Synthesis of D*-Threosamine and* D*-Erythrosamine*[1]

By Juji YOSHIMURA, Yoshiaki OHGO
and Tetsuo SATO

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In the course of studies on the glycosylation of aminosugars[2], the requirement of a lower 2-aminosugar had arisen, so we attempted to synthesize 2-amino-D-tetroses. Recently, the synthesis of them was reported by Kuhn et al.[3], in which the hydrochlorides of D-threosamine and D-erythrosamine were obtained by catalytic half reduction of *N*-benzyl-D-tetrosaminonitriles (III_b and IV_b) prepared by acidic hydrolysis of corresponding acetone derivatives (I_b and II_b).

It prompts us to record further observations related to their work. To obtain *N*-substituted-D-tetrosaminonitriles (III and IV) two paths shown in Fig. 1 were examined. By treatment of D-glyceraldehyde[4] with amines (aniline, benzylamine and isopropylamine respectively) and hydrogen cyanide, *N*-phenyl-D-threosaminonitrile (IV_a), m. p. 114~116°C, $[\alpha]_D-247.2°$ (*c* 0.72, ethanol), Found: C, 62.38; H, 6.30; N, 14.5, Calcd. for $C_{10}H_{12}O_2N_2$: C, 62.48; H, 6.29; N, 14.58%, and *N*-isopropyl-D-erythrosaminonitrile (III_c), m. p. 103~104°C, $[\alpha]_D+48.1°$ (*c* 0.21, methanol), Found: C, 53.43; H, 8.90; N, 17.48. Calcd. for $C_7H_{14}O_2N_2$: C, 53.14; H, 8.92; N, 17.71%, were obtained as colorless needles.

On the other hand, when acetone-D-glyceraldehyde[5] was treated in the same manner, two epimeric pairs of the corresponding acetone-aminonitriles (I_a, II_a, I_b and II_b) were separated in crystalline forms (acetone-*N*-phenyl-D-erythrosaminonitrile (I_a), m. p. 124°C, $[\alpha]_D+157.9°$ (*c* 0.69, methanol), yield 7.4%, Found: C, 66.30, H, 6.85; N, 12.06, Calcd. for $C_{13}H_{16}O_2N_2$: C, 67.22; H, 6.94; N, 12.06%, acetone-*N*-phenyl-D-threosaminonitrile (IIa), m. p. 100~102°C, $[\alpha]_D-149.4°$ (*c* 0.86, methanol), yield 30%, Found: C, 67.40; H, 7.04; N, 11.94. Calcd. for $C_{13}H_{16}O_2N_2$: C, 67.22; H, 6.94; N, 12.06%. The physical properties of *N*-benzyl derivatives, I_b and II_b, are entirely consistent with those of the substances reported by Kuhn et al.[3] respectively.

In addition to them, a trace of rhombic colorless crystal, m. p. 115~116°C, $[\alpha]_D+15°$ (*c* 0.77, methanol), having the same analytical values as the epimeric pair (Found: C, 67.06; H, 7.02; N, 11.92%) in the case of *N*-phenyl derivatives and a small amount of crystals corresponding to $C_{13}H_{18}O_4N_2$, m. p. 255~256°C, and $C_{16}H_{16}O_2N_2$, m. p. 216~218°C in the case of *N*-benzyl derivatives were obtained.

To prepare *N*-substituted D-tetrosaminonitriles the above acetone derivatives were subjected to hydrolysis in a mineral acid, to which *N*-benzyl derivatives (I_b and II_b) showed such an extraordinary resistance that it was impracticable to obtain hydrolyzates of I_b and II_b even in 2 N hydrochloric acid solution of 80% ethanol at room temperature for 24 hr., although Kuhn et al. carried out successfully by exsiccating the 2 N hydrochloric acid solution of I_b or II_b on phosphorus pentoxide at room temperature. *N*-Phenyl derivatives (I_a and II_a) changed gradually in their optical rotation in a 1 N mineral acid solution of 80% ethanol at room temperature [I_a: $[\alpha]_D+107°$ (5 min.) → +156° (3 hr.) → +165° (22 hr. approximately const.), II_a: $[\alpha]_D-164°$ (3 min.) → −177° (1 hr.) → −220° (20 hr.) → −222° (41 hr.) → −228° (92 hr. const.)]. Colorless needles, m. p. 114~116°C, obtained from the reaction mixture of II_a, was agreed with IV_a described above.

The presumption whether these aminonitrile derivatives belong to the threo-type or the erythro-type was deduced from the general survey on their yields and their optical rotational data. In general, an epimer in which -NHR group has trans configuration to the hydroxyl gronp attached to the adjacent carbon precedes the cis isomer in their yield[6]. Moreover, the one having -NHR group on the right hand in the Fischer projection shows generally more positive optical rotation than the other, when they are measured in an inert solvent. This relationship seems to be closely akin to the acid-amide rule[7] in the sugar series. Fortunately, Kuhn et al. established the configurations of I_b and II_b by converting them into the configurationally known α-amino-β, γ-dihydroxybutyric acid[8], and the result coincides with the above mentioned presumption.

To obtain pure epimeric pair of aminosugars,

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[1] This work was presented at the 14th Annual Meeting of the Chemical Society of Japan, Tokyo, April, 1961.

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[7] C. S. Hudson and S. Komatsu, *J. Am. Chem. Soc.*, **40**, 813 (1918); ibid., **41**, 1141 (1919).

[8] E. E. Hamel and E. P. Painter, ibid., **75**, 1362 (1953).

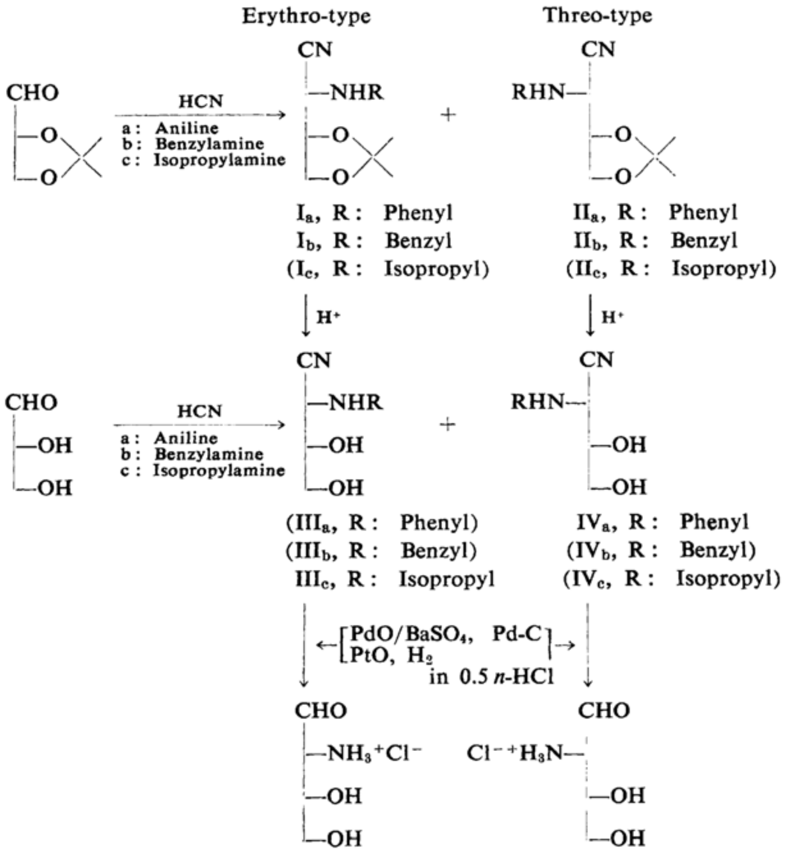

Fig. 1. Substances in parentheses could not be isolated as crystals.

N-phenyl-D-threosaminonitrile IV_a and *N*-phenyl-D-erythrosaminonitrile III_a which was derived by hydrolysis of I_a were subjected to catalytic half reduction in hydrochloric acid solution to afford D-threosamine hydrochloride and D-erythrosamine hydrochloride which showed the same behavior as depicted by Kuhn et al.3)

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Laboratory of Organic Chemistry
Tokyo Institute of Technology
Meguro-ku, Tokyo