of 550 ml. of concentrated hydrochloric acid and refrigeration of the solution. The weight of product, collected by filtration and dried *in vacuo*, was 5.088 g., 89.0% of that expected from the total quantity of diacetylaminoacridine used. The amount of tritium in the product was found to be 395 millicuries, 61.4% of that initially in the hydrogen gas. The chloride content, determined gravimetrically,[16] was 23.77%; the theoretical value for acriflavine hydrochloride is 23.94%. The picrate melted at 245–246°; the melting point reported[17] for the picrate of acriflavine is 244°. Analysis of product by filter paper partition chromatography, using the method of Lederer[18] modified by developing the chromatograph with *n*-octyl alcohol saturated with 1.5 *N* ammonium hydroxide, and calibrating with known mixtures, indicated the presence of 1% of proflavine.

(16) R. K. Snyder, *Bull. Natl. Formulary Comm.*, **9**, 248 (1941).

(17) A. Bolliger, *Quart. J. Pharm. and Pharmacol.*, **13**, 1 (1940).

(18) M. Lederer, *Anal. Chim. Acta*, **6**, 267 (1952).

LEMONT, ILLINOIS

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF COLUMBIA UNIVERSITY]

Studies on α-Pyridones. II. Derivatives of Pyrindine

BY FAUSTO RAMIREZ AND ALBERT P. PAUL[1]

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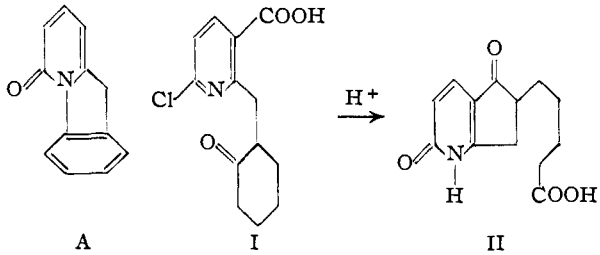
The action of mineral acids on 2-(2′-oxocyclohexyl)-methyl-6-chloronicotinic acid (I) leads to 6-(4′-carboxy)-butyl-2-hydroxy-5-oxo-6,7-dihydro-1,5H-pyrindine (II). This rearrangement, which provides a novel route to derivatives of pyrindine, is interpreted as involving the acid-catalyzed cyclization of the keto acid I to a spiro-β-diketone (C) followed by cleavage of C to the keto acid II. The structure of II follows from chemical and spectral data and is proven by an unequivocal synthesis starting from ethyl 2-bromomethyl-6-chloronicotinate. Ultraviolet absorption data of a number of α-pyridone derivatives in the pyridine and pyrindine series are provided.

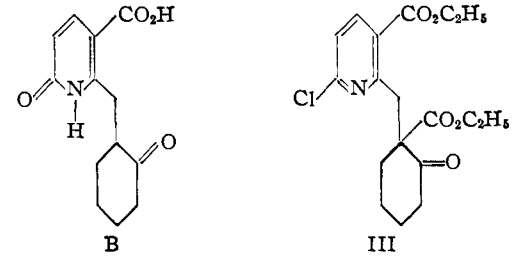
Our exploration[2] of possible routes to α-pyridone derivatives of benzo[b]pyrrocoline (A) has led us to the examination of the action of mineral acids on 2-(2′-oxocyclohexyl)-methyl-6-chloronicotinic acid (I). The present paper furnishes chemical and spectroscopic evidence for the formulation I → II



A I II

as the over-all result of the action of mineral acids on I. An interpretation of the course of this rearrangement, which provides a route to derivatives of 1,5H-pyrindine and bears on the more general question of acid catalysis in the condensation of ketones with carboxylic acids, is also presented. Some correlations between structure and ultraviolet absorption spectra among α-pyridones are discussed.

2-(2′-Oxocyclohexyl)-methyl-6-chloronicotinic acid (I) was obtained from the previously synthesized[2] ethyl 2-(1′-carbethoxy-2′-oxocyclohexyl)-methyl-6-chloronicotinate (III) by alkaline hydrolysis and decarboxylation. Ultraviolet and infrared (see Experimental) absorption spectra leave no doubt concerning the structure of this α-chloronicotinic acid derivative. I formed a 2,4-dinitrophenylhydrazone whose ultraviolet spectrum (λ_{max} 368 mμ) is fully consistent with the structure shown. The action of either 85% phosphoric acid or of a mixture of hydrochloric acid and acetic acid on I gave a high melting (m.p. 263–264°) crystalline substance of formula $C_{13}H_{15}NO_4$. It soon became apparent that a simple α-pyridone[3] formulation (B) for this ketoacid was untenable. For example, the substance formed a deep red 2,4-dinitrophenylhydrazone (λ_{max} 397 mμ) indicative of a high degree of conjugation for the hydrazone group. In view of this and of other data described below, the possibility of a deep-seated rearrangement during the acid treatment was considered and the structural hypothesis II was advanced for the substance, m.p. 263–264°.



B III

The presence of an α-pyridone structure in II was evident from its infrared spectrum showing the characteristically strong band at 6.05 μ; at this point the ultraviolet spectrum of II (Fig. 1) was of little diagnostic value due to the limited spectral-structural correlations in the α-pyridone series now in existence.[2] Esterification of the keto acid II using alcoholic hydrochloric acid gave the corresponding ethyl and methyl esters (IV and V, respectively), of ultraviolet spectra (Fig. 1) similar to that of the parent carboxylic acid. Alkylation of the sodio salt of the α-pyridone V with methyl iodide gave the N-methyl-α-pyridone VI; VI is obtainable also from the carboxylic acid II upon treatment with diazomethane in ether–methanol. This example of N-alkylation of an α-pyridone with diazomethane is of interest, inasmuch as it has been stated[4] that

(1) David W. and Ellen A. Ferguson Fellow, 1953–1954. From part of the Ph.D. Thesis of A. P. Paul.

(2) F. Ramirez and A. P. Paul, *J. Org. Chem.*, **19**, 183 (1954).

(3) The conversion of α-chloropyridines into α-pyridones by mineral acids was recently described (ref. 2).

(4) H. S. Mosher in "Heterocyclic Compounds," edited by R. C. Elderfield, John Wiley & Sons, Inc., New York, N. Y., Vol. I, p. 435, 534 (1950).

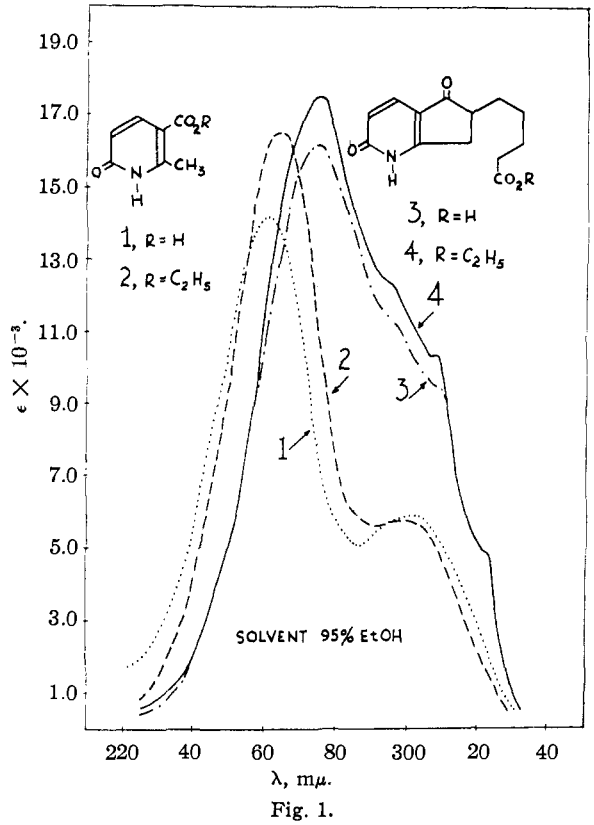


Fig. 1.

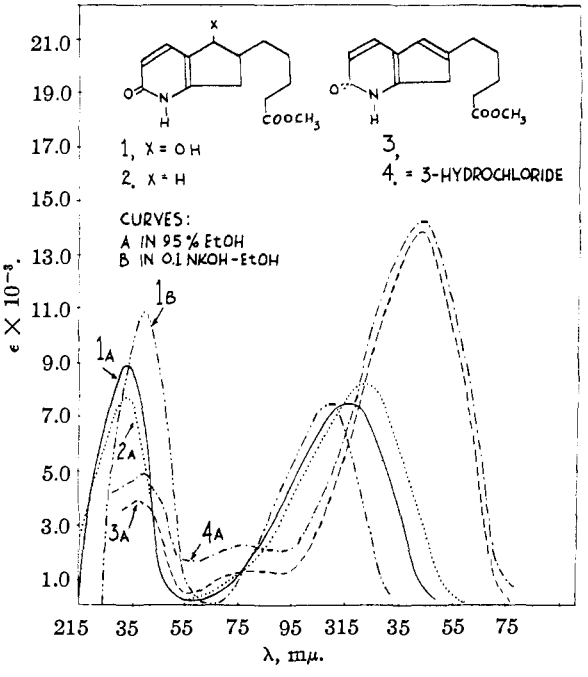
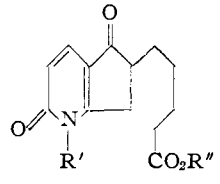


Fig. 2.

treatment of 2-hydroxypyridine with diazomethane gives only 2-methoxypyridine. A deep red 2,4-dinitrophenylhydrazone (λ_{max} 400 mμ) was also furnished by the N-alkyl-α-pyridone VI.



IV, R′ = H, R″ = C_2H_5
V, R′ = H, R″ = CH_3
VI, R′ = R″ = CH_3

Sodium borohydride reduction of the keto ester V gave a pyridone–alcohol–ester whose spectral characteristics indicated *no conjugation between the carbomethoxy group and the α-pyridone group* (*cf.* Figs. 2 and 3) a situation consistent with structure VII. Oxidation of VII with the chromium trioxide–pyridine reagent[5] gave the original ketone V. It is of interest to note that α-pyridones having an electron-attracting group in the *para*-position to the carbonyl of the pyridone (group 1) such as IV, V, VI and the simpler compounds shown in Fig. 3 differ from α-pyridones lacking such a structural feature (group 2) represented by VII, IX and the simpler compounds of Fig. 3, in two respects: (a) compounds in group 1 show markedly different ultraviolet spectra in neutral and alkaline solutions, while compounds of group 2 show fairly similar ultraviolet spectra in neutral and alkaline solutions[6]; (b) compounds of group 1 give no detectable color with ferric chloride solution while compounds of group 2 show a deep red color with ferric chloride solution as befit phenolic derivatives.

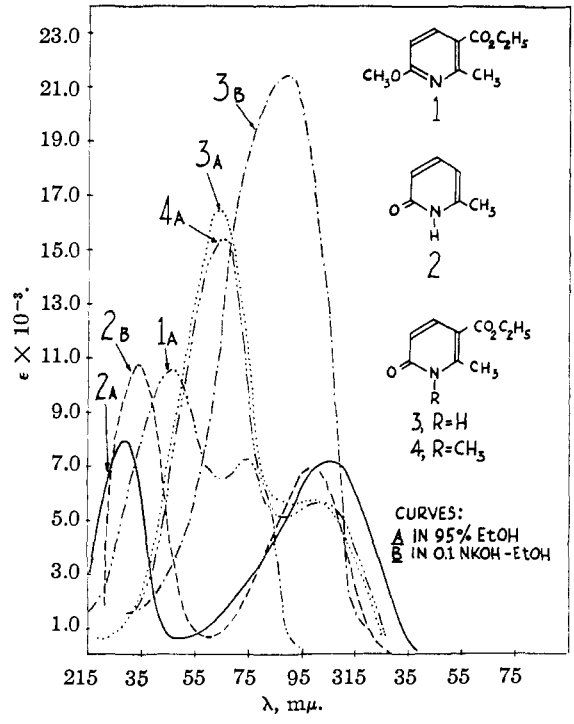
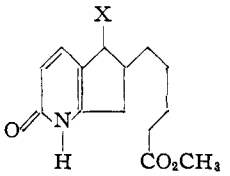


Fig. 3.

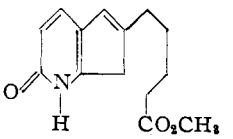
An attempt to replace the hydroxyl group of VII with chlorine (to yield VIII) by means of thionyl chloride in the presence of pyridine led to the elimination of hydrogen chloride and formation of an unsaturated pyridone X (*cf.* Fig. 2). The double bond of X can be selectively hydrogenated to yield IX without affecting the pyridone system by means of a palladium-on-charcoal catalyst.

(5) G. I. Poos, G. E. Arth, R. E. Beyler and L. H. Sarett, THIS JOURNAL, 75, 422 (1953).

(6) This observation may be of diagnostic value and reconciles contradictory statements in the literature. *Cf.* ref. 2, footnote 9.

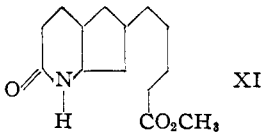


VII, X = OH
[VIII, X = Cl]
IX, X = H



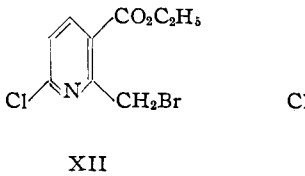
X

Catalytic hydrogenation of either the keto ester IV or the alcohol ester VII with a platinum oxide catalyst in acetic acid solution containing some hydrochloric acid proceeded smoothly to the same saturated lactam XI with absorption of four and three moles of hydrogen, respectively. In neutral alcoholic solution the pyridone ring was not attacked.

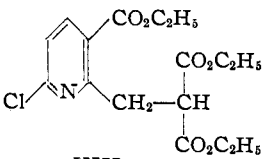


XI

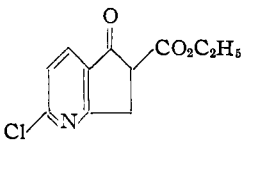
A final confirmation of the structure of II was sought and obtained by an unequivocal synthesis. Alkylation of the sodio salt of malonic ester with the previously described[2] ethyl 2-bromomethyl-6-chloronicotinate XII gave the expected triester XIII which in turn underwent smooth cyclization in the form of its sodio salt. The cyclization was accompanied by elimination of ethyl carbonate to yield the desired keto ester XIV. The cleavage of the quaternary bond during the cyclization is not unexpected and has been previously reported.[7] At this point a compound analogous to the keto pyridone acid II was prepared to furnish more information concerning structural–spectral correlations in this series. Thus, treatment of 6-carbethoxy-2-chloro-5-oxo-6,7-dihydro-1,5H-pyrindine (XIV) with phosphoric acid yielded 2-hydroxy-5-oxo-6,7-dihydro-1,5H-pyrindine (XV).



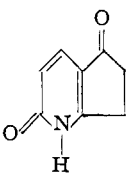
XII



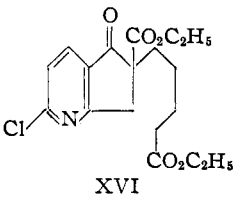
XIII



XIV



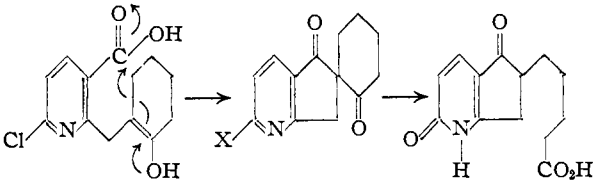
XV



XVI

Alkylation of the β-keto ester XIV with ethyl 5-iodovalerate furnished 6-carbethoxy-6-(4′-carbethoxy)-butyl-2-chloro-5-oxo-6,7-dihydro-1,5H-pyrindine (XVI), which, when submitted to phosphoric acid treatment, gave a substance identical in all respects to the previously obtained material II of m.p. 263°.

The following course is proposed for the rearrangement of I on treatment with mineral acids



I C II

The formation of the intermediate spiro-β-diketone C from the keto acid I[8] would appear to be an example of acid-catalyzed Claisen condensation, as previously observed[9] among acyclic keto acids. The opening of the β-diketone C to the keto acid II, a reversal of the previous condensation, finds an analogy in the alcoholysis of certain 1,3-diketones in the presence of hydrogen chloride studied by Adkins, Kutz and Coffman.[10]

The generality of acid-catalyzed condensations of keto acids is under investigation.

Experimental[11]

2-(2′-Oxocyclohexyl)-methyl-6-chloronicotinic Acid (I).—A mixture of 6.0 g. (0.0162 mole) of crude ethyl 2-(1′-carbethoxy-2′-oxocyclohexyl)-methyl-6-chloronicotinate (III)[2] and 28 ml. of 5% aqueous sodium hydroxide solution (1.44 g., 0.0357 mole of sodium hydroxide) was refluxed for 15 hours. The hot solution was acidified with 50% aqueous sulfuric acid to *ca.* *p*H 4, cooled and extracted with chloroform. The combined chloroform extracts were refluxed for 3 hours with Norit, filtered and dried over anhydrous sodium sulfate. The dark residue obtained upon removal of the solvent was recrystallized from ethanol–water (Norit) to give 1.46 g. (35%) of colorless crystals, m.p. 134–137°. The analytical sample of I was obtained from water as short, colorless needles, m.p. 138–139°; λ_{max}^{EtOH} 230 mμ, ε 8,310; 274 mμ, ε 4,210; 278 mμ, ε 3,600; bands at 5.88, 6.33 and 6.41 (weak) μ, and broad band in the 2.8–4.4 μ region (chloroform).

Anal. Calcd. for $C_{13}H_{14}ClNO_3$: C, 58.3; H, 5.3; N, 5.2. Found: C, 58.4; H, 5.5; N, 5.3.

The **2,4-dinitrophenylhydrazone** of I, was obtained as yellow-orange needles, m.p. 209–210°, from glacial acetic acid; λ_{max}^{Chl} 272 mμ, ε 13,800; 368 mμ, ε 21,000.

Anal. Calcd. for $C_{19}H_{18}ClN_5O_6$: C, 51.0; H, 4.1; N, 15.6; Cl, 7.9. Found: C, 51.3; H, 4.1; N, 15.7; Cl, 8.1.

Treatment of 2-(2′-Oxocyclohexyl)-methyl-6-chloronicotinic Acid (I) with Mineral Acids. 6-(4′-Carboxy)-butyl-2-hydroxy-5-oxo-6,7-dihydro-1,5H-pyrindine (II). (a).—A mixture containing 1.3 g. of I and 15 ml. of 85% phosphoric acid was heated at 185° for 30 minutes. The cooled reaction mixture was poured onto 100 g. of crushed ice and

(7) A. D. Mitchell and J. F. Thorpe, *J. Chem. Soc.*, 997, 2261 (1910).

(8) Here written as the enol as suggested (M. J. S. Dewar, "The Electronic Theory of Organic Chemistry," Oxford University Press, London, 1949, p. 126) for acid-catalyzed aldol condensations.

(9) (a) C. F. Koelsch and H. M. Walker, THIS JOURNAL, **72**, 346 (1950); (b) A. D. Campbell, C. L. Carter and S. N. Slater, *J. Chem. Soc.*, 1741 (1948).

(10) H. Adkins, W. Kutz and D. D. Coffman, THIS JOURNAL, **52**, 3212 (1930).

(11) The microanalyses were carried out by Micro-Tech Laboratories, Skokie, Ill., and Schwarzkopf Microanalytical Laboratories, Woodside, New York. The ultraviolet absorption spectra were taken in a Cary Recording Spectrophotometer, Model 11, in the solvents indicated. The infrared absorption spectra were determined in a Baird Associates, Inc., spectrophotometer. Melting points are uncorrected.

filtered to give 1.0 g. (86%) of yellow crystals, m.p. 260–263° (dec., darkens at 250°); this material was soluble in 5% aqueous sodium bicarbonate solution with gas evolution. The analytical sample of II was obtained from water as very pale yellow needles, m.p. 263–264° (dec., darkens at 255°); λ_{max}^{EtOH} 275 mμ, ε 16,100; 295 mμ, ε 11,400; 308 mμ, ε 9,500; 323 mμ, ε 4,900; bands at 5.82, 5.91, 6.13 μ, and broad band in the 3.0–4.0 μ region (Nujol mull).

Anal. Calcd. for $C_{13}H_{15}NO_4$: C, 62.6; H, 6.1; N, 5.6. Found: C, 62.9; H, 5.8; N, 5.5.

Treatment of II, in methanolic solution with the 2,4-dinitrophenylhydrazine reagent gave the **2,4-dinitrophenylhydrazone of 6-(4′-carbomethoxy)-butyl-2-hydroxy-5-oxo-6,7-dihydro-1,5H-pyrindine** (V) as deep red needles, m.p. 260° dec. (glacial acetic acid); $\lambda_{max}^{Chl.}$ 264 mμ, ε 18,400; 304 mμ, ε 11,200; 397 mμ, ε 32,600.

Anal. Calcd. for $C_{20}H_{21}N_5O_7$: C, 54.2; H, 4.8; N, 15.8. Found: C, 54.1; H, 4.8; N, 16.0.

(b).—A mixture containing 0.50 g. of I, 10 ml. of glacial acetic acid and 5 ml. of concentrated hydrochloric acid was refluxed for 2.5 hours. The solvent was removed by distillation *in vacuo*, and the dry residue was recrystallized from water (Norit) to give 0.25 g. (56%) of yellowish crystals of II, m.p. 222° dec., raised to 263–264° dec. on repeated recrystallizations from water.

(c).—II was the only product isolated when I was treated with 100% phosphoric acid or polyphosphoric acid in a manner similar to that described in part (a). The yields obtained with these reagents were 64 and 86%, respectively.

Treatment of Ethyl 2-(1′-Carbethoxy-2′-oxocyclohexyl)-methyl-6-chloronicotinate (III) with Mineral Acids. 6-(4′-Carboxy)-butyl-2-hydroxy-5-oxo-6,7-dihydro-1,5H-pyrindine (II). (a).—A stirred mixture containing 2.00 g. of III and 20 ml. of 85% phosphoric acid was heated at 185° for 30 minutes. The mixture was cooled, poured onto 120 g. of crushed ice, and filtered to give 0.60 g. (47%) of brownish crystals, m.p. 248–253° dec., whose infrared spectrum was identical to that of II previously obtained.

(b).—A mixture containing 5.0 g. of III and 15 ml. of concentrated hydrochloric acid was refluxed for 14 hours. The reaction mixture was cooled, poured onto 40 g. of crushed ice, and filtered to give 1.05 g. (32%) of yellowish crystals, m.p. 248–252° dec., whose infrared spectrum was identical to that of II.

6-(4′-Carbethoxy)-butyl-2-hydroxy-5-oxo-6,7-dihydro-1,5H-pyrindine (IV).—A mixture of 0.15 g. of II and 10 ml. of 5% ethanolic hydrochloric acid was refluxed overnight under anhydrous conditions. The solvent was removed by distillation *in vacuo*, and the residue was recrystallized from benzene–hexane (Norit) to give 0.12 g. (71%) of colorless crystals, m.p. 155–156°. The analytical sample was obtained as colorless plates, m.p. 156–157°, from benzene–hexane; λ_{max}^{EtOH} 275 mμ, ε 17,400; 296 mμ, ε 12,300; 308 mμ, ε 10,400; 323 mμ, ε 5,100; in 0.1 *N* ethanolic potassium hydroxide: λ_{max} 282 mμ (shoulder); 314 mμ, ε 24,600; 327 mμ, ε 18,800; bands at 5,82, 5.86, 6.08 (strong), 6.18, and 6.30 (weak) μ; broad band in the 3.2–3.8 μ region (chloroform).

Anal. Calcd. for $C_{15}H_{19}NO_4$: C, 64.9; H, 6.9; N, 5.0. Found: C, 64.9; H, 7.0; N, 4.4.

6-(4′-Carbomethoxy)-butyl-2-hydroxy-5-oxo-6,7-dihydro-1,5H-pyrindine (V).—A mixture of 1.98 g. of II and 25 ml. of 5% methanolic hydrochloric acid was refluxed for 12 hours under anhydrous conditions. The solvent was removed by distillation *in vacuo*, and the residue was recrystallized from methanol to give 1.43 g. (70%) of colorless crystals, m.p. 192–193°. The analytical sample was obtained from methanol as colorless plates, m.p. 193–194°; λ_{max}^{EtOH} 275 mμ, ε 17,300; 294 mμ, ε 12,400; 308 mμ, ε 10,300; 323 mμ, ε 5,200; in 0.1 *N* ethanolic potassium hydroxide: λ_{max} 282 mμ (shoulder); 315 mμ, ε 25,600; 327 mμ, ε 18,800. Bands at 5.80, 5.88, 6.08 (strong), 6.19, 6.31 (weak) μ; broad band in the 3.0–3.8 μ region (chloroform). This substance gave no color with ethanolic ferric chloride.

Anal. Calcd. for $C_{14}H_{17}NO_4$: C, 63.9; H, 6.5; N, 5.3. Found: C, 64.0; H, 6.4; N, 5.3.

The **2,4-dinitrophenylhydrazone of V** was prepared in the usual manner, melted at 258° dec. and was identical to the product obtained from II as described above.

1-Methyl-6-(4′-carbomethoxy)-butyl-2,5-dioxo-1,2,6,7-tetrahydro-1,5H-pyrindine (VI). (a).—A suspension of the pyridone acid II (0.62 g.) in 50 ml. of 1:1 ether–methanol was treated dropwise with a solution of diazomethane (*ca.* 0.6 g.) in ether (20 ml.). The mixture was allowed to stand for 30 minutes, and the solvent was removed in a current of air. The residue was recrystallized from a benzene–hexane mixture (Norit) to give 0.35 g. (58%) of cream-colored crystals, m.p. 117–118°. The analytical sample of VI was obtained from benzene–hexane as very pale, cream-colored crystals, m.p. 118–119° (sintering at 114°); λ_{max}^{EtOH} 277 mμ, ε 18,500; 295 mμ, ε 12,600; 306 mμ, ε 10,400; 320 mμ, ε 5,500; bands at 5.81, 5.88, 6.05 (strong), 6.23 (weak), and 6.37 μ (chloroform).

Anal. Calcd. for $C_{15}H_{19}NO_4$: C, 65.0; H, 6.9; N, 5.1. Found: C, 65.3; H, 7.2; N, 5.1.

The **2,4-dinitrophenylhydrazone of VI**, prepared in the usual manner, was obtained from benzene–hexane as deep red crystals, m.p. 200–203° dec., λ_{max}^{EtOH} 266 mμ, ε 17,100; 307 mμ, ε 12,000; 400 mμ, ε 31,800.

Anal. Calcd. for $C_{21}H_{23}N_5O_7$: C, 55.1; H, 5.1; N, 15.3. Found: C, 55.2; H, 5.2; N, 15.1.

(b).—The sodio salt of V was prepared from 0.30 g. of V and 0.03 g. of sodium hydride in 30 ml. of anhydrous benzene. The mixture was refluxed for 24 hours and treated dropwise, over a 30-minute period, with a solution of methyl iodide (5 ml.) in anhydrous benzene (15 ml.). After a 24 hour reflux period the mixture was poured into 200 ml. of ice-water and the organic layer was separated. The aqueous layer was extracted with chloroform, and the combined benzene and chloroform extracts were dried over anhydrous sodium sulfate. After removal of the organic solvents, the residue was recrystallized from benzene–hexane to give 0.25 g. (78%) of cream-colored crystals, m.p. 118–119° alone and mixed with previously prepared VI. The infrared spectra of both products were identical.

(c).—A mixture containing 0.50 g. V, 20 drops of methyl iodide, 0.40 g. of potassium carbonate (anhydrous, ignited), and 20 ml. of acetone was refluxed for 16 hours under anhydrous conditions. The residue remaining after removal of the solvents was treated with *ca.* 25 ml. of water and filtered to give 0.35 g. of crystalline product. From the aqueous filtrate, 0.16 g. of additional product was obtained upon chloroform extraction. The combined material gave on recrystallization 0.42 g. (80%) of VI, m.p. 118–119° whose identity was further confirmed by its infrared spectrum.

6-(4′-Carbomethoxy)-butyl-2,5-dihydroxy-6,7-dihydro-1,5H-pyrindine (VII).—To a stirred solution of sodium borohydride (0.46 g.) in 50% aqueous methanol (20 ml.) cooled in an ice-bath, there was added in small portions 1.06 g. of the ketopyridone ester V. The resulting mixture was stirred for 15 hours while being allowed to reach room temperature. At the end of this time 20 ml. of water was added, and the mixture was stirred at room temperature for 3 hours. The mixture was acidified to *p*H 5 with 10% hydrochloric acid and filtered to give 0.70 g. (66%) of colorless crystals, m.p. 168–173°. This material did not form a precipitate when treated with 2,4-dinitrophenylhydrazine reagent. The analytical sample of VII was obtained from acetonitrile as colorless plates, m.p. 152–156° (softens at 145° and effervesces at the melting point); λ_{max}^{EtOH} 233 mμ, ε 8,900; 317 mμ, ε 7,400; in 0.1 *N* ethanolic potassium hydroxide: λ_{max} 239 mμ, ε 10,800; 307 mμ, ε 7,200; bands at 3.11, 5.80, 6.09 and 6.20 μ; broad band in the 3.0–4.0 μ region (Nujol mull). The product gave a deep orange color with ethanolic ferric chloride.

Anal. Calcd. for $C_{14}H_{19}NO_4$: C, 63.4; H, 7.2; N, 5.3. Found: C, 63.2; H, 7.2; N, 5.0.

6-(4′-Carbomethoxy)-butyl-2-hydroxy-5-oxo-6,7-dihydro-1,5H-pyrindine (V) from 6-(4′-Carbomethoxy)-butyl-2,5-dihydroxy-6,7-dihydro-1,5H-pyrindine (VII).—A solution of 0.30 g. of VII in 3 ml. of pyridine was added to a mixture of 0.34 g. of chromic oxide in 3 ml. of pyridine (prepared according to the directions of Sarett). The reaction mixture was allowed to stand at room temperature for 24 hours, water was added, and the mixture was filtered to remove inorganic material. The filtrate was extracted with chloroform, and the combined chloroform extracts, after thorough washing with water, were dried over anhydrous sodium sulfate. Removal of the solvent left a residue from which 0.27 g. (90%) of V, m.p. 193–194°, was obtained after one recrystallization from methanol. Mixed m.p. and infrared spectra confirmed the identity of V.

6-(4'-Carbomethoxy)-butyl-2-hydroxy-1,7H-pyrindine Hydrochloride (X-Hydrochloride).—To a stirred suspension of the hydroxypyridone ester VII (0.50 g., 0.0019 mole) in anhydrous benzene (10 ml.) containing pyridine (0 15 g., 0.0019 mole) kept at 5–10°, was added a solution of thionyl chloride (0.44 g., 0.0038 mole) in benzene (10 ml.). The addition lasted 30 minutes. The mixture was stirred at room temperature for an additional 3-hour period and filtered. The dark crystalline material obtained was recrystallized from acetone (Norit) and yielded 0.43 g. (80%) of tan crystals, m.p. 171–175° (sinters at 108°). The analytical sample of X-hydrochloride was obtained as pale, cream-colored crystals, m.p. 171–175° (gas evolution, sinters at 108°), from acetone; λ_{max}^{EtOH} 238 mμ, ε 4,800; 244 mμ, ε 4,100 (shoulder); 277 mμ, ε 2,200; 345 mμ, ε 14,200; bands at 3.12 (weak), 5.81, and 6.10 μ (Nujol mull).

Anal. Calcd. for $C_{14}H_{18}ClNO_3$: C, 59.3; H, 6.4; N, 4.9; Cl, 12.5. Found: C, 59.6; H, 6.5; N, 5.3.

6-(4'-Carbomethoxy)-butyl-2-hydroxy-1,7H-pyrindine (X).—Two hundred mg. of X-hydrochloride was triturated with 5 ml. of 5% aqueous sodium bicarbonate; effervescence was observed during this treatment. The reaction mixture was filtered, and the residue was recrystallized from benzene–hexane to give 0.16 g. (94%) of cream-colored crystals, m.p. 146–147°. The analytical sample of X was obtained from benzene–hexane as cream-colored crystals, m.p. 147–148°; λ_{max}^{EtOH} 238 mμ, ε 3,900; 280 mμ, ε 1,200; 345 mμ, ε 13,700; bands at 5.80, 6.08, 6.22 (weak), 6.42 μ, and broad band in the 3.0–4.0 μ region (chloroform). This material gave a deep wine-red color with ethanolic ferric chloride.

Anal. Calcd. for $C_{14}H_{17}NO_3$: C, 68.0; H, 6.9; N, 5.7. Found: C, 68.7; H, 7.0; N, 5.7.

6-(4'-Carbomethoxy)-butyl-2-hydroxy-6,7-dihydro-1,5H-pyrindine (IX).—A solution of 0.102 g. of X in 10 ml. of absolute ethanol was hydrogenated at atmospheric pressure in the presence of 0.013 g. of 10% palladium-on-charcoal catalyst. A total of 7.1 ml. of hydrogen was absorbed at 23° over a 1.5-hour period. The mixture was filtered, and the solvent was evaporated on the steam-bath to yield 0.10 g. of yellowish crystals, which on recrystallization from cyclohexane afforded 0.078 g. (78%) of colorless needles, m.p. 141–142°. The analytical sample of IX was obtained from cyclohexane as short, colorless needles, m.p. 141–142°; λ_{max}^{EtOH} 233 mμ, ε 7,600; 323 mμ, ε 8,100; bands at 5.81, 6.07 (strong), 6.20 μ, and broad band in the 3.2–4.0 μ region (chloroform). This material gave a deep wine-red color with ethanolic ferric chloride.

Anal. Calcd. for $C_{14}H_{19}NO_3$: C, 67.4; H, 7.7; N, 5.6. Found: C, 67.4; H, 7.6; N, 5.4.

6-(4'-Carbomethoxy)-butyl-2-oxo-octahydro-1,5H-pyrindine (XI). **(a) From 6-(4'-Carbomethoxy)-butyl-2-hydroxy-5-oxo-6,7-dihydro-1,5H-pyrindine (V).**—A solution of 0.40 g. of V in 15 ml. of glacial acetic acid containing one drop of concentrated hydrochloric acid was hydrogenated at atmospheric pressure in the presence of platinum oxide catalyst (0.04 g.). A total of 157 ml. of hydrogen was absorbed at 27° over a 5-hour period. The reaction mixture was filtered, the solvent distilled *in vacuo*, the residue treated with 10 ml. of 5% sodium bicarbonate solution, and the mixture extracted with chloroform. The combined chloroform extracts were dried over anhydrous sodium sulfate, and distilled. The oily residue yielded on recrystallization from hexane 0.35 g. (90%) of colorless crystals, m.p. 68–70°. Repeated recrystallization from hexane gave the analytical sample of XI as short needles, m.p. 74–75°; bands at 3.13 (weak), 5.76, and 6.01 (strong) μ (carbon tetrachloride).

Anal. Calcd. for $C_{14}H_{23}NO_3$: C, 66.4; H, 9.1; N, 5.5. Found: C, 66.0; H, 8.8; N, 5.7.

(b) From 6-(4'-Carbomethoxy)-butyl-2,5-dihydroxy-6,7-dihydro-1,5H-pyrindine (VII).—A solution of 0.065 g. of VII in 10 ml. of glacial acetic acid containing one drop of concentrated hydrochloric acid was hydrogenated at atmospheric pressure, in the presence of 0.010 g. of platinum oxide catalyst. A total of 21.0 ml. of hydrogen was absorbed at 27° over a 1.5-hour period. The product was worked up as in (a) to yield 0.034 g. (52%) of XI, m.p. 72–74° (hexane).

Ethyl 2-(2',2'-Dicarbethoxy)-ethyl-6-chloronicotinate (XIII).—Ethyl 2-bromomethyl-6-chloronicotinate (XII) was prepared from 13.6 g. of ethyl 2-methyl-6-chloronicotinate, 12.2 g. of N-bromosuccinimide, 200 ml. of carbon tetrachloride and 0.10 g. of benzoyl peroxide as previously described.[3] The sodio salt of diethyl malonate was prepared by adding at room temperature over a 30-minute period a solution of 9.9 g. of diethyl malonate in 80 ml. of anhydrous benzene to a stirred suspension of 1.64 g. of sodium hydride in 120 ml. of anhydrous benzene and 40 ml. of anhydrous dimethylformamide under anhydrous conditions; the mixture was stirred for 1 hour at room temperature.

A solution of the crude bromide in 40 ml. of anhydrous benzene was added over a 0.5-hour period to the stirred mixture of the sodio salt of diethyl malonate kept at room temperature. Stirring was continued for an additional 16-hour period at room temperature. The reaction mixture was poured into 400 ml. of ice-water containing 4 ml. of concentrated hydrochloric acid. The organic layer was separated and combined with benzene extracts of the aqueous layer. The organic solvent was distilled and the remaining oil was heated at 100° (0.3 mm.) to effect the removal of diethyl malonate. The residue was recrystallized from petroleum ether (b.p. 30–60°) to give 13.30 g. of pale yellow crystals, m.p. 39–42°. From the mother liquors 2.71 g. of ethyl 2-methyl-6-chloronicotinate and 2.91 g. of additional XIII (b.p. 175° at 0.2 mm.) were obtained by distillation in a molecular still. The total yield of XIII was 16.21 g. (74%).

The analytical sample of XIII was obtained as colorless crystals, m.p. 42–43°, from petroleum ether (b.p. 30–60°); λ_{max}^{EtOH} 233 mμ, ε 11,300; 273 mμ, ε 5,200; 279 mμ, ε 4,300; bands at 5.82 (strong), 6.31 and 6.38 (weak) μ (chloroform).

Anal. Calcd. for $C_{16}H_{20}ClNO_6$: C, 53.7; H, 5.6; N, 3.9; Cl, 9.9. Found: C, 53.2; H, 5.4; N, 3.9; Cl, 9.1.

6-Carbethoxy-2-chloro-5-oxo-6,7-dihydro-1,5H-pyrindine (XIV).—To a stirred suspension of 0.12 g. of sodium hydride in 75 ml. of anhydrous benzene, was added dropwise over a 30-minute period a solution of 1.50 g. of XIII in 25 ml. of anhydrous benzene. The mixture was stirred and refluxed for 13 hours. The cooled reaction mixture was poured into 200 ml. of ice-water containing 2 ml. of concentrated hydrochloric acid. After separation of the organic layer, the aqueous layer was extracted with benzene, and the combined benzene extracts were dried over anhydrous sodium sulfate. Removal of the benzene gave a residue which was recrystallized from methanol to yield 0.72 g. (72%) of colorless crystals, m.p. 97–98°. The analytical sample of XIV was obtained as shiny, colorless needles, m.p. 97–98°, from methanol; λ_{max}^{EtOH} 239 mμ, ε 7,500; 291 mμ, ε 11,600; 297 mμ, ε 12,400; 309 mμ, ε 8,700; bands at 5.80, 5.85, 6.08 (weak), 6.19 (weak), and 6.30 μ; broad band in the 2.9–3.1 μ region (chloroform). This material gave a deep blue color with ethanolic ferric chloride.

Anal. Calcd. for $C_{11}H_{10}ClNO_3$: C, 55.1; H, 4.2; N, 5.8; Cl, 14.8. Found: C, 55.1; H, 4.4; N, 5.9; Cl, 14.7.

The **2,4-dinitrophenylhydrazone of XIV**, prepared in the usual manner, was obtained from *n*-propyl alcohol as dark orange crystals, melting and resolidifying at 149° and remelting at 174–175°; λ_{max}^{Chl} 258 mμ, ε 11,800; 314 mμ, ε 6,600; 382 mμ, ε 34,800; 326 mμ, ε 7,800.

Anal. Calcd. for $C_{17}H_{14}ClN_5O_6$: C, 48.6; H, 3.4; N, 16.7; Cl, 8.5. Found: C, 48.6; H, 3.7; N, 16.4; Cl, 8.6.

2-Hydroxy-5-oxo-6,7-dihydro-1,5H-pyrindine (XV).—A mixture containing 0.40 g. of XIV and 4 ml. of 85% phosphoric acid was heated for 30 minutes at 185°. The cooled reaction mixture was poured onto 40 g. of crushed ice, and the resulting solution after neutralization with solid sodium bicarbonate, was evaporated to dryness on the steam-bath. The residue was extracted with ethanol, from which 0.15 g. (70%) of pale yellow crystals, m.p. 288–289° dec., was obtained on concentration. The analytical sample of XV was obtained from ethanol as colorless crystals, m.p. 292–293° dec.; λ_{max}^{EtOH} 273 mμ, ε 17,900; 295 mμ, ε 11,900; 308 mμ, ε 10,000; 323 mμ, ε 5,100; in 0.1 *N* ethanolic potassium hydroxide: λ_{max} 281 mμ, ε 11,600 (shoulder); 314 mμ, ε 25,200; 325 mμ, ε 18,400; bands at 5.99, 6.12, 6.22, 6.30 μ and broad band in the 3.2–3.8 μ region (Nujol mull). The product gave no color with ethanolic ferric chloride.

Anal. Calcd. for $C_8H_7NO_2$: C, 64.4; H, 4.7; N, 9.4. Found: C, 64.5; H, 4.6; N, 9.5.

The **2,4-dinitrophenylhydrazone of XV**, prepared in the usual manner, was obtained as deep red needles, m.p. 330° dec., from glacial acetic acid. The analytical sample was

dried *in vacuo* at 125°; λ_{max}^{Chl} 264 mμ, ε 13,600; 303 mμ, ε 8,600; 395 mμ, ε 24,800.

Anal. Calcd. for $C_{14}H_{11}N_5O_5$: C, 51.1; H, 3.4; N, 21.3. Found: C, 50.8; H, 3.4; N, 21.3.

6-Carbethoxy-6-(4′-carbethoxy)-butyl-2-chloro-5-oxo-6,7-dihydro-1,5H-pyrindine (XVI).—To a solution of sodium ethoxide (prepared by dissolving 0.58 g. of sodium in 100 ml. of anhydrous ethanol) was added 6.10 g. of XIV. The mixture was heated to reflux, and a solution of 7.00 g. of ethyl 5-iodovalerate[12] in 10 ml. of absolute ethanol was added dropwise over a 0.5-hour period. The mixture was refluxed for 3.5 hours longer and the solvent was removed *in vacuo*, water was added, and the oil which separated was extracted with ether. The combined ether extracts were washed with 10% aqueous sodium hydroxide and water, and were dried over anhydrous sodium sulfate.

The combined alkaline and water washings were acidified with concentrated hydrochloric acid and extracted with ether. Removal of the solvent gave 2.58 g. of XIV, m.p. 93–96°.

The combined ether extracts from above were distilled to remove solvent and unreacted 5-iodovalerate (2.44 g., b.p. 60–65° at 0.5 mm.). The residue was submitted to a molecular distillation giving 3.42 g. of XVI at 190° (0.05 mm.). A two-stage molecular distillation (145° at 0.001 mm.) gave the analytical sample of XIV as a clear, pale yellow, mobile oil: λ_{max}^{EtOH} 238 mμ, ε 10,300; 289 mμ, ε 11,900; 297 mμ, ε 11,400; bands at 5.80, 5.85, 6.30 and 6.35 μ (chloroform).

Anal. Calcd. for $C_{18}H_{22}ClNO_5$: C, 58.8; H, 6.0; N, 3.8; Cl, 9.6. Found: C, 58.7; H, 5.8; N, 4.1; Cl, 9.9.

6-(4′-Carboxy)-butyl-2-hydroxy-5-oxo-6,7-dihydro-1,5H-pyrindine (II) from 6-Carbethoxy-6-(4′-carbethoxy)-butyl-2-chloro-5-oxo-6,7-dihydro-1,5H-pyrindine (XVI).—A mixture of 0.30 g. of XVI and 3 ml. of 85% phosphoric acid was heated at 185° for 30 minutes. The cooled reaction mixture was poured onto 18 g. of crushed ice and filtered to give 0.18 g. (90%) of pale yellow crystals, m.p. 260–261° (dec., darkens at 255°), which did not depress the melting point of II, and whose infrared spectrum was identical to that of II.

The **2,4-dinitrophenylhydrazone** of the product obtained in this experiment melted at 256–257° dec. and did not depress the melting point of the 2,4-dinitrophenylhydrazone of II.

1,6-Dimethyl-5-carbethoxy-2-pyridone (XVII) and Ethyl 2-Methyl-6-methoxynicotinate (XVIII). (a).—A mixture containing 7.24 g. of ethyl 2-methyl-6-oxynicotinate,[2] 11.36 g. of methyl iodide, 8.40 g. of potassium carbonate (anhydrous, ignited) and 50 ml. of acetone was refluxed with stirring for 16 hours. The solvent was evaporated on the steam-bath, and the residue was treated with *ca.* 50 ml. of water. The resulting mixture was extracted with chloroform, and the combined chloroform extracts were dried over anhydrous sodium sulfate. Removal of the solvent gave a residue which was recrystallized from cyclohexane to give 6.20 g. (80%) of colorless crystals, m.p. 79–80°. The analytical sample of XVII was obtained as fine, colorless needles, m.p. 80–81°, from cyclohexane; λ_{max}^{EtOH} 265 mμ, ε 15,400; 303 mμ, ε 5,600; bands at 5.88, 6.06 (strong), 6.26 (weak), and 6.50 μ, and narrow band in the 3.0–4.0 μ region (chloroform).

Anal. Calcd. for $C_{10}H_{13}NO_3$: N, 7.2. Found: N, 6.9.

The cyclohexane filtrate from above was evaporated to dryness on the steam-bath to give 1.02 g. (13%) of yellowish oil, whose infrared spectrum showed it to be the O-alkylated product XVIII. On distillation this material afforded a colorless oil, b.p. 65–67° (0.2 mm.), $n^{25}D$ 1.5107. The analytical sample of XVII was obtained as a colorless oil, $n^{25}D$ 1.5098, by a two-stage molecular distillation (bath temperature 80°, 0.4 mm.); λ_{max}^{EtOH} 247 mμ, ε 10,600; 274 mμ, ε 7,300; 282 mμ, ε 5,500; bands at 5.86, 6.25 (strong), and 6.34 (weak) μ (chloroform).

Anal. Calcd. for $C_{10}H_{13}NO_3$: N, 7.2. Found: N, 7.0.

(b).—To a stirred mixture of the sodio salt of ethyl 2-methyl-6-oxynicotinate (prepared by refluxing for 20 hours under anhydrous conditions a stirred mixture of 3.00 g. of the pyridone) and 0.44 g. of sodium hydride in 35 ml. of anhydrous benzene was added 4.0 ml. of methyl iodide over a 0.5-hour period. The reaction mixture was refluxed for 18 hours, an additional 5 ml. of methyl iodide was added and refluxing continued for 6 hours longer. The solvent and excess methyl iodide were removed by distillation *in vacuo* and the colorless residue was treated with water and extracted with chloroform. The combined chloroform extracts were washed with 10% aqueous sodium hydroxide, then water, and finally dried over anhydrous sodium sulfate. On removal of the chloroform, the residue was steam distilled, and the pot residue was extracted with ether. After drying over anhydrous magnesium sulfate, the ether was distilled to give 0.80 g. (26%) of XVII, m.p. 68–75°.

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(12) N. J. Leonard and W. E. Goode, THIS JOURNAL, **72**, 5404 (1950).

NOTES

Illumination of *cis*- and *trans*-Stilbenes in Dilute Solutions

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In connection with studies of the photochemical isomerization of *trans*-stilbene to *cis*-stilbene it was observed[1] that *cis*-stilbene itself underwent photochemical decomposition to give a product reported[1b] to have an absorption spectrum peak at 247 mμ in hexane. In the present investigation the illumination of *cis*- and *trans*-stilbene in dilute solutions with a mercury arc has been carried out and the main product has been identified as phenanthrene.

Most of the experiments were carried out on solutions of the stilbenes of concentration suitable (about 5×10^{-5} *M*) for the measurement of the high absorption peak characteristic of phenanthrene in the neighborhood of 250 mμ. From this peak (molar absorbancy index or molar extinction coefficient about 6.6×10^4) the extent of phenanthrene formation was estimated. In cyclohexane, illumination for ten minutes converted 95% of the *cis*-stilbene to phenanthrene. In 60 minutes about 70% of the *cis*-stilbene in either 95% ethyl alcohol or acetonitrile was converted to phenanthrene. No higher conversion was observed in any case on continued illumination because phenanthrene, itself, underwent a slow decomposition on illumination. In carbon tetrachloride it was evident that the phenanthrene decomposed so fast that it did not accumulate in solution. The spectrum of phenanthrene was also observed for illuminated, dilute solutions (*ca.* 5×10^{-5} *M*) of *trans*-stilbene in cyclohexane, acetonitrile and 95% ethyl alcohol. No absorption peaks characteristic of phenanthrene

(1) (a) G. N. Lewis, T. T. Magel and D. Lipkin, THIS JOURNAL, **62**, 2973 (1940); (b) A. Smakula, *Z. physik. Chem.*, **B25**, 90 (1934).