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SYNTHESIS OF 2-(6-AMINOHEXANAMIDO)ETHYL 1-THIO-β-D-GALACTOPYRANOSIDE AND 1-THIO-β-D-GLUCOPYRANOSIDE, AND RELATED COMPOUNDS*

REIKO T. LEE AND YUAN CHUAN LEE**

Department of Biology and McCollum-Pratt Institute, Johns Hopkins University, Baltimore, Maryland 21218 (U. S. A.)

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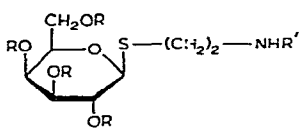
ABSTRACT

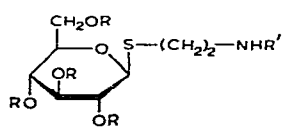
2-(6-Aminohexanamido)ethyl 1-thio-β-D-galactopyranoside (**5**) and 1-thio-β-D-glucopyranoside (**9**) were prepared by the following scheme: 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-aldopyranoses, generated from 2-*S*-(2,3,4,6-tetra-*O*-acetyl-β-D-aldopyranosyl)-2-thiopseudourea hydrobromides, were aminoethylated with ethylenimine, followed by *N*-acylation of the products with 6-(trifluoroacetamido)hexanoic acid (**1**), and *O*-deacylation. These reactions could be carried out consecutively without isolation of intermediates, and the products obtained after gel chromatography were de(trifluoroacetyl)ated to obtain the final products. The chain lengths of the aglycons were further extended by repeating the acylation and the de(trifluoroacetyl)ation. An analog containing glycerol *in lieu* of a sugar was prepared by a similar reaction-scheme.

INTRODUCTION

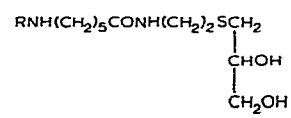
As part of a program for the preparation of thioglycosides having aglycons bearing terminal amino groups, glycosides useful for affixation to solid matrices, we



	R	R'
2	CH_3CO-	H
2a	H	H
5	H	$H_2N(CH_2)_5CO-$
6	CH_3CO-	$F_3CCONH(CH_2)_5CO-$
6a	H	$F_3CCONH(CH_2)_5CO-$
7	H	$H_2N(CH_2)_5CONH(CH_2)_5CO-$



	R	R'
9	H	$H_2N(CH_2)_5CO-$
10	CH_3CO-	$F_3CCONH(CH_2)_5CO-$
11	H	$H_2N(CH_2)_5CONH(CH_2)_5CO-$
12	H	$F_3CCONH(CH_2)_5CONH(CH_2)_5CO-$



13 R = H

14 R = $H_2N(CH_2)_5CO-$

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have previously reported the synthesis[1] of 6-aminohexyl 1-thioglycosides and *p*-(6-aminohexanamido)phenyl 1-thio-β-D-galactopyranoside. We now describe methods for the preparation of aminoacyl derivatives of 2-aminoethyl 1-thio-β-D-galactopyranoside, 1-thio-β-D-glucopyranoside, and 1-thio-DL-glycerol.

EXPERIMENTAL

Materials. — 2,3,4,6-Tetra-*O*-acetyl-α-D-galactopyranosyl bromide and 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (Sigma Chemical Co.) were used without purification. Ethylenimine (J. T. Baker and Co.) was redistilled just before the aminoethylation reaction was performed. 6-Aminohexanoic acid and 2-ethoxy-*N*-(ethoxycarbonyl)-1,2-dihydroquinoline (EEDQ) (Aldrich Chemical Co.) were used without purification. 1-Thio-DL-glycerol (95%) was obtained from Evans Chemetics, Inc. (Darien, Conn.). Fluorescamine (4-phenylspiro[furan-2(3*H*),1′-phthalan]-3,3′-dione) was obtained from Roche Diagnostics (Nutley, N.J.). All other chemical reagents were of reagent grade, and were used without purification.

Analytical methods. — Proton magnetic resonance (p.m.r.) spectra were recorded with a JEOLCO MH-100 spectrometer. Labile hydrogen atoms in the samples to be measured were routinely exchanged with deuterium by dissolving samples in deuterium oxide (99.8%) and evaporating to dryness. Optical rotations at 589 nm were measured with a Cary 16 spectropolarimeter. Unless otherwise mentioned, colorimetric measurements were made in test tubes (13 × 100 mm) with a Bausch and Lomb Spectronic 20 colorimeter.

Carbohydrate was determined by a modified phenol–sulfuric acid method[2]. Amino groups were determined either by a modified method[2] employing 2,4,6-trinitrobenzenesulfonic acid (TNBS) or by a fluorescamine method[3]; the latter was especially useful when interference caused by ammonia in the samples was to be avoided[4,5]. 6-Aminohexanoic acid was used as a reference compound for both methods of amino-group determination. Thiol groups were determined by a variation of the Ellman method[6]: to samples (2 ml) of solutions containing 10 to 100 nmolar equivalents of thiol group were added 1 ml of 0.2M sodium borate buffer (pH 8.0) and 20 μl of 5,5′-dithiobis(2-nitrobenzoic acid) (0.4% in 0.1M sodium phosphate buffer, pH 7.0). After 5 to 10 min, the intensity of the yellow color developed was measured at 412 nm. For the determination of the glycol grouping, Hanahan and Olley's method[7] was modified: to a sample solution containing 10 to 150 nmoles of the glycol in 0.25 ml were added 0.1 ml each of 0.1M sodium periodate and M sulfuric acid. After exactly 5 min, 0.1 ml of 10% sodium hydrogen sulfite solution was added, followed by 2.5 ml of chromotropic acid in 12M sulfuric acid. The mixture was mixed well, heated in a boiling-water bath for 30 min, and cooled; half-saturated thiourea in water (0.25 ml) was added, and the intensities at 570 nm were read. Ester groups were determined by use of a modified hydroxamate method[8].

Thin-layer chromatography (t.l.c.) was usually performed on aluminum (E. Merck) or plastic sheets (J. T. Baker) pre-coated with a layer of silica gel. The

eluants used were (*A*) 3:2:1 (v/v) ethyl acetate–acetic acid–water; (*B*) 9:4:2 (v/v) ethyl acetate–isopropyl alcohol–water; or (*C*) 70% (v/v) ethanol–water. Detection of the compounds was accomplished either by spraying with 10% sulfuric acid in 95% ethanol and charring by heating for a few minutes at 140° (carbohydrates), spraying with 0.3% ninhydrin in acetone and heating similarly (amino group), or spraying with periodate–benzidine reagent (glycol grouping[9]).

General procedures. — All evaporations were conducted *in vacuo* at 35–45° in a Rinco rotary evaporator. Prior to elementary analysis or component analysis of a crystalline compound, samples were dried overnight in a vacuum desiccator heated at 40–45°. Elementary analyses were made by Galbraith Laboratories, Oak Ridge, Tenn.

Deacetylation was accomplished either with sodium methoxide or anion-exchange resins [Dowex 1 X-8 (OH^-) (100–200 mesh) or Amberlite IRA-400 (OH^-) (200–400 mesh)]. Sodium methoxide removed *O*-acetyl groups only, whereas the resins very effectively removed both trifluoroacetyl and *O*-acetyl groups. In the methoxide method, enough methanolic solution of sodium methoxide was added to the sample in dry methanol to make it ~0.05M in sodium methoxide. The solution was kept overnight at room temperature, and then usually acidified with acetic acid and evaporated.

Dowex 1 or Amberlite IRA-400 resin was converted into the OH^- form with 2M sodium hydroxide, and this form was washed with water and stored, as a suspension in 50% ethanol, in a tightly capped jar. Samples to be deacylated were dissolved in 50% ethanol, an excess (~2-fold) of the resin was added (calculated on the estimated capacity of 0.8 meq per ml of packed resin), and the suspension was gently stirred. De(trifluoroacetyl)ation was complete within 1 h, but total deacetylation usually required 5–6 h. The extent of deacetylation was checked by the hydroxamate method. After deacylation, the resin was filtered off, and the filtrate evaporated.

Gel chromatography was effectively used for purification of reaction products (see Discussion). The two systems used were Bio Gel P-2 (fine mesh) (5 × 150 cm) eluted with 0.1M acetic acid, and Sephadex LH-20 (4 × 150 cm) eluted with 95% ethanol. Elution was always conducted at room temperature, at 150–180 ml per h (Bio Gel) or 100–150 ml per h (LH-20).

For coupling of the amino group with the carboxyl group, EEDQ was routinely used. For this reaction, the acid, the amine, and EEDQ were mixed in 1.1:1.0, 1.0:1.0, and 1.15:1.0 molar ratios. The mixture of anhydrous reactants was dissolved in absolute ethanol (usually, the smallest volume required in order to effect complete dissolution) and the solution was kept overnight at room temperature.

6-(Trifluoroacetamido)hexanoic acid (**1**). — Trifluoroacetic anhydride (40 ml, 270 mmoles) was slowly added to 6-aminohexanoic acid (13.1 g, 100 mmoles) contained in a 100-ml, round-bottomed flask. The rate of addition was so controlled that insufficient heat to evaporate off trifluoroacetic anhydride was produced (periodical cooling under cold tap-water during the addition was found helpful). After all of the anhydride had been added, the homogeneous solution was kept for 1 h at room temperature, and evaporated to a thick syrup which was mixed with 100 ml of cold

water and stirred overnight in the cold. The crystalline product was filtered off, washed with cold water, dried, and recrystallized from ether; yield 61%, m.p. 88–89°. The product displayed the same characteristics as the compound prepared by another method[1].

2-Aminoethyl 2,3,4,6-tetra-O-acetyl-1-thio-β-D-galactopyranoside (**2**) *and 2-aminoethyl 1-thio-β-D-galactopyranoside* (**2a**). — 2-*S*-(2,3,4,6-Tetra-*O*-acetyl β-D-galactopyranosyl)-2-thiopseudourea hydrobromide (**3**) was prepared from 2,3,4,6-tetra-*O*-acetyl-α-D-galactosyl bromide by the method described by Horton[10]. Conversion of **3** into 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-galactopyranose (**4**) was achieved by boiling a suspension of it in carbon tetrachloride–aq. sodium hydrogen sulfite solution[11].

Freshly distilled ethylenimine (b.p. 55–56°; 2 ml, 56 mmoles) was added to a solution (carbon tetrachloride) of **4** prepared from 20 mmoles of **3**. The course of the reaction was monitored by measurement of SH content (see Fig. 1). The reaction was essentially complete within 30 min; the mixture was then evaporated to a syrup, and the residual water was removed by azeotropic evaporation with toluene. The resulting, syrupy **2** was used directly in the next step.

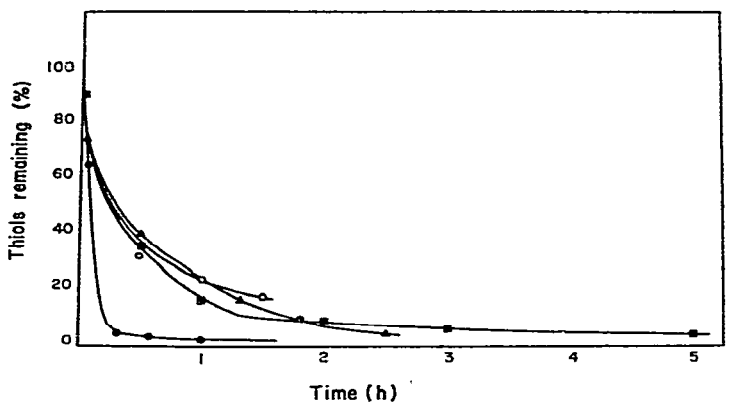

Fig. 1. Aminoethylation of thiols with ethylenimine. ●, compound **4** in carbon tetrachloride; ○, compound **4** in chloroform; ▲, compound **8** in carbon tetrachloride–chloroform; and ■, 1-thio-DL-glycerol in absolute ethanol.

For its identification, the syrup (**2**) was deacetylated with sodium methoxide in methanol, and the product was fractionated on a column of Bio Gel. The elution profile showed two, overlapping, sugar peaks: the minor peak did not contain amino groups, but the major peak had ~1 equivalent of amino group per mole of galactose. By p.m.r. spectroscopy, the component in the minor peak was identified as *N*-acetylated **2a**, presumably formed during the deacetylation (see Discussion). The eluate containing the major peak (which became very dark upon evaporation and standing) was decolorized with charcoal, and then applied to a column (1.1 × 13 cm)

of Dowex 50 (H^+) (200–400 mesh). Sucecssive elution with water and then with 1M ammonia each produced a single peak. The ammoniacal eluate was evaporated to dryness, and the product was decolorized, and crystallized from ethanol–ether; m.p. 130–131°. A sample of this crystalline material gave 97% of the theoretical amount of galactose, and 95% (by TNBS) and 110% (by fluorescamine) of the theoretical amount of amino group (with cystamine dihydrochloride as the standard).

2-(6-Aminohexanamido)ethyl 1-thio-β-D-galactopyranoside (**5**). — Compound **5** was prepared from **1** plus **2** with EEDQ in ethanol (see *General procedures*). The reaction mixture was evaporated to dryness, the residue dissolved in chloroform, the solution washed with cold 0.5M sulfuric acid (twice) and saturated sodium hydrogen carbonate solution (twice) (to remove remaining reactants and quinoline derivatives), dried (sodium sulfate), and evaporated to a syrup containing 2-[6-(trifluoroacetamido)-hexanamido]ethyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-galactopyranoside (**6**).

The syrup was deacetylated by sodium methoxide (see *General procedures*), and the syrupy product was fractionated on a column of Bio Gel P-2 (see Fig. 2). The

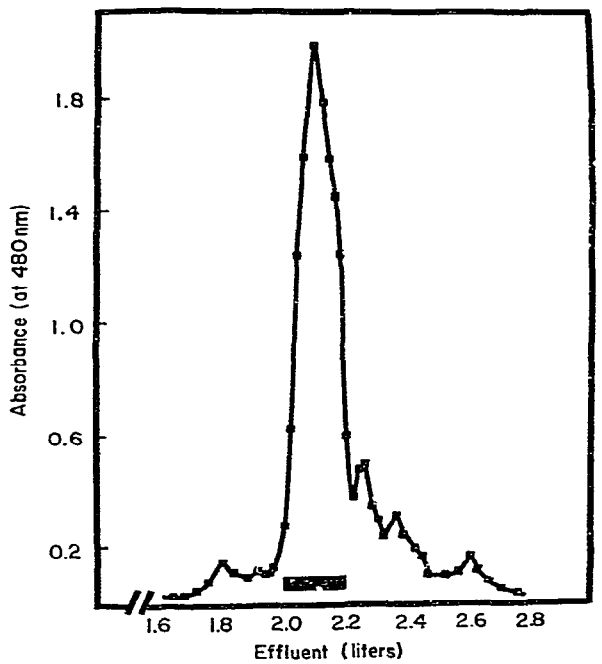

Fig. 2. Gel filtration (Bio Gel P-2) of compound **6a**. Elution was performed with 0.1M acetic acid, and the effluent was analyzed by the phenol–sulfuric acid method. (For details, see *General procedures*.)

portion containing the main peak (elution volume, 2.0–2.2 liters), which contained about 11 mmoles of galactose (55% yield from **3**), was evaporated to dryness. De(trifluoroacetyl)ation of the 2-[6-(trifluoroacetamido)hexanamido]ethyl 1-thio-

β-D-galactopyranoside (**6a**) thus obtained* was accomplished with Dowex 1 (OH^-) resin, to yield **5**, which was twice recrystallized from 95% ethanol–ether; 38.5% yield (based on **3**). Recrystallization from 2-propanol yielded crystals, m.p. 158–159°, $[\alpha]_D^{25}$ −16.0° (*c* 4.80, water); homogeneous by t.l.c. in solvents (*A*) and (*C*), as detected both by ninhydrin reagent and by charring; p.m.r. data (D_2O): δ 1.2–1.8 (m, 8, C–CH_2), 2.24 (t, 2, ND_2–CH_2), 2.6–3.1 (m, 4, S–CH_2 and COND–CH_2), 3.2–4.05 (m, 8, O–CH_2 and CO–CH_2), and 4.60 (d, 1, anomeric C–H, *J* 8 Hz).

Anal. Calc. for $C_{14}H_{28}N_2O_6S$ (352.45 daltons): C, 47.70; H, 8.00; N, 7.95; S, 9.10. Found: C, 47.93; H, 8.08; N, 7.81; S, 8.98.

*2-[6-(6-Aminohexanamido)hexanamido]ethyl 1-thio-β-*D*-galactopyranoside* (**7**). — The aglycon in **5** was elongated to give **7** by dissolving compounds **5**, **1**, and EEDQ in dry ethanol. After being kept overnight, the mixture was evaporated to syrup which was fractionated on a column of Sephadex LH-20; the elution profile is shown in Fig. 3. Evaporation of the portion containing the major peak resulted in a white, crystalline product, presumably *N*-trifluoroacetylated **7**. Recrystallization from 95%

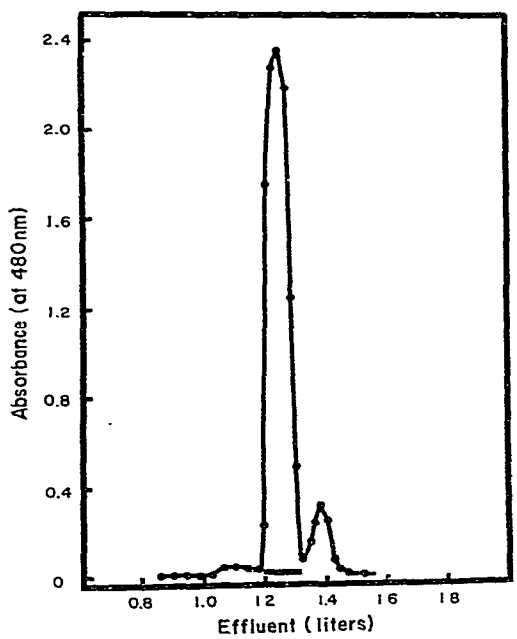

Fig. 3. Gel filtration (Sephadex LH-20) of *N*-(trifluoroacetyl)ated **7**. Elution was performed with 95% ethanol, and the effluent was analyzed by the phenol–sulfuric acid method. (The major peak was *N*-trifluoroacetylated **7**, and the minor peak was unreacted compound **5** used in the condensation reaction. For details, see *General procedures*.)

*Compound **6a**, obtained from **6** by treatment with sodium methoxide, was water-soluble, showed only a single spot in t.l.c., and did not react with TNBS. The masked amino group was, however, readily liberated by the treatment with Dowex 1 (OH^-) resin. Therefore, **6a** was tentatively identified as *O*-deacylated **6**.

ethanol produced two crops of crystals, in 62.5 and 16.5% yield, respectively, having m.p. 169–170°. The trifluoroacetyl group was removed by treatment with Dowex 1 (OH^-) as already described. After evaporation of the filtrate, compound **7** was crystallized from absolute ethanol–ether in 90.5% yield; homogeneous by t.l.c. in solvent (*A*), m.p. 173–174°, $[\alpha]_D^{25}$ −10.0° (*c* 5.10, 50% ethanol).

Anal. Calc. for $C_{20}N_{39}N_3O_7S$ (465.60 daltons): C, 51.58; H, 8.44; N, 9.02; S, 6.88. Found: C, 51.49; H, 8.59; N, 8.85; S, 6.90.

*2-(6-Aminohexanamido)ethyl 1-thio-β-*D*-glucopyranoside* (**9**). — The D-glucose analogs of **2**, **3**, **4**, and **5** were prepared by procedures similar to those already described, with some minor changes. 2,3,4,6-Tetra-*O*-acetyl-1-thio-β-D-glucopyranose (**8**) was generated and extracted into carbon tetrachloride as described for the D-galactose counterpart (**4**). Extraction with acid and water in the cold could not be performed, because of the limited solubility of **8** in carbon tetrachloride; therefore, about an equal volume of chloroform was added to the solution of **8** in carbon tetrachloride, and washing was conducted at room temperature with cold 0.5M sulfuric acid and then cold water.

In the next step (aminoethylation of **8**), the disappearance of SH was much slower than that observed for the galactose analog (**4**) (see Fig. 1), probably due to lower concentrations of the reactants, as well as the inclusion of chloroform. When **4** was treated with ethylenimine in chloroform, reaction proceeded more slowly than in carbon tetrachloride, even though the concentrations of the reactants were higher than in carbon tetrachloride.

In some preparations of **9**, 2-[6-(trifluoroacetamido)hexanamido]ethyl 1-thio-β-D-glucopyranoside (**10**) (the D-glucose analog of **6**) was treated directly with Dowex 1 resin to remove both the acetyl and the trifluoroacetyl groups. Purification of the resulting **9** was accomplished by gel filtration on Bio Gel P-2, which yielded an elution profile** similar to that depicted in Fig. 2. The yield of **9** in the major peak was ~70%, as determined by carbohydrate analysis. Although **9** obtained from the column of Bio Gel P-2 was homogeneous by t.l.c., and it had an equimolar ratio of amino group to glucose (1.0:1.0), crystallization of **9** was extremely difficult, because of its hygroscopicity. Compound **9** was fractionally precipitated from ethanolic solution by adding successive amounts of ether. Crystals of **9** were obtained in 26% yield by pooling the middle fractions and then successively recrystallizing from ethanol–ether (twice) and isopropanol in a dry atmosphere, the crystals being collected each time by decantation (not filtration). The crystals were dried thoroughly in a vacuum desiccator. The product was homogeneous in t.l.c., and had $[\alpha]_D^{25}$ −28.9° (*c* 7.05 in water, as determined by the phenol–sulfuric acid method); its p.m.r. spectrum was similar to that of **5** (anomeric proton, $\delta = 4.6$, J 8 Hz).

2-[6-(Trifluoroacetamido)hexanamido]ethyl 1-thio-β-D-glucopyranoside (the D-glucose analog of **6a), obtained by treatment of **10** with sodium methoxide, can be purified by gel filtration prior to de(trifluoroacetyl)ation. The elution profile was practically identical to that obtained from **10** treated with Dowex 1 resin.

2-[6-(Acetamido)hexanamido]ethyl 2,3,4,6-tetra-O-acetyl-1-thio-β-D-glucopyranoside (**9b**). — As determination of the m.p. of **9**, or its elementary composition, was extremely difficult because of its hygroscopicity, **9** was identified as its acetate. Acetylation of **9** in 1:1 dry pyridine–acetic anhydride was conducted overnight at room temperature, and the mixture was evaporated after addition of dry methanol, and again after addition of a small volume of water, with addition of toluene. The residue was twice recrystallized from absolute ethanol–ether. The product exhibited a single (sugar) spot in t.l.c. with solvent (*B*), and had m.p. 119–120°.

Anal. Calc. for $C_{24}H_{38}N_2O_{11}S$ (562.63 daltons): C, 51.23; H, 6.81; N, 4.98; S, 5.70. Found: C, 51.14; H, 6.68; N, 5.23; S, 5.86.

2-[6-(6-Aminohexanamido)hexanamido]ethyl 1-thio-β-D-glucopyranoside (**11**). — The trifluoroacetyl derivative (**12**) of **11** was prepared by coupling **9** with **1** in the presence of EEDQ as already described. The reaction mixture was evaporated to a syrup, and this was washed with ether by decantation. A solution of the residue in a small volume of 95% ethanol was applied to a column of Sephadex LH-20; elution of this column produced two peaks similar to those shown in Fig. 3. The yield from the first peak, which contained **12**, was 70% (based on the amount of D-glucose). The material in the first peak was deacylated with Amberlite IRA-400 (OH^+), to yield, upon evaporation, a white solid. Recrystallization from ethanol–ether gave, in 76% yield, **11** which was non-hygroscopic. Thrice-recrystallized material gave a single spot in t.l.c. with solvent (*A*); it had m.p. 147–148°, and $[\alpha]_D^{25}$ −23.6° (*c* 3.98, water).

Anal. Calc. for $C_{20}H_{39}N_3O_7S$ (465.60 daltons): C, 51.58; H, 8.44; N, 9.02; S, 6.88. Found: C, 51.39; H, 8.47; N, 8.96; S, 7.00.

1-S-[2-(6-Aminohexanamido)ethyl]-1-thio-DL-glycerol (**13**). — To a solution of 1-thio-DL-glycerol (4.4 g, 40 mmoles) in absolute ethanol (20 ml) was added freshly distilled ethylenimine (4 ml, 112 mmoles). The course of aminoethylation was monitored by measuring the disappearance of the thiol group (see Fig. 1). After 6 h, the mixture was evaporated to a syrup, which was used directly for coupling with **1** as described in the synthesis of **5**. The product, 1-*S*-[2-(6-trifluoroacetamidohexanamido)-ethyl]-1-thio-DL-glycerol, was dissolved in water, and the solution washed with toluene (twice) to remove the quinoline derivatives. The aqueous solution was evaporated to a syrup, which was dissolved in 95% ethanol, and purified on a column of Sephadex LH-20. The materials in the main-peak fractions, as determined by the analysis for glycol grouping, were combined and de(trifluoroacetyl)ated by means of Amberlite IRA-400 as already described, to afford syrupy **13** in 56% yield (based on 1-thio-DL-glycerol). It was homogeneous by t.l.c. in solvent (*A*) (ninhydrin and periodate reagents), but crystallized only after fractional precipitation from ethanolic solution with ether. Of the three fractions of ethanol–ether precipitate, the second and the third (which precipitated as solids) were recrystallized from ethanol–ether, to give a combined yield of 21%; m.p. 78–80°. Analyses for glycol grouping and amino groups on thrice-recrystallized material gave 97 and 104%, respectively, of the theoretical values. The p.m.r. spectrum indicated the presence of 6-aminohexanoyl and aminoethylthio groups (by comparison with the spectra of **5** and **9**).

*1-S-{2-[6-(6-Aminohexanamido)hexanamido]ethyl}-1-thio-*DL*-glycerol* (**14**). — Compound **14** was prepared from **1** plus **13** as described for the synthesis of **7** and **11**. The EEDQ reaction-mixture yielded, upon evaporation, a white solid which was successively washed with ether (twice), toluene (twice), and ether (twice). The residue was de(trifluoroacetyl)ated as already described, and the syrupy product was purified by passage through a column of Sephadex LH-20. The major peak fractions, containing both amino groups and glycol groupings, were evaporated to dryness, and the residue was crystallized from 95% ethanol–ether in 50% overall yield. The crystalline **14** was homogeneous by t.l.c. with solvent (*A*), and had m.p. 115–117°. Thrice-recrystallized material showed, by component analyses, 102 and 97.5%, respectively, of the theoretical amount of amino group (TNBS method) and glycol grouping.

DISCUSSION

In a previous report[1], we described the synthesis of some 6-aminohexyl 1-thio-β-D-aldopyranosides. As an alternative route to such thioglycosides, we have now explored the possibility of aminoethylation of 1-thioaldose derivatives with ethylenimine, as such a method would obviate the necessity for the availability of amino-protected aminoalkyl halides. This approach has proved successful, thus providing a simpler method for the preparation of thioglycosides having a terminal amino group.

The most crucial factor in the reaction scheme was found to be the purity of the ethylenimine. In early experiments, the ethylenimine used for aminoalkylations leading to **5** had previously been redistilled and then stored for a few days at room temperature. Although the batches of crystalline **5** obtained in these experiments showed an equimolar ratio of galactose to amino group, they exhibited heterogeneity by t.l.c., and their sulfur content was lower than expected. Gel filtration of these batches of **5** revealed that they were contaminated by compounds of higher molecular weight, all having equimolar galactose–NH_2 ratios. This problem was almost completely eliminated by using freshly distilled ethylenimine. A small amount of contaminants of higher molecular weights formed during the reaction was removed by gel filtration (see Fig. 2) and by repeated recrystallization. In the case of the galactose derivative **5**, the successive recrystallizations caused a slight decrease in m.p., accompanied by an increase in the sulfur content of the product.

As pointed out previously[1], *O*-deacetylation of compounds containing amino groups by the conventional method, with a catalytic amount of sodium methoxide or barium methoxide, posed some difficulties. *O*-Deacetylation of **2** by sodium methoxide produced, instead of the desired **2a**, a large proportion (sometimes 100%) of *N*-acetylated **2a**. This problem was solved by employing a strong anion-exchanger (Dowex 1 or Amberlite IRA-400) in the OH form. Presumably, *N*-acetylation during *O*-deacetylation with methoxide results from aminolysis of *O*-acetyl ester on the sugar residue, or from methyl acetate formed after *O*-deacetylation of the sugar acetate. By using a large excess of the anion exchanger in aqueous alcohol, saponification (instead of transesterification) occurs, and *N*-acetylation is prevented. In

addition, the resin accomplishes *N*-de(trifluoroacetyl)ation concomitantly with *O*-deacetylation for such compounds as **6** and **10**.

The thioglycosides described herein have been successfully coupled to BrCN-activated Sepharose beads, and they are being examined for biological applications.

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