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6-CHLORO-3-β-D-ERYTHROFURANOSYL-1-PHENYL- AND -1-*p*-TOLYL-PYRAZOLO-[3,4-*b*]QUINOXALINE*

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ABSTRACT

The *C*-nucleoside analogs 6-chloro-3-β-D-erythrofuranosyl-1-phenylpyrazolo-[3,4-*b*]quinoxaline (**5**) and 3-β-D-erythrofuranosyl-1-*p*-tolylpyrazolo[3,4-*b*]quinoxaline (**10**) were prepared by dehydration of the polyhydroxyalkyl chain of 6(7)-chloro-1-phenyl-3-(D-*arabino*-tetritol-1-yl)-pyrazolo(3,4-*b*]quinoxaline and 3-(D-*arabino*-tetritol-1-yl)-1-*p*-tolylpyrazolo[3,4-*b*]quinoxaline, respectively. The structure and anomeric configuration of **5** and **10** were determined by high-resolution, n.m.r spectroscopy. The mass spectra and biological activities of some of these compounds are discussed.

INTRODUCTION

Current research in nucleoside antibiotics[2,3] has stimulated interest in the synthesis of *C*-nucleoside analogs[4] of a variety of heterocyclic bases, which are more amenable than *N*-nucleosides for biochemical investigations, due to the greater stability of the carbon–carbon than of the carbon–nitrogen linkage towards hydrolytic and enzymic reagents. The synthesis of *C*-nucleoside analogs having pyrazoloquinoxaline and triazole moieties, by dehydrative cyclization of the polyhydroxyalkyl chain of the corresponding saccharide heterocyclic derivative, has been reported recently[1,5]. The use of high-resolution, n.m.r. spectroscopy for their anomeric determination[6] can increase the utility of this method for *C*-nucleoside synthesis.

Pyrazolo[3,4-*b*]quinoxaline derivatives are of biological interest. Some of these derivatives have pharmacological properties and show tuberculostatic activity *in vitro*[7], but the chemotherapeutic properties of saccharide pyrazolo[3,4-*b*]quinoxalines have not been thoroughly investigated. In this work, two types of saccharide pyrazolo[3,4-*b*]quinoxaline derivatives, substituted in the base moieties, have been

*C-Nucleoside Pyrazolo[3,4-*b*]quinoxaline Analogs, Part II For Part I, see ref 1
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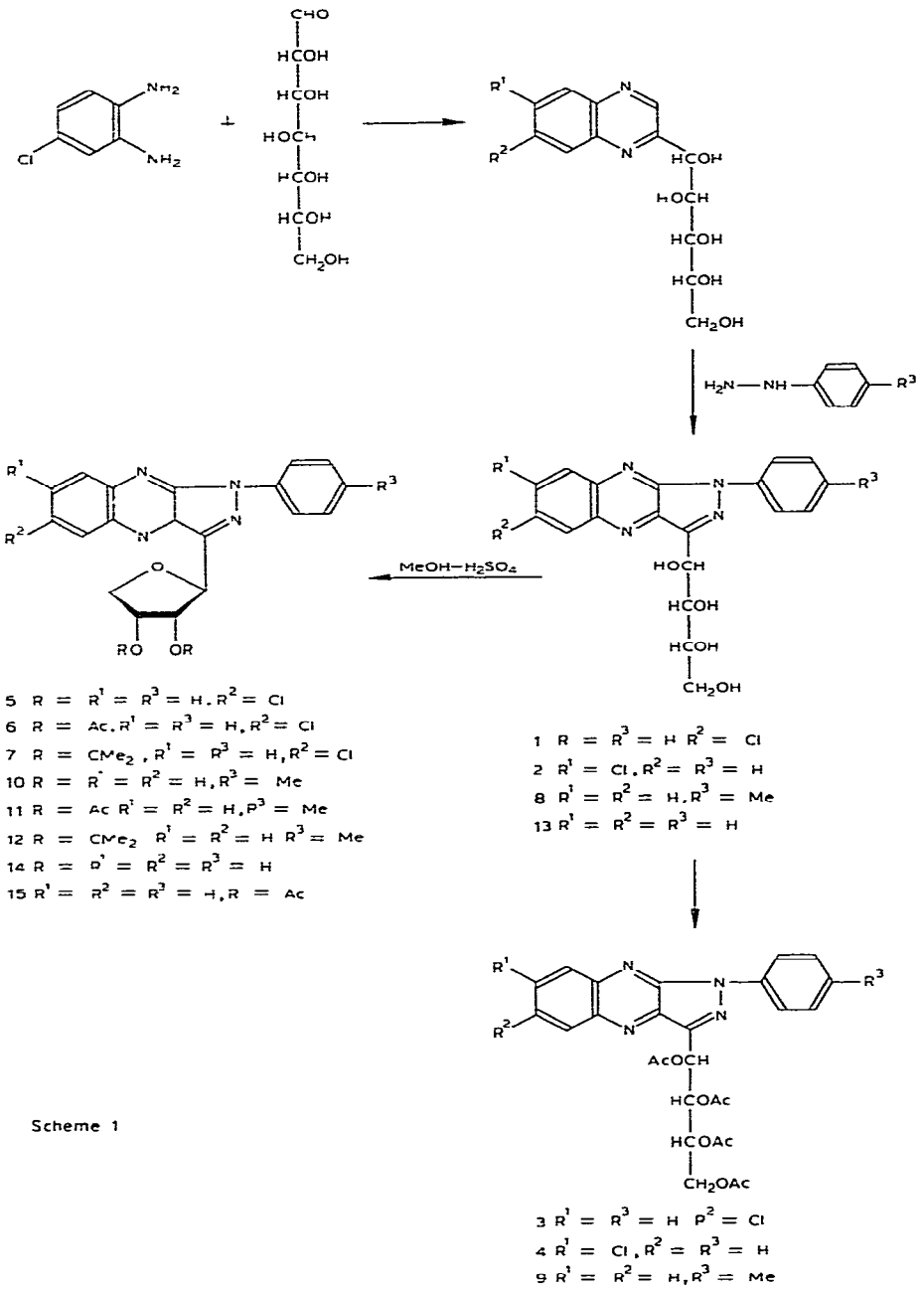
prepared, and converted into their *C*-nucleoside analogs. The structure and anomeric configuration of the latter were determined by n.m.r. spectroscopy. The biological activity of some of these compounds is reported.



5 R = R^1 = R^3 = H, R^2 = Cl
6 R = Ac, R^1 = R^3 = H, R^2 = Cl
7 R = CMe_2, R^1 = R^3 = H, R^2 = Cl
10 R = R^1 = R^2 = H, R^3 = Me
11 R = Ac R^1 = R^2 = H, R^3 = Me
12 R = CMe_2 R^1 = R^2 = H R^3 = Me
14 R = R^1 = R^2 = R^3 = H
15 R^1 = R^2 = R^3 = H, R = Ac

1 R = R^3 = H R^2 = Cl
2 R^1 = Cl, R^2 = R^3 = H
8 R^1 = R^2 = H, R^3 = Me
13 R^1 = R^2 = R^3 = H

3 R^1 = R^3 = H R^2 = Cl
4 R^1 = Cl, R^2 = R^3 = H
9 R^1 = R^2 = H, R^3 = Me

Scheme 1

DISCUSSION

Similarly to *o*-phenylenediamine, 4-substituted phenylenediamines react with sugar derivatives, giving isomeric mixtures of 6- and 7-substituted quinoxaline derivatives[8,9]. In many cases[10–13], the 6-substituted isomer is the preponderant isomer. The reaction of 4-chloro-*o*-phenylenediamine with D-*glycero*-D-*gulo*-heptose and phenylhydrazine afforded a mixture of 6- and 7-chloro-1-phenyl-3-(D-*arabino*-tetritol-1-yl)-pyrazolo[3,4-*b*]quinoxalines (**1** and **2**) in the ratio of 3 : 2 as estimated by t.l c. The preponderance of the 6-isomer can be explained on the basis of the relative reactivities of the two amino groups in 4-chloro-*o*-phenylenediamine. The 1-amino group, being the more reactive[14], condenses with the sugar carbonyl group, giving the preponderant, 6-chloro isomer **1**. The condensation of the less-reactive, 2-amino group with the sugar carbonyl leads to the minor, 7-chloro isomer **2**. The two isomers, **1** and **2**, could not be separated by fractional recrystallization, and attempts to separate them by acetylation gave a mixture of the tetraacetates **3** and **4** which, on deacetylation, regenerated a mixture of **1** and **2**. However, refluxing of the isomeric mixture of **1** and **2** with methanolic sulfuric acid solution resulted in the separation of the preponderant isomer as its *C*-nucleoside derivative **5** (see Scheme 1), which was purified by recrystallization, leaving the minor isomer in the mother liquor.

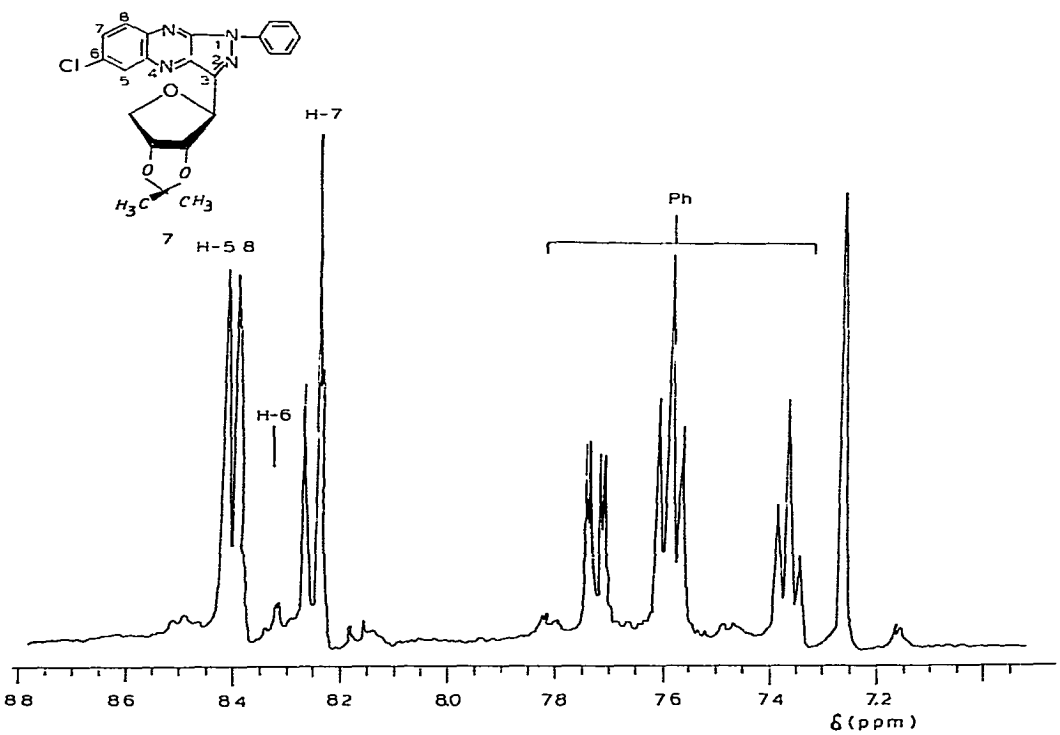


Fig 1. N.m.r. spectrum, at 360 MHz, of 6-chloro-3-(2,3-*O*-isopropylidene-β-D-erythrofuranosyl)-1-phenylpyrazolo[3,4-*b*]quinoxaline (**7**) (high resolution of the base moiety).

Acetylation of **5** with acetic anhydride–pyridine afforded the diacetyl derivative **6**, whose n.m.r. spectrum showed two methyl signals at δ 2.03 and 2.13, attributable to two acetyl groups. The anomeric proton of **6** appeared as a doublet, centered at δ 5.60, having J 6.0 Hz. This coupling-constant value made the anomeric assignment of compound **6** uncertain[1]. However, the high-resolution, n.m.r. spectrum (360 MHz) of the isopropylidene derivative **7** showed the anomeric proton as a singlet at δ 5.85, consistent[15–17] with the trans arrangement of H-1′ and H-2′, which is in agreement with the *β*-D-*erythro* configuration.

Additional evidence for the *β*-D configuration was obtained from the value of the difference ($\Delta\delta$) between the chemical shift of the methyl signals of the 2,2-dimethyldioxolane ring: the difference of 0.20 (1.662 — 1.462) between the chemical shifts of the two methyl protons of **7** is consistent[18–20] with the *β*-D configuration.

The 6-chloro substituent on the pyrazolo[3,4-*b*]quinoxaline moiety was proved by comparing the aromatic regions of the high-resolution, n.m.r. spectrum (360 MHz) of **7** (see Fig. 1) with those of the phenyl analog **15** (see Fig. 2). The latter showed H-6 as a doublet, centered at δ 8.30, and H-7 as a doublet at δ 8.20, having $J_{6,7}$ 8.5 Hz. The presence of H-6 downfield to H-7 is attributed to its proximity to the glycosyl ring, which has a deshielding effect[17]. However, the spectrum of com-

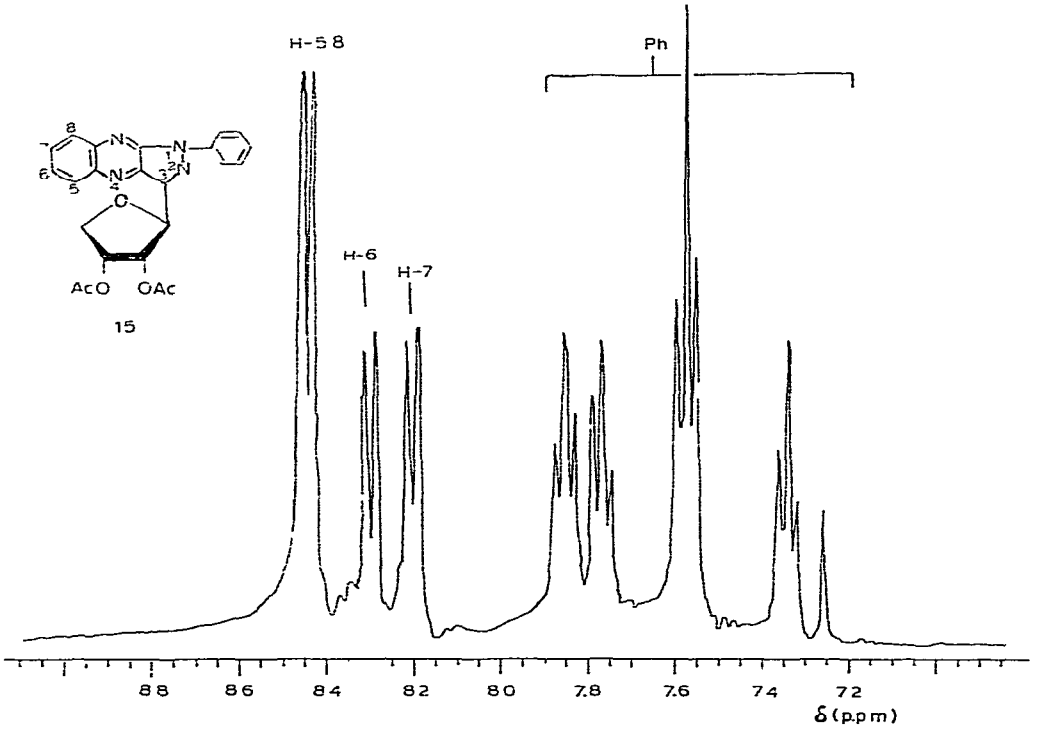


Fig. 2. N m.r. spectrum, at 360 MHz, of 3-(2,3-di-*O*-acetyl-*β*-D-erythrofuranosyl)-1-phenylpyrazolo[3,4-*b*]quinoxaline (**15**) (high resolution of the base moiety).

pound **7** lacked the lower-field doublet assigned to H-6, and showed a small downfield shift for H-7, due to the electronegativity of the neighboring chlorine atom.

3-(D-*arabino*-Tetritol-1-yl)-1-*p*-tolylpyrazolo-[3,4-*b*]quinoxaline (**8**) was prepared by the reaction of D-*glycero*-D-*gulo*-heptose with *o*-phenylenediamine and *p*-tolylhydrazine. Acetylation of **8** with acetic anhydride–pyridine afforded the tetra-*O*-acetyl derivative **9**, whose n.m.r. spectrum showed the four acetyl groups as four methyl singlets, at δ 1.97, 2.07, 2.13, and 2 20. The *p*-tolyl methyl group appeared as a singlet at δ 2.47.

Refluxing of **8** with methanolic sulfuric acid afforded the *C*-nucleoside analog, namely, 3-β-D-erythrofuranosyl-1-*p*-tolylpyrazolo[3,4-*b*]quinoxaline (**10**). Acetylation of **10** by refluxing with acetic anhydride afforded the di-*O*-acetyl derivative **11**, whose n.m.r. spectrum showed two methyl signals, at δ 2.07 and 2.18, attributable to two acetyl groups. The different substitution at the base moieties of **6** and **11** did not show any appreciable change in the coupling constant of the anomeric proton Compound **11** showed the anomeric proton at δ 5.80 as a doublet having $J_{1',2'}$ 6.4 Hz. The same value of the coupling constant was obtained for the phenyl analog[1], and consequently, the anomeric configuration could not be ascertained. However, by the same method of anomeric assignment, the isopropylidene derivative **12** was prepared, and its high-resolution, n.m.r. spectrum showed the anomeric proton as a singlet at δ 5.86. The zero value of the coupling constant for the anomeric proton of **12** proved unequivocally[21,22] the trans arrangement of H-1′ and H-2′, that is, the β-D-*erythro* configuration. The difference, $\Delta\delta$ = 0.201 (1.662–1.461), between the two methyl signals of the 2,2-dimethyldioxolane ring of compound **12** confirmed the β-D configuration.

From the foregoing results, it seems that the stereo-course of the dehydration process of saccharide pyrazoloquinoxaline analogs is not affected by substitution in the base moiety. The β-D configuration is the favored one for the liberated *C*-nucleoside, and is obtained by inversion in the configuration of C-1 of the D-*arabino*-tetritol chain. This inversion was confirmed by c.d. studies for the phenyl analog[1]. The α anomer, obtained without inversion, was not detected in the products by t.l.c. The preponderance of the β anomer may be explained by its higher conformational stability during the acid-catalyzed, dehydrative cyclization process. The bulky, base

α (^2E) β (^2E)

B = substituted pyrazolo [3,4-*b*] quinoxaline moiety

Fig. 3. The preponderant conformers of anomeric pyrazolo[3,4-*b*]quinoxaline *C*-nucleoside analogs.

TABLE I

K_B TEST FOR PYRAZOLO [3,4-*b*]QUINOXALINE DERIVATIVES

Concentration (μg/mL)	ED_{50}				
	Compound **1.2**	**13**	**5**	**14**	**6**
	Solvent *dil. EtOH*	*dil. Me_2SO*	*dil. Me_2SO*	*dil. Me_2SO*	*dil. EtOH*
100	10	04	03	06	14
	09	03	01	05	15
10	17	13	13	12	14
	16	14	12	11	15
1	19	14	13	12	15
	20	13	14	13	15
0.1	18	20	14	13	16
	19	19	15	14	14
0.01	19	18	15	15	16
	20	17	16	14	17

moiety is positively charged in the acidic medium, and, accordingly, tends to occupy the equatorial β-position rather than the axial α-position, by the reverse anomeric effect[23], as indicated by the ^2E conformer (see Fig. 3), which is predominant for purine nucleosides[24], and this is in agreement with the value for $J_{1',2'}$ (6.4 Hz). Additionally, the α anomer has a nonbonded, *syn*-axial interaction[25] between the bulky, axially attached, base moiety and the C-3′ hydroxyl group, which would provide a conformational-instability factor.

The mass spectrum of compound **5** showed the molecular ion at *m/z* 282 and 284, due to the chlorine isotopes; the base peak at *m/z* 77 represents the Ph group. The spectrum showed the characteristic fragments of the pyrazoloquinoxaline *C*-nucleosides[1]; $BCHO^+H$, BCHO, and BCH_2 as strong peaks, with their chlorine-isotope fragments (see Experimental section). The fragments BH and B were more intense than expected for common *C*-nucleosides[6], perhaps because of the bulkiness of the pyrazoloquinoxaline moiety. The mass spectrum of the acetyl derivative **6** showed the molecular ion peak at *m/z* 466 and 468. The base peak at *m/z* 43 corresponds to a CH_3CO group.

Biological activity studies for compounds **1**, **2**, and **5**, as well as their phenyl analogs[1] **13** and **14**, showed cytotoxicity *in vitro* to K_B cells (see Table I). The *C*-nucleoside **5** showed stronger activity than its acyclic precursors **1** and **2** Compound **6** was inactive. The different ED_{50} values for these analogs may be attributed to a solubility factor.

EXPERIMENTAL

General. — Melting points are uncorrected, and evaporations were performed under diminished pressure below 60°. Thin-layer chromatography (t.l.c.) was conducted on silica gel (Kiesel gel G, Merck), with solvent *A*, 3:1 benzene–ethanol, or solvent *B*, butanone saturated with water. I.r. absorption spectra were recorded with a Unicam SP 1025 instrument. N.m.r. spectra were recorded with Varian T-(60 MHz), EM-360, and NTC (360 MHz) instruments, using internal tetramethylsilane as the standard. Mass spectra were recorded with AEI MS-902 and Dupont MS 21-492B spectrometers. Combustion analyses were performed in the Department of Chemistry, Purdue University, W. Lafayette, Indiana, U.S.A.

*6(7)-Chloro-1-phenyl-3-(β-*D*-arabino-tetritol-1-yl)pyrazolo[3,4-*b*]quinoxalines* (**1** *and* **2**). — A solution of D-*glycero*-D-*gulo*-heptose (2 g) in water (150 mL) was heated with 4-chloro-*o*-phenylenediamine (1.5 g), phenylhydrazine hydrochloride (8 g), and acetic acid (2.5 mL) in a sealed flask for 8 h in a boiling-water bath. The flask was cooled, and opened, and the yellow precipitate was filtered off, washed successively with water, 50% methanol, and ether, and dried: yield 2 g. Recrystallization from propyl alcohol gave yellow needles, m.p. 230–232°; ν_{max}^{KBr} 3300 (OH) and 1600 cm^{-1} (C=N). T.l.c. showed two spots, R_F 0.32, 0.28 (solvent *A*) and 0.68, 0.61 (solvent *B*). The two spots could not be separated by fractional recrystallization from propyl or methyl alcohol.

Anal. Calc. for $C_{19}H_{17}ClN_4O_4$: C, 57.0; H, 4.3; N, 14.0. Found: C, 56.8; H, 4.3; N, 13.7.

*6(7)-Chloro-1-phenyl-3-(tetra-*O*-acetyl-*D*-arabino-tetritol-1-yl)-pyrazolo[3,4-*b*]-quinoxalines* (**3** *and* **4**). — A solution of the mixture of **1** and **2** (0.2 g) in pyridine (4 mL) was treated with acetic anhydride (4 mL) for 24 h at room temperature; it was then poured onto crushed ice, and the acetate was filtered off, washed with water, and dried; yield 0.2 g. It was recrystallized from dilute methanol, to give yellow needles, m.p. 157–158°; m.s., accurate measurement of the molecular-ion peak: Found 568.135 (Calc. 568.136).

Anal. Calc. for $C_{27}H_{25}ClN_4O_8$: C, 57.04; H, 4.40; N, 9.85. Found: C, 57.08; H, 4.67; N, 9.63.

Deacetylation of the acetate mixture **4** *and* **5**. — A mixture of **4** and **5** (10 mg) was treated with 20% methanolic ammonia for 24 h at room temperature. Evaporation of the methanol gave yellow needles which showed two spots at the same R_F values as those of the mixture of **1** and **2**.

*6-Chloro-3-β-*D*-erythrofuranosyl-1-phenylpyrazolo[3,4-*b*]quinoxaline* (**5**). — A suspension of the isomeric mixture of **1** and **2** (0.5 g) in 7% methanolic sulfuric acid (300 mL) was boiled under reflux for 72 h; complete dissolution occurred within 5 h. The reaction was monitored by t.l.c.; complete dehydration was found after 72 h (only one spot). The solution was poured into hot water, the methanol was evaporated under diminished pressure, and the yellow precipitate obtained was collected, washed thoroughly with water until neutral, and dried; yield 0.4 g. It was recrystallized from

methanol, to give yellow needles, m.p. 188°; t.l.c. showed one spot, R_F 0.86 (solvent *B*). For compound **5**, ν_{max}^{KBr} 3390 (OH) and 1605 cm^{-1} (C=N); mass-spectral data (principal peaks): *m/z* 282, 284 (20, 15; M), 323, 325 (26, 14), 310, 312 (19, 8; BHCHO⁻H, where B = 6-chloro-1-phenylpyrazolo[3,4-*b*]quinoxaline moiety), 309, 311 (73, 23; BCHO⁻H), 308, 310, (16, 19; BCHO), 293, 295 (18, 17; BCH_2), 281, 283 (19, 3; BH_2), 280, 282 (11, 6; BH), 279, 281 (25, 19; B), 254, 256 (71, 12; BH_2 + H — CN), 255, 257 (9, 23; BH_2 — CN), 93 (32, $PhNH_2$), 81 (74), and 77 (100, Ph); accurate measurement of the molecular-ion peak: Found 382.083 (Calc. 382.083).

Anal. Calc. for $C_{19}H_{15}ClN_4O_3$: C, 59.68; H, 3.92; N, 14.66. Found: C, 59.46; H, 4.09; N, 14.20.

*6-Chloro-3-(2,3-di-O-acetyl-β-*D*-erythrofuranosyl)-1-phenylpyrazolo[3,4-*b*]-quinoxaline* (**6**). — A solution of **5** (0.1 g) in pyridine (2 mL) was treated with acetic anhydride (2 mL) for 24 h at room temperature; it was then poured onto crushed ice, and the acetate was filtered off, washed with water, and dried: yield 0.10 g. It was recrystallized from methanol, to give yellow needles, m.p. 145–146°; n.m.r. data (60 MHz, $CDCl_3$): δ 2.03 and 2.13 (d, 6 H, 2 CH_3CO), 4.17 and 4.63 (2 q, 2 H, ABX system of the methylene group at C-4', $J_{3',4'}$ 3.5 and $J_{3',4''}$ 4.5 Hz, with a geminal coupling-constant of 10.1 Hz), 5.60 (d, 1 H, H-1', $J_{1',2'}$ 6.0 Hz), 5.80–5.95 (m, 1 H, H-3'), 6.25 (q, 1 H, H-2', $J_{2',3'}$ 5.0 Hz), 7.19–8.50 (m, 8 H, aromatic protons); mass-spectral data (principal peaks): *m/z* 466, 468 (1, 1; M), 348, 350 (8, 2; M — 2 OAc), 347, 349 (23, 10; M — H — 2 OAc), 309, 311 (1, 1; BCHO⁻H), 308, 310 (3, 1; BCHO), 279, 281 (3, 2; B), 256, 258 (64, 3; BH_2 + H — CN), 255, 257 (2, 17; BH_2 — CN), 115 (19), 93 (12, $PhNH_2$), 81 (38), 77 (13, Ph), and 43 (100, CH_3CO); accurate measurement of the molecular-ion peak: Found 466.102 and 468.104 (Calc. 468.102 and 468.102).

Anal. Calc. for $C_{23}H_{19}ClN_4O_5$: C, 59.22; H, 4.08; N, 12.02. Found: C, 59.10; H, 4.06; N, 11.92.

*6-Chloro-3-(2,3-O-isopropylidene-β-*D*-erythrofuranosyl)-1-phenylpyrazolo[3,4-b]quinoxaline* (**7**). — A solution of **5** (60 mg) in dry acetone (20 mL) was treated with *p*-toluenesulfonic acid (300 mg), with stirring. After 1 h, t.l.c. showed the reaction to be complete [one spot, R_F 0.83 (solvent *B*)]. The mixture was poured into an ice-cold solution of sodium hydrogencarbonate, and the resulting precipitate was filtered off, washed with water, and dried; yield 80 mg. It was recrystallized from methanol, to give yellow needles, m.p. 198–200°; n.m.r. data (360 MHz; $CDCl_3$): δ 1.462 and 1.662 (d, 6 H, CMe_2, $\Delta\delta$ 0.20), 4.14 (q, 1 H, H-4'', $J_{3',4'}$ 3.7 Hz), 4.211 (d, H-4', $J_{4',4''}$ 10.6 Hz), 5.23 (q, 1 H, H-3'), 5.57 (d, 1 H, H-2', $J_{2',3'}$ 6.0 Hz), 5.85 (s, 1 H, H-1'), 7.34–7.74 (m, 5 H, Ph), 8.23–8.27 (t, 1 H, H-7), 8.39 (s, 1 H, H-8), and 8.41 (s, 1 H, H-5).

Anal. Calc. for $C_{22}H_{19}ClN_4O_3$: C, 62.55; H, 4.54; N, 13.17. Found: C, 62.35; H, 4.32; N, 13.41.

*3-(*D*-arabino-Tetritol-1-yl)-1-*p*-tolylpyrazolo[3,4-b]quinoxaline* (**8**). — A solution of D-*glycero*-D-*gulo*-heptose (1.5 g), *o*-phenylenediamine (0.8 g), *p*-tolylhydrazine hydrochloride (5.5 g), and acetic acid (1.5 mL) in water (200 mL) was treated as for

compounds **1** and **2**; yield 1.10 g. It was recrystallized from propyl alcohol, to give yellow needles, m.p. 230–232°; ν_{max}^{KBr} 3500 (OH) and 1620 cm^{-1} (C=N).

Anal. Calc. for $C_{20}H_{20}N_4O_4$: C, 63.13; H, 5.26; N, 14.73. Found: C, 63.13; H, 5.18; N, 14.72.

*1-Phenyl-3-(tetra-*O*-acetyl-*D*-arabino-tetritol-1-yl)-1-p-tolylpyrazolo[3,4-b]-quinoxaline* (**9**). — A solution of compound **8** (0.1 g) was acetylated with acetic anhydride–pyridine (8 mL), and processed as described for **3** and **4**; yield 0.12 g. It was recrystallized from dilute methanol, to give yellow needles, m.p 166–168°; n.m.r. data (60 MHz): δ 1.97, 2.07, 2.13 and 2.20 (4 s, 12 H, 4 CH_3CO), 2.47 (s, 3 H, tolyl CH_3), 4.0–6.5 (m, 5 H, alditol protons), and 7.2–8.4 (m, 8 H, aromatic protons)

Anal. Calc. for $C_{28}H_{28}N_4O_4$: C, 61.29; H, 5.15; N, 10.20. Found: C, 61 38; H, 5.29; N, 10.25.

*3-β-*D*-Erythrofuranosyl-1-p-tolylpyrazolo[3,4-b]quinoxaline* (**10**). — A suspension of **9** (0.52 g) in 6% methanolic sulfuric acid (200 mL) was boiled under reflux, with stirring, for 21 h; complete dissolution occurred within 1 h, and the reaction was complete, as monitored by t.l.c. (only one spot), after 21 h. The solution was poured into hot water, the methanol evaporated, and the yellow precipitate filtered off, washed with water, and dried; yield 0.45 g (92%). It was recrystallized from dilute methanol, to give yellow needles, m.p. 205–207°; n.m r. data (360 MHz; Me_2SO-d_6): δ 1.243 (s, 3 H, tolyl CH_3), 2.717 (dd, 1 H, H-4″, $J_{3',4'}$ 2.54 Hz), 3.208 (q, 1 H, H-4′, $J_{3',4'}$ 4.45, $J_{4',4''}$ 9.2 Hz), 3.294 (m, 1 H, H-3′), 3.752 (q, 1 H, H-2′), 4.01 (d, 1 H, OH), 4.08 (d, 1 H, OH), 4 14 (d, 1 H, H-1′, $J_{1',2'}$ 6.4 Hz), 6.268–6 841 (m, 4 H, AB system of the tolyl aromatic protons), and 7.01–7.207 (m, 4 H, H-5,6,7,8); after addition of CD_3CO_2D, the two hydroxyl protons disappeared.

Anal. Calc. for $C_{20}H_{18}N_4O_3$: C, 66.27; H, 5.01; N, 15.47. Found: C, 66.57, H, 4.98; N, 15.18.

*3-(2,3-Di-*O*-acetyl-β-*D*-erythrofuranosyl)-1-p-tolylpyrazolo[3,4-b]quinoxaline* (**11**). — Compound **10** (0.18 g) was refluxed with acetic anhydride (5 mL) for 2 h, and the solution evaporated to a syrup; the last traces of the acetic anhydride were removed by rotary evaporation with toluene. The yellow product was recrystallized from dilute methanol, to give yellow needles, m.p. 166–168°; n.m.r. data (360 MHz; $CDCl_3$); δ 2.068, 2.179 (d, 6 H, 2 CH_3CO), 2.428 (s, 3 H, tolyl CH_3), 4.156–4.186 (q, 1 H, H-4″), 4.635–4.674 (q, 1 H, H-4′, $J_{3',4'}$ 4.4, $J_{4',4''}$ 9.47 Hz), 5.80 (d, 1 H, H-1′, $J_{1',2'}$ 6.4 Hz), 5.875–5.886 (m, 1 H, H-3′), 6.244–6.275 (dd, 1 H, H-2′, $J_{2',3}$ 5.3 Hz), 7.244–7.859 (m, 4 H, AB pattern of tolyl aromatic protons), and 8.18–8.34 (m, 4 H, H-5,6,7,8).

Anal. Calc. for $C_{24}H_{22}N_4O_5$: C, 64.55; H, 4.97; N, 12.55 Found: C, 64.76; H, 4.96; N, 12.36.

*3-(2,3-*O*-Isopropylidene-β-*D*-erythrofuranosyl)-1-p-tolylpyrazolo[3,4-b]quinoxaline* (**12**). — Compound **10** (0.12 g) was dissolved in dry acetone and treated with *p*-toluenesulfonic acid (0.25 g) as described for compound **5**; the yellow precipitate obtained was recrystallized from dilute methanol, to give yellow needles, m.p. 126–

128°; t.l.c., R_F 0.96 (solvent *B*); n.m.r. data (360 MHz, $CDCl_3$): δ 1.662 and 1.461 (d, 6 H, CMe_2, $\Delta\delta$ 0.201), 2.425 (s, 3 H, tolyl CH_3), 4.151–4.197 (m, 2 H, H-4′,4″), 5.249–5.258 (m, 1 H, H-3′), 5.574 (dd, 1 H, H-2′), 5.859 (s, 1 H, H-1′), 7.25–7.854 (m, 4 H, AB pattern of the aromatic *p*-tolyl protons), and 8.191–8.288 (m, 4 H, H-5,6,7,8).

Anal. Calc. for $C_{22}H_{22}N_4O_3$: C, 67.66; H, 5.68; N, 14.36. Found: C, 67.71; H, 5.51; N, 14.08.

Biological tests. — Compounds **1**, **2**, **5**, **13**, and **14** showed cytotoxic activity towards K_B cells (a human, epidermoid carcinoma). The *in vitro* cytotoxicity test was performed by the Cell Culture Laboratory of the Purdue University Cancer Center. The compounds were tested as suspensions in dilute, aqueous ethanol or dilute, aqueous dimethyl sulfoxide. Compound **6** was inactive.

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