D-Erythronolactone as a C_4 building unit. Part 2.[1] A short and efficient synthesis of both enantiomers of *epi*-muricatacin, a diastereoisomer of the native acetogenin from *Annona muricata*

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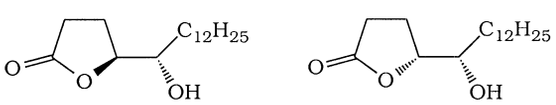
Both enantiomers of *epi*-muricatacin (+)- and (−)-2 have been prepared from 2,3-*O*-isopropylidene-D-erythrose 7. The enantiomers (+)- and (−)-2 are obtained in good yields and with high diastereoisomeric and enantiomeric purity. The aim of the synthesis is to obtain both enantiomers of the target molecule from one chiral precursor. This was made possible by the reaction sequence for the introduction of the two different side chains being exchangeable.

Introduction

Epi-Muricatacin **2** (Scheme 1) is the epimer of the naturally occurring acetogenin muricatacin **1**, which was extracted from the seeds of *Annona muricata*.[2] Muricatacin **1** is the simplest of the known native acetogenins, bearing only two chiral centres and having no tetrahydrofuran moiety unlike other members of this class of natural products. The relative stereochemistry of the diol moiety in **1** is *threo*. Both the natural product and its unnatural epimer **2** are biologically active showing cytotoxicity in KB and VERO cell lines.[3]



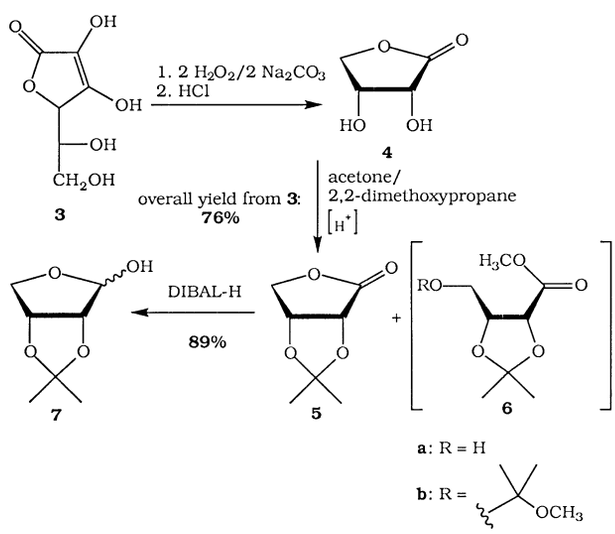
threo (4*R*,5*R*) (-)-**1** *erythro* (4*R*,5*S*) (-)-**2**

Scheme 1

Muricatacin **1** has been synthesized by several groups because it belongs to the highly interesting class of substituted γ-lactones, which can be found in many natural products.[2–9] Presently two syntheses of *epi*-muricatacin **2** are known,[3,10] one of them using a stereochemically unselective ketone reduction.[3] In the course of our work on the use of *erythro* C_4 building units in natural product synthesis,[1,11–13] we here present the synthesis of both enantiomers of *epi*-muricatacin **2** starting with 2,3-*O*-isopropylidene-D-erythrose **7** which is easily accessible in two steps from D-isoascorbic acid **3** (Scheme 2).[14,15]

Results and Discussion

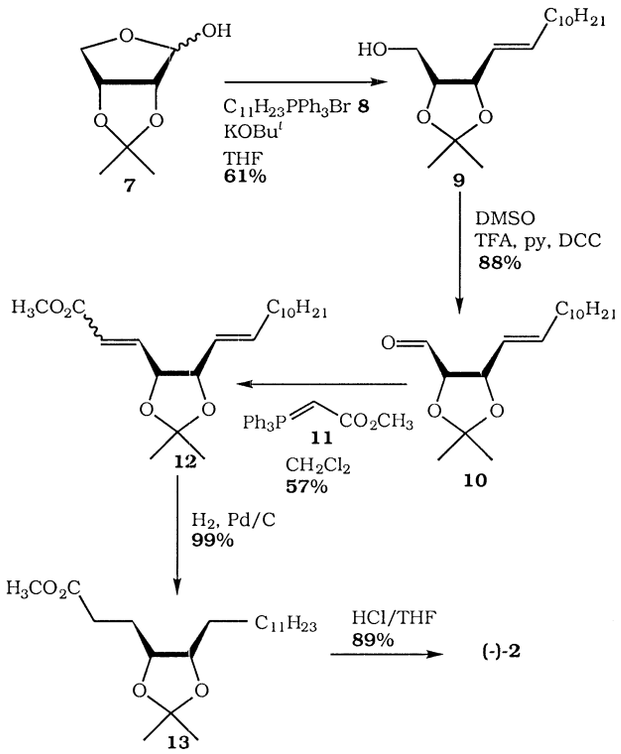
D-Isoascorbic acid **3** was oxidized with aqueous hydrogen peroxide (2 equiv.) to give D-erythronolactone **4** (77%). D-Erythronolactone **4** was then acetalized with a mixture of acetone, 2,2-dimethoxypropane and catalytic amounts of toluene-*p*-sulfonic acid to afford 2,3-*O*-isopropylidene-D-erythronolactone **5** (76%). As a by-product we observed the formation of 2,3-*O*-isopropylidene-D-erythronic acid methyl ester **6a**; the acetonide-protected erythronic acid derivative **6b** found by Cohen *et al.*[14,15] was not detected. Compound **5** was reduced with diisobutylaluminium hydride in dichloromethane as a solvent (yield 89%) to give, diastereoselectively, the β-anomer (monitored by ^{1}H NMR).



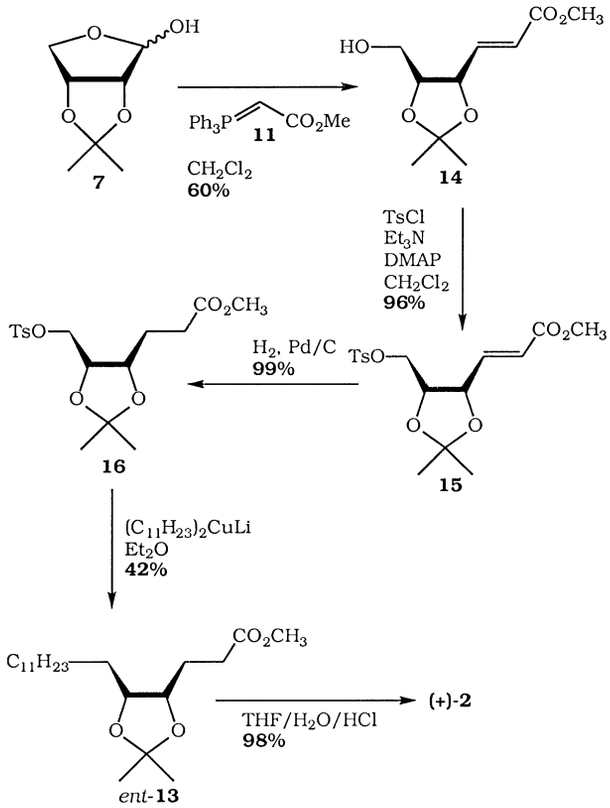
Scheme 2

The synthesis of (−)-**2** from 2,3-*O*-isopropylidene-D-erythrose **7** is depicted in Scheme 3. Wittig reaction of **7** with undecyl(triphenyl)phosphonium bromide **8** (from the reaction of undecyl bromide with triphenylphosphine in refluxing toluene[16]) and potassium *tert*-butoxide in tetrahydrofuran leads to the alcohol **9** (61%). The formation of the alkene is *E*-selective (> 95:5 determined by ^{1}H NMR). Compound **9** was then oxidized with activated dimethyl sulfoxide according to the method of Pfitzner and Moffat to the aldehyde **10** (88%).[17,18] Subsequent Wittig reaction of this with the stabilized ylide methyl (triphenylphosphoranylidene)acetate **11** in tetrahydrofuran led to the diene **12** (57%). Hydrogenation of this on a Pd/C contact afforded the saturated methyl ester **13** which was deprotected under acidic conditions (THF, HCl, MeOH) and cyclized to (−)-*epi*-muricatacin (−)-**2**. The ring closure to the γ-lactone occurs immediately according to Baldwin's rules.[19]

To synthesize the enantiomer (+)-**2** (Scheme 4), 2,3-*O*-isopropylidene-D-erythrose **7** was first treated with methyl (triphenylphosphoranylidene)acetate **11** in refluxing dichloromethane to give the α,β-unsaturated ester **14** [60%; again completely *E*-selective (determined by ^{1}H NMR)]. In order to establish the aliphatic side-chain of (+)-**2** the hydroxy group was activated as a tosylate **15**. The double bond was hydrogenated on a Pd/C contact in ethanol under a hydrogen atmosphere (5 bar) to **16**; overall yield of 95% over two steps. The removal



Scheme 3



Scheme 4

of the double bond is necessary to avoid a side reaction of the Michael system in the following cuprate addition. Alkylation of the tosylate **16** with lithium di(undecyl)cuprate (prepared from undecyllithium **17** and cuprous iodide) at −78 °C in diethyl ether afforded the ester *ent*-**13** (42%). Cyclization in THF with catalytic amounts of aqueous hydrochloric acid yielded *epi*-muricatacin (+)-**2** from *ent*-**13** quantitatively, analogous to the conversion of **13** into (−)-**2**.

Our synthesis of both enantiomers of *epi*-muricatacin (+)-**2** and (−)-**2** confirms the versatility of D-erythronolactone as a C_4 building unit as demonstrated by us earlier.[1,11–13] By means of a change in the sequence of side-chain introduction our strategy leads to an efficient synthesis of both enantiomers **2** from one chiral precursor.

Experimental

^{1}H NMR: Varian VXR 300; 300 MHz, $\delta = 0$ for TMS used as internal standard, $\delta = 7.26$ for $CHCl_3$. ^{13}C NMR: Varian VXR 300; 75 MHz, $\delta = 0$ for TMS used as internal standard, $\delta = 77.0$ for $CHCl_3$. The multiplicity of the carbon nuclei was determined by the APT technique. Melting points are uncorrected: Büchi melting point apparatus 510. Specific optical rotations: Perkin-Elmer polarimeter 241. Column liquid chromatography: Merck Silica gel 60. Thin layer chromatography: Merck Silica gel 60 F_{254} analytic aluminium plates. IR: Perkin-Elmer PE 1750 FT. MS: Varian MAT 212 (normal conditions: EI, 70 eV, 1 mA, 200 °C. CH analyses: Heraeus CHNO Rapid.

(2*R*,3*R*)-*O*-Isopropylidene-D-erythronolactone 5

This compound was prepared (76%) from D-isoascorbic acid **3** according to the procedure cited in the literature[14,15]; mp 66 °C (lit.,[14,15] 68–68.5 °C); $[\alpha]_D^{25}$ −103.4 (*c* 1.0 in H_2O) {lit.,[14] $[\alpha]_D^{25}$ −112 (*c* 1.5 in H_2O)}; $\delta_H(CDCl_3)$ 1.40, 1.49 [2 s, 6 H, $C(CH_3)_2$], 4.45 (d, *J* 2.4, 2 H, 4-H), 4.77 (d, 2 H, *J* 5.7, 2-H) and 4.90 (dd, *J* 5.7, 2.4, 1 H, 3-H); $\delta_C(CDCl_3)$ 25.6, 26.8 (2 CH_3), 70.3 (C-4), 74.7, 75.6 (C-3, C-2), 114.0 [*C*$(CH_3)_2$] and 174.3 (C=O).

As a by-product we obtained methyl 2,3-*O*-isopropylidene-erythronate **6a**; $\delta_H(CDCl_3)$ 1.35, 1.43 [2 s, 6 H, $C(CH_3)_2$], 3.80 (s, 3 H, OCH_3), 4.05 (d, *J* 6.0, 1 H, 2-H), 4.26 (d, *J* 5.0, 2 H, 4-H) and 4.31 (dd, *J* 6.0, 5.5, 1 H, 3-H); $\delta_C(CDCl_3)$ 25.1, 26.4 (2 CH_3), 52.5 (OCH_3), 65.3 (C-4), 71.0, 71.4 (C-3, C-2), 110.0 [*C*$(CH_3)_2$] and 172.7 (C=O).

(2*R*,3*R*)-2,3-*O*-Isopropylidene-D-erythrose 7

To a solution of the protected D-erythronolactone **5** (5.0 g, 32 mmol) in dichloromethane (100 ml) was added *via* a dropping funnel a 1.0 M solution of diisobutylaluminium hydride in dichloromethane (50 ml, 50 mmol) added at −72 °C under an inert atmosphere. The resulting mixture was stirred for 3 h at −72 °C, after which methanol (16 ml) was to it cautiously, to destroy the remaining diisobutylaluminium hydride. After being warmed to room temperature, the reaction mixture was poured into a mixture of ethyl acetate and water (1:1). The mixture was acidified to pH 3 (monitored with a pH-meter) with dilute sulfuric acid and the layers were separated. The aqueous phase was extracted with ethyl acetate and the extract evaporated to give the lactol **7** (4.5 g, 89%) as a pale yellow solid, the spectroscopic data of which were identical with those cited in the literature.[1,14]

Undecyl(triphenyl)phosphonium bromide 8

A solution of undecyl bromide (50 g, 0.21 mol) and triphenylphosphine (56 g, 0.21 mol) in dry toluene (300 ml) was heated under reflux for 48 h,[16] and then evaporated. The remaining solid **8** was dried *in vacuo* to give the title compound (106 g, 100%); $\delta_H(CDCl_3)$ 0.88 (t, *J* 7.1, CH_3), 1.20 (br m, 14 H, CH_2), 1.63–3.70 (br m, 6 H, CH_2) and 7.18–7.80 (br m, 15 H, Ar H); $\delta_C(CDCl_3)$ 14.1 (CH_3), 22.6, 29.2, 29.2, 29.5, 30.3, 30.5, 31.2 (CH_2), 125.3, 128.2, 129.0, 130.5, 130.6, 133.5, 133.7, 135.1, 135.1 and 137.7 (aromatic C).

(4*R*,5*S*)-2,2-Dimethyl-4-hydroxymethyl-5-[(*E*)-dodec-1-enyl]-1,3-dioxolane 9

A suspension of undecyl(triphenyl)phosphonium bromide **8** (28.1 g, 57 mmol) in dry tetrahydrofuran (100 ml) was cooled to −78 °C and treated with potassium *tert*-butoxide (6.4 g, 57

mmol). The orange solution was stirred at −20 °C for an additional hour, after which a solution of the lactol **7** (3.0 g, 19 mmol) in dry tetrahydrofuran (10 ml) was added to it *via* a dropping funnel. The cooling bath was removed and the reaction mixture was stirred overnight. It was then treated with water (50 ml) and diluted with diethyl ether (200 ml). The phases were separated and the aqueous phase was extracted with diethyl ether (× 3). The extract was dried ($MgSO_4$) and evaporated and the residue purified by column chromatography using as eluent ethyl acetate–hexane (1:1) (R_f 0.23). Compound **9** was a yellow syrup (3.4 g, 61%); $[\alpha]_D^{20}$ −35.3 (*c* 1.13 in $CHCl_3$); ν_{max}(KBr)/cm^{-1} 3481 (OH) and 1658 (C=C); δ_H($CDCl_3$) 0.88 (t, *J* 6.4, 3 H, CH_3), 1.27 (br m, 16 H, CH_2), 1.39 [2 s, 6 H, $C(CH_3)_2$], 2.08 (m, 2 H, CH_2), 2.41 (br s, 1 H, OH), 3.55 (d, *J* 5.0, 2 H, CH_2OH), 4.23 (dt, *J* 6.4, 5.0, 1 H, 4-H), 4.99 (ddd, *J* 6.4, 7.7, 1.0, 1 H, 5-H), 5.43 (ddd, *J* 11.4, 8.7, 0.7, 1 H, CH=) and 5.35 (ddd, *J* 11.4, 7.7, 1.1, 1 H, CH=); δ_C($CDCl_3$) 14.1 (CH_3), 22.7, 27.9, 29.3, 29.4, 29.50, 29.57, 29.63, 29.65, 32.0 (9 CH_2), 25.3, 27.99 [$C(CH_3)_2$], 62.2 (CH_2OH), 73.0, 78.5 (C-4, C-5), 108.5 [$C(CH_3)_2$], 124.4 and 135.5 (CH=); *m/z* (%) 298 (1) [$M^{\cdot+}$], 238 (23), 223 (35), 97 (81) and 59 (100). $C_{18}H_{34}O_3$ (298.46) (Found: C, 72.12; H, 11.17; *M*, 298.46. Calc. for $C_{18}H_{34}O_3$: C, 72.43; H, 11.48%).

(4*S*,5*S*)-2,2-Dimethyl-4-formyl-5-[(*E*)-dodec-1-enyl]-1,3-dioxolane 10

Trifluoroacetic acid (0.3 ml) and pyridine (0.5 ml) were added to a solution of compound **9** (2.3 g, 8 mmol) in a mixture of dimethyl sulfoxide (15 ml) and dry toluene (15 ml). The resulting mixture was stirred for 5 min after which it was treated with dicyclohexylcarbodiimide (4.9 g) and stirred overnight. After this the mixture was filtered to remove precipitated dicyclohexylurea, diluted with diethyl ether, washed with deionized water (40 ml), dried ($MgSO_4$) and evaporated. The residue was purified by column chromatography to give the title compound (2.0 g, 88%); ν_{max}(KBr)/cm^{-1} 1734 (C=O) and 1688 (C=C); δ_H($CDCl_3$) 0.88 (t, *J* 6.6, 3 H, CH_3), 1.27 (br m, 16 H, CH_2), 1.44, 1.61 [2 s, 6 H, $C(CH_3)_2$], 2.08 (m, 2 H, CH_2), 4.38 (dd, *J* 7.4, 3.4, 1 H, 4-H), 5.18 (td, *J* 7.4, 1.0, 1 H, 5-H), 5.34 (ddd, *J* 11.4, 7.4, 0.7, 1 H, C=H), 5.70 (ddd, *J* 11.1, 7.1, 1.0, 1 H, C=H) and 9.55 (d, *J* 3.4, 1 H, CHO); δ_C($CDCl_3$) 14.1 (CH_3), 22.7, 24.7, 25.5, 28.1, 29.5, 29.62, 29.65, 32.0, 35.0 (9 CH_2), 25.3, 27.5 [$C(CH_3)_2$], 74.6, 82.3 (C-4, C-5), 111.0 [$C(CH_3)_2$], 122.8, 136.8 (CH=) and 199.7 (C=O); *m/z* (%) 296 (2) [$M^{\cdot+}$], 239 (38), 209 (26), 100 (100), 85 (74) and 83 (43). $C_{18}H_{32}O_3$ (296.44) (Found: C, 72.57; H, 10.44; *M*, 296.44. Calc. for $C_{18}H_{32}O$: 72.93, H, 10.88%).

(4*R*,5*S*)-2,2-Dimethyl-4-methoxycarbonylethenyl-5-[(*E*)-dodec-1-enyl}-1,3-dioxolane 12

A solution of methyl (triphenylphosphoranylidene)acetate **11** (5.7 g, 17 mmol) was added to a solution of the aldehyde **10** (1.8 g, 6 mmol) in dry tetrahydrofuran (50 ml). After the solution had been refluxed for 24 h it was diluted with deionized water and diethyl ether and the phases were separated. The aqueous phase was extracted with diethyl ether (× 3) and the combined extracts were dried ($MgSO_4$) and worked up. Column chromatography then gave **12** (1.2 g, 57%) as a syrup; ν_{max}(KBr)/cm^{-1} 1724 (C=O) and 1651 (C=C); δ_H($CDCl_3$) 0.88 (t, *J* 7.1, 3 H, CH_3), 1.27 (br m, 16 H, CH_2), 1.37, 1.42 [2 s, 6 H, $C(CH_3)_2$], 2.08–2.30, 2.42–2.66 (2 m, 2 H, CH_2), 3.69, 3.74 (s, 3 H, OCH_3), 4.71 (ddd, *J* 8.4, 7.05, 1.7, 1 H, 4-H), 5.05 (ddd, *J* 8.7, 6.7, 1.0, 1 H, 5-H), 5.31 (ddd, *J* 11.4, 7.4, 0.7, 1 H, 1-H), 5.65 (ddd, *J* 11.1, 7.1, 1.0, 1 H, 1-H), 6.08 (dd, *J* 15.5, 1.7, 1 H, H_3CO_2C-C*H*=C) and 6.77 (dd, *J* 14.8, 5.7, 1 H, H_3CO_2C-C=C*H*); δ_C($CDCl_3$) 14.1 (CH_3), 22.7, 24.7, 25.45, 25.52, 27.90, 27.94, 29.27, 29.38, 29.47, 29.51, 29.58, 29.64, 29.67, 32.0, 35.0 [2 $C(CH_3)_2$, 9 CH_2], 51.6, 55.8 (OCH_3), 74.35, 74.75, 75.51, 76.6 (CHO), 109.32 [$C(CH_3)_2$], 122.15, 122.22, 124.66, 124.80, 125.26, 135.1, 135.5, 144.5 (C=C) and 166.4 (C=O); *m/z* (%) 352 (3) [$M^{\cdot+}$], 239 (25), 157 (19), 156 (40) and 98 (100) (Found: C, 71.65; H, 10.48; *M*, 352.51. Calc. for $C_{21}H_{36}O_4$: C, 71.55; H, 10.29%).

(4*R*,5*S*)-2,2-Dimethyl-4-methoxycarbonylethyl-5-dodecyl-1,3-dioxolane 13

A 200-ml glass autoclave was charged with compound **12** (1.0 g, 2.8 mmol) as a solution in ethanol (100 ml) together with a catalytic amount of palladium-on-charcoal (10%). After hydrogenation under an atmosphere of hydrogen (5 bar), the mixture was filtered through Celite® to remove the catalyst. Evaporation of the filtrate yielded **13** as a colourless syrup (0.93 g, 99%); ν_{max}(KBr)/cm^{-1} 1774 (C=O); δ_H($CDCl_3$) 0.88 (t, *J* 7.1, CH_3), 1.27 (br m, 22 H, CH_2), 1.33, 1.42 [2 s, 6 H, $C(CH_3)_2$], 1.74–1.80, 2.42–2.66 (2 m, 4 H, CH_2), 3.68 (s, 1 H, OCH_3) and 4.05 (m, 2 H, CHO); δ_C($CDCl_3$) 14.1 (CH_3), 22.7, 25.45, 26.0, 26.4, 28.56, 29.38–29.73, 30.6, 32.0 [14 CH_2, 2 $C(CH_3)_2$], 51.6 (OCH_3), 76.98, 77.96 (C-4, C-5), 107.6 [$C(CH_3)_2$] and 174.0 (C=O); *m/z* (%) 341 (26) [$M^{\cdot+}$ − CH_3], 239 (19), 81 (34), 74 (37) and 55 (100) (Found: C, 71.01; H, 11.53; *M*, 356.54. Calc. for $C_{21}H_{40}O_4$: C, 70.74, H, 11.31%).

(4*R*,5*S*)-2,2-Dimethyl-4-hydroxymethyl-5-[(*E*)-methoxycarbonylethenyl}-1,3-dioxolane 14

A solution of the protected D-erythrose **7** (5.0 g, 31 mmol) and methyl (triphenylphosphoranylidene)acetate **11** (15.5 g, 47 mmol) in dichloromethane (100 ml) was refluxed for 3 days and then evaporated. The residue was extracted overnight with pentane in a Soxhlet extractor after which the extract was evaporated. The residue when chromatographed on silica gel with ethyl acetate–hexane (1:1) gave **14** as a colourless syrup (4.0 g 60%); [α] + 13.2 (*c* 1.05 in CH_2Cl_2); ν_{max}(neat)/cm^{-1} 3495 (OH), 1719 (C=O) and 1647 (C=C); δ_H($CDCl_3$) 1.38, 1.54 [2 s, 6 H, $C(CH_3)_2$], 2.30 (br s, 1 H, OH), 3.45 (dd, *J* 11.8, 5.2, 1 H, CH_2OH), 3.60 (dd, *J* 11.8, 3.5, 1 H, CH_2OH), 3.73 (s, 3 H, OCH_3), 4.57 (ddd, *J* 7.0, 5.2, 3.5, 1 H, 5-H), 5.60 (td, *J* 7.0, 1.6, 1 H, 4-H), 5.95 (dd, *J* 11.5, 1.3, 1 H, C=CH) and 6.40 (dd, *J* 11.5, 7.0, 1 H, C=CH); δ_C($CDCl_3$) 24.7, 27.4 (CH_3), 51.7 (OCH_3), 61.5 (CH_2OH), 74.8, 78.9 (C-4, C-5), 108.9 [$C(CH_3)_2$], 120.6, 147.6 (C=C) and 166.4 (C=O); *m/z* (%) 201 (34) [$M^{\cdot+}$ − CH_3], 141 (72) and 98 (90) (Found: C, 55.67; H, 7.45; *M*, 216.2. Calc. for $C_{10}H_{16}O_5$: C, 55.55; H, 7.46%).

(4*S*,5*S*)-2,2-Dimethyl-4-tosyloxymethyl-5-[(*E*)-methoxycarbonylethenyl]-1,3-dioxolane 15

Tosyl chloride (3.3 g, 17 mmol) was added to a stirred solution of compound **14** (3.0 g, 14 mmol), triethylamine (2.8 g, 28 mmol) and *N*,*N*-dimethylaminopyridine (0.1 g, 1 mmol) in dichloromethane (100 ml) at 0 °C in small portions. The mixture was stirred for 1 h at 0 °C, allowed to warm to room temperature and then stirred for additional 2 h. It was then diluted with diethyl ether (150 ml) and washed with brine (× 2). The aqueous layer was back-extracted with diethyl ether (2 × 100 ml). The combined organic layers were dried ($MgSO_4$), filtered and evaporated to yield the crude tosylate. This was chromatographed on silica gel with ethyl acetate–hexane (1:1) to yield **15** as a colourless syrup (4.9 g, 96%); $[\alpha]_D^{20}$ + 102.0 (*c* 0.94 in CH_2Cl_2); ν_{max}(neat)/cm^{-1} 3414, 3000, 2947, 1751 (C=O) and 1598; δ_H($CDCl_3$) 1.33, 1.41 [2 s, 6 H, $C(CH_3)_2$], 2.44 (s, 3 H, aryl-CH_3), 3.71 (s, 3 H, OCH_3), 3.83 (dd, *J* 10.4, 5.5, 1 H, CH_2OTos), 4.01 (dd, *J* 10.4, 3.5, 1 H, CH_2OTos), 4.64 (ddd, *J* 6.9, 5.5, 3.5, 1 H, 4-H), 5.57 (dd, *J* 6.9, 1.9, 1 H, 5-H), 5.83 (dd, *J* 11.5, 1.9, 1 H, CH=), 6.27 (dd, *J* 11.5, 6.9, 1 H, CH=), 7.34 (m, 2 H, ArH) and 7.77 (m, 2 H, ArH); δ_C($CDCl_3$) 21.6 (aryl CH_3), 24.9, 27.2 (CH_3), 51.8 (OCH_3), 68.5 (CH_2OTos), 74.6, 75.4 (C-4, C-5), 109.6 [$C(CH_3)_2$], 121.7 (CH=), 128.0 (2 ArCH), 129.8 (2 ArC), 132.8 (ArC), 144.9 (ArC), 145.5 (CH=) and 165.9 (C=O); *m/z* (%) 370 (3) [$M^{\cdot+}$], 355 (28) [$M^{\cdot+}$ − CH_3], 295 (57), 155 (74) and 91 (100) (Found: C, 55.32; H, 6.03; *M*, 370.42. Calc. for $C_{17}H_{22}O_7S$: C, 55.12; H, 5.99%).

(4*S*,5*S*)-2,2-Dimethyl-4-tosyloxymethyl-5-methoxycarbonylethyl-1,3-dioxolane 16

Catalytic amounts of Pd/C were added to a solution of compound **15** (3.0 g, 8 mmol) in ethanol (50 ml) and the hydrogenation carried out under hydrogen (5 bar) for 24 h. The mixture was then filtered through Celite® to remove the catalyst and evaporated to yield **16** quantitatively as a colourless syrup (2.9 g, 99%); $[\alpha]_D^{20}$ + 11.4 (*c* 0.54 in CH_2Cl_2); $\nu_{max}(Et_2O)/cm^{-1}$ 2950, 2930 and 1720 (C=O); $\delta_H(CDCl_3)$ 1.28, 1.32 [2 s, 6 H, $C(CH_3)_2$], 1.6–1.9 (m, 2 H), 2.45 (s, 3 H, aryl-CH_3), 2.25–2.6 (m, 2 H), 3.68 (s, 3 H, OCH_3), 3.95–4.25 (m, 4 H), 7.37 (m, 2 H, ArH) and 7.81 (m, 2 H, ArH); $\delta_C(CDCl_3)$ 21.7 (CH_3-aryl), 24.4 (CH_2), 25.4, 27.9 (2 CH_3), 30.8 (CH_2), 51.7 (OCH_3), 67.7 (CH_2OTos), 74.6, 75.8 (C-4, C-5), 108.9 [*C*$(CH_3)_2$], 128.1, 129.9 (4 ArCH), 132.6 (ArC), 145.1 (ArC) and 173.6 (C=O); *m/z* (%) 357 (60) [$M^{\cdot+}$ − CH_3], 143 (51) and 129 (100) (Found: C, 54.98; H, 6.61; *M*, 372.42. Calc. for $C_{17}H_{24}O_7S$: C, 54.82; H, 6.49%).

Preparation of undecyllithium 17

Lithium powder (2.2 g, 310 mmol) was added to a solution of undecyl chloride (24.8 g, 130 mmol) in pentane (50 ml) at 0 °C. The resulting slurry was sonificated with ultrasound for 2 h at 0 °C. The yellowish solution containing **17** was then titrated against diphenylacetic acid (0.74 mol l^{-1}).

(4*S*,5*R*)-2,2-Dimethyl-4-methoxycarbonylethyl-5-dodecyl-1,3-dioxolane *ent*-13

Undecyllithium **17** in pentane (0.74 mol l^{-1}; 7 ml, 5.2 mmol) was added dropwise to a stirred slurry of purified cuprous iodide (0.5 g, 2.6 mmol) in diethyl ether (25 ml) at −40 °C; the reaction mixture turned black immediately. After complete addition of the undecyllithium, the mixture was warmed to 0 °C to give a clear black solution which was cooled to −78 °C and treated with the tosylate **16** (0.5 g, 1.3 mmol) dissolved in diethyl ether (5 ml), added dropwise. After 2 h the reaction was quenched with saturated aqueous ammonium chloride at 0 °C. The organic layer was separated, washed with brine (× 2); the combined aqueous layers were then back-extracted once with diethyl ether. The combined organic layers were dried ($MgSO_4$), filtered and evaporated to afford a colourless syrup which was chromatographed on silica gel with diethyl ether–pentane (1:3) to yield *ent*-**13** as a colourless oil (0.17 g, 42%). The physical properties and spectroscopic data are in agreement with those of compound **13**.

(4*R*,5*S*)-(−)-*epi*-Muricatacin (−)-2 and (4*S*,5*R*)-(+)-*epi*-muricatacin (+)-2. Concentrated hydrochloric acid (5 ml) was added to a solution of compound **13** (0.4 g, 1.2 mmol) in a mixture of tetrahydrofuran (200 ml) and deionized water (60 ml); the reaction was monitored by TLC [hexane–ethyl acetate (5:1)]. After completion of the reaction the mixture was neutralized with sodium hydrogen carbonate and diluted with diethyl ether. After separation of the phases, the aqueous layer was extracted with diethyl ether (× 3). The combined extracts were dried ($MgSO_4$) and evaporated to give *epi*-muricatacin (−)-**2** as a colourless solid (0.3 g, 89%), mp 69–70 °C (lit.,[3] 69 °C); $[\alpha]_D^{20}$ −30.5 (*c* 1.87 in $CHCl_3$) {lit.,[3] $[\alpha]_D^{20}$ −32 (*c* 1.87 in $CHCl_3$)}; ν_{max}(KBr)/cm^{-1} 3422 (OH) and 1762 (C=O); $\delta_H(CDCl_3)$ 0.88 (t, *J* 6.4, CH_3), 1.26 (br m, 22 H, CH_2), 2.08–2.30, 2.42–2.66 (m, 5 H, CH_2, C*H*OH), 3.94 (m, 1 H, CHO*H*), 4.44 (dt, *J* 7.1, 3.0, 1 H, CHO-lactone); $\delta_C(CDCl_3)$ 14.1 (CH_3), 21.1, 22.7, 25.7, 28.73, 29.36–29.65, 31.91, 31.92 (13 CH_2), 71.4, 82.8 (C-3, C-4) and 177.5 (C=O); *m/z* (%) 284 (2) [$M^{\cdot+}$], 87 (23) and 86 (100) (Found: C, 70.65; H, 10.98; *M*, 284. Calc. for $C_{17}H_{32}O_3$: C, 71.07; H, 11.34%).

Compound *ent*-**13** (0.11 g, 0.31 mmol) was treated with a catalytic amount of aqueous hydrochloric acid in tetrahydrofuran at room temperature for 2 h and then evaporated to dryness. Recrystallisation of the residue from diethyl ether–pentane yielded (+)-**2** as white crystals (0.09 g, 98%). The spectroscopic data are in agreement with that of (−)-**2**; $[\alpha]_D^{20}$ + 31.5 (*c* 1.07 in $CHCl_3$).

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