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Olefin Metathesis by Molybdenum Imido Alkylidene Catalysts

Richard R. Schrock

Department of Chemistry 6-331, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139

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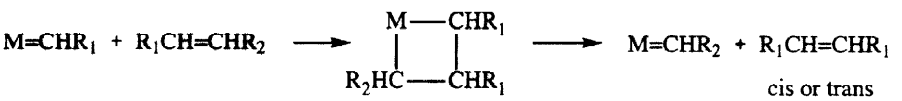
Abstract: A "well-defined" alkylidene complex of the type $Mo(CHCMe_2Ph)(N\text{-}2,6\text{-}i\text{-}Pr_2C_6H_3)[OCMe(CF_3)_2]_2$ has proven to be a useful initiator in catalytic olefin metathesis reactions of interest to organic chemists. A variety of related molybdenum imido alkylidene complexes can be prepared readily from a common precursor. This article is a summary of what is known about the details of the steps in a metathesis reaction catalyzed by complexes of the type $Mo(CHR')(NAr)(OR)_2$, and how the activity and stability of complexes of this type change upon altering each of the ligands in the pseudo-tetrahedral species. Some recent asymmetric ring-closing metathesis reactions are also discussed briefly.

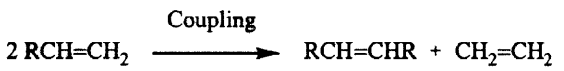
Olefin metathesis is a catalytic process whose key step is a reaction between an olefin and a transition metal alkylidene complex, usually M=CHR (equation 1) or $M{=}CH_2$, in a 2+2 fashion to give an unstable intermediate metalacyclobutane ring.[1] In the last several years two "well-defined" molybdenum catalysts have become



(1)

available commercially (from Strem Chemicals, Inc.) that have the formula $Mo(CHCMe_2Ph)(N\text{-}2,6\text{-}i\text{-}Pr_2C_6H_3)(OR)_2$ (OR = $OCMe_3$ or $OCMe(CF_3)_2$). That in which OR = $OCMe(CF_3)_2$ has been shown to be especially reactive in a variety of metathesis reactions.[2-7] In this paper I will discuss how this and related molybdenum catalysts are believed to function, in particular with respect to some processes of current interest in organic chemistry. Since such species are relatively reactive toward oxygen, water, and functionalities that contain relatively reactive protons, metathesis reactions must be carried out in an atmosphere of dinitrogen or argon using dry and pure solvents and substrates. In contrast, a later metal metathesis catalyst such as $Ru(CHPh)Cl_2(PR'_3)_2$[5,7-11] is more tolerant of water and oxygen, is significantly less active for a given substrate,[12] and the mechanism or mechanisms of its reactions are not as well-understood as the mechanism of the Mo catalysts.[13] In many circumstances, *e.g.*, formation of a trisubstituted or a tetrasubstituted double bond, the higher reactivity of Mo catalysts is required. In addition, enantiomerically pure Mo catalysts are now available and have been used successfully for asymmetric ring closing reactions, a topic that is discussed here, while equally successful Ru-based catalysts for asymmetric reactions have not yet been reported.

Several potentially useful types of metathesis reactions for monoolefins or diolefins are shown in equations 2 through 5. Perhaps the most interesting of these in the last several years has been the ring-closing metathesis (RCM) reaction (*e.g.*, equation 4);[5] the coupling reaction (equation 2) and its extension to oligomers and polymers (ADMET;[14-17] equation 3) are potential alternatives to RCM. Some cyclic olefins also can be opened



(2)

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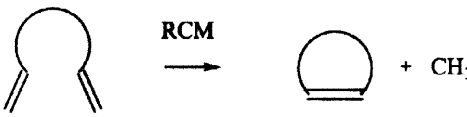
$$y\ CH_2{=}CH(CH_2)_xCH{=}CH_2 \xrightarrow{\text{ADMET}} \{CH(CH_2)_xCH\}_y + y\ CH_2{=}CH_2 \quad (3)$$



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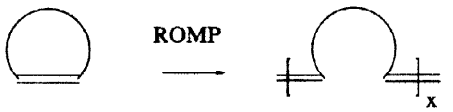
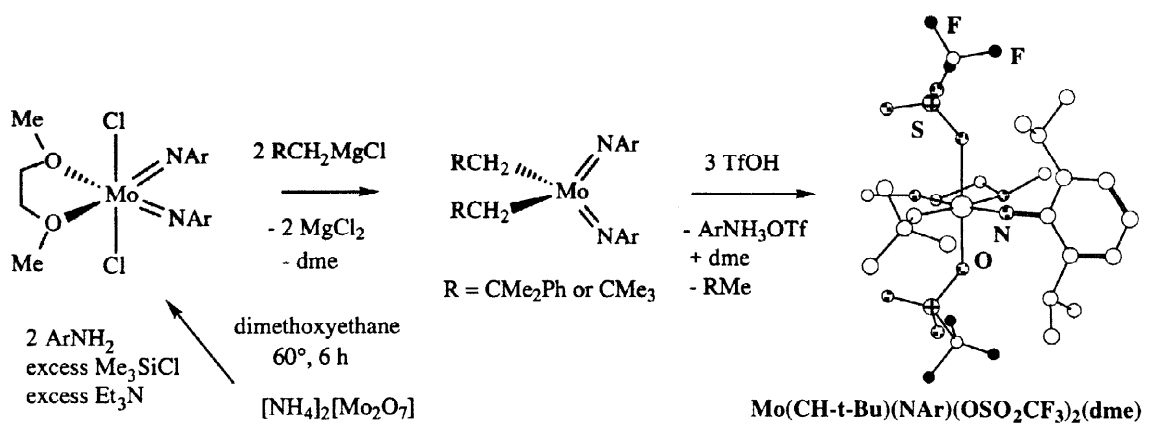


(5)

and oligomerized or polymerized (ring opening metathesis polymerization or ROMP;[1,18,19] equation 5), especially norbornenes and cyclobutenes. If one also considers that *cis* or *trans* olefins can be formed in any metathesis step, that all possible alkylidenes can form ($M{=}CH_2$, M=CHR, and $M{=}CR_2$, if applicable; see also the discussion of rotamers later), that alkylidenes and olefins can vary by many orders of magnitude in their reactivity, and that all reactions are reversible to a greater or lesser extent, then the potential complexity of even a superficially simple metathesis reaction becomes apparent.

Initiator Synthesis and Stability

A variety of molybdenum complexes of the type $Mo(CHR')(NAr)(OR)_2$ can be synthesized by treating $Mo(CHCMe_2Ph)(NAr)(triflate)_2(dme)$ (Scheme 1) with the desired alkoxide.[20,21] The "universal precursor," $Mo(CHCMe_2Ph)(NAr)(triflate)_2(dme)$, can be synthesized on a relatively large scale and can be stored indefinitely at room temperature under an inert atmosphere. The availability of a given imido (NAr) group in the final catalyst depends upon whether the imido group in question can be carried through the three steps shown in Scheme 1. Although some variations of the imido's substituent have been successful (*e.g.*, 2-t-BuC_6H_4, 2-i-PrC_6H_4, 2-PhC_6H_4, 2-$CF_3C_6H_4$, 1-adamantyl),[22-24] sterically bulky 2,6-disubstituted aryl imido ligands (2,6-$Me_2C_6H_3$ or 2,6-i-$Pr_2C_6H_3$) have given rise to the most successful catalysts so far. The triflate complex in which Ar = 2,6-diisopropylphenyl currently is available commercially (from Strem Chemicals, Inc.), so a variety of dialkoxide complexes that contain this relatively successful imido group can be prepared, potentially even *in situ*.



Scheme 1. Synthesis of $Mo(CHCMe_2Ph)(NAr)(triflate)_2(dme)$.

The first metathesis catalysts of the general type $M(CHR')(NAr)(OR)_2$ contained tungsten,[25] and many studies have employed tungsten.[21] The structure of $W(CHPh)(NAr)[OCMe(CF_3)_2]_2$ shown in Figure 1, the product of a metathesis reaction between $W(CH\text{-}t\text{-}Bu)(NAr)[OCMe(CF_3)_2]_2$ and styrene, is typical of a pseudo-tetrahedral complex in this category.[26] It should be noted that the phenyl group lies in the C-W-N plane and points toward the imido nitrogen, the W-N-C_{ipso} angle is essentially linear, and the plane of the aryl ring is perpendicular to the C-W-N plane. However, molybdenum complexes currently are preferred over tungsten complexes for a variety of reasons: (i) molybdenum complexes are synthesized more easily; (ii) tungsten is several times more expensive than molybdenum; (iii) molybdenum is believed to be more tolerant of functionalities such as the carbonyl group; (iv) molybdacyclobutane complexes are much less stable than tungstacyclobutane complexes and unsubstituted metalacyclobutane complexes therefore are less often "sinks" in which the metal can be sequestered in an inactive form.

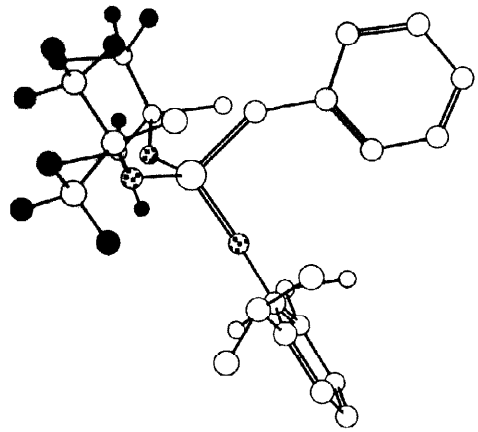


Figure 1. The X-Ray Structure of $W(CHPh)(NAr)[OCMe(CF_3)_2]_2$.

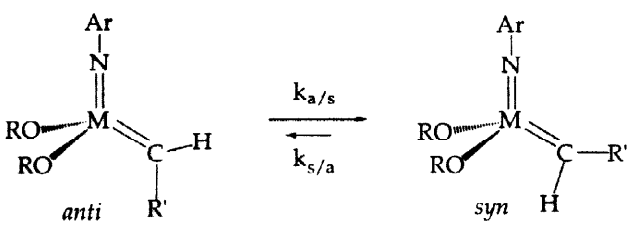
It is important to note that $Mo(CHR')(NAr)(OR)_2$ complexes are electron deficient 14 electron species. (The lone pair on the imido nitrogen is included in the electron count, since a Mo-N-C_{ipso} angle that approaches 180° implies that the imido ligand donates its π electrons to the metal.) Therefore $Mo(CHR')(NAr)(OR)_2$ complexes would react bimolecularly with themselves in a variety of ways, among them ligand redistribution reactions, if they were not prevented from doing so for steric reasons. Bimolecular reactions are discouraged if potentially bridging ligands (which include all three types of ligands in the complex) are sterically protected. Therefore it is imperative that the NAr ligand, the OR ligands, and at least the initial alkylidene all be relatively bulky in order to isolate an initiator. For this reason neopentylidene and the cheaper neophylidene ligand are employed, since these alkylidenes generally yield stable, isolable, pseudo-tetrahedral species, as long as the NAr and OR groups themselves are relatively bulky.

Catalyst Stability and Reactivity as a Function of the Alkylidene

Although the NAr and OR groups are permanently bound to the metal throughout a successful metathesis reaction, the nature of the alkylidene changes as metathesis proceeds, and consequently the reactivity and stability of intermediates in the catalytic cycle usually change dramatically. Perhaps the most important intermediate to consider is a methylene complex. Few methylene complexes can be isolated, or even observed in solution by NMR methods, in part because they are the most reactive alkylidenes, and consequently also the most susceptible toward bimolecular decomposition reactions.[27] Although experimental data are not yet available, irreversible decomposition of methylene species may turn out to be the major mode of decomposition in many metathesis reactions, so that activity steadily decreases as the reaction proceeds, unless the reaction is highly dilute (which is, in fact, sometimes the case). In this context it would be highly desirable to develop a supported, but still well-defined (*i.e.*, tethered) catalyst, one in which bimolecular decomposition of methylene intermediates is virtually absent. Mo=CHR' species are much less reactive than $Mo{=}CH_2$ species, while $Mo{=}CR'_2$ species are the least reactive by far. Unfortunately, few hard numbers are available, in part because relative reactivities depend upon the olefin substrate in question, but also because determining the reactivities of

Mo=CHR' species is complicated by the presence of rotamers, as is discussed immediately below. It should be clear that whether ethylene is removed rapidly, slowly, or not at all from a metathesis reaction could dramatically alter the course and/or rate of the desired reaction, as ethylene is the most reactive of the common substrates, and a methylene complex is generated when ethylene reacts with an alkylidene complex. The importance of an ethylene atmosphere versus an atmosphere of dinitrogen or argon in one type of ruthenium-catalyzed metathesis reactions has been documented in the literature.[28,29]

Two Mo=CHR' rotamers are possible as a consequence of the fact that the d orbital that is employed for π bonding of the imido ligand to the metal is the one that lies in the N-M-C plane. Therefore the alkylidene must lie in the N-Mo-C plane and two rotamers (*syn* and *anti*; equation 6) are possible. X-ray and solution studies reveal that in most cases the most stable form, and often the only observable form, is the *syn* form (see also Figure 1). The *syn* form can convert into the *anti* form either by rotation of the alkylidene about the M=C bond, or as a consequence of a reaction with an olefin in a metathesis step. It turns out that *syn* and *anti* forms can have dramatically different reactivities, a fact that complicates our predicting the course of a given metathesis reaction if both forms can be present during the metathesis process.

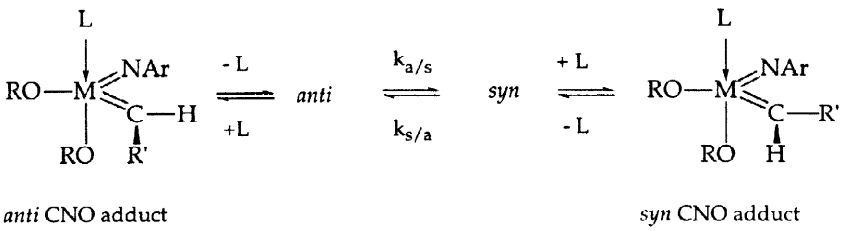


(6)

The Alkoxide Effect, Rotamer Interconversion, and Adducts

The electron withdrawing ability of an alkoxide ligand in a given alkylidene complex is one of the most important determinants of reactivity. In general, the more electron withdrawing the alkoxide, the more electrophilic the metal, and the more active the catalyst, *i.e.*, the $OCMe_3$ catalyst is much less reactive than the $OCMe(CF_3)_2$ catalyst. The effect on the metal of changing the alkoxide from $OCMe_3$ to $OCMe(CF_3)_2$ is enormous, especially since two alkoxides are present. In both the $OCMe_3$ and $OCMe(CF_3)_2$ catalysts only the *syn* rotamer is readily observable in solution by proton or carbon NMR.

Adducts of $M(CH\text{-}t\text{-}Bu)(NAr)(OR)_2$ (Ar = 2,6-i-$Pr_2C_6H_3$; OR = $OCMe_3$ or $OCMe(CF_3)_2$) complexes were employed as models for the initial olefin adduct in an olefin metathesis reaction,[30] but these studies also gave rise to some early information concerning rotamers. For example, PMe_3 was found to attack the CNO face of *syn*-$M(CH\text{-}t\text{-}Bu)(NAr)[OCMe(CF_3)_2]_2$ to give first a *syn*-TBP species in which the phosphine is bound in an axial position (equation 7; Figure 2). It should be noted that this adduct is chiral and that the opposite enantiomer would be the result of addition of the phosphine to the other CNO face in a pseudo-tetrahedral $M(CH\text{-}t\text{-}Bu)(NAr)[OCMe(CF_3)_2]_2$ complex, which corresponds basically to addition of the phosphine to the



(7)

anti CNO adduct

syn CNO adduct

other side of the M=C bond. The base is bound to the metal most strongly when the alkoxide is electron-withdrawing, so that adducts are isolable only when OR = $OCMe(CF_3)_2$, not when OR = $OCMe_3$. The *syn* rotamer is formed initially when OR = $OCMe(CF_3)_2$ since it is virtually the only one present ($K_{eq} \approx 10^3$), the phosphine is bound relatively strongly, and, as was shown later (see below), the rate of conversion of the phosphine-free *syn* rotamer to the *anti* rotamer when OR = $OCMe(CF_3)_2$ is relatively slow ($k_{s/a} \approx 10^{-5}$ s^{-1}). With time, however, the *anti* adduct forms in the absence of olefin via loss of PMe_3 from the *syn* adduct, followed by slow rotation of the alkylidene to give unobservable *anti*-M(CH-*t*-Bu)(NAr)$(OR)_2$, and trapping of the apparently more reactive *anti* form by PMe_3. The adduct of the *syn* rotamer is believed to be less stable than the adduct of the *anti* rotamer because steric interaction develops between the R' substituent (the t-butyl group in Figure 2) in the *syn* alkylidene and the isopropyl groups on the aryl ring of the NAr ligand, which lies in the trigonal plane in the adduct.[30] Several theoretical studies have concluded that an olefin should add to a CNO face of a catalyst.[31-37] They also have suggested that the stability of the base-free *syn* form compared to the base-free *anti* form can be attributed in part to an "agostic" interaction[38] of the alkylidene C-H_α electron pair and the metal in the *syn* rotamer,[39] one that is not possible in the *anti* rotamer. The fact that a two electron donor can bind strongly to an electrophilic, reactive alkylidene suggests that the most electrophilic catalysts may not be the most desirable in the presence of certain relatively Lewis basic functionalities. It should be noted that at least three out of four ligands in a M(CH-*t*-Bu)(NAr)$(OR)_2$ complex at any given time contribute to a crowded pseudo-tetrahedral coordination sphere. Therefore a typical basic donor ligand (nitrile, ester, etc.) is likely to be labile to some degree, and metathesis activity therefore possible, although a strongly coordinated base (*e.g.*, pyridine) can virtually block reactivity at room temperature.

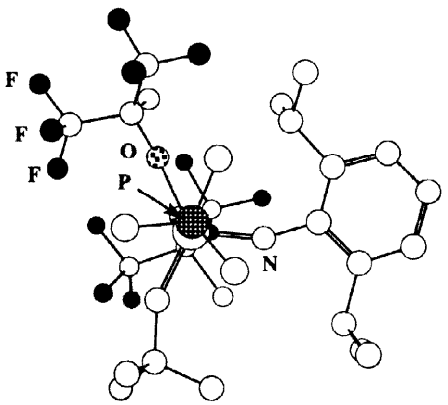
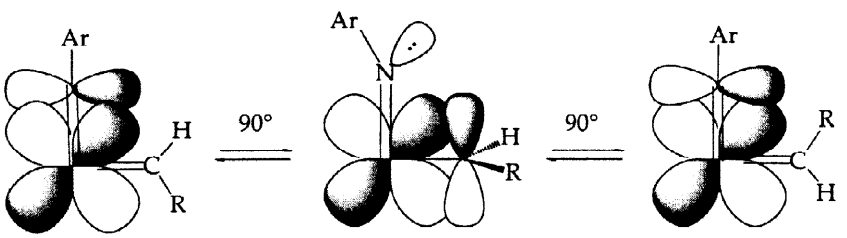


Figure 2. X-ray Structure of Mo(CHCMe3)(NAr[OCMe(CF3)2]2(PMe3).

A detailed investigation of alkylidene rotation rates in Mo$(CHCMe_2Ph)(NAr)(OR)_2$ complexes (where OR = $OCMe_2(CF_3)$, $OCMe(CF_3)_2$, $OC(CF_3)_3$, or $OC(CF_3)_2(CF_2CF_2CF_3)$)[40,41] revealed that values for $k_{a/s}$ varied by up to six orders of magnitude (at 298K), the smallest values for $k_{a/s}$ being found in complexes that contain the most electron-withdrawing alkoxides, while equilibrium constants ($K_{eq} = k_{a/s}/k_{s/a}$) at 25°C varied by only two orders of magnitude at most. Values for $k_{s/a}$ at 298K could be calculated from $k_{a/s}$ and K_{eq} and found to vary by up to six orders of magnitude in the same general direction as $k_{a/s}$. The main conclusion was that the rate of interconversion of *syn* and *anti* rotamers was "fast" for *t*-butoxide complexes ($k_{s/a} \approx 1$ sec^{-1} at 298 K), but "slow" for hexafluoro-*t*-butoxide complexes ($k_{s/a} \approx 10^{-5}$ sec^{-1} at 298 K). The intermediate in which the



anti *syn* (8)

alkylidene has rotated by 90° can be stabilized by the d orbital involved in π bonding of the imido ligand to the metal, so the imido ligand must give up its π bond and bend in the transition state (equation 8). The ease of alkylidene rotation therefore varies significantly with the nature of the imido ligand. For example, although there is little difference between the rates of alkylidene ligand rotation in hexafluoro-*t*-butoxide complexes that contain N-2,6-i-$Pr_2C_6H_3$ or N-2,6-$Me_2C_6H_3$ ligands, the alkylidene ligand in an analogous N-2-*t*-BuC_6H_4 complex rotates ~1500 times faster, *i.e.*, the unsymmetrically substituted phenylimido ligand can bend more easily in the ground state, thereby making the transition state shown in equation 8 more readily accessible.

It is interesting to note that in alkylidene complexes that contain phenoxide ligands (*e.g.*, O-2,6-$Me_2C_6H_3$, biphenolates, and binaphtholates - see later), the energy difference between *syn* and *anti* rotamers is lower, as is the barrier to their interconversion. In several cases *syn* and *anti* rotamers are both observable and have been found to *interconvert rapidly on the NMR time scale* (~100 s^{-1}) at room temperature. Phenoxide complexes have been studied little, although the data which are available suggest that they can be nearly as reactive as the $OCMe(CF_3)_2$ complex. However, determining the reactivity of a given alkylidene complex requires that we have intimate knowledge of the rate of alkylidene interconversion, as well as the reactivity of "pure" *syn* and *anti* rotamers.

The reactivity difference between *anti* and *syn* Mo(CH-t-Bu)(NAr)$[OCMe(CF_3)_2]_2$ species toward 2,3-$(CF_3)_2$norbornadiene was estimated to be ~10^5, with the *anti* rotamer, the one that is present in only low concentration, being the most reactive.[41] Since *syn* and *anti*-Mo(CH-t-Bu)(NAr)$(OCMe_3)_2$ interconvert readily (~1 s^{-1}), the difference in reactivity could not be documented for the $OCMe_3$ species. Relative reactivity will also depend on the monomer, the alkylidene, and possibly also the imido ligand, so we cannot be certain that the *anti* rotamer will always be as many as five orders of magnitude more reactive than the *syn* rotamer. It is important to note that the *syn* rotamer *may* react with an olefin. For example, in the $OCMe(CF_3)_2$ catalyst it is believed to be the *syn* rotamer that reacts exclusively with 2,3-$(CF_3)_2$norbornadiene; in the $OCMe_3$ catalyst the *anti* rotamer is believed to react exclusively with 2,3-$(CF_3)_2$norbornadiene to give a *syn* product, but that the *syn* rotamer is then transformed into the *anti* rotamer faster than it reacts with monomer. The presence of Mo=CHR' rotamers with greatly different reactivities complicates attempts to understand in detail the steps in a given metathesis reaction, especially when the rotamers interconvert rapidly.

All of what has been discussed so far concerning rotamers will depend upon the reactivity of the olefin or olefins in question, as the magnitude of the rate constant for reaction of a given alkylidene with various olefins is likely to span several orders of magnitude. A dramatic illustration of the degree to which the monomer itself can be a factor in determining which rotamer will be involved in a metathesis reaction were revealed in studies of the exceedingly slow polymerization of 1,7,7-trimethylbicyclo[2.2.1]hept-2-ene by Mo$(CHCMe_2Ph)(NAr)(OCMe(CF_3)_2]_2$. Careful studies showed that under some conditions conversion of a *syn* to an *anti* rotamer is the *rate limiting step* in this reaction,[42-45] *i.e.*, only the *anti* rotamer will react with this particular norbornene; presumably steric factors severely limit the rate of reaction of this particular monomer with the *syn* rotamer.

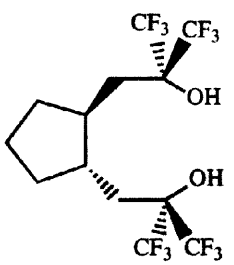
Ring Closing Metathesis

Ring closing metathesis (RCM) is the most recent and most exciting application of olefin metathesis to organic chemistry.[2-7,11,46,47] The advantage of starting a metathesis reaction with a known amount of a well-defined initiator that is 100% active is a significant advantage compared to "classical" metathesis recipes where the amount, the identity, and the stability of a catalyst is not known. Therefore low yields, irreproducibility, and

intolerance of functionalities tended to be common when classical catalysts were employed for RCM. With the advent of well-defined catalysts reproducibility and yields have improved markedly and many functionalities are now known to be tolerated.

The two main types of catalysts that are used for RCM currently are $Mo(CHCMe_2Ph)(N\text{-}2,6\text{-}i\text{-}Pr_2C_6H_3)[OCMe(CF_3)_2]_2$ and $Ru(CHPh)Cl_2(PCy_3)_2$. The ruthenium catalyst has the advantage of a greater tolerance of functionality, but sacrifices speed.[12] The molybdenum catalyst has the advantage of being able to form rings in sterically more demanding circumstances, but is relatively intolerant of protons on heteroatoms (carboxylic acids, alcohols, thiols, etc.) and some functionalities (*e.g.*, aldehydes).[3-5,48] The rate of metathesis by Ru is attenuated sometimes to the point of preventing a practical metathesis reaction entirely, as in the presence of donors such as S, P, or nitriles. In contrast, there are indications that molybdenum will tolerate S, P, and nitrile functionalities, perhaps because of the relatively crowded pseudo-tetrahedral coordination sphere, and possibly also in some cases a "mis-match" between a relatively "hard" electrophilic metal center and a "soft" donor such as S or P. A review of RCM by molybdenum catalysts has appeared elsewhere recently.[2]

Molybdenum catalysts that contain diolates have been studied little compared to $Mo(CHCMe_2Ph)(N\text{-}2,6\text{-}i\text{-}Pr_2C_6H_3)[OCMe(CF_3)_2]_2$. Catalysts that contain C_2 symmetric diolates became prime targets for controlling the structure of polymers prepared by ROMP. In fact it was found that the structure of a living polymer could be controlled to a high degree by a combination of enantiomorphic site control and chain-end control using racemic catalysts.[49-52] Interestingly, the success of this control depended dramatically upon the nature of the imido ligand. In one case, an N-2,6-$Me_2C_6H_3$ catalyst produced essentially pure *cis,isotactic* ring-opened polymer, while the N-2,6-i-$Pr_2C_6H_3$ catalyst produced polymer that contained a significant percentage of *trans* linkages as a consequence of chain propagation via *anti* rotamers competing with chain propagation via *syn* rotamers.[52] Enantiomerically pure versions of these catalysts became the most plausible targets for asymmetric metathesis reactions such as asymmetric RCM (ARCM). Enantiomerically pure molybdenum catalysts have been prepared that contain a tartrate-based diolate,[52] a binaphtholate,[50] or a diolate derived from a *trans*-1,2-disubstituted cyclopentane (A).[53,54] The enantioselectivity of the molybdenum catalyst that contains the dolate



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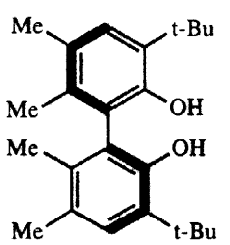

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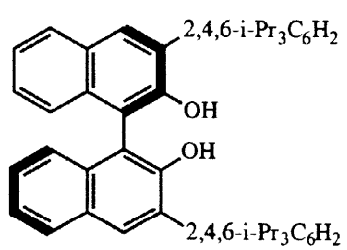

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derived from A in several simple kinetic resolutions was not high, perhaps primarily as a consequence of the "floppy" nature of the nine-membered ring that contains the metal. On the other hand, a binaphtholate or biphenolate ligand forms a relatively rigid seven-membered ring containing the metal, and *syn* and *anti* rotamers are known to interconvert readily in such catalysts. Hence a catalyst that contains an enantiomerically pure binaphtholate or biphenolate ligand appeared to offer more opportunities for ARCM. Four potentially reactive CNO sites are available in any enantiomerically pure catalyst in which rotamers interconvert readily. Understanding and predicting which of these is the most rapid yet efficient for asymmetric metathesis steps is a

challenge.

Two publications have appeared recently that demonstrate the high potential of ARCM reactions. In the first[55] 5,5',6,6'-tetramethyl-3,3'-di-*tert*-butyl-1,1'-biphenyl-2,2'-diol (**B**; H_2t-Bu_2Me_4BIPHEN) was prepared in two steps and resolved via a phosphorus-based procedure to give the pure S-(-)-enantiomer. A molybdenum catalyst of the type *syn*-Mo(CHCMe$_2$Ph)(NAr)[(-)-t-Bu_2Me_4BIPHEN] (**1a**; Ar = 2,6-i-$Pr_2C_6H_3$) was then prepared from Mo(CHCMe$_2$Ph)(NAr)(triflate)$_2$(dme) in the usual manner. An X-ray crystal structure (Figure 3) established the absolute configuration of the complex and the identity of the predominant rotamer in the solid state as *syn*. Catalyst **1a** was then employed as an initiator in attempted kinetic resolutions.

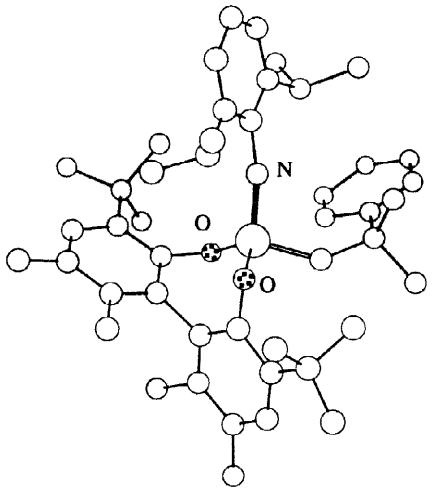
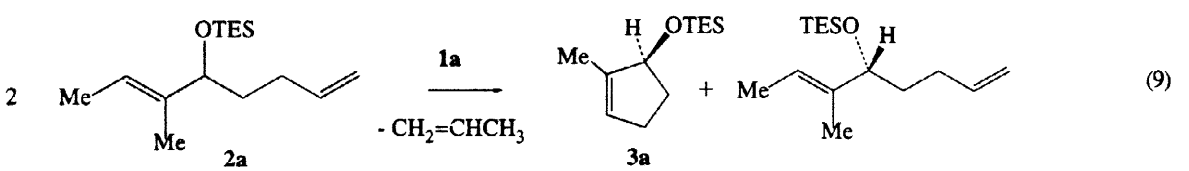
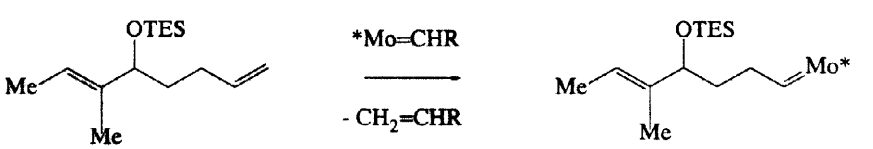


Figure 3. X-ray structure of complex **1a**.

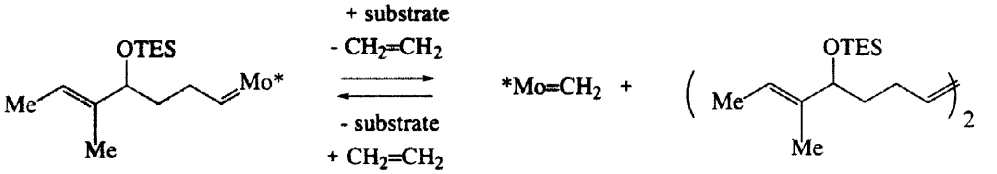
When the unsaturated TES ether **2a** (equation 9) is subjected to 5 mol % **1a** (benzene, argon atm, 22°C), after only 10 minutes 43% **3a** and 38% of the dimeric product formed via coupling of terminal olefins (equations 10 and 11) are formed. Most importantly, **3a** is obtained in 93% ee and the ee of unreacted **2a** (19%) is >99%. Formally propylene is generated, although it is likely that propylene is metathesized to some extent during the reaction to give ethylene and 2-butenes. The mechanism of this ARCM reaction is believed to involve attack by the initial Mo alkylidene at the most reactive terminal olefin to give the "tethered" alkylidene shown in equation 10. This species can then ring-close to give **3a** and an ethylidene complex, react with more substrate to give a methylene complex, ethylene, and dimer (equation 11), or react with other metathesis products (*e.g.*, ethylene) that are present in the reaction mixture. Dimer formation should not be irreversible, although the rate of dimer cleavage is likely to be the fastest if a methylene complex is involved, and the rate of reaction of the methylene complex versus all other steps (including removal of ethylene from the system) therefore may vary widely depending upon conditions. The enantioselective step is believed to be the formation of a crowded bicyclic intermediate containing the metal followed by essentially irreversible loss



(9)



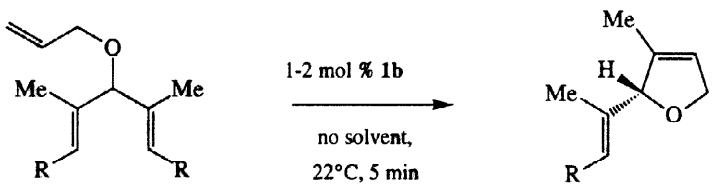
(10)



(11)

of one enantiomer and formation of an ethylidene complex. When the OTES group is moved to the allylic position of the terminal olefin in the substrate, enantioselectivity is poor, consistent with the proposal that formation of the "tethered" alkylidene does not occur with significant stereodifferentiation. It is estimated that the relative rate of ring closure of one enantiomer of **2a** versus the other is approximately 50.

In addition to the enantioselective synthesis of unsaturated carbocycles, ARCM offers opportunities for the preparation of enantiomerically enriched heterocycles.[56] More attractive than kinetic resolution in some ways is a catalytic enantioselective "desymmetrization" that delivers the derived heterocycles in high optical purity and ideally in 100% yield. This has been carried out successfully, as shown (for example) in equation 12. In this case a catalyst variation that contains the N-2,6-$Me_2C_6H_3$ imido ligand (**1b**) proved most expedient, perhaps as a consequence of the more crowded nature of the bicyclic species formed in the enantioselective step. With **1a** the cyclization reaction was relatively slow when the substrate contained a trisubstituted olefin (R = Me), although enantioselectivity was high in the product that was obtained. It is important to note that in the case of **2a** and **2b**, the ring-closing reaction can be carried out in the absence of solvent.

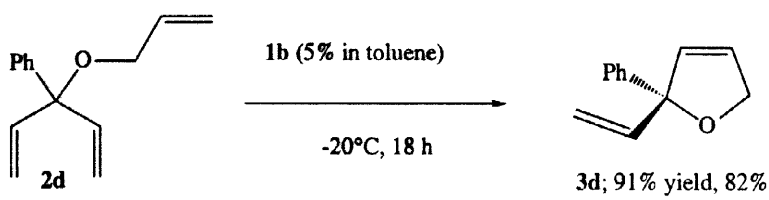


(12)

2b R = H (1 mol % **1b**) (*R*)-**3b** *93% ee, 85% yield*

2c R = Me (2 mol % **1b**) (*R*)-**3c** *99% ee, 93% yield*

The possibility of controlling the absolute stereochemistry of quaternary carbon stereogenic centers has also been examined. As shown in equation 13, **2d** can be cyclized by **1b** at -20°C to give product **3d** in 91% yield and 82% ee. Lower ee's are found in reactions carried out at room temperature. The reaction is slow (35% complete in 18h) and the ee is relatively low (16%) in reactions carried out at room temperature with catalyst **1a** .



(13)

3d; 91% yield, 82%ee

Although very few substrates have been tested, initial findings with catalysts **1a** and **1b** suggest that six-membered rings are not formed with high enantioselectivity. Therefore we have begun to develop new types of catalysts. In a third publication[57] a new catalyst (**1c**) is reported that contains a substituted binaphtholate derived from R-(+)-binaphthol in which the aryl group in the position ortho to the oxygen is 2,4,6-triisopropylphenyl (**C**). Unlike catalysts **1a** and **1b**, catalyst **1c** can be isolated only as a THF adduct. The X-ray structure of the pyridine adduct (Figure 4) confirms that the configuration of the binaphtholate is R, that pyridine is bound to one of the CNO faces, as in all other adducts to date, and that the base has bound to the *syn* rotamer.

The THF adduct of **1c** has been found to be relatively slow-acting at room temperature, although it will catalyze the formation of *six*-membered rings with relatively high enantioselectivity. For example, as shown in equation 14, at 25°C 32% product (84% ee) is formed in 3.7 h at 25°, along with 34% dimer, while at 65°, a 50% yield of product (81% ee) and 27% dimer is realized in 40 minutes. In comparison, catalyst **1a** yields 47% product (45% ee) and 11% dimer in 30 minutes at 25°, with 42% starting material left over (57% ee). At this stage it is not known whether catalyst **1c** is slower than **1a** because of competitive inhibition by THF, because the coordination sphere several angstroms away from the metal is more crowded in **1c**, or for more complex reasons having to do with rotamers and relative rotamer reactivities. In any case it is noteworthy also that the ee does not suffer significantly at 65° compared to 25°.

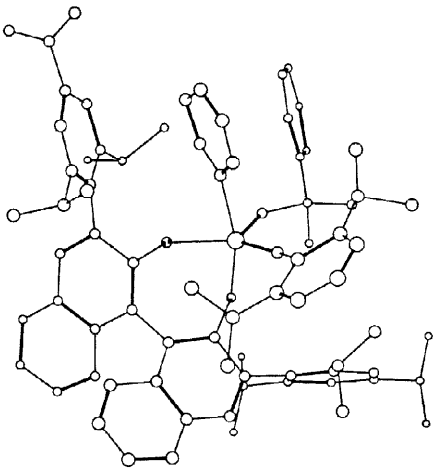
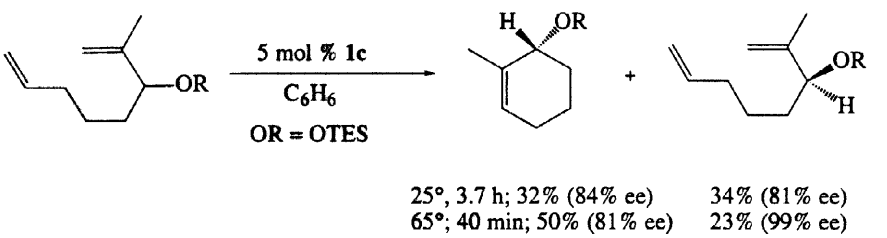


Figure 4. X-ray structure of the pyridine adduct of catalyst **1c**.



(14)

25°, 3.7 h; 32% (84% ee) 34% (81% ee)
65°; 40 min; 50% (81% ee) 23% (99% ee)

Comments and Conclusions

A moderately good understanding of the mechanism of reaction of "well-defined" molybdenum catalysts of the type $Mo(CHR)(NAr)(OR')_2$ has been obtained in the last several years. Crucial details such as rotamer interconversion rates and relative reactivities are extremely difficult to extract, however, and are likely to be highly dependent upon the particular alkoxide, imido, alkylidene, and substrate in question. Nevertheless, awareness of the details in even a qualitative sense should allow further applications in organic chemistry. With regard to new asymmetric catalysts, it should be pointed out that racemic catalysts may prove useful in applications where enantioselectivity is not the primary issue, as their reactivity may differ in important ways from that of $Mo(CHCMe_2Ph)(N\text{-}2,6\text{-}i\text{-}Pr_2C_6H_3)[OCMe(CF_3)_2]_2$, or in order to optimize conditions for substrate conversion before focusing on enantioselectivity. As we become aware of the factors that limit a catalyst's lifetime and selectivity, conditions will be found that will produce higher turnover numbers. In this context it would be desirable to develop a catalyst that is tethered to an insoluble support in order (it would be hoped) to extend catalyst life and increase turnover number. Above all, however, it must be remembered that no "magic catalyst" will accomplish all of the most demanding tasks, especially asymmetric reactions, with equal ease, and that therefore catalyst design will play a significant role in optimizing conditions for forming a specific type of product. Finally, it would be desirable to develop a reliable method of *in situ* synthesis of asymmetric catalysts so that optimization of activity and enantioselectivity for a given type of substrate can be explored using combinatorial techniques.

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