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A pyridine-containing ruthenium–indenylidene complex: Synthesis and activity in ring-closing metathesis

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Abstract

The reaction of $Cl_2Ru(PCy_3)_2$(3-phenylindenylidene) with excess pyridine leads to the new pyridine-containing ruthenium-based complex: $Cl_2Ru(PCy_3)(Py)_2$(3-phenylindenylidene) in good yield. This catalyst has been fully characterized and tested in ring-closing metathesis. Its moderate activity has been examined by kinetic studies using several substrates and different reaction conditions.

Keywords: Ruthenium; Metathesis; Ring-closing metathesis; Indenylidene

1. Introduction

Among the large number of organic and organometallic reactions allowing the formation of carbon–carbon double bonds, the metathesis of olefin is one of the most powerful and is becoming more widely employed in synthetic schemes. As a result of the impact of this reaction, the 2005 Nobel Prize in chemistry was awarded to Chauvin, Schrock and Grubbs for their seminal contributions to the understanding of the mechanism and for the development of well-defined, efficient catalysts [1]. One of the major advances in this field was the discovery of well-defined homogeneous ruthenium–benzylidene species, such as the Grubbs' catalyst **1a** [2] and, complexes containing *N*-heterocyclic carbenes **1b** [3] and **1c** [4] (Fig. 1). Theses complexes are tolerant to harsh reaction conditions and extremely compatible with functional groups. However their reactivity profile in terms of turnover frequencies (TOF) are moderate especially when compared to catalytic systems used in hydrogenation and cross-coupling reactions [5]. This modest activity appears general to date with the exception of activity in ring-opening metathesis polymerizations (ROMP). In order to increase this reactivity, many catalysts based on the Ru–benzylidene scaffold have been developed, albeit with varied success. In 2002, Grubbs and co-workers reported the synthesis of substitution labile pyridine-containing complexes **2a** [6] and **2c** [7]. According to mechanistic studies on metathesis, the initiation step involves the 14-electron intermediate Cl_2Ru(ligand)(alkylidene) [8] formation which is accelerated by the presence of labile ligands. Pre-catalyst **2c** displayed good activity in ROMP, however, for both cross metathesis (CM) and ring-closing metathesis (RCM) no significant improvement was observed when compared to previous catalysts. Activity and stability being intimately related, the catalytic species is more easily generated when labile ligands are present, which unfortunately also translates into rapid degradation in view of slower propagation kinetics. The use of ruthenium–3-phenylindenylidene complexes such as **3a** and **3b** [9,10] showing a higher thermal stability than their benzylidene counterparts appears an as attractive alternative or at least worthy of investigation (Fig. 1).

We now report the synthesis and full characterization of a novel metathesis pre-catalyst: $Cl_2Ru(PCy_3)$(pyridine)$_2$(3-phenylindenylidene) (**4**). Kinetics studies enabling the

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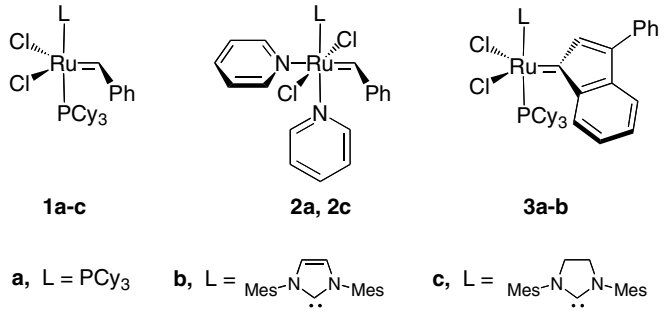
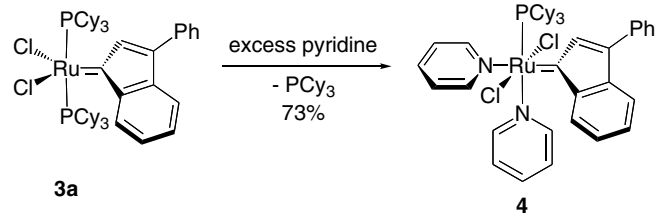


Fig. 1. Various ruthenium-based pre-catalyst architectures.

evaluation of the stability and catalytic activity of **4** in ring-closing metathesis are also presented.

Treatment of complex **3a** with an excess of pyridine leads to a rapid color change of the reaction mixture from red to black, subsequent addition of hexanes results in the formation of a precipitate. Further filtration at −40 °C cleanly produced the bis(pyridine) adduct $Cl_2Ru(PCy_3)$-(pyridine)$_2$(3-phenylindenylidene) (**4**) as an air and moisture sensitive brownish red solid. The ^{1}H NMR spectrum contains the characteristic signal of CH–C=Ru appearing as a singlet at 7.80 ppm (vs. 7.98 ppm for complex **3a**). Integration of ^{1}H NMR signals and comparison with the spectrum of starting compound **3a** clearly indicate the coordination of two pyridines to the metal center and the loss of one tricyclohexylphosphine ligand. Moreover, the ^{13}C and ^{31}P NMR spectra respectively confirm the presence of a ruthenium–carbon double bond (signal at 309.3 ppm) and of a phosphine (signal at 18.4 ppm vs. 33.5 ppm for complex **3a**) (Scheme 1).

Crystallization carried out in a glovebox using a mixture of dichloromethane and pentane afforded suitable crystals for X-ray determination. Ball-and-stick representation of $Cl_2Ru(PCy_3)(py)_2$-(3-phenylindenylidene) (**4**) is shown in Fig. 2 and representative bond lengths and angles are reported in Table 1. The X-ray crystal structure determination confirmed a distorted octahedral geometry for **4** and clearly showed coordination of the Ru center to the indenylidene moiety. To the best of our knowledge, the Ru=C(1) (indenylidene carbon) bond length of 1.899(4) Å is the longest observed to date. This bond is significantly longer than those in five-coordinated benzylidene–ruthenium catalysts (d(Ru=Cα) between 1.795(11) and 1.841(11) Å) [10c] as well as the one in the ruthenium–indenylidene complex bearing a *N*-heterocyclic carbene IPr (1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene), 1.861(4) Å [10a]. According



Scheme 1. Synthesis of ruthenium bis(pyridine) adduct complex **4**.

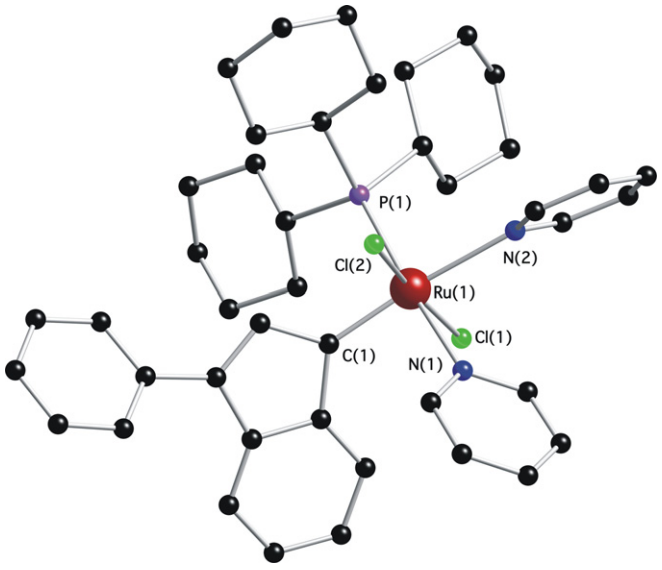


Fig. 2. Ball-and-stick representation of $Cl_2Ru(PCy_3)(py)_2$-(3-phenylindenylidene) (**4**) (hydrogen atoms have been omitted for clarity).

to the literature [7a], the presence of a pyridine ligand *trans* to the carbene leads to the substantial elongation of the Ru=Cα bond. However, coordination of an additional ligand has no effect on the length of the Ru–P(1) bond, 2.401(1) Å. Interestingly, the two Ru–Cl bonds differ by 0.02 Å. The same trend is observed for the two Ru–N bonds ($\Delta = 0.23$ Å), confirming the distinctive influences of *trans* substituents (indenylidene and phosphine).

In order to evaluate the activity in RCM of **4**, kinetic studies were carried out under different reaction conditions (temperature and catalyst loading). Using diethyldiallylmalonate (**5a**) as model substrate, we performed reactions at room temperature and with low pre-catalyst loading (1 mol%) to slow the RCM reaction in order to obtain an accurate comparison of pre-catalyst activity (Fig. 3). Under these conditions, pre-catalyst **4** initiates RCM well, conversion reached 29% after 10 min and the color of the reaction

Table 1
Selected bond length and angles for $Cl_2Ru(PCy_3)(py)_2$-(3-phenylindenylidene) (**4**)

Atoms	Bond distances (Å)	Atoms	Bond angles (°)
Ru(1)–C(1)	1.899(4)	C(1)–Ru(1)–N(1)	89.9(1)
Ru(1)–N(1)	2.178(4)	C(1)–Ru(1)–N(2)	171.3(1)
Ru(1)–N(2)	2.338(4)	N(1)–Ru(1)–N(2)	82.4(1)
Ru(1)–Cl(1)	2.381(1)	C(1)–Ru(1)–Cl(1)	95.2(1)
Ru(1)–Cl(2)	2.414(1)	N(1)–Ru(1)–Cl(1)	86.5(1)
Ru(1)–P(1)	2.401(1)	N(2)–Ru(1)–Cl(1)	88.2(1)
		C(1)–Ru(1)–P(1)	93.5(1)
		N(1)–Ru(1)–P(1)	176.60(7)
		N(2)–Ru(1)–P(1)	94.32(8)
		Cl(1)–Ru(1)–P(1)	92.73(3)
		C(1)–Ru(1)–Cl(2)	89.3(1)
		N(1)–Ru(1)–Cl(2)	86.31(7)
		N(2)–Ru(1)–Cl(2)	86.36(8)
		Cl(1)–Ru(1)–Cl(2)	171.52(4)
		P(1)–Ru(1)–Cl(2)	93.18(3)

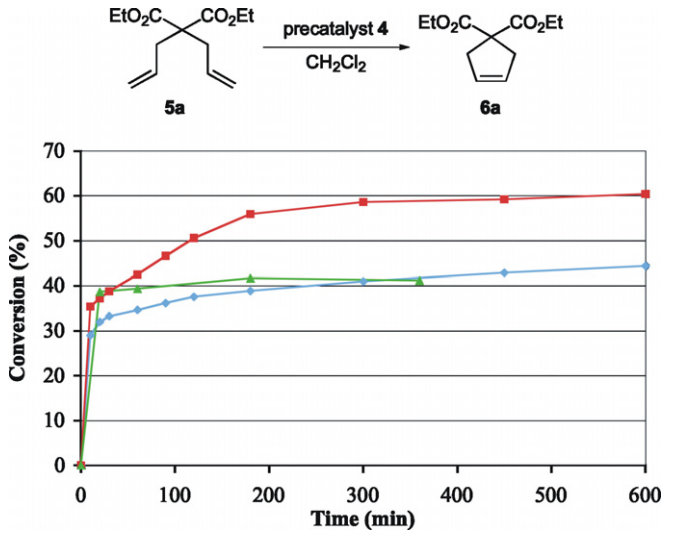


Fig. 3. RCM of **5a** with pre-catalyst **4** in CH_2Cl_2 (◆, 1 mol%, rt), (■, 5 mol%, rt) and (▲, 1 mol%, 40 °C).

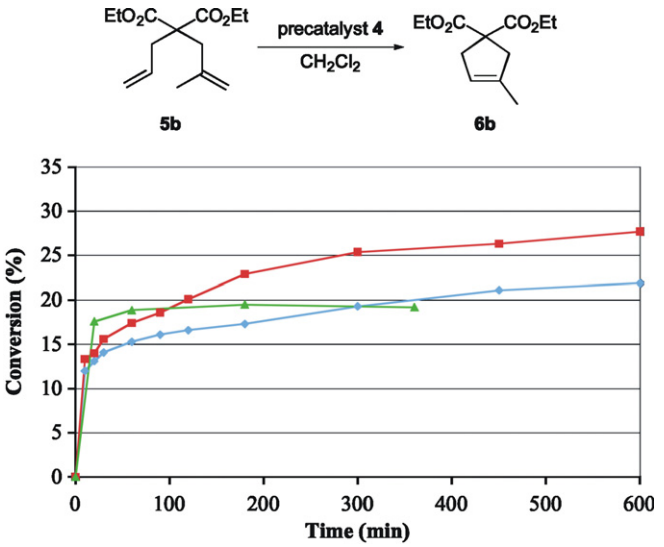


Fig. 4. RCM of **5b** with pre-catalyst **4** in CH_2Cl_2 (◆, 1 mol%, rt), (■, 5 mol%, rt) and (▲, 1 mol%, 40 °C).

mixture changed rapidly from red to orange. As mentioned previously, the greater lability of the pyridine ligand in comparison with phosphine enhances the formation of the active species, however after 30 min the reaction rate decreased indicating a degradation of the 14-electron intermediate. It is noteworthy that a similar study carried out with pre-catalyst **2a** under the same conditions, showed a complete loss of activity after 15 min [6]. It was previously reported that only ~20% conversion with 4 mol% of **2a** was achieved. Attempts to stabilize the active species by adding 10 equiv. of pyridine lead to ~10% conversion. This report concluded that the propagating species was unstable under these reactions conditions. The RCM of **5a** using complex **4** progressed gradually reaching until 44% conversion after 10 h, showing the robustness of the Ru–indenylidene architecture. In order to obtain complete conversion, we then increased the loading of pre-catalyst from 1 to 5 mol%. This translated into a notable improvement in substrate conversion (35% after 10 min and 60% conversion after 10 h); nevertheless, it has to be noted that to approximately double the conversion, we had to increase the catalyst loading by a factor of 5. At this point, we believe that the increase of catalyst loading is associated with a higher concentration of pyridine in the reaction mixture leading to a more rapid decomposition of the catalytic species. We also studied the effect of temperature on the reaction and catalyst stability by performing the reaction at 40 °C with 1 mol% of pre-catalyst **4**. A smooth reaction was observed for the first 20 min (39%), however no further conversion was reached after 2 h. These results suggest that thermal activation should be avoided when using pre-catalyst **4**.

In order to confirm these initial results, we then carried out the same studies with a more hindered substrate, the diethylallymethallylmalonate (**5b**) (Fig. 4). Overall, the same trend as with **5a** was observed. At 40 °C, the catalytic activity is completely quenched after only 20 min (18% conversion), whereas at room temperature, the reactions progresses for 10 h (25% with 1 mol% of **4** and 29% using 5 mol%). Again, degradation of the catalyst occurs more slowly at room temperature; therefore we suspect the remainder of the unactivated initial loading of pre-catalyst acts as a reservoir of the active species.

In addition to **5a** and **5b,** heteroatom containing substrates the diallyltosylamine (**5c**) and the more hindered allylmethallyltosylamine (**5d**) were also examined as potential substrates (Fig. 5). For these two compounds, the initiation rate is equally fast but after 5 h the catalyst shows no further activity. Surprisingly, **5c** reached better conversion than **5a** (54% conversion vs. 44%). Conversely, the

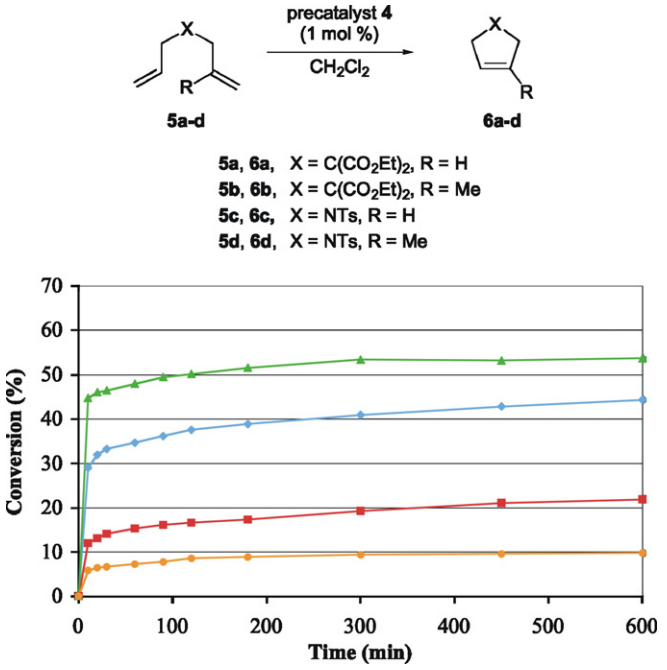


Fig. 5. RCM of different substrats with pre-catalyst **4** in CH_2Cl_2, 1 mol%, rt (◆, **5a**), (■, **5b**), (▲, **5c**), and (●, **5d**).

more hindered substrates **5b** and **5d** showed, as might be expected, the opposite trend (10% conversion using **5d** and 22% with **5b**).

In conclusion, we have synthesized and fully characterized a new ruthenium-based complex, $Cl_2Ru(PCy_3)(py)_2$-(3-phenylindenylidene) (**4**). X-ray characterization shows the longest ruthenium–carbon double bond reported to date. Kinetic studies were carried out to evaluate the activity of pre-catalyst **4** in RCM. Despite a rapid initiation, the presence of pyridine in lieu of a better binding ligand in the reaction mixture seems to have a negative effect on the stability of the active species and only moderate catalytic conversions were obtained. In view of these results and how they compare to the activity of other Ru–alkylidene fragments, the robustness of the Ru–indenylidene moiety appears promising. Further developments making use of this easily synthesized scaffold are ongoing in our laboratory.

2. Experimental

2.1. Preparation of $Cl_2Ru(PCy_3)(Py)_2$(3-phenylindenylidene) (4)

In a glovebox, $Cl_2Ru(PCy_3)_2$(3-phenylindenylidene) (500 mg, 0.54 mmol) was dissolved in a minimum volume of pyridine (ca. 1 mL). The mixture was stirred 30 min at room temperature before adding 20 mL of hexanes. The mixture was again stirred 30 min at room temperature before cooling at −40 °C overnight. The resulting precipitate was filtered on a collection frit, washed with hexanes (3 × 10 mL), and dried under vacuum to yield an air-sensitive brownish red solid (310 mg, 73% yield). ^{1}H NMR (C_6D_6, 500 MHz) δ 9.32 (s, 3H), 8.64 (d, $J = 7.3$ Hz, 1H), 8.58 (s, 2H), 8.04 (d, $J = 7.3$ Hz, 1H), 7.80 (s, 1H), 7.31 (t, $J = 7.3$ Hz, 1H), 7.23 (d, $J = 7.3$ Hz, 1H), 7.02 (t, $J = 7.3$ Hz, 2H), 7.00 (t, $J = 7.3$ Hz, 1H), 6.76 (m, 3H), 6.50 (m, 1H), 6.16 (m, 2H), 3.57 (m, 3H), 2.33 (m, 3H), 2.17 (m, 6H), 2.02 (m, 6H), 1.72 (m, 6H), 1.57 (m, 3H), 1.22 (m, 6H). ^{13}C NMR (C_6D_6, 125 MHz) δ 309.3 (*C*=Ru), 159.7 (*C*), 154.5 (*C*H), 151.4 (2*C*H), 145.0 (*C*), 143.8 (*C*H), 142.5 (*C*), 138.4 (*C*), 136.5 (*C*H), 136.4 (*C*H), 130.8 (*C*H), 130.6 (*C*H), 130.1 (2*C*H), 128.9 (*C*H), 128.8 (*C*H), 128.7 (*C*H), 128.5 (*C*H), 126.7 (2*C*H), 124.0 (2*C*H), 123.3 (*C*H), 118.7 (*C*H), 37.7 (d, $J_{CP} = 17.6$ Hz, 3 *C*H), 30.3 (6*C*H$_2$), 29.0 (d, $J_{CP} = 9.4$ Hz, 6*C*H$_2$), 27.3 (3*C*H$_2$). ^{31}P NMR (C_6D_6, 121.4 MHz) δ 18.4 (s). Anal. Calc. for $C_{43}H_{53}Cl_2N_2PRu$: C, 64.49; H, 6.67; N, 3.50. Found: C, 64.22; H, 6.90; N, 3.80%.

2.2. General procedure for kinetic studies

In a glovebox, a vial was charged with the diene (1 mmol) and dichloromethane (10 mL), then pre-catalyst **4** (0.01 mmol, 8 mg) was added. Progress of the reaction was monitored by ^{1}H NMR by drawing aliquots from the reaction solution and by integrating the characteristic signals for allylic proton resonances.

3. Supplementary material

Crystallographic data for **4** as supplementary Publication No. CCDC-609698. Copies of the data can be obtained free of charge on applications to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, fax: +44 1223 336 033; e-mail: deposit@ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk.

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