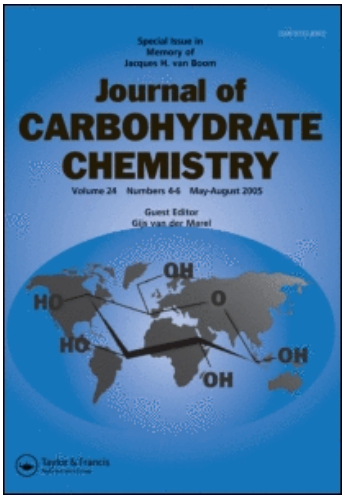

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A New Synthesis of 2-C-Methyl-d-Ribono-1,4-Lactone and the C-9/C-13 Fragment of Methynolide

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A NEW SYNTHESIS OF 2-C-METHYL-D-RIBONO-1,4-LACTONE AND THE C-9/C-13 FRAGMENT OF METHYNOLIDE

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ABSTRACT

The synthesis of the glucosaccharino lactone, 2-C-methyl-D-ribono-1,4-lactone **7** from 2,3-O-isopropylidene-D-glyceraldehyde **1** is reported. Lactone **7** was transformed into (2R,3R)-2,3-dihydroxy-2-methylpentanoic acid **18** (the C-9/C-13 fragment of Methynolid) by two new procedures which improve on existing alternatives: conversion of the epoxide derivative **9** to the episulfide **14** and subsequent reduction; and reductive opening of the 5-bromo derivative of 2,3-O-isopropylidene-2-C-methyl-D-ribono-1,4-lactone and subsequent hydrogenation.

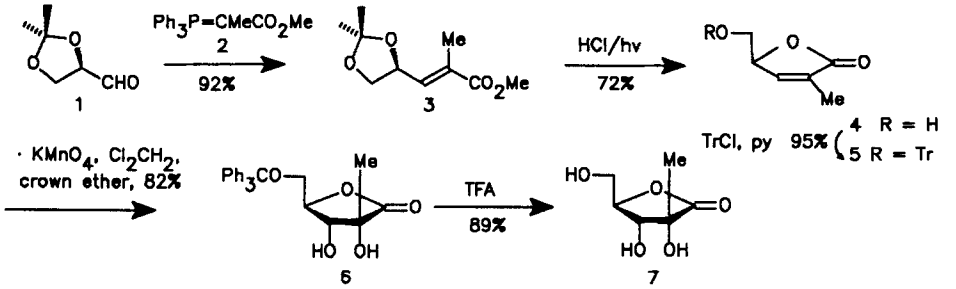
INTRODUCTION

The growing interest in the development of acyclic asymmetric synthesis, particularly in relation to the preparation of macrolide antibiotics,[1] led us to study the stereochemistry of aldol-like condensations of sulphur ylides[2] or α-diazocarbonyl compounds[3] with simple monosaccharides and their potential for the synthesis of useful synthons. These studies resulted in the development of (a) a good synthetic procedure for enantiomerically pure *threo*-α-methyl-β-hydroxycarbonyl compounds,[4] a usual structural unit of macrolides and other natural products, and (b) a stereoselective synthesis for glycidic amides with a variety of synthetic possibilities. The work involved entailed preparing (2R,3R)-2,3-dihydroxy-2,3-di-

O-isopropylidene-2-methyl-pentanoic acid **18**, the C-9/C-13 fragment of the aglycone of methymycin, a current synthon in macrolide chemistry.[1] This paper reports two new syntheses for **18**, in addition to an effective procedure for preparation of the 2-C-methyl-D-ribono-1,4-lactone **7**, a very useful adduct in the synthesis of many products of pharmacological interest,[5] and the starting product for the synthesis of **18**. These new syntheses improve on existing alternatives[6,7] based on a similar strategy.

RESULTS AND DISCUSSION

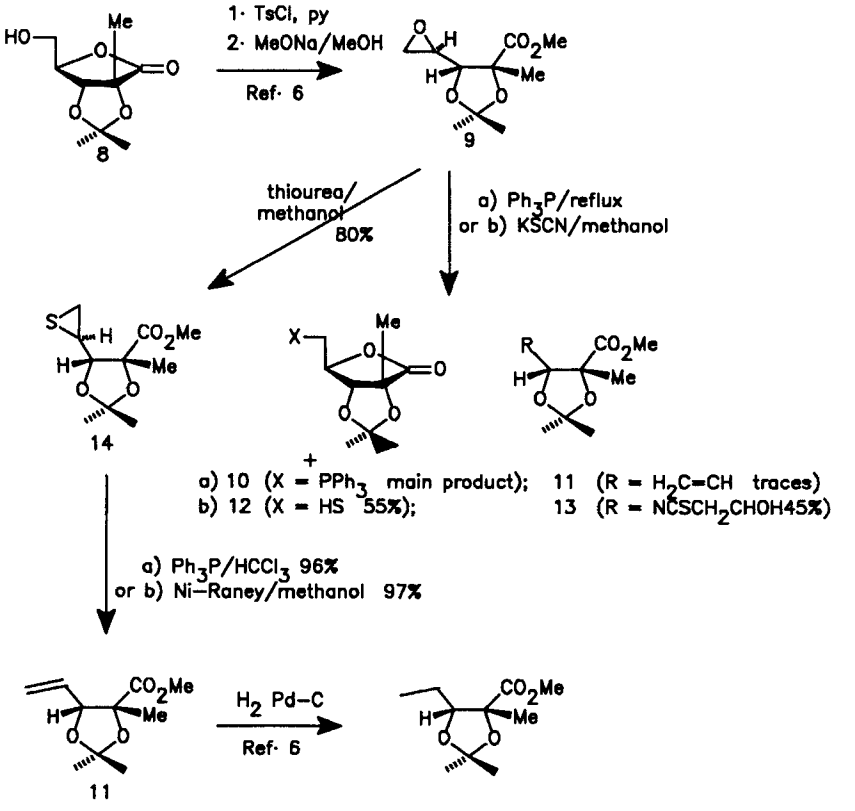
The glucosaccharino lactone, 2-C-methyl-D-ribono-1,4-lactone **7**, has two chiral centers (C-2 and C-3) of identical configuration and suitable functionalization as present in the target molecule, the acyclic acid **18**. The synthesis of **7** was first achieved by Killiani[9] from β-D-fructose by treatment with calcium hydroxide. However, the process is rather tedious, the yield is very low (10%) and the reaction time too long (a few months). This led us to explore an alternative route to **7** that offered a better yield despite the fact it involved more steps. Condensation of 2,3-O-isopropylidene-D-glyceraldehyde **1** with (1-methoxycarbonyl-ethylidene)triphenylphosphorane **2** gave the methyl E-(S)-4,5-dihydroxy-4,5-O-isopropylidene-2-methyl-2-pentenoate **3** in high yield (92%) and stereoselectivity (E isomer >98%). Its trans configuration was established by NMR.[10] Hydrolysis of **3** and photochemical isomerization with subsequent lactonization led to the butenolide **4** in a 72.2% yield. Tritylation at C5 led to **5** and hydroxylation with potassium permanganate gave, in 82% yield, the corresponding diol **6** stereospecifically. The removal of the triphenylmethyl group with trifluoracetic acid gave the 2-C-methyl-D-ribono lactone **7**. Its physical and chemical properties were the same as those of the lactone obtained by Killiani's method and consistent with literature data.[11]



Scheme 1

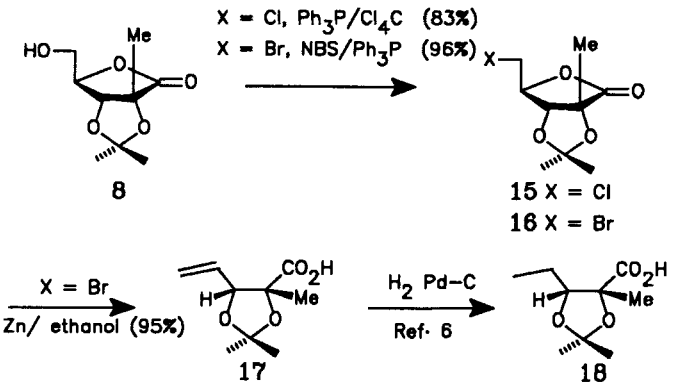
In order to transform lactone **7** into **18**, we first attempted deoxygenation with triphenylphosphine of the epoxide **9**, prepared from **7** as described elsewhere.[6] However, the

main reaction product was the triphenylphosphonium salt **10**, whose structure was assigned based on ^{1}H NMR spectra, and traces of the alkene **11** under strong reaction conditions. In a second approach, we attempted conversion of **9** into the corresponding episulphide **14** by reaction with potassium thiocyanate in methanol. However, the expected episulphide was obtained in a low yield (less than 10%), to the benefit of two main products, **12** and **13**, identified on the basis of their ^{1}H NMR and MS data.[12] Fortunately, the reaction of **9** with thiourea in methanol led to the episulphide **14** in a higher yield (80% after purification) than previously achieved[6] with potasium selenocyanate in the absence of side products **12** and **13**. The disparate behaviour of the epoxide **9** towards various nucleophilic reagents may be attributed to the preferred evolution of the initial alkoxide adduct. Thus, with triphenylphosphine and sodium thiocyanate, alkoxide lactonization was favoured, whereas with thiourea, attachment of the alkoxy group to the higher reactive imonium intermediate takes place preferentially. Finally, the episulphide **14** was converted into the methyl (2R,3R)-2,3-dihydroxy-2,3-O-isopropylidene-2-methyl-4-pentenoate **11** quantitatively by two procedures: (a) triphenylphosphine in $CHCl_3$ at room temperature for 5h; and (b) Ni/Raney in methanol under reflux for 18h.



Scheme 2

Our second approach to **18** from **7** started with the reductive opening of the 5-halo-1,4-lactone **15** and **16**.[13] Treatment of the 5-chloro lactone **15** (prepared directly from **8**) with sodium metal in dry ether led to a complex mixture of products. Fortunately, treatment of the 5-bromo derivative **16** [prepared directly from **8** in a very high yield (96% after purification) by direct halogenation of **8** with N-bromosuccinimide[14]] with zinc powder in ethanol under reflux yielded the acid **17** in a 95% yield. Finally, catalytic hydrogenation of **17** yielded the target molecule, the pentanoic acid **18** in a 94.3% yield, which was identified from spectroscopic data. While this work was in progress, a related four-step process for conversion of **8** into **18** was reported.[7]



Scheme 3

EXPERIMENTAL

Melting points are given uncorrected. IR spectra were recorded on a Beckman Aculab IV spectrophotometer; wavenumbers are expressed in cm^{-1}. ^{1}H-NMR spectra at 200 MHz were obtained on a Bruker WP 200 SY using $CDCl_3$ as solvent. Chemical shifts (δ) are expressed in ppm taking the signal of $CHCl_3$ as internal reference with notations indicating the signal multiplicity (s, singlet; d doublet; t triplet; q, quadruplet; m, multiplet). Coupling constants are expressed as J values in Hertz units. Mass spectra were recorded on a Hewlett-Packard 5988A instrument. Microanalyses were performed by the "Servicio de Microanálisis de la Universidad de Málaga". Specific rotations were measured with a Perkin-Elmer 241 polarimeter. Photochemical reactions were conducted on a Rayonet apparatus with low pressure Hg lamps of 8 w. Silica gel for column chromatography was Merck silica-gel 60 No. 7736. Analytical thin-layer chromatography was performed on Merck silica-gel 60 No. 7747.

Methyl E-(4S)-4,5-dihydroxy-4,5-O-isopropylidene-2-methyl-2-pentenoate (3). To a solution of (1-methoxycarbonylethylidene)triphenylphosphorane **2** (11 g) in 50 mL of dry

dichloromethane at 0 °C was added, dropwise, a solution of 2,3-O-isopropylidene-D-glyceraldehyde **1** (4.1g) in the same solvent (10 mL). The reaction mixture was stored overnight and then concentrated and diluted with hexane. Triphenylphosphine oxide was removed by filtration and the filtrate cooled at 5 °C. Additional precipitate was removed by filtration and the filtrate was concentrated. The crude product **3** was obtained in 92 % yield (5.8 g). Further purification of **3** was achieved by distillation at 76 °C and 0.4 mm Hg, to give 4.57 g (54%): ^{1}H NMR ($CDCl_3$) δ 6.70 (dq, 1H, J = 1.5 and 6.7 Hz, H-3), 4.87 (q, 1H, J = 6.7 Hz, H-4), 4.17 (dd, 1H, J = 8.2 and 6.7 Hz, H-5), 3.75 (s, 3H, -COOMe), 3.67 (dd, 1H, J = 8.2 and 6.7 Hz, H-5'), 1.87 (d, 3H, J = 1.5 Hz, Me at C-2), 1.46 and 1.42 (2s, 6H, CMe_2); ^{13}C NMR ($CDCl_3$) δ 167.7 (C-1), 138.5(C-3), 130.6 (C-2), 109.7 ($\underline{C}Me_2$), 72.6 (C-4), 68.6 (C-5), 51.9 ($CO_2\underline{Me}$), 26.5 and 25.7($C\underline{Me}_2$), 12.9 (Me at C-2).

Anal. Calcd for $C_{10}H_{16}O_4$: C, 59.98; H, 8.05. Found: C, 60.06; H, 8.12.

(4S)-4-hydroxymethyl-2-methyl-butenolide (4). A solution of 1g of **3** in 20 mL of methanol in the presence of 1 mL of concentrated HCl was irradiated at 253.4 nm for 16 h. The mixture was neutralized with sodium hydrogen carbonate, solids removed by filtration, the solvent evaporated at a low pressure and the product distilled at 126 °C and 1.5 mm Hg to give 0.48 g of lactone **4** (72.2%). The NMR spectral data was consistent with literature.[11]

(4S)-4-triphenylmethyloxymethyl-2-methyl-butenolide (5). The lactone **4** (5 g) was dissolved in 20 mL of anhydrous pyridine and to the solution was added triphenylmethyl chloride (15 g). The solution was kept at r.t. for 24 h. Water was added to the solution and the resulting suspension was extracted with chloroform (3 x 1 mL). The organic solution was washed with cadmium chloride solution, filtered, dried over anhydrous sodium sulphate and concentrated to dryness to give a mixture of the protected lactone and triphenylmethyl chloride. Excess triphenylmethyl chloride was removed by washing with hexane and product **5** was crystallized from methanol to give 13.7 g as a white solid (yield 95%): mp 120-121 °C; ^{1}H NMR ($CDCl_3$) δ 7.43-7.22 (m, aromatic protons, 15 H), 6.93 (d, 1H, J= 1.4 Hz; H-3), 4.94 (m, 1H, H-4), 3.31 (d, 2H, J= 5.1 Hz; H-5, H-5'), 1.92 (s, 3H, Me at C-2); ^{13}C NMR ($CDCl_3$) δ 173.9 (C-1), 146.3 (C-2), 143.3 (C-3), 128.52, 127.9, 127.66, 127.4, 127.2 (aromatic carbons), 86.9 ($\underline{C}Ph_3$), 79.9 (C-4), 63.9 (C-5), 10.7 (Me at C-2).

Anal. Calcd for $C_{25}H_{22}O_3$: C, 81.08; H, 5.94. Found: C, 80.83; H, 5.97.

5-O-Triphenylmethyl-2-C-methyl-D-ribono-1,4-lactone (6). Oxidation of **5** (3 g) was accomplished using the method of Mukaiyama,[15] but at -15 °C and for 2 h. The diol formed was crystallized as a white solid from chloroform, to give 2.8 g of pure lactone **6** (yield 82%): mp 143-145 °C; ^{1}H NMR ($CDCl_3$) δ 7.5-7.2 (m, 15H, aromatic protons), 4.40 (ddd, 1H, J= 3.7, 5.0 and 6. 0 Hz, H-4), 3.94 (d, 1H, J= 6.0 Hz, H-3), 3.47 (dd, 1H, J= 3.7 Hz and 10.7 Hz, H-5), 3.28 (dd, 1H, J= 5.0 Hz and 10.7 Hz, H-5'), 1.47 (s, 3H, Me at C-2); ^{13}C NMR

(CD_3COCD_3) δ 175.1 (C-1), 148.9, 129.04, 128.8, 128.5, 128.3, 128.0, 127.8 ($C\underline{Ph}_3$), 84.12 (C-4), 82.25 ($\underline{C}Ph_3$), 73.52 (C-3), 73.22 (C-2), 61.14 (C-5), 21.55 (Me at C-2).

Anal. Calcd for $C_{25}H_{24}O_5$.x $1H_2O$: C, 71.07; H, 6.20. Found: C, 71.29; H, 6.25.

2-C-methyl-D-ribono-1,4-lactone (7): The lactone **6** (2.8 g) in 30 mL of ethyl acetate was treated with a TFA solution (1 mL in 10 mL of water) for 3 h. The solution was neutralized with sodium hydrogen carbonate, concentrated to dryness and redissolved in hot ethyl acetate. Lactone **7** crystallized as a white solid (1 g, 89%): $[\alpha]_D^{20}$(water) +93°; mp 150-154 °C; IR., ν_{max} (cm^{-1}): 3410-3330 (-OH); 1750 (C=O, γ-lactone); ^1H NMR (D_2O) δ 4.48 (ddd, 1H, J= 3.0, 4.5 and 7.5 Hz, H-4), 4.06 (dd, 1H, J=3.0 and 15.5 Hz, H-5), 4.05 (d, 1H, J= 7.5 Hz, H-3), 3.75 (dd, 1H, J= 4.5 and 15.5 Hz, H-5'), 1.42 (s, 3H, -Me at C-2).

Methyl (2R,3S,4S)-2,3-dihydroxy-2,3-O-isopropylidene-2-methyl-4,5-epithio-pentanoate (14). To a solution of 1 g of methyl (2R,3S,4R)-2,3-O-isopropylidene-2,3-dihydroxy-2-methyl-4,5-epoxy-pentanoate **9**, (prepared by the method of Hoffmann et al.[6]), in 5 mL of methanol was added 0.61 g of thiourea previously recrystallized from methanol. The solution was stirred at room temperature for 24 h. The solvent was then evaporated under vacuum. Column chromatography on silica gel (elution with EtOAc/hexane 25:75) provided 0.8 g of the episulphide **14** as a colourless liquid (80%): ^1H NMR ($CDCl_3$) δ 3.75 (s, 3H, -CO_2Me), 3.35 (d, 1H, J= 8.6 Hz, H-3), 2.78 (ddd, 1H, J = 5.4 , 6.4 and 8.6 Hz, H-4), 2.50 (dd, 1H, J= 1.7 and 6.4 Hz, H-5), 2.26 (dd, 1H, J= 1.7 and 5.4 Hz, H-5'), 1.6 and 1.35 (2s, 6H, CMe_2), 1.55 (s, 3H, Me at C-2); ^{13}C NMR ($CDCl_3$) δ 172.31 (C-1), 110.30 ($\underline{C}Me_2$), 89.67 (C-3), 83.41 (C-2), 52.07 ($CO_2\underline{Me}$), 31.85 (C-4), 26.45 and 26.37 ($C\underline{Me}_2$), 23.30 (-Me at C-2), 20.72 (C-5); MS: 217 (M^+ -15).

Anal. Calcd for $C_{10}H_{16}O_4S$: C, 51.72; H, 6.89. Found: C, 51.84; H, 7.00.

Methyl (2R,3R)-2,3-dihydroxy-2,3-O-isopropylidene-2-methyl-4-pentenoate (11): **Procedure A**: An amount of 200 mg of the episulphide **14** was dissolved in 2 mL of chloroform and an equimolar amount of triphenylphosphine was added. The reaction was complete after 5 h, at room temperature, with quantitative conversion of **14** into the alkene **11**. The solvent was evaporated and product **11** purified by TLC (eluent, 25% EtOAc/hexane) to give 165 mg (96%).

Procedure B: An amount of 200 mg of **14** was added to a suspension of 2 g of activated Ni/Raney in 5 mL of methanol. The suspension was treated under reflux for 18 h to achieve quantitative conversion to the methyl pentenoate **11** (170 mg): ^1H NMR ($CDCl_3$) δ 5.7 (ddd, 1H, J= 6.8, 10.3 and 17.1 Hz, H-4), 5.43 (dd, 1H, J= 1.3 and 17.1 Hz, H-5), 5.27 (dd, 1H, J= 1.3 and 10.3 Hz, H-5'), 4.35 (d, 1H, J= 6.8 Hz, H-3), 3.68 (s, 3H,-CO_2Me), 1.53 (s, 3H, Me at C-2), 1.61 and 1.45 (2s, 6H, CMe_2); ^{13}C NMR ($CDCl_3$) δ 172.5 (C-1), 131.6 (C-4), 119.4 (C-5), 111.1 ($\underline{C}Me_2$), 86.2 (C-3), 84.5 (C-2), 51.7 (-CO_2Me), 26.9 and 26.7 ($C\underline{Me}_2$), 22.6 (Me at C-2).

5-Chloro-2,3-O-isopropylidene-2-C-methyl-D-ribono-1,4-lactone (15). To a solution of 2 g of **8** in 200 mL of CCl_4 were added 2 g of triphenylphosphine. The mixture was kept under reflux for 16 h, after which the reaction was checked to be complete by TLC. The solvent was evaporated under vacuum and the crude purified by column chromatography on silica gel (elution with 25% EtOAc/hexane) to give 1.8 g of **15** as a white solid (83%): mp 38 °C; ^{1}H NMR ($CDCl_3$) δ 4.69 (ddd, 1H, J= 1.0, 3.7 and 5.8 Hz, H-4), 4.48 (d, 1H, J= 1.0 Hz, H-3), 3.76 (dd, 1H, J=3.7 and 12.1 Hz, H-5), 3.65 (dd, 1H, J= 5.8 and 12.1 Hz, H-5'), 1.65 (s, 3H, Me at C-2), 1.42 (s, 6H, CMe_2); ^{13}C NMR ($CDCl_3$) δ 175.17 (C-1), 113.42 ($\underline{C}Me_2$), 82.26 (C-4), 82.03 (C-2), 81.27 (C-3), 43.45 (C-5), 26.78 and 26.66 ($C\underline{Me}_2$), 20.38 (Me at C-2); MS: 205 (M^+ -15), 207(M^+ +2-15).

Anal. Calcd for $C_9H_{13}O_4Cl$: C, 48.98; H, 5.89. Found: C, 48.78; H, 6.22.

5-Bromo-2,3-O-isopropylidene-2-C-methyl-D-ribono-1,4-lactone (16). A solution of 0.8 g of lactone **8** and 1.38 g of N-bromosuccinimide in 40 mL of dichloromethane was cooled to 0 °C and 2.04 g of triphenylphosphine was slowly added with stirring. On addition, the mixture turned to a strong orange colour. Then, 0.32 g of barium carbonate was added and the mixture heated under reflux for 30 minutes. The suspension was cooled, solids removed by filtration, and the filtrate was washed with water twice. The solvent was then evaporated under vacuum and the crude residue was diluted with hexane to precipitate the triphenylphosphine oxide. Column chromatography on silica gel (elution with EtOAc/hexane 25:75) provided 1 g of the bromo lactone **16** as a green solid (96%): mp 39 °C; ^{1}H NMR ($CDCl_3$) δ 4.70 (ddd, 1H, J= 1.0, 7.3 and 4.1 Hz, H-4), 4.45 (d, 1 H, J= 1.0 Hz, H-3), 3.59 (dd, 1H, J= 4.1 and 11.1 Hz, H-5'), 3.41 (dd, 1H, J= 7.3 and 11.1 Hz, H-5), 1.65 (s, 3H, Me at C-2), 1.43 (s, 6H, CMe_2); ^{13}C NMR ($CDCl_3$) δ 175.12 (C-1), 113.63 ($\underline{C}Me_2$), 83.01 (C-4), 82.02 (C-2), 80.93 (C-3), 30.63 (C-5), 26.95 and 26.81 ($C\underline{Me}_2$), 20.81 (Me at C-2); MS: 249 (M^+ -15), 251(M^+ +2-15).

Anal. Calcd for $C_9H_{13}O_4Br$: C, 40.75; H, 4.91. Found: C, 40.34; H, 4.83.

(2R,3R)-2,3-dihydroxy-2,3-O-isopropylidene-2-methyl-4-pentenoic acid (17). A suspension of 1.16 g of the 5-bromo derivative **16** in 20 mL of ethanol and 1.23 g of zinc powder was heated under reflux for 2 h. The suspension was cooled at room temperature and solids removed by filtration. The filtrate was diluted with water and acidified with formic acid to pH 4. The product was extracted with chloroform (3 x 1mL)and the solvent was evaporated under vacuum to yield 0.77 g of the pentenoic acid **17** (95%): IR (film) 3500, 3097, 2881, 1786 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.8 (ddd, 1H, J= 6.8, 10.3 and 17.1 Hz, H-4), 5.44 (dd, 1H, J= 1.3 and 17.1 Hz, H-5), 5.37 (dd, 1H, J= 1.3 and 10.3 Hz, H-5'), 4.37 (d, 1H, J= 6.8 Hz, H-3), 1.53 (s, 3H, Me at C-2), 1.59 and 1.43 (2s, 6H, CMe_2); ^{13}C NMR ($CDCl_3$) δ 175.99 (C-1), 131.26 (C-4), 119.84 (C-5), 110.73 ($\underline{C}Me_2$), 85.60 (C-3), 83.96 (C-2), 26.78 and 26.25($C\underline{Me}_2$), 22.30(Me at C-2).

(2R,3R)-2,3-dihydroxy-2,3-O-isopropylidene-2-methyl-pentanoic acid (18). A solution of 0.278 g of **17** in 100 mL of ethyl acetate was hydrogenated at a pressure of 45 l/inch^2 and room temperature using Pd-C as catalyst for12 h. Solids were removed by filtration and the filtrate concentrated to dryness. The crude obtained was the pure pentanoic acid **18** in liquid form (0.265 g, 94.3%): IR (film) 3500, 3000, 1750 cm^{-1}; $[\alpha]_D^{23}$ +13.0°(chloroform); ^{1}H NMR ($CDCl_3$) δ 3.79 (dd, 1H, J= 3.7 and 8.5 Hz,H-3), 1.55 (m, 2H, H-4 and H-4'), 1.51 (s, 3H, Me at C-2), 1.46 and 1.37 (2s, 6H, CMe_2), 1.1 (t, 3H, J= 7.4 Hz, H-5,5',5"); ^{13}C NMR ($CDCl_3$) δ 177 (C-1), 109 ($\underline{C}Me_2$), 86 (C-2), 83 (C-3), 26. 1 and 26.8 ($C\underline{Me}_2$), 23 (Me at C-2), 22 (C-4), 11 (C-5).

Anal. Calcd for $C_9H_{16}O_4$: C,57.44; H, 8.51. Found: C, 57.12; H, 8.47.

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REFERENCES AND NOTES

1. a) K. C. Nicolau, *Tetrahedron*, **33**, 683 (1977);
   b) S. Masamune, G. S. Bates, J. W. Corcoran, *Angew. Chem. Int. Ed. Engl.*, **16**, 585 (1977);
   c) T. G. Black, *Tetrahedron*, **33**, 3041 (1977);
   d) S. Masamune, C. U. Kim, K. E. Wilson, G. O. Spessard, P. E. Georghiou, G. S. Bates , *J. Am. Chem. Soc.*, **97**, 3512 (1975);
   e) I. Paterson, M. M. Mansuri, *Tetrahedron*, **41**, 3569 (1985).

2. M. Valpuesta-Fernández, P. Durante-Lanes, F. J. López-Herrera, *Tetrahedron*, **46**, 7911 (1990).

3. F. J. López-Herrera, M. Valpuesta-Fernández, S. García-Claros, *Tetrahedron*, **46**, 7165 (1990).

4. F. J. López-Herrera and F. Sarabia-García, *Tetrahedron Lett.*, **34**, 3467 (1993).

5. a) K. Ando, T. Yamada, Y. Takaishi and M. Shibuya, *Heterocycles*, **29**, 1023 (1989);
   b) R. E. Ireland, R. C. Anderson, R. Badoud, B. J. Fitzsimmons, G. J. McGarvey, S. Thaisrivongs, C. S. Wilcox, *J. Am. Chem. Soc.*, **105**, 1988 (1983);
   c) E. Walton et al., *J. Med. Chem.*, **12**, 306 (1961).

6. R. W. Hoffmann, W. Ladner, *Chem. Ber.*, **116**, 1631 (1983).

7. B. Deguin, J. C. Florent, C. Monneret, *J. Org. Chem.*, **56**, 405 (1991).

8. L. D. Bergel´son, E. D. Dyatlovitskaya, M. Tichy, V. V. Voronkova, *Izv. Akad. Nauk. SSSR, Ser. Khim.*, 1612 (1962).

9. H. Killiani, *Berichte*, **15**, 2953 (1882).

10. F. J. López-Aparicio, I. Izquierdo-Cubero, M. D. Portal-Olea, *Carbohydr. Res.*, **103**, 158 (1982).

11. F. J. López-Aparicio, I. Izquierdo-Cubero, M. D. Portal-Olea, *Carbohydr. Res.*, **129**, 99 (1984).

12. ^{1}H NMR data for **10** ($CDCl_3$) δ 7.5-7.1 (m, 15 H, Ph_3P); 4.4 (ddd, 1H, H-4); 4.3 (d, 1H, H-3); 3.95 (dd, 1H, H-5); 3.87 (dd, 1H, H-5'); 1.55 (s, 3H, Me at C-2); 1.35 and 1.27 (2s, 6H, $-CMe_2$). ^{1}H NMR data for **12** ($CDCl_3$) δ 4.61 (dt, 1H, H-4); 4.3 (d,1H, H-3); 2.95 (dd, 1H, H-5); 2.83 (dd, 1H, H-5'); 1.61 (s,3H, -Me at C-2); 1.40 and 1.39 (2s, 6H, $-CMe_2$); MS (m/z): 203 (M^+-15). ^{1}H NMR data for **13** ($CDCl_3$) δ 4.81 (q, 1H, H-4); 4.05 (d, 1H, H-3); 3.79 (s, 3H, $-CO_2Me$); 3.56 (d, 2H, H-5 and H-5'); 1.62 (s, 3H, Me at C-2); 1.57 and 1.41 (2s, 6H, $-CMe_2$); MS (m/z): 261 (M^++1 - 15).

13. a) J. C. Florent, J. Ughetto-Monfrin, C. Monneret, *J. Org. Chem.*, **52**, 1051 (1987);
b) C. S. Wilcox, L. M. Thomasco, *J. Org. Chem.*, **50**, 546 (1985);
c) V. Jäger, B. Häfele, *Synthesis*, 801 (1987);
d) B. Häfele, D. Schröter, V. Jäger, *Angew. Chem. Int. Ed. Engl.*, **25**, 87 (1986);
e) B. Bernet, A. Vasella, *Helv. Chim. Acta*, **67**, 1328 (1984).

14. S. Hanessian, M. M. Ponpipom, P. Lavallee, *Carbohydr. Res.*, **24**, 45 (1972).

15. T. Mukaiyama, F. Tabusa, K. Suzuki, *Chem. Lett.*, 173-174 (1983).