# Olefin Cross-Metathesis with Monosubstituted Olefins

**Oliver Brümmer, Anke Rückert, and Siegfried Blechert***

**Abstract**: The applicability of olefin cross-metathesis for the synthesis of different unsymmetrically substituted functionalized olefins is described. The coupling of different functionalized olefins in the presence of Grubbs' ruthenium catalyst or Schrock's molybdenum catalyst afforded the crossed products in good yields and with very high selectivities. Derivatives of jasmonic acid and functionalized allylsilanes were prepared by this catalytic method for carbon–carbon double bond formation.

**Keywords**
alkenes · allylsilanes · C–C coupling · cross-metathesis · jasmonates · molybdenum · ruthenium

## Introduction

During recent years olefin metathesis has gained a position of increasing significance.[1] This method for carbon–carbon double-bond formation has been stimulated by the development of new catalysts like Grubbs' ruthenium catalyst[2] $Cl_2(PCy_3)_2$-Ru=CHPh (= **Ru**, Cy = cyclohexyl) and Schrock's molybdenum catalyst[3] $PhMe_2CCH{=}Mo{=}N$-(2,6-$i$Pr$_2$C$_6$H$_3$)[OCMe-$(CF_3)_2]_2$ (= **Mo**). Numerous accounts have been given of ring-closing metathesis leading even to strained rings and macrocycles.[4] In contrast, there are only a few examples for selective cross-metathesis in the presence of functional groups. This interesting method for the formation of carbon–carbon double bonds has not yet found widespread application, because general conditions that give high selectivity are not known. In addition to a driving force, the suppression of self-metathesis is required. Until now, selective cross-metathesis has been reported in a few cases for styrenes,[5] acrylonitrile,[6] and allylsilanes.[7a, b] Based on these experiments, selectivity was explained in terms of the delocalizable carbon–carbon double bonds (aryl or cyano substituent) and nucleophilicity of the olefins. According to this model, the $\beta$-effect of silicon is supposed to play an important role in cross-coupling reactions with allyltrimethylsilane. In the course of our studies into cross-metathesis,[8] we observed a large number of selective cross-couplings of monosubstituted olefins that could not be explained by the above-mentioned effects.

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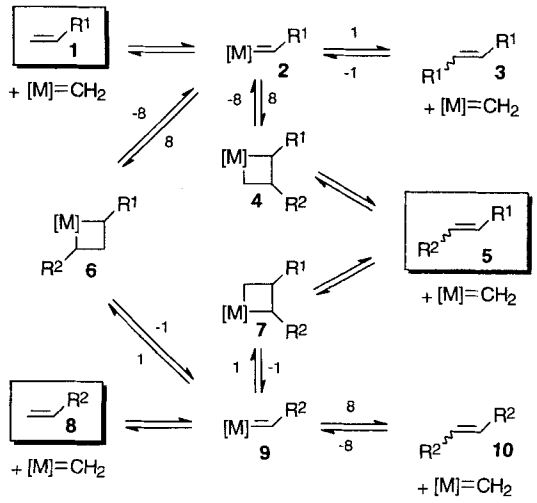
## Results and Discussion

Olefin metathesis proceeds by sequential [2+2] cycloaddition and cycloreversion.[9] The simplified reaction between two different olefins is shown in Scheme 1. Generally, the reaction between two different olefins, **1** and **8**, can afford the three disubstituted products **3**, **5**, and **10**. From **Mo** and **Ru**, a catalytically active metal methylidene complex is preformed. It can react with olefins **1** and **8** to form metal alkylidene complexes **2** and **9**, respectively. Subsequent cycloaddition reaction with the starting olefins leads to the metallacyclobutanes **4**, **6**, or **7**. Only the cycloreversion reaction of the mixed metallacyclobutanes **4** and **7** furnishes the desired cross-product **5**, and the metal methyl-




Scheme 1. Mechanism of olefin cross-metathesis. Ethene, which is a stochiometric cross-metathesis by-product formed in the cycloreversion reaction steps, has been omitted for clarity.

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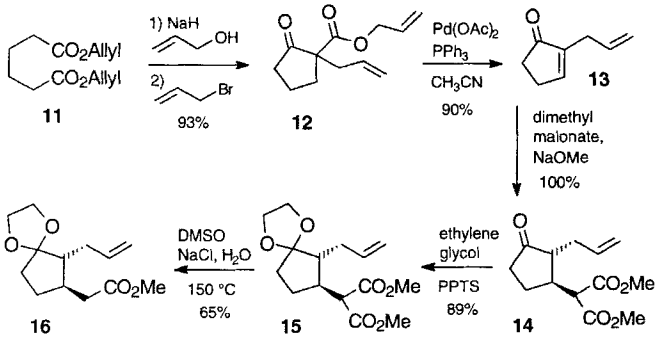
idene complex is regenerated. The other reaction pathways are not productive or lead to the homodimers **3** and **10**.

The composition of products depends on the ratio of the concentrations of **2** and **9** as well as on their specific reactivities towards **1** and **8**. Olefin metathesis proceeds more slowly with sterically hindered olefins,[10] although it cannot be ruled out that the catalytically active metal methylidene complex reacts preferentially with the more hindered olefin. The deceleration of the dimerization might be due to increased steric interactions between the incoming olefin and the metal alkylidene complex in the productive cycloaddition. Consequently, we are interested in the olefin metathesis between two olefins with different steric demands.

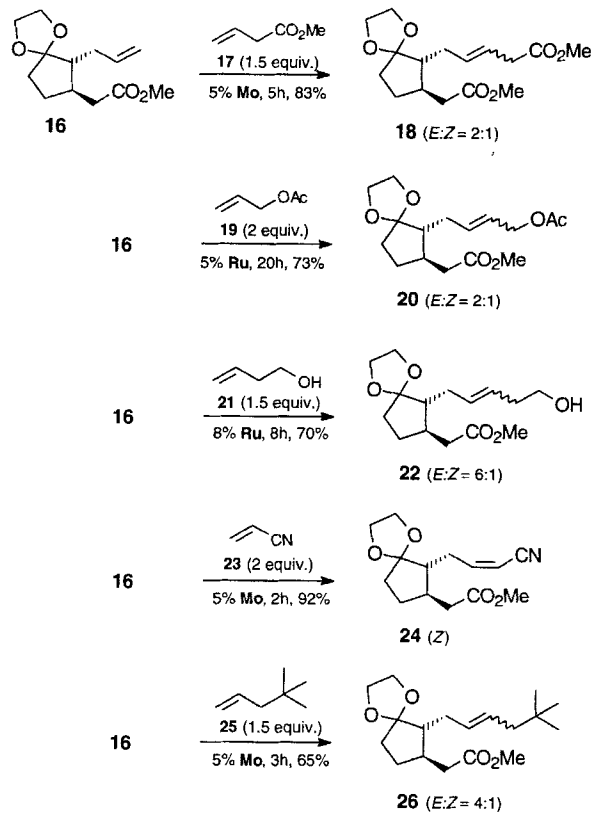
In the course of our studies into the biological activity of derivates of jasmonic acid,[11] we were searching for a simple method for modifying the olefinic side chain. In some cases, classic Wittig olefination gave unsatisfactory results. As an alternative, we decided to employ the cross-metathesis between readily accessible **16** and diverse sterically less demanding olefins.

Compound **16** was synthesized according to the procedure of Tsuji et al. (Scheme 2).[12] Starting with commercially available diallyl adipate **11**, the cyclopentenone derivative **13** was synthesized by a Dieckmann condensation, alkylation, and Pd-catalyzed enone formation. Michael addition, formation of an acetal, and decarboxylation furnished compound **16** in good yield.




Scheme 2. Synthesis of the metathesis precursor **16** (PPTS = pyridinium *p*-toluenesulfonate).

Owing to the sensitivity of the catalysts (paricularly of **Mo**) towards atmospheric oxygen, all cross-metathesis reactions were performed under argon. Because of the importance of the ethylene concentration, all reactions were carried out in refluxing methylene chloride. A mixture of **16** and various monosubstituted olefins (1.1–2 equiv) was refluxed in the presence of **Mo** or **Ru**. After purification by flash chromatography on silica gel, the main cross-metathesis products were isolated in good yields (Scheme 3). Probably, because of the above-mentioned steric effects, the acetal **16** showed no self-metathesis under these conditions. Thus, olefin metathesis reactions were performed successfully with olefins containing ester, acetate, cyano, hydroxy, and *tert*-butyl groups. In the reaction with **17** and **19**, the homodimers of these compounds were formed in 26 and 12% yield, respectively. These undesired by-products were readily separated from the cross-metathesis products by distillation. In all other cases, only small amounts, if any, of the self-metathesis




Scheme 3. Synthesis of jasmonic acid derivatives.

products were observed. Cross-coupling reactions with **19** and **21** only proceeded with the **Ru** catalysis, whereas acrylonitrile and **16** could only be coupled with the **Mo** catalyst.

Considerably lower coupling yields were obtained when the ketone was used instead of acetal **16**. In some cases, olefination of the ketone took place, and the catalyst was consumed.

The stereochemistry of the disubstituted double bond is presumably fixed during the cycloaddition step (Scheme 1, **4** and **7**). With the exception of compound **24**, the observed (*E*)/(*Z*) selectivities are low. The (*E*)/(*Z*) ratio was determined by NMR spectroscopy and GC. In the case of jasmonic acid derivatives, the formation of stereoisomers was of no great disadvantage, because we needed to test both the *cis* and *trans* isomers for structure–activity studies. We are currently investigating whether the selective cross-metathesis described above can be applied more generally to other systems.

In the course of our studies we observed that the rate of metathesis is also influenced by heteroatoms, such as oxygen and nitrogen. We therefore performed a series of cross-metathesis reactions of 4,4-dimethyl-1-pentene (**25**) with oxygen-bearing olefins. In all the examples examined, we observed good selectivities. For instance, the reaction of benzyl pentenyl ether (**27**) with **25** (1.3 equiv) in the presence of 5% **Mo** furnished exclusively the unsymmetrically substituted olefin **28** (Scheme 4). Remarkably, when **25** and **27** were allowed to react separately under the same conditions, the respective homodimers were obtained.

From a preparative point of view, the cross-metathesis with allyltrimethylsilane (**29**) is more interesting,[7b] since functionalized allylsilanes can be used for nucleophilic addition to elec-



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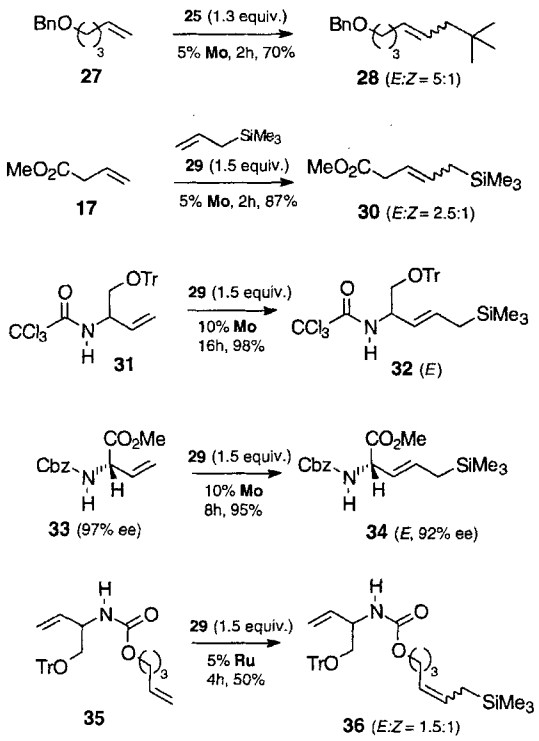


Scheme 4. Synthesis of allylsilanes.

trophilic carbon centers.[13] In our studies, **25** and **29** showed comparable reactivities. The reaction of **27** with a 1:1 mixture of **25** and **29** revealed no difference in the reactivities of the two alkenes. Apparently, the $\beta$-effect of silicon does not play an important role during metathesis.

The further examples shown in Scheme 4 prove the applicability of olefin metathesis to the formation of functionalized allylsilanes. Allyltrimethylsilane (**29**) reacts in good yields with vinyl acetic ester **17** as well as with the sterically demanding compound **31**, which was synthesized by tritylation of the corresponding alcohol.[14] Disubstituted allylsilanes, such as **34**, could also be prepared in high enantiomeric excess. The *ee* values of the commercially available starting material **33** and product **34** were determined by chiral HPLC. Despite the fact that vinyl glycine esters are highly unstable, little isomerization was observed, and this was presumed to have taken place during workup. The reaction of allyltrimethylsilane **29** with **35**, which was synthesized by esterification of **31** with 4-penten-1-ol, shows that chemoselective cross-coupling is possible. The regioisomer was not formed, although the bisallylsilane of **29** was recovered in 5% yield.

The examples described above demonstrate that polar groups have a positive influence on the selectivity of olefin cross-metathesis. This could be explained by a precomplexation of the catalyst by free electron pairs in a polar olefin.

All reactions described can be catalyzed by **Mo** and **Ru**, except for the cross-couplings of **19** and **21**, which only proceed with **Ru**, because **Mo** does not tolerate free alcohol and acetate groups; also, **Ru** failed to catalyze the reaction between acrylonitrile (**23**) and **16**. **Mo** generally requires shorter reaction times and affords higher yields. Certainly, its sensitivity towards atmospheric oxygen is a disadvantage. The olefin cross-metathesis proceeds at ambient temperatures under neutral conditions; this means that sensitive compounds such as **33** react without isomerization.

## Conclusion

The examples described demonstrate the applicability of cross-metathesis for the synthesis of unsymmetrically substituted functionalized olefins. A broad variety of functional groups is tolerated. The preparation of derivatives of jasmonic acid and of allylsilanes shows that this catalytic method for the synthesis of olefins is an interesting alternative to other procedures, because it proceeds under neutral and very mild conditions. The main disadvantage at present is the lack of stereoselectivity. Certainly, the results described do not represent general conditions for successful selective cross-metathesis. However, they indicate the importance of steric parameters and how neighboring group effects of hetero atoms (e.g., O and N) can be utilized. The electronic character of the double bond stressed by other authors[7b] does not seem to play an important role, at least in our examples. The tendency of an olefin to dimerize is not the only criterion for the selectivity of cross-metathesis. Further studies into the factors affecting selectivity of olefin metathesis are in progress.

## Experimental Section

MS and HRMS: Varian MAT 711 and MAT 955Q mass spectrometer (EI) with an ionization potential of 70 eV. IR: Nicolet 750 FT infrared spectrometer. $^1$H NMR: Bruker AM 400 and AC 200; chemical shifts relative to $CDCl_3$. $^{13}$C NMR spectra, including DEPT: Bruker AM 400 and AC 200. TLC: performed on Merck $^{60}F_{240}$ (0.2 mm) sheets, which were visualized with a solution of molybdophosphoric acic in acetic acid, UV light, or an aqueous solution of $KMnO_4$. Preparative flash chromatography: performed on Merck (0.04–0.063 mm) silica gel with a positive pressure of air; PE (light petroleum, b.p. 40–60 °C), MTBE (methyl *tert*-butyl ether) as eluent. GC: Hewlett Packard 5890 Series II. *ee*: determined by chiral HPLC (DAICEL Chemical Industries, Chiracel OD-H, 300–4 nm, Hex/IPA (10+0.5), 1 mL L$^{-1}$, 254 nm UV and IR detection). Unless otherwise stated, all starting materials were of the highest commercially available purity and were used without further purification.

**General procedure:** Cross-metatheses were performed in a glove-box under an atmosphere of argon. A solution of **Mo** or **Ru** in $CH_2Cl_2$ was added to a solution of the two olefins in $CH_2Cl_2$. The resulting mixture was refluxed for several hours and monitored by TLC and GC. The solvent was removed under reduced pressure, and the crude residue was chromatographed on silica gel. The configuration of the resulting double bond was determined by NMR spectroscopy and GC.

**Allyl 1-allyl-2-oxocyclopentane-1-carboxylate (12)**: Allyl alcohol (2.86 mL, 40 mmol) was added at room temperature under argon to a stirred suspension of NaH (5.05 g of 80% paraffin oil suspension, 0.168 mol) in dry toluene (150 mL). Diallyl adipate (**11**) (33.6 g, 0.149 mol) was added dropwise over 30 min to the mixture, and the resulting mixture was stirred at 90 °C for 2 h. After this time, more NaH (1.5 g of 80% paraffin oil suspension, 50 mmol) was added, and the mixture was heated to 90 °C for another 30 min. Then, excess allyl alcohol was distilled off from this mixture azeotropically (110 °C), whereby another 60 mL of toluene was added for the complete removal of allyl alcohol. Once allyl alcohol could no longer be detected in the reaction mixture, allyl bromide (18.36 mL, 0.217 mol) was added dropwise over 10 min at 100 °C. After having been stirred for 16 h, the mixture was cooled to room temperature, washed with 5% aq. NaCl, sat. $NaHCO_3$, and brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was distilled to give **12** (29 g, 0.139 mol, 93%) as a colorless oil, b.p. 90 °C

$CDCl_3$): $\delta$ = 28.0 ($CH_2$), 29.8 ($CH_2$), 53.0 (CH), 64.1 ($CH_2$), 65.3 ($CH_2$), 86.3 ($C_q$), 115.0 ($CH_2$), 115.5 ($CH_2$), 126.9 (CH), 127.9 (2 × CH), 128.3 (2 × CH), 136.2 (CH), 137.4 (CH), 143.5 ($C_q$), 155.9 ($C_q$). IR (ATR): $\tilde{\nu}$ = 3059, 3032, 3022, 2953, 2925, 2869, 2854, 1710 1641, 1597, 1491, 1449, 1415, 1333, 1296, 1220, 1091, 1076, 1033, 1002, 992, 918, 900, 774, 765, 746, 705 $cm^{-1}$. MS (70 eV, EI): *m/z* (%) = 440 (6, $M^+$), 244 (18), 243 (100), 228 (25), 215 (16), 165 (76). HRMS: calcd. for $C_{29}H_{30}O_3N$: 440.2226, found 440.2226.

**6-Trimethylsilanylhex-4-enyl (1-trityloxymethylallyl)carbamate (36)**: Following the general procedure, a solution of **35** (60 mg, 0.14 mmol), allyltrimethylsilane (**29**) (18 mg, 0.16 mmol, 1.1 equiv), and **Ru** (5 mg, 0.006 mmol, 5 mol%) in $CH_2Cl_2$ (2.5 mL) was refluxed for 9 h. Separation of the reaction mixture by flash chromatography (MTBE/PE 1:9) afforded **36** (37 mg, 0.07 mmol, 50% yield) as a 1.5:1 mixture of (*E*)/(*Z*) isomers (colorless oil) and the bisallylsilane (4 mg, 0.0065 mmol, 5%). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = −0.30 (s, 5.4H, *E*), −0.25 (s, 3.6H, *Z*), 1.36 (d, $^3J$ = 8 Hz, 1.2H, *E*), 1.36 (d, $^3J$ = 8 Hz, 0.8H, *Z*), 1.66 (m, 2H), 2.04 (m, 2H), 3.20 (d, $^3J$ = 6 Hz, 2H), 4.05 (dt, $^3J$ = 5 Hz, $^4J$ = 1 Hz, 2H), 4.38 (m, 1H), 4.95 (d, $^3J$ = 8 Hz, 1H, NH), 5.20 (ddd, $^2J$ = 1 Hz, $^3J$ = 10.5 Hz, $^4J$ = 1 Hz, 1H), 5.23 (m, 1H), 5.25 (ddd, $^2J$ = 1 Hz, $^3J$ = 17 Hz, $^4J$ = 1 Hz, 1H), 5.40 (dtt, $^3J$ = 17, 8 Hz, $^4J$ = 1 Hz, 1H), 5.91 (ddd, $^3J$ = 17, 10.5, 5 Hz, 1H), 7.21–7.33 (m, 9H), 7.43 (m, 6H). $^{13}$C NMR (50 MHz, $CDCl_3$): $\delta$ = −2.0 (0.6$CH_3$, *E*), −1.8 (0.4$CH_3$, *Z*), 18.4 ($CH_2$), 22.6 (0.6$CH_2$, *E*), 23.3 (0.4$CH_2$, *Z*), 29.0 (0.6$CH_2$, *E*), 29.3 (0.4$CH_2$, *Z*), 53.3 (CH), 64.5 (0.6$CH_2$, *E*), 64.7 (0.4$CH_2$, *Z*), 65.5 ($CH_2$), 86.5 ($C_q$), 115.7 ($CH_2$), 126.1 (0.6CH, *E*), 126.4 (0.4CH, *Z*), 127.1 (CH), 127.2 (0.6CH, *E*), 127.4 (0.4CH, *Z*), 127.8 (2 × CH), 128.6 (2 × CH), 136.4 (CH), 143.7 ($C_q$), 156.2 ($C_q$). IR (ATR): $\tilde{\nu}$ = 3451, 3088, 3062, 3024, 2956, 2929, 2874, 1727, 1646, 1598, 1495, 1449, 1406, 1325, 1248, 1215, 1153, 1093, 1078, 1034, 925, 899 $cm^{-1}$. MS (70 eV, EI): *m/z* (%) = 527 (<1, $M^+$), 284 (12), 254 (12), 243 (100), 204 (14), 165 (34), 153 (19), 105 (10), 73 (50). HRMS: calcd. for $C_{33}H_{41}O_3NSi$: 527.2856, found 527.2856.

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