[Chem. Pharm. Bull. 12 (4) 454 ~ 459]

UDC 547.456'495.2

67. Tyunosin Ukita, Akira Hamada, and Mitsuaki Yoshida : Synthesis of 1-(β-D-Ribofuranosyl)urea and Related Compounds.

(*Faculty of Pharmaceutical Sciences, University of Tokyo*[*1])

The general methods in synthesis of glycosylurea hitherto appeared in the literature can be classified into two types of reactions : 1) condensation of an aldohexose or aldopentose and urea in the presence of acid catalysts such as sulfuric acid, hydrochloric acid or cationic resins, and 2) reaction of ammonia with glycosyl isocyanate protected in the hydroxyl groups. The first type of reaction seems suitable to obtain several pyranosylurea, thus 1-(β-D-glucopyranosyl)-[1,2] and 1-arabinopyranosylurea[3] are reported to be obtained in considerable yields. The application of this method to the synthesis of ribosylurea, however, was not necessarily favorable. Benne and Jones[4] reported that the condensation of D-ribose and urea furnished mainly ribopyranosylurea with a small amount of ribofuranosylurea and the former was proved by Naito, *et al.*[5] to be a mixture of α- and β-anomers.

As for the second type of reaction, the syntheses of arabinosyl-,[6] xylosyl-,[6] and glucosylureas[7,8] are encountered in classical reports. In these cases, however, the ammonolysis generally gave the final product in poor yields for preparative purpose and the ammonolysis occurred not only at the isocyanate group but also at the protecting groups of their sugar moiety, *i.e.* no intermediate acylglycosylureas were isolated.

Recently, Naito and Sano,[9] using this type of reaction, reported a synthesis of 1-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)thiourea (Ⅷ) in an excellent yield. But they could not obtain a successful result in synthesizing benzoylated derivative of the ribofuranosylurea (Ⅴ) by a similar procedure.[*2]

In the course of our research on syntheses of modified ribonucleosides, it was required to have 1-(β-D-ribofuranosyl)urea with protected hydroxyl groups in a preparative amount. This paper deals with the syntheses of 1-(β-D-ribofuranosyl)urea (Ⅶ) and of 1-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)urea (Ⅴ) in the yields enough for the subsequent syntheses of pyrimidine nucleosides.

2,3,5-Tri-O-benzoyl-D-ribofuranosyl chloride (Ⅰ) was heated with silver isocyanate in anhydrous toluene and from the petroleum ether soluble part of the reaction mixture, a colorless syrup (Ⅱ) was obtained in a yield of ca. 90%. This compound gave a strong absorption at 2245 cm^{-1} characteristic of N=C=O stretching vibration.[10] The product (Ⅱ), on warming with ethanol, gave colorless crystals, m.p. 223~226°, elemental analysis of which was in good accord with that of N-(2,3,5-tri-O-benzoyl-D-ribofuranosyl)urethane (Ⅲ). From the petroleum ether insoluble part of the above reaction mixture colorless long needles (Ⅳ), 229~230°, were isolated. The same compound was

*1 Motofuji-cho, Bunkyo-ku, Tokyo (浮田忠之進, 浜田 昭, 吉田光昭).

*2 M. Sano : Private communication.

1) M. N. Schrool : Rec. Trav. Chim., **22**, 1 (1903).
2) A. Hynd : Biochem. J., **20**, 195, 205 (1926).
3) B. Helferich, W. Kosche : Ber., **59**, 69 (1926).
4) H. Benne, A. S. Jones : J. Chem. Soc., **1960**, 3837.
5) T. Naito, T. Kawakami : This Bulletin, **10**, 627 (1962).
6) T. B. Johnson, W. Bergmann : J. Am. Chem. Soc., **60**, 1916 (1938).
7) E. Fischer : Ber., **47**, 1377 (1914).
8) T. B. Johnson, W. Bergmann : J. Am. Chem. Soc., **54**, 3360 (1932).
9) T. Naito, M. Sano : This Bulletin, **9**, 709 (1961).
10) H. Hoyer : Chem. Ber., **89**, 2677 (1956).

also obtained from II when the dioxane solution was treated with water. The compound (IV) gave analytical data corresponding to 1,3-bis(2,3,5-tri-O-benzoyl-D-ribofuranosyl)urea.

The above observations support that the compound (II) has a structure of 2,3,5-tri-O-benzoyl-D-ribofuranosyl isocyanate represented by II.

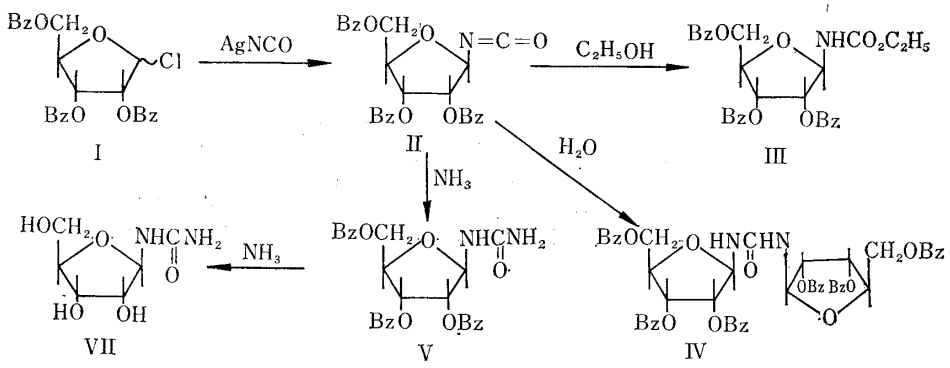


Chart 1.

The ammonolysis of the isocyanate derivative (II) was first performed by adding a methanolic ammonia to the chloroform solution at 0° and the product on subsequent recrystallization from chloroform-petroleum ether furnished colorless needles (V), m.p. 184~186°, in a yield of 50%. Better yield was obtained when the ammonolysis was performed directly for the filtered reaction mixture of I and silver isocyanate in anhydrous toluene. Thus, when ammonia gas was bubbled to the toluene solution, V was precipitated as crystals in 75% yield.

The product (V) gave analytical data corresponding to 1-(2,3,5-tri-O-benzoyl-D-ribofuranosyl)urea and revealed absorptions at 1650 and 1530 cm^{-1} characteristic of -CO-NH- group. When V was benzoylated with benzoyl chloride in pyridine, a product (VI), m.p. 176~177°, was obtained as colorless needles. This product (VI) was identified by mixed fusion with a standard sample of 1-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)-3-benzoylurea which was derived from authentic 1-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)thiourea (VIII).[9] That is to say, the thiourea (VIII) synthesized by the procedure of

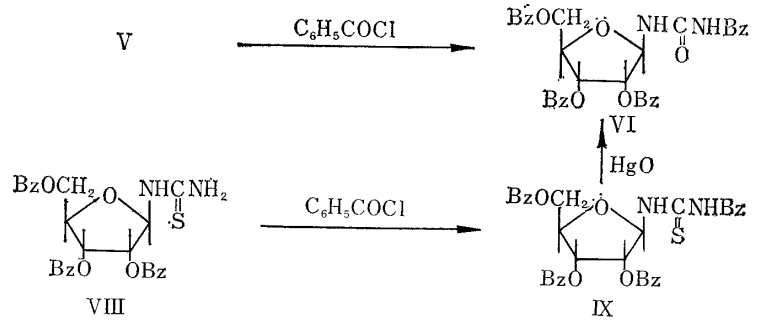


Chart 2.

Naito, *et al.*[9] was benzoylated to 1-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)-3-benzoylthiourea (IX), m.p. 128~129° and the latter (IX) was desulfured by a modified method of Shah, *et al.*[11] with yellow mercuric oxide in a mixed solvent of aqueous ethanol and chloroform to give 1-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)-3-benzoylurea (VI) as needles, m.p. 175~176°.

11) M. H. Shah, M. Y. Mlasalkar : J. Sci. & Ind. Research., **18B**, 202 (1959).

The above identification supported that 1-(2,3,5-tri-O-benzoyl-D-ribofuranosyl)urea (V) had a β-configuration at anomeric center, therefore, II, III, and IV should have β-configurations. In order to have another evidence concerning the configuration, V was converted to a thymine riboside. The compound (V) was condensed with 2-methyl-3-methoxyacryloyl chloride in pyridine by a modified method of Naito, *et al.*[9] After

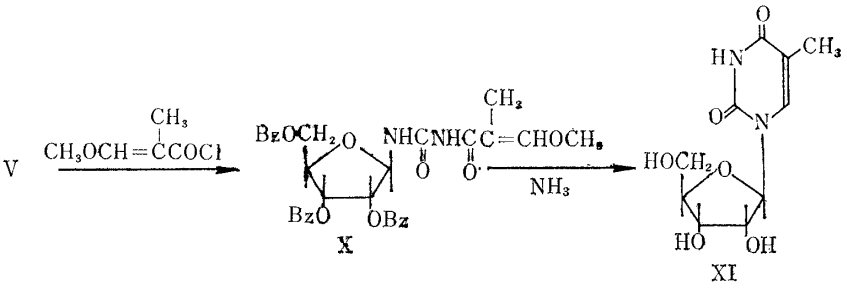


Chart 3.

separation of the reaction products by silica gel column chromatography, a product, 1-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)-3-(2-methyl-3-methoxyacryloyl)urea (X), was obtained as a pale yellow powder in 75.6% yield. On ring closure and simultaneous deacylation of this compound by treatment with ammonia, colorless needles (XI), m.p. 179~180°, were isolated. The product, XI, gave analytical data corresponding to those of ribofuranosylthymine and was identified by mixed fusion with an authentic (β-D-ribofuranosyl)thymine synthesized by Fox's method.[12] The ultraviolet spectra and behaviours in paper chromatography in three solvents of these compounds also showed their identity.

From the above observations, the anomeric center of V, therefore those of II, III, and IV, should confirmatively be assigned as β-configurations. 1-(2,3,5-Tri-O-benzoyl-β-D-ribofuranosyl)urea (V) was debenzoylated with ammonia in methanol and the mixture was purified by cellulose column chromatography. From the fraction which contained a compound (VII) ($Rf_1=0.15$), fine needles, m.p. 120~122.5°, $[\alpha]_D^{24}$ +1.98 (in water), was obtained in a yield of 375 mg. (51.8%). This compound (VII) was confirmed to be 1-(β-D-ribofuranosyl)urea by elemental analysis, periodate oxidation, infrared spectra and paper chromatography. A mixture of this compound (VII) with authentic 1-(β-D-ribopyranosyl)urea (m.p. 181~183)*3 melted at 99~115°. On periodate oxidation at 2~5°, VII consumed exactly one mole of the reagent when checked after 30 minutes and 24 hours without liberation of formic acid. In infrared spectrum, VII showed four absorption bands in the region of 730~960 cm^{-1} (918, 898, 846, and 806 cm^{-1})*4 characteristic of furanosyl compounds.[13] In paper chromatography, VII showed $Rf_1=0.15$ and $Rf_2=0.09$ in contrast to 1-(β-D-ribopyranosyl)urea ($Rf_1=0.10$ and $Rf_2=0.04$) and the relation between Rf values of these compounds well coincided with earlier observation that in D-ribose series furanosyl compounds travel faster than pyranosyl compounds.[14]

The compound (VII) was found unstable in an aqueous solution, thus it was slowly converted to ribopyranosylurea by keeping the solution at room temperature. The conversion was found more rapid in acidic or alkaline media. On above debenzoylation of V, the reaction mixture contained a trace amount of ribopyranosylurea and ribose besides the main product (VII) and the amount of the side products increased by keeping the mixture at room temperature.

*3 The sample was kindly supplied by Dr. T. Naito of Daiichi Seiyaku Co., Ltd.

*4 1-(β-D-Ribopyranosyl)urea showed three absorption bands: 955, 915, and 886 cm^{-1}.

12) J. J. Fox, N. Yung, G. B. Brown: J. Am. Chem. Soc., **78**, 2117 (1956).
13) S. A. Barker, R. Stephens: J. Chem. Soc., **1954**, 4550.
14) F. A. Isherwood, M. A. Jermyn: Biochem. J., **48**, 515 (1951).

Experimental*5

Paper chromatography was carried out ascendingly on Toyo Roshi No. 53 paper. The solvents used were 1) BuOH-EtOH-H_2O(4:1:5), 2) iso-BuOH saturated with H_2O, and 3) iso-PrOH-NH_4OH-H_2O (7:1:2). The Rf values for these solvents are represented by Rf_1, Rf_2, and Rf_3 respectively.

2,3,5-Tri-O-benzoyl-β-D-ribofuranosyl Isocyanate (II)——2,3,5-Tri-O-benzoyl-D-ribofuranosyl chloride (I) prepared according to the method of Kissman[15] from 5 g. of 1-O-acetyl-2,3,5-tri-O-benzoyl-D-ribose[16] was dissolved in 30 ml. of anhyd. toluene. The solution was added to a suspension of 3 g. of AgNCO[17] in 50 ml. of anhyd. toluene and the mixture heated at 100~110° for 2.5 hr. under stirring. After cooling, AgCl that precipitated was removed by filtration, washed with toluene and the washings were combined with filtrate. The combined solution was concentrated to ca. 40~50 ml. under reduced pressure and to the solution was added 100~150 ml. of anhyd. petr. ether. After standing for 30 min. at room temperature, the supernatant layer was separated by decantation from a small amount of white syrup that precipitated. On removal of the solvent, 4.5 g. of colorless syrup was obtained. IR cm^{-1}: $\nu_{N=C=O}$ 2245 (KBr).

1-(2,3,5-Tri-O-benzoyl-β-D-ribofuranosyl)urea (V)——a) By the reaction of II with NH_3 in MeOH at 0°: To a solution of 780 mg. of II in 3 ml. of anhyd. $CHCl_3$ was added 0.4 ml. of MeOH containing 82 mg. of NH_3 and the mixture was stirred for 40 min. at 0°. The solvent and NH_3 was removed from the mixture under reduced pressure at 20°. The residual white crystalline mass (813 mg.) was triturated with 20 ml. of $CHCl_3$ and washed three times with the same solvent and the residue was dissolved in 20 ml. of $CHCl_3$ containing 1 ml. of MeOH. The crystals that appeared on addition of petr. ether to the above solution, after standing overnight, were filtered and dried over $CaCl_2$ *in vacuo*. Colorless needles, m.p. 186~187°, were obtained in a yield of 400 mg. (50%). *Anal.* Calcd. for $C_{27}H_{24}O_8N_2$: C, 64.27; H, 4.80; N, 5.55. Found: C, 64.07; H, 4.72; N, 5.64. IR cm^{-1}: $\nu_{-NH-CO-}$ 1650, 1530 (KBr).

b) Preparative method: AgCl was removed by filtration from a reaction mixture of I (prepared from 10.0 g. of 1-O-acetyl-2,3,5-tri-O-benzoyl-D-ribose) and 6 g. of AgNCO in toluene. When the filtrate was bubbled with NH_3 under stirring at 0°, white crystals appeared immediately. The stirring and bubbling were continued for 40~50 min. and the crystals were filtered and dissolved in a mixture of $CHCl_3$-MeOH (20:1). Addition of petr. ether to the solution gave colorless needles, m.p. 184~186° in a yield of 7.5 g. (75.0%). A mixed fusion of this product with 1-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)-urea (V) obtained above showed no depression of the melting point. The absorption in IR region of the product also well coincided with those of V.

N-(2,3,5-Tri-O-benzoyl-β-D-ribofuranosyl)urethane (III)——A solution of 277 mg. of II in 15 ml. of abs. EtOH was warmed at 40~50°. The white precipitate that occurred was filtered and recrystallized from EtOH to furnished colorless needles, m.p. 223~226°, which were dried over P_2O_5 *in vacuo*. *Anal.* Calcd. for $C_{29}H_{27}O_9N$: C, 65.27; H, 5.10; N, 2.62. Found: C, 65.28; H, 5.09; N, 3.03.

1,3-Bis(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)urea (IV)——To a solution of 500 mg. of II in 10 ml. of dioxane was added trace of H_2O. The crystals that appeared immediately were separated by filtration and recrystallized from $CHCl_3$ by addition of petr. ether to colorless needles, m.p. 229~230°, in a quantitative yield and dried over P_2O_5 *in vacuo*. *Anal.* Calcd. for $C_{53}H_{44}O_{15}N_2$: C, 67.08; H, 4.67; N, 2.96. Found: C, 66.72; H, 4.84; N, 3.08.

A small amount of this compound was also obtained during the purification of II when the toluene-petr. ether insoluble syrup was recrystallized from $CHCl_3$-petr. ether. This compound might be resulted by hydrolysis of II with a trace of H_2O contaminated in the reaction mixture.

1-(β-D-Ribofuranosyl)urea (VII)——A suspension of 1.9 g. of V in 35 ml. of MeOH was saturated with NH_3 at 0° and the mixture was kept in a sealed tube for 48 hr. at room temperature. The solvent was removed under reduced pressure and the residue was extracted with Et_2O (3×30 ml.). The Et_2O insoluble residue was dissolved in a small amount of aq. EtOH and applied to a cellulose column (3.0×50 cm.). The column was eluted with BuOH-EtOH-H_2O (4:1:5) and each 10 ml. of the eluate was taken. The fractions (tube No. 61~72) which contained a compound having Rf_1 0.15 and colored yellow with the Ehrlich's reagent were combined and solvent was evaporated. To the residual syrup, anhyd. EtOH was added and recovered by evaporation. The syrup (540 mg., 74.5%) was scratched under cooling in an ice bath to crystallize. Recrystallization from EtOH containing a trace of H_2O gave colorless needles, m.p. 120~122.5°, with a yield of 375 mg. (51.8%). *Anal.* Calcd. for $C_6H_{12}O_5N_2$: C, 37.51; H, 6.29; N, 14.58. Found: C, 37.72; H, 6.23; N, 14.57. $[\alpha]_D^{24}$ +1.98 (c=1.06, H_2O). Rf_1=0.15 and Rf_2=0.09. IR ν_{max}^{KBr} cm^{-1}: 918, 898, 846, and 806 (furanose ring). On oxidation of this compound (VII) with

*5 All melting points are uncorrected.

15) H. M. Kissman, C. Pidacks, B. R. Barker: J. Am. Chem. Soc., **77**, 18 (1955).
16) E. F. Records, H. Rinderkneckt: Herv. Chim. Acta, **42**, 1171 (1959).
17) G. Dean: J. Chem. Soc., **1904**, 1371.

periodate at 2~5°, it consumed 1.00, 1.00, and 1.01 moles of the reagent per mole after respective 30 min., 1 and 24 hr. without liberation of HCOOH. When an aqueous solution of Ⅶ was kept standing at room temperature for several weeks, a part of Ⅶ was converted to ribopyranosylurea which was detected by paper chromatography (solvent 1). The conversion was more rapidly in acidic medium, thus in 0.5*N* HCl solution at 20° after 2 hr. a considerable amount of ribopyranosylurea and a small amount of ribose were formed in the solution.

1-(2,3,5-Tri-O-benzoyl-β-D-ribofuranosyl)-3-benzoylthiourea (IX)——One gram of 1-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)thiourea (Ⅷ) prepared by Naito's[9] method was dissolved in 5 ml. of pyridine. To the solution was added 0.35 g. of BzCl under cooling and the mixture was set aside overnight at room temperature. The solvent was removed under reduced pressure and the residue dissolved in $CHCl_3$. The solution was washed with 5% $NaHSO_4$, 5% $NaHCO_3$ and H_2O, successively, and dried over Na_2SO_4. The solution was evaporated under reduced pressure to leave a pale yellow syrup, which was crystallized on ice cooling. Recrystallization from EtOH gave colorless needles, m.p. 128~129°, which were dried over P_2O_5 *in vacuo*. Yield, 350 mg. (29.2%). *Anal.* Calcd. for $C_{34}H_{28}O_8N_2S$: C, 65.37; H, 4.52; N, 4.48. Found : C, 65.46; H, 4.89; N, 4.45.

Desulfation of IX to 1-(2,3,5-Tri-O-benzoyl-β-D-ribofuranosyl)-3-benzoylurea (VI)——Desulfation was carried out according to the method of Shah.[11] To a solution of 135 mg. of Ⅸ in a mixture of 15 ml. of aq. EtOH and 2 ml. of $CHCl_3$ was added 70 mg. of yellow HgO and the mixture was stirred at 50~60° for 3 hr. The black precipitate that appeared was filtered and the filtrate was concentrated under reduced pressure. The residual crystals were recrystallized from EtOH to colorless needles, m.p. 175~176°, yield, 65 mg. (50%) and dried over P_2O_5 *in vacuo*. *Anal.* Calcd, for $C_{34}H_{28}O_9N_2$: C, 67.09; H, 4.64; N, 4.60. Found : C, 67.07; H, 4.85; N, 4.59.

Synthesis of VI from 1-(2,3,5-Tri-O-benzoyl-D-ribofuranosyl)urea (V)——The compound (V) was benzoylated by a similar method that used for 1-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)thiourea (Ⅷ). The product (Ⅵ) was obtained as colorless needles, m.p. 176~177° in a yield of 9.7%. A mixed fusion of this product with that obtained by desulfation of Ⅸ showed no depression of the melting point and IR spectra of the both compounds were identical.

1-(2,3,5-Tri-O-benzoyl-β-D-ribofuranosyl)-3-(2-methyl-3-methoxyacryloyl)urea (X)——To a suspension of 2.13 g. of V in 15 ml. of $CHCl_3$ was added 0.9 g. of 2-methyl-3-methoxyacryloyl chloride[18] and 0.8 g. of pyridine. The mixture was stirred for 2 days at room temperature to give a pale yellow clear solution. The solvent was evaporated under reduced pressure, the residue was dissolved in $CHCl_3$ and washed with 5% $NaHSO_4$, 5% $NaHCO_3$ and H_2O, successively. The dried solution was evaporated under reduced pressure to leave a pale yellow glassy solid. This solid was triturated with EtOH and supernatant was removed by decantation. These procedure were repeated three times. A pale yellow powder thus obtained was dissolved in a small portion of $CHCl_3$. The solution was submitted to a silica gel column (3×45 cm.) chromatography, the column was eluted with $CHCl_3$ and each 10 ml. of the effluents were taken. The fractions (tube No. 26~46) that showed UV absorption were combined and concentrated under reduced pressure to furnish 1.93 g. (75.6%) of the pale yellow powder, which was dried over P_2O_5 *in vacuo*. *Anal.* Calcd. for $C_{32}H_{30}O_{10}N_2 \cdot H_2O$: C, 61.80; H, 5.16; N, 4.51. Found : C, 61.88; H, 4.92; N, 4.07.

N-(β-D-Ribofuranosyl)thymine (XI)——To a solution of 1.1 g. of X in 3 ml. of hot EtOH was added 6 ml. of conc. NH_4OH in 5 to 7 portion within 4 hr. at 80~90°. When the mixture became no longer turbid by further addition of NH_4OH, the mixture was concentrated under reduced pressure and extracted with $CHCl_3$ for removal of benzamide and ethyl benzoate produced. The aqueous layer was evaporated to dryness under reduced pressure. The residue was dissolved in a small portion of EtOH and applied to a cellulose column (2.8×40 cm.). The column was eluted with BuOH-EtOH-H_2O (4:1:5) and each 10 ml. of the effluents were taken. The fractions (tube No. 24~30) that showed UV absorption were combined and concentrated to dryness under reduced pressure. The residual syrup was dissolved in ca. 3 ml. of EtOH, filtered and the filtrate was evaporated to a small volume and allowed to cool. The crystals appeared were recrystallized from EtOH to colorless needles, m.p. 179~180°, yield, 17.8%, which were dried over P_2O_5 *in vacuo*. *Anal.* Calcd. for $C_{10}H_{14}O_6N_2$: C, 46.62; H, 5.47; N, 10.85. Found : C, 46.95; H, 5.75; N, 10.54. UV mμ (ε) : $\lambda_{max}^{pH\ 7.2}$ 267 (9700), $\lambda_{min}^{pH\ 7.2}$ 235 (2920). $[\alpha]_D^{20}$ −12.9 (c=0.80, H_2O). Rf_1=0.36, Rf_2=0.23, Rf_3=0.72. The admixture of the product with an authentic N-(β-D-ribofuranosyl)thymine synthesized by Fox's procedure[12] showed no depression of the melting point. Furthermore, the both compounds gave identical spectra in UV- and IR-region.

The authors are indebted to Takeda Chemical Industries Co., Ltd. for their kind supply of the starting materials for the present syntheses and to Dr. T. Naito of the Central Research Laboratory, Daiichi Seiyaku Co. Ltd. for supplying of samples. Thanks are also due to Mr. D. Ōhata of the Medical Institute of the Sasaki Foundation and the Central Analysis Room of this Faculty for carring out the elemental analysis and optical measurements.

18) G. Shaw, R. N. Warrener : J. Chem. Soc., **1958**, 153.

Summary

1-(β-D-Ribofuranosyl)urea (Ⅶ) was synthesized *via.* 2,3,5-tri-O-benzoyl-β-D-ribofuranosyl isocyanate (Ⅱ) and 1-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)urea (Ⅴ). One of the intermediate, Ⅴ, which is an important starting material for the synthesis of ribonucleosides, was obtained in a yield of 75.0% by direct ammonolysis at 0° of the reaction mixture of 2,3,5-tri-O-benzoyl-D-ribofuranosyl chloride and silver isocyanate. The structure of Ⅴ was confirmed by converting it to (β-D-ribofuranosyl)thymine.

(Received November 5, 1963)

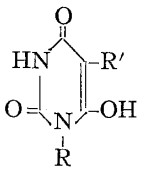
[Chem. Pharm. Bull. 12 (4) 459 ~ 465]

UDC 547.457'854.5 : 615.771.7

68. Tyunosin Ukita, Mitsuaki Yoshida, Akira Hamada, and Yoshio Kato*2 : The Syntheses of Glycosylbarbiturate.*3

(*Faculty of Pharmaceutical Science, University of Tokyo**1)

In our previous paper,[1] it was shown that the 5-phenylcarbamoylbarbituric acids (I) revealed a remarkable inhibitory activity against the multiplication of the rat ascites hepatoma (AH 130) cells *in vitro* and also *in vivo* test of Ehrlich ascites carcinoma in mice. However, the assays of the anti-tumor activities were made difficult on account of the poor solubility in water of this series of compounds. It was, therefore, desired to modify the structures of these compounds to be more soluble without decrease in the activities.



I R : H, CH_3, C_6H_5
R′ : $CONHC_6H_5$
Ⅱ R : glycosyl
R′ : suitable substituents

Chart 1.

As the first step of this type of research, in this paper, syntheses of 1-β-D-glucopyranosyl- (Ⅵ) and 1-β-D-ribofuranosylbarbituric acid (X) were attempted. Of these glycosides, the latter compound (X), especially, seemed to be interesting in biochemical point of view, because it has a structure of 6-hydroxyuridine, the synthesis and properties of which have never been reported.

As for the synthesis of glycosylbarbituric acids, Goodman, *et al.*[2] reported on the condensation of 2,4,6-trimethoxypyrimidine and 2,3,4,6-tetra-O-acetyl-α-D-glucopyranosyl bromide by Hilbert-Johnson's method,[3] but they failed to obtain the desired condensation product. Bergmann, *et al.*[4] treated 1-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)urea with malonic acid in acetic anhydride, but the product was found to be N,N′-bis-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosylcarbamoyl)malondiamide instead of

*1 Hongo, Motofuji-cho, Bunkyo-ku, Tokyo (浮田忠之進, 吉田光昭, 浜田 昭, 加藤好雄).
*2 Present address : c/o Sanshikagaku Research Institute, Hyakunin-cho, Shinjuku-ku, Tokyo.
*3 From the thesis of Yoshio Kato for the degree of Doctor of Pharmaceutical Sciences, University of Tokyo (1962).

1) T. Ukita, Y. Kato, M. Hori, H. Nishizawa : This Bulletin, 8, 1021 (1960).
2) I. Goodman, P. Newmark : J. Am. Chem. Soc., **79**, 6446 (1957).
3) G.E. Hilbert and T.B. Johnson : *Ibid.*, **52**, 2001, 4489 (1930).
4) T.B. Johnson, W. Bergmann : *Ibid.*, **60**, 1916 (1938).