

Chemoselective cross-metathesis reaction between electron-deficient 1,3-dienes and olefins

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Abstract

Chemoselective cross-metathesis reactions between methyl sorbate or 1,3-dienic amides and various olefins in the presence of the Grubbs–Hoveyda catalyst have been investigated. Cross-metathesis reactions turned out to be more chemoselective with 1,3-dienic amides than with 1,3-dienic esters.

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1. Introduction

In the last decade, metal-catalyzed olefin metathesis has emerged as one of the most powerful and reliable organometallic transformations for carbon-carbon bond formation in organic synthesis [1], and particularly, ring-closing metathesis (RCM) and cross-metathesis (CM) [2] reactions have been thoroughly investigated. These convenient synthetic techniques have recently gained prominence due to the commercial availability of molybdenum catalyst [Mo]-I [3] and robust ruthenium carbene complexes such as [Ru]-I [4], [Ru]-II [5], and [Ru]-III [6], which exhibit good activities, operational simplicity, and remarkable functional group tolerance (Fig. 1). Therefore, the metathesis has become a powerful synthetic tool that has been widely used in the synthesis of natural products [7].

Although the RCM between 1,3-dienes and olefins has been used to synthesize complex naturally occurring molecules [8], CM reactions involving conjugated 1,3-dienes have been scarcely investigated [9]. Only recently, CM reac-

tions have been described between conjugated electron-deficient olefins such as ethyl sorbate and various olefin cross-partners [10]. When ethyl sorbate (1) and 5-hexenyl acetate (2) were heated in refluxing CH_2Cl_2 in the presence of catalyst [Ru]-II (10 mol%), 1,3-diene 3 and olefin 4 were obtained as an inseparable 4/1 mixture (Scheme 1). Indeed, the ester functionality in ethyl sorbate (1) does not sufficiently deactivate the α,β -double bond towards CM and thus when [Ru]-II is used, both olefins of the diene react. By reducing the electron density at the α,β -double bond, as well as by increasing steric hindrance at the α -carbon, the CM is more chemoselective [10].

As the phosphine-free ruthenium complex [Ru]-III exhibits superior activity towards electron-deficient olefins compared to [Ru]-II [11], we initiated a systematic study designed to explore the construction of substituted 1,3-dienes of type A by performing CM reactions between methyl sorbate (5) and diverse olefin partners. Furthermore, we also investigated the corresponding dienic amides 14–16 in order to increase the chemoselectivity of the CM reaction, which would result in the selective formation of dienes of type A and therefore would decrease the formation of olefins of type B (Scheme 2).

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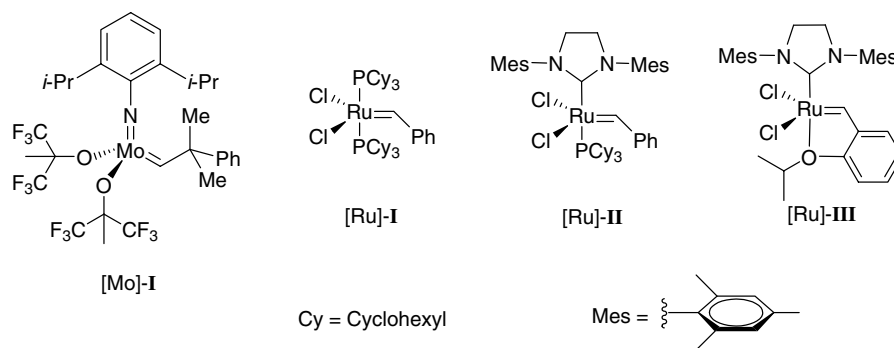
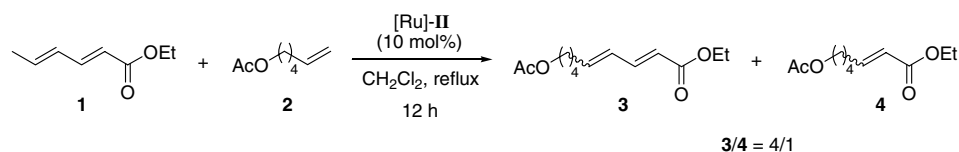
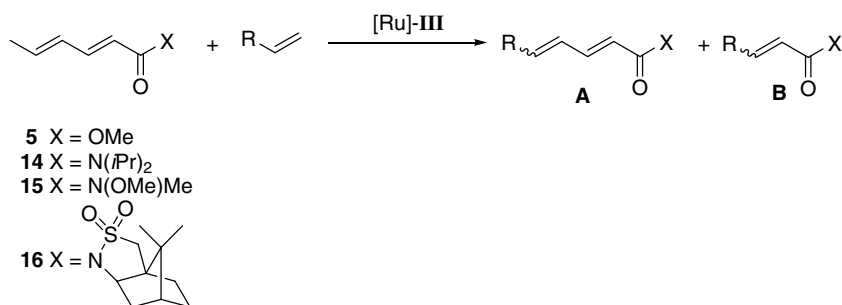


Fig. 1. Commercially available metal carbenes used in RCM and CM reactions.



Scheme 1.



Scheme 2.

2. CM reactions with methyl sorbate (5)

When methyl sorbate (**5**) and oct-1-ene (5 equiv.) were stirred in CH₂Cl₂ at rt (*c* = 0.2 M) for 48 h in the presence of [Ru]-III (5 mol%), the desired conjugated diene **6** was isolated as an inseparable mixture of (*E,E*)-**6** and (*E,Z*)-**6** stereoisomers in a 10/1 ratio, accompanied by the corresponding mono-olefin of type **B** (A/B = 2.5/1) with a global yield of 68% (Table 1, entry 1). In the case of the CM between methyl sorbate (**5**) and allyl trimethylsilane, dienic ester **7** was obtained as a mixture of stereoisomers (*E,E*)-**7** and (*E,Z*)-**7** in a 5/1 ratio in addition to being contaminated with olefin of type **B** (A/B = 6/1). When styrene was used, the conjugated diene **8** was formed in 35% yield with an excellent stereoselectivity as only the (*E,E*)-**8** isomer was isolated and no trace of the mono-olefin of type **B** was observed (Table 1, entry 3) [12].

Other olefins such as diethyl allylphosphonate, allyl bromide and *N*-allyl-*p*-toluenesulfonamide were also examined in the cross-metathesis reaction with methyl sorbate (**5**). In each case, the corresponding CM products were formed in moderate yields (45–56%) and were sometimes accompanied by the mono-olefin of type **B** (Table 1, entries 4–6) [12].

The CM reaction with electron-deficient olefins such as methyl vinyl ketone and *tert*-butyl acrylate was also studied and, respectively, afforded the CM products **12** and **13** in poor yields (13–30%) (Table 1, entries 7 and 8) [12].

3. CM with dienic amides

It was hypothesized the kinetics of the CM reaction with α,β -unsaturated amides was decreased by the chelation of the amide carbonyl group on the ruthenium center, and therefore, the efficiency of CM between α,β -unsaturated amides and olefins was affected by the substituents on the amide nitrogen [13]. Since the dienic esters did not show good chemoselectivity in CM, we turned our attention to dienic amides possessing more electron-rich carbonyl groups. In the case of (*E,E*)-dienic amides, easily accessible from sorbic acid [14], the chelation as well as the steric hindrance should avoid the CM with the α,β -unsaturation and the CM product at the γ,δ -position should be obtained selectively. In consequence, CM reactions between dienic amides **14**–**16** with a variety of electron-rich olefins were examined. The results are reported in Table 2.

Table 1
CM reactions between methyl sorbate (**5**) and a variety of cross-partners

Entry	R	Product A (<i>E,E</i>)/(<i>E,Z</i>)	Ratio A/B Yield ^a
1	Hex	Hex 6 10/1	2.5/1 68%
2	TMS	TMS 7 5/1	6/1 71%
3	Ph	Ph 8 100/0	35% ^{b,c}
4	(EtO) ₂ P	(EtO) ₂ P 9 5.5/1	4/1 ^c 56%
5	Br	Br 10 32/1	48% ^{b,c}
6	TsHN	TsHN 11 11.5/1	4/1 45%
7		12 100/0	13% ^{b,c}
8	<i>t</i> -BuO	<i>t</i> -BuO 13 50/1	30% ^{b,c}

^a Isolated yield for the mixture of **A** and **B**.

^b No trace of **B** was detected.

^c A trienic compound was identified by GC/MS and NMR spectroscopy (see Section 5).

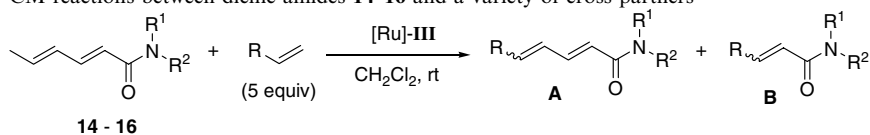
When the dienic *N,N*-diisopropylamide **14** was utilized in the CM reaction with oct-1-ene (5 equiv.) in the presence of 10 mol% of [Ru]-**III** at rt for 24 h, the cross-metathesis product **17** was isolated in 36% yield in a 28/1 (*E,E*)/(*E,Z*) ratio and no trace of mono-olefin of type **B** was detected (Table 2, entry 1). Under the same conditions (oct-1-ene, 5 equiv.; [Ru]-**III** 10 mol%, CH₂Cl₂, rt, 24 h), the dienic Weinreb amide **15** was transformed into the dienic amide **18** [(*E,E*)/(*E,Z*) = 6/1] and into the corresponding mono-olefin of type **B** in 65% yield in a 3.5/1 A/B ratio (Table 2, entry 2). In order to decrease the formation of the mono-olefin of type **B**, the amount of the [Ru]-**III** catalyst was decreased to 5 mol%. After 24 h, the dienic compound **18** and the mono-olefin of type **B** were obtained in 60% yield in a 5/1 ratio, and under these conditions the (*E,E*)-**18**/(*E,Z*)-**18** ratio was 29/1 (Table 2, entry 3). It is worth noting that, when the reaction was stopped after 1 h, the (*E,E*)-**18** and (*E,Z*)-**18** ratio was increased to 49/1, the isolated yield of **18** along with the corresponding mono-olefin of type **B** was 64%, and the A/B ratio was interestingly increased to 13/1 (Table 2, entry 4). Thus, the increase of the **18A**/**18B** ratio by decreasing the reaction time seems to indicate that compound **18B** would be formed from the putative kinetic diene **18A**, which would imply an insertion of the [Ru] in its α,β -double bond. To ver-

ify this hypothesis, compound **18A** was treated with catalyst [Ru]-**III** (5 mol%) in the presence of 5 equiv. of oct-1-ene (Scheme 3) [15]. After 4.5 h a negligible amount of monoolefin **18B** was formed, the main product of the reaction being dimer **C**. After 24 h, the amount of dimer **C** increased without significant augmentation of the monoolefin **18B**. However, at this stage, partial decomposition of **18A** was ascertained. An additional amount of 5 mol% of catalyst [Ru]-**III** was subsequently added and after 3 days of stirring diene **18A** was almost totally decomposed and **18B** was not formed anymore. So it seems that the decrease of the **18A**/**18B** ratio by increasing the reaction time could be due to the decomposition of diene **18A**. Furthermore, when **18A** was stirred alone with catalyst [Ru]-**III** (10 mol%) for 24 h, only traces of **18B** were detected and no significant decomposition of **18A** occurred. However, as the formation of dimer **C** was noticed, it seems that catalyst [Ru]-**III** slowly inserts in the γ,δ -double bond of diene **18A**. According to these results, it seems that the main active species is intermediate **Z** which principally inserts in the γ,δ -double bond of amide **15** to give **18A**, and to a minor extent in the α,β -double bond of **15** to give **18B**. Finally, by decreasing the amount of catalyst [Ru]-**III** and the reaction time, the chemoselectivity can be improved.

When allyl bromide was involved in the CM reaction with Weinreb amide **15**, for 14 h at rt, with 5 mol% of [Ru]-**III**, the corresponding dienic amide **19** was formed in 39% yield with a very good (*E,E*)/(*E,Z*) ratio of 19/1. Interestingly, no trace of mono-olefin of type **B** was detected (Table 2, entry 5). In the case of the CM reaction between Weinreb amide **15** and (*Z*)-1,4-dichloro-2-butene the best results were obtained when the reaction was carried out with 5 mol% of [Ru]-**III**, at rt for 30 min. Under these conditions, compound **20** was isolated in 59% yield [(*E,E*)/(*E,Z*) = 32/1] with a A/B ratio of 13/1 (Table 2, entries 6 and 7). When amide **15** was involved in the cross-metathesis reaction with 1-acetoxy-but-3-ene, allyltrimethylsilane, and (*Z*)-1,4-diacetoxy-but-2-ene, the dienic cross-metathesis products were isolated as a mixture of (*E,E*)- and (*E,Z*)-stereoisomers. In the case of the CM between amide **15** and 1-acetoxy-but-3-ene (24 h, 10 mol% [Ru]-**III**), compound **21** was obtained along with the corresponding mono-olefin of type **B** in a 24/1 ratio and 46% overall yield. With allyltrimethylsilane, the cross-product **22** was isolated in 45% yield with a (*E,E*)-**22**/(*E,Z*)-**22** ratio of 4/1 and **23** was formed in 42% yield with a (*E,E*)-**23**/(*E,Z*)-**23** ratio of 5/1 when (*Z*)-1,4-diacetoxy-but-2-ene was used in the CM reaction with amide **15** (Table 2, entries 8–10). Interestingly in these three latter cases, the formation of **B** was probably kinetically decreased due to either a complexation of the ruthenium complex with participation of carbonyl group of the acetate as previously reported [13,16] (Scheme 4; Table 2, entries 8 and 10) or by steric hindrance of the olefin partner (Table 2, entry 9).

In the case of more hindered dienic amides such as camphorsultamide **16**, a good chemoselectivity was

Table 2

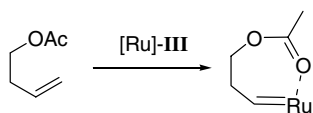
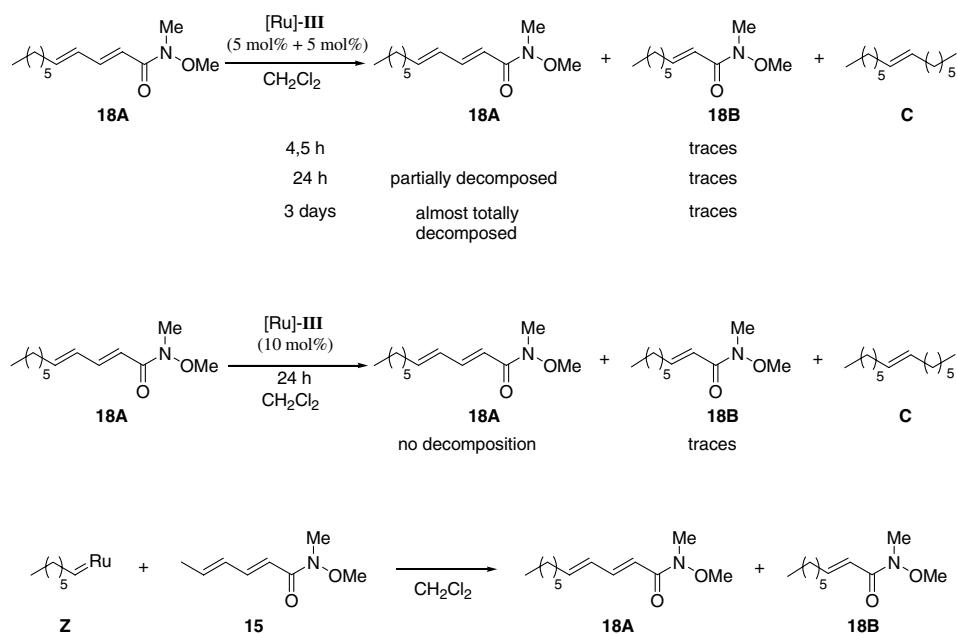
CM reactions between dienic amides **14–16** and a variety of cross-partners

Entry	Amide	R-CH=CH ₂	t (h)	[Ru]-III mol %	diene A (E,E)/(E,Z)	Ratio A/B yield ^a	
1			24	10		— ^c 36%	
2			24	10		28/1 ^b 6/1	3.5/1 65%
3	15		24	5	18	29/1	5/1 60%
4	15		1	5	18	49/1	13/1 64%
5	15		14	5		19/1	— ^c 39%
6	15		24	10		18/1	2/1 70%
7	15		0.5	5	20	32/1	13/1 59%
8	15		24	10		7/1	24/1 46%
9	15		24	10		4/1 ^b	— ^c 45%
10	15		24	10		5/1	— ^c 42%
11			24	10		10/1	— ^c 61%
12	16		24	10		9/1	— ^c 40%
13	16		24	10		5/1	— ^c 40%

(continued on next page)

Table 2 (continued)

Entry	Amide	R	t (h)	[Ru]-III mol %	diene A (E,E)/(E,Z)	Ratio A/B yield ^a
14	16		24	10		— ^c 57%

^a Global yield of the mixture of **A** and **B**.^b (E,E) and (E,Z) isomers were separated.^c **B** was not detected by GC/MS and ¹H NMR.

observed as the desired cross-metathesis products of type **A** were isolated in moderate to good yields with no trace of mono-olefin of type **B** (Table 2, entries 11–14). Indeed, when a reaction mixture consisting of camphorsultamide **16**, oct-1-ene (5 equiv.), and catalyst [Ru]-III (10 mol%) was stirred in CH₂Cl₂ at rt for 24 h, the cross-metathesis product **24** was isolated in 61% yield with a 10/1 (E,E)-**24**/(E,Z)-**24** ratio (Table 2, entry 11). When the 1-acetoxybut-3-ene and the (Z)-1,4-diacetoxybut-2-ene were involved in the CM reaction with camphorsultamide **16**,

dienic amides **25** and **26** were isolated in similar yields (40%) with a (E,E)/(E,Z) ratio of 9/1 and 5/1, respectively (Table 2, entries 12 and 13). Finally, when the (Z)-1,4-dichlorobut-2-ene was utilized in the CM with **16**, diene **27** was isolated in 57% yield with an (E,E)-**27**/(E,Z)-**27** ratio of 16/1 (Table 2, entry 14).

4. Conclusion

Cross-metathesis reactions between dienic amides and a variety of olefins turned out to be highly chemoselective at the γ,δ -double bond producing mostly the corresponding dienes of type **A**. When a mixture of diene of type **A** and mono-olefin of type **B** is obtained, a decrease in the amount of catalyst and/or the reaction time can result in higher chemoselectivity in favor of **A**. This method allows

the formation of functionalized dienic amides under mild conditions. As the Weinreb amides **18–23** can be transformed into aldehydes, ketones or carboxylic acids and as the optically active amides **24–27** can be involved in diastereoselective reactions, the CM reaction of dienic amides provides a valuable alternative for the preparation of useful intermediates.

5. Experimental

5.1. General comments

Flash chromatography was performed with Merck Geduran Si60 silica gel (40–63 μm). Infrared (IR) spectra were recorded on a Bruker TENSOR™ 27 (IRFT), wavenumbers are indicated in cm^{-1} . ^1H NMR spectra were recorded on a Bruker AVANCE 400 at 400 MHz and data are reported as follows: chemical shift in ppm from tetramethylsilane as an internal standard, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet or overlap of non-equivalent resonances), integration. ^{13}C NMR spectra were recorded on a Bruker AVANCE 400 at 100 MHz and data are reported as follows: chemical shift in ppm from tetramethylsilane with the solvent as an internal indicator (CDCl_3 δ : 77.0 ppm). Mass spectra with electronic impact (MS-EI) were recorded from a Hewlett-Packard tandem 5890 A GC (12 m capillary column) – 5971 MS (70 eV). High resolution mass spectra (HRMS) were performed by the Centre de Spectrochimie de l'École Normale Supérieure Ulm (Paris).

5.2. General procedure for CM reactions between methyl sorbate and olefin cross-partners

To a solution of methyl sorbate (150 mg, 1.2 mmol, 1 equiv.) and olefin partner (6 mmol, 5 equiv.) in CH_2Cl_2 ($c = 0.1\text{--}0.2\text{ M}$) was added the Grubbs–Hoveyda catalyst [Ru]-III (18.5 mg, 0.030 mmol, 0.025 equiv.). After 24 h stirring, another portion of Grubbs–Hoveyda catalyst [Ru]-III was added (0.025 equiv.). After 24 h, silica was added to the reaction mixture and after evaporation of the solvent, the pad of silica was loaded on top of a silica gel column and a flash chromatography purification was achieved.

5.2.1. Methyl (2E,4E)-undeca-2,4-dienoate (**6**)

Purification on silica gel (Et_2O /Petroleum Ether: 5/95 to 10/90) afforded **6** in 68% yield as a mixture of dienes (*E,E*)-**6**/*E,Z*)-**6** (10/1), contaminated by the mono-olefin of type **B** (**A/B**: 2.5/1).

IR (neat): 1724, 1656, 1436 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ : 7.27 (dd, $J = 15.4, 10.2$ Hz, 1H), 6.22–6.08 (m, 2H), 5.78 (d, $J = 15.4$ Hz, 1H), 3.73 (s, 3H), 2.23–2.12 (m, 2H), 1.50–1.37 (m, 2H), 1.36–1.20 (m, 6H), 0.88 (t, $J = 7.0$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ : 167.2, 149.9, 140.4, 138.7, 120.6, 51.3, 32.1, 31.4, 29.6, 28.7,

22.4, 13.9; Mass (EI) m/z : 196 (M^+ , 18), 165 ($\text{M} - \text{OMe}^+$, 16), 111 ($\text{M} - \text{Hex}^+$, 100), 81 (49).

5.2.2. Methyl (2E,4E)-6-(trimethylsilyl)hexa-2,4-dienoate (**7**)

Purification on silica gel (Et_2O /Petroleum Ether: 5/95 to 10/90) afforded **7** in 71% yield as a mixture of (*E,E*)-**7**/*E,Z*)-**7** (5/1), contaminated by mono-olefin of type **B** (**A/B**: 6/1).

IR (neat): 1658, 1465, 1453 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ : 7.27 (dd, $J = 15.6, 11.0$ Hz, 1H), 6.18 (dt, $J = 15.0, 8.5$ Hz, 1H), 6.04 (dd, $J = 15.6, 11.0$ Hz, 1H), 5.71 (d, $J = 15.0$ Hz, 1H), 3.73 (s, 3H), 1.68 (d, $J = 8.5$ Hz, 2H), 0.02 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3) δ : 168.1, 145.9, 143.0, 126.9, 116.5, 51.3, 25.2, –1.9 (3C); Mass (EI) m/z : 198 (M^+ , 9), 167 ($\text{M} - \text{OMe}^+$, 6), 73 (TMS^+ , 100), 66 (55).

5.2.3. Methyl (2E,4E)-5-phenylpenta-2,4-dienoate (**8**)

Purification on silica gel (Et_2O /Petroleum Ether: 5/95 to 10/90) afforded (*E,E*)-**8** in 35% yield, contaminated by methyl 7-phenylhexa-2,4,6-trienoate (**A**/triene: 4/1).

IR (neat): 1707, 1624, 1491, 1433 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ : 7.50–7.40 (m, 3H), 7.39–7.28 (m, 3H), 6.83–6.95 (m, 2H), 6.00 (d, $J = 15.3$ Hz, 1H), 3.77 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ : 167.5, 144.8, 140.5, 135.9, 129.1, 128.8 (2C), 127.2 (2C), 126.1, 120.8, 51.5; Mass (EI) m/z : 188 (M^+ , 25), 157 ($\text{M} - \text{OMe}^+$, 18), 129 ($\text{M} - \text{CO}_2\text{Me}^+$, 100), 128 (75), 77 (Ph^+ , 8); HRMS (ESI): calculated for $\text{C}_{12}\text{H}_{12}\text{O}_2\text{Na}$ [$\text{M} + \text{Na}$] $^+$: 211.0739, found 211.0735.

5.2.4. Methyl (2E,4E)-6-(diethoxyphosphoryl)hexa-2,4-dienoate (**9**)

Excess of diethyl allylphosphonate was removed from the crude mixture under vacuum. Purification on silica gel (AcOEt /Petroleum Ether: 20/80 to 100/0) afforded **9** in 56% yield as a mixture of (*E,E*)/(*E,Z*) stereoisomers in a 5.5/1 ratio, along with mono-olefin of type **B** (**A/B** = 4/1), and contaminated by traces of methyl 8-(diethoxyphosphoryl)octa-2,4,6-trienoate detectable by GC/MS.

IR (neat): 3467, 1716, 1644, 1617, 1436 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ : 7.27 (dd, $J = 15.5, 11.0$ Hz, 1H), 6.32 (ddd, $J = 15.5, 11.0, 5.2$ Hz, 1H), 6.07 (m, 1H), 5.86 (dd, $J = 15.5, 2.4$ Hz, 1H), 4.11 (m, 4H), 3.74 (s, 3H), 2.72 (dd, $J = 23.1, 7.6$ Hz, 2H), 1.32 (t, $J = 7.1$ Hz, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ : 167.2, 143.7, 132.6, 131.7, 120.7, 62.1, 51.5, 31.2, 16.4; Mass (EI) m/z : 262 (M^+ , 16), 247 ($\text{M} - \text{OMe}^+$, 10), 124 (100), 109 (32); HRMS (CI^+ , NH_3): calculated for $\text{C}_{11}\text{H}_{20}\text{O}_5\text{P}$ [$\text{M} + \text{H}$] $^+$: 263.1048, found 263.1044.

5.2.5. Methyl (2E,4E)-6-bromohexa-2,4-dienoate (**10**)

Purification on silica gel (AcOEt /Petroleum Ether: 2/98 to 5/95) afforded **10** in 48% yield as a mixture of (*E,E*)/(*E,Z*) stereoisomers in a 32/1 ratio, contaminated by methyl 8-bromoocta-2,4,6-trienoate (**A**/Triene = 6/1).

IR (neat): 1713, 1643, 1614, 1434, cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ : 7.19 (dd, $J = 15.4, 11.0$ Hz, 1H), 6.32 (dd, $J = 15.0, 11.0$ Hz, 1H), 6.18 (dt, $J = 15.0, 7.5$ Hz, 1H), 5.87 (d, $J = 15.4$ Hz, 1H), 3.97 (d, $J = 7.5$ Hz, 2H), 3.69 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ : 166.9, 142.8, 136.7, 131.9, 122.8, 51.8, 31.2; Mass (EI) m/z : 206 (M^+ , ^{81}Br , 15), 204 (M^+ , ^{79}Br , 15), 175 (M^+ , $^{81}\text{Br} - \text{OMe}^+$, 15), 173 (M^+ , $^{79}\text{Br} - \text{OMe}^+$, 15), 125 (100), 93 (57), 66 (50).

5.2.6. Methyl (2E,4E)-6-(4-methylphenylsulfonamido)-hexa-2,4-dienoate (11)

Purification on silica gel (AcOEt/Hexanes: 5/95 to 40/60) afforded **11** in 45% yield as a mixture of (*E,E*)/(*E,Z*) stereoisomers in a 11.5/1 ratio, contaminated by mono-olefin of type **B** (A/B = 4/1) and also by traces of *p*-toluenesulfonamide.

IR (neat): 3238, 1694, 1650, 1620, 1597, 1438 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ : 7.66 (d, $J = 8.3$ Hz, 2H), 7.21 (d, $J = 8.3$ Hz, 2H), 7.03 (dd, $J = 15.4, 11.0$ Hz, 1H), 6.12 (dd, $J = 15.2, 11.1$ Hz, 1H), 5.82 (dt, $J = 15.2, 5.5$ Hz, 1H), 5.68 (d, $J = 15.4$ Hz, 1H), 5.36 (br s, NH), 3.63 (s, 3H), 3.58 (m, 2H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ : 167.3, 143.5, 143.3, 139.4, 136.9, 129.9 (2C), 127.1 (2C), 126.3, 121.4, 51.6, 44.6, 21.5; Mass (EI) m/z : 295 (M^+ , 1), 264 ($\text{M} - \text{OMe}^+$, 5), 155 (19), 140 (44), 111 (100), 108 (84), 91 (77), 80 (61); HRMS (CI^+ , NH_3): calculated for $\text{C}_{14}\text{H}_{21}\text{N}_2\text{O}_4\text{S}$ [$\text{M} + \text{NH}_4$] $^+$: 313.1222, found 313.1216.

5.2.7. Methyl (2E,4E)-6-oxohepta-2,4-dienoate (12)

Purification on silica gel (AcOEt/Hexanes: 3/97 to 20/80) afforded (*E,E*)-**12** as a single stereoisomer in 13% yield, contaminated by dimethyl octa-2,4,6-trienedioate (A/Triene: 6/1).

IR (neat): 1717, 1660, 1627, 1599, 1436 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ : 7.27 (dd, $J = 15.4, 11.5$ Hz, 1H), 7.07 (dd, $J = 15.5, 11.5$ Hz, 1H), 6.36 (d, $J = 15.5$ Hz, 1H), 6.18 (d, $J = 15.4$ Hz, 1H), 3.72 (s, 3H), 2.26 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ : 197.8, 166.2, 141.5, 139.1, 136.3, 128.6, 52.0, 27.9; Mass (EI) m/z : 154 (M^+ , 46), 139 ($\text{M} - \text{Me}^+$, 100), 123 ($\text{M} - \text{OMe}^+$, 20), 111 (76), 95 (37).

5.2.8. tert-Butyl methyl (2E,4E)-hexa-2,4-dienoate (13)

Purification on silica gel (AcOEt/Hexanes: 0/100 to 3/97) afforded **13** in 30% yield as a mixture of (*E,E*)/(*E,Z*) stereoisomers in a 50/1 ratio, contaminated by methyl 7-phenyl-hexa-2,4,6-trienoate (A/Triene: 9/1).

IR (neat): 1699, 1609 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ : 7.24 (dd, $J = 15.0, 11.5$ Hz, 1H), 7.14 (dd, $J = 14.8, 11.5$ Hz, 1H), 6.10 (d, $J = 15.0$ Hz, 1H), 6.06 (d, $J = 14.8$ Hz, 1H), 3.71 (s, 3H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3) δ : 166.5, 165.2, 141.3, 139.7, 130.6, 127.3, 81.2, 51.9, 28.1 (3C); Mass (EI) m/z : 213 ($\text{M} + \text{H}^+$, 1), 212 (M^+ , 1), 181 ($\text{M} - \text{OMe}^+$, 20), 157 (100), 139 ($\text{M} - \text{OtBu}^+$, 77), 111 (54), 57 (67); HRMS (CI^+ , NH_3): calculated for $\text{C}_{11}\text{H}_{17}\text{O}_4$ [$\text{M} + \text{H}$] $^+$: 213.1127, found 213.1121.

5.3. General procedure for CM reactions with dienic amides

To a solution of sorbamide (1 mmol, 1 equiv.) and the olefin partner (5 mmol, 5 equiv.) in CH_2Cl_2 ($c = 0.1$ – 0.2 M) was added Grubbs–Hoveyda catalyst [Ru]-**III** (64 mg, 0.10 mmol, 0.1 equiv.). The solution was stirred for 24 h and silica was then added to the reaction mixture. After evaporation of the solvent, the pad of silica was loaded on top of a silica gel column and a flash chromatography purification was achieved.

5.3.1. (2E,4E)-N,N-Diisopropylundeca-2,4-dienamide (17)

Purification on silica gel (AcOEt/Petroleum Ether: 15/85 to 20/80) afforded **17** in 36% yield as a mixture of the dienes (*E,E*)-**17**/(*E,Z*)-**17** (28/1).

IR (neat): 1659, 1630, 1606, 1460, 1411, 1376 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ : 7.19 (dd, $J = 14.6, 10.5$ Hz, 1H), 6.09 (d, $J = 14.6$ Hz, 1H), 6.07 (dd, $J = 15.2, 10.5$ Hz, 1H), 6.02 (dt, $J = 15.2, 6.9$ Hz, 1H), 4.02 (m, 1H), 3.79 (m, 1H), 2.14 (q_{app}, $J = 7.0$ Hz, 2H), 1.50–1.10 (m, 20H), 0.88 (t, $J = 7.0$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ : 166.5, 142.1, 141.7, 128.9, 121.3, 47.6 (br), 45.8 (br), 32.9, 31.6, 28.8 (2C), 22.6, 21.5 (2C, br), 20.8 (2C, br), 14.1; Mass (EI) m/z : 265 (M^+ , 36), 250 ($\text{M} - \text{Me}^+$, 13), 222 ($\text{M} - \text{Pr}^+$, 26), 208 ($\text{M} - \text{Bu}^+$, 22), 194 ($\text{M} - \text{Pent}^+$, 9), 180 ($\text{M} - \text{Hex}^+$, 36), 165 ($\text{M} - \text{NiPr}_2^+$, 100), 100 (NiPr_2^+ , 54), 95 (95), 81 (61).

5.3.2. (2E,4E)-N-Methoxy-N-methylundeca-2,4-dienamide (18)

Only 5 mol% of catalyst [Ru]-**III** were used and the reaction was stopped after 1 h. Purification on silica gel (AcOEt/Petroleum Ether: 20/80), afforded **18** in 64% yield as a mixture of the dienes (*E,E*)-**18**/(*E,Z*)-**18** (49/1), contaminated by mono-olefin of type **B** (A/B: 13/1). When the reaction was stirred for 24 h, a 5/1 A/B ratio was observed.

IR (neat): 1659, 1630, 1606, 1460, 1411, 1376 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ : 7.31 (dd, $J = 15.2, 10.6$ Hz, 1H), 6.37 (d, $J = 15.2$ Hz, 1H), 6.23 (dd, $J = 15.1, 10.7$ Hz, 1H), 6.12 (dt, $J = 15.1, 6.5$ Hz, 1H), 3.70 (s, 3H), 3.25 (s, 3H), 2.16 (q_{app}, $J = 7.0$ Hz, 2H), 1.50–1.37 (m, 2H), 1.36–1.20 (m, 6H), 0.88 (t, $J = 7.0$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ : 167.5, 144.1, 144.0, 128.7, 116.8, 61.7, 33.0, 32.5, 31.6, 28.9, 28.7, 22.6, 14.1; Mass (EI) m/z : 225 (M^+ , 2), 165 ($\text{M}^+ - \text{N}(\text{OMe})\text{Me}$, 100), 81 (85); HRMS (ESI): calculated for $\text{C}_{13}\text{H}_{23}\text{NO}_2\text{Na}$ [$\text{M} + \text{Na}$] $^+$: 248.1634, found 248.1626.

5.3.3. (2E,4E)-6-Bromo-N-methoxy-N-methylhexa-2,4-dienamide (19)

Purification on silica gel (AcOEt/Petroleum Ether: 10/90 to 20/80) afforded **19** in 39% yield as a mixture of (*E,E*)/(*E,Z*) stereoisomers in a 19/1 ratio.

IR (neat): 1655, 1625, 1605, 1414, 1380 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ : 7.30 (dd, $J = 15.2, 11.0$ Hz, 1H), 6.54 (d, $J = 15.2$ Hz, 1H), 6.46 (dd, $J = 15.0, 11.0$ Hz, 1H), 6.24

(dt, $J = 15.0, 7.8$ Hz, 1H), 4.05 (d, $J = 7.8$ Hz, 1H), 3.71 (s, 3H), 3.26 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ : 166.5, 141.3, 135.8, 132.7, 121.0, 61.9, 32.4, 31.7; Mass (EI) m/z : 235 ($\text{M}^+ - ^{81}\text{Br}$, 7), 233 ($\text{M}^+ - ^{79}\text{Br}$, 8), 176 (7), 175 ($\text{M}^+ - ^{81}\text{Br} - \text{N}(\text{OMe})\text{Me}$, 99), 173 ($\text{M}^+ - ^{79}\text{Br} - \text{N}(\text{OMe})\text{Me}$, 100), 154 (64), 94 (63), 66 (79); HRMS (CI^+ , NH_3): calculated for $\text{C}_8\text{H}_{13}^{79}\text{BrNO}_2$ [$\text{M} + \text{H}$] $^+$: 234.0130, found 234.0134, calculated for $\text{C}_8\text{H}_{13}^{81}\text{BrNO}_2$ [$\text{M} + \text{H}$] $^+$: 236.0110, found 236.0114.

5.3.4. (2E,4E)-N-Methoxy,N-methyl-6-chlorohexa-2,4-dienamide (20)

Only 5 mol% of catalyst [Ru]-III were used and the reaction was stopped after 30 min. Purification on silica gel (AcOEt/Petroleum Ether: 20/80) afforded **20** in 59% yield as a mixture of the dienes (*E,E*)-**20**/*E,Z*-**20** (32/1), contaminated by the mono-olefin of type **B** (**A/B**: 13/1). When the reaction was stirred for 24 h with 10 mol% of catalyst [Ru]-III a 2/1 **A/B** ratio was observed.

IR (neat): 1656, 1628, 1606, 1413, 1378 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ : 7.26 (dd, $J = 15.2, 11.0$ Hz, 1H), 6.49 (d, $J = 15.4$ Hz, 1H), 6.44 (dd, $J = 15.0, 11.0$ Hz, 1H), 6.12 (dt, $J = 15.0, 6.9$ Hz, 1H), 4.10 (dd, $J = 6.9, 1.0$ Hz, 2H), 3.66 (s, 3H), 3.21 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ : 166.4, 141.3, 135.4, 131.9, 120.7, 61.7, 44.0, 32.3; Mass (EI) m/z : 191 ($\text{M}^+ - ^{37}\text{Cl}$, 2), 189 ($\text{M}^+ - ^{35}\text{Cl}$, 6), 154 ($\text{M} - \text{Cl}^+$, 20), 131 ($\text{M}^+ - ^{37}\text{Cl} - \text{N}(\text{OMe})\text{Me}$, 34), 129 ($\text{M}^+ - ^{35}\text{Cl} - \text{N}(\text{OMe})\text{Me}$, 100); HRMS (ESI): calculated for $\text{C}_8\text{H}_{13}\text{NO}_2^{35}\text{Cl}$ [$\text{M} + \text{H}$] $^+$: 190.0638, found 190.0635.

5.3.5. (2E,4E)-N-Methoxy,N-methyl-7-acetoxyhepta-2,4-dienamide (21)

Purification on silica gel (AcOEt/Petroleum Ether: 35/65), afforded **21** in 46% yield as a mixture of the dienes (*E,E*)-**21**/*E,Z*-**21** (7/1), contaminated by mono-olefin of type **B** (**A/B**: 24/1).

IR (neat): 1735, 1655, 1628, 1605, 1414, 1379 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ : 7.24 (dd, $J = 15.2, 11.0$ Hz, 1H), 6.38 (d, $J = 15.2$ Hz, 1H), 6.26 (dd, $J = 15.3, 11.2$ Hz, 1H), 6.02 (dt, $J = 15.3, 7.0$ Hz, 1H), 4.04 (t, $J = 6.7$ Hz, 2H), 3.66 (s, 3H), 3.20 (s, 3H), 2.46 (q_{app} , $J = 6.7$ Hz, 2H), 2.00 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ : 170.7, 166.8, 142.7, 137.6, 130.8, 118.0, 62.8, 61.5, 32.1, 31.9, 20.6; Mass (EI) m/z : 227 (M^+ , 8), 184 ($\text{M} - \text{Ac}^+$, 1), 167 ($\text{M}^+ - \text{N}(\text{OMe})\text{Me}$, 15), 107 (100); HRMS (ESI): calculated for $\text{C}_{11}\text{H}_{18}\text{NO}_4$ [$\text{M} + \text{H}$] $^+$: 228.1240, found 228.1236.

5.3.6. (2E,4E)-N-Methoxy,N-methyl-6-(trimethylsilyl)-hexa-2,4-dienamide (22)

Purification on silica gel (AcOEt/Petroleum Ether: 20/80) afforded (*E,E*)-**22** in 37% yield and (*E,Z*)-**22** in 8% yield ((*E,E*)/(*E,Z*): 4/1).

IR (neat): 1664, 1640, 1621, 1462, 1416, 1381 cm^{-1} ; Major isomer (*E,E*)-**22**: ^1H NMR (400 MHz, CDCl_3) δ : 7.31 (dd, $J = 15.1, 10.5$ Hz, 1H), 6.29 (d, $J = 15.4$ Hz, 1H), 6.17 (dt, $J = 14.9, 8.0$ Hz, 1H), 6.09 (dd, $J = 14.9,$

10.5 Hz, 1H), 3.70 (s, 3H), 3.24 (s, 3H), 1.67 (d, $J = 7.9$ Hz, 2H), 0.02 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3) δ : 167.9, 144.5, 142.0, 127.4, 114.7, 61.7, 32.5, 25.1, -1.9 (3C); Minor isomer (*E,Z*)-**22**: ^1H NMR (400 MHz, CDCl_3) δ : 7.31 (dd, $J = 15.0, 11.6$ Hz, 1H), 6.42 (d, $J = 15.0$ Hz, 1H), 6.12 (dd, $J = 11.6, 10.8$ Hz, 1H), 6.09 (dt, $J = 10.8, 9.2$, 1H), 3.71 (s, 3H), 3.25 (s, 3H), 1.85 (dd, $J = 9.2, 1.2$ Hz, 2H), 0.02 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3) δ : 167.7, 138.7, 138.3, 124.7, 117.3, 61.7, 32.4, 21.0, -1.8 (3C); Mass (EI) m/z : 227 (M^+ , 7), 212 ($\text{M} - \text{Me}^+$, 2), 196 ($\text{M} - \text{OMe}^+$, 2), 180 (1), 167 ($\text{M}^+ - \text{N}(\text{OMe})\text{Me}$, 34), 151 (44), 109 (2), 73 (TMS^+ , 100), 66 (9), 59 (5); HRMS (ESI): calculated for $\text{C}_{11}\text{H}_{21}\text{NO}_2\text{SiNa}$ [$\text{M} + \text{Na}$] $^+$: 250.1247, found 250.1239.

5.3.7. (2E,4E)-N-Methoxy,N-methyl-6-acetoxyhexa-2,4-dienamide (23)

Purification on silica gel (AcOEt/Petroleum Ether: 35/65) afforded **23** in 42% yield as a mixture of the dienes (*E,E*)-**23**/*E,Z*-**23** (5/1).

IR (neat): 1737, 1659, 1632, 1607, 1417, 1380 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ : 7.29 (dd, $J = 15.2, 11.2$ Hz, 1H), 6.51 (d, $J = 15.2$ Hz, 1H), 6.24 (dd, $J = 15.3, 11.0$ Hz, 1H), 6.11 (dt, $J = 15.3, 5.8$ Hz, 1H), 4.65 (d, $J = 5.8$ Hz, 2H), 3.70 (s, 3H), 3.24 (s, 3H), 2.08 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ : 170.2, 166.3, 141.5, 134.1, 130.8, 119.9, 63.5, 61.5, 32.0, 20.5; Mass (EI) m/z : 213 (M^+ , 4), 153 ($\text{M}^+ - \text{N}(\text{OMe})\text{Me}$, 20), 111 (100); HRMS (ESI): calculated for $\text{C}_{10}\text{H}_{16}\text{NO}_4$ [$\text{M} + \text{H}$] $^+$: 214.1079, found 214.1055.

5.3.8. N-[(2E,4E)-Undeca-2,4-dienoyl]-(S)-2,10-camphorsultam (24)

Purification on silica gel (AcOEt/Petroleum Ether: 10/90) afforded **24** in 61% yield as a mixture of the dienes (*E,E*)-**24**/*E,Z*-**24** (10/1).

M.p. 84–86 °C; $[\alpha]_D^{20} + 64.4$ (c 0.56, CHCl_3); IR (neat): 1682, 1638, 1607, 1456, 1412, 1392, 1328, 1271 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ : 7.35 (dd, $J = 14.8, 10.0$ Hz, 1H), 6.51 (d, $J = 14.8$ Hz, 1H), 6.24 (dd, $J = 15.2, 10.0$ Hz, 1H), 6.17 (dt, $J = 15.2, 6.2$ Hz, 1H), 3.93 (dd, $J = 7.5, 5.1$ Hz, 1H), 3.50 (d, $J = 13.8$ Hz, 1H), 3.46 (d, $J = 13.8$ Hz, 1H), 2.16 (q_{app} , $J = 6.5$ Hz, 2H), 2.16–2.04 (m, 2H), 1.96–1.84 (m, 3H), 1.60–2.40 (m, 10H), 1.16 (s, 3H), 0.96 (s, 3H), 0.85 (m, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ : 164.5, 146.6, 146.1, 128.6, 118.3, 65.1, 53.1, 48.4, 47.7, 44.6, 38.5, 33.0, 32.8, 31.6, 28.8, 28.5, 26.5, 22.5, 20.8, 19.8, 14.0; Mass (EI) m/z : 379 (M^+ , 12), 294 ($\text{M} - \text{Hex}^+$, 28), 165 ($\text{M} - \text{CO} - \text{Sultam}^+$, 100); HRMS (CI^+ , CH_4): calculated for $\text{C}_{21}\text{H}_{34}\text{NSO}_3$ [$\text{M} + \text{H}$] $^+$: 380.2259, found 380.2253.

5.3.9. N-[(2E,4E)-7-Acetoxyhepta-2,4-dienoyl]-(S)-2,10-camphorsultam (25)

Purification on silica gel (AcOEt/Petroleum Ether: 15/85) afforded **25** in 40% yield as a mixture of the dienes (*E,E*)-**25**/*E,Z*-**25** (9/1).

$[\alpha]_D^{20} + 82.1$ (c 0.39, CHCl_3); IR (neat): 1735, 1676, 1634, 1606, 1456, 1413, 1326, 1271 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.29 (dd, $J = 14.8, 11.0$ Hz, 1H), 6.51 (d, $J = 14.8$ Hz, 1H), 6.5 (dd, $J = 15.2, 11.0$ Hz, 1H), 6.15 (dt, $J = 15.2, 7.0$ Hz, 1H), 4.08 (t, $J = 6.5$ Hz, 2H), 3.88 (dd, $J = 7.4, 5.2$ Hz, 1H), 3.47 (d, $J = 13.8$ Hz, 1H), 3.39 (d, $J = 13.8$ Hz, 1H), 2.45 (q_{app}, $J = 6.5$ Hz, 2H), 2.12–2.02 (m, 2H), 1.98 (s, 3H) 1.92–1.77 (m, 3H), 1.37 (m, 1H), 1.30 (m, 1H), 1.11 (s, 3H), 0.92 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 170.3, 163.8, 143.7, 136.6, 130.1, 121.4, 65.0, 63.4, 52.9, 48.3, 47.6, 44.5, 38.3, 32.6, 32.1, 26.3, 20.8, 20.7, 19.7; Mass (EI) m/z : 381 (M^+ , 1), 338 ($\text{M} - \text{Ac}^+$, 1), 135 ($\text{M} - \text{AcOH} - \text{Sultam}^+$, 11), 107 (100); HRMS (Cl^+ , CH_4): calculated for $\text{C}_{19}\text{H}_{28}\text{NO}_5\text{S}$ [$\text{M} + \text{H}$] $^+$: 382.1688, found 382.1682.

5.3.10. *N*-[*(2E,4E)*-6-Acetoxyhexa-2,4-dienoyl]-(*S*)-2,10-camphorsultam (**26**)

Purification on silica gel (AcOEt/Petroleum Ether: 15/85) afforded **26** in 40% yield as a mixture of the dienes (*E, E*)-**26**/*(E, Z)*-**26** (5/1).

$[\alpha]_D^{20} + 44.9$ (c 0.90, CHCl_3); IR (neat, cm^{-1}): 1738, 1676, 1639, 1609, 1455, 1413, 1374, 1327, 1270 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.32 (dd, $J = 14.8, 11.1$ Hz, 1H), 6.62 (d, $J = 14.8$ Hz, 1H), 6.43 (dd, $J = 15.3, 11.2$ Hz, 1H), 6.15 (dt, $J = 15.3, 5.50$ Hz, 1H), 4.65 (d, $J = 5.5$ Hz, 2H), 3.91 (dd, $J = 7.4, 5.2$ Hz, 1H), 3.49 (d, $J = 13.8$ Hz, 1H), 3.42 (d, $J = 13.8$ Hz, 1H), 2.16–2.04 (m, 2H), 2.06 (s, 3H) 1.96–1.80 (m, 3H), 1.40 (m, 1H), 1.33 (m, 1H), 1.13 (s, 3H), 0.94 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 170.3, 163.8, 143.7, 136.6, 130.1, 121.4, 65.0, 63.4, 52.9, 48.3, 47.6, 44.5, 38.3, 32.6, 26.3, 20.7 (2C), 19.7; HRMS (Cl^+ , CH_4): calculated for $\text{C}_{18}\text{H}_{26}\text{NO}_5\text{S}$ [$\text{M} + \text{H}$] $^+$: 368.1532, found 368.1536.

5.3.11. *N*-[*(2E,4E)*-6-Chloro-hexa-2,4-dienoyl]-(*S*)-2,10-camphorsultam (**27**)

Purification on silica gel (AcOEt/Petroleum Ether: 10/90) afforded **27** in 57% yield as a mixture of the dienes (*E, E*)-**27**/*(E, Z)*-**27** (16/1).

$[\alpha]_D^{20} + 81.1$ (c 0.54, CHCl_3); IR (neat): 1675, 1634, 1607, 1456, 1413, 1373, 1328, 1271 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.34 (dd, $J = 14.8, 11.1$ Hz, 1H), 6.70 (d, $J = 14.8$ Hz, 1H), 6.17 (dd, $J = 14.9, 11.1$ Hz, 1H), 6.09 (dt, $J = 14.9, 6.9$ Hz, 1H), 4.13 (d, $J = 6.9$ Hz, 2H), 3.92 (dd, $J = 7.4, 5.3$ Hz, 1H), 3.50 (d, $J = 13.8$ Hz, 1H), 3.43 (d, $J = 13.8$ Hz, 1H), 2.16–2.04 (m, 2H), 1.96–1.80 (m, 3H), 1.41 (m, 1H), 1.34 (m, 1H), 1.15 (s, 3H), 0.95 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 163.7, 143.2, 137.5, 131.3, 122.1, 65.0, 53.0, 48.4, 47.7, 44.6, 43.7, 38.3, 32.7, 26.4, 20.7, 19.8;. HRMS (Cl^+ , CH_4): calculated for $\text{C}_{16}\text{H}_{23}\text{NO}_3\text{S}^{35}\text{Cl}$ [$\text{M} + \text{H}$] $^+$: 344.1087, found 344.1093.

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