Synthesis of the C7–C23 Fragment Related to Iriomoteolide-1a via *B*-Alkyl Suzuki–Miyaura Cross-Coupling and Indium-Mediated Aldehyde Allylation

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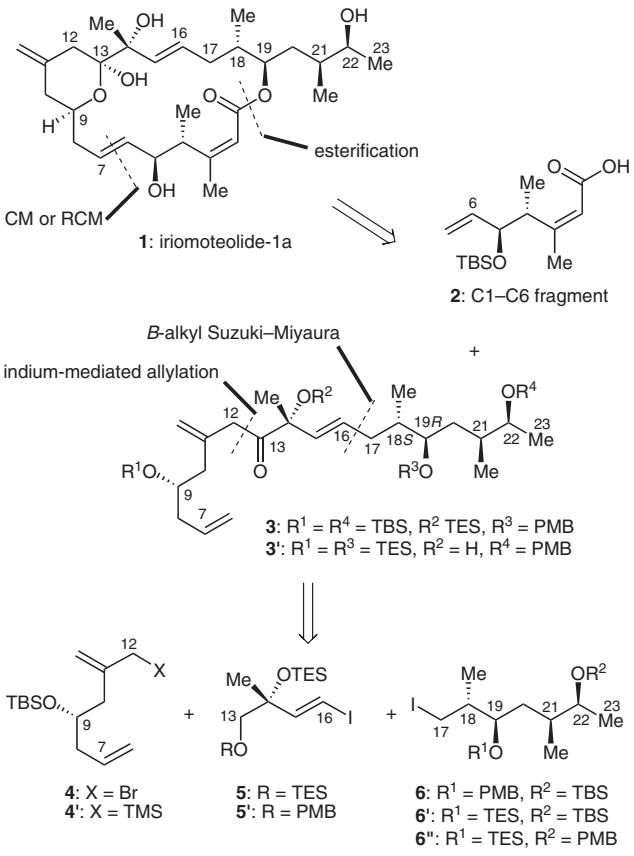
Received 17 May 2010

Abstract: Synthesis of the C7–C23 fragment and its 18*R*,19*S*-diastereomer of iriomoteolide-1a has been accomplished from the C7–C12 allyl bromide, the C13–C16 vinyl iodide, and the C17–C23 alkyl iodide fragments. These fragments were assembled first by the *B*-alkyl Suzuki–Miyaura cross-coupling to give the C13–C23 intermediate. The latter, after being transformed into the C13 aldehyde, was coupled to the C7–C12 allyl bromide in the presence of indium powder in THF–H_2O (1:1) at 70 °C to the fully functionalized C7–C23 fragment with orthogonal protecting groups at C19 (PMB ether), and C9, C14, and C22 (TBS, TES, and TBS ethers, respectively). Formation of the characteristic six-membered C9/C13-hemiacetal ring has been demonstrated after global desilylation using pyridine-buffered HF.

Key words: allylation, *B*-alkyl Suzuki–Miyaura cross-coupling, indium, iriomoteolide, macrolide

Up to date, three 20-membered iriomoteolide-1a, -1b, and -1c have been reported.[1] These macrolides are produced by the marine dinoflagellate *Amphidinium* sp. (HYA024 strain) which was monoclonally separated from sea sand collected off Iriomote Island, Japan. The structures of iriomoteolide-1a (**1**, Scheme 1)[1a,c] and -1b have been proposed while the absolute configurations at C22 and C23 of the side chain of iriomoteolide-1c have not been determined.[1b] Both iriomoteolide-1a and -1c share the same macrolactone core possessing the characteristic C11 exocyclic methylene, six-membered C9/C13-hemiacetal (tetrahydropyran) ring, and C2–C3 trisubstituted *Z*-double bond,[1c] in addition to the C14 tertiary alcohol and two *E*-endogenous double bonds. Preliminary studies showed that iriomotolide-1a and -1c exhibited potent cytotoxicity against human B lymphocyte DG-75 cells (IC_{50} value of 0.002 μg/mL for both macrolides) and Epstein–Barr virus (EBV)-infected human B lymphocyte Raji cells (IC_{50} values of 0.003–0.004 μg/mL).[1] It was suggested that the C9/C13-hemiacetal ring and/or the C11 exocyclic methylene are essential for the observed potent cytotoxicity of iriomoteolide-1a and -1c.[1b] The intriguing molecular architecture and potent biological activity of iriomotolide-1a have attracted considerable attention for its total synthesis.[1c,2] Yang,[2a] Ghosh,[2b] and Paterson[2h] have reported the preparation of the C1–C12 (or C1–C9) fragment while Zhao,[2e] Loh,[2f,g] and Paterson[2h] have accomplished the synthesis of the C13–C23 fragment. The advanced C7–C23 fragment **3′** and the proposed structure of iriomoteolide-1a were constructed by Horne[1c,2d] using Sakurai reaction[3] of the allylsilane **4′**,[2c] *B*-alkyl Suzuki–Miyaura cross-coupling[4] of the alkyl iodide **6″**, and RCM reaction at C6–C7 (Scheme 1).



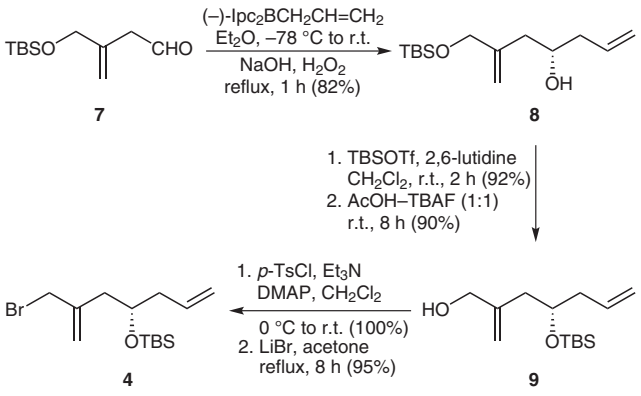
Scheme 1 Retrosynthetic bond disconnections of iriomoteolide-1a (**1**) leading to the fragments **2**–**6** along with some known analogues

Moreover, Xu and Ye's team has accomplished the core of **1** via RCM at the C15–C16 *E*-double bond.[2i] We envisaged synthesis of iriomoteolide-1a from the four small fragments **2** and **4**–**6** according to the critical bond disconnections shown in Scheme 1. Some related fragments **4′**,[2c] **5′**,[2h] **6′**,[2h] and **6″**[2d] appeared recently in the literature, we

SYNLETT 2010, No. 14, pp 2184–2188
Advanced online publication: 16.07.2010
DOI: 10.1055/s-0030-1258507; Art ID: W07610ST

focused on a strategic choice of the orthogonal protecting groups, which should allow selective release of the C19–OH at a later stage, and the method/sequence for the fragment assembly. Our strategy is flexible and it allows quick access to structural analogues. We report here on synthesis of the C7–C23 fragment **3** and its 18*R*,19*S*-diastereomer via *B*-alkyl Suzuki–Miyaura cross-coupling[2d,h,4] and the indium-mediated aldehyde allylation,[5] which is the first demonstration in the total synthesis of iriomoteolide-1a.

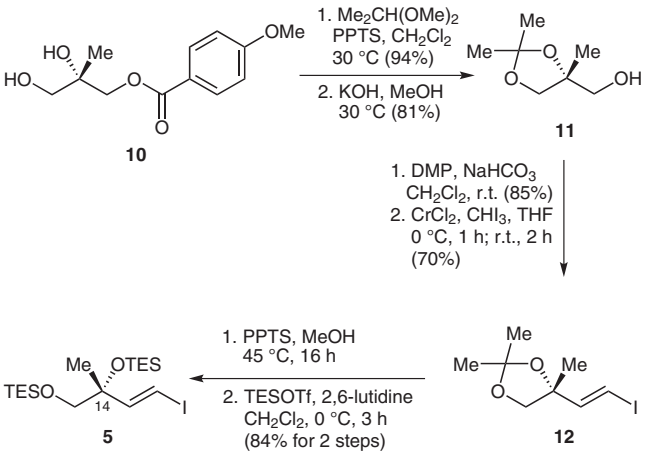
We prepared the allyl bromide **4** from the known aldehyde **7**[2a] as shown in Scheme 2. Reaction of **7** with (–)-*B*-allyldiisopinocampheylborane[6] gave the chiral homoallyl alcohol **8** in 82% yield. Protection of **8** as the bis-TBS ether (92%) was followed by selective removal of the primary TBS group, affording the allyl alcohol **9** (90%). Treatment of **9** with *p*-TsCl and Et_3N in the presence of DMAP formed the corresponding tosylate which was transformed into the allyl bromide **4**[7] (LiBr, refluxing acetone) in 95% overall yield for the two steps.



Scheme 2 Synthesis of the C7–C12 allyl bromide **4**

The chiral diol **10** is readily available by using the modified Sharpless asymmetric dihydroxylation (AD) of the corresponding *para*-methoxybenzoate.[8] In our previous total synthesis of amphidinolide X and Y,[9] we used **10** and its antipodal for construction of the stereogenic oxygenated quaternary carbons at C7 and C18(C19), respectively. In the current work, we applied this versatile chiral building block for assembling the vinyl iodide **5**[2d,h] possessing the C14-oxygenated quaternary carbon (Scheme 3). Protection of the diol **10** as the acetonide followed by alkaline hydrolysis of the ester produced the alcohol **11** in 76% overall yield. Oxidation of **11** using Dess–Martin periodinane (DMP) gave the volatile aldehyde, which was then subjected to the Takai olefination[10] using $CrCl_2$ and CHI_3, affording the vinyl iodide **12** in good overall yield.[11] Finally, the acetonide moiety in **12** was replaced to give the bis-TES-protected vinyl iodide **5**[2d] in 84% overall yield for the two steps.

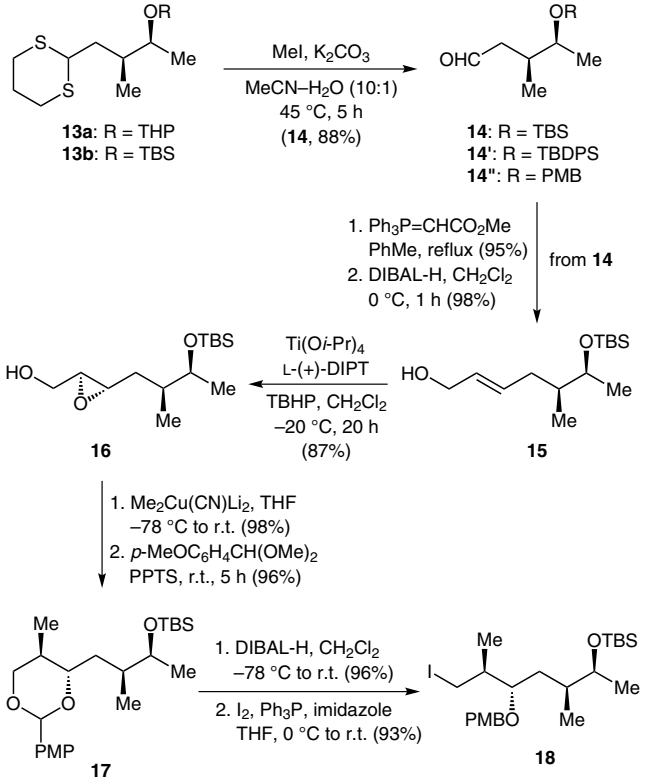
The aldehyde **14** and the related **14′** and **14″**, containing the *syn*-aldol moiety, have been reported (Scheme 4). Loh and Zhao prepared the TBS-protected **14**[2f] and the TBDPS-protected **14′**[2e,g] from (*S*)-lactates while



Scheme 3 Synthesis of the C13–C16 vinyl iodide **5**

Paterson[2h] obtained **14** from the crotylation of acetaldehyde with (*Z*)-crotyldiisopinocamphenylborane. Alternatively, Horne[2d] synthesized the PMB-protected **14″** from (3*S*)-methyl hydroxybutyrate via *anti*-selective allylation. In our recent work on total synthesis of marine butenolides,[12] we used the THP-protected dithiane **13a** obtained from the *syn*-selective aldol reaction of acetaldehyde with the norephedrine-derived chiral propionate.[13] We prepared the TBS-protected **13b** in the same manner and found that the minor *anti*-diastereomer could be separated by column chromatography. Removal of the dithiane moiety in **13b** gave the aldehyde **14** in 88% yield. The latter was subjected to Wittig olefination with the stabilized ylide and the resultant α,β-unsaturated ester was reduced to the allyl alcohol **15** in excellent overall yield. For introducing 18*R*,19*S*-configuration, the epoxide **16** was obtained in 87% yield in a single diastereomer as confirmed by ^1H NMR analysis. Treatment of **16** with $Me_2Cu(CN)Li_2$ in THF at –78 °C gave the 1,3-diol which was transformed into the cyclic acetal **17** in excellent stereoselectivity and overall yield. After regioselective reductive ring opening of the cyclic acetal the resultant primary alcohol was converted into the iodide **18**[7] which is the 18*R*,19*S*-diastereomer of **6**.

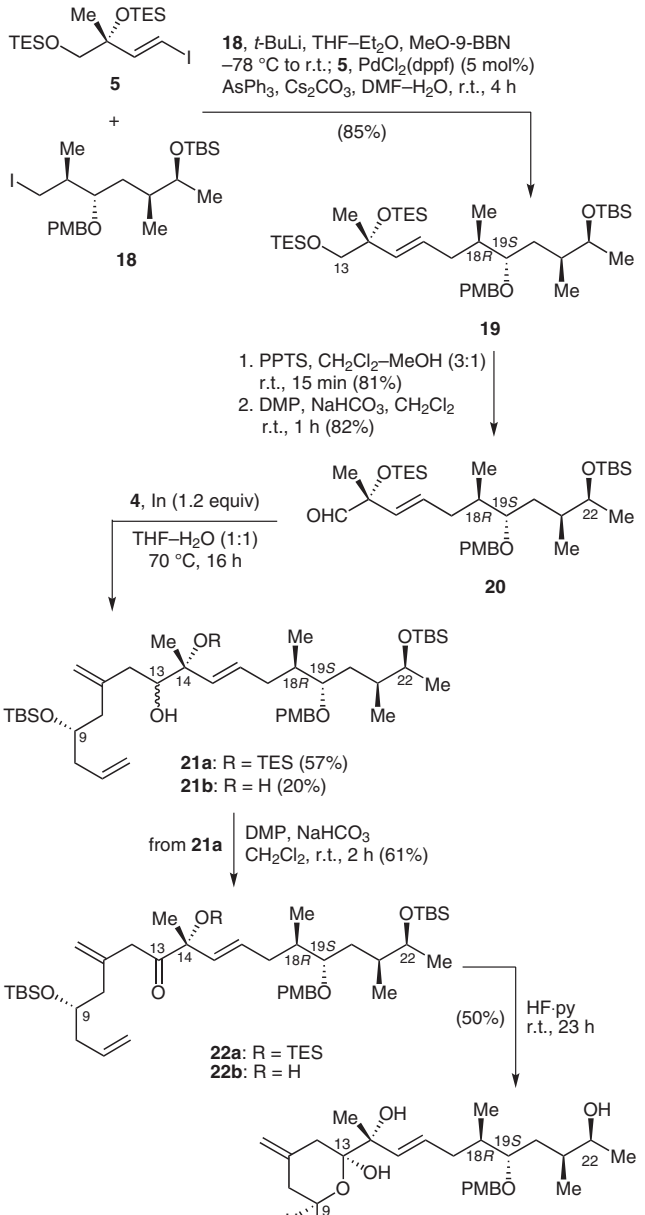
With the fragments **4**, **5**, and **18** in hand, we investigated the sequence for their assembly (Scheme 5). In order to minimize protection–deprotection operations at C13, we first coupled the vinyl iodide **5** with the alkyl iodide **18**. Treatment of **18** with *t*-BuLi formed the corresponding alkyllithium, which reacted with MeO-9-BBN to afford the *B*-alkyl boronate. The latter was then subjected to the coupling with the vinyl iodide **5** in the presence of $PdCl_2(dppf)$ (5 mol%), $AsPh_3$, and Cs_2CO_3 in mixed DMF and H_2O at room temperature to furnish **19**[14] in 85% yield.[2d,h,4] The C13-TES ether in **19** was selectively cleaved, and the resultant primary alcohol was oxidized to **20** in 66% overall yield for the two steps. We initially tried the indium-mediated allylation of the aldehyde **20** with the allyl bromide **4** at room temperature but no reaction was detected. We rationalized the failure as the result of steric hindrance imposed by the bulky substitutions at the



Scheme 4 Synthesis of the diastereomeric C17–C23 alkyl iodide **18**

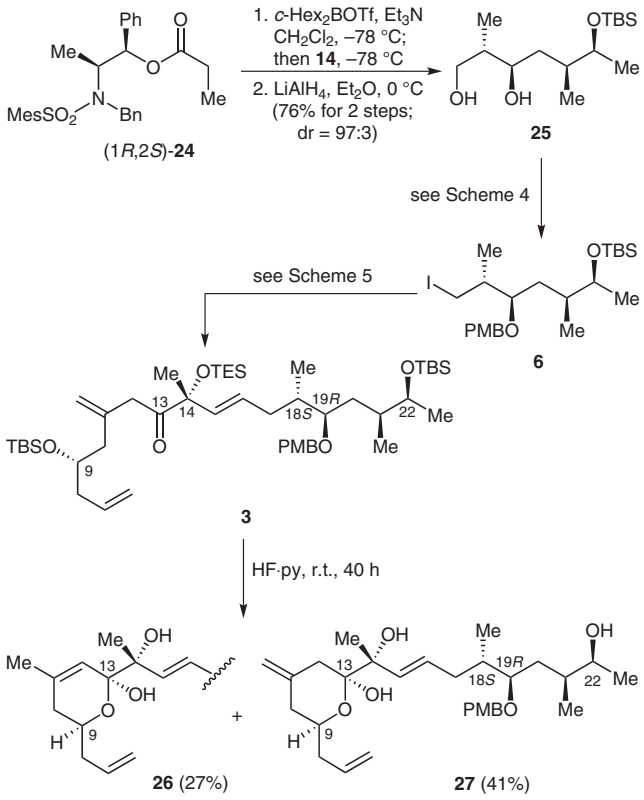
α-carbon of the aldehyde. By running the allylation at 70 °C, we were pleased to find that the expected allylation took place smoothly to give a mixture of two epimers of the C13-alcohol **21a** (57% combined yield) along with a C14-desilylated diol **21b** (20% combined yield of two epimers). Oxidation of the epimeric **21a** using DMP gave the ketone **22a**[15] in 61% yield (not optimized). Finally, we carried out global desilylation of **22a** using pyridine-buffered HF (r.t., 23 h) to form the C9/C13-hemiacetal **23**[16] (50% yield) along with a partially desilylated compound, the C14-alcohol **22b** (9%).

Finally, we synthesized the C7–C23 ketone fragment **3** of iriomoteolide-1a (Scheme 6). In order to shorten the reaction sequence an *anti*-selective aldol reaction of (1*R*,2*S*)-**24**[13] with **14** was performed to give, after $LiAlH_4$ reduction, the 1,3-diol **25** in 76% overall yield and in an excellent diastereomer ratio. By following the same procedures used in Scheme 4, the diol **25** was transformed into the chiral iodide **6**.[7] The latter was then sequentially assembled with the vinyl iodide **5** and the allyl bromide **4** according to the established procedures in Scheme 5, furnishing the ketone **3**.[7] Exposure of **3** upon pyridine-buffered HF at room temperature for about 10 hours gave a major product, the C9/C13-hemiacetal **27**, according to TLC analysis.[17] A minor product of low polarity was also found and was thought to be a partial desilylation intermediate. However, after stirring for 40 hours, the minor product increased significantly, and it was tentatively assigned as the isomerized byproduct **26** (27% yield) by ^1H NMR analysis: (a) disappearance of the two exocyclic methyl-



Scheme 5 Synthesis of the C7–C23 ketone fragment **22a** and the corresponding hemiacetal **23**

ene protons at C11; and (b) appearance of a new singlet vinyl proton and a new singlet methyl group at δ = 6.10 and 2.04 ppm, respectively. Nevertheless, it should be possible to suppress formation of **26** by controlling the reaction time. A related hemiacetal was prepared by Horne[2d] from the corresponding C9-TES-protected ketone **3′** (see Scheme 1). Our results on successful cleavage of the C9-TBS ether in **22a** and **3** using pyridine-buffered HF are different from those observed in Horne's model study.[2c] Our findings indicate that the C9-TBS-protected ketone **3** is the suitable advanced intermediate which should enable further manipulation of the functional groups for completing the total synthesis of iromoteolide-1a.



Scheme 6 Synthesis of the C7–C23 ketone fragment **3** and the corresponding hemiacetal **27**

In summary, we have accomplished synthesis of the C7–C23 fragment and its 18*R*,19*S*-diastereomer of iriomoteolide-1a in both forms of the C13-ketone **3/22a** and the C9/C13-hemiacetal **23/27**. Our synthesis highlights a sequence of *B*-alkyl Suzuki–Miyaura cross-coupling and indium-mediated aldehyde allylation for formation of the C16–C17 sp^2–sp^3 and the C12–C13 sp^3–sp^3 bonds, respectively. Our work offers the first demonstration of the indium-mediated aldehyde allylation (70 °C, THF–H_2O) and cleavage of the C9-TBS ether (HF·py, r.t.) in the synthesis of the advanced intermediates related to iriomoteolide-1a.

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synlett.

Acknowledgment

The Laboratory of Asymmetric Catalysis and Synthesis is established under the Cheung Kong Scholars Program of The Ministry of Education of China. This work is supported by Zhejiang University, Zhejiang University Education Foundation, and Department of Chemistry, HKUST.

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(14) **Procedure for the Synthesis of Alkene 19**
A flame-dried 50 mL two-neck flask was charged with the alkyl iodide **18** (680.0 mg, 1.31 mmol). The loaded flask was evacuated and backfilled with nitrogen for five times. A solution of 9-MeO-BBN (1 M in hexanes, 5.0 mL, 5.00 mmol) and dry Et_2O (12.0 mL) were then added successively at ambient temperature (about 18 °C). The resultant colorless solution was cooled to –78 °C and kept at the same temperature for 5 min. A solution of *t*-BuLi (1.6 M in heptane, 2.0 mL, 3.20 mmol) was rapidly added in one portion at –78 °C. The resultant yellow suspension was stirred for 10 min at the same temperature. Dry THF (12.0 mL) was added and the mixture turned clear. After stirring for an additional 10 min, the cold bath was removed followed by stirring at ambient temperature for 1.5 h to give a pale yellow homogeneous solution of the *B*-alkyl boronate. A separate 50 mL two-neck flask was charged with

$PdCl_2(dppf)\cdot CH_2Cl_2$ (40.0 mg, 4.9×10^{-2} mmol), $AsPh_3$ (44.0 mg, 0.14 mmol), and Cs_2CO_3 (1.04 g, 3.2 mmol). The loaded flask was evacuated and backfilled with nitrogen for five times. A solution of the vinyl iodide **5** (360.0 mg, 0.79 mmol) in degassed DMF (12.0 mL) was added through a syringe followed by adding degassed H_2O (0.36 mL, 20 mmol). Some blocky solid in the resultant yellow suspension was crushed with ultrasonication. After stirring at ambient temperature for 5 min, the above solution of the *B*-alkyl boronate was added via a syringe followed by stirring for another 4 h at ambient temperature. The reaction was quenched with sat. aq NH_4Cl solution. The resultant mixture was extracted with EtOAc (3 × 30 mL). The combined organic layer was washed with brine, dried over anhyd Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography (silica gel, first with PE and then with 2% EtOAc in PE) to afford the coupling product **19** (485.0 mg, 85%).

Characterization Data for Alkene 19

Colorless oil. $[\alpha]_D^{20}$ –18.1 (*c* 2.50, $CHCl_3$). R_f = 0.21 (100% PE). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.25 (d, *J* = 7.6 Hz, 2 H), 6.86 (d, *J* = 7.6 Hz, 2 H), 5.60 (dt, *J* = 16.0, 6.4 Hz, 1 H), 5.51 (d, *J* = 16.0 Hz, 1 H), 4.50 and 4.32 (ABq, *J* = 11.2 Hz, 2 H), 3.80 (s, 3 H), 3.73–3.64 (m, 1 H), 3.41–3.34 (m, 1 H), 3.37 (s, 2 H), 2.10–1.80 (m, 3 H), 1.71–1.60 (m, 1 H), 1.51 (br dd, *J* = 12.8, 10.8 Hz, 1 H), 1.28 (s, 3 H), 1.20 (br dd, *J* = 12.8, 12.0 Hz, 1 H), 1.07 (d, *J* = 6.0 Hz, 3 H), 1.00–0.90 (m, 18 H), 0.88 (br s, 12 H), 0.78 (d, *J* = 6.4 Hz, 3 H), 0.58 (q, *J* = 8.0 Hz, 12 H), 0.02 (br s, 6 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.0, 136.7, 131.3, 129.2 (2×), 127.5, 113.6 (2×), 79.7, 75.6, 72.7, 71.4, 70.7, 55.3, 36.3, 36.0, 35.3, 33.6, 25.9 (3×), 24.5, 20.9, 18.1, 14.1, 13.1, 7.1 (3×), 6.8 (3×), 6.7 (3×), 4.4 (3×), –4.3, –4.8. HRMS (+ESI): *m/z* [M + Na^+] calcd for $C_{40}H_{78}O_5Si_3Na$: 745.5049; found: 745.5013.

(15) **Procedure for the Synthesis of Ketone 22a**

A mixture of the allyl bromide **4** (63.0 mg, 0.20 mmol), the aldehyde **20** (100.0 mg, 0.16 mmol), and indium powder (24.0 mg, 0.20 mmol) in THF–H_2O (1:1, 0.4 mL) was stirred at 70 °C for 16 h in a sealed pressurized vial. After cooling to r.t., the reaction mixture was diluted with 10% aq $NaHCO_3$ (2 mL) and extracted with EtOAc (3 × 5 mL). The combined organic layer was washed with brine, dried over anhyd Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, 9% EtOAc in hexane) to provide the alcohol **21a** (79.0 mg, 57%) along with the diol **21b** (24.2 mg, 20%).

To a suspension of the alcohol **21a** (69.0 mg, 8.1×10^{-2} mmol) and solid $NaHCO_3$ (68.0 mg, 0.81 mmol) in CH_2Cl_2 (1 mL) cooled at 0 °C was added Dess–Martin periodinane (0.3 M in CH_2Cl_2, 0.83 mL, 0.25 mmol) followed by stirring at 25 °C for 2 h. The reaction was quenched by adding sat. aq $Na_2S_2O_3$ and sat. aq. $NaHCO_3$. The resultant mixture was extracted with EtOAc (3 × 5 mL), and the combined organic layer was washed with brine, dried over anhyd Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, 9% EtOAc in hexane) to provide the ketone **22a** (42.0 mg, 61%).

Characterization Data for Ketone 22a

Colorless oil. $[\alpha]_D^{20}$ +16.4 (*c* 1.13, $CHCl_3$). IR (film): 2956, 1722, 1514, 1465, 1251, 1083 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.24 (d, *J* = 8.8 Hz, 2 H), 6.86 (d, *J* = 8.8 Hz, 2 H), 5.87–5.68 (m, 2 H), 5.44 (d, *J* = 15.2 Hz, 1 H), 5.07–4.99 (m, 2 H), 4.96 (s, 1 H), 4.83 (s, 1 H), 4.48 and 4.33 (ABq, *J* = 11.2 Hz, 2 H), 3.82–3.75 (m, 1 H), 3.80 (s, 3 H), 3.71–3.64 (m, 1 H), 3.43 and 3.38 (ABq, *J* = 18.0 Hz, 2 H), 3.36–3.31 (m, 1 H), 2.30–1.49 (m, 10 H), 1.44 (s, 3 H), 1.18 (br dd, *J* = 12.4, 11.6 Hz, 1 H), 1.07 (d, *J* = 6.0 Hz, 3 H), 0.97 (t, *J* = 8.4 Hz, 9 H), 0.87–0.84 (m, 21 H), 0.78 (d, *J* = 6.4 Hz, 3 H), 0.68–0.60 (m, 6 H), 0.05–0.01 (m, 12 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 210.2, 159.0, 140.8, 135.1, 133.9, 131.2, 130.3, 129.2 (2×), 117.0, 116.5, 113.7 (2×), 82.4, 79.9, 72.6, 71.0, 70.8, 55.3, 43.7, 43.5, 41.8, 36.1 (2×), 35.4, 33.7, 25.9 (6×), 24.4, 20.8, 18.1, 18.1, 14.2, 13.4, 7.1 (3×), 6.6 (3×), –4.3, –4.5 (2×), –4.8. HRMS (+ESI): *m/z* [M + Na^+] calcd for $C_{48}H_{88}O_6Si_3Na$: 867.5781; found: 867.5781.

(16) **Procedure for the Synthesis of Hemiacetal 23**

To a solution of the ketone **22a** (7.8 mg, 9.2×10^{-3} mmol) in dry THF (1.0 mL) was added pyridine-buffered HF (0.15 mL, prepared from 0.5 mL of HF·pyridine, 0.7 mL of pyridine, and 1.6 mL of THF) at r.t. After stirring at the same temperature for 1 h, no reaction had taken place according to TLC analysis. Additional HF·pyridine (0.25 mL) was added followed by stirring at r.t. for 23 h. The reaction was quenched by adding sat. aq $NaHCO_3$. The mixture was extracted with EtOAc (3 × 5 mL). The combined organic layer was washed with brine, dried over anhyd Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, 33% EtOAc in hexane) to give the hemiacetal **23** (2.3 mg, 50%) along with the hydroxy ketone **22b** (0.6 mg, 9%).

Characterization Data for Hemiacetal 23

Pale yellow oil. $[\alpha]_D^{20}$ –17.6 (*c* 0.23, $CHCl_3$). IR (film): 3459, 2924, 1613, 1514, 1264, 1035 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.25 (d, *J* = 8.8 Hz, 2 H), 6.87 (d, *J* = 8.8 Hz, 2 H), 5.88–5.70 (m, 3 H), 5.11–5.03 (m, 2 H), 4.87 (d, *J* = 2.0 Hz, 1 H), 4.83 (d, *J* = 2.0 Hz, 1 H), 4.53 and 4.32 (ABq, *J* = 11.0 Hz, 2 H), 3.95–3.84 (m, 1 H), 3.80 (s, 3 H), 3.79–3.70 (m, 1 H), 3.42–3.33 (m, 1 H), 3.03 (d, *J* = 1.6 Hz, 1 H), 2.40 (s, 1 H), 2.36–2.20 (m, 4 H), 2.17–1.84 (m, 5 H), 1.71–1.50 (m, 2 H), 1.35–1.17 (m, 2 H), 1.31 (s, 3 H), 1.12 (d, *J* = 6.6 Hz, 3 H), 0.89 (d, *J* = 6.5 Hz, 3 H), 0.83 (d, *J* = 7.0 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.2, 141.5, 134.4, 133.9, 129.5 (2×), 129.3, 117.2, 113.8 (3×), 111.3, 99.2, 80.3, 77.1, 70.8, 70.7, 70.5, 55.3, 40.2, 39.3, 37.8, 36.7, 36.5, 34.9, 32.5, 21.0, 19.6, 14.5, 13.7. MS (+TOF LD): *m/z* (%) = 525 (100) [M + Na^+], 467 (55) [M^+ – H_2O – OH]. HRMS (+TOF CI): *m/z* [M^+ – H_2O – OH] calcd for $C_{30}H_{43}O_4^+$: 467.3161; found: 467.3158.

(17) **Characterization Data for Hemiacetal 27**

Pale yellow oil. $[\alpha]_D^{20}$ –2.3 (*c* 0.28, $CHCl_3$). IR (film): 3445, 2967, 2919, 1613, 1513, 1248, 1036 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.25 (d, *J* = 8.8 Hz, 2 H), 6.87 (d, *J* = 8.8 Hz, 2 H), 5.85–5.70 (m, 3 H), 5.12–5.03 (m, 2 H), 4.87 (s, 1 H), 4.83 (s, 1 H), 4.47 and 4.38 (ABq, *J* = 11.5 Hz, 2 H), 3.95–3.85 (m, 1 H), 3.80 (s, 3 H), 3.74–3.66 (m, 1 H), 3.42–3.35 (m, 1 H), 3.09 (s, 1 H), 2.45 (br s, 1 H), 2.35–2.14 (m, 5 H), 2.07–1.93 (m, 3 H), 1.90 (dd, *J* = 12.5, 12.5 Hz, 1 H), 1.75–1.60 (m, 2 H), 1.45–1.32 (m, 2 H), 1.29 (s, 3 H), 1.09 (d, *J* = 7.0 Hz, 3 H), 0.90 (d, *J* = 6.5 Hz, 3 H), 0.88 (d, *J* = 7.0 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 159.3, 141.6, 134.4, 133.8, 129.5 (2×), 129.3, 117.1, 113.9, 113.9 (2×), 111.2, 99.2, 80.0, 77.1, 70.7, 70.6, 70.0, 55.3, 40.2, 39.4, 37.9, 36.0, 36.0, 35.0, 32.7, 21.1, 20.1, 14.8, 14.6. HRMS (+TOF EI): *m/z* [M^+] calcd for $C_{30}H_{46}O_6^+$: 502.3294; found: 502.3316.