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Supporting Information

69451 Weinheim, Germany

Direct Synthesis of (+)-Erogorgiaene by Means of a Kinetic Enantiodifferentiating Step

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Section A: General Information.

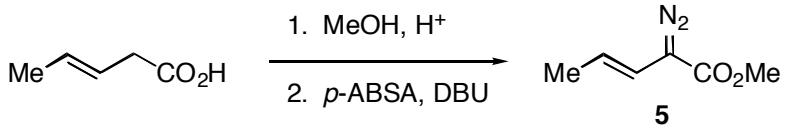
Commercial reagents from Aldrich Chemical Company and Acros Organics were purchased at the highest commercial purity and used without further purification unless otherwise stated. All moisture sensitive reactions were performed using glassware that was oven dried overnight (60°C) and then flame dried under vacuum prior to use. Tetrahydrofuran (THF), hexanes, dichloromethane (DCM), acetonitrile and toluene were used either directly from the solvent purification system (solvent was passed through two columns with activated alumina) purchased from MBRAUN, or distilled following the procedures of Perrin and Armarego.[1] 2,2-dimethylbutane (2,2-DMB) was purchased from Lancaster Synthesis, passed through activated silica gel (heated to 120°C overnight) and distilled from sodium under argon. All other solvents were of reagent grade. Hydrogenations were carried out using a Parr hydrogenator at the specified H_2 pressure or using H_2 filled balloons. Reaction solvents used in rhodium carbenoid transformations were degassed by bubbling argon gas through for 15 to 20 minutes prior to use. Organic reaction mixtures were concentrated using a Buchi rotary evaporator. Optical rotations were measured using a Jasco DIP-370 digital polarimeter. Analytical TLC was performed on 250μm Whatman silica gel (Aluminum backing, UV 254 nm) plates using UV light and phosphomolybdic acid (10% in ethanol) as visualizing agents. Column chromatography was carried out using E. Merck silica 60 (230-400 mesh) or ICN 60 (32-64 mesh) following the method of Still.[2]

[1] D. D. Perrin, W. L. F. Armarego, In *Purification of Laboratory Chemicals*; 3rd ed.; Pergamon: Oxford, 1988
[2] W. C. Still, M. Kahn, A. Mitra, A. J. *J. Org. Chem.* **1978**, *43*, 2923

^{1}H NMR spectra were recorded on a Varian Nuclear Magnetic Resonance spectrometer at 300, 400, or 500 MHz and ^{13}C spectra were recorded at 75 or 125 MHz, with the sample solvent being $CDCl_3$, unless otherwise noted. The following abbreviations are used to explain the multiplicities: s, singlet; d, doublet; t, triplet; q, quartet; dd, doublet of doublets; dt, doublet of triplets; dq, doublet of quartets; ddd, doublet of doublet of doublets. Infrared spectra were obtained on a Nicolet Impact 420 FT-IR spectrometer. High-resolution mass spectra were obtained from the Mass Spectroscopy Facility at the University at Buffalo, The State University of New York. Diastereomeric ratios were determined by values derived from the 500 MHz ^{1}H NMR spectra of the crude reaction. Enantiomeric excess was determined by high performance liquid chromatography (HPLC) using chiral analytical columns (specified for each compound) with 2-propanol (ipa) in hexane as the eluent (% ipa specified for each compound).

Section B: Preparation of Diazo compounds

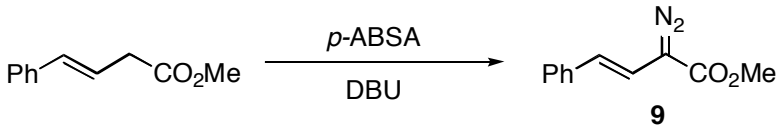
Preparation of starting materials (diazo compounds).



5

Methyl (*E*)-2-diazo-3-pentenoate (5): To a stirred solution of *trans*-pent-3-enoic acid (3.0 g, 30.0 mmol) in methanol (20 mL) was added concentrated H_2SO_4 (1 mL). The reaction mixture was stirred for 12 h at room temperature and then slowly neutralized with saturated sodium bicarbonate ($NaHCO_3$). The aqueous layer was extracted with dichloromethane and the combined organic layers were washed with brine and dried

(Na_2SO_4). The solvent was removed under reduced pressure and the remaining clear oil (3.30 g, 96% yield) was used for the next step, without further purification. To a stirred solution of methyl *trans*-pent-3-enoate (1.0 g, 8.76 mmol) and *p*-ABSA[3] (3.15 g, 13.1 mmol) in CH_3CN (20 mL) cooled to 0ºC, was added DBU (2.66 g, 17.5 mmol) in one portion. The reaction mixture was allowed to warm to room temperature over 7 h then quenched with saturated ammonium chloride (NH_4Cl). The aqueous layer was extracted with diethyl ether and the combined organic layers were washed with brine and dried (Na_2SO_4). The solvent was removed under reduced pressure and the residue was purified by flash chromatography (SiO_2, pentane) to give the title compound (**5**) (0.80 g, 65% yield) as an orange oil, which was stored in pentane below –10ºC until ready for use. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.77-5.74 (d, 1H, J = 16.0 Hz), 5.37-5.33 (m, 1H), 3.82 (s, 3H), 1.86-1.84 (d, 3H, J = 6.0 Hz). The spectroscopic data are consistent with the previously reported data.[4]



9

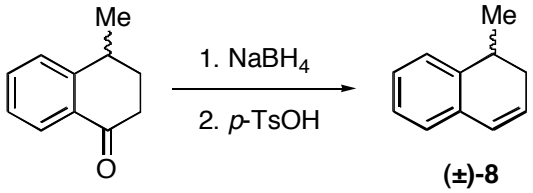
Methyl (*E*)-2-diazo-4-phenyl-3-butenoate (9): Prepared according to the procedure of Davies.[5] To a stirred solution of methyl *trans*-4-phenylbut-3-enoate (1.0 g, 5.68 mmol) and *p*-ABSA[3] (1.64 g, 6.82 mmol) in CH_3CN (150 mL) cooled to 0ºC, was added DBU (0.95 g, 6.25 mmol) in one portion. The reaction mixture was allowed to warm to room temperature over 7 h then quenched with saturated ammonium chloride (NH_4Cl). The aqueous layer was extracted with diethyl ether and the combined organic layers were

[3] *p*-Acetamidobenzenesulfonyl azide (*p*-ABSA) was prepared using the procedure outlined in : J. S. Baum, D. A. Shook, H. M. L. Davies, D. H. Smith, *Synth. Commun.* **1987**, *17*, 1709.
[4] H. M. L. Davies, B. Hu, *J. Org. Chem.* **1992**, *57*, 3186
[5] H. M. L. Davies, T. J. Clark, H. D. Smith, H. D. *J. Org. Chem.* **1991**, *56*, 3817

washed with brine and dried (Na_2SO_4). The solvent was removed under reduced pressure and the residue was triturated with a solution of pentane/diethyl ether (1:1). The solid was filtered off and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (SiO_2, pentane/diethyl ether (15:1)) to give the title compound (**9**) (0.92 g, 80% yield) as an orange oil, which was stored neat at –10°C until ready for use. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36-7.20 (m, 5 H), 6.50 (d, 1H, *J* = 16.0 Hz), 6.22 (d, 1H, *J* = 16.0 Hz), 3.85 (s, 3H). The spectroscopic data are consistent with the previously reported data.[5]

Section C: Preparation of Dihydronapthalenes

Preparation of starting materials (substrates).



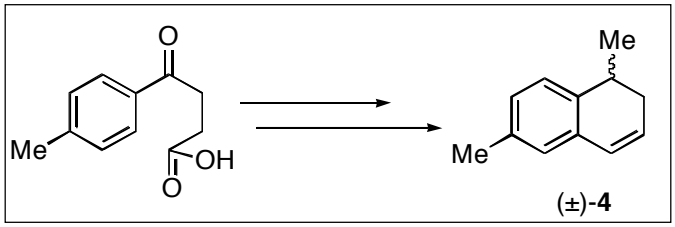
(±)-8

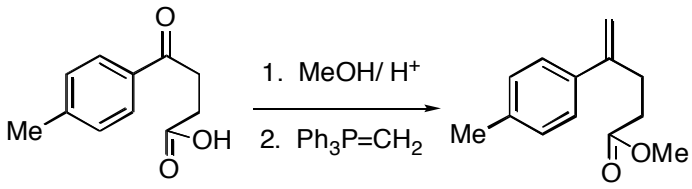
1,2-dihydro-1-methylnaphthalene(±)-8: Prepared using a similar procedure to that reported by Ferraz.[6] To a stirred solution of commercially available 4-methyl-α-tetralone (0.50 g, 3.12 mmol) in methanol (50 mL) was added $NaBH_4$ (0.35 g, 9.36 mmol) portionwise. The reaction mixture was followed by TLC and after complete consumption of the starting material (approx. 2 h), was quenched with saturated $NaHCO_3$. The aqueous layer was extracted with diethyl ether, dried ($MgSO_4$), filtered and the solvent was removed under reduced pressure. The crude alcohol was dissolved in toluene (15 mL) and a few crystals of *p*-TsOH were added. The reaction mixture was stirred overnight, then neutralized by slow addition of saturated sodium bicarbonate ($NaHCO_3$)

[6] H. M. C. Ferraz, L. F. Silva Jr, T. O. Vieira, *Tetrahedron*, **2001**, *57*, 1709.

and extracted with diethyl ether. The combined organic layers where washed with brine, dried ($MgSO_4$), filtered, and the solvent was removed under reduced pressure. The product was purified by flash chromatography (SiO_2, hexanes) to give the title compound **8** as a clear oil (0.35 g, 78% yield). The title compound is volatile and cannot be dried for long periods (>30 min) under high vacuum. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (m, 3 H), 7.03 (br m, 1 H), 6.46 (d, 1H, *J* = 9.6 Hz), 5.97 (dt, 1H, *J* = 9.6, 4.8 Hz), 2.96 (sextet, 1H, *J* = 7 Hz), 2.54-2.44 (m, 1H), 2.18-2.10 (m, 1H), 1.25 (d, 3H, *J* = 6.8 Hz). The spectroscopic data are consistent with the previously reported data.[6]

*Preparation of 1,2-dihydro-1,6-dimethylnaphthalene(±)-***4**

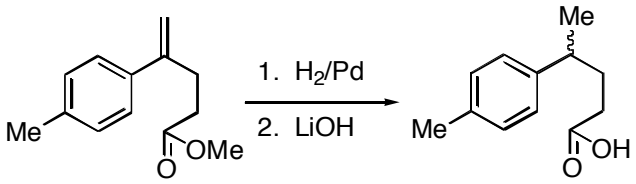




To a stirring solution of commercially available 4-oxo-4-*p*-tolylbutanoic acid (1.0 g, 5.20 mmol) in methanol (20 mL) was added concentrated H_2SO_4 (1 mL). The reaction mixture was stirred for 12 h at room temperature and then slowly neutralized with saturated sodium bicarbonate ($NaHCO_3$). The aqueous layer was extracted with diethyl ether and the combined organic layers were washed with brine and dried (Na_2SO_4). The solvent was removed under reduced pressure and the remaining white solid (0.99 g, 92% yield) was used for the next step, without further purification. ^{1}H NMR (500 MHz,

$CDCl_3$) δ 7.88 (d, *J* = 8.0 Hz, 2 H), 7.27 (d, *J* = 6.0 Hz, 2 H), 3.71 (s, 3H), 3.30 (dd, 2H, *J* = 6.5, 6.5 Hz), 2.76 (dd, 2H, *J* = 6.5, 7.0 Hz), 2.41 (s, 3H). The spectroscopic data are consistent with the previously reported data.[7]

To a cloudy white suspension of methyl triphenylphosphonium bromide (7.14 g, 19.9 mmol) in THF (35 mL) at room temperature was added KO^{t}Bu (2.02 g, 17.9 mmol). The reaction changed color to yellow upon addition of base, and was allowed to stir for 15 min before addition of a THF solution (20 mL) of the ester (2.06g, 10.0 mmol). The yellow color of the reaction mixture dissipated over 2 hours and after complete consumption of the ester (followed by TLC) the reaction was quenched with water. The aqueous layer was extracted with diethyl ether and the combined organic layers were washed with brine and dried ($MgSO_4$). The solvent was removed under reduced pressure, and the residue was purified using flash chromatography (SiO_2, pentane:diethyl ether (9:1 to 5:1)) to give the alkene (1.66 g, 81% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 (d, 2H, *J* = 10.0 Hz), 7.14 (d, 2H, *J* = 10.0 Hz), 5.28 (s, 1H), 5.04 (dd, 1H, *J* = 1.5 Hz), 3.66 (s, 3H), 2.82 (dd, 2H, *J* = 11.0, 8.0 Hz), 2.48 (dd, 2H, *J* = 9.5, 7.5 Hz), 2.34 (s, 3H). The spectroscopic data are consistent with the previously reported data.[7]

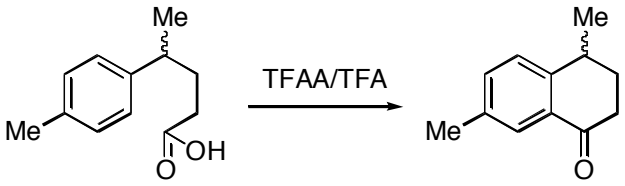


To a solution of the alkene (1.66 g, 8.13 mmol) in ethanol (45 mL) was added palladium on carbon (10 mol%) and pressurized to 30 psi of hydrogen for 3 h. The reaction mixture was then filtered through a pad of celite, washed with diethyl ether and concentrated under reduced pressure to give a clear oil (1.65 g, 98% yield), which

[7] X-X. Xu, H-Q. Dong, *J. Org. Chem.* **1995**, *60*, 3039.

required no further purification. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.10 (d, 2H, *J* = 7.5 Hz), 7.06 (d, 2H, *J* = 8.0 Hz), 3.62 (s, 3H), 2.68 (m 1H), 2.32 (s, 3H), 2.19 (m, 2H), 1.89 (m, 2H), 1.25 (d, 3H, *J* = 7.0 Hz). The spectroscopic data are consistent with the previously reported data.[8]

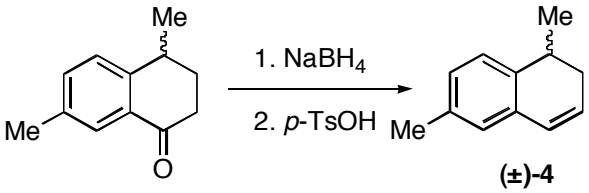
A solution of the ester (1.65 g, 8.00 mmol) was prepared in a mixture of THF:MeOH:H_2O (2:1:1), to which was added LiOH (1.34 g, 32.0 mmol). The reaction mixture was heated to 50°C for 3 hours, and then allowed to cool to room temperature. 10% aqueous hydrochloric acid was added dropwise to the reaction mixture until the pH of the solution reached pH 3. The aqueous layer was then extracted with diethyl ether, dried using $MgSO_4$ and filtered to give the carboxylic acid as an oil (1.50 g, 98% yield) which was used immediately for the next step.



Following the procedure reported by Zubaidha,[9] a solution of trifluoroacetic anhydride (6.55 g, 31.2 mmol) in trifluoroacetic acid (1.5 mL) was prepared and added to the carboxylic acid (1.50 g, 7.80 mmol) which was cooled to 0°C. The reaction mixture was allowed to stir overnight. Water (3 mL) was added to the reaction mixture while the reaction mixture was stirring and the acid was neutralized by the portionwise addition of solid $NaHCO_3$. After all the acid was neutralized, concentrated sodium hydroxide was added until the pH reached pH 10, and the reaction mixture was allowed to stir for 2 hours. The orange aqueous mixture was extracted diethyl ether, dried with $MgSO_4$ and

[8] M. Ono, Y. Ogura, K. Hatogai, H. Akita, *Bull. Chem. Soc. Jpn.*, **2001**, *49*, 1581.
[9] P. K. Zubaidha, S. P. Chavan, U. S. Racherla, N. R. Ayyangar, *Tetrahedron*. **1991**, *47*, 5759.

concentrated under reduced pressure to give the tetralone as a pale yellow oil (0.867 g, 64% yield), which did not require further purification. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (br s, 1 H), 7.33 (dd, 1H, *J* = 8.0, 8.5 Hz), 7.22 (dd, 1H, *J* = 7.5 Hz,), 3.05 (m, 1H), 2.76 (m, 1H), 2.60 (m, 1H), 2.36 (s, 3H), 2.23 (m, 1H), 1.88 (m, 1H), 1.38 (d, 3H, *J* = 7.0 Hz). The spectroscopic data are consistent with the previously reported data.[10].



(±)-4

1,2-dihydro-1,6-dimethylnaphthalene(±)-4: Following a similar procedure to that reported by Ferraz.[6] To a stirred solution of 4-methyl-α-tetralone (0.867 g, 4.98 mmol) in methanol (20 mL) was added $NaBH_4$ (0.56 g, 14.9 mmol) portionwise. The reaction mixture was followed by TLC and after complete consumption of the starting material (approx. 2 h), was quenched with saturated $NaHCO_3$. The aqueous layer was extracted with diethyl ether, dried ($MgSO_4$), filtered and the solvent was removed under reduced pressure. The crude alcohol was dissolved in toluene (25 mL) and a few crystals of *p*-TsOH were added. The reaction mixture was stirred overnight, then neutralized by slow addition of saturated sodium bicarbonate ($NaHCO_3$) and extracted with diethyl ether. The combined organic layers where washed with brine, dried ($MgSO_4$), filtered, and the solvent was removed under reduced pressure. The product was purified by flash chromatography (SiO_2, hexanes) to give the title compound **4** as a clear oil (0.479 g, 61% yield). The title compound is volatile and cannot be dried for long periods (>30 min) under high vacuum. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.06 (d, 1H, *J* = 8.0 Hz), 6.97 (d, 1H,

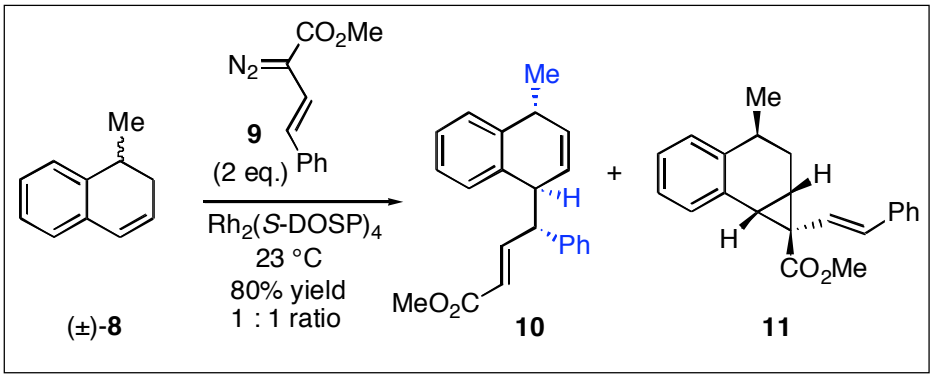
[10] S. P. Chavan, V. D. Dhondge, S. S. Patil, Y. T. S. Rao, C. A. Govande, *Tetrahedron : Asymmetry*, **1997**, *8*, 2517.

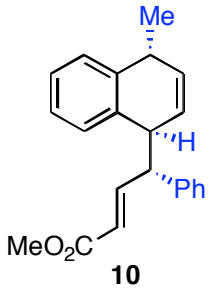
J = 7.5 Hz), 6.87 (s, 1H), 6.40 (d, 1H, *J* = 9.5 Hz), 5.95 (dt, 1H, *J* = 9.5, 4.5 Hz), 2.89 (m, 1H), 2.44 (m, 1H), 2.31 (s, 3H), 2.11 (m, 1H), 1.22 (d, 3H, *J* = 7.0 Hz). The spectroscopic data are consistent with the previously reported data.[11]

[11] K. Adachi, M. Mori, *Bull. Chem. Soc. Jpn.* **1983**, *56*, 651.

Section D: Experimental Procedures for Rhodium(II) Catalyzed Reactions

Products from Rhodium(II) catalyzed reactions.



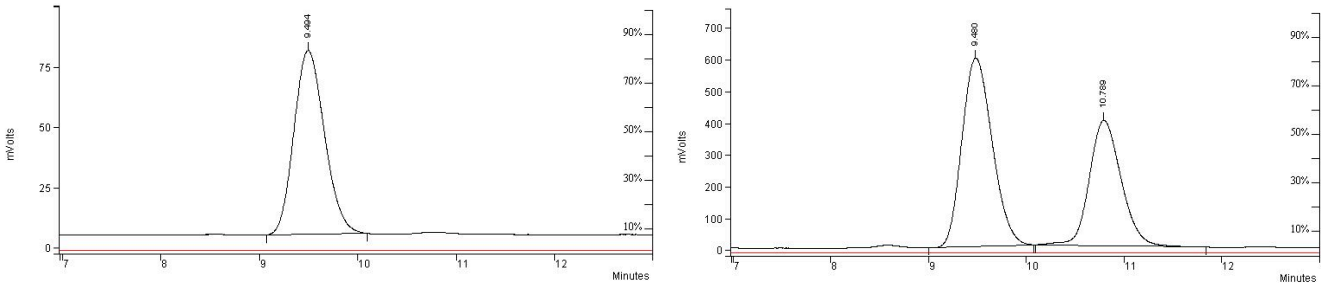


(*R*,2*E*)-methyl 4-((1*R*,4*S*)-1,4-dihydro-1-methylnaphthalen-4-yl)-4-phenylbut-2-enoate (10). To a flame dried 25 mL round bottom flask with a magnetic stir bar was added 1,2-dihydro-1-methylnaphthalene(±)-**8** (51 mg, 0.354 mmol) and Rh_2(*S*-DOSP)$_4$ (13.3 mg, 7x10^{-3} mmol), dissolved in 2,2-DMB (2 mL) under argon at room temperature. In a 10 mL syringe a solution of methyl *E*-2-diazo-4-phenyl-3-butenoate **9** (143 mg, 0.707 mmol) was prepared in 2,2-DMB (5 mL). The solution of diazo compound was added via syringe pump at a rate of 2.4 mL/h (~2 h addition time). After the diazo addition was complete the reaction mixture was allowed to stir for an additional 0.5 h, the solvent was removed under reduced pressure. Crude ^{1}H NMR showed a 1:1 ratio of products **10 : 11,** >98% de for both products. Purification by column chromatography (SiO_2, pentane : ether (17 : 1)) gave a combined mass of 90.1 mg (80% yield) in three

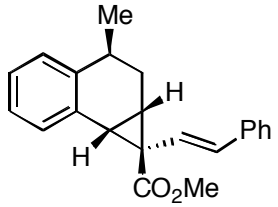
fractions (39 mg of **10**, 42 mg of **11** and 9.1 mg as a mixture of **10** and **11**): 39 mg (35% yield) of **10** as a clear oil. R_f = 0.51 (6:1 pentane:ether) 98% *ee* by HPLC using Chiralcel OD-H, 0.7 mL/min., 1.0% 2-propanol in hexane, t_R = 9.4 (minor) and 10.7 (major) min, UV 254 nm). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (dd, 1H, *J* = 15.5, 8.0 Hz), 7.20-7.10 (m, 8 H), 6.90 (br dd, 2H, *J* = 8.0, 1.5 Hz), 5.87 (m, 1H), 5.82 (dd, 1H, *J* = 17.0, 1.5 Hz), 3.90 (br m, 1H), 3.76 (br m, 1H), 3.72 (s, 3H), 2.66 (br m, 1H), 1.26 (d, 3H, *J* = 7.5 Hz). This material was directly submitted to the hydrogenation step because it had a tendency to undergo a retro-Cope rearrangement. All other spectroscopic data was obtained on hydrogenated compound **15**.

10 from Rh_2(*S*-DOSP)$_4$ (98% *ee*) catalyzed reaction

10 from Rh_2(*S*-DOSP)$_4$&Rh_2(*R*-DOSP)$_4$ catalyzed reaction

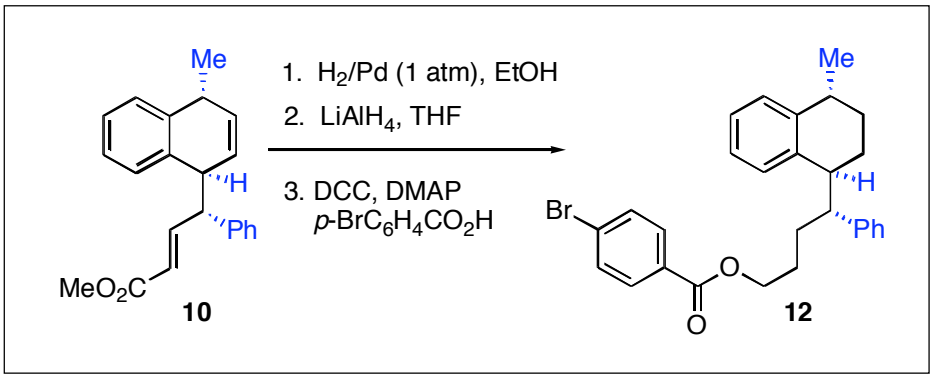


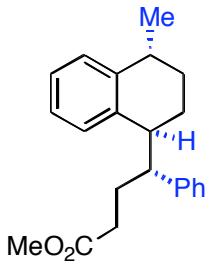
HPLC traces of **10**.



11

(1*R*,1a*S*,3*S*,7b*S*)-methyl-1a,2,3,7b-tetrahydro-3-methyl-1-styryl-1*H*-cyclopropa[*a*]naphthalene-1-carboxylate (**11**). 42 mg (37% yield) of **11** as a clear oil R_f = 0.55 (6:1 pentane:ether) (>98% de by ^{1}H NMR), 98% *ee* by HPLC using Chiralcel OD-H, 0.7 mL/min., 1.0% 2-propanol in hexane, t_R = 9.4 (minor) and 10.4 (major) min, UV 254 nm). $[\alpha]_D^{25}$ = -1.60 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 (dd, 1H, *J* = 7.0, 1.0 Hz), 7.22-7.18 (m, 5H), 7.15 (dd, 1H, *J* = 6.5, 1.5 Hz), 7.08 (dd, 2H, *J* = 7.5, 7.0 Hz), 6.23 (d, 1H, *J* = 16.5 Hz), 5.83 (d, 1H, *J* = 16.0 Hz), 3.73 (s, 3 H), 2.97 (d, 1H, *J* = 9.5 Hz), 2.61 (m, 1H), 2.35 (m, 1H), 2.00 (m, 1H), 1.86 (m, 1H), 1.26 (d, 3H, *J* = 7.0 Hz), ^{13}C NMR (75 MHz; $CDCl_3$): δ 174.5, 142.3, 137.4, 135.9, 131.7, 130.7, 128.4, 127.3, 127.0, 126.9, 126.2, 126.0, 121.4, 52.4, 31.7, 29.9, 29.6, 26.6, 26.3, 22.3; FTIR (CH_2Cl_2) 3027, 2958, 2922, 2871, 2851, 1717, 1492, 1435, 1265, 1237 cm^{-1}; HRMS (EI) *m/z* calcd for $[M]^+$ $(C_{22}H_{22}O_2)^+$: 318.1614 found: 318.1602.





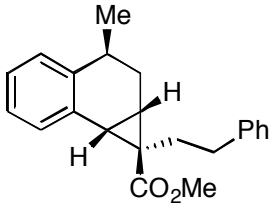
15

(*R*)-methyl-4-((1*R*,4*S*)-1,2,3,4-tetrahydro-1-methylnaphthalen-4-yl)-4-phenylbutanoate (15).[12] To a flame dried 25 mL round bottom flask with a magnetic stir bar was added 1,2-dihydro-1-methylnaphthalene(±)-**8** (72 mg, 0.50 mmol) and Rh_2(*S*-DOSP)$_4$ (13 mg, 6.9x10^{-3} mmol), dissolved in 2,2-DMB (2 mL) under argon at room temperature. In a 10 mL syringe a solution of methyl *E*-2-diazo-4-phenyl-3-butenoate **9** (120 mg, 0.59 mmol) was prepared in 2,2-DMB (5 mL). The solution of diazo compound was added via syringe pump at a rate of 2.4 mL/h (~2 h addition time). After the diazo addition was complete the reaction mixture was allowed to stir for an additional 0.5 h, the solvent was removed under reduced pressure. Crude ^{1}H NMR showed a 1:1 ratio of products **10 : 11,** >98% de for both products.

The crude reaction mixture was taken up in ethanol (20 mL) and palladium on carbon (Pd/C) (0.10 g, 10% Pd) was added. The reaction mixture was purged with H_2 gas using

[12] Due to the tendency of product **10** to readily undergo the retro-Cope rearrangement, compound **15** was isolated by conducting a 2-step 1-pot procedure (rhodium(II) mediated C-H/Cope rearrangement followed by global hydrogenation).

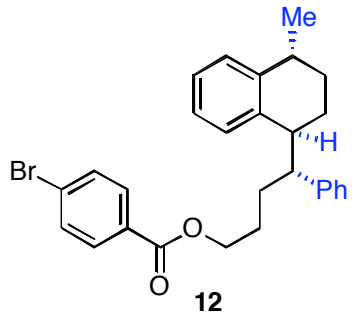
a water aspirator and a balloon filled with hydrogen gas. The reaction mixture was kept under a H_2 atmosphere (1 atm) for 5 hours before it was passed through a pad of celite. The celite pad was further washed with diethyl ether, and the combined solutions were concentrated in vacuo. Purification by column chromatography (SiO_2, pentane : ether, 17 : 1) gave a combined mass of 125 mg (78% yield): 50 mg (31% yield) of **15** as a clear oil R_f = 0.55 (6:1 pentane:ether) (>98% de); $[\alpha]_D^{25}$ = -2.50 (*c* = 0.4, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30-7.10 (m, 9H), 3.54 (s, 3H), 2.98 (br m, 1H), 2.80 (br m, 2H), 1.94 (br m, 4H), 1.68 (m, 1H), 1.49 (m, 1H), 1.30-1.22 (m, 2H), 1.20 (d, 3H, *J* = 7.0 Hz). ^{13}C NMR (75 MHz; $CDCl_3$): δ 174.0, 142.9, 142.7, 138.8, 130.5, 128.4, 127.9, 126.3, 126.2, 124.8, 51.3, 49.4, 44.4, 32.8, 31.3, 29.7, 29.4, 27.0, 23.3, 21.9; FTIR (CH_2Cl_2) 2951, 2926, 2902, 2870, 1736, 1454, 1369, 1166 cm^{-1}; HRMS (EI) *m/z* calcd for $[M+ Na]^+$ $(C_{22}H_{26}O_2Na)^+$: 345.1825 found: 345.1825.



18

(1*R*,1a*S*,3*S*,7b*S*)-methyl-1a,2,3,7b-tetrahydro-3-methyl-1-phenethyl-1*H*-cyclopropa-[*a*]naphthalene-1-carboxylate (**18**). 65 mg (40% yield) of **18** as a clear oil. R_f = 0.57 (6:1 pentane:ether) $[\alpha]_D^{25}$ = -12.4 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27 (m, 1H), 7.18-7.06 (m, 6H), 6.89 (d, 2H, *J* = 7.0 Hz), 3.78 (s, 3H), 2.75 (m, 1H), 2.69 (d, 1H, *J* = 9.5 Hz), 2.65 (m, 2H), 2.12 (m, 1H), 2.05 (ddd, 1H, *J* = 14.5, 9.5, 2.0), 1.76 (dt, 1H, *J* = 10.5, 5.0 Hz), 1.74 (m, 1H), 1.53 (m, 1H), 1.28 (d, 3H, *J* = 7.0 Hz); ^{13}C NMR (75

MHz; $CDCl_3$): δ 175.3, 144.1, 142.6, 131.1, 130.9, 128.3, 128.2, 127.8, 126.9, 126.2, 125.6, 51.9 34.4, 33.7, 32.8, 27.7, 26.9, 25.8, 23.9, 21.7; FTIR (CH_2Cl_2) 3025, 2952, 2931, 2868, 1719, 1492, 1454, 1312 cm^{-1}; HRMS (EI) *m/z* calcd for $[M]^+$ $(C_{22}H_{24}O_2)^+$: 320.1771 found: 320.1773.

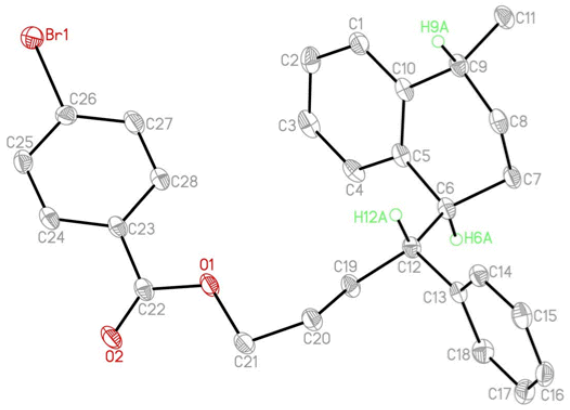


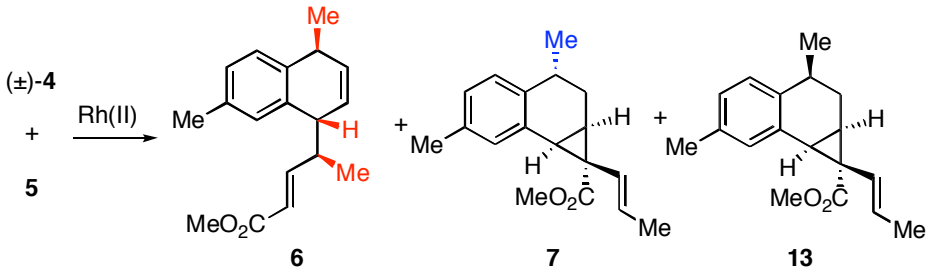
12

(*R*)-4-((1*R*,4*S*)-1,2,3,4-tetrahydro-1-methylnaphthalen-4-yl)-4-phenylbutyl-4-bromobenzoate (**12**). To a cooled (0°C) solution of **15** (40 mg, 0.12 mmol) in THF (20 mL) was added a solution lithium aluminum hydride (0.40 mL, 0.37 mmol, 1.6 M in THF) dropwise over 10 mins. The reaction mixture was quenched after 2 hours by adding a few drops of water (dropwise over 15 min). After the effervescence ceased, 10% HCl was added to dissolve the aluminum salts and extracted with diethyl ether, dried ($MgSO_4$), filtered and concentrated in vacuo. Crude ^1H NMR showed complete conversion to the alcohol. The crude alcohol was taken up in DCM (25 mL) cooled to 0°C, to which was added 4-bromo-phenylacetic acid (49.8 mg, 0.25 mmol) and DMAP (1.5 mg, 12.4 μmol). The reaction mixture was allowed to stir for 5 min, then dicyclohexylcarbodiimide (0.30 mL, 0.25 mmol, 1.0 M in DCM) was added dropwise and the reaction mixture was allowed to stir overnight. A white solid formed overnight and the slurry was filtered and washed with diethyl ether. The filtrate was washed with

brine, dried ($MgSO_4$), filtered and concentrated in vacuo. The crude product was purified by column chromatography (SiO_2, pentane : ether, 5 : 1) to give the title compound (**12**) 37.8 mg (64% yield) as a white solid. The solid was recrystallized from hexanes to give white needle-like crystals suitable for X-ray analysis. $R_f = 0.74$ (6:1 pentane:ether); $[\alpha]_D^{25}$ = +20.0 (*c* = 0.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, 2H, *J* = 8.0 Hz), 7.56 (d, 2H, *J* = 8.4 Hz), 7.29-7.17 (m, 9H), 4.17 (dd, 1H, *J*= 6.5, 6.5 Hz), 3.0 (m, 1H), 2.84 (m, 1H), 1.98 (m, 1H), 1.87 (m, 1H), 1.72 (m , 2H), 1.45 (m, 3 H), 1.31 (m, 3H), 1.20 (d, 3H, *J* = 7.0 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 165.8, 143.6, 142.7, 138.9, 131.6, 131.0, 130.6, 128.33 (2C), 128.30 (2C), 128.0, 126.2, 126.1, 124.6, 65.0, 49.4, 44.4, 31.3, 30.5, 27.1, 26.9, 23.5, 21.9; FTIR (CH_2Cl_2) 3058, 3026, 2955, 2929, 2870, 1719, 1591, 1486, 1455, 1398, 1250 cm^{-1}; HRMS (EI) *m/z* calcd for $[M]^+$ $(C_{28}H_{29}O_2{}^{81}Br)^+$: 478.1325 found: 478.1324.

ORTEP drawing of **12**

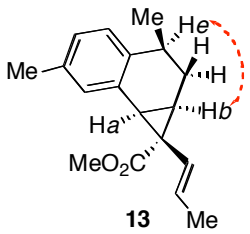




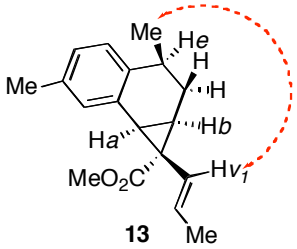
Rh(II)	yield, % (**6** + **7** + **13**)	ratio **6** : **7** : **13**
$Rh_2(OOct)_4$	73	3 : 61 : 36

To a flame dried 25 mL round bottom flask with a magnetic stir bar was added 1,2-dihydro-1,6-dimethylnaphthalene(±)-**4** (50.0 mg, 0.316 mmol) and $Rh_2(Oct)_4$ (9.9 mg, 0.013 mmol), dissolved in 2,2-DMB (5 mL) under argon at room temperature. In a 10 mL syringe a solution of methyl (*E*)-2-diazo-4-methyl-3-butenoate **5** (88.6 mg, 0.632 mmol) was prepared in 2,2-DMB (8 mL). The solution of diazo compound was added via syringe pump at a rate of 3.9 mL/h (~2 h addition time). After the diazo addition was complete the reaction mixture was allowed to stir for an additional 0.5 h, the solvent was removed under reduced pressure. Crude ^{1}H NMR showed a 3:61:36 ratio of products **6 : 7 : 13**. Purification using column chromatography (SiO_2, pentane : ether, 9 : 1) gave an inseparable mixture of **7**&**13** 62.3 mg (73% yield). Major diastereomer **7** : ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.11 (s, 1H), 7.01 (m, 2H), 5.35 (dq, 1H, *J* = 15.5, 6.5 Hz), 5.08 (d, 1H, *J* = 15.5 Hz), 3.71 (s, 3H), 2.77 (d, 1H, *J* = 9.5 Hz), 2.59 (ddq, 1H, *J* = 19.5, 13.0, 6.5 Hz), 2.30 (s, 3H), 2.21 (m, 1H), 1.94 (ddd, 1H, *J* = 14.5, 10.0, 5.0 Hz). 1.79 (m, 1H), 1.52 (d, 3H, *J* = 6.5 Hz), 1.25 (d, 3H, *J* = 7.0 Hz). Further characterization data was collected on Minor diastereomer **7:** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.08 (s, 1H), 6.96 (m, 2H), 5.47 (dq, 1H, *J* = 16.0, 6.5 Hz), 4.84 (d, 1H, *J* = 15.5 Hz), 3.72 (s, 3H), 2.85 (m, 1H), 2.68 (d, 1H, *J* = 9.5 Hz), 2.31 (m, 1H), 2.30 (s, 3H), 2.10 (m, 1H), 1.50 (d, 3H, *J* = 7.0 Hz). 1.23

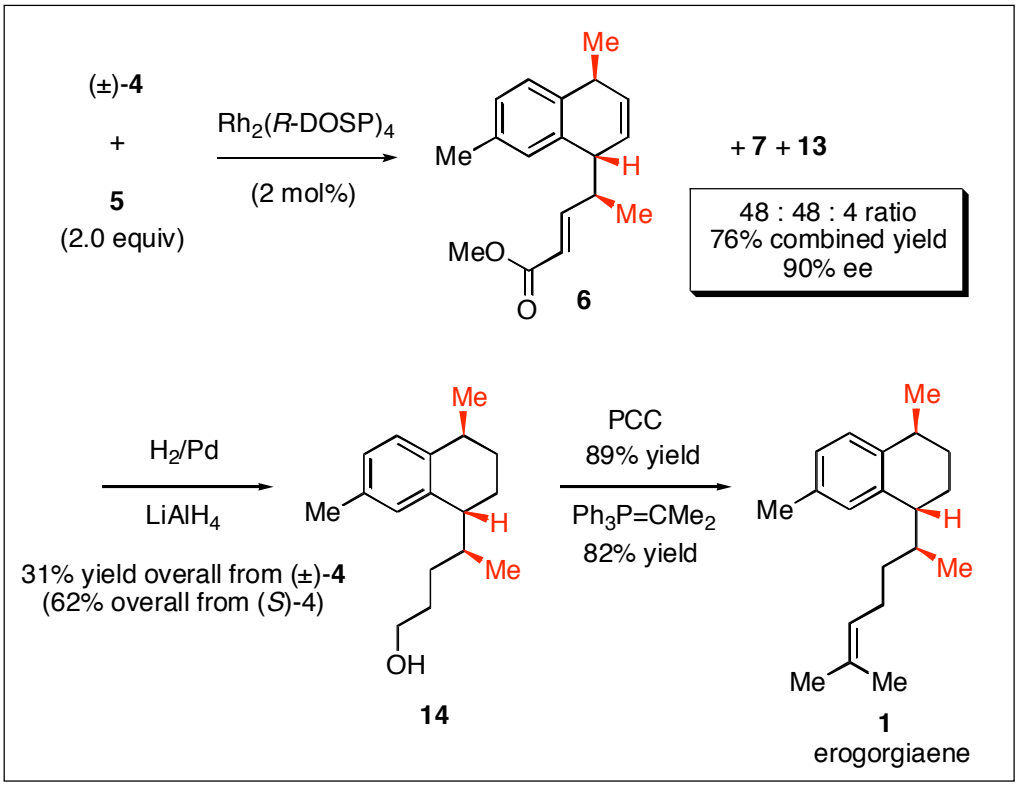
(d, 3H, J = 7.0 Hz). Relative configuration of minor diastereomer **13** was confirmed by studies, key proton irradiations are shown below.



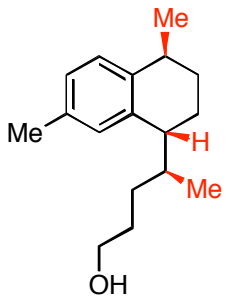
nOe observed between H*b* & H*e*



nOe observed between Hv_1 & -CH_3



Enantiomeric excess of **6** was determined after hydrogenation and reduction of **6** to **14** (90% *ee*). The experimental data are given below.



14

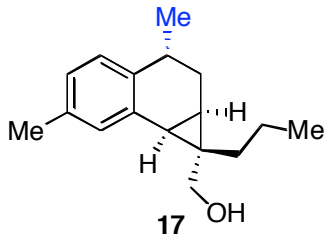
(*S*)-4-((1*S*,4*R*)-1,2,3,4-tetrahydro-1,6-dimethylnaphthalen-4-yl)pentan-1-ol (14). To a flame dried 25 mL round bottom flask with a magnetic stir bar was added 1,2-dihydro-

1,6-dimethylnaphthalene(±)-**4** (0.20 g, 1.26 mmol) and Rh_2(*R*-DOSP)$_4$ (95.0 mg, 0.050 mmol), dissolved in 2,2-DMB (5 mL) under argon at room temperature. In a 10 mL syringe a solution of methyl (*E*)-2-diazo-4-methyl-3-butenoate **5** (354 mg, 2.53 mmol) was prepared in 2,2-DMB (8 mL). The solution of diazo compound was added via syringe pump at a rate of 3.9 mL/h (~2 h addition time). After the diazo addition was complete the reaction mixture was allowed to stir for an additional 0.5 h, the solvent was removed under reduced pressure. Crude ^{1}H NMR showed a 48:48:4 ratio of products **6 : 7 : 13**, >98% de for both products. To determine the yield a separate reaction was purified by column chromatography (SiO_2, pentane ether (9:1)) to give a mixture of **6** and **7** in 76% yield (0.234 mg) (using 0.18 mg (1.13 mmol) of **4**, 0.318 mg (2.27 mmol) of **5**, and 86 mg (0.046 mmol) of Rh_2(*R*-DOSP)$_4$).

The crude reaction mixture was taken up in ethanol (20 mL) and palladium on carbon (Pd/C) (0.10g, 10% Pd) was added. The reaction mixture was pressurized with H_2 gas at 30 psi and allowed to shake for 4 h. The crude mixture was passed through a pad of celite and washed with diethyl ether and concentrated under reduced pressure.

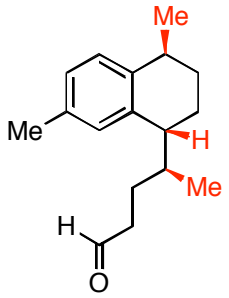
The residue was dissolved in THF (15 mL) and cooled to 0°C. Lithium aluminum hydride (2.37 mL, 3.79 mmol, 1.6M in THF) was added dropwise over 5 min and the reaction mixture was allowed to warm to room temperature over 2 h. Excess reducing agent was quenched by slow addition (dropwise) of water, and then washed with 10% aqueous hydrochloric acid. The aqueous layer was extracted with diethyl ether and the combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Purification by column chromatography (SiO_2, pentane : ether (3 : 1)) gave a combined mass of 192.2 mg (62% yield): 96.1 mg (31% yield, from reaction enantiomer of **4**; 62%

yield from **4**) of **14** as a clear oil. R_f = 0.22 (3:1 pentane:ether) 90% *ee* by HPLC using Chiralcel OD-H, 0.7 mL/min., 1.0% 2-propanol in hexane, t_R = 23.7 (minor) and 25.4 (major) min, UV 254 nm). $[\alpha]_D^{25}$ = +36.5 (*c* = 0.81, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.14 (d, 1H, *J* = 7.5 Hz), 7.03 (br s, 1H), 6.94 (d, 1H, *J* = 8.0 Hz), 3.69 (dd, 2H, *J* = 7.0, 6.5 Hz), 2.88 (br m, 1H), 2.72 (br m, 1H), 2.30 (s, 3H), 2.14 (m, 1H), 1.92 (m, 1H), 1.82 (m, 1H), 1.68 (m, 4H), 1.64-1.33 (m, 6H), 1.26 (d, 3H, *J* = 6.5 Hz); ^{13}C NMR (75 MHz; $CDCl_3$): δ 140.4, 139.7, 134.7, 128.0, 126.5, 126.1, 63.4, 41.7, 37.6, 32.8, 31.7, 31.1 (2C), 21.9, 21.5, 21.1, 14.6; FTIR (CH_2Cl_2) 3340, 2952, 2982, 2867, 1497, 1456, 1376, 1056 cm^{-1}; HRMS (EI) *m/z* calcd for $[M]^+$ $(C_{17}H_{26}O)^+$: 246.1982 found: 246.1978.



17

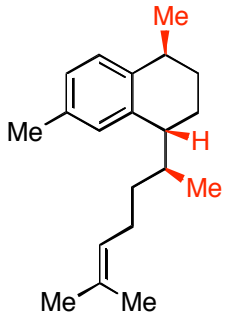
((1*S*,1a*R*,3*R*,7b*R*)-1a,2,3,7b-tetrahydro-3,6-dimethyl-1-propyl-1*H*-cyclopropa[*a*]naphthalen-1-yl)methanol (17). 95.7 mg (31% yield) of **17** as a clear oil. R_f = 0.25 (3:1 pentane:ether) $[\alpha]_D^{25}$ = -87.3 (*c* = 3.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.99 (br s, 1H), 6.95 (d, 1H, *J* = 7.5 Hz), 6.90 (d, 1H, *J* = 7.5 Hz), 3.67 (d, 1H, *J* = 11.0 Hz), 3.36 (d, 1H, *J* = 11.0 Hz), 2.67 (br m, 1H), 2.28 (s, 3H), 1.95 (ddd, 1H, *J* = 14.0, 9.0, 2.5 Hz), 1.78 (d, (d, 1H, *J* = 8.5 Hz), 1.67 (dt, 1H, *J* = 11.0, 5.5), 1.49-1.46 (m, 3H), 1.27 (br m, 3H), 1.24 (d, 3H, *J* = 7.0 Hz), 0.75 (dd, 3H, *J* = 7.5, 7.0 Hz); ^{13}C NMR (75 MHz; $CDCl_3$): δ 141.2, 135.3, 133.0, 131.1, 127.0, 126.7, 69.8, 33.7, 27.3, 26.6, 23.5, 22.5, 21.0, 19.0, 16.7, 14.5; FTIR (CH_2Cl_2) 3375, 2946, 2927, 2868, 1497, 1459, 1374, 1265, 1017 cm^{-1}; HRMS (EI) *m/z* calcd for $[M]^+$ $(C_{17}H_{24}O)^+$: 244.1822 found: 244.1821.



16

(*S*)-4-((1*S*,4*R*)-1,2,3,4-tetrahydro-1,6-dimethylnaphthalen-4-yl)pentanal (16). To a stirring solution of **14** (34 mg, 0.138 mmol) in DCM (15 mL) was added pyridinium chlorochromate (0.119 g, 0.552 mmol) and the reaction mixture was allowed to stir for 12 h. Celite was then added and the reaction mixture was passed through a pad of

celite/silica gel (mixture of 3:2) washed with DCM and concentrated under reduced pressure. The residue was purified using flash chromatography (SiO_2, pentane:diethyl ether (7:1)) to give the title compound **16** (30 mg, 89% yield) as a clear oil. R_f = 0.50 (9:1 pentane:ether); $[\alpha]_D^{25}$ = +52.6 (c = 0.81, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.82 (s, 1H), 7.13(d, 1H, J = 7.6 Hz), 6.96 (m, 2H), 2.87 (m, 1H), 2.72 (m, 1H), 2.51 (m, 2H), 2.29 (s, 3H), 1.94 (m, 1H), 1.78 (m, 1H), 1.76-1.54 (m, 4H), 1.34 (m, 1H), 1.26 (d, 3H, J = 8.5 Hz), 0.67 (d, 3H, J = 6.4 Hz); ^{13}C NMR (75 MHz; $CDCl_3$): δ 202.7, 140.3, 139.1, 134.8, 128.0, 126.6, 126.3, 42.4, 41.7, 36.9, 32.7, 31.4, 27.2, 21.9, 21.6, 21.1, 14.4; FTIR (CH_2Cl_2) 2957, 2927, 2869, 1725, 1498, 1457, 1377 cm^{-1}; HRMS (EI) m/z calcd for $[M]^+$ $(C_{17}H_{24}O)^+$: 244.1821 found: 244.1822.



1

Erogorgiaene (1).[13] To a yellow suspension of diisopropyltriphenylphosphonium iodide (0.212 g, 0.491 mmol) in THF (10 mL) cooled to 0°C was added NaHMDS (0.24 mL, 0.47 mmol, 2.0 M in THF). After 5 min a THF solution (7 mL) of aldehyde **16** (30.0 mg, 0.123 mmol) was added and the reaction mixture was allowed to stir overnight. The reaction mixture was concentrated under reduced pressure and purified using column chromatography (SiO_2, hexane) to give erogorgiaene **1** (27.2 mg, 82% yield) as a clear

[13] a) A. D. Rodriguez, C. Ramirez, *J. Nat. Prod.* **2001**, *64*, 100-102. b) R. R. Cesati, J. De Armas, A. H. Hoveyda, *J. Am. Chem. Soc.* **2004**, *126*, 96-101.

oil. R_f = 0.63 (pentane) $[\alpha]_D^{25}$ = +21.4 (*c* = 0.14, $CHCl_3$); ref. 13a lit. $[\alpha]_D^{25}$ = +24.4 (*c* = 3.2, $CHCl_3$); ref. 13b $[\alpha]_D^{20}$ = +40.6 (*c* = 0.14, $CHCl_3$); H NMR (500 MHz, $CDCl_3$) δ 7.13 (d, 1H, *J* = 7.5 Hz), 7.03 (br s, 1H), 6.94 (d, 1H, *J* = 7.5 Hz), 5.17 (br t, 1H, *J* = 6.5 Hz), 2.91-2.84 (m, 1H), 2.75-2.68 (m, 1H), 2.30 (s, 3H), 2.18-2.00 (m, 3H), 1.93 (m, 1H), 1.80 (m, 1H), 1.72 (s, 3H), 1.64 (s, 3H), 1.54 (m, 1H), 1.52-1.45 (m, 1H), 1.30 (m, 2H), 1.26 (d, 3H, *J* = 6.8 Hz), 0.63 (d, 3H, *J* = 6.8 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 140.4, 139.9, 134.7, 131.3, 128.1, 126.4, 126.0, 124.9, 41.5, 37.0, 35.2, 32.8, 31.8, 26.3, 25.7, 21.9, 21.6, 21.1, 17.7, 14.6. The spectroscopic data are consistent with the previously reported data.[13a,b]

^{1}H NMR of Erogorgiaene (*Synthetic*)