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Reaction of Nucleophilic Reagents with D-Glycosyl- and D-Gluconyl Isothiocyanates[1]

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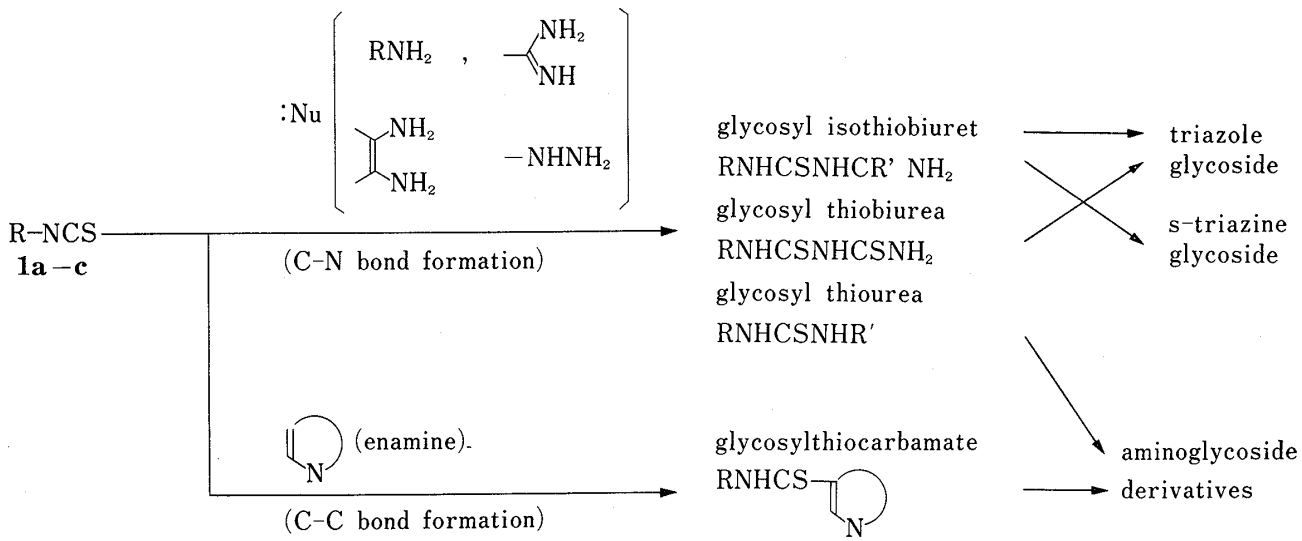
Reactions of various amino compounds with D-glycosyl- and D-gluconyl isothiocyanates gave the corresponding thioureides in good yields.

Attempts to cause the ring closure of N-glucopyranosyl-N'-phenyl thioureide with methyl cyanoacetate or methyl propiolate under acidic conditions were unsuccessful.

Keywords——glycosyl isothiocyanate; gluconyl isothiocyanate; N-glycosyl-N'-substituted thioureide; N-gluconyl-N'-substituted thioureide; nitrogen nucleophiles; carbon nucleophiles; N-glycosyl-N'-phenyl thioureide

Syntheses glycosyl isocyanates and isothiocyanates have been reported by Fischer,[3] and Johnson and Bergman.[4] In addition, syntheses of glycosyl ureides or thioureides and appli-



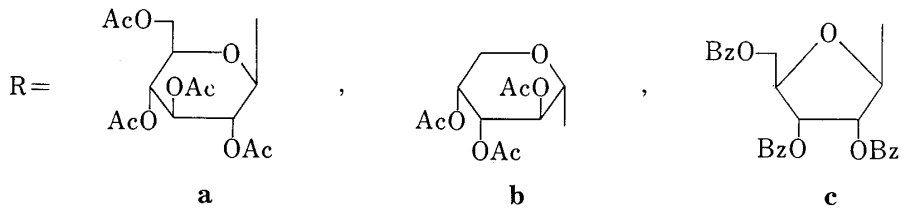


Chart 1

1) Previous paper: M. Sakaguchi, Y. Miyata, H. Ogura, K. Gonda, S. Koga, and T. Okamoto, *Chem. Pharm. Bull.* (Tokyo), **27**, 1094 (1979); This constitutes Part XXVI in a series entitled "Studies on Heterocyclic Compounds."
2) Location: *5-9-1 Shirokane, Minato-ku, Tokyo 108, Japan.*
3) E. Fischer, *Ber.*, **47**, 1377 (1914).
4) T.B. Johnson and W. Bergman, *J. Am. Chem. Soc.*, **54**, 3360 (1932).

cations to the preparation of nucleosides were reported by Goodman,[5] Naito,[6] Ukita,[7] and Sorm.[8] These publications are the only ones dealing with the synthesis of N-nucleosides using glycosyl isothiocyanates. In the present paper, we wish to report syntheses of modified

Table I. N-Glycosyl-N′-substituted Thioureides

Compd. No.	mp (°C)	Yield (%)	IR ν_{max}^{KBr} cm^{-1}	Formula	Analysis (%) Calcd. (Found) C	H	N
2a	205—207 (dec.)[a]	87	3500, 1250, 1150	$C_7H_{14}N_2O_5S$	35.28 (35.45	5.92 5.72	11.76 11.74)
2b	Syrup	74	3500, 1260, 1110	$C_6H_{12}N_2O_4S$	36.60 (34.57	5.81 5.76	13.45 13.32)
2c	163—165[b]	82	3500, 3400, 1710, 1605, 1580, 750	$C_{27}H_{24}N_2O_7S$	62.30 (62.15	4.65 4.60	5.38 5.34)
3a	136—139	95	3450, 1740, 1610, 1570, 750	$C_{21}H_{26}N_2O_0S$	52.28 (52.25 (M$^+$, *m/e* 482)	5.43 5.40	5.81 5.83)
3b	170—172	97	3450, 1740, 1605, 1580, 720	$C_{28}H_{22}N_2O_7S$	63.39 (63.40 (M$^+$, *m/e* 530)	4.18 4.26	5.28 5.25)
3c	167—168	95	3500, 1710, 1610, 1580, 750	$C_{33}H_{28}N_2O_7S$	66.43 (66.37	4.73 4.71	4.70 4.68)
4a	156—158	92	3500, 3450, 1740, 1580	$C_{19}H_{24}N_4O_9S$	47.10 (47.18 (M$^+$, *m/e* 484)	4.99 4.94	11.56 11.62)
4b	162—165	87	3450, 1740, 1560	$C_{16}H_{20}N_4O_7S$	46.60 (46.57 (M$^+$, *m/e* 412)	4.89 4.92	13.59 13.60)
4c	167—170	90	3500, 1710, 1580	$C_{31}H_{25}N_4O_7S$	62.30 (62.26	4.22 4.18	9.38 9.43)
5a	120—124	95	3400, 3270, 2900, 1740	$C_{25}H_{36}N_2O_9S$	55.54 (55.55	6.71 6.68	5.18 5.24)
5b	Syrup[c]	97	3450, 3200, 1740	$C_{22}H_{32}N_2O_7S$	56.39 (56.27	6.88 6.92	5.98 5.80)
5c	Syrup[d]	95	3450, 2950, 1710	$C_{37}H_{38}N_2O_7S$	67.87 (67.92	5.85 5.84	4.28 4.30)
6a	145—147	87	3400, 3270, 1740, 1680	$C_{21}H_{26}N_4O_{10}S$	47.91 (47.87 (M$^+$, *m/e* 526)	4.98 4.95	10.64 10.42)
6b	151—155	85	3450, 3250, 1740, 1680	$C_{28}H_{22}N_4O_8S$	58.53 (58.50 (M$^+$, *m/e* 574)	3.86 3.84	9.75 9.74)
6c	175—176	92	3400, 3300, 1710, 1610	$C_{33}H_{28}N_4O_8S$	61.87 (61.92	4.41 4.43	8.75 8.68)
7a	139—141	85	3460, 3260, 1740, 1610, 1590	$C_{27}H_{33}N_5O_{11}S_2$	48.57 (48.72	4.98 4.85	10.49 10.63)
7b	syrup[e]	87	3450, 3250, 1740, 1610, 1580	$C_{24}H_{29}N_5O_9S_2$	48.40 (48.32	4.91 4.90	11.76 11.72)
8a	134—136	70	3400, 3270, 1740, 1580	$C_{25}H_{29}N_5O_{11}S_2$	46.94 (46.98	4.57 4.73	10.95 10.98)
8b	syrup[f]	92	3500, 3250, 1740, 1580	$C_{22}H_{25}N_5O_9S_2$	46.56 (46.59	4.44 4.53	12.34 12.28)

a) Reported[6] mp 207—210° (dec.).
b) Reported[6] mp 158—161°.
c) TLC (silica gel) *Rf* 0.74 (benzene acetone=3: 2).
d) TLC (silica gel) *Rf* 0.82 (benzene–acetone=3: 2).
e) TLC (silica gel) *Rf* 0.55 (benzene–acetone=4: 1).
f) TLC (silica gel) *Rf* 0.50 (benzene–acetone=4: 1).

5) I. Goodman, "Advances in Carbohydrate Chemistry," Vol. 13, Academic Press, New York, 1958, p. 215.
6) T. Naito and M. Sano, *Chem. Pharm. Bull.* (Tokyo), **9**, 709 (1961).
7) T. Ukita, A. Hamada, and Y. Yoshida, *Chem. Pharm. Bull.* (Tokyo), **12**, 454 (1964).
8) A. Piskala and F. Sorm, *Coll. Czech. Chem. Comm.*, **29**, 2060 (1964).

nucleoside analogs from glycosyl isothiocyanates as starting materials. The synthetic approaches to nucleoside analogs are shown in Chart 1. These are:

(i) C–N bond formation at the C-1 position by the reaction of isothiocyanates with nitrogen nucleophiles (amine, diamine,[9] hydrazino compounds,[10] and guanyl compounds[11]).

(ii) C–C bond formation at the C-1 position by the reaction of isothiocyanates with carbon nucleophiles (enamines[12]). It is known that isothiocyanates undergo various reactions due to the isothiocyanate group.[13] Glycosyl isothiocyanates (**1a**—**c**) or gluconyl isothiocyanate (**1d**) in appropriate solvents reacted smoothly with amino compounds at room temperature to give the corresponding N-glycosyl- and N-gluconyl-N′-substituted thioureides in good yields.

Treatment of 2,3,4,6-tetra-*O*-acetyl-*β*-D-glucopyranosyl isothiocyanate (**1a**) or 2,3,4-tri-*O*-acetyl-*α*-D-arabinopyranosyl isothiocyanate (**1b**) with NH_3–MeOH under cooling gave **2a** or **b** in 74—87% yield. Similar treatment of 2,3,5-tri-*O*-benzoyl-*β*-D-ribofuranosyl isothiocyanate (**1c**) with NH_3–MeOH afforded **2c** in 95% yield. Reactions of **1a**, **b**, **c** and **d** with

Table II. N-Gluconyl-N′-substituted Thiourecides

Compd. No.	mp (°C)	Yield (%)	IR ν_{max}^{KBr} cm^{-1}	NMR ($CDCl_3$, δ)	Analsis (%)	Calcd.	Found
						$C_{23}H_{28}N_2O_{11}S$ (M^+, *m/e* 540)	
3d	Syrup[a]	95	3450, 3400, 1740		C	51.11	51.08
					H	5.22	5.17
					N	5.18	5.24
						$C_{21}H_{23}N_4O_{11}S$ (M^+, *m/e* 542)	
4d	127—129	78	3450, 1740, 1590	7.80 (1H, t, 5-H), 8.68 (2H, d, 4-H, 6-H), 10.76, 13.08 (2H, bs, $(NH)_2$)	C	46.49	46.53
					H	4.83	4.92
					N	10.33	10.30
						$C_{27}H_{38}N_2O_{11}S$	
5d	Syrup[b]	90	3400, 3300, 1740, 1610	1.70, 2.15 (15H, m, CH_2, CH), 8.08, 9.80 (2H, bs, $(NH)_2$)	C	54.17	54.25
					H	6.40	6.35
					N	4.68	4.72
						$C_{23}H_{28}N_4O_{12}S$ (M^+, *m/e* 584)	
6d	Syrup[c]	72	3200, 1740, 1600, 760, 690	7.70, 8.61 (4H, d, pyridine ring), 9.33, 9.84, 13.58 (3H, bs, $(NH)_3$)	C	47.26	47.32
					H	4.83	4.80
					N	9.58	9.73
						$C_{29}H_{35}N_5O_{13}S_2$	
7d	110—112	95	3480, 1740, 1580	2.40, 2.57 (6H, s, Me_2), 9.00, 11.98 (2H, bs, $(NH)_2$)	C	47.99	47.95
					H	4.86	4.93
					N	9.65	9.64
						$C_{27}H_{31}N_5O_{13}S_2$	
8d	Syrup[d]	92	3480, 1740, 1600, 700	7.00 (1H, t, 5-H), 8.01 (4H, m, Ph), 9.00, 11.98 (2H, bs, $(NH)_2$)	C	46.48	46.53
					H	4.48	4.40
					N	10.04	10.10

a) TLC (silica gel) R^6 0.85 (benzene–acetone=3:2).
b) TLC (silica gel) *Rf* 0.48 ($CHCl_3$–MeOH=9:1).
c) TLC (silica gel) *Rf* 0.62 ($CHCl_3$–MeOH=9:1).
d) TLC (silica gel) *Rf* 0.58 ($CHCl_3$–MeOH=9:1).

9) H. Ogura, H. Takahashi, K. Takeda, M. Sakaguchi, N. Nimura, and H. Sakai, *Heterocycles*, **3**, 1129 (1975).
10) H. Ogura, H. Takahashi, and E. Kudo, *J. Carbohydr. Nucleosides Nucleotides*, **5**, 329 (1978); H. Ogura, H. Takahashi, and M. Sakaguchi, *Nucleic Acids Res.*, **S5**, 251 (1978).
11) H. Ogura and H. Takahashi, presented at the 21st Symposium on the Chemistry of Natural Products, Sapporo, 1978.
12) H. Ogura, H. Takahashi, K. Takeda, and N. Nimura, *Nucleic Acids Res.*, **S2**, 7 (1976).
13) S. Patai, "The Chemistry of Cyanates and Their Thio Derivatives," John Wiley and Sons, 1977.

Table III. N-Glucopyranosyl-N′-substituted Thioureides (**11a**, **12a**, **13a**, **14a**)

Compd. No.	mp (°C)	Yield (%)	IR ν_{max}^{KBr} cm^{-1}	Formula	Analsis (%) Calcd. (Found) C	H	N
11a	126—128	80	3300, 1740, 1580, 720, 695	$C_{22}H_{28}N_2O_9S$	53.22 (53.20 (M$^+$, *m/e* 596)	5.68 5.65	5.64 5.60)
12a	162—165	94	3350, 1740, 1590, 740	$C_{22}H_{26}N_4O_9S$	50.57 (50.54	5.02 5.04	10.72 10.69)
13a	170—181	84	3300, 1740, 1590, 750	$C_{22}H_{25}N_3O_9S_2$	48.97 (48.85 (M$^+$, *m/e* 539)	4.67 4.65	7.79 7.82)
14a	148—150	70	3350, 1740, 1620, 740	$C_{21}H_{25}BrN_2O_9S$	44.93 (44.98	4.49 4.50	4.99 4.87)

aniline, 2-aminopyrimidine, 1-adamantylamine or sulfamines in benzene or xylene also proceeded well to afford the corresponding N-glycosyl- and N-gluconyl-N′-substituted thioureides. Similar treatment of **1a**, **b**, **c** and **d** with isonicotinylhydrazine in acetonitrile gave **6a**, **b**, **c**, and **d** in fair yields (Table I and II). Similar reactions of 2,3,4,6-tetra-*O*-acetyl-*β*-D-glucopyranosyl isothiocyanate (**1a**) with amino compounds (benzylamine, 2-aminobenzimidazole, 2-aminobenzothiazole or *o*-bromoaniline) gave N-glycosyl-N′-substituted thioureides in excellent yields (Table III), and similar treatments of **1d** with 2-aminopyridine or 5-amino-1-phenylpyrazole-4-carboxylate afforded N-gluconyl-N′-substituted thioureides in 75—82% yield. Treatment of N-(2,3,4,6-tetra-*O*-acetyl-*β*-D-glucopyranosyl)-N′-phenyl thioureide (**3a**) with methyl cyanoacetate in Ac_2O with heating gave 53% N-acetylanilide and 42% **1a**. In this case, it appears that **3a** dissociated back to the starting material (**1a**) on heating. It is known

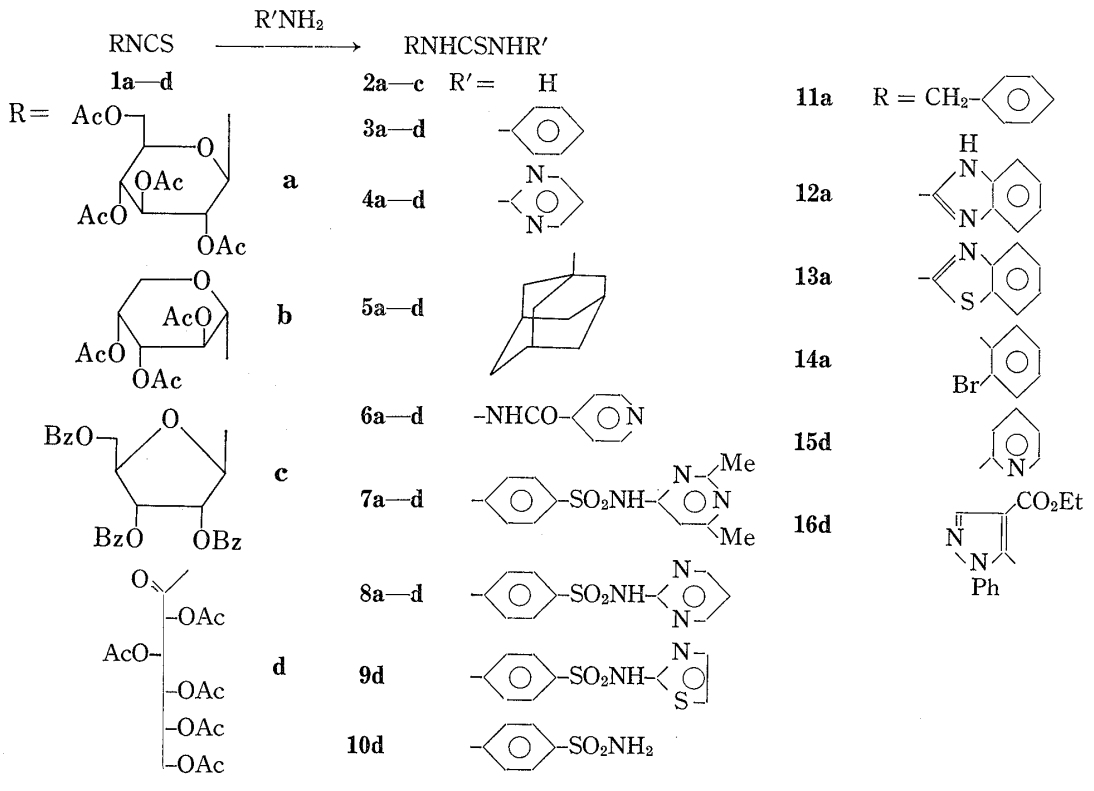


Chart 2

that ureas having a bulky group dissociate on heating.[14] Reaction of **3a** with methyl propiolate in Ac_2O under reflux gave the N-acetyl compound (**17a**) in 87% yield. The nuclear magnetic resonance (NMR) spectrum of **17a** showed a singlet peak at δ 2.45 due to the N-acetyl group. In the mass spectrum (MS), a molecular ion peak appeared at *m/e* 524 (6%). Thus, attempts to cause ring closure of a glycosyl thioureide (**3a**) by heating or under acidic conditions to give **18a** were unsuccessful.

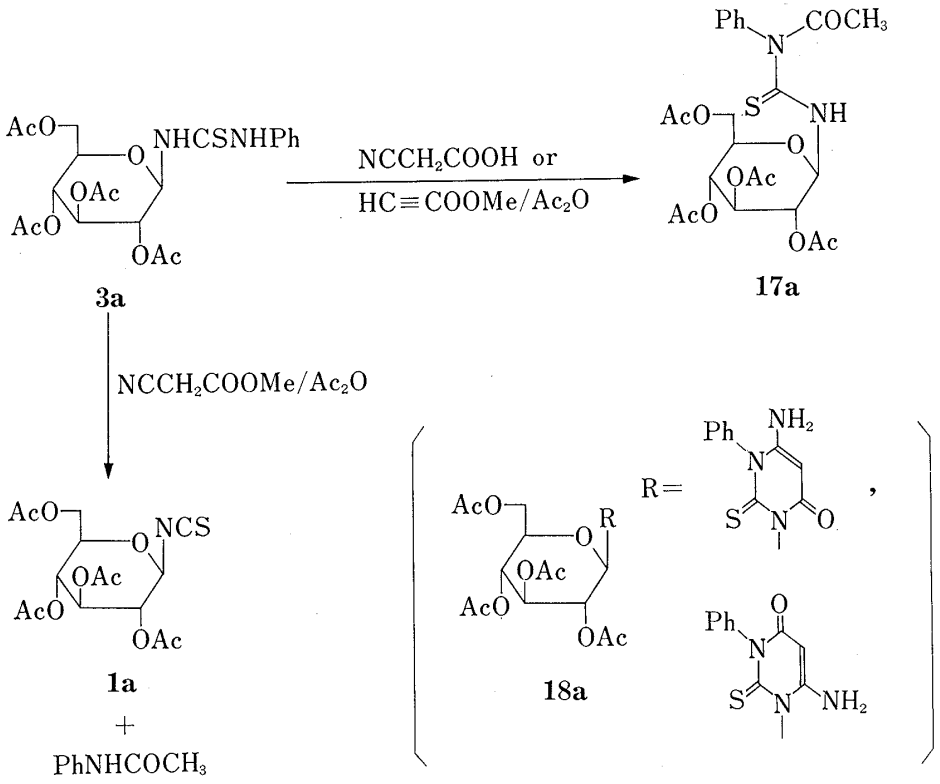


Chart 3

Experimental

All melting points are uncorrected. Infrared spectra (IR) were measured with a JASCO A-2 spectrometer and NMR spectra on a Varian T-60 spectrometer; tetramethylsilane was used as an internal reference. Mass spectra were determined with a JMS-D-100 spectrometer using a direct inlet system at 75 eV.

N-Glycosyl Thioureide (2a, b) and N-(2,3,5-Tri-*O*-benzoyl-*β*-D-ribofuranosyl)thioureide (2c)——a) **1a, b** or **c** (0.003 mol) was dissolved in NH_3–MeOH (10 ml) and kept at 0—5° for 1—2 hr with stirring. The separated crystals were collected by filtration, washed with MeOH (3—5 ml) and dried. **2a** or **c** was obtained as colorless prisms or needles. Analytical samples were recrystallized from EtOH. In the case of **1b**, the filtrate was evaporated down under reduced pressure to give **2b** as a colorless syrup.

N-Glycosyl- and N-Gluconyl-N′-phenylthioureide (3a, b, c and d)——a) A mixture of D-glycosyl isothiocyanate (**1a, b** or **c**) (0.001 mol) and aniline (93 mg, 0.001 mol) in dry xylene (10 ml) was refluxed for 3 hr and allowed to stand at room temperature. Separated crystals were collected by filtration, followed by recrystallization from benzene to give **3a, b** or **c** as fine colorless needles.

b) A solution of 2,3,4,5,6-penta-*O*-acetyl-D-gluconyl isothiocyanate (**1d**; 447 mg, 0.001 mol) and aniline (93 mg, 0.001 mol) in acetonitrile (15 ml) was stirred for 2 hr at room temperature. Removal of the solvent by evaporation left a syrup which was purified by chromatography on silica gel with $CHCl_3$ to give **3d** as a colorless syrup.

14) W.B. Bennet, J.H. Saunders, and E.E. Hardy, *J. Am. Chem. Soc.*, **75**, 2101 (1953); T. Mukaiyama and Y. Fujita, *Bull. Chem. Soc. Jpn.*, **29**, 54 (1956); J.C. Stowell and S.J. Padegimas, *J. Org. Chem.*, **39**, 2448 (1974).

N-Glycosyl- and N-Gluconyl-N′-(pyrimidin-2-yl)thioureides (4a, b, c and d)——A mixture of **1a, b, c** or **d** (0.001 mol) and 2-aminopyrimidine (95 mg, 0.001 mol) in dry benzene (15 ml) was refluxed for 2—10 hr and evaporated down under reduced pressure to give a syrup which yielded crystals on standing in EtOH. Recrystallization from EtOH gave **4a, b, c** or **d** as fine colorless needles.

N-Glycosyl- and N-Gluconyl-N′-(2-adamantyl)thioureides (5a, b, c and d)——A solution of **1a, b, c** or **d** (0.001 mol) and 1-adamantylamine (150 mg, 0.001 mol) in dry benzene (10 ml) was refluxed for 1—3 hr and evaporated down under reduced pressure to give a residue. The residue was crystallized from ether to give **5a** as a colorless precipitate. Recrystallization from EtOH gave **5a** as colorless needles. In the cases of **1b, c** and **d**, the reaction solution was treated as described for **3d** to give **5b, c** or **d** as a slightly yellow syrup. This syrup was dissolved in $CHCl_3$ (1 ml) and then chromatographed on silica gel with $CHCl_3$. From the eluate with $CHCl_3$, **5b, c** or **d** was obtained as a colorless syrup.

N-Glycosyl- and N-Gluconyl-2-(isonicotinylhydrazine)carboxamide (6a, b, c and d)——A mixture of **1a, b** or **c** (0.001 mol) and isonicotinylhydrazine (136 mg, 0.001 mol) in dry benzene (20 ml) was refluxed for 2—5 hr and evaporated down under reduced pressure to give **6a, b** or **c**. Recrystallization from benzene or CCl_4 gave **6a, b** or **c** as fine colorless needles. In the case of **1d**, the reaction mixture was purified by chromatography on silica gel with $CHCl_3$ to give **6d** as a colorless syrup.

N^1-(2,4-Dimethylpyrimidin-6-yl)-N^4-(2-glycosylthioamido)sulfanilamide (7a, b) and N^1-(2,4-Dimethylpyrimidin-6-yl)-N^4-(2-gluconylthioamido)sulfanilamide (7d)——A mixture of **1a, b** or **d** (0.001 mol) and N-(2,6-dimethyl-4-pyrimidyl)sulfanilamide (278 mg, 0.001 mol) in tetrahydrofuran (THF) (15 ml) was stirred for 3—5 hr at room temperature and evaporated down under reduced pressure to give a residue. The residue was crystallized from ether to give **7a** or **d** as slightly yellow crystals. Recrystallization from ether–$CHCl_3$ (5: 1) gave **7a** or **d** as slightly yellow needles. In the case of **1b, 7b** was obtained as a yellow syrup after chromatography.

N^1-(Pyrimidin-2-yl)-N^4-(2-glycosylthioamido)sulfanilamide (8a, b) and N^1-(Pyrimidin-2-yl)-N^4-(2-gluconylthioamido)sulfanilamide (8d)——A mixture of **1a, b** or **d** (0.001 mol) and N-(2-pyrimidyl)sulfanilamide (250 mg, 0.001 mol) in THF (10 ml) was treated as described above (**7a, b** or **d**) and yielded **8a, b** or **d** as slightly yellow crystals or a slightly yellow syrup.

N^1-(Thiazol-2-yl)-N^4-(2-gluconylthioamido)sulfanilamide (9d)——A mixture of **1d** (447 mg, 0.001 mol) and 2-sulfanilamidothiazole (255 mg, 0.001 mol) in dry THF (20 ml) was stirred for 3 hr at room temperature and evaporated to dryness. The residue obtained was purified by chromatography on silica gel using $CHCl_3$ to give 641 mg (92%) of **9d** as a slightly yellow syrup. *Rf* 0.47 (benzene–acetone=3: 2). IR ν_{max}^{KBr} cm^{-1}: 3480 (NH), 1740 (ester), 1580 (phenyl), 1220, 1110, 750. *Anal.* Calcd. for $C_{26}H_{30}N_4O_{13}S_3$: C, 44.44; H, 4.30; N, 7.97. Found: C, 44.72; H, 4.50; N, 7.98.

***α*-Gluconylthioureidoamino-*p*-toluenesulfonamide (10d)**——A mixture of **1d** (447 mg, 0.001 mol) and α-amino-*p*-toluenesulfonamide (186 mg, 0.001 mol) in dry THF (15 ml) was stirred for 20 min at room temperature and treated as described for **9d** to give 545 mg (87%) of **10d** as a colorless syrup. *Rf* 0.52 (benzene–acetone =3: 2). IR ν_{max}^{KBr} cm^{-1}: 3450, 3300 (NH_2, NH), 1740 (ester), 1605 (phenyl), 1210, 1110, 695. *Anal.* Calcd. for $C_{24}H_{31}N_3O_{13}S_2$: C, 45.50; H, 4.93; N, 6.63. Found: C, 45.73; H, 5.00; N, 6.60.

General Procedure of N-Glucopyranosyl-N′-substituted Thioureide (11a, 12a, 13a, 14a)——A mixture of **1a** (389 mg, 0.001 mol) and a heterocycle (benzylamine, 2-aminobenzimidazole, 2-aminobenzothiazole, *o*-bromoaniline, 2-aminopyridine or 5-amino-4-carboethoxy-1-phenylpyrazole) (0.001 mol) in dry benzene or MeCN (10 ml) was refluxed for 0.5—1 hr. Crystals that separated were collected by filtration, followed by recrystallization from benzene to give **11a, 12a, 13a** or **14a** as fine colorless needles or prisms (Table III).

N-(2,3,4,5,6-Penta-*O*-acetyl-D-gluconyl)-N′-(pyrid-2-yl)thioureide (15d)——A solution of **1d** (447 mg, 0.001 mol) and 2-aminopyridine (94 mg, 0.001 mol) in dry benzene (10 ml) was refluxed for 4 hr and evaporated to dryness. The syrup was purified by chromatography on silica gel, and 443 mg (82%) of **15d** was obtained from the benzene–acetone (25: 1) eluate as a colorless syrup. *Rf* 0.82 (benzene–acetone=3: 2). IR ν_{max}^{KBr} cm^{-1}: 3450 (NH), 1740 (ester), 1590, 1210, 1070, 780. *Anal.* Calcd. for $C_{22}H_{27}N_3O_{11}S$: C, 48.80; H, 5.03; N, 7.76. Found: C, 48.92; H, 5.23; N, 7.65. NMR ($CDCl_3$) δ: 7.20, 7.70, 8.38 (4H, m, pyridine), 9.08 (1H, bs, NH), 13.40 (1H, bs, NH). MS *m/e*: 541 (M^+).

N-(2,3,4,5,6-Penta-*O*-acetyl-D-gluconyl)-N′-(4-carboethoxy-1-phenylpyrazol-5-yl)thioureide (16d)——A mixture of **1d** (447 mg, 0.001 mol) and 5-amino-1-phenylpyrazole-4-carboxylate (231 mg, 0.001 mol) in dry benzene (10 ml) was refluxed for 10 hr and evaporated to dryness. The syrup was chromatographed on silica gel with benzene–acetone (10: 1) to give 499 mg (75%) of **16d** as a colorless syrup. *Rf* 0.75 (benzene–acetone=3: 2). IR ν_{max}^{KBr} cm^{-1}: 3450, 3200 (NH), 1740 (ester), 1590, 1580 (phenyl), 1210, 1050, 750. *Anal.* Calcd. for $C_{28}H_{34}N_4O_{13}S$: C, 50.45; H, 5.14; N, 8.40. Found: C, 50.30, H, 5.14; N, 8.60. NMR ($CDCl_3$) δ: 1.30 (3H, t, Me), 7.48 (5H, m, Ph), 8.08 (1H, s, 3-H), 9.48 (1H, bs, NH), 11.72 (1H, bs, NH).

Attempted Ring Closure of N-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)-N′-phenyl Thioureide (3a)——a) With Methyl Cyanoacetate: A mixture of **3a** (482 mg, 0.001 mol) and methyl cyanoacetate (99 mg, 0.001 mol) in Ac_2O (10 ml) was refluxed for 2 hr and poured into ice-H_2O (100 ml). The reaction mixture was extracted with $CHCl_3$ (50 ml) and the organic layer was washed with saturated $NaHCO_3$ and dried over $MgSO_4$. Removal of the solvent by evaporation left a brown residue. Ether was added to the residue and the separated crystals were collected by filtration. They were identical with the starting material (**1a**).

The filtrate was concentrated under reduced pressure to give 105 mg (77%) of N-acetylanilide (mp 112—114°, reported mp 114°[15]).

b) With Cyanoacetic Acid in Ac_2O: A solution of **3a** (480 mg, 0.001 mol) and cyanoacetic acid (85 mg, 0.001 mol) in Ac_2O (5 ml) was heated at 85—90° for 5 hr and poured into ice-H_2O (100 ml). The reaction mixture was treated as described in section a) to give a brown residue. The residue was chromatographed on silica gel with $CHCl_3$–acetone. The eluate with $CHCl_3$–acetone (19: 1) gave 456 mg (87%) of N-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-N′,N′-acetylphenyl thioureide (**17a**) as a colorless syrup. *Rf* 0.82 (benzene–acetone=3: 2). IR ν_{max}^{KBr} cm^{-1}: 3350 (NH), 1740 (ester), 1700 (CO), 1605, 1580 (phenyl), 1210, 1110, 750. *Anal.* Calcd. for $C_{23}H_{28}N_2O_{10}S$: C, 52.67; H, 5.38; N, 5.34. Found: C, 52.74; H, 5.42; N, 5.40. MS *m/e*: 524 (M^+).

c) With Methyl Propiolate in Ac_2O: A solution of **3a** (480 mg, 0.001 mol) and methyl propiolate (85 mg, 0.001 mol) in Ac_2O (5 ml) was gently refluxed for 2.5 hr and poured into ice–H_2O (50 ml). Extraction with $CHCl_3$ gave a dark brown residue which showed five spots on thin-layer chromatography (TLC). The residue was treated as described in section b) and from the eluate with benzene–acetone (49: 1), 193 mg (37%) of **17a** was obtained as a colorless syrup.

15) Zvi Rapport, "Handbook of Tables for Organic Compound Identification (3rd Edit.)," The Chemical Rubber Co., 1967.