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Preliminary communication

The synthesis of *C*-nucleoside precursors: 3-(alditol-1-yl)-5-phenyl-1,2,4-triazolo[3,4-*a*]phthalazines*

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The synthesis[2] of *C*-nucleosides and their analogs is gaining impetus as a result of their multifarious biological activities[3]. Dehydrative cyclization of the polyhydroxyalkyl chains of heterocyclic compounds carrying alditolyl groups (acyclic *C*-nucleoside analogs) is one good approach for the synthesis of *C*-nucleosides[4]. As part of a program aimed at the synthesis of alditolyl derivatives of condensed heterocyclic compounds, and their conversion into *C*-nucleosides, we have described[1] the synthesis of 3-(alditol-1-yl)-1,2,4-triazolo[3,4-*a*]phthalazines.

In this communication, we report the synthesis of the title compounds by condensation of aldopentoses and aldohexoses with 1-hydrazino-4-phenylphthalazine[5] (**1**). Whereas D-ribose (**3**), D-galactose (**4**), and D-mannose (**6**) gave yellow crystalline products, D-arabinose (**2**) and D-glucose (**5**) gave colorless products. The yellow product from D-ribose, m.p. 230°, had an elemental analysis agreeing with that calculated for the molecular formula $C_{19}H_{20}N_4O_4$. The electronic spectrum (in EtOH) of this product showed three absorption bands at 246, 248, and 344 nm, and its molecular spectrum (in KBr) showed bands at 3520, 3440, and 3300 (OH and NH) and 1630 cm^{-1} (C=N). These data are in agreement with the hydrazone structure **8**, which is also supported by the n.m.r. spectrum (in Me_2SO-d_6) having a 9-proton-multiplet signal between δ 8.6 and 7.7 due to the phenyl and phthalazine rings, the protons of the alditolyl chain and hydroxyl groups appeared between δ 5.9 and 3.0. Similar hydrazone structures (**9** and **11**) were assigned to the yellow products obtained from D-galactose and D-mannose, respectively.

Auto- or catalytic dehydrogenation of the hydrazone **8** by prolonged heating in ethanol or by brief heating in ethanol containing 10% palladium-on-charcoal gave a colorless, crystalline product, m.p. 215°, having the molecular formula $C_{19}H_{18}N_4O_4$. The electronic spectrum of this product (in EtOH) showed only one absorption band, at 246 nm, and lacked the other two bands of the parent hydrazone. The molecular absorption spectrum of the product was similar to that of the parent hydrazone. The product was, therefore, assigned the structure of 5-phenyl-3-(D-*ribo*-tetritol-1-yl)-1,2,4-triazolo[3,4-*a*]phthalazine (**13**). The mass-spectral fragmentation-pattern was in harmony with this assignment, it showed the base peak (100%) at *m/z* 246, corresponding to the

*Reactions of Sugars with Amidrazones and Hydrazidines, for Part 1, see ref. 1.
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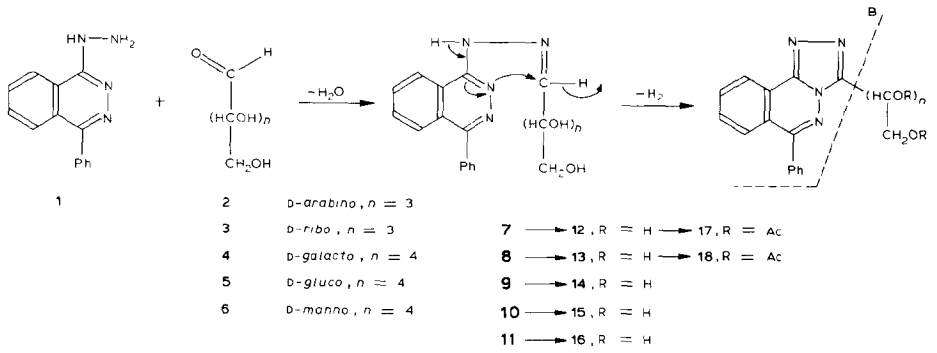
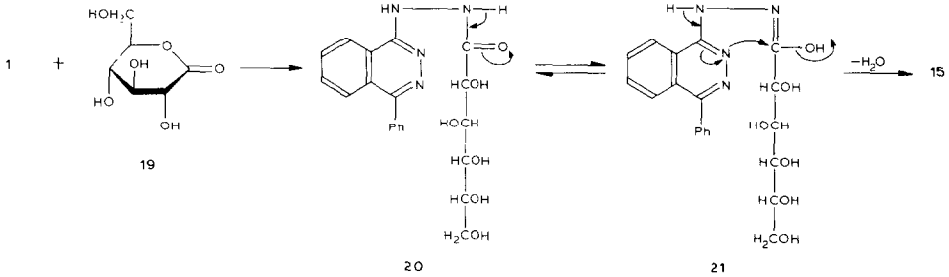
mass of the heterocyclic base (BH), in addition to peaks at 305 (B–CHOH–CHO^+, 12.4%), and 289 (B–CH_2–$CHOH^+$, 11.3%). Other peaks characteristic of the fragmentation of the heterocyclic base, as well of as the sugar moiety, also appeared in the spectrum.



Reaction of **1** with D-arabinose and D-glucose gave directly the colorless, cyclized products **12** and **15**, respectively, as a result of the simultaneous condensation and autodehydrogenative cyclization of the intermediate hydrazones **7** and **10**, respectively.

3-(D-*gluco*-Pentitol-1-yl)-5-phenyl-1,2,4-triazolo[3,4-*a*]phthalazine (**15**) was also obtained by the reaction of **1** with D-glucono-1,5-lactone (**19**). Cyclization occurred here through autodehydration of the enolized form (**21**) of the intermediate hydrazone (**20**).



Acetylation of **13** with acetic anhydride in the presence of pyridine gave the tetra-*O*-acetyl derivative **18**, m.p. 148°, $C_{27}H_{26}N_4O_8$. The n.m.r. spectrum (in $CDCl_3$) of **18** showed the following signals, which confirm the assigned structure: δ 8.9 (m, 9 H, aromatic protons), δ 6.8 (d, 1 H, alditolyl H-1), δ 6.0 (q, 1 H, alditolyl H-2), δ 5.3 (m, 1 H, alditolyl H-3), δ 4.2 (m, 2 H, alditolyl CH_2), δ 2.15 (s, 3 H, acetyl CH_3), δ 2.0 (s, 6 H, 2 acetyl CH_3), and δ 1.80 (s, 3 H, acetyl CH_3).

Acetylation of the cyclized product **12**, from D-arabinose, gave the corresponding tetra-*O*-acetyl derivative (**17**), m.p. 172°.

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