from benzoin and 1,2 hydrazinedicarboxyamidine, using the method of Kreutzberger, and was recrystallized from ethanol, m.p. 256–260° (lit.[5] m.p. 233–234°).

Anal. Calcd. for $C_{15}H_{13}N_3$: C, 76.57; H,5.57; N, 17.86; equiv. wt., 235. Found: C, 76.60; H, 5.45; N, 17.86; equiv. wt., 234.

4,5-Di(4-methoxyphenyl)-2-aminoimidazole.—This compound was prepared from anisoin as described above, and was recrystallized from ethanol, m.p. 245–248° (lit.[5] m.p. 225–226°).

Anal. Calcd. for $C_{17}H_{17}N_3O_2$: C, 69.15; H, 5.76; N, 14.24; equiv. wt., 295. Found: C, 69.91; H, 5.98; N, 14.31; equiv. wt., 298.

4,5-Di(2-pyridyl)-2-aminoimidazole, recrystallized from acetone, had m.p. 238–240° (lit.[5] m.p. 230–231°).

Anal. Calcd. for $C_{13}H_{11}N_5$: C, 65.81; H, 4.67; N, 29.52; equiv. wt., 239. Found: C, 65.63; H, 4.86; N, 29.79; equiv. wt., 238.

4,5-Di-(6-methyl-2-pyridyl)-2-aminoimidazole, recrystallized from ethanol, had m.p. 263–266° (equiv. wt.: calcd., 265; found, 267). This compound was very prone to autooxidation and consistent elemental analyses could not be obtained. The infrared spectrum and the equivalent weight of a freshly recrystallized sample showed that such a sample was indeed the compound in a high state of purity. All samples used for pK_a measurements were freshly recrystallized just prior to the run.

pK_a Determinations.—Solutions of the unsubstituted and alkyl-substituted 2-aminoimidazolium salts were prepared at a concentration of about 8×10^{-3} *M* in 0.10 *N* KCl and in 1:1 (v./v.) 0.10 *N* KCl–ethanol solutions. These salts were titrated with 0.10 *N* NaOH. The diaryl compounds were not soluble in water; they were prepared as solutions of the free base form at about 8×10^{-3} *M* in the 0.10 *N* KCl–ethanol solution, and titrated with 0.10 *N* HCl. The pH determinations were made with a Beckman pH meter (Model G) equipped with a glass electrode and a sealed calomel electrode. Titrations were carried out at 25.0° in a constant-temperature bath; the solutions being titrated were stirred with a magnetic stirrer. The pK_a values were calculated from the titration curves. The meter was calibrated against standard 0.10 *N* HCl and 0.10 *N* NaOH. The correction in the pH reading was independent of the actual pH. Blank titrations of KCl and KNO_3 at the same concentrations used for the imidazolium salts were carried out with both the acid and base titrant to check the procedure and to make sure that the small amount of added salt did not affect the meter calibration. From the base titration of KCl as a blank, a pK_w of 13.79 was calculated; with KNO_3 the value was 13.80, in good agreement with the value of 13.78 calculated for these conditions.[10] In the ethanolic system, the pK_w values obtained from the blank titrations were 14.72 and 14.73, respectively.

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[10] H. S. Harned and B. B. Owen, "The Physical Chemistry of Electrolytic Solutions," 2nd Ed., Reinhold Publishing Corp., New York, N. Y. 1950, pp. 481–486.

The Thermal Decomposition of Dialkyl Chelidamates and Related Esters

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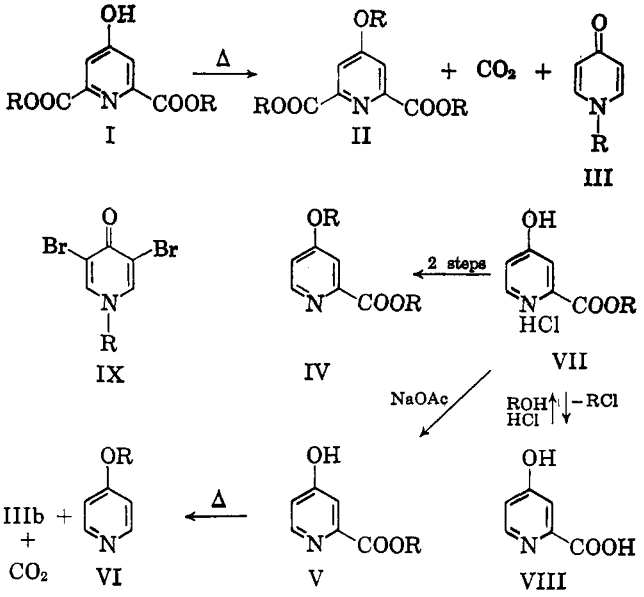
Recently it was observed in this laboratory that dimethyl 4-hydroxydipicolinate (Ia) when heated to 200–210° lost carbon dioxide and was converted to a mixture containing dimethyl 4-methoxypyridine-2,6-dicarboxylate (IIa) and N-methyl-4-pyridone (IIIa). Additional, tarry decomposition products were also formed but not further investigated. The decomposition of diethyl 4-hydroxydipicolinate (Ib) proceeded similarly although a slightly higher reaction temperature was required. Also, in addition to the expected diethyl 4-ethoxypyridine-2,6-dicarboxylate (IIb) and N-ethyl-4-pyridone (IIIb) some ethyl 4-ethoxypicolinate (IVb) was isolated. The pyrolysis of ethyl 4-hydroxypicolinate (Vb) produced predominantly N-ethyl-4-pyridone and a small amount of 4-ethoxypyridine (VIb). No ethyl 4-ethoxypicolinate was isolated from this reaction. In contrast to these results, ethyl 4-hydroxypicolinate hydrochloride (VIIb) decomposed to ethyl chloride and 4-hydroxypicolinic acid (VIII) when it was heated to 180–210°.



a, R = methyl
b, R = ethyl

Ethyl 4-ethoxypicolinate (IVb), which was obtained in small quantity on pyrolysis of diethyl 4-hydroxydipicolinate, was also synthesized from 4-hydroxypicolinic acid (VIII) by esterification and replacement of the hydroxyl by chlorine and, subsequently, by an ethoxy group.

Since N-alkyl-4-pyridones are hygroscopic substances,[1] they were converted to derivatives for identification. In this connection it was observed that the melting point of N-ethyl-3,5-dibromo-4-pyridone differs considerably from the one stated in the literature.[2] No analytical data for this compound are included in the paper cited, whereas satisfactory values were obtained for the material prepared during this investigation. Therefore, the melting point of N-ethyl-3,5-dibromo-4-pyridone (IXb) given in the experimental part is probably more nearly the correct one.

Experimental[3]

Decomposition of Dimethyl 4-Hydroxydipicolinate.[4]—A batch of 11.7 g. (0.055 mole) of this ester was placed in a small distilling flask and immersed in a metal bath which was preheated to 210°. This temperature was maintained for 75 min. while carbon dioxide (0.071 mole) was evolved. After this period of time the evolution of gas had ceased and the residue in the flask was distilled. Fractions of boiling range 150–182° at 2 mm. (4.3 g.) and 183–189° at 2 mm. (2.1 g.) were collected. The lower boiling

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[1] D. G. Markees, *J. Org. Chem.*, **23**, 1030 (1958).

[2] T. Ishii, *J. Pharm. Soc. Japan*, **71**, 1092 (1951).

[3] All melting points were determined on a Mel-Temp apparatus and are corrected. The boiling points are not corrected.

[4] L. R. Fibel and P. E. Spoerri, *J. Am. Chem. Soc.*, **70**, 3908 (1948).

material was almost pure **dimethyl 4-methoxydipicolinate**, m.p. 125–126° (lit.[5] 125–127°) after two recrystallizations from water.

Anal. Calcd. for $C_{10}H_{11}NO_5$: C, 53.33; H, 4.92; N, 6.22. Found: C, 53.23; H, 5.03; N, 6.31.

No melting point depression was observed when this material was mixed with authentic dimethyl 4-methoxydipicolinate.

Recrystallization of the higher boiling fraction from water gave another 0.8 g. of **dimethyl 4-methoxydipicolinate** (total yield, 0.023 mole). The aqueous mother liquor was distilled and yielded 1.1 g. (0.010 mole) of **N-methyl-4-pyridone**, b.p. 188–192° at 2.4 mm. A 300-mg. sample of this substance was treated with bromine water (35 ml.); the water was evaporated and the residue was made alkaline with 1 *M* sodium carbonate. **N-Methyl-3,5-dibromo-4-pyridone** (130 mg., 18%) was collected and recrystallized from water, m.p. 194–195° (lit.[2] 194°), no depression on admixture to a sample prepared from authentic N-methyl-4-pyridone. Another 300-mg. sample was converted to the **picrate**, m.p. 186–187.5°.

Anal. Calcd. for $C_{12}H_{10}N_4O_8$: N, 16.56. Found: N, 16.62.

Diethyl 4-Hydroxydipicolinate.[6]—The hydrate of this ester was obtained in 55–85% yield by esterification of chelidamic acid with ethanol in the presence of sulfuric acid. The excess alcohol was removed from the reaction mixture, water was added to the residue, and the crude product was collected by filtration. It was recrystallized from dilute ethanol and dehydrated at 78° (2 mm.), m.p. 120–121° (lit.[6] 113°).

Anal. Calcd. for $C_{11}H_{13}NO_5$: C, 55.22; H, 5.48; N, 5.86. Found: C, 55.22; H, 5.60; N, 5.78.

For preparative purposes the water of hydration was removed azeotropically with boiling benzene.

Decomposition of Diethyl 4-Hydroxydipicolinate.—Anhydrous diethyl 4-hydroxydipicolinate (11.0 g., 0.046 mole) was placed in a small Claisen flask and immersed in a metal bath which was preheated to 230°. After the evolution of carbon dioxide (0.047 mole) had ceased, the residue in the flask was distilled and arbitrarily divided into two fractions of boiling range up to 150° at 0.5 mm. (2.2 g.) and 150–176° at 0.9 mm. (4.1 g.). Both fractions were washed with water and the washings were combined. Repeated distillation of the lower boiling material gave a small amount of **ethyl 4-ethoxypicolinate**, b.p. 127° at 1.3 mm.

Anal. Calcd. for $C_{10}H_{13}NO_3$: C, 61.53; H, 6.71; N, 7.17. Found: C, 61.49; H, 6.91; N, 7.19.

A sample was converted to the **picrate**; after careful drying at 78° (0.3 mm.), it melted at 104–105.5°. Admixture of an authentic specimen did not depress this melting point.

From the higher boiling fraction crystallized 3.0 g. (0.010 mole) of **diethyl 4-ethoxydipicolinate**, m.p. 85–87° (lit.[5] 85–87°) after one recrystallization from petroleum ether of boiling range 90–100°. No melting point depression was observed on admixture of an authentic sample.

The aqueous washings were combined, the water was evaporated, and the residue (1.8 g.) was distilled. The main fraction, boiling range 180–195° at 1.3 mm. (0.8 g., 0.0065 mole), crystallized readily on cooling. A sample of the hygroscopic material was treated with picric acid to give **N-ethyl-4-pyridone picrate**, m.p. 196–198° (lit.[1,2] 197–198°), undepressed on admixture of an authentic sample. Bromine water converted the crude distillate to **N-ethyl-3,5-dibromo-4-pyridone**, m.p. 157–159°, undepressed on admixture of an authentic sample.

N-Ethyl-3,5-dibromo-4-pyridone.—Bromine water (approximately 150 ml.) was added to a stirred solution of 1.5 g. of N-ethyl-4-pyridone[1] in 10 ml. of water until a red oil began to separate. The mixture was concentrated on the steam bath and the crystalline material (3.4 g.) was collected and redissolved in water. This solution was made alkaline with 2.5 *M* sodium hydroxide and 1.8 g. (52%) of crude product was collected. Recrystallization from water gave the analytical sample, m.p. 157–159° (lit.[2] 209–210°).

Anal. Calcd. for $C_7H_7Br_2NO$: C, 29.92; H, 2.53; Br, 56.88. Found: C, 30.11; H, 2.72; Br, 57.03.

Ethyl 4-Hydroxypicolinate Hydrochloride.—A mixture of 6.4 g. of crude 4-hydroxypicolinic acid[7] and 90 ml. of 6 *M* absolute alcoholic hydrochloric acid was refluxed for 6 hr. When the resulting solution was concentrated and cooled, 5.4 g. (58%) of ethyl 4-hydroxypicolinate hydrochloride was deposited, m.p. 174.5–176° dec. (from ethanol–ether).

Anal. Calcd. for $C_8H_9NO_3 \cdot HCl$: C, 47.19; H, 4.95; Cl, 17.41; N, 6.88. Found: C, 46.85; H, 5.15; Cl, 17.81; N, 7.13.

Ethyl 4-Hydroxypicolinate.—Crude ethyl 4-hydroxypicolinate hydrochloride (10.2 g.) was added to a solution of 7.5 g. of sodium acetate trihydrate in 50 ml. of water. The product was taken up with chloroform; the extracts were combined, washed with a little water, and dried with sodium sulfate. The crude ester (4.7 g., 56%) crystallized after removal of the solvent. Recrystallization from benzene gave the analytical sample, m.p. 126–128°.

Anal. Calcd. for $C_8H_9NO_3$: C, 57.48; H, 5.43; N, 8.38. Found: C, 57.51; H, 5.55; N, 8.44.

Decomposition of Ethyl 4-Hydroxypicolinate.—When ethyl 4-hydroxypicolinate (2.7 g., 0.016 mole) was heated to 210–235°, slightly more than the equimolecular amount of carbon dioxide was evolved. Distillation of the residue gave 30 mg. of a fore-run boiling up to 104° at 2 mm., 30 mg. of an intermediate fraction, boiling range 104–104° at 2 mm., and 1.2 g. (0.010 mole) of a fraction of boiling range 180–195° at 1.3 mm. The highest boiling material was found to consist chiefly of **N-ethyl-4-pyridone**, demonstrated as picrate and dibromoderivative. Addition of picric acid to the two low-boiling fractions produced in each case a **picrate** of m.p. 126–127° whose melting point was not depressed by **4-ethoxypyridine picrate**, m.p. 126–127.5°.

A sample of **4-ethoxypyridine** was prepared from 4-chloropyridine hydrochloride and excess sodium ethoxide in alcohol–dimethylformamide solution, b.p. 86–88° at 14 mm. (lit.[2] 94° at 14 mm.). Addition of picric acid gave the picrate, m.p. 126–127.5° (lit.[8] 129–130°).

Anal. Calcd. for $C_{14}H_{12}N_4O_8$: N, 15.38. Found: N, 15.70.

Ethyl 4-Chloropicolinate.—A mixture of 5.0 g. of ethyl 4-hydroxypicolinate hydrochloride and 20 ml. of thionyl chloride was refluxed for 10 hr. The excess thionyl chloride was then removed and the crystalline residue was decomposed with 0.5 *M* sodium carbonate. The free chloro ester was taken up with ether and the ether solution was washed with water and dried. Distillation gave 2.6 g. (57%) of an oil of b.p. 93–96° at 1.3 mm. The analytical sample, b.p. 94° at 1.4 mm., was obtained by redistillation of the crude product.

Anal. Calcd. for $C_8H_8ClNO_2$: Cl, 19.10; N, 7.55. Found: Cl, 19.38; N, 7.27.

Ethyl 4-Ethoxypicolinate.—A solution of 2.2 g. of ethyl 4-chloropicolinate in 10 ml. of absolute ethanol was mixed with a solution of 0.4 g. of sodium in 12 ml. of absolute ethanol. Dimethylformamide (8 ml.) was added and the mixture was refluxed for 10 min. after the initial reaction had subsided. The volatile parts were then removed, water was added to the residue, and the crude product was taken up with ether. The ethereal solution was washed with water, dried, and distilled. Redistillation of the crude product (0.9 g., 37%) gave the analytical sample, b.p. 122–124° at 0.9 mm.

Anal. Calcd. for $C_{10}H_{13}NO_3$: C, 61.53; H, 6.71; N, 7.17. Found: C, 61.33; H, 6.89; N, 7.07.

A sample of this ester was converted to the **picrate**; it was recrystallized from water and after careful drying melted at 104–105.5°.

Anal. Calcd. for $C_{16}H_{16}N_4O_{10}$: N, 13.20. Found: N, 13.28.

Decomposition of Ethyl 4-Hydroxypicolinate Hydrochloride.—This ester hydrochloride (1.8 g., 0.0089 mole) was heated to 180–210°. The gas which evolved was condensed by passage through ice–water. The condensate was taken up with benzene and identified as **ethyl chloride** by vapor phase chromatography. The residue in the reaction vessel (1.2 g., 0.0086 mole) solidified at the reaction temperature. After repeated recrystallization from water, it melted at 259–261° dec. This melting point suggested that the compound was **4-hydroxypicolinic acid** (lit.[7,9] m.p. 250°, 255–258°).

Anal. Calcd. for $C_6H_5NO_3 \cdot H_2O$: C, 45.87; H, 4.49; N, 8.91. Found: C, 46.02; H, 4.77; N, 8.96.

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