Communications to the Editor

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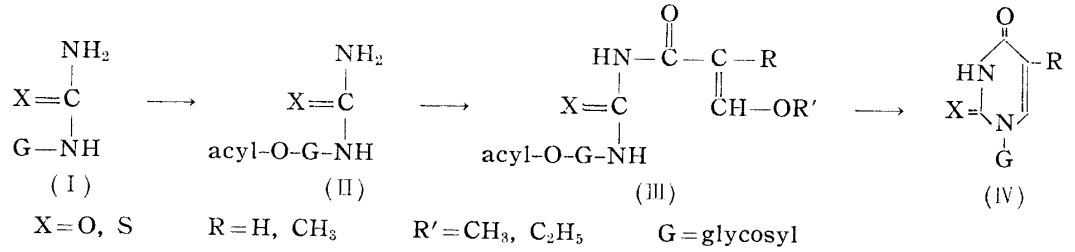
A New Synthetic Method for Pyrimidine Nucleoside

In order to synthesize pyrimidine nucleoside from glycosylurea and glycosylthiourea, D-glucose, D-arabinose, and D-ribose were each reacted with urea and thiourea according to the method of Helferich[1] and Hynd,[2] and 1-β-D-glucopyranosylurea, 1-β-D-glucopyranosylthiourea, 1-D-arabopyranosylurea, and two kinds of 1-D-ribopyranosylurea (A and B) were obtained. These compounds (I), after protecting the hydroxyls in the sugar portion by acetylation to (II), were condensed with β-ethoxyacryloyl chloride and α-methyl-β-methoxyacryloyl chloride to form the intermediate (III), which was warmed with dilute ammonia to effect pyrimidine cyclization to (IV). Thus, a new method was established for the syntheses of 1-β-D-glucopyranosyluracil, 1-β-D-glucopyranosyl-2-thiouracil, 1-β-D-glucopyranosylthymine, 1-β-D-glucopyranosyl-2-thiothymine, 1-D-arabopyranosylthymine, and two kinds of 1-D-ribopyranosylthymine.



Recently, Benn and Jones[3] reported the formation of two kinds of 1-D-ribosylurea, $[\alpha]_D^{18}$ −27°, RG 0.91, and $[\alpha]_D^{23}$ +24°, RG 1.26,*1 from D-ribose and urea. They failed to give the melting points of these compounds and assumed them, from the result of periodate oxidation, to be 1-D-ribopyranosylurea and 1-D-ribofuranosylurea. These were assumed to be identical with the substances obtained as above in this laboratory, from the comparison of optical rotation and RG (1.27 for (A) and 0.96 for (B)*2).

The ring structure of the sugar portion in two kinds of 1-D-ribosylthymine, m.p. 250° and m.p. 234°, respectively derived from (A) and (B), was determined in the following manner. Admixture of both these thymine derivatives with 1-β-D-ribofuranosylthymine,[4] m.p. 183~185°, showed depression in the melting point. Condensation of tri-O-acetyl-β-D-ribopyranosyl bromide and tri-O-benzoyl-β-D-ribopyranosyl bromide each with dithyminylmercury according to the method of Fox[4] afforded the same 1-D-ribopyranosylthymine of m.p. 234° from both. Condensation of tri-O-acetyl-β-D-ribopyranosyl bromide and 2,4-diethoxy-5-methylpyrimidine, following the method of Visser,[5] gave two kinds of 1-D-ribopyranosylthymine, one of m.p. 250° as reported by him and the other of m.p. 234°, identical with the one obtained as above. These two substances (A and B) were found to be identical with the substances synthesized as above, from the result of mixed fusion and comparison of infrared absorption spectra. This has proved that the ring structure of the sugar portion is a pyranose type and the two kinds of 1-D-ribosylurea (A and B) are both

*1 Solvent system : BuOH-EtOH-H_2O = 4:1:5.
*2 Solvent system : BuOH-AcOH-H_2O = 4:1:5.

1) B. Helferich : Ber., **56**, 59 (1926).
2) A. Hynd : Biochem. J., **20**, 195, 205 (1926).
3) M. H. Benn, A. S. Jones : Chem. & Ind. (London), **1959**, 997; J. Chem. Soc., **1960**, 3837.
4) J. J. Fox : J. Am. Chem. Soc., **78**, 2117 (1956).
5) D. W. Visser : *Ibid.*, **70**, 1926 (1948).

1-D-ribopyranosylurea. However, the configuration of the C-1 is still undetermined, whether it is α or β type.

As shown above, it is difficult to obtain 1-D-ribofuranosylurea by the reaction of D-ribose and urea. Consequently, 1-(tri-O-benzoyl-β-D-ribofuranosyl)thiourea was prepared from tri-O-benzoyl-D-ribofuranosyl isothiocyanate, and 1-β-D-ribofuranosyl-2-thiouracil and 1-β-D-ribofuranosyl-2-thiothymine were obtained by similar reactions as shown in the Chart.

The properties of the compounds (I) to (IV) described above are summarized in Table I.

Table I.

Sugar portion	X	(I) m.p. (°C) $[\alpha]_D$ (in H_2O)	(II) m.p. (°C) $[\alpha]_D$ (in H_2O)	R	(III) m.p. (°C) UV $\lambda_{max}^{H_2O}$ mμ (log ε)	(IV) m.p. (°C) $[\alpha]_D$ (in H_2O) UV $\lambda_{max}^{H_2O}$ mμ (log ε)
1-β-D-Glucopyranose	O	207 −18.9°	95 −13.2°	CH_3	145 262.2 (4.199)	266～267 + 8.20° 264.5 (3.99)
				H	151 253 (4.347)	200～205 + 20.9° 258 (3.98)
	S	207～210 −43.9°	171～173 +8.68°	CH_3	Amorphous 267, 289 (−, −)	226～228 + 14.5° 282 (4.194)
				H	Amorphous 273.5 (−)	226～227 + 18.5° 227 (4.18)
1-D-Arabopyranose	O	193 −52.1°	213 −44.0°	CH_3	152 262.0 (4.170)	243～244 − 62.9° 264.5 (3.968)
1-D-Ribopyranose	O	(A) 184 +24.45°	194 −8.12°	CH_3	Amorphous 265.0 (−)	250 −108° 268 (3.983)
		(B) 184 −39.7°	194 −2.01°		Amorphous 261.5 (−)	234 − 6.5° 264 (3.978)
			O-Bz Compd.			
1-β-D-Ribofuranose	S	163～164 +124°	163～164 −44.8°	CH_3	Amorphous ——	215～217 + 30.5° 273 (4.176)
				H	Amorphous ——	212～214 + 38.5° 275 (4.136)

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