

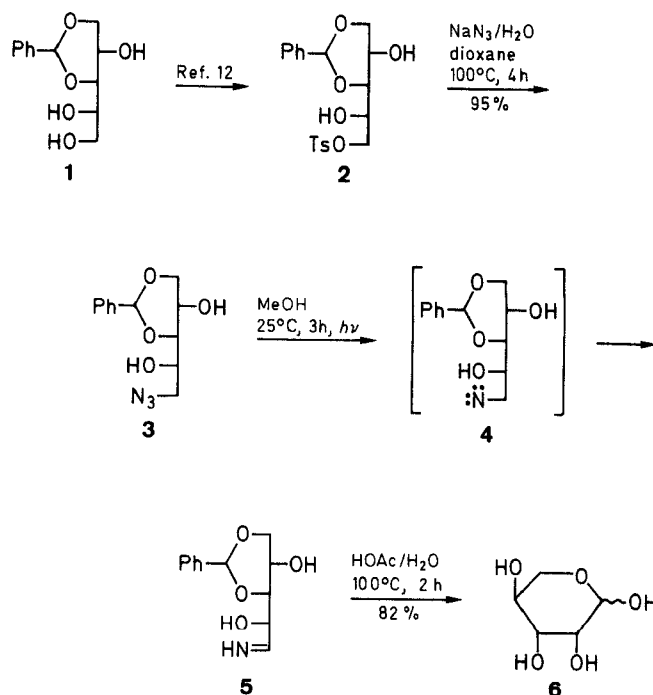
Synthesis of L-Lyxose from L-Arabinitol via Photolysis of an Azido Derivative

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1,3-*O*-Benzylidene-L-arabinitol (**1**) was converted via its 5-*O*-sulfonyl derivative **2** to the corresponding 5-azido compound which upon photolysis and hydrolysis afforded L-Lyxose (**6**).

Among transformations between monosaccharides and their acyclic derivatives, the important conversion of alditols to the corresponding aldoses is the most ambiguous. Several such procedures, mainly oxidative ones, have been reported.¹⁻⁴ Other approaches, which have been used for the preparation of terminal aldehyde derivatives of saccharides, are the photochemical oxidation of *O*-pyruvoyl derivatives⁵ or photolysis of azido-deoxy derivatives in combination with a mild acid hydrolysis of an aldimine formed.⁶ Recently, an example of the latter possibility has been investigated for the selective transformation alditol aldose for of 1-azido-1-deoxy-3,4-*O*-isopropylidene-D-mannitol to D-mannose.⁷ A similar route, but however for a useful conversion L-arabinitol to L-lyxose (**6**) is shown here. Otherwise, L-lyxose (**6**) has usually been prepared from L-galactonic acid by the Ruff degradation,⁸ periodate oxidation of 3,4,5-tri-*O*-benzyl-D-galactitol and deprotection,⁹ or by the molybdate catalyzed epimerization of L-lyxose.¹⁰



1,3-Benzylidene-L-arabinitol (**1**)¹¹ possessing a free hydroxymethyl group was transformed by a known procedure¹² to 5-*O*-(4-methylbenzenesulfonyl) derivative **2**. Reaction of **2** with an excess of sodium azide in a mixture of dioxane and water gave the 5-azido derivative **3** in 95% yield. The presence of a free hydroxy group neighboring to the primary sulfonyloxy (or halogeno one¹³) to be substituted thus facilitates the reaction due to the possibility of proceeding via an oxirane intermediate.¹²

Photolysis of the azide **3** with unfiltered mercury arc light in methanol was accomplished within 3 h. It has been shown,¹⁴ that upon irradiation of alkyl azides, "activated" nitrenes are formed as primary products, which undergo intramolecular rearrangement to form aldimines. Hence, the photoproduct **4** rearranged to the aldimine **5**, which without isolation was further hydrolyzed to yield L-lyxose (**6**). To obtain the pure sugar, the product had to be passed through a cation exchange resin in the H-form to remove minor byproducts (ca. 15%) probably originating from a competitive solvent-proton abstraction by the nitrene intermediate **4** (cf. Ref. 14).

The sequence of the reactions enabled to achieve 35% conversion of L-arabinitol to L-lyxose (**6**).

All reagents were of commercial quality from freshly opened containers. NaN₃ was purchased from Fluka Chemical Co. and Dowex 50 W X-8, 200–400 mesh from Dow Chemical Co. Other reagents, including solvents and chromatographic materials were purchased from Lachema. Melting points were measured on a Kofler stage and are uncorrected. Microanalyses were obtained using a Perkin-Elmer 240 element analyser and optical rotations at the Na-D line were obtained at 20 °C using a Perkin-Elmer 141 polarimeter. IR spectra were recorded on a Perkin-Elmer 983 spectrophotometer. ¹³C-NMR spectra were obtained using a Bruker AM-300 spectrometer.

1,3-*O*-Benzylidene-L-arabinitol (**1**) was prepared according to a method¹¹ reported for the D-isomer; yield: 86%; mp 149–152 °C; $[\alpha]_D + 7.5^\circ$ ($c = 2.0$, pyridine) (For 1,3-*O*-benzylidene-D-arabinitol, Lit.¹¹ mp 151–152 °C; $[\alpha]_D - 7.6^\circ$ ($c = 2.0$, pyridine)).

¹³C-NMR (75 MHz, DMSO-*d*₆/TMS): $\delta = 61.61$ (C-2), 62.54 (C-5), 69.27 (C-4), 72.29 (C-1), 78.58 (C-3), 99.98 (C₆H₅), 126.13, 127.77, 128.41, 138.72 (C_{arom}).

1,3-*O*-Benzylidene-5-*O*-(4-methylbenzenesulfonyl)-L-arabinitol (**2**) was prepared according to a reported method;¹² yield: 54%; mp 111–114 °C; $[\alpha]_D - 19.5^\circ$ ($c = 2.0$, pyridine) (Lit.¹² mp 109–112 °C and 127 °C (dimorphic); $[\alpha]_D - 18.0^\circ$ ($c = 1.9$, pyridine)); TLC (silica gel, benzene/MeOH, 9:1): $R_f = 0.3$.

¹³C-NMR (75 MHz, DMSO-*d*₆/TMS): $\delta = 21.02$ (CH₃), 60.99 (C-2), 65.95 (C-4), 72.04 (C-1), 72.04 (C-5), 77.73 (C-3), 99.59 (C₆H₅), 125.89, 127.49, 128.39, 138.33 (C₆H₅), 127.71, 129.96, 132.05, 144.66 (C₆H₄).

5-Azido-1,3-*O*-benzylidene-5-deoxy-L-arabinitol (**3**):

A solution of **2** (3.0 g, 7.5 mmol) in dioxane (45 mL) is added to a solution of NaN₃ (1.1 g, 17.0 mmol) in H₂O (12 mL) is refluxed 4 h

(until disappearance of **2**; TLC control). The solvents are evaporated at reduced pressure and the residue is extracted with acetone (150 mL) and crystallized; yield: 1.9 g (95%); mp 167–169 °C; $[\alpha]_D - 25.6^\circ$ ($c = 1.0$, MeOH); TLC (silica gel, benzene/MeOH, 9:1): $R_f = 0.2$.

C₁₂H₁₅N₃O₄ calc. C 54.34 H 5.66 N 15.85
(265.3) found 54.25 5.70 15.81

IR (KBr): $\nu = 2099$ (N₃).

¹³C-NMR (75 MHz, DMSO-*d*₆/TMS): $\delta = 53.45$ (C-5), 61.25 (C-2), 67.68 (C-4), 72.22 (C-1), 79.24 (C-3), 100.02 (C₆H₅), 126.15, 127.86, 128.52, 138.56 (C_{arom}).

L-Lyxose (**6**):

A solution of **3** (1.5 g, 5.7 mmol) in MeOH (500 mL) is irradiated in a photochemical reactor with unfiltered light from a 125 W high-pressure mercury arc for 3 h (until disappearance of **3**; TLC control). The solvent is evaporated at reduced pressure. The residue is dissolved in 5% HOAc (30 mL) and refluxed for 2 h. The cooled mixture is washed with benzene (20 mL) and the aqueous layer is evaporated at reduced pressure. The residue not containing HOAc (removed by repeated evaporation of the residue with H₂O) is dissolved in H₂O (5 mL) and passed through a Dowex 50 W column (30 × 2 cm, H-form) using H₂O as an eluent. The collected eluant (150 mL) was concentrated at reduced pressure to give sirupy **6**, which crystallizes from MeOH; yield 0.7 g (82%); mp 102–104 °C; $[\alpha]_D + 13.4^\circ$ ($c = 2.0$, H₂O) (Lit.¹⁰ mp 103–104 °C; $[\alpha]_D + 13^\circ$ ($c = 2.0$, H₂O)).

¹³C-NMR (75 MHz, D₂O/TMS_{ext}): $\delta = 64.23$ (C-5 α), 65.38 (C-5 β), 67.73 (C-4 β), 68.78 (C-4 α), 71.26 (C-2 α), 71.37 (C-2 β), 71.74 (C-3 α), 73.93 (C-3 β), 95.27 (C-1 α), 95.42 (C-1 β).

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