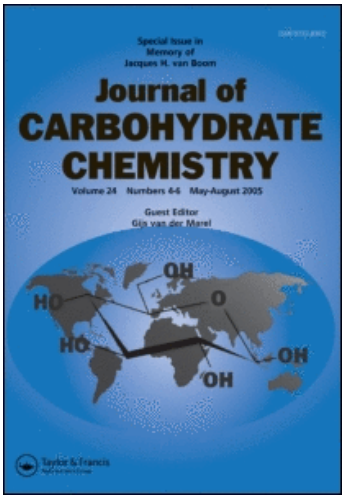

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Valentine Rocherolle[a]; J. Cristobal Lopez[a]; Alain Olesker[a]; Gabor Lukacs[a]
[a] Institut de Chimie des Substances Naturelles du C.N.R.S., Gif-sur-Yvette Cedex, France

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SYNTHESIS OF GEMINAL ALKYL AND EQUATORIALLY FUNCTIONALIZED GEMINAL ALKYL DERIVATIVES OF HEXOPYRANOSIDES BY CARBOPALLADATION

Valentine Rocherolle, J. Cristobal Lopez, Alain Olesker and Gabor Lukacs*

Institut de Chimie des Substances Naturelles du C.N.R.S., 91198 Gif-sur-Yvette Cedex, France.

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ABSTRACT

Carbohydrate ketoenolates gave gem-di-C-methyl derivatives in the presence of methyl iodide. The oximes of the latter furnished equatorially functionalized gem-di-C-alkyl derivatives by cyclo-palladation-oxidation followed by reduction.

INTRODUCTION

The use of carbohydrates as chiral building blocks for the synthesis of natural products implies a choice of the sugar derivative[1,2] on the basis of easy accessibility, latent functionalities, and versatility. Extension of the scope of carbohydrates as suitable building blocks relies on the development of convenient key intermediates capable of meeting these requirements. We were interested in preparing carbohydrate derivatives bearing geminal alkyl substituents on the pyranoside ring and also the same type of compounds in which the alkyl substituents were differentiated and functionalized for further manipulations.[3]

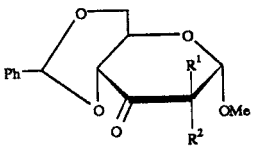
RESULTS AND DISCUSSION

Considerable interest was devoted in recent years to the synthesis of gem-di-C-alkyl derivatives of carbohydrates.[4-11] An elegant method utilizing stereoselective Claisen rearrangement of alkyl vinyl ethers was also reported for the preparation of such compounds, functionalized in one of the alkyl groups.[12]

We report here that gem-di-C-methyl derivatives 6, 7 and 8 can be obtained from 2,3:4,6-di-O-benzylidene-α-D-mannopyranoside 4[13] and from ketones 2[14] and 3,[15] respectively. Yields were modest in the preparation of 6 and excellent and good, respectively, in the synthesis of 7 and 8. Since our initial efforts to dialkylate the ketoenolates from 1,[13] 2 and 3 with the help of lithium diisopropylamide as base were not successful, we attempted the use of 2,2,6,6-tetramethylpiperidine.[16] The ketoenolates were prepared in ether solution in an argon atmosphere at -35°C in the presence of butyl-lithium and 2,2,6,6-tetramethylpiperidine. The enolates were allowed to react with methyl iodide and hexamethylphosphoramide furnishing products consisting of the desired gem-di-C-methyl derivatives. When the reaction was applied to ketone 1, the corresponding gem-di-C-methyl derivative 6 was present in the reaction mixture only in a very small amount. Therefore, the lithium enolate 5 was prepared from 4 according to Chapleur[5] and treated as indicated above. In case of ketone 3, the reaction gave also the β-elimination product 11 in about 28% yield.

Recent investigations have shown the potential of the Shaw reaction[17] in preparing stereospecifically equatorially functionalized gem-di-C-methyl derivatives from ketoximes substituted by gem-di-C-methyl groups at the α-position.[18-20] Application of this reaction, according to the methodology of Baldwin and co-workers,[18,19] to the gem-di-C-methyl carbohydrates 12, 13 and 14 gave in good yield the desired products 17, 18 and 19, respectively.

The ketoximes 12, 13 and 14 were prepared from the corresponding ketones 6, 7 and 8, respectively, in quantitative yield.



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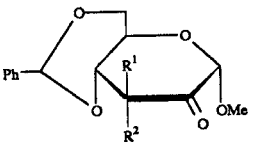
6 $R^1 = R^2 = Me$

9 $R^1 = H$; $R^2 = Me$

10 $R^1 = Me$; $R^2 = H$



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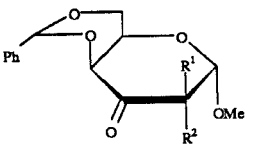

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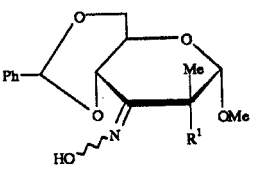

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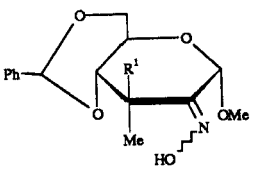
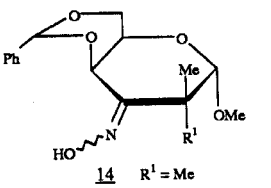
17 $R^1 = CH_2OAc$



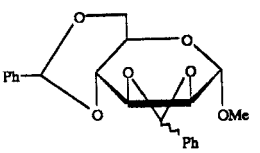
13 $R^1 = Me$

18 $R^1 = CH_2OAc$



14 $R^1 = Me$

19 $R^1 = CH_2OAc$



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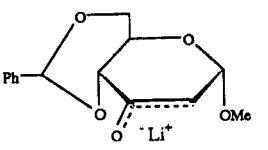

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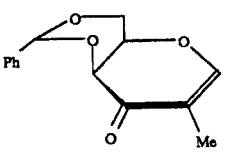

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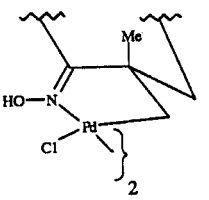

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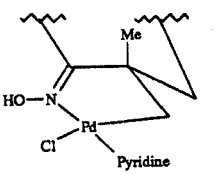

16

When the oximes 12, 13 and 14 were allowed to react with disodium tetrachloropalladate and sodium acetate, the corresponding dimeric organopalladium compounds of general structure 15 were obtained in excellent yields. The dimeric organopalladium compounds were then converted by treatment with pyridine in tetrahydrofuran solution into the corresponding monomeric complexes of general structure 16. Oxidation of these complexes by lead tetra-acetate, followed by reduction with sodium borohydride afforded the corresponding acetoxy oximes 17, 18 and 19.

Stereochemistry of the oximes

Carbon-13 NMR spectroscopy has been shown to be extremely useful for the determination of the configuration of ketoximes.[21] In an extensive investigation on the ^{13}C chemical shifts of these compounds, Hawkes, Herwig and Roberts have found that ketoximes with α quaternary carbons were always single isomers which were believed to have the oxime OH anti to the quaternary carbon.[21] This hypothesis was substantiated by the observation of a consistent pattern of α-anti and α-syn carbon shift changes upon transformation of a ketone to an oxime. The resonances of both α-carbons were shown to be shielded on oxime formation, with the effect for the α-syn carbon being considerably greater than for the α-anti carbon.

Interestingly, conversion of ketone 6 to the corresponding oxime 12 afforded a 1:1 mixture of two isomers while similar transformation of ketones 7 and 8 to their oximes furnished only a single isomer, as judged from their carbon-13 NMR spectra in $CDCl_3$ solution. In case of the oximes 12, resulting from ketone 6, the chemical shift of C-4 could be easily assigned. The Δδ value of 3.8 ppm for C-4 of these two compounds was attributed, in agreement with expectation, to the configuration of the oxime OH group. Thus, the chemical shift value of C-4 of the oxime anti to the quaternary carbon was 76.5 ppm while C-4 of the oxime syn to the quaternary carbon was 80.3 ppm.

After functionalization of the equatorial C-methyl group, oxime 17 revealed to be quite surprisingly a single isomer. Furthermore, the chemical shift of C-4 in compound 17 being 80.1 ppm, we would be tempted to draw the unexpected conclusion that the oxime OH of this compound is syn to its quaternary carbon atom in $CDCl_3$ solution. No explanation can be put forward at this moment for this observation. The chemical shift difference of C-2 between the syn and anti oximes, resulting from ketone 6, is too small for being taken into account for structural assignments.

No final conclusion can be advanced concerning the configuration of the oximes 13 and 14 derived as single isomers from ketones 7 and 8, respectively.

Stereochemistry at the quaternary carbon centers

Application of carbon-13 N.M.R. spectroscopy has permitted the determination of the configuration of the substituents of quaternary centers for the new α-acetoxy ketoximes prepared during this investigation. The spectral study of appropriate model compounds appeared to be extremely useful. Thus, the chemical shift of the C-methyl group in the ^{13}C NMR spectrum of the isomeric models 9[22] and 10[22] was 8.6 and 16.2 ppm, respectively, in $CDCl_3$ solution.

The very high field shift of the C-methyl group in the spectrum of 9 was interpreted, on the one hand, by the cis-relationship between the C-methyl group and the anomeric substituent and by the coplanar arrangement of the C-3 ketone and the C-2 substituent, on the other. The C-methyl group in the spectrum of 10 is shielded only by the axially disposed H-4. From these results, the 25.5 and 19.1 ppm chemical shifts in the spectrum of 6 could be easily assigned to the axial and equatorial C-methyl groups, respectively. The downfield shifts, relative to the monosubstituted compounds 9 and 10, are the consequence of the β-effect due to the additional methyl group in 6.

Upon oxime formation both C-methyl groups were slightly deshielded. The chemical shift of the remaining C-methyl group in

the spectrum of 17 was 21.2 ppm. In view of the shielding γ-effect, due to the oxygen atom of the acetoxy group, it appeared clear that the 21.2 ppm resonance had to be assigned to an axially oriented C-methyl group. A Δδ value of 5.1 ppm for the axially disposed C-methyl groups of 17 and 12 was found in agreement with the theory.[23]

The stereochemistry of the quaternary centers of 18 and 19 was established by using identical considerations, although, the corresponding isomeric axially and equatorially monosubsituted C-methyl compounds were not available.

The chemical shifts of the axial and equatorial C-methyl group of 8 was 24.3 ppm and 19.4 ppm, respectively. Again, upon oxime formation, these resonance positions moved slightly downfield to 26.2 ppm and 21.3 ppm, respectively in 14. The chemical shift of the remaining C-methyl group in the spectrum of 19 was 21.2 ppm. A Δδ value of 5.0 ppm for the C-methyl group of 14 and 19 indicated that the acetoxymethyl function of 19 was equatorially oriented. Similar conclusions were reached for the acetoxymethyl group of 18, although the situation was not as clear as in the previously discussed cases. However, the Δδ value of 5.1 ppm, between the spectrum of 13 and 18, was again in favour of an axially disposed C-methyl group in 18.

In conclusion, functionalization of the equatorial C-methyl group of the gem-di-C-methyl derivatives occured stereospecifically during the cyclopalladation reaction. This result, in agreement with previous investigations,[15,16] can be explained by the coplanar arrangement of the oximes and the equatorial methyl groups.

EXPERIMENTAL

General Procedures. The melting points were determined with a Büchi apparatus and are uncorrected. A Perkin-Elmer Model 141 MC polarimeter and 1-dm tubes were used for measurement of specific rotations. ^{1}H NMR spectra were recorded in chloroform-d solution at 400 MHz. The ^{13}C NMR spectra were measured in chloroform-d

solution at 50.31 MHz with a Bruker WP-200 spectrometer. Chemical shifts are given in parts per million, and tetramethylsilane was the internal standard (δ 0.000). Carbon-13 chemical shifts for aromatic carbons are not given. Microanalyses were performed by the Service Central de Microanalyse du CNRS. Silica gel 60 PF_{254} (Merck) activated at 120°C was the support for TLC and for column chromatography.

Methyl 4,6-O-benzylidene-2-deoxy-2-C-dimethyl-α-D-erythro-hexopyranosid-3-ulose (6). To a solution of 1.6M butyl-lithium (37 mL, 60 mmol, 2.2 eq.) in dry tetrahydrofuran (400 mL) was added 2,3:4,6-di-O-benzylidene-α-D-mannopyranoside 4 (27 mmol) and the mixture was stirred at -40°C for 1 h under an argon atmosphere. Then, 2,2,6,6-tetramethyl-piperidine (930 μL, 5.45 mmol) was added to neutralize the excess of butyl-lithium and the temperature was allowed to warm up to 25°C for 10 min. The temperature of the solution was then cooled to -40°C and the lithium salt of 2,2,6,6-tetramethylpiperidine was added to it [the lithium salt was prepared by adding 1.6M butyl-lithium (28 mL, 46 mmol) to 2,2,6,6-tetramethylpiperidine (7.85 mL, 46 mmol) in tetrahydrofuran solution (100 mL) at room temperature]. Then, to the reaction mixture were added hexamethylphosphoramide (47 mL, 270 mmol) and methyl iodide (17 mL, 270 mmol). The temperature of the solution was kept at -40°C for 3 h and then at -10°C for 42 h. A saturated solution of ammonium chloride (400 mL) was added to the mixture, the organic phase was washed with a 0.5N solution of hydrochloric acid (2 x 100 mL), dried over magnesium sulfate and concentrated in vacuo. The crude material was further purified by flash chromatography (hexane/ethyl acetate, 8:2) to afford the ketone 6 (1.34 g, 17%), and a mixture of methyl-4,6-O-benzylidene-2-deoxy-α-D-erythro-hexopyranosid-3-ulose 1 (2.9 g, 40%) and methyl 4,6-O-benzylidene-2-deoxy-2-C-methyl-α-D-ribo-hexopyranosid-3-ulose 9 (1.5 g, 20%). Repetition of the reaction using the latter two compounds raised the overall yield of 6 to 25%. Pure 6 is a syrup, $[\alpha]_D^{22}$ = + 54° (c = 0.9, chloroform); mass spectrum (chemical ionization) (M^+ + H) 293; ^1H NMR δ 7.32-7.48 (m, 5H, Ph); 5.54

(s, 1H, H-7); 4.54 (s, 1H, H-1); 4.53 (d, 1H, $J_{4,5}$ = 11 Hz, H-4); 4.35 (q, 1H, $J_{5,6}$ = 5 Hz, J_{gem} = 11 Hz, H-6 eq); 4.12 (m, 1H, H-5); 3.93 (t, 1H, $J_{5,6\ ax}$ = J_{gem} = 11 Hz, H-6 ax); 3.35 (s, 3H, OMe); 1.36 (s, 3H, C-2Me_{ax}); 1.10 (s, 3H, C-2Me_{eq}); ^{13}C NMR δ: 202.7 (C-3); 108.5 (C-1); 102.3 (C-7); 80.0 (C-4); 69.7 (C-6); 65.8 (C-5); 55.3 (OMe); 51.5 (C-2); 25.5 (C-2Me_{ax}); 19.1 (C-2Me_{eq}).

Anal. Calcd for $C_{16}H_{20}O_5$: C, 65.74; H, 6.90; O, 27.36. Found: C, 65.99; H, 6.75.

Methyl 4,6-O-benzylidene-3-deoxy-3-C-dimethyl-α-D-erythro-hexopyranosid-2-ulose (7). To a solution of 1.6M butyl-lithium (3.12 mL, 5.7 mmol) in anhydrous ether (25 mL) was added 2,2,6,6-tetramethylpiperidine (0.9 mL, 5.7 mmol) and the mixture was stirred at room temperature for 10 min under an argon atmosphere. The mixture was then cooled to -10°C and methyl 4,6-O-benzylidene-3-deoxy-α-D-arabino-hexopyranosid-2-ulose 2 (500 mg, 1.9 mmol) was added to it. After two hours ether was evaporated and replaced by tetrahydrofuran and then methyl iodide (1.19 mL, 19 mmol) in hexamethylphosphoramide (3.3 mL, 19 mmol) was added to the mixture which was kept at 0°C for 36 h. Working-up, as indicated above for the preparation of 6, furnished a crude reaction mixture which without purification was treated again as above except that the enolate was formed at 0°C. The final residue was purified by flash chromatography (hexane/ethyl acetate, 3:1) affording pure 7 (470 mg, 85%), mp 150-152°C; $[\alpha]_D^{22}$ = + 49° (c = 0.3, chloroform); mass spectrum (chemical ionization) (M^+ + H) 293; ^{1}H NMR δ 7.40-7.52 (m, 5H, Ph); 5.55 (s, 1H, H-7); 4.70 (s, 1H, H-1); 4.42 (q, 1H, $J_{5,6}$ = 5 Hz, J_{gem} = 11 Hz, H-6 eq); 4.31 (m, 1H, H-5); 3.77 (t, 1H, $J_{5,6\ ax}$ = J_{gem} = 11 Hz, H-6 ax); 3.56 (d, 1H, $J_{4,5}$ = 11 Hz, H-4); 3.53 (s, 3H, OMe); 1.35 (s, 3H, C-3Me_{eq}); 1.26 (s, 3H, C-3Me_{ax}); ^{13}C NMR δ: 202.3 (C-2); 100.7 (C-1); 100.6 (C-7); 82.8 (C-4); 68.6 (C-6); 59.3 (C-5); 55.6 (OMe); 47.5 (C-3); 20.1 (C-3Me_{ax}); 18.2 (C-2Me_{eq}).

Anal.Calcd for $C_{16}H_{20}O_5$: C, 65.74; H, 6.90; O, 27.36. Found: C, 65.96; H, 6.76.

Methyl 4,6-O-benzylidene-2-deoxy-2-C-dimethyl-α-D-threo-hexopyranosid-2-ulose (8) and 4,6-O-benzylidene-1,2-deoxy-2-C-methyl-D-threo-hex-1-enopyran-3-ulose (11). To a solution of 1.6M butyllithium (3.12 mL, 5.7 mmol) in anhydrous ether (25 mL) was added 2,2,6,6-tetramethylpiperidine (0.9 mL, 5.7 mmol) and the mixture was stirred at room temperature for 10 min under an argon atmosphere. The mixture was then cooled to -40°C and methyl 4,6-O-benzylidene-2-deoxy-α-D-threo-hexopyranosid-3-ulose 3 (500 mg, 1.9 mmol) was added to it. After one hour ether was evaporated and replaced by tetrahydrofuran and then methyl iodide (1.2 mL, 19 mmol) in hexamethylphosphoramide (3.3 mL, 19 mmol) was added to the mixture which was kept at 0°C for 36 h. Working-up, as described above for the preparation of 6, furnished a crude reaction mixture which was flash chromatographed (hexane/ethyl acetate, 8:2) affording 8 (340 mg, 65%) and 11 (135 mg, 28%).

Analytically pure 8 was obtained by crystallization from hexane/ethyl acetate, mp 159-161°C, $[\alpha]_D^{22}$ = + 69° (c = 0.57, chloroform); mass spectrum (chemical ionization) (M^+ + H) 293; ^{1}H NMR δ 7.30-7.45 (m, 5H, Ph); 5.48 (s, 1H, H-7); 4.63 (s, 1H, H-1); 4.38 (d, 1H, J_{gem} = 11 Hz, H-6 eq); 4.25 (d, 1H, $J_{4,5}$ = 2 Hz, H-4); 4.17 (q, 1H, $J_{5,6ax}$ = 2 Hz, J_{gem} = 11 Hz, H-6 ax); 3.87 (m, 1H, H-5); 3.35 (s, 3H, OMe); 1.48 (s, 3H, C-2Me); 1.06 (s, 3H, C-2Me); ^{13}C NMR δ: 204.1 (C-3); 107.5 (C-1); 100.9 (C-7); 78.9 (C-4); 69.1 (C-6); 63.0 (C-5); 55.3 (OMe); 49.4 (C-2); 24.3 (C-2Me$_{ax}$); 19.4 (C-2Me$_{eq}$).

Anal. Calcd for $C_{16}H_{20}O_5$: C, 65.74; H, 6.90; O, 27.36. Found: C, 65.94; H, 6.90.

Analytically pure 11 was obtained by crystallization from hexane/ethyl acetate mp 145°C; $[\alpha]_D^{22}$ = +147° (c = 1.07, chloroform); mass spectrum (chemical ionization) (M^+ + H) 247; ^{1}H NMR δ 7.33-7.48 (m, 5H, Ph); 7.40 (s, 1H, H-1); 5.60 (s, 1H, H-7); 4.48 (d, 1H, J_{gem} = 11 Hz, H-6 eq); 4.20 (2s, 2H, H-4 and H-5); 4.13 (q, 1H, $J_{5,6\ ax}$ = 2 Hz, J_{gem} = 11 Hz, H-6 ax); 1.73 (s, 3H, C-2Me); ^{13}C NMR δ: 186.7 (C-3); 160.7 (C-1); 112.7 (C-2); 100.9 (C-7); 73.3 (C-4); 68.3 (C-6); 10.7 (C-2Me).

Anal. Calcd for $C_{14}H_{14}O_4$: C, 68.28; H, 5.73. Found: C, 68.30; H, 5.55.

General procedure for the preparation of the oximes. To a solution of ulose (100 mg, 0.36 mmol) in dry pyridine was added hydroxylamine hydrochloride (86 mg, 1.37 mmol) and the mixture was stirred at room temperature for 5 h. The solution was diluted with ice water and extracted with dichloromethane. The organic phase was washed with cold 1N hydrochloric acid, dried over magnesium sulfate and evaporated, affording the oximes (95-98%).

Methyl 4,6-O-benzylidene-2-deoxy-2-C-dimethyl-α-D-erythro-hexopyranosid-3-ulose oxime (12). ^{13}C NMR δ: 151.6 and 150.2 (C-3, C-3'). 107.1 and 106.6 (C-1, C-1'); 102.9 and 102.1 (C-7, C-7'); 80.3 and 76.5 (C-4, C-4'); 69.7 and 69.7 (C-6, C-6'); 64.4 and 63.9 (C-5, C-5'); 55.3 (OMe, OMe'); 45.2 and 44.5 (C-2, C-2'); 26.3 and 25.5 (C-2Me_{ax}, C-2'Me_{ax}); 23.9 and 21.7 (C-2Me_{eq}, C-2'Me_{eq}).

Methyl 4,6-O-benzylidene-3-deoxy-3-C-dimethyl-α-D-erythro-hexopyranosid-2-ulose oxime (13). mp = 120-122°C, $[\alpha]_D^{22}$ = + 7° (c = 1.82, chloroform); ^1H NMR δ 7.42-7.58 (m, 5H, Ph); 5.86 (s, 1H, H-1); 5.60 (s, 1H, H-7); 4.37 (q, 1H, $J_{5,6}$ = 5 Hz, J_{gem} = 11 Hz, H-6 eq); 4.17 (m, 1H, H-5); 3.73 (t, 1H, $J_{5,6\ ax} = J_{gem}$ = 11 Hz, H-6 ax); 3.53 (s, 3H, OMe); 3.48 (d, 1H, $J_{4,5}$ = 10 Hz, H-4); 1.37 (s, 3H, C-3Me_{ax}); 1.30 (s, 3H, C-3Me_{eq}); ^{13}C NMR δ: 158.3 (C-2); 101.5 (C-7); 92.0 (C-1); 83.4 (C-4); 69.3 (C-6); 60.0 (C-5); 55.5 (OMe); 39.7 (C-3); 22.5 (C-2Me_{ax}); 21.2 (C-2Me_{eq}).

Methyl 4,6-O-benzylidene-2-deoxy-2-C-dimethyl-α-D-threo-hexo-pyranosid-3-ulose oxime (14). mp = 125-127°C, $[\alpha]_D^{22}$ = + 184° (c = 1.45, chloroform); ^1H NMR δ 7.43-7.60 (m, 5H, Ph); 5.66 (s, 1H, H-7); 5.53 (d, 1H, $J_{4,5}$ = 2 Hz, H-4); 4.53 (s, 1H, H-1): 4.37 (d, 1H, J_{gem} = 10 Hz, H-6 eq); 4.23 (q, 1H, $J_{5,6\ ax}$ = 2 Hz, J_{gem} = 10 Hz, H-6 ax); 3.70 (m, 1H, H-5); 3.40 (s, 3H, OMe); 1.50 (s, 3H, C-2Me_{ax}); 1.15 (s, 3H, C-2Me_{eq}); ^{13}C NMR δ: 156.0 (C-3); 106.7 (C-1); 101.1 (C-7); 69.5 (C-6); 65.1 (C-4); 55.1 (OMe); 40.4 (C-2); 26.2 (C-2Me_{ax}); 21.3 (C-2Me_{eq}).

General procedure for the palladation of the oximes, for the oxidation of the organopalladium compounds and for the preparation of the equatorially functionalized geminal alkyl derivatives. A solution of disodium tetrachloropalladate (360 mg, 1.22 mmol), sodium acetate (100 mg, 1.22 mmol) and ulose oxime (250 mg, 0.81 mmol) in ethanol (7 mL) was stirred at room temperature for 5 days. Then, the solvent was evaporated and the residue dissolved in ethyl acetate was filtered through kieselguhr. Evaporation of the solvent gave crystalline dimeric palladated oximes 15 (90%); ^{1}H NMR δ 2.20 ± 0.03 (d, 1H, J_{gem} = 7 Hz, Pd-CH_2-) and 3.06 ± 0.02 (d, 1H, J_{gem} = 7 Hz, Pd-CH_2-).

To a solution of the dimeric organopalladium compound 15 (100 mg, 0.12 mmol) in dry tetrahydrofuran (4.5 mL) was added pyridine (0.18 mL, 0.24 mmol) and the mixture was stirred at room temperature for 10 min. Then a solution of lead tetraacetate (105 mg, 0.24 mmol) in acetic acid (1.8 mL) was added at 0°C to the reaction mixture which was stirred for another 2 h while the temperature was allowed to rise to 25°C. A solution of sodium borohydride (18 mg, 0.48 mmol) in 1N aqueous sodium hydroxide (1.2 mL) was then added and the mixture stirred for 30 min. The black suspension was filtered, the filtrate extracted with ethyl acetate, washed with water and sodium hydrogen carbonate, dried over magnesium sulfate and evaporated. The crude reaction products were purified by preparative thin layer chromatography.

Methyl 2(S)2-C-acetoxymethylene-4,6-O-benzylidene-2-deoxy-2-C-methyl-α-D-erythro-hexopyranosid-3-ulose oxime (17). Syrup, (80%), $[\alpha]_D^{22}$ = + 31°, (c = 1.4, chloroform); ^{1}H NMR δ 7.38-7.47 (m, 5H, Ph); 5.61 (s, 1H, H-7); 4.77 (d, 1H, $J_{4,5}$ = 10 Hz, H-4); 4.54 (s, 1H, H-1); 4.35 (q, 1H, $J_{5,6}$ = 5 Hz, J_{gem} = 11 Hz, H-6 eq); 4.22 (m, 1H, H-5); 3.88 (t, 1H, $J_{5,6ax}$ = J_{gem} = 11 Hz, H-6 ax); 3.38 (s, 3H, OMe); 2.07 (s, 3H, OAc); 1.38 (s, 3H, C-2Me); ^{13}C NMR δ: 170.6 (OAc); 149.5 (C-3); 103.7 (C-1); 103.1 (C-7); 80.1 (C-4); 69.8 (C-6); 66.7 (CH_2OAc); 63.8 (C-5); 55.6 (OMe); 47.0 (C-2); 21.2 (C-2Me); 21.0 (OAc).

Anal. Calcd for $C_{18}H_{23}NO_7$: C, 59.17; H, 6.34; N, 3.83; O, 30.65. Found: C, 60.04; H, 6.17; N, 3.92.

Methyl 3(S)3-C-acetoxymethylene-4,6-O-benzylidene-3-deoxy-3-C-methyl-α-D-erythro-hexopyranosid-3-ulose oxime (18). Syrup, (20%), $[\alpha]_D^{22}$ = + 14°, (c = 5.8, chloroform); ^{1}H NMR δ 7.43-7.57 (m, 5H, Ph); 5.83 (s, 1H, H-1); 5.62 (s, 1H, H-7); 4.40 (q, 1H, $J_{5,6}$ = 5 Hz, J_{gem} = 11 Hz, H-6 eq); 4.25 (m, 1H, H-5); 4.13 and 4.60 (2d, 2H, J_{gem} = 10 Hz, CH_2OAc); 3.90 (d, 1H, $J_{4,5}$ = 10 Hz, H-4); 3.82 (t, 1H, $J_{5,6ax} = J_{gem}$ = 11 Hz, H-6 ax); 3.55 (s, 3H, OMe); 2.03 (s, 3H, OAc); 1.36 (s, 3H, C-3Me); ^{13}C NMR δ: 168.8 (OAc); 156.0 (C-2); 100.7 (C-7); 92.0 (C-1); 77.6 (C-4); 69.3 (C-6); 64.0 (CH_2OAc); 55.7 (OMe); 55.3 (C-5); 47.2 (C-3); 20.9 (OAc); 17.4 (C-3Me).

Anal. Calcd for $C_{18}H_{23}NO_7$: C, 59.17; H, 6.34; N, 3.83; O, 30.65. Found: C, 59.32; H, 6.21; N, 3.63.

Methyl 2(S)2-C-acetoxymethylene-4,6-O-benzylidene-2-deoxy-2-C-methyl-α-D-threo-hexopyranosid-3-ulose oxime (19). Syrup, (65%), $[\alpha]_D^{22}$ = + 139°, (c = 1.25, chloroform); ^{1}H NMR δ 7.32-7.50 (m, 5H, Ph); 5.60 (s, 1H, H-7); 5.50 (1s, 1H, H-4); 4.68 (s, 1H, H-1); 4.32 (d, 1H, J_{gem} = 11 Hz, H-6 eq); 4.27 (s, 2H, CH_2OAc); 4.19 (q, 1H, $J_{5,6ax}$ = 2 Hz, J_{gem} = 11 Hz, H-6 ax); 3.70 (m, 1H, H-5); 3.35 (s, 3H,OMe); 2.10 (s, 3H, OAc); 1.53 (s, 3H, C-2 Me); ^{13}C NMR δ: 171.2 (OAc); 153.7 (C-3); 103.7 (C-1); 101.3 (C-7); 69.5 (C-6); 66.9 (C-4); 64.8 (CH_2OAc); 61.7 (C-5); 55.4 (OMe); 43.0 (C-2); 21.2 (C-2Me); 20.8 (OAc).

Anal. Calcd for $C_{18}H_{23}NO_7$: C, 59.17; H, 6.34; N, 3.83; O, 30.65. Found: C, 59.40; H, 6.51; N, 3.70.

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