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# Lewis Acid Assisted Ruthenium-Catalyzed Metathesis Reactions

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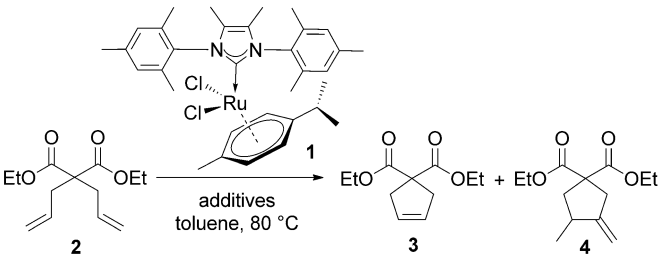
The combination of a ruthenium–arene complex, a noncoordinating salt, and a Lewis acid facilitates access to a highly active and selective in situ metathesis catalyst. The catalyst is formed from an inexpensive ruthenium precursor and olefins are used as the substrates. RCM = Ring-closing metathesis, acac = acetylacetonate.

Since its discovery in the mid 1960s, metathesis has become a valuable tool for organic syntheses and polymer chemistry, particularly in industry. Therein, ill-defined catalysts[1] dominated for the first three decades, before well-defined catalysts established metathesis as an indispensable tool for organic synthesis.[2] In this regard, ruthenium-based complexes have notably experienced tremendous growth in interest.[3] These latter complexes emerged to form efficient and highly tolerant catalysts for all kinds of metathesis reactions. Hence, numerous elegant synthetic applications have been realized.[4] However, despite the clear advantages of well-defined activators, olefin metathesis is still limited by irreversible catalyst deactivation, which necessitates, in most cases, high catalyst loadings.[5] Therefore, approaches that can be used to generate the active catalyst from readily available and stable precursors significantly extend the impact of olefin metathesis for industrial applications, which is demonstrated by a number of reported examples.[6] In this respect, compounds of the type [(NHC)(*p*-cymene)$RuCl_2$] (NHC = N-heterocyclic carbene) constitute easily available ruthenium complexes; complexes of this type have been known since the pioneering report of Nolan et al. in 1999.[7] Unfortunately, the use of such complexes, apart from the desired ring-closing metathesis (RCM) reaction, also results in unwanted cycloisomerizations in the benchmark reaction of diethyl diallylmalonate (see below).[6i] Therefore, several efforts have been undertaken to perform selective metathesis transformations in the presence of arene complexes such as [(L)(*p*-cymene)$RuCl_2$]. Common concepts are photochemical activation[6a–c] and activation by carbene precursors such as trimethyldiazomethane[6d,e] and alkyne.[6f–i] Interestingly, Delaude and co-workers reported that the homobimetallic ruthenium complex [(*p*-cymene)Ru(μ-Cl)$_3$RuCl($\eta^2$-$C_2H_4$)(IMes)] [IMes = 1,3-bis(2,4,6-trimethylphenyl)imidazol-2-ylidene] does not require any aforementioned activators to initiate the metathesis reactions.[8] Nonetheless, the benchmark reactions of diethyl diallylmalonate and *N*,*N*-diallyltosylamide again resulted in mixtures of cycloisomerization and RCM products.

Herein, we report that the addition of noncoordinating salts and Lewis acids enhances the metathesis activity of ruthenium arene complexes of the type [(NHC)(*p*-cymene)$RuCl_2$] to effectively suppress such undesired cycloisomerization reactions accompanied with a very high productivity.

The RCM reaction of diethyl diallylmalonate (Scheme 1) was chosen as a benchmark reaction to demonstrate the influence of different additives by using complex **1** as the catalyst precursor. Preliminary studies showed that full conversion of the




**Scheme 1.** Ring-closing metathesis of diethyl diallylmalonate by using catalyst **1** and additives.

substrate could be achieved in toluene at 80 °C for catalyst **5**.[7] However, in the presence of **1** (1 mol%), only 33% of desired RCM product **3** and 32% of undesired cycloisomer **4** were obtained within 1 h (Table 1, entry 1).

To our delight, the addition of $NaPF_6$ (5 mol%) raised the productivity to 76%, and the cycloisomerization was completely suppressed. Any further increase or decrease in the noncoordinating anion did not result in any increase in the amount of product formed (Table 1, entries 2–4). Notably, the addition of $AgPF_6$ caused complete deactivation of the catalyst.

Interestingly, the addition of Lewis acids such as $Fe(acac)_3$ (acac = acetylacetonate) and $AlCl_3$ also successfully inhibited the formation of cycloisomerization product **4** (Table 1, entries 7 and 9). Consequently, we applied a combination of

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**Table 1.** Effect of additives on the activity of **1** in the RCM of diethyl diallylmalonate.

| Entry[a] | Additive [mol%] | Conv. **2** [%][b] | Yield **3** [%][b] |
|---|---|---|---|
| 1[e] | – | 65 | 33 |
| 2 | $NaPF_6$ (1) | 67 | 21 |
| 3 | $NaPF_6$ (5) | 76 | 76 |
| 4 | $NaPF_6$ (10) | 72 | 63 |
| 5 | $PdCl_2(PPh_3)_2$ (5) | 46 | 26 |
| 6 | $PdCl_2(PPh_3)_2$ (5)/$NaPF_6$ (5) | 64 | 61 |
| 7 | $AlCl_3$ (5) | 34 | 34 |
| 8 | $AlCl_3$ (5)/$NaPF_6$ (5) | 94 | 94 |
| 9 | $Fe(acac)_3$ (5) | 48 | 46 |
| 10 | $Fe(acac)_3$ (5)/$NaPF_6$ (5) | 97 | 97 |
| 11 | $Fe(acac)_3$ (5)/$NaPF_6$ (5) | 94 | 87[c] |
| 12 | $Fe(acac)_3$ (5)/$NaPF_6$ (5) | 67 | 62[d] |
| 13 | $Fe(OAc)_2$ (5)/$NaPF_6$ (5) | >99 | 97 |

[a] Reaction conditions: diethyl diallylmalonate (4 mmol), (*p*-cymene)Ru($Me_2$IMes)$Cl_2$ (**1**, 1 mol%), additive, toluene (100 mL), Ar bubbling, 80 °C, 1 h. [b] Determined by GC with hexadecane as an internal standard. [c] Technical-grade toluene (100 mL); reaction performed in air. [d] Degassed water (50 μL) was added. [e] See Figure S1.

$NaPF_6$ and a Lewis acid, which resulted in excellent performance; the RCM product was delivered in up to 97% yield with exclusive selectivities (Table 1, entries 6, 8, 10, 13).

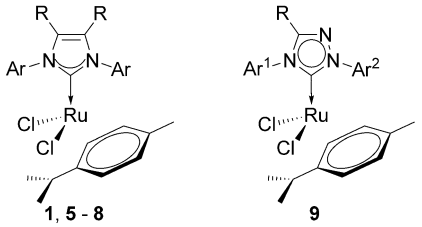
Moreover, the oxidation state of iron apparently has no influence on the activation; thus, $Fe(acac)_3$ and $Fe(OAc)_2$ behave in the same manner (97%; Table 1, entries 10, 13). Inspired by these excellent results, other $M(acac)_x$ salts (M = $Fe^{II}$, $Co^{I,II}$, $Ni^{II}$, $Cr^{III}$, $Cu^{II}$, $Mn^{II,III}$) were employed together with $NaPF_6$. However, these combinations revealed a lower performance in RCM than the use of only $NaPF_6$.

Given that all of the starting materials are air stable, we were interested in keeping an industrial focus. Therefore, we executed the RCM reaction in air and successfully obtained **3** in 87% yield (Table 1, entry 11), for which small amounts of water were tolerated (Table 1, entry 12).

In further experiments, the conditions of the new catalyst system were optimized for temperature and solvent as a result of the properties of the additive; 80 °C in toluene was best, whereas dichloromethane, dichloroethane, 1,4-dioxane, and isobutyl alcohol resulted in full deactivation of the catalyst.

Noteworthy, the preparation of the ruthenium complex in situ from $[(p\text{-cymene})RuCl_2]_2$, $Me_2$IMesHCl, and NaO*t*Bu resulted in comparable productivities (52% of **3**). In doing so, the experiment was also successfully conducted with the isolated free carbene, $Me_2$IMes, which confirmed no negative influence of the base on the catalytic activity (see the Supporting Information, Table S3).

Next, various ruthenium complexes of the type [(NHC)(*p*-cymene)$RuLCl_2$] were applied to the RCM reaction; mesitylene-substituted imidazol-2-ylidenes **1** and **5** offered significantly better results than 1,3-bis(2,6-diisopropylphenyl)-substituted imidazol-2-ylidenes **6** and **7** (Figure 1). Interestingly, if the 4,5-positions of the imidazol-2-ylidenes were substituted by methyl groups, formation of the product dramatically increased to 97%; thus, complex **1** served as the best ring-closing metathesis precursor.

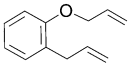
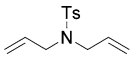
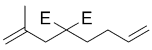
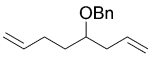
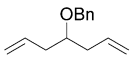
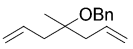
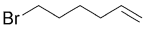



| | | Yield **3** [%]: |
|---|---|---|
| **1**: R = Me; | Ar = 2,4,6-trimethylphenyl | 97 |
| **5**: R = H; | Ar = 2,4,6-trimethylphenyl | 48 |
| **6**: R = Me; | Ar = 2,6-di-*i*PrPh | 22 |
| **7**: R = H; | Ar = 2,6-di-*i*PrPh | 14 |
| **8**: R = MeO-Ph; | Ar = 2-Me, 5-*t*Bu-Ph | 44 |
| **9**: R = Me; | $Ar^1$ = 2-Me-Ph; | |
| | $Ar^2$ = 2,4,6-trimethylphenyl | 3 |

**Figure 1.** Effect of the NHC on productivity in the RCM of diethyl diallylmalonate.

Subsequently, we investigated the application of our new catalyst system consisting of **1** with $NaPF_6$ and $Fe(acac)_3$ as additives for different metathesis reactions (Table 2). The RCM of 1-allyl-2-(allyloxy)benzene (**10**) was performed with 1 and

**Table 2.** RCM and cross-metathesis reactions promoted by **1** and assisted by $NaPF_6$ and $Fe(acac)_3$.

| Entry[a] | Substrate | | *t* [h] | Conv. [%][b] | RCM Yield [%][b] |
|---|---|---|---|---|---|
| 1 |  | **10** | 0.5 | 94 | 85 |
| 2[c] | | | 3 | 94 | 81 |
| 3[d] | | | 3 | 16 | 9 |
| 4 |  | **11**[g] | 3 | 14 | 12 |
| 5 |  | **12**[h] | 3 | 50 | 24 |
| 6[e] |  | **13**[i] | 3 | 85 | 41 |
| 7 |  | **14** | 3 | 90 | 81 |
| 8 |  | **15** | 3 | 95 | 94 |
| 9[f] |  | **16** | 3 | 23 | 13 |
| 10[f] |  | **17** | 3 | 54 | 21 |

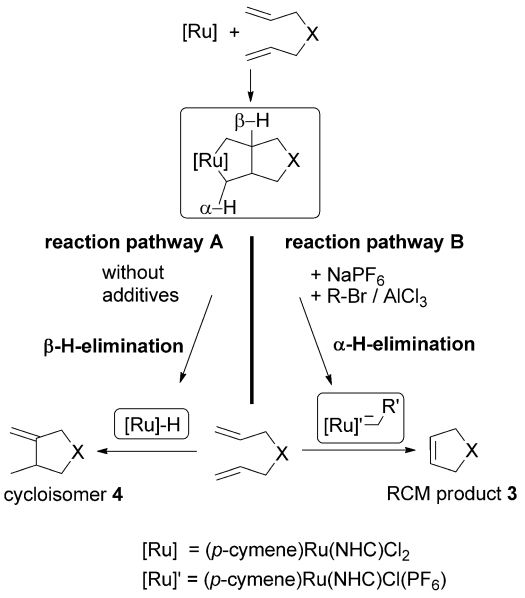
[a] Reaction conditions: substrate (4 mmol), (*p*-cymene)Ru($Me_2$IMes)$Cl_2$ (**1**, 1 mol% related to diene), $NaPF_6$ (5 mol%), $Fe(acac)_3$ (5 mol%), toluene (100 mL), Ar bubbling, 1 h. [b] Determined by GC with hexadecane as an internal standard. [c] Compound **1** (0.1 mol%), $NaPF_6$ (0.5 mol%), and $Fe(acac)_3$. [d] Compound **1** (0.01 mol%), $NaPF_6$ (0.5 mol%), and $Fe(acac)_3$, 110 °C. [e] 1,2-Dibromocyclohexane (1 mol%).[12] [f] Compound **1** (10 mol%), $NaPF_6$ (50 mol%), and $Fe(acac)_3$. [g] Ts = tosyl. [h] E = $CO_2$Et. [i] Bn = benzyl.

0.1 mol% of **1**, and excellent conversions and yields were obtained (Table 2, entries 1 and 2). Amide **11** and sterically hindered olefin **12** were converted to lesser degrees and provided the desired product in only 12 and 24% yield, respectively, (Table 2, entries 4 and 5). In the course of this, the formation of five-membered rings **14** and **15** were more efficient than

the formation of six-membered ring **13** (Table 2, entries 6, 7, and 8).

Moreover, in addition to ring-closing metathesis, we were pleased to successfully apply the catalytic system to the self-metathesis of styrene (**16**) and 6-bromohexene (**17**). However, the yields were low owing to a missing enthalpic driving force (ring strain), which is often observed for self- and cross-metathesis reactions.[9]

With respect to the mechanism, we believe that both competing reaction pathways are induced by the formation of a metallacycle intermediate formed through oxidative cyclization, as shown in Scheme 2.[10] So, in pathway A, subsequent




**Scheme 2.** Cycloisomerization versus Ru–alkylidene formation.

β-hydride elimination forms the catalytically active ruthenium hydride species, which releases undesired cycloisomerization product **4** after reductive elimination. However, for the case in which the β position is blocked, α-hydride elimination appears to be the next most favorable process, which represents reaction pathway B, and this results in desired product **3** (Scheme 2). This α-hydrogen abstraction is known for other M alkylidene complexes (M = W, Mo, Ta, Re)[11] as well. We assume that the presence of a Lewis acid (e.g., $AlCl_3$), a noncoordinating salt (e.g., $NaPF_6$), and an organic halogen-containing compound[12] enable the commonly disfavored α-hydride elimination, which proceeds through desired reaction pathway B. Here, a carbocation, for instance, $R^+Br{-}AlCl_3^-$, is formed from the organic halogen compound and the Lewis acid ($AlCl_3$), which initiates the generation of a metathesis-active ruthenium alkylidene complex. In agreement with this proposal, in the formation of their rhenium alkylidene complex, Gladysz et al. also observed that the carbocation allows α-hydride elimination despite the presence of β hydrogen atoms.[13] Hence, it is reasonable to suspect that α-hydride elimination is more rapid than β-hydride elimination in the presence of a carbocation.

Recent reports showed that complete conversion of diethyl diallylmalonate could be achieved with NHC-containing Ru–alkylidenes at catalyst loadings as low as 25–50 ppm.[5,14] Thus, to effectively perform the RCM reaction, only trace amounts of alkylidenes have to be generated, which are below the detection limit.

In summary, the metathesis activity of catalysts of the type [(*p*-cymene)Ru(NHC)$Cl_2$] was significantly improved by the addition of $NaPF_6$ and a Lewis acid, which effectively eliminate undesired side reactions, specifically cycloisomerizations. To the best of our knowledge, this is the first application of a new type of metathesis catalyst in which the initiator is generated by means of the alkene that is used as a substrate and not by external alkyne or diazomethane activators. Notably, the catalyst can be generated in situ from inexpensive, air-stable, and commercially available starting materials, and the activity is highly dependent on the structure of the imidazolylidene ligand. In addition, the novel catalytic system was successfully employed in ring-closing metathesis and cross-metathesis reactions.

## Experimental Section

### Ring-closing metathesis of 2 and 10–17 with additives

Representative procedure: The noncoordinating salt, $NaPF_6$ (0.50–0.05 mmol), and Lewis acid, for example, $Fe(acac)_3$ (0.50–0.05 mmol), were weighed directly into a 50 mL, three-necked flask. A magnetic stirrer bar, two septa, and a cooling unit were attached, and after careful evaporation and purging with argon, substrate **2** or **10**–**17** (1.0 mmol), hexadecane (0.5 mmol), and dry and degassed toluene (25 mL) were added. (*p*-cymene)Ru($Me_2$IMes)$Cl_2$ (0.001–0.10 mmol) was dissolved in toluene (4.0 mL) in a 5 mL Schlenk tube and was added by syringe to the warm ($T = 80\,^{\circ}C$) reaction solution, which was bubbled continuously with argon and stirred at 80 °C for 3 h. The reaction was monitored by GC. Details on screening experiments and the preparation of the substrates and complexes are reported in the Supporting Information.

**Keywords:** carbene ligands · homogenous catalysis · Lewis acids · metathesis · ruthenium

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