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Synthesis of γ-lactones by desymmetrization. A synthesis of (−)-muricatacin

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ABSTRACT

A short synthesis of the natural potent cytotoxic agent (−)-muricatacin **1** and related unsaturated lactones from a versatile common intermediate, dienedioate **2**, derived from D-mannitol or tartaric acid, is described. The strategy depends upon the desymmetrization of **7** by dihydroxylation and elaboration of the hydroxy alkyl sidechain. A route to unsaturated lactones is also described using a cis selective Wittig reaction. Since the enantiomers of **2** are available from the corresponding tartaric acids, this method provides access to both enantiomers of the described compounds and a wide range of derivatives.

1. Introduction

γ-Butyrolactones are widely distributed throughout nature and this moiety occurs in a variety of natural compounds with interesting biological activities. For example, it is present in muricatacin **1**, a simple biologically active acetogenin derivative isolated[1] from the seeds of *Annona muricata* (Annonaceae). Numerous works have been published on the synthesis of either (+) or (−)[2,6,7] or *epi*- or aza-analogues[3] of muricatacin. The chirality for these syntheses either originated from natural sources or was introduced through asymmetric transformations such as Sharpless asymmetric dihydroxylation,[2a,2m] epoxydation[2g] or prepared by α- and α′-C–H functionalization of tetrahydrofuran.[2s] An elegant synthesis using RCM has also recently appeared.[2t] In this paper we present a strategy, which is applicable to the preparation of diverse optically pure γ-lactones starting from readily available diendioldioate **2** and is here exemplified by a new synthesis of (−)-muricatacin **1**. We have previously studied the desymmetrization of **2** for the synthesis of some heterocyclic sugar analogues[4,5] and we expected to apply a similar strategy for a short syntheses of a variety of optically pure lactones. The publication of an article[6] on the synthesis of muricatacin via asymmetric dihydroxylation and another starting from tartaric acid[7] has prompted us to report our findings on this subject.

Several saturated lactones and dilactones were obtained by chemical manipulation of **2**. Desymmetrization via monodesilylation[4] of the C_2 symmetric saturated disilylated diol **3**[8] afforded the monolactone **4** and saturation of the diol **2** produced **5**, which lactonized to afford only the di-γ-lactone **6** and no δ-lactone.[9,2b,2e] Although compound **4** has the basic structure for muricatacin and a chain extension at the ester group would afford the title compound or derivatives we decided to base our synthesis on the formation of an aldehyde derived from **7** by monodihydroxylation and periodate cleavage followed by Wittig technology.

The diene **7** was monodihydroxylated (Scheme 1) according to a previously reported procedure[4] affording **8** in 83% yield. The diol was then cleaved with $NaIO_4$, utilizing a method described by Heathcock et al.[10] to afford the aldehyde **9** ($[\alpha]_D$ +27 (*c* 1.9, $CHCl_3$)) in 88% yield, after chromatographic purification, and was used immediately since degradation occurred slowly even at −20 °C. Diene **10** was obtained by Wittig olefination of **9** with the phosphorane generated by treatment of *n*-undecyltriphenylphosphonium bromide with butyllithium in THF at −78 °C. A freshly prepared and dried phosphonium bromide was crucial to obtain a good yield. Quenching of the reaction, either with water, methanol, or a saturated NH_4Cl solution resulted in low yields but simple evaporation of solvent and purification by preparative chromatography furnished the diene **10** in a moderate to good yield (73%; $[\alpha]_D$ −16.20 (*c* 1.0, $CHCl_3$)), which had, as expected, almost exclusively the *Z* configuration at the newly formed C=C bond confirmed by the coupling constant J_{cis}=11.16 Hz versus

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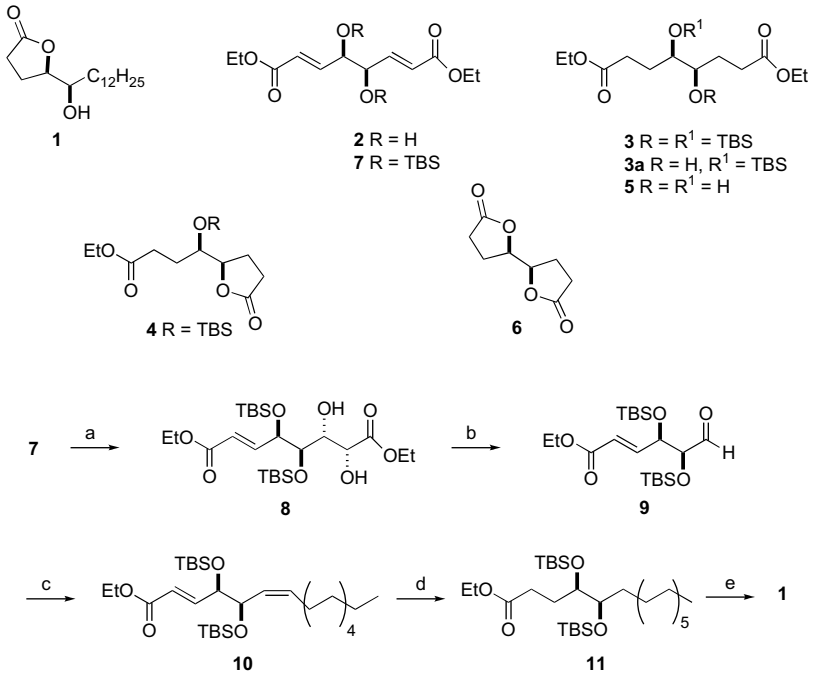
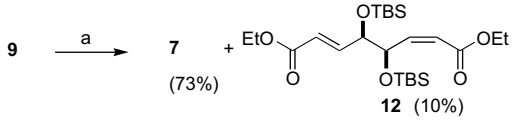


Scheme 1. (a) NMO, acetone/H_2O, OsO_4, 83%; (b) $NaIO_4$, EtOH, NaOH, 88%; (c) BuLi, $Ph_3P^+C_{11}H_{23}$, Br^-, 57–73%; (d) H_2, Pd/C, 95%; (e) TBAF, THF, 74%.

J_{trans}=15.63 Hz for the *E* configured C=C bond. This product was hydrogenated in the presence of 10% Pd/C. Shaking for 1 h at 60 psi resulted in almost complete saturation of the conjugated C=C bond. Prolonged treatment at 60 psi overnight still gave incomplete conversion even after the addition of more catalyst. A two-step sequence was necessary to achieve a good yield of the required product **11**. After shaking for 1 h, the mixture was filtered through Celite and further hydrogenated overnight with new catalyst to afford the expected saturated compound **11** ($[\alpha]_D$ +36.9 (*c* 1.2, $CHCl_3$)) in 95% yield. This was sufficiently pure to proceed directly to the deprotection of the silylated alcohol. Desilylation was achieved with TBAF in THF and as expected, the product spontaneously cyclized, affording **1** in 74% yield after column chromatography (mp 72.5–72.9 °C; $[\alpha]_D$ −22.1 (*c* 1.0, $CHCl_3$); lit.:[2f] mp 71 °C; $[\alpha]_D$ −22 (*c* 0.64, $CHCl_3$)). The ^1H and ^{13}C NMR spectra were also in complete agreement with the literature data.[2f,2r]

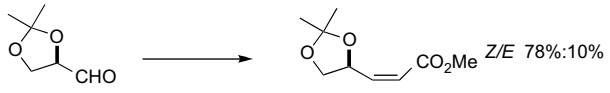
Unsaturated γ-lactones are important building blocks for the synthesis of related natural compounds[6] and we expected to prepare unsaturated lactones using the common intermediate **9**. This implied the preparation of a (*E*,*Z*) dienedioate; the γ-hydroxy-α,β-unsaturated *Z* enoates would cyclize to the lactone, while the *E* alkene would be unable to. Wittig reaction of aldehyde **9** with a stabilized ylide gave, as expected, the *E*,*E* diene (73%) **7** and only 10% of the required *E*,*Z* isomer **12** (Scheme 2).



Scheme 2. (a) Ph_3PCHCO_2Et, MeOH, 0 °C.

Isopropylidene glyceraldehyde reacts with a stabilized ylide to form an approximately 8:1 (*Z*/*E*) mixture of isomers[11] (Scheme 3).

This reaction appears to be general for isopropylidene bound vicinal heteroatom systems. We thus assumed that the aldehyde **15** derived from the isopropylidene protected dienedioate **13**[4] should undergo a similar stereoselective olefination (Scheme 4).



Scheme 3. (a) $Ph_3P{=}CHCO_2Me$, MeOH, 0 °C.

Dihydroxylation of **13**[4,8] gave the vicinal diol **14** in 54% yield (72% including recovered starting material) as a 2:1 separable mixture of isomers. Cleavage of the mixture with $NaIO_4$ gave the crude aldehyde **15**, which was used without purification for the olefination reaction with [(ethoxycarbonyl)methylene]triphenylphosphorane. The dienedioate **16** was obtained in 81% yield as a 88:12 mixture of *E*,*Z* and *E*,*E* dienedioate (determined by GC). Hydrolysis of the dioxolane with TFA in THF/H_2O 4:1 afforded lactone **17** in 51% yield.

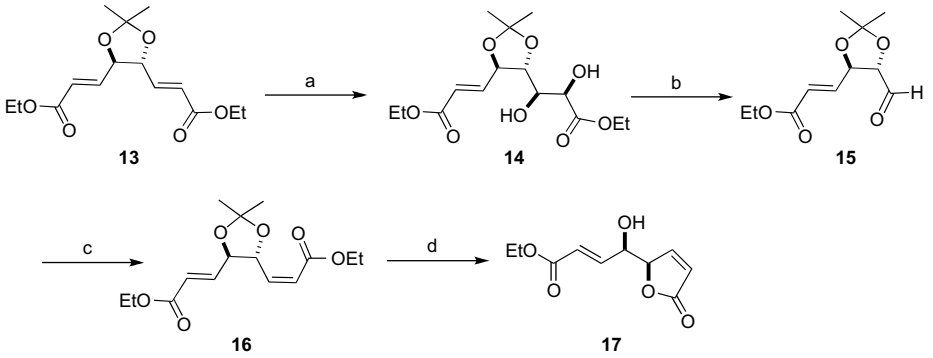
2. Conclusion

A chiral pool approach, from readily available and inexpensive starting materials has been applied to the synthesis of a range of γ-lactones including the biologically active natural product muricatacin. This strategy is also useful for the synthesis of unsaturated lactones. Flexibility is built into the synthesis and a large number of derivatives are available by slight modification to these procedures. The enantiomers of these compounds are readily available starting from the appropriate tartaric acid.

3. Experimental

3.1. General

Melting points were determined on a Buchi Melting Point apparatus and are uncorrected. Infrared spectra (neat product for oil or KBr pellets for solids) were recorded on a Mattson Research Series FTIR spectrometer. Optical rotations were recorded on a Perkin Elmer 241 polarimeter using a 0.5 dm cell. Concentrations



Scheme 4. (a) NMO, acetone/H_2O, OsO_4, 54% (*anti*/*syn* 2:1); (b) $NaIO_4$, EtOH, NaOH; (c) Ph_3PCHCO_2Et, 82% for two steps, *Z*/*E* 88:12; (d) TFA, THF/H_2O, 51%.

are given in g/100 mL. NMR spectra were recorded on a Brüker AMX300 spectrometer (^1H: 300 MHz, ^{13}C: 75 MHz) in $CDCl_3$ solution using Me_4Si as an internal reference for ^1H and the solvent peak at δ 77.0 ppm for ^{13}C. Chemical shifts are expressed in parts per million downfield. Analytical thin layer chromatography was performed on precoated Merck plates (silica gel 60) with fluorescence indicator (254 nm). Elemental analyses were performed by the Microanalytical Laboratory, operated by the Analytical Department at the IST (Portugal).

3.2. 1-(4*R*,5*R*)-4-(*tert*-Butyldimethylsilanyloxy)-4-(5-oxotetrahydrofuran-2-yl)-butyric acid ethyl ester 4

A solution of **3a** (0.1027 g, 0.27 mmol), in 4 mL of dry THF, was added to a suspension of 10 mg (1.5 equiv) of NaH in 2 mL of dry THF under argon. The mixture was stirred for 0.5 h, then NH_4Cl saturated solution (15 mL) was added and the mixture was extracted with ether (3×20 mL). The organic phase was washed with brine and dried on $MgSO_4$. The solvent was evaporated in vacuo and the residue purified by medium pressure column chromatography (2×19 cm, Hex/AcOEt 85:15) to give **4** (0.0839 g, 93%) as a colorless oil. $[\alpha]_D$ −20.5 (*c* 1.04, $CHCl_3$). IR (cm^{-1}): 1781.1 (C=O), 1734.5 (C=O). ^1H NMR ($CDCl_3$): 4.43 (dt, 1H, *J*=5.0, 7.62, H-5), 4.12 (q, 2H, OCH_2CH_3), 3.75 (m, 1H, *J*=5.0, H-4), 2.61–2.39 (m, 4H, H-2,2′,7,7′), 2.29–2.17 (m, 1H, H-6), 2.08–1.85 (m, 2H, H-6′, H-3), 1.80–1.68 (m, 1H, H-3′), 1.26 (t, 3H, OCH_2CH_3), 0.90 (s, 9H, Si–*t*-Bu), 0.10 (s, 3H, $SiCH_3$), 0.08 (s, 3H, $SiCH_3$). ^{13}C NMR: 176.9 (C-1), 173.2 (C-8), 81.7 (C-4), 76.6 (C-5), 60.5 (OCH_2CH_3), 29.7, 28.5, 27.7 (C-2, C-7, C-3), 25.8 (Si–*t*-Bu), 23.7 (C-6), 18.0 (quat., Si–*t*-Bu), 14.2 (OCH_2CH_3), −4.5, −4.6 ($SiCH_3$). Anal. Calcd for $C_{16}H_{39}O_5Si$: C, 58.15; H, 9.15. Found C, 57.90; H, 9.06.

3.3. 1-(2*R*,2′*R*)-(−)Tetrahydro-[2,2′]-bifuranyl-5,5′-dione 6

A solution of **2** (0.20 g 0.77 mmol) in 4 mL of EtOH was shaken in the presence of 41 mg of 10% Pd/C under a pressure of 30 psi. After 1 h, 20 mg more catalyst was then added and the product was hydrogenated overnight at 30 psi. The catalyst was filtered off on Celite that was washed successively with EtOH (100 mL), then AcOEt (100 mL). The combined filtrates were concentrated in vacuo and the residue was dissolved in dry THF under argon. $Ti(O\text{-}iPr)_4$ (0.223 g) was added and the mixture refluxed for 1.5 h. The reaction was quenched with 5 mL of saturated solution of NH_4Cl, the solid was filtered on Celite and washed with 200 mL of AcOEt. Evaporation of solvent and purification of the resulting oil by medium pressure column chromatography (2×16 cm, AcOEt) gave 0.062 g (51% for two steps) of **6** as a white oil that crystallized spontaneously. Mp 78.3–79.2 °C. $[\alpha]_D$ −82.5 (*c* 1.0, $CHCl_3$); lit.:[8] mp 78–79 °C; $[\alpha]_D$ −81 (*c* 0.99, $CHCl_3$). IR (cm^{-1}): 1781.1 (C=O). ^1H NMR ($CDCl_3$): 4.57–4.62 (m, 2H, H-2,2′), 275–2.63 (m, 2H, H-4,4′), 2.59–2.48 (m, 2H, H-4,4′), 2.44–2.24 (m, 4H, 3-CH_2, 3′-CH_2). ^{13}C NMR: 176.2 (C-5,5′), 79.8 (C-2,2′), 27.8 (C-4,4′), 23.7 (C-3,3′).

3.4. 1-(4*R*,5*S*)-4,5-Bis-(*tert*-butyldimethylsilanyloxy)-6-oxohex-2-(*E*)-enoic acid ethyl ester 9

To a solution of **8** (0.20 g, 0.38 mmol) in 3 mL of EtOH and cooled in an ice-bath was added a suspension of 0.246 g (3 equiv) of $NaIO_4$ and 8 mg of NaOH in 1 mL of water. The mixture was stirred at rt for 45 min, then diluted with 15 mL of water. Extraction with DCM (4×15 mL), washing of the organic phase with brine (15 mL), drying on $MgSO_4$, and evaporation of solvent gave 0.175 g of crude product that was purified by preparative TLC (Hex/AcOEt 4:1) to give 0.139 g (87%) of **9** as a colorless viscous oil. $[\alpha]_D$ +27 (*c* 1.9, $CHCl_3$). IR (cm^{-1}): 1724.8 (C=O). ^1H NMR ($CDCl_3$): 9.58 (d, 1H, *J*=1.7, H-6), 7.03 (dd, 1H, *J*=15.6, 4.3, H-3), 6.03 (dd, 1H, *J*=15.6, 1.9, H-2), 4.55 (dt, 1H, *J*=4.3, 1.9, H-4), 4.25–4.01 (m, 2H, OCH_2CH_3), 6.00 (dd, 1H, J=1.7, 4.7, H-5), 1.27 (t, 3H, OCH_2CH_3), 0.90, 0.90 (2s, 18H, *t*-Bu), 0.06 (s, 6H, SiMe), 0.04 (s, 3H, SiMe), 0.04 (s, 3H, SiMe). ^{13}C NMR: 201.9 (C-6), 165.9 (C-1), 145.9 (C-3), 122.2 (C-2), 79.5, 73.3 (C-4, C-5), 60.4 (OCH_2CH_3), 25.6 (Si–*t*-Bu), 18.2, 18.1 (quat., Si–*t*-Bu), 14.2 (OCH_2CH_3), −4.7, −5.2 ($SiCH_3$).

3.5. 2-(4*R*,5*R*)-4,5-Bis-(*tert*-butyldimethylsilanyloxy)-heptadeca-2(*E*),6(*Z*)-dienoic acid ethyl ester 10

A solution of *n*-undecyltriphenylphosphonium bromide (0.25 g, 1.3 equiv/aldehyde) in 4.0 mL of dry THF cooled by an ice bath was treated with 0.342 mL (1.05 equiv/phosphonium bromide) of a 1.59 M solution of BuLi in hexane for 20 min, then cooled to −78 °C. Aldehyde **9** (0.17 g, 0.40 mmol) dissolved in 3 mL of dry THF under argon was added to the orange solution and stirred for 25 min to give a pale yellow solution. Evaporation of the solvent and purification of the crude product by preparative TLC (Hex/AcOEt 95:5) gave 0.16 g (73%) of **10** as a colorless oil. $[\alpha]_D$=−16.2 (*c* 1.0, $CHCl_3$). IR (cm^{-1}, neat): 1724.1 (C=O), 1658.9 (C=C). ^1H NMR ($CDCl_3$): 7.07 (dd, 1H, *J*=15.6, 4.1, H-3), 6.00 (dd, 1H, *J*=15.6, 1.9, H-2), 5.46 (dt, 1H, *J*=14.3, 6.9, H-7), 5.17 (m, 1H, H-6), 4.42 (dd, 1H, *J*=5.0, 9.1, H-4), 4.28 (m, 1H, H-5), 4.24–4.14 (m, 2H, OCH_2CH_3), 2.00 (m, 2H, H-8,8′), 1.38–1.22 (m, 19H, H-9,9′, H-10,10′, H-11,11′, H-12,12′, H-13,13′, H-14,14′, H-15,15′, H-16,16′, OCH_2CH_3), 1.00–0.80 (m, 21H, 2Si–*t*-Bu, CH_3), 0.07, 0.06, 0.05, 0.03 (4s, 12H, 4SiMe). ^{13}C NMR: 165.5 (C-1), 148.1 (C-3), 132.7 (C-6), 128.7 (C-7), 121.4 (C-2), 75.7, 71.6 (C-4, C-5), 60.2 (OCH_2CH_3), 31.9 (C-8), 29.6, 29.6, 29.3, 28.3 (C-9,10,11,12,13,14,15), 25.9, 25.8 (2Si–*t*-Bu), 22.7 (C-16), 18.3, 18.1 (quat., Si–*t*-Bu), 14.2, 14.1 (C-17, OCH_2CH_3), −4.4, −4.7, −4.7, −4.8 ($SiCH_3$). Anal. Calcd for $C_{31}H_{62}O_4Si_2$: C, 67.09; H, 11.26. Found C, 67.08; H, 11.17.

3.6. 3-(4*R*,5*R*)-4,5-Bis-(*tert*-butyldimethylsilanyloxy)-heptadecanoic acid ethyl ester 11

Diene **10** (0.073 g, 0.13 mol) was dissolved in EtOH (3.5 mL) and hydrogenated in the presence of 14 mg of Pd/C 10% under 60 psi of H_2 for 1 h. The mixture was filtered on a small pad of Celite that was washed successively with EtOH and AcOEt. Solvents were evaporated and the resulting colorless oil was further hydrogenated in 3.5 mL of EtOH overnight with 14 mg of new catalyst. Treatment as described above gave 0.07 g (95%) of **11** as a colorless oil that was used without purification for the next reaction. $[\alpha]_D$ +36.9 (*c* 1.18, $CHCl_3$). IR (neat, cm^{-1}): 1739.5 (C=O). ^1H NMR: 4.19–4.04 (m, 2H, OCH_2CH_3), 3.61–3.52 (m, 2H, H-4, H-5), 2.43 (ddd, 1H, *J*=5.4, 9.5, 15.8, H-2), 2.25 (ddd, 1H, *J*=6.9, 9.1, 15.6, H-2′), 2.04–1.91 (m, 1H, H-3), 1.67–1.10 (m, 26H, OCH_2CH_3, H-3′, H-6,6′ to H-16,16′), 1.00–0.80 (m, 21H, 2 Si–*t*-Bu; CH_3), 0.06, 0.05 (m, 12H,SiMe). ^{13}C NMR: 173.9 (C-1), 75.2, 74.3 (C-4, C-5), 60.2 (OCH_2CH_3), 31.9 (C-2), 31.4 (C-3), 29.9, 29.7, 29.4, 25.8 (2Si–*t*-Bu), 25.6 (C-9,10,11,12,13,14,15), 22.7 (C-16), 18.0 (quat., Si–*t*-Bu), 14.2, 14.1 (C-17, OCH_2CH_3), −4.1, −4.6, −4.7 ($SiCH_3$). Anal. Calcd for $C_{31}H_{66}O_4Si_2$: C, 66.60; H, 11.90. Found C, 66.39; H, 11.80.

3.7. 4-(5*R*,1′*R*)-5-(1′-Hydroxytridecyl)-dihydrofuran-2-one [(−)-muricatacin] 1

Silyl ether **11** (0.08 g, 0.14 mmol) was dissolved under argon in 2 mL of dry THF. A 1 M solution of TBAF (0.866 mL) in THF (6 equiv) was added at rt and the mixture was stirred for 3 h (monitored by TLC Hex/AcOEt 95:5). H_2O (10 mL) was added and the product was extracted with ether (3×30 mL), washed with brine, and dried on $MgSO_4$. Evaporation of solvents gave 0.055 g of crude product that was purified by medium pressure column chromatography (2×19 cm, Hex/AcOEt 70:30) to give 0.03 g (74%) of **1** as a white solid that was recrystallized from hexane. Mp 72.5–72.9 °C. $[\alpha]_D$ −22.1 (*c* 1.0, $CHCl_3$); lit.:[2f] mp 71 °C; $[\alpha]_D$=−22 (*c* 0.64, $CHCl_3$). IR (KBr, cm^{-1}): 3400 (OH), 1744.3 (C=O). IR ($CHCl_3$, cm^{-1}): 1772.5; lit.:[2k] 1767 cm^{-1} ($CHCl_3$). ^1H NMR: 4.42 (dt, 1H, *J*=4.5, 7.4, H-5), 3.57 (m, 1H, H-1′), 2.68–2.44 (m, 2H, H-3,3′), 2.31–2.04 (m, 2H), 1.93 (br s, 1H, OH), 1.59–1.20 (m, 22H), 0.88 (t, 1H, *J*=6.7, CH_3). ^{13}C NMR: 177.1 (C-2), 82.9 (C-5), 73.6 (C-1′), 32.9 (C-3), 31.9 (C-4), 29.6, 29.6 (2C), 29.6, 29.5 (2C), 29.3, 28.7, 25.4, 24.1, 22.7, 14.1 (C-13′). Anal. Calcd for $C_{17}H_{32}O_3$: C 71.79; H 11.34. Found: C 71.61; H 11.46.

3.8. 5-(4*R*,5*R*)-{5-[2″(*Z*)-Ethoxycarbonyl-vinyl]-2′,2′-dimethyl-[1′,3′]-dioxolan-4-yl}-(*E*)-acrylic acid ethyl ester 16

Dioxolane **14** (0.41 g, 1.2 mmol) was dissolved in 10 mL of EtOH. A solution of $NaIO_4$ (0.79 g, 3 equiv) and NaOH (34 mg) in H_2O was added at rt and the mixture was stirred for 0.5 h. H_2O (15 mL) was added and the product was extracted with DCM (3×15 mL), washed with brine, and dried on $MgSO_4$. Evaporation of the solvent gave crude **15** that was dissolved in dry methanol (20 mL) under argon and cooled by an ice-bath. [(Ethoxycarbonyl)methylene]-triphenylphosphorane (0.573 g, 1.33 equiv) was added in three portions and the mixture was stirred at 0 °C overnight. Evaporation of the solvent and purification of the crude product by flash column chromatography (Hex/AcOEt 8:2 then 7:3) gave 0.36 g (97%) of **16** as a 88:12 mixture of (*E*,*Z*) and (*E*,*E*) diene. ^1H NMR (400 MHz, major isomer): 6.95 (dd, 1H, *J*=15.6, 5.4, H-3), 6.19 (dd, 1H, *J*=11.7, 8.1, H-1″), 6.10 (dd, 1H, *J*=15.6, 1.4, H-2), 5.97 (dd, 1H, *J*=11.7, 1.3, H-2″), 5.44 (dt, 1H, *J*=8.2, 1.3, H-5′), 4.30–4.24 (m, 1H, *J*=8.2, 1.5, 5.4, H-4), 4.24–4.13 (m, 4H, $2OCH_2CH_3$), 1.48–1.47 (m, 6H, $2CH_3$), 1.33–1.25 (m, 6H, $2OCH_2CH_3$). ^{13}C NMR (100 MHz): 165.9, 165.1 (C=O), 143.6, 143.2 (C-3, C-1″), 123.7, 122.4 (C-2, C-2″), 110.7 (C-2′), 80.0, 76.1 (C-4, C-5′), 60.7, 60.5 ($2OCH_2CH_3$), 27.1, 26.8 ($2CH_3$), 14.2 ($2OCH_2CH_3$).

3.9. 6-(4*R*,5*R*)-4-(5-Oxo-2,5-dihydro-furan-2-yl)-but-2 (*E*)-enoic acid ethyl ester 17

A 88:12 mixture of **16** and (*E*,*E*) isomer **13** (0.50 g, 1.7 mmol) dissolved in 10 mL of THF/H_2O 4:1 was heated at 65 °C with 2 mL (15 equiv) of trifluoroacetic acid. The reaction was monitored by TLC (Hex/AcOEt 1:1). After 1.5 h, the reaction was quenched with 15 mL of $NaHCO_3$ saturated solution and the product extracted with AcOEt (2×50 mL), dried on $MgSO_4$, and concentrated in vacuo. The resulting oil was purified by medium pressure column chromatography (2×31 cm, Hex/AcOEt 1:1) to give 0.160 g of **17** (51%) as a colorless oil that crystallized spontaneously. Mp 57–60 C. $[\alpha]_D$ +145 (*c* 1.0, $CHCl_3$). IR (KBr, cm^{-1}): 3329 (OH), 1731 (C=O), 1664.4 (C=C). ^1H NMR: 7.55 (dd, 1H, *J*=5.8, 1.5, H-3′), 6.88 (dd, 1H, *J*=15.6, 5.0, H-3), 6.23 (dd, 1H, *J*=5.8, 1.9, H-4′), 6.19 (dd, 1H, *J*=15.6, 1.7, H-2), 5.12 (dt, 1H, *J*=5.0, 1.9, H-5′), 4.56 (dt, 1H, *J*=5.0, 1.9, H-4), 4.20 (q, 2H, OCH_2CH_3), 1.29 (t, 3H, OCH_2CH_3). ^{13}C NMR: 172.8 (C-5′), 165.9 (C-1), 153.2 (C-3′), 143.3 (C-3,), 123.8, 123.2 (C-2, C-4′), 85.1 (C-2′), 76.9(C-4), 60.8 (OCH_2CH_3), 14.0 (OCH_2CH_3). Anal. Calcd for $C_{10}H_{12}O_5$: C, 56.60; H, 5.70. Found: C, 56.45; H, 5.42.

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References and notes

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