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COMMUNICATION

Phosphites as ligands in ruthenium-benzylidene catalysts for olefin metathesis†

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The use of phosphites in second generation, ruthenium-based olefin metathesis pre-catalysts leads to an improvement in catalyst stability and activity at low catalyst loadings.

With the ultimate recognition of the Chemistry Nobel Prize awarded to Chauvin, Grubbs and Schrock in 2005 for their seminal contributions to the discovery and development of olefin metathesis,[1] this transformation is now one of the most useful tools in organic chemistry, finding countless applications in various fields of chemistry.[2] Since the initial reports dealing with the activity of ruthenium alkylidene complexes,[3] the development of longer-living and more active pre-catalysts has been the focus of numerous studies. The replacement of a labile phosphine ligand by a *N*-heterocyclic carbene (NHC) was a major breakthrough, allowing for a dramatic increase in terms of pre-catalyst reactivity and stability, leading to a new generation of complexes (**G-II**, Fig. 1).[4]

We recently reported the facile synthesis of indenylidene-type phosphite-containing ruthenium complexes from the corresponding pyridine adduct (**Caz-1** in Fig. 1). Such complexes have not only shown an unexpected *cis*-dichloro structural arrangement but also an enhanced activity at low catalyst loadings.[5] Their efficiency is probably related to an increased stability conferred by a synergy between the π-acidic phosphite and the strong σ-donor NHC.[6] We reasoned that such an effect could also be of interest in benzylidene-type complexes, especially in the context of performing metathesis transformations at low catalyst loadings.[7]

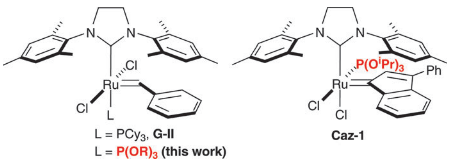

Fig. 1 Ruthenium complexes bearing phosphite ligands in two frequently-encountered olefin metathesis architectures.

Scheme 1 Synthesis of complexes **1a** and **1b**.

As an initial synthetic strategy to reach our goal, the pyridine adduct **G-III** was used as a starting material.[8] Two different phosphites, $P(O^iPr)_3$ and $P(OEt)_3$, that provided respectively excellent and more modest results in the indenylidene series,[9] were used in the present study. Reaction of **G-III** with 1 equivalent of these ligands in dichloromethane at room temperature allowed for the isolation of the desired complexes in good yields (Scheme 1).†

The ^{13}C-{^{1}H} NMR spectra of **1a** and **1b**, with a $^{2}J_{C-P}$ between the carbenic carbon and the phosphorus of *ca.* 140 Hz, indicate a *trans* arrangement of the complexes, which is in contrast with the *cis* configuration observed with **Caz-1**. This structural feature in **1a** and **1b** was unambiguously confirmed by X-ray diffraction studies on single crystals. Graphical representations of the structure of **1a** and **1b** are provided in Fig. 2. **1a** and **1b** present a slightly distorted square pyramidal geometry, with the benzylidene moiety sitting at the apex of the pyramid. When compared to **G-II** pre-catalyst (L = PCy_3), complexes **1a** and **1b** present a slightly shorter Ru–P bond (**1a**, 2.3496(11) Å; **1b**, 2.3213(10) Å; **G-II**, 2.4245(5) Å, respectively).[10] These metrical parameters suggest stronger Ru–P bonds in phosphite-containing complexes.[11]

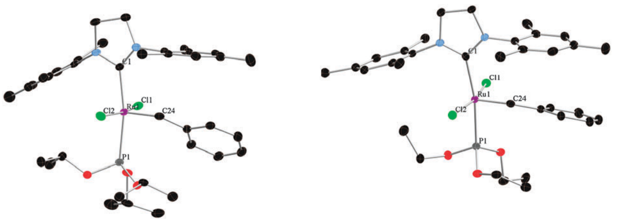

Fig. 2 Molecular representations of **1a** (left) and **1b** (right). H atoms are omitted for clarity. Selected bond distances (Å) and angles (°): **1a**: Ru-C(24), 1.836(4); Ru-C(1), 2.114(4); Ru-P, 2.3496(11); Ru-Cl(1), 2.3605(10); Ru-Cl(2), 2.4008(10); C(1)-Ru-P, 169.23(11); C(1)-Ru-Cl(1), 90.22 (10); C(1)-Ru-Cl(2), 87.09(10); C(24)-Ru-C(1), 98.47(16); **1b**: Ru-C(24), 1.843(4); Ru-C(1), 2.125(3); Ru-P, 2.3213(10); Ru-Cl(1), 2.3820(10); Ru-Cl(2), 2.3985 (11); C(1)-Ru-P, 169.04(9); C(1)-Ru-Cl(1), 89.13(9); C(1)-Ru-Cl(2), 88.86(9); C(24)-Ru-C(1), 99.76(14).

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† Electronic supplementary information (ESI) available: Experimental details and characterisation of complexes and metathesis products. CCDC 811896 and 811897. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c1cc10825e

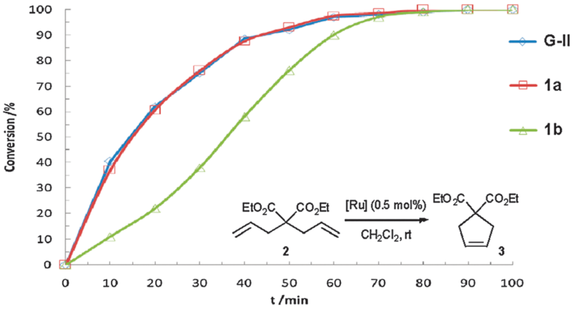


Fig. 3 Reaction profiling in the RCM of diallyldiethylmalonate. Reaction conditions: **2** (0.25 mmol), pre-catalyst (0.5 mol%), CH_2Cl_2 (2.5 mL). Conversions were determined by GC. Average of two runs for each reaction.

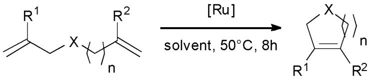
The activity profile of complexes **1a** and **1b** was then evaluated in ring closing metathesis (RCM) using **2** as model substrate and compared to the activity displayed by **G-II**. The results of this series of reactions are illustrated in Fig. 3.

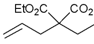
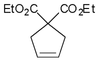
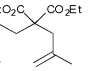
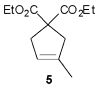
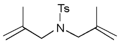
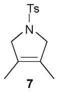
Complete conversion of diallyldiethylmalonate **2** was achieved with all pre-catalysts after 1.5 h when 0.5 mol% of the organoruthenium complex was used. Surprisingly, **1a** and **G-II** displayed similar conversion profiles, when a slower activation could have been expected for **1a** considering the observed shorter Ru–P bond in the structural study. This exact behaviour was observed for **1b**, featuring the $P(OEt)_3$ ligand, where **1b** exhibited a slower activation but nevertheless permitted complete conversion after 1.5 h.

In order to highlight any marked differences between the complexes, low catalyst loading experiments were performed. Catalytic reactions were therefore conducted using 0.025 mol% catalyst loading and, to reduce the time necessary to conduct the experiment, an operating temperature of 50 °C was selected. Results of these low catalytic concentration studies are presented in Table 1.

In toluene, after 8 h, **G-II** and **1a** led to similar catalytic activity while **1b** displayed a slightly lower performance (Table 1, entries 1–3). Changing the solvent to dichloromethane allowed for improved results, **1a** giving this time a slightly better conversion than **G-II** whilst **1b** showed again poorer efficiency (entries 4–6). Interestingly, the use of methyl *tert*-butylether (MTBE), which is considered to be a good alternative to chlorinated solvents,[7b] proved to be a judicious choice as a nearly quantitative conversion was obtained with **1a** (Table 1, entries 7–9). A similar beneficial effect of MTBE compared to toluene and to a smaller extent to CH_2Cl_2 was again observed in the RCM of malonate derivative **4** (Table 1, entries 10–18). Indeed, comparable activities were displayed in toluene in the presence of 0.025 mol% of pre-catalyst but the use of dichloromethane led to higher conversions with **1a** (**1a** > **G-II** > **1b**) whereas MTBE allowed for higher conversions to product (Table 1, entries 16–18). The RCM of the "challenging" substrate **6** leading to the tetrasubstituted olefin **7** was next evaluated in refluxing dichloromethane. In the presence of 2 mol% of pre-catalyst, the previously observed reactivity trend for the two test substrates was again observed as **1a** allowed for 65% conversion after 8 h whilst **G-II** could not reach more than 40% (Table 1, entries 19–20). The use of MTBE amplified this difference as **G-II** and **1a** allowed for 25 and 63% conversion, respectively (Table 1, entries 22–23).

Table 1 Comparison of **1a** and **1b** with **G-II** in RCM[a]



Entry	Substrate	Product	Pre-catalyst	Solvent	Conv. (%)[b]
1/2/3 4/5/6 7/8/9	 2	 3	**G-II**/**1a**/**1b** **G-II**/**1a**/**1b** **G-II**/**1a**/**1b**	toluene CH_2Cl_2 MTBE	72/74/65 83/87/70 89/98/89
10/11/12 13/14/15 16/17/18	 4	 5	**G-II**/**1a**/**1b** **G-II**/**1a**/**1b** **G-II**/**1a**/**1b**	toluene CH_2Cl_2 MTBE	77/77/77 81/86/75 91/93/93
19/20/21 22/23/24	 6	 7	**G-II**/**1a**/**1b** **G-II**/**1a**/**1b**	CH_2Cl_2 MTBE	40^c/65^c/33^c 25^c/63^c/42^c

[a] Reaction conditions: substrate (0.25 mmol), pre-catalyst (0.025 mol%), solvent (0.5 mL), 50 °C, 8 h. [b] Conversions determined by GC, average of at least two runs. [c] Pre-catalyst (2 mol%) loading. MTBE = methyl *tert*-butylether.

These promising results prompted us to evaluate further the catalytic potential of **1a** in diverse metathesis reactions.

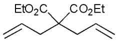
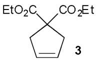
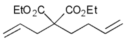
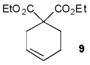
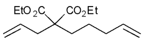
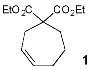
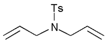
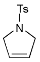
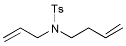
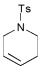
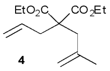
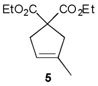
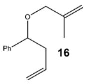
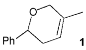
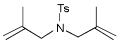
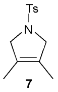
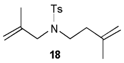
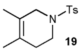
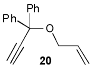
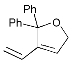
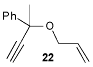
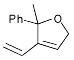
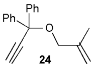
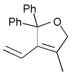
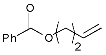
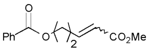
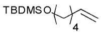
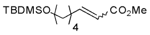
The catalytic activity of **1a** was hence next evaluated at low catalyst loading in various ring closing metatheses (RCM), in enyne metathesis as well as in cross-metathesis (CM). The results of these studies are summarised in Table 2. The reaction conditions chosen were similar to those described above (50 °C, 8 h), and the solvent selected was MTBE.

The RCM of unhindered alkenes (**2**, **8**, **10**, **12**, **14**) was first examined (Table 2, entries 1–5). 5-Membered rings were obtained in excellent yields using catalyst loadings of 0.05–0.025 mol% (Table 2, entries 1 and 4) whilst the synthesis of 6-membered rings required 0.1–0.05 mol% Ru to proceed to completion (Table 2, entries 2 and 5). Similarly, the 7-membered ring congener **11** could be obtained in high yield using 0.2 mol% Ru (Table 2, entry 3). More hindered olefins, such as **4** and **16**, were efficiently ring-closed using low catalyst loading (0.025–0.075 mol%, Table 2, entries 6 and 7). Finally, the ring closing metathesis of challenging substrates, leading to the formation of tetra-substituted double bonds (**7** and **19**), was achieved in good yields but in the presence of higher catalyst loadings (Table 2, entries 8 and 9).

Pre-catalyst **1a** was also evaluated in enyne metathesis reactions. The system displayed excellent activity as the furan derivatives could be obtained in very high yields using only 0.05–0.1 mol% ruthenium loadings (Table 2, entries 10 and 11). The very challenging enyne substrate **24**, when subjected to the optimum conditions, leads to the desired product **25** in 87% isolated yield (Table 2, entry 12). This is, to the best of our knowledge, the best catalytic performance reported to date on this substrate.[12] Additionally, **1a** was tested in the cross-metathesis of olefins **26** and **28** with methyl acrylate. Good yields and excellent selectivity were obtained using Ru-loadings of 0.2 and 0.5 mol% (Table 2, entries 13 and 14).

In conclusion, two benzylidene Ru complexes bearing a NHC and a phosphite ligand were synthesised, fully characterised and

Table 2 Evaluation of **1a** in RCM and CM[a]

Entry	Substrate	Product	Pre-catalyst (mol%)	Yield (%)[b]
1	 **2**	 **3**	**1a** (0.025) **G-II** (0.025)	98 (97) 89
2	 **8**	 **9**	**1a** (0.05)	99 (89)
3	 **10**	 **11**	**1a** (0.2)	78 (76)
4	 **12**	 **13**	**1a** (0.05)	97 (91)
5	 **14**	 **15**	**1a** (0.1)	>99 (94)
6	 **4**	 **5**	**1a** (0.025) **G-II** (0.025)	95 (91) 91
7	 **16**	 **17**	**1a** (0.075)	96 (94)
8	 **6**	 **7**	**1a** (2)	63 (62)
9	 **18**	 **19**	**1a** (5)	86 (86)
10	 **20**	 **21**	**1a** (0.05)	98 (91)
11	 **22**	 **23**	**1a** (0.1)	99 (78)
12	 **24**	 **25**	**1a** (5) **G-II** (5)	92 (87) 81
13[c]	 **26**	 **27**	**1a** (0.2) **G-II** (0.2)	75 (72) [>20 : 1][d] 72
14[c]	 **28**	 **29**	**1a** (0.5)	91 (83) [>20 : 1][d]

[a] Reaction conditions: substrate (0.25 mmol), pre-catalyst, MTBE (0.5 mL), 50 °C, 8 h. [b] Isolated yields in parentheses; average of at least two runs. [c] Methyl acrylate (5 equiv.) as coupling partner. [d] *E*/*Z* ratios in brackets determined by ^{1}H NMR.

tested in olefin metathesis. This represents, to the best of our knowledge, the first example of P(OR)$_3$-containing ruthenium benzylidene complexes fully characterised and shown efficient in olefin metathesis reactions. Complex **1a**, featuring a P(O^{i}Pr)$_3$ ligand, proved superior to its PCy$_3$ and P(OEt)$_3$ analogues, in particular for challenging substrates. **1a** is efficient for RCM reactions using catalyst loadings as low as 0.025 mol%, and proved highly efficient for very challenging substrates, including in enyne metathesis. **1a** was also shown active and selective in cross-metathesis. In addition to these attractive features, **1a**, bearing a phosphite, is potentially more economically viable than its congener **G-II** which bears tricyclohexylphosphine.[13] Because of such remarkable catalytic activity and lower production costs, this new family of catalysts shows great promise. Studies aimed at addressing synthetic and mechanistic issues of this NHC/P(OR)$_3$ synergy are ongoing in our laboratories.

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