of water was added and the mixture was refluxed for three hours. The mixture was cooled, acidified with dilute sulfuric acid, and extracted several times with benzene. The benzene extracts were extracted with 2 *N* sodium carbonate solution and with water, the benzene was evaporated, and the residue was distilled under reduced pressure, the colorless viscous liquid distilling at 134–137° at 0.4 mm. being collected; weight, 12.4 g. (57%).

Anal. Calcd. for $C_{13}H_{18}O$: C, 82.1; H, 9.5. Found: C, 81.8; H, 9.4.

The acid obtained by acidification of the alkaline washings was esterified with methanolic hydrochloric acid, purified by distillation (7 g., b. p. 128–133° at 0.4 mm.), and this recovered ester could be used in subsequent reductions.

β - [1 - (3 - Methyl - 1,2,3,4 - tetrahydronaphthyl)]-ethyl Bromide.—A mixture of 5.0 g. of the above alcohol and 2 cc. of phosphorus tribromide was heated on a steam-bath for two hours. The mixture was taken up in benzene and washed with 2 *N* sodium carbonate solution and then with water. The residue obtained by evaporation of the benzene was distilled, the colorless liquid distilling at 137–140° at 0.4 mm. being collected; weight, 5.2 g. (75%).

Anal. Calcd. for $C_{13}H_{17}Br$: Br, 31.6. Found: Br, 31.8.

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The Preparation of Pentaacetyl-*d*-gluconyl Chloride

BY CHARLES E. BRAUN, S. H. NICHOLS, JR., J. L. COHEN AND THEIS E. AITKEN

In the course of work being carried out in these laboratories a method has been developed for the preparation of pentaacetyl-*d*-gluconyl chloride in quantity. This new procedure, based upon that of Major and Cook,[1] involves much less manipulation and gives consistently good results. The details are presented here for those interested.

Anhydrous pentaacetylgluconic acid[2] (25 g. or 0.062 mole) was dissolved in 185 cc. of anhydrous ethyl ether and an excess of phosphorus pentachloride (15 g. or 0.072 mole) was added without cooling. The reactants were allowed to stand at room temperature from four to twelve hours (usually overnight). The excess phosphorus pentachloride was then filtered off on a sintered glass funnel, and the ethereal filtrate concentrated to about one-half of its volume *in vacuo* at room temperature. The concentrated solution was kept at zero degrees or below[3] for fifteen to twenty-four hours. The mother liquor was then decanted, *care being taken not to break up or disturb the crystals which had formed on the bottom of the flask.* The crystalline mass was next broken up, mechanically removed and filtered on a sintered glass funnel. After thorough washing with petroleum ether (Eastman Kodak Company, practical, b. p. 35–55°), the crystalline acid chloride was preserved *in vacuo* over calcium chloride and potassium hydroxide at room temperature.

The decanted mother liquor, after being concentrated *in vacuo* at room temperature to one-half of its volume, was allowed to stand at zero degrees or below for another twenty-four hours. The second crop of crystals thus obtained was treated as described above. The concentrated mother liquor which contained all of the phosphorus oxychloride was usually discarded. By this procedure pentaacetyl-*d*-gluconyl chloride was produced as large colorless crystals; m. p. 68–71°; $[\alpha]^{21}D$ +1.71° (alcohol-free chloroform, *c*, 4.38).

Anal. Calcd. for $C_{16}H_{21}O_{11}Cl$: Cl, 8.35. Found: Cl, 8.20.

The yields obtained in five typical preparations were 83%, 86%, 92%, 88% and 93%, or an average yield of 88.4%.

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(1) Major and Cook, THIS JOURNAL, **58**, 2477 (1936).

(2) Major and Cook, *ibid.*, **58**, 2475 (1936).

(3) At higher temperatures the yields are decreased appreciably due to the increase in solubility of the acid chloride in the anhydrous ether.

Additional Observations on the Vitamin K Activity of Quinones

BY ERHARD FERNHOLZ, H. B. MACPHILLAMY AND S. ANSBACHER

Several months ago we reported that phlorone (2,5-dimethyl-1,4-benzoquinone) has vitamin K activity,[1] an observation recently confirmed by H. J. Almquist.[2] In this connection it seemed of interest to investigate whether 2-methyl-5,6,7,8-tetrahydro-1,4-naphthoquinone possesses the great potency of the parent substance. The hydrogenated quinone, first synthesized by Chuang and Han,[3] was prepared by catalytic hydrogenation of 2-methyl-1,4-naphthoquinone. It was found to be active at 1 mg., a degree of activity which should be considered practically negligible, since it is common to a great number of quinones.

We have also studied the analogous hydrogenation product of vitamin K_1 (β,γ,5,6,7,8-hexahydrovitamin K_1). It showed no vitamin K activity, not even in a dose of 2 mg. In contrast to this, Fieser, Tishler, and Sampson[4] reported it to have slight activity, although the dosage is not indicated.

We wish to point out that we have prepared and assayed the naphthotocopherol and its quin-

(1) Ansbacher and Fernholz, *J. Biol. Chem.*, **131**, 399 (1939).

(2) 52nd Annual Meeting, Am. Physiol. Soc., New Orleans, May 16 (1940).

(3) Chuang and Han, *Ber.*, **68**, 876 (1935).

(4) Fieser, Tishler and Sampson, THIS JOURNAL, **62**, 996 (1940).

oid oxidation product recently mentioned by Fieser, *et al.*[4] The latter authors gave no biological data for the oxidation product and stated that the tocopherol was active at 0.3 mg. We found that 1 mg. of the tocopherol was totally inactive, but the oxidation product was fully active at that dose.[5]

Experimental

2 - Methyl - 5,6,7,8 - tetrahydro - 1,4 - naphthoquinone.—A solution of 1.72 g. of 2-methyl-1,4-naphthoquinone in glacial acetic acid was completely hydrogenated using platinum oxide catalyst. The reaction mixture was decanted from the catalyst, diluted with water and extracted with ether. The ethereal solution was washed, dried and the solvent evaporated. The quinone was obtained by steam distilling a suspension of the crude hydroquinone in a ferric chloride solution. The distillate was extracted with ether, the extract dried and the solvent evaporated. The residue after recrystallization from light petroleum ether yielded 1.6 g. (94%) of quinone melting at 58–59°.

Anal. Calcd. for $C_{11}H_{12}O_2$: C, 74.97; H, 6.87. Found: C, 74.95; H, 6.71.

β,γ-5,6,7,8-Hexahydro Vitamin K_1.—One gram of the synthetic vitamin was hydrogenated as described above. The hydroquinone was oxidized with silver oxide in dry ether. The yield was 0.95 g. (95%) of yellow oil giving with alcoholic alkali a pink color which darkened to brown on standing.

Anal. Calcd. for $C_{31}H_{52}O_2$: C, 81.52; H, 11.47. Found: C, 81.17; H, 11.60.

Naphthotocopherol.—A mixture of 3.5 g. of 2-methyl-1,4-naphthoquinone, 5 g. of phytol, 5 g. of anhydrous zinc chloride and 50 cc. of xylene[6] was refluxed for twenty-four hours. The solvent was removed *in vacuo* and the residue taken up in ether. The ethereal solution was washed repeatedly with 2% potassium hydroxide solution containing hydrosulfite and finally with dilute hydrochloric acid and water. After drying and removal of the solvent, the remaining brown oil was taken up in petroleum ether (b. p. 40–60°), and extracted with Claisen alkali. The small amount of yellow oil obtained on working up the soluble portion gave the typical Dam–Karrer reaction for vitamin K_1.

The petroleum ether portion was washed, dried and the solvent evaporated. The residue was purified by chromatographic adsorption on activated alumina in petroleum ether solution. The yield was about 1.0 g. (13% based on phytol), of reddish-brown oil which strongly reduced an alcoholic silver nitrate solution in the cold.

Anal. Calcd. for $C_{31}H_{48}O_2$: C, 82.24, H, 10.70. Found: C, 82.48; H, 10.72.

Oxidation of Naphthotocopherol.—Two hundred milligrams of the above tocopherol was oxidized with ferric chloride in alcoholic solution. The reaction mixture was diluted with water, extracted with ether, and the ethereal solution washed, dried and concentrated. The residue was purified by chromatographing in petroleum ether solution on activated calcium sulfate. About 100 mg. (48%) of dark orange oil was obtained.

Anal. Calcd. for $C_{31}H_{48}O_3$: C, 79.43; H, 10.30. Found: C, 79.42; H, 10.03.

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(5) Reported by the senior author in a lecture at Columbia University on December 4, 1939.

(6) Jacob, Sutcliffe and Todd, *J. Chem. Soc.*, 331 (1940), report an unsuccessful attempt to effect this condensation in boiling decalin. In our experience the tocopherol is destroyed at that temperature.

Collidine Treatment of 2-Bromocholestanone

BY ROBERT P. JACOBSEN

In the course of preparation of certain steroids for photochemical study, the author has had occasion to employ the collidine method of Butenandt, *et al.*,[1] for the splitting of hydrogen bromide from 2-bromocholestanone to form 1-cholestenone. On refluxing a collidine solution of the bromo compound for two hours, these workers obtained the α,β-unsaturated ketone (m. p. 95°, $[\alpha]_D$ + 64.5°) in 77% yield. Butenandt and Wolff[2] had earlier reported the preparation of 1-cholestenone (m. p. 111–112°, $[\alpha]_D$ −32.1°; oxime, m. p. 146–147°), in poor yield by the potassium acetate–acetic acid treatment of 2-bromocholestanone. This latter compound the German workers now call "hetero-Δ^1-cholestenone" and state that the "normal Δ^1-ketone" is the substance melting at 95°.

In the experience of the author, the collidine reaction appears to follow a less straightforward course than that indicated by Butenandt and his collaborators. 2-Bromocholestanone (m. p. 169°) was refluxed in collidine[3] for two, four, or six hours without effecting the complete fission of hydrogen bromide. After twelve hours of boiling, a non-homogeneous, crystalline, halogen-free product (m. p. 89–92° to a sludge which cleared at about 100°) was obtained in 74% yield. By repeated crystallization from methanol this gave a very small amount of material, m. p. 126–127.5° (nearly pure cholestanone), which showed no selective absorption[4] in the ultraviolet region between 2200 and 2600 Å. No pure 1-cholestenone could be obtained from the intermediate fractions by crystallization, although some sam-

(1) Butenandt, Mamoli, Dannenberg, Masch and Paland, *Ber.*, **72**, 1617 (1939).

(2) Butenandt and Wolff, *ibid.*, **68**, 2091 (1935).

(3) Obtained from the Research Department of the Barrett Company, 90% of the material boiling in the range 170.7–171.9°.

(4) Ultraviolet absorption measurements by Dr. P. A. Cole and Mr. C. Z. Nawrocki of this Laboratory.