Flexuosin.—*H. flexuosum* was collected near Tallahassee in June, 1956. The air-dried whole plant, wt. 12 oz., on extraction in the usual manner, yielded 11 g. of gummy material which could not be induced to crystallize. Chromatography over 40 g. of alumina (eluate benzene) gave 7 g. of viscous material; the more polar fractions were highly colored and discarded. The fractions eluted with benzene were rechromatographed over freshly-ignited alumina. Benzene eluted 5 g. of non-crystalline gum; ethanol eluted partially crystalline material which on crystallization from ethanol furnished 0.24 g. of colorless crystals, m.p. 221°, $[\alpha]_D$ −90° (95% ethanol, *c* 0.50).

Anal. Calcd. for $C_{15}H_{18}O_4$: C, 68.68; H, 6.92. Calcd. for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63. Found: C, 68.18; H, 6.74.

TALLAHASSEE, FLA.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, TEMPLE UNIVERSITY]

The Reaction of Triphenylphosphine with Some Aromatic Amine Oxides[1]

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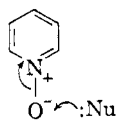
A new method is presented for the deoxygenation of pyridine-N-oxides by the use of triphenylphosphine. The yields of the corresponding pyridine and triphenylphosphine oxide are good. The reaction between 4-nitropyridine-N-oxide and triphenylphosphine gave triphenylphosphine oxide as the only product which could be isolated; a kinetic study showed this reaction to be first order with respect to each of the reactants.

Pyridine-N-oxide has received considerable attention recently as an intermediate in the synthesis of pyridine derivatives.[2,3] Substitution reactions in the pyridine ring are much more difficult than in the benzene ring owing to electronic effects exerted by the hetero nitrogen atom. If, however, pyridine is converted to the N-oxide, the over-all distribution of electrons is modified. The effect is an increased concentration of electrons at the 2- and 4-positions, facilitating electrophilic substitution in these positions.

Deoxygenation of pyridine-N-oxides may be accomplished by a variety of methods. A nucleophilic reagent (Nu) may attack the oxygen atom of pyridine-N-oxide as[3]



Electron donors such as phosphorus trichloride can supply an electron pair to the oxygen atom and cause deoxygenation. The most common laboratory method for accomplishing the deoxygenation consists in refluxing a chloroform solution of the N-oxide with phosphorus trichloride.

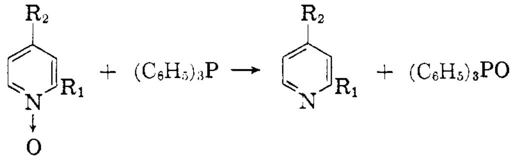
Our search for a reagent of wider applicability has led to the use of triphenylphosphine as the deoxygenating agent. Although triphenylphosphine is substantially stable in air, it is attacked by a wide variety of oxygen-containing compounds with the formation of triphenylphosphine oxide. This property of triphenylphosphine, and of phosphines in general, has been utilized in the removal of oxygen atoms of several substrate molecules.[4]

It has been reported[4] that aliphatic amine oxides, such as trimethylamine oxide, react quantitatively with tertiary phosphines in boiling glacial acetic acid to form the corresponding amine and phosphine oxide. The same authors reported that, in

$$(CH_3)_3N \longrightarrow O + PR_3 \longrightarrow (CH_3)_3N + OPR_3$$

contrast, the N-oxides of pyridine and quinoline were found to be quite stable toward both triphenylphosphine and triethylphosphine. It was observed that the ease of removal of the oxygen from amine oxides often decreases with the dipole moment of the amine oxide, *e.g.*, trimethylamine oxide 5.04 D., pyridine-N-oxide 4.24 D.

In our investigation it was discovered that triphenylphosphine will cause deoxygenation of a variety of aromatic amine oxides at high temperatures



$I, R_1 = R_2 = H$
$II, R_1 = CH_3, R_2 = H$
$III, R_1 = H, R_2 = CH_3$
$IV, R_1 = H, R_2 = OCH_3$

Quinoline-N-oxide is also smoothly deoxygenated by triphenylphosphine.

The optimum method for performing this reaction is to heat the reactants in the absence of a solvent. At temperatures considerably above 200° the amine distils from the reaction mixture in good yield in most cases. Triphenylphosphine oxide was isolated from the residue by recrystallization from a water–methanol solvent pair. In the reactions of 4-methoxypyridine-N-oxide and quinoline-N-oxide the products were isolated by column chromatography. The only solvent found suitable for the reaction was triethylene glycol; however, there is no apparent advantage derived from its use. Observations of the reaction of triphenylphosphine with several amine oxides are summarized in Table I.

Considerable difficulty was encountered in the reaction of triphenylphosphine with 4-nitropyridine-N-oxide. Upon heating the reactants in the absence of a solvent a vigorous exothermic reaction

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[1] From a thesis submitted by William F. Olszewski in partial fulfillment of the requirements for the M.A. degree, Temple University, June, 1958.

[2] E. Ochiai, *J. Org. Chem.*, **18**, 534 (1953).

[3] A. R. Katritzky, *Quart. Revs.* (*London*), **10**, 395 (1956).

[4] L. Horner and H. Hoffmann, *Angew. Chem.*, **68**, 480 (1956).

TABLE I

REACTION OF TRIPHENYLPHOSPHINE WITH AMINE OXIDES

Amine-N-oxide	Solvent	Reaction temp., °C.	Time (hr.)	Yield of product, % Amine	Yield of product, % $(C_6H_5)_3$-PO
Pyridine	Chloroform[a]	Reflux	1.5	..	..
	Ethanol (95%)[b]	Reflux	1.0	..	..
	Chlorobenzene[a]	Reflux	1.0	..	..
	Dibutyl carbitol	250–260	1.0	..	..
	None	230–233	0.6	89.8	72.6
	Triethylene glycol	250–260	.5	86.8	65.2
4-Picoline	None	275–280	.7	92.8	30.4
	Triethylene glycol	270–280	.3	56.3	51.1
2-Picoline	None	275–280	.6	51.6	49.0
	Triethylene glycol	230–240	.8	50.0	50.2
4-Methoxy-pyridine	None[c]	270–275	.8	61.6	83.0
	Triethylene glycol[d]	270–275	.8	..	..
Quinoline	None[c]	270–280	.3	89.2	94.3
	Triethylene glycol[d]	280–285	.8	..	..
4-Nitropyridine	Chloroform[e]	Reflux	5.0	..	..
	Dimethylformamide[f]	Reflux	3.0	..	..
	None[g]	130	..	..	53.7
	Triethylene glycol	170–175	3.8	..	..

[a] No evidence of a reaction until the solvent was removed by distillation and a free flame applied. [b] 77.8% of triphenylphosphine was recovered. [c] Products were isolated by column chromatography. [d] Attempted isolation of products by column chromatography was too slow to be feasible. [e] 78.8% of triphenylphosphine was recovered. [f] Ultraviolet studies revealed the presence of triphenylphosphine oxide, but not 4-nitropyridine. [g] Violent reaction was observed; triphenylphosphine oxide was isolated by column chromatography.

occurred, accompanied by the evolution of brown nitrous fumes. The only product that could be isolated from the reaction mixture was triphenylphosphine oxide. Investigation of the reaction mixture according to the method of den Hertog[5] showed that neither of the known decomposition products of 4-nitropyridine, N-(4′-pyridyl)-4-pyridone nor 4-pyridone, was present. When the reaction was repeated in refluxing chloroform and dimethylformamide the conditions were found to be too mild for the reaction to proceed to any considerable extent.

A kinetic study of the reaction between triphenylphosphine and 4-nitropyridine-N-oxide in triethylene glycol was performed using a spectrophotometric method. Ultraviolet spectra of the four components of the system were determined in absolute methanol, and it was found that at 328 mμ 4-nitropyridine-N-oxide had a strong, unique absorption peak (ϵ 15970). 4-Nitropyridine was prepared for spectral purposes from 4-nitropyridine-N-oxide according to the method of Ochiai.[2] The concentration of 4-nitropyridine-N-oxide throughout the course of the reaction was determined from the ultraviolet spectra by the application of Beer's law. A plot of the reciprocal of the concentration of 4-nitropyridine-N-oxide against time resulted in a straight line, indicating a second-order reaction (*k* 0.0020 liter/mole-sec.). In more detailed calculations it was shown that the effect of the small absorbancies of the other components at 328 mμ was negligible.

Experimental

Materials.—Quinoline-N-oxide dihydrate, 4-methoxypyridine-N-oxide and 4-nitropyridine-N-oxide (all Beacon Chemical Industries) were used as received. Pyridine-N-oxide and 2-picoline-N-oxide (both Reilly Tar and Chemical Corp.) were distilled twice at reduced pressure. 4-Picoline-N-oxide (Reilly Tar and Chemical Corp.) was used as received. Triphenylphosphine (Eastman Kodak Co., White Label) and triethylene glycol (Eastman Kodak Co., Yellow Label) were used as received. Chromatographic separations were performed on Alcoa alumina.

Equipment.—Ultraviolet studies were carried out on a Beckman model DK-2 spectrophotometer using quartz cells with a 1-cm. path length. The absorption spectra were measured between 220 and 340 mμ.

General Procedure.—The reaction between triphenylphosphine and the amine oxides was performed by heating the reactants in a small distilling flask using a Wood metal-bath to allow better temperature control. Pyridine, 2-picoline and 4-picoline distilled from the reaction mixture at the temperature indicated in Table I. The residue was recrystallized from a water–methanol solvent pair to obtain triphenylphosphine oxide.

In the reactions of quinoline-N-oxide and 4-methoxypyridine-N-oxide with triphenylphosphine the products were isolated by column chromatography. After heating, the dark-colored reaction mixture was dissolved in a minimum amount of methanol, poured onto a chromatographic column, and eluted with petroleum ether (75–90°) followed by cyclohexane. The free amine and triphenylphosphine oxide appeared in the early and late fractions, respectively.

All reactions were carried out using approximately equimolar quantities of the amine oxide and triphenylphosphine. In each case the amine was identified by conversion to its picrate. The concentration of solvent, whenever used, varied from 56–91% by weight.

Kinetic Study.—A mixture of 0.3548 g. (0.002532 mole) of 4-nitropyridine-N-oxide and 0.6642 g. (0.002532 mole) of triphenylphosphine was placed in a 10-ml. volumetric flask which was nearly filled with triethylene glycol. The flask was inserted in a bath maintained at 170–175° and as soon as the solids had melted the volume was brought up to the mark by adding more solvent. Then, 0.1-ml. aliquots were withdrawn and suitably diluted with methanol. Ultraviolet absorption spectra were determined for these solutions. The concentration of 4-nitropyridine-N-oxide was calculated by the application of Beer's law. Some transient absorption in the 4-nitro-pyridine region (282.5 mμ) was observed, but this band disappeared during the course of the reaction.

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(5) H. J. den Hertog, F. Broekman and W. Combé, *Rec. trav. chim.*, **70**, 105 (1951).