Carbohydrate Research, 95 (1981) 51–60
Elsevier Scientific Publishing Company, Amsterdam – Printed in The Netherlands

THE SYNTHESIS OF 3-(ALDITOL-1-YL)-1,2,4-TRIAZOLO[3,4-*a*]PHTHALAZINES*

MOHAMMED A. E. SHABAN**†, RAAFAT S. ALI, AND SOUSAN M. EL-BADRY

Departments of Chemistry, Faculties of Science and Pharmacy, Alexandria University, Alexandria (Egypt)

(Received March 2nd, 1981; accepted for publication, April 14th, 1981)

ABSTRACT

Condensation of 1-hydrazinophthalazine (hydralazine) with D-lyxose, D-ribose, D-xylose, D-mannose, and L-rhamnose gave the corresponding *aldehydo*-sugar phthalazin-1-ylhydrazones. D-Arabinose and D-galactose, on the other hand, gave the corresponding 3-(alditol-1-yl)-1,2,4-triazolo[3,4-*a*]phthalazines through the autodehydrogenative cyclization of the hydrazones. A rationale for this difference is discussed. Acetylation of the latter gave the poly-*O*-acetyl derivatives. Catalytic, dehydrogenative cyclization with palladium-on-charcoal, or acetylation, transforms the hydrazones into the triazolophthalazines, or their acetates. The mass spectra of the synthesized compounds were discussed.

INTRODUCTION

We have been interested in the reactions of aroylhydrazines with monosaccharides[1,2], aldosuloses[3,4], aldosulose 1-aroylhydrazones[4], aldosulose 1-arylhydrazones[5,6], and aldaric acids[7,8], and in conversion of the resulting hydrazones and hydrazides into 1,2,3-triazole[3,4] and 1,3,4-oxadiazole[1,2,7,8] derivatives. Currently, we are involved in a program aimed at studying the reactions of sugars and their derivatives with cyclic and acyclic amidrazones and hydrazidines. The latter are related to hydrazines, and offer versatile starting-materials for a wide variety of heterocyclic systems[9].

We now describe the reaction of monosaccharides (**2–8**) with a medicinally important, cyclic amidrazone, namely, 1-hydrazinophthalazine[10] (hydralazine, apresoline) (**1**). 1-Hydrazinophthalazine and its Schiff bases are among the most effective, hypotensive agents[11]; they act on the arteriolar, smooth muscles (vasodilators). In addition, they exhibit moderate anti-inflammatory activity[12]. Because

*Reactions of Sugars with Amidrazones and Hydrazidines. Part I.

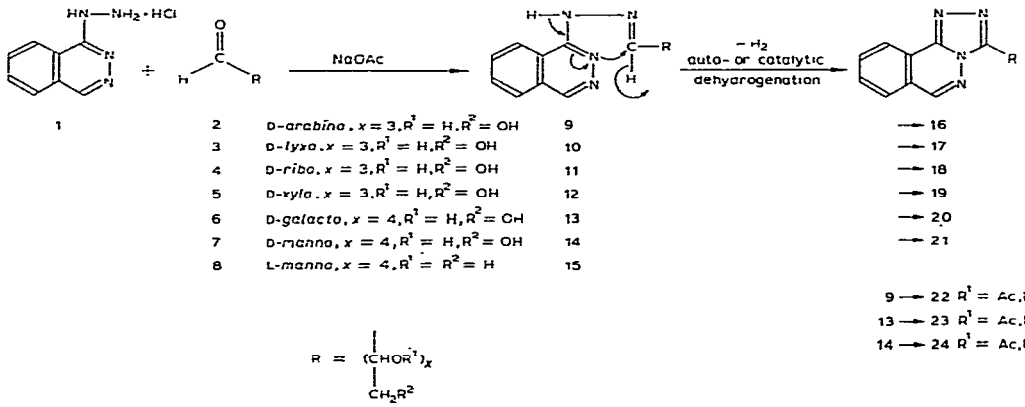
**Present address: Department of Chemistry, Faculty of Science, King Abdulaziz University, P. O. Box 9028, Jeddah, Saudi Arabia.
†To whom correspondence should be addressed.

0008-6215/81/0000–0000/$ 02.50,

they bear a resemblance to Schiff bases, we anticipated that *aldehydo*-sugar phthalazin-1-ylhydrazones (**9–15**) might be more potent hypotensives, as sugar moieties usually increase the penetration of a drug into biological systems as a result of the increase in hydrophilicity.

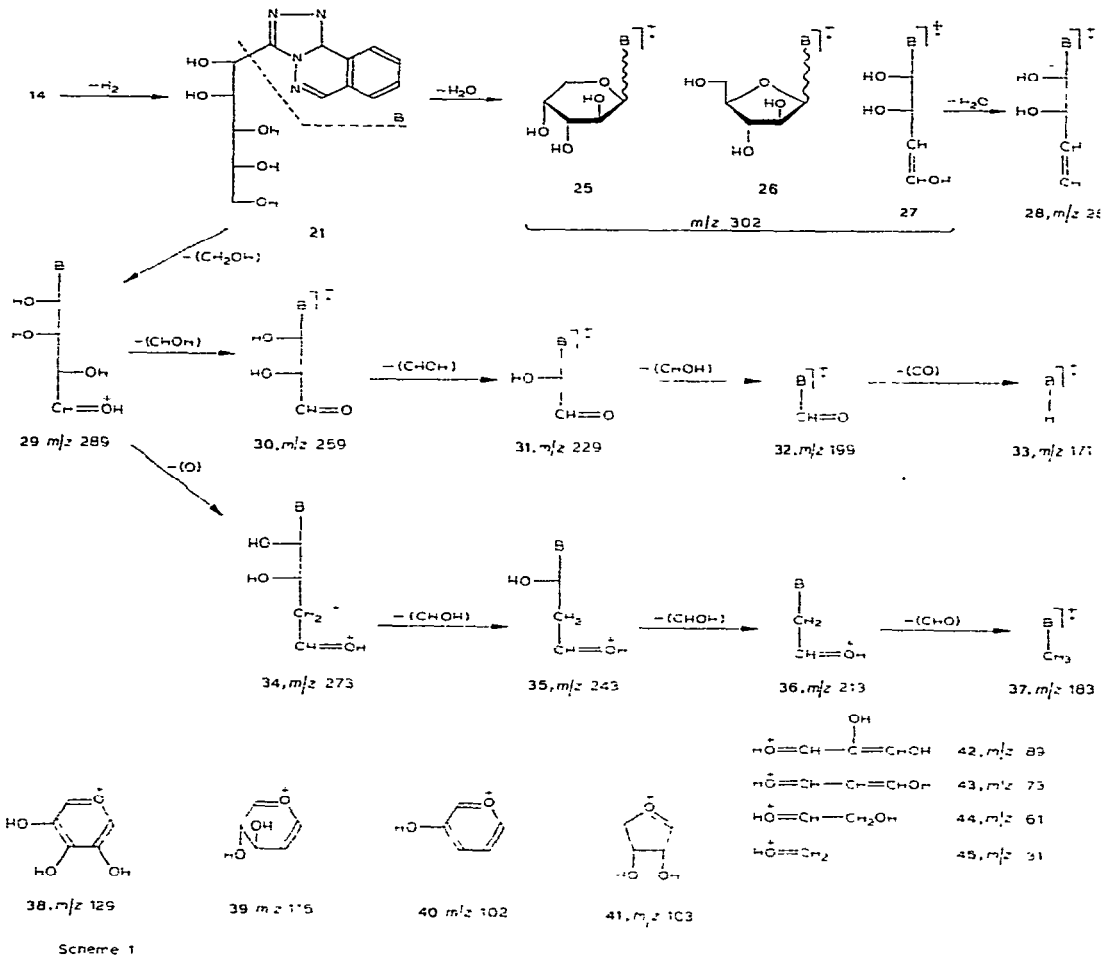
RESULTS AND DISCUSSION

Aqueous solutions of D-arabinose (**2**), D-lyxose (**3**), D-ribose (**4**), and D-xylose (**5**) (aldopentoses), D-galactose (**6**) and D-mannose (**7**) (aldohexoses), and L-rhamnose (**8**) (a 6-deoxyaldohexose) were condensed with one equivalent of 1-hydrazinophthalazine hydrochloride (**1**) in the presence of sodium acetate. Whereas the reaction products (**10–12**, **14**, and **15**) of D-lyxose, D-ribose, D-xylose, D-mannose, and L-rhamnose were yellow to orange, those (**9** and **13**) of D-arabinose and D-galactose were colorless.



The orange product (**14**) obtained from the condensation of 1-hydrazinophthalazine with D-mannose (**7**) had an elemental analysis agreeing with that calculated for $C_{14}H_{18}N_4O_5$, that is, one molecule of water less than the sum of the two reactants. The infrared spectrum of the product showed a broad band at 3400 cm^{-1} due to NH and OH absorptions, and a C=N absorption band at 1630 cm^{-1}. These data pinpoint the condensation of D-mannose (**7**) with **1**, with the elimination of one molecule of water, to give *aldehydo*-D-mannose phthalazin-1-ylhydrazone (**14**).

The mass spectrum of **14** (see Scheme 1) did not show a molecular-ion peak, but revealed a fragmentation pattern in agreement with the assigned structure. The hydrazone loses a hydrogen molecule and cyclizes to the triazolophthalazine structure **21** before it undergoes fragmentation. This is in agreement with previous reports documenting the ease of dehydrogenative cyclization of hydrazones of this type upon heating[13,14]. The cyclized product **21** loses a water molecule, giving a low-intensity peak at *m/z* to which structures **25–27** may be assigned. Elimination of a hydroxyl group from any of these structures gives a fragment at *m/z* 285. The structure



Scheme 1

of the fragment obtained from **27** is probably **28**. Comparable structures containing one double bond in the furanoside or pyranoside rings may be assigned to those obtained from **25** and **26**, respectively. Alternatively, **21** loses a CH_2OH group to give **29** (*m/z* 289). The latter affords **30** and **34** on elimination of a CHOH group, or oxygen atom, respectively. Both **30** and **34** undergo sequential loss of CHOH groups, giving fragments **31–33** and **35–37**, respectively. Also appearing in the spectrum are fragments **38–45**, resulting from the breakdown of the sugar chain.

D-Ribose (**4**), D-xylose (**5**), and D-lyxose (**3**) reacted with 1-hydrazinophthalazine (**1**) similarly to D-mannose, to give the yellow *aldehydo*-D-ribose (**11**), *aldehydo*-D-xylose (**12**), and *aldehydo*-D-lyxose phthalazin-1-ylhydrazone (**10**). All of these hydrazones showed infrared absorption bands at 1650–1610 (C=N) and broad bands at 3400 cm^{-1} (NH + OH), and their elemental analyses were in agreement with the molecular formula $C_{13}H_{16}N_4O_4$. The mass spectra of **11** and **10** did not show molecular-ion peaks, but their fragmentation patterns were comparable to that of the

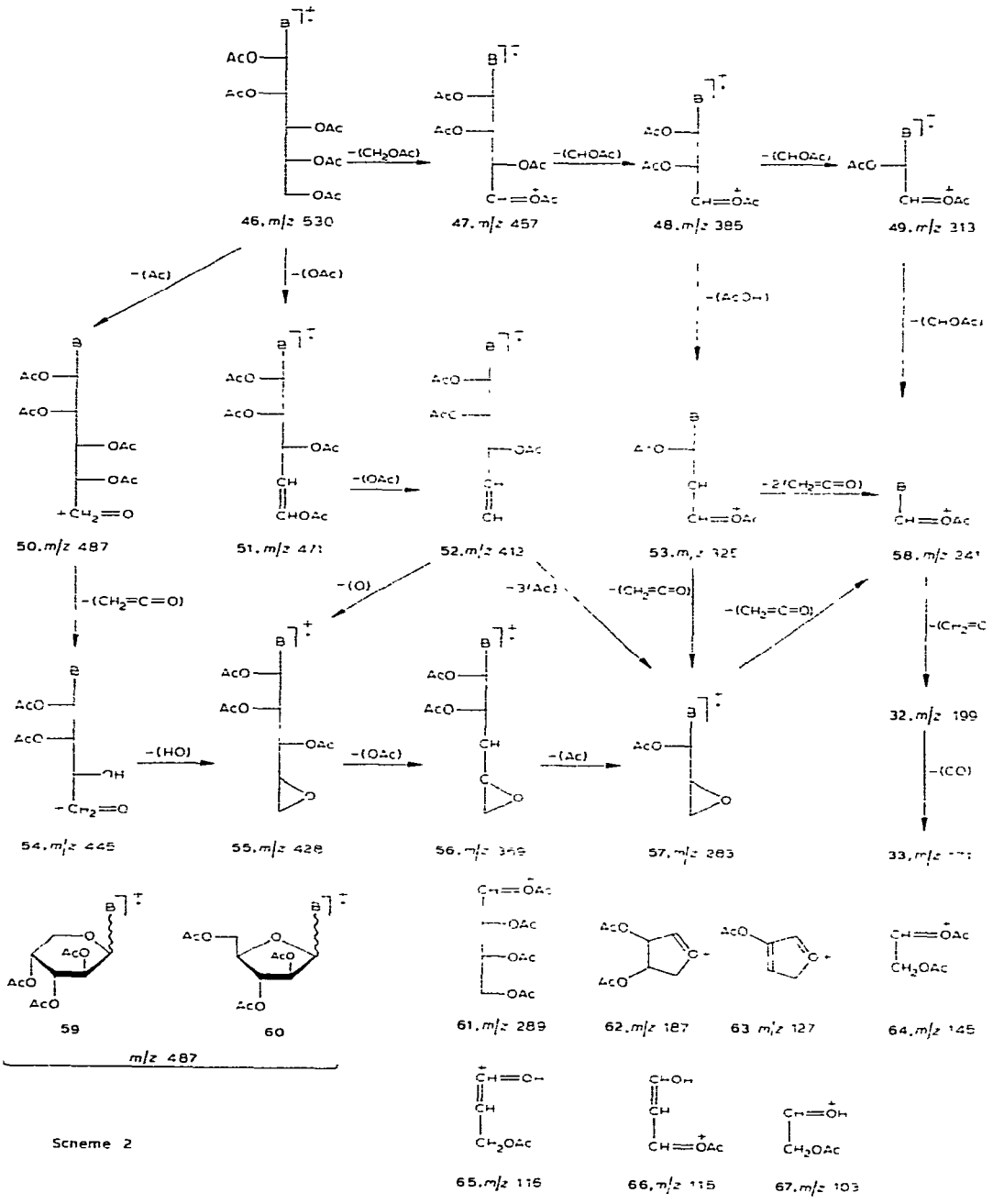
D-mannose derivative (**14**). The mass spectrum of *aldehydo*-D-xylose phthalazin-1-ylhydrazone (**12**), however, showed an $(M + 1)^+$ peak at *m/z* 293. The fragmentation of the latter followed a pattern closely similar to that of **14**.

L-Rhamnose (**8**; 6-deoxy-L-mannose) also gave a yellow hydrazone (**15**; *aldehydo*-L-rhamnose phthalazin-1-ylhydrazone, or 6-deoxy-*aldehydo*-L-mannose phthalazin-1-ylhydrazone), which showed infrared absorptions at 3420 (OH), 3320, 3200 (NH), 1628 (C=N), and 1615 cm^{-1}, and its elemental analysis agreed with the molecular formula $C_{14}H_{18}N_4O_4$.

The colorless condensation product of D-galactose (**6**) with 1-hydrazinophthalazine (**1**) gave elemental analysis data that agreed with the molecular formula $C_{14}H_{16}N_4O_5$, which is two hydrogen atoms less than that of the expected hydrazone **13**. The infrared spectrum of the product showed C=N absorption at 1650 cm^{-1}, and OH absorption at 3350 cm^{-1}. The product was, therefore, assigned the structure of 3-(D-*galacto*-pentitol-1-yl)-1,2,4-triazolo[3,4-*a*]phthalazine (**20**). All attempts to prepare the hydrazone **13**, under a variety of conditions, gave **20**. The cyclic triazolophthalazine (**20**) is believed to be formed by autodehydrogenation of the initially formed hydrazone **13**. The cyclic structure (**20**) assigned is in harmony with previously reported results[13], as well as with the mass-spectral fragmentation pattern of **20**. The mass spectrum of the latter did not show the expected molecular ion at *m/z* 320, and yet it showed fragments, similar to those of the cyclized D-mannose derivative **21**, at *m/z* 289 (**29**), 259 (**30**), 229 (**31**), 199 (**32**), 171 (**33**), 243 (**35**), and 213 (**36**), in addition to smaller fragments (**38–45**) due to the breakdown of the sugar moiety.

D-Arabinose (**2**) behaved like D-galactose, giving the colorless, cyclic 3-(D-*arabino*-tetritol-1-yl)-1,2,4-triazolo[3,4-*a*]phthalazine (**16**). Its elemental analysis gave values agreeing with the molecular formula $C_{13}H_{14}N_4O_4$, and its mass spectrum showed the molecular ion (M^+) of this formula as a low-intensity peak at *m/z* 290. The structures of the other fragments are similar to those just discussed (**29–45**).

That sugars **3–5**, **7**, and **8** gave colored hydrazones, whereas D-arabinose (**2**) and D-galactose (**6**) afforded colorless, cyclic dehydrogenation-products may be attributed to the low solubility of the hydrazones of the former group which permits their separation from the reaction mixture before they become dehydrogenated. The intermediate hydrazones (**9** and **13**) of **2** and **6** probably are sufficiently soluble to remain in solution and be dehydrogenated. To substantiate this speculation, the colored hydrazones were subjected to catalytic, dehydrogenative cyclization by heating their aqueous methanolic solutions with 10% palladium-on-charcoal. By this treatment, the phthalazin-1-ylhydrazones (**10–12**, and **14**) gave colorless products whose elemental analyses showed two hydrogen atoms less than for the parent, colored hydrazones. The infrared spectra of the products showed absorptions at 3400–3350 (OH) and 1635 cm^{-1} (C=N). The dehydrogenation products were, accordingly, formulated as 3-(D-*ribo*-, 3-(D-*xylo*-, and 3-(D-*lyxo*-tetritol-1-yl)-1,2,4-triazolo[3,4-*a*]phthalazine (**18**, **19**, and **17**) and 3-(D-*manno*-pentitol-1-yl)-1,2,4-triazolo[3,4-*a*]phthalazine (**21**), respectively. These results, therefore, support the


46, m/z 530
47, m/z 457
48, m/z 385
49, m/z 313
50, m/z 487
51, m/z 471
52, m/z 413
53, m/z 325
58, m/z 241
54, m/z 445
55, m/z 428
56, m/z 369
57, m/z 283
32, m/z 199
33, m/z 171
59
60
m/z 487
61, m/z 289
62, m/z 187
63 m/z 127
64, m/z 145
65, m/z 116
66, m/z 115
67, m/z 103

Scheme 2

suggested rationale as to why some monosaccharides gave hydrazones, whereas others gave cyclization products.

Acetylation of **14** with acetic anhydride in the presence of pyridine gave, unexpectedly, a colorless acetate having the molecular formula $C_{24}H_{26}N_4O_{10}$, that is, two hydrogen atoms less than for the expected, colored hydrazone pentacetate such as those obtained by acetylation of monosaccharide arylhydrazones under the same conditions[15]. The infrared spectrum of the acetate obtained lacked an NH absorption, and showed C=N and *O*-acetyl absorption at 1640 and 1760 cm^{-1}, respectively. These results indicated that the compound was the penta-*O*-acetyl derivative of the cyclic, dehydrogenation structure, namely, 3-(1,2,3,4,5-penta-*O*-acetyl-D-*manno*-pentitol-1-yl)-1,2,4-triazolo[3,4-*a*]phthalazine (**24**). In full agreement with this structure was the mass spectrum of **24** (see Scheme 2), which showed the molecular ion (M^+) at *m/z* 530 (**46**). On losing CH_3CO, CH_3COO, or CH_2OCOCH_3 fragments, the latter gave the peaks at *m/z* 487 (**50**), 471 (**51**), and 457 (**47**), respectively. Fragment **50** may also exist in the alternative pyranoside (**59**) or furanoside (**60**) structures. Fragments **47**, **50**, and **51** undergo further, sequential breakdown, typical[16,17] of polyacetoxyalkyl chains, as shown in Scheme 2.

Acetylation of the colorless 3-(D-*galacto*-pentitol-1-yl)-1,2,4-triazolo[3,4-*a*]-phthalazine (**20**) with acetic anhydride in the presence of pyridine gave 3-(1,2,3,4,5-penta-*O*-acetyl-D-*galacto*-pentitol-1-yl)-1,2,4-triazolo[3,4-*a*]phthalazine (**23**), which showed infrared absorption bands at 1760 (OAc), and 1640 cm^{-1} (C=N). The mass spectrum of **23** showed its molecular ion at *m/z* 530, and had a fragmentation pattern exactly like that of the corresponding D-mannose derivative **24**.

That the acetylation product **24** from the open-structure hydrazone **14** of D-mannose is similar to that of the D-galactose derivative **23**, originating from the cyclic structure **20**, is an additional proof of the concomitant dehydrogenative cyclization and acetylation of **24**.

Acetylation of 3-(D-*arabino*-tetritol-1-yl)-1,2,4-triazolo[3,4-*a*]phthalazine (**16**) with acetic anhydride–pyridine gave the expected 3-(1,2,3, 4-tetra-*O*-acetyl-D-*arabino*-tetritol-1-yl)-1,2,4-triazolo[3,4-*a*]phthalazine (**22**).

EXPERIMENTAL

General methods. — Melting points were determined with a Kofler block and are uncorrected. The infrared spectra were recorded, for potassium bromide discs or Nujol mulls, with a Unicam SP200 or Pye-Unicam SP-1100 spectrophotometer. The mass spectra were recorded with a Varian M-66 mass spectrometer. The homogeneity of nonpolar compounds was checked by thin-layer chromatography on plates precoated with Merck Silica gel G (layer thickness 0.25 mm), used without pretreatment. The distance of solvent travel was 5 cm, and the spots were detected by spraying the chromatograms with 1:1:18 anisaldehyde–concentrated sulfuric acid–ethanol[18], or with 20% sulfuric acid, followed by heating on a hot plate for a few minutes. Evaporations were performed in a rotary evaporator, the bath temperature

being kept below 50°. The microanalyses were performed in the Chemistry Department, Faculty of Science, Cairo University.

aldehydo-D-*Ribose phthalazin-1-ylhydrazone* (**11**). — A solution of D-ribose (**4**; 0.75 g) in water (1 mL) was treated with sodium acetate (0.8 g) and a solution of[10] **1** (1 g) in a mixture of water (3 mL) and methanol (30 mL). The mixture was heated on a boiling-water bath for 10 min, and kept for 24 h at room temperature. The product that separated was filtered off, and washed with, and recrystallized from, water–methanol, to give 1.2 g (80%) of **11** as yellow clusters, m.p. 150°; ν_{max} 3400 (broad, NH and OH), 1640 (C=N), and 1620 cm^{-1}.

Anal. Calc. for $C_{13}H_{16}N_4O_4$: C, 53.4; H, 5.5; N, 19.2. Found: C, 53.4; H, 5.1; N, 19.7.

3-(D-ribo-*Tetritol-1-yl*)-*1,2,4-triazolo*[*3,4*-a]*phthalazine* (**18**). — A solution of **11** (1 g) in a mixture of water (20 mL) and methanol (30 mL) was mixed with 10% palladium-on-charcoal (0.5 g), the mixture boiled for 1 h under reflux, and the suspension cooled to room temperature. The catalyst was filtered off, and the filtrate was evaporated to dryness. Crystallization of the residue from methanol gave 0.7 g of **18** (70%), m.p. 218°; ν_{max} 3250 (OH) and 1635 cm^{-1} (C=N).

Anal. Calc. for $C_{13}H_{14}N_4O_4$: C, 53.8; H, 4.8; N, 19.3. Found: C, 54.0; H, 5.0; N, 19.4.

3-(D-arabino-*Tetritol-1-yl*)-*1,2,4-triazolo*[*3,4*-a]*phthalazine* (**16**). — A solution of D-arabinose (**2**; 0.75 g) in water (1 mL) was treated with a solution of a mixture of sodium acetate (0.8 g) and **1** (1 g) in water (3 mL) and methanol (30 mL). The mixture was heated on a boiling-water bath for 30 min, and allowed to cool. The product that separated was filtered off, and recrystallized from methanol, to give 1 g (68%) of **16**, m.p. 225°; ν_{max} 3380 (broad, NH and OH) and 1640 cm^{-1} (C=N).

Anal. Calc. for $C_{13}H_{14}N_4O_4$: C, 53.8; H, 4.8; N, 19.3. Found: C, 53.9; H, 4.9; N, 19.0.

3-(*1,2,3,4-Tetra-*O-*acetyl-*D-arabino-*tetritol-1-yl*)-*1,2,4-triazolo*[*3,4-a*]*phthalazine* (**22**). — A solution of **16** (1 g) in pyridine (3 mL) was treated with acetic anhydride (3 mL) for 24 h at room temperature, and evaporated under diminished pressure; the residue was dried by several additions and evaporations of toluene, and crystallized from methanol, to give 1.3 g (82%) of **22**, m.p. 135°; ν_{max} 1750 (OAc) and 1635 cm^{-1} (C=N).

Anal. Calc. for $C_{21}H_{23}N_4O_8$: C, 55.2; H, 4.8; N, 12.5. Found: C, 55.8; H, 4.6; N, 12.1.

aldehydo-D-*Xylose phthalazin-1-ylhydrazone* (**12**). — A mixture of D-xylose (**5**; 0.75 g) and water (1 mL) was shaken, filtered through a fritted-glass funnel, and the filtrate treated with a filtered solution of a mixture of sodium acetate (0.8 g) and **1** (1 g) in water (3 mL) and methanol (30 mL). The mixture was heated on a boiling-water bath for 10 min, and then kept for 16 h at room temperature. The yellow, crystalline **12** was filtered off, washed with pre-filtered methanol, and dried (yield 1.3 g; 88%), m.p. 202°; ν_{max} 3400 (broad, NH and OH), 1650 (C=N), and 1630 cm^{-1}. The hydrazone is insoluble in methanol or ethanol, and sparingly soluble in water.

Anal. Calc. for $C_{13}H_{16}N_4O_4$: C, 53.4; H, 5.5; N, 19.2. Found: C, 53.0; H, 5.9; N, 19.5.

3-(D-xylo-*Tetritol-1-yl*)-*1,2,4-triazolo*[*3,4-a*]*phthalazine* (**19**). — To a solution of **12** (1 g) in water (100 mL) and methanol (30 mL) was added 10% palladium-on-charcoal (0.5 g), and the mixture was boiled under reflux for 3 h, cooled to room temperature, the catalyst filtered off, and the filtrate evaporated to dryness. Crystallization of the residue from methanol gave 0.8 g of **19** (80%), m.p. 210°; ν_{max} 3350 (OH) and 1635 cm^{-1} (C=N).

Anal. Calc. for $C_{13}H_{14}N_4O_4$: C, 53.8; H, 4.8; N, 19.3. Found: C, 53.6; H, 5.1; N, 18.6.

aldehydo-D-*Lyxose phthalazin-1-ylhydrazone* (**10**). — A mixture of D-lyxose (**3**; 0.75 g) and water (1 mL) was shaken, filtered through a fritted-glass funnel, and the filtrate treated with a filtered solution of sodium acetate (0.8 g) and **1** (1 g) in water (3 mL). Pre-filtered methanol (30 mL) was added, and the mixture was heated on a boiling-water bath for 10 min, and cooled to room temperature. After 16 h, the yellow, crystalline **10** that had separated was filtered off, washed with methanol, and dried (yield 1.1 g; 75%), m.p. 162°; ν_{max} 3400 (NH and OH) and 1630 cm^{-1} (C=N). The hydrazone is insoluble in methanol or ethanol, and sparingly soluble in water.

Anal. Calc. for $C_{13}H_{16}N_4O_4$: C, 53.4; H, 5.5; N, 19.2. Found: C, 52.8; H, 5.8; N, 19.9.

3-(D-lyxo-*Tetritol-1-yl*)-*1,2,4-triazolo*[*3,4-*a]*phthalazine* (**17**). — To a solution of **10** (1 g) in water (60 mL) and methanol (30 mL) was added 10% palladium-on-charcoal (0.5 g), and the mixture was boiled under reflux for 3 h, cooled to room temperature, the catalyst filtered off, and the filtrate evaporated to dryness. Crystallization of the residue from methanol gave 0.5 g (50%) of **17**, m.p. 185°; ν_{max} 3350 and 1635 cm^{-1} (C=N).

Anal. Calc. for $C_{13}H_{14}N_4O_4$: C, 53.8; H, 4.8; N, 19.3. Found: C, 54.1; H, 4.8; N, 19.2.

aldehydo-D-*Mannose phthalazin-1-ylhydrazone* (**14**). — A mixture of D-mannose (**7**; 0.9 g) and water (1 mL) was shaken, filtered through a fritted-glass funnel, and the filtrate treated with a filtered solution of **1** (1 g) and sodium acetate (0.8 g) in water (3 mL). Methanol (30 mL) was added, the mixture was boiled on a boiling-water bath for 10 min, cooled, and kept for 16 h at room temperature. The product that separated was filtered off, washed with methanol, and dried (yield 1.5 g; 91%), to give **14** as orange, needle-like crystals, m.p. 215°; ν_{max} 3400 (broad, NH and OH), 1630 (C=N), and 1600 cm^{-1} (Ph); insoluble in methanol and ethanol.

Anal. Calc. for $C_{14}H_{18}N_4O_5$: C, 52.2; H, 5.6; N, 17.4. Found: C, 52.0; H, 5.4; N, 17.6.

3-(D-manno-*Pentitol-1-yl*)-*1,2,4-triazolo*[*3,4-a*]*phthalazine* (**21**). — A solution of **14** (1 g) in water (100 mL) and methanol (50 mL) was mixed with 10% palladium-on-charcoal (0.5 g), and the mixture was boiled under reflux for 3 h, cooled, the catalyst filtered off, and the filtrate evaporated to dryness. Crystallization of the

residue from methanol gave 0.6 g (60%) of **21**, m.p. 220°; ν_{max} 3400 (OH) and 1635 cm^{-1} (C=N).

Anal. Calc. for $C_{14}H_{16}N_4O_5$: C, 52.4: H, 5.0; N, 17.5. Found: C, 52.4; H, 5.3: N, 17.9.

*3-(1,2,3,4,5-Penta-*O*-acetyl-*D*-manno-pentitol-1-yl)-1,2,4-triazolo[3,4-a]phthalazine* (**24**). — A solution of **21** (1 g) in dry pyridine (5 mL) was treated with acetic anhydride (3 mL) for 24 h at room temperature. The mixture was diluted with ice–water (100 mL) and extracted with chloroform (5 × 40 mL). The extracts were combined, successively washed with 10% aqueous solution of potassium hydrogensulfate, a saturated aqueous solution of sodium hydrogencarbonate, and water, dried (Na_2SO_4), and evaporated, affording a residue that crystallized from methanol to give 0.9 g (55%) of **24**, m.p. 170°; ν_{max} 1760 (OAc) and 1640 cm^{-1} (C=N).

Anal. Calc. for $C_{24}H_{26}N_4O_{10}$: C, 54.3; H, 4.9: N, 10.6. Found: C, 54.2: H, 5.4; N, 10.5.

*3-(*D*-galacto-Pentitol-1-yl)-1,2,4-triazolo[3,4-a]phthalazine* (**20**). — A solution of D-galactose (**6**; 0.9 g) in water (1 mL) was treated with a solution of **1** (1 g) and sodium acetate (0.8 g) in water (3 mL) and methanol (30 mL). The mixture was boiled on a boiling-water bath for 10 min, and allowed to cool to room temperature. The product that separated was filtered off, and recrystallized from water, to give 1.4 g (87%) of **20**, m.p. 194°; ν_{max} 3350 (OH), 1650 (C=N), and 1630 cm^{-1}.

Anal. Calc. for $C_{14}H_{16}N_4O_5$: C, 52.4; H, 5.0; N, 17.5. Found: C, 52.2; H, 5.0: N, 17.4.

*3-(1,2,3,4,5-Penta-*O*-acetyl-*D*-galacto-pentitol-1-yl)-1,2,4-triazolo[3,4-a]phthalazine* (**23**). — A solution of **20** (1 g) in dry pyridine (3 mL) was treated with acetic anhydride (5 mL) for 24 h at room temperature, diluted with ice–water, and extracted with chloroform (6 × 30 mL). The extracts were combined, successively washed with 10% aqueous potassium hydrogensulfate solution, saturated aqueous sodium hydrogencarbonate solution, and water, dried (Na_2SO_4), and evaporated, affording a residue that crystallized from methanol, to give 0.9 g (55%) of **23**, m.p. 203°; ν_{max} 1760 (OAc) and 1640 cm^{-1} (C=N).

Anal. Calc. for $C_{24}H_{26}N_4O_{10}$: C, 54.3; H, 4.9; N, 10.6. Found: C, 54.1; H, 5.1; N, 10.4.

aldehydo-L-*Rhamnose phthalazin-1-ylhydrazone* (**15**). — A mixture of L-rhamnose (**8**; 0.9 g) and water (1 mL) was shaken, filtered through a sintered-glass funnel, and the filtrate treated with a filtered solution of **1** (1 g) and sodium acetate (0.8 g) in water (3 mL) and methanol (30 mL). The mixture was boiled for 10 min on a boiling-water bath, and then cooled, and kept for 16 h at room temperature. The yellow, crystalline **15** was filtered off, washed with pre-filtered methanol, and dried (yield, 1.3 g, 80%), m.p. 208°; ν_{max} 3420 (OH), 3320 (NH), and 1628 cm^{-1} (C=N). The hydrazone is sparingly soluble in water, and insoluble in methanol or ethanol.

Anal. Calc. for $C_{14}H_{18}N_4O_4$: C, 54.9; H, 5.9; N, 18.3. Found: C, 54.5: H, 5.7; N, 18.4.

REFERENCES

1 H. EL KHADEM, M. A. E. SHABAN, AND M. A. M. NASSR, *Carbohydr. Res.*, 13 (1970) 470–471; 23 (1972) 103–109.
2 M. A. E. SHABAN AND M. A. M. NASSR, *Org. Prep. Proced. Int.*, 8 (1976) 107–112.
3 H. EL KHADEM AND M. A. E. SHABAN, *Carbohydr. Res.*, 2 (1966) 178–180; *J. Chem. Soc., C*, (1967) 519–520.
4 H. EL KHADEM, M. A. M. NASSR, AND M. A. E. SHABAN, *J. Chem. Soc., C*, (1968) 1465–1467.
5 H. EL KHADEM AND M. A. E. SHABAN, *Carbohydr. Res.*, 3 (1967) 416–423.
6 H. EL KHADEM, M. M. A. ABDEL RAHMAN, AND M. A. E. SHABAN, *Carbohydr. Res.*, 6 (1968) 465–469.
7 M. A. E. M. SHABAN AND M. A. M. NASSR, *Carbohydr. Res.*, 36 (1974) c12–c13; *Org. Prep. Proced. Int.*, 8 (1976) 113–118.
8 M. A. E. SHABAN, E. H. EL ASHRY, M. A. M. NASSR, AND V. N. REINHOLD, *Carbohydr. Res.*, 42 (1975) c1–c3; *Org. Prep. Proced. Int.*, 9 (1977) 267–270.
9 S. PATAI, *The Chemistry of Amidines and Imidates*, Wiley, New York, 1976.
10 F. GROSS, J. DRUEY, AND R. MEIER, *Experientia*, 6 (1950) 19–23.
11 W. T. COMER AND A. W. GOMOLL, in A. BURGER (Ed.), *Medicinal Chemistry*, Wiley–Interscience, New York, 1970, pp. 1027–1064.
12 R. JAQUES, *Helv. Physiol. Pharmacol. Acta*, 23 (1965) 54–59.
13 D.-I. SHIHO AND S. TAGAMI, *J. Am. Chem. Soc.*, 82 (1960) 4044–4054.
14 J. DRUEY AND B. H. RINIGIER, *Helv. Chim. Acta*, 34 (1951) 195–199.
15 L. MESTER, *Dérivés Hydraziniques des Glucides*, Hermann, Paris, 1967.
16 J. SZAFRANEK, C. D. PFAFFENBERGER, AND E. C. HORNING, *Carbohydr. Res.*, 38 (1974) 97–105.
17 B. A. DMITRIEV, L. V. BACKINOWSKY, O. S. CHIZHOV, B. M. ZOLOTAREV, AND N. K. KOCHETKOV, *Carbohydr. Res.*, 19 (1971) 432–435.
18 P. J. DUNPHY, J. D. KERR, J. F. PENNOCK, AND K. J. WHITTLE, *Chem. Ind. (London)*, (1966) 1549–1550.