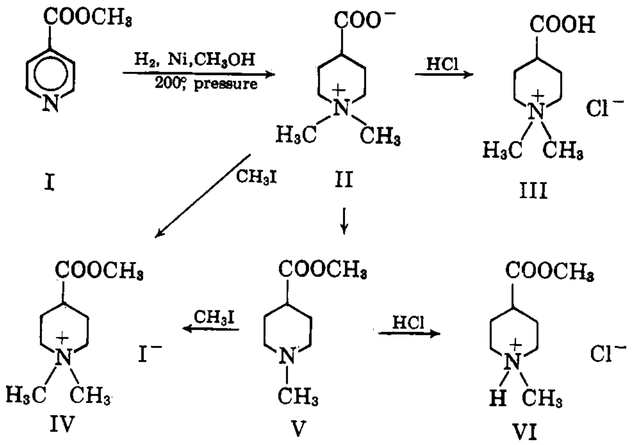
This liquid must be methyl N-methylisonipecotate (V) since V forms a methyl iodide identical with that from both an authentic sample of methyl N-methylisonipecotate and the solid betaine II. Likewise V yields a hydrochloride different from the hydrochloride of II.



While the attack of amines by alcohol solvents in hydrogenation reactions is a well established reaction,[2,3] the alkylation of nitrogen with an alkyl fragment from an ester is less expected. The ready alkylation of simple piperidines with alcohols ar 200° by Raney nickel has been reported.[3] The formation of alkyl N-alkylisonipecotates would be expected to be the predominant reaction under the conditions we have described as leading to a betaine. The formation of ethyl N-ethylnipecotate has been reported from the reduction of ethyl nicotinate with Raney nickel in ethanol.[2] No mention was made in the report of betaine formation.

Some generality of betaine formation from amino esters is suggested by the reduction of I to II in ethanol which gave a solid, very impure, but with the solubility characteristics of II. The presence of methanol is thus not essential to betaine formation, although methanol has been reported to be an inhibitor of some hydrogenation reactions.[4] Also, the reported hydrogenation of methyl isonicotinate in methanol with ruthenium proceeds nicely at 100—150° to yield methyl isonipecotate,[5] while our results indicate that if the temperature is allowed to rise to 200° some betaine formation is observed.

Several possible mechanisms are being investigated as well as the applications of this reaction.

Experimental[6]

1,1-Dimethyl-4-carboxypiperidine Betaine (II).—Methyl isonicotinate (137.1 g., 1.0 mole) was dissolved in 100 ml. of absolute methanol and treated with about 10 g. of W-2 Raney nickel and hydrogen at 1000–1500 lb./in.² pressure in an Aminco shaking pressure apparatus. Hydrogen uptake began at 150°; the temperature was maintained at 175–200° until hydrogen absorption ceased (6 hr.). The cooled reaction mixture was filtered free of catalyst and evaporated in a rotating vacuum evaporator to a pasty mass. Treatment of this mass with acetone resulted in a copious precipitate which when filtered and dried in a vacuum desiccator weighed 137.8 g. (87.5%). The material is extremely hygroscopic. After drying over phosphorus pentoxide for 48 hr., the material decomposed at 259–260°.

Elemental analyses were completely irreproducible.

1,1-Dimethyl-4-carboxypiperidinium Chloride (III).—This compound was prepared by dissolving II in concentrated aqueous hydrochloric acid, evaporating first in a stream of air and then in a vacuum desiccator over potassium hydroxide and finally recrystallizing from ethanol–ether. The pure material melted at 244–245°.

Anal. Calcd. for $C_8H_{16}NO_2Cl$: C, 49.61; H, 8.33; N, 7.23. Found: C, 49.58; H, 8.12; N, 7.11.

Methyl N-Methylisonipecotate (V).—Crude II was heated in a distilling flask immersed in a silicone fluid bath at 270–280° whereupon the product slowly distilled. The distillate was dissolved in ether, dried with sodium sulfate, and redistilled to yield a clear, colorless oil boiling at 200–202°.

This material was also synthesized by the methylation of methyl isonipecotate with formaldehyde and formic acid according to the procedure used by Hanby and Rydon for the methylation of diethanolamine.[7] The product, after working up in the usual manner, boiled at 200–202° and displayed an infrared spectrum superimposable on that of the same compound prepared by the thermal rearrangement of II.

Anal. Calcd. for $C_8H_{15}NO_2$: C, 61.12; H, 9.62; N, 8.61. Found: C, 60.69; H, 9.61; N, 8.96.

Methyl Isonipecotate.—This ester was prepared according to the procedure of Freifelder and Stone.[5]

1,1-Dimethyl-4-carbomethoxypiperidinium Iodide (IV).—This compound was prepared according to identical procedures from II or V (V in turn prepared by two methods). The starting material was dissolved in anhydrous methanol and excess methyl iodide added. The solution was then evaporated to dryness in a vacuum and the solid recrystallized from ethanol–ether: from II, m.p. 145–148°; from V by way of authentic methyl isonipecotate, m.p. 149–150°; from V by way of rearrangement of II, m.p. 150–152°; lit.[8] m.p., 147–148°. The infrared spectra of all three samples described are superimposable. The compound prepared from V by way of rearrangement of II was analyzed.

Anal. Calcd. for $C_9H_{18}NO_2I$: C, 36.30; H, 6.04; N, 4.67. Found: C, 36.34; H, 5.92; N, 4.60.

1-Methyl-4-carbomethoxypiperidine Hydrochloride (VI).—Hydrogen chloride was slowly bubbled through a cold solution of V (prepared by rearrangement of II) in anhydrous ether. The precipitated salt was filtered and recrystallized from ethanol–ether to yield colorless crystals melting at 193–195°, lit.[9] m.p. 193°.

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(2) H. Adkins, L. F. Kuick, M. Farlow, and B. Wojcik, *J. Am. Chem. Soc.*, **56**, 2425 (1934).

(3) C. F. Winans, and H. Adkins, *ibid.*, **54**, 306 (1932).

(4) K. Folkers, and H. Adkins, *ibid.*, **54**, 1145 (1932).

(5) M. Freifelder, and G. R. Stone, *J. Org. Chem.*, **26**, 3805 (1961).

(6) Infrared spectra were obtained on a Perkin-Elmer Infracord. Melting points were uncorrected and were obtained in sealed capillaries in a Mel-Temp apparatus. Microanalyses were performed by Alfred Bernhardt, Max-Planck Institute für Kohlenforschung, Mulheim, Ruhr, Germany.

(7) W. E. Hanby, and H. N. Rydon, *J. Chem. Soc.*, 513 (1947).

(8) R. E. Lyle, E. F. Perlowski, H. J. Troscianiec, and G. G. Lyle, *J. Org. Chem.*, **20**, 1761 (1955).

(9) Beilstein, "Handbuch der Chemie," Vol. XXII (1), 1935, p. 486.

The Reaction of Calcium with Pyridine and Its Methyl Derivatives[1]

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We have found that calcium reacts with pyridine and its methyl derivatives to form deeply colored, highly reactive, nonvolatile, insoluble, thermally unstable products. Although these properties prevented purification and thoroughly adequate characterization, we

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(1) Taken from the dissertation submitted to the University of Iowa by A. R. U. in partial fulfillment of the requirements for a Ph.D. degree, 1963.

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were able to collect interesting data about these novel substances, and report them here.

The reaction of pyridine with calcium directly is extremely slow, even at 115°. In contrast, at temperatures well below −34° pyridine reacts almost instantaneously with a solution of calcium in liquid ammonia, rapidly destroying its characteristic blue color and forming a dark green precipitate. No appreciable quantity of hydrogen is evolved. When one mole of pyridine per mole of calcium is added, the blue color of the solution disappears completely, and no further change is observed on addition of more pyridine. There is, however, a difference in the composition of the nonvolatile residue after extended evacuation. The 1:1 reaction leaves a green solid of empirical composition $Ca(C_5H_5N)(NH_3)$. When two or more moles of pyridine per mole of calcium are used, the product is black and has the formula, after evacuation at 0°, $Ca(C_5H_5N)_2$. When heated with a large excess of pyridine, this precipitate dissolves forming a deep blue solution, from which the black solid reprecipitates on cooling. With this exception, these products appeared to be insoluble in common solvents.

The material of composition $Ca(C_5H_5N)(NH_3)$ very slowly loses both ammonia and pyridine when heated under vacuum at 90°, changing in 20 hr. to a composition approximating $Ca(C_5H_5N)_{0.8}(NH_3)_{0.6}$. The material of composition $Ca(C_5H_5N)_2$ very slowly loses pyridine at 25° *in vacuo* and after 20–30 hr. at 110° is converted to black $Ca(C_5H_5N)$. Thermal decomposition of both $Ca(C_5H_5N)(NH_3)$ and $Ca(C_5H_5N)$ *in vacuo* up to 360° liberated only traces of pyridine or other volatile products, including a small amount of colorless crystalline sublimate identified as 4,4′-dipyridyl. Most of the material remained nonvolatile.

In air the calcium–pyridine products became very hot, evolving smoke, and usually becoming incandescent. They reacted vigorously with water, liberating only 2–5% of the theoretical hydrogen, and only about one-fourth of the original pyridine. Another fourth remained as insoluble organic residue with the calcium hydroxide, and the remaining half could be extracted from the hydrolysis products with hydrochloric acid or ether. The ether extract was isolated as an orange oil that rapidly became insoluble in all common solvents. Combustion analysis of the oil gave varying results from different preparations, approximating $C_5H_{7-9}NO$, suggesting a probably polymeric, partially hydrogenated pyridine oxide or hydrate. The hydrolysis evidently consisted of a complex set of reactions. The absence of much hydrogen was probably the result of easy ring hydrogenation, and the partially hydrogenated pyridines are known to be very unstable.[4]

Substances of similar physical and chemical properties were prepared from methyl pyridines, as summarized in Table I.

A very limited amount of light on the nature of these products is provided by some possibly similar sodium–pyridine compounds studied by Emmert[5] and by LeBeau and Picon.[6] Emmert postulated for $Na(C_5H_5N)$ that it was actually dimeric, for hydrolysis followed by air oxidation produced good yields of 4,4′-dipyridyl, and more recently electron spin resonance studies by Ward[7] tend to support this suggestion. However, Emmert also obtained an unstable yellow hydrolysis product, and LeBeau and Picon likewise, resembling somewhat the initially either soluble product of the hydrolysis of the calcium compounds. In the calcium work we found no dipyridyls in the hydrolysis products.

TABLE I

CALCIUM–PYRIDINE PRODUCTS

Reagent (R)	Empirical formula[a]	Color	Air reactivity[b]
Pyridine	CaRA	Green	M
	CaR_2	Black	M
	CaR	Black	M
2-Picoline	CaRA	Green	M
	$CaR_{1.46}$	Royal blue	
	CaR_2	Royal blue	M
	$CaR_{0.88}$	Black	M
3-Picoline	CaRA	Red-brown	M
	$CaR_{1.91}$	Green	
	$CaR_{0.86}$	Green-black	M
4-Picoline	CaRA	Tan	M
	CaR_2	Brown	
	CaR	Black	M
2,6-Lutidine	$CaR_{0.80}A_{0.69}$	Light green	H
	CaR	Blue	H

[a] A = NH_3. [b] H = high reactivity, incandescence, sometimes throwing off sparks; M = medium reactivity, immediate color change with evolution of heat and smoke, sometimes setting fire to paper in contact with it.

Experimental

Reagents.—Calcium metal was about 98% pure electrolytic lump from Fisher Scientific Co. Spectrographic analysis showed the major impurities to be Mg and Sr, with minor amounts of Mn, Al, and Cu, and only a trace of Fe. It was granulated in an inert atmosphere (drybox) immediately before use. Pyridine was Mallinckrodt reagent grade stored over potassium hydroxide and refluxed over barium oxide prior to distillation for use. Picolines, lutidine, and collidine were Eastman products similarly treated before use.

Apparatus and General Procedure.—The reaction vessel was a 100-ml. flask with two vertical side arms to permit immersion in a dewar flask. These were fitted with stopcocks. This vessel was provided with a magnetic stirring bar, evacuated, and weighed. Calcium (0.4 to 0.8 g., 10–20 mg.-atoms) was added in an atmosphere of dry oxygen-free nitrogen or helium. The vessel was evacuated again and reweighed, to determine calcium by difference. It was then cooled to −80° and dried ammonia led in until about 60 ml. of liquid was collected, giving a solution about 0.2–0.4 *M*. The pyridine was added through a microburet, determining its weight from the volume and density. The cooling bath was then removed and the reaction mixture stirred while permitting the ammonia to vaporize and leave the flask, to be absorbed in water and carry any hydrogen into a buret. When essentially all excess ammonia had evaporated (requiring about 2 hr.), the exit line was connected to a vacuum pump through two traps cooled to −196°. Evacuation was continued, with periodic weighings of flask and contents (usually 15–30 hr.) until the rate of weight loss had leveled off to a very low value, less than 0.2% (2 mg.) per hour. The composition of the nonvolatile residue was determined from the weight of the flask contents, the weights of calcium and pyridine used, and from analysis of the trap contents. These were taken up in dilute hydrochloric acid and analyzed by use of a Cary ultraviolet Model 11 recording spectrophotometer.

Samples of the nonvolatile solid product were removed in oxygen-free dry nitrogen or helium in the drybox and tested for solubility, and taken from the box for observing the action of air

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[4] E. Klingsberg, "The Chemistry of Heterocyclic Compounds," Interscience Publishers, Inc., New York, N. Y., 1960, p. 77.

[5] B. Emmert, *Ber.*, **47**, 2598 (1914); **49**, 1060 (1916); **50**, 31 (1917); B. Emmert and R. Buchert, *ibid.*, **54B**, 204 (1921).

[6] LeBeau and M. Picon, *Com t. rend.*, **173**, 1178 (1921); *Bull soc. chim. France*, **31**, 181 (1922).

[7] R. Ward, *J. Am. Chem. Soc.*, **83**, 3623 (1961).

or water. Hydrolysis was carried out either by placing the sample directly in water or dilute hydrochloric acid, or by adding it to a mixture of 40 ml. of ether and 10 ml. of 95% ethanol in a nitrogen atmosphere, stirring for 25 min., and adding 5 ml. of water.

Calcium–Pyridine, 1:1.—Compositions of products of five reactions, C_5H_5N per Ca, were 1.00, 1.00, 0.96, 0.98, 1.00; NH_3 1.01, 1.07, 0.91, 0.79, 0.98; av. $Ca(C_5H_5N)_{0.99}(NH_3)_{0.95}$. Only traces of hydrogen were formed. Combustion analysis of four yellow insoluble hydrolysis products were C, 57.79, 59.02, 67.88, 60.76; H, 7.74, 8.43, 8.05, 7.40; N, 9.72, 11.22, 13.27, 11.28; O (by difference), 24.75, 21.33, 10.80, 20.56; av. empirical formula, $C_5H_{7.7}N_{0.8}O_{1.2}$. Evacuation of two original products at 90° for 20 hr. left empirical compositions, $Ca(C_5H_5N)_{0.81}(NH_3)_{0.63}$ and $Ca(C_5H_5N)_{0.80}(NH_3)_{0.49}$.

Calcium–Pyridine, 1:2 (or More).—Compositions of products of ten reactions, when evacuated at 30°, were $Ca(C_5H_5N)_{1-2}$. Only traces of hydrogen were produced. Evacuation at 0° left $Ca(C_5H_5N)_{2.08}$ and $Ca(C_5H_5N)_{2.21}$ in two preparations. Evacuation at 110° for 20–30 hr. produced, in three preparations- $Ca(C_5H_5N)_{0.84}$, $Ca(C_5H_5N)_{1.12}$, and $Ca(C_5H_5N)_{1.06}$ These ma, terials smoked in air and changed from black to tan. Hydrolysis by ether–alcohol–water gave a semisolid yellow product; combustion analyses: C, 68.61; H, 6.28; N, 10.29; O, 14.82. Decomposition of $Ca(C_5H_5N)$ at 110–360° produced a very small amount of sublimate, 4,4′-dipyridyl, identified by infrared spectrum, m.p. 108° (lit. m.p. 112°), and combustion analysis: C, 77.9; H, 5.7 (theory: C, 76.90; H, 5.16).

Calcium–2-Picoline, 1:1.—Two reactions were run. Each went rapidly, evolving only traces of hydrogen. One product was evacuated for 24 hr. at 0° and then for 6 hr. at 28°, then having the composition $Ca(pic)_{0.98}(NH_3)_{1.09}$. Its reactivity with air and water appeared very similar to that of $Ca(C_5H_5N)(NH_3)$. Hydrolysis with dilute hydrochloric acid liberated 35.4% of the original picoline. The other initial product was evacuated for 9 hr. at 30° and then for 24 hr. at 110°, then having the composition $Ca(pic)_{0.82}(NH_3)_{0.77}$.

Calcium–2-Picoline, 1:Excess.—One reaction with an 8:1 excess of picoline, and another with a 12:1 excess, both formed green precipitates which turned red at −80° and back to green again near −33°. Evaporation of the bulk of ammonia left a dark blue solid, which after a 27-hr. evacuation at 25° had the composition $Ca(pic)_{1.46}$. This lost additional picoline at 120°, leaving a greenish black solid, $Ca(pic)_{0.80}$. This resembled the pyridine compounds in its vigorous reaction with air and water, and formed a viscous yellow oil by ether–alcohol–water hydrolysis. Evacuation of the product of the second reaction left a dark blue $Ca(pic)_{1.87}$ after 18 hr. at 0°, which lost picoline during 22 hr. at 110° becoming black $Ca(pic)_{0.88}$, similar to the first product.

Calcium–3-Picoline, 1:1.—Addition of this picoline to the ammonia solution of calcium produced promptly a bright yellow-green precipitate which changed to brown as most of the excess ammonia was removed, and evacuation for 27 hr. at 28° left a red-brown solid of empirical composition, $Ca(pic)_{0.99}(NH_3)_{1.10}$. This was very reactive in air. Hydrolysis with dilute hydrochloric acid gave a clear yellow solution which was shown to contain 38.2% of the original picoline.

Calcium–3-Picoline, 1:8.—Addition of the picoline to the Ca–NH_3 solution produced promptly a bright yellow-green precipitate which turned to a viscous, red-brown sludge when most of the liquid ammonia had evaporated. Evacuation for 21 hr. at 28° left a glassy, olive green solid of composition, $Ca(pic)_{1.91}$. This was heated to 110° *in vacuo* for 11 hr., which reduced the picoline content to $Ca(pic)_{0.86}$, a green-black solid. In air, this turned tan at once, with evolution of considerable heat and smoke. Hydrolysis by the ether–alcohol–water method gave an orange yellow oil which solidified partially on addition of water, but became an oil again when subjected to evacuation.

Calcium–4-Picoline, 1:1.—Addition of the picoline turned the ammonia solution light green with production of a precipitate and evolution of no more than a trace of hydrogen. Evaporation of the ammonia left a yellow solid which turned tan after 45 hr. evacuation at 28°, and had the composition, $Ca(pic)_{0.99}(NH_3)_{1.13}$. This material became quite hot in air and smoked. It reacted vigorously with water with no evolution of hydrogen. The insoluble solid hydrolysis product dissolved in dilute hydrochloric acid giving a deep orange, almost red solution. Spectrophotometric examination of this solution showed it to contain 54.4% of the original 4-picoline.

Calcium–4-Picoline, 1:8.—Addition of the picoline turned the mixture dark brown, and after evaporation of the ammonia and 17 hr. evacuation at 29°, a dark brown solid having the composition $Ca(pic)_{2.02}$ remained. Heating this material for 19 hr. *in vacuo* at 120° produced black $Ca(pic)_{1.04}$, a water-reactive substance that in air became somewhat warm and turned brown in 2 min. Hydrolysis by the ether–alcohol–water method led to isolation of a tacky, orange polymeric material which was not further examined.

Calcium–2,6-Lutidine, 1:1.—Addition of the lutidine caused appearance of a yellow precipitate. The ammonia was allowed to evaporate and collected in dilute hydrochloric acid. This solution was found by spectrophotometric analysis to contain a small amount of lutidine. Additional lutidine was collected in traps at −196° while the reaction flask was being evacuated at 29° for 22 hr. From these quantities and the original amounts of reagents, the composition of the light green residual solid was found to be $Ca(lut)_{0.80}(NH_3)_{0.69}$. In air this quickly evolved smoke, became incandescent, and turned orange. It reacted vigorously with dilute hydrochloric acid, giving a yellow solution containing 28.1% of the lutidine in the compound.

Calcium–2,6-Lutidine, 1:8.—A greenish yellow precipitate appeared when the lutidine was added. Evaporation of the ammonia left a blue-green solid initially containing 2.7 moles of lutidine per mole of calcium. Evacuation at 31° for 24 hr. reduced the lutidine content to the more stable Ca(lut), a sky blue solid of high reactivity. In air it smoked, became incandescent while throwing off sparks, and turned tan. Hydrolysis by the ether–alcohol–water method left a white precipitate [presumably chiefly $Ca(OH)_2$] and a yellow solution, from which a yellow oil was separated by evaporation of the ether. Addition of water to this oil changed it to a semisolid, but subsequent evacuation changed it back to a yellow-orange oil.

Calcium–2,4,6-Collidine.—Collidine was found to react with calcium in a similar manner but more detailed studies were not completed.

Calcium and Liquid Ammonia Alone.—Several experiments were run to determine the maximum rate of amide formation likely under the experimental conditions used for the pyridine reactions, by dissolving the usual size sample of calcium in liquid ammonia and, without adding pyridine, measuring the hydrogen evolution as the ammonia was allowed to evaporate. For reasons not known, inconsistent results were obtained, the amount of amide after 90 min. in four similar experiments being 37, 36, 56, and 18%. Nevertheless, these experiments showed consistently less than 10% reaction in the first 15 min. at −34°, whereas the pyridine reactions were all conducted at temperatures close to −70° and occurred almost instantaneously, reacting with all the calcium present before the solution could become warmer. It was, therefore, concluded that only traces of calcium amide could have been present when the pyridine reactions took place.

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Condensation of Aromatic Aldehydes with Dimethyl Sulfone[1,2]

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Direct condensations of methyl *p*-tolyl sulfone with benzaldehyde in the presence of alkoxide or hydroxide

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[1] Reaction of Resonance Stabilized Anions, part XI. For part X, see H.-D. Becker, G. J. Mikol, and G. A. Russell, *J. Am. Chem. Soc.*, **85**, 3410 (1963).

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[3] Alfred P. Sloan Foundation Fellow, 1959–1963.