DOI: 10.1002/cssc.201200320

Methyl Ricinoleate as Platform Chemical for Simultaneous Production of Fine Chemicals and Polymer Precursors

Antoine Dupé,[a, b] Mathieu Achard,[a] Cédric Fischmeister,*[a] and Christian Bruneau*[a]

The modification of methyl ricinoleate by etherification of the hydroxyl group was accomplished by using a nonclassical ruthenium-catalyzed allylation reaction and also by esterification. Methyl ricinoleate derivatives were engaged in ring-closing metathesis (RCM) reactions leading to biosourced 3,6-dihydropyran and α,β-unsaturated lactone derivatives with concomitant production of polymer precursors. Sequential RCM/hydrogenation and RCM/cross-metathesis were also implemented as a straightforward method for the synthesis of tetrahydropyran and lactone derivatives as well as valuable monomers (i.e., polyamide precursors).

Introduction

The sustainable utilization of biomass as a renewable source of raw materials is a domain of strong economic and environmental interest in a context of fossil-resource shortage.[1] Owing to their long carbon chains, fatty acid methyl esters (FAMEs) offer interesting perspectives for the polymer industry[2] and for the preparation of surfactants.[3] Typically, these compounds can be derivatized by C=C bond transformations, among which efficient and selective catalytic processes are preferable.[4] Since the early seventies, olefin metathesis has been used for the transformation of FAMEs,[5] but it is only recently that the incorporation of functional groups by olefin metathesis was made possible thanks to the development of highly active and functional-group tolerant catalysts.[6] For example, cross-metathesis reactions with methyl acrylate have been first reported by Meier et al.,[7] whereas our group focused on cross-metathesis transformations with acrylonitrile to produce polyamide monomers.[8] In particular, we reported the direct synthesis of amino esters by a tandem cross-metathesis/C=C bond and CN hydrogenation reaction.[9] We have become interested in the transformation of methyl ricinoleate (*R*-12-hydroxy-*cis*-9-octadecenoic acid methyl ester) as it presents the double advantage of being a nonedible oil derivative and incorporating a hydroxyl functional group, which enables a thermal rearrangement towards the valuable methyl 10-undecenoate[10] and 1-heptanal.

To the best of our knowledge, the preliminary derivatization of methyl ricinoleate through the hydroxyl group by ring-closing metathesis (RCM) has not been reported. We envisioned that the introduction of allylic ethers or acrylic ester substituents (Scheme 1) would lead to 3,6-dihydropyran and α,β-unsaturated lactone derivatives, which are compounds of interest in medicine, pharmacology, and flavors.[11] These products would be obtained with coproduction of methyl 9-decenoate, another important raw material for the polymer industry (Scheme 2). Herein, we report on the transformation of methyl ricinoleate into designed diene derivatives and their RCM reaction leading to dihydropyran and unsaturated lactone derivatives. We show that the choice of catalyst can drive the selectivity of the reaction and that domino ring-closing/cross-metathesis and tandem RCM/hydrogenation can be implemented, leading to a variety of products of interest for fine chemistry and polymer synthesis.

Results and Discussion

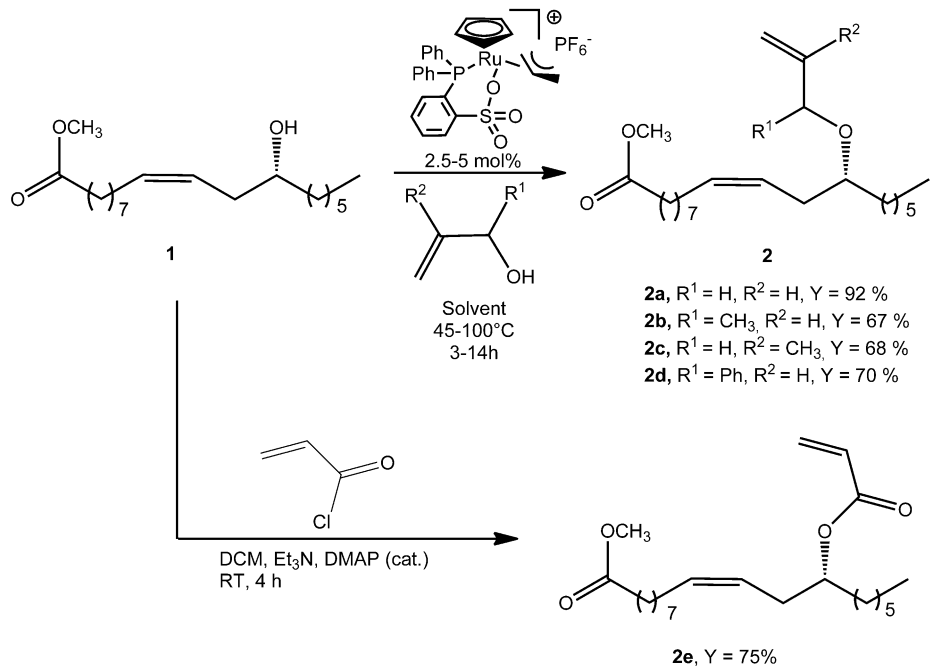
Methyl ricinoleate derivatization

The allylation of the hydroxyl group of methyl ricinoleate was attempted by a standard NaH deprotonation in the presence of allyl bromide, but this method failed to provide the desired product **2a** in good yield due to competitive transesterification reactions. Other Pd^0-catalyzed allylation methods[12] were also unsuccessful. The catalytic allylation of methyl ricinoleate directly with branched allyl alcohol was successfully achieved by extension of a recently reported procedure using [RuCp(DPPSA)(η^3-propenyl)] (Cp = cyclopentadienyl, DPPSA = *ortho*-diphenylphosphinesulfonate) as a catalyst (Scheme 1).[13] Structural diversity was achieved by the utilization of various allylic alcohols, which regioselectively provided the products featuring a terminal allylic group in good to high yields using 2.5–5 mol% of catalyst at 45–100 °C. Various solvents including

[a] *A. Dupé, Dr. M. Achard, Dr. C. Fischmeister, Dr. C. Bruneau*
Institut des Sciences Chimiques de Rennes
Organométalliques: Matériaux et Catalyse
UMR 6226-CNRS-Université de Rennes 1, Campus de Beaulieu
263, avenue du général Leclerc. 35042 Rennes (France)
Fax: (+33) 223236939
E-mail: cedric.fischmeister@univ-rennes1.fr
christian.bruneau@univ-rennes1.fr

[b] *A. Dupé*
ADEME
20, avenue du Grésillé
49004 Angers cedex 01 (France)

Supporting Information for this article is available on the WWW under http://dx.doi.org/10.1002/cssc.201200320.



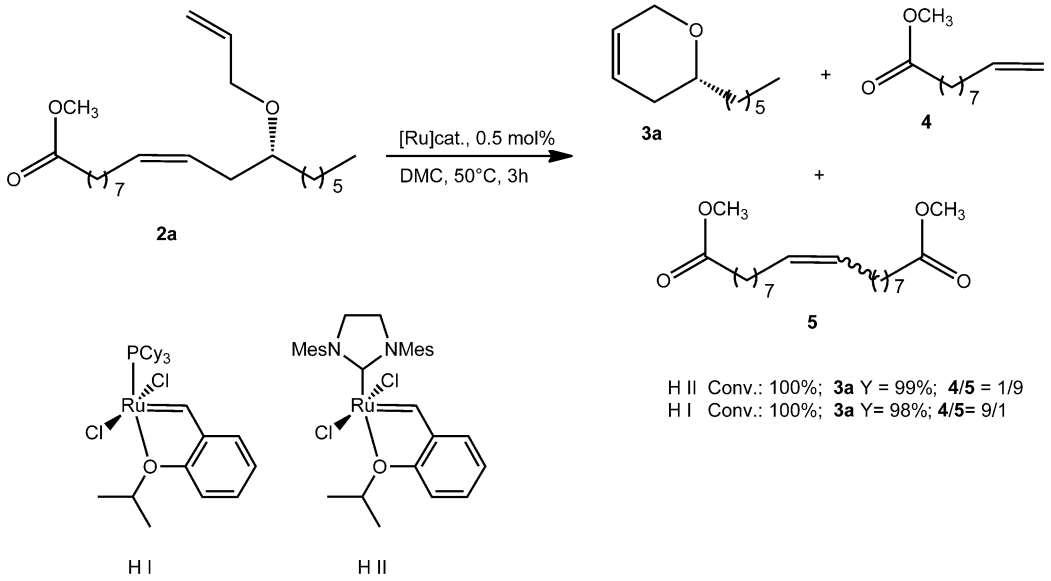
Scheme 1. Preparation of methyl ricinoleate derivatives.

dimethyl carbonate (DMC) and diethyl carbonate (DEC) were used as greener alternatives to the conventional dichloromethane and dichloroethane.[14] The esterification of methyl ricinoleate was achieved using acryloyl chloride in dichloromethane to yield the desired diester **2e** in 75% yield (Scheme 1).

Ring Closing Metathesis transformations

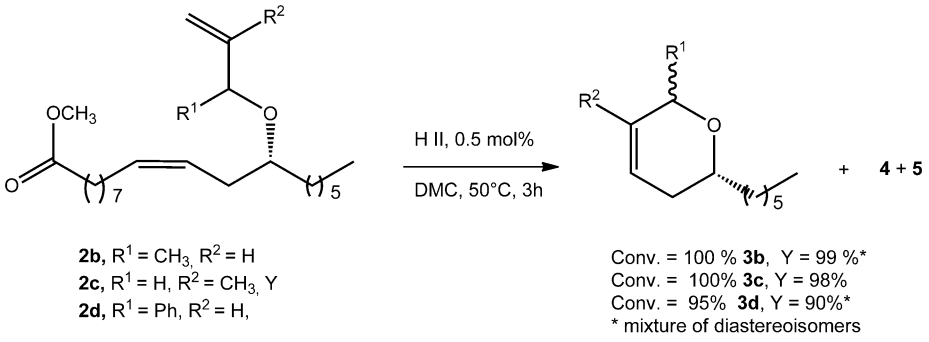
The RCM of **2a** was first attempted as a model reaction using the second generation Hoveyda catalysts (HII) in DMC.[15] This reaction led almost quantitatively to the desired dihydropyran (**3a**) isolated in 99% yield and to the mono- and diesters **4** and **5** obtained in a 1/9 ratio on the basis of yields calculated by GC (Scheme 2). As other diesters, **5** is an interesting compound for the production of polyesters[16] and is accessible by self-metathesis[17] of methyl oleate or fermentation of oleic acid.[18–19] In this case, **5** was most likely obtained by self-metathesis of **4** producing also ethylene through a secondary metathesis reaction rather than by self-metathesis of the starting **2a** because no trace of 7,12-(bis-allyloxy)octadec-8-ene could be detected.

With this first result we envisioned the same reaction in the presence of the first generation Hoveyda catalyst (HI). Indeed, first generation catalysts are generally effective for promoting RCM reactions, but they are less efficient in promoting cross-metathesis transformations and should thus lead to the same dihydropyrane **3a** and the two esters **4** and **5**, but with a reverse selectivity relative to HII. Thus, in the reaction of **2a** with HI at 50 °C in DMC for 3 h, **2a** was fully transformed and **3a** was again isolated in high yield, but as anticipated the monoester **4** was now obtained as the major coproduct (**4**/**5** = 9:1, Scheme 2). It was thus demonstrated that it is possible to select one of the reaction products (polymer precursor) without interfering with the synthesis of the other product (fine chemical) simply by switching between first and second generation ruthenium catalysts.

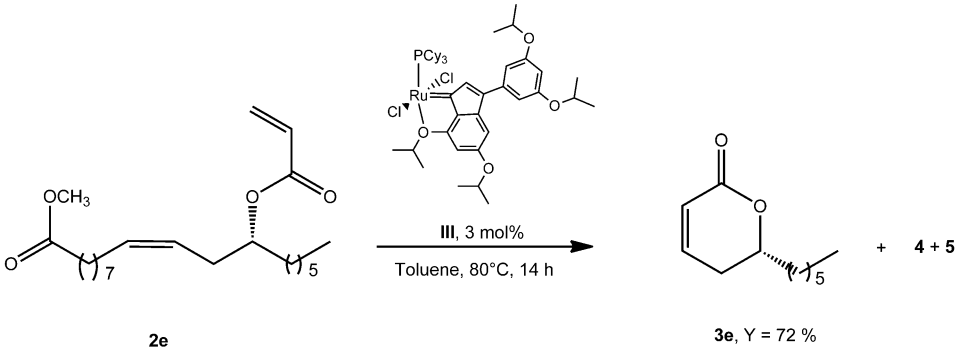


Scheme 2. RCM of *O*-allyl methyl ricinoleate.

Although the molecular structure of the 3,6-dihydropyran derivative was imposed at the α-ether position by the nature of the starting methyl ricinoleate, molecular diversity was obtained using derivatives **2b–d**. In the presence of HII (0.5 mol%), these compounds were efficiently transformed into the corresponding 3,6-dihydropyrans in high yields with concomitant formation of diester **5**, whereas monoester **4** was detected in low amounts as in the case of **2a** (Scheme 3).



Scheme 3. Synthesis of 3,6-dihydropyran derivatives.



Scheme 4. Synthesis of methyl ricinoleate derived α,β-unsaturated lactone.

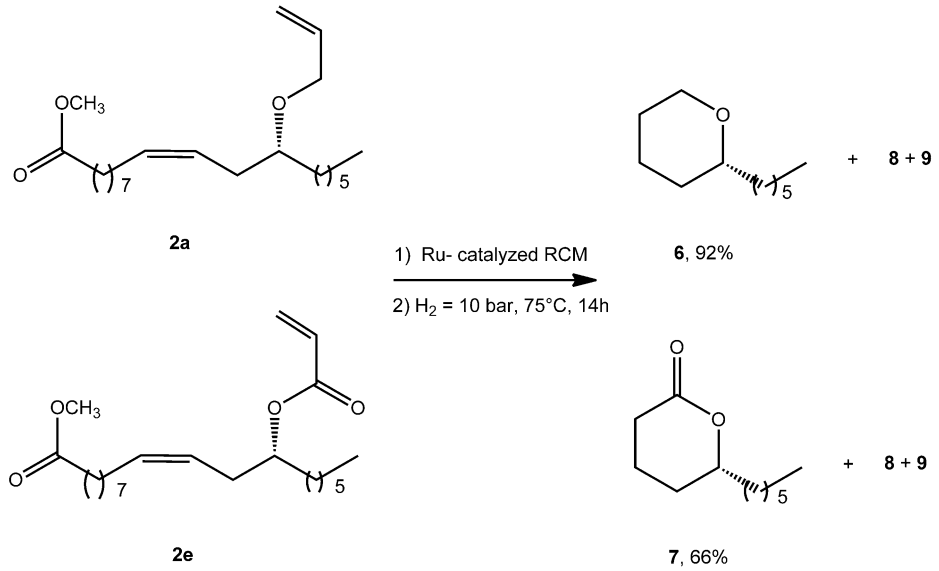
The transformation of precursor **2e** into the corresponding α,β-unsaturated lactone was next attempted.[20] As pointed out in the literature, the formation of lactones by RCM does not perform very well and usually requires high catalyst loadings.[11b,c,f,20] In our case, catalyst loadings of 3 mol% were necessary to ensure high conversions. When HII was used at 50 °C in DMC for 14 h, the reaction proceeded with full conversion, but led to the formation of side products arising from double bond migration in the main chain. HI was thus used in toluene at 80 °C for 14 h and indeed furnished a cleaner reaction mixture, but with lower efficiency (conversion of 45%) leading to **3e** in 40% yield. Recently, we[21] and others[22] have reported on a new family of first generation olefin-metathesis catalysts based on a chelating indenylidene architecture (Scheme 4, **III**). More specifically, we have shown that the combination of high thermal stability and slow activation of complex **III** resulted in some cases in improved RCM performance.[21a] Thus, when the RCM of **2e** was attempted with **III**, the reaction proceeded smoothly reaching 75% conversion in 14 h and furnishing **3e** in 72% yield (Scheme 4). As with the synthesis of **3a** in the presence of HI, **4** was the major coproduct (**4**/**5** = 6:1 by GC analysis). This first example constitutes an entry towards other unsaturated lactones with molecular diversity in terms of substitution pattern and ring sizes that could be accessible using the same synthetic strategy.

Tandem RCM/Hydrogenation

Having demonstrated the efficiency of the RCM reaction for the production of various 3,6-dihydropyrans and α,β-unsaturated lactone derivatives, the tandem[23] RCM/hydrogenation sequence[8c,24] was attempted to prepare tetrahydropyran and lactone derivatives that are also compounds of interest in various domains, such as fragrance and pharmacy.[25] For that purpose, the RCM reactions of **2a** and **2e** were repeated as already described (Scheme 2 and 4) and the crude reaction mixtures were transferred into a high pressure reactor. After 14 h at 75 °C under H_2 (10 bar), products **6** and **7** were isolated in 92 and 66% yield, respectively, with concomitant production of a mixture of the saturated monoester **8** and diester **9** (**8**/**9** = 1:9 by GC analysis for the transformation of **2a** and 6:1 by ^{1}H NMR analysis for the transformation of **2e**) resulting from the hydrogenation of **4** and **5**, respectively (Scheme 5).

Cascade RCM/cross-metathesis

As mentioned earlier, the RCM reactions of methyl ricinoleate derivatives **2a–d** furnished compounds **3a–d** with concomitant formation of mono- and diesters **4** and **5** that are useful reagents or raw materials for the polymer industry. For example, **5** and methyl 10-undecenoate (one extra carbon atom with regard to **4**) have recently been used for the preparation of polyamide monomers through cross-metathesis reactions with acrylonitrile.[8a,c,9] Examples of diester synthesis by cross-metathesis of FAMEs with methyl acrylate have also been recently reported.[7] The synthesis of the same compounds (i.e., α,ω-nitrile ester and α,ω-diester) was attempted in a cascade RCM/cross-metathesis sequence involving the initial RCM reaction of **2a** leading to 3,6-dihydropyran **3a**, followed by a cross-metathesis reaction with methyl acrylate and acrylonitrile (Scheme 6). Compound **2a** underwent a RCM reaction in the presence of methyl acrylate (2 equiv) at 100 °C in toluene. The



Scheme 5. Tandem RCM/hydrogenation transformations.

cascade reaction with methyl acrylate proceeded with full conversion of **2a** furnishing the RCM product **3a** in 93% yield and the cross-metathesis product **10** in 91% yield. The same reaction with acrylonitrile turned out to be more difficult and required a higher catalyst loading to ensure efficient formation of **11**. With 1 mol% of catalyst HII, **3a** and **11** were isolated in 92 and 65% yield, respectively (whereas with an initial catalyst loading of 0.5 mol%, **3a** and **11** were isolated in 91 and 43% yield, respectively). As generally observed, cross-metathesis with methyl acrylate furnished exclusively the *E* isomer, whereas the *Z* isomer was obtained as the major product for the cross-metathesis with acrylonitrile. This cascade or domino protocol is thus another example where a fine chemical and a polymer precursor are produced efficiently and simultaneously in a one-pot reaction.

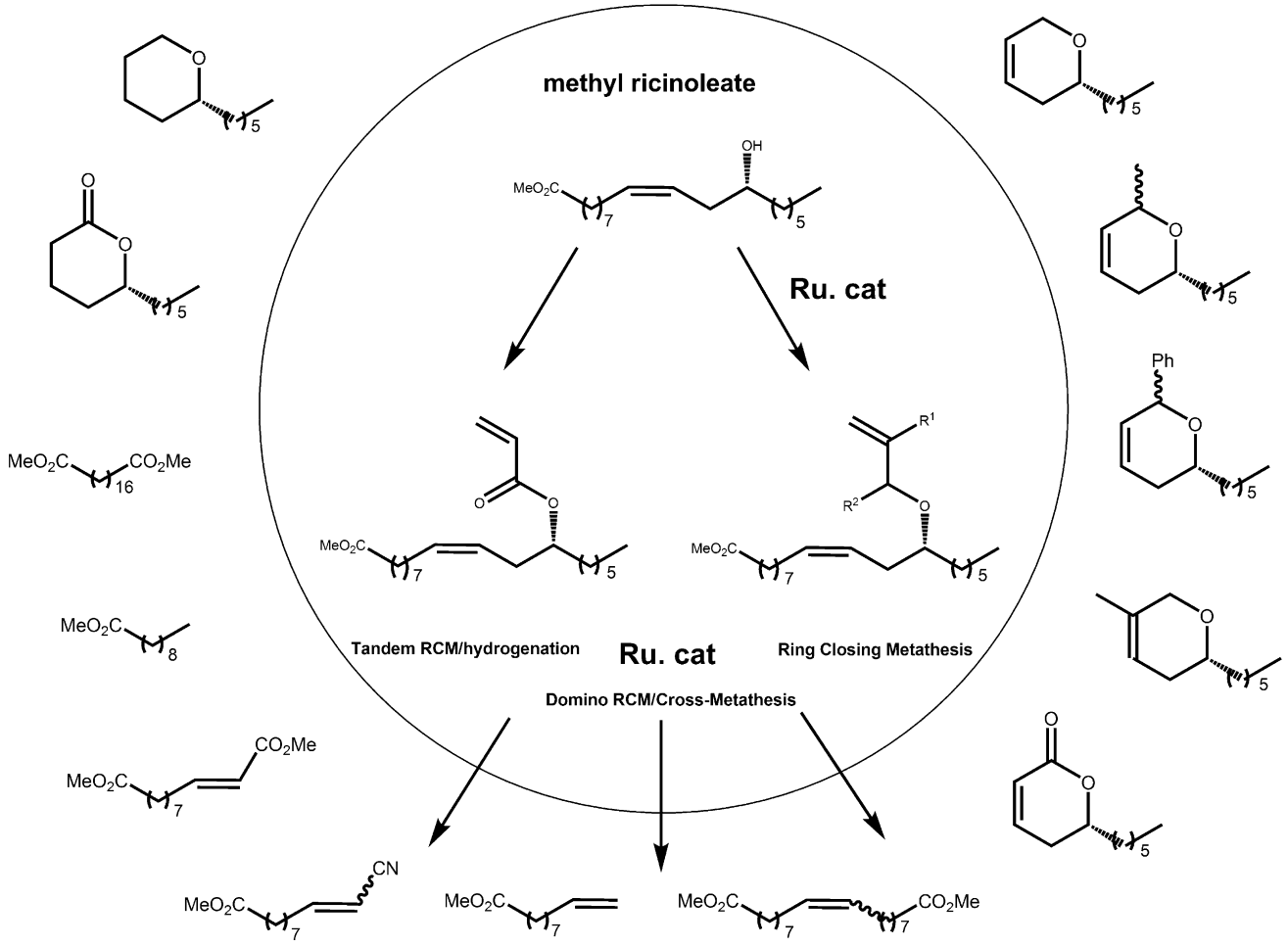
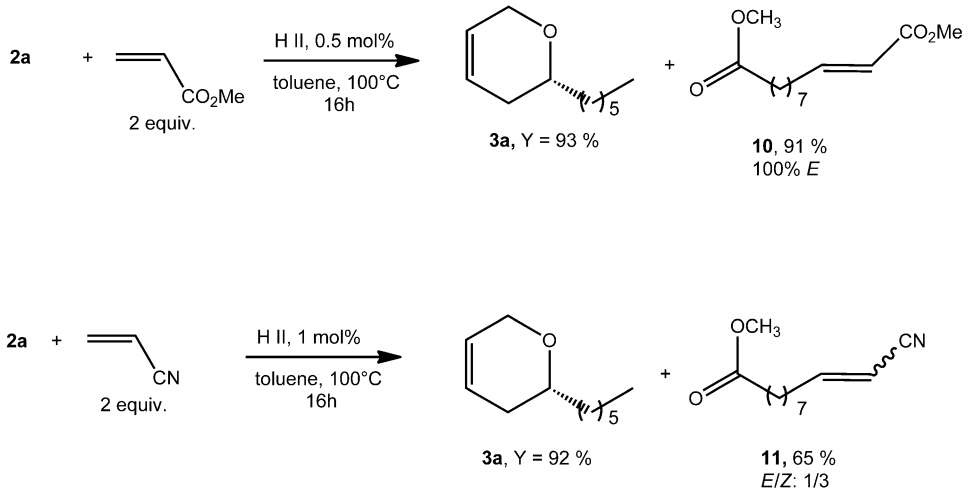


Figure 1. Methyl ricinoleate as a platform chemical.

Conclusions

We have shown that methyl ricinoleate can be used as a platform chemical for the synthesis of a variety of functional compounds of interest both in fine chemistry and polymer synthesis (Figure 1). These products were prepared using efficient olefin metathesis transformations performed as a single reaction or by sequential transformations. These first examples open up the route towards further utilization of methyl ricinoleate for the production of a broad range of functional molecules potentially accessible by the appropriate initial derivatization of the hydroxyl group preferentially using efficient and selective catalytic methods.



Scheme 6. Cascade RCM/cross-metathesis transformations.

Acknowledgements

The authors thank ADEME and the Region Bretagne for a PhD grant to AD.

Keywords: hydrogenation · lactones · metathesis · renewable resources · ruthenium

[1] a) P. N. R. Vennestrøm, C. M. Osmundsen, C. H. Christensen, E. Taarning, *Angew. Chem.* **2011**, *123*, 10686; *Angew. Chem. Int. Ed.* **2011**, *50*, 10502; b) P. Gallezot, *Chem. Soc. Rev.* **2012**, *41*, 1538; c) A.-L. Marshall, P. Alaimo, *Chem. Eur. J.* **2010**, *16*, 4970; d) C. H. Christensen, J. Raas-Hansen, C. C. Marsden, E. Taarning, K. Egeblad, *ChemSusChem* **2008**, *1*, 283; e) R. Diercks, J.-D. Arndt, S. Freyer, R. Geier, O. Machhammer, J. Schwartze, M. Volland, *Chem. Eng. Technol.* **2008**, *31*, 631; f) A. Corma, S. Iborra, A. P. Velty, *Chem. Rev.* **2007**, *107*, 2411.

[2] a) L. Montero de Espinosa, M. A. R. Meier, *Eur. Polym. J.* **2011**, *47*, 837; b) J. C. Ronda, G. Lligadas, M. Galià, V. Cadiz, *Eur. J. Lipid Sci. Technol.* **2011**, *113*, 46; c) Y. Xia, R. C. Larock, *Green Chem.* **2010**, *12*, 1893; d) M. A. R. Meier, *Macromol. Chem. Phys.* **2009**, *210*, 1073; e) D. Quinzler, S. Mecking, *Angew. Chem.* **2010**, *122*, 4402; *Angew. Chem. Int. Ed.* **2010**, *49*, 4306; f) Y. Lu, R. C. Larock, *ChemSusChem* **2009**, *2*, 136; g) M. A. R. Meier, J. O. Metzger, U. S. Schubert, *Chem. Soc. Rev.* **2007**, *36*, 1788; h) F. Pardal, S. Salhi, B. Rousseau, M. Tessier, S. Claude, A. Fradet, *Macromol. Chem. Phys.* **2008**, *209*, 64; i) S. Warwel, J. Tillack, C. Demes, M. Kunz, *Macromol. Chem. Phys.* **2001**, *202*, 1114; j) H. Mutlu, M. A. R. Meier, *Eur. J. Lipid. Sci. Technol.* **2010**, *112*, 10.

[3] P. Foley, A. Kermanshahi pour, E. S. Beach, J. B. Zimmerman, *Chem. Soc. Rev.* **2012**, *41*, 1499.

[4] a) U. Biermann, U. Bornscheuer, M. A. R. Meier, J. O. Metzger, H. J. Schäfer, *Angew. Chem.* **2011**, *123*, 3938; *Angew. Chem. Int. Ed.* **2011**, *50*, 3854; b) A. Behr, A. Westfechtel, J. Perez Gomes, *Chem. Eng. Technol.* **2008**, *31*, 700.

[5] a) P. B. van Dam, M. C. Mittelmeijer, C. J. Boelhouver, *J. Chem. Soc. Chem. Commun.* **1972**, 1221.

[6] a) G. C. Vougioukalakis, R. H. Grubbs, *Chem. Rev.* **2010**, *110*, 1746; b) C. Samojlowicz, M. Bieniek, K. Grela, *Chem. Rev.* **2009**, *109*, 3708; c) P. H. Deshmukh, S. Blechert, *Dalton Trans.* **2007**, 2479; d) C. E. Diesendruck, E. Tzur, N. G. Lemcoff, *Eur. J. Inorg. Chem.* **2009**, 4185; e) C. Fischmeister, P. H. Dixneuf, *Metathesis Chemistry: From Nanostructure Design to Synthesis of Advanced Materials* (Eds.: Y. İmamoğlu, V. Dragutan), Springer, Dordrecht, Netherlands, **2007**, pp. 3; f) R. R. Schrock, A. H. Hoveyda, *Angew. Chem.* **2003**, *115*, 4740; *Angew. Chem. Int. Ed.* **2003**, *42*, 4592.

[7] a) A. Rybak, M. A. R. Meier, *Green Chem.* **2008**, *10*, 1099; b) A. Rybak, M. A. R. Meier, *Green Chem.* **2007**, *9*, 1356.

[8] a) X. Miao, R. Malacea, C. Fischmeister, C. Bruneau, P. H. Dixneuf, *Green Chem.* **2011**, *13*, 2911; b) C. Bruneau, C. Fischmeister, X. Miao, R. Malacea, P. H. Dixneuf, *Eur. J. Lipid Sci. Technol.* **2010**, *112*, 3; c) R. Malacea, C. Fischmeister, C. Bruneau, J.-L. Dubois, J.-L. Couturier, P. H. Dixneuf, *Green Chem.* **2009**, *11*, 152.

[9] a) X. Miao, C. Fischmeister, C. Bruneau, P. H. Dixneuf J.-L. Dubois, J.-L. Couturier, *ChemSusChem* **2012**, *5*, 1410; b) C. Bruneau, J-L. Couturier, P. Dixneuf, J.-L. Dubois, C. Fischmeister, X. Miao, WO2011138051, **2011**.

[10] M. Van der Steen, C. V. Stevens, *ChemSusChem* **2009**, *2*, 692.

[11] a) T. A. Adams, M. E. Welker, C. S. Day, *J. Org. Chem.* **1998**, *63*, 3683; b) I. Collins, *J. Chem. Soc. Perkin Trans. 1* **1999**, 1377; c) A. Schwäblein, J. Martens, *Eur. J. Org. Chem.* **2011**, 4335; d) A. B. Penissi, M. E. Vera, M. L. Mariani, M. I. Rudolph, J. P. Ceñal, J. C. de Rosas, T. H. Fogal, C. E. Tonn, L. S. Favier, O. S. Giordano, R. S. Piezzi, *Eur. J. Pharmacol.* **2009**, *612*, 122; e) S.-M. Lee, W.-G. Lee, Y.-C. Kim, H. Ko, *Bioorg. Med. Chem. Lett.* **2011**, *21*, 5726; f) A. D'Annibale, L. Ciaralli, M. Bassetti, C. Pasquini, *J. Org. Chem.* **2007**, *72*, 6067; g) P. V. Ramachandran, M. Venkat Ram Reddy, H. C. Brown, *Tetrahedron Lett.* **2000**, *41*, 583; h) J. A. Marco, M. Carda, S. Rodriguez, E. Castillon, M. N. Kneeteman, *Tetrahedron* **2003**, *59*, 4085.

[12] a) B. Schmidt, S. Nave, *Adv. Synth. Catal.* **2006**, *348*, 531; b) A. R. Haight, E. J. Stoner, M. J. Peterson, V. K. Grover, *J. Org. Chem.* **2003**, *68*, 8092.

[13] a) B. Sundararaju, M. Achard, B. Demerseman, L. Toupet, G. V. M. Sharma, C. Bruneau, *Angew. Chem.* **2010**, *122*, 2842; *Angew. Chem. Int. Ed.* **2010**, *49*, 2782; b) Z. Sahli, N. Derrien, S. Pascal, B. Demerseman, T. Roisnel, F. Barrière, M. Achard, C. Bruneau, *Dalton Trans.* **2011**, *40*, 5625.

[14] a) B. Schäffner, F. Schäffner, S. P. Verevkin, A. Börner, *Chem. Rev.* **2010**, *110*, 4554; b) H. Doucet, C. Fischmeister, *Green Chem.* **2011**, *13*, 741.

[15] For examples of utilization of DMC in metathesis reactions, see: a) X. Miao, C. Fischmeister, C. Bruneau, P. H. Dixneuf, *ChemSusChem* **2008**, *1*, 813; b) V. Le Ravalec, C. Fischmeister, C. Bruneau, *Adv. Synth. Catal.* **2009**, *351*, 1115; c) V. Le Ravalec, A. Dupé, C. Fischmeister, C. Bruneau, *ChemSusChem* **2010**, *3*, 1291; d) H. Bilel, N. Hamdi, F. Zagrouba, C. Fischmeister, C. Bruneau, *Green Chem.* **2011**, *13*, 1448.

[16] a) S. Warwel, C. Demes, G. Steinke, *J. Polym. Sci. Part A* **2001**, *39*, 1601; b) S. Warwel, J. Tillack, C. Demes, M. Kunz, *Macromol. Chem. Phys.* **2001**, *202*, 1114.

[17] J. C. Mol, *Green Chem.* **2002**, *4*, 5.

[18] D. Fabritius, H. J. Schäfer, A. Steinbüchel, *Appl. Microbiol. Biotechnol.* **1998**, *50*, 573.

[19] Long chain α,ω-diesters are also accessible by methoxycarbonylation reactions, see Ref.[2a] and: a) C. Jiménez-Rodriguez, G. R. Eastham, D. J. Cole-Hamilton, *Inorg. Chem. Commun.* **2005**, *8*, 878; b) M. R. L. Furst, R. Le Goff, D. Quinzler, S. Mecking, C. H. Botting, D. J. Cole-Hamilton, *Green*

Chem. **2012**, *14*, 472; c) Y. Zhu, J. Patel, S. Mujcinovic, W. Roy Jackson, A. J. Robinson, *Green Chem.* **2006**, *8*, 746.

[20] During the preparation of this manuscript, the synthesis of lactone derivatives by ruthenium-catalyzed allylation and RCM reactions was reported. K. Takii, N. Kanbayashi, K. Onitsuka, *Chem. Commun.* **2012**, *48*, 3872.

[21] a) A. Kabro, T. Roisnel, C. Fischmeister, C. Bruneau, *Chem. Eur. J.* **2010**, *16*, 12255; b) A. Kabro, G. Ghattas, T. Roisnel, C. Fischmeister, C. Bruneau, *Dalton Trans.* **2012**, *41*, 3695.

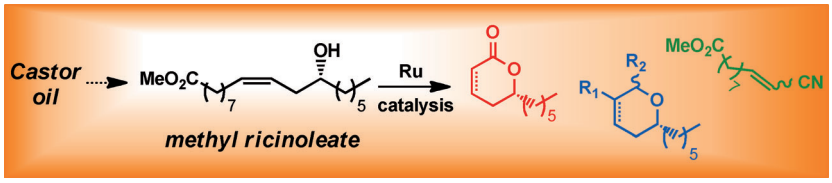
[22] a) L. R. Jimenez, B. J. Gallo, Y. Schrodi, *Organometallics* **2010**, *29*, 3471; b) W. Holtcamp, C. A. Faler, C. P. Huff, M. S. Bedoya, J. R. Hagadorn, US 2011/0112349.

[23] The terms cascade, tandem are used according to: D. Fogg, E. N. dos Santos, *Coord. Chem. Rev.* **2004**, *248*, 2365.

[24] For examples of tandem RCM/hydrogenation reactions, see: a) A. Fürstner, A. Leitner, *Angew. Chem.* **2003**, *115*, 320; *Angew. Chem. Int. Ed.* **2003**, *42*, 308; b) J. Louie, C. W. Bielawski, R. H. Grubbs, *J. Am. Chem. Soc.* **2001**, *123*, 11312; c) S. D. Drouin, F. Zamanian, D. E. Fogg, *Organometallics* **2001**, *20*, 5495; d) X. Miao, C. Fischmeister, C. Bruneau, P. H. Dixneuf, *ChemSusChem* **2009**, *2*, 542.

[25] a) M. O'Brien, S. Cahill, L. A. Evans, *Chem. Commun.* **2008**, 5559; b) H. Oertling, C. Brocke, H. Loges, A. Machinek, Eur. Pat. Appl., EP 2168957A2 20100331, **2010**; c) A. Goswami, P. Pratim Saikia, B. Saikia, D. Chaturvedi, N. C. Barua, *Tetrahedron Lett.* **2011**, *52*, 5133; d) R. F. Reátegui, J. B. Gloer, J. Campbell, C. A. Shearer, *J. Nat. Prod.* **2005**, *68*, 701; e) E. A. Crane, K. A. Scheidt, *Angew. Chem.* **2010**, *122*, 8494; *Angew. Chem. Int. Ed.* **2010**, *49*, 8316; f) E. Sarrazin, E. Frerot, A. Bagnoud, K. Aeberhardt, M. Rubin, *J. Agric. Food Chem.* **2011**, *59*, 6657.

Received: May 10, 2012
Published online on ■■ ■■, 0000



A. Dupé, M. Achard, C. Fischmeister, C. Bruneau**

■■ – ■■

Methyl Ricinoleate as Platform Chemical for Simultaneous Production of Fine Chemicals and Polymer Precursors

The derivatization of methyl ricinoleate followed by ring-closing metathesis (RCM) or sequential RCM/hydrogenation and RCM/cross-metathesis lead to a variety of biosourced compounds of interest for fine chemistry and polymer synthesis. 3,6-Dihydropyran, and α,β-unsaturated lactone derivatives have been prepared with concomitant production of polymer precursors. Tetrahydropyran and lactone derivatives as well as valuable monomers in particular polyamide precursors have also been prepared.

