Tetrahedron 69 (2013) 7408–7415

Contents lists available at SciVerse ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Efficient, durable and reusable olefin metathesis catalysts with high affinity to silica gel

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ARTICLE INFO

Article history:
Received 8 February 2013
Received in revised form 7 June 2013
Accepted 17 June 2013
Available online 24 June 2013

Keywords:
Olefin metathesis
Catalysis
Reusable catalyst
Ruthenium removal
Organometallic reagents

ABSTRACT

The new Scorpio type olefin metathesis catalysts with very high affinity to silica gel are reported. After completion of the reaction, those complexes can be efficiently separated from reaction product by direct filtration of reaction mixture through a short pad of silica gel. Products obtained by this methodology are contaminated with low amounts of residual ruthenium. Especially, catalyst $(H_2IPr)(Cl)_2Ru{=}C(H)(C_6H_4OR)$ (**5b**, R=CH(Me)(C(O)N(Me)OMe) exhibited very high activity and could be easily recovered and reused. Additionally, this catalyst was found to be effective already at 0.1–0.5 mol % and showed good compatibility with environmentally benign solvents.

1. Introduction

Olefin metathesis is a powerful transformation that is widely used in organic synthesis for the formation of carbon–carbon double bonds.[1–5] The continuing success of olefin metathesis is due to the development of efficient and stable catalysts for this transformation (Fig. 1).

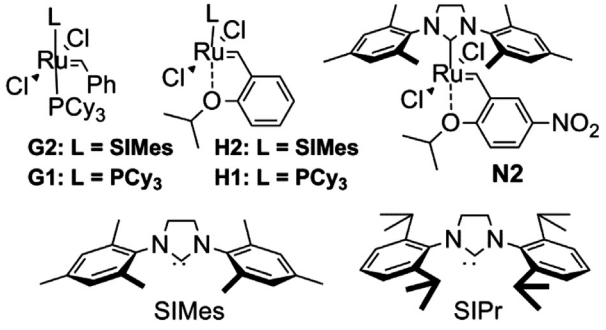

Fig. 1. Classical metathesis catalysts and NHC ligands.

For current applications, commercially available first- and second-generation catalysts **G1** and **G2** are already remarkably efficient.[1,2] The Hoveyda catalyst **H1**,[6] and its second-generation congener **H2**, possess reactivity comparable to that of **G2** and they are efficient for the metathesis of highly electron-deficient substrates (e.g., acrylonitrile).[7] Grela et al. demonstrated that the 4-nitro-substituted complex **N2** initiates olefin metathesis dramatically faster than the parent Hoveyda–Grubbs catalyst **H2**.[8,9] Later on, it was reported that replacement of the terminal isopropyl substituent of the hemilabile ether functionality by an ester group, originally selected also on account of its electron-withdrawing properties led to the isolation of the new complex **E2** (Fig. 2).

E2 was the first example of the so called Scorpio catalyst, where the added ester group coordinates to the metal, thereby contributing to the overall stability of the complex.[10,11] Recently, Grela published further catalysts with other functional groups installed as terminal substituents of the benzylidene ether ligand, such as **E2′**, **Kme2**, **Ket2** and **Carb2** that were found to be very active.[12,13] One of the major problems in the application of olefin metathesis, particularly in pharmaceutical industry, is related to the residual ruthenium removal.[2] Ruthenium level in orally administrative drugs must not exceed 10 ppm. Additionally ruthenium hydride complexes, formed after decomposition of metathesis catalysts can also lead to unwanted side reactions during product isolation and purification.[14] Several protocols for separation of metal containing impurities from metathesis products have been developed so far.[15]

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0040-4020/$ – see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.tet.2013.06.056

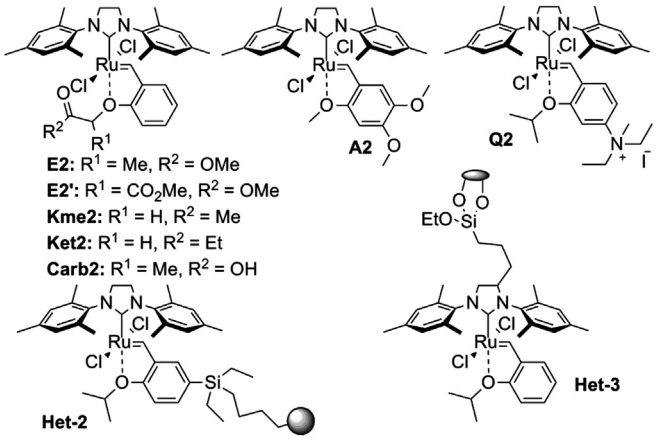


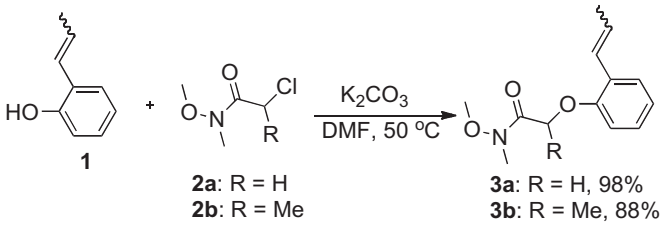
Fig. 2. Modified olefin metathesis catalysts.

For example, extraction with supercritical carbon dioxide,[16] treatment with aqueous hydrogen peroxide and filtration through silica gel[17] as well as the use of various scavengers[18] allow to reduce the ruthenium content to 10–60 ppm. Alternatively, two cycles of chromatography combined with 12 h incubation with activated charcoal was shown to reduce the amount of residual ruthenium to 60 ppm.[19] However, those methods are time consuming and in some cases can provoke side reactions. In a different approach catalysts with high affinity to silica gel, such as **A2**[20] and **Q2**[21] (Fig. 2) or heterogenic complexes, such as **Het-2**[22] and **Het-3**[23] and others were synthesized.[24–37] Homogeneous catalysts with classical NHC ligand and modified benzylidene ligand allow to obtain product having from 12 to 420 ppm of ruthenium with the use of simple purification step. Heterogenic catalysts can give superior results, but their synthesis is much more complicated. Inspired by those reports we developed novel catalysts bearing a hydroxamic ester group as terminal substituent of the styrenyl ether. Our intention was to combine high activity observed for Scorpio type catalysts with the possibility of simple purification of products from catalyst and ruthenium containing impurities. Additionally, we were interested in developing an easy and efficient method for catalyst recovery and reuse. The introduction of a hydroxamic ester into the catalyst structure resulted in a very high affinity to silica gel, which depends however on the solvent used. Herein we present the results on the synthesis and activity of those new catalysts. Additionally, the removal of residual ruthenium from products as well as catalyst recovery and reuse experiments is reported. Finally, experiments showing high activity of the catalyst when performing reaction in green solvents are presented.

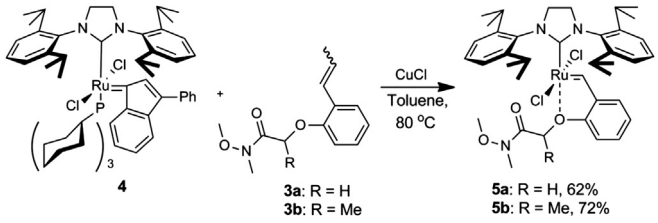
2. Results and discussion

In the presented approach, the appropriate carbene ligand precursors **3a** and **3b**, being hydroxamic ester-substituted styrenyl ethers, were prepared in Williamson reaction using commercially available 2-propenylphenol **1** and suitable alkylating agents **2a** and **2b**, respectively (Scheme 1).

It is quite well known that SIPr ligand provide higher catalyst stability.[38] Therefore, we decided to synthesize new catalysts bearing SIPr ligand. New complexes were obtained in the reaction of ligands **3a** and **3b** with indenylidene complex **4** (Scheme 2). The reaction was carried out in toluene at 80 °C in the presence of copper(I) chloride, commonly used as a phosphine scavenger[6] affording the desired catalysts **5a** and **5b** with good yields. Complexes **5a** and **5b** were stable during purification on silica gel. Both **5a** and **5b** were very stable in the solid state—no signs of decomposition were observed after 3 months storage.



Scheme 1. Preparation of benzylidene ligands **3a** and **3b**.



Scheme 2. Preparation of catalysts **5a**,**b**.

Activity of complexes **5a** and **5b** was tested using standard RCM substrate **6** and results were compared with those obtained with commercially available **H2** and **N2** (Fig. 3). Those reactions were run in dry, degassed dichloromethane under argon. Catalyst **5b** exhibited activity comparable to that presented by **N2**, which is known to be a fast initiator, giving almost full conversion of substrate after 20 min. Interestingly, the activity of **5a** was low when compared with **5b** and was comparable with that observed for **H2** catalyst.

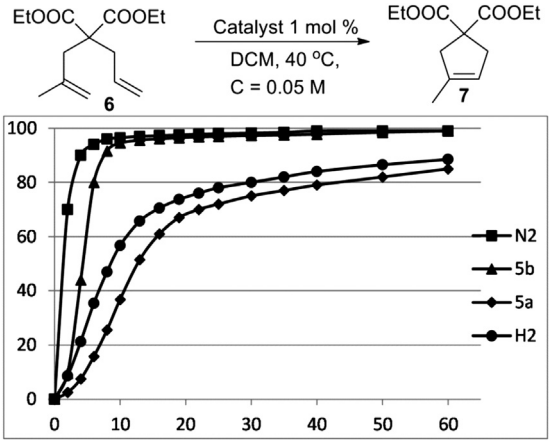
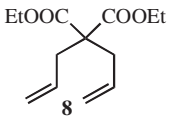
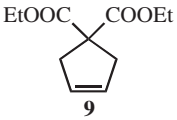
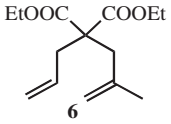
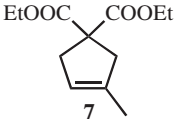
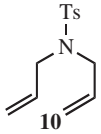
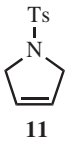
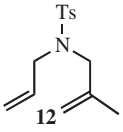
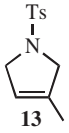
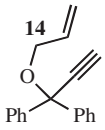
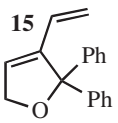
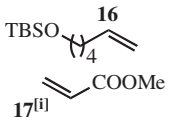
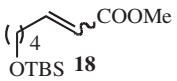


Fig. 3. RCM of diethyl allylmethallylmalonate (**6**).

Next complexes **5a** and **5b** were tested in various metathetical transformations to establish the scope of their application (Table 1). Noteworthy, those reactions were run in non-degassed DCM without protective atmosphere of inert gas. For comparison reactions under the same conditions with the use of **N2** and **H2** were also carried out. In turn, results obtained with the use of **E2**, **Q2** and **A2** are presented as reported in the literature.

In general, catalysts **5a** and **5b** were found to give better results than **H2**, **E2**, **A2**, **Het-2** and **Het-3** in all the tested reactions. The obtained results with the use **5a** and **5b** were comparable with **Q2**, this includes the residual ruthenium levels found in the reaction products. The latter however binds to the silica gel strongly and this fact makes impossible its recovery and reuse. Noticeably, the residual ruthenium level in all products obtained using our new catalysts was from 5 to 400 times lower than that observed in the products synthesized with **N2** or **H2**. For product purification, we used a straightforward procedure, which involved only filtration of

Table 1
Activity tests in various metathesis transformations catalyzed by **5a**, **5b**, **N2** and **H2** on air and in non-degassed solvent.[a] For comparison, results obtained with **E2**, **Q2** and **A2** reported in the literature

Entry	Substrate	Product	Cat.	Time [min]	Yield[b] [%]	Ru[c] [ppm]
1	 **8**	 **9**	**5a**	60	94	41
2			**5b**	30	98	14
3			**N2**	30	99	2180
4			**E2**[d]	360	(70)	ND
5			**Q2**[e]	60	(99)	12
6	 **6**	 **7**	**5a**	150	97	17
7			**5b**	60	96	9
8			**N2**	50	98	1950
9			**H2**	120	94	3640
10			**A2**[f]	1080	(75)	ND
11			**Q2**[e]	90	(96)	ND
12			**Het-2**[g]	180	(41)	ND
13	 **10**	 **11**	**5b**	20	>98	36
14			**N2**	10	99	1980
15			**E2**[d]	60	(55)	ND
16			**Q2**[e]	30	99	68
17			**Het-2**[g]	420	(95)	ND
18			**Het-3**[h]	120	(>95)	<5 ppb
19	 **12**	 **13**	**5b**	40	>98	32
20			**N2**	20	99	2210
21	 **14**	 **15**	**5a**	45	99	37
22			**5b**	30	>98	15
23			**N2**	30	99	1430
24			**E2**[d]	15	99	ND
25			**Q2**[e]	30	98	ND
26	 **16** **17**[i]	 **18**	**5a**	120	93	113
27			**5b**	50	92	143
28			**N2**	15	94	704
29			**H2**	40	87	2550
30			**E2**[d]	960	89	ND

[a] Reaction conditions: catalyst 1 mol %, CH_2Cl_2, reflux, C=0.05 M.
[b] Isolated yield after column chromatography. In parentheses yield determined by GC.
[c] Determined by ICP-MS.
[d] Ref. 13, reaction conditions: catalyst 1 mol %, CH_2Cl_2 (for entry 30 reaction was performed in commercially grade CH_2Cl_2), 0 °C (45 °C for entry 24), C=0.02 M.
[e] Ref. 21, reaction conditions: catalyst 5 mol %, CH_2Cl_2 25 °C, C=0.02 M.
[f] Ref. 20, reaction conditions: catalyst 2.5 mol %, CH_2Cl_2 25 °C.
[g] Ref. 22, reaction conditions: catalyst 5.0 mol %, CH_2Cl_2 45 °C, C=0.02 M.
[h] Ref. 23, reaction conditions: catalyst 0.4 mol %, C_6H_6 30 °C. ND—not determined.

reaction mixture through a short pad of silica gel (SiO_2/substrate mass ratio=7) (Fig. 4). When DCM was used as an eluent, **5a** and particularly **5b** showed high affinity to silica gel what allowed to obtain products with low residual ruthenium (determined by inductively coupled plasma mass spectroscopy, ICP-MS). Only in the case of the CM was the ruthenium content in the product over 100 ppm (Table 1, entries 26, 27).

In Table 2 we present few examples of reactions catalyzed by low amount of catalyst **5b** in non-degassed toluene and without protective atmosphere of inert gas. Dropwise addition of catalyst allows for reduction of its loading to 0.1 mol % in the case of RCM reactions (entries 2, 4). We observed a positive effect of slow addition of catalyst also in CM and this reaction was completed with 0.3 mol % of catalyst (entry 8). Interestingly, enyne ring closing proceeded better when the catalyst was added in one portion (entry 5). This transformation turned out to be quite challenging and 0.5 mol % of catalyst was necessary to achieve a good yield.

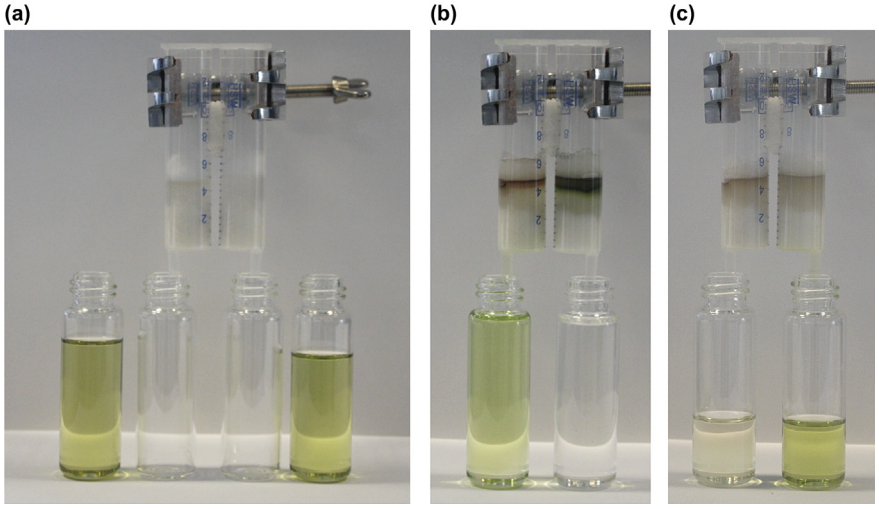


Fig. 4. Filtration of the reaction mixture through a short pad of silica. (a) Mixture after metathesis reaction with the use of **H2** (on the left) and **5b** (on the right) before filtration; (b) mixture after filtration and washed with DCM (**H2** on the left and **5b** on the right); (c) catalyst **5b** can be subsequently washed with EtOAc and reused (**H2** on the left and **5b** on the right).

Table 2
Low loading experiments in non-degassed toluene and without protective atmosphere of inert gas.[a] NI—not isolated

Entry	Substrate	Product	**5b** mol %	Time [min]	Conversion[b] [%]	Yield [%]
1	**10**	**11**	0.1	60	76	NI
2			0.1[c]	60	97	94
3	**12**	**13**	0.1	60	55	NI
4			0.1[c]	60	98	96
5	**14**	**15**	0.5	300	94	92
6			0.5[c]	300	86	NI
7	**16**, **17**[d]	**18**	0.3	180	68	NI
8			0.3[c]	180	94	90

[a] Reaction conditions: toluene, 70 °C, *C*=0.1 M.
[b] Determined by GC.
[c] Added dropwise with the use of syringe pump.
[d] **17** (5 equiv) was used.

Examples of much lower loadings are known from the literature however, they usually require special conditions, such as running the reaction at high concentration,[39] robotic equipment[40] or performing reaction in a glove box.[41] Recently, fast olefin metathesis at low catalyst loading was reported by Plenio et al., but still all these reactions needed an argon atmosphere and the use of dry solvents to go to completion.[42] The use of our catalysts therefore, is advantageous because it does not require a protective atmosphere of an inert gas, nor specially dried and degassed solvents, thus making our catalysts especially suitable for industrial applications.

High stability, activity and efficiency of **5b** give us the opportunity to its recovery and reuse. For this experiment we used protocol reported by Grela et al.[21] After filtration of reaction mixture through silica gel and removal of product with an additional portion of DCM, the catalyst was eluted with ethyl acetate. The sequence consisting of RCM, enyne, RCM, CM and RCM was performed. Similar approach was previously reported for heterogenic catalyst **Het-2**.[22] However, both **Het-2**[23] and **Het-3**[23] as well as **A2**[20] showed noticeable decrease in activity after 3–4 cycles and were relatively slow initiators. Notably, in our case the products were eluted quantitatively and did not contaminate the subsequent reaction mixture, moreover we did not observe any traces of isomerization by-products and full conversion of substrate was noted in each run. The results of **5b** recycling and reuse are presented in Table 3. After fifth run the purity of crude **5b** was checked

Table 3
Recovery and reuse of catalyst **5b**[a]

Cycle	Substrate	Product	Time [min]	Product			**5b** Yield [%], (mg)
				Yield[b] % (mg)	Purity[c] [%]	Ru [ppm]	
1	**10**	**11**	20	97 (983)	>99	161	86 (61)
2	**14**	**15**	30	>99 (962)	>99	58	89 (54)
3	**12**	**13**	50	>99 (825)	98	113	85 (46)
4	**16**, **17**	**18**	50	77[d] (610)	>99	ND	97 (40)
5	**10**	**11**	35	97 (553)	98	184	90 (36)

[a] Conditions: **5b** 2 mol %, *C*=0.05 M, dry DCM, 40 °C.
[b] Isolated yield.
[c] Determined by GC.
[d] Reaction with 2 equiv of **17**, after separation of catalyst, product was purified by column chromatography; 17% of a dimer of **16** was obtained as well.

by ^{1}H NMR and an equimolar mixture of **5b** and dimer of **3b** was observed. Nonetheless, this mixture still efficiently mediate metathesis reactions and no sign of **3b** was observed in products. As shown in Fig. 4 the classical **H2** complex does not provide such an opportunity. Relatively high catalysts loadings (2 mol %) are needed in recovery/reuse experiments. This fact can be explained by the lack of the previously suggested boomerang effect in Hoveyda-type catalysts.[7b,c] Experiments with lower catalyst loadings resulted a decrease in the yields of the reaction products.

Nowadays, the chemical industry, in particular fine-chemical and pharmaceutical industry, use large amounts of solvents per mass of final products. Therefore, solvents define a major part of the environmental performance of a process and also impact on cost, safety and health issues. The goal to minimize the environmental impact resulting from the use of solvents in chemical production as well as their impact on safety and health is expressed by the idea of '*green*' solvents.[43,44] In that respect, straight-chain alkanes (e.g., hexane, heptane), ethers (diethyl ether, methyl *tert*-butyl ether [TBME] or cyclopentyl methyl ether [CPME]), simple alcohols and esters (e.g., ethyl acetate) are considered as green solvents. In Table 4 we show an example of RCM reaction catalyzed by **5b** carried out in such green solvents. In the tested reaction good to excellent conversions are observed after 60 min reaction time at 40 °C. It should be noted that all reactions were performed in ACS grade solvents and under an air atmosphere. These results clearly show that catalyst **5b** is suitable for industrial applications where the need to perform reactions under eco-friendly conditions is very important. It has to be added that

the use of catalysts **H2** and **E2** resulted in much lower conversions (Table 4).

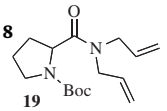
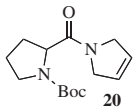
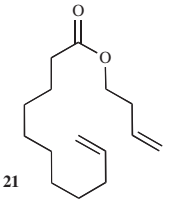
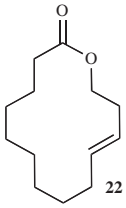
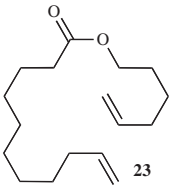
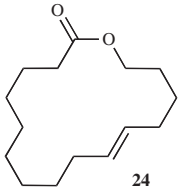
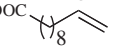
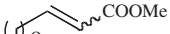
In order to further test the performance and utility of catalyst **5b** in green solvents, we have applied it in the RCM reaction of bio-like substrate **19** to obtain the desired cyclic compound **20** (Table 5 entry 2). Catalyst **5b** was also very efficient in the RCM reaction leading to 14- and 16-membered lactones **22** and **24**, respectively (Table 5 entries 3 and 4). These results are important because the macrocyclic motif is widely prevalent in a number of natural products and pharmaceuticals[45] and also provides the backbone for a unique class of olfactory compounds, termed macrocyclic musks.[46] Finally, **5b** was used in the CM reaction of methyl 10-undecenoate (**25**) with methyl acrylate (**17**) yielding the desired product **26** using *i*-PrOH as solvent (Table 5 entry 5). This result is valuable because 10-undecylenic acid derivatives constitute feedstock readily available from castor oil and have already been used for the industrial production of C11-polyamide (PA11) in the Rilsan® process.

Table 4
RCM of **8** promoted by **5b**, **E2** and **H2** in ACS grade green solvents on air[a]

Entry	Solvent	Catalyst (mol %)	Conversion[b] [%]
1	MeOH	**5b** (0.5)	52
2	MeOH	**E2** (0.5)	7
3	MeOH	**H2** (0.5)	17
4	*i*-PrOH	**5b** (0.5)	94
5	*i*-PrOH	**E2** (0.5)	10
6	*i*-PrOH	**H2** (0.5)	30
7	CPME	**5b** (0.2)	98
8	CPME	**E2** (0.2)	36
9	CPME	**H2** (0.2)	54
10	*n*-Heptane	**5b** (0.2)	96
11	AcOEt	**5b** (0.2)	>99
12	AcOEt	**E2** (0.2)	65
13	AcOEt	**H2** (0.2)	88

[a] Reaction conditions: 40 °C, *C*=0.1 M, 60 min.
[b] Determined by GC.

Table 5
RCM and CM products obtained in ACS grade AcOEt under an air atmosphere[a]

Entry	Substrate	Product	**5b** (mol %)	Yield[b] [%]
1[c]	**8**  **19**	**9**  **20**	0.1	93
2[c]			0.1	92
3[d,e]	 **21**	 **22**	0.5	97
4[d,f]	 **23**	 **24**	0.5	95
5[g]	**25** MeOOC  **17** COOMe	COOMe  COOMe **26**	0.5	88

[a] Reaction conditions: catalyst added with the syringe pump over 1 h, reaction time 1.5 h.
[b] Yields for isolated products.
[c] *C*=0.1 M, 40 °C.
[d] *C*=0.005 M, 70 °C.
[e] *E*/*Z* 9/1.
[f] *E*/*Z* 8/2.
[g] **17** (6 equiv), catalyst added over 2 h with syringe pump, reaction time 3 h, *C*=0.1 M, 70 °C, solvent *i*-PrOH, *E*/*Z* 9/1, selectivity towards CM product (96%), conversion (92%) and yield were determined by GC using dodecane as internal standard.

3. Conclusions

In conclusion, we presented new Scorpio type catalysts bearing hydroxamic ester group. Those catalysts can be easily obtained from commercially available substrates. Particularly, complex **5b** exhibited high activity and efficiency. Recovered, crude **5b** maintained activity and efficiency for at least five subsequent reactions. Importantly, products obtained using complex **5b** have low level of residual ruthenium after implementation of simple purification step. This fact along with the possibility of using low loadings of **5b** and its high efficiency in ACS grade green solvents (TON up to 920) make this catalyst especially suitable for industrial applications, in particular in fine-chemical and pharmaceutical industry.

4. Experimental part

4.1. General information

Solvents were dried by distillation over the following drying agents and were transferred under argon: toluene (Na), *n*-pentane, CH_2Cl_2 (CaH_2). Column chromatography was performed with the use of Merck silica gel 60 (230–400 mesh). NMR spectra were recorded on Bruker Avance 300 MHz spectrometer in $CDCl_3$; chemical shifts (δ) are given in parts per million (ppm) downfield from trimethylsilane as referenced to residual protio solvent peaks, coupling constants (*J*) are reported in hertz (Hz). GC analysis: Trace GC Ultra, Thermo Electron Corporation, HP-5 column. MS (ESI): LCT PremierXE Waters mass spectrometer. Ru content was evaluated using ICP-MS. IR spectra were recorded on a Perkin–Elmer 1600 FTIR spectrometer.

4.2. Preparation of catalyst 4

A 100 mL Schlenk flask was purged with argon and charged with dry hexane (10 mL) and commercially available 1,3-bis(2,6-diisopropylphenyl)-4,5-dihydroimidazolium tetrafluoroborate [**SIPr·BF$_4$**, CAS 282109-83-5] (182 mg, 0.379 mmol) followed by the addition of potassium *tert*-pentoxide (0.207 mL of 1.7 M solution in toluene, 0.352 mmol). The resulting mixture was stirred at room temperature for 1 h. After that time commercially available dichloro(3-phenyl-1*H*-inden-1-ylidene)bis(tricyclohexylphosphine) ruthenium(II) [**M1**, CAS 250220-36-1] (250 mg, 0.271 mmol) was added and the resulting mixture was stirred at reflux for 30 min. After completion of the reaction the reaction mixture was cooled down to room temperature and concentrated in vacuo. Crude product was purified by column chromatography (EtOAc/cyclohexane 1/10) affording the desired ruthenium complex **4** as a red solid (260 mg, 92.9% yield). Spectroscopic analysis was consistent with the literature data.[47] ^{1}H NMR (300 MHz, CD_2Cl_2): δ 8.90 (d, *J*=7.0 Hz, 1H), 7.62 (d, *J*=7.0 Hz, 2H), 7.50–7.49 (m, 1H), 7.44–7.36 (m, 6H), 7.25 (t, *J*=7.2 Hz, 1H), 7.19 (t, *J*=7.3 Hz, 1H), 7.11 (d, *J*=7.1 Hz, 1H), 6.82 (s, 1H), 6.80 (d, *J*=7.7 Hz, 1H), 6.69 (d,

J=6.5 Hz, 1H), 6.62 (d, *J*=7.5 Hz, 1H), 4.41–4.35 (m, 1H), 4.18–4.09 (m, 2H), 4.05–4.00 (m, 1H), 3.90–3.80 (m, 2H), 3.61–3.55 (m, 1H), 3.03–2.95 (m, 1H), 2.00–1.94 (m, 3H), 1.75–0.90 (m, 51H), 0.65 (d, *J*=6.2 Hz, 3H).

4.3. Protocol for the synthesis of ligands 3a and 3b

To the solution of 2-propenylphenol (**1**), (1 equiv, mixture of *E* and *Z* isomers) in DMF (*C*=0.5 M) solid K_2CO_3 (2 equiv) was added, and the resulting mixture was stirred at room temperature for 15 min. Next, the appropriate alkylating reagent **2a** or **2b** (1.2 equiv) was added and the reaction mixture was heated at 50 °C for 20 h with vigorous stirring. After that time, solvent was removed under vacuum and water was added to the residue. The aqueous phase was extracted with EtOAc and the organic layer was washed with brine and dried over $MgSO_4$. Crude products were purified by column chromatography using mixture of EtOAc/*c*-hexane as eluent.

*4.3.1. (E/Z)-N-Methoxy-N-methyl-2-(2-[prop-1-en-1-yl]phenoxy) acetamide (**3a**).* Yield 97%, light yellow oil. Isomer mixture *E*/*Z*=5/1. *E* isomer, ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45 (dd, *J*=7.5, 1.6 Hz, 1H), 7.20–6.80 (m, 4H), 6.30 (dq, *J*=16.0, 6.4 Hz, 1H), 4.83 (s, 2H), 3.73 (s, 3H), 3.25 (s, 3H), 1.89 (dd, *J*=6.7, 1.7 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.9, 130.4, 127.6, 127.0, 126.8, 126.6, 125.6, 120.9, 112.3, 66.3, 61.6, 32.4, 19.0. IR, ν_{max} (KBr): 3501, 2937, 1688, 1598, 1579, 1487, 1446, 1328, 1294, 1226, 1178, 1122, 1062, 989, 855, 750, 629, 591, 466, 434 cm^{-1}. HRMS calcd for $C_{13}H_{17}NO_3$ $(M)^+$ *m*/*z* 236.1287 found 236.1290.

*4.3.2. (E/Z)-N-Methoxy-N-methyl-2-(2-[prop-1-en-1-yl]phenoxy) propanamide (**3b**).* Yield 88%, yellow oil. Isomer mixture *E*/*Z*=6/1. *E* isomer, ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42 (dd, *J*=7.7, 1.7 Hz, 1H), 7.30–6.70 (m, 4H), 6.24 (dq, *J*=15.9, 6.6 Hz, 1H), 5.15–5.08 (m, 1H), 3.70 (s, 3H), 3.22 (s, 3H), 1.90 (dd, *J*=6.6, 1.8 Hz, 3H), 1.60 (d, *J*=6.7 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.3, 130.4, 127.6, 126.8, 126.4, 125.7, 121.6, 121.0, 113.4, 71.8, 61.5, 32.6, 18.9, 17.7. IR, ν_{max} (KBr): 3501, 3345, 2937, 1682, 1597, 1579, 1486, 1452, 1387, 1295, 1239, 1176, 1148, 1078, 1039, 992, 944, 751, 620, 555, 433 cm^{-1}. HRMS calcd for $C_{14}H_{19}NNaO_3$ $(M+Na)^+$ *m*/*z* 272.1263 found 272.1250.

4.4. General protocol for the synthesis of catalysts 5a,b

Ligand **3a** or **3b** (1.2 equiv) and CuCl (1.5 equiv) were placed in an Schlenk flask. The flask was filled with argon and then dry toluene (*C*=0.1) was added. Afterwards complex **4** (1 equiv) was added and the resulting solution was stirred at 80 °C for 20 min. Then reaction mixture was cooled down to room temperature and concentrated under vacuum. The resulting material was dissolved in a minimum amount of DCM and purified by flash chromatography (*c*-hexane/EtOAc 7/3).

Catalyst **5a**, yield 62%, green microcrystalline solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 16.47 (s, 1H), 7.56–7.44 (m, 3H), 7.42–7.32 (m, 4H), 7.00–6.86 (m, 2H), 6.81 (d, *J*=8.2 Hz, 1H), 4.83 (s, 2H), 4.14 (s, 4H), 3.63 (s, 7H), 3.04 (s, 3H), 1.31–1.16 (m, 24H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 298.5, 213.7, 167.8, 153.0, 149.1, 146.2, 138.2, 128.9, 128.1, 124.3, 122.2, 113.3, 65.4, 61.4, 54.6, 32.5, 28.6, 26.5, 23.7. IR, ν_{max} (KBr): 3440, 3066, 3039, 2963, 2928, 2867, 1935, 1652, 1592, 1475, 1454, 1404, 1327, 1296, 1260, 1232, 1105, 1048, 993, 931, 875, 804, 758, 748, 647, 598, 555, 434, 462 cm^{-1} HRMS calcd for $C_{38}H_{51}ClN_3O_3Ru$ $(M-Cl)^+$ 734.2662 found 734.2662.

Catalyst **5b**, yield 72%, green microcrystalline solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 16.46 (s, 1H), 7.53–7.35 (m, 7H), 6.90–6.74 (m, 3H), 5.27 (q, *J*=6.3 Hz, 1H), 4.14 (s, 4H), 3.70–3.61 (m, 7H), 2.97 (s, 3H), 1.55 (d, *J*=6.3 Hz, 3H), 1.33–1.12 (d, *J*=6.8 Hz, 24H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 297.7, 214.1, 170.6, 151.8, 149.0, 145.9, 138.1, 128.9, 128.1, 124.9, 122.6, 112.5, 72.1, 61.4, 54.6, 32.5, 29.6, 26.4, 23.6, 17.6. IR, ν_{max} (KBr): 3439, 3069, 2968, 2864, 1792, 1663, 1592, 1574, 1455, 1400, 1391, 1327, 1296, 1400, 1252, 1216, 1176, 1107, 1045, 993, 936, 850, 860, 803, 743, 648, 556, 461, 438 cm^{-1}. HRMS calcd for $C_{39}H_{53}N_3O_3ClRu$ $(M-Cl)^+$ 748.2819 found 748.2844.

4.5. General procedure for olefin metathesis

Under argon the substrate (1 mmol) was dissolved in dry, degassed DCM (20 mL, *C*=0.05 M), and solid catalyst (1 mol %) was added in one portion. The reaction mixture was stirred at reflux and the reaction progress was monitored by GC. After cooling down, the reaction mixture was filtered through a pad of silica gel (SiO_2/substrate mass ratio=7). The product was eluted with additional portion of reagent grade DCM (20 mL). The solvent was removed, the product was dried on vacuum and its purity was determined by GC.

4.6. General procedure for low catalyst loading experiments

The substrate (1 mmol) was dissolved in dry, non-degassed toluene (*C*=0.1 M), and catalyst was added (in one portion or drop by drop with the use of syringe pump). The reaction mixture was stirred at 70 °C and the reaction progress was monitored by GC. After cooling down, the reaction mixture was filtered through a pad of silica gel (SiO_2/substrate mass ratio=7). The product was eluted with additional portion of reagent grade toluene. The solvent was removed, product was dried on vacuum.

4.7. General procedure for catalyst recovery experiment

The substrate was dissolved in dry DCM (*C*=0.05 M), and solid catalyst (2 mol %) was added in one portion. The reaction mixture was stirred at reflux and the reaction progress was monitored by GC. After cooling down, the reaction mixture was filtered through a pad of silica gel (SiO_2/substrate mass ratio=7). The product was eluted with additional portion of reagent grade DCM. The solvent was removed, the product was dried on vacuum and its purity was determined by GC. Catalyst was removed from silica gel with reagent grade AcOEt. After removal of solvent, the crude catalyst was washed with *n*-pentane and dried on vacuum. The recovered catalyst was used in next reaction without additional purification.

4.8. General procedure for RCM of substrates 19, 21 and 23

The substrate was dissolved in appropriate green solvent (0.6 mmol, *C*=0.1 M for **19** and *C*=0.005 M in case of **21** and **23**) and was treated with catalyst **5b** (stock solution prepared in DCM). Reaction mixture was heated at 40 °C (70 °C for **21** and **23**) and conversions were measured by GC.

4.9. General procedure for CM reactions of 25 with 17

Substrate (0.6 mmol, *C*=0.1 M) and dodecane (0.6 mmol) were dissolved in *i*-PrOH and was treated with catalyst **5b** (stock solution prepared in DCM). Reaction mixture was heated at 70 °C and conversions and selectivity were measured by GC.

4.10. Characterization of the metathesis products

*4.10.1. Diethyl 3-methyl-3-cyclopentene-1,1-dicarboxylate (**7**).*[48] ^{1}H NMR (300 MHz, $CDCl_3$) δ: 5.10–5.09 (m, 2H), 4.07 (q, *J*=7.2 Hz, 4H),

2.87–2.82 (m, 2H), 2.80–2.78 (m, 2H), 1.63–1.61 (m, 3H), 1.15 (t, *J*=7.2 Hz, 6H).

*4.10.2. Diethyl 3-cyclopentene-1,1-dicarboxylate (**9**).*[48] ^{1}H NMR (300 MHz, $CDCl_3$) δ: 5.53–5.51 (m, 2H), 4.08 (q, *J*=7.2 Hz, 4H), 2.92–2.89 (m, 4H), 1.15 (t, *J*=7.2 Hz, 6H).

*4.10.3. N-Tosyl-2,5-dihydropyrrole (**11**).*[49] ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm: 7.74–7.68 (m, 2H), 7.33–7.29 (m, 2H), 5.66–5.62 (m, 2H), 4.12–4.08 (m, 4H), 2.41 (s, 3H).

*4.10.4. N-Tosyl-3-methyl-2,5-dihydropyrrole (**13**).*[50] ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm: 7.72–7.69 (m, 2H), 7.32–7.29 (m, 2H), 5.24–5.22 (m, 1H), 4.07–4.03 (m, 2H), 3.97–3.95 (m, 2H), 2.41 (s, 3H), 1.64 (s, 3H).

*4.10.5. 2,2-Diphenyl-3-vinyl-2,5-dihydrofuran (**15**).*[51] Colourless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm: 7.37–7.28 (m, 10H), 6.28–6.20 (m, 2H), 5.32 (d, *J*=14.1 Hz, 1H), 5.11 (d, *J*=8.4 Hz, 1H), 4.81–4.80 (m, 2H).

*4.10.6. 7-(tert-Butyl-dimethyl-silanyloxy)-hept-2-enoic acid methyl ester (**18**).*[52] ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm: 6.89 (dt, *J* = 15.7, 7.0 Hz, 1H), 5.82 (dt, *J* = 15.7, 1.6 Hz), 3.71 (s, 3H), 3.62–3.58 (m, 2H), 2.24–2.18 (m, 2H), 1.53–1.51 (m, 4H), 0.88 (s, 9H), 0.03 (s, 6H).

*4.10.7. 2-(2,5-Dihydropyrrole-1-carbonyl)-pyrrolidine-1-carboxylicacid tert-butyl ester (**20**).*[53] ^{1}H NMR (300 MHz, CD_2Cl_2) δ ppm: 5.87–5.69 (m, 2H), 4.54–4.08 (m, 5H), 3.61–3.29 (m, 2H), 2.20–2.04 (m, 2H), 1.92–1.74 (m, 2H), 1.40–1.32 (m, 9H).

*4.10.8. (E,Z)-Oxacyclotetradec-11-en-2-one (**22**).*[54] *E* isomer—^{1}H NMR (300 MHz, $CDCl_3$) δ ppm: 5.51–5.30 (m, 2H), 4.14–4.10 (m, 2H), 2.39–2.33 (m, 4H), 2.04–1.98 (m, 2H), 1.63–1.55 (m, 2H), 1.38–1.27 (m, 10H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ ppm: 174.1, 132.8, 127.8, 64.3, 35.1, 31.9, 31.3, 26.6, 26.1, 25.8, 25.6, 23.88, 23.80.

*4.10.9. (E,Z)-Oxacyclohexadec-11-en-2-one (**24**).*[49] *E* isomer—^{1}H NMR (300 MHz, $CDCl_3$) δ ppm: 5.40–5.25 (m, 2H), 4.16–4.04 (m, 2H), 2.35–2.25 (m, 2H), 2.06–1.96 (m, 4H), 1.66–1.56 (m, 4H), 1.41–1.20 (m, 12H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ ppm: 173.9, 131.8, 130.3, 63.9, 34.7, 32.06, 32.02, 28.37, 28.31, 28.2, 28.0, 27.2, 26.5, 25.5, 25.2.

*4.10.10. (E,Z)-Dodec-2-enedioic acid dimethyl ester (**26**).*[55] *E* isomer—^{1}H NMR (300 MHz, $CDCl_3$) δ ppm: 7.01–6.91 (m, 1H), 5.83–5.77 (m, 1H), 3.71 (s, 3H), 3.66 (s, 3H), 2.32–2.27 (m, 2H), 2.21–2.14 (m, 2H), 1.63–1.56 (m, 2H), 1.49–1.39 (m, 2H) 1.28 (s, 8H).

Acknowledgements

Apeiron Synthesis acknowledges the National Centre for Research and Development for financial support within 'IniTech' programme. M.B. acknowledges the Foundation for Polish Science for financial support within 'INNOWATOR' programme.

Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2013.06.056.

References and notes

1. Vougioukalakis, G. C.; Grubbs, R. H. *Chem. Rev.* **2010**, *110*, 1746–1787.
2. Samojlowicz, C.; Bieniek, M.; Grela, K. *Chem. Rev.* **2009**, *109*, 3708–3742.
3. Monfette, S.; Fogg, D. E. *Chem. Rev.* **2009**, *109*, 3783–3816.
4. Michalak, M.; Gulajski, L.; Grela, K. In *Alkene Metathesis*; de Meijere, A., Ed.; Science of Synthesis: Houben-Weyl Methods of Molecular Transformations; Georg Thieme: Stuttgart, Germany, 2010; Vol. 47a, p 327; (Alkenes).
5. Clavier, H.; Grela, K.; Kirschning, A.; Mauduit, M.; Nolan, S. P. *Angew. Chem., Int. Ed.* **2007**, *46*, 6786–6801.
6. Kingsbury, J. S.; Harrity, J. P. A.; Bonitatebus, P. J.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1999**, *121*, 791–799.
7. (a) Gillingham, D. G.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2007**, *46*, 3860–3864 For recent articles on the boomerang mechanism see; (b) Vorfalt, T.; Wannowius, K.-J.; Plenio, H. *Angew. Chem., Int. Ed.* **2010**, *49*, 5533–5536; (c) Vorfalt, T.; Wannowius, K. J.; Thiel, V.; Plenio, H. *Chem.—Eur. J.* **2010**, *16*, 12312–12315.
8. Grela, K.; Harutyunyan, S.; Michrowska, A. *Angew. Chem., Int. Ed.* **2002**, *41*, 4038–4040.
9. (a) Michrowska, A.; Bujok, R.; Harutyunyan, S.; Sashuk, V.; Dolgonos, G.; Grela, K. *J. Am. Chem. Soc.* **2004**, *126*, 9318–9325; (b) Olszewski, T. K.; Bieniek, M.; Skowerski, K.; Grela, K. *Synlett* **2013**, *24*, 903–919.
10. (a) Priority date: August 2, 2003, DE 103 35 416, Inventor Dieter Arlt; (b) Bieniek, M.; Bujok, R.; Cabaj, M.; Lugan, N.; Lavigne, G.; Arlt, D.; Grela, K. *J. Am. Chem. Soc.* **2006**, *128*, 13652–13653.
11. Bieniek, M. *Substituted Hoveyda–Grubbs Catalysts-activity Control and Applications in Olefin Metathesis* Ph.D. Thesis; Institute of Organic Chemistry, PAS: Warsaw, 2008.
12. Bieniek, M.; Samojlowicz, C.; Sashuk, V.; Bujok, R.; Sledz, P.; Lugan, N.; Lavigne, G.; Arlt, D.; Grela, K. *Organometallics* **2011**, *30*, 4144–4158.
13. Gawin, R.; Makal, A.; Wozniak, K.; Mauduit, M.; Grela, K. *Angew. Chem., Int. Ed.* **2007**, *46*, 7206–7209.
14. Hong, S. H.; Day, M. W.; Grubbs, R. H. *J. Am. Chem. Soc.* **2004**, *126*, 7414–7415.
15. Vougioukalakis, G. C. *Chem.—Eur. J.* **2012**, *18*, 8868–8880.
16. Gallou, F.; Saim, S.; Doenig, K. J.; Bochniak, D.; Horhota, S. T.; Yee, N. K.; Senanayake, C. *Org. Process Res. Dev.* **2006**, *10*, 937–940.
17. Knight, D. W.; Morgan, I. R.; Proctor, A. J. *Tetrahedron Lett.* **2010**, *51*, 638–640.
18. Lambeth, R. H.; Pederson, S. J.; Baranoski, M.; Rawlett, A. M. *J. Polym. Sci., Part A: Polym. Chem.* **2010**, *48*, 5752–5757.
19. Cho, J. H.; Kim, B. M. *Org. Lett.* **2003**, *5*, 531–533.
20. Grela, K.; Kim, M. *Eur. J. Org. Chem.* **2003**, *6*, 963–966.
21. Michrowska, A.; Gułajski, Ł.; Kaczmarska, Z.; Mennecke, K.; Kirschning, A.; Grela, K. *Green Chem.* **2006**, *8*, 685–688.
22. Grela, K.; Tryznowki, M.; Bieniek, M. *Tetrahedron Lett.* **2002**, *43*, 6425–6428.
23. Allen, D. P.; van Wingerden, M. M.; Grubbs, R. H. *Org. Lett.* **2009**, *11*, 1261–1264.
24. Yinghuai, Z.; Kuijin, L.; Huimin, N.; Chuanzhao, L.; Stubbs, L. P.; Siong, C. F.; Muihua, T.; Peng, S. C. *Adv. Synth. Catal.* **2009**, *351*, 2650–2656 and references cited therein.
25. Kingsbury, J. S.; Garber, S. B.; Giftos, J. M.; Gray, B. L.; Okamoto, M. M.; Farrer, R. A.; Fourkas, J. T.; Hoveyda, A. H. *Angew. Chem. Int., Ed.* **2001**, *40*, 4251–4256.
26. De Clercq, B.; Lefebvre, F.; Verpoort, F. *New J. Chem.* **2002**, *26*, 1201–1208.
27. De Clercq, B.; Lefebvre, F.; Verpoort, F. *Appl. Catal., A* **2003**, *247*, 345–364.
28. Lee, B. S.; Namgoong, S. K.; Lee, S. *Tetrahedron Lett.* **2005**, *46*, 4501–4503.
29. Michalek, F.; Mädge, D.; Rühe, J.; Bannwarth, W. *Eur. J. Org. Chem.* **2006**, 577–581.
30. Michalek, F.; Mädge, D.; Rühe, J.; Bannwarth, W. *J. Organomet. Chem.* **2006**, *691*, 5172–5180.
31. Lim, J.; Lee, S. S.; Riduan, S. N.; Ying, J. Y. *Adv. Synth. Catal.* **2007**, *349*, 1066–1076.
32. Keraani, A.; Fischmeister, C.; Renouard, T.; Le Floch, M.; Baudry, A.; Bruneau, C.; Rabiller-Baudry, M. *J. Mol. Catal. A: Chem.* **2012**, *357*, 73–80.
33. Melis, K.; De Vos, D.; Jacobs, P.; Verpoort, F. *J. Mol. Catal. A: Chem.* **2001**, *169*, 47–56.
34. Mayr, M.; Buchmeiser, M. R.; Wurst, K. *Adv. Synth. Catal.* **2002**, *344*, 712–719.
35. Allen, D. P.; Van Wingerden, M. M.; Grubbs, R. H. *Org. Lett.* **2009**, *11*, 1261–1264.
36. Krause, J. O.; Lubbad, S.; Nuyken, O.; Buchmeiser, M. R. *Adv. Synth. Catal.* **2003**, *345*, 996–1004.
37. Vehlow, K.; Maechling, S.; Köhler, K.; Blechert, S. *J. Organomet. Chem.* **2006**, *691*, 5267–5277.
38. Dıez-Gonzalez, S.; Nolan, S. P. *Coord. Chem. Rev.* **2007**, *251*, 874–883.
39. Gatti, M.; Vieille-Petit, L.; Luan, X.; Mariz, R.; Drinkel, E.; Linden, A.; Dorta, R. *J. Am. Chem. Soc.* **2009**, *131*, 9498–9499.
40. Kuhn, K. M.; Bourg, J.-B.; Chung, C. K.; Virgil, S. C.; Grubbs, R. H. *J. Am. Chem. Soc.* **2009**, *31*, 5313–5320.
41. Urbina-Blanco, C. A.; Leitgeb, A.; Slugovc, C.; Bantreil, X.; Clavier, H.; Slawin, A. M.; Nolan, S. P. *Chem.—Eur. J.* **2011**, *17*, 5045–5053.
42. Peeck, H. L.; Savka, R. D.; Plenio, H. *Chem.—Eur. J.* **2012**, *18*, 12845–12853.
43. Capello, Ch.; Fischer, U.; Hungerbuhler, K. *Green Chem.* **2007**, *9*, 927–934.
44. Jessop, P. G. *Green Chem.* **2011**, *13*, 1391–1398.
45. (a) Gallenkamp, D.; Furstner, A. *J. Am. Chem. Soc.* **2011**, *133*, 9232–9235; (b) Hickmann, V.; Kondoh, A.; Gabor, B.; Alcarazo, M.; Furstner, A. *J. Am. Chem. Soc.* **2011**, *133*, 13471–13480; (c) Micoine, K.; Furstner, A. *J. Am. Chem. Soc.* **2010**, *132*, 14064–14066.
46. (a) Rimkus, G. G. *The Handbook of Environmental Chemistry*; Springer: Berlin, 2004; Vol. 3X; (b) Rowe, D. J. *Chemistry and Technology of Flavors and Fragrances*; Blackwell: Oxford, U.K, 2005; (c) Ohloff, G.; Pickenhagen, W.; Kraft, P. *Scent and Chemistry: the Molecular World of Odors*; Helvectica Acta: Zurich, 2011.
47. Clavier, H.; Urbino-Blanco, C. A.; Nolan, S. P. *Organometallics* **2009**, *28*, 2848–2854.

48. Ritter, T.; Hejl, A.; Wenzel, A. G.; Funk, T. W.; Grubbs, R. H. *Organometallics* **2006**, *25*, 5740–5745.
49. Furstner, A.; Liebl, M.; Lehmann, C. W.; Piquet, M.; Kunz, R.; Bruneau, C.; Touchard, D.; Dixneuf, P. H. *Chem.—Eur. J.* **2000**, *6*, 1847–1857.
50. Wu, Q.; Ren, J. H. X.; Zhou, J. *Chem.—Eur. J.* **2011**, *17*, 11553–11558.
51. Furstner, A.; Ackermann, L.; Gabor, B.; Goddard, R.; Lehmann, C. W.; Mynott, R.; Stelzer, F.; Thiel, O. R. *Chem.—Eur. J.* **2001**, *7*, 3236–3253.
52. Schmid, T. E.; Bantreil, X.; Citadelle, C. A.; Slawin, A. M. Z.; Cazin, C. S. J. *Chem. Commun.* **2011**, 7060–7062.
53. Cabrera, J.; Padilla, R.; Dehn, R.; Deuerlein, S.; Gułajski, Ł.; Chomiszczak, E.; Teles, J. H.; Limbach, M.; Grela, K. *Adv. Synth. Catal.* **2012**, *354*, 1043–1051.
54. Marx, V. M.; Herbert, M. B.; Keitz, B. K.; Grubbs, R. H. *J. Am. Chem. Soc.* **2013**, *135*, 94–97.
55. Miao, X.; Fischmeister, C.; Dixneuf, P. H.; Bruneau, C.; Dubois, J.-L.; Couturier, J.-L. *Green Chem.* **2012**, *14*, 2179–2183.