Tetrahedron Vol. 46, No. 20, pp. 7165-7174, 1990
Printed in Great Britain

0040 4020/90 $3.00+.00
Pergamon Press plc

REACTION OF METHYL DIAZOACETATE WITH 2,3 O-ISOPROPYLIDENE-D-GLYCERALDEHYDE. STEREOSELECTIVITY IN THE SYNTHESIS OF 2-DEOXY-D-ALDONATES AND 2-DEOXY-γ,D-ALDONOLACTONES.

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(*Received in UK* 31 *May* 1990)

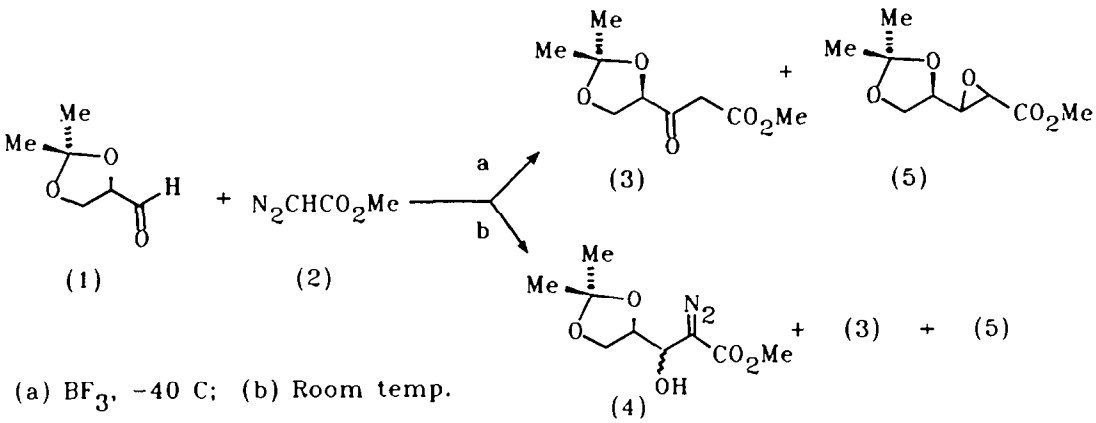
Abstract: The reaction of 2,3-*O*-isopropylidene-D-glyceraldehyde with diazoacetates are revised. In the absence of catalyst, the methyl (3S, 4R) and (3R, 4R)-4,5-*O*-isopropylidene-2-diazo-3,4,5-trihydroxypentanoate (**4a** and **4b**) were the new and main products in a high stereoselective reaction (84:16). These products were easily converted into the corresponding 2-deoxy-3-ulosonates (**3**), 2-deoxy-aldonates (**6**, **7** and **8**) and 2-deoxy-γ,D-aldonolactones (**9** and **10**).

One of the more attractive and difficult problems of synthesis is how can we control stereochemically the synthesis of acyclic compounds[1]. Monosacharides and derivatives are often employed as chiral synthons or templates for stereospecific synthesis of several types of compounds with multiple asymmetric centers[2].

We report in this paper, the first results of a stereochemical study of the reaction of 2,3-*O*-isopropylidene-D-glyceraldehyde (**1**) with methyl diazoacetate (**2**). This reaction was previously studied in this laboratory[3] to facilitate the synthesis of ß-ketoesters derived from sugars. These compounds are potentially useful for synthetic processes because of the well established reactivity of their ß-ketoester groups. Consequently, these compounds have been used for the synthesis of polyhydroxyalkyl-pyrimidine derivatives and pyrimidine-C-nucleosides[4]. These previous works describe only the synthesis of this type of ß-ketoester product (**3**). However, this present work revealed that slight modifications of the reaction gave rise to different results, and this observation suggests new applications and possibilities.

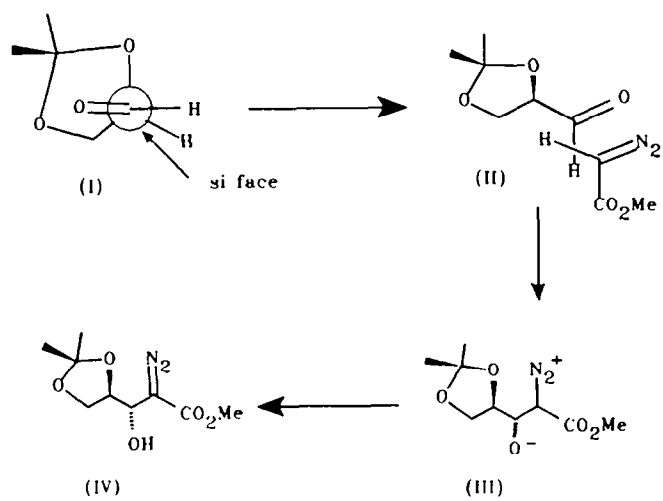
For example, the previously described[3] reaction between (**1**) and (**2**) in ethyl ether, at -40° C, and in the presence of a catalytic amount of borontrifluoride gives a high yield of the ß-ketoester only (**3**). In the absence of the catalyst, the reaction gives a mixture of (3S, 4R) and (3R,4R)-4,5-O-isopropylidene-2-diazo--3,4,5-trihydroxypentanoates (**4a**) and (**4b**) (84:16) plus small amounts of (**3**) and traces of the epoxyderivatives (**5**) (11/59/< 5; (**3**)/(**4**)/(**5**)). The formation of products similar to (**4**) is described by other autors[5], as the result of a reaction between a potassium or lithium salt of ethyl diazoacetate and aldehydes. Analogously, the formation of epoxiderivatives similar to (**5**), has been described in the reaction of (**1**) with diazoalkanes[6]. Thus the greater acidity of the α-proton of diazoacetates in neutral media appears to be sufficient for its removal by the intermediate alkoxide, to form mainly ß-hydroxy-α-diazoesters; unlike the similar reactions with diazomethane and other less acidic diazoalkanes which give rise mainly to the epoxiderivatives. The presence of catalytical amounts of acid (BF_3-etherate), were sufficient to: a) reduce

the nucleophyllic alkoxide activity required to produce the epoxide; and b) to reduce the basicity required to produce the ß-hydroxy-α-diazoacetate; and c) this, in turn, via the ß-hydrogen-shift, favours the formation of the ß-ketoester (3) (Scheme I).



Scheme I

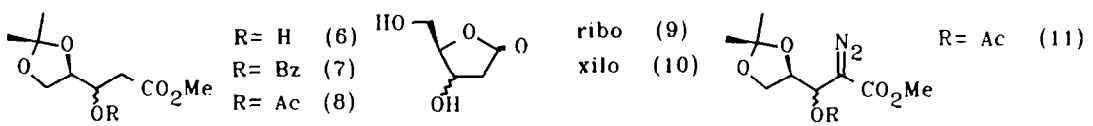
The stereoselectivity observed in the formation of the 3-hydroxy-2-diazo-acetates (4) is easy to understand because the diazoacetate approaches more easily the *si* face of the aldehydic carbonyl group of (1), in the preferred conformation (I). The additional, mutual, electrostatic stabilization between the N_2^+ and O^- groups during the formation of the adduct (II) must lead prefentially to a *like* (*lk*) approach (*si,si*) with *unlike*-1,2 (*ul*-1,2) relative topology (*si*,R), a *lk,ul-1,2* process[7], to give a *like, unlike* (*l,u*) product (III). This is finally



Scheme II

transformed by the transfer of a proton to (**IV**) (a *l* product, **4a**) as the main product. The formation o (**4b**), a *u* product,could be explained as the result of a *lk* (less favoured) aproximation to the *re* face of (**1**), a *lk,lk*-1,2 process.

Column chromatography (hexane-ethyl acetate 3:2) gave pure (**3**), an unresolvable mixture of the two isomers (**4**) and also another mixture of stereoisomers of (**5**). The latter was partially resolved by column chromatography (hexane-ethyl acetate 3:1) into a mixture of the *trans*-isomers of (**5**) and one of the *cis*-isomers of (**5**) in pure state. The structure of compounds (**4**) were established by two tests, or two steps. Firstly, the typical absorbtion of diazo group appeared in the infrared at 2080 cm^{-1}. Secondly, their C-3 configurations were determined by their stereospecific transformation into a mixture of isomers (**6**), that were separated and characterized by reference to the same products described in the literature[8,9].



Scheme III

Reduction of (**3**) with $NaBH_4$ in methanol, was shown to be non-stereoselective, and gave a 57:43 proportion of the compounds (**6b:6a**), respectively. Nevertheless, the higher stereoselectivity shown during the preparation of (**4**) (84:16, **4a:4b**) allowed us to convert them into (**6**) by catalytic hydrogenation in ethyl acetate, and this suggested an alternative and more stereoselective route to compounds (**6a**). The same reaction in methanol, produced the two lactones (**9**) and (**10**). In both cases, the process did not affect the configuration at C-3, and the original stereocomposition was maintained.

The *cis,trans* configuration of the three isomers (**5**) was assigned by ^{1}H-NMR spectroscopy. Thus, the pure isolate isomer shows a $J_{2,3}$ of 4.4 Hz, a typical value for a *cis*-epoxide. The mixture of the two unresolvable epoxides have values of 1.89 and 1.81 Hz, typical for *trans*-epoxides. Moreover, the ^{1}H-NMR spectra of these epoxides are very similar to those of the corresponding N,N-dimethyl amides[10].

The mixed compounds (**6**) were benzoylated and acetylated to give the two mixtures (**7**) and (**8**), in the usual way, and separated by column chromatography. The acetate mixture (**8**) was also obtained from the mixture of (**4**); this offers a more stereoselective route to the (**8a**) isomer. In addition, both the mixture (**6**) and each of its isolated components were converted respectively, into both or one of the corresponding lactones (**9**) or (**10**), by acid hydrolysis, and this confirmed the previous configurational assignments o compounds (**4**) and (**6**).

As mentioned earlier in this present work, many of these compounds are potential chirons for synthetic processes and we are studying some of these transformation for the synthesis of products of possible pharmaceutical interest.

EXPERIMENTAL PART

General methods. IR spectra were recorded in chloroform soluion with a Perkin-Elmer 883 spectrometer. UV spectra were recorded with a HP-5482A spectrophotometer. Optical rotations were measured at 18-20°C with a Perkin-Elmer mod. 241 polarimeter. Low resolution mass spectra in the electron impact (EIMS) mode were recorded with a HP-5988; high resolution specta were obtained in the Ottawa-Carlenton Universities Mas Spectrometry Centre. ^{1}H and ^{13}C-NMR spectra were recorded using a Bruker WP 200 SY spectrometer. Proton chemical shifts are referenced to the residual chloroform signal (δ 7.24) and carbon chemical shifts to the solvent ($^{13}CDCl_3$ = 77 ppm). The multiplicity of ^{13}C resonances was determined by INEPT experiments. TLC were performed on silicagel 60 F 254 plates and column chromatography was caried out on silicagel 60 (70-230 mesh).

Reaction of 2,3-O-isopropylidene-D-glyceraldehyde (1) with methyl diazoacetate (2). Synthesis of methyl (4R)-4,5-O-isopropylidene-3-keto-4,5-dihydroxypentanoate (3) and methyl (3S,4R) and (3R,4R)--4,5-O-isopropylidene-2-diazo-3,4,5-trihydroxypentanoates (4a) and (4b).

Method A: 2.04 g (15.7 mmol) of 2,3-O-isopropylidene-D-glyceraldehyde (**1**) were mixed with 1.90 g (19.0 mmol) of methyl diazoacetate (**2**) and left over-night at room temperature. Afterwards, the mixture showed two new spots (TLC on silicagel, hexane-ethyl acetate, 4:1), which were separated by column chromatography with the same eluent. The less polar product (0.35 g, 11%), gave a positive test with $FeCl_3$, and showed to be methyl (4R)-4,5-O-isopropylidene-3-keto-4,5-dihydroxypentanoate (**3**)[3]. The second product (2.13 g, 59%) proved to be a mixture of methyl (3S,4R) and (3R,4R)-4,5-O-isopropylidene-2-diazo-3,4,5--trihydroxypentanoates (**4a**) and (**4b**), in a (84:16) proportion. In addition, there were traces of glycidic esters (**5**), (< 5 % by ^{1}H-NMR).

Method B: To a cooled (-40°C) mixture of 5.43 g (42 mmol) of 2,3-O-isopropylidene-D-gliceraldehyde (**1**) and 4.18 g (42 mmol) of methyl diazoacetate (**2**), 5 ml of diethyl ether containing a few drops o borontrifluoroetherate were slowly added. Fifteen minutes later, when temperature had risen to -30°C, a slow evolution of nitrogen was observed. The reactants were allowed to rise to room temperature, and kept overnight. The final column chromatography yield was 6.0 g (71%) of methyl (4R)-4,5-O-isopropylidene--3-keto-4,5-dihydroxypentanoate (**3**), plus traces of glycidic esters (**5**), (< 5 % by ^{1}H-NMR).

(**3**)[3]: colourless oil, b.p. 88°C (0.3 mm Hg); Rf 0.52 (hexane-ethyl acetate, 3:1); $[\alpha]_D^{20}$ +44.69° (c 0.98, MeOH); UV λ_{max} nm MeOH: 242 and 208 ; ^{1}H-NMR ($CDCl_3$) δ ppm: 4.48 (dd, 1H, J = 7.7 and 5.3 Hz, H-4), 4.17 (dd, 1H, J = 8.8 and 7.7 Hz, H-5), 4.04 (dd, 1H, J = 8.8 and 5.3 Hz, H-5'), 3.70 (s, 3H, OMe), 3.62 (d, 1H, 17.0 Hz, H-2), 3.58 (d, 1H, 17.0 Hz, H-2'), 1.44 and 1.34 (two s, 6H, CMe_2), 11.8 (s, OH enolic form), 5.45 (s, vinylic proton in the enolic form). ^{13}C-NMR, ($CDCl_3$) : 203.0 (C-3), 167.0 (C-1), 110.9

($\underline{C}Me_2$), 79.7 (C-4), 66.1 (C-5), 51.8 (OMe), 45.0 (C-2), 25.6 and 24.5 ($C\underline{Me}_2$).

(4a and 4b): yellow oil; Rf= 0.23 (hexane-ethyl acetate, 3:1); UV λ_{max} nm MeOH (log ϵ) : 258 (8.62) and 206 (8.07); IR ν_{max} cm^{-1} (NaCl): 3400, 3000-2800, 2080 and 1670; E.M. m/e: 187 (M^+ -N_2 -Me), 101 (100%, dioxolane ring), 43 (CH_3CO^+).

Exact mass calcd for $C_9H_{14}O_5N_2$ - N_2 - Me 187.0603, found 187.0630

(4a): ^{1}H-NMR ($CDCl_3$) δ ppm: 4.49 (dd, 1H, J= 6.6 and 5.9 Hz, H-3), 4.25 (ddd, 1H, J= 6.6, 6.3 and 5.0 Hz, H-4), 4.10 (dd, 1H, J= 8.7 and 6.3 Hz, H-5), 3.93 (dd, 1H, J= 8.7 and 5.0 Hz, H-5'), 3.77 (s, 3H, OMe), 1.40 and 1.33 (two s, 6H, CMe_2); ^{13}C-NMR ($CDCl_3$) δ ppm: 167.0 (C-1), 110.0 ($\underline{C}Me_2$), 76.7 (C-4), 68.1 (C-3), 66.6 (C-5), 51.9 (OMe), 26.4 and 24.9 ($C\underline{Me}_2$).

(4b): ^{1}H-NMR ($CDCl_3$) δ ppm: 4.52-4.44 (m, 1H, H-3), 4.20-4.28 (m, 1H, H-4), 4.05 (dd, 1H, J= 8.7 and 6.5 Hz, H-5), 3.89 (dd, 1H, J= 8.7 and 5.4 Hz, H-5'), 3.76 (s, 3H, OMe), 1.45 and 1.35 (two s, 6H, CMe_2).

(5)-cis: ^{1}H-NMR ($CDCl_3$) δ ppm: 4.14 (dd, 1H, J= 9.9 and 7.8 Hz, H-5), 4.06 (dd, 1H, J= 9.9 and 5.9 Hz, H-5'), 4.15-4.0 (m, 1H, H-4), 3.77 (s, 3H, OMe), 3.56 (d, 1H, J= 4.4 Hz, H-2), 3.16 (dd, 1H, J= 7.3 and 4.4 Hz, H-3), 1.41 and 1.27 (two s, 6H, CMe_2)

(5)-trans-1: ^{1}H-NMR ($CDCl_3$) δ ppm: 4.1-4.0 (m, 2H, H-4 and H-5), 3.9-3.8 (m, 1H, H-5'), 3.85 (s, 3H, OMe), 3.41 (d, 1H, J= 1.89 Hz, H-2), 3.24-3.19 (m, 1H, H-3), 1.34 and 1.29 (two s, 6H, CMe_2)

(5)-trans-2: ^{1}H-NMR ($CDCl_3$) δ ppm: 4.1-4.0 (m, 1H, H-5), 3.9-3.8 (m, 2H, H-4 and H-5'), 3.86 (s, 3H, OMe), 3.36 (d, 1H, J= 1.81 Hz, H-2), 3.24-3.19 (m, 1H, H-3), 1.34 and 1.29 (two s, 6H, CMe_2).

Reduction of methyl (4R)-4,5-O-isopropylidene-3-keto-4,5-dihydroxypentanoate (3). Synthesis of (3R,4R) and (3S,4R)-4,5-O-isopropylidene-3,4,5-trihydroxypentanoate (6b) and (6a).

To a solution of 1 g (4.5 mmol) of methyl (4R)-4,5-O-isopropylidene-3-keto-4,5-dihydroxypentanoate (3) in 3 mL of anhydrous methanol at 0°C, 61.7 mg (1.63 mmol) of sodium borohydride were slowly added. The reaction mixture was neutralized with 1.2 N hydrochloric acid and extracted with diethyl ether (3x10 ml). The organic layers were dried over sodium sulfate and concentrated to yield 0.65 g (64.4%) of a mixture of methyl (3R,4R) and (3S,4R)-O-isopropylidene-3,4,5-trihydroxypentanoate **(6b:6a)** in a 57:43 proportion. These were then separated by column chromatography using a hexane-ethyl acetate, 4:1 eluent.

(6a and 6b): colourless oil; Rf= 0.18 (hexane-ethyl acetate, 3:1); IR, MS and Elem.Anal. were found to be identical with the reported literature value[8,9].

(6a): $[\alpha]^{20}_D$ -11.8 (c 0.6, $CHCl_3$) (reported [8], $[\alpha]^{20}_D$ -11.2 (c 0.6, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ ppm: 4.15-3.95 (m, 4H, H-3, H-4, H-5 and H-5'), 3.70 (s, 3H, OMe), 2.70 (dd, 1H, J= 16.7 and 2.8 Hz, H-2), 2.46 (dd, 1H, J= 16.7 and 8.4 Hz, H-2'), 1.38 and 1.32 (two s, 6H, CMe_2). ^{13}C-NMR ($CDCl_3$) δ ppm: 172.1 (C-1), 109.7 ($\underline{C}Me_2$), 77.6 (C-4), 68.3 (C-3), 65.6 (C-5), 51.8 (-OMe), 38.1 (C-2), 26.3 and 25.1 ($C\underline{Me}_2$).

(6b): $[\alpha]^{20}_D$ +13.3 (c 1.2, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ ppm: 4.12-3.98 (m, 3H, H-3, H-4 and H-5), 3.83

(dd, 1H, J= 5.9 and 8.0 Hz, H-5'), 3.70 (s, 3H, OMe), 2.55 (dd, 1H, J= 15.9 and 7.5 Hz, H-2), 2.46 (dd, 1H, J= 15.9 and 4.9 Hz, H-2'), 2.10 (broad s, 1H, OH), 1.43 and 1.33 (two s, 6H, CMe_2); ^{13}C-NMR ($CDCl_3$) δ ppm: 173.0 (C-1), 109.2 ($\underline{C}Me_2$), 77.2 (C-4), 69.3 (C-3), 66.6 (C-5), 51.8 (-OMe), 37.6 (C-2), 26.6 and 25.1 ($C\underline{Me}_2$).

Catalytic hydrogenation of methyl (3S,4R) and (3R,4R)-4,5-O-isopropylidene-2-diazo-3,4,5-trihydroxypentanoates (4a and 4b). Synthesis of (3S,4R) and (3R,4R)-4,5-O-isopropylidene-3,4,5-trihydroxypentanoate (6a) and (6b) or 2-deoxy-D-ribono and xilono-γ-lactones (9) and (10).

233 mg of **(4)** (84:16, **4a:4b**) were dissolved in ethyl acetate (50 mL) and hydrogenated at room temperature in a low pressure hydrogenator together with a small amount of Pd/C for 24 hr. The reaction mixture was filtered, the solvent removed under vaccuo and the residue purified by thick layer chromatography (hexane-ethyl acetate, 4:1), to yield 65.7 mg (32%) of the mixture **(6)** (5:1, **6a:6b**).

In the same way, but using methanol as the solvent instead of ethyl acetate, we obtained a mixture of the lactones **(9)** and **(10)** in a 93% (5:1, **9/10**) of yield. The spectroscopic and other physical data are given bellow.

Benzoylation of methyl (3S,4R) and (3R,4R)-4,5-O-isopropylidene-3,4,5-trihydroxypentanoate (6a and 6b). Synthesis of (3S,4R) and (3R,4R)-4,5-O-isopropylidene-3-benzoyl-3,4,5-trihydroxypentanoate (7a and 7b).

To a solution of 100 mg (0.5 mmol) of the previous reduction mixture **(6)** in 0.8 ml of anhydrous pyridine, 0.12 mL (1 mmol) of benzoyl chloride were added. The resulting mixture was stirred for 20 h at room temperature and chloroform (10 mL) was then added. The solution was washed with 10 mL of 1% of hydrochloric acid and then with 10 ml of a saturated solution of $NaHCO_3$. The organic layer was dried over $MgSO_4$, and the solvent removed under vaccuo to yield a nearly quantitative mixture (1:1) of the benzoylated products **(7a)** and **(7b)** which could not be separated in pure state. Nevertheless, column chromatography (hexane-ethyl acetate, 6:1) yielded different fractions with one of the two isomers present in higher proportion.

(7a) and (7b): Rf = 0.37 (hexane-ethyl acetate, 4:1); E.M. m/e: 293 (M$^+$ -Me), 105 (100%, PhCO$^+$), 101 (dioxolane ring, $C_5H_9O_2^+$), 43 (CH_3CO^+).

Anal.Calcd for $C_{16}H_{20}O_6$: C, 62.32; H, 6.54. Found: C, 62.57; H, 6.65.

(7a): ^{1}H-NMR ($CDCl_3$) δ ppm: 8.1-7.9 (m, 2H), 7.6-7.3 (m, 3H), 5.48 (dt, 1H, J= 6.1 and 5.8 Hz, H-3), 4.37 (m, 1H, H-4), 4.09 (dd, 1H, J= 8.7 and 7.3 Hz, H-5), 3.89 (dd, 1H, J= 8.7 and 5.4 Hz, H-5'), 3.64 (s, 3H, OMe), 2.80 (d, 2H, J= 6 Hz, H-2 and H-2'), 1.40 and 1.34 (two s, 6H, CMe_2).

(7b): ^{1}H-NMR ($CDCl_3$) δ ppm: 8.1-7.9 (m, 2H), 7.6-7.3 (m, 3H), 5.57 (dt, 1H, J= 6.7 and 3.7 Hz, H-3), 4.41 (ddd, 1H, J= 6.8, 5.7 and 3.7 Hz, H-4), 4.05 (dd, 1H, J= 8.7 and 6.8 Hz, H-5), 3.86 (dd, 1H, J= 8.7

and 5.7 Hz, H-5'), 3.64 (s, 3H, OMe), 2.82 (d, 2H, J = 6.7 Hz, H-2 and H-2'), 1.45 and 1.34 (two s, 6H, CMe_2).

Acetylation of methyl (3S,4R) and (3R,4R)-4,5-O-isopropylidene-3,4,5-trihydroxypentanoate (6a and 6b). Synthesis of (3S,4R) and (3R,4R)-4,5-O-isopropylidene-3-acetyl-3,4,5-trihydroxypentanoate (8a) and (8b).

To a stirred solution of 310 mg (1.5 mmol) of the previous reduction mixture (**6**) in 2 ml of triethylamine, 0.4 mL (4.2 mmol) of acetic anhydride were added. The reaction mixture was stirred under an argon atmosphere for 24 h and then extracted with ethyl acetate 2x10 mL. The extracts were treated as for the mixture of (**7**) **above**, then showed a practically quantitative reaction, to yield 278 mg (74.3%) of a mixture of (**8a**) and (**8b**).

(8a) and (8b): Rf = 0.34 (hexane-ethyl acetate, 3:1), IR ν_{max} cm^{-1} (NaCl): 2965, 2925, 2865, 1720, 1240-1200, 1070-1020; E.M. m/e: 231 (M^+ -Me), 186 (M^+ -$MeCO_2H$), 171 (M^+ -$MeCO_2H$ -Me), 101 (dioxolane ring, $C_5H_9O_2$), 43 (100%, CH_3CO^+).

Anal. Calcd for $C_{11}H_{18}O_6$: C, 53.65; H, 7.37. Found: C, 53.27; H, 7.16.

(8a): ^{1}H-NMR ($CDCl_3$) δ ppm: 5.17 (ddd, 1H, J = 7.6, 5.8 and 4.6 Hz, H-3), 4.15 (ddd, 1H, J = 5.8, 5.9 and 6.5 Hz, H-4), 3.99 (dd, 1H, J = 8.6 and 6.5 Hz, H-5), 3.72 (dd, 1H, J = 8.6 and 5.9 Hz, H-5'), 3.61 (s, 3H, OMe), 2.65 (dd, 1H, J = 15.9 and 4.6 Hz, H-2), 2.55 (dd, 1H, J = 15.9 and 7.6 Hz, H-2'), 2.00 (s, 3H, OAc), 1.35 and 1.27 (two s, 6H, CMe_2).

(8b): ^{1}H-NMR ($CDCl_3$) δ ppm: 5.27 (ddd, 1H, J = 7.3, 5.8 and 4.0 Hz, H-3), 4.2 (ddd, 1H, J = 7.9, 5.3 and 4.0 Hz, H-4), 3.95 (dd, 1H, J = 8.6 and 7.9 Hz, H-5), 3.72 (dd, 1H, J = 8.6 and 5.3 Hz, H-5'), 3.61 (s, 3H, OMe), 2.65 (dd, 1H, J = 16.2 and 5.8 Hz, H-2), 2.55 (dd, 1H, J = 16.2 and 7.3 Hz, H-2'), 2.00 (s, 3H, OAc), 1.35 and 1.27 (two s, 6H, CMe_2).

Reaction of (3RS,4R)-4,5-O-isopropylidene-2-diazo-3,4,5-trihydroxypentanoates (4) with trifluoroacetic acid.

50 mg of the mixture (**4**) were dissolved in 0.5 ml of $CDCl_3$ in an NMR tube and a drop of TFA was added, which caused evolution of nitrogen and the disappearance of the yellow color of the initial product. In few minutes, the ^{1}H-NMR spectra reveal the complete transformation into the ß-ketoester (**3**).

Efect of heat on the mixture of (3RS,4R)-4,5-O-isopropylidene-2-diazo-3,4,5-trihydroxypentanoates (4).

101 mg (0.44 mmol) of the mixture of (**4**) was heated under vaccuo at 150°C for few minutes to cause the disappearance of the yellow color of the starting products. ^{1}H-NMR and TLC reveal that the resulting product was the ß-ketoester (**3**).

Photolysis of the mixture of (3RS,4R)-4,5-O-isopropylidene-2-diazo-3,4,5-trihydroxypentanoates (4).

84.8 mg (0.37 mmol) of the mixture of (**4**) were dissolved in 15 ml of benzene and irradiated with a Hg lamp of medium pressure and with a Pyrex filter. The reaction was followed measuring its absorvance at 394 nm. After 5 h, the concentrated product (71.5 mg, 96%) show to be the ß-ketoester (**3**).

Acid hydrolysis of (6). Synthesis of 2-deoxy-D-ribono and D-xylono-þ-lactones (9) and (10).

67.5 mg of (**6**) (5:1, **6a:6b**) were treated with 1 ml of TFA:water 1:1 for 3 hr. The solvents were eliminated under vaccuo and the residue was washed several times by adding benzene and them remouving it by evaporation. Finally, the residue was purified by column chromatography (hexane-ethyl acetate 1:4) to yield (**9**) and (**10**) (77.8% in a 5:1).

In the same way, (**6a**) gives (**9**) and (**6b**) gives (**10**) with similar yields.

(**9**)[9,11,12]: ^{1}H-NMR, ($(CD_3)_2CO$-$CDCl_3$) δ ppm: 4.48 (ddd, 1H, J = 6.8, 2.8 and 2.2 Hz, H-3), 4.35 (ddd, 1H, J = 3.5, 3.4 and 2.2 Hz, H-4), 3.76 (dd, 1H, J = 12.3 and 3.1 Hz, H-5), 3.68 (dd, 1H, J = 12.3 and 3.5 Hz, H-5'), 2.83 (dd, 1H, J = 17.9 and 6.8 Hz, H-2), 2.34 (dd, 1H, J = 17.9 and 2.8 Hz, H-3); ^{13}C-NMR (D_2O) δ ppm: 179.4 (C-1), 88.8 (C-4), 67.7 (C-3), 60.9 (C-5) and 37.5 (C-2).

(**10**)[11,13]: $[\alpha]_D^{20}$ +49.3 (c 0.56, methanol);^{1}H-NMR ($(CD_3)_2CO$-$CDCl_3$) δ ppm: 4.67 (ddd, 1H, J = 6.3, 2.7 and 4.8 Hz, H-3), 4.43 (ddd, 1H, J = 4.8, 4.4 and 5.1 Hz, H-4), 4.02 (dd, 1H, J = 12.3 and 4.4 Hz, H-5), 3.95 (dd, 1H, J = 12.3 and 5.1 Hz, H-5'), 2.74 (dd, 1H, J = 17.8 and 6.3 Hz, H-2), 2.52 (dd, 1H, J = 17.8 and 2.7 Hz, H-3); ^{13}C-NMR (D_2O) δ ppm: 179.2 (C-1), 85.5 (C-4), 68.1 (C-3), 59.7 (C-5) and 38.6 (C-2).

Acetylation of methyl (3S,4R) and (3R,4R)-4,5-O-isopropylidene-2-diazo3,4,5-trihydroxypentanoate (4a) and (4b). Synthesis of (3S,4R) and (3R,4R)-4,5-O-isopropylidene-3-acetyl-2-diazo-3,4,5-trihydroxypentanoate (11a) and (11b).

To a solution of 310 mg of (**4**) in 3 ml of anhydrous pyridine, 0.4 ml of acetic anhydride were added. The reaction was left at room temperature overnight and then poured into 20 ml of water. This gave a yellow organic layer that was extracted with 3x10 ml of chloroform. The joint organic layers were dried with sodium sulphate and concentrated to give 357 mg (97.4 %) of the unresolvable mixture (**11**).

(11a) and (11b): yellow oil; Rf = 0.36 (hexane-ethyl acetate, 3:1); IR ν_{max} cm^{-1} (NaCl): 2060, 1720-1700 and 1675-1655; E.M. m/e: 229 (M^+ -43), 187 , 172 , 101 (100%, dioxolane ring, $C_5H_9O_2^+$), 69, 43.

Exact mass calcd for $C_{11}H_{16}O_6N_2$ -N_2 -Me 229.0708, found 229.0687.

(11a): ^{1}H-NMR ($CDCl_3$) δ ppm: 5.53 (d, 1H, J = 4.8 Hz, H-3), 4.52 (ddd, 1H, J = 4.8, 6.7 and 5.7 Hz, H-4), 4.09 (dd, 1H, J = 8.8 and 6.7 Hz, H-5), 3.74 (dd, 1H, J = 8.8 and 5.7 Hz, H-5'), 3.76 (s, 3H, OMe), 2.07

(s, 3H OAc), 1.44 and 1.33 (two s, 6H, CMe_2); ^{13}C-NMR ($CDCl_3$) δ ppm: 169.6 and 165.4 (carbonyl groups), 110.3 ($\underline{C}Me_2$), 75.4 (C-4), 69.6 (C-3), 66.2 (C-5), 57.8 (C-2), 51.9 (-OMe), 25.9 and 24.7 ($C\underline{Me}_2$) and 20.6 (-OCO$\underline{Me}$).

(11b): ^{1}H-NMR ($CDCl_3$) δ ppm: 5.58 (d, 1H, J = 5.9 Hz, H-3), 4.58 (ddd, 1H, J = 6.7, 5.1 and 5.9 Hz, H-4), 4.03 (dd, 1H, J = 8.9 and 6.7 Hz, H-5), 3.79 (dd, 1H, J = 8.9 and 5.1 Hz, H-5'), 3.75 (s, 3H, OMe), 2.10 (s, 3H, OAc), 1.42 and 1.33 (two s, 6H, CMe_2); ^{13}C-NMR ($CDCl_3$) δ ppm: 170.0 and 165.1 (carbonyl groups), 106.9 ($\underline{C}Me_2$), 76.2 (C-4), 69.3 (C-3), 65.7 (C-5), 57.8 (C-2), 51.9 (-OMe), 26.1 and 25.2 ($C\underline{Me}_2$) and 20.6 (-OCO$\underline{Me}$).

Catalytic hydrogenation of (3S,4R) and (3R,4R)-4,5-O-isopropylidene-3-acetyl-2-diazo-3,-4,5-trihydroxypentanoate (11a) and (11b). Synthesis of (3S,4R) and (3R,4R)-4,5-O-isopropylidene-3--acetyl-3,4,5-trihydroxypentanoate (8a) and (8b).

154 mg of **(11)** were dissolved in 50 ml of ethyl acetate and hydrogenated as above for **(4)**, giving quantitatively a mixture (5:1) of **(8a:8b)**.

ACKNOWLEDGMENT

The autors thank to "Comision Interministerial de Ciencia y Tecnología" (ref. PB85/471) and to Consejería de Educación y Ciencia de la Junta de Andalucia for partial financial support.

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