Synthesis of C-Nucleosides. 5-Amino-2-ribofuranosylimidazole Derivatives

By JEAN IGOLEN* and TAM HUYNH DINH

(*Service de Chimie Thérapeutique, Institut Pasteur, Paris, France*)

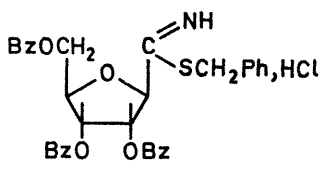
Summary Benzyl tri-*O*-benzoylribofuranosylthioformimidite reacts with α-aminocyanoacetic acid derivatives to yield *C*-imidazole nucleosides which are further cyclized into purines.

IN the last few years, interest has focused on *C*-nucleosides —pseudouridine, showdomycin, formycins, and pyrazomycin. These nucleosides are characterized by the unusual carbon–carbon linkage between the carbohydrate and the heterocycle, and seemed to be powerful tools for biochemical investigations and antimitotic or antiviral research.[1]

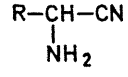
We have developed a convenient route for the synthesis of a series of imidazole *C*-nucleosides: the modified Pinner reaction,[2] on tri-*O*-benzoyl-β-D-ribofuranosyl cyanide[3] gives a good yield of the thioformimidite (I) which reacts with α-aminocyanoacetic acid derivatives $H_2N{\cdot}CHR{\cdot}CN$ (II) to give 5-amino-2-tri-*O*-benzoylribofuranosylimidazoles (III a—d).

The interest of this synthesis lies in the fact that aminoimidazoles, and especially the 5-amino-4-imidazolecarboxamide ribotide, are key intermediates in the biosynthesis of purines. The imidazole derivatives (III a, b) are indeed successfully ring-closed by heating under reflux with formamidine acetate[4] or diethoxymethyl acetate,[5] yielding 8-tri-*O*-benzoylribofuranosylpurines (IV a, b).

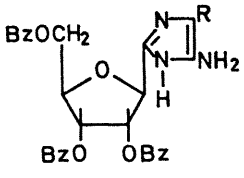
All crystalline compounds gave analytical and spectral data in accord with the assigned structures. Anticancer activity for these promising new compounds is under evaluation.



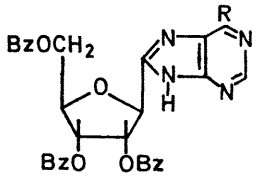
(I)



(II) a; R = CN
b; R = $CONH_2$
c; R = CO_2Me
d; R = CO_2Et



(III) a; R = CN
b; R = $CONH_2$
c; R = CO_2Me
d; R = CO_2Et



(IV) a; R = NH_2
b; R = OH

We thank Professor Marc Julia for his interest in this work and helpful discussions; also the "Ligue Nationale Française contre le Cancer" for a subvention.

(*Received, August 5th*, 1971; *Com.* 1367.)

[1] S. Hanessian and T. H. Haskell, in "The Carbohydrates", 2nd edn, vol. 2, Academic Press, New York, 1970, p. 139; R. J Suhadolnik, "Nucleoside Antibiotics", Wiley, Interscience, New York, 1970.
[2] M. Julia and T. Huynh Dinh, *Bull. Soc. chim. France*, 1971, 1303.
[3] M. Bobek and J. Farkas, *Coll. Czech. Chem. Comm.*, 1969, **34**, 247.
[4] E. C. Taylor and R. W. Hendess, *J. Amer. Chem. Soc.*, 1965, **87**, 1995.
[5] R. J. Rousseau, R. K. Robins, and L. B. Townsend, *J. Amer. Chem. Soc.*, 1968, **90**, 2661.