

# Olefin metathesis in ionic liquids

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Received 14th May 2008

First published as an Advance Article on the web 22nd August 2008

DOI: 10.1039/b711482f

This *tutorial review* covers the use of ionic liquids as (co)solvents for the olefin metathesis reaction. Olefin metathesis is a simple and effective synthetic tool used to create many compounds which otherwise would require complex multistep syntheses. It is expected that the application of ionic liquids (IL) as well as the development of IL-enabled catalysts and separation techniques will create a green aspect to this important methodology.

## Introduction to olefin metathesis

Since the development of the first stable and well-defined catalysts, olefin metathesis<sup>1</sup> has provided synthetic chemists with an efficient tool to access compounds for which conventional syntheses would consist of many tedious steps. Development of new catalysts and optimisation of the conditions have led to the establishment of metathesis methodology in organic chemistry, which finally resulted in the award of the Nobel Prize to Chauvin, Grubbs and Schrock in 2005.

Olefin metathesis (the term is derived from the Greek word *μεταθεσις* with the same pronunciation, which means transposition) is basically an alkylidene exchange between two reacting olefins, mediated by transition metal alkylidene complexes. The mechanism has been correctly explained by Chauvin, who proposed the formation of the metalacyclobutane as the

transition product (Fig. 1).<sup>2</sup> Several types of olefin metathesis have been identified so far, among them ring closing metathesis (RCM) and cross-metathesis (CM) being widely and successfully applied in the synthesis of biologically active complex compounds.

Ring closing metathesis occurs when a diene undergoes intramolecular metathesis, affording a cyclic olefin. On the other hand, when a cyclic olefin is metathesized with another olefin, ring opening metathesis (ROM) takes place. Under certain conditions, cyclic olefins may polymerize, resulting in the formation of an unsaturated polymer, through a process called ring opening metathesis polymerization (ROMP). For acyclic dienes, the oligomerization (which may lead to polymerization as well) is called the ADMET (acyclic diene metathesis) process. Last, but not least, enyne metathesis occurs, when an alkyne and an alkene react to form a 1,3-diene. The same intramolecular reaction of an enyne is sometimes called enyne cycloisomerisation or enyne RCM (Fig. 2).

To date, catalysts **1–4** shown in Fig. 3 have been the most widely used in olefin metathesis. Schrock molybdenum alkylidene **1**,<sup>3</sup> Grubbs 1st (**2**) and 2nd generation (**3**)<sup>4</sup> ruthenium benzylidenes and the phosphine-free Hoveyda–Grubbs complex (**4**)<sup>5</sup> were among the first catalysts commercially available.<sup>6</sup> Molybdenum-based catalysts, developed by

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Paweł Śledź was born in 1985 in Szczecin, Poland. He has just obtained his MSc degree in chemistry, done jointly at the Warsaw University and University of Virginia, performing crystallographic structural studies of proteins under the supervision of Krzysztof Wozniak and Wladek Minor. Before moving to structural biochemistry, he conducted work on olefin metathesis studying new Ru-based catalysts with Karol Grela in 2004–2006. In 2006 as a Summer Undergraduate Research Fellow at the California Institute of Technology (USA) he studied aqueous olefin metathesis with Robert H. Grubbs.

Marc Mauduit was born in Longjumeau, France in 1971. He received his undergraduate training and PhD from the University of Paris XI-Orsay (France) under the guidance of Yves Langlois. In 1999, he carried out postdoctoral studies with Stephen Hanessian at the University of Montréal. In 2001, he moved to Rennes (France) as a Chargé de Recherche (CNRS) at the Ecole Nationale Supérieure de Chimie. His research interests focus on organometallic chemistry, in particular olefin metathesis, conducted in unusual media (ionic liquid and aqueous solvents), and development of new chiral N-heterocyclic carbenes for asymmetric catalysis.

Karol Grela was born in Warsaw, Poland in 1970. He received a PhD degree from the Institute of Organic Chemistry, Polish Academy of Sciences (IChO PAN), in 1998 under supervision of Mieczysław Mąkosza. After postdoctoral research with Alois Fürstner at the Max-Planck-Institut für Kohlenforschung, Mülheim an der Ruhr, Germany, he returned to Warsaw and, after completing Habilitation in 2003, was promoted to Associate Professor at IChO PAN where he leads a small but very efficient research group of dedicated co-workers. His research interests focus on organic and organometallic chemistry.

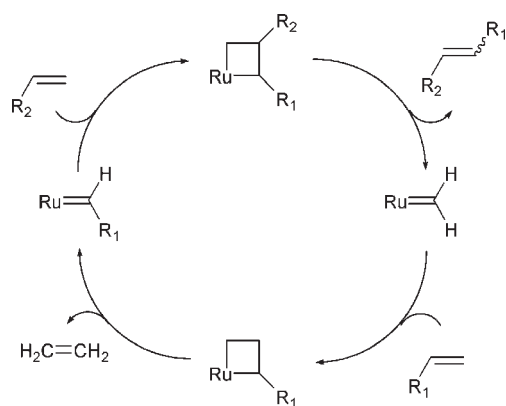


Fig. 1 Metalacyclobutane mechanism proposed by Chauvin.

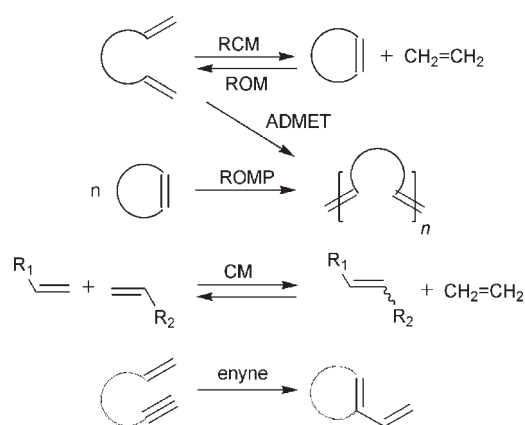


Fig. 2 The most important types of olefin metathesis.

Schrock, are generally more reactive than Ru-based catalysts, but their instability to air and moisture have made them less popular than Ru complexes. Nonetheless, chiral Mo complexes are widely used in enantioselective metathesis.<sup>3</sup>

Importantly, Hoveyda complex **4** can be easily recovered after the reaction. According to the so-called boomerang mechanism<sup>5</sup> (Fig. 4), the propagating 14-electron species **A** and **B**, formed during the initiation step, can re-coordinate to 2-isopropoxystyrene, regenerating the initial pre-catalyst at the end of the reaction. This behaviour could not be observed for Mo-based complexes and phosphine-containing Ru-catalysts **2** and **3**.

With the expansion of the olefin metathesis method to the synthesis of biologically important compounds, problems arose with incomplete catalyst separation, leading to

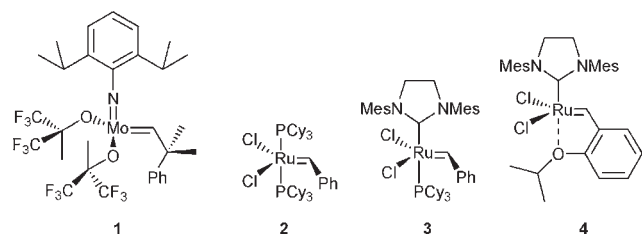


Fig. 3 Commercially available metathesis catalysts (Cy = cyclohexyl, Mes = 2,4,6-trimethylphenyl).

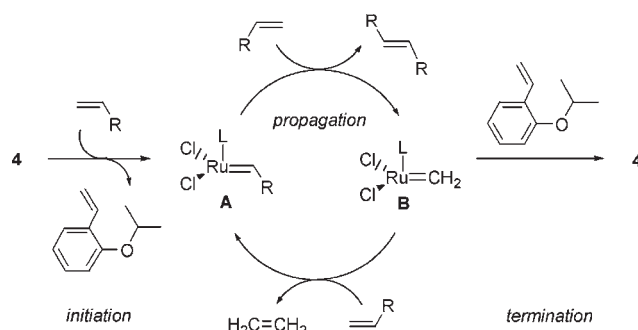


Fig. 4 Self-regeneration of **4** according to the boomerang mechanism.

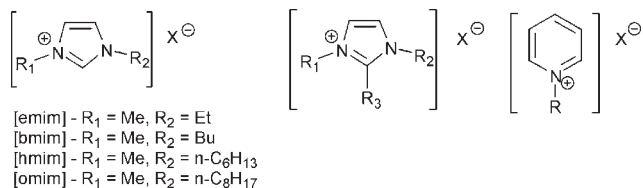
side-reactions and contamination of the product with heavy metals.<sup>7</sup> The acceptable Ru content in pharmaceutically active substances is <10 ppm, while most conventional purification methods, such as silica-gel based chromatography or charcoal-treatment lead to products containing 100–1000 ppm of Ru. Therefore, several methods to decrease the ruthenium level have been developed.<sup>7</sup> Treatment of crude metathesis products with substances like Ph<sub>3</sub>P=O, DMSO or Pb(OAc)<sub>4</sub> followed by column chromatography allowed the obtainment of Ru levels ranging from 200 ppm to 2000 ppm. Various other scavengers have been tested as well.<sup>7</sup> Immobilization of the catalyst on solid supports has been studied as a general solution to the purification and recovery problems.<sup>7</sup> The application of a biphasic system, employing the ionic liquid as a catalyst-carrying solvent is a new and promising concept in olefin metathesis. It is expected that this approach will allow multiple reuse of the homogeneous well-defined catalysts and minimize Ru contamination of product.

## Room temperature ionic liquids

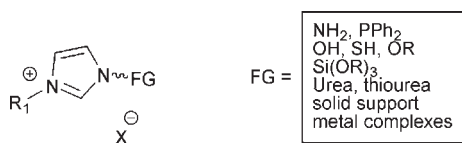
Room temperature ionic liquids (RTILs), especially 1,3-dialkylimidazolium salts, since their first water-stable representative was prepared by Wilkes and Zaworotko in 1992,<sup>8</sup> have been receiving an increasing amount of attention as an innovative media for metal-catalyzed organic reactions. Their interesting features, such as non-flammability, facile recoverability and negligible vapour pressure, make them a “green” and safe<sup>9</sup> alternative for conventional organic solvents.<sup>10</sup> Nevertheless, studies on their toxic effects on humans and the environment are currently in progress and special efforts to develop efficient and biodegradable versions have been made.<sup>11</sup>

The crucial properties of ionic liquids, such as affinity to water and miscibility with other solvents, can be adjusted by the proper choice of alkyl substituents and escorting counterion. Besides 1,3-dialkylimidazolium salts, 1,2,3-trialkylimidazolium and *N*-alkylpyridinium salts are widely used (Fig. 5).

As the development of ionic liquid supported catalysis advanced, the term task specific ionic liquids (TSILs) was introduced into the literature.<sup>12</sup> Various organic and inorganic functionalities can be appended into a molecule of ionic liquid to make it suitable to selectively catalyze desired reactions in the ionic solvent environment (Fig. 6).



**Fig. 5** Most commonly used RTILs. X = BF<sub>4</sub>, PF<sub>6</sub>, CH<sub>3</sub>COO, CF<sub>3</sub>SO<sub>3</sub>, NTF<sub>2</sub> (Tf = CF<sub>3</sub>SO<sub>2</sub>).

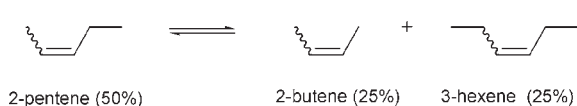


**Fig. 6** TSILs—task specific ionic liquids.

Reactions catalyzed by metal complexes in RTILs are receiving an increasing amount of attention, becoming the most vigorously developing field in IL research.<sup>13</sup> So far, several catalytic systems, including rhodium, vanadium and ruthenium complexes, have been applied to numerous transformations in organic synthesis.<sup>10,12</sup> Basically, three major approaches to the metal-catalyzed reactions in ionic solvents are known. Reactions can be run (i) in pure ionic liquid, (ii) in a biphasic system of ionic liquid and organic solvent or (iii) in organic solvent with a tiny amount of an ionic liquid as the immobilising matrix for a metal complex. The routine procedure for the reaction work-up is phase separation, so the catalyst remains in the ionic solvent and the reaction product is extracted into the organic phase. Development of these methods is expected to give easy access to effective catalyst separation, and is currently under vigorous study.

### Olefin metathesis in RTILs—the early example

The first example in the literature of using ionic solvents in the olefin metathesis reaction was published in 1995 by Chauvin and Olivier-Bourbigou.<sup>14</sup> Using W(OAr)<sub>2</sub>Cl<sub>4</sub> (ArOH = 2,6-diphenylphenol or 2,4,6-trimethylphenol) dissolved in [bmim]Cl–AlCl<sub>3</sub>–EtAlCl<sub>2</sub> ionic liquid, good results in the self-metathesis of 2-pentene were obtained (Fig. 7). Importantly, active species were found to be arrested in the ionic environment, allowing efficient catalyst separation and recycling through a decantation of the hydrocarbon layer. In this way, 1-pentene could be converted into ethylene and 4-octene while the mixture of cyclopentene and 2-pentene afforded the expected telomers.

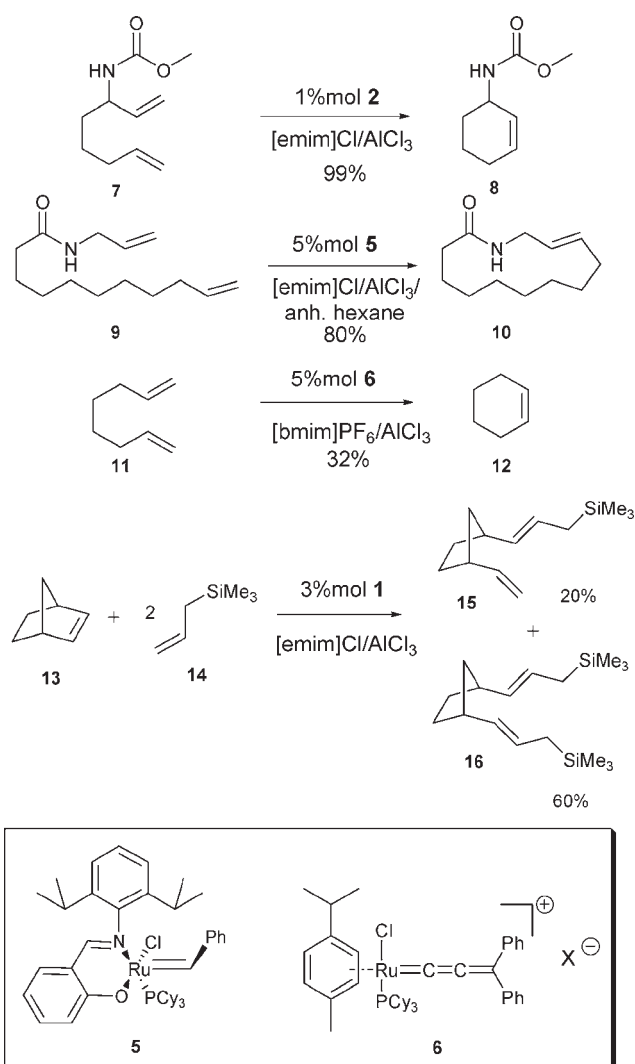


**Fig. 7** First example of olefin metathesis in RTILs developed by Chauvin in 1995.

### Applications of untagged olefin metathesis catalysts

Five years later, the application of catalysts **1**, **2**, the Schiff-base bearing catalyst **5**,<sup>15</sup> and the cationic allenylidene **6** (X = OTf)<sup>16</sup> in imidazole- and pyridine-based ionic liquids mixed with a stoichiometric amount of ammonium chloride was disclosed by Bayer AG. It should be noted that except for **6**, catalysts used in this study are non-charged species, originally designed for application in neutral organic solvents. Catalyst **5**, especially successful in this study, was able to perform the RCM reaction of several dienes both in pure ionic liquids and in a two-phase system composed of anhydrous hexane and an ionic liquid (Fig. 8). For example, RCM of substrate **9** was performed at 40 °C for 14 h, affording the desired product **10** in 80% yield (*E* : *Z* 5 : 1). Interestingly, ruthenium allenylidene salt **6** was moderately effective under these conditions.<sup>17</sup>

This patent is one of only two examples where the sensitive Schrock catalyst **1** was applied in IL. In the other one, recently published by Bowden and Miller, **1** is shown to be effective in RCM and CM reactions, and to exhibit some activity toward



**Fig. 8** Metathesis in ionic liquids reported by Bayer AG.

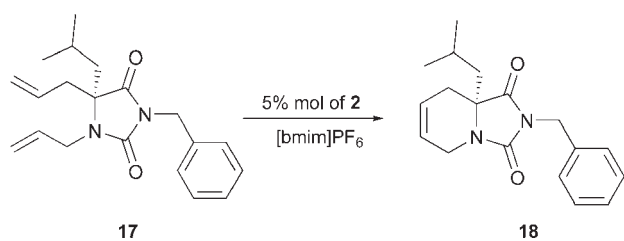


Fig. 9 Bicyclic hydantoin **18** synthesis performed by Buijsman.

uncontrolled ROMP.<sup>18</sup> Moreover, a very interesting approach to product separation, based on extraction in a Soxhlet apparatus equipped with polydimethylsiloxane thimbles, was reported in this paper. Nonetheless, besides these two examples, most of the work with well-defined catalysts in IL have been performed with Ru-based catalysts.

The mechanism of olefin metathesis in ionic liquids does not differ from the aforementioned general mechanism (Fig. 1), although there was an alternative mechanism with ill-defined Mo and W based olefin metathesis catalysts reported in the literature by Kucherov and co-workers.<sup>19</sup> Namely, a reaction catalyzed by  $WCl_6$  species involves a reduction step ( $W^{6+}$  to  $W^{5+}$ ) not observed in the reaction in a conventional solvent, and a reaction with  $MoCl_6$  species leads to the formation of some side-products (isomerisation). These conclusions have been reached after an intensive EPR study.

The work done by Buijsman and co-workers can be considered as the first systematic study on practical synthetic application of ionic liquids as a medium for olefin metathesis.<sup>20</sup> The motivation for this work was to decrease the ruthenium contamination within the product by the immobilization of the Ru species in the ionic liquid phase. The substrate chosen for the study was **17**, which RCM was supposed to afford bicyclic hydantoin **18** (Fig. 9). It was found, that for the reaction catalyzed by Grubbs 1st generation catalyst **2**, [bmim]PF<sub>6</sub> is the optimal solvent, and quantitative conversion could be achieved after only 1 h at 80 °C. However, the catalyst-containing ionic liquid phase could be reused only up to three times with a significant loss of activity in the last cycle. The catalyst was used in the pure ionic liquid, and the products were isolated from the reaction mixture by extraction with diethyl ether.

Buijsman and co-workers have also tested Grubbs 2nd generation catalyst **3** in RTILs. Metathesis of several substrates has been performed (Table 1) and, what is noteworthy, in some cases RCM in ionic liquid gave better results than the reaction in dichloromethane (DCM) under the same conditions. Unfortunately, the catalyst-containing phase could be recycled only 3 times and significant Ru residual contamination within the final product was detected (1300–1600 ppm). It should be pointed out, that all the results presented by Buijsman *et al.* were accompanied by diligent residual Ru content data.

Kiddle and co-workers exceeded the work of Buijsman by applying microwave irradiation to affect RCM reactions.<sup>21</sup> Application of [bmim]BF<sub>4</sub> allowed the achievement of quantitative conversions with Grubbs 2nd generation catalyst **3** after 15 s of irradiation for substrates **19**, **21**, **29** and **30** (Fig. 10). No recovery studies and ruthenium contamination measurements

Table 1 Additional substrates studied by Buijsman. All reactions were carried out at 80 °C

Substrate	Product	Catalyst (mol%), conditions	Conv. (%)
		<b>3</b> (5), 1 h, [bmim]PF <sub>6</sub>	100
		<b>3</b> (5), 1 h, [bmim]PF <sub>6</sub>	100
		<b>3</b> (5), 20 h, [bmim]PF <sub>6</sub>	75
		<b>3</b> (5), 20 h, [bmim]PF <sub>6</sub>	73
		<b>3</b> (5), 1 h, [bmim]PF <sub>6</sub>	75

were performed in this work. The authors suggested that the enhancement in catalyst activity was caused by the non-thermal effects of microwave irradiation (by direct increase in reacting species energy, not through the solvent heating) which was supported by a study performed in dichloromethane (a microwave-transparent solvent). More detailed research was performed by Kappe, Lavastre and co-workers in 2003.<sup>22</sup> Microwave-assisted RCM was investigated in organic solvents like CCl<sub>4</sub> and DCM, both pure and doped with ionic liquids such as [bmim]PF<sub>6</sub>. Although very high conversion (98%) could be achieved for substrate **19** with catalyst **3** in DCM doped with 0.04 M [bmim]PF<sub>6</sub> after only 15 s of irradiation, and the protocol was effective for other substrates in DCM, it was proved that the rate enhancement occurs purely due to the thermal effect.

In 2002, following the pioneer works of Buijsman, Astruc and co-workers attempted the RCM reaction of poly-olefin **31**

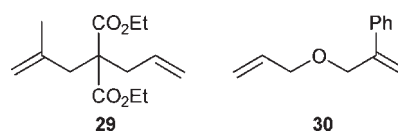
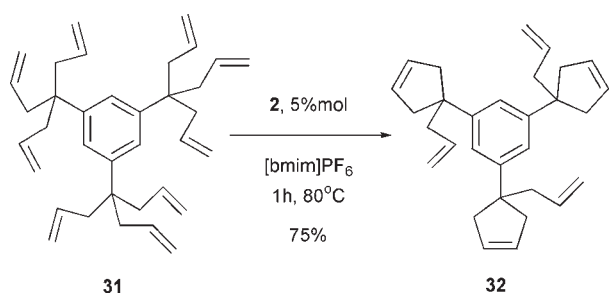


Fig. 10 Representative RCM substrates quantitatively metathesized by Kiddle with **3** in [bmim]BF<sub>4</sub> under microwave irradiation conditions.



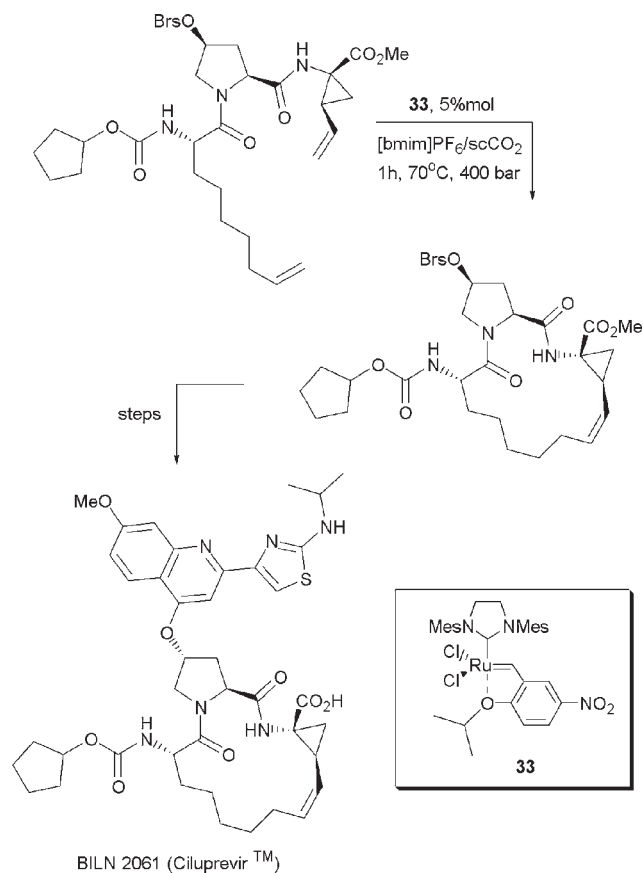
**Fig. 11** Formation of polycyclic cyclopentenylaryl derivative via RCM performed by Astruc using **2** in [bmim]PF<sub>6</sub>.

to form polycyclic cyclopentenylaryl derivative **32** (Fig. 11). The reaction was performed in a [bmim]PF<sub>6</sub> medium at 80 °C giving the desired product in 75% yield after extraction with ether.<sup>23</sup>

Later, in 2006, Williams and co-workers showed the application of selected commercially available catalysts to olefin cross metathesis in ionic liquids.<sup>24</sup> Self-metathesis of 1-octene, which is supposed to afford 7-tetradecene, was studied using several ionic liquids (not only *n*-butyl (bmim), but also methyl, ethyl, *n*-hexyl and *n*-octyl substituted imidazolium salts). Among the catalysts investigated by the authors, the Hoveyda–Grubbs catalyst **4** proved to be the most active and selective, leaving reasonably low Ru contamination within the product in comparison with other catalysts (less than 2% of the catalyst had leached into the organic layer). Various reaction conditions were investigated, including liquid–liquid biphasic systems or using imidazolium salts bearing a halide counterion as an additive. Moreover, careful study of the alkyl chain influence on the catalyst performance in the 1,3-disubstituted and 1,2,3-trisubstituted imidazolium salts was performed. It appeared that alkyl chains of short length usually enhanced catalyst activity, while longer ones inhibited it. Furthermore, for 1,2,3-trialkylimidazolium salts, the influence of the longer chains was not as significant as for 1,3-dialkylimidazolium ones. Optimized reaction protocols led to obtaining very promising results, for example 90% conversion with 98% selectivity in [emim]NTf<sub>2</sub> or 91% conversion with 98% selectivity in [bdmim]NTf<sub>2</sub> (1-butyl-2,3-dimethylimidazolium bis(trifluoromethylsulfonyl)imide). Both reactions were conducted in biphasic IL–substrate mixtures.

An interesting biphasic catalytic system composed of IL and supercritical carbon dioxide (scCO<sub>2</sub>)<sup>25</sup> phases has been recently developed.<sup>26</sup> Ionic liquids were used as an immobilizing matrix for the highly potent nitro catalyst **33**<sup>27</sup> and the metathesis reaction was conducted in supercritical carbon dioxide (Fig. 12). Complex **33** is poorly soluble in [bmim]BF<sub>4</sub>, so more lipophilic IL [bmim]PF<sub>6</sub> was applied. This technology was used *inter alia* for the macrocyclisation of some pharmaceutical precursors, including BILN 2061, a cyclic peptide that has shown anti-hepatitis C virus (HCV) effect in humans (Fig. 12).<sup>26</sup> Catalyst **33** immobilised in IL–scCO<sub>2</sub> can be used in a continuous-flow setup, which makes this protocol especially suitable for industrial applications.<sup>26</sup>

In 2006, Tang and co-workers evaluated the 2nd generation Grubbs catalyst **3** in the self cross-metathesis reaction of styrene derivatives performed in [bmim]PF<sub>6</sub> media.<sup>28</sup> Using



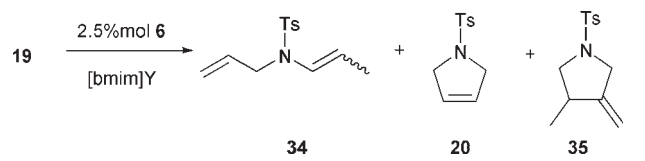
**Fig. 12** Application of the nitro-catalyst **33** in ionic liquid and supercritical carbon dioxide. Brs = SO<sub>2</sub>C<sub>6</sub>H<sub>4</sub>Br.

2.5 to 5 mol% of catalyst loading, the catalytic system in ionic media can be recycled 4 times yielding 43 to 89% of the self-metathesis products. Unfortunately, no measurements of Ru-contamination are given.

### Application of charged catalyst systems

Despite occasional positive results, in general, systems based on non-charged, commercially available catalysts (Fig. 3) exhibit some limitations, namely the catalyst, or its decomposition products, often leach into the organic phase, which results in the gradual loss in activity of the catalyst-containing IL layer. This is a significant problem to overcome. The application of charged catalyst species, in order to improve the immobilization of the catalyst by increasing catalyst affinity to the ionic liquid, was successfully performed in 2002.<sup>29</sup> The charged metathesis catalyst **6** was shown to be efficient in ionic liquids, despite the fact that previous results published in Bayer's patent were not very promising.<sup>17</sup> Dixneuf *et al.* tested **6** in the family of [bmim] ionic liquids, discussing the influence of conditions on the outcome of selected model metathesis reactions (Table 2). It was found, that desired product **20** could be formed selectively in quantitative yield, when both counterions—of the catalyst and IL—were TfO<sup>−</sup>, while the reaction is run at room temperature for 18 h. No residual Ru content examination was performed in this study.

**Table 2** Study of RCM of **19** in ionic liquids with **6** as catalyst. Reactions were run at 80 °C with 2.5% mol of catalyst



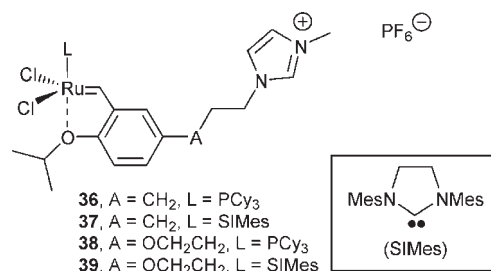
Catalyst counter-ion	Solvent counterion	Time/h	<b>34</b> (%)	<b>20</b> (%)	<b>35</b> (%)	Total conversion (%)
PF <sub>6</sub>	PF <sub>6</sub>	5	2	58	5	65
BF <sub>4</sub>	BF <sub>4</sub>	6	8	37	30	75
TfO	BF <sub>4</sub>	5	6	23	31	60
TfO	PF <sub>6</sub>	5	—	83	2	85
TfO	TfO	2.5	—	97	3	100
TfO	TfO	18 <sup>a</sup>	—	100	—	100

<sup>a</sup> Reaction carried out at room temperature.

It is noteworthy that Dixneuf and co-workers were the first to use an ionic liquid in the biphasic system for a metathesis reaction (2002). Results obtained with catalyst **6** applied in [bmim]BF<sub>4</sub>-toluene were better than those for the reaction conducted in pure ionic solvent—a conversion of 96% was achieved after 5.25 h at 80 °C, while for the reaction conducted in pure [bmim]BF<sub>4</sub> the yield after 5.5 h was only 40%. The allenylidene complex was also tested in ROMP of norbornene, where up to 6 successful catalytic cycles in biphasic toluene-[bdmim]PF<sub>6</sub> mixtures were achieved.<sup>30</sup>

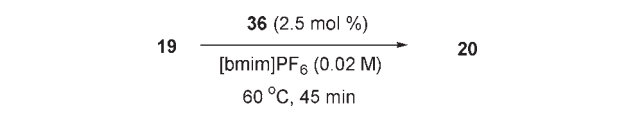
Meanwhile, work on new catalysts that incorporate the structural motif of an imidazolium salt ionic liquid was conducted simultaneously in France and the United States. The attachment of the imidazolium moiety into Hoveyda's 2-isopropoxybenzylidene ligand was chosen in both cases (Fig. 13).

Catalyst **36**, prepared by Mauduit, Guillemin and co-workers, exhibited fairly good activity and excellent recyclability when used in [bmim]PF<sub>6</sub>.<sup>31</sup> In a model RCM reaction of diallyltsylamine **19** (Table 3), Grubbs 1st generation **2** and Hoveyda 2nd generation **4** catalysts, despite similar activity in the first cycle, could not be effectively recycled and gave significantly worse results than **36** in the subsequent cycles. Presumably, it is due to the catalyst leaching into the organic layer during the extraction of the reaction product from the ionic liquid. Mauduit's catalyst **36** was shown to be well immobilized in the ionic liquid [bmim]PF<sub>6</sub>, and no significant loss in catalyst activity was observed even after 10 cycles (Table 3). However, in the



**Fig. 13** First catalysts bearing an imidazolium cation motif.

**Table 3** Recyclability of Mauduit's 1st generation catalyst **36**



Catalyst	Cycle (conversion, %)									
	1	2	3	4	5	6	7	8	9	10
<b>36</b>	>98	>98	>98	>98	>98	96	92	92	92	95
<b>2</b>	>98	20	—	—	—	—	—	—	—	—
<b>4</b>	>98	40	20	—	—	—	—	—	—	—

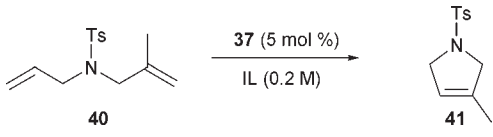
formation of trisubstituted carbon-carbon double bonds and in RCM of some oxygen-containing substrates its recyclability was limited to only three or four cycles.<sup>31</sup>

To improve catalyst stability and performance in the metathesis of these more challenging substrates, the 'second generation IL catalyst' **37** was prepared by Mauduit and co-workers (Fig. 13).<sup>32</sup> Under similar conditions, no significant differences in recyclability could be observed. Nonetheless, quantitative conversion in the formation of trisubstituted double bonds could not be achieved under milder conditions (lower temperature: 40 °C instead of 60 °C), and no recyclability could be performed then. Switching the ionic solvent to a less viscous one (from [bmim]PF<sub>6</sub> to [bmim]NTf<sub>2</sub>) led to an increase in catalyst mobility in the ionic phase, which resulted in an increased reactivity and good recyclability (up to 6 times). However, the increased solubility of toluene—an extracting medium—in [bmim]NTf<sub>2</sub> led to some problems with product separation. The best optimized system effectively to promote metathesis and allow efficient recyclability is biphasic [bmim]PF<sub>6</sub>-toluene at 25 °C. Products containing di-, tri- and in one case even tetrasubstituted C-C double bonds could be formed effectively under such conditions. Moreover, **37** can be recycled at least 8 times, leading to extremely low Ru contamination of products (1 to 22 ppm) even at high catalyst loading (5 mol%), which are the best results in this field so far (Table 4). However, the main disadvantage of this process devoted to reducing Ru-waste is undoubtedly the need to pass the organic extract phase through a plug of silica gel to remove the residual traces of the ionic phase. Indeed, some micro-emulsions can be formed from the toluene-[bmim]PF<sub>6</sub> biphasic system and a decantation process does not allow their complete elimination.

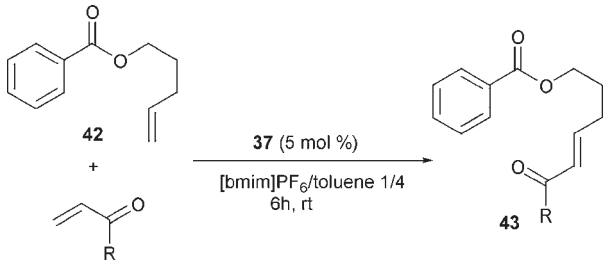
Mauduit and co-workers have also investigated the scope of the new catalyst in challenging cross metathesis reactions of electron-deficient alkenes (Table 4). Reasonably good conversions could be achieved, but the recyclability was significantly lower when compared to the applications in RCM (Table 4). Therefore, while catalyst **37** is able to make many metathesis reactions practical, further progress in the area is necessary.

A very similar approach was independently presented by Yao and Zhang. Their 1st generation catalyst **38** (Fig. 13) showed excellent recyclability, comparable to the performance of the previously discussed Mauduit's catalyst.<sup>33</sup> Complex **38** remained active for ten cycles with only a minor decrease in activity (Table 5) and was shown to be useful for RCM of several dienes, leading to cyclic products containing di- and

**Table 4** Performance of Mauduit's 2nd generation catalyst **37** in RCM and CM reactions



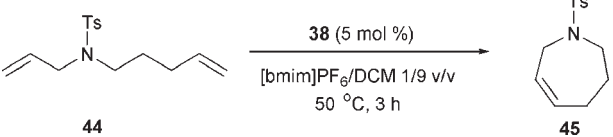
Solvent	Conditions	Cycle (conversion, %)							
		1	2	3	4	5	6	7	8
[bmim]PF <sub>6</sub>	60 °C, 4 h	>98	97	91	68	16	—	—	—
[bmim]PF <sub>6</sub>	40 °C, 4 h	76	—	—	—	—	—	—	—
[bmim]NTf <sub>2</sub>	40 °C, 4 h	>98	97	91	89	74	50	—	—
[bmim]PF <sub>6</sub>	40 °C, 4 h	>98	>98	>98	96	85	63	—	—
toluene 1 : 1									
[bmim]PF <sub>6</sub>	40 °C, 3 h	>98	>98	>98	97	94	93	90	88
toluene 1 : 3									
[bmim]PF <sub>6</sub>	25 °C, 3 h	>98	>98	>98	>98	>98	>98	95	95
toluene 1 : 3									
Ru content (ppm)		16.9	5.4	1.6	3.3	1.2	22	5.7	2.3



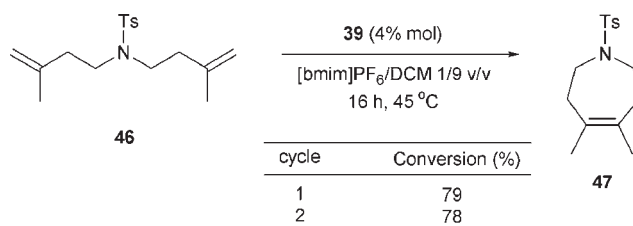
R	Cycle	Isolated yield (%)
Me	1	88
	2	87
	3	35
H	1	92
	2	32

trisubstituted C–C double bonds. The difference between Yao's and Mauduit's biphasic approaches is the use of dichloromethane instead of toluene as a second liquid phase. The second generation Yao's catalyst, **39** (Fig. 13), derived from a similar ligand was shown to be, similarly to analogous Mauduit's catalyst **37**, very active in formation of di- and trisubstituted olefins *via* RCM.<sup>34</sup> Moreover, one example of the formation of a tetrasubstituted double bond in RCM promoted by **39** was also disclosed (Fig. 14). Unfortunately, no Ru residual content study has been performed in this work. As the reaction conditions applied by Mauduit and Yao are slightly different, the direct comparison of the catalysts'

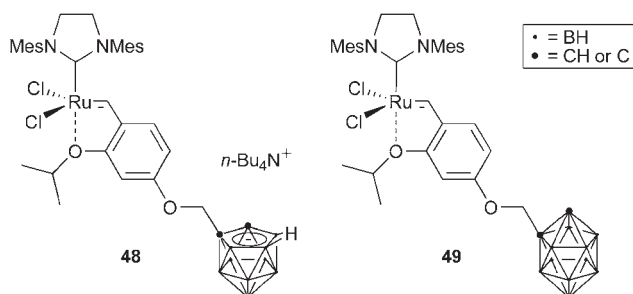
**Table 5** Recyclability of Yao's 1st generation catalyst **38**



Cycle (conversion, %)									
1	2	3	4	5	6	7	8	9	10
>98	>98	97	96	95	94	92	92	91	90



**Fig. 14** A challenging RCM promoted by catalyst **39**.



**Fig. 15** The first anion-tagged Ru-complex **48** and its neutral analogue **49**.

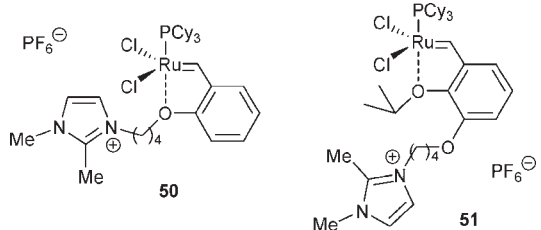
performance cannot be done; however, the application profiles of **37** and **39** seem to be—in general—similar.

An interesting strategy for the attachment of an ionic-tag to the benzylidene fragment of the Hoveyda–Grubbs pre-catalyst has recently been attempted by Wang and co-workers.<sup>35</sup> The anionic tag, [*nido*-7,8-C<sub>2</sub>B<sub>9</sub>H<sub>11</sub>]<sup>−</sup>, was used, leading to robust and recyclable complex **48**, remarkably suitable for the non-covalent immobilization concept (Fig. 15). Although **48** shows slightly reduced activity as compared with **4** and the not-charged *closo*-1,2-carborane analogue **49** it can be recovered in up to ten cycles in the RCM of diallyltsylamine **19** performed in [bmim]PF<sub>6</sub> using 2.5 mol% catalyst loading. It should be noted that neutral **49** is deactivated after only 2 recycles under the same conditions.

Despite the pretty good application profiles exhibited by the above mentioned tagged catalysts **36–39** and **48**, several attempts have been made to obtain catalysts of even higher activity, like the nitro-Hoveyda–Grubbs catalyst **33**,<sup>27</sup> but more compatible with RTILs. Wakamatsu and Blechert have shown that an increase in the steric hindrance at the *ortho* position to the chelating isopropoxy group of Hoveyda–Grubbs complex **4** greatly improves its activity.<sup>36</sup> It is also well known that modification of the chelating alkoxy ligand in **4** can have a pronounced effect on the catalyst activity and stability.<sup>37</sup>

Thus, Dixneuf and co-workers have recently reported two new ionic-tagged catalysts **50** and **51**, designed to perform olefin metathesis in pure [bmim]PF<sub>6</sub> media (Table 6).<sup>38</sup> Unfortunately, both of these new complexes exhibit rather low recyclability. This could be explained by catalyst destabilisation caused either by the replacement of the isopropyl ether fragment with the *n*-alkyl ether chain in **50** (it is known that Hoveyda-type catalysts bearing methyl ether fragment are less stable as compared with **4**)<sup>37</sup> or by the presence of the additional *ortho*-substituent in **51**.<sup>38</sup> These two complexes, as well as the parent Hoveyda–Grubbs catalyst, have been

**Table 6** Catalytic performance and recyclability of catalysts **50** and **51** in RCM



19		20	
catalyst (2.5% mol)			
[bmim]PF <sub>6</sub>			
45 min., rt or 60 °C			
Cycle (conversion, %)			
Catalyst	1	2	3
<b>50</b> <sup>a</sup>	90	85	60
<b>51</b> <sup>b</sup>	89	77	46

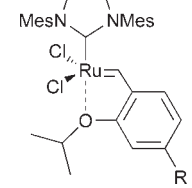
21		22		
catalyst (5% mol)				
[bmim]NTf <sub>2</sub>				
1 h, rt				
Cycle (conversion, %)				
Catalyst	1	2	3	4
<b>50</b>	24	22	22	16
<b>51</b>	53	39	23	8

<sup>a</sup> Reaction at 60 °C. <sup>b</sup> Reaction at room temperature (rt).

recently used in an ethenolysis reaction of methyl oleate producing 1-decene and methyl 9-decenoate, two useful intermediates in the synthesis of lubricants and polyesters.<sup>39</sup> Optimal conditions are reached when reactions are performed in [bdmim]NTf<sub>2</sub> at 20 °C using 5 mol% of catalysts. Whereas 38% conversion is observed with **50**, complex **51** displayed more suitable activity yielding 89% of the desired products without any traces of self-CM by-products. Interestingly, recycling attempts with **51** failed but were more successful with neutral Hoveyda–Grubbs catalysts, where up to 85% was reached after the third cycle of reuse.

It was demonstrated that complex **33** initiates the olefin metathesis dramatically faster than the parent Hoveyda–Grubbs catalyst **4**. The authors proposed that the electron-withdrawing (EWG) nitro group in the benzylidene fragment of **33** weakens the O→Ru chelation and facilitates initiation of the catalytic cycle.<sup>40</sup> In accordance with this assumption, complex **52**,<sup>41</sup> bearing the electron-donating (EDG) diethylamino group shows no activity in olefin metathesis in CH<sub>2</sub>Cl<sub>2</sub>, while its EWG-derivative, **53** is of high activity.<sup>42,43</sup> The screening of catalysts **52–54** in RTILs was performed as a joint project of Mauduit's and Grela's groups.<sup>44</sup> Although the activity was good in the first run, recyclability was poor and a significant loss in activity was observed even after the first cycle (Table 7). The surprisingly high activity of **52** in [bmim]PF<sub>6</sub> remains unclear at present.

**Table 7** Amino- and ammonium-tagged catalysts tested in RTILs



Catalyst	R
<b>52</b>	NEt <sub>2</sub>
<b>53</b>	NEt <sub>2</sub> Me <sup>+</sup> PF <sub>6</sub> <sup>-</sup>
<b>54</b>	NEt <sub>2</sub> Me <sup>+</sup> I <sup>-</sup>

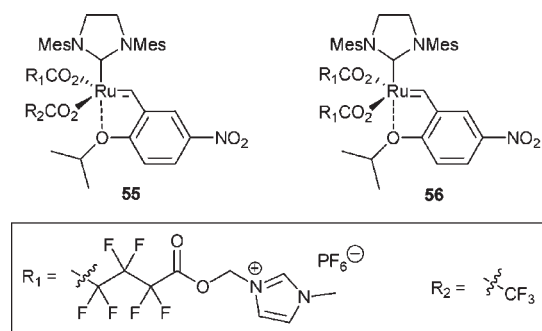
Catalyst	Cycle (conversion, %)		
	1	2	3
<b>52</b>	98	38	< 1
<b>53</b>	90	53	< 1
<b>54</b>	98	33	2

Reaction conditions: **40** → **41**, catalyst 2.5 mol%, [bmim]PF<sub>6</sub>/toluene 1/4 v/v

To improve the solubility of nitro-catalyst **33** in [bmim]BF<sub>4</sub>, two IL-tagged derivatives were designed (Fig. 16).<sup>26</sup> Since the IL-pendant in **55** and **56** is attached directly to the Ru centre instead of the dissociating benzylidene ligand (*cf.* the boomerang mechanism, Fig. 4), perfect recoverability should therefore be expected. Unfortunately, no following reports on the catalytic activity and reusability of these new complexes are known.

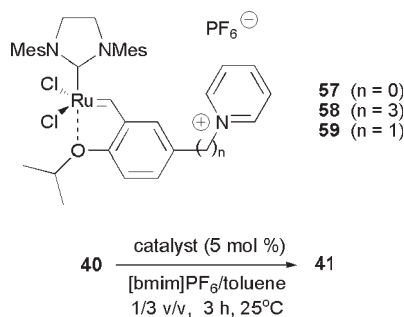
A new family of ionic liquid tagged metathesis catalysts bearing a pyridinium cation has been reported jointly by Grela, Mauduit and co-workers.<sup>45</sup> Catalysts **57–59** were tested both in imidazolium- and pyridinium-based ionic liquids. Activated pyridinium catalyst **57**, while being the fastest IL-tagged metathesis catalyst so far,<sup>44</sup> could not be recovered well (Table 8). Non-activated pyridinium catalyst **58** could be recovered much more efficiently than activated catalyst **57**.<sup>44,45</sup> This is probably due to the aforementioned electronic destabilization—reanchoring of the propagating 14-electron Ru species **A**, **B** (Fig. 4) to the weaker coordinating EWG-substituted styrene of **57** is handicapped in this case, which may result in the migration of Ru into the organic layer. As was concluded by the authors, unfortunately, the desired increased activity of **57** is counter-balanced by a diminished reusability of this complex in RTILs.

Clearly, the best compromise is to be found between these antinomic properties. Recently, it was reported by the same

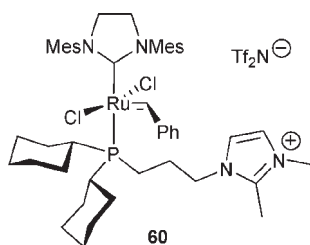


**Fig. 16** Ionic-tagged versions of Grela's nitro-catalyst **33**.



**Table 8** Pyridinium-tagged catalysts' performance in RCM of **40**

Catalyst	Cycle (conversion, %)					
	1	2	3	4	5	6
<b>57</b>	>98	95	65	5	—	—
<b>58</b>	>98	>98	>98	>98	>98	>98
<b>59</b>	>98	>98	>98	>98	>98	>98

**Fig. 17** Ionophilic phosphine-based Ru-complex **60**.

team that catalyst **59**, employing a methylene “spacer” between the benzylidene and pyridinium cation, exhibits increased activity but not diminished recyclability.<sup>44</sup> Obviously, a balance of the antinomic properties—activity and recyclability—can be reached by carefully adjusting the length of the hydrocarbon linker between the activating EWG-tag and the benzylidene moiety. It is expected that this observation will lead to the design of a new generation of catalysts of even better application profiles in RTILs.

The majority of the above described tagged catalysts are based on the Hoveyda–Grubbs catalyst **4** parent structure; however, different approaches have also been taken. In 2008, Consorti, Dupont and co-workers synthesized an ionophilic phosphine-based Ru-complex **60** (Fig. 17).<sup>46</sup> The attachment of the imidazolium tag onto the phosphine entity allows efficient recovery of the metathesis complex in [bmim]PF<sub>6</sub>–toluene biphasic media, up to 8 cycles in the RCM of 1,7-octadiene. Very low levels of ruthenium by-products in the toluene phase are detected after each recycling (down to 2 ppm when 0.25 mol% of catalyst is loaded). Nevertheless, in the case of tetrasubstituted alkene formation, the ionic-tagged complex showed lower activity, yielding only 10% of the product.

## Conclusions

In summary, the recent years have witnessed a rapid yet rational evolution of the olefin metathesis catalysts suitable

for use in ionic liquids.<sup>47</sup> From the first timid attempts to apply existing catalysts in ionic media new methods were developed. Subsequently, as the need for more efficient catalysts arose, complexes bearing structural motifs that mimic ionic liquids have been prepared. Recent developments have provided synthetic chemists with access to effective and clean processes, which, along with efficient catalyst recyclability, promises a great future for the “green” metathesis in ionic liquids both in scientific research, and in industrial or pharmaceutical applications.

## Acknowledgements

KG thanks the Foundation of Polish Science for the “Mistrz” professorship. Research support by the Institute of Organic Chemistry PAN (internship to PS) is gratefully acknowledged. MM thanks the CNRS, The French Ministry of the Research and the National Agency of the Research (RDR-2 Program) for their financial support.

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