Highly Active Metathesis Catalysts Generated In Situ from Inexpensive and Air-Stable Precursors**

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The preparation of well-defined ruthenium alkylidene complexes bearing *N*-heterocyclic carbene ligands such as 1,3-dimesitylimidazol-2-ylidene (**1**) and 4,5-dihydroimidazol-2-ylidene (**2**) have led to catalysts (such as **3** and **4**; see Figure 1) which are highly active in ring-closing metathesis (RCM), cross metathesis (CM), and ring-opening metathesis polymerization (ROMP).[1] These catalysts show increased thermal stability and similar tolerance to oxygen and moisture when compared to their parent bisphosphane complexes, $[(PCy_3)_2Cl_2Ru{=}CHPh]$ (**5**, Figure 1).[2] Since all synthetic routes to catalysts **3** and **4** proceed through the transformation of a ruthenium bisphosphane carbene,[3] a direct route through readily available starting materials is still desirable.

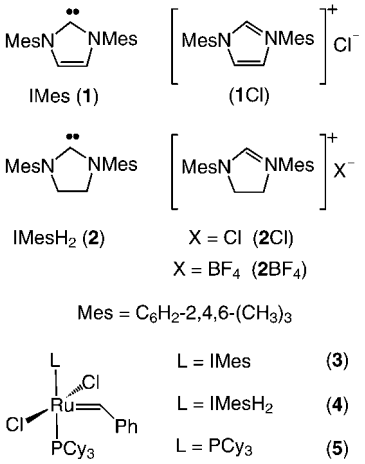
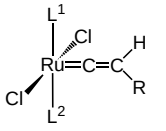


Figure 1. Well-defined ruthenium benzylidene complexes **3**–**5** possessing phosphane or imidazolylidene ligands **1** and **2**.

Ruthenium vinylidene complexes can be easily prepared from commercially available terminal alkynes and ruthenium sources.[4] Unfortunately, such complexes have displayed only limited metathesis activity, such as the ROMP of highly strained norbornenes and the RCM of unsubstituted α,ω-dienes.[4, 5] As observed in other systems,[1] ruthenium vinylidene compounds coordinated with an imidazolylidene ligand should exhibit increased activity and thus facilitate a broader range of metathesis reactions.

Our initial efforts were directed towards preparing and measuring the metathesis activity of various imidazolylidene ruthenium vinylidene complexes. The reaction of 1,3-diisopropyl-4,5-dimethylimidazol-2-ylidene (*i*PrIm)[6] and $[(PCy_3)_2Cl_2Ru{=}C{=}CHPh]$ (**6a**; Figure 2)[4] quantitatively afforded $[(i\text{PrIm})_2Cl_2Ru{=}C{=}CHPh]$ (**7**) as a bright blue solid. Disappointingly, RCM of diethyl diallylmalonate using this complex was not observed, even under forcing conditions.[7] This is somewhat surprising since the analogous bisimidazolylidene benzylidene complex is a known RCM catalyst.[8]



$L^1 = L^2 = PCy_3$, R = Ph (**6a**)
$L^1 = L^2 = PCy_3$, R = *t*Bu (**6b**)
$L^1 = L^2 =$ *i*Prim, R = Ph (**7**)
L^1 = IMes, $L^2 = PCy_3$, R = *t*Bu (**8**)

Figure 2. Ruthenium vinylidene complexes.

The mechanism of olefin metathesis appears to involve ligand (phosphane or imidazolylidene) dissociation and it is known that imidazolylidene ligands have relatively high binding energies.[9] However, carbenes bearing a mixed ligand set, that is, one imidazolylidene and one phosphane, have more pronounced activities than their $[L_2Cl_2Ru{=}CHR]$ (L = phosphane or imidazolylidene) counterparts. Thus, a ruthenium vinylidene complexes possessing a mixed ligand system was prepared and investigated for RCM activity. Simple phosphane displacement of the known complex $[(PCy_3)_2Cl_2Ru{=}C{=}C(H)t\text{Bu}]$ (**6b**, Figure 2)[4] by bulky 1,3-dimesitylimidazol-2-ylidene (**1**) afforded vinylidene complex **8** in 85 % yield as a brown solid. Complex **8** catalyzed the RCM of diethyl diallylmalonate in 86 % yield (Table 1, entry 1 a), although the reaction rate was much slower than with the ruthenium carbene complexes **3**–**5**. The slow rate of reaction may result from slow initiation since the propagating species, presumably methylidene, should be the same as that produced by carbene complex **3**. Noteworthy is that the replacement of a phosphane with an imidazolylidene in neutral allenylidene complexes does not provide a metathesis-active catalyst.[10]

These results indicated that increased ligand dissociation (i.e., of phosphane) was necessary to accelerate inititation and thereby enhance catalytic activity. Previously, addition of phosphane sponges, such as copper salts or acids, has been used to facilitate RCM catalyzed by ruthenium carbenes. An alternative approach would involve the direct generation of the phosphane-free active species in situ, thus circumventing the need to add additional reagents to remove phosphane. Ruthenium vinylidene complexes can be conveniently prepared by adding two equivalents of phosphane and a terminal alkyne to $[\{(p\text{-cymene})RuCl_2\}_2]$ (**9**).[4] As shown in Table 1 (entry 1 b), the combination of 2.5 mol % dimer **9**, 5 mol % ligand **1**, and 5 mol % of *tert*-butyl acetylene catalyzed the RCM of diethyl diallylmalonate affording the ring-closed product in 95 % yield (80 °C, 12 h). The complex formed in situ displayed higher catalytic activity than vinylidene complex **8** (86 %, 65 °C, 24 h), which suggests that a vinylidene complex with a low coordination number, such as phosphane-free **8′** (Scheme 1), may be formed as a catalyst precursor (see below).

The scope of the reagents needed to generate vinylidene catalysts in situ was investigated further. As expected, the

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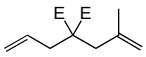
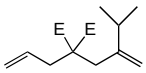
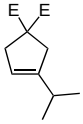
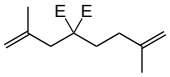
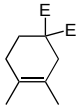
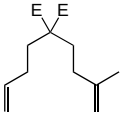
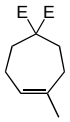
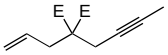
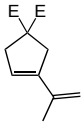
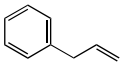
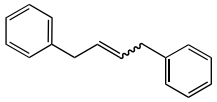
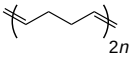
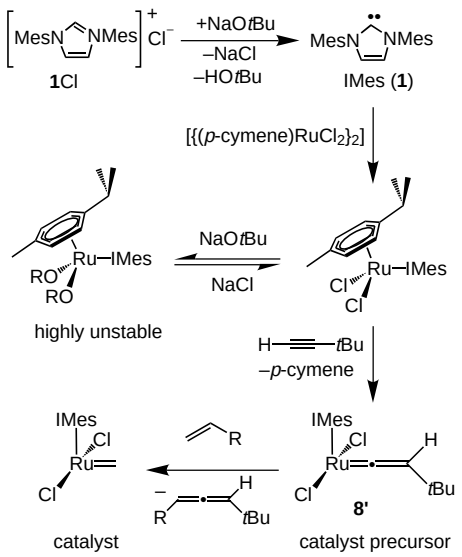
Table 1. Metathesis reactions using [{(*p*-cymene)$RuCl_2$}$_2$] (**9**), **1**Cl, NaO*t*Bu, and *tert*-butyl acetylene;[a] E = CO_2Et.

Entry	Substrate	Product	*t* [h]	Yield [%][b]
1a			24[d]	86[c]
b			12[e,f]	95[c]
c			2[e,f,h]	51[c,i]
d			2[e,f]	86[c,i]
e			2[e,g,h]	44[c,i]
f			2[e,g]	73[c,i]
g			10	96
h			10[h]	0
2			10	98
3			24	96
4			24	79
5			10	76
6			10	80
7			8	93
8			1[j]	95

[a] Performed at 80 °C with 2.5 mol % of **9** in hexanes unless otherwise indicated. [b] Yield of isolated product. [c] Determined by ^{1}H NMR spectroscopy or GC using 1,3,5-mesitylene as an internal standard. [d] 5 mol % **8** as catalyst at 65 °C. [e] Performed with ligand **1** instead of **1**Cl and NaO*t*Bu. [f] Toluene as solvent. [g] THF as solvent. [h] No *tert*-butyl acetylene was added. [i] Percent conversion. [j] No solvent.

absence of a ruthenium source **9** or ligand **1** failed to provide any ring-closed product. Unfortunately, other ruthenium sources such as [$RuCl_2(PPh_3)_3$] and [{$RuCl_2$(cod)}$_n$] (cod = 1,5-cyclooctadiene), afforded no metathesis active species. While the absence of alkyne (*tert*-butyl acetylene) did provide ring-closed product, the reaction rates were slower (Table 1, compare entries 1c and d). Presumably, [(*p*-cymene)(IMes)$RuCl_2$], a known RCM catalyst precursor, was generated in situ.[11] However, when the RCM reaction was performed in THF the inclusion of alkyne resulted in substantially higher yields (compare entries 1 e and f). It was also apparent from these control reactions that solvent plays an important role in the generation of a metathesis catalyst in situ (see below).



Scheme 1. Proposed pathways for catalyst generation and decomposition.

Although a number of imidazolylidene compounds are stable as their free carbene, an easier method would involve the generation of the free imidazolylidene carbene in situ from the appropriate salt and base. Such a method has been used to generate complexes **3** and **4** as well as PdL (L = imidazolylidene), a highly efficient aryl-amination catalyst.[12] In hope of extending this methodology, we examined the RCM of diethyl diallymalonate using [{(*p*-cymene)-$RuCl_2$}$_2$], NaO*t*Bu, and **2**BF_4, **2**Cl, or **1**Cl under various conditions. Unfortunately, all the RCM reactions with the ligand **2**X (X = BF_4, Cl) failed to give a cyclized product and may be related to the instability of the saturated imidazolylidene-free carbene.[13] Alternatively, the formation of the vinylidene precursor may be blocked because of deprotonation of the alkyne by base, although addition of alkyne as the final reagent afforded only starting material. Similar results were obtained with **1**Cl when the reactions were performed in either toluene or THF. However, dramatically different results were obtained in hexanes. For example, diethyl diallylmalonate was converted into the corresponding ring-closed product in 96 % yield (Table 1, entry 1g). In the absence of alkyne, it is possible that a highly unstable and unsaturated alkoxide ruthenium complex is generated by the presence of NaO*t*Bu since no product was formed under these conditions (entry 1h).[14] A proposed mechanism for the generation of the active species and the decomposition product is shown in Scheme 1. The combination of a low concentration of metal complex that is soluble in hexanes as well as the generation of a vinylidene complex from the addition of alkyne may produce a stable ruthenium vinylidene species resistant to decomposition.

A variety of metathetical reactions were performed using this system (Table 1). Interestingly, in addition to RCM, the catalyst generated in situ was also effective in CM, ene–yne metathesis, and ROMP. While reaction times were longer,

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sterically hindered olefins were cyclized in comparable yields to those obtained by using complexes **3** and **4**.

Since all of the starting materials are air stable, we tried setting up the RCM reaction on the benchtop, thus eliminating the use of a drybox or vacuum line. The solid components (commercially available) were weighed in air into a reaction flask. The atmosphere was purged with argon followed by the addition of reagent grade hexanes, *tert*-butyl acetylene, and diethyl diallylmalonate. After 10 h at 80 °C, ring-closed product was obtained in 88 % yield. The reaction rate and yield were comparable to those when degassed solvents and drybox procedures were employed (96 %, Table 1, entry 1 g).

In conclusion, when coordinated to a bulky imidazolylidene ligand, ruthenium vinylidene complexes are effective catalysts for a variety of metathetical reactions. Although reaction rates were slower, their general reactivity profile towards a variety of substrates was similar to the analogous highly active ruthenium alkylidenes (**3** and **4**). In addition, the catalysts can be generated in situ from inexpensive, air stable, and commercially available starting materials, which circumvents the need for a drybox or special Schlenk equipment.

Experimental Section

Representative procedure: In a drybox, [{(*p*-cymene)$RuCl_2$}$_2$] (0.02 mmol), ligand **1**Cl (0.045 mmol), and NaO*t*Bu (0.045 mmol) were weighed directly into a screw cap vial. A stir bar was added followed by hexanes (2 mL). Substrate (0.85 mmol) and *tert*-butyl acetylene (0.045 mmol) were added and the vial was sealed with a PTFE lined cap. The vial was removed from the drybox and the contents stirred at 80 °C. The reaction was monitored by GC and after complete consumption of substrate, the products were purified by chromatography on silica gel. All products listed in Table 1 have been previously characterized.

Selected NMR data for **8**: ^{1}H NMR (300 MHz, C_6D_6): $\delta = 6.76$ (s, 2H; NCHCHN), 5.99 (s, 1H; C(*t*Bu)H), 2.78 – 2.67 (m, 3H, 3CH of PCy_3), 2.44 (s, 9H; $3CH_3$), 2.14 (s, 9H; $3CH_3$), 2.14 – 2.09 (m, 8H; CH_2 of PCy_3), 1.69 – 1.58 (m, 14H; CH_2 of PCy_3), 1.28 – 1.17 (m, 8H; CH_2 of PCy_3), 1.12 (s, 9H; $C(CH_3)_3$); ^{31}P NMR (121.4 MHz, C_6D_6): $\delta = 17.4$ (s).

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Highly Enantioselective Palladium-Catalyzed Ene-Type Cyclization of a 1,6-Enyne**

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Dedicated to Professor Barry M. Trost on the occasion of his 60th birthday

Transition metal catalyzed ene-type carbocyclizations of 1,6-enynes such as cycloisomerization[1] and the ene reaction[2] are powerful synthetic methods leading to five-membered rings.[3–5] However, examples for the corresponding enantioselective catalysis are limited,[6] hence it is a challenge to establish high levels of asymmetric induction as well as high yields. Herein we report a highly efficient catalysis by chiral palladium(II) complexes for enantioselective ene-type carbocyclizations of the 1,6-enyne **1** leading to highly enantioenriched five-membered rings [Eq. (1)].

The palladium(II)-catalyzed carbocyclization reactions of 1,6-enynes have generally been performed with $Pd(OAc)_2$ or by the combined use of Pd^0 species (e.g. $[Pd_2(dba)_3]\cdot CHCl_3$) (dba = *trans*,*trans*-dibenzylidene acetone) and a weak acid such as acetic acid or trifluoroacetic acid.[3] However, in the presence of a chiral bidentate phosphane ligand, such as BINAP (BINAP = 2,2′-bis(diphenylphosphanyl)-

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