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Formal syntheses of (±)-Asterisca-3(15),6-diene and (±)-Pentalenene using Rh(I)-catalyzed [(5+2)+1] cycloaddition

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ABSTRACT

Efficient formal syntheses of (±)-Asterisca-3(15),6-diene, a natural product with a bicyclo[6.3.0]undecane skeleton, and (±)-Pentalenene, a natural product with a tricyclo[6.3.0.0^{4,8}]undecane skeleton, have been achieved by using Rh(I)-catalyzed [(5+2)+1] cycloaddition. The [(5+2)+1] reaction provides an expeditious approach to reach the bicyclic cyclooctenone **4**, which was quickly transformed (via hydroboration then oxidation) to diketone **14**, a key advanced intermediate for the total synthesis of (±)-Asterisca-3(15),6-diene. Through further transformations, **14** was converted to diene **18**, an advanced intermediate for the total synthesis of (±)-Pentalenene.

1. Introduction

Terpenoids exist widely in nature. They usually have complex carbocyclic skeletons with unusual arrays of rings and functionalities (Fig. 1), which endow them with a broad range of biological properties.[1] Due to this, developing new synthetic methods and strategies for the synthesis of terpene natural products, especially those directed toward the construction of the carbocyclic skeletons presented in terpenes, is highly demanded. For example, the eight-membered carbocycle is one such skeleton found in many terpene and other natural products (e.g., Taxol). However, synthesis of eight-membered carbocycles is usually difficult due to unfavorable entropic factors and transannular interactions associated with the ring closure transition state.[2] To facilitate access to natural products and potential drugs containing eight-membered rings, we recently developed a Rh(I)-catalyzed [(5+2)+1] cycloaddition that can efficiently synthesize eight-membered carbocycles (Scheme 1).[3] This

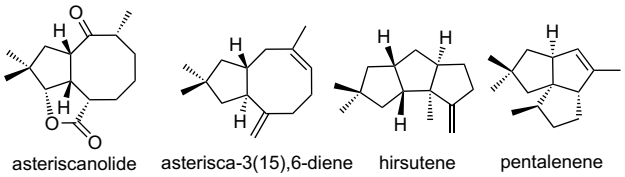
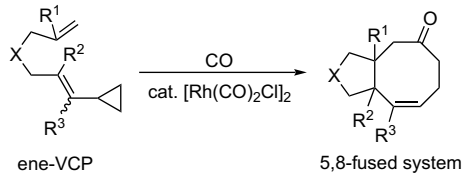


Figure 1. Selected terpene natural products.



Scheme 1. The [(5+2)+1] cycloaddition.

[(5+2)+1] reaction can also be extended to the synthesis of a linear triquinane skeleton,[4] via either a tandem [(5+2)+1]/aldol or a stepwise approach, as demonstrated by the total syntheses of Hirsutene and (±)-1-Desoxyhypnophilin from our group.[5]

Asterisca-3(15),6-diene and Pentalenene belong to the class of sesquiterpenes and are classified as the rare bicyclo[6.3.0]undecane family and tricyclo[6.3.0.0^{4,8}] system, respectively. Since their isolation,[6] intensive efforts have been directed toward syntheses of these structurally intriguing molecules,[7–11] but only limited methodologies are available for the rapid acquisition of these all-carbon natural products. As a part of our ongoing research program syntheses of natural products using the Rh(I)-catalyzed [(5+2)+1] cycloaddition, we report herein a new general approach to synthesize (±)-Asterisca-3(15),6-diene and (±)-Pentalenene.

2. Retrosynthetic plan

Our synthetic strategy (Scheme 2) was inspired by the pioneering work accomplished by Mehta's group and Pattenden's group.[7,8a] We envisaged that both (±)-Asterisca-3(15),6-diene and

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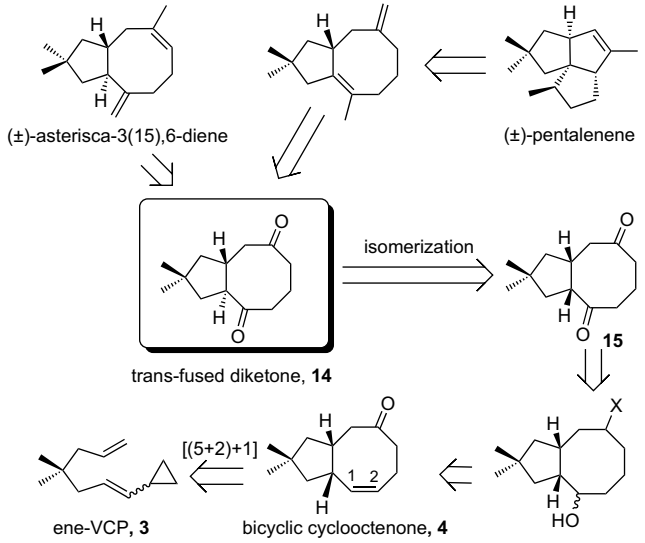
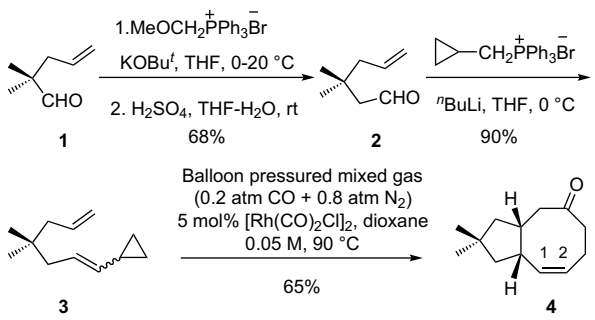


Scheme 2. Retrosynthetic analysis.

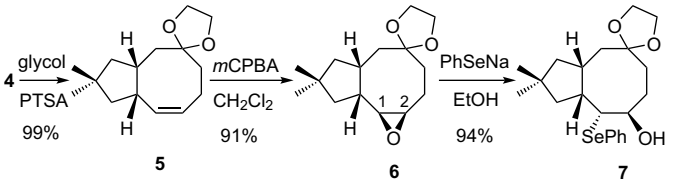
(±)-Pentalenene can be accessed from trans-fused unsymmetric diketone **14**, which could be obtained from a cis-fused unsymmetric diketone **15** through an acid or base induced isomerization. The central transformation in our synthesis plan is to regioselectively introduce a hydroxyl group at the C-1 position of the intermediate **4**. To realize this conversion, several standard methodologies, for example, epoxide opening reaction, hydroboration–oxidation, and oxymercuration–demercuration reaction, would give us flexible approaches. One salient feature of this synthetic plan is that the key advanced intermediate, the bicyclic cyclooctenone **4**, can be expeditiously obtained from ene-vinylcyclopropane (ene-VCP) **3** using [(5+2)+1] cycloaddition. Another feature of the synthetic plan is that both target natural products can be synthesized through a common advanced intermediate, the unsymmetric diketone **14**.

3. Results and discussion

Our synthesis started with the preparation of the bicyclic cyclooctenone **4** (Scheme 3).[5b] Commercially available aldehyde **1** was converted to ene-VCP **3** in two steps (the *Z*/*E* ratio of **3** is 1:1.3, the *Z*- and *E*-isomers cannot be separated by column chromatography on silica gel). Compound **3** was then transformed to the bicyclic cyclooctenone **4** as a single cis-diastereomer with a reaction yield of 65% under the optimal Rh(I)-catalyzed [(5+2)+1] cycloaddition conditions (balloon pressured mixed gas of 0.2 atm CO+0.8 atm N_2, 5 mol % $[Rh(CO)_2Cl]_2$ as catalyst, dioxane as solvent,



Scheme 3.



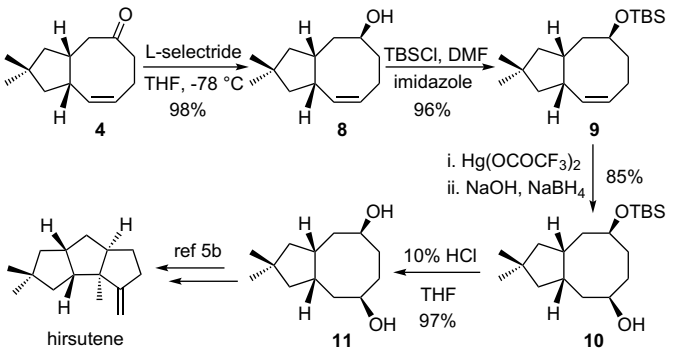
Scheme 4.

90 °C). The high stereoselectivity in the [(5+2)+1] cycloaddition is consistent with our previous observations.[3]

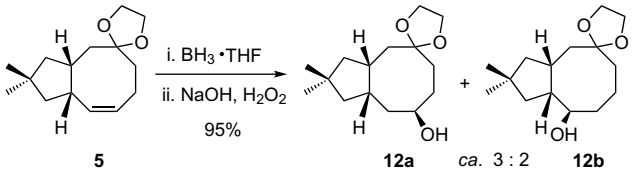
3.1. Studies on the regioselective introduction of a hydroxyl group to intermediate 4

With the key intermediate bicyclic cyclooctenone **4** in hand, our attention was directed to introducing a hydroxyl group at C-1 through functionalization of the double bond in **4** regioselectively. First, we explored the feasibility of regiocontrolled opening of the epoxide **6**, which was obtained in two steps from protection of the carbonyl in **4** by glycol, and epoxidation of ketal **5** with *m*-CPBA (Scheme 4). We reasoned that due to steric bulk sodium phenylselenide would attack the epoxide **6** at the less hindered C-2 position to give the desired β-hydroxyl selenide product. To our disappointment, the sodium phenylselenide attacked at the C-1 position to give the undesired selenide **7** as the sole product in 94% yield. The stereo- and regiochemistry of **7** was assigned by chemical correlation and details are given in the Supplementary data.[12] Currently, the reason for this regioselectivity is not clear.

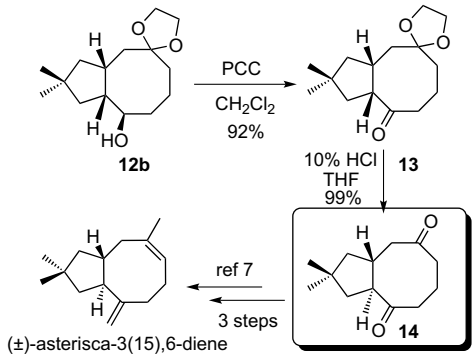
Next, an oxymercuration–demercuration process was explored (Scheme 5). Unfortunately, such a strategy failed to direct oxymercuration of either **4** or **5** to the desired products. Therefore, the TBS protected ether **9** was prepared by sequential stereoselective reduction of the carbonyl group in **4** with L-selectride and protection of the secondary alcohol **8** to its TBS ether. Surprisingly, treatment of **9** with mercury(II) trifluoroacetate in THF/H_2O, followed by reduction of the resulting organomercurials with basic aqueous $NaBH_4$ gave the undesired alcohol **10** as a single diastereo- and regioisomer in 85% yield. The structure of **10** was unambiguously confirmed by its conversion to diol **11**, whose structure has been determined by X-ray analysis in our previous work.[5b] However, continued efforts to reverse this regioselectivity proved to be unsuccessful. Here we want to point out that **11** is an advanced intermediate for the synthesis of Hirsutene and the synthetic route from **4** to **11** represents another approach for the formal synthesis of Hirsutene.[5b] Finally, hydroboration–oxidation reaction was tested. A series of boron reagents (BH_3·THF, 9-BBN, Evans' rhodium-catalyzed procedure with catecholborane[13]) were tried with the ketal **5** and TBS ether **9**. The best result was obtained



Scheme 5.



Scheme 6.



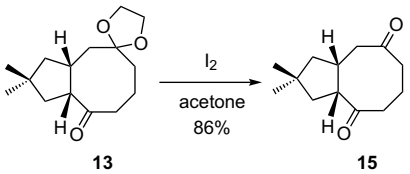
Scheme 7.

from the reaction of ketal **5** with $BH_3 \cdot THF$ complex in THF (Scheme 6). After a standard oxidative alkaline workup with H_2O_2/NaOH, secondary alcohols **12a** and **12b** were obtained in high yield as a 3:2 mixture of regioisomers.[14] These two compounds were readily separated by column chromatography on silica gel. Attempts to run this reaction at lower temperature did not improve the regioselectivity.

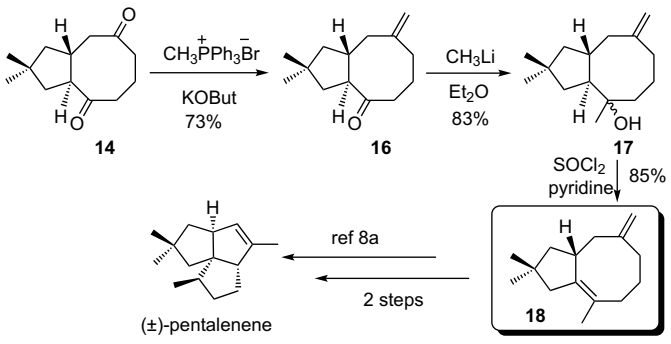
3.2. Formal syntheses of (±)-Asterisca-3(15),6-diene and (±)-Pentalenene

After the above studies, we began our journey of synthesis toward (±)-Asterisca-3(15),6-diene and (±)-Pentalenene. Synthesis of (±)-Asterisca-3(15),6-diene was commenced with alcohol **12b** (Scheme 7). Oxidation of **12b** by PCC afforded ketone **13** in 92% yield. To our delight, treatment of **13** with 10% HCl in THF not only recovered the carbonyl group, but also induced a cis to trans isomerization to generate the desired trans-diketone **14** quantitatively. Interestingly, the cis-diketone **15** could also be obtained through a molecular iodine-catalyzed deprotection procedure (Scheme 8).[15,16] Compound **14** has been transformed to (±)-Asterisca-3(15),6-diene by Mehta's group in three steps.[7,16] Therefore, a concise and step-economy formal synthesis of (±)-Asterisca-3(15),6-diene was achieved from commercially available compound **1** to **14** in seven steps with an overall yield of 14%. To the best of our knowledge, our approach represents the second route for the synthesis of this 5,8-ring fused sesquiterpene.

Now, our effort was focused on synthesis of (±)-Pentalenene (Scheme 9). Regioselective Wittig olefination of **14** afforded ketoolefin **16**, followed by methylation of **16** with methyllithium and dehydration with thionyl chloride and pyridine to obtain diene **18**



Scheme 8.



Scheme 9.

in 71% yield for two steps. The ^1H and ^{13}C NMR data of **18** exactly match those reported by Pattenden and Teague.[8a] Diene **18** has been used as an advanced intermediate for total synthesis of (±)-Pentalenene by Pattenden and others[8] through $RhCl_3$-catalyzed alkene isomerization and boron trifluoride promoted transannular cyclization. Therefore, the present work represents a formal synthesis of branched triquinane (±)-Pentalenene from **1** to **18** with an overall yield of 7% in 10 steps.

4. Conclusion

In summary, short and efficient formal syntheses of terpenoids of (±)-Asterisca-3(15),6-diene and (±)-Pentalenene have been achieved by utilizing the trans-fused diketone **14** as a common intermediate. The key common strategy-level step for these syntheses was the Rh(I)-catalyzed [(5+2)+1] cycloaddition, which proved to be an efficient method for rapid construction of the core skeleton of some 5,8-ring fused and 5,5,5-ring fused natural products. Further development and application of the [(5+2)+1] cycloaddition in natural product synthesis are underway in our group.

5. Experimental section

5.1. General

Air and moisture sensitive reactions were carried out in oven-dried glassware sealed with rubber septa under a positive pressure of dry argon. Similarly sensitive liquids and solutions were transferred via an oven-dried syringe. Tetrahydrofuran, diethyl ether, benzene, and toluene were distilled from sodium and benzophenone prior to use. Dichloromethane was distilled from CaH_2 prior to use. Dioxane (extra dry, water<50 ppm) was commercially available and used as received. Chemical reagents were used as received without further purification, unless otherwise indicated. NMR spectra were measured on Varian Mercury 200 (^1H at 200 MHz, ^{13}C at 50 MHz), Varian Mercury Plus 300 (^1H at 300 MHz, ^{13}C at 75 MHz), and Bruker ARX400 (^1H at 400 MHz, ^{13}C at 100 MHz) nuclear magnetic resonance spectrometers. Infrared spectra were recorded on an AVATAR 330 Fourier transform spectrometer (FTIR) with an OMNI sampler and are reported in wavenumbers (cm^{-1}). Mass spectra (MS) and high-resolution mass spectra (HRMS) were recorded on VG-ZAB-HS (EI, 70 eV) and Bruker APEX IV (ESI) mass spectrometers.

5.2. (±)-(1*R*, 8*R*)-10,10-Dimethylbicyclo[6.3.0]undec-6-en-3-one (4)

$[Rh(CO)_2Cl]_2$ (47 mg, 0.12 mmol) was charged in a base-washed, oven-dried Schlenk flask under an atmosphere of nitrogen, and

then a solution of the *Z*/*E* mixture of ene-VCP substrate **3** (400 mg, 2.4 mmol) in degassed dioxane (50 mL) was added. The solution was bubbled with the mixed CO gas (0.2 atm CO+0.8 atm N_2) for 5 min. The reaction mixture was then stirred at 90 °C under the balloon pressured mixed gas of 0.2 atm CO and 0.8 atm N_2 for 120 h. After being cooled to room temperature, the mixture was concentrated and the residue was purified by flash column chromatography on silica gel (eluted with petroleum ether/ethyl acetate 80:1) to afford the cycloaddition product **4** (304 mg, 65%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): 1.0 (s, 3H), 1.12 (s, 3H), 1.16–1.20 (m, 1H), 1.48–1.53 (m, 2H), 1.81 (dd, *J*=7.9 and 13.6 Hz, 1H), 2.17–2.34 (m, 4H), 2.42–2.55 (m, 3H), 2.74–2.82 (m, 1H), 5.47 (t, *J*=9.5 Hz, 1H), 5.82–5.91 (m, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$): 214.2, 135.4, 128.2, 47.5, 47.4, 46.2, 43.9, 40.3, 39.6, 37.6, 31.6, 31.4, 23.5. FTIR: ν=2951, 2930, 2865, 1701, 1383, 1365 cm^{-1}; MS (EI): *m*/*z* (%)=192 (M^+, 50), 177 (50), 151 (40), 135 (30), 107 (40), 93 (50), 83(100), 55 (65); HRMS calcd for $C_{13}H_{20}O$: 192.1514, found: 192.1516.

5.3. (±)-(*Z*)-(1*R*,8*R*)-10,10-Dimethylbicyclo[6.3.0]undec-6-en-3-one ethylene glycol ketal (5)

To a stirred solution of **4** (800 mg, 4.2 mmol) in 35 mL benzene were added glycol (9.4 mL, 168 mmol) and PTSA hydrate (160 mg, 0.84 mmol). The resulting mixture was refluxed for 20 h. Then the reaction mixture was cooled to room temperature and diluted with Et_2O, quenched by addition of 5 mL aqueous $NaHCO_3$. The aqueous layer was separated and the organic phase was washed successively with saturated aqueous $NaHCO_3$ and brine, dried over Na_2SO_4, and concentrated. The crude product was purified by flash column chromatography on silica gel (eluted with petroleum ether/ethyl acetate 50:1) to afford **5** (968 mg, 99%) as a colorless oil. ^{1}H NMR (300 MHz, C_6D_6): 0.94 (s, 3H), 1.03 (s, 3H), 1.13 (t, *J*=12.6 Hz, 1H), 1.38 (m, 2H), 1.65 (dd, *J*=9.7, 11.5 Hz, 1H), 1.77 (m, 2H), 2.03 (dd, *J*=11.8, 13.9 Hz, 1H), 2.12 (m, 2H), 2.34 (m, 1H), 2.57 (m, 1H), 3.25 (m, 1H), 3.52 (m, 4H), 5.28 (m, 1H), 5.58 (m, 1H); ^{13}C NMR (75.5 MHz, C_6D_6): 24.9, 30.9, 31.5, 36.9, 37.3, 39.5, 39.9, 40.5, 49.0, 49.5, 63.9, 64.6, 112.1, 130.2, 134.2; FTIR: ν=2951, 2865, 1737, 1463, 1366, 1111, 1055 cm^{-1}; HRMS (ESI) $[M+H]^+$ $C_{15}H_{25}O_2$ calcd 237.1849, found 237.1846.

5.4. (±)-(1*R*,7*R*,8*R*)-10,10-Dimethyl-7-hydroxybicyclo[6.3.0]-undecan-3-one ethylene glycol ketal (12b)

To a stirred solution of **5** (927 mg, 3.9 mmol) in 25 mL anhydrous THF under argon was added BH_3·THF (9.8 mL, 1 M in THF, 9.8 mmol) slowly at 0 °C. The resulting mixture was stirred at 0 °C for 2.5 h, then 3 M NaOH (7 mL) and 30% H_2O_2 (7 mL) were added very slowly. The resulting mixture was stirred at room temperature for 30 min and diluted with 100 mL of ethyl acetate. After separation of the aqueous layer, the organic phase was washed with brine, dried over $MgSO_4$, and concentrated. The crude product was purified by flash column chromatography on silica gel (eluted with petroleum ether/ethyl acetate 8:1 to 3:1) to afford **12a** (566 mg) as a white solid and **12b** (377 mg) as a colorless film in 95% yield (ca. **12a**/**12b**=3:2). Compound **12b**: ^{1}H NMR (400 MHz, C_6D_6): 0.91 (s, 3H), 0.92 (m, 1H), 1.02 (s, 3H), 1.13 (m, 2H), 1.35–1.49 (m, 3H), 1.56 (m, 1H), 1.64–1.87 (m, 6H), 1.97–2.08 (m, 2H), 2.60 (quintet, *J*=9.2 Hz, 1H), 3.48–3.53 (m, 4H); ^{13}C NMR (100 MHz, C_6D_6): 19.2, 28.2, 30.3, 35.3, 36.0, 36.3, 40.1, 40.9, 46.5, 48.0, 52.8, 64.25, 64.32, 72.1, 111.6; FTIR: ν=3448, 2949, 2931, 2866, 1462, 1364 cm^{-1}; HRMS (ESI) $[M+Na]^+$ $C_{15}H_{26}O_3Na$ calcd 277.1774, found 277.1773. Compound **12a**: ^{1}H NMR (400 MHz, C_6D_6): 0.92 (s, 3H), 0.97 (s, 3H), 1.05 (m, 2H), 1.42–1.74 (m, 8H), 1.85 (dt, *J*=14.7, 8.9 Hz, 1H), 1.96 (dd, *J*=11.3, 14.7 Hz, 1H), 2.08 (dd, *J*=10.1, 14.6 Hz, 1H), 2.68 (m, 2H), 3.52 (m, 4H), 3.72 (m, 1H); ^{13}C NMR (100 MHz, C_6D_6): 27.5, 29.4, 30.0, 30.4, 31.9, 35.6, 36.6, 37.2, 39.4, 51.7, 51.9, 64.2, 64.4, 69.3, 111.8. FTIR: ν=3426, 2947, 2927, 2868, 1463, 1365 cm^{-1}. HRMS (ESI): $[M+Na]^+$ $C_{15}H_{26}O_3Na$ calcd 277.1774, found 277.1772. Mp 84–86 °C.

5.5. (±)-(1*R*,8*R*)-10,10-Dimethyl-7-oxobicyclo[6.3.0]undecan-3-one ethylene glycol ketal (13)

To a stirred solution of **12b** (190 mg, 0.75 mmol) in 10 mL CH_2Cl_2 was added PCC (323 mg, 1.5 mmol) at room temperature. The resulting mixture was stirred for 3 h, then diluted with 10 mL Et_2O. The suspension was filtered through an Al_2O_3 column and concentrated. The crude product was purified by flash column chromatography on silica gel (eluted with petroleum ether/ethyl acetate 100:1 to 80:1) to afford **13** (173 mg, 92%) as a colorless film. ^{1}H NMR (400 MHz, $CDCl_3$): 0.98 (s, 3H), 1.09 (s, 3H), 1.26 (t, *J*=12.3 Hz, 1H), 1.43–1.58 (m, 4H), 1.73 (m, 2H), 1.91–2.07 (m, 3H), 2.31 (ddd, *J*=4.1, 9.0, 12.6 Hz, 1H), 2.47 (ddd, *J*=4.4, 9.7, 12.4 Hz, 1H), 2.72 (m, 1H), 3.44 (dt, *J*=10.3, 8.0 Hz, 1H), 3.87–3.96 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): 19.4, 27.6, 28.6, 36.2, 37.6, 37.9, 39.0, 43.6, 47.3, 49.7, 50.8, 64.0, 64.5, 110.9, 216.3; FTIR: ν=2951, 2866, 1968, 1460, 1364, 1099 cm^{-1}; HRMS (ESI) $[M+Na]^+$ $C_{15}H_{24}O_3Na$ calcd 275.1618, found 275.1615.

5.6. (±)-(1*S*,8*R*)-10,10-Dimethylbicyclo[6.3.0]undecan-2,6-dione (14)

To a stirred solution of **13** (400 mg, 1.6 mmol) in 25 mL THF was added 21 mL 10% HCl at room temperature. The resulting mixture was stirred at room temperature for 36 h, then 22 mL 3 M aqueous NaOH was added and the resulting mixture was diluted with 120 mL Et_2O. After separation of the aqueous layer, the organic layer was washed with water and brine, dried over $MgSO_4$, and concentrated. The crude product was purified by flash column chromatography on silica gel (eluted with petroleum ether/ethyl acetate 3:1) to afford **14** (329 mg, 99%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): 1.07 (s, 3H), 1.10 (s, 3H), 1.30 (t, *J*=11.9 Hz, 1H), 1.60 (dd, *J*=7.6, 12.9 Hz, 1H), 1.81–1.87 (m, 2H), 2.07 (m, 1H), 2.28–2.59 (m, 8H), 2.91 (dt, *J*=7.5, 11.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 21.5, 30.9, 31.4, 36.6, 42.6, 42.9, 43.4, 44.5, 46.8, 49.5, 56.2, 211.8, 213.7; FTIR: ν=2952, 2863, 1696, 1462, 1363, 1250 cm^{-1}; HRMS (ESI) $[M+Na]^+$ $C_{13}H_{20}O_2Na$ calcd 231.1356, found 231.1354. Mp 95–97 °C.

5.7. (±)-(1*S*,8*R*)-10,10-Dimethyl-6-methylidene-bicyclo[6.3.0]undecan-2-one (16)

To a stirred suspension of methyl triphenylphosphonium bromide (257 mg, 0.72 mmol) in 5 mL anhydrous benzene was added solid KO^{t}Bu (65 mg, 0.58 mmol) under argon. The resulting mixture was stirred at 60 °C for 40 min, then cooled to room temperature. A solution of **14** (100 mg, 0.48 mmol) in 4 mL benzene was added dropwise, the resulting mixture was stirred at 80 °C for 3.5 h, then cooled to room temperature, quenched by addition of 3 mL water, and diluted with 15 mL Et_2O. After separation of aqueous layer, the organic phase was washed with water and brine, dried over $MgSO_4$, and concentrated. The crude product was purified by flash column chromatography on silica gel (eluted with petroleum ether/ethyl acetate 50:1) to afford **16** (72 mg, 73%) as a white solid. ^{1}H NMR (400 MHz, C_6D_6): 0.93 (s, 3H), 0.97 (m, 1H), 1.01 (s, 3H), 1.42 (dd, *J*=7.6, 13.0 Hz, 2H), 1.50 (dd, *J*=7.0, 12.5 Hz, 2H), 1.80 (m, 2H), 1.91 (dd, *J*=11.1, 12.9 Hz, 1H), 1.93–1.99 (m, 1H), 2.02–2.10 (m, 2H), 2.23 (m, 2H), 2.53 (dt, *J*=7.4, 11.1 Hz, 1H), 4.78 (m, 1H), 4.80 (m, 1H); ^{13}C NMR (100 MHz, C_6D_6): 23.9, 31.3, 31.7, 36.5, 36.8, 39.7, 42.2, 44.6, 48.3, 49.5, 55.4, 115.6, 147.1, 212.2; FTIR: ν=3066, 2947, 2857, 1691, 1450, 1220 cm^{-1}; HRMS (ESI) $[M+H]^+$ $C_{14}H_{23}O$ calcd 207.1743, found 207.1744. Mp 65–67 °C.

5.8. (±)-(1*S*,8*R*)-6-Methylidene-2,10,10-trimethylbicyclo[6.3.0]undecan-2-ol (17)

To a stirred solution of **16** (37 mg, 0.18 mmol) in 4 mL anhydrous Et_2O was added CH_3Li (0.17 mL, 1.6 M, 0.27 mmol) under argon at 0 °C. The resulting mixture was stirred at 0 °C for 4 h, then quenched by addition of 4 mL water and diluted with 15 mL Et_2O. After separation of the aqueous layer, the organic phase was washed with water and brine, dried over $MgSO_4$, and concentrated. The crude product was purified by flash column chromatography on silica gel (eluted with petroleum ether/ethyl acetate 30:1) to afford **17** (33 mg, 83%) as a colorless oil. ^{1}H NMR (400 MHz, C_6D_6): 0.98 (s, 3H), 0.99 (s, 3H), 1.06 (s, 3H), 1.13 (ddd, *J*=1.7, 5.2, 12.9 Hz, 1H), 1.30–1.46 (m, 4H), 1.61–1.71 (m, 4H), 1.91–2.01 (m, 3H), 2.13 (m, 1H), 2.27 (m, 1H), 2.36 (dd, *J*=5.4, 13.0 Hz, 1H), 4.76 (m, 1H), 4.86 (m, 1H); ^{13}C NMR (100 MHz, C_6D_6): 22.5, 29.1, 29.5, 29.9, 36.1, 37.7, 38.0, 39.6, 43.9, 46.6, 50.2, 51.0, 72.1, 114.1, 149.3; FTIR: ν=3472, 2932, 2865, 1446, 1364 cm^{-1}; HRMS (ESI) $[M+Na]^+$ $C_{15}H_{26}ONa$ calcd 245.1876, found 245.1875.

5.9. (±)-6-Methylidene-2,10,10-trimethylbicyclo[6.3.0]-undec-1-ene (18)

To a stirred solution of **17** (30 mg, 0.14 mmol) in 2 mL pyridine was added $SOCl_2$ (20 μL, 0.28 mmol) at 0 °C. The resulting mixture was stirred at 0 °C for 2.5 h, then quenched by addition of 2 mL cold water and diluted with 15 mL Et_2O. After separation of the aqueous layer, the organic phase was washed with saturated aqueous NH_4Cl and brine, dried over $MgSO_4$, and concentrated. The crude product was purified by flash column chromatography on silica gel (eluted with pentane) to afford **18** (23 mg, 85%) as a colorless oil. ^{1}H NMR (400 MHz, C_6D_6): 0.84 (s, 3H), 1.05 (s, 3H), 1.06 (m, 1H), 1.44–1.58 (m, 2H), 1.61 (m, 3H), 1.70–1.85 (m, 4H), 1.96 (d, *J*=14.1 Hz, 1H), 2.10 (dd, *J*=1.5, 14.1 Hz, 1H), 2.23 (dd, *J*=5.3, 12.9 Hz, 1H), 2.34 (dd, *J*=3.7, 12.3 Hz, 1H), 2.45 (dt, *J*=5.3, 13.5 Hz, 1H), 2.64 (m, 1H), 4.82 (m, 1H), 4.95 (m, 1H); ^{13}C NMR (100 MHz, C_6D_6): 19.0, 27.3, 27.4, 28.9, 31.5, 32.2, 37.3, 41.8, 45.0, 49.1, 49.5, 111.9, 125.4, 139.9, 150.6.

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Supplementary data

Experimental procedures, spectral data (^{1}H NMR, ^{13}C NMR, IR, HRMS), and copies of ^{1}H NMR, ^{13}C NMR for all compounds described in the paper. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2009.04.020.

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