Phosphabicyclononane-Containing Ru Complexes: Efficient Pre-Catalysts for Olefin Metathesis Reactions

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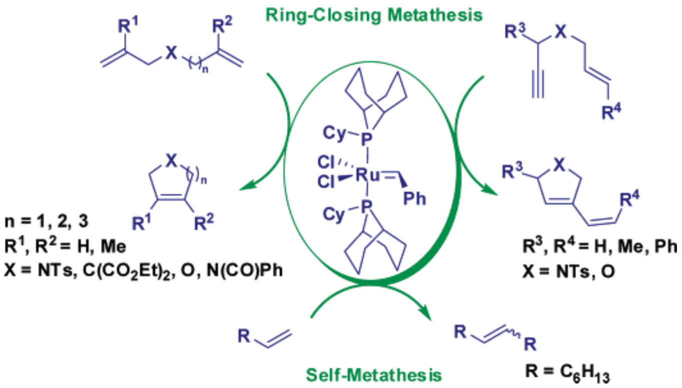

The catalytic performances of three Phosphabicyclononane (Phoban)-containing ruthenium-based pre-catalysts have been evaluated for metathesis transformations. A wide screening of substrates in ring-closing metathesis reactions reveals the greater efficiency of pre-catalyst **4**. Comparison of the catalytic activities of **4** with Grubbs' first-generation pre-catalyst illustrates the key role of the Phoban ligand. Additionally, a comparative study of three Phoban-containing pre-catalysts has been conducted for the self-metathesis of 1-octene at low catalyst loading (25−100 ppm).

Introduction

Olefin metathesis represents a powerful tool in modern synthetic chemistry. Remarkably, its range of applications[1] spans from ring-closing metathesis (RCM) and cross metathesis (CM) to ring-opening metathesis polymerization (ROMP) and acyclic diene metathesis polymerization (ADMET). Because ruthenium-based complexes are recognized as efficient catalysts and are tolerant to various functionalities, they have been the focus of considerable attention over the past decade.[2] Subsequent to the discovery by Grubbs of catalyst **1a**[3] in 1995, the replacement of a tricyclohexylphosphine ligand by a N-heterocyclic carbene (NHC) led to analogues **1b**,**c**[4] and allowed for an improved stabilization of the active species. Following this groundbreaking

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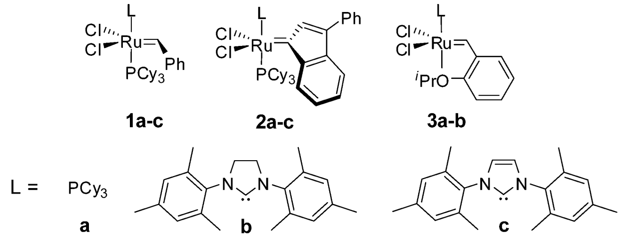

FIGURE 1. Representative Ru-based metathesis pre-catalysts.

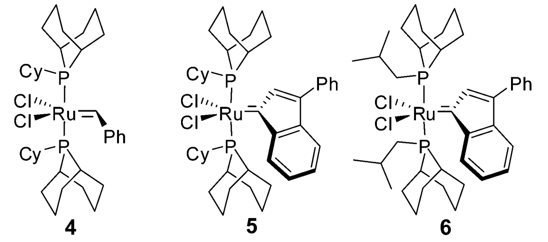

FIGURE 2. Structures of Phoban-containing pre-catalysts.

modification, further developments have focused on the modification of the alkylidene moiety, and this approach has led to new families of catalysts such as the indenylidene-containing pre-catalysts **2a**−**c**[5] and isopropoxybenzylidene-containing phosphine-free complexes **3a**,**b** (Figure 1).[6] Thus, even if many different ruthenium-based pre-catalysts have been synthesized to date, little attention has been paid during this rapid development to the tuning of phosphine ligands. In these systems, it was long thought that only PCy_3 (or tricyclopentylphosphines) were viable ligands. Changing the phosphine affects phosphine dissociation and rebinding to ruthenium and therefore has a profound influence on the catalytic activity. By comparing the dissociation from ruthenium of a series of substituted triarylphosphines (PAr_3) with tricyclohexylphosphine (PCy_3), Grubbs and co-workers[7] showed that the faster phosphine exchange was observed with PPh_3. This effect was also observed by Nolan and co-workers in their early studies on second-generation systems.[4] Nevertheless, this high lability and the lack of bulkiness of PPh_3 translated into a decreased stability of the corresponding complex which is one of the reasons PCy_3 is still preferentially used. The choice of the ancillary ligand remains a crucial parameter in finding the adequate compromise between lability and stabilization. Phosphabicyclononane (Phoban) ligands, initially developed in the 1960s,[8] are interesting candidates for developing active catalysts because they fulfill the requirements of steric bulk and basicity for metathesis reactions.

The first synthesis of a Ru−Phoban complex was reported in 2004 by Forman and co-workers[9] (Figure 2). They employed the relatively inexpensive 9-cyclohexyl-9-phospha-bicyclononane as ligand for the synthesis of complex **4** and briefly evaluated its efficacy in several metathesis reactions. The investigation of self-metathesis (SM) and ethenolysis reactions of methyl oleate catalyzed by complexes **4** and **5** showed interesting results in terms of activity.[10] Moreover, several calculations and computational studies[11] have been carried out examining catalyst **4**, but to the best of our knowledge, the catalytic performance of these complexes in RCM has not been thoroughly investigated.

Herein, we report the evaluation of the catalytic activity of Phoban-containing ruthenium pre-catalysts in metathesis transformations. First, a comparative study of complexes **4**,[9] **5**, and **6**[12] in RCM reactions has been performed. Additionally, the influence of the alkylidene moiety and Phoban ligand variations on 1-octene metathesis activity has been investigated at different temperatures and concentrations in the presence of these pre-catalysts.

Results and Discussion

Ring-Closing Metathesis Experiments. To carry out a thorough evaluation of pre-catalysts **4**, **5** and **6**, we tested their catalytic activity in RCM involving different substrate types. The results were compared to the ones obtained with reference catalysts **1a** and **2a**. The benchmark substrates include variously substituted and functionalized dienes and enynes. The reactions were carried out with 2 mol % of catalyst, and reaction times as well as temperatures have been optimized (Table 1).

As a general trend, pre-catalyst **4** exhibited a greater activity for all tested substrates in this early study. The cyclization of simple five- and six-membered ring substrates was achieved in quantitative yields in less than 1 h (entries 1 and 4). Interestingly, both trisubstituted olefins and enyne could be cyclized efficiently in short reaction times (entries 2, 3, and 5). Similar results were obtained with complexes **1a** and **4** in the cyclization of diallyldiethylmalonate **7**. The examination of more challenging substrates revealed a significantly higher activity of cyclohexylphoban-containing pre-catalyst **4**. For instance, compounds **9** and **11** were converted into the corresponding trisubstituted olefins **10** and **12** in quantitative yields after 2 h using **4**, while 6 h were necessary to reach a complete conversion using Grubbs' catalyst **1a** (entries 2 and 3). The formation of ether **14** was twice as fast using **4** when compared to **1a** (entry 4). This difference of activity was also noticed in enyne ring-closing metathesis (entry 5) because **16** was isolated after 2 h with **4** while the use of **1a** in this reaction required 5 h to reach completion. This difference of activity was previously communicated,[13] and Chen[14] mentioned that ligand symmetries and conformational behavior could explain that kind of phenomenon. However, by comparing indenylidene-containing pre-catalysts **5** and **6** with **2a**, the superiority of Phoban- vs tricyclohexylphosphine-containing complexes is not evident. Indeed, for all

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[10] Forman, G. S.; Bellabarba, R. M.; Tooze, R. P.; Slawin, A. M. Z.; Karch, R.; Winde, R. *J. Organomet. Chem.* **2006**, *691*, 5513−5516.

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[13] Dwyer, C. L.; Kirk, M. M.; Meyer, W. H.; Janse van Rensburg, W.; Forman, G. S. *Organometallics* **2006**, *25*, 3806−3812.

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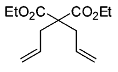
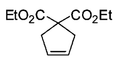
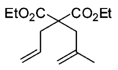
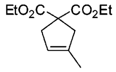
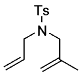
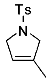
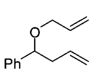
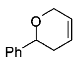
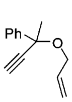
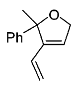
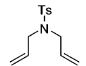
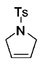
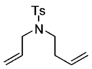
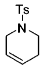
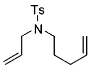
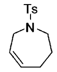
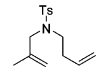
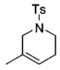
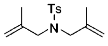
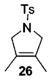
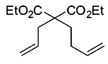
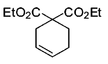
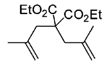
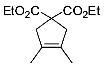
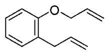
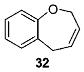
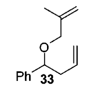
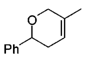
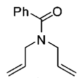
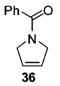
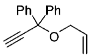
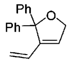
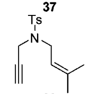
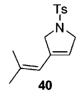
TABLE 1. Comparison of Pre-Catalysts 1, 2a, 4, 5, and 6 in the RCM of Benchmark Substrates[a]

Entry	Substrate	Product	Pre-catalyst	Time (h)	Isolated yield (%)
1	 **7**	 **8**	**1a**	0.25	>99
			2a	0.25	98
			4	0.5	>99
			5	3	99
			6	2	96
2	 **9**	 **10**	**1a**	6	93
			2a	6	89
			4	2	>99
			5	8	80
			6	2	98
3	 **11**	 **12**	**1a**	6	87
			2a	6	89
			4	2	>99
			5	8	98
			6	5	>99
4	 **13**	 **14**	**1a**	2	94
			2a	2	98
			4	1	>99
			5	5	98
			6	5	99
5	 **15**	 **16**	**1a**	5	93
			2a	5	89
			4	2	>99
			5	5	98
			6	10	68[b]

[a] Reactions performed in CH_2Cl_2 at rt using 2 mol % of pre-catalyst. [b] Reaction performed at 40 °C.

TABLE 2. Scope Extension for Pre-Catalysts 4 and 6[a]

Entry	Substrate	Product	Pre-catalyst	Time (h)	Isolated yield (%)
1	 **17**	 **18**	**4**	0.33	>99
			6	6.5	93
2	 **19**	 **20**	**4**	0.75	>99
			6	3	>99
3	 **21**	 **22**	**4**	1.5	>99
			6	6.75	89
4	 **23**	 **24**	**4**	5.5	98
			6	7.5	>99
5	 **25**	 **26**	**4**	24	15[b]
			6	24	26[b]
6	 **27**	 **28**	**4**	0.5	>99
			6	2	>99
7	 **29**	 **30**	**4**	24	<2[b]
			6	24	<2[b]
8	 **31**	 **32**	**4**	3	96
			6	7.5	>99
9	 **33**	 **34**	**4**	3	95
			6	8.5	29[c]
10	 **35**	 **36**	**4**	3.5	>99
			6	7.5	>99
11	 **37**	 **38**	**4**	3	>99
			6	8	>99
12	 **39**	 **40**	**4**	8	>99
			6	6.5	>99[c]

[a] Reactions performed in CH_2Cl_2 at rt using 2 mol % of pre-catalyst. [b] Reaction performed in CH_2Cl_2 at 40 °C using 5 mol % of pre-catalyst. [c] Reaction performed at 40 °C.

substrates described in Table 1, the catalytic activity of **2a** remains superior (entries 1−4) or at least equivalent (entry 5) to **5**. Moreover, an improvement of activity is only observed for trisubstituted olefins with **6** (entries 2 and 3), while **2a** displays a higher activity for all other substrates tested (entries 1, 4, and 5).

These observations confirm that it remains difficult to predict the activity of a pre-catalyst in RCM because it is a highly substrate-dependent reaction, and these further highlight the differences between benzylidene- and indenylidene-containing pre-catalysts. On the other hand, pre-catalysts **5** and **6** bearing an indenylidene moiety were found to be efficient in mediating the metathesis cyclization transformations of various substrates in a few hours. Unfortunately, pre-catalyst **6** was not suitable for the enyne metathesis reaction of **15** (entry 5). However, the cyclizations of trisubstituted olefins using pre-catalyst **6** were achieved under mild conditions and in short reaction times, especially for malonate **9**.

Overall, 9-isobutyl-9-phospha-bicyclononane-containing pre-catalyst **6** gives better results than 9-cyclohexyl-9-phospha-bicyclononane-containing complex **5** except for enyne **15**. It is important to note that the two different Phoban ligands are not behaving in an analogous manner in RCM of trisubstituted olefins because pre-catalyst **6** is the most active for this application.

All these observations led us to investigate a wider range of substrates using pre-catalyst **4** as well as pre-catalyst **6** that was found to be particularly efficient in the RCM of trisubstituted olefins. Special attention was focused on the influence of ring size as well as the degree of substitution of the unsaturated bonds and finally on functional group tolerance (Table 2).

Overall, the catalytic activity of pre-catalyst **4** proved to be greater than that of **6**. Several tosylamine-containing dienes were used (entries 1−5). First, compounds **18** and **20** were isolated in high yields with both pre-catalysts, but the use of **4** allowed for a significant decrease of the reaction time when compared to **6** (entries 1 and 2). Seven-membered ring product **22** was isolated in quantitative yield after 1.5 h of reaction at room temperature with pre-catalyst **4**, while **6** required a longer reaction time to reach completion. As expected, this type of cyclization involves longer reaction times than for smaller rings. The RCM of trisubstituted olefin **23** was achieved within 5.5 and 7.5 h, respectively, using complexes **4** and **6** (entry 4). Despite the use of 5 mol % of catalyst loading, only low yields were observed for tetrasubstituted olefin **26** (entry 5) even after heating the reaction mixture at 40 °C for 24 h. Similar conditions were applied for the cyclization of substrate **29**, and no conversion was observed. Seven-membered ring ether **32** was isolated in good yield with both pre-catalysts but with a shorter reaction time with the benzylidene complex (entry 8). RCM reactions with substrates **33** and **39** (entries 9 and 12) particularly emphasize the fact that **4** is more active than **6**. Thus, thermal activation was necessary to observe the formation of products **34** and **40** in the presence of **6**, while complete conversions at room temperature in relatively short times were observed with

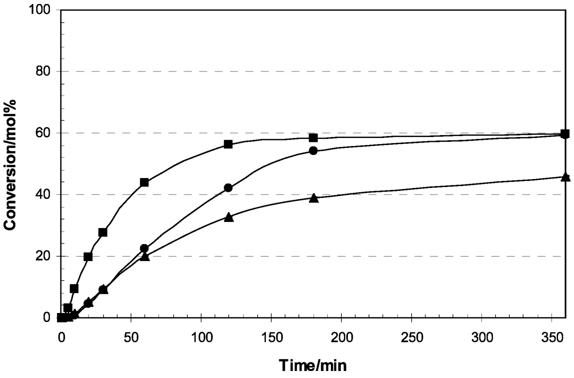


FIGURE 3. Conversion of 1-octene at 40 °C with pre-catalysts **4**−**6** (25 ppm [Ru]). ■, **4**; ●, **5**; ▲, **6**.

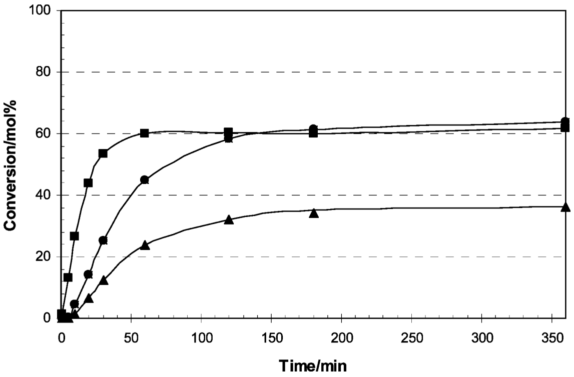


FIGURE 4. Conversion of 1-octene at 50 °C with pre-catalysts **4**−**6** (25 ppm [Ru]). ■, **4**; ●, **5**; ▲, **6**.

4. Finally, quantitative yields of **36** and **38** were obtained with both pre-catalysts; however, reaction times were once again shorter with **4** (entries 10 and 11).

Self-Metathesis of Terminal Alkenes. Self-metathesis represents an attractive reaction for the conversion of low value feedstock into useful chemical products in the field of petrochemicals and polymers.[15] In this context, the activity of pre-catalysts **4**−**6** was first investigated in the self-metathesis reaction of 1-octene for temperatures ranging from 40 to 60 °C, at ruthenium metal concentrations of 25 ppm with a 1-octene/Ru ratio of 27 000 (Figures 3−5). The initial reaction rates increase in the order **6** < **5** < **4** above 40 °C, and **6** ≈ **5** < **4** at 40 °C. However, similar conversions were reached with **4** and **5** after 24 h of reaction at all investigated temperatures (Table 3). These results indicate a slower initiation[16] of the phenyl−indenylidene complex **5** compared to its benzylidene analogue **4**. Because after initiation, **5** and **4** both form the same catalytic species with the same metathesis activity and decomposition behavior, it is not surprising to obtain the same final conversions.

When the reaction temperature was raised to 60 °C, lower conversions were reached with **4** and **5** which indicate the increasing decomposition of the active species at this temperature. Concerning complex **6**, such a stability effect was already observed at 50 °C. The magnitude of the conversion decrease indicates a lower stability of the isobutylphoban catalyst **6** as compared to the cyclohexylphoban catalysts **5** and **4** (Table 3).

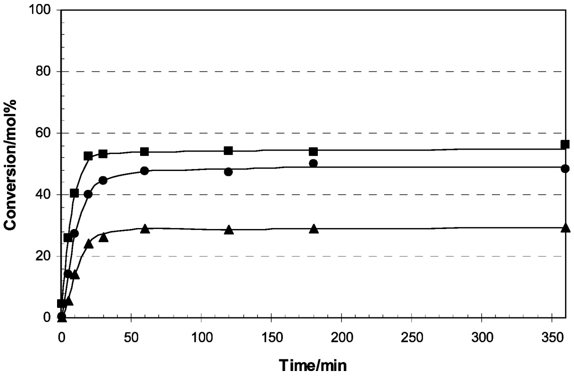


FIGURE 5. Conversion of 1-octene at 60 °C with pre-catalysts **4**−**6** (25 ppm [Ru]). ■, **4**; ●, **5**; ▲, **6**.

TABLE 3. Final Conversions in 1-Octene Self-Metathesis after 24 h Using 25 ppm of [Ru]

entry	temperature (°C)	pre-catalyst	conversion[a] (%)
1	40	**4**	61
		5	64
		6	50
2	50	**4**	63
		5	63
		6	37
3	60	**4**	55
		5	48
		6	30

[a] Monitored by GC.

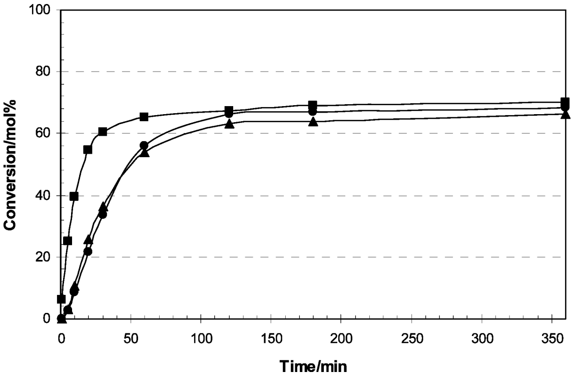


FIGURE 6. Conversion of 1-octene at 50 °C with pre-catalysts **4**−**6** (100 ppm [Ru]). ■, **4**; ●, **5**; ▲, **6**.

Increasing the catalyst loading from 25 [Ru] to 100 ppm [Ru] (Figure 6) results in a similar performance of complexes **5** and **6** with respect to conversion rate and final conversion in the metathesis of 1-octene at 50 °C. It should be noted that higher final conversions for **4** were previously obtained for 1-octene/Ru = 9000 when the catalyst was introduced as a solid, rather than as a toluene solution.[17]

Conclusions

To summarize, the use of complex **4** allows for the RCM of dienes and enynes bearing various functionalities (tosylamides, esters, ethers, and amides). This catalyst was found particularly efficient in the RCM preparation of trisubstituted olefins, and

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a comparison between Grubbs' catalyst and pre-catalyst **4** highlighted a significantly improved activity of the cyclohexylphoban-containing complex. However, it should be noted that the limitation of this catalyst is apparent in tetrasubstituted olefin formation that often represents a challenge.[18] The superior performance of the cyclohexylphoban ligand over its isobutyl counterpart for indenylidene-containing pre-catalysts was clearly pointed out by studying 1-octene metathesis at a ruthenium concentration of 25 ppm, whereas at 100 ppm, no difference is apparent under the experimental conditions. The carbene moiety (**4** vs **5**) influenced catalyst initiation rather than achievable conversion.

Experimental Section

General Procedure for RCM Reactions. A Schlenk flask was filled under argon with the diene or the enyne (0.5 mmol) and DCM (5 mL) before the addition of the pre-catalyst (0.01−0.025 mmol). Progress of the reaction was monitored by TLC. The solvent was removed under a vacuum, and the crude residue was purified by flash column chromatography to yield the pure product.

General Procedure for the Self-Metathesis of 1-Octene. A three-necked round-bottom flask (100 mL) equipped with a condenser, an argon inlet, and a thermometer was charged with 1-octene (15 mL) and nonane (0.5 mL, internal standard) and heated to the desired reaction temperature under argon. Stock solutions of the respective catalysts in toluene were prepared before each reaction. An amount of 4 mL of the stock solution was added to the flask, and the reaction was stirred for 22 h. Samples (0.4 mL) were withdrawn by syringe at regular time intervals, quenched with a solution of toluene (0.5 mL) and *tert*-butyl-hydrogen peroxide (2 drops), and then analyzed by GC/FID. Conversions are reported as the molar % of 1-octene that was converted to the desired products, 7-tetradecene and ethylene.

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Supporting Information Available: Compound characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

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