tallization from acetone afforded colorless needles of 3α-cholesterol melting at 140–142° identical in all respects with an authentic sample.

When 50 mg. of the enol acetate of cholestenone was dissolved in 20 ml. of dry pyridine containing 100 mg. of sodium borohydride and the mixture stored at room temperature for two hours, 25 mg. of crystalline enol acetate was recovered after addition of ether followed by washing with hydrochloric acid and water. The mother liquors were essentially pure enol acetate as judged by infrared spectrometry. Under similar conditions 17β-hydroxyetiocholan-3-one was reduced to the 3α and β diols in almost quantitative yield.

Cholesterol from Δ⁴-Cholesten-3-one.—A solution of 766 mg. of cholestenone in ether was added to a Grignard reagent prepared from 1.9 g. of *t*-butyl chloride and 480 mg. of magnesium. The solution was heated under reflux for 20 min. and then poured into a stirred and cooled solution of 1.20 g. of sodium borohydride in 200 ml. of 80% aqueous ethanol. The mixture was allowed to stand for 30 min. and cholesterol was isolated as described in the preceding experiment. From the digitonin precipitate 290 mg. (37%) of pure cholesterol melting at 146–148° was obtained after two crystallizations from acetone.

SLOAN-KETTERING INSTITUTE FOR CANCER RESEARCH
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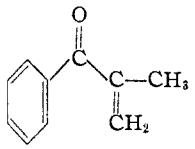
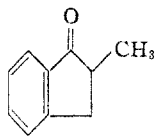
A Thiophene Isostere of 2-Methyl-1-indanone

BY J. H. BURCKHALTER AND JOSEPH SAM

It has been demonstrated that α-methylacrylophenone (I), obtained from steam distillation of β-dimethylamino-α-methylpropiophenone hydrochloride,[1] will undergo ring closure to form 2-methyl-1-indanone (II).[2] Later studies have shown that α-methyl-2-acrylothienone (III), an analog of I, can

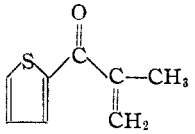


I

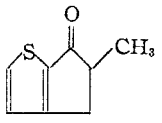


II

be readily obtained from the analogous Mannich base.[3] The present report records the ring closure of III to form IV. Proof that a substance of struc-



III



IV

ture IV has been obtained was afforded by a comparison of the 2,4-dinitrophenylhydrazine derivatives of III and IV. Further confirmatory evidence is supplied by the molecular refractivity of IV and by a distinctive odor which is also characteristic of the benzene isostere of IV.

We are grateful to Dr. Austin M. Patterson, of Xenia, Ohio, for advice on the systematic naming of IV (see Experimental part).

Experimental[4]

4,5-Dihydro-5-methyl-6*H*-cyclopenta[*b*]thiophen-6-one (IV).—Eighteen grams of α-methyl-2-acrylothienone (III)[3] was poured slowly with stirring into 100 ml. of concentrated sulfuric acid which had been at room temperature. The mixture turned to a clear reddish color and became slightly warm. After the liquid had been allowed to cool to room temperature, it was poured with stirring into a liter of cold water. The milky oil which separated was extracted with three portions of ether and the extract dried over sodium sulfate. After removal of the ether, 14 g. (78% yield) of cyclic ketone (IV) was distilled at 95.5° (2 mm.); $n^{20}D$ 1.5808, d^{20}_{20} 1.1890, M_D calcd. 41.80, found 42.48.

Anal. Calcd. for C_8H_8OS: C, 63.13; H, 5.30. Found: C, 62.83; H, 5.47.

A red **2,4-dinitrophenylhydrazone** of IV decomposed at 248°, after recrystallization from ethyl acetate.

Anal. Calcd. for $C_{14}H_{12}N_4O_4S$: C, 50.59; H, 3.64. Found: C, 50.81; H, 3.64.

A derivative of α-methyl-2-acrylothienone (III), considered to be **1-(2,4-dinitrophenyl)-3-(2-thienyl)-4-methylpyrazoline** by analogy with other results,[3] was prepared as a red crystalline product from III and 2,4-dinitrophenylhydrazine, m.p. 222°, after recrystallization from ethyl acetate. A mixed melting point with the 2,4-dinitrophenylhydrazone of IV showed a decided depression.

Anal. Calcd. for $C_{14}H_{12}N_4O_4S \cdot {}^1/_2H_2O$: C, 49.26; H, 3.84. Found: C, 49.12; H, 3.90.

DEPARTMENT OF PHARMACEUTICAL CHEM.
UNIVERSITY OF KANSAS
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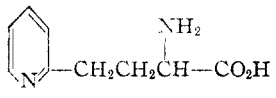
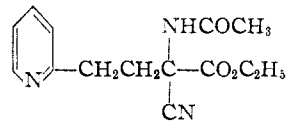
α-Amino-γ-2-pyridinebutyric Acid

BY J. H. BURCKHALTER AND VERLIN C. STEPHENS[1]

As a part of a study of unnatural amino acids as possible antimetabolites,[2] α-amino-γ-2-pyridinebutyric acid (I) was prepared. Ethyl α-acetamido-α-cyano-γ-2-pyridinebutyric acetate (II) was ob-



I



II

tained in 53% yield by a base-catalyzed condensation of 2-vinylpyridine with ethyl acetamidocyanoacetate.[3] Acid hydrolysis of II gave I in only 51%yield, because its extensive solubility in water made separation from the by-product ammonium chloride rather difficult.

Experimental[4]

Ethyl α-Acetamido-α-cyano-γ-2-pyridinebutyrate (II).—To a boiling solution of 17 g. (0.1 mole) of ethyl acetamidocyanoacetate, 2 g. of sodium ethoxide and 200 ml. of benzene, 10.5 g. (0.1 mole) of 2-vinylpyridine[5] was added dropwise with vigorous stirring. The solution was maintained at reflux temperature for seven hours under a slow stream of nitrogen. After cooling and filtering, the benzene solution was concentrated *in vacuo* until solid began forming. A saturated solution of sodium bisulfite was added, and the mixture of liquids was allowed to stand for two hours with occasional shaking. The solid which had gradually formed was collected by filtration. A little more product was obtained by further concentration. The yield of crude ester was 14.5 g. (53%), m.p. 116–120°. Recrystallization from aqueous methanol gave 12 g., m.p. 120–122°.

Anal. Calcd. for $C_{14}H_{17}N_3O_3$: C, 61.07; H, 6.23. Found: C, 60.88; H, 6.13.

(1) Mannich and Heilner, *Ber.*, **55**, 356 (1922).
(2) Burckhalter and Fuson, THIS JOURNAL, **70**, 4184 (1948).
(3) Blicke and Burckhalter, *ibid.*, **64**, 453 (1942).
(4) Microanalyses by Mr. Charles Beazley, Skokie, Illinois.

(1) Fellow of the American Foundation for Pharmaceutical Education, 1948–1950.
(2) Burckhalter and Stephens, THIS JOURNAL, **73**, 56 (1951).
(3) Doering and Weil, *ibid.*, **69**, 2461 (1947), have used the same general method for the preparation of γ-2-pyridinebutyric acid.
(4) C and H analyses by Mr. C. W. Beazley, Skokie, Illinois.
(5) Obtained through the courtesy of Reilly Tar and Chemical Co., Indianapolis, Indiana.