one pellet of potassium hydroxide in 5 ml. of absolute ethanol. After 42 hr. at 25°, the mixture was cooled in ice and scratched to induce crystallization of the product. After one recrystallization from aqueous ethanol, the orange prisms melted at 125–126°.

Anal. Calcd. for $C_{17}H_{19}NO_2$: C, 78.33; H, 5.74; N, 4.81. Found: C, 78.56; H, 5.88; N, 4.72.

Lithium aluminum hydride reduction of 1-acetyl-3-ethoxypyrrocoline. 1-Ethyl-3-ethoxypyrrocoline. A solution of 2.8 g. (13 mmoles) of 1-acetyl-3-ethoxypyrrocoline in 70 ml. of anhydrous ether was added to a suspension of 0.57 g. (15 mmoles) of lithium aluminum hydride in 50 ml. of ether. The mixture was heated at the reflux temperature for 2.5 hr., the excess hydride was destroyed cautiously with water, and the mixture was steam distilled. About 800 ml. of distillate was collected before the yellow oil stopped distilling. The layers of the distillate were separated, the aqueous layer was extracted with ether, and the organic extracts were combined, dried, and the ether was removed. The residue was distilled through a Holzman column at 147.5–152° (13 mm.) as an orange mobile liquid, yield 1.80 g. (75%).

Anal. Calcd. for $C_{12}H_{15}NO$: C, 76.15; H, 7.99; N, 7.40. Found: C, 76.46; H, 8.24; N, 8.06.

The infrared spectrum (liquid film) confirmed the complete reduction of the carbonyl function (disappearance of the band at 1645 $cm.^{-1}$ present in the spectrum of 1-acetyl-3-ethoxypyrrocoline); C—H stretching bands appeared at 3100, 2980, 2940, and 2680 $cm.^{-1}$ The ultraviolet spectrum exhibited maxima at 241 mμ (log ε 4.30), 285 (3.50), 296 (3.50), and 382 (3.17) and a well defined minimum at 291 (3.40). The other minima were broad, located approximately at 275 and 315 mμ.

Hydrolysis of 1-acetyl-3-ethoxypyrrocoline. 3-(2′-Pyridyl)-4-ketopentanoic acid hydrochloride. A solution of 0.5 g. of 1-acetyl-3-ethoxypyrrocoline and 1.0 ml. of 12*N* hydrochloric acid was warmed on the steam bath for 2 hr. The mixture was placed in a vacuum desiccator over potassium hydroxide. Crystals soon formed, which were hygroscopic, but washing with boiling chloroform removed this property, m.p. 158–167° [reported[21] 156° (dec.)].

Anal. Calcd. for $C_{10}H_{12}ClNO_3$: C, 52.20; H, 5.27; N, 6.10. Found: C, 52.21; H, 5.33; N, 6.02.

The infrared spectrum (Nujol) indicated the presence of ketone (1710 $cm.^{-1}$) and acid (1725) carbonyls, amine salt (2550), and the pyridinium grouping (1635). Additional bands were present at 1830, 1890, 1955, and 2015 $cm.^{-1}$

URBANA, ILL.

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

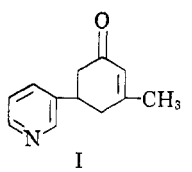
Preparation of the Pyridalacetones and the Inductive Effect of Nitrogen on the Dehydration of the Intermediate Aldols*[1]

C. S. MARVEL AND J. K. STILLE

Received April 29, 1957

The *trans*-isomers of 2-, 3-, and 4-pyridalacetone have been prepared by two synthetic approaches. The tendency for an olefin-forming elimination by the intermediate ethyl 3-hydroxy-3-pyridyl-2-acetopropionates and the 4-hydroxy-4-pyridyl-2-butanones increases as the position of substitution on the pyridine ring is changed from 2 to 3 to 4, which suggests that the inductive effect of the nitrogen plays an important role in the chemistry of these compounds.

The preparation of the pyridalacetones, which was first attempted by application of the procedures described for benzalacetone[2] and the pyridine analogs of chalcone,[3] was unsuccessful. Acid catalyzed condensations using hydrogen chloride[4] and boron fluoride[5] did not yield the desired products. In order to learn more about the properties of the pyridalacetones so that the more direct synthesis route from the pyridine aldehydes and acetone could be effected, the pyridalacetones were prepared from the ethyl pyridalacetoacetates. The synthesis was first attempted with pyridine-3-aldehyde by the method of Knoevenagel,[6] but it became apparent that even at the low temperature (−20°) or during subsequent steps a large amount of Michael addition of acetoacetic ester to ethyl 2-(3′-pyridal)acetoacetate (VII) was taking place, since distillation after the decarboxylation step yielded a 3-methyl-5-(3′-pyridyl)-Δ^2-cyclohexenone (I). (The position of the double



I

bond has not been definitely fixed in the cyclohexenone ring. It may have migrated to the Δ^5 position.) In order to avoid this side reaction, the condensation was run in an ether solution. In this manner the product crystallized as it was formed, and the ethyl 2-pyridalacetoacetates were obtained relatively free from acetoacetic ester.

* This paper is a contribution in honor of Lyndon F. Small, former Editor of the Journal.

(1) The work discussed herein was performed as a part of the polymer research project sponsored by the National Science Foundation.

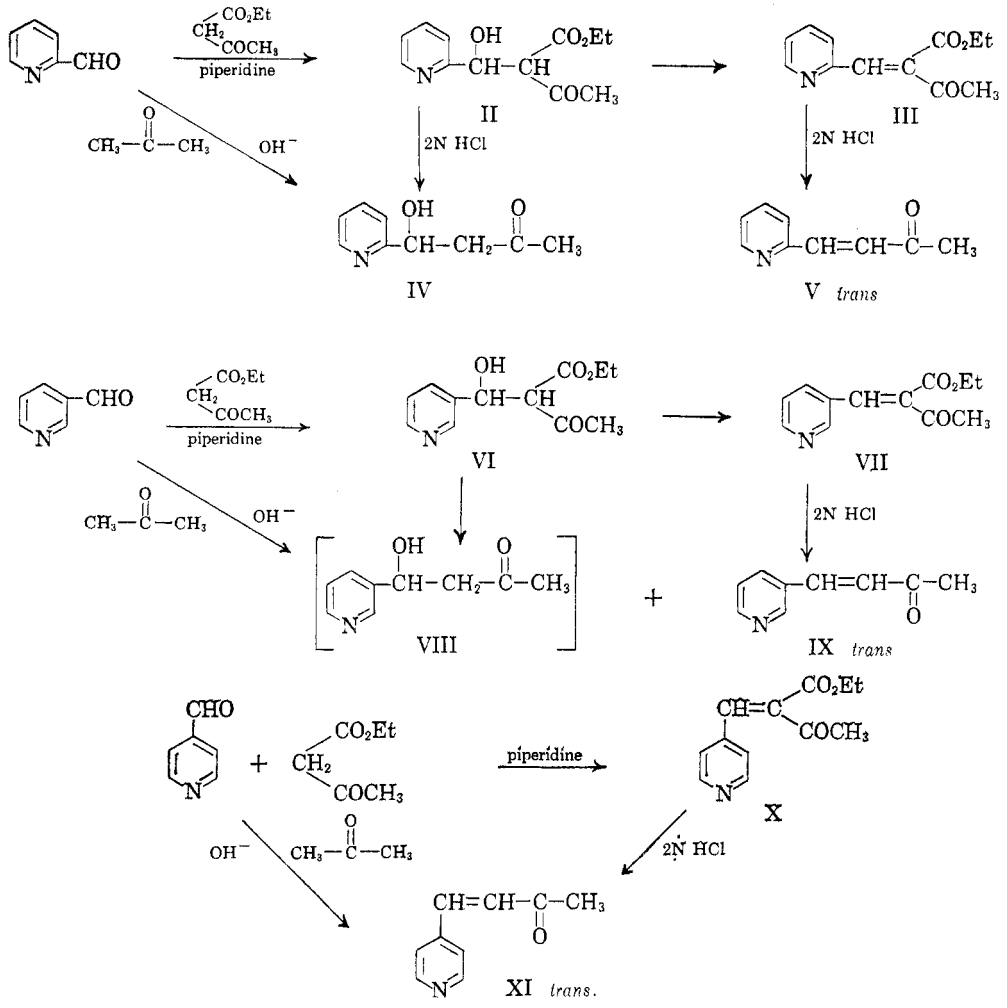
(2) N. L. Drake and P. Allen, Jr., *Org. Syntheses*, **Coll. Vol. 1**, 77, (1920).

(3) C. S. Marvel, L. E. Coleman, Jr., and G. P. Scott, *J. Org. Chem.*, **20**, 1785 (1955).

(4) R. E. Lyle and L. P. Paradis, *J. Am. Chem. Soc.*, **77**, 6667 (1955).

(5) C. S. Marvel and J. K. Stille, *J. Org. Chem.*, **21**, 1313 (1956).

(6) E. Knoevenagel, *Ber.*, **29**, 172 (1896).

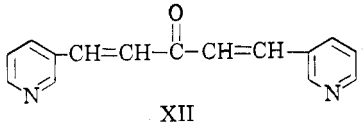


The product isolated in the reaction of pyridine-2-aldehyde was ethyl 3-hydroxy-3-(2′-pyridyl)-2-acetopropionate (II) which was found to be stable when dry and free from impurities, but it underwent an olefin-forming elimination at room temperature when in solution or in the presence of impurities to produce ethyl 2-(2′-pyridal)acetoacetate (III). The elimination is base-catalyzed, since the one step hydrolysis and decarboxylation of a mixture of II and III produced 4-hydroxy-4-(2′-pyridyl)-2-butanone (IV) and 2-pyridalacetone (V). The elimination of water from IV to yield V proved to be even more difficult. Acid catalyzed eliminations were unsuccessful and base catalysis apparently produced V which underwent further reactions to produce a mixture of products similar to the products formed from the base catalyzed condensation of pyridine-2-aldehyde and acetone at room temperature.

The reactions of pyridine-3-aldehyde were similar, yielding ethyl 3-hydroxy-3-(3′-pyridyl)-2-acetopropionate (VI), ethyl 2-(3′-pyridal) acetoacetate (VII), 4-hydroxy-4-(3′-pyridyl)-2-butanone (VIII), and 3-pyridalacetone (IX), but the elimination of water from VI and VIII proceeded with greater ease as the amount of VIII produced was considerably less than with the 2-isomer. None of the corresponding ethyl 3-hydroxy-3-(4′-pyridyl)-2-acetopropionate or 4-hydroxy-4-(4′-pyridyl)-2-butanone could be obtained, and even the infrared spectra of the crude materials failed to show the presence of these products. Apparently the elimination reaction takes place with extreme ease in this case to produce ethyl-2-(4′-pyridal)acetoacetate (X) which decarboxylates to yield 4-pyridalacetone (XI).

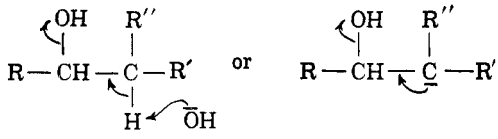
During the course of investigation of these reactions, it was learned that chloroform was the best of the few solvents which would extract the pyridalacetones from an aqueous medium, and that the reactive pyridine aldehydes required low temperatures in their base catalyzed condensation reactions. The reactions of the pyridine aldehydes with acetone were then investigated with various reaction temperatures and orders of addition of reactants and base.[3] Although the reaction of pinacolone with pyridine-2-aldehyde proceeded normally, it was found that the reaction of acetone with the pyridine aldehydes gave the best yields of products at temperatures near −20°. The previously observed elimination trends were also observed in this reaction series. Pyridine-2-aldehyde and acetone produced only IV, while pyridine-3-aldehyde and acetone gave a mixture of VIII and IX and the

4-isomer yielded only XI. Also isolated from the reaction mixture in the case of pyridine-3-aldehyde was a product which is thought to be 3,3′-dipyridalacetone (XII).



XII

The behavior of these three isomers can be conveniently explained if the inductive effect of nitrogen in the pyridine ring is considered. This effect would be that of electron withdrawal from the carbon atom bearing the hydroxyl group, and would increase as the distance from nitrogen to that carbon decreased. This effect is shown to some extent in vinylpyridines where sigma for the vinyl group has been measured.[7] Thus the elimination process becomes more difficult, whether the elimination proceeds by a concerted or an anionic mechanism. This is shown by the fact that in the case of the 4-isomer, all of the product produced is the olefin, and



R = 2, 3, or 4 pyridyl

R′ = $-\overset{O}{\overset{\|}{C}}-CH_3$

R″ = H or CO_2Et

with the 2-isomer the alcohol is a major product in the Knoevenagel condensation and the only product in the aldol condensation. This trend has been observed in the pyridalacetophenone series.[8] It would be expected then that pyridine-2-aldehyde would be the most reactive isomer of the series when the reaction is one which depends upon an electropositive carbonyl carbon. This has been previously shown in the boron fluoride catalyzed reaction of pyridine-2-aldehyde.[5] In all the reactions, the yields of products have decreased in going from the 2-isomer to the 4-isomer. This may be due either to the reactivity of the aldehyde or to the fact that the olefin formed undergoes Michael addition or further condensation with another mole of aldehyde to form a dipyridalacetone thereby reducing the yield of the desired product.

The ultraviolet spectra of the 2-, 3-, and 4-pyridalacetones are as shown in Fig. 1. These spectra are quite different from that of *trans*-benzalacetone[8] in that there is a hypsochromic shift of about 30 mμ and a hypochromic shift of 5,000 in ε from benzalacetone to pyridalacetone. Furthermore, the

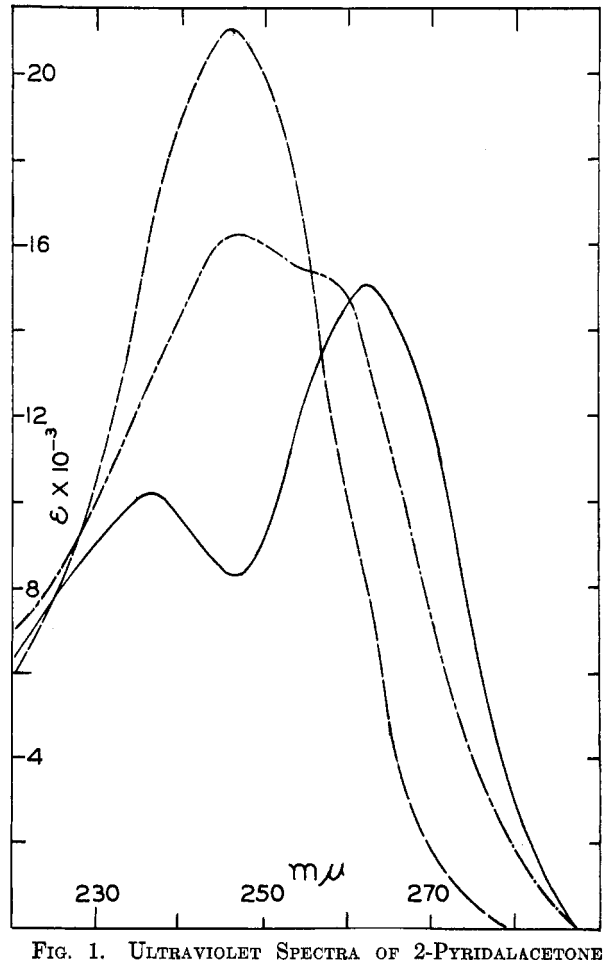


FIG. 1. ULTRAVIOLET SPECTRA OF 2-PYRIDALACETONE (—); 4-PYRIDALACETONE (— — —); AND 3-PYRIDALACETONE (— — — — —).

2- and 3-isomers give a double maximum in the 230–270 mμ region. Two maxima are also present in the ultraviolet spectra of 2-vinylpyridine,[9] 3-vinylpyridine and 3-acetylpyridine.[10] Coleman[11] has reported the ultraviolet spectra of the pyridalacetophenones and the β-pyridalacrylic acids. In these spectra the shapes of the ultraviolet absorption curves are very similar to those of the pyridalacetones. The bathochromic shift of 40 mμ from the pyridalacetones to the pyridalacetophenones might be expected, considering the relative electron-withdrawing effect of the methyl group compared with the phenyl group.[12] When the absorbing system involves the benzene ring instead of the pyridine ring, such as is the case with 2-cinnamoylpyridine, only one maximum is observed.

The absorption curves of the pyridalacetones in the 220–280 mμ region can be easily resolved as

(7) A. Pietrizky, R. Wiley, and D. McDaniel, *J. Org. Chem.*, **22**, 83 (1957).

(8) R. A. Friedel and M. Orchin, *Ultra Violet Spectra of Aromatic Compounds*, John Wiley and Sons, Inc., New York (1951).

(9) R. P. Mariella, L. F. A. Peterson, and R. C. Ferris, *J. Am. Chem. Soc.*, **70**, 1494 (1948).

(10) M. L. Swain, A. Eisner, C. F. Woodword, and B. A. Brice, *J. Am. Chem. Soc.*, **71**, 1341 (1949).

(11) L. E. Coleman, Jr., *J. Org. Chem.*, **21**, 1193 (1956) and unpublished data.

(12) H. H. Szmant and H. J. Planmsek, *J. Am. Chem. Soc.*, **76**, 1193 (1954) and earlier papers.

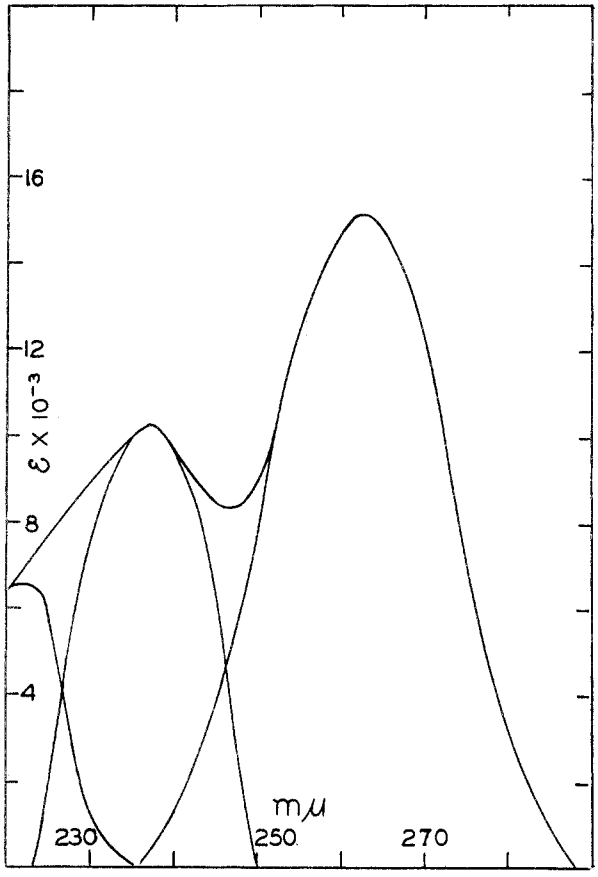


FIG. 2.—ULTRAVIOLET SPECTRUM OF 2-PYRIDALACETONE.

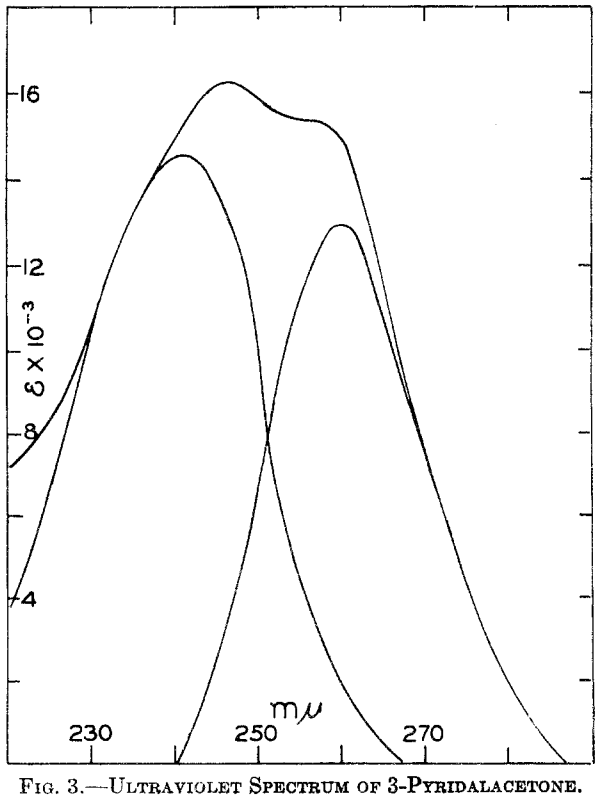


FIG. 3.—ULTRAVIOLET SPECTRUM OF 3-PYRIDALACETONE.

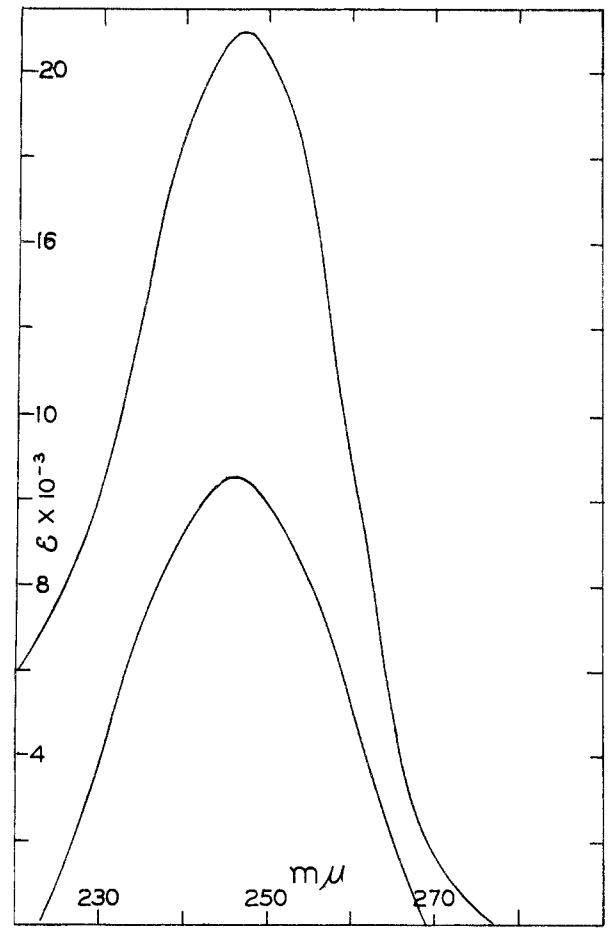


FIG. 4.—ULTRAVIOLET SPECTRUM OF 4-PYRIDALACETONE.

contributions from two absorption peaks (Fig. II–IV). It has been shown[13,14] that λ_{max} is dependent upon the length of the absorbing system, and that it is generally necessary that the excited states shall have ionic wave functions for absorption in the ultraviolet.[15] If the length of the absorbing system in the pyridalacetones can be considered to be from the carbonyl oxygen to nitrogen, it is possible that the position of the two maxima observed are due to the two possible absorption paths around the pyridine ring. Thus when the two paths are equal, as in the case of 4-pyridalacetone, only one maximum is observed. Both bathochromic and hypsochromic shifts from this maximum are noted with the 2- and 3-isomers, the largest shifts being noted with the 2-isomer where the path lengths differ the most.

EXPERIMENTAL

Ethyl 3-hydroxy-3-(2'-pyridyl)-2-acetopropionate (II). This method was developed by modification of the method of Knoevenagel[6] in order to remove the product as it was

(13) G. W. Wheland, *Resonance in Organic Chemistry*, John Wiley and Sons, Inc., New York (1955), p. 676.

(14) A. L. Wilds, L. W. Beck, W. J. Close, C. Djerassi, J. N. Johnson, Jr., T. L. Johnson, and C. H. Shunk, *J. Am. Chem. Soc.*, **69**, 1985 (1947).

(15) R. S. Mulliken, *J. Chem. Phys.*, **7**, 364 (1939).

formed, and obtain a product relatively free from difficultly removable impurities.

To 53.5 g. (0.5 mole) of pyridine-3-aldehyde[16] dissolved in 125 ml. of anhydrous ether was added a solution of 65.1 g. (0.5 mole) of ethylacetoacetate in 125 ml. of anhydrous ether. The resulting solution was cooled to −20°, and a few drops of an ether solution of piperidine were added (25 g. of piperidine in 50 g. of ether). Three such batches were prepared. The reaction mixture was allowed to stand in a deep freeze refrigerator at −20° for at least 24 hr. The white crystals which separated were removed by filtration on a Buchner funnel. A 1-g. portion of this product was removed and recrystallized from absolute ether at −20°, m.p. 54–54.5°.

Anal. Calcd. for $C_{12}H_{15}NO_4$: C, 60.76; H, 6.37; N, 5.91. Found[17]: C, 60.94; H, 6.29; N, 5.93.

The infrared spectrum (Nujol mull) exhibited absorption maxima for —OH (3170 cm.$^{-1}$), ester (1732, 1220 cm.$^{-1}$), ketone (1710 cm.$^{-1}$), and aromatic C=N and C=C (1605, 1581 cm.$^{-1}$ respectively).[18]

Ethyl 2-(2′-pyridal)acetoacetate (III). The remainder of the product was transferred to a large crystallizing dish and placed under reduced pressure (0.05 mm.) at room temperature for 24 hr. A portion of the bright yellow crystals which had formed (284 g., 86.1%) was recrystallized from cyclohexane, m.p. 115–116°.

Anal. Calcd. for $C_{12}H_{13}NO_3$: C, 65.74; H, 5.98; N, 6.39. Found: C, 65.84; H, 5.91; N, 6.50.

The infrared spectrum (Nujol mull) exhibited absorption maxima for a conjugated β-keto ester (1727 cm.$^{-1}$),[19] β-ester ketone (1667 cm.$^{-1}$), C=C (1630 cm.$^{-1}$), and aromatic C=N and C=C (1582 and 1568 cm.$^{-1}$ respectively). The infrared spectrum of the crude product showed a mixture of II and III.

4-Hydroxy-4-(2′-pyridyl)-2-butanone (IV). To 284 g. of the crude ethyl 2-(2′-pyridal)acetoacetate (III) mixed with hydrated product (II) was added 1200 ml. of 2*N* hydrochloric acid. The solution was transferred to a 2-l. round-bottomed flask fitted with a reflux condenser, at the top of which was fastened a delivery tube. The solution was heated at the reflux temperature for 30 hr., after which time the evolution of carbon dioxide had ceased. The dark solution was neutralized with 10% sodium hydroxide and extracted 12 times with 200-ml. portions of chloroform. The extracts were combined and the chloroform was removed under reduced pressure. The dark oily liquid was distilled into three fractions, the second of which (b.p. 62.5–63°/0.055 mm.) 91.95 g. (41.6%), consisted mainly of 2-pyridalacetone (V) contaminated with the hydrated product (IV). The third fraction (b.p. 78–83°/0.05 mm.) was recrystallized from ether at −20°, m.p. 75.5–76°, 30.11 g. (12.1%).

Anal. Calcd. for $C_8H_{11}NO_2$: C, 65.43; H, 6.71. Found: C, 65.29; H, 6.81.

The infrared absorption spectrum (Nujol mull) exhibited absorption maxima for OH (3110 cm.$^{-1}$), C=O (1721 cm.$^{-1}$), aromatic C=N and C=C (1603 and 1580 cm.$^{-1}$ respectively), and C—O— (1077 cm.$^{-1}$).

trans-2-Pyridalacetone (V). Attempts to separate the hydrated product (IV) from 2-pyridalacetone in the second fraction by distillation or crystallization were incomplete. Analysis of this fraction showed 13% of the material was the hydrated product (IV). In order to effect removal, 20 g. of the mixture was heated overnight on a steam bath with 5.05 g. (0.034 mole) of phthalic anhydride. The reaction flask was protected from moisture by use of a drying tube. The mixture was then neutralized with 10% potassium hydroxide and extracted with chloroform. No potassium salt of the half ester could be isolated from the aqueous layer. The chloroform was removed from the extract under reduced pressure, and the oil residue was distilled, b.p. 59–59.5/10.05 mm., to give 9 g. which represents an overall yield of 18.7%, n_D^{20} 1.5785.

Anal. Calcd. for C_9H_9NO: C, 73.44; H, 6.16. Found: C, 73.62; H, 6.32.

The infrared spectrum exhibited absorption maxima for C=O (1695, 1677 cm.$^{-1}$), C=C (1625 cm.$^{-1}$), aromatic C=N and C=C (1585 and 1568 cm.$^{-1}$ respectively), and *trans* C=C (984 cm.$^{-1}$). The two carbonyl absorption maxima were ascribed one to the carbonyl conjugated with the carbon-carbon double bond and the other to some sort of interaction of the conjugated side chain with the aromatic portion of the molecule.

4-Hydroxy-4-(2′-pyridyl)-2-butanone (IV) *from acetone and pyridine-2-aldehyde.* In order to find a more suitable method for the preparation of 2-pyridalacetone, a method was developed by modification of the method described in *Organic Syntheses*.[2] To 35 g. (0.3 mole) of pyridine-2-aldehyde, 44 g. (0.822 mole) of acetone, and 30 ml. of water mixed and cooled to −20° in a 500-ml. three-necked, round bottomed flask fitted with a motor stirrer, thermometer, and a dropping funnel, was slowly added 25 ml. of 10% sodium hydroxide so that the temperature remained at −20° during the entire course of the reaction. The addition required about 10 min. After a total time of 40 min., the reaction was stopped by neutralization with hydrochloric acid while the mixture was kept at −20°. The product was then extracted with chloroform and the chloroform was removed from the extract under reduced pressure. The paste residue was crystallized from *Skelly C* (b.p. 90–110°) yielding 20.4 g. (41.2%) white crystalline product, m.p. 76–77°. The infrared spectrum was identical to that reported above.

When this reaction was run at 0° or higher temperatures, the product was a yellow powder which could be purified neither by crystallization nor chromatography. The powder is believed to be a mixture of the Michael addition product of acetone to 2-pyridalacetone and 2,2′-dipyridal acetone (infrared). The order of addition of reactants or variations in the concentrations of the reactants did not give better results.

trans-2-Pyridalpinacolone. Since no pyridalacetone could be obtained at reaction temperatures of 0° or higher, the synthesis of 2-pyridalpinacolone was attempted to find out if it proceeded in a normal manner. A solution of 11 g. of sodium hydroxide in 100 ml. of water was cooled to 10° in a three necked 300-ml. flask. To this solution was slowly added 54 g. (0.5 mole) of pyridine-2-aldehyde followed by 25 g. (0.25 mole) of pinacolone. The solution was then allowed to come to room temperature, and was stirred for 4 hr. The bright yellow oil which formed the upper layer was separated from the aqueous layer, washed with water, and dried over magnesium sulfate. Distillation of this oil under reduced pressure yielded 20.3 g. (43.0%) of 2-pyridalpinacolone, b.p. 92°C. (0.1 mm.), n_D^{20} 1.5412.

Anal. Calcd. for $C_{12}H_{15}NO$: N, 7.40. Found: N, 7.23.

The infrared spectrum exhibited absorption maxima for C=O (1687 cm.$^{-1}$), C=C (1622 cm.$^{-1}$), aromatic C=N and C=C (1589 and 1573 cm.$^{-1}$ respectively), and C=C *trans* (995 cm.$^{-1}$).

3-Methyl-5-(3′-pyridyl)-Δ²-cyclohexenone (I). To 53.5 g. (0.5 mole) of pyridine-3-aldehyde and 65 g. (0.5 mole) of ethyl acetoacetate mixed and chilled to −5°C. was added a solution of 0.5 g. of piperidine in 1.0 g. of ethanol. The

(16) The pyridine aldehydes were obtained from Dr. F. Raschig G.M.B.H., Chem. Fabrik, Ludwigshafen, and were freshly distilled before use.

(17) The microanalyses were performed by Mr. Jozsef Nemeth, Mrs. R. Maria Benassi, Mrs. Lucy Chang, Miss Claire Higham and Mrs. Maria Stingl, University of Illinois; Clark Microanalytical Laboratory, Urbana, Ill.; and Micro-Tech. Laboratories, Skokie, Ill.

(18) The infrared spectra were determined by Mr. James Brader, Mrs. Louise Griffith and S. Portnow. The spectra were obtained from a Perkin-Elmer model 21 spectrophotometer.

(19) N. J. Leonard, H. S. Gutowsky, W. J. Middleton, and E. M. Peterson, *J. Am. Chem. Soc.*, **74**, 4070 (1952).

mixture was allowed to remain in the refrigerator at 0° for 24 hr. The reaction mixture, a liquid, was then placed under reduced pressure (0.05 mm.) at room temperature in order to remove any unreacted starting materials. To this crude product (120 g.) was added 360 ml. 2*N* hydrochloric acid and the resulting solution was heated at the reflux temperature for 12 hr., after which time the solution was neutralized with 10% sodium hydroxide. The upper oily layer which formed was distilled under reduced pressure, b.p. 111°/0.01 mm., 15.20 g. (41%), n_D^{25} 1.5632.

Anal. Calcd. for $C_{12}H_{13}NO$: C, 76.99; H, 7.00; N, 7.48. Found: C, 76.99; H, 7.22; N, 7.78.

Infrared spectrum maxima were observed at 1665 and 1637 cm.$^{-1}$

Ethyl 3-hydroxy-3-(3'-pyridyl)-2-acetopropionate (VI). The reaction using pyridine-3-aldehyde was run exactly as described for the 2-isomer, except that a total of 500 ml. of ether and 1.0 molar amounts of reactants were used. It was noted that freshly distilled pyridine-3-aldehyde must be used, and that sometimes it is necessary to seed the reaction mixture. A 5-g. portion of the crude product formed was recrystallized from 25 ml. of ether at −20°, m.p. 74°.

Anal. Calcd. for $C_{12}H_{15}NO_4$: C, 60.76; H, 6.37; N, 5.91. Found: C, 60.74; H, 6.13; N, 5.79.

The infrared spectrum exhibited absorption maxima for OH (3160 cm.$^{-1}$), C=O ester (1738 cm.$^{-1}$), C=O carbonyl (1717 cm.$^{-1}$), aromatic C=N and C=C (1604 and 1589 cm.$^{-1}$ respectively).

Ethyl 2-(3'-pyridal)acetoacetate (VII). The remaining crude product turned yellow and melted on standing. This is due to unsaturation by loss of water as confirmed by infrared analysis of the resulting liquid. The ethyl 3-hydroxy-(3-pyridyl)-2-acetopropionate is reasonably stable at room temperature, however, if it is free from impurities. A 5-g. portion of this product was distilled under reduced pressure, collecting the fraction which boiled at 93° (0.07 mm.), n_D^{25} 1.5442.

Anal. Calcd. for $C_{12}H_{13}NO_3$: C, 65.74; H, 5.98; N, 6.39. Found: C, 65.96; H, 6.31; N, 6.12.

The infrared spectrum exhibited absorption maxima for C=O conjugated ester (1725 cm.$^{-1}$), C=O conjugated ketone (1670 cm.$^{-1}$), C=C (1630 cm.$^{-1}$), aromatic C=N and C=C (1593 and 1572 cm.$^{-1}$ respectively), and —C—O— (1258 cm.$^{-1}$).

trans-3-Pyridalacetone (IX). The remaining crude product was placed under reduced pressure (0.03 mm.) at room temperature for 24 hr. in order to remove unreacted starting materials. To the 140 g. (68.6%) of crude liquid obtained was added 600 ml. of 2*N* hydrochloric acid, and the resulting solution was heated at the reflux temperature for 25 hr., after which time the evolution of CO_2 had ceased. The solution was cooled and neutralized with 431 ml. of 10% sodium hydroxide. A dark red oil of unknown composition which separated was removed, and the aqueous portion was extracted 20 times with 50-ml. portions of chloroform. The chloroform extracts were treated as described for the 2-isomer. The oil residue was distilled under reduced pressure, and the fraction boiling at 65–72° (0.05 mm.) was collected. This fraction showed mainly the desired product (infrared) contaminated with the hydrated product. The material was redistilled, b.p. 69.5–70° (0.05 mm.), yielding 17.6 g. (12.0%) n_D^{25} 1.5855.

Anal. Calcd. for C_9H_9NO: C, 73.45; H, 6.16; N, 9.52. Found: C, 73.49; H, 6.27; N, 9.27.

The infrared spectrum exhibited absorption maxima for C=O (1695 and 1678 cm.$^{-1}$ also present in the 2-isomer), C=C (1621 cm.$^{-1}$), aromatic C=N and C=C (1596 and 1577 cm.$^{-1}$ respectively), and *trans* C=C (982 cm.$^{-1}$).

trans-3-Pyridalacetone (IX) *from acetone and pyridine-3-aldehyde.* The reaction of pyridine-3-aldehyde with acetone was carried out exactly as described for the 2-isomer. The oil residue left from the chloroform extracts was distilled under reduced pressure, collecting the fraction which boiled at 68.5–70° (0.05 mm.), 12.4 g. (28%), and whose infrared spectrum was as described above. Another fraction which was collected (93°/0.05 mm.) was found to be mainly the hydrated product. In other trials in which pyridine-3-aldehyde was added to a sodium hydroxide solution of acetone, a 50–50 mixture (14% yield each) of 3-pyridal acetone and 4-hydroxy-4-(3-pyridyl)2-butanone was obtained.

TABLE I

ULTRAVIOLET ABSORPTION MAXIMA AND MOLAR EXTINCTION COEFFICIENTS OF THE PYRIDALACETONES

Isomer	Solvent	λ Å	$\epsilon \times 10^{-4}$
2	Water	2365	1.03
		2625	1.51
	Ethanol	2380	1.18
		2610	1.37
3	Water	2460	1.62
		2600	1.48
	Ethanol	2440	1.55
		2610	1.25
4	Water	2460	2.11
	Ethanol	2420	1.93

3,3'-Dipyridalacetone (XII). The residue from the previous distillation was extracted with chloroform, and the chloroform was removed under reduced pressure leaving a light brown powder. The powder was dissolved in hot *Skelly C*, and on cooling a light yellow fluffy precipitate formed. This material was reprecipitated several times yielding 0.5 g. (1.4%), m.p. 144°.

Anal. Calcd. for $C_{15}H_{12}N_2O$: C, 76.25; H, 5.12; N, 11.68. Found: C, 75.75; H, 4.84; N, 11.48.

The infrared spectrum (Nujol mull) exhibited absorption maxima for C=O (1657 cm.$^{-1}$), C=C (1628 cm.$^{-1}$), aromatic C=N and C=C (1605 and 1590 cm.$^{-1}$ respectively), and *trans* C=C (980 cm.$^{-1}$).

Ethyl 2-(4'-pyridal)acetoacetate (X). The preparation of ethyl 2-(4'-pyridal)acetoacetate was carried out as described for the other isomers, except that 3.5 molar amounts were used. The white crystalline product formed could not be identified even after several recrystallizations from ether. Of the 365 g. obtained, 5 g. was distilled (113°/0.03 mm.) yielding a light yellow liquid, n_D^{25} 1.5415.

Anal. Calcd. for $C_{12}H_{13}NO_3$: C, 65.74; H, 5.98; N, 6.39. Found: C, 65.89; H, 6.05; N, 6.67.

The product showed some anomalous infrared absorption maxima: 3400, 1727, 1710, 1675, 1635, 1600, and 1553 cm.$^{-1}$.

trans-4-Pyridalacetone (XI). The white crystals obtained above were allowed to remain at room temperature for several days, and were then placed under reduced pressure (0.05 mm.) for 48 hr. At the end of this treatment, most of the solid had turned to a yellow oil. The oil was dissolved in 1200 ml. of 2*N* hydrochloric acid, the temperature of the solution was raised to a point just below the reflux temperature (80°) for 24 hr., and finally to the reflux temperature for 12 hr., at the end of which time the evolution of carbon dioxide had ceased. A continuous extraction apparatus was used to extract the neutral solution with chloroform. The extract was worked up as described for the other two isomers, 15.6 g. (3%), b.p. 86–87° (0.05 mm.). This liquid crystallized on standing and was recrystallized from ether at −20°, m.p. 40°.

Anal. Calcd. for C_9H_9NO: C, 73.45; H, 6.16; N, 9.52. Found: C, 73.52; H, 5.92; N, 9.21.

The infrared spectrum (melt) exhibited absorption maxima for C=O (1692, weak, and 1670 cm.$^{-1}$), C=C (1622 cm.$^{-1}$), aromatic C=N and C=C (1599 and 1555 cm.$^{-1}$ respectively), and *trans* C=C (978 cm.$^{-1}$).

trans-4-Pyridalacetone (XI) *from acetone and pyridine-4-aldehyde.* The reaction of pyridine-4-aldehyde with acetone was carried out as described for the 2-isomer. After 5 drops of 10% sodium hydroxide had been added, the temperature

rose rapidly from −20° to 0°, and there was formed a mass of white solid. The reaction mixture was quickly cooled again to −20°, and the rest of the base was added slowly. The mixture turned a red-violet color after 20 min., and at the end of 30 min. the reaction was stopped by the addition of hydrochloric acid. Upon extraction with chloroform, a brown oil which was not identified separated from the aqueous phase, producing three phases. The chloroform extract was worked up in the usual manner, yielding 19.1 g. (20.7%) of a light yellow liquid, b.p. 86–87° (0.07 mm.), which crystallized on standing. This product was recrystallized from ether at −20°, m.p. 40°, with an infrared spectrum identical with that reported above.

Ultraviolet spectra.—The ultraviolet spectra of the pyridalacetones were run in water and ethanol at concentrations from 1.0×10^{-5} to 7.0×10^{-5} molar (Table I).

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Influence of a 9(11)-Double Bond on the Course and Mechanism of Alkyl-Oxygen Cleavage Reactions of Unsaturated Steroids*

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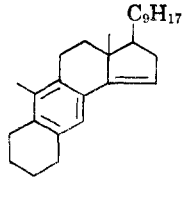
The rate of the buffered solvolysis of dehydroergosteryl tosylate was found to be slightly slower than the solvolysis rate of ergosteryl tosylate which indicates no homoallylic participation of the 9(11)-double bond in this reaction. The product of solvolysis of ergosteryl tosylate was 3,5-cyclo-7,22-ergostadien-6β-ol (XV) and not the isomeric 3,5-cyclo-6,22-ergostadien-8-ol when prepared in boiling aqueous acetone containing potassium bicarbonate. The same conditions yielded *i*-dehydroergosterol from dehydroergosteryl tosylate and the kinetic data together with the conditions of its preparation prove that the original formulation of this compound as 3,5-cyclo-7,9(11),22-ergostatrien-6β-ol (III) is correct. The failure of the 9(11)-double bond to participate in a typical homoallylic reaction makes it difficult or impossible to account for the acid-catalyzed elimination reaction of dehydroergosterol on the basis of a homoallylic mechanism. In the acid-catalyzed conversion of dehydroergosterol to 5,7,9(11),14,22-ergostapentaene (VI) the hypothesis is offered that the 5-double bond migrates first into the 4-position (I → IV) and that the dehydration proceeds by an allylic mechanism (IV → V).

The acid-catalyzed reactions of 3,5-cyclo-7,22-ergostadien-6β-ol (*i*-ergosterol, XV) and of 3,5-cyclo-7,9(11),22-ergostatrien-6β-ol (*i*-dehydroergosterol, III) in ethanol were also studied quantitatively and qualitatively. The 9(11)-dehydro compound (III) reacted *ca.* 50% faster than XV. This is considered as evidence that the 9(11)-double bond participates in allylic alkyl-oxygen cleavage to but a small extent. *i*-Ergosterol yielded *ca.* 70% of an *i*-hydrocarbon (3,5-cyclo-6,8(14),22-ergostatriene, XVI) and *ca.* 30% of ergosteryl ethyl ether while *i*-dehydroergosterol yielded *ca.* 85% of dehydroergosteryl ethyl ether (X) and *ca.* 15% of an *i*-hydrocarbon [3,5-cyclo-6,8(14),9(11),22-ergostatetraene (VIII)]. The influence of the 9(11)-double bond on the course of this acid-catalyzed reaction is interpreted, *inter alia*, as a conformational effect. Ergosteryl tosylate when submitted to hot pyridine readily underwent elimination to give the *i*-hydrocarbon, but dehydroergosteryl tosylate failed to react analogously and a conformational influence of the 9(11)-double bond is also suggested for this reaction.

Preparative conditions for obtaining 3,5-cyclo-6,8(14),22-ergostatriene and 3,5-cyclo-6,8(14),9(11),22-ergostatetraene are described.

When dehydroergosterol (I) and its derivatives undergo alkyl-oxygen cleavage at C-3, two types of initial product have been shown to arise depending on the conditions of the reaction and the nature of the esterifying group. Thus, solvolysis of the tosylate (II) in aqueous acetone leads to rearrangement and the production of a 3,5-cyclosterol (*i*-dehydroergosterol) for which structure III (3,5-cyclo-7,9(11),22-ergostatrien-6β-ol) has been suggested,[1] while treatment of the free alcohol (I) with hydrogen chloride in chloroform leads to dehydration and the formation of unrearranged hydrocarbons such as 5,7,9(11),14,22-ergostapentaene (VI),[2] which can further undergo a rearrangement to give anthraergostapentaene (VII).[3a,3b] That the anthrasteroid rearrangement[3] proceeds as

(3b) Note added in proof: A. W. Burgstahler (Abstracts of papers presented before the New York meeting of the American Chemical Society, September 8–13, 1957, page 25P) has recently achieved hydroxylation of an analog, anthracholestatetraene (W. R. Nes, R. B. Kostic and E. Mosettig, *J. Am. Chem. Soc.*, **78**, 436 (1956)), of VII with osmium tetroxide. The resulting glycol was cleaved with lead tetraacetate yielding a keto-aldehyde which underwent a reverse Michael reaction to give a tricyclic ketone which in turn on reduction with lithium aluminum hydride followed by dehydrogenation furnished 3,9-dimethylanthracene. It has previously been shown in this laboratory that the anthrasteroid rearrangement involves scission of either the C_1–C_{10} bond or the C_9–C_{11} bond.[3] Burgstahler's work establishes that the former is correct. Were the latter true, he would have obtained 2,9-dimethylanthracene. It follows from his degradation that the complete structure of VII is



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(1) R. W. Rees and C. W. Shoppee, *J. Chem. Soc.*, 3422 (1954).

(2) W. R. Nes, *J. Am. Chem. Soc.*, **78**, 193 (1956).

(3a) W. R. Nes and E. Mosettig, *J. Am. Chem. Soc.*, **75**, 2787 (1953); **76**, 3182 (1954).