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Enantioselective total synthesis and correction of the absolute configuration of megislactone

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Abstract

The title compound, one of the constituents from *Iryanthera megistophylla*, has been synthesized in enantiopure forms. The stereogenic centers at C-2 and C-3 were constructed by using a chiral auxiliary induced asymmetric aldolization and the C-4 was derived from the corresponding optically active lactates. The carbon–carbon double bond in the side chain was derived from a pure *cis* vinyl iodide using a Suzuki coupling with an alkyl borane formed in situ from the corresponding terminal alkene. A previously unknown (partial) cis to trans transformation of an isolated C–C double bond in a long alkyl chain was observed during the deprotection of TBS group with CAN. Somewhat unexpectedly, the otherwise undetectable co-presence of the trans isomer of the remote double bond in a long alkyl chain was clearly revealed in ^{1}H and ^{13}C NMR in the presence of a lactone ring. The present work unambiguously shows that the absolute configuration of the natural compound is the antipode of the one originally reported. Some errors in the previous ^{1}H and ^{13}C NMR signal assignments are also corrected.
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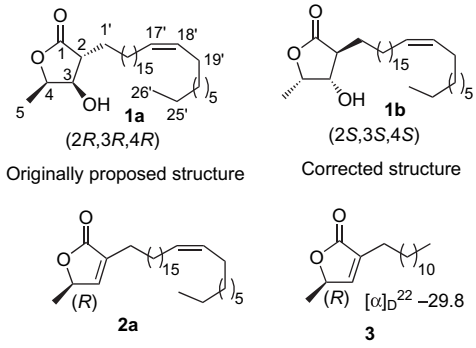
Keywords: Aldols; Lactones; Condensation; Cyclization; Heterocycles

1. Introduction

Megislactone (**1**) was isolated from the bark of *Iryanthera megistophylla* in 2002 by Hudson and Towers.[1] The original structure of this compound was proposed to be **1a**, with the relative configuration determined by NMR spectroscopy and the absolute configuration established by comparison of the optical rotation of a derivative (alleged to be **2a**) with that of a known/similar compound (**3**).

Aldol motif-containing compounds are one of the types of compounds that are particularly interesting to our group.[2] As an extension of our synthesis of blastmycinone and antimycin A_{3b}, we started the synthesis of megislactone. Herein we wish to report the details.



2. Results and discussions

Our synthetic plan is outlined in Scheme 1. In a previous[2d] work, we observed that removal of a similar TES protecting group on the hydroxyl group γ to the carbonyl group bonded to a chiral auxiliary led to immediate formation of a five-membered lactone. Although the relative configurations of the three stereogenic center-array in aldol **4a** are less favorable (unable

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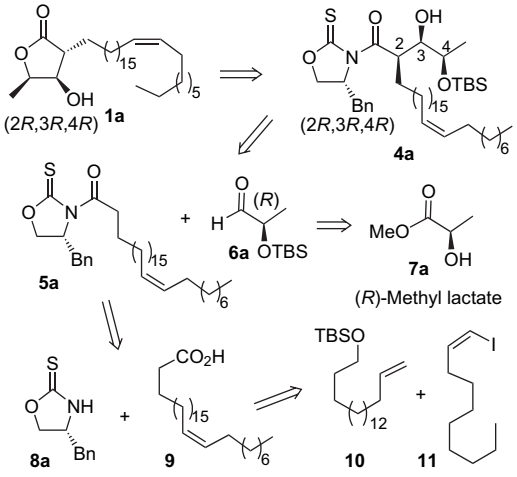


Scheme 1.

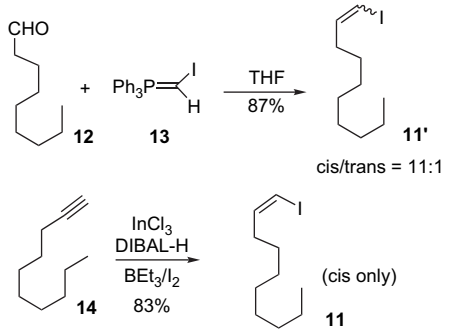
to form all-trans substituted lactone ring) than those in blastmycinone, we still thought that this concurrent deprotection–lactonization deserved a try here.

The stereogenic centers at C-2/C-3 were planned to form by an asymmetric aldolization between **5a** and **6a** under the conditions[3] developed by Crimmins. The aldehyde **6a** could be obtained from lactate **7a**, a common commercially available reagent. And the chiral auxiliary **8a** can be readily prepared from (*R*)-phenylalanine using a practical procedure[4] recently developed by our group. Thus, the major challenge of the synthetic work appears to be associated with the long chain carboxylic acid **9**.

An important and unavoidable task in the synthesis of **9** is to secure the geometry of the carbon–carbon double bond. Because this double bond is located in a long alkyl chain and remote from any other functionality, separation of the double bond isomers would be extremely difficult. Even spectroscopic detection of the presence of the double bond isomers may be unfeasible. Therefore, from the beginning Suzuki coupling[5] of a *cis* vinyl iodide was opted for constructing this isolated double bond because of its high level of stereoselectivity. Hence, it follows that the geometry of the double bond in the end product is determined by that of the vinyl iodide precursor (**11**).

One of the reliable ways to prepare pure *cis*-**11**[6] is to reduce the corresponding terminal iodoalkyne with diimide.[6] However, because both the precursor and the reagent ($KO_2CN{=}NCO_2K$) are potentially hazardous compounds, in the first try we chose to use the perhaps less selective but much more feasible protocol[7] reported by Stork and Zhao. Starting from the known aldehyde **12** and Wittig reagent **13** (prepared in situ from $Ph_3P^+CIHI^-$ by treatment with NaHMDS) the expected vinyl iodide was formed smoothly in 87% yield as a 11:1 mixture of the cis and trans isomers as shown by ^{1}H NMR. Although the desired cis isomer predominated, removal of the minor isomer by chromatography turned out to be unfeasible (Scheme 2).

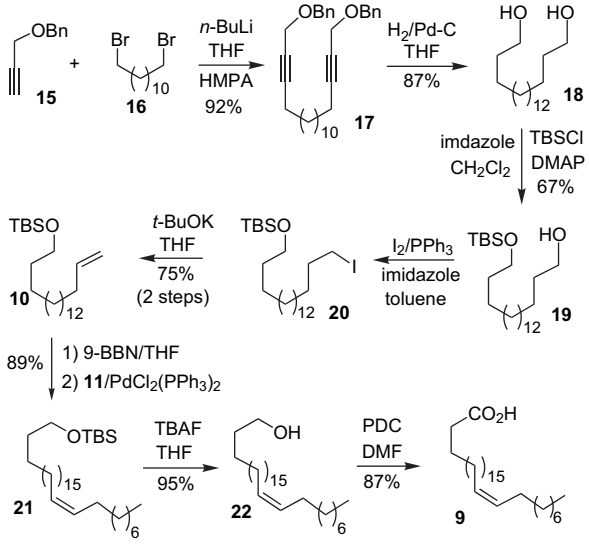
Failed to obtain the pure *cis* iodide by the Wittig olefination, our attention was next paid to the $InCl_3$/DIBAL-H/Et_3B/I_2 protocol developed by Oshima[8] and co-workers. Following the procedure of the literature with commercially



Scheme 2.

available **14** as the starting material, the anticipated **11** was isolated in 83% yield, with the content of the trans isomer well below the detection limits of 300 MHz ^{1}H NMR.

Another fragment (**10**) needed for the Suzuki coupling was synthesized as shown in Scheme 3. Alkylation of the known propargyl ether **15**[9] with commercially available dibromide **16** led to **17** in 92% yield. Exposure of **17** to H_2 (50 atm)/Pd–C for 3 days led to saturation of the triple bonds and concurrent removal of the benzyl protecting groups. One of the two hydroxyl groups in the known diol **18**[10] was then protected as TBS (*tert*-butyldimethylsilyl) ether, leaving the other ready for transformation into the corresponding iodide. After the subsequent elimination mediated by *t*-BuOK in THF, the terminal alkene **10** was obtained in 75% yield from **19**.

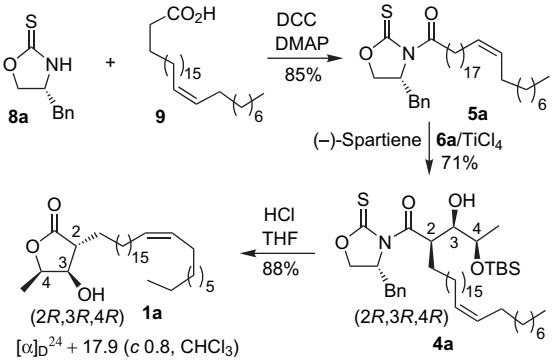


Scheme 3.

The Suzuki coupling is usually performed with $PdCl_2$(dppf) or $Pd(PPh_3)_4$ as the catalyst. However, in the present work the coupling product was also obtained in good yields using $PdCl_2(PPh_3)_2$,[11] which is readily accessible and more stable than $Pd(PPh_3)_4$.

The isolated **21** was then treated with *n*-Bu_4NF (TBAF) to remove the TBS protecting group, affording alcohol **22**. Finally, the hydroxyl group was oxidized into the corresponding carboxylic acid with pyridinium dichromate[12] (PDC) in DMF, affording the desired acid **9** in 87% yield.

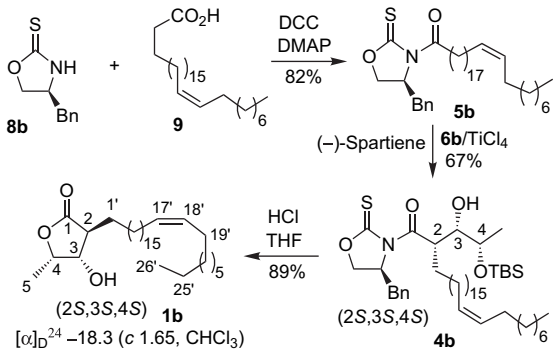
Acylation of chiral auxiliary **8a** with acid **9** was performed under the conditions[13] of Andrade. The aldolization between **5a** and **6a** mediated by $TiCl_4$ gave the enantiopure *syn* aldol **4a** in 71% yield (Scheme 4). Further treatment of **4a** with 4 N HCl to remove the TBS protecting group resulted in spontaneous lactonization, affording the target compound **1a**.



Scheme 4.

All the spectroscopic data of our synthetic **1a** are consistent[14] with those reported[1] in the literature, except that the optical rotation (+17.9) has an opposite sign. It seems what we obtained is the antipode of the natural product. As the absolute configurations of all stereogenic centers in this work are secured by the methodologies adopted, we next looked into the original assignment for the natural compound again to seek possible explanation for the opposite rotation. It was then noticed that the absolute configuration of the isolated natural compound was entirely based on comparison of the sign of the optical rotation of their **2a** (obtained by treatment of the natural megislactone with Al_2O_3 without specifying the yield) with that of **3** reported in the literature. However, without $^1H/^{13}C$ NMR and IR data, the correct molecular weight (i.e., MS result) alone cannot guarantee the genuine identity of the sample—it is not impossible that their '**2a**' was some other compound generated on Al_2O_3 during the intended dehydration, with the same molecular weight but a different structure from **2a**.

The antipode of **1a** was then synthesized using the same route but with an auxiliary and an aldehyde of the opposite configuration (i.e., **6b** and **8b**) to replace **6a** and **8a** (Scheme 5). The enantiopure end product (**1b**) thus obtained indeed shows a compatible optical rotation ($[\alpha]_D^{28}$ −18.3 (*c* 1.65, $CHCl_3$)) with that ($[\alpha]_D^{20}$ −13 (*c* 1.0, $CHCl_3$)) of the natural megislactone. And the ^1H and ^{13}C NMR data are also consistent with those reported for the natural megislactone.



Scheme 5.

Comparison of the ^1H and ^{13}C NMR data of **1b** with those reported for the natural one is given in Tables 1 and 2. It appears that the two sets of data agree very well with each other. However, a few minor errors in the original assignments are also detected during careful analysis of the spectroscopic data: C5 and C26′ are now switched, because in the HMQC spectrum the carbon connected to the methyl protons (doublet) at δ 1.40 is that at δ 13.8, not at δ 14.1. The HMQC spectrum also unmistakably reveals that the four protons in the region of δ 1.74−1.41 are connected to C-1′ and C-2′ in this way: on going from 1.74 to 1.41, the first two protons are linked to C-1′ and the next two are attached to C-2′.

To gain further evidence for the absolute configuration, formal dehydration of synthetic **1a** and **1b** was also performed by converting the OH into corresponding mesylate followed by treatment with Bu_4NF. Without involving any carbocation intermediate, an indirect elimination of water is expected to be much less likely to cause any carbon framework rearrangement compared with direct[1] dehydration of water over Al_2O_3. The elimination product from **1a** and **1b** gave an optical rotation of −16.6 and +16.2, respectively (Scheme 6),

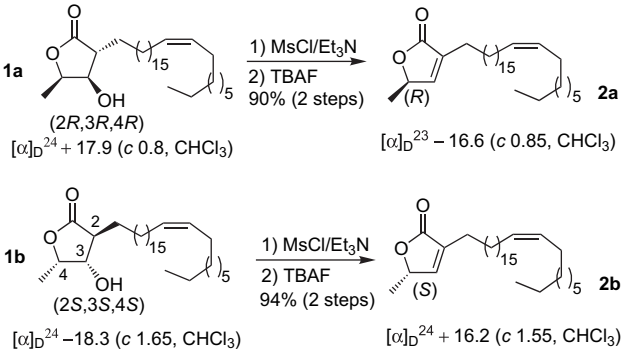
Table 1
Comparison of ^1H NMR data of the synthetic and natural megislactone (**1b**)

Synthetic **1b** (this work)	Natural **1b**	Previous assignment	Present assignment
5.34 (t, *J*=4.7 Hz, 2H)	5.33 (dt, *J*=9.4, 4.6 Hz, 2H)	H-17′ and H-18′	H-17′ and H-18′
4.62 (dq, *J*=4.8, 6.4 Hz, 1H)	4.61 (dq, *J*=4.6, 6.5 Hz, 1H)	H-4	H-4
4.19 (ddd, *J*=4.6, 4.3, 3.9 Hz, 1H)	4.19 (dd, *J*=3.9, 4.6 Hz, 1H)	H-3	H-3
2.53 (m, 1H)	2.52 (m, 1H)	H-2	H-2
2.50−2.36 (br s, 1H)	(not given)		OH
2.02−1.93 (m, 4H)	2.00 (m, 4H)	H-16′ and H-19′	H-16′ and H-19′
1.74−1.68 (m, 1H)	1.70 (m, 1H)	H-1′a	H-1′a
1.59−1.52 (m, 1H)	1.51 (m, 2H)	H-2′	H-1′b
1.50−1.41 (m, 2H)	1.45 (m, 1H)	H-1′b	H-2′
1.40 (d, *J*=6.7 Hz, 3H)	1.39 (d, *J*=6.5 Hz, 3H)	H-5	H-5
1.39−1.20 (s, 38H)	1.38−1.20 (m, 38H)	H-3′ to H-15′, H-20′ to H-25′	H-3′ to H-15′, H-20′ to H-25′
0.87 (t, *J*=7.1 Hz, 3H)	0.86 (t, *J*=6.5 Hz, 3H)	H-26′	H-26′

Table 2
Comparison of ^{13}C NMR data of the synthetic and natural megislactone (**1b**)

Synthetic **1b** (this work)	Natural **1b**	Previous assignment	Present assignment
178.0	177.6	C-1	C-1
129.8	129.9	C-17′	C-17′
129.8	129.9	C-18′	C-18′
78.4	78.2	C-4	C-4
73.9	74.1	C-3	C-3
49.3	49.2	C-2	C-2
31.9			C-24′[a]
29.8–29.1	31.9–29.3	C-3′ to C-5′ and C-20′ to C-24′	C-3′ to C-5′ and C-20′ to C-23′
	29.0	C-2′	
28.4	28.4	C-1′	C-1′
27.22	27.2	C-19′	C-2′
27.15	27.2	C-16′	C-16′ and C-19′
22.6	(Not given)		C-25′
14.1	14.1	C-5	C-26′
13.8	13.9	C-26′	C-5
178.0	177.6	C-1	C-1

[a] This carbon is assigned as C-24′ rather than C-20′ on the basis of the following arguments: (a) Compound **10** does not show this carbon in ^{13}C NMR, which contains the C-20′, but **11** does. (b) ^{13}C NMR simulation using ChemDraw 9.0 suggests that the third carbon from the terminal methyl group has a chemical shift of 31.8, whereas that for C-20′ would be 29.9.



Scheme 6.

with all spectroscopic data fully consistent with their structures. Thus, the absolute configuration of the natural megislactone must be as shown by structure **1b**, the antipode of the originally proposed **1a**.

It is interesting to note that the final deprotection–lactonization could also be achieved by using CAN (ceric ammonium nitrate)/MeOH, a set of conditions known for cleaving silyl protecting groups. However, the product obtained under such conditions shows slight difference at the –CH=CH– region in ^{1}H NMR and ^{13}C NMR (Fig. 1). In ^{1}H NMR, an additional set of lines partially overlapped with the original broadened triplet was observed. In ^{13}C NMR, an extra line appeared at 130.34. Because in such a molecular setup, any changes in the relative configurations of the stereogenic centers in the lactone ring inevitably lead to unmistakable changes in ^{1}H NMR, the only possible explanation for the additional signals in NMR must be co-presence of a trans double bond isomer. As no trans isomer could be detected with the **1a** prepared using HCl instead of CAN, the isomerization must be caused by CAN.

3. Conclusions

Both (+)- and (−)-megislactone have been synthesized through a highly stereoselective route. The spectroscopic data of the synthetic sample clearly show that absolute configuration of the natural compound must be the antipode of the originally proposed. Some minor corrections are also made to the original spectroscopic assignments. An interesting partial isomerization of the cis carbon–carbon double bond mediated by CAN was observed during the desilylation–cyclization step.[15] The otherwise undetectable co-presence

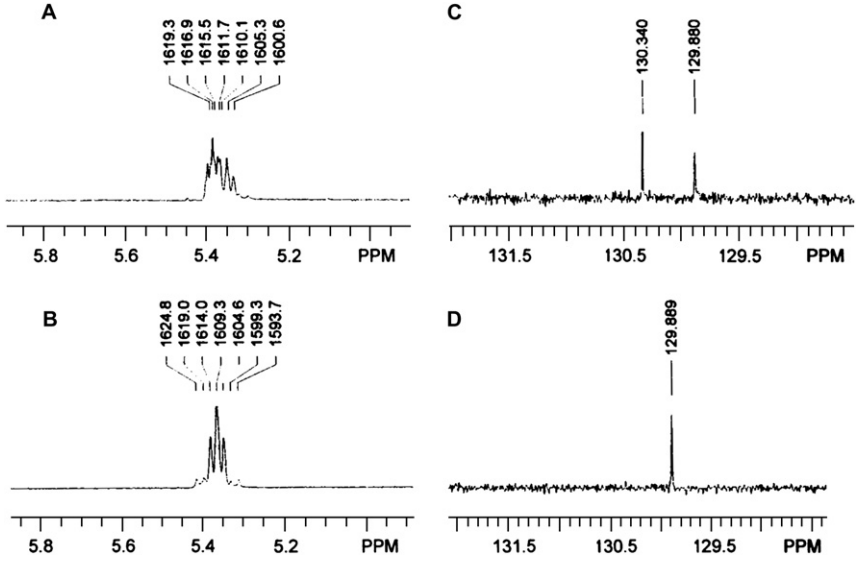


Figure 1. Comparison of the ^{1}H and ^{13}C NMR spectra. (A) and (B): partial ^{1}H NMR of the **1b** formed using CAN and HCl, respectively. (C) and (D): partial ^{13}C NMR of the **1b** formed using CAN and HCl, respectively. The extra signal at δ 5.35 in (A) and δ 130.3 in (C) stem from the trans C–C double bond isomer. Other parts of the ^{1}H and ^{13}C NMR spectra of the two samples are identical to each other.

of the trans isomer revealed by the remote lactone ring in the end product is also noteworthy.

4. Experimental

4.1. General

Unless otherwise stated, the ^{1}H NMR and ^{13}C NMR spectra were recorded in deuterochloroform at ambient temperature using a Varian Mercury 300 or a Bruker Avance 300 instrument (operating at 300 MHz for proton). The FTIR spectra were scanned with a Nicolet Avatar 360 FTIR spectrometer. EIMS and EIHRMS were recorded with an HP 5989A and a Finnigan MAT 8430 mass spectrometer, respectively. The ESIMS and ESIHRMS were recorded with a PE Mariner API-TOF and an APEX III (7.0 Tesla) FTMS mass spectrometer, respectively. The melting points were uncorrected. Optical rotations were recorded on a Jasco P-1030 polarimeter. Dry THF was distilled from Na/Ph_2CO under N_2. Dry HMPA, DMF, and DMSO were stirred with CaH_2 at ambient temperature under N_2 for 4 d before being distilled under reduced pressure and kept under N_2 over activated 4 Å molecular sieves. Dry CH_2Cl_2 was distilled over CaH_2 and kept over activated 4 Å molecular sieves. All other solvents and reagents were commercially available and used as-received without any further purification. PE (chromatography eluent) stands for petroleum ether (bp 60–90 °C). DCC stands for *N*,*N*′-dicyclohexyldiimide. DMAP stands for 4-dimethylamino-pyridine. DMF stands for *N*,*N*′-dimethylformamide.

4.2. Alkylation of alkyne **15** with dibromide **16** (**17**)

n-BuLi (2.5 M in hexanes, 16.7 mL, 41.7 mmol) was added dropwise to a solution of the propargyl ether **15** (6.100 g, 41.7 mmol) in dry THF (40 mL) stirred at 0 °C under N_2. The stirring was continued at 0 °C for 10 min before dry HMPA (10 mL) was introduced, followed by a solution of dibromodecane **16** (3.281 g, 10.0 mmol) in dry THF (10 mL). The stirring was continued at ambient temperature for 48 h. The reaction was quenched with water. The mixture was extracted with Et_2O. The organic phase was washed with water and brine, and dried over Na_2SO_4. Removal of the solvent and chromatography on silica gel (40:1 PE–Et_2O) gave the bisbenzyl ether **17** (4.219 g, 0.20 mmol, 92%) as a yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38–7.26 (m, 10H), 4.59 (s, 4H), 4.16 (t, J=2.3 Hz, 4H), 2.26–2.20 (m, 4H), 1.56–1.41 (m, 4H), 1.38–1.26 (m, 16H); ^{13}C NMR (75 MHz, $CHCl_3$) δ 137.6, 128.3, 128.0, 127.7, 87.3, 75.7, 71.3, 57.7, 29.6, 29.5, 29.1, 28.8, 28.6, 18.7; FTIR (film) 3087, 3030, 2927, 2854, 1496, 1454, 1072, 736 cm^{-1}. EIMS *m*/*z* (%) 367 ([M–Bn]$^+$, <0.7), 91 (100). Anal. Calcd for $C_{32}H_{42}O_2$: C, 83.79; H, 9.23. Found C, 84.06; H, 9.41.

4.3. Conversion of bisbenzyl ether **17** into diol **18**

A mixture of **17** (2.440 g, 5.32 mmol) and 10% Pd–C (244 mg) in THF (20 mL) in a stainless steel bomb was stirred at ambient temperature under H_2 (50 atm) for 3 d. The solids were filtered off. The filtrate was concentrated on a rotary evaporator. The residue was chromatographed on silica gel (3:1 PE–THF) to yield the known diol **18**[10] (1.320 g, 4.61 mmol, 87%) as a white powder: mp 95–96 °C (lit.[16] 97 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.64 (t, J=6.6 Hz, 4H), 1.54 (m, 4H), 1.26 (s, 26H).

4.4. Monosilyl protection of diol **18** (**19**)

TBSCl (787 mg, 5.16 mmol) was added in portions to a solution of diol **18** (1.343 g, 4.69 mmol), imidazole (351 mg, 5.16 mmol) and DMAP (57 mg, 0.47 mmol) in dry CH_2Cl_2 (470 mL). The mixture was then stirred at ambient temperature for 24 h before being washed with aq saturated $NaHCO_3$, water and brine, and dried over Na_2SO_4. The solvent was removed by rotary evaporation. The residue was purified by flash chromatography on silica gel (4:1 PE–THF) to furnish the mono TBS ether **19** (1.266 g, 3.17 mmol, 67%) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.68 (t, J=7.2 Hz, 2H), 3.65 (t, J=6.6 Hz, 2H), 1.62–1.46 (m, 4H), 1.31 (s, 28H), 0.95 (s, 9H), 0.10 (s, 6H); ^{13}C NMR (75 MHz, $CHCl_3$) δ 63.4, 63.0, 32.9, 32.8, 29.7–29.4 (all the remaining/unresolved alkyl carbons), 26.0, 25.8, 25.7, 18.4, −5.3; FTIR (film) 3449, 2926, 2854, 1466, 1400, 1255, 1102, 836, 775 cm^{-1}. ESIMS *m*/*z* 401.5 ([M+H]$^+$). ESIHRMS calcd for $C_{24}H_{53}O_2Si$ ([M+H]$^+$): 401.3809; found: 401.3525.

4.5. Transformation of alcohol **19** into iodide **20**

I_2 (64 mg, 0.253 mmol) was added to a solution of **19** (78 mg, 0.195 mmol), imidazole (20 mg, 0.293 mmol) and PPh_3 (78 mg, 0.293 mmol) in dry toluene (2 mL) stirred at ambient temperature. After 20 min, another portion of imidazole (7 mg, 0.097 mmol) was introduced, followed by PPh_3 (26 mg, 0.097 mmol), and I_2 (21 mg, 0.097 mmol). When the reaction was complete as shown by TLC, aq saturated aqueous $Na_2S_2O_3$ (5 mL) was added, followed by EtOAc. The phases were separated. The organic layer was washed in turn with water and brine before being dried over $NaSO_4$. Removal of the solvent and column chromatography (50:1 PE–Et_2O) gave iodide **20** (95 mg, 0.186 mmol, 95%) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.61 (t, J=6.8 Hz, 2H), 3.20 (t, J=7.0 Hz, 2H), 1.81 (q, J=7.1 Hz, 2H), 1.51 (m, 2H), 1.27 (s, 28H), 0.90 (s, 9H), 0.06 (s, 6H); ^{13}C NMR (75 MHz, $CHCl_3$) δ 63.3, 33.6, 32.9, 30.5, 29.7–29.4 (all the remaining/unresolved alkyl carbons), 28.5, 26.0, 25.8, 18.4, 7.3, −5.3. FTIR (film) 2926, 2854, 1436, 1254, 1101, 836, 775, 761 cm^{-1}; EIMS *m*/*z* (%) 453 ([M–C_4H_9]$^+$, 12), 325 (7), 215 (10), 125 (27), 111 (58), 97 (99), 75 (100); EIHRMS calcd for $C_{20}H_{42}OSiI$ ([M–C_4H_9]$^+$) 453.2050; found 453.2064.

4.6. Synthesis of alkene **10** from iodide **20**

t-BuOK (1.564 g, 14.0 mmol) was added in one portion to a solution of **20** (1.362 g, 2.67 mmol) in dry THF (20 mL) and

stirred at ambient temperature. When TLC showed completion of the reaction, H_2O (5 mL) was added, followed by EtOAc (100 mL). The phases were separated. The organic layer was washed with water and brine before being dried over $NaSO_4$. Rotary evaporation and column chromatography (PE) afforded the terminal alkene **10** (803 mg, 2.10 mmol, 79%) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.82 (ddt, J=17.1, 10.2, 6.6 Hz, 1H), 5.02–4.90 (m, 2H), 3.60 (t, J=6.6 Hz, 2H), 2.05 (dt, J=6.6 Hz, 2H), 1.58–1.42 (m, 2H), 1.26 (s, 26H), 0.90 (s, 9H), 0.06 (s, 6H); ^{13}C NMR (75 MHz, $CHCl_3$) δ 139.3, 114.1, 63.3, 33.8, 32.9, 29.7–29.2 (all the remaining/unresolved alkyl carbons), 28.94, 26.0, 25.8, 18.4, −5.3; FTIR (film) 2927, 2855, 1464, 1255, 1102, 836, 775 cm^{-1}; EIMS *m/z* (%) 367 ([M−CH_3]$^+$, 0.74), 325 (32), 297 (7), 75 (100), 55 (14); EIHRMS calcd for $C_{23}H_{47}OSi$ ([M−CH_3]$^+$): 367.3396; found: 367.3404.

4.7. Transformation of alkyne *14* into cis vinyl iodide *11*

DIBAL-H (1.0 M solution in cyclohexane, 6.5 mL) was added to a solution of anhydrous $InCl_3$ (1.499 g, 6.75 mmol) in dry THF (20 mL) and stirred at −78 °C under N_2. The stirring was continued at that temperature for 0.5 h. Alkyne **14** (651 mg, 4.72 mmol) was then added, followed by Et_3B (1.0 M solution in THF, 1.0 mL). After stirring at −78 °C for another 3 h, iodine (7.62 g, 30.0 mmol) was introduced. The stirring was continued at −78 °C for 30 min. The mixture was poured into aq saturated $NaHCO_3$. The excess I_2 was decomposed by addition of aq saturated NaS_2O_3. The mixture was filtered through Celite. The filtrate was extracted with Et_2O. The phases were separated. The organic layer was washed with water and brine, and dried over Na_2SO_4. Rotary evaporation and chromatography on silica gel (*n*-hexane) yielded the known vinyl iodide **11**[6] (1.045 g, 3.93 mmol, 83%) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.18–6.15 (m, 2H), 2.16–2.10 (m, 2H), 1.43–1.27 (m, 12H), 0.89 (t, J=6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CHCl_3$) δ 141.4, 82.1, 34.7, 31.8, 29.4, 29.2, 29.1, 27.9, 22.7, 14.1.

4.8. Suzuki coupling between *10* and *11* (*21*)

A solution of 9-BBN (0.5 M solution in THF, 1.0 mL, 0.5 mmol) and the terminal olefin **10** (76 mg, 0.2 mmol) in dry THF (2 mL) was stirred at ambient temperature for 3 h before aq NaOH (1 N, 0.6 mL) was added. The stirring was continued at ambient temperature for an additional 30 min. The reaction mixture was then transferred via a syringe to a mixture of vinyl iodide **11** (48 mg, 0.18 mmol) and $Pd(PPh_3)_2Cl_2$ (28 mg, 0.04 mmol) in THF–H_2O (3:1 v/v, 2 mL). The resulting mixture was stirred at ambient temperature for 1 h. The solids were filtered off through Celite. The filtrate was washed in turn with 1 N aq NaOH, H_2O, and brine, before being dried over anhydrous Na_2SO_4. Rotary evaporation and flash chromatography on silica gel (*n*-hexane) gave the cis alkene **21** (84 mg, 0.16 mmol, 89%) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.34 (t, J=4.5 Hz, 2H), 3.60 (t, J=6.7 Hz, 2H), 2.04–1.98 (m, 4H), 1.53–1.43 (m, 2H), 1.26 (s, 42H), 0.89 (s, 9H), 0.88 (t, J=7.1 Hz, 3H), 0.06 (s, 6H); ^{13}C NMR (75 MHz, $CHCl_3$) δ 129.9 (2C's), 63.3, 32.9, 31.9, 29.8–29.3 (all the remaining/unresolved alkyl carbons), 27.2 (2C's), 26.0, 25.8, 22.7, 18.4, 14.1, −5.3; FTIR (film) 3004 (w), 1464, 1255, 1102, 836, 761 cm^{-1}; EIMS *m/z* (%) 465 ([M−C_4H_3]$^+$, 12.6), 325 (56), 297 (8), 105 (100), 75 (87); EIHRMS calcd for $C_{30}H_{61}OSi$ ([M−C_4H_9]$^+$): 465.4492; found: 465.4499.

4.9. Removal of the TBS group in *21* (*22*)

A solution of the alkene **21** (378 mg, 0.72 mmol) and TBAF (1.0 M solution in THF, 1.44 mL) in dry THF (5 mL) was stirred at ambient temperature for 2 h. H_2O (5 mL) was then added to the reaction mixture, followed by Et_2O. The phases were separated. The organic layer was washed with water, brine, and dried over anhydrous Na_2SO_4. Removal of the solvent and flash chromatography (4:1 PE–EtOAc) gave the alcohol **22** (280 mg, 0.69 mmol, 95%) as a white solid: mp 46–48 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.34 (t, J=4.5 Hz, 2H), 3.64 (t, J=6.5 Hz, 2H), 2.00 (m, 4H), 1.59–1.53 (m, 2H), 1.26 (s, 42H), 0.88 (t, J=6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CHCl_3$) δ 129.9 (2C's), 63.1, 32.8, 31.9, 29.8–29.3 (all the remaining/unresolved alkyl carbons), 27.2 (2C's), 25.7, 22.7, 14.1; FTIR (KBr) 3327, 2920, 2851, 719 cm^{-1}; EIMS: *m/z* (%) 390 ([M−H_2O]$^+$, 2.19), 110 (20), 96 (67), 92 (74), 69 (69), 55 (100), 41 (64); EIHRMS calcd for $C_{28}H_{54}$ ([M−H_2O]$^+$): 390.4226; found: 390.4228.

4.10. PDC oxidation of *22* (*9*)

A mixture of **22** (95 mg, 0.233 mmol) and PDC (524 mg, 1.39 mmol) in dry DMF (5 mL) was stirred at ambient temperature until TLC showed completion of the reaction. Water (10 mL) was then added to the mixture, followed by Et_2O. The phases were separated. The organic layer was washed with water, brine, and dried over anhydrous Na_2SO_4. Rotary evaporation and column chromatography on silica gel (6:1 to 3:1 PE–EtOAc) afforded the acid **9** (85 mg, 0.201 mmol, 86%) as a white solid: mp 46–47 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.34 (t, J=4.5 Hz, 2H), 2.34 (t, J=7.4 Hz, 2H), 2.02–1.98 (m, 4H), 1.63 (m, 2H), 1.25 (s, 40H), 0.88 (t, J=6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CHCl_3$) δ 180.3, 129.9 (2C's), 34.1, 31.9, 29.8–29.1 (all the remaining/unresolved alkyl carbons), 27.2 (2C's), 24.7, 22.7, 14.1; FTIR (KBr) 3449, 2918, 2850, 1696, 1472, 942, 718 cm^{-1}; ESIMS *m/z* 421.3 ([M−H]$^-$). ESIHRMS calcd for $C_{28}H_{54}NaO_2$ ([M+Na]$^+$): 445.4016; found: 445.4014.

4.11. Acylation of chiral auxiliary *8a* with acid *9* (*5a*)

DCC (132 mg, 0.642 mmol, 1.5 equiv) was added in one portion to a suspension of the acid **9** (181 mg, 0.428 mmol), DMAP (10 mg, 0.086 mmol, 0.2 equiv), and the chiral auxiliary **8a** (91 mg, 0.471 mmol, 1.1 equiv) in dry CH_2Cl_2 (1 mL) and stirred at 0 °C. The mixture was stirred at the same temperature for 10 min and then at ambient temperature

until TLC showed full consumption of the starting **9**. The mixture was filtered through Celite. The filtrate was concentrated and chromatographed on silica gel (5:1 PE–CH_2Cl_2) to yield **5a** (217 mg, 0.363 mmol, 85%) as a colorless oil: $[\alpha]_D^{27}$ −52.8 (*c* 0.85, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34–7.21 (m, 5H), 5.35 (t, *J*=4.8 Hz, 2H), 4.97–4.89 (m, 1H), 4.35–4.25 (m, 2H), 3.44–3.18 (m, 3H), 2.76 (dd, *J*=13.4, 10.0 Hz, 1H), 2.02–1.95 (m, 4H), 1.78–1.67 (m, 2H), 1.26 (s, 40H), 0.89 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CHCl_3$) δ 185.4, 174.2, 135.3, 129.9 (2C's), 129.4, 129.0, 127.4, 70.2, 59.9, 37.6, 37.5, 31.9, 29.7–29.0 (all the remaining/unresolved alkyl carbons), 27.2 (2C's), 24.4, 22.7, 14.1; FTIR (KBr) 3064, 2924, 2853, 1702, 1465, 1366, 1324, 1192, 967, 743, 701 cm^{-1}; ESIMS: *m/z* 620.2 ([M+Na]$^+$). ESIHRMS calcd for $C_{38}H_{63}NO_2SNa$ ([M+Na]$^+$): 620.4472; found: 620.4479.

4.12. Aldol condensation between *5a* and *6a* (*4a*)

Freshly distilled $TiCl_4$ (42 μL, 0.381 mmol) was added via a syringe to a solution of **5a** (217 mg, 0.363 mmol) in dry CH_2Cl_2 (3 mL) and stirred at ambient temperature under an argon atmosphere. The resulting yellow solution was stirred for 5 min before neat (−)-sparteine (0.21 ml, 0.908 mmol) was added dropwise (giving a purple solution). After stirring at ambient temperature for 20 min, the reaction flask was placed into a −78 °C cooling bath. With stirring, a solution of aldehyde **6a** (340 mg, 1.81 mmol) in dry CH_2Cl_2 (1 mL) was introduced via syringe. The resultant mixture was stirred at −78 °C for 2 h and at 0 °C for another 2 h. The reaction was quenched with aq NH_4Cl. The mixture was filtered through Celite. The filtrate was washed in turn with water and brine. The organic phase was dried over anhydrous Na_2SO_4. Rotary evaporation and column chromatography on silica gel (8:1 PE–EA) yielded the aldol **4a** (204 mg, 0.26 mmol, 71%) as a colorless oil: $[\alpha]_D^{27}$ −23.9 (*c* 1.95, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34–7.25 (m, 5H), 5.35 (t, *J*=4.6 Hz, 2H), 4.95 (m, 1H), 4.86 (m, 1H), 4.33–4.19 (m, 2H), 3.87–3.73 (m, 2H), 3.31 (dd, *J*=13.4, 3.1 Hz, 1H), 2.76 (dd, *J*=13.2, 10.6 Hz, 1H), 2.46 (d, *J*=6.0 Hz, 1H), 2.08–1.96 (m, 4H), 1.79–1.64 (m, 1H), 1.49–1.41 (m, 1H), 1.38–1.21 (s, 43H), 0.89 (s, 9H), 0.88 (t, *J*=7.4 Hz, 3H), 0.07 (d, *J*=7.4 Hz, 6H); ^{13}C NMR (75 MHz, $CHCl_3$) δ 184.7, 175.1, 135.3, 129.9 (2C's), 129.4, 129.0, 127.4, 74.9, 70.0, 69.9, 60.4, 45.3, 37.6, 31.9, 29.9–29.3 (all the remaining/unresolved alkyl carbons), 27.2 (2C's), 26.6, 26.4, 25.8, 22.7, 20.6, 17.9, 14.1, −3.9, −4.9; FTIR (film) 3544, 3064, 2925, 2854, 1694, 1497, 1372, 1321, 964, 837, 778, 744 cm^{-1}; ESIMS *m/z* 786.7 ([M+H]$^+$). ESIHRMS calcd for $C_{47}H_{84}NO_4SSi$ ([M+H]$^+$): 786.5885; found: 786.5889.

4.13. Synthesis of *1a*

A solution of **4** (39 mg, 49.7 μmol) and HCl (4 N, 0.10 mL, 0.40 mmol, 8.0 equiv) in THF (2 mL) was stirred at ambient temperature for 12 h. After neutralization with aq saturated $NaHCO_3$, the mixture was extracted with Et_2O (three times). The combined organic phases were washed in turn with water and brine before being dried over anhydrous Na_2SO_4. Rotary evaporation and column chromatography on silica gel (6:1 PE–EtOAc) gave **1a** (21 mg, 44.0 μmol, 88%) as a white powder: mp 52–53 °C. $[\alpha]_D^{27}$ 17.9 (*c* 0.8, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.35 (t, *J*=4.8 Hz, 2H), 4.62 (dq, *J*=4.9, 6.6 Hz, 1H), 4.19 (m, 1H), 2.53 (m, 1H), 2.01 (m, 5H), 1.79–1.70 (m, 1H), 1.63–1.58 (m, 1H), 1.55–1.42 (m, 2H), 1.40 (d, *J*=6.2 Hz, 3H), 1.25 (s, 38H), 0.88 (t, *J*=7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CHCl_3$) δ 177.7, 129.9 (2C's), 78.2, 74.1, 49.2, 31.9, 29.8–29.3 (all the remaining/unresolved alkyl carbons), 28.4, 27.3, 27.2 (2C's), 22.7, 14.1, 13.9; FTIR (KBr) 3435, 2926, 2850, 1759, 1472, 1194, 1050, 963, 719 cm^{-1}; ESIMS *m/z* 479.4 ([M+H]$^+$), 501.4 ([M+Na]$^+$). ESIHRMS calcd for $C_{31}H_{58}O_3Na$ ([M+Na]$^+$): 501.4278; found: 501.4287.

4.14. Conversion of *1a* into *2a*

Et_3N (44 μL, 0.314 mmol) and MsCl (27 μL, 0.314 mmol) were added dropwise to a solution of **1a** (15 mg, 0.031 mmol) in dry CH_2Cl_2 (1.5 mL) and stirred in an ice-water bath. The cooling bath was removed. The mixture was stirred at ambient temperature for 5 h. H_2O (5 mL) and Et_2O (20 mL) were added to the reaction mixture. The phases were separated. The aqueous phase was back-extracted with Et_2O (3·10 mL). The combined organic phases were washed with brine and dried over anhydrous Na_2SO_4. The solvent was removed by rotary evaporation. The residue was dissolved in dry acetone (2 mL) and treated with TBAF (1.0 M solution in THF, 102 μL, 3.0 equiv) at ambient temperature until TLC showed completion of the reaction. H_2O (5 mL) and Et_2O (10 mL) were added. The phases were separated. The aqueous phase was back-extracted with Et_2O (3·10 mL). After removal of the solvent, the residue was chromatographed on silica gel (15:1 PE–Et_2O) to give **19** as a white powder (13 mg, 90% from **1a**): mp 25–26 °C. $[\alpha]_D^{27}$ −16.6 (*c* 0.85, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.99 (s, 1H), 5.34 (m, 2H), 5.00 (m, 1H), 2.27 (t, *J*=7.0 Hz, 2H), 2.01 (m, 4H), 1.54–1.42 (m, 2H), 1.40 (d, *J*=6.6 Hz, 3H), 1.26 (s, 38H), 0.88 (t, *J*=6.5 Hz, 3H); ^{13}C NMR (75 MHz, $CHCl_3$) δ 173.0, 148.8, 134.3, 129.9 (2C's), 77.4, 31.9, 29.8–29.2 (all the remaining/unresolved alkyl carbons), 27.4, 27.2 (2C's), 25.2, 22.7, 19.2, 14.1; FTIR (KBr) 2925, 2853, 1762, 1465, 1317, 1075, 951, 856, 721 cm^{-1}; ESIMS *m/z* 461.3 ([M+H]$^+$), 483.3 ([M+Na]$^+$). ESIHRMS calcd for $C_{31}H_{57}O_2$ ([M+H]$^+$): 461.4353; found: 461.4369.

4.15. Acylation of *8b* with acid *9* (*5b*)

The procedure was the same as that for synthesis of **5a** given above. Yield: 82%. Data for **5b**: $[\alpha]_D^{27}$ +51.9 (*c* 1.45, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37–7.21 (m, 5H), 5.35 (t, *J*=4.8 Hz, 2H), 4.96–4.90 (m, 1H), 4.33–4.25 (m, 2H), 3.38–3.18 (m, 3H), 2.76 (dd, *J*=13.3, 10.1 Hz, 1H), 2.02–1.91 (m, 4H), 1.75–1.68 (m, 2H), 1.26 (s, 40H), 0.89 (t, *J*=7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CHCl_3$) δ 185.3,

174.1, 135.3, 129.83, 129.81, 129.4, 128.9, 127.3, 70.2, 59.9, 37.6, 37.5, 31.9, 29.7–29.0 (all the remaining/unresolved alkyl carbons), 27.2 (2C's), 24.4, 22.6, 14.1; FTIR (KBr) 2924, 2853, 1700, 1465, 1456, 1400, 1367, 1324, 1192, 967, 743, 722, 701 cm^{-1}; ESIMS *m/z* 620.2 ($[M+Na]^+$). ESIHRMS calcd for $C_{38}H_{63}NO_2SNa$ ($[M+Na]^+$): 620.4472; found: 620.4470.

4.16. Aldol condensation between **5b** and **6b** (**4b**)

The procedure was the same as that for synthesis of **4a** given above. Yield: 67%. Data for **4b**: $[\alpha]_D^{27}$ +23.8 (*c* 1.85, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ 7.34–7.23 (m, 5H), 5.35 (t, *J*=4.6 Hz, 2H), 4.95 (m, 1H), 4.86 (m, 1H), 4.33–4.16 (m, 2H), 3.87–3.75 (m, 2H), 3.31 (dd, *J*=13.0, 3.0 Hz, 1H), 2.76 (dd, *J*=13.1, 10.0 Hz, 1H), 2.45 (d, *J*=6.0 Hz, 1H), 2.05–1.99 (m, 4H), 1.78–1.64 (m, 1H), 1.49–1.41 (m, 1H), 1.26 (s, 43H), 0.89 (s, 9H), 0.88 (t, *J*=7.4 Hz, 3H), 0.07 (d, *J*=7.4 Hz, 6H); ^{13}C NMR (75 MHz, $CHCl_3$) δ 184.7, 175.1, 135.3, 129.9 (2C's), 129.4, 129.0, 127.4, 74.9, 70.0, 69.9, 60.4, 45.3, 37.6, 31.9, 29.9–29.3 (all the remaining/unresolved alkyl carbons), 27.2 (2C's), 26.6, 26.4, 25.8, 22.7, 20.6, 17.9, 14.1, −3.9, −4.9; FTIR (film) 3544, 3064, 2925, 2854, 1694, 1497, 1372, 1321, 964, 837, 778, 744 cm^{-1}; ESIMS *m/z* 808.5 ($[M+Na]^+$). ESIHRMS calcd for $C_{47}H_{83}NO_4SSiNa$ ($[M+Na]^+$): 808.5704; found: 808.5709.

4.17. Synthesis of **1b**

The procedure was the same as that for synthesis of **1a** from **4a** given above. Yield: 89%. Data for **1b**: mp 53–54 °C (lit.[1] 53–54 °C). $[\alpha]_D^{28}$ −18.3 (*c* 1.65, $CHCl_3$) (lit.[1] $[\alpha]_D^{20}$ −13 (*c* 1.0, $CHCl_3$)). ^1H NMR (300 MHz, $CDCl_3$) δ 5.35 (t, *J*=4.7 Hz, 2H), 4.62 (dq, *J*=4.8, 6.4 Hz, 1H), 4.19 (ddd, *J*=3.9, 4.3, 4.6 Hz, 1H), 2.53 (m, 1H), 2.50–2.36 (br, 1H), 2.02–1.93 (m, 4H), 1.74–1.68 (m, 1H), 1.59–1.52 (m, 1H), 1.50–1.41 (m, 2H), 1.40 (d, *J*=6.7 Hz, 3H), 1.39–1.20 (s, 38H), 0.87 (t, *J*=7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CHCl_3$) δ 178.0, 129.8 (2C's), 78.4, 73.9, 49.3, 31.9, 29.7–29.1 (all the remaining/unresolved alkyl carbons), 28.4, 27.22, 27.15 (2C's), 22.6, 14.1, 13.8; FTIR (KBr) 3445, 2918, 2850, 1759, 1472, 1207, 1051, 986, 718 cm^{-1}; ESIMS: *m/z* 501.4 ($[M+Na]^+$). ESIHRMS calcd for $C_{31}H_{58}O_3Na$ ($[M+Na]^+$): 501.4278; found: 501.4277.

4.18. Conversion of **1b** into **2b**

The procedure was the same as that for synthesis of **2a** from **1a** given above. Yield: 94% from **1b**. Data for **2b**: mp 26–27 °C. $[\alpha]_D^{27}$ +16.2 (*c* 1.55, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ 6.99 (d, *J*=1.1 Hz, 1H), 5.34 (t, *J*=4.8 Hz, 2H), 5.00 (m, 1H), 2.26 (t, *J*=7.5 Hz, 2H), 2.01 (m, 4H), 1.57–1.41 (m, 2H), 1.40 (d, *J*=6.7 Hz, 3H), 1.26 (s, 38H), 0.88 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CHCl_3$) δ 173.9, 148.8, 134.3, 129.8 (2C's), 77.4, 31.9, 29.7–29.2 (all the remaining/unresolved alkyl carbons), 27.3, 27.2 (2C's), 25.1, 22.6, 19.2, 14.1; FTIR (KBr) 2925, 2853, 1760, 1318, 1027 cm^{-1}; ESIMS *m/z* 461.4 ($[M+H]^+$), 483.4 ($[M+Na]^+$). ESIHRMS calcd for $C_{31}H_{56}O_2Na$ ($[M+Na]^+$): 483.4173; found: 483.4174.

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References and notes

1. Ming, D. S.; Lopez, A.; Hillhouse, B. J.; French, C. J.; Hudson, J. B.; Towers, G. H. N. *J. Nat. Prod.* **2002**, *65*, 1412–1416.
2. See, e.g.: (a) Wu, Y.-K.; Shen, X.; Tang, C.-J.; Chen, Z.-L.; Hu, Q.; Shi, W. *J. Org. Chem.* **2002**, *67*, 3802–3810; (b) Wu, Y.-K.; Shen, X.; Yang, Y.-Q.; Hu, Q.; Huang, J.-H. *J. Org. Chem.* **2004**, *69*, 3857–3865; (c) Wu, Y.-K.; Sun, Y.-P. *Chem. Commun.* **2005**, 1906–1908; (d) Yang, Y.-Q.; Wu, Y.-K. *Chin. J. Chem.* **2005**, *23*, 1519–1522; (e) Sun, Y.-P.; Wu, Y.-K. *Synlett* **2005**, 1477–1479 (and erratum *Synlett* **2006**, 1132); (f) Wu, Y.-K.; Sun, Y.-P. *J. Org. Chem.* **2006**, *71*, 5748–5751; (g) Wu, Y.-K.; Sun, Y.-P. *Org. Lett.* **2006**, *8*, 2831–2834; (h) Wu, Y.-K.; Yang, Y.-Q. *J. Org. Chem.* **2006**, *71*, 4296–4301; (i) Shen, X.; Yang, Y.-Q.; Hu, Q.; Huang, J.-H.; Gao, J.; Wu, Y.-K. *Chin. J. Chem.* **2007**, *25*, 802–807.
3. (a) Crimmins, M. T.; King, B. W.; Tabet, E. A. *J. Am. Chem. Soc.* **1997**, *119*, 7883–7884; (b) Crimmins, M. T.; King, B. W. *J. Am. Chem. Soc.* **1998**, *120*, 9084–9085.
4. Wu, Y.-K.; Yang, Y.-Q.; Hu, Q. *J. Org. Chem.* **2004**, *69*, 3990–3992.
5. Miyaura, N.; Ishiyama, T.; Sasaki, H.; Ishikawa, M.; Satoh, M.; Suzuki, A. *J. Am. Chem. Soc.* **1989**, *111*, 314–321.
6. (a) Coleman, B. E.; Cwynar, V.; Hart, D. J.; Havas, F.; Mohan, J. M.; Patterson, S.; Ridenour, S.; Schmidt, M.; Smith, E.; Wells, A. J. *Synlett* **2004**, 1339–1342; (b) Dieck, H. A.; Heck, R. F. *J. Org. Chem.* **1975**, *40*, 1083–1090.
7. Stork, G.; Zhao, K. *Tetrahedron Lett.* **1989**, *30*, 2173–2174.
8. Takami, K.; Mikami, S.; Yorimitsu, H.; Shinokubo, H.; Oshima, K. *J. Org. Chem.* **2003**, *68*, 6627–6631.
9. Ishikawa, T.; Mizuta, T.; Hagiwara, K.; Aikawa, T.; Kudo, T.; Saito, S. *J. Org. Chem.* **2003**, *68*, 3702–3705.
10. Murphy, K. E.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2003**, *125*, 4690–4691.
11. (a) King, A. O.; Negishi, E.-i.; Villani, F. J., Jr.; Silveira, A., Jr. *J. Org. Chem.* **1978**, *43*, 358–360; (b) Tsuji, J. *Organic Synthesis with Palladium Compounds*; Springer: New York, NY, 1980; p 3.
12. Corey, E. J.; Schmidt, G. *Tetrahedron Lett.* **1979**, *20*, 399–402.
13. Andrade, C. K. Z.; Rocha, R. O.; Vercillo, O. E.; Silva, W. A.; Matos, R. A. F. *Synlett* **2003**, 2351–2352.
14. However, the vicinal coupling (9.4 Hz) between the two cis olefinic protons at δ 5.33 (dt, *J*=9.6, 4.6 Hz, 2H) reported in the Ref. 1 is absent in our spectrum (cf. Fig. 1). To our knowledge if two vicinal or geminal protons have an identical chemical shift in ^1H NMR, no line-splitting corresponding to the coupling between them can be observed.
15. The intermediates prepared using the cis–trans mixture of **9** showed identical ^1H and ^{13}C NMR and $[\alpha]_D$ data to those prepared from pure *cis*-**9**.
16. Pattision, F. L. M.; Howell, W. C.; Mcnamara, A. J.; Schneider, J. C.; Walker, J. F. *J. Org. Chem.* **1956**, *21*, 739–747.