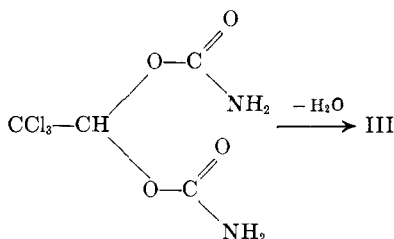
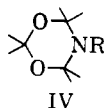


A possible mechanism for the reaction could be through dehydration of an intermediate biscarbamate.



The only other examples of 1,3,5-dioxazines that have been described previously are the dihydro derivatives (IV, R = H, CH₂COOH, CH₂COOEt, CH₂CONH₂, Cl, NO₂, NH₂).³



Experimental

2-Trichloromethyl-4-keto-6-amino-4H-1,2,5-dioxazine.—To a solution of 16.6 g. (0.1 mole) of chloral hydrate in 250 ml. of tetrahydrofuran was added 26.0 g. (0.4 mole) of sodium cyanate. The mixture was chilled and 29.7 ml. (0.4 mole) of trifluoroacetic acid was added. The mixture was stirred for 2 hr. at room temperature and filtered to remove the sodium trifluoroacetate (more tetrahydrofuran may be added). The filtrate was evaporated at 25°, *in vacuo*, leaving an oil (35 g.). The infrared spectra of the oil showed no absorption at 4.4 μ (isocyanate). The oil solidified on standing, better on stirring with a little water; the solid was collected and dried in a desiccator. It was recrystallized twice from acetone–water or from tetrahydrofuran and petroleum ether (b.p. 60–70°), m.p. 240° dec.

Anal. Calcd. for C₄H₃Cl₃N₂O₃: C, 20.58; H, 1.30; Cl, 45.56; N, 12.00. Found: C, 20.88; H, 1.31; Cl, 45.58; N, 11.93.

The n.m.r. showed a single peak ($\overset{|}{\text{C}}\text{---H}$) at 348 c.p.s. (5.81 p.p.m.). The near-infrared showed an absorption (---C---H)

at 2.82 and a triplet at 5.55–5.78 μ from a tautomeric carbonyl. Attempts to determine the molecular weight by nonaqueous titration or cryoscopically gave inconsistent values ranging from 239 to 248 (theoretical, 233.45). The p*K*_a determined in 50% aqueous ethanol was 8.15.

When chloral was treated with sodium cyanate and trifluoroacetic acid under the same conditions described previously, *no reaction occurred*, and chloral was recovered.

(3) (a) T. Curtius and R. Jay, *Ber.*, **23**, 740 (1890); M. Bergmann, M. Jacobsohn, and H. Schotte, *Z. Physiol. Chem.*, **131**, 20 (1923). (b) NOTE ADDED IN PROOF.—After this work had been submitted, we learned of an article by F. W. Hoover, H. B. Stevenson, and H. S. Rothrock, *J. Org. Chem.*, **29**, 1825 (1963), in which is described the reaction of chloral with free isocyanic acid to give CCl₃CH(OH)NCO.

A New Conversion of Isonitriles to Isocyanates

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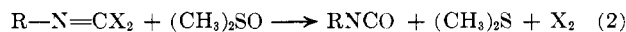
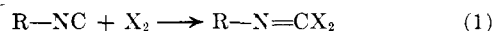
An apparently new oxidation of isonitriles with dimethyl sulfoxide in the presence of small amounts of halogen has been encountered in these laboratories.

(1) National Science Foundation Undergraduate Research Participant.

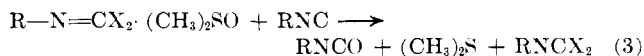
Previously isonitriles have been converted to isocyanates by the action of mercuric oxide,² ozone,³ and similar reagents. The reaction of isonitrile dihalides with water to yield an amine, presumably *via* the isocyanate, was reported.⁴

In the studies of the effect of solvent on the reaction of silver cyanide with alkyl halides, isopropyl iodide and silver cyanide were heated in dimethyl sulfoxide for 24 hr. Examination of the infrared spectrum indicated the presence of an isocyanate (maximum, 2220 cm.⁻¹).⁵ Further study of the reaction showed that isopropyl isonitrile (prepared by the dehydration of isopropylformamide with *p*-toluenesulfonyl chloride in quinoline⁶) was stable to dimethyl sulfoxide at the same temperatures and times, thus indicating that a direct oxidation of the isonitrile was not involved. Addition of 5 mole % of bromine to an equimolar mixture of isopropyl isonitrile and dimethyl sulfoxide in chloroform solvent at refluxing temperatures led to smooth formation of isopropyl isocyanate and dimethyl sulfide, both identified by comparison with authentic samples. The yield of isocyanate was approximately equal (±10%) to that of dimethyl sulfide. The chloroform and dimethyl sulfoxide used in this study were dried with calcium hydride to obviate the possible hydrolysis of isonitrile dihalide.⁴ A preliminary infrared study of the reaction showed that the isonitrile maximum (2120 cm.⁻¹) decreased steadily with time. No peak at 1690 cm.⁻¹ (isonitrile dihalide) was observed, and the spectrum could be described by the superposition of the maxima of the isonitrile, isocyanate, dimethyl sulfoxide, and the chloroform. Addition of dimethyl sulfoxide to preformed isonitrile dibromide in chloroform (infrared maximum, 1690 cm.⁻¹) gave isocyanate in a rapid exothermic reaction at room temperature. Dimethyl sulfide was again identified as the other product.

On the basis of the information presently available, the most probable course of the reaction appears to be that shown in eq. 1 and 2. A chain reaction (presumably ionic) is implied by the necessity for the halogen coupled with the fact that only 5 mole % is required for the conversion. Equation 1 indicates a well known reaction of isonitriles.⁴



What is written as eq. 2 is probably a multistep process, and the halogen may never be formed *per se*, but may be transferred from some intermediate adduct of dimethyl sulfoxide and isonitrile dihalide directly to another mole of isonitrile (eq. 3). Further study of the reaction is required to settle these points. It is, how-



ever, apparent that process 1 is not greatly faster than process 2, otherwise the build-up of the 1690 cm.⁻¹ isonitrile dihalide maximum would have been observed.

(2) A. Gautier, *Ann. chim. (Paris)* [4] **17**, 229 (1869).

(3) H. Feuer, H. Rubinstein, and A. T. Nielsen, *J. Org. Chem.*, **23**, 1107 (1958).

(4) H. Guillemand, *Ann. chim. (Paris)*, [8] **14**, 311 (1908); *Bull. Soc. Chem.*, (1904); J. J. Nef, *Ann.*, **270**, 257 (1892).

(5) H. Hoyer, *Ber.*, **89**, 2677 (1956).

(6) J. Casanova, Jr., R. E. Schuster, and N. D. Werner, *J. Chem. Soc.* **4280** (1963). We thank Professor Casanova for a preprint of this paper.

Addition of iodine to a mixture of isopropyl isonitrile and dimethyl sulfoxide also led to isocyanate, but the reaction was slower and some tar was produced. The use of chlorine was also successful. Phenylisonitrile also gave phenyl isocyanate with bromine and dimethyl sulfoxide.

Kornblum has observed oxidations of benzyl halides with dimethyl sulfoxide to yield carbonyl compounds.⁷ The reaction of isonitrile dihalides with dimethyl sulfoxide has some analogies in the reaction of acid chlorides and acid anhydrides with dimethyl sulfoxide.^{8,9}

Preliminary results with W. H. Krutzsch show that pyridine N-oxide also reacts with isonitriles in the presence of halogen (but not in their absence) to yield isocyanates. These results will be reported later in detail.

Experimental

Isopropylformamide.—This compound was prepared in 85% yield by refluxing 85.6 ml. of isopropylamine with 80.5 ml. of ethyl formate for 4 hr.¹⁰ The product distilled at 198–199°.

Isopropylisonitrile.—The isonitrile was prepared from the formamide by the method of Casanova.⁸ To a well stirred solution of 41 g. of *p*-toluenesulfonyl chloride in 100 ml. of distilled quinoline was added 18.4 g. of isopropylformamide at 75°. The system was maintained at 70 mm. and the isopropylisonitrile distilled to a receiver cooled in liquid nitrogen as it formed. The yield was 4.2 g. (30%), b.p. 88–89° (735 mm.),¹¹ on redistillation.

Substitution of benzenesulfonyl chloride for the *p*-toluenesulfonyl chloride specified by Casanova gave substantially lower yields.

Isopropyl Isocyanate.—A solution of 0.38 g. of isopropyl isocyanide (5.5 mmoles) and 0.70 g. of dimethyl sulfoxide (10 mmoles), which had been dried over and distilled from calcium hydride in 5 ml. of chloroform which had been dried over calcium hydride, was prepared; 0.034 g. of bromine (0.21 mmole of dry bromine in 0.2 ml. of chloroform) was added. The solution was refluxed for 24 hr. Infrared spectra were recorded prior to the addition of the bromine and periodically throughout the rest of the reflux time. Following completion of the reflux period, approximately 0.5 ml. of isopropylamine was added to the cooled reaction mixture. The crystals which formed were removed by filtration and recrystallized from ethanol to yield diisopropylurea, m.p. 190–191°. An authentic sample of isopropyl isocyanate was prepared from isopropyl iodide and silver cyanate; reaction of the isocyanate with isopropylamine gave an authentic sample of diisopropylurea,¹² m.p. and m.m.p. 190–191° with the preceding sample. The infrared spectra of the two samples were identical.

The gases from the reaction mixture were passed through a liquid nitrogen trap, and the material which collected was subjected to vapor phase chromatography (4-ft. silicone column operated at room temperature). Chloroform and a maximum of retention time identical with that of dimethyl sulfide appeared; infrared spectra of the isolated dimethyl sulfide and an authentic sample were identical. The yield of dimethyl sulfide appeared to be essentially equivalent ($\pm 10\%$) to the yield of isocyanate as judged by the area of the dimethyl sulfide v.p.c. maximum compared with calibrated isocyanate infrared determinations. The yield of isocyanate was approximately 80% from infrared measurements.

(7) N. Kornblum, J. W. Powers, G. J. Anderson, W. J. Jones, H. O. Carlson, O. Levand, and W. M. Weaver, *J. Am. Chem. Soc.*, **79**, 6562 (1957); I. M. Hunsberger and J. M. Tien, *Chem. Ind. (London)*, **88** (1959).

(8) L. Horner and P. Kaiser, *Ann.*, **626**, 19 (1959); H. W. Kircher, *Anal. Chem.*, **30**, 1540 (1958).

(9) F. G. Bordwell and B. M. Pitt, *J. Am. Chem. Soc.*, **77**, 572 (1955); T. Enkvist and C. Naupert, *Finska Kemistamfundets Medd.*, **69**, 98 (1961).

(10) J. Moffat, M. Newton, and G. Papenheimer, *J. Org. Chem.*, **27**, 4058 (1962).

(11) I. Ugi and R. Meyr, *Ber.*, **93**, 237 (1960).

(12) A. W. Hoffman, *ibid.*, **15**, 756 (1882).

To 10 ml. of chloroform was added 1 ml. of isopropylisonitrile. Bromine was added until its color persisted in the solvent. The solvent was evaporated. The viscous liquid (isopropylimido-carbonyl dibromide)³ which formed was washed with chloroform by decantation; then 10 ml. of chloroform and 1 ml. of dimethyl sulfoxide were added. After completion of the vigorous exothermic reaction, infrared spectra indicated that the isonitrile absorption were missing and had been replaced by the isocyanate maximum (yield, 82%). V.p.c. of the reaction mixture on a silicone column gave a fraction whose retention time and infrared spectrum were identical with those of an authentic sample of isopropyl isocyanate. Dimethyl sulfide was identified by v.p.c. Diisopropylurea,¹² m.p. 190–191°, was formed upon addition of isopropylamine.

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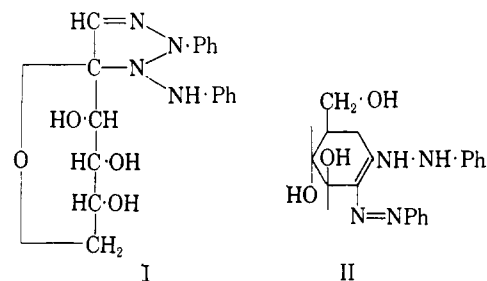
Analysis of the Structure of Dehydro-D-glucosazone by Nuclear Magnetic Resonance and by Comparison of Its Optical Isomers

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Mester and Moczar¹ found structure II for dehydro-D-glucosazone rather than structure I previously proposed by Diels and co-workers.²



The gross structure (II) has now been confirmed by application of nuclear magnetic resonance spectroscopy. However, the n.m.r. evidence requires the *D-ribo* rather than the *D-arabino* configuration for II, a conclusion supported by chemical evidence reported herein. The n.m.r. spectrum of tri-*O*-acetyl-dehydro-D-glucosazone was determined at 60 Mc.p.s. in deuterated chloroform and the spectrum is shown in Fig. 1. The presence of three *O*-acetyl groups, five hydrogens attached to the sugar carbon chain, two hydrogens on nitrogen, and two phenyl groups was indicated by integration. The sharp doublet at 6.2 p.p.m. and well shifted chemically from other signals requires the presence of a hydrogen coupled with one only neighboring hydrogen. The spacing for this signal, 3 c.p.s., is found in the quartet of intensity one centered at 5.3 p.p.m. The position of the latter signal is characteristic of hydrogens on secondary carbons in carbohydrate structures which are

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(2) O. Diels, E. Cluss, H. J. Stephan, and R. König, *Ber.*, **71**, 1189 (1938).