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THE MOLECULAR COMPLEX OF 4-(N-PYRIDINIUM)PYRIDINE-N-OXIDE CHLORIDE WITH TETRACYANOETHYLENE IN THE SYNTHESIS OF SUBSTITUTED PYRIDINE N-OXIDES

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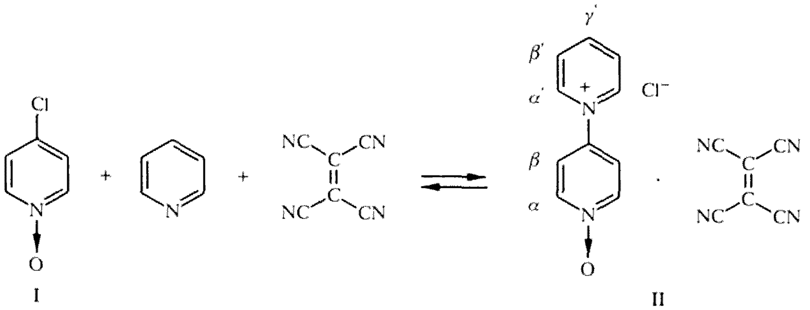
The structure of the complex of 4-(N-pyridinium)pyridine-N-oxide chloride with tetracyanoethylene was studied by ^{13}C NMR spectroscopy. The results of the investigation, suggesting the use of this complex in the synthesis of substituted pyridine derivatives, were confirmed experimentally by its reaction with oxygen and with nitrogen-containing nucleophiles.

Earlier we were the first to show on the example of the reaction of the N-oxide of 4-chloropyridine (I) with pyridine and tetracyanoethylene, that the binding of aromatic substances in complexes with charge transfer II substantially facilitates their interaction with nucleophiles [1].


I

II

In the absence of tetracyanoethylene this process does not occur. The structure of complex II was confirmed by the IR and UV spectra and by qualitative reactions. In an attempt to isolate the chloride of 4-(N-pyridinium)pyridine-N-oxide in the free state from the complex II, for example, by column or preparative thin-layer chromatography, it breaks down quantitatively to the starting materials. Nonetheless, a more detailed investigation of the complex II is both of theoretical and of practical interest, especially in connection with the possibility of using it in the synthesis of 4-substituted derivatives of pyridine N-oxide.

It is known that the ability of aromatic substrates for nucleophilic substitution depends on the presence of sufficiently good leaving groups and a high total electron deficiency of the π-system. Actually, complex II contains one of the most nucleophilic substituents — the pyridinium cation, and its higher (in comparison with the N-oxide I) electron deficiency was confirmed by ^{13}C NMR spectroscopy (Table 1), in comparison with the model compound — pyridinium hydrochloride (V).

In agreement with the literature data [2], one group of signals in the spectrum of compound II corresponds to the pyridinium cation, and the other is characteristic of the N-oxide fragment. In this case the signals from the $C_{(\alpha)}$ and $C_{(\beta)}$ atoms are slightly shifted in the weak-field direction on account of the overall unshielding of the aromatic system of the N-oxide when the chlorine atom is replaced by a pyridinium cation and a complex is formed with tetracyanoethylene. Evidently the weakest-field shift (about 3 ppm) is observed for the $C_{(\gamma)}$ atom. Correspondingly, complex II should be more sensitive to nucleophilic attack than the N-oxide I.

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TABLE 1. ^{13}C NMR Spectra of Compounds I, II, and V

Compound	Chemical shift (δ, ppm)					
	$2C(\alpha)$	$2C(\beta)$	$C(\gamma)$	$2C(\alpha')$	$2C(\beta')$	$C(\gamma')$
I	140,39	127,00	129,88	—	—	—
II*	140,56	127,30	132,84	142,09	127,64	146,80
V*	—	—	—	141,90	127,60	146,90

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*For graphical comparison, the numeration of the atoms in the pyridinium cation (compounds II and V) is shown with a prime.

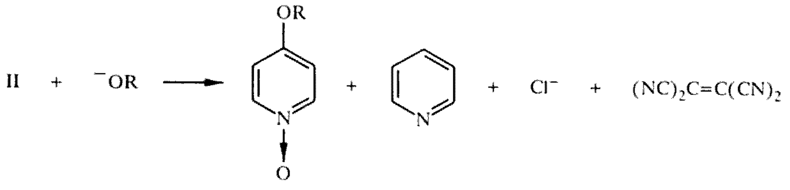
TABLE 2. Characteristics of the N-Oxides Synthesized, IIIa-e, IVa,b

N-Oxide	T_m, °C	IR spectrum, $\nu_{N\text{-oxide}}$, cm^{-1}	Yield, %
III a	240 (with dec.)	—	82
III b	82	1275	87
III c	124...126 (picrate)	1270	74
III d	175...176	1273	93
III e	129...130	1295	68
IVa	75...76	1235	74
IV b	184...185 (hydrochloride)	1242	69

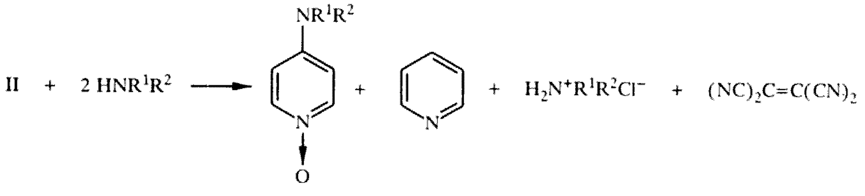
Actually, when complex II is treated with potassium hydroxide, sodium alkoxides, sodium phenolate, or aromatic amines under mild conditions, 4-substituted N-oxides of pyridine are formed (Table 2).

When the N-oxide I is used, these reactions proceed under more rigorous conditions for a longer time. Thus, for example, its interaction with morpholine occurs only at 135°C in a sealed ampule for 5 h [3]. Moreover, under these conditions N-oxides have a tendency for appreciable deoxidation [4].

The direct addition of sodium alkoxide or secondary amines to a mixture of the N-oxide I and tetracyanoethylene (but not complex II) to activate nucleophilic substitution of the chloride ion does not lead to the desired result. In this case an interaction of tetracyanoethylene with nucleophiles and the formation of tricyanovinyl derivatives of the $(NC)_2C = C(CN)\text{-}X$ ($X = OR$, NR^1R^2) type are observed [5, 6], and the N-oxide I is regenerated in unchanged form. The use of complex II as an intermediate permits nucleophilic substitution in the N-oxide I.



III a-e



IV a, b

IIIa $R = H$, b $R = CH_3$, c $R = C_2H_5$, d $R = CH_2C_6H_5$, e $R = C_6H_5$; IVa $R^1 = R^2 = C_2H_5$, b $NR^1R^2 =$ N-Morpholino

EXPERIMENTAL

The ^{13}C NMR spectra were recorded on a Gemini-200 spectrometer (200 MHz), with solvent DMSO-D_6 and internal standard TMS. The IR spectra of 2% solutions of the substances in chloroform were recorded on an IKS-29 instrument. Complex II was synthesized according to the procedure of [1].

4-Hydroxypyridine N-Oxide (IIIa). A mixture of 337 mg (1 mmole) of the complex II, 0.28 g (5 mmoles) potassium hydroxide, and 5 ml of water was heated for 4 h at 40°C, acidified to pH 6 with acetic acid, and evaporated under vacuum until a precipitate formed. The reaction product was filtered off, washed with water, and recrystallized from ethanol. Yield 91 mg (82%), T_m 240°C (with dec.).

4-Methoxypyridine N-Oxide (IIIb). To a mixture of 337 mg (1 mmole) of the complex II in 5 ml of absolute methanol we added a solution of 115 mg (5 mmoles) of metallic sodium in 5 ml of methanol. The dark-red solution was left for 24 h at room temperature, the solvent was evaporated under vacuum, the residue was carefully triturated with anhydrous chloroform (4 × 5 ml), the chloroform extract was evaporated to dryness under vacuum, and the residue was recrystallized from a mixture of benzene and acetone (1:1). Yield 109 mg (87%), T_m 82°C.

The following were produced analogously: 4-ethoxypyridine N-oxide (IIIc), using absolute ethanol as the solvent; 4-benzyloxypyridine N-oxide (IIId) — solvent benzyl alcohol; and 4-phenoxypyridine N-oxide (IIIe) — mixture of dioxane with ethanol, 1:1 (the reaction was conducted with sodium phenolate at 70°C).

4-(N-Morpholino)pyridine N-Oxide (IVb). A mixture of 337 mg (1 mmole) of the complex II, 3 ml of water, and 0.5 ml (5 mmoles) morpholine was heated for 3 h at 90°C, then evaporated to dryness under vacuum. The reaction product was isolated as in the preceding experiment, and recrystallized from a mixture of benzene and acetone (2:1). Yield 0.14 g (74%), T_m 75-76°C.

4-N,N-Diethylaminopyridine N-oxide (IVa) was produced analogously (Table 2).

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