

PREPARATION OF A COMPOUND WHICH MAY BE HYDROGEN ISOCYANIDE

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The possibility of the gas chromatographic identification of the long-postulated compound hydrogen isocyanide** has turned up as an interesting side line in a recent study of the pyrolyzates of the substituted barbituric acids. Though the primary focus of the investigation was the applicability of pyrolytic gas chromatography to a toxicological problem of forensic importance, the repeated appearance of an unknown peak was felt to justify at least a limited detour into an old problem of pure chemistry.

During the preparation of hydrogen cyanide as a standard for the determination of its retention time, it was found that a substance in the vapor above the sample of dry KCN had a retention time which differed from that of HCN prepared by adding acid to KCN. In a 4-ft. column packed with polypropylene glycol 10% on celite 100/120 the retention times in minutes, at a flow rate of 50 ml/min, were:

<i>Temperature °C</i>	<i>HCN</i>	<i>Unknown</i>
50	4.6	6.6
75	2.15	3.2

Both HCN and the unknown vapor were unusual in that they produced negative peaks with the ⁹⁰Sr radioactive detector in the Pye gas chromatograph. The peaks were reasonably sharp and slightly asymmetrical. Substances which give negative peaks with the ⁹⁰Sr ionization detector when argon is the carrier gas are comparatively few in number. They are substances whose ionization potential is greater than the excitation potential of the argon atoms (11.6 eV), *viz.*:

Br ₂	H ₂	O ₂	CO ₂	HCN	H ₂ O
Cl ₂	Kr	Xc	CF ₄	HCl	N ₂ O
I ₂	Ne	BF ₃	(CN) ₂	HF	SO ₂
He	N ₂	CO	HBr	HI	SF ₆

Methane, C₂H₄ and C₂H₆, though they fall into this category so far as their ionization potentials are concerned, do, however, ionize sufficiently to give positive peaks.

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** Alternative names: hydrogen isonitrile, hydrogen carbylamine.

Water gives a negative peak at low temperatures and a positive peak over 100° . Most organic compounds have molecules whose ionization potentials are less than the excitation potential of the argon atoms, and hence give positive peaks.

Hydrogen cyanide is believed to exist in two forms because it gives rise to two kinds of alkyl derivatives: the alkyl cyanides, RCN, which are derivatives of hydrogen cyanide, HCN, and the alkyl isocyanides, RNC, which are derivatives of hydrogen isocyanide, HNC.

EARLIER APPROACHES TO THE PREPARATION OF HNC

USHERWOOD¹ calculated from the ratio of specific heats of gaseous HCN that the equilibrium mixture contains a few tenths of 1 % of HNC. ENKLAAR² claimed to have isolated the isomerides of which HCN was thought to consist by means of their methyl mercuric salts. He claimed that the isocyanide could be prepared by the action of H_2S on a solution of AgCN, of $Hg(CN)_2$ or of AgCN in KCN, or by the action of H_2SO_4 on $Na_4Fe(CN)_6$. He later³ attempted to calculate the relative proportions of the isomers in ordinary prussic acid from boiling-point data. COATES, HINKEL AND ANGEL⁴ attempted to repeat ENKLAAR's work with mercuric methyl cyanides. All of their preparations gave the usual mercuric methyl cyanide, and they found no evidence for its alleged isomer.

DADIEU⁵ from a study of the Raman spectrum of HCN deduced evidence for the presence of two types of molecules in the gaseous state, but the amount of hydrogen isocyanide was of the order of 0.5 % or under. GORDY AND WILLIAMS⁶ examined the infrared spectrum of aqueous solutions of HCN and deduced that a weak band was due to 2-4 % of HNC. From a similar study of the Raman spectrum HERZBERG⁷ found no evidence to support the view that traces of HNC were present in HCN. REICHEL AND STRASSER⁸ studied the ultraviolet curve of HCN and concluded that at most it contains only a few parts per hundred of the isomer.

The alkyl and aryl isocyanides form isothiocyanates by direct union with sulfur. However, efforts made by McCROSKY, BERGSTROM AND WAITKINS⁹ to parallel this synthesis and form isothiocyanic acid from hydrogen isocyanide (presumed to be present in HCN) resulted in failure. They concluded that HNC cannot be present in pure HCN except in extremely small concentrations.

ESCUBÓS, VARGAS, AND SOLS¹⁰ argue the presence of HNC in HCN from its inhibiting action on phosphomonoesterases.

More recently a group of chemists at Cambridge University¹¹, approaching the problem from the theoretical side, have concluded that under mild conditions the preparation of hydrogen isocyanide should be possible. Their conclusion was based upon the fact that the energy potential of a proton brought into juxtaposition with the C-N group shows a minimum in the position appropriate to HCN and another, somewhat higher, corresponding to HNC.

TWO APPROACHES USED IN THIS STUDY

The unknown compound isolated gas-chromatographically in this study has been investigated by (a) excluding possible known compounds and (b) attempting to prepare it by alternative routes.

Survey of possible known compounds

Cyanogen, $(\text{CN})_2$, was prepared by adding a solution of KCN to a solution of CuSO_4 . The retention time at 50° was 0.75 min; negative peak.

Cyanic acid, HOCN , was prepared by dry distillation of cyanuric acid. It gave a very flat, extremely asymmetrical positive peak with retention times at 75° varying from 7.5 to 15 min, depending upon the amount injected.

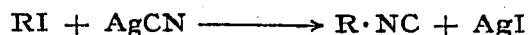
Hydrazine, $\text{H}_2\text{N}\cdot\text{NH}_2$. Attempts were made to prepare hydrazine from the sulfate with strong potassium hydroxide. Two positive peaks were obtained from the vapor; the retention times were 2.8 min and 6.5 min.

Ammonia, NH_3 ; positive peak at 1.55 min.

Hydroxylamine, $\text{HO}\cdot\text{NH}_2$. Attempts were made to prepare hydroxylamine by adding alkali (dil. KOH, conc. KOH and moist $\text{Ca}(\text{OH})_2$) to the hydrochloride. In each case the vapor gave a small positive peak at 1.0 min. It is reported to be unstable and to decompose rapidly at room temperature, especially in the presence of moisture and CO_2 .

Attempts to prepare hydrogen isocyanide

1. One of the general methods for preparing isocyanides is by heating an alkyl iodide with silver cyanide in aqueous ethanolic solution.:

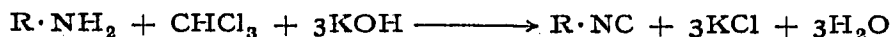


A small amount of alkyl cyanide is also formed. On the other hand, if KCN is used, the major product is cyanide and traces only of isocyanide are obtained¹².

If HI had been heated with AgCN in aqueous ethanolic solution, any possible peak due to hydrogen isocyanide would have been obscured by the positive ethanol peak if the polypropylene glycol column was used. AgCN reacted rapidly with hydriodic acid (in the absence of ethanol) but the product appeared to be mainly HCN.

When AgCN was reacted with HCl, either dilute or concentrated, no negative peak at 3.2 min (75°) was observed. However, when dry hydrogen chloride was reacted with dry AgCN the resulting vapor produced a small negative peak at 3.2 min.

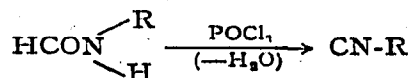
2. Heating a mixture of a primary amine and chloroform with ethanolic potassium hydroxide is a method for preparing isocyanides and is also the well-known carbylamine test for a primary amine.



FINAR¹² points out that it has been argued by analogy that using ammonia as the primary amine might lead to the formation of hydrogen isocyanide.

When a small amount of chloroform was warmed with ammonia and potassium hydroxide, some samples of the vapor in the test tube produced small negative peaks. The negative peak corresponding with the presumed hydrogen isocyanide was variable in relative size from experiment to experiment, and was frequently absent. The optimum conditions for this preparation have not yet been determined.

3. Isocyanides may be prepared by reacting N-substituted formamides with POCl_3 ^{13,14}.



On the other hand, alkyl cyanides may be prepared by treating acid amides with P_2O_5 or $POCl_3$. Formamide might, therefore, give either HCN or HNC when it reacts with P_2O_5 or $POCl_3$.

When formamide was treated with P_2O_5 , either cold or with heating, the product was HCN in which none of the substance sought could be detected. However, when $POCl_3$ was used, the chromatograph indicated that there was a significant amount of the supposed isocyanide present in the products, which consisted mainly of HCN. In test-tube experiments with $POCl_3$ in excess, the vapors contained HCN and the presumed hydrogen isocyanide in a ratio of 10 or 20 to 1. When, however, formamide was in excess, the ratio of HCN to the supposed HNC was about 2 or 3 to 1. Attempts were made to scale up this preparation, but the resulting product appeared to be mainly HCN in which only trace amounts of the substance sought could be detected with the gas chromatograph. The reaction of formamide with $POCl_3$ is exothermic, and the heat so produced may depress yields of the supposed isocyanide.

HCN prepared by treating KCN with dilute sulfuric acid contained no trace of hydrogen isocyanide. Attempts to prepare HNC by treating potassium ferrocyanide or potassium silver cyanide complexes with acid have also been unsuccessful up to the present.

Although the existence of hydrogen isocyanide has not yet been proved, there is enough evidence here to justify further investigation.

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SUMMARY

To hydrogen isocyanide, long-postulated isomer of hydrogen cyanide, may be attributed a small negative peak which was observed with a ^{90}Sr detector. Tentative partial identification by synthesis of the compound is here reported. The peak appeared repeatedly in a study of the pyrolytic gas chromatography of the substituted barbituric acids.

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