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Activated pyridinium-tagged ruthenium complexes as efficient catalysts for ring-closing metathesis

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Abstract

New pyridinium-tagged ruthenium catalysts have been synthesised to perform olefin metathesis in several media including both organic and aqueous solvents and room temperature ionic liquids (RTILs). High activity was obtained in the ring-closing metathesis (RCM) of a variety of di- or tri-substituted and/or oxygen-containing dienes. However, only fair levels of recycling combined with low to moderate residual ruthenium levels (25–173 ppm) have been observed showing clearly the difficulty of associating high activity and recyclability.

Keywords: Olefin metathesis; Ionic-tagged-catalyst; Ruthenium; Ionic liquid

1. Introduction

Second generation Grubbs's olefin metathesis catalysts **1a**–**c** [1] or the Hoveyda's boomerang analogues **2a**,**b** [2] and their activated parents recently developed by Grela **3** and **4** and Blechert **5** [3,4] (Scheme 1) have gained considerable attention in synthetic organic chemistry [5]. From a synthetic strategic point of view, these powerful catalysts led to significantly simplify the synthetic pathways in many natural and unnatural molecules syntheses [6]. Unfortunately, the use of these efficient homogeneous catalysts is associated to difficult disposal of the ruthenium wastes from the final products [7]. Even after repeated purifications by silica gel column chromatography, a large quantity of ruthenium by-products (>2000 ppm) remains detectable [8]. As a result, these valuable catalysts are incompatible with industrial processes when biologically active compounds are produced [6]. Several purification processes have recently emerged to overcome this problem using: (i) hydrosoluble phophines or phosphine oxides [9] (ii) several scavengers [9a,10] and (iii) supported phosphines [11] allowing to reduce the residual ruthenium levels down to 200 ppm. The best purification method (60 ppm) was reported by Kim and co-workers with treatment of the crude media by activated charcoal following by silicagel chromatography [12]. An alternative solution to reduce the ruthenium by-product is the use of supported catalysts [13]. Concerning solid supported catalysts [14], in most of cases the Ru-waste disposal is efficient only after purification by a silicagel filtration (55 ppm) [9a] whereas the use of soluble polymers can afford the same level of contamination without any supplementary purification [15]. To the best of our knowledge, the lowest contamination detected in the metathesis product was reported by Buchmeiser and co-workers reaching 0.01 ppm of Ru with a perfluro-tagged solid supported catalyst [16]. As the latest environmentally friendly process, the use of ionic-tagged Ru-catalysts **6a**–**b** in ionic solvents was recently introduced by our group as an original alternative to minimise the Ru-wastes in metathesis products [17,18]. This new homogeneous catalytic system combine excellent recyclability

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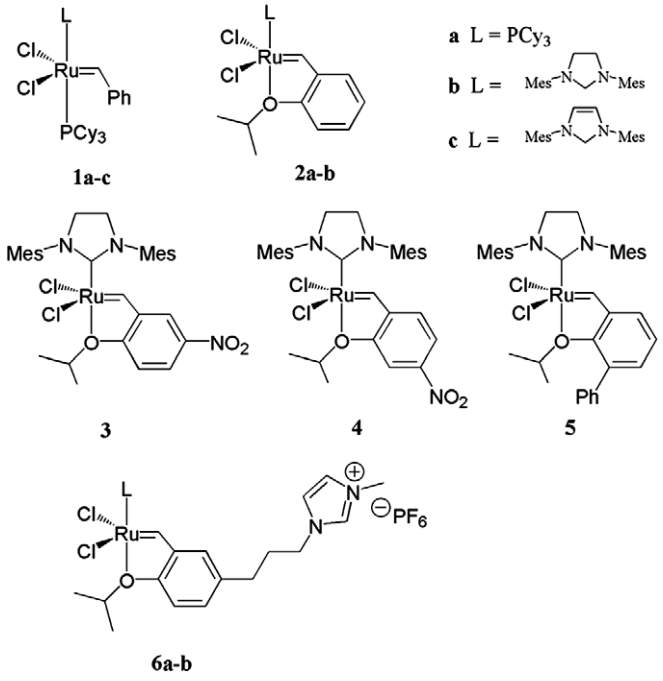
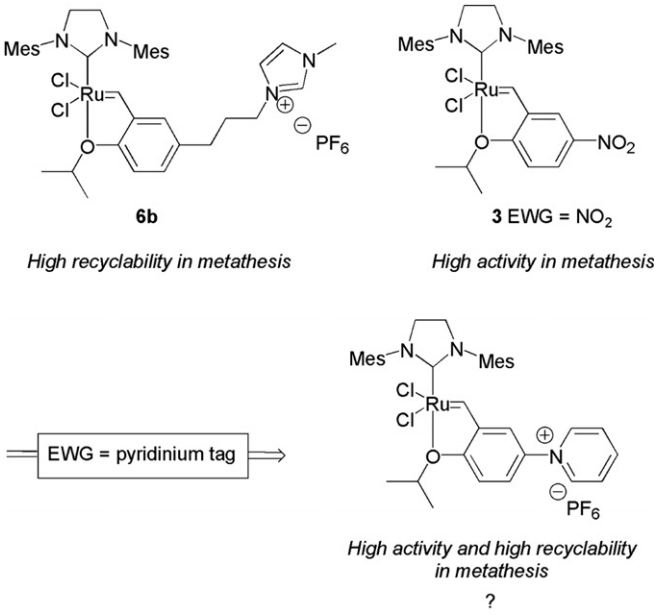


Scheme 1. Selected ruthenium catalysts for RCM. Cy = cyclohexyl; Mes = 2,4,6-trimethylphenyl.



Scheme 2. Concept of activation of the metathesis catalyst via an ionic tag.

(up to 8 runs) without loss of activity (>95%) and very weak Ru-contamination rates, in average 7 ppm have been detected per run [19].

Capitalising on our efforts aimed at developing more environmentally friendly olefin metathesis processes [19], we describe herein the synthesis of new air-stable pyridinium-containing ruthenium catalysts for which the ionic tag is anchored to the styrenyl-ether benzylidene fragment [20]. This specific ionic-tag enhances the catalytic activity and allows the use of a wide range of media such as organic, aqueous, and ionic solvents with low to moderate residual ruthenium levels in the metathesis products.

2. Results and discussion

2.1. Catalysts design and synthesis

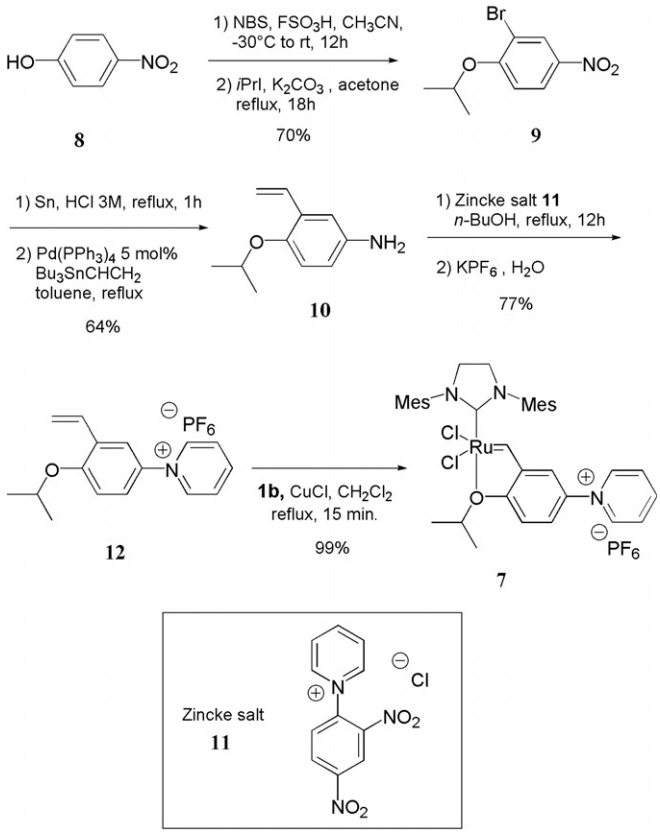
2.1.1. Catalysts design

The introduction of an electron-with drawing group (EWG) such as a nitro function on the benzylidene moiety of the Hoveyda-Grubbs boomerang catalyst has been recently reported [3]. The unprecedented high activity of this modified catalyst is directly linked to the nitro-EWG group that weakens the O–Ru chelation allowing an easier leaching of the styrenyl-ether ligand and then a faster initiation rate is obtained. This assumption has been confirmed by introducing electron-donating groups (EDG) such as diethylamino; the resulting catalyst exhibited an noticeably lower activity [21]. Using this concept and our experience in recyclable ionic-tagged Ru-catalysts, we designed an activated catalyst possessing an ionic EWG substituent in order to obtain high activity as well as an excellent recyclability (Scheme 2). The choice of a pyridinium fragment as the ionic tag instead of an imidazolium was guided by: (i) the absence of acidic protons, to avoid the formation of carbenic by-products (ii) the easy access in one-step procedure from aniline by using the Zincke reaction [22].

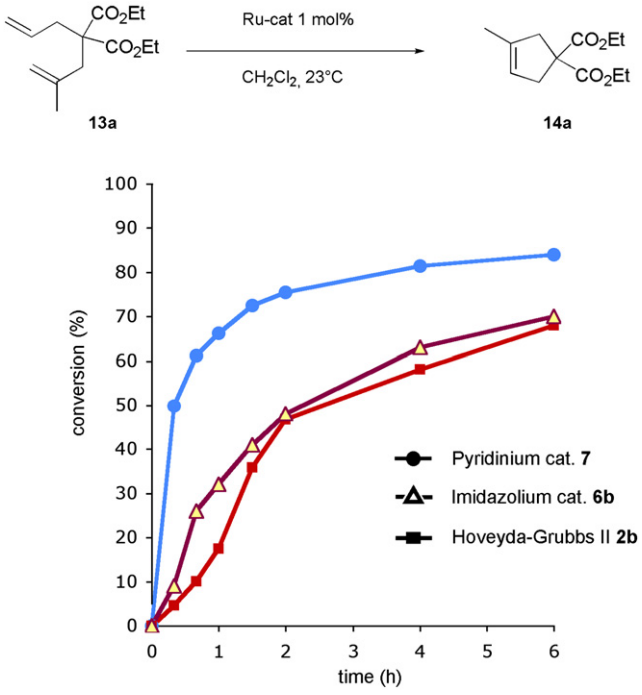
2.1.2. Synthesis of the pyridinium-activated catalyst 7

As illustrated in Scheme 3, we started with a selective *ortho*-bromination of commercially available 4-nitrophenol **8** by *N*-bromosuccinimide in the presence of fluorosulfonic acid in acetonitrile [23]. Etherification of the phenol group with isopropyliodide and K_2CO_3 in acetone produced the bromophenol ether **9** in 70% yield (from **8**). Reduction of the nitro group with metallic Tin in refluxed 3 M HCl aqueous solution followed by Pd-catalysed Stille coupling to introduce the vinyl group afforded the styrenyl-ether aniline **10** in 64% overall yield. The key step, the introduction of the pyridinium group, is achieved using a Zincke reaction between the aniline **10** and the pyridinium salt **11** in refluxing *n*-butanol. This remarkable transformation allows to isolate in good yield the expected pyridinium chloride salt. Finally, the anion exchange is accomplished by treatment with KPF_6 in water to afford the corresponding pyridinium hexafluorophosphate salt **12** in 77% yield (over two steps) after purification by silica gel chromatography.

The pyridinium-tagged ruthenium catalyst **7** is readily obtained from the 2nd generation Grubbs'catalyst **1 b** by simple exchange of the styrenyl group with the pyridinium ligand **12** in presence of CuCl. After washing the crude product with ethyl acetate and pentane, the resulting catalyst **7** is isolated in a pure form in 99% yield as an air-stable olive-green micro-crystalline solid.



Scheme 3. Synthesis of pyridinium-tagged catalyst **7**.



Scheme 4. Comparative activities of catalysts **2b**, **6b** and **7**.

2.2. Catalytic performance and recyclability of 7

2.2.1. Catalytic performance

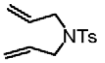
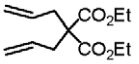
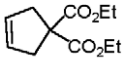
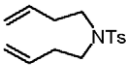
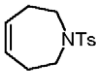
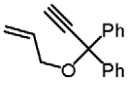
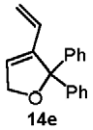
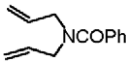
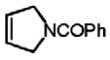
To compare the activities of catalysts **2b**, imidazolium-tagged **6b** and pyridinium-containing **7**, we studied the ring-closing metathesis of diethyl 2-allyl-2-methallylmalonate **13a** under identical conditions i.e. 1 mol% of catalyst in CH_2Cl_2 at room temperature (Scheme 4).

As expected, the presence of the pyridinium-tag as an activated group in the complex **7** led to a faster initiation step of the metathesis catalytic cycle. After only 15 min, the yield of the cyclised product **14a** is 50% as opposed to 5% and 9% reached by the Hoveyda-Grubbs II catalyst **2b** and the imidazolium non-activated homologue **6b** respectively. After 6 h, the difference of activity is less pronounced; whereas 84% of conversion is observed with catalyst **7**, 68% and 70% are obtained with **2b** and **6b** respectively. These results are in good accordance with those obtained with the nitro-containing catalysts **3** and **4**. The catalytic activity of the Hoveyda-Grubbs catalyst **2b** is enhanced by EWG on the styrenyl-ether ligand. These EWGs decrease the coordinating ability of the ether function and thus favour the first steps of the catalytic cycle; i.e. coordination of the substrate and loss of the styrenyl-ether ligand leading to the deliverance of the active specie.

We next focused on its catalytic performance through the evaluation of a wide range of substrates for RCM and also enyne-cycloisomerisation in organic solvent and in several aqueous media (Table 1). To perform catalytic reactions in aqueous media is a challenge from both economic and environmental point of views; recent efforts in this area have been reported [24], especially in metathesis reactions [25]. In traditional solvent, as expected, the ionic activated catalyst **7** showed a high activity in RCM (Table 1, entries 1, 3, 4 and 9). Nevertheless, lower activity is observed in aqueous media (EtOH/water: entry 2 or MeOH/water: entry 5) where only 40–50% of substrate reacted. Intriguingly, this difference of activity was not observed in the enyne-cycloisomerisation reaction of **13e** leading to complete conversion after 0.5 h at 25 °C (entries 6, 7 and 8). At this time, we are unable to explain this difference, but several experiments, notably with variation of the counter-anion, are presently ongoing.

In addition to the improvement of the catalytic activity, another advantage should be highlighted: the good affinity of the pyridinium-containing catalyst towards silica gel should improve the removal of the Ru-wastes in the metathesis products. The inductive coupled plasma mass spectroscopy (ICP-MS) analysis of several samples showed moderate to low levels of Ru-wastes down to 25 ppm (entry 6). Even if the levels of remaining ruthenium are interesting, they are higher to those observed with the imidazolium catalyst **6b** in biphasic ionic media. Whereas only 2.5 ppm of ruthenium were detected in the product **14d** [19] with the imidazolium-containing catalyst **6b,** 113 ppm of ruthenium contaminated the metathesis product using the activated catalyst **7** (entry 3). The significant difference in levels of Ru-wastes shows clearly the challenge to associate an

Table 1
Metathesis reactions catalysed by **7**[a]

Entry	Substrate	Product	Solvent	Time (h)	Conversion (%)[b]	Ru (ppm)[c]
1	 **13b**	 **14b**	CH_2Cl_2	0.5	99	138
2			$EtOH/H_2O$	24	50	
3	 **13c**	 **14c**	CH_2Cl_2	2	78	113
4	 **13d**	 **14d**	CH_2Cl_2	0.5	99	173
5			$MeOH/H_2O$	24	40	
6	 **13e**	 **14e**	CH_2Cl_2	0.5	99	25
7			$MeOH/H_2O$	0.5	99	28
8			$EtOH/H_2O$	0.5	99	
9	 **13f**	 **14f**	CH_2Cl_2	0.5[d]	99	

[a] Conditions: 5 mol% of catalyst, CH_2Cl_2 or $MeOH/H_2O$ v/v 5:2 $c = 0.02$ mol/L, 25 °C.
[b] Conversions were determined by analysis of ^1H NMR or GC/MS of crude reaction mixture.
[c] Determined by ICP-MS spectroscopy analysis and showed as parts per million.
[d] With 2.5 mol% of catalyst.

enhanced activity due to the pyridinium EWG with an effective boomerang ligand allowing a good recyclability and a low contamination in ruthenium. We then attempted to recycle the pyridinium-activated catalyst **7** in ionic solvents.

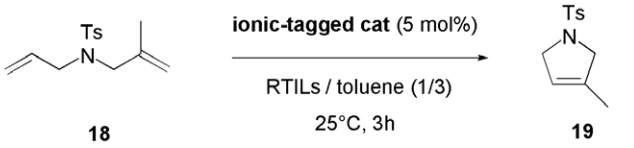
2.2.2. Recyclability in ionic solvents

Usually, to perform olefins metathesis reactions in homogenous conditions, unpolar organic solvent are used and the recovery of the catalyst needs silica gel purification. Ionic solvents represent alternative attractive media due to their good ability to solvate organometallic species, their remarkable reusability, and their modular immiscibility with many usual organic solvents (allowing an easier extraction of the organic products) [26,27]. To perform metathesis reactions in these new media with ionic-containing boomerang catalysts [28] allows to recycle with efficiency the catalytic system without loss of activity [18,19].

To evaluate the recyclability of the new activated pyridinium-catalyst **7**, we performed the ring-closing metathesis of 2-allyl-2-methallyltosylamine **18** using 5 mol% of ionic catalyst in two different ionic solvents ($BMI \cdot PF_6$ and $BMPy \cdot BF_4$) with toluene as co-organic solvent (Scheme 5). Whereas the non-activated catalyst **6b** exhibited a very high level of reusability (>98% up to 6 runs, entry 1) in $BMI \cdot PF_6$/toluene medium [18,19], the activated pyridinium catalyst **7** showed a good activity in the first two cycles (>98%). Nevertheless, the activity decreases rapidly to reach 65% of conversion in the third cycle and no activity in the fourth (entry 2). As expected, the decrease of conversions was progressively obtained due to the extraction of the 14-electron catalytic species (which is unable to reanchor its pyridinium-ligand) to the organic phase during the isolation of the RCM product.

To evaluate to a reel effect of the pyridinium function in terms of activity and recyclability, we then prepared the complex **15**. This pyridinium-containing catalyst, equivalent to **6b**, possesses the same C3 alkyl linker between the ionic tag and the benzenylidene pattern. As illustrated in Scheme 6, complex **15** could be easily synthesised in a three-step procedure in good yield. Starting from the alkyl bromide **16** [17], the alkylation of the pyridine afforded the corresponding pyridinium-tagged benzylidene ligand **17**, which can react with a slight excess of Grubbs II catalyst **1b** in the presence of CuCl to give the complex **15** isolated as an air-stable green powder in 83% yield.

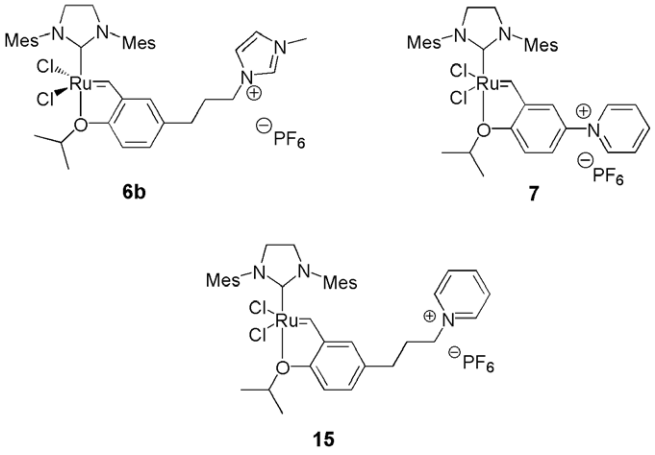
The direct comparison between the imidazolium-tagged catalyst **6b** (entry 1), and its pyridinium-containing equiva-



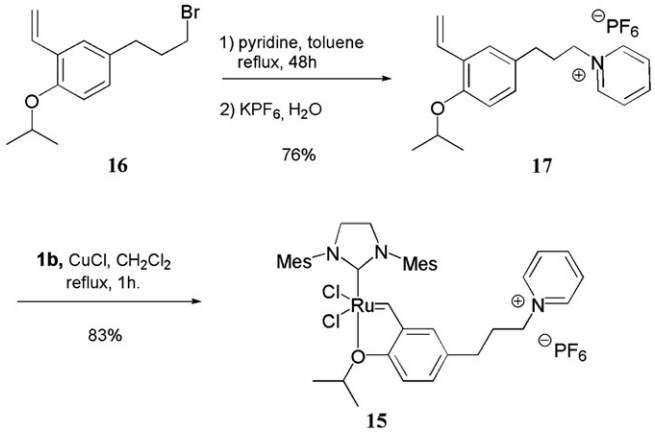
18 19

entry	catalyst	RTILs	cycle (% conv.)[a]					
			1	2	3	4	5	6
1	**6b**	BMI.PF_6	>98	>98	>98	>98	>98	>98
2	**7**	BMI.PF_6	>98	95	65	6	-	-
3	**15**	BMI.PF_6	>98	>98	>98	>98	93	91
4	**7**	BMPy.BF_4	>98	89	26	-	-	-
5	**15**	BMPy.BF_4[b]	>98	>98	97	92	88	74

[a] Determined by ^{1}H NMR spectroscopic analysis at 400 MHz.
[b] reaction performed at 40°C



Scheme 5. Comparative recyclability of ionic-tagged catalysts **6b**, **7** and **15** in ionic media.



Scheme 6. Synthesis of non-activated pyridinium-tagged catalyst **15**.

lent **15** showed similar conversions and reuses over 6 cycles (Scheme 5, entry 3). This result shows clearly that the nature of the cationic tag does not interfere in the activity and the recyclability of catalyst. We then focused on the influence of the counter-anion of the ionic solvent. We therefore performed the metathesis reaction in 1-butyl-4-methyl pyridinium tetrafluoroborate (BMPy · BF_4) possessing the same cationic fragment but a different counter-anion. Regarding the activated pyridinium-catalyst **7**, a slight difference of activity is observed with a good activity only in the first cycle (>98%) to reach 89% in the second cycle, and 26% yield in the third run (entry 4). Concerning the non-activated equivalent **15**, good activity and levels of recyclability were observed with excellent conversions over 4 cycles to reach 74% in the sixth run (entry 5). Nevertheless, higher temperatures (40 °C instead of 23 °C) are required to obtain these good results of reusability. This difference of activity could be explained by a better solubility of the ionic catalyst at this temperature, probably due to the difference of the counter-anion between the catalyst (PF_6) and the ionic solvent (BF_4).

3. Conclusion

This work reports the development of novel pyridinium-containing catalysts **7** and **15** to perform metathesis reactions in traditional but also in aqueous and ionic media. Whereas a high activity is generally observed, the recyclability levels of this activated catalyst were very low in ionic solvents. Moreover, low to moderate residual ruthenium levels were detected by ICP-MS in the final products (up to 25 ppm). All these results show clearly the difficulty to associate a higher activity by introducing activating groups such as ionic tag on a boomerang ligand with an efficient reusability of the catalyst. This study led us to develop a new generation of ionic-tagged catalysts possessing more suitable activating spacers between the ionic tag and the benzylidene fragment in order to obtain more efficient and recyclable catalysts. These results will be reported in due course.

4. Experimental

4.1. General

^{1}H (400 MHz), ^{13}C (100 MHz), ^{31}P (162 MHz) and ^{19}F (36.5 MHz) NMR spectra were recorded on a Bruker ARX400 spectrometer with complete proton decoupling for nucleus other than ^{1}H. Chemical shifts are reported in parts per million from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$, ^{1}H: δ 7.27 ppm, ^{13}C: δ 77.0 ppm, CD_2Cl_2, ^{1}H: δ 5.31 ppm, ^{13}C: δ 53.7 ppm and $(CD_3)_2CO$: ^{1}H: δ 2.05 ppm, ^{13}C: δ 205.1 ppm). Data are reported as follows: chemical shift (δ) in ppm, multiplicity (s = singlet, d = doublet, t = triplet, q = quadruplet, sept = septuplet, br = broad, m = multiplet), coupling constants (Hz), integration and attribution. High-resolution mass spectra (HRMS) were recorded at the Centre Régional de Mesures Physiques de l'Ouest (CRMPO), Université

de Rennes 1 on a Micromass ZABSpecTOF instrument. Elemental analyses were also performed at the CRMPO.

4.2. Materials

All non-aqueous reactions were performed under an argon atmosphere using oven-dried glassware. Toluene was distilled from sodium metal under nitrogen. Tetrahydrofuran and diethyl ether were distilled from sodium metal/benzophenone ketyl under nitrogen. Dichloromethane and triethylamine were distilled from calcium hydride under nitrogen. Dimethylformamide was distilled from phosphorous pentoxide under vacuum and stored under argon. Dienes and alkenes used were synthesised and purified according to literature procedures [3,19]. BMI · PF_6 was prepared and purified as reported previously [19] and dried overnight at 70 °C under high vacuum to remove traces of water. All others chemical reagents and solvents were obtained from commercial sources and used without further purification. Analytical TLC were performed on Merck silica gel $60F_{254}$ plates, and visualised under UV-light. Chromatographic purifications were performed on a column with 230–400 mesh silica gel (Merck 9385) using the indicated solvent system.

4.2.1. 2-Bromo-1-isopropoxy-4-nitrobenzene (*9*)

To a solution of 2-bromo-4-nitrophenol [23] (5.45 g, 25 mmol) in dry acetone (80 mL) were added at room temperature K_2CO_3 (6.9 g, 50 mmol, 2 equiv.) and isopropyl iodide (5 mL, 50 mmol, 2 equiv.). The reaction mixture was stirred at reflux for 48 h. After cooling and concentration under vacuum, the resulting mixture was diluted in ethyl acetate (100 mL) and washed two times with a saturated solution of sodium hydrogenocarbonate and one time with brine, dried over magnesium sulfate, filtered and concentrated. Purification by silica gel chromatography (pentane/ethyl acetate, 8/2) afforded the desired product **9** as a pale yellow solid (4.5 g, 70%). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 1.45 (d, J(H,H) = 6.1 Hz, 6H, $2CH_3$), 4.72 (sept, J(H,H) = 6.1 Hz, 1H, CH), 6.92 (dd, J(H,H) = 2.9 Hz and J(H,H) = 8.6 Hz, 1H, CH_{Ar}), 8.20 (d, J(H,H) = 8.6 Hz, 1H, CH_{Ar}), 8.46 (d, J(H,H) = 8.6 Hz, 1H, CH_{Ar}). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 159.7, 140.9, 129.3, 124.5, 112.8, 112.4, 72.8, 21.7 (2C).

4.2.2. 3-Bromo-4-isopropoxyaniline

To a solution of 2-bromo-1-isopropoxy-4-nitrobenzene **9** (1.3 g, 5 mmol) in aqueous 3 M HCl solution (25 mL) was added tin (0.9 g, 7.5 mmol, 1.5 equiv.) at room temperature. The reaction mixture was stirred for 3.5 h at reflux and then poured onto a 1 N NaOH solution (120 mL). The organic phase was extracted with EtOAc, washed with brine, dried over sodium sulfate and then concentrated. Purification by silica gel chromatography (pentane/ethyl acetate, 8/2) afforded the desired product as a brown oil (780 mg, 68%). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 1.33 (d, J(H,H) = 6.1 Hz, 6H, $2CH_3$), 3.48 (s large, 2H, NH_2), 4.34 (sept, J(H,H) = 6.1 Hz, 1H, CH), 6.57 (dd, J(H,H) = 2.9 Hz and J(H,H) = 8.6 Hz, 1H, CH_{Ar}), 6.79 (d, J(H,H) = 8.6 Hz, 1H, CH_{Ar}), 6.91 (d, J(H,H) = 8.6 Hz, 1H, CH_{Ar}). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 147.4, 141.7, 119.8, 119.7, 115.5, 115.0, 73.8, 22.1 (2C).

4.2.3. 4-Isopropoxy-3-vinylaniline (*10*)

A Schlenk flask was charged with dry toluene (3 mL) and tetrakis(triphenylphosphine)palladium (58 mg, 0.058 mmol, 0.1 equiv.). The mixture was degassed and 3-bromo-4-isopropoxyaniline (0.134 g, 0.58 mmol) diluted in dry toluene (3 mL) was added dropwise through a syringe. The resulting mixture was stirred 15 min before adding tributylvinylstannane (369 mg, 1 mmol, 2 equiv.). The flask was heated at 110 °C over 62 h. After cooling to room temperature, the mixture was filtrated on a plug of Celite and washed with diethyl ether. The solvent was evaporated off under vacuum and a purification by silica gel chromatography using pentane/ethyl acetate (8/2) as the eluent afforded the desired product **10** as a brown oil (98 mg, 95%). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 1.30 (d, J(H,H) = 6.1 Hz, 6H, $2CH_3$), 3.45 (s large, 2H, NH_2), 4.33 (sept, J(H,H) = 6.1 Hz, 1H, CH), 5.21 (dd, J(H,H) = 1.6 Hz and J(H,H) = 11 Hz, 1H, CH_{vinyl}), 5.67 (dd, J(H,H) = 1.6 Hz and J(H,H) = 17.8 Hz, 1H, CH_{vinyl}), 6.58 (dd, J(H,H) = 8.5 Hz and J(H,H) = 11.2 Hz, 1H, CH_{Ar}), 6.75 (d, J(H,H) = 8.6 Hz, 1H, CH_{Ar}), 6.86 (d, J(H,H) = 2.8 Hz, 1H, CH_{Ar}), 7.02 (dd, J(H,H) = 11.2 Hz and J(H,H) = 17.8 Hz, 1H, CH_{vinyl}). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 148.4, 140.3, 131.9, 129.4, 117.8, 115.9, 113.7, 112.8, 72.6, 22.2 (2C).

4.2.4. 1-(4-Isopropoxy-3-vinylphenyl)-pyridinium hexafluorophosphate (*12*)

A 10 mL round bottomed flask equipped with a condenser was charged with 4-isopropoxy-3-vinylaniline (**10**) (630 mg, 3.56 mmol), the Zincke salt **11** [22b] (1.0 g, 3.56 mmol, 1 equiv.) and *n*-butanol (3.9 mL). The mixture was stirred overnight at 120 °C then the solvent was evaporated off. The residue was dissolved in distilled water (30 mL) and filtered through a plug of Celite to remove the 2,4-dinitro-phenyl-ammonium chloride salt. The aqueous phase was washed with small volume of EtOAc (3 × 10 mL) and then treated with potassium hexafluorophosphate (982 mg, 5.34 mmol, 1.5 equiv.). After 10 min stirring, dichloromethane and brine were added. The organic phase was washed with brine, dried over magnesium sulfate, filtrated and concentrated. A purification by silica gel chromatography using dichloromethane/acetone (3/1) as the eluent afforded the desired pyridinium · PF_6 salt **12** as a yellow solid (1.37 g, 77% (two steps)). ^{1}H NMR (400 MHz, $(CD_3)_2CO$) δ (ppm): 1.41 (d, J(H,H) = 6.0 Hz, 6H, $2CH_3$), 4.87 (m, 1H, CH), 5.41 (dd, J(H,H) = 1.2 Hz and J(H,H) = 11.2 Hz, 1H, CH_{vinyl}), 5.97 (dd, J(H,H) = 1.2 Hz and J(H,H) = 17.9 Hz, 1H,

CH_{vinyl}), 7.11 (dd, J(H,H) = 11.3 Hz and J(H,H) = 17.9 Hz, 1H, CH_{vinyl}), 7.39 (d, J(H,H) = 9.1 Hz, 1H, CH_{Ar}), 7.82 (dd, J(H,H) = 2.9 Hz and J(H,H) = 8.8 Hz, 1H, CH_{Ar}), 8.13 (d, J(H,H) = 3.1 Hz, 1H, CH_{ar}), 8.43 (t, J(H,H) = 7.3 Hz, 2H, CH_{Py}); 8.89 (tt, J(H,H) = 1.3 Hz and J(H,H) = 7.9 Hz, 2H, CH_{Py}), 9.38 (m, 1H, CH_{Py}) ^{13}C NMR (100 MHz, $(CD_3)_2CO$) δ (ppm): 158.5, 147.9 (2C), 146.5 (2C), 131.8, 130.4, 130.0 (2C), 126.3, 124.1, 117.9, 116.1, 72.7, 22.8 (2C). ^{31}P NMR (162 MHz, $(CD_3)_2CO$) δ (ppm): −143.2 (sept, 1P, J(F,P) = 707.5 Hz). ^{19}F NMR (376 MHz, $(CD_3)_2CO$) δ (ppm): −73.0 (d, 6F, J(F,P) = 707.5 Hz).

4.2.5. Pyridinium-activated catalyst (7)

Grubbs II catalyst **2b** (0.069 g, 0.08 mmol), CuCl (0.012 g, 0.12 mmol) and CH_2Cl_2 (3.5 mL) were placed in a Schlenk flask equipped with a condenser. A solution of **12** (0.037 g, 0.096 mmol) in CH_2Cl_2 (1.3 mL) was then added and the resulted solution was stirred under argon at 45 °C for 15 min. From this point forth, all manipulations were carried out in air with reagent-grade solvents. The reaction mixture was concentrated in vacuo and to the residue EtOAc (10 mL) was added. The solution was filtered off. After removal of solvent, the solid was washed with a small amount of cold *n*-pentane and dried under vacuum to give the pyridinium catalyst **7** as olive microcrystalline solid (0.067 g, 99%). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 1.43 (m, 6H, $2CH_3$), 2.33–2.49 (m, 18H, $6CH_{3Mes}$), 4.16 (m, 4H, $2CH_2$), 4.89 (m, 1H, CH), 7.09 (s, 4H, CH_{Mes}), 7.90 (m, 1H, CH_{Ar}), 7.99 (m, 2H, CH_{Ar}), 8.47 (m, 4H, CH_{Py}), 8.57 (m, 1H, CH_{Py}), 16.58 (s, 1H, CH). HRMS (FAB) calc. for C^+: 704.1748, found: 704.1766.

4.2.6. 1-[3-(4-Isopropoxy-3-vinylphenyl)propyl]-pyridinium hexafluorophosphate (17)

A 10 mL round bottomed flask equipped with a condenser was charged with 4-(3-bromo-propyl)-1-isopropoxy-2-vinyl-benzene **16** [17] (362 mg, 1 mmol), pyridine (810 μL, 10 mmol, 10 equiv.) and dry toluene (5 mL). The mixture was stirred overnight at 100 °C then the solvent was evaporated off. The residue was dissolved in distilled water (30 mL) and washed with small volume of EtOAc (3 × 10mL) and then treated with potassium hexafluorophosphate (239 mg, 1.3 mmol, 1.3 equiv.). After 10 min stirring, dichloromethane and brine were added. The organic phase was washed with brine, dried over magnesium sulfate, filtrated and concentrated. A purification by silica gel chromatography using dichloromethane/acetone (3/1) as the eluent afforded the desired pyridinium · PF_6 salt **17** as a pale yellow solid (324 mg, 76% two steps). ^{1}H NMR (400 MHz, MeOD) δ (ppm): 1.30 (d, J(H,H) = 6.0 Hz, 6H, $2CH_3$), 2.36 (quint, J(H,H) = 7.5 Hz, 2H, CH_2), 2.71 (t, J(H,H) = 7.5 Hz, 2H, CH_2), 4.54 (sept, J(H,H) = 6.0 Hz, 1H, CH), 4.66 (t, J(H,H) = 7.5 Hz, 2H, CH_2), 5.18 (dd, J(H,H) = 1.2 Hz and J(H,H) = 11.3 Hz, 1H, CH_{vinyl}), 5.72 (dd, J(H,H) = 1.7 Hz and J(H,H) = 17.8 Hz, 1H, CH_{vinyl}), 6.87 (d, J(H,H) = 8.1 Hz, 1H, CH_{ar}), 6.98 (dd, J(H,H) = 11.3 Hz and J(H,H) = 17.9 Hz, 1H, CH_{vinyl}), 7.07 (dd, J(H,H) = 2.2 Hz and J(H,H) = 8.4 Hz, 1H, CH_{Ar}), 7.31 (d, J(H,H) = 2.2 Hz, CH_{Ar}), 8.05 (t, J(H,H) = 7.1 Hz, 2H, CH_{Py}), 8.54 (td, J(H,H) = 7.9 Hz and J(H,H) = 1.3 Hz, 2H, CH_{Py}), 8.94 (d, J(H,H) = 5.6 Hz, 1H, CH_{Py}). ^{13}C NMR (400 MHz, MeOD) δ (ppm): 22.9 (2C), 33.1, 34.2, 63.4, 72.6, 114.8, 116.4, 127.7, 129.6, 129.8, 130.3, 133.5 (2C), 133.8, 146.3, 147.2 (2C), 155.5. ^{31}P NMR (162 MHz, $CDCl_3$) δ (ppm): −143.2 (sept, 1P, J(F,P) = 710.1 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm): −72.3 (d, 6F, J(F,P) = 710.1 Hz).

4.2.7. Pyridinium non-activated catalyst (15)

In a Schlenk flask, 1-[3-(4-isopropoxy-3-vinylphenyl)propyl]-pyridinium hexafluorophosphate **7** (21.3 mg, 0.05 mmol) was diluted in dry dichloromethane (5 mL). Copper(I) chloride (5 mg, 0.05 mmol, 1 equiv.) and Grubbs II catalyst **2b** (42.5 mg, 0.05 mmol, 1 equiv.) were introduced. The resulting solution was degassed three times (vacuum/argon) and stirred for 1 h at 30 °C. The solvent was evaporated under vacuum, the residue was dissolved in dry acetone (10 mL) and the insoluble materials were removed by filtration and washed with acetone (2 × 5 mL). The filtrate was evaporated under vacuum and then purified through a plug of silica gel to afford the pyridinium catalyst **15** as a green powder (37 mg, 83%). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 1.40 (d, J(H,H) = 6.0 Hz, 6H, $2CH_3$), 2.24 (m, 2H, CH_2), 2.5-2.7 (m, 18H, $6CH_{3Mes}$), 3.03 (t, J(H,H) = 7.3 Hz, 2H, CH_2), 4.42 (m, 4H, CH_2), 5.07 (m, 3H, CH, CH_2), 6.82 (d, J(H,H) = 1.9 Hz, 1H, CH_{Ar}), 7.10 (d, J(H,H) = 8.2 Hz, 1H, CH_{Ar}), 7.25 (s, 4H, CH_{Mes}), 7.65 (dd, J(H,H) = 1.9 Hz and J(H,H) = 8.2 Hz, CH_{Ar}), 8.30 (t, J(H,H) = 6.9 Hz, 2H, CH_{Py}), 8.78 (t, J(H,H) = 7.8 H, 2H, CH_{Py}), 9.26 (d, J(H,H) = 6.4 Hz, 1H, CH_{Py}), 16.49 (s, 1H, Ru=CH). ^{31}P NMR (162 MHz, $(CD_3)_2CO$) δ (ppm): −143.0 (sept, 1P, J(F,P) = 708 Hz). ^{19}F NMR (376 MHz, $(CD_3)_2CO$) δ (ppm): −72.9 (d, 6F, J(F,P) = 708 Hz).

4.3. General procedure for RCM reactions in CH_2Cl_2

A reaction tube equipped with a magnetic stirring bar was charged with pyridinium-catalyst **7** (1–5 mol%), substrate (0.2 mmol) and CH_2Cl_2. The reaction mixture was stirred at 25 °C. After complete conversion (followed by TLC), the reaction mixture was passed through a cartridge containing silica gel (1–2 g). The cartridge was washed with an additional portion of CH_2Cl_2 (10–20 mL). The solvent was removed under reduced pressure to yield crude cyclised product.

4.4. General procedure for RCM reactions in $MeOH/H_2O$ (5/2 v/v) and $EtOH/H_2O$ (5/2 v/v)

A reaction tube equipped with a magnetic stirring bar was charged with catalyst **7** (6 mg, 0.007 mmol, 5 mol%)

and non-degassed water (2 mL). To the resulting suspension a solution of substrate **13e** (0.14 mmol) in MeOH or EtOH (5 mL) was added. The reaction mixture was stirred at 25 °C. After complete conversion (followed by TLC), the reaction mixture was evaporated to dryness, dissolved in CH_2Cl_2 (5 mL) and passed through a cartridge containing silica gel (1–2 g). The cartridge was washed with an additional portion of CH_2Cl_2 (15–25 mL). The CH_2Cl_2 fraction was concentrated under reduced pressure to yield crude product **14e**.

4.5. General procedure for RCM reactions in BMI · PF_6/toluene (1/3 v/v) and BMPy · BF_4/toluene (1/3 v/v)

$BMI \cdot PF_6$ or $BMPy \cdot BF_4$ (1.25 mL) was introduced into a Schlenk flask and dried for 2 h under vacuum at 70 °C then washed with dry toluene (3×10 mL). The ionic-tagged catalyst was added and the mixture was stirred for 1 h at room temperature under vacuum to afford a complete dissolution of the catalyst. The diene (1 mmol, $c = 0.2$ M) was then introduced followed by dry toluene (3.75 mL) and the reaction mixture was stirred at the indicated temperature. The progress of the reaction could be followed by ^1H NMR or by TLC. The product was then extracted from the reaction mixture with dry toluene (4×10 mL). The combined toluene extract layers were evaporated to afford the crude product.

4.6. Procedure for ICP-MS measurement

All samples were prepared by weighing 5 mg of the crude compound (that was previously filtered through a plug of silica gel in order to remove $BMI \cdot PF_6$ traces) and then adding 10 mL of 0.12 M hydrochloric acid in glacial acetic acid. The analyses were performed on a PE Instrument Elan 6000 Inductive Coupled Plasma Mass Spectrometer (ICP-MS) using ^{99}Ru and ^{101}Ru isotopes, which are not interfered by molybdenum oxide. All samples were diluted 10 times in ultra pure water. The Ru level was determined by comparison with a standard Ru sample (10 μg/mL). The analyses have been realised by UT2A Company, France (http://www.univ-pau.fr/ut2a).

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