Pergamon

Tetrahedron Letters 40 (1999) 4787–4790

TETRAHEDRON
LETTERS

Ruthenium Carbene Complexes with Imidazolin-2-ylidene Ligands Allow the Formation of Tetrasubstituted Cycloalkenes by RCM

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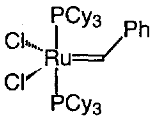
Received 24 March 1999; accepted 6 May 1999

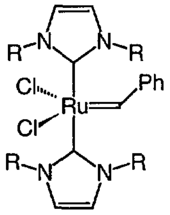
Abstract: Chemically quite robust ruthenium carbene complexes **2-8** bearing one or two imidazolin-2-ylidene ligands are highly active catalysts for all types of ring closing metathesis reactions (RCM). Importantly, they even allow the formation of tetrasubstituted alkenes that were previously out of reach of ruthenium-based metathesis catalysts. © 1999 Elsevier Science Ltd. All rights reserved.

Key Words: Alkenes, Carbenes, Imidazolin-2-ylidenes, Metathesis, Ruthenium

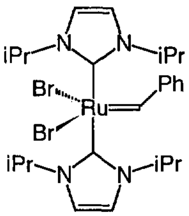
The discovery of Grubbs et al. that the ruthenium carbene complex **1** constitutes a highly efficient metathesis pre-catalyst tolerating most functional groups has triggered an avalanche of interest in this specific transformation.[1,2] As a consequence, many investigations have been reported which aim at gaining facile access to this exceedingly useful reagent,[3] at finding equipotent alternatives,[4] and at improving its application profile even further.[5] In this context it has been proposed to replace one or both of the PCy_3 ligands in **1** by imidazolin-2-ylidenes which are easily accessible and known to be more Lewis-basic than PCy_3, and which may allow a fine tuning of the reactivity pattern by systematic variations of the R groups.[6,7] Preliminary data show that this is indeed possible.[6] Prompted by a recent publication of Grubbs et al. describing the favorable features of one member of this new series in ring closing metathesis (RCM) reactions,[8] we now disclose a more comprehensive and comparative investigation in this field.



1



2 R = Cy
3 R = i-Pr
4 R = CHMePh
5 R = CHMe(Naphthyl)



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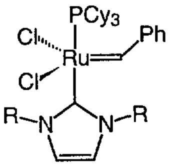
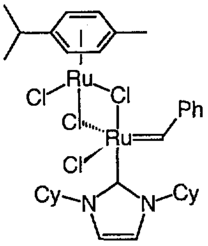


7 R = CHMePh



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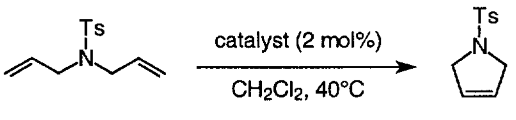
Complexes **2-8** have been obtained according to the general procedure outlined previously.[6] All of them were found to catalyze the conversion of diene **9** into dihydropyrrole **10**, although significant differences in

PII: S0040-4039(99)00919-3

their behavior have been noticed (Table 1). Thus, compounds **4** and **5** bearing benzylic residues on the N-heterocyclic carbene ligands exhibit the lowest activity, whereas little difference was noticed between complexes **2** (R = Cy) and **3** (R = i-Pr); both of them result in essentially quantitative conversion after 24 h at 40°C. This result is in contrast to the behavior of the parent catalyst **1**, in which replacement of PCy_3 by $P(i\text{-}Pr)_3$ results in a noticeable loss of catalytic performance.[9]

Table 1. Screening of Different Ruthenium Carbene Complexes Containing Imidazolin-2-ylidene Ligands.



9 **10**

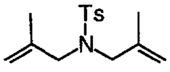
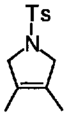
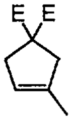
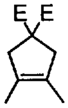
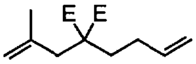
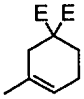
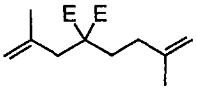
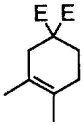
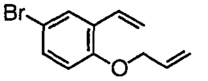
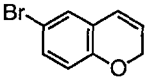
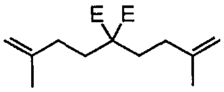
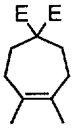
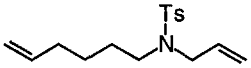
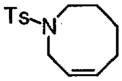
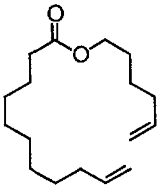
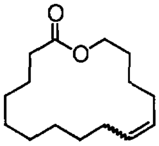
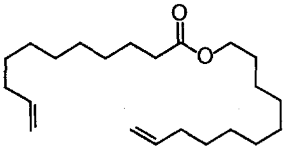
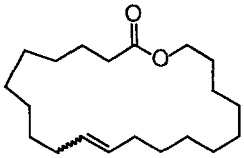
t (h)	2	3	4	5	6	7	8
	Conversion (GC %)						
2.5	80		16	70	77	93	93
5	82	44	17	70	79	95	95
24	93	90	21	71	89	95	95

A characteristic feature of the present class of metathesis catalysts relates to the fact that complexes **7** and **8** bearing only *one* N-heterocyclic carbene entity were found to be significantly more active than those which incorporate two of them. This observation is mechanistically reassuring, since the mixed ligand sphere allows them to populate the dissociative pathway[10] of RCM reactions more easily: because the dissociation of the phosphine from the ruthenium center is more facile than that of an imidazolin-2-ylidene, a higher concentration of an electronically and coordinatively unsaturated species thought to be responsible for productive RCM will form if **7** is used instead of **2** as the pre-catalyst. The same argument holds true for **8**, in which the chloride bridged cymene(ruthenium) template is prone to decoordination and thereby opens the required vacant site on the active species in solution.[11]

Another noteworthy result is the comparison of **3** and its dibromo analogue **6**, which were found to be essentially equipotent catalysts. This reactivity pattern is in sharp contrast to that of the parent system **1**, in which the performance drops significantly if the chloride ligands are replaced by bromide or iodide.[9] A detailed mechanistic interpretation of this finding has to await further studies.

From the preparative viewpoint, complexes **2-8** constitute valuable tools for any kind of RCM reaction. As can be seen from the results compiled in Table 2, they effect the smooth cyclization of a representative panel of diene substrates to the corresponding cycloalkenes independent of the ring size formed; this includes macrocyclic products such as the commercially relevant perfume ingredient Exaltolid® (entries 14-16).[12] Their compatibility with functional groups seems to be essentially identical to that of complex **1**. A rather unexpected yet very useful feature, however, is their ***excellent performance in the formation of tri- and even of tetra-substituted cycloalkene products***. The latter cannot be formed with **1**[13] and have therefore been a domain of the more active but also significantly more sensitive Schrock alkylidene catalyst $Mo(=NAr)(=CHCMe_2Ph)[OCMe_2(CF_3)_2]$ (**11**).[14] In view of the good accessibility and excellent stability of **2-8** even against air and moisture, they constitute a valuable alternative to **11** and will almost certainly find many applications in advanced organic synthesis.

Table 2. RCM Reactions Catalyzed by Ruthenium-Carbene Complexes Containing Imidazolin-2-ylidene Ligands (conditions: CH_2Cl_2 at 40°C); E = COOMe.

Entry	Substrate	Product	Catalyst (mol%)	t (h)	Yield (%)
1			**7** (5%)	16	80
2			**8** (5%)	16	63
3			**7** (2%)	2.5	91 [a]
4			**8** (2%)	3	81 [a]
5			**7** (5%)	24	64 [a]
6			**8** (2%)	16	95
7			**7** (5%)	14	96
8			**8** (5%)	14	88
9			**8** (2%)	3	93 [a]
10			**7** (5%)	13	83
11			**8** (5%)	13	65
12			**7** (2%)	15	69
13			**8** (4%)	22	52
14			**2** (4%)	55	81 [a,b]
15			**7** (2%)	19	72 [b]
16			**8** (4%)	55	88 [a,b]
17			**2** (4%)	20	73 [a,c]
18			**7** (4%)	38	76 [c]
19			**8** (4%)	24	80 [a,c]

[a] GC-Yield. [b] *E*:*Z* = 3.2 (± 0.1) : 1. [c] *E*:*Z* = 2.4 (± 0.1) : 1.

Acknowledgement. Generous financial support by the Fonds der Chemischen Industrie (stipends to L. A. and T. W.), the Deutsche Forschungsgemeinschaft (Leibniz program), and the Bayerischen Forschungsstiftung (FORKAT program) are acknowledged with gratitude.

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