sample was obtained by recrystallization from approximately 1:1 benzene–hexane: mp 129–130° (lit.[16] 133°); ir (KBr) 3400 (OH), 1710 cm^{-1} (acid C=O); nmr (acetone-d_6) τ 2.6–3.2 (m, 8, aromatic), 4.4 (s, 2, OH, CO_2H).

Anal. Calcd for $C_{12}H_{10}O_3S$: C, 61.52; H, 4.29; S, 13.69. Found: C, 61.36; H, 4.26; S, 13.54.

3-Thienylphenylacetic Acid (10).—Into a 50-ml three-necked flask maintained at 20° and fitted with a thermometer and stirrer were added α-(3-thienyl)mandelic acid (**13**, 2.0 g, 8.85 mmol), stannous chloride (3.30 g, 0.0175 mol), water (0.68 ml, 0.0378 mol), and 28 ml of acetic acid. The flask was maintained at 15–22° for 15 min while hydrogen chloride was bubbled through the mixture. During this time essentially all the stannous chloride disappeared, and the mixture darkened considerably. The mixture was concentrated under reduced pressure and the residue was partitioned between water and ether. The aqueous layer was extracted with two portions of ether. The combined ether layers were washed with ten portions of water and two portions of brine and dried ($MgSO_4$). Evaporation left 1.44 g (78%) of solid, mp 85–87°. An analytical sample was obtained by recrystallization from benzene–hexane followed by sublimation at 80–83° (0.01 mm), mp 88.5–90°: ir (KBr) 1690 cm^{-1} (acid C=O); nmr (acetone-d_6) τ 2.4–3.0 (m, 8, aromatic), 4.83 (s, 1, methine); nmr ($CDCl_3$) τ −1.8 (s, 1, CO_2H).

Anal. Calcd for $C_{12}H_{10}O_2S$: C, 66.03; H, 4.62; S, 14.69. Found: C, 66.05; H, 4.68; S, 14.43.

4*H*-Indeno[1,2-*b*]thiophene-4-carboxylic Acid (5).—Into a 100-ml three-necked flask fitted with a reflux condenser and calcium chloride drying tube were added 15 ml of dry benzene and 100 g (4.27 mmol) of 3-thienylmandelic acid (**13**). The mixture was cooled below 0° and the 1.71 g (1.28 × 10^{-2} mol) of aluminum chloride was added in one portion *via* a Gooch tube. The resulting red mixture was refluxed for 3 hr; a continuous evolution of hydrogen chloride was observed. The mixture was cooled in an ice bath and decomposed with a mixture of ice, 10 ml of water, and 5.6 ml of 12 *M* hydrochloric acid. Trituration produced a white crystalline solid which was dissolved in ether. The aqueous phase was washed twice with ether. The combined ether solutions were extracted three times with 10% sodium carbonate. The basic solution was treated with Norite at 60–70°, filtered, cooled, and acidified with 12 *M* hydrochloric acid. The aqueous suspension was extracted three times with ether. The ether solution was washed three times with water and twice with brine and dried ($MgSO_4$). Evaporation left 0.84 g (91%) of solid, mp 167–178°. Recrystallization from benzene–hexane left 0.35 g (38%) of white crystalline solid, mp 209–210° (lit.[3] 212–213° dec). The nmr and ir spectra of this material were identical with those of an authentic specimen of **5** prepared as described in the literature.[3]

Registry No.—**5**, 23062-44-4; **6**, 27921-48-8; **8**, 27921-49-9; **9**, 27921-50-2; **10**, 16199-72-7; **11**, 27921-52-4; **13**, 3193-25-7.

Acknowledgment.—The authors wish to thank Messrs. Robert Smith, James Wisowaty, and Bruce Heitke for recording the nmr spectra.

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[16] M. Robba and R. Moreau, *Ann. Pharm. Fr.*, **23**, 103 (1965).

Studies in the Chemistry of Di-2-pyridylglyoxal

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Addition, disproportionation, and alkylation reactions of di-2-pyridylglyoxal are discussed. Two addition products, 1,2-diethoxy-1,2-dihydroxy-1,2-di(2-pyridyl)ethane dihydrochloride and 1,2-di(2-pyridyl)-1,1,2,2-tetrahydroxyethane dihydrochloride, were prepared and characterized. The tetrahydroxy derivative was found to be stable in the solid state for at least 3 months. However, it completely decomposed after being allowed to reflux 10 min in water under nitrogen. Picolinic acid, 2-pyridinemethanol, and considerable tar were isolated from the reaction mixture. Di-2-pyridylglyoxal is stable in ethanol but rapidly decomposes to give 1,2-di-2-pyridyl-1,2-ethenediol and ethyl picolinate when catalytic amounts of acid are added. Attempts to alkylate di-2-pyridylglyoxal with methyl iodide in either alcohol or nitrobenzene were unsuccessful. When alkylation was attempted in ethanol, disproportionation of the di-2-pyridylglyoxal occurred apparently under the catalytic influence of hydrogen iodide formed by the alcoholysis of the methyl iodide. A general mechanism for the acid-catalyzed disproportionation of di-2-pyridylglyoxal in either alcohol or water under acidic or basic conditions is discussed.

There are many recent reviews of the general chemistry of carbonyl compounds.[2,3] There are also specific treatments of the chemistry of heterocyclic carbonyl compounds.[4] It is interesting to note that the chemistry of pyridine aldehydes and ketones is sometimes quite different from that found with benzene analogs.

Pyridine carbonyl compounds, especially 2- (or 4-) substituted ones such as picolinaldehyde, isonicotinaldehyde, or their quaternary salts, undergo addition easily because of the electron-withdrawing power of the heterocyclic ring. Thus pyridoxal in the crystalline state is mainly in the form of the hemiacetal;[5] 2- (and 4-) formyl-1-methylpyridinium salts form stable hemiacetals and *gem*-glycols.[6] The 2-substituted hemiacetal readily cleaves on refluxing with aqueous sodium hydroxide.[7] 2-Formyl-1-methylpyridinium iodide forms an isolable hydroxylamine adduct which dehydrates on heating.[8]

It was reported that di-2-pyridylglyoxal (**1**) does not undergo the benzilic acid rearrangement in aqueous alkali but decomposes into picolinic acid (**2**) and a small amount of 2-pyridinemethanol (**3**) accompanied by liberation of ammonia.[9] Poziomek, Kronenberg, and Havinga[10] found that di-2-pyridylglyoxal decomposed in refluxing aqueous solution to give 1,2-di(2-pyridyl)-1,2-ethenediol (**4**), **2**, and traces of **3** and pico-

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[1] To whom reprint requests should be addressed at the Physical Research Laboratory, Edgewood Arsenal.

[2] S. Patai, Ed., "The Chemistry of the Carbonyl Group," Interscience, New York, N. Y., 1966.

[3] S. Coffey, Ed., "Rodd's Chemistry of Carbon Compounds," 2nd ed, Vol. I, Part D, Elsevier, New York, N. Y., 1962.

[4] E. Klingsberg, Ed., "Pyridine and Its Derivatives," Part 3, Interscience, New York, N. Y., 1962.

[5] D. Heinert and A. E. Martell, *J. Amer. Chem. Soc.*, **81**, 3933 (1959).

[6] G. M. Steinberg, E. J. Poziomek, and B. E. Hackley, Jr., *J. Org. Chem.*, **26**, 368 (1961).

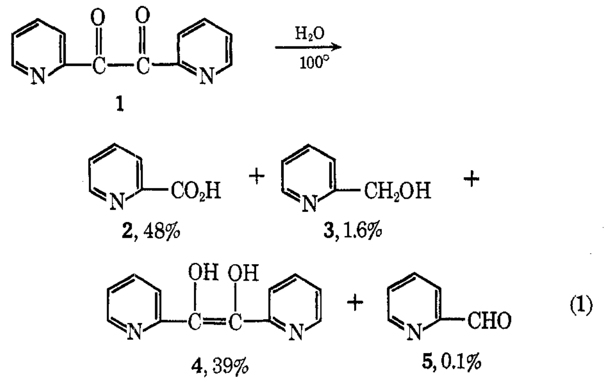
[7] S. Golding and A. R. Katritzky, *Can. J. Chem.*, **43**, 1250 (1965).

[8] E. J. Poziomek, D. N. Kramer, B. W. Fromm, and W. A. Mosher, *J. Org. Chem.*, **26**, 423 (1961).

[9] D. Oda, *Nippon Kagaku Zasshi*, **82**, 478 (1961); *Chem. Abstr.*, **56**, 10089*b* (1962).

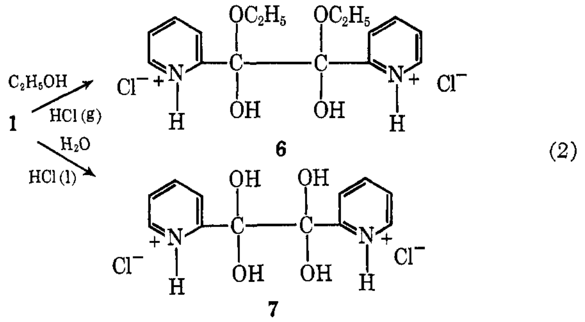
[10] E. J. Poziomek, M. E. Kronenberg, and E. Havinga, *Recl. Trav. Chim. Pays-Bas*, **85**, 791 (1966).

linaldehyde (**5**) (eq 1). It is the purpose of the present study to investigate the chemistry of **1** under acidic conditions.

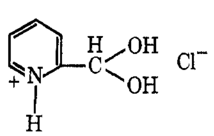


Results and Discussion

Addition Reactions of Di-2-pyridylglyoxal (1).—Two additional products, 1,2-diethoxy-1,2-dihydroxy-1,2-di(2-pyridyl)ethane dihydrochloride (**6**) and 1,2-di-(2-pyridyl)-1,1,2,2-tetrahydroxyethane dihydrochloride (**7**), were prepared with good yields by treating **1** with ethanolic hydrogen chloride and concentrated hydrochloric acid, respectively (eq 2). Structural assignments were made on the basis of elemental analysis and the absence of carbonyl stretching bands in the infrared absorption spectra. The starting material, **1**, exhibits a well-defined carbonyl doublet (1717, 1695 cm^{-1}).



The isolation of the stable addition compounds **6** and **7** was not surprising since picolinaldehyde hydrochloride was reported by Harries and Lenart[11] to form a stable hydrate **8** though the structure was not discussed. A *gem*-glycol assignment can be made on the basis of the absence of a carbonyl stretching band in the infrared absorption spectrum. Actually, the infrared spectra of **7** and **8** are very similar to each other. Mathes, Sauermilch, and Klein[12] reported the isolation of the hydrochloride of **1** from concentrated hydrochloric acid but gave no elemental analyses.



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Effect of Solution on 1,2-Di(2-pyridyl)-1,1,2,2-tetrahydroxyethane Dihydrochloride (7).—The tetrahydroxyethane derivative **7** was found to be stable in the solid state. No decomposition was noted after storage at room temperature for at least 3 months. Attempts to obtain an ultraviolet absorption spectrum in water indicated that **7** decomposes in solution. The decomposition was studied in detail at various temperatures; the results are summarized in Table I. Little reaction occurred in the cold as evidenced by an 85.1% recovery of the parent compound **1** after the solution was allowed to stand for 3 days. However, **7** completely decomposed after the solution was refluxed for 10 min under nitrogen. This gave mainly picolinic acid, a small amount of 2-pyridinemethanol, and considerable tar. Compound **4** was isolated as a decomposition product at room temperature. However, it is unstable in hot aqueous acid which may account why none was isolated in the reflux experiment. The acid-catalyzed decomposition of **4** in alcohol is described later.

Table I

Decomposition of 1,2-Di(2-pyridyl)-1,1,2,2-tetrahydroxyethane Dihydrochloride (7) in Water

Conditions	Products, yield, % (isolated) 1	2	3	4
Reflux, N_2, 10 min[a]		42 ± 2[b]	6.5 ± 0.2[b]	
Room temperature, N_2, 69 hr[c]	16.4	13.1		16.4
5°, N_2, 69 hr[c]	85.1	6.1		

[a] 5.0 g of 7 in 65 ml of water. [b] Reproducibility based on two experiments. [c] 5.0 g in 50 ml of water.

Disproportionation of Di-2-pyridylglyoxal (1).—The reactions of **1** in ethanol containing catalytic amounts of acid were studied under a wide variety of experimental conditions (Table II). Compound **1** is stable in ethanol but decomposes rapidly when acid is added. Little difference was found between the use of hydriodic and hydrochloric acids.

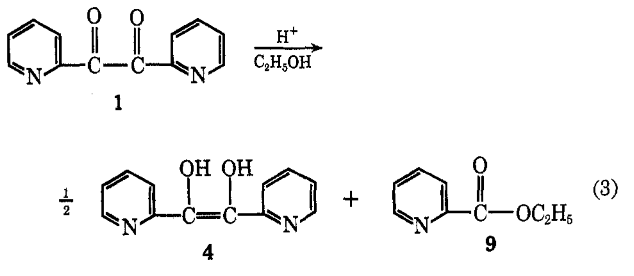
Table II

Reactions of Di-2-pyridylglyoxal in Ethanol with Catalytic Amounts of Acid

Conditions	Products, yield, % (isolated) 1	4	9
Room temperature, 10 days, HI[a]		21.8	64.2[b]
Room temperature, 10 days, HCl[a]		26.3	46.1[b]
Room temperature, 10 days, no acid[a]	100		
Reflux, 12 hr, N_2, HCl[c]		31.5	63.0[b]
	7.5	22.2	63.7[b]
Reflux, 12 hr, O_2, HCl[c]			71.4[b]
			96.0[b]

[a] 1 (5 g), 300 ml of EtOH, and 0.1 ml of concentrated acid. [b] Yield based on crude weight. [c] 1 (5 g), 100 ml of EtOH, and 0.1 ml of concentrated acid.

It is evident that **1** disproportionates to **4** and **9** under the influence of acid in ethanol (eq 3). The isolation of



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[11] C. Harries and G. H. Lenart, *Justus Liebigs Ann. Chem.*, **410**, 95 (1915).

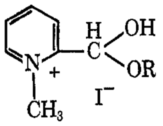
[12] W. Mathes, W. Sauermilch, and T. Klein, *Chem. Ber.*, **84**, 452 (1951).

more than 50% yield of **9** is expected since the other product, **4**, decomposes under the conditions of the experiment to give ethyl picolinate. The absence of any **4** product in the experiment in which air was bubbled through the reaction solution is explained on the basis of an oxidation of **4** to **1**, followed by a decomposition of **1** to **4** and **9**, etc.

Decomposition of 1,2-Di-2-pyridyl-1,2-ethenediol (4).—It was found that when 100 ml of ethanolic solution containing 5% **4** and 0.1 ml of concentrated hydrochloric acid is refluxed, 37% decomposition occurs. Part of this decomposition is due to the oxidation of **4** to **1** by air. (Air oxidation of **4** is a reported method of preparing **1**.[13]) Only 26% decomposition of **4** occurred when the solution was refluxed under nitrogen. Any **1** formed in the acid-catalyzed decomposition of **4** would be subject to disproportionation. Under the conditions of this experiment, the decomposition of **1** is essentially complete.

Logical decomposition paths of **4** are summarized in Scheme I. Ethyl picolinate was clearly identified in the infrared absorption spectrum of the reaction residue. The spectrum also indicated the presence of a hydroxy component, probably 2-pyridinemethanol.

Reaction of Di-2-pyridylglyoxal with Methyl Iodide.—It was previously reported that 2-(alkoxyhydroxymethyl)-1-methylpyridinium iodide (**10**) can be prepared by reaction of methyl iodide with picolinaldehyde in alcohol.[6] In view of this as well as the isolation of **6** and **7** and the acid-catalyzed decomposition of **1** in hydroxylic solvents, it was thought that reaction of **1** in ethanol with methyl iodide would lead to **11**. Compound **11** might be expected to disproportionate to **4** and 2-carboethoxy-1-methylpyridinium iodide (**12**) (eq 4).



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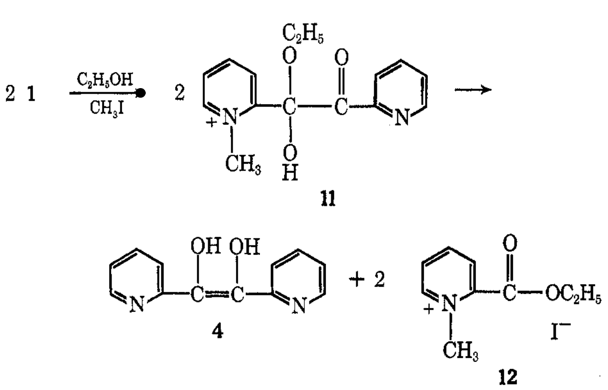


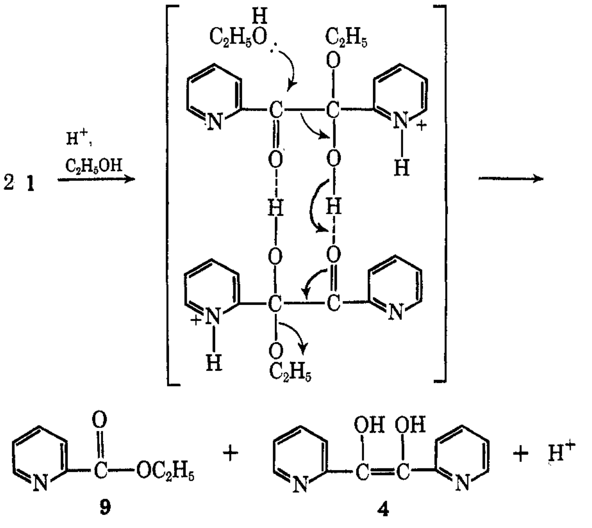
(4)

A number of repeated experiments with **1** and methyl iodide in ethanol led consistently to the formation of **4** and **9** but no **12** (see the Experimental Section for details). When **1** was refluxed with methyl iodide in nitrobenzene, only a small amount of a very hygroscopic gum was isolated. It was also established that appreciable methylation of ethyl picolinate (**9**) does not occur under the conditions used with **1** in alcohol.

Methyl iodide is subject to alcoholysis or hydrolysis in alcohol or water.[14,15] In the attempted reaction of **1** with methyl iodide, disproportionation of **1** apparently occurred under the catalytic influence of hydrogen iodide (formed from alcoholysis of methyl iodide).

Under the experimental conditions, the disproportionation of **1** was complete in each case. However, the yield of **4** was higher in more concentrated solutions. This effect was not investigated further but it seems to indicate that the conversion of **1** to **4** is a second-order reaction. Obviously this is complicated by the acid-catalyzed decomposition of **4** itself.

Mechanism Considerations.—Poziomek, Kronenberg, and Havinga[10] proposed that the combination of cleavage, oxidation, and reduction of **1** in water occurs through linear or cyclic hydrogen-bonded complexes or hemiketals. The same general mechanism can be used to explain the disproportionation of **1** in either alcohol or water under acidic conditions. Protonation of the pyridine nitrogen (or carbonyl oxygen) serves to increase the susceptibility of the carbonyl carbon to attack by hydroxylic solvent. (In the absence of added acid, **1** was recovered without change after being allowed to reflux in ethanol.) One possible intermediate in the reaction of **1** with ethanolic hydrogen chloride is shown in eq 5. The physical reality of a ten-membered cyclic transition state in ethanol is questionable, but essentially an intermolecular transfer of hydride ion is indicated. Various modifications can be made by using other intermolecular linear or cyclic hydrogen bonded hemiketals or ketals without affecting the reaction course.



(5)

Essentially the same mechanism can be used for the disproportionation of **1** in alkali. Oda[9] did not find an appreciable amount of **4** in the reaction of **1** with alkali. He proposed a cleavage into picolinaldehyde and picolinic acid followed by a Cannizzaro reaction of picolinaldehyde. Actually under the conditions of Oda's experiment (heat was used), **4** is susceptible to decomposition; it is not surprising that very little **4** was iso-

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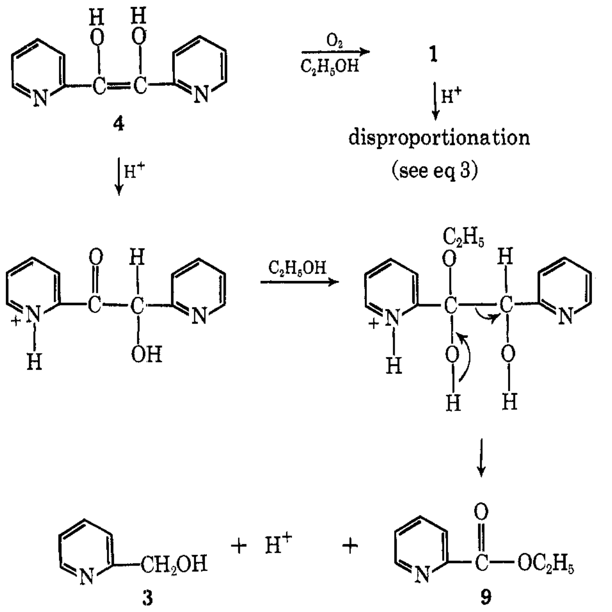
[13] E. Klingsberg, Ed., "Pyridine and Its Derivatives," Part 4, Interscience, New York, N. Y., 1964, p 140.

[14] E. A. Moelwyn-Hughes, *Proc. Roy. Soc., Ser. A*, **164**, 295 (1938).

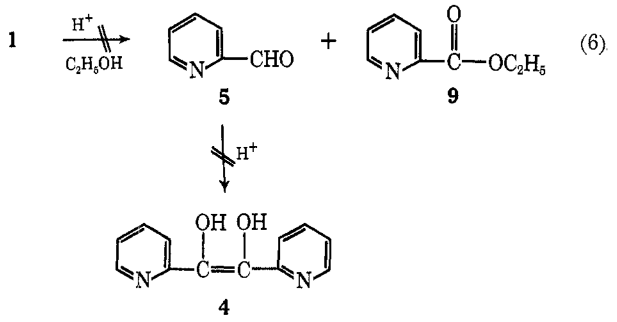
[15] J. D. Roberts and M. C. Caserio, "Basic Principles of Organic Chemistry," W. A. Benjamin, New York, N. Y., 1965, p 386.

Scheme I



lated. A 22% yield of **4** can be obtained by simply adding **1** to a cooled aqueous solution of sodium hydroxide and allowing the mixture to stir for 30 min.[16]

Cleavage of **1** into **5** and **9**, followed by a condensation of **5** to give **4** (eq 6), can be eliminated as reaction



pathways in the present work. Though it has been reported that picolinaldehyde (**5**) when dissolved in acid forms **4**,[17] no 1,2-di(2-pyridyl)-1,2-ethenediol was obtained from picolinaldehyde under the conditions in which acid catalysis led to the isolation of **4** from **1**.

Experimental Section

General.–All pH measurements were made at room temperature with a Fisher Accumet pH meter precalibrated with standard buffer solution. Gas chromatographic analyses of reaction products were performed with a F & M Model 5750 research chromatograph using a 6 ft × 0.25 in. o.d. stainless steel column packed with 3% GE Type XE60 silicone on 60–80 mesh Chromosorb G. All melting points were determined using a Thomas-Hoover capillary melting point apparatus and are corrected. In every experiment the reaction products were identified by comparison of their infrared absorption spectra with those of authentic samples. The infrared absorption spectra of solids were determined in potassium bromide disks; liquids were placed between sodium chloride plates. A Beckman Model IR-8 spectrophotometer was used. Elemental analyses were performed by the Analytical Chemistry Dept., Chemical Research Laboratory, Edgewood Arsenal, Md. The nmr spectra were obtained on a Varian Model A-60 spectrometer by the Physical Chemistry Dept., Chemical Research Laboratory, Edgewood Arsenal, Md.

Samples of compounds **1–4** and **9** were obtained from either Distillation Products Industries or Aldrich Chemical Co. Authenticity was verified by a comparison of infrared absorption spectra with those published by Sadtler Research Laboratories, Inc. However, it was noticed that the Sadtler spectrum of **4** is actually that of a mixture of **1** and **4**.

Preparation of 1,2-Diethoxy-1,2-dihydroxy-1,2-di(2-pyridyl)-ethane Dihydrochloride (6).—Into a stirred solution of 5.0 g (0.024 mol) of **1** in 100 ml of absolute ethanol was bubbled anhydrous HCl gas. The reaction flask was fitted with a condenser and a tube for gas delivery. The top of the condenser was connected to a drying tube containing $CaCl_2$. The reaction flask was cooled in an ice bath during the addition of the HCl gas. The gas was bubbled through the reaction mixture at approximately 500 ml/min for a total of 8 min. Diethyl ether (1 l.) was added to the solution and a white, tacky solid precipitated. The precipitate was collected, washed with ether, and air-dried to give 8.08 g (0.022 mol) of a colorless solid: mp 174° dec; nmr (D_2O) δ 1.19 (6 H, t, CH_3), 3.66 (4 H, q, CH_2), 4.82 (2 H, s, OH), 8.0–9.0 (8 H, m, pyridine ring hydrogens); ir (KBr), 3181 (broad), 1608 (s), 1519 (m), 1453 (m), 1144 (s), 768 cm^{-1} (s).

Anal. Calcd for $C_{16}H_{22}Cl_2N_2O_4 \cdot {}^1/_2H_2O$: C, 49.8; H, 6.0; Cl, 18.4; N, 7.4; O, 18.6. Found: C, 49.0; H, 5.7; Cl, 18.8; N, 7.9; O, 18.4.

The poor analysis is probably due to a loss of part of the ethanol during the course of handling the sample.

Preparation of 1,2-Di(2-pyridyl)-1,1,2,2-tetrahydroxyethane Dihydrochloride (7).—Compound **1** (2.85 g, 0.013 mol) was added slowly to 20 ml of magnetically stirred 36 *N* HCl. Some slight evolution of heat was noted upon addition of **1**. The compound immediately dissolved, giving a light yellow solution from which a white solid precipitated after several minutes. The mixture was stirred an additional hour at room temperature. The mixture was filtered and the precipitate was washed with three 50-ml portions of acetone. The solid was dried for 1 hr at 64° in a vacuum oven to give 4.21 g (97.7%) of product. The solid gradually turned a light brown on standing. During the melting point determination, the compound started to turn from brown to yellow at 153° and then slowly back to brown at 160°. The sample decomposed at 166–167°: nmr (D_2O) δ 5.01 (4 H, s, OH), 8.0–9.0 (8, H, m, pyridine ring hydrogens); ir (KBr), 3139 (broad), 2778 (broad), 1610 (s), 1517 (m), 1457 (m), 1139 (s), 778 cm^{-1} (s).

Anal. Calcd for $C_{12}H_{14}Cl_2N_2O_4$: C, 45.0; H, 4.1; Cl, 22.2; N, 8.8; O, 20.0. Found: C, 44.6; H, 4.5; Cl, 22.4; N, 8.5; O, 20.2.

Preparation of 2-(Dihydroxymethyl)pyridine Hydrochloride (8).—Freshly distilled **5** (2.0 g, 0.0187 mol) was added to 10 ml of concentrated HCl. There was slight amount of heat evolved. The solution was poured into 200 ml of acetone. The mixture was stirred for 15 min in an ice–water bath and then was filtered. The solid was washed with several portions of acetone and dried under vacuum to give 2.24 g (74.3%) of colorless product: mp 109–110° (lit.[11] 103–107°); ir (Nujol 1612 and 1530 cm^{-1} (C=N and/or C=C).

Anal. Calcd for $C_6H_8ClNO_2$: C, 44.6; H, 5.0; N, 8.7. Found: C, 44.8; H, 5.0; N, 8.6.

The Effect of Water on 1,2-Di(2-pyridyl)-1,1,2,2-tetrahydroxyethane Dihydrochloride (7). A. Reflux under Nitrogen.—A solution of 5.0 g (0.016 mol) of **7** in 65 ml of distilled deionized water was placed in a reaction flask. The flask was equipped with a reflux condenser and a tube for bubbling nitrogen into the reaction mixture. The top of the condenser was connected to a bubbler containing Nujol to prevent air from entering the reaction flask. The solution was nitrogen purged for 10 min before heating was begun. The starting solution was a light, clear yellow-orange, which became deep red on heating. Approximately 15 min was required to bring the solution to reflux. The solution was allowed to reflux for 10 min in a nitrogen atmosphere. The solution was cooled in an ice bath and the pH adjusted to 7.0 with 1 *N* NaOH. The solution was then cooled in an ice bath for 45 min and slowly turned a muddy brown; however, no precipitate formed. The pH of the solution was adjusted to 10.0 using 1 *N* NaOH. The solution was then ex-

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[16] E. J. Poziomek, unpublished results.

[17] J. P. Schaefer and J. L. Bertram, *J. Amer. Chem. Soc.*, **89**, 4121 (1967).

tracted with three 100-ml and two 50-ml portions of diethyl ether. The extract was dried with Na_2SO_4 and evaporated *in vacuo* to give 0.221 g (0.4%) of a light green oil, identified as **3**. The pH of the aqueous portion was adjusted to 3.0 with 0.5 *N* HCl. The solution was then concentrated to 30 ml *in vacuo*. Ethanol (25 ml) was added to the slurry and the mixture was filtered to give 2.96 g of NaCl. The filtrate was concentrated *in vacuo* until a brown slurry formed. Addition of chloroform and slight heating caused the crude product to dissolve leaving 0.84 g of unidentified tar. The chloroform was removed under vacuum from the extract to give 2.32 g of crude **2**. The impure acid was sublimed at 100–110° (5.0 mm) to give 1.74 g (44.2%) of pure **2**, mp 135–137° (lit.[18] 135–137°). The purified acid was slightly yellow and gradually turned light pink on standing exposed to light.

The experiment was repeated, using the method described above and gave 2.93 g of NaCl, 0.234 g (6.7%) of **3**, 1.57 g (39.9%) of **2**, and 1.95 g of unidentified tar.

B. In Water at 5°.—A solution of 5.0 g (0.016 mol) of **7** in 50 ml of distilled, deionized water was placed in a glass-stoppered flask and allowed to stand at 5.0° for 69 hr. (The solution was purged with nitrogen before the storage period.) Dissolution of the starting material gave a clear orange solution which turned deep red upon standing. The pH was adjusted from 1.7 to 7.0 with 0.5 *N* NaOH. Bright orange crystals started to precipitate at pH 3.0. The solution was cooled and stirred for an additional 45 min before filtering. Filtration of the mixture gave 2.89 g (85.1%) of **1**, mp 154° (lit.[11] mp 154–155°). Adjustment of the pH of the filtrate to 10.0 with 0.5 *N* NaOH caused the solution to become a murky green color; however, no precipitate formed. The solution was extracted with four 50-ml portions of chloroform but the extract failed to give any product upon evaporation. The pH of the aqueous layer was adjusted to 1.0 with 1 *N* HCl acid.

A brown solid resulted when the solution was evaporated to dryness *in vacuo*. Ethanol was added to the flask and the resulting mixture was filtered to give 1.75 g of sodium chloride. The filtrate was concentrated *in vacuo* to give 0.58 g of crude **2**. The crude product was sublimed *in vacuo* at 110° (3 mm) to yield 0.24 g (6.1%) of pure **2** and 0.21 g of unidentified residue.

C. In Water at Room Temperature.—The same experimental procedure described in the preceding section was repeated except the solution was continuously stirred and the experiment was conducted at room temperature. After 69 hr the reaction mixture was a deep red color. The pH was adjusted from 1.0 to 7.0 with 0.5 *N* NaOH. Orange crystals started to precipitate at pH 3.0. The solution was cooled and filtered to give 1.12 g of a 1:1 mixture of **1** (16.4%) and **4** (16.4%). The amount of each component in the mixture was estimated from analysis of the ir spectrum.

The filtrate was acidified to pH 1.0, evaporated to dryness, extracted with ethanol, and filtered to give 2.3 g of NaCl. Vacuum evaporation of the filtrate gave 1.42 g (37.5%) of crude **2**. Purification *via* sublimation gave 0.52 g (13.1%) (mp 135–136°).

Reactions of Di-2-pyridylglyoxal in Ethanol with Catalytic Amounts of Acid. A. Room Temperature. (1) Under Air with HCl.—To 5.0 g (0.024 mol) of **1** in 300 ml of ethanol was added 0.1 ml of concentrated HCl. The flask was sealed with parafilm, covered with aluminum foil, and stirred at room temperature for 10 days. A light orange solution formed immediately on addition of the acid; this changed to a deep red color with time. The volume was reduced to 50 ml using a rotary evaporator under vacuum. The mixture was cooled and filtered to give 1.35 g (26.7%) of **4**, mp 153° (lit.[11] mp 156°).

Anal. Calcd for $C_{12}H_8N_2O_2$: C, 67.3; H, 4.7; N, 13.1; O, 14.9. Found: C, 67.5; H, 4.6; N, 13.3; O, 15.0.

The filtrate was stripped of any remaining ethanol *in vacuo* at 40° (7 mm) using a rotary evaporator to give 5.89 g of a brown viscous liquid identified as crude **9**.

(2) Under Air with HI.—The experimental procedure and reaction time are the same as used in the preceding experiment except that 0.1 ml of 58% HI was added instead of HCl. A light orange solution resulted when the acid was added which changed to a clear deep red solution on standing.

The volume was reduced to 50 ml using a rotary evaporator under vacuum. The mixture was cooled and filtered to give 1.12 g (21.7%) of **4**. The filtrate was further evaporated at 40° (7 mm) to give 4.66 g of a brown viscous liquid identified as crude **9**.

(3) Under Air without Acid.—The experimental procedure and reaction time are the same as described in the previous two experiments except no acid was added. A light yellow heterogeneous mixture formed when **1** was added to the ethanol. After the mixture was allowed to stand 10 days, the solvent was evaporated *in vacuo* using a rotary evaporator to give 5.0 g of **1** (quantitative recovery).

B. Elevated Temperature. (1) Under Air with HCl.—To a stirred solution of 5.0 g (0.024 mol) of **1** in 100 ml of ethanol was added 0.10 ml of concentrated HCl. The reaction flask was fitted with a heating mantle, reflux condenser, and a delivery tube for bubbling in a continuous stream of air. The top of the condenser was connected to a $CaCl_2$ drying tube. Air was continuously bubbled through the reaction mixture which was allowed to reflux for 12 hr. The mixture was cooled and filtered to give 0.634 g (12.3%) of **4**, mp 150°. The filtrate was concentrated to 30 ml by removing the ethanol *in vacuo*. The solution was cooled and filtered to give 1.08 g (21.2%) of **1**, mp 151°. The filtrate was concentrated *in vacuo* to give 5.18 g of crude **9**. The experiment was repeated using the above procedure and yielded 6.97 g of crude **9**.

(2) Under Nitrogen with HCl.—The experimental procedure and apparatus are the same as used in the preceding experiment except nitrogen instead of air was continuously bubbled through the reaction mixture. Nitrogen was bubbled through the reaction mixture for 20 min before heating. The color of the solution before heating was a light orange; it gradually darkened to a deep red when heated. Nitrogen was continuously bubbled through the solution which was refluxed 12 hr. The reaction mixture was cooled and filtered giving 1.62 g (31.5%) of **4**. The remaining ethanol was removed *in vacuo* at 40° (7 mm) to give 4.57 g (crude) of **9**.

The run was repeated using the same procedure and conditions to give 1.14 g (22.2%) of **4**, 0.38 g (7.5%) of **1**, and 4.62 g (crude) of **9**.

Reactions of 1,2-Di-2-pyridyl-1,2-ethenediol (4) in Ethanol with Catalytic Amounts of HCl. A. Refluxed under Nitrogen.—To a magnetically stirred solution of 5.0 g (0.023 mol) of purified **4** in 100 ml of ethanol was added 0.10 ml of 36 *N* HCl. The reaction flask was equipped with a reflux condenser and a tube for bubbling nitrogen through the reaction mixture. The top of the condenser was connected to a bubbler trap containing Nujol to prevent air from entering the reaction flask. Nitrogen was bubbled through the reaction mixture for 30 min before heating was started. The reaction mixture was allowed to reflux for 12 hr while a slow stream of nitrogen was bubbled through the mixture. The reaction mixture turned from orange to deep red on refluxing. The mixture was filtered to give 3.64 g (74.6%) of starting material. The filtrate was concentrated (volume reduced to 25 ml) *in vacuo*, cooled, and filtered to give 0.221 g (12.6%) of **1**, mp 151°. The remaining filtrate was further concentrated *in vacuo* at 40° (7 mm) to give 1.41 g of crude **9**.

B. Refluxed under Air.—The experimental procedure and apparatus are the same as described for the previous experiment, except air was bubbled through the reaction mixture instead of nitrogen. Work-up of the reaction mixture gave 3.13 g (63.5%) of starting material, 0.124 g (2.5%) of **1** (mp 153°), and 1.80 g of crude **9**.

Attempted Alkylation of Di-2-pyridylglyoxal (1) with Methyl Iodide.—Methyl iodide (6.7 g, 0.047 mol) was added to a magnetically stirred mixture of 5.0 g (0.024 mol) of **1** in 300 ml of ethanol. The mixture was refluxed for 3 hr, cooled in an ice bath, and filtered to give 0.83 g (16.1%) of **4**. The filtrate was evaporated *in vacuo* to give 6.03 g of crude **9**.

The crude **9** was fractionated as follows.

Fraction	Bp, °C	Pressure, mm	Wt, g	Estimated purity, %
1	60–80	7	0.710	95
2	108–109	7	0.857	99
3	110–111	7	1.914	99
R			2.206	

Fractions 1, 2, and 3 each contained a light yellow liquid which darkened on standing. The purity of each fraction was deter-

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[18] "The Merck Index," 6th ed, Merck and Co., Rahway, N. J., 1952, p 757.

mined using gas chromatography. Fraction 2 was submitted for elemental analysis: $n^{20}D$ 1.5115 (lit.[19] $n^{20}D$ 1.5104)

Anal. Calcd for $C_8H_9NO_2$: C, 63.6; H, 6.0; N, 9.3. Found: C, 63.2; H, 6.0; N, 9.3.

The experiment was repeated using the procedure outlined above except the reactants were refluxed in 100 ml of ethanol to give 1.80 g (35%) of 4 and 5.3 g of crude **9**.

Registry No.—**1**, 492-73-9; **6**, 27784-64-1; **7**, 27784-65-2.

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[19] R. C. Weast, Ed., "Handbook of Chemistry and Physics," 49th ed, Chemical Rubber Publishing Co., Cleveland, Ohio, 1968, p C520.

The Thermal Rearrangement of O-(2-Pyridyl) Oximes

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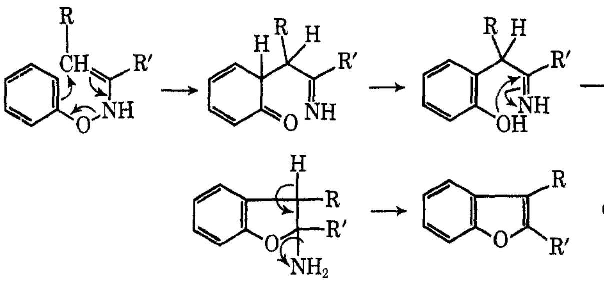
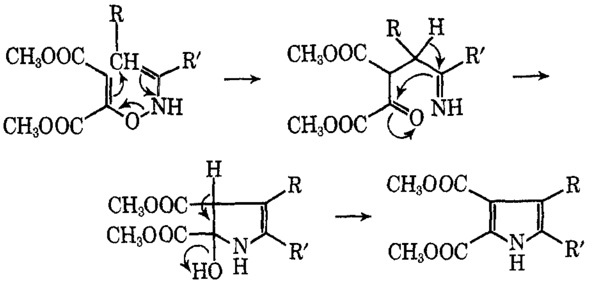
O-(2-Pyridyl) oximes of cyclopentanone, cyclohexanone, acetophenone, 1-indanone, and 1-tetralone (**1a–e**) were prepared by treating the respective oximes with 2-fluoropyridine. On heating, compounds **1** rearranged to yield 3-(2-oxoalkyl)-2-pyridones (**5**), of which two (**5b** and **5e**) were cyclized to the corresponding furo[2,3-*b*]pyridines (**6**). The mechanism of this rearrangement and its relationship to the Fischer indole synthesis are discussed.

Rearrangements of O-substituted oximes containing α-methylene groups have been recently reported by us[1,2] and by others.[3–5]

The rearrangement involves concerted cleavage of the nitrogen–oxygen bond and formation of a new carbon–carbon bond to give initially 4-imino ketones. These highly reactive species, however, cyclize spontaneously forming either furans (path A, observed in the case of O-phenyl oximes[6]) or pyrroles (path B, observed in the case of O-vinyl oximes[2]).



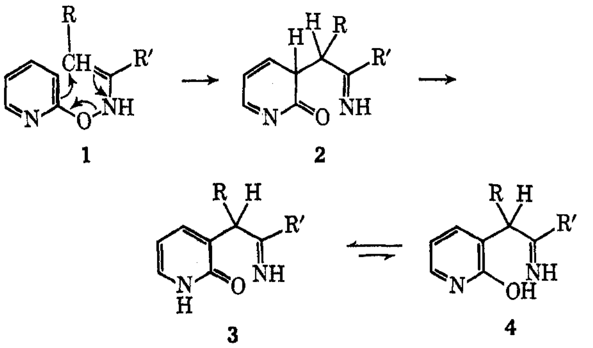
(A)



(B)

Path A is completely analogous to the Fischer indole synthesis[6,7] and involves rearrangement, aromatization to a phenol, and nucleophilic attack by the hydroxyl on the imine. Path B in which the initial intermediate retains the keto form involves a nucleophilic attack by the imine on the carbonyl.

We wish to report now the rearrangement of O-(2-pyridyl) oximes (**1**) (path C). We were interested in this peculiar case as it differs from those previously studied. Aromatization of the intermediate **2** should lead to **3**, as 2-hydroxypyridines are known to exist predominantly as 2-pyridones.[8] Cyclization to a furopyridine (path A mechanism) can proceed by nucleophilic action of the hydroxyl group in the minor tautomer **4**, but this course is unlikely in view of the available information on the reactivity of 2-pyridones.[9] On the other hand the amidic carbonyl in the pyridone **3** should be inert toward a nucleophilic attack by the imine (path B mechanism), thus excluding the possibility of cyclization to a pyrrole (7-azaindole in this case).



(C)

Termination of path C at compound **3** and isolation of an uncyclized product would further confirm the mechanisms suggested earlier (paths A and B) and provide new synthetic utility of the rearrangement.

The initial step (**1** → **2**) involves an electrophilic attack on the electron-deficient pyridine ring. It is to be expected that use of an acid catalyst would lead to further deactivation in this step because of protonation of the pyridine nitrogen. A thermal process,[10,11] by

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[8] A. R. Katritzky and J. M. Lagowsky, *Advan. Heterocycl. Chem.*, **1**, 339 (1963).

[9] H. Meislich in "Pyridine and Its Derivatives," Vol. 3, E. Klingsberg, Ed., Interscience, New York, N. Y., 1962, p 509.

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