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VEGYÉSZMÉRNÖKI ÉS BIOMÉRNÖKI KAR
OLÁH GYÖRGY DOKTORI ISKOLA

Metathesis of conjugated polyenes



Gábor Turczel

Ph.D. student

MTA TTK

Supervisor: **Róbert Tuba**

Head of Green Chemistry Research Group

MTA TTK AKI

BME

MTA TTK AKI

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1. Aims and objectives

The aim of this work is the valorization of low value conjugated feedstock *via* olefin metathesis reaction. Naturally occurring, non-edible conjugated fatty acids and their derivatives are excellent candidates for such feedstock. Nature is also abundant in non-conjugated polyenes, which could be readily converted to a mixture of conjugated isomers by catalytic isomerization and utilized in metathesis reaction. These renewable materials can be considered as a potential sustainable feedstock for polyurethane and polyester monomer synthesis. Conjugated petrochemical side-products were also investigated as potential raw materials. The key objective is the utilization of conjugated systems as resource of building blocks for the synthesis of high-value chemicals (Figure 1).

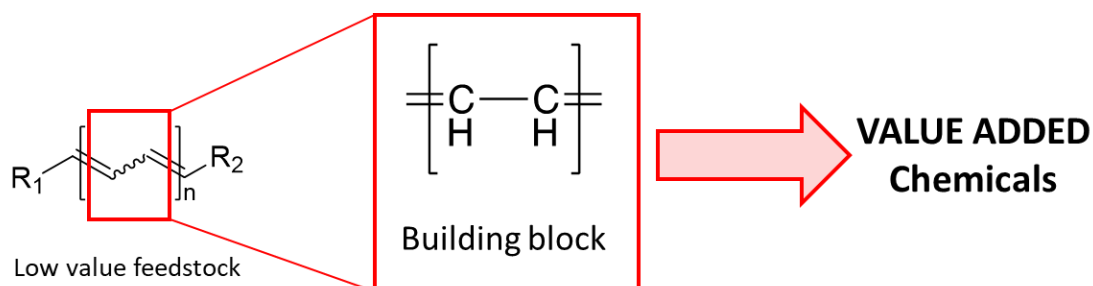
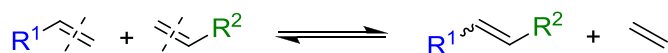


Figure 1. Utilization of low value conjugated feedstock as building block

In this work, Grubbs metathesis catalyst systems were employed to convert the =CH-CH= unit of the conjugated starting materials into high-value chemicals having potential industrial applications.

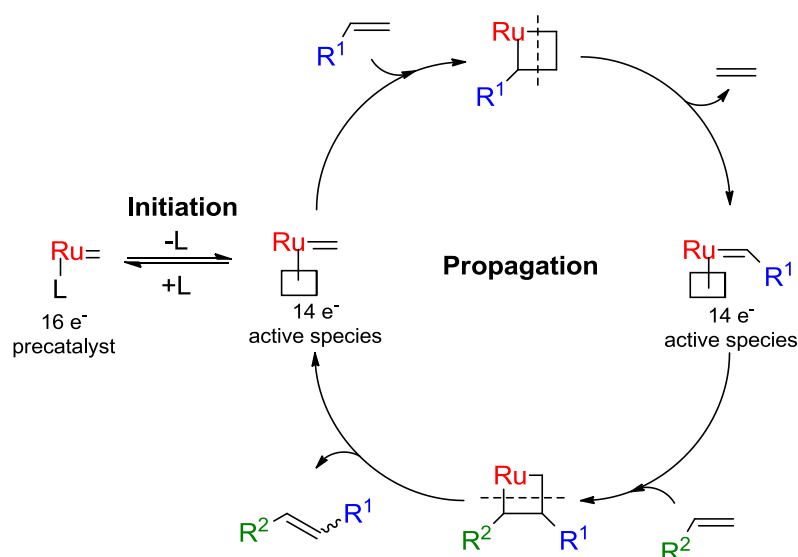
2. Introduction

Formally, the olefin metathesis reaction can be described as the splitting of the C=C double bond, which is followed by reorganization and the formation of new alkene species (Scheme 1). Olefin metathesis is a reversible reaction, which usually leads to a mixture of the starting materials and products through a catalytic cycle.



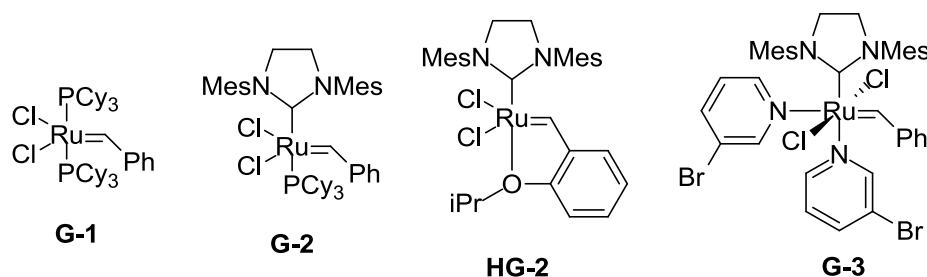
Scheme 1. Formal reaction scheme of olefin metathesis

The actual mechanism involves a series of cycloaddition and cycloreversion steps, through the formation of metallacyclobutane intermediates (Scheme 2).



Scheme 2. Mechanism of Ru alkylidene catalyzed olefin metathesis

Following the discovery of the first well-defined ruthenium alkylidene metathesis catalyst¹, extensive research led to a wide range of catalytically active compounds with increased activity, selectivity and stability. The first commercially available metathesis catalyst (**G-1**, Scheme 3) showed exceptional methathesis polymerization reactivity enabling its industrial application.² Latter iterations of Grubbs metathesis catalysts (**G-2**,³ **HG-2**,⁴ and **G-3**,⁵ Scheme 3) showed exceptional metathesis efficiency towards cross metathesis (**CM**), ring-opening cross metathesis (**ROCM**) and ring closing metathesis reactions thus promoting their industrial applications.



Scheme 3. Commercially available Grubbs metathesis catalysts

¹ S. B. T. Nguyen, L. K. Johnson, R. Grubbs, *J. Am. Chem. Soc.* **1992**, *114*, 3974–3975.

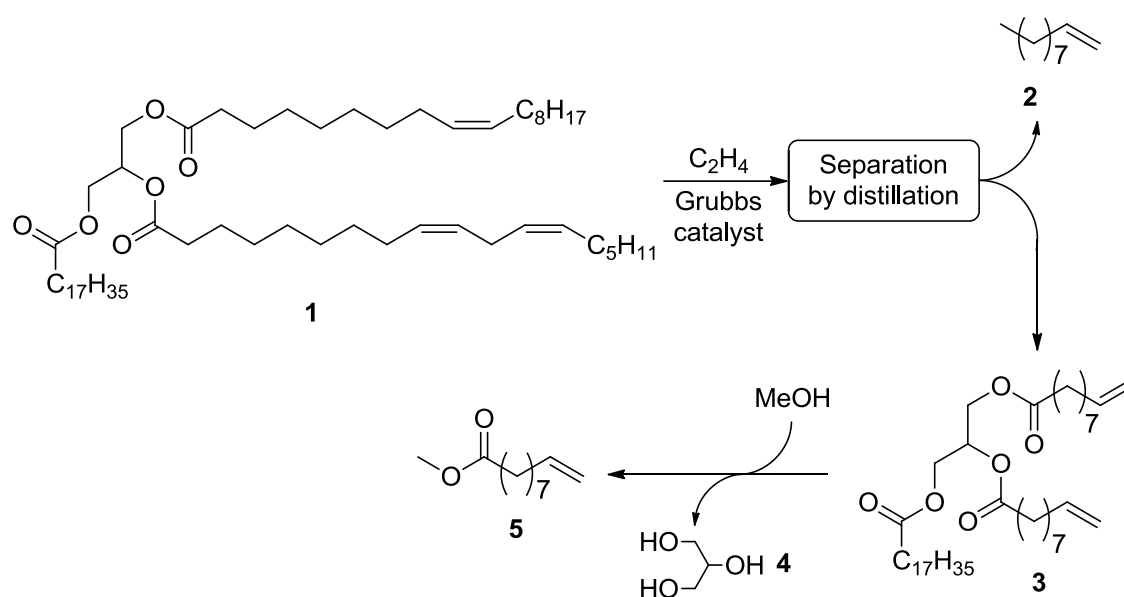
² P. Schwab, M. B. France, J. W. Ziller, R. H. Grubbs, *Angew. Chemie Int. Ed.* **1995**, *34*, 2039–2041.

³ M. Scholl, S. Ding, C. W. Lee, R. H. Grubbs, *Org. Lett.* **1999**, *1*, 954–956.

⁴ S. B. Garber, J. S. Kingsbury, B. L. Gray, A. H. Hoveyda, *J. Am. Chem. Soc.* **2000**, *122*, 8168–8179.

⁵ J. A. Love, J. P. Morgan, T. M. Trnka, R. H. Grubbs, *Angew. Chemie - Int. Ed.* **2002**, *41*, 4035–4037.

This led to the development of a metathesis-based palm oil biorefinery plant, located in Indonesia.⁶ The refinery converts the natural triglycerides (**1**) found in the oil to olefins (**2**), ω -unsaturated esters (**5**), saturated mono and diesters (Scheme 4). The initial step is the CM of **1** with ethylene, forming terminal olefins, mainly 1-decene (**2**) and shorter chain triglycerides (**3**). **3** is then reacted with methanol to produce glycerol (**4**) and **5**, which can be further derivatized to additional value-added compounds. These renewable-based products are utilized as polymer building blocks,⁷ lubricants, surfactants and their intermediates⁸ and antimicrobials⁹.



Scheme 4. Natural oil processing *via* ethenolysis

From a metathesis point of view, the most important renewable raw materials are the monounsaturated fatty acid esters. While some terpenes also find utilization, there are additional compounds of interest in this field, especially polyenes.

α -Linoleic acid (**6**, Scheme 5) is the main fatty acid component of numerous seed oils including safflower, poppyseed, melon and grape. These oils contain approximately 70% of **6** as glycerol esters. The well-known utilization of **6** is the production of its conjugated mixture, which is recognized as a dietary supplement.

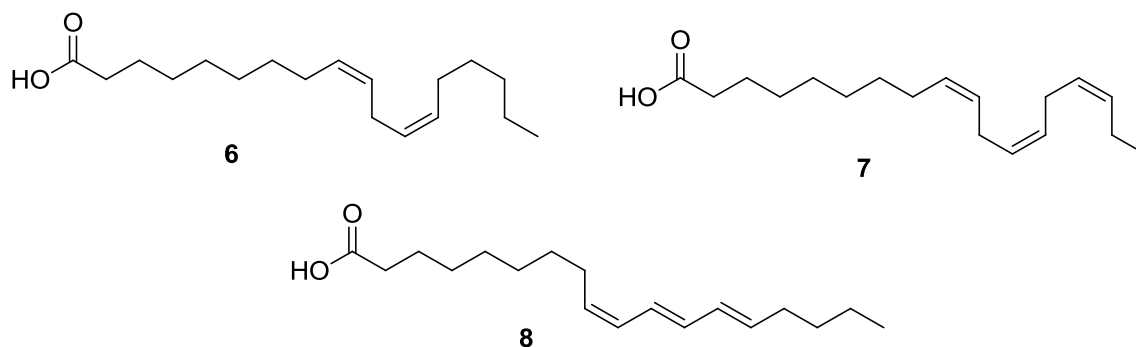
⁶ D. Stoianova, A. Johns, R. Pederson, in *Handb. Metathesis Second Ed.* (Eds.: R.H. Grubbs, D.J. O'Leary), Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim, **2015**, pp. 699–726.

⁷ S. Warwel, F. Brüse, C. Demes, M. Kunz, M. R. gen. Klaas, *Chemosphere* **2001**, *43*, 39–48.

⁸ J. L. Zullo, J. C. Anderson, H. Kaido, R. L. Pederson, Y. Schrodi, S. W.H., M. J. Tupy, E. H. Wagener, *Surface Coating Compositions and Methods*, **2011**, US7951232B2.

⁹ M. L. De Souza, J. L. Zullo, J.C. Anderson, R. L. Pederson, Y. Schrodi, *Antimicrobial Compositions, Methods and Systems*, **2006**, US20080033026A1.

While the above-mentioned crops yield edible vegetable oils that can be used as cooking oils in food preparation, some polyunsaturated non-edible seed oils are also available in vast amount. Linseed oil can contain up to 50% α -linolenic acid (**7**, Scheme 5) as triglycerides. The application of linseed oil is somehow limited due to its high sensitivity to oxidation.



Scheme 5. α -Linoleic acid (**6**), α -Linolenic acid (**7**) and α -eleostearic acid (**8**)

A typical example for the non-edible vegetable oil is the α -eleostearic acid (**8**, Scheme 5) produced from the nugget of the tung tree. The tung oil contains about 80% of **8**. **8** is a conjugated triene, which is even more sensitive to oxidation than **7**. Although **7** and **8** are highly unsaturated polyenes, their utilization *via* metathesis is not yet fully explored.

Besides naturally occurring polyenes, petrochemical based ones are also available on a vast scale. Ethylene production *via* steam-cracking is currently one of the key steps in the processing of crude oil. The product distribution is heavily dependent on the feed and the technology applied. Among the products, 1,3-butadiene and aromatics are considered as a value-added side-products, while cyclopentadiene (**CPD**) and other cyclic olefins are often hydrogenated and re-cracked. The proportion of these side-products are significant, for example producing 100 kg ethylene could lead to 4 kg of **CPD**.

3. Experimental methods

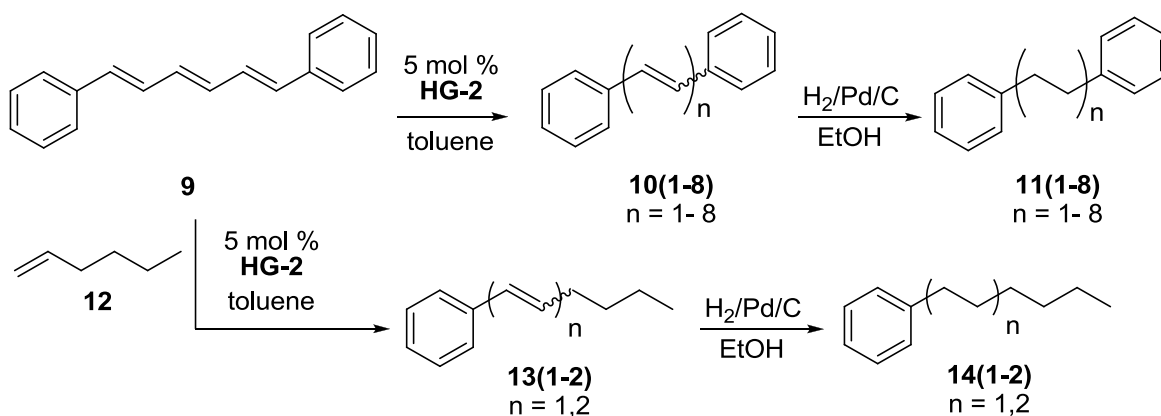
All reactions were conducted under nitrogen atmosphere using *Schlenk*-technique or under argon atmosphere in an MBraun (Labmaster PRO) glovebox. Cyclopentadiene (**CPD**) was freshly prepared from dicyclopentadiene at 210°C under nitrogen atmosphere.

The overall yield has been determined for each reaction product using GC and ^1H NMR techniques, utilizing ethyl benzene as internal standard. Quantitative ^{13}C NMR studies were carried out by Attila Domján.

4. Results and discussion

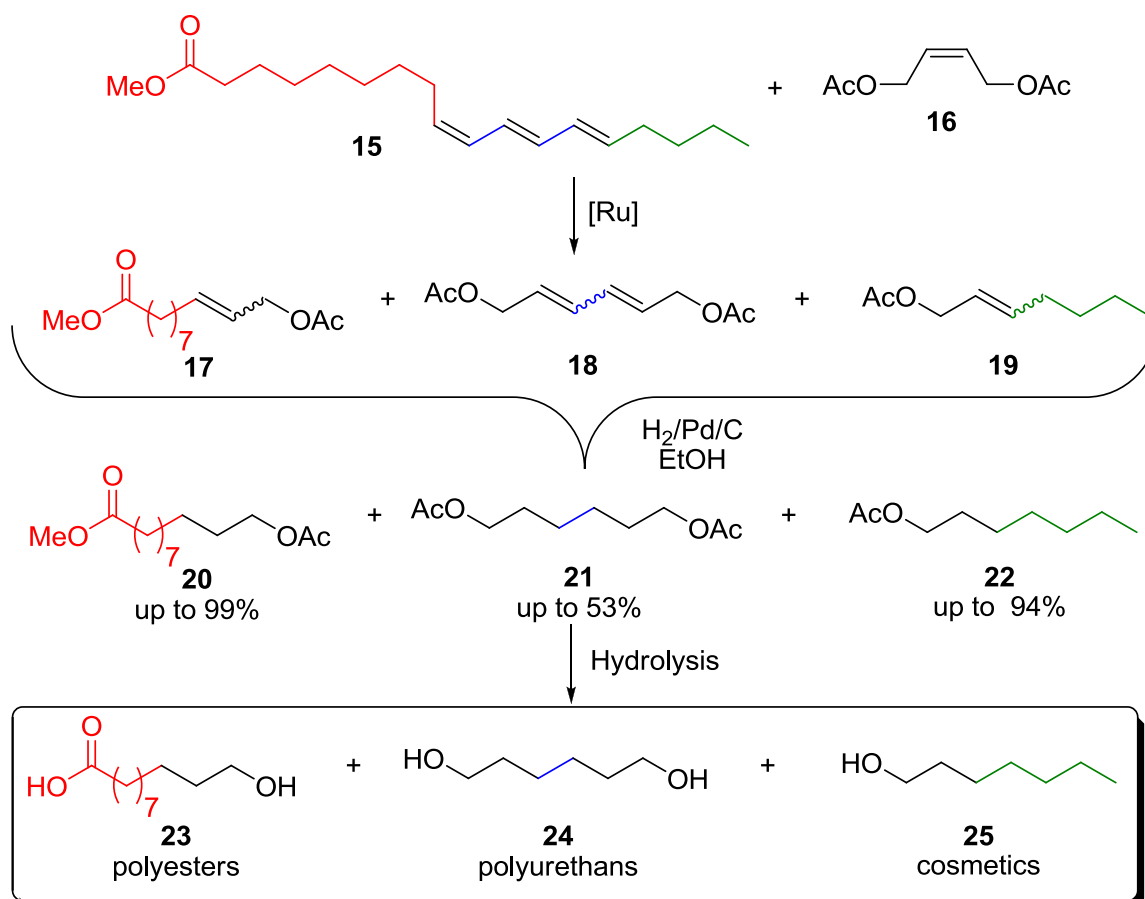
Throughout my work, the metathesis of different low value conjugated compounds was evaluated. Utilizing Grubbs metathesis catalysts systems, both bio-based and petroleum-based conjugated starting materials were converted to value-added polyurethane and polyester intermediates.

First, the metathesis of conjugated systems was investigated on commercially available model compounds, such as 1,6-diphenyl-1,3,5-hexatriene (**9**, Scheme 6).^[P1] Self- and cross-metathesis (**CM**) reactions revealed the formation of low solubility polymeric side-products, even at excess of the **CM** agent. The homologue formation can be explained by the recombination of the conjugated $-\text{CH}=\text{CH}-$ units in the molecule, thus allowing them to be recognized as building blocks.



Scheme 6. Homologue formation in the self- and cross-metathesis of **9**

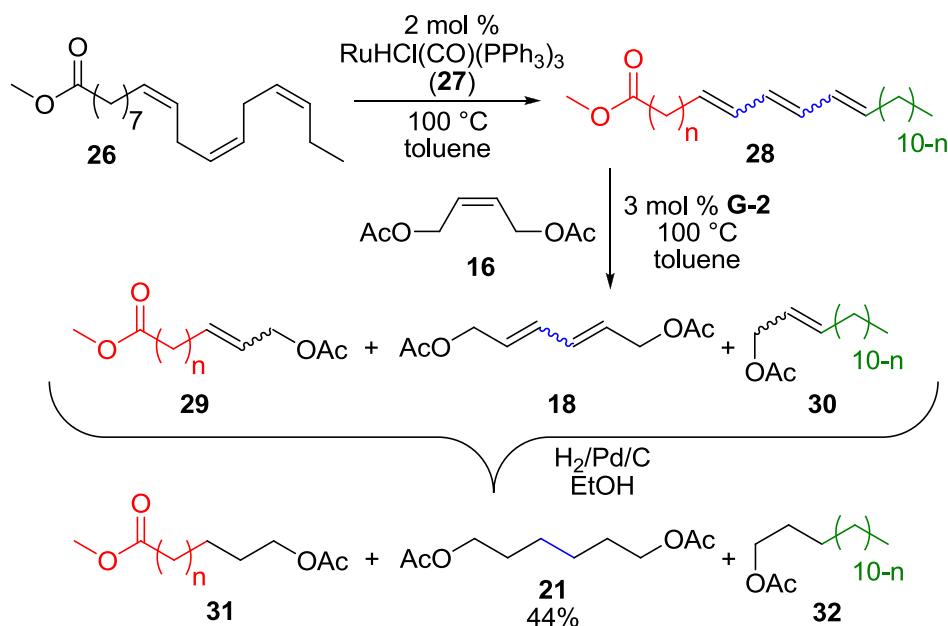
Following the initial model reactions, the metathesis of renewable methyl eleostearate (**15**) and tung oil was carried out with different ruthenium alkylidene catalysts (**G-2**, **HG-2** and **G-3**).^[P2] Methyl eleostearate (**15**) was prepared from commercially available tung oil *via* trans esterification with methanol. Applying **16** diester as **CM** agent formed the expected monomer intermediate **21** after hydrogenation, up to 53 % yield (Scheme 7).



Scheme 7. Metathesis of methyl eleostearate (**15**)¹⁰

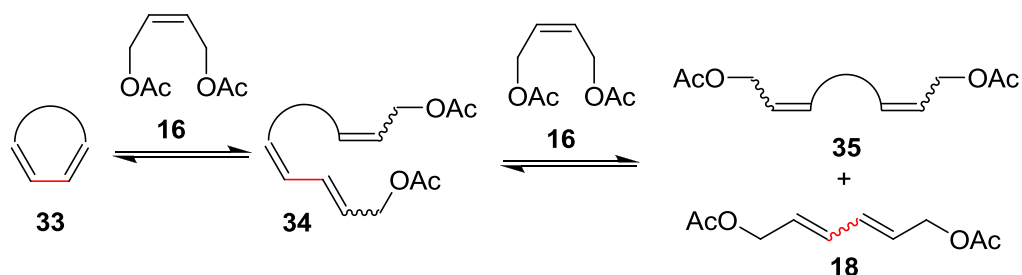
Conversion of pretreated tung oil was also carried out resulting in lower yield (26%) of **21**, which can be explained by the acidic, and possibly peroxide impurities in the natural oil. After establishing the metathesis of conjugated fatty acid esters to produce **21** value added intermediate, the feasibility of extending this procedure to non-conjugated renewable feedstock was investigated. Methyl linolenate (**26**) is a promising candidate for such transformation since its isolated double bonds can be readily isomerized, resulting in a mixture of conjugated fatty acid esters (**28**).^[P2] This procedure involved subsequent isomerization, metathesis and hydrogenation in one-pot, to yield the value added **21** (Scheme 8). The **CM** with **16** resulted in similar yield (44%) of **21** as that of the metathesis of **15**.

¹⁰ Different products (**20**, **21**, **22**) comes from the different color coded part of the starting material (**15**). Yields determined for **20**, **21**, **22** are based on **15**.



Scheme 8. Isomerization and metathesis of methyl linolenate (26)¹¹

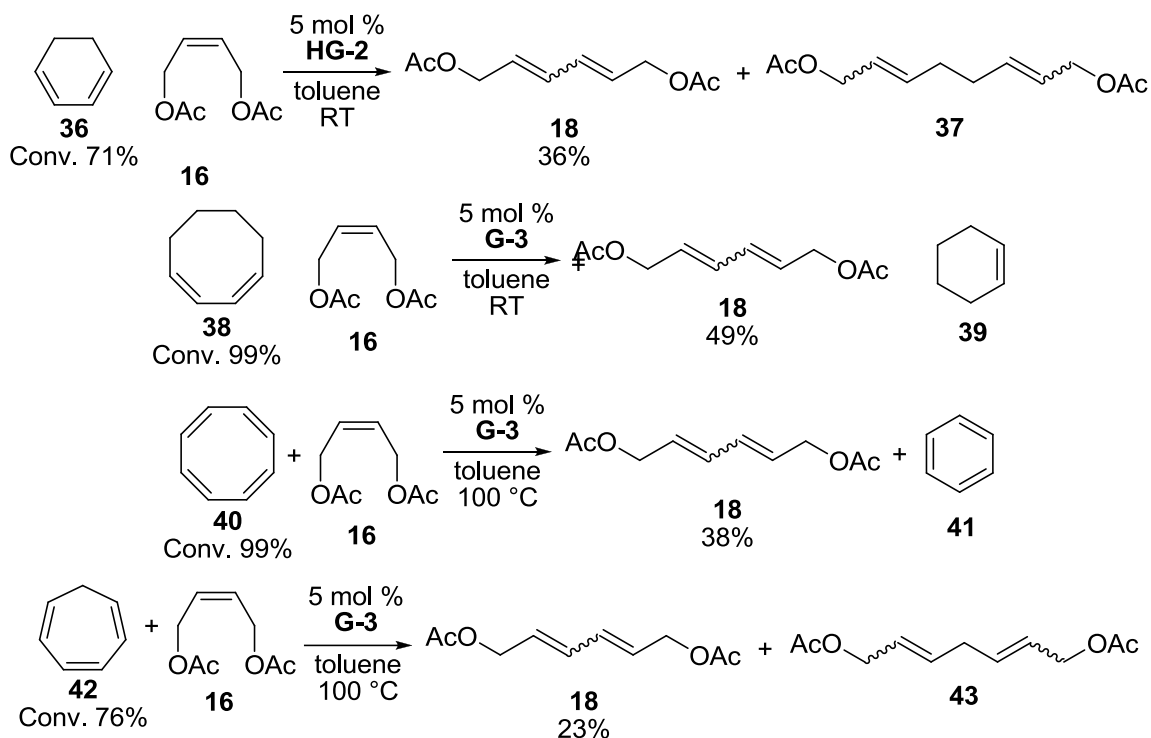
Petrochemical-based small cyclic polyenes (33) were also reacted with 16 in a subsequent **ROCM/CM** fashion (Scheme 9 and 10), forming the anticipated 18, among other diesters (35) and self-metathesis products.



Scheme 9. **CM** of small, conjugated polyenes with 16

Each case, four-fold excess of **CM** reagent (16) were applied per double bond of the corresponding polyene. Using this, relatively high excess of **CM** agent resulted in only trace amounts of the possible ring-opened polyene intermediate (34) as the **ROCM** reaction was immediately followed by a consecutive **CM** step leading to the formation of derivatives of 35 and 18 (Scheme 10) in reasonable yield.

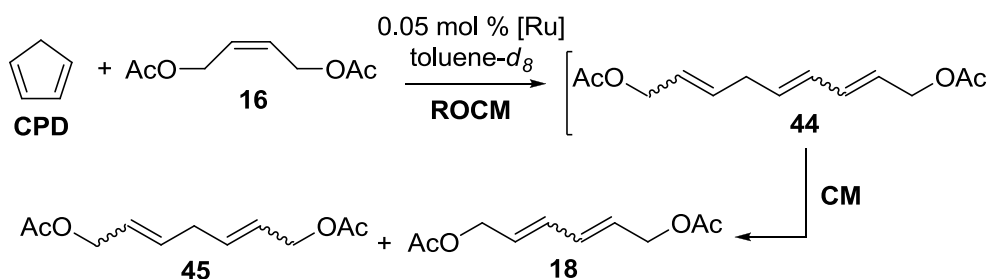
¹¹ Different products (21, 31, 23) comes from the different color coded part of the starting material (28). Yield determined for 21 is based on 26.



Scheme 10. Producing **18** monomer intermediate from cyclic polyenes

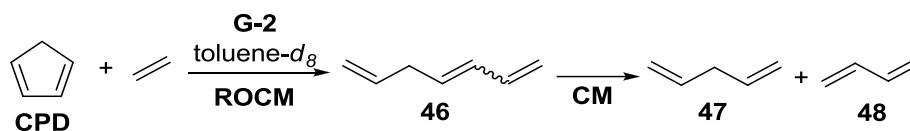
In conclusion, **CM** of cyclic polyolefines proceeded with good conversion and reasonable selectivity giving **18** as target molecule. The featured reactions clearly indicated that the application of the **CM** reagent in excess promotes the secondary metathesis products formation in a consecutive **ROCM/CM** tandem reaction.

Following the metathesis of different small cyclic polyenes, the **CM** of cyclopentadiene (**CPD**) was investigated in detail.^[P3] The **CM** of **CPD** was carried out, utilizing **16** diester as **CM** agent (Scheme 11). Catalyst loadings as low as 0.05 mol % showed good conversion (> 90%) and produced the expected polyurethane and polyester intermediates (**18** [59%], **45** [59%]) in good yield.



Scheme 11. Metathesis of **CPD** with **16**

Finally, the ethenolysis of **CPD** was carried out, producing butadiene (**48**) and 1,4-pentadiene (**47**) in moderate yield (Scheme 12).^[P3] This lower yield can be explained by the appearance of ruthenium methyldiene intermediates throughout the reaction, which is known for its decreased stability and reduced metathesis activity.



Scheme 12. Ethenolysis of **CPD**

5. Theses

1. Applying Grubbs metathesis catalyst, a model reaction with (*Z*)-stilbene was carried out to utilize the conjugated unit of the bio-based methyl eleostearate to form alkene homologues with increased chain length.**[P1]**
2. Utilizing different Grubbs metathesis catalysts, renewable starting material methyl eleostearate was converted to monomer intermediate hexane-1,6-diyl diacetate in moderate yield.**[P2]**
3. Methyl linolenate was utilized to synthesize hexane-1,6-diyl diacetate in one-pot: methyl linolenate was isomerized to a mixture of conjugated esters utilizing $\text{RuHCl}(\text{CO})(\text{PPh}_3)_3$ catalyst, which was metathesized applying Grubbs metathesis catalyst, followed by subsequent catalytic hydrogenation (Pd/C).**[P2]**
4. Cross metathesis of cyclopentadiene was carried out, utilizing (*Z*)-but-2-ene-1,4-diyl diacetate as cross metathesis agent to form hexane-1,6-diyl diacetate and heptane-1,7-diyl diacetate in good yield after subsequent hydrogenation (Pd/C).**[P3]**

Articles accepted by the Ph.D. commission:

- P1.** Kovács E.; SÁghy P.; **Turczel G.**; Tóth I.; Lendvay Gy.; Domján A.; Anastas P. T.; Tuba R.: Metathesis of renewable polyene feedstocks - Indirect evidences of the formation of catalytically active ruthenium allylidene species, *J. Organomet. Chem.* **2017**, 847, 213–217. [IF (2017): 1.946, independent citation: 1, participation: 100%]
- P2.** Kovács E.; **Turczel G.**; Szabó L.; Varga R.; Tóth I.; Anastas P. T.; Tuba R.: Synthesis of 1,6-Hexandiol, Polyurethane Monomer Derivatives *via* Isomerization Metathesis of Methyl Linolenate, *ACS Sustain. Chem. Eng.* **2017**, 5, 11215–11220. [IF (2017): 6.140, independent citation: 2, participation: 90%]
- P3.** **Turczel G.**; Kovács E.; Csizmadia E.; Nagy T.; Tóth I.; Tuba R.: One-pot Synthesis of 1,3-Butadiene and 1,6-Hexanediol Derivatives from Cyclopentadiene (CPD) *via* Tandem Olefin Metathesis Reactions, *ChemCatChem*, **2018**, 10, 4884–4891. [IF (2017): 4.674, independent citation: 1, participation: 80%]
- P4.** **Turczel G.**; Kovács E.; Tuba R.: Megújuló polialkének metatézise, *XL. Kémiai Előadói Napok, Szeged, 2017*. Conference proceeding, 216-219. [participation: 100%]

Additional articles:

Turczel G.; Kovács E.; Merza G.; Philip C.; Anastas P. T.; Tuba R.: Synthesis of Semiochemicals *via* Olefin Metathesis, *ACS Sustain. Chem. Eng.* **2019**, 7, 33-48. [IF (2017): 6.140, participation: 100%]

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Könczöl L.; **Turczel G.**; Szpisjak T.; Szieberth D.: The stability of η^2 -H₂ borane complexes – a theoretical investigation, *Dalton Transactions* **2014**, *43*, 13571-13577. [IF (2014): 4.197, independent citation: 5, participation: 10%]

Presentations/Posters:

XXXV. Kémiai Előadói Napok: Szeged 2012. (Oral presentation) **Turczel G.**;

Kovács E.; Faigl F.: Oxiránok erős bázisokkal indukált átrendeződése

XL. Kémiai Előadói Napok: Szeged 2017. (Oral presentation) **Turczel G.**; Kovács

E.; Tuba R.: Megújuló polialkének metatézise

12th European Workshop in Phosphorus Chemistry: Kassel 2015. (Poster)

Turczel G.; Pánczél J.; Szieberth D.; Nyulászi L.: Theoretical study of the hydrolysis mechanism of the phosphorus-chlorine bond

256th ACS National Meeting & Exposition: Boston 2018. (Oral presentation)

Turczel, G.; Csizmadia, E.; Kovács E.; Tóth, I.; Anastas P. T; **Tuba R.**: Metathesis of Conjugated Polyunsaturated Materials

256th ACS National Meeting & Exposition: Boston 2018. (Oral presentation)

Kovács, E.; **Turczel, G.**; Szabó L.; Varga R.; Tóth I.; Anastas P. T; Tuba R.: Synthesis of Polyurethane Monomers from Renewable Resources *via* One-pot Isomerization Metathesis Reactions

256th ACS National Meeting & Exposition: Boston 2018. (Poster) **Turczel, G.**;

Csizmadia E.; **Kovács E.**; Tóth I.; Anastas P. T; Tuba R.: Synthesis of supramolecular vinyl alcohol (VA) copolymers *via* ring-opening metathesis polymerization (ROMP) for biogenic amine delivery

256th ACS National Meeting & Exposition: Boston 2018. (Poster) **Kovács E.**;

Turczel, G.; Nagyházi M.; Szálás G.; Sággy P.; Tuba R.: Synthesis of water-soluble CAAC catalyst ligands