Experimental

During the course of the synthesis of *m*-*t*-butylphenol,[2] several derivatives were prepared which have not previously been reported.

2,4,6-Tribromo-3-*t*-butylaniline.—*m*-*t*-Butylaniline (b.p. 118–118.5° at 15 mm., 127–128° at 35 mm.) was brominated at room temperature in glacial acetic acid to give 2,4,6-tribromo-3-*t*-butylaniline, colorless needles from dilute methanol, m.p. 117–118°.

Anal. Calcd. for $C_{10}H_{12}NBr_3$: Br, 61.6. Found: Br, 61.4.

Derivatives of *m*-*t*-Butylphenol.—The following derivatives were prepared in the usual manner: (a) 3-*t*-butylphenoxyacetic acid, m.p. 113.5–114°, colorless needles from dilute ethanol; calcd. for $C_{12}H_{16}O_3$, neut. equiv., 208; found, neut. equiv., 207.5. (b) 3,5-dinitrobenzoate, m.p. 103.5–104°, shiny plates from dilute ethanol.

Anal. Calcd. for $C_{17}H_{16}O_6N_2$: N, 8.14. Found: N, 8.16.

Alkylation of *m*-*t*-Butylphenol.—Five grams of *m*-*t*-butylphenol[2] and 3.1 g. of *t*-butyl chloride were heated to 50–60°. Evolution of hydrogen chloride began immediately. During the course of the heating, an additional 2 g. of *t*-butyl chloride was added to replace entrainment losses carried past the condenser by the evolved gas. After warming for 24 hours, crystals formed on cooling. The product, recrystallized from petroleum ether (35–75°), m.p. 120.5–121° (lit. value[2] for 2,5-di-*t*-butylphenol, 118–119°). The yield of crude product was essentially quantitative, of recrystallized material, 6.0 g. (87%). Mixed melting point with an authentic sample prepared by the procedure of Carpenter, *et al.*,[2] showed no depression.

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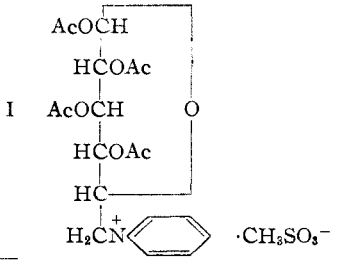
Salts of 6-Pyridinium-6-desoxy-D-glucose

BY B. M. ISELIN[1] AND JOHN C. SOWDEN[2]

Numerous investigators have reported the synthesis of sugar derivatives in which carbon-1 is linked with cyclic tertiary amines such as pyridine or nicotinamide by replacement of the hemiacetal hydroxyl.[3] The present note describes the preparation of derivatives in which the tertiary amine, pyridine, is linked to carbon-6 of the D-glucose chain by replacement of the primary alcoholic hydroxyl. When 1,2,3,4-tetraacetyl-6-methanesulfonyl-β-D-glucose[4] was heated with anhydrous pyridine, there resulted, in good yield, 1,2,3,4-tetraacetyl - 6 - pyridinium - 6 - desoxy - β - D-glucose methanesulfonate, I. Replacement of the methanesulfonyl anion by bromide ion was accomplished by means of ion exchange to give 1,2,3,4 - tetraacetyl - 6 - pyridinium - 6 - desoxy - β - D-glucose bromide. While tetraacetyl-D-glucosylpyridinium bromide is reduced readily in the aromatic nucleus to the corresponding 1,2-dihydropyridine derivative by treatment with sodium dithionite ($Na_2S_2O_4$),[3b] the attempted reduction of the 6-pyridinium-6-desoxy-D-glucose salts was unsuccessful. This is not surprising in view of the fact that N-alkylpyridinium salts, analogous to tetraacetyl-6-pyridinium-6-desoxy-D-glucose salts, undergo secondary changes upon treatment with sodium dithionite.[5] The amino-acetal linkage, present in tetraacetyl-D-glucosylpyridinium salts, seems to facilitate the partial reduction of the aromatic nucleus.[6]



Removal of the acetyl groups from tetraacetyl-6-pyridinium-6-desoxy-β-D-glucose methanesulfonate by catalytic saponification with sodium methoxide in chloroform solution gave crystalline 6-pyridinium-6-desoxy-D-glucose methanesulfonate.

Experimental

1,2,3,4-Tetraacetyl-6-pyridinium-6-desoxy-β-D-glucose Methanesulfonate (I).—A solution of 8 g. of 1,2,3,4-tetraacetyl-6-methanesulfonyl-β-D-glucose in 80 ml. of anhydrous pyridine was refluxed for 2.5 hours. On cooling, the dark red reaction mixture deposited a gelatinous precipitate which solidified on gradual addition of 150 ml. of ether. The crude product (7.83 g.) was dissolved in 1 l. of boiling acetone, 0.5 g. of decolorizing carbon was added, and the hot solution was filtered. After concentration to 300 ml., the clear filtrate yielded 5.65 g. (60%) of tetraacetyl-6-pyridinium-6-desoxy-β-D-glucose methanesulfonate as felted needles showing m.p. 225–226° and $[\alpha]^{24}D$ −16° in chloroform, *c* 1.27.

Anal. Calcd. for $C_{20}H_{27}O_{12}NS$: C, 47.52; H, 5.39; N, 2.77; acetyl, 34.1. Found: C, 47.16; H, 5.41; N, 2.77; acetyl, 34.3.

The substance showed an ultraviolet absorption spectrum typical for pyridinium salts with a maximum at $\lambda_{max.}^{alc.}$ 260 mμ (log ε 3.62).

1,2,3,4-Tetraacetyl-6-pyridinium-6-desoxy-β-D-glucose Bromide.—A solution of 1 g. of tetraacetyl-6-pyridinium-6-desoxy-β-D-glucose methanesulfonate in 25 ml. of water was passed through a column containing 50 g. of Amberlite IRA-400 ion-exchange resin which had been pretreated with dilute hydrogen bromide solution. The sulfur-free effluent was concentrated to dryness at 0.3 mm. pressure and room temperature. The solid residue was recrystallized from methyl ethyl ketone to give 520 mg. of the bromide, melting at 232–234°. Two additional recrystallizations from the same solvent gave the pure product showing m.p. 238–239° and $[\alpha]^{24}D$ −15° in water, *c* 0.95.

Anal. Calcd. for $C_{19}H_{24}O_9NBr$: Br, 16.3. Found: Br, 16.7.

6-Pyridinium-6-desoxy-D-glucose Methanesulfonate.—To a solution of 1.65 g. of tetraacetyl-6-pyridinium-6-desoxy-β-D-glucose methanesulfonate in 15 ml. of dry chloroform at −10° was added 1.65 ml. (0.5 eq.) of a 1 *N* solution of sodium methoxide in absolute methanol. After standing for 90 minutes at this temperature, 5 ml. of water was added and the mixture was neutralized with dilute sulfuric acid. The aqueous layer was treated with decolorizing carbon, evaporated to dryness at 0.3 mm. and room temperature and the residue extracted with hot methanol. After removal of inorganic material by centrifugation, the solution was concentrated to dryness at reduced pressure and the residual sirup (1.07 g.) was dissolved in ethanol. On prolonged standing, the solution deposited prisms of 6-pyridinium-6-desoxy-D-glucose methanesulfonate. Recrystallization from methanol–ether gave 638 mg. (58%) of the product melting at 152–155°. After several recrystallizations from methanol–acetone, the substance showed m.p. 155–157°; $[\alpha]^{24}D$

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(3) (a) E. Fischer and K. Raske, *Ber.*, **43**, 1750 (1910); (b) P. Karrer, B. Ringier, J. Büchi, H. Fritzsche and U. Solmssen, *Helv. Chim. Acta*, **20**, 55 (1937); (c) L. J. Haynes and A. R. Todd, *J. Chem. Soc.*, 303 (1950).

(4) B. Helferich and A. Gnüchtel, *Ber.*, **71**, 712 (1938).

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+42° after three minutes, +36° (constant) after two hours, in water, c 1.3; $\lambda_{max.}^{alc.}$ 260 mμ (log ε 3.68).

Anal. Calcd. for $C_{12}H_{19}O_8NS$: C, 42.72; H, 5.68; N, 4.15; S, 9.50. Found: C, 42.99; H, 5.90; N, 4.30; S, 9.79.

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BANTING AND BEST DEPARTMENT OF MEDICAL RESEARCH
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The Synthesis of Methylamine-C^{14} and Diazomethane-C^{14} [1]

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In connection with the preparation of radioactive steroid hormones, a satisfactory micromethod was demanded for the conversion of $C^{14}O_2$, through methylamine, to diazomethane for use in Arndt–Eistert extensions. Isotopic methylamine has previously been prepared from $NaC^{13}N$ by chromous chloride reduction (Hershberg, *et al.*[4]), and from sodium acetate-1,2-C^{14}, bacteriologically prepared, or from methyl labeled acetic acid, obtainable from $C^{14}H_3I$ (Gal, *et al.*[5]).

In this instance it was desired to employ the readily available $NaC^{14}N$.[6] While many reductions of cyanide are described (reviewed by Migrdichian[7]), none was well suited to the present purpose either because of the formation of amine mixtures or difficulty of small scale adaptation. Hydrogenation of cyanide was re-examined *ab initio*, and found to proceed almost exclusively to the monoamine (85% yield) in the presence of a slight excess of hydrochloric acid which arrests reduction at this stage. It is essential however that pure hydrogen and freshly prepared Adams–Shriner platinum catalyst be employed for satisfactory reduction at N.T.P. Aged platinum oxide (approximately six months or more) and certain tank hydrogens (even scrubbed as described below) are unsuitable.

The conversion of methylamine to diazomethane was conducted in the usual manner[8] in apparatus scaled to size. In C^{14} runs, isotope dilution (usually about fivefold) was made with C^{12}-methylurea at this stage. To minimize loss of precipitated nitroso-C^{14}-methylurea without diminution of yield, the procedure of nitrosylation was reversed —*i.e.*, acid was added to the methylurea–nitrite solution. Nitroso-C^{14}-methylurea decomposes on thin plating with loss of 93% of the C^{14} as volatile product. In bulk it is reasonably stable and gives rise to diazomethane-C^{14} with the correct molar count. The over-all yield of diazomethane from cyanide is consistently 40% or slightly better and radioactive product with specific activity up to 15 million counts/min./mg. has been prepared.

(1) A summary report has previously appeared; *Nucleonics*, **7**, No. 3, 53 (1950). Supported by the Cancer Grants Division, United States Public Health Service, and the Medical Research Division, National Research Council (Ottawa).

(2) Donner Foundation Fellow.

(3) Contributed in partial fulfillment of the requirements for the degree of Master of Science.

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(7) Migrdichian, "The Chemistry of Organic Cyanogen Compounds," Reinhold Publishing Corp., New York, N. Y., 1947, p. 151.

(8) Arndt, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, pp. 165, 966.

Experimental

Counts were ascertained from infinitely thin plates in the windowless flow gas chamber (Nuclear Instruments) operating at 40–50% efficiency, and are expressed below as disintegrations registered per minute per millimole.

Hydrogenation of $HC^{14}N$.—The sketch illustrates the vessels employed, the respective capacities of A and B being 125 and 30 ml. The vertical joint C was pivoted to allow rocking of the system by means of an arm driven from an eccentric and clipped to the neck of flask A. Flexible plastic tubing led from D to the usual vacuum line–hydrogen reservoir system. The reservoir was of the gas buret type (250-ml. capacity) which contained hydrogen generated (Kipp) from arsenic-free zinc and reagent grade hydrochloric acid, and scrubbed through solutions (20%) of potassium hydroxide, silver nitrate and saturated potassium permanganate.

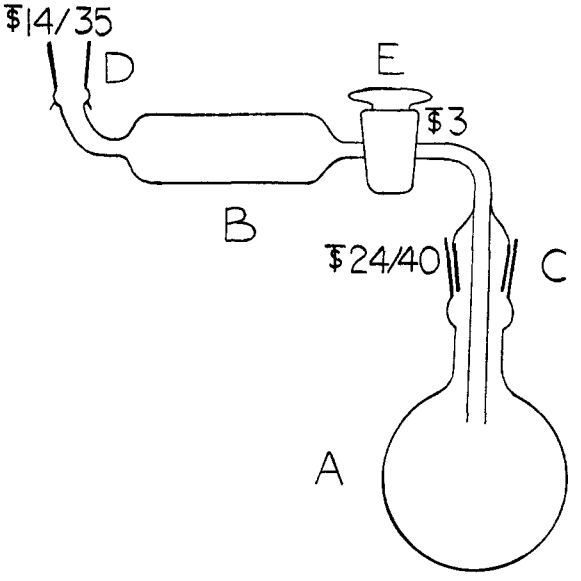

Fig. 1.

To vessel A was added a solution (50 ml.) of $NaC^{14}N$ (205 mg.; approximately 8.4 millicuries in 4.18 mmoles) in 2.24 molar proportions excess of sodium hydroxide. The $NaC^{14}N$ was prepared as previously described[6] from triphenylacetic acid-1-C^{14} which had 3.0×10^9 cts./min./mmole.

The solution was then taken to dryness *in vacuo* at 30°. After assembly to B, A was evacuated and sto co closed. Vessel B was then charged with 5 ml. of glacial acetic acid and 85 mg. of freshly prepared Adams–Shriner platinum oxide catalyst. After reduction of the latter, the apparatus was dismantled at D, and 0.96 ml. (11.5 mmoles) of concentrated hydrochloric acid in 5 ml. of acetic acid introduced to B. The system was refilled with hydrogen, and, after tilting B toward A, the contents of B were released to the evacuated vessel A on opening of the widebore stopcock E. Shaking was then commenced and hydrogenation continued until uptake of hydrogen ceased (4 to 7 hours) with the utilization of the theoretical two moles (210 ml.). Sodium chloride precipitates but is not detrimental to the reduction. After removal of catalyst by filtration (gravity), and washing with dilute hydrochloric acid, the filtrate was taken to dryness *in vacuo* to give a residue of monomethylamine hydrochloride and sodium chloride, which without further purification is suited to conversion[8] to methylurea and diazomethane.

For qualitative identification, the residue from an inactive run was triturated with hot butanol. The latter was concentrated to 3 ml. and, on refrigeration, gave mono-