in this case; the relative proportions of products of type Ⅶ and Ⅹ, and of other by-products, depends very markedly upon the substitution pattern of the octalone studied: between 80% of indane in cases a and c, to 80% of tetralin in cases b and d.

The most remarkable features of this aromatization are its ease and cleanliness in the case where no angular methyl group hinders it, with HBr/AcOH, *p*-TsOH/AcOH, CF_3CO_2H or polyphosphoric acid (PPA). For example the trimethyloctalone (Ⅵc) with PPA at 150° gives quantitatively the trimethyltetralin (Ⅷc) in two minutes.

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Synthesis of 8-Hydroxypurine Nucleosides

Recently, 8-hydroxynucleosides draw attention of many investigators, because of their biological interest.[1~3] From the chemical point of view, they also are interest as the key intermediate of the synthesis of purine cyclonucleosides[4,5] having O-anhydro linkage.

In order to meet this requirement, many attempts were made in this laboratory to hydrolyze halogen atom substituted at 8-position. However, the acid lability of purine nucleoside and alkaline instability of 8-hydroxypurine nucleoside gave only unsatisfactory results.

We found that, when 8-bromo derivatives of adenosine and guanosine were heated in acetic acid with excess of sodium acetate, desired 8-hydroxy compounds were obtained in a good yield. 8-Bromoguanosine (Ⅰ) was heated with ten fold excess of anhydrous sodium acetate (fused freshly) in glacial acetic acid at 118° for 3 hours. Resulting white solid has $\lambda_{max}^{pH\,2}$ mμ: 242, 292; $\lambda_{max}^{pH\,7}$ mμ: 242, 292; $\lambda_{max}^{pH\,10}$ mμ: 251, 279. The similar solubility of this compound with that of sodium acetate in many solvents made it difficult to purify this specimen. In order to circumvent this difficulty 2′,3′-O-isopropylidene-8-bromoguanosine (Ⅱ) was reacted in acetic acid with sodium acetate and 2′,3′-O-isopropylidene-8-hydroxyguanosine*1 (Ⅲ) was obtained as a hard glass. Acidic removal of isopropylidene group gave 8-hydroxyguanosine (Ⅳ), m.p. >180°(decomp.), in 38% yield. *Anal.* Calcd. for $C_{10}H_{13}O_6N_5\cdot\frac{1}{2}H_2O$: C, 38.96; H, 4.54; N, 22.72. Found: C, 38.80; H, 4.72; N, 22.21. Ultraviolet absorption properties: $\lambda_{max}^{pH\,2}$ mμ: 245.5, 292.5; $\lambda_{max}^{pH\,7}$ mμ: 245.5, 292.5; $\lambda_{max}^{pH\,10}$ mμ: 258, 280. Infrared absorption ν_{max}^{Nujol} cm^{-1}: 1720 (8-CO). Paper chromatography: Rf 0.10 (1-butanol-water, 86:14), Rf 0.69 (water, pH 10). This sample was identical in many respects with that obtained above. 8-Hydroxyguanosine

*1 Although 8-hydroxypurine may be obtained *via* an 8-acetoxy compound, the latter compound could not be isolated.

1) H. S. Forrest, D. Hatfield and J. M. Lagowski: J. Chem. Soc., **1961**, 963.
2) R. Lohrmann, J. M. Lagowski, H. S. Forrest: *Ibid.*, **1964**, 452.
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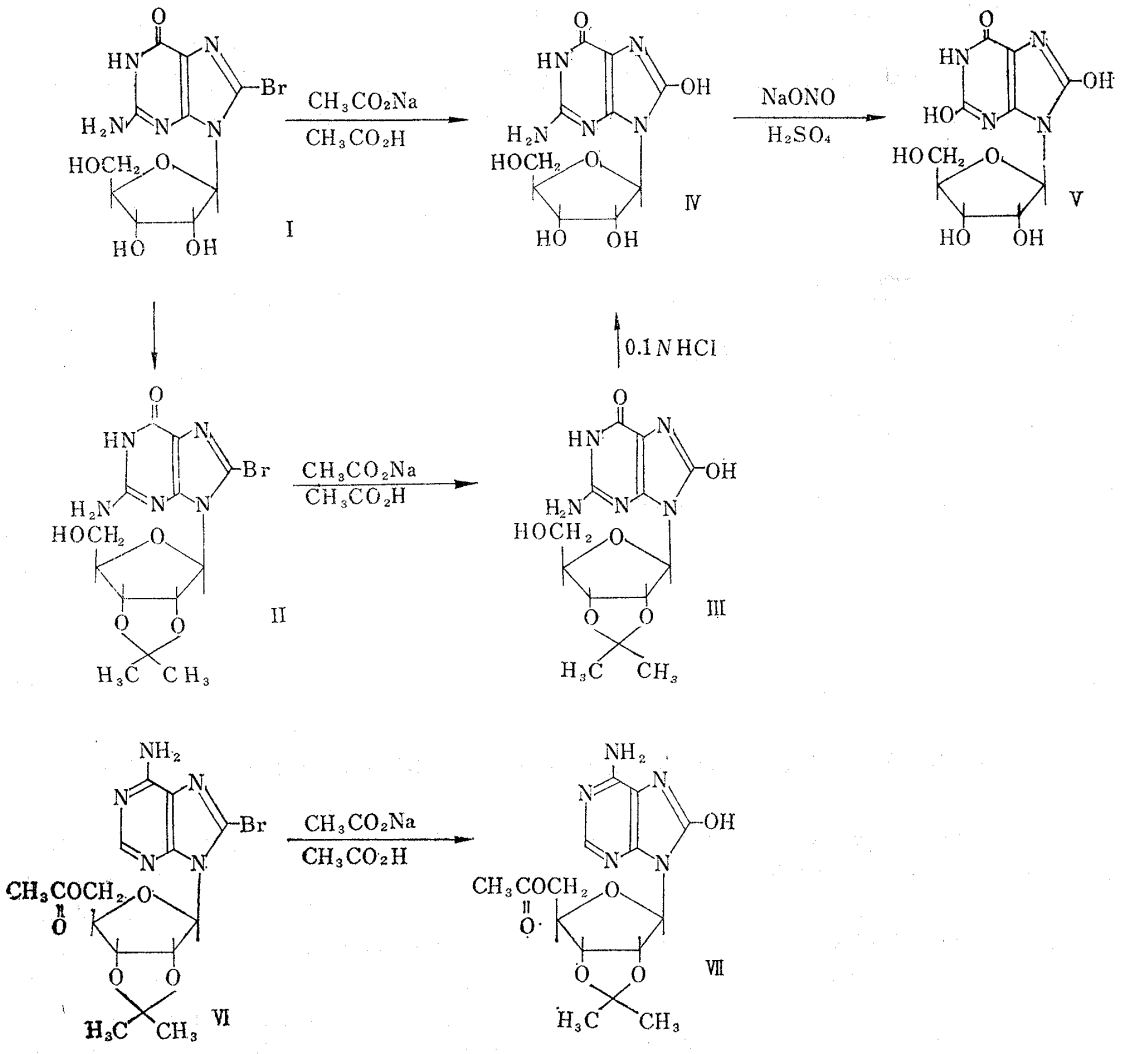
5) M. Ikehara, H. Tada, K. Muneyama: This Bulletin, **13**, 639 (1965).



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was fairy stable to the acidic treatment (0.1*N* hydrochloric acid at 100° for 1 hour) and labile to the alkaline hydrolysis (0.1*N* sodium hydroxide even at room temperature) as reported in the case of uric acid riboside.[1] When 8-hydroxyguanosine (Ⅳ) was reacted with nitrous acid in 20% sulfuric acid,*2 a compound having ultraviolet absorption properties (λ_{max}^{pH1} mμ : 232, 289; λ_{max}^{pH10} mμ : 248, 303) was obtained. Paper chromatography (Rf 0.21 in 1-butanol-water, 86:14; Rf 0.64 in water, pH 10) also indicated the identical properties reported for uric acid 9-riboside.*3,3)

This reaction was then applied to 8-bromo-5′-O-acetyl-2′,3′-O-isopropylideneadenosine (Ⅵ) using 5 equivalents of sodium acetate. After the reflux of 2.5 hours 8-hydroxy derivative (Ⅶ) was obtained as a hard glass in the quantitative yield. Ultraviolet absorption properties : $\lambda_{max}^{0.1N\ HCl}$ mμ : 262, 284; $\lambda_{max}^{0.1N\ NaOH}$ mμ : 280. Infrared absorption : ν_{max}^{Nujol} cm^{-1} : 1740 (ester CO), 1715 (8-CO). Thin-layer chromatography : Rf 0.28 (silica gel, chloroform-ethanol, 35:5). Paper chromatography : Rf 0.70 (1-butanol-water-conc. ammonia, 7:1:2). Acidic hydrolysis of this compound gave 8-hydroxyadenine, $\lambda_{max}^{pH\ 9}$ mμ :

*2 When the deamination reaction was carried out in dilute acetic acid, ultraviolet absorption was diminished after 2 hr. at room temperature (unpublished experiments by K. Muneyama).

*3 After completion of this experiments, we were aware of the work of Holmes, *et al.*[6] of the synthesis of uric acid 9-riboside by another route.

6) R. E. Holmes, R. K. Robins : J. Am. Chem. Soc. 87, 1772 (1962).

277; $\lambda_{max}^{pH\,4}$ mμ : 268; $\lambda_{max}^{pH\,1}$ mμ : 263, 278 (identical with those reported by Cavalieri and Bendich[7]). Paper chromatography : Rf 0.26 (1-butanol-water, 86:14).

Thus a versatile method of introduction of hydroxyl group to the 8-position of purine nucleosides was established. The application of this method to the various nucleosides is in progress in this laboratory.

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A Total Synthesis of Coenzyme A *via* Thiazoline Intermediate*1

In the previous paper,[1] the authors described a novel synthesis of D-pantethine (IIIa), one of the biosynthetic intermediates of coenzyme A from D-pantothenic acid,[2] which comprises the interim formation of thiazoline derivative from D-pantothenonitrile (Ia) followed by acid hydrolysis thereof (hereafter referred to as the thiazoline method). This method seems to be applicable to the syntheses of other metabolites from D-pantothenic acid including coenzyme A itself. The present communication deals with the syntheses of coenzyme A and dephospho coenzyme A by the thiazoline method.

Three independent papers on the total synthesis of coenzyme A[3~5] have so far been published, each of which employed in principle the condensation of D-pantetheine derivatives with adenine nucleotides, differing in the procedure for pyrophosphate bond formation. The present method is characterized in building up aletheine moiety in coenzyme A structure in the last step of the synthetic route.

The key intermediates used in the present experiment are P^1-adenosine-3′-phosphate-5′P^2-D-pantothenonitrile 4′-pyrophosphate (Ib) for coenzyme A, and P^1-adenosine-5′P^2-D-pantothenonitrile 4′-pyrophosphate (Ic) for dephospho coenzyme A. For the preparation of Ib and Ic, it is essential at the outset to establish the synthesis of D-pantothenonitrile 4′-phosphate (V). D-Pantothenonitrile (Ia) was treated with dibenzyl phosphorochloridate in anhydrous pyridine to furnish a syrupy substance (IV), $[\alpha]_D^{23}$ +19.1° (EtOH), in 73.2% yield. Catalytic hydrogenation of IV over palladium-charcoal afforded V, $[\alpha]_D^{25}$ +11.4° (H_2O), IR ν_{max}^{KBr} cm^{-1} : 2250 (C≡N), in 69% yield as its barium salt ($C_9H_{15}O_6N_2PBa \cdot 2H_2O$).

*1 A part of this communication was read at the Kanto Branch Meeting of the Pharmaceutical Society of Japan, May, 1965, Tokyo.

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