CHAPTER 7

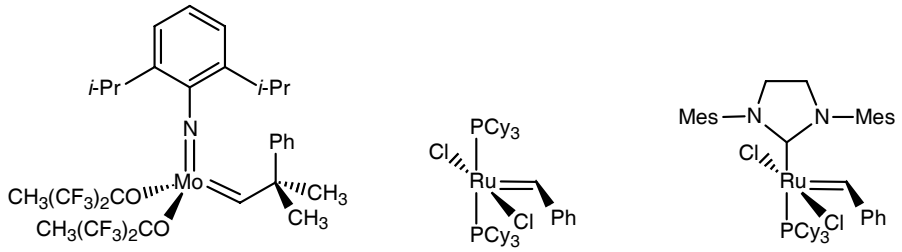
Formation of Trisubstituted Olefins via Ruthenium-Catalyzed Cross-Metathesis

Formation of Trisubstituted Olefins via Ruthenium-Catalyzed Cross-Metathesis

Abstract Symmetric trisubstituted alkenes can be prepared via intermolecular olefin cross-metathesis between α-olefins and isobutylene using a second-generation ruthenium benzylidene catalyst. Mechanistic studies of the reaction pathway in isobutylene cross-metathesis reveal that formation of the ruthenium isopropylidene is kinetically favored over the formation of the ruthenium methylidene. In order to kinetically favor the desired cross-metathesis product, 2-methyl-2-butene was employed as an isobutylene surrogate. Cross-metathesis of 2-methyl-2-butene with a variety of α-olefins constitutes a particularly mild and effective method to generate isoprenoid/prenyl groups, requiring only benchtop manipulations, standard glassware, low (room) temperatures, and low catalyst loadings. Understanding of the reactivity patterns of geminally-disubstituted and trisubstituted olefins in cross-metathesis has allowed the formation of trisubstituted olefins via the ring-opening cross-metathesis of low strain cyclic olefins and three-component cross-metathesis reactions.

Introduction

The development of new synthetic methods to create trisubstituted olefins remains an ongoing challenge in synthetic organic chemistry as trisubstituted olefins are present in a wide range of natural products and other molecules of biological and medicinal interest. While Wittig olefinations remain the most commonly used method to synthesized trisubstituted olefins,[1] olefin cross-metathesis (CM) offers a mild and convenient route to these structures that is orthogonal to Wittig chemistry. The commercial availability of well-defined single-component homogeneous olefin metathesis catalysts,[2] such as the molybdenum imido catalyst **7.1** (Figure 7.1) developed by Schrock *et al.*,[3] and ruthenium benzylidene catalyst **7.2** developed by Grubbs *et al.*,[4] has helped olefin metathesis gain prominence in synthetic organic chemistry as a facile methodology for



7.1 **7.2** **7.3**

Figure 7.1. Olefin metathesis catalysts

olefin formation.[5,6] In particular, the combination of high activity and high functional group tolerance of late transition metal ruthenium metathesis catalysts such as **7.2** and **7.3**[7] has made the olefin metathesis reaction practical for small molecule and natural product synthesis.

The molybdenum imido catalyst **7.1** displays mixed reactivities toward 1,1-disubstituted olefins. While Wagener *et al.* showed this catalyst was able to polymerize 2-methyl-1,5-hexadiene via acyclic diene metathesis (ADMET) polymerization to reasonable molecular weights,[8] Crowe *et al.* found during cross-metathesis of the same diene with styrene that the geminally disubstituted olefin was unreactive (Figure 7.2).[9]

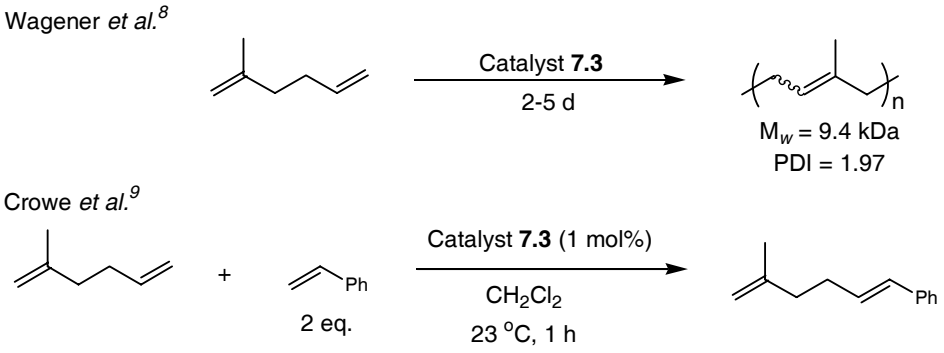
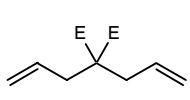
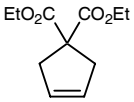
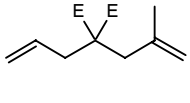
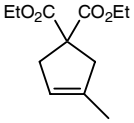
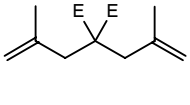
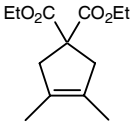


Figure 7.2. Reactivity of 1,1-disubstituted olefins in cross-metathesis with **7.3**

Ring-closing metathesis (RCM) reactions have been widely utilized in the construction of a variety of organic molecules.[6,10] The ring-closing metathesis activity of catalysts **7.1-3** with a

variety of substrates was examined by Grubbs *et al.*, as shown in Table **7.1**.[7a] While the molybdenum catalyst **7.1** is able to form even tetrasubstituted olefins via RCM, the less reactive bisphosphine-based ruthenium catalyst **7.2** affords only low yields of trisubstituted product and cannot form tetrasubstituted olefins. Fortunately, the development of *N*-heterocyclic carbene-based "second-generation" ruthenium metathesis catalysts such as **7.3** has resulted in catalysts with higher functional group tolerance than **7.2**, yet recovering much (if not all) of the activity loss associated with moving to a late transition metal.[2b,7] Catalyst **7.3** can produce trisubstituted olefins via RCM easily and can afford moderate yields of tetrasubstituted products as well. This

Table 7.1. Formation of substituted olefins via ring-closing metathesis[7a]

Substrate	Product	Time	^{1}H NMR Conversion 7.1	7.2	7.3
		10 min	quant.	quant.	quant.
		10 min	quant.	20 %	quant.
		24 h	93 %	0 %	31 %

E = CO_2Et

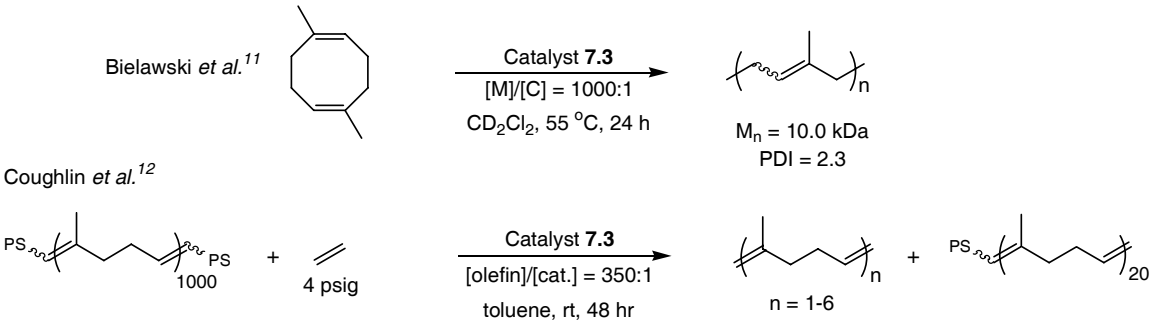
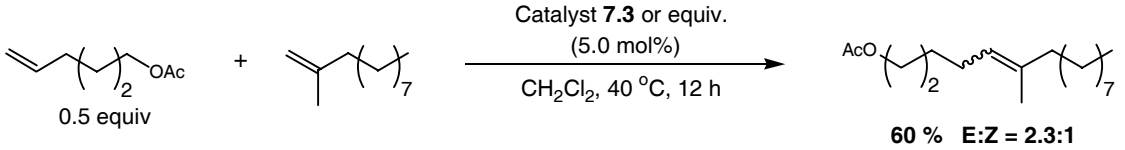


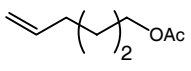
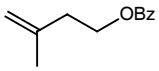
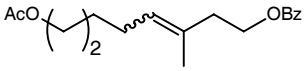
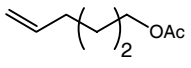
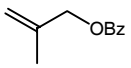
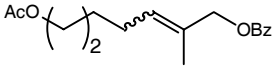
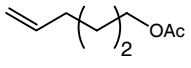
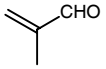
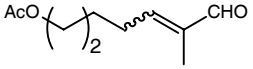
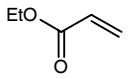
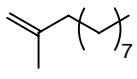
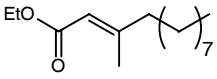
Figure 7.3. Polyisoprene structures in olefin metathesis catalyzed by **7.3**

increased tolerance to olefin substitution by **7.3** is also illustrated by its ability to polymerize 1,5-dimethyl-1,5-cyclooctadiene to form poly-1,4-isoprene[11] and to depolymerize poly(styrene-*b*-1,4-isoprene) in the presence of ethylene to polystyrene and polyisoprene oligomers (Figure 7.3).[12]

Formation of Trisubstituted Olefins via Cross-Metathesis The high functional group tolerance of **7.3**, coupled with its high reactivity with more substituted olefins, has renewed interest in the formation of trisubstituted olefins via intermolecular cross-metathesis.[1] Initial explorations showed that catalyst **7.3** is able to catalyze the formation of trisubstituted olefins from geminally disubstituted olefins with a wide variety of terminal olefins, including α,β-unsaturated carbonyl compounds, some of which are shown in Table 7.2.[1,13,14] Unfortunately, the low stereoselectivities of these reactions (an issue that has long complicated the use of cross-metathesis as a general synthetic technique) reduces the synthetic utility of the cross-metathesis approach.[5,15]

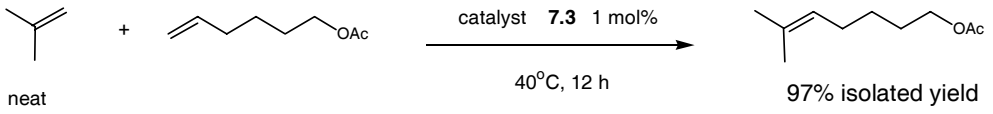
Table 7.2. Synthesis of trisubstituted olefins via cross-metathesis[1,13,14]

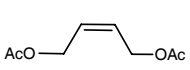
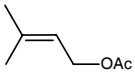
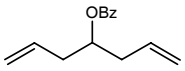
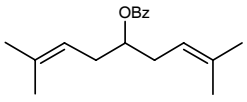
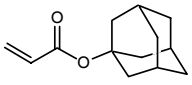
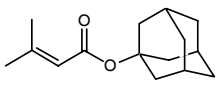
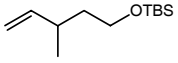
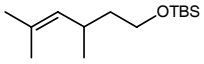
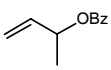
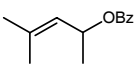


α-Olefin	1,1-Disubstituted Olefin	Product	Yield (%)	E/Z ratio
			80	2.8:1
			81	4.1:1
			92	> 20:1
			55	2:1

However, cross-metathesis reactions using disubstituted olefins with identical geminal substituents are not complicated by the issue of poor stereoselectivity. A number of 1,1-disubstituted olefins have been successfully employed in cross-metathesis using catalyst **7.3,** with isobutylene being the most important and convenient example.[16] Most importantly, these reactions offer a synthetically convenient alternative to Wittig-type olefinations of aldehydes in the formation of prenyl groups. A number of examples of cross-metathesis performed in neat isobutylene are shown in Table 7.3.[16] Although a small amount of tetramethylethylene (2,3-dimethyl-2-butene) was formed during the reaction, this background reaction did not lower overall cross-metathesis efficiency. The inability of isobutylene to undergo homodimerization via CM allows it to serve both as a reaction solvent and as an effective cross partner. This is evidenced by the very low amount of catalyst loading required relative to the amount of bulk olefin in the reaction (~ 0.0001 eq.).

Table 7.3. Cross-metathesis with isobutylene[16]



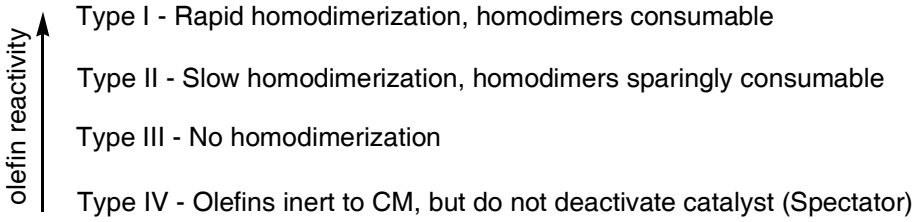
Entry	Metathesis Partner	Product	Isolated Yield
1			88
2			96
3			83
4			72
5			99

As a general synthetic technique, formation of trisubstituted olefins by ruthenium-catalyzed cross-metathesis is limited by the generally poor tolerance to geminal substituents larger than a methyl group.[1,13,14] In order to tune the ligand system of **7.3** to accommodate bulkier substituents or afford higher stereoselectivities, a more detailed understanding of the mechanistic pathway involved in this reaction is required. Isobutylene, with its low cost, ready availability, and symmetric structure, is the most promising geminally disubstituted olefin for use as a probe into the intricacies of this catalytic process.

Results and Discussion

Systematic evaluation of a wide variety of cross-metathesis reactions with a number of commercially available catalysts has enabled a general ranking of olefin reactivities to be established.[14] Since the actual catalytic process involves numerous ruthenium alkylidene intermediates reacting with starting materials to form products, undergoing degenerate metathesis, and performing secondary metathesis on product olefins, a complete understanding of the mechanistic pathways responsible for product formation requires a detailed analysis of a vary large number of substrate and catalyst specific rate constants. The empirical olefin categorization approach dramatically simplifies this analysis by generalizing reactivities of classes of olefins in terms of the accessibility of their respective ruthenium alkylidenes, their rates of homodimerization, and the susceptibility of their homodimers to undergo secondary metathesis events (Figure 7.4).[14]

Understanding of reactivities of general classes of olefin reactivities allows the prediction of product selective cross-metathesis reactions and facilitates the planning of cross-metathesis reactions as part of a larger synthetic effort. Selective reactions occur when olefins of different reactivities are employed in a cross-metathesis reaction. Since the less reactive olefin can only be consumed in reactions with the more reactive olefin (or its homodimer), as the reaction is driven to completion by the removal of ethylene the product mixture is driven towards the desired cross-product (Figure 7.5).[14]



Reaction between two olefins of Type I = *Statistical CM*
Reaction between two olefins of same type (Type II or III) = *Non-selective CM*
Reaction between olefins of two different types = *Selective CM*

Figure 7.4. Olefin categorization and rules for product selectivity[14]

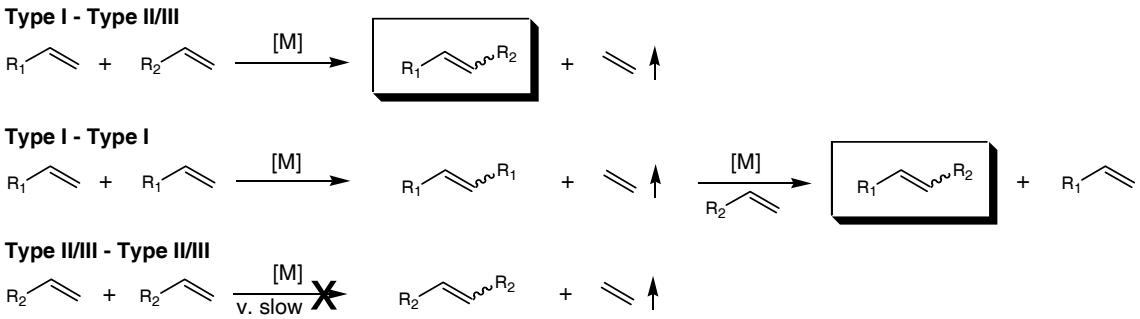


Figure 7.5. Primary reactions in cross-metathesis of Type I with Type II/III olefins[14]

While this approach is useful as a general guide towards the successful application of olefin metathesis in organic synthesis, it offers insufficient insight into the actual catalytic process upon which to base ligand and catalyst design decisions. In order to develop catalysts (i.e., ligand sets) with higher stereoselectivities, it would be useful to understand if the primary mechanistic pathway(s) involves coordination of the 1,1-disubstituted olefin to the monosubstituted ruthenium alkylidene, coordination of the α-olefin to the geminally disusbstituted ruthenium alkylidene, or both.

Kinetic Products of Catalyst Reactions with Substituted Olefins Consistent with earlier findings,[4b] the kinetic reaction product of ruthenium catalysts **7.3** with a simple terminal olefin such as propene (or *cis*-2-butene) is the formation of the ruthenium ethylidene **7.4** and styrene

(Figure 7.6). Because this pseudo-degenerate alkylidene "exchange" reaction is kinetically favored, CM reactions are driven to completion using Le Chatlier's principle (in this case, the removal of ethylene from the system). Only after extended reaction time was the ruthenium methylidene **7.5** characteristic of a productive metathesis event observed. The ability of olefins such as 3,3-dimethyl-1-butene to participate in CM reactions, yet not react to form the *t*-butyl-substituted ruthenium alkylidene, was rationalized by the ability of the metallacycle to form with the bulky *t*-butyl group located on the opposite corner of the metallacyclobutane ring.[4b] Because of the additional bulk of the geminal methyl groups of isobutylene, it was presumed that similar behavior would predominate and result in the formation of the ruthenium methylidene as the kinetic and thermodynamic product of the reaction between **7.3** and isobutylene. Surprisingly, NMR experiments showed that the ruthenium isopropylidene **7.6** was formed as the kinetic

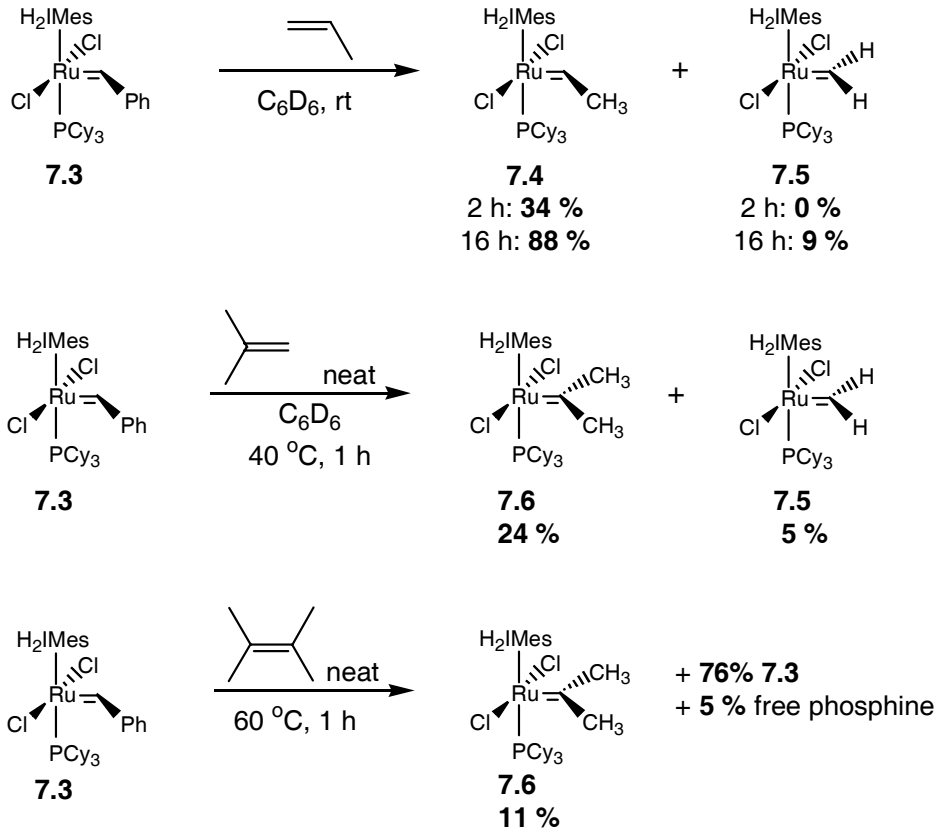


Figure 7.6. NMR initiation experiments with substituted olefins

product. Consistent with the low overall reactivity of isobutylene, this initiation reaction required heating at moderate temperatures for extended reaction times to achieve moderate conversions. Apparently, the additional sterics imparted by the geminal methyl groups is insufficient to disfavor the formation of the more electron rich ruthenium isopropylidene. During the extended reactions, **7.6** was observed to react with additional isobutylene to form 2,3-dimethyl-2-butene and methylidene **7.5.** Isopropylidene **7.6**, unlike the ruthenium benzylidenes **7.3**, is relatively unstable and could not be isolated by column chromatography from **7.5** and residual **7.3**. Use of more reactive catalysts such as the triphenylphosphine and bispyridine-based catalysts (**7.7** and **7.8**, respectively (Figure 7.7) led only to an acceleration of the overall process. The rates of initiation (L-type ligand dissociation) and further reaction are apparently similar between the benzylidene and isopropylidene.[17] Interestingly, NMR tube experiments show that the bisphosphine catalyst **7.2** also forms the isopropylidene as the kinetic product. If catalyst **7.2** can form the isopropylidene, it begs the question why this catalyst is unable to perform productive cross-metathesis with isobutylene.

Catalyst **7.3** was also able to initiate with the tetrasubstituted olefin 2,3-dimethyl-2-butene, albeit at higher temperatures and longer reaction times with low efficiency. This indicates the facile formation and reaction of tetrasubstituted olefins via intermolecular cross-metathesis is a future possibility. Catalyst **7.3** has sufficient reactivity to perform the reaction; however, the mesityl groups are perhaps too bulky to accommodate the additional sterics of the

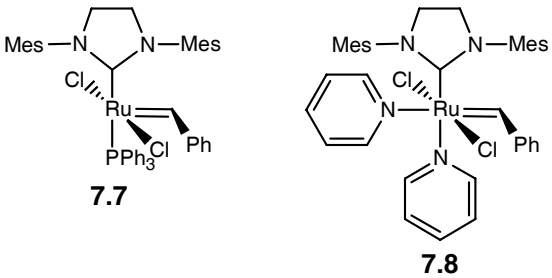


Figure 7.7. Metathesis catalysts with faster initiation rates

heavily substituted metallacycle. A number of approaches to scale back ligand bulk and enable the synthetically useful formation of tetrasubstituted olefins via RCM and CM are underway in our lab.[18]

Cross-Metathesis with 2-Methyl-2-Butene While the rate of reaction of **7.3** with simple terminal olefins is significantly higher than with isobutylene, the huge excess of isobutylene likely renders this process competitive. Unfortunately, the kinetic products of these reactions are not the desired cross-products. In order to design a reaction in which the *gem*-dimethyl groups would be transferred to the product olefin in the kinetic product, we sought to take advantage of the preference of the ruthenium catalysts to form electron rich alkylidenes while being tolerant of the bulk of a simple methyl group. 2-Methyl-2-butene seemed to be an ideal isobutylene surrogate for these types of cross-metathesis reactions. Reaction with the terminal olefin cross-partner should be much faster than with the trisubstituted olefin, ensuring a high relative concentration of the desired ruthenium alkylidene. The sterics and electronics of the subsequent metallacyclobutane formation should now lead to the desired cross-product being the kinetic product (as shown in Figure 7.8).

Productive reaction affords ruthenium isopropylidene and methyl-substituted product

Productive reaction affords ruthenium ethylidene and desired product

Figure 7.8. Regiochemistry of metallacyclobutane formation

Reaction of catalyst **7.3** with 2-methyl-2-butene affords exclusive production of the ruthenium ethylidene **7.4** as expected (Figure 7.9). In addition, this reaction proceeds more

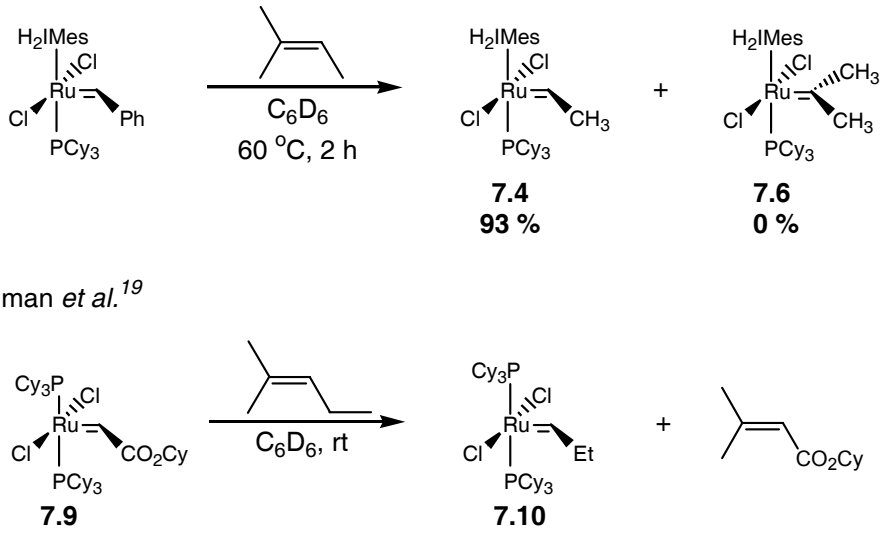
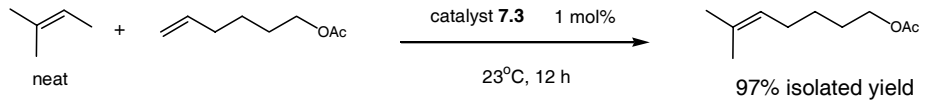


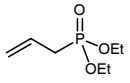
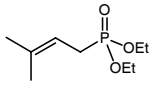
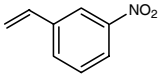
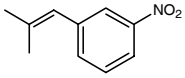
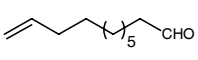
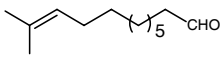
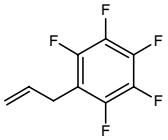
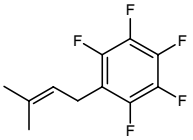
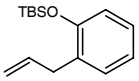
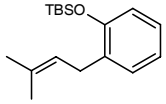
Figure 7.9. NMR initiation experiments with trisubstituted olefins

rapidly than reaction with the disubstituted isobutylene, indicating that benefits of the more electron rich olefin and less bulky resultant alkylidene outweigh the steric hindrance due to the additional methyl group during metallacyclobutane formation. The regioselectivity of the cross-metathesis reaction is identical to that observed by Ulman *et al.* with the bisphosphine-based enoic carbene **7.9**.[19] While the parent catalyst **7.2** was unreactive with trisubstituted olefins, catalyst **7.9** undergoes one turnover with 2-methyl-2-pentene to afford the ruthenium ethylidene **7.10** exclusively.

Unlike the high boiling tetrasubstituted 2,3-dimethyl-2-butene (bp 73 °C), 2-methyl-2-butene (bp 35-38 °C) serves as a synthetically useful isobutylene surrogate in cross-metathesis (Table 7.4).[16] The higher boiling point of 2-methyl-2-butene relative to isobutylene allows for reactions to be run with a standard reflux condenser rather than in more specialized pressure vessels and the higher reactivity of 2-methyl-2-butene allows reactions to be run efficiently at room temperature with lower catalyst loadings (~1 mol%). In addition to greatly enhancing the synthetic ease of the reaction relative to the use of isobutylene, this use of 2-methyl-2-butene represents the first productive CM of trisubstituted olefins at room temperature. Cross-metathesis

Table 7.4. Cross-metathesis with 2-methyl-2-butene[16]



Entry	Metathesis Partner	Product	Isolated Yield
1			97
2			96
3			91
4			91
5			99

with diethyl allylphosphonate (Entry 1, Table 7.4) affords diethyl prenylphosphonate, a useful Wittig-type reagent. Unprotected aldehydes are readily tolerated as well, illustrating the direct orthogonality of this cross-metathesis approach to Wittig methods (Entry 4, Table 7.4). Perhaps the most important example is the CM reaction with a protected phenolic allylbenzene, affording nearly quantitative yields of the prenyl compound (Entry 5 Table 7.4). This cross-metathesis reaction is a convenient alternative to the standard synthetic route involving the Claisen rearrangement of a tertiary allylic phenoxy ether.

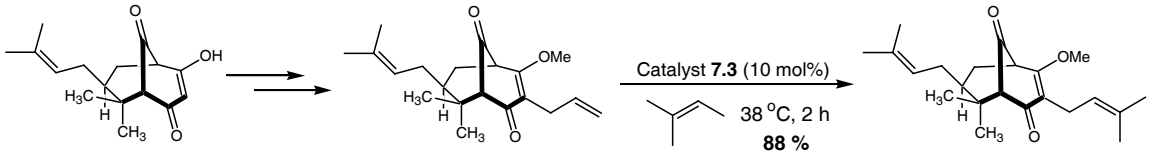


Figure 7.10. Synthesis of polyprenylated core of Garsubellin A[20]

This CM methodology has been employed by Stoltz *et al.* in the synthesis of the bicyclic core of the polyprenylated phloroglucin natural product Garsubellin A (as shown in Figure 7.10). In this synthesis, installation of an allyl group via a simple alkylation is followed by a Claisen rearrangement. Conversion of the allyl group to a prenyl group was achieved in high yield via cross-metathesis with 2-methyl-2-butene. This masking of prenyl groups as more robust allyl groups capable of being converted to prenyl groups via metathesis with 2-methyl-2-butene is being considered as the end-game strategy of other planned syntheses of polycyclic polyprenylated acylphloroglucinols.[21]

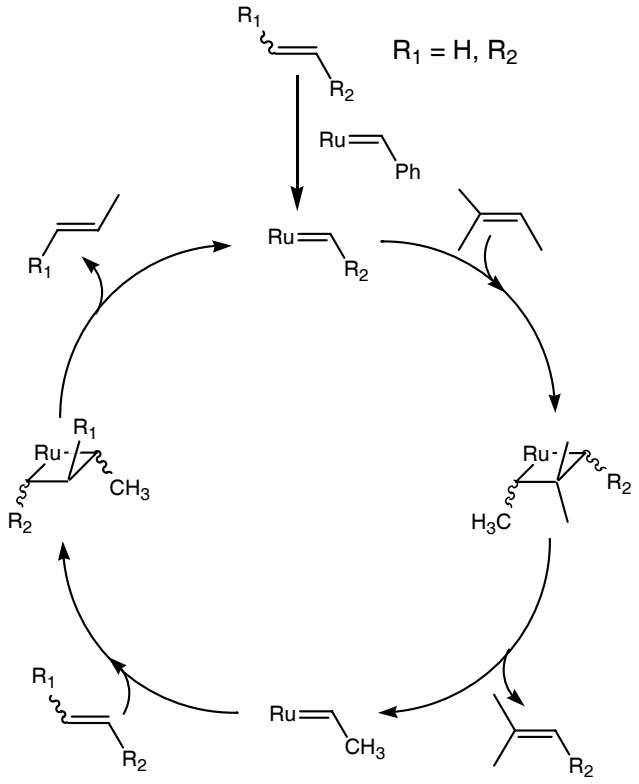
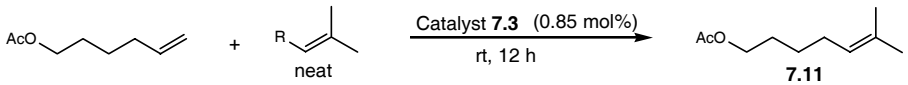


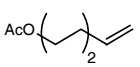
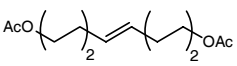
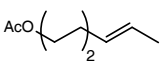
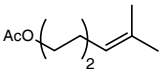
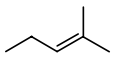
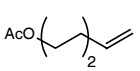
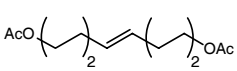
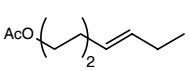
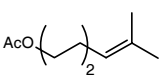
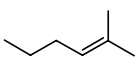
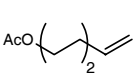
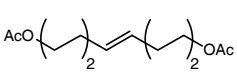
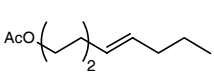
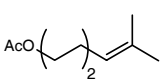
Figure 7.11. Proposed 2-methyl-2-butene cross-metathesis reaction pathway

These results indicate that the general reaction pathway for 2-methyl-2-butene cross-metathesis is that shown in Figure 7.11. Due to the higher reactivity of terminal olefins towards

CM, a significant portion of the terminal olefin may homodimerize via self-metathesis before the CM reaction with 2-methyl-2-butene (represented by $R_1 = R_2$). However, these homodimers are still generally more reactive than a trisubstituted olefin, ensuring facile access to the appropriately substituted ruthenium alkylidene. Cross-metathesis with 2-methyl-2-butene produces the ruthenium ethylidene and the geminally dimethyl-substituted product. Depending upon the nature of R_2, this trisubstituted olefin may be kinetically resistant to further metathesis. The ruthenium ethylidene reacts with another equivalent of olefin to regenerate the appropriate ruthenium alkylidene and release a methyl-substituted olefin. In the case where R_1 = H or CH_3, this volatile propene or 2-butene boils off at room temperature effectively removing the methyl endgroups from the reaction and driving the reaction towards the desired product. Higher molecular weight homologues of 2-methyl-2-butene such as 2-methyl-2-pentene and 2-methyl-2-hexene may be used as well; however, the higher boiling butene and pentene fragments are more difficult to drive out of the system at room temperature, resulting in a larger fraction of ethyl- and propyl-substituted products (Table 7.5).

Table 7.5. Cross-metathesis with 2-methyl-2-butene homologues



Trisubstituted Olefin	^{1}H NMR Product Distribution				
	 0%	3%	 7.12	 5%	 92%
	 0%		 0%	 17%	 83%
	 18%		 21%		 61%

Reaction with 2-methyl-2-butene performed by Arnab K. Chatterjee (Grubbs Group)

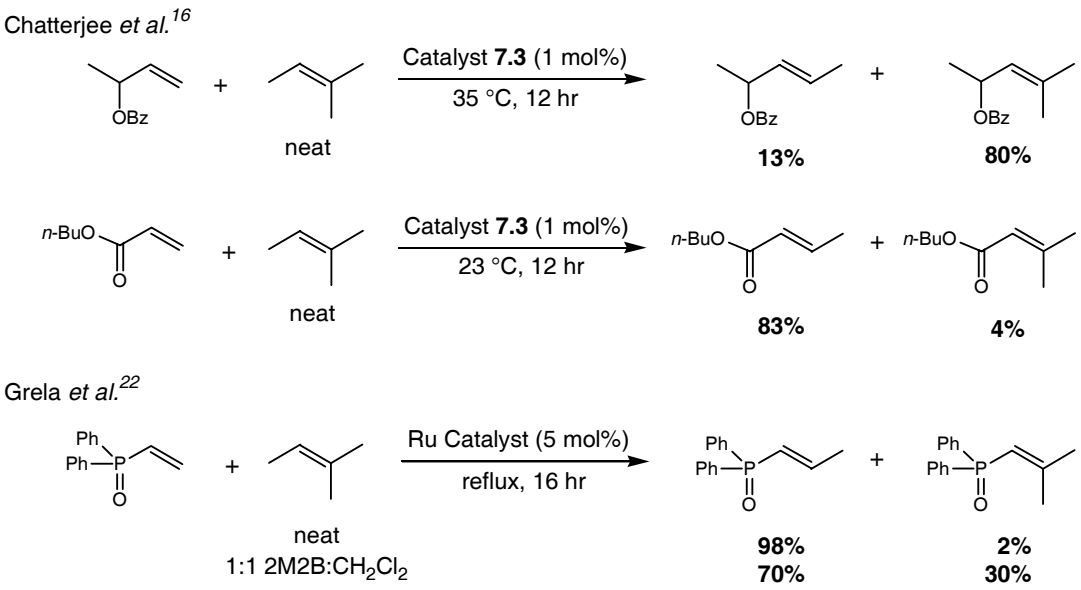


Figure 7.12. 2-Methyl-2-butene cross-metathesis with less active olefins[16]

While cross-metathesis with 2-methyl-2-butene is highly efficient for reactive olefins (Type I olefins), reaction with the less reactive allylic benzoate (Figure 7.12) results in a 6:1 mixture of dimethyl- and methyl-substituted products which cannot be driven to produce the desired cross-product in high conversion.[16] With even more unreactive olefins (Type II olefins, Figure 7.4), a mechanistic reversal is observed. This reversal is exemplified by the cross-metathesis of *n*-butyl acrylate with 2-methyl-2-butene which affords *E*-*n*-butyl crotonate in 83% conversion by ^{1}H-NMR.[16]

Unlike the examples shown in Table 7.4, when it is unfavorable for the terminal olefin to cross onto the ruthenium (such as in the case of acrylates), a second reaction pathway illustrated in Figure 7.13 is primarily responsible for the observed product distribution. In this system, the 2-methyl-2-butene is the more reactive olefin and reacts with the catalyst to produce a ruthenium ethylidene. This ethylidene species undergoes a productive metathesis reaction with the terminal olefin to produce a methyl-substituted olefin and ruthenium methylidene. The methylidene subsequently reacts with the large excess of 2-methyl-2-butene to produce isobutylene and

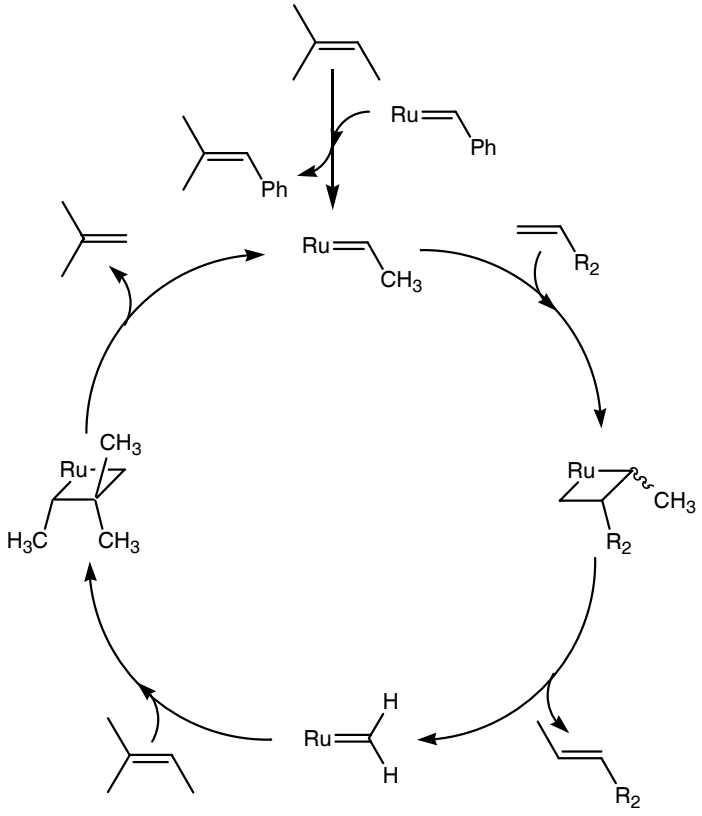


Figure 7.13. Proposed cross-metathesis pathway with less reactive olefins

regenerate the propagating ethylidene. In this pathway, the isobutylene boils off and effectively removes the geminal methyl endgroups from the reaction, resulting in the preferential generation of methyl-substituted olefins. With these less reactive olefinic substrates, the 2-methyl-2- butene may serve as practical substitute for propene or 2-butene in cross-metathesis. In terms of the categorization model discussed previously, 2-methyl-2-butene lies somewhere on the boundary between Types II and III. It serves as a moderately reactive Type III olefin when reacting with Type I and Type II olefins; however, its ability to form a new ruthenium ethylidene by reacting with the catalyst presumably will allow it to act like a Type II olefin during reaction with Type III olefins.

Grela *et al.* have subsequently employed this methodology in the synthesis of diphenyl-(*Z)*-prop-1-enyl phosphine oxide from diphenyl vinylphosphine oxide (Figure 7.12).[22] Using neat

2-methyl-2-butene, the methyl to dimethyl-substituted product ratio was 98:2; however, using less trisubstituted olefin (1:1 2-methyl-2-butene:CH_2Cl_2) resulted in a significantly higher ratio of disubstituted product (70:30).[22] Grela's results offer additional support for the mechanistic pathways for metathesis with 2-methyl-2-butene outlined here.

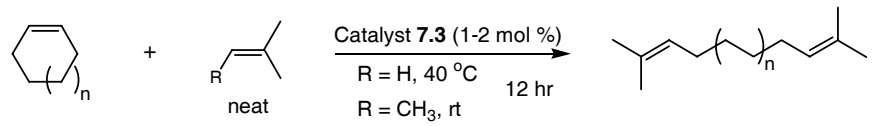
In order to convert simple terminal olefins into prenyl groups, cross-metathesis with 2-methyl-2-butene is the preferred methodology. However, given the inability to separate the methyl-substituted products via standard silica gel chromatography, cross-metathesis with isobutylene is the preferred route to the desired cross-product with substrates that form methyl-substituted products resistant to secondary metathesis and the only route to exclusively dimethyl-substituted products when less reactive olefins (such as Type II olefins) are used.

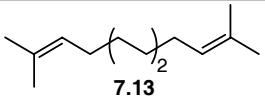
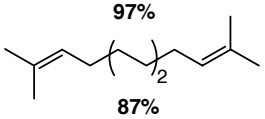
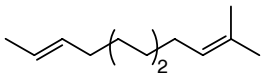
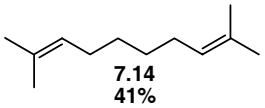
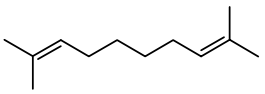
Formation of Trisubstituted Olefins via Ring-Opening Cross Metathesis Ring-opening cross-metathesis (ROCM) involves the ring-opening metathesis of a cyclic olefin in the presence of an acyclic olefin to generate a ring-opened structure with functionalized end-groups. Recent work has shown that 5-and 6-membered rings such as cyclopentene and cyclohexene with low ring-strain can be ring-opened in the presence of an electron deficient olefin such as an acylate in moderate yields.[5b, 23] While the equilibria in these reactions lie heavily on the side of the ring-closed starting material, ring-opening reactions which lead to the formation of an electron-deficient olefin such as the α, β-unsaturated ester allow the olefin to resist the secondary metathesis necessary for ring-closing.[24] The high reactivity of the electron-deficient ruthenium enoic carbenes results in the formation of monomeric and ring-opened structures with α, β-unsaturated ester endgroups.[23a] Instead of relying on olefin electronics to afford ring-opened product, use of sterically bulky endgroups should offer similar capabilities. As shown previously, the reluctance of the catalyst to couple *gem*-dimethyl-substituted olefins to form 2,3-dimethyl-2-butene is greater than its reluctance to couple α, β-unsaturated esters to form fumarates or

maleates.[14] Therefore, ROCM of cyclohexene in isobutylene should afford the monomeric 2,9-dimethyl-2,9-decadiene.

The ROCM of cyclooctene and cyclohexene with isobutylene and 2-methyl-2-butene are shown in Table 7.6. The higher ring-strain of cyclooctene results in quantitative conversion of ring-opened product. The lower reactivity of internal olefins slows secondary metathesis and results in a small amount of monomethyl-substituted product in the case of 2-methyl-2-butene. With cyclohexene, only the product with both olefins capped with *gem*-dimethyl groups is sufficiently resistant to subsequent RCM. Both isobutylene and 2-methyl-2-butene offer similar conversions under identical conditions (pressure vessel, 40 °C). These results are comparable to the results of ROCM using acrylates.[23a,b]

Table 7.6. Ring-opening cross-metathesis of cyclic olefins

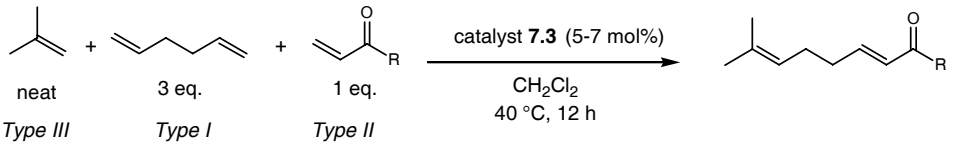


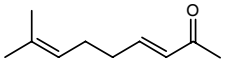
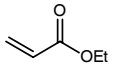
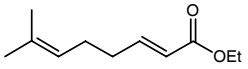
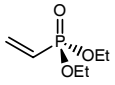
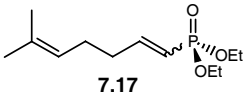
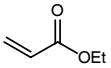
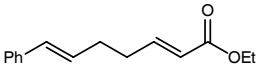
Trisubstituted Olefin	Cyclic Olefin	Products (% isolated yield)
		 **7.13** **97%**
		 **87%**  **13%**
		 **7.14** **41%**
		 **19%** RT **29%** F-P bottle, 40 °C

ROCM of cyclohexene with isobutylene performed in conjuction with Arnab K. Chatterjee (Grubbs Group)

Three Component Olefin Metathesis Reactions: As mentioned previously, use of the categorization model allows for the design of highly selective cross-metathesis reactions. One of the first reactions to be conceived by this approach was a three component coupling reaction between a Type I α,ω-diene and Type II and Type III olefin.[14] The inability of the Type II and Type III olefins to efficiently couple via metathesis is the key to preventing these olefins from being consumed in non-productive metathesis reactions. The ability of isobutylene to serve as a reactive solvent and as a Type III olefin makes it an ideal choice for such a reaction. Three component coupling reactions between 1,5-hexadiene, isobutylene, and a variety of Type II olefins are shown in Table 7.7.[14] Coupling of a Type I and a Type II olefin to a Type I α,ω-diene in a stepwise reaction (Entry 4, Table 7.7) is considerably less efficient than using a Type III olefin in a simultaneous one-pot strategy (Entries 1-3, Table 7.7).

Table 7.7. Three component cross-metathesis reactions[14]



Entry	Method	CM partner Y	CM partner Z	Ratio (Diene:Y:Z)	Product	Isolated Yield (%)
1[a]	A			3:neat:1	 **7.15**	89
2	A			3:neat:1	 **7.16**	60
3	A			1:neat:1	 **7.17**	57[b]
4[a]	B			1:3:1	 **7.18**	34

[a] Reaction performed by Arnab K. Chatterjee (Grubbs Group) [b] *E/Z* = 8:1 by ^{1}H NMR [c] Reaction at 23 °C
Method A = Added all components at one time
Method B = Added component Z, then added component Y after 4 hours

The origin of the remarkably high product selectivity in the reaction can be understood by looking at the various mechanistic pathways outlined in Figure 7.14. Since the isobutylene solvent is the least active towards metathesis, the majority of the α,ω-diene starting material is preferentially consumed in cross-metathesis reactions with the Type II acrylate or in self-metathesis reactions leading to oligoalkenamers. Stoichiometry is used to ensure roughly one Type II olefin is coupled to each α,ω-diene. The remaining terminal olefins undergo reaction with the Type III olefin. If an α,ω-diene is capped on both ends by *gem*-dimethyl endgroups, these trisubstituted olefins are simple 2-methyl-2-butene homologues which will react regioselectively with the Type II olefin to form the desired product. Presumably, any olefin formed via the reaction of the α,ω- diene with the Type II olefin is the least reactive olefin towards secondary metathesis and redistribution. Since premature coupling of all the isobutylene to form 2,3-dimethyl-2-butene is unlikely, the key limiting reactions (provided the catalyst is

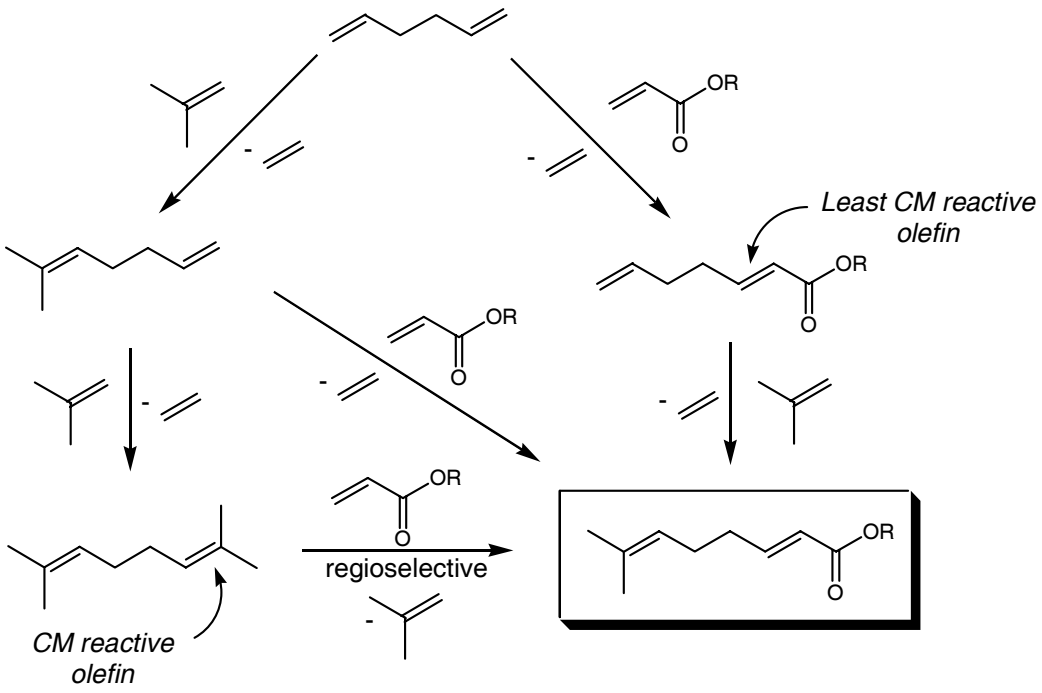


Figure 7.14. Mechanistic pathways for 3-component cross-metathesis reaction

sufficiently long-lived) are the homodimerization of the Type II olefin and cross-metathesis of the Type II olefin with isobutylene, both of which form a product olefin (such as a fumarate) which is kinetically inert to further metathesis.

Conclusions

In conclusion, a mechanistic understanding of the cross-metathesis reactions between isobutylene and terminal olefins employing the ruthenium benzylidenes catalyst **7.3** has been presented. This mechanistic understanding of the reactivity of olefins with various substitution patterns with the ruthenium catalyst has enabled the discovery of the ability of 2-methyl-2-butene to serve as a synthetically convenient surrogate for the gaseous olefins isobutylene or propene/2-butene in cross-metathesis reactions with Type I and Type II olefin cross-partners, respectively. Of particular interest is the convenient conversion of terminal olefins to prenyl groups. In order to achieve exclusively trisubstituted olefin cross-products, the more convenient 2-methyl-2-butene may be employed with reactive terminal olefins; however, the more rigorous route using isobutylene must be employed with less reactive substrates to prevent the formation of 1,2-disubstituted products. Ring-opening cross-metathesis of unstrained cyclic olefins may be achieved using geminally-disubstituted olefin cross-partners. In addition, the unique reactivity of isobutylene and prenyl-type olefins in cross-metathesis has allowed the development of highly product-selective three-component cross-metathesis reactions. In total, these methods allow for the efficient one-step formation of trisubstituted olefins under mild reaction conditions and low catalyst loadings, and further demonstrate the utility of olefin metathesis in organic synthesis.

Experimental

Materials: All air sensitive manipulations and polymerizations were carried out in an N_2-filled drybox or using standard Schlenk techniques. All solvents were rigorously degassed in 18 L reservoirs and passed through two sequential purification columns consisting of activated alumina.[25] All starting materials were procured from Aldrich and used as received unless

otherwise noted. Ruthenium olefin metathesis catalysts **7.2** and **7.3** were obtained from Materia, Inc. Catalysts **7.7** and **7.8** were synthesized according to the literature procedures.[26]

***Methods**:* Nuclear magnetic resonance (NMR) spectra were obtained using a Varian *Mercury 300* spectrometer (^{1}H: 300 MHz, ^{13}C: 75 MHz). Shifts for NMR spectra are reported in ppm relative to the chemical shift of the residual proteo solvent. ^{31}P NMR spectra are reference to an external H_3PO_4 standard ($\delta = 0$). High-resolution mass spectra (EI and FAB) were provided by either the Caltech Mass Spectrometry Facility or the UCLA Mass Spectrometry Facility (University of California, Los Angeles).

Typical Isobutylene Cross-Metathesis Procedure: To an oven dried, 100 mL Fischer-Porter bottle with Teflon stir bar, ruthenium metathesis catalyst (15.0 mg, 0.018 mmol, 1.0 mol%) was added. The bottle was capped with a rubber septum and flushed with dry nitrogen and cooled to -78 °C (or temperature sufficient to freeze substrate). Substrate (1.0 mmol) was injected into the bottle. Once the substrate was frozen, a pressure regulator was attached to the bottle. The bottle was evacuated and backfilled with dry nitrogen 3 times. Subsequently, isobutylene (5-10 mL, 50-100 equiv.) was condensed into the bottle. The bottle was backfilled to ~2 psi with nitrogen, sealed, and allowed to slowly warm to room temperature, at which time it was transferred to an oil bath at 40 °C. After stirring for 12-18 hours, the bottle was removed from the oil bath and allowed to cool to room temperature. The isobutylene was slowly vented off at room temperature until the pressure apparatus could be safely disassembled. The remaining mixture was taken up in organic solvent for subsequent purification via silica gel chromatography and/or spectroscopic characterization.

Typical 2-Methyl-2-Butene Cross-Metathesis Procedure: Substrate (1.5 mmol) and 2-methyl-2-butene (3.2 mL) were added simultaneously via syringe to a flask containing catalyst **7.3** (0.015 mmol, 1.0 mol%) equipped with a reflux condenser under a nitrogen atmosphere. The reaction was allowed to stir at room temperature while cold water was circulated through the reflux

condenser to prevent evaporation of 2-methyl-2-butene. After 12 hours, the reaction mixture was reduced in volume to 0.5 mL and purified directly on a silica gel column to provide the cross-metathesis product.

Typical NMR Initiation Reaction: In a N_2-filled drybox, catalyst **7.3** (15.0 mg, 17.6 μmol) was added to screw-cap NMR tube along with 1 mL of C_6D_6. A teflon septum screwcap was used to seal the NMR tube. The substrate olefin was added to the NMR tube using microsyringe injection for liquid olefins or by bubbling the gaseous olefin through the NMR tube solution for 2-5 minutes with the aid of a long needle attached to the tank regulator. The NMR tube was heated in a temperature-controlled oil bath and removed at designated intervals for spectroscopic analysis.

(H_2Imes)(PCy_3)Cl_2Ru(=CHMe) (7.4). The ruthenium ethylidene was independently synthesized via reaction of **7.3** with cis-2-butene or propene. ^{31}P NMR (C_6D_6): δ = 29.05 (s). ^{1}H NMR (C_6D_6): δ = 19.03 (q, *J* = 5.7 Hz, 1H, Ru=C*H*CH_3), 2.81 (s, 6H, ortho CH_3), 2.57 (s, 6H, ortho CH_3), 2.18 (s, 3H, para CH_3), 2.10 (s, 3H, para CH_3), 1.91 (d, *J* = 5.7 Hz, 3H, Ru=CHC*H*$_3$).

(H_2Imes)(PCy_3)Cl_2Ru(=CH_2) (7.5). For complete spectroscopic characterization of the ruthenium methylidene, see reference 7b.

(H_2Imes)(PCy_3)Cl_2Ru(=C(CH_3)$_2$) (7.6). The ruthenium isopropylidene is extremely air sensitive and decomposes rapidly upon exposure to air. Only moderate amounts of isopropylidene in a mixture of other catalyst species could be obtained. As such, isolation via standard techniques was not possible. The isopropylidene could only be characterized via NMR spectroscopy. The far upfield shift of the tricyclohexylphosphine resonance is consistent with the shift observed by Trnka et al. for a related cyclic disubstituted complex (H_2Imes)(PCy_3)Cl_2Ru(=C(CH_2)$_3$).[27] ^{31}P NMR (C_6D_6): δ = 19.94 (s). ^{1}H NMR (C_6D_6): δ = 2.85 (s, 6H, ortho CH_3), 2.57 (s, 6H, ortho CH_3), 2.26 (s, 6H, Ru=C(C*H*$_3$)$_2$), 2.21 (s, 3H, para CH_3), 2.14 (s, 3H, para CH_3).

Reaction of 5-Hexenyl-1-Acetate with:

(A). 2-Methyl-2-butene. 2-Methyl-2-butene (3.0 mL) and 5-hexenyl-1-acetate (230 μL, 1.47 mmol) were reacted according to the general procedure (see above) using catalyst **7.3** (11 mg, 0.013 mmol, 0.85 mol%) under a nitrogen atmosphere for 12 hours. The flask was allowed to stir at room temperature for 12 hours. ^{1}H NMR analysis of the initial product distribution (analysis of vinylic protons) indicated the presence of 92% 2-methyl-hept-2-enyl-7-acetate (**7.11**), ~ 5% 5-heptenyl-1-acetate (**7.12**), and 3% 1,10-diacetoxy-*trans*-5-decene(**7.13**).

(B). 2-Methyl-2-pentene. 2-Methyl-2-pentene (1.18 g, 1.73 mL) and 5-hexenyl-1-acetate (0.200 g, 220 μL, 1.41 mmol) were reacted according to the general procedure (see above) using catalyst **7.3** (10.2 mg, 0.012 mmol, 0.85 mol%) under a nitrogen atmosphere for 12 hours. The flask was allowed to stir at room temperature for 12 hours. ^{1}H NMR analysis of the initial product distribution (analysis of vinylic protons) indicated the presence of 83% 2-methyl-hept-2-enyl-7-acetate (**7.11**), 17% 5-octenyl-1-acetate (**7.12**).

(C). 2-Methyl-2-hexene. 2-Methyl-2-hexene (3.0 mL) and 5-hexenyl-1-acetate (0.200 g, 220 μL, 1.41 mmol) were reacted according to the general procedure (see above) using catalyst **7.3** (10.2 mg, 0.012 mmol, 0.85 mol%) under a nitrogen atmosphere for 12 hours. The flask was allowed to stir at room temperature for 12 hours. ^{1}H NMR analysis of the initial product distribution (analysis of vinylic protons) indicated the presence of 61% 2-methyl-hept-2-enyl-7-acetate (**7.11**), ~ 21% 5-octenyl-1-acetate/1,10-diacetoxy-*trans*-dec-5-ene(**7.12**), and 18% 5-hexenyl-1-acetate starting material.

2-Methyl-hept-2-enyl-7-acetate (7.11). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.10 (tm, J = 5.4 Hz, 1H), 4.06 (2H, t, J = 6.9 Hz), 2.05 (s, 3H), 2.01 (m, 2H), 1.69 (s, 3H), 1.60 (s, 3H), 1.70-1.55 (m, 2H), 1.41-1.31 (m, 2H). R_f = 0.32 (20:1 hexane:ethyl acetate). HRMS-[GC-EI+] (m/z): [M•]+ calc'd for $C_{10}H_{18}O_2$, 170.1307; found, 170.1315.

1,10-Diacetoxy-*trans*-dec-5-ene (7.12). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.37 (t, J = 3.6 Hz, 2H, m), 4.02 (4H, t, J = 6.6 Hz, 4H), 2.02 (s, 6H), 2.00 (m, 4H), 1.60(m, 4H), 1.38 (m, 4H). R_f = 0.31 (85:15 hexane:ethyl acetate). ^{13}C NMR ($CDCl_3$, 75 MHz, ppm): δ 171.41, 130.40, 64.63, 32.25, 28.21, 25,96, 21.17. HRMS-[GC-EI+] (m/z): [M•]+ calc'd for $C_{14}H_{24}O_4$, 256.1675; found, 256.1664.

Ring-Opening Cross-Metathesis of Cyclic Olefins:

2,11-Dimethyl-dodeca-2,10-diene (7.13). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.13 (t, J = 2.5 Hz, 2H), 1.97 (d, J = 6.9 Hz, 4H), 1.69 (s, 6H), 1.61 (s, 6H), 1.29 (m, 8H). R_f = 0.87 (20:1 hexane:ethyl acetate). ^{13}C NMR ($CDCl_3$, 75 MHz, ppm): δ 131.29, 125.13, 30.08, 29.44, 28.23, 25.91, 17.85. HRMS-[GC-EI+] (m/z): [M•]+ calc'd for $C_{14}H_{26}$, 194.2035; found, 194.2038.

2,9-Dimethyl-deca-2,8-diene (7.14). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.13 (t, J = 2.5 Hz, 2H), 1.97 (d, J = 6.9 Hz, 4H), 1.70 (s, 6H), 1.61 (s, 6H), 1.33 (m, 4H). R_f = 0.90 (20:1 hexane:ethyl acetate). HRMS-[GC-EI+] (m/z): [M•]+ calc'd for $C_{12}H_{22}$, 166.1722; found, 166.1707.

Three Component Cross-Metathesis Reactions:

For characterization of **7.15** and **7.18**, see reference 14.

9-Methyl-deca-2,8-dienoic acid ethyl ester (7.16). 1,5-Hexadiene (266 μL, 2.25 mmol) and ethyl acrylate (81 μL, 0.75 mmol) were reacted with catalyst **7.3** (31.8 mg, 0.037 mmol, 5.0 mol%) according to the general isobutylene cross-metathesis procedure. After 12 hours at 40 °C, the reaction mixture was then reduced in volume to 0.5 ml and purified directly on a silica gel column (4x15 cm), eluting with 20:1 pentanes:diethyl ether to afford a clear oil (82 mg, 0.45 mmol, 60% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.92 (dt, J = 15.6, 6.3 Hz, 1H), 5.77 (dt, J = 15.6, 1.5 Hz, 1H), 5.12-5.02 (m, 1H), 4.13 (q, J = 7.2 Hz, 2H), 2.26-2.05 (m, 4H), 1.64 (s, 3H), 1.56 (s, 3H), 1.24 (t, J = 7.8 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ 166.85, 149.08,

132.86, 123.04, 121.56, 60.25, 32.59, 26.73, 25.80, 17.85, 14.41. R_f = 0.39 (20:1 hexane:ethyl acetate). HRMS (GC-EI) calcd for $C_{11}H_{18}O_2$ [M•] 182.1307, found 182.1314.

(8-Methyl-nona-1,7-dienyl)-phosphonic acid diethyl ester (7.17). 1,5-Hexadiene (266 μL, 2.25 mmol) and diethyl vinyl phosphonate (115 μL, 0.75 mmol) were reacted with catalyst **7.3** (31.8 mg, 0.037 mmol, 5.0 mol%) according to the general isobutylene cross-metathesis procedure. After 12 hours at 40 °C, the reaction mixture was then reduced in volume to 0.5 ml and purified directly on a silica gel column (4x15 cm), eluting with 1:2 hexane:ethyl acetate to afford a clear oil (104 mg, 0.427. mmol, 57% yield) *E:Z* = 8:1. *E* isomer: ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.85-6.60 (m, 1H), 5.59 (dd, *J* = 21.3, 17.1 Hz, 1H,), 5.10-4.95 (m,1H), 4.01 (q, *J* = 7.2 Hz, 4H,), 2.35-2.00 (m, 4H), 1.62 (s, 3H), 1.54 (s, 3H), 1.26 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ 153.66, 132.89, 122.92, 117.07 (d, *J* = 186 Hz), 61.73, 53.58, 34.58, 34.30, 26.47, 25.79, 17.87, 16.53. ^{31}P NMR (121 MHz, $CDCl_3$, ppm): δ 19.85. R_f = 0.24 (1:2 hexane:ethyl acetate). HRMS (FAB) calcd for $C_{12}H_{24}O_3P$ $[M + H]^+$ 247.1463, found 247.1455.

References and Notes

(1) Chatterjee, A. K.; Grubbs, R. H. *Org. Lett.* **1999**, *1*, 1751-1753 and references therein.

(2) For recent reviews on development of olefin metathesis catalysts, see: (a). Schrock, R. R. In *Handbook of Olefin Metathesis*, vol 1., Grubbs, R. H., Ed. Wiley-VCH, **2004**, pp. 8-32. (b). Nguyen, S. T..; Trnka, T. M. In *Handbook of Olefin Metathesis*, vol 1., Grubbs, R. H., Ed. Wiley-VCH, **2004**, pp. 61-85. (c). Grubbs, R. H. *Tetrahedron* **2004**, *60*, 7117-7140. (d). Trnka, T. M.; Grubbs, R. H. *Acc. Chem. Res.* **2001**, *34*, 18-29.

(3) (a). Schrock, R. R.; Murdzek, J. S.; Bazan, G. C.; Robbins, J.; Dimare, M.; O'Regan, M. *J. Am. Chem. Soc.* **1990**, *112*, 3875-3886. (b). Bazan, G. C.; Khosravi, E.; Schrock, R. R.; Feast, W. J.; Gibson, V. C.; O'Regan, M. B.; Thomas, J. K.; Davis, W. M. *J. Am. Chem.*

Soc. **1990**, *112*, 8378-8387. (c). Bazan, G. C.; Oskam, J. H.; Cho, H. N.; Park, L. Y.; Schrock, R. R. *J. Am. Chem. Soc.* **1991**, *113*, 6899-6907.

(4) (a). Schwab, P.; France, M. B.; Ziller, J. W.; Grubbs, R. H. *Angew. Chem. Int. Ed. Eng.* **1995**, *34*, 2039-2041. (b). Schwab, P.; Grubbs, R. H.; Ziller, J. W. *J. Am. Chem. Soc.* **1996**, *118*, 100-110. (c). Belderrain, T. R.; Grubbs, R. H. *Organometallics* **1997**, *16*, 4001-4003.

(5) For recent reviews on olefin cross-metathesis, see: (a). Chatterjee, A. K. In *Handbook of Olefin Metathesis*, vol 2., Grubbs, R. H., Ed. Wiley-VCH, **2004**, pp. 246-295. (b). Connon, S. J.; Blechert, S. *Angew. Chem. Int. Ed.* **2003**, *42*, 1900-1923.

(6) For recent reviews on the application of olefin metathesis to the synthesis of small and complex molecules, see: (a). Love, J. A. In *Handbook of Olefin Metathesis*, vol 2., Grubbs, R. H., Ed. Wiley-VCH, **2004**, pp. 296-322. (b). Furstner, A. *Angew. Chem. Int. Ed.* **2000**, *39,* 3012-3043.

(7) (a). Scholl, M.; Ding, S.; Lee, C. W.; Grubbs, R. H. *Org. Lett.* **1999**, *1*, 953-956. (b). Sanford, M. S.; Love, J. A.; Grubbs, R. H. *J. Am. Chem. Soc.* **2001**, *123*, 6543-6554.

(8) Konzelman, J.; Wagener, K. B.; *Macromolecules* **1995**, *28*, 4686-4692.

(9) Crowe, W. E.; Zhang, Z. *J. Am. Chem. Soc.* **1993**, *115*, 10998-10999.

(10) For reviews on ring-closing metathesis, see: (a). Maier, M. E. *Angew. Chem. Int. Ed.* **2000**, *39*, 2073-2077. (b). Grubbs, R. H.; Miller, S. J.; Fu, G. C. *Acc. Chem. Rec.* **1995**, *28*, 446-452.

(11) Bielawski, C. W.; Grubbs, R. H. *Angew. Chem. Int. Ed.* **2000**, *39*, 2903-2906.

(12) Craig, S. W.; Manzer, J. A.; Coughlin, E. B. *Macromolecules* **2001**, *34*, 7929-7931.

(13) Chatterjee, A. K.; Morgan, J. P.; Scholl, M.; Grubbs, R. H. *J. Am. Chem. Soc.* **2000**, *122*, 3783-3784.

(14) Chatterjee, A. K.; Choi, T.-L.; Sanders, D. P.; Grubbs, R. H. *J. Am. Chem. Soc.* **2003**, *125*, 11360-11370.

(15) Leading references using **7.1** and **7.2** in CM: (a). Crowe, W. E.; Goldberg, D. R. *J. Am. Chem. Soc.* **1995**, *117*, 5162-5163. (b). Brummer, O.; Ruckert, A.; Blechert, S. *Chem. Eur. J.* **1997**, *3*, 441-446. (c). Blackwell, H. E.; O'Leary, D. J.; Chatterjee, A. K.; Washenfelder, R. A.; Bussmann, D. A.; Grubbs, R. H. *J. Am. Chem. Soc.* **2000**, *122*, 58-71.

(16) Chatterjee, A. K.; Sanders, D. P.; Grubbs, R. H. *Org. Lett.* **2002**, *4*, 1939-1942.

(17) This is identical to the results of Schwab *et al.* who were unable to isolate the isopropyl-substituted ruthenium alkylidene $(PCy_3)_2Cl_2Ru(=CH$*i*-Pr) from the reaction of **7.2** with 3-methyl-1-butene. A small constant concentration of the desired alkylidene was observed via NMR throughout the reaction. See reference 4b.

(18) Funk, T.; Chelnov, A.; Grubbs, R. H. *Unpublished results.*

(19) Ulman, M.; Belderrain, T. R.; Grubbs, R. H. *Tetrahedron Lett.* **2000**, *41*, 4689-4693.

(20) Spessard, S. J.; Stoltz, B. M. *Org. Lett.* **2002**, *4*, 1943-1946.

(21) Ciochina, R.; Grossman, R. B. *Org. Lett.* **2003**, *5*, 4619-4621.

(22) Demchuk, O. M.; Pietrusiewicz, K. M.; Michrowska, A.; Grela, K. *Org. Lett.* **2003**, *5*, 3217-3220.

(23) (a). Choi, T.-L.; Lee, C. W.; Chatterjee, A. K.; Grubbs, R. H. *J. Am. Chem. Soc.* **2001**, *123*, 10417-10418. (b). Randl, S.; Connon, S. J.; Blechert, S. *Chem. Commun.* **2001**, 1796-1797. (c). Morgan, J. P.; Morrill, C.; Grubbs, R. H. *Org. Lett.* **2002**, *4*, 67-70.

(24) Enoic carbene complexes such as **7.9** undergo stoichiometric reactions with cyclohexene to afford the new ruthenium alkylidene $(PCy_3)_2Cl_2Ru(=CH(CH_2)_4CH=CHCO_2Cy)$. See reference 19.

(25) Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K. Trimmers, F. J. *Organometallics* **1996**, *15*, 1518-1520.

(26) Sanford, M. S.; Love, J. A.; Grubbs, R. H. *Organometallics* **2001**, *20*, 5314-5318.

(27) Trnka, T. M. *Ph.D. Dissertation* California Institute of Technology, **2003**.