

Cross-metathesis of 1,3-dienes with electron-deficient olefins

Purnama Dewi, Stefan Randl and Siegfried Blechert*

Technische Universität Berlin, Institut für Chemie, Strasse des 17. Juni 135, D-10623 Berlin, Germany

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Abstract—Cross-metathesis reactions between 1,3-dienes and electron-deficient olefins have been investigated. Terminal monosubstituted 1,3-dienes afforded low yields of the desired CM products due to competing cleavage of the internal double bond. This undesired cleavage is successfully suppressed in the case of 1,3-dienes containing a sterically more congested internal double bond. Methyl vinyl ketone as the coupling partner was shown to provide the best yields.

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In the last decade, olefin metathesis has emerged as a powerful tool for C–C-bond formation.¹ Especially in the last few years, cross-metathesis reactions (CM) have been thoroughly examined and a variety of selective cross-coupling reactions have been described.² Although the potential of ring-closing metathesis (RCM) reactions between 1,3-dienes and unconjugated olefins has been recognized for some time and reactions of this type have been successfully employed in the synthesis of complex natural products,³ CM reactions involving 1,3-dienes have been investigated and applied surprisingly scarcely.⁴ Only recently, Snapper et al. have described cross-coupling reactions between substituted butadienes and electron-neutral olefins.^{5,6} In a previous communication, we have presented a first example of a CM between a 1,3-diene and methyl vinyl ketone.⁷ A feasible domino process of enyne RCM and CM with electron-deficient alkenes was reported afterwards.^{6a} However, the reaction behavior of isolated butadienes can be different. Such an example is presented in this letter. Following our earlier work on CM reactions, we were interested in examining the general substrate scope of CM reactions between electron-deficient olefins and 1,3-dienes.

We chose the phosphine-free ruthenium complex [Ru-2]⁸ for the CM reactions since it was shown to exhibit super-

ior activity toward electron-deficient olefins⁹ compared to the second-generation *Grubbs* catalyst [Ru-1]¹⁰ (Fig. 1).

In our initial experiments, we employed terminal monosubstituted 1,3-butadienes **1**, **2**, and **3** and methyl vinyl ketone (MVK) as the coupling partner (Table 1). In these reactions, the desired dienones **4**, **6**, and **9** were obtained in yields of less than 40%. Unlike the CM reactions between unconjugated alkenes and electron-deficient olefins, in which the products are provided with complete *E*-stereoselectivity,¹¹ the newly formed double bond was generated with moderate *E/Z* stereoselectivity.

As a first example, both the *E*- and *Z*-isomers of diene **1** were converted to a chromatographically inseparable 4:1 mixture of *E/Z* stereoisomers of the corresponding dienones **4**. Attempts to optimize product yields by varying either the equivalents of MVK, reaction time or temperature proved unsuccessful.

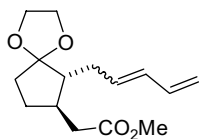
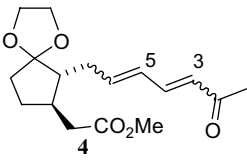
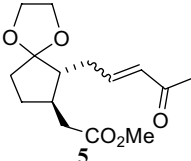
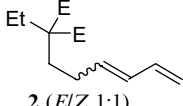
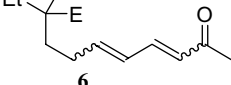
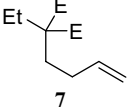
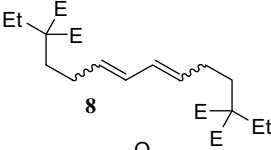
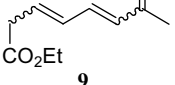
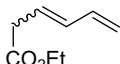
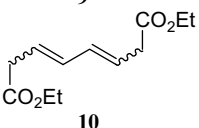
Other isolated products from further substrates, such as enone **5** or dimers **8** and **10**, indicate that the low yields are mainly due to unselective attack of the metathesis catalyst on the 1,3-diene system. Their formation can be rationalized by cleavage of the diene at the internal double bond.

To suppress the competing catalyst attack on the internal double bond, we decided to employ 1,3-dienes, which are sterically less accessible, that is, with higher substituted internal double bond (Table 2). Both acyclic

Keywords: Cross metathesis; Butadienes; Enones; Dienones; Ruthenium catalyst.

*Corresponding author. Tel.: +49 30 31422255; fax: +49 30 31423619; e-mail: blechert@chem.tu-berlin.de

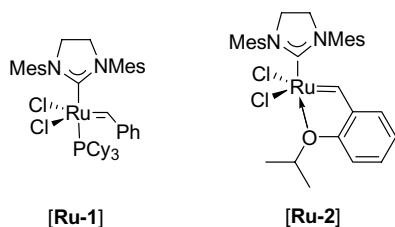
Table 1. CM reactions between terminal 4-substituted 1,3-dienes and MVK

Entry	Substrate	Products	Yield (%)
1	 1 (<i>E/Z</i> 1:1)	 4	35 (3 <i>E</i> ,5 <i>E</i>):(3 <i>Z</i> ,5 <i>E</i>):(3 <i>E</i> ,5 <i>Z</i>):(3 <i>Z</i> ,5 <i>Z</i>) 4:4:1:1 ^a
		 5	38 <i>E/Z</i> 1:1 ^a
2	 2 (<i>E/Z</i> 1:1)	 6	38 ^b
		 7	11
		 8	13 ^b
		 9	24 ^b
3	 3 (<i>E/Z</i> 1:1)	 10	6 ^b

Reaction conditions: CH₂Cl₂ (*c* = 0.05 M), 45 °C, 3 equiv MVK, 5 mol % [Ru-2], 3 h.

^a Determined by ¹H NMR.

^b *E/Z* not determined.

**Figure 1.** Ru-metathesis catalysts.

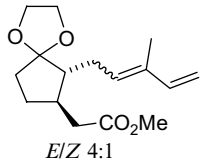
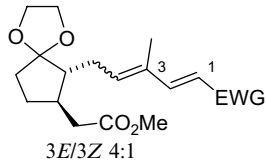
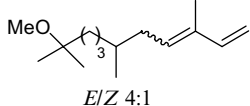
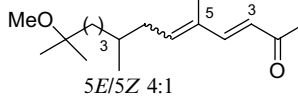
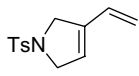
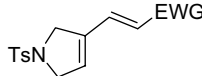
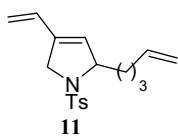
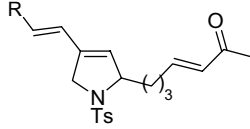
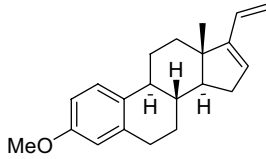
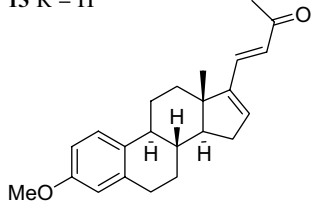
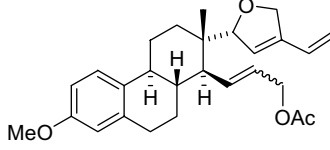
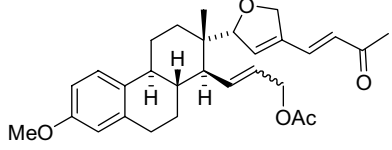
(entries 1 and 2) and cyclic dienes (entries 3–6), whose internal double bonds are incorporated in ring systems, were tested. We would like to point out that the latter were conveniently prepared via enyne metathesis. In the reactions with MVK, the desired CM products were obtained in moderate to good yields. Gratifyingly, in all cases, the dienones were formed with complete stereochemistry (*E/Z* > 20:1). As expected, the products formed by the cleavage of the internal double bond were not detected. The ene-diene **11** reacted smoothly with

3 equiv MVK to give the double-CM product **12**. It is however possible to differentiate between the two double bonds. Using 1.2 equiv of MVK, mono-CM product **13** was formed in 68% yield, exhibiting the higher reactivity of the unconjugated double bond toward metathesis.

Electron-deficient olefins other than MVK gave lower yields. Whereas moderate yields were obtained with methyl acrylate, the more electron-deficient acrolein and acrylonitrile gave low yields even at a higher reaction temperature and most of the starting material was recovered.

Previously, we have reported that enyne **14** affords ring-rearrangement products **11** upon treatment with ethylene or **15a** with the TBS-protected allyl alcohol after 1–3 h in the presence of the first-generation Grubbs-catalyst (PCy₃)₂Cl₂Ru(=CHPh) [Ru-3].¹² We were interested in whether the CM products **12** or **13** (see Table 2) are also obtainable directly from **14** under comparable condition. Surprisingly, in the reactions of **14** with

Table 2. CM reactions between terminal 3,4-disubstituted 1,3-dienes and electron-deficient alkenes

Entry	Substrate	Product	Yield (%)
1	 E/Z 4:1	 3E/3Z 4:1 EWG = COMe EWG = CO ₂ Me EWG = CHO EWG = CN	73 37 23 14 ^a
2	 E/Z 4:1	 5E/5Z 4:1	77
3		 EWG = COMe EWG = CO ₂ Me	85 45
4	 11	 12 R = COMe 13 R = H	84 68 ^b
5			39 ^c
6			70

Reaction conditions: CH₂Cl₂ (*c* 0.05 M), 3 equiv CH₂ = CH(EWG), 5 mol % [Ru-2], 45 °C, 3 h.

^a (1*E*,3*E*)/(1*Z*,3*E*)/(1*E*,3*Z*)/(1*Z*,3*Z*) 4:12:1:3.

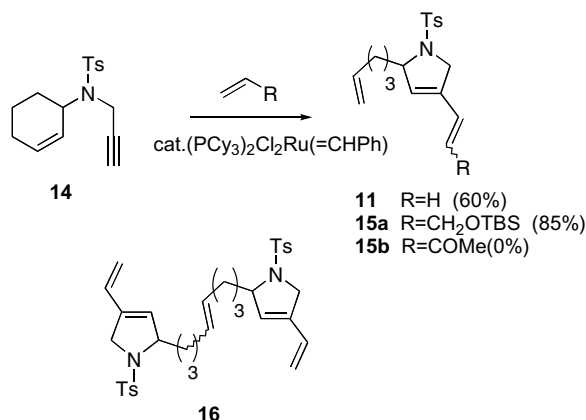
^b 1.2 eq MVK.

^c 24 h reaction time.

MVK no such products were formed using catalysts [Ru-1], [Ru-2], or [Ru-3]; dimer **16** was isolated as the only ring-rearranged product, as shown in Scheme 1. In the reactions using the second-generation catalysts [Ru-1] or [Ru-2], the MVK mainly dimerized to afford (*E*)-hex-3-ene-2,5-dione. This major difference between the reaction of an isolated butadiene and of its precursor **14** indicates, according to our opinion, different reaction pathways and intermediates are occurring.⁷

In summary, we have investigated selective CM reactions between 1,3-dienes and electron-deficient olefins.

High yields of the desired products are only achieved in case the internal double bond is sterically congested and thus protected from catalyst attack. Methyl vinyl ketone turned out to be the most effective coupling partner. With the exception of acrylonitrile,¹³ the products are provided with complete *E/Z*-selectivity. Taking the well-known high functional group tolerance of the Ru catalysts into account, we are confident that this reaction provides a valuable alternative for the preparation of dienones to existing methods such as the Horner–Wadsworth–Emmons reaction, especially for base-sensitive substrates.



Scheme 1. Attempted ring-rearrangement metathesis between **14** and MVK.

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