A most user-friendly protocol for ring closing metathesis reactions

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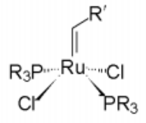
Ring closing metathesis reactions (RCM) can be conveniently achieved in a photo-assisted manner simply by heating a solution of the diene substrate, catalytic amounts of commercially available [(*p*-cymene)RuCl$_2$]$_2$ 4 and PCy$_3$ in CH$_2$Cl$_2$ under neon light.

The advent of well-defined ruthenium-based metathesis pre-catalysts has triggered an explosive growth of interest in this transformation in both the organic and polymer chemists' communities.[1] Among them, the ruthenium carbene complexes **1** (R' = Ph, CH=CPh$_2$) developed by Grubbs *et al.* set the standards in the field.[2] These reagents turned out to be very efficient and highly tolerant pre-catalysts for all kinds of metathesis reactions and have therefore found numerous applications in the synthesis of complex target molecules and the preparation of speciality polymers.[1,3]

Although the rapidly increasing demand has led to the development of considerably improved methods for the preparation of **1**,[4,5] the recent literature also documents a search for alternative metathesis initiators of comparable performance and improved accessibility. In this context, we have introduced the cationic, 18-electron ruthenium allenylidene species **2** as a versatile pre-catalyst for various ring closing metathesis (RCM) reactions.[6] This compound is easily prepared by cleaving the chloride bridges of commercially available [(*p*-cymene)RuCl$_2$]$_2$ **4** with PCy$_3$, followed by treatment of the resulting monomer **3** with 1,1-diphenylprop-2-ynyl alcohol in the presence of NaPF$_6$. Other groups have reported alternative methods for activating compound **3**: thus, Noels *et al.* found that this complex converts into an efficient catalyst for ring opening metathesis polymeri-



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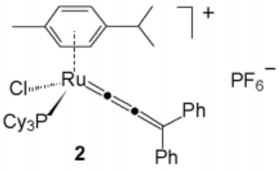

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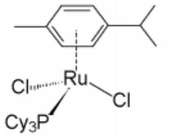
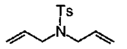
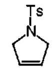
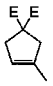
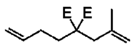
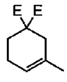
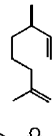
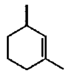
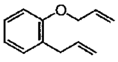
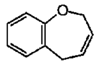
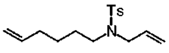
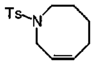
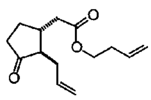
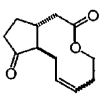
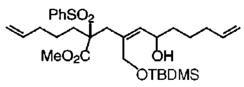
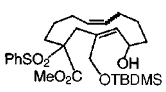
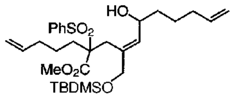
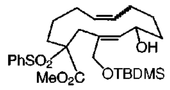
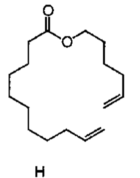
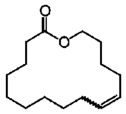
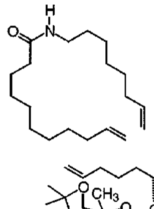
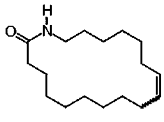
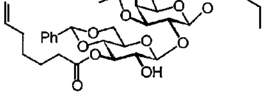
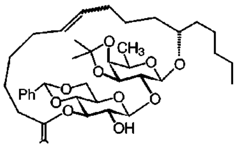
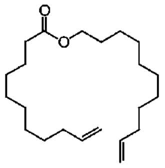
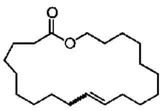


3

[(*p*-cymene)RuCl$_2$]$_2$

4

Table 1 Neon light driven RCM using [(*p*-cymene)RuCl$_2$]$_2$ **4** (2.5 mol%) + PCy$_3$ (5.5 mol%) in CH$_2$Cl$_2$ as an *in situ* catalyst mixture

Entry	Substrate	Product	Yield (%)	Ref.
1			90	6
2			$90^{a,b}$	
3	 E = CO$_2$Me		86	12
4	 E = CO$_2$Me		87	12
5			82^{b}	
6			78	
7			77	6
8			65^{c}	13
9			68^{d}	14
10			70^{c}	14
11			80	15
12			75	15
13			70^{c}	16
14			72	15

[a] Using (*p*-cymene)Ru(PCy$_3$)Cl$_2$ **3** (2.5 mol%) as the pre-catalyst instead of the *in situ* mixture. [b] GC yield. [c] Using [(*p*-cymene)RuCl$_2$]$_2$ (5 mol%) + PCy$_3$ (11 mol%). [d] Using [(*p*-cymene)RuCl$_2$]$_2$ (15 mol%) + PCy$_3$ (30 mol%).

zations (ROMP) upon treatment with diazo alkanes,[7] whereas Hafner *et al*. initiated ROMP reactions with **3** after exposure to UV light (200 W Hg lamp).[8] These latter procedures, however, either require hazardous additives or special photochemical equipment and have not yet been applied to RCM.

We now report an even more convenient method for the activation of this key compound. Thus, heating a solution of a diene in the presence of catalytic amounts of **3** or, preferably, a mixture of commercially available [(*p*-cymene)RuCl$_2$]$_2$ **4** and PCy$_3$ effects a clean and very efficient cyclization of the substrate, provided that the reactions are exposed to neon light or strong daylight.† Several aspects of this method are noteworthy:

(i) Light emitted by neon tubes commonly used for the lighting of laboratories is sufficient.

(ii) The reactions are performed in standard laboratory glassware (DURAN®) which absorbs 50% of UV light with λ = 300 nm and more than 95% of UV light with $\lambda \leqslant$ 285 nm.[9]

(iii) Control experiments carried out in the dark clearly prove the photochemical effect on the rate of reaction.[10]

(iv) Refluxing CH_2Cl_2 turned out to be the best solvent.[11]

(v) Under these photo-assisted conditions, the reactions proceed very cleanly and reproducibly and neither activation by hazardous diazo alkanes nor any special photochemical devices or equipment is necessary.

(vi) Although the rate of reaction is slower than that observed with Grubbs carbenes, the isolated yields are good to excellent and comparable to those obtained with **1** in all RCM experiments carried out so far. Note that a slow initiation is a disadvantage in polymerization reactions, whereas it is of minor importance for RCM.

(vii) As can be seen from the examples compiled in Table 1, this new procedure tolerates a wide range of functional groups in the substrates, including esters, amides, ketones, ethers, silyl ethers, acetals, glycosides, sulfones, sulfonamides, and even unprotected secondary hydroxy groups.

(viii) This new procedure applies to all ring sizes including medium-sized and macrocyclic ones. Furthermore it allows the preparation of even trisubstituted olefins in the five- and six-membered ring series as shown in entries 3–5 of Table 1.[12]

Finally—and most importantly—we would like to stress that this new protocol is distinguished by a hitherto unrivaled ‘low tech’ nature. It requires only commercially available reagents, avoids the (multi-step) preparation of peculiar complexes as well as the use of hazardous additives and needs no special equipment whatsoever; importantly, however, its efficiency and scope favorably compare with all current alternatives described in the literature. Therefore we believe that this extremely simple, yet highly productive methodology may help to increase the popularity of RCM even further and should find many applications in advanced organic synthesis.

Studies to elucidate the mechanism of the photochemical activation step on a molecular level are underway and will be reported in due course.

Notes and references

† *Representative procedure*: A solution of *N*,*N*-bis(allyl)toluene-*p*-sulfonamide (1.00 g, 3.99 mmol), [(*p*-cymene)RuCl$_2$]$_2$ **4** (61 mg, 0.1 mmol) and PCy$_3$ (62 mg, 0.22 mmol) in CH_2Cl_2 (40 ml) was refluxed under Ar for 16 h in a well-illuminated hood. The solvent was removed *in vacuo* and the residue was purified by flash chromatography on silica using hexane–EtOAc (10:1) as eluent. This affords *N*-tosyl-2,5-dihydro-1*H*-pyrrole as colorless crystals (799 mg, 90%), mp 123-124 °C; δ_H(300 MHz, $CDCl_3$) 7.70 (d, *J* 8, 2H), 7.29 (d, *J* 8, 2H), 5.63 (s, 2H), 4.10 (s, 4H), 2.41 (s, 3H); δ_C(75 MHz, $CDCl_3$) 143.8, 134.7, 130.1, 127.8, 125.8, 55.2, 21.9; *m/z* 223 (35, [M$^+$]), 155 (32), 91 (77), 68 (100), 41 (24).

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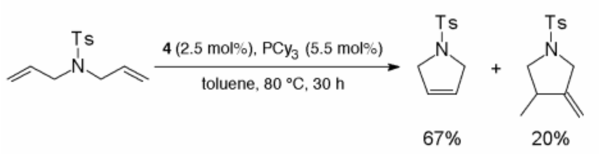
8 A. Hafner, A. Mühlebach and P. A. van der Schaaf, *Angew. Chem*., 1997, **109**, 2213.

9 Constant irradiation of the reaction mixture with a UV emitting quartz lamp dipped into the solution at room temperature is inappropriate, leaving 98% of the substrate unchanged after 16 h reaction time.

10 Reaction of *N*,*N*-bis(allyl)toluene-*p*-sulfonamide in refluxing CH_2Cl_2 with **4** (2.5 mol%) and PCy$_3$ (5.5 mol%) in the dark shows that 92% of the substrate (GC) is unchanged after 16 h. Note that after this period of time, the photoassisted reaction is quantitative.†

11 RCM can also be carried out in toluene at 80 °C; in this medium, however, the reactions tend to be less selective as shown by the following prototype experiment:



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