Note

Conversion of cytidine into 1-β-D-arabinofuranosylcytosine

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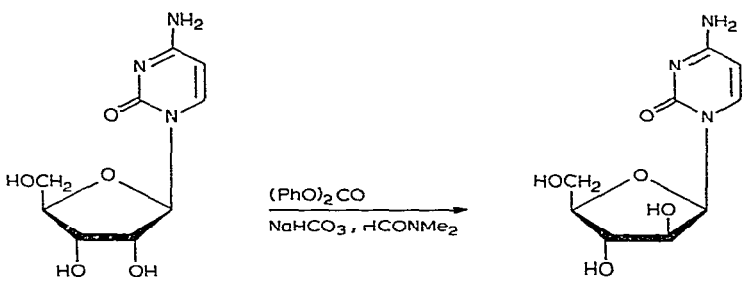
1-β-D-Arabinofuranosylcytosine (ara-C), a cytoxic, antiviral nucleoside[1] has recently been shown to be active against some acute leukemias[2] Shimizu and Shimizu[3] and Sanchez and Orgel[2] have achieved syntheses of ara-C by building the molecule from sugar precursors Nagyvary[4,5] has converted cytidine 3′-phosphate into the 3′-phosphate of ara-C We now report a simple conversion of cytidine into ara-C

The conditions used are those that readily effect conversion of uridine into $O^2,2'$-anhydrouridine[6] Under these conditions cytidine should be converted into $O^2,2'$-anhydrocytidine, which should be rapidly converted[7] into ara-C Thus cytidine (100 mg), diphenyl carbonate (115 mg) and sodium hydrogen carbonate (5 mg) were heated for 15 min at 150° in *N,N*-dimethylformamide (0 2 ml) The solution was applied to a t l c plate of silica gel (20 × 20 cm , silica gel DSF-5, Mondray Ltd , Montreal, Quebec) which was developed first with 7 3 chloroform–ethanol and then with ethanol The band containing ara-C separated cleanly and was eluted with ethanol Concentration gave pure ara-C (yield 40%), λ_{max}^{2MHCl}. 280 and 210 nm, λ_{max}^{EtOH} 275 and 232 nm, λ_{max}^{2MNaOH} 276 and 223 nm, λ_{max} 6 05, 6 57 μm, the compound was identical in all respects to authentic ara-C (Sigma Chemical Co , St Louis, Missouri)



The reaction was conducted at several temperatures and monitored by paper chromatography (see Table I) The optimum conditions found were those reported here For example, at 135° cytidine was completly decomposed after 60 min, with a

maximum yield of ara-C of 32% At 140° the yield reached a maximum of 35% after 45 min

TABLE I

CHROMATOGRAPHIC R_F VALUES

Compound	R_F[a]	R_F[b c]	R_F[b d]
Ara-C (authentic)	0 58	0 50	0 67
Product ara-C	0 58	0 50	0 67
Cytidine	0 48	0 44	0 62

[a]T l c Eastman Chromagram 6060, with fluorescent indicator and ethanol as developer [b]Whatman 3 MM paper [c]Isopropyl alcohol–ammonium hydroxide–water (7 1 2) as developer [d]Ethanol–water (7 3) as developer

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