TABLE I

NITROPYRIDINECARBOXYLIC ACIDS

Group position NO_2	Group position COOH	All recryst. from water M.p., °C.	Dec. temp., °C.	Yield, %	Formula	Analyses, % Calculated Carbon	Calculated Hydrogen	Found Carbon	Found Hydrogen
3	2	105	105	45	$C_6H_4N_2O_4$	42.85	2.38	43.21	2.43
4	2	152	152	51	$C_6H_4N_2O_4$	42.85	2.38	43.12	2.72
5	2	210	212	30	$C_6H_4N_2O_4$	42.85	2.38	42.92	2.49
6	2	168	169	45	$C_6H_4N_2O_4 \cdot H_2O$	38.71	3.22	39.00	3.15
2	3	156	157	42	$C_6H_4N_2O_4$	42.85	2.38	43.07	2.43
4	3	120	120	45	$C_6H_4N_2O_4 \cdot H_2O$	38.71	3.22	39.01	3.02
5	3	172	250	40	$C_6H_4N_2O_4$	42.85	2.38	43.05	2.35
6	3	183	184	52	$C_6H_4N_2O_4$	42.85	2.38	42.85	2.54
2	4	175	177	37	$C_6H_4N_2O_4$	42.85	2.38	42.90	2.61
3	4	222	219	35	$C_6H_4N_2O_4$	42.85	2.38	42.74	2.42

scribed above for the preparation of 2-chloro-3-nitro-5-methylpyridine. There was obtained 3.5 g. (80%) of 2-chloro-3-nitro-4-methylpyridine melting at 45–47°. Recrystallization from petroleum ether gave a product melting at 46–47°. *Anal.* Calcd. for $C_6H_5N_2O_2Cl$: C, 41.71; H, 2.90. Found: C, 41.87; H, 3.25.

3-Nitro-4-methylpyridine.—2-Chloro-3-nitro-4-methylpyridine (3.25 g.) was mixed with 7 g. of benzoic acid[4] and heated to 150°. Copper powder (5 g.) was then added slowly with stirring over a period of five minutes. After stirring a short while the melt was allowed to cool and was then extracted with a mixture of chloroform and 20% sodium carbonate solution. The mixture was filtered, separated and extracted twice more with chloroform. The extracts were combined and evaporated to give 1.8 g. (70%) of 3-nitro-4-methylpyridine.

6(2)-Methyl-3(5)-nitropyridine.—2-Chloro-3-nitro-6-methylpyridine[2] (4 g.) was subjected to the same treatment[4] with benzoic acid and copper powder as described above to give 2.5 g. (80%) of 6(2)-methyl-3(5)-nitropyridine[2,3] which after recrystallization from petroleum ether melted at 107–108°.

4-Nitro-2-methylpyridine.—4-Amino-2-methylpyridine[5] (20 g.) was dissolved in 100 ml. of concentrated sulfuric acid and dropped into a mixture of 350 ml. of fuming sulfuric acid (15%) and 175 ml. of 30% hydrogen peroxide keeping the temperature at 10–20°. After the final addition, the reaction mixture was stirred one hour at 20° and then allowed to come to room temperature and stand two days. At the end of this time it was poured onto cracked ice, neutralized with sodium hydroxide and extracted with benzene. Evaporation of the solvent left 14 g. (55%) of product which after recrystallization melted at 32–34°. *Anal.* Calcd. for $C_6H_6N_2O_2$: C, 52.17; H, 4.35. Found: C, 57.80; H, 4.19.

4-Nitro-3-methylpyridine.—4-Amino-3-methylpyridine (23.5 g.) was oxidized in the manner just described for the 2-methyl isomer. There was obtained 24.5 g. (82%) of crude product which after recrystallization from petroleum ether melted at 28–29°. *Anal.* Calcd. for $C_6H_6N_2O_2$: C, 52.17; H, 4.35. Found: C, 52.27; H, 4.50.

Preparation of the Nitropyridinecarboxylic Acids.—All of the acids were prepared in the same manner, *i.e.*, 1.4 g. of the nitropicoline and 100 ml. of water were heated to 90° and treated with 3 g. of potassium permanganate over a period of one-half hour while stirring. The reaction mixture was cooled to 50° and filtered. The manganese dioxide was washed first with water and then with benzene to remove unchanged starting material and then the filtrate was extracted three times with benzene. The aqueous layer was evaporated to small volume and treated with somewhat more than the calculated amount of sulfuric acid with cooling. The crude acid was filtered and recrystallized from hot water. Ether extraction of the acid mother liquid afforded a small second crop. The yields are calculated after subtracting the amount of recovered starting material and the data are shown in Table I.

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

Condensation Reactions of Picoline 1-Oxides

BY ROGER ADAMS AND SEIJI MIYANO[1]

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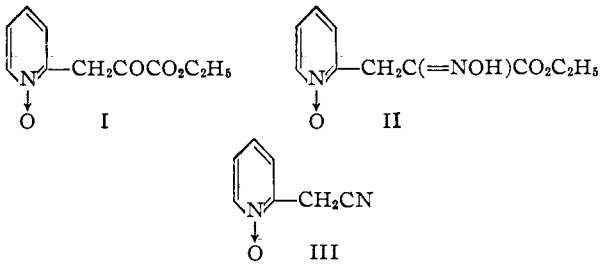
2- and 4-picoline 1-oxides and 6-benzyloxy-2-methylpyridine 1-oxide condense with ethyl oxalate to give the corresponding ethyl pyridylpyruvate 1-oxides. The pyruvates upon treatment with hydroxylamine form α-oximino derivatives which by means of alkali are converted to the corresponding acetonitriles. Peroxide in acetic acid converts the pyruvates from the 2- and 4-picoline 1-oxides to the corresponding picolinic acid 1-oxides. Peracetic acid reacts with 6-benzyloxy-2-methylpyridine 1-oxide to give a mixture of 2-picolinic acid 1-oxide and 6-benzyloxy-2-pyridylacetic acid 1-oxide. The ester of this latter compound and the 6-benzyloxy-2-methylpyridine 1-oxide upon hydrogenation or hydrolysis give the corresponding 1-hydroxy-2-pyridones.

Many reactions of 2- and 4-picoline have been known and attributed to the inherent electron-attracting nature of the ring nitrogen atom which imparts a positive character to the α-carbon atom. But neither 2-picoline[2] nor 4-picoline condenses with ethyl oxalate. Since the nitrogen oxide group should enhance the polarization, 2- and 4-picoline 1-oxides should be more reactive than the 2- and 4-picolines. This is in fact so and these oxides undergo condensation with ethyl oxalate in the presence of potassium ethoxide to give the corresponding potassium salts of the pyruvates from which ethyl 2-pyridylpyruvate 1-oxide (I) and ethyl 4-pyridylpyruvate 1-oxide are obtained upon acidification.

With hydroxylamine, the corresponding ethyl 2-(and 4)-pyridyl-(α-oximino)-propionate 1-oxides

(1) Rotary Foundation Fellow for advanced study, 1952–1953.

(2) R. Adams and A. W. Schrecker, THIS JOURNAL, **71**, 1190 (1949).

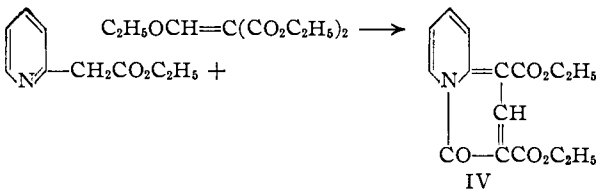


are formed (II). By aqueous alkaline hydrolysis of these followed by vacuum sublimation of the resulting products 2-(and 4)-pyridylacetonitrile 1-oxides (III) are obtained. Probably the 2-(and 4)-pyridyl-(α-oximino)-propionic acid 1-oxides are first formed and during vacuum sublimation lose carbon dioxide and water.

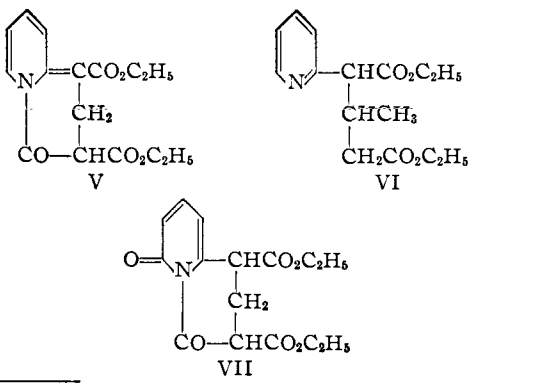
Ice-cold aqueous sodium hydroxide and 30% hydrogen peroxide convert the pyruvates (I) to 2- and 4-picoline 1-oxides. On the other hand, 30% hydrogen peroxide and acetic acid at 65–70° oxidize the pyruvates to 2- and 4-picolinic acid 1-oxides.

Although pyridine and its derivatives are usually converted merely to the corresponding nitrogen oxides upon being treated with hydrogen peroxide and acetic acid, ethyl 2-pyridylacetate is degraded simultaneously to 2-picolinic acid 1-oxide. 1,3-Dicarbethoxy-2,3-dihydro-4-quinolizone (V) and diethyl α-(2-pyridyl)-β-methylglutarate (VI) likewise yield 2-picolinic acid 1-oxide under similar conditions.

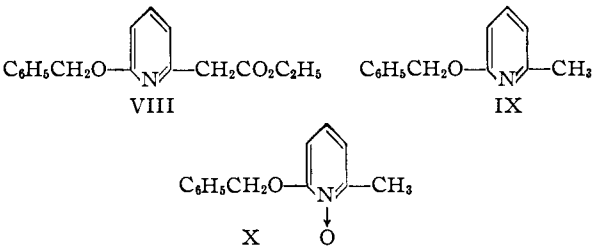
The condensation reactions just reported are of interest since they might be applied to the synthesis of a pyridone suitable for the synthesis of cytisine. Boekelheide and Lodge[3] have reported the condensation of ethyl 2-pyridylacetate and diethyl ethoxymethylenemalonate to give 1,3-dicarbethoxy-4-quinolizone (IV).



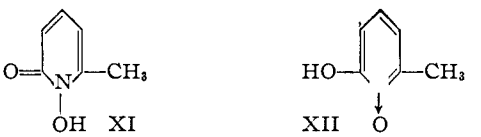
In a similar manner, we have shown that ethyl 2-pyridylacetate and ethyl methylenemalonate give 1,3-dicarbethoxy-2,3-dihydro-4-quinolizone (V), though in low yield. It was also possible to condense ethyl 2-pyridylacetate with ethyl crotonate to form diethyl α-(2-pyridyl)-β-methylglutarate (VI).



The synthesis of ethyl 6-benzyloxy-2-pyridylacetate (VIII) was undertaken since by a similar condensation followed by debenzylation and rearrangement, a product VII would be available from which cytisine might possibly be synthesized. 6-Bromo-2-methylpyridine and sodium benzyloxide react to form 6-benzyloxy-2-methylpyridine (IX) which by the action of peracetic acid is converted to its 1-oxide X.

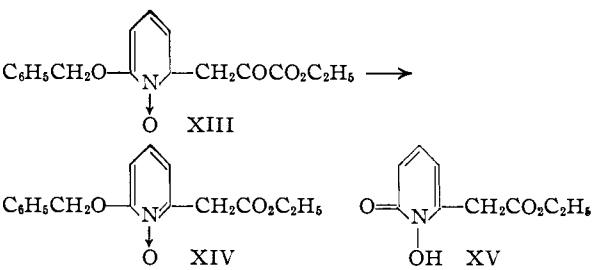


This product (X) is readily debenzylated either by hydrolysis with hydrochloric acid or by hydrogenation over a palladium catalyst with the formation of 1-hydroxy-6-methyl-2-pyridone (XI). The infrared spectrum shows a strong absorption band at 1640 cm.$^{-1}$ which indicates this as the structure rather than the tautomeric form XII. Structure



XI is also supported by the results of Shaw[4] who obtained 1-benzyloxy-2-pyridone by benzylation of 1-hydroxy-2-pyridone. Phosphorus trichloride converts X to 6-methyl-2-pyridone.

6-Benzyloxy-2-methylpyridine 1-oxide (X) with ethyl oxalate gives the corresponding pyruvate XIII. This reacts differently from the 2-(and 4)-pyridylpyruvate 1-oxide with aqueous sodium peroxide. It gives a mixture of 6-benzyloxy-2-methylpyridine and 6-benzyloxy-2-pyridylacetic acid 1-oxide which was esterified to 6-benzyloxy-2-pyridylacetate 1-oxide (XIV). Attempts to remove the N-oxide grouping by the methods usually employed failed. Elimination of the benzyl group always occurred with the formation of ethyl 1-hydroxy-2-pyridone-6-acetate (XV).

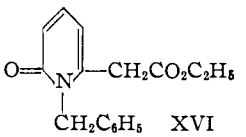


Another approach to a satisfactory intermediate for introducing a second ring between the nitrogen and 2-carbon in a pyridone is through ethyl 1-benzyl-2-pyridone-6-acetate (XVI), prepared by the

(3) V. Boekelheide and J. P. Lodge, Jr., THIS JOURNAL, 73, 3681 (1951).

(4) E. Shaw, *ibid.*, 71, 67 (1949).

action of sodium peroxide on the corresponding pyruvate followed by esterification. This product, however, could not be debenzylated by the ordinary methods.



XVI

Experimental

All melting points are corrected.

Ethyl 2-Pyridylpyruvate 1-Oxide (I).—To a solution of 8 g. of potassium in 120 ml. of absolute ethanol prepared under a stream of nitrogen and cooled to room temperature was added 20.4 g. of freshly distilled ethyl oxalate and the mixture stirred for 15 minutes. Into this, a solution of 26.4 g. of 2-picoline 1-oxide in 20 ml. of absolute ethanol was introduced dropwise. The mixture was stirred for 30 minutes and then allowed to stand for 20 hours before concentration to one-third of its volume by distillation under reduced pressure on a steam-bath. Upon addition of 25 ml. of dry benzene the potassium salt of the keto ester separated as a dense yellow powder.

The crude potassium salt was treated with 35 ml. of 10% hydrochloric acid and extracted three times with chloroform. The extract was dried over anhydrous magnesium sulfate and the solvent removed. The residual liquid solidified to yield 17.5 g. (34.6%) of yellow crystals. After recrystallization from benzene–petroleum ether (b.p. 90–110°), it formed light-yellow needles, m.p. 72–73°.

Anal. Calcd. for $C_{10}H_{11}NO_4$: C, 57.42; H, 5.26; N, 6.69. Found: C, 57.30; H, 5.10; N, 6.92.

Ethyl 2-Pyridyl-(α-oximino)-propionate 1-Oxide (II).—To a solution of 6.6 g. of crude potassium salt of ethyl 2-pyridylpyruvate 1-oxide in 32 ml. of absolute ethanol, 2 g. of hydroxylamine hydrochloride and 3.3 g. of potassium acetate were added. The mixture was refluxed for 6 hours on a steam-bath. After filtration to remove the precipitated inorganic salt, white crystals separated which weighed 2.2 g. (35.1%). The ester was recrystallized from 25% ethanol; colorless needles, m.p. 172–173°.

Anal. Calcd. for $C_{10}H_{12}N_2O_4$: C, 53.57; H, 5.36; N, 12.50. Found: C, 53.70; H, 5.23; N, 12.40.

2-Pyridylacetonitrile 1-Oxide (III).—A mixture of 1.5 g. of ethyl 2-pyridylpyruvate 1-oxide and 8 ml. of 2 *N* aqueous sodium hydroxide was refluxed for 13 hours. The yellow reaction mixture was acidified with 30% acetic acid and evaporated to dryness under reduced pressure. The residue was sublimed at 120° (1.5 mm.) to give 0.4 g. (43.9%) of colorless prisms. After resublimation they melted at 134–135°.

Anal. Calcd. for $C_7H_6NO_2$: C, 62.69; H, 4.48. Found: C, 62.63; H, 4.40.

Ethyl 4-Pyridylpyruvate 1-Oxide.—The procedure described for making ethyl 2-pyridylpyruvate 1-oxide was used. The potassium salt of the keto ester, however, separated directly from the reaction mixture and was washed with absolute ether. Acidification, then extraction with chloroform gave after evaporation of the solvent a light-yellow crystalline mass in 48% yield. It was recrystallized from acetone–petroleum ether (b.p. 90–110°); light yellow prisms, m.p. 122–123°.

Anal. Calcd. for $C_{10}H_{11}NO_4$: C, 57.42; H, 5.26; N, 6.70. Found: C, 57.73; H, 5.39; N, 6.60.

Ethyl 4-Pyridyl-(α-oximino)-propionate 1-Oxide.—The product was made in the same manner as the 2-(α-oximino)-propionate. The yield was 57.5%. The ester was recrystallized from water; colorless needles, m.p. 221–222°.

Anal. Calcd. for $C_{10}H_{12}N_2O_4$: C, 53.57; H, 5.36; N, 12.50. Found: C, 53.20; H, 5.47; N, 12.72.

4-Pyridylacetonitrile 1-Oxide.—The procedure described for making 2-pyridylacetonitrile 1-oxide was used. The product was obtained in 49.3% yield and purified by sublimation, m.p. 184–185°.

Anal. Calcd. for $C_7H_6N_2O$: C, 62.69; H, 4.48; N, 20.90. Found: C, 63.01; H, 4.56; N, 21.24.

2-Picolinic Acid 1-Oxide.—A solution of 3 g. of ethyl 2-pyridylacetate[5] in 10 ml. of 30% hydrogen peroxide and 8 ml. of acetic acid was heated to 75–80° for 10 hours. Removal of the solvent gave 1.3 g. (78.9%) of pale yellow crystals. By recrystallization from ethanol or vacuum sublimation at 120° (1 mm.), colorless needles formed, m.p. 162–163° (lit.[6] m.p. 161°).

Anal. Calcd. for $C_6H_5NO_3$: C, 51.79; H, 3.59; N, 10.10. Found: C, 52.01; H, 3.72; N, 10.22.

Ethyl 2-pyridylpyruvate 1-oxide, 1,3-dicarbethoxy-2,3-dihydro-4-quinolizone and diethyl α-(2-pyridyl)-β-methylglutarate were also converted to picolinic acid 1-oxide by the same procedure.

4-Picolinic Acid 1-Oxide.—The procedure for the oxidation of the ethyl 2-pyridylacetate to the 2-picolinic acid 1-oxide was used. The oxidation of ethyl 4-pyridylpyruvate gave a 67.6% yield of 4-picolinic acid 1-oxide which after recrystallization from methanol melted at 265–266° (lit.[7] m.p. 266°). It was identical with an authentic sample of 4-picolinic acid 1-oxide prepared by oxidation of isonicotinic acid.

6-Bromo-2-methylpyridine.—A solution of 54 g. of 6-amino-2-methylpyridine in 247 ml. of 48% hydrobromic acid was placed in an ice–salt-bath. With mechanical stirring 75 ml. of bromine was added dropwise while the temperature was kept at 0°. A solution of 85 g. of sodium nitrite in 130 ml. of water was then introduced at such a rate that the temperature of the reaction mixture did not rise above 5°. After stirring for an additional 30 minutes to complete the reaction, the dark brown solution was made alkaline by adding 190 g. of sodium hydroxide in 200 ml. of water. The light yellow reaction mixture was extracted three times with ether. The extract was dried and after removal of solvent, the product was fractionated *in vacuo*, b.p. 102–103° (20 mm.) (lit.[8] b.p. 198–201°). The yield was 68 g. (79%).

6-Benzyloxy-2-methylpyridine (IX).—To a hot solution of 31.5 g. of sodium in 490 ml. of benzyl alcohol was added dropwise 210 g. of 6-bromo-2-methylpyridine. The mixture was refluxed for 8 hours with stirring. The inorganic salt was filtered, the reaction mixture was poured into water and extracted three times with ether. The extract was dried over anhydrous magnesium sulfate, the ether removed by distillation, and the residue was fractionated. The product distilled at 166–171° (20 mm.) and weighed 144 g. (61%). It solidified to colorless prisms, m.p. 51–52° (lit.[9] m.p. 45–46°). This compound was previously made by benzylation of 6-methyl-2-pyridone but the yield was lower than by the method described above.

6-Benzyloxy-2-methylpyridine 1-Oxide (X).—To a solution of 58 g. of 6-benzyloxy-2-methylpyridine in 40 ml. of acetic acid, 58 g. of 40% peracetic acid was added carefully. The resulting mixture was heated at 55–60° for 6 hours and at 70–80° for 4 hours. After acetic acid was removed by distillation under reduced pressure, 25 ml. of 20% hydrochloric acid was poured onto the residue. The resulting solution was shaken with ether and the aqueous layer made alkaline with 30% aqueous potassium hydroxide. Brown crystals separated which were recrystallized from 35% ethanol to yield 41 g. (66%) of colorless crystals, m.p. 99–100°.

Anal. Calcd. for $C_{13}H_{13}NO_2$: C, 72.55; H, 6.05; N, 6.51. Found: C, 72.78; H, 6.11; N, 6.61.

Ethyl 6-Benzyloxy-2-pyridylpyruvate 1-Oxide (XIII).—Following the procedure used for making ethyl 2-pyridylpyruvate 1-oxide, 6-benzyloxy-2-methylpyridine 1-oxide was converted to the pyruvate. The product was obtained in 64% yield. Recrystallization from 30% ethanol gave yellow needles, m.p. 103–104°.

Anal. Calcd. for $C_{17}H_{17}NO_5$: C, 64.76; H, 5.40; N, 4.44. Found: C, 64.77; H, 5.20; N, 4.40.

Ethyl 6-Benzyloxy-2-pyridyl-(α-oximino)-propionate.—The ethyl 6-benzyloxy-2-pyridylpyruvate 1-oxide was converted to the α-oximino derivative by the method previously

(5) R. B. Woodward and E. C. Kornfeld, *Org. Syntheses*, **29**, 44 (1949).

(6) O. Diels and R. Meyer, *Ann.*, **513**, 129 (1934).

(7) E. Ghigi, *Ber.*, **75B**, 1318 (1942).

(8) H. D. T. Willink, Jr., and J. P. Wibaut, *Rec. trav. chim.*, **53**, 417 (1934).

(9) N. J. Leonard and J. H. Boyer, THIS JOURNAL, **72**, 2980 (1950).

described. The yield was 0.45 g. (69%). Recrystallization from 95% ethanol yielded colorless needles, m.p. 136–137°.

Anal. Calcd. for $C_{17}H_{18}N_2O_5$: C, 61.82; H, 5.45; N, 8.48. Found: C, 62.16; H, 5.46; N, 8.89.

6-Benzyloxy-2-pyridylacetic Acid 1-Oxide.—A mixture of 37 ml. of 10% aqueous sodium hydroxide and 19 ml. of 30% hydrogen peroxide was added carefully to 4.6 g. of ethyl 6-benzyloxy-2-pyridylpyruvate 1-oxide in an ice-bath. After standing for 36 hours the resulting solution was filtered to remove a small amount of crystalline material. Manganese dioxide was added to the filtrate to destroy the peroxide and the mixture was then filtered and acidified with 10% hydrochloric acid. Tan-colored crystals separated which were washed with ice-cold water. The yield was 1.35 g. (36%), m.p. 147–151° with effervescence. Attempts to purify the product were unsuccessful.

The small amount of crystals obtained in filtration of the original reaction mixture was purified by recrystallization from 35% ethanol, m.p. 103–104°. It proved to be 6-benzyloxy-2-methylpyridine 1-oxide. The yield was 0.81 g. (25.7%).

Ethyl 6-Benzyloxy-2-pyridylacetate 1-Oxide (XIV).—A mixture of 6 g. of crude 6-benzyloxy-2-pyridylacetic acid 1-oxide, 40 ml. of absolute ethanol and one drop of concentrated sulfuric acid was refluxed for 5 hours. After removing ethanol by distillation under reduced pressure the residue was neutralized with 20% aqueous sodium carbonate and extracted with chloroform. The extract was dried over anhydrous sodium sulfate, the chloroform removed, and a small amount of absolute ether was added to cause the residue to crystallize. The yield was 5.6 g. (67%). Recrystallization from benzene–petroleum ether (b.p. 90–110°) gave colorless needles, m.p. 55–56°. The ester sublimes at 25° (15 mm.).

Anal. Calcd. for $C_{16}H_{17}NO_4$: C, 66.90; H, 5.92; N, 4.88. Found: C, 66.76; H, 6.06; N, 4.83.

Ethyl 1-Hydroxy-2-pyridone-6-acetate (XV).—A solution of 0.45 g. of ethyl 6-benzyloxy-2-pyridylacetate 1-oxide in 20 ml. of absolute ethanol was shaken with 20 mg. of palladium catalyst (5% on charcoal). Reduction was complete in about 45 minutes. Concentration of the filtered solution gave 0.23 g. (80%) of ethyl 1-hydroxy-2-pyridone-6-acetate. Sublimation at 120° (1.0 mm.) gave small colorless prismatic needles, m.p. 128.5°–129.

Anal. Calcd. for $C_9H_{11}NO_4$: C, 54.82; H, 5.58; N, 7.46. Found: C, 55.10; H, 5.58; N, 7.69.

1-Hydroxy-6-methyl-2-pyridone (XI) (A).—A solution of 0.5 g. of 6-benzyloxy-2-methylpyridine 1-oxide in 20 ml. of absolute ethanol was shaken with 20 mg. of palladium catalyst (5% on charcoal). The reduction was complete in 40 minutes. Concentration of the filtered solution gave 0.21 g. (72.2%) of 1-hydroxy-6-methyl-2-pyridone which was purified by sublimation at 120° (3 mm.), m.p. 141–142°.

Anal. Calcd. for $C_6H_7NO_2$: C, 57.60; H, 5.60; N, 11.20. Found: C, 57.87; H, 5.65; N, 11.26.

(B).—A mixture of 2.2 g. of 6-benzyloxy-2-methylpyridine 1-oxide and 25 ml. of 15% hydrochloric acid was refluxed for 30 minutes. The reaction mixture was shaken with benzene to remove benzyl chloride and the aqueous layer was evaporated to dryness *in vacuo*. Sublimation of the residue at 120° (1 mm.) gave 0.75 g. (58.5%) of 1-hydroxy-6-methyl-2-pyridone.

Reduction and Debenzylation of 6-Benzyloxy-2-methylpyridine 1-Oxide to 6-Methyl-2-pyridone.—To 2.2 g. of 6-benzyloxy-2-methylpyridine 1-oxide (X) suspended in 20 ml. of acetic acid, 5 ml. of phosphorus trichloride was added and the mixture was refluxed for 5 hours. The reaction mixture was made alkaline by addition of aqueous sodium hydroxide and taken to dryness. Sublimation of the residue at 120° (1 mm.) gave 0.29 g. of 6-methyl-2-pyridone, m.p. 159–160°.

Attempted Oxidative Decarboxylation of Ethyl 4-Pyridylpyruvate 1-Oxide.—To an ice-cold mixture of 9 ml. of 10% aqueous sodium hydroxide and 2.8 ml. of 30% hydrogen peroxide, 2.1 g. of ethyl 4-pyridylpyruvate 1-oxide was added carefully and the mixture allowed to stand in the ice-box for 2 days. After adding powdered manganese dioxide the mixture was filtered, acidified with dilute hydrochloric acid and then extracted with three portions of 30 ml. of chloroform. After distilling off the solvent, 0.62 g. (56.8%) of colorless crystals were obtained and purified by vacuum sublimation; m.p. 183–184°. It proved to be 4-picoline 1-oxide.

Under the same conditions 1.7 g. of ethyl 2-pyridylpyruvate 1-oxide was converted to 0.38 g. (42.9%) of 2-picoline 1-oxide.

1,3-Dicarbethoxy-2,3-dihydro-4-quinolizone.—To a solution of 1.1 g. of sodium in 25 ml. of absolute ethanol was added 7 g. of ethyl 2-pyridylacetate, followed by 7 g. of ethyl methylenemalonate.[10] The mixture was refluxed for 3 hours. After acidifying with 30% acetic acid, ethanol was removed by distillation under reduced pressure and the residue was extracted 3 times with chloroform. The extract was dried over anhydrous sodium sulfate and after distillation of the chloroform the residue was fractionated *in vacuo*. Ethyl 2-pyridylacetate and ethyl methylenemalonate were recovered and 5.4 g. of dark red oil remained in the distilling flask. Yellow crystals separated and were recrystallized from 20% ethanol; yield 0.81 g. (6.5%), m.p. 120–121°.

Anal. Calcd. for $C_{15}H_{17}NO_5$: C, 61.85; H, 5.83. Found: C, 61.55; H, 5.43.

Diethyl α-(2-Pyridyl)-β-methylglutarate (VI).—To a solution of 2.14 g. of sodium in 30 ml. of absolute ethanol, 13.1 g. of ethyl 2-pyridylacetate was added, followed by 10.6 g. of ethyl crotonate. The resulting mixture was refluxed for 2 hours with mechanical stirring. After distilling the ethanol under reduced pressure, 16 ml. of 30% acetic acid was added to neutralize the residue. It was then extracted four times with chloroform. The extract was dried over anhydrous magnesium sulfate, the chloroform removed by distillation and the residue fractionated to give 13 g. (58.9% based on ethyl pyridylacetate) of pale-yellow oil, b.p. 143–145° (1.5 mm.).

Anal. Calcd. for $C_{15}H_{21}NO_4$: C, 64.52; H, 7.53; N, 5.02. Found: C, 64.73; H, 7.27; N, 5.04.

1-Benzyl-2-pyridone-6-acetic Acid.—A solution of 2.1 g. of ethyl 1-benzyl-2-pyridone-6-pyruvate[9] in a mixture of 12 ml. of 10% aqueous sodium hydroxide and 5 ml. of 30% hydrogen peroxide was kept in the ice-bath for 36 hours. Manganese dioxide was added to the resulting solution and then filtered. The filtrate was acidified with 10% hydrochloric acid. Crystals separated which weighed 0.82 g. (48.2%). Recrystallization from water gave colorless needles, m.p. 167° (with effervescence).

Anal. Calcd. for $C_{14}H_{13}NO_3$: C, 69.09; H, 5.35; N, 5.76. Found: C, 69.12; H, 5.49; N, 5.76.

Ethyl 1-Benzyl-2-pyridone-6-acetate (XVI).—A mixture of 4 g. of 1-benzyl-2-pyridone-6-acetic acid, 120 ml. of absolute ethanol and 1 ml. of concentrated sulfuric acid was refluxed for 2 hours. After removing ethanol by distillation under reduced pressure, the residue was neutralized with potassium carbonate and extracted with ether. When the ether was removed the residue crystallized. The yield was 4.2 g. (94.1%). Purified from 40% ethanol, it formed colorless prisms, m.p. 78–79°.

Anal. Calcd. for $C_{16}H_{17}NO_3$: C, 71.21; H, 6.70; N, 5.16. Found: C, 70.22; H, 6.47; N, 5.25.

In spite of the apparent purity of this product the carbon content was low in two analyses. Attempts to debenzylate with palladium-on-charcoal in neutral or acid media failed.

URBANA, ILLINOIS

(10) G. B. Bachman and H. A. Tanner, *J. Org. Chem.*, **4**, 500 (1939).