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An efficient construction of bicyclic systems containing a seven-membered ring by tandem ring-closing metathesis reactions of dienynes

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Abstract

Various (5–7) and (6–7) bicyclic dienes bearing quaternary methyl group and ester functionality have been synthesized from acyclic dienynes by tandem ring-closing metathesis (RCM) reaction. Epoxidation of these conjugated dienes led to bicyclic vinyl oxiranes which undergo acid-catalyzed addition of alcohols to afford highly oxygenated compounds.

Keywords: Seven-membered ring; Dienynes; Tandem ring-closing metathesis

1. Introduction

Bridged and fused carbobicyclic systems containing medium-sized rings are widely found in biologically active natural products and development of new synthetic approach to these skeletons continues to be an important goal. In particular, the occurrence of fused ($n - 7$) bicyclic framework ($n = 5$, 6 or 7) is found in several natural products such as guanacastepenes, cyathane diterpenes and colchicine (Fig. 1). Different methods based on transition metal-mediated reactions have been developed for the synthesis of such systems [1]. Among them tandem ring-closing metathesis (RCM) reaction of dienynes, first described by Grubbs and co-workers, arose as one of the most exciting and powerful method [2,3].

Starting from acyclic precursor substrates such as **1** (Fig. 2), this cascade process generates complex polycyclic structures containing the 1,3-diene functionality. Thus, the triple bond positioned between the two olefins, acts as an olefin metathesis relay. When exposed to an RCM catalyst such as **2** [4a] or **3** [4b], **1** undergoes an initial RCM *enyne* metathesis reaction [5] followed by a second ring-closing α,ω-*diene* metathesis reaction to produce fused bicyclic [m.n.0] systems. In these highly efficient tandem processes, two rings are formed in a single step generally in high yields [6,7].

For these metatheses, multiple pathways and products are possible: the starting substrate can cyclize with either left-to-right or right-to-left endedness to give isomeric dienes **4** (via **A**) or **5** (via **B**) (Fig. 2). Therefore, site-selective initiation seems necessary for selectivity. This can be achieved by modifying the reactivity of the alkene moiety with steric and/or stereoelectronic factors. In general, the initial alkylidenation occurs on the more kinetically reactive alkene usually the unhindered terminal monosubstituted double bond [8].

In previous reports, we described the application of this technique for the preparation of polyoxygenated fused bicyclic systems containing medium-sized rings from carbohydrates [9] and for a concise formal synthesis of guanacastepene A [10]. In a recent work, we also described some effects of substituents on the multiple bonds on the tandem RCM of dienynes [11]. In an extension to this

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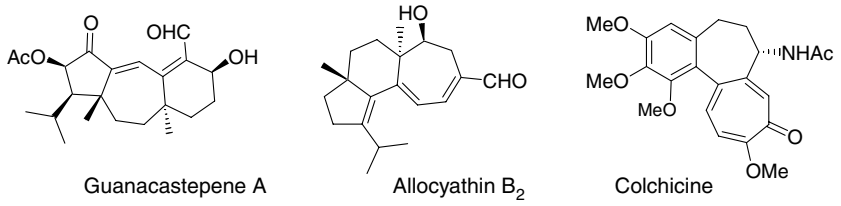


Fig. 1.

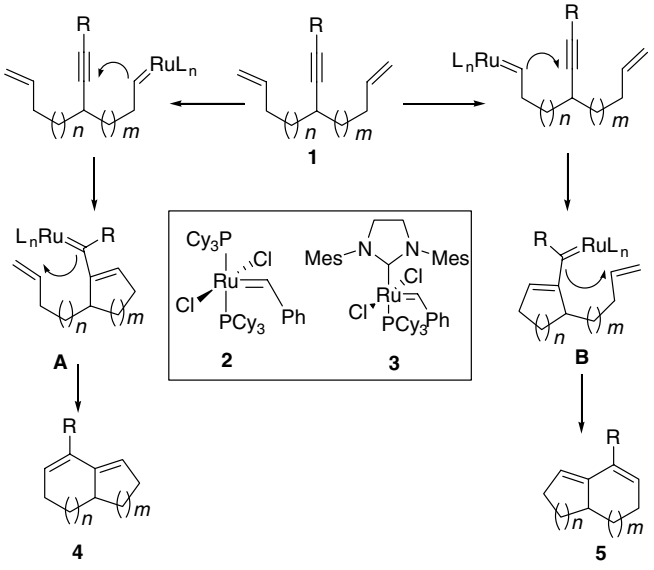


Fig. 2.

work, we report now the synthesis of bicyclic systems containing a seven-membered ring possessing both an angular methyl group and functionality able to further manipulation.

2. Results and discussion

Dienynes **6**–**11**, precursors to the (5–7) and (6–7) bicyclic ring systems, were prepared [12] and subjected to RCM reactions using catalyst **3** to afford bicycles **12**–**18** in high yield. The results, summarized in Table 1, merit some comments. First, in all cases, catalyst **2** was found to be ineffective and starting dienyne was recovered unchanged. Second, for these substrates, a high selectivity for the ring sizes as well as for ring functionalization has been achieved by steric differentiation between the two tethered alkenes. For dienynes **6** and **9**, initiation of the reaction occurs at the least substituted terminal alkene according to the left-to-right process leading to bicycles **12** and **16** in which the ester group is located on the five- and six-membered ring respectively (entries 1 and 4). By contrast, the highly oxygenated bicycle **13** (entry 2) is derived from reaction initiation at the alkene lacking substitution at the allylic position (right-to-left) bringing the ester group on the seven-membered ring. As expected, dienynes **10** and **11**, which possess symmetrically tethered alkenes, undergo the tandem process selectively to furnish [5.4.0] bicyclic derivatives **17** and **18** in good yield. The formation of the (6–6) bicycle **19** from **11** results from an initial isomerization of both double bonds before the RCM reaction [13].

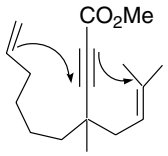
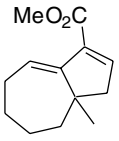
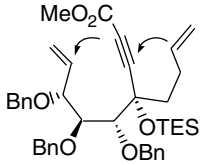
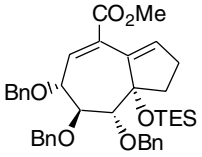
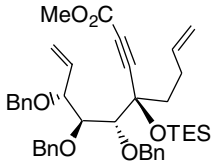
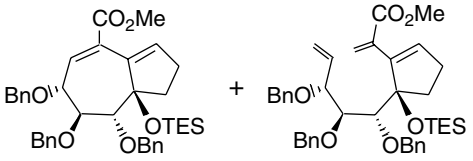
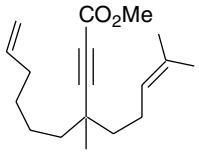
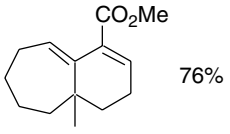
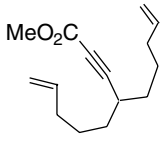
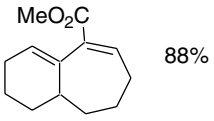
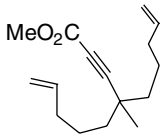
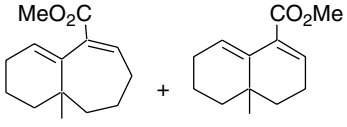
The stereochemistry of the triethylsilyl ether at the propargylic position in **7** and **8** has a notable effect on the tandem RCM (entries 2 and 3). Whereas dienyne **7** easily underwent the tandem process, its β-epimer **8** led to a mixture of bicycle **14** (55%) and the monocyclization product **15** (42%), even after a long reaction time. In this case the closure to the seven-membered ring is difficult as the resulting [5.3.0] bicycle **14** is thought to be destabilized due to the transannular ring strain arising from the β-OTES group (entry 3).

The synthesis of fused (7–7) bicycle **20** was next attempted starting from dienyne **21** (Scheme 1). Treatment of **21** with catalyst **3** in toluene at 80 °C produced a mixture of products. The main fraction, isolated by chromatography on silica gel, was found to be an inseparable mixture of the monocyclization product **22** and the starting dienyne (68%, 1:1 ratio). In the presence of ethylene, the RCM reaction of **21** afforded a mixture of bicycles **16** and **19** in 8% and 55%, respectively. These products are identical in all aspect to those obtained from dienynes **9** and **11**. In the same way, when the mixture of **21** and **22** obtained above was exposed to catalyst **3** in the presence of ethylene, compounds **16** and **19** were isolated in 75% (1:1 ratio). As for dienyne **11**, compounds **16** and **19** result from an initial isomerization of one or two double bonds before the RCM reaction [13]. All attempts to produce the desired [5.5.0] bicyclic product **20** from dienyne **21** failed. This result is the consequence of combined unfavorable factors: a hindered alkene, long tether chains and the presence of an ester group.

With these bicyclic compounds at hand, we became interested in the possibility of introducing further functionalities. In the course of our synthesis of guanacastepene A we found that epoxide **24** derived from bicyclic diene **23** underwent a regio- and stereoselective acid- catalyzed 1,6-addition of alcohols through S_N2' type process to give **25** (Scheme 2) [10,14].

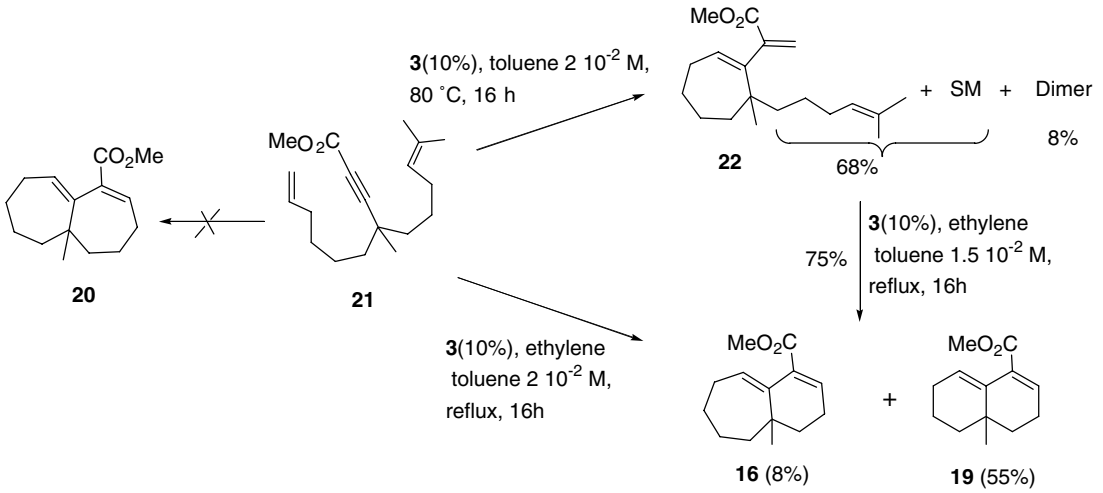
In order to explore the use of bicyclic compounds prepared above in the synthesis of natural products, we applied this two-step transformation to compounds **12** and **16**. The result is summarized in Scheme 3. Oxidation of these dienes with *m*-chloroperbenzoic acid (*m*-CPBA) occurred exclusively on the less deactivated double bond

Table 1
Tandem RCM of acyclic dienyenes[a]

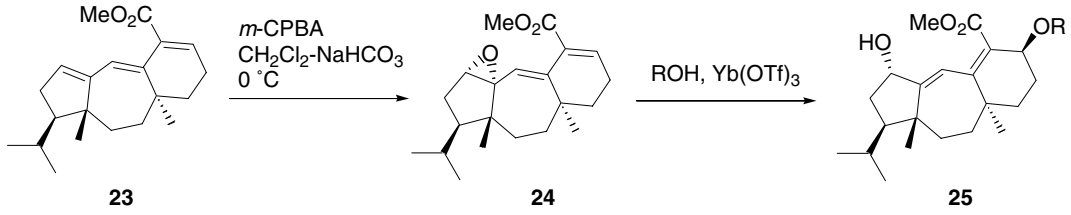
Entry	Dienyne	Catalyst (%), time	Product	Yield (%)
1	 **6**	**3** (5), 4 h	 **12**	92
2	 **7**	**3** (10), 2 h	 **13**	95
3	 **8**	**3** (10), 18 h	 **14** (55%) + **15** (42%)	
4	 **9**	**3** (5), 3 h	 76% **16**	76
5	 **10**	**3** (20), 3.5 h CH_2Cl_2 10^{-3} M	 88% **17**	88
6	 **11**	**3** (20), 3.5 h CH_2Cl_2 10^{-3} M	 **18** (80%) + **19** (9%)	

[a] All reactions were carried out using catalyst **3** in refluxing dichloromethane.

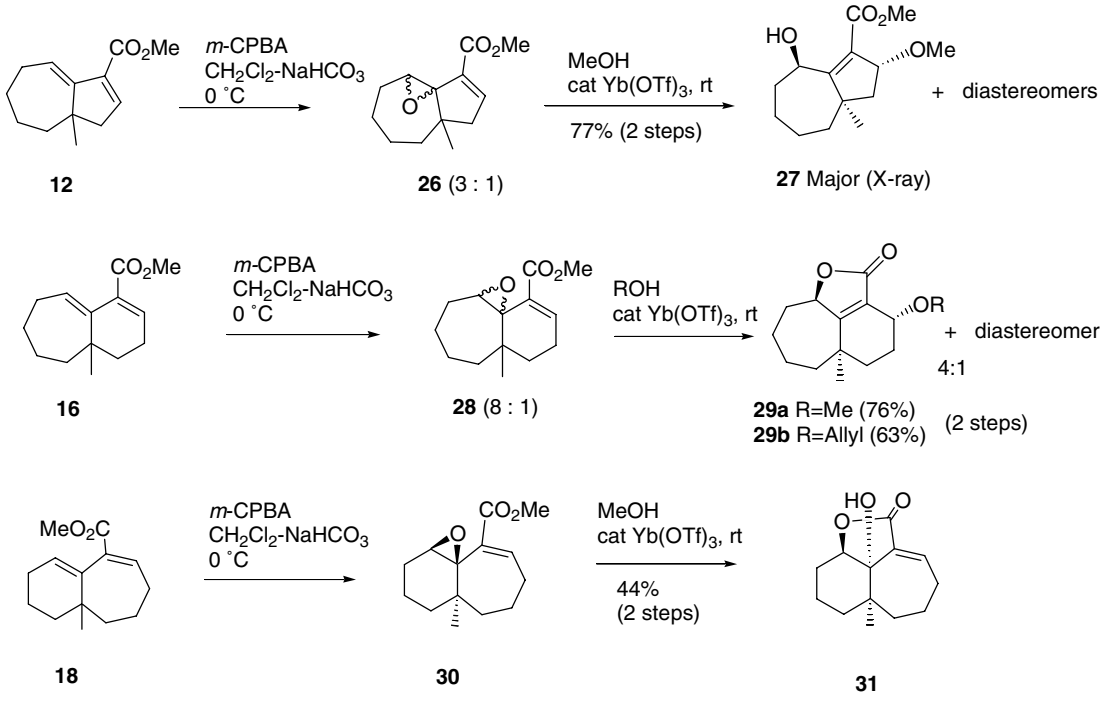
affording epoxides **26** and **28**, respectively. Whereas the stereoselectivity of epoxidation was high for the (7–6) bicyclic compound **16** (8:1 ratio), it is only moderate (3:1) for its (7–5) counterpart **12**. In each case epoxidation occurred preferably from the less hindered face, opposite to the angular methyl group, affording the anti stereoisomer as the major product. When these epoxides were treated with methanol in the presence of catalytic ytterbium triflate [$Yb(OTf)_3$],1,4-dioxygenated derivatives **27** and **29** were obtained respectively. In both cases, nucleophilic attack of alcohol occurred regioselectively on the double bond according to the S_N2' process. Thus, stirring the crude



Scheme 1.



Scheme 2.



Scheme 3.

epoxide **26** in methanol with $Yb(OTf)_3$ for 1 h led to a mixture of diastereoisomers from which alcohol **27** was isolated as the major component in 77% combined yield. The structure of **27** was unambiguously established by X-ray crystallographic analysis. By contrast, under the same conditions epoxide **28** gave lactone **29a** as a mixture of

two diastereoisomers (4:1) in 76% combined yield. This result could be easily understood in terms of rings strain: lactonization of **27** would lead to a highly strained tricyclic system. The stereochemistry of the major isomer **29a** was tentatively assigned by analogy with **27**. Similarly, lactone **29b** was obtained when allyl alcohol was used instead of methanol.

Under the same conditions, (7–6) bicyclic diene **18**, in which the ester group is located on the seven-membered ring, underwent the two-step transformation giving exclusively lactone **31**. This structure was assigned on the basis of analytical and spectroscopic data. In particular, the IR spectrum shows the presence of characteristic bands of hydroxyl and carbonyl groups at ν_{max} 3444 and 1724 cm^{-1}, respectively. ^{13}C and ^{1}H NMR spectra confirmed the disappearance of the methyl ester group and the ^{13}C NMR spectrum displays two carbon resonances at δ 84.1 (CH) and 78.3 (C) ppm which correspond to two sp^3 C–O bonds. The stereochemistry was tentatively assigned by analogy with **27**. For this substrate, opening of the intermediate epoxide **30** with methanol occurred only according to 1,2-process. Unexpectedly, instead methyl ether, only the free alcohol was isolated. The notable difference in reactivity of epoxide **30** compared to its isomer **28** is unclear at present. However, it is likely that the conformation adopted by the seven-membered ring in **30** slows down the S_N2' process.

3. Conclusion

In summary, we have shown that tandem ring-closing metathesis of dienynes is an efficient method for the construction of functionalized (5–7) and (6–7) bicyclic 1,3-dienes. In this reaction, selectivity of ring sizes was effectively controlled utilizing steric differentiation of terminal alkenes. Epoxidation of resulting dienes led to bicyclic vinyl oxiranes which undergo acid-catalyzed addition of alcohols to afford highly oxygenated products. Given the simplicity of this three-step transformation, this process holds out a promise to enhance the efficiency of the total synthesis of polycyclic natural products containing seven-membered rings.

4. Experimental

4.1. General

Infrared spectra were recorded as neat or in solutions in CCl_4. ^{1}H and ^{13}C NMR spectra were recorded on a 300 or 400 MHz instrument as solutions in $CDCl_3$, using residual protic solvent $CHCl_3$ ($\delta_H = 7.27$ ppm) or $CDCl_3$ ($\delta_C = 77.0$ ppm) as internal reference. Mass spectra were obtained either by electronic impact (EI) or chemical ionization with ammonia (CI, NH_3). All reactions were monitored by TLC carried out on 0.2 mm aluminium silica gel (60 F_{254}) pre-coated plates using UV light and 5% ethanolic phosphomolybdoic acid and heat as developing agent. Flash chromatography was performed on 40–63 μm (400–230 mesh) silica gel 60 with ethyl acetate (EtOAc)–petroleum ether (PE) (b.p. 40–60 °C) or cyclohexane as eluents.

4.2. Procedure for the metathesis reaction

4.2.1. Bicyclic diene 12

To a degassed solution of dienyne **6** (93 mg, 0.35 mmol) in dry methylene chloride (20 mL) was added catalyst **3** (14.5 mg, 5 mol%). The mixture was heated at reflux for 4 h. The solvent was removed under reduce pressure and the residue was purified by flash chromatography (ethyl acetate/petroleum ether 2.5/97.5) to give **9** (66 mg, 92%) as a colorless oil. ^{1}H NMR: $\delta = 6.79$ (br s, 1H), 6.52 (dd, $J = 8$, 4 Hz, 1H), 3.75 (s, 3H), 2.50–2.20 (m, 4H), 1.90–1.15 (m, 6H), 1.18 (s, 3H). ^{13}C NMR: $\delta = 165.1$ (C), 150.7 (C), 144.3 (CH_2), 123.5 (C), 51.3 (CH_3), 49.1 (CH_2), 46.8 (C), 40.2 (CH_2), 29.1 (CH_2), 28.0 (CH_2), 27.0 (CH_2), 24.2 (CH_3). IR (CCl_4): 1725 cm^{-1}. CI MS: NH_3 m/z 207 ($M^{+\cdot}+1$), 224 ($M^{+\cdot}+18$). HMRS (EI) m/z calc. for $C_{13}H_{18}O_2$, 206.13068, found: 206.13072%.

4.2.2. Bicyclic diene 13

Prepared from dienyne **7** (400 mg, 0.597 mmol) by the same procedure as for **12** using **3** (10 mol%) to give **13** (370 mg, 96%) as a colorless oil. R_f: 0.35 (EtOAc/cyclohexane 5:95). ^{1}H NMR: $\delta = 7.40$–7.22 (m, 15H), 6.93 (br s, 1H), 6.48 (br s, 1H), 5.02–4.72 (m, 6H), 3.83–3.75 (m, 3H), 3.79 (s, 3H), 2.43–2.24 (m, 3H), 2.00–1.84 (m, 1H), 0.88 (t, $J = 7.5$ Hz, 9H), 0.58 (q, $J = 7.5$ Hz, 6H). ^{13}C NMR: $\delta = 167.5$ (C), 141.3 (CH), 138.9 (C), 138.6 (C), 138.5 (C), 137.9 (C), 136.1 (CH), 128.2–127.0 (CH Bn), 89.2 (CH), 88.8 (C), 87.1 (CH), 78.6 (CH), 75.1 (CH_2), 74.6 (CH_2), 73.5 (CH_2), 51.8 (CH_3), 37.7 (CH_2), 30.9 (CH_2), 7.0 (CH_3), 6.2 (CH_2). IR (film): 1721 cm^{-1}. HMRS (EI) m/z calc. for $C_{39}H_{48}O_6Si$, 640.3220, found: 640.3251%.

4.2.3. Bicyclic diene 14

Prepared from dienyne **8** (150 mg, 0.22 mmol) by the same procedure as for **12** using **3** (10 mol%) to give 64 mg of **15** (42%) and 79 mg of **14** (55%) as colorless oils. **14**: R_f: 0.5 (EtOAc/cyclohexane 1:9). $\delta = 7.35$–7.22 (m, 15H), 7.06 (d, $J = 2.4$ Hz, 1H), 5.92 (s, 1H), 5.11, 4.63 (ABq, $J = 11.4$ Hz, 2H), 4.92–4.72 (m, 4H), 4.08–3.98 (m, 2H), 3.75 (s, 3H), 3.25 (d, $J = 7.8$ Hz, 1H), 2.46–2.39 (m, 2H), 2.31–2.20 (m, 1H), 1.96–1.87 (m, 1H), 0.89 (t, $J = 7.5$ Hz, 9H), 0.56 (q, $J = 7.5$ Hz, 6H). ^{13}C NMR: $\delta = 166.4$ (C), 142.9 (CH), 139.8 (C), 138.9 (2 C), 138.4 (C), 132.9 (CH), 128.3–127.2 (CH Bn), 89.3 (CH), 86.2 (C), 80.9 (CH), 80.5 (CH), 76.3 (CH_2), 76.0 (CH_2), 73.7 (CH_2), 51.9 (CH_3), 37.1 (CH_2), 29.4 (CH_2), 7.0 (CH_3), 6.4 (CH_2). IR (film): 1721 cm^{-1}. HMRS (EI) m/z calc. for $C_{39}H_{48}O_6Si$, 640.32202, found: 640.31970%.

4.2.4. Triene **15**

R_f: 0.6 (EtOAc/cyclohexane 5:95). $\delta = 7.33$–7.21 (m, 15H), 6.43–6.41 (br s, 1H), 6.01–5.88 (m, 3H), 5.27–5.15 (m, 2H), 4.85–4.64 (m, 4H), 4.40–4.34 (m, 2H), 4.18 (d, $J = 4$ Hz, 1H), 4.01 (dd, $J = 7$, 4 Hz, 1H), 3.90 (t, $J = 4$ Hz, 1H), 3.74 (s, 3H), 2.87–2.78 (m, 1H), 2.46–2.44 (m, 2H), 1.88–1.79 (m, 1H), 0.87 (t, $J = 7.5$ Hz, 9H), 0.54 (q, $J = 7.5$ Hz, 6H). ^{13}C NMR: $\delta = 168.1$ (C), 139.4 (C), 139.2 (C), 139.1 (C), 138.5 (C), 137.9 (CH), 136.8 (CH), 135.1 (C), 128.3–126.9 (CH Bn), 123.0 (CH_2), 118.3 (CH_2), 91.0 (C), 82.8 (CH), 80.7 (CH), 78.2 (CH), 74.3 (CH_2), 73.7 (CH_2), 70.7 (CH_2), 51.8 (CH_3), 33.7 (CH_2), 30.7 (CH_2), 7.2 (CH_3), 6.1 (CH_2). IR (film): 1726 cm^{-1}. HMRS (EI) m/z calc. for $C_{41}H_{52}O_6Si$, 668.35333, found: 668.35310%.

4.2.5. Bicyclic diene **16**

Prepared from dienyne **9** (161 mg, 0.58 mmol) by the same procedure as for **12** to give **16** (98 mg, 76%) as a colorless oil. ^{1}H NMR: $\delta = 6.22$ (br s, 1H), 5.90 (t, $J = 6.4$ Hz, 1H), 3.74 (s, 3H), 2.15–2.20 (m, 4H), 1.90–1.10 (m, 8H), 1.04 (s, 3H). ^{13}C NMR: $\delta = 170.3$, (C), 139.8 (C), 135.0 (C), 131.6 (CH), 129.8 (CH), 51.8 (CH_3), 40.1 (CH_2), 38.1 (CH_2), 37.9 (C), 27.1 (CH_2), 26.4 (CH_2), 24.1 (CH_2), 22.6(CH_2), 21.3 (CH_3). IR (CCl_4): 1723 cm^{-1}. CI MS: NH_3 m/z 221 ($M^{+\cdot}$+1), 238 ($M^{+\cdot}$+18). HMRS (EI) m/z calc. for $C_{14}H_{20}O_2$, 220.14633, found: 220.14630%.

4.2.6. Bicyclic diene **17**

To a degassed solution of dienyne **10** (47 mg, 0.20 mmol) in dry CH_2Cl_2 (200 mL) was added catalyst **3** (34 mg, 20 mol%). The mixture was heated at reflux for 3.5 h. The solvent was removed under reduce pressure and the residue was purified by flash chromatography on silica gel (EtOAc/cyclohexane 5:95) to give **17** (36 mg, 88%) as a colorless oil. Colorless oil. R_f: 0.35 (EtOAc/cyclohexane 5:95). ^{1}H NMR: $\delta = 6.79$ (t, $J = 6.3$ Hz, 1H), 5.74 (t, $J = 3.9$ Hz, 1H), 3.71 (s, 3 H), 2.40–2.05 (m, 5H), 1.80–1.45 (m, 8H). ^{13}C NMR: $\delta = 169.0$ (C), 140.2 (CH), 137.3 (C), 134.8 (C), 129.1 (CH), 51.7 (CH_3), 36.6 (CH), 35.8 (CH_2), 29.7 (CH_2), 28.8 (CH_2), 25.6 (CH_2), 24.9 (CH_2), 17.7 (CH_2). IR (neat): 1715, 1652 cm^{-1}. HMRS (EI) m/z calc. for $C_{13}H_{18}O_2$, 206.13068, found: 206.13072%.

4.2.7. Bicyclic diene **18**

Prepared from dienyne **11** (60 mg, 0.24 mmol) by the same procedure as for **17** to give a mixture of **18** and **19** (9:1) (53 mg, 89%) as a colorless oil which could be separated by preparative TLC. **18**: colorless oil. R_f: 0.20 (EtOAc/cyclohexane 2:98). ^{1}H NMR: $\delta = 6.91$ (t, $J = 5.3$ Hz, 1H), 5.48 (t, $J = 3.7$ Hz, 1H), 3.70 (s, 3H), 2.24 (q, $J = 4.6$ Hz, 2H), 2.18–2.00 (m, 2H), 1.67–1.30 (m, 8H), 0.98 (s, 3H). ^{13}C NMR: $\delta = 168.8$ (C), 140.7 (CH), 138.3 (C), 135.0 (C), 128.3 (CH), 51.7 (CH_3), 41.9 (CH_2), 38.9 (CH_2), 36.5 (C), 29.9 (CH_2), 26.5 (CH_3), 25.7 (CH_2), 20.9 (CH_2), 18.6 (CH_2). IR (neat): 1715, 1652 cm^{-1}. HMRS (EI) m/z calc. for $C_{14}H_{20}O_2$, 220.1463, found: 220.1462%.

4.2.8. Bicyclic diene **19**

Colorless oil. R_f: 0.22 (EtOAc/cyclohexane 1:99). ^{1}H NMR: $\delta = 6.51$ (t, $J = 3.3$ Hz, 1H), 6.05 (d, $J = 3.3$ Hz, 1H), 3.74 (s, 3H), 2.32–2.03 (m, 4H), 1.80–1.25 (m, 6H), 1.00 (s, 3H). ^{13}C NMR: $\delta = 168.6$ (C), 135.5 (C), 134.9 (CH), 131.1 (C), 125.6 (CH), 51.6 (CH_3), 38.1 (CH_2), 36.3 (CH_2), 32.2 (C), 26.4 (CH_2), 23.0 (CH_2), 22.9 (CH_3), 18.0 (CH_2). IR (neat): 1718 cm^{-1}.

4.3. Representative procedure for the preparation and the ring opening of epoxides

4.3.1. Epoxide **28**

m-CPBA (80%, 46 mg) was added to a biphasic mixture of **16** (46 mg, 0.209 mmol), CH_2Cl_2 (1 mL) and saturated aqueous sodium bicarbonate (1 mL) cooled at 0 °C. The heterogeneous mixture was stirred vigorously for 30 min and then quenched with saturated sodium sulfite (0.5 mL). The mixture was stirred for 15 min while slowly warmed up to r.t. The CH_2Cl_2 layer was separated and the aqueous layer was extracted three times with CH_2Cl_2. The combined organic layers were washed with saturated $NaHCO_3$, brine, dried ($MgSO_4$) and evaporated under reduced pressure to give 54 mg of crude epoxide **28** as a mixture of diastereoisomers (8:1 ratio), which was used without further purification in the next reaction. Colorless oil. Major isomer: ^{1}H NMR: $\delta = 6.77$ (br t, $J = 3.2$ Hz, 1H), 3.76 (d, $J = 6.4$ Hz, 1H), 3.69 (s, 3H), 2.53–2.40 (m, 4H), 1.20–1.90 (m, 8H), 0.98 (s, 3H). ^{13}C NMR: $\delta = 168.6$, (C), 142.1 (CH), 132.8 (C), 62.3 (CH), 62.0 (C), 52.0 (CH_3), 40.1 (CH_2), 35.4 (CH_2), 37.9 (C), 27.9 (CH_2), 24.9 (CH_2), 23.8 (CH_2), 23.0 (CH_2), 18.3 (CH_3). IR (CCl_4): 1723 cm^{-1}.

4.3.2. Lactone **29a**

To a solution of 32 mg of the above epoxide **28** in methanol (1.0 mL) was added at room temperature ytterbium triflate hydrate [Yb(OTf)$_3$] (3 mg, 4.8 μmol, 0.035 equiv.). After being stirred at room temperature for 0.75 h, methanol was removed under reduced pressure and the residue was purified by flash chromatography on silica gel (EtOAc/PE 1:4). Concentration of the appropriate fractions afforded 22 mg of colorless oil of lactone **29a** (76%) as a mixture of two isomers (4:1 ratio). R_f: 0.40 (EtOAc/PE 1:4). ^{1}H NMR: $\delta = 4.95$ (m, 1H), 3.98 (m, 1H), 3.46 (s, 3H), 2.40–1.30 (m, 12H), 1.11 (s, 3H). ^{13}C NMR: $\delta = 175.5$ (C), 172.8, (C), 124.7 (C), 81.6 (CH), 77.0 (CH), 57.6 (CH_3), 38.8 (CH_2), 36.3 (C), 32.6 (CH_2), 32.4 (CH_2), 25.6 (CH_3), 24.9 (CH_2), 23.0 (CH_2), 22.0 (CH_2). IR (CCl_4): 1763 cm^{-1}. CI MS: NH_3 m/z 237 ($M^{+\cdot}$+1), 254 ($M^{+\cdot}$+18).

*4.3.3. Lactone **29b***

Prepared from **16** by the same procedure as for **29a** (63%) using allyl alcohol instead of MeOH. ^{1}H NMR: $\delta = 5.93$ (m, 1H), 5.33 (d, $J = 17$ Hz, 1H), 5.15 (d, $J = 10$ Hz, 1H), 4.92 (m, 1H), 4.19 (br s, 1H), 4.17 (br s, 1H), 4.13 (m, 1H), 2.40–1.30 (m, 12H), 1.10 (s, 3H). ^{13}C NMR: $\delta = 175.3$ (C), 172.7, (C), 135.3 (CH), 124.8 (C), 116.8 (CH_2), 81.5 (CH), 70.9 (CH_2), 65.8 (CH), 57.6 (CH_3), 38.7 (CH_2), 36.2 (C), 32.2 (CH_2), 32.1 (CH_2), 25.7(CH_2), 25.6 (CH_3), 23.0 (CH_2), 22.0 (CH_2). IR (CCl_4): 1764 cm^{-1}. CI MS: NH_3 m/z 263 ($M^{+\cdot}$+1), 280 ($M^{+\cdot}$+18).

*4.3.4. Ester **27** (major isomer)*

Prepared by the two steps procedure from **12** as for **29a**. M.p. 78–80 °C (PE). ^{1}H NMR: $\delta = 6.23$ (d, $J = 11.6$ Hz, 1H), 4.45 (d, $J = 6$ Hz, 1H), 4.12 (td, $J = 11.6$, 2.8 Hz, 1H), 3.82 (s, 3H), 3.36 (s, 3H), 2.30–1.42 (m, 10H), 1.31 (s, 3H). ^{13}C NMR: $\delta = 178.8$ (C), $\delta = 168.1$, (C), 127.4 (C), 83.9 (CH), 69.7 (CH), 57.2 (CH_3), 52.3 (CH_3), 50.6 (C), 41.7 (CH_2), 39.0 (CH_2), 38.3 (CH_2), 28.9 (CH_3), 27.6 (CH_2), 22.7 (CH_2). IR (CCl_4): 3409, 1691 cm^{-1}. CI MS: NH_3 m/z 255 ($M^{+\cdot}$+1), 272 ($M^{+\cdot}$+18). HMRS (EI) m/z calc. for $C_{14}H_{22}O_4$, 254.15181, found: 254.15280%.

*4.3.5. Epoxide **30***

Prepared from **18** by the same procedure as for **28** and used in the next step without further purification. Colorless oil. ^{1}H NMR: $\delta = 7.37$ (dd, $J = 9$, 5.1 Hz, 1H), 3.26 (t, $J = 4.2$ Hz, 1H), 2.71–2.60 (m, 1H), 2.32–2.22 (m, 2H), 2.11–0.88 (m, 9H), 1.05 (s, 3H). ^{13}C NMR: $\delta = 166.9$ (C), 149.6 (CH), 135.0 (C), 62.3 (C), 61.3 (CH), 51.6 (CH_3), 42.6 (CH_2), 36.8 (CH_2), 32.8 (C), 27.4 (CH_2), 24.0 (CH_2), 21.8 (CH_3), 21.6 (CH_2), 16.7 (CH_2). HMRS (EI) m/z calc. for $C_{14}H_{20}O_3$, 236.1413, found: 236.1413%.

*4.3.6. Lactone **31***

Prepared from **27** by the same procedure as for **29a** (15 mg, 44%, 2 steps). White solid. ^{1}H NMR: $\delta = 7.22$ (dd, $J = 9$, 5.1 Hz, 1H), 4.30 (t, $J = 7.2$ Hz, 1H), 2.84 (tdd, $J = 10$, 5.1, 3 Hz, 1H), 2.40–2.20 (m, 3H), 2.15–1.22 (m, 12H), 1.10 (s, 3H). ^{13}C NMR: $\delta = 168.8$ (C), 145.1 (CH), 135.7 (C), 84.1 (CH), 78.3 (C), 40.6 (CH_2), 34.8 (C), 32.7 (CH_2), 25.5 (CH_2), 23.2 (CH_2), 22.4 (CH_3), 21.8 (CH_2), 16.1 (CH_2). IR (film): 3444, 1724, 1674 cm^{-1}. HMRS (EI) m/z calc. for $C_{13}H_{18}O_3$, 222.1256, found: 222.1270%.

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Appendix A. Supplementary material

Experimental procedures and characterization data for dienynes **6–11**. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.jorganchem.2006.07.014.

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