Anal. Calcd. for $C_{11}H_{16}O_8$: C, 47.80; H, 5.84. Found: C, 47.80; H, 5.87.

Benzyl β-D-arabinopyranoside triacetate cleaved at a slower rate than the α-form and was complete in 40 minutes. The sirup, impure 2,3,4-triacetyl-α-D-arabinopyranose, showed $[\alpha]^{25}D$ −123.5° (chloroform) calculated as triacetyl arabinose, and mutarotated to a constant value of −107.2°. It has not been crystallized.

Benzyl α-L-arabinopyranoside triacetate responded to reductive cleavage in a manner similar to the α-D form to give a 60% yield of 2,3,4-triacetyl-α-L-arabinopyranose melting at 105–108° and showing $[\alpha]^{25}D$ +50.1° (*c*, 2, chloroform).

Anal. Calcd. for $C_{11}H_{16}O_8$: C, 47.80; H, 5.84. Found: C, 47.95; H, 5.96.

A trace of acid causes mutarotation of this product in chloroform solution, and an equilibrium value $[\alpha]^{25}D$ +110.5° results.

MADISON 6, WISCONSIN RECEIVED JULY 5, 1950

[CONTRIBUTION FROM THE CHEMICAL RESEARCH DIVISION OF SCHERING CORPORATION]

Catalytic Hydrogenation of Cholesterol

BY E. B. HERSHBERG, EUGENE OLIVETO, MARTIN RUBIN, HEINZ STAEUDLE AND LOIS KUHLEN

Strong acids have been shown to act as promoters for the low-pressure hydrogenation of cholesterol using Adams platinum oxide catalyst. When perchloric acid was used as the promoter, cholestanol was obtained in 87–90% yield. Cholestane, cholestanyl acetate and coprostanol were formed as by-products.

For many years the catalytic hydrogenation of cholesterol has been an outstanding example of a difficult and capricious hydrogenation. Despite the relative ease of reaction reported by W. F. Bruce,[1] in this Laboratory the authors found that the specified amount of platinum catalyst produced only a slight absorption of hydrogen. Even excessively large amounts of catalyst permitted only a slow and halting reaction. Neither careful crystallization of the commercial material to the highest recorded constants of melting point and optical rotation nor a pretreatment with Raney nickel[2,3] accelerated its rate of hydrogenation. This was in sharp contrast to the hydrogenation of sitosterol and stigmasterol which proceeded smoothly at room temperature in acetic acid solution and which indicated that the catalyst was not at fault. Even cholesterol resynthesized from 25-norcholestenolone[4] did not absorb hydrogen at an appreciable rate.

A pretreatment of the cholesterol dissolved in acetic acid and warmed on the steam-bath for 7 hours with a small amount of 30% hydrogen peroxide gave a product which would reduce reliably though slowly at room temperature with Adams catalyst, approximating the rate observed in the "Organic Syntheses" procedure.[1] Other oxidizing agents accomplished the same improvement though the process could still not be considered practical for the preparation of large amounts of cholestanol.

In the search for promoters for this reaction perchloric acid was found to have a powerful activating effect. So little of it was necessary to accelerate the rate of hydrogenation that it could not be considered to be an oxidizing agent. This interpretation was later substantiated by the observation that many other acids produced the same effect roughly parallel to their acid strength. Thus, sulfuric, maleic, oxalic, phosphoric, hydrochloric, *p*-toluenesulfonic and citric acids, all lower than *pK* 3, were effective promoters. Acetic acid (*pK* 4.76) and benzoic acid (*pK* 4.20) produced a slow and incomplete reaction while desoxycholic acid and catechol showed no promoter effect.

Using perchloric acid as an accelerator, it was no longer necessary to limit the hydrogenation to acetic acid as a solvent or to conduct the hydrogenation much above room temperature, though the heat evolved by the now rapid hydrogenation maintained the temperature of the resultant solution at 40–50°. Usually, the hydrogenation solution was warmed initially to 40–50° in order to dissolve and hydrogenate a greater amount of cholesterol in the hydrogenator at our disposal. The use of ethyl acetate, which is a good solvent for cholesterol, had the additional advantage that very little cholestanyl acetate was formed, whereas acetic acid in the presence of platinum catalyst caused considerable ester formation and it was then necessary to hydrolyze the entire product in order to obtain pure cholestanol.[1]

It is interesting to note that of the seven active promoters found, perchloric,[5] sulfuric,[6] phosphoric,[6] *p*-toluenesulfonic,[6] hydrochloric[7] and oxalic[8] acids are known to form addition products with cholesterol.

A procedure was developed in which a suspension of 1.25 kg. of cholesterol in 17 l. of ethyl acetate was hydrogenated completely in 30–45 min. with 25 g. of Adams platinum oxide catalyst using 1–2 ml. of 72% perchloric acid promoter. From 87 to 90% of the theoretical amount of cholestanol was obtained, and this product gave a negative Liebermann–Burchard reaction.

The best yield of cholestanol obtained in large scale hydrogenations using perchloric acid as a promoter was about 90% of the theoretical. A careful large scale chromatographic separation of the residues remaining after the crystallization of the cholestanol indicated the presence of small amounts of three other compounds: cholestanyl acetate, coprostanol and cholestane, all by-products

(1) *Org. Syntheses*, **17**, 45 (1937), also Coll. Volume II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 191.

(2) A. Wilds and C. Djerassi, THIS JOURNAL, **68**, 1712 (1946).

(3) J. R. Durland, Ph.D., Thesis, University of Wisconsin, 1939.

(4) A. Ryer, W. Gebert and N. Morrill, THIS JOURNAL, **72**, 4247 (1950).

(5) W. Lange, R. G. Folzenlogen and D. G. Kolp, *ibid.*, **71**, 1733 (1949).

(6) A. Ryer and W. Gebert, this Laboratory, unpublished work.

(7) U. S. Patent 2,322,906.

(8) L. Yoder, O. R. Sweeney and L. K. Arnold, *Ind. Eng. Chem.*, **37**, 374 (1945).

of the hydrogenation and not present in the initial cholesterol.

Cholestanyl acetate was undoubtedly formed by ester interchange of either the starting material or of the product with the ethyl acetate.

The formation of coprostanol is another example of the formation of significant amounts of a coprostane derivative in the catalytic hydrogenation of a $\Delta^{5,6}$-double bond.[9]

The hydrogenolysis of a hydroxyl group in the presence of hydrogen, platinum and perchloric acid has been noted before[10] and this may explain the presence of cholestane.

Experimental[11]

Hydrogenation of Cholesterol

In order to make a comparison of the products of the hydrogenation of cholesterol with the starting material a large lot of cholesterol was carefully crystallized from ethyl acetate. The material obtained melted at 148.6–149.8°, $[\alpha]^{24}D$ −40.26°. Upon chromatographic analysis of a 20-g. sample using a column of Florosil there was obtained only 0.12 g. of material melting at 139–145° (0.6%) while the remainder was substantially pure cholesterol.

A solution of 1250 g. of this purified cholesterol in 17 l. of C.P. ethyl acetate at 40–50° was hydrogenated in a reciprocating type hydrogenator with the aid of 25 g. of platinum oxide catalyst[12] and 2.0 cc. of 70–72% perchloric acid. The initial pressure was 15 lb./sq. in. and the hydrogenation was complete in approximately 30 minutes.[13] The heat of hydrogenation kept the solution at about the starting temperature. After displacing the hydrogen with nitrogen the solution was treated with 1 cc. of 50% sodium hydroxide solution, filtered with suction to remove the catalyst, cooled to 10° and held overnight at this temperature. There was thus obtained 579 g. of β-cholestanol, m.p. 139–141°, $[\alpha]^{24}D$ +22.3°. The mother liquors were evaporated to dryness under reduced pressure and the residue was recrystallized from 17 l. of methanol. Two more crops were obtained which weighed 526.5 g., m.p. 139–142°, thus givng a total yield of 1105.5 g. (88.0%) of cholestanol. The same yield was obtained from different samples of unrecrystallized U.S.P. cholesterol using this procedure. Further concentration of the mother liquors gave material melting below 100°.

In order to separate this residue into its components the methanolic mother liquors were evaporated to dryness leaving 143 g. of light brown material, m.p. 75–88°. A 20-g. sample was dissolved in 200 ml. of hexane and adsorbed onto a 1-meter column of 100–200 mesh Florosil. Successive elutions with hexane, hexane–chloroform (95:5), hexane–chloroform (85:15), and chloroform gave four fractions. From the hexane eluate there were obtained three fractions. The first, 1.6 g., m.p. 63.4–72.8°, gave cholestane m.p. 79.8–81.6°, $[\alpha]^{23}D$ +27.3°, after one crystallization from acetone.

Anal. Calcd. for $C_{27}H_{48}$: C, 87.02; H, 12.98. Found: C, 87.14; H, 13.00.

The next fraction, 2.04 g., reached a maximum melting point at 104° and ranged from m.p. 85–104–98°. It was crystallized from acetone and from methanol and gave cholestanyl acetate m.p. 109.0–110.0°, $[\alpha]^{22}D$ +12.34°.

Anal. Calcd. for $C_{29}H_{50}O_2$: C, 80.87; H, 11.70. Found: C, 80.73; H, 11.55.

The third and last fraction from the hexane eluate weighed 4.26 g., m.p. 73–103–83°. Three crystallizations of this fraction from methanol gave coprostanol, m.p. 99.2–100.4°, $[\alpha]^{22}D$ +23.84°

Anal. Calcd. for $C_{27}H_{48}O$: C, 83.43; H, 12.45. Found: C, 83.45; H, 12.10.

Each of the above three compounds was compared with authentic samples by mixture melting point and by direct comparisons of the infrared spectra. In each case no differences were observed.

From the hexane–chloroform eluates there was obtained 8.1 g. of substantially pure cholestanol. Allowing for the cholestanol in the residue the over-all yield obtained from the hydrogenation was 92.5%, while approximately 1–2% of cholestane, 1–2% of cholestanyl acetate and 2.5–3.5% of coprostanol were formed as by-products.

BLOOMFIELD, NEW JERSEY RECEIVED AUGUST 18, 1950

(9) T. Reichstein and A. Lardon, *Helv. Chim. Acta*, **24**, 955 (1941).

(10) K. Kindler and D. Kwok, *Ann.*, **554**, 9 (1943); K. Rosenmund and E. Karg, *Ber.*, **75**, 1850 (1942).

(11) All melting points are corrected. Optical rotations were determined in a 1% chloroform solution. The optical data and microanalyses were determined by Mr. W. Tarpley, Mr. Edwin Conner and their Staff.

(12) Baker and Company, Newark, New Jersey.

(13) FOOTNOTE ADDED IN PROOF.—Only 20 minutes was required in a rotary hydrogenator [E. B. Hershberg, F. Bertsch, H. Kaplan and H. Brown, *Ind. Eng. Chem.*, **42**, 2336 (1950)].

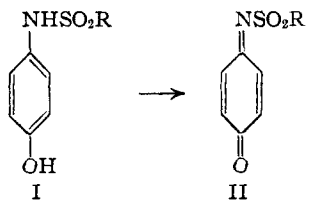
[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Quinone Imides. IV. p-Quinone Monosulfonimides

BY ROGER ADAMS AND J. H. LOOKER

Lead tetraacetate oxidation of the benzenesulfonyl, *p*-toluenesulfonyl and methanesulfonyl derivatives of *p*-aminophenol give the corresponding *p*-quinone imides. The 2-methyl, 3-methyl, 2-chloro, 3-chloro and 2,6-dichloro derivatives of 4-benzenesulfonamidophenol have been oxidized similarly. The *p*-quinone imides are (1) readily reduced, (2) hydrolyzed by hot water to the quinone and sulfonamide and (3) add hydrogen chloride or thiophenol to give the corresponding chloro- or phenylmercapto-4-sulfonamidophenol. The primary products of the addition reactions have the entering groups ortho to the hydroxyl. The sulfonamidophenols are best prepared from the aminophenols and sulfonyl chlorides in pyridine.

The conversion of the disulfonamides of *p*-phenylenediamine, 1,4-naphthylenediamine and their derivatives to *p*-quinone disulfonimides by oxidation with lead tetraacetate has been described in previous papers.[1] The identical procedure is equally adaptable to the sulfonamides of *p*-aminophenol and its derivatives and leads to the formation of *p*-quinone monosulfonimides. Thus, the benzenesulfonyl, *p*-toluenesulfonyl and methanesulfonyl derivatives of *p*-aminophenol (I) are oxidized to the corresponding *p*-quinone imides II.



I II

R = phenyl, *p*-tolyl, methyl

The benzenesulfonyl derivatives of 2-chloro-, 2,6-

(1) R. Adams and A. S. Nagarkatti, THIS JOURNAL, **72**, 4601 (1950); R. Adams and R. A. Wankel, *ibid.*, **73**, 131 (1951); see also R. Adams and J. H. Anderson, *ibid.*, **72**, 5154 (1950).