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A Symmetry-Based Synthesis of the Heterobicyclic Core of the Zaragozic Acids/Squalestatins

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Dedicated to Professor Hans-Ulrich Reißig on the occasion of his 60th birthday.

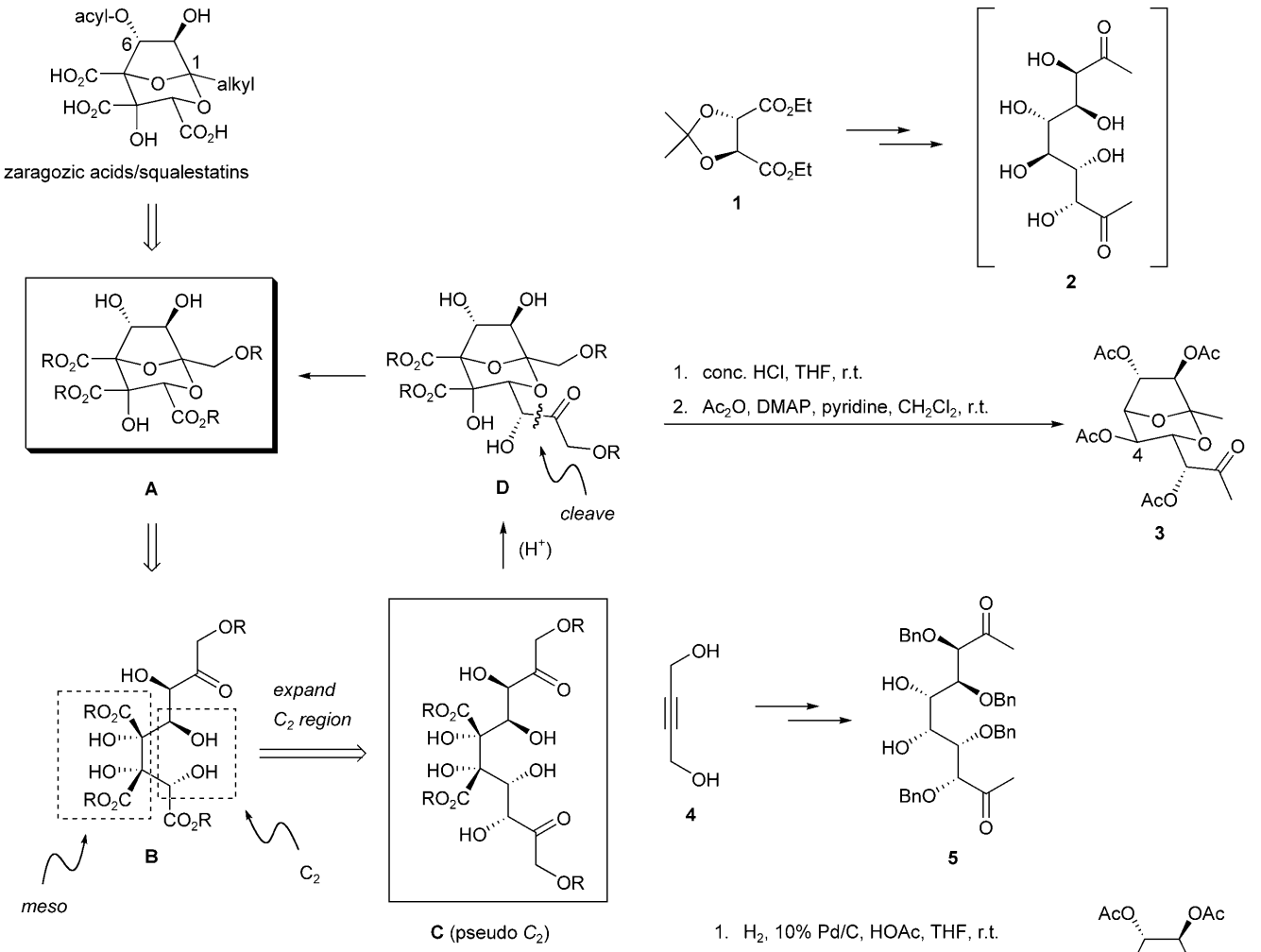
Abstract: The pseudo C_2-symmetrical diketone **22** was efficiently constructed from furan-3,4-dimethanol (**7**) using a two-directional route featuring a double asymmetric dihydroxylation. Acidic hydrolysis of the cyclopentylidene acetals of **22** triggered a selective cyclization of the resulting hexaol diketone to generate the 2,8-dioxabicyclo[3.2.1]octane core of the zaragozic acids/squalestatins. Chemoselective oxidative cleavage of a superfluous two-carbon appendage and further functional group manipulations yielded the enantiomerically pure triester **30**, which offers itself as a general heterobicyclic building block for naturally occurring zaragozic acids/squalestatins and unnatural analogues.

Keywords: aldol reaction; asymmetric catalysis; chemoselectivity; cyclization; dihydroxylation; two-directional synthesis

The zaragozic acids/squalestatins isolated from various fungi are potent inhibitors of squalene synthase and in part *ras*-farnesyl protein transferase, too.[1] More recent studies show that these natural products can also cure prion-infected neurons and protect against prion neurotoxicity[2] as well as sensitize acute myeloid leukemia cells (AML) to radiochemotherapy.[3] Almost all of these compounds feature the 2,8-dioxabicyclo[3.2.1]octane core with an unusually high density of polar oxygen functions, while structural differences reside in the alkyl side chain at C-1 and the ester side chain at C-6. Due to their strong physiological effects and complex molecular structure, the zaragozic acids/squalestatins have stimulated enormous synthetic efforts. Thus, the total synthesis of several of these natural products has been accomplished, and many synthetic studies toward the heterobicyclic core as well as detailed investigations on structure-activity relationships have been carried out.[1,4,5]

Here we report the enantioselective synthesis of a heterobicyclic system of type **A**, which rests on the symmetry-based concept depicted in Scheme 1.[5,6] A retrosynthetic disconnection of the acetal of **A** leads to polyhydroxy ketone **B** that exhibits regions with local *meso* and C_2 symmetry. Expansion of the C_2 region in **B** by addition of a two-carbon unit to the ester terminus enhances the molecular complexity, however, a pseudo C_2-symmetric diketone **C** is attained that should be rapidly accessible by two-directional synthesis.[7] Synthetically, diketone **C** might serve as a surrogate for **B**, provided its intramolecular acetalization would lead to **D** in a chemoselective fashion and with simultaneous differentiation of the two diastereotopic γ,ε-dihydroxy ketone moieties. Finally, the superfluous appendage in **D** can be removed *via* a chemoselective oxidative cleavage[8] to generate **A**. Due to its functionality, **A** can be regarded as a general building block for zaragozic acids/squalestatins and non-natural analogues. In this respect, the protected hydroxymethyl group at C-1 of **A** offers the possibility to attach different alkyl side chains, while the hydroxy group at C-6 allows the connection of diverse ester side chains by position-selective acylation.[9]

Previous model studies relevant to the present work are summarized in Scheme 2. Thus, we recently communicated a concise synthesis of the C_2-symmetric linear model compound **2** from the diethyl tartrate derivative **1**.[5a] Under suitable conditions, the hexahydroxy diketone **2** cyclized with completely chemoselective participation of the γ,ε-hydroxy groups to afford the 2,8-dioxabicyclo[3.2.1]octane derivative **3**, which is epimeric at C-4 to the heterobicyclic core of the zaragozic acids/squalestatins in high yield after peracetylation. More advanced model studies showed that the pseudo C_2-symmetric tetrabenzyl ether **5** could be readily accessed from alkyne **4** through



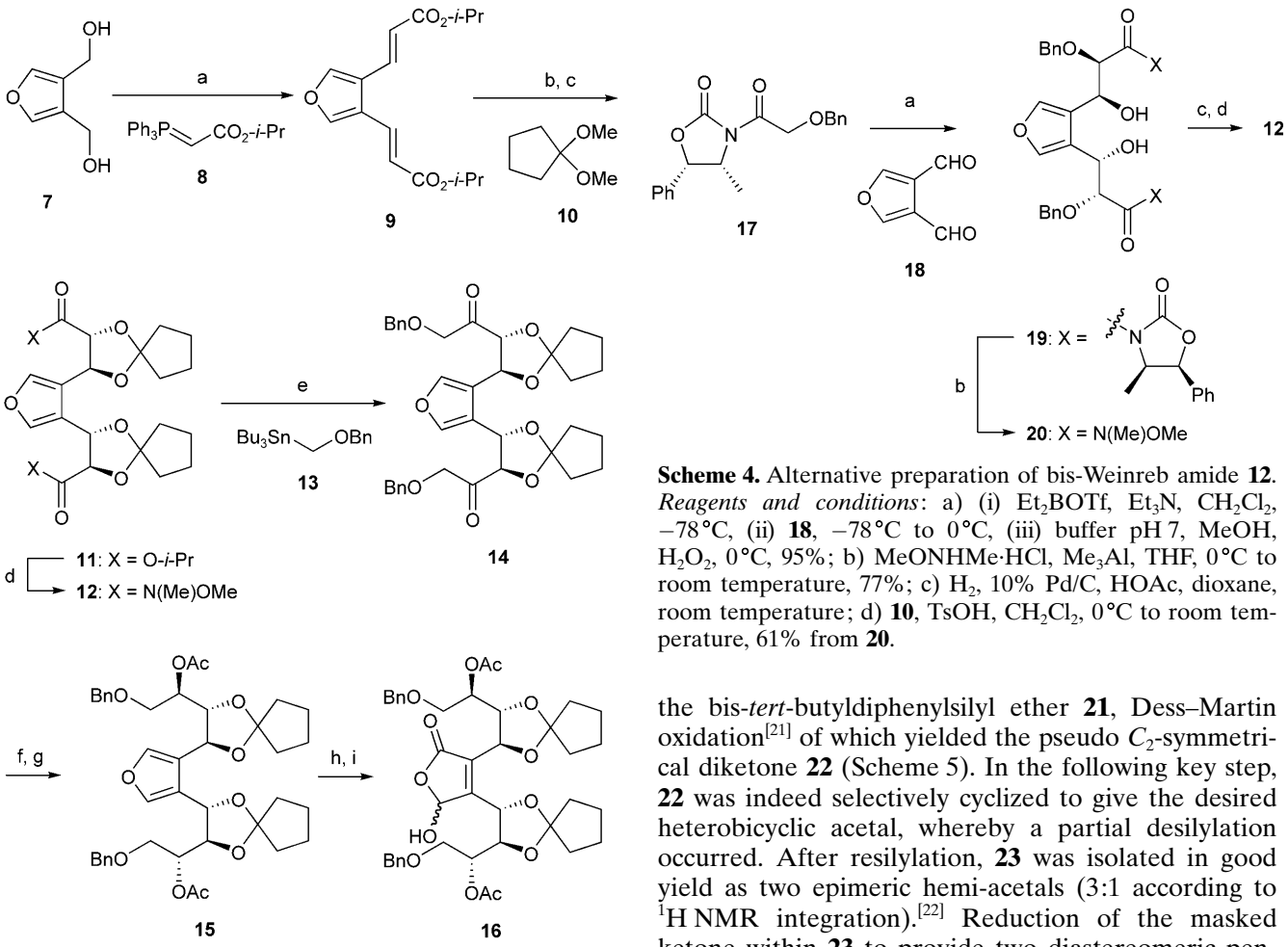
Scheme 1. Concept for the synthesis of the heterobicyclic core of the zaragozic acids/squalestatins.

Sharpless AD methodology.[5b] Under optimized conditions, the derived hexahydroxy diketone smoothly underwent a chemoselective intramolecular acetalization to give the desired γ,ε-cyclization product **6** as a model for the heterobicyclic core upon treatment with acetic anhydride.

The successful execution of a symmetry-based route according to Scheme 1 to a fully substituted compound of type **A** is illustrated in Scheme 3, Scheme 4, Scheme 5, and Scheme 6.

A two-directional, sequential Swern oxidation/Wittig reaction[10] converted the disubstituted furan **7**[11] into the (*E,E*) configured bis-isopropyl ester **9** in a one-pot process. Double asymmetric dihydroxylation[12] of **9** with a modified "AD-mix-α"[13] furnished a tetraol that was subsequently derivatized to give the bis-cyclopentylidene acetal **11** (Scheme 3). The furan nucleus of **9**, which introduces two latent carboxylic acids into the system with C-2 and C-5, also assumes the role of the alkyne spacer utilized in the model series[5b] to avoid an undesired cyclization after the first AD reaction as well as to ensure high catalyst control for the second AD process. The smooth two-fold AD transformation fortunately observed for **9** in contrast to the model substrate[5b] can probably be rationalized with a better solubility of the diol intermediate produced from **9** in the organic layer. Use of isopropylmagnesium chloride[14] allowed a chemoselective exchange of the ester functions against Weinreb amides, whereupon the resulting product **12** was converted into diketone **14** with the lithium species[15] derived from **13**. At this point, it proved advisable to mask the two carbonyl groups temporarily as protected alcohols in order to prevent undesired cyclizations in the course of the furan oxidation. Diacetate **15** obtained with complete diastereoselectivity[16] was then transformed to the two lactol lactone epimers **16** (4:1 according to ^{1}H NMR integration) uneventfully.[17]

Scheme 2. Model studies.



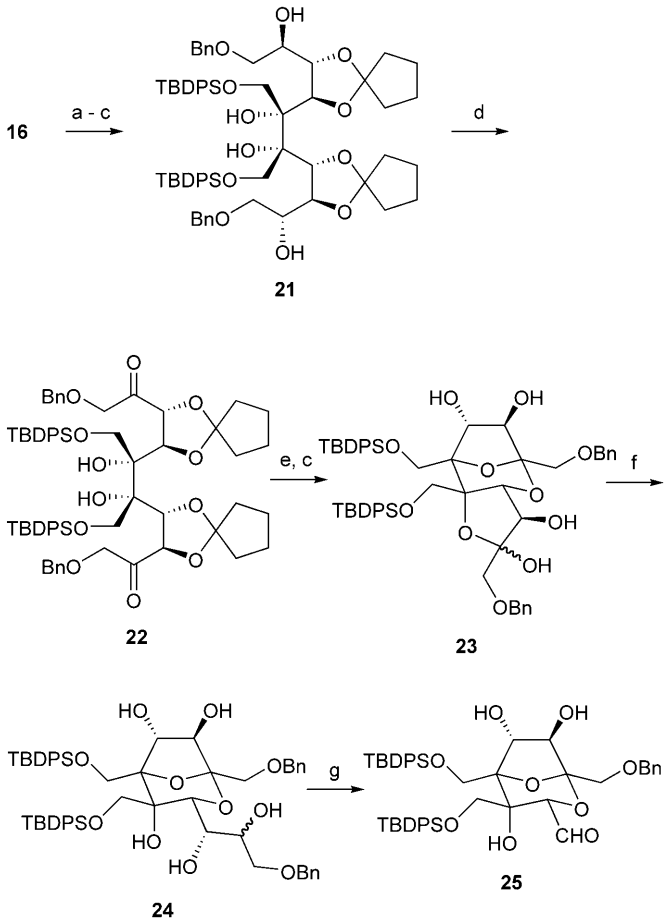
Scheme 3. Two-directional synthesis of lactol lactone **16**. *Reagents and conditions*: a) (i) DMSO, $(COCl)_2$, Et_3N, CH_2Cl_2, −78 °C to 0 °C, (ii) **8**, 0 °C to room temperature, 86%; b) 2.5 mol% $K_2OsO_2(OH)_4$, $K_3[Fe(CN)_6]$, 5 mol% $(DHQ)_2PHAL$, K_2CO_3, $NaHCO_3$, $MeSO_2NH_2$, *t*-BuOH, H_2O, 0 °C; c) **10**, TsOH, CH_2Cl_2, 0 °C to room temperature, 92% from **9**; d) MeONHMe·HCl, *i*-PrMgCl, THF, −20 °C, 98%; e) **13**, BuLi, THF, −78 °C, 100%; f) Li(*s*-Bu)$_3$BH, THF, −100 °C to −78 °C; g) Ac_2O, DMAP, Et_3N, CH_2Cl_2, 0 °C to room temperature, 97% from **14**; h) Br_2, K_2HPO_4, THF, H_2O, 0 °C; i) CrO_3, H_2SO_4, acetone, 0 °C, 93% from **15**.

The high enantioselectivity of the double AD reaction in Scheme 3 was proven by an alternative preparation of bis-Weinreb amide **12** *via* an Evans aldol reaction[18] of the enantiomerically pure glycolic acid derivative **17**[19] with dialdehyde **18**,[20] which succeeded efficiently in a two-directional fashion (Scheme 4). The resultant C_2-symmetrical product **19** was transformed to **12** by cleavage of the auxiliaries[19] to give **20** followed by debenzylation and acetalization {**12** from **9**: $[\alpha]_D^{22}$: −39.9 (*c* 0.96, $CHCl_3$); **12** from **17**: $[\alpha]_D^{22}$: −39.1 (*c* 0.98, $CHCl_3$)}.

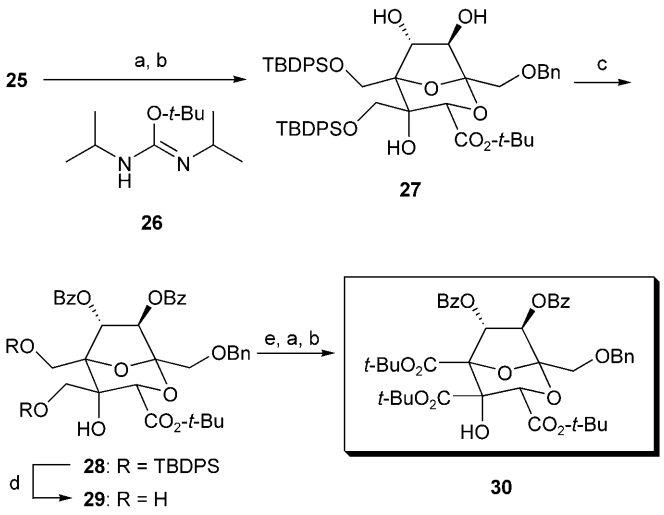
A sequence consisting of dihydroxylation, global reduction of all carbonyl groups and chemoselective blocking of the two primary alcohols converted **16** to the bis-*tert*-butyldiphenylsilyl ether **21**, Dess–Martin oxidation[21] of which yielded the pseudo C_2-symmetrical diketone **22** (Scheme 5). In the following key step, **22** was indeed selectively cyclized to give the desired heterobicyclic acetal, whereby a partial desilylation occurred. After resilylation, **23** was isolated in good yield as two epimeric hemi-acetals (3:1 according to ^{1}H NMR integration).[22] Reduction of the masked ketone within **23** to provide two diastereomeric pentaols **24** (5:1 according to ^{1}H NMR integration) set the stage for a chemoselective[8] oxidative cleavage of the superfluous two-carbon appendage with sodium periodate that led to aldehyde **25** with high efficacy.

Scheme 4. Alternative preparation of bis-Weinreb amide **12**. *Reagents and conditions*: a) (i) Et_2BOTf, Et_3N, CH_2Cl_2, −78 °C, (ii) **18**, −78 °C to 0 °C, (iii) buffer pH 7, MeOH, H_2O_2, 0 °C, 95%; b) MeONHMe·HCl, Me_3Al, THF, 0 °C to room temperature, 77%; c) H_2, 10% Pd/C, HOAc, dioxane, room temperature; d) **10**, TsOH, CH_2Cl_2, 0 °C to room temperature, 61% from **20**.

Due to its sensitivity, aldehyde **25** was directly converted to *tert*-butyl ester **27** by chlorite oxidation[23] and esterification with *O*-alkylisourea **26**[24] (Scheme 6). An X-ray diffraction analysis of **27** with anomalous X-ray scattering provided an independent proof of the absolute configuration.[25] After chemoselective *O*-benzoylation of the two secondary alcohols to give **28**, desilylation to furnish **29** proceeded without competing acyl shift.[26] Finally, the reaction sequence double Swern oxidation, double chlorite oxidation and double esterification with **26** resulted in tri-*tert*-butyl ester **30**, which represents a largely orthogonally protected derivative of the desired heterobicyclic building block **A** for zaragozic acids/squalestatins and, thus, warrants high flexibility regarding an elaboration to these natural products or analogues thereof. Differentiation between the C-6 and C-7 hydroxy groups can be achieved according to the method developed by Carreira,[9] and attachment of several C-1 alkyl side chains proceeds readily after debenzylation of **30** followed by Swern oxidation.



Scheme 5. Construction of the heterobicyclic aldehyde **25**. *Reagents and conditions*: a) OsO_4, pyridine, toluene, 0 °C; b) $LiAlH_4$, Et_3N, THF, CH_2Cl_2, 0 °C to 65 °C; c) TBDPSCl, DMAP, Et_3N, CH_2Cl_2, room temperature, 43% **21** from **16**, 66% **23** from **22**; d) Dess–Martin periodinane, pyridine, CH_2Cl_2, room temperature, 91%; e) TFA, CH_2Cl_2, H_2O, 0 °C to room temperature; f) $LiBH_4$, Et_3N, THF, 0 °C, 94%; g) $NaIO_4$, pyridine, MeOH, H_2O, room temperature, 93%.



Scheme 6. Completion of the synthesis of tri-*tert*-butyl ester **30**. *Reagents and conditions*: a) $NaClO_2$, KH_2PO_4, isoprene, *t*-BuOH, H_2O, 0 °C to room temperature; b) **26**, CH_2Cl_2, room temperature, 80% **27** from **25**, 50% **30** from **29**; c) PhCOCl, DMAP, CH_2Cl_2, 0 °C to room temperature, 100%; d) HF·pyridine, THF, pyridine, room temperature, 94%; e) DMSO, $(COCl)_2$, Et_3N, CH_2Cl_2, −78 °C.

Due to the two-directional strategy employed, the 24-steps route from **7** to **30** compares well to previous syntheses of the fully functionalized heterobicyclic core in terms of efficiency and stereoselectivity. Application of **30** toward the total synthesis of naturally occurring zaragozic acids/squalestatins is the subject of ongoing work.

Experimental Section

Double AD Reaction of 9 and Acetalization to Give Diester 11

A mixture of $K_3Fe(CN)_6$ (15.804 g, 48 mmol), K_2CO_3 (6.624 g, 48 mmol), $NaHCO_3$ (4.032 g, 48 mmol), $K_2OsO_2(OH)_4$ (73.6 mg, 0.2 mmol) and $(DHQ)_2PHAL$ (311.6 mg, 0.4 mmol) in water (100 mL) and *t*-BuOH (70 mL) was stirred for 1 h at room temperature. After cooling to 0 °C, methanesulfonamide (1.53 g, 16 mmol) was added followed by a solution of bis-enoate **9** (2.336 g, 8 mmol) in *t*-BuOH (30 mL). Stirring at 0 °C was continued for 24 h, sodium sulfite (23 g) was added, and the mixture was stirred for 1 h at 0 °C. The layers were separated, and the aqueous layer was extracted with ethyl acetate (4× 50 mL). After drying the combined organic layers with Na_2SO_4 and concentration under vacuum, the oily residue was passed through a short silica gel column (ethyl acetate). The crude tetraol obtained was dissolved in dry CH_2Cl_2 (20 mL), and the resultant solution was cooled to 0 °C. 1,1-Dimethoxycyclopentane (21 g) and TsOH (152 mg, 0.8 mmol) was added, and stirring was continued overnight while allowing the mixture to warm to room temperature. The mixture was diluted with diethyl ether (80 mL), washed with semi-saturated $NaHCO_3$ solution (10 mL) and water (10 mL), dried with $MgSO_4$, and concentrated under vacuum. Purification of the residue by flash chromatography on silica gel (diethyl ether/pentane, 1:3) gave the bis-acetal **11** as a colorless oil; yield: 3.638 g (92%). $R_f = 0.37$ (diethyl ether/pentane, 1:3); $[\alpha]_D^{22}$: −23.13 (*c* 0.83, $CHCl_3$); IR (ATR): $\nu = 2978$ (m), 2876 (w), 1746 (s), 1727 (s), 1554 (w), 1468 (w), 1454 (w), 1434 (w), 1375 (m), 1337 (m), 1279 (m), 1194 (s), 1098 (s), 1039 (m), 969 (s), 877 (m), 820 (m), 821 (m), 752 (m), 604 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 1.24$ (d, $J = 5.9$ Hz, 6H), 1.26 (d, $J = 5.9$ Hz, 6H), 1.65–1.83 (m, 10H), 1.95–2.06 (m, 6H), 4.62 (d, $J = 7.4$ Hz, 2H), 5.02–5.14 (m, 4H), 7.51 (s, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 21.65$ (q), 21.71 (q), 23.13 (t), 24.00 (t), 36.19 (t), 36.43 (t), 69.08 (d), 73.30 (d), 78.75 (d), 121.18 (s), 121.38 (s), 143.03 (d), 170.43 (s); MS (ESI): $m/z = 510.2$ [$M + NH_4^+$]; anal. calcd. for $C_{26}H_{36}O_9$: C 63.40, H 7.37; found: C 63.41, H 7.56.

Preparation of Aldehyde 25 from Diketone 22 *via* Selective Cyclization, Resilylation, Reduction and Oxidative Cleavage

A solution of diketone **22** (2.95 g, 2.57 mmol) in CH_2Cl_2 (52 mL) cooled to 0 °C was treated with water (0.463 g, 25.72 mmol) and TFA (2.932 g, 25.72 mmol). After stirring for 1 h at 0 °C and 24 h at room temperature, the reaction was quenched by addition of saturated $NaHCO_3$ solution (36 mL). The layers were separated, the aqueous layer was extracted with CH_2Cl_2 (3×60 mL), and the solvent was removed under vacuum. Purification by flash chromatography on silica gel (diethyl ether/CH_2Cl_2, 1:6) gave hemi-acetal **23** (yield: 1.17 g, 46%) and partially desilylated material (yield: 0.724 g, 37%) as white solids. The latter material was dissolved in dry CH_2Cl_2 (19 mL) and treated with triethylamine (241 mg, 2.31 mmol), DMAP (5.8 mg, 0.05 mmol) and TBDPSCl (315.5 mg, 1.15 mmol). After stirring for 50 h at room temperature, the mixture was filtered through a pad of silica gel (diethyl ether). Concentration under vacuum and purification by flash chromatography on silica gel (diethyl ether/CH_2Cl_2, 1:6) gave additional (520 mg) **23** as a white solid; total yield from **22**: 1.69 g (66%). R_f=0.26 (diethyl ether/CH_2Cl_2, 1:6); IR (ATR): ν=3452 (br., w), 3070 (w), 2931 (w), 2857 (w), 1469 (m), 1457 (m), 1427 (m), 1391 (w), 1363 (w), 1184 (w), 1106 (s), 1072 (s), 1043 (s), 1000 (m), 939 (m), 820 (m), 793 (m), 738 (s), 783 (m), 697 (s), 609 (m) cm^{-1}; MS (ESI): *m/z*=1014.5 [M+NH_4^+], 1019.4 [M+Na^+], 1035.4 [M+K^+].

A solution of hemi-acetal **23** (1.061 g, 1.064 mmol) in dry THF (32 mL) was treated with triethylamine (129 mg, 1.277 mmol). After stirring for 30 min at room temperature, the mixture was cooled to 0 °C, lithium borohydride (81.44 mg, 3.724 mmol) was added, and stirring at 0 °C was continued for 4 h. The reaction was quenched by dropwise addition of 2N NaOH (10 mL) followed by stirring for 30 min. Extraction with ethyl acetate (3×20 mL), drying of the organic layer with Na_2SO_4 and removal of the solvent under vacuum left a residue, which was purified by flash chromatography on silica gel (diethyl ether/CH_2Cl_2, 1:6) to give pentaol **24** as a white solid; yield: 1.002 g (94%). R_f=0.23 (diethyl ether/CH_2Cl_2, 1:6); IR (ATR): ν=3410 (br., w), 3071 (w), 2931 (w), 2858 (w), 1457 (m), 1427 (m), 1363 (w), 1108 (s), 1072 (s), 936 (w), 821 (m), 783 (m), 698 (s), 610 (m) cm^{-1}; MS (ESI): *m/z*=1016.5 [M+NH_4^+], 1021.4 [M+Na^+]; anal. calcd. for $C_{58}H_{70}O_{11}Si_2$: C 69.71, H 7.06; found: C 69.85, H 6.96.

A solution of sodium periodate (343.5 mg, 1.61 mmol) in water (4 mL) was added dropwise to a solution of pentaol **24** (802 mg, 0.803 mmol) and pyridine (190 mg, 2.41 mmol) in methanol (28 mL). After stirring for 20 h at room temperature, additional sodium periodate (86 mg, 0.402 mmol) in a mixture of water (0.5 mL) and methanol (3 mL) was added, and stirring was continued for 6 h. Dilution with ethyl acetate, drying with Na_2SO_4, and removal of the solvent under vacuum left a residue, which was purified by flash chromatography on silica gel (diethyl ether/CH_2Cl_2, 1:15) to give aldehyde **25** as a white solid; yield: 786 mg (93%). R_f=0.24 (CH_2Cl_2/ethyl acetate, 15:1); mp 57.5–58.6 °C; $[\alpha]_D^{22}$: +6.63 (*c* 1.19, CH_2Cl_2); IR (ATR): ν=3436 (br., w), 3068 (w), 2931 (m), 2858 (m), 1739 (m), 1457 (m), 1427 (m), 1390 (w), 1108 (s), 1073 (s), 820 (m), 739 (m), 699 (s), 610 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ=0.96 (s, 9H), 1.04 (s, 9H), 2.56 (d, *J*=2.6 Hz, 1H), 3.49 (s, 1H), 3.58 (d, *J*=11.6 Hz, 1H), 3.66 (d, *J*=10.1 Hz, 1H), 3.85 (d, *J*=11.6 Hz, 1H), 3.86 (d, *J*=10.1 Hz, 1H), 3.87 (d, *J*=11.7 Hz, 1H), 3.93 (d, *J*=8.3 Hz, 1H), 4.06 (d, *J*=11.7 Hz, 1H), 4.53 (apparent t with *J*=2.7 Hz, 1H), 4.60 (d, *J*=11.9 Hz, 1H), 4.69 (d, *J*=11.9 Hz, 1H), 4.71 (d, *J*=0.8 Hz, 1H), 4.86 (dd, *J*=2.9 Hz, *J*=8.3 Hz, 1H), 7.28–7.44 (m, 17H), 7.56–7.58 (m, 4H), 7.60–7.62 (m, 2H), 7.66–7.68 (m, 2H), 9.54 (d, *J*=0.8 Hz, 1H, CHO); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ=19.07 (s), 26.69 (q), 26.74 (q), 62.39 (t), 62.85 (t), 72.29 (t), 73.18 (s, C4), 74.03 (t), 77.69 (d), 79.13 (d), 84.38 (d), 87.21 (s), 103.00 (s), 127.74 (d), 127.84 (d), 127.86 (d), 128.05 (d), 128.58 (d), 130.03 (d), 130.12 (d), 131.63 (s), 131.72 (s), 131.92 (s), 132.21 (s), 135.49 (d), 135.66 (d), 135.74 (d), 135.81 (d), 137.27 (s), 199.20 (d); MS (ESI): *m/z*=864.4 [M+NH_4^+], 896.4 [M+MeOH+NH_4^+], 901.4 [M+MeOH+Na^+]; anal. calcd. for $C_{49}H_{58}O_9Si_2$: C 69.47, H 6.90; found: C 69.55, H 6.80.

Preparation of Tri-*tert*-butyl Ester 30 from Triol 29

A solution of dry DMSO (135 mg, 1.726 mmol) in dry CH_2Cl_2 (1 mL) was added dropwise to a solution of oxalyl dichloride (109.6 mg, 0.863 mmol) in dry CH_2Cl_2 (4 mL) cooled to −78 °C under argon. After stirring for 10 min, a solution of triol **29** (216 mg, 0.332 mmol) in dry CH_2Cl_2 (3.4 mL) was added dropwise, and stirring was continued at −78 °C for 45 min. Dry triethylamine (262 mg, 2.59 mmol) was added, and the mixture was stirred for 30 min at −78 °C. The reaction was quenched by addition of 1M KH_2PO_4 (3.4 mL). The mixture was extracted with CH_2Cl_2 (3×10 mL), and the combined organic layers were dried with Na_2SO_4. The crude dialdehyde obtained after removal of the solvent under vacuum was dissolved in a mixture of *t*-BuOH (31 mL) and isoprene (7.7 mL). The resultant solution was cooled to 0 °C, and a 1M solution of $NaClO_2$ in 1M KH_2PO_4 (3.3 mL, 3.3 mmol) was added dropwise. After stirring the reaction mixture for 1 h at 0 °C and 4 h at room temperature, another portion of the 1M solution of $NaClO_2$ in 1M KH_2PO_4 (3.3 mL, 3.3 mmol) was added dropwise, and stirring was continued for further 19 h. The mixture was treated with brine (5 mL) and a pH 2 KH_2PO_4 buffer (5 mL) followed by extraction with ethyl acetate (5×15 mL). The combined organic layers were dried with Na_2SO_4, and the solvent was removed under vacuum to give a crude diacid, which was dissolved in dry CH_2Cl_2 (15 mL) and treated with *N,N′*-diisopropyl-*O*-*tert*-butylisourea (664 mg, 3.32 mmol) under argon. After stirring for 24 h at room temperature, another portion of *N,N′*-diisopropyl-*O*-*tert*-butylisourea (664 mg, 3.32 mmol) was added, and stirring was continued for further 24 h. The white precipitate formed was filtered off, and the solvent was removed under vacuum. Purification of the residue by flash chromatography on silica gel (diethyl ether/CH_2Cl_2, 1:20) furnished tri-*tert*-butylester **30** as a white foam; yield: 131 mg (50%). R_f=0.20 (diethyl ether/CH_2Cl_2, 1:20); $[\alpha]_D^{22}$: +68.01 (*c* 1.31, CH_2Cl_2); IR (ATR): ν=3447 (br., w), 2981 (w), 2935 (w), 2876 (w), 1727 (s), 1454 (m), 1369 (m), 1315 (m), 1252 (s), 1150 (s), 1108 (s), 1063 (s), 1026 (m), 998 (m), 968 (w), 911 (w), 838 (m), 708 (s), 602 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ=1.29 (s, 9H), 1.47 (s, 9H), 1.62 (s, 9H), 3.97 (d,

$J = 12.1$ Hz, 1H), 4.02 (d, $J = 12.1$ Hz, 1H), 4.20 (s, 1H), 4.71 (d, $J = 11.5$ Hz, 1H), 4.96 (d, $J = 11.5$ Hz, 1H), 5.16 (s, 1H), 5.86 (d, $J = 1.7$ Hz, 1H), 6.86 (d, $J = 1.7$ Hz, 1H), 7.24–7.29 (m, 3H), 7.38–7.46 (m, 6H), 7.54–7.60 (m, 2H), 7.99–8.03 (m, 4H); ^{13}C NMR (125.8 MHz, $CDCl_3$): $\delta = 27.81$ (q), 27.95 (q), 28.09 (q), 68.86 (t), 74.13 (t), 74.23 (s), 75.49 (d), 76.20 (d), 78.48 (d), 83.92 (s), 84.28 (s), 86.50 (s), 90.72 (s), 104.30 (s), 127.46 (d), 127.84 (d), 128.22 (d), 128.35 (d), 128.53 (d), 128.97 (s), 129.04 (s), 129.81 (d), 130.05 (d), 133.44 (d), 133.54 (d), 138.22 (s), 163.51 (s), 164.22 (s), 164.99 (s), 165.22 (s), 168.49 (s); MS (ESI): $m/z = 808.5$ $[M + NH_4^+]$; HR-MS (EI): $m/z = 733.2477$, calcd. for $[M^+ - t\text{-Bu}]$: 733.2496.

Acknowledgements

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