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Synthetic efforts towards the protoilludenes. A formal synthesis of Δ7-protoilludene

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Abstract—An improved route to 5,8,8-trimethylbicyclo[4.3.0]-4-nonen-3-one, a key intermediate for the synthesis of the protoilludane skeleton and in particular Δ7-protoilludene, is reported. Attempts on an alternative synthesis of Δ6-protoilludene based on a phenylsulfonyl allene cycloaddition reaction is also presented.

In the past two decades sesquiterpenes with the 4/6/5 ring system have been isolated from natural sources and characterized.[1] Δ6-Protoilludene (**1**) is the parent compound of one subclass, the protoilludanes, while Δ7-protoilludene (**2**) is another. Δ6-Protoilludene (**1**) has been isolated form the fungi *Fomitopsis insularis*, *Omphalotus olerius*[2a] and *Ceratocycstis piceae*[1e] and interesting antibacterial activity has been reported. Δ6-Protoilludene (**1**) has also been postulated as an intermediate in the biosyntheses of other sesquiterpenes.[1c,2b,c] The carbon skeleton of **1** represents a synthetic challenge, and syntheses of **1** and **2** have appeared in the literature.[3] In addition, synthetic effort towards the basic ring system has been published.[4] The present paper reports studies of an intramolecular phenylsulfonyl allene cycloaddition reaction as the key step towards **1**, and it also describes an improved route to the ketone **3**, an intermediate in the synthesis of racemic Δ7-protoilludene (**2**) (Fig. 1).[3c]

1. Results and discussion

We have previously attempted the assembly of the 4/6/5 ring system by an intramolecular allene–ene reaction of the cyclopentane derivative **4**,[3d] but the 4/5/5 ring compound **5** was the product obtained (Scheme 1). Padwa and co-workers[5] have shown that the 4/6/5 ring system is indeed formed in a similar cycloaddition reaction, provided the allene is substituted with a phenylsulfonyl group. Hence, we decided to prepare the phenylsulfonyl substituted allene **6** and attempt the thermal cycloaddition to compound **7**, which we envisioned could be further transformed into Δ6-protoilludene (**1**)[6] (Scheme 2).

The acid chloride obtained from the acid **8**[3d,7] was converted into the bromide **9** in 85% yield using a Barton reaction.[8] Treatment of **9** with the lithium derivative of trimethylprop-2-ynyloxysilane followed by deprotection furnished the alcohol **10b**, which was transformed[9] via the sulfoxide **11** to the crystalline sulfone **6** in 50% overall yield.

The allene **6** exhibited absorptions at 1971, 1958 and 851 cm^{-1} in the IR spectrum, characteristic of a terminal allene function with a polar substituent. The NMR data were

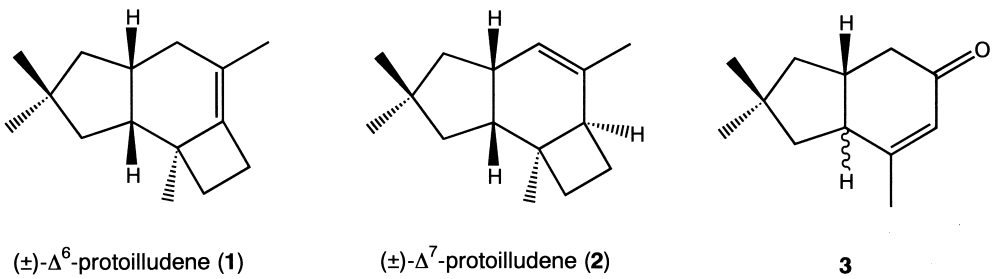

Figure 1.

Keywords: protoilludene; cycloaddition; allene.
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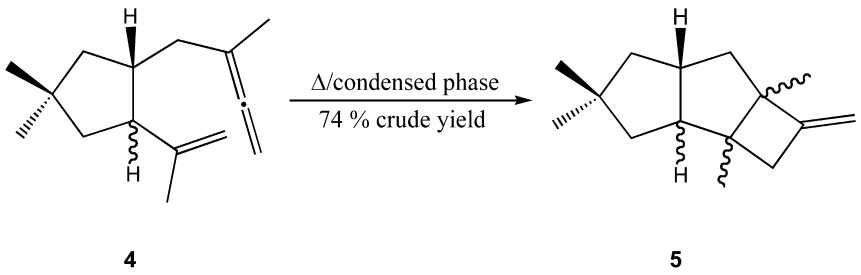
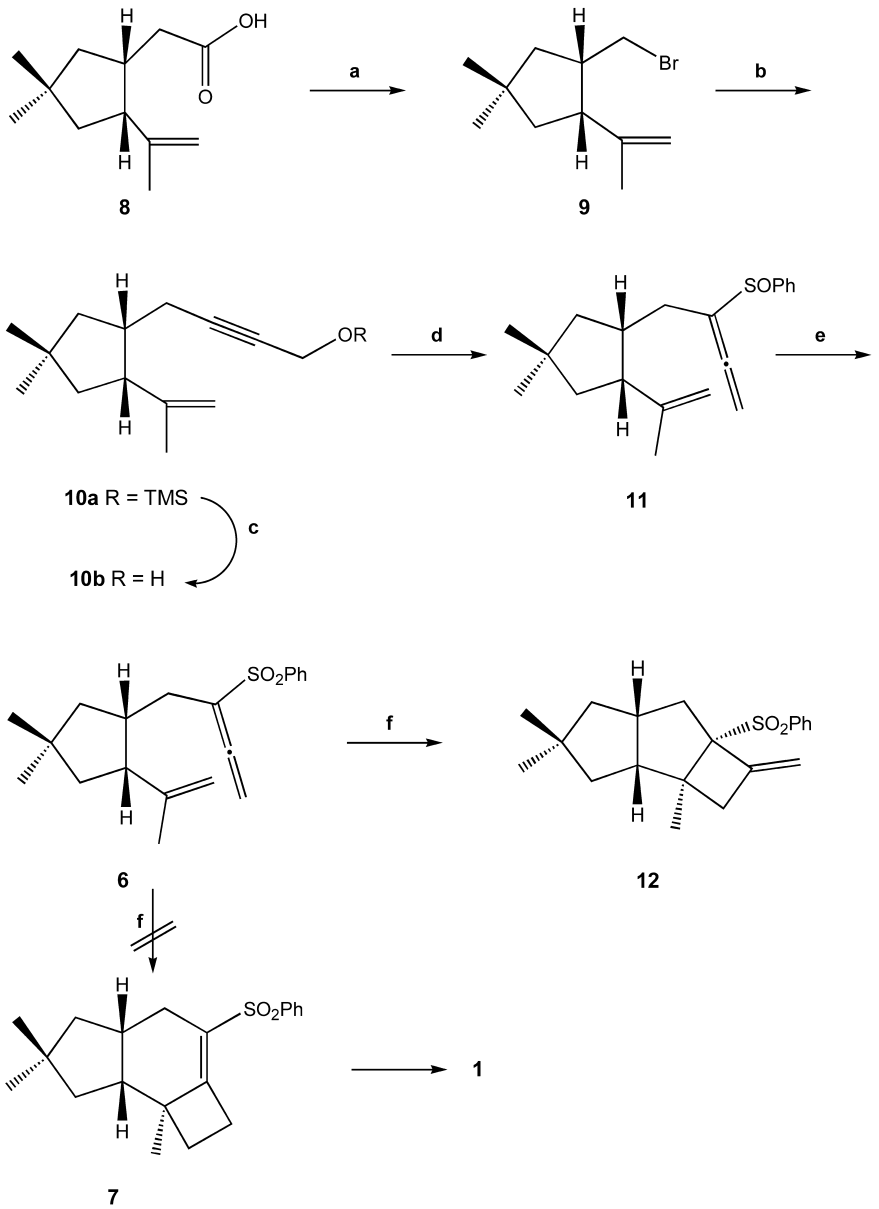


4 **5**

Scheme 1.

also in agreement with the assigned structure; in the ^{1}H NMR spectrum a singlet was observed at 4.68 ppm for 2 protons indicating a 1,1-disubstituted allene. Furthermore, in the ^{13}C and DEPT spectra, signals were observed at 209.52 and 90.67 ppm for two quaternary carbons.

With the phenylsulfonyl allene **6** in hand, we could study the thermal intramolecular [2+2] cycloaddition reaction. No conversion took place when **6** was heated under reflux in toluene for 98 h. However, using *o*-xylene as the solvent and heating under reflux for 80 h, only one volatile product was



8 **9** **11** **6** **12** **7** **1**

Scheme 2. *Reagents and conditions*: (a) (1) $(COCl)_2/CH_2Cl_2$, (2) 2-mercaptoyridine-1-oxide sodium salt, $CBrCl_3$, AIBN, benzene, △, 85%; (b) MeLi, CuI/Et_2O, −10°C, trimethylprop-2-ynyloxysilane, 87%; (c) K_2CO_3, MeOH, 96%; (d) PhSCl, Et_3N, Et_2O, −20 to 25°C, 74%; (e) Oxone, Na_2CO_3, MeOH, H_2O, 81%; (f) △, decalin, 28%.

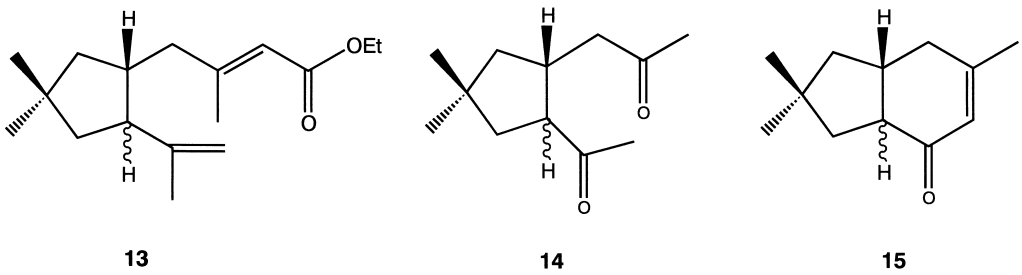


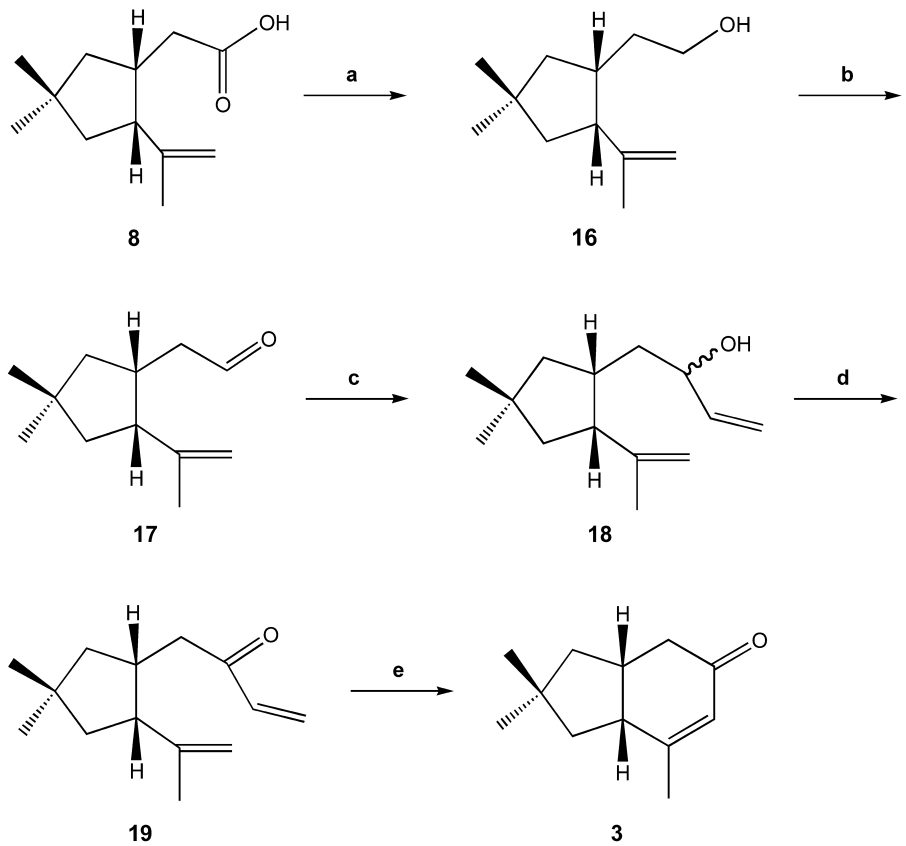
Figure 2.

formed in small amounts according to GLC analysis of the crude reaction mixture. The product was separated by preparative TLC and assigned the tricyclic structure **12** based on spectral data. The absence of any observable nOe between the bridgehead methyl group and the vicinal bridgehead proton supports the assigned stereochemistry. Prolonged reaction time caused extensive polymerization. Increasing the reaction temperature to approximately 185–195°C using decalin as the solvent gave after 84 h of reflux only a slightly higher yield (28%) of compound **12**, which was formed as the sole product according to GLC analysis. Passing **6** through a packed column (quartz wool) at 310 or 360°C gave no detectable conversion to either **7** or **12**. Instead, substantial polymerisation took place.

Some precedence for these results may be found in the literature where Padwa et al. have reported a similar result from their study of intramolecular [2+2] phenylsulfonyl allene ene reactions.[5c] When 1,1-disubstituted olefins were subjected to thermal conditions, a bicyclo[3.2.0]heptane system was formed, most likely via a diradical intermediate. These cycloadducts were formed by a [2+2]-cycloaddition across the most activated double bond, resulting in a different regioselectivity compared to that reported in their initial study.[5a] Our result support their findings.

We have recently published an improved preparation of the ester **13**,[3d] an intermediate in the synthesis of **1** reported by Oppolzer and Nakao[3b] (Fig. 2).

The bicyclic ketone **3**[4c] is an intermediate in the synthesis of racemic Δ^7-protoilludene (**2**) reported by Takeshita et al.[3c] They prepared the ketone *cis*-**3** starting from 4,4-dimethylcyclopentene, which is available only by a multistep synthesis.[10] We have also reported a synthesis of *cis*-**3** based on an intramolecular aldol condensation of the diketone **14**, but the major product is the isomeric ketone **15**.[4c] Hence, an improved route to **3** was desired and this was successfully achieved as depicted in Scheme 3.



Scheme 3. *Reagents and conditions*: (a) $LiAlH_4$, Et_2O, 0°C, 88%; (b) PCC/CH_2Cl_2, 79%; (c) $CH_2{=}CHMgCl$, Et_2O, 0–25°C, 84%; (d) MnO_2, $CHCl_3$, 87%; (e) $RuCl_2(=CHPh)[1,3\text{-}(Mes)_2ImH_2]P(CY)_3/CH_2Cl_2$, reflux, 5 h, 80%.

The acid **8**, obtained as the *cis*-isomer by a literature procedure,[3d] was transformed in two steps to the aldehyde **17**. Subsequent addition of vinylmagnesium chloride afforded the alcohol **18** that was converted to the ketone **19** by oxidation with active manganese dioxide. The overall yield of the vinyl ketone **19** from the acid **8** was 51%. A solution of the ketone **19** in dichloromethane underwent a metathesis reaction when heated in the presence of tricyclohexylphosphine[1,3-bis(2,4,6-trimethylphenyl)-4,5-dihydroimidazol-2-ylidene][benzylidene]ruthenium(IV)-dichloride (Grubbs' second generation catalyst)[11] for 5 h, furnishing the ketone **3** in 80% yield.

The preparation of **3** by our route in 41% overall yield constitutes formally a new synthesis of **2**, which compares favorably with that reported with respect to both yield and simplicity.

2. Experimental

2.1. General

The NMR spectra were recorded on a Varian Mercury 300 instrument using $CDCl_3$ as solvent. ^1H and ^{13}C NMR spectra were recorded at 300 and 75 MHz, respectively. IR spectra were recorded on a Perkin–Elmer Paragon 500 FT Spectrometer. Analytical GLC was performed on a 25 m SP2100 capillary column on a Varian GC 3300 instrument. Mass spectra were recorded at 70 eV with Fission's VG Pro spectrometer. All reactions were carried out under an atmosphere of nitrogen. When purified by chromatography this refers to flash chromatography using silica gel (230–400 mesh).

2.1.1. *cis*-1-Bromomethyl-2-isopropenyl-4,4-dimethylcyclopentane (9). To a solution of the acid **8**[3d] (1.24 g, 6.32 mmol) in dry CH_2Cl_2 (15 mL) oxalyl chloride (0.96 g, 7.58 mmol) was added dropwise at room temperature. After stirring for 2 h at this temperature, the solvent was removed and the crude acid chloride was used as such in the next step. The acid chloride in benzene (10 mL) was added to a suspension of AIBN (0.1 g, 0.6 mmol) and the sodium salt of 2-mercaptopyridine-1-oxide (0.99 g, 6.64 mmol) in bromotrichloromethane (6.6 mL). The reaction mixture was heated under reflux for 6 h. Removal of solvent and purification by column chromatography (silica, hexane) afforded the bromide **9** (1.23 g, 85%) as a colorless oil; R_f=0.68 (5% EtOAc in hexane); IR (film): 3056, 1642, 588 cm^{-1}; δ_H (300 MHz): 1.02 (3H, s, C*H*$_3$-C), 1.09 (3H, s, C*H*$_3$-C), 1.16 (1H, dd, *J*=10.0, 12.0 Hz, C–C*H*H–CH), 1.22 (1H, dd, *J*=10.0, 12.0 Hz, C–C*H*H–CH), 1.44–1.47 (1H, m, C–C*H*H–CH), 1.49 (1H, dd, *J*=10.0, 12.0 Hz, C–C*H*H–CH), 1.82 (3H, s, C*H*$_3$–C=C), 2.04 (1H, m, C*H*–CH$_2$Br), 2.14 (1H, ddd, *J*=8.0, 10.0, 10.8 Hz, C*H*–C=C), 3.24–3.29 (2H, m, C*H*$_2$Br), 4.74 (2H, s, C=C*H*$_2$); δ_C (75 MHz): 21.79 (CH_3), 27.58 (CH_3), 28.56 (CH_3), 29.65 (C), 37.13 (CH_2), 39.62 (CH_2), 42.63 (CH), 45.75 (CH_2), 47.39 (CH), 125.76 (CH_2), 147.19 (C); HRMS calcd for $C_{11}H_{19}^{79}Br$ (M^+): 230.0670, found 230.0655, HRMS calcd for $C_{11}H_{19}^{81}Br$ (M^+): 232.0650, found 232.0640.

2.1.2. *cis*-4-(2-Isopropenyl-4,4-dimethylcyclopentyl)but-2-yn-1-ol (10b). A solution of trimethylprop-2-ynyloxysilane (0.64 g, 5.02 mmol) in dry THF (25 mL) was added over a period of 90 min to a stirred solution of CuI (190 mg, 1.0 mmol) and MeLi in ether (1.65 M, 5.02 mmol, 3.0 mL), kept at −10°C. Stirring was continued for an additional 45 min at this temperature. The bromide **9** (1.16 g, 5.0 mmol) in dry THF (10 mL) was added dropwise during 30 min and the reaction mixture was allowed to warm to room temperature and stirred for another 10 h at this temperature. After quenching the reaction with saturated aqueous NH_4Cl (20 mL), the reaction mixture was extracted with ether (5×25 mL), washed with brine (20 mL), and dried ($MgSO_4$). The crude protected alcohol **10a** (1.22 g, 4.4 mmol) was dissolved in MeOH (50 mL) and K_2CO_3 (3.46 g, 25 mmol) was added. The mixture was heated to reflux for 5 h. The solvent was removed and the product purified by column chromatography (silica, 20% EtOAc in hexane), which yielded the alcohol **10b** (0.87 g, 84% overall yield in two steps) as a pale yellow colored oil; R_f=0.30 (20% EtOAc in hexane); IR (film): 3528, 2339 cm^{-1}; δ_H (300 MHz): 1.00 (3H, s, C*H*$_3$–C), 1.08 (3H, s, C*H*$_3$–C), 1.18 (1H, dd, *J*=10.0, 12.0 Hz, C–C*H*H–CH), 1.25 (1H, dd, *J*=10.0, 12.0 Hz, C–C*H*H–CH), 1.40–1.45 (1H, m, C–C*H*H–CH), 1.48 (1H, dd, *J*=10.0, 12.0 Hz, C–C*H*H–CH), 1.82 (3H, s, C*H*$_3$–C=C), 1.97 (1H, m, CH$_2$-C*H*–CH$_2$), 2.15 (1H, ddd, *J*=8.0, 10.0, 10.8 Hz, C*H*–C=C), 2.66 (1H, brs, O*H*), 3.24–3.29 (2H, m, CH–C*H*$_2$–C≡C), 4.22 (2H, t, *J*=2.2 Hz, C≡C–C*H*$_2$–OH), 4.78 (2H, s, C=C*H*$_2$); δ_C (75 MHz): 20.45 (CH_2), 21.21 (CH_3), 27.38 (CH_3), 28.96 (CH_3), 30.45 (CH), 32.93 (C), 38.81 (CH_2), 42.12 (CH), 48.95 (CH_2), 59.76 (CH_2), 77.82 (C), 85.39 (C), 124.61 (CH_2), 148.34 (C); HRMS calcd for $C_{14}H_{22}O$ (M^+): 206.1671, found 206.1659.

2.1.3. *cis*-4-(2-Isopropenyl-4,4-dimethylcyclopentyl)-3-(phenylsulfonyl)-1,2-butadiene (6). To a cold (−20°C) solution of the alcohol **10b** (0.86 g, 4.17 mmol) in dry ether (15 mL) and Et_3N (0.42 g, 4.17 mmol), benzenesulfenylchloride (0.60 g, 4.17 mmol) was added dropwise during a period 20 min. Stirring was continued for another 30 min at this temperature and then the reaction mixture was warmed to room temperature. After 1 h of stirring at room temperature, water (10 mL) was added, and the organic phase was separated and dried ($MgSO_4$). Removal of the solvent and purification of the residue by column chromatography (silica, 25% EtOAc in hexane) afforded *cis*-4-(2-isopropenyl-4,4-dimethylcyclopentyl)-3-(phenylsulfinyl)-1,2-butadiene (**11**) (0.93 g, 74%) as a yellow colored oil; R_f=0.25 (50% EtOAc in hexane); IR (film): 1953, 1038 cm^{-1}; δ_H (300 MHz): 1.04 (3H, s, C*H*$_3$–C), 1.07 (3H, s, C*H*$_3$–C), 1.20 (1H, dd, *J*=10.0, 12.5 Hz, C–C*H*H–CH), 1.28 (1H, dd, *J*=10.0, 12.5 Hz, C–C*H*H–CH), 1.39–1.46 (4H, m, C–C*H*$_2$–CH+C*H*$_2$–C=C=C), 1.73 (3H, s, C*H*$_3$–C=C), 1.98 (1H, m, CH$_2$–C*H*–CH$_2$), 2.18 (1H, ddd, *J*=8.0, 10.0, 10.8 Hz, C*H*–C=C), 4.52 (2H, brs, C=C=C*H*$_2$), 4.70 (2H, brs, C=C*H*$_2$), 7.55 (2H, t, *J*=7.5 Hz, *m*-*H*–Ar), 7.66 (1H, t, *J*=7.5 Hz, *p*-*H*–Ar) 7.89 (2H, d, *J*=7.5 Hz, *o*-*H*–Ar); HRMS calcd for $C_{20}H_{26}OS$ (M^+): 314.1704, found 314.1696.

To a cold (0°C) solution of **11** (0.91 g, 3.01 mmol) in 1:1 water–MeOH (100 mL) was added Na_2CO_3 (106 mg,

1.0 mmol) and then Oxone™ (6.15 g, 10.0 mmol, 49.5% $KHSO_5$). The resulting slurry was stirred for 4 h at room temperature, diluted with water (50 mL), and extracted with $CHCl_3$ (3×50 mL) and dried ($MgSO_4$). Removal of the solvent afforded the sulfone **6** (0.77 g, 81%) as white crystals, mp 136–138°C (dec.); IR (KBr): 1971, 1958, 1584, 1320, 1152, 851 cm^{-1}; δ_H (300 MHz): 1.01 (3H, s, C*H*$_3$–C), 1.06 (3H, s, C*H*$_3$–C), 1.26 (1H, dd, *J*=10.0, 13.5 Hz, C–C*H*–CH), 1.32 (1H, dd *J*=10.0, 12.8 Hz, C–C*H*–CH), 1.40–1.44 (1H, m, CH_2–C*H*–CH_2), 1.70 (3H, s, C*H*$_3$–C═C), 2.12–2.35 (3H, m, C–C*H*$_2$–C*H*), 2.54–2.65 (2H, m, C*H*$_2$–C═C═C), 4.68 (2H, brs, C═C═C*H*$_2$), 4.76 (2H, s, C═C*H*$_2$), 7.54 (2H, t, *J*=7.5 Hz, *m*-*H*–Ar), 7.65 (1H, t, *J*=7.5 Hz, *p*-*H*–Ar) 7.90 (2H, d, *J*=7.5 Hz, *o*-*H*–Ar); δ_C (75 MHz): 23.24 (CH_3), 32.29 (CH_3), 32.41 (CH_3), 38.85 (C), 39.76 (CH), 41.72 (CH_2), 46.34 (CH), 46.71 (CH_2), 52.08 (CH_2), 85.72 (CH_2), 90.67 (C), 115.32 (CH_2), 128.67 (2×CH), 129.72 (2×CH), 133.28 (CH), 139.62 (C) 146.08 (C), 209.52 (C); MS: *m*/*z* 178 (18); HRMS calcd for $C_{20}H_{26}SO_2$ (M^+): 330.1653, found 330.1648.

2.1.4. *cis*–*anti*–*cis*-2,9,9-Trimethyl-4-methylene-5-(phenylsulfonyl)tricyclo[5.3.0.0^{2,5}]decane (12). A solution of the sulfone **6** (32 mg, 0.1 mmol) in *o*-xylene (5 mL) was heated under reflux for 80 h. The solvent was then removed under reduced pressure, and the title compound **12** (5 mg, 16%) was isolated from the reaction mixture using preparative TLC (R_f=0.22, 50% EtOAc in hexane). Recrystallization from chloroform and hexane afforded pale yellow crystal; mp 131–133°C (dec.); IR (KBr): 1686, 1296, 1146, 874 cm^{-1}; δ_H (300 MHz): 1.03 (3H, s, C*H*$_3$–C), 1.08 (3H, s, C*H*$_3$–C), 1.32 (1H, dd, *J*=8.5, 13.0 Hz, C–C*H*–CH), 1.40 (1H, ddd, *J*=8.5, 10.0, 13.0 Hz, C–C*H*–CH), 1.44–1.48 (1H, m, CH_2–C*H*–CH_2), 1.65 (3H, s, C*H*$_3$–C), 1.84 (1H, dd, *J*=6.5, 12.8 Hz, C–C*H*–CH), 2.08 (1H, m, CH–C*H*(CH)–C), 2.36–2.54 (2H, m, C–C*H*–CH+CH–C*H*–C), 2.59 (1H, dt, *J*=2.4, 15.5 Hz, C–C*H*–CH), 2.78 (1H, dt, *J*=2.4, 15.5 Hz, C–C*H*–CH), 3.16 (1H, dd, *J*=8.1, 13.5 Hz, CH–C*H*–C) 4.48 (1H, t, *J*=2.4 Hz, C═C*H*H), 4.78 (1H, t, *J*=2.4 Hz, C═CH*H*), 7.56 (2H, t, *J*=7.5 Hz, *m*-*H*–Ar), 7.68 (1H, t, *J*=7.5 Hz, *p*-*H*–Ar), 7.89 (2H, d, *J*=7.5 Hz, *o*-*H*–Ar); δ_C (75 MHz): 24.32 (CH_3), 32.09 (CH_3), 32.78 (CH_3), 36.13 (C), 40.11 (C), 41.26 (CH_2), 41.91 (CH), 43.72 (CH), 46.3 (CH_2), 50.46 (CH_2), 60.77 (CH_2), 78.18 (C), 113.66 (CH_2), 128.61 (2xCH), 129.88 (2xCH), 133.35 (CH), 139.81 (C), 142.26 (C); MS: *m*/*z* 189 (20), 142 (12); HRMS calcd for $C_{20}H_{26}SO_2$ (M^+): 330.1653, found 330.1645.

2.1.5. *cis*-(2-Isopropenyl-4,4-dimethylcyclopentyl)acetaldehyde (17). The acid **8**[3d] (1.12 g, 5.7 mmol) in dry ether (25 mL) was slowly added to a cold (0°C) suspension of $LiAlH_4$ (175 mg, 4.6 mmol) in dry ether (30 mL) and then the reaction mixture was heated under reflux for 5 h. After cooling to room temperature, water (1.0 mL) was carefully added, followed by addition of a solution of NaOH (1.0 M, 1.0 mL) and water (3 mL). The precipitated lithium–aluminum salts were filtered and washed with ether. After drying ($MgSO_4$) and removal of the solvent the alcohol **16** (914 mg, 88%) was obtained as a yellow colored oil; IR (film): 3475, 1646 cm^{-1}; ^1H NMR (300 MHz): 1.02 (3H, s, C*H*$_3$-C), 1.08 (3H, s, C*H*$_3$–C) 1.17 (1H, dd, *J*=10.0, 12.5 Hz, C–C*H*–CH), 1.40–1.45 (1H, m, CH_2–C*H*–CH_2), 1.48 (1H, dd, *J*=6.5, 12.5 Hz, C–C*H*–CH), 1.52–1.60 (1H, m, CH_2–C*H*–C═C), 1.65 (3H, s, C*H*$_3$–C═C), 2.06 (1H, dd, *J*=11.0, 15.5 Hz, C–C*H*–CH), 2.15 (1H, dd, *J*=4.5, 13.0 Hz, C–C*H*–CH), 2.50–2.55 (1H, brs, O*H*), 2.60–2.68 (2H, m, CH–C*H*$_2$–CH_2), 3.45–3.51 (2H, m, C*H*$_2$–OH), 4.72 (2H, s, C═C*H*$_2$); ^{13}C NMR (75 MHz): 22.87 (CH_3), 29.91 (CH_3), 31.03 (CH_3), 35.34 (C), 37.10 (CH_2), 37.23 (CH_2), 38.76 (CH_2), 43.60 (CH), 47.83 (CH), 61.80 (CH_2), 111.00 (CH_2), 149.08 (C); HRMS calcd for $C_{12}H_{22}O$ (M^+): 182.1671, found 182.1659.

A solution of the alcohol **16** (900 mg, 4.94 mmol) in CH_2Cl_2 (25 mL) was added dropwise during 30 min to a suspension of PCC (4.85 g, 15.0 mmol) in CH_2Cl_2 (50 mL). After stirring at ambient temperature for another 3 h, ether (75 mL) was added and the extracted residue washed with water. After drying ($MgSO_4$) and removal of solvent, the residue was purified by column chromatography (silica, 15% EtOAc in hexane), to give 703 mg (79%) of the aldehyde **17** as a yellow colored oil; R_f=0.31 (25% EtOAc in hexane); IR (film): 1710, 1644 cm^{-1}; ^1H NMR (300 MHz): 1.00 (3H, s, C*H*$_3$–C), 1.09 (3H, s, C*H*$_3$–C), 1.20 (1H, dd, *J*=10.0, 12.5 Hz, C–C*H*–CH), 1.50 (1H, dd, *J*=6.5, 12.5 Hz, C–C*H*–CH), 1.54–1.58 (1H, m, CH_2–C*H*(CH)–C), 1.67 (3H, s, C*H*$_3$–C═C), 2.10 (1H, dd, *J*=11.0, 15.5 Hz, C–C*H*–CH), 2.17 (1H, dd, *J*=4.5, 13.0 Hz, C–C*H*–CH), 2.24–2.29 (2H, m, C*H*$_2$–CHO), 2.72–2.77 (1H, m, CH_2–C*H*(CH)–CH_2), 4.72 (2H, s, C═C*H*$_2$), 9.79 (1H, s, C*H*O); HRMS calcd for $C_{12}H_{20}O$ (M^+): 180.1514, found 180.1510.

2.1.6. *cis*-1-(2-Isopropenyl-4,4-dimethylcyclopentyl)but-3-en-2-ol (18). Vinylmagnesium chloride (1.7 M, 4.66 mmol, 2.74 mL) was added dropwise to a cold (0°C) solution of the aldehyde **17** (700 mg, 3.88 mmol) in dry ether (25 mL). Stirring was continued for another 30 min and the reaction mixture was allowed to warm to room temperature and stirred for another 16 h at this temperature. Saturated aq. NH_4Cl (15 mL) was added and the product was extracted with ether (3×20 mL). Drying ($MgSO_4$) and removal of the solvent afforded **18** (680 mg, 84%) as a pale yellow colored oil in a 1:1 diasteromeric mixture; R_f=0.22 (25% EtOAc in hexane); IR (film): 3437, 1640 cm^{-1}; ^1H NMR (300 MHz): 1.00 (3H, s), 1.01 (3H, s), 1.07 (3H, s), 1.08 (3H, s) 1.18–1.21 (2H, m), 1.42–1.43 (2H, m), 1.58–1.62 (4H, m), 1.67 (3H, s), 1.68 (3H, s), 2.06–2.09 (2H, m), 2.20 (1H, dd, *J*=4.5, 13.0 Hz), 2.23–2.30 (3H, m), 2.60–2.65 (2H, m), 2.64–2.68 (2H, brs), 3.91–3.93 (2H, m), 4.77 (2H, s), 4.79 (2H, s), 5.88–5.90 (2H, m), 6.08–6.09 (2H, m), 6.35–6.36 (2H, m); ^{13}C NMR (75 MHz): 23.06 (CH_3), 23.09 (CH_3), 30.52 (CH_3), 30.58 (CH_3), 31.45 (CH_3), 31.47 (CH_3), 35.64 (C), 35.70 (C), 37.71 (CH_2), 37.74 (CH_2), 38.99 (CH_2), 39.02 (CH_2), 42.70 (CH), 42.74 (CH), 46.49 (CH_2), 46.52 (CH_2), 47.61 (CH), 47.63 (CH), 72.79 (CH), 72.80 (CH), 110.91 (CH_2), 110.92 (CH_2), 115.12 (CH_2), 115.14 (CH_2), 139.98 (CH), 139.99 (CH), 145.49 (C), 145.52 (C); HRMS calcd for $C_{14}H_{24}O$ (M^+-H_2O): 190.1827, found 190.1819.

2.1.7. *cis*-1-(2-Isopropenyl-4,4-dimethylcyclopentyl)but-3-en-2-one (19). To a solution of the alcohol **18** (675 mg, 3.24 mmol) in $CHCl_3$ (30 mL) was added portionwise MnO_2 (4.22 g, 48.6 mmol) over a period of 5 h at ambient

temperature. Stirring was continued for another 20 h at this temperature. The reaction mixture was filtered through a plug of silica and evaporation of solvent afforded **19** (582 mg, 87%) as a colorless oil; R_f=0.36 (25% EtOAc in hexane); IR (film): 1728, 1640 cm^{-1}; ^1H NMR (300 MHz): 1.01 (3H, s, C*H*$_3$–C), 1.07 (3H, s, C*H*$_3$–C), 1.20 (1H, dd, *J*=10.0, 12.5 Hz, C–C*H*H–CH), 1.42–1.44 (1H, m, CH$_2$–C*H*(CH)–CH$_2$), 1.53 (1H, dd, *J*=6.5, 12.5 Hz, C–C*H*H–CH), 1.69 (3H, s, C*H*$_3$–C=C), 2.09 (1H, dd, *J*=11.0, 15.5 Hz, C–C*H*H–CH), 2.21 (1H, dd, *J*=4.5, 13.0 Hz, C–C*H*H–CH), 2.60–2.65 (1H, m, CH$_2$–C*H*(CH)–C=C), 2.85–2.88 (2H, m, CH–C*H*$_2$–C=O), 4.79 (2H, s, C=C*H*$_2$), 6.15 (1H, dd, *J*=2.5, 9.0 Hz, CH=C*H*H), 6.44 (1H, dd, *J*=9.0, 15.0 Hz, C*H*=CH$_2$), 6.52 (1H, dd, *J*=2.5, 15.0 Hz, CH=CH*H*); ^{13}C NMR (75 MHz): 23.20 (CH$_3$), 30.78 (CH$_3$), 31.41 (CH$_3$), 35.54 (C), 37.54 (CH$_2$), 42.21 (CH), 44.04 (CH$_2$), 46.02 (CH$_2$), 48.40 (CH), 110.24 (CH$_2$), 126.93 (CH$_2$), 138.54 (CH), 146.42 (C), 199.37 (C); HRMS calcd for $C_{14}H_{22}O$ (M^+): 206.1671, found 206.1664.

2.1.8. *cis*-5,8,8-Trimethylbicyclo[4.3.0]-4-nonen-3-one (3).[3c] The ketone **19** (206 mg, 1.0 mmol) was dissolved in dry CH_2Cl_2 (100 mL) and to this was tricyclohexylphosphine[1,3-bis(2,4,6-trimethylphenyl)-4,5-dihydroimidazol-2-ylidene][benzylidene]ruthenium(IV)dichloride (Grubbs' second generation catalyst)[11] added (85 mg, 0.1 mmol) under an atmosphere of argon. The reaction mixture was heated under reflux for 5 h. After removal of the solvent, the residue was purified by column chromatography (silica, 15% EtOAc in hexane) to afford the ketone **3**[3c] (142 mg, 80%) as a pale yellow oil; R_f=0.26 (15% EtOAc in hexane); IR (film): 2970 (s), 1676 (s) cm^{-1}; ^1H NMR (300 MHz): 0.99 (3H, s, C*H*$_3$–C), 1.02 (3H, s, C*H*$_3$–C), 1.23 (1H, dd, *J*=8.5, 13.0 Hz, C–C*H*H–CH), 1.50 (1H, ddd, *J*=8.5, 10.5 Hz, 13.0 Hz, C–C*H*H–CH), 1.50–1.56 (1H, m, CH$_2$–C*H*(CH)–CH$_2$), 1.79 (1H, dd, *J*=6.7, 13.0 Hz, C–C*H*H–CH), 1.84 (3H, s, C*H*$_3$–C=C), 2.15–2.33 (2H, m, C–C*H*H–CH+CH$_2$–C*H*(CH)–C), 2.60–2.70 (2H, m, CH–C*H*$_2$–C=O), 5.75 (1H, s, C=C*H*); ^{13}C NMR (75 MHz): 23.12 (CH$_3$), 30.20 (CH$_3$), 30.75 (CH$_3$), 37.27 (CH$_2$), 38.32 (C), 40.63 (CH$_2$), 43.70 (CH), 45.52 (CH), 46.37 (CH$_2$), 125.32 (CH), 164.03 (C), 199.19 (C); HRMS calcd for $C_{12}H_{18}O$ (M^+): 178.1358, found 178.1350.

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