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Synthesis of Alkyl-Substituted Six-Membered Lactones through Ring-Closing Metathesis of Homoallyl Acrylates. An Easy Route to Pyran-2-ones, Constituents of Tobacco Flavor

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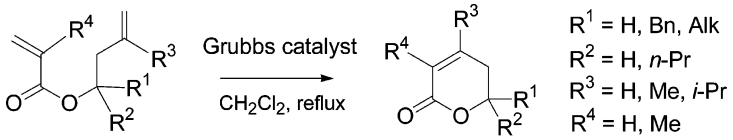

The ring-closing metathesis (RCM) reactions of homoallylic acrylates bearing alkyl substituents on various positions of their skeleton afford the corresponding pentenolides in the presence of carbene ruthenium catalysts. For $R^3 = R^4 = H$, or $R^3 = Me$, $R^4 = H$, the reactions are catalyzed by complex $[RuCl_2(PCy_3)_2(=CHPh)]$, while a second-generation Grubbs catalyst is required when $R^3 = H$ and $R^4 = Me$, $R^3 = R^4 = Me$, or $R^3 = i$-Pr and $R^4 = H$. Alkyl substitution at the homoallylic carbon (R^1, R^2) increases the yield of the reaction when both the acrylic and/or homoallylic double bonds are methyl-substituted. The interaction of the catalyst with the substrate in the initiation stage involves the homoallylic double bond rather than the acrylic moiety, and the resulting alkylidene species from the first-generation Grubbs catalyst can be observed by ^1H and ^{31}P NMR. The racemic tobacco constituents 4-isopropyl-5,6-dihydropyran-2-one and 4-isopropyltetrahydropyran-2-one are prepared via a short reaction sequence, involving the RCM reaction as the key transformation.

Introduction

Five- and six-membered lactones are widely present as structural subunits in a large number of natural compounds showing important biological activities.[1] Since the olefin ring-closing metathesis (RCM) reaction represents a powerful tool to obtain cyclic alkenes,[2] various syntheses of unsaturated lactones by RCM of α,ω-diolefins have been reported in the literature.[3] Diene esters are suitable substrates for these reactions, and the catalysts are molybdenum or ruthenium carbene complexes.[2,4]

When the organic precursors are acrylates, Lewis acids can be used as additives to promote the reactions catalyzed by first-

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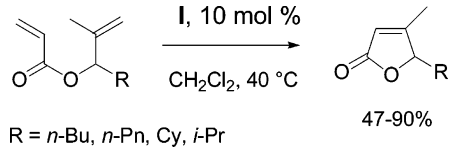
SCHEME 1. RCM of Allylic Acrylates Catalyzed by Complex [$RuCl_2(PCy_3)_2$(=CHPh)] (I)



generation Grubbs catalysts. For instance, Ti(*i*-OPr)$_4$ in stoichiometric or catalytic amounts increases the reactivity of the electron-poor acrylic double bond toward RCM, as an effect of weak coordination of the ester group.[5] The substrate reactivity is further inhibited by an alkyl substituent on either the (homo)-allylic or the acrylic double bond, as the result of steric hindrance. With regards to the synthesis of lactones with tri- or tetrasubstituted double bonds through RCM reaction, some examples are reported in literature, employing second-generation[6a,c,d] or, exceptionally, first-generation Grubbs catalysts.[6b] Although the use of either additives or the most efficient metal catalysts renders the RCM reaction a useful procedure for the preparation of lactones, the optimal reaction conditions with respect to the structural features of the acrylic diene precursor and/or the type of the required catalyst have not been specifically discussed.

We have previously reported on the RCM of acrylic esters bearing a methyl group on the allylic double bond, for the preparation of α,β-unsaturated 4,5-disubstituted γ-lactones (Scheme 1).[7]

Although the combination of an electron-deficient acrylic double bond and a methyl group on the allylic moiety was expected to be incompatible with a first-generation Grubbs catalyst,[2,6a] we obtained 4-methyl-5-alkyl-γ-lactones in good to high yields, using complex [$RuCl_2(PCy_3)_2$(=CHPh)] (**I**) as catalyst and in the absence of other promoters. The proximity of the two double bonds in the diene and the stability of the resulting five-membered lactones may have counterbalanced the unfavorable steric and electronic features of the acrylates. In addition, we optimized the activity of the catalyst by using high dilution conditions as well as by providing a constant supply of fresh catalyst via dropwise addition of solutions of complex **I** to the reaction mixture. While the slow addition of the catalyst was adopted only occasionally in the lactone synthesis,[3a,f,6b] this procedure or the related portion-wise addition for large scale preparations has been widely employed in RCM reactions.[3a,8]

We now report on the preparation of six-membered α,β-unsaturated lactones, starting from homoallylic acrylate precursors. In particular, we have focused our attention on the effect of alkyl substitution on the RCM reaction. In fact, while the presence of alkyl groups on the double bonds poses increasing limits to the reactivity of the diene precursors in the ring-closing process, naturally occurring pentenolides of synthetic interest are characterized by specific alkyl substitution patterns.[1] Therefore, the influence of this structural feature on reaction parameters, such as catalyst loading, reaction times, and the choice of the appropriate catalyst, is the subject of this work. We then report on a straightforward synthetic route to isopropyl-substituted six-membered lactones, as an application of the RCM approach to the preparation of racemic pyran-2-one tobacco constituents.

Results and Discussion

We have investigated the RCM reaction of homoallyl acrylates **3**−**6** by catalysis of carbene ruthenium complexes chosen among the commercially available compounds **I**−**IV**, which are commonly used in olefin metathesis (Scheme 2).

Esters **3**−**6**, bearing different alkyl substituents along the carbon chain, were prepared by acylation of homoallylic alcohols $R^1R^2C(OH)CH_2C(R^3)$=CH_2 **1** and **2** with acryloyl or methacryloyl chloride (for experimental procedures and yields of **3**−**6**, see Supporting Information).

The RCM reactions of acrylates **3a**−**d**, which are functionalized with two monosubstituted double bonds, were carried out upon addition of catalyst **I** (Scheme 3), in order to test the activity of the first-generation Grubbs catalyst on these sterically unhindered diene systems.

In a typical experiment, complex **I** in 16 mL of dichloromethane (0.17 mmol, 0.01 M) was added dropwise to a refluxing solution of **3** in 160 mL of dichloromethane (1.7 mmol, 0.01 M). The consumption of the substrate was checked by TLC, and the reaction was stopped after 6 h, when starting material could no longer be detected. The expected lactones **7a**−**d** were isolated in good yields, as reported in Table 1.

The yields of the reaction are not affected by the presence of an alkyl substituent (R^1) on the homoallylic carbon (entries 1−3) or by an increase in its substitution degree (entry 4, $R^1 = R^2 =$ *n*-Pr). Substrates **3**, functionalized with unhindered double bonds, appear to be insensitive toward a potential *gem*-dialkylic effect, which is otherwise known to produce a dramatic increase on yields and rates of many ring-closing reactions, including RCM.[9] The reaction of the homoallylic acrylate **3c** can be performed with catalyst loads lower than 10 mol %, without affecting the yield of the six-membered lactone **7c** (entries 1, 5, and 6). We have previously observed in the RCM of methallyl acrylate esters shown in Scheme 1 that comparable reaction yields were obtained using either 5 or 10 mol % of complex **I**.[7] Thus, these experiments confirm our previous findings; that is, the acrylic double bond is not a crucial functionality for the first-generation Grubbs catalyst.

The subsequent step was the evaluation of the reactivity of dienic esters **4** bearing a methyl group on the homoallylic double bond. Compound **4a**, when reacted under similar conditions as compounds **3**, gave the expected lactone in a 20% yield (entry 7). For comparison, it is reported that compound **4a** afforded

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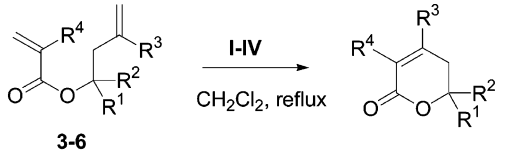
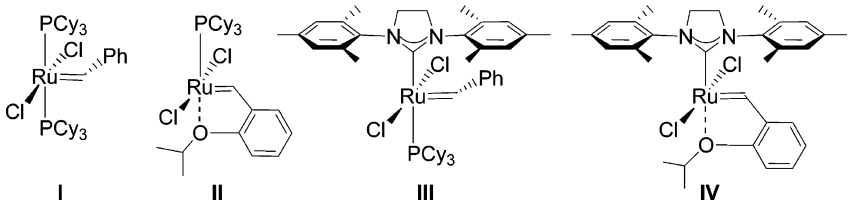
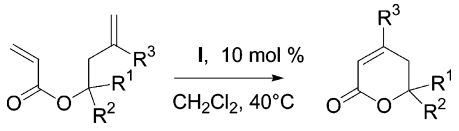
SCHEME 2. RCM of Homoallyl Acrylates 3−6, Catalyzed by Complexes I−IV, to Yield Alkyl-Substituted Six-Membered α,β-Unsaturated Lactones





SCHEME 3. RCM of Homoallyl Acrylates 3 and 4 to Pentenolides 7 and 8



3 R^3 = H 6h **7**
4 R^3 = Me 18h **8**

TABLE 1. RCM of Homoallyl Acrylates 3 and 4 to Pentenolides 7 and 8

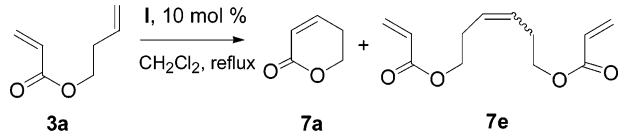
entry	substrate	R^1	R^2	R^3	**I** (mol %)	time (h)	product	yield[a] (%)
1	**3a**	H	H	H	10	6	**7a**	65
2	**3b**	*n*-C_9H_{19}	H	H	10	6	**7b**	62
3	**3c**	Bn	H	H	10	6	**7c**	67
4	**3d**	*n*-Pr	*n*-Pr	H	10	6	**7d**	68
5	**3c**	Bn	H	H	5	6	**7c**	58
6	**3c**	Bn	H	H	2	6	**7c**	61
7	**4a**	H	H	CH_3	10	18	**8a**	20
8	**4b**	*n*-Bu	H	CH_3	10	18	**8b**	55
9	**4c**	*n*-C_9H_{19}	H	CH_3	10	18	**8c**	74

[a] Yields of isolated products.

8a in 73% yield using the second-generation Grubbs catalyst **III** (5 mol %) after 20 h in toluene at 80 °C.[6a] On the other hand, we noticed that the presence of an alkyl group on the homoallylic carbon atom raised significantly the yield of the corresponding six-membered lactones **8b**,**c** (entries 8 and 9), suggesting that the chain conformation imposed by an alkyl group could assist the reaction of these difficult substrates.

The reaction of the acrylate **3a** was followed by GC, in order to clarify if the moderate yield of lactone could be due to the formation of side products during the RCM process. The analysis after 4 h of reaction showed the presence of **3a** (18%), the expected lactone **7a** (50%), and of a secondary product **7e** (32%) (Scheme 4). After an additional 2 h at reflux, the relative GC percentages **3a**:**7a**:**7e** changed into 4:71:24, indicating further conversion of the mixture into **7a**. When the reaction was left at reflux overnight, the substrate totally disappeared, but there was no increase in the GC percentage of **7a** with respect to **7e**. However, upon addition of a second load of complex **I** (10 mol %) to the mixture at 6 h reaction time, compound **7e** was converted overnight into the six-membered lactone. On the basis of the molecular mass found at m/z = 247.18 (**7e**−Na^+ adduct) in the ESI-MS spectrum, compound

SCHEME 4. Product Analysis for the RCM Reaction of the Homoallylic Acrylate 3a



7e was identified as the product of a cross-metathesis (CM) reaction of **3a** involving presumably the homoallylic double bond. So, the formation of **7e** observed in the reaction of **3a** accounts for the yields of the desired lactones **7a**−**d** in the range of 60−70% (Table 1).

An analogous GC analysis performed on the reaction of the homomethallylic acrylate **4a** showed the presence of the substrate and of the 3-methyl-substituted lactone **8a** with relative GC percentages of 81 and 16% (4 h), respectively, with other significant peaks not being observed. The conversion into **8a** reached the 23% value at 20 h of reaction, and no further changes were observed for longer reaction times.

The interaction of complex **I** with the homoallylic acrylate **3a** and with the homomethallylic acrylate **4a** in the initial stages of the reaction was investigated by ^1H and ^{31}P NMR. Five minutes after addition of **3a** (5 μL, 0.038 mmol) to a solution of complex **I** in CD_2Cl_2 (0.0077 mmol, 0.015 M) at rt, the high-frequency region of the spectrum showed the benzylidene proton of **I** at 20.01 ppm, a triplet at 19.35 ppm (J = 5 Hz), and a singlet at 18.94 ppm. This was accompanied by the formation of a triplet at 4.48 ppm (J = 6 Hz). The peak of **I** and the nearby triplet disappeared over 3 h at room temperature, or in 30 min when the NMR tube was heated to 38 °C; the only peak left in the high-frequency region was the singlet at 18.97 ppm, due to the methylidene group of the catalyst resting state [$RuCl_2$-$(PCy_3)_2$(=CH_2)] (**Ia**).[10] When the same NMR experiments were carried out on a mixture of homomethallylic acrylate **4a** and complex **I**, this showed to be stable at rt, as indicated by the presence of its benzylidene proton, while the transformation into the active methylidene complex occurred upon heating the sample to 38 °C, with the intermediate species not being detected. The ^1H NMR spectra for the reactions of **I** with either **3a** or **4a**, showing the corresponding carbenoid species, are displayed in Figure 1. On the other hand, the species **Ia** was not detected by NMR when complex **I** was treated with ethyl acrylate either at rt or at 38 °C.

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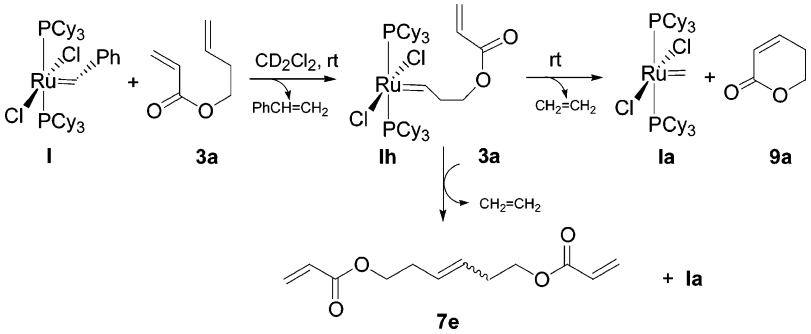
SCHEME 5. Initiation Stage of Complex I in the Reaction with Homoallyl Acrylate 3a, Yielding the Catalyst Resting State $[RuCl_2(PCy_3)_2{=}CH_2]$ (Ia)



These experiments indicate that the attack of complex **I** to the substrate occurs selectively at the homoallylic double bond during the initiation stage of the catalytic process, yielding, in the case of the monosubstituted homoallylic acrylate **3a**, the detectable intermediate $[RuCl_2(PCy_3)_2(=CH(CH_2)_2OCOCH=CH_2)]$ **Ih**. This species is characterized by the proton resonances of the Ru=CH− (19.35 ppm) and $-CH_2O-$ (4.48 ppm) groups and by a ^{31}P NMR peak at 35.5 ppm, just next to the one of complex **I** at 36.1 ppm. A GC analysis of the reaction mixture of **I** and **3a** from the NMR tube after 2 h at rt showed the presence of **3a**, **7a**, and **7e** with relative GC percentages of 72, 3, and 24%, respectively, indicating that, under the conditions of the NMR experiment, the product from CM, in stereoisomeric ratio 4:1, is formed abundantly in the early part of the reaction. Therefore, the initiation stage of the process can be depicted as in Scheme 5.

We studied next the effect of a geminal methyl group on the conjugated double bond on the RCM outcome. In this case, the reactivity of the electron-poor acrylic moiety is further impaired by steric hindrance. The reaction mixtures of the homoallyl methacrylate esters **5** with the chosen catalyst were kept at reflux

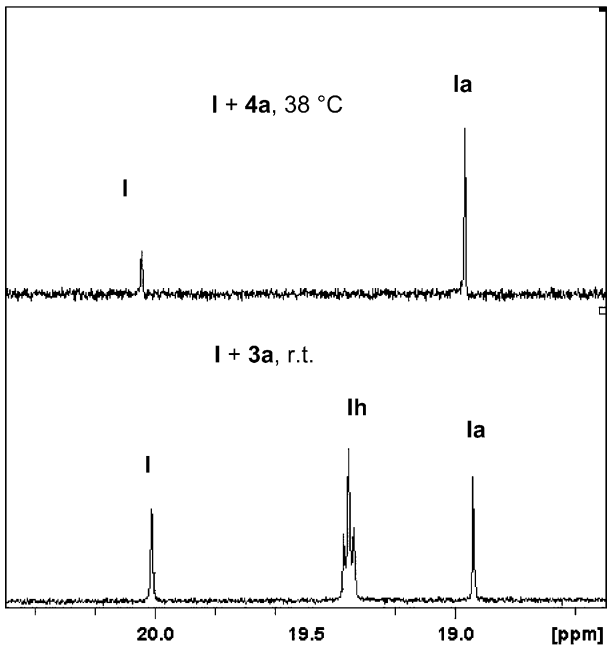


FIGURE 1. High-frequency region of the ^1H NMR spectra of complex **I** in the presence of the homoallylic acrylate **3a** (lower trace, rt, 25 min) and of the homomethallylic acrylate **4a** (upper trace, 38 °C, 15 min). Chemical shift calibration was performed at each temperature.

SCHEME 6. Products of the RCM Reaction of Homoallyl Methacrylate Esters 5, in the Presence of a Ruthenium Catalyst I−IV

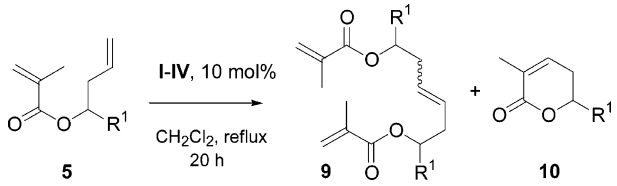


TABLE 2. RCM Reactions of Homoallyl Methacrylate Esters 5, in Refluxing Dichloromethane[a]

entry	substrate	R^1	catalyst (10 mol %)	product **9** (% yield)[b]	product **10** (% yield)[b]
1	**5a**	H	**I**	**9a** (25)	
2	**5b**	Bn	**I**	**9b** (23)	
3	**5a**	H	**II**	**9a** (34)	
4	**5a**	H	**III**	**9a** (48)	**10a** (24)
5	**5b**	Bn	**III**	*c*	**10b** (49)
6	**5a**	H	**IV**	**9a** (25)	**10a** (16)

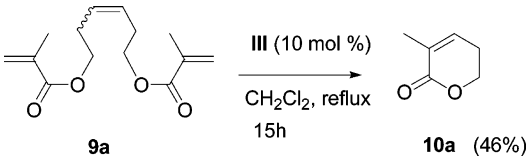
[a] 20 h. [b] Yields of isolated products. [c] Not isolated.

for 20 h, according to standard metathesis conditions for *gem*-dialkyl-substituted olefins, which generally require prolonged reaction times.[6a]

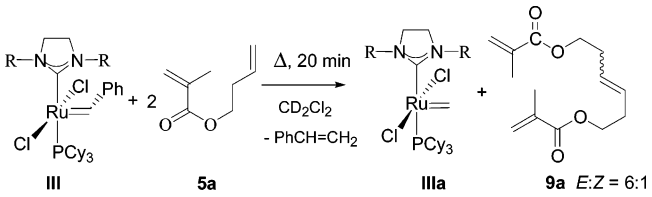
The RCM reactions of the homoallylic methacrylate esters **5a**,**b** were performed using complexes **I**−**IV** (Scheme 6), and the results obtained under comparable conditions are reported in Table 2. Both the first-generation Grubbs catalysts **I** or the Hoveyda−Grubbs catalyst **II**[11] afforded in modest yield only the dimeric species **9**, as the result of a cross-metathesis process involving the monosubstituted alkene (Table 2, entries 1−3). To increase the reactivity of the sterically hindered acrylic double bond of esters **5** toward RCM, we employed complexes with expected higher activity, namely, the second-generation catalysts **III** or **IV**.[12] The model compound **5a** was reacted with **III**, showing a modest conversion into the desired lactone **10a** and the prevalent formation of the dimer **9a**. On the other hand, treatment of **5a** with complex **IV** afforded both compounds **9a** and **10a** in poor yield.

The reaction of **5a** with **III** was also monitored by GC−MS. After 4 h, the analysis showed the substrate **5a**, the lactone **10a**, and the dimeric species **9a** in 18:26:55 relative percentage ratios. Afterward, the conversion into **10a** increased only modestly and reached 30% after 22 h of reaction, and no further changes were observed after this time. On the other hand, a second addition in one portion of 10 mol % of complex **III** brought the relative GC percentage ratio of the six-membered lactone to 69:21 versus that of the dimer after an overnight reaction. This last result

SCHEME 7. RCM of Compound 9a Catalyzed by the Second-Generation Grubbs Catalyst III



SCHEME 8. Initiation Stage of Complex III in the Reaction with the Homoallyl Methacrylate Ester 5a



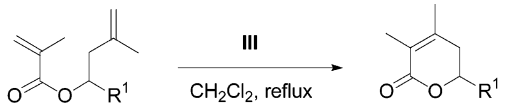
suggested that the side products **9a**,**b**, even though undesired, were good RCM substrates themselves. In fact, in the presence of catalyst **III**, an isolated pure sample of **9a** afforded **10a** in moderate yield, as the result of a RCM process between the methacrylic alkene moiety and the internal double bond (Scheme 7).

Thus, these results indicate the preference of the ruthenium catalyst to attack the more electron-rich double bond of **5a** and, subsequently, to perform a cross-metathesis reaction, a process fiercely competitive with the desired RCM process. It is evident that only the more active catalysts **III** or **IV** can subsequently convert the CM product into the desired lactone.

The use of internal olefins as starting materials or as intermediates is common in cross-metathesis reactions promoted by complexes of type **III**.[13] Although the ruthenium catalysts bearing N-heterocyclic carbene ligands are known to catalyze the RCM process involving two methyl-substituted alkene groups and affording tetrasubstituted olefins,[6a,13,14] to the best of our knowledge, there are no other examples describing the RCM of a methacrylate double bond with an internal olefin. On the other hand, the formation of an acyclic dimer and its conversion via a retrometathesis process to form a macrolide, catalyzed by various Grubbs catalysts, were previously described in detail.[15]

The initial interaction of the second-generation Grubbs catalyst **III** with **5a** was followed by NMR in CD_2Cl_2. Complex **III**, characterized by the benzylidene proton resonance at 19.1 ppm and by a ^{31}P NMR peak at 29.4 ppm, is stable at rt in the presence of the homoallyl methacrylate ester. While the situation does not change upon mild heating to 32 °C, complete conversion of **III** into the corresponding methylidene complex **IIIa** (17.7 ppm, Ru=CH_2) is observed after 20 min at 40 °C, other carbenoid species are not detected in the ^1H NMR spectrum. At this stage, the GC analysis of the reaction mixture under the conditions of the NMR experiment ([**III**] = 5.9×10^{-3} M; [**5a**] = 6×10^{-2} M) shows 45% of substrate, 4% of the lactone **10a**, and 50% of the CM product **9a** in stereoisomeric ratio of 6:1. When compared to the behavior of the first-generation Grubbs catalyst in the presence of the homoallyl acrylate **3a**, it is obvious that complex **III**, in contrast to complex **I**, requires a thermal activation for the conversion into the catalyst resting state **IIIa** (Scheme 8). This observation is consistent with the intrinsic reactivity of complexes **I** and **III**. In both cases, the first step of the reaction involves dissociation of one PCy_3 ligand to afford a 14-electron coordinatively unsaturated intermediate. This process is rate determining for the N-heterocyclic carbene complex **III** and faster by almost 2 orders of magnitude in the bisphosphine complex **I**.[16]

SCHEME 9. RCM of Esters 6 Catalyzed by the Second-Generation Grubbs Catalyst III



6a (R^1 = H)	10 + 10 mol %	48 h	**11a** (40%)
6b (R^1 = *n*-C_9H_{19})	10 mol %	24 h	**11b** (64%)

Since it is known that the activity of the second-generation catalysts can overcome the difficulty of combining two *gem*-disubstituted olefin moieties, even when one is electron-poor by conjugation,[6a] we extended our study to the synthesis of 3,4-disubstituted-5,6-dihydropyran-2-ones. The reactions of esters **6** catalyzed by complex **III** gave the expected products **11** under the conditions and yields indicated in Scheme 9.

The conversion of **6a**, followed by GC, required the addition of a second load of catalyst **III** after 24 h to reach a 44% value before the final work up (48 h), with the reaction mixture containing unreacted substrate. A similar reaction yield (42%) was reported for the preparation carried out in toluene at 80 °C (**III**, 5 mol %, 40 h),[6a] which evidently benefits from the higher temperature accessible in this solvent. It is worth noting that the presence of an alkyl substituent R^1 on the homoallylic carbon atom of the methacrylate affects positively the formation of the tetrasubstituted pentenolide **11b**, with respect to both yields (64 vs 40%) and catalyst load. Similarly, appreciable yield increments are observed in the preparation of the trisubstituted α,β-unsaturated lactones **10** (Table 2, entries 4 and 5) and **8** (Table 1, entries 7−9), rather than for compounds **7** formed from the homoallyl acrylates **3a**−**d** (Table 1, entries 1−4).

The higher yield observed for **11b** than for **10b** was at first surprising. It may reflect the fact that the *gem*-disubstitution on the double bonds in **6b** hinders substantially the dimerization of the homomethallylic moiety,[17] thus favoring the RCM reaction of the alkylidene intermediate with the methacrylate group.

On the basis of the results concerning the preparation of 4-methyl-5,6-dihydropyran-2-ones from homomethallyl acrylates (Scheme 3),[6a] we wished to extend the use of RCM as the key step in the synthesis of two naturally occurring δ-lactones, components of tobacco flavor and widely used as aromatizers in the cigarette manufacturing, that is, (±)-4-isopropyl-5,6-

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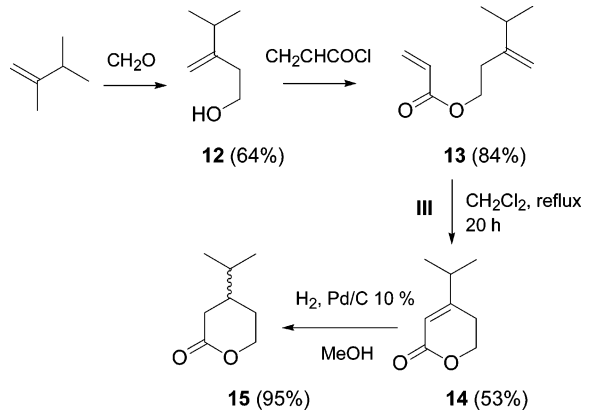
SCHEME 10. RCM-Based Synthetic Pathway to Tobacco Lactones 14 and 15



dihydropyran-2-one **14** and (±)-4-isopropyltetrahydropyran-2-one **15**.[18] A RCM-based retrosynthetic approach led us to choose the ester **13**, attainable from alcohol **12**, as the suitable precursor of the target molecules. The synthetic pathway to the tobacco lactones is shown in Scheme 10.

The alcohol **12** was prepared according to a literature procedure through an ene reaction between formaldehyde and 2,3-dimethylbut-1-ene[19] and then acylated with acryloyl chloride. The resulting ester **13** cyclized satisfactorily (53% yield) to **14** in the presence of the second-generation Grubbs catalyst **III**. The catalytic hydrogenation of **14** on Pd/C afforded the racemic tobacco lactone **15**.[20] Ester **13** gave no evidence of either cyclization or cross-metathesis in the presence of complex **I**. Evidently, the increased steric bulk of the *gem*-dialkylic group on going from methyl to isopropyl inhibits the efficiency of the first-generation catalyst.

Conclusions

The reactivity of alkyl-substituted homoallyl acrylates toward RCM is dependent on the catalyst used for the purpose. A methyl group on the homoallylic double bond is still compatible with the use of catalyst **I**, while a bulkier group, such as isopropyl, requires the use of the second-generation Grubbs catalyst **III**. When the acrylic double bond is methyl-substituted, the homoallylic moiety undergoes preferentially a cross-metathesis reaction yielding a dimeric product, which turns into the desired α,β-unsaturated lactone only in the presence of a second-generation Grubbs catalyst. The key feature which distinguishes the activity of first- and second-generation Grubbs catalysts is the ability of the latter to promote more efficiently the RCM between the acrylic moiety and an internal olefin. ^{1}H NMR spectroscopy and reaction products show that the interaction of the catalyst with the substrate in the initiation stage involves the homoallylic double bond.

Experimental Section

4-Propyl hept-1-en-4-ol (1d): Colorless oil (52% yield); IR ($CHCl_3$) 3420, 2970, 1471, 1130 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ = 0.91 (6H, t, J = 6.6 Hz), 1.37 (9H, m), 2.19 (2H, d, J = 7.3 Hz), 5.09 (2H, m), 5.83 (1H, ddt, J_1 = 16.8 Hz, J_2 = 11.0 Hz, J_3 = 7.3 Hz) ppm; ^{13}C NMR ($CDCl_3$, 200 MHz) δ = 14.6, 16.7, 41.6, 44.0, 73.9, 118.3, 134.0 ppm; MS (EI) m/z = 114 (21%), 71 (100). Anal. Calcd for $C_{10}H_{20}O$: C, 76.86; H, 12.90. Found: C, 76.74; H, 12.66.

But-3-enyl acrylate (3a): Colorless oil (56% yield); IR ($CHCl_3$) 1717, 1419, 1306 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ = 2.39 (2H, qt, J_1 = 6.6 Hz, J_2 = 1.4 Hz), 4.18 (2H, t, J = 6.6 Hz), 5.10 (2H, m), 5.78 (1H, dd, J_1 = 10.2 Hz, J_2 = 1.4 Hz), 5.78 (1H, ddt, J_1 = 16.8 Hz, J_2 = 10.2 Hz, J_3 = 6.6 Hz, overlapped), 6.08 (1H, dd, J_1 = 16.8 Hz, J_2 = 10.2 Hz), 6.37 (1H, dd, J_1 = 16.8 Hz, J_2 = 1.4 Hz) ppm; ^{13}C NMR ($CDCl_3$, 200 MHz) δ = 33.0, 63.5, 117.1, 128.5, 130.4, 133.9, 166.0 ppm. Anal. Calcd for $C_7H_{10}O_2$: C, 66.65; H, 7.99. Found: C, 66.52; H, 8.08.

1-Nonylbut-3-enyl acrylate (3b): Colorless oil (60% yield); IR ($CHCl_3$) 2970, 1712, 1416, 1307 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ = 0.87 (3H, t, J = 7.3 Hz), 1.24 (14H, m), 1.55 (2H, m), 2.33 (2H, t, J = 6.6 Hz), 5.02 (3H, m), 5.75 (1H, ddt, J_1 = 17.5 Hz, J_2 = 10.2 Hz, J_3 = 6.6 Hz, overlapped), 5.78 (1H, dd, J_1 = 10.2 Hz, J_2 = 2.1 Hz), 6.09 (1H, dd, J_1 = 16.8 Hz, J_2 = 10.2 Hz), 6.37 (1H, dd, J_1 = 16.8 Hz, J_2 = 2.1 Hz) ppm; ^{13}C NMR (50 MHz, $CDCl_3$) δ = 14.0, 22.6, 25.2, 29.3, 29.4, 29.5, 31.8, 33.6, 38.6, 73.6, 117.6, 128.9, 130.1, 133.7, 165.8 ppm; MS (EI) m/z = 211 (8%), 139 (16), 97 (14), 83 (37), 67 (24), 55 (100). Anal. Calcd for $C_{16}H_{28}O_2$: C, 76.14; H, 11.18. Found: C, 76.26; H, 11.41.

1-Benzylbut-3-enyl acrylate (3c): Colorless oil (43% yield); IR ($CHCl_3$) 2960, 1717, 1417, 1306, 1048, 984 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ = 2.38 (2H, m), 2.89 (1H, dd, J_1 = 13.9 Hz, J_2 = 5.8 Hz), 2.97 (1H, dd, J_1 = 13.9 Hz, J_2 = 6.6 Hz), 5.10 (2H, m), 5.23 (1H, qd, J_1 = 6.6 Hz, J_2 = 5.8 Hz), 5.80 (1H, dd, J_1 = 10.2 Hz, J_2 = 1.4 Hz, overlapped), 5.81 (1H, ddt, J_1 = 17.6 Hz, J_2 = 9.5 Hz, J_3 = 7.3 Hz, overlapped), 6.09 (1H, dd, J_1 = 17.6 Hz, J_2 = 10.2 Hz), 6.38 (1H, dd, J_1 = 16.8 Hz, J_2 = 1.4 Hz), 7.24 (5H, m) ppm; ^{13}C NMR ($CDCl_3$, 50 MHz) δ = 37.7, 39.8, 74.0, 117.9, 126.4, 128.3, 129.4, 130.3, 133.4, 137.3, 165.5 ppm; MS (EI) m/z = 144 (41%), 129 (47), 91 (53), 65 (18), 55(100). Anal. Calcd for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 77.68; H, 7.56.

1,1-Di-*n*-propylbut-3-enyl acrylate (3d): Colorless oil (24% yield); IR ($CHCl_3$) 2970, 1710, 1473, 1431, 1311, 1130 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ = 0.89 (6H, t, J = 7.3 Hz), 1.27 (4H, m), 1.80 (4H, m), 2.61 (2H, d, J = 7.3 Hz), 5.08 (2H, m), 5.70 (1H, ddt, J_1 = 16.8 Hz, J_2 = 9.5 Hz, J_3 = 7.3 Hz, overlapped), 5.71 (1H, dd, J_1 = 10.2 Hz, J_2 = 1.4 Hz), 6.02 (1H, dd, J_1 = 16.8 Hz, J_2 = 10.2 Hz), 6.28 (1H, dd, J_1 = 16.8 Hz, J_2 = 1.4 Hz) ppm; ^{13}C NMR ($CDCl_3$, 50 MHz) δ = 14.4, 16.5, 37.7, 40.0, 86.9, 118.0, 129.2, 130.1, 133.2, 165.2 ppm; MS (EI) m/z = 169 (11%), 95 (9) 71 (6), 55 (100). Anal. Calcd for $C_{13}H_{22}O_2$: C, 74.24; H, 10.54. Found: C, 74.16; H, 10.62.

1-Nonyl-3-methylbut-3-enyl acrylate (4b): Colorless oil (74% yield); IR ($CHCl_3$) 3035, 2970, 1711, 1432, 1307, 1045 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ = 0.86 (3H, t, J = 6.6 Hz), 1.24 (14H, m), 1.56 (2H, m), 1.74 (3H, s), 2.21 (1H, dd, J_1 = 13.9 Hz, J_2 = 5.8 Hz), 2.32 (1H, dd, J_1 = 13.9 Hz, J_2 = 7.3 Hz), 4.73 (2H, m), 5.11 (1H, dq, J_1 = 7.3 Hz, J_2 = 5.8 Hz), 5.77 (1H, dd, J_1 = 10.2

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Hz, J_2 = 2.2 Hz), 6.08 (1H, dd, J_1 = 16.8 Hz, J_2 = 10.2 Hz), 6.37 (1H, dd, J_1 = 16.8 Hz, J_2 = 2.2 Hz) ppm; ^{13}C NMR ($CDCl_3$, 50 MHz) δ = 14.0, 22.5, 22.6, 22.6, 25.3, 29.3, 29.5 (overlapped peaks), 31.8, 34.1, 42.9, 72.5, 113.2, 128.9, 130.0, 141.7, 165.8 ppm; MS (EI) *m*/*z* = 194 (14%), 138 (9), 110 (8), 95 (18), 82 (24), 67 (9), 55 (100). Anal. Calcd for $C_{17}H_{30}O_2$: C, 76.64; H, 11.35. Found: C, 76.47; H, 11.48.

1-Butyl-3-methylbut-3-enyl acrylate (4c): Colorless oil (63% yield); IR ($CHCl_3$) 3165, 1751, 1455, 1347, 1069, 1004 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ = 0.86 (3H, t, J = 6.6 Hz), 1.29 (4H, m), 1.55 (2H, m), 1.72 (3H, s), 2.19 (1H, dd, J_1 = 13.9 Hz, J_2 = 5.8 Hz), 2.31 (1H, dd, J_1 = 13.9 Hz, J_2 = 7.3 Hz), 4.72 (2H, m), 5.09 (1H, dq, J_1 = 7.3 Hz, J_2 = 5.8 Hz), 5.75 (1H, dd, J_1 = 10.2 Hz, J_2 = 1.4 Hz), 6.07 (1H, dd, J_1 = 17.5 Hz, J_2 = 10.2 Hz), 6.34 (1H, dd, J_1 = 17.5 Hz, J_2 = 2.2 Hz) ppm; ^{13}C NMR ($CDCl_3$, 50 MHz) δ = 13.9, 22.5, 27.4, 33.7, 42.8, 72.4, 113.2, 128.9, 130.0, 141.6, 165.8 ppm. Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.35; H, 10.37.

But-3-enyl methacrylate (5a): Colorless oil (46% yield); IR ($CHCl_3$) 3050, 2895, 1712, 1640, 1526, 1433, 1044 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ = 1.89 (3H, s), 2.38 (2H, q, J = 6.6 Hz), 4.15 (2H, t, J = 6.6 Hz), 5.08 (2H, m), 5.49 (1H, br s), 5.76 (1H, ddt, J_1 = 16.8 Hz, J_2 = 10.2 Hz, J_3 = 6.6 Hz), 6.05 (1H, br s) ppm; ^{13}C NMR ($CDCl_3$, 50 MHz) δ = 18.0, 33.0, 63.5, 117.0, 125.0, 133.9, 136.4, 167.2 ppm; MS (EI) *m*/*z* = 99 (9%), 69 (100), 54 (47). Anal. Calcd for $C_8H_{12}O_2$: C, 68.54; H, 8.63. Found: C, 68.42; H, 8.74.

1-Benzylbut-3-enyl methacrylate (5b): Colorless oil (73% yield); IR ($CHCl_3$) 3030, 2900, 1709, 1525, 1430, 1044 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ = 1.91 (3H, s), 2.38 (2H, m), 2.88 (1H, dd, J_1 = 13.9 Hz, J_2 = 6.6 Hz), 2.98 (1H, dd, J_1 = 13.9 Hz, J_2 = 6.6 Hz), 5.10 (2H, m), 5.19 (1H, dq, J_1 = 6.6 Hz, J_2 = 5.8 Hz), 5.52 (1H, m), 5.80 (2H, dddd, J_1 = 16.8 Hz, J_2 = 9.5 Hz, J_3 = 7.3 Hz, J_4 = 6.6 Hz), 6.08 (1H, m), 7.24 (5H, m) ppm; ^{13}C NMR ($CDCl_3$, 50 MHz) δ = 18.2, 37.7, 39.8, 74.2, 117.9, 125.0, 126.4, 128.3, 129.5, 133.5, 136.6, 137.4, 166.8 ppm; MS (EI) *m*/*z* = 144 (72%), 129 (66), 91 (40), 69 (100). Anal. Calcd for $C_{15}H_{18}O_2$: C, 78.23; H, 7.88. Found: C, 78.04; H, 8.01.

3-Methyl-1-nonylbut-3-enyl methacrylate (6b): Colorless oil (49% yield); IR ($CHCl_3$) 2935, 1705, 1468, 1332, 1171 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ = 0.85 (3H, t, J = 5.8 Hz), 1.23 (14H, m), 1.56 (2H, m), 1.72 (3H, s), 1.90 (3H, s), 2.19 (1H, dd, J_1 = 13.9 Hz, J_2 = 5.1 Hz), 2.32 (2H, dd, J_1 = 13.9 Hz, J_2 = 7.3 Hz), 4.70 (2H, m), 5.05 (1H, dq, J_1 = 7.3 Hz, J_2 = 6.6 Hz), 5.48 (1H, m), 6.05 (1H, m) ppm; ^{13}C NMR ($CDCl_3$, 50 MHz) δ = 14.0, 22.4, 22.5, 22.6, 25.3, 29.3, 29.5, 31.9, 34.0, 41.3, 42.8, 72.6, 113.2, 124.7, 136.8, 141.8, 167.0 ppm; MS (EI) *m*/*z* = 194 (16%), 138 (7), 95 (12), 81 (14), 69 (100), 55 (10). Anal. Calcd for $C_{18}H_{32}O_2$: C, 77.09; H, 11.50. Found: C, 77.03; H, 11.64.

3-Isopropyl but-3-enyl acrylate (13): Colorless oil (84% yield); IR ($CHCl_3$) 3097, 2956, 1710, 1467, 1312, cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ = 1.03 (6H, d, J = 6.6 Hz), 2.26 (1H, septuplet, J = 6.6 Hz), 2.40 (2H, t, J = 7.3 Hz), 4.27 (2H, t, J = 7.3 Hz), 4.78 (2H, m), 5.81 (1H, dd, J_1 = 10.2 Hz, J_2 = 1.4 Hz), 6.11 (1H, dd, J_1 = 17.5 Hz, J_2 = 10.2 Hz), 6.50 (1H, dd, J_1 = 16.8 Hz, J_2 = 1.4 Hz) ppm; ^{13}C NMR ($CDCl_3$, 50 MHz) δ = 21.6, 33.1, 34.1, 63.5, 108.7, 128.6, 130.4, 151.5, 166.1 ppm. Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.31; H, 9.75.

General Procedure for the Preparation of Pentenolides 7, 8, 10, 11, and 14. First, 1.6 mmol of esters **3**−**6** or **13** was dissolved in dry CH_2Cl_2 (160 mL) under argon atmosphere; a 0.01 M solution of the suitable catalyst **I**−**IV** (0.16 mmol in 16 mL of CH_2Cl_2) was added dropwise and the refluxing mixture stirred overnight. When the starting material could no longer be detected by TLC, the solvent was removed under reduced pressure, and the residue was separated on a silica gel column eluted with light petroleum ether/Et_2O to afford the desired products **7**, **8**, **10**, **11**, or **14** as oils, and in some cases (see Results and Discussion) also the more polar homodimers **9**.

6-Nonyl-5,6-dihydro-2*H*-pyran-2-one (7b): Colorless oil (6 h, 62% yield); IR ($CHCl_3$) 3025, 1714, 1400, 1248, 1039 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ = 0.84 (3H, t, J = 6.6 Hz), 1.23 (14H, m), 1.44 (4H, m), 2.30 (2H, m), 4.38 (1H, m), 5.97 (1H, dt, J_1 = 9.5 Hz, J_2 = 1.4 Hz), 6.85 (1H, ddd, J_1 = 9.5 Hz, J_2 = 4.4 Hz, J_3 = 3.6 Hz) ppm; ^{13}C NMR ($CDCl_3$, 50 MHz) δ = 14.0, 22.5, 24.7, 29.2, 29.3, 29.4, 31.8, 34.8, 77.9, 121.3, 144.9, 165.4 ppm; MS (EI) *m*/*z* = 164 (12%), 97 (100), 81 (16), 68 (80), 55 (31). Anal. Calcd for $C_{14}H_{24}O_2$: C, 74.95; H, 10.78. Found: C, 74.78; H, 10.98.

6-Benzyl-5,6-dihydro-2*H*-pyran-2-one (7c): Colorless oil (6 h, 67% yield); IR ($CHCl_3$) 2950, 1720, 1396, 1265, 1042 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ = 2.30 (2H, m), 2.95 (1H, dd, J_1 = 13.9 Hz, J_2 = 6.6 Hz), 3.16 (1H, dd, J_1 = 13.9 Hz, J_2 = 5.8 Hz), 4.65 (1H, dddd, J_1 = 8.8 Hz, J_2 = 7.3 Hz, J_3 = 6.6 Hz, J_4 = 5.8 Hz), 6.00 (1H, m), 6.84 (1H, ddd, J_1 = 9.5 Hz, J_2 = 4.4 Hz, J_3 = 3.6 Hz), 7.25 (5H, m) ppm; ^{13}C NMR ($CDCl_3$, 50 MHz) δ = 28.6, 41.1, 78.3, 121.4, 126.9, 128.6, 129.5, 136.0, 144.8, 164.1 ppm; MS (EI) *m*/*z* = 188 (4%), 97 (100), 91 (45), 69 (52). Anal. Calcd for $C_{12}H_{12}O_2$: C, 76.57; H, 6.43. Found: C, 76.43; H, 6.52.

6-Nonyl-4-methyl-5,6-dihydro-2*H*-pyran-2-one (8c): Colorless oil (18 h, 74% yield); IR ($CHCl_3$) 3055, 1748, 1436, 1232, 1064 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ = 0.86 (3H, t, J = 6.6 Hz), 1.24 (14H, m), 1.60 (2H, m), 1.96 (3H, s), 2.16 (1H, dd, J_1 = 17.6 Hz, J_2 = 4.4 Hz), 2.32 (2H, dd, J_1 = 17.5 Hz, J_2 = 10.9 Hz), 5.35 (1H, m), 5.78 (1H, s) ppm; ^{13}C NMR ($CDCl_3$, 50 MHz) δ = 14.0, 22.6, 22.9, 24.8, 29.2, 29.3, 29.4, 31.8, 34.7, 34.8, 77.2, 116.5, 156.9, 165.3 ppm. Anal. Calcd for $C_{15}H_{26}O_2$: C, 75.58; H, 10.99. Found: C, 75.49; H, 11.19.

6-Benzyl-3-methyl-5,6-dihydropyran-2-one (10b): Colorless oil (20 h, 49% yield); IR ($CHCl_3$) 3050, 1720, 1327 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ = 1.91 (3H, s), 2.25 (2H, m), 2.94 (1H, dd, J_1 = 13.9 Hz, J_2 = 7.3 Hz), 3.16 (1H, dd, J_1 = 13.9 Hz, J_2 = 5.8 Hz), 4.61 (1H, m), 6.52 (1H, m), 7.26 (5H, m) ppm; ^{13}C NMR ($CDCl_3$, 50 MHz) δ = 18.5, 32.4, 38.9, 77.9, 120.4, 125.5, 128.4, 129.8, 134.2, 137.4, 163.8 ppm. Anal. Calcd for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98. Found: C, 77.13; H, 7.04.

6-Nonyl-3,4-dimethyl-5,6-dihydropyran-2-one (11b): Colorless oil (24 h, 64% yield); IR ($CHCl_3$) 2970, 1716, 1411, 1321, 1279, 1147, 1085 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ = 0.87 (3H, t, J = 6.6 Hz), 1.26 (14H, m), 1.56 (2H, m), 1.88 (3H, s), 1.91 (3H, s), 2.14 (1H, dd, J_1 = 17.5 Hz, J_2 = 3.7 Hz), 2.36 (1H, m), 4.28 (1H, m) ppm; ^{13}C NMR ($CDCl_3$, 50 MHz) δ = 14.0, 20.2, 20.4, 22.56, 22.62, 24.8, 29.2, 29.4, 29.5, 31.8, 34.8, 36.0, 76.2, 122.2, 148.4, 166.6 ppm. Anal. Calcd for $C_{16}H_{28}O_2$: C, 76.14; H, 11.18. Found: C, 76.09; H, 11.36.

1,6-Dimethacryloyloxyhex-3-ene (9a): *E*/*Z* mixture, colorless oil (20 h, 25−48% yield range); IR ($CHCl_3$) 3025, 1711, 1526, 1433, 1224, 1044 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ = 1.91 (6H, s), 2.40 (4H, m), 4.13 (4H, td, J_1 = 6.6 Hz, J_2 = 1.5 Hz), 5.52 (4H, m), 6.07 (2H, m) ppm; ^{13}C NMR ($CDCl_3$, 50 MHz) δ = 18.2, 26.9, 32.0, 63.9, 125.2, 127.4, 128.4, 136.4, 167.3 ppm. Anal. Calcd for $C_{14}H_{20}O_4$: C, 66.65; H, 7.99. Found: C, 66.58; H, 7.90.

1,6-Diphenyl-2,5-dimethacryloyloxyoct-4-ene (9b): *E*/*Z* mixture, colorless oil (20 h, 23% yield); IR ($CHCl_3$) 3095, 1705, 1638, 1459, 1309, 1082 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ = 1.90 (6H, s), 2.33 (4H, m), 2.88 (4H, m), 5.14 (2H, m), 5.52 (4H, m), 6.05 (2H, m), 7.26 (10H, m) ppm; ^{13}C NMR ($CDCl_3$, 50 MHz, *E*/*Z* mixture) δ = 18.2, 31.4, 36.5, 40.0, 39.7, 74.4, 125.1, 126.4, 128.3, 129.4, 136.5, 137.4, 166.7 ppm; MS (EI) *m*/*z* = 198 (39%), 107 (32), 91 (42), 69 (100). Anal. Calcd for $C_{28}H_{32}O_4$: C, 77.75; H, 7.46. Found: C, 77.70; H, 7.50.

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Supporting Information Available: Preparation of esters **3**−**6**, general procedure for RCM reactions, characterization data, charts of ^{1}H and ^{13}C NMR spectra, and references of the compounds described in the text. This material is available free of charge via the Internet at http://pubs.acs.org.

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