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An Atom-Economic and Stereospecific Access to Trisubstituted Olefins through Enyne Cross Metathesis Followed by 1,4-Hydrogenation

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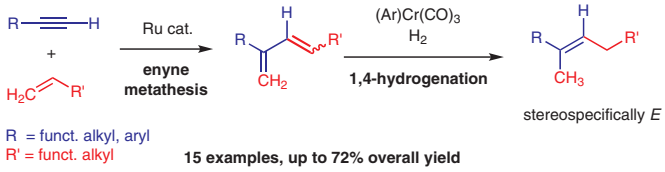

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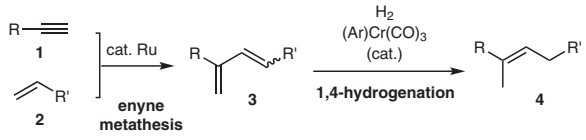
Abstract The combination of intermolecular enyne cross metathesis and subsequent 1,4-hydrogenation opens a stereocontrolled and atom-economic access to trisubstituted olefins. By investigating different combinations of functionalized alkyne and alkene substrates, we found that the outcome (yield, *E*/*Z* ratio) of the Grubbs II-catalyzed enyne cross-metathesis step depends on the substrate's structure, the amount of the alkene (used in excess), and the (optional) presence of ethylene. In any case, the 1,4-hydrogenation, catalyzed by 1,2-dimethoxybenzene-Cr(CO)$_3$, proceeds stereospecifically to yield exclusively the *E*-products from both the *E*- and *Z*-1,3-diene intermediates obtained by metathesis. A rather broad scope and functional group compatibility of the method is demonstrated by means of 15 examples.

Key words Ru catalysis, enyne cross metathesis, 1,4-hydrogenation, synthesis of alkenes, diastereoselectivity, 1,3-dienes

The development of new synthetic strategies for the stereoselective synthesis of trisubstituted olefins, a widespread structural motif of natural products, is a topic of high interest in synthetic organic chemistry. This is because most of the established methods, such as olefination,[1] cross-coupling,[2] or carboalumination/cross-coupling[3], also have drawbacks – in spite of their usefulness. For instance, the laborious synthesis of functionalized building blocks (e.g. for cross-couplings[4]) or a lack of *E*/*Z*-stereoselectivity[5] may hamper the applicability of the existing protocols, most of which are also far from being atom-efficient.[6] Thus, the search for novel atom-economic methods for the synthesis of trisubstituted olefins still represents a relevant challenge.

Against this background, we reasoned that the intermolecular cross metathesis[7] of an alkyne **1** and an alkene **2** followed by 1,4-hydrogenation[8] of the resulting 1,3-diene intermediate **3** should open a general access to *E*-olefins **4** (Scheme 1).



Scheme 1 Envisioned two-step reaction sequence

A literature search revealed (almost surprisingly) that such a sequence has never been described in the literature[9,10] and we therefore decided to explore the feasibility of this concept. We herein report the results of our study, which has indeed led to the development of a facile two-step protocol for the stereospecific synthesis of trisubstituted olefins of type **4**.

To investigate the scope and limitations of the envisioned sequence we selected the set of alkyne and alkene building blocks shown in Figure 1.

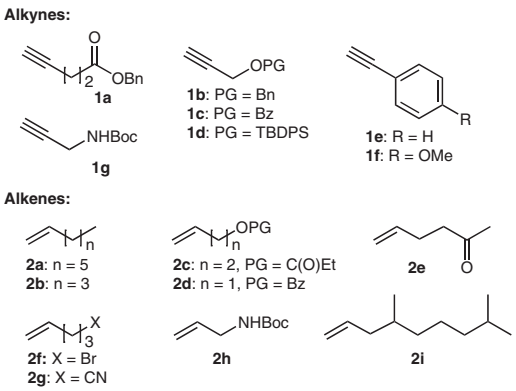
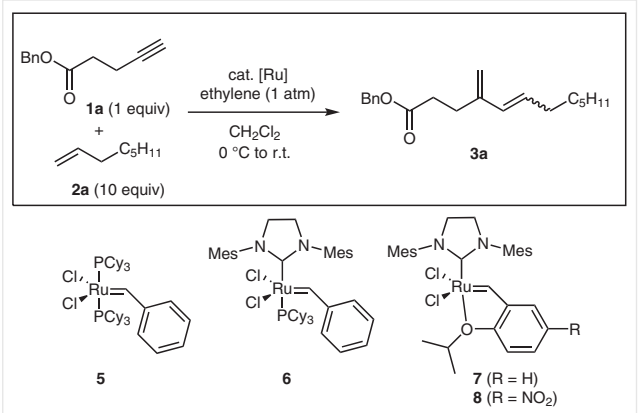


Figure 1 Alkyne and alkene building blocks used in this study

As a positive influence of ethylene on enyne metathesis, discovered by Mori,[11] is well documented in the literature,[12] we chose the ethylene-promoted procedure of Lee et al.[13] to test and optimize the enyne-metathesis step. At first, we

performed a brief catalyst screening employing substrates **1a** and **2a** and four different commercially available ruthenium catalysts **5**–**8**[14] (Scheme 2). The Grubbs II[14c] (**6**) and the Hoveyda–Grubbs[14d] catalyst (**7**) delivered comparably good results (Table 1) and we therefore used the less expensive catalyst **6** for all further experiments. On a small scale (about 1 mmol) we generally performed the reactions with 10 mol% of catalyst while at larger scales (>1.5 mmol) the catalyst amount could be slightly reduced (7–8 mol%). Lower catalyst loadings (<5%) usually resulted in incomplete conversion even after prolonged reaction times (50 h).



Scheme 2 Test reaction and catalysts screened (see Table 1)

The reactions were carried out in CH_2Cl_2 as solvent under an atmosphere of ethylene (1 atm) and run until complete consumption of the alkyne starting material (GC–MS monitoring, 24–72 h). The product **3a** was then isolated after flash chromatography and the *E*/*Z* ratio determined by means of ^{1}H NMR spectroscopy.

Table 1 Results of the Catalyst Screening According to Scheme 2

Entry	Catalyst	Loading (mol%)	Reaction time (h)	Isolated yield (%)	*E*/*Z*[a]
1	**5**	10	72	48	50:50
2	**6**	10	24	51	>99:1
3	**6**	8	48	57	>99:1
4	**6**	10	72	66	>99:1
5	**7**	5	24	–[b]	n.d.
6	**7**	10	48	60	>99:1
7	**8**	1	24	–[c]	n.d.
8	**8**	10	48	43	>99:1

[a] Determined by ^{1}H NMR spectroscopy.
[b] Only 40 % conversion (GC–MS).
[c] < 2% conversion (GC–MS and NMR).

We next tested the scope and limitations of the cross-metathesis protocol by employing the different alkynes and alkenes depicted in Figure 1. In all cases, a solution of the alkyne (1 equiv), the alkene (10 equiv), and the catalyst **6** (7–10 mol%) in CH_2Cl_2 was stirred under an ethylene atmosphere until complete consumption of the alkyne (24–72 h). Table 2 shows 17 successful examples, in which the expected products were formed in moderate to good yield. As a trend, the propargyl benzoate **1c** gave rise to higher yields than the corresponding propargyl benzyl ether **1b** (Table 2, entries 2, 3 and 12, 13, respectively). Remarkably, mixtures of *E*/*Z*-diastereomers were obtained in the case of alkene substrates with ester, keto, or cyano functionalities (i.e., **2c**–**e**,**g**), while virtually pure *E*-products were formed in the case of unfunctionalized olefins, such as **2a**,**b**,**i**. The cyano-substituted diene **3n** (formed in only 34% yield as an *E*/*Z* mixture) could be better synthesized by S_N2 chemistry[15] from the bromide **3m** (see below), which was obtained in 61% as a pure *E*-isomer – in contrast to **3l** (with an OBn instead of an OBz unit), which was isolated as an *E*/*Z*-mixture in lower yield. Here, an unexpected and subtle dependency of the diastereoselectivity on the substrate structure became apparent.

Table 2 Outcome of the Enyne Cross Metathesis with Different Substrates

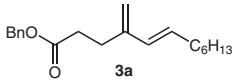
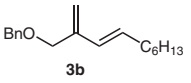
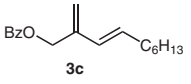
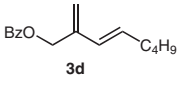
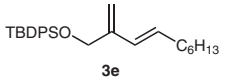
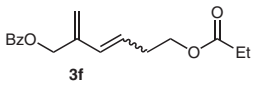
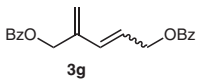
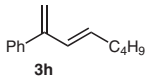
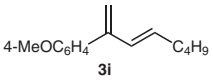
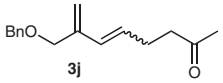
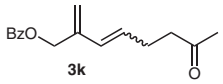
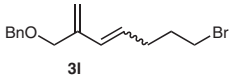
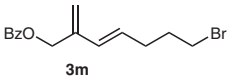
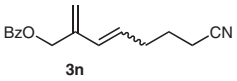
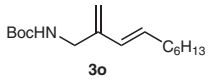
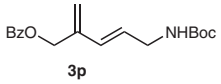
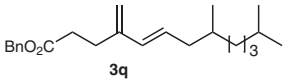
Entry	Substrates (time)	Product	Yield (%)	*E*/*Z*
1	**1a** + **2a** (72 h)	 **3a**	66	>99:1
2	**1b** + **2a** (24 h)	 **3b**	66	>99:1
3	**1c** + **2a** (72 h)	 **3c**	75	>99:1
4	**1c** + **2b** (72 h)	 **3d**	73	>99:1
5	**1d** + **2a** (48 h)	 **3e**	40	>99:1
6	**1c** + **2c** (72 h)	 **3f**	54	62:38
7	**1c** + **2d** (72 h)	 **3g**	56	79:21

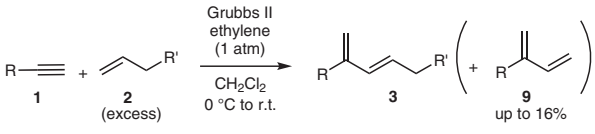
Table 2 (continued)

Entry	Substrates (time)	Product	Yield (%)	*E*/*Z*
8	**1e** + **2b** (24 h)	 **3h**	55	>99:1
9	**1f** + **2b** (24 h)	 **3i**	64	>99:1
10	**1b** + **2e** (24 h)	 **3j**	36	79:21
11	**1c** + **2e** (72 h)	 **3k**	61	84:16
12	**1b** + **2f** (48 h)	 **3l**	54	60:40
13	**1c** + **2f** (48 h)	 **3m**	61	>99:1
14	**1c** + **2g** (24 h)	 **3n**	34 (+ 23)[a]	52:48
15	**1g** + **2a** (24 h)	 **3o**	40	>99:1
16	**1c** + **2h** (24 h)	 **3p**	54	>99:1
17	**1a** + **2i** (48 h)	 **3q**	57	>95:5

[a] With slight impurities.

Table 2 reflects the general usefulness of the enyne-metathesis protocol used. Noteworthy, small amounts of monosubstituted 1,3-butadienes of type **9** were also formed (Scheme 3), especially in some of the highly *E*-selective reactions. These byproducts arising from reaction of the alkyne with ethylene were separated off by chromatography on $AgNO_3$-doped silica[16] and only isolated if formed in larger amounts (16% in entry 1; 21% in entry 3, 10% in entry 4; 14% in entry 9).

Although both the *E*- and the *Z*-isomers of the enyne-metathesis products of type **3** can be employed in the following 1,4-hydrogenation step to deliver the same product (see below), we were puzzled by the 'fluctuating' diastereo-

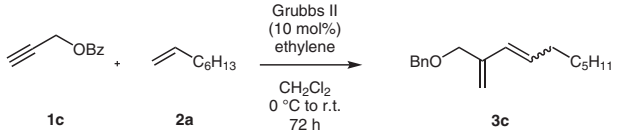


Scheme 3 Formation of side products of type **9** during enyne cross metathesis in the presence of ethylene

selectivity of the metathesis reaction (Table 2). As already mentioned, the dienes **3** were formed with high *E*-selectivity (>95:5) in the majority of the examples, while rather low *E*/*Z* ratios (in the range of 4:1 to 1:1) were observed in other cases, in accordance with literature reports.[13]

Using the reaction of **1c** with **2a** as a model system we could show that the stereoselectivity (as well as the yield) depends on the amount of the alkene used in excess. The highest yield and *E*-selectivity (dr >99:1) was achieved with 10 equivalents of **2a** while both the yield and the *E*/*Z* ratio dropped significantly when only 5 or 3 equivalents of **2a** were used (Table 3).

Table 3 Dependence of Yield and Stereoselectivity on the Excess of Alkene



Entry	Alkene (equiv)	Yield (%)	*E*/*Z*
1	10	75	>99:1
2	5	57	77:23
3	3	38	55:45

We also investigated the influence of ethylene on the yield and the diastereoselectivity of the enyne cross metathesis by performing reactions of **2a** with three different alkynes **1a–c** both in the presence and the absence of ethylene. As the results shown in Table 4 indicate, a virtually complete *E*-selectivity was achieved for alkynes **1a** and **1c** also in the absence of ethylene (Table 4, entries 2 and 7), and in the case of **1a** the product **3a** was formed even in improved yield (Table 4, entry 2). For substrate **2b**, however, the diastereoselectivity was completely lost in the absence of ethylene and the yield dropped to 25% (Table 4, entry 4). This demonstrates that certain enyne cross-metathesis reactions indeed benefit from the presence of ethylene while others do not. In any case, the use of a large (typically ten-fold) excess of the alkene component is recommended to promote both yield and *E*-selectivity.

Noteworthy, the reaction time also had an important influence on the yield (Table 4, compare entries 5 and 6). Even though the alkyne starting material **1c** was completely consumed after 24 h (GC–MS control), the yield of the cross-

Table 4 Influence of Ethylene on the Yield and Diastereoselectivity of the Reaction of **2a** with Alkynes **1a–c**

Entry	Alkyne (1 equiv)	Alkene (10 equiv)	Ethylene	Reaction time (h)	Yield (%)[a]	*E*/*Z*[b]
1	**1a**	**2a**	yes	72	66	>99:1
2	**1a**	**2a**	no	72	78	>99:1
3	**1b**	**2a**	yes	24	66	>99:1
4	**1b**	**2a**	no	48	25	50:50
5	**1c**	**2a**	yes	24	53	>99:1
6	**1c**	**2a**	yes	72	75	>99:1
7	**1c**	**2a**	no	24	55	>99:1

[a] Isolated yield.
[b] Determined by ^{1}H NMR spectroscopy.

metathesis product **3c** increased from 53% to 75% upon prolonging the reaction time from 24 h to 72 h in this case. This is possibly due to a slow conversion of the side product **9** (see Scheme 3) to the desired product **3c** through diene-ene cross metathesis. In the absence of ethylene, none or only negligible amounts of **9** were formed.

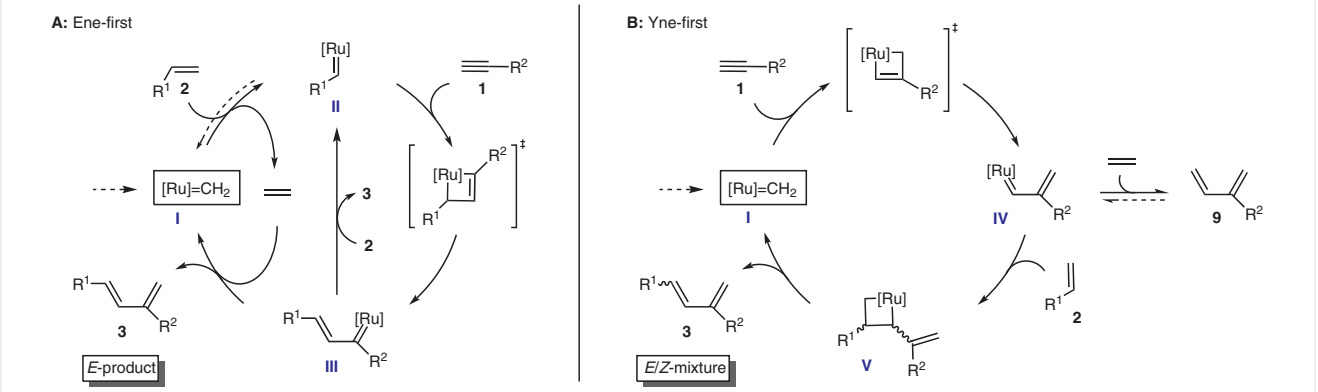
All these results let us rethink the mechanism of the intermolecular enyne metathesis, which is still the subject of debate.[17] Two mechanistic pathways have been proposed, which are depicted in Scheme 4. In the 'ene-first' pathway (cycle **A**) the catalyst **I** first reacts reversibly with the alkene **2**, and the new Ru carbene **II** then fuses with the alkyne **1** to generate the vinylcarbene **III**, which finally may react either with ethylene or directly with the next molecule of the alkene **2**. In both cases, the catalytic cycle would be closed under formation of the product **3**. In the 'yne-first' pathway (cycle **B**) the catalyst **I** reacts first with the alkyne to generate the intermediate **IV**, which then combines with the alkene via the metallacyclobutane **V** to release the product under regeneration of the catalyst.

On the basis of a Hammett analysis Diver et al. found that the Grubbs II catalyzed metathesis of substituted styrenes with 1-butyn-3-yl benzoate appears to proceed via an 'ene-first' mechanism,[18] and Lippstreu and Straub also suggested (based on DFT calculations) that an 'ene-first' pathway should be energetically favored, with the alkyne insertion being the only irreversible and therefore regioselectivity-determining step.[19]

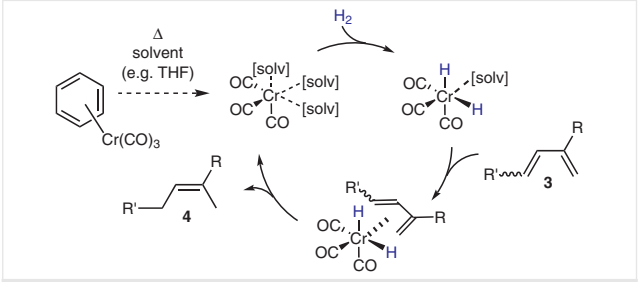
However, in other cases reactions were shown to proceed via the 'yne-first' pathway,[17] and our observation of side products of type **9** also indicates the involvement of intermediate **IV**.[20] On the other hand, only the 'ene-first' mechanism should selectively afford the *E*-product, because the alkyne insertion is expected to generate the *E*-configurated intermediate **III** only.[19] In contrast, both diastereomers can arise from the 'yne-first' route as the formation of cycloadduct **V** does not necessarily proceed in a stereoselective fashion. Thus, we suggest that the highly *E*-selective enyne metathesis reactions (see Table 2) proceed via the 'ene-first' mechanism (cycle **A**), which is kinetically fostered by a large excess of the alkene. The detrimental effect of polar donor functionalities in the alkene unit (as part of R^1) on the diastereoselectivity may be explained by assuming a chelate coordination to the Ru atom in **II** and thus a kinetic retardation of the alkyne insertion in cycle **A**. As a result, such reactions will proceed (at least partly) via cycle **B** and, accordingly, with reduced stereoselectivity.

Fortunately, the configuration of dienes **3** was not important for our study (Scheme 1) because both isomers were expected to yield the same *E*-configurated 1,4-hydrogenation product **4**. The (arene)Cr(CO)$_3$-catalyzed 1,4-hydrogenation of conjugated dienes, first reported in 1968 by Frankel, proceeds regio- and stereospecifically and presumably involves a 'synchronous' transfer of the two hydrogen atoms to the ends of the diene unit kept in a *s*-cis conformation by η^4-complexation (Scheme 5).[21,22]

Hydrogenation experiments were performed according to the procedure of Le Maux,[23] however, higher temperatures and longer reaction times were needed to achieve full conversion. After testing four catalysts available in our laboratory (Table 5) we selected (veratrole)Cr(CO)$_3$ (**10**) for all further experiments.



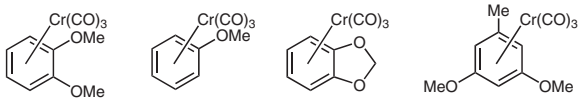
Scheme 4 The two possible mechanistic pathways of enyne cross metathesis



Scheme 5 Proposed mechanism of the (arene)$Cr(CO)_3$-catalyzed 1,4-hydrogenation[20,21]

Typically, a solution of the substrate (**3**) and 5 mol% of **10** in THF was stirred in an autoclave at 50–60 bar H_2 at 120 °C for 24 h. Under these optimized conditions, the (arene)$Cr(CO)_3$-catalyzed 1,4-hydrogenation was performed with all seventeen dienes obtained before by enyne metathesis (Table 6).

Table 5 Results of the Catalyst Screening in the 1,4-Hydrogenation[a]



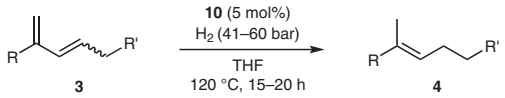
10 **11** **12** **13**

Entry	Catalyst	Substrate	Temp (°C)	Conversion (%)[b]	Yield (%)
1	**10**	**3a**	100	100	96
2	**11**	**3a**	100	100	84
3	**12**	**3a**	100	100	n.d.
4	**13**	**3a**	100	83	n.d.
5	**10**	**3c**	120	100	85
6	**11**	**3c**	120	100	76

[a] Reaction conditions: 5 mol% (Ar)$Cr(CO)_3$, H_2 (50–55 bar), THF, 17–20 h.
[b] Determined by GC–MS.

As Table 6 shows, the 1,4-hydrogenation of the dienes **3** proceeded smoothly in most cases to afford the desired trisubstituted olefins of type **4** as single isomers, as analyzed by GC–MS and NMR spectroscopy. The expected *E*-configuration was confirmed through H,H-NOESY experiments. Particularly good results were achieved for dienes **3a**–**e** and **3h**,**i**, respectively, which all carry long aliphatic side chains (Table 6, entries 1–5 and 9). In a similar manner substrate **3q** (carrying a branched 'terpenoid' side chain) delivered the 1,4-hydrogenated product **4q** in excellent yield (91%, Table 6, entry 17). Functional groups on the 'western' (alkyne-derived) terminus of the molecules were generally well tolerated, albeit the *O*-benzyl-protected substrates again performed slightly worse in comparison to the corresponding *O*-benzoyl-protected analogues (Table 6, entries 2, 3 and 10, 11, respectively). Somewhat lower yields were obtained in the cases of the Boc-protected amine **4o** (54%, Table 6, entry 15) and the phenyl-substituted product **4h** (43%, Table 6, entry 8).

Table 6 Outcome of the 1,4-Hydrogenation of Various Substrates



3 **4**

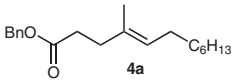
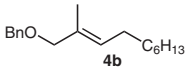
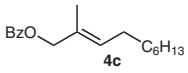
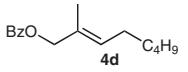
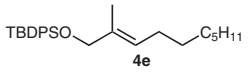
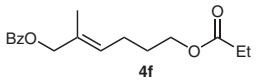
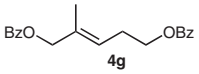
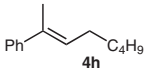
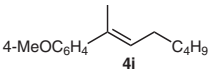
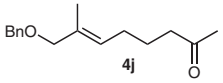
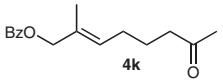
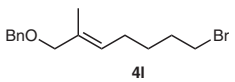
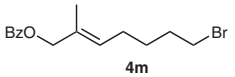
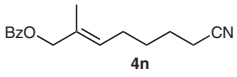
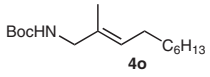
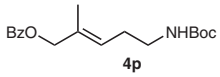
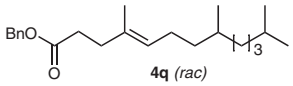
Entry	Substrate	Product	Yield (%)[a]
1	**3a**	 **4a**	88
2	**3b**	 **4b**	65
3	**3c**	 **4c**	96
4	**3d**	 **4d**	>99
5	**3e**	 **4e**	78[b]
6	**3f**	 **4f**	61
7	**3g**	 **4g**	–[c]
8	**3h**	 **4h**	43[d]
9	**3i**	 **4i**	90[d]
10	**3j**	 **4j**	68
11	**3k**	 **4k**	89
12	**3l**	 **4l**	–[e]
13	**3m**	 **4m**	24[b]

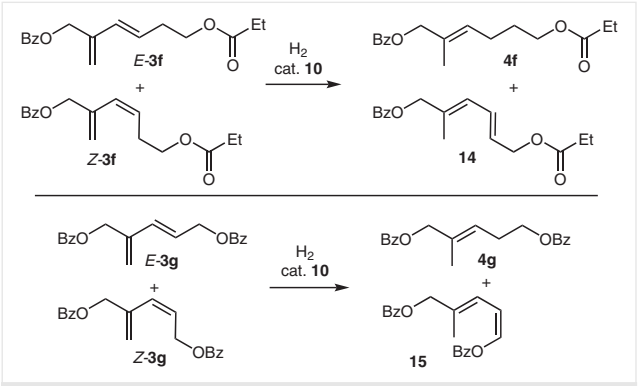
Table 6 (continued)

Entry	Substrate	Product	Yield (%)[a]
14	**3n**	 **4n**	74[f]
15	**3o**	 **4o**	54
16	**3p**	 **4p**	23
17	**3q**	 **4q** *(rac)*	91[d]

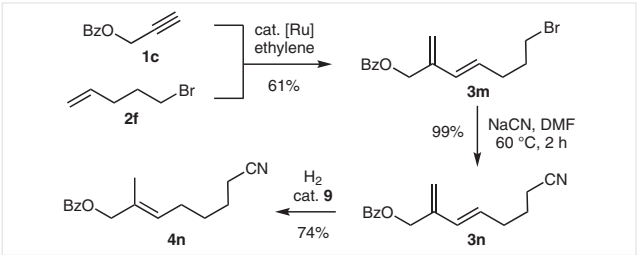
[a] Isolated yield.
[b] 20 mol% of catalyst **10** were used.
[c] ca. 40 % of an inseparable mixture were obtained.
[d] 10 mol% of catalyst **10** were used.
[e] No product detected, starting material re-isolated.
[f] The diene **3n** synthesized from **3m** was employed.

In contrast, functional groups on the 'eastern' (i.e., the alkene-derived) side of the substrates had a more pronounced influence on the outcome of the 1,4-hydrogenation. While the propionate **4f**, the ketones **4j**,**k**, as well as the nitrile **4n** were formed in good yields, the benzoate **4g**, the bromides **4l**,**m**, as well as the carbamate **4p** could not be isolated in useful yields and/or purities. Noteworthy, the ester-functionalized substrates **3f** and **3g**, which were both employed as *E*/*Z*-diastereomeric mixtures, led also to the formation of the isomerized side products **14** and **15**, respectively (Scheme 6). Similar Cr-catalyzed isomerizations of *Z*-configurated dienes had been described by Shibasaki et al.[24] While pure **4f** was obtained in 61% yield after chromatographic separation, **4g** was isolated only as a constituent of an inseparable mixture also containing the isomerization product **15** (resulting from *Z*-**3g** through a Cr-assisted 1,5-H shift)[24] and remaining starting material **3g**. Obviously, the bromides **3l** and **3m** do not represent suitable substrates for the 1,4-hydrogenation (Table 6, entries 12 and 13).

In conclusion, we have demonstrated that the combination of enyne cross metathesis and a subsequent 1,4-hydrogenation opens a straightforward, atom-economic, and stereospecific access to a variety of functionalized triple-substituted alkenes of type **4** as pure *E*-isomers.[25] Despite their broad general applicability, both the Ru-catalyzed enyne cross metathesis and the arene-$Cr(CO)_3$-catalyzed hydrogenation fail for certain particular substrates. However, the interconversion of functional groups at the stage of the diene intermediates **3** allows the application of the methodology also for the synthesis of 'difficult' products, which cannot be directly prepared under the standard conditions. As an example, the cyano-substituted alkene **4n** was synthesized in good overall yield from the readily available starting materials **1c** and **2f** via the three-step sequence shown in Scheme 7. Thus the feasibility of the concept was proven and we are optimistic that it will find application in organic synthesis in the future.



Scheme 6 Isomerization in case of allylic (**3f**) and homoallylic (**3g**) substrates



Scheme 7 Overall synthesis of the functionalized *E*-alkene **4n**

Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0036-1591528.

References and Notes

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(25) Detailed experimental procedures and characterization data are given in the Supporting Information.

General Procedure for Enyne Metathesis

A Schlenk flask was filled under argon with 0.1 equiv of catalyst **6**, cooled to 0 °C and flushed with ethylene. Then, dry CH_2Cl_2 (2.0 ml/mmol alkyne), 1.0 equiv of the alkyne (**1**) and 10 equiv of the alkene **2** were added, and the reaction mixture was stirred at r.t. for 24–72 h. The catalyst was removed by stirring the reaction mixture with active charcoal. The suspension was then filtered over silica, and the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography on SiO_2/$AgNO_3$ (cHex/EtOAc) to afford the diene **3** as colorless oil.

Analytical Data of Selected Dienes

Compound **3a**: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.38–7.30 (m, 5 H,), 6.04 (d, $^3J_{H,H}$ = 15.8 Hz, 1 H), 5.72 (dt, $^3J_{H,H}$ = 15.8 Hz, 6.9 Hz, 1 H), 5.12 (s, 2 H), 4.90 (s, 1 H), 4.84 (s, 1 H), 2.56 (m, 4 H), 2.11–2.06 (m, 2 H), 1.41–1.35 (m, 2 H), 1.32–1.25 (m, 6 H), 0.88 (t, $^3J_{H,H}$ = 6.9 Hz, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 173.2, 144.6, 136.1, 131.5), 130.9, 128.7, 128.3, 113.6, 66.4, 33.3, 33.0, 31.8, 29.4, 29.0, 27.4, 22.7, 14.2 ppm. HRMS (ESI): *m/z* calcd $[M+H]^+$ for $C_{20}H_{28}O_2$: 301.21621; found: 301.21666.

Compound **3d**: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.08–8.06, 7.58–7.54 (m, 1 H), 7.46–7.43 (m, 2 H), 6.12 (d, $^3J_{H,H}$ = 16.0 Hz, 1 H), 5.81 (dt, $^3J_{H,H}$ = 16.0 Hz, 6.9 Hz, 1 H), 5.22 (s, 1 H), 5.14 (s, 1 H), 4.99 (s, 2 H), 2.14–2.10 (m, 2 H), 1.42–1.36 (m, 2 H), 1.35–1.30 (m, 2 H), 0.89 (t, $^3J_{H,H}$ = 7.2 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.4, 140.7, 133.1, 132.1, 130.3, 129.8, 129.3, 128.5, 115.4, 64.8, 32.8, 31.5, 22.3, 14.0 ppm. HRMS (ESI): *m/z* calcd $[M + H]^+$ for $C_{16}H_{20}O_2$: 245.15361; found: 245.15396.

Compound **3i**: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.26–7.24 (m, 2 H), 6.88–6.85 (m, 2 H), 6.28 (d, $^3J_{H,H}$ = 15.6 Hz, 1 H), 5.67 (dt, $^3J_{H,H}$ = 15.6 Hz, 7.0 Hz, 1 H), 5.11 (d, $^4J_{H,H}$ = 1,4 Hz, 1 H), 5.01 (d, $^3J_{H,H}$ = 1.8 Hz, 1 H), 3.81 (s, 3 H), 2.14–2.10 (m, 2 H), 1.40–1.28 (m, 4 H), 0.89 (t,$^3J_{H,H}$ = 7.2 Hz, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.1, 147.7, 134.5, 133.3, 131.6, 129.4, 113.7, 113.6, 55.4, 32.7, 31.6, 22.4, 14.1 ppm.

General Procedure for 1,4-Hydrogenation

Under argon atmosphere, 1.00 equiv of the diene were dissolved in dry THF (4.0 ml/mmol diene) in a glass reaction vial. Then 0.05 equiv of the (arene)$Cr(CO)_3$ catalyst were added, and the vial was placed in a Parr autoclave. After sealing the autoclave and purging it three times with hydrogen (30 bar), the hydrogen pressure was set to 41–59 bar, and the temperature raised to 120 °C for 15–20 h (overnight). After cooling to r.t., the solvent was evaporated under reduced pressure, and the crude product was dissolved in EtOH (4.0 ml/mmol diene). To oxidize the remaining catalyst, 1.0 equiv of anhydrous $FeCl_3$ were added, and nitrogen was bubbled through the mixture for 30 min. Then, water was added, and the mixture was extracted 3 times with petrol ether or cyclohexane. The combined organic layers were dried over Na_2SO_4 under reduced pressure, and the crude product was purified by column chromatography on silica (cHex/EtOAc).

Analytical Data of Selected Trisubstituted Olefins

Compound **4a**: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.37–7.30 (m, 5 H), 5.16–5.13 (m, 1 H), 5.10 (s, 2 H), 2.48–2.45 (m, 2 H), 2.33–2.31 (m, 2 H), 1.96–1.93 (m, 2 H), 1.59 (s, 3 H), 1.32–1.23 (m, 10 H), 0.88 (t, $^3J_{H,H}$ = 7.0 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 173.4, 136.2, 133.1, 128.7, 128.3, 128.3, 125.9, 66.2, 34.8, 33.4, 32.0, 29.9, 29.4, 29.4, 28.0, 22.8, 16.0, 14.3 ppm. HRMS (EI): *m/z* calcd $[M]^+$ for $C_{20}H_{30}O_2$: 302.2245; found: 302.232.

Compound **4d**: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.07–8.05 (m, 2 H), 7.57–7.53 (m, 1 H), 7.45–7.42 (m, 2 H), 5.58–5.55 (m, 1 H), 4.71 (s, 2 H), 2.09–2.04 (m, 2 H), 1.74 (s, 3 H), 1.41–1.35 (m, 2 H), 1.34–1.27 (m, 4 H), 0.89 (t, $^3J_{H,H}$ = 7.0 Hz, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 166.6, 133.0, 130.6, 130.3, 130.0, 129.7, 128.5, 70.9, 31.7, 29.1, 27.9, 22.7, 14.2, 14.2 ppm. HRMS (ESI): *m/z* calcd $[M + Na]^+$ for $C_{16}H_{22}O_2$: 269.15120; found: 269.15154.

Compound **4i**: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.33–7.30 (m, 2 H), 6.86–6.83 (m, 2 H), 5.72–5.69 (m, 1 H), 3.80 (s, 3 H), 2.17 (q,

$^3J_{H,H}$ = 7.3 Hz, 2 H), 2.00 (s, 3 H), 1.47–1.41 (m, 2 H), 1.34–1.31 (m, 4 H), 0.90 (t, $^3J_{H,H}$ = 6.9 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.5, 136.8, 133.9, 127.4, 126.7, 113.6, 55.4, 31.8, 29.6, 28.9, 22.8, 15.9, 14.3 ppm.

Compound **4k**: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.06–8.05 (m, 2 H), 7.57–7.54 (m, 1 H), 7.46–7.43 (m, 2 H), 5.54–5.51 (m, 1 H), 4.71 (s, 2 H), 2.44 (t, $^3J_{H,H}$ = 7.4 Hz, 2 H), 2.14 (s, 3 H), 2.09 ('q', $^3J_{H,H}$ = 7.6 Hz, 2 H), 1.73 (s, 3 H), 1.68 ('p', $^3J_{H,H}$ = 7.4 Hz) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 208.9, 166.5, 133.0, 131.2, 130.5, 129.7, 128.7, 128.5, 70.5, 43.1, 30.1, 27.1, 23.4, 14.2 ppm.

Compound **4n**: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.07–8.04 (m, 2 H), 7.59–7.54 (m, 1 H), 7.47–7.42 (m, 2 H), 5.53 (t, $^3J_{H,H}$ = 7.2 Hz, 1 H), 4.71 (s, 2 H), 2.35 (t, $^3J_{H,H}$ = 6.9 Hz, 2 H), 2.13 ('q', $^3J_{H,H}$ = 7.2 Hz, 2 H), 1.74 (s, 3 H), 1.71–1.64 (m, 2 H), 1.61–1.51 (m, 2 H) ppm.^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.5, 133.1, 131.3, 130.5, 129.7, 128.5, 128.3, 119.8, 70.5, 28.4, 27.0, 25.1, 17.2, 14.2 ppm. HRMS (EI): *m/z* calcd $[M]^+$ for $C_{16}H_{19}NO_2$: 257.1416; found: 257.143.