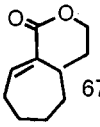
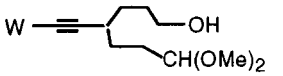
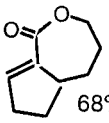
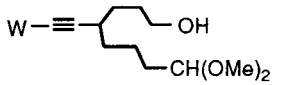
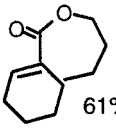
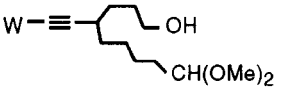
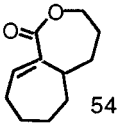
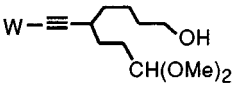
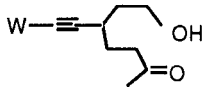
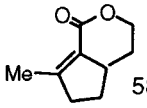
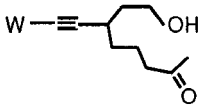
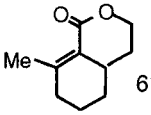
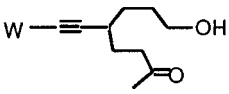
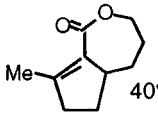
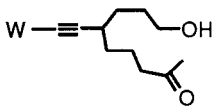
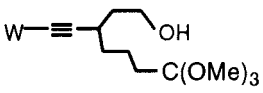
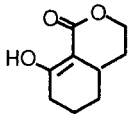


An alternative use of tungsten−η^1-oxacyclic dienes is to provide a short synthesis of oxacyclic dienes via demetalations with anhydrous Me_3NO in CH_3CN.[52] As mentioned previously, use of $Me_3NO{\cdot}2H_2O$ in the demetalation, following cyano-[4+2]-cycloaddition, affords good yields of furopyridine derivatives.[51] It is unclear about the role of water that drastically changes the chemoselectivity in demetalation of η^1-oxacyclic dienes. Solvents are critical determinants of the yields of oxacyclic dienes. CH_3CN is the best solvent, whereas CH_2Cl_2 and $CHCl_3$ give α-alkylidene lactones (see Scheme 3 and Table 1) as a byproduct. The results are summarized in Table 7. A small amount of cyano-[4+2]-cycloaddition product is present as a byproduct (<5%). Reasonable yields are obtained for dihydrofuranyl and -pyranyl dienes, including those for the intramolecular Diels−Alder reactions. Heating the oxacyclic dienes (entries 5−7) in refluxing toluene leads to intramolecular cycloaddition reactions with excellent diastereoselectivities. Only one single diastereomer is produced with the methyl acrylate group approaching the diene with endo overlap and on the face opposite the phenyl group.[52]

E. Carbonylation Reaction

As shown in Scheme 9, the reaction of alkynyltungsten compounds with $Co_2(CO)_8$ at ambient conditions generates a carbenoid intermediate that can be trapped by a tethered olefin to give a cyclopropane derivative in 86% yield.[53] Heating this trinuclear species in toluene affords a tungsten−η^1-cyclopentenone in 58% yield, further leading to cyclopentenone in 86% yield after demetalation with a concentrated HCl solution. This reaction pathway is distinct from the conventional $Co_2(CO)_8$-mediated Pauson−Khand reaction[24,25] which cannot be applied to elec-

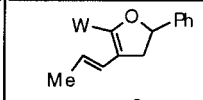
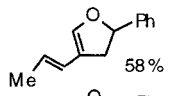
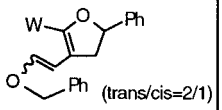
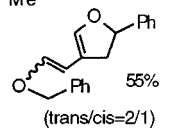
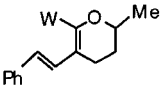
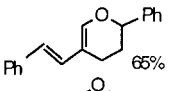
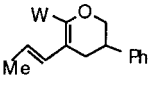
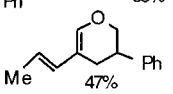
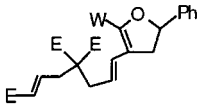
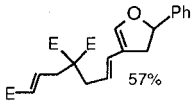
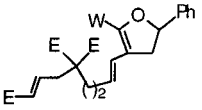
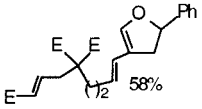
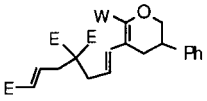
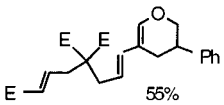
Table 6. Isolated Yields for Bicyclic Lactones (W = CpW(CO)$_3$)

entry	tungsten-alkynol[a]	bicyclic lactones[b]
1		 81%
2		 67%
3		 68%
4		 61%
5		 54 %
6		—
7		 58%
8		 61%
9		 40%
10		—
11		 61%

[a] One equivalent of $BF_3{\cdot}Et_2O$ was used, and diethyl ether was used as the solvent. [b] Yields are calculated based on tungsten−η^1-alkynol compounds.

tron-deficient olefins such as styrene, unsaturated esters, and nitriles. $Co_2(CO)_8$ reacts with electron-deficient olefins to give mainly diene derivatives. Scheme 9 shows the results for synthesis of various cyclopentenone derivatives from alkynyltungsten compounds bearing a tethered alkene. The reaction works well for a variety of alkenes including styrene, unsaturated esters, and nitriles. The resulting tungsten−η^1-cyclopentenone species are smoothly demetalated with concentrated HCl solution to give

Table 7. Yields for Demetalation of η^1-Oxacyclic Dienes with Anhydrous Me_3NO[a]

Entries	η^1-Oxacyclic Dienes	Oxacyclic Dienes
1		 58 %
2	 (trans/cis=2/1)	 55% (trans/cis=2/1)
3		 65%
4		 47%
5		 57%
6		 58%
7		 55%

[a] W = CpW(CO)$_3$, Z = CO_2Me.

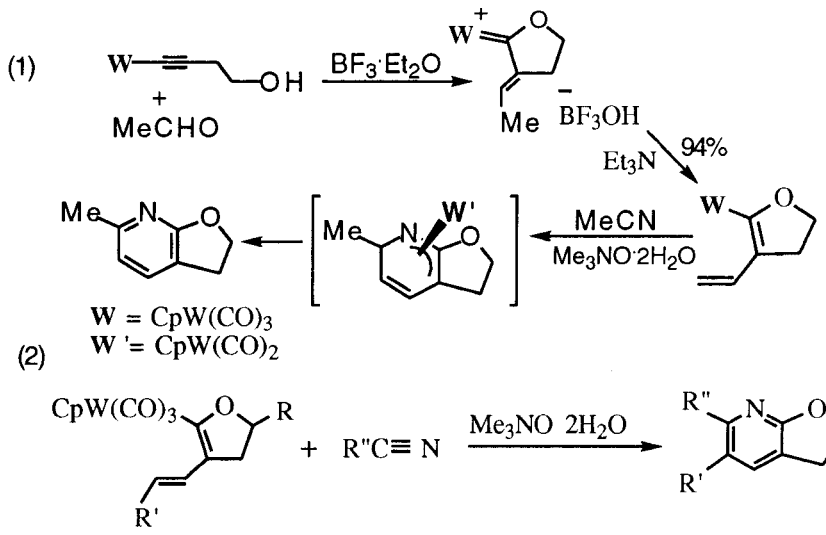
organic cyclopentenones in good yields. Unfortunately, the intramolecular [2+2+1]-cycloaddition is not applicable to the synthesis of larger carbocycles such as [3.4.0]-bicyclic cyclopentenones.

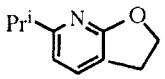
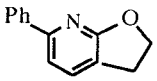
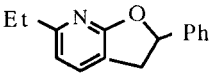
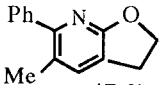
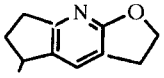
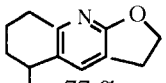
Protonation of alkynylmetal complexes for short reaction periods is known to give metal−η^1-vinylidenium species.[37] Nevertheless, it was found[54] that excess CF_3SO_3H could induce oxidative carbonylation of alkynyltungsten organometallics over a prolonged reaction period, as shown in Scheme 10. By tethering a 4-methoxyphenyl group to an alkynyltungsten complex, the key intermediate in the reaction was found to be a highly electrophilic W(IV)−acyl species that can be isolated and characterized.[54] In the cases of complexes having more highly electron-rich aryl groups, reactions with CF_3SO_3H lead to intramolecular carbonylations, affording indanones in good yields (>80%). Formation of indanones is envisaged to derive from attack of the aryl moiety at the W(IV)−CO group, and a W(IV)−H is also formed during this cyclization. Subsequent reduction of the α-methylene cyclopentanone intermediate with this W(IV)−hydride species affords the observed product. The thiophene group can also be carbonylated by CF_3SO_3H to give a 32% yield of indanone together with an acid (28%) as the byproduct (eq 2).

F. Via Vinylidenium Intermediates

Treatment of alkynyliron(II), -molybdenum(II), and -tungsten(II) species with electrophiles is known to generate metal−vinylidenium complexes. The iron cations are utilized for synthesis of β-lactams via a

Scheme 8



Entry	Dienes	R"CN	Cond.	Products
1	R = R' = H	R" = Pr^i	$Me_3NO\ 2H_2O$ 23 °C (8 h)	 58 %
2	R = R' = H	R" = Pr^i	hν (23 °C, 48 h)	**6** (47%)
3	R = R' = H	R" = Ph	$Me_3NO\ 2H_2O$ 23 °C (8 h)	 82 %
4	R = Ph, R' = H	R" = Et	$Me_3NO\ 2H_2O$ 23 °C (8 h)	 67 %
5	R = H, R' = Me	R" = Ph	$Me_3NO\ 2H_2O$ 23 °C (8 h)	 47 %
6	R = H R' = CH-$(CH_2)_2$CN Ph	——	$Me_3NO\ 2H_2O$ CH_2Cl_2 (reflux, 42 h)	 50 %
7	R = H R' = CH-$(CH_2)_3$CN Ph	——	$Me_3NO\ 2H_2O$ CH_2Cl_2 (reflux, 12 h)	 77 %

[2+2]-cycloaddition with imines.[55,56] Scheme 11 shows an example for the reaction of iron−vinylidenium with imines to give iron−carbeniums in which the diastereomeric ratios are 8/5 and 3/1 for R = Ph, CH=CHPh, respectively. Demetalation of the iron−carbeniums can be achieved by air-oxidation to give β-lactam in overall 18−19% yields based on the starting iron−vinylideniums. This [2+2]-cycloaddition is believed to proceed in a stepwise manner. The iron−vinylidenium also undergoes a [2+2]-cycloaddition with a variety of 2-thiazolines to afford bicyclic iron carbenium in 51−82% yields. The resulting carbenium salts exist in good diastereomeric ratios (15:1−6:1). PhIO-oxidation of one of these carbenium salts (R^1 = Me, R^2 = CO_2Me) gives a 52% yield of bicyclic γ-lactam, which is an important intermediate in pharmaceutic synthesis.

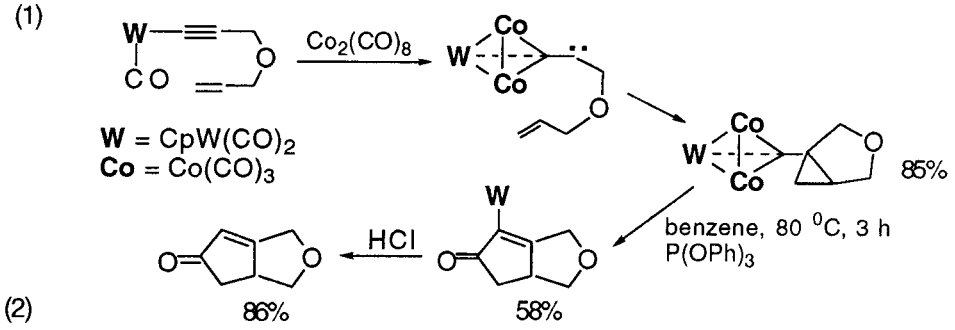
III. η^1-Allyl and π-Allyl Complexes

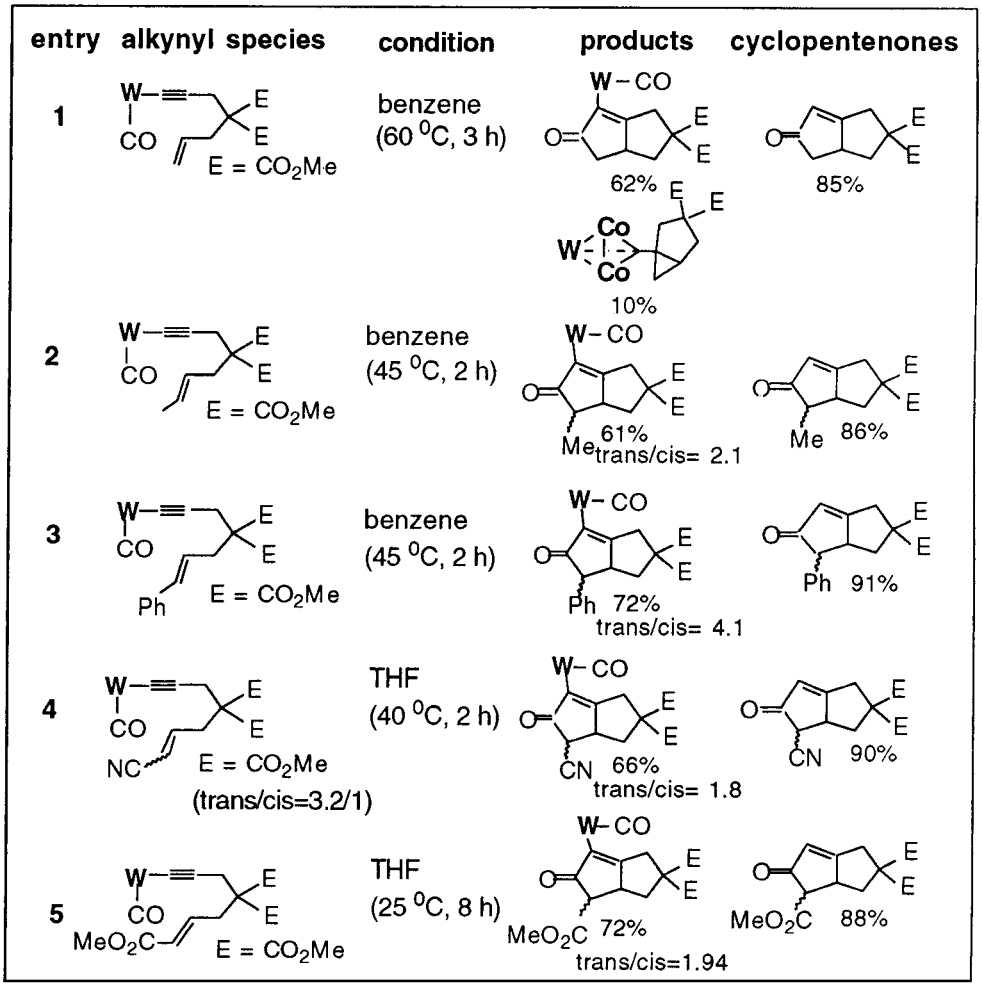
1. Synthesis of η^1- and η^3-Allyl Compounds

A. Metalation of Allyl Halides

Reactions of $CpM(CO)_nNa$ (M = Fe, n = 2; M = Mo, W, n = 3) and allyl halides (halide = Cl, Br, and I) or tosylates in THF normally affords $CpM(CO)_n$-(η^1-allyl) (M = Fe, n = 2; M = Mo, W, n = 3) in 50−70% yields.[23] The molybdenum and tungsten η^1-allyl species can be converted to their π-allyl complexes preferably by Me_3NO-promoted decarbonylation reaction in 50−65% yields. The *syn*/*anti* ratios of these π-allyl products are generally consistent with the *cis*/*trans* composition of the starting allyl halides.[57] CpFe(CO)(π-allyl) compounds can be prepared in moderate yields (40−55%) by photolysis of their η^1-

Scheme 9. Pauson−Khand Reaction Derived from Alkynyltungsten Species



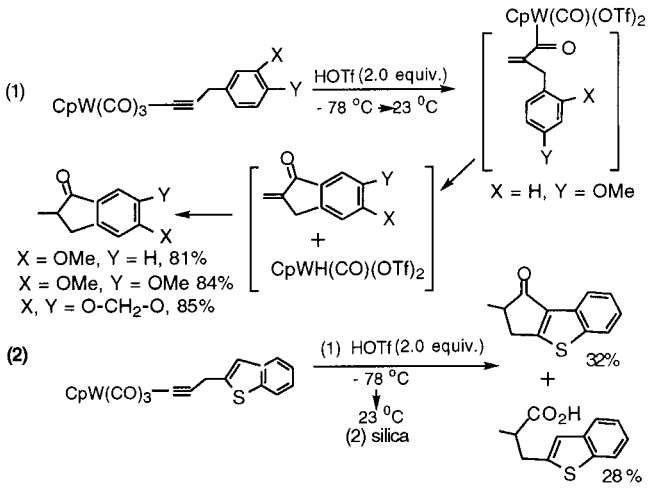


allyl derivatives. Iron−π-allyl complexes are not as useful as molybdenum and tungsten analogues. A main restriction in the synthesis of these allylmetal complexes is that it operates only with primary halides $XCH_2CR{=}CR_2$; $CpMo(CO)_3X$ is formed exclusively for reactions involving secondary and tertiary halides.

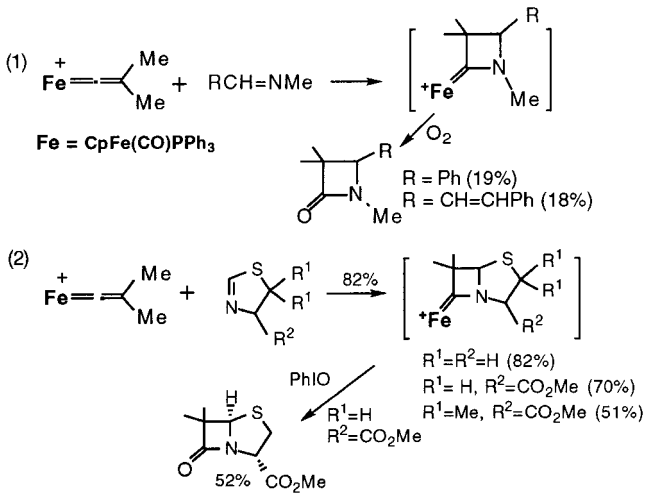
B. Oxidative Addition of Allyl Halides

Oxidative addition of $M(CO)_3(CH_3CN)_3$ (M = Mo, W) to allyl halides followed by MCp (M = Li, Na) treatment is the most convenient and practical method to prepare $CpM(CO)_2(\pi\text{-allyl})$ (M = Mo, W) compounds in high yields.[58] In contrast, allylic tosylates and methanesulfonates are too unstable to be generally useful. Allylic acetates have been successfully used in several cases,[59,60] and there is a report of allylic diphenylphosphinates being employed as efficient precursors.[61] The reactions are also effective for synthesis of cyclic molybdenum−π-allyl compounds and applicable to the synthesis of $CpMo(CO)_2$(*anti*-π-allyl) through oxidative addition of *R-cis*-3-allylic halide with $Mo(CO)_3(CH_3CN)_3$.[62] The *anti*-η^3-allyl compounds can be also prepared either from $CpMo(CO)_3Na$ and *R-cis*-allylic halides as mentioned above or by $NaBH_4$ reduction of the $CpMo(CO)_2(\eta^4$-*cis*-diene$)^+$ cation. The stereochemical course of oxidative addition of the chiral allylic acetates with $Mo(CO)_3(CH_3CN)_3$ has been elucidated.[31b] The outcome is that the formation of the Mo−allylic bond proceeds via retention of configuration with respect to the acetate−carbon bond cleavage as shown in

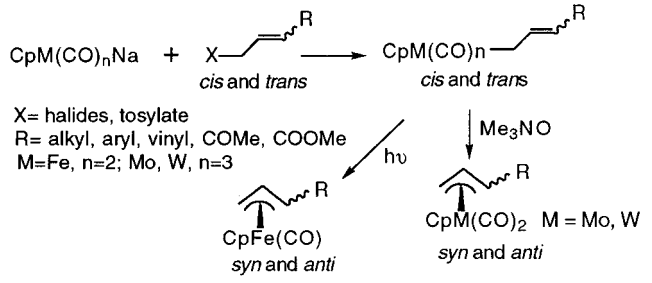
Scheme 10



Scheme 11

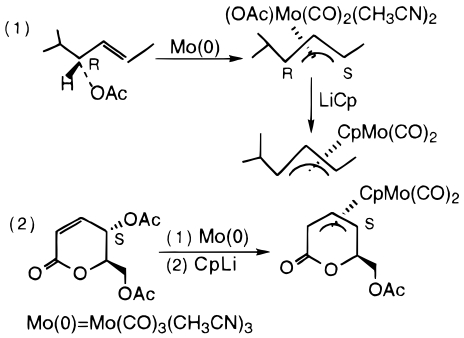


Scheme 12



Scheme 14. Similarly, the reaction between this Mo(0) species and the chiral cyclic allylic acetate gave the product with retention of configuration. The observed stereochemistry here is distinct from the corresponding reactions of Pd(0) complexes which proceed via inversion of configuration.[63] Owing to the labile CH_3CN ligand of $Mo(CO)_3(CH_3CN)_3$, it is likely that before oxidative cleavage of the allylic−acetate

Scheme 14



bond, formation of a chelation intermediate through coordination of the allylic C=C bond and the carbonyl group to molybdenum center accounts for the retention of stereochemistry.

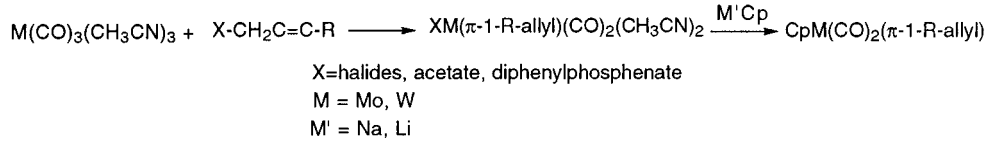
In contrast, the reactions between $Mo(CO)_3(CH_3CN)_3$ and chiral allylic bromides proceed via inversion with respect to cleavage of the allylic carbon−halide bond. Examples are provided by the work of Liebeskind[64] shown in Scheme 15. The ring conformation is important for the reaction. An interesting case is the chiral trans bromide isomer (eq 1) of which the pseudoaxial bromide group can be displaced by $Mo(CO)_3(CH_3CN)_3$ presumably by an S_N2 mechanism. The cis isomer (eq 2) with bromide in the pseudoequatorial site fails to react with Mo(0) species.

2. η^1-Allyl Complexes in Organic Synthesis

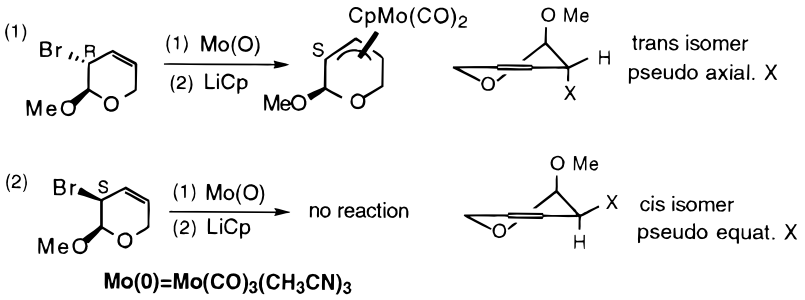
A. Cycloaddition with Reactive Olefins

η^1-Allyliron complexes can undergo facile [3+2]-cycloadditions with electron-deficient alkenes via a stepwise mechanism, affording five-membered carbocyclic compounds.[14] These cycloadditions were first developed by Rosenblum and Wojcicki two decades ago.[14] Although these reactions have been studied extensively, only limited examples are useful for organic synthesis because very electron-deficient olefins are required to achieve good yields of cycloadducts.[65,66] Scheme 16 shows the types of olefins applicable to the cycloadditions. Diastereomeric mixtures with a 1:1 ratio of products are found for the reaction of η^1-allyliron species with *trans*-dimethyl-2-cyano-2-butenedioate (entry 1), indicating that the mechanism involves a zwitterionic intermediate. These iron−η^1-cyclopentyl species are further demetalated by a Ce(IV) oxidation to afford the methyl ester in reasonable yields. The reaction of this iron−allyl complex with a reactive alkyne such as dimethyl acetylenedicarboxylate gives a mixture of products,[65,66] and the desired iron−cyclopentyl product is obtained in 42% yield. Several η^1-allyliron derivatives with a methoxy group at the C_2 and C_3 position have also been examined.[67,68] The iron−η^1-2-methoxyallyl

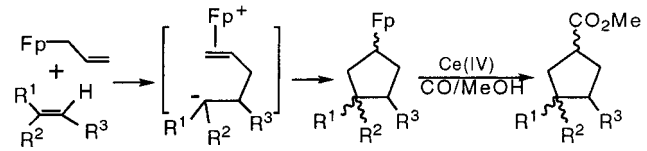
Scheme 13



Scheme 15

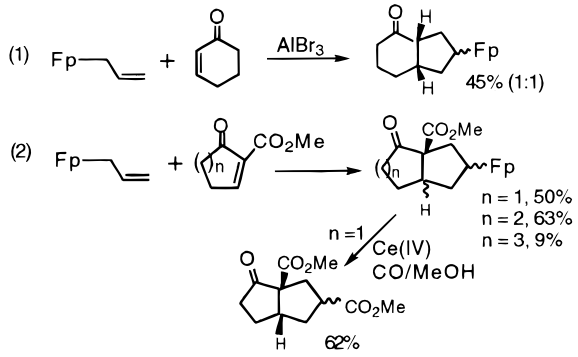


Scheme 16



entry	R^1	R^2	R^3	Fe–η^1-complex	ester
1	CO_2Et	CN	CO_2Et	81% (1:1)	60%
2	CO_2Et	CO_2Et	H	70%	62%
3	CO_2Me	CO_2Me	CO_2Me	50%	63%
4	CN	CN	CO_2Et	67%	77%
5	CO_2Me	CO_2Me	H	64%	—

Scheme 17

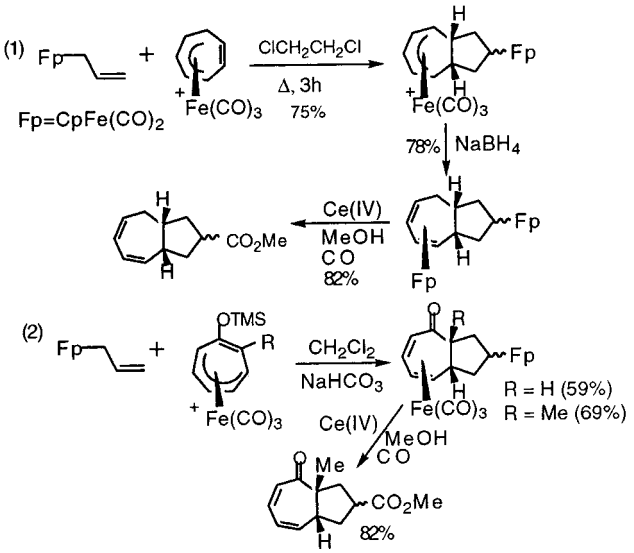


species reacts sluggishly with reactive alkenes to give a mixture of three products. Although the cycloaddition works well for iron–η^1-3-methoxyallyl complex and reactive alkenes, less reactive alkenes such as dimethyl fumarate and dimethyl maleate fail to undergo cycloaddition.

Scheme 17 shows an $AlBr_3$-promoted cycloaddition of cyclohexenone with η^1-allyliron complex to afford a 1:1 mixture of *cis*-fused bicyclic ketones in 45% yield.[69] The reaction of η^1-allyliron compounds with reactive 2-ethoxycarbonyl-cycloalkenone can proceed without acid catalyst to yield five-membered carbocycles as a mixture of two diastereomers (eq 2);[69] the yields of products depend on the ring sizes (n = 1, 50%; n = 2, 63%; and n = 3, 9%). Ce(IV) oxidation of iron–[3.3.0]-bicyclic compounds in a CO/MeOH mixture affords the methyl esters in 62% yield.

η^1-AllylIron complexes can also undergo [3+2]-cycloaddition with iron–η^5-tropylium salts without Lewis acid (Scheme 18), giving an iron–η^5-hydroazulenium salt (78% yield) as a mixture of two diastereomers.[70,71] These cationic salts are subsequently converted to the bicyclic esters in 82% yield via sequential $NaBH_4$ reduction and Ce(IV) oxidation. The synthetic utility of this method can be extended to functionalized iron–η^5-tropylium salts that afford 4-ketohydro-azulenyl complexes in 59–69% yields (eq 2).[71a] These iron azulenyl compounds are demetalated by Ce(IV) oxidation to give dienone esters in 82% yield.

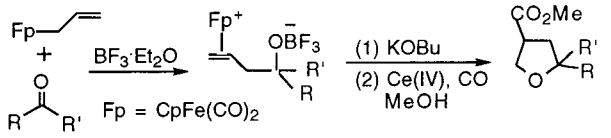
Scheme 18



B. Cycloaddition with C=X Bonds

The majority of allyl organometallics of main group metals undergo addition reactions with aldehydes and ketones,[1–8] but the reaction often requires Lewis acid. Several allylsilanes such as (η^1-allyl)$SiMe_2Ph$ can undergo [3+2]-cycloaddition with organic carbonyl compounds.[8] In the presence of $BF_3{\cdot}Et_2O$, η^1-allyliron complexes react with aldehydes and ketones in CH_2Cl_2 to form an isolable zwitterionic salt consisting of η^2-homoallylic alcohol as shown in Scheme 19.[72,73] Release of homoallylic alcohols from this iron salt is conducted with good yields via treatment with NaI, and $CpFe(CO)_2I$ is the major organometallic product. Treatment of these iron salts with Bu_4NF does not induce [3+2]-cycloaddition. However, addition of KOBu (1.0 equiv) to these salts in CH_2Cl_2 effects a cyclization reaction to give Fe–η^1-3-tetrahydrofuranyl complexes[73] that are subsequently oxidized by Ce(IV) in MeOH/CO to liberate 3-tetrahydrofuran esters in moderate yields. The yields of esters are 40–45% for iron–olefin species derived from aldehydes and about 20% for iron–olefin complexes derived from ketones.

Scheme 19

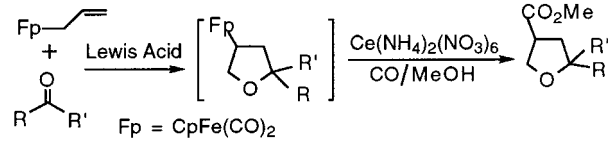


organic carbonyl	Fe-olefins	cycloadducts (yield, ratio[a])
R'=Ph, R =H	80%[b]	45%[c] (1.5:1)
R'=3-PhNO$_2$, R =H	80%	43% (1.2:1)
R'=3-PhOMe, R =H	75%	45% (1.2:1)
R, R' = (CH$_2$)$_6$	45%	19%
R'=Ph, R =Me	50%	20% (1.2:1)

[a] The ratio of two diastereomeric products. [b]The yields are calculated based on iro−allyl species. [c]These yields are reported based on iron−olefin complexes.

η^1-Allyliron complexes undergo direct cycloaddition with aldehydes if $ZnCl_2$ is used in the reaction.[74] Solvents and reaction temperatures are critical for the yields of cycloproducts. The reaction is best carried out in CH_2Cl_2 at room temperature. A summary of $ZnCl_2$-promoted synthesis of tetrahydrofurans is shown in Scheme 20. This $ZnCl_2$-catalyzed

Scheme 20

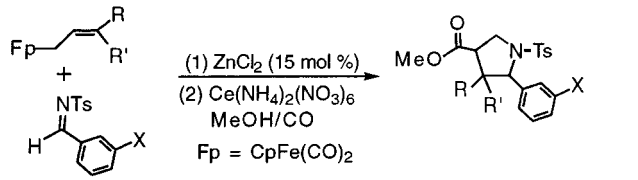


Organic carbonyl	Lewis Acid[a]	Product yield[b] (ratio)[c]
R'=3-PhNO$_2$, R =H	ZnCl$_2$ (15%)	71% (3.1:1)
	no Lewis Acid	60% (1.9:1)
R'=2-PhNO$_2$, R =H	ZnCl$_2$ (15%)	62% (2.1:1)
	no Lewis Acid	45% (1.9:1)
R'=Ph, R =H	ZnCl$_2$ (15%)	36% (2.1:1)
	ZnCl$_2$ (100%)	40% (1.1:1)
	no Lewis Acid	8% (1.8:1)
R'=2-PhOMe, R =H	ZnCl$_2$ (15%)	31% (2.0:1)
	ZnCl$_2$ (100%)	28% (1.2:1)
R'=PhCHMe, R =H	ZnCl$_2$ (100%)	16% (1.5:1)
	TiCl$_4$ (200%)	15% (1.5:1)
R, R' = (CH$_2$)$_6$	ZnCl$_2$ (200%)	0%
	TiCl$_4$ (200%)	37%
R'=Ph, R =Me	ZnCl$_2$ (200%)	0%
	TiCl$_4$ (200%)	15% (1.0:1)

[a] CH_2CI_2, 25 °C. [b]Yields are calculated based on iron−allyl complex. [c]The ratio of two diastereomeric products.

cycloaddition reaction has limited use because only reactive aldehydes such as nitrobenzaldehyde give good yields of tetrahydrofuran ester. A catalytic amount of $ZnCl_2$ (15 mol %) suffices the reaction in these cases. The yields of tetrahydrofuran ester decrease significantly to 30−36% for benzaldehyde and 2-methoxybenzaldehyde. The reaction does not work for ketones. This $ZnCl_2$-catalyzed [3+2]-cycloaddition also works for *N*-tosylimines,[75] leading to

Scheme 21



Allyliron species	Imine	Yields (diastereomeric ratio)
R = R' =H	X = H	55% (2.5:1)
	X = NO$_2$	42% (2.5:1)
R = Me, R'=H	X = H	28% (2.5:1)

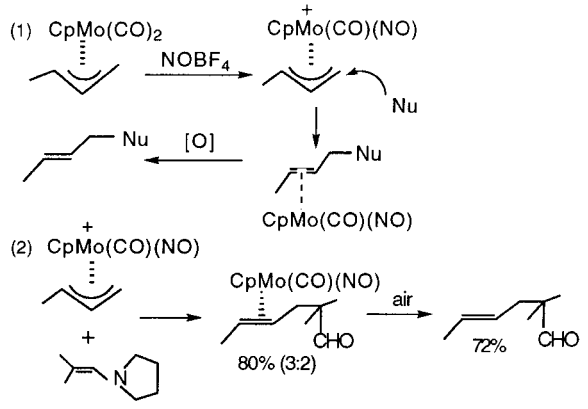
the synthesis of pyrrolidine derivatives (Scheme 21). The yields are fair (40−55%) for the pyrrolidine ester derived from the iron−allyl complex and low (28%) for the product derived from the iron−crotyl complex.

3. π-Allyl Complexes for Organic Synthesis

A. Demetalations

(i) α-Functionalized Olefins from [CpMo(NO)CO(π-Allyl)]$^+$ Salts. Complexes of the type CpM(CO)$_2$(π-allyl) (M = Mo,W) can be easily converted to an allyl cation or anion equivalent with ligand substitution of the two carbonyl groups. The carbonyl group of CpM(CO)$_2$(π-allyl) (M = Mo,W) is easily replaced by $NOBF_4$ to give the cationic salt [CpMo(CO)(NO)(π-allyl)]$^+$,[27−29] which shows facile reactivity toward numerous nucleophiles to give CpMo(CO)(NO)(Nu−CH_2CH=CH_2). The latter is easily oxidized by air or Ce(IV) oxidation to liberate α-functionalized olefins. Scheme 22 shows a regiocontrolled attack of

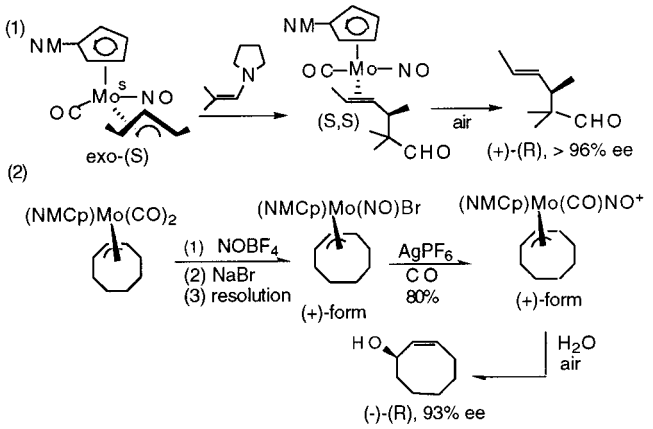
Scheme 22



the enamine of isobutaldehyde at the CpMo(CO)$_2$(π-*syn*-crotyl) cation, affording a π-olefin complex in 80% yield as a mixture of two diastereomers (3:2), further preceding to 2,2-dimethylhex-4-enal in 73% yield after air oxidation[76]

A few chiral CpMo(CO)(NO)(π-allyl)$^+$ cationic complexes have been prepared and used for enantioselective synthesis of α-functionalized olefins. Introduction of a chiral neomenthyl (NM) group onto the cyclopentadienyl group such as the complex[76] in eq 1 (Scheme 23) allows simple resolution of its *S*-enantiomer. The chiral molybdenum center effects

Scheme 23

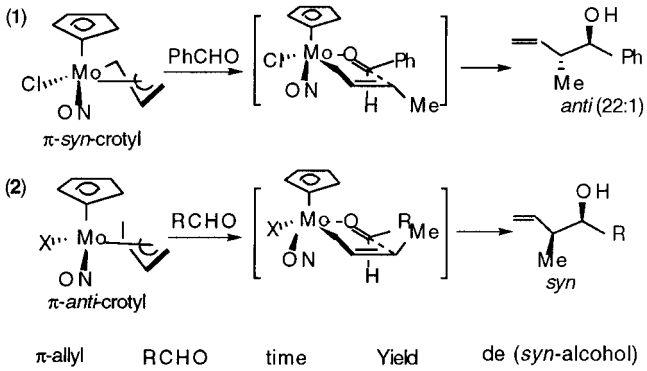


enantiofacial attack of enamines at one of its two allylic carbons, affording molybdenum−η^2-2,2,3-trimethylhex-4-enal complex. Air oxidation of this chiral molybdenum−η^2-olefin species liberates 2,2,3-trimethylhex-4-enal with ee > 96%. Yields are not reported for this sequence of reaction. Chiral complex (+)-(NMCp)Mo(NO)Br(π-cyclooctenyl)[77] is also resolved from diastereomeric mixtures of (NMCp)Mo(NO)Br(π-C_8H_{13}). Treatment of this compound with $AgPF_6$ in the presence of CO yields the chiral cation (eq 2) with retention of configuration (80% yield). Nucleophilic attack of this allyl cation with water proceeds with high enantioselectivity to give (−)-(*R*)-3-hydroxylcyclooctene in 93% ee with quantitative yield.

(ii) Homoallylic Alcohols from CpM(NO)X(π-Allyl) Complexes. Stereoselective synthesis of a secondary homoallylic alcohol is an important topic in organic reactions. CpMo(NO)X(π-allyl) (X = halides) compounds[30−32] are easily prepared from LiX and CpMo(NO)(CO)(π-allyl)$^+$. These π-allyl complexes reacted facily with aldehydes to give secondary homoallylic alcohol efficiently. The reaction is stereospecific as manifested in two instances in Scheme 24. Upon treatment with benzaldehyde, Mo−π-*syn*-crotyl complex generated anti homoallylic alcohol (de = 92%) in quantitative yields. A series of Mo−π-*anti*-crotyl compounds were also prepared, and their reactions with benzaldehyde and dihydrocinnamaldehyde were studied. The results are given in eq 2 (Scheme 24). All halide ligands (X = OTs, Cl, Br and I) produced the syn alcohol with good diastereoselectivities. The tosylate and chloride reacted faster than the iodide. Faller suggests that the Mo−π-allyl bonding of these complexes is not symmetric because of different electronic properties of halide versus nitrosyl groups. The allyl terminus opposite the nitrosyl group tends to dissociate to leave an empty site for aldehyde to coordinate to form a chairlike transition state to control the stereoselection.

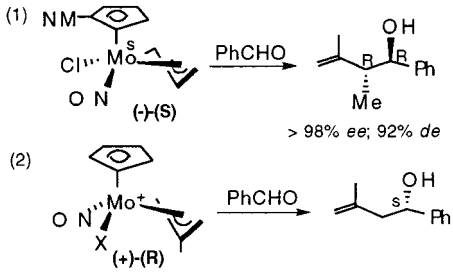
Chiral compounds of this class condensed with aldehydes to give homoallylic alcohols with a high degree of enantiomeric excess. As shown in Scheme 25, reaction of (−)-(*S*)-(neomenthylcyclopentadienyl)-Mo(NO)Cl(π-*syn*-crotyl) with benzaldehyde afforded (+)-(*R*,*R*)-2-methyl-1-phenyl-3-buten-1-ol in >98% ee[78] (Scheme 25, eq 1). Treatment of benzaldehyde

Scheme 24



π-allyl	RCHO	time	Yield	de (*syn*-alcohol)
X = I	PhCHO	1 h	45%	98%
X = I	PhCHO	24 h	99%	85%
X = Br	PhCHO	1 h	66%	85%
X = Cl	PhCHO	1 h	83%	94%
X = OTs	PhCHO	1 h	94%	94%
X = I	PhC_2H_4CHO	1 h	43%	88%
X = Br	PhC_2H_4CHO	1 h	83%	84%

Scheme 25



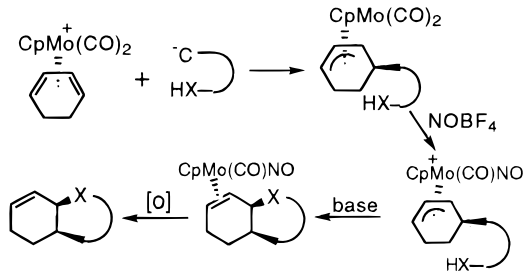
π-allyl	concn	time	conversion	*ee*
X = I	0.25	45h	91%	88%
X = Br	0.31	14 h	90%	90%
X = Cl	0.24	11 h	100%	98%
X = camphor-sulfonate	0.32	11 h	100%	94%

with enantiomerically pure (+)-(*R*)-CpMo(NO)(π-methallyl)X (X = camphorsulfonate, Cl, Br, I) yielded the chiral homoallylic alcohol (*S*)-(−)-3-methyl-1-phenyl-3-buten-1-ol with ee values between 88% and 98%. The iodide complex gave the slowest rate and also the lowest ee value (88%), whereas the chloride species gave the highest reaction rates and the best ee value (98%).

B. CpM(CO)$_2$(π-Allyl) Complexes for Heterocycles

(i) Nucleophilc Addition at CpM(CO)$_2$(η^4-Diene)$^+$ (M = Mo, W) Salts. The CpMo(CO)$_2$(π-diene)$^+$ cation can be attacked by a variety of carbon nucleophiles to give functionalized CpMo(CO)$_2$(π-allyl) complex. Scheme 26 shows an application of this method to construct a *cis*-fused bicyclic ring; in this case a carbon nucleophile is tethered with a HX (X = O, N) group. Treatment of the resulting molybdenum−π-allyl complexes with $NOBF_4$ produced an allyl cation equivalent to effect an intramolecular cyclization via attack of the tethered XH group at the π-allyl terminus to furnish bicyclic heterocyclic compounds.

Scheme 26



Both nucleophilic additions approach the π-organic moieties opposite the molybdenum fragment to give the products in *cis*-fused configuration.

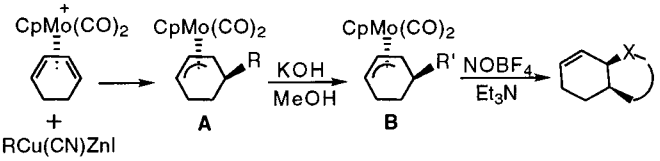
Scheme 27 shows the attack of Knochel reagent RCu(CN)ZnI on molybdenum−η^4-cyclohexadiene cation to give high yields of π-cyclohexenyl complexes.[79,80] The tethered CO_2Et, OAc, and SAc groups of these allyl complexes were subsequently hydrolyzed by KOH in MeOH to afford the corresponding XH (X = CO_2, O, S) products in 45−100% yields. Treatment of these π-allyl complexes with $NOBF_4$ and Et_3N effected an intramolecular cyclization to give η^2-olefin intermediates, which upon air oxidation afforded *cis*-fused bicyclic heterocycles including δ-lactone, tetrahydropyran, and -thiopyran. A major drawback in this method is the low yields (35−43%) in the cyclization step. There is no attempt to extend this method for synthesis of various sizes of bicyclic heterocycles besides the [4.4.0]-bicyclic rings.

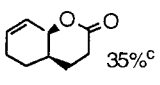
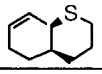
The molybdenum−π-allyl and −η^4-diene cations undergo facile interconversion by nucleophilic addition and hydride abstraction.[77] In this manner, it is easy to establish two cis substituents R^1 and R^2 to a π-allyl fragment on cyclohexane and -heptane rings as shown in Scheme 28.[77,81,82] Pearson reported[82] the synthesis of a series of *cis*-fused bicyclic lactones via treatment of $CpMo(CO)_2$(cyclohexadiene)$^+$ with disodium acetate derivatives. The resulting π-allyl complexes were subsequently oxidized by I_2 to yield a highly electrophilic Mo(IV) species, and the tethered carboxylic acid of these Mo(VI) species can attack the π-allyl carbon end opposite to the molybdenum center to furnish a *cis*-fused bicyclic lactone ring. This method seems to be efficient and stereoselective because both π-allyl complexes and bicyclic lactones are obtained in good yields. The use of I_2 for oxidative demetalation of dicarbonylmolybdenum(π-allyl) complexes also appears to be very effective. One of the bicyclic lactone products is transformed into an acyclic molecule which has a relative stereochemistry corresponding to the C(4), C(5), and C(6) centers in the macrolide antibiotics tylosin and magnamycin B (eq 3).

The organic utilization of cyclopentadienone is difficult to develop as the compound is unstable at ambient temperatures. Liebeskind reported[83] that molybdenum−η^4-cyclopentadienone cation reacted with organolithium, -magnesium, and -copper reagents with regiochemistry at the C_α carbon rather than at the C_β carbon like Michael reaction as shown in Scheme 29. Equations 2 and 3 illustrate the use of two enolates as nucleophiles to construct polycyclic oxacycles. Demetalation of these π-allyl complexes is conducted with ICO_2CF_3 to generate a highly electrophilic Mo(IV) intermediate, subsequently inducing an intramolecular cyclization to give tricyclic and bicyclic furan derivatives in 82% and 75% yields, respectively. The reactions again use molybdenum−π-allyl fragment as a stereotemplate, leading to *cis*-fused products for such double additions.

Pearson investigated the addition of chiral oxazolidinone enolates to the cations of molybdenum−η^4-cyclohexadiene and −η^4-cycloheptadiene species.[84] The enolates of these chiral oxazolidinone are generated by LDA in THF at −78 °C. Chiral molybdenym−π-allyl compounds are obtained in good yields for both dienes as shown in Scheme 30. The level of ee values are more satisfactory for the six-membered ring system (ee > 65%) than for its seven-membered counterpart (15−32%). The enolates of chiral oxazolidinones (**a** and **b**) add preferentially to the pro-*S* terminus of the diene moiety to give (*S*)-π−allyl complex, whereas the enolates of chiral oxazolidinones (**c**-**e**)

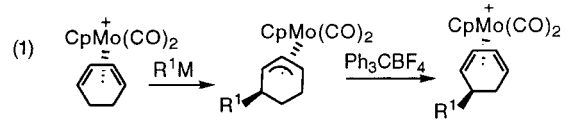
Scheme 27

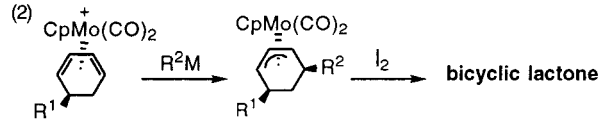


RCu(CN)ZnI	π-allyl (**A**)	π-allyl (**B**)	bicyclic product
R=$(CH_2)_3CO_2Et$	90%[a]	R'=$(CH_2)_3CO_2H$ 94%[b]	n.a
R=$(CH_2)_2CO_2Et$	73%	R'=$(CH_2)_2CO_2H$ 100%	 35%[c]
R=$(CH_2)_3OAc$	90%	R'=$(CH_2)_3OH$ 100%	 43%
R=$(CH_2)_3SAc$	96%	R'=$(CH_2)_3SH$ 45%	 34%

n.a = not available. [a]Yield was calculated based on diene salt. [b]Yield was calculated based on allyl species **A**. [c]Yield was calculated based on allyl species **B**.

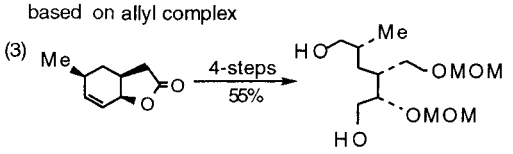
Scheme 28



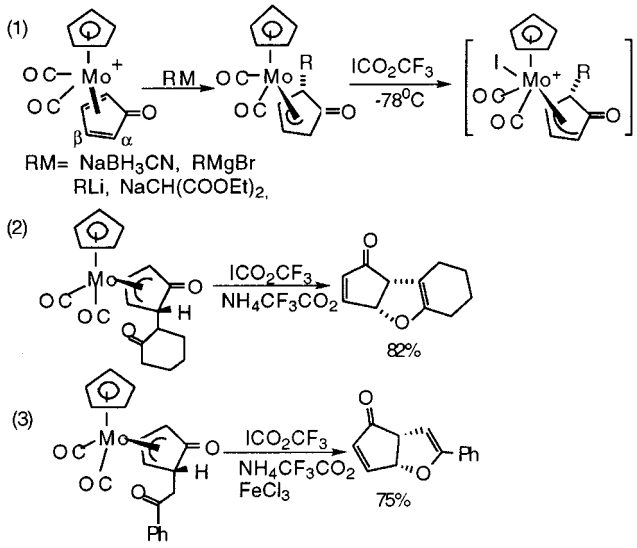


R^1	R^2M	π-allyl	bicyclic lactone
H	$NaCH(CO_2Me)CO_2Na$	98%[a]	75%[b]
H	$NaCMe(CO_2Me)CO_2Na$	70%	64%
H	$NaCH_2CO_2Na$	97%	64%
Me	$NaCH(CO_2Me)CO_2Na$	95%	90%
Me	$NaCH_2CO_2Na$	85%	64%

[a]Yields are calculated based on diene salt. [b] Yields are calculated based on allyl complex



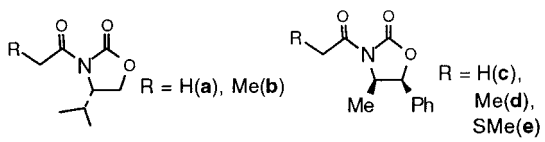
Scheme 29

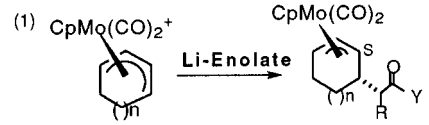


add preferentially to the pro-*R* terminus to give (*R*)-π-allyl species. However, there is no report for further use of these chiral organometallics in enantiomeric synthesis. In principle, they can provide a short and enantioselective synthesis of bicyclic lactones according to the reaction sequence in Scheme 28.

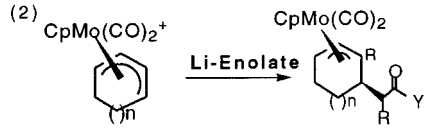
(ii) Metal−π−allyl fragment as a stereotemplate. *(ii-a) Alkylation Reaction.* The enolates of molybdenum−allyl complexes can be generated by LDA to effect carbon−carbon bond forming reaction via alkylation and aldol reaction. Pearson reported[85]

Scheme 30





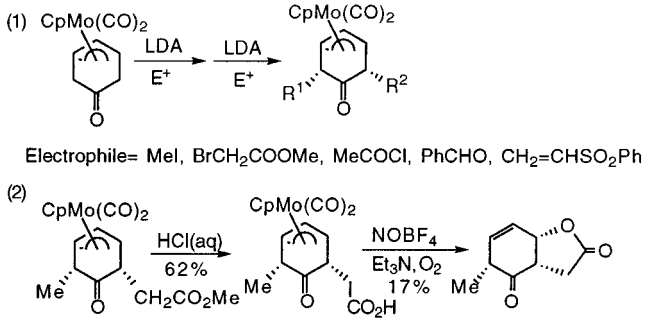
Diene	Enolate	Yield	ee value
n = 1	a	79%	65%
n = 1	b	70%	85%
n = 2	a	65%	15%
n = 2	b	65%	30%



Diene	Enolate	Yield	*ee* value
n = 1	c	74%	65%
n = 1	d	60%	80%
n = 2	c	76%	10%
n = 2	d	60%	32%
n = 2	e	52%	0%

a double alkylation of $CpMo(CO)_2$(π-cyclohexen-3-on-1-yl) complex via treatment of its enolate with various electrophiles as illustrated in Scheme 31.

Scheme 31

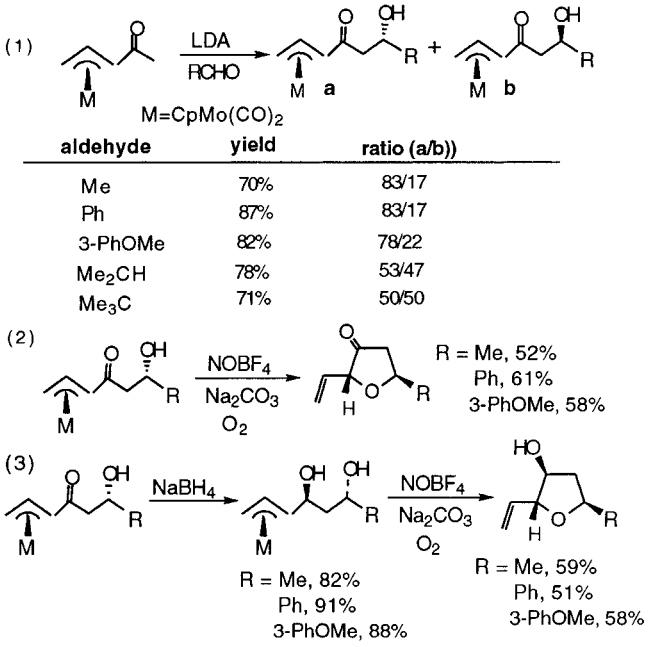


Equation 2 shows an instance to use one of the dialkylation products for synthesis of heterocycles. Following Faller's method, the acid derived from this ester is converted to a bicyclic lactone via treatment with $NOBF_4$, Et_3N, and air oxidation. The yield of bicyclic lactone in the cyclization of molybdenum−π-allyl complex is very low (17%) compared to those lacking a lactone (Scheme 28).

The enolate of $CpMo(CO)_2$(π-1-acetylallyl) is easily generated by LDA,[57] and its reaction with aldehydes affords two diastereomeric products, easily separable on a silica column. The diastereoselectivities (**a/b**) are fair for methyl and aryl aldehydes but very poor for

bulky Me_3CCHO (Scheme 32, eq 1). This π-allyl

Scheme 32

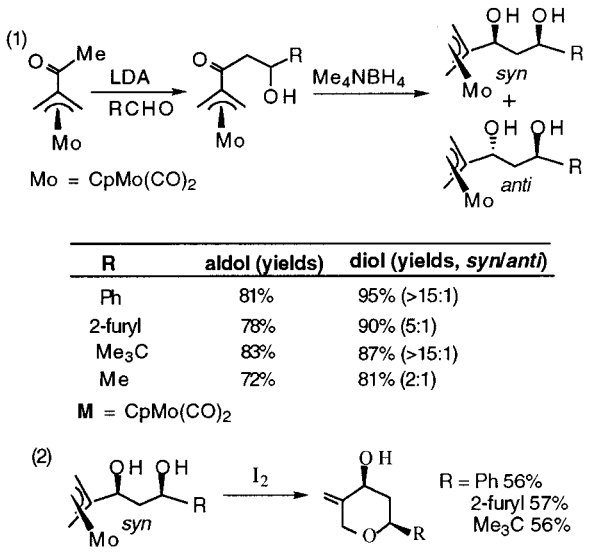


enolate, however, fails to react with ketones and epoxide. For molybdenum α-ketone allyl compounds, the allyl and ketone groups retain a sickled-shape conformation, and $NaBH_4$ reduction of these compounds proceeds with excellent stereoselectivities. The major aldol products **a** and their allyllic α,γ-1,3-diol derivatives are further utilized for stereoselective syntheses of 3-oxo-5-R-2-vinyl-tetrahydrofuran (eq 2) and 3-hydroxy-5-R-2-vinyl-tetrahydrofurans (eq 3) based on $NOBF_4$-promoted demetalation;[50] the yields are fair 50−60%. The stereochemistries of these products indicate that the furanyl rings are formed from intramolecular attack of the tethered alcohol at the π-allyl terminus opposite the $CpMo(CO)_2$ fragment.

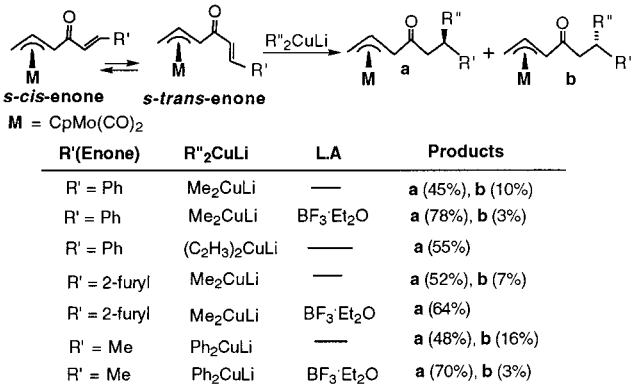
The enolate of $CpMo(CO)_2(\pi$-2-acetylallyl) is readily generated by deprotonation with lithium diisopropylamide at −78 °C,[86] and its condensation with aldehydes gives the aldol products with the yields exceeding 85%. The crystal structures of these aldol products reveal that there exists a strong intramolecular hydrogen bond between hydroxyl and α-ketone groups. Utilization of this hydrogen-locked chairlike conformation effects stereoselective generation of a 1,3-diol by reduction of the compounds with Bu_4NBH_4 in methanol/benzene (1:1 ratio). The diastereomeric ratios of the resulting diols depend on the R substituent as shown in Scheme 33. The *syn*-diol isomer is exclusively formed for bulky aryl and *tert*-butyl groups, and the *syn*/*anti* ratio becomes small (2.0) for methyl group. Treatment of these *syn*-1,3-diol with 1.5 equiv of I_2 in CH_3CN leads to demetalation to give 2-R-4-hydroxyl-5-methylene-tetrahydropyran compounds in 56−57% yields.

(ii-b) Michael Reaction. Conjugate additions of organocopper reagents to molybdenum π-allyl enones are investigated.[87,88] The *s-cis* enone conformer is the major solution species in equilibrium with its minor *s-trans* enone conformer. Minor *s-trans*-enone conformer apparently reacts more rapidly with organocopper reagent than the *s-cis*-enone conformer to control product stereochemistry. Organocopper reagents presumbly approach the enone group of the two conformers opposite the metal fragment. The results appear in Scheme 34. At −40 °C, the reactions

Scheme 33



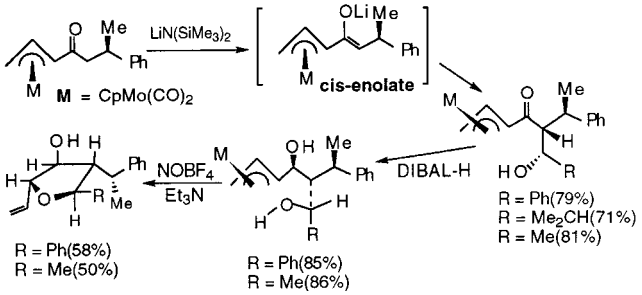
Scheme 34



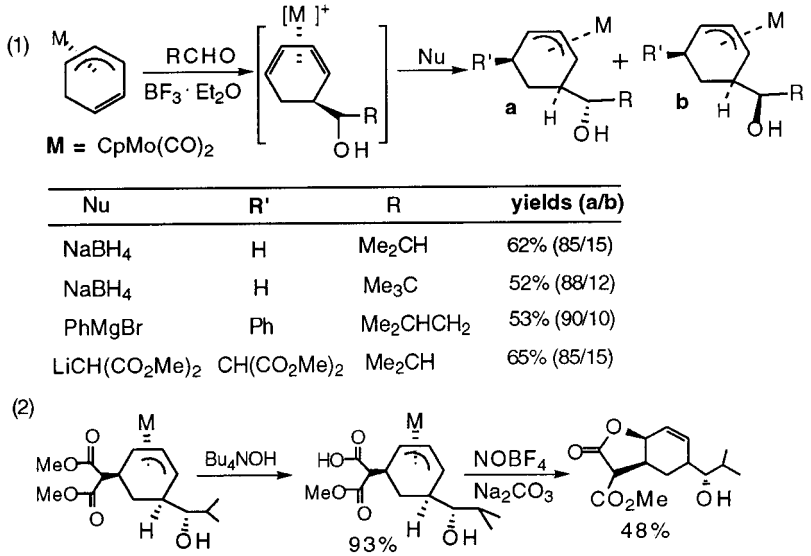
proceed in reasonable diastereselectivities **a**/**b** = 3/1−16/1 for various substituents of R′ and R″, and this ratio is improved drastically in the presence of $BF_3{\cdot}Et_2O$ (1.0 equiv) to afford **a** as the only diastereomer. The coordinated $BF_3{\cdot}O{=}C$ fragment of *s-cis*-enone conformer is expected to exert steric hindrance with its C=C bond, which thus decreases its concentration.

Scheme 35 shows the utilization of conjugated addition products for stereoselective synthesis of

Scheme 35

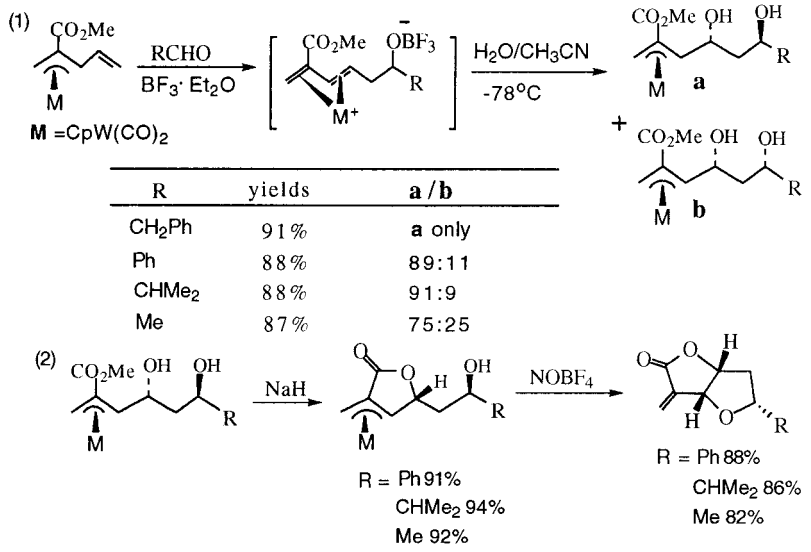


Scheme 36



Nu	R'	R	yields (a/b)
$NaBH_4$	H	Me_2CH	62% (85/15)
$NaBH_4$	H	Me_3C	52% (88/12)
PhMgBr	Ph	Me_2CHCH_2	53% (90/10)
$LiCH(CO_2Me)_2$	$CH(CO_2Me)_2$	Me_2CH	65% (85/15)

Scheme 37



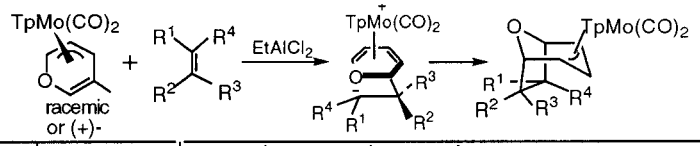
R	yields	a/b
CH_2Ph	91%	**a** only
Ph	88%	89:11
$CHMe_2$	88%	91:9
Me	87%	75:25

2,3,4,5-tetrasubstituted tetrahydrofuran compounds. Treatment of one major product with $LiN(SiMe_3)_2$ selectively generates *cis*-enolate anion that condenses with aldehydes to afford the aldol product in good yields and selectivities. Further reduction of the resulting π-allyl compound with DIBAL-H, gives the allylic α-hydroxyl alcohol as a single diastereomer in 86% yield. Treatment of this π-allyl complex with $NOBF_4$ and Et_3N using the Faller method effects a cyclization to deliver tetrasubstituted furan compounds in fair yields (50−58%).

(ii-c) Condensation of Aldehydes with Tethered Olefins. Being similar to R_3Si as an electron-donating group, the $CpMo(CO)_2$ fragment can stabilize a β-carbocation center that is isolable from reaction mixtures. $CpMo(CO)_2$(π-cyclohexadienyl) derivatives undergo BF_3-promoted addition reaction[89] with aldehydes through generation of molybdenum−η^4-cyclohexadiene cationic precipitates in cold diethyl ether; the protocol is shown in Scheme 36. The molybdenum−π-cyclohexadiene cations also react well with nucleophiles such as $NaBH_4$, RMgBr, and $LiCH(COOMe)_2$ to furnish good yields (>60%) of difunctionalized molybdenum−π-cyclohexenyl complexes. These nucleophiles do not cause a deprotonation reaction on π-diene salts. The two substituents of these π-allyl complexes are generated from one nucleophile and one electrophile, respectively, and this feature is distinct from generation of two nucleophiles on π-allyl complexes in Faller and Pearson's protocol.[77,81,82] The malonate product is converted to the acid derivative (93%) and further to bicyclic lactone in 48% yield by a $NOBF_4$-promoted intramolecular cyclization.

Acyclic tungsten−π-pentadienyl complexes also undergo electrophilic addition with aldehydes, and the *s-trans*-diene cationic intermediates are isolated as precipitates in nonpolar solvent.[90,91] This cation is highly electrophilic to react with water with excellent regioselectivity and stereoselectivity; the yields exceed 85%. The yields and selectivities are shown in Scheme 37. The diastereoselectivities **a**/**b** increase with increasingly sterically demanding aldehydes. These BF_3-promoted reactions are synthetically useful because they create simultaneously two asymmetric secondary hydroxylic carbons in a one-

Table 8. [5 + 2]-Cycloaddition of η^3-Pyranylmolybdenum Complexes



Entry	alkene	condns	yields exo/endo	product	R^1	R^2	R^3	R^4	*ee*(%)
1	CH_2=CHCHO	20%,[a] rt	87%, 10:1	*exo*	HCO	H	H	H	—
				endo	H	H	H	HCO	—
2	CH_2=CHCOMe	10%, rt	94%, 8.4:1	*exo*	MeCO	H	H	H	—
				endo	H	H	H	MeCO	—
3	CH_2=CHCO$_2$Me	20%, rt	88%, 3.5:1	*exo*	CO_2Me	H	H	H	95%
				endo	H	H	H	CO_2Me	95%
4		20%, rt	93%, 1.0:0	*exo*	$-CO(CH_2)_3-$		H	H	96%
				endo	H		H	$-CO(CH_2)_3-$	96%
5	CH_2=CHCN	120%, rt	57%, 0.64:1	*exo*	CN	H	H	H	23%
				endo	H	H	H	CN	23%
6		110%, rt	99%, 8:1	*exo*	-CON(Me)CO-		H	H	97%
				endo	H		H	-CON(Me)CO-	>90%
7		20%, rt	91%, 1:1.2	*exo*	HCO	Ph	H	Me	—
				endo	Me	Ph	H	CHO	—
8	PhCH=C(CN)$_2$	20%, rt	96%, 1.0:0	*exo*	NC	Ph	H	CN	—
				endo	NC	H	Ph	CN	—
9	DMAD	110%, rt	43%	—	CO_2Et	CO_2Et	C—C		—

[a] Molar percentage of $EtAlCl_2$ was used in the reaction

pot synthesis. To demonstrate this synthetic utility, tungsten−allyllic α,γ-diols are converted to their lactone derivatives, which are subsequently transformed into bicyclic α-methylene-γ-butyrolactones via $NOBF_4$-promoted intramolecular cyclization and air oxidation. Synthesis of bicyclic lactones based on this method is very efficient because each reaction step proceeds with high yields.

(ii-d) Cycloaddition Reaction. Although CpMo(CO)$_2$(π-*anti*-pentadienyl) undergoes [5+2]-cycloaddition with TCNE, the reaction is not useful because tetracyanoethylene is the only applicable electrophile.[92] Liebeskind recently reported[93] that TpMo(CO)$_2$(π-pyranyl) (Tp = hydridotrispyrazolylborate) complex underwent a very effiecient regio- and stereoselective [5+2]-cycloaddition with a variety of electron-deficient olefins to afford substituted π-oxabicyclo[3.2.1]octenyl complexes. The reaction protocol is shown in Table 8. Lewis acid $EtAlCl_2$ is required in the cycloaddition to generate a zwitterionic intermediate. In this manner, thermodynamically more stable *exo*-forms of oxabicyclic products are produced preferentially in most cases. High *exo*/*endo* ratios (>8.0) of products are observed for reactive olefins such as acrolein, methylvinyl ketone, and 2-cyclohexenone. The ratios are moderate or low for less reactive alkenes such as methyl acrylate and acrylonitrile. Entries 3, 4, and 6 demonstrate the use of (+)-TpMo(CO)$_2$(π-pyranyl) (ee = 97%) complex in the reaction; it reacts with methyl acrylate, cyclohexenone, and *N*-methylmaleimide (entries 3 and 4) to give oxabicyclic products with a high degree of enantiomeric excess (ee > 90%). The ee value is somewhat low (23% ee) in the case of acrylonitrile due to its low reactivity. A control experiment indicates that $EtAlCl_2$ slowly epimerizes the (+)-molybdenum−π-pyranyl complex to its racemic form. The prolonged reaction period and the use of a large amount of $EtAlCl_2$ are expected to yield products with low ee values. The mechanism of this unexpected epimerization is not rationalized at this stage.

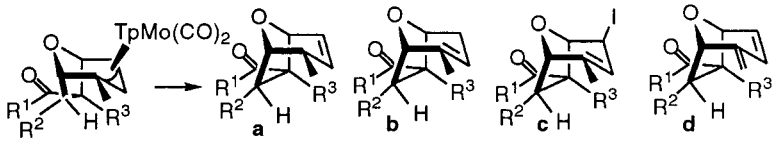
The resulting oxabicyclic allylmolybdenum complexes were demetalated in high yields by (i) treatment with strong acid or by (ii) oxidative demetalation with I_2 or Ce(IV). A summary of the yields of π-oxabicyclo[3.2.1]octenes is shown in Table 9. The action of strong acid on these three π-allyl complexes provided the major diastereomer **a**, an alkene resulting from protonation at the molybdenum center and reductive elimination to the more substituted terminal carbon of the π-allyl group. In such a protonation step, the control of reaction time was critical for complete conversion and good selectivity. Iododemetalation also proceeded in good yields with the use of I_2 and gave the allylic iodide product **c** having the most substituted double dond. Oxidative demetalation with ceric ammonium nitrate in the presence of a base gave dienes **b** as products (72−87%). Notably, the three demetalations give the products with the same level of ee values if chiral molybdenum−π-allyl complexes are used. Table 9 shows a good match of enantiopurities (96% ee) between the starting π-allyl complexes and the products from the three protocols.

IV. η^1-Propargyl Complexes

1. Preparation and General Feature

One important feature for propargylmetal complexes of borane, silane, stannane, titanium, and zinc is the presence of an equilibrium between the propargyl and allenyl species.[1] The position of this equilibrium is very important because it will affect the chemoselectivity in electrophilic addition reac-

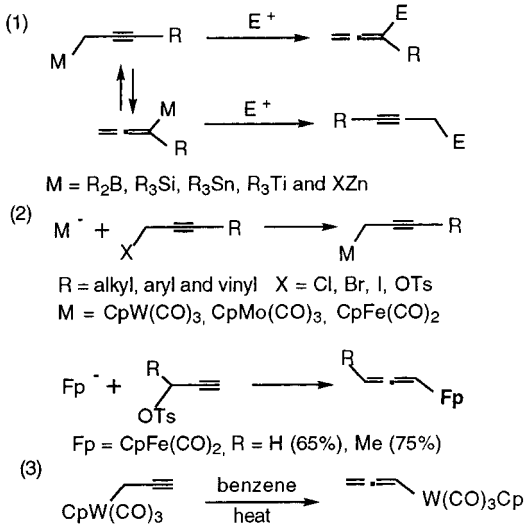
Table 9. Demetalation of Molybdenum−π-Cycloadduct



Mo-π-allyl exo	R^1	R^2	R^3	condn's	Product (yields)
rac-	$-(CH_2)_3-$		H	xsTFA, CH_2Cl_2, 20 min	86% (**a**/**b**=8.1)
	"		"	I_2, CH_2Cl_2, 2.5 min	**65%** (c)
	"		"	Ce(IV), THF/H_2O/Et_3N	**87%** (d)
97%ee	−N(Me)CO−		H	HCl, MeCN, 60°C, 20 h	100%(**a**/**b**=8.1, 97%ee)
	"		"	I_2, CH_2Cl_2, 2.5 min	**98%** (c)
	"		"	Ce(IV), THF/H_2O/Et_3N	**82%** (d)
rac-	H	Ph	Me	xsTFA, CH_2Cl_2, 20 min	89% (**a**/**b**>25)
	"	"	"	I_2, CH_2Cl_2, 4.0 min	**66%** (c)
	"	"	"	Ce(IV), THF/H_2O/Et_3N	**77%** (d)

tions. Propargyl and allenyl complexes of Fe(II), Mo(II), and W(II) species can be selectively prepared from propargyl halides and tosylates according to the procedures in Scheme 38 (eq 2).[94−97] In contrast with their main group analogues, these metal complexes do not show any sign of the propargyl and allenyl equilibrium, probably because the complexes are already in the most stable form. Unsubstituted tungsten−η^1-propargyl complexes are shown to undergo isomerization to the allenyl species upon heating in benzene; the mechanism involves a 1,3-shift of tungsten fragment according to a deuterium-labeling experiment.[98]

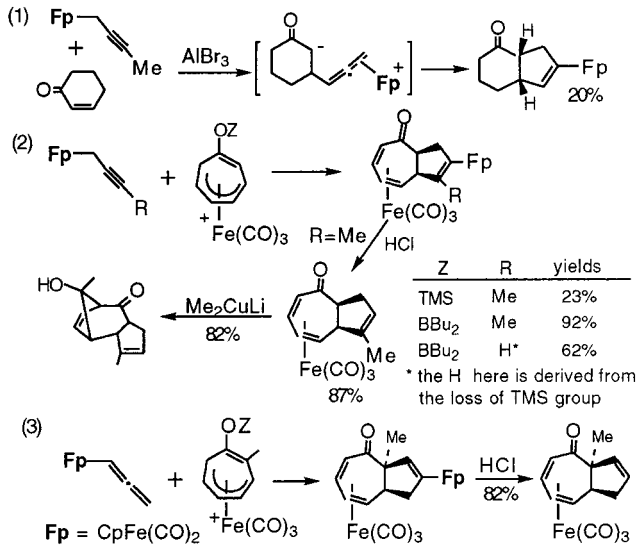
Scheme 38



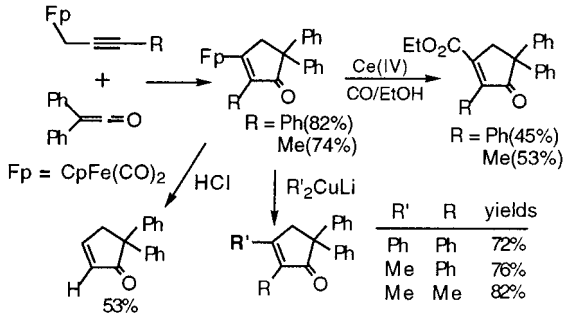
2. Cycloaddition with C=X Bonds.

A. Carbocyclic Compounds. Similar to its allyl complexes, iron−propargyl complexes also undergo [3+2]-cycloaddition with reactive alkenes to give iron−cyclopentenyl complexes.[14,15] Unfortunately, the adducts derived from the alkenes bearing mutliple CN, CO_2Me_2 and CF_3, groups are not useful in organic synthesis. Scheme 39 shows one instance for cycloaddition of iron−η^1-propargyl compound with cyclohexenone in the presence of $AlBr_3$; the adduct is obtained in only 23% yield.[69] The 1,2-shift of iron fragment in the bicyclic product suggests a zwitterionic intermediate involved in the mechanism (eq 1). The iron−propargyl compounds react with η^5-troponeiron salt to afford diiron−(η^4,$\eta^{1)}$-4-ketohydroazulenyl complex;[71] the yields depend on the activating group Z: 23% for Z = TMS group and 62−92% for Z = BBu_2 group. Hydrodemetalation of the diron−(η^4,η^1)-azulenyl (R = Me) complex via treatment with HCl cleaves the Fe−C bond of the adduct to give iron−η^4-4-ketoazulene complex in 87% yield. Interestingly, addition of Me_2CuLi to this iron−η^4-dienone species affords the tricyclic carbocyclic compound in 82% yield. [71c] Unsubstituted iron−η^1-allenyl complex shows a similar activity toward η^5-troponeiron salt to furnish the expected diiron−(η^4,η^1)-azulenyl species (eq 3). Treatment of this diiron species with HCl

Scheme 39



Scheme 40



produces iron−η^4-dienone complex in 82% yield. Removal of iron fragment from the Fe(η^4-dienone) in eq 2 can be conducted conveniently with Ce(IV) oxidation but it is not performed here.

The iron−η^1-propargyl complex reacts with ketene in a [3+2]-cycloaddition pathway to furnish iron−η^1-cyclopentenonyl compound (Scheme 40), and no Lewis acid is required here.[99] The iron−enonyl bond of this complex is cleanly cleaved by organocuprates R'_2CuLi to cause the replacement of iron fragment by R′ group to form a 2,3-disubstituted enone with good yields (72−82%). The cyclopentenone framework can be retained by demetalation using Ce(IV) salt or HCl. Oxidative carboxylation with $Ce(NH_4)_2(NO_3)_6$ produces 3-carboethoxy-2-cyclopentenone in moderate to good yields (46−53%) on a preparatively useful scale (2−4 mmol), and acid cleavage gives the protonated product in 53% yield.

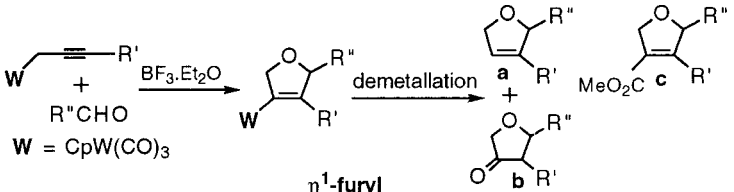
A. Heterocyclic Compounds

Propargylmetal complexes of silanes, boranes, stannanes, titanium, and zinc normally react with aldehydes to give allenyl alcohols exclusively.[1] These addition reactions often require Lewis acids as a promoter. A few cases are known for allenylsilanes which can undergo [3+2]-cycloaddition with aldehydes and imines to afford 1,2-dihydrofurans or -pyrroles. Propargylmolybdenum and -tungsten complexes prefer [3+2]-cycloaddition with aldehydes rather than addition reactions.[100−102] In the presence of $BF_3.Et_2O$, the cycloaddition proceeds smoothly to afford η^1-2,5-dihydrofuryl compounds in good yields (>85%) as shown in Scheme 41. The reaction does not proceed with ketone, epoxide, and unsaturated ketone in the intermolecular system. These η^1-2,5-dihydrofuryl species are transformed into η^1-2,5-dihydrofuran derivatives upon demetalation with $Me_3NO{\cdot}H_2O$ or by Ce(IV) oxidation. Hydrated $Me_3NO{\cdot}2H_2O$ is not effective for complete demetalation over a prolonged period. Use of $Me_3NO{\cdot}H_2O$ leads to hydrodemetalation to give mainly 2,5-dihydrofurans (51−60% yields) and 3-oxo-2,5-dihydrofuran as byproducts (11−13%). Demetalation with anhydrous Me_3NO and pyridine oxide gives 2,5-dihydrofurans and 3-oxo-2,5-dihydrofurans in nearly 1:1 ratio. Oxidation of tungsten−η^1-2,5-dihydrofuryl species by $Ce(NH_4)_2(NO_3)_6$ in a CO/MeOH mixture affords 3-carbomethoxy-2,5-dihydrofurans in fair yields (52−56%).

The propargyltungsten complexes also form 2,5-dihydropyrrole[103] in the reaction with *N*-tosylimines and $BF_3{\cdot}Et_2O$; the yield is 75%. Similar to the aldehyde adduct, use of $Me_3NO{\cdot}H_2O$ in demetalation gives the 2,5-dihydropyrrole **a** and 3-oxodihydropyrrole **b** in 51% and 36% yields, respectively. Ce(IV) oxidation in MeOH/CO affords the 3-carbomethoxy-2,5-hidydropyrrole in 37% yield. Bicyclic-2,5-dihydrofurans can be prepared[104] from intramolecular [3+2]-cycloaddition of tungsten−propargyl species bearing a tethered aldehyde, and the protocol is shown in Scheme 43. Metal anions $CpW(CO)_3Na$, $CpFe(CO)_2Na$, and $Re(CO)_5Na$ are used to examine their kinetic differentiation toward the substrate, and it is desired that the metal anion reacts more facily with propargylbromide rather than aldehyde. The resulting propargylmetal complexes were extracted with diethyl ether and subsequently treated with $BF_3{\cdot}Et_2O$ to induce cyclizations. Among the three metal anions, $CpW(CO)_3Na$ gives the best result to afford a 57% yield of η^1-2,5-bicyclic furyanyl product. Ce(IV) oxidation of this bicyclic organometallic produced the bicyclic unsaturated ester in 46% yield.

The scope of intramolecular [3+2]-cycloaddition is shown in Table 10. Two classes of substrates are used for the cycloadditions: propargyl bromides with a

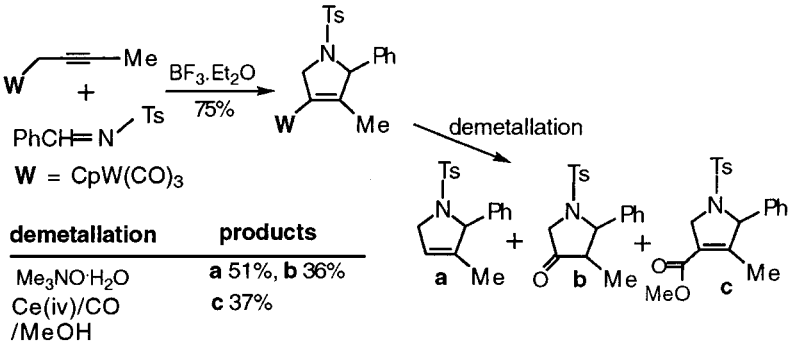
Scheme 41



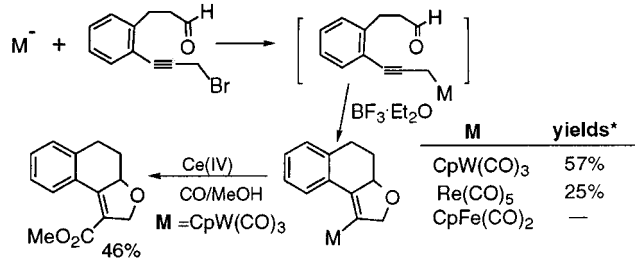
entries	propargyl	R"CHO	η^1-furyl (yields)[a]	demetallation	(yields)[b]
1	R' = Ph	R" = Et	90%	$Me_3NO{\cdot}H_2O$	**a** 58%, **b** 11%
2	"	"		Me_3NO	**a** 35%, **b** 32%
3	"	"		pyridine-oxide	**a** 32%, **b** 34%
4	R' = vinyl	R" = Me_2CH	85%	$Me_3NO{\cdot}H_2O$	**a** 60%, **b** 12%
5	R' = vinyl	R" = Ph	91%	$Me_3NO{\cdot}H_2O$	**a** 60%, **b** 13%
6	"	"		Ce(IV)/CO/MeOH	**c** 56%
7	R' = ≡—Ph	R" = Ph	80%	$Me_3NO{\cdot}H_2O$	**a** 51%
8	"	"		Ce(IV)/CO/MeOH	**c** 52%

[a] Yields are calculated based on alkynyltungsten complexes. [b] Yields are calculated based on η^1-furyl complexes.

Scheme 42

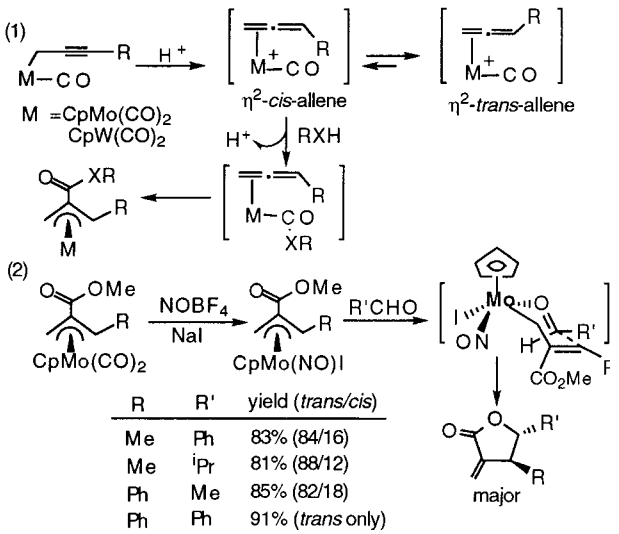


Scheme 43



Yields are calculated based on bromo-propargyl substrate.

Scheme 44



tethered aldehyde (entries 1−7) or a tethered ketone group (entries 8−10). In most cases, Lewis acids such as $BF_3.Et_2O$ or $LiClO_4$ are added to the diethyl ether solution of propargyltungsten compounds that were previously extracted from the reaction mixtures of $CpW(CO)_3Na$ and bromopropargyl substrate. No Lewis acid is required for synthesis of five-membered carbocycles (entries 1 and 4). The cycloaddition proceeds well with the aldehyde and ketone groups, affording η^1-2,5-dihydrofuranyl species in moderate to good yields (40%-65%). The cyclizations are also applicable to the syntheses of five-, six-, and seven-membered carbocycles including those bearing functionalities such as a dioxolane or a triethylsiloxyl group. The tungsten η^1-2,5-dihydrofuranyl species are decomplexed with $(NH_4)_2Ce(NO_3)_6$ in CH_3OH/CH_2Cl_2 under a stream of CO (1 atm) to afford the bicyclic unsaturated esters in 50−65% yields in most cases. Demetalation of the [3.3.0]-bicyclic tungsten species (entry 4) with Ce(IV) oxidation fails to give the desired bicyclic furan, probably due to its highly strained structure.

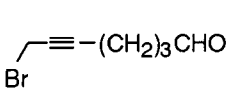
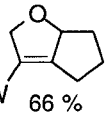
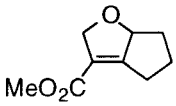
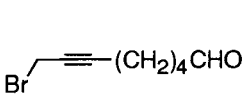
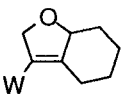
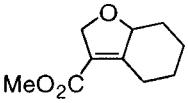
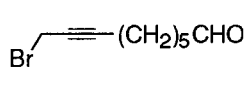
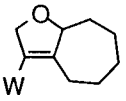
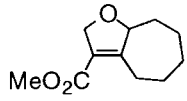
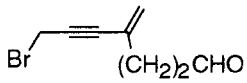
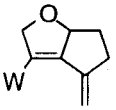
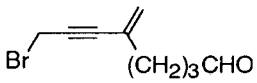
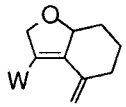
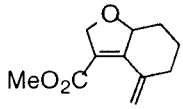
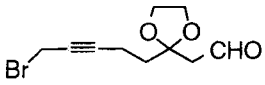
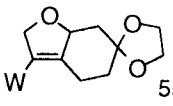
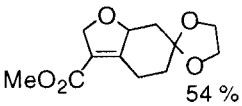
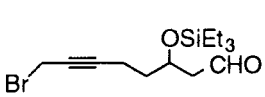
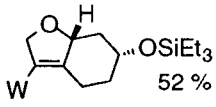
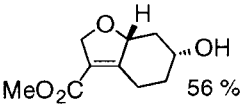
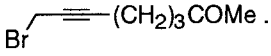
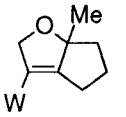
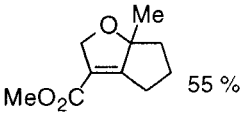
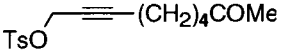
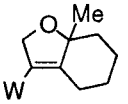
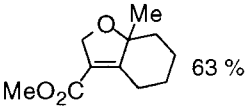
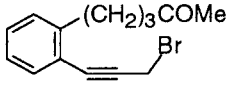
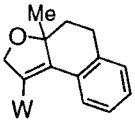
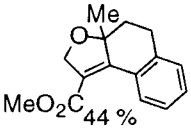
3. Alkoxycarbonylation of η^1-Propargyl Complexes

A. Synthesis of α-Methylene Butyrolactones

Protonation of propargylmetal complexes of Mo(II) and W(II) in cold diethyl ether forms the precipitate of metal−*cis*-η^2-allene cation as the kinetically favorable product (Scheme 44).[105] Treatment of this species with RXH (RX = HO, RO, RS, R_2N) in cold diethyl ether leads to formation of metal−*syn*-π-allyl complex,[106] the yields generally exceed 80%. This alkoxycarbonylation reaction fails to work with iron(II) complexes.[107,108] One major use of the resulting molybdenum−2-carbomethoxyallyl species is to provide a short synthesis of α-methylene butyrolactone.[109] In a standard procedure, the molybdenum−π-allyl species are sequentially treated with $NOBF_4$ and NaI in cold CH_3CN to form the $CpMo(NO)I(\pi$-allyl) derivative, which reacts in situ with aldehyde to give *trans*-γ-lactone preferably.[109] The *trans*/*cis* ratio of γ-lactones increases with increasing sizes of the R and R′ group, and the *trans*-selectivity is rationalized based on a chairlike transition state with R and R′ substituents on the equatorial sites. The tungsten species also give good yields of α-methylene butyrolactones following the same reaction sequence (vide infra).

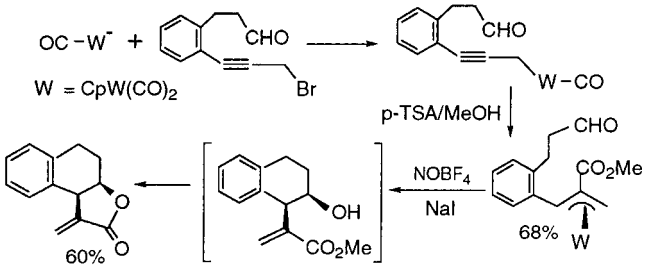
Bicyclic α-methylene butyrolactones are prepared efficiently via intramolecular coupling of molybdenum−[110] or tungsten[111]−η^3-2-carbomethoxyallyl complexes with tethered aldehydes or ketones. As shown in preceding sections, propargyl bromides with tethered aldehydes are good substrates for short synthesis of 2,5-dihydrofurans fused with five-, six-, and seven carbocycles based on propargyltungsten chemistry. The same substrates are utilized for the synthesis of bicyclic α-methylene butyrolactones as shown by an example in Scheme 45. The propargyltungsten complexes generated from $NaCpW(CO)_3$ and propargyl bromide are treated with *p*-toluenesulfonic acid (0.20 equiv) in MeOH to afford tungsten−π-2-carbomethoxy-allyl complexes in overall 68% yield in this two-step reaction. Sequential treatment of this π-allyl complex with $NOBF_4$ and NaI in cold

Table 10. Isolated Yields of Tungsten−η^1-2,5-dihydrofuryl Complexes and Fused 3-Methoxycarbonyl-2,5-dihydrofurans (W = CpW(CO)$_3$)

Entry	Substrate[a]	L. A.[b]	2,5-Dihydro-3-furyl	Unsaturated Ester
1		--	 66 %	 56 %
2		$LiClO_4$	 60 %	 58 %
3		$BF_3{\cdot}Et_2O$	 50 %	 55 %
4		--	 40 %	-----
5		$BF_3{\cdot}Et_2O$	 52 %	 50 %
6		$BF_3{\cdot}Et_2O$	 55 %	 54 %
7		$BF_3{\cdot}Et_2O$	 52 %	 56 %
8		$BF_3{\cdot}Et_2O$	 59 %	 55 %
9		$BF_3{\cdot}Et_2O$	 68 %	 63 %
10		$BF_3{\cdot}Et_2O$	 52 %	 44 %

[a] Equimolar ratios of CpW(CO)$_3$Na and organic substrates were used. [b] Lewis acid in equimolar proportions was used.

Scheme 45

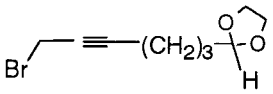
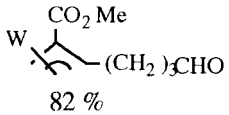
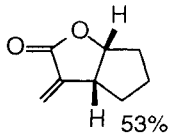
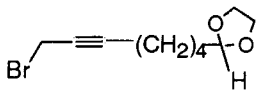
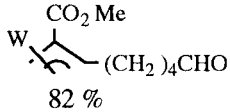
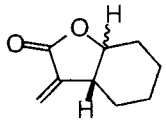
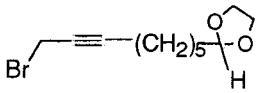
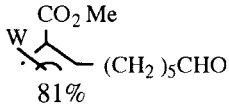
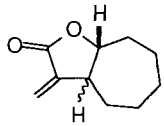
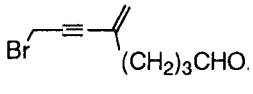
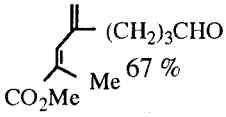
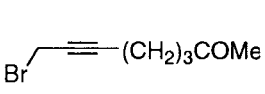
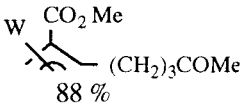
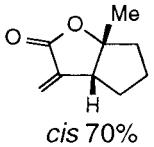
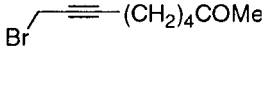
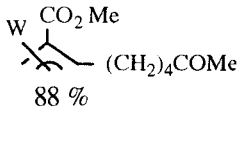
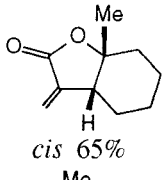
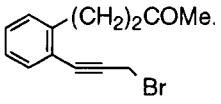
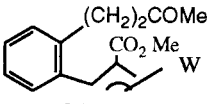
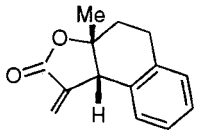
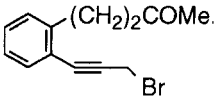
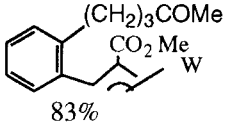
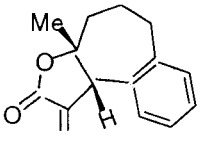


CH_3CN effects an intramolecular allylation to give *cis*-fused tricyclic α-methylene butyrolactone in 60% yield.

A series of the substrates is prepared and used for the synthesis of α-methylene butyrolactones fused with various sizes; the scope of reaction is shown in Table 11. Alkoxycarbonylation of these propargyl complexes proceeds smoothly, except for vinylpropargyltungsten complexes that suffer from hydrodemetalation of the allyl complex. This synthetic method is effective to obtain α-methylene butyrolactones fused with five-, six-, and seven-membered carbocycles. The reaction proceeds well with both tethered aldehydes and ketones. The stereoselectivities depend on the ring sizes and carbonyl groups. *Cis*-fused products are produced exclusively for five-membered carbocyclic compounds and also for the substrates bearing a ketone group (entries 5−6) and a fused phenyl group (entries 7−8). Control of the observed *cis*-stereoselectivities by ring sizes and functionalities is rationalized based on a bicyclic transition state structure via coordination of the carbonyl group to tungsten center.[110]

Common lactones can also be synthesized based on intramolecular alkoxycarbonylation of tungsten−alkynol complexes.[112,113] Scheme 46 shows the formation of tungsten−π-allyl complexes through treat-

Table 11. Isolated Yields of Tungsten−η^3-2-methoxycarbonylallyl Complexes and Fused α-Methylenebutyrolactones (W = CpW(CO)$_3$)

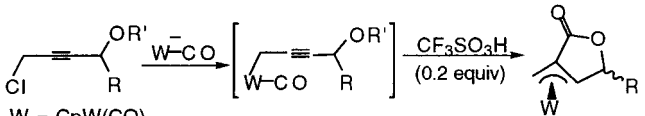
entry	substrate[a]	π-allyl [b,c]	α-methylene-butyrolactones[d,e]
1		 82 %	 53%
2		 82 %	 *trans* 36%; *cis* 15%
3		 81%	 *trans* 27%; *cis* 28%
4		 67 %	----
5		 88 %	 *cis* 70%
6		 88 %	 *cis* 65%
7		 84%	 *cis* 62%
8		 83%	 *cis* 56%

[a] Equimolar ratios of CpW(CO)$_3$Na and organic substrates were used. [b] These organometallic compounds were purified on a silica column. [c] Isolated yields after chromatographic purification. [d] Isolated yields after purification by preparative silica TLC. [e] Yields were estimated based on tungsten−allyl compounds.

ment of tungsten−alkynol species with CF_3SO_3H catalyst (0.20 equiv). A mixture of *syn*- and *anti*-isomers is produced from the alcohol substrate; separation of these isomers is unsuccessful by column chromatography. The *syn*-π-allyl diastereomers are produced selectively for the substrate having a tethered *tert*-butyldimethylsilyl group. The mechanism of the *syn*-stereoselection has been elucidated[112,113] by an isotopic oxygen-labeling study and by isolation of a reaction intermediate.

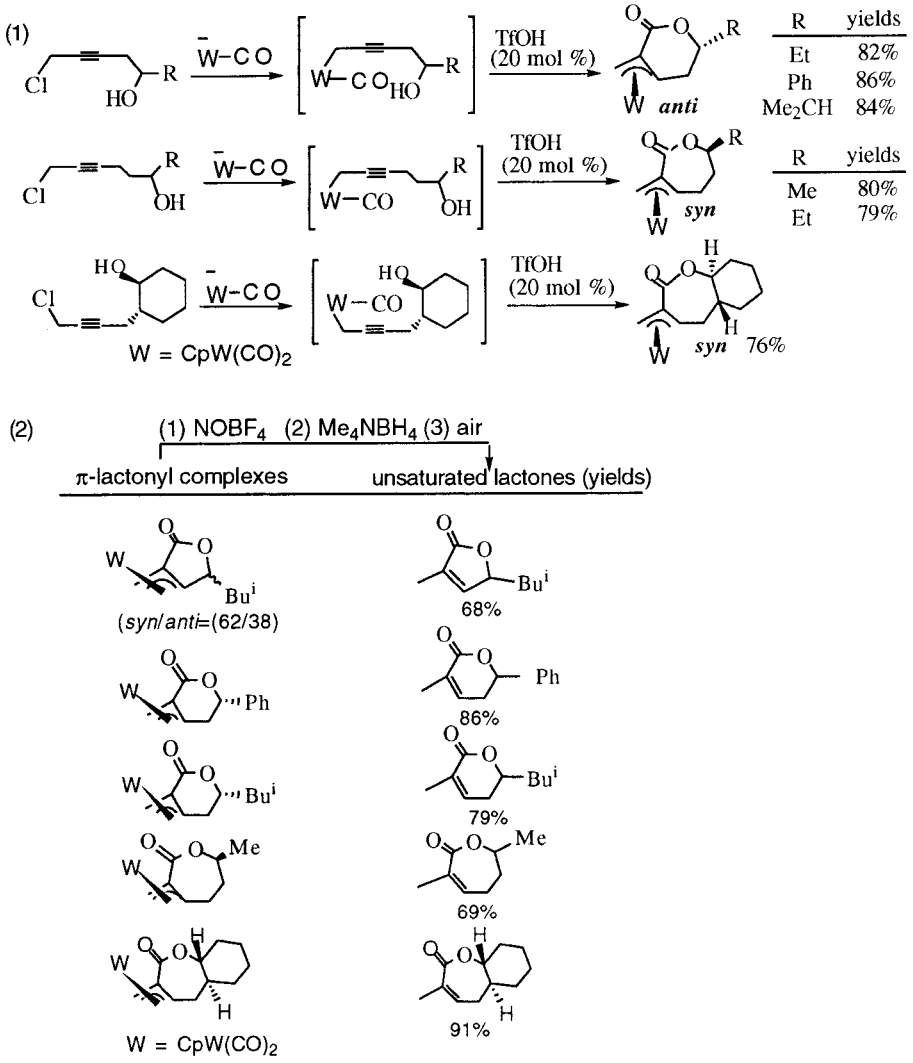
The acid-catalyzed cyclocarbonylation reaction can be extended to the synthesis of tungsten−π−δ and ϵ-lactonyl complexes with the use of 1-chloropent-2-yn-4-ols and 1-chlorohex-2-yn-5-ols as starting materials.[113] A Lewis acid catalyst (20 mol %) is employed

Scheme 46



propargyl chloride	π-lactone(*syn*/*anti*)	yields
R' = H		
R = Et	71/29	80%
i-Bu	62/38	81%
i-Py	49/51	80%
R' = $SiMe_2$(t-Bu)		
R = Me	***syn***	83%
Et	***syn***	82%
i-Bu	***syn***	81%

Scheme 47

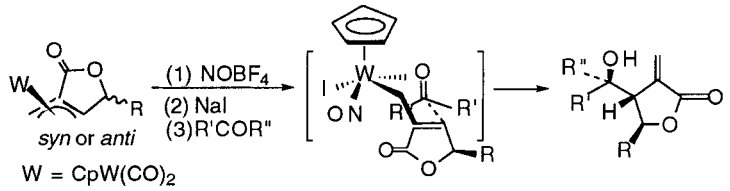


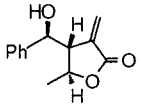
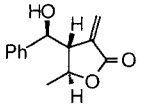
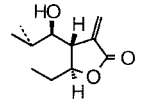
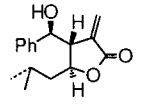
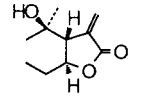
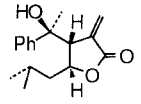
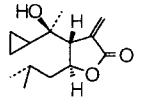
to promote the cyclizations, which proceed with excellent diastereoselectivities to afford only *anti*-π-allyl isomer for the six-membered ring and *syn*-π-allyl isomer for the seven-membered ring. Equation 1 shows an efficient example to construct a bicyclyc ϵ-lactonyl framework from the easily available chloropropargyl derivative, and the *syn*-π-allyl complex is obtained in 76% yield. The resulting π-allyl complexes are considered to be the less sterically hindered ones among the two possible π-allyl isomers. To demonstrate the use of such cyclocarbonylation reactions, the above π-lactonyl complexes are demetalated by treatment with $NOBF_4$ and Bu_4NBH_4 to give unsaturated lactones in good yields, and the results are summarized in Scheme 47. During the demetalation, the hydride attacks exlusively at the less substituted terminus of tungsten−allyl complexes to give furanone and pyranone derivatives exclusively. Such regiochemistry is very common for complexes of CpMo(NO)(CO)(π-allyl) cation.[28−29]

B. Synthesis of Functionalized α-Methylene Butyrolactones

Many naturally occurring compounds not only have an α-methylene butyrolactone unit but often bear an additional hydroxyl group, particularly in the family of sesquiterpenes.[114−117] α-Methylene butyrolactones comprising a homoallylic alcohol are the most frequently encountered. Stereocontrolled synthesis of such functionalized α-methylene butyrolactones has attracted considerable attentions.[118−121] A short synthesis of the compounds is easily achieved from preceding tungsten−π-lactonyl species.[113] Entries 1 and 2 in Scheme 48 show the use of the *syn*- or *anti*-$\pi-\gamma$-lactonyl complex for preparation of such functionalized γ-lactones. The *anti*-π-allyl complexes are selectively prepared from tungsten−η^1-vinylpropargyl complexes.[122] Notably, both π-allyl isomers afford the same functionalized α-methylene butyrolactone in condensation of their CoW(NO)I derivatives with benzaldehyde. This information suggests that these two isomeric species will have the same transition state in the allylation of aldehydes.[113] In this chair-like transition state, the C−C bond forming process preferably proceeds opposite to the R-substituent. Entry 3 shows the use of a mixture of *syn*- and *anti*-π-allyl complexes in the reaction, affording only one single diastereomeric product in 61% yield. The reaction also works for small organic ketones. Methyl ketone derivatives (entries 5−7) including acetone, phenyl methyl ketone, and cyclopropyl methyl ketone

Scheme 48



Entry	Allyl	R'COR"	Product	Yields
1	R = Me **syn**			60%
2	R = Me **anti**			61%
3	R = Et **syn+anti (71/29)**			61%
4	R = iBu **syn**			67%
5	R = Et **syn**			61%
6	R = iBu **syn**			60%
7	R = iBu **syn**			55%

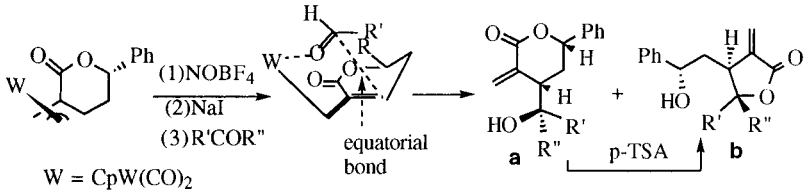
are also applicable to the reaction to give only one diastereomeric product in 55−61%. No condensation product is found for diethyl ketone.

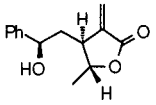
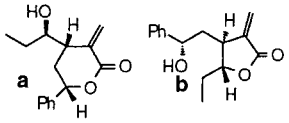
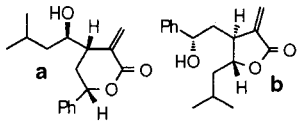
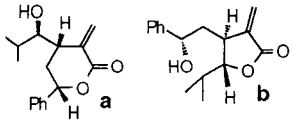
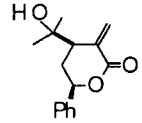
The preceding tungsten−η^3-δ-lactonyl complex is also useful for synthesis of α-methylene butyrolactones bearing a β-hydroxy carbon chain[113] following the same reaction sequence (Scheme 49). Condensation of the CpW(NO)I(π-allyl) derivatives of these complexes with aldehydes or acetone proceeds with excellent diastereoselectivities. Although two products are produced in this reaction, the primary product α-methylene δ-lactone (**a)** undergoes a facile acid-catalyzed transacylation reaction to yield its γ-lactone derivative (**b**) in quantitative yields. The stereochemical outcome of the product (**a**) is also rationalized based a bicyclic transition state with coordination of an organic carbonyl group to the tungsten center. In this transition state, addition of aldehyde to the ϵ-lactone ring proceeds preferentially from the equatorial position of the cyclohexenyl ring.[113] According to this model, a bulky phenyl group at the δ-lactonyl ring is required to enhance the reaction stereoselectivities.

Similarly, tungsten−η^3-ϵ-lactonyl complex can be extended to the synthesis of α-methylene butyrolactones bearing a γ-hydroxy carbon chain (Scheme 50).[113] In the condensation of their CpW(NO)I(π-allyl) derivatives with organic carbonyl groups, the expected seven-membered lactone appears to be unstable in the reaction medium and all of these species undergo transacylation reaction to form more stable α-methylene butyrolactone in 43−64% yields. Only one single diastereomer is found for bulky trimethylacetaldehyde and cyclopropylmethyl ketone, but the yields are relatively low 43−46%. Although benzaldehyde gives good yields of products, two diastereomers are formed. In this reaction sequence, the major diastereomer **a** is transformed into a triol derivative that has a better X-ray crystallinity for X-ray diffraction study, thus identifying the structure of **a**. The major diastereomer **a** is considered as a kinetically favored product because it is formed from the addition of aldehyde to the lactonyl ring on the same side with metal fragment.

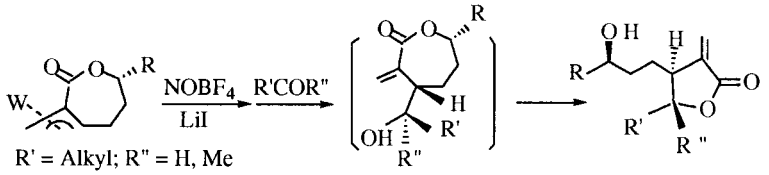
As chloropropargyl alcohols are the starting material for synthesis of functionalized α-methylene butyrolactones, these alcohols are readily prepared in enantiomerically pure forms. The above method provides an easy route to asymmetric synthesis of α-methylene butyrolactones as shown in Scheme 51. This chiral chloropropargyl chloride is conveniently prepared in several steps from D-(+)-xylose.[123] Trans-

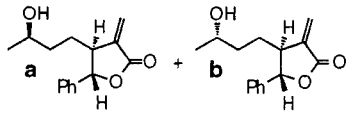
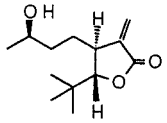
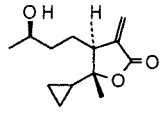
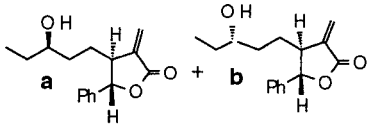
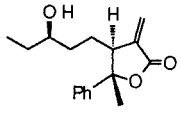
Scheme 49



Entry	R'COR"	Product	Yields(%)
1			68%
2			**a**(10%) **b**(58%)
3			**a**(20%) **b**(48%)
4			**a**(16%) **b**(51%)
5			57%

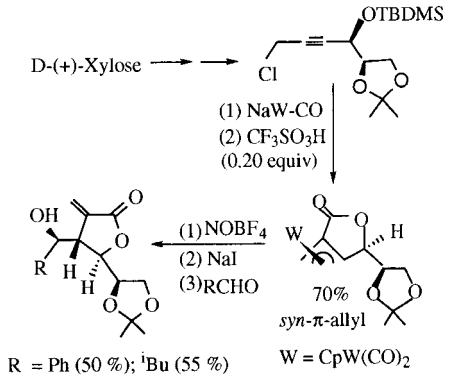
Scheme 50



Reagents	R'COR"	Products	Yield(%)
R = Me			64% (**a**/**b**=5.4)
R = Me			46%
R = Me			43%
R = Et			64% (**a**/**b**=5.3)
R = Et			58%

formation of this chiral chloropropargyl derivative into *syn*-π-allyl complex is achieved in 70% yield using the standard procedure.[113] In this transformation, the cyclocarbonylation reaction proceeds with

Scheme 51

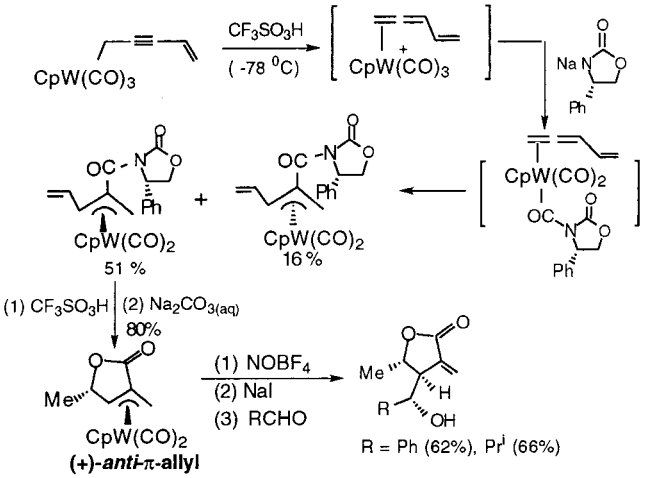


retention of stereochemistry in the C−O bond formation and the *syn*-selection of the tungsten−π-allyl bonding is controlled by the *tert*-butyldimethylsiloxyl group. Allylation of aldehyde with the CpW(NO)I(π-allyl) derivative of this dicarbonyl complex affords the optically active α-methylene butyrolactone in 50−55% yields (98% ee).[113] Again, aldehyde is added to the γ-lactonyl ring trans to the dioxlane substituent accompanied by generation of an *anti*-homoallylic alcohol.

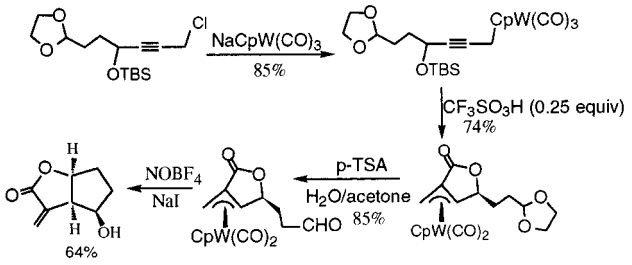
Use of chiral auxiliaries is an alternative approach for asymmetric synthesis of functionalized α-methylene butyrolactones.[124] Attempts to use chiral secondary alcohols such as (+)-menthol and (+)-neomenthol to induce enantioselective alkoxycarbonylation of vinylpropargyltungsten species are unsuccessful. The resulting products consist of 1:1 diastereomeric mixtures that are unseparable by fractional crystallization and column chromatography. (*S*)-4-Phenyl-2,5-oxazolidinone is found to be an effective chiral auxiliary for enantioselective aminocarbonylation of this propargyltungsten species to yield two diastereomeric products in 51% and 16% yields, respectively (Scheme 52). The major diastereomer is subsequently converted to chiral (+)-π-*anti*-allyl complex, ultimately preceding to α-methylene butyrolactones with good enantiopurity (ee = 93−94%).

Tungsten−π-allyl complexes are elaborated for stereocontrolled synthesis of *cis*-fused α-methylene butyrolactones bearing a homoallylic alcohol.[125] The synthetic protocol is shown in Scheme 53, which uses

Scheme 52



Scheme 53



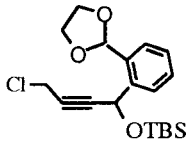
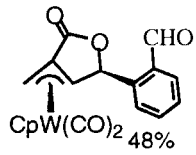
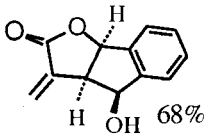
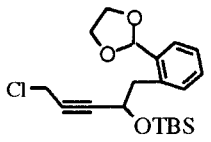
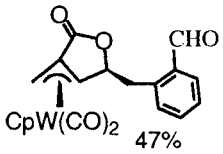
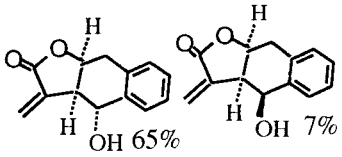
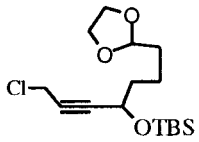
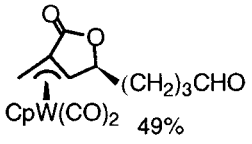
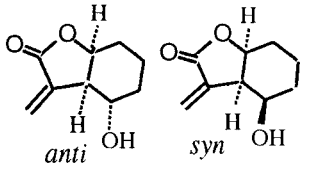
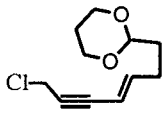
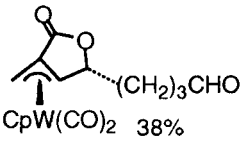
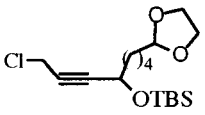
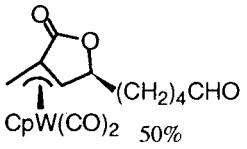
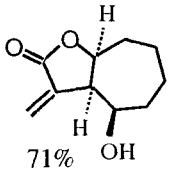
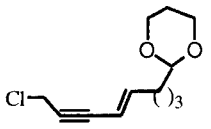
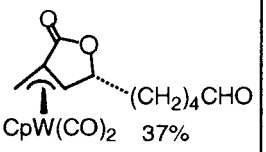
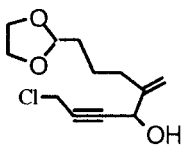
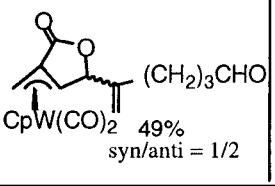
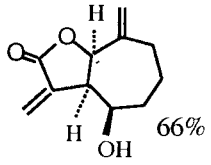
chloropropargyl substrates bearing an alcohol and an aldehyde. The whole reaction sequence comprises two key steps: (1) cyclocarbonylation of propargyltungsten complexes to form a *syn*-π-allyl complex and (2) intramolecular allylation of aldehyde using Faller's method. The two steps proceed with good yields and high diastereoselectivities. The resulting bicyclic α-methylene butyrolactone has a *cis*-fused ring bearing a *syn*-homoallylic alcohol. This information suggests that the reaction mechanism involves a tricyclic transition state with aldehyde coordinating to tungsten center. An open transition state is expected to yield *cis*-fused bicyclic lactone with an *anti*-homoallylic alcohol.[125] A semi-emperical calculation with the pm3(tm) using the program suit SPARTAN 5.0 suggests that the observed product has the lowest energy in its transition state among the four possible products.

Table 12 shows a variety of substrates for construction of α-methylene butyrolactones fused with five-, six-, and seven-membered carbocyclic rings. Entries 1−3 show the use of tungsten−π-*syn*-allyl complexes, which are presumbly easier to use to achieve a tricyclic transition state than their π-*anti*-allyl isomers because the tethered aldehyde and tungsten center are on the same side. The resulting five-membered carbocyclic compounds also has a *cis*-fused ring bearing a *syn*-homoallylic alcohol. Although the resulting six-membered ring products in entries 2 and 3 have the expected *cis*-fused rings, the alcohols have an *anti*-configuration as the major diastereomers. The minor diastereomers in these two cases have a *cis*-fused ring bearing a *syn*-homoallylic alcohol. In the case of a seven-membered ring (entry 5), the resulting product has a *cis*-fused ring with a *syn*-homoallylic alcohol. Although *anti*-π-allyl complexes seem to have difficulties to achieve a tricyclic transition state because the aldehyde chain and tungsten are on the opposite side, the species are still effective in the allylation reaction to give the same compositions of products such as their *syn*-isomers as shown in entries 4 and 6. The final case shows the use of a mixture of *syn*- and *anti*-allyl complexes for cyclization, affording only one diastereomer that has a *syn*-fused ring bearing a *syn*-alcohol. The *cis*-stereoselection can be rationalized by a tricyclic transition state mechanism that is also supported by a semi-emperical calculation.

C. Application to Natural Product Synthesis

The α-methylene butyrolactone bearing a homoallylic alcohol as shown in Scheme 48 is not only an

Table 12. Intramolecular Allylation of Tethered Aldehydes

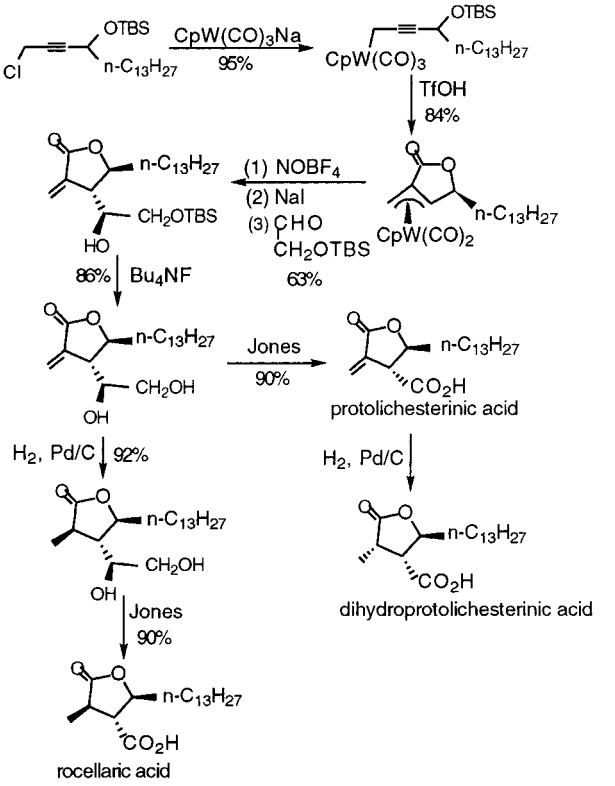
entry	substrates	π-allyl complexes	products and yields
1			
2			
3			
4			66% (*anti/syn*=10.1) 68% (anti/syn=9.9)
5			
6			69%
7			

important substructure for numerous natural products.[115,116] but also serve as an useful intermediate for natural product synthesis. Propargyltungsten compounds can provide a short synthesis of natural α-methylene butyrolactones including their enantiopure forms. Scheme 54 shows an efficient method[126] for total synthesis of natural monocyclic α-methylene butyrolactones such as the family of paraconic acids[127,128] including protolichesterinic acid, rocellaric acid, and dihydroprotolichesterinic acid. The synthetic protocol is based on organotungsten chemistry. There are two key steps in the synthesis: (i) intramolecular alkoxycarbonylation and (ii) condensation with $TBSOCH_2CHO$. The resulting functionalized α-methylene butyrolactones from the allylation reaction are treated with Bu_4NF and oxidatively cleaved by Jones reagent to afford protolichesterinic acid in good yield. Hydrogenation of protolichesterinic acid over Pd/C catalyst is shown to lead to dihydroprotolichesterinic acid. Similarly, rocellaric acid is also obtained in good yields from the γ-lactone bearing a diol group through sequential treatment with hydrogenation and Jones oxidation.

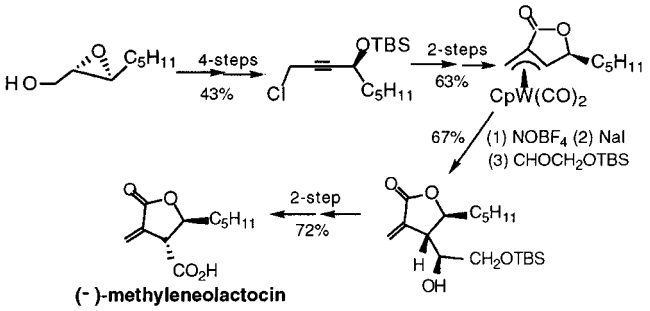
As chiral chloropropargyl alcohol is easily prepared from various synthetic methods, enantioselective synthesis of natural α-methylene butyrolactones can be achieved using organotungsten chemistry. Shown in Scheme 55 is an effcient synthesis[129] of natural (−)-methyleneolactocin[130−132] according to the same reaction sequence. This natural lactone is obtained in an overall yield of 30.4% and 96% ee based on the starting chiral chloropropargyl alcohol.

The same α-methylene butyrolactones are also useful for synthesis of naturally occurring bislactones such as (+)-dihydrocanadensolide,[133−134] (±)-avenociolide, and (±)-isoavenociolide.[135−138] Total syntheses of these three bislactones have attracted considerable attention because of their diverse and potent biological activities. Scheme 56 shows the use of organotungsten compound for asymmetric synthesis of (+)-dihydrocanadensolide.[139] The key chloropropargyl diol is prepared in high enantiopurity (ee 96%) by

Scheme 54

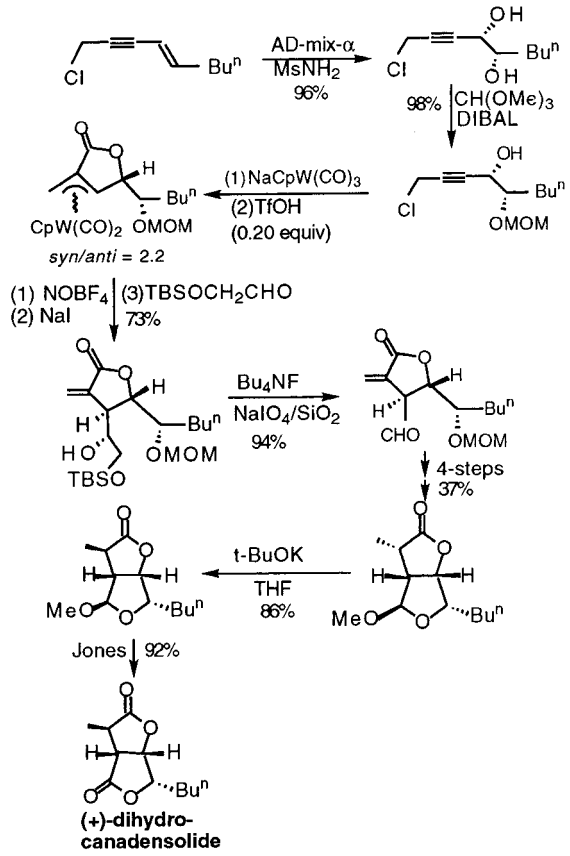


Scheme 55



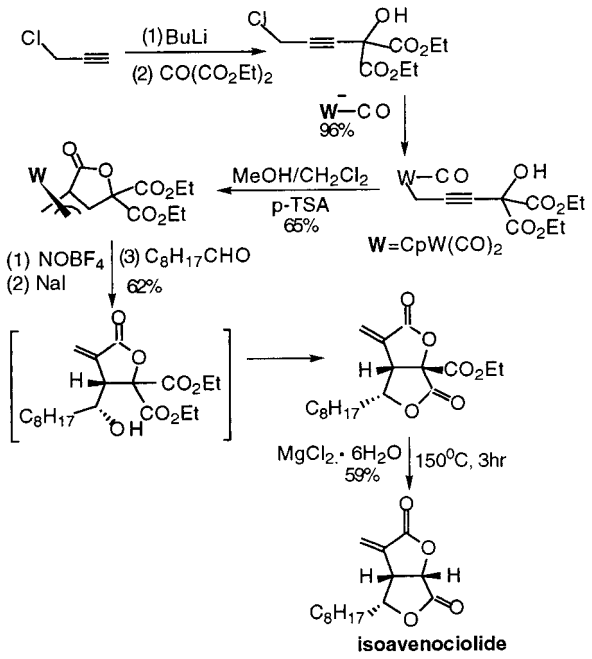
Sharpless asymmetric dihydroxylation of vinylpropargyl chloride. These chiral chloropropargyl species are employed for the synthesis of tungsten−π-allyl complexes through cyclocarbonylation reactions, and the products are obtained as a mixture of *syn*- and *anti*-π-allyl diastereomers. There is no need to separate the two isomers because their CpW(NO)I derivatives give the same diastereomeric product in the Faller's reaction.[30−32] Following a similar approach, the γ-lactone bearing a diol group is oxidatively cleaved to afford the aldehyde in 94%, finally proceding to a bicyclic lactol after a four-step transformation with an overall 34% yield. Use of this lactol for synthesis of (+)-dihydrocanadensolide proceeds smoothly following a base epimerization and Jones oxidation. One drawback of this methodology is the generation of *trans*-lactone in the aldehyde condensation. The *trans*-configuration of the product inevitably adds more steps to the synthesis in order to construct a fused [3.3.0]-bicyclic ring. Efforts to extend this method to the asymmetric synthesis of another natural bislactone, i.e., (+)-canadensolide, were unsuccessful.

Scheme 56

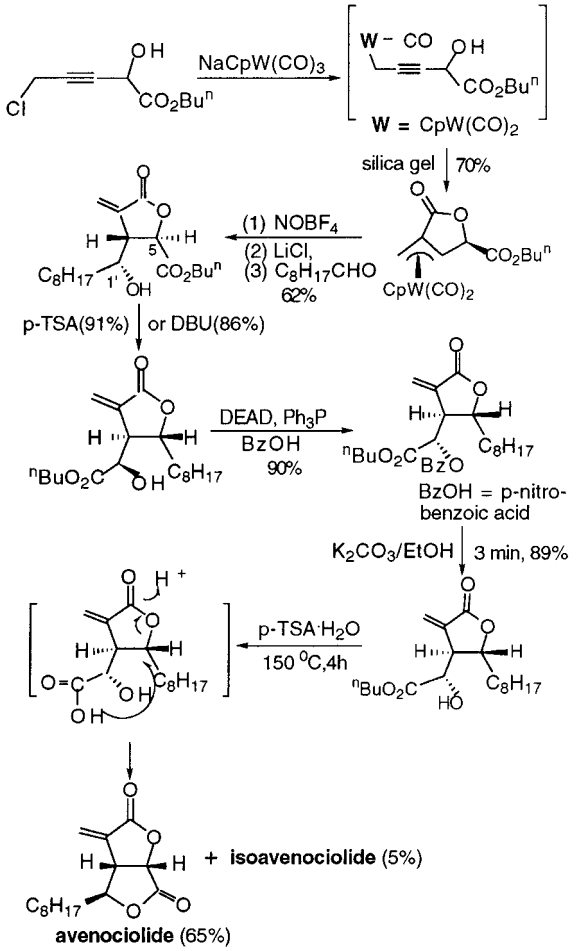


The most impressive accomplishment in the use of propargyltungsten compound is a three-step total synthesis of isoavenociolide[139,140] from the easily available chloropropargyl alcohol. The first two steps follow the standard procedures to give π-allyl complex in good yield. In this synthetic protocol, a malonate group is introduced onto the chloropropargyl substrate because this functional group effects a lactonization during condensation of tungsten−π-allyl complex with $C_8H_{17}CHO$, yielding a bicyclic lactone in 62% yield. Further heating of this bicyclic lactone with $MgCl_2$ at elevated temperatures leads to decarboxylation to afford isoavenociolide in 59% yield. The total synthesis of avenociolide using a propargyltungsten complex[139,140] is not as easy as those for isoavenociolide. As shown in Scheme 58, *trans*-α-methylene butyrolactone generated from the allylation with $C_8H_{17}CHO$ requires two inversions of stereochemistry at the C5 and C1′ carbons to complete the synthesis of avenociolide. Treatment of this *trans*-γ-lactone product with p-TSA or DBU fails to epimerize the C5 carbon but induces a transacylation reaction to yield another *trans*-α-methylene butyrolactone. Epimerization of the secondary alcohol of this new γ-lactone proceeds smoothly according to Mitsunobu reaction. Heating this Mitsunobu product with p-TSA·H_2O (p-TSA = *p*-toluenesulfonic acid) effects an intramolecular cyclization to afford avenociolide in 66% yield. In this transformation, the ester group of the γ-lactone is first hydrolyzed by TSA·H_2O to a free acid which subsequently attacks[135c,136] the lactonyl C5-carbon to accomplish the second inversion; this process is facilitated in the presence of Bronsted acid.

Scheme 57



Scheme 58



V. Conclusion

This review article has disclosed the construction of carbocyclic and heterocyclic frameworks from cyclopentadienyliron, -molybdenum, and -tungsten compounds comprising an allyl, propargyl, or alkynyl group. Compared to their main group metal analogues, considerable differences in reaction chemistry are observed between the two classes of metals, particularly for alkynyl- and propargylmetal complexes. We envision that these transition metal complexes are good complementary reagents to organometallic reagents of silanes, stannanes, boranes, and zinc. Several important classes of oxygen heterocycles can be efficiently synthesized with these transition metal complexes. Many reactions run by these complexes can be carried out on multigram scales and handled by routine operations.[46,83,91,113,126,129,139] The reliability of these reactions is manifested by application to the synthesis of natural products.

VI. Acknowledgment

The contribution of this laboratory to the development of alkynyl-, allyl-, and propargyltungsten compounds was supported by National Science Council, Taiwan. We thank our co-workers who are mentioned in the references.

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