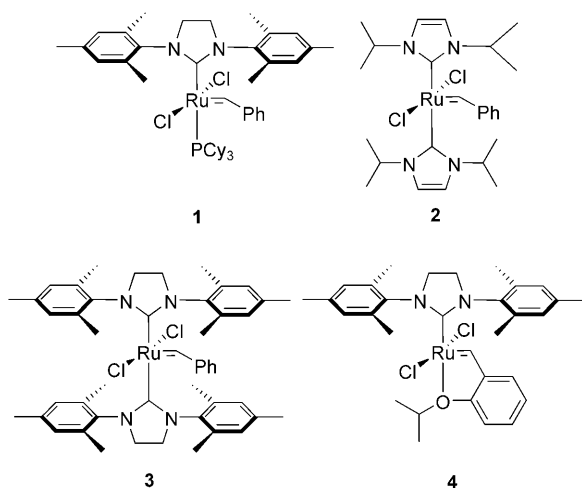


An [(NHC)(NHC_{EWG})RuCl₂(CHPh)] Complex for the Efficient Formation of Sterically Hindered Olefins by Ring-Closing Metathesis**

Tim Vorfalt, Steffen Leuthäuser, and Herbert Plenio*

We recently learned that *N,N'*-diarylimidazolin-2-ylidenes with electron-withdrawing substituents, such as 4-toluenesulfonyl-substituted aryl groups, have electron-donating properties that are comparable to tricyclohexylphosphine, PCy₃.^[1,2] In second-generation catalysts for olefin metathesis,^[3–5] the latter ligand is important, as dissociation of PCy₃ is the initiating step for olefin metathesis.^[6] Consequently, the synthesis of complexes derived from **1** (Scheme 1) with an



Scheme 1. Ruthenium NHC complexes for olefin metathesis. Cy = cyclohexyl.

electron-deficient *N*-heterocyclic carbene (NHC) ligand instead of PCy₃ appears to be an interesting target. The obvious motivation is that NHC ligands with diminished donor capacity might be more willing to act as leaving groups, just as PCy₃ does in second-generation complexes. Furthermore, the absence of a phosphine ligand in the ruthenium

complex should increase the stability of such complexes towards oxidation and also avoid degradation pathways that can arise in the presence of phosphine ligands.^[7]

Complexes of the type [(NHC)₂RuCl₂(CHPh)], such as **2**, were reported as early as 1998 to be catalytically active in the ring-opening metathesis polymerization (ROMP) of 2-norbornene and cyclooctadiene.^[8] Additional work by Grubbs et al. with the complex **3** later revealed poor activities in various RCM and ROMP reactions.^[9] Those later studies, together with the knowledge that NHC ligands bind more strongly to metal centers than phosphines, may have been the reason why such complexes have been studied only scarcely in recent years. Modest ring-closing metathesis (RCM) and ROMP activities were reported by He et al. with [(NHC)₂RuCl₂(CHPh)] (NHC = *N,N'*-diarylimidazol-2-ylidene)^[10] and by Ledoux, Verpoort et al.^[11] for [(NHC)₂RuCl₂(CHPh)] (NHC = *N,N'*-aryl,alkyl-imidazol-2-ylidene) complexes. The latter authors also realized that in certain [(NHC)₂RuCl₂(CHPh)] complexes, one NHC ligand can be replaced by other ligands.^[12]

These results led us to believe that such complexes also provide new opportunities. The synthesis of tetrasubstituted olefins by olefin metathesis still poses significant problems with ruthenium-based catalysts.^[13–17] The conditions used for an example from Grubbs et al. illustrates some problems:^[18] Elevated temperatures (60–80 °C), high catalyst loading (5 mol %), and extended reaction times (24 h) are required for the RCM of such olefins; even under such conditions, several olefins are incompletely converted, and others do not react at all. In 2007, Clavier and Nolan reported indenylidene-based ruthenium complexes; at 80 °C, 2.5–5 mol % of catalyst are required to effect the 89–97 % conversion into various tetrasubstituted olefins.^[19] In 2008, several groups reported improvements: a) by reducing the steric bulk of the NHC ligand,^[20,21] b) by designing NHC ligands with inhibited rotation of the *N*-aryl groups to diminish C–H activation,^[22] and c) by using solvents of low dielectric constant, such as hexafluorobenzene or octafluorotoluene.^[23,24]

Herein we report a new type of ruthenium complex with mixed NHC ligands, one of them being electron-rich, the other one being (relatively) electron-deficient. The latter ligand should be released from ruthenium to generate the catalytically active species.

First, facile synthetic access to NHC ligands substituted with electron-withdrawing groups was required. The nitro group is a strongly electron-withdrawing substituent that is easily introduced into aromatic systems. The *N,N'*-dimesitylimidazolinium salt was converted into the tetranitrated

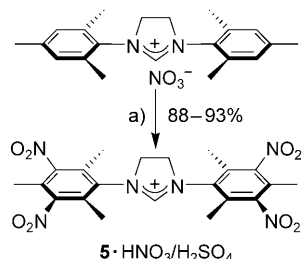
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NHC = *N*-heterocyclic carbene. NHC_{EWG} = *N*-heterocyclic carbene
with electron-withdrawing groups.

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imidazolium salt **5** in about 90% yield by employing a mixture of concentrated sulfuric and nitric acid (Scheme 2).

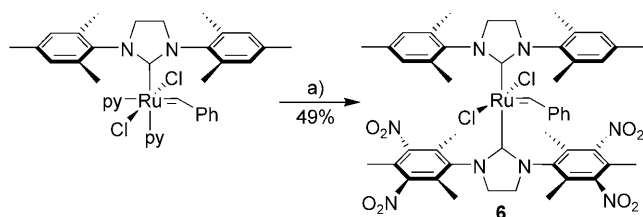
To probe the electron-releasing capacity of the NHC ligand **5**, the synthesis of the complexes [(**5**)IrCl(cod)] (cod =



Scheme 2. Synthesis of nitrated imidazolium salt **5**. Reagents and conditions: a) $\text{H}_2\text{SO}_4/\text{HNO}_3$; 18 h, 0°C .

1,5-cyclooctadiene) and [(**5**)IrCl(CO)₂] was undertaken. [(**5**)IrCl(cod)] is available by standard routes,^[1] whereas the synthesis of [(**5**)IrCl(CO)₂] failed. To quantify the electron donation of the NHC ligand **5**, the redox potential of [(**5**)IrCl(cod)] was determined to be $E_{1/2} = 1.041\text{ V}$, which is significantly more anodic than that of the 4-toluenesulfonyl-substituted complex ($E_{1/2} = 0.910\text{ V}$) previously reported.^[1] Plotting the redox potentials of several [(NHC)IrCl(cod)] complexes against the respective $\nu_{\text{av}}(\text{CO})$ values (see the Supporting Information; based on data recently reported)^[1] allows an extrapolation of the $\nu_{\text{av}}(\text{CO})$ values for the hypothetical complex [(**5**)IrCl(CO)₂] to 2034.5 cm^{-1} . This value lies between the $\nu_{\text{av}}(\text{CO})$ of [($\text{P}(\text{iPr})_3$)IrCl(CO)₂] (2032 cm^{-1}) and [(PEt_3)IrCl(CO)₂] (2038 cm^{-1}),^[25] thus placing NHC ligand **5** among the least electron-donating NHC ligands reported to date.^[26,27]

The tetranitrocarbene **5**, generated in situ from the tetranitroimidazolium salt, was used to synthesize the [(NHC)(NHC_{EWG})RuCl₂(CHPh)] complex **6** in 49% yield (Scheme 3).



Scheme 3. Synthesis of complex **6**. Reagents and conditions: a) KOtBu , $5 \cdot \text{H}_2\text{SO}_4/\text{HNO}_3$, toluene; 20 min, 80°C .

Complex **6** was tested in the RCM of various alkenes. The screening results are summarized in Table 1. Complex **6** does not display significant olefin metathesis activity at room temperature, which was established by the RCM of diallyltosylamide. Employing a 0.5 mol % loading of **6** led to no product formation at all after 24 h at 25°C , and even after 24 h at 50°C , only 20% of product was formed. The catalyst displays significant activity only at temperatures above 60°C .

Consequently, all of the screening reactions were carried out at 80°C .

The RCM of diethyl diallylmalonate and diallyltosylamide was performed as an initial test for the reactivity of **6** at elevated temperatures (Table 1, entries 1, 2). At 80°C , 0.1 mol % of complex **6** is sufficient to effect the quantitative conversion (99%) of both substrates within 60 min. Following these two simple RCM transformations, we attempted the synthesis of a trisubstituted alkene (Table 1, entry 3) with intermediate bulk. Initially 0.5 mol %, then 0.25 mol %, and finally 0.1 mol % of complex **6** were employed. Quantitative conversion was observed for all reactions, even when using as little as 0.1 mol % of complex **6**. This compares well with a specialized Grubbs–Hoveyda complex recently reported, which produces 93% conversion of this substrate at 60°C with a tenfold higher catalyst loading of 1 mol %.^[22]

To enable the proper evaluation of the catalytic activity of **6**, we screened three additional ruthenium complexes under the same conditions as **6**: a Grubbs first-generation complex, the Grubbs second-generation complex **1**, and the Grubbs–Hoveyda complex **4**. The results for the Grubbs first-generation complex are not listed in Table 1, as no conversion was observed for any of the eight reactions (entries 4–11) under the conditions specified in Table 1. From the data listed in Table 1, it is also apparent that the performance of the Grubbs second-generation complex **1** can not match that of the bis(NHC) complex **6**. Observed conversions range between 2–52% (Table 1, entries 4–11) at 0.5 mol % loading and 80°C . But for entry 11, even 0.25 mol % of **6** is sufficient to effect full conversion. Even a drastically increased catalyst loading for **1** of 2.5 mol % (Table 1, entries 4, 7, 9, 10) cannot match the performance of complex **6**. The small increase in conversion between 0.5 and 2.5 mol % loading indicates that the decomposition of **1** is limiting the catalytic activity. The performance of **4** for a few substrates gives respectable results, but less-efficient RCM reactions are nonetheless observed for entries 9, 10, and 11 (90%, 60%, and 58% conversion), whereas for all other reactions (Table 1, entries 4–8), **6** performs much better than **4**. The reaction in entry 7 using **6**, **1**, and **4** was followed by recording the time-conversion curves for each catalyst (see the Supporting Information). Within the first few minutes of the reaction, **1** converts a significant amount of reactant, whereas both **6** and **4** remain latent. Those two complexes only start to produce product after about 10 min, with **6** being much faster than **4**.

The superior performance of complex **6** can be demonstrated more convincingly by comparing the conversion data for this complex with data provided by other groups for other ruthenium complexes, as those data were presumably obtained under optimized conditions for the respective catalytic system. The tetrasubstituted alkene substrates screened (Table 1, entries 4–11) were tested by several other groups using modified Grubbs second-generation complexes,^[18,20,21,28] Grubbs–Hoveyda species,^[29] and indenylidene catalysts.^[19,30] Typical conditions employed by those groups are 5 mol % of ruthenium complex at 60°C or 2.5–5 mol % at 80°C . In contrast, between 0.25–1.0 mol % of complex **6** are sufficient to obtain excellent yields of various tetrasubstituted alkenes (Table 1, entries 4–11, except for

Table 1: Ring-closing metathesis to form tetrasubstituted olefins.^[a]

Entry	Metathesis reaction	Catalyst loading [mol %]	6	1	4
1		0.1 ^[b]	99%	–	–
2		0.1 ^[b]	99%	–	–
3		0.1 0.25 ^[b] 0.5 ^[b]	99% 99% 99% (> 95%)	–	–
4		0.5 0.5 ^[c] 1.0 2.5	48% 65% 78% (75%) –	3% – – 19%	6% – – –
5		0.5 0.5 ^[d]	98% (> 95%) 3% (–)	11% –	28% –
6		0.5	26% (> 20%)	2%	3%
7		0.5 2.5	98% ^[e] –	23% 31%	68% –
8		0.5	80% ^[e]	25%	25%
9		0.25 0.5 2.5	64% 99% (> 95%) –	25% 26% 35%	64% 90% –
10		0.5 1.0 0.5 ^[d] 2.5	60% 87% (87%) 7% ^[d] (–) –	14% – – 23%	– 50% – –
11		0.25 0.5	99% (> 95%) 99%	37% 52%	58% 99%

[a] General procedure for metathesis screen: 0.4 mmol substrate (0.02 M in toluene), toluene stock solution of **6**, **1**, or **4**; 3 h at 80 °C. Conversion determined by GC analysis (yields of isolated product in brackets); all GC peaks characterized by GC/MS; isolated RCM products identified by NMR spectroscopy. Ts = 4-toluenesulfonyl. [b] 60 min. [c] Five times 0.1 mol %. [d] [(NHC)₂RuCl₂(CHPh)], **3**. [e] Products too volatile for isolation.

entry 6). The results reported herein also compare favorably with the conversion data recently reported for a RCM in hexafluorobenzene using 1–5 mol % of catalyst.^[23] None of the lactone (Table 1, entry 6) was formed when using 5 mol % of a Grubbs catalyst.^[20] D'Annibale et al. reported a 40% yield of this product when employing two times 10 mol % (to give 20 mol %) of second-generation catalyst.^[31] For the formation of a cycloheptene derivative (Table 1, entry 10) the use of 5 mol % in a set of five different ruthenium complexes enables conversions in the range of 34–87% at 60 °C.^[18,20] The formation of a tetrasubstituted alkene (Table 1, entry 11) was recently reported with various ruthenium complexes using 2 mol %, 24 h at 40 °C in 80% yield.^[30] or 1 mol % at 70 °C in 99% yield,^[29] or with 1 mol % at 80 °C in 99% yield.^[23]

and can thus be monitored conveniently by UV/Vis spectroscopy. For complex **6** dissolved in pyridine, the replacement of NHC **5** is fast and requires less than 4 min at 60 °C. For the symmetrical complex **3** this reaction is much slower and takes more than 1 h under the same reaction conditions. The absence of a well-defined isosbestic point in the high-temperature experiments is indicative of some decomposition of the pyridine complex. Consequently, the same experiment was repeated at 25 °C (Figure 1). The absorption maximum $\lambda_{\text{max}} = 339$ nm is due to complex **6**, and the new λ_{max} at 365 nm fits well with the $\lambda_{\text{max}} = 368$ nm for an isolated sample of [(NHC)RuCl₂(CHPh)(py)₂]. The reaction of pyridine with complex **3** is much slower at 25 °C; after 60 minutes, the absorption band at 335 nm shows only little change, and at least 600 minutes are required until the reaction with pyridine

It is our working hypothesis that the diminished electron-donating properties of the tetranitrated NHC **5** turn this ligand into a better leaving group.^[32] This proposal was tested by screening two RCM reactions of sterically demanding substrates (Table 1, entries 5 and 10, indicated by footnote [d]) with 0.5 mol % of complex **3**, which has two conventional NHC ligands. In the first reaction (Table 1, entry 5), complex **6** gives virtually quantitative conversion, whereas the use of **3** results in virtually no product formation. In the second example (Table 1, entry 10), complex **6** again displays drastically higher efficiency than **3**. This supports our idea that less electron-donating NHC ligand **5** is a better leaving group. It is, however, likely that the increased steric bulk of the hexasubstituted *N*-aryl groups of NHC **5** also contribute to its leaving group quality by imposing some steric strain in ruthenium complex **6**.

To provide additional evidence for the ability of NHC ligands to act as leaving groups, we probed the substitution of the tetranitrated NHC in complex **6** and the mesityl NHC in complex **3** ligands by pyridine. The related reaction for the Grubbs second-generation complex leading to the replacement of a PCy₃ ligand by pyridine is known to be facile, and the formation of the green complex [(NHC)RuCl₂(CHPh)(py)₂] is complete within a few minutes at room temperature. Such ligand substitution reactions involve significant color changes,

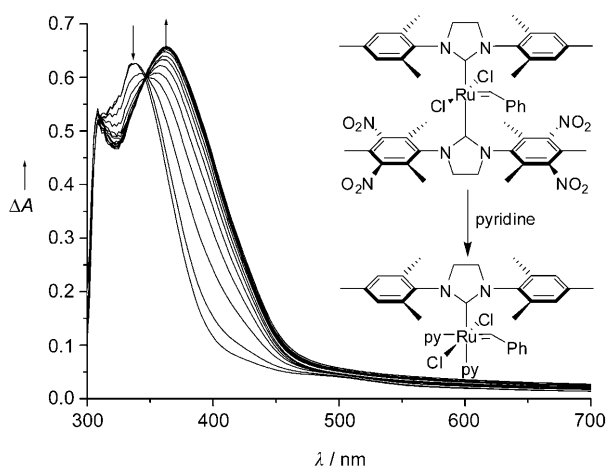


Figure 1. UV/Vis spectra of the NHC substitution reaction for **6** (4×10^{-5} M) in pyridine solvent. Each trace corresponds to 10 min reaction time.

is finished. In contrast to the reaction of **6** with pyridine, there is also no clear evidence for the formation of $[(\text{NHC})\text{RuCl}_2(\text{CHPh})(\text{py})_2]$ from **3** and pyridine.

In conclusion, the tetranitrated NHC **5**- $\text{HNO}_3/\text{H}_2\text{SO}_4$ can be synthesized in excellent yields by direct nitration of the respective imidazolium salt. The electron-donating capacity of **5** is comparable to that of $\text{P}(\text{t}^{\text{Bu}})_3$ and PEt_3 , placing it among the least electron-donating NHC ligands. A UV/Vis experiment provides evidence for the tetranitro NHC being a better leaving group than the mesityl NHC ligand. The easily synthesized complex **6**, of the general type $[(\text{NHC})-(\text{NHC}_{\text{EWG}})\text{RuCl}_2(\text{CHPh})]$, is a highly efficient pre-catalyst for the ring-closing metathesis of substituted alkenes; the formation of tetrasubstituted alkenes require loadings of only 0.25–1 mol %, and for a trisubstituted alkene, as little as 0.1 mol % is sufficient. We are currently studying the activity of complex **6** in other olefin metathesis reactions as well as modifying the nature of both NHC ligands to obtain even more active catalysts.

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