Synthesis and Properties of Isomeric Di- and Mono-Glucopyranosyl Hypoxanthines

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Four isomeric glucosyl hypoxanthines, bis-1,9-(β -D-glucopyranosyl) hypoxanthine (I), bis-1,7-(β -D-glucopyranosyl) hypoxanthine (II), 7- β -D-glucopyranosyl hypoxanthine (III) and 9- β -D-glucopyranosyl hypoxanthine (IV) were synthesized simultaneously by using the so-called Davoll-Lowy's method. Their synthetic procedures and structural evidences are presented.

In a recent communication,¹⁾ we have reported that when the bromomercury derivative of hypoxanthine was refluxed with acetobromoglucose in xylene two isomeric diglucosyl hypoxanthines are produced simultaneously (12.7% and 12.3%) besides two expected monoglucosides (6.0% and 10.2%). The structures of the four isomeric glucosyl hypoxanthines were bis-1,9-(β -D-glucopyranosyl) hypoxanthine (I), its 1,7-position isomer (II), 7- β -D-glucopyranosyl hypoxanthine (III) and its 9-position isomer (IV) as identified with infra-red, NMR and ultraviolet absorption spectra and some other experimental results.¹⁾

In this paper the procedures of the above reactions are described in detail and some additional evidences in support of the N-1 glucosides for compounds I and II are also discussed.

When compound I was treated with 1N hydrochloric acid for 1.5 hr at 100°C, monoglucosyl hypoxanthine was obtained in a 50% yield, and it was determined as 1- β -D-glucopyranosyl

hypoxanthine (V) spectrophotometrically. Compound II also gave 1- β -D-glucopyranosyl hypoxanthine (V) by the acid treatment.¹⁾ This result revealed that the glucosidic linkage at the N-1 position is more resistant than at any of the nitrogen atoms in the imidazole ring against the acid hydrolysis and that the N-1 glucoside of hypoxanthine seemed to be 3-glycosyl-6-hydroxypyrimidine. When 3- β -D-ribofuranosyl uracil was treated with 1N hydrochloric acid for 3 hr at 100°C, a 43% yield of uracil was obtained.²⁾ But the N-9 glycosidic bond of purine nucleosides was completely hydrolyzed by N-hydrochloric acid at 100°C for 1 hr.³⁾ Moreover, one of the two anomeric protons of compound I (δ , 5.72 and 6.08 ppm) and compound II (δ , 5.98 and 6.02 ppm) on their NMR spectra gave almost the same chemical shift as the proton of compound V (δ , 6.02 ppm) (Figs. 1, 2 and 3).

The ring opening of a purine nucleoside having a substituent on one of the pyrimidine ring nitrogen atoms was observed by several

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CHART 1

CHART 2

FIG. 1. NMR Spectrum of Bis-1,9-(β -D-glucopyranosyl) Hypoxanthine (I) in Deuterium Oxide (60 Mc).

FIG. 2. NMR Spectrum of Bis-1,7-(β -D-Glucopyranosyl) Hypoxanthine (II) in Deuterium Oxide (60 Mc).

investigators.^{4,5)} Treatment of N-1-alkylinosine with alkali gave 5-amino-1-(β -D-ribofuranosyl)

imidazole-4-alkylcarboxamide.⁶⁾ Bis-1,9-(β -D-glucopyranosyl) hypoxanthine (I) and its 1,7-isomer (II) were quite unstable in alkaline

4) J. A. Montgomery and H. J. Thomas, *J. Org. Chem.*, **28**, 2304 (1963).

5) M. A. Stevens, H. W. Smith and G. B. Brown, *J. Am. Chem. Soc.*, **81**, 1734 (1959).

6) E. Shaw, *J. Am. Chem. Soc.*, **80**, 3899 (1959); *ibid.*, **81**, 6021 (1959); *ibid.*, **83**, 4770 (1961).

FIG. 3. NMR Spectrum of 1-β-D-Glucopyranosyl Hypoxanthine(V) in Deuterium Oxide (60 Mc).

FIG. 4. Bis-1,9-(β-D-glucopyranosyl) hypoxanthine was dissolved in 0.05 N sodium hydroxide. The ultraviolet absorption pattern was immediately obtained with a Shimadzu recording spectrophotometer (solid line). Both blank cuvette and sample cuvette were set aside at room temperature. Absorption patterns were obtained after 5 min, 10 min, 60 min, 240 min and 1500 min. Percent hydrolysis was obtained spectrally.

solution. When they were stored in 0.05 N sodium hydroxide solution at room temperature, the absorption maximum of compound I shifted from 252 mμ to 274 mμ (Fig. 4), and that of compound II shifted from 256 mμ to

FIG. 5. The ultraviolet absorption patterns of bis-1,7-(β-D-glucopyranosyl) hypoxanthine in 0.05 N sodium hydroxide were obtained after 0 min, 5 min, 10 min, 30 min, 60 min (dotted and dashed line), 120 min (solid line), 240 min (dotted line) and 1500 min (solid line), as the same manner as described in FIG. 1. Percent hydrolysis was also obtained.

291 mμ (Fig. 5). By replacing the alkyl group of the pyrimidine ring nitrogen with glucosyl group, alkaline hydrolysis is expected to proceed more easily.

The above-mentioned chemical natures of the diglucosyl hypoxanthines, compound I and

CHART 3

CHART 4

II, may provide strong additional evidence that one of the two glucosyl moieties in the respective compounds is linked to the pyrimidine nitrogen as described previously.

From the results obtained in the alkaline hydrolysis of N-1-alkylinosine,⁶⁾ compounds I and II were expected to give 5-amino-1-(β -D-glucopyranosyl) imidazole-4-(β -D-glucopyranosyl) carboxamide (I') and 5-amino-3-(β -D-glucopyranosyl) imidazole-4-(β -D-glucopyranosyl) carboxamide (II'), respectively, and this

was actually confirmed by the following evidence. The products I' and II' obtained by alkaline hydrolysis possessed arylamino group, as detected by the Bratton-Marshall's diazotization reaction,^{7,8)} and their infrared spectra revealed the presence of carboxamide C=O stretching (1620 cm^{-1} and 1630 cm^{-1} , re-

7) A.C. Bratton and E.K. Marshall, *J. Biol. Chem.*, **128**, 537 (1939).

8) J. Baddiley, J.G. Buchanan, F.E. Hardy and J. Stewart, *J. Chem. Soc.*, **1959**, 2892.

spectively) (cf. the C=O stretching of compounds I and II were $1690\sim 1700\text{ cm}^{-1}$).

Since free glucose could not be detected in the reaction mixture by the Fehling reaction as well as by paper chromatography, N-glucosylcarboxamide bonds in both compounds I' and II' were retained under such a condition as described above. Moreover, sodium formate, a by-product of this reaction, was detected by the reaction with mercuric chloride.⁹⁾ Then, the acetylated compounds III and IV (III'' and IV'') were reacted with mercuric bromide in an alkaline medium to obtain respective bromomercury derivatives. The ultraviolet absorption spectra of the bromomercury derivatives of III'' and IV'' in aqueous ethanol revealed the patterns similar to those of acetylated compounds II and I (II'' and I''), respectively (the details are shown in experimental). These derivatives were coupled with acetobromoglucose under the usual conditions of the Davoll-Lowy's method.¹⁰⁾ The coupling product (23.3% Yield) obtained from III'' was identical with compound II'', and the product (17% Yield) from IV'' was identical with I''. Thus, the allocations of bromomercury moieties to the position 1 of hypoxanthine in the bromomercury derivatives of acetylated compounds III and IV (III'' and IV'') were reasonably suggested.¹¹⁾

The result indicates that the attachment of mercury to hypoxanthine would be at least the (N-1)-(O-6) grouping, besides the known N-7 or N-9.¹¹⁾

It is then assumed that the bromomercury derivative of hypoxanthine obtained under the above-mentioned conditions would be a mixture of mono- (1:1) and di- (2:1) bromomercury hypoxanthines¹¹⁾ and that the incoming acetobromoglucose attacks the nitrogen bearing the

mercury of the bromomercury groups to displace the metal group. If the assumption is true, it is expected that the mono- (1:1) bromomercury hypoxanthine reacts with one more equivalent of mercuric bromide in alkaline medium, and that the obtained di- (2:1) bromomercury hypoxanthine requires one more equivalent of acetobromoglucose to be coupled to give diglucosides. In fact, this was confirmed by the following experiment.

Monobromomercury hypoxanthine was reacted with mercuric bromide in 1N sodium hydroxide and the obtained (2:1) derivative was refluxed with two molar equivalents of acetobromoglucose. The ratio of the yield of diglucosides against that of monoglucoside was increased by 2.5 times.

EXPERIMENTAL

Methods. The melting points were determined on a Yanagimoto micromelting point apparatus, and corrected. The ultraviolet spectra were measured with a Model-139 Hitachi Perkin-Elmer spectrophotometer, and the infrared spectra were measured with a model AR-275 Shimadzu spectrophotometer using potassium bromide disks unless otherwise stated. The NMR spectra were recorded on a Varian A-60 spectrophotometer in CDCl_3 and D_2O solvents using tetramethylsilane and D.S.S. as reference compounds. The $[\alpha]_D$ values were determined with a Rex photoelectric polarimeter and the ORD curves were measured with a JASCO automatic recording spectropolarimeter. The R_f values were obtained by descending chromatography on Whatman No. 1 paper with the solvent systems, pyridine: butanol: water = 1:1:1 v/v (solvent-A), butanol: acetic acid: water = 12:3:5 v/v (solvent-B) and isobutyric acid: water: ammonium hydroxide (d , 0.88): 0.1 M-versene = 100:55.8:4.2:1.6 v/v (solvent-C).

Bromomercury hypoxanthine. To a hot solution of 6.0 g (46 mmoles) of hypoxanthine in 250 ml of water containing 1.8 g (46 mmoles) of sodium hydroxide was added with stirring 16.5 g (46 mmoles) of mercuric bromide in hot alcohol. Precipitate formed immediately and the resulting suspension was stirred at room temperature for 45 min and then chilled. The precipitate was collected by centrifugation. It was washed with deionized water until free from bromide ion and then with ethanol and ether. It was dried for 24 hr at 110°C (2 mmHg) over phosphoric

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10) J. Davoll and B. A. Lowy, *J. Am. Chem. Soc.*, **73**, 1650 (1951).

11) J. A. Montgomery and H. J. Thomas, *J. Org. Chem.*, **31**, 1411 (1966).

anhydride, yield 15.18 g (83%). *Anal.* Found: N, 13.75. Calcd. for $C_8H_3ON_4HgBr$: N, 13.48%.

Bis-1,9-(2',3',4',6'-tetra-O-acetyl)- β -D-glucopyranosyl hypoxanthine (I''), Bis-1,7-(2',3',4',6'-tetra-O-acetyl)- β -D-glucopyranosyl hypoxanthine (II''), (2',3',4',6'-Tetra-O-acetyl)-7- β -D-glucopyranosyl hypoxanthine (III'') and (2',3',4',6'-Tetra-O-acetyl)-9- β -D-glucopyranosyl hypoxanthine (IV''). The finely ground mixture of 7.0 g (17.0 mmoles) of bromomercury hypoxanthine and 7.0 g of Celite No. 545 was previously dried for 24 hr at 110°C (2 mm-Hg) over phosphoric anhydride and suspended in 300 ml of dry xylene. The suspension was subjected to azeotropic distillation and cooled to room temperature. To the resulting suspension was added at once 6.9 g (16.8 mmoles) of acetobromoglucose dissolved in dry xylene (ca. 90 ml). The mixture was heated for 2 hr under reflux with stirring and then filtered. The filter cake was washed with hot chloroform (three 100 ml-portions). The hot xylene filtrate was evaporated to dryness *in vacuo* at below 40°C, and the residue was dissolved in 100 ml of warm chloroform and this was combined with the chloroform washings. The combined solution was washed with 30% potassium iodide solution (two 100 ml-portions) and with water (two 100 ml-portions), dried with magnesium sulfate and evaporated to dryness *in vacuo*. Crude coupling product (6.8 g) was obtained as a glass.

The t.l.c. on alumina* in ethylacetate-methanol (20:1) showed four zones under an UV-lamp and with vanadic acid-sulfuric acid spray at the following *R_f* values: compound I'', 0.90; compound II'', 0.83; compound III'', 0.20; compound IV'', 0.02. The crude product was acetylated with pyridine-acetic anhydride in the usual manner and chromatographed on a column packed with 150 g of neutralized alumina.* Elution with 650 ml of ethylacetate removed 4.2 g of the first fraction (fully acetylated glucose, compound I'' and compound II''). Further elution with about 800 ml of ethylacetate-methanol (3:1) removed 1.5 g of another fraction (compound II'' and compound I''). The former fraction was concentrated and chromatographed again on a column packed with 150 g of silicic acid.** Elution with 88 ml of ethylacetate-chloroform (3:1) removed 0.7 g of fully acetylated glucose and successive elution with 110 ml of the same solvent removed 1.8 g

of compound I'' (*R_f* 0.90). Further 40 ml of the eluate was set aside and elution with about 1 liter of ethylacetate removed 1.7 g of compound II'' (*R_f* 0.83). Each fractionated material was dissolved in 100 ml of chloroform and washed with water. Evaporation of the dried chloroform solution *in vacuo* gave 1.70 g (12.7%) of compound I'' as a glass, and 1.64 g (12.3%) of compound II'' as a glass. Both products were crystallized from ethanol.

Compound I'' mp 139.5~141.0°C $\lambda_{\max}^{EtOH}$ $m\mu(\epsilon)$: 243 (9300), 250 (8700), 271 (4700). $\lambda_{\min}^{EtOH}$ $m\mu(\epsilon)$: 224 (4100), 248 (8400), 261 (5300). *Anal.* Found: N, 7.20***. Calcd. for $C_{33}H_{40}O_{19}N_4$: N, 7.03%.

Compound II'' mp 150.5~152.0°C $\lambda_{\max}^{EtOH}$ $m\mu(\epsilon)$: 255 (5500), 247 (sh), 265 (sh). $\lambda_{\min}^{EtOH}$ $m\mu(\epsilon)$: 233 (4000). *Anal.* Found: N, 6.71***. Calcd. for $C_{33}H_{40}O_{19}N_4$: N, 7.03%.

The latter fraction of the alumina column chromatography was concentrated and chromatographed again on a column packed with 150 g of neutralized alumina. Elution with 120 ml of ethylacetate-chloroform-methanol (4:1:2) removed 190 mg of the impurities and next 120 ml of elution removed 520 mg of compound III'' (*R_f* 0.20). Further elution with 500 ml of the same solvent and 900 ml of ethylacetate-ethanol (1:1) removed 910 mg of compound IV'' (*R_f* 0.02). These fractionated materials were dissolved in 200 ml of chloroform and washed with two 20 ml-portions of water. Evaporation of the dried chloroform solution *in vacuo* gave 470 mg (6.0%) of compound III'' and 800 mg (10.2%) of compound IV''. Compound III'' and IV'' were crystallized from ethanol and from ethyl-acetate, respectively. Both compounds were recrystallized from ethanol.

Compound III'' mp 243.5~245.0°C $\lambda_{\max}^{EtOH}$ $m\mu(\epsilon)$: 252 (10,200). $\lambda_{\min}^{EtOH}$ $m\mu(\epsilon)$: 217 (6200). $[\alpha]_D^{25} - 4.4^\circ$ ($c = 1.28$, $CHCl_3$). *Anal.* Found: C, 48.82; H, 4.83; N, 12.20. Calcd. for $C_{19}H_{22}O_{10}N_4$: C, 48.93; H, 4.75; N, 12.01%.

Compound IV'' mp 266.0~267.0°C $\lambda_{\max}^{EtOH}$ $m\mu(\epsilon)$: 244 (11,000). $\lambda_{\min}^{EtOH}$ $m\mu(\epsilon)$: 217 (4200). $[\alpha]_D^{25} - 26.2^\circ$ ($c = 1.54$, $CHCl_3$). *Anal.* Found: C, 48.94; H, 4.76; N, 12.01. Calcd. for $C_{19}H_{22}O_{10}N_4$: C, 48.93; H, 4.75; N, 12.01%.

Bis-1,9-(β -D-glucopyranosyl) hypoxanthine (I). One g of compound I'' was dissolved in 80 ml of methanolic ammonia saturated at 0°C. The reaction mixture was stored overnight in an ice-box (5°C). After evaporation of the solvent the residue was dissolved

* Purchased from E. Merck AG, Darmstadt.

** Purchased from Mallinkrodt, New York, U.S.A.

*** Microanalysis of C and H was not performed.

in 10 ml of water and washed with chloroform. The aqueous layer was evaporated to dryness. The residue was treated with boiling ethanol and chilled. Amorphous powder was obtained by filtration. It was recrystallized three times from ethanol and dried over phosphoric anhydride at 110°C (2 mmHg) overnight: Yield, 423 mg (73.0%), mp, 215.5~216.5°C; $\lambda_{\max}^{0.05\text{ N HCl}}$ $m\mu(\epsilon)$: 251 (9600), $\lambda_{\max}^{\text{H}_2\text{O}, \text{pH}6}$ $m\mu(\epsilon)$: 251 (9500), $\lambda_{\max}^{0.05\text{ N NaOH}}$ $m\mu$: 252; $[\alpha]_D^{25} + 15.0^\circ$ ($c=2.2$, H_2O); R_f value 0.13 (solvent-B), 0.38 (solvent-C). The ORD curve was positive plain in the range of 350 $m\mu$ to 700 $m\mu$.

Anal. Found: D, 43.47; H, 5.66; N, 11.81. Calcd. for $\text{C}_{17}\text{H}_{24}\text{O}_{11}\text{N}_4 \cdot \frac{1}{2}\text{H}_2\text{O}$: C, 43.49; H, 5.37; N, 11.93%.

Bis-1,7-(β -D-glucopyranosyl) hypoxanthine (II). Similarly, 910 mg of compound II' was deacetylated, affording 376 mg (71.2%) of the titled compound. mp, 221.5~223.0°C (sintered at 212°); $\lambda_{\max}^{0.05\text{ N HCl}}$ $m\mu(\epsilon)$: 254 (7000), $\lambda_{\max}^{\text{H}_2\text{O}, \text{pH}6}$ $m\mu(\epsilon)$: 256 (6200), $\lambda_{\max}^{0.05\text{ N NaOH}}$ $m\mu$: 256; $[\alpha]_D^{25} + 20.0^\circ$ ($c=2.07$, H_2O); R_f value 0.15 (solvent-B), 0.40 (solvent-C). The ORD curve was positive plain in the range of 350 $m\mu$ to 700 $m\mu$. *Anal.* Found: C, 43.21; H, 5.63; N, 11.62. Calcd. for $\text{C}_{17}\text{H}_{24}\text{O}_{11}\text{N}_4 \cdot \frac{1}{2}\text{H}_2\text{O}$: C, 43.49; H, 5.37; N, 11.93.

7- β -D-Glucopyranosyl hypoxanthine (III). Deacetylation of 525 mg of compound III' in 25 ml of methanolic ammonia afforded 250 mg (74.4%) of compound III, mp, 200.5~203.5°C. The compound was first crystallized from 50% ethanol, recrystallized from water and dried over phosphoric anhydride at 110°C (2 mmHg) overnight. mp, 203.5~205.0°C; $\lambda_{\max}^{0.05\text{ N HCl}}$ $m\mu(\epsilon)$: 253.5 (9000), $\lambda_{\max}^{\text{H}_2\text{O}, \text{pH}6}$ $m\mu(\epsilon)$: 252 (8800), $\lambda_{\max}^{0.05\text{ N NaOH}}$ $m\mu(\epsilon)$: 263 (9200); $[\alpha]_D^{18} - 48.0^\circ$ ($c=1.17$, 1 N NaOH), $[\alpha]_D^{33} + 8.7^\circ$ ($c=1.5$, H_2O); R_f value 0.61 (solvent-A), 0.19 (solvent-B), 0.52 (solvent-C). The ORD curve was negative plain in the range of 350 $m\mu$ to 700 $m\mu$. *Anal.* Found: C, 41.89; H, 5.31; N, 17.82. Calcd. for $\text{C}_{11}\text{H}_{14}\text{O}_6\text{N}_4 \cdot \text{H}_2\text{O}$: C, 41.77; H, 5.10; N, 17.72%.

9- β -D-Glucopyranosyl hypoxanthine (IV). Deacetylation of 1.0 g of compound IV' in 50 ml of methanolic ammonia afforded 560 mg (80.7%) of compound IV. It was recrystallized from water and dried over phosphoric anhydride overnight (2 mmHg). mp, 275.0~276.0°C (dec), $\lambda_{\max}^{0.05\text{ N HCl}}$ $m\mu(\epsilon)$: 249 (11,000), $\lambda_{\max}^{\text{H}_2\text{O}, \text{pH}6}$ $m\mu(\epsilon)$: 248 (14,800), $\lambda_{\max}^{0.05\text{ N NaOH}}$ $m\mu(\epsilon)$: 254 (12,900); $[\alpha]_D^{22} - 38.4^\circ$ ($c=2.11$, 1 N NaOH), $[\alpha]_D^{31} - 2.1^\circ$ ($c=0.9$, H_2O); R_f value 0.60 (solvent-A), 0.16 (solvent-B), 0.47 (solvent-C). *Anal.* Found: C, 41.79; H, 5.08; N, 17.84. Calcd. for $\text{C}_{11}\text{H}_{14}\text{O}_6\text{N}_4 \cdot \text{H}_2\text{O}$: C, 41.77; H, 5.10; N, 17.72%.

1- β -D-Glucopyranosyl hypoxanthine (V) from Bis-1,9-(β -D-glucopyranosyl) hypoxanthine (I) and Bis-1,7-(β -D-glucopyranosyl) hypoxanthine (II). Fifty mg of compound I was dissolved in 5 ml of 1 N hydrochloric acid and heated on a steam bath for 1.5 hr. The reaction mixture was evaporated to dryness with several additions of methanol *in vacuo* at below 40°C. The residue was triturated with methanol and filtered. The collected white powder was dissolved in minimum amount of boiling water and neutralized with dilute ammonium hydroxide and chilled.

Colorless crystals were deposited and filtered. Yield, 16 mg (49.4%), mp, 273.5~275.0°C (dec). It was recrystallized from water for analysis. $\lambda_{\max}^{0.05\text{ N HCl}}$ $m\mu(\epsilon)$: 249 (9400), $\lambda_{\max}^{\text{H}_2\text{O}, \text{pH}6}$ $m\mu(\epsilon)$: 250.5 (8800), $\lambda_{\max}^{0.05\text{ N NaOH}}$ $m\mu(\epsilon)$: 260.5 (9300); $[\alpha]_D^{31.0} + 16.2^\circ$ ($c=0.88$, H_2O); R_f value 0.60 (solvent-A). *Anal.* Found: C, 43.99; H, 4.91; N, 18.34. Calcd. for $\text{C}_{11}\text{H}_{14}\text{O}_6\text{N}_4$: C, 44.29; H, 4.72; N, 18.79%.

Fifty mg of compound II was hydrolyzed with acid in the manner described above to give 10 mg (31.0%) of compound V.

Bis-1,9-(β -D-glucopyranosyl) hypoxanthine (I) from (2',3',4',6'-Tetra-O-acetyl)-9- β -D-glucopyranosyl hypoxanthine (IV').

a) Bromomercury derivative of compound IV'. Three hundred and twenty mg of compound IV' was dissolved in 15 ml of boiling deionized water containing 250 mg (0.69 mmole) of mercuric bromide, and 0.69 ml of 1 N sodium hydroxide solution was gradually added into this reaction mixture. The solution was heated on a steam bath for 1.5 hr and stored overnight in an ice box. The precipitate was filtered and washed with a small amount of cold water. Yield, 227 mg (44.3%), mp 191.0~192.5°C. $\lambda_{\max}^{50\%\text{ EtOH}}$ $m\mu$: 248, 250, $\lambda_{\min}^{50\%\text{ EtOH}}$ $m\mu$: 224. cf. Compound I' $\lambda_{\max}^{50\%\text{ EtOH}}$ $m\mu$: 245, 251, $\lambda_{\min}^{50\%\text{ EtOH}}$ $m\mu$: 226.

b) Bis-1,9-(β -D-glucopyranosyl) hypoxanthine (I). Two hundred and twenty five mg of the bromomercury derivative of compound IV' was dried for 24 hr at 110°C (2 mmHg) over phosphoric anhydride and suspended in 10 ml of dry xylene. One hundred and twenty mg of acetobromoglucose was added to the suspension and refluxed for 1 hr. The insoluble material was removed and identified as compound IV'. The xylene solution was concentrated *in vacuo* and the residue was dissolved in chloroform. The solution was washed with water, dried with magnes-

um sulfate and evaporated. The oily product was chromatographed on a 20 g of silicic acid column under the same condition as mentioned previously, and 40 mg of compound I'' (17%) was obtained. Deacetylation of this compound by methanolic ammonia gave 14 mg of compound I which was identical with an authentic sample in every respect examined.

Bis-1,7-(β -D-glucopyranosyl) hypoxanthine (II) from (2',3',4',6'-Tetra-O-acetyl)-7- β -D-glucopyranosyl) hypoxanthine (III'').

a) Bromomercury derivative of compound III''. Two hundred and eighty four mg (55.5% yield) of the bromomercury derivative of compound III'' was obtained from 320 mg of compound III'' in the same manner as described above. mp, 189~191.0°C, $\lambda_{\max}^{50\% \text{ EtOH}}$ m μ : 251~253, $\lambda_{\min}^{50\% \text{ EtOH}}$ m μ : 233. cf. compound II'', $\lambda_{\max}^{50\% \text{ EtOH}}$ m μ : 254, $\lambda_{\min}^{50\% \text{ EtOH}}$ m μ : 232.

b) Bis-1,7-(β -D-glucopyranosyl) hypoxanthine (II). Two hundred and eighty mg of the bromomercury derivative of compound III'' was reacted with 130 mg of acetobromoglucose in 10 ml of xylene and 70 mg (23.3% yield) of compound II'' was obtained by column chromatography (30 g of silicic acid). Deacetylation by methanolic ammonia gave 20 mg of II'' which was identical with an authentic sample in every respect examined.

Bis-bromomercury hypoxanthine. Bromomercury hypoxanthine (5.3 g, 13.0 mmoles) and Celite 545 (2.1 g) were suspended in 13.0 ml of 1 N sodium hydroxide, and 4.7 g (13.0 mmoles) of mercuric bromide in hot alcohol was added to the suspension. The reaction mixture was refluxed with stirring for 1 hr and stored in an ice-box overnight and filtered. The filter cake (pale red-brown solid) was washed well with deionized water and with alcohol, and then dried over phosphoric anhydride overnight. Yield, 9.2 g* (80.0%, calcd. as bis-bromomercury derivative of hypoxan-

thine). *Anal.* Found: N, 8.06. Calcd. for $\text{C}_5\text{H}_2\text{ON}_4\text{-Hg}_2\text{Br}_2$: N, 7.83%.

Glucosidation of bis-bromomercury hypoxanthine with two equimolar amount of acetobromoglucose. The bis-bromomercury derivative of hypoxanthine (7.0 g, 10.2 mmoles) and Celite (2.1 g) 545 were suspended in 100 ml of xylene and the suspension was subjected to azeotropic distillation (60 ml). Then, 8.36 g (10.2 mmoles) of acetobromoglucose was added. The mixture was refluxed for 2 hr with vigorous stirring. After 10 min the red color due to the bis-bromomercury derivative of hypoxanthine turned to pale yellow. The reaction mixture was filtered while warm and the filter cake was washed with chloroform (400 ml). The filtrate was evaporated *in vacuo* and dissolved in 600 ml of chloroform. The chloroform washings and the solution obtained were combined and washed with 30% potassium iodide (two 160 ml-portions) and water (two 200 ml-portions) to give 10.2 g of an oily product. This oily product was subjected to column chromatography in the same manner as described above. The yields of four products were: compound I'' 2.46 g (15.2%), compound II'' 1.86 g (11.5%), compound III'' 280 mg (2.9%), compound IV'' 400 mg (4.2%).

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* This yield includes 2.1 g of Celite; therefore, the yield of pure product was 7.1 g. For preparation of the analytical sample of the bis-bromomercury hypoxanthine, the Celite was not added in a small run.