Tetrahedron Vol 45 No 16 pp 4945 to 4950 1989
Printed in Great Britain

0040-4020/89 $3 00+ 00

Homochiral Ketals in Organic Synthesis Enantioselective Synthesis and Absolute Configuration of (-)-Modhephene[1]

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(*Received in USA* 14 *February* 1989)

The sesquiterpene (-)-modhephene, (-)-(1), isolated from the plant Isocoma wrightii by Zalkow and coworkers in 1978,[2] was the first natural product shown to possess the interesting carbocyclic [3 3 3]propellane skeleton Although a number of inventive syntheses of racemic modhephene have appeared,[3] no enantioselective synthesis has yet been disclosed, nor has proof of the absolute stereochemistry of this sesquiterpene been obtained Completion of the first enantioselective synthesis of modhephene and assignment of its absolute configuration are outlined in Scheme I and discussed below

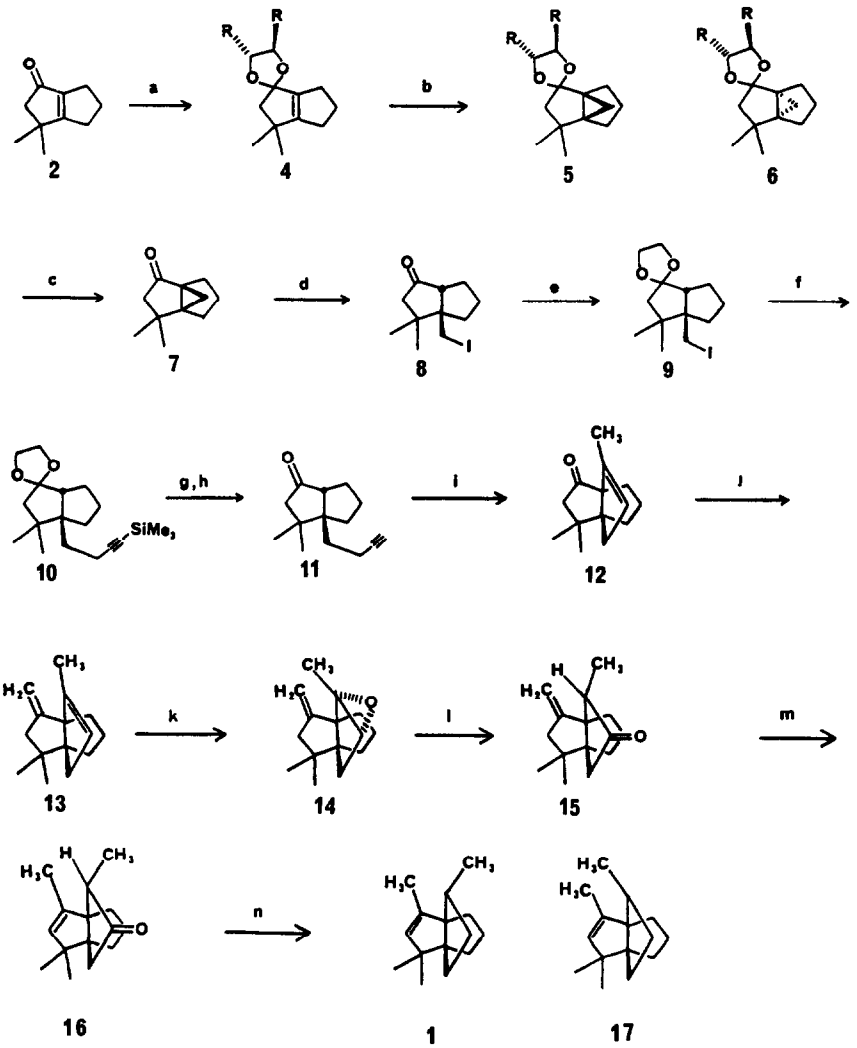
Ketalization of 3,3-dimethyl-2,3,5,6-tetrahydro-1H,4H-pentalen-1-one (2)[3d] (Scheme I) using the bis(trimethylsilyl ether) of 1,4-di-O-methyl-D-threitol (3)[4] and trimethylsilyl trifluoromethanesulfonate[5] produced in 64% yield homochiral ketal 4 Treatment of this ketal with the Simmons-Smith reagent[6] in refluxing ether gave, after 2 h and in 84% chemical yield, an inseparable 8 1 mixture of diastereomeric cyclopropane ketals 5 and 6 as determined by 62 9-MHz ^{13}C NMR spectroscopy [7]

Hydrolysis of the mixture of cyclopropane ketals (aqueous HCl, MeOH, room temperature, 3 h) provided in 94% yield enantiomerically enriched cyclopropyl ketone 7, mp 48-50 °C, $[\alpha]^{25}_D$ - 31 5° (c 3 9, $CHCl_3$) Assignment of the (3aS, 6aS) absolute stereochemistry to 7 was based upon application of the "reversed octant rule"[8] in interpreting its CD spectrum [1] This assignment was in accord with all previously examined cyclopropyl ketones [6 8-11]

Treatment of 7 with excess trimethylsilyl iodide (2 1 equiv, CCl_4, -10 °C, 3 h) produced, via regioselective cyclopropane ring opening,[12] iodomethyl ketone 8 in 85% yield Ketalization of 8 using the bis(trimethylsilyl ether) of ethylene glycol and trimethylsilyl trifluoromethanesulfonate[5] gave the corresponding iodomethyl ketal 9 in 96% yield Treatment of 9 with an excess of the lithium salt of 1-trimethylsilyl-1-propyne[13] (2 equiv, ether/tetramethylethylenediamine/HMPA, -25 °C, 1 h) gave acetylenic ketal 10 Ketal 10 was subjected to hydrolysis (aqueous HCl, MeOH, room temperature, 3 h) and to desilylation (nBu_4NF, THF, 24 h) to give enantiomerically enriched acetylenic ketone 11, $[\alpha]^{25}_D$ -117 9° (c 3 5, $CHCl_3$) in 82% yield from iodoketal 9 Ketone (-)-11 exhibited physical properties and gave spectral data consistent with those published for racemic 11 [3d]

Thermolysis[3d,14] of acetylenic ketone 11, (decalin, 360 °C, 100 min) provided tricyclic

SCHEME I Enantioselective Synthesis of (-)-Modhephene (1)



Reagents

(a) 1,4-Di-O-methyl-2,3-di-O-trimethylsilyl-D-threitol, TMS-OTf

(b) Zn(Cu), CH_2I_2, Et_2O, heat

(c) Aq HCl, CH_3OH

(d) TMS-I, CCl_4

(e) $TMSOCH_2CH_2OTMS$, TMS-OTf, CH_2Cl_2

(f) $Li^{\oplus}{}^{\ominus}CH_2C{\equiv}CTMS$, TMED, HMPA, Et_2O

(g) Aq HCl, CH_3OH

(h) $nBu_4N^{\oplus}F^{\ominus}$, THF, H_2O

(i) 360 °C, decalin

(j) CH_2I_2, Zn, $TiCl_4$, THF

(k) MCPBA, Na_2HPO_4, CH_2Cl_2

(l) BF_3 Et_2O, CH_2Cl_2

(m) I_2, C_6H_6, heat

(n) NH_2NH_2, K_2CO_3 diethylene glycol, heat

ketone 12 in 57% yield Olefination[15] of 12 (CH_2I_2, Zn, $TiCl_4$) gave diene 13 in 52% yield (81% based on unrecovered ketone) Regio- and stereoselective monoepoxidation[3d] of 13 (MCPBA, Na_2HPO_4, CH_2Cl_2) produced the desired epoxide 14 in 53% yield Isomerization[3d] of 14 using BF_3 Et_2O in CH_2Cl_2 produced olefinic ketone 15 in 43% yield Exocyclic alkene 15 was equilibrated[3d] with its endocyclic isomer 16 using iodine in refluxing benzene At equilibrium, the ratio of 15 to 16 was approximately 1 2 These isomers were chromatographically separable Wolff-Kishner deoxygenation[3d] of 16 produced in our hands in 66% yield an inseparable 5 1 mixture[3b] of (-)-modhephene, (-)-1, and epimodhephene 17 as determined by 250-MHz ^1H and 62 9-MHz ^{13}C NMR spectra of our synthetic material with those of (±)-1 graciously provided by Professor Paul Wender [3h]

Since natural modhephene was unavailable to us for comparison purposes, we were forced to compare its optical rotation as calculated[16] from the reported ORD data[17] with the rotations measured for synthetic modhephene The data are summarized in Table 1

Previously, Zalkow [2,17] and others[18] speculated that modhephene and the co-occurring sesquiterpene isocomene might be derived biosynthetically from (1R,9S)-caryophyllene Assignment of the (3aS, 4S, 6aR) absolute stereochemistry to natural (-)-modhephene is not in accord with the postulated biosynthetic pathway [19]

Table 1 Rotations for Natural and Synthetic Modhepenes

	[α],deg			[α],deg	
λ,nm	Natural[a]	Synthetic[b,c]	λ,nm	Natural[a]	Synthetic[b,c]
589	-4 21	-5 22	404		-17 2
578		-5 66	400	-14 70	
550	-6 71		365		-26 5
546		-6 68	350	-22 49	
500	-7 99		334		-38 0
450	-9 31		302		-59 8
435		-14 0	300	-41 32	

[a] calculated from the reported ORD data
[b] (c 1 6, $CHCl_3$)
[c] corrected to 100% e e

3,3-Dimethyl-3,4,5,6-tetrahydropentalen-1(2H)-one 1,4-Di-O-methyl-D-threitol Ketal (4). To a well-stirred solution of trimethylsilytrifluoromethanesulfonate (50 μL, 5 mol %) in CH_2Cl_2 (1 mL) at -78 °C were added 1,4-di-O-methyl-2,3-di-O-trimethylsilyl-D-threitol (1 1 g, 4 69 mmol) and enone 2 (750 mg, 5 0 mmol) dropwise The reaction mixture was warmed from -78 °C to 25 °C over several hours After 20 h the reaction was quenched by addition of dry pyridine (500 μL) and volatiles were removed in vacuo Chromatography of the residue on silica gel 60 (200 g) eluted with 35% ethyl acetate/hexanes gave ketal 4 as a pale yellow oil homogenous by TLC (R_f 0 48, 35% EtOAc/hexanes), $[\alpha]^{25}_D$-3 00° (c 3 00, $CHCl_3$), yield 830 mg, 2 96 mmol, 64%, IR ($CHCl_3$) cm^{-1} 3014, 2957, 2930, 1454, 1222, 1210, 1135, 1095, 962 and 823, ^1H NMR ($CDCl_3$) δ 1 03 (3,s), 1 04 (3,s), 1 09-2 28 (8,m), 3 33 (3,s), 3 34 (3,s), 3 34-3 47 (4,m), and 3 85-3 86 (2,m), ^{13}C NMR (CDl_3) δ 25 66 (CH_2), 27 22 (CH_2), 27 36 (CH_3), 27 43 (C), 57 91 (CH_2), 59 24 (CH), 59 32 (CH), 73 21 (CH_2), 73 26 (CH_2), 76 91 (CH_3), 77 73 (CH_3), 115 61 (C), 141 84 (C) and 162 34 (C), mass spectrum (70 eV) m/z (rel intensity) 282 (23), 267 (34), 237 (12), 177 (4), 151 (22), 175 (100), 115 (54), 107 (18), 91 (23), 87 (30), 77 (19), 71 (13), 59 (18), 55 (15), 52 (3), exact mass calcd for $C_{16}H_{26}O_4$ 282 1831, obsd 282 1831

(3aS,6aS)-3,3-Dimethyl-3,4,5,6-tetrahydro-3a,6a-methanopentalen-1(2H)-one 1,4-Di-O-methyl-D-threitol Ketals (5 and 6). To a well-stirred suspension of freshly prepared Zn-Cu couple (1 9 g, 14 3 mmol) and anhydrous K_2CO_3 (1 1 g, 7 68 mmol) in ether (4 mL) at reflux were added a large crystal of I_2 and CH_2I_2 (620 μL, 7 68 mmol) After 20 min at reflux, the ketal 4 (721 mg, 2 56 mmol) was added as a solution in ether (2 mL) After 2 h the mixture was cooled to 0 °C and quenched with saturated aqueous K_2CO_3 (700 μL) After stirring at room temperature for 30 min, the gray-black precipitate was removed by filtration through a powder funnel plugged with glass wool and the precipitate was washed well with ether The organic extracts were washed with saturated aqueous NH_4Cl, saturated aqueous $NaHCO_3$, and

saturated aqueous NaCl, dried ($MgSO_4$), filtered, and concentrated in vacuo Chromatography of the residue on silica gel 60 (50 g) eluted with 20% EtOAc/hexanes gave the product 5 and 6 as a colorless oil homogenous by TLC (R_f 0 50, 20% EtOAc/hexanes), $[\alpha]^{25}_D$ +0 82° (c 3 5, $CHCl_3$), yield 640 mg, 2 16 mmol, 84%, IR ($CHCl_3$) cm^{-1} 3017, 2958, 2871, 1458, 1364, 1308, 1292, 1213, 1195, 1100 and 975, ^1H NMR ($CDCl_3$) δ 0 55 (1,d), 0 82 (1,d), 0 89 (3,s), 1 04 (3,s), 1 30-1 98 (8,m), 3 29-3 84 (12,m), ^{13}C NMR ($CDCl_3$) δ 14 48 (CH_2), 24 08 (CH_2), 24 28 (CH_2), 26 39 (CH_3), 26 52 (CH_3), 27 52 (CH_2), 36 63 (C), 42 72 (C), 45 62 (C), 54 42 (CH_2), 59 28 (CH), 73 05 (CH_2), 76 92 (CH_3), 77 00 (CH_3), 116 79 (C), mass spectrum (70 eV) m/z (rel intensity) 296 (7), 240 (70), 215 (3), 201 (3), 164 (3), 149 (12), 122 (18), 115 (100), 107 (44), 93 (20), 79 (26), 71 (12), 55 (21), 51 (4), exact mass calcd for $C_{17}H_{28}O_4$ 296 1988, obsd 296 1988

(3aS,6aS)-3,3-Dimethyl-3,4,5,6-tetrahydro-3a,6a-methanopentalene-1(2H)-one (7). To a solution of the ketals 5 and 6 (1 3 g, 4 4 mmol) in CH_3OH (22 mL) at room temperature was added 2 7 M aqueous HCl (1 4 mL) After 3 h the solution was poured into saturated aqueous $NaHCO_3$ (40 mL) and the mixture was extracted with ether (4x50 mL) The combined ether extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo Chromatography of the residue on silica gel 60 (50 g) eluted with 20% EtOAc/hexanes gave 7 as a white solid, m p 48-50 °C, homogeneous by TLC (R_f 0 20, 1% MeOH/CH_2Cl_2), $[\alpha]^{25}_D$-31 5° (c 3 9, $CHCl_3$), yield 675 mg, 4 12 mmol, 94%, IR ($CHCl_3$) cm^{-1} 3075, 3017, 2961, 2871, 1701, 1455, 1368, 1280, 1268, 1221, 1219, 1138, 1063, 1016 and 941, ^1H NMR ($CDCl_3$) δ 1 05 (3,s), 1 08 (3,s), 1 21 (1,d,J^3=5 7 Hz), 1 47-1 60 (4,m), 1 82-1 90 (4,m), 2 37 (1,d,J^3=16 9 Hz), ^{13}C NMR ($CDCl_3$) δ 22 22 (CH_2), 23 51 (CH_2), 23 95 (CH_2), 25 61 (CH_3), 26 89 (CH_2), 27 36 (CH_3), 35 83 (C), 49 01 (C), 51 65 (C), 53 30 (CH_2) and 211 21 (C), mass spectrum (70 eV) m/z (rel intensity) 165 (25), 164 (17), 149 (40), 122 (100), 107 (91), 93 (41), 79 (39), 67 (6), 55 (5), exact mass calcd for $C_{11}H_{16}O$ 164 1202, obsd 164 1198

Anal Calcd for $C_{11}H_{16}O$ C, 80 44, H, 9 82 Found C, 80 13, H, 9 79

(3aR,6aS)-3,3-Dimethyl-3a-iodomethyl-3,3a,4,5,6,6a-hexahydropentalene-1(2H)-one (8). To a well-stirred solution of the cyclopropylketone 7 (305 mg, 1,86 mmol) in CCl_4 (10 mL) at 0 °C was added trimethylsilyl iodide (556 μL, 3 91 mmol) After 2 h at 0 °C, the reaction mixture was diluted with ether (100 mL) The organic phase was washed with saturated aqueous Na_2SO_3 (50 mL), dried ($MgSO_4$), filtered, and solvents were removed in vacuo Chromatography of the residue on silica gel 60 (200 g) eluted with 20% EtOAc/hexanes gave the product 8 as a white solid, mp 38-40 °C, homogenous TLC (R_f 0 31, 20% EtOAc/hexanes) $[\alpha]^{25}_D$ -33 11° (c 3 2, $CHCl_3$), Yield 462 mg, 1 56 mmol, 85%, IR ($CHCl_3$) cm^{-1} 3019, 2962, 2875, 1731, 1371, 1223, 1220, 1215, and 820, ^1H NMR ($CDCl_3$) δ 1 14 (3,s), 1 27 (3,s), 1 63-2 11 (7,m), 2 33-2 41 (2,m) and 3 26-3 39 (2,m), ^{13}C NMR ($CDCl_3$) δ 11 89 (CH_2), 23 92 (CH_3), 24 57 (CH_2), 26 45 (CH_3), 28 09 (CH_2), 34 84 (CH_2), 39 07 (C), 53 65 (CH_2), 56 30 (C), 58 30 (CH) and 218 83 (C), mass spectrum (70 eV) m/z (rel intensity) 293 (11), 253 (2), 235 (2), 207 (1), 165 (66), 147 (20), 137 (8), 123 (37), 109 (15), 95 (22), 81 (100), 67 (10), exact mass calcd for $C_{11}H_{17}O$ (M-I) 165 1280, obsd 165 1279

(3aR,6aS)-3,3-Dimethyl-3a-iodomethyl-3,3a,4,5,6,6a-hexahydropentalen-1(2H)-one Ethylene Ketal (9). To a well-stirred solution of TMSOTf (5 μL, 5 mole %) in CH_2Cl_2 (1 mL) at -78 °C were added ethylene glycol bis(trimethylsilyl) ether (235 μL, 0 992 mmol) and the iodoketone 8 (160 mg, 0 540 mmol) The reaction mixture was warmed from -78 °C to 25 °C over several hours After 8 h the reaction mixture was quenched by addition of pyridine (60 μL) and solvents were removed in vacuo Chromatography of the residue on silica gel 60 (50 g) eluted with 20% EtOAc/hexanes gave the product 9 as a pale yellow oil homogeneous by TLC (R_f 0 43, 20% EtOAc/hexanes), $[\alpha]^{25}_D$ +21 67° (c 5 5, $CHCl_3$), Yield 177 mg, 0 520 mmol, 96%, IR ($CHCl_3$) cm^{-1} 3017, 2879, 1470, 1369, 1327, 1222, 1210, 1189, 1024, 966 and 948, ^1H NMR ($CDCl_3$) δ 1 11 (3,s), 1 19 (3,s), 1 57-1 85 (7,m), 1 97 (1,d,J=13 9 Hz), 2 15-218 (1,m), 3 20-3 40 (2,m), and 3 65-3 86 (4,m), ^{13}C NMR ($CDCl_3$) δ 15 48 (CH_2), 24 59 (CH_3), 25 30 (CH_3), 25 33 (C), 26 68 (CH_2), 34 77 (CH_2), 40 00 (CH_2), 52 77 (CH_2), 58 33 (CH), 58 47 (C), 63 85 (CH_2), 63 94 (CH_2), and 114 70 (C), mass spectrum (70 eV) m/z (rel intensity) 277 (1), 235 (1), 209 (69), 165 (4), 153 (14), 127 (38), 123 (100), 113 (4), 81 (19), 67 (5), exact mass calcd for $C_{13}H_{21}O_2$ (M-I) 209 1542, obsd 209 1545

(3aR,6aS)-3a-(3-Butyn-1-1)-3,3-dimethyl-3,3a,4,5,6,6a-hexahydropentalen-1(2H)-one (11). To n-BuLi (12 6 mmol) freed from solvent (hexanes) at -35 °C were added ether (15 mL), tetramethylethylenediamine (1 9 mL) and 1-trimethylsilyl propyne (2 8 mL, 18 9 mmol) After 4 h at -20 °C the mixture was cooled to -35 °C and the iodoketal 9 (2 1 g, 6 29 mmol) in ether (5 mL) and HMPA (13 mL) were added After 15 min the reaction mixture was poured into cold saturated aqueous NH_4Cl (700 mL) The aqueous phase was separated and extracted with ether (3x200 mL) The ether phases were combined, dried ($MgSO_4$), filtered, and concentrated in vacuo

The crude trimethylsilyl ketal 10 from above was taken up in MeOH (40 mL) containing 3N HCl (3 mL) After 3 h at room temperature, the reaction mixture was diluted with ether, washed with saturated aqueous $NaHCO_3$, dried ($MgSO_4$), filtered, and concentrated in vacuo

The crude trimethylsilyl ketone from above was taken up in THF (60 mL) Tetrabutylammonium fluoride (6 3 mL, 6 3 mmol, 1M solution in THF) was added at room temperature After 24 h the reaction mixture was diluted with ether, washed with saturated aqueous $NaHCO_3$, dried ($MgSO_4$), filtered, and concentrated in vacuo Chromatography of the residue on silica gel 60 (500 g) eluted with 20% EtOAc/hexanes gave the product 11 as a colorless oil homogeneous by TLC (Rf 0 38, 20% EtOAc/hexanes), $[\alpha]^{25}_D$ -117 88° (c 3 5, $CHCl_3$), yield 1 06 g, 5 20 mmol, 82%, IR ($CHCl_3$) cm^{-1} 3305, 2959, 2877, 2249, 2117, 1729, 1455, 1372 and 1214, ^1H NMR ($CDCl_3$) δ 1 07 (3,s), 1 10 (3,s), and 1 50-2 37 (14,m), ^{13}C NMR δ 15 38, 19 63, 24 61, 24 81, 26 99, 28 52, 31 72, 33 75, 38 87, 53 17, 56 37, 59 27, 68 33 and 221 69, mass spectrum (70 eV) m/z (rel intensity) 204 (0 8), 119 (18), 105 (37), 92 (100), 91 (51), 81 (52), 68 (11), 56 (44), exact mass calcd for $C_{14}H_{20}O$ 204 1515, obsd 204 1461

Anal Calcd for $C_{14}H_{20}O$ C, 82 30, H, 9 80 Found C, 82,17, H, 9 92

(1S,5S)-4,4,8-Trimethyltricyclo[3 3 3 $0^{1,5}$] undec-7-en-2-one (12) A solution of 11 (537 mg, 2 63 mmol) in decalin (12 mL) was split into four portions Each portion was placed in Carrius combustion tube (capacity 10 mL) and subjected to a freeze-thaw procedure under vacuum three times The tube was then sealed under vacuum The solution was then heated at 360 °C for 100 min in a bath of molten lead The solution was then allowed to cool to room temperature, then placed on a silica gel column (25 g) and eluted with hexane, then ether, to give a total of 500 mg of crude 12 Purification by chromatography on silica gel 60 (200 g) eluted with 19 1 hexanes Et_2O afforded 308 mg (1 51 mmol, 57%) of 12 as a colorless oil, $[\alpha]^{24}_D$ +107° (c 2 67, $CHCl_3$), ^1H NMR ($CDCl_3$) δ 0 97 (3,s), 1 43-1 94 (7,m) 1 75 (3,bs), 1 98 (1,d,J=16 Hz), 2 50 (1,d,J=16 Hz), 2 62 (1,dt,J=15,3 Hz) and 5 21 (1,bs), ^{13}C NMR ($CDCl_3$) δ 13 61, 23 91, 25 17, 26 35, 35 70, 37 05, 37 14, 39 95, 52 10, 64 63, 74 47, 126 12, 141 05 and 219 45

(1S,5R)-2-Methylene-4,4,8-trimethyltricyclo[3 3 3 $0^{1,5}$]undec-7-ene (13). To a suspension of zinc dust (1 45 g, 22 41 mmol) in THF (25 mL) was added 1,1,diiodomethane (1 0 mL, 3 32 g, 12 45 mmol) and the mixture was stirred at room temperature for 30 min The mixture was then cooled to 0 °C and $TiCl_4$ (546 μL, 945 mg, 5 0 mmol) was added dropwise The temperature was allowed to reach 25 °C over 30 min to produce a chocolate brown solution A solution of 12 (503 mg, 2 49 mmol) in THF (5 mL) was added to this mixture and the resulting solution stirred at room temperature for 3 h, then quenched by the addition of 1M HCl The phases were separated and the aqueous phase was extracted with ether The combined organic extracts were washed with brine, dried ($MgSO_4$), filtered and concentrated Chromatography on silica gel 60 eluted with 19 1 hexanes Et_2O afforded 184 mg (0 90 mmol, 36%) of recovered 12 and 264 mg (1 31 mmol, 52%) of 13 as a colorless oil, $[\alpha]^{24}_D$ +40° (c 4 0, $CHCl_3$), ^1H NMR ($CDCl_3$) δ 0 92 (3,s), 0 96 (3,s) 1 2-1 85 (6,m), 1 76 (3,bs), 1 95-2 05 (1,m), 2 12(1,dt,J=14 2 Hz, 1 5 Hz), 2 37 (1,dt,J=14 2 Hz, 1 5 Hz), 2 52 (1,m), 4 80 (2,m) and 5 16 (1,bs), ^{13}C NMR ($CDCl_3$) δ 13 89, 22 68, 24 45, 24 57, 26 98, 37 21, 39 09, 40 09, 40 80, 49 88, 67 32, 103 84, 124 75, 142 98 and 158 47

(1R,2S,3R,5S)-2,3-Epoxy-8-methylene-2,6,6 trimethyl tricyclo[3 3 3 $0^{1,5}$]undecane (14). To a slurry of Na_2HPO_4 (400 mg, 2 8 mmol) and 13 (205 mg, 1 01 mmol) in CH_2Cl_2 (4 mL) at 0 °C was added MCPBA (198 mg, 1 15 mmol) The mixture was stirred for 30 min at this temperature then quenched with $NaHCO_3$ solution The aqueous phase was extracted with CH_2Cl_2 The combined organic extracts were washed with saturated $NaHCO_3$ solution, brine, dried ($MgSO_4$) and concentrated Chromatography on silica gel 60 eluted with 19 1 hexanes Et_2O gave 134 mg (0 61 mmol, 61%) of 14 as a pale yellow oil, $[\alpha]^{24}_D$ +26° (c 3 53, $CHCl_3$), ^1H NMR ($CDCl_3$) δ 0 85 (3,s), 0 91 (3,s), 1 40 (3,s), 1 55-2 10 (8,m), 2 30-2 45 (2,m), 3 35 (1,d,J=1 7 Hz), 4 85 (1,m) and 4 95 (1,m), ^{13}C NMR ($CDCl_3$) δ 15 25, 22 99, 24 93, 28 37, 35 81, 35 88, 37 55, 41 31, 49 89, 67 03, 68 01, 69 46, 70 66, 108 74 and 157 00

(1R,2S,5S)-8-Methylene-2,6,6-trimethyltricyclo[3 3.3 $0^{1,5}$]undecan-3-one (15) To a solution of 14 (134 mg, 0 61 mmol) in CH_2Cl_2 (5 mL) at 0 °C was added BF_3 Et_2O (132 μL, 1 10 mmol) The resulting solution was stirred for 5 min then quenched with water This mixture was extracted with Et_2O and the organic phase washed with brine, dried ($MgSO_4$) and concentrated Chromatography on silica gel 60 eluted with 9 1 hexanes Et_2O gave 71 mg (0 32 mmol, 53%) of 15 as a pale yellow oil, $[\alpha]^{24}_D$ +10 3°(c 2 5, $CHCl_3$), ^1H NMR ($CDCl_3$) δ 0 91 (3,s), 0 95-2 05 (7 m), 1 03 (3,s), 1 16 (3,d,J=7 2 Hz), 2 12 (1,d,J=14 6 Hz), 2 48-2 67 (2,m), 2 72 (1,dd,J=19 2 Hz, 2 0 Hz) and 4 8 (2,dm,J=9 4 Hz), ^{13}C NMR ($CDCl_3$) δ 11 77, 19 51, 23 84, 26 06, 35 84, 38 70, 40 22, 45 90, 48 69, 53 54, 61 48, 62 78, 103 95, 161 88 and 221 18

(1R,5S,8S)-2,4,4,8-Tetramethyltricyclo[3.3.3.$0^{1,5}$]undec-2-en-7-one (16). To a solution of 15 (96 mg, 0 44 mmol) in benzene (8 mL) was added a single crystal of iodine (12 mg) and the resulting solution was heated at reflux for 2 h Upon cooling the solution was diluted with Et_2O and washed with $Na_2S_2O_5$, brine, dried ($MgSO_4$), and concentrated Chromatography on silica gel 60 eluted with 19 1 hexanes Et_2O gave 32 mg of recovered 18 (0 15 mmol, 34%) and 64 mg (0 29 mmol, 66%) of 16 as a pale yellow oil, $[\alpha]^{24}_D$ + 77° (c 1 26, $CHCl_3$), ^1H NMR ($CDCl_3$) δ 0 98 (3,s), 1 06 (3,s), 1 09 (3,d,J=7 1 Hz), 1 3-1 65 (5,m), 1 40 (3,m), 1 88-2 95(2,m), 2 32 (3,dq,J=7 1 Hz, 1 8 Hz), 2 82 (1,dd,J=19 3 Hz, 1 8 Hz) and 5 01 (1,bs), ^{13}C NMR ($CDCl_3$) δ 11 42, 13 57, 24 65, 25 71, 29 62, 29 92, 38 53, 46 15, 46 42, 53 41, 59 27, 69 35, 134 62, 142 24 and 221 2

(1R,5S,8R)-2,4,4,8-Tetramethyltricyclo[3.3.3.$0^{1,5}$]undec-2-ene (-)-(1). A well-stirred mixture of 16 (44 mg, 0 20 mmol), hydrazine hydrate (100 µl, 2 0 mmol) and potassium carbonate (358 mg, 2 6 mmol) in diethylene glycol (2mL) was heated at 160° for 2 h then at 240°C for a further 2 h Upon cooling, the reaction mixture was diluted with water and extracted with hexanes The combined organic extracts were washed with water, dried ($MgSO_4$) and concentrated Chromatography on silica gel 60 eluted with hexanes gave 27 mg (0 13 mmol, 66%) of (-)- 1 as a colorless oil, $[\alpha]^{25}$ D -4 1° (c 1 6, $CHCl_3$), ^1H NMR ($CDCl_3$) δ 0 96 (6,s), 0 97 (3,d,J=6 Hz), 1 08 - 2 18 (8,m), 1 58 (3,d,J=1 5 Hz) and 4 81 (1,m)

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19 Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research Partial support of this research by the American Heart Association, Arizona Affiliate, is gratefully acknowledged