colored intermediates react slowly at 25° to give a mixture of 20 or more products.

Experimental Section[7]

Synthesis of Thiolcarbonates.—S-Phenyl O-isopropyl thiocarbonate was prepared by stirring a mixture of 32 g (0.27 mol) of O-phenylthiocarbonyl chloride (K and K Laboratories), 30 g of potassium carbonate, and 210 g of 2-propanol overnight at 25° and for 5 hr at 85°. Gas evolution was noted at 85°. Filtration and fractionation through a spinning-band column gave 9 g (17%) of product: bp 77–80° (0.3 mm); nmr δ 7.44 (m, 5), 5.11 (septet, 1), 1.28 (d, 6).

Anal. Calcd for $C_{10}H_{12}O_2S$: C, 60.94; H, 6.54; S, 16.26. Found: C, 61.00; H, 6.23; S, 16.06.

The other thiolcarbonates were prepared by treating tetrahydrofuran solutions of phenyl or hexyl mercaptans first with an equimolar amount of butyllithium in hexane and then with chloromethyl, chloroethyl, or chlorophenyl carbonates. Data are in Table IV.

TABLE IV
THIOLCARBONATES

RSCOOR′	Yield, %	Bp (mm) or mp, °C	Lit. bp (mm) or mp, °C
$C_6H_5SCOOCH_3$[a] (1)	69	88–89.5 (2.4)	
$H_{13}C_6SCOOCH_3$[b]	67	70–71 (2.0)	
$C_6H_5SCOOC_2H_5$	80	69.5–70 (0.3)	130 (16)[c]
$C_6H_5SCOOC_6H_5$	47	50–60	56[c]

[a] *Anal.* Calcd for $C_8H_8O_2S$: C, 57.13; H, 4.79. Found: C, 57.63; H, 4.96. [b] *Anal.* Calcd for $C_8H_{16}O_2S$: C, 54.51; H, 9.15. Found: C, 54.70; H, 9.25. [c] H. Rivier, *Bull. Soc. Chim. Fr.*, (4) 1, 733 (1907).

Nmr Tube Experiments.—Mixtures of solvent, 1, and catalyst in the ratio 40:10:1 by weight (Table I) and 40:5:1 (solvent-effect experiments) were prepared. Samples were placed in nmr tubes and heated in an oil bath thermostatically controlled at 85 ± 1° for 1.0 hr. The compositions of the resulting mixtures were estimated from the integrals of the methyl peaks of 1 at δ 3.78 and 2 at δ 2.37. Other products were seldom detected, never in amounts exceeding 2%.

Similarly, a solution of 0.20 g of 1 and 0.02 g of tetraethylammonium fluoride in 0.78 g of acetonitrile-d_3 were heated at 35° for 64 hr; nmr analysis showed 97% conversion into 2. A solution of 0.20 g of 1 in 0.80 g of pyridine gave 72% conversion into 2 and 28% unreacted 1 under these conditions.

Thermal Stability of O-Methyl S-Phenyl Thiocarbonate (1).—An nmr tube containing 1 was heated in an oil bath at 154° for 4 hr. The nmr spectrum was unchanged. When a sample was heated for 3 days at 180°, nmr analysis showed 12% conversion into $C_6H_5SCH_3$, 88% unchanged starting material.

Methyl Phenyl Sulfide (2).—A mixture of 1.00 g of trioctylphosphine in 5.00 g (0.030 mol) of 1 was heated at 100 ± 1° for 19 hr in a Schlenck tube. Slow evolution of gas was noted. Flash distillation at 1 μ gave 3.72 g (100%) of colorless 2. Glpc at 125° on a 2-m column of 20% Triton X-305® on Gas Chrom R® showed 99.6% purity.

Hexyl Methyl Sulfide.—This reaction was run similarly using 8.82 g (0.05 mol) of S-hexyl O-methyl thiocarbonate. Flash distillation gave 6.50 g (98% of *n*-hexyl methyl sulfide, 97% pure by glpc on a 1-m column of 20% Triton X-305® on Gas Chrom R® with linear programming from 100 to 250°.

Ethyl Phenyl Sulfide.—A mixture of 11.1 g (0.061 mol) of O-ethyl S-phenyl thiocarbonate and 0.3 g of tetraethylammonium fluoride was heated and stirred at 70°. No gas evolved. Acetonitrile (11.6 g) was added to give a homogeneous solution. Heating at 70° was continued for 20 hr as gas slowly evolved. Glpc on a 0.6-m column of 10% Apiezon L® on Gas Chrom R® with linear programming from 100 to 250° showed 98% conversion into product and 2% conversion into an unidentified by-product. Distillation gave 7.48 g (89%) of ethyl phenyl sulfide, bp 81–83° (8.6 mm) [lit.[8] bp 86–87° (14 mm)].

(7) Melting and boiling points are uncorrected. Infrared spectra were determined using a Perkin-Elmer Model 21 spectrophotometer. Nmr spectra were produced on a Varian Model A-60 device using 49:1 $CDCl_3$–Me_4Si as solvent, except as noted.

(8) H. Brintzinger and M. Langheck, *Ber.*, **87**, 325 (1954).

Isopropyl Phenyl Sulfide.—A solution of 8.0 g of O-isopropyl S-phenyl thiocarbonate and 0.23 g of tetraethylammonium fluoride in 20 g of N,N-dimethylformamide was stirred at 130° for 16 hr. Little or no gas evolved. The solution was heated at reflux for 10 hr. Gas evolved slowly. The solution was poured into water. The oil was extracted with methylene chloride, dried, and concentrated. Analysis by glpc and nmr showed approximately 24% conversion into product (nmr δ 3.33) and 50% unchanged starting material.

S-Benzyl O-Methyl Xanthate (3).—To a solution of 43.4 g (0.33 mol) of sodium methyl xanthate in 300 ml of acetonitrile was slowly added 57.1 g (0.33 mol) of benzyl bromide at 10–20°. The solution was concentrated under high vacuum and filtered, always keeping the product at 25° or lower. The residue was 67 g (100%) of product, 99% pure by nmr [δ 7.29 (5), 4.35 (2), 4.12 (3)]. Distillation gave 28 g of 3, bp 107–109° (0.4 mm), containing several per cent isomer 4 and sulfide 5.

Rapid addition of benzyl bromide to an equimolar amount of sodium methyl xanthate in warm methanol gave a fast, exothermic reaction. A 42% yield of benzyl methyl sulfide, bp 72° (2.4 mm), was obtained by fractionation of the product.

Reactions of 3.—These reactions were performed in nmr tubes or the equivalent as described above. The methyl and methylene peaks of isomer 4 were at δ 2.36 and 4.35, respectively. The corresponding peaks of sulfide 5 were at δ 1.93 and 3.62.

O-Methyl S-(*p*-Nitrobenzyl) Xanthate.—A solution of 16.6 g (0.013 mol) of sodium methyl xanthate and 27.4 g (0.013 mol) of *p*-nitrobenzyl bromide in 300 ml of acetonitrile was kept at 25° for 3 hr. Solvent removal and recrystallized from toluene–methanol gave 21.7 g (70%) of product: mp 76.5–77.5°; nmr δ 7.88 (q, 4), 4.48 (2), 4.20 (3); ir no C=O peak.

Anal. Calcd for $C_9H_9NO_3S_2$: C, 44.43; H, 3.73; N, 5.76; S, 26.36. Found: C, 44.54; H, 3.90; N, 5.70; S, 26.38.

O-Ethyl S-(*p*-Nitrobenzyl) Xanthate.—This ester, mp 62–63° (lit.[9] mp 65–66°), was prepared as described above for the methyl ester in 83% yield. The product was recrystallized from toluene–pentane: nmr δ 7.84 (4), 4.65 (q, 2), 4.43 (2), 1.40 (t, 3); ir no C=O peak.

Anal. Calcd for $C_{10}H_{11}NO_3S_2$: C, 46.67; H, 4.27; N, 5.44; S, 24.92. Found: C, 46.85; H, 4.26; N, 5.44; S, 24.91.

Reactions of S-(*p*-Nitrobenzyl) Xanthates.—Treatment of these xanthates with soluble F^-, CN^-, or N_3^- salts gave intensely violet colors which slowly faded during several days. Acetonitrile solutions containing equimolar quantities of the O-methyl xanthate and Et_4NF had λ_{max} 520 mμ (ε 2500), 303 (11,000), 277 (12,800); aging caused these peaks to shift in wavelength and intensity. Nmr study of such solutions showed that mixtures were present at all times. Chromatography of a week-old solution gave more than 20 colored fractions.

Registry No.—1, 3186-52-5; 3, 17659-13-1; 5-phenyl O-isopropyl thiocarbonate, 17659-14-2; $H_{13}C_6SCOOCH_3$, 17659-15-3; O-methyl S-(*p*-nitrobenzyl) xanthate, 15183-56-9; O-ethyl S-(*p*-nitrobenzyl) xanthate, 17659-17-5.

Acknowledgment.—We are indebted to Mr. Jake Graff and Mr. Paul Sanders for technical assistance and to Dr. R. A. Clement for helpful discussions.

(9) A. L. Morrison and F. R. Atherton, British Patent 675,779 (1952).

The Specific Debenzylation of Alkylated Carbohydrates *via* Bromination–Hydrolysis

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We wish to report a new method for the debenzylation of carbohydrates. This method has been used successfully with hexopyranosides, an acyclic hexose,

oligosaccharides, and a polysaccharide. The method appears to be specific for debenzylation, *i.e.*, appended hydroxyl and methoxyl groups as well as heterooxygen bonds remain intact.

Recently, in this laboratory, tri-*O*-benzylamylose was prepared and subjected to methanolysis; the products were then methylated to give a homologous series of perbenzylated methyl terminal 4-*O*-methylmaltooligosaccharides.[1] Debenzylation of these oligosaccharides was unsuccessful when the usual procedures were followed.

Benzylation is frequently used to protect hydroxyl groups during carbohydrate reactions because the resulting benzyl ethers are stable to acids and bases, oxidizing agents, and reducing agents such as sodium borohydride and lithium aluminum hydride. For the most part, hydroxyl groups are subsequently easily regenerated, usually by catalytic hydrogenolysis.[2] Benzylated monosaccharides, for example, are easily debenzylated this way. On the other hand, only slight debenzylation of oligo-[3] and polysaccharides is effected when they are treated by the same methods because of their lower solubility and because they coat the catalyst, making it inaccessible to other molecules.[4]

We have now worked out an apparently general scheme whereby carbohydrate derivatives can be debenzylated rapidly, specifically, and with retention of configuration. The scheme consists of free-radical bromination in chloroform, carbon tetrachloride, benzene, or Sulfolane[5] at 0–25° followed by hydrolysis in saturated sodium carbonate or calcium hydroxide solutions. By this reaction sequence, carbohydrate derivatives can be debenzylated rapidly and with retention of configuration. The experimental procedure is illustrated by several examples in the Experimental Section. A critical discussion of the reaction mechanism is being prepared.

This method was also successfully applied to the debenzylation of perbenzylated methyl terminal 4-*O*-methylmaltooligosaccharides. Tlc analysis of the products revealed a homologous series of compounds identical with that obtained by hydrogenolysis using an excess of Raney nickel.[1] Acid-catalyzed hydrolysis of the products yielded only D-glucose and 4-*O*-methyl-D-glucose which were not present originally. There was no evidence of glycosidic bond cleavage; *i.e.*, there was no indication of the formation of D-glucose, 4-*O*-methyl-D-glucose, methyl D-glucopyranoside, or D-gluconic acid or its lactones during either the bromination or the work-up. Likewise, debenzylation of tri-*O*-benzylamylose was accomplished in one treatment (infrared analysis) with no breakdown of the polymer chain (chromatographic analysis).

(1) J. N. BeMiller and R. E. Wing, Abstracts, 153rd National Meeting of the American Chemical Society, Miami Beach, Fla., April 1967, No. C45; R. E. Wing, Ph.D. Dissertation, Southern Illinois University, 1967; J. N. BeMiller and R. E. Wing, *Carbohyd. Res.*, **6**, 197 (1968).

(2) Debenzylation methods have been reviewed by W. H. Hartung and R. Simonoff, *Org. Reactions* **7**, 263 (1953), and by G. M. McCloskey, *Advan. Carbohyd. Chem.*, **12**, 137 (1957).

(3) R. J. Rebhahn, Ph.D. dissertation, Rutgers—The State University, New Brunswick, N. J., 1966.

(4) Debenzylation of oligosaccharides has been accomplished with amounts of Raney nickel far in excess of what is normally considered to be catalytic.[1]

(5) A trademark of the Shell Chemical Co. for tetramethylene sulfone. Commercial samples normally contain up to 5% water and were used as received.

By using an incandescent lamp the reaction proceeds slowly enough that hydrogen bromide is released to the atmosphere before its concentration effects degradations. Flushing the beaker with dry air or nitrogen is often helpful. With compounds devoid of acid-labile groups, temperature, moisture, and hydrogen bromide concentration need to be less carefully controlled. For example, pure D-glucitol was obtained in very high yield when a solution of hexa-*O*-benzyl-D-glucitol in chloroform was treated with bromine, irradiated with an ultraviolet lamp, then shaken with lime water.

This new procedure should be useful in removing benzyl ether groups from molecules which contain groups that are reduced or cleaved by catalytic hydrogenation but cannot be used in the presence of triphenylmethyl ethers because of their facile cleavage by hydrogen bromide nor in the presence of benzylidene cyclic acetals. Both methyl 6-*O*-triphenylmethyl-α-D-glucopyranoside and methyl 4,6-*O*-benzylidene-α-D-glucopyranoside are converted into methyl α-D-glucopyranoside when allowed to react under the conditions described in the examples given.

Experimental Section

Procedure. A.—Methyl 2,3-di-*O*-benzyl-α-D-glucopyranoside was prepared according to the method of Bell and Lorber.[6] In an open beaker a solution of 0.500 g (1.34×10^{-3} mol) of this substance in 50 ml of Sulfolane was maintained at 20–25° by the use of an acetone–Dry Ice bath.[7] Bromine (0.14 ml, 2.70×10^{-3} mol; 1.0 mol per mole of benzyl ether group) was added all at once and the stirred reaction mixture was irradiated for 3 hr from above with a 60-W incandescent bulb. An additional 0.14 ml of bromine was added, and irradiation was continued for an additional 1.5 hr. The reaction mixture was then shaken with 100 ml of a saturated sodium carbonate solution for 15 min. Several extractions of this mixture with chloroform removed the Sulfolane. The remaining water layer was treated with a mixed anion–cation-exchange resin and evaporated to dryness to yield 0.253 g (97%). Tlc of this syrup revealed only one component which corresponded to methyl α-D-glucopyranoside. Crystallization of the syrup from absolute ethanol converted it into a white solid, mp 164–165°, which was identical with that of standard methyl α-D-glucopyranoside and of a mixture of the two.

B.—Methyl 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranoside was prepared by the method of Tate and Bishop.[8] This substance (1.659 g, 3.0×10^{-3} mol) was dissolved in 50 ml of Sulfolane maintained at 20–25° in an open beaker. Bromine (0.28 ml. 5.40×10^{-3} mol; 0.45 mol per mole of benzyl ether group) was added, and the mixture was irradiated directly with a 60-W incandescent bulb. After 1.5, 3.0, and 4.5 hr, respectively, additional 0.28-ml portions of bromine were added. After a total of 6 hr, the reaction was worked up as described above to yield 0.426 g (73%) of a syrup which by tlc was proved to be identical with an authentic sample of methyl α-D-glucopyranoside.

The above reactions were also effected in benzene, chloroform, or carbon tetrachloride in place of Sulfolane and sodium bicarbonate or calcium hydroxide in place of sodium carbonate. Similar yields of methyl α-D-glucopyranoside were obtained.

C.—Hexa-*O*-benzyl-D-glucitol (0.500 g, 6.92×10^{-3} mol; containing trace impurities of partially benzylated D-glucitol as shown by tlc), prepared by the procedure of Tate and Bishop,[8] was dissolved in 50 ml of chloroform. To the solution, maintained at room temperature in an open beaker, bromine (1.0 ml, 1.93×10^{-2} mol; 2.3 mol per mole of benzyl ether) was added, and the reaction mixture was irradiated for 80 min with a long-wavelength ultraviolet lamp. A precipitate formed during the reaction when chloroform was used as the solvent which has tentatively been identified as an α-bromo ether. (These results will

(6) D. Bell and J. Lorber, *J. Chem. Soc.*, 453 (1940).

(7) This bath was used to control the temperature so as not to expose the open beaker to extra water vapor.

(8) M. E. Tate and C. T. Bishop, *Can. J. Chem.*, **41**, 1801 (1963).

be reported in the critical discussion being prepared.) The reaction mixture was then stirred for 30 min with 100 ml of a saturated calcium hydroxide solution. The precipitate which had formed during the reaction disappeared during this treatment with base. Carbon dioxide was bubbled through the solution until it was neutral, and the calcium carbonate was removed by filtration. The layers were separated and evaporated under reduced pressure. Chromatographic examination of the chloroform layer revealed no carbohydrates. The water layer was stirred with a mixed ion-exchange resin and, after filtration and evaporation, a syrup was obtained [0.125 g (100%)]. Analysis of the syrup by tlc and glpc showed the product to be identical with an authentic sample of D-glucitol.

D.—Methyl terminal 4-*O*-methylmaltooligosaccharides have been prepared in this laboratory.[1] A homologous series (0.100 g) was dissolved in 50 ml of chloroform maintained at 0–10° in an open beaker. Bromine (0.28 ml, 5.40×10^{-3} mol) was added dropwise over a 15-min period, while the stirred mixture was irradiated with a 60-W incandescent bulb. After 1.5 and 3.0 hr, respectively, additional 0.28-ml portions of bromine were added. After a total of 6.0 hr, the reaction mixture, which contained a precipitate, was worked up as described for the D-glucitol reaction to yield 0.04 g. Tlc analysis of the resulting syrup showed the components to be identical with the products obtained when the same compounds were treated with excess Raney nickel.[1] The syrup was hydrolyzed with 30 ml of 2 *N* sulfuric acid for 36 hr. After neutralization (resin) and evaporation, the products were converted into their per(trimethylsilyl) derivatives and analyzed by glpc. Only D-glucose and 4-*O*-methyl-D-glucose were indicated to be present.

E.—Tri-*O*-benzylamylose has been prepared in this laboratory.[1] This substance (0.172 g) was dissolved in 50 ml of chloroform maintained at 0–10° in an open beaker. Bromine (0.2 ml, 3.86×10^{-3} mol) was added all at once, while the stirred reaction mixture was irradiated with a 60-W incandescent light. After 1.5 and 3.0 hr, respectively, additional 0.2-ml portions of bromine were added. After a total of 4.5 hr, the reaction mixture, which contained a precipitate, was worked up as described for the D-sorbitol reaction to yield 0.08 g. Tlc analysis of this product showed no degradation products (D-glucose, D-gluconic acid, or D-gluconolactone). Infrared analysis showed the absence of benzyl ether groups. The product gave a blue color on treatment with iodine solution, indicating that amylose (DP >20) was present.

Registry No.—Methyl 2,3-di-*O*-benzyl-α-D-glucopyranoside, 17791-36-5; methyl 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranoside, 17791-37-6; hexa-*O*-benzyl-D-glucitol, 17791-38-7.

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Steroid Tetrazoles[1]

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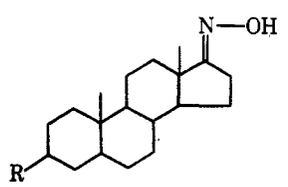
Tetrazoles are known to be formed when an excess of azide is used in the Schmidt reaction,[2,3] and by the reaction of oximes with sodium azide in the presence of sulfuric acid or chlorosulfonic acid.[3,4]

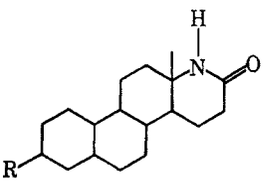
In this Note we wish to report the reaction of sodium azide with steroidal C-17 oximes, which proceeds with concomitant ring D rearrangement, to yield pentacyclic steroid tetrazoles.

Reaction of hydrazoic acid (generated by the action of sodium azide on chlorosulfonic acid) with 5α-androstan-17-one oxime (**1a**) afforded a mixture of lactam **2a** and tetrazole **3a**. The nuclear magnetic resonance (nmr) spectrum of this compound (**3a**), as well as that of the other tetrazoles described here, is characterized by the strong deshielding of the 18-methyl protons (1.36 ppm) by the tetrazole ring.

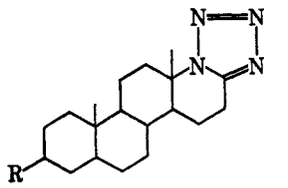
The same reaction with the 3β-acetoxy 17-oxime (**1b**)[5] provided a mixture containing 48% lactam **2b** and 9.5% the expected tetrazole (**3b**). Alkaline hydrolysis of the 3-acetoxyl group in **3b**, gave the corresponding alcohol (**3c**) which was oxidized with chromic acid in acetone[6] to the 3 ketone (**3d**). The latter was



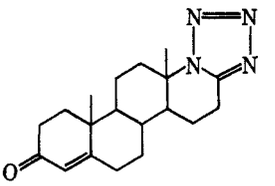
1a, R = H
b, R = AcO



2a, R = H
b, R = AcO



3a, R = H
b, R = AcO
c, R = OH
d, R = ketone
e, 2,4-dibromo; R = ketone



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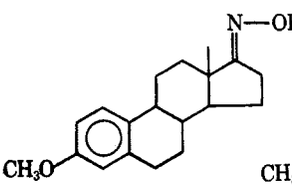

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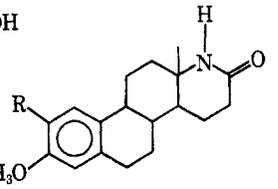
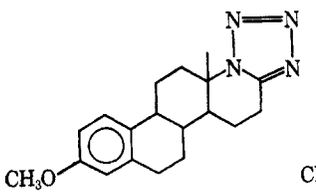


6a, R = H
b, R = SO_2Cl



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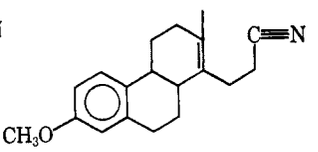

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(1) Publication no. 332 from the Syntex Institute of Steroid Chemistry. For no. 331, see P. Crabbé, H. Carpio, A. Cervantes, J. Iriarte, and L. Tökes, *Chem. Commun.*, **2**, 79 (1968).

(2) M. A. Spielman and F. L. Austin, *J. Amer. Chem. Soc.*, **59**, 2658 (1937).

(3) For a leading reference, see H. Wolff, *Org. Reaction*, **3**, 307 (1946).

(4) See also (a) K. F. Schmidt, German Patent 855,711 (Nov 17, 1952); *Chem. Abstr.*, **52**, 15592g (1958); (b) Fr. R. Benson, *Chem. Rev.*, **41**, 1 (1947).

(5) R. Anliker, M. Müller, J. Wohlfahrt, and H. Heusser, *Helv. Chim. Acta*, **38**, 1404 (1955).

(6) K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc.*, 39 (1946).

(7) K. L. Williamson and W. S. Johnson, *J. Org. Chem.*, **26**, 4563 (1961).