

together with the melting points and analyses of the 7-thiabicyclo[2.2.1]heptane derivatives.

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(16) E. Pesch and S. L. Friess, *J. Am. Chem. Soc.*, **72**, 5756 (1950).

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[CONTRIBUTION FROM THE BIOLOGICAL LABORATORIES OF AMHERST COLLEGE]

Reaction of *N*- and *O*-Alkylchelidamic Acids with Thionyl Chloride¹

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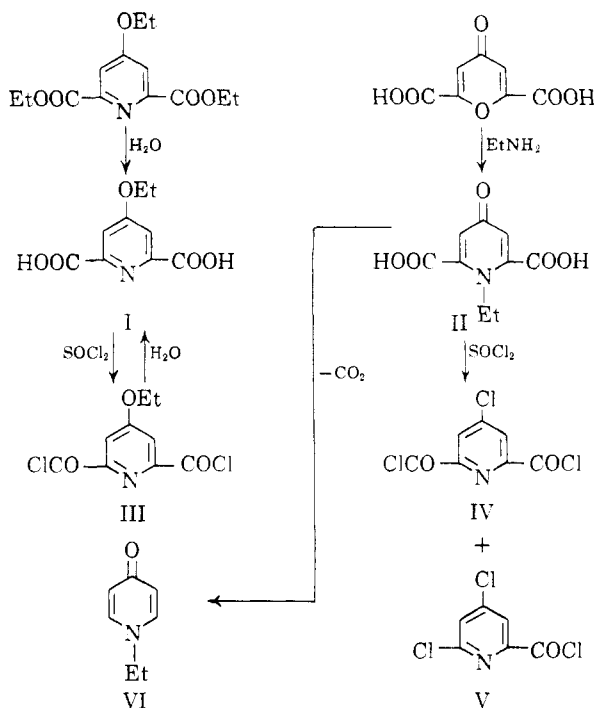
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The reactions of *N*-alkyl-4-pyridone-2,6-dicarboxylic acids and of the isomeric 4-alkoxypyridine-2,6-dicarboxylic acids with thionyl chloride are described. The latter yield the expected 4-alkoxypyridine-2,6-dicarboxylic acid chlorides while the former furnish mixtures of 4-chloropyridine-2,6-dicarboxylic acid dichloride and 4,6-dichloropicolinic acid chloride. Derivatives of the various acids are described and some of their physical constants are presented. Also included is the description of *N*-ethyl-4-pyridone.

In a recent publication² we described the reaction of sodium ethoxide with diethyl 4-chloropyridine-2,6-dicarboxylate which gave diethyl 4-ethoxy-pyridine-2,6-dicarboxylate. On hydrolysis of this ester the corresponding acid (I) was obtained. Since its melting point did not agree with the one reported in the literature³ the isomer *N*-ethyl-4-pyridone-2,6-dicarboxylic acid (II) was prepared for comparison from 4-pyrone-2,6-dicarboxylic acid and ethylamine. Although the formation of the two acids presents in itself some evidence for their constitution, additional proof of structure seemed to be desirable. Their reaction with thionyl chloride was found to serve this purpose. However no conclusions can be drawn as to the structure of the acid prepared by the British authors³ since their work was not repeated.

On treatment with thionyl chloride, the compound obtained by hydrolysis of diethyl 4-ethoxy-pyridine-2,6-dicarboxylate gave smoothly the corresponding acid chloride (III) which could be converted to the original acid and to the amide and anilide. On the other hand, the isomer *N*-ethyl-4-pyridone-2,6-dicarboxylic acid (II) gave under comparable conditions a mixture of two products. In addition to the expected⁴ 4-chloropyridine-2,6-dicarboxylic acid dichloride (IV) 4,6-dichloropic-

olinic acid chloride (V) was isolated as the predominant product. Both acid chlorides were characterized by hydrolysis to the parent acids and by conversion to several derivatives.



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(1) This investigation was supported by a grant (CY-2924) from the National Institutes of Health, U. S. Public Health Service, to Professor G. W. Kidder, whom the author wishes to thank for his continued interest in this work.

(2) D. G. Markees and G. W. Kidder, *J. Am. Chem. Soc.*, **78**, 4130 (1956).

(3) J. N. Collie and G. Bishop, *J. Chem. Soc.*, **127**, 962 (1925).

(4) See e.g. H. Maier-Bode and J. Altpeter, *Das Pyridin und seine Derivate in Wissenschaft und Technik*, Wilhelm Knapp, Halle (Saale) 1934, p. 147.

The literature describes several similar reactions in the pyridine series. It was observed that *N*-methyl-5-methoxy-4-pyridone-2-carboxylic acid reacts with thionyl chloride to give 4,6-dichloro-5-methoxypicolinic acid chloride.⁵ An earlier report,⁶ however, indicates that the corresponding nor-acid, 5-methoxy-4-pyridone-2-carboxylic acid furnishes 4-chloro-5-methoxypicolinic acid chloride under

(5) K. Heyns and G. Vogelsang, *Ber.*, **87**, 1377 (1954).

(6) T. Yabuta, *J. Chem. Soc.*, **125**, 575 (1924).

similar conditions. Furthermore, the reaction of picolinic acid with thionyl chloride has been described.⁷ On prolonged heating of the components 4-chloropicolinic acid chloride was formed, which under extremely vigorous conditions was converted to 4,6-dichloropicolinic acid dichloride. The much milder conditions under which *N*-alkyl-4-pyridone-carboxylic acids react to give 4,6-dichloropicolinic acid chlorides suggest that a different mechanism is operating in these cases.

The ready loss of one carboxyl group of *N*-ethylchelidamic acid (II) in thionyl chloride prompted an attempt to prepare *N*-ethyl-4-pyridone-2-carboxylic acid by decarboxylation of II under relatively mild conditions. However, the only product which could be isolated after heating II in pyridine in the presence of copper bronze was the picrate of *N*-ethyl-4-pyridone.⁸ This pyridone (VI) although mentioned, does not seem to be described adequately in the literature^{8,9} and its preparation and some of its physical properties are therefore included.

Finally *N*-methyl-4-pyridone-2,6-dicarboxylic acid¹⁰ and 4-methoxypyridine-2,6-dicarboxylic acid were prepared and subjected to the reaction with thionyl chloride. As expected, 4-methoxypyridine-2,6-dicarboxylic acid dichloride was obtained from the latter, while the former gave a mixture of 4-chloropyridine-2,6-dicarboxylic acid dichloride and 4,6-dichloropicolinic acid chloride. The last two compounds were methanolyzed and identified as methyl esters while 4-methoxypyridine-2,6-dicarboxylic acid dichloride was analyzed as such and furthermore converted to several derivatives, which are included in Table I.

EXPERIMENTAL¹¹

4-Ethoxypyridine-2,6-dicarboxylic acid. A mixture of 5.4 g. of diethyl 4-ethoxypyridine-2,6-dicarboxylate² and 30 ml. of 10% sodium hydroxide was refluxed for 3 hr. The solid which separated on cooling was filtered, dissolved in 50 ml. of warm water, and the solution acidified with 10% hydrochloric acid. A crop of 2.1 g. (46%) of crude material was obtained. A sample was recrystallized several times from water, dried *in vacuo* at 180° and recrystallized once more from ethyl acetate, m.p. 182–184° (dec.) (Lit.³ 200°).

Anal. Calcd. for C₈H₉NO₅: C, 51.19; H, 4.30; N, 6.64. Found: C, 51.23; H, 4.43; N, 6.57.

4-Methoxypyridine-2,6-dicarboxylic acid. Alkaline hydrolysis of dimethyl 4-methoxypyridine-2,6-dicarboxylate² and subsequent acidification gave this acid in 86% yield. A sample was recrystallized from water and obtained as hydrate, m.p. 222.5–223.5° (dec.) after some darkening.

Anal. Calcd. for C₈H₉NO₅·H₂O: C, 44.65; H, 4.22; N, 6.51. Found: C, 44.24; H, 3.93; N, 6.75.

(7) H. Meyer and R. Graf, *Ber.*, **61**, 2210 (1928).

(8) T. Ishii, *J. Pharm. Soc. Japan*, **71**, 1092 (1951).

(9) H. Ost, *J. Prakt. Chem.*, [2] **29**, 378 (1884).

(10) E. R. Riegel and M. C. Reinhard, *J. Am. Chem. Soc.*, **48**, 1334 (1926); E. Spaeth and E. Tschelnitz, *Monatsh.*, **42**, 251 (1921).

(11) All melting points were determined on a Fisher-Johns apparatus and are corrected unless stated otherwise.

N-Ethyl-4-pyridone-2,6-dicarboxylic acid. A mixture of 1.3 g. of chelidonic acid and 50 ml. of 33% aqueous ethylamine was refluxed for 7 hr. After cooling it was acidified with hydrochloric acid and the precipitate filtered. The yield was 0.6 g. (40%) and a sample recrystallized from water melted at 186–188° if heated slowly and at 196–198° if heated rapidly.

Anal. Calcd. for C₈H₉NO₅: C, 51.19; H, 4.30; N, 6.64. Found: C, 51.10; H, 4.41; N, 6.55.

N-Ethyl-4-pyridone. A batch of 11.0 g. of *N*-ethyl-4-pyridone-2,6-dicarboxylic acid was heated in a distillation flask at reduced pressure. An oil of boiling range 190–200°/1–2 mm. distilled over and crystallized on cooling. Repeated distillation gave the analytical sample b.p. 178°/0.8 mm., m.p. 62–64°.¹² This material was sealed immediately after distillation. Exposed to air it becomes liquid accompanied by weight increase.

Anal. Calcd. for C₇H₉NO: C, 68.27; H, 7.37; N, 11.4. Found: C, 67.71; H, 7.25; N, 11.2.

Decarboxylation of N-ethylchelidamic acid (II) in pyridine. A mixture of 2.5 g. of *N*-ethylchelidamic acid, 0.5 g. of copper bronze, and 15 ml. of pyridine was refluxed until the evolution of carbon dioxide ceased. The copper catalyst was filtered off, the filtrate evaporated down and the residue taken up with a little water. This solution was treated with charcoal and then with an excess of aqueous picric acid to give a crop of 2.8 g. (67%) of yellow crystals of *N*-ethyl-4-pyridone picrate, m.p. 195–196° (Lit.⁸ 196°); no depression of this melting point was observed on admixture with authentic *N*-ethyl-4-pyridone picrate.

4-Ethoxypyridine-2,6-dicarboxylic acid dichloride. A mixture of 2.0 g. of 4-ethoxypyridine-2,6-dicarboxylic acid and 10 ml. of thionyl chloride was heated until a clear, brown solution was obtained. The excess halogenating agent was then removed with the aid of some benzene and upon addition of petroleum benzene a crop of 1.5 g. (64%) of crude crystalline material was obtained. A sample, recrystallized from the same solvent, melted at 77–78°.

Anal. Calcd. for C₈H₇Cl₂NO₅: Cl, 28.6; N, 5.65. Found: Cl, 28.5; N, 5.46.

Hydrolysis of this compound produced 4-ethoxypyridine-2,6-dicarboxylic acid of m.p. 182–184°, undepressed on admixture with an authentic sample.

4-Methoxypyridine-2,6-dicarboxylic acid dichloride. This compound was obtained similarly in nearly quantitative yield. A sample, recrystallized from hexane, melted at 97–99°.

Anal. Calcd. for C₈H₇Cl₂NO₅: N, 5.98. Found: N, 5.90.

Hydrolysis of this compound produced 4-methoxypyridine-2,6-dicarboxylic acid of m.p. 222–224°. No m.p. depression on admixture with an authentic sample was observed.

Reaction of N-ethyl-4-pyridone-2,6-dicarboxylic acid with thionyl chloride. A mixture of 8.0 g. of crude *N*-ethyl-4-pyridone-2,6-dicarboxylic acid and 32 ml. of thionyl chloride was refluxed for 3 hr. The excess thionyl chloride was then removed with the aid of benzene and the residue distilled *in vacuo*. Two fractions of boiling range 92–104°/1.6 mm. (3.2 g., 40%) and of b.p. 117°/1.3 mm. (3.4 g., 38%) were obtained, the latter of which solidified on cooling. Fractionation of the liquid material gave a sample of 4,6-dichloropicolinic acid chloride b.p. 87°/1.3 mm.

Anal. Calcd. for C₈H₇Cl₂NO: N, 6.66. Found: N, 6.63.

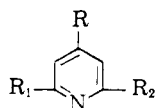
A sample of the solid product was recrystallized several times from petroleum ether, m.p. 97–98°. Analysis and conversion to derivatives proved it to be 4-chloropyridine-2,6-dicarboxylic acid dichloride.

Anal. Calcd. for C₇H₇Cl₂NO₅: N, 5.87. Found: N, 5.67.

Reaction of N-methyl-4-pyridone-2,6-dicarboxylic acid with thionyl chloride. Refluxing 4.0 g. of *N*-methyl-4-pyridone-2,6-dicarboxylic acid with thionyl chloride furnished, after removal of the excess halogenating agent, 1.9 g. of material

(12) Sealed capillary, bath, uncorrected.

TABLE I
DERIVATIVES OF PICOLINIC ACID AND PYRIDINE-2,6-DICARBOXYLIC ACID OF THE STRUCTURE



R	R ₁	R ₂	Start- ing Mate- rial	Yield, ^a %	M.P.	Recryst. from	Calcd., % N	Found, % N	Empirical Formula
CH ₃ O	CONH ₂	CONH ₂	^b	90	>300°	H ₂ O-AcOH	21.5	21.3	C ₈ H ₉ N ₃ O ₃
CH ₃ O	CONHC ₆ H ₅	CONHC ₆ H ₅	^b	80	275-277°	Dioxane	12.1	11.8	C ₂₀ H ₁₇ N ₃ O ₃
C ₂ H ₅ O	CONH ₂	CONH ₂	III	70	289°	H ₂ O	20.1	20.4	C ₉ H ₁₁ N ₃ O ₃
C ₂ H ₅ O	CONHC ₆ H ₅	CONHC ₆ H ₅	III	80	258-259°	EtOH	11.7	11.4	C ₂₁ H ₁₉ N ₃ O ₃
Cl	Cl	COOH	V	80	114-116° ^o	H ₂ O ^d	7.30	7.11	C ₆ H ₃ Cl ₂ NO ₂
Cl	Cl	COOCH ₃	V	90	78.5-79.5° ^e	H ₂ O-MeOH	6.79	6.48	C ₇ H ₃ Cl ₂ NO ₂
Cl	Cl	CONH ₂	V	80	176.5-178.5° ^f	H ₂ O-EtOH	14.7	14.5	C ₈ H ₄ Cl ₂ N ₂ O
Cl	Cl	CONHC ₆ H ₅	V	75	172.5-174.5° ^c	EtOH	10.5	10.3	C ₁₂ H ₈ Cl ₂ N ₂ O
Cl	COOH	COOH	IV	60	218-219° ^g	H ₂ O	^h	^h	C ₇ H ₄ ClNO ₄
Cl	CONH ₂	CONH ₂	IV	95	>300°	H ₂ O	21.1	20.6	C ₇ H ₆ ClN ₃ O ₂
Cl	CONHC ₆ H ₅	CONHC ₆ H ₅	IV	65	272°	AcOH	11.9	11.5	C ₁₃ H ₁₄ ClN ₃ O ₂

^a Round figures. ^b 4-Methoxypyridine-2,6-dicarboxylic acid dichloride. ^c Lit. 111-112°. ^d Also sublimed *in vacuo*. ^e Lit. 73-74°. ^f Lit. 172-174°. ^g Lit. 220° (dec.). ^h Calcd.: C, 38.28; H, 2.75. Found: C, 38.04; H, 2.86.

boiling up to 110°/4 mm. and 1.0 g. of a residue which solidified on cooling. Samples of the two products were methanolized, the former giving *methyl 4,6-dichloropicolinate* of m.p. 78-79°, while the latter yielded *dimethyl 4-chloropyridine-2,6-dicarboxylate* of m.p. 143-144°. No depression of these melting points was observed on admixture with authentic samples.

Derivatives of substituted pyridinecarboxylic acids. The various acid chlorides reported above were converted to a number of derivatives. Hydrolyses and alcoholyses were carried

out by mixing the reactants without a solvent. The amides and anilides were prepared by treating benzene solutions of the acid chlorides with ammonia and aniline, respectively. Analyses and more preparative information is contained in Table I.

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(13) A. P. Sedgwick and N. Collie, *J. Chem. Soc.*, 67, 401 (1895).

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Olefinic Derivatives of 2,4-Diamino-s-triazines

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The reaction of *N*-alkylaminoalkyl vinyl ethers with cyanogen chloride gave the corresponding cyanamides. Amidonitriles containing vinyl ether or methacryloyl groups were obtained respectively by the successive cyanoalkylation and acylation of aminoethyl vinyl ether or the reaction of aminonitriles with methacryloyl chloride. Condensation of these cyanamides or amidonitriles with dicyandiamide gave the related derivatives of 2,4-diamino-*s*-triazine, a new group of triazines which undergo addition polymerization.

Olefinic derivatives of 2,4-diamino-*s*-triazines are potentially monomers from which cross-linked polymers may be prepared by successive alternate polymerization procedures. The few compounds of this type which have been described are limited to derivatives having the olefinic group joined directly to the heterocyclic nucleus.¹

Three new classes of olefinic triazines have been prepared whose common structural feature is separation of the olefin group from the heterocyclic ring

by a short chain containing oxygen, nitrogen, or both. Two of these classes are vinyl ethers, the third derivatives of methacrylamide. By appropriate selection of starting materials, a wide variety of monomeric triazines were obtained. These compounds showed good addition polymerization and copolymerization characteristics and could be cured by cross-linking reactions to insoluble polymers.

N-Vinoxyalkylcyanamides (I) were formed by the cyanation of appropriately substituted aminoalkyl vinyl ethers with cyanogen chloride. Subsequent condensation with dicyandiamide in the

(1) J. T. Thurston, U. S. Patent 2,461,943 (Feb. 15, 1949); C. G. Overberger and S. L. Shapiro, *J. Am. Chem. Soc.*, 76, 1061 (1954).