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ORIGINAL PAPER

Reactivity of terminal phenylpentenes in a ruthenium-catalyzed cross-metathesis reaction: construction of linear bifunctional C-8 alkenes

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Abstract In the present study the behavior of 1-functionalized 2-phenylpent-4-enes in the presence of ruthenium-based metathesis catalysts was investigated. The experimental observations revealed that the outcome of the reaction depends very much on the combination of olefinic partners used in the reaction; only certain combinations delivered satisfactory amounts of unsymmetrical cross-metathesis products, i.e., bifunctional C-8 alkenes.

Keywords Metathesis · Catalysis · Alkenes · Ruthenium · Isomerization

Introduction

Alkenes represent important intermediates in the preparation of complex molecular architectures, either naturally or non-naturally occurring compounds, as well as in the production of polymers [1–3], because their π-bond is sufficiently reactive to be used in a wide range of transformations and the attached functionalities can participate in functional group interconversion reactions, thus altering the reactivity and characteristics of the alkenes [4, 5]. Furthermore, alkenes are substrates for the catalytic metathesis reaction, which has become one of the most powerful tools for the selective formation of new carbon–carbon bonds [6–9]. Olefin metathesis reactions allow a facile and straightforward access to more substituted olefins and generally do not produce by-products, except ethylene, which can be easily removed by evaporation. The development of well-defined transition-metal alkylidene metathesis catalysts has advanced organic synthesis (on both the academic and industrial levels), natural product synthesis, specialty materials production, and polymer science [10–18]. Although molybdenum-based catalysts [19] are generally considered to be more reactive towards highly substituted and electron-rich olefins, Grubbs' ruthenium-based complexes [20] have attracted more attention due to their high functional group tolerance and remarkable stability towards air and moisture. The incorporation of N-heterocyclic carbene (NHC) ligands into ruthenium alkylidene complexes, for example **2**, led to increased activity relative to **1** [21].

Cross-metathesis [22–24] (CM) still remains an underrepresented area when compared to ring-closing metathesis [25] (RCM) and ring-opening metathesis polymerization [26]. This has largely resulted from the low catalyst activity, poor product selectivity, and insufficient stereoselectivity in CM reactions. Very recently, Grubbs et al., succeeded in the preparation of new ruthenium catalysts capable of performing the olefin CM with excellent *Z*-selectivity [27]. To better understand the olefin cross-metathesis selectivity and to predict the reaction outcome, the same research group reported a classification of olefins according to their ability to dimerize, which is based purely on an empirical approach [28]. However, the olefin CM represents a convenient route to higher olefins containing a wide range of pendant functionalities from simple alkene

This work is dedicated to Professor Slovenko Polanc on the occasion of his 65th birthday.

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precursors. The CM was successfully applied in the transformations of unsaturated acid derivatives with functional olefins to bifunctional fatty acids esters and α, ω-nitrile esters [29–31]. Similarly, the CM of fatty acids esters derived from plant oils with methyl acrylate delivered α, ω-dicarboxylic acid esters [32] while the reaction of methyl oleate with *cis*-2-butene-1,4-diyl diacetate resulted in protected α-hydroxy-ω-carboxylic acid derivatives [33]. The CM reaction of a poly(2-oxazoline) featuring terminal double bonds in the side chains with acrylates allowed the introduction of functional groups along the polymer backbone [34]. It was recently reported that the solventless CM of terminal olefins with ethyl acrylate can be performed by using NHC-ruthenium complexes with loadings as low as 100 ppm thus demonstrating increased stability and activity of 2nd generation catalysts [35]. The preparation of trialkyl-substituted isoprenoid olefins as key intermediates in tocopherol synthesis was accomplished by ruthenium-catalyzed CM [36], which was also applied to access the C-8-alkene containing terminal hydroxy groups as an early intermediate in the multi-step synthesis of Annonaceous acetogenins, a diverse class of biologically active compounds [37]. The use of the catalytic metathesis reaction has been successfully demonstrated in the synthesis of renin inhibitors [38], such as aliskiren or its analogues, in which the main C-8 skeleton **A** can be constructed by the CM reaction from appropriate terminal alkenes [39, 40] (Fig. 1). Moreover, a macrocyle route toward aliskiren has been reported by Hanessian et al., where the selective RCM reaction was crucial for the production of the nine-membered lactone as a key intermediate in the convergent total synthesis [41]. We have already reported the formation of macrocycles containing an unsaturated C1-C8 unit by RCM, which can subsequently be opened to give the asymmetric linear alkene skeleton with a good *E*/*Z* ratio [42].

Herein we report on a detailed study of the cross-metathesis reaction using different combinations of 1-functionalized 2-phenylpent-4-enes, leading directly to linear C-8 alkenes with different pendant functionalities.

Results and discussion

As the model substrates we chose differently functionalized phenylpentenes **5** (methyl ester **5a**, mesylate **5b**, phenyl ketone **5c**, alcohol **5d**, bromide **5e**, dibenzyl amide **5f**, Weinreb amide **5 g**) due to their easy preparation from readily available 2-phenylpent-4-enoic acid [43]. At the outset of our experiments, we examined the activity of four different ruthenium-based catalysts **1**-**4** in the CM between ester **5a** and mesylate **5b** in the molar ratio 2:1. The Hoveyda-Grubbs second-generation catalyst (**3**) turned out to be the catalyst of choice, since the highest conversion (72 %) of mesylate into the cross-metathesis product **6ab** was observed when using 2.5 mol % of **3** in refluxing dichloromethane after 2 h (Scheme 1).

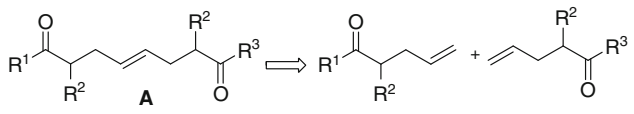
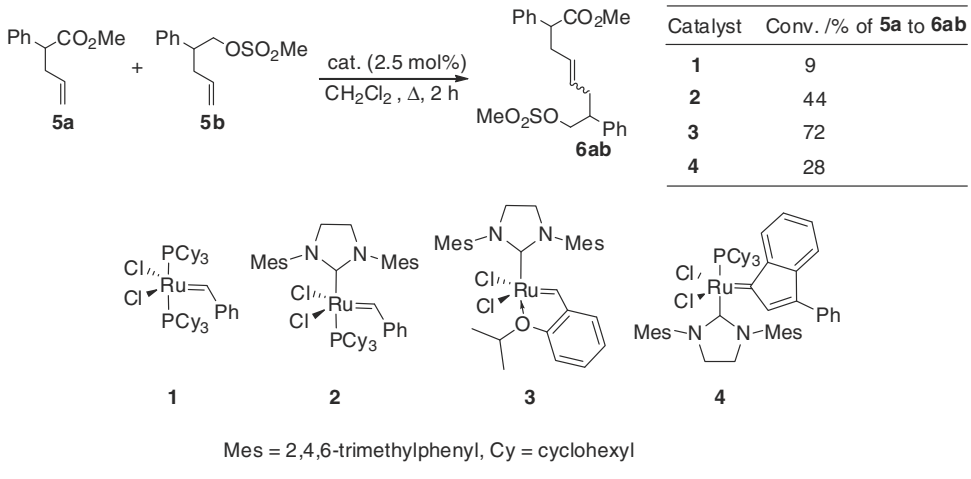


Fig. 1 Retrosynthetic pathway to C-8 skeleton

In continuation, the catalyst **3** was used in the CM reactions between different phenylpentenes **5**, but for 24 h in order to consume at least one metathesis partner. With regard to the alkenes **5** subjected to the CM reaction, different distributions of the heterodimers **6**, homodimers **7**, and isomerized starting compounds **8** were observed under otherwise identical conditions; full details are summarized in Table 1.

The CM reaction of methyl ester **5a** and mesylate **5b** led to the formation of the unsymmetrically substituted C-8 alkene **6ab**, which was isolated by column chromatography as a mixture of two stereoisomers in a 28 % yield. The ester **5a** showed a significant tendency towards homodimerization, as besides the desired product **6ab**, the diester **7a** was isolated in a 35 % yield. Conducting the same reaction in refluxing toluene did not improve the yield of **6ab**. Interestingly, when almost equimolar quantities of phenyl ketone **5c** and alcohol **5d** were reacted in the presence of the catalyst **3**, a higher yield (36 %) of the isolated heterodimeric product **6cd** was obtained. The substrates **5c** and **5d** also tend to isomerize [44] under the applied conditions and, consequently, the internal olefins **8c** and **8d** were isolated in 12 and 20 % yields, respectively. The ester **5a** was the most compatible metathesis partner in the reaction with bromide **5e**, and the heterodimeric product **6ae** was isolated in a yield of 40 %, which was the highest yield obtained for an unsymmetrical alkene. Surprisingly, the combination of alcohol **5d** and mesylate **5b** did not lead to the formation of dimer products, neither in dichloromethane nor in refluxing toluene, and only the isomerized products **8d** and **8b** together with the starting compounds were isolated. The reaction of alcohol **5d** with dibenzyl amide **5f** gave only 16 % of the cross-product **6df** after column chromatography purification. Additionally, a very small amount (3 %) of alcohol dimer **7d** was isolated, while isomeric alcohol **8d** and isomeric amide **8e** were isolated in 24 and 41 % yields, respectively. The latter result shows that alkene isomerization predominates over CM in this particular combination of olefins. Practically the same yield (17 %) of the cross-product **6af** was obtained in the reaction of ester **5a** and dibenzyl amide **5f**. Here again, the ester

Scheme 1



Mes = 2,4,6-trimethylphenyl, Cy = cyclohexyl

5a dimerized to give **7a** in a 10 % yield. On the other hand, the reaction of mesylate **5b** and dibenzyl amide **5f** gave the unsymmetrical C-8 alkene **6bf** in only a 3 % isolated yield, but important amounts of starting materials were recovered. Finally, the reaction of mesylate **5b** and Weinreb amide **5g** for 40 h in refluxing dichloromethane did not deliver any metathesis or non-metathesis products and only the starting materials were recovered using chromatography purification of the reaction mixture. The low reactivity of dibenzyl amide **5f** in the CM reactions and the inability of Weinreb amide **5g** to metathesize could be explained by the coordination of their carbonyl oxygen to the ruthenium center of the carbene intermediate formed in the metathesis between the amide and the catalyst **3** [45]. If such a six-membered chelate becomes too stable, this can inhibit the catalyst for any further metathesis reaction, which is more pronounced with the amides **5f** and **5g** than the ester **5a** or phenyl ketone **5c**. In addition, Weinreb amide **5g** could form a stable 5-membered chelate with ruthenium. On the other hand, the amide **5f** is more prone to double-bond isomerization as significant amounts of isomerized products were isolated in the reactions where **5f** was used as a metathesis partner.

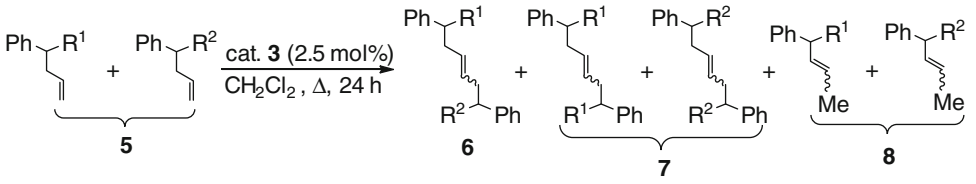
It is worth noting that the separation of reaction mixtures by column chromatography was rather difficult due to the similar R_f of the products, which consequently resulted in low isolated yields. Regarding the ^{1}H NMR spectra, most of the metathesis and isomerized products were isolated as mixtures of two stereoisomers, referred to as major and minor isomers. The NMR patterns of the olefinic protons were complex and; hence, it was not possible to find out whether the predominant isomer was *trans* or *cis*. On the basis of literature data [17, 22, 46] on metal-catalyzed alkene transformations we assumed that the major isomers in the isolated products were *trans* and the minor *cis*.

In conclusion, this study revealed that 1-functionalized 2-phenylpent-4-enes can be used as substrates in ruthenium-catalyzed CM reactions and that only certain combinations successfully led to the formation of synthetically valuable, unsymmetrical C-8 alkenes. It was also shown that in some combinations of alkene substrates the double-bond isomerization competed with CM in the presence of the Hoveyda-Grubbs second-generation catalyst, thus giving significant amounts of isomerized starting olefins. This was particularly pronounced with dibenzyl amide and alcohol when used as metathesis partners. The methyl ester turned out to be a good partner in CM since in all combinations in which it was used (with mesylate, bromide, and dibenzyl amide) the desired heterodimeric products were obtained. On the other hand, dibenzyl amide and Weinreb amide showed a somewhat lower reactivity in CM, most probably due to the formation of the more stable ruthenium chelate intermediates in the catalytic cycle, if compared to the ester and ketone. Although the isolated yields of the metathesis products were low, this study importantly contributes to a better understanding of the behavior of differently functionalized alkenes in CM reactions, which need further investigations because of their great synthetic potential.

Experimental

NMR spectra were recorded at 29 °C with a Bruker Avance DPX 300 in DMSO-d_6 or $CDCl_3$. ^{1}H NMR spectra were recorded at 300 MHz using TMS as an internal standard. ^{13}C NMR spectra were recorded at 75.5 MHz and are referenced against the central line of the solvent signal (DMSO-d_6 septet at $\delta = 39.5$ ppm, $CDCl_3$ triplet at $\delta = 77.0$ ppm). The coupling constants (J) are given in Hz. For minor isomers of products **6**, **7**, and **8** only selected ^{1}H

Table 1 CM of functionalized phenylpentenes **5**



Run	Starting olefins **5**	Products; yield/ %[b] (n_{minor}:n_{major})[c]				
	R^1:R^2 (n_1:n_2)[a]	**6**	**7**		**8**	
1	CO_2Me (**5a**):CH_2OMs (**5b**)	**6ab**	**7a**	–	–	–
	(2:1)	28 (1:4)	35 (1:4.5)			
2	COPh (**5c**):CH_2OH (**5d**)	**6cd**	–	–	**8c**	**8d**
	(1:1.2)	36 (1:4)			12 (1:2.2)	20 (1:2.5)
3	CO_2Me (**5a**):CH_2Br (**5e**)	**6ae**	–	**7e**[d]	–	–
	(1:2)	40		25		
4	CH_2OMs (**5b**):CH_2OH (**5d**)	–	–	–	**8b**	**8d**
	(1:2)				30 (1:2)	21 (1:8.2)
5	CH_2OH (**5d**):$CONBn_2$ (**5f**)	**6df**	**7d**	–	**8d**	**8f**
	(2:1)	16	3		24 (1:6)	41 (1:3.2)
6	CO_2Me (**5a**):$CONBn_2$ (**5f**)	**6af**	**7a**	–	–	**8f**
	(2:1)	17 (1:1.5)	10 (1:2.2)			10 (1:2)
7	CH_2OMs (**5b**):$CONBn_2$ (**5f**)	**6bf**	–	–	–	–
	(2:1)	3				
8[e]	CH_2OMs (**5b**):CON(OMe)Me (**5g**)	–	–	–	–	–
	(1:2)					

[a] Molar ratio between substrates **5**

[b] Isolated yield by column chromatography

[c] Ratio between minor and major isomer determined on the basis of ^{1}H NMR of olefinic protons for **6** and **7**, and methyl protons for **8**.

[d] Product not confirmed by MS

[e] Reaction time 40 h

NMR resonances are given. IR spectra were obtained with a Bio-Rad FTS 3000MX spectrometer. The MS spectra were recorded with a VG-Analytical AutoSpec Q spectrometer. Flash chromatography was performed on 230–400 mesh silica gel. Merck silica gel 60 PF_{254} containing gypsum was used to prepare chromatotron plates. The 2-Phenylpent-4-enoic acid was prepared according to a published procedure [43]. Anhydrous toluene and THF were obtained using standard drying techniques. All other reagents and solvents were used as received from commercial suppliers.

Methyl 2-phenylpent-4-enoate (**5a**)

A mixture of 0.51 g 2-phenylpent-4-enoic acid (2.89 mmol), 20 cm^3 methanol, and 0.5 cm^3 conc. H_2SO_4 was refluxed for 16 h. After evaporation of methanol under reduced pressure, 15 cm^3 CH_2Cl_2 was added to a residue and washed with 3 × 15 cm^3 sat. $NaHCO_3$. The aqueous layers were additionally extracted with 15 cm^3 CH_2Cl_2. The combined organic extracts were dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo to give 456 mg (83 %) **5a** as a yellow oil. The NMR spectroscopic data are consistent with reported data [47].

2-Phenylpent-4-enyl methanesulfonate (**5b**, $C_{12}H_{16}O_3S$)

To a cold solution (0 °C) of 790 mg 2-phenylpent-4-en-1-ol (**5d**, 4.877 mmol) and 0.5 cm^3 methanesulfonyl chloride (6.472 mmol) in 20 cm^3 CH_2Cl_2, 2 cm^3 triethylamine (14.33 mmol) was added. The reaction mixture was allowed to warm to room temperature at which it was stirred for 15 h. Then 20 cm^3 H_2O was added, layers were separated, and the aqueous layer was extracted with 2 × 15 cm^3 CH_2Cl_2. The combined organic extracts were washed with 20 cm^3 1 M HCl, dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo to give 1.065 g **5b** (91 %) as an orange oil. ^{1}H NMR (300 MHz, $CDCl_3$):

δ = 2.41–2.60 (*m*, 2H, CH_2CH=), 2.77 (*s*, 3H, CH_3), 3.06–3.15 (*m*, 1H, CH), 4.35 (*d*, *J* = 6.7 Hz, 2H, CH_2O-SO_2CH_3), 5.00–5.09 (*m*, 2H, H_2C=CH), 5.61–5.75 (*m*, 1H, H_2C=C*H*), 7.20–7.28 (*m*, 3H, Ar), 7.31–7.36 (*m*, 2H, Ar) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 36.0, 37.0, 44.8, 72.9, 117.3, 127.2, 127.8, 128.6, 134.8, 140.0 ppm; IR (NaCl): $\bar{\nu}$ = 3,065, 3,028, 2,978, 2,938, 1,642, 1,495, 1,454, 1,354, 1,175, 958, 927, 837, 702 cm^{-1}; HRMS (ES+, TOF): calcd for $C_{12}H_{16}O_3SNa$ ($[M + Na]^+$) 263.0718, found 263.0716.

1,2-Diphenylpent-4-en-1-one (**5c**)

A mixture of 356 mg 2-phenylpent-4-enoic acid (2.02 mmol), 0.35 cm^3 oxalyl chloride (4.08 mmol), and 5 cm^3 dry toluene was refluxed for 1 h. The volatiles were evaporated in vacuo and the oily residue was dissolved in 5 cm^3 dry THF. To the resulting cold (0 °C) solution 0.8 cm^3 phenylmagnesium bromide (2.4 mmol, 3 M in Et_2O) was slowly added under Ar. The reaction mixture was stirred for 1.5 h at the same temperature and then allowed to warm to room temperature at which it was stirred for 15 h. Then 15 cm^3 sat. NH_4Cl was added and extracted with 3 × 10 cm^3 Et_2O. The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated in vacuo. Purification of the crude product by radial chromatography (petroleum ether/EtOAc = 20/1) yielded 300 mg (63 %) **5c** as a colorless oil. NMR spectroscopic data are consistent with reported data [48].

2-Phenylpent-4-en-1-ol (**5d**)

To a cold solution (0 °C) of 356 mg 2-phenylpent-4-enoic acid (2.02 mmol) in 8 cm^3 dry THF, 3 cm^3 suspension of $LiAlH_4$ (6 mmol, 2 M in THF) was slowly added. The reaction mixture was allowed to warm to room temperature at which it was stirred for 15 h. The reaction was quenched by the successive addition of 1 cm^3 H_2O, 1 cm^3 2 M aqueous NaOH, and 1.5 cm^3 H_2O. The solid was filtered and washed with 3 × 10 cm^3 CH_2Cl_2. The organic layer was washed with 20 cm^3 H_2O, dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo to give 256 mg **5d** (78 %) as an orange oil. The NMR spectroscopic data are consistent with reported data [49].

5-Bromo-4-phenylpent-1-ene (**5e**)

A mixture of 563 mg **5b** (2.34 mmol), 1.95 g LiBr (22.4 mmol), and 18 cm^3 acetone was refluxed for 5 h. Then the volatiles were evaporated in vacuo, 50 cm^3 H_2O was added to the oily residue and extracted with 3 × 15 cm^3 CH_2Cl_2. The combined organic extracts were dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. Purification of the crude product by radial chromatography (petroleum ether/EtOAc = 10/1) yielded 374 mg (71 %) **5e** as a yellow oil. NMR spectroscopic data are consistent with reported data [50].

N,N-dibenzyl-2-phenylpent-4-enamide (**5f**, $C_{25}H_{25}NO$)

A mixture of 1 g 2-phenylpent-4-enoic acid (5.68 mmol), 1 cm^3 oxalyl chloride (11.64 mmol), and 15 cm^3 dry toluene was refluxed for 1 h. The volatiles were evaporated in vacuo and the oily residue was dissolved in 20 cm^3 dry CH_2Cl_2. To the resulting cold (0 °C) solution, 3 cm^3 dibenzylamine (15.51 mmol) was added. The reaction mixture was allowed to warm to room temperature at which it was stirred for 15 h. Then 40 cm^3 1 M HCl was added, the layers were separated, and the aqueous layer was extracted with 3 × 10 cm^3 CH_2Cl_2. The combined organic extracts were dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo to give 1.433 g **5f** (71 %) as a colorless oil. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.30–2.39 (*m*, 1H, CH_aH_bCH=), 2.72–2.82 (*m*, 1H, CH_aH_bCH=), 4.01 (*dd*, *J* = 6.3, 8.4 Hz, 1H, CH), 4.24 (*d*, *J* = 15.0 Hz, 1H, $NCH_{a1}H_{b1}Ph$), 4.36 (*d*, *J* = 16.9 Hz, 1H, $NCH_{a1}H_{b1}Ph$), 4.55 (*d*, *J* = 16.9 Hz, 1H, $NCH_{a2}H_{b2}Ph$), 4.70 (*d*, *J* = 15.0 Hz, 1H, $NCH_{a2}H_{b2}Ph$), 4.92–5.01 (*m*, 2H, H_2C=CH), 5.62–5.75 (*m*, 1H, H_2C=CH), 7.03–7.08 (*m*, 4H, Ar), 7.21–7.34 (*m*, 11H, Ar) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 39.6, 48.3, 49.3, 49.6, 116.7, 126.4, 127.1, 127.2, 127.5, 127.9, 128.0, 128.4, 128.77, 128.80, 136.2, 136.5, 137.4, 139.6, 173.0 ppm; IR (NaCl): $\bar{\nu}$ = 3,064, 3,029, 2,921, 1,647, 1,495, 1,452, 1,438, 1,207, 1,178, 699 cm^{-1}; HRMS (ES+, TOF): calcd for $C_{25}H_{26}NO$ ($[M + H]^+$) 356.2014, found 356.2002.

N-Methoxy-N-methyl-2-phenylpent-4-enamide (**5g**, $C_{13}H_{17}NO_2$)

A mixture of 1 g 2-phenylpent-4-enoic acid (5.68 mmol), 1 cm^3 oxalyl chloride (11.64 mmol), and 15 cm^3 dry toluene was refluxed for 1 h. The volatiles were evaporated in vacuo and the oily residue was dissolved in 20 cm^3 dry CH_2Cl_2. To the resulting cold (0 °C) solution, 848 mg *N*,*O*-dimethylhydroxylamine hydrochloride (8.52 mmol) and 2 cm^3 triethylamine (14.33 mmol) were added. The reaction mixture was allowed to warm to room temperature at which it was stirred for 15 h. Then 40 cm^3 1 M HCl was added, the layers were separated, and the aqueous layer was extracted with 3 × 10 cm^3 CH_2Cl_2. The combined organic extracts were dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. Purification of the crude product by radial chromatography (petroleum ether/EtOAc = 25/1) yielded 772 mg (62 %) **5g** as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.41–2.50 (*m*, 1H, CH_aH_bCH=), 2.79–2.89 (*m*, 1H, CH_aH_bCH=), 3.15 (*s*, 3H, CH_3), 3.46 (*s*, 3H, OCH_3), 4.07 (*m*, 1H, CH), 4.95–5.08 (*m*, 2H, H_2C=CH), 5.67–5.81 (*m*, 1H, H_2C=CH), 7.19–7.34 (*m*, 5H, Ar) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 32.3, 38.2, 47.6, 61.2, 116.5, 126.9, 128.1, 128.5, 136.0, 139.6, 173.9 ppm; IR (NaCl): $\bar{\nu}$ = 3,075, 3,030, 2,974, 2,938,

2,820, 1,730, 1,662, 1,455, 1,440, 1,417, 1,383, 1,175, 992, 700 cm^{-1}; HRMS (ES+, TOF): calcd for $C_{13}H_{18}NO_2$ ($[M + H]^+$) 220.1338, found 220.1335.

General procedure for the metathesis reaction of olefins ***5***

A mixture of two different olefins **5** in the molar ratio 1 : 1.2–2, 15 cm^3 CH_2Cl_2, and 16 mg Hoveyda-Grubbs catalyst (**3**) (0.025 mmol, 2.5 mol %) was refluxed for 24 h. Then the reaction mixture was evaporated under reduced pressure and the residue was purified by column chromatography on silica gel to give different distributions of products **6**, **7**, and **8**. For full details see Table 1.

Methyl 8-(methylsulfonyloxy)-2,7-diphenyloct-4-enoate (**6ab**, $C_{22}H_{26}O_5S$)

Obtained in the reaction of 380 mg **5a** (2 mmol) and 240 mg **5b** (1 mmol). Column chromatography (petroleum ether/EtOAc, 25:1, then 5:1) afforded 113 mg (28 %) **6ab**. ^{1}H NMR (300 MHz, $CDCl_3$): minor 5.25–5.31 (*m*, 0.5H, CH=CH); major $\delta = 2.30$–2.47 (*m*, 3H, CH_2CH=$CHCH_aH_b$), 2.67–2.77 (*m*, 1H, CH_aH_bCH=CH), 2.74 (*s*, 3H, OSO_2CH_3), 2.87–3.03 (*m*, 1H, CH_2CHCH_2), 3.53 (*dd*, $J = 7.3$, 7.7 Hz, 1H, $CHCO_2CH_3$), 3.63 (*s*, 3H, CO_2CH_3), 4.26 (*m*, 2H, $CH_2OSO_2CH_3$), 5.31–5.39 (*m*, 2H, CH=CH), 7.10–7.16 (*m*, 2H, Ar), 7.22–7.33 (*m*, 8H, Ar) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): major $\delta = 33.5$, 36.5, 38.4, 44.7, 51.8, 52.1, 72.5, 126.4, 127.0, 127.1, 127.5, 128.1, 129.2, 136.6, 139.8, 173.2 ppm; IR (NaCl): $\bar{\nu} = 3{,}029$, 2,949, 2,925, 2,853, 1,734, 1,495, 1,455, 1,436, 1,354, 1,173, 956, 838, 701 cm^{-1}; HRMS (ES+, TOF): calcd for $C_{22}H_{26}O_5SNa$ ($[M + Na]^+$) 425.1399, found 425.1406.

8-Hydroxy-1,2,7-triphenyloct-4-en-1-one (**6cd**, $C_{26}H_{26}O_2$)

Obtained in the reaction of 236 mg **5c** (1 mmol) and 195 mg **5d** (1.2 mmol). Column chromatography (petroleum ether/EtOAc, 20:1, then 10:1, then 3:1) afforded 133 mg (36 %) **6cd**. ^{1}H NMR (300 MHz, $CDCl_3$): minor $\delta = 4.34$ (*t*, $J = 7.3$ Hz, 0.25H, CHCOPh), 5.26–5.30 (*m*, 0.5H, CH=CH); major $\delta = 1.54$ (*rs*, 1H, OH), 2.19–2.48 (*m*, 3H, CH_2CH= and $CHCH_2OH$), 2.65–2.88 (*m*, 2H, CH_2CH= CH), 3.58–3.70 (*m*, 2H, H_2COH), 4.47 (*t*, $J = 7.3$ Hz, 1H, CHCOPh), 5.34–5.38 (*m*, 2H, CH=CH), 7.09–7.48 (*m*, 13H, Ar), 7.88–7.91 (*m*, 2H, Ar) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): major $\delta = 35.3$, 37.0, 48.3, 54.0, 66.6, 126.6, 127.0, 127.9, 128.1, 128.42, 128.44, 128.6, 128.8, 129.4, 130.0, 132.8, 136.7, 139.1, 142.0, 199.3 ppm; IR (NaCl): $\bar{\nu} = 3{,}425$, 3,061, 3,027, 2,920, 1,681, 1,598, 1,494, 1,449, 699 cm^{-1}; HRMS (ES+, TOF): calcd for $C_{26}H_{27}O_2$ ($[M + H]^+$) 371.2011, found 371.2014.

Methyl 8-bromo-2,7-diphenyloct-4-enoate (**6ae**, $C_{21}H_{23}BrO_2$)

Obtained in the reaction of 190 mg **5a** (1 mmol) and 450 mg **5e** (2 mmol). Column chromatography (petroleum ether/EtOAc, 20:1) afforded 155 mg (40 %) **6ae**. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 2.29$–2.52 (*m*, 3H, CH_2CH=$CHCH_aH_b$), 2.67–2.76 (*m*, 1H, CH_aH_bCH=CH), 2.94 (*m*, 1H, CH_2CHCH_2Br), 3.43–3.49 (*m*, 2H, CH_2Br), 3.53 (*m*, 1H, $CHCO_2Me$), 3.63 (*s*, 3H, CO_2CH_3), 5.23–5.44 (*m*, 2H, CH=CH), 7.07–7.15 (*m*, 2H, Ar), 7.21–7.34 (*m*, 8H, Ar) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): major $\delta = 36.8$, 37.1, 38.3, 47.8, 51.6, 52.5, 126.8, 127.2, 127.8, 128.3, 128.8, 129.2, 129.7, 138.9, 141.6, 173.5 ppm; IR (NaCl): $\bar{\nu} = 3061$, 3,029, 2,951, 2,922, 2,848, 1,736, 1,495, 1,452, 1,435, 1,267, 1,224, 1,197, 1,161, 971, 700 cm^{-1}; HRMS (ES+, TOF): calcd for $C_{21}H_{24}BrO_2$ ($[M + H]^+$) 387.0960, found 387.0960.

N,N-Dibenzyl-8-hydroxy-2,7-diphenyloct-4-enamide (**6df**, $C_{34}H_{35}NO_2$)

Obtained in the reaction of 355 mg **5f** (1 mmol) and 324 mg **5d** (2 mmol). Column chromatography (petroleum ether/CH_2Cl_2, 1:5, then CH_2Cl_2, then CH_2Cl_2/MeOH, 10:1) afforded product **6df** (78 mg, 16 %). ^{1}H NMR (300 MHz, $CDCl_3$): major $\delta = 1.65$ (*rs*, 1H, OH), 2.27–2.60 (*m*, 3H, CH_2CH=$CHCH_aH_b$), 2.68–2.96 (*m*, 2H, CH_aH_bCH= and $CHCH_2OH$), 3.64–3.80 (*m*, 3H, CH_2OH and CHCON), 4.12–4.26 (*m*, 2H, NCH_2Ph), 4.48–4.58 (*m*, 1H, NCH_aH_bPh), 4.97–5.12 (*m*, 1H, NCH_aH_bPh), 5.29–5.43 (*m*, 2H, CH=CH), 7.03–7.34 (*m*, 20H, Ar) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): major $\delta = 35.6$, 48.3, 49.6, 66.7, 126.4, 126.7, 127.0, 127.2, 127.5, 127.9, 128.0, 128.5, 128.7, 128.8, 136.6, 137.4, 139.6, 142.2, 173.1 ppm; IR (NaCl): $\bar{\nu} = 3{,}448$, 3,062, 3,027, 2,925, 1,645, 1,494, 1,453, 1,437, 1,030, 971, 700 cm^{-1}; HRMS (ES+, TOF): calcd for $C_{34}H_{36}NO_2$ ($[M + H]^+$) 490.2746, found 490.2737.

Methyl 8-(dibenzylamino)-8-oxo-2,7-diphenyloct-4-enoate (**6af**, $C_{35}H_{35}NO_3$)

Obtained in the reaction of 380 mg **5a** (2 mmol) and 355 mg **5f** (1 mmol). Column chromatography (petroleum ether/EtOAc, 20:1) afforded 88 mg **6af** (17 %). ^{1}H NMR (300 MHz, $CDCl_3$): minor $\delta = 3.42$ (*t*, $J = 7.7$ Hz, 1H, $CHCO_2Me$), 3.57 (*s*, 2H, CO_2CH_3); major $\delta = 2.30$–2.56 (*m*, 2H, $CH_{2a}CH$=), 2.67–2.91 (*m*, 2H, $CH_{2b}CH$=), 3.52 (*t*, $J = 7.7$ Hz, 1H, CHC_2OMe), 3.61 (*s*, 3H, CO_2CH_3), 3.65–3.71 (*m*, 1H, CHCON), 4.12–4.23 (*m*, 2H, NCH_2Ph), 4.46–4.54 (*m*, 1H, NCH_aH_bPh), 4.94–5.05 (*m*, 1H, NCH_aH_bPh), 5.23–5.48 (*m*, 2H, CH=CH), 7.00–7.02 (*m*, 2H, Ar), 7.08–7.10 (*m*, 2H, Ar), 7.21–7.34 (*m*, 16H, Ar) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): major $\delta = 36.9$, 38.9, 48.8, 49.6, 50.0, 51.9, 52.3, 126.9, 127.7, 128.0, 128.3, 128.4, 128.46, 128.49, 128.9, 129.0, 129.2, 129.3, 137.0, 137.8, 139.1,

140.0, 173.5, 174.4 ppm; IR (NaCl): $\bar{\nu}$ = 3,061, 3,028, 2,950, 2,922, 1,737, 1,646, 1,493, 1,454, 1,436, 1,267, 1,221, 1,156, 970, 698 cm^{-1}; HRMS (ES+, TOF): calcd for $C_{35}H_{36}NO_3$ ($[M + H]^+$) 518.2695, found 518.2695.

8-(Dibenzylamino)-8-oxo-2,7-diphenyloct-4-enyl methanesulfonate (**6bf**, $C_{35}H_{37}NO_4S$)
Obtained in the reaction of 480 mg **5b** (2 mmol) and 355 mg **5f** (1 mmol). Column chromatography (petroleum ether/EtOAc, 25:1) afforded 17 mg **6bf** (3 %). ^{1}H NMR (300 MHz, $CDCl_3$): major δ = 2.25–2.41 (*m*, 3H, CH_2CHCH_2CH= and $COCHCH_aH_bCH$=), 2.73 (*s*, 3H, OSO_2CH_3), 2.77–2.86 (*m*, 1H, $COCHCH_aH_bCH$=), 2.92–3.02 (*m*, 1H, CH_2CHCH_2CH=), 3.62–3.71 (*m*, 1H, CHCON), 4.10–4.27 (*m*, 4H, CH_2O and NCH_2Ph), 4.45–4.54 (*m*, 1H, NCH_aH_bPh), 4.93–5.08 (*m*, 1H, NCH_aH_bPh), 5.22–5.46 (*m*, 2H, CH=CH), 6.99–7.01 (*m*, 2H, Ar), 7.07–7.13 (*m*, 4H, Ar), 7.21–7.33 (*m*, 14H, Ar) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): major δ = 37.1, 72.8, 126.5, 127.2, 127.3, 127.86, 127.93, 128.1, 128.5, 128.6, 128.78, 128.83, 136.7, 137.5, 139.5, 140.3, 173.1 ppm; HRMS (ES+, TOF): calcd for $C_{35}H_{38}NO_4S$ ($[M + H]^+$) 568.2522, found 568.2527.

Dimethyl 2,7-diphenyloct-4-enedioate (**7a**, $C_{22}H_{24}O_4$)
Obtained in the reaction of 380 mg **5a** (2 mmol) and 240 mg **5b** (1 mmol). Column chromatography (petroleum ether/EtOAc, 25:1, then 5:1) afforded 123 mg (35 %) **7a**. ^{1}H NMR (300 MHz, $CDCl_3$): minor δ = 2.47–2.56 (*m*, 0.5H, 2 × CH_aH_b), 2.78–2.86 (*m*, 0.5H, 2 × CH_aH_b), 3.45 (*t*, *J* = 7.8 Hz, 0.5H, 2 × CH), 3.62 (*s*, 1.5H, 2 × OCH_3), 5.28–5.31 (*m*, 0.5H, CH=CH); major δ = 2.35–2.43 (*m*, 2H, 2 × CH_aH_b), 2.67–2.76 (*m*, 2H, 2 × CH_aH_b), 3.52 (*dd*, *J* = 6.9, 7.7 Hz, 2H, 2 × CH), 3.63 (*s*, 6H, 2 × OCH_3), 5.37–5.41 (*m*, 2H, CH=CH), 7.20–7.32 (*m*, 10H, Ar) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): major δ = 36.9, 51.5, 52.0, 127.9, 128.3, 128.6, 129.4, 139.1, 173.1 ppm; IR (NaCl): $\bar{\nu}$ = 2,956, 2,925, 2,854, 1,742, 1,457, 1,378, 1,159 cm^{-1}; HRMS (ES+, TOF): calcd for $C_{22}H_{25}O_4$ ($[M + H]^+$) 353.1753, found 353.1757.

2,7-Diphenyloct-4-ene-1,8-diol (**7d**, $C_{20}H_{24}O_2$)
Obtained in the reaction of 355 mg **5f** (1 mmol) and 324 mg **5d** (2 mmol). Column chromatography (petroleum ether/CH_2Cl_2, 1:5, then CH_2Cl_2, then CH_2Cl_2/MeOH, 10:1) afforded product **7d** (9 mg, 3 %). ^{1}H NMR (300 MHz, $CDCl_3$): major δ = 1.26 (rs, 2H, 2 × OH), 2.22–2.41 (*m*, 4H, 2 × CH_2CH=), 2.69–2.82 (*m*, 2H, 2 × CH), 3.62–3.77 (*m*, 4H, 2 × CH_2OH), 5.29–5.35 (*m*, 2H, CH=CH), 7.13–7.35 (*m*, 10H, Ar) ppm; IR (NaCl): $\bar{\nu}$ = 3,361, 3,026, 2,923, 2,888, 1,631, 1,494, 1,452, 1,054, 973, 701 cm^{-1}; HRMS (ES+, TOF): calcd for $C_{20}H_{25}O_2$ ($[M + H]^+$) 297.1855, found 297.1852.

2,7-Diphenyl-1,8-dibromo-4-octene (**7e**, $C_{20}H_{22}Br_2$)
Obtained in the reaction of 190 mg **5a** (1 mmol) and 450 mg **5e** (2 mmol). Column chromatography (petroleum ether/EtOAc, 20:1) afforded 106 mg **7e** (25 %). ^{1}H NMR (300 MHz, $CDCl_3$): major δ = 2.30–2.38 (*m*, 2H, 2 × CH_aH_bCH=), 2.47–2.53 (*m*, 2H, 2 × CH_aH_bCH=), 2.95 (*m*, 2H, 2 × CH), 3.44 (*m*, 4H, 2 × CH_2Br), 5.25–5.29 (*m*, 2H, CH=CH), 7.06–7.09 (*m*, 2H, Ar), 7.24–7.34 (*m*, 8H, Ar) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): major δ = 37.5, 38.1, 47.2, 126.5, 127.0, 127.8, 128.5, 142.6 ppm.

2-Phenylpent-3-enyl methanesulfonate (**8b**, $C_{12}H_{16}O_3S$)
Obtained in the reaction of 240 mg **5b** (1 mmol) and 324 mg **5d** (2 mmol). Column chromatography (petroleum ether/CH_2Cl_2, 1:1) afforded 72 mg (30 %) **8b**. ^{1}H NMR (300 MHz, $CDCl_3$): major δ = 1.68 (*dd*, *J* = 6.7, 1.5 Hz, 3H, CH_3CH=), 2.78 (*m*, 3H, OSO_2CH_3), 3.67–3.73 (*m*, 1H, CH), 4.32–4.39 (*m*, 2H, CH_2), 5.56–5.64 (*m*, 2H, CH=CH), 7.20–7.36 (*m*, 5H, Ar) ppm; HRMS (ES+, TOF): calcd for $C_{12}H_{16}O_3SNa$ ($[M + Na]^+$) 263.0718, found 263.0716.

1,2-Diphenylpent-3-en-1-one (**8c**, $C_{17}H_{16}O$)
Obtained in the reaction of 236 mg **5c** (1 mmol) and 195 mg **5d** (1.2 mmol). Column chromatography (petroleum ether/EtOAc, 20:1, then 10:1, then 3:1) afforded 28 mg **8c** (12 %). ^{1}H NMR (300 MHz, $CDCl_3$): minor δ = 1.75 (*dd*, *J* = 1.7, 6.9 Hz, 1.36H, CH_3CH=), 5.52 (*d*, *J* = 6.6 Hz, 0.45H, CHCH=); major δ = 1.71 (*dd*, *J* = 1.2, 6.5 Hz, 3H, CH_3CH=), 5.24 (*d*, *J* = 8.1 Hz, 1H, CHCH=), 5.49–5.61 (*m*, 1H, CH_a=CH_b), 5.95–6.06 (*m*, 1H, CH_a=CH_b), 7.19–7.51 (*m*, 8H, Ar), 7.94–7.99 (*m*, 2H, Ar) ppm; HRMS (ES+, TOF): calcd for $C_{17}H_{16}ONa$ ($[M + Na]^+$) 259.1099, found 259.1096.

2-Phenylpent-3-en-1-ol (**8d**, $C_{11}H_{14}O$)
Obtained in the reaction of 236 mg **5c** (1 mmol) and 195 mg **5d** (1.2 mmol). Column chromatography (petroleum ether/EtOAc, 20:1, then 10:1, then 3:1) afforded 39 mg **8d** (20 %). ^{1}H NMR (300 MHz, $CDCl_3$): minor δ = 1.70 (*dd*, *J* = 1.5, 6.7 Hz, 1.2H, H_3CCH=); major δ = 1.50 (*rs*, 1H, OH), 1.72 (*d*, *J* = 4.5 Hz, 3H, H_3CCH=), 3.43–3.50 (*m*, 1H, CH), 3.71–3.77 (*m*, 2H, CH_2OH), 5.55–5.64 (*m*, 2H, CH=CH), 7.21–7.26 (*m*, 3H, Ar), 7.30–7.35 (*m*, 2H, Ar) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): major δ = 18.1, 51.7, 66.4, 126.7, 127.8, 128.1, 128.7, 130.9, 141.4 ppm; HRMS (ES+, TOF): calcd for $C_{11}H_{15}O$ ($[M + H]^+$) 163.1123, found 163.1131.

N,N-dibenzyl-2-phenylpent-3-enamide (**8f**, $C_{25}H_{25}NO$)
Obtained in the reaction of 355 mg **5f** (1 mmol) and 324 mg **5d** (2 mmol). Column chromatography (petroleum ether/CH_2Cl_2, 1:5, then CH_2Cl_2, then CH_2Cl_2/MeOH, 10:1)

afforded product **8f** (146 mg, 41 %). ^{1}H NMR (300 MHz, $CDCl_3$): minor $\delta = 1.44$ (*dd*, $J = 1.8$, 6.9 Hz, 0.94H, CH_3CH=); major $\delta = 1.67$ (*dd*, $J = 1.3$, 6.4 Hz, 3H, CH_3CH=), 4.12–4.56 (*m*, 4H, NCH_2Ph, NCH_aH_bPh and CHCH=), 4.94–4.99 (*m*, 1H, NCH_aH_bPh), 5.31–5.43 (*m*, 1H CH_a=CH_b), 5.91–6.00 (*m*, 1H, CH_a=CH_b), 7.01–7.38 (*m*, 15H, Ar) ppm; IR (NaCl): $\bar{\nu} = 3{,}030$, 2,926, 1,630, 1,443, 1,214, 976, 699 cm^{-1}; HRMS (ES+, TOF): calcd for $C_{25}H_{26}NO$ ($[M + H]^+$) 356.2014, found 356.2021.

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