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A Versatile and Highly Z-Selective Olefin Metathesis Ruthenium Catalyst Based on a Readily Accessible *N*-Heterocyclic Carbene.

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ABSTRACT: A ruthenium catalyst for Z-selective olefin metathesis has been synthesized from a readily accessible N-heterocyclic carbene (NHC) ligand that is prepared thanks to an efficient, practical and scalable multicomponent synthesis. The desired ruthenium complex with cyclometalated NHC ligand is obtained by means of selective C(sp^3)-H activation at the adamantyl fragment and X-ray diffraction analysis unambiguously confirmed the structure of the precatalyst. The catalyst demonstrated attractive catalytic performance in self- and cross-metathesis at low catalyst loading to afford the desired internal olefins with high conversion and very high Z-selectivity (up to >99%). The versatility of the chelated catalyst is illustrated by the high cis-selectivity (up to >98%) and high tacticity control (up to >98% syndiotactic) achieved in ring-opening-polymerization, allowing for the production of highly microstructurally controlled norbornene, norbornadiene and cyclopropene-derived polymers.

KEYWORDS: *Olefin metathesis, Z-selective catalyst, Syndiotactic polymers, NHC ligand, Ruthenium Complex.*

During the last two decades, olefin metathesis has evolved to become a highly versatile tool for the construction of C-C double bonds.[1] The development of efficient and robust transition metal-based catalysts for olefin metathesis has allowed important applications in natural product synthesis,[2] biochemistry[3] and material science.[4] Among the key advances, the incorporation of N-heterocyclic carbenes (NHC) as ancillary ligands has enabled new generations of ruthenium-based catalysts with improved properties.[5] In the recent years, particular attention has been given to the development of Ru-based complexes capable of Z-selective olefin metathesis,[6, 2b] as an alternative to more sensitive W-,[7] and Mo-based catalysts.[8] Attractive applications in selective olefin metathesis transformations have been achieved with unsymmetrical NHC ligands,[9] and recent breakthrough works by Grubbs and co-workers evidenced the benefits provided by a chelating unsymmetrical NHC ligand in ruthenium-catalyzed Z-selective olefin metathesis transformations,[10] that opened the door to the development of catalysts with improved activity and Z-selectivity.[11] The most efficient cyclometalated Z-selective ruthenium catalyst **Ru-1** was recently obtained using the unsymmetrical saturated NHC ligand combining a *N*-adamantyl and a bulky *N*-2,6-diisopropylphenyl (Dipp) group (Figure 1).[12] Indeed, catalyst **Ru-1** delivered exceptional level of Z-selectivity in broad scope of transformations,[6b] with the exception of ring-opening-cross metathesis.[13] Nevertheless, and despite the advantageous properties conferred to the cyclometalated-metal species by this unsymmetrical NHC, the cost arising from the multi-step synthesis of such ligands may render their use prohibitive for industrial applications.[14] In fact, the ligands surrounding the metal are the most expensive component of a (Z-selective) metathesis catalyst. This is reinforced by the fact that despite the metal, the ligands cannot be recycled. Therefore, the development of readily accessible NHC ligand for the design of new ruthenium-based catalyst displaying high versatility and high selectivity in the production of Z-olefins is of high interest. Recently, we described a practical and efficient multicomponent procedure for the highly selective synthesis of unsymmetrical unsaturated NHC ligand precursors that provide a cost-effective alternative to the multistep synthesis of their saturated analogues.[15] Notably, this approach allows for the straightforward preparation at multi-gram scale in good yield of the unsymmetrical imidazolium salt **1** bearing the *N*-Dipp and *N*-adamantyl substituents (Figure 1). Herein, we report on the synthesis of a new chelated ruthenium-based catalyst incorporating an unsymmetrical unsaturated NHC, which demonstrated its great versatility and high selectivity in the construction of internal Z-olefins. Moreover, no modification of the Ru-based catalyst is required to produce highly tactic polymers (up to >98% syndiotactic) with very high cis-content (up to >98%).

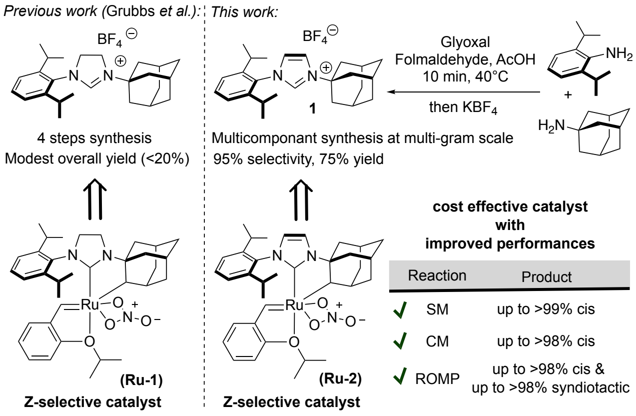
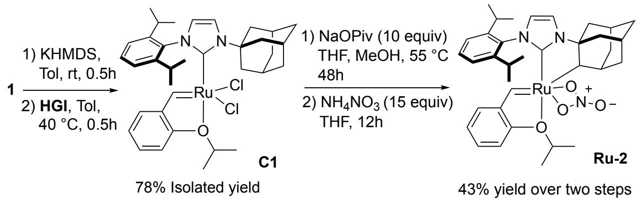


Figure 1. Highly *Z*-selective ruthenium catalyst **Ru-1** based on the saturated unsymmetrical NHC precursor (left). New synthetic approach to the lower-cost highly *Z*-selective ruthenium catalyst **Ru-2** (right). Self-metathesis (SM), cross-metathesis (CM), ring-opening-cross metathesis (ROMP).

We initiated our study by the preparation of complex **Ru-2** incorporating our readily accessible unsymmetrical unsaturated NHC ligand combining the *N*-Dipp and *N*-adamantyl substituents. First, deprotonation of the tetrafluoroborate imidazolium salt **1** with potassium bis(trimethylsilyl)amide (KHMDS) followed by the addition of a stoichiometric amount of the first generation Hoveyda-Grubbs complex (HGI) afforded the expected second generation type complex **C1** with good 78% isolated yield (Scheme 1). X-ray diffraction analysis of this new species allowed us to confirm the prerequisite close proximity between the ruthenium center and the adamantyl C-H bond (2.89 Å) (Figure 2, left).[16] Serenely, the cyclometalation procedure by means of carboxylate-assisted C-H bond activation strategy was engaged in the presence of an excess of sodium pivalate (Scheme 1).[17] Isolation and full characterization, including X-ray crystallography of the stable nitrato-complex **Ru-2** confirmed the five-membered chelating architecture, which is critical for successful stereoselectivity in catalysis (Figure 2, right).[18]

Scheme 1. NaOPiv-Mediated C(sp^3)-H Activation at the Adamantly Fragment to Form the Cyclometalated Ru-2 Complex



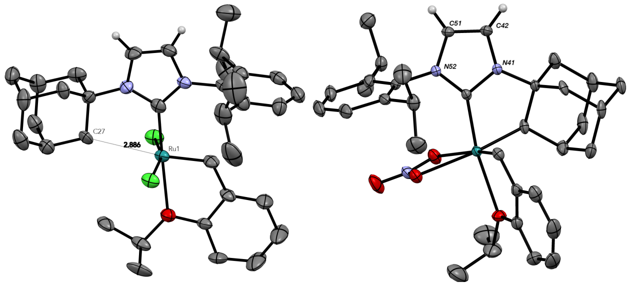
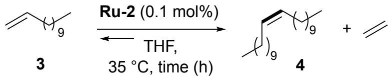


Figure 2. Solid-state structure of complex **C1** (left) and complex **Ru-2** (right) from single crystal X-ray diffraction. Displacement ellipsoids are drawn at 50% probability. Most hydrogen atoms have been omitted for clarity (N in blue, C in grey, Cl in green, O in red, H in white. For complex **C1**: distance between C27 and Ru = 2.89 Å. For complex **Ru-2**: distance between C27 and Ru = 2.06 Å.

The efficiency of this new catalyst was first evaluated in the self-metathesis of an unfunctionalized terminal olefin;[11a] *i.e* 1-dodecene (Table 1). Interestingly, the catalyst **Ru-2** demonstrated excellent catalytic performances at low 0.1 mol% catalyst loading and afforded after 2 hours the desired internal olefin with 88% conversion and with very high >99% selectivity towards primary metathesis products (PMP).[19] Furthermore, high 98% Z-selectivity could be maintained at high conversion without any detectable amount of undesired olefin walking product, suggesting good stability of the cyclometalated catalyst **Ru-2** (Table 1, entry 3).

Table 1. Evaluation of Catalyst Ru-2 in the Self-Metathesis of 1-Dodecene[a]

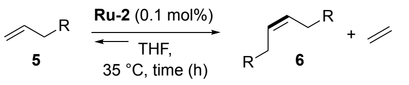


entry	time (h)	Conv. (%)	Z:E ratio	PMP-selectivity (%)
1	1	76	>99:1	>99
2	2	88 (82)[b]	>99:1	>99
3	6	95	98:2	>99
4	22	98	98:2	>99

[a]Conversions, molar ratio of *E* and *Z* isomers, and PMP-selectivity were monitored by GC analysis using tetradecane as internal standard. [b]Isolated yield

The efficiency of our new catalyst was further evaluated in the homometathesis of two more challenging substrates (Table 2). First, while modest reactivity is generally observed for substrates with allylic functionality,[11a,d] the efficiency of the catalyst was illustrated in the self-metathesis of allylacetate to produce the desired self-metathesis product **6a** in high conversion (>98%) and high 97% Z-selectivity with very little alteration of the product configuration after an extended period of time (table 2, entry 4). Regarding allylbenzene, which is easily isomerized to *β*-methylstyrene, **Ru-2** homometathesized allylbenzene with full conversion and excellent 97% Z-selectivity after 6h with very low amount (<5%) of allylbenzene isomerization (Table 2, entry 7). It is important to note that very similar behaviors were described with catalyst **Ru-1**, which afforded the self-metathesis products **6a** and **6b** with very comparable rate of conversion and selectivity.

Table 2. Self-Metathesis of Allylacetate and Allylbenzene

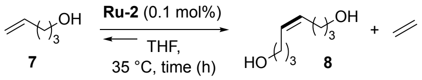


entry	substrate	time (h)	Conv. (%)[a]	Z:E ratio[b]
1	R = OAc (**5a**)	1	70	98:2
2		2	93	97:3
3		4	>98 (89)[c]	97:3
4		8	>98	96:4
5	R = Ph (**5b**)	1	84	>99:1
6		3	96(90)[c]	98:2
7		6	>98	97:3
8		20	>98	85:15

[a]Determined by 1H NMR spectroscopy. [b]Molar ratio of *E* and *Z* isomers were determined by GC. [c]Isolated Yields.

Ruthenium-based olefin metathesis catalysts have demonstrated variable degree of stability in the presence of alcohols.[20] In fact, the free hydroxyl-function may participate in catalyst deactivation and/or decomposition into isomerization active species such as ruthenium hydrides.[21] Therefore, 4-pentanol was established as a particularly challenging benchmark substrate for cylometalated ruthenium catalysts, which demonstrated low activities and/or major erosion of *Z*-selectivity.[22] Interestingly, catalyst **Ru-2** afforded good catalytic activity in the self-metathesis of 4-pentenol (**7**), while attaining and maintaining high *Z*-selectivity at high conversion, surpassing all previously described *Z*-selective cyclometalated catalysts, notably **Ru-1** (Table 3).

Table 3. Self-Metathesis of 4-Pentenol by Catalyst Ru-2[a]

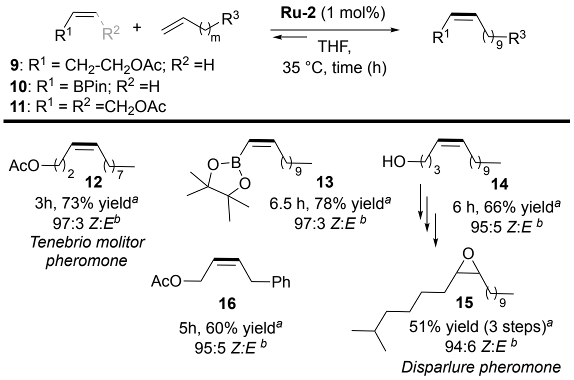


Entry	Time (h)	Conversion (%)	Z:E ratio (%)
1	1	14	>98:2
2	2	50(49)[b]	97:3
3	4	84	93:7
4	6	84	93:7

[a]Conversions and molar ratio of *E* and *Z* isomers were determined by 1H NMR spectroscopy. [b]Isolated Yield

The excellent selectivity obtained in self-metathesis prompted us to further evaluate catalyst **Ru-2** in cross-metathesis (Scheme 2). The reaction between 3-butenyl acetate (**9**) and 1-decene afforded the desired internal olefin product **12**, a *Z*-insect pheromone**,** in good 73% yield and with high 97:3 *Z*:*E* ratio. While cross metathesis with vinyl boronates catalyzed by non-cyclometalated Grubbs type complexes leads to highly *E* isomer products,[23] high 97% *Z*-selectivity was observed with catalyst **Ru-2** for the production in good 78% yield of the vinyl pinacol boronate cross product **13**.[24] Interestingly, 4-pentenol (**7**) could also be engaged efficiently in cross-metathesis with 1-dodecene (**3**) to produce **14** in satisfactory yield and high 95% *Z*-selectivity. The latter was converted in three steps to the disparlure pheromone **15** with high 94% *cis*-epoxy content.[25] While cyclometalated Ru-based catalysts proved inefficient in reacting internal olefins with trans configuration, the substrate scope for cross-metathesis with this family of catalysts is not restricted to terminal olefins.[26] Indeed symmetrical internal *Z*-olefins can be useful coupling partners in such transformations. The CM reaction between allyl benzene (**5b**) and *cis*-1,4-diacetoxybutene (**11**) afforded the desired unsymmetrical internal olefin **16** in good yield and with high 95:5 *Z*:*E* ratio.

Scheme 2. *Z*-selective Cross-Metathesis with Ru-2



[a]Isolated yields. [b]Determined by ^{1}H NMR spectroscopy.

Recently, *Z*-selective Ru-based catalysts have demonstrated their capacity to produce norbornene and norbornadiene-derived polymers with specific microstructures.[27] Nevertheless, while high *cis*-selectivity is often attained with cyclometalated Ru-based catalyst, the production of polymers exhibiting high tacticity is more challenging and requires special catalyst design. In fact, Grubbs and co-workers demonstrated that a modification of the chelating fragment by replacement of the *N*-adamantyl substituent for the less encumbered *N*-tert-butyl group allowed for lower unfavorable interactions that resulted in higher syndioselectivity,[13] but at the expense of catalyst stability.[27b] A close look at the structural parameters of complex **Ru-2** and comparison with the crystal structure of the previously reported complex **Ru-1** evidenced no significant difference.[28] In fact, the planar geometry of the unsaturated NHC ligand (N(42)-C(51)-C(42)-N(41) torsional angle of 0.63°) induced no dramatic change to the topographic steric map of the catalytic pocket and the resulting calculated buried volume for **Ru-2** was only slightly lower than for complex **Ru-1** (45.9 *vs* 46.4) (Figure 3).[29]

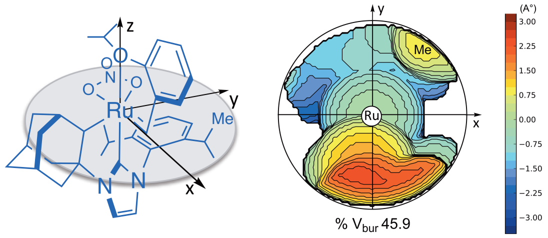
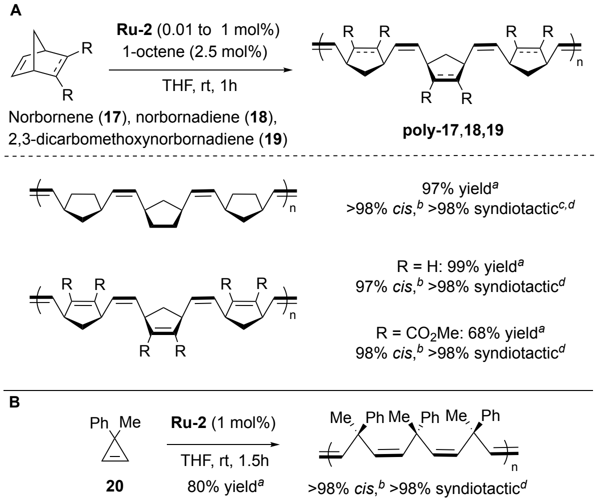


Figure 3. Steric map of complex **Ru-2**. The complex is oriented according to the scheme on the left; the steric map is reported on the right.

Because very small changes in the electronic and steric properties of the ancillary NHC ligand can translate in dramatic differences in catalytic properties, we decided to probe the potential benefit provided by our readily accessible catalyst for the control of tacticity in ring-opening-polymerization (Scheme 3). Our first attempt using catalyst **Ru-2** (0.01 mol%) in the ROMP of norbornene afforded a polymer material with very low solubility that prevented its spectroscopic analysis. On the other hand, norbornene ROMP with the addition of 2.5 mol % of 1-octene as a chain transfer agent, generated **poly-17** with high *cis*-content (>98% *Z*-selectivity). Furthermore, the ^{13}C NMR spectrum of the hydrogenated material was consistent with highly syndiotactic polymer (>98%) (Scheme 3, A). Under the same conditions, the norbornadiene ROMP afforded the polymeric product **poly-18** in high yield with the same level of selectivity control (97% *cis*, >98% syndiotactic). Moreover, the polymerization of the more complex monomer **19** using 1 mol% of **Ru-2** produced a highly *cis* and syndiotactic material (**poly-19**), which was isolated in 68% yield. Finally, we turned our attention to the chiral cyclopropene monomer **20** that was only previously considered with Mo- and W-based catalysts.[30] Once again, excellent stereogenic metal control was observed with **Ru-2** producing **poly-20** with very high *cis,syndio*-selectivity, since microstructural errors were below the detection level (Scheme 3, B).

Scheme 3. Ring-Opening Metathesis Polymerization of Norbornyl (Part A) and Cyclopropenyl Substrates (Part B)



[a]Isolated yield; [b]Determined by ^{1}H NMR spectroscopy; [c]Tacticity of the hydrogenated polymer; [d]Determinated by ^{13}C spectroscopy (isotactic sequences were below the detection limit).

In summary, we have developed a new highly *Z*-selective ruthenium catalyst based on a readily accessible unsaturated unsymmetrical NHC ligand. The catalyst **Ru-2** afforded a stable catalytic system with excellent activities in the self-metathesis and cross-metathesis of (functionalized) terminal olefins, attaining and maintaining high *Z*-selectivity at high conversion, with the capacity to surpass the efficiencies of previously described *Z*-selective cyclometalated catalysts. Moreover, no structural modification of the Ru-based catalyst is required to achieve high tacticity (up to >98% syndiotactic) and high *cis*-selectivity (up to >98%) in ring-opening-polymerization allowing for the production of highly microstructurally controlled norbornene, norbornadiene and cyclopropene-derived polymers.

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

NMR spectra of products, GC analyses, experimental procedures, X-ray crystallographic data (PDF)

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Notes

The authors declare no competing financial interests

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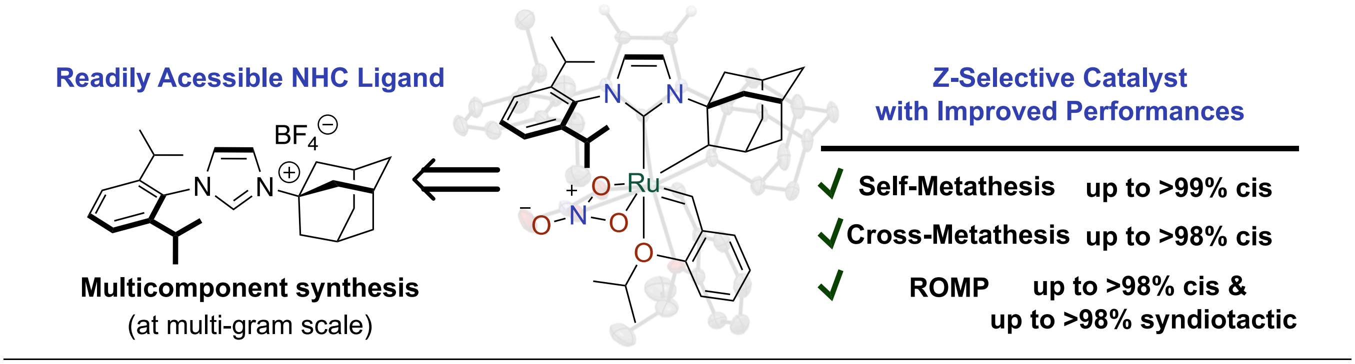
Readily Acessible NHC Ligand
BF4
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Multicomponent synthesis
(at multi-gram scale)
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Z-Selective Catalyst
with Improved Performances
✓ Self-Metathesis up to >99% cis
✓ Cross-Metathesis up to >98% cis
✓ ROMP up to >98% cis &
up to >98% syndiotactic