cc. of octane-1,1,1,8,8,8-d_6, b.p. 121°, $n^{25}D$ 1.3945, d^{25}_4 0.7354.

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Depolymerization of a Dextran with Sonic Vibrations or Ultraviolet Light[1]

BY P. R. WATSON AND I. A. WOLFF

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In addition to studies on acid hydrolysis[2] and thermal[3] procedures for partial depolymerization of the dextran produced by *Leuconostoc mesenteroides* NRRL B-512, limited attention has been given at this Laboratory to dextran depolymerization with sonic vibrations or with ultraviolet light. This paper records our experiments with these latter procedures.

Lockwood, *et al.*,[4] Stacey[5] and Pautard[6] have investigated the ultrasonic degradation of a highly branched dextran and stated that the degraded dextrans produced in the course of the reaction were less polydisperse than an acid-hydrolyzed dextran. However, no data were presented on the percentage of 1,6′-glucosidic linkages in the resulting products. Pautard[6] suggested that ultrasonic degradation may be analogous to a thermal process. The periodate oxidation data[7] presented here (Table I) are in accord with Pautard's postulation since the sonically degraded samples, like thermally degraded NRRL B-512 dextran[3] and in contrast with fractions prepared from acid-hydrolyzed material, have a lower percentage of 1,6′-linkages than the parent raw material. It also is seen in Table I that under the conditions of irradiation used, a more extended time of treatment would be required for preparation of a fraction of inherent viscosity near 0.25, of suitable molecular size for injection purposes.[8]

TABLE I

PROPERTIES OF SONICALLY DEPOLYMERIZED NRRL B-512 DEXTRAN

Treatment time, min.	Max. power, %	Properties of products: Inherent viscosity[a]	Properties of products: 1,6′-like[b] links, %
0	..	1.17	94.6
5	100	0.78	..
10	100	.59	..
15	100	.52	93.8
5	50	.82	92.4
10	50	.67	..
30	50	.45	92.5

[a] Measured in water at 25° at a relative viscosity of 1.1–1.2. [b] Those units (linked at position 1 only or at positions 1 and 6) which give formic acid on periodate oxidation (reducing end-groups disregarded).

(1) Article not copyrighted.

(2) I. A. Wolff, C. L. Mehltretter, R. L. Mellies, P. R. Watson, B. T. Hofreiter, P. L. Patrick and C. E. Rist, *Ind. Eng. Chem.*, **46**, 370 (1954).

(3) I. A. Wolff, P. R. Watson, J. W. Sloan and C. E. Rist, *ibid.*, **45**, 755 (1953).

(4) A. R. Lockwood, A. E. Jones and F. G. Pautard, *Research (London)*, **4**, 46 (1951).

(5) M. Stacey, *ibid.*, **4**, 48 (1951).

(6) F. G. Pautard, *Chemistry & Industry*, 1316 (1953).

(7) Allene Jeanes and C. A. Wilham, THIS JOURNAL, **72**, 2655 (1950).

(8) U. S. Government military medical purchase description for dextran injection, stock number 1-161-890, May 24, 1951.

Solid B-512 dextran on irradiation with ultraviolet light was partially depolymerized (Table II). Oxidation probably took place concurrently since the products were slightly acidic and discolored during moisture-determination analysis at 100° *in vacuo*. The apparent percentage of 1,6′-linkages is increased with time of exposure to the light, but the formic acid values from periodate oxidation studies should be accepted with reservation in view of our incomplete knowledge of the structure of the irradiated products. The irradiated samples were water-soluble. Pautard[9] has reported that irradiation of dextran sensitized with dichromate caused its insolubilization.

TABLE II

PROPERTIES OF NRRL B-512 DEXTRAN IRRADIATED WITH ULTRAVIOLET LIGHT

Treatment time, hr.	Properties of Products: Inherent viscosity[a]	Properties of Products: 1,6′-like[a] links, %
0	1.17	94.6
4	1.07	94.6
8	0.91	95.1[b]
15	.84	95.9[b]
24	.90	96.9[b]

[a] Terms have same meaning as in Table I. [b] Corrected for acidity of the original sample.

Experimental

Sonic treatments were carried out in a Raytheon[10] (specification number T-049A, model 10 KC, power output 200 watts) instrument on 2% solutions of native NRRL B-512 dextran, which had been produced in whole culture. Cooling water was used to prevent excessive temperature rise of the solutions being treated. The degraded dextrans were recovered in solid form by alcoholic precipitation.

Ultraviolet light treatment involved exposure of air-equilibrated solid dextran, in the form of a finely divided powder, to radiation from a high-pressure, quartz, mercury arc lamp operated without a filter. The dextran was exposed in thin layers (0.5 g. dextran spread over 33.2 sq. cm.), 20 inches from the light source.

Acknowledgment—The assistance of B. H. Alexander and J. C. Rankin in carrying out the periodate oxidation analyses is gratefully acknowledged.

(9) F. G. Pautard, *Nature*, **171**, 302 (1953).

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

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Hydroxylation of Δ^{17}-20-Cyanopregnenes by Potassium Permanganate

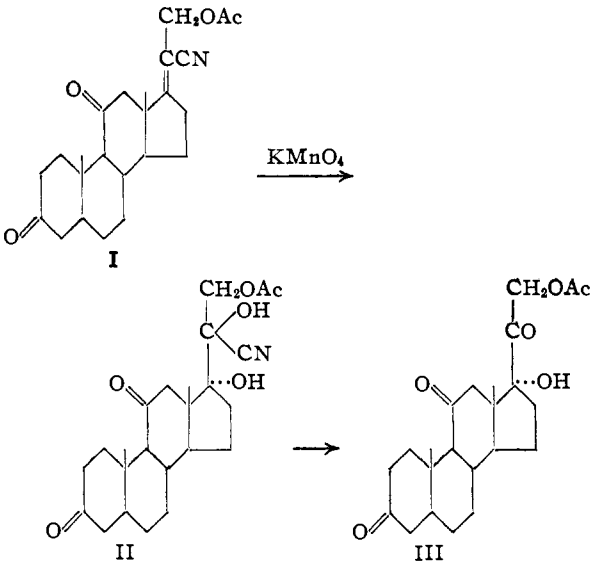
BY ROGER TULL, R. E. JONES, S. A. ROBINSON AND MAX TISHLER

RECEIVED AUGUST 13, 1954

A search for hydroxylating agents other than osmium tetroxide for the introduction of a hydroxyl group into position-17 of the pregnane molecule led to a practical method for the utilization of potassium permanganate in the conversion of Δ^{17}-20-cyanopregnene-21-ol-3,11-dione acetate (I) into pregnane-17α,21-diol-3,11,20-trione 21-acetate (III) an intermediate in Sarett's partial synthesis of cor-

tisone acetate.[1] The use of potassium permanganate in the transformation of Δ^{17}-20-cyanopregnenes, unsubstituted in ring C, into 17α-hydroxy-20-ketopregnanes in yields of 40–50% has already been reported by Heer and Miescher.[2]

We had observed that the cyanopregnene I reacted with potassium permanganate in acetone to give an intermediate cyanohydrin II, which was converted without isolation into the 17α-hydroxy-20-ketopregnane (III) by treatment with potassium carbonate, the over-all yield being 45%. When the reaction was carried out in acetone containing

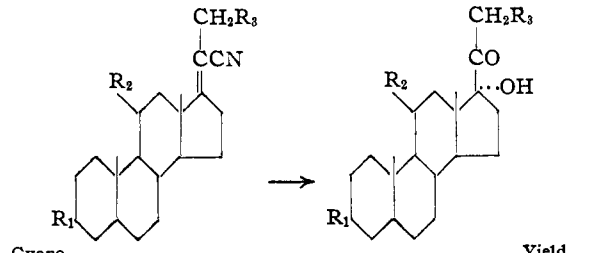


an organic base such as piperidine, the over-all yield was improved to 70%. A further increase in yield was achieved through a study of the change in alkalinity during the course of the hydroxylation reaction. By conducting the reaction in the presence of a glass electrode, it was observed that an immediate drop in the apparent *p*H of the anhydrous system from 11.5 to 9.5 occurred when potassium permanganate was added to the solution of steroid and piperidine in acetone. As the permanganate was consumed, the apparent *p*H rose gradually to 11, at which point the hydroxylation reaction slowed down considerably. The gradual addition of acetic acid to the reaction mixture as a means of maintaining the *p*H about 9 brought about the further improvement in yield to 80–90%.

In a similar manner, the geometrical isomer IV of the cyanopregnene I[3] was transformed into III in 69% yield and pregnane-3α,17α,21-triol-11,20-dione 3,21-diacetate (VI) was isolated from Δ^{17}-20-cyanopregnene-3α,21-diol-11-one diacetate (V) in a yield of 75%.

Some success was had in the hydroxylation of cyanopregnenes possessing free hydroxyl groups. Δ^{17}-20-Cyanopregnene-3α,21-diol-11-one 21-acetate (VII) yielded 75% of the corresponding ketol; Δ^{17}-20-cyanopregnene-11β,21-diol-3-one 21-acetate (X) was hydroxylated to the extent of only 39% and no product was isolated from the reaction of Δ^{17}-20-cyanopregnene-3α,21-diol-11-one (IX) with potassium permanganate. A summary of our findings is recorded in Table I.

TABLE I



Cyanopregnene[a]	R_1	R_2	R_3	Ketol	Yield, %
I	=O	=O	-OAc	III	80–90
IV	=O	=O	-OAc	III	69
V	α-OAc	=O	-OAc	VI	75
VII	α-OH	=O	-OAc	VIII	75
IX	α-OH	=O	-OH	None	
X	=O	β-OH	-OAc	XI	39

[a] With the exception of IV, all cyanopregnene derivatives belong to the same geometrical series.

The application of potassium permanganate to $\Delta^{5,17}$-20-cyanopregnadiene-3α-ol acetate was poor since only 10% of the corresponding ketol could be obtained.[4] This observation is of interest since the corresponding cyanopregnadiene containing an acetoxyl group in position-21 is converted into the ketol in 50% yield.[2]

Further application of the permanganate procedure has been reported recently from these laboratories in a description of the total synthesis of cortisone acetate,[5] wherein *dl*-$\Delta^{5,17}$-20-cyano-3-ethylenedioxypregnadien-21-ol-11-one acetate was converted into the corresponding 17-hydroxy-20-keto derivative in 89% yield.

Acknowledgment.—We are indebted to Miss Jane Alden and Mr. Fred Kocher for valuable technical assistance.

Experimental

Pregnane-17α,21-diol-3,11,20-trione 21-Acetate (III) from I.—Ninety grams (0.226 mole) of Δ^{17}-20-cyanopregnene-21-ol-3,11-dione acetate (I)[6] (m.p. 195–199°) dissolved in 2.9 l. of acetone was placed in a 12-l. three-necked flask equipped with a thermometer and mechanical stirrer. To the solution cooled to −5° was added 108 ml. of piperidine and 86.3 g. (0.545 mole) of granular potassium permanganate. The mixture was stirred for 30 minutes, whereupon a solution of 18 ml. of glacial acetic acid in 225 ml. of acetone was added in a dropwise manner over a period of 20 minutes, the temperature being kept below 2°. The mixture was stirred for an additional four hours at 0–2°. At the end of this period there was added 1.8 l. of chloroform at a rate which did not allow the temperature to rise above 3°. In the same manner there was added a solution of 270 ml. of concentrated hydrochloric acid in 1350 ml. of water followed by the addition of a solution of 126 g. of sodium bisulfite in 900 ml. of water. The mixture was warmed to room temperature and stirred for one hour. The layers were separated and the aqueous layer was extracted twice with chloroform. The chloroform extracts were combined and stirred for one hour with 2.7 l. of 5% potassium carbonate. The

(1) L. H. Sarett, THIS JOURNAL, **70**, 1454 (1948); **71**, 2443 (1949); U. S. Patent 2,597,190 (1952).

(2) J. Heer and K. Miescher, *Helv. Chim. Acta*, **34**, 359 (1951).

(3) For a discussion of the chemistry of geometrical isomerism in the cyanopregnene series, see: Huang-Minlon, R. Tull and J. Babcock, THIS JOURNAL, **76**, 2396 (1954).

(4) Carried out by Dr. H. E. Mertel of our laboratories.

(5) G. I. Poos, R. M. Lukes, G. E. Arth and L. H. Sarett, THIS JOURNAL, **76**, 5031 (1954).

(6) R. E. Jones and F. Kocher, *ibid.*, **76**, 3682 (1954).

aqueous layer was extracted with 700 ml. of chloroform and the chloroform extracts were combined and washed with 1350 ml. of water. The chloroform solution was concentrated under reduced pressure to a volume of 450 ml. The mixture was cooled to 0–5°. To the slurry was added slowly 3150 ml. of petroleum ether, the temperature being maintained at 0–5°. After stirring for one hour, the ketol III was collected on a filter, washed with a mixture of petroleum ether and chloroform (4:1), finally with petroleum ether and dried in air at 60°; yield 83.5 g. (90.7%), m.p. 229–231°, $[\alpha]^{25}D$ 79° (*c* 1, acetone).

Essentially pure material was obtained by stirring the product with a mixture of 210 ml. of isopropyl alcohol and 210 ml. of absolute ether at 20–25° for 30 minutes and then at 0–5° for 30 minutes. The purified ketol was collected and washed with 82 ml. of absolute ether; weight 73.8 g. (recovery 88.4%, over-all, 80%), m.p. 232.5–234.5°, $[\alpha]^{25}D$ 82.3° (*c* 1, acetone).

Pregnane-17α,21-diol-3,11,21-trione 21-Acetate (III) from IV.—Ten grams (0.025 mole) of the isomeric cyanopregnane[6] IV (m.p. 132–134°) oxidized according to the above procedure, yielded 7 g. (69%) of III, m.p. 232–234°. The ketol was isolated from a mixture of petroleum ether and chloroform with ratio of 3 to 1 instead of 7 to 1, thus the purification step was unnecessary.

Pregnane-3α,17α,21-triol-11,20-dione 3,21-Diacetate (VI) from V.—From 11.1 g. (0.052 mole) of Δ^{17}-20-cyanopregnene-3α,21-diol-11-one diacetate (V)[3] there was obtained 8.43 g. (74.6%) of the corresponding ketol VI; m.p. 237–238°. No melting point depression was observed when mixed with an authentic sample of VI.

Pregnane-3α,17α,21-triol-11,20-dione 21-Acetate (VIII).—Five grams of Δ^{17}-20-cyanopregnene-3α,21-diol-11-one 21-acetate (VII)[1] was treated with potassium permanganate in the manner described previously. The triol 21-acetate VIII was obtained in 75% yield; m.p. 222–226.5°. Inasmuch as the melting point of VIII is not depressed by admixture with III, it was necessary to convert it into the 3,21-diacetate, m.p. 232–235°, by treatment with acetic anhydride in pyridine (93% yield). The structure of the resulting 3,21-diacetate was confirmed by mixed melting point determinations with samples of III and VI. As expected, admixture with III showed depression while the mixture of diacetate with VI showed no depression.

Oxidation of Δ^{17}-20-Cyanopregnene-3α,21-diol-11-one (IX).—Five grams of IX was treated with potassium permanganate in the usual manner. An oil was obtained which was acetylated to give a semi-crystalline product from which no 3α,21-diol diacetate was isolated.

Pregnane-11(β),17(α),21-triol-3,20-dione 21-Acetate (XI).—From 3.12 g. of Δ^{17}-20-cyanopregnene-11(β),21-diol-3-one 21-acetate[7] (X) there was obtained 2.28 g. of crude XI; m.p. 198–205°. Recrystallization of the crude material from acetone–petroleum ether gave 1.24 g. (39%) of XI; m.p. 218–220°—no melting point depression with an authentic sample of XI.

(7) N. L. Wendler, R. P. Graber, R. E. Jones and M. Tishler, THIS JOURNAL, **74**, 3630 (1952).

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[CONTRIBUTION NO. 1239 FROM THE STERLING CHEMISTRY LABORATORY OF YALE UNIVERSITY]

Bolaform Electrolytes. IV. Conductance of α,ω-Bispyridinium Polymethylene Bromides and β,β′-Bisquaternary Substituted Diethyl Ethers in Methanol

BY JAMES C. NICHOL[1] AND RAYMOND M. FUOSS

RECEIVED JULY 26, 1954

The conductances of the following bolaform electrolytes have been measured in methanol at 25°: 1,2-ethane-N,N′-bispyridinium dibromide (I), 1,4-butane-N,N′-bispyridinium dibromide (II), 1,10-decane-N,N′-bispyridinium dibromide (III), diethyl ether bis-β,β′-trimethylammonium diiodide (IV), diethyl ether β-trimethylammonium, β′-methyldiethylammonium diiodide (V), diethyl ether bis-β-methyldiethylammonium diiodide (VI), diethyl ether bis-β-trimethylammonium dimethosulfate (VII) and diethyl ether bis-β-pyridinium dichloride (VIII) over the approximate concentration range 0.05×10^{-3} to 1.5×10^{-3} *N*. The dependence of limiting conductances, reciprocal association constants and intercharge distances between the cationic sites on chain length and structure of end groups is discussed.

The first three papers of this series[2–4] describe conductance studies of 2-1 salts whose cations were made up of a chain of atoms terminated at each end by a trimethylammonium group. In some cases, the chain consisted solely of methylene groups while in others ester or amide linkages were present. Recently, some α,ω-bispyridinium polymethylene salts were described by Dr. J. Hartwell[5] of the National Cancer Institute; these are similar to the salts prepared by Chu but differ in having terminal pyridinium groups rather than alkyl-substituted ammonium groups. Furthermore, Dr. J. Fakstorp[6] of Pharmacia Laboratories (Copenhagen) reported the preparation of a series of salts in which the cations were obtained by substituting various quaternary groups in the terminal β,β′-positions of diethyl ether. These compounds are similar to those of Edelson and Eisenberg, differing in the replacement of ester or amide linkages by an ether linkage in the middle of the cation. Through the kindness of Dr. Hartwell and of Dr. Fakstorp, we received samples of a number of these new salts, which made it possible for us to compare their electrical properties with those of the previously investigated compounds of related structure. This comparison is based on the conductance at 25° of dilute solutions of the salts in absolute methanol.

(1) On leave of absence from Willamette University, Salem, Oregon. Grateful acknowledgment is made to the California Research Corporation for a research fellowship for the academic year 1953–1954.

(2) R. M. Fuoss and D. Edelson, THIS JOURNAL, **73**, 269 (1951).

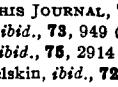
(3) R. M. Fuoss and V. F. H. Chu, *ibid.*, **73**, 949 (1951).

(4) H. Eisenberg and R. M. Fuoss, *ibid.*, **75**, 2914 (1953).

(5) J. L. Hartwell and M. A. Pogorelskin, *ibid.*, **72**, 2040 (1950).

(6) J. Fakstorp, J. Christiansen and J. G. A. Pedersen, *Acta Chem. Scand.*, **7**, 134 (1953).

Experimental

Materials.—The compounds provided by Dr. Hartwell consisted of 1,2-ethane-N,N′-bispyridinium dibromide (I), 1,4-butane-N,N′-bispyridinium dibromide (II) and 1,10-decane-N,N′-bispyridinium dibromide (III). Dr. Fakstorp's compounds included diethyl ether bis-β,β′-trimethylammonium diiodide (IV), diethyl ether β-trimethylammonium, β′-methyldiethylammonium diiodide (V), diethyl ether bis-β-methyldiethylammonium diiodide (VI), diethyl ether bis-β-trimethylammonium dimethosulfate (VII) and diethyl ether bis-β-pyridinium dichloride (VIII). For reference in later discussion, the structural formulas of these compounds, together with code symbols, are given in Table A. The symbol "Py$^+$" means the group  .