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Treatment of 1-(2,3-*O*-isopropylidene-β-D-ribofuranosyl)-2-oxo-4-imidazoline-4-carboxylic acid methyl ester with formaldehyde gave the 5-hydroxymethyl derivative which, after acetylation, gave the 5-cyanomethyl derivative by treatment with tetra-*n*-butylammonium cyanide. The 2,5′-*O*-cyclo derivative of the 5-cyanomethylimidazole-4-carboxylate was converted to the title compound by treatment with ammonia. The present sequence of reactions furnished the chemical conversion of uridine to a 3-deazaguanosine *via* the imidazole nucleoside as the intermediate.

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Sir:

3-Deazaguanosine was recently synthesized (1) by the condensation of an imidazole base with a sugar portion followed by the ring closure of the pyridine moiety. This unique guanosine analog was found to be effective against various viral infections in mice (2). In our continuing studies of the chemical transformation of naturally occurring nucleosides to other nucleosides of potential biochemical interests, we have recently achieved (3) the converison of uridine to inosine. In the present report we wish to describe a conversion of an imidazole derivative readily accessible from uridine (4) to the 8,5′-*O*-cyclo-3-deazaguanosine.

Treatment of 1-(2,3-*O*-isopropylidene-β-D-ribofuranosyl)-2-oxo-4-imidazoline-4-carboxylic acid methyl ester (**1**) (3,5) with 37% formaldehyde in 1*N* sodium hydroxide for 2 days at room temperature afforded the 5-hydroxymethyl derivative in the form of the carboxylate salt (**2**). Esterification of **2** with methyl iodide gave the foamy compound (**3**); ms: m/e 329 (M - 15); nmr (100 MHz, DMSO-d_6): δ 1.30, 1.49 (s, 3 + 3, Me_2C), 3.32 (s, 3, MeO), 3.40-3.70 (m, 2, 5′-H), 3.88-4.12 (m, 1, 4′-H), 4.54 (d, 1, 5-Ha), 4.78 (d, 1, 5-Hb), 4.64-4.88 (dd, 1, 3′-H), 5.34 (dd, 1, 2′-H), 5.80 (d, 1, 1′-H, $J_{1',2'}$ = 2.0 Hz), 10.90 (bs, 1, NH); uv (water): λ max 270 nm (ε, 12,000), λ min. 232 nm (ε, 1360). Treatment of **3** with acetic anhydride in pyridine followed by a chromatographic purification afforded the di-*O*-acetate (**4**) in 76% yield; ms: m/e 428 (M^+), 413 (M - 15); nmr (deuteriochloroform): δ 1.38, 1.57 (s, 3 + 3, Me_2C), 2.06, 2.11 (s, 3 + 3, Ac_2), 3.88 (s, 3, MeO), 4.30 (bs, 3, 4′,5′-H), 4.97 (dd, 1, 3′-H), 5.24 (d, 1, 5-Ha), 5.48 (dd, 1, 2′-H), 5.57 (d, 1, 5-Hb), 5.66 (d, 1, 1′-H, $J_{1',2'}$ = 2.0 Hz), 10.35 (bs, 1, NH); uv (methanol): λ max 273.5 nm (ε, 12,000), λ min 233 nm (ε, 1,400). The 5-acetoxy group in **4** was expected to be a good leaving group for nucleophilic displacement by taking account of the fact that 4-acetoxymethylimidazole is rapidly hydrolyzed by way of the *exo*-methylene intermediate (6). Treatment of **4** with tetra-*n*-butylammonium cyanide in chloroform at room temperature and successive purification through a silica gel column gave the 5-cyanomethyl derivative (**5**) in 82% yield; ir (potassium bromide): 2270 cm^{-1} (CN); nmr (deuteriochloroform): δ 1.38, 1.58 (s, 3 + 3, Me_2C), 2.06 (s, 3, Ac), 3.91 (s, 3, MeO), 3.98 (d, 1, 5-Ha), 4.33 (d, 1, 5-Hb), 4.10-4.38 (m, 3, 4′,5′-H), 4.96 (dd, 1, 3′-H), 5.49 (dd, 1, 2′-H), 5.72 (d, 1, 1′-H, $J_{1',2'}$ = 1.5 Hz), 9.88 (bs, 1, NH). Compound **5** was deacetylated with methanolic ammonia to give **6**. The 5′-*O*-tosylation of **6** gollowed by cyclization by treatment with triethylamine in chloroform afforded 2,5′-*O*-cyclo-1-(2,3-*O*-isopropylidene-β-D-ribofuranosyl)-5-cyanomethyl-2-oxyimidazole-4-carboxylic acid methyl ester (**7**) in 67% yield as crystals, m.p. 225-227°; ms: m/e: 335 (M^+), 320 (M - 15); ir (potassium bromide): 2260 cm^{-1} (CN); nmr (deuteriochloroform): δ 1.36, 1.56 (s, 3 + 3, Me_2C), 3.89 (s, 3, MeO), 4.80 (d, 1, 5′-Ha), 4.20 (d, 1, 5-Hb, J gem = 18.0 Hz), 4.42 (dd, 1, 5′-Hb, J gem = 13.0 Hz), 4.59 (d, 1, 5-Ha), 4.71 (bs, 1, 4′-H), 4.84 (d, 1, 3′-H), 5.07 (d, 1, 2′-H), 5.78 (s, 1, 1′-H); uv (methanol): λ max 243 nm (ε, 9,100). The 2,5′-*O*-cyclo compound (**7**) was treated with methanolic ammonia at 100° for 2.5 hours in a sealed tube to give, after purification with preparative thin layer chromatography, 8,5′-*O*-cyclo-2′,3′-*O*-isopropylidene-8-oxy-3-deazaguanosine (**8**) in 40.5% yield. The spectral data; ms: m/e: 320 (M^+); uv (1*N* hydrochloric acid): λ max 312, 276 nm (ε, 7,200, 8,600), λ min 299, 243 nm (ε, 6,700, 3,300); (water): λ max 306, 265 nm (ε, 7,800, 10,800), λ min 286, 231 nm (ε, 5,500, 2,300), (1*N* sodium hydroxide): λ max 287 sh, 271 nm (ε, 8,700, 10,700), λ min 236 nm (ε, 3,800) and nmr (DMSO-d_6): δ 1.30, 1.46 (s, 3 + 3, MeC), 3.92 (d, 1, 5′-Ha), 4.50 (dd, 1, 5′-Hb, J gem = 13.0 Hz), 4.66 (bs, 1, 4′-H), 4.82 (d, 1, 3′-H), 5.04 (d, 1, 2′-H, $J_{2',3'}$ = 6.0 Hz), 5.53 (s, 1, 1′-H), 5.54 (bs, 2, NH_2), 5.78 (s, 1, 3-H), 10.18 (bs, 1, NH) are well assignable to the structure of **8**. The initially formed 4-carboxamide derived from **7** must have cyclized completely under these reaction conditions.

Since the cleavage of the cyclo linkage with hydrazine and successive oxidative dehydrazination was realized in

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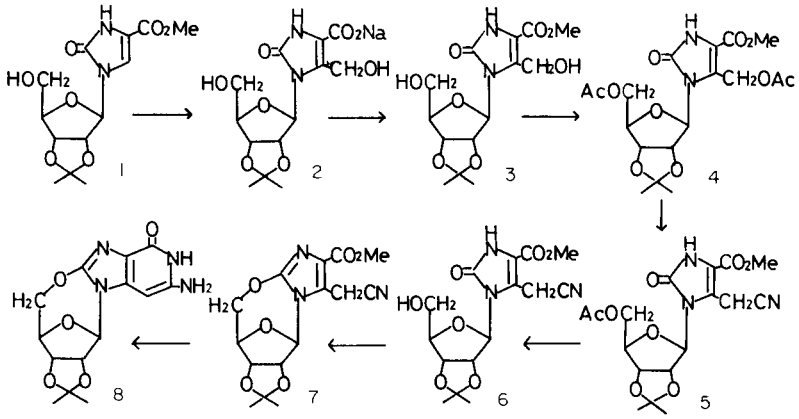

the conversion of 8,2′-*O*-cycloadenosine to arabinofuranosyladenine by Reese, *et al.* (7), the formation of **8** would mean the synthesis of 3-deazaguanosine from uridine by the manipulation of the heterocyclic moiety (8).

REFERENCES AND NOTES

(1) P. D. Cook, R. J. Rousseau, A. M. Mian, P. Dea, R. B. Meyer Jr., and R. K. Robins, *J. Am. Chem. Soc.*, **98**, 1492 (1976).

(2) L. B. Allen, J. H. Huffman, P. D. Cook, R. B. Meyer Jr., R. K. Robins, and R. W. Sidwell, *Antimicrob. Agents Chemother.*, **12**, 114 (1977).

(3) H. Tanaka and T. Ueda, *Nucleic Acids Research Special Publication*, **3**, 17 (1977).

(4) B. A. Otter, E. A. Falco, and J. J. Fox., *J. Org. Chem.*, **33**, 3593 (1968); *idem., ibid.*, **34**, 2636 (1969).

(5) H. Tanaka, T. Takahashi, H. Togashi, and T. Ueda, *Chem. Pharm. Bull.*, **26**, 33 (1978).

(6) T. C. Bruice and T. H. Fife, *J. Am. Chem. Soc.*, **83**, 1124 (1961).

(7) J. B. Chattopadhyaya and C. B. Reese, *J. Chem. Soc., Chem. Commun.*, 414 (1977).

(8) Satisfactory elemental analyses have been obtained for the newly synthesized compounds.