SYNTHETIC STUDIES ON HETEROCYCLES FROM SUGAR DERIVATIVES II*.

PREPARATION OF 3,4-DI-*O*-ACETYL-6,*N*-ANHYDRO[*cis*-1,2-*b*]DIHYDROBENZOTHIAZINE AND RELATED COMPOUNDS

M. SEKIYA AND S. ISHIGURO†

Kyorin Chemical Laboratory, Ukima 1-3-32, Kita-ku, Tokyo (Japan)

(Received October 27th, 1971; accepted, in revised form, December 15th, 1971)

ABSTRACT

D-Mannopyrano[*cis*-1,2-*b*]dihydrobenzothiazine or its 6-chlorodihydrobenzothiazine analog was converted into 3,4-di-*O*-acetyl-6,*N*-anhydro-D-mannopyranochloro[*cis*-1,2-*b*]dihydrobenzothiazine (**8**) or the corresponding 6-chloro derivative via the intermediate 3,4-di-*O*-acetyl-6-*O*-tosyl-D-mannopyrano[*cis*-1,2-*b*]dihydrobenzothiazine or the corresponding 6-chloro derivative. Selective deacetylation of **8** with chilled sodium methoxide in methanol, followed by mesylation of the resulting syrup, afforded 3-*O*-acetyl-4-*O*-mesyl-6,*N*-anhydro-D-mannopyrano[*cis*-1,2-*b*]dihydrobenzothiazine, which was further transformed into 3,4-anhydro-6,*N*-anhydro-D-mannopyrano[*cis*-1,2-*b*]dihydrobenzothiazine. N.m.r. spectroscopy helped greatly in the determination of the structure of the products.

INTRODUCTION

Recently, much effort has been expended on synthesis of heterocycles from saccharide derivatives[2]. In the previous report[1], with the aim of studying neighboring-group participation reactions in aryl glycosides, the formation of new tricyclic heterocycles containing both nitrogen and sulfur was achieved.

This paper deals with the transformation of the tricyclic heterocycles into compounds having a more complicated ring-system.

RESULTS AND DISCUSSION

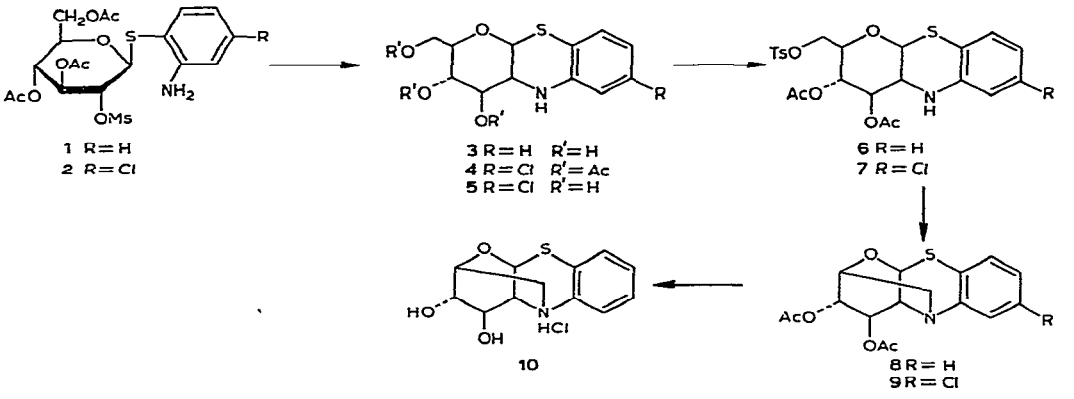
D-Mannopyrano[*cis*-1,2-*b*]dihydrobenzothiazine** (**3**) and the corresponding 6-chlorodihydrobenzothiazine analog (**5**) were synthesized by a slight modification of the method previously reported[1].

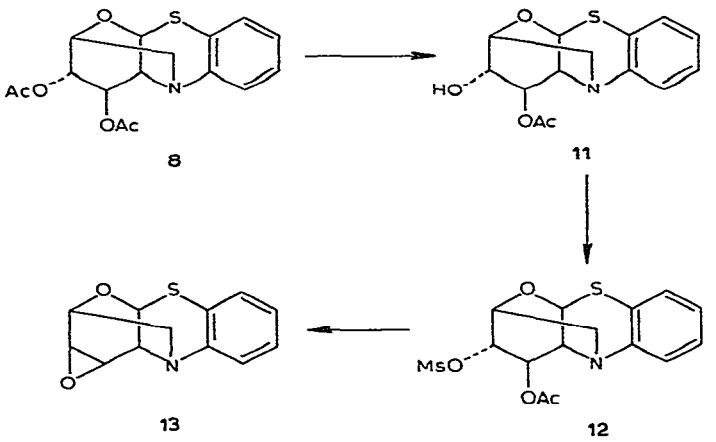
*For Part I, see Ref. 1.

†To whom correspondence should be sent: present address: Department of Biochemistry, Purdue University, West Lafayette, Ind. 47907, U. S. A.

**An officially approved system of nomenclature for compounds of this class has not yet been developed.

Tosylation of **3** or **5** with 1.1 molar-equiv. of tosyl chloride in pyridine and subsequent acetylation of the reaction mixture gave the 6-*p*-toluenesulfonate (**6**) in 85% or the 6′-chloro analog (**7**) in 70% yield, respectively. Cyclization of the resulting sulfonate, **6** or **7**, by use of an excess of sodium acetate in boiling ethanol–chloroform for 2 h gave colorless crystals (**8**) in 76% or (**9**) in 30% yield, respectively. The i.r. spectra of **8** and **9** showed no absorption near 3400 (NH), or 1170 cm^{-1} (OTs), but





showed a new band near 1580 cm^{-1} attributable to the benzene ring resulting from the formation of the new ring-system. The n.m.r. spectrum of **8** or **9** showed two acetyl-proton signals at τ 7.83, 8.70 or τ 7.83, 8.62, respectively. The large upfield shift of one of the acetyl signals suggested that some significant structural change might have occurred during the reaction. Inspection of Dreiding models of **8** or **9** suggests that an "abnormal" acetyl group is present at the pyranoid C-3 adjacent to the bridgehead. The protons attached to the pyranoid ring were assigned sequentially by double-resonance experiments. It is noteworthy that the methylene protons situated at C-6 show separate signals, having chemical shifts at τ 5.96, 6.54 or τ 5.99, and 6.54,

respectively, arising from the syn and anti configurations with respect to the lone pair of electrons on the nitrogen atom. The u.v. spectra of **8** or **9** show moderate absorption near 306 or 315 nm, apparently characteristic of the –S–Ph–N– group. The mass spectrum of **8** or **9** shows the molecular ion (M^+) at *m/e* 335 or 369, respectively.

From the foregoing it is speculated that **8** or **9** have the structure of 3,4-di-*O*-acetyl-6,*N*-anhydro-D-mannopyrano[*cis*-1,2-*b*]dihydrobenzothiazine or the corresponding 6-chloro derivative, respectively. The elemental analyses are in good agreement with these postulated structures.

Several papers[3–8] have described intramolecular *N*-alkylation in carbohydrate chemistry, but the formation of **8** or **9** through intramolecular nucleophilic substitution of a primary tosyloxy group by an aromatic, secondary amine is the first such example to the authors' knowledge.

The hydrochloride of **8** was easily prepared by deacetylation with methanolic sodium methoxide followed by treatment with ethereal hydrogen chloride.

In the next step, it was proposed to modify the 3 and 4-hydroxyl group in **8**. Deacetylation of **8** with chilled methanolic sodium methoxide gave a colorless, syrupy product (**11**) that retained one acetyl group, as indicated by i.r. and the n.m.r. spectra. Since the acetyl group at the pyranoid C-3 of **8** is sterically hindered, compound **8** resists complete deacetylation with chilled alkali.

Mesylation of **11** gave crystals of compound **12** in 89% yield; the n.m.r. spectrum of **12** showed methyl-proton signals for one mesyl group and one acetyl group.

Thus, the structures of **11** and **12** were assigned as 3-*O*-acetyl-6,*N*-anhydro-D-mannopyrano[*cis*-1,2-*b*]dihydrobenzothiazine and corresponding 4-methanesulfonate, respectively.

Treatment of **12** with an excess of sodium methoxide in boiling methanol–chloroform for 3 h gave colorless needles (**13**), in 83% yield. Compound **13** showed neither acetyl nor mesyl groups by i.r. and n.m.r. spectroscopy. The mass spectrum of **13** showed M^+ at *m/e* 233. The identification of an epoxide ring is based on the observation that epoxide protons usually resonate at slightly higher field (τ 6.40–7.0) than a proton adjacent to oxygen in pyranoid ring[9]. These data support the presence of the 3,4-anhydro group. The configuration of **13** was assigned as D-*talo* from the predicted direction of nucleophilic rearside attack by the alkoxy anion at C-3 upon treatment with alkali.

Thus, compound **13** was assigned as 3,4-anhydro-6,*N*-anhydro-D-talopyrano-[*cis*-1,2-*b*]dihydrobenzothiazine.

EXPERIMENTAL

General. — Unless stated otherwise, solvents were evaporated in *vacuo* at a bath temperature of 40° in a rotary evaporator. Reactions were monitored by t.l.c. on Silica Gel G (E. Merck, Darmstadt, Germany), with solvent systems 2:1 (*v/v*) benzene–ether, 19:1 (*v/v*) benzene–methanol, and 65:23:12 (*v/v*) ethyl acetate–isopropyl alcohol–water. Detection was effected with sulfuric acid or iodine vapor.

Melting points were determined with a micro melting point apparatus and are uncorrected. Optical rotations were measured in 1-dm tubes with a Applied Electric Lab., Ltd. automatic polarimeter MP-1T. I.r. spectra were recorded with a JASCO infrared spectrophotometer DS-301. U.v. spectra were recorded with a Hitachi spectrometer 124. N.m.r. spectra were measured at 100 MHz with a JEOL, JNM-4H-100 spectrometer in chloroform-*d*. Chemical shifts are given on the τ scale and coupling constants (J) in Hz, with tetramethylsilane as the internal standard. Mass spectra were obtained with a Hitachi RMU-6-E mass spectrometer, modified for direct introduction of the sample, at an ionizing potential of 75 eV.

*2-Amino-4-chlorophenyl 3,4,6-tri-*O*-acetyl-2-*O*-mesyl-1-thio-β-*D*-glucopyranoside* (**2**). — A solution of 3,4,6-tri-*O*-acetyl-2-*O*-mesyl-α-D-glucopyranosyl bromide[10] (12 g) in chloroform (50 ml) was added to a solution of sodium 2-amino-4-chlorobenzenethiolate[11] (6.1 g) in methanol (50 ml), and the mixture was heated for 40 min under reflux. During the course of the reaction, the mixture became turbid and sodium bromide precipitated. After cooling, the reaction mixture was poured into ice–water. The water layer was extracted with chloroform (50 ml). The combined chloroform layers were washed with 10% sodium hydroxide solution and water, and dried over sodium sulfate. The solution was evaporated to a syrup that crystallized from a small amount of ethanol. Recrystallization from the same solvent afforded crystals (8 g, 59%), m.p. 153–155° (decomp.), $[\alpha]_D^{19}$ −7.5° (*c* 0.4, chloroform); ν_{max}^{KBr} 3370 (NH), 1750 (OAc), 1180 (OMs), 830 (phenyl) cm^{-1}; λ_{max}^{EtOH} 312 nm (ε 4,760); n.m.r. data: τ 2.64, 3.26, 3.35 (each 1-proton doublets and triplet, phenyl), 4.93 (1-proton doublet, $J_{1,2}$ 10, H-1), 5.80 (2-proton singlet, NH), 6.79 (3-proton singlet, OMs), 7.87, 7.90, 7.95 (each 3-proton singlets, OAc); *m/e* 429 (M^+ −96).

Anal. Calc. for $C_{19}H_{24}ClNO_{10}S_2$: C, 43.38; H, 4.60; N, 2.66; S, 12.19. Found: C, 42.73; H, 4.49; N, 2.26; S, 12.40.

D-*Mannopyrano*[cis-*1,2*-b]*dihydrobenzothiazine* (**3**). — To a suspension of *o*-aminophenyl 3,4,6-tri-*O*-acetyl-2-*O*-mesyl-1-thio-β-D-glucopyranoside[1] (**1**), (30 g) in methanol (200 ml) was added methanol (200 ml) saturated with dry hydrogen chloride gas at 0°, and the mixture was kept for 2 h at room temperature. Complete removal of the solvent afforded a syrup that was suspended in saturated aqueous sodium hydrogen carbonate (200 ml). After addition of ethanol (200 ml), the mixture was heated for 20 min under reflux. Removal of the solvent gave a crystalline mass that was washed with chilled water and ethanol, and filtered to give **3** (13.2 g, 80%), m.p. 203–206°. This product was indistinguishable with an authentic sample[1] by t.l.c. and i.r. spectrum.

*3,4,6-Tri-*O*-acetyl-D-mannopyrano*[cis-*1,2*-b]-*6'-chlorodihydrobenzothiazine* (**4**). — To a suspension of **2** (9.5 g) in methanol (100 ml) was added methanol (100 ml saturated with dry hydrogen chloride gas at 0°, and the reaction mixture was treated as in the preparation of **3**. Removal of the solvent gave a powder that was acetylated with 1:1 (*v*/*v*) pyridine–acetic anhydride (80 ml). The reaction mixture was poured into ice–water. The resulting white precipitate was collected, washed with water, and air-dried. Recrystallization from boiling ethanol gave pure **4** (6.2 g, 67%),

m.p. 150–151°, $[\alpha]_D^{12}$ −44° (*c* 0.4, chloroform); ν_{max}^{KBr} 3390 (NH), 1740 (OAc), 785 (phenyl), no absorption near 1170–1180 cm^{-1} (OMs); λ_{max}^{EtOH} 312 nm (ε 3,440); n.m.r. data: τ 3.04 (1-proton doublet, $J_{7,8}$ 7.5, phenyl-8), 3.34 (1-proton quartet, $J_{5,7}$ 2.5, phenyl-7), 3.47 (1-proton doublet, phenyl-5), 4.66 (1-proton doublet, $J_{1,NH}$ 4.5, NH), 4.50 (1-proton triplet, $J_{4,5}$ 10, H-4), 4.66 (1-proton quartet, $J_{3,4}$ 5, H-3), 5.05 (1-proton quartet, $J_{1,2}$ 1.5, H-1), 5.78 (2-proton doublet, H-6), 6.06 (1-proton quartet, $J_{2,3}$ 4.8, H-2), 6.19 (1-proton quartet, $J_{5,6}$ 4, H-5), 7.88, 7.93 (9-proton singlets, OAc); *m/e* 429 (M^+).

Anal. Calc. for $C_{18}H_{20}ClNSO_7$: C, 50.29; H, 4.69; N, 3.26; S, 7.46. Found: C, 50.60; H, 4.58; N, 3.11; S, 7.59.

From the mother liquor of **4** colorless needles were precipitated. Recrystallization from ethanol gave pure material (0.3 g), m.p. 146–148°, $[\alpha]_D^{12}$ −18° (*c* 0.4, chloroform); ν_{max}^{KBr} 3380 (NH), 1740 (OAc), 1692 (NAc), 793 (phenyl), no absorption near 1170 cm^{-1} (OMs); n.m.r. data: τ 1.36 (1-proton singlet, NH), 1.5, 2.52, 2.95 (each 1-proton doublets and quartet, phenyl), 4.31–4.64 (2-proton multiplet, sugar protons), 5.04 (1-proton doublet, $J_{1,2}$ 1.8, H-1), 5.55–6.60 (6-proton multiplet, sugar protons), 7.69 (3-proton singlet, NAc), 7.87, 7.94 (each 3-proton singlets, OAc), 8.22 (3-proton singlet, unidentified methyl signal), 8.76 (3-proton triplet, CH_3CH_2–). *m/e* 517 (M^+).

Anal. Calc. for $C_{22}H_{28}ClNO_9S$: C, 51.01; H, 5.45; N, 2.70; S, 6.19. Found: C, 50.64; H, 5.42; N, 2.50; S, 6.52.

D-*Mannopyrano*[cis-*1,2*-b]-*6'-chloro-dihydrobenzothiazine* (**5**). — To a suspension of **4** (2 g) in dry methanol (20 ml) was added 0.1M methanolic sodium methoxide (1 ml). The reaction mixture was heated for 30 min under reflux, and cooled. After the addition of acetic acid (1 drop), the solvent was evaporated to dryness to give the crude product (**5**) (1.45 g), containing a small amount of sodium acetate but which was suitable for the next step; ν_{max}^{KBr} 3370 (NH, OH), 1583, 785 cm^{-1} (phenyl); λ_{max}^{EtOH} 315 nm; *m/e* 285 (M^+ −18), 183 (6-chlorobenzothiazine ion).

3,4-Di-O-*acetyl-6*-O-*tosyl*-D-*mannopyrano*[cis-*1,2*-b]*dihydrobenzothiazine* (**6**). — To a chilled solution of **3** (18 g) in pyridine (300 ml) was added tosyl chloride (13.5 g). The mixture, protected from moisture, was stirred for 1 h at 0°, and then kept overnight at 4°. Acetic anhydride (200 ml) was then added dropwise at 0°, and the reaction mixture was kept overnight at 4°. The mixture was poured into ice–water, and extracted with chloroform. The chloroform layer was washed successively with dilute sulfuric acid, aqueous sodium hydrogen carbonate, and water, and dried over sodium sulfate. The solution was evaporated to give **6** as a crystalline (28.8 g, 85%), which was recrystallized from chloroform–petroleum ether to give pure material, m.p. 117–119°, $[\alpha]_D^{20}$ −26° (*c* 0.5, chloroform); ν_{max}^{KBr} 3390 (NH), 1740 (OAc), 1587, 751 (phenyl), 1170 cm^{-1} (OTs); λ_{max}^{EtOH} 304 nm (ε 3,400); n.m.r. data: τ 2.2–2.85 (4-proton multiplet, phenyl in tosyl), 2.95–3.6 (4-proton multiplet, phenyl), 5.8–6.2 (1-proton singlet, NH), 7.62 (3-proton singlet, tosyl), 7.90, 7.94 (each 3-proton singlets, OAc); *m/e* 335 (M^+ −172).

Anal. Calc. for $C_{23}H_{25}NO_8S_2$: C, 54.74; H, 4.97; N, 2.76; S, 12.63. Found: C, 54.73; H, 4.81; N, 2.27; S, 12.68.

3,4-Di-O-acetyl-6-O-tosyl-D-mannopyrano[cis-*1,2*-b]-*6-chlorodihydrobenzothiazine* (**7**). — To a chilled solution of **5** (1.45 g) in pyridine (50 ml) was added tosyl chloride (1 g). The mixture was stirred for 1 h at 0°, kept overnight at 4°, and acetic anhydride (30 ml) was added and the mixture again kept overnight at 4°. The reaction mixture was treated as in the preparation of **6** to afford crystals which, upon recrystallization from ethanol gave pure **7** (1.75 g, 70%), m.p. 123–125° (decomp.), $[\alpha]_D^{17}$ −44° (*c* 0.37, chloroform); ν_{max}^{KBr} 3400 (NH), 1740 (OAc), 1580, 760 (phenyl), 1172 cm^{-1} (OTs); λ_{max}^{EtOH} 312 nm (ε 4,610); n.m.r. data: τ 2.23–2.84 (4-proton multiplet, phenyl in tosyl), 3.05–3.67 (3-proton multiplet, phenyl), 5.8–6.2 (1 proton, NH), 7.60 (3-proton singlet, tosyl), 7.90, 7.93 (each 3-proton singlets, OAc); *m/e* 369 (M^+ −172).

Anal. Calc. for $C_{23}H_{24}ClNO_8S$: C, 50.97; H, 4.46; N, 2.58 S, 11.83. Found: C, 50.95; H, 4.73; N, 2.30; S, 11.76.

3,4-Di-O-acetyl-6,N-anhydro-D-mannopyrano[cis-*1,2*-b]*dihydrobenzothiazine* (**8**). — To a solution of **6** (28 g) in chloroform (150 ml) and ethanol (150 ml) was added anhydrous sodium acetate (18 g). The mixture was heated for 2 h under reflux. After cooling, the reaction mixture was poured into ice–water and the water layer was extracted with chloroform. The combined chloroform layers were washed with water, dried over sodium sulfate, and evaporated to give a syrup that crystallized from a small amount of ethanol. Recrystallization from the same solvent gave colorless crystals (17 g, 76%), m.p. 168°, $[\alpha]_D^{19}$ −102° (*c* 1, chloroform); ν_{max}^{KBr} 1745, 1737 (OAc), 1582, 1557, 740, 712 (phenyl), no absorption near 3400 cm^{-1} (NH); λ_{max}^{EtOH} 306 nm (ε 2,560); n.m.r. data: τ 2.9–3.35 (4-proton multiplet, phenyl), 4.7 (1-proton quartet, $J_{3,4}$ 2, H-3), 4.85 (1-proton doublet, $J_{1,2}$ 2, H-1), 5.41 (1-proton triplet, $J_{5,6syn}$ 6, H-5), 5.43 (1-proton quartet, $J_{4,5}$ 6, H-4), 5.96 (1-proton quartet, $J_{6syn,6anti}$ 9, H-6syn), 6.54 (1-proton doublet, *H*-6anti), 6.55 (1-proton quartet, $J_{2,3}$ 5, H-2), 7.83 (3-proton singlet, C-4 OAc), 8.70 (3-proton singlet, C-3 OAc); *m/e* 335 (M^+).

Anal. Calcd. for $C_{16}H_{17}NO_5S$: C, 57.31; H, 5.11; N, 4.18; S, 9.56. Found: C, 57.02; H, 4.98; N, 4.12; S, 9.67.

3,4-Di-O-acetyl-6,N-anhydro-D-mannopyrano[cis-*1,2*-b]-*6'-chlorodihydrobenzothiazine* (**9**). — To a solution of **7** (7 g) in chloroform (30 ml) and ethanol (30 ml) was added anhydrous sodium acetate (4 g). The mixture was heated for 2 h under reflux. The reaction mixture was treated as in the preparation of **8** to give crystals. Recrystallization from ethanol gave pure **9** (1.4 g, 30%), m.p. 132–134°, $[\alpha]_D^{19}$ −146° (*c* 0.3, chloroform); ν_{max}^{KBr} 1745 (OAc), 1578, 1550, 810, 790 cm^{-1} (phenyl); λ_{max}^{EtOH} 315 nm (ε 5,800); n.m.r. data: τ 2.97–3.31 (3-proton multiplet, phenyl), 4.68 (1-proton quartet, $J_{3,4}$ 2, H-3), 4.88 (1-proton doublet, $J_{1,2}$ 2, H-1), 5.41 (1-proton triplet, $J_{5,6syn}$ 6, H-5), 5.42 (1-proton quartet, $J_{4,5}$ 6, H-4), 5.99 (1-proton quartet, $J_{6syn,6anti}$ 9, H-6syn), 6.51 (1-proton quartet, $J_{2,3}$ 6, H-2), 6.54 (1-proton doublet, H-6anti), 7.83 (3-proton singlet, C-4 OAc), 8.62 (3-proton singlet, C-3 OAc); *m/e* 369 (M^+).

Anal. Calc. for $C_{16}H_{16}ClNO_5S$: C, 51.96; H, 4.36; N, 3.79; S, 8.67. Found: C, 52.28; H, 4.12; N, 3.66; S, 8.55.

6,N-Anhydro-D-mannopyrano[cis-*1,2*-b]*dihydrobenzothiazine hydrochloride* (**10**).

— A mixture of **8** (2 g) in dry methanol (25 ml) containing sodium (0.2 g) was stirred for 2 h at room temperature. After glacial acetic acid (1 ml) had been added, the solvent was evaporated to dryness to give a syrupy residue that extracted with chloroform (50 ml). The chloroform layer was washed with aqueous sodium hydrogen carbonate and water, dried over calcium chloride, and evaporated to give a slightly yellow syrup that was dissolved in ethanol (10 ml). The solution was added dropwise to dry ether (30 ml) saturated with dry hydrogen chloride gas at 0°. The resulting white precipitate was washed with ether until acid-free to give the pure salt **10** (1.65 g, 99.5%), m.p. 154–164°, $[\alpha]_D^{25}$ −12° (*c* 0.4, water); ν_{max}^{KBr} 3325 (OH), 2220 (R_3N^+H), 1590, 754 cm^{-1} (phenyl); λ_{max}^{EtOH} 306 nm (ε 2,470); *m/e* 250 (M^+ −36).

Anal. Calc. for $C_{12}H_{13}ClNO_3$: C, 50.08; H, 4.90; N, 4.87; S, 11.18. Found: C, 50.17; H, 5.21; N, 4.55; S, 11.38.

*3-O-Acetyl-6,*N*-anhydro-*D*-mannopyrano*[cis-*1,2*-b]*dihydrobenzothiazine* (**11**).— A mixture of **8** (10 g) and sodium methoxide in dry methanol (100 ml) containing sodium (0.4 g) was stirred for 45 min at 0°. After adding glacial acetic acid (5 ml), the solvent was evaporated to give a syrupy residue, which dissolved in chloroform (100 ml), and then poured into ice–water. The chloroform layer was washed with aqueous sodium hydrogen carbonate and water, dried over sodium sulfate, and evaporated to give a slightly yellow syrup **11** (8.2 g, 94%), $[\alpha]_D^{17}$ −47° (*c* 0.7, chloroform); ν_{max}^{KBr} 3400 (OH), 1742 (OAc), 1585, 1559, 750 cm^{-1} (phenyl); λ_{max}^{EtOH} 306 nm (ε 2,330); n.m.r. data in methyl sulfoxide-d_6: τ 8.83 (3-proton singlet, C-3 OAc), no methyl proton signal near 7.8–8.0 corresponding to C-4 OAc; *m/e* 293 (M^+).

*3-O-Acetyl-4-O-mesyl-6,*N*-anhydro-*D*-mannopyrano*[cis-*1,2*-b]*dihydrobenzothiazine* (**12**). — To a chilled solution of **11** (7 g) in pyridine (70 ml) was added mesyl chloride (7 g) and the mixture, protected from moisture, was kept overnight at 4°. After chloroform (100 ml) had been added, the reaction mixture was poured into ice–water (500 ml). The product was treated as in the preparation of **6** to give a crystalline mass (9.8 g, 89%). Recrystallization from ethanol gave colorless needles, m.p. 200–201°, $[\alpha]_D^{17}$ −71° (*c* 0.3, chloroform); ν_{max}^{KBr} 1750 (OAc), 1585, 1560, 746 (phenyl), 1170 cm^{-1} (OMs); u.v. λ_{max}^{EtOH} 305 nm (ε 2,650); n.m.r. data in methyl sulfoxide-*d*: τ 2.89–3.84 (4-proton multiplet, phenyl), 4.59 (1-proton quartet, $J_{3,4}$ 5.2, H-3), 4.91 (1-proton doublet, $J_{1,2}$ 2.2, H-1), 5.25–5.41 (2-proton multiplet, H-4 and H-5), 6.01 (1-proton quartet, $J_{5,6syn}$ 6, $J_{6syn,6anti}$ 9, H-6syn), 6.28 (1-proton quartet, $J_{2,3}$ 5.5, H-2), 6.56 (1-proton doublet, $J_{5,6anti}$ 0, H-6anti), 6.7 (3-proton singlet, OMs), 8.76 (3-proton singlet, OAc); *m/e* 371 (M^+).

Anal. Calc. for $C_{15}H_{17}NO_6S_2$: C, 48.52; H, 4.62; N, 3.77; S, 17.26. Found: C, 48.46; H, 4.64; N, 3.67; S, 17.35.

*3,4-Anhydro-6,*N*-anhydro-*D*-mannopyrano*[cis-*1,2*-b]*dihydrobenzothiazine* (**13**). — A mixture of **12** (5 g) and sodium methoxide in dry methanol (100 ml) containing sodium (1.1 g) was heated for 3 h under reflux. After cooling, the reaction mixture was poured into ice–water (300 ml) and extracted with chloroform. The chloroform layer was washed with water, dried over sodium sulfate, and filtered. The solvent was removed to give a colorless oil that showed two components by t.l.c. The product was

dissolved in benzene and chromatographed on silica gel (150 g). successive with elution by petroleum and benzene. The latter effluent was evaporated to give a colorless oil that crystallized from ethanol. Recrystallization from the same solvent gave fine needles (2.6 g, 83%), m.p. 104–105°, $[\alpha]_D^{17}$ −30° (*c* 0.3, chloroform); ν_{max}^{KBr} 1585, 1558, 755, 745 cm^{-1} (phenyl); λ_{max}^{EtOH} 305 nm (ε 2,640); n.m.r. data: τ 2.86–3.35 (4-proton multiplet, phenyl), 5.06 (1-proton doublet, $J_{1,2}$ 3.5, H-1), 5.30 (1-proton triplet, $J_{5,6syn}$ 5, H-5), 6.21 (1-proton quartet, $J_{6syn,6anti}$ 8.7, H-6syn), 6.52 (1-proton quartet, $J_{4,5}$ 5, H-4), 6.59 (1-proton quartet, $J_{3,4}$ 5, H-3), 6.77 (1-proton doublet, H-6anti), 6.86 (1-proton quartet, $J_{2,3}$ 5, H-2); *m/e* 233 (M^+).

Anal. Calc. for $C_{12}H_{11}NO_2S$: C, 61.80; H, 4.75; N, 6.01; S, 13.74. Found: C, 61.85; H, 5.04; N, 5.85; S, 13.49.

ACKNOWLEDGMENTS

The authors thank Professor S. Tejima for his interest in this work and Miss N. Arakawa for her help in preparation of the starting materials. The authors also thank all staffs of the analytical room of this Laboratory for n.m.r., mass spectra, and elemental analyses.

REFERENCES

1 M. SEKIYA AND S. ISHIGURO, *Tetrahedron Lett.*, (1971) 431. *Carbohyd. Res.*, 22 (1972) 325.
2 H. EL KHADEM, *Advan. Carbohyd. Chem. Biochem.*, 25 (1970) 351.
3 J. CLÉOPHAX, J. LEBOUL, A. M. SEPULCHRE, AND S. D. GÉRO, *Bull. Soc. Chim. Fr.*, (1970) 4412.
4 J. CLÉOPHAX, J. HILDESHEIM, A. M. SEPULCHRE, AND S. D. GÉRO, *Bull. Soc. Chim. Fr.*, (1969) 153.
5 J. CLÉOPHAX, S. D. GÉRO, AND A. M. SEPULCHRE, *Carbohyd. Res.*, 7 (1968) 505.
6 W. MEYER ZU RECKENDORF, *Chem. Ber.*, 97 (1964) 1275; 101 (1968) 3802.
7 G. T. LOURENS, *Carbohyd. Res.*, 17 (1971) 35.
8 J. S. BRIMACOMBE AND A. M. MOFTI, *Carbohyd. Res.*, 18 (1971) 157.
9 D. H. BUSS AND L. HOUGH, *Tetrahedron*, 21 (1965) 69.
10 B. HELFERICH AND J. ZIRNER, *Chem. Ber.*, 95 (1962) 2604.
11 K. J. FARRINGTON AND W. K. WARBURTON, *Aust. J. Chem.*, 8 (1955) 545.