these are given in the last line, and show satisfactory agreement over better than a three-fold concentration range.

TABLE I

THE IONIZATION CONSTANT OF ACI-NITROETHANE AT 23°

(1)	Init. concn. Ba nitroethane	0.04039	0.02467	0.01268
(2)	Acid added	HCl	HCl	H_2SO_4
(3)	Concn. of added acid	0.03975	0.02429	0.01226
(4)	*p*H	3.01	3.10	3.28
(5)	Concn. H^+ ion $\times 10^4$	9.77	7.94	5.25
(6)	Concn. nitro ion $\times 10^3$	1.62	1.17	0.95
(7)	Concn. $CH_3CH{=}NOOH$	0.03877	0.02350	0.01173
(8)	$K_1 \times 10^6$ (av. 4.09 ± 0.10)	4.08	3.95	4.25

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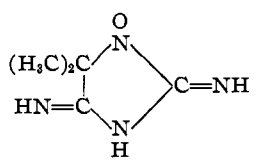
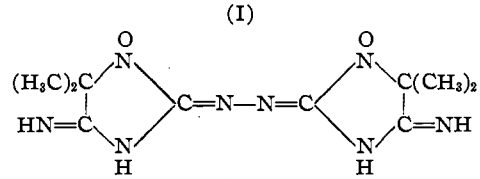
α-Hydroxylaminoisobutyronitrile—an Intermediate in the Synthesis of Porphyrexide and Porphyrindine

BY CURT C. PORTER AND LESLIE HELLERMAN

Kuhn and Franke[1] have shown that porphyrexide (I) and porphyrindine (II)[2,3] constitute, with their respective reductants, rapidly reversible oxidation–reduction systems, the characteristics of which may be measured potentiometrically.



(I)



(II)

Thermodynamically, they stand among the most powerfully oxidizing of the organic systems (E_0' at[4] *p*H 7 = +0.725 or +0.565, respectively).[1] The oxidants, which are unusually interesting "free radicals," have been employed recently for the estimation of certain mercaptans and of the sulfhydryl groups of certain proteins; as such, they have been used in the study of *protein denaturation*.[5,6]

The first step in the synthesis of these substances, involving the addition of hydrocyanic acid to acetoxime to give α-hydroxylaminoisobutyronitrile, requires the use of concentrated aqueous hydrocyanic acid and may be difficult to control. We have modified the procedure by substituting for liquid hydrocyanic acid a suitable cyanide–phosphate buffer. This device may have value also in certain other cases where concentrated hydrocyanic acid has been specified.

Preparation of α-Hydroxylaminoisobutyronitrile, $(H_3C)_2C(NHOH)CN$.—Powdered acetoxime, 94.9 g. (1.3 moles), and 626 g. (4.6 moles) of potassium dihydrogen phosphate (KH_2PO_4) are placed in a 2-liter round-bottomed flask with ground connections for a glass stopper (which preferably carries a stopcock); water, 260 cc., is added, and the mixture is placed in an ice-bath. *Subsequent operations are conducted in an excellently ventilated hood.* To the reaction mixture is added an ice-cold solution of 112.7 g. (2.3 moles) sodium cyanide dissolved in 280 cc. of water; the addition is made rather slowly while the reagents are kept well mixed. The mixture is allowed to warm to room temperature (about 20°) during which it is shaken occasionally. A yellow surface layer will have formed. The flask with contents is conveniently placed in a large closed vessel (desiccator) and allowed to stand (under the hood) at room temperature for about eighteen hours and no longer. The whole mixture is subjected to three ether extractions (total of 640 g. of purified ether) and from the extracts without preliminary drying the hydrocyanic acid and ether are removed in a stream of clean air. The residual aqueous suspension of crystals (which may be concentrated further, if necessary, in a vacuum desiccator) is ice-cooled, transferred to a cold suction filter, freed of mother liquor, and washed thrice with 2-cc. portions of ice water.

The crude product, consisting of nitrile and unchanged oxime, is dried in a vacuum desiccator over phosphorus pentoxide; then the oxime is completely removed by means of trituration with four or five 100-cc. portions of petroleum ether (b. p. 30–35°); oxime recoverable from the extracts amounts to 20–25 g. The α-hydroxylaminoisobutyronitrile is purified further, if required, by being washed with small portions of cold *n*-butanol, followed by recrystallization from ether and petroleum ether; yield 25 g.; m. p. 100°.

The procedure is reliable and convenient. Yields are not as large as those reported by Kuhn and Franke.[1] No difficulty is encountered in the subsequent steps of the porphyrexide synthesis, particularly if the ethanol, required as solvent in the preparation of the iminoester dihydrochloride (derived from nitrile) and of the related amidine hydrochloride, is properly dried.

For the oxidation of α-hydroxylaminoisobutyramidine hydrochloride to the corresponding nitroso compound, the calculated quantity of a standard solution of sodium hypochlorite may be substituted for chlorine gas. However, in order to prevent the formation of N-chloro derivatives, enough hydrochloric acid must be present in the reaction mixture to "cover" the amidine grouping and to generate chlorine *in situ*.

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(1) R. Kuhn and W. Franke, *Ber.*, **68B**, 1528 (1935).
(2) O. Piloty and B. Schwerin, *ibid.*, **34**, 1863, 1870, 2354 (1901).
(3) O. Piloty and W. Vogel, *ibid.*, **36**, 1283 (1903).
(4) W. M. Clark and B. Cohen, *Pub. Health Repts.*, **38**, 666 (1923); reprinted in *Hygienic Lab. Bull.* No. **151**, 13 (1928).
(5) R. Kuhn and P. Desnuelle, *Z. physiol. Chem.*, **251**, 14 (1938).
(6) J. P. Greenstein, *J. Biol. Chem.*, **125**, 501 (1938).