Synthesis of Purine Cyclonucleoside having 8,3'-O-Anhydro Linkage*¹

Since the first purine cyclonucleoside has been reported,¹⁾ a number of purine nucleosides having 8,2'-(S- and -O)-,²⁻⁴⁾ 8,5'-(S- and -O)-,^{5,6)} and 8,3'-S-²⁾ anhydro linkage were synthesized. However, the synthesis of a cyclonucleoside having 8,3'-O-anhydro linkage could not be performed, mainly because of the difficulty in the cyclization of 3'-tosylated 8-oxyadenosine presumably due to a large steric distortion.³⁾ As the first 2,3'-cyclonucleoside has been synthesized in the pyrimidine deoxyribonucleoside,⁷⁾ we attempted to synthesize 8,3'-anhydro-8-oxy-9- β -D-(2-deoxythreopentofuranosyl)adenine (I) starting from 2'-deoxyadenosine.

8-Bromo-2'-deoxyadenosine⁸⁾ was converted to 5'-trityl derivative*³ (III) (UV: $\lambda_{\max}^{pH 1}$ 263 m μ , $\lambda_{\max}^{EtOH}$ 265 m μ , $\lambda_{\max}^{pH 1}$ 265 m μ . IR: $\nu_{\max}^{KBr}$ cm⁻¹: 1075 (sugar C-O-C), 700 (trityl). Paper chromatography: Rf (A)*³ 0.84, Rf (B) 0.91, Rf (C) 0.90 in the yield of 78%.

*¹ A preliminary account of this study has been presented at the XXI International Congress IUPAC, 1967, Praha.

*² All crystalline compounds appeared in this paper had the elemental analysis value satisfactorily in agreement with the theoretical one.

*³ Rf (A) stands for the Rf value in the solvent A. Solvent used were: A, *n*-BuOH-H₂O, 86:14; B, iso-PrOH-ammonia-H₂O, 7:1:2; C, *n*-BuOH-AcOH-H₂O, 5:2:3; D, *n*-PrOH-H₂O (pH 6.5), 3:1; E, EtOH-M NH₄OAc (pH 7.5), 7:3.

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Compound III was then tosylated with 1.5 equivalents of tosyl chloride. 3'-O-Tosyl-5'-O-trityl-8-bromoadenosine (VI) (Prisms from EtOH-dioxane, m.p. 176~177°. UV: $\lambda_{\max}^{\text{pH } 11}$ m μ : 264, 272 (shoulder); $\lambda_{\max}^{\text{EtOH}}$ 264 m μ ; $\lambda_{\max}^{\text{pH } 11}$ 264 m μ . IR: $\nu_{\max}^{\text{KBr}}$ cm $^{-1}$: 1570 (covalent tosylate), 1070 (sugar C-O-C), 700 (trityl). Paper chromatography: Rf (A) 0.87, Rf (B) 0.82, Rf (C) 0.89, thus obtained, was converted to 8-oxy derivative by the treatment with anhydrous sodium acetate in acetic anhydride, which was superior to acetic acid⁹⁾ in preventing cleavage of the glycosidic linkage in 2'-deoxynucleoside. Resulting 8-oxy compound (V) (amorphous powder. UV: $\lambda_{\max}^{\text{pH } 11}$ 287 m μ ; $\lambda_{\max}^{\text{EtOH}}$ 283 m μ ; $\lambda_{\max}^{\text{pH } 11}$ 267 m μ ; 301 m μ . IR $\nu_{\max}^{\text{KBr}}$ cm $^{-1}$: 1740~1745 (8-CO), 1700~1710 (acetamide), 1170 (covalent tosylate). Paper chromatography: Rf (A) 0.89, Rf (B) 0.83, Rf (C) 0.90) was finally subjected to cyclization

Fig. 1. Optical Dispersion Curve of 8,3'-Anhydro-8-oxy-9- β -D-(2-deoxythreopentofuranosyl)adenine

bathochromic region from those of 8-methoxyadenosine¹⁰⁾ and elemental analysis data suggested the structure 8,3'-anhydro-8-oxy-9- β -D-(2-deoxythreopentofuranosyl)adenine for compound I. This structure was further supported by the optical rotatory dispersion study of I. As shown in Fig. 1, the optical rotatory dispersion (ORD) curve of I has a positive Cotton effect around 260 m μ . This is in contrast to the natural purine nucleoside, which has negative Cotton effect in the major absorption region.¹¹⁾ The inversion of the Cotton effect could be ascribed to the rotation of base around the nucleosidic linkage and the fixation at certain angle by the anhydro linkage.¹²⁾

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Received June 5, 1967

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