TABLE III

PREPARATION OF ISOCYANATOSILANES FROM CHLOROSILANES AND ISOCYANIC ACID

Starting chlorosilane	Molar fraction	Conversion, %[a]	Isocyanato-silane	Yield, %[b]	B.p., mm.	$n^{20.5}D$
$SiCl_4$	0.071	96	$Si(NCO)_4$	60	73/2[c]	1.4595[c]
$(CH_3)_3SiCl$	.51	83	$(CH_3)_3SiNCO$	57	89/754[d]	1.3940[d]
$(CH_3)_2SiCl_2$	.083	97	$(CH_3)_2Si(NCO)_2$	58	130–132[e]	1.4195[e]

[a] By titration of chloride from trimethylammonium chloride formed in the reaction. [b] Based on a quantitative conversion. [c] Reported,[7] b.p. 185.6°/760 mm. and n^{20} 1.4610. [d] Reported,[8] b.p. 91° and n^{20} 1.3960. [e] Reported,[8] b.p. 131.2° and n^{20} 1.4221.

TABLE IV

PREPARATION OF PHOSPHOR(DIISOCYANATIDITES) FROM PHOSPHORODICHLORIDITES AND ISOCYANIC ACID

R	Conversion, %	Yield, %[a]	B.p., °C./mm.[b]	n_D/t	Formula	C		H		N		P	
						Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found
CH_3[c]	94	64.3	56/18	1.4815/22	$C_3H_3N_2O_3P$	24.67	24.72	2.07	2.18	19.19	19.02	21.21	20.7
C_2H_5	90	51.5	70/27	1.4720/22	$C_4H_5N_2O_3P$	30.01	29.93	3.15	3.70	17.50	17.04	19.35	19.3
C_6H_5	88	61	76–78/0.20–0.25	1.5505/21	$C_8H_5N_2O_3P$	46.17	46.06	2.42	2.78	13.46	13.19	14.88	14.6

[a] By titration of chloride from either pyridine hydrochloride or trimethylammonium chloride formed in the reaction. [b] Based on a quantitative conversion. [c] Bisbenzylamine derivative, m.p. 122–123° (from ethanol). *Anal.* Calcd. for $C_{17}H_{21}N_4O_3P$: C, 56.66; H, 5.88; N, 15.55; P, 8.60. Found: C, 56.76; H, 6.03; N, 15.34; P, 8.4.

Phosphor(diisocyanatidites)(V).—These compounds were prepared by reactions of the corresponding phosphorodichloridites with isocyanic acid in ether in the presence of either pyridine or trimethylamine. The reaction products were purified by distillation through a spinning band column. The experimental details are given in Table IV.

Diphenyl Phosphorochloridite, $(C_6H_5O)_2PCl$.—This material, b.p. 170–173° (4 mm.), always was obtained during the preparation of phenyl phosphorodichloridite.

Diphenyl Phosphor(isocyanatidite), $(C_6H_5O)_2PNCO$.—Reaction of diphenyl phosphorochloridite with a 25% excess of isocyanic acid in ether in the presence of trimethylamine gave a 70% yield of diphenyl phosphor(isocyanatidite), b.p. 149–150° (1.2 mm.), $n^{21}D$ 1.5716. Conversion was found by chloride titration to be 88%.

Anal. Calcd. for $C_{13}H_{10}NO_3P$: C, 60.24; H, 3.89; N, 5.40 P, 11.95. Found: C, 60.34; H, 4.02, N, 5.62; P, 12.4.

The Cyanomethylation of Indole

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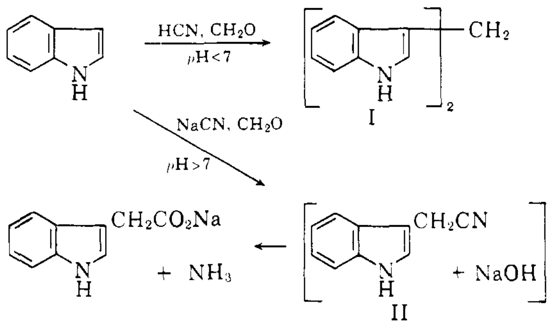
The utility of 3-indolacetonitrile as a precursor of tryptophan[1] has prompted a study of the cyanomethylation of indole. The preparation of the nitrile directly from indole, formaldehyde, and an alkali cyanide is reported in the patent literature.[2–4] Our efforts to confirm these reports have met with only limited success, due to two competing reactions under the conditions employed. In neutral or acidic solution, the reaction was found to be predominantly between indole and formaldehyde, yielding 3,3′-diindolylmethane. Under alkaline conditions, on the other hand, cyanomethylation of the indole to 3-indoleacetonitrile (II) did occur. However, alkali hydroxide was also formed, and under the conditions required to accomplish the cyanomethylation reaction, the nitrile product was hydrolyzed almost as rapidly as it was produced to 3-indoleacetic acid.



A variety of conditions have been investigated in an attempt to arrest the reaction of indole, formaldehyde, and an alkali cyanide at the nitrile stage. Use of a dipotassium phsophate buffer was found to repress the hydrolysis of the nitrile somewhat, but the yield of nitrile based on indole was still low (*i.e.*, approximately 15%).[5] On the other hand, alumina was found to be completely inoperable as a buffer, a salt of 3-indoleacetic acid being obtained as the main product. No cyanomethylation products resulted in experiments in which either magnesium acetate or dimethylamine acetate was used as the buffer. Likewise no reaction was observed when zinc cyanide or cuprous cyanide was used in place of the alkali cyanide. It should be noted that the reaction of 1-acetyl-3-acetoxymethylindole, obtained by heating gramine with acetic anhydride and fused sodium acetate,[6] with potassium cyanide gave a 38% yield of the nitrile.

Experimental[7]

3-Indoleacetonitrile from Indole, Formaldehyde, and Potassium Cyanide.—Indole (39 g., 0.33 mole), potassium cyanide (22 g., 0.34 mole), dipotassium phosphate trihydrate (85 g., 0.37 mole), and aqueous formaldehyde (30 ml. 36.2% solution equivalent to 10.9 g. or 0.36 mole) were mixed with ethanol (100 ml.) and water (70 ml.). The mixture was sealed in a Hastelloy B-lined shaker tube under nitrogen and heated for 4 hr. at 150°. After cooling to 0–5°, the mixture was discharged and filtered.

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(1) J. N. Coker, W. L. Kohlhase, M. Fields, A. O. Rogers, and M. A. Stevens, *J. Org. Chem.*, **27**, 850 (1962).

(2) W. Salzer and H. Andersag, German Patent 722,809.

(3) K. Bauer and H. Andersag, U. S. Patents 2,222,344 and 2,315,661.

(4) Japanese Patent 16,544.

(5) O. B. Mathre, U. S. Patent 2,927,117.

(6) E. Leete and L. Marion, *Can. J. Chem.*, **31**, 775 (1953).

(7) All melting points are uncorrected.

The filtrate was freed of solvent by heating *in vacuo*. Vacuum distillation of the oily residue yielded 17.5 g. of unchanged indole (b.p. 90–110°/0.1–0.3 mm.) and 3.4 g. 3-indoleacetonitrile (0.021 mole; 14.5% yield at 6.5% conversion) (b.p. 160–180°/0.2 mm.). The nitrile was characterized as its 1,3,5-trinitrobenzene complex, m.p. 138–139.5°.

Carrying out the above procedure with alumina (6 g., Alcoa F-20) and potassium acetate (5 g., 0.05 mole) in place of the dipotassium phosphate produced 3-indoleacetic acid in 55% yield and 3,3′-diindolylmethane in 20% yield.

3-Indoleacetonitrile from 1-Acetyl-3-acetoxymethylindole.—1-Acetyl-3-acetoxymethylindole (4.6 g., 0.02 mole) and potassium cyanide (2.6 g., 0.04 mole) were placed in ethanol (30 ml.) and water (30 ml.) and the mixture refluxed gently for 4 hr. Most of the solvent was then removed by heating *in vacuo*, and the residue obtained extracted with ether (three 50-ml. portions). These extracts were combined, dried over anhydrous sodium carbonate, and the ether removed by gentle heating. The residue (2.4 g.) was vacuum distilled and yielded 1.2 g. (0.0076 mole, 38%) 3-indoleacetonitrile (b.p. 155–163°/0.10–0.15 mm.). The product was characterized as its 1,3,5-trinitrobenzene adduct, m.p. 138.5–139.5°.

Experiments in the Synthesis of Pyridinium Amidines and Imino Esters

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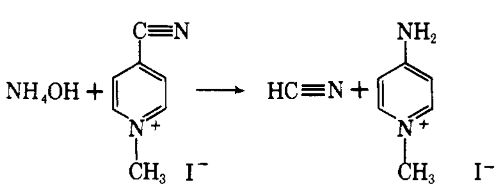
A comparison of the previously reported chemistry of formylpyridinium salts[1,2] and chloral[3] coupled with the ease of trichloroacetonitrile addition reactions[4,5] led us to investigate the possibility of forming pyridinium amidines and imino esters from 4-cyano-1-methylpyridinium iodide (I) with amines and alcohols.

The reaction of I with ethanol, either in the presence or absence of an equimolar quantity of hydrogen iodide led to a recovery of starting materials. Additionally, starting reagents were recovered in attempted reactions of I with aniline or 4-amino-1-methylpyridinium iodide (II). However, the reaction of I with ammonium hydroxide led to an over-all displacement of the cyano function and formation of II. This displacement reaction is analogous to the formation of methyl-4-pyridone from I with excess alkali.[6]

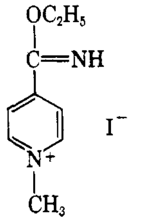


I II

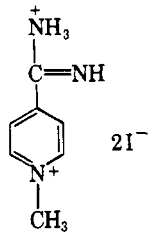
The ammonolysis results using I led us to experiment under similar conditions with the corresponding carbamyl, carboxy, and carbomethoxy derivatives, as well as with isonicotinonitrile, and *p*-nitrobenzonitrile However, the formation of an amine was specific to I.

A blue color followed by red was noticed in the reaction of I with bases. Patton[6] also noticed the transient blue color, the nature of which he did not investigate further. It was reported previously that pyridinalchlorimine dimethyl sulfate gave a brilliant blue color with excess triethylamine.[7] Presumably 4-cyano-1-methylpyridinium methyl sulfate was formed by the elimination of hydrogen chloride, and further reaction of the cyano compound with base resulted in color. It was also found that addition of aqueous base to mixtures of 4-formyl-1-methylpyridinium iodide oximes with acetic anhydride gave a blue color, again through the probable formation of I.[8] The *anti* oxime produced color at a faster rate but quantitative data are not available. In all of these studies the chromogenic substance was present in low concentrations and could not be isolated. The blue color may be related to the formation of free radicals in the reduction of I by some reaction intermediate.[9]

Though no success was met in synthesizing amidines and imino ester derivatives from I, isonicotinimidic acid ethyl ester methiodide (III) and 4-amidino-1-methylpyridinium iodide hydroiodide (IV) were obtained through an alternate route involving methylation of the appropriate pyridine base.



III



IV

It was interesting to find that whereas 2,2,2-trichloroacetamidine is unstable at room temperature and trimerizes spontaneously to give a mixture of triazines,[10] IV is stable both in the solid state and in refluxing ethanol. This may indicate a decrease in the nucleophilic character and basic strength of the imino group of IV relative to the same function in 2,2,2-trichloroacetamidine, thus leading to an inhibition of the trimerization reaction.

Reaction of the imino ester III with ammonium hydroxide gave a complicated mixture of products. Chromatographic separation followed by infrared analysis indicated II and 4-carbamyl-1-methylpyridinium iodide as two of the components. Since under similar ammonolysis conditions 4-carbomethoxy-1-methylpyridinium iodide did not give the 4-amino derivative the intermediate formation of I would be deduced logically.

The general results of this investigation indicate that the strongest electrophilic site in I exists on the ring

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[3] (a) H. W. Post, *ibid.*, **6**, 830 (1941); (b) P. K. Chang and T. L. V. Ulbricht, *J. Am. Chem. Soc.*, **80**, 976 (1958).

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[5] F. Cramer, K. Pawelzik, and H. J. Baldauf, *Chem. Ber.*, **91**, 1049 (1958).

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