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Thermal intramolecular cycloaddition of 4-alkenylfulvene; highly regio- and diastereoselective formation of [4+2] adduct

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Abstract—4-Alkenylfulvenes were prepared by the annulation of 1,4-ynediones and allylidenetriphenylphosphorane and subjected to a thermal reaction. Highly regio- and stereoselective [4+2] cycloaddition is accomplished with 4-((*R*)-3-benzyloxypent-4-en-1-yl)fulvene and the resulting adduct is transformed into bicyclo[3.3.0]octene derivative.

1. Introduction

Construction of fused ring-systems has been an attractive subject of organic chemists. A variety of pericycloaddition reactions have been successfully employed in natural product synthesis, such as intramolecular Diels–Alder reaction. The 6π electrons of fulvene allowed thermal [4+2], [6+2], and [6+4] cycloaddition reactions with dienophiles, 1,3-dipolarophiles and dienes to form a variety of ring systems.[1] The competition among these cycloaddition reactions has been a subject of several recent publications.[2] Intramolecular cycloaddition of fulvenes could provide powerful tool as shown in the elegant synthesis of triquinane sesquiterpenes,[3] but the utility is limited due to the general inaccessibility of substituted fulvene, especially in a regioselective manner. Fulvenes have been usually prepared by the base-catalyzed condensation of cyclopentadienes with aldehydes and ketones but this method leads to the formation of a regioisomeric mixture in many cases.[4] We have demonstrated a single-step preparation of functionalized fulvenes by the condensation of allylidenetriphenylphosphorane with 1,4-ynediones.[5] The reaction proceeds smoothly at room temperature and with the high regioselection. Thus, we set out to study the regio- and stereoselectivity of intramolecular cycloaddition of various alkenylfulvenes. We now report synthesis and thermal intramolecular cycloaddition of 4-alkenylfulvenes in which high diastereoselective cycloaddition is accomplished with 4-((*R*)-3-benzyloxypent-4-en-1-yl)fulvene.

2. Results and discussion

Synthesis of the fulvene tethered by an alkenyl chain bearing a chiral center was initiated from preparation of the corresponding 1,4-ynedione, since a limited number of 1,4-ynediones has been reported so far. *O*-Benzyl-(*R*)-pantolactone was converted into (3*S*)-3-benzyloxy-2,2-dimethyl-pent-4-enal **1** in 63% overall yield via a straightforward sequence consisted of reduction with DIBAL, Wittig olefination and then Swern oxidation.[6] Carbon elongation of **1** to **2** was carried out in 68% overall yield by Wittig reaction with methoxymethylidenetriphenylphosphorane and then acid hydrolysis. Conversion of aldehyde **2** to the desired 1,4-ynedione **5** was accomplished in a following manner. The aldehyde **2** was at first treated with ethynylmagnesium bromide to give **3** in 80% yield. The hydroxy group of **3** was protected with TMSCl and then subjected to the Sonogashira reaction with benzoyl chloride to afford **4** in 55% yield after deprotection. Oxidation of **4** with MnO_2 furnished unstable 1,4-ynedione **5** in 47% yield along with recovery of **4** (33%).

Preparation of fulvene **7** from 1,4-ynedione **5** was next examined according to the method reported previously.[5] When **5** was treated with 2-ethoxyallylidenetriphenylphosphorane **6** in THF at 0°C, cyclization underwent nicely in a highly regioselective manner to give deep-red colored fulvene as a mixture of *Z*-isomer *Z*-**7** (56%) and *E*-isomer *E*-**7** (22%) (Scheme 1). The *E*- and *Z*-geometry were estimated on the basis of H-6 chemical shift in their NMR spectra (6.77 ppm for *Z*-**7**, 8.29 ppm for *E*-**7**). It is evident that the fulvenes are formed via initial Michael addition of

Keywords: fulvene; intramolecular cycloaddition; allylidenetriphenylphosphorane; 1,4-ynedione.

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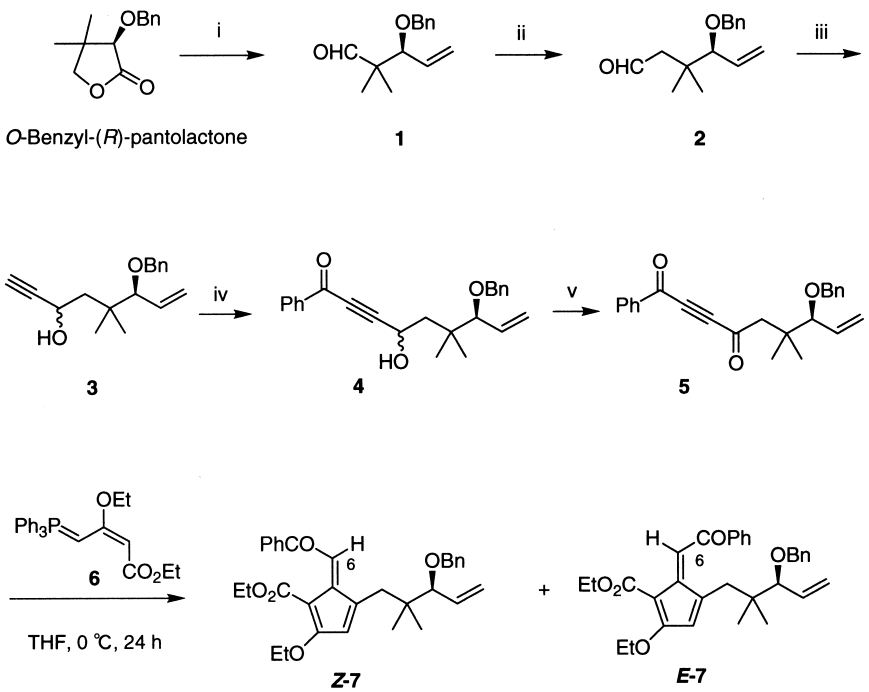
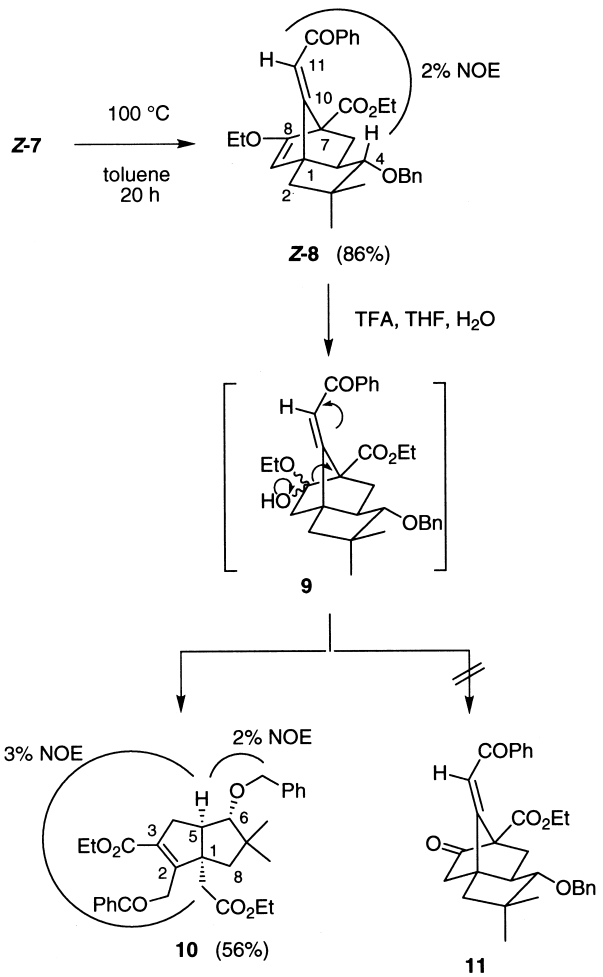


Scheme 1. *Reagents and conditions*: (i) (1) DIBAL, toluene, −78°C, 2 h; (2) $Ph_3P^+CH_3Br^-$, BuLi, room temperature, 3 h; (3) Swern Oxidation, 63% (3 steps). (ii) (1) $Ph_3P^+CH_2OCH_3Cl^-$, *sec*-BuLi, THF, 0°C; (2) TsOH, acetone, H_2O, 0°C, 68% (2 steps). (iii) ethynylmagnesium bromide, THF, 0°C, 1 h, 80%. (iv) (1) TMSCl, Et_3N, ether, room temperature, 12 h; (2) PhCOCl, $(Ph_3P)_2PdCl_2$, CuI, Et_3N, benzene, room temperature, 15 h; (3) citric acid, MeOH, room temperature, 20 min, 55% (3 steps). (v) MnO_2 (5 equiv.), CH_2Cl_2, room temperature, 24 h, 47%.



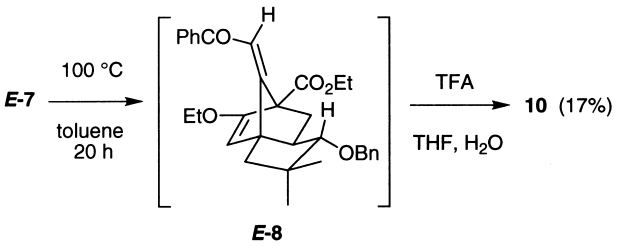
Scheme 2.

phosphorane **6** to the 3 position of 1,4-ynedinone **5** followed by intramolecular Wittig reaction with the 4-keto group. The low temperature conditions were found to be essential for minimizing the generation of the by-products.

Thermal cycloaddition of *Z*-isomer *Z*-**7** was effected by heating in toluene at 100°C for 20 h and [4+2] adduct *Z*-**8** was obtained in 86% yield with a high diastereoselection (ds 96:4) (Scheme 2). Other cyclization products involving [6+2] adduct were not detected in the reaction mixture. In the NMR experiment the major product showed the NOE between the C-11 vinyl proton and the C-4 benzyloxymethine proton, supporting to have the stereochemistry depicted in the structure *Z*-**8**.

In an attempt to convert the adduct *Z*-**8** into the corresponding ketones **11**, we found that the compound *Z*-**8** could be readily transformed into bicyclo[3.3.0]octene **10** by the mild acid treatment and no formation of **11** was observed under the reaction conditions. The structure of **10** was confirmed by a combination of COSY, HMQC and HMBC spectra in the NMR experiment. The stereochemical feature was supported by the NOE observation depicted in the structure **10**. The ring opening would involve C–C bond cleavage through an intermediary hemiacetal **9** and proceeds faster than hydrolysis to form ketone **11**. Easy C–C bond cleavage may be addressed to release of ring strain and existence of the two electron-withdrawing groups at the 7 and 11 positions (Scheme 2).[7]

When the *E*-isomer *E*-**7** was subjected to thermal reaction under the same conditions, an inseparable mixture generated. Treatment of the mixture with aqueous TFA and subsequent column chromatography allowed isolating compound **10** in 17% yield, which could arise from [4+2]



Scheme 3.

adduct *E*-**8** (Scheme 3). Thus, the both fulvenes *Z*-**7** and *E*-**7** proceeded intramolecular cycloaddition in a [4+2] fashion with high diastereoselection. The highly diastereoselective formation of the [4+2] adducts and subsequent transformation of them to **10** may provide an access to quinane skeleton.

3. Conclusion

We have demonstrated that the thermal intramolecular cycloaddition reaction of 4-alkenylfulvenes prepared from 1,4-ynedione and allylidenephosphorane proceeded in a [4+2] fashion with a high diastereoselection. The resulting [4+2] adduct could be converted into bicyclo[3.3.0]octene skeleton by mild acid treatment. An application of this strategy to synthesis of pentalenic acid is underway.

4. Experimental

4.1. General

All mps were measured on a Yanagimoto hot stage apparatus and are uncorrected. IR spectra were recorded on a Hitachi 270-30 spectrometer. ^{1}H NMR spectra were measured at 500 MHz in $CDCl_3$ on a JEOL Lambda 500 spectrometer, using $SiMe_4$ as the internal standard. *J*-Values are given in Hz. ^{13}C NMR spectra were recorded at 125 MHz on the spectrometer and solvent peak ($CDCl_3$: δ_C 77.0) was used for the internal standard. Mass spectra were recorded on a Shimadzu GCMS-QP5000 spectrometer or a JEOL JMS-700T spectrometer. All reactions were carried out under Ar in dried glassware. Flash chromatography was performed on Wakogel C-300. Extracts were dried over $MgSO_4$ and evaporated under reduced pressure. THF was distilled from sodium benzophenone ketyl under Ar prior to use. All commercially available reagents were used as received. MnO_2 (Chemical treated) was purchased from Wako Pure Chemical Industries Ltd.

4.1.1. (3*S*)-3-Benzyloxy-2,2-dimethyl-4-pentenal (1).[6] To a solution of *O*-benzyl-(*R*)-pantolactone (500 mg, 2.26 mmol) in toluene (5 ml) was added a 1.01 M solution of DIBAL in toluene (2.68 ml) at −78°C. The mixture was stirred for 2 h at that temperature, poured into an aq NH_4Cl solution and extracted with EtOAc. The extract was dried and evaporated. The residue was purified by flash chromatography (hexane–EtOAc) to give an oil (484 mg, 2.19 mmol). The oil (424 mg, 1.91 mmol) was dissolved in THF (5 ml) and the solution was added at 0°C to a solution of methylidenetriphenylphosphorane prepared from methyltriphenylphosphonium bromide (3.41 g, 9.55 mmol) and a 1.59 M solution of BuLi in hexane (6.0 ml) in THF (30 ml). The mixture was stirred for 3 h at 0°C, poured into an aq NH_4Cl solution and extracted with EtOAc. The extract was dried and evaporated. The residue was purified by flash chromatography (hexane–EtOAc) to give (3*S*)-3-benzyloxy-2,2-dimethyl-4-penten-1-ol as an oil (323 mg). δ_H ($CDCl_3$): 0.89 (s, 3H), 0.90 (s, 3H), 2.83 (bs, 1H), 3.46 (d, 1H, *J*=10.9 Hz), 3.53 (d, 1H, *J*=10.9 Hz), 3.62 (d, 1H, *J*=8.2 Hz), 4.29 (d, 1H, *J*=11.9 Hz), 4.61 (d, 1H, *J*=11.9 Hz), 5.30 (m, 2H), 5.81 (m, 1H), 7.31 (m, 5H); δ_C ($CDCl_3$): 138.10, 134.91, 128.40, 127.76, 127.63, 119.67, 88.03, 71.15, 70.40, 38.58, 22.48, 19.80; $[\alpha]_D^{21}$=−0.28° (*c*=0.645, $CHCl_3$); ν_{max} (neat): 3448, 2958, 2864, 1420, 1096, 698 cm^{-1}.

To a solution of oxalyl chloride (0.31 ml, 1.47 mmol) in CH_2Cl_2 (5 ml) was added a dry DMSO (0.52 ml, 1.47 mmol) at −78°C. The mixture was stirred for 2 min at −15°C, mixed with a solution of the above oil (323 mg, 1.47 mmol) in CH_2Cl_2 (4 ml) and the stirring was then continued for 15 min at the same temperature. The reaction mixture was cooled at −78°C, treated with Et_3N (1.42 ml, 7.34 mmol) and then warmed up gradually at room temperature. The mixture was poured onto ice-water and extracted with CH_2Cl_2. The extract was dried and evaporated. The residue was purified by flash chromatography (hexane–EtOAc) to give **1** as an oil (310 mg, 63% (3 steps)). δ_H ($CDCl_3$): 0.99 (s, 3H), 1.10 (s, 3H), 3.88 (d, 1H, *J*=8.5 Hz), 4.30 (d, 1H, *J*=11.9 Hz), 4.59 (d, 1H, *J*=11.9 Hz), 5.36 (m, 2H), 5.75 (m, 1H), 7.30 (m, 5H), 9.54 (s, 1H); δ_C ($CDCl_3$): 205.57, 133.70, 133.47, 128.40, 127.79, 127.55, 120.65, 84.12, 70.75, 46.34, 19.50, 16.65; $[\alpha]_D^{21}$=−0.85° (*c*=0.495, $CHCl_3$); ν_{max} (neat): 1720, 1454, 930, 734, 696 cm^{-1}; HRMS (EI): calcd for $C_{14}H_{18}O_2$: 218.1307. Found: 218.1274. Anal. calcd for $C_{14}H_{18}O_2$: H, 8.31; C, 77.03. Found: H, 8.53; C, 77.21.

4.1.2. (4*S*)-4-Benzyloxy-3,3-dimethyl-5-hexenal (2). To a solution of methoxymethyltriphenylphosphonium chloride (1.07 g, 3.12 mmol) in THF (10 ml) was added a 1.01 M solution of *sec*-BuLi in hexane (3.19 ml, 3.12 mmol) at −78°C and the mixture was stirred for 1 h at 0°C. The mixture was cooled at −78°C, treated with a solution of **1** (568 mg, 2.60 mmol) in THF (3 ml) and then stirred for 3 h at room temperature. The mixture was poured into an aq NH_4Cl solution at 0°C and extracted with EtOAc. The extract was dried and evaporated. The residue was purified by passing through a short column of SiO_2 with hexane–EtOAc and dissolved in a 1:1 solution (6 ml) of acetone and H_2O containing TsOH (10 mg). The mixture was stirred for 2 h at 0°C, diluted with water and extracted with EtOAc. The extract was washed with brine, dried and evaporated. The residue was purified by flash chromatography (hexane–EtOAc) to give **2** as an oil (411 mg, 68%). δ_H ($CDCl_3$): 0.98 (s, 3H), 1.00 (s, 3H), 2.17 (d, 1H, *J*=14.8 Hz), 2.33 (d, 1H, *J*=14.8 Hz), 3.40 (d, 1H, *J*=6.9 Hz), 4.18 (d, 1H, *J*=11.6 Hz), 4.48 (d, 1H, *J*=11.6 Hz), 5.24 (m, 2H), 5.69 (m, 1H), 7.23 (m, 5H), 9.72 (s, 1H); δ_C ($CDCl_3$): 202.87, 138.33, 134.70, 128.25, 127.75, 127.42, 120.00, 87.18, 70.29, 53.07, 38.10, 25.30, 23.21; $[\alpha]_D^{21}$=−0.82° (*c*=0.487, $CHCl_3$); ν_{max} (neat): 2956, 2864, 1712, 1066, 738, 698 cm^{-1}; *m/z* (EI) 233 (M^++1, 11), 126 (25), 107 (44), 91 (100); HRMS (EI):

calcd for $C_{15}H_{20}O_2$: 232.1463. Found: 232.1471. Anal. calcd for $C_{15}H_{20}O_2$: H, 8.67; C, 77.55. Found: H, 8.73; C, 77.72.

4.1.3. (3*S*,6*RS*)-3-Benzyloxy-4,4-dimethyl-6-hydroxy-1-octen-7-yne (3). To a solution of **2** (176 mg, 0.76 mmol) in THF (2 ml) was added a 0.6 M solution of ethynylmagnesium bromide (2.53 ml, 1.52 mmol) in THF at 0°C. The mixture was stirred for 1 h at the same temperature, poured into an aq NH_4Cl solution and then extracted with EtOAc. The extract was washed with brine, dried and evaporated. The residue was purified by flash chromatography (hexane–EtOAc) to give **3** as an oil (157 mg, 80%). δ_H ($CDCl_3$): 0.89 (s, 3H×1/2), 0.98 (s, 3H×1/2), 1.00 (s, 3H×1/2), 1.06 (s, 3H×1/2), 1.57 (dd, 1H×1/2, *J*=15.0, 2.7 Hz), 1.79 (dd, 1H×1/2, *J*=15.0, 8.5 Hz), 1.89 (dd, 1H×1/2, *J*=15.0, 4.3 Hz), 2.04 (dd, 1H×1/2, *J*=15.0, 9.8 Hz), 2.37 (d, 1H×1/2, *J*=2.1 Hz), 2.42 (d, 1H×1/2, *J*=2.1 Hz), 3.23 (bs, 1H×1/2), 3.44 (d, 1H×1/2, *J*=8.6 Hz), 3.49 (d, 1H×1/2, *J*=8.6 Hz), 4.23 (bs, 1H×1/2), 4.29 (d, 1H×1/2, *J*=11.6 Hz), 4.31 (d, 1H×1/2, *J*=11.9 Hz), 4.51 (m, 1H×1/2), 4.52 (m, 1H×1/2), 4.61 (d, 1H×1/2, *J*=11.6 Hz), 4.63 (d, 1H×1/2, *J*=11.9 Hz), 5.25 (m, 2H×1/2), 5.38 (m, 2H×1/2), 5.79 (m, 1H×1/2), 5.91 (m, 1H×1/2), 7.30 (m, 5H×1/2), 7.33 (m, 5H×1/2); δ_C ($CDCl_3$): 137.98, 137.33, 135.02, 134.44, 128.48, 128.36, 128.09, 127.94, 127.89, 127.62, 120.60, 120.09, 88.22, 88.03, 86.25, 85.94, 72.04, 71.47, 70.79, 70.41, 59.60, 59.22, 47.82, 46.71, 37.20, 37.09, 27.54, 26.19, 24.16, 23.09; $[\alpha]_D^{22}=-0.26°$ (*c*=0.531, $CHCl_3$); ν_{max} (neat): 3292, 2960, 2864, 1452, 1386, 736, 698 cm^{-1}; HRMS (EI): calcd for $C_{17}H_{20}O$ $[M-H_2O]^+$: 240.1514. Found: 240.1494.

4.1.4. (7*S*)-7-Benzyloxy-6,6-dimethyl-1-phenylnon-8-en-2-yne-1,4-dione (5). To a solution of **3** (201 mg, 0.79 mmol) in dry ether (5 ml) were added Et_3N (0.18 ml, 1.3 mmol) and TMSCl (0.16 ml, 1.3 mmol) at 0°C. The mixture was stirred for 12 h at room temperature, poured onto ice-water and extracted with EtOAc. The extract was dried and evaporated. The resulting silyl ether of **3** was purified by passing through a short column of SiO_2 and dissolved in a mixture of Et_3N (4 ml) and benzene (1 ml). The solution was mixed with benzoyl chloride (88 μl, 0.87 mmol), CuI (18 mg, 0.093 mmol) and then $(Ph_3P)_2$ $PdCl_2$ (18 mg, 0.025 mmol) and the stirring was continued for 15 h at room temperature After the addition of MeOH (2 ml), the mixture was evaporated and the residue was taken into benzene. The benzene layer was washed with brine, dried and evaporated. The residue was dissolved in MeOH (5 ml) containing citric acid (2.6 mg, 1.7 mol%). The mixture was stirred for 20 min at room temperature, poured into water and extracted with EtOAc. The extract was dried and evaporated. The residue was purified by flash chromatography (hexane–EtOAc) to give crude **4** as an oil (189 mg, 55%). δ_H ($CDCl_3$): 0.92 (s, 3H×1/2), 1.02 (s, 3H×1/2), 1.06 (s, 3H×1/2), 1.13 (s, 3H×1/2), 1.70 (d, 1H×1/2, *J*=15.2 Hz), 1.90 (d, 1H×1/2, *J*=14.7 Hz), 2.17 (d, 1H×1/2, *J*=15.2 Hz), 2.37 (d, 1H×1/2, *J*=14.7 Hz), 3.49 (d, 1H×1/2, *J*=8.6 Hz), 3.52 (d, 1H×1/2, *J*=8.6 Hz), 4.28 (d, 1H×1/2, *J*=11.3 Hz), 4.32 (d, 1H×1/2, *J*=11.6 Hz), 4.64 (d, 1H×1/2, *J*=11.3 Hz), 4.65 (d, 1H×1/2, *J*=11.6 Hz), 4.68 (d, 1H×1/2, *J*=11.3 Hz), 4.80 (d, 1H×1/2, *J*=11.3 Hz), 5.29 (m, 2H×1/2), 5.34 (m, 2H×1/2), 5.82 (m, 1H×1/2), 5.93 (m, 1H×1/2), 7.32 (m, 5H), 7.46 (m, 2H), 7.58 (m, 1H), 8.14 (m, 2H); δ_C ($CDCl_3$): 177.81, 177.76, 137.05, 136.47, 134.66, 134.09, 134.04, 129.63, 129.59, 129.52, 128.53, 128.48, 128.41, 128.37, 128.25, 128.10, 127.97, 127.93, 127.79, 127.69, 120.85, 120.69, 96.03, 88.10, 87.96, 81.34, 70.85, 70.44, 60.33, 59.84, 59.56, 46.89, 45.84, 37.37, 37.21, 27.56, 26.40, 24.15, 23.34, 20.97; ν_{max} (neat): 3400, 2236, 1640, 1262, 1066, 700 cm^{-1}; *m*/*z* (EI) 361 (M^+-1, 5), 219 (5), 205 (5), 120 (24), 105 (100), 77 (100).

The oil was taken into CH_2Cl_2 (2 ml) and mixed with MnO_2 (activated) (500 mg, 0.52 mmol) for 24 h at room temperature The mixture was filtered through celite and the filtrate was evaporated. The residue was purified by flash chromatography (hexane–EtOAc) to give **5** (87 mg, 47%) and **4** (54 mg, 33%).

Compound **5**. Oil; δ_H ($CDCl_3$): 1.04 (s, 6H), 2.59 (d, 1H, *J*=14.3 Hz), 2.79 (d, 1H, *J*=14.3 Hz), 3.55 (d, 1H, *J*=8.2 Hz), 4.22 (d, 1H, *J*=11.6 Hz), 4.50 (d, 1H, *J*=11.6 Hz), 5.27 (m, 2H), 5.67 (m, 1H), 7.24 (m, 5H), 7.50 (t, 2H, *J*=7.6 Hz), 7.57 (t, 1H, *J*=7.6 Hz), 7.95 (d, 2H, *J*=7.6 Hz); δ_C ($CDCl_3$): 185.76, 165.34, 138.50, 135.74, 134.91, 134.61, 128.24, 127.60, 137.36, 120.23, 111.96, 88.15, 86.76, 82.67, 70.30, 53.77, 39.34, 26.01, 24.72, 23.11; $[\alpha]_D^{27}=-1.37°$ (*c*=0.292, $CHCl_3$); ν_{max} (neat): 2956, 2920, 1648, 1594, 1258, 1174 cm^{-1}; *m*/*z* (EI) 269 (M^+-91, 11), 255 (15), 105 (100), 91 (98), 77 (89); HRMS (EI): calcd for $C_{24}H_{24}O_3$: 360.1726. Found: 360.1688.

4.1.5. Ethyl 4-((3*S*)-3-benzyloxy-2,2-dimethyl-pent-4-en-1-yl)-2-ethoxy-5(*Z*)-benzoylmethylidene-1,3-cyclopentadiene-1-carboxylate (*Z*-7) and ethyl 4-((3*S*)-3-benzyloxy-2,2-dimethyl-pent-4-en-1-yl)-2-ethoxy-5(*E*)-benzoylmethylidene-1,3-cyclopentadiene-1-carboxylate (*E*-7). To a solution of (2-ethoxy-3-ethoxycarbonyl-2-propenylidene)triphenylphosphorane **6** (58 mg, 0.137 mmol) in THF (6 ml) was added a solution of **5** (45 mg, 0.125 mmol) in THF (2 ml) at 0°C and the mixture was stirred for 24 h at 0°C. The mixture was filtered and the filtrate was evaporated. The residue was purified by flash chromatography (hexane–EtOAc) to give *Z*-**7** (35 mg, 56%) and *E*-**7** (14 mg, 22%).

Compound Z-**7**. Oil; δ_H ($CDCl_3$): 0.88 (t, 3H, *J*=7.4 Hz), 0.92 (s, 3H), 0.99 (s, 3H), 1.40 (t, 3H, *J*=7.0 Hz), 2.54 (d, 1H, *J*=13.7 Hz), 2.68 (d, 1H, *J*=13.7 Hz), 3.46 (d, 1H, *J*=8.2 Hz), 3.75 (q, 2H, *J*=7.0 Hz), 4.22 (q, 2H, *J*=7.4 Hz), 4.27 (d, 1H, *J*=12.2 Hz), 4.61 (d, 1H, *J*=12.2 Hz), 5.32 (m, 2H), 5.81 (m, 1H), 6.21 (s, 1H), 6.77 (s, 1H), 7.26 (m, 5H), 7.49 (t, 2H, *J*=7.6 Hz), 7.52 (t, 1H, *J*=7.6 Hz), 7.94 (d, 2H, *J*=7.6 Hz); δ_C ($CDCl_3$): 194.08, 171.88, 163.03, 145.36, 144.47, 138.79, 137.28, 135.25, 132.90, 129.45, 128.94, 128.50, 128.26, 127.41, 127.33, 121.94, 119.92, 98.10, 87.32, 70.10, 67.32, 59.60, 38.50, 34.43, 24.78, 23.37, 15.27, 13.88; $[\alpha]_D^{20}=-4.25°$ (*c*=0.961, $CHCl_3$); ν_{max} (neat): 2968, 1678, 1594, 1240, 1104 cm^{-1}; *m*/*z* (EI) 500 (M+, 11), 395 (8), 105 (100), 91 (88), 77 (30); HRMS (EI): calcd for $C_{32}H_{36}O_5$: 500.2563. Found: 500.2609.

Compound E-**7**. Oil; δ_H ($CDCl_3$): 0.66 (s, 3H), 0.72 (s, 3H), 1.34 (t, 3H, *J*=7.3 Hz), 1.41 (t, 3H, *J*=7.3 Hz), 2.45 (d, 1H, *J*=14.3 Hz), 2.50 (d, 1H, *J*=14.3 Hz), 3.22 (d, 1H, *J*=8.2 Hz), 4.17 (q, 2H, *J*=7.3 Hz), 4.15 (d, 1H, *J*=11.9 Hz),

4.26 (q, 2H, J=7.3 Hz), 4.49 (d, 1H, J=11.9 Hz), 5.12 (m, 2H), 5.59 (m, 1H), 6.02 (s, 1H), 7.27 (m, 5H), 7.44 (t, 2H, J=7.5 Hz), 7.56 (t, 1H, J=7.6 Hz), 7.98 (d, 2H, J=7.5 Hz), 8.29 (s, 1H); δ_C ($CDCl_3$): 194.87, 170.93, 163.91, 145.81, 144.58, 138.89, 137.33, 135.16, 133.91, 133.60, 129.30, 128.64, 128.18, 127.59, 127.25, 124.26, 119.44, 98.28, 87.63, 70.15, 67.18, 59.25, 38.95, 36.32, 23.47, 23.02, 15.18, 14.45; $[\alpha]_D^{22}=-0.40°$ (c=0.801, $CHCl_3$); ν_{max} (neat): 2964, 1728, 1702, 1574, 1204, 1064 cm^{-1}; m/z (EI) 500 (M+, 8), 105 (100), 91 (84), 77 (63); HRMS (EI): calcd for $C_{32}H_{36}O_5$: 500.2563. Found: 500.2554.

4.1.6. Ethyl (1*R*,4*S*,5*R*,7*S*)-4-benzyloxy-8-ethoxy-3,3-dimethyl-10(*Z*)-benzoylmethylidene-tricyclo[5.2.1.0^{1,5}]-dec-8-ene-7-carboxylate (*Z*-8). A solution of *Z*-**7** (28 mg, 0.056 mmol) in toluene was heated for 20 h at 100°C in a sealed tube. The cooled mixture was evaporated and the residue was purified by flash chromatography (hexane–EtOAc) to give *Z*-**8** as a solid (24 mg, 86%). Mp 143–144°C; δ_H ($CDCl_3$): 0.95 (t, 3H, J=7.0 Hz), 1.12 (s, 3H), 1.14 (s, 3H), 1.23 (t, 3H, J=7.0 Hz), 1.84 (d, 1H, J=14.7 Hz), 1.93 (d, 1H, J=14.7 Hz), 2.03 (dd, 1H, J=11.9, 9.2 Hz), 2.33 (m, 2H), 3.25 (d, 1H, J=11.1 Hz), 3.72 (m, 1H), 3.81 (m, 2H), 4.17 (m, 1H), 4.54 (d, 1H, J=11.6 Hz), 4.62 (d, 1H, J=11.6 Hz), 4.92 (s, 1H), 6.14 (s, 1H), 7.32 (m, 5H), 7.44 (t, 2H, J=7.0 Hz), 7.54 (t, 1H, J=7.0 Hz), 7.92 (d, 2H, J=7.0 Hz); δ_C ($CDCl_3$): 191.61, 169.03, 167.12, 161.34, 139.17, 132.90, 128.69, 128.47, 128.25, 128.20, 128.04, 127.29, 127.10, 104.28, 102.35, 91.15, 72.52, 64.84, 60.42, 56.97, 53.78, 43.75, 37.87, 30.25, 29.60, 25.60, 14.12, 13.81; $[\alpha]_D^{22}=-0.71°$ (c=0.591, $CHCl_3$); ν_{max} (Nujol): 1736, 1274, 1100 cm^{-1}; m/z (EI) 500 (M^+, 15), 409 (8), 105 (100), 91 (96), 77 (38); HRMS (EI): calcd for $C_{32}H_{36}O_5$: 500.2563. Found: 500.2551. Anal. calcd for $C_{32}H_{36}O_5$: H, 7.25; C, 76.77. Found: H, 7.44; C, 77.07.

4.1.7. Ethyl (1*S*,5*R*,6*S*)-2-benzoylmethyl-6-benzyloxy-1-ethoxycarbonylmethyl-7,7-dimethyl-bicyclo[3.3.0]oct-2-ene-3-carboxylate (10). A solution of *Z*-**8** (24 mg, 0.048 mmol) in a 4:4:1 mixture (1 ml) of THF, CF_3CO_2H and H_2O was stirred for 5 h at room temperature The mixture was diluted with water (5 ml) and extracted with EtOAc. The extract was washed successively with brine and saturated aq $NaHCO_3$ solution, dried and evaporated. The residue was purified by flash chromatography (hexane–EtOAc) to give **10** as an oil (14 mg, 56%). δ_H ($CDCl_3$): 1.06 (t, 3H, J=7.3 Hz), 1.07 (s, 3H), 1.12 (s, 3H), 1.20 (t, 3H, J=7.3 Hz), 1.53 (d, 1H, J=13.4 Hz), 1.80 (d, 1H, J=13.4 Hz), 2.53 (d, 1H, 14.0 Hz), 2.62 (d, 1H, J=14.0 Hz), 2.63 (d, 1H, J=16.8 Hz), 2.80 (t, 1H, J=8.6 Hz), 2.89 (dd, 1H, J=16.8, 8.6 Hz), 3.45 (d, 1H, J=8.6 Hz), 3.76 (d, 1H, J=17.1 Hz), 4.05 (q, 2H, J=7.3 Hz), 4.06 (q, 2H, J=7.3 Hz), 4.48 (d, 1H, J=17.1 Hz), 4.68 (d, 2H, J=1.5 Hz), 7.33 (m, 5H), 7.48 (t, 2H, J=7.6 Hz), 7.57 (t, 1H, J=7.6 Hz), 8.01 (d, 2H, J=7.6 Hz); δ_C ($CDCl_3$): 196.06, 171.05, 165.38, 153.96, 139.18, 137.10, 133.01, 129.67, 128.59, 128.32, 128.30, 128.07, 127.41, 127.37, 94.30, 73.61, 60.38, 60.01, 58.44, 49.86, 47.35, 44.38, 41.97, 37.87, 36.60, 28.31, 23.13, 14.03; $[\alpha]_D^{21}=-1.29°$ (c=0.680, $CHCl_3$): ν_{max} (neat): 2920, 1726, 1696, 1106, 730 cm^{-1}; m/z (EI) 518 (M^+, 21), 427 (7), 105 (100), 91 (74), 77 (38); HRMS (EI): calcd for $C_{32}H_{38}O_6$: 518.2668. Found: 518.2666.

4.1.8. Thermal reaction of ethyl 4-((3*S*)-3-benzyloxy-2,2-dimethyl-pent-4-en-1-yl)-2-ethoxy-5(*E*)-benzoylmethyl-idene-1,3-cyclopentadiene-1-carboxylate (*E*-7). A solution of *Z*-**7** (34 mg, 0.068 mmol) in toluene was heated for 20 h at 100°C in a sealed tube. The cooled mixture was evaporated and the residue was dissolved in a 4:4:1 mixture (1 ml) of TFA, THF and H_2O. The mixture was stirred for 5 h at room temperature, diluted with water, and extracted with EtOAc. The extract was washed in turn with brine and saturated aq $NaHCO_3$ solution, dried, and then evaporated. Flash chromatography (hexane–EtOAc) and preparative GPC gave **10** as an oil (6 mg, 17%).

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