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SYNTHESIS OF 2,3-AZIRIDINO-2,3-DIDEOXY-D-LYXONO-γ-LACTONE 5-PHOSPHONATE FROM D-RIBOSE, A NEW MEMBER OF THE 2,3-AZIRIDINO-γ-LACTONE FAMILY OF SYNTHONS

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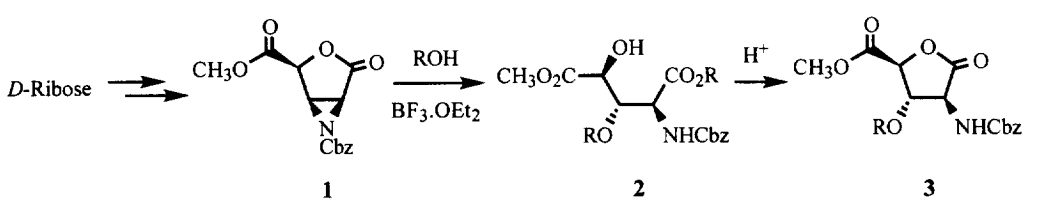
*Abstract : A formal synthesis of the novel (1S,4S,5R)-N-(benzyloxycarbonyl)-4-(diethoxyphosphinyl)methyl-3-oxa-6-azabicyclo[3.1.0]hexan-2-one **4** from D-ribose is presented. A key step involves the use of the 2,3-sulfate **12** for introduction of the C-3 azide functionality prior to aziridine ring formation.* © 1997 Elsevier Science Ltd.

INTRODUCTION

The hydrolytic stability of the phosphonate group has motivated a great deal of research aimed at replacing the more labile phosphate group of biologically important molecules by this moiety. Thus, a certain number of phosphonylated nucleoside analogues have been shown to display antiviral activity,[1] while phosphonate analogues of phosphorylated carbohydrates have been used for mechanistic studies of enzymatic and metabolic processes.[2] Such considerations have also motivated the recent synthesis of phosphonate analogues of sphingosine-1-phosphate (involved in cell proliferation, and cell death) starting from D-galactose or D-xylose.[3] The phosphonate group may also be viewed as an isostere of the carboxylate functionality. As such, phosphonate analogues of glutamate (e.g., 2-amino-5-phosphonopentanoic acid (AP5)) and derivatives are presently one of the most intensively studied classes of glutamate receptor antagonists,[4] glutamate being the major excitatory neurotransmitter of the central nervous system, the hyperactivity of which can lead to a number of neurodegenerative diseases.[5]

We are currently developing 4-substituted 2,3-aziridino-γ-butyrolactones as polyvalent synthons for the preparation of stereochemically pure substances, notably α- and β-amino acids.[6-8] Among these butyrolactones, we have recently described the synthesis (from D-ribose) and the reactivity of the 4-methyl carboxylate derivative **1** (Scheme 1).[8] The latter reacts with hard nucleophiles such as alcohols to give



1 **2** **3**

Scheme 1

3,4-disubstituted L-glutamate derivatives of type **2** which, under acidic conditions, can undergo cyclization to the 2,3,4-trisubstituted γ-butyrolactones **3**. Compound **1** can thus be viewed either as a precursor of substituted glutamic acid analogues (such as **2**) or, after incorporation of a purine or pyrimidine base at C-1 of compound **3**, as a precursor of nucleoside analogues.

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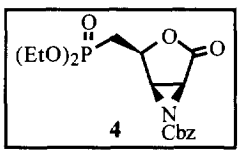
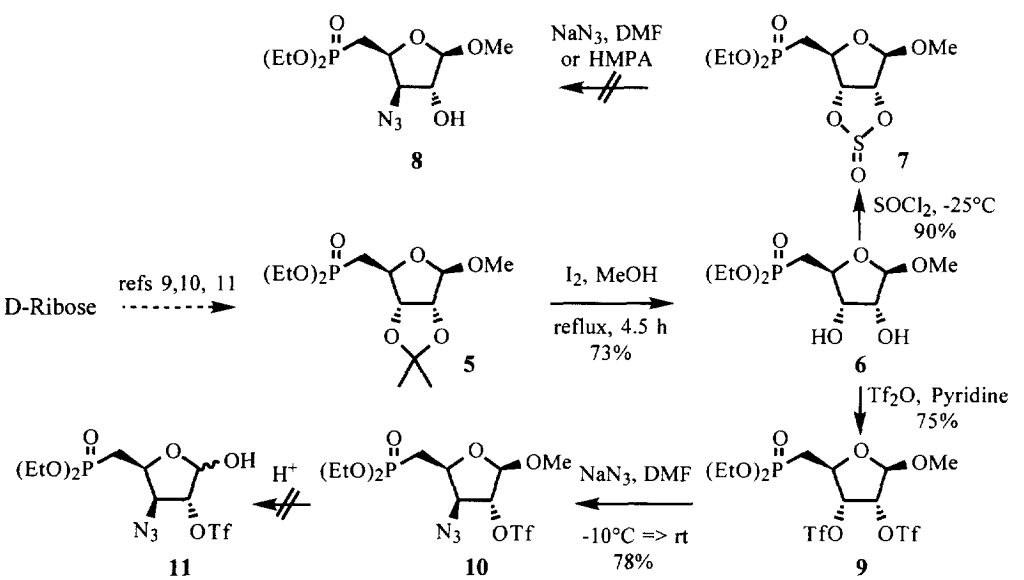
In view of the current interest in phosphonate derivatives of these two classes of pharmacologically important compounds, it appeared important to be able to employ our methodology to approach the synthesis of such molecules. It is with this intention that we present, in this paper, a formal synthesis of the C-5 phosphonate analogue of **1**, that is, **4**, from D-ribose.



4

RESULTS AND DISCUSSION

The starting material for our synthesis of **4** was the protected 5-C-diethylphosphonate ribofuranoside derivative **5**[9] (Scheme 2) which can be prepared in good yields from the 5-iodo precursor[10] (itself prepared from D-ribose)[11] via an Arbuzov reaction with triethylphosphite. Compound **5** being sensitive to acidic conditions, the 2,3-O-isopropylidene group could be efficiently removed by refluxing **5** in methanol in the presence of a catalytic amount of iodine.[12] The best yields of diol **6** (73%) were obtained when a Dean-Stark apparatus was used in order to prevent any reversible formation of the starting acetonide.

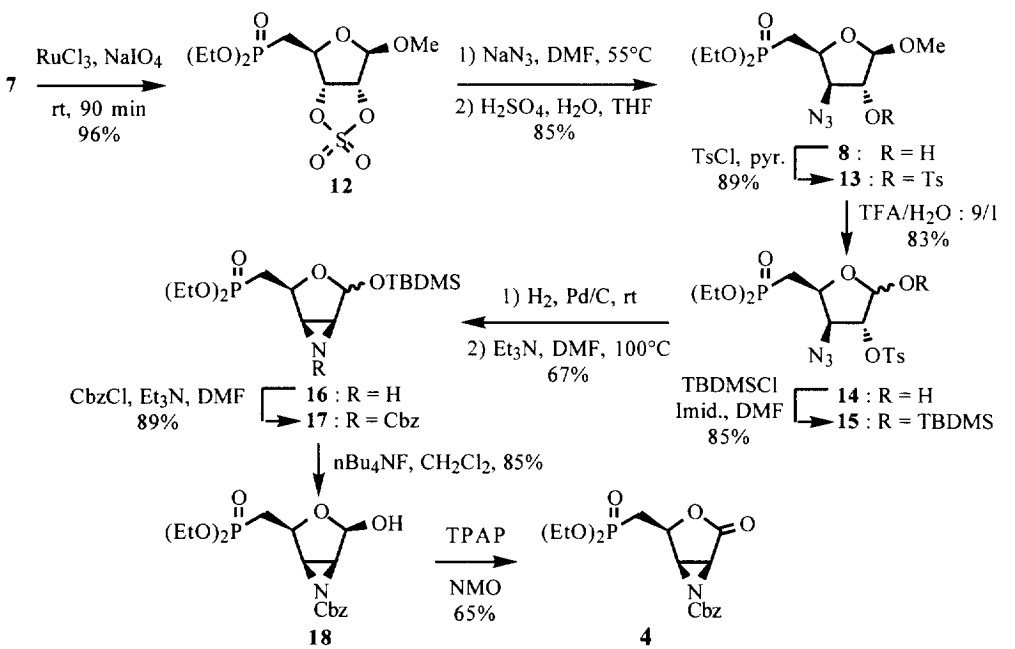


Scheme 2

The *cis*-2,3-diols of methyl furanosides have been our general point of entry to the 2,3-aziridino-γ-lactone motif, the general strategy involving activation of the C-3 position by formation of a 2,3-O-cyclic sulfite followed by regiospecific opening of the sulfite at C-3 by azide anion.[8,13] Diol **6** was thus treated with thionyl chloride and triethylamine at -25°C,[14] affording cyclic sulfite **7** as a 1:1 mixture of the *endo* and *exo* isomers in excellent yields. However, introduction of an azide group by heating **7** in DMF or HMPA in the presence of sodium azide was not successful, only degradation products, instead of **8**, being observed. The failure of this reaction in the case of **7** is probably not the result of steric interference from the phosphonate group since it has been successfully applied to the very sterically hindered 5-O-trityl analogue.[8] On the other

hand, the enhanced acidity of the C-5 protons due to the adjacent phosphonate group may, under the somewhat vigorous, basic conditions of the reaction, lead to parasitic reaction pathways. A better leaving group for C-3, i.e., one which would allow introduction of the azide function at moderate or low temperature, was thus sought. The triflate group has been successfully used by others for the introduction of an azide functionality on sugars by nucleophilic displacement.[15] While selective formation of the C-3 triflate of **6** proved difficult, the ditriflate derivative **9** could be efficiently prepared by treatment of **6** with excess triflic anhydride and pyridine. Compound **9**, sufficiently stable to allow its purification by flash chromatography on silica gel, then reacted cleanly with sodium azide in DMF at room temperature to give the 3-azido-2-O-triflate **10** in 78% yield. Incorporation of the azide group at C-3 was inferred from the observation that H-1 appeared as a singlet in the ^{1}H-nmr spectrum of **10**, pointing to a *trans* relationship with H-2, impossible if the C-2 triflate rather than the C-3 triflate had been displaced (in S_N2 fashion) by azide anion.

As shown in our previous studies,[8,13] successful formation of the aziridine-lactone motif from a methyl furanoside such as **10** requires, at this stage, replacement of the anomeric methyl group by an alkylsilyl group since the latter, unlike the former, can be removed under conditions compatible with the presence of an aziridine ring (i.e., using F^-). Disappointingly, however, all attempts at hydrolytic cleavage of the methoxy group of **10** to give **11** led to formation of degradation products, probably a consequence of the presence of the labile triflate group. Finally, a solution to these problems was found in the form of the cyclic sulfate **12**, obtained by ruthenium chloride mediated oxidation of the sulfite derivative **7** (Scheme 3).[16]



Scheme 3

The improved leaving group capacity of sulfate compared to sulfite then allowed introduction of azide at C-3 by heating **12** in DMF at 55°C in the presence of 2 eq of sodium azide. Mild acidic hydrolysis of the intermediate C-2 sulfate then afforded the desired 3-azido-2-hydroxy furanoside **8** in high yield. Exclusive C-3 attack of the azide anion was again indicated by the ^{1}H nmr spectrum of **8** which displayed a singlet for the anomeric proton at δ 4.83 and thus a *trans* arrangement with H-2. In preparation for formation of the aziridine ring, the free hydroxy group of **8** was then tosylated to give **13** in 89% yield.

Transformation of **13** into the required anomeric O-silylated derivative was then studied. Thus, after some experimentation, the optimal conditions for hydrolysis of the anomeric methoxy function of **13** were found to be the use of a mixture of trifluoroacetic acid and water (9:1) at 20°C repeated in two cycles of 48 h. This technique afforded furanose **14** in 83% yield. Treatment of the latter with tert-butyldimethylsilyl chloride and imidazole in DMF then gave the corresponding silylated furanoside **15** as a 2:3 mixture of α-and β-anomers which were not separated.

With derivative **15** in hand, the sequential formation of the aziridine ring and the lactone functionality could be undertaken. Catalytic hydrogenation of **15** in methanol provided the C-3 amino derivative which, after removal of the catalyst (palladium on carbon) by filtration and evaporation of the solvent, was treated with triethylamine in DMF at 100°C for 4 h to effect cyclization to the aziridine **16** in 67% overall yield.[17] The amine functionality of the aziridine ring of **16** was then protected with a carbobenzyloxy (Cbz) group by reaction with benzyl chloroformate and triethylamine in DMF, affording **17**.

Finally, the furanoside **17** was transformed into the desired lactone **4** by first effecting O-desilylation using tetrabutylammonium fluoride, giving furanose **18** in 85% yield. The anomeric hydroxyl group of **18** was then oxidized by treatment with catalytic tetrapropylammonium perruthenate[18] in the presence of 4-methylmorpholine N-oxide as co-oxidant in acetonitrile. Aziridino-lactone **4** was thus obtained in 65% yield. Spectroscopic data for **4** were in complete accord with the assigned structure. In particular, the IR spectrum showed two bands at 1790 and 1735 cm^{-1}, corresponding to the carbonyl absorptions of the lactone and carbamate functionalities, respectively. Moreover, in the ^{1}H-nmr spectrum of **4**, H-2 and H-3[19] gave rise to, respectively, a doublet at δ 3.59 and a doublet of doublets at δ 3.89, a characteristic pattern observed for other 2,3-aziridino-γ-lactone derivatives we have synthesized.[8,13]

In conclusion, the formal synthesis of a new member of the 2,3-aziridino-γ-lactone family of compounds, the 5-phosphonate derivative **4**, from D-ribose, has been realized. This result indicates that the methodology we have developed for the synthesis of the aziridino-γ-lactone structure is compatible with a number of side-chain functional groups (ether, ester, phosphonate) pending minor modifications in the procedure. The use of **4** as a stereochemically pure synthon for the preparation of pharmacologically relevant substances will be reported in due course.

EXPERIMENTAL PROCEDURE

General methods

Melting points were determined on a Büchi apparatus and are uncorrected. IR spectra of samples were obtained as films (i.e., by application of a $CHCl_3$ solution to an NaCl plate followed by evaporation of the solvent) with a Nicolet 205 FT-IR spectrometer. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AC 200 (200 MHz), Bruker WP250 (250 MHz) or Bruker Aspect 3000 (300 MHz) instrument. Chemical shifts are given as δ values with reference to Me_4Si which was used as internal standard. Electron impact (EI), chemical ionization (CI) and high resolution (HR) mass spectra were respectively recorded on an AEI MS-50, AEI MS-9 and a Kratos 80RF spectrometer. Optical rotations were determined with a Perkin-Elmer 241 polarimeter. Thin-layer chromatography was performed on Merck silica gel 60 plates with fluorescent indicator. The plates were visualized with UV light (254 nm) and with a 20% solution of phosphomolybdic acid in ethanol. All column chromatography was conducted on Merck 60 silica gel (230-240 mesh) at medium pressure (200 mbar). TPAP, 4-methylmorpholine N-oxide and benzyl chloroformate were purchased from Aldrich Chemical Co. and were used without further purification. Elemental analyses were performed at the ICSN, CNRS, Gif-sur-Yvette, France.

Methyl 5-deoxy-5-C-diethoxyphosphinyl-β-D-ribofuranoside (6).- A solution of acetonide **5**[9] (2.75 g, 8.48 mmol) and iodine (450 mg, 1.77 mmol) in methanol (50 mL) was refluxed for 4.5 h, the 2,2-dimethoxypropane generated being continuously removed with a Dean-Stark apparatus. The reaction mixture was then cooled to room temperature and sodium thiosulfate pentahydrate (880 mg, 3.54 mmol) was added to reduce the iodine. After removal of the solvent, chromatography of the oily yellow residue on silica gel

(dichloromethane-ethanol, 97:3) first gave a small amount of unreacted starting material (200 mg, 7%) followed by the title compound **6** (1.75 g, 73%), isolated as a colorless oil. $[\alpha]_D^{27}$ - 48.1 (c 2, $CHCl_3$) ; ^{1}H-NMR (300 MHz, $CDCl_3$) : δ = 1.35 (2t, 6H, J = 7.0 Hz, $P(OCH_2C\underline{H}_3)_2$), 2.02 (ddd, 1H, $J_{5,4}$ = 9.6 Hz, $J_{5,5'}$ = -15.0 Hz, $J_{5,P}$ = 17.1 Hz, H-5), 2.36 (ddd, 1H, $J_{5',4}$ = 4.3 Hz, $J_{5',P}$ = 19.7 Hz, H-5'), 3.35 (s, 3H, $OC\underline{H}_3$), 4.13 (m, 7H, H-2, H-3, H-4 and $P(OC\underline{H}_2)_2$), 4.80 (d, 1H, $J_{1,2}$ = 2.4 Hz, H-1) ; ^{13}C-NMR (75 MHz, $CDCl_3$) : δ = 16.3 and 16.4 ($P(OCH_2\underline{C}H_3)_2$), 31.7 (d, $J_{C-5,P}$ = 137.0 Hz, C-5), 55.1 ($O\underline{C}H_3$), 62.1 and 62.4 (2d, $J_{OCH_2,P}$ = 6.6 Hz, $P(O\underline{C}H_2)_2$), 75.2 (C-4), 76.0 (d, $J_{C-3,P}$ = 8.0 Hz, C-3), 77.7 (C-2), 108.4 (C-1) ; IR (film) : ν (cm^{-1}) = 3375 (OH), 1210 (P=O), 1035 and 977 (P-OC) ; HRMS (CI) : calcd for $C_{10}H_{22}O_7P$ m/z 285.1103 ; found m/z 285.1098 ; Anal. Calcd for $C_{10}H_{21}O_7P$: C, 42.25 ; H, 7.45. Found : C, 42.55 ; H, 7.35.

*Methyl 5-deoxy-5-C-diethoxyphosphinyl-2,3-O-sulfinyl-β-D-ribofuranoside (**7**).-* Freshly distilled thionyl chloride (0.405 mL, 5.55 mmol) in dichloromethane (5 mL) was added dropwise to a stirred solution of diol **6** (1.05 g, 3.70 mmol) and triethylamine (1.6 mL, 11.1 mmol) in dichloromethane (30 mL) at -25°C under an inert atmosphere. After 15 min of addition and a further 15 min of stirring at -25°C, the reaction mixture was diluted with dichloromethane (50 mL) and washed with brine (3 x 100 mL). The organic phase was dried over Na_2SO_4 and then evaporated to dryness under reduced pressure providing sulfite **7** (1.1g, 90%) as a lightly colored oil which was not further purified. ^{1}H-NMR (250 MHz, $CDCl_3$) : δ = 1.35 (t, 6H, J = 7.1 Hz, $P(OCH_2C\underline{H}_3)_2$), 2.23 (m, 2H, H-5 and H-5'), 3.40 (s, 1.5H, $OC\underline{H}_3$ *endo* (or *exo*)), 3.41 (s, 1.5H, $OC\underline{H}_3$ *exo* (or *endo*)), 4.15 (m, 4H, $P(OC\underline{H}_2)_2$), 4.59 (ddd, 0.5H, $J_{4,5}$ = 6.0 Hz, $J_{4,5'}$ = 9.0 Hz, H-4 *endo* (or *exo*)), 4.80 (ddd, 0.5H, $J_{4,5}$ = 6.0 Hz, $J_{4,5'}$ = 9.0 Hz, H-4 *exo* (or *endo*)), 5.07 (d, 0.5H, $J_{1,4}$ = 1.5 Hz, H-1 *endo* (or *exo*)), 5.13 (d, 0.5H, $J_{2,3}$ = 6.4 Hz, H-2 *endo* (or *exo*)), 5.27 (d, 0.5H, $J_{1,4}$ = 1.5 Hz, H-1 *exo* (or *endo*)), 5.34 (d, 0.5H, $J_{2,3}$ = 6.0 Hz, H-2 *exo* (or *endo*)), 5.45 (d, 0.5H, H-3 *endo* (or *exo*)), 5.60 (d, 0.5H, H-3 *exo* (or *endo*)) ; ^{13}C-NMR (62.5 MHz, $CDCl_3$) : δ = 15.8 and 15.9 ($P(OCH_2\underline{C}H_3)_2$), 31.6 (d, $J_{C-5,P}$ = 140.0 Hz, C-5 *endo* (or *exo*)), 31.7 (d, $J_{C-5,P}$ = 140.0 Hz, C-5 *exo* (or *endo*)), 54.7 ($O\underline{C}H_3$), 61.6 (d, $J_{OCH_2,P}$ = 5.8 Hz, $P(O\underline{C}H_2)_2$), 80.4 and 81.0 (C-4 *exo* and*endo*)), 87.2 (C-2 *endo* (or *exo*)), 87.4 (d, $J_{C-3,P}$ = 6.0 Hz, C-3 *endo* (or *exo*)), 90.1 (d, $J_{C-3,P}$ = 7.0 Hz, C-3 *exo* (or *endo*)), 90.4 (C-2 *exo* (or *endo*)), 107.7 and 108.2 (C-1 *exo* and *endo*)) ; IR (film) : ν (cm^{-1}) = 1450, 1250 (P=O), 1220 (S=O), 1110 (C-O), 1060 (C-O), 1030 and 980 (P-OC) ; MS (CI) : m/z 331 [M^+ + H].

*Methyl 5-deoxy-5-C-diethoxyphosphinyl-2,3-O-di-trifluoromethanesulfonyl-β-D-ribofuranoside (**9**).-* To a stirred solution of diol **6** (253 mg, 0.89 mmol) and pyridine (345 µL, 4.27 mmol) in dichloromethane (15 mL) was added dropwise at -40°C under nitrogen, a solution of trifluoromethanesulfonic anhydride (350 µL, 2.13 mmol) in dichloromethane (3 mL). After one hour of stirring between -40°C and 0°C, the reaction mixture was neutralized with 5% aqueous sodium carbonate (15 mL) and then extracted with dichloromethane (20 mL). The organic phase was washed with water (20 mL) and dried over Na_2SO_4. Removal of the solvent and column chromatography of the residue on silica gel (ethyl acetate-heptane, 2:1) afforded the title compound **9** (370 mg, 75%) as an unstable colorless oil. ^{1}H-NMR (200 MHz, $CDCl_3$) : δ = 1.36 (2t, 6H, J = 7.0 Hz, $P(OCH_2C\underline{H}_3)_2$), 2.12 (ddd, 1H, $J_{5,4}$ = 9.7 Hz, $J_{5,5'}$ = -15.3 Hz, $J_{5,P}$ = 17.2 Hz, H-5), 2.29 (ddd, 1H, $J_{5',4}$ = 4.7 Hz, $J_{5',P}$ = 19.5 Hz, H-5'), 3.48 (s, 3H, $OC\underline{H}_3$), 4.17 (2q, 4H, J = 7.0 Hz, $P(OC\underline{H}_2)_2$), 4.62 (dddd, 1H, $J_{4,3}$ = 5.7 Hz, $J_{4,P}$ = 9.4 Hz, H-4), 5.13 (s, 1H, H-1), 5.18 (d, 1H, $J_{2,3}$ = 4.2 Hz, H-2), 5.38 (dd, 1H, H-3) ; IR (film) : ν (cm^{-1}) = 1428 (SO_2CF_3), 1250 (P=O), 1220 and 1140 (SO_2CF_3), 1030 and 970 (P-OC) ; MS (CI) : m/z 549 [M^+ + H].

*Methyl 3-azido-3,5-dideoxy-5-C-diethoxyphosphinyl-2-O-trifluoromethanesulfonyl-β-D-xylofuranoside (**10**).-* To a stirred solution of compound **9** (410 mg, 0.748 mmol) in DMF (6 mL) held at -10°C was added under nitrogen sodium azide (53 mg, 0.815 mmol). After 3 h of stirring between -10°C and 20°C, the reaction mixture was evaporated to dryness. The colored oily residue was then purified by column chromatography on silica gel (ethyl acetate-heptane, 3:1) providing the azido derivative **10** (260 mg, 78%) as a colorless oil. ^{1}H-NMR (250 MHz, $CDCl_3$) : δ = 1.36 (2t, 6H, J = 7.0 Hz, $P(OCH_2C\underline{H}_3)_2$), 2.24 (ddd, 1H, $J_{5,4}$ = 6.5 Hz, $J_{5,5'}$ = -15.3 Hz, $J_{5,P}$ = 19.0 Hz, H-5), 2.33 (ddd, 1H, $J_{5',4}$ = 7.4 Hz, $J_{5',P}$ = 18.3 Hz, H-5'), 3.45 (s, 3H, $OC\underline{H}_3$), 4.15

(2q, 4H, J = 7.0 Hz, $P(OC\underline{H}_2)_2$), 4.29 (dd, 1H, $J_{3,2}$ = 1.1 Hz, $J_{3,4}$ = 5.1 Hz, H-3), 4.68 (m, 1H, H-4), 5.03 (s, 1H, H-1), 5.13 (d, 1H, H-2) ; ^{13}C-NMR (62.5 MHz, $CDCl_3$) : δ = 16.2 and 16.3 ($P(OCH_2\underline{C}H_3)_2$), 27.7 (d, $J_{C-5,P}$ = 140.0 Hz, C-5), 56.2 ($O\underline{C}H_3$), 62.0 (d, $J_{OCH2,P}$ = 4.0 Hz, $P(O\underline{C}H_2)_2$), 65.7 (d, $J_{C-3,P}$ = 7.0 Hz, C-3), 76.4 (C-4), 91.2 (C-2), 106.2 (C-1), 120.9 ($OSO_2\underline{C}F_3$) ; IR (film) : ν (cm^{-1}) = 2115 (N_3), 1420 (SO_2CF_3), 1250 (P=O), 1210 and 1140 (SO_2CF_3), 1040 and 970 (P-OC) ; MS (CI) : m/z 442 [M^+ + H].

Methyl 5-deoxy-5-C-diethoxyphosphinyl-β-D-ribofuranoside-2,3-sulfate (12).- The crude sulfite **7** (1.10 g, 3,33 mmol) dissolved in acetonitrile (7.5 mL), carbon tetrachloride (7.5 mL) and water (11 mL) was treated with ruthenium trichloride hydrate (15 mg, 0.072 mmol) and sodium metaperiodate (1.60 g, 7.48 mmol). After 90 min of vigorous stirring at room temperature, the reaction mixture was diluted with water (20 mL) and extracted with dichloromethane (3 x 30 mL). The organic phases were combined and dried over Na_2SO_4, concentrated under vacuum and purified by column chromatography on silica gel (ethyl acetate-heptane, 3:1) yielding sulfate **12** (1.12 g, 96%) as a faintly colored oil. $[\alpha]_D^{27}$ - 49.8 (c 1.5, $CHCl_3$) ; ^{1}H-NMR (250 MHz, $CDCl_3$) : δ = 1.36 (t, 6H, J = 7.1 Hz, $P(OCH_2C\underline{H}_3)_2$), 2.21 (ddd, 1H, $J_{5,4}$ = 7.1 Hz, $J_{5,5'}$ = -15.2 Hz, $J_{5,P}$ = 17.7 Hz, H-5), 2.29 (ddd, 1H, $J_{5',4}$ = 5.1 Hz, $J_{5',P}$ = 20.0 Hz, H-5'), 3.42 (s, 3H, $OC\underline{H}_3$), 4.17 (m, 4H, $P(OC\underline{H}_2)_2$), 4.77 (m, 1H, H-4), 5.20 (d, 1H, $J_{2,3}$ = 5.7 Hz, H-2), 5.21 (s, 1H, H-1), 5.55 (dd, 1H, $J_{3,4}$ = 0.6 Hz, H-3) ; IR (film) : ν (cm^{-1}) = 1395 (SO_2), 1230 (P=O), 1215 (S=O), 1025 and 970 (P-OC) ; HRMS (CI) : calcd for $C_{10}H_{20}O_9PS$ m/z 347.0566 ; found m/z 347.0582

Methyl 3-azido-3,5-dideoxy-5-C-diethoxyphosphinyl-β-D-xylofuranoside (8).- A solution of sulfate **12** (1.0 g, 2.90 mmol) in DMF (15 mL) was heated at 55°C for 2.5 h in the presence of sodium azide (380 mg, 5.80 mmol). After removal of the solvent, the slightly colored solid residue was taken up in THF (15 mL). Concentrated sulfuric acid (156 µL, 2.90 mmol) followed by water (53 µL, 2.90 mmol) were added and the reaction mixture was stirred at room temperature for 1 h. The solution was then neutralized by addition of saturated aqueous sodium hydrogen carbonate before being extracted by ethyl acetate (3 x 20 mL). The combined organic phases were dried over Na_2SO_4 and evaporated under reduced pressure leaving a yellow oil which was purified by flash chromatography on silica gel (ethyl acetate) providing the azido derivative **8** (770 mg, 85%) as a colorless oil. $[\alpha]_D^{27}$ - 79.2 (c 0.5, $CHCl_3$) ; ^{1}H-NMR (250 MHz, $CDCl_3$) : δ = 1.34 and 1.35 (2t, 6H, J = 7.0 Hz, $P(OCH_2C\underline{H}_3)_2$), 2.21 (ddd, 1H, $J_{5,4}$ = 6.8 Hz, $J_{5,5'}$ = -15.2 Hz, $J_{5,P}$ = 18.6 Hz, H-5), 2.29 (ddd, 1H, $J_{5',4}$ = 7.0 Hz, $J_{5',P}$ = 18.3 Hz, H-5'), 3.40 (s, 3H, $OC\underline{H}_3$), 4.01 (d, 1H, $J_{3,4}$ = 4.6 Hz, H-3), 4.13 (m, 4H, $P(OC\underline{H}_2)_2$), 4.28 (m, 1H, H-2), 4.58 (d, J = 3.7 Hz, 1H, exchangeable with D_2O, OH), 4.68 (pseudo dq, 1H, $J_{4,P}$ = 7.0 Hz, H-4), 4.83 (s, 1H, H-1) ; ^{13}C-NMR (75 MHz, $CDCl_3$) : δ = 16.3 and 16.4 ($P(OCH_2\underline{C}H_3)_2$), 27.7 (d, $J_{C-5,P}$ = 140.0 Hz, C-5), 55.9 ($O\underline{C}H_3$), 62.0 and 62.2 (2d, $J_{OCH2,P}$ = 6.2 Hz, $P(O\underline{C}H_2)_2$), 67.8 (d, $J_{C-3,P}$ = 8.0 Hz, C-3), 75.7 (C-4), 79.7 (C-2), 109.8 (C-1) ; IR (film) : ν (cm^{-1}) = 3330 (OH), 2110 (N_3), 1250 (P=O), 1030 and 970 (P-OC) ; MS (CI) : m/z 310 [M^+ + H] ; Anal. Calcd for $C_{10}H_{20}N_3O_6P$: C, 38.84 ; H, 6.52 ; N, 13.59. Found : C, 38.84 ; H, 6.49 ; N, 13.57.

Methyl 3-azido-3,5-dideoxy-5-C-diethoxyphosphinyl-2-O-tosyl-β-D-xylofuranoside (13).- To a stirring solution of compound **8** (750 mg, 2.42 mmol) in anhydrous pyridine (20 mL) was added at 0°C freshly recrystallized p-toluenesulfonyl chloride (1.4 g, 7.2 mmol). After 70 h at room temperature, the reaction mixture was evaporated to dryness under vacuum, the solid residue was taken up in ethyl acetate (40 mL) and the solution was washed with water (40 mL). After separation and drying of the organic phase (Na_2SO_4), the solvent was removed and the yellow oil remaining was purified by flash chromatography on silica gel (ethyl acetate-heptane, 2:1) yielding the tosylate **13** (1.0 g, 89%) as a colorless oil. $[\alpha]_D^{27}$ - 64.7 (c 1, $CHCl_3$) ; ^{1}H-NMR (250 MHz, $CDCl_3$) : δ = 1.31 (t, 6H, J = 7.0 Hz, $P(OCH_2C\underline{H}_3)_2$), 2.14 (ddd, 1H, $J_{5,4}$ = 6.7 Hz, $J_{5,5'}$ = -15.2 Hz, $J_{5,P}$ = 18.8 Hz, H-5), 2.23 (ddd, 1H, $J_{5',4}$ = 7.1 Hz, $J_{5',P}$ = 18.5 Hz, H-5'), 2.46 (s, 3H, $ArC\underline{H}_3$), 3.29 (s, 3H, $OC\underline{H}_3$), 4.06 (m, 1H, H-3), 4.10 (m, 4H, $P(OC\underline{H}_2)_2$), 4.55 (pseudo dq, 1H, $J_{4,3}$ = 5.2 Hz, $J_{4,P}$ = 7.1 Hz, H-4), 4.72 (s, 1H, H-2), 4.79 (s, 1H, H-1), 7.39 (d, 2H, J = 8.3 Hz, $Ar\underline{H}_{meta}$), 7.81 (d, 2H, $Ar\underline{H}_{ortho}$) ; ^{13}C-NMR (75 MHz, $CDCl_3$) : δ = 16.3 and 16.4 ($P(OCH_2\underline{C}H_3)_2$), 21.7 ($Ar\underline{C}H_3$), 27.7 (d, $J_{C-5,P}$ = 140.0 Hz, C-5), 56.1 ($O\underline{C}H_3$), 62.0 and 62.1 (2d, $J_{OCH2,P}$ = 5.6 Hz, $P(O\underline{C}H_2)_2$), 65.7 (d, $J_{C-3,P}$ = 8.0 Hz, C-3), 76.0 (C-4), 86.1

(C-2), 106.8 (C-1), 128.1 and 130.3 ($\underline{C}H_{arom.}$), 132.5 and 145.9 ($\underline{C}_{arom.}$) ; IR (film) : ν (cm^{-1}) = 2112 (N_3), 1375, 1190 and 1178 (SO_2), 1250 (P=O), 1025 and 975 (P-OC) ; MS (CI) : m/z 464 [M^+ + H] ; Anal. Calcd for $C_{17}H_{26}N_3O_8PS$: C, 44.06 ; H, 5.65 ; N, 9.07 ; P, 6.68 ; S, 6.92. Found : C, 44.29 ; H, 5.63 ; N, 8.99 ; P, 6.33 ; S, 6.91.

3-Azido-3,5-dideoxy-5-C-diethoxyphosphinyl-2-O-tosyl-α,β-D-xylofuranose (14).- A solution of compound **13** (784 mg, 1.69 mmol) in trifluoroacetic acid and water (20 mL of a 90/10 mixture) was stirred at room temperature for 48 h. The solvents were removed and the residue was redissolved in the same solvent mixture and stirred for a further 48 h at room temperature. The solution was then evaporated to dryness, the residue was taken up in ethyl acetate (50 mL) and washed with 5% aqueous sodium carbonate (2 x 20 mL). The combined aqueous phases were extracted with ethyl acetate (2 x 20 mL) and the organic phases were combined and dried over Na_2SO_4. After removal of the solvent, the residual yellow oil was purified by flash chromatography on silica gel (ethyl acetate-heptane, 2:1). Unreacted starting material (108 mg, 14%) was first eluted, followed by the title compound **14** (630 mg, 83%), isolated as a colorless oil. ^{1}H-NMR (250 MHz, $CDCl_3$) : δ = 1.32 and 1.33 (2t, 6H, J = 7.0 Hz, α- and β-P($OCH_2\underline{C}H_3$)$_2$), 1.95-2.35 (m, 2H, α- and β-H-5 and H-5'), 2.47 (s, 3H, Ar$\underline{C}H_3$), 4.04 (d, 0.6H, $J_{3,4}$ = 2.5 Hz, β-H-3), 4.12 (m, 4H, α- and β-P($O\underline{C}H_2$)$_2$), 4.28 (dd, 0.4H, $J_{3,2}$ = 4.3 Hz, $J_{3,4}$ = 5.7 Hz, α-H-3), 4.52 (m, 0.6H, β-H-4), 4.60 (dd, 0.4H, $J_{2,1}$ = 4.2 Hz, α-H-2), 4.66 (m, 0.4H, α-H-4), 4.74 (s, 0.6H, β-H-2), 5.21 (s, 0.6H, β-H-1), 5.38 (d, 0.4H, α-H-1), 7.39 (d, 2H, J = 8.2 Hz, Ar$\underline{H}_{meta}$), 7.85 (d, 2H, Ar$\underline{H}_{ortho}$) ; ^{13}C-NMR (62.5 MHz, $CDCl_3$) : δ = 16.0 and 16.1 (α- and β-P($OCH_2\underline{C}H_3$)$_2$), 21.4 (Ar$\underline{C}H_3$), 27.1 and 27.4 (2d, $J_{C\text{-}5,P}$ = 140.0 Hz, α- and β-C-5), 62.0 and 62.2 (2d, $J_{OCH2,P}$ = 5.6 Hz, α- and β-P($O\underline{C}H_2$)$_2$), 65.4 and 65.7 (2d, $J_{C\text{-}3,P}$ = 7.6 Hz, α- and β-C-3), 71.4 and 74.9 (α- and β-C-4), 82.3 and 86.8 (α- and β-C-2), 93.8 and 100.4 (α- and β-C-1), 127.8, 127.9, 129.8 and 130.1 ($\underline{C}H_{arom.}$), 145.3 and 145.6 ($\underline{C}_{arom.}$) ; IR (film) : ν (cm^{-1}) = 3300 (OH), 2100 (N_3), 1370, 1190 and 1170 (SO_2), 1250 (P=O), 1025 and 965 (P-OC) ; HRMS (CI) : calcd for $C_{16}H_{25}N_3O_8PS$ m/z 450.1100 ; found m/z 450.1073.

tert-Butyldimethylsilyl 3-azido-3,5-dideoxy-5-C-diethoxyphosphinyl-2-O-tosyl-α,β-D-xylofuranoside (15).- A solution of compound **14** (630 mg, 1.4 mmol), imidazole (316 mg, 2.1 mmol) and *tert*-butyldimethylsilyl chloride (190 mg, 2.8 mmol) in DMF (5 mL) was stirred at room temperature under nitrogen for 24 h. After removal of the solvent, the reaction mixture was taken up in ethyl acetate (30 mL) and washed with water (20 mL). The organic phase was dried over Na_2SO_4, evaporated to dryness under vacuum and purified by column chromatography on silica gel (ethyl acetate-heptane, 6:4 followed by 2:1) yielding the silyl derivative **15** (670 mg, 85%) as a colorless oil (mixture of α/β anomers : 2/3). ^{1}H-NMR (250 MHz, $CDCl_3$) : δ = 0.04, 0.06 and 0.12 (3s, 6H, α- and β-Si($C\underline{H}_3$)$_2$), 0.81 and 0.90 (2s, 9H, α- and β-SiC($C\underline{H}_3$)$_3$), 1.31 and 1.32 (3t, 6H, J = 7.0 Hz, α- and β-P($OCH_2\underline{C}H_3$)$_2$), 1.90-2.35 (m, 2H, α- and β-H-5 and H-5'), 2.46 (s, 3H, Ar$\underline{C}H_3$), 4.00 (d, 0.6H, $J_{3,4}$ = 4.6 Hz, β-H-3), 4.10 (m, 4H, α- and β-P($O\underline{C}H_2$)$_2$), 4.25 (pseudo t, 0.4H, J = 6.2 Hz, α-H-3), 4.46 (m, 0.6H, β-H-4), 4.47 (dd, 0.4H, $J_{2,1}$ = 4.0 Hz, $J_{2,3}$ = 5.5 Hz, α-H-2), 4.65 (m, 1H, β-H-2 and α-H-4), 5.15 (s, 0.6H, β-H-1), 5.35 (d, 0.4H, α-H-1), 7.38 (2d, 2H, J = 8.0 Hz, Ar$\underline{H}_{meta}$), 7.83 (2d, 2H, J = 8.0 Hz, Ar$\underline{H}_{ortho}$) ; ^{13}C-NMR (62.5 MHz, $CDCl_3$) : δ = -4.8 and -4.5 (α- and β-Si($\underline{C}H_3$)$_2$), 16.3 and 16.4 (α- and β-P($OCH_2\underline{C}H_3$)$_2$), 17.7 and 18.0 (α- and β-Si$\underline{C}$), 21.7 (Ar$\underline{C}H_3$), 25.4 and 25.6 (α- and β-SiC($\underline{C}H_3$)$_3$), 27.5 and 27.6 (2d, $J_{C\text{-}5,P}$ = 140.0 Hz, α- and β-C-5), 61.8 and 62.0 (2d, $J_{OCH2,P}$ = 7.0 Hz, α- and β-P($O\underline{C}H_2$)$_2$), 65.0 and 65.4 (2d, $J_{C\text{-}3,P}$ = 6.7 Hz, α- and β-C-3), 71.7 and 75.8 (α- and β-C-4), 83.1 and 87.5 (α- and β-C-2), 94.2 and 100.8 (α- and β-C-1), 127.9, 128.0, 130.1 and 130.3 ($\underline{C}H_{arom.}$), 132.7, 132.9, 145.4 and 145.8 ($\underline{C}_{arom.}$) ; IR (film) : ν (cm^{-1}) = 2113 (N_3), 1375, 1191 and 1180 (SO_2), 1254 ($SiCH_3$ and P=O), 1030 and 966 (P-OC), 832 (SiC(CH_3)$_3$) ; MS (CI) : m/z 564 [M^+ + H] ; Anal. Calcd for $C_{22}H_{38}N_3O_8PSSi$: C, 46.88 ; H, 6.80 ; N, 7.46 ; P, 5.50 ; S, 5.68 ; Si, 4.97. Found : C, 46.88 ; H, 6.71 ; N, 7.73 ; P, 5.35 ; S,5.45 ; Si, 5.06.

tert-Butyldimethylsilyl 2,3-aziridino-5-C-diethoxyphosphinyl-2,3,5-trideoxy-α,β-D-lyxofuranoside (16).- A solution of the azido derivative **15** (650 mg, 1.15 mmol) in methanol (30 mL) was hydrogenated at atmospheric pressure for 2 h at room temperature in the presence of 10% palladium on carbon (200 mg). The

catalyst was then removed by filtration through celite and the filtrate was evaporated to dryness, leaving an oily residue. The latter was dissolved in DMF (15 mL) and the solution was heated at 100°C for 4 h in the presence of triethylamine (2 mL). After removal of the solvent, the remaining brownish oil was purified by column chromatography on silica gel (dichloromethane-ethanol, 97:3 followed by 95:5) providing the aziridine **16** (280 mg, 67%) as a colored oil (mixture of α/β anomers : 3/7). ^{1}H-NMR (250 MHz, $CDCl_3$) : δ = 0.11, 0.12 and 0.14 (3s, 6H, α- and β-Si($C\underline{H}_3$)$_2$), 0.88 and 0.90 (2s, 9H, α- and β-SiC($C\underline{H}_3$)$_3$), 1.33 and 1.34 (2t, 6H, J = 7.0 Hz, α- and β-P($OCH_2C\underline{H}_3$)$_2$), 1.96-2.23 (m, 2H, α- and β-H-5 and H-5'), 2.58 (d, 0.3H, $J_{2,3}$ = 3.6 Hz, α-H-2), 2.63 (d, 0.7H, $J_{2,3}$ = 3.6 Hz, β-H-2), 2.67 (d, 0.7H, β-H-3), 2.83 (m, 0.3H, α-H-3), 4.13 (m, 4H, α- and β-P($OC\underline{H}_2$)$_2$), 4.22 (pseudo q, 0.7H, J = 6.7 Hz, β-H-4), 4.43 (pseudo q, 0.3H, J= 6.9 Hz, α-H-4), 5.27 (d, 0.3H, $J_{1,2}$ = 0.9 Hz, α-H-1), 5.35 (s, 0.7H, β-H-1) ; ^{13}C-NMR (75 MHz, $CDCl_3$) : δ = -4.8, -4.4 and -4.3 (α- and β-Si($\underline{C}H_3$)$_2$), 16.4 and 16.5 (α- and β-P($OCH_2\underline{C}H_3$)$_2$), 17.9 and 18.0 (α- and β-Si$\underline{C}$), 25.7 (α- and β-SiC($\underline{C}H_3$)$_3$), 27.9 and 28.5 (2d, $J_{C\text{-}5,P}$ = 140.0 Hz, α- and β-C-5), 36.0 and 37.2 (2d, $J_{C\text{-}3,P}$ = 7.0 Hz, α- and β-C-3), 38.5 and 39.7 (α- and β-C-2), 61.6 and 61.9 (2d, $J_{OCH_2,P}$ = 6.8 Hz, α- and β-P($O\underline{C}H_2$)$_2$), 71.2 and 71.7 (α- and β-C-4), 97.6 and 97.7 (α- and β-C-1) ; IR (film) : ν (cm^{-1}) = 3260 (NH), 1250 (Si(CH_3)$_2$), 1230 (P=O), 1025 and 962 (P-OC) ; HRMS (CI) : calcd for $C_{15}H_{33}NO_5PSi$ m/z 366.1866 ; found m/z 366.1839.

tert-Butyldimethylsilyl 2,3-N-(benzyloxycarbonyl)aziridino-5-C-diethoxyphosphinyl-2,3,5-trideoxy-α,β-D-lyxofuranoside (17).- To a stirring solution of aziridine **16** (280 mg, 0.766 mmol) and triethylamine (215 µL, 1.53 mmol) in DMF (10 mL) held at 0°C was added dropwise under an inert atmosphere benzyl chloroformate (220 µL, 1.53 mmol). After 30 min at 0°C and a further 2 h at 20 °C, the reaction mixture was diluted with dichloromethane (20 mL) and washed with water (15 mL). The organic phase was dried over Na_2SO_4, evaporated to dryness under vacuum and the residue was purified by flash chromatography on silica gel (ethyl acetate-heptane, 3:1) affording the title compound **17** (340 mg, 89%) as a colorless oil. ^{1}H-NMR (250 MHz, $CDCl_3$) : δ = 0.10 and 0.14 (2s, 6H, α- and β-Si($C\underline{H}_3$)$_2$), 0.88 and 0.90 (2s, 9H, α- and β-SiC($C\underline{H}_3$)$_3$), 1.29 (t, 6H, J = 7.0 Hz, α- and β-P($OCH_2C\underline{H}_3$)$_2$), 2.19-2.35 (m, 2H, α- and β-H-5 and H-5'), 3.20 (d, 0.3H, $J_{2,3}$ = 4.4 Hz, α-H-2), 3.26 (d, 0.7H, $J_{2,3}$ = 3.7 Hz, β-H-2), 3.39 (d, 0.7H, β-H-3), 3.44 (d, 0.3H, α-H-3), 4.08 (m, 4H, J = 7.0 Hz, α- and β-P($OC\underline{H}_2$)$_2$), 4.17 (m, 0.7H, β-H-4), 4.39 (m, 0.3H, α-H-4), 5.11 (2d, 0.6H, J = 12.2 Hz, α-Ar$C\underline{H}_2$), 5.12 (s, 1.4H, β-Ar$C\underline{H}_2$), 5.31 (s, 0.7H, β-H-1), 5.37 (s, 0.3H, α-H-1), 7.35 (s, 5H, Ar$\underline{H}$) ; ^{13}C-NMR (75 MHz, $CDCl_3$) : δ = -4.8, -4.5, -3.9 and -3.7 (α- and β-Si($\underline{C}H_3$)$_2$), 16.7 and 16.8 (α- and β-P($OCH_2\underline{C}H_3$)$_2$), 18.2 and 18.5 (α- and β-Si$\underline{C}$), 26.1 and 26.2 (α- and β-SiC($\underline{C}H_3$)$_3$), 27.6 and 28.6 (2d, $J_{C\text{-}5,P}$ = 140.0 Hz, α- and β-C-5), 43.2 and 44.3 (2d, $J_{C\text{-}3,P}$ = 6.6 Hz, α- and β-C-3), 45.3 and 45.5 (α- and β-C-2), 62.1 and 62.3 (2d, $J_{OCH_2,P}$ = 6.3 Hz, α- and β-P($O\underline{C}H_2$)$_2$), 68.7(Ar$\underline{C}H_2$), 71.8 and 71.9 (α- and β-C-4), 96.3 and 97.1 (α- and β-C-1), 128.5, 128.7, 128.9 and 129.0 (α- and β-$\underline{C}H_{arom.}$), 135.9 and 136.0 (α- and β-$\underline{C}_{arom.}$), 161.5 and 162.3 (α- and β-C=O) ; IR (film) : ν (cm^{-1}) = 1730 (C=O), 1260 (SiCH_3), 1035 and 965 (P-OC), 840 (SiC(CH_3)$_3$) ; MS (EI) : m/z 499 [M^+] ; Anal. Calcd for $C_{23}H_{38}NO_7PSi$: C, 55.29 ; H, 7.67 ; N, 2.80 ; P, 6.20. Found : C, 55.43 ; H, 7.56 ; N, 2.72 ; P, 6.36.

2,3-N-(benzyloxycarbonyl)aziridino-5-C-diethoxyphosphinyl-2,3,5-trideoxy-β-D-lyxofuranose (18).- To a stirring solution of the silyl derivative **17** (110 mg, 0.22 mmol) in dichloromethane (2 mL) held at -60°C was added under nitrogen tetrabutylammonium fluoride trihydrate (76 mg, 0.24 mmol). The reaction mixture was slowly allowed to warm to room temperature over 2 h. The solvent was then evaporated under reduced pressure leaving a colored oily residue which was purified by flash chromatography on silica gel (ethyl acetate-ethanol, 98:2) yielding lactol **18** (72 mg, 85%) as a white solid. M.p. 125.5°C ; ^{1}H-NMR (250 MHz, $CDCl_3$) : δ = 1.28 (2t, 6H, J = 7.0 Hz, P($OCH_2C\underline{H}_3$)$_2$), 2.27 (dd, 2H, $J_{5,4}$ = 6.9 Hz, $J_{5,P}$ = 18.5 Hz, H-5 and H-5'), 3.29 (d, 1H, $J_{2,3}$ = 4.4 Hz, H-2), 3.43 (dd, 1H, $J_{3,4}$ = 0.6 Hz, H-3), 4.06 (pseudo quint., 4H, J = 7.3 Hz, P($OC\underline{H}_2$)$_2$), 4.50 (pseudo q, 1H, J = 6.8 Hz, H-4), 5.12 (s, 2H, Ar$C\underline{H}_2$), 5.42 (s, 1H, H-1), 5.52 (m, 1H, exchangeable with D_2O, OH), 7.35 (s, 5H, Ar$\underline{H}$) ; ^{13}C-NMR (75 MHz, $CDCl_3$) : δ = 16.3 and 16.4 (P($OCH_2\underline{C}H_3$)$_2$), 27.1 (d, $J_{C\text{-}5,P}$ = 140.0 Hz, C-5), 42.8 (d, $J_{C\text{-}3,P}$ = 8.6 Hz, C-3), 44.5 (C-2), 61.9 and 62.3 (2d, $J_{OCH_2,P}$ = 6.6 Hz, P($O\underline{C}H_2$)$_2$), 68.4 (Ar$\underline{C}H_2$), 70.9 (C-4), 95.4 (C-1), 128.3, 128.4 and 128.6 ($\underline{C}H_{arom.}$), 135.4 ($\underline{C}_{arom.}$), 161.2 (C=O) ; IR (film) : ν (cm^{-1}) = 3170 (OH), 1730 (C=O), 1260 (P=O), 1025 and 965 (P-

OC) ; MS (CI) : m/z 386 [M^+ + H] ; Anal. Calcd for $C_{17}H_{24}NO_7P$: C, 52.99 ; H, 6.28 ; N, 3.63 ; P, 8.04. Found : C, 52.96 ; H, 6.29 ; N, 3.46 ; P, 8.29.

(1S, 4S, 5R) N-(Benzyloxycarbonyl)-4-(diethoxyphosphinyl)methyl-3-oxa-6-azabicyclo[3.1.0]hexan-2-one (4).- A solution of lactol **18** (69 mg, 0.179 mmol) in acetonitrile (4 mL) was stirred at 20°C under nitrogen in the presence of anhydrous 4-methylmorpholine *N*-oxide (32 mg, 0.273 mmole), tetrapropylammonium perruthenate (9 mg, 0.025 mmole) and finely ground 4Å molecular sieves (90 mg). After 3 h, the reaction mixture was concentrated under reduced pressure and filtered through a pad of silica gel (ethyl acetate) affording the desired lactone **4** (45 mg, 65%) as a colorless oil. $[\alpha]_D^{20}$ -38.4 (c 1, $CHCl_3$) ; ^{1}H-NMR (250 MHz, $CDCl_3$) : δ = 1.29 and 1.31 (2t, 6H, J = 7.0 Hz, $P(OCH_2\underline{C}H_3)_2$), 2.32 (ddd, 1H, $J_{Ha,4}$ = 5.3 Hz, $J_{Ha,Hb}$ = -15.1 Hz, $J_{Ha,P}$ = 19.2 Hz, PCH_a), 2.44 (ddd, 1H, $J_{Hb,4}$ = 8.5 Hz, $J_{Hb,P}$ = 18.1 Hz, PCH_b), 3.59 (d, 1H, $J_{1,5}$ = 4.3 Hz, H-1), 3.89 (dd, 1H, $J_{5,4}$ = 2.7 Hz, H-5), 4.10 (2qd, 4H, J = 7.2 Hz, $P(O\underline{C}H_2)_2$), 4.83 (pseudo ddt, 1H, H-4), 5.16 (s, 2H, $Ar\underline{C}H_2$), 7.36 (s, 5H, $Ar\underline{H}$) ; ^{13}C-NMR (75 MHz, $CDCl_3$) : δ = 16.3 and 16.4 ($P(OCH_2\underline{C}H_3)_2$), 27.9 (d, $J_{C,P}$ = 140.0 Hz, CH_2P), 39.1 (C-1), 43.3 (d, $J_{C\text{-}5,P}$ = 6.5 Hz, C-5), 62.1 and 62.4 (2d, $J_{OCH_2,P}$ = 6.8 Hz, $P(O\underline{C}H_2)_2$), 69.5 ($Ar\underline{C}H_2$), 74.7 (C-4), 128.5, 128.7 and 128.8 ($\underline{C}H_{arom.}$), 134.7 ($\underline{C}_{arom.}$), 159.6 ($C{=}O_{carbamate}$), 166.7 ($C{=}O_{lactone}$) ; IR (film) : ν (cm^{-1}) = 1790 (OC=O), 1735 (NC=O), 1256, 1168, 1025 and 965 (P-OC) ; HRMS (CI) : calcd for $C_{17}H_{23}NO_7P$ m/z 384.1292 ; found m/z 384.1253.

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17. During the conversion of the azido-tosylate **15** to the aziridine **16**, the cyclization step takes place more easily with the β-anomer due to steric interactions between the tosyl and the bulky silyl groups when the latter lies in the α face. This results in different α:β ratio (2:3 for compound **15** then 3:7 for the aziridine **16**), the β-anomer being formed in major quantity.
18. For a review, see : Ley, S.V.; Norman, J.; Griffith, W.P.; Marsden, S.P. *Synthesis* **1994**, 639.
19. Corresponding to H-1 and H-5, respectively, in the IUPAC nomenclature for compound **4**.

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