Alkene Metathesis for Transformations of Renewables

Christian Bruneau, Cedric Fischmeister

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1 Introduction

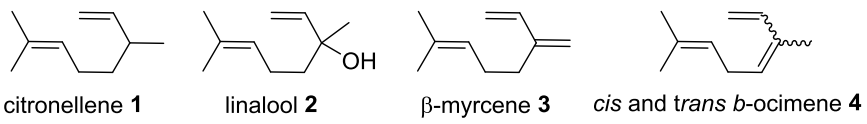
With the depletion of fossil resources and the concerns about climate changing and environment protection, biomass is intensively considered as a sustainable source of raw material for the chemical industry and for the production of biofuels.[1-4] Beside the very abundant carbohydrate and lignocellulosic biomass, lipids and to a lesser extend terpenes are envisioned as promising candidates for the production of bio-sourced compounds with a broad range of applications.[5,6] Terpenes are of most importance in fragrance composition whereas fats and oils have already found application as bio-diesel fuel and they are also foreseen as a renewable source of polymers. The transformation of these renewable compounds into valuable molecules for the chemical industry using efficient and selective processes is therefore of prime importance. In this context, catalysis plays a pivotal role by offering efficient tools for converting biomass to more value added chemicals through economically and environmentally competitive processes.[7,8] In particular, olefin metathesis is one of the modern catalysed reaction which as impacted the world of homogeneous organometallic catalysis over the last 25 years.[9-11] Continuous improvements of catalysts performances[12] and stability with better knowledge of activation and deactivation pathways[13-15] have rendered this process compatible with the transformation of bio-sourced compounds of variable purity.[16] In this chapter, we will review the main recent achievements and progress obtained in the valorisation of terpenes and lipids thanks to olefin metathesis.

2 Metathesis of unsaturated terpene derivatives

Terpenes are found in essential oils and constitutes a class of natural products that find direct applications and serve as feedstocks in flavor and fragrances industry and other potential applications due to their biological properties [17]. Terpenoids are chemically modified terpenes, essentially oxygenated derivatives such as alcohols, epoxides, ketones, aldehydes, carboxylic acids and esters. Chemical transformations of terpene derivatives have been investigated with the objective of producing new fine chemicals with high added value for diverse applications. Catalytic isomerization, rearrangements, cyclization, ring opening, hydrogenation, dehydrogenation, epoxidation, oxidation, hydration, hydroformylation, cyclopropanation are the most studied reactions [19-21]. Recent transformations of unsaturated terpenes and terpenoids based on olefin metathesis processes include ring closing metathesis of dienes, cross metathesis with ethylene and functional olefins to produce fine chemicals, ring opening metathesis and ring opening/cross metathesis for the production of reticulated polymers.

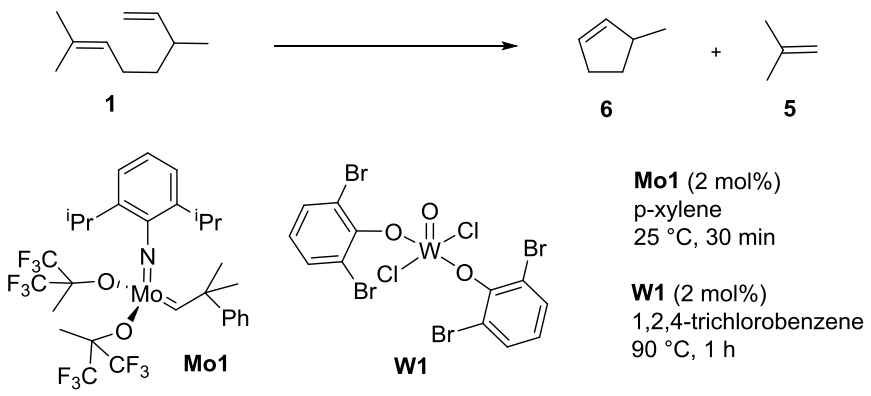
2.1 Ring closing metathesis

The ring closing metathesis of terpenes has been investigated with the monoterpenes citronellene **1**, linalool **2**, β-myrcene **3** and β-ocimene **4** (Scheme 1). Under RCM conditions, these terpenes containing a 1,6-diene structure eliminate isobutene and form cyclopentene derivatives from citronellene, linalool, and myrcene, and 2-methyl-1,3-cyclopentadiene in the case of β-ocimene.



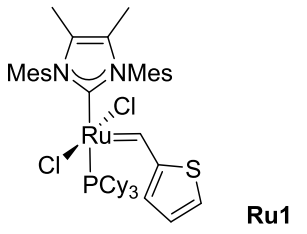
Scheme 1. Terpenes used in ring closing metathesis

The first ring closing metathesis transformations of a monoterpene have been carried out with citronellene **1** in the presence of molybdenum and tungsten catalysts. With a catalyst loading as low as 0.1 mol%, the Schrock catalyst Mo(=CHC(Me)$_2$Ph)((CF$_3$)$_2$MeCO)$_2$(2,6-^{i}Pr$_2$(C$_6$H$_3$N) **Mo1** catalyzed the ring closing metathesis of (-)-citronellene at room temperature into 3-methylcyclopentene **6** in 60% isolated yield without epimerization [22]. Each optically pure (*R*)- and (*S*)-citronellene enantiomer was converted into the corresponding (***R***)-**6** and (***S***)-**6** 3-methylcyclopentene in 68-70% isolated yield and 97% enantiomeric excess with retention of configuration at 90 °C in 1,2,5-trichlorobenzene for 1 h in the presence of 2 mol% of WOCl$_2$(2,6-Br$_2$C$_6$H$_3$O)$_2$ **W1** as catalyst (Scheme 2) [23].



Scheme 2 Ring closing metathesis of citronellene **1** with Mo and W catalysts

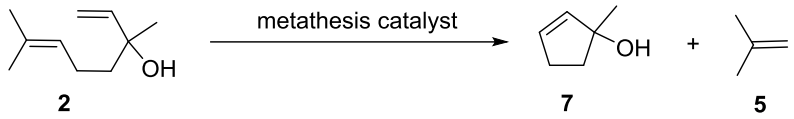
Later on, this RCM reaction was achieved with full conversion of (*R*)-citronellene **1** with 0.5 mol% of the ruthenium catalyst **Ru1** (Scheme 3) in toluene at 80 °C using microwave heating during 20 min [24].



Scheme 3. Structure of complex **Ru1**

A conversion of 93% of citronellene **1** was obtained during RCM at 60 °C for 6 h catalyzed by 84 ppm of second generation Hoveyda catalyst immobilized on silica [25,26]. In toluene at 80 °C, a TON of 16000 was obtained with very high conversion and selectivity, whereas the reaction carried out without solvent also gave full conversion of **1** but only 30% of **6** was formed together with high amounts of oligomers, and homometathesis and cycloisomerization by-products.

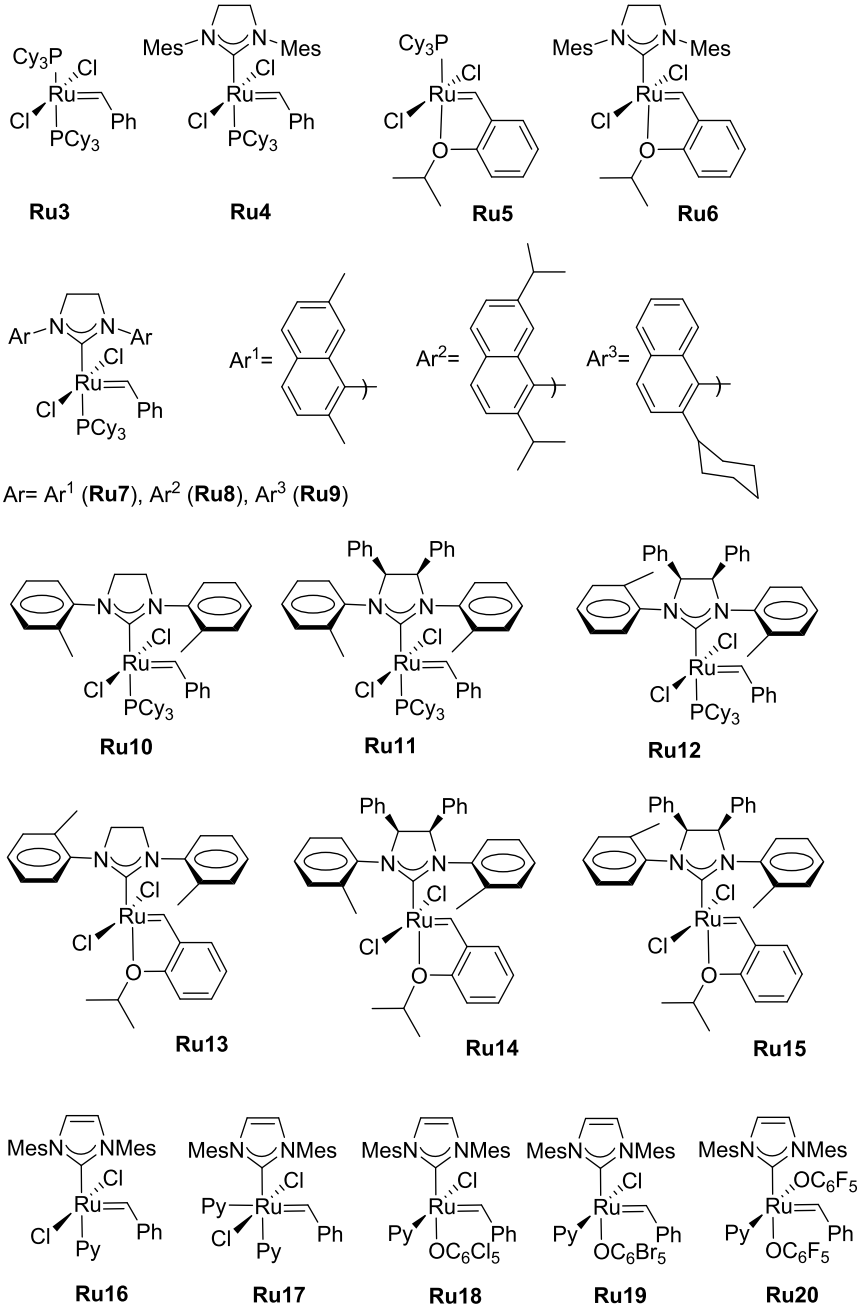
Ring closing metathesis of linalool **2** leading to isobutene **5** and 1-methylcyclopent-2-en-1-ol **7** as primary products, has been very often used as a model reaction to evaluate the catalytic properties of new ruthenium catalysts (Scheme 4).



Scheme 4 Ring closing metathesis of linalool **2**

Several well-defined benzylidene ruthenium complexes and *in situ* generated ruthenium carbene moieties featuring a bidentate Schiff base ligand derived from salicylaldehyde [27-29], and a benzylidene ruthenium complex containing a tridentate phosphinesulfonate ligand [30] have revealed modest activities.

The most efficient ruthenium catalysts that have been used for this RCM reaction are presented in Scheme 5.



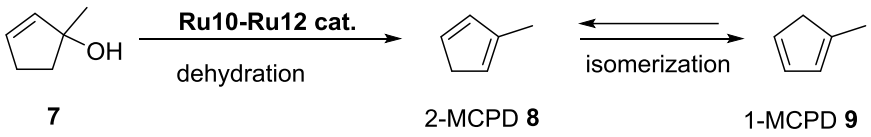
Scheme 5. Selected ruthenium catalysts used for linalool ring closing metathesis

In the presence of the first generation Grubbs catalyst **Ru3** at room temperature in $CDCl_3$ the reactivity of linalool **2** was one order of magnitude higher than that of citonellene **1**, whereas the *O*-methoxy-protected linalool presented no reactivity even at 65 °C. These two results highlight the beneficial effect of the allylic alcohol functionality on the rate of the metathesis reaction as compared to isostructural terpene derivatives [31]. The second generation Grubbs catalyst **Ru4** also gave full conversion whereas the Hoveyda-Grubbs catalysts **Ru5** and **Ru6** exhibited a slightly lower activity (Table 1 - entries 1-4) [32,33]. Other second generation ruthenium complexes (**Ru7**, **Ru8** and **Ru9**), equipped with a very bulky *N*-heterocyclic carbene ligand containing substituted naphthyl groups gave full conversion with excellent yields of isolated 1-methylcyclopent-2-en-1-ol **6** under mild conditions with 1 mol% of catalyst (Table 1 - entries 5-7) [34]. With **Ru1** (Scheme 3) it was possible to reach full conversion within 10 min by increasing the catalyst loading to 0.5 mol% (Table 1- entries 8-10) [24]. The authors confirmed that the presence the allylic alcohol functionality increased the reaction rate since the full conversion of citronellene under similar conditions required a double time of 20 min.

The RCM of linalool has been investigated with Grubbs (**Ru11**, **Ru12**) and Hoveyda (**Ru14**, **Ru15**) second generation catalysts featuring frozen saturated *N*-heterocyclic imidazolinylidene ligands substituted on the backbone of the five-membered ring by two phenyl groups in *syn*-position and by *ortho*-tolyl groups at the nitrogen atoms with a *syn* or *anti*-conformation [35]. Full conversions of linalool were obtained with the Grubbs type catalysts **Ru11**, **Ru12** and the less sterically hindered catalyst **Ru10** when the reactions were performed with 1 mol% of catalyst in dichloromethane at 30 °C within 7 to 13 min (Table 1-entries 11-13). With a lower catalyst loading of 0.1 mol%, the higher catalytic activity of the *syn*-isomer **Ru11** was evidenced. The RCM reactions carried out at 60 °C in deuterated benzene in the presence of 1 mol% of the Hoveyda type catalysts **Ru13**, **Ru14** and **Ru15** led to full conversion within 6 min (Table 1 - entries 17-19). With these catalysts operating at 60 °C, full conversion were also obtained in one hour with 0.1 mol% catalyst loading of **Ru13** and **Ru14**, whereas the *anti*-isomer **Ru15** was less efficient giving only 90% conversion (Table 1 - entries 20-22).

With catalysts **Ru10**, **Ru11** and **Ru12**, complete dehydration of the alcohol took place after formation of 1-methylcyclopent-2-en-1-ol **7**, to give first

2-methylcyclopentadiene (2-MCPD) **8** within 2 h, and then a mixture with its isomer 1-methylcyclopentadiene (1-MCPD) **9** (Scheme 7). With the phosphine-free Hoveyda type catalysts **Ru13-Ru15**, these subsequent reactions from **7** were much less pronounced.



Scheme 6 Dehydration of 1-methylcyclopent-2-en-1-ol **6** catalyzed by Grubbs type catalyst

The second generation Hoveyda type complex **Ru6** appeared as a good catalyst making the full conversion of **2** possible under neat conditions at room temperature with a catalyst loading of 0.1 mol% (Table 1 - entry 23) [36]. The Grubbs type catalysts **Ru3** and **Ru10** were less efficient and dehydration of 1-methylcyclopent-2-en-1-ol **7** to methylcyclopentadienes was observed with **Ru3** and **Ru6** when the temperature was increased to 60 °C.

Ruthenium complexes **Ru17**-**Ru20** equipped with a benzylidene and a pyridine ligand with at least one chloride atom substituted by another halide or an alkoxide have been evaluated in ring closing metathesis of dienes [37,38]. In the presence of 0.05 mol% of catalyst in refluxing $CDCl_3$, linalool was converted into 1-methylcyclopent-2-en-1-ol **7**. **Ru20** featuring two pentafluorophenoxy ligands exhibited an exceptional activity leading to full conversion in 1 hour, whereas the other catalyst precursors showed conversions located in the range 17-34% (Table 1 – entries 27-31). Nevertheless, all these ruthenium-pseudohalide catalysts led to 100% conversion in 15 min when the catalyst loading was as low as 0.5 mol%.

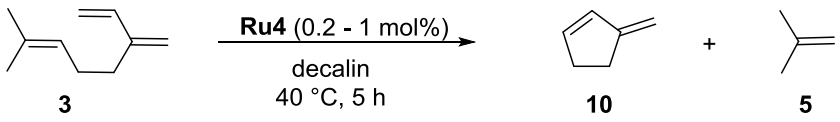
Table 1. Efficient ring closing metathesis of linalool **2**

Entry	Catalyst	Catalyst (mol%)	Solvent	T (°C)	t (min)	Conversion[a] or yield*[b] (%)	Ref
1	**Ru3**	5	$CDCl_3$	rt	60	100	17
2	**Ru4**	5	$CDCl_3$	rt	60	100	17
3	**Ru5**	5	$CDCl_3$	rt	60	65	17
4	**Ru6**	5	$CDCl_3$	rt	60	95	17
5	**Ru7**	1	CH_2Cl_2	rt	30	92*	18
6	**Ru8**	1	CH_2Cl_2	rt	6	88*	18
7	**Ru9**	1	CH_2Cl_2	rt	6	94*	18
8	**Ru1**	0.1	toluene	80	60	43	8
9	**Ru1**	0.1	DMC	80	60	40	8
10	**Ru1**	0.5	toluene	80	10	100	8
11	**Ru10**	1	CD_2Cl_2	30	13	100	19
12	**Ru11**	1	CD_2Cl_2	30	7	100	19
13	**Ru12**	1	CD_2Cl_2	30	10	100	19
14	**Ru10**	0.1	CD_2Cl_2	30	60	30	19
15	**Ru11**	0.1	CD_2Cl_2	30	60	59	19
16	**Ru12**	0.1	CD_2Cl_2	30	60	33	19
17	**Ru13**	1	C_6D_6	60	6	100	19
18	**Ru14**	1	C_6D_6	60	6	100	19
19	**Ru15**	1	C_6D_6	60	6	100	19
20	**Ru13**	0.1	C_6D_6	60	6	>98	19
21	**Ru14**	0.1	C_6D_6	60	6	>98	19
22	**Ru15**	0.1	C_6D_6	60	6	90	19

23	**Ru6**	0.1	neat	rt	45	100	20
24	**Ru6**	0.01	neat	rt	60	44	20
25	**Ru10**	0.1	neat	60	30	36	20
26	**Ru3**	0.1	neat	45	60	55	20
27	**Ru16**	0.05	$CDCl_3$	reflux	60	24	21
28	**Ru17**	0.05	$CDCl_3$	reflux	60	29	21
29	**Ru18**	0.05	$CDCl_3$	reflux	60	17	21
30	**Ru19**	0.05	$CDCl_3$	reflux	60	34	21
31	**Ru20**	0.05	$CDCl_3$	reflux	60	100	21

[a] Conversion determined by ^{1}H NMR or GC. [b] Isolated yield

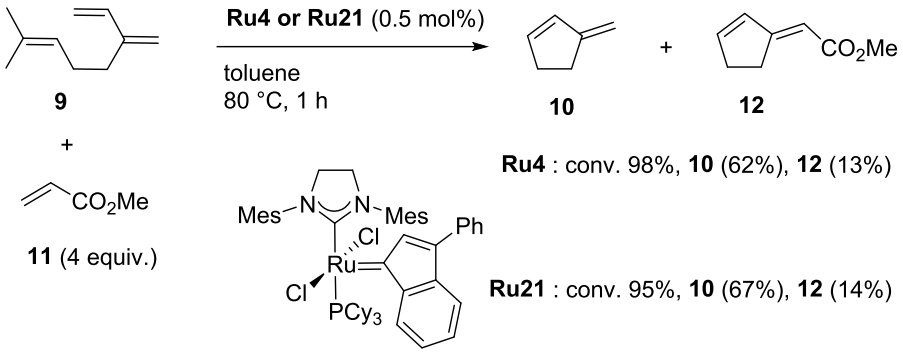
The ring closing metathesis of β-myrcene **3** has been achieved with the second generation catalyst **Ru4** at 40 °C in decalin as solvent (Scheme 7) [39]. From this triene **3**, full conversion into 3-methylenecyclopentene **10** was obtained in the presence of 1 mol% of catalyst.



Scheme 7 Ring closing metathesis of β-myrcene **3** into 3-methylenecyclopentene **10**

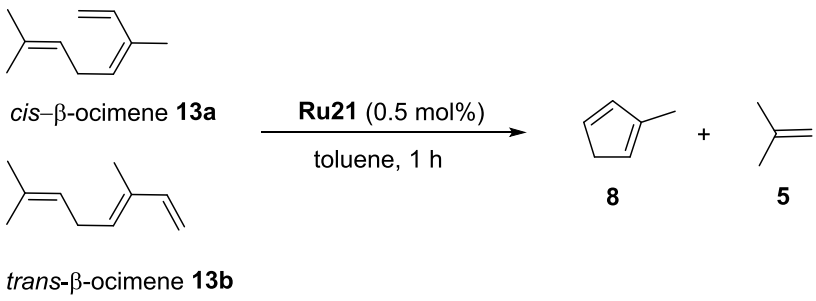
The diene **10** was then used for controlled cationic polymerization with a catalytic system based on ^{i}BuOCH(Cl)Me/$ZnCl_2$/Et_2O in toluene.
It has been shown that even in the presence of methyl acrylate **11** as cross metathesis partner, the ring closing metathesis of β-myrcene was favoured over the cross metathesis reaction [40]. The second generation benzylidene and indenylidene ruthenium catalysts **Ru4** and **Ru21** were led to excellent conversion of β-myrcene at 80 °C in the presence of 0.5 mol% of catalyst

within 1 h with production of **10** in 62-67% GC yields and the cross metathesis product **12** in 13-14% (Scheme 8).



Scheme 8 Ring closing metathesis of β-myrcene in the presence of methyl acrylate

The RCM of *cis*- and *trans*-β-ocimene **13a** and **13b,** isomers of β-myrcene, (Scheme 9) has been studied in the presence of catalyst **Ru21**. The *cis*-derivative **13a** was very reactive and led to 94% conversion after 1 h at 80 °C, whereas only 33% of the *trans*-isomer **13b** was converted under the same conditions. However, the expected 2-methylcyclopentadiene **8** was formed in only 24% yield indicating that side or subsequent reactions took place.

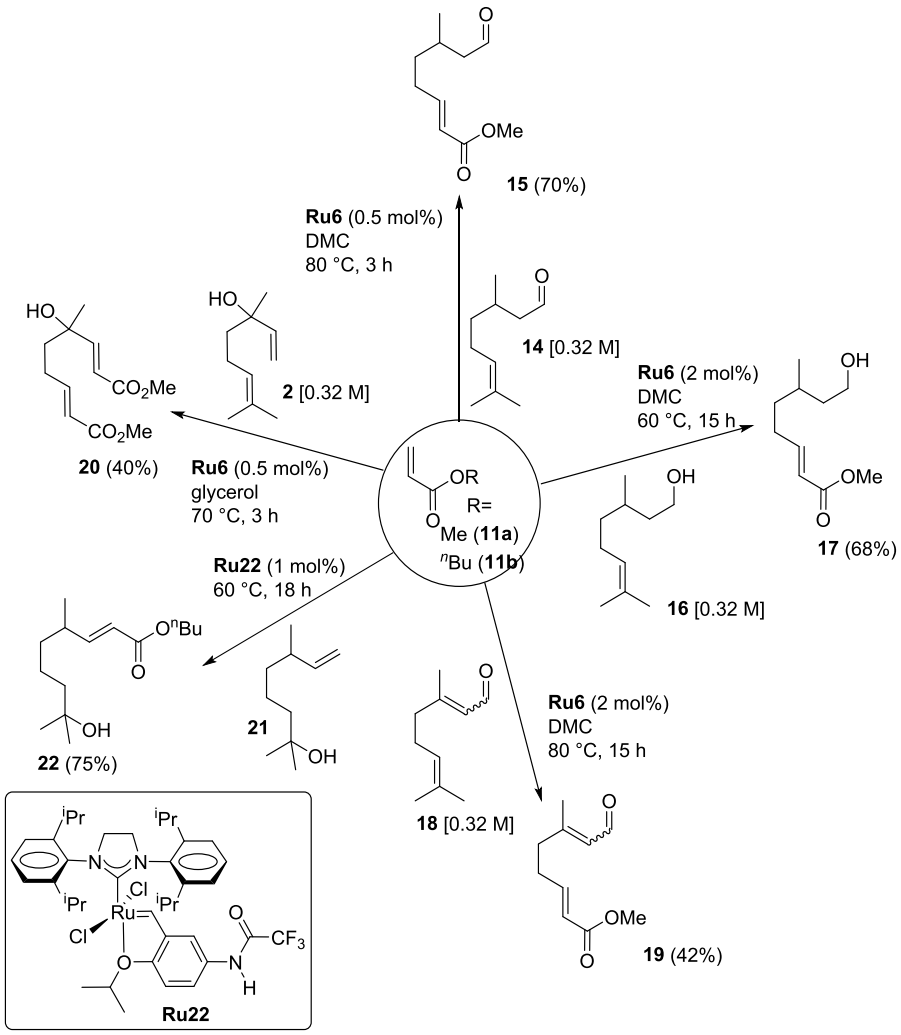


Scheme 9. RCM of cis- and trans- β-ocimene in the presence of **Ru21** as catalyst

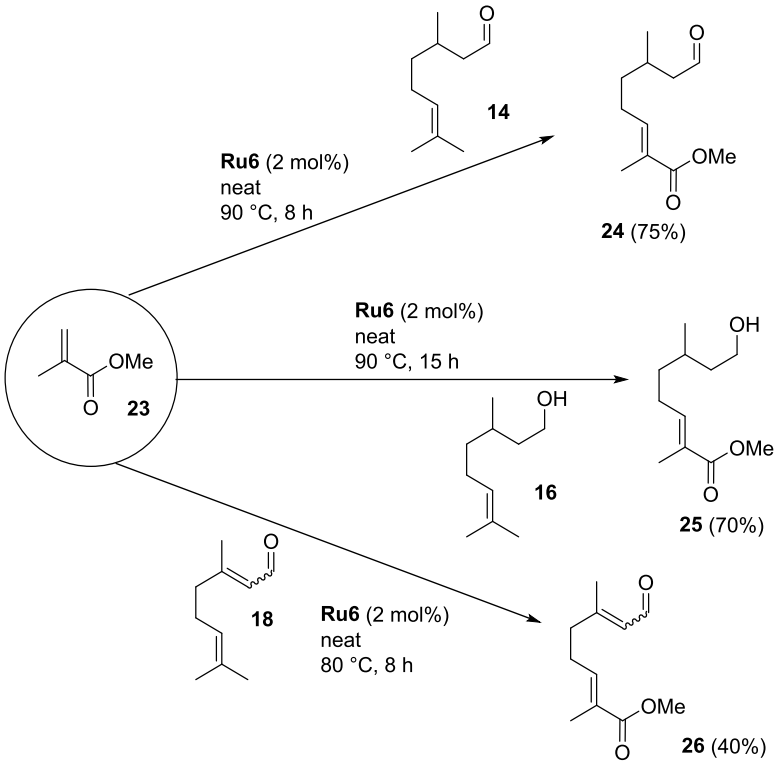
2.2 Cross Metathesis (CM)

2.2.1 Cross metathesis of terpenes with electron deficient olefins

The second generation Hoveyda catalysts have been found to be the most efficient catalysts for cross metathesis of terpenes and terpenoids with acrylic substrates. The cross metathesis of methyl acrylate **11a** with the diterpenes citronellal **15**, citronellol **16** and citral **17** was achieved in the presence of catalytic amounts of **Ru6** in the green solvent dimethyl carbonate (DMC) at 60-80 °C leading to the cross metathesis products isolated in 42-70% yield (Scheme 10) [41]. With an acrylate as cross metathesis partner, not surprisingly the resulting double bond presented an *E*-configuration, exclusively. Dichloromethane [42] and glycerol [43] have also been used as solvent to perform these cross metathesis reactions with **Ru4** and **Ru6** as catalyst. In the case of linalool, the terminal and prenyl double bonds were involved in the cross metathesis process leading to the formation of the 1,9-diester **20** with two (*E*)-double bonds in 40% yield obtained with only 0.5 mol% of catalyst **Ru6** (Scheme 10) [43]. Dihydromyrcenol **21**, a diterpenoid featuring one terminal double bond has been used in cross metathesis with *n*-butyl acrylate **11b** in the presence of 1 mol% of **Ru22** to give the (*E*)-isomer **22** in 75% yield after 18 h at 60 °C without solvent (Scheme 10) [44].
Cross metathesis of the more sterically hindered methyl methacrylate **23** required more demanding conditions. It was found that the best conditions for the transformation of **14**, **16** and **18** were obtained under neat conditions at 80-90 °C with catalyst **Ru6** (Scheme 11) [41]. Again, the reaction was stereoselective and only the (*E*)-isomers **24**, **25**, **26** were isolated in 75, 70 and 40% yield, respectively. These products formally correspond to new terpenoids with an oxidized prenyl group obtained without oxidation steps and generation of large amounts of wastes.



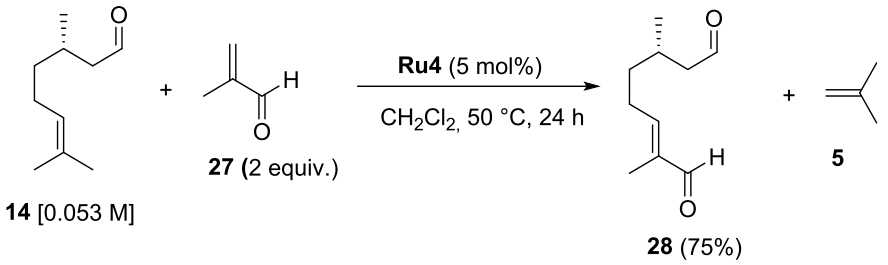
Scheme 10 Cross metathesis of terpenoids with acrylates



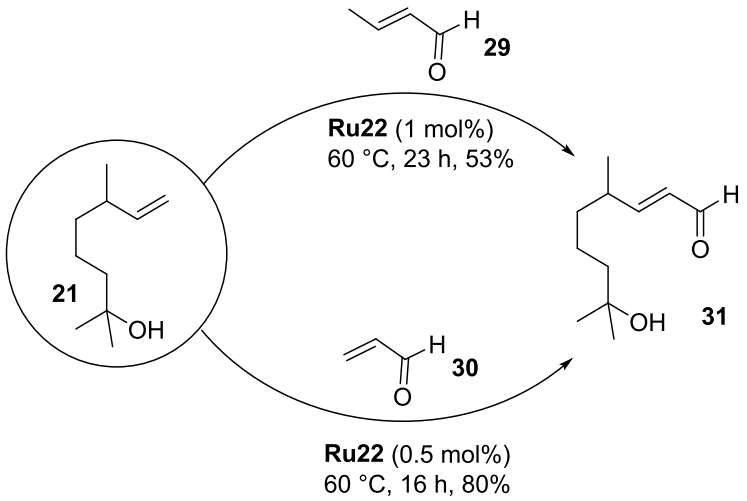
Scheme 11 Cross metathesis of terpenoids with methyl methacrylate

Cross metathesis of (*S*)-citronellal **(S)-14** with methacrolein **27** was used to produce the optically pure dialdehyde **28** as the first step of the synthesis of the biologically active (-)-fusarisetin A [45]. The reaction was achieved in 75% yield with 5 mol% of the second generation Grubbs catalyst **Ru4** in CH_2Cl_2 at 50 °C for 24 h (Scheme 12).

With the catalyst **Ru22**, the cross metathesis of neat **21** performed at 60 °C with the α,β-unsaturated aldehydes **29** and **30** gave the same product, namely (*E*)-8-hydroxy-4,8,dimethylnon-2-enal **31**, with high stereoselectivity (E/Z= 95:5 and 94:6, respectively), but acrolein **30** was more reactive than crotonaldehyde **29** leading to higher conversion with lower catalyst loading (Scheme 13) [44].



Scheme 12 Cross metathesis of (*S*)-citronellal with methacrolein

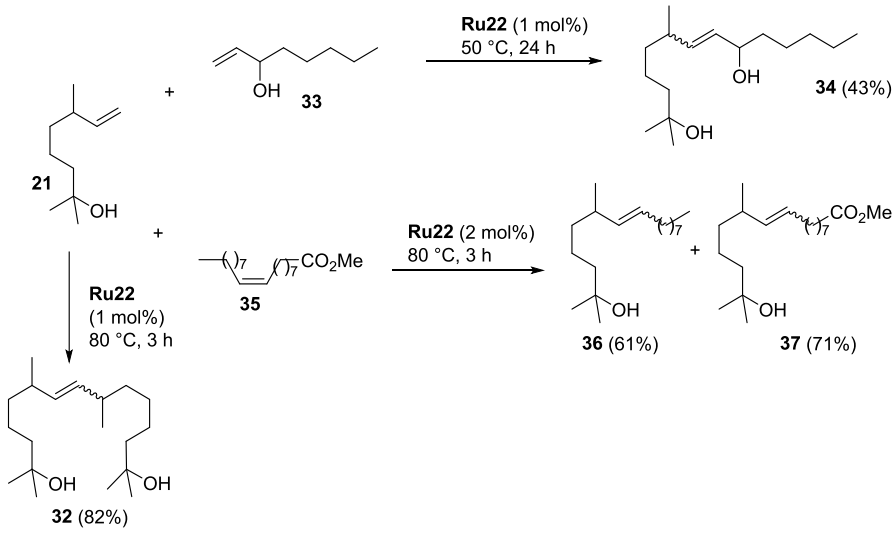


Scheme 13 Cross metathesis of dihydromyrcenol with acrylic aldehyde

2.2.2 Cross metathesis of acyclic terpenes with terminal and internal olefins

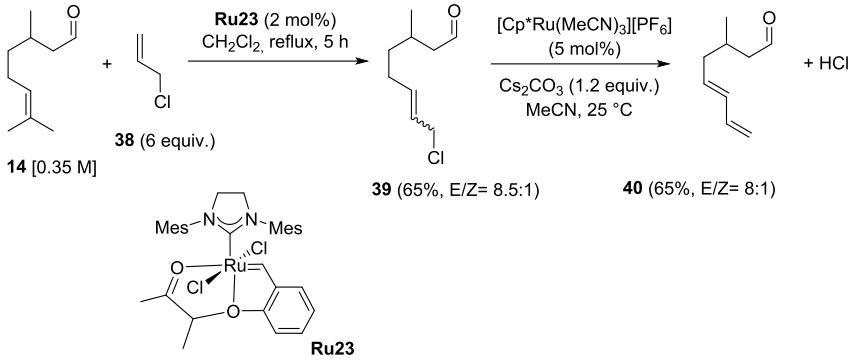
A mixture of stereoisomers of the self-metathesis product **32** was produced in 82% yield when dihydromyrcenol **21** was treated at 80 °C for 3 h with 1 mol% of catalyst **Ru22** under neat conditions (Scheme 14) [44]. When the terminal allylic alcohol **33** was used as cross metathesis partner, **34** was obtained in 43% yield after 24 h at 50 °C. Cross metathesis with methyl oleate **35** featuring a *cis* internal double bond led to **36** and **37** in 61% and

71%yield, respectively. These two products correspond to the reaction of **21** with each side of the double bond of **35** (Scheme 14). In this case, the (*E*)-stereoisomers are the major ones (*E/Z*= 86:14 and 87:13) but as expected in a much less pronounced ratio than with the previous electron deficient olefins **11a-b**, **23**, **27**, **29**, **30**.



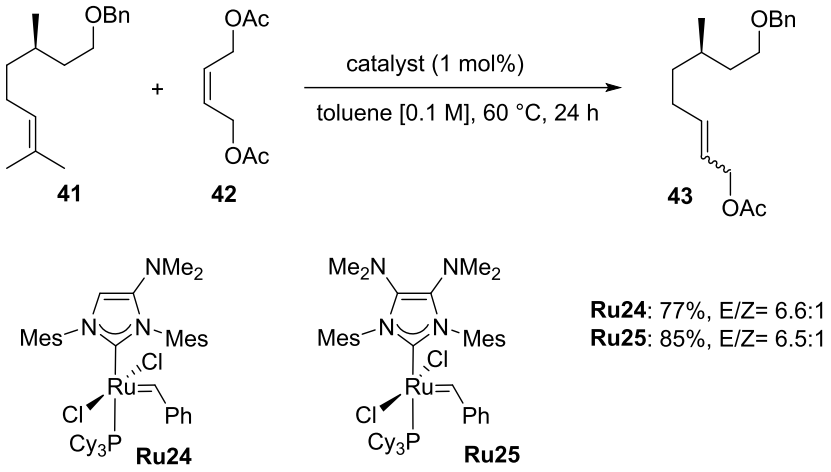
Scheme 14 Cross metathesis of dihydromyrcenol 21with non-activated olefins

The conjugated diene **40** was prepared in two steps in two steps from citronellal **14**. The cross metathesis of **14** with allyl chloride **38** was first carried out in the presence of 2 mol% of catalyst **Ru23** in refluxing dichloromethane for 5 h with an excess of **38** leading to the isolation of **39** in 65% yield with a *E/Z* ratio of 8.5:1. The ruthenium-catalysed dehydrochlorination reaction was then performed at room temperature with 5 mol% of [Cp*Ru(MeCN)$_3$][PF$_6$] as catalyst and provided **40** in 65% yield with a *E/Z* ratio of 8:1. (Scheme 15) [46].



Scheme 15 Cross metathesis of citronellal with allyl chloride followed by diene formation

The ruthenium complexes **Ru24**-**Ru25** featuring a 4-NMe_2-substituted and 4,5-$(NMe_2)_2$-disubstituted imidazolylidene carbene ligand were evaluated in the cross metathesis of citronellol benzyl ether **41** with *cis*-1,4-diacetoxybut-2-ene **42** containing an internal double bond (Scheme 16) [47]. Under the conditions reported in Scheme 16, these ruthenium benzylidene complexes led to the formation of **43** in 77 and 85% yield, respectively. It is noteworthy that under similar conditions Hoveyda type catalysts equipped with the same *N*-heterocyclic ligands were less efficient as they delivered **43** with only 25% yield.



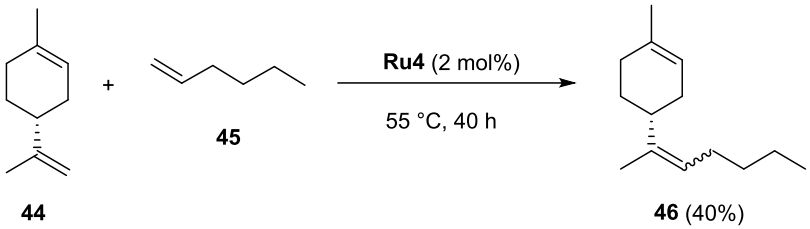
Scheme 16 Cross metathesis of citronellol benzyl ether **41** with *cis*-1,4-diacetoxybut-2-ene **42**

2.2.3 Ethenolysis: double bond scission

Ethenolysis of terpene derivatives, which corresponds to cross metathesis with ethylene [48,49] and cleavage of internal double bonds to produce two different products has been used for degradation and analytical purposes rather than for target oriented synthesis. These applications involve terpenes with a high number of isoprene motifs and are not reported in details in this chapter. Among them, the triterpene squalene and the tetraterpene β-carotene have been selectively cleaved into shorter polyenes with ruthenium catalysts [50,51]. Ethenolysis has also been used to degrade polyisoprene and polyisoprene-containing copolymers in the presence of various catalysts based on molybdenum, tungsten or ruthenium [52-59]. Alkenolysis, which corresponds to cleavage with short internal alkenes has also been investigated [60,61] with limonene [62,63] and β-pinene [64], which have been used to produce terpene-terminated oligomers of isoprene.

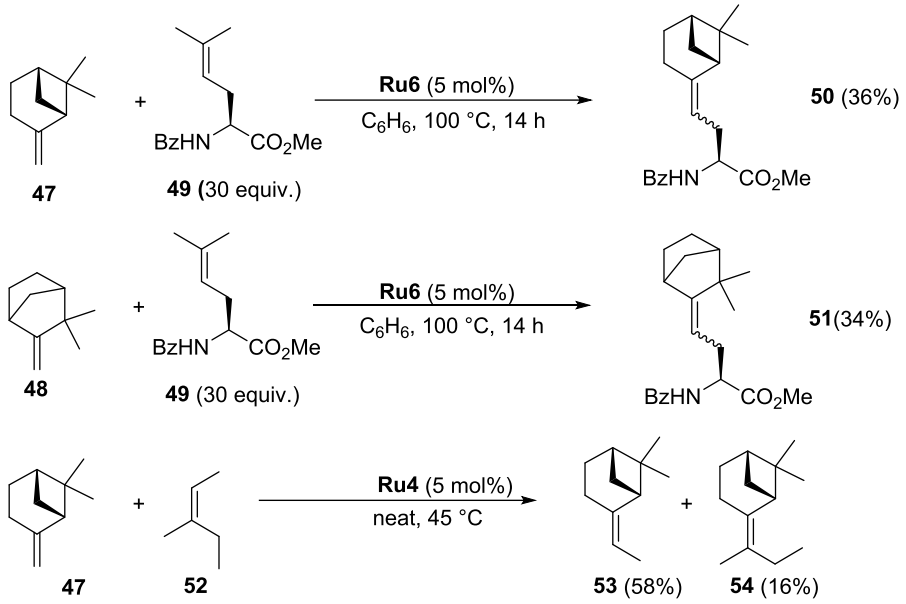
2.2.4 Cross metathesis of cyclic terpenes

Cyclic terpenes are more sterically hindered than the acyclic ones, and the access to the reactive catalytic center might be difficult in some cases. However, with the non-functional terminal olefin 1-hexene **45**, limonene **44** reacted in the presence of 2 mol% of **Ru4** at 55 °C without solvent to give the cross metathesis product **46** in 40% yield (Scheme 17) [65].



Scheme 17 Cross metathesis of (D)-limonene with 1-hexene

This reactivity of limonene with a terminal olefin has been extended to the production of co-oligomers starting from 1,5-hexadiene in the presence of **Ru4** (1 mol% with respect to the diene) in an excess of limonene as solvent (30 equiv.) at 45 °C. Polyhexadiene was formed together with hexadiene oligomers featuring one or two limonene ends [65].
It has been shown that β-pinene **47** and camphene **48** failed to give the cross metathesis reaction with *N*,*O*-protected allylglycine. On the other hand, the cross metathesis of these sterically hindered terpenes with the prenylglycine derivative **49** was possible with 5 mol% of **Ru6** at 100 °C in the presence of a large excess of the cross metathesis partner and the modified terpenes **50** and **51** were obtained in 36 and 34% yield, respectively (Scheme 18) [66]. The cross metathesis with the aliphatic internal olefin (*Z*)-3-methylpent-2-ene **52** with β-pinene has also been carried out with 5 mol% of catalyst **Ru4** at 45 °C without solvent and the two possible cross metathesis products **53** and **54** have been observed (Scheme 18) [64].

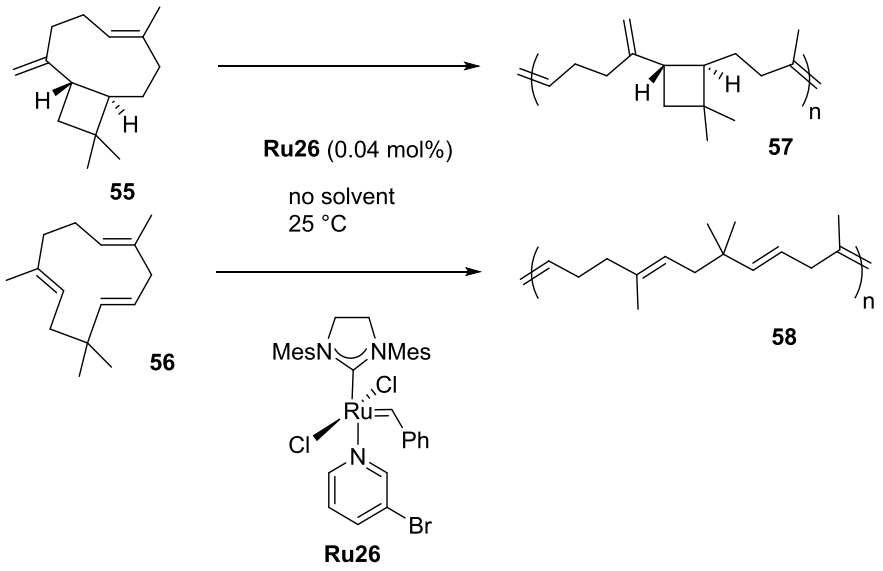


Scheme 18 Cross metathesis involving β-pinene **47** and camphene **48**

The general idea to make these cross metathesis reactions with bulky double bonds successful was to favour the productive with respect to the non-productive pathway by playing with the steric parameters of the cross metathesis partner [66,67]. Hence, the cross metathesis of β-pinene and camphene appeared to be more efficient with a trisubstituted olefin as cross metathesis partner than with a terminal olefin. This is in line with the computational studies, which indicated that non-productive metathesis of β-pinene in the presence of another olefin takes place in the presence of second generation ruthenium catalysts *via* formation of a carbene involving the pinene substrate, and that its self-metathesis does not occur because it is inhibited both by kinetic and thermodynamic factors [55].

2.3. Ring opening metathesis polymerization

Ring opening metathesis of terpenes is extremely scarce. Only recently, the ring opening metathesis of the sesquiterpenes caryophyllene **55** and humulene **56** has been reported [68]. The ruthenium catalysts **Ru4** and **Ru26** appeared to be the most active for this polymerization where only trisubstituted double bonds were involved (Scheme 19). Complete conversion of **55** was achieved even with 0.04 mol% of **Ru26** at 25 °C and its exocyclic methylene group was not involved in the polymerization process.



Scheme 19 Ring opening metathesis of two sesquiterpenes

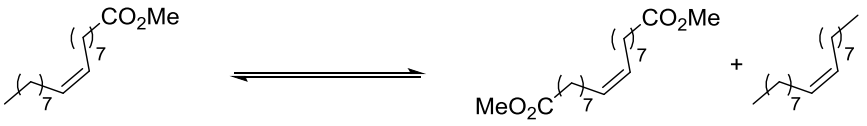
Finally, functional hyperbranched polymers have been produced *via* ring opening metathesis polymerization of dicyclopentadiene in the presence of terpenes. D-Limonene, limonene oxide, β-pinene, carvone have been used as chain transfer agent to modify the physical properties and thermal stability of thermosets based on polydicyclopentadiene [69,70].

3 Metathesis of unsaturated fatty acid derivatives

Triglycerides are the main components of fats and oil leading to fatty acid and esters following hydrolysis or transesterification, respectively. They originate essentially from plant seeds or algaes and are composed of essentially mono- or poly-unsaturated linear carbon chain and a terminal carboxylic functional group. Oleochemistry is a well-developed domain in food industry as well as in biofuels and is based on the reactivity of the terminal carboxylic functional group or carbon-carbon double bond [71-73] and in some case on the presence of other functional groups present in the linear carbon chain, a typical example being castor oil.[74-75] Among the portfolio of carbon-carbon double bond transformations, olefin metathesis appears as a very efficient and versatile catalytic transformation offering a broad range of potential applications for the transformation and valorisation of fatty esters. The main transformations of fatty esters by olefin metathesis will be considered hereafter focusing on recent contributions.

3.1 Self metathesis

The early days of olefin metathesis of fatty esters concerned essentially the self-metathesis reaction promoted by heterogeneous catalysts.[76] This reaction later developed with homogeneous catalysts offers an easy access to fatty dieters of interest for the production of polyesters. As depicted in Scheme 20, methyl oleate **59** can be converted into dimethyl 9-octadecene-1,18-dioate **60** and 9-octadecene **61** in general in an equilibrium mixture unless polyunsaturated fatty esters are used.[77] A number of reviews cover this topic that will not be further developed in this chapter.[78-80]



59 **60** **61**

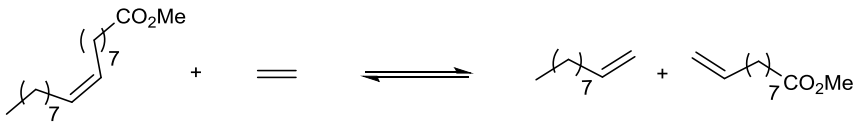
Scheme 20: Self-metathesis of methyl oleate **59**

3.2 Cross Metathesis

Cross metathesis is another important transformation that allows the introduction of a variety of functional groups.[81] In contrast to self-metathesis, cross-metathesis can easily be brought to high conversion and selectivity using an excess of one of the reagent in general the less prone to self-metathesis and/or the less expensive. Two different reactions can be applied to fatty esters derivatives. The first one, cross-metathesis with ethylene ("*ethenolysis*") has been used in order to cleave fatty esters into 2 terminal olefins whereas cross-metathesis with functional olefins aims at preparing bi-functional molecules as polymer precursors.

3.2.1 Ethenolysis

The ethenolysis of fatty esters has been used to shorten the chain length of fatty esters thereby producing valuable medium chain compounds for polymer industry. For instance, the ethenolysis of methyl oleate **59** produces methyl 9-decenoate **62** and *n*-1-decene **63**, two compounds with many applications in fragrance, polymers and surfactants (Scheme 21).[48,49]

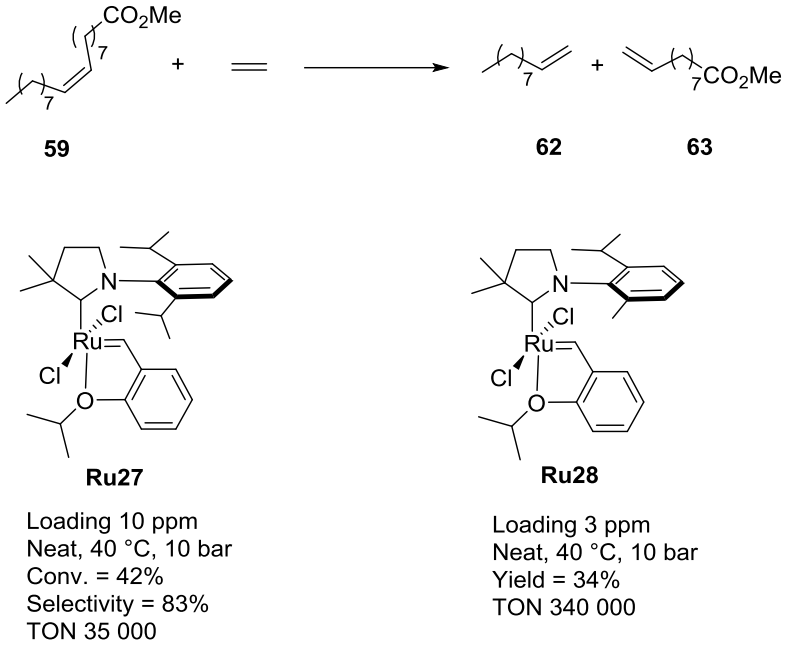


59 **62** **63**

Scheme 21 Ethenolysis of methyl oleate

An early report by Mol in 1981 paved the way to future developments in ethenolysis of fatty esters. This work identified what will be one of the major challenge of ethenolysis. Indeed, selectivity to the desired products **62** and **63** is hampered by self-metathesis reactions leading to undesired compounds **60** and **61**. However, the ethylene pressure is an efficient manifold to access high selectivity. For instance a Re/Al/Sn catalyst delivered up to 29% of self-metathesis products when the reaction was conducted under 2 bar of

ethylene pressure but self-metathesis was almost totally suppressed when the reaction was conducted with 50 bar of ethylene pressure.[84] Since this first report, many improvements have been achieved owing to the development of well-defined catalysts. In a thorough experimental and computational study, researchers at Dow Chemical reported a TON of 15000 obtained with Grubbs catalyst **Ru3** in the ethenolysis of methyl oleate hence raising the issue of the economic viability of this process for which a TON of 50000 would be required.[85] A major improvement came in 2008 when the group of Schrodi reported a TON of 35000 and selectivity of 83% obtained with the Ru-CAAC **Ru27** (CAAC: CycloAlkylAminoCarbene) catalyst ~~**Ru27**~~ (Scheme 22).[86] More recently, Grubbs and Bertrand studied the structure/activity relationship of a series of Ru-CAAC complexes where they reported the highest TON ever reported in ethenolysis with a slightly different catalyst **Ru28** (Scheme 22).[87] Of note, they highlighted the dramatic influence of the feed purity. If the necessity to use low hydroperoxide-containing methyl oleate is a known issue necessitating pre-treatment of the oil feed,[88-92] the influence of the ethylene gas purity was studied and found to be also a major parameter to consider for achieving high TONs. The highest TON still reported to date (340 000) was thus obtained at 40 °C with a catalyst loading of 1 ppm and an ethylene purity and pressure of 99.995% and 10 bar, respectively. If the vast majority of ethenolysis transformation of fatty esters has been performed with ruthenium based catalysts, this reaction was also reported with molybdenum catalyst but with moderate TONs.[93]



Scheme 22. Ru-CAAC catalyst in ethenolysis of methyl oleate

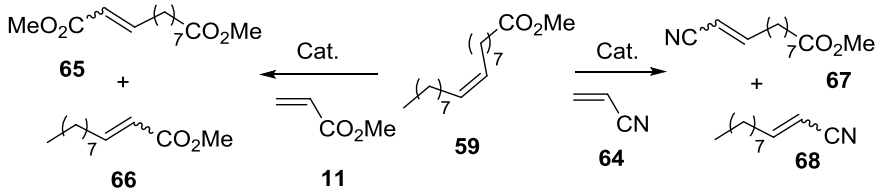
3.2.2 Alkenolysis

Beside the cleavage by ethenolysis of fatty esters, researchers sought a more efficient cleavage process by considering the formation of ruthenium methylidene species as the Achilles' heel of this reaction. Another type of fatty ester cleavage denoted as alkenolysis was thus investigated. In 2006, Jackson and Robinson reported the cross-metathesis of natural oils with 2-butene. At that time, the purity of both methyl oleate and 2-butene were identified as key issues for achieving high TONs. A productivity as high as 470 000 was achieved at – 5 °C and Hoveyda catalyst **Ru6** with triply distilled methyl oleate and 2-butene free of 1,3-butadiene, which acted as a catalyst poison. [94] In 2012, Meier used the cross-metathesis of oil-derived biodiesel with 1-hexene in order to shorten the chain length of the fatty ester chains. Best results (TONs > 2000) were obtained with Umicore M51 **Ru23**. [95] It must be noted that alkenolysis was also used for the simple determination of double bond positions in long chain olefins including fatty esters.[96] Alkenolysis of fatty esters was transferred into an industrial process by Elevance in a joint venture with Wilmar. This metathesis process is used to produce chemical intermediates by cross-metathesis of natural oils

with 1-butene.[97,98] Very recently, Mecking extended alkenolysis to algaes' based poly-unsaturated fatty derivatives in particular the penta-unsaturated eicosapentaenoic ester. Several ruthenium catalysts were evaluated in the butenolysis reaction of this compound with 2-butene searching for high conversion and selectivity. Most second generation ruthenium catalysts were found competent for this reaction but the selectivity for the desired methyl 5-heptenoate was not exceeding 48%. However, increasing the catalyst loading to 0.2 mol% per double bond led to a selectivity of 95% for the desired product.[99] Interestingly, the self-metathesis of eicosapentaenoic acid opens the way toward the synthesis of biosourced benzene.[100]

3.2.3 Cross Metathesis with functional olefins

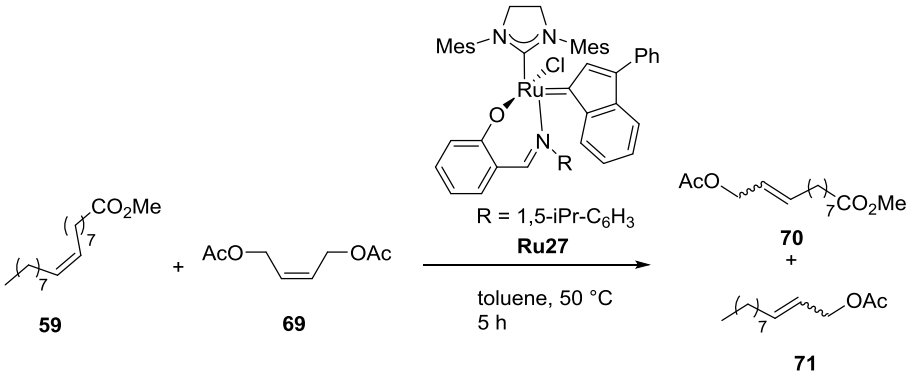
Olefin metathesis has been used for the polymerization of long chain fatty esters under various manners. [101] The cross metathesis of fatty esters with functional olefins is a one stone two birds process as it shortens the carbon chain length while introducing a second functional group. The prepared homo- or hetero-bifunctional compounds are of great interest for the preparation of short chain polymer precursors. Cross-metathesis with acrylic derivatives have been extensively studied for the preparation for diesters [102-105] and nitrile-esters [106-111] derivatives for the production of polyesters and polyamides, respectively (Scheme 23). Other cross metathesis partners such as allyl chloride, [112] acrolein [113, 92] and alkynes [114, 115] have also been used.



Scheme 23 Cross-metathesis of methyl oleate with methyl acrylate and acrylonitrile

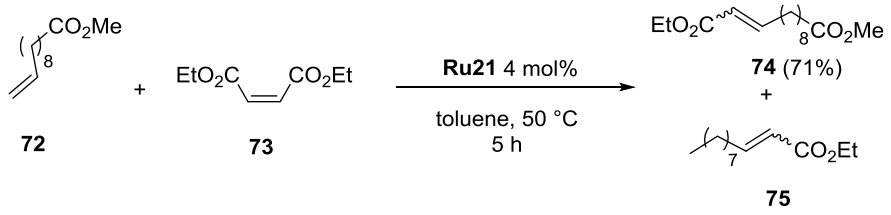
Following these pioneering researches on the preparation of bifunctional monomers using terminal functional olefins, several groups investigated cross metathesis reactions with internal olefins bearing one or two functional

groups. As presented earlier for alkenolysis of methyl oleate, this process would be an ethylene free process when fatty esters such as methyl oleate **59** are used. In 2011, Behr reported the cross metathesis of methyl oleate **59** with *cis*-2-butene-1,4-diyl diacetate **69** (Scheme 24). The Schiff-base ruthenium catalyst was found the most efficient for this reaction leading to high conversion of methyl oleate. However, high selectivity could not be obtained even with a catalyst loading of 2 mol% [116]



Scheme 24 CM of methyl oleate with cis-2-butene-1,4-diyl diacetate

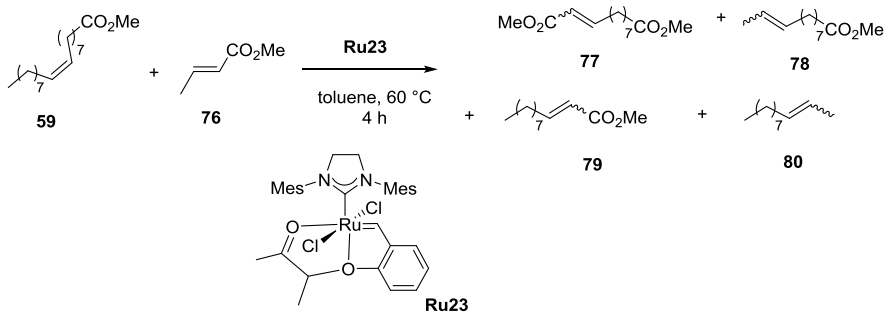
At the same period, this group also investigated the cross metathesis of methyl 10-undecenoate **72** (arising from the pyrolysis of castor oil) with diethyl maleate **73** leading to the diester **74** (Scheme 25).[117] Experimental parameters as well as various ruthenium-based catalysts were investigated. Again, the best results were obtained with a high catalyst loading (4 mol%) of the indenylidene catalyst **Ru21** and the formation of the self-metathesis product of **72** could not be reduced below 25%. Similarly, the investigation of the cross metathesis of **72** with dimethyl maleate and methyl acrylate **11** was realized. It was demonstrated that at 80 °C in toluene, the cross metathesis with methyl acrylate was faster and required lower catalyst loading (0.5 mol%) than the cross metathesis involving dimethyl maleate.[118]



Scheme 25 CM of methyl 10-undecenoate **72** with diethyl maleate **73**

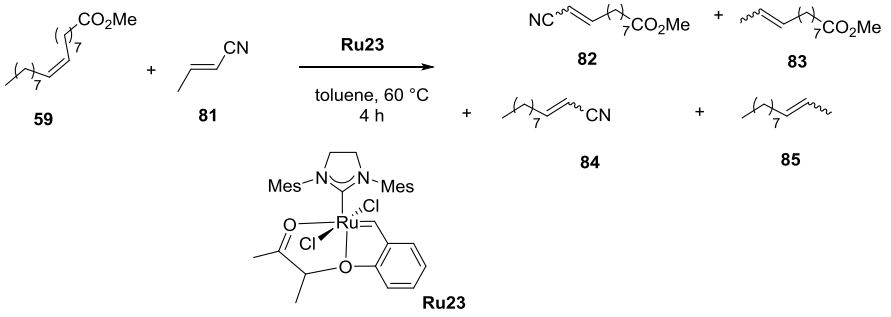
The direct synthesis of bifunctional compounds incorporating a carboxylic acid function was reported by Schrekker. [119] In this comparative study, the benefit of using acrylic acid or maleic acid instead of methyl acrylate or maleate was established. Better conversion and selectivity were obtained using ultra-pure methyl oleate **59** and Hoveyda catalyst **Ru6** in THF at 60 °C. It is postulated that these results are likely due to the higher steric hindrance of esters *vs* acid.

An important contribution came in 2015 from the group of Gauvin. It was demonstrated that the use of methyl crotonate **76** as cross metathesis partner led to significant improvements in terms of activity and selectivity for the cross metathesis products (Scheme 26). [120] As an example, a productive TON of 35450 was obtained with 26 ppm of catalyst **Ru23**. This protocol was scaled up to 50 g using an industrial grade feed under bulk conditions at 60 °C. A high conversion and selectivity for cross products of 96% and 97% were obtained, respectively.



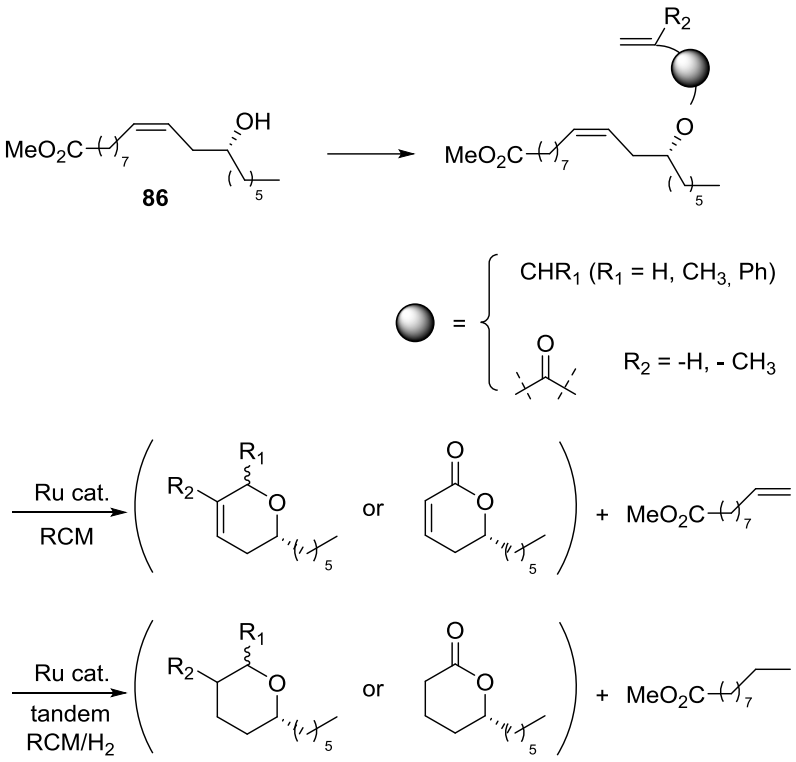
Scheme 26 CM of methyl oleate **59** with methyl crotonate **76**

Similarly, the same group investigated the influence of nitrile-functionalized olefins on the outcome of cross metathesis with methyl oleate. Cross metathesis of methyl oleate was conducted with either acrylonitrile or crotonitrile (Scheme 27).[121] Under similar conditions i.e. **Ru23** 1 mol% , toluene, 60 °C, 4 h, a higher conversion was obtained with crotonitrile (75% *vs* 22%) but the highest selectivity was obtained with acrylonitrile (86% *vs* 82%). However, higher selectivity could be obtained at 110 °C but the process suffered from a rather high catalyst loading limiting the TON to values below 250.



Scheme 27 CM of methyl oleate **59** with crotonitrile **81**

As exemplified here above the transformation of fatty esters by olefin metathesis aims almost exclusively at the synthesis of polymer precursors. In 2012, the use of methyl ricinoleate **86** as a platform chemical for the synthesis of high-added value chemicals was reported (Scheme 28). The synthetic strategy involved the functionalisation of methyl ricinoleate using the hydroxyl group present in the carbon chain and further ring closing metathesis. This methodology enabled the synthesis of a variety of compounds of interest for flavour or fragrance composition.[124] The esters by-products of these reactions can be directly valorised by cross-metathesis transformations as described in 3.2.3.



Scheme 28 High added-value compounds from methyl ricinoleate (castor oil)

4 Conclusion

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