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Carbohydrate Research 299 (1997) 307–310

CARBOHYDRATE RESEARCH

Note

# Preparation of 2-deoxyaldoses from aldose phenylhydrazones

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Received 13 September 1996; accepted 10 January 1997

**Abstract**

Acetylation of D-mannose phenylhydrazone gives acetylated D-*arabino*-1-phenyl-azo-1-(*E*)-hexene. Subsequent reduction with sodium borohydride produces 2-deoxy-D-*arabino*-hexose phenylhydrazone which, on hydrolysis, gives 2-deoxy-D-*arabino*-hexose. By a similar procedure 2-deoxy-D-*lyxo*-hexose, 2,6-dideoxy-L-*arabino*-hexose, and 2-deoxy-D-*erythro*-pentose can be prepared from D-galactose, L-rhamnose, and D-arabinose, respectively. © 1997 Elsevier Science Ltd.

*Keywords:* Aldose phenylhydrazones; 1-Phenylazo-1-hexenes; 2-Deoxyaldoses

Treatment of acetylated aldosediphenylformazans with nucleophiles may result in substitution of the 2-*O*-acetyl group and formation, e.g. with ammonia, of 2-amino-2-deoxy-aldoseformazans which, on hydrolysis, provide 2-amino-2-deoxy-aldonolactones [1,2]. Reduction of acetylated formazans with sodium borohydride led to 2-deoxy-formazans [3]. These reactions were assumed to proceed via elimination–addition reactions through bis(phenylazo)hexene intermediates, which were not isolated [1,3].

Tetraacetoxy-1-phenylazo-1-hexenes, such as **1a**, are readily prepared by base-catalyzed acetylation of hexose phenylhydrazones [4–7]. It has been shown that phenylazoalkenes undergo conjugate addition of nucleophiles, such as mercaptides [8] and carbanions [9], to give phenylhydrazone derivatives. It therefore appeared likely that they would react with hydride ions to give 2-deoxy-phenylhydrazones, analogously to bis(phenylazo)hexenes. In order to ascertain this point, a number of tri- and tetra-acetoxy-1-phenylazo-1-pentenes or hexenes have been reduced with sodium borohydride to yield phenylhydrazones of 2-deoxy-sugars. The latter have been hydrolyzed to the free 2-deoxy-sugars.

The phenylhydrazones of D-mannose, D-galactose, L-rhamnose, and D-arabinose were converted into the acetylated 1-phenylazo-1-alkenes **1a**, **1b**, **4**, and **7**, respectively, by a known procedure involving acetylation and elimination of the 2-*O*-acetyl group [5–7] (Scheme 1). The yields of crystalline **1a**, **1b**, and **4** were only ~ 50%, perhaps due to *cis*/*trans* isomerization in solution. The D-*erythro*-derivative **7** could not be crystallized and the crude product was used for further reaction. The phenylazoalkenes were then treated with an excess of sodium borohydride, keeping the pH at 8 to avoid deacetylation. After reduction, the resulting 2-deoxy phenylhydrazones were deacetylated to give **2a**, **2b**, **5**, and **8**, respectively, which were characterized through their $^{13}C$ NMR spectra. Subsequent hydrolysis gave the 2-deoxy-sugars **3a**, **3b**, **6**, and 2-deoxy-D-*erythro*-pentose. 2-

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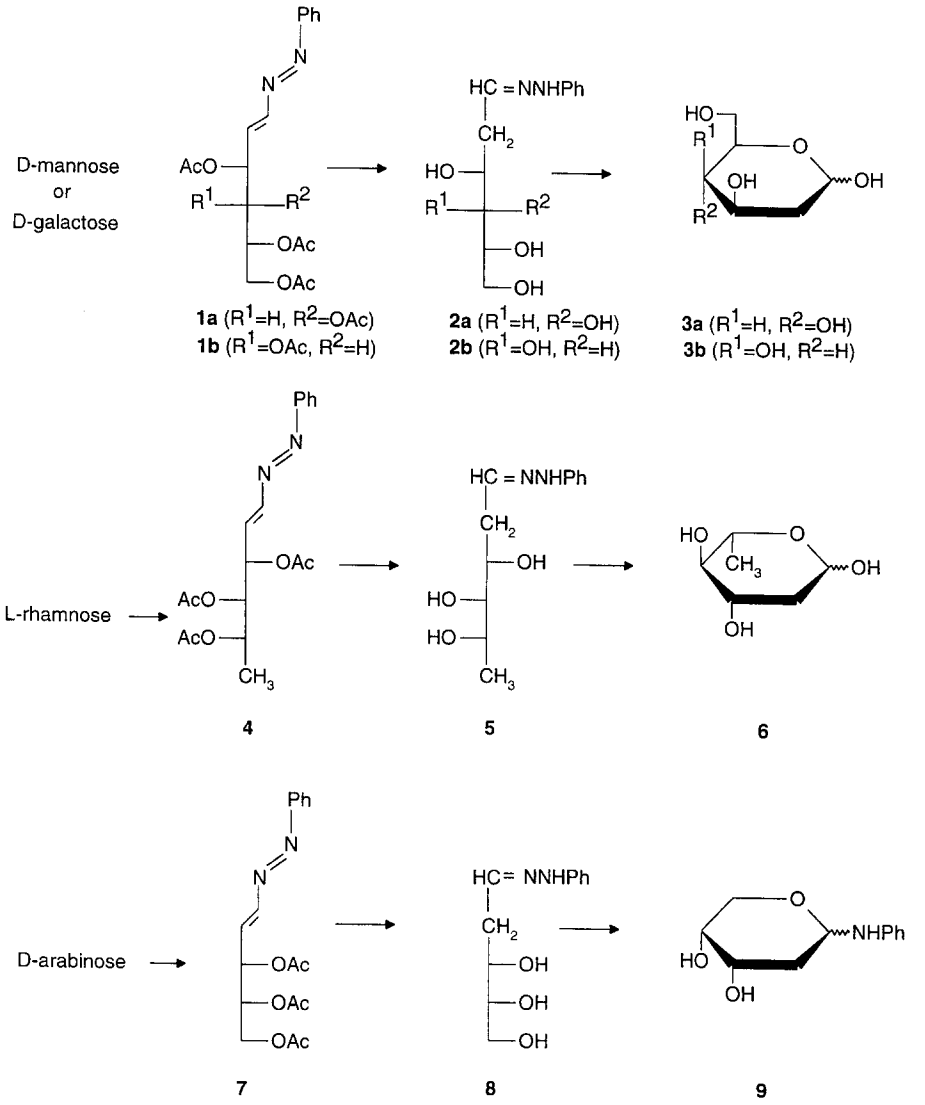
*PII* S0008-6215(97)00022-0




Scheme 1.

Deoxy-D-*arabino*-hexose (**3a**) was obtained crystalline in 65% yield, 2-deoxy-D-*lyxo*-hexose (**3b**) in 35% yield (68% as a syrup), and 2,6-dideoxy-L-*arabino*-hexose (**6**) as a syrup in 80% yield. 2-Deoxy-D-*erythro*-pentose (50% as a syrup) was isolated as the glycosylamine **9** in 40% yield.

## 1. Experimental

*General methods.*—Melting points are uncorrected. Optical rotations were measured on a Perkin–Elmer 141 polarimeter. NMR spectra were recorded on Bruker AC-250 or AM-500 instruments. Tetramethylsilane was used as internal reference in organic solvents and dioxane (67.4 ppm) for $^{13}C$ NMR spectra measured in $D_2O$ solns.

*3,4,5,6-Tetra-*O*-acetyl-*D*-arabino-1-phenylazo-1-(*E*)-hexene* (**1a**).—Prepared as described [7] and obtained in 45–50% yield after recrystallization from EtOH: mp 121–122 °C; $[\alpha]_D^{20}$ −7° (2 min) → −3.4° (48 h) (*c* 1.1, $CHCl_3$), lit. −0.5° [7]. The $^{13}C$ NMR spectrum was identical with that reported [7]. The discrepancy between the observed and reported optical rotation may be due to *cis/trans* isomerization at the N=N double bond. The $^1H$ NMR spectrum (500 MHz) measured in a freshly prepared $CDCl_3$ soln showed only one product. After ~4 h at room temperature, 10% of an isomer was formed. Both products showed a *trans*-2,3-coupling (13.5 Hz). $^1H$ NMR ($CDCl_3$, 500 MHz) of the main component: δ 7.27–7.46 (m, 5 H, Ph), 7.33 (dd, 1 H, $J_{1,2}$ 13.5, $J_{1,3}$ 1.4 Hz, H-1), 6.78 (dd, 1 H, $J_{2,3}$ 5.9 Hz, H-2), 5.93 (ddd, 1 H, $J_{3,4}$ 3.2 Hz, H-3), 5.52 (dd, 1 H, $J_{4,5}$ 8.4 Hz, H-4), 5.29 (ddd, 1 H, $J_{5,6}$ 2.8, $J_{5,6'}$ 4.8 Hz, H-5), 4.30 (dd, 1 H, $J_{6,6'}$ 12.5 Hz, H-6), 4.20 (dd, 1 H,

H-6′). The minor component gave the following spectrum: δ 7.09 (dd, $J_{1,2}$ 13.2, $J_{1,3}$ 1.2 Hz, H-1), 6.86 (dd, $J_{2,3}$ 6.2 Hz, H-2), 5.69 (ddd, $J_{3,4}$ 3.5 Hz, H-3), 5.43 (dd, $J_{4,5}$ 8.2 Hz, H-4), 5.21 (ddd, $J_{5,6}$ 2.7, $J_{5,6'}$ 5.0 Hz, H-5), 4.25 (dd, $J_{6,6'}$ 12.5 Hz, H-6), 4.15 (dd, H-6′).

*3,4,5,6-Tetra*-O-*acetyl*-D-lyxo-*1-phenylazo-1*-(E)-*hexene* (**1b**).—Prepared from D-galactose phenylhydrazone by the same procedure. Yield 40–45%; mp 82–83 °C, lit. 86–87 °C [7]; $[\alpha]_D^{20}$ −75° (2 min) → −64° (48 h) (*c* 1.2, $CHCl_3$), lit. −70.5° [7]. The $^{13}C$ NMR spectrum was identical with that reported [7].

*3,4,5-Tri*-O-*acetyl-6-deoxy*-L-arabino-*1-phenylazo-1*-(E)-*hexene* (**4**).—L-Rhamnose phenylhydrazone [10], (11.3 g) was treated with pyridine (55 mL) and $Ac_2O$ (30 mL) overnight at +5 °C [7]. Precipitation with ice–water (500 mL) gave an oil which was boiled for 15 min in a mixture of EtOH (100 mL), water (50 mL), and pyridine (15 mL). On cooling and dilution with water (50 mL), the product crystallized as yellow needles: 8.5 g (50%); mp 86–88 °C. Recrystallization from 1:1 MeOH–water gave a product with mp 93–94 °C, $[\alpha]_D^{20}$ +22° (2 min) → +40° (1 h) (*c* 1.1, $CHCl_3$). $^1H$ NMR ($CDCl_3$, 500 MHz): δ 7.4–7.8 (m, 5 H, Ph), 7.35 (dd, 1 H, $J_{1,2}$ 13.5, $J_{1,3}$ 1.0 Hz, H-1), 6.79 (dd, 1 H, $J_{2,3}$ 6.0 Hz, H-2), 5.89 (ddd, 1 H, $J_{3,4}$ 6.0 Hz, H-3), 5.43 (dd, 1 H, $J_{4,5}$ 6.5 Hz, H-4), 5.12 (dq, 1 H, $J_{5,6}$ 6.5 Hz, H-5), 2.05, 2.11, 2.13 (9 H, AcO), 1.27 (d, 3 H, H-6). $^{13}C$ NMR: δ 169.9, 169.7 (C=O), 152.3 (Ph), 150.1 (C-1), 136.6 (C-2), 131.4, 129.0, 128.8 (Ph), 73.7, 69.6, 67.4 (C-3,4,5), 21.0, 20.7 (OAc), 16.0 (C-6). Anal. Calcd for $C_{18}H_{22}N_2O_6$: C, 59.66; H, 6.12; N, 7.73. Found: C, 59.88; H, 6.17; N, 7.66.

*2-Deoxy*-D-arabino-*hexose* (**3a**).—The azo compound **1a** (9.3 g) was dissolved in a mixture of EtOH (450 mL) and phosphate buffer (200 mL, pH ~ 7). The buffer was prepared from 750 mL of 2 M NaOH and 250 mL of phosphoric acid. A soln of sodium borohydride (8–9 g) in water (25 mL) was added with stirring during 4–5 h at room temperature until **1a** was not observed on TLC (2:3 EtOAc–hexane). The mixture was then filtered and most of the EtOH was evaporated to a pale yellow suspension which was diluted with water and extracted with EtOAc (3 × 75 mL). The extract was washed with water, dried ($Na_2SO_4$), and evaporated. The yellow residue (~ 10 g) was deacetylated with NaOMe in MeOH, diluted with water, and concd to give a soln of 2-deoxy-D-*arabino*-hexose phenylhydrazone (**2a**). $^{13}C$ NMR ($D_2O$): δ 146.2, 130.4, 121.0, 114.0 (Ph), 144.3 (C-1), 73.4, 71.9, 69.0 (C-3,4,5), 63.9 (C-6), 36.8 (C-2).

Ion-exchange resin IR-120 ($H^+$) (50 mL) was then added and the suspension was stirred for 1 h. It was then filtered and the filtrate was neutralized with Amberlite IRA 67 ($OH^-$) ion-exchange resin (10 mL). Filtration and concn gave a colourless syrup (~ 3.6 g) which was concd twice from a mixture of EtOH (20 mL) and acetone (20 mL). The residue was crystallized from acetone (40 mL) and a few drops of EtOH to give 2.4 g (65%) of **3a**, mp 138–140 °C. Recrystallization from EtOH–EtOAc gave a product with mp 145–146 °C, $[\alpha]_D^{20}$ +46.0° (*c* 1.5, $H_2O$); reported for the β-anomer: mp 145–146 °C, $[\alpha]_D$ +46° [11].

*2-Deoxy*-D-lyxo-*hexose* (**3b**).—Reduction of **1b** (7.5 g), followed by deacetylation as described above, gave a soln of 2-deoxy-D-*lyxo*-hexose phenylhydrazone (**2b**). $^{13}C$ NMR ($D_2O$): δ 144.5 (C-1), 146.2, 130.4, 121.0, 114.2 (Ph), 73.8, 71.0, 69.9, 63.9 (C-3,4,5,6), 36.5 (C-2). Hydrolysis with ion-exchange resin gave 2 g (68%) of crude **3b**, which was crystallized from MeOH (10 mL), 1.0 g (34%), mp 114–115 °C. Recrystallization gave a product with mp 116–117 °C, lit. 120–121 °C [12]; $[\alpha]_D^{20}$ +58.5° (*c* 1.2, $H_2O$), lit. +59° [12]. The $^{13}C$ NMR spectrum in $D_2O$ soln showed a mixture containing 85% α + β-pyranoses and 15% furanoses.

*2,6-Dideoxy*-L-arabino-*hexose* (**6**).—Reduction and deacetylation of **4** (4.1 g), as described above gave crude 2,6-dideoxy-L-*arabino*-hexose phenylhydrazone. $^{13}C$ NMR ($D_2O$): δ 144.2 (C-1), 146.5, 133.4, 121.0, 114.0 (Ph), 77.4, 67.9 (C-3,4,5), 36.8 (C-2), 19.0 (C-6). Hydrolysis with ion-exchange resin, concn, and drying, gave 1.35 g (80%) of syrupy **6**, $[\alpha]_D^{20}$ −18.7° (*c* 1.5, $H_2O$), lit. −18.2° [13]. The $^{13}C$ NMR spectrum was identical with that reported previously [14].

*2-Deoxy*-N-*phenyl*-D-erythro-*pentopyranosylamine* (**9**).—D-Arabinose phenylhydrazone [15] (3.5 g) was suspended in an ice-cold mixture of pyridine (10 mL) and $Ac_2O$ (10 mL), and the mixture was stirred until a homogeneous soln was obtained. It was kept overnight at 5 °C and then poured into ice–water (150 mL). The resulting precipitate was separated by decantation and dissolved in EtOH (30 mL). Water (10 mL) and pyridine (3 mL) was added and the mixture was boiled for 15 min. After cooling, the red soln was poured into water (150 mL), precipitating 3,4,5-tri-*O*-acetyl-D-*erythro*-1-phenylazo-1-pentene (**7**) as a red syrup which could not be crystallized. $^{13}C$ NMR ($CDCl_3$): δ 152.2, 150.4, 135.8, 131.4,

129.0, 122.7 (Ph, C-1,2), 71.3, 70.0 (C-3,4), 61.5 (C-5), 20.7, 20.6 (AcO). The water was separated, and the crude product was dissolved in EtOH (125 mL) and phosphate buffer (100 mL) and reduced as described above with sodium borohydride (4 g) to give an aq soln of 2-deoxy-D-*erythro*-pentose phenylhydrazone (**8**). $^{13}C$ NMR ($D_2O$): $\delta$ 146.2, 130.4, 121.0, 114.1 (Ph), 144.4 (C-1), 75.1, 70.8 (C-3,4), 63.3 (C-5), 31.3 (C-2).

The phenylhydrazone was hydrolyzed and neutralized with ion-exchange resins as described above. The filtrate was concd to give 1 g of syrupy 2-deoxy-D-*erythro*-pentose, which was dissolved in MeOH (4 mL) and water (3 mL). Aniline (0.70 g) was added and the mixture was kept overnight at +5 °C. Filtration then gave 1.2 g (40%) of the title compound, mp 169–170 °C. Recrystallization from 1:1 MeOH–water gave a product with mp 171–172 °C, lit. 172–173° [16]; $[\alpha]_D^{20}$ +175° → +59.5° (*c* 0.9, pyridine), lit. +171° → +46° [16]. $^{13}C$ NMR ($Me_2SO$-$d_6$): $\delta$ 146.6, 128.8, 117.0, 113.3 (Ph), 80.1 (C-1), 68.1, 66.8, 65.9 (C-3,4,5), 34.7 (C-2).

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