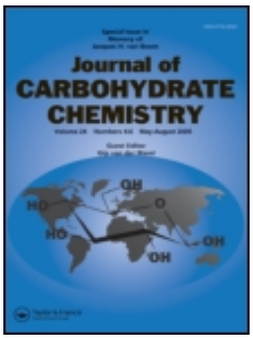

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Synthesis of New Pseudo-*C*-Nucleosides Containing Pyrazole Rings in their Structure

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ABSTRACT

Synthetic approaches to new 4-(furanos-4-*C*-yl)-1*H*-pyrazole and 3-(furanos-4-*C*-yl)-1*H*-pyrazole derivatives are described, including its pyrazole-5-carboxylate derivative, which is a pyrazofurin analogue. Preparation of related 5-acetoxy-1-acetyl-1*H*-pyrazole, 5-acetoxy-1*H*-pyrazole-1-carboxylate, and 4,5-dihydro-1-phenyl-1*H*-pyrazol-5-one derivatives is also reported. The formation of the pyrazole rings was accomplished either by reaction of enones and of 1,3-diketones with *N*-nucleophiles or by ring closure of a diazoketone.

Key Words: Pyrazoles; Pseudo-*C*-Nucleosides; 1,3-Diketones; Hydrazones.

INTRODUCTION

The pyrazole ring system is of some practical importance, because many drugs contain a pyrazole unit in their structure. 1-Phenylpyrazoles were evaluated for inhibitory activity against xanthine oxidase, some of them being potent inhibitors, displaying long-lasting hypouricemic action.[1] 1-Naphthylpyrazole-5-carboxamides were found to be nonbasic factor Xa inhibitors, showing significantly increased enzyme specificity and oral bioavailability than related lead structures.[2]Antagonists of the CB1 cannabinoid receptor were described as possessing the pyrazole-3-carboxamide moiety in their structure.[3] Pyrazole derivatives were also evaluated as antitumor and antiangiogenic agents.[4] The antipyretic action of a pyrazole derivative has been known since 1884,[5] and since then a diversity of bioactivities has been reported for this type of compounds.

Pyrethroid acid oxime-esters containing a pyrazole ring were found to possess plant antiviral activities.[6] The herbicidal activity of substituted phenyl pyrazoles,[7] the acaricidal activity of pyrazole-5-carboxamides,[8] and the fungicidal activity of 1*H*-pyrazole derivatives make these types of compounds important for pest management.[9,10] Recently, the interest on the synthesis of new substituted pyrazole derivatives has increased. Reaction of 1,3-diketones with *N*-nucleophiles[11] reaction of Baylis-Hillman adducts with hydrazine hydrochlorides,[12] and the microwave-assisted synthesis of pyrazoles by Vilsmeier cyclization of hydrazones[13] and of pyrazole libraries by means of cellulose beads as solid support[14] are some of the reported achievements in this field. Pyrazole *C*-nucleosides have been frequently mentioned in the literature. Since the isolation from *S. Candidus* of the pyrazole *C*-nucleoside pyrazofurin,[15] which has a broad spectrum of antiviral and antitumor activities, there has been considerable interest in synthetic approaches to new analogues of this compound. Synthesis and antiviral activity of 5′-deoxypyrazofurin was reported in the literature, being more selective and less toxic than pyrazofurin.[16] Isothiazole derivative analogues to this *C*-nucleoside antibiotic were synthesized, but no significant inhibition of tumor cell growth or of viral replication was detected.[15]

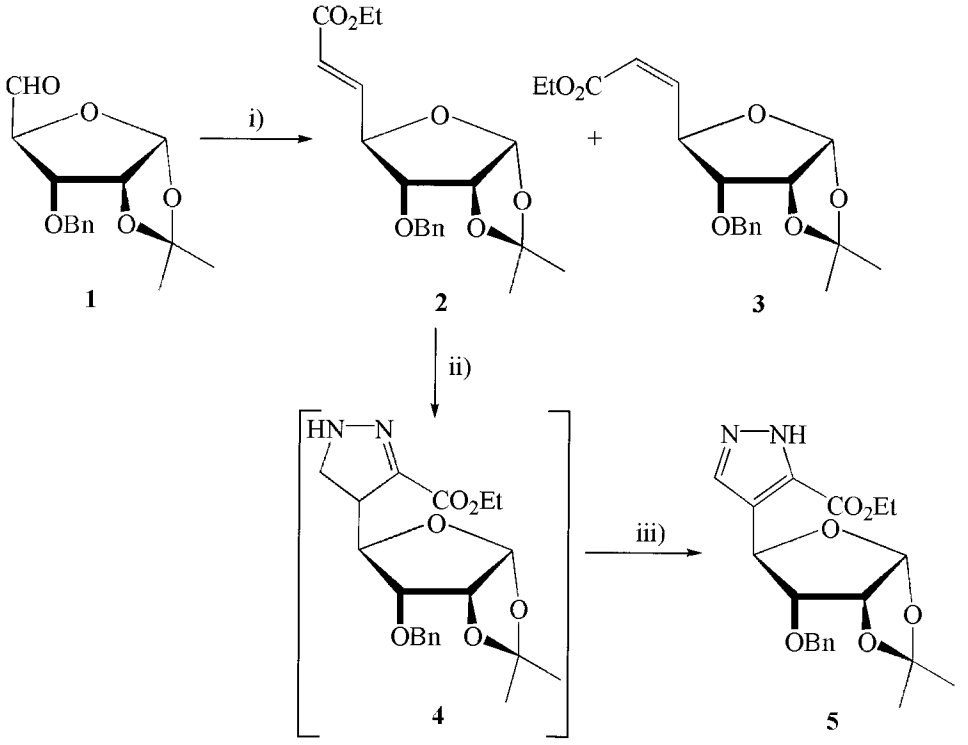
A variety of strategies is known for the synthesis of pyrazole *C*-nucleosides, namely the reaction of an alkyne acetal with acetic acid and aqueous HCl, followed by addition of hydrazine hydrate,[17] palladium catalyzed glycal coupling with iodopyrazoles,[18] and metal catalyzed reaction of keto esters with alkyl cyanoformates.[19] Recently the preparation of pyrazole *C*-nucleosides was described via reaction of ribofuranosyl cyanides with

β-dicarbonyl compounds promoted by tin (IV) chloride.[20] Heptenuloses underwent ring closure reactions with various *N*-nucleophiles to give acyclic pyrazole *C*-nucleosides.[21]

We report now synthetic approaches leading to new *C*-nucleoside analogues, which contain the pyrazole ring bonded to C-4 of the furanosyl moiety, therefore being known as pseudo-*C*-nucleosides. A goal of the investigation is the preparation of new sugar derivatives possessing the pyrazole unit bonded to C-4 for further evaluation of their bioactivity in various domains, namely as pesticides, due to the bioactivity found for other pseudo-*C*-nucleosides and analogues containing thiazole and thiazolidinone moieties in their structure.[22]

RESULTS AND DISCUSSION

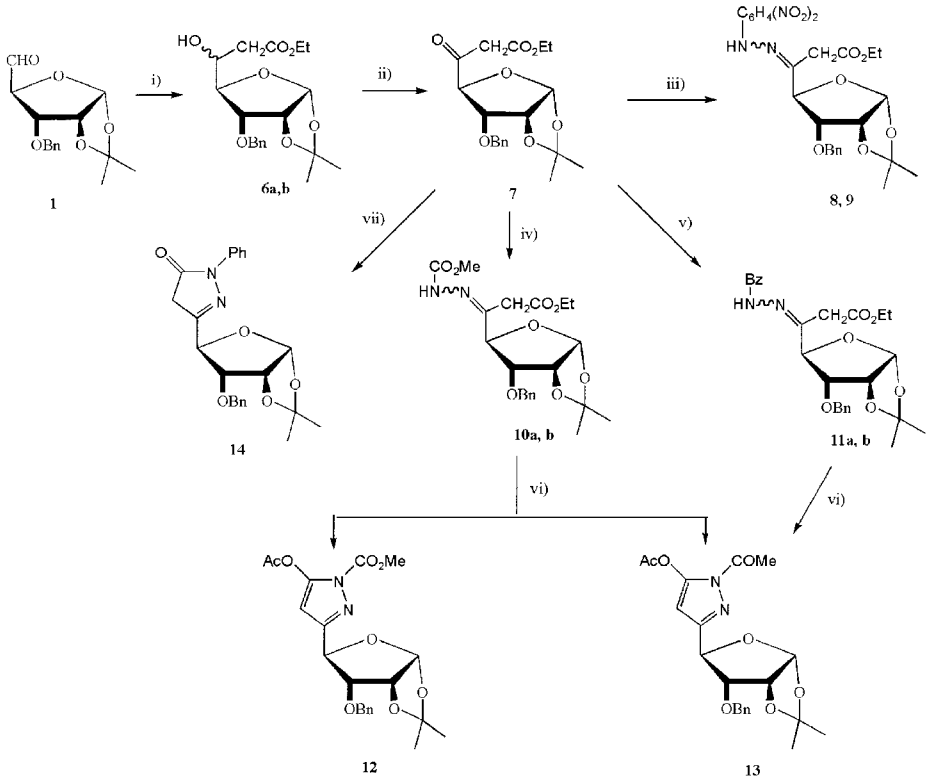
Synthesis of the ethyl 4-[(4*R*)-α-D-erythrofuranos-4-*C*-yl]pyrazole-5-carboxylate derivative **5** was accomplished by Wittig reaction of 3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-*ribo*-pentodialdo-1,4-furanose (**1**)[23] with [(ethoxycarbonyl)methylene]triphenylphosphorane to give the *E*- and *Z*-isomers **2** and **3** in 74% and 10% yield, respectively. Treatment of **2** with diazomethane in diethyl ether at 0°C[24] for 2 h and dehydrogenation of the intermediate pyrazoline **4** with Cl_2/CCl_4 gave the target molecule in 84% yield (Sch. 1). The evidence that helped to elucidate the stereochemistry of **2** and **3** is based



Scheme 1. i) $Ph_3P = CHCO_2Et$, $CHCl_3$, rt, 30 min, 74% for **2**, 10% for **3**; ii) CH_2N_2, Et_2O, 0°C, 2 h; iii) Cl_2/CCl_4, rt, 3 h, 84%.

on their NMR data. The signal of H-4 of the *Z*-isomer appears in a multiplet at δ 5.76–5.73, due to the neighbourhood of the carbonyl group, while the resonance of H-4 of the *E*-isomer is included in the multiplet at δ 4.63–4.54. This effect has also been found in *Z*-alkenes bonded to pyranosidic moieties.[25] The same effect justifies that H-5 of the *E*-isomer appears at lower field (δ 6.92) than H-5 of the *Z*-isomer (included in the multiplet at δ 5.97–5.95). The coupling constant $J_{5,6} = 16$ Hz for **2** is also in agreement with the stereochemistry assigned. Compound **5** is analogous to *C*-nucleosides containing 5-carboxamido-4-(β-D-ribofuranosyl)pyrazole moieties, which were moderate inhibitors of the *in vitro* growth of tumor cell lines, and showed a moderate *in vitro* antiviral activity towards the rabies virus.[26]

Reformatsky reaction of **1** with ethyl bromoacetate in THF in the presence of activated zinc at 45°C gave the ethyl *allo-*/*talo*-heptofuranuronate **6a,b** in 65% yield in a 1 : 1 ratio (Sch. 2). Its oxidation with pyridinium dichromate in the presence of powdered molecular sieve (3 Å) and acetic acid in dichloromethane at rt for 30 min gave **7** in 75%

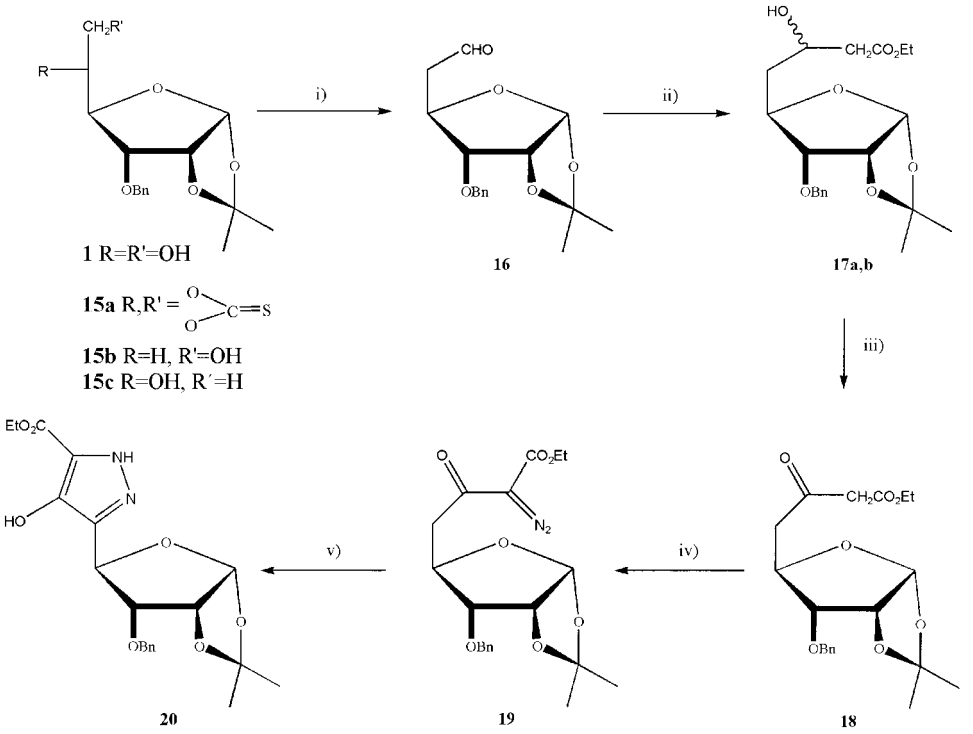


Scheme 2. i) $BrCH_2CO_2Et$, Zn, THF, 45°C, 1 hr, 65%; ii) PDC, molecular sieves powder 3 Å, CH_2Cl_2, AcOH, 25°C, 30 min, 75%; iii) $H_2NNHC_6H_3(NO_2)_2$, EtOH, AcOH, 80°C, 5 hr, 46% for **8**, 47% for **9**; iv) H_2NNHCO_2Me, EtOH, AcOH, 80°C, 5 hr, 80%; v) $H_2NNHCOPh$, EtOH, AcOH, 80°C, 5 hr, 80%; vi) Ac_2O, NaOAc, 100°C, 4 hr, 72% for **12**, 16% for **13** starting from **10a,b**; 85% for **13** starting from **11a,b**.

yield. This derivative contains a 2-methylene-1,3-dicarbonyl moiety, which, after reaction with hydrazine derivatives, afforded the corresponding hydrazones **8, 9, 10a,b,** and **11a,b**, when 2,4-dinitrophenyl hydrazine, methyl hydrazinocarboxylate, and benzoyl hydrazine were used. Separation by column chromatography of the *Z*/*E* isomers was only possible with the 2,4-dinitrophenylhydrazono derivatives **8** and **9,** which were isolated in 46% and 47% yield, respectively. The *Z*/*E* stereochemistry was assigned by means of the chemical shift of H-4, which appeared at a lower field for the *Z*-isomer, due to the neighborhood of NH, than the corresponding signals of the *E*-isomer (δ 4.80) and of the 1,3-dicarbonyl starting material (included in the multiplet at δ 4.67–4.57). Intramolecular cyclization of **10a,b** promoted by acetic anhydride and sodium acetate at 100°C for 4 hr gave the expected pyrazole **12** in 72% yield, together with the 1-acetyl-1*H*-pyrazole derivative **13** in 16% yield. The formation of the pyrazole ring was confirmed by NMR data. The signal of the olefinic H-4 appeared at δ 6.09 (for **12**) and δ 6.52 (for **13**) and the signals of C-3, C-4, and C-5 appeared at δ 153.0, 98.1, and 148.8 (for **12**) and at δ 155.7, 103.4, and 144.4 (for **13**). The presence of the methoxy group was detected in **12** by the ^{1}H- and ^{13}C NMR signals at δ 4.02 and δ 54.7, respectively, which were absent in the corresponding spectra of **13**. They also exhibited the resonances due to the methyl group of two acetyl groups at δ 2.51, and 2.25 and δ 23.3 and 20.9, confirming the proposed structure for **13,** which was also obtained by treatment of **12** with acetic anhydride and sodium acetate. When the hydrazone **11a,b** was treated with acetic anhydride and sodium acetate under the same conditions, only compound **13** was obtained in 85% yield. Replacement of the methoxycarbonyl group or of the benzoyl group by the acetyl group in **13** was caused by reaction with acetic anhydride present in a large excess.

Reaction of 1,3-dicarbonyl compound **7** with phenyl hydrazine gave the 1-phenyl-1*H*-pyrazole derivative **14** in 72% yield. The structure of the pyrazole ring was confirmed by ^{1}H NMR due to the presence of the expected phenyl protons and of the methylene group, which appeared at δ 3.28 and 2.79, as an AB system with $J_{A,B} = 24$. ^{13}C NMR spectrum showed the signals corresponding to C-3 at δ 155.5, C-4 at δ 38.7, C-5 at δ 170.2, and the resonances of the aromatic ring, which appear with those of the phenyl ring of the benzyl group.

Synthesis of 3-*O*-benzyl-5-deoxy-1,2-*O*-isopropylidene-α-D-*ribo*-hexodialdo-1,4-furanose (**16**) was accomplished by oxidation of 3-*O*-benzyl-5-deoxy-1,2-*O*-isopropylidene-α-D-*ribo*-hexofuranose (**15b**) with PCC and powdered molecular sieves (4 Å) in CH_2Cl_2 at rt for 15 min in 80% yield. The starting material **15b** was obtained by reaction of **1**[23] with *N,N′*- thiocarbonyldiimidazole[27] to give the intermediate thiocarbonate **15a**, which was treated with tributyltin hydride and azoisobutyronitrile in toluene,[28] a reaction that also gave compound **15c** (Sch. 3). An alternative procedure consisted of a classic approach based on tritylation of **1**, followed by iodination with triphenylphosphine/iodine/imidazole, detritylation, and reduction with lithium aluminium hydride to give **15b** in 55% overall yield.[29] Reformatsky reaction of **16** with ethyl bromoacetate and zinc gave **17a,b** in 60% yield, which oxidation with PCC for 40 min under the reaction conditions previously described for **15**, gave the ketoester **18** in 92% yield. Its reaction with tosyl azide and triethylamine in acetonitrile at rt for 30 min afforded the diazoester **19** in 93.5% yield. The pyrazofurin analogue **20** was synthesized by intramolecular cyclization of **19** with NaH in 20% yield, according to the procedure described by Chen and Schneller.[16]



Scheme 3. i) PCC, molecular sieves powder 4 Å, CH_2Cl_2, rt, 15 min, 80%; ii) $BrCH_2CO_2Et$, Zn, THF, 55°C, 40 min, 60%; iii) PCC, molecular sieve powder 4 Å, CH_2Cl_2, rt, 40 min, 92%; iv) TsN_3, Et_3N, MeCN, rt, 30 min, 93.5%; v) NaH, THF, rt, 20 hr, 20%.

EXPERIMENTAL

General Methods

Melting points were determined with a melting point apparatus (Leitz-Biomed) with platinium plate and are uncorrected. Optical rotations were measured with an Atago Polax-D polarimeter and IR spectra were recorded with a Biorad FTS 25 PC spectrophotometer. ^{1}H NMR spectra were run with a Bruker AC-250 P spectrometer. Chemical shifts are expressed in parts per million (ppm) downfield from TMS and the coupling constants J in Hz. The ^{13}C NMR spectra were run at 62.90 MHz in the same spectrometer. The experiments were performed in chloroform-d. The progress of all reactions was monitored by thin layer chromatography (TLC) using aluminium sheets precoated with silica gel $60F_{254}$ to a thickness of 0.2 mm (Merck). Preparative TLC was performed with aluminium plates coated with silica gel $60F_{254}$ to a thickness of 0.5 mm (Merck). Compounds were detected with UV light (254 nm) and/or by spraying the sheets with a 3% vanillin-sulfuric acid solution. Column chromatography (CC) was conducted under low pressure by elution of the columns filled with silica gel (0.040–0.063 mm, Merck).

Ethyl 3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene-α-D-*ribo*-hept-5(*E*)-enefuranuronate (2) and ethyl 3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene-α-D-*ribo*-hept-5(*Z*)-enefuranuronate (3). A solution of **1**[23](2.0 g, 7.2 mmol) in chloroform (35 mL) was added to a solution of [(ethoxycarbonyl)methylene]triphenylphosphorane (5.1 g, 14.6 mmol) in chloroform (35 mL). The mixture was stirred at rt for 30 min. After concentration under reduced pressure the residue was purified by CC eluted with ethyl acetate/toluene (1 : 4) to give **2** (1.85 g, 74%) and **3** (0.25 g, 10%). Physical and spectroscopic data for **2**: R_f 0.78 (ethyl acetate/toluene 1 : 1); [a] $^{25}_{D} = +47.5^\circ$ (*c* 2, $CHCl_3$); IR (neat) (cm^{-1}): 1725 (C = O), 1660 (C = C); UV ($\lambda_{máx.}$ nm) ethanol: 203 ($\varepsilon = 12320$); ^{1}H NMR: 7.34 (s, 5H, Ph), 6.92 (dd, 1H, H-5, $J_{4,5} = 5$, $J_{5,6} = 16$), 6.12 (d, 1H, H-6), 5.76 (d, 1H, H-1, $J_{1,2} = 3.4$), 4.72 (part A of AB system, 1H, CH_2, Bn, $J_{AB} = 12$), 4.63–4.56 (m, 3H, H-2, H-4 and part B of AB system, CH_2, Bn), 4.19 (q, 2H, CH_2, Et, $J_{CH2,CH3} = 7$), 3.53 (dd, 1H, H-3, $J_{2,3} = 4$, $J_{3,4} = 9$), 1.61 (s, 3H, CH_3, isop), 1.36 (s, 3H, CH_3, isop), 1.29 (t, 3H, CH_3,Et); ^{13}C NMR: 166.4 (C-7), 143.9 (C-5), 137.5 (Cq, Ph), 128.9, 128.5, 128.4 (CH, Ph), 122.9 (C-6), 113.6 (Cq, isop), 104.4 (C-1), 82.3 (C-3), 77.9 (C-2), 77.4 (C-4), 72.9 (CH_2, Bn), 60.9 (CH_2, Et), 27.2 (CH_3, isop), 26.8 (CH_3, isop), 14.6 (CH_3, Et).

Anal. Calcd for $C_{19}H_{24}O_6$: C 65.50, H 6.94; Found: C 65.83, H 6.57.

Data for **3:** R_f 0.74 (ethyl acetate/toluene 1 : 1); $[\alpha]_D^{25} = -8^\circ$ (c 1.25, $CHCl_3$); IR (neat) (cm^{-1}): 1730 (C = O), 1680 (C = C); UV ($\lambda_{máx.}$ nm) (ethanol): 204 ($\varepsilon = 16759$); ^{1}H NMR: 7.32 (s, 5H, Ph), 5.97–5.95 (m, 2H, H-5, H-6), 5.76–5.73 (m, 2H, H-1, H-4), 4.74–4.56 (m, 3H, H-2, CH_2, Bn), 4.18 (q, 2H, CH_2, Et, $J_{CH_2CH_3} = 7$), 3.53 (dd, 1H, H-3, $J_{2,3} = 4.2$, $J_{3,4} = 9$), 1.66 (s, 3H, CH_3, isop), 1.37 (s, 3H, CH_3, isop), 1.29 (t, 3H, CH_3, Et); ^{13}C-NMR: 165.3 (C-7), 142.9 (C-5), 137.4 (Cq, Ph), 128.3, 128.0, 127.8 (CH, Ph), 124.4 (C-6), 113.3 (Cq, isop), 103.9 (C-1), 82.0 (C-3), 77.8 (C-2), 73.2 (C-4), 72.0 (CH_2, Bn), 60.5 (CH_2, Et), 26.8 (CH_3, isop), 26.7 (CH_3, isop), 14.1 (CH_3, Et).

Anal. Calcd for $C_{19}H_{24}O_6$: C 65.50, H 6.94; Found: C 65.80, H 6.75.

Ethyl 4-[(4*R*)-3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-erythrofuranos-4-*C*-yl]-1*H*-pyrazole-5-carboxylate (5). A solution of **2** (2.79 g, 8 mmol) in diethyl ether (60 mL) was cooled to 0°C and added dropwise to a solution of diazomethane in diethyl ether (32 mmol, 500 mL). The mixture was stirred at 0°C for 2 hr. Glacial acetic acid was added dropwise to get a colorless reaction mixture, due to the elimination of the diazomethane that did not react. Concentration in vacuum gave a residue, which was dissolved in carbon tetrachloride (40 mL). A saturated chlorine solution in carbon tetrachloride (200 mL) was added dropwise, and the mixture was stirred at rt for 3 hr. The solvent was removed by evaporation under reduced pressure, and the residue was dissolved in diethyl ether (50 mL), extracted with a saturated solution of sodium hydrogen carbonate (50 mL), and washed with water (50 mL). The organic phase was dried (Na_2SO_4) and concentrated under reduced pressure. The residue was purified by CC with ethyl acetate/toluene (3 : 2) to give **5** (2.5 g, 84%). R_f 0.43 (ethyl acetate/toluene 2 : 1); $[\alpha]_D^{25} = +43.8^\circ$ (*c* 1.6, $CHCl_3$); IR (neat) (cm^{-1}): 3443 (N-H), 1722 (C = O), 1592 (C = C); UV ($\lambda_{máx.}$ nm) ethanol: 237 ($\varepsilon = 12903$), 209 ($\varepsilon = 12974$); ^{1}H NMR: 13.80 (s, 1H, N-H), 7.75 (s, 1H, H-3), 7.30–7.15 (m, 5H, Ph), 5.86 (d, 1H, H-1′, $J_{1',2'} = 3.7$), 5.56 (d, 1H, H-4′, $J_{3',4'} = 9$), 4.70 (t, 1H, H-2′, $J_{2',3'} = 3.9$), 4.62, 4.50 (2 H, AB system, CH_2, Bn, $J_{AB} = 12$), 4.35 (q, 2H, CH_2, Et, $J_{CH_2CH_3} = 7$), 3.95 (dd, 1H, H-3′), 1.70 (s, 3H, CH_3, isop), 1.42 (s, 3H, CH_3, isop), 1.36 (t, 3H, CH_3, Et);^{13}C NMR: 162.1 (C = O), 139.5 (C-5), 137.2 (Cq, Ph), 132.0 (C-3), 128.5, 128.2, 127.8 (CH, Ph), 120.5

(C-4), 112.8 (Cq, isop), 103.6 (C-1′), 82.3 (C-3′), 77.6 (C-2′), 72.0 (CH_2, Bn), 71.7 (C-4′), 61.0 (CH_2, Et), 26.8 (CH_3, isop), 26.5 (CH_3, isop), 14.2 (CH_3, Et).

Anal. Calcd for $C_{20}H_{24}N_2O_6$: C 61.84, H 6.23, N 7.21; Found: C 62.15, H 6.53, N 7.45.

General Procedure for the Reformatsky Reaction

A solution of ethyl bromoacetate (10 mmol) in anhydrous THF (4 mL) was added at rt under nitrogen to the suspension of activated granulated zinc 20 mesh (0.34 g, 5.32 mmol) in the solution of the carbonyl compound (3.6 mmol) in anhydrous THF (2 mL). The reaction mixture was heated under nitrogen. After cooling to rt, a 10% hydrochloric acid solution (25 mL), previously cooled to 0°C, was added. The organic phase was extracted with dichloromethane (3 × 25 mL), neutralized with a 2.5% sodium hydrogen carbonate solution (25 mL), and then dried (Na_2SO_4). Concentration under reduced pressure afforded a residue, which was purified by CC eluted with ethyl acetate/toluene (1 : 5).

Ethyl 3-*O*-benzyl-6-deoxy-1,2-*O*-isopropylidene-α-D-*allo*/*talo*-heptofuranuronate (6a,b). Starting from 1[23] (1 g, 3.6 mmol), the reaction mixture was heated at 45°C for1 hr to give **6a,b,** (0.86 g, 65%). R_f 0.53 (ethyl acetate/toluene 1 : 1); IR (cm^{-1}) 3460 (O-H), 1730 (C = O); ^{1}H NMR: 7.37–7.17 (m, 10 H, Ph), 5.69 (t, 2H, H-1a, H-1b, $J_{1,2} = 3.4$), 4.69 (part A of AB system, 2H, CH_2a and CH_2b, Bn, $J_{AB} = 12$), 4.53–4.48 (m, 4H, H-2a, H-2b and part B of AB system, CH_2a, CH_2b, Bn), 4.34–4.31 (m, 1H, H-5a); 4.14–4.03 (m, 7H, H-4a, H-4b, H-5b, CH_2a, CH_2b, Et), 3.95–3.90 (m, 2H, H-3a, H-3b), 3.47 (brs, 1H, OH-5a), 3.29 (d, 1H, OH-5b, $J_{5b,OH\text{-}5b} = 7$), 2.64–2.49 (m, 4H, CH_2-6a, CH_2-6b), 1.53 (s, 6H, CH_3, isop), 1.30 (s, 6H, CH_3, isop), 1.18 (t, 6H, CH_3, Et, $J_{CH_2CH_3} = 7$); ^{13}C NMR: 172.0, 171.8 (C = O, C-7a, C-7b), 137.8, 137.7 (Cq, Ph), 129.0, 128.4, 128.2, 127.9, 127.9 (CH, Ph), 112.8 (Cq, isop), 104.3, 104.2 (C-1a, C-1b), 80.8, 80.5 (C-4a, C-4b), 78.2, 77.8 (C-2a, C-2b), 77.7, 77.1 (C-3a, C-3b), 72.0, 71.8 (CH_2-a, CH_2-b, Bn), 67.0, 66.5 (C-5a, C-5b), 60.5, 60.5 (CH_2-a, CH_2-b, Et), 39.1, 37.3 (C-6a, C-6b), 26.9 (CH_3, isop), 26.7 (CH_3, isop), 14.1 (CH_3, Et).

Anal. Calcd for $C_{19}H_{26}O_7$: C 62.28, H 7.15; Found: C 62.15, H 7.20.

Ethyl 3-*O*-benzyl-5,7-dideoxy-1,2-*O*-isopropylidene-α-D-*allo*/*talo*-octofuranuronate (17a,b). Starting from **16** (1.05 g, 3.60 mmol), the reaction mixture was heated at 55°C for 40 min to give **17a,b** (0.82 g, 60%); R_f 0.53 (ethyl acetate/toluene 1 : 1); IR (neat) (cm^{-1}) 3500 (OH), 1740 (C = O); ^{1}H NMR: 7.32–7.28 (m, 5H, Ph), 5.69 (d, 1H, H-1, $J_{1,2} = 3.5$), 4.76 (part A of AB system, 1H, CH_2, Bn, $J_{AB} = 11.8$), 4.54–4.49 (m, 2H, H-2, part B of AB system, CH_2, Bn), 4.25–4.08 (m, 4H, H-4, H-6, CH_2, Et), 3.45 (dd, 1H, H-3, $J_{2,3} = 3.9$, $J_{3,4} = 8.2$), 3.32 (brs, 1H, OH-6), 2.48–2.45 (m, H, H-7) 1.90–1.65 (m, H, H-5), 1.58 (s, 3H, CH_3, isop), 1.33 (s, 3H, CH_3, isop), 1.25 (t, 3H, CH_3, Et, $J_{CH_2CH_3} = 7.2$); ^{13}C NMR: 171.8, 171.71 (C-8), 137.0 (Cq, Ph), 128.7, 128.2, 127.8 (CH, Ph), 112.5 (Cq, isop), 103.8, 103.6 (C-1), 81.6, 81.3 (C-3), 76.6, 76.4 (C-2), 76.0, 75.2 (C-4), 71.8 (CH_2, Bn), 66.1, 65.3 (C-6), 60.2 (CH_2, Et), 41.6, 41.3 (C-7), 38.6, 38.4 (C-5).

Anal. Calcd for $C_{20}H_{28}O_7$: C 63.14, H 7.42; Found: C 63.15, H 7.25.

Ethyl 3-*O*-benzyl-6-deoxy-1,2-*O*-isopropylidene-α-D-*ribo*-hept-5-ulofuranuronate (7). Compounds **6a,b** (1.83 g, 5 mmol), activated powdered molecular sieves (4 Å, 5.0 g) and pyridinium dichromate (3.2 g, 15 mmol) were added to dichloromethane (24 mL), previously dried over molecular sieves 4 Å, and cooled at 5°C. The mixture

was cooled at 0°C and stirred for 5 min. Glacial acetic acid (0.49 mL) was added dropwise. The reaction mixture was warmed at 25°C and stirred for 30 min. Ethyl acetate (30 mL) was then added, and the suspension was filtered and concentrated under reduced pressure. Toluene (3 × 20 mL) was added to the slushy mixture and concentrated. The residue was purified by CC eluted with ethyl acetate/toluene (1 : 1) to give **7** (1.36 g, 75%). R_f 0.62 (ethyl acetate/toluene 1 : 2); $[\alpha]_D^{25} = +50^\circ$ (*c* 2.5, $CHCl_3$); IR (neat) (cm^{-1}) 1737 (C = O); ^{1}H NMR: 7.37–7.27 (m, 5H, Ph), 5.77 (d, 1H, H-1, $J_{1,2} = 3.1$), 4.73 (1H, part A of the AB system, CH_2, Bn, $J_{AB} = 11.9$), 4.67–4.57 (m, 3H, H-2, H-4, part B of the AB system, Bn), 4.12 (q, 2H, CH_2, Et, J = 7,3), 3.93 (dd, 1H, H-3, $J_{2,3} = 2,8$, $J_{3,4} = 7.6$), 3.61, 3.51 (AB system, 2H, H-6, H-6′, $J_{AB} = 16$), 1.56 (s, 3H, CH_3, isop), 1.34 (s, 3H, CH_3, isop), 1.21 (t, 3H, CH_3, Et); ^{13}C NMR: 200.3 (C-5), 171.7 (C-7), 136.6 (Cq, Ph), 128.0, 127.5 (CH, Ph), 113.1 (Cq, isop), 103.9 (C-1), 82.1 (C-3), 78.8 (C-2), 77.5 (C-4), 71.8 (CH_2, Bn), 60.8 (CH_2, Et), 45.5 (C-6), 26.5 (CH_3, isop), 26.1 (CH_3, isop), 13.6 (CH_3, Et).

Anal. Calcd for $C_{19}H_{24}O_7$: C 62.63, H 6.64; Found: C 62.52, H 6.81.

General Procedure for the Reaction of Keto Sugars with Hydrazine Derivatives

A mixture of the keto sugar **7** (1 g, 2.75 mmol) and the hydrazine derivative (3.0–4.78 mmol) in ethanol (10 mL) was stirred for 5 min at rt. Glacial acetic acid (0.1 mL) was added dropwise. The reaction mixture was heated at 80°C for 5 hr, then cooled and concentrated. The residue was purified by CC.

Ethyl 3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene-5(*Z*)-(2,4-dinitrophenyl) hydrazono-α-D-*ribo*-heptofuranuronate (8) and ethyl 3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene-5(*E*)-(2,4-dinitrophenyl)hydrazono-α-D-*ribo*-heptofuranuronate (9). Reaction with 2,4-dinitrophenyl hydrazine (0.6 g, 3.0 mmol) and purification of the residue with ethyl acetate/toluene (1 : 10) gave **8** (0.69 g, 46%) and **9** (0.70 g, 47%). Data for **8**: R_f 0.57 (ethyl acetate/toluene 1 : 5); $[\alpha]_D^{25} = +56.6^\circ$ (*c* 1.7, $CHCl_3$); IR (neat) (cm^{-1}) 3230 (N-H), 1728 (C = O); UV ($\lambda_{máx.}$ nm) ethanol: 354 ($\varepsilon = 19306$), 202 ($\varepsilon = 45054$); ^{1}H NMR: 12.32 (s, 1H, N-H), 9.07 (d, 1H, H-3′, $J_{3',5'} = 2.9$), 8.30 (dd, 1H, H-5′), 7.90 (d, 1H, H-6′, $J_{5',6'} = 9.7$), 7.28 (s, 5H, Ph), 5.98 (d, 1H, H-1, $J_{1,2} = 3.5$), 5.04 (d, 1H, H-4, $J_{3,4} = 9$), 4.82, 4.57 (AB system, 2H, CH_2, Bn, $J_{AB} = 12$), 4.63 (t, 1H, H-2, $J_{2,3} = 3.7$), 4.22–4.13 (m, 3H, H-3, CH_2, Et), 3.58, 3.42 (AB system, 2H, H-6a, H-6b, $J_{AB} = 16$), 1.63 (s, 3H, CH_3, isop), 1.39 (s, 3H, CH_3, isop), 1.26 (t, 3H, CH_3, Et, $J_{CH_2CH_3} = 7$); ^{13}C NMR: 164.5 (C-7), 149.0 (C-5), 144.9 (C-4′, Ph-NO_2), 138.1 (C-2′, PhNO_2), 136.3 (Cq, Ph), 129.6 (C-5′), 128.5, 128.3, 128.2 (CH, Ph), 123.2 (C-3′), 116.2 (C-6′), 114.1 (Cq, isop), 104.7 (C-1), 80.5 (C-3), 76.7 (C-2 and C-4), 72.5 (CH_2, Bn), 61.2 (CH_2, Et), 40.6 (C-6), 26.7 (CH_3, isop), 26.5 (CH_3, isop), 14.1 (CH_3, Et).

Anal. Calcd for $C_{25}H_{28}O_{10}N_4$: C 55.15, H 5.18, N 10.29; Found C 55.40, H 5.04, N 10.46.

Data for **9**: R_f 0.51 (ethyl acetate/toluene 1 : 5); $[\alpha]_D^{25} = -6.7^\circ$C (*c* 1.5, $CHCl_3$); IR (neat) (cm^{-1}) 3266 (N-H), 1730 (C = O); UV ($\lambda_{máx.}$ nm) ethanol: 351 ($\varepsilon = 4571$), 206 ($\varepsilon = 6656$); ^{1}H NMR: 11.60 (s, 1H, N-H), 9.14 (d, 1H, H-3′, $J_{3',5'} = 2.2$), 8.31 (dd, 1H, H-5″), 7.98 (d, 1H, H-6′, $J_{5',6'} = 9.4$), 7.28 (s, 5H, Ph), 5.85 (d, 1H, H-1, $J_{1,2} = 3.5$),

4.80 (d, 1H, H-4, $J_{3,4} = 9.2$), 4.74, 4.58 (AB system, 2H, CH_2, Bn, $J_{AB} = 12.2$), 4.65 (t, 1H, H-2, $J_{2,3} = 3.7$), 4.19 (q, 2H, CH_2, Et, J = 7), 3.96 (dd, 1H, H-3), 3.47, 3.36 (AB system, 2H, H-6a, H-6b, $J_{AB} = 15.4$), 1.67 (s, 3H, CH_3, isop), 1.40 (s, 3H, CH_3, isop), 1.26 (t, 3H, CH_3, Et, $J_{CH_2CH_3} = 7$); ^{13}C NMR: 167.1 (C-7), 147.9 (C-5), 145.0 (C-4′, $PhNO_2$), 138.7 (C-2′, $PhNO_2$), 137.0 (Cq, Ph), 129.8 (C-5′), 128.3, 128.0, 127.9 (CH, Ph), 123.0 (C-3′), 117.1 (C-6′), 113.6 (Cq, isop), 104.1 (C-1), 80.9 (C-3), 79.2 (C-4), 76.9 (C-2), 72.5 (CH_2, Bn), 62.4 (CH_2, Et), 32.9 (C-6), 26.8 (CH_3, isop), 26.4 (CH_3, isop), 14.0 (CH_3, Et).

Anal. Calcd for $C_{25}H_{28}O_{10}N_4$: C 55.15, H 5.18, N 10.29; Found: C 54.95, H 5.30, N 10.04.

Ethyl 3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene-5(*E*)/5(*Z*)-methoxycarbonylhydrazono-α-D-*ribo*-heptofuranuronate (10a,b). Reaction with methyl hydrazinocarboxylate (0.18 g, 3.02 mmol) and purification of the residue by CC eluted with ethyl acetate/toluene (1 : 5) gave **10a,b** (0.96 g, 80%). R_f 0.45 (ethyl acetate/toluene 1 : 3); IR (cm^{-1}) 3626 (N-H), 1725 (C = O), 1720 (C = O); ^{1}H NMR: 8.15 (s, 1H, N-H), 7.73 (s, 1H, N-H), 7.36–7.16 (m, 10 H, Ph), 5.74, 5.73 (each d, 1H, H-1, $J_{1,2} = 3.8$, $J_{1,2} = 3.7$), 4.95 (d, 1H, H-4, $J_{3,4} = 8.7$), 4.82–4.72 (m, 3H, H-2, part A of AB system, Bn), 4.64–4.52 (m, 3H, H-2, H-4, part B of AB system, CH_2, Bn), 4.08 (q, 4H, CH_2, Et, J = 7.1), 4.40, 3.93 (2 dd, 1H, H-3, $J_{2,3} = 4.3$, $J_{3,4} = 8.9$), 3.83 (s, 3H, OCH_3), 3.65 (s, 3H, OCH_3), 3.62, 3.38 (AB system, 2H, H-6, H-6′, $J_{AB} = 17$), 3.28, 3.22 (AB system, 2H, H-6, H-6′, $J_{AB} = 14$), 1.60, 1.59 (s, each 3H, CH_3, isop), 1.42, 1.37 (2s, each 3H, CH_3, isop), 1.21 (t, 6H, CH_3, Et); ^{13}C NMR: 170.6 (C-7), 168.3 (Cq, COOMe), 154.5, 148.4 (C-5), 137.5, 135.7 (Cq, Ph), 128.8, 128.4, 128.3, 128.2, 128.0, 127.8 (CH, Ph), 113.7, 113.3 (Cq, isop), 104.9, 103.7 (C-1), 81.3, 78.7 (C-3), 80.8, 77.7 (C-2), 77.3, 76.3 (C-4), 72.7, 72.1 (CH_2, Bn), 62.1, 60.7 (CH_2, Et), 52.8, 52.4 (OCH_3), 39.6, 33.2 (C-6), 26.8, 26.68 (CH_3, isop), 26.5, 26.3 (CH_3, isop), 14.0, 13.8 (CH_3, Et).

Anal. Calcd for $C_{21}H_{28}N_2O_8$: C 57.79, H 6.47, N 6.42; Found: C 57.55, H 6.90, N 6.39.

Ethyl 5(*E*)/5(*Z*)-benzoylhydrazono-3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene-α-D-*ribo*-heptofuranuronate (11a,b). Reaction with benzoyl hydrazine (0.65 g, 4.78 mmol) and CC eluted with ethyl acetate/toluene (1 : 2) gave **11a,b** (1.06 g, 80%). R_f 0.27 (ethyl acetate/toluene 1 : 2); IR (cm^{-1})3450 (N-H), 1730 (C = O), 1690 (C = O); ^{1}H NMR (C_3D_6O): 10.81, 9.75 (each s, 1H, N-H), 7.84 (dd, 4H, H-2, Ph, H-4, Ph) 7.53–7.12 (m, 16H, Ph), 5.90, 5.88 (each d, 1H, H-1, $J_{1,2} = 3.6$, $J_{1,2} = 3.7$), 5.17 (d, 1H, H-4, $J_{3,4} = 9.1$), 4.98 (t, 1H, H-2, $J_{2,3} = 3.9$), 4.87–4.63 (m, 6H, CH_2, Bn, H-2, H-4), 4.67 (dd, 1H, H-3, $J_{2,3} = 4$, $J_{3,4} = 9$), 4.17–4.07 (m, 5H, H-3, CH_2, Et,), 3.66 (s, 2H, H-6, H-6′), 3.54, 3.36 (AB system, 2H, H-6, H-6′, $J_{AB} = 16.5$), 1.57, 1.52 (each s, 3H, CH_3, isop), 1.37, 1.32 (each s, 3H, CH_3, isop), 1.19 (t, 6H, CH_3, Et); ^{13}C-NMR: 170.7 (C-7), 164.3 (C = O), 152.5 (C-5), 135.4 (Cq, Ph), 132.4 (Cq, Ph, Bz), 131.8, 128.6, 128.4, 128.1, 128.0, 127.8, 127.2 (CH, Ph), 114.0 (Cq, isop), 105.0 (C-1), 81.6 (C-3), 77.2 (C-2), 76.3 (C-4), 73.0 (CH_2, Bn), 60.9 (CH_2, Et), 40.0 (C-6), 26.9 (CH_3, isop), 26.7 (CH_3, isop), 14.1 (CH_3, Et).

Anal. Calcd for $C_{26}H_{30}N_2O_7$: C 64.72, H 6.27, N 5.81; Found: C 64.35, H 7.56, N 5.49.

3-[(4*R*)-3-*O*-Benzyl-1,2-*O*-isopropylidene-α-D-erythrofuranos-4-*C*-yl]-4,5-dihydro-,1-phenyl-1*H*-pyrazol-5-one (14). Reaction with phenyl hydrazine (0.5 g, 4.6 mmol) and purification by CC eluted with ethyl acetate/toluene (1 : 4 v/v) gave **14** (0.81 g, 72%).

$R_f = 0.49$ (ethyl acetate/toluene 1/1);$[\alpha]_D^{25} = +80^\circ$ (*c* 1.5, $CHCl_3$); IR 1714 (C = O) cm^{-1}; ^1H NMR: 7.84 (d, 2H, Ph), 7.45–7.18 (m, 8H, Ph), 5.79 (d, 1H, H-1′, $J_{1',2'} = 3.5$), 4.83 (d, 1H, H-4′, $J_{3',4'} = 9.1$), 4.87, 4.54 (AB system, 2H, CH_2, Bn, $J_{AB} = 12.4$), 4.70 (t, 1H, H-2′, $J_{2',3'} = 3,9$), 3.85 (dd, 1H, H-3′), 3.28, 2.79 (AB system, 2H, CH_2-4, $J_{AB} = 24$), 1.66 (s, 3H, CH_3, isop), 1.40 (s, 3H, CH_3, isop); ^{13}C-NMR: 170.2 (C-5), 155.5 (C-3), 138.8, 137.7 (Cq, Ph), 129.1, 128.8, 128.6, 128.3, 125.3, 118.9 (CH, Ph), 113.6 (Cq, isop), 104.1 (C-1′), 79.1 (C-3′), 77.2 (C-2′), 76.5 (C-4′), 72.5 (CH_2, Bn), 38.7 (C-4), 26.7 (CH_3, isop), 26.4 (CH_3, isop).

Anal. Calcd for $C_{23}H_{24}N_2O_5$: C 67.63, H 5.92; Found: C 67.58, H 6.20, N 5.80.

General Procedure for the Cyclisation of Hydrazones to Pyrazoles

The solution of the hydrazone (1.1 mmol) in chloroform (2 mL) was added to the mixture of sodium acetate (164 mg, 2 mmol) and acetic anhydride (2.8 mL, 30 mmol). The reaction mixture was stirred at 100°C for 4 hr. Concentration in vacuum gave a residue, which was extracted with chloroform (3 × 50 mL), the organic phase was washed with water, dried (Na_2SO_4), and concentrated under reduced pressure to give a residue, which was purified by CC eluted with ethyl acetate/toluene (1 : 6).

Methyl 5-acetoxy-3-[(4*R*)-3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-erythrofuranos-4-*C*-yl]-1*H*-pyrazole-1-carboxylate (12) and **5-acetoxy-1-acetyl-3-[(4*R*)-3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-erythrofuranos-4-*C*-yl]-1*H*-pyrazole (13).** Starting from **10a,b** (0.48 g, 1.1 mmol), the residue obtained was subjected to CC to give **12** (0.34 g, 72%) and **13** (0.073 g, 16%). Starting from **11a,b** (0.53 g, 1.1 mmol) only **13** (0.39 g, 85%) was obtained.

Data for **12**: R_f 0.54 (ethyl acetate/toluene 1 : 1); $[\alpha]_D^{25} = +17^\circ$ (*c* 1.8, $CHCl_3$); IR (neat) (cm^{-1}): 1798, 1766 (C = O), 1591 (C = C); UV ($\lambda_{máx.}$ nm) ethanol: 228 ($\varepsilon = 7424$), 209 ($\varepsilon = 8398$); ^1H NMR: 7.28 (s, 5H, Ph), 6.09 (s, 1H, H-4), 5.83 (d, 1 H, H-1′, $J_{1',2'} = 3.6$), 5.06 (d, 1H, H-4′, $J_{3',4'} = 9$), 4.67-4.60 (m, 3H, H-2′, CH_2, Bn), 4.02 (s, 3H, OCH_3), 3.90 (dd, 1H, H-3′, $J_{2',3'} = 4$), 2.36 (s, 3H, CH_3, Ac), 1.64 (s, 3H, CH_3, isop), 1.25 (s, 3H, CH_3, isop); ^{13}C NMR: 171.2 (C = O), 166.9 (C = O, Ac), 153.0 (C-3), 148.8 (C-5), 137.1 (Cq, Ph), 128.3, 128.1, 127.8 (CH, Ph), 113.2 (Cq, isop), 104.0 (C-1′), 98.1 (C-4), 81.1 (C-3′), 77.7 (C-2′), 74.8 (C-4′), 72.1 (CH_2, Ph), 54.7 (CH_3, OCH_3), 26.7 (CH_3, isop), 26.5 (CH_3, isop), 20.4 (CH_3, Ac).

Anal. Calcd for ($C_{21}H_{24}O_8N_2$): C 58.33, H 5.59, N 6.48; Found C 57.95, H 5.45, N 6.93.

Data for **13**: R_f 0.69 (ethyl acetate/toluene 1 : 1); $[\alpha]_D^{25} = +25^\circ$ (*c* 2.3, $CHCl_3$); IR (neat)(cm^{-1}): 1780, 1755 (C = O), 1579 (C = C); UV ($\lambda_{máx.}$ nm) ethanol: 240 ($\varepsilon = 8693$), 208 ($\varepsilon = 8861$); ^1H NMR: 7.30–7.15 (m, 5H, Ph), 6.52 (s, 1H, H-4), 5.74 (d, 1H, H-1′, $J_{1',2'} = 3.5$), 5.65 (d, 1H, H-4′, $J_{3',4'} = 8.9$), 4.67, 4.45 (AB system, 2H, CH_2, Bn, $J_{AB} = 12$), 4.63 (t, 1H, H-2′, $J_{2',3'} = 3.8$), 3.98 (dd, 1H, H-3′), 2.51 (s, 3H, CH_3, Ac), 2.25 (s, 3H, CH_3, Ac), 1.62 (s, 3H, CH_3, isop), 1.34 (s, 3H, CH_3, isop); ^{13}C NMR: 170.0, 167.1 (C = O), 155.7 (C-3), 144.4 (C-5), 137.0 (Cq, Ph), 129.0, 128.4, 128.0 (CH, Ph), 113.6 (Cq, isop), 104.2 (C-1′), 103.4 (C-4), 82.2 (C-3′), 77.6 (C-2′), 72.5 (C-4′), 72.1 (CH_2, Bn), 27.0 (CH_3, isop), 26.9 (CH_3, isop), 23.3 (CH_3, Ac), 20.9 (CH_3, Ac).

Anal. Calcd for ($C_{21}H_{24}O_7N_2$): C 60.57, H 5.81, N 6.73; Found C 60.67, H 5.50, N 7.12.

3-*O*-benzyl-5-deoxy-1,2-*O*-isopropylidene-α-D-*ribo*-hexofuranose (15b) and 3-*O*-benzyl-6-deoxy-1,2-*O*-isopropylidene-α-D-allofuranose (15c). *N,N′*-thiocarbonyldiimidazole (1.9 g, 10 mmol) was added to a solution of **1**[23] (3.0 g, 9.7 mmol) in THF (20 mL). The reaction mixture was refluxed for 30 min under nitrogen. Evaporation of the solvent under reduced pressure gave a residue that was dissolved in dichloromethane (90 mL) and washed with cold HCl 2M (11 mL) to which cold water was added (2 mL). The organic layer was dried with sodium sulphate and the solvent evaporated to give the intermediate 3-*O*-benzyl-1,2-*O*-isopropylidene-5,6-*O*-thiocarbonyl-α-D-allofuranose (**15a**) (2.7 g, 80%). The thiocarbonate (2.7 g, 7.7 mmol), Bu_3SnH (4.5 g, 15.3 mmol), and AIBN (0.11 g, 0.67 mmol) in dry toluene (150 mL) was added dropwise to refluxing toluene (80 mL) under argon for 45 min. Subsequent addition of the Bu_3SnH (2 × 2.2 g, 7.5 mmol) together with AIBN (2 × 0.06 g, 0.37 mmol) after 2 hr and 4 hr was necessary. The reaction was complete in 6 hr. The solution was then treated with aqueous NaOH (10%, 80 mL) and stirred at 40°C for 12 hr. The organic layer was separated and the aqueous layer was reextracted with diethyl ether. The combined organic phases were washed repeatedly with water until free of base and dried with sodium sulfate. Concentration to a syrup, followed by CC eluted with ethyl acetate/toluene (1 : 5) gave **15b** (2.34 g, 30%) and **15c** (2.34 g, 30%).

Data for **15b**: R_f 0.37 (ethyl acetate/toluene 1 : 1); $[\alpha]_D^{25} = +120^\circ$ (*c* 1.3, $CHCl_3$); IR (neat) (cm^{-1}): 3430 (OH); ^{1}H NMR: 7.37–7.28 (m, 5H, Ph), 5.72 (d, 1H, H-1, $J_{1,2} = 3.7$), 4.79 (part A of AB system, 1H, CH_2, Bn, $J_{AB} = 11.8$), 4.59–4.51 (m, 2H, H-2, part B of AB system), 4.13 (ddd, 1H, H-4, $J_{3,4} = 9$, $J_{4,5} = 4.7$), 3.71 (t, 2H, H-6, $J_{5,6} = 5.7$), 3.48 (dd, 1H, H-3, $J_{2,3} = 4.3$), 2.78 (brs, 1H, OH-6), 1.99-1.87 (m, 1H, H-5a), 1.84–1.68 (m, 1H, H-5b), 1.59 (s, 3H, CH_3, isop), 1.35 (s, 3H, CH_3, isop); ^{13}C NMR: 136.9 (Cq, Ph), 128.2, 128.0, 127.9 (CH, Ph), 112.6 (Cq, isop), 103.7 (C-1), 81.4 (C-3), 76.7 (C-4), 76.5 (C-2), 71.8 (CH_2, Bn), 59.8 (C-6), 34.6 (C-5), 26.4 (CH_3, isop), 26.2 (CH_3, isop).

Anal. Calcd for ($C_{16}H_{22}O_5$): C 65.29, H 7.53; Found C 65.43, H 7.50.

Data for **15c**: R_f 0.66 (ethyl acetate/toluene 1 : 1); $[\alpha]_D^{25} = +107.4^\circ$ (*c* 1.5, $CHCl_3$); IR (neat) (cm^{-1}): 3460 (OH); ^{1}H NMR: 7.39–7.31 (m, 5H, Ph), 5.71 (d, 1H, H-1, $J_{1,2} = 3.7$), 4.75 (part A of AB system, 1H, CH_2, Bn, $J_{AB} = 11.6$), 4.58–4.54 (m, 2H, H-2, part B of AB system), 4.05–3.99 (m, 2H, H-4, H-5), 3.89 (dd, 1H, H-3, $J_{2,3} = 4.3$, $J_{3,4} = 8.4$), 2.54 (brs, 1H, OH-5), 1.59 (s, 3H, CH_3, isop), 1.35 (s, 3H, CH_3, isop), 1.21 (d, 3H, H-6, $J_{5,6} = 6.5$); ^{13}C NMR: 137.2 (Cq, Ph), 128.3, 128.0, 127.9 (CH, Ph), 112.8 (Cq, isop), 103.8 (C-1), 81.3 (C-4), 77.6 (C-2), 76.9 (C-3), 71.8 (CH_2, Bn), 66.3 (C-5), 26.7 (CH_3, isop), 26.5 (CH_3, isop), 17.4 (C-56).

Anal. Calcd for ($C_{16}H_{22}O_5$): C 65.29, H 7.53; Found C 65.38, H 7.49.

3-*O*-benzyl-5-deoxy-1,2-*O*-isopropylidene-α-D-*ribo*-hexodialdo-1,4-furanose (16). 3-*O*-benzyl-5-deoxy-1,2-*O*-isopropylidene-α-D-*ribo*-hexofuranose (**15b**) (1.2 g, 4.1 mmol) was added to a suspension of pyridinium chlorochromate (2 g, 9.2 mmol) and molecular sieve powder 4 Å (4 g) in dichloromethane (20 mL). The reaction mixture was stirred at rt for 15 min. Ethyl acetate was then added (30 mL) and the mixture stirred at rt for 10 min. The suspension was filtered and concentrated under reduced pressure. The residue was purified by CC eluted with ethyl acetate/toluene (1 : 4) to give **16** (0.96 g, 80%); R_f 0.65 (ethyl acetate/toluene 1 : 1); $[\alpha]_D^{25} = +80^\circ$ (*c* 1.5, $CHCl_3$); IR(cm^{-1}): 1726 (C = O); ^{1}H NMR: 9.72 (t, 1H, H-6, $J_{5,6} = 2$), 7.35–7.32 (m, 5H, Ph), 5.73 (d, 1H, H-1, $J_{1,2} = 3,7$),

4.78 (part A of AB system, 1H, CH_2,Bn, $J_{AB} = 11.8$), 4.59–4.45 (m, 3H, H-2, H-4, part B of AB system), 3.51 (dd, 1H, H-3, $J_{2,3} = 4.2$, $J_{3,4} = 9$), 2.73–2.43 (m, 2H, H-5, H-5′), 1.61 (s, 3H, CH_3, isop), 1.36 (s, 3H, CH_3, isop); ^{13}C NMR: 199.8 (Cq, C-6), 137.0 (Cq, Ph), 128.4, 128.3, 127.9 (CH, Ph), 112.9 (Cq, isop), 104.0 (C-1), 81.0 (C-3), 76.3 (C-4), 72.9 (C-2), 72.0 (CH_2, Bn), 45.5 (C-6), 26.5 (CH_3, isop), 26.2 (CH_3, isop).

Anal. Calcd for $C_{16}H_{20}O_5$: C 65.74, H 6.90; Found C 66.05, H 6.78.

Ethyl 3-*O*-benzyl-5,7-dideoxy-1,2-*O*-isopropylidene-α-D-*ribo*-oct-6-ulofuranuronate (18). A solution of **17a,b** (1.3 g, 3.4 mmol) in dry dichloromethane (3 mL) was added to a suspension of PCC (2.45 g, 11.4 mmol) and powdered molecular sieves (4 Å, 3.42 g) in dry dichloromethane (17 mL). The mixture remained under stirring at rt for 40 min. Absolute ethyl acetate was added (30 mL), and the mixture was stirred for 10 min. After filtration, the filtrate was concentrated under reduced pressure at rt to give **18** (1.2 g, 92%); R_f 0.66 (ethyl acetate/toluene 1 : 1); $[\alpha]_D^{25} = +46^\circ$ (*c* 2.5, $CHCl_3$); IR (neat) (cm^{-1}): 1744 (C = O), 1720 (C = O); UV ($\lambda_{máx.}$ nm) ethanol: 230 ($\varepsilon = 7222$), 204 ($\varepsilon = 6476$); ^{1}H NMR: 7.36–7.30 (m, 5H, Ph), 5.70 (d, 1H, H-1, $J_{1,2} = 3,7$), 4.78 (part A of AB system, 1H, CH_2, Bn, $J_{AB} = 11.9$), 4.56–4.51 (m, 2H, H-2, part B of AB system of CH_2, Bn), 4.37 (ddd, 1H, H-4), 4.17 (q, 2H, CH_2, Et, $J_{CH_2CH_3} = 7.2$), 3.55 (dd, 1H, H-3, $J_{2,3} = 4.2$, $J_{3,4} = 9$), 3.49 (s, 2H, H-7, H-7′), 2.90–2.58 (m, 2H, H-5, H-5′), 1.60 (s, 3H, CH_3, isop), 1.35 (s, 3H, CH_3, isop), 1.26 (t, 3H, CH_3, Et); ^{13}C NMR: 200,4 (C-6), 167.0 (C-8), 137,2 (Cq, Ph), 128.4, 128.0 (CH, Ph), 113.1 (Cq, isop), 104.0 (C-1), 80.8 (C-3), 76.6 (C-2), 74.1 (C-4), 72.2 (CH_2, Bn), 61.3 (CH_2, Et), 49.9 (C-7), 44.7 (C-5), 26.7 (CH_3, isop), 26.5 (CH_3, isop), 14.0 (CH_3, Et).

Anal. Calcd for $C_{20}H_{26}O_7$: C 63.48, H 6.92; Found C 64.04, H 6.45.

Ethyl 3-*O*-benzyl-7-diazo-5,7-dideoxy-1,2-*O*-isopropylidene-α-D-*ribo*-oct-6-ulofuranuronate (19). Tosyl azide (2.14 g, 10.8 mmol) and triethylamine (0.56 mL, 4.06 mmol) were added to a solution of **18** (1.5 g, 3.97 mmol) in anhydrous acetonitrile (18 mL). The mixture was kept under stirring at rt for 30 min. The mixture was filtered and concentrated under reduced pressure. The residue was purified by CC eluted with ethyl acetate/toluene (1 : 6) to give **19** (1.5 g, 93.5%); R_f 0.60 (ethyl acetate/toluene 1 : 2); $[\alpha]_D^{25} = +69^\circ$ (*c* 1.45, $CHCl_3$); IR (neat) (cm^{-1}): 2150 (C = N_2), 1730 (C = O), 1660 (C = O); UV ($\lambda_{máx.}$ nm) ethanol: 257 ($\varepsilon = 7855$), 216 ($\varepsilon = 12535$); ^{1}H NMR: 7.37–7.23 (m, 5H, Ph), 5,71 (d, 1H, H-1, $J_{1,2} = 3.7$), 4.78 (part A of AB system, 1H, CH_2, Bn, $J_{AB} = 11.8$), 4.57–4.50 (m, 3H, H-2, H-4, part B of AB system of CH_2, Bn), 4.27 (q, 2H, CH_2, Et, $J_{CH_2CH_3} = 7.1$), 3.63 (dd, 1H, H-3, $J_{2,3} = 4.2$, $J_{3,4} = 9$), 3.16–3.13 (m, 2H, H-5), 1.60 (s, 3H, CH_3, isop), 1.35 (s, 3H, CH_3, isop), 1,31 (t, 3H, CH_3, Et); ^{13}C NMR (C_3D_6O): 189.3 (C-6), 161.1 (C-8), 137.4 (Cq, Ph), 128.4, 127.9 (CH, Ph), 113.1 (Cq, isop), 104.0 (C-1), 81,3 (C-3), 76,8 (C-4), 76.7 (Cq, C-7), 74.2 (C-2), 72.2 (CH_2, Bn), 61.4 (CH_2, Et), 42.0 (C-5), 26.7 (CH_3, isop), 26.4 (CH_3, isop), 14.3 (CH_3, Et).

Anal. Calcd for ($C_{20}H_{24}O_7N_2$): C 59.40, H 5.98, N 6.93; Found: C, 59.65; H, 5.78; N, 7.28.

Ethyl 3-[(4*R*)-3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-erythrofuranos-4-*C*-yl]-4-hydroxy-1*H*-pyrazole-5-carboxylate (20). A solution of **19** (1 g, 2.48 mmol) in dry THF (13.5 mL) was added dropwise to a suspension of 95% sodium hydride (0.3 g, 12.4 mmol) in dry THF (13.5 mL) under nitrogen at 0°C. After complete addition, the reaction mixture was stirred at 20°C for 20 hr. The mixture was cooled to 0°C, a solution of glacial acetic acid (0.71 mL, 12.4 mmol) in THF (2 mL) was added dropwise, and the mixture was concentrated under reduced pressure. The residue was extracted with $CHCl_3$ (2 × 50 mL) and water (50 mL). THF (20 mL) was added to the aqueous phase,

and the solution was extracted with $CHCl_3$ (50 mL). The organic phases were dried (Na_2SO_4) and concentrated. The residue was purified by CC eluted with ethyl acetate/toluene (1 : 10) to give **20** (0.2 g, 20%); mp 161–161.5°C; R_f 0.57 (*n*-hexane/ethyl acetate 1 : 3); $[\alpha]_D^{25} = +15^\circ$ (*c* 2.0, $CHCl_3$); IR (KBr) (cm^{-1}): 3431 (N-H), 3300 (O-H), 1724 (C = O), 1691 (C = C); UV ($\lambda_{máx.}$ nm) ethanol: 230 ($\varepsilon = 7635$), 207 ($\varepsilon = 8938$); ^{1}H NMR: 7.30–7.25 (m, 5H, Ph), 6.87 (s, 1H, N-H), 5.85 (d, 1H, H-1′, $J_{1',2'} = 3.6$), 5.17 (d, 1H, H-4′, $J_{3',4'} = 9.2$), 4.67–4.24 (m, 3H, H-2′, CH_2, Bn), 4.44 (q, 2H, CH_2, Et, $J_{CH_2CH_3} = 7.1$), 4.30 (dd, 1H, H-3′, $J_{2',3'} = 4.2$), 1.67 (s, 3H, CH_3, isop), 1.39 (s, 3H, CH_3, isop), 1.43 (t, 3H, CH_3, Et); ^{13}C NMR: 161.8 (C = O), 144.6 (C-3), 137.3 (Cq, Ph), 131.5 (C-5), 128.5, 128.2, 127.9 (CH, Ph), 122.7 (C-4), 113.2 (Cq, isop), 103.8 (C-1), 79.6 (C-3), 77.5 (C-2), 72.5 (CH_2, Bn), 72.1 (C-4), 61.4 (CH_2, Et), 26.7 (CH_3, isop), 26.4 (CH_3, isop), 14.3 (CH_3, Et).

Anal. Calcd for $C_{20}H_{24}O_7N_2$: C 59.40, H 5.98, N 6.93; Found: C 59.34, H 5.81, N 7.14.

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