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Selective ring opening cross metathesis of cyclopropenone ketal: a one step synthesis of protected divinyl ketones

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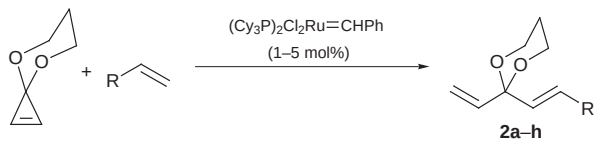
Grubbs ruthenium complex efficiently catalyses ring opening cross metathesis of cyclopropenone ketal and terminal olefins to afford 1,4-divinyl ketone ketals in good yields.

Since the Grubbs and Schrock groups described new alkenylidene-ruthenium and -molybdenum catalysts, olefin metathesis has attracted increasing attention.[1] The ring closing metathesis (RCM) reaction using these catalysts has in particular been studied, and syntheses of numerous cyclic structures (from five-membered rings to larger rings) have been reported.[2] In addition, ring opening metathesis of cyclic olefins has been widely used for the realisation of 'living' polymerisation.[3] Recently, the combination of ring opening metathesis (ROM) and selective cross coupling between strained bicyclic olefins and monosubstituted olefins[4,5] has shown another aspect of this powerful reaction which adheres to the 'atom economy' concept.[6] This was cleverly exemplified by Snapper in a very short synthesis of viridiene from bicyclo[3.2.0]heptadiene and butadiene.[4] So far, an identical process starting from cyclopropenes has not been reported, probably because of the steric hindrance of the substituents on the cyclopropenyl ring.[7,8]

In connection with our ongoing interest in the Nazarov cyclisation reaction,[9] an easy access to substituted divinyl ketones was desirable. Considering ring opening cross metathesis promotes selective reaction, we initiated studies on the synthesis of divinyl ketals from cyclopropenone ketals and terminal olefins (Scheme 1).

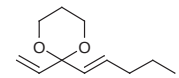
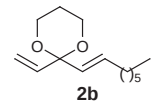
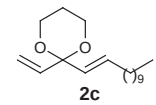
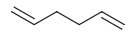
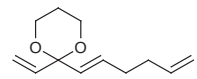
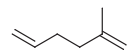
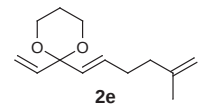
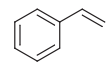
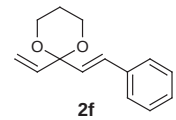
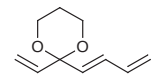
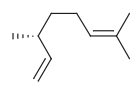
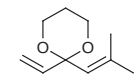
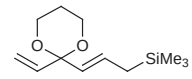
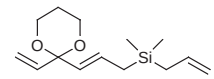
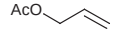
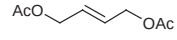
Following observations of the high reactivity of allylsilanes,[5,10] we initially employed 3 equiv. of allyltrimethylsilane and cyclopropenone propane-1,3-diyl ketal **1**[11] with 1% of Grubbs catalyst [$Cl_2(Cy_3P)_2Ru{=}CHPh$] (≡ [Ru]). The reaction was completed in less than 15 min and led only to the monomeric ring opening cross metathesis product **2i**† in 86% yield. Other possible cross metathesis or self metathesis by-products were not detected. A subsequent attempt was run with an equimolar ratio of the starting products, which provided an identical yield and selectivity for the *E* configuration of the created double bond (*E*:*Z* = 95:5). Moreover, we found that 0.04 mol% of catalyst was sufficient to complete this reaction in 2 h (Scheme 1).

In order to determine the scope and limitations of the reaction, other terminal olefins were reacted under similar conditions. The results are shown in Table 1.‡ With non-functionalized terminal olefins, optimal yields were obtained when benzene was used as solvent. High *E* selectivities were observed in all cases. The reaction was found to be extremely dependant on the substitution on carbon atoms 2 or 3 of the terminal olefins. For example, the reaction between 2-methylhexa-1,5-diene (Table 1, entry 5) and **1** occurred regioselectively on the monosubstituted olefin. On the other hand, methallyltrimethylsilane, 3,3-dimethylbutene or vinyltri-

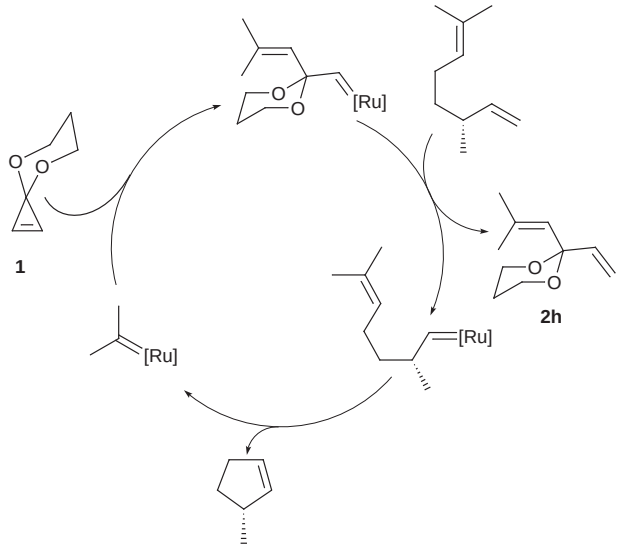


Scheme 1

Table 1 Ring opening cross metathesis of **1** with various olefins

Entry	Alkene	*T*/°C	*t*/h	Product	Yield (%) (*E*:*Z*)
1		room temp.	2	 **2a**	83 (87:13)
2		80	0.5	 **2b**	79 (86:14)
3		80	2	 **2c**	69 (82:18)
4		80	3	 **2d**	32 (86:14)
5		80	2	 **2e**	76 (85:15)
6		80	5	 **2f**	86 (96:4)
7[a]		0	2	 **2g**	28 (80:20)
8		80	5	 **2h**	52
9		room temp.	0.12	 **2i**	86 (95:5)
10		room temp.	3	 **2j**	52 (95:5)
11[b]		room temp.	1.5		78

[a] Obtained as a separable 30:70 mixture of **2g** and the Diels–Alder adduct derived from **1** and butadiene (norcar-3-en-7-one propane-1,3-diyl ketal). [b] **1** was recovered after work-up.

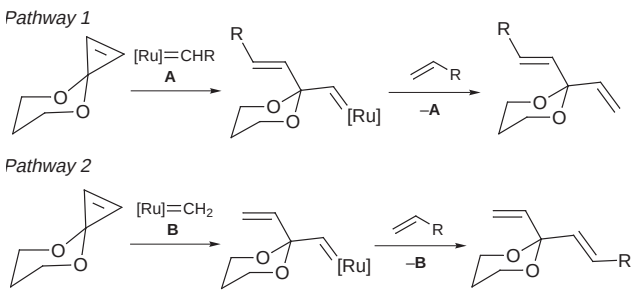


Scheme 2

methylsilane did not give metathesis products. The reaction was also found to be sensitive to electronic effects. With allyl acetate (Table 1, entry 11), no ring opening cross olefin metathesis product was detected. Only the self metathesis reaction took place, affording 1,4-diacetoxybut-2-ene.

In order to introduce a chiral center, we investigated reaction between **1** and the inexpensive (*R*)-citronellene (Table 1, entry 8). Unfortunately, the expected triene was not obtained and, instead, the reaction afforded **2h** (in 52% yield) and 3-methylcyclopentene. To explain this result, which contrasts with the others, we believe that product **2h** is obtained *via* a cascade reaction involving a ring opening cross metathesis[12] associated with a ring closing metathesis (Scheme 2). The above sequence overcomes the limitation imposed by the substitution of olefins and therefore, other 1,6-dienes could be use to introduce a disubstituted alkenyl fragment.

To better understand the reaction mechanism, stoichiometric ROM was performed in $CDCl_3$ at room temperature and examined by ^1H NMR spectroscopy. This experiment showed that cyclopropenone ketal **1** does not react with Grubbs catalyst. As a consequence, an olefin must be present to promote the metathesis reaction. This was illustrated by the reaction performed with styrene (Table 1, entry 6) where the structure of the active species is similar to that of the initial catalyst. Two credible reaction sequences could summarise the catalytic activity.[5,13] Pathway 1 (Scheme 3) utilises substituted alkylidene complex **A**, while the methylene complex **B** displays metathesis activity in pathway 2. A reaction performed with citronellene distinguished between the two mechanistic hypotheses, as the formation of divinyl ketal **2h** as the unique product strongly supports pathway 1. Moreover, we believe that the active catalytic species exhibits a structure different to the starting catalyst. According to the Chauvin mechanism[14] (formation of a metallacyclobutane followed by a cycloreversion process) and following the rational studies of Grubbs,[15] steric reasons could thus largely explain the *E* selectivity.



Scheme 3

In conclusion, under Grubbs ruthenium complex catalysis, cyclopropenone ketal reacts with terminal olefins *via* a ring opening cross metathesis reaction to provide selectively protected 1,4-divinyl ketones with a preferential *E* configuration. Studies to extend this reaction to other cyclopropene structures are currently underway and will be reported in due course.

Notes and references

† *Selected data* for *E*-**2i**: δ_H(200 MHz, $CDCl_3$) 5.78 (1H, dt, *J* 17.6, 7.8), 5,75 (1H, dd, *J* 17.6, 10.7), 5.34 (1H, dd, *J* 17.6, 1.9), 5.21 (1H, dd, *J* 17.6, 2), 5.20 (1H, dd, *J* 10.7, 2), 3.90 (4H, m), 1.70 (2H, m), 1.55 (2H, dd, *J* 7.8, 1.9), 0.01 (9H, s); δ_C(50.3 MHz, $CDCl_3$) 139.5, 131.2, 128.1, 115.9, 98.9, 61.1(2C), 26.0, 23.0, −1.7 (3C)

‡ General procedure for the ring opening cross metathesis summarised in Table 1: To a degassed solution of catalyst $Cl_2(Cy_3P)_2Ru$=CHPh (37 mg, 5 mol%) in anhydrous benzene (5 ml) was added a mixture of cyclopropenone ketal **1** (0.1g, 0.9 mmol) and olefin (1.05 mmol) in solution of benzene (3 ml). Then the red solution was heated to reflux. The reaction was checked by GC. After conversion was complete, the solvent was removed under vacuum. The crude product was purified by column chromatography (silica gel deactivated with Et_3N; light petroleum–Et_2O = 9:1). All new compounds were fully characterised spectroscopically.

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