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 repeatedwith 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.

(7) L. M. White and G. E. Secor, *Arch. Biochem. Biophys.*, **43**, 60 (1953).

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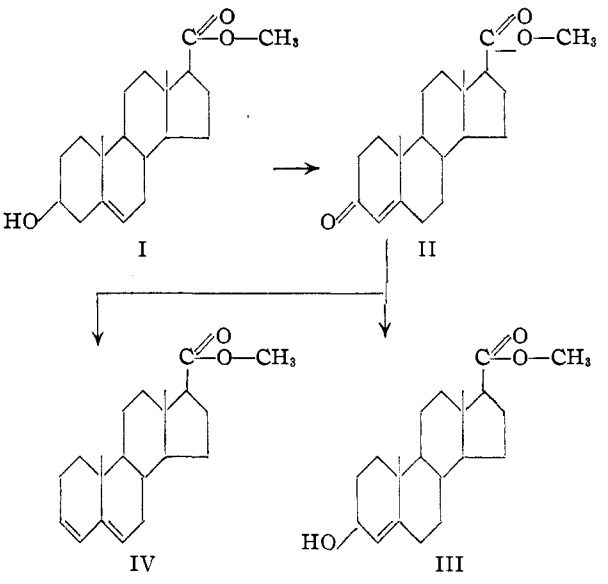
The Reduction of Methyl 3-Oxo-Δ^4-etiocholenate with Sodium Borohydride[1]

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.

(3) Pl. A. Plattner, H. Heusser and A. B. Kulkarni, *Helv. Chim. Acta*, **32**, 265 (1949).

(4) K. Miescher and A. Wettstein, *ibid.*, **22**, 1268 (1939).

(5) H. McKennis, Jr., and G. W. Gaffney, *J. Biol. Chem.*, **175**, 217 (1948).

(6) C. W. Shoppee and G. H. R. Summers, *J. Chem. Soc.*, 687 (1950).

Experimental

Methyl 3β-Hydroxy-Δ⁴-etiocholenate (III).—The starting material for this synthesis was methyl 3β-hydroxy-Δ⁵-etiocholenate (I) which was converted by an Oppenauer oxidation[4] to methyl 3-oxo-Δ⁴-etiocholenate (II). To a solution of 990 mg. (3.0 mmoles) of the latter in 40 ml. of methanol and 10 ml. of ethyl acetate was added a solution of 228 mg. (6.0 mmoles) of sodium borohydride in 40 ml. of methanol and 10 ml. of ethyl acetate and the mixture allowed to stand at room temperature for 16 hours under exclusion of moisture. At the end of this time, 1.0 ml. of water was added and the solution adjusted to *p*H 7 with acetic acid. The solvent was then evaporated *in vacuo* at 40–45° to near-dryness, the residue taken up with 15 ml. of warm methanol and transferred quantitatively to 150 ml. of water. After refrigeration for one hour, the separating crystalline material was filtered by suction and allowed to dry. This dry material was dissolved in 100 ml. of absolute ethanol, added to a solution of 3100 mg. of digitonin in 170 ml. of absolute ethanol and 40 ml. of water and allowed to stand under refrigeration for 20 hours. The resulting digitonide was filtered by suction, washed with two 15-ml. portions of absolute ether, then transferred to a mortar and pulverized. This was extracted thoroughly with 200 ml. of absolute ether, filtered and washed several times with the same solvent. The digitonide thus treated was transferred to a 500-ml. erlenmeyer flask, covered with 93 ml. of pure pyridine and allowed to dissolve.

In the meantime, the alcoholic filtrate, combined with the ether washings, was evaporated *in vacuo* at 40–45°. When the volume had diminished to about 100 ml. a further, small quantity of the digitonide separated. This was filtered, washed with absolute ether and transferred to the flask containing the main bulk of the digitonide. The pyridine solution of the now decomposed digitonide was diluted with 800 ml. of absolute ether, centrifuged and filtered. The separating digitonin was washed with the same solvent and the washings combined with the filtrate, all of which was evaporated to dryness *in vacuo*. This treatment resulted in 906 mg. (91%) of methyl 3β-hydroxy-Δ⁴-etiocholenate which, when recrystallized twice from methanol, gave needles, m.p. 209–211° (Fisher–Johns block), $[\alpha]^{25}D$ +92° (*c* 1.98, $CHCl_3$).

Anal. Calcd. for $C_{21}H_{32}O_3$: C, 75.86; H, 9.70. Found: C, 75.64; H, 9.58.

Methyl Δ³,⁵-Etiocholadienate (IV).—The alcoholic filtrate from the preceding preparation, reduced in volume and combined with the ether washings, was evaporated to dryness *in vacuo* at 50°, leaving a residue consisting of material not precipitable with digitonin plus a small amount of unused digitonin. This was taken up with ether, filtered, evaporated and dried for 15 minutes at 50° under a reduced pressure of 0.1 mm. This resulted in a light yellow oil which was placed on a column of Fisher reagent grade silicic acid and chromatographed. Benzene and benzene–ether (99.5–0.5) eluates gave 60 mg. (6%) of crude methyl Δ³,⁵-etiocholadienate which, when recrystallized three times from methanol, gave long, fine needles, m.p. 141–142° (Fisher–Johns block), λ_{max}^{alc} 234 (4.3).

Anal. Calcd. for $C_{21}H_{30}O_2$: C, 80.21; H, 9.61. Found: C, 79.77; H, 9.50.

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Dialkoxyalkanenitriles. II.[1] Reaction of Dialkoxyacetonitriles with Dicyanodiamide

BY V. P. WYSTRACH AND JOHN G. ERICKSON[2]

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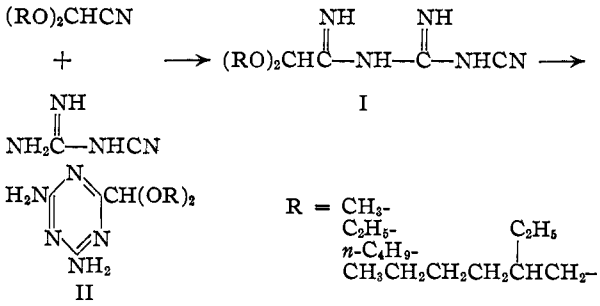
The base-catalyzed reaction of dialkoxyacetonitriles with dicyandiamide in 2-methoxyethanol or 1-butanol solution produces dialkoxyacetoguanamines (II), acetals of 4,6-diamino-2-*s*-triazinecarboxaldehyde. The reactions take place very rapidly, and excellent yields of pure materials are obtained. The first step in the reaction probably involves the formation of dialkoxyacetimidodicyandiamides (I), followed by cyclization to the triazine.



Although the method is essentially an extension of a reaction already reported in the patent literature[3] for the preparation of simple guanamines, the products represent a new series of *s*-triazine derivatives. A survey of the literature has shown that the only *s*-triazinecarboxaldehyde derivatives reported heretofore are the oximinoacetoguanamides prepared by Ostrogovich and co-workers.[4]

In earlier work,[5] it had been found that dialkoxyacetonitriles are easily cleaved by solutions of ammonia in alcohols. The successful preparation of these guanamines from dialkoxyacetonitriles in alcoholic solutions containing much stronger bases than ammonia was, accordingly, unexpected. Apparently, the reactions of dialkoxyacetonitriles with dicyandiamide are much faster than the cleavage reactions. We have observed that dialkoxyacetonitriles are considerably more reactive toward dicyandiamide, as well as other reagents, than are simple aliphatic nitriles. On the other hand, α,α-dimethoxypropionitrile does not react in the same manner with dicyandiamide. With this compound, apparently, the cleavage reaction predominates over the reaction with dicyandiamide.

Acknowledgment.—Analyses were performed by the Microanalytical Group of the Stamford Research Laboratories.

Experimental[6]

The preparation of the dialkoxyalkanenitriles from hydrocyanic acid and the alkyl esters of ortho acids has already been reported.[1]

Dimethoxyacetoguanamine.—A mixture of dimethoxyacetonitrile (30.3 g., 0.3 mole), dicyandiamide (27.7 g., 0.33 mole), potassium hydroxide (85% pure, 1.0 g., 0.015 mole) and 2-methoxyethanol (75 ml.) was stirred and heated in a suitably equipped three-necked flask. At 60°, the source of heat was removed and the temperature of the solution rose rapidly to 132°, where the mixture refluxed vigorously. After the exothermic reaction had subsided, the mixture was refluxed 15 minutes longer, cooled to 15°, filtered, washed with ethanol and dried. This gave 49.6 g. (89.4%) of guanamine as white prisms, m.p. 207–210°. It was recrystallized twice from water (decolorized with charcoal); m.p. 208–209°.

(1) Previous paper in this series, John G. Erickson, THIS JOURNAL, **73**, 1338 (1951).

(2) Research Dept., General Mills, Inc., Minneapolis, Minn.

(3) W. Zerweck and W. Brunner, U. S. Patent 2,302,162 (Nov. 17, 1942); J. E. Castle, U. S. Patent 2,548,772 (April 10, 1951); J. K. Simons, U. S. Patent 2,522,419 (Dec. 5, 1950); D. W. Kaiser and B. C. Redmon, U. S. Patent 2,510,981 (June 13, 1950); D. W. Kaiser, U. S. Patent 2,606,904 (Aug. 12, 1952).

(4) A. Ostrogovitch and V. Crasu, *Gazz. chim. ital.*, **64**, 800 (1934); **66**, 653 (1936); A. Ostrogovitch and J. Cadariu, *ibid.*, **71**, 505, 515, 524 (1941).

(5) To be reported elsewhere.

(6) Melting points are not corrected.