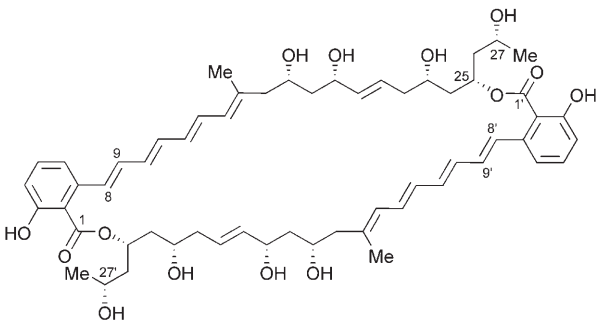

1: marinomycin A (*trans* $\Delta^{8,9}$, *trans* $\Delta^{8',9'}$)
2: marinomycin B (*cis* $\Delta^{8,9}$, *cis* $\Delta^{8',9'}$)
3: marinomycin C (*trans* $\Delta^{8,9}$, *cis* $\Delta^{8',9'}$)

Scheme 1. Structures of marinomycins A–C (**1**–**3**).

Natural Product Synthesis

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Total Synthesis of Marinomycins A–C**

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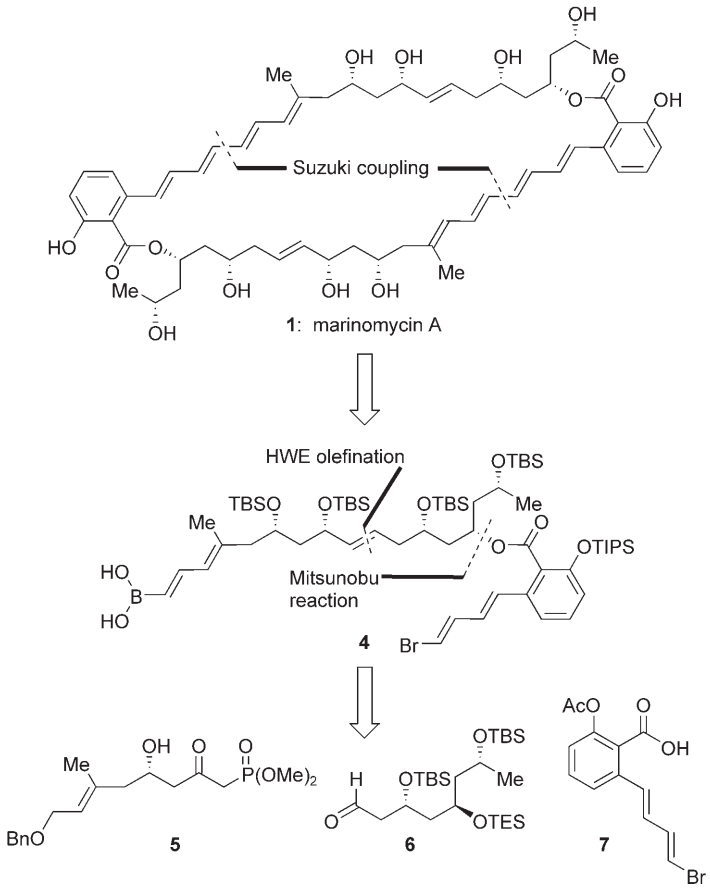
Marinomycins A–C (**1**–**3**, Scheme 1) are recently discovered natural products with imposing molecular architectures and impressive biological properties.[1] Isolated from actinomycete *Marinispora* strain CNQ-140 cultured from a sediment collected from the bottom of the ocean offshore of La Jolla, California (USA), by Fenical and co-workers,[1] these novel compounds exhibit significant antibiotic activities (minimum inhibitory concentration, MIC = 0.1–0.6 μM) against methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococcus faecium* (VREF), and inhibit cancer cell proliferation against the National Cancer Institute's 60 cancer cell line panel (LC_{50} = 0.2–2.7 μM). In particular, these marinomycins **1**–**3** showed potent and selective cytotoxicities against six of the eight melanoma cell lines of that panel.[1] Their novel and sensitive polyunsaturated structures coupled with their potentially useful biological activities prompted our interest in these molecules. Herein, we report the total synthesis of marinomycins A–C (**1**–**3**) and of two of their hitherto unknown monomeric homologues, mono-marinomycin A (**m-1**) and *iso*-mono-marinomycin A (**m-2**, Scheme 7).

Given that **1**, the most abundant of the marinomycins, is photolytically convertible to a mixture of all three (i.e. **1**, **2**, and **3**),[1] a total synthesis of marinomycin A (**1**) would constitute syntheses of **2** and **3** as well. Scheme 2 depicts our



Scheme 2. Retrosynthetic analysis of marinomycin A (**1**). HWE = Horner–Wadsworth–Emmons, TBS = *tert*-butyldimethylsilyl, TES = triethylsilyl.

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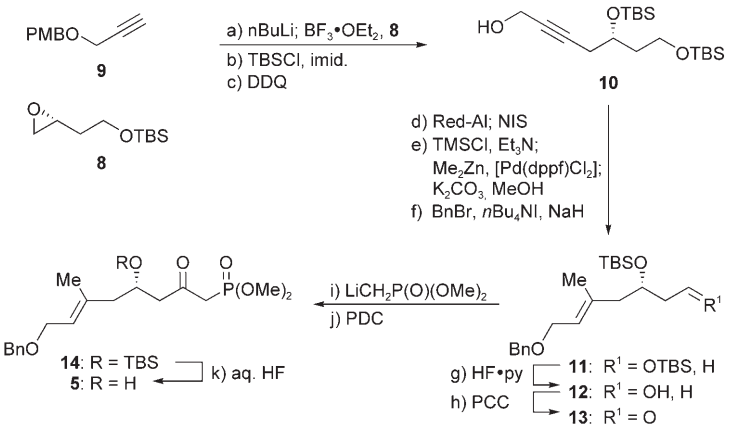
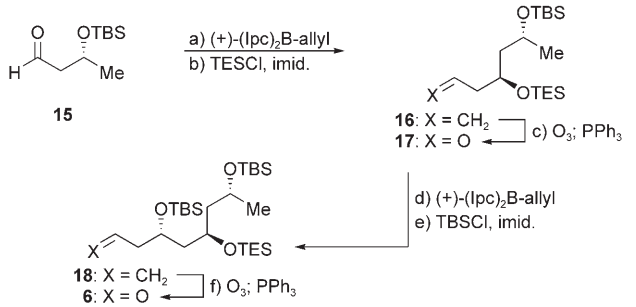
original retrosynthetic analysis of marinomycin A (**1**). The symmetrical structure of the molecule renders it suitable for several retrosynthetic disconnections; the one shown in Scheme 2 was chosen to highlight and test the Suzuki reaction as a means to construct large and complex macrocycles.[2] The appropriately functionalized vinyl boronic acid vinyl bromide **4** needed for the originally intended dimerization was traced to the three key building blocks ketophosphonate **5**, aldehyde **6**, and carboxylic acid **7**, through the indicated Horner–Wadworth–Emmons (HWE) olefination and Mitsunobu reactions. It was expected that dimer versus monomer formation in the cyclization process would be subject to concentration conditions.

The required building blocks **5**–**7** were synthesized in their enantiomerically pure forms as summarized in Schemes 3–5. Starting with the construction of ketophosphonate **5** (Scheme 3), the enantiomerically pure epoxide **8**[3] was regioselectively opened in the presence of $BF_3{\cdot}OEt_2$ with the lithium reagent derived from propargylic ether **9**[4] and *n*BuLi at −78 °C, leading to the corresponding secondary alcohol (89 % yield), whose silylation (TBSCl, 96 % yield) and de-*p*-methoxybenzylation (DDQ, 79 % yield) afforded the chain-extended propargylic alcohol **10**. Exposure of the latter compound to Red-Al, followed by addition of NIS, furnished the corresponding hydroxy vinyl iodide (66 % yield), whose temporary silylation (TMSCl) and subsequent coupling with $ZnMe_2$ in the presence of $[Pd(dppf)Cl_2]$ (cat.) gave, upon basic (K_2CO_3, MeOH) workup, the corresponding primary allylic alcohol (81 % yield). Benzylation of the latter compound (88 % yield) followed by desilylation (HF·py, 77 % yield) and oxidation with PCC afforded aldehyde **13** (73 % yield). Reaction of aldehyde **13** with the lithium species derived from dimethyl methyl phosphonate and *n*BuLi followed by oxidation (PDC) of the resulting epimeric mixture of alcohols led to ketophosphonate **14** in 64 % overall yield (two steps). Finally, fluoride-induced (aq HF/MeCN) desilylation of **14** gave the desired hydroxy ketophosphonate **5** in 92 % yield.

The synthesis of fragment **6** began with the readily available aldehyde **15**[5] and involved two iterations of Brown allylation[6] [(+)-$(ipc)_2$B-allyl]/ozonolysis (PPh_3) sequences with appropriate protections of the resulting secondary alcohols (Scheme 4). Proceeding through intermediates **16**–**18**, this sequence afforded the desired compound **6** in good overall yield (47 % from **15**, six steps) and with high diastereoselectivity (>40:1 d.r.).



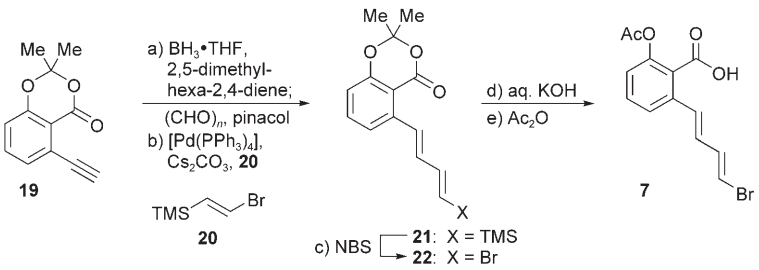
Scheme 3. Preparation of ketophosphonate **5**. Reagents and conditions: a) **9** (2.0 equiv), *n*BuLi (2.5 M in hexanes, 2.0 equiv), THF, −78 °C, 45 min; then $BF_3{\cdot}OEt_2$ (1.2 equiv), **8** in THF, −78 °C, 4 h, 89 %; b) TBSCl (1.2 equiv), imid. (3.0 equiv), DMF, 25 °C, 6 h, 96 %; c) DDQ (1.5 equiv), CH_2Cl_2, pH 7 phosphate buffer, 25 °C, 3 h, 79 %; d) Red-Al (3.33 M in toluene, 1.7 equiv), THF, 25 °C, 45 min; then NIS (1.8 equiv), THF, −78 °C, 30 min, 66 %; e) TMSCl (2.0 equiv), Et_3N (5.0 equiv), 25 °C, 2 h; then $[Pd(dppf)Cl_2]$ (0.05 equiv), Me_2Zn (2.0 equiv), THF, 65 °C, 12 h; then K_2CO_3 (0.1 equiv), MeOH, 25 °C, 4 h, 81 %; f) NaH (1.6 equiv), BnBr (1.7 equiv), nBu_4NI (0.1 equiv), THF, 25 °C, 6 h, 88 %; g) HF·py, THF, 0 °C, 3 h, 77 %; h) PCC (2.0 equiv), $NaHCO_3$ (0.5 equiv), 25 °C, 3 h, 73 %; i) $CH_3P(O)(OMe)_2$ (4.0 equiv), *n*BuLi (2.5 M in hexanes, 4.0 equiv), THF, −78 °C, 2 h; then **13** in THF, −78 °C, 2 h; j) PDC (2.1 equiv), 4-Å M.S., DMF, 25 °C, 12 h, 64 % over two steps; k) HF (48 % aq), MeCN, 25 °C, 3 h, 92 %. Bn = benzyl, DDQ = 2,3-dichloro-5,6-dicyano-1,4-benzoquinone, dppf = bis(diphenylphosphino)ferrocene, DMF = *N*,*N*-dimethylformamide, imid. = imidazole, PMB = *p*-methoxybenzyl, M.S. = molecular sieves, NIS = *N*-iodosuccinimide, PCC = pyridinium chlorochromate, PDC = pyridinium dichromate, py = pyridine, THF = tetrahydrofuran, TMS = trimethylsilyl.



Scheme 4. Preparation of aldehyde **6**. Reagents and conditions: a) (−)-B(Ipc)$_2$OMe (1.7 equiv), allylMgBr (1.0 M in Et_2O, 1.7 equiv), Et_2O, −78→25 °C, 2 h; then **15** in Et_2O, −78 °C, 4 h, −78→25 °C, 1 h, 95 % (>40:1 d.r.); b) TESCl (1.8 equiv), imid. (4.0 equiv), DMF, 25 °C, 4 h; c) O_3, CH_2Cl_2, −78 °C, 4 h; then PPh_3 (1.3 equiv), −78 °C, 2 h, −78→25 °C, 1 h, 64 % over two steps; d) (−)-B(Ipc)$_2$OMe (1.7 equiv), allylMgBr (1.0 M in Et_2O, 1.7 equiv), Et_2O, −78→25 °C, 2 h; then **17** in Et_2O, −78 °C, 4 h, −78→25 °C, 1 h, 85 % (>40:1 d.r.); e) TBSCl (2.0 equiv), imid. (5.0 equiv), DMF, 25 °C, 4 h; f) O_3, CH_2Cl_2, −78 °C, 4 h; then PPh_3 (1.3 equiv), −78 °C, 2 h, −78→25 °C, 1 h, 91 % over two steps. Ipc = isopinocampheyl.

The dienyl bromide carboxylic acid **7** was synthesized from known acetonide acetylene **19**[7] (Scheme 5). Thus, **19** was reacted with the adduct of $BH_3{\cdot}THF$ with 2,5-dimethylhexa-2,4-diene,[8] and the resulting borane (87 % yield) was coupled with commercially available TMS vinyl bromide **20** in the presence of $[Pd(PPh_3)_4]$ (cat.) and Cs_2CO_3 to afford TMS diene **21** (89 % yield). Exposure of the latter compound, **21**, to NBS gave bromide **22** (88 % yield), which was converted into acetoxy carboxylic acid **7** through saponification (KOH, 87 % yield) and acetylation (Ac_2O, $Mg(ClO_4)_2$;[9] 96 % yield).

The assembly of fragments **5**–**7** and elaboration of the growing molecule to the targeted enyne bromide **28** is shown in Scheme 6. Thus, coupling of ketophosphonate **5** and aldehyde **6** proceeded smoothly under the influence of $Ba(OH)_2$ to afford the enone in 95 % yield. Hydroxy-directed reduction of this enone with Et_2BOMe and $NaBH_4$[10] at



Scheme 5. Preparation of aryl diene fragment **7**. Reagents and conditions: a) 2,5-dimethylhexa-2,4-diene (5.5 equiv), BH_3·THF (2.5 equiv), THF, 0 °C, 3 h; then **19**, 0 °C, 1.5 h; then H_2O, 0→25 °C, 1 h; then $(CH_2O)_n$, 25 °C, 1 h; then pinacol (2.0 equiv), 25 °C, 24 h, 87%; b) $[Pd(PPh_3)_4]$ (0.1 equiv), Cs_2CO_3 (10 equiv), **20** (1.3 equiv), THF/H_2O (2:1), 55 °C, 1 h, 89%; c) NBS (1.2 equiv), MeCN, 25 °C, 15 min, 88%; d) KOH (5.0 equiv), THF/H_2O (1:1), 55 °C, 18 h, 87%; e) $Mg(ClO_4)_2$ (0.03 equiv), Ac_2O (1.1 equiv), 25 °C, 48 h, 96%. NBS = *N*-bromosuccinimide.

−78 °C resulted in the exclusive formation of the corresponding allylic alcohol (89% yield), whose silylation (TBSCl) led to the fully protected hexaol **23** (89% yield). The benzyl group was then cleaved from the terminal oxygen atom of this compound, **23**, with Ca in liquid NH_3 (75% yield), and the resulting primary alcohol was oxidized with DMP to furnish aldehyde **25** (87% yield). Enyne **26** was then generated from aldehyde **25** upon acetylene installment ($TMSCHN_2$-LDA;[11] 85% yield) and selective desilylation (TES) with PPTS in ethanol (77% yield). Accompanied by inversion of configuration at C25 (marinomycin numbering scheme), the Mitsunobu reaction between hydroxy compound **26** and carboxylic acid **7** (DEAD, PPh_3) proceeded in 93% yield to afford ester **27**. Exchanging the Ac groups for a TIPS group (K_2CO_3, MeOH; TIPSOTf, 2,6-lut.) then furnished the targeted bromo enyne **28** in excellent yield (92% overall). This latter switch of protecting groups was necessary because of difficulties encountered in the subsequent hydroboration and Suzuki coupling steps using the Ac-protected and free phenol carboxylic acid variants of **28**.

The stage was now set for the anticipated Suzuki dimerization/cyclization in the hope of reaching marinomycins A–C (see Scheme 7). Thus, the required boronic acid **4** was generated from enyne **28** by reaction with catecholborane and catalytic amounts of dicyclohexylborane (THF, 25 °C; then H_2O) and exposed to the action of TlOEt (4.0 equiv) and $[Pd(PPh_3)_4]$ (cat.) in THF/H_2O (4:1) at ambient temperature[12] and 0.01 M concentration, to afford, much to our surprise, only the monomeric product **29** (72% yield over the two steps). Increasing the concentration (up to 1.0 M) did not have much effect on the outcome of this reaction, suggesting that the precursor had a well-preorganized disposition towards cyclization once the palladium species was inserted. However, the use of 300 equivalents of TlOEt produced, in addition to **29**, the dimeric product **1** in approximately 2% yield (see Scheme 6), after global desilylation. Fluoride-induced global desilylation (TBAF) of **29** (see Scheme 7) gave the all-*trans* 22-membered ring **m-1** (mono-marinomycin A) and the all-*trans* 24-membered ring **m-2** (*iso*-mono-marinomycin A), where the lactone had shifted during desilylation, in 85% yield as a separable 1:1 mixture. The mono-marinomycins A (**m-1** and **m-2**) were isolated and characterized in pure form by preparative plate chromatography (silica, CH_2Cl_2/MeOH 93:7, two elutions) in the dark, followed by HPLC (C18-Dynamax column, 60 Å, 10 mm × 250 mm, 45% MeCN in H_2O). *iso*-Mono-marinomycin A (**m-2**) yielded crystals (mp: 213 °C (dec.), $CDCl_3$-D_3COD) that were suitable for X-ray crystallographic analysis (see ORTEP representation, Figure 1),[13] which confirmed its assigned structure as well as that of its sibling, mono-marinomycin A (**m-1**) and their precursors. The NOESY, ROESY, and COSY NMR data were also consistent with the assigned structures of **m-1** (Table 1) and **m-2**.

Having realized the propensity of dienyl bromide boronic acid **4** to cyclize before dimerization,

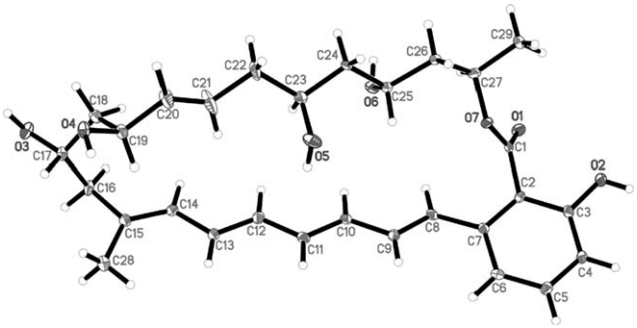
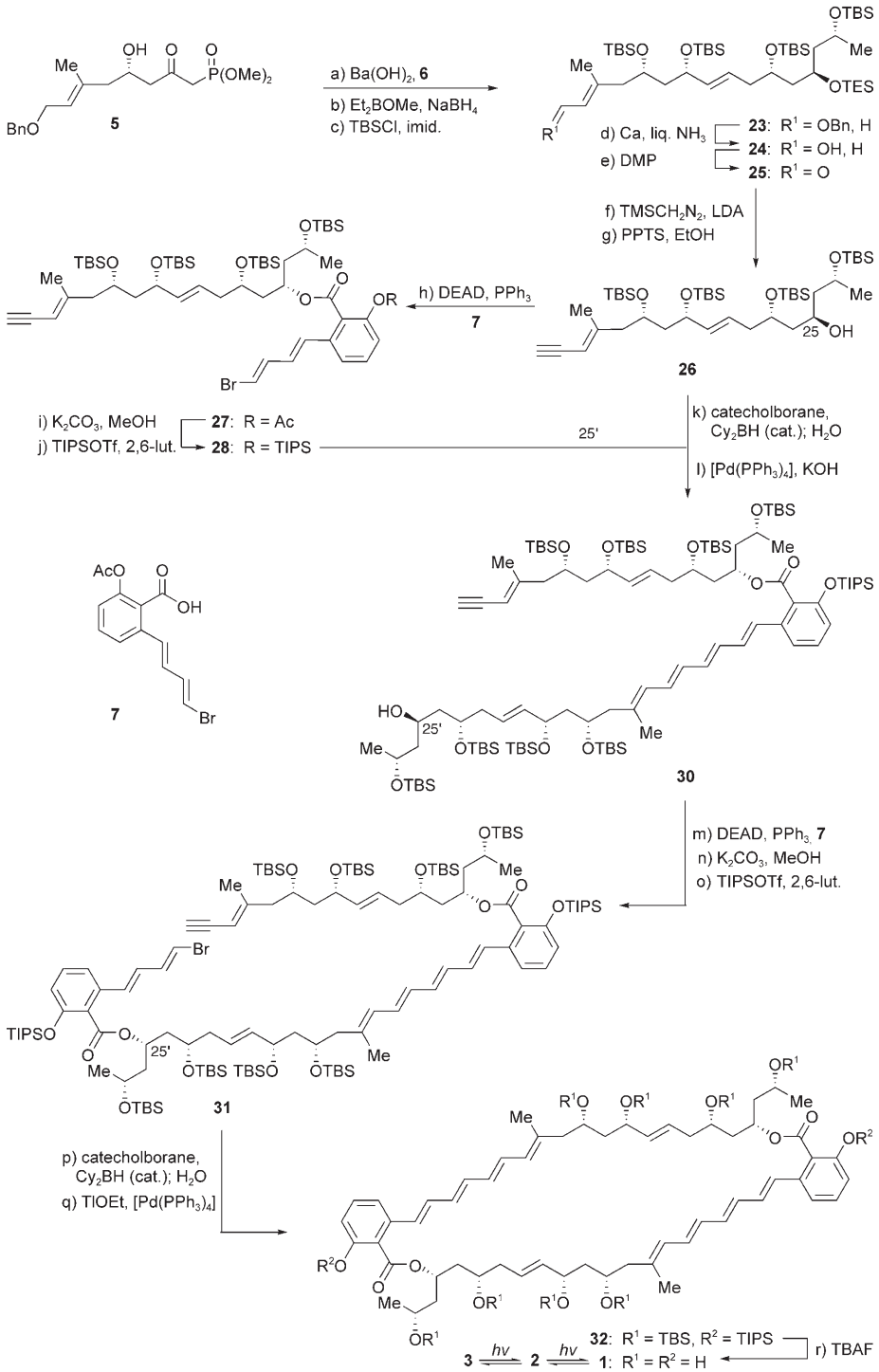


Figure 1. ORTEP representation of *iso*-mono-marinomycin A (**m-2**) with thermal ellipsoids shown at the 30% probability level. Hydrogen atoms are shown as white spheres.

we resorted to a stepwise approach to marinomycins A–C. The same key building blocks, **7** (Scheme 5), **26** (Scheme 6), and **28** (Scheme 6) were required, and the revised strategy is continued in Scheme 6. Thus, regioselective hydroboration of hydroxy enyne **26** with catecholborane catalyzed by dicyclohexylborane gave the corresponding boronic acid, whose Suzuki coupling (KOH (10 equiv), $[Pd(PPh_3)_4]$ (cat.), THF/H_2O (4:1)) with dienyl bromide **28** (0.67 equiv) led to hydroxy polyene **30** (63% yield based on **28**). Mitsunobu reaction of the latter compound, **30**, with carboxylic acid **7** proceeded with inversion of configuration at C25′ to afford, after exchange of the Ac group for a TIPS group, enyne ester **31** (78% overall yield for the three steps; Table 1).

Reaction of enyne **31** with catecholborane under the catalytic influence of dicyclohexylborane (THF, 25 °C) furnished, after H_2O quench, the corresponding boronic acid, which was, without isolation, treated with $[Pd(PPh_3)_4]$ (stoichiometric) and TlOEt (300 equiv) at ambient temperature to afford the fully protected macrocycle **32**. The product was used without purification in the next step, which involved global deprotection of **32** to give marinomycin A (**1**) in 23% overall yield for the three steps from **31**. Synthetic marinomycin A (**1**) was purified by HPLC (C8-Luna 5μ column, 100 Å, 250 mm × 10 mm, 60% MeCN in H_2O) and exhibited identical physical properties (R_f, R_t, UV spectral, α_D^{25}, mass

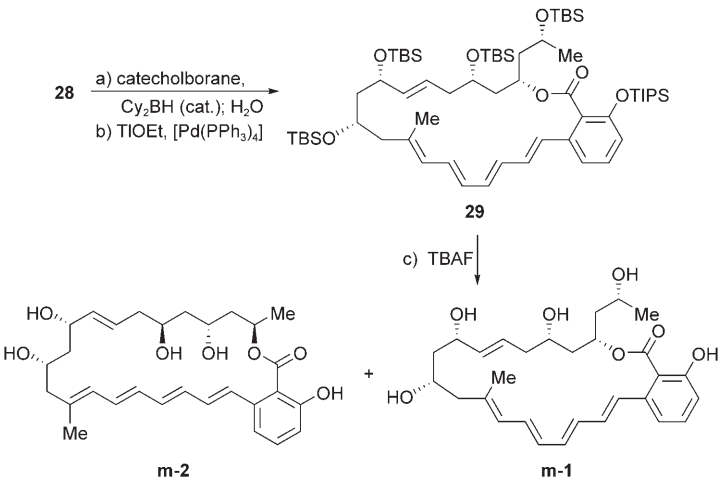


Scheme 6. Preparation of Suzuki coupling precursor **28** and completion of the total synthesis of marinomycins A–C (**1**–**3**). Reagents and conditions: a) **5** (1.0 equiv), **6** (1.1 equiv), $Ba(OH)_2{\cdot}H_2O$ (0.75 equiv), THF/H_2O (20:1), 25 °C, 1 h, 95 %; b) Et_2BOMe (1.0 M in THF, 1.1 equiv), $NaBH_4$ (1.1 equiv), THF/MeOH (4:1), −78 °C, 3 h, 89 %; c) TBSCl (4.0 equiv), imid. (8.0 equiv), DMF, 25 °C, 8 h, 89 %; d) **23** in THF/*i*PrOH (3:1); then liq. NH_3; then Ca (30 equiv), −78 °C, 1 h, 75 %; e) DMP (1.6 equiv), $NaHCO_3$ (10 equiv), CH_2Cl_2, 25 °C, 30 min, 87 %; f) iPr_2NH (1.8 equiv), *n*BuLi (2.5 M in hexanes, 1.5 equiv), THF, −78→0 °C, 30 min, $TMSCH_2N_2$ (1.5 equiv), THF, −78 °C, 30 min; then **25**, −78 °C , 1 h, −78→25 °C, 2 h, 85 %; g) PPTS (0.1 equiv), EtOH, 25 °C, 3 h, 77 %; h) DEAD (6.0 equiv), PPh_3 (6.0 equiv), **7** (6.0 equiv), THF, 25 °C , 1 h, 93 %; i) K_2CO_3 (0.05 equiv), THF/MeOH (1:1), 25 °C, 15 min; j) TIPSOTf (30 equiv), 2,6-lut. (60 equiv), CH_2Cl_2, 25 °C, 18 h, 92 % over two steps; k) catecholborane (3.0 equiv), Cy_2BH (0.1 M in THF, 0.2 equiv), THF, 25 °C, 1 h; then H_2O (5.0 equiv); l) KOH (10 equiv), $[Pd(PPh_3)_4]$ (0.1 equiv), THF/H_2O (4:1), 25 °C, 1 h, 63 % based on **28**; m) DEAD (6.0 equiv), PPh_3 (6.0 equiv), **7** (6.0 equiv), THF, 25 °C, 1 h; n) K_2CO_3 (0.05 equiv), THF/MeOH (1:1), 25 °C, 15 min; o) TIPSOTf (30 equiv), 2,6-lut. (60 equiv), CH_2Cl_2, 25 °C, 18 h, 78 % over three steps; p) catecholborane (3.0 equiv), Cy_2BH (0.1 M in THF, 0.2 equiv), THF, 25 °C, 1 h; then H_2O (5.0 equiv); q) TlOEt (300 equiv), $[Pd(PPh_3)_4]$ (1.0 equiv), THF/H_2O (10:1), 25 °C, 4 h; r) TBAF (50 equiv), THF, 25 °C, 18 h, 23 % over three steps. Cy = cyclohexyl, DMP = Dess–Martin periodinane, DEAD = diethyl azodicarboxylate, LDA = lithium diisopropylamide, lut. = lutidine, PPTS = pyridinium *p*-toluenesulfonate, TBAF = tetra-*n*-butylammonium fluoride, Tf = trifluoromethanesulfonyl, TIPS = triisopropylsilyl.

Table 1: Selected physical properties for compounds **m-1** and **31**.

m-1: $R_f = 0.54$ (silica gel, $CHCl_3$/MeOH/H_2O 40:9:1); $[\alpha]_D^{37} = -276.6$ ($c = 0.06$, $CDCl_3$); IR (film): $\tilde{\nu}_{max} = 3352, 2926, 2851, 1709, 1656, 1595, 1449, 1376, 1259, 1218, 1118, 1065, 999\ cm^{-1}$; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 7.35$ (t, $J = 7.8$ Hz, 1H), 7.13 (d, $J = 14.4$ Hz, 1H), 6.92 (d, $J = 8.4$ Hz, 1H), 6.77 (d, $J = 7.2$ Hz, 1H), 6.47 (dd, $J = 14.4$, 11.4 Hz, 1H), 6.34 (t, $J = 11.4$ Hz, 1H), 6.16–6.03 (m, 3H), 5.91 (d, $J = 10.8$ Hz, 1H), 5.38–5.20 (m, 3H); 4.16 (br, 1H, OH), 4.06 (m, 1H), 3.95 (m, 1H), 3.71 (t, $J = 9.0$ Hz, 1H), 3.65 (m, 1H), 3.58 (br, 1H, OH), 3.29 (br, 1H, OH), 2.56 (d, $J = 10.8$ Hz, 1H), 2.19 (d, $J = 13.8$ Hz, 1H), 2.14 (t, $J = 10.8$ Hz, 1H), 1.97–1.85 (m, 4H), 1.88 (s, 3H), 1.79–1.75 (m, 2H), 1.70–1.62 (m, 3H), 1.20 ppm (d, $J = 6.0$ Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 171.9, 162.4, 141.7, 135.8, 135.3, 134.6, 134.5, 133.3, 132.8, 131.9, 131.1, 130.3, 129.7, 128.2, 120.1, 117.0, 73.1, 72.5, 66.4, 65.8, 65.6, 50.4, 48.3, 45.5, 43.8, 42.5, 23.4, 17.8, 14.2$ ppm; HRMS (ESI-TOF) calcd for $C_{29}H_{38}O_7Na$ [M+Na^+]: 521.2510; found: 521.2530.

31: $R_f = 0.57$ (silica gel, hexanes/EtOAc, 8:1); $[\alpha]_D^{37} = -98.8$ ($c = 0.09$, CH_2Cl_2); IR (film): $\tilde{\nu}_{max} = 2952, 2828, 2856, 1729, 1570, 1465, 1255, 835, 775\ cm^{-1}$; ^1H NMR (600 MHz, C_6D_6, mixture of two rotamers around the aryl–carbonyl bond, ca. 1:1 ratio): $\delta = 7.15$ ($J = 8.4$ Hz, 1H), 7.11 (d, $J = 8.4$ Hz, 1H), 7.03–6.96 (m, 2H), 6.94–6.89 (m, 3H), 6.85 (dd, $J = 15.6$, 10.8 Hz, 1H), 6.75 (d, $J = 7.8$ Hz, 1H), 6.72 (d, $J = 7.8$ Hz, 1H), 6.61 (dd, $J = 13.2$, 13.2 Hz, 1H), 6.55 (dd, $J = 13.8$, 11.4 Hz, 1H), 6.49–6.37 (m, 2H), 6.31 (dd, $J = 15.6$, 10.8 Hz, 1H), 6.16 (d, $J = 11.4$ Hz, 1H), 6.03 (d, $J = 13.8$ Hz, 1H), 5.85 (dt, $J = 15.0$, 7.2 Hz, 1H), 5.83 (dt, $J = 15.0$, 7.2 Hz, 1H), 5.66 (dd, $J = 15.6$, 7.2 Hz, 1H), 5.59 (dd, $J = 15.6$, 7.2 Hz, 1H), 5.51–5.45 (m, 2H), 5.46 (s, 1H), 4.38 (q, $J = 7.2$ Hz, 1H), 4.28 (q, $J = 7.2$ Hz, 1H), 4.16–4.05 (m, 6H), 2.83 (d, $J = 2.4$ Hz, 1H), 2.49–2.40 (m, 4H), 2.33–2.25 (m, 2H), 2.23–2.10 (m, 6H), 2.05–1.92 (m, 5H), 2.04 (s, 3H), 1.86 (s, 3H), 1.85–1.79 (m, 2H), 1.70 (ddd, $J = 13.2$, 7.2, 4.8 Hz, 1H), 1.35–1.28 (m, 12H), 1.19–1.16 (m, 36H), 1.07 (s, 9H), 1.06 (s, 9H), 1.06 (s, 27H), 1.05 (s, 9H), 1.02 (s, 9H), 1.01 (s, 9H), 0.28 (s, 3H), 0.26 (s, 6H), 0.23 (s, 3H), 0.21 (s, 3H), 0.20 (s, 3H), 0.19 (s, 3H), 0.19 (s, 3H), 0.19 (s, 3H), 0.16 (s, 6H), 0.15 (s, 3H), 0.15 (s, 3H), 0.14 (s, 3H), 0.14 (s, 3H), 0.12 ppm (s, 3H); ^{13}C NMR (150 MHz, C_6D_6, mixture of rotamers around the aryl–carbonyl bond, ca. 1:1 ratio): $\delta = 167.4$ (0.5 C), 167.4 (0.5 C) 167.1, 153.9, 153.8 (0.5 C), 153.8 (0.5 C), 150.8, 137.8 (3 C), 137.7, 137.2, 137.1, 136.4, 136.2 (0.5 C), 136.2 (0.5 C), 135.7, 132.4 (0.5 C), 132.3 (0.5 C), 131.5 (0.5 C), 130.9 (0.5 C), 130.9, 130.1, 130.1 (0.5 C), 130.0, 129.9 (0.5 C), 129.1, 129.0, 126.5 (0.5 C), 126.4 (0.5 C), 126.3 (0.5 C), 126.2 (0.5 C), 118.1, 117.9, 117.9, 117.4, 110.6, 110.4 (0.5 C), 110.3 (0.5 C), 107.8, 81.9, 80.7, 72.0, 71.9 (0.5 C), 71.8 (0.5 C), 71.5, 71.4, 69.8 (0.5 C), 69.7 (0.5 C), 68.7, 68.2, 66.5, 66.4 (2 C), 51.7, 48.6, 47.4, 47.2, 46.7, 45.6, 45.5, 42.6, 42.5, 41.0, 30.2, 26.3 (9 C), 26.2 (9 C), 26.2 (3 C), 26.2 (3 C), 24.5, 24.4, 20.3, 18.3 (8 C), 17.9 (12 C), 12.7 (6 C), −3.4, −3.4, −3.8 (2 C), −3.9 (3 C), −3.9, −4.0, −4.1 (4 C), −4.2, −4.3, −4.4 ppm; HRMS (ESI-TOF) calcd for $C_{124}H_{226}BrO_{14}Si_{10}$ [$M-H^-$]: 2298.3853; found: 2298.3852.



Scheme 7. Formation of mono-marinomycins **m-1** and **m-2**. Reagents and conditions: a) catecholborane (3.0 equiv), Cy_2BH (0.1 M in THF, 0.2 equiv), THF, 25 °C, 1 h; then H_2O (5.0 equiv); b) TlOEt (4.0 equiv), [$Pd(PPh_3)_4$] (0.1 equiv), THF/H_2O (4:1), 25 °C, 30 min, 72% over two steps; c) TBAF (30 equiv), THF, 18 h, 85% yield.

spectrometric, and ^1H and ^{13}C NMR spectral data) to those recorded for the naturally occurring substance.[1,14] When allowed to isomerize in ambient light, marinomycin A (**1**) formed mixtures with marinomycins B (**2**) and C (**3**) as previously reported (**1**/**2**/**3** ≈ 16:2:9 after 30 min; ca. 1:1:1 after 2 h by HPLC).[1,15]

The success of the Suzuki reaction in these syntheses underscores its usefulness in the construction of complex molecules. Besides rendering the naturally occurring marinomycins A–C (**1**–**3**) readily available, the described synthetic technology also provides access to their monomeric derivatives, mono-marinomycin A (**m-1**) and its isomer *iso*-mono-marinomycin A (**m-2**), and opens the way to the construction of other members of the class of natural or designed origins.

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[14] We thank Professor William Fenical and Dr. Hak Cheol Kwon for an authentic sample and spectra of marinomycins A–C (**1**–**3**).
[15] Exact ratios of marinomycins A–C (**1**–**3**) varied from one experiment to another.

