SYNTHESIS OF SOLAMIN

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Abstract —Total synthesis of an annonaceous acetogenin, solamin (**1**) is described. Direct coupling between γ-lactone (**13**) and mono-THF unit (**12**) prepared from D-glutamic acid in 16 steps gave the product (**14**) in excellent yield, which was converted to the title compound (**1**) in sequential 3 steps.

INTRODUCTION

More than 280 annonaceous acetogenins have been isolated[1] since the isolation of Uvaricin[2] in 1982. These compounds have strong and wide spectra of biological activities *i.e.* cytotoxic, antitumoral, antimalarial, immunosupressive, pesticidal, or antifeedant.[3] The skeleton of these polyketide derivatives is similar and one synthetic route has wide utility. Here we report a total synthesis of solamin,[4] a basic mono-THF acetogenin, *via* a new and potentially applicable route. Our synthetic plan is based on direct alkylation of activated γ-lactone (**A**) with long chain halogen group (**B**) with proper functionality including furan as shown in **Figure 1**. Described below is our synthetic scheme in detail.

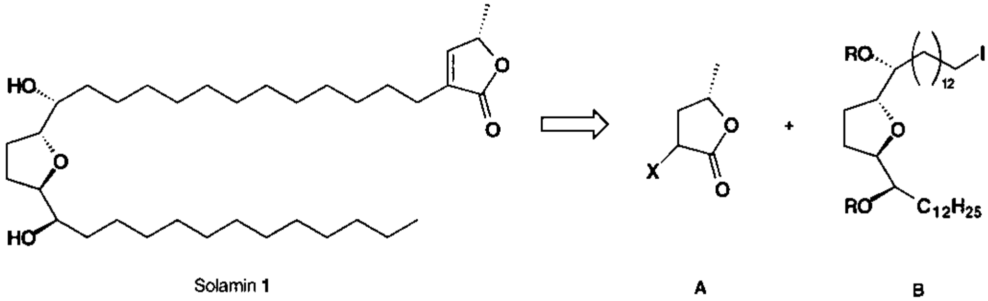
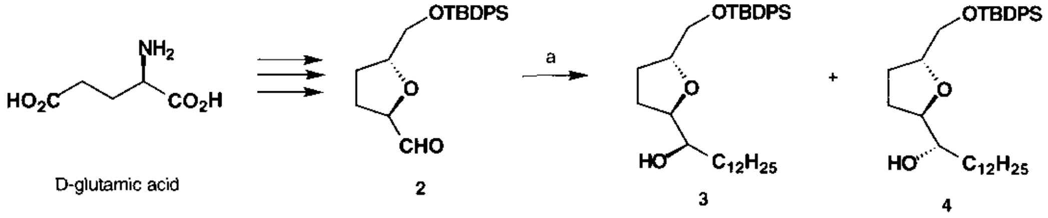


Figure 1.

RESULTS AND DISCUSSION

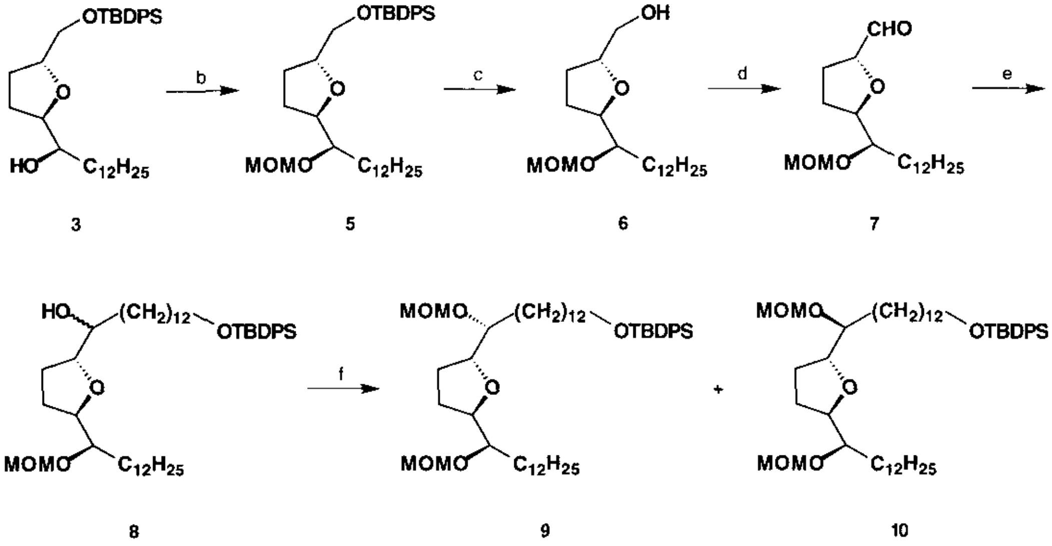
The aldehyde (**2**) was prepared from D-glutamic acid in 8 steps (12%) as reported.[5] The chelation controlled Grignard reaction[6] of **2** with *n*-dodecylmagnesium bromide in the presense of catalytic amount of cuprous bromide dimethy sulfide complex gave alkylated products (**3**) (65%) and (**4**) (9%) (**Scheme 1**).

Both diastereomers were separated by gravity column chromatography, and the absolute configulations of the compounds were determined by ^{1}H-NMR analysis of their MTPA ester.[7] The $\Delta\delta_H$ (δ_S-δ_R) values of major product showed positive values on the chain side and negative values on the THF-ring side and that of minor product showed negative values on the chain side and positive values on the THF-ring side.[8] These data indicate that at C-1' major product has *R* configulation and minor product has *S* configulation.



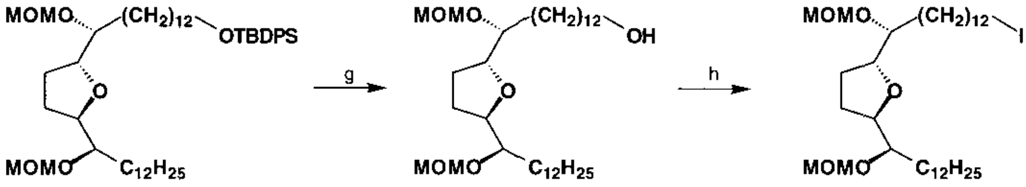
Scheme 1. a) $C_{12}H_{25}MgBr$, $CuBr{\cdot}SMe_2$, Et_2O, **3** 65%, **4** 9%.,

Protection of the hydroxy group of **3** using methoxymethyl chloride and diisopropylethylamine gave **5** (99%). The bis-ether (**5**) was treated with tetrabutylammonium fluoride to afford **6** (97%). The primary alcohol (**6**) was oxidized with Dess-Martin periodinane to give aldehyde (**7**) (93%). The Grignard reaction of the aldehyde (**7**) with ω-*tert*-butyldiphenylsilyloxydodecylmagnesium bromide gave an unseparable mixture of products. This was treated with excess amount of methoxymethyl chloride and diisopropylethylamine to give **9** (48%) and **10** (12%) after purification by silica gel column chromatography (**Scheme 2**).



Scheme 2. b) MOMCl, DIPEA, CH_2Cl_2, 99%. c) TBAF, THF, 97%. d) Dess-Martin periodinane, CH_2Cl_2, 93%. e) $BrMg(CH_2)_{12}OTBDPS$, $CuBr{\cdot}SMe_2$, Et_2O. f) MOMCl, DIPEA, **9** 48%, **10** 12%.

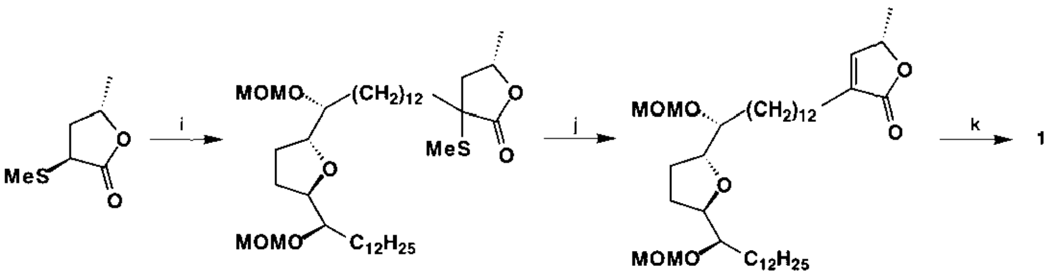
Deprotection of **9** by treating with tetrabutylammonium fluoride gave alcohol (**11**) (92%). The primary hydroxy group was converted to iodide by treating with triphenylphosphine, imidazole and iodine to finish the construction of mono-THF unit (**12**) (**Scheme 3**).



9 **11** **12**

Scheme 3. g) TBAF, THF, 92%. h) TPP, imid., I_2, Et_2O-CH_3CN, 98%.

Sodium enolate of **13**[9] was treated with **12** in HMPA to give **14** in high yield (86%). The sulfide (**14**) was oxidized with *m*-chloroperbenzoic acid to sulfoxide, followed by thermal elimination in refluxing toluene in the presence of calcium carbonate to afford unsaturated lactone (**15**) (97%). Finally , removal of methoxymethyl groups by treating with boron trifluoride diethy ether complex in dimethyl sulfide yielded solamin (**1**) as white solid, which was recrystallized from hexane to give pure **1** (**Scheme 4**). The data of our synthetic **1** are identical to those of authentic sample.[4]



trans **- 13** **14** **15**

Scheme 4. i) NaHMDS, THF, then **12**, HMPA, 86%. j) I; *m*-CPBA, CH_2Cl_2. II; tol., $CaCO_3$, Δ, 97%. k) BF_3-Et_2O, SMe_2, 90%

In conclusion, we completed the synthesis of solamin (**1**), one of the typical annonaceous acetogenins in overall 2.3% yield through 19 steps from D-glutamic acid *via* direct coupling of long chain iodide with γ-lactone (**13**). This procedure must be applicable to other acetogenins as a general and efficient method, and these works are now in progress in our laboratory.

ACKNOWLEDGEMENT

We thank Ajinomoto Co., Ltd. generous gift of D-glutamic acid, and Professors Takayuki Oritani and Akira Tanaka for the spectra of solamin. This work was partly supported by the Grant in Aid for Scientific Reserch from the Ministry of Education, Science, Culture and Sports.

EXPERIMENTAL SECTION

IR spectra: Jasco FT / IR 230 spectrometer. ^{1}H-NMR spectra: Bruker AC-300 spectrometer (300 MHz) . Specific rotations: Jasco DIP-371 polarimeter. Refractive indeces: Atago 1T refractometer. Column chromatography: Merck Kieselgel 60 (Art. Nr. 7734). Melting points: Yanako micro-melting point apparatus. Melting points are uncorrected.

(2*R*,5*R*,1'*R*)-5-[(*tert*-Butyldiphenylsilyloxy)methyl]-2-(1'-hydroxytridecyl)tetrahydrofuran (**3**) and
(2*R*,5*R*,1'*S*)-5-[(*tert*-Butyldiphenylsilyloxy)methyl]-2-(1'-hydroxytridecyl)tetrahydrofuran (**4**)

A solution of 25.3 g (102 mmol) of 1-bromododecane in ether (90 mL) was added dropwise to 4.50 g (185 mmol) of magnesium turnings covered with 18 mL of ether after dibromoethane-initiation and the reaction mixture was stirred for 1 h at rt. To this was added 85 mL of ether and 2.32 g (11.3 mmol) of CuBr·SMe$_2$ at -50 °C. After 10 min, the reaction mixture was warmed to -30 °C for 30 min and then cooled down to -50 °C again. To this was added dropwise a solution of 6.80 g (18.4 mmol) of aldehyde (**2**) in 40 mL of ether and the mixture was allowed to warm to rt overnight. The reaction mixture was poured into saturated aqueous NH$_4$Cl solution and was extracted three times with ether. The combined organic layers were washed with brine dried with MgSO$_4$ and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (Hexane / Ether = 6 / 1) to afford 3.03 g (65%) of **3** and 893 mg (9%) of **4** as colorless oil. **3** IR (film): ν = 3467, 2926, 2855, 1464, 1428, 1114, 740, 702 cm^{-1}; ^{1}H-NMR (300 MHz in CDCl$_3$): δ = 0.88 (3H, t, *J* = 6.7 Hz, 13'-H), 1.05 (9H, s, -C(CH_3)$_3$), 1.16-1.48 (22H, m, 2'- to 12'-H), 1.61-2.17 (4H, m, 3- and 4-H), 3.34-3.40 (1H, m, 1'-H), 3.66 (2H, d, *J* = 4.7 Hz, -CH_2OTBDPS), 3.78-3.85 (1H, m, 2-H), 4.07-4.15 (1H, m, 5-H), 7.33-7.45 and 7.61-7.71 (10H, m, -*Ph*); Anal. Calcd for $C_{34}H_{54}O_3$ Si: C, 75.78; H, 10.10. Found: C, 75.97; H, 10.05; $[\alpha]_D^{22}$ +3.4° (*c* 0.52 in CHCl$_3$); $n_D^{19.5}$ 1.5169.
4 IR (film): ν = 3458, 2927, 2855, 1464, 1428, 1113, 740, 702 cm^{-1}; ^{1}H-NMR (300 MHz in CDCl$_3$): δ = 0.88 (3H, t, *J* = 6.7 Hz, 13'-H), 1.05 (9H, s, -C(CH_3)$_3$), 1.14-1.43 (22H, m, 2'- to 12'-H), 1.71-2.07 (4H, m, 3- and 4-H), 3.65 (2H, d, *J* = 4.7 Hz, -CH_2OTBDPS), 3.72-3.82 (1H, m, 1'-H), 3.82-3. 91 (1H, m, 2-H), 4.08-4.20 (1H, m, 5-H), 7.35-7.42 and 7.66-7.71 (10H, m, -*Ph*); Anal. Calcd for $C_{34}H_{54}O_3$ Si: C, 75.78; H, 10.10. Found: C, 75.37; H, 10.10; $[\alpha]_D^{25}$ +0.36° (*c* 1.06 in CHCl$_3$); $n_D^{19.7}$ 1.5171.

(1'*R*,2*R*,5*R*)-5-[(*tert*-Butyldiphenylsilyloxy)methyl]-2-[(1'-methoxymethoxy)tridecyl]tetrahydrofuran (**5**)
MOMCl (2.20 mL, 29.0 mmol) was added to a solution of alcohol (**3**) (6.38 g, 11.8 mmol) and DIPEA (9.9 mL, 56.8 mmol) in CH$_2$Cl$_2$ (25 mL) at 0 °C, and the mixture was stirred overnight at rt. The reaction mixture was quenched with saturated aqueous NH$_4$Cl solution, extracted with ether. The extract was washed with water and brine, dried with Na$_2$SO$_4$ and concentrated *in vacuo*. The residue was purified by silica gel column chlomatography (Hexane / Ether = 20 / 1 - 8 / 1) to afford 6.85 g (99%) of **5** as colorless oil. IR (film): ν = 2926, 2855, 1465, 1428, 1113, 1039, 919, 823, 741, 703, 613 cm^{-1}; ^{1}H-NMR (300 MHz in CDCl$_3$): δ = 0.88 (3H, t, *J* = 6.7 Hz, 13'-H), 1.04 (9H, s, -C(CH_3)$_3$), 1.18-1.51 (22H, m, 2'- to 12'-H), 1.60-2.01 (4H, m, 3- and 4-H), 3.40 (3H, s, -OCH$_2$OCH_3), 3.45-3.50 (1H, m, 1'-H),

3.65 (2H, d, J = 4.7 Hz, -CH_2OTBDPS), 3.98-4.05 (1H, m, 2-H), 4.09-4.17 (1H, m, 5-H), 4.69 and 4.84 (2H, d, J = 6.8 Hz, -OCH_2OCH_3), 7.34-7.44 and 7.67-7.71 (10H, m, -*Ph*); Anal. Calcd for $C_{36}H_{58}O_4$ Si: C, 74.18; H, 10.03. Found: C, 74.01; H, 10.05; $[\alpha]_D^{21}$ +17.6° (*c* 1.11 in $CHCl_3$); $n_D^{18.8}$ 1.5109.

(1'*R*,2*R*,5*R*)-5-(Hydroxymethyl)-2-[(1'-methoxymethoxy)tridecyl]tetrahydrofuran (**6**)

A solution of **5** (6.54 g, 11.2 mmol) in THF (100 mL) was treated with Bu_4NF (4.36 g, 16.7 mmol). After stirring the mixture for 1 h, saturated aqueous NH_4Cl solution and water were added. The reaction mixture was extracted three times with ether. The combined organic layers were washed with brine, dried with $MgSO_4$ and concentrated *in vacuo*. After silica gel column chromatography (Hexane / AcOEt = 6 / 1 - 2 / 1) 3.77 g (97%) of **6** was obtained as colorless oil. IR (film): ν = 3457, 2925, 2854, 1466, 1149, 1041, 919 cm^{-1}; ^{1}H-NMR (300 MHz in $CDCl_3$): δ = 0.88 (3H, t, J = 6.7 Hz, 13'-H), 1.16-1.40 (22H, m, 2'- to 12'-H), 1.58-1.80 and 1.83-2.08 (4H, m, 3- and 4-H), 3.40 (3H, s, -OCH_2OC*H_3*), 3.40-3.56 (1H, m, 1'-H), 3.47 and 3.66 (2H, dd, J = 3.0 and 11.6 Hz, -CH_2OH), 3.92-4.06 (1H, m, 2-H), 4.06-4.17 (1H, m, 5-H), 4.70 and 4.80 (2H, d, J = 6.8 Hz, -OCH_2OCH_3); Anal. Calcd for $C_{20}H_{40}O_4$ Si: C, 69.72; H, 11.70. Found: C, 69.77; H, 11.67; $[\alpha]_D^{25}$ +17.9° (*c* 1.21 in $CHCl_3$); $n_D^{19.7}$ 1.4612.

(1'*R*,2*R*,5*R*)-(1'-Methoxymethoxytridecyl)tetrahydrofuran-2-carbaldehyde (**7**).

To alcohol (**6**) (500 mg, 1.28 mmol) in CH_2Cl_2 (9 mL) was added Dess-Martin periodinane (740 mg, 1.75 mmol). After 90 min, the solution was poured into 10% aqueous $Na_2S_2O_3$ solution, the aqueous layer was extracted with ether, and the organic layer was washed with satd. aqueous $NaHCO_3$ and brine, dried with $MgSO_4$ and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (Hexane / Ether = 4 / 1) to afford 464 mg (93 %) of **7** as colorless oil. IR (film): ν = 2924, 2850, 1736, 1466, 1150, 1040, 919 cm^{-1}; ^{1}H-NMR (300 MHz in $CDCl_3$): δ = 0.88 (3H, t, J = 6.7 Hz, 13'-H), 1.18-1.50 (22H, m, 2' to 12'H), 1.70-2.24 (4H, m, 3- and 4-H), 3.40 (3H, s, -OCH_2OC*H_3*), 3.50-3.56 (1H, m, 1'-H), 4.09-4.16 (1H, m, 5-H), 4.31-4.37 (1H, m, 2-H), 4.70 and 4.80 (2H, d, J = 6.8 Hz, -OCH_2OCH_3), 9.67 (1H, d, J = 1.8 Hz, -C*H*O); Anal. Calcd for $C_{20}H_{40}O_4$ Si: C, 69.72; H, 11.70. Found: C, 69.77; H, 11.67; $[\alpha]_D^{25}$ +17.9° (*c* 1.21 in $CHCl_3$); $n_D^{19.7}$ 1.4612.

(2*R*, 5*R*, 13'*R*, 1"*R*)-2-(1'-*tert*-Butyldiphenylsilyloxy-13'-methoxymethoxytridecyl)-5-(1"-methoxymethoxytridecyl)tetrahydrofuran (**9**) and (2*R*, 5*R*, 13'*S*, 1"*R*)-2-(1'-*tert*-butyldiphenylsilyloxy-13'-methoxymethoxytridecyl) -5-(1"-methoxymethoxytridecyl)tetrahydrofuran (**10**)

A solution of 6.80 g (13.5 mmol) of 1-bromo-12-*tert*-butyldiphenylsilyloxydodecane in ether (25 mL) was added dropwise to 656 mg (27 mmol) of magnesium turnings covered with 3 mL of ether after dibromoethane-initiation and the reaction mixture was stirred for 1 h at rt. To this were added 11 mL of ether and 307 mg (1.49 mmol) of CuBr·SMe_2 at -50 °C. After 10 min, the reaction mixture was warmed to -30 °C for 30 min and then cooled down to -50 °C again. To this was added dropwise a solution of 463 mg (1.35 mmol) of aldehyde (**7**) in 3 mL of ether and the mixture was allowed to warm to rt overnight. The reaction mixture was poured into saturated aqueous NH_4Cl solution and was extracted three times with ether. The combined organic layers were washed with brine, dried with $MgSO_4$ and concentrated *in vacuo*. To a solution of this crude mixture and DIPEA (9.9 mL, 56.8 mmol) in CH_2Cl_2

(25 mL) was added MOMCl (2.20 mL, 29.0 mmol) at 0 °C and the mixture was stirred overnight at rt. The reaction mixture was quenched with saturated aqueous NH_4Cl solution, extracted with ether. The extract was washed with water and brine, dried with Na_2SO_4 and concentrated *in vacuo.* The residue was purified by silica gel column chlomatography (Hexane / AcOEt = 10 / 1 - 6 / 1) to afford 529 mg (48%) of **9** and 127 mg (12%) of **10** as colorless oil. **9** IR (film): ν = 2925, 2854, 1465, 1149, 1105, 1038, 919, 823, 740 cm^{-1}; ^{1}H-NMR (300Mhz in $CDCl_3$); δ = 0.88 (3H, t, J = 6.7Hz, 13”-H), 1.04 (9H, s, $-C(CH_3)_3$), 1.15-1.55 (46H, m, 2’- to 12’- and 2”- to 12”-H), 1.55-1.73 and 1.86-2.15 (4H, m, 3- and 4-H), 3.39 (6H, s, $-OCH_2OCH_3$), 3.38-3.50 (2H, m, 13’- and 13”-H), 3.64 (2H, t, J = 6.5 Hz, 1”-H), 3.90-4.03 (2H, m, 2- and 5-H), 4.67 and 4.84 (4H, d, J = 6.8 Hz, $-OCH_2OCH_3$), 7.30-7.49 and 7.58-7.78 (10H, m, *-Ph*); Anal. Calcd for $C_{50}H_{86}O_6Si$: C, 74.02; H, 10.68. Found: C, 73.92; H, 10.78; $[\alpha]_D^{27}$ +30.2° (*c* 0.60 in $CHCl_3$); $n_D^{19.3}$ 1.4952. **10** IR (film): ν = 2925, 2854, 1465, 1149, 1105, 1039, 920, 823, 740 cm^{-1}; ^{1}H-NMR (300 MHz in $CDCl_3$): δ = 0.88 (3H, t, J = 6.7 Hz, 13”-H), 1.04 (9H, s, $-C(CH_3)_3$), 1.15-1.55 (46H, m, 2’- to 12’- and 2”- to 12”-H), 1.55-1.73 and 1.86-2.15 (4H, m, 3- and 4-H), 3.39 (3H and 3H, s, $-OCH_2OCH_3$), 3.40-3.52 (1H, m, 1”-H), 3.65 (2H, t, J = 6.5 Hz, 1’-H), 3.61-3.70 (1H, m, 13’-H), 3.90-4.01 (2H, m, 2- and 5-H), 4.65, 4.67, 4.78 and 4.83 (4H, d, J = 6.8 Hz, $-OCH_2OCH_3$), 7.32-7.46 and 7.62-7.70 (10H, m, *-Ph*); Anal. Calcd for $C_{50}H_{86}O_6Si$: C, 74.02; H, 10.68. Found: C, 73.92; H, 10.78; $[\alpha]_D^{20}$ +9.2° (*c* 0.50 in $CHCl_3$); $n_D^{19.6}$ 1.4971.

(2*R*,5*R*,1’*R*,1”*R*)-2-(13’-Hydroxy-1’-methoxymethyloxytridecyl)-5-(1”-methoxymethyloxytridecyl)-tetrahydrofuran (**11**)

A solution of **9** (523 mg, 0.645 mmol) in THF (7.8 mL) was treated with Bu_4NF (337 mg, 1.29 mmol). After stirring the mixture for 8 h, saturated aqueous NH_4Cl solution and water were added. The reaction mixture was extracted three times with ether. The combined organic layers were washed with brine, dried with $MgSO_4$ and concentrated *in vacuo.* After silica gel column chromatography (Hexane / AcOEt = 10 / 1 - 4 / 1) 341 mg (92%) of **11** was obtained as white wax. **11** IR (film): ν = 3519, 2920, 2851, 1469, 1150, 1032, 921 cm^{-1}; ^{1}H-NMR (300 MHz in $CDCl_3$): δ = 0.88 (3H, t, J = 6.7 Hz, 13”-H), 1.13-1.98 (46H, m, 2’- to 12’-, 2”- to 12”-, 3- and 4-H), 3.39 (6H, s, $-OCH_2OCH_3$), 3.42-3.50 and 3.92-4.02 (4H, m, 1”-, 2-, 5- and 13’-H), 3.64 (2H, t, J = 6.6 Hz, 13’-H), 4.66 and 4.83 (4H, d, J = 6.8 Hz, $-OCH_2OCH_3$); Anal. Calcd for $C_{34}H_{68}O_6$: C, 71.28; H, 11.96. Found: C, 70.86; H, 11.86; $[\alpha]_D^{22}$ +44.5° (*c* 1.00 in $CHCl_3$); mp 33-34 °C.

(2*R*,5*R*,13’*R*,1”*R*)-2-(1’-Iodo-13’-methoxymethoxytridecyl)-5-(1”-methoxymethoxytridecyl)-tetrahydrofuran (**12**)

To a solution of **11** (327 mg, 0.57 mmol) in 2:3 CH_3CN-Et_2O (5.5 mL) were added imidazole (85.5 mg, 1.27 mmol), PPh_3 (299 mg, 1.14 mmol), and I_2 (348 mg, 1.37 mmol) at –15 °C. After being stirred for 10 min, the reaction mixture was poured into 10% aqueous $Na_2S_2O_3$ solution and the aqueous layer was extracted with ether. The extract was washed with saturated aqueous $NaHCO_3$ solution and brine, dried with $MgSO_4$, and concentrated *in vacuo.* The residue was purified by silica gel column chromatography (Hexane / Ether = 4 / 1) to afford 385 mg (98%) of **12** as colorless oil. IR (film): ν = 2925, 2853, 1465, 1149, 1102, 1037, 919 cm^{-1}; ^{1}H-NMR (300 MHz in $CDCl_3$): δ = 0.88 (3H, t, J = 6.7 Hz, 13”-H), 1.15-

1.51 (46H, m, 2’- to 12’- and 2”- to 12”-H), 1.51-1.71 and 1.88-2.00 (4H, m, 3- and 4-H), 3.19 (2H, t, *J* = 7 Hz, 1’-H), 3.36 (6H, s, $\mathrm{-OCH_2OC}\mathit{H}_3$), 3.42-3.56 and 3.90-4.05 (4H, m, 1”, 2, 5, and 13’-H), 4.66 and 4.84 (4H, d, *J* = 6.8 Hz, $\mathrm{-OC}\mathit{H}_2\mathrm{OCH_3}$); Anal. Calcd for $C_{34}H_{67}IO_5$: C, 59.81; H, 9.89. Found: C, 60.23; H, 9.91; $[\alpha]_D^{23}$ +38.3° (*c* 0.62 in $CHCl_3$); $n_D^{19.6}$ 1.4818.

(1’”*R*,2”*R*,3*RS*,5*S*,5”*R*,13’*R*)-3-{13’-Methoxymethoxy-13’-[5”-(1’”-methoxymethoxytridecyl)-2”-furyl]tridecyl}-5-methyl-3-(methylsulfinyl)furan-2-one (**14**)

To a solution of *trans*-**13** (26.3 mg, 0.18 mmol) in THF (540 μL) was added sodium bis(trimethylsilyl)amide (180 μL, 1.0 M solution in THF) and the mixture was stirred for 1 h. To this was added the iodide (**12**) (123 mg, 0.18 mmol) in HMPA (540 μL) and the mixture was stirred for 2 h at rt. The reaction mixture was poured into saturated aqueous NH_4Cl solution and extracted with ether. The combined organic layers were washed with brine, dried with $MgSO_4$ and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (Hexane / AcOEt = 6 / 1 - 3 / 2) to afford 108 mg (86%) of **14**. IR (film): ν = 2925, 2853, 1762, 1465, 1343, 1186, 1149, 1103, 1038, 919 cm^{-1}; ^{1}H-NMR (300 MHz in $CDCl_3$): δ = 0.88 (3H, t, *J* = 6.7 Hz, 13’”-H), 1.18-1.98 (52H, m, 1’- to 12’-, 2’”- to 12’”-, 3”-, 4”- and 4-H), 1.50 (3H, d, J = 6.4 Hz *methyl* at C-5), 2.16 (3H, s, $\mathrm{-SC}\mathit{H}_3$), 3.39 (6H, s, $\mathrm{-OCH_2OC}\mathit{H}_3$), 3.42-3.52 and 3.90-4.02 (4H, m, 1’”-, 2”, 5”, 13’-H), 4.51-4.66 (1H, m, 5-H), 4.63 and 4.84 (4H, d, *J* = 6.8 Hz, $\mathrm{-OC}\mathit{H}_2\mathrm{OCH_3}$); Anal. Calcd for $C_{40}H_{76}O_7S$: C, 68.53; H, 10.93. Found: C, 68.18; H, 10.80; $[\alpha]_D^{24}$ +27.3° (*c* 0.72 in $CHCl_3$); $n_D^{19.9}$ 1.4731.

Bis-MOM solamin (**15**)

To a solution of **14** (68.1 mg, 0.097 mmol) in CH_2Cl_2 (7 mL) was added *m*-CPBA (19.5 mg, 0.113 mmol) in CH_2Cl_2 (1.2 mL) at -78 °C. After stirring for 1 h, the reaction mixture was poured into 10% aqueous $Na_2S_2O_3$ solution and the aqueous layer was extracted with ether. The extract was washed with saturated aqueous $NaHCO_3$ and brine, dried with Na_2SO_4 and concentrated *in vacuo*. The residue was dissolved in toluene (1.7 mL) and $CaCO_3$ (10 mg, 0.100 mmol) was added. After being refluxed for 15 min, the reaction mixture was filtered through Celite and the filtrate was concentrated *in vacuo*. The residue was purified by silica gel column chromatography (Hexane / AcOEt = 4 / 1) to afford 61.5 mg (97%) of **15**. IR (film): ν = 2925, 2853, 1760, 1464, 1149, 1034, 919 cm^{-1}; ^{1}H-NMR (300 MHz in $CDCl_3$): δ = 0.88 (3H, t, *J* = 6.7 Hz, 13’”-H), 1.15-1.98 (50H, m, 2’”- to 12’”-, 3”-, 4”-, and 1’- to 12’-H), 1.40 (3H, d, *J* = 6.4 Hz, *methyl* at C-5), 2.26 (2H, t, *J* = 7.7 Hz, 1’-H), 3.39 (6H, s, $\mathrm{-OCH_2OC}\mathit{H}_3$), 3.40-3.50 and 3.91-4.00 (4H, m, 1’”-, 2”-, 5”-, 13’-H), 4.67 and 4.76 (4H, d, *J* = 6.8 Hz, $\mathrm{-OC}\mathit{H}_2\mathrm{OCH_3}$), 4.86-5.03 (1H, m, 5-H), 6.98 (1H, d, *J* = 1.5 Hz, vinyl-H); Anal. Calcd for $C_{39}H_{72}O_7$: C, 71.74; H, 11.11. Found: C, 72.10; H, 11.23; $[\alpha]_D^{19}$ +45.8° (*c* 0.52 in $CHCl_3$); $n_D^{19.5}$ 1.4772.

Solamin (**1**)

To a solution of **15** (52.6 mg, 0.0806 mmol) in dimethyl sulfide (4.0 mL) was added $BF_3{\cdot}Et_2O$ (319 μL, 2.52 mmol) at -15 °C. After being stirred for 40 min at rt , the reaction was quenched with saturated Na_2CO_3 solution. The reaction mixture was diluted with AcOEt and washed with water and brine, dried with Na_2SO_4 and concentrated *in vacuo*. The residue was purified by silica gel column chromatography

(Hexane / AcOEt = 6 / 1 - 2 / 1) to afford 47.9 mg (90%) of **1**. IR (film): ν = 3454, 2917, 2849, 1737, 1469, 1082, 799 cm^{-1}; ^{1}H-NMR (300 MHz in CDCl$_3$): δ = 0.88 (3H, t, J = 6.7 Hz), 1.20-2.10 (52H, m), 1.40 (3H, d, J = 6.4 Hz), 2.26 (2H, t, J = 7.7 Hz), 3.38-3.44 and 3.79-3.85 (2H and 2H, m), 5.00 (1H, m), 6.98 (1H, d, J = 1.5 Hz); Anal. Calcd for $C_{35}H_{64}O_5$: C, 74.42; H, 11.42. Found: C, 74.15; H, 11.35; $[\alpha]_D^{22}$ +24° (c 0.28 inMeOH) [lit.,[4] 21.2° (c 0.16, MeOH)]; mp 68-70 °C (lit.,[4] 64-68 °C).

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8. $\Delta\delta_H$ (δ_S-δ_R)
   major product
   chain side (0.11 positive), C-2 (0.12 negative), C-5 (0.002 negative), C-3 and C-4 (> 0.1 negative)
   minor product
   chain side (0.09 negative), C-2 (0.15 positive), C-5 (0.05 positive), C-3 and C-4 (> 0.1 positive)
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