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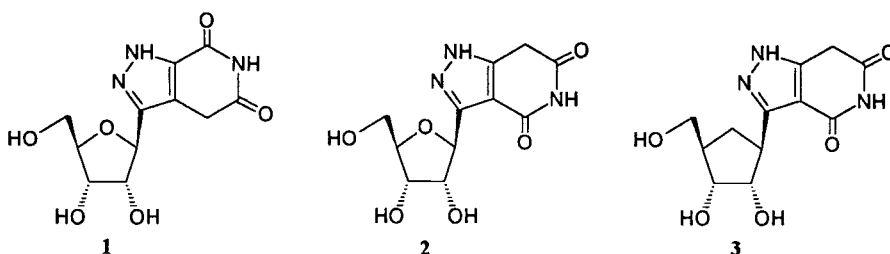
THE SYNTHESIS OF ENANTIOMERICALLY PURE PYRAZOLO[4,3-*c*]PYRIDINE CARBARIBO C-NUCLEOSIDE

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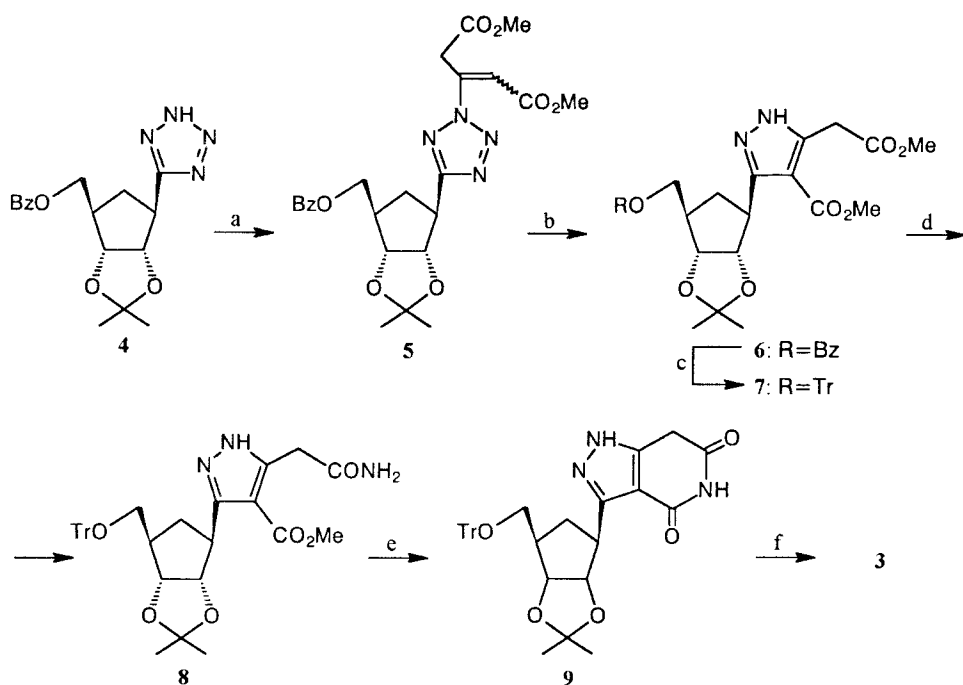
Abstract: The synthesis of (-)-3-[(1*S*,2*S*,3*R*,4*R*)-2,3-dihydroxy-4-(hydroxymethyl)cyclopentan-1-yl]-1*H*-pyrazolo[4,3-*c*]pyridine-4,6(5*H*,7*H*)-dione **3** was accomplished *via* enantiomerically pure carbocyclic 5-(β-*D*-ribofuranosyl)tetrazole **4**.

Recent studies focused on non-standard base pairs possessing an expanding genetic alphabet patterns support a need for new xanthosine analogues with favourable pK_a values.¹ The pK_a values of xanthosine analogues are certainly the outcome of the number and positions of nitrogens in the base. In this respect, the dioxo derivatives of pyrazolo[3,4-*c*]pyridine² **1** and pyrazolo[4,3-*c*]pyridine³ **2** families of *C*-nucleosides represent interesting and novel classes of compounds of this kind.



Herein, we report on the use of the tetrazole synthon **4**⁴ in the formation of sugar modified target *C*-nucleosides. The regiospecific linear synthesis of **2** which has been reported earlier³ seemed adequate to extend on the enantiomerically pure compound **4** to yield a carbocyclic nucleoside **3** related to 7-substituted 3,7-deaza-8-azaxanthosine **2**.

Thus, tetrazole **4**⁴ (Scheme) was transformed into 2-alkenyl tetrazole **5** by its conjugative addition to dimethyl 1,3-allenedicarboxylate.⁵ The compound **5** was thermally



(a) $\text{MeOCOCH}_2\text{C}(\text{Cl})=\text{CHCO}_2\text{Me}$ / Et_3N / THF, -5°C (η 73%)

(b) xylene, 140°C (η 61%)

(c) i, NaOMe/ MeOH; ii, Ph_3CCl / Et_3N / DMAP/ $(\text{CH}_2\text{Cl})_2$, 50°C (η 86%)

(d) 25% NH_3 in MeOH (η 97%)

(e) 0.8M NaOMe in MeOH, reflux (η 60%)

(f) 60% aq. $\text{CH}_3\text{CO}_2\text{H}$ (η 90%)

Scheme

rearranged in xylene into pyrazole 6 via the ring opening by loss of nitrogen and subsequent intramolecular cyclization. The diester 7 was ammonolyzed to give the monoamide 8, which readily cyclized after treatment with sodium methylate in boiling methanol to pyrazolo[4,3-c]pyridine 9. Deprotection of 9 with 60% aq. acetic acid furnished the target compound 3.⁶

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- (3) (a) Prhavic, M.; Townsend, L.B.; Kobe, J. *ibid*, **1991**, *10*, 729. (b) Prhavic, M.; Kobe, J. *ibid*, **1996**, accepted.
- (4) Mohar, B.; Štimac, A; Kobe, J. *ibid*, **1993**, *12*, 793.
- (5) A mixture of tetrazole **4**, Et₃N (1.4 mole equiv.), and dimethyl 3-chloro-2-pentenedioate (1.2 mole equiv.) in THF is stirred at -5°C for 4 h, and concentrated. The residue is dissolved in EtOAc, washed with water, brine, and dried (Na₂SO₄). The concentrated residue is chromatographed on silica gel (eluent petroleum ether/ EtOAc 4:1) to furnish **5** as a light yellow syrup.
- (6) Light amber solid, m.p. = 214-5°C (from abs. ethanol). $[\alpha]_D^{21} = -48.6$ (c 0.5, H₂O). ¹H NMR (299.94 MHz, D₂O/ TMS): δ 1.51 (m, 1H, H-5'a), 2.29 (m, 2H, H-4', H-5'b), 3.68 (m, 4H, CH_aH_bOH, H-7_a, H-7_b), 3.91 (m, 1H, H-1'), 3.99 (m, 1H, H-3'), 4.18 (m, 1H, H-2') ppm. ¹³C NMR (75.43 MHz, Me₂SO-d₆): δ 30.07 (C-5'), 31.86 (br C-7), 40.57 (br C-1'), 46.89 (C-4'), 63.28 (CH₂OH), 73.18 (C-3'), 75.55 (C-2'), 106.23 (C-3a), 148.60 and 149.33 (br C-3, br C-7a), 162.18 (C-4), 171.33 (br C-6) ppm. IR (KBr): 3400 (NH, OH), 1704 (CO) cm⁻¹. FABMS *m/z* 282 (MH⁺).