containing a mixture of 1.4 g. (0.003 mole) of Ia and 0.1 g. of 10% palladium on charcoal catalyst in 25 ml. of absolute ethanol. The mixture was shaken for 1 hr. at room temperature (22°) during which time the theoretical amount of hydrogen required for the cleavage of the azo link (0.006 mole) was absorbed. The catalyst was then removed by heating the mixture to the boiling point and filtering hot. The transparent beige colored filtrate was evaporated to dryness rendering 1.4 g. of 3-amino-2,5-diphenylpyrrole (XI) (quantitative yield). Recrystallization from a methanol-water mixture furnished XI as silver-gray crystals melting at 186–187°. The authenticity of XI was established by an undepressed mixed melting point of a mixture with a specimen of XII obtained by an independent route (see above). The infrared spectrum was identical with that of an authentic sample.[11]

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[CONTRIBUTION FROM THE FRICK CHEMICAL LABORATORY, PRINCETON UNIVERSITY]

Pyridine 1-Oxides. IX. Further Oxidative Dimerizations of 4-Nitro-3-picolines[1a,b]

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Further experiments are described which verify the structure of the oxidative dimerization product of 4-nitro-3-picoline 1-oxide (I) as 1,2-di(1′-oxy-4′-nitro-3′-pyridyl)ethane (II) and elucidate its mode of formation. It is shown that II may be formed by treatment of I with sodium ethoxide *in the absence of external oxidizing agents;* since 4-nitro-3-picoline (VII) is recovered unchanged under similar conditions, it is concluded that the *N*-oxide grouping rather than the 4-nitro group is the effective oxidizing agent in the conversion of I to II. However, treatment of VII with 30% potassium hydroxide in ethanol in the presence of oxygen of 0° yields 1,2-di(4′-nitro-3′-pyridyl)ethane (VIII), identical with the product of phosphorus trichloride deoxygenation of II. Treatment of VII with 30% potassium hydroxide in ethanol in the presence of oxygen at room temperature yields 1,2-di(4′-ethoxy-3′-pyridyl)ethylene (X. R = C_2H_5), and it is shown that 1,2-di(4′-nitro-3′-pyridyl)ethane (VIII) is an intermediate in this conversion. Under similar conditions, 4-nitro-3-picoline 1-oxide (I) can be converted with sodium ethoxide in ethanol to 1,2-di(1′-oxy-4′-methoxy-3′-pyridyl)ethylene (XI. R = C_2H_5), which on deoxygenation gives X (R = C_2H_5). A similar series of reactions is described with the corresponding 4-methoxy derivatives. Catalytic reduction of XI (R = CH_3) yields 1,2-di(4′-methoxy-3′-pyridyl)ethane (XII. R = CH_3), identical with the reduction product of X (R = CH_3). Oxidation of XII (R = C_2H_5) with peracetic acid yields 1,2-di(1′-oxy-4′-ethoxy-3′-pyridyl)ethane (III. R = C_2H_5) which is identical with the product of the action of sodium ethoxide on 1,2-di(1′-oxy-4′-chloro-3′-pyridyl)ethane (IV). Compound II can be converted to XI (R = C_2H_5) with sodium ethoxide.

Previous work from this laboratory[2] had shown that treatment of 4-nitro-3-picoline 1-oxide (I) with *n*-butyl nitrite in the presence of sodium ethoxide resulted in oxidative dimerization to yield 1,2-(1′-oxy-4′-nitro-3′-pyridyl)ethane (II). The present investigation was undertaken in an effort to provide further evidence for the structure of II and to elucidate its mode of formation.

It has now been found that the oxidative dimerization product II is formed in moderate yield (20–35%) by treatment of 4-nitro-3-picoline 1-oxide (I) with sodium ethoxide alone. The same product is formed in comparable yield even when the reaction is run in a nitrogen atmosphere. This result can only mean that either the *N*-oxide group or the 4-nitro group is functioning as the oxidizing agent in the conversion of I to II, and that the *n*-butyl nitrite originally employed was presumably not essential for the conversion but merely served as an additional and perhaps more efficient oxidizing agent. As one would predict, deliberate addition of a better oxidizing agent such as sodium hypochlorite resulted in considerably increased yields of II.

In order to resolve the question of whether the *N*-oxide group or the nitro group was the active oxidizing agent, 4-nitro-3-picoline (VII),[3] prepared by deoxygenation of I with phosphorus trichloride in chloroform at 0°, was treated with sodium ethoxide in ethanol under nitrogen. No reaction took place and starting material was recovered. Thus, the *N*-oxide group is apparently serving as the oxidizing agent in the conversion of I to II. Activation of the 3-methyl group by the 4-nitro group is presumably also important, however, for 4-ethoxy-3-picoline 1-oxide could not be dimerized with sodium ethoxide, even when external oxidizing agents were also employed. This conclusion is further emphasized by the observation that 4-nitro-3-picoline (VII) with 30% potassium hydroxide in ethanol solution at 0° in the presence of oxygen gave an oxidative coupling product, 1,2-di(4′-nitro-3′-pyridyl)ethane (VIII), in 79% yield. This compound proved to be identical with the

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[1] (a) This work was supported in part by a research grant (C-2551) to Princeton University from the National Cancer Institute, National Institutes of Health, Public Health Service. (b) For the previous paper in this series, see E. C. Taylor and J. S. Driscoll, *J. Org. Chem.*, **26**, 3001 (1961). (c) Parke, Davis and Co. Fellow in Chemistry, 1957–1958: Monsanto Chemical Co. Fellow, 1958–1959.

[2] E. C. Taylor, A. J. Crovetti, and N. E. Boyer, *J. Am. Chem. Soc.*, **79**, 3549 (1957).

[3] This compound is rapidly converted to a mixture of 3-methyl-4-pyridone and 1-(3′-methyl-4′-pyridyl)-3-methyl-4-pyridone by moisture and care must be exercised to maintain anhydrous conditions in handling it. For details see ref. 1b.

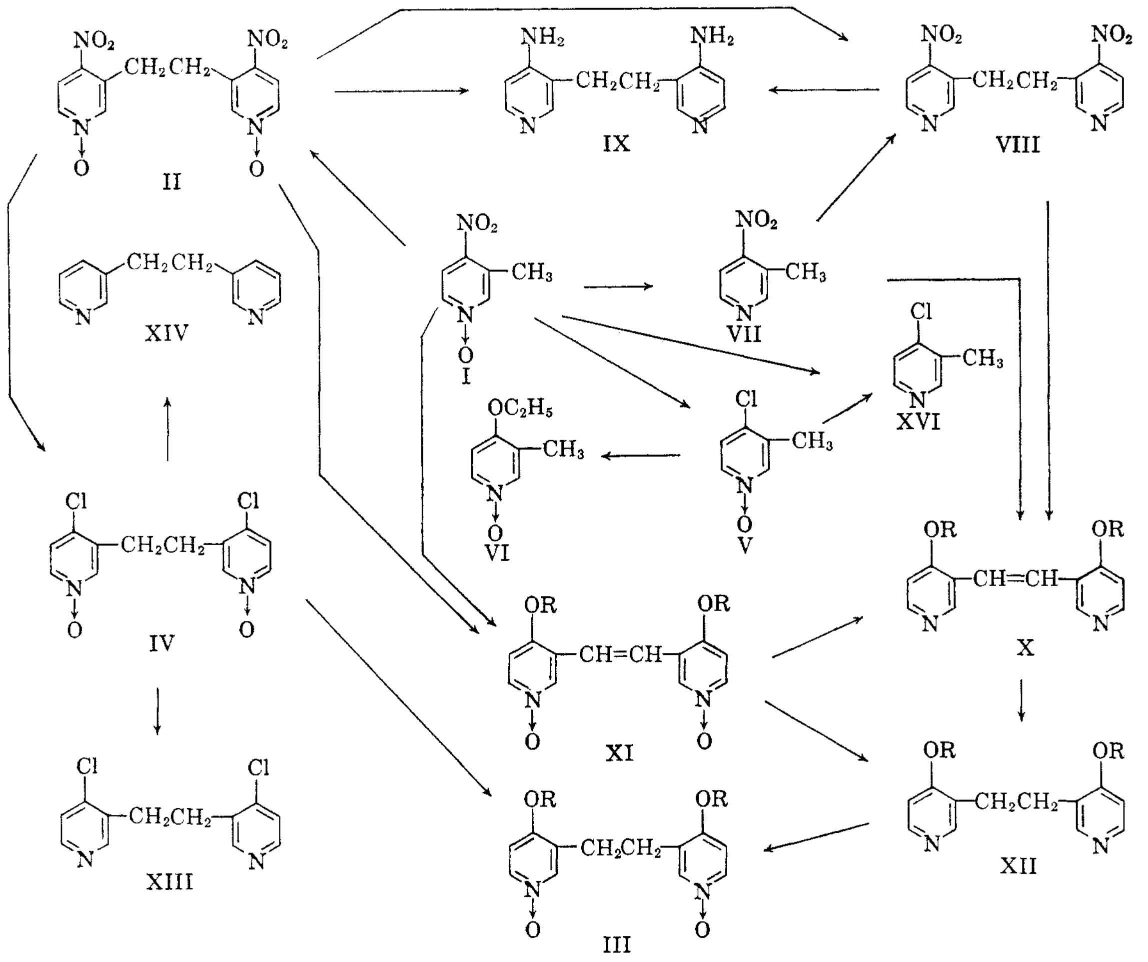


Figure 1

product of phosphorus trichloride deoxygenation of 1,2-di(1′-oxy-4′-nitro-3′-pyridyl)ethane (II). Catalytic reduction of either II or VIII gave 1,2-di(4′-amino-3′-pyridyl)ethane (IX).[2]

When 4-nitro-3-picoline (VII) was treated with 30% potassium hydroxide in methanol solution *at room temperature* in the presence of oxygen, a compound of empirical formula C_7H_7NO was formed. It rapidly decolorized solutions of aqueous potassium permanganate and bromine in carbon tetrachloride, and a chloroform solution of this compound gave an intense yellow color with tetranitromethane. A molecular weight determination showed it to be dimeric, and the compound thus must be 1,2-di(4′-methoxy-3′-pyridyl)ethylene (X. R = $-CH_3$). The corresponding ethoxy derivative (X. R = $-C_2H_5$) was prepared by treatment of VII with 30% potassium hydroxide in ethanol solution in like manner. From both reactions 1,2-di(4′-nitro-3′-pyridyl)ethane (VIII) could be isolated during the cold stage (0°) of the reaction. Removal of the ice bath resulted in dissolution of the yellow precipitate of VIII, and the ethers were then subsequently isolated. Both X (R = $-CH_3$) and X (R = $-C_2H_5$) were formed in high yield when 1,2-di(4′-nitro-3′-pyridyl)ethane (VIII) was employed as the starting material.

It was then found that treatment of 4-nitro-3-picoline 1-oxide (I) under similar conditions, or indeed, with sodium ethoxide in ethanol solution at room temperature in the absence of *n*-butyl nitrite, yielded an unsaturated dimeric ether, 1,2-di(1′-oxy-4′-ethoxy-3′-pyridyl)ethylene (XI. R = $-C_2H_5$). Deoxygenation with phosphorus trichloride gave 1,2-di(4′-ethoxy-3′-pyridyl)ethylene (X. R = $-C_2H_5$), identical in every respect with the product obtained either from VII or from VIII as described above. It was a surprise to find that XI (R = $-C_2H_5$) was identical with the product previously formulated[2] as 1,2-di(1′-oxy-4′-ethoxy-3′-pyridyl) ethane (III. R = $-C_2H_5$), which had been isolated from the original oxidative dimerization reaction. This previous structural assignment is thus in error. The compound originally reported as 1,2-di(1′-oxy-4′-hydroxy-3′-pyridyl)ethane, prepared from the ether by hydrolysis, should now be correctly represented as the corresponding ethylene derivative. A similar series of interconversions was carried out with the corresponding 4-methoxy derivatives with similar results (see Experimental and Fig. 1).

Catalytic reduction of 1,2-di(1′-oxy-4′-methoxy-3′-pyridyl)ethylene (XI. R = $-CH_3$) yielded 1,2-di(4′-methoxy-3′-pyridyl)ethane (XII. R = $-CH_3$), identical with the reduction product of 1,2-di(4′-methoxy-3′-pyridyl)ethylene (X. R = $-CH_3$). Oxidation of XII(R = $-C_2H_5$) with peracetic acid yielded 1,2-di(1′-oxy-4′-ethoxy-3′-pyridyl)ethane (III. R = $-C_2H_5$) which was identical with the product of the action of sodium ethoxide on 1,2-di-(1′-oxy-4′-chloro-3′-pyridyl)ethane (IV).

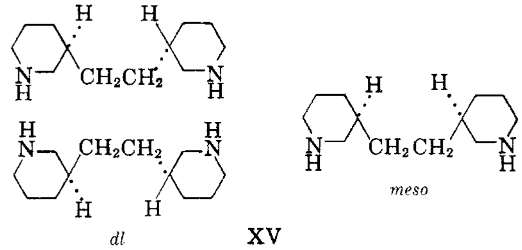
In view of the facile conversion of 1,2-di(4′-nitro-3′-pyridyl)ethane (VIII) to 1,2-di(4′-methoxy (or ethoxy)-3′-pyridyl)ethylene (X) described above, the previously reported[2] failure of attempts to react 1,2-di(1′-oxy-4′-nitro-3′-pyridyl)ethane (II) with sodium ethoxide seemed puzzling. It has now been found that II reacts smoothly with sodium ethoxide in the presence of air, but not in a sealed tube, to give XI in good yield.

The fact that the saturated nitro dimers (II and VIII) were isolated from the oxidative coupling reactions run at 0°, and that such compounds are intermediates in the formation of the corresponding ethylene derivatives X and XI, reveals that the former reaction is more facile than displacement of the 4-nitro group by alkoxide ion (at 0°). Apparently the methylene groupings of the ethane bridge must be activated by the 4-nitro group before oxidation can take place, for although VIII is readily converted to X, 1,2-di(4′-methoxy-3′-pyridyl)ethane (XII) cannot be oxidized to X under the same conditions. Also, once oxidation of the saturated to the unsaturated dimer has taken place, replacement of the nitro group by alkoxide seems to be rapid and complete, for it has not been possible in any instance to isolate unsaturated nitro dimers from the reaction mixtures. This observation stands in contrast to the results previously observed in analogous aromatic reactions, where nitro stilbenes are commonly observed products of oxidative dimerizations of *o*-nitrotoluenes,[4–6] and displacement of nitro groups is never observed.

Spectral evidence is completely in accord with the structures assigned above to the dimeric products. The unsaturated dimers (X and XI) have an absorption band in the region 972–976 cm.$^{-1}$, characteristic of a *trans* ethylenic carbon-hydrogen out-of-plane deformation vibration.[7] This absorption disappears on reduction of the ethylenic double bond. The ultraviolet absorption spectra of the dimers are also in complete accord with the assigned structures (see Table I). The positions of the absorption maxima in the saturated dimers are in every instance almost identical with the positions of maximum absorption exhibited by the corresponding 3-picolines, but the extinction coefficients are uniformly almost twice as great. The ethylenic compounds, on the other hand, absorb at longer wave lengths and have higher extinction coefficients as compared with the corresponding saturated dimers. It is interesting to note that the reported spectra of *p*-methoxystilbene[8] and 4-styrylpyridine[9] are very similar to the spectra of 1,2-di(4′-ethoxy-3′-pyridyl)ethylene (X. R = $-C_2H_5$) and 1,2-di-(4′-methoxy-3′-pyridyl)ethylene (X. R = $-CH_3$), and that the spectrum of 2,6-dimethyl-4-methoxypyridine[10] is very similar to the spectra of 1,2-di-(4′-ethoxy-3′-pyridyl)ethane (XII. R = $-C_2H_5$) and 1,2-di(4′-methoxy-3′-pyridyl)ethane (XII. R = $-CH_3$).

Only monopicrates were formed from the unsaturated dimers, while only dipicrates were formed from the corresponding saturated dimers. Apparently deactivation of the second ring by transmission of positive charge *via* the ethylenic bridge effectively prohibits dipicrate formation with the former derivatives.

We wish to record a few additional reactions which were carried out with some of the above compounds during the course of this investigation. A preliminary attempt to deoxygenate 1,2-di(1′-oxy-4′-chloro-3′-pyridyl)ethane (IV) by catalytic reduction using platinum oxide catalyst resulted in the formation of two isomeric products, $C_{12}H_{26}N_2Cl_2$, in which the halogens are ionically bound and in which the heterocyclic rings are reduced. As two asymmetric centers are formed during this reduction, it seems probable that the two compounds isolated are the *dl* and the *meso* forms of 1,2-di-(3′-piperidyl)ethane (XV). Catalytic reduction of IV with Raney nickel yielded 1,2-di(4′-chloro-3′-pyridyl)ethane (XIII), while reduction with Raney nickel alloy in sodium hydroxide (Papa, Schwenk, and Ginsberg conditions)[11] yielded 1,2-di(3′-pyridyl)ethane(XIV).



dl *meso*

XV

Initial attempts to deoxygenate 4-nitro-3-picoline 1-oxide (I) with phosphorus trichloride in chloroform at 70° yielded a halogen-containing oil

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TABLE I

Ultraviolet Absorption Spectra

Compound	Solvent	λ_{max} mμ	ϵ
4-Nitro-3-picoline (VII)	C_2H_5OH	280.5	2,750
	0.1N HCl	283	
1,2-Di(4′-nitro-3′-pyridyl)ethane (VIII)	C_2H_5OH	282.5	5,050
	0.1N HCl	286	
4-Chloro-3-picoline 1-oxide (V)	0.1N HCl	263	15,200
1,2-Di(1′-oxy-4′-chloro-3′-pyridyl)ethane (IV)	0.1NHCl	264.5	32,750
4-Ethoxy-3-picoline 1-oxide (VI)	C_2H_5OH	269.5	15,100
	0.1N HCl	250	11,600
1,2-Di(1′-oxy-4′-ethoxy-3′-pyridyl)ethane (III. R = —C_2H_5)	C_2H_5OH	269.5	36,750
1,2-Di(1′-oxy-4′-ethoxy-3′-pyridyl)ethylene (XI. R = —C_2H_5)	C_2H_5OH	273.2	43,500
		357	7,550
	0.1N HCl	238.5	34,700
		310 (s)	16,600
3-Picoline	C_2H_5OH	262.5	2,950
		269	2,500
1,2-Di(3′-pyridyl)ethane (XIV)	C_2H_5OH	262	6,300
		268.5	4,700
1,2-Di(4′-methoxy-3′-pyridyl)ethane (XII. R = —CH_3)	C_2H_5OH	241	19,800
1,2-Di(4′-ethoxy-3′-pyridyl)ethane (XII. R = —C_2H_5)	0.1N HCl	225	19,000
		256.5 (s)	
		263.5 (s)	
1,2-Di(4′-methoxy-3′-pyridyl)ethylene (X. R = —CH_3)	C_2H_5OH	309.5	21,800
	0.1N HCl	229.5	31,950
		294	18,150
1,2-Di(4′-ethoxy-3′-pyridyl)ethylene (X. R = —C_2H_5)	C_2H_5OH	310	22,600

which, by analysis of its picrate, was assigned the structure 4-chloro-3-picoline (XVI). This was confirmed by deoxygenation of 4-chloro-3-picoline 1-oxide (V) under similar conditions to give the same compound. Selective removal of the oxygen atom from I without displacement of the 4-nitro group can, as mentioned above, be effected by carrying out the reaction at 0°.

EXPERIMENTAL[12]

1,2-Di(1′-oxy-4′-nitro-3′-pyridyl)ethane (II). *Method A.* A solution of 2.0 g. of 4-nitro-3-picoline 1-oxide and 0.1 g. of *p*-benzoquinone in 100 ml. of ethanol was placed in a 250-ml. flask equipped with a calcium chloride tube, a gas inlet tube, and a dropping funnel, cooled to 0°, and a stream of nitrogen gas was bubbled through the solution for 1 hr. To this solution was added dropwise, and at 0°, a solution of 0.36 g. of sodium in 10 ml. of ethanol which had likewise been deoxygenated with nitrogen. Nitrogen flow was then discontinued, and the mixture was stirred for 3 hr. at 0°. The dark brown solution was filtered and the collected brown solid (0.65 g.) recrystallized from concentrated hydrochloric acid to give yellow crystals, m.p 233–234° dec., identical with an authentic sample.[2]

Method B. To a cold solution of 1 g. of 4-nitro-3-picoline 1-oxide in 25 ml. of absolute ethanol was added with stirring 5 ml. of 5% sodium hypochlorite. A solution of 0.1 g. of sodium in 4 ml. of ethanol was then added over a period of 30 sec. After stirring at 0° for 5 hr., 0.43 g. (43%) of yellow crystals was collected by filtration. Recrystallization from concentrated hydrochloric acid yielded yellow crystals, m.p. 239° dec. The products obtained by Methods A and B were identical as judged by a comparison of infrared spectra.

4-Ethoxy-3-picoline 1-oxide (VI). To a solution of 4.0 g. of 4-chloro-3-picoline 1-oxide[13] in 100 ml. of ethanol was added a solution of 0.66 g. of sodium in 20 ml. of ethanol. The mixture first turned dark green and then lightened rapidly. It was refluxed for 5 hr. and then filtered to remove sodium chloride (1.47 g.). The filtrate was diluted with 50 ml. of water and was then extracted with three 100-ml. portions of chloroform. The combined extracts were dried over anhydrous sodium sulfate and evaporated under reduced pressure to give a brown oil which solidified upon rubbing. After drying at 60° for 20 hr., this material weighed 4.0 g. (94%) and melted at 136–138°. The analytical sample, m.p. 138–139°, was prepared by sublimation at 110°/0.15 mm. This material is reported to melt at 139–140°.[2]

Anal. Calcd. for $C_8H_{11}NO_2$: C, 62.7; H, 7.2; N, 9.1. Found: C, 62.5; H, 7.1; N, 9.1.

4-Chloro-3-picoline (XVI) *picrate. Method A.* To a solution of 2.0 g. of 4-nitro-3-picoline 1-oxide in 20 ml. of chloroform was added 4.0 ml. of phosphorus trichloride, and the mixture was stirred at 0° for 5 min. and then at 70° for 1 hr. The light yellow solution was added to 50 ml. of water, the chloroform layer separated, and the aqueous layer adjusted to *p*H 10 with 10% aqueous sodium carbonate. The resulting brown emulsion was extracted with two 100-ml. portions of chloroform, and the combined extracts and the chloroform layer from the reaction mixture were combined, dried over anhydrous sodium sulfate and evaporated under reduced pressure. The residual brown oil was dissolved in warm ethanol and a saturated ethanolic solution of picric acid was added to give 1.76 g. (38%) of the picrate of 4-chloro-3-picoline, m.p. 150–155°. Recrystallization from water raised the m.p. to 153–155°.

Anal. Calcd. for $C_{12}H_9N_4O_7Cl$: C, 40.4; H, 2.55; N, 15.7. Found: C, 40.1; H, 2.85; N, 15.3.

Method B. To a stirred solution of 1.0 g. of 4-chloro-3-picoline 1-oxide in 15 ml. of chloroform at 3° was added 2.0 ml. of phosphorus trichloride. The mixture was then heated at 70° for 1 hr., added to ice water, and the mixture worked up as described above to give 1.19 g. (51%) of the picrate

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(12) All melting points are uncorrected. We are indebted for the microanalyses to Dr. Joseph F. Alicino, Metuchen, N. J., and to the Schwartzkopf Microanalytical Laboratory, New York, N. Y.

(13) A. R. Katritzky, *J. Chem. Soc.*, 2404 (1956).

of 4-chloro-3-picoline, m.p. 153–155°, identical with the product prepared by Method A.

1,2-Di(4′-nitro-3′-pyridyl)ethane (VIII). *Method A*. Oxygen was bubbled through a stirred solution of 30 g. of potassium hydroxide in 330 ml. of absolute ethanol at 3° for 10 min. To this solution was added, dropwise, a solution of 6.0 g. of 4-nitro-3-picoline[14] in 30 ml. of ethanol. The reaction mixture was stirred with oxygen at 3° for 1 hr. before the crystalline yellow precipitate which had formed was collected by filtration; yield, 4.69 g. (78%), m.p. 151–153°. Recrystallization from ethanol raised the m.p. to 152–155°.

Anal. Calcd. for $C_{12}H_{10}N_4O_4$: C, 52.55; H, 3.7; N, 20.4. Found: C, 52.8; H, 3.6; N, 20.65.

The picrate of this material, m.p. 173° dec., was prepared in ethanol solution.

Anal. Calcd. for $C_{24}H_{16}N_{10}O_{18}$: C, 39.35; H, 2.2; N, 19.1. Found: C, 39.4; H, 2.4; N, 19.2.

Method B. A mixture of 2.0 g. of 1,2-di(1′-oxy-4′-nitro-3′-pyridyl)ethane and 8.0 ml. of phosphorus trichloride in 50 ml. of chloroform was heated at 60° for 3.5 hr. and then added to 125 ml. of water. Sodium carbonate was added to *p*H 8 and the mixture was extracted with four 25-ml. portions of chloroform. The combined extracts were dried over anhydrous sodium sulfate and evaporated under reduced pressure to give 1.67 g. of a brown solid, m.p. 93–96°. Fractional recrystallization of this material from 50% aqueous ethanol yielded 0.42 g. (23%) of impure 1,2-di(4′-nitro-3′-pyridyl)ethane, m.p. 130–135°. Further recrystallization from the same solvent raised the m.p. to 147–149°. The infrared spectrum of this compound was identical with the spectrum given by the product obtained by Method A.

Concentration of the filtrates from the recrystallizations above gave 0.51 g. of brown needles which exhibited a strong Beilstein test and which did not depress the melting point of an authentic sample of 1,2-di(4′-chloro-3′-pyridyl)ethane (XIII).[2]

1,2-Di(4′-amino-3′-pyridyl)ethane (IX). A solution of 1.0 g. of 1,2-di(4′-nitro-3′-pyridyl)ethane in 150 ml. of hot methanol was cooled to room temperature, approximately 1 g. of Raney nickel catalyst (washed with methanol) added and the mixture shaken under 3 atm. of hydrogen at room temperature for 16.5 hr. Removal of the catalyst by filtration and concentration of the methanol filtrate under reduced pressure gave 0.74 g. (95%) of light tan crystals, m.p. 242–243°. Recrystallization from water raised the m.p. to 244–245°. This material is reported to melt at 250–251°.[2] Comparison of infrared spectra and a mixed melting point determination with an authentic sample showed them to be identical.

1,2-Di(4′-methoxy-3′-pyridyl)ethylene (X. R = — OH_3). *Method A*. A rapid stream of oxygen was bubbled through 10 ml. of a 30% solution of potassium hydroxide in methanol at 2° for 10 min. A solution of 1.05 g. of 4-nitro-3-picoline in 10 ml. of methanol was then added dropwise over a period of 5 min. into the cold, stirred solution. The color of the reaction mixture changed from clear to red-brown, and within 10 min. a yellow precipitate separated, which was shown by a mixed melting point determination and by comparison of infrared spectra to be 1,2-di(4′-nitro-3′-pyridyl)-ethane. The red-brown mixture containing this yellow precipitate was stirred for 1 hr. at 2° in a stream of oxygen, the ice bath was removed, and the mixture was stirred with oxygen for 5 hr. at room temperature. Addition of 100 ml. of water caused the separation of 0.39 g. of white crystals, m.p. 173–177°. An additional 0.13 g. (total yield, 0.52 g., 57%) separated from the filtrate upon standing. Recrystallization from water raised the melting point to 180–183°.

Anal. Calcd. for $C_{14}H_{14}N_2O_2$: C, 694.; H, 5.8; N, 11.6 mol. wt. 242. Found: C, 69.4; H, 5.7; N, 11.4 mol. wt. 254.

Method B. A stream of air was blown through a stirred solution of 0.5 g. of 1,2-di(4′-nitro-3′-pyridyl)ethane in 50 ml. of 30% potassium hydroxide in methanol for a period of 3 hr. at room temperature. Addition of 100 ml. of water, chilling and filtering then yielded 0.36 g. (91%) of white crystals, m.p. 168–172°. Recrystallization from water raised the m.p. to 180–183°.

Method C. To a stirred solution of 0.25 g. of 1,2-di(1′-oxy-4′-methoxy-3′-pyridyl)ethylene in 30 ml. of chloroform was added 1.0 ml. of phosphorus trichloride. A white solid separated immediately. The resulting suspension was heated at 70° for 1 hr., cooled and added to 50 ml. of water. The *p*H was adjusted to 8 with sodium carbonate, the chloroform layer was separated and the aqueous layer was extracted with two 100-ml. portions of chloroform. The chloroform solutions were combined, dried over anhydrous sodium sulfate, and evaporated under reduced pressure to give 0.16 g. (73%) of a white solid, m.p. 173–175°. Recrystallization from water raised the m.p. to 180–183°.

Determination of mixed melting points and comparison of infrared spectra showed the products obtained by Methods A, B, and C to be identical.

1,2-Di(4′-ethoxy-3′-pyridyl)ethylene (X. R = — C_2H_5). *Method A*. A solution of 1.18 g. of 4-nitro-3-picoline in 100 ml. of 30% potassium hydroxide in ethanol was stirred with a stream of oxygen at 4° for 1 hr., and then at room temperature for 4 hr. Ethanol was added at half-hour intervals because of evaporation. The reaction mixture was then diluted with 150 ml. of water, extracted with two 250-ml. portions of chloroform, and the extracts dried and evaporated under reduced pressure. Sublimation of the red residue gave a small amount of white crystals, m.p. 128–129°.

Anal. Calcd. for $C_{16}H_{18}N_2O_2$: C, 71.1; H, 6.7; N, 10.4. Found: C, 71.3; H, 7.0; N, 10.5.

Method B. Treatment of 0.25 g. of 1,2-di(1′-oxy-4′-ethoxy-3′-pyridyl)ethylene in chloroform solution with phosphorus trichloride as described above in Method B yielded 0.11 g. (49%) of a light yellow solid, m.p. 122–123°. Sublimation at 120°/0.2 mm. yielded white crystals, m.p. 124–126°. A mixed melting point determination and comparison of infrared spectra showed the products prepared by Methods A and B to be identical.

1,2-Di(1′-oxy-4′-methoxy-3′-pyridyl)ethylene (XI. R = —CH_3). *Method A*. Air was bubbled through 200 ml. of 30% potassium hydroxide in methanol for 10 min. at 3°, and then 2.0 g. of 4-nitro-3-picoline 1-oxide in 100 ml. of methanol was added with stirring over a period of 5 min. The reaction mixture, which immediately turned dark green, was stirred with a current of air for 1 hr. at 3° and then for 2 hr. at room temperature. The mixture was diluted with 200 ml. of water and extracted with three 250-ml. portions of chloroform. The extracts were combined, dried over anhydrous sodium sulfate and evaporated under reduced pressure to give 1.04 g. (59%) of yellow crystals, m.p. 229–230° dec. Recrystallization from nitromethane raised the melting point to 242° dec.

Anal. Calcd. for $C_{14}H_{14}N_2O_4$: C, 61.3; H, 5.15; N, 10.2. Found: C, 61.3; H, 5.3; N, 10.3.

The picrate, prepared in ethanol solution and recrystallized from water, melted with decomposition at 237–238°.

Anal. Calcd. for $C_{20}H_{17}N_5O_{11}$: C, 47.7; H, 3.4; N,13.9. Found: C, 47.7; H, 3.5; N, 14.1.

Method B. A suspension of 1.0 g. of 1,2-di(1′-oxy-4′-nitro-3′-pyridyl)ethane in 100 ml. of 30% potassium hydroxide in methanol was stirred at room temperature for 12 hr. with a steady stream of air. Methanol was added at intervals to keep the volume approximately constant. Addition of 100 ml. of water resulted in the separation of 0.36 g. of a yellow solid, m.p. 227° dec., while extraction of the filtrate with three 100-ml. portions of chloroform and concentration of the extracts yielded an additional 0.38 g. of product (total yield, 0.74 g., 83%). Recrystallization raised the decomposition point to 242°. The infrared spectra of the products prepared by methods A and B were identical.

1,2-Di(1′-oxy-4′-ethoxy-3′-pyridyl)ethylene (XI. R = — C_2H_5). *Method A*. A solution of 5.0 g. of 4-nitro-3-picoline

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(14) W. Herz and L. Tsai, *J. Am. Chem. Soc.*, 76, 4184 (1954).

1-oxide in 180 ml. of ethanol at 40° was added rapidly to a solution of 3.0 g. of sodium in 50 ml. of ethanol at 5°, and the resulting mixture was stirred for 1 hr. at 5° and then for 2.5 hr. at room temperature. It was then diluted with 350 ml. of water and extracted with four 250-ml. portions of chloroform. Concentration of the dried chloroform extracts yielded 2.08 g. (42%) of yellow crystals, m.p. 231–232° dec. Recrystallization from water raised the decomposition point to 239°. The compound lost 8–11% of its weight upon drying for analysis.

Anal. Calcd. for $C_{16}H_{18}N_2O_4$: C, 63.6; H, 6.0; N, 9.3. Found: C, 63.5; H, 6.2; N, 9.5.

The picrate, prepared in ethanol and recrystallized from water, melted with decomposition at 211–212°.

Anal. Calcd. for $C_{22}H_{21}N_5O_{11}$: C, 49.7; H, 4.0; N, 13.2. Found: C, 49.4; H, 4.2; N, 13.2.

Method B. A suspension of 0.5 g. of 1,2-di(1′-oxy-4′-nitro-3′-pyridyl)ethane in 50 ml. of ethanol containing 0.5 g. of sodium was stirred in contact with air for 24 hr. at room temperature. The resulting dark brown solution was diluted with 100 ml. of water and extracted with three 100-ml. portions of chloroform. The combined extracts were dried and evaporated under reduced pressure to give 0.36 g. of a brown solid, m.p. 226–228° dec. Recrystallization from water gave yellow crystals, m.p. 240° dec. The infrared spectra of the products prepared by methods A and B were identical.

1,2-Di(4′-methoxy-3′-pyridyl)ethane (XII. R = $-CH_3$). *Method A.* A mixture of 0.6 g. of 1,2-di(4′-methoxy-3′-pyridyl)ethylene, 1.0 g. of platinum oxide catalyst and 100 ml. of ethanol was shaken at 45° under 3 atm. of hydrogen for 16.5 hr. The catalyst was removed by filtration and the filtrate concentrated under reduced pressure to give 0.44 g. (73%) of a white solid, m.p. 160–169°. Recrystallization from water raised the m.p. to 170°.

Anal. Calcd. for $C_{14}H_{16}N_2O_2$: C, 68.8; H, 6.6; N, 11.5. Found: C, 68.65; H, 6.9; N, 11.4.

The picrate, prepared in ethanol and recrystallized from water, melted with decomposition at 232–233°.

Anal. $C_{26}H_{22}N_8O_{16}$: C, 44.45; H, 3.2; N, 15.95. Found: C, 44.35; H, 3.1; N, 16.0.

Method B. Hydrogenation of 3.0 g. of 1,2-di(1′-oxy-4′-methoxy-3′-pyridyl)ethylene with platinum oxide catalyst in ethanol solution at 44° and 3 atm. pressure for 17 hr., and isolation of the product as described above, gave 2.33 g. (87%) of a white solid, m.p. 160–168°. Recrystallization from water raised the m.p. to 170°. Comparison of infrared spectra showed the products obtained by Methods A and B to be identical.

1,2-Di(4′-ethoxy-3′-pyridyl)ethane (XII. R = $-C_2H_5$). Catalytic hydrogenation of 1,2-di(1′-oxy-4′-ethoxy-3′-pyridyl)ethylene as described above for the 4′-methoxy analog yielded 1,2-di(4′-ethoxy-3′-pyridyl)ethane in 55% yield as white crystals, m.p. 122°.

Anal. Calcd. for $C_{16}H_{20}N_2O_2$: C, 70.6; H, 7.4; N, 10.3. Found: C, 70.8; H, 7.6; N, 10.4.

The picrate, prepared in ethanol and recrystallized from water, melted with decomposition at 242°.

Anal. Calcd. for $C_{28}H_{26}N_8O_{16}$: C, 46.0; H, 3.6; N, 15.3. Found: C, 46.2; H, 3.6; N, 15.1.

1,2-Di(1′-oxy-4′-methoxy-3′-pyridyl)ethane (III. R = $-CH_3$). A solution of 1.0 g. of 1,2-di(1′-oxy-4′-chloro-3′-pyridyl)ethane in 50 ml. of methanol containing 2.0 g. of sodium methoxide was sealed in a glass ampoule and heated on a steam bath for 24 hr. After cooling, the sodium chloride which had separated was removed by filtration and the filtrate was evaporated to dryness under reduced pressure. The residue was dissolved in 100 ml. of water and the *p*H adjusted to 6–7 by the addition of dilute hydrochloric acid. The resulting solution was evaporated to dryness and the residue extracted with 100 ml. of hot ethanol. Evaporation of the ethanol extract then yielded 0.88 g. of an orange solid, m.p. 195–196° dec. Recrystallization from aqueous acetone yielded light yellow crystals, m.p. 221° dec.

Anal. Calcd. for $C_{14}H_{16}N_2O_4$: C, 60.9; H, 5.8; N, 10.1. Found: C, 60.7; N, 5.8; N, 10.2.

1,2-Di(1′-oxy-4′-ethoxy-3′-pyridyl)ethane (III. R = $-C_2H_5$). *Method A.* A solution of 1.0 g. of 1,2-di(1′-oxy-4′-chloro-3′-pyridyl)ethane in 75 ml. of ethanol containing 0.68 g. of sodium was heated in a sealed glass ampoule on a steam bath for 24 hr. The reaction mixture was then worked up as described above to give 0.98 g. (92%) of yellow crystals, m.p. 224–225° dec. Recrystallization from aqueous acetone raised the decomposition point to 231–232°.

Anal. Calcd. for $C_{16}H_{20}N_2O_4$: C, 63.1; H, 6.6; N, 9.2. Found: C, 63.4; H, 6.5; N, 9.4.

Method B. A solution of 1.5 g. of 1,2-di(4′-ethoxy-3′-pyridyl)ethane in 60 ml. of glacial acetic acid containing 15 ml. of 40% peracetic acid was stirred at room temperature for 1 hr. and then at 70–80° for 6 hr. A small amount of charcoal was added to catalyze the decomposition of residual peroxide, the mixture was filtered and the filtrate diluted with 100 ml. of water. The *p*H was adjusted to 7 with 20% aqueous sodium hydroxide and a small amount of starting material which had separated was removed by filtration. Evaporation of the filtrate to dryness, extraction of the residue with chloroform, and evaporation of the chloroform extracts yielded 0.79 g. of a yellow solid, m.p. 209–221° dec. This solid was extracted in turn with dry acetone. Recrystallization of the acetone-insoluble fraction from aqueous acetone yielded white crystals, m.p. 229–231° dec., which were identical in every respect with the product obtained by Method A.

1,2-Di(4′-chloro-3′-pyridyl)ethane (XIII). A suspension of 0.5 g. of 1,2-di(1′-oxy-4′-chloro-3′-pyridyl)ethane in 30 ml. of chloroform and 2.0 ml. of phosphorus trichloride was heated at 72° for 1 hr. and then added to 50 ml. of water. The *p*H was adjusted to 8 with 10% sodium carbonate, the chloroform layer separated, and the aqueous layer extracted with two 100-ml. portions of chloroform. Combination of the chloroform solutions, drying and evaporation under reduced pressure yielded 0.36 g. (81%) of tan crystals, m.p. 109–111°. This compound is reported to melt at 110°.[2] This compound proved to be identical with an authentic sample, as judged by a mixed melting point determination and by a comparison of infrared spectra.

1,2-Di(3′-pyridyl)ethane (XIV). To a solution of 5.0 g. of 1,2-di(1′-oxy-4′-chloro-3′-pyridyl)ethane in 400 ml. of 10% sodium hydroxide at 90° was added cautiously (foaming) and in small portions, 15 g. of Raney nickel alloy over a period of 1.25 hr. The mixture was heated at 90° for an additional hour and then filtered. The nickel catalyst was washed with 200 ml. of water, and the combined filtrates were extracted with two 300-ml. portions of chloroform. The combined extracts were dried over anhydrous sodium sulfate and evaporated under reduced pressure to give 1.78 g. (55%) of almost white crystals, m.p. 51–58°. Distillation (b.p. 128°/0.4 mm.) raised the m.p. to 54–59°.

Anal. Calcd. for $C_{12}H_{12}N_2$: C, 78.2; H, 6.6; N, 15.2. Found: C, 78.2; H, 6.5; N, 15.2.

The picrate, prepared in ethanol and recrystallized from water, melted with decomposition at 245°.

Anal. Calcd. for $C_{24}H_{18}N_8O_{14}$: C, 44.9; H, 2.8; N, 17.4. Found: C, 44.4; H, 3.0; N, 17.6.

1,2-Di(3′-piperidyl)ethane dihydrochloride (XV). A suspension of 1.0 g. of 1,2-di(1′-oxy-4′-chloro-3′-pyridyl)ethane and 0.5 g. of platinum catalyst in 100 ml. of ethanol was shaken for 3 hr. at 43° under 3 atm. of hydrogen. The mixture was heated to boiling, filtered while hot, and the filtrate evaporated to dryness under reduced pressure to give 0.42 g. of a yellow solid, m.p. 293–297° dec. Recrystallization from a mixture of ethanol and ether gave white crystals, m.p. 304° dec.

Anal. Calcd. for $C_{12}H_{26}N_2Cl_2$: C, 53.7; H, 9.7; N, 10.45. Found: C, 53.6; H, 9.6; N, 10.7.

The material which was collected by the filtration above (which includes the catalyst) was extracted with 25 ml. of water. Evaporation of the extract then gave 0.36 g. of white crystals, m.p. > 360°, which were purified by recrystallization from aqueous acetone.

Anal. Calcd. for $C_{12}H_{26}N_2Cl_2$: C, 53.7; H, 9.7; N, 10.45. Found: C, 53.6; H,9.6; N, 10.5.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF ROCHESTER]

Amine Oxides. A Comparison of 2-Vinylpyridine *N*-Oxide and the 2,3-Dihydroisoxazolo[2,3-a]pyridinium Ion[1]

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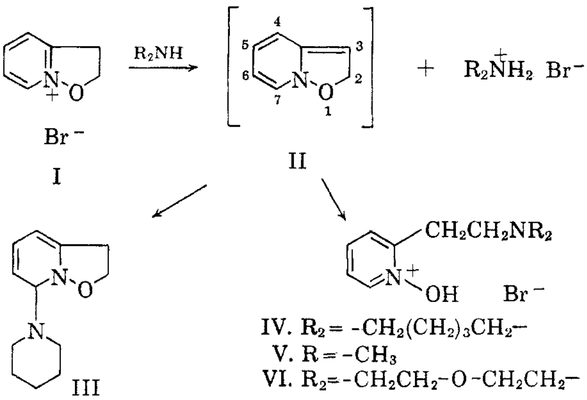
The reaction of 2-vinylpyridine *N*-oxide with nucleophilic reagents occurs readily and follows a course similar to that of 2-vinylpyridine. The adducts obtained with secondary amines are the same as the major products resulting from the reaction of secondary amines with 2,3-dihydroisoxazolo(2,3-a)pyridinium bromide.

Previously,[3] we reported on the preparation of some cyclic quaternary salts derived from pyridine *N*-oxide and their decomposition with base. The reaction of 2,3-dihydroisoxazolo (2,3-a)-pyridinium bromide (I) with aqueous piperidine led to the separation of an unstable crystalline product (III), m.p. 124–126°, of unusual chemical and spectral properties. The composition of this product corresponded to the empirical formula $C_{12}H_{18}N_2O$, which is in accord with that required for an adduct of piperidine and 2-vinylpyridine *N*-oxide. However, the ultraviolet absorption spectrum of the unstable product and its behavior on hydrogenation clearly eliminated this possibility.

Reinvestigation of this reaction has led to the isolation of an additional product (IV), m.p. 167–168.5°, whose composition is in accord with the empirical formula $C_{12}H_{19}N_2OBr$. Although the yields of III and IV varied in individual experiments, IV was predominant in each instance and the sum of III and IV accounted for all the 2,3-dihydrooxazolo (2,3-a) pyridinium bromide employed. As IV had the characteristics of a hydrobromide salt, it was converted to the corresponding free base which was an oil markedly different from III in its spectral properties.

The ultraviolet absorption spectrum of IV showed a single maximum at 263 mμ (ε 11,500), suggesting the possibility that it was a simple pyridine or pyridine *N*-oxide derivative. In the color test devised by Katritzky,[4] IV gave a positive result for the presence of an *N*-oxide function. Treatment of IV, then, with phosphorus trichloride effected removal of the *N*-oxide group and yielded an oil identical in its infrared spectrum and other properties with 2-[β-(*N*-piperidino)ethyl]pyridine. The identity was further established by comparison of the dipicrate derivatives. Thus, IV must be the hydrobromide salt of 2-[β-(*N*-piperidino)ethyl] pyridine *N*-oxide and a possible explanation for its formation is illustrated below.



The reaction of dihydroisoxazolo-[2,3-a]pyridinium bromide (I) with aqueous dimethylamine and with morpholine was also studied and, in each case, gave a single product in high yield. The structure of the dimethylamine product V was established by independent synthesis. The structure VI assigned to the product with morpholine is based on its physical and spectral properties as well as analogy.

Although the structure of I seems clearly established, particularly in view of its spectral properties, a possible explanation for its easy conversion to IV, V and VI on treatment with secondary amines might lie in the existence of an equilibrium between I and the corresponding salt of 2-vinyl pyridine *N*-oxide (VII). To test this possibility a sample of 2-vinylpyridine *N*-oxide was prepared and converted to its picrate. It was readily demonstrated that this picrate was different from, and not easily interconvertible with, the picrate of I.

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[4] N. A. Coats and A. R. Katritzky, *J. Org. Chem.*, **24**, 1836 (1959).