binose (4.00 g.) was dissolved in 15 ml. of methylene chloride and the solution treated with a solution of 1.9 g. of *p*-nitrobenzoyl chloride in a mixture of 10 ml. of methylene chloride and 3 ml. of dry pyridine. After standing overnight at room temperature the methylene chloride solution was washed successively with 1*N* hydrochloric acid, aqueous sodium bicarbonate, and water. Moisture was removed with sodium sulfate and the solution concentrated to give 5.4 g. of sirup which crystallized spontaneously. Recrystallization from methanol afforded 4.64 g. (86%) of a mixture of the anomeric esters melting at 75–92° and showing $[\alpha]_D^{20}$ +11.0° in methylene chloride (*c*, 6.8).

Through fractional crystallization from ether-pentane the anomers were separated. The less soluble anomer crystallized as large plates, m.p. 77–78° and $[\alpha]_D^{20}$ +43.9° (*c*, 5.4 methylene chloride). The more soluble anomer crystallized as long needles, m.p. 96–97°, $[\alpha]_D^{20}$ −59° (*c*, 2.0 methylene chloride). In accord with the usual convention, the dextrorotatory isomer is designated the β-anomer (XIb) and the levorotatory isomer designated the α-anomer (XIa). From the rotations of the two pure substances it is apparent that the original mixture consisted of approximately 68% of the β-anomer.

Anal. Calcd. for $C_{33}H_{31}NO_8$ (569.59): C, 69.58; H, 5.49; N, 2.46. Found: (β-anomer) C, 69.86; H, 5.60; N, 2.42; (α-anomer) C, 69.65; H, 5.59; N, 2.49.

1,4-Anhydro-L-arabitol tri-p-nitrobenzoate (XIV). (*a*) *via 2,3,5-tri-O-benzyl-L-arabinosyl bromide* (XII). Two grams of a mixture of the anomeric 2,3,5-tri-*O*-benzyl-1-*O*-*p*-nitrobenzoyl-L-arabinofuranoses, dissolved in methylene chloride, was treated with 30 ml. of a 0.15*N* solution of hydrogen bromide in methylene chloride. After 5 min. the precipitated *p*-nitrobenzoic acid was filtered off and washed with methylene chloride; yield 565 mg. (96%). The filtrate and washings were concentrated to a reddish sirup which was dissolved in 10 ml. of tetrahydrofuran and treated with 5 ml. of a 2.0*M* solution of lithium aluminum hydride in tetrahydrofuran. When the reaction mixture had cooled to room temperature ethyl acetate was added cautiously to destroy the excess of reducing agent. It was then acidified with 50 ml. of 5*N* hydrochloric acid and extracted twice with 50-ml. portions of methylene chloride. The combined extracts were washed with saturated aqueous sodium bicarbonate and with water. Moisture was removed with sodium sulfate and the solvent removed to leave 1.31 g. of a sirup which showed only minor hydroxyl absorption in the infrared. Adsorption of the whole sample on alumina, followed by elution with methylene chloride, afforded a colorless sirup (1.15 g.) showing neither hydroxyl nor carbonyl components in the infrared. It was then dissolved in absolute ethanol and reduced in the presence of palladium on charcoal. Hydrogen absorption was slow, several hours being required to reach the theoretical value. The catalyst was removed and the filtrate concentrated to give a sirup which failed to crystallize. Chromatography, using Whatman No. 1 paper and *n*-butyl alcohol–water (86:14), revealed only one component, having an R_f of 0.6. On the basis of a molecular weight of 134, the sirup consumed 0.97 molar equivalent of sodium metaperiodate. Acylation of 910 mg. of this 1,4-anhydro-L-arabitol (prepared in a similar run) with *p*-nitrobenzoyl chloride in the usual manner afforded 3.49 g. (88%) of crystalline product which was recrystallized successively from benzene, chloroform–carbon tetrachloride and aqueous acetone: m.p. 80–82°; $[\alpha]_D^{20}$ +85.1° in chloroform (*c*, 0.5).

Anal. Calcd. for $C_{26}H_{19}N_3O_{13}$ (581.43): C, 53.71; H, 3.29; N, 7.23. Found: C, 53.75; H, 3.52; N, 7.00.

(b) *From ethyl 5-O-benzoyl-1-thio-β-L-arabinoside* (XV). Ethyl 5-*O*-benzoyl-1-thio-β-L-arabinoside[7] (587.1 mg.) was suspended in *ca.* 20 ml. of absolute alcohol with two teaspoonfuls of freshly prepared W-2 Raney nickel[17] and the mixture stirred for 13 hr. It was then boiled under reflux for 5.5 hr. and filtered, the nickel being washed generously with hot alcohol. On concentration *in vacuo*, there was obtained a sirup (378.2 mg.) which was dissolved in absolute methanol and debenzoylated with barium methoxide. The solution was deionized with a mixed-bed ion exchange resin, filtered and concentrated *in vacuo* to give a sirup: 226.1 mg. Acylation with *p*-nitrobenzoyl chloride in the usual manner gave 394.1 mg. (34%, based on the thioarabinoside) of crystalline material. Recrystallized twice from aqueous acetone it melted at 81–82° and showed $[\alpha]_D^{20}$ +85.1° in chloroform (*c*, 0.87). Mixed with the ester obtained in (a) above it melted at 80–82°.

Acknowledgment. Analyses were performed in the Analytical Services Unit of this Laboratory under the direction of Mr. H. G. McCann.

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[CONTRIBUTION FROM DEPARTMENT OF AGRICULTURAL BIOCHEMISTRY, UNIVERSITY OF MINNESOTA]

Synthesis of Xylobiose (4-*O*-β-D-Xylopyranosyl-D-xylose)[1]

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The synthesis of xylobiose (4-*O*-β-D-xylopyranosyl-β-D-xylose) (IX) has been achieved by condensing benzyl 2,3-di-*O*-benzyl-D-xylopyranoside (V), with 2,3,4-tri-*O*-acetyl-α-D-xylosyl bromide (VI) to give benzyl 4-*O*-(2,3,4-tri-*O*-acetyl-D-xylosyl)-2,3-di-*O*-benzyl-D-xyloside (VII). Saponification to remove acetyl groups followed by hydrogenation to remove the benzyl groups yielded xylobiose (IX).

Chemical or biochemical hydrolysis of polysaccharides leading to the formation of disaccharides provides a valuable approach to the determination of the general structure of polysaccharides.[2] Thus

(1) Paper No. *4530*, Scientific Journal Series, Minnesota Agricultural Experiment Station. Work supported in part by funds from the U. S. Department of Agriculture, Regional Project NC-25.

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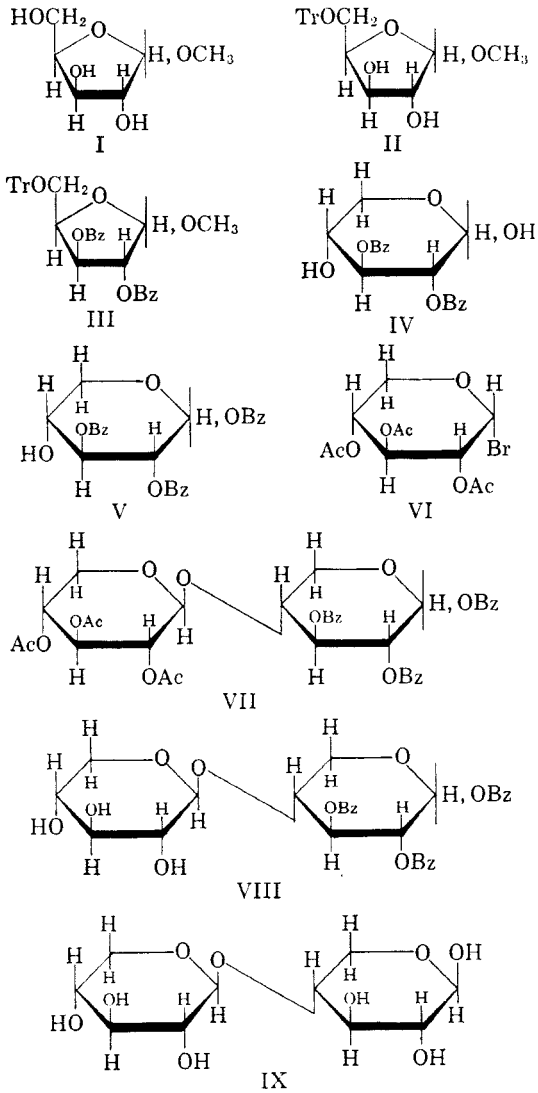
for example, cellobiose,[3] maltose,[4] 6-*O*-β-D-glucopyranosyluronic acid-D-galactose,[5] and 4-*O*-β-D-xylopyranosyl-D-xylose (xylobiose)[6] have been obtained from cellulose, starch, plant gums, and xylans, respectively. The structures of these disaccharides have been established by the classical methylation method[7] and by degradation studies.[8]



In certain instances evidence in support of the structure of beta-linked disaccharides has been forthcoming from synthetic experiments. Thus, the structure of cellobiose,[9] 6-*O*-β-D-glucopyranosyluronic acid-D-galactose,[10] lactose,[11] sophorose,[12] and of gentiobiose,[13] among others, have been confirmed by synthesis.

This paper is concerned with the synthesis for the first time, as far as we are aware, of 4-*O*-β-D-xylopyranosyl-D-xylose (xylobiose) (IX), a disaccharide which may be obtained by acid[6] or enzymic[14,15] hydrolysis of polysaccharides of the xylan type. This synthesis was achieved by condensing benzyl 2,3-di-*O*-benzyl-D-xylopyranoside (V) with 2,3,4-tri-*O*-acetyl-α-D-xylosyl bromide (VI) in the presence of mercuric cyanide,[16,17] a reaction improved by adding the glycosyl halide at intervals of two hours.

The 2,3,4-tri-*O*-acetyl-α-D-xylosyl bromide (VI) required for the condensation was prepared in the usual way[18] whereas the benzyl 2,3-di-*O*-benzyl-D-xylopyranoside was obtained as follows: methyl α- and β-D-xylofuranoside[19] (I) was treated with trityl chloride in pyridine to give methyl 5-*O*-trityl-α- and -β-D-xyloside (II) which was converted into methyl 2,3-di-*O*-benzyl-5-*O*-trityl-α- and -β-D-xyloside (III). Simultaneous detritylation and hydrolysis of III yielded 2,3-di-*O*-benzyl-D-xylose (IV) which was transformed into the required benzyl 2,3-di-*O*-benzyl-D-xylopyranoside (V), the *beta*-form of which crystallized.

Following the condensation of V and VI, the disaccharide derivative, benzyl 4-*O*-(2,3,4-tri-*O*-acetyl-D-xylosyl)-2,3-di-*O*-benzyl-D-xyloside (VII) and unchanged benzyl 2,3-di-*O*-benzyl-D-xyloside (V) were separated from 2,3,4-tri-*O*-acetyl-D-xylosyl bromide (VI) by saponification, and extraction of VII and V from aqueous solution with chloroform. Hydrogenation[20] of the disaccharide derivative, benzyl 4-*O*-(β-D-xylopyranosyl)-2,3-di-*O*-benzyl-D-xyloside (VIII) afforded 4-*O*-β-D-xylopyranosyl-D-xylose (IX). The specific rotation $[\alpha]^{23}$ −15° of the product so formed differed from that of xylobiose due probably to the presence of some α-1→4 linked xylobiose, and consequently

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the xylobiose failed to crystallize even when nucleated. After acetylation of the sirupy xylobiose, however, the crystalline 4-*O*-β-D-xylopyranosyl-D-xylose hexaacetate[6] was readily isolated. This proved to be identical with a specimen prepared[21] from pure xylobiose isolated from corn hull hemicellulose. Deacetylation of the hexaacetate then yielded the required crystalline xylobiose (IX).

EXPERIMENTAL

All evaporations were carried out at 40–50° (bath temp.) under reduced pressure.

Methyl 5-O-trityl-α- and δ-β-D-xyloside. D-Xylose (10 g.) was refluxed with 0.012% methanolic hydrogen chloride (630 ml.) for 4 hr. after which the optical rotation had changed to +30.5°.[19] The solution was neutralized with silver carbonate (0.5 g.), filtered and evaporated to a sirup (10.8 g.). No attempt was made to separate the methyl furanoside from the pyranoside and the unchanged xylose. The sirupy product was dissolved in pyridine (85 ml.), trityl chloride (10 g.) was added, and the mixture heated for 1 hr. at 90–100°, ingress of water from the atmosphere being prevented by a calcium chloride drying tube. After standing overnight at room temperature, the reaction mixture was treated with water until a turbidity was produced and then poured into ice water (600 ml.). The sirupy precipitate consisting of methyl 5-*O*-trityl-α- and δ-β-D-xyloside did not crystallize. The aqueous suspension was extracted with chloroform (3 × 200 ml.) and the combined extracts were decolorized with charcoal (1 g.), dried (magnesium sulfate), and evaporated to a sirupy mixture of methyl 5-*O*-trityl-α- and δ-β-D-xyloside.

Methyl 5-O-trityl-2,3-di-O-acetyl-α-D-xyloside. In a separate experiment methyl α-D-xylofuranoside, m.p. 84°, was isolated[19] from the mixture of glycosides (1.15 g.) prepared as described above by separation on a cellulose column using butanone-water azeotrope as the irrigating solvent.[19,22]

A solution of the methyl α-D-xylofuranoside (0.440 g.) in dry pyridine (15 ml.) was treated with trityl chloride (0.74 g.) for 18 hr. at room temperature. The reaction mixture was heated for 1 hr. at 90–100° and then cooled to room temperature. The reaction mixture was treated with water until it became turbid and then poured with stirring into ice water (300 ml.). After standing for 1 hr. the sirupy precipitate was extracted from the aqueous solution with three 100-ml. portions of chloroform and the combined chloroform extracts were dried (potassium carbonate). Evaporation of the solution provided methyl 5-*O*-trityl-α-D-xyloside as a sirup (1.063 g.) which had $[\alpha]_D^{22}$ +71° (*c*, 5 in chloroform).

A portion of the methyl 5-*O*-trityl-α-D-xyloside (0.543 g.) was allowed to stand at room temperature for 24 hr. with acetic anhydride (4 ml.) and pyridine (10 ml.). The acetylation mixture was poured with stirring into ice water (200 ml.) and allowed to stand for about 6 hr. at 0° until all the acetic anhydride had decomposed. The product was extracted with chlofororm (3 × 75 ml.), and the combined chloroform extracts were dried (potassium carbonate). Evaporation of the chloroform solution gave a sirup which crystallized spontaneously upon the addition of a few drops of ethanol. After three recrystallizations from ethanol the methyl 2,3-di-*O*-acetyl-5-*O*-trityl-α-D-xyloside had a m.p. of 131° and $[\alpha]_D^{23}$ +81° (*c*, 1.2 in chloroform).

Anal. Calcd. for $C_{29}H_{30}O_7$: C, 71.02; H, 6.12; OCH_3, 6.3; $COCH_3$, 17.55; $(C_6H_5)_3C$, 49.6. Found: C, 71.23; H, 6.21; OCH_3, 7.1; $COCH_3$, 18.0; $(C_6H_5)_3C$, 50.9.

The method employed for the determination of the triphenyl methyl content corresponded to that of Helferich and Becker[23] with the exception that the trityl alcohol was isolated by extraction with chloroform rather than by filtration.

Methyl 5-O-trityl-2,3-di-O-benzyl-α- and δ-β-D-xyloside. Benzyl chloride (125 ml.) and powdered potassium hydroxide (20 g.) were added to the sirupy material consisting of methyl 5-*O*-trityl-α- and δ-β-D-xyloside and the mixture was stirred at 90–100° for 6 hr. The reaction mixture was cooled, water (100 ml.) was added and the two layers were separated. Chloroform (100 ml.) was added to the upper organic layer and the mixture was washed with water (3 × 100 ml.). The chloroform and excess benzyl chloride were removed by distillation *in vacuo* and the residue was retreated with benzyl chloride and potassium hydroxide as described above to give methyl 2,3-di-*O*-benzyl-5-*O*-trityl-α- and δ-β-D-xyloside (27.4 g.).

2,3-Di-O-benzyl-D-xylopyranose. The methyl 2,3-di-*O*-benzyl-5-*O*-trityl-α- and δ-β-D-xyloside was dissolved in acetic acid (60 ml.) in the cold and 27% hydrobromic acid in acetic acid (15 ml.) was added. A precipitate of trityl bromide formed after a few seconds, and after 1 min. the solution was filtered into ice water (250 ml.) which was contained in the filter flask. The precipitate so formed was washed with cold glacial acetic acid (20 ml.). Chloroform (200 ml.) was added to the combined filtrate and washings and the chloroform solution was washed several times with a saturated aqueous solution of sodium bicarbonate until it was free of acid and twice with water. The chloroform solution was dried (magnesium sulfate) and evaporated to give 2,3-di-*O*-benzyl-D-xylopyranose which contained a small amount of trityl alcohol as an impurity. (Found: OCH_3, none).

Benzyl 2,3-di-O-benzyl-D-xylopyranoside. 2,3-Di-O-benzyl-D-xylopyranose (2.3 g.) was heated for 4 hr. at 95–100° with benzyl alcohol (15 ml.) and *p*-toluenesulfonic acid (0.5 g.) under reduced pressure (water aspirator). After cooling the reaction mixture to room temperature, chloroform (70 ml.) was added and the mixture was washed with dilute ammonium hydroxide (40 ml.) and with water until neutral. The organic layer was dried (sodium carbonate), evaporated and the excess benzyl alcohol and a small amount of trityl alcohol were removed by distillation at 150–170° (bath temp.) and about 0.005 mm. The benzyl 2,3-di-*O*-benzyl-α- and δ-β-D-xylopyranoside was distilled (2.1 g.) b.p. 225–235° (bath temp.) at 0.001 mm., $[\alpha]_D^{23}$ +15° (*c*, 2 in chloroform). Part of the distillate crystallized spontaneously and after recrystallization from methanol, benzyl 2,3-di-*O*-benzyl-β-D-xylopyranoside was obtained, m.p. 122° and $[\alpha]_D^{22}$ −71° (*c*, 0.2 in chloroform).

Anal. Calcd. for $C_{26}H_{28}O_5$: C, 74.29; H, 6.66. Found: C, 74.08; H, 6.81.

Reaction of benzyl 2,3-di-O-benzyl-D-xylopyranoside with 2,3,4-tri-O-acetyl-α-D-xylosyl bromide. A mixture of benzyl 2,3-di-*O*-benzyl-D-xylopyranoside (0.50 g.), 2,3,4-tri-*O*-acetyl-α-D-xylosyl bromide (0.2 g.),[18] mercuric cyanide (1.8 g.),[16,17] calcium sulfate (1 g.), and benzene (15 ml.) was shaken at room temperature for 2 hr. At this time and at subsequent 2-hr. intervals freshly prepared 2,3,4-tri-*O*-acetyl-α-D-xylosyl bromide (0.2-g. portions) in benzene (10 ml.) was added to the reaction mixture until a total of 1.6 g. of the bromo derivative had been added. The shaking was continued for a further 24 hr. after which time the inorganic salts were removed by filtration and washed with benzene. The combined benzene filtrate and washings were washed successively with water, 2*N* sodium hydroxide (4 × 50 ml.) and with water (50-ml. portions) until the washings were neutral. The benzene layer was separated, dried (potassium carbonate), filtered and evaporated to a

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thick sirup (1.13 g.) which was dissolved in ethanol (50 ml.) and 2*N* aqueous sodium hydroxide (20 ml.) was added. The solution was warmed to 50–60° for 1 hr., evaporated to 25 ml., diluted with water (100 ml.), and chloroform (100 ml.) was added. The chloroform layer was separated and washed with water until neutral, dried (potassium carbonate) and evaporated to give benzyl 4-*O*-(β-D-xylopyranosyl)-2,3-di-*O*-benzyl-D-xyloside as a sirup (0.44 g.).

Hydrogenation of benzyl 4-O-(β-D-xylopyranosyl)-2,3-di-O-benzyl-D-xyloside. The aforementioned sirup (0.44 g.) was dissolved in ethanol (50 ml.), and palladium-charcoal catalyst (1.4 g.) was added. The catalyst was prepared by dissolving palladium chloride (0.3 g.) in 2 *N* hydrochloric acid to which acid-washed charcoal (1.5 g.) was added and the mixture was shaken with hydrogen at atmospheric pressure until the supernatant solution was colorless (about 2 hr.). The palladium-charcoal catalyst was filtered, washed with water until the washings were free of chloride ion, then with ethanol (500 ml.), and the catalyst was used immediately. The hydrogenation apparatus and reaction flask were flushed with hydrogen and the reaction mixture was shaken for 24 hr. after which time no more hydrogen was taken up. The charcoal catalyst was removed by filtration, washed with aqueous methanol, and the combined filtrates were evaporated to a sirup (0.22 g.). Chromatographic analysis with 1-butanol-ethanol-water (4:1:5) and *p*-anisidine hydrochloride spray reagent indicated three components, xylose, xylobiose and an unknown component which had an R_F value between the other two compounds. (This unknown compound was probably a 1:1′-linked xylose disaccharide.)

Isolation of 4-O-β-D-xylopyranosyl-β-D-xylose (xylobiose). The mixture of three components described above was applied to three pieces of Whatman No. 3 MM filter paper (8 × 22 in.) and the paper was irrigated with 1-butanol-ethanol-water (4:1:5) for 3 days. Elution of the appropriate section of the paper with aqueous methanol and evaporation of the eluant provided xylobiose (67 mg.) which had $[\alpha]_D^{23}$ −15° (*c* 2.2 in water) and migrated as a single spot on a paper chromatogram and on electrophoresis with borate buffer. However, even after nucleating this material with an authentic sample it did not crystallize. Since the optical rotation {$[\alpha]_D^{23}$ −15° (*c*, 2.2 in water)} was more positive than the literature value {$[\alpha]_D$ −25.5° (equil. value)} it appeared that some of the α 1→4 linked disaccharide was present.

The xylobiose obtained above was heated at 95–100° for 2 hr. with acetic anhydride (5 ml.), sodium acetate (0.15 g.) and acetic acid (1 ml.) and evaporated to dryness under reduced pressure. Water (25 ml.) and chloroform (25 ml.) were added to the residue and after separation of the layers the aqueous layer was washed with chloroform (3 × 25 ml.). The combined chloroform extracts were dried (potassium carbonate) and evaporated to give 120 mg. of a sirup which crystallized when nucleated with an authentic sample of xylobiose hexaacetate, m.p. and mixed m.p. 155–156°, $[\alpha]_D^{22}$ −76° (*c*, 1 in chloroform) after recrystallization from ethanol.

Anal. Calcd. for $C_{22}H_{30}O_{11}$: C, 49.44; H, 5.62; Found: C, 49.57; H, 5.69.

A solution of xylobiose hexaacetate (41 mg.) in methanol (10 ml.) was treated with metallic sodium (3 mg.). After keeping overnight the solution was evaporated to dryness and the residue recrystallized from methanol. The 4-*O*-β-D-xylopyranosyl-β-D-xylose (xylobiose) thus obtained had a m.p. and mixed m.p. of 184°, $[\alpha]_D^{23}$ −23° (equil. value, *c*, 0.5 in water); lit.[6,21] m.p. 185–186°, $[\alpha]_D^{25}$ −32° to −25.5°.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF UTAH]

Synthesis of Quaternary Ammonium Salts by Displacement of Benzenesulfonate Esters with Trimethylamine

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Quaternary salts have been prepared directly by the reaction of trimethylamine with 1,6-di-*O*-benzenesulfonyl-D-mannitol, 1,6-di-*O*-benzenesulfonyl-3,4-*O*-isopropylidene-D-mannitol, 1,6-di-*O*-benzenesulfonyl-2,5-anhydro-D-glucitol, and pentaerythritol tetrabenzenesulfonate.

The syntheses of certain bis- and other quaternary ammonium salts were undertaken as a result of our interest in compounds with ganglionic blocking activity. Bisquaternary salts have been prepared by reaction of ditosylates with secondary amines followed by reaction with methyl iodide.[2] Diepoxides were converted into bistertiary amines by reaction with secondary amines.[3] Quaternization was effected with methyl iodide or dimethyl sulfate. In the work described herein, the direct formation of quaternary salts was realized by the nucleophilic displacement of benzenesulfonate esters with trimethylamine.

Quaternary salts of pyridine have been obtained by refluxing sulfonic acid esters of primary alcohols with anhydrous pyridine. 2,3-*O*-Isopropylidene-1-*O*-tosyl-D,L-glyceritol,[4] 2,3:4,5-di-*O*-isopropyli-

(1) The portion of this paper by Donald L. Schmidt constitutes a part of a dissertation to be presented to the faculty of the University of Utah in candidacy for the degree of Doctor of Philosophy.

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