hydrochloric acid. The liberated organic acids were usually redissolved in ether and purified. The experiments using cinnamic acid (II) used 14.8 g. (0.10 *M*) of II and 0.25 mole of the Grignard reagent.

3-Methylpentanoic acid (I + III) was formed in 40% yield (11.6 g.); b.p. 112–113° at 37 mm., $n^{25}D$ 1.4139, neut. equiv., 116 (calcd. for $C_6H_{12}O_2$: neut. equiv., 116); amide, m.p. 123–124° (petroleum ether) (lit.[3a] m.p. 125°); no depression of m.p. when mixed with an authentic sample.[3b] There were 7.3 g. of a higher boiling acidic fraction and 2.5 g. of a neutral product.

3-Phenylbutyric acid (I + V) was formed in 40% yield (16.3 g.); b.p. 122° at 2 mm., m.p. 35–36° (petroleum ether) (lit.[4] m.p. 37–38°), neut. equiv., 164 (calcd. for $C_{10}H_{12}O_2$: neut. equiv., 164). Amide, m.p. 105–106 (water) (lit.[4] 105–106°). Anilide m.p. 136–137° (ethanol–water) (lit.[4] 136–137°). There were 4.1 g. of a higher boiling acidic fraction and 16.0 g. of a neutral product.

3,4,4-Trimethylpentanoic acid (I + IV) was formed in 3% yield (1.2 g.); b.p. 88–92° at 3 mm. (lit.[5] 97–98° at 4 mm.), $n^{25}D$ 1.4348 (lit.[5] $n^{21}D$ 1.4320), neut. equiv., 142 (calcd. for $C_8H_{16}O_2$: neut. equiv., 144); amide, m.p. 166–167° (ethanol–water) (lit.[5] 166–167°). In this reaction 10.7 g. (50%) of I was recovered, b.p. 105–107° at 40 mm., m.p. 69–70° (no depression of melting point when mixed with a sample of authentic crotonic acid). There were 8.9 g. of a higher boiling acidic fraction and 2.7 g. of a neutral fraction.

3-Phenylpentanoic acid (II + III) was formed in 42% yield (7.5 g.); b.p. 135° at 3 mm., m.p. 60–61° (petroleum ether) (lit.[6] 58°), neut. equiv., 179 (calcd. for $C_{11}H_{14}O_2$: neut. equiv., 178); benzylamine salt, m.p. 111–112° (ethyl acetate) (lit.[6] 96.5°). Calcd. for $C_{18}H_{23}NO_2$: C, 75.7; H, 8.1. Found[7]: C, 75.2; H, 8.0. The higher boiling acidic fraction weighed 5.0 g. and the neutral fraction 2.6 g.

***β-t*-Butylhydrocinnamic Acid** (II + IV).—In this reaction the acidic portion was distilled, collecting 11.3 g. of a product boiling up to 142° at 2 mm. There was 4.4 g. of a residue. The distillate was analyzed spectroscopically (ultraviolet and infrared absorption[8]). It consisted of 2.0 g. (13% recovery) of II and 9.3 g. (45% yield) of the *t*-butylhydrocinnamic acid. The distillate was crystallized several times from an ethanol–water mixture until a constant melting point of 115–116° (4.1 g.) was reached (lit.[9] 114–116°). Its neutral equivalent was 207 (calcd. for $C_{13}H_{18}O_2$: 206). The neutral fraction in this experiment was 1.9 g.

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(8) We wish to thank Dr. R. A. Friedel of U. S. Bureau of Mines, Bruceton, Pa., for these analyses.

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CONTRIBUTION NO. 914 FROM
DEPARTMENT OF CHEMISTRY
UNIVERSITY OF PITTSBURGH
PITTSBURGH 13, PENNA.

Crystalline 2,4-Dinitrophenylhydrazones of D-Fructose

BY LAWRENCE M. WHITE AND GERALDINE E. SECOR

RECEIVED AUGUST 4, 1953

Attempts in this Laboratory to synthesize D-fructose 2,4-dinitrophenylhydrazone by methods used for the formation of the 2,4-dinitrophenylhydrazones of certain aldose sugars[1–3] yielded an orange-colored mass that behaved somewhat like a thixotropic gel. The mass, probably cryptocrystalline, could not be purified easily and no conditions were found that gave recognizable crystals from ethanol. No synthesis of a crystalline D-fructose 2,4-dinitrophenylhydrazone has been reported

The authors have found that D-fructose and 2,4-dinitrophenylhydrazine react rapidly in cold or hot dioxane containing favorable amounts of water and acid to form very small needles of the dioxane solvate of D-fructose 2,4-dinitrophenylhydrazone. Conditions favoring a slower reaction produce trichitic crystals or long needles usually growing in spherulitic clusters and sheaves. Although the corresponding pyridine solvate can be made in small yield by the reaction of D-fructose and 2,4-dinitrophenylhydrazine in pyridine, it is most easily prepared from the dioxane solvate by a simple crystallization procedure.

The solvates are soluble in cold or hot pyridine; slightly soluble in cold or hot 95% ethanol, acetone, water, dioxane and ethyl acetate; and insoluble in cold or hot ethyl ether, chloroform, benzene and petroleum ether (b.p. 64–70°).

Free fructose can be regenerated from the solvated hydrazones and, under certain conditions, the dioxane and pyridine can be removed quantitatively from the molecule.

The optical, X-ray and crystallographic properties and the analytical applications of these compounds will be reported elsewhere.

Experimental

Reagents.—Reagent grade dioxane was passed through chromatographic grade activated alumina.[4,5] Immediately before use, the dioxane was made to contain 3% water and 0.3% hydrochloric acid (sp. gr. 1.19).

Reagent grade 2,4-dinitrophenylhydrazine was recrystallized from ethyl acetate before use.[5]

Reagent grade D-fructose was used without further purification.

D-Fructose 2,4-Dinitrophenylhydrazone Dioxane Solvate.—A mixture of 1 g. of D-fructose, 1 g. of 2,4-dinitrophenylhydrazine and 50 ml. of acidified, aqueous dioxane was agitated vigorously at room temperature. After 3 to 5 minutes, fine chrome yellow needles began to form. The needles were filtered under nitrogen,[6] washed with reagent grade dioxane and ethyl ether, and dried to constant weight at room temperature *in vacuo;* yield 1.85 g. (82%), m.p. (cor.) 176–178° dec., $[\alpha]^{26}D$ −35.4° (*c* 1, pyridine).

Anal. Calcd. for $C_{12}H_{16}N_4O_9 \cdot C_4H_8O_2$: C, 42.86; H, 5.40; N, 12.50. Found: C, 42.9; H, 5.47; N, 12.3.

D-Fructose 2,4-Dinitrophenylhydrazone Pyridine Solvate.—D-Fructose 2,4-dinitrophenylhydrazone dioxane solvate (1.83 g.) was dissolved in 25 ml. of pyridine at room temperature and 25 ml. of 95% ethanol was added. Large, yellow, blade-like crystals grew slowly. The product was filtered under nitrogen[6] and dried to constant weight at room temperature *in vacuo;* yield 1.43 g. (79.9%), m.p. (cor.) 173–175° dec., $[\alpha]^{26}D$ −34.7 (initial and final) (*c* 1, pyridine).

Anal. Calcd. for $C_{12}H_{16}N_4O_9 \cdot C_5H_5N$: C, 46.47; H, 4.82; N, 15.94. Found: C, 46.5; H, 4.85; N, 15.7.

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(4) W. Dasler and C. D. Bauer, *Ind. Eng. Chem., Anal. Ed.*, **18**, 52 (1946).

(5) Unpurified reagent and practical grades of dioxane adjusted to the proper water and acid contents, and unrecrystallized reagent grade 2,4-dinitrophenylhydrazine were used successfully in unreported experiments.

(6) Since the crystals are readily oxidized when wet, they must be kept from contact with air until they are dry; thereafter they are reasonably stable to air and light. This precaution was used only when preparing samples for analysis.

A second crop of crystals having the same appearance under low-power magnification was taken by evaporating the mother liquor to 3 ml. on the steam-bath, cooling and adding 3 ml. of ethanol. The crystals were filtered under nitrogen and dried at room temperature *in vacuo*. Yield for this crop was 0.21 g. (11.7%). Total yield for the two crops was 1.64 g. (91.6%).

Chromatography.—Approximately 15 micrograms of D-fructose 2,4-dinitrophenylhydrazone pyridine solvate was applied 6 cm. from one end of a 6 × 38 cm. strip of Whatman No. 1 paper. The paper was equilibrated for 6 hours in a 2-liter graduated cylinder containing 100 ml. of *n*-butyl alcohol saturated with water, then the solvent was allowed to ascend the paper for 16 hours. The D-fructose 2,4-dinitrophenylhydrazone traveled as a single discrete yellow spot, R_f value 0.67. Spraying this, and more heavily loaded chromatograms, with resorcinol failed to reveal the presence of any free fructose in the D-fructose 2,4-dinitrophenylhydrazone pyridine solvate.

Cleavage of the D-Fructose 2,4-Dinitrophenylhydrazone Solvates.—Each of the solvates was cleaved in aqueous solution with benzaldehyde in the usual manner. Chromatographic examination[7] of the resulting mother liquors revealed the presence of a sugar indistinguishable from D-fructose.

Removal of Dioxane and Pyridine from the Solvates.—Vacuum-dried samples of D-fructose 2,4-dinitrophenylhydrazone dioxane solvate (51.52 mg.) and D-fructose 2,4-dinitrophenylhydrazone pyridine solvate (50.87 mg.) were exposed to water-saturated nitrogen[6] for several days and then dried to constant weight at room temperature *in vacuo* over anhydrous magnesium perchlorate. Weight lost by the dioxane solvate, 9.98 mg. (19.4%); calcd. for complete loss of one mole of dioxane and no uptake of water, 10.12 mg. (19.65%). Weight lost by the pyridine solvate, 9.07 mg. (17.8%); calcd. for complete loss of one mole of pyridine and no uptake of water, 9.16 mg. (18.00%).

D-Fructose 2,4-dinitrophenylhydrazone pyridine solvate (7.977 mg.) was dissolved in 15 ml. of hot acetone, the acetone blown off with nitrogen and the treatment repeated with 10 ml. of hot acetone. After removal of the acetone, the residue was dried *in vacuo* overnight at room temperature. The residue contained 1.005 mg. of N (12.6%); calcd. for complete loss of one mole of pyridine, 1.017 mg. of N (12.75%).

Acknowledgment.—The authors wish to thank Dr. Frank E. Young of this Laboratory for the determination of the optical rotations.

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WESTERN REGIONAL RESEARCH LABORATORY
ALBANY, CALIFORNIA

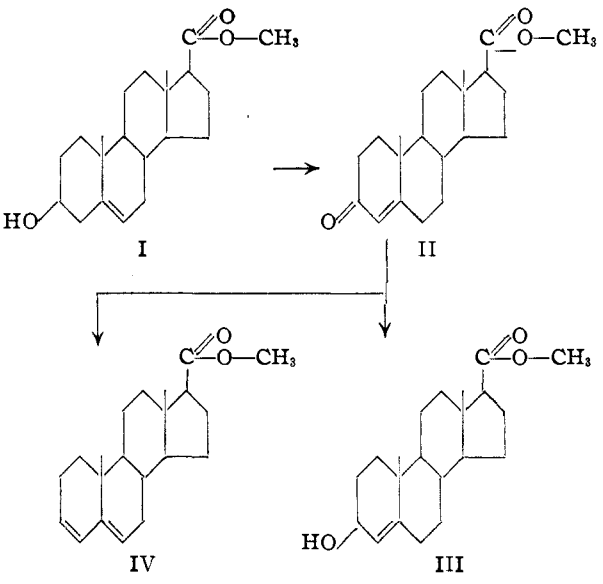
The Reduction of Methyl 3-Oxo-Δ^4-etiocholenate with Sodium Borohydride[1]

BY W. WERNER ZORBACH

RECEIVED AUGUST 19, 1953

During a current investigation designed to convert methyl 3β-hydroxy-Δ^5-etiocholenate (I)[2] to methyl 3β,5-dihydroxyetiocholanate by paralleling earlier work in the cholestane series,[3] it was necessary first to convert I to the corresponding 3-oxo-Δ^4 derivative (II),[4] and thence proceed to methyl 3β-hydroxy-Δ^4-etiocholenate (III).

To effect the reduction of II, sodium borohydride was chosen, since this reagent reduces neither double bonds nor ester linkages. It was noted in



an earlier paper that a similar reduction of Δ^4-cholesten-3-one was accomplished employing lithium aluminum hydride,[5] but here the power of this reagent to attack ester linkages was of little concern. These workers reported a 50–50 conversion to 3α- and 3β-Δ^4-cholestenol in quantitative yield and it was, therefore, surprising when preliminary experiments in our own case revealed a high degree of conversion to the 3β-Δ^4-stenol (III), although studies by Shoppee and Summers[6] presaged the possibility of a stereospecific reduction. In this work, Δ^5-cholesten-3-one and cholestan-3-one were reduced with lithium aluminum hydride to give 90% or better conversion to cholesterol and cholestan-3β-ol, respectively. In each case, small amounts of the corresponding α-epimers were obtained.

Of especial interest is the reduction of methyl 3-oxo-Δ^4-etiocholenate (II) in this Laboratory for reasons of both a high degree of conversion (91%) to the desired 3β-Δ^4-stenol III and the remarkable absence of any methyl 3α-hydroxy-Δ^4-etiocholenate which would, normally, be expected on the basis of the studies noted above.

A number of reductions were accomplished and all were carried out in methanol and ethyl acetate, the latter of which was introduced to ensure against possible saponification of the ester linkage. Despite carefully controlled conditions of temperature and *p*H, none of the α-epimer could be obtained. Separation of the β-epimer III from the reaction products *via* the digitonide left an oil which could not be crystallized. This oil was further resolved by chromatography over silicic acid, resulting in a small amount of crystalline material which analyzed for methyl $\Delta^{3,5}$-etiocholadienate (IV). Determination of the ultraviolet spectrum, λ_{max}^{alc} 234 (4.3), confirmed this structure. This is not an unreasonable consequence since it is well-known that, due to a tendency to form a conjugated system, Δ^4-stenols readily undergo dehydration. This could satisfactorily account for the formation of small amounts of the diene IV.

(1) Supported in part by a grant from the Washington, D. C., Heart Association.

(2) Generously supplied by Dr. A. C. Shabica, Ciba Pharmaceutical Products, Inc., Summit, N. J.

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