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Synthesis of optically pure di- to tetra-substituted cyclopentanes from sugar-derived norbornene derivatives*

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ABSTRACT

The chiral norbornene derivative **2** obtained from Lewis acid-catalyzed reaction of an L-arabinose-derived dienophile **1** and cyclopentadiene was oxidized with OsO_4–$NaIO_4$ to the dialdehyde **3**, a tetrasubstituted cyclopentane. Mild treatment of **3** with $[Rh(dppp)_2]Cl$ [dppp = $Ph_2P(CH_2)_3PPh_2$] (**4**) selectively epimerized the aldehyde adjacent to the methoxycarbonyl group to give the epi-aldehyde **8**. Under more vigorous conditions, this group was decarbonylated to give the monoaldehyde **11**, and more strenuous treatment removed the second aldehyde group to give the didecarbonylated cyclopentane derivative **5**. The structure and optical purity of **5** was confirmed by its transformation into (1*S*,2*S*)-cyclopentane-1,2-dicarboxylic acid (**7**).

INTRODUCTION

The Lewis acid-catalyzed cycloaddition of methyl (*E*)-4,5,6,7-tetra-*O*-acetyl-2,3-dideoxy-L-*arabino*-hept-2-enonate (**1**, obtained by Wittig chain-extension from *aldehydo*-L-arabinose tetraacetate) to cyclopentadiene gives the crystalline *si-exo* carboxylate norbornene adduct **2** as the major product among the four possible stereoisomeric adducts[1]. This reaction may be considered as transferring the chirality of the sugar precursor to a potential tetrasubstituted cyclopentane derivative having four functional substituents of defined absolute stereochemistry. Variation of the reaction conditions for the cycloaddition permits access to the other three adducts[1,2], and use of D-arabinose as the precursor[1] allows preparation of the four enantiomers and consequently eight of the sixteen possible tetrasubstituted cycloalkanes. The norbornene ring constrains two of the substituents on the the cyclopentane component to the *cis* disposition.

Here we describe detailed studies on the dialdehyde **3** formed by the OsO_4–$NaIO_4$ oxidation[3] of norbornene derivative **2** (compound **3** has the same absolute stereochemistry as the chiral positions in prostaglandin $PGF_{1\alpha}$ and its analogs), and show that it may be specifically monoepimerized, presumably at the position adjacent to the methoxycarbonyl group, to form the *trans*-dialdehyde. It may be noted that this conversion affords, in principle, consequent access to all sixteen stereoisomeric tetrasubstituted cycloalkanes by chirality transfer from the arabinoses. Specific decarbonylation may

* Dedicated to Professor Grant Buchanan on the occasion of his 65th birthday.

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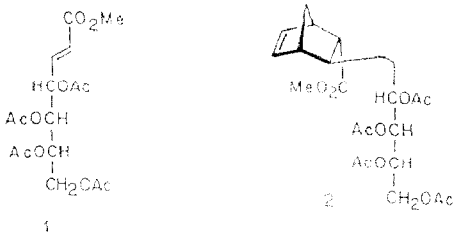
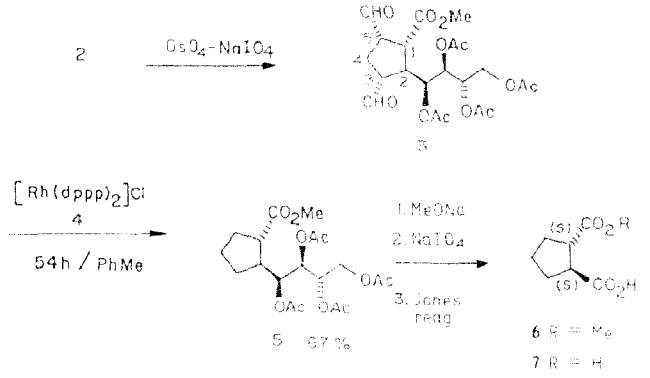


also be effected at this same position to furnish the trisubstituted cyclopentane derivatives, and didecarbonylation is likewise feasible to provide the disubstituted analogs, with full retention of optical purity.

The key reagent for these transformations is the cationic rhodium complex[4] $[Rh(dppp)_2]Cl$ (**4**) used for decarbonylation[2] as an alternative to the more commonly used Wilkinson complex $[RhCl(PPh_3)_3]$. For our purposes, compound **4** was much superior to the Wilkinson complex. The required stoichiometric amount of the latter complex amounted to four times the weight of the substrate dialdehyde, and t.l.c. monitoring of the reaction was complicated by the fact that spots of the reactants and products were masked by the spot of the reagent. Thus in the didecarbonylation of **3** (to give **5**) with the Wilkinson reagent was extremely difficult to monitor, isolation of the product was difficult, and yields were low*. In contrast, the reaction could be readily effected with a catalytic amount of **4** and the transformation was clearly observed by t.l.c., as the cationic complex **4** remained at the baseline with a developing reagent that allowed observation of reactant and product.

RESULTS AND DISCUSSION

Oxidation of the norbornene adduct[1] **2** with OsO_4–$NaIO_4$ gave the dialdehyde **3** in quantitative yield. Some difficulties in the isolation of **3** noted in the earlier paper[1] were

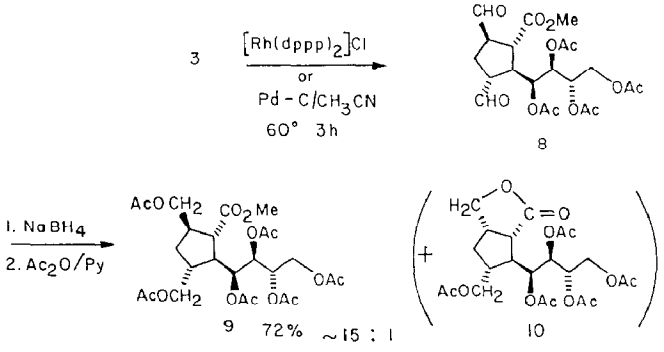


* The identity of the decarbonylated product **5** obtained from both reactions was confirmed by ^1H-n.m.r. spectroscopic comparison. However, because of the low yield (~15%), the reaction with Wilkinson's complex was not examined further.

circumvented by using solid OsO_4 rather than a solution in 1-butanol. The product was amorphous and tended to undergo partial hydration (see Experimental Section), but it was nevertheless fully characterized.

Treatment of **3** with 0.2 mol equivalents of the complex **4** in boiling toluene for 54 h gave the optically pure didecarbonylated cyclopentane derivative **5** crystalline in 67% yield. The structure attributed to **5** was supported by elemental analysis and mass spectrometry, by the disappearance of two aldehydic protons in the ^{1}H-n.m.r. spectrum, and by the appearance of three methylene carbons (δ 31.5, 29.6, and 25.4) in the ^{13}C n.m.r. spectrum that resonated as triplets in a gated-decoupling spectrum.

The absolute configuration of the chiral centers on the cyclopentane ring of **5** was confirmed through transformation of **5** into the known[5] (1*S*,2*S*)-cyclopentane-1,2-dicarboxylic acid (**7**) by sequential *O*-deacetylation, periodate degradation of the polyol chain, oxidation of the resutant aldehyde to the acid affording the monoester **6**, and mild saponification of the ester; the melting points and specific rotations of the product were in good agreement with literature values. It was thus concluded that the decarbonylation of the two aldehyde groups in compound **3** had been effected without any skeletal rearrangement or inversion of the configuration at the remaining chiral centers.

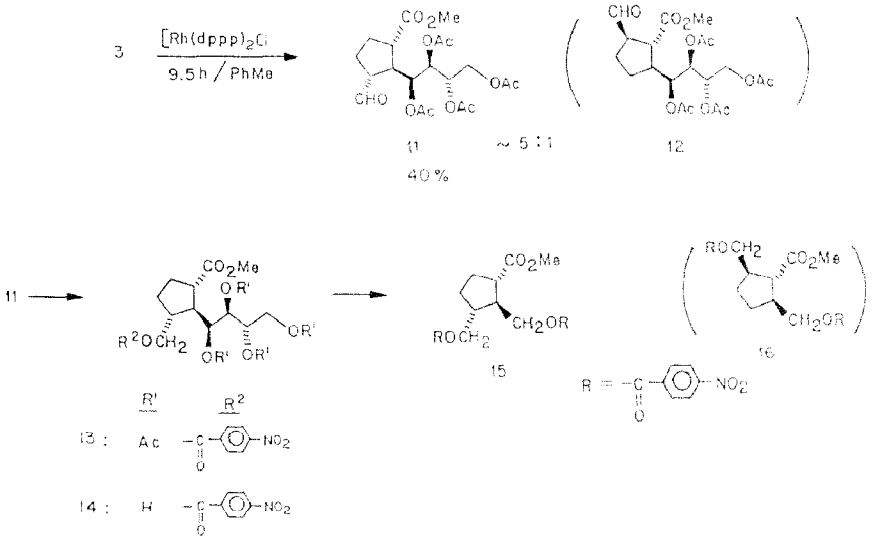


One of the two aldehyde groups in **3** was found to epimerize readily, and an epi-dialdehyde presumed to have structure **8** was shown to be the major product at a very early stage of the treatment of **3** with the reagent **4**, being manifested as a slightly faster-migrating component in t.l.c. before the onset of decarbonylation. The reaction was more conveniently effected by simply treating **3** in MeCN solution with palladium-on-carbon for 3 h at 60°, which afforded the isomeric dialdehyde **8** in 84% yield. (For another example of epimerization of an aldehyde group under heterogeneous catalysis, see ref. 4 of the preceding paper[2]).

It may be rationalized that the aldehyde group adjacent and *cis* to the methoxycarbonyl group would be the more prone to epimerize and that the *trans* product **8** would be the favored product at equilibrium. Strong evidence that this is indeed so was established by reducing the dialdehyde and acetylating the resultant diol. The product obtained, in 72% net yield on all steps from the precursor alkene **2**, had elemental analysis and spectral data consistent with its being the diacetoxymethyl analog **9** of the

precursor dialdehyde **8**, and not a monoacetoxy lactone epimeric with lactone **10** at the acetoxymethyl position. It had earlier been established that this reduction–acetylation sequence conducted on dialdehyde **3** (having an aldehyde group *cis* to the vicinal methoxycarbonyl group) gives[1] the bicyclic lactone **10**.

A very small proportion of lactone[1] **10** isolated along with **9** as the principal product may be attributed to a minor amount of dialdehyde **3** remaining in equilibrium with **8** in the product of the epimerization reaction. The possibility of a double epimerization of **3** is considered remote, as the second aldehyde group lacks and adjacent ester group and is already *trans* to the adjacent sugar chain.



The decarbonylation of dialdehyde **3** by the rhodium complex[4] could be performed selectively, giving a monodecarbonylated product at reaction times intermediate between those causing initial epimerization and those leading to didecarbonylation. The principal monodecarbonylation product was formulated as **11**, arising through removal of the aldehyde group adjacent to the methoxycarbonyl group. A minor proportion of an isomeric monoaldehyde tentatively formulated as **12** was also isolated.

The structure of the monoaldehyde **11** was established by a degradative sequence involving borohydride reduction, *p*-nitrobenzoylation to the ester **13**, selective *O*-deacetylation to the tetrol **14**, glycol cleavage–borohydride reduction and *p*-nitrobenzoylation of the resultant alcohol to give the ester **15** in 91% net yield from **14**. This product was still optically active and showed in its ^{1}H-n.m.r. spectrum nonequivalent methine groups on the cyclopentane ring. This evidence rules out a possible alternative formulation as **16** that would have resulted had the decarbonylation of **3** taken place at the position adjacent to the sugar chain. The symmetry of **16** would have made it optically inactive, and the two methine groups in the ring would have been equivalent.

In conclusion, oxidative cleavage of the double bond in the chiral norbornene

adduct **2** obtained from a sugar-derived dienophile **1**, and subsequent decarbonylation by using the cationic rhodium complex **4**, provides a route to vicinally di-, tri-, and tetra-substituted cyclopentanes, having carbon functionality at each position capable of differential functional elaboration, in optically pure form. With the ready availability[1,2] of a stereoisomeric range of substituted norbornene derivatives through the Diels–Alder reaction of sugar dienophiles and cyclopentadiene, the transformation described here should be of general interest for the syntheses of chirally substituted cycloalkanes.

EXPERIMENTAL

For general procedures, see the preceding paper[2].

*Methyl (1*R,*2*S,*3*R,*5*S*)-2-(1,2,3,4-tetra*-O-*acetyl*-L-arabino-*tetritol-1-yl)-3,5-di-formylcyclopentanecarboxylate* (**3**) *by OsO_4–$NaIO_4$ oxidation of methyl (5*S,*6S)-6-*exo-*(1,2,3,4-tetra*-O-*acetyl*-L-arabino-*tetritol-1-yl)bicyclo[2.2.1]hept-2-eno-5*-endo-*carboxylate* (**2**). — To a solution of **2** (1.42 g, 3.22 mmol) in THF (25 mL) and water (1 mL) was added OsO_4 (41 mg, 0.16 mmol), and the solution was stirred at room temperature for 10 min. To the dark, tan-colored solution an aqueous solution (11 mL) of $NaIO_4$ (1.5 g, 7.01 mmol) was added dropwise over ~3 min, and the solution was stirred at room temperature for 16 h, after which time the tan color disappeared. The resultant solid was filtered off, and the filtrate was concentrated to an aqueous mixture which was extracted with EtOAc (30 mL + 3 × 10 mL). The combined extracts were washed with saturated brine (4 × 5 mL), dried (Na_2SO_4), and evaporated to dryness. Toluene was evaporated from the residue, which on drying *in vacuo* gave **3** as viscous syrup; yield 1.58 g (quantitative), which was used directly in the next decarbonylation reaction. For analytical purposes it was freeze-dried from benzene to give an amorphous powder (which turned into a glassy solid upon heating to ~40°).

Dialdehyde **3** thus obtained was suspected not to be a single chemical species, as its n.m.r. spectra lacked good resolution and showed some broadening of the signals near the base line, presumably because of partial formation of hydrated aldehydes (acyclic or cyclic forms). Up to ~20% of such species may have been present, as judged from the CO_2CH_3 signals in the ^{1}H-n.m.r. spectrum. The product showed a somewhat diffuse spot on t.l.c. (R_F ~0.3, 1:2 toluene–EtOAc) that could not be characterized as a definite single entity; $[\alpha]_D^{25}$ −10° (*c* 1.2, $CHCl_3$); i.r. (KBr) *ν* 2960, 1720–1760 (C=O), 1380, 1200–1260, 1040, 960 cm^{-1}; ^{1}H-n.m.r. *δ* 9.66 (d, 1 H, *J* 0.6 Hz, CHO), 9.57 (d, 1 H, *J* 0.5 Hz, CHO), 5.35 (dd, 1 H, $J_{1',2'}$ 3, $J_{2',3'}$ 8 Hz, H-2'), 5.20 (dd, 1 H, $J_{2,1'}$ 8 Hz, H-1'), 5.11 (ddd, 1 H, $J_{3',4'a}$ 3, $J_{3',4'b}$ 5.2 Hz, H-3'), 4.25 (dd, 1 H, $J_{4\ gem}$ 12.5 Hz, H-4'a), 4.07 (dd, 1 H, H-4'b), 3.675 (s, 3 H, CO_2CH_3), 3.19 (m, 2 H, H-1,2), 3.06 (apparent q, 1 H, *J* ~8 Hz, H-5 or 3), 2.74 (m, 1 H, H-3 or 5), 2.1–2.5 (m, 2 H, CH_2 of C-4); ^{13}C-n.m.r. *δ* 199.7 (CHO), 190.5 (CHO), 170.9–169.7 (C=O of Ac and CO_2CH_3), 71.3, 69.2, 68.8 (C-1',2',3'), 61.6 (C-4'), 52.9, 52.5, 52.2 (two carbons of cyclopentane and CO_2CH_3), 47.0, 43.1 (two carbons of cyclopentane), 26.0 (C-4 of cyclopentane), 19.9–21.1 (CH_3 of Ac).

Anal. Calc. for $C_{21}H_{28}O_{12}$: C, 53.40; H, 5.97. Found: C, 53.23; H, 6.02.

Decarbonylation of dialdehyde **3** *to methyl (1S,2S)-2-(1,2,3,4-tetra-O-acetyl-*L*-arabino-tetritol-1-yl)cyclopentanecarboxylate* (**5**). — Compound **3** (1.05 g, 2.15 mmol) in toluene (100 mL) was treated with 400 mg (0.430 mmol) of [Rh(dppp)$_2$]Cl (**4**) in the same general manner as described in the preceding paper[2]. After 54 h, the mixture was filtered, and the filtrate was evaporated to ~10 mL. It was applied onto a short column of silica gel (10 g, dry column) and eluted with 1:1 toluene–EtOAc. Evaporation of the eluate gave a solid (648 mg) which was purified on a column of silica gel (8 g, 2:1 hexane–EtOAc, R_f 0.35 with this solvent) to give **5** as crystals; yield 605 mg (67% from alkene **2**). Recrystallization from ~1:5 EtOAc–hexane gave an analytical sample: m.p. 105–106°, $[\alpha]_D^{27}$ +4.3° (*c* 2.4, $CHCl_3$); i.r. (KBr) ν 2960, 1725–1755 (C=O), 1370, 1210–1270, 1030, 970, 610 cm^{-1}; ^{1}H-n.m.r.: δ 5.32 (dd, 1 H, $J_{1',2'}$ 2, $J_{2',3'}$ 8.9 Hz, H-2'), 5.11 (dd, 1 H, $J_{1',2'}$ 9.8 Hz, H-1'), 5.01 (ddd, 1 H, $J_{3',4'a}$ 2.8, $J_{3',4'b}$ 4.8 Hz, H-3'), 4.21 (dd, 1 H, $J_{4'gem}$ 12.5 Hz, H-4'a), 4.08 (dd, 1 H, H-4'b), 3.66 (s, 3 H, CO_2CH_3), ~2.5 (m, 2 H, H-1,2), 2.15, 2.07, 2.05, 2.02 (each s, 3 H, 4 × Ac), 1.3–2 (m, 6 H, CH_2 of C-3,4,5); ^{13}C-n.m.r.: δ 176.4 (CO_2CH_3), 170.6, 170.5, 169.8 (C=O of Ac), 73.6, 69.6, 68.4 (C-1',2',3'), 61.9 (C-4'), 51.6 (CO_2CH_3), 47.1, 44.4 (C-1,2), 31.5, 29.6 (C-3,5), 25.4 (C-4), 20.8, 20.6 (triple intensity, CH_3 of Ac); *m/z* (rel. intensity, composition) 385 (<1, $M^+ - OCH_3$), 158 (16, $C_7H_{10}O_4$), 43 (100, CH_3CO).

Anal. Calc. for $C_{19}H_{28}O_{10}$ (416.4): C, 54.80; H, 6.78. Found: C, 54.89; H, 6.80.

Transformation of **5** *into (1S,2S)-*trans*-cyclopentane-1,2-dicarboxylic acid* (**7**). — Compound **5** was conventionally deacetylated with catalytic NaOMe in MeOH to give the corresponding tetrol; yield 92%; m.p. 126–127°, $[\alpha]_D^{26}$ +45° (*c* 0.9, MeOH); i.r. (KBr) ν 3360 (br.), 1715 (C=O), 1450, 1275, 1080, 1020 cm^{-1}; ^{1}H-n.m.r. (C_5D_5N): δ 4.14–4.5 (5H, H-1',2',3',4'), 3.63 (s, 3 H, CO_2CH_3), 3.16 (m, 2 H, H-1,2), ~1.9 and ~1.5 (each m, 3 H, total 6H, CH_2 of C-3,4,5).

Anal. Calc. for $C_{11}H_{20}O_6$ (248.3): C, 53.21; H, 8.12. Found: C, 53.26; H, 8.14.

The foregoing tetrol (210 mg, 0.845 mmol) in MeOH (10 mL) was treated with an aqueous solution (5 mL) of $NaIO_4$ (605 mg, 2.83 mmol) for 0.5 h at room temperature. Extractive work up (CH_2Cl_2) in a manner similar to that described for the OsO_4–$NaIO_4$ oxidation of **2**, and evaporation, gave a residue that was subsequently oxidized with the Jones reagent[6] (0.5 mL, in acetone, 0.5 h, 0°) to give the monomethyl ester **6** as an oil; yield 140 mg (96%); $[\alpha]^{26}_{578}$ +84° (*c* 0.6, MeOH); ^{1}H-n.m.r.: δ 3.71 (s, 3 H, CO_2CH_3), 3.15 (m, 2 H, H-1,2), 1.7–2.2 (6 H, 3 × CH_2).

The monomethyl ester **6** (70 mg, 0.41 mmol) in MeOH (0.5 mL) was hydrolyzed with 2M NaOH (0.6 mL) for 2 h at room temperature. The solution was then evaporated to about half the original volume, water (~0.5 mL) was added, and the solution was washed with ether (2 × 1 mL). The aqueous layer was then acidified (6M HCl) and extracted with EtOAc (6 × ~1 mL) to give 53 mg (82%) of crystalline **7**. Recrystallization from hot water gave an analytical sample; m.p. 183–185°, $[\alpha]_D^{26}$ +81° (*c* 1.4, MeOH). lit.[5a] m.p. 180–181°, $[\alpha]_D$ +87.6° (MeOH); ^{1}H-n.m.r. ($CDCl_3$ + acetone-d_6): δ ~2.1, ~3.7 (very br. CO_2H), 3.16 (m, 2 H), 2.08 (m, 2 H), 1.91 (m, 2 H), 1.75 (m, 2 H).

Anal. Calc. for $C_7H_{10}O_4$ (158.2): C, 53.16; H, 6.37. Found: C, 53.06; H, 6.41.

Epimerization of dialdehyde **3** *to the 1*R*,2*S*,3*R*,5*R *isomer* **8** *and characterization as*

*methyl (1S,2S,3R,5R)-3,5-bis(acetoxymethyl)-2-(tetra-*O*-acetyl-*L*-arabino-tetritol-1-yl)cyclpentanecarboxylate* (**9**). — To a suspension of 10% palladium-on-carbon (160 mg) in MeCN (5 mL) (pretreated under 50 lb. in $^{-2}$ of H_2 in a Parr hydrogenation apparatus for 3 min with subsequent purging of H_2 by bubbling N_2 through the suspension for a few min) was added a solution of **3** (387 mg 0.819 mmol) in MeCN (5 mL), and the stirred mixture was heated for 3 h at 60°. T.l.c. of the mixture showed that the spot of **3** had almost disappeared and the epi-aldehyde **8** (R_F 0.43, 1:2 toluene–EtOAc) was the sole product. The entire mixture was transferred to a column of silica gel (4 g, dry column) which was eluted with EtOAc to give **8** as a glassy solid; yield 318 mg (84% from **2**); ^{1}H-n.m.r.: δ 9.65 (d, 1 H, $J \sim 1$ Hz, CHO), 9.63 (d, 1 H, $J \sim 1$ Hz, CHO), 5.34 (dd, 1 H, $J_{1',2'}$ 4, $J_{2',3'}$ 7.4 Hz, H-2'), 5.23 (dd, 1 H, $J_{1',2'}$ 6 Hz, H-1'), 5.11 (ddd, 1 H, $J_{3',4'a}$ 3, $J_{3',4'b}$ 5.4 Hz, H-3'), 4.27 (dd, 1 H, $J_{4\ gem}$ 12.5 Hz, H-4'a), 4.08 (dd, 1 H, H-4'b), 3.74 (s, 3 H, CO_2CH_3), ~3.2 (m, 2 H, H-1, 3 or 5), 3.04 (apparent q, 1 H, $J \sim 7$ Hz, H-2), 2.77 (m, 1 H, H-5 or 3), 2–2.3 (m, 2 H, CH_2 of C-4), 2.115, 2.055 (× 2), 2.047 (each s, 3 H, Ac).

Conversion of **8** *into* **9**. — The foregoing compound **8** (300 mg, 0.635 mmol) was treated with $NaBH_4$ (55 mg, 1.5 mmol) in MeOH (5 mL) for 0.5 h under ice-bath cooling. The solution was then acidified with M HCl (1.5 mL) and evaporated to an aqueous mixture, extractive processing (CH_2Cl_2) of which gave a solid (289 mg), 245 mg of which was acetylated with Ac_2O (0.2 mL) and pyridine (2 mL). The crude product was chromatographed on a column of silica gel (14 g, 1:1 hexane–EtOAc) to give crystals of **9**; yield 207 mg, 72% overall from alkene **2**. Recrystallization from ether–hexane (~1:1) gave an analytical sample; m.p. 70–73°, $[\alpha]_D^{27}$ −22° (*c* 2.3, $CHCl_3$); i.r. (KBr) ν 1725–1750 (C=O), 1370, 1230 (br.), 1030 cm^{-1}; ^{1}H-n.m.r.: δ 5.32 (dd, 1 H, $J_{1',2'}$ 3.5, $J_{2',3'}$ 7 Hz, H-2'), 5.26 (dd, 1 H, H-1'), 5.07 (ddd, 1 H, $J_{3',4'a}$ 3, $J_{3',4'b}$ 5.6 Hz, H-3'), 4.25 (dd, 1 H, $J_{4'gem}$ 12.4 Hz, H-4'a), 4.07 (dd, 1 H, H-4'b), 4.14, 4.05, 3.96, 3.955 (2 sets of AB part of ABX system, total 4 H, $J_{AB} \sim 11$ and ~11, $J_{AX} \sim 7$ and ~7, $J_{BX} \sim 6$ and ~7 Hz, C*H*$_2$OAc on C-3 and C-5), 3.71 (s, 3 H, CO_2CH_3), ~2.5 (m, 2 H skeletal H), ~1.7 (m, 1 H skeletal H), other skeletal protons on the cyclopentane ring were overlapped by Ac signals), 2.04, 2.055 (× 2), 2.06, 2.10, 2.12 (each, s, 3 H, Ac); *m/z* (rel. intensity, composition): 529 (1, $M^+ - OCH_3$), 487 (2, 529 − CH_2CO), 43 (100, CH_3CO).

Anal. Calc. for $C_{25}H_{36}O_{14}$ (560.6): C, 53.57; H, 6.47. Found: C, 53.58; H, 6.50.

A slower-moving fraction from the foregoing silica gel column gave the bicyclic lactone[1] **10** (12 mg).

Selective decarbonylation of dialdehyde **3** *to methyl (1S,2S,3R)-3-formyl-2-(tetra-*O*-acetyl-*L*-arabino-tetritol-1-yl)cyclopentanecarboxylate* (**11**) *and its (5R) formyl isomer* (**12**). — Compound **3** (348 mg, 0.734 mmol) in toluene (30 mL) was heated with 80 mg (0.086 mmol) of rhodium complex **4** in the same way as described for the preparation of **5**, but the reaction was terminated after 9.5 h. The mixture became homogeneous, and the resulting solution was evaporated to ~5 mL and applied to a column of silica gel (4 g, dry column). Elution with 1:1 toluene–EtOAc gave a mixture (204 mg) which consisted mostly of isomeric monoaldehydes (**11** and **12**, ~5:1 by ^{1}H-n.m.r.) and a small amount of **5**. Chromatographic separation on a column of silica gel (20 g, 1:1 hexane–

EtOAc) gave 126 mg (40%) of crystalline **11** (R_F 0.36 with the foregoing solvent) and 12 mg of **12** as a glassy solid (R_F 0.29 with the same solvent). An analytical sample of **11** was obtained by recrystallization from ~1:5 EtOAc–hexane; m.p. 103–105.5°, $[\alpha]_D^{27}$ +2° (*c* 1.4, $CHCl_3$); i.r. (KBr) *v* 1725–1755 (C=O), 1370, 1200–1260, 1160, 1060, 1025, 975, 610 cm^{-1}; ^{1}H-n.m.r.: δ 9.58 (d, 1 H, J ~1 Hz, CHO), 5.31 (dd, 1 H, $J_{1',2'}$ 2.9, $J_{2',3'}$ 8.2 Hz, H-2'), 5.21 (dd, 1 H, $J_{1,2}$ 8.5 Hz, H-1'), 5.07 (ddd, 1 H, $J_{3',4'a}$ 3, $J_{3',4'b}$ 5.1 Hz, H-3'), 4.23 (dd, 1 H, $J_{4\ gem}$ 12.5 Hz, H-4'a), 4.06 (dd, 1 H, H-4'b), 3.69 (s, 3 H, CO_2CH_3), 3.15 (ddd, 1 H, $J_{1,2}$ and/or $J_{2,3}$ 5.2, 6.8 Hz, H-2), ~2.7 (m, 2 H, H-1,3), 1.7–2 (m, 4 H, CH_2 of C-4,5), 2.14, 2.06 (×2) 2.045 (each, s, 3 H, Ac); ^{13}C-n.m.r.: δ 200.3 (CHO), 174.8 (CO_2CH_3), 170.6, 170.4, 170.0, 169.8 (C=O of Ac), 72.2, 69.4, 68.8 (C-1',2',3'), 61.8 (C-4'), 54.1 (C-3), 51.9 (CO_2CH_3), 46.9, 42.6 (C-1,2), 30.2, 26.8 (C-4,5), 20.8, 20.6 (CH_3 of Ac); *m/z* (rel. intensity, composition) 413 (2, $M^+ - OCH_3$), 371 (3, 413 – CH_2CO), 43 (100, CH_3CO).

Anal. Calc. for $C_{20}H_{28}O_{11}$ (444.4): C, 54.05; H, 6.35. Found: C, 54.04; H, 6.39.

^{1}H-N.m.r. data for compound **12**: δ 9.62 (d, 1 H, J 0.8 Hz, CHO), 5.29 (dd, 1 H, $J_{1',2'}$ 2.2, $J_{2',3'}$ 8.7 Hz, H-2'), 5.15 (dd, 1 H, $J_{1',2'}$ 9.6 Hz, H-1'), 5.02 (ddd, 1 H, $J_{3',4'a}$ 2.8, $J_{3',4'b}$ 4.7 Hz, H-3'), 4.21 (dd, 1 H, $J_{4\ gem}$ 12.5 Hz, H-4'a), 4.08 (dd, 1 H, H-4'b), 3.70 (s, 3 H, CO_2CH_3), ~3 (m, 2 H), 2.57 (m, 1 H), 1.37 (m, 1 H), 2.15, 2.07, 2.05, 2.03 (each, s, 3 H, Ac).

Transformation of **11** *into methyl (1S,2S,3R)-2,3-bis(*p*-nitrobenzoyloxymethyl)-cyclopentanecarboxylate* (**15**). — Monoaldehyde **11** (298 mg, 0.671 mmol) was reduced with $NaBH_4$ (44 mg, 0.86 mmol) in the same manner as described in the preparation of **9**, affording 302 mg (quant.) of a thick syrup, 296 mg of which was treated in pyridine (3 mL) with *p*-nitrobenzoyl chloride (145 mg, 0.781 mmol) for 1 h at room temperature. Conventional extractive processing ($CHCl_3$) gave **13** as a viscous syrup; yield 354 mg (90%); $[\alpha]_D^{25}$ –13° (*c* 1, $CHCl_3$); i.r. (KBr) *v* 1725–1750 (C=O), 1530 (NO_2), 1370, 1275, 1220 (br.) cm^{-1}; ^{1}H-n.m.r.: δ 8.29 (m, 4 H, aromatic H), ~5.37 (m, 2 H, H-1',2'), 5.10 (m, 1 H, $J_{3',4'a}$ 2.8, $J_{3',4'b}$ 6.0 Hz, H-3'), 4.40 (m, 2 H, AB part of ABX, $CH_2OCOC_6H_4NO_2$), 4.26 (dd, 1 H, $J_{4\ gem}$ 12.3 Hz, H-4a), 4.04 (dd, 1 H, H-4b), 3.70 (s, 3 H, CO_2CH_3), 2.96 (m, 1 H, H-1), 2.59 (m, 1 H, H-2), 1.7–2.3 (m, 5H, skeletal H on cyclopentane), 2.09, 2.075, 2.02, 2.00 (each, s, 3 H, Ac).

Anal. Calc. for $C_{27}H_{33}NO_{14}$ (595.6): C, 54.45; H, 5.58; N, 2.35. Found: C, 54.51; H, 5.66; N, 2.18.

Compound **13** was selectively deacylated as follows[7]. To a solution of **13** (314 mg, 0.5 mmol) in dry MeOH (2.5 mL) was added ~0.35M HCl in MeOH (2.5 mL of a solution prepared by adding 0.2 mL of AcCl to 10 mL of dry MeOH). The solution was kept for 12 h at room temperature and then heated for 4 h at 60°. Evaporation of the solution afforded crystals of **14**. The residual liquid (~1 mL) was taken out by pipette, and the crystals were further washed with cold MeOH (2 × 1 mL) in the same way, and finally collected by filtration with the aid of ether, giving 167 mg of **14**; total yield 74%; m.p. 139–141°. One recrystallization from MeOH raised the m.p. to 141–143°; $[\alpha]_D^{26}$ +1° (*c* 0.4, MeOH); i.r. (KBr) *v* 3400, 3300, 1740, 1725 (C=O), 1525, 1520 (NO_2), 1285, 720 cm^{-1}.

Anal. Calc. for $C_{19}H_{25}NO_{10}$ (427.4): C, 53.39; H, 5.89; N, 3.28. Found: C, 53.22; H, 5.94; N, 3.24.

A 143-mg (0.335 mmol) sample of **14** was treated with $NaIO_4$ (230 mg, 1.08 mmol) in a manner similar to that described for the transformation of **5** into **7**. The resulting aldehyde (113 mg, oil, quant.) was reduced with $NaBH_4$ (20 mg, 0.53 mmol) in MeOH (3 mL) to give the 2-hydroxymethyl derivative (103 mg, oil, 96%), which was then treated with *p*-nitrobenzoyl chloride (75 mg, 0.40 mmol) in pyridine (1 mL) (15 min at 0° and then 1 h at room temperature). Conventional extractive processing ($CHCl_3$) gave a syrup (164 mg) which was purified on a column of silica gel (4 g, 10:1 toluene–EtOAc) to give **15** as a thick syrup; yield 141 mg, 95%, (91% overall from **14**); $[\alpha]_D^{24}$ +7° (*c* 1, $CHCl_3$); i.r. (KBr) *v* 2960, 1715–1745 (C=O), 1520, 1530 (NO_2), 1350 (br.) 1270–1280, 1100, 715 cm^{-1}; ^{1}H-n.m.r.: δ 8.24 (m, 8 H, aromatic), 4.57 and 4.42 (AB part of ABX, 2 H, J_{AB} 11.2, J_{AX} 5.3, J_{BX} 7 Hz), 4.45 (AA′ part of AA′X, 2 H, foregoing total 4 H, 2 × $CH_2COC_6H_4NO_2$), 3.65 (s, 3 H, CO_2Me), 2.82, 2.66, 2.35 (each, m, 1 H, total 3 H), 1.9–2.1 (m, 3 H), 1.75 (m, 1 H).

Anal. Calc. for $C_{23}H_{22}N_2O_{10}$ (486.4): C, 56.79; H, 4.56; N, 5.76. Found: C, 56.84; H, 4.59; N, 5.72.

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