

CLEAVAGE OF 8,2'-ANHYDRO-8-OXY-9- β -D-ARABINOFURANOSYLADENINE
WITH HYDROGEN SULFIDE AND ITS INTERCONVERSION WITH 8,5'-CYCLONUCLEOSIDE

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We have reported previously (1) on the synthesis of 8,2'-anhydro-8-oxy-9- β -D-arabino-furanosyladenine (I) and its acid hydrolysis. As we have developed a method suitable for synthesizing I in quantity (2), reaction of its cleavage with hydrogen sulfide and dilute alkali was investigated.

When compound I was heated with excess hydrogen sulfide in pyridine at 100° for 14 hr, a compound having mp 154°(decomp.) (II) (3) was obtained in a yield of 74.4%. This compound had UV absorption properties ($\lambda_{\text{max}}^{\text{pH1}}$ 223, 242, 298 (sh), 308 (ϵ 21,900); $\lambda_{\text{max}}^{\text{pH7}}$ 238, 298, 305.5 (ϵ 24,800); $\lambda_{\text{max}}^{\text{pH13}}$ 228, 296.5 nm (ϵ 21,100), 303 nm (sh)), which resembled with those of 8-mercaptadenosine (4). NMR of compound II showed signals at 8.07 δ (s, H-2, 1H), 6.82 δ (s, NH₂-6, 2H) and 6.70 δ (d, H-1', 1H, J_{1'-2'}=6 cps). Paper electrophoresis in 0.05M borate buffer (pH 6.8) gave R_{adenosine} 0.72. Paper chromatography : R_f 0.43 (A), 0.36 (B) and 0.25 (C) (5). These properties suggested a structure, 8-mercapto-9- β -D-arabinofuranosyl-adenine (II) for this compound.

Compound II was then desulfurized with Raney nickel (W-2). Recrystallization of the product from methanol gave a compound having mp 260°(decomp.) (III) in a yield of 36.7%. UV absorption properties of III : $\lambda_{\text{max}}^{\text{pH1}}$ 258 (ϵ 15,100), $\lambda_{\text{max}}^{\text{pH7}}$ 260 (ϵ 15,400), $\lambda_{\text{max}}^{\text{pH13}}$ 260 nm (ϵ 15,000). In NMR spectra it showed a singlet peak of H-8 at 8.12 δ (s, 1H), together with peaks at 8.18 δ (s, H-2, 1H), 7.18 δ (s, NH₂-6, 2H) and 6.27 δ (d, H-1', 1H, J_{1'-2'}=4.8 cps).

Migration in paper electrophoresis (borate) showed $R_{\text{adenosine}} = 0.63$, which suggested arabinosyl configuration. R_f 's were 0.43 (A), 0.09 (B) and 0.42 (C). Direct comparison of III with an authentic sample (6) of 9- β -D-arabinofuranosyladenine shows completely identical properties of both specimens. This reaction constitutes the first chemical conversion of the naturally occurring adenosine to arabinosyladenine.

When compound I was heated with 0.01N sodium hydroxide at 60° for 3 hr, a crystalline compound (IV) was obtained in a yield of 37% together with the starting material (38%). Compound IV had UV absorption: $\lambda_{\text{max}}^{\text{pH1}}$ 261 (ϵ 17,400), 272; $\lambda_{\text{max}}^{\text{pH7}}$ 261.5 (ϵ 18,300); $\lambda_{\text{max}}^{\text{pH13}}$ 261.5 nm (ϵ 17,900). In NMR spectrum it lacks H-8 signal and had peaks at 8.02 δ (s, H-2, 1H), 6.82 δ (s, NH₂-6, 2H) and 6.25 δ (d, H-1', 1H, $J_{1'-2'} = 6$ cps). R_f 's were 0.44 (A) and 0.39 (C). These properties suggested an arabinofuranosyl nucleoside having the cyclonucleoside structure. As shown in CD curve in Fig. 1, compound IV had a very large Cotton effect around 260 nm (B-band region). As predicted from the magnitude of Cotton effect of purine β nucleosides (7), $\theta = 25,000$ suggested 8,5'-O-cyclonucleoside structure for IV. This conclusion was further supported by the conversion of IV with 0.01N sodium hydroxide (60°, 3 hr) to give an equilibrium mixture of 8,2'- and 8,5'-9- β -D-arabinofuranosylcyclonucleoside (I and IV) in ca 60 : 40. This fact eliminates a possibility of 8,3'-O-cyclonucleoside structure for compound IV.

This type of interconversion of cyclonucleosides has not been reported in pyrimidine nucleoside series and should be investigated in future.

References

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3. All crystalline compounds gave satisfactory elemental analysis values.

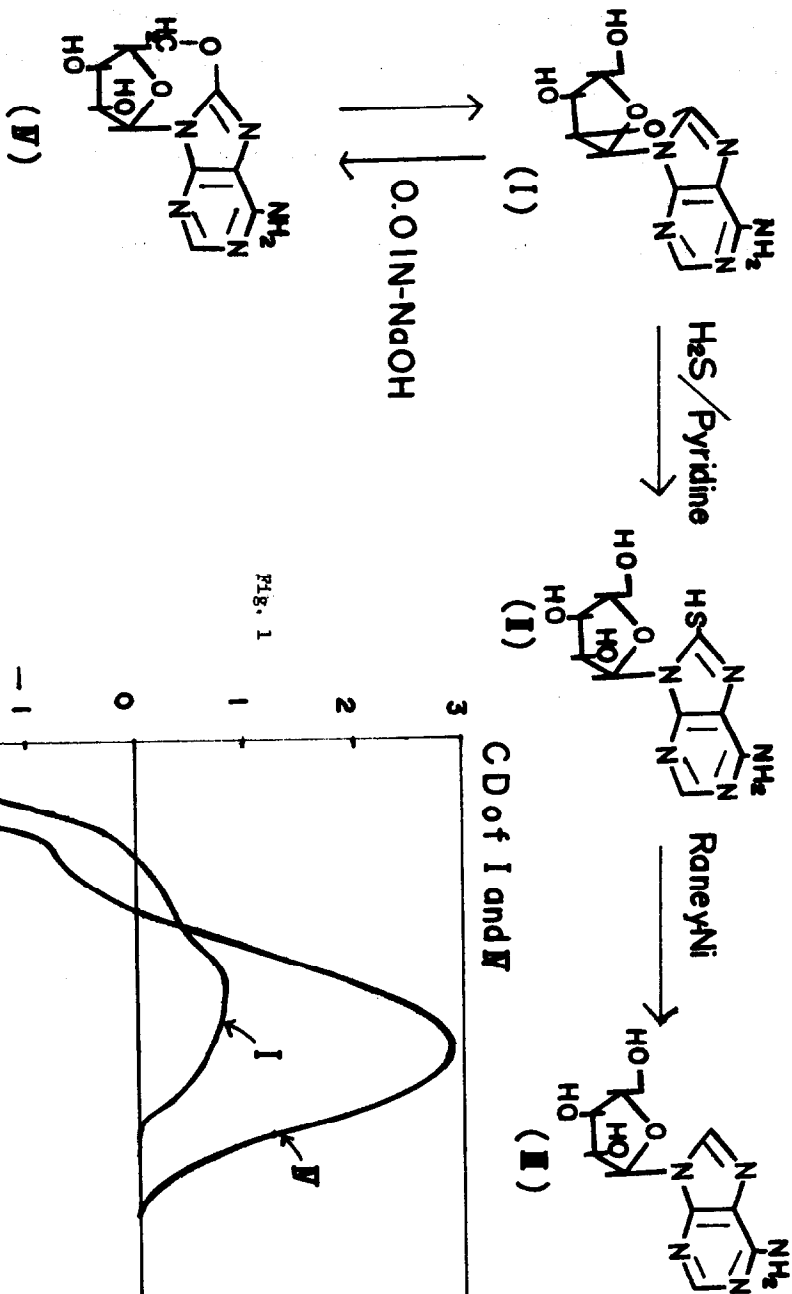
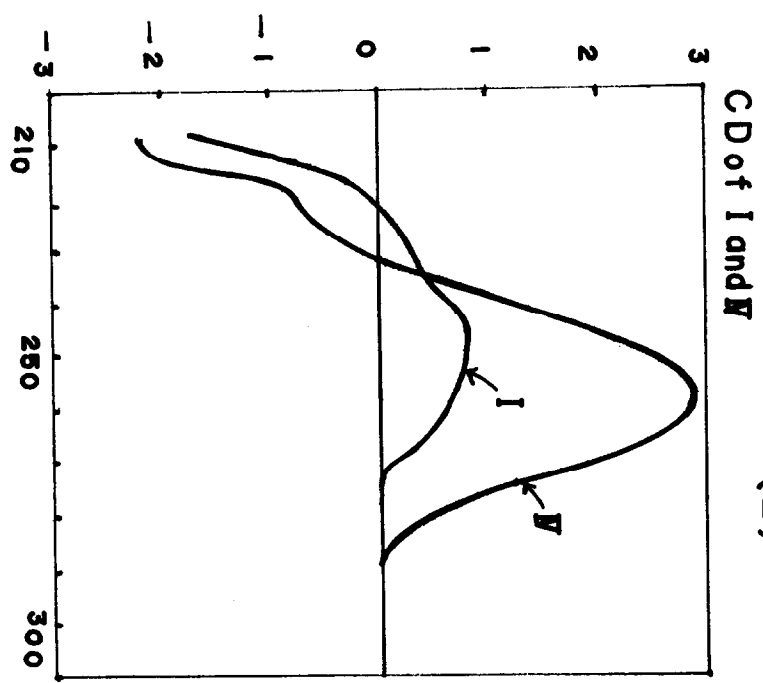


Fig. 1



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5. Solvent A, water adjusted to pH 9 with ammonia; B, n-butanol-water (86 ; 14);
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