SUPPORTING INFORMATION

FOR

Enantioselective Syntheses of Tremulenediol A and Tremulenolide A

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Experimental Procedures:

Solvents and reagents were reagent-grade and used without purification unless otherwise noted. Dichloromethane (CH_2Cl_2), triethylamine (Et_3N), and diisopropylamine were distilled from calcium hydride and stored under nitrogen. Tetrahydrofuran (THF) and diethyl ether (Et_2O) were passed through a column of neutral alumina and stored under argon. Methanol (MeOH) and dimethylformamide (DMF) were passed through a column of molecular sieves and stored under argon. Toluene was passed through a column of Q5 reactant and stored under argon. All reactions were done in flame-dried glassware under nitrogen unless otherwise indicated. ^1H nuclear magnetic resonance (NMR) spectra were obtained at either 500, 400 or 300 MHz as solutions in CDCl_3 . ^{13}C NMR were obtained at either 125, 100 or 75 MHz as solutions in CDCl_3 . Chemical shifts are reported in parts per million (ppm, δ), and referenced from the solvent. Coupling constants are reported in Hertz (Hz). Spectral splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; comp, complex; and br, broad. Infrared (IR) spectra were obtained using a Perkin-Elmer FTIR 1600 spectrophotometer using sodium chloride plates as indicated, and reported as wave numbers. Low resolution chemical ionization mass spectra were obtained with a Finnigan TSQ-70 instrument. High resolution measurements were made with a VG Analytical ZAB2-E instrument. Analytical thin layer chromatography was performed using Merck 250 micron 60F-254 silica gel plates. The plates were visualized with UV light, ninhydrin, phosphomolybdic acid, *p*-anisaldehyde, and potassium permanganate. Flash column chromatography was performed according to Still's procedure (Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923) using ICN Silitech 32-63 D 60A silica gel.

13

2-(4-Benzyloxy-but-2-ynyl)-2-[3-(2S,3S)-(2-carboxycyclopropyl)-but-2-enyl]-malonic acid dimethyl ester (13). Pd(PPh₃)₄ (81 mg, 73 μmol) and PPh₃ (190 mg, 0.725 mmol) were added sequentially to a solution of **4** (100 mg, 0.725 mmol) in degassed THF (4 mL) at room temperature, and the resulting solution was stirred for 20 min. In a separate flask, **5** (462 mg, 1.59 mmol) was added to a slurry of NaH (58 mg of a 60% mineral oil suspension, 1.45 mmol) in degassed THF (4 mL) at room temperature. After stirring for 20 min at room temperature, the resulting homogeneous solution was transferred *via* cannula to the flask containing the catalyst and substrate. The mixture was heated under reflux for 4 h. The resulting dark brown solution was allowed to cool to room temperature by removal of the oil bath and then cooled to 0 °C. Aqueous 1M NaHSO₄ (8 mL) was added, and the layers were separated. The aqueous phase was extracted with CH₂Cl₂ (3 x 10 mL). The combined organic fractions were washed with saturated aqueous NaCl (10 mL), dried (Na₂SO₄) and concentrated under reduced pressure. The crude residue was purified by flash chromatography eluting with hexanes/EtOAc (2:1 to 1:1) to give 220 mg (71%) of **13** as a clear, yellow oil: ¹H NMR (500 MHz) δ 7.35-7.27 (comp, 5 H), 5.13 (t, *J* = 7.4, 1.5 Hz, 1 H), 4.57 (s 2 H), 4.07 (t, *J* = 1.0 Hz, 6 H), 3.68 (s, 3 H), 3.66 (s, 3 H), 2.83 (br s, 2 H, C9-H), 2.81 (br s, 2 H, C7-H), 1.95 (br q, *J* = 16.2, 8.1 Hz, 1 H), 1.81 (m, 1 H), 1.70 (s, 3H), 1.36 (m, 1 H), 1.10 (m, 1 H); ¹³C NMR (125 MHz) δ 175.9, 170.5, 137.5, 128.4, 128.2, 127.8, 127.8, 121.1, 82.0, 78.8, 71.2, 57.1, 52.7, 30.7, 29.7, 22.8, 19.6, 17.3, 17.3; IR (CDCl₃) 2952, 2259, 1735, 1698, 1436, 1291, 1211, 1070 cm⁻¹; mass spectrum (CI) *m/z* 429.1907 [C₁₆H₁₉O₅ (M+1) requires 429.1913] 399, 321, 279.

14

(3a*S*,7*S*)-8-Benzyloxymethyl-7-formyl-4-methyl-3,3a,6,7-tetrahydro-1*H*-azulene-2,2-dicarboxylic acid dimethyl ester (14). [Rh(CO)₂Cl]₂ (2 mg, 4.8 μmol) was dissolved in degassed toluene (2 mL), and a solution of **13** (20 mg, 0.048 mmol) in degassed toluene (5 mL) was added. The resulting mixture was heated for 30 min at 110 °C (bath temperature). The mixture was allowed to cool to room temperature by removal of the oil bath, and then filtered through a short plug of neutral alumina. The filtrate was concentrated under reduced pressure, and the crude residue was purified by flash chromatography eluting with hexanes/EtOAc (3:1) to give **17** mg (85%) of **14** as a clear, colorless oil: ¹H NMR (500 MHz) δ 9.59 (s, 1 H), 7.36-7.27 (comp, 5 H), 5.51-5.49 (m, 1 H), 4.51 (d, *J* = 11.6 Hz, 1 H), 4.46 (d, *J* = 11.8 Hz, 1 H), 4.01 (app dt, *J* = 12.1, 1.2 Hz, 1 H), 3.76 (s, 3 H), 3.74 (s, 3 H), 3.37 (br s, 1 H), 3.23 (dd, *J* = 17.3, 2.0 Hz, 1 H), 3.20 (t, *J* = 6.0 Hz, 1 H), 2.89 (dd, *J* = 16.7, 1.4 Hz, 1 H), 2.73 (ddd, *J* = 12.4, 7.4, 2.0 Hz, 1 H), 2.68-2.59 (m, 1 H), 2.35-2.29 (m, 1 H), 2.07 (t, *J* = 12.7 Hz, 1 H), 1.68 (d, *J* = 0.6 Hz, 1 H); ¹³C NMR (125 MHz) δ 200.4, 171.7, 171.4, 142.5, 138.2, 134.3, 128.4, 127.7, 127.6, 122.8, 71.9, 71.2, 57.3, 52.9, 52.8, 51.7, 44.5, 39.3, 39.3, 26.4, 24.2; IR (CDCl₃) 3022, 2954, 1732, 1698, 1436, 1374, 1291, 1211, 1071 cm⁻¹; mass spectrum (CI) *m/z* 413.1956 [C₂₄H₂₉O₆ (M+1)] 413, 305 (base), 273, 245.

bla-II-249-dist
 Pulse Sequence: s2pu1
 Solvent: CDCl3
 Ambient temperature
 File: bla-II-249
 INOVA-500 "nmr1"

Relax. delay 1.000 sec
 Pulse 10.6 degrees
 Acq. time 5.975 sec
 Width 4996.9 Hz
 8 repetitions
 OBSERVE H1, 299.888293 MHz
 DATA PROCESSING
 FT size 65536
 Total time 0 min, 55 sec

bla-II-181-repurified
Pulse Sequence: s2pu1
Solvent: CDCl3
Ambient temperature
File: bla-II-181
INOVA-500 "nmr"

Relax. delay 1.000 sec
Pulse 10.6 degrees
Acq. time 5.975 sec
Width 4996.9 Hz
8 repetitions
OBSERVE H1, 299.8882300 MHz
DATA PROCESSING
FT size 65536
Total time 0 min, 55 sec

exp3 std1h

SAMPLE DEC. 6 VT
 date Oct 15 98
 solvent CDCl3
 file exp 30
 ACQUISITION
 sfrq 300.150
 in H1 dm nm
 at 4.290 daf 200
 np 32000 dseq undefined
 sw 3730.0 dres undefined
 fb 2000 homo n
 bs 16
 tpwr 57 1b
 pw 3.0 wfile 0.10
 di 1.000 proc ft
 tof 401.0 fa not used
 nt 16 math not used
 ct 16
 alock n
 gain not used
 flags not used
 il n
 in y
 dp y
 hs nm
 DISPLAY
 sp -6.6
 wp 2399.7
 vs 162
 sc 0
 wc 250
 hzmm 9.60
 is 391.36
 rfi 2570.2
 rfp 2179.1
 th 20
 ins 1.000
 nm
 ph

b1a-II-284-f1
 Pulse Sequence: s2pu1
 Solvent: CDCl3
 Ambient temperature
 File: b1a-II-284
 INOVA-500 "nmr1"
 Relax delay 1.000 sec
 Pulse 10.6 degrees
 Acq. time 5.975 sec
 Width 4995.9 Hz
 16 repetitions
 OBSERVE H1 299.8882306 MHz
 DATA PROCESSING
 FT size 65536
 Total time 1 min, 51 sec

12

b1a-III-71-f2
 Pulse Sequence: s2pul
 Solvent: CDCl3
 Ambient temperature
 UNITplus-300 "nmr3"
 PULSE SEQUENCE
 Relax. delay 1.000 sec
 Pulse 10.6 degrees
 Acq. time 5.975 sec
 Width 4996.9 Hz
 16 repetitions
 OBSERVE H1, 299.3882301 MHz
 DATA PROCESSING
 Line broadening 0.1 Hz
 FT size 65536
 Total time 1 min, 51 sec

bia-III-82-post3102
 Pulse Sequence: szp11
 Solvent: CDCl3
 Ambient temperature
 UNITplus-300 "nmr3"
 PULSE SEQUENCE
 Relax: delay 1.000 sec
 Pulse: 10.8 degrees
 Acq. time 5.375 sec
 Width 4996.9 Hz
 16 repetitions
 OBSERVE H1, 299.8082313 MHz
 DATA PROCESSING
 Line broadening 0.1 Hz
 FI size 65536
 Total time 1 min, 51 sec

b1a-III-186-f2
 Solvent: CDCl3
 Ambient temperature
 UNITplus-300 "nmr2"
 PULSE SEQUENCE
 Relax. delay 1.000 sec
 Pulse 30.0 degrees
 Acq. time 3.813 sec
 Width 4196.4 Hz
 16 repetitions
 OBSERVE H1, 300.1390317 MHz
 DATA PROCESSING
 Line broadening 0.1 Hz
 FI size 32768
 Total time 1 minute

bls-VI-259-f1

Pulse Sequence: szpu1

Solvent: CDCl3

Ambient temperature

Mercury-400BB "nmr6"

Relax. delay 2.000 sec

Pulse 47.8 degrees

Acq. time 2.856 sec

Width 5602.2 Hz

16 Repetitions

OBSERVE H1 400.2669771 MHz

DATA PROCESSING

Line broadening 0.1 Hz

FT size 32768

Total time 1 min, 20 sec

bla-VI-272

expi s2put

SAMPLE		DEC. & VT	
date	Jan 22 2004	dfrq	499.349
solvent	CDCl3	dn	H1
file	exp	dpwr	30
ACQUISITION		dof	0
sfrq	499.349	dm	nmn
tn	H1	dmf	C
at	4.865	dseq	200
np	64000	dres	1.0
sw	6577.3	homo	27.0
fb	4000	temp	0.10
bs	32	PROCESSING	
ss	4	lb	0.10
tpwr	54	wtfile	ft
pw	2.00	proc	not used
di	297.8	fn	f
tof	84	math	not used
nt	84	werf	n
ct	n	wexp	n
alock	40	wbs	n
gain	40	wnt	n
11	n	wft	
in	y		
dp	nm		
hs	nm		
DISPLAY			
sp	-249.8		
wp	5243.1		
vs	220		
sc	0		
wc	250		
hzmm	20.37		
is	7181.32		
rf1	4129.8		
rfp	3615.3		
th	1.000		
ai	cdc	ph

Jw

b1a-VI-233

Pulse Sequence: s2pu1

Solvent: CDCl3

Ambient temperature

Mercury-400BB "nmr5"

Relax. delay 2.000 sec

Pulse 47.8 degrees

Acq. time 2.836 sec

Width 5602.2 Hz

84 repetitions

OBSERVE H1, 400.2669771 MHz

DATA PROCESSING

Line broadening 0.1 Hz

FT size 32768

Total time 5 min, 21 sec

blA-VIII-23-f2

Pulse Sequence: s2pu1

Solvent: CDCl3

Ambient temperature

Mercury-400B "nmr6"

Relax. delay 2.000 sec

Pulse 15.5 degrees

Acq. time 2.856 sec

Width 5802.4 Hz

16 Repetitions

OBSERVE H1 400.2669775 MHz

DATA PROCESSING

Line broadening 0.1 Hz

FT size 32768

Total time 1 min, 20 sec

BLA-VIII-165

exp3 s2pu1

SAMPLE		DEC. 8 VT	
date	Nov 23 2004	dfrq	499.349
solvent	CDC13	dn	H1
file	exp	dpr	30
ACQUISITION		dof	0
sfrq	499.349	dm	nmh
in	H1	dmm	C
at	4.865	dmt	200
np	64000	dseq	1.0
sw	6577.3	dres	n
fb	4000	homo	27.0
bs	32	temp	0.10
ss	54	PROCESSING	
tpwr	2.0	lb	0.10
pw	2.000	wf1le	ft
dl	297.6	proc	not used
tof	128	fn	f
nt	128	math	
ct	40	werr	
alock	n	wexp	
gain	40	wds	
FLAGS		wnt	
fl	n		
in	y		
dp	nm		
hs			
DISPLAY			
sp	-249.7		
wp	5243.1		
vs	3074		
sc	0		
wc	250		
h2mm	20.97		
is	41258.44		
rfl	504.2		
rtp	7		
th	2.000		
als			
al	cdc ph

bia VIII 168

expi s2pu1

SAMPLE DEC. & VT
 date Dec 1 2004 dfrq 499.867
 solvent CDC13 dn H1
 file exp 30
 ACQUISITION dof 0
 sfrq 499.868 dm nmh
 tn H1 dmm C
 at 3.996 dmf 200
 np 73980 dseq
 sw 9256.0 dres 1.0
 fb not used homo
 bs 32 temp 27.0
 tpwr 57 PROCESSING 0.10
 pw 1.0 lbfile
 dl 2.000 wfile ft
 tof 1124.6 proc
 nt 64 fn not used f
 ct 64 math
 gain 30 n
 il 30 weff
 in n weff
 dp n wbs
 hs Y wlt
 DISPLAY -250.0
 sp 5248.5
 wp 1603
 vs 0
 sc 250
 wc 20.99
 hzmm 14475.29
 is 1016.6
 rfi 0
 rfp 7
 th 1.000
 ins
 al ph

9 8 7 6 5 4 3 2 1 0 ppm