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ONE STEP REARRANGEMENT OF 8,5'-O-CYCLOADENOSINE TO N^3,5'-CYCLONUCLEOSIDE

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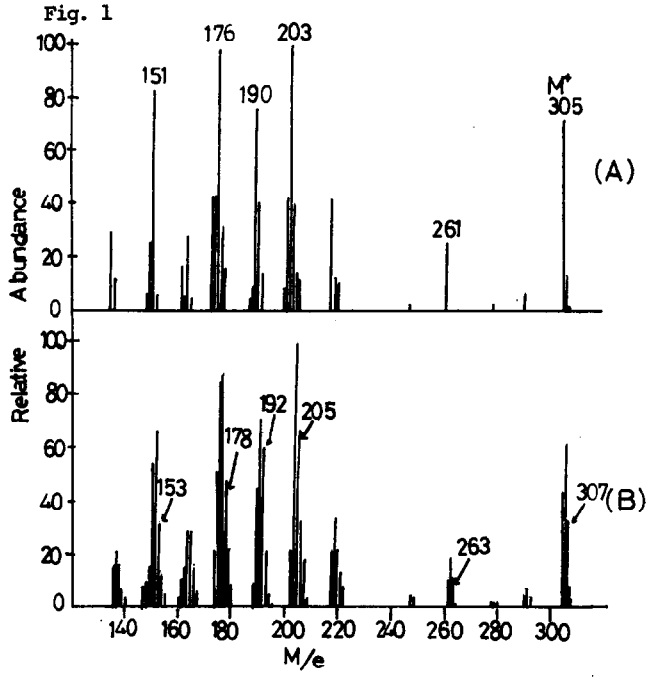
Previously we have reported several examples of one step rearrangement of purine 8-cyclonucleosides. 8,2'- and 8,3'-O-cycloadenosine rearranged to 8,5'-O-cyclonucleosides having a arabino- or xylofuranose moiety by the weak alkaline treatment (1). 8,3'-S-Cycloadenosine sulfoxide also rearranged to 8,5'-O-cyclo-3'-xylosulfinic acid by the same treatment (2). In this communication we report a one step rearrangement of 8,5'-O-cycloadenosine (I) to an N^3,5'-cyclonucleoside (II).

When compound I (3) (615 mg, 2 mmoles) was heated with sodium chloride (dried at 70° for 12 hr over phosphorus pentoxide in a vacuum of 30 mm/Hg) in dimethylsulfoxide (20 ml) at 130-140° for 9 hr under atomosphere of nitrogen, a non-migrating spot other than that of starting material appeared on TLC. Amount of this material increased during 9 hrs' heating. Evaporation and extraction of the reaction mixture with water gave a residue, which was recrystallized from water-methanol mixture. Colorless prisms (II), mp 270° (decomp.), were obtained in the yield of 215 mg (35%). Examination of the water insoluble material by TLC (silica gel, $CHCl_3$-EtOH, 10:1) showed existence of another compound having Rf 0.50 in small amount and the starting material (recovered 27 mg). The compound having Rf 0.50 showed λ_{max}^{EtOH} at 265 nm, but the structure was unknown.

Compound II had UV absorption properties: $\lambda_{max}^{H^+}$ (ε) 223 (24200), 393 (23000); $\lambda_{max}^{H_2O}$ (ε) 220 (26500), 300 (18300); $\lambda_{max}^{OH^-}$ (ε) 308 nm (26500). In an alkaline solution at room temperature UV absorption at 240-300 nm decreased rapidly. Elemental analysis suggests a molecular formula of $C_{13}H_{15}O_4N_5$ (M.W.= 305). The molecular weight was also supported from a molecular ion peak, M^+ 305 (62%) in mass spectrum (Fig. 1a). A fragment ion $(M-102)^+$ appeared as a base peak corresponding to an ion (V), which indicated that an N-C bond other than the nucleosidic linkage was formed. Other principal peaks were similar to those found in mass spectra of adenine cyclonucleosides (4). IR spectrum of II gave a C=O band at 1700 cm^{-1}, which appeared at lower wave number than 8-C=O of 8-ketoadenosine. NMR spectra taken in d_6-DMSO at 90 MHz (tetramethylsilane

Fig. 1



as internal standard) gave following peaks (ppm): δ 1.2 and 1.4 (s, CH_3), 4.4-4.8 (m, sugar Hs), 5.9 (s, 1 H, H-1'), 7.2-7.5 (m, 2 H, NH, disappeared in D_2O), 8.0 (s, 1 H, H-2). Two active protons were also proved from the mass spectrum of deuterated II (M^+ 307, 33%) (Fig. 1b). CD spectrum (taken in water at 0.2 OD/ml concentration in a 10 mm light path cell) of compound II was as shown in Fig. 2. A positive cotton band at 297 nm suggested N^3,5'-cyclonucleoside structure (5), which had a syn conformation. Reaction of compound II with $NaNO_2$ in acetic acid showed no change in UV spectra suggesting that NH_2 group was not present. From these data we assigned the compound II to 2',3'-O-isopropylidene-N^3,5'-anhydro-8-oxyadenosine. Finally, from 2',3'-O-isopropylidene-5'-O-tosyl-8-oxyadenosine (IIIa) (UV: $\lambda_{max}^{H^+}$ 268, 280; λ_{max}^{MeOH} 269; $\lambda_{max}^{OH^-}$ 285 nm) compound II was obtained by refluxing in dioxane to give compound IV (UV: $\lambda_{max}^{H^+}$ 294, $\lambda_{max}^{H_2O}$ 295, $\lambda_{max}^{OH^-}$ 310 nm) followed by the brief treatment with ammonia. This sample was identical with the sample obtained above.

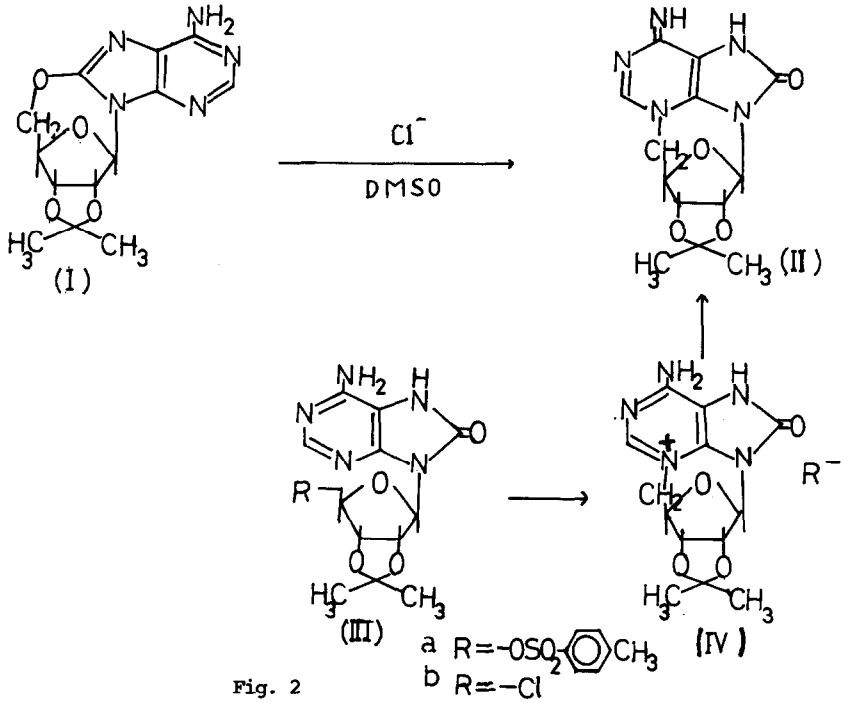
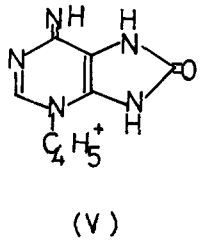
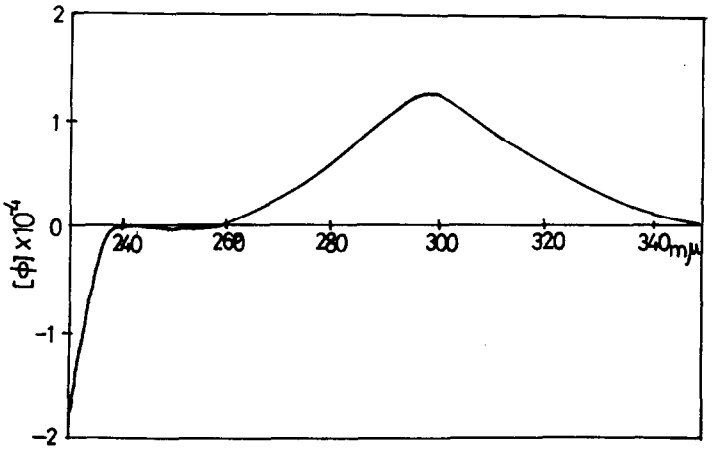

Cl⁻
DMSO
(I)
(II)
(III)
(IV)
a R=-OSO2-C6H4-CH3
b R=-Cl

Fig. 2



(V)


2
1
0
-1
-2
[φ]x10⁻⁴
240
260
280
300
320
340mμ

From these results we concluded that the chloride anion attacked first at 5'-carbon to give 8-oxy-5'-deoxy-5'-chloro adenosine (IIIb), which was subsequently cyclized to N^3,5'-cyclonucleoside as in the case of 5'-tosylate (IIIa).

References

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