CHAPTER III

Experimental

Elemental Analyses

Analyses for carbon, hydrogen, nitrogen, sulfur and chlorine were performed by the laboratory of Chemistry Department of the Australian National University, Canberra, Australia and the Laboratory of the Department of Chemistry, Mahidol University, Bangkok.

Melting Points

All melting points were taken either on a Lietz microscope melting-point apparatus or an Electrothermal capillary melting point apparatus and both are uncorrected.

Infrared Absorption Spectra

All Infrared absorption spectra were obtained with a Perkin-Elmer 283 Grating Infrared Spectrophotometer.

Nuclear Magnetic Resonance Spectra

All Nuclear Magnetic Resonance Spectra were obtained with

a Variant Spectrophotometer, by the courtesy of Dr. William D. Crow of the Chemistry Department, The Australian National University, Canberra, Australia. They are all ^{13}C N.M.R. and ^{1}H -decoupled, using Tetramethylsilane as an internal standard and d6 DMSO as a log signal.

Chemical

The starting materials used here, including rhodanine and aldehydes were supplied by Aldrich Chemical Co. Benzaldehyde, p-dimethylaminobenzaldehyde, anhydrous sodium acetate, D-glucose, and acetic anhydride were supplied by May & Baker Co. Vanillin and Ethyl vanillin by Rhodiarome. Acetobromoglucose was partially supplied by Sigma Chemical Co. THF, siliga-gel for TLC and column chromatography were supplied by E-Merck Co. The solvents used were all BP. grade.

5-Benzylidenerhodanine

6.66 g. rhodanine (0.05 mole) was dissolved in 50 ml. of glacial acetic acid, then 12.3 g. anhydrous sodium acetate (0.15 mole) was added. After the mixture became clear, 5.31 g. (5.07 ml. or 0.05 mole) of benzaldehyde was added, and the reaction mixture was refluxed for 45 minutes. After it was cooled to room temperature, yellow crystals were formed. The whole mixture was kept in the refrigerator overnight. The crystals were separated by filtration and washed several times with water. The filtrate was poured into 300 ml. of water and kept in the refrigerator for another night.A yellow precipitate was formed and was separated by filtration. The precipitate was washed with water. The crude product was dried in the oven at 60°C with reduced pressure. Recrystalization from toluene yielded 8.8 g. of the product (80 % yield), m.p. 202-6 (lit m.p. 204-5) (99)

5-(3-Methoxy-4-hydroxybenzylidene) rhodanine

To a solution of 6.66 g. (0.05 mole) rhodanine in 30 ml. of glacial acetic acid was added 11.4 g. of anhydrous sodium acetate followed by 7.60 g. (0.05 mole) of vanillin. The reaction mixture was refluxed for 40 minutes and was cooled to room temperature, and yellowish orange crystals appeared, 50 ml of water was then added to the mixture. It was stirred for a few minutes and kept in the refrigerator overnight. The product was separated

by filtration and washed with water. The filtrate was poured into another 200 ml. water and kept in the refrigerator for another night. The precipitate was collected by filtration and washed with water. The crude product was dried in the oven at 60°C with reduced pressure. The total product weighed 12.03 g. or 89.98 % yield. After recrystalization from methanol, it gave yellowish orange crytals with m.p. 225-7°C (lit m.p. 227-8°C (128); and 228-230°C (83))

5-(3-Ethoxy-4-hydroxybenzylidene) rhodanine

6.66 g. (0.05 mole) rhodanine was dissolved in 30 ml. glacial acetic acid, then 11.40 g. anhydrous sodium acetate was added. After the solution became clear, 8.31 g.(0.05 mole) ethyl vanillin was added and the mixture was refluxed for 60 minutes. After cooling the mixture to room temperature, reddish yellow crystals were formed. The mixture was kept in the refrigerator overnight, then the crystals were separated by filtration and washed with water. The filtrate and washed water was combined and poured into 300 ml. of distilled water. This aqueous mixture was kept in the refrigerator for another night. The yellow precipitate was obtained by filtration and dried in the oven at 60°C with reduced pressure. The total weight of the product was 13.6 g. or 96.9 %. It was recrystalized from 95 % ethanol and the crystals had an of m.p.217.5 - 218.5°C (lit m.p. 216°) (30).

5-(4-Dimethylaminobenzylidene) rhodanine

25.0 g. of anhydrous sodium acetate was added into a solution of 13.3 g.(0.1 mole) rhodanine in 150 ml. glacial acetic acid, followed by 14.9 g. (0.1 mole) p-dimethylamino benzaldehyde. The mixture was refluxed on a water bath for 60 minutes. Then it was cooled to room temperature and kept in the refrigerator overnight. Red needle crystals were formed. The crystals were separated by filtration and washed with water. The filtrate was then poured into 100 ml. water and put into the refrigerator for another night. More precipitate was formed which was separated by filtration and washed with water. The product was dried in the oven under reduced pressure at 60°C. The total product weighed 19.6 g. or 74.2 % yield with m.p. 247° dec. after recrystalization from toluene. (lit m.p. Feigl reported a m.p. 246° (129). Mackie reported a m.p. 240°C dec (130))

5-(4-Chlorobenzylidene) rhodanine

6.66 g. (0.05 mole) rhodanine was dissolved in 50 ml. glacial acetic acid, then 12.3 g. of anhydrous sodium acetate was added. The mixture was warmed on a water bath to get a clear solution, then 7.03 g.(0.05 mole) p-chlorobenzaldehyde was added and the mixture was refluxed for 60 minutes. After the reaction mixture was cooled to room temperature, yellow needle crystals were formed. The mixture in the refrigerator overnight and the crystals

were separated by filtration. The crystals were washed with water. The filtrate and the washed water were mixed and poured into 250 ml. of water. This mixture was kept in the refrigerator for another night. The second crop of the product was filtered and the precipitate was washed with water. The total crude product was dried in the oven at 60°C under reduced pressure. The total yield weighed 12.08 g. or 94.9 % yield with m.p. 221-5°C Recrystalization from ethanol gave yellow needle crystals m.p. 223-5°C (lit m.p. 227°C) (131)

5-(2,6-Dichlorobenzylidene) rhodanine

6.66 g. (0.05 mole) rhodanine and 12.3 g.(0.15 mole) anhydrous sodium acetate were mixed in 50 ml glacial acetic acid. The mixture was warmed on a water bath until a clear solution was obtained. Then 8.75 g. (0.05 mole) of 2,6 dichlorobenzaldehyde was added to the solution. The mixture was refluxed for 60 minutes and yellow needle crystals formed during the reflux. The reaction mixture was kept in the refrigerator overnight to get more crystals which were separated by filtration. The crystals were washed with water several times. The filtrate was poured into another 100 ml of water and kept in the refrigerator overnight. The second crop of precipitate was filtered and washed with water. The crude product was dried in an oven at 60°C under reduced pressure. The total crude product weighed 13.85 g. or 95.4 % yield and gave m.p.

179-181°C after recrystization from methanol (lit m.p.184-6°C)(54).

5-(3-Nitrobenzylidene) rhodanine

A mixture of 13.3 g. (0.1 mole) rhodanine and 24.6 g.(0.3 mole) anhydrous sodium acetate in 100 ml. glacial acetic acid was warmed on a water-bath until a clear solution was obtained. Then 15.1 g (0.1 mole) of m-nitrobenzaldehyde was added to the solution and was refluxed for 60 minutes. Yellow crystals were formed in the reaction mixture which was kept in the refrigerator overnight. The crystals were separated by filtration and washed with water. The filtrate was poured into another 100 ml. of water and the mixture was kept in the refrigerator for another night to allow more product to be formed. The product was separated by filtration and washed with water. The total weight of the product was 25.9 g. or 97.3 % yield. Recrystalization from tetrahydrofuran gave yellow needle crystals with m.p. 263-dec. (lit m.p. 260 dec.) (111).

5-(4-nitrobenzylidene) rhodanine

13.3 g. (0.1 mole) rhodanine and 24.6 g. anhydrous sodium acetate were added to 100 ml. glacial acetic acid. The mixture was warmed on a water bath to get a clear solution, then 15.1 g. of p-nitrobenzaldehyde (0.1 mole) was added. The reaction mixture was refluxed for 45 minutes. After cooling the mixture to room temperature, yellow crystals formed. The mixture was kept in the

refrigerator overnight and the crystals were separated by filtration and washed with water. The filtrate was poured into another 200 ml. of water. This aqueous mixture was kept in the refrigerator for another night to obtain more crystals which were separated by filtration. The crystals were washed with water. The crude product was dried in an oven at 60°C under reduced pressure. The total weight of the product was 26.02 g. or 97.7 % yield and the m.p. was 257-8°C with decompose, after recrystalization from acetone. (lit m.p. 273-4°C) (130).

5-(3-Metayl-2-thienylmethylene) rhodanine

To a solution of 6.66 g. (0.05 mole) rhodanine and 12.5 g. anhydrous sodium acetate in 100 ml. glacial acetic acid, 6.31 g. 0.05 mole) of 3-methyl-2-thiophenecarboxaldehyde was added. The mixture was refluxed for 60 minutes, and after cooling to room temperature, yellow needle crystals formed. The mixture was kept in the refrigerator overnight to allow more crystals to form and these were separated by filtration and washed with water. The filtrate was poured into 100 ml. water and the aqueous mixture was kept in the refrigerator for another night. The second crop of the product was filtered and washed with water. The crude product was dried in a desicator over anhydrous calcium chloride. The total weight of the product was 6.45 g. or 53.5 % yield. Recrystalization from methanol gave yellow needle crystals with m.p.226-8

(lit m.p. 226-227.5°) (133).

5-(5-Bromo-2-thienylmethylene)rhodanine

A mixture of 6.66 g.(0.05 mole) rhodanine and 12.5 g.(0.15 mole) anhydrous sodium acetate in 200 ml. glacial acetic acid was warmed on a water bath until a clear solution was obtained. Then 9.6 g.(0.05 mole) 5-Bromo-2-thiophene carboxaldehyde was added. After refluxing the mixture for 15 minutes, a browish yellow precipitate formed. The mixture was kept in the refrigerator overnight. The precipitate was separated by filtration and washed with water. The filtrate was poured into 100 ml. of water which was then kept in the refrigerator for another night. A second crop of the product was filtered and washed with water. The crude product was dried in an oven at 60°C under reduced pressure. The total product weighed 9.24 g. or 67.4 % yield with m.p.242-5 °C after recrystalization from methanol. (lit m.p. 245.5-246.5°C)(133).

5-(3-Pyridylmethylene) rhodanine

Rhodanine 13.3 g (0.1 mole) was mixed with anhydrous sodium acetate 25.0 g.(0.3 mole) in 250 ml. glacial acetic acid. The mixture was warmed on a water-bath to get a clear solution, then Pyridine-3-carboxaldehyde 10.7 g.(0.1 mole) was added. The mixture was refluxed for 30 minutes and yellow crystals formed during the period. The reaction mixture was cooled to room temperature and poured into 500 ml. of water. The whole mixture was kept in the

refrigerator overnight. The product was filtered and washed with water. The crude product was dried in an oven at 60°C under reduced pressure. The total weight of the product was 15.13 g. or 68.3 % yield with m.p. over 300°C decompose (lit m.p. 318-320°C decompose)(132).

5-(4-Pyridylmethylene) rhodanine

9.63 g (0.09 mole) Pyridine-4-carboxaldehyde was added into solution of 11.97 g. (0.09 mole) rhodanine and 22.14 g. (0.27 mole) anhydrous sodium acetate in 225 ml. of glacial acetic acid. The mixture was refluxed on a water bath for 30 minutes. A yellow precipitate formed. The mixture was cooled to room temperature, and poured into 500 ml. of water. Then it was kept in the refrigerator overnight. The yellow product was filtered to separate the precipitate and washed with water. The crude product was dried at 60°C in an oven under reduced pressure. The total weight of the product was 17.18 g. or 86.3 % yield with m.p.over 300°C with decompose (lit m.p.320 - 322°C decompose)(132).

α-D-Acetobromoglucose:(2,3,4,6-Tetra-O-acetyl-α-D-glucopyranosylbromide

200 ml. of acetic anhydride, in a 500 ml. three necked flask, equipped with an effecient stirrer and a thermometer, was cooled in an ice-bath, then 1.2 ml. of perchloric acid was added dropwisely to the acetic anhydride. 50 g. of D-glucose anhydrous

was portionly added, while stirring the solution, over a period of one hour and at a rate which kept the temperature between 30-40°C. After the addition of sugar, the mixture was stirred again for another 15 minutes and at this step, a white viscous suspension was obtained. The suspension was cooled to 20°C, then 15 g. of red phosphorus was portionly added. 90 g.(29.5 ml) of bromine(Maclinkod) was then slowly added to the suspension, at a rate which kept the temperature of the whole mixture below 20°C. After the bromination reaction 18 g. of water was slowly added, so that the temperature would not exceed 20°C. The suspension was stirred in a cool temperature for another 30 minutes and then the temperature of the whole mixture was raised to room temperature for a 2 hour period. Then 150 ml. of chloroform was poured into the mixture, and the red particles of phosphorous were stirred and filtered off with glass wool. However, the phosphorous particles may or may not be filtered off completely. The reactor flask and funnel were rinsed with 50 ml. chloroform, and the two portions were combined and poured into 400 ml. of ice-water while stirring vigorously. The chloroform layer was separated with an addequate separator funnel and the extraction of the mother liquid portion was repeated with another 50 ml. of chloroform. The chloroform portion was combined and the product was separated by filtration through glass wool. The acid was neutralized and left in the chloroform portion with saturated sodium bicarbonate solution until effervescence ceased. The chloroform layer was separated and washed with two portions of

250 ml. of cooled water. The chloroform portion was dried with 10g. of magnesium sulfate anhydrous. After the filtration, a faint yellow viscous solution was obtained. The solution was evaporated at 40°C under reduced pressure to obtain a yellow syrup. The syrup was transferred to a meter with 250 ml. of a mixture of petroleum ether and ether (2:1) and the mixture was ground after adding 1 g. of previously dried calcium carbonate for a few minutes, after which white crystals appeared. The product was filtered, and washed with cool dry ether and dried in a desicator over a sodium hydroxide pellet. The ethereal filtrate was evaporated to reduce the volume so that the second crop of the product could form. The total yield of the product was 99 g. or 86.8 % yield with a m.p.82-87°C. After recrystalization from ether, its m.p. was improved to 87-88°C (lit m.p.88-89°C) (134).

The product must be kept in a tight container and stored in a refrigerator. When being used, it must be dissolved in dry acetone and the precipitate of calcium carbonate filtered off.

α-D-Acetobromoglucose from Sigma Chemical Co.

Acetobromo α-D-glucose, supplied by Sigma Chemical Co. (catalog No. A-1750), and containing 1% of calcium carbonate as a stabilizer, was dissolved in dry acetone and the salt was filtered off before it was used.

N-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl)-5-benzylidene rhodanine

6.63 g. (0.03 mole) of 5-benzylidene rhodanine was dissolved in 650 ml. acetone, then 12.3 g. (0.03 mole) of acetobromoglucose was added to the solution, followed by the addition of 12.0 ml. of 10 % sodium hydroxide solution. The mixture was stirred by a magnetic stirrer at room temperature for 3 days, then the reaction mixture was filtered and the filtrate was evaporated at 60°C under reduced pressure, to remove the solvent. A yellow precipitate was obtained, and was recrystalized from methanol to give yellow needle crystals which were dried in a desiccator over anhydrous $CaCl_2$. The total yield was 11.84 g. or 71.7 % yield with m.p. yield with m.p. 187-9°C (lit. m.p. 192-4°C; $[\alpha]_D^{20}$ — 171°C pyridine) (54).

$[\alpha]_D^{25}$ = -36.7 (l=2, C=0.91, THF)

IR(KBr) ν 1750 (C=O) ; 1225 (C=S); 910 (β-form) cm^{-1}

N-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl)-5-(3-methoxy-4-hydroxybenzylidene) rhodanine

To a solution of 5-(3-methoxy-4-hydroxybenzylidene) rhodanine 8.02 g.(0.03 mole) in 400 ml. acetone, 12.3 g. acetobromoglucose was added, followed by 12.0 ml. of 10 % sodium hydroxide. The mixture was stirred by a magnetic stirrer at room temperature for 3 days, then the reaction solution was filtered and the filtrate

was evaporated at 60°C under reduced pressure to remove the acetone. A yellow precipitate was obtained and was recrystalized from methanol. The crystals were dried in a desiccator over anhydrous. $CaCl_2$ to get the total yield of 13.9 g. (77.6%) Further recrystalization from methanol gave yellow needle crystals (m.p.258-9°C)

$[\alpha]_D^{25}$ = -119.6 (l = 1;C=0.39; THF)

calculated for $C_{25}H_{27}O_{12}NS_2$

Calc. C, 50.20; H. 4.54 ; N, 2.34 ; S 10.73

found C, 50.40; H. 4.61 ; N, 2.29 ; S 10.63

IR(KBr) : 1744 (C=O); 1225 (C=S); 909(β-form)cm^{-1}

N-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl)-5-(3-ethoxy-4-hydroxybenzylidene) rhodanine

A mixture of 8.44 g. (0.03 mole) 5-(3-Ethoxy-4-hydroxybenzylidene) rhodanine and 12.3 g. acetobromoglucose was dissolved in 450 ml. acetone containing 12.0 ml. of 10 % sodium hydroxide solution. The mixture was stirred on a magnetic stirrer at room temperature for 3 days, then any precipitate was filtered off. The filtrate was evaporated at 60°C under reduced pressure to remove the acetone. A yellow precipitate was obtained, and was crystalized from methanol. After drying in a desiccator over anhydrous $CaCl_2$, 14.68 g.(80.0 %) of the product was obtained. Recrystalization from methanol gave yellow needle crystals (m.p. 234.5-236°C).

$[\alpha]_D^{25}$ = -154.8 (l=1; C=0.37;THF)

Calculate for $C_{26}H_{29}O_{12}NS_2$

calc. C, 51.05; H, 4.76; N, 2.29; S, 10.49

found C, 50.87; H, 4.89; N, 2.10; S, 10.39

IR(KBr) : ν 1748(C=O); 1222 (C=S); 910(β-form)cm^{-1}

N-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl)-5-(4-dimethylamino benzylidene) rhodanine

2.64 g. (0.01 mole)5-(4-dimethylaminobenzylidene) rhodanine was incompletely dissolved in 500 ml. acetone, and 150 ml. tetrahydrofuran(THF) was added to dissolved the crystals, with the assistance of heat. Then 4.11 g. (0.01 mole) acetobromoglucose was added to the solution followed by 4 ml. of 10 % sodium hydroxide. The mixture was stirred by a magnetic stirrer at room temperature for 3 days. Then the solution was filtered and the filtrate was evaporated at 60°C under reduced pressure to remove the solvent. A reddish precipitate was obtained. After crystalization from methanol, the solution gave red crystals which were dried in a desiccator over anhydrous $CaCl_2$. The total yield was 4.59 g. (77.4%)with m.p. 195-8°C (lit m.p. 197-201°C $[\alpha]_D^{20}$ = -104.0° THF) (54).

$[\alpha]_D^{25}$ = -270.2 (l=1; C=0.38; THF)

IR(KBr) ν 1750 (C=O); 1225 (C=S); 899(β-form)cm^{-1}

N-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl)-5-(4-chlorobenzylidene) rhodanine

5-(4-chlorobenzylidene) rhodanine 7.67 g. (0.03 mole) was dissolved in 600 ml. acetone. Then 12.3 g. acetobromoglucose and 12 ml. of 10 % sodium hydroxide solution were added. The mixture was stirred by a magnetic stirrer at room temperature for 4 days. The reaction solution was filtered and the filtrate was evaporated at 60°C under reduced pressure to remove the solvent. A yellow precipitate was obtained and was crystalized from methanol to give yellow needle crystals with m.p. 225-6°C. The product was dried in a desicator over anhydrous $CaCl_2$. The total yield was 12.64 g. (71.8 %) (lit m.p. 226-8°C; $[\alpha]_D^{20}$ = -170.0° pyridine)(54).

$[\alpha]_D^{25}$ = -160.8 (l = 2; C = 1.6; THF)

Calculate for $C_{24}H_{24}NO_{10}S_2Cl$

Calc. C, 49.19; H, 4.13; N. 2.39; S. 10.94

found C, 49.36; H, 4.10; N, 2.17; S, 10.83

IR (KBr): ν 1745 (C=O); 1230 (C=S); 908 (β-form)cm^{-1}

N-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl)-5-(2,6,dichlorobenzylidene) rhodanine

12.3 g. (0.03 mole) Acetobromoglucose was added to a solution of 8.71 g.(0.03 mole) 5-(2-6-dichlorobenzylidene) rhodanine in 300 ml. acetone, then 12.0 ml. of 10 % sodium hydroxide solution

was slowly added to the stirred solution, The mixture was kept at room temperature for 3 days with continous stirring, then the reaction mixture was filtered and the filtrate was evaporated at 50°C under reduced pressure. A yellow sticky mass was obtained and dried in a desiccator under reduced pressure. The yellow product weighed 11.95 g. (64.5%). **This crude product was purified by column chromatography as follow :**

50 g. of silica gel (230-400 mesh; E. -merck) was suspended in n-hexane : ethyl acetate mixture (2:1) and the suspension was poured into a glass column 1 inch in diameter and 30 inches long. The column was settled for 24 hours, then approximately 1 gm of the sample was ground with a small amount of silica gel to dryness and was transfered to the top of the column. Elution was carried out using the mix solvent system. Several yellow bands were observed, and the third band from the bottom, which was the major band, was collected. After removal of the solvent, a yellow sticky mass was obtained and was dried in a desiccator over anhydrous $CaCl_2$. The product was solidified and gave m.p. 78-80°C (lit m.p. 78-81; $[\alpha]_D^{20}$ = -52.0° pyridine) (54).

$[\alpha]_D^{25}$ = -72.5 (l = 2, C = 0.95, THF)

IR(KBr) : ν 1750 (C=O); 1225 (C=S); 900(β-form) cm^{-1}

<u>N-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl)-5-(3-methyl-2-thienyl-methylene) rhodanine</u>

2.42 g (0.01 mole)5-(3-Methyl-2-thienylmethylene) rhodanine was dissolved in 400 ml. acetone. Then 4.1 g.(0.01 mole) aceto-bromoglucose was added to this solution followed by 4 ml. of 10 % sodium hydroxide solution, which was slowly added to the stirred solution. The mixture was kept at room temperature and stirred for 4 days. Then the mixture was filtered and the filtrate was evaporated at 60°C to remove the acetone. A yellow product was obtained and was recrystalized from methanol to give yellow needle crystals which were dried in a desicator over anhydrous $CaCl_2$. The total yield was 3.43 g. (60.0 %) with m.p. 184-6°C (lit m.p. 192-3°C, $[\alpha]_D^{20}$ = -210.0° pyridine) (54)

$[\alpha]_D^{25}$ = -183.2° (l = 2, C = 1.42, THF)

IR (KBr) : ν 1750 (C=O); 1234 (C=S); 900 (β-form) cm^{-1}

N-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl)-5-(5-bromo-2-thienyl methylene) rhodanine

To a solution of 3.06 g. (0.01 mole) 5-(5-Bromo-2-thienyl-methylene) rhodanine in 600 ml of acetone, 4.1 g (0.01 mole) aceto-bromoglucose was added followed by 4.0 ml. of 10 % sodium hydroxide solution. The mixture was stirred by a magnetic stirrer at room temperature for 3 days, then the mixture was filtered to remove any precipitate. The filtrate was evaporated until dryness at 60°C under reduced pressure. A yellow product was obtained and was

crystalized from methanol to give yellow needle crystals. These were then dried in a desicator over anhydrous $CaCl_2$. The total yield was 4.33 g. (68.9 %) with m.p. 187-9 (lit m.p.182-7°C $[\alpha]_D^{20}$ = -130.0°, pyridine)(54).

$[\alpha]_D^{25}$ = -141.7° (l = 2, C = 1.4, THF)

IR(KBr) : 1745 (C=O); 1210 (C=S); 899(β-form)cm^{-1}

N-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl)-5-(3-pyridylmethylene) rhodanine

8.2 g. (0.02 mole) Acetobromoglucose was added into a suspension of 5-(3-pyridylmethylene) rhodanine 4.44 g.(0.02 mole) in 1000 ml. of acetone containing 8.0 ml. of 10 % sodium hydroxide solution. The suspension was stirred by a magnetic stirrer at room temperature for 6 days. After this period the solution was still not completely clear. However the reaction mixture was filtered to get a clear solution and the filtrate was evaporated at 60°C under reduced pressure to remove the solvent. A brownish-yellow precipitate was obtained and was crystalized from methanol to give yellow needle crystals, which were dried in a desicator over anhydrous $CaCl_2$. The total product weighed 10.17 g. (92.8 %) and the m.p. was 189-192°C (lit m.p.191-3°; $[\alpha]_D^{20}$ = -195.0°THF) (54).

$[\alpha]_D^{25}$ = -138.0 (l=2; C=1.06; THF)

IR(KBr) : ν = 1744(C=O); 1224 (C=S); 908 (β-form)cm^{-1}

N-β-D-Glucopyranosyl-5-benzylidenerhodanine

2.56 g (0.0046 mole) N-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl) -5-benzylidenerhodanine was suspended in 700 ml. methanol, then 9.2 ml. of 2.0 M hydrochloric acid was added. The reaction mixture was stirred on a magnetic stirrer at room temperature. The suspension became clear after 3 days, but stirring was continued for another day. The solution was filtered and the filtrate was evaporated in a Rota-evapotator at 60°C under reduced pressure. A yellow precipitate was obtained to which a minimum volume of 95% ethanol was added to dissolve the product, then water was added dropwise to the ethanolic solution until cloudiness appeared, The cloudly solution was warmed until it was clear and the solution was kept in the refrigerator overnight. A yellow precipitate was formed and was separated by filtration. This product was dried in a desicator over anhydrous $CaCl_2$. The total yield was 1.7 g. (96 %) with m.p. 118-130°C. The crude product was purified by means of column chromatography using silica gel (230-400 mesh, E-merck) as an adsorbent and ethyl-acetate as an eluent. The major band, which was strongly adsorbed near the top of the column, was collected and the solvent was removed by evaporation under reduced pressure. A yellow precipitate was obtained and was recrystalized from ethyl acetate giving yellow crystals with m.p. 156-8°C (lit m.p. 104-110; $[\alpha]_D^{20}$ = -78.0° pyridine) (54).

$[\alpha]_D^{25}$ = -49.9 (l=2, C=1.1, THF)

Calculate for $C_{16}H_{17}NO_6S_2 \cdot \frac{1}{2} H_2O$

calc. C, 48.97; H, 4.61; N, 3.57; S 16.32

found C, 48.68; H, 4.69; N, 3.43; S 16.02

IR(KBr) : 3500-3300 (OH); 1100-1050(C-OH);887(β-form)
1714(C=C); 1230 (C=S)cm^{-1}

N-β-D-Glucopyranosyl-5-(3-methoxy-4-hydroxybenzylidene) rhodanine

A suspension of 3.12 g (0.0046 mole) N-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-5-(3-methoxy-4-hydroxybenzylidene) rhodanine in 400 ml. of methanol, containing 9.2 ml. of 2M.hydrochloric acid solution, was stirred by a magnetic stirrer at room temperature for 3 days. The mixture became clear, but it was further stirred for another day. The solution was then filtered and the filtrate was evaporated at 60°C under reduced pressure. A reddish yellow product was obtained and completely dissolved in a minimum volume of 95 % ethanol. Then water was added dropwise to the ethanolic solution until cloudiness appeared. The ethanolic solution was warmed on a water bath to make it clear and was kept in the refrigerator. A yellow precipitate was formed and was separated by filtration. The total crude yield was 2.07 g.(92.4 %) with m.p. 197-200°C. The product was recrystalized from methanol and gave yellow crystals (m.p.201-2°C)

$[\alpha]_D^{25}$ = -53.8 (l=2,C=0.90, THF)

Calculate for $C_{17}H_{19}NO_8S_2 \cdot 2\frac{1}{2} H_2O$

Calc. C, 43.03; H, 5.08; N, 2.95; S, 13.50

found C, 43.32; H, 5.16; N, 2.81; S, 13.23

IR(KBr) : ν 3500 - 3300 (OH) : 1100-1060(C-OH); 890(β-form); 1710 (C=O); 1220 (C=S)cm^{-1}

N-β-D-Glucopyranosyl-5-(3-ethoxy-4-hydroxybenzylidene) rhodanine

To a suspension of 3.19 g.(0.0052 mole) N-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-5-(3-ethoxy-4-hydroxybenzylidene) rhodanine in 400 ml. of methanol, 10.4 ml. of 2M. hydrochloric acid was added. The mixture was stirred at room temperature for 7 days using a magnetic stirrer. Then the solution was filtered and the filtrate was evaporated at 60°C under reduced pressure. A reddish yellow precipitate was obtained, and was purified by dissolving it in a minimum volume of 95 % ethanol. Then water was added dropwise until cloudiness appeared. This mixture was warmed to make the solution completely clear and then kept in the refrigerator overnight. A yellow precipitate was formed and was separated by filtration. After drying it in a desiccator it gave 2.26 g (98 %) of the product with m.p. 155-159°C. The product was purified several times by fractional recrystalization from a mixture of ethanolic water, which improved the m.p. to 167-170°C

$$[\alpha]_D^{25} = -48.2 \ (l = 2; \ C = 0.86; \ THF)$$

Calculate for. $C_{18}H_{21}NO_8S_2 \cdot \frac{1}{2}H_2O$

Calc. C, 47.78; H, 4.89; N, 3.09

found.C, 47.57; H, 4.99; N, 2.81

IR(KBr) : ν 3500 - 3320(CH); 1090-1055(C-OH);888 (β-form); 1705(C=O); 1220 (C=S)cm^{-1}

N-β-D-Glucopyranosyl-5-(4-chlorobenzylidene) rhodanine

1.46 g (0.0025 mole)N-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl)-5-(4-chlorobenzylidene) rhodanine was suspended in 300 ml. methanol, then 5 ml. of 2M.hydrochloric acid was added. The mixture was stirred overnight and was then refluxed on a water bath until a clear solution was obtained. The reaction mixture was furthur stirred overnight at room temperature, resulting in the reappearance of a suspension. This suspension was refluxed for about 2 hours and was stirred at room temperature for another 24 hours. It was then filtered and the filtrate was evaporated at 60°C under reduced pressure. A yellow product was obtained and a minimum volume of 95 % ethanol was used to dissolve this product. Then water was carefully added until cloudiness first appeared and was redissolved by heat to give a clear solution. After keeping it in the refrigerator overnight, a yellow jelly-like mass formed, which was separated by filtration and dried in a desiccator over anhydrous $CaCl_2$. The total yield was 1.03 g or 99 % yield. Recrystalization from ethyl-acetate gave yellow needle crystals with m.p. 118-9°C

$[\alpha]_D^{25}$ = -52.3(1=2, C=0.89, THF)

Calculate for $C_{16}H_{16}NO_6S_2Cl$

Calc. C, 45.99; H, 3.83; N, 3.35 ; Cl, 8.50

found C, 45.80; H, 4.36; N, 2.84; Cl, 8.45

IR(KBr) : $\bar{\nu}$ 3500 - 3300 (OH); 1100 - 1050(C-OH); 890(β-form); 1720 (C=O); 1230(C=S)cm^{-1}

N-β-D-Glucopyranosyl-5-(2,6-dichlorobenzylidene) rhodanine

To a solution of 1.44 g. (0.0023 mole) N-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl)-5-(2,6-dichlorobenzylidene) rhodanine in 200 ml. methanol, 4.6 ml. of 2M hydrochloric acid was added. The solution was stirred on a magnetic stirrer at room temperature for 4 days. The solution was then filtered and the filtrate was evaporated at 60°C under reduced pressure. A yellow sticky mass was obtained and was dissolved in a minimum amount of 95 % ethanol. Then water was carefully added untill cloudiness first appeared. The mixture was warmed to give a clear yellow solution and was kept in the refrigerator overnight. Again a yellow sticky mass formed and was separated by filtration. This crude mass was dried in a desiccator and gave 0.74 g. (71.5 %) of the product. Column chromatography was used to purity this product using silica gel (230-400 mesh, E-merck) as an adsorbent and ethyl acetate as an eluent. Several yellow bands were observed on the chromatogram but only the major band which was more strongly adsorbed and

remaining near the top of the column, was collected. The collected portion was evaporated to remove the solvent and yielded a yellow sticky mass which was dried in a desicator. The product solidified and gave m.p. 121-124°C

$[\alpha]_D^{25}$ = -27.0 (l=2; C=1.27; THF)

Calculate for $C_{16}H_{15}NO_6S_2Cl_2$

Calc. C, 42.48; H 3.33; N, 3.09;

Found C, 42.79; H 3.59; N, 2.83

IR(KBr) : 3500-3300 (OH); 1100-1050 (C-OH); 885 (β-form) 1716(C=O), 1230(C=S)cm^{-1}

N-β-D-Glucopyranosyl-5-(5-bromo-2-thienylmethylene) rhodanine

A mixture of 2.52 g. (0.004 mole) N-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl)-5-(5-bromo-2-thienylmethylene) rhodanine was suspended in 350 ml. methanol containing 5 ml of 2M hydrochloric acid, and was stirred by a magnetic stirrer at room temperature for 4 days. The reaction solution was filtered and the filtrate was evaporated at 60°C under reduced pressure. A reddish-brown precipitate was obtained and was dissolved in a minimum amount of hot 95 % ethanol. After cooling this ethanolic solution in the refrigerator overnight, reddish-yellow crystatls were obtained. Separation was effected by filtration and drying in a desiccator, and 1.76 g. or 93.8 % yield of the product with m.p. 199-201° was produced. Fractional recrystalization from ethanol

improved up to 207-9°C dec.

$[\alpha]_D^{25}$ = -68.2 (l=2; C=0.63; THF)

Calculate for $C_{14}H_{14}NO_6S_3Br$

Calc. C, 35.90; H, 3.00; N 2.99; S 20.51

found C, 35.54; H, 3.02; N 2.68; S 20.47

IR(KBr) : 3500-3300(OH), 1100-1050 (C-OH); 883 (β-form); 1710(C=O); 1230 (C=S) cm^{-1}

TABLE I. 5 - ARYLMETHYLENE RHODANINE DERIVATIVES

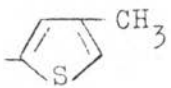
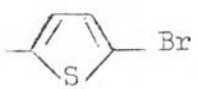
Aryl group	Empirical formula	m.p. °C	yield %	Reference
C_6H_5	$C_{10}H_7NS_2O$	202 - 206	80	99
$3\text{-}OCH_3\text{-}4\text{-}OH\text{-}C_6H_3$	$C_{11}H_6NS_2O_3$	225 - 227	89.9	128, 83
$3\text{-}OC_2H_5\text{-}4\text{-}OH\text{-}C_6H_3$	$C_{12}H_{11}NS_2O_3$	217.5-218.5	96.9	80
$4\text{-}Cl\text{-}C_6H_4$	$C_{10}H_6NS_2OCl$	223 - 225	94.9	131
$2,6,\text{-}Cl_2\text{-}C_6H_3$	$C_{10}H_5NS_2OCl_2$	179 - 181	95.4	54
$4\text{-}(CH_3)_2\text{-}N\text{-}C_6H_4$	$C_{12}H_{12}N_2S_2O$	247 dec.	74.2	129,130
$3\text{-}NO_2\text{-}C_6H_4$	$C_{10}H_6N_2S_2O_3$	263 dec.	97.3	111
$4\text{-}NO_2\text{-}C_6H_4$	$C_{10}H_6N_2S_2O_3$	257 - 258	97.7	132
	$C_9H_7NS_3O$	226 - 228	53.5	133
	$C_8H_4NS_3O$	242 - 245	67.4	133
	$C_9H_6N_2S_2O$	> 300	68.3	132
	$C_9H_6N_2S_2O$	> 300	86.3	132

TABLE II N-(2,3,4,6-TETRA-ACETYL-β-D-GLUCOPYRANOSYL)-5-ARYLMETHYLENE RHODANINE DERIVATIVES

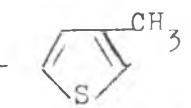
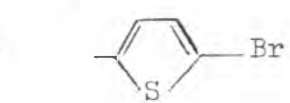
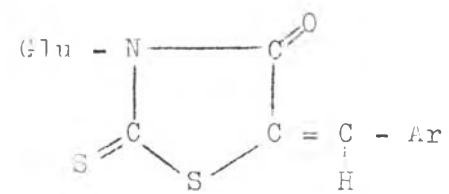
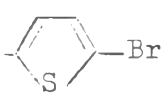
Aryl group	Empirical formula	Yield %	M.P. °C	$[\alpha]_D^{25}$ THF	IR(KBr) cm^{-1}
- C_6H_5	$C_{24}H_{25}NO_{10}S_2$	71.7	187 - 189	- 36.7	1750;1225;910
- 3-OCH_3-4-OH-C_6H_3	$C_{25}H_{27}O_{12}NS_2$	77.6	258 - 259	-119.6	1744;1225;909
- 3-OC_2H_5-4-OH-C_6H_3	$C_{26}H_{29}O_{12}NS_2$	80.0	234.5-236	-154.8	1748;1222;910
- 4-ClC_6H_4	$C_{24}H_{24}NO_{10}S_2Cl$	71.8	225 - 226	-160.8	1745;1230;908
- 2,6-$Cl_2C_6H_3$	$C_{24}H_{23}NO_{10}S_2Cl_2$	64.5	78 - 80	- 72.5	1750;1225;900
- 4-$(CH_3)_2N$-C_6H_4	$C_{26}H_{30}N_2O_{10}S_2$	77.4	195 - 198	-270.2	1750;1225;899
	$C_{23}H_{25}NO_{10}S_3$	60.0	184 - 186	-183.2	1750;1234;900
	$C_{22}H_{22}NO_{10}S_3Br$	68.9	187 - 189	-141.7	1745;1210;899
	$C_{23}H_{24}N_2O_{10}S_2$	92.8	189 - 192	-138.0	1744;1224;908

TABLE III N-β-D-GLUCOPYRANOSYL-5-ARYLMETHYLENE RHODANINE DERIVATIVES



Aryl group	Empirical formula	M.P. °C	$[\alpha]_D^{25}$ THF, l=2	Yield %	IR (KBr) cm^{-1}				
					OH	C-OE	β form	C=O	C=S
$-C_6H_5$	$C_{16}H_{17}NO_6S_2 \cdot \frac{1}{2}H_2O$	156-158	-49.9	96	3500-3300	1100-1050	887	1714	1230
$-3-OCH_3-4-OHC_6H_3$	$C_{17}H_{19}NO_8S_2 \cdot 2\frac{1}{2}H_2O$	201-202	-53.8	92.4	3500-3300	1100-1060	890	1710	1220
$-3-OC_2H_5-4-OHC_6H_3$	$C_{18}H_{21}NO_8S_2 \cdot \frac{1}{2}H_2O$	167-170	-48.2	98	3500-3320	1090-1055	888	1705	1220
$-4-ClC_6H_4$	$C_{16}H_{16}NO_6S_2Cl$	118-119	-52.3	99	3500-3300	1100-1050	890	1720	1230
$-2,6\ Cl_2C_6H_3$	$C_{16}H_{15}NO_6S_2Cl_2$	121-124	-27.0	71.5	3500-3300	1100-1050	885	1716	1230
	$C_{14}H_{14}NO_6S_3Br$	207-209	-68.2	93.8	3500-3300	1100-1050	883	1710	1230