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.

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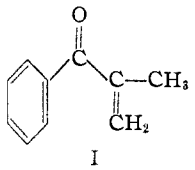
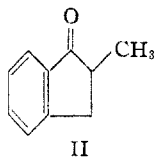
A Thiophene Isostere of 2-Methyl-1-indanone

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

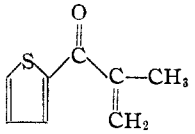


I

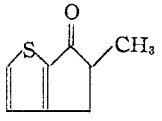


II

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.

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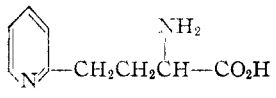
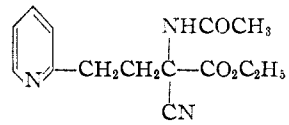
α-Amino-γ-2-pyridinebutyric Acid

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.

α-Amino-γ-2-pyridinebutyric Acid (II) Monohydrate.—A solution of 38.5 g. (0.14 mole) of ethyl α-acetamido-α-cyano-γ-2-pyridinebutyrate in 75 ml. of concentrated hydrochloric acid was refluxed for six hours. After evaporation of the solution to dryness under reduced pressure, a small quantity of ice was added and the solution was made slightly basic by the addition of ammonia solution. It was warmed on a steam-bath until all the solid formed by the evaporation process had dissolved. The nearly neutral solution was again cooled, and the solid which formed was removed by filtration. After washing once with alcohol, 35 g. of solid was obtained (a mixture of the desired product with ammonium chloride), m.p. 230° dec. Recrystallization from a very small amount of water gave 14 g. (51%) of a chloride-free product, m.p. 276° dec. A second recrystallization from aqueous alcohol gave material which melted at 280° dec., when the m.p. bath was preheated to 240°.

Anal. Calcd. for $C_9H_{12}N_2O_2 \cdot H_2O$: C, 54.53; H, 7.12. Found: C, 54.91; H, 6.97.

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The Mechanism of the Pyrolyses of Pinenes

BY ROBERT L. BURWELL, JR.

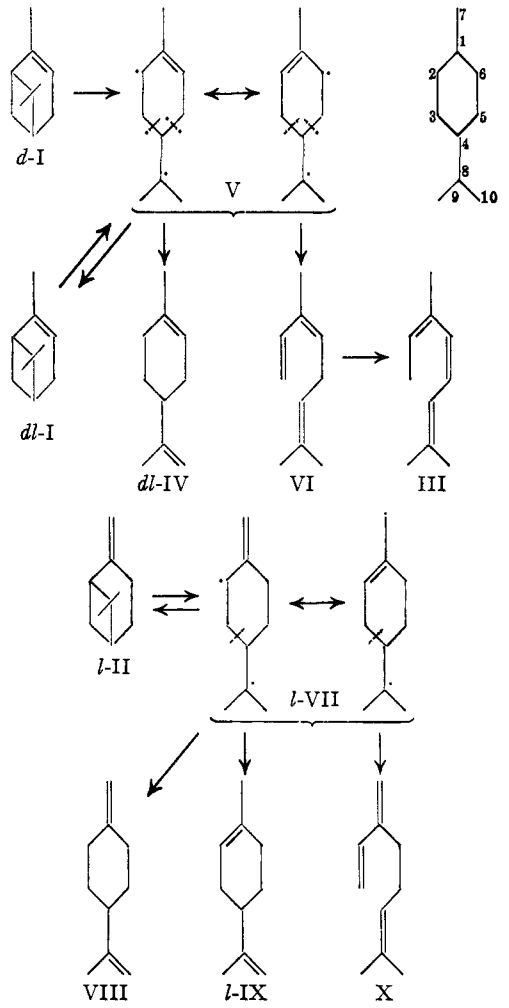
In view of the current interest in biradicals as reaction intermediates, it should be noted that a biradical provides an exceptionally attractive explanation of reactions occurring during pyrolyses of α-pinene (I) and β-pinene (II). The hypothesis permits one to deduce the relative rates of the reactions undergone by such biradicals. This biradical is unusual in that one of the odd electrons is part of an allylic resonance hybrid. The energetics, kinetics and products are consequent to this.

Savich and Goldblatt,[1] Fuguitt and Hawkins[2] and earlier workers have shown that vapor or liquid phase pyrolysis of α-pinene in the temperature range 200 to 500° results initially in three simultaneous reactions, all first order:[2] (a) racemization of α-pinene, (b) isomerization to *allo*-ocimene (III), and (c) isomerization to almost inactive limonene (IV). The relative rate of reaction (c) declines slowly with increasing temperature. The activation energy for the total reaction is about 41 kcal.[2] Frequency factors accord with those expected for unimolecular processes.[2]

If the three reactions are first order, racemization cannot involve either *dl*-limonene or *allo*-ocimene as an intermediate.[3] Furthermore, nearly *dl*-limonene is formed as such since *l*-limonene resists racemization under the reaction conditions.[1]

The biradical (V) coördinates these facts. It is a resonance hybrid like the allyl free radical and is similarly stabilized. Reforming the broken bond leads to *dl*-I since recombination may occur to each stereochemical antipode. As models show, intramolecular hydrogen atom transfer is possible only from one of the six hydrogen atoms on the isopropyl residue (positions (9) and (10)) to the equivalent positions (2) or (6). Such a process forms *d*-IV and *l*-IV with equal probability. Rupture of either of the bonds indicated by dotted lines (3–4 or 4–5) forms VI which like ocimene[4] should readily conjugate to III at reaction temperatures. Intermediate V probably possesses a folded structure intermediate between *d*-I and *l*-I.

This mechanism, then, proposes a rate determining isomerization of I to the biradical which further reacts with probabilities which are temperature dependent.



Szwarc and Sheon[5] report the process $CH_2{=}CH{-}CH_2{-}CH_3 \rightarrow CH_2{=}CH{-}CH_2\cdot + CH_3\cdot$ to involve an activation energy of 62 kcal./mole. Allowance for the bond strain in a cyclobutane ring would reduce this value about to the activation energy reported for pyrolysis of α-pinene. The bond between carbon atoms (2) and (3) does not rupture at a rate detectable in comparison with the bond between (2) and (8) presumably owing to the greater stability of the tertiary free radical formed in the latter case.

Rice and Rice[6] proposed that a biradical like V should be formed from α-pinene and should im-

(1) T. R. Savich and L. A. Goldblatt, THIS JOURNAL, 67, 2027 (1945).

(2) R. E. Fuguitt and J. E. Hawkins, *ibid.*, 67, 242 (1945); 69, 319 (1947).

(3) R. L. Burwell, Jr., *ibid.*, 70, 2865 (1948).

(4) J. L. Simonsen, "The Terpenes," 2nd ed., Vol. I, University Press, Cambridge, 1947, p. 20.

(5) M. Szwarc and A. H. Sheon, *J. Chem. Phys.*, 18, 237 (1950).

(6) F. O. Rice and K. K. Rice, "The Aliphatic Free Radicals," The Johns Hopkins Press, Baltimore, Md., 1935, p. 164.