g. Crystallization from methanol–chloroform gave the analytical sample of 4-azido-4-deoxy-D-xylose (**12**), mp 110–114°, $[\alpha]^{21}D$ +81° (*c* 1, water).

Anal. Calcd for $C_5H_9N_3O_4$: C, 34.3; H, 5.18; N, 24.0. Found: C, 34.1; H, 5.30; N, 23.8.

4-Acetamido-1,2,3,5-tetra-*O*-acetyl-4-deoxy-D-xylofuranose (14).—To a cold (0°) mixture of 254 ml of glacial acetic acid, 254 ml of acetic anhydride, and 15.1 ml of concentrated sulfuric acid was added 4.9 g (23.7 mmoles) of methyl 4-acetamido-4-deoxy-α-D-xylopyranoside (**9**) with stirring. The reaction was stored at *ca.* 0° for 47 hr, then 59 g of anhydrous sodium acetate was added, and the mixture was evaporated to dryness *in vacuo*. The residue was partitioned between water and ether. The ether layer was washed with water, saturated aqueous sodium bicarbonate, and, finally, water, and then it was dried and evaporated to dryness *in vacuo* to give 5.85 g (69%) of product (**14**) as a syrup, λ_{max}^{film} 5.70 (OAc), 5.95 μ (NAc). There was no evidence for NH absorption at 3.0 μ or amide II absorption at 6.5 μ. The nmr spectrum was compatible with the furanose structure (**14**) and showed H-1 absorption occurring as a singlet (τ 3.62) and a doublet (τ 3.42, J = 5 cps) to suggest approximately equal amounts of α and β anomers.

Anal. Calcd for $C_{15}H_{21}NO_9$: C, 50.1; H, 5.89; N, 3.90. Found: C, 50.4; H, 6.15; N, 3.75.

The original aqueous extract from the ether–water partition was further extracted with chloroform. The chloroform layer was washed and dried in same fashion as was the previously described ether layer, then was evaporated to dryness to yield 1.88 g of a syrup. Thin layer chromatography using ethyl acetate as the developing solvent showed that in addition to the furanose (**14**) there was also another slower moving component. The infrared spectrum showed the presence of NH absorption at 2.9 μ and amide II absorption at 6.5 μ in addition to the expected carbonyl bands, thus indicating the presence of small amounts of the pyranose (**16**). An additional 1.4 g (16%) of pure furanose was obtained by partition of this fraction between benzene and water. The pure furanose component was obtained from the benzene fraction.

9-(4-Acetamido-4-deoxy-β-D-xylofuranosyl)adenine (17).—To a mixture of 5.13 g (14.3 mmoles) of 4-acetamido-1,2,3,5-tetra-*O*-acetyl-4-deoxy-D-ribofuranose and 13.2 g (18 mmoles) of chloromercuri-6-benzamido purine (64% on Celite) on 540 ml of 1,2-dichloroethane was added 2.3 ml (19.5 mmoles) of titanium tetrachloride. The reaction was refluxed with stirring for 24 hr, then was cooled to room temperature and stirred for 4 hr with 12 ml of saturated aqueous sodium bicarbonate. The mixture was filtered and the precipitate was washed with chloroform. The organic layer was separated and washed with 10 ml of 30% aqueous potassium iodide, then with two 10-ml portions of water. The solution was dried, then evaporated to dryness to give 5.7 g (73%) of crude blocked nucleoside.

A solution of the crude blocked nucleoside in 133 ml of methanol was treated with 13.3 ml of 1 *N* methanolic sodium methoxide at room temperature for 15 hr, then was neutralized to pH 7 with IRC 50 (H) and evaporated to dryness *in vacuo*. The residue was partitioned between chloroform and water; then the aqueous phase was evaporated to dryness to give 2.48 g of crude nucleoside (**17**). Crude **17** was dissolved in the minimum amount of water and applied to a column of 150 g of Dowex 1 (OH).[15] Elution of the column began with 500 ml of pure water, then proceeded through 100 ml of methanol–water (3:7), 300 ml of methanol–water (1:1), 900 ml of methanol–water (7:3), and finally 500 ml of pure methanol. Two ultraviolet absorbing peaks were eluted using methanol-water (7:3). The main fraction weighed 0.98 g and was crystallized from methanol–chloroform to give 0.97 g (22%) of crystalline **17**, mp 227–230°, which was homogeneous on thin layer chromatography using 1-propanol–ethyl acetate–water (3:2:1) as the developing agent.

Recrystallization from methanol gave the analytical sample: mp 228–230° dec; $[\alpha]^{21}D$ −101° (*c* 0.55, water); $\lambda_{max}^{pH\ 1}$ 258 mμ (ε 14,520); $\lambda_{max}^{pH\ 7}$ 259 mμ (ε 14,590); $\lambda_{max}^{pH\ 13}$ 260 mμ (ε 14,640); λ_{max}^{Nujol} 2.90, 3.04, 3.22 (OH and NH), 6.00, 6.16, 6.24 μ (aromatic). There was no amide II absorption at 6.5 μ.

Anal. Calcd for $C_{12}H_{16}N_6O_4$: C, 46.8; H, 5.23; N, 27.3. Found: C, 46.7; H, 5.30; N, 27.1.

9-(4-Acetamido-2,3,5-tri-*O*-acetyl-4-deoxy-β-D-xylofuranosyl)-adenine (19).—To a cold (0°) mixture of 0.5 g (14.4 mmoles) of 9-(4-acetamido-4-deoxy-β-D-xylofuranosyl)adenine (**17**) in 35 ml of dry pyridine was added 1.4 ml of acetic anhydride with stirring. The reaction was stirred at 0° for 1 hr, then stored at *ca.* 0° for 44 hr and decomposed by the addition of 10 ml of methanol, with stirring and cooling. The reaction was evaporated to dryness *in vacuo* and the residue was partitioned between 30 ml each of chloroform and water. The water layer was extracted with two additional 10-ml portions of chloroform. The organic extracts were combined and washed with 10 ml of water, dried, and evaporated to dryness *in vacuo* to give 0.87 g of syrup. Treatment of this syrup with ether caused the product to solidify. Precipitation from benzene with petroleum ether gave 0.52 g (83%) of **19**: mp 101–110°; $[\alpha]^{22}D$ −66° (*c* 1, chloroform).

Anal. Calcd for $C_{18}H_{22}N_6O_7$: C, 49.8; H, 5.11; N, 19.4. Found: C, 49.9; H, 5.08; N, 18.9.

Registry No.—**2**, 13143-91-4; **3**, 13143-92-5; **4**, 13143-93-6; **5**, 13143-94-7; **6**, 13143-95-8; **7**, 13143-96-9; **8**, 13143-97-0; **9**, 13143-98-1; **10**, 13143-99-2; **11**, 13131-52-7; **12**, 13144-00-8; **14**, 13144-01-9; **17**, 13144-02-0; **19**, 13144-03-1.

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Silica Gel Catalyzed Detritylation of Some Carbohydrate Derivatives[1]

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Methyl 2,3,4-tri-*O*-acetyl-α-D-glucopyranoside (I) and 1,2,3,4-tetra-*O*-acetyl-β-D-glucopyranose (II) were prepared in 81 and 87% yields, respectively, from methyl 2,3,4-tri-*O*-acetyl-6-*O*-trityl-α-D-glucopyranoside (III) and 1,2,3,4-tetra-*O*-acetyl-6-*O*-trityl-β-D-glucopyranose (IV). A column of silica gel was used as the acidic detritylation catalyst and it also served as an adsorbent for the chromatographic separation of the reaction products.

In 1924, Helferich and Becker[3] prepared the first trityl[4] ether of a carbohydrate. Since then, the trityl ether has been extensively used in carbohydrate chemistry as a protecting group for primary hydroxyl groups.[5] The ethers are base stable and acid labile. A number of procedures have been developed for cleaving trityl ethers and regenerating the hydroxyl groups, but each has its limitations. For example, catalytic hydrogenolysis proceeds with difficulty in the presence of sulfur-containing compounds[6] and is

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(2) This is a laboratory of the Northern Utilization Research and Development Division, Agricultural Research Service, U. S. Department of Agriculture.

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(4) This is an abbreviation for the triphenylmethyl group.

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capricious.[7] Acid-catalyzed detritylations are often accompanied by acyl migration (HCl,[8] HBr in acetic acid,[9] and acetic acid[10]) and yields are low. Compound I was previously prepared in only 46% yield from compound III and hydrogen bromide in acetic acid[11] and compound II in only 55% yield from compound IV and hydrogen bromide in acetic acid.[12]

Even though silica gel is an acidic adsorbent, it has often been used successfully for the chromatographic purification of trityl ethers.[13] In 1962, Buchanan and Schwarz[14] stated that it was necessary to pretreat with ammonium hydroxide the silica gel used for the chromatographic purification of trityl ethers. In 1965, Buchanan and Fletcher[10a] reported the simultaneous silica gel catalyzed detritylation and epoxide ring opening of methyl 4-*O*-acetyl-2,3-anhydro-6-*O*-trityl-α-D-guloside (V) to give methyl 4-*O*-acetyl-α-D-galactopyranoside. However, when V was treated with 80% acetic acid, methyl 6-*O*-acetyl-α-D-galactopyranoside was isolated. The two silica gel catalyzed detritylations recorded here were not accompanied by acyl migration. Apparently silica gel does not catalyze the migration of the acetyl group on the C-4 hydroxyl to the C-6 hydroxyl on pyranose rings having the *gluco* or *galacto* configuration. This condition is not true in the glycerol series. Borgstrom[15] noted that acyl migration occurred during the chromatographic purification of 2-*O*-acyl glycerides on silica gel.

For the preparative detritylation of compounds III and IV on silica gel columns, the optimum conditions were sought. The compounds to be detritylated were dissolved in a small amount of dry benzene and the solution was poured onto a dry silica gel column. The column was completely developed with an additional amount of dry benzene and then left at room temperature for 16 hr. During column development, a considerable amount of heat was generated and the upper three-fourths of the column turned a brilliant yellow. Heat evolution occurred with each one of the activated silica gel samples. The yellow color occurred only with silica gel samples having detritylation activity. At constant column loading, the intensity of color and the fraction of the column colored were a crude measure of adsorbent activity. As activity of the silica gel increased, color intensity increased and the area of the column colored decreased; *i.e.*, the amount of silica gel necessary to detritylate the sample completely was reduced. Apparently the yellow color is caused by the trityl cation[16] formed by ionization of the ether and retained on the column. Elution with 5% ethyl acetate in chloroform or 5% ethyl acetate in benzene decomposed the trityl cation and removed the resultant triphenylcarbinol. The detritylated sugar was then eluted with ethyl acetate and recrystallized from an appropriate solvent.

Initially it was thought that the amount of residual acid in the silica gel determined the extent of cleavage of the trityl ethers. The pH of a 10% aqueous suspension of silica gel was used as a measure of the residual acid. Four kinds of silica gel[17] containing different quantities of residual acid were selected to evaluate trityl ether cleavage. The pH of their 10% suspensions ranged from 3.75 to 7.20 (Table I). The adsorbent activity of silica gel as measured by Brockmann dyes is a function of the amount of water added to the silica gel (Table II).[18] The relationship between detritylation activity and adsorption activity, as measured by Brockmann dyes, was evaluated with Davison Grade 12 silica gel. The percentage detritylation at constant column loading was used to measure detritylation activity of the silica gels (Table II). Activities of various silica gels in cleaving trityl ethers were determined by measuring the percentage detritylation at constant loading (0.66 g of isopropyl trityl ether/100 g of silica gel). The results are summarized in Table I. Davison Grade 12 and Whatman SG 31 were active catalysts. Mallinckrodt silicic acid, which contained an appreciable amount of residual acid, had negligible activity. Merck silica gel H, which was slightly basic, had moderate activity. Therefore, it appears that the detritylation activity of these silica gels is not directly related to the quantity of residual acid they contain.

TABLE I

DETRITYLATION ACTIVITY AND pH OF SOME SILICA GELS[a]

Silica gel	pH	Detritylation, %
Merck silica gel H[b]	7.20	59
Whatman SG 31	5.75	100
Mallinckrodt silicic acid	4.70	2
Davison Grade 12	3.75	100

[a] Activity grade I. See ref 18. [b] See ref 17.

TABLE II

RELATIONSHIP BETWEEN ADSORPTION ACTIVITY AND DETRITYLATION ACTIVITY

Activity grade	Water added, %	Detritylation, %
I	0	100
II	5	100
III	15	100
IV	25	68
V	38	2

Experimental Section

All melting points were taken in Kimax capillary tubes on a Mel-Temp apparatus, Laboratory Devices, Cambridge, Mass., and are uncorrected. The silica gels used were silica gel Grade 12, mesh size 28–200, Grace Davison Chemical, Baltimore, Md.; Whatman silica gel SG 31, mesh size 80% 100–200, Scien-

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(17) The mention of firm names or trade products does not imply that they are endorsed or recommended by the U. S. Department of Agriculture over other firms or similar products not mentioned.

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tifica, Clifton, N. J.; silica gel H for thin layer, E. Merck (Brinkmann Instruments, Westbury, N. Y.); silicic acid, 100 mesh, Mallinckrodt Chemical Works, St. Louis, Mo. Thin layer chromatography (tlc) was carried out on silica gel G (Merck). The plates were prepared with a Desaga applicator set at 0.25 mm. Before the plates were used, they were heated in an oven at 110° for 1 hr. The plates were developed with an ethyl acetate–hexane mixture (1:3) and visualized by spraying with 5% sulfuric acid in ethanol and then charring on a hot plate set at 200°. Spots containing the trityl group were a brilliant yellow. The benzene used to dissolve the trityl ethers was dried over "dri-Na"[19] for at least 24 hr before use. Isopropyl trityl ether was used in the investigation of the parameters affecting detritylation.

Methyl 2,3,4-Tri-*O*-acetyl-α-D-glucopyranoside (I).—To a 2.2 cm × 46 cm column prepared from 100 g of Davison Grade 12 silica gel, activity grade I, was added a solution composed of 1.000 g of methyl 2,3,4-tri-*O*-acetyl-6-*O*-trityl-α-D-glucopyranoside[3] in 8 ml of benzene. The column was developed with an additional 170 ml of benzene. After 16 hr at room temperature, the column was eluted with 600 ml of 10% ethyl acetate in benzene. Analysis of eluate by tlc showed triphenylcarbinol and a trace of starting material. The column was then eluted with 600 ml of 25% methanol in ethyl acetate. The solvent was removed on a rotary evaporator and dried in a vacuum desiccator. The residue (553 mg, 98%) was dissolved in a small amount of ether and hexane was added until the solution became cloudy. The solution was cooled overnight in a refrigerator. The long needlelike crystals were filtered and dried to yield 457 mg (81%): mp 109–110°, $[\alpha]^{26}D$ +148 ($CHCl_3$); lit.[11] mp 111°, $[\alpha]^{20.5}D$ +148.8° ($CHCl_3$).

1,2,3,4-Tetra-*O*-acetyl-β-D-glucose (II).—The procedure followed is essentially the same as described above except for the following. Triphenylcarbinol was eluted from the column with 500 ml of 5% ethyl acetate in chloroform; the product was eluted with 500 ml of ethyl acetate and recrystallized by dissolving in a small amount of chloroform and adding ether until the solution was cloudy. The product weighed 515 mg (87%): mp 125–127°, $[\alpha]^{26}D$ +12° ($CHCl_3$); lit.[12] mp 128–129°, $[\alpha]^{20}D$ +12.1° ($CHCl_3$).

Detritylation Activity of Different Silica Gels.—Each sample of silica gel was heated at 300° for 3 hr and then placed in a desiccator to cool. A dry column (2.2 cm o.d.) containing 38 g of silica gel was prepared. A benzene solution (5 ml) containing 250 mg of isopropyl trityl ether was added to the column. It was completely developed with benzene and kept at room temperature for 1 hr. Benzene eluted any remaining starting material and ethyl acetate eluted the triphenylcarbinol. The solvents were evaporated by blowing air over the tared collection beakers. After the residues were dried in a vacuum desiccator, they were weighed and their yields calculated. Melting points and thin layer chromatograms were used for identification and to determine purity (Table I).

Detritylation as Related to Adsorbent Activity.—Davison Grade 12 silica gel was used to evaluate the effect of added water on detritylation activity. Samples having activities II–V were prepared by the addition of water to silica gel activity grade I.[18] A 2.2-cm-o.d. column containing a 100-g sample of silica gel was prepared for each activity grade. A 500-mg sample of isopropyl trityl ether was dissolved in 5 ml of benzene and added to each of the dry columns. The column was completely developed with benzene and then kept at room temperature for 1 hr. Any starting material that remained was eluted with 100 ml of benzene and the product, triphenylcarbinol, was eluted with ethyl acetate (200 ml). The benzene eluate from activity grade IV contained both materials. They were easily separated by triturating the residue with a little cold hexane and then filtering. Triphenylcarbinol is quite insoluble in hexane. The solvents were removed by blowing air over the collection beakers. The residues were then dried in a vacuum desiccator, weighed, and identified by melting point and tlc (Table II).

Registry No.—I, 7432-72-6; II, 13100-46-4.

(19) A granular sodium–lead alloy purchased from J. T. Baker Chemical Co., Phillipsburg, N. J.

Displacement and Elimination Reactions of 5α,6α-Epoxy-3β-cholestanyl *p*-Toluenesulfonate in Dimethylformamide

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Products of the solvolysis of 5α,6α-epoxy-3β-cholestanyl *p*-toluenesulfonate in dimethylformamide containing lithium carbonate and/or lithium chloride have been isolated and characterized. These products appear to be formed by successive displacement and elimination reactions. Convenient preparations of 2,4,6-cholestatriene and 5α,6α-epoxy-3α-cholestanyl formate are described, as well as an example of displacement with over-all retention brought about by successive displacements of chloride.

In the course of our studies on direct displacement and solvolysis reactions of 2,4-cholestadienes substituted at the 6α and 6β positions with appropriate leaving groups, we developed a synthetic route to 6β-(2,6-dichlorobenzoyloxy)-2,4-cholestadiene.[2] The key intermediate in this series of reactions was 5α,6α-epoxy-2-cholestene (**5**), which we prepared by a six-step synthesis from cholesterol (**1a**). In view of the success of Bowers and co-workers[3] in preparing other steroidal 5α,6α-epoxy-2-enes from the corresponding 3β-*p*-toluenesulfonates in refluxing dimethylacetamide containing lithium carbonate, we set out to investigate a similar route to 5α,6α-epoxy-2-cholestene. The reaction proved to be more complex than we had anticipated; therefore we have investigated it in some detail.

Results and Discussion.

The 5α,6α-epoxy-3β-cholestanyl *p*-toluenesulfonate (**2b**) which was required for our study had been reported by Bourdon and Ranisteano.[4] These workers prepared it by the perbenzoic acid epoxidation of cholesteryl *p*-toluenesulfonate (**1b**). We have repeated their preparation, modified in that *m*-chloroperbenzoic acid was substituted for perbenzoic acid (route A), and we have also employed the alternate route, tosylation of cholesterol α-epoxide (**2a**) (route B). In our hands, route A appears to be preferable in that the product is more readily purified, as discussed below. When the material prepared by route A

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