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Note

Chemical modification of 1-(3,4-di-*O*-acetyl-2-deoxy-2-hydroxyimino-α- and -β-D-*erythro*-pentopyranosyl)pyrazole at C-2 and C-3

ZYGFRYD SMIATACZ AND HENRYK MYSZKA
Institute of Chemistry, The University of Gdańsk, 80-952 Gdańsk (Poland)

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We have described the use of 1-(3,4,6-tri-*O*-acetyl-2-deoxy-2-hydroxyimino-α- and -β-D-*arabino*- and -D-*lyxo*-hexopyranosyl)pyrazoles[1,2] and the methyl esters of some *N*-protected *O*-(3,4,6-tri-*O*-acetyl-2-deoxy-2-hydroxyimino-α,β-D-*arabino*-hexopyranosyl)-hydroxy-α-L-amino acids[3] in the synthesis of corresponding D-glycopyranosides, 2-acetamido-2-deoxy-D-glycopyranosides, and 3-azido- or 3-acetamido-2-deoxy-2-hydroxyimino-D-glycopyranosides. We now report on analogous syntheses from 1-(3,4-di-*O*-acetyl-2-deoxy-2-hydroxyimino-α- and -β-D-*erythro*-pentopyranosyl)pyrazole.

1-(3,4-Di-*O*-acetyl-2-deoxy-2-hydroxyimino-β- and -α-D-*erythro*-pentopyranosyl)pyrazoles[4] (**1** and **2**) were converted into the 1-(2,3,4-tri-*O*-acetyl-D-pentopyranosyl)pyrazoles **3**–**5** *via* the reaction sequence $\geq C{=}N{-}OH \rightarrow \geq C{=}O \rightarrow \geqslant C{-}OH \rightarrow \geqslant C{-}OAc$. The deoximation was accomplished with acetaldehyde in the presence of hydrochloric acid[5] and the ketones were reduced with sodium borohydride[6]. Thus, **1** yielded 1-(2,3,4-tri-*O*-acetyl-β-D-arabinopyranosyl)pyrazole (**3**; $^1C_4$ conformer, $J_{1,2} \approx J_{3,4} \approx 3.5$, $J_{2,3} \sim 8$, $J_{4,5a} \sim 4$, $J_{4,5e} \sim 2$ Hz) and the β-D-*ribo* isomer **4** ($^4C_1$ conformer, $J_{1,2} \sim 8$, $J_{2,3} \approx J_{4,5e} \approx 3$, $J_{4,5a} \sim 9$ Hz) in the ratio ~2:1 and in a combined yield of ~70%. However, application of this reaction sequence to **2** gave mainly the α-D-*arabino* derivative **5** ($^1C_4$ conformer, $J_{1,2} \approx J_{2,3} \approx 9$, $J_{3,4} \sim 3.5$, $J_{4,5a} \sim 2.5$, $J_{4,5e} \sim 1.5$ Hz).

Reduction of the ketone, formed by deoximation of **1**, to yield products of both the axial (**3**) and equatorial (**4**) addition of hydride ion to C-2 is compatible with predictions on stereoelectronic interactions in the transition state of the reaction[7]. The stereospecific reduction of the product of deoximation of **2** to give **5** was unexpected. The structure of **5** was confirmed, by synthesis, by the reaction of 2,3,4-tri-*O*-acetyl-β-D-arabinopyranosyl bromide with pyrazole by the Koenigs–Knorr method.

Hydrogenation (Pd/C, AcOH) of the 2-hydroxyimino group in **1** was also not stereospecific and, after acetylation, the β-D-*arabino* (**6**; $^1C_4$ conformer, $J_{1,2} \approx J_{3,4}$

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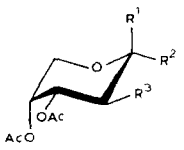
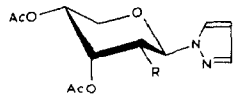


3 R^1 =  , R^2 = H, R^3 = OAc



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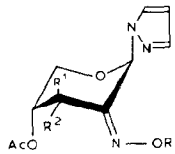
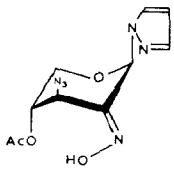
7 R = NHAc



8 R = H, R^1 = H, R^2 = N_3
9 R = H, R^1 = N_3, R^2 = H
14 R = Ac, R^1 = H, R^2 = NHAc
15 R = Ac, R^1 = NHAc, R^2 = H

5 R^1 = H, R^2 =  , R^3 = OAc

6 R^1 =  , R^2 = H, R^3 = NHAc



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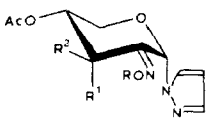
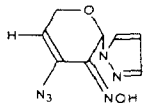


11 R = H, R^1 = H, R^2 = N_3
13 R = H, R^1 = N_3, R^2 = H
16 R = Ac, R^1 = H, R^2 = NHAc



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$\approx J_{4,5e} \approx 3$, $J_{2,3} \sim 10$ Hz) and β-D-*ribo* (**7**; $^4C_1$ conformer, $J_{1,2} \sim 9$, $J_{2,3} \approx J_{3,4} \approx J_{4,5e} \approx 3$, $J_{4,5a} \sim 10$ Hz) products were obtained.

Literature evidence[8–10] and previous findings[1–3] concerning OAc as the leaving group in the system R–O–C–C=N–Y–H (Y = O or NHPh, R = Ac) prompted the modification of **1** and **2** at C-3. Thus, **1** reacted with sodium azide in boiling ethanol to give the β-D-*erythro* derivative **8** ($J_{3,4} \approx J_{4e,5a} \approx 3$, $J_{4e,5e} \sim 1.5$ Hz), the product of equatorial substitution of AcO-3, as well as the β-D-*threo* derivative **9** and **10** ($J_{3,4} \approx J_{4,5e} \approx 1.5$, $J_{4,5a} \sim 3$ Hz), the products of axial substitution. The **8**:**9**:**10** ratio was 6:4.5:1. The oxime groups in **8** and **9** have the *Z* configuration, whereas the configuration in **10** is *E*. The *Z*:*E* ratio was 9.5:1.

Under similar conditions of reaction, **2** afforded **11–13** in the ratio 5:3:1. The α-D-*threo* derivative **11** ($J_{3,4} \approx J_{4a,5a} \approx 8$, $J_{4a,5e} \sim 3$ Hz) was formed by equatorial displacement of AcO-3, whereas the α-D-*erythro* derivative **13** ($J_{3,4} \approx J_{4,5e} \approx 3$, $J_{4,5a} \sim 8$ Hz) was the product of axial substitution. Compound **12** was identified as 1-(3-azido-2,3,4-trideoxy-2-hydroxyimino-α-D-*glycero*-pent-3-enopyranosyl)pyrazole, formed probably from **13** *via trans*-elimination of AcO-4 and H-3.

The mechanism of formation of the products with different configurations at C-3 and of the oxime has been suggested elsewhere[3].

Compounds **8**, **9**, and **11** were then hydrogenolysed over Pd/C. The reactions were rapid (4 h) and selective, and left the hydroxyimino group intact. Subsequent

TABLE I

^{1}H-N.M.R. DATA [a] FOR **3–16**

Compound	*H-1*	*H-2*	*H-3*	*H-4*	*H-5e*	*H-5a*	$\Delta\delta_{H\text{-}5e,H\text{-}5a}$	*Ac*	*Pyrazole*	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5e}$	$J_{4,5a}$	J_{gem}
3	6.03 d	5.28 dd	5.38 dd	5.34 m	4.30 dd	3.73 dd	0.61	1.76, 3 H 1.90, 3 H 2.00, 3 H	6.18, 1 H 7.43, 1 H 7.51, 1 H	3.5	8.0	3.5	1.5	4.0	12
4	5.60 d	5.48 dd	5.78 dd	5.15 m	3.98 dd	3.88 dd	0.10	1.75, 3 H 1.90, 3 H 2.08, 3 H	6.25, 1 H 7.50, 2 H	8.0	3.5	3.0	3.0	9.0	10
5	5.70 d	5.35 dd	5.20 dd	5.30 m	4.10 dd	3.80	0.30	1.76, 3 H 1.93, 3 H 2.10, 3 H	6.35, 1 H 7.63, 1 H 7.73, 1 H	9.0	9.0	3.5	1.5	2.5	13
6	5.87 d	4.57 dd	5.25 dd	4.97 m	4.20 dd	3.65 dd	0.55	1.67, 3 H 1.92, 3 H 2.10, 3 H	6.22, 1 H 7.65, 1 H 7.69, 1 H	3.0	10.0	3.0	2.0	4.0	11
7	6.00 d	5.20 dd	5.55 dd	4.55 m	3.82 dd	3.68 dd	0.14	1.62, 3 H 1.72, 3 H 1.81, 3 H	6.24, 1 H 7.55, 2 H	8.0	3.0	3.0	3.0	9.0	10
8	7.04 s		5.01 d	5.40 m	4.12 dd	3.90 dd	0.22	2.13, 3 H	6.40, 1 H 7.60, 1 H 7.70, 1 H			3.5	1.5	3.0	12
9	6.83 s		4.78 dd	4.45 m	4.07 dd	3.70 dd	0.37	2.00, 3 H	6.33, 1 H 7.68, 2 H			1.5	1.5	3.0	11
10	6.30 s		5.40 d	4.85 m	4.10 dd	3.87 dd	0.27	2.10, 3 H	6.23, 1 H 7.75, 2 H			1.5	1.5	3.0	10
11	6.95 s		5.15 d	5.10 m	3.88 dd	3.60 dd	0.28	2.08, 3 H	6.15, 1 H 7.63, 1 H 7.70, 1 H			8.0	3.0	9.0	11
12	7.00 s			5.90 dd	4.25 m				6.38, 1 H 7.68, 2 H						
13	6.88 s		5.48 d	4.93 dd	4.17 dd	3.95 dd	0.22	2.08, 3 H	6.40, 1 H 7.68, 2 H			3.0	3.0	8.5	12
14	6.93 s		6.00 d	5.50 dd	4.15 dd	3.90	0.25	2.03, 3 H 2.10, 6 H	6.45, 1 H 7.65, 1 H 7.75, 1 H			3.5	1.5	2.5	12
15	6.88 s		5.10 dd	4.95 m	4.18 dd	3.85	0.33	2.00, 3 H 2.05, 6 H	6.50, 1 H 7.68, 1 H 7.85, 1 H			1.5	1.0	3.0	12
16	6.90 s		5.83 dd	5.25 m	4.02 dd	3.72	0.30	2.00, 6 H 2.10, 3 H	6.50, 1 H 7.70, 1 H 7.78, 1 H			9.0	3.0	9.0	10

[a]Chemical shifts (δ scale) and coupling constants (Hz, ±0.5 Hz) determined by first-order analysis.

acetylation gave β-D-*erythro* (**14**; $^1C_4$ conformer, $J_{3,4}$ ~3.5, $J_{4,5e}$ ~1.5, $J_{4,5a}$ ~2.5 Hz), β-D-*threo* (**15**; $^1C_4$ conformer, $J_{3,4} \approx J_{4,5e} \approx 1.5$, $J_{4,5a}$ ~3 Hz), and α-D-*threo* (**16**; $^4C_1$ conformer, $J_{3,4} \approx J_{4,5a} \approx 9$, $J_{4,5e}$ ~3 Hz) products, respectively. The ^{1}H-n.m.r. data for **3**–**16** are given in Table I.

EXPERIMENTAL

Melting points are uncorrected. Optical rotations were determined (Hilger–Watt instrument) for solutions in chloroform (*c* 0.5). T.l.c. was performed on Silica Gel G with toluene–ethyl acetate (*A*, 2:1; *B*, 5:1) and carbon tetrachloride–acetone (*C*, 3:1; *D*, 1:1). Column chromatography was performed on Kieselgel (<0.08 mm). ^{1}H-N.m.r. spectra ($CDCl_3$, internal Me_4Si) were recorded with a Tesla-BS 487C (80 MHz) spectrometer. I.r. spectra were recorded for Nujol mulls with a Perkin–Elmer 257 spectrophotometer. F.d.-mass spectra were recorded on a MAT 711 mass spectrometer.

1-(3,4-Di-*O*-acetyl-2-deoxy-2-hydroxyimino-β-D-*erythro*- and -α-D-*erythro*-pentopyranosyl)pyrazole (**1** and **2**) were prepared according to the literature procedure[4].

1-(2,3,4-Tri-O-acetyl-β-D-arabino- and -β-D-ribo-pyranosyl)pyrazole (**3** *and* **4**). — A solution of **1** (3 mmol, 0.892 g), acetaldehyde (9 mmol, 0.396 g), and M hydrochloric acid (3 mL) in acetonitrile (20 mL) was stirred for 6 days at room temperature, then cooled to 0°, and sodium borohydride (18 mmol, 0.684 g) was added in small portions. The resulting solution was stirred for 3 h at ~20°, then cooled to 0°, neutralized with acetic acid, and concentrated. The residue was treated conventionally with acetic anhydride–pyridine. Column chromatography (solvent *A*) of the product gave, first, **3** (45%), isolated as a syrup, $[\alpha]_D^{20}$ −104°, R_F 0.52 (solvent *A*); ν_{max} 1740 cm^{-1} (ester CO).

Anal. Calc. for $C_{14}H_{18}N_2O_7$: C, 51.53; H, 5.64; N, 8.59. Found: C, 51.45; H, 5.58; N, 8.50.

Eluted second was **4** (25%), isolated as a syrup, $[\alpha]_D^{20}$ −6°, R_F 0.33, ν_{max} 1745 cm^{-1} (ester CO).

Anal. Found: C, 51.42; H, 5.52; N, 8.55.

1-(2,3,4-Tri-O-acetyl-α-D-arabinopyranosyl)pyrazole (**5**). — (*a*) On treatment of **2**, as described for **1**, deoximation required 5 days at ~20°. The crude product crystallized from ether to give **5** (62%), m.p. 88–90°, $[\alpha]_D^{20}$ −39°, R_F 0.36 (solvent *A*); ν_{max} 1735 cm^{-1} (ester CO).

Anal. Calc. for $C_{14}H_{18}N_2O_7$: C, 51.53; H, 5.64; N, 8.59. Found: C, 51.50; H, 5.59; N, 8.55.

(*b*) To a solution of 2,3,4-tri-*O*-acetyl-β-D-arabinopyranosyl bromide (3 mmol, 1.017 g) and pyrazole (3.3 mmol, 0.224 g) in benzene (17 mL) and nitromethane (17 mL) was added $Hg(CN)_2$ (3 mmol, 0.76 g), and the mixture was stirred for 24 h at room temperature. T.l.c. (solvent *A*) then showed complete conversion of the bromide into one major product. The mixture was filtered, treated with ether, filtered, diluted with chloroform, washed with water, dried ($MgSO_4$), and concentrated, and the residue was crystallized from ether to gave **5** (80%).

*1-(2-Acetamido-3,4-di-*O*-acetyl-2-deoxy-β-*D*-arabino- and -β-*D*-ribo-pyranosyl)pyrazole* (**6** *and* **7**). — A solution of **1** (3 mmol, 0.89 g) in ethanol (25 mL) and acetic acid (1.5 mL) was stirred under hydrogen (1 atm.) in the presence of 5% Pd/C (0.6 g) for 7 days at ~20°, then filtered, and concentrated, and the residue was treated conventionally with acetic anhydride–pyridine. Column chromatography (solvent *C*) of the oily product gave, first, **6** (32%), isolated as a syrup, $[\alpha]_D^{20}$ −95°, R_F 0.36 (solvent *C*); ν_{max} 1740 (ester CO) and 1670 cm^{-1} (amide CO).

Anal. Calc. for $C_{14}H_{19}N_3O_6$: C, 51.67; H, 5.87; N, 12.92. Found: C, 51.55; H, 5.72; N, 13.02.

Eluted second was **7** (36%), isolated as a syrup, $[\alpha]_D^{20}$ −15°, R_F 0.21; ν_{max} 1750 (ester CO) and 1680 cm^{-1} (amide CO).

Anal. Found: C, 51.60; H, 5.71; N, 12.88.

(Z)-*1-(4-*O*-Acetyl-3-azido-2,3-dideoxy-2-hydroxyimino-β-*D*-*erythro*-pentopyranosyl)pyrazole* (**8**), *and* (Z)- (**9**) *and* (E)-*1-(4-*O*-acetyl-3-azido-2,3-dideoxy-2-hydroxyimino-β-*D*-*threo*-pentopyranosyl)pyrazole* (**10**). — A suspension of sodium azide (13.5 mmol, 0.88 g) in a solution of **1** (3.36 mmol, 1 g) in ethanol (100 mL) was stirred and boiled under reflux. T.l.c. (solvent *C*) after 2 h showed complete conversion of **1** into three products. The solution was filtered and concentrated, and the residue was extracted with ether. The extract was filtered, diluted with dichloromethane (250 mL), washed with water (3 × 100 mL), dried ($MgSO_4$), and concentrated. Column chromatography of the resulting syrup (solvent *B*) gave, first, **8** (42%), isolated as a syrup, $[\alpha]_D^{20}$ −156°, R_F 0.46 (solvent *B*); ν_{max} 3320 (OH), 2120 (N_3), and 1735 cm^{-1} (ester CO).

Anal. Calc. for $C_{10}H_{12}N_6O_4$: C, 42.86; H, 4.32; N, 29.99. Found: C, 42.36; H, 4.24; N, 29.80.

Eluted second was **9** (32%), isolated as a syrup, $[\alpha]_D^{20}$ −226°, R_F 0.31; ν_{max} 3320 (OH), 2110 (N_3), and 1730 cm^{-1} (ester CO).

Anal. Found: C, 42.57; H, 4.28; N, 29.74.

Eluted third was **10** (8%), syrup, $[\alpha]_D^{20}$ −110°, R_F 0.24; ν_{max} 3300 (OH), 2110 (N_3), and 1735 cm^{-1} (ester CO).

Anal. Found: C, 42.61; H, 4.30; N, 29.70.

*1-(4-*O*-Acetyl-3-azido-2,3-dideoxy-2-hydroxyimino-α-*D*-threo- and -α-*D*-erythro-pentopyranosyl)pyrazole* (**11** *and* **13**) *and 1-(3-azido-2,3,4-trideoxy-2-hydroxyimino-α-*D*-glycero-pent-3-enopyranosyl)pyrazole* (**12**). — A suspension of sodium azide (12 mmol, 0.78 g) in a solution of **2** (3 mmol, 0.891 g) in ethanol (80 mL) was stirred and boiled under reflux. After 2 h, t.l.c. (solvent *C*) showed the conversion of **2** into three products. The mixture was processed as described above for **8**–**10**, and column chromatography (solvent *C*) of the resulting syrup gave, first, **11** (40%), isolated as a syrup, $[\alpha]_D^{20}$ +97°, R_F 0.68 (solvent *C*); ν_{max} 3300 (OH), 2120 (N_3), and 1740 cm^{-1} (ester CO).

Anal. Calc. for $C_{10}H_{12}N_6O_4$: C, 42.86; H, 4.32; N, 29.99. Found: C, 42.80; H, 4.29; N, 29.73.

Eluted second was **12** (24%), isolated as a syrup, $[\alpha]_D^{20}$ +153°, R_F 0.59; ν_{max} 3250 (OH) and 2110 (N_3).

Anal. Calc. for $C_8H_8N_6O_2$: C, 43.63; H, 3.66; N, 38.17. Found: C, 43.51; H, 3.57; N, 38.09.

Eluted third was **13** (9%), isolated as a syrup, $[\alpha]_D^{20}$ +180°, R_F 0.50; ν_{max} 3300 (OH), 2120 (N_3), and 1735 cm^{-1} (ester CO).

Anal. Calc. for $C_{10}H_{12}N_6O_4$: C, 42.86; H, 4.32; N, 29.99. Found: C, 42.78; H, 4.10; N, 29.82.

*1-(3-Acetamido-2-acetoxyimino-4-O-acetyl-2,3-dideoxy-β-*D-erythro-*pentopyranosyl)pyrazole* (**14**). — A solution of **8** (1 mmol, 0.28 g) in ethanol (10 mL) was stirred under hydrogen (1 atm.) in the presence of 5% Pd/C (0.25 g) for 3 h at ~20°, then filtered, and concentrated to dryness, and the residue was treated conventionally with pyridine–acetic anhydride. The product crystallized from ether to give **14** (75%), m.p. 196–198°, $[\alpha]_D^{20}$ −238°, R_F 0.18 (solvent *C*); ν_{max} 3250 (NH), 1710 (ester CO), and 1680 cm^{-1} (amide CO).

Anal. Calc. for $C_{14}H_{18}N_4O_6$: C, 49.70; H, 5.36; N, 16.56. Found: C, 49.58; H, 5.30; N, 16.41.

*1-(3-Acetamido-2-acetoxyimino-4-O-acetyl-2,3-dideoxy-β-*D-threo-*pentopyranosyl)pyrazole* (**15**). — Compound **15** (69%), obtained from **9** as described above for **14**, was crystallized from ether and had m.p. 168–170°, $[\alpha]_D^{20}$ −113°, R_F 0.14 (solvent *C*); ν_{max} 3200 (NH), 1730 (ester CO), and 1675 cm^{-1} (amide CO).

Anal. Calc. for $C_{14}H_{18}N_4O_6$: C, 49.70; H, 5.36; N, 16.56. Found: C, 49.50; H, 5.33; N, 16.45.

*1-(3-Acetamido-2-acetoxyimino-4-O-acetyl-2,3-dideoxy-α-*D-threo-*pentopyranosyl)pyrazole* (**16**). — Compound **16** (75%), obtained from **11** as described above for **14**, was crystallized from ether and had m.p. 163–166°, $[\alpha]_D^{20}$ +172°, R_F 0.47 (solvent *D*); ν_{max} 3260 (NH), 1740 (ester CO), and 1680 cm^{-1} (amide CO).

Anal. Calc. for $C_{14}H_{18}N_4O_6$: C, 49.70; H, 5.36; N, 16.56. Found: C, 49.68; H, 5.30; N, 16.44.

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