Convergent Synthesis of *trans*-Fused Oxane Ring Systems Based on Ni^{II}/Cr^{II}-Mediated Cross-coupling Reactions

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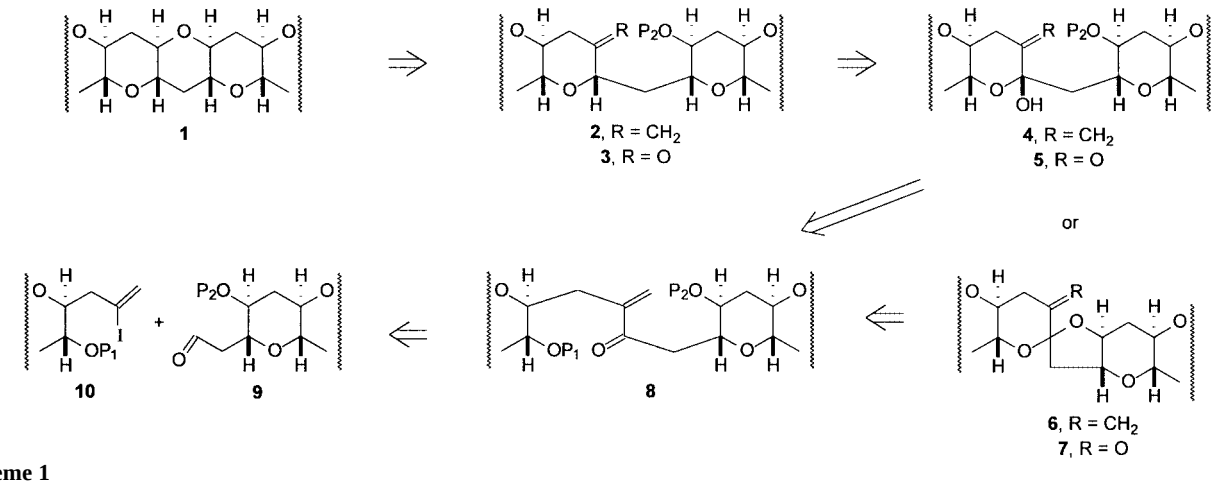
Abstract: A general method for the convergent assembly of polyether structures has been developed based on a Ni^{II}/Cr^{II}-mediated cross-coupling reaction of alkenyl iodides with aldehydes. The present method allowed coupling to oxane rings via acetal cyclization and reductive etherification reactions.

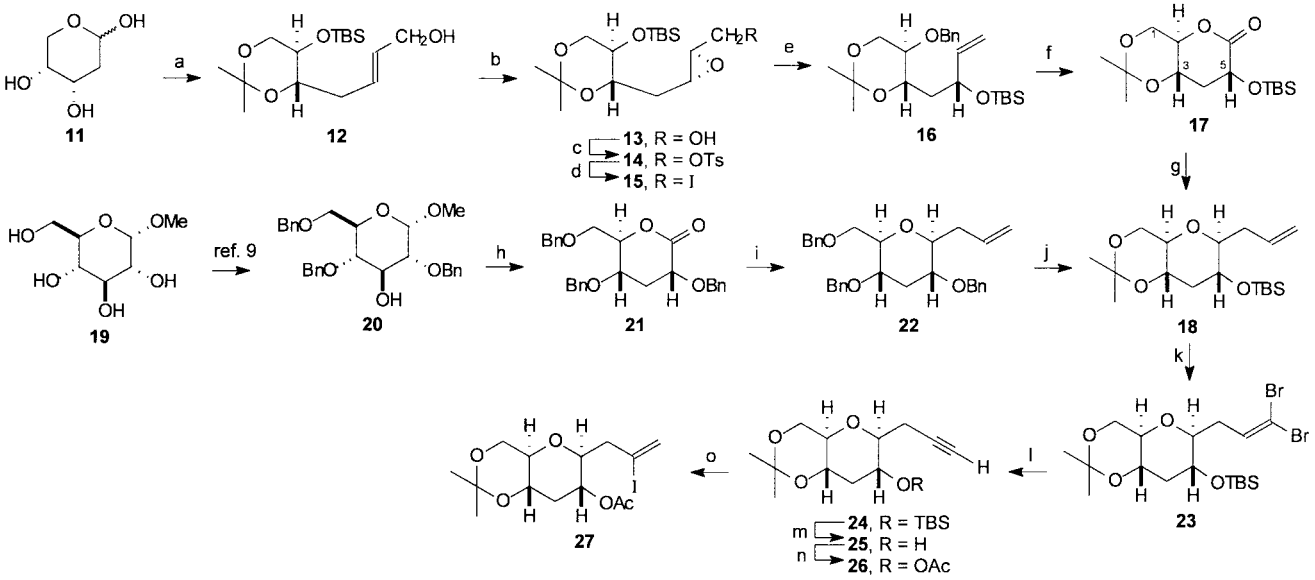
Key words: coupling reactions, tetrahydropyrans, polyethers, toxins

The reductive intramolecular coupling of hydroxy-ketones in reactions with silane-Lewis acids (SI-LA) to generate oxane rings in C-linked oxacycles is affected by the conformational preference of the hemiacetal intermediates.[1] This finding implies that the convergent synthesis of *trans*-fused polyethers may be conducted on driving ring closure of hydroxy-ketones to oxane rings under thermodynamic conditions. Recently, we have shown[2] that SI-LA-induced reductive cleavage of the anomeric center in allyl spiroketals can be conducted chemo-, regio- and stereoselectively to give C-linked oxacycles. As a part of a larger project to synthesize *trans*-fused polyethers related to ciguatoxin and congeners,[3] both reductively conducted possibilities are being considered[4] (Scheme 1). In this communication, we report on results related to the **5** → **1** cyclization approach based on very simple models. Our synthetic plan began with the Ni^{II}/Cr^{II}-mediated coupling[5] between fragments **9** and **10** followed by oxidation to the α,β-unsaturated ketone **8**. These reactions establish all the requisite framework which should allow us to study sequentially the double SI-LA reductive process.

Schemes 2 and 3 summarize the synthesis of the starting models, alkenyl iodide **27** (Scheme 2) and aldehyde **33** (Scheme 3). The synthesis of the allyl intermediate **18** began with 2-deoxyribose (**11**), which was converted into olefin **12** by a Wittig reaction followed by sequential selective protection involving 1,3-dioxacetalization and silylation. DIBAL-H reduction led to alcohol **12** (73% overall yield). Sharpless asymmetric epoxidation[6] of **12** using (-)-diethyl tartrate as the chiral auxiliary gave the epoxide **13** in 90% yield. Iodination of the tosyl derivative followed by base treatment gave, after benzylation,[7] compound **16** (89% overall yield, three steps). Vinyl fragmentation followed by oxidation of the resulting hemiacetal gave the lactone **17** (61% yield). The equatorial C-glycosidation to give **18** was stereoselectively accomplished by addition of allylmagnesium bromide to the lactone **17** followed by silane reduction.[8] Compound **18** was alternatively synthesized via lactone **21** following a protocol identical with that used for **17** to **18** conversion. Lactone **21** was prepared from the D-glucopyranoside derivative **20**[9], with the free hydroxyl group being removed under Barton [10] conditions. Vinyl fragmentation in **18** followed by dibromoolefination of the resulting aldehyde[11] gave the vinyl dibromide **23** which was converted to the acetylene derivative **24** by further treatment with n-Buli. Removal of the silyl group from **24**[12] then led to the alcohol **25** which was converted to the acetate **26**. Iodoboration[13] of **26** gave the alkenyl iodide **27**.[14]



Scheme 1

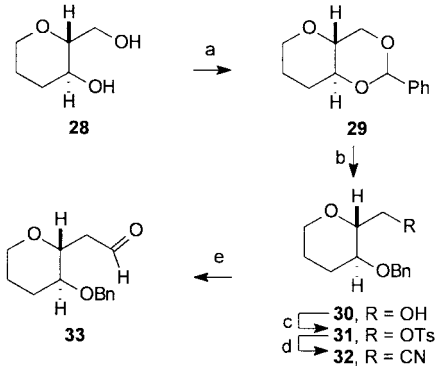


Scheme 2 Preparation of intermediate **27**. Reagents and conditions: (a) i, 1.2 equiv of Ph_3PCHCO_2Me, THF, 80ºC, 5 h, 99%; ii, 1.5 equiv of $Me_2C(OMe)_2$, CSA cat., CH_2Cl_2, 40ºC, 12 h, 93%, iii, 1.4 equiv of TBSOTf, 2.0 equiv of Et_3N, CH_2Cl_2, 0-25ºC, 1 h, 98%; iv, 2.5 equiv of DIBAL-H, Et_2O, 0-25ºC, 5 h, 81%. (b) 0.3 equiv of Ti (O-i-Pr)$_4$, 0.2 equiv of (-)-diethyl tartrate, 3.0 equiv of t-BuOOH (5-6 N in decane), 4 Å MS, CH_2Cl_2, -20ºC, 24 h, 90%. (c) 1.1 equiv of TsCl, 0.05 equiv of 4-DMAP, 2.0 equiv of Et_3N, CH_2Cl_2, 0-25ºC, 3 h, 98%. (d) 2.3 equiv of NaI, 2.0 equiv of $NaHCO_3$, butanone, 60ºC, 2 h, 97%. (e) i, 2.0 equiv of t-BuLi, Et_2O, -78ºC, 30 min, 94%; ii, 1.1 equiv of BnBr, 1.1 equiv of NaH, (n-Bu)$_4$NI cat., THF, 0-25ºC, 12 h, 93%. (f) i, 3.0 equiv of NMO, OsO_4 cat., THF-H_2O-acetone (1:1:1), 25ºC, 12 h, 91%; ii, H_2, Pd (C) 5% cat., EtOAc, 12 h, 99%; iii, 1.5 equiv of (n-Bu)$_4$ NIO_4, CH_2Cl_2, 0-25ºC; iv, 3.0 equiv of PCC, 0.3 equiv of NaOAc, 3 Å MS, CH_2Cl_2, 25ºC, 12 h, 80%. (g) i, 1.2 equiv of allylmagnesium bromide, THF, -78ºC, 1 h; ii, 1.5 equiv of Et_3SiH, 1.5 equiv of TMSOTf, CH_2Cl_2, -78ºC, 5 h, 68%. (h) i, 1.6 equiv of NaH, 3.3 equiv of CS_2, 1.8 equiv of MeI, imidazole cat., THF, 0-20ºC, 1 h; ii, 1.5 equiv of Bu_3SnH, AIBN cat., toluene, 110ºC, 36 h, 87% (two steps); iii, 0.1 equiv of AcOH, 0.5 equiv of HCl 1N, 60ºC, 48 h, 69%; iv, 3.0 equiv of $(COCl)_2$, 9.0 equiv of DMSO, 15.0 equiv of Et_3N, CH_2Cl_2, -78-0ºC, 2 h, 70%. (i) i, 1.1 equiv of allylmagnesium bromide, THF, -78ºC, 1 h; ii, 1.5 equiv of Et_3SiH, 1.5 equiv of $BF_3{\cdot}Et_2O$, CH_2Cl_2, 0ºC, 2 h, 64% (two steps). (j) i, Na, NH_3 liq, THF, -60ºC, 2 h, 100%; ii, 1.5 equiv of 2,2-dimethoxypropane, $POCl_3$ cat., DMF, 20ºC, 12 h, 60%; iii, 1.2 equiv of t-BuMe_2SiCl, 2.5 equiv of imidazole, CH_2Cl_2, 20ºC, 48 h, 96%. (k) i, 1.5 equiv of 4-methylmorpholine N-oxide, OsO_4 cat., H_2O: THF (1:1), 20ºC, 12 h; ii, 1.5 equiv of $NaIO_4$, MeOH: H_2O (8:1), 0ºC, 90% (two steps); iii, 4.0 equiv of Ph_3P, 2.0 equiv of CBr_4, 5.0 equiv of Et_3N, CH_2Cl_2, hexane, 0ºC, 3 h, 97%. (l) 1.0 equiv of n-BuLi, THF, -78ºC, 2 h, 65%. (m) 1.3 equiv of n-BuLi, THF, 0ºC, 2 h, 98%. (n) 1.5 equiv of Ac_2O, 2.5 equiv of Et_3N, DMAP cat., CH_2Cl_2, 20ºC, 2 h, 89%. (o) i, 1.2 equiv of B-I-9-BBN (1.0 M in hexane), n-pentane, -20-20ºC, 8 h, then 0.02 equiv of AcOH, 0ºC, 30 min, then NaOH, H_2O_2 35%, 0ºC, 30 min; ii, 1.5 equiv of 2,2-dimethoxypropane, $POCl_3$ cat., CH_2Cl_2, 20ºC, 12 h; iii, 1.5 equiv of Ac_2O, 2.5 equiv of Et_3N, DMAP catalyst, CH_2Cl_2, 20ºC, 1 h, 53% (three steps).

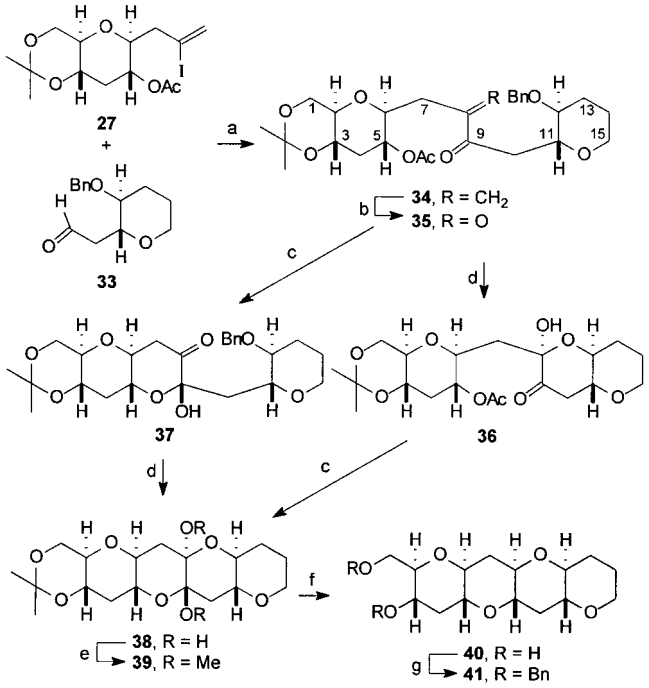
For the synthesis of aldehyde **33** (Scheme 3), diol **28**[15] was selectively protected involving 1,3-benzylidene ketalization followed by DIBAL-H reduction to give **30**. Tosylation and displacement of the tosyl group with cyanide provided **32** which was further reduced to the aldehyde **33** (62% overall yield).

The completion of the synthesis is shown in Scheme 4. The Ni^{II}/Cr^{II}-mediated coupling[5] of **27** with **33** proceeded smoothly to yield the two expected allylic alcohols, which were oxidized to the α,β-unsaturated ketone **34**.[16] Subsequent ozonolysis led to diketone **35**. Base-induced hydrolysis of diketone **35** gave hemiacetal **37**. Debenzylation of **35** gave hemiacetal **36**. Hemiacetals **36** and **37** were independently converted to the common bis-hemiacetal **38**.

O-Methylation of bis-hemiacetal **38** under the base conditions reported by Mori[1j] gave the methyl diacetal **39**, which was doubly reduced by SI-LA treatment to the tetracyclic diol **40**, further protected as its dibenzyl ether derivative **41**.[1j]



Scheme 3 Preparation of aldehyde **33**. Reagents and conditions: (a) 1.5 equiv of $PhCH(OMe)_2$, 0.01 equiv of CSA, DMF, 50ºC, 3 h, 85%. (b) 3.0 equiv of DIBAL-H, CH_2Cl_2, 0ºC, 24 h, 97%. (c) 1.2 equiv of TsCl, 0.05 equiv of 4-DMAP, 1.5 equiv of Et_3N, CH_2Cl_2, 25ºC, 24 h, 100%. (d) 3.0 equiv of KCN, DMSO, 60ºC, 24 h, 87%. (e) 1.5 equiv of DIBAL-H, Et_2O, 20ºC, 12 h, 86%.



Scheme 4 Synthesis of compound **41**.[1j] Reagents and conditions: (a) i, 4.0 equiv of $CrCl_2$, 0.1 equiv of $NiCl_2$, DMSO, 20ºC, 12 h, 86%; ii, 3.0 equiv of oxalyl chloride, 9.0 equiv of DMSO, 15.0 equiv of Et_3N, CH_2Cl_2, -78°C, 2 h, 96%. (b) O_3, CH_2Cl_2, -78ºC, 20 min, then 3.0 equiv of Ph_3P, 20°C, 1 h, 56-60%. (c) 1.1 equiv of K_2CO_3, MeOH, 20ºC, 2 h, 79%. (d) H_2, Pd-C 10% cat., EtOAc, 20ºC, 2 h, 55-63%. (e) 2.5 equiv of NaH, 5.0 equiv of MeI, DMF, 0ºC, 6 h, 62%. (f) 10.0 equiv of Et_3SiH, 4.0 equiv of TMSOTf, CH_2Cl_2, 0ºC, 3 h, 66%. (g) 2.5 equiv of BnBr, 2.5 equiv of NaH, n-Bu_4NI (cat.), THF-DMF (3:1), 25ºC, 3 h, 76%.

The present strategy will be extended for synthesizing polycyclic marine toxins, which will be reported in due course.

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(14) Data for selected compounds included in Scheme 2: **17**: colorless foam. $[\alpha]^{27}_D$ +14.5 (c 4.93, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.53 (1H, dd, J = 7.7, 7.7 Hz, H-5), 4.46 (1H, ddd, J = 3.6, 7.6, 8.4 Hz, H-3), 4.20 (1H, ddd, J = 5.3, 6.9, 8.4 Hz, H-2), 4.11 (1H, dd, J = 6.9, 8.7 Hz, H-1), 3.77 (1H, dd, J = 5.3, 8.7 Hz, H-1), 2.44 (1H, ddd, J = 3.6, 7.7, 13.1 Hz, H-4), 2.25 (1H, ddd, J = 7.6, 7.6, 13.1 Hz, H-4), 1.45 (3H, s), 1.34 (3H, s), 0,91 (9H, s), 0.16 (3H, s), 0.14 (3H, s). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.4 (C_q, C_6), 110.2 (C_q), 77.1 (CH, C_3), 76.2 (CH, C_2), 67.8 (CH, C_5), 66.2 (CH_2, C_1), 33.1 (CH_2, C_4), 26.3 (CH_3), 25.7 (CH_3), 24.6 (CH_3), 18.2 (C_q), -4.8 (CH_3), -5.3 (CH_3). IR (KBr): ν_{max} 1790 cm^{-1}. Anal. calcd for $C_{15}H_{28}O_5Si$: C, 56.93; H, 8.93. Found C, 56.94, H, 8.87. **27**: Oil. $[\alpha]^{20}_D$ -28.5 (c 1.4, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.06 (1H, brs, H-9), 5.74 (1H, brs, H-9), 4.69 (1H, ddd, J = 4.8, 9.8, 11.0 Hz, H-5), 3.88 (1H, dd, J = 5.2, 10.8 Hz, H-1), 3.65 (1H, dd, J = 10.8, 10.8 Hz, H-1), 3.62 (1H, ddd, J = 3.5, 8.8, 9.8 Hz, H-6), 3.59 (1H, ddd, J = 4.2, 9.4, 9.8 Hz, H-3), 3.21 (1H, ddd, J = 5.2, 9.4, 10.8 Hz, H-2), 2.61 (1H, brdd, J = 3.5, 15.1 Hz, H-7), 2.44 (1H, brdd, J = 8.8, 15.1 Hz, H-7), 2.35 (1H, ddd, J = 4.2, 4.8, 11.4 Hz, H-4), 2.04 (3H, s), 1.56 (1H, ddd, J = 11.4, 11.4, 11.4 Hz, H-4), 1.45 (3H, s), 1.37 (3H, s). ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.9 (C_q), 128.1 (CH_2, C_9), 105.6 (C_q, C_8), 99.3 (C_q), 77.9 (CH, C_6), 74.4 (CH, C_2), 70.0 (CH, C_5), 68.4 (CH, C_3), 62.6 (CH_2, C_1), 47.4 (CH_2, C_7), 35.3 (CH_2, C_4), 29.1 (CH_3), 21.1 (CH_3), 19.1 (CH_3). HRMS calcd for the deacetylated derivative $C_{12}H_{19}IO_4$, m/z M^+ 354.03281. Found, 354.03317.

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(16) Data for selected compounds included in Scheme 4: α,β-Unsaturated ketone **34**: Oil. $[\alpha]^{20}_D$ +0.02 (c 0.55, $CHCl_3$).^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32-7.26 (5H, m, ϕH), 5.98 (1H, s, =CH), 5.78 (1H, s, =CH), 4.62 (1H, d, J = 11.7 Hz, ϕCH), 4.58 (1H, ddd, J = 4.9, 9.8, 9.8 Hz, H-5), 4.39 (1H, d, J = 11.7 Hz, ϕCH), 3.82 (1H, brd, J = 11.5 Hz, H-15), 3.79 (1H, dd, J = 5.2, 10.8 Hz, H-1), 3.71 (1H, ddd, J = 3.0, 8.9, 8.9 Hz, H-11), 3.58 (1H, dd, J = 10.8, 10.8 Hz, H-1), 3.56 (1H, ddd, J = 4.1, 9.4, 11.6 Hz, H-3), 3.48 (1H, ddd, J = 3.0, 9.8, 9.3 Hz, H-6), 3.35 (1H, ddd, J = 2.7, 11.5, 11.7 Hz, H-15), 3.14 (1H, ddd, J = 5.2, 9.4, 10.8 Hz, H-2), 3.09 (1H, dd, J = 3.0, 15.8 Hz, H-10), 3.08 (1H, ddd, J = 5.0, 8.9, 9.3 Hz, H-12), 2.75 (1H, dd, J = 8.9, 15.8 Hz, H-10), 2.66 (1H, brdd, J = 2.2, 14.7 Hz, H-7), 2.32 (1H, ddd, J = 4.5, 4.5, 11.3 Hz, H-4), 2.28 (1H, brd, J = 12.4 Hz, H-13), 2.18 (1H, dd, J = 8.9, 14.7 Hz, H-7), 2.03 (3H, s), 1.70-1.65 (1H, m, H-14), 1.63-1.56 (1H, m, H-14), 1.47 (1H, ddd, J = 11.3, 11.3, 11.3 Hz, H-4), 1.43 (3H, s), 1.44-1.38 (1H, m, H-13), 1.36 (3H, s). ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.6 (C_q, C_9), 170.1 (C_q), 144.8 (C_q, C_8), 138.4 (C_q), 128.4 (CH), 127.8 (CH), 127.7 (CH), 126.6 (CH_2), 99.2 (C_q), 77.6 (CH, C_6), 77.6 (CH, C_{11}), 76.8 (CH, C_2), 74.1 (CH, C_{12}), 70.8 (CH, C_5), 70.4 (CH_2), 68.5 (CH, C_3), 67.8 (CH_2, C_{15}), 62.6 (CH_2, C_1), 40.9 (CH_2, C_{10}), 35.2 (CH_2, C_4), 33.4 (CH_2, C_7), 29.7 (CH_2, C_{13}), 29.1 (CH_3), 25.3 (CH_2, C_{14}), 21.1 (CH_3), 19.1 (CH_3). HRMS, calcd for $C_{28}H_{38}O_8$ m/z M^+ 502.25667. Found, m/z 502.25632. Diketone **35**: Oil. $[\alpha]^{20}_D$ -8.9 (c 0.59, $CHCl_3$) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32-7.23 (5H, m, ϕH), 4.55 (1H, ddd, J = 4.4, 9.3, 11.2 Hz, H-5), 4.54 (1H, d, J = 11.5 Hz, ϕCH), 4.33 (1H, d, J = 11.5 Hz, ϕCH), 3.86 (1H, ddd, J = 3.3, 9.3, 9.3 Hz, H-6), 3.80 (1H, brdd, J = 4.5, 11.4 Hz, H-15), 3.76 (1H, dd, J = 5.3, 10.8 Hz, H-1), 3.68 (1H, ddd, J = 5.6, 7.8, 8.8 Hz, H-11), 3.58-3.52 (2H, m, H-1, H-3), 3.32 (1H, ddd, J = 2.7, 11.7, 11.7 Hz, H-15), 3.15 (1H, ddd, J = 5.0, 10.0, 10.0 Hz, H-2), 3.11 (1H, ddd, J = 4.4, 9.3, 10.6 Hz, H-12), 3.02 (1H, dd, J = 5.5, 15.3 Hz, H-10), 2.90 (1H, dd, J = 7.7, 15.3 Hz, H-10), 2.78 (1H, dd, J = 8.9, 16.7 Hz, H-7), 2.62 (1H, dd, J = 3.4, 16.7 Hz, H-7), 2.36 (1H, ddd, J = 4.4, 4.4, 11.2 Hz, H-4), 2.24 (1H, brdd, J = 3.0, 12.2 Hz, H-13), 1.98 (3H, s), 1.68-1.62 (1H, m, H-14), 1.60-1.57 (1H, m, H-14), 1.47 (1H, ddd, J = 11.2, 11.2, 11.2 Hz, H-4), 1.46 (3H, s), 1.37-1.34 (1H, m, H-13), 1.35 (3H, s). ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.7 (C_q, C_8), 196.5 (C_q, C_9), 137.9 (C_q), 128.5 (CH), 128.4 (CH), 127.9 (CH), 127.8 (CH), 99.3 (C_q), 77.4 (CH, C_{12}), 77.3 (CH, C_{11}), 75.1 (CH, C_6), 74.4 (CH, C_2), 70.5 (CH, C_5), 70.4 (CH_2), 68.3 (CH, C_3), 67.8 (CH_2, C_{15}), 62.4 (CH_2, C_1), 40.1 (CH_2, C_{10}), 38.5 (CH_2, C_7), 35.1 (CH_2, C_4), 29.1 (CH_3), 29.0 (CH_2, C_{13}), 25.2 (CH_2, C_{14}), 21.0 (CH_3), 19.1 (CH_3). HRMS calcd for $C_{27}H_{36}O_9$ m/z 504.23561. **36**: Colorless foam $[\alpha]^{20}_D$ -22.5 (c, 0.32, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.82 (1H, ddd, J = 4.4, 10.7, 11.2 Hz, H-5), 3.95-3.88 (3H, m, H-6, H-12, H-15), 3.84 (1H, dd, J = 5.2, 10.7 Hz, H-1), 3.67-3.60 (2H, m, H-1, H-3), 3.35 (1H, ddd, J = 3.3, 11.0, 11.0 Hz, H-15), 3.22 (1H, ddd, J = 4.8, 10.7, 10.7 Hz, H-2), 3.17 (1H, ddd, J = 4.2, 7.0, 9.8 Hz, H-11), 2.84 (1H, J = 9.8, 13.5 Hz, H-10), 2.67 (1H, dd, J = 5.0, 13.5 Hz, H-10), 2.39 (1H, brddd, J = 4.4, 5.0, 11.2 Hz, H-4), 2.31 (1H, brdd, J = 2.0, 15.0 Hz, H-13), 2.10-2.03 (1H, m, H-7), 2.04 (3H, s), 1.77 (1H, brdd, J = 8.0, 15.0 Hz, H-13), 1.78-1.70 (2H, m, 2 × H-14), 1.47 (1H, ddd, J = 11.2, 12.0, 12.0 Hz, H-4), 1.46 (3H, s), 1.40-1.36 (1H, m, H-7), 1.37 (3H, s). ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.5 (C_q, C_9), 169.7 (C_q), 99.5 (C_q), 97.2 (C_q, C_8), 78.1 (CH, C_{11}), 77.7 (CH, C_6), 74.8 (CH, C_2), 69.8 (CH, C_5), 69.6 (CH, C_{12}), 68.1 (CH, C_3), 67.7 (CH_2, C_{15}), 62.3 (CH_2, C_1), 42.3 (CH_2, C_{10}), 35.2 (CH_2, C_{13}), 35.0 (CH_2, C_4), 29.0 (CH_2, CH_3), 29.0 (CH_2, C_7), 25.2 (CH_2, C_{14}), 21.0 (CH_3), 19.0 (CH_3). HRMS, calcd for $C_{20}H_{30}O_9$ m/z M^+ 414.18898. Found, m/z 414.18778. **37**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35-7.26 (5H, m, ϕH), 4.61 (1H, d, J = 11.4 Hz, ϕCH), 4.46 (1H, d, J = 11.4 Hz, ϕCH), 4.10 (1H, ddd, J = 4.4, 9.5, 11.8 Hz, H-5), 3.88 (1H, dd, J = 5.1, 10.7 Hz, H-1), 3.88 (1H, dd, J = 5.1, 10.7 Hz, H-15), 3.69-3.64 (1H, m, H-3), 3.68 (1H, dd, J = 10.5, 10.7 Hz, H-1), 3.63 (1H, ddd, J = 5.0, 5.4, 10.1 Hz, H-11), 3.36-3.26 (3H, m, H-6, H-12, H-15), 3.20 (1H, ddd, J = 5.2, 10.0, 10.5 Hz, H-2), 2.85 (1H, dd, J = 12.3, 12.5 Hz, H-7), 2.70 (1H, dd, J = 5.1, 13.5 Hz, H-7), 2.47 (1H, dd, J = 5.0, 15.1 Hz, H-10), 2.26 (1H, brddd, J = 4.1, 4.1, 11.4 Hz, H-13), 2.24 (1H, brd, J = 11.8 Hz, H-4), 1.86 (1H, dd, J = 5.0, 15.1 Hz, H-10), 1.70-1.60 (2H, m, 2 × H-14), 1.56 (1H, ddd, J = 11.4, 11.4, 11.8 Hz, H-4), 1.53 (1H, brs, C_9-OH), 1.48 (3H, s), 1.43-1.34 (1H, m, H-13), 1.39 (3H, s). ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.9 (C_q, C_8), 137.6 (C_q), 128.5 (CH), 128.1 (CH), 99.4 (C_q), 96.7, (C_q, C_9), 77.9 (CH, C_{11}), 77.7 (CH, C_6), 77.0 (CH, C_{12}), 73.6 (CH, C_2), 70.7 (CH_2), 69.4 (CH, C_3), 68.1 (CH, C_5), 68.0 (CH_2, C_{15}), 62.6 (CH_2, C_1), 41.9 (CH_2, C_7), 36.7 (CH_2, C_{10}), 35.0 (CH_2, C_4), 29.2 (CH_3), 29.0 (CH_2, C_{13}), 25.1 (CH_2, C_{14}), 19.1 (CH_3). **39**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.90 (1H, brd, J = 11.0 Hz, H-15), 3.87 (1H, dd, J = 5.1, 10.8 Hz, H-1), 3.67 (1H, dd, J = 10.8, 10.8 Hz, H-1), 3.63 (1H, ddd, J = 4.1, 11.0, 11.2 Hz, H-3), 3.49 (1H, ddd, J = 4.0, 9.2, 11.2 Hz, H-5), 3.38 (1H, ddd, J = 5.0, 11.0, 13.0 Hz, H-12), 3.36-3.33 (1H, m, H-15), 3.29 (1H, ddd, J = 5.2, 11.2, 11.7 Hz, H-6), 3.26 (6H, s, 2 × CH_3O), 3.20 (1H, ddd, J = 5.1, 10.8, 11.0 Hz, H-2), 3.14 (1H, ddd, J = 5.0, 9.5, 11.0 Hz, H-11), 2.19-2.13 (3H, m, H-4, H-7, H-10), 1.96 (1H, dd, J = 11.7, 11.7 Hz, H-7), 1.96-1.93 (1H, m, H-13), 1.93 (1H, dd, J = 11.0, 11.0 Hz, H-10), 1.75-1.70 (2H, m, 2 × H-14), 1.64 (1H, ddd, J = 11.2, 11.2, 11.2 Hz, H-4), 1.56-1.52 (1H, m, H-13), 1.46 (3H, s, CH_3), 1.39 (3H, s, CH_3).). ^{13}C NMR (125 MHz, $CDCl_3$) δ 99.3 (C_q), 98.6 (C_q, C_8), 98.4 (C_q, C_9), 76.2 (CH, C_6), 76.2 (CH, C_{11}), 75.2 (CH, C_2) 70.7, (CH, C_{12}), 69.8 (CH, C_3), 69.1 (CH, C_5), 68.3 (CH_2, C_{15}), 62.7 (CH_2, C_1), 47.3 (CH_3, CH_3O), 47.2 (CH_3, CH_3O), 34.7 (CH_2, C_4), 29.5 (CH_2, C_7), 29.3 (CH_2, C_{10}), 29.2 (CH_3), 28.8 (CH_2, C_{13}), 25.9 (CH_2, C_{14}), 19.1 (CH_3). HRMS, calcd for $C_{20}H_{32}O_8$, m/z M^+ 400.20968. Found, m/z 400.20963.

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