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ORIGINAL PAPER

Stereoselective total synthesis of protected sulfamisterin and its analogues

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The stereoselective synthesis of sulfamisterin *I* and its unnatural analogues *II* and *V* in their protected form was achieved through a common strategy. The Wittig reaction of aldehydes *VIII* and *IX* with the C_{14} hydrophobic side-chain *X* served as the key C—C connecting transformation. Subsequent functional group inter-conversions in the coupling products *XI* and *XX* completed the total synthesis.

Keywords: sulfamisterin, total synthesis, stereoselective, α-substituted α-amino acid, Wittig reaction, serine palmitoyltransferase

Introduction

(+)-Sulfamisterin *I*, (2*S*,3*R*)-2-amino-(2-hydroxymethyl)-12-oxo-3-(sulphooxy)octadecanoic acid (Fig. 1), is a new, natural, antifungal product that has been isolated from the culture broths of *Pycnidiella* sp. AB5366 (Sato et al., 2005; Yamaji-Hasegawa et al., 2005). This compound is reported to be responsible for both in vivo and in vitro inhibitory activity (Sato et al., 2005; Yamaji-Hasegawa et al., 2005) towards serine palmitoyltransferase (Hanada, 2003), an enzyme playing a crucial role in the sphingolipid biosynthesis.

The structure-elucidation study (Sato et al., 2005; see also references herein) revealed that *I* is an unusual α-substituted α-amino acid derivative possessing a C_{18} straight carbon chain with the C═O group at C-12, two stereogenic centres which are (2*S*,3*R*)-configured and C-3 alcohol function bearing a sulphate moiety. The inhibitory profile of *I* and related compounds depends on the stereochemistry at the C-2 quaternary centre and the 2*S* configuration is essential for high activity (Sato et al., 2005; Yamaji-Hasegawa et al., 2005). On the other hand, the stereochemistry of the 3-hydroxy group as well as its sulphation plays no essential role in the biological activity (Sato et al., 2005; Yamaji-Hasegawa et al., 2005). Although *I* and also its analogues *II*, *III*, and *IV* have an interesting β-hydroxy-α-substituted serine motif (Kang et al., 2005; Ohfune & Shinada, 2005; Byun et al., 2006) and exhibit remarkable bioactivity, only one total synthesis of *I* and its structurally-related derivatives has been reported to date (Sato et al., 2005). Prompted by these facts, and pursuing our interest in the construction of structures containing a densely functionalised quaternary centre (Gonda et al., 2006; Martinková et al., 2006, 2008, 2010, 2012a, 2012b), we focused on the synthesis of *I* and its desulphated congeners *II* and *V* (Sato et al., 2005) in their protected form.

Experimental

All commercial reagents were used with the highest available purity from Aldrich, Fluka, Merck or Acros Organics, without further purification. Solvents were dried and purified prior to use following standard procedures. Kieselgel 60 (0.040–0.063 mm, Merck) was used for flash column chromatography. Solvents

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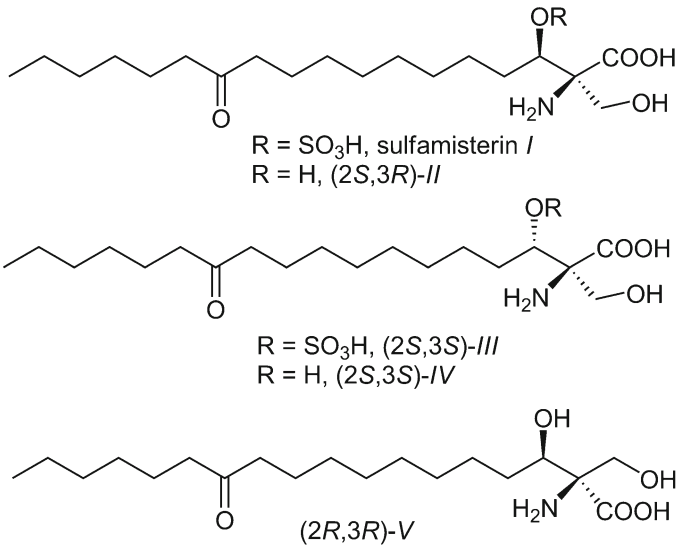

Fig. 1. Sulfamisterin (*I*) and its analogues.

for flash chromatography (hexane, EtOAc, CH_3OH, CH_2Cl_2) were distilled prior to use. Thin layer chromatography was performed using Merck silica gel 60 F_{254} analytical plates; detection was performed with either ultraviolet light (254 nm) or spraying with a solution of phosphomolybdic acid, a basic potassium permanganate solution, or a solution of concentrated H_2SO_4, with subsequent heating. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ and CD_3OD on a Varian Mercury Plus 400 FT NMR (400.13 MHz for ^1H, 100.6 MHz for ^{13}C) or on a Varian Premium Compact 600 (599.87 MHz for ^1H, 150.84 MHz for ^{13}C) spectrometer using TMS as internal reference. For the assignment of signals, homonuclear COSY and heteronuclear 2D correlated (HSQC, HMBC) techniques were used. Optical rotations, $[\alpha]_D$ (c in grams per 1000 mL, solvent), were measured on a P-2000 Jasco polarimeter. Melting points were recorded on a Kofler hot block and are uncorrected. All reactions were performed under an atmosphere of nitrogen, unless noted otherwise.

(5R,6S)-8,8-Dimethyl-2-oxo-3,7,9-trioxa-1-azaspiro[4.5]decane-6-carbaldehyde (VIII)

2-Iodoxybenzoic acid (IBX) (0.62 g, 2.21 mmol) was added to a solution of alcohol *VI* (0.32 g, 1.47 mmol) in CH_3CN (7.6 mL) and the resulting mixture was heated to reflux for 15 min. Once the starting material was completely consumed (TLC), the reaction was stopped and allowed to cool to ambient temperature. The insoluble materials were removed by filtration, the solvent was evaporated under reduced pressure, and the residue was purified by flash chromatography on silica gel (EtOAc) to afford 0.30 g (94 %) of aldehyde *VIII* as white amorphous solids, $[\alpha]_D^{20} = +39.7°$ ($c = 3.2$ g L^{-1}, $CHCl_3$).

(5S,6S)-8,8-Dimethyl-2-oxo-3,7,9-trioxa-1-azaspiro[4.5]decane-6-carbaldehyde (IX)

Using the procedure described for the preparation of *VIII*, alcohol *VII* (0.15 g, 0.69 mmol) and IBX (0.29 g, 1.04 mmol), after purification by flash chromatography on silica gel (EtOAc), afforded crystalline aldehyde *IX* (0.14 g, 94 %); $[\alpha]_D^{25} = -72.1°$ ($c = 4.2$ g L^{-1}, $CHCl_3$).

(5R,6R)-6-[(1′Z)-8′-(2″-Hexyl-1″,3″-dioxolan-2″-yl)oct-1′-en-1′-yl]-8,8-dimethyl-3,7,9-trioxa-1-azaspiro[4.5]decan-2-one ((Z)-XI) and (5R,6R)-6-[(1′E)-8′-(2″-hexyl-1″,3″-dioxolan-2″-yl)oct-1′-en-1′-yl]-8,8-dimethyl-3,7,9-trioxa-1-azaspiro[4.5]decan-2-one ((E)-XI)

n-BuLi (2.43 mL of 1.6 M solution in hexane) was added to a solution of 1,1,1,3,3,3-hexamethyldisilazane (0.83 mL, 3.89 mmol) in dry THF (4.1 mL) at ambient temperature. The solution of lithium bis(trimethylsilyl)azanide (LHMDS) thus generated was treated with the known phosphonium salt *X* (2.66 g, 4.45 mmol), and the resulting dark mixture was stirred at ambient temperature for 5 min. A solution of aldehyde *VIII* (0.30 g, 1.39 mmol) in dry THF (4.1 mL) was then added drop-wise, and the reaction mixture was stirred at ambient temperature for 30 min. Following complete conversion of the starting material (TLC), the mixture was poured into a saturated aqueous NH_4Cl solution (30 mL) and extracted with EtOAc (3 × 25 mL). The combined organic layers were dried with Na_2SO_4, the solvent was evaporated, and the residue was chromatographed on silica gel (hexane/EtOAc, $\varphi_r = 1 : 1$) to afford 0.51 g (81 %) of a mixture of isomers *XI* as a colourless oil. A small amount of the mixture of olefins *XI* was separated by

column chromatography on silica gel (hexane/EtOAc, $\varphi_r = 1 : 1$) to afford only (*Z*)-*XI* in pure form as a colourless oil; $[\alpha]_D^{25} = -23.2°$ ($c = 8.6$ g L^{-1}, $CHCl_3$).

(5R,6R)-6-[8′-(2″-Hexyl-1″,3″-dioxolan-2″-yl)octyl]-8,8-dimethyl-3,7,9-trioxa-1-azaspiro[4.5]decan-2-one (XII)

20 % $Pd(OH)_2/C$ (37 mg) was added to a solution of olefins *XI* (0.49 g, 1.08 mmol) in dry EtOH (11.7 mL). The resulting mixture was stirred at ambient temperature for 1 h in an atmosphere of H_2 and then filtered through a short pad of Celite. Evaporation of the solvent under reduced pressure followed by column chromatography of the crude product on silica gel (hexane/EtOAc, $\varphi_r = 1 : 1$) afforded 0.46 g (94 %) of *XII* as a colourless oil; $[\alpha]_D^{25} = +15.6°$ ($c = 3.4$ g L^{-1}, $CHCl_3$).

(5R,6R)-tert-Butyl 6-[8′-(2″-hexyl-1″,3″-dioxolan-2″-yl)octyl]-8,8-dimethyl-2-oxo-3,7,9-trioxa-1-azaspiro[4.5]decane-1-carboxylate (XIII)

Di-*tert*-butyl bicarbonate (Boc_2O) (0.43 g, 1.97 mmol) and 4-dimethylaminopyridine (DMAP) (0.12 g, 0.98 mmol) were successively added to a solution of *XII* (0.45 g, 0.99 mmol) in dry CH_3CN (1.9 mL). After stirring at ambient temperature for 15 min, the solvent was removed under reduced pressure, and the residue was purified by flash chromatography on silica gel (hexane/EtOAc, $\varphi_r = 5 : 1$) to afford 0.54 g (99 %) of *XIII* as a colourless oil; $[\alpha]_D^{25} = +20.0°$ ($c = 2.8$ g L^{-1}, $CHCl_3$).

tert-Butyl {(4R,5S)-4-[8′-(2″-hexyl-1″,3″-dioxolan-2″-yl)octyl]-5-(hydroxymethyl)-2,2-dimethyl-1,3-dioxan-5-yl}carbamate (XIV)

Cs_2CO_3 (0.09 g, 0.28 mmol) was added to a solution of *XIII* (0.53 g, 0.95 mmol) in CH_3OH (14.2 mL). After stirring at ambient temperature for 1.5 h, the reaction mixture was concentrated under reduced pressure, and the residue was subjected to flash chromatography on silica gel (hexane/EtOAc, $\varphi_r = 3 : 1$) to afford 0.47 g (93 %) of *XIV* as a colourless oil; $[\alpha]_D^{25} = +26.5°$ ($c = 9.2$ g L^{-1}, $CHCl_3$).

(4R,5S)-5-[(tert-Butoxycarbonyl)amino]-4-[8′-(2″-hexyl-1″,3″-dioxolan-2″-yl)octyl]-2,2-dimethyl-1,3-dioxane-5-carboxylic acid (XV)

$(COCl)_2$ (0.13 mL, 1.51 mmol) in CH_2Cl_2 (1.56 mL) was added to a solution of DMSO (0.21 mL, 2.96 mmol) in dry CH_2Cl_2 (1.56 mL) pre-cooled to –78 ℃ and the resulting mixture was stirred at –78 ℃ for 1 h. A solution of alcohol *XIV* (0.47 g, 0.89 mmol) in CH_2Cl_2 (3.65 mL) was added drop-wise to this mixture at the same temperature. After stirring at –78 ℃ for 3 h, the mixture was allowed to warm to 0 ℃ then Et_3N (2.60 mL) and a saturated aqueous $NaHCO_3$ solution (21 mL) were added successively. The aqueous phase was extracted with further portions of CH_2Cl_2 (2 × 15 mL). The combined organic layers were dried with Na_2SO_4, stripped of solvent and the residue was passed through a small pad of silica gel (hexane/EtOAc, $\varphi_r = 7 : 1$) to afford crude aldehyde (0.45 g, 97 %) that was immediately used in the subsequent reaction without NMR analysis.

A solution of $NaClO_2$ (0.74 g, 8.18 mmol) and $NaH_2PO_4 \cdot 2H_2O$ (0.92 g, 5.90 mmol) in water (4.1 mL) was added to the solution of crude aldehyde (0.45 g, 0.85 mmol) in a mixture of CH_3CN/*tert*-butanol/2-metylbut-2-ene ($\varphi_r = 4 : 4 : 1$, 18 mL) at 0 ℃. After stirring at 0 ℃ for 30 min, the solvent was removed under reduced pressure, and the residue was chromatographed on silica gel (hexane/EtOAc, $\varphi_r = 1 : 2$) to afford 0.46 g (99 %) of acid *XV* as a colourless oil; $[\alpha]_D^{25} = +50.0°$ ($c = 1.6$ g L^{-1}, CH_3OH).

(2S,3R)-2-Acetamido-3-acetoxy-2-(acetoxymethyl)-12-oxooctadecanoic acid (XVI)

A mixture of TFA/H_2O ($\varphi_r = 2 : 1$, 3.5 mL) was added to a solution of *XV* (52 mg, 0.10 mmol) in THF (1.2 mL) and then stirred and heated at 50 ℃ for 3.5 h. Following complete consumption of the starting material (^{1}H NMR monitoring), the reaction was stopped, the mixture was allowed to cool to ambient temperature and the solvent was evaporated. The crude product was immediately dissolved in pyridine (1.8 mL), treated with Ac_2O (1.76 mL, 18.6 mmol) and stirred at ambient temperature for 1 h, then poured into a saturated aqueous NaCl solution (5.6 mL) and extracted with EtOAc (5 × 10 mL). The combined organic layers were dried with Na_2SO_4, the solvent was removed under reduced pressure and the residue was purified by flash chromatography on silica gel (CH_2Cl_2/CH_3OH, $\varphi_r = 6 : 1$) to afford 36 mg (78 %) of *XVI* as a colourless oil; $[\alpha]_D^{25} = +35.1°$ ($c = 6.4$ g L^{-1}, CH_3OH).

(4R,5S)-Benzyl 5-[(tert-butoxycarbonyl)amino]-4-[8′-(2″-hexyl-1″,3″-dioxolan-2″-yl)octyl]-2,2-dimethyl-1,3-dioxane-5-carboxylate (XVII)

K_2CO_3 (28 mg, 0.20 mmol) and benzyl bromide (BnBr) (36 μL, 0.30 mmol) were successively added to a solution of *XV* (0.11 g, 0.20 mmol) in dry DMF (1 mL). The mixture was stirred at ambient temperature for 30 min, then poured into water (5 mL) and extracted with Et_2O (3 × 10 mL). The combined organic layers were dried with Na_2SO_4, the solvent was evaporated and the residue purified by

flash chromatography on silica gel (hexane/EtOAc, $\varphi_r = 7 : 1$) to afford 0.11 g (85 %) of *XVII* as a colourless oil; $[\alpha]_D^{20} = +43.6°$ ($c = 4.2$ g L^{-1}, $CHCl_3$).

(2S,3R)-Benzyl 2-{[(benzyloxy)carbonyl] amino}-3-hydroxy-2-(hydroxymethyl)-12-oxooctadecanoate (XVIII)

A solution of *XVII* (0.10 g, 0.16 mmol) in a mixture of TFA/H_2O ($\varphi_r = 10 : 3$, 0.78 mL) was stirred at ambient temperature for 1 h. Next, the solvents were evaporated under reduced pressure, the residue was dissolved in THF (1.9 mL) and treated with a saturated aqueous solution of $NaHCO_3$ (1.9 mL). After stirring at ambient temperature for 15 min, benzyl chloroformate (CBzCl) (14 μL, 0.24 mmol) was added and stirring continued at the same temperature for 30 min. The mixture was diluted with CH_2Cl_2 (10 mL), the organic layer was separated and the aqueous layer extracted with CH_2Cl_2 (2 × 10 mL). The combined organic layers were dried with Na_2SO_4, the solvent was evaporated, and the residue chromatographed on silica gel (hexane/EtOAc, $\varphi_r = 3 : 1$) to afford 83 mg (90 %) of *XVIII* as a colourless oil; $[\alpha]_D^{20} = +19.1°$ ($c = 1.6$ g L^{-1}, $CHCl_3$).

(2S,3R)-Benzyl 2-{[(benzyloxy)carbonyl] amino}-3-hydroxy-12-oxo-2-[(trityloxy)methyl] octadecanoate (XIX)

Triphenylmethyl chloride (TrCl) (0.39 g, 1.40 mmol) and DMAP (69 mg, 0.56 mmol) were successively added to a solution of *XVIII* (82 mg, 0.14 mmol) in dry pyridine (1.35 mL). After stirring and heating at 60 °C for 30 h, the reaction mixture was allowed to cool to ambient temperature, poured into water (8 mL), and extracted with Et_2O (3 × 15 mL). The combined organic layers were dried with Na_2SO_4, the solvent was evaporated, and the residue was purified by flash chromatography on silica gel (hexane/EtOAc, $\varphi_r = 7 : 1$) to afford 91 mg (78 %) of *XIX* as a colourless oil; $[\alpha]_D^{21} = +31.3°$ ($c = 4.8$ g L^{-1}, $CHCl_3$).

(2S,3R)-Benzyl 2-{[(benzyloxy)carbonyl] amino}-12-oxo-3-(sulphooxy)-2-[(trityloxy)methyl]octadecanoate (XX)

Sulphur trioxide pyridine complex (0.18 g, 1.13 mmol) was added to a stirred solution of *XIX* (91 mg, 0.11 mmol) in dry pyridine (3.4 mL). After heating at 80 °C for 30 min, the reaction mixture was allowed to cool to ambient temperature, co-evaporated three times with toluene and the residue was chromatographed on silica gel (CH_2Cl_2/CH_3OH, $\varphi_r = 15 : 1$) to afford 95 mg (95 %) of *XX* as a colourless oil; $[\alpha]_D^{21} = +16.4°$ ($c = 5.2$ g L^{-1}, $CHCl_3$).

(2S,3R)-2-Amino-12-oxo-3-(sulphooxy)-2-[(trityloxy)methyl]octadecanoic acid (XXI)

Using the same procedure as for the preparation of *XII*, compound *XX* (91 mg, 0.10 mmol) was hydrogenated with 20 % $Pd(OH)_2/C$ (32 mg) for 22 h to afford, after flash chromatography on silica gel (CH_2Cl_2/CH_3OH, $\varphi_r = 7 : 1$), 62 mg (90 %) of *XXI* as white crystals; $[\alpha]_D^{22} = -1.7°$ ($c = 5.8$ g L^{-1}, CH_3OH).

(5S,6R)-6-[8′-(2″-Hexyl-1″,3″-dioxolan-2″-yl)octyl]-8,8-dimethyl-3,7,9-trioxa-1-azaspiro[4.5]decan-2-one (XXIII)

Using the procedure as for the preparation of *XI*, compound *IX* (0.14 g, 0.65 mmol) was converted to an inseparable mixture of olefins *XX* (0.17 g, 58 %, colourless oil, hexane/EtOAc, $\varphi_r = 1 : 1$).

Using the procedure as for the preparation of *XII*, the corresponding mixture of alkenes *XX* (0.16 g, 0.35 mmol) was hydrogenated with 20 % $Pd(OH)_2/C$ (12 mg) for 2 h to afford, after flash chromatography on silica gel (hexane/EtOAc, $\varphi_r = 1 : 1$), 155 mg (97 %) of *XXIII* as a colourless oil; $[\alpha]_D^{25} = +28.5°$ ($c = 3.2$ g L^{-1}, $CHCl_3$).

(5S,6R)-tert-Butyl 6-[8′-(2″-hexyl-1″,3″-dioxolan-2″-yl)octyl]-8,8-dimethyl-2-oxo-3,7,9-trioxa-1-azaspiro[4.5]decane-1-carboxylate (XXIV)

Using the procedure as for the preparation of *XIII*, compound *XXIII* (65 mg, 0.14 mmol) was converted to *XXIV* (72 mg, 91 %, colourless oil, hexane/EtOAc, $\varphi_r = 5 : 1$); $[\alpha]_D^{25} = +14.7°$ ($c = 3.8$ g L^{-1}, $CHCl_3$).

tert-Butyl {(4R,5R)-4-[8′-(2″-hexyl-1″,3″-dioxolan-2″-yl)octyl]-5-(hydroxymethyl)-2,2-dimethyl-1,3-dioxan-5-yl}carbamate (XXV)

Using the procedure as for the preparation of *XIV*, compound *XXIV* (72 mg, 0.13 mmol) and Cs_2CO_3 (13 mg, 0.04 mmol) afforded, after flash chromatography on silica gel (hexane/EtOAc, $\varphi_r = 3 : 1$), 60 mg (88 %) of *XXV* as a colourless oil; $[\alpha]_D^{20} = -16.6°$ ($c = 3.2$ g L^{-1}, $CHCl_3$).

(4R,5R)-5-[(tert-Butoxycarbonyl)amino]-4-[8′-(2″-hexyl-1″,3′′-dioxolan-2″-yl)octyl]-2,2-dimethyl-1,3-dioxane-5-carboxylic acid (XXVI)

Using the procedure as for the preparation of *XV*, compound *XXV* (59 mg, 0.11 mmol) was converted to carboxylic acid *XXVI* (60 mg, 99 %, colourless oil, hexane/EtOAc, $\varphi_r = 1 : 2$); $[\alpha]_D^{20} = +8.9°$ ($c = 3.2$ g L^{-1}, $CHCl_3$).

(2R,3R)-2-Acetamido-3-acetoxy-2-(acetoxymethyl)-12-oxooctadecanoic acid (XXVII)

Using the procedure as for the preparation of *XVI*, compound *XXVI* (60 mg, 0.11 mmol) was converted to *XXVII* (35 mg, 66 %, colourless oil, EtOAc/AcOH, $\varphi_r = 50 : 1$); $[\alpha]_D^{25} = +4.6°$ ($c = 6.0$ g L^{-1}, $CHCl_3$).

(S)-4-[(R)-1′-Hydroxy-10′-oxohexadecyl]-4-(hydroxymethyl)oxazolidin-2-one (XXVIII)

A solution of *XXIII* (86 mg, 0.19 mmol) in a mixture of AcOH/H_2O ($\varphi_r = 7 : 3$, 18.6 mL) was stirred and heated at 80 ℃ for 6 h and then at 40 ℃ for 12.5 h. The solvent was removed under reduced pressure, and the residue was subjected to flash chromatography on silica gel (EtOAc) to afford 65 mg (92 %) of crystalline *XXVIII*; $[\alpha]_D^{25} = +11.9°$ ($c = 3.0$ g L^{-1}, $CHCl_3$).

(S)-4-[(R)-1′-Hydroxy-10′-oxohexadecyl]-4-[(trityloxy)methyl]oxazolidin-2-one (XXIX)

TrCl (0.22 g, 0.79 mmol) and DMAP (39 mg, 0.32 mmol) were added successively to a solution of *XXVIII* (60 mg, 0.16 mmol) in dry pyridine (1.6 mL) and the mixture was stirred and heated at 60 ℃ for 23 h. The mixture was allowed to cool to ambient temperature, poured into water (5 mL), and extracted with Et_2O (3 × 10 mL). The combined organic layers were dried with Na_2SO_4, the solvent was evaporated under reduced pressure, and the residue was chromatographed on silica gel (hexane/EtOAc, $\varphi_r = 2 : 1$) to afford 90 mg (91 %) of *XXIX* as a colourless oil; $[\alpha]_D^{25} = +27.5°$ ($c = 4.0$ g L^{-1}, $CHCl_3$).

(R)-10-Oxo-1-{(S)-2′-oxo-4′-[(trityloxy)methyl]oxazolidin-4′-yl}hexadecyl benzoate (XXX)

Benzoyl chloride (BzCl) (0.10 mL, 0.86 mmol) and DMAP (1.71 mg, 14.0 μmol) were added successively to a solution of *XXIX* (86 mg, 0.14 mmol) in dry pyridine (1.4 mL). The reaction mixture was stirred at ambient temperature for 4 h, then poured into water (5 mL), and extracted with Et_2O (3 × 10 mL). The combined organic phases were dried with Na_2SO_4, the solvents were removed under reduced pressure, and the residue was subjected to flash chromatography on silica gel (hexane/EtOAc, $\varphi_r = 4 : 1$) to afford 97 mg (96 %) of *XXX* as a colourless oil; $[\alpha]_D^{25} = -1.8°$ ($c = 4.8$ g L^{-1}, $CHCl_3$).

(R)-1-[(S)-4′-(Hydroxymethyl)-2′-oxooxazolidin-4′-yl]-10-oxohexadecyl benzoate (XXXI)

To a solution of *XXX* (95 mg, 0.13 mmol) in CH_2Cl_2/CH_3OH ($\varphi_r = 2 : 1$, 1.65 mL) was added *p*-TsOH (74 mg, 0.39 mmol) in three portions at 10 min intervals and the mixture was stirred at ambient temperature for 24 h. The acid was then neutralised with Et_3N (37.0 μL), the solvent was removed under reduced pressure and the residue was purified by flash chromatography on silica gel (hexane/EtOAc, $\varphi_r = 1 : 2$) to afford 51 mg (81 %) of *XXXI* as a colourless oil; $[\alpha]_D^{25} = +21.3°$ ($c = 2.2$ g L^{-1}, $CHCl_3$).

(S)-4-[(R)-1′-(Benzoyloxy)-10′-oxohexadecyl]-2-oxooxazolidine-4-carboxylic acid (XXXII)

IBX (42 mg, 0.15 mmol) was added to a solution of *XXXI* (48 mg, 0.10 mmol) in CH_3CN (2 mL) and the mixture was heated to reflux for 45 min. Next, the mixture was allowed to cool to ambient temperature, the solids were removed by filtation, and the solvent was removed under reduced pressure. The aldehyde thus obtained (47 mg, 98 %) was used immediately in the subsequent reaction without further purification.

A solution of $NaClO_2$ (86 mg, 0.95 mmol) and $NaH_2PO_4 \cdot 2H_2O$ (0.11 g, 0.71 mmol) in water (0.47 mL) was added drop-wise to the solution of crude aldehyde (47 mg, 0.10 mmol) in a mixture of CH_3CN/*tert*-butanol/2-metylbut-2-ene ($\varphi_r = 4 : 4 : 1$, 2.1 mL) at 0 ℃ and the mixture was stirred at 0 ℃ for 15 min and then at ambient temperature for 45 min. Evaporation of the solvent and purification of the residue by chromatography on silica gel (CH_2Cl_2/CH_3OH, $\varphi_r = 8 : 1$) afforded 46 mg (94 %) of carboxylic acid *XXXII* as a colourless oil; $[\alpha]_D^{25} = +47.5°$ ($c = 1.4$ g L^{-1}, $CHCl_3$).

Transformation of XXXII into XVI

NaOH (10 mass % aqueous solution, 3.2 mL) was added to a solution of *XXXII* (45 mg, 0.09 mmol) in CH_3OH (3.2 mL) at ambient temperature; the mixture was stirred and heated at 80 ℃ for 2 h, cooled to ambient temperature and neutralised with 10 mass % aqueous HCl solution. The solids were removed by filtration and the solvent was evaporated. The crude product was immediately dissolved in pyridine (1.7 mL), followed by the addition of Ac_2O (1.68 mL, 17.8 mmol). The reaction mixture was stirred at ambient temperature for 1 h, poured into a saturated aqueous NaCl solution (5.3 mL), and extracted with EtOAc (5 × 10 mL). The combined organic layers were dried with Na_2SO_4, the solvent was evaporated under reduced pressure, and the residue chromatographed on silica gel (CH_2Cl_2/CH_3OH, $\varphi_r = 6 : 1$) to afford 34 mg (77 %) of *XVI*.

Results and discussion

The oxazolidinones *VI* and *VII* obtained using a previous approach (Martinková et al., 2012a) are effectively capable of further transformation to the desired

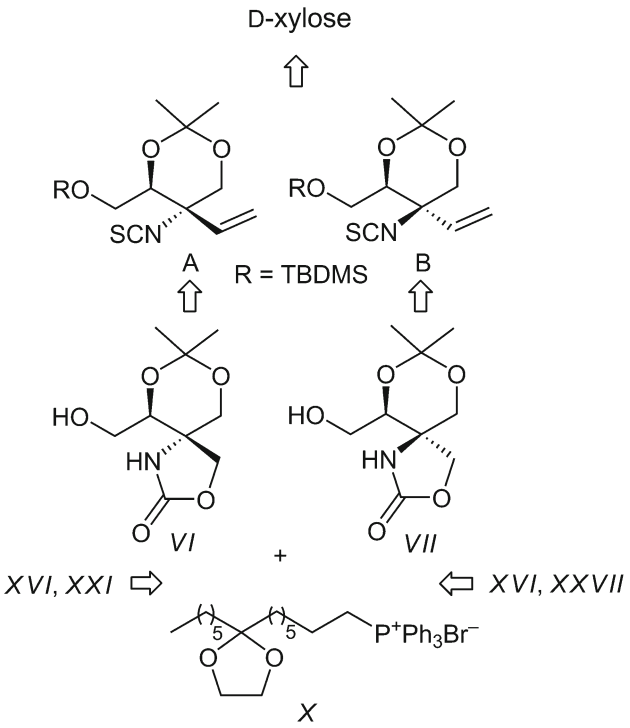

Fig. 2. Retrosynthetic pathway.

target molecules, following the strategy illustrated in Fig. 2.

Retrosynthetically, the carbon backbone of the final molecules *XVI*, *XXI*, and *XXVII* would be constructed from the highly functionalised fragments, the derivatives *VI* and/or *VII* referred to above (Martinková, et al., 2012a) and the hydrophobic C_{14} counterpart *X* (Payette & Just, 1981; Sano et al., 1995). The known phosphonium salt *X* was prepared on a multigram scale, applying combined modifications of protocols from the literature (Payette & Just, 1981; Sano et al., 1995; Shioiri et al., 1998). The isothiocyanates A and B derived from D-xylose (Martinková, et al., 2012a) with a defined configuration on both the stereogenic centres were chosen as the starting material to afford *VI* and *VII*, respectively.

Transformation of VI to α-substituted α-amino acids XVI and XXI

Synthesis of sulfamisterin *I* and its desulphated analogue *II* in their protected forms (see amino acids *XXI* and *XVI*, respectively) commenced with the branched aminopolyol *VI*, prepared in a larger amount (more than 5 g) together with its congener, diastereoisomer *VII* (Martinková et al., 2012a). Its oxidation with IBX (More & Finney, 2002; Satam et al., 2010) in CH_3CN afforded the stable aldehyde *VIII* with a 94 % yield (Fig. 3). Wittig olefination of *VIII* with non-stabilised ylide derived from the known phosphonium salt *X* (Payette & Just, 1981; Sano et al., 1995) employing LHMDS (freshly prepared from *n*-BuLi and $NH(SiMe_3)_2$) (Azuma et al., 2000) as the

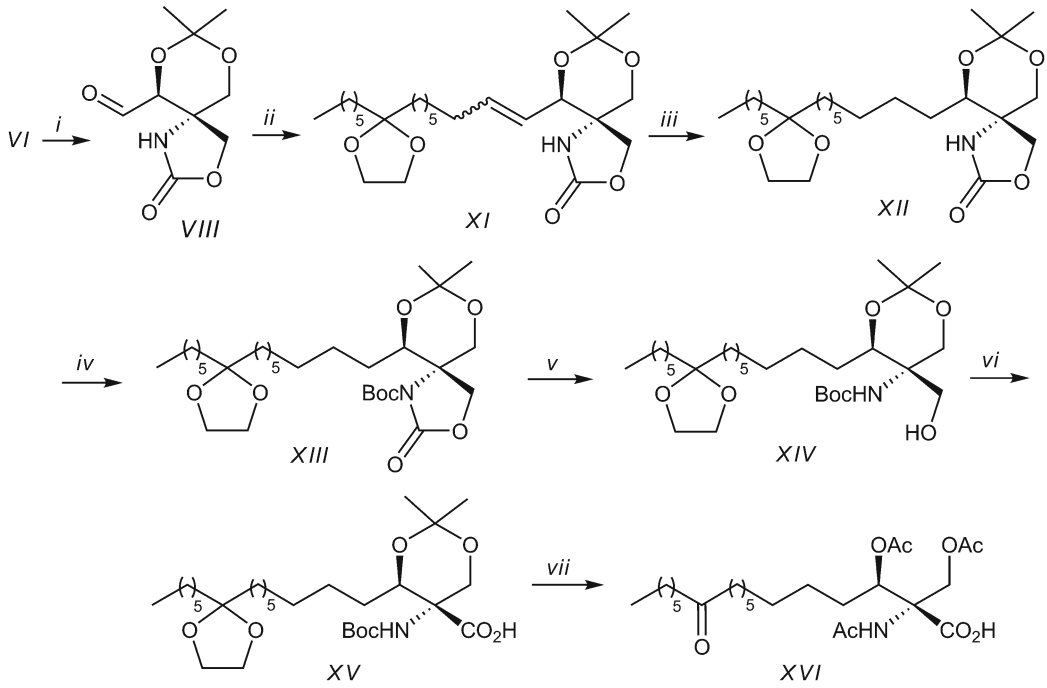

Fig. 3. Synthesis of *XVI*. Reagents and conditions: *i*) IBX, CH_3CN, reflux, 94 %; *ii*) LHMDS, *X*, THF, r.t., 81 %; *iii*) H_2, $Pd(OH)_2/C$, EtOH, r.t., 94 %; *iv*) Boc_2O, CH_3CN, DMAP, a.rt., 99 %; *v*) Cs_2CO_3, CH_3OH, r.t., 93 %; *vi*) DMSO, $(COCl)_2$, Et_3N, –78 °C, 97 %, then $NaClO_2$, CH_3CN/*tert*-BuOH/2-methylbut-2-ene, 0 °C, 99 %; *vii*) TFA/H_2O/THF, 50 °C, then Ac_2O, pyridine, r.t., 78 % (after two steps).

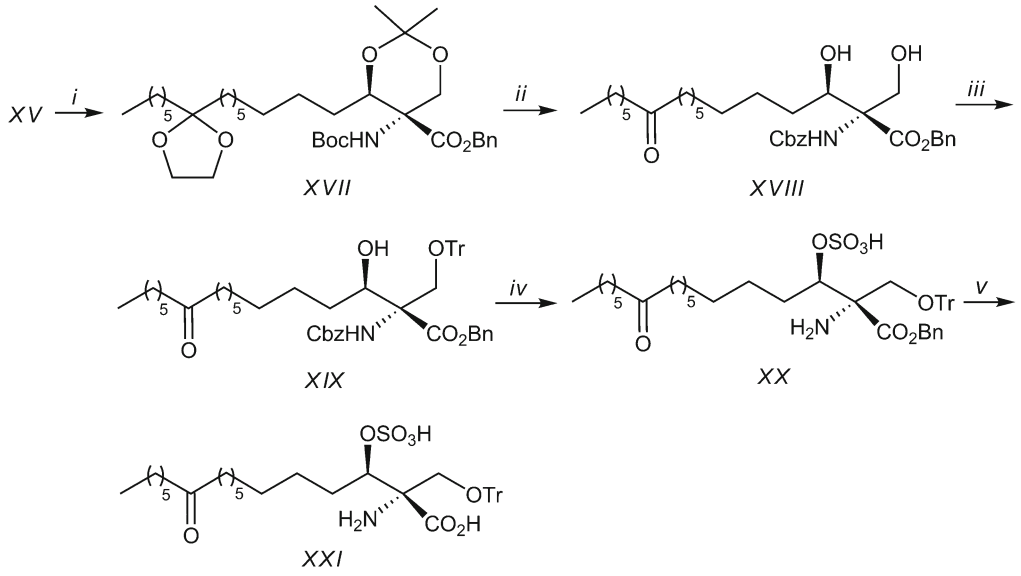

Fig. 4. Synthesis of *XXI*. Reagents and conditions: *i*) BnBr, K_2CO_3, DMF, r.t., 85 %; *ii*) TFA/H_2O, r.t., then CBzCl, aqueous $NaHCO_3$, THF, r.t., 90 % (after two steps); *iii*) TrCl, pyridine, DMAP, 60 °C, 78 %; *iv*) sulphur trioxide pyridine complex, pyridine, 80 °C, 95 %; *v*) H_2, $Pd(OH)_2/C$, CH_3OH, r.t., 90 %.

base, resulted in the formation of a barely separable mixture of olefins *XI* ($Z/E \approx 3:1$ ratio, determined by ^{1}H NMR) with a 81 % yield. A small amount of the mixture of diastereomeric olefins *XI* was separated using silica gel chromatography to yield only (*Z*)-*XI* in pure form. The geometry of the C=C bond was confirmed on the basis of the vinyl proton coupling constant value (J_{cis} = 11.6 Hz). Hydrogenation of *XI* in the presence of $Pd(OH)_2/C$ in EtOH afforded the saturated derivative *XII* (94 %, Fig. 3).

Once the coupling product *XII* was achieved, it was possible to explore its modification into the desired α-substituted α-amino acids *XVI* and *XXI,* utilising the stereoselective functional group transformations. First, protection of the carbamate nitrogen atom in *XII* with a Boc group by treatment with Boc_2O and DMAP in CH_3CN (Hansen et al., 1995) provided *XIII* with excellent yield (99 %, Fig. 3). Selective cleavage of the cyclic carbamate moiety in *XIII* was achieved with catalytic amounts of Cs_2CO_3 (Mita et al., 2007) in CH_3OH, affording the corresponding compound *XIV* with 93 % yield. Swern oxidation of the primary hydroxyl group in *XIV* followed by $NaClO_2$ treatment afforded the carboxylic acid *XV* (Fig. 3). The simultaneous removal of all protecting groups in *XV* by acid hydrolysis (TFA/H_2O) and the subsequent acetylation with Ac_2O in pyridine afforded derivative *XVI* (78 %, Fig. 3) as the protected form of *II*.

Having secured an appropriate route to *II*, the next task was to modify the corresponding amino acid *XV* into sulfamisterin *I*. The reaction of *XV* with benzyl bromide in dry DMF and in the presence of K_2CO_3 produced ester *XVII* with a yield of 85 % (Fig. 4). Its acid hydrolysis (TFA/H_2O), followed by treatment with benzyl chloroformate (CBzCl) in the presence of $NaHCO_3$, resulted in the formation of the known CBz-derivative *XVIII* (Sato et al., 2005) with a yield of 90 %. The ^{1}H NMR spectrum of *XVIII* exhibited small differences from Chida's product (Sato et al., 2005), probably due to its measurement at 400 MHz (see Experimental). Its ^{13}C NMR data were in full accord with those reported in the literature (Sato et al., 2005), but the value of the specific rotation ($[\alpha]_D^{20}$ = +19.1°, c = 1.6 g L^{-1}, $CHCl_3$) was distinct from the published value (Sato et al., 2005; $[\alpha]_D^{23}$ = +4.9°, c = 14.1 g L^{-1}, $CHCl_3$). The primary hydroxyl group present in *XVIII* was selectively protected as the triphenylmethyl ether *XIX* using trityl chloride (TrCl) in pyridine at 60 °C. The remaining alcohol function in *XIX* was then treated with the sulphur trioxide pyridine complex (Liav & Goren, 1984; Sanders et al., 1997) in pyridine at 80 °C to afford compound *XX* with a yield of 95 % (Fig. 4). Unfortunately, the final catalytic hydrogenation using $Pd(OH)_2/C$ as a catalyst removed only the Cbz and benzyl groups to afford compound *XXI* (90 %) as the protected form of *I* (Fig. 4). The addition of further portions of the catalyst proved ineffective and led to the generation of unidentified decomposition products. Substitution of the *tert*-butyldimethylsilyl group for trityl was assayed but its deprotection with tetra-*n*-butylammonium fluoride (TBAF) was accompanied by desulphatation.

Modification of VII into amino acids XVI and XXVII

In a parallel fashion, diastereoisomer *VII* (Martinková et al., 2012a) was converted to (2*R*,3*R*)-configured analogue *XXVII* in eight reaction steps and with an overall yield of 27 % (Fig. 5). First, IBX-

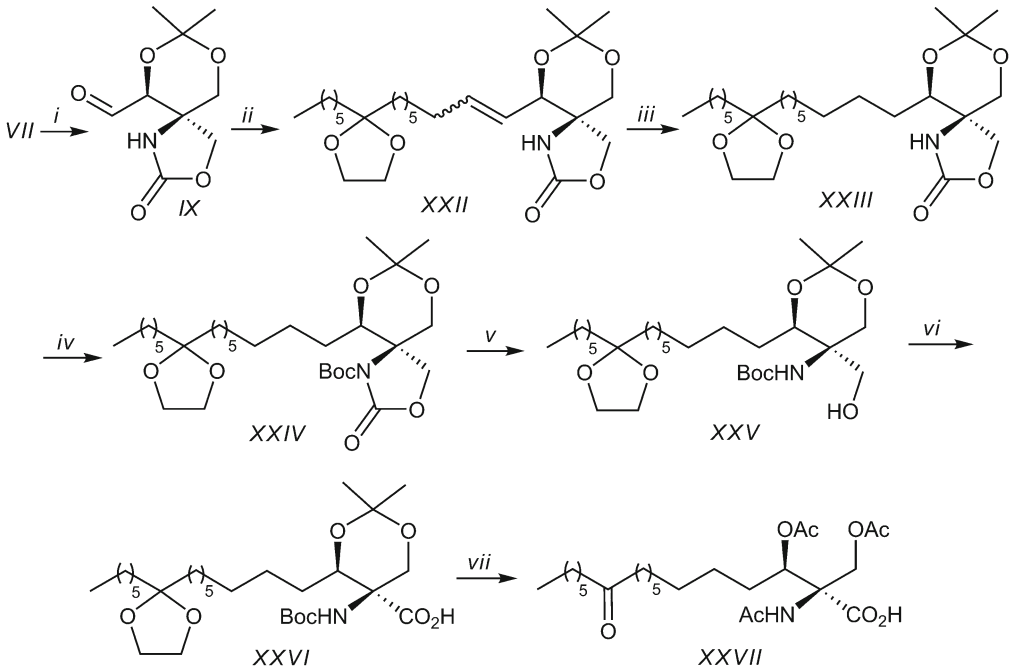

Fig. 5. Synthesis of *XXVII*. Reagents and conditions: *i*) IBX, CH_3CN, reflux, 94 %; *ii*) LHMDS, *X*, THF, r.t., 58 %; *iii*) H_2, $Pd(OH)_2/C$, EtOH, r.t., 97 %; *iv*) Boc_2O, CH_3CN, DMAP, r.t., 91 %; *v*) Cs_2CO_3, CH_3OH, rt, 88 %; *vi*) DMSO, $(COCl)_2$, Et_3N, –78 °C, 99 %, then $NaClO_2$, CH_3CN/*tert*-BuOH/2-methylbut-2-ene, 0 °C, 99 %; *vii*) TFA/H_2O/THF, 50 °C, then Ac_2O, pyridine, r.t., 66 % (two steps).

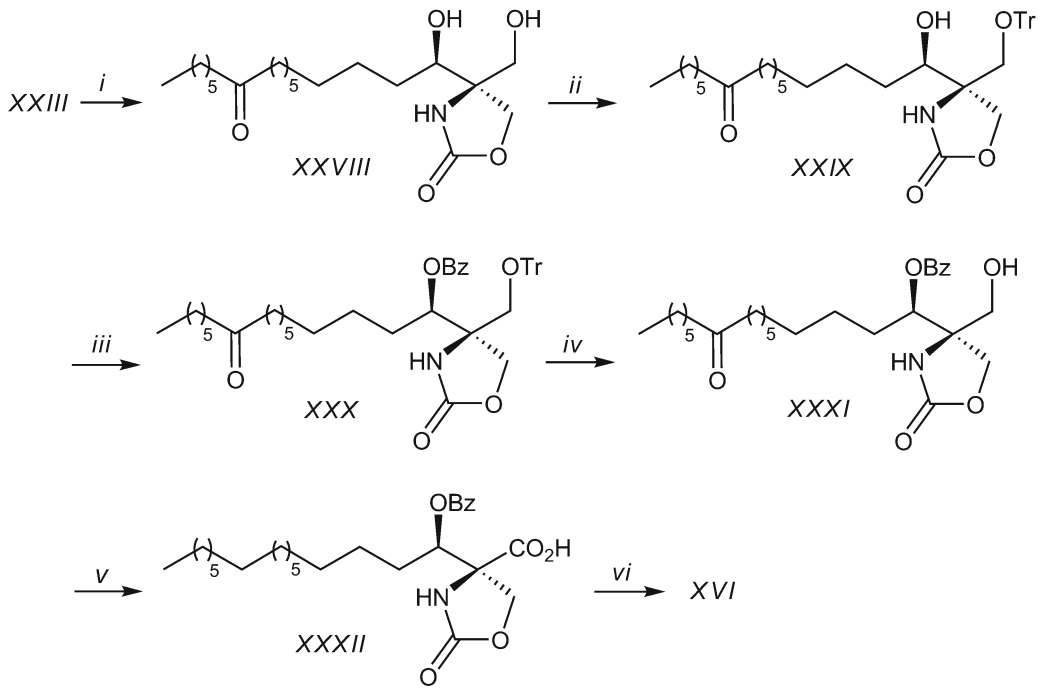

Fig. 6. Synthesis of *XVI*. Reagents and conditions: *i*) AcOH/H_2O, 80 °C to 40 °C, 92 %; *ii*) TrCl, DMAP, pyridine, 60 °C, 91 %; *iii*) BzCl, pyridine, DMAP, r.t., 96 %; *iv*) *p*-TsOH, CH_3OH/CH_2Cl_2, r.t., 81 %; *v*) IBX, CH_3CN, reflux, 98 %, then $NaClO_2$, CH_3CN/*tert*-BuOH/2-methylbut-2-ene, 0 °C, 94 %; *vi*) 10 mass % aqueous NaOH, CH_3OH, 80 °C, then Ac_2O, pyridine, r.t., 77 % (two steps).

mediated oxidation of *VII* afforded the corresponding crystalline aldehyde *IX* (94 %, Fig. 5). Its coupling reaction with an ylide derived from the known *X* (Payette & Just, 1981; Sano et al., 1995) afforded an inseparable mixture of alkenes *XXII* ($Z/E \approx 3:1$ ratio, determined by ^{1}H NMR). Unlike the coupling of

Table 1. Characterisation data of the newly prepared compounds

Compound	Formula	M_r	w_i(calc.)/% w_i(found)/%			Yield	M.p.
			C	H	N	%	°C
VIII	$C_9H_{13}NO_5$	215.20	50.23	6.09	6.51	94	–
			50.20	6.15	6.45		
IX	$C_9H_{13}NO_5$	215.20	50.23	6.09	6.51	94	148–150
			50.29	6.02	6.58		
XI[a]	$C_{25}H_{43}NO_6$	453.61	66.19	9.55	3.09	81	–
(*Z*)-*XI*	$C_{25}H_{43}NO_6$	453.61	66.19	9.55	3.09	–	–
			66.15	9.59	3.05		
XII	$C_{25}H_{45}NO_6$	455.63	65.90	9.95	3.07	94	–
			65.95	9.93	3.09		
XIII	$C_{30}H_{53}NO_8$	555.74	64.84	9.61	2.52	99	–
			64.88	9.63	2.59		
XIV	$C_{29}H_{55}NO_7$	529.75	65.75	10.46	2.64	93	–
			65.72	10.45	2.67		
XV	$C_{29}H_{53}NO_8$	543.73	64.06	9.82	2.58	99	–
			64.00	9.85	2.63		
XVI	$C_{25}H_{43}NO_8$	485.61	61.83	8.93	2.88	78	–
			61.81	8.95	2.95		
XVII	$C_{36}H_{59}NO_8$	633.86	68.22	9.38	2.21	85	–
			68.26	9.31	2.26		
XVIII	$C_{34}H_{49}NO_7$	583.76	69.95	8.46	2.40	90	–
			69.89	8.49	2.36		
XIX	$C_{53}H_{63}NO_7$	826.07	77.06	7.69	1.70	78	–
			77.01	7.75	1.66		
XX	$C_{53}H_{63}NO_{10}S$	906.13	70.25	7.01	1.55	95	–
			70.31	7.05	1.51		
XXI	$C_{38}H_{51}NO_8S$	681.88	66.93	7.54	2.05	90	142–144
			66.85	7.59	2.01		
XXII[a]	$C_{25}H_{43}NO_6$	453.61	66.19	9.53	3.09	58	–
XXIII	$C_{25}H_{45}NO_6$	455.63	65.90	9.95	3.07	97	–
			65.93	9.98	3.05		
XXIV	$C_{30}H_{53}NO_8$	555.74	64.84	9.61	2.52	91	–
			64.80	9.65	2.49		
XXV	$C_{29}H_{55}NO_7$	529.75	65.75	10.46	2.64	88	–
			65.79	10.43	2.61		
XXVI	$C_{29}H_{53}NO_8$	543.73	64.06	9.82	2.58	99	–
			64.08	9.80	2.55		
XXVII	$C_{25}H_{43}NO_8$	485.61	61.83	8.93	2.88	66	–
			61.87	8.90	2.85		
XXVIII	$C_{20}H_{37}NO_5$	371.51	64.66	10.04	3.77	92	69–70
			64.69	10.00	3.73		
XXIX	$C_{39}H_{51}NO_5$	613.83	76.31	8.37	2.28	91	–
			76.29	8.42	2.33		
XXX	$C_{46}H_{55}NO_6$	717.93	76.96	7.72	1.95	96	–
			76.92	7.75	1.91		
XXXI	$C_{27}H_{41}NO_6$	475.62	68.18	8.69	2.94	81	–
			68.22	8.65	2.91		
XXXII	$C_{27}H_{39}NO_7$	489.60	66.24	8.03	2.86	94	–
			66.27	8.00	2.90		

a) Elemental analysis of compound (a mixture of geometric isomers) was not performed.

VIII with *X*, the lower yield (58 %) for this step was most probably due to the formation of some minor unidentified products. Hydrogenation of *XXII* with $Pd(OH)_2/C$ in EtOH afforded the saturated product *XXIII* with a yield of 97 % (Fig. 5). Protection of the carbamate nitrogen of *XXIII* using the conditions as described for the preparation of *XIV* successfully provided *XXIV* (91 %), of which the base treatment (Cs_2CO_3, CH_3OH) resulted in the formation of the corresponding derivative *XXV* with a yield of 88 %. Step-wise oxidation of the primary alcohol *XXV* (DMSO, oxalyl chloride followed by $NaClO_2$) afforded

Table 2. Spectral data of the newly prepared compounds

Compound	Spectral data
VIII	^{1}H NMR (400 MHz, $CDCl_3$), δ: 1.48 (s, 3H, CH_3), 1.53 (s, 3H, CH_3), 3.71 (d, 1H, $J_{10,10}$ = 11.7 Hz, H-10), 4.04 (d, 1H, $J_{10,10}$ = 11.7 Hz, H-10), 4.34 (d, 1H, $J_{4,4}$ = 9.8 Hz, H-4), 4.42 (s, 1H, H-6), 4.48 (d, 1H, $J_{4,4}$ = 9.8 Hz, H-4), 7.10 (br s, 1H, NH), 9.72 (s, 1H, CH═O) ^{13}C NMR (100 MHz, $CDCl_3$), δ: 18.7 (CH_3), 28.3 (CH_3), 55.6 (C-5), 67.4 (C-10), 70.9 (C-4), 76.6 (C-6), 100.0 (C-8), 159.3 (C-2), 199.4 (CH═O)
IX	^{1}H NMR (400 MHz, $CDCl_3$), δ: 1.50 (s, 3H, CH_3), 1.55 (s, 3H, CH_3), 3.78 (d, 1H, $J_{10,10}$ = 12.0 Hz, H-10), 3.89 (d, 1H, $J_{10,10}$ = 12.0 Hz, H-10), 3.93 (d, 1H, $J_{4,4}$ = 9.4 Hz, H-4), 4.14 (s, 1H, H-6), 4.62 (d, 1H, $J_{4,4}$ = 9.4 Hz, H-4), 6.63 (br s, 1H, NH), 9.56 (s, 1H, CH═O) ^{13}C NMR (100 MHz, $CDCl_3$), δ: 18.7 (CH_3), 28.4 (CH_3), 56.0 (C-5), 66.7 (C-4), 67.6 (C-10), 76.4 (C-6), 100.0 (C-8), 157.8 (C-2), 200.7 (CH═O)
(*Z*)-*XI*	^{1}H NMR (400 MHz, $CDCl_3$), δ: 0.88 (t, 3H, J = 7.0 Hz, CH_3), 1.25–1.37 (m, 16H, 8 × CH_2), 1.38 (s, 3H, CH_3), 1.52 (s, 3H, CH_3), 1.57–1.61 (m, 4H, 2 × CH_2), 1.99–2.08 (m, 1H, H-3′), 2.11–2.20 (m, 1H, H-3′), 3.74 (d, 1H, $J_{10,10}$ = 11.5 Hz, H-10), 3.93 (s, 4H, 2 × H-4″, 2 × H-5″), 3.95 (d, 1H, $J_{10,10}$ = 11.5 Hz, H-10), 4.28 (d, 1H, $J_{4,4}$ = 9.5 Hz, H-4), 4.61–4.65 (m, 2H, H-4, H-6), 5.39 (ddt, 1H, $J_{2',1'}$ = 11.6 Hz, $J_{6,1'}$ = 8.1 Hz, $J_{3',1'}$ = 1.6 Hz, $J_{3',1'}$ = 1.6 Hz, H-1′), 5.78 (dddd, 1H, $J_{2',1'}$ =11.6 Hz, $J_{3',2'}$ = 8.5 Hz, $J_{3',2'}$ = 6.3 Hz, $J_{6,2'}$ = 0.9 Hz, H-2′), 6.82 (br s, 1H, NH) ^{13}C NMR (100 MHz, $CDCl_3$), δ: 14.0 (CH_3), 18.5 (CH_3), 22.6 (CH_2), 23.7 (CH_2), 23.8 (CH_2), 28.3 (C-3′), 28.9 (CH_3), 29.1 (CH_2), 29.2 (CH_2), 29.6 (2 × CH_2), 31.8 (CH_2), 37.1 (2 × CH_2), 56.5 (C-5), 64.8 (C-4″, C-5″), 67.8 (C-10), 69.7 (C-6), 70.1 (C-4), 99.2 (C-8), 111.8 (C-2″), 122.2 (C-1′), 138.8 (C-2′), 159.6 (C-2)
XII	^{1}H NMR (400 MHz, $CDCl_3$), δ: 0.87 (t, 3H, J = 6.9 Hz, CH_3), 1.24–1.36 (br s, 22H, 11 × CH_2), 1.36 (s, 3H, CH_3), 1.44 (s, 3H, CH_3), 1.57–1.61 (m, 4H, 2 × CH_2), 3.71 (d, 1H, $J_{10,10}$ = 11.5 Hz, H-10), 3.72–3.75 (m, 1H, H-6), 3.85 (d, 1H, $J_{10,10}$ = 11.5 Hz, H-10), 3.93 (s, 4H, 2 × H-4″, 2 × H-5″), 4.28 (d, 1H, $J_{4,4}$ = 9.5 Hz, H-4), 4.55 (d, 1H, $J_{4,4}$ = 9.5 Hz, H-4), 6.34 (br s, 1H, NH) ^{13}C NMR (100 MHz, $CDCl_3$), δ: 14.1 (CH_3), 18.5 (CH_3), 22.6 (CH_2), 23.8 (2 × CH_2), 25.6 (CH_2), 28.0 (CH_2), 28.8 (CH_3), 29.3 (CH_2), 29.4 (2 × CH_2), 29.6 (CH_2), 29.8 (CH_2), 31.8 (CH_2), 37.1 (2 × CH_2), 56.3 (C-5), 64.8 (C-4″, C-5″), 68.0 (C-10), 70.0 (C-4), 73.8 (C-6), 99.3 (C-8), 111.9 (C-2″), 159.4 (C-2)
XIII	^{1}H NMR (400 MHz, $CDCl_3$), δ: 0.87 (t, 3H, J = 6.8 Hz, CH_3), 1.22–1.34 (br s, 20H, 10 × CH_2), 1.36 (s, 3H, CH_3), 1.39–1.44 (m, 2H, CH_2), 1.53 (s, 3H, CH_3), 1.55–1.61 (m, 13H, 3 × CH_3, 2 × CH_2), 3.62 (d, 1H, $J_{10,10}$ = 10.9 Hz, H-10), 3.92 (s, 4H, 2 × H-4″, 2 × H-5″), 4.25 (d, 1H, $J_{4,4}$ = 9.6 Hz, H-4), 4.49 (d, 1H, $J_{4,4}$ = 9.6 Hz, H-4), 4.59–4.63 (m, 2H, H-6, H-10) ^{13}C NMR (100 MHz, $CDCl_3$), δ: 14.1 (CH_3), 19.0 (CH_3), 22.6 (CH_2), 23.8 (2 × CH_2), 25.3 (CH_2), 28.0 (3 × CH_3, CH_2), 28.8 (CH_3), 29.2 (CH_2), 29.3 (CH_2), 29.5 (CH_2), 29.6 (CH_2), 29.8 (CH_2), 31.8 (CH_2), 37.1 (2 × CH_2), 60.0 (C-5), 64.8 (C-4″, C-5″), 65.4 (C-10), 67.3 (C-4), 70.4 (C-6), 84.5 (C_q), 99.6 (C-8), 111.8 (C-2″), 149.2 (C═O), 159.4 (C-2)
XIV	^{1}H NMR (400 MHz, CD_3OD), δ: 0.88 (t, 3H, J = 6.6 Hz, CH_3), 1.22–1.31 (m, 20H, 10 × CH_2), 1.31 (s, 3H, CH_3), 1.42 (s, 9H, 3 × CH_3), 1.49 (s, 3H, CH_3), 1.51–1.58 (m, 6H, 3 × CH_2), 3.58 (d, 1H, $J_{H,H}$ = 11.4 Hz, CH_2OH), 3.80 (d, 1H, $J_{6,6}$ = 11.1 Hz, H-6), 3.88 (s, 4H, 2 × H-4″, 2 × H-5″), 3.97 (d, 1H, $J_{H,H}$ = 11.4 Hz, CH_2OH), 4.15 (d, 1H, $J_{6,6}$ = 11.1 Hz, H-6), 4.50–4.53 (m, 1H, H-4), 6.01 (br s, 1H, NH) ^{13}C NMR (100 MHz, CD_3OD), δ: 14.6 (CH_3), 19.9 (CH_3), 23.7 (CH_2), 25.0 (2 × CH_2), 27.4 (CH_2), 28.8 (3 × CH_3), 29.3 (CH_3), 29.5 (CH_2), 30.4 (CH_2), 30.6 (CH_2), 30.7 (CH_2), 30.8 (CH_2), 31.0 (CH_2), 33.1 (CH_2), 38.1 (2 × CH_2), 56.2 (C-5), 60.5 (CH_2OH), 62.4 (C-6), 65.9 (C-4″, C-5″), 72.7 (C-4), 80.4 (C_q), 100.1 (C-2), 113.0 (C-2″), 157.2 (C═O)
XV	^{1}H NMR (400 MHz, $CDCl_3$), δ: 0.88 (t, 3H, J = 6.9 Hz, CH_3), 1.24–1.36 (m, 22H, 11 × CH_2), 1.43 (s, 9H, 3 × CH_3), 1.51 (s, 3H, CH_3), 1.56–1.62 (m, 4H, 2 × CH_2), 1.70 (s, 3H, CH_3), 3.75 (d, 1H, $J_{6,6}$ = 11.9 Hz, H-6), 3.92 (s, 4H, 2 × H-4″, 2 × H-5″), 4.85 (d, 1H, $J_{6,6}$ = 11.9 Hz, H-6), 4.93–4.95 (m, 1H, H-4), 5.71 (br s, 1H, NH) ^{13}C NMR (100 MHz, $CDCl_3$), δ 14.1 (CH_3), 18.9 (CH_3), 22.6 (CH_2), 23.8 (2 × CH_2), 25.3 (CH_2), 28.2 (3 × CH_3), 29.0 (CH_3), 29.3 (CH_2), 29.4 (CH_2), 29.6 (2 × CH_2), 29.8 (2 × CH_2), 31.8 (CH_2), 37.1 (2 × CH_2), 57.1 (C-5), 62.0 (C-6), 64.8 (C-4″, C-5″), 69.7 (C-4), 80.3 (C_q), 100.7 (C-2), 111.8 (C-2″), 153.6 (C═O), 171.3 (COOH)
XVI	^{1}H NMR (400 MHz, CD_3OD), δ: 0.85 (t, 3H, J = 6.8 Hz, CH_3), 1.23 (m, 16H, 8 × CH_2), 1.43–1.53 (m, 4H, 2 × CH_2), 1.54–1.60 (m, 1H, CH_2), 1.71–1.78 (m, 1H, CH_2), 1.93 (s, 3H, CH_3CO), 1.95 (s, 3H, CH_3CO), 2.01 (s, 3H, CH_3CO), 2.38 (t, 4H, J = 7.3 Hz, 2 × CH_2), 4.45 (d, 1H, $J_{H,H}$ = 11.3 Hz, CH_2O), 4.64 (d, 1H, $J_{H,H}$ = 11.3 Hz, CH_2O), 5.40 (dd, 1H, $J_{4,3}$ = 10.7 Hz, $J_{4,3}$ = 1.6 Hz, H-3) ^{13}C NMR (100 MHz, CD_3OD), δ: 14.4 (CH_3), 20.8 (CH_3CO), 20.9 (CH_3CO), 23.1 (CH_3CO), 23.6 (CH_2), 24.9 (2 × CH_2), 27.3 (CH_2), 30.0 (CH_2), 30.3 (CH_2), 30.5 (3 × CH_2), 31.2 (CH_2), 32.8 (CH_2), 43.5 (CH_2), 43.5 (CH_2), 63.3 (CH_2O), 65.9 (C-2), 73.6 (C-3), 172.2 (C═O), 172.4 (C═O), 172.9 (C═O), 173.5 (COOH), 214.3 (C-12)
XVII	^{1}H NMR (400 MHz, CD_3OD), δ: 0.91 (t, 3H, J = 6.8 Hz, CH_3), 1.24–1.41 (m, 37H, 11 × CH_2, 5 × CH_3), 1.57–1.64 (m, 4H, 2 × CH_2), 3.77–3.79 (m, 1H, H-4), 3.90–3.95 (m, 5H, 2 × H-4″, 2 × H-5″, H-6), 4.51 (d, 1H, $J_{6,6}$ = 11.8 Hz, H-6), 5.15 (s, 2H, CH_2Ph), 7.31–7.42 (m, 5H, Ph) ^{13}C NMR (100 MHz, CD_3OD), δ: 14.5 (CH_3), 22.3 (CH_3), 23.7 (CH_2), 24.9 (2 × CH_2), 25.9 (CH_3), 27.3 (CH_2), 28.8 (3 × CH_3), 30.5 (2 × CH_2), 30.7 (CH_2), 30.8 (CH_2), 31.0 (CH_2), 31.3 (CH_2), 33.0 (CH_2), 38.1 (2 × CH_2), 63.4 (C-5), 65.9 (C-4″, C-5″), 66.2 (C-6), 68.0 (CH_2Ph), 73.8 (C-4), 80.7 (C_q), 101.5 (C-2), 113.0 (C-2″), 129.2 (CH_{Ph}), 129.5 (2 × CH_{Ph}), 129.6 (2 × CH_{Ph}), 137.2 (C_i), 157.1 (C=O), 171.8 (C═O)

Table 2. (continued)

Compound	Spectral data
XVIII	^{1}H NMR (400 MHz, $CDCl_3$), δ: 0.87 (t, 3H, J = 7.0 Hz, CH_3), 1.22–1.40 (m, 17H, 8 × CH_2 and 1H of CH_2), 1.50–1.59 (m, 5H, 2 × CH_2 and 1H of CH_2), 2.35–2.39 (m, 4H, 2 × CH_2), 3.08 (br s, 1H, OH), 3.67 (br s, 1H, OH), 3.95–4.07 (m, 3H, CH_2OH, H-3), 5.10 (br s, 2H, CH_2Ph), 5.17–5.25 (m, 2H, CH_2Ph), 5.89 (br s, 1H, NH), 7.31–7.36 (m, 10H, Ph) ^{13}C NMR (100 MHz, $CDCl_3$), δ: 14.0 (CH_3), 22.5 (CH_2), 23.8 (2 × CH_2), 25.9 (CH_2), 28.9 (CH_2), 29.1 (CH_2), 29.2 (4 × CH_2), 31.6 (CH_2), 42.7 (CH_2), 42.8 (CH_2), 64.2 (CH_2OH), 67.3 (CH_2Ph), 67.6 (CH_2Ph), 69.0 (C-2), 74.0 (C-3), 128.1 (CH_{Ph}), 128.2 (2 × CH_{Ph}), 128.3 (CH_{Ph}), 128.4 (CH_{Ph}), 128.6 (5 × CH_{Ph}), 135.3 (C_i), 135.9 (C_i), 157.0 (C═O), 170.9 (C═O), 211.8 (C-12)
XIX	^{1}H NMR (400 MHz, $CDCl_3$), δ: 0.88 (t, 3H, J = 6.9 Hz, CH_3), 1.00–1.61 (m, 22H, 11 × CH_2), 2.34–2.39 (m, 4H, 2 × CH_2), 3.32 (d, 1H, $J_{H,H}$ = 9.4 Hz, CH_2O), 3.67–3.75 (m, 1H, H-3), 3.93 (d, 1H, $J_{H,H}$ = 9.4 Hz, CH_2O), 4.18 (d, 1H, $J_{3,OH}$ =11.4 Hz, OH), 5.08–5.15 (m, 2H, CH_2Ph), 5.19 (d, 1H, $J_{H,H}$ = 12.2 Hz, CH_2Ph), 5.24 (d, 1H, $J_{H,H}$ = 12.2 Hz, CH_2Ph), 5.81 (br s, 1H, NH), 7.21–7.41 (m, 25H, Ph) ^{13}C NMR (100 MHz, $CDCl_3$), δ: 14.0 (CH_3), 23.5 (CH_2), 23.8 (2 × CH_2), 25.9 (CH_2), 28.9 (CH_2), 29.2 (CH_2), 29.3 (4 × CH_2), 31.6 (CH_2), 42.8 (2 × CH_2), 64.2 (CH_2O), 67.1 (CH_2Ph), 67.5 (CH_2Ph), 67.7 (C-2), 74.0 (C-3), 87.4 (CPh_3), 127.3 (3 × CH_{Ph}), 127.9 (2 × CH_{Ph}), 128.0 (6 × CH_{Ph}), 128.1 (CH_{Ph}), 128.3 (4 × CH_{Ph}), 128.4 (6 × CH_{Ph}), 128.5 (3 × CH_{Ph}), 135.4 (C_i), 136.2 (C_i), 142.9 (3 × C_i), 156.5 (C═O), 170.4 (C═O), 211.6 (C-12)
XX	^{1}H NMR (400 MHz, CD_3OD), δ: 0.88 (t, 3H, J = 6.9 Hz, CH_3), 0.95–1.35 (m, 16H, 8 × CH_2), 1.40–1.56 (m, 6H, 3 × CH_2), 2.37–2.43 (m, 4H, 2 × CH_2), 3.60 (d, 1H, $J_{H,H}$ = 9.7 Hz, CH_2O), 3.74 (d, 1H, $J_{H,H}$ = 9.7 Hz, CH_2O), 4.71–4.73 (m, 1H, H-3), 5.00–5.13 (m, 4H, 2 × CH_2Ph), 7.15–7.35 (m, 18H, Ph), 7.41–7.47 (m, 7H, Ph) ^{13}C NMR (100 MHz, CD_3OD), δ: 14.4 (CH_3), 23.6 (CH_2), 24.9 (CH_2), 25.0 (CH_2), 26.6 (CH_2), 30.0 (CH_2), 30.2 (CH_2), 30.3 (2 × CH_2), 30.4 (CH_2), 32.2 (CH_2), 32.8 (CH_2), 43.5 (2 × CH_2), 62.6 (CH_2O), 67.1 (C-2), 67.4 (CH_2Ph), 68.4 (CH_2Ph), 81.9 (C-3), 88.1 (CPh_3), 127.9 (3 × CH_{Ph}), 128.7 (6 × CH_{Ph}), 128.9 (CH_{Ph}), 129.3 (CH_{Ph}), 129.5 (6 × CH_{Ph}), 129.6 (CH_{Ph}), 130.2 (7 × CH_{Ph}), 136.9 (C_i), 138.3 (C_i), 145.3 (3 × C_i), 156.9 (C═O), 171.8 (C═O), 214.4 (C-12)
XXI	^{1}H NMR (400 MHz, CD_3OD), δ: 0.87 (t, 3H, J = 6.7 Hz, CH_3), 1.15–1.37 (m, 18H, 9 × CH_2), 1.46–1.57 (m, 4H, 2 × CH_2), 2.39–2.43 (m, 4H, 2 × CH_2), 3.35 (d, 1H, $J_{H,H}$ = 9.3 Hz, CH_2O), 3.76 (d, 1H, $J_{H,H}$ = 9.3 Hz, CH_2O), 4.71 (m, 1H, H-3), 7.21–7.35 (m, 9H, Ph), 7.43–7.51 (m, 6H, Ph) ^{13}C NMR (100 MHz, CD_3OD), δ: 14.4 (CH_3), 23.6 (CH_2), 24.9 (2 × CH_2), 27.0 (CH_2), 30.0 (CH_2), 30.3 (2 × CH_2), 30.4 (CH_2), 30.5 (CH_2), 32.0 (CH_2), 32.8 (CH_2), 43.5 (2 × CH_2), 64.0 (CH_2O), 68.7 (C-2), 81.2 (C-3), 89.0 (CPh_3), 128.4 (3 × CH_{Ph}), 129.0 (6 × CH_{Ph}), 130.2 (6 × CH_{Ph}), 144.5 (3 × C_i), 173.7 (COOH), 214.4 (C-12)
XXIII	^{1}H NMR (400 MHz, $CDCl_3$), δ: 0.87 (t, 3H, J = 6.9 Hz, CH_3), 1.28 (m, 20H, 10 × CH_2), 1.42 (s, 3H, CH_3), 1.44 (s, 3H, CH_3), 1.47–1.55 (m, 2H, CH_2), 1.57–1.61 (m, 4H, 2 × CH_2), 3.65–3.67 (m, 1H, H-6), 3.74 (d, 1H, $J_{10,10}$ = 11.8 Hz, H-10), 3.82 (d, 1H, $J_{4,4}$ = 9.3 Hz, H-4), 3.84 (d, 1H, $J_{10,10}$ = 11.8 Hz, H-10), 3.93 (s, 4H, 2 × H-4″, 2 × H-5″), 4.03 (d, 1H, $J_{4,4}$ = 9.3 Hz, H-4), 6.14 (br s, 1H, NH) ^{13}C NMR (100 MHz, $CDCl_3$), δ: 14.0 (CH_3), 18.6 (CH_3), 22.5 (CH_2), 23.7 (2 × CH_2), 25.3 (CH_2), 28.2 (CH_2), 28.8 (CH_3), 29.3 (CH_2), 29.4 (2 × CH_2), 29.5 (CH_2), 29.8 (CH_2), 31.8 (CH_2), 37.0 (2 × CH_2), 57.0 (C-5), 64.8 (C-4″, C-5″), 67.8 (C-4), 67.8 (C-10), 73.9 (C-6), 99.4 (C-8), 111.8 (C-2″), 158.1 (C-2)
XXIV	^{1}H NMR (400 MHz, $CDCl_3$), δ: 0.84 (t, 3H, J = 6.9 Hz, CH_3), 1.25 (m, 22H, 11 × CH_2), 1.28 (s, 3H, CH_3), 1.41 (s, 3H, CH_3), 1.54 (m, 13H, 3 × CH_3, 2 × CH_2), 3.45 (m, 1H, H-6), 3.49 (d, 1H, $J_{10,10}$ = 11.1 Hz, H-10), 3.78 (d, 1H, $J_{4,4}$ = 9.1 Hz, H-4), 3.90 (s, 4H, 2 × H-4″, 2 × H-5″), 4.26 (d, 1H, $J_{10,10}$ = 11.1 Hz, H-10), 4.35 (d, 1H, $J_{4,4}$ = 9.1 Hz, H-4) ^{13}C NMR (100 MHz, $CDCl_3$), δ: 14.0 (CH_3), 22.5 (CH_2), 22.9 (CH_3), 23.7 (2 × CH_2), 24.2 (CH_3), 26.2 (CH_2), 27.4 (CH_2), 28.0 (3 × CH_3), 29.3 (2 × CH_2), 29.4 (CH_2), 29.5 (CH_2), 29.8 (CH_2), 31.7 (CH_2), 37.0 (2 × CH_2), 61.9 (C-10), 64.8 (C-4″, C-5″), 65.3 (C-5), 69.7 (C-4), 72.9 (C-6), 84.4 (C_q), 101.6 (C-8), 111.7 (C-2″), 149.5 (C═O), 152.7 (C-2)
XXV	^{1}H NMR (400 MHz, $CDCl_3$), δ: 0.88 (t, 3H, J = 6.8 Hz, CH_3), 1.24–1.40 (m, 25H, 11 × CH_2, CH_3), 1.43 (s, 3H, CH_3), 1.46 (s, 9H, 3 × CH_3), 1.56–1.60 (m, 4H, 2 × CH_2), 3.43 (t, 1H, $J_{H,H}$ = 11.6 Hz, $J_{H,OH}$ = 11.6 Hz, CH_2OH), 3.64–3.68 (m, 1H, H-4), 3.77 (d, 1H, $J_{6,6}$ = 12.3 Hz, H-6), 3.93 (s, 4H, 2 × H-4″, 2 × H-5″), 3.94–3.97 (m, 1H, CH_2OH), 4.00 (d, 1H, $J_{6,6}$ = 12.3 Hz, H-6), 4.81 (m, 1H, OH), 5.37 (br s, 1H, NH) ^{13}C NMR (100 MHz, $CDCl_3$), δ: 14.1 (CH_3), 18.5 (CH_3), 22.5 (CH_2), 23.8 (2 × CH_2), 25.4 (CH_2), 28.3 (3 × CH_3), 28.6 (CH_3), 29.3 (2 × CH_2), 29.4 (CH_2), 29.5 (2 × CH_2), 29.8 (CH_2), 31.8 (CH_2), 37.1 (2 × CH_2), 55.6 (C-5), 64.8 (C-4″, C-5″, CH_2OH), 64.9 (C-6), 74.6 (C-4), 80.2 (C_q), 98.8 (C-2), 111.8 (C-2″), 157.2 (C═O)
XXVI	^{1}H NMR (400 MHz, $CDCl_3$), δ: 0.88 (t, 3H, J = 6.9 Hz, CH_3), 1.24–1.37 (m, 22H, 11 × CH_2), 1.43 (s, 3H, CH_3), 1.45 (s, 3H, CH_3), 1.47 (s, 9H, 3 × CH_3), 1.56–1.63 (m, 4H, 2 × CH_2), 3.94 (m, 4H, 2 × H-4″, 2 × H-5″), 4.12 (m, 1H, H-4), 4.21 (br s, 2H, 2 × H-6), 5.27 (br s, 1H, NH) ^{13}C NMR (100 MHz, $CDCl_3$), δ: 14.1 (CH_3), 18.6 (CH_3), 22.6 (CH_2), 23.6 (CH_2), 23.7 (CH_2), 25.4 (CH_2), 28.2 (3 × CH_3), 28.9 (CH_2), 29.1 (CH_3), 29.3 (CH_2), 29.5 (2 × CH_2), 29.6 (2 × CH_2), 31.8 (CH_2), 37.0 (CH_2), 37.1 (CH_2), 60.0 (C-5), 63.8 (C-6), 64.8 (C-4″, C-5″), 73.1 (C-4), 81.0 (C_q), 99.3 (C-2), 112.0 (C-2″), 156.5 (C═O), 172.2 (COOH)

Table 2. (continued)

Compound	Spectral data
XXVII	^{1}H NMR (400 MHz, CD_3OD), δ: 0.83 (t, 3H, J = 6.9 Hz, CH_3), 1.22 (m, 18H, 9 × CH_2), 1.42–1.52 (m, 4H, 2 × CH_2), 1.91 (s, 3H, CH_3CO), 1.92 (s, 3H, CH_3CO), 1.99 (s, 3H, CH_3CO), 2.37 (t, 4H, J = 7.3 Hz, 2 × CH_2), 4.51 (d, 1H, $J_{H,H}$ = 10.7 Hz, CH_2O), 4.65 (d, 1H, $J_{H,H}$ = 10.7 Hz, CH_2O), 5.45–5.50 (m, 1H, H-3) ^{13}C NMR (100 MHz, CD_3OD), δ: 14.4 (CH_3), 20.7 (CH_3CO), 21.0 (CH_3CO), 23.3 (CH_3CO), 23.6 (CH_2), 24.9 (2 × CH_2), 27.0 (CH_2), 30.0 (CH_2), 30.3 (2 × CH_2), 30.4 (2 × CH_2), 31.0 (CH_2), 32.8 (CH_2), 43.5 (2 × CH_2), 64.6 (CH_2O), 65.2 (C-2), 75.0 (C-3), 172.1 (C═O), 172.6 (C═O), 172.9 (C═O), 173.2 (COOH), 214.4 (C-12)
XXVIII	^{1}H NMR (400 MHz, $CDCl_3$), δ: 0.88 (t, 3H, J = 6.8 Hz, CH_3), 1.27 (m, 17H, 8 × CH_2 and 1H of CH_2), 1.50–1.60 (m, 5H, 2 × CH_2 and 1H of CH_2), 2.39 (t, 4H, J = 7.4 Hz, 2 × CH_2), 3.62–3.72 (m, 3H, CH_2OH, H-1′), 3.99 (br s, 1H, OH), 4.22 (d, 1H, $J_{5,5}$ = 8.7 Hz, H-5), 4.31 (d, 1H, $J_{5,5}$ = 8.7 Hz, H-5), 4.39 (br s, 1H, OH), 6.93 (br s, 1H, NH) ^{13}C NMR (100 MHz, $CDCl_3$), δ: 14.0 (CH_3), 22.5 (CH_2), 23.8 (2 × CH_2), 26.0 (CH_2), 28.9 (CH_2), 29.2 (CH_2), 29.3 (2 × CH_2), 29.4 (CH_2), 30.6 (CH_2), 31.6 (CH_2), 42.7 (CH_2), 42.8 (CH_2), 64.2 (CH_2OH), 65.9 (C-4), 68.8 (C-5), 72.4 (C-1′), 161.0 (C-2), 212.1 (C-10′)
XXIX	^{1}H NMR (400 MHz, $CDCl_3$), δ: 0.88 (t, 3H, J = 6.9 Hz, CH_3), 1.13–1.32 (m, 17H, 8 × CH_2 and 1H of CH_2), 1.51–1.58 (m, 5H, 2 × CH_2 and 1H of CH_2), 2.38 (t, 4H, J = 7.3 Hz, 2 × CH_2), 2.47 (br s, 1H, OH), 3.22 (d, 1H, $J_{H,H}$ = 9.5 Hz, CH_2O), 3.39 (d, 1H, $J_{H,H}$ = 9.5 Hz, CH_2O), 3.74–3.79 (m, 1H, H-1′), 4.00 (d, 1H, $J_{5,5}$ = 8.9 Hz, H-5), 4.28 (d, 1H, $J_{5,5}$ = 8.9 Hz, H-5), 5.83 (br s, 1H, NH), 7.22–7.33 (m, 9H, Ph), 7.38–7.42 (m, 6H, Ph) ^{13}C NMR (100 MHz, $CDCl_3$), δ: 14.0 (CH_3), 22.5 (CH_2), 23.8 (2 × CH_2), 26.0 (CH_2), 28.9 (CH_2), 29.1 (CH_2), 29.3 (2 × CH_2), 29.7 (CH_2), 30.2 (CH_2), 31.6 (CH_2), 42.7 (CH_2), 42.8 (CH_2), 64.0 (C-4), 65.5 (CH_2O), 69.1 (C-5), 72.8 (C-1′), 87.2 (CPh_3), 127.4 (3 × CH_{Ph}), 128.1 (6 × CH_{Ph}), 128.5 (6 × CH_{Ph}), 142.9 (3 × C_i), 159.4 (C-2), 211.8 (C-10′)
XXX	^{1}H NMR (400 MHz, $CDCl_3$), δ: 0.86 (t, 3H, J = 7.0 Hz, CH_3), 1.15–1.22 (m, 8H, 4 × CH_2), 1.23–1.40 (m, 9H, 4 × CH_2 and 1H of CH_2), 1.41–1.58 (m, 5H, 2 × CH_2 and 1H of CH_2), 2.32–2.38 (m, 4H, 2 × CH_2), 3.21 (d, 1H, $J_{H,H}$ = 9.5 Hz, CH_2O), 3.41 (d, 1H, $J_{H,H}$ = 9.5 Hz, CH_2O), 3.99 (d, 1H, $J_{5',5'}$ = 8.9 Hz, H-5′), 4.36 (d, 1H, $J_{5',5'}$ = 8.9 Hz, H-5′), 5.55 (d, 1H, $J_{2,1}$ = 10.4 Hz, $J_{2,1}$ = 2.2 Hz, H-1), 6.41 (br s, 1H, NH), 7.20–7.29 (m, 9H, Ph), 7.39–7.47 (m, 8H, Ph), 7.55–7.60 (m, 1H, Ph), 7.94–7.98 (m, 2H, Ph) ^{13}C NMR (100 MHz, $CDCl_3$), δ: 14.0 (CH_3), 22.4 (CH_2), 23.7 (CH_2), 23.8 (CH_2), 25.7 (CH_2), 28.9 (2 × CH_2), 29.1 (2 × CH_2), 29.2 (2 × CH_2), 31.6 (CH_2), 42.7 (CH_2), 42.8 (CH_2), 63.7 (C-4′), 65.2 (CH_2O), 68.8 (C-5′), 74.0 (C-1), 87.2 (CPh_3), 127.3 (3 × CH_{Ph}), 128.0 (6 × CH_{Ph}), 128.3 (C_i), 128.5 (8 × CH_{Ph}), 129.7 (2 × CH_{Ph}), 133.3 (CH_{Ph}), 142.8 (3 × C_i), 159.1 (C-2′), 166.1 (C═O), 211.7 (C-10)
XXXI	^{1}H NMR (400 MHz, $CDCl_3$), δ: 0.87 (t, 3H, J = 6.8 Hz, CH_3), 1.19–1.39 (m, 16H, 8 × CH_2), 1.48–1.57 (m, 4H, 2 × CH_2), 1.63–1.75 (m, 2H, CH_2), 2.36 (m, 4H, 2 × CH_2), 3.34 (br s, 1H, OH), 3.64 (d, 1H, $J_{H,H}$ = 11.9 Hz, CH_2OH), 3.68 (d, 1H, $J_{H,H}$ = 11.9 Hz, CH_2OH), 4.32 (d, 1H, $J_{5',5'}$ = 9.0 Hz, H-5′), 4.39 (d, 1H, $J_{5',5'}$ = 9.0 Hz, H-5′), 5.38 (d, 1H, $J_{2,1}$ = 9.9 Hz, $J_{2,1}$ = 3.1 Hz, H-1), 6.30 (br s, 1H, NH), 7.44–7.47 (m, 2H, Ph), 7.58–7.62 (m, 1H, Ph), 8.03–8.05 (m, 2H, Ph) ^{13}C NMR (100 MHz, $CDCl_3$), δ: 14.0 (CH_3), 22.5 (CH_2), 23.7 (CH_2), 23.8 (CH_2), 25.6 (CH_2), 28.7 (CH_2), 28.9 (CH_2), 29.1 (3 × CH_2), 29.2 (CH_2), 31.6 (CH_2), 42.7 (CH_2), 42.8 (CH_2), 64.4 (C-4′), 64.4 (CH_2OH), 68.9 (C-5′), 74.2 (C-1), 128.6 (2 × CH_{Ph}), 129.0 (C_i), 129.8 (2 × CH_{Ph}), 133.7 (CH_{Ph}), 159.5 (C-2′), 166.8 (C=O), 211.8 (C-10)
XXXII	^{1}hH NMR (400 MHz, CD_3OD), δ: 0.87 (t, 3H, J = 7.0 Hz, CH_3), 1.18–1.37 (m, 16H, 8 × CH_2), 1.44–1.54 (m, 4H, 2 × CH_2), 1.65–1.72 (m, 2H, CH_2), 2.35–2.40 (m, 4H, 2 × CH_2), 4.53 (d, 1H, $J_{5,5}$ = 9.2 Hz, H-5), 4.69 (d, 1H, $J_{5,5}$ = 9.2 Hz, H-5), 5.57–5.60 (m, 1H, H-1′), 7.44–7.48 (m, 2H, Ph), 7.57–7.61 (m, 1H, Ph), 8.03–8.05 (m, 2H, Ph) ^{13}C NMR (100 MHz, CD_3OD), δ: 14.0 (CH_3), 23.6 (CH_2), 24.9 (2 × CH_2), 26.9 (CH_2), 30.0 (CH_2), 30.2 (2 × CH_2), 30.3 (3 × CH_2), 32.8 (CH_2), 43.5 (2 × CH_2), 69.2 (C-4), 69.8 (C-5), 76.6 (C-1′), 129.7 (2 × CH_{Ph}), 130.9 (2 × CH_{Ph}), 131.0 (C_i), 134.5 (CH_{Ph}), 161.0 (C-2), 167.4 (C═O), 175.1 (COOH), 214.3 (C-10′)

product *XXVI* in the quantitative yield (Fig. 5). Using the same reaction sequence as for the preparation of *XVI*, compound *XXVI* was then transformed into the triacetyl derivative *XXVII* (Fig. 5).

Having established the synthetic pathway to *XXVII*, the next step was to utilise the common intermediate *XXIII* (Fig. 5) for the construction of (2*S*,3*R*)-configured amino acid *XVI* (prepared from diastereomeric *XI*, see Fig. 3). In this context, it was necessary to modify the quaternary stereogenic centre in *XXIII* so that the hydroxymethyl moiety of the 1,3-*O*-isopropylidene ring in *XXIII* ultimately formed the carboxylic acid group of *XVI* and the masked primary alcohol in the oxazolidinone fragment became the hydroxymethyl side chain. Thus, removal of the acid-labile protecting groups in *XXIII* ($AcOH/H_2O$, Fig. 6) provided diol *XXVIII* (92 %). The primary hydroxyl group in *XXVIII* was selectively protected as triphenylmethyl ether *XXIX* with a yield of 91 % using TrCl and DMAP in dry pyridine. The reaction of *XXIX* with BzCl in pyridine in the presence of a catalytic amount of DMAP resulted in the formation of benzoate ester *XXX* (96 %, Fig. 6). Its detritylation was achieved under mild conditions (*p*-TsOH, CH_3OH/CH_2Cl_2), and the alcohol *XXXI* thus obtained (81 %, Fig. 6) was oxidised using a two-step protocol to afford the corresponding acid *XXXII* with a yield of 94 %. The final saponification with 10

mass % aqueous NaOH in CH_3OH followed by acetylation (Ac_2O, pyridine) produced the corresponding triacetyl derivative of *II* with a yield of 77 %.

Conclusions

In summary, the following total syntheses were achieved: *XXI* (12 steps with 32 % overall yield from *VI*), *XVI* (8 steps with 49 % overall yield from *VI* or in 9 steps with 25 % overall yield from *VII*) and *XXVII* (8 steps with 27 % overall yield from *VII*), as the protected forms of the naturally occurring sulfamisterin *I* and its unnatural analogues *II* and *V*, respectively. The coupling of two polar fragments *VIII* and *IX* with the aliphatic tail substrate *X* was achieved by a Wittig olefination to establish the complete carbon framework of the above target compounds. It is worth noting that these syntheses effectively utilised all of the functional groups of the starting oxazolidinones *VI* and *VII*.

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