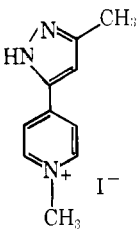
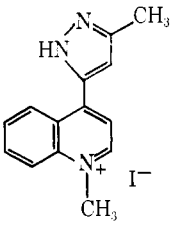


1



2

Experimental Section[5]

4-[5(3)-Methyl-3(5)-pyrazolyl]quinoline.—A mixture of 2.9 g (0.014 mole) of 4-acetoacetylquinoline[2] and 5.8 ml (0.12 mole) of 100% NH_2NH_2 was stirred at room temperature for 15 min, heated on a steam bath for 15 min, and diluted with H_2O. Filtration gave 2.1 g (66%) of tan crystals, mp 122–125°. Sublimation gave yellow crystals, mp 123–126°. *Anal.* ($C_{13}H_{11}N_3 \cdot H_2O$) C, H, N.

1-Methyl-4-[5(3)-methyl-3(5)-pyrazolyl]quinolinium Iodide.—A solution of 1.9 g (0.008 mole) of 4-[5(3)-methyl-3(5)-pyrazolyl]-quinoline, 10 ml of MeI, and 100 ml of EtOH was heated under reflux with stirring for 2 hr. The solvent was distilled, and the residue was triturated with Et_2O to leave 2.1 g of yellow crystals, mp 180–185°. Two recrystallizations (EtOH) gave 1.6 g (55%) of yellow crystals: mp 211–213° [*Anal.* ($C_{14}H_{14}IN_3 \cdot 0.5H_2O$) C, H, I, N]; uv (MeOH) 243 mμ (ε 30,900) and 352 mμ (ε 12,700), uv (0.1 *N* NaOH) 392 mμ (ε 14,100).

(5) Melting points were determined in a Hershberg apparatus and are uncorrected. Microanalyses were performed by Mr. L. M. Brancone and staff; where analyses are indicated only by symbols of the elements, analytical results obtained for those elements were within 0.4% of the theoretical values. Uv spectra were determined with a Cary 11 spectrophotometer by Mr. W. Fulmor and staff.

Some 9-(2,3,4-Tri-O-benzyl-D-arabinopyranosyl)purines[1]

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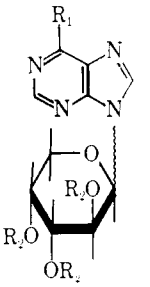
The arabinofuranoside of 6-mercaptopurine (6-MP) has interesting antitumor activity.[2] To compare the effect of a change in ring size, we recently synthesized the α- and β-arabinopyranosides of 6-MP (**1a** and **1b**).[3,4] We have now prepared their O-benzyl-blocked derivatives (**2a** and **2b**), whose greatly altered solubility properties may influence their biological properties. The synthesis of **2a** and **2b** became feasible when a practical separation of their precursors **3a** and **3b**[5] was found. The conversion of **3** by nitrous acid to **4** and the thiation of **4** to **2** proceeded in good yields by standard procedures. Compounds **2a**, **2b**, **4a**, and **4b** were inactive against leukemia L1210 in mice.[6]



1. $R_1 = SH$; $R_2 = H$
2. $R_1 = SH$; $R_2 = CH_2C_6H_5$
3. $R_1 = NH_2$; $R_2 = CH_2C_6H_5$
4. $R_1 = OH$; $R_2 = CH_2C_6H_5$

a = α anomer

b = β anomer

Experimental Section[7]

Separation of 3a and 3b.—Column chromatography experiments with silica gel and alumina did not give good separation of these anomers. However, Florisil[8] was satisfactory. A synthetic mixture of 1.30 g of **3a** and 1.43 g of **3b** in 10 ml of warm toluene was placed on a 60-g column (2.2 × 47 cm) of 100–200 mesh Florisil[8] and eluted with Et_2O. The first fraction of 500 ml of eluent was discarded. The next two fractions of 1.1 l. of Et_2O and 250 ml of EtOAc–Et_2O (1:4) contained 1.32 g of **3b** (92.5% recovery). The fourth fraction, 100 ml of EtOAc–Et_2O (1:4), contained 0.09 g of **3a** and **3b**. The final two fractions of 500 ml of EtOAc–Et_2O (1:4) and 500 ml of EtOAc contained 1.21 g (93%) of **3a**. The separation was followed by tlc in solvent A with R_f 0.50 and 0.22 for **3b** and **3a**, respectively.

This procedure was applied to the crude reaction mixtures of **3a** and **3b**[5] from which about 10–15% of the less soluble **3a** had been first removed by fractional crystallization from toluene and ether.

9-(2,3,4-Tri-O-benzyl-D-arabinopyranosyl)hypoxanthine (4a and 4b).—Stirring 1.0 g (1.9 mmoles) of 9-(2,3,4-tri-O-benzyl-α-D-arabinopyranosyl)adenine (**3a**) with $NaNO_2$ (3.5 g, 40 mmoles) in 59 ml of AcOH, 50 ml of H_2O, and 2.5 ml of 1 *N* HCl for 24 hr afforded 60–70% of **4a**: mp 150–151° after recrystallization from toluene and trituration with Et_2O; $\lambda_{max}^{pH\ 1}$ 250 mμ (ε 11,200), $\lambda_{max}^{pH\ 7}$ 249 (11,800), $\lambda_{max}^{pH\ 13}$ 253 (13,600); $[\alpha]^{23}D$ −13.6° (*c* 1.38, CH_2Cl_2); R_f 0.10 in solvent A. *Anal.* ($C_{31}H_{30}N_4O_5$) C, H, N.

Compound **4b**, similarly prepared in 66% yield had mp 162–163° (triturated with Et_2O); $\lambda_{max}^{pH\ 1}$ 251 mμ (ε 11,200), $\lambda_{max}^{pH\ 7}$ 249 (12,000), $\lambda_{max}^{pH\ 13}$ 253 (13,800); $[\alpha]^{23}D$ +34.5° (*c* 1.50, CH_2Cl_2); R_f 0.34 in solvent A. *Anal.* ($C_{31}H_{30}N_4O_5$) C, H, N.

9-(2,3,4-Tri-O-benzyl-D-arabinopyranosyl)-9H-purine-6-thiol (2a and 2b).—A solution of 0.50 g (0.93 mmole) of **4b** and 1.7 g of P_2S_5 in 30 ml of dry C_5H_5N was heated at reflux for 3.5 hr under N_2 and then worked up to afford 0.48 g (93%) of **2b**, mp 177.5–179.0°. Recrystallization from EtOAc afforded 0.35 g (68%) of the β anomer **2b**: mp 199–200°; the solubility of **2b** was too low for determining λ_{max} at pH 1; λ_{max}^{MeOH} 322 mμ (ε 23,100), $\lambda_{max}^{pH\ 13}$ 313 (23,400); $[\alpha]^{21}D$ −21° (*c* 0.50, DMF); R_f 1.00 in solvent B. *Anal.* ($C_{31}H_{30}N_4O_4S$) C, H, N.

The preparation of the α anomer **2a** was similar except that a larger amount of P_2S_5 (3.0 g) for 0.50 g of **4a** was required for complete reaction. The yield was 0.37 g (72%) of the α anomer **2a**: mp 226–230°; $\lambda_{max}^{pH\ 1}$ 323 mμ (ε 20,300), $\lambda_{max}^{pH\ 7}$ 321 (19,300), $\lambda_{max}^{pH\ 13}$ 312 (21,600); $[\alpha]^{22}D$ +23° (*c* 0.50 DMF); R_f 0.81 in solvent B (R_f 0.31 for **4a**). *Anal.* ($C_{31}H_3PN_4O_4S$) C, H, N.

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(2) A. P. Kimball, G. A. LePage, and B. Bowman, *Can. J. Biochem.*, **42**, 1753 (1964).

(3) A. P. Martinez and W. W. Lee, *J. Org. Chem.*, **34**, 416 (1969).

(4) The formulas are written in the completely aromatic form for convenience, although the 6-hydroxy and 6-thiol derivatives exist as the keto tautomers.

(5) A. P. Martinez, W. W. Lee, and L. Goodman, *ibid.*, **34**, 92 (1969).

(6) These compounds were screened for antitumor activity by Chemotherapy, National Cancer Institute, according to its protocol described in *Cancer Chemotherapy Rept.*, **25**, 1 (1962).

(7) Melting points were determined in a Fisher-Johns apparatus and are uncorrected. Tlc was run on silica gel HF (E. Merck AG Darmstadt) in the following solvents: A, EtOAc; B, MeOH–EtOAc (1:9). The spots were detected by uv light. For the uv spectra, the samples were dissolved in MeOH or 2-methoxyethanol and diluted either five- or tenfold with 0.1 *N* HCl pH 7 buffer or 0.1 *N* NaOH, as required. Where analyses are indicated only by symbol of the elements or functions, analytical results obtained for those elements or functions were within ±0.4% of the theoretical values.

(8) Trade name for the magnesium silicate product of the Floridin Co.