washed with *n*-butyl alcohol and ether to give 24.9 g. (89%) of product, m.p. 207–209°. This was recrystallized from ethanol to give 19.0 g. of solid, m.p. 208–209°, whose infrared spectrum was identical with that of **3** (Table I).

Acknowledgment.—The authors are grateful to M. Blitz and W. Greenfield for the ultraviolet spectra and to Mrs. O. Kitrey for the infrared spectra.

3-Isothiazolone–*cis*-3-Thiocyanoacrylamide Equilibria[1,2]

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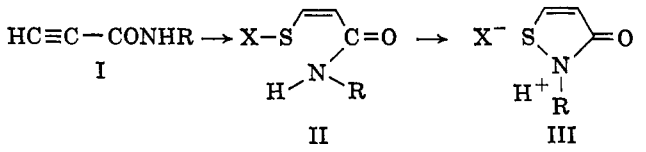
cis-3-Thiocyanoacrylamides (II) were obtained by the addition of hydrogen thiocyanate to the propiolamides. Conversion to the correspondingly substituted 3-isothiazolones (III) was effected readily by treatment with acid or with the stoichiometric quantities of metal salt (Fe^{2+}, Ni^{2+}) and alkali. Cyanide ion rapidly regenerated the *cis*-3-thiocyanoacrylamides from the 3-isothiazolones, and the S–N bond in the latter was also cleaved by treatment with sodium thiophenolate, sodium *t*-butyl mercaptide, hydrogen sulfide, and sulfite ion. Several methods were developed which provide evidence for equilibria between 3-isothiazolones (+HCN) and *cis*-3-thiocyanoacrylamides.

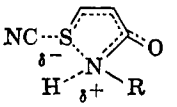
Formation of the 3-isothiazolone nucleus by an unpredicted ring contraction of the 1,4-thiazepine ring system[5] led us to investigate the synthesis of 3-isothiazolones. In a recent communication[6] we introduced a new synthesis which follows the sequence I → III (X = CN or SO_3^-). Since initial experiments with the Bunte salts (II, X = SO_3^-) failed to yield



I II III

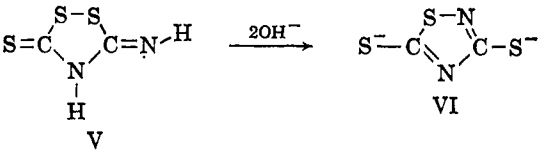
crystalline intermediates, the major part of the investigation was carried out using the *cis*-3-thiocyanoacrylamides (II, X = CN). Detailed consideration of the properties of the 3-thiocyanoacrylamides has revealed very interesting relationships between these compounds and the corresponding 3-isothiazolones.

On the basis of recent developments in the chemistry of isothiazoles,[7] we designed the synthesis of 3-isothiazolones along lines suggested by the isothiazole synthesis of Wille, Capeller, and Steiner.[7g] We reasoned that the proximity of the weakly nucleophilic amide nitrogen to the sulfur attached to two electron-withdrawing groups would facilitate S–N orbital overlap, thus lowering the activation energy for the cyclization process, II → III. Postulation of a range of possible transition states (IV) in which the developing formal charges on S and N could be dispersed not only through the conjugated system but also by stretching of the S–CN and/or N–H bonds suggested potential roles for solvation, for proton removal, and for removal of cyanide ion in effecting the ring closure.



IV

Some support for the projected synthesis was drawn from the work of Hantzsch and Wolvekamp[8] on isoperthiocyanic acid (V) and perthiocyanates (VI). The reaction is complex, involving the formation and



V VI

the redissolution of sulfur.[9] Some similarity of mechanism may exist between this process and the isothiazole synthesis due to Hatchard.[7c] Finally, an example closer to our process is found in the work of Reissert and Manns,[10] who observed the formation of 4,5-benz-3-isothiazolone from 2,2′-dicarboxamidodiphenyl disulfide.

The *cis*-3-thiocyanoacrylamides (II) were obtained readily by the addition of hydrogen thiocyanate to the propiolamides. The stereochemical assignments for the products were made from the n.m.r. coupling constants: $J_{2,3}$ = 9 c.p.s. for *cis* and 14 c.p.s. for *trans*.[11] The *cis* product (*i.e.*, from *trans* addition) was expected to predominate[12–14] and, in fact, constituted about 85% of the product obtained from propiolamide (I, R = H). In the case of the N-alkylpropiolamides (I, R = CH_3 or C_2H_5) the yields of the corresponding 3-thiocyanoacrylamides were lower and no *trans* product was ob-

(1) This investigation was supported by a research grant (USPHS-GM-05829-06) from the National Institutes of Health, U. S. Public Health Service, to whom we are pleased to acknowledge our thanks.

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(3) On leave from the Australian National University, Canberra, A. C. T., 1964–1965.

(4) To whom requests for reprints should be addressed.

(5) N. J. Leonard and G. E. Wilson, Jr., *Tetrahedron Letters*, **No. 23**, 1471 (1964).

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(8) A. Hantzsch and M. Wolvekamp, *Ann.*, **331**, 265 (1931). See also H. J. Emeleus, A. Haas, and N. Sheppard, *J. Chem. Soc.*, 3165, 3168 (1963).

(9) E. Söderbäck, *Acta Chem. Scand.*, **1**, 529 (1947).

(10) A. Reissert and E. Manns, *Ber.*, **61**, 1308 (1928).

(11) L. M. Jackman, "Applications of Nuclear Magnetic Personance Spectroscopy in Organic Chemistry," Pergamon Press Ltd., London, 1959, p. 85.

(12) A. Michael, *J. prakt. Chem.*, **52**, 344 (1895).

(13) W. E. Truce and R. F. Heine, *J. Am. Chem. Soc.*, **79**, 5311 (1957).

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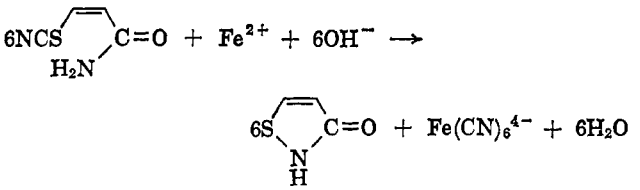
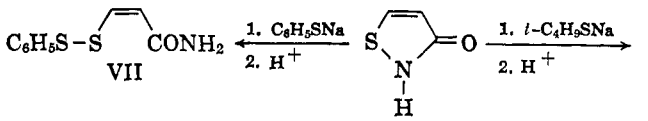
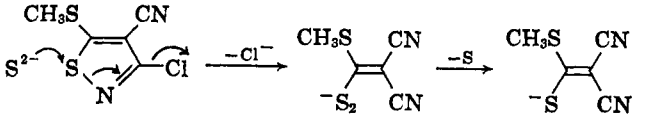
served under the conditions employed. When solutions of the *cis*-3-thiocyanoacrylamides (II) in dilute acid were allowed to stand or were refluxed briefly, hydrogen cyanide was evolved and cyclization to the 3-isothiazolones occurred in high yield. By contrast, *trans*-3-thiocyanoacrylamide was recovered unchanged from such treatment, and it could be readily freed from the *cis* isomer by this method.

The ease of cyclization suggested that in the postulated transition (IV) from thiocyanoacrylamide to isothiazolone the negative charge on the cyanide portion of the molecule was already developed to some extent. It seemed worthwhile, therefore, to attempt coordinative removal of cyanide ion with metal ions. In order to obtain a final pH near neutrality, the *cis*-3-thiocyanoacrylamides were treated with the stoichiometric quantities of alkali and metal salt. The amides dissolved readily in alkali,[15] and on treatment with the selected salt—Fe^{2+} and Ni^{2+} proved particularly suitable—underwent rapid cyclization at 0° in near quantitative yield.



The facility of cyclization by this means prompted us to investigate the reverse reaction—fission of the S–N bond in 3-isothiazolones by nucleophiles. Cyanide ion rapidly regenerated the *cis*-3-thiocyanoacrylamides (II) from the 3-isothiazolones (III). The action of sodium thiophenolate and of sodium *t*-butyl mercaptide on 3-isothiazolone led to the production of mixed disulfides (VII, VIII). In the case of thiophenol the mixed disulfide, *cis*-3-phenyldithioacrylamide (VII), underwent ready attack to yield diphenyl disulfide. Crystallization of the mixed disulfide VII from hydroxylic solvents likewise led to contamination with diphenyl disulfide, due probably to a certain amount of cyclization, with elimination of thiophenolate as a good leaving group. This effect was not observed with the mixed disulfide from *t*-butyl mercaptan, *cis*-3-*t*-butyldithioacrylamide (VIII). The action of hydrogen sulfide was predictable from the results with sodium thiophenolate; sulfur was the only product isolated. Hatchard[7c] observed a similar nucleophilic attack of sulfide ion on 3-chloro-4-cyano-5-methyl-





(15) Spectrophotometric titration indicated $pK_a \sim 7.2$ for II, R = H. As will be seen later, this is not the pK_a of the acrylamide but that of 3-isothiazolone. The *trans* isomer did not dissolve in alkali, although it did react slowly, presumably giving a thiol and cyanate ion.

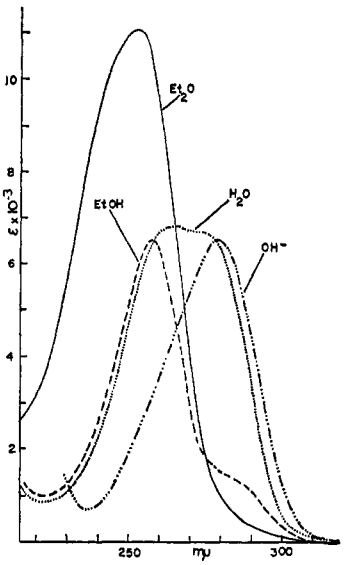
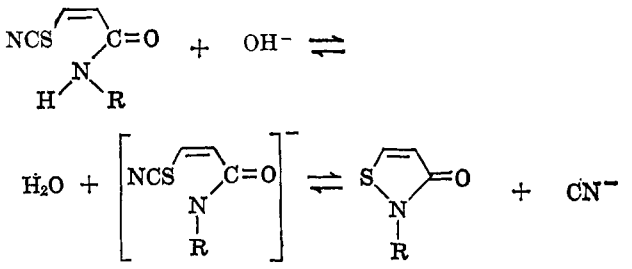


Figure 1.—Ultraviolet absorption spectra showing fate of *cis*-3-thiocyanoacrylamide (II, R = H) in different solvents.

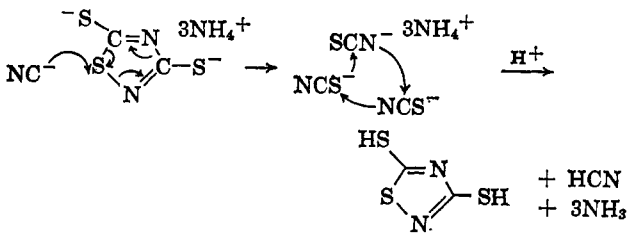
thioisothiazole, leading to the elimination of the 3-chlorine atom.[16] Spectroscopic methods indicated that the S–N bond in 3-isothiazolone was also broken by SO_3^{2-}, leading presumably to the Bunte salt (II, R = H, X = SO_3^-), but that nitrite, thiocyanate, and halide ions were without effect in aqueous solution.

The ease of both forward and reverse reactions for the 3-thiocyanoacrylamides led inevitably to the conclusion that an equilibrium probably existed in hydroxylic solvents. The ultraviolet absorption spectrum of *cis*-3-thiocyanoacrylamide (Figure 1) showed considerable dependence upon solvent. The curves in 95% ethanol or water were practically superposable on those for 3-isothiazolone. In the presence of increasing amounts of added cyanide, however, the spectrum gradually approached that shown by an ethereal solution, indication that the measured spectra[17] in hydroxylic solvents are actually those of equilibrium mixtures. The existence of the equilibria (Scheme I)

SCHEME I



(16) The susceptibility of the S–N bond to nucleophilic attack was also foreshadowed by the use of ammonium perthiocyanate for the removal of hydrogen cyanide from coke oven gas in a cyclic process involving acidification to regenerate the perthiocyanic acid [German Patent 1,118,175 (Nov. 11, 1959); *Chem. Abstr.*, **56**, 14550 (1962)].



(17) The equilibrium is essentially established within 5–10 min. in solution.

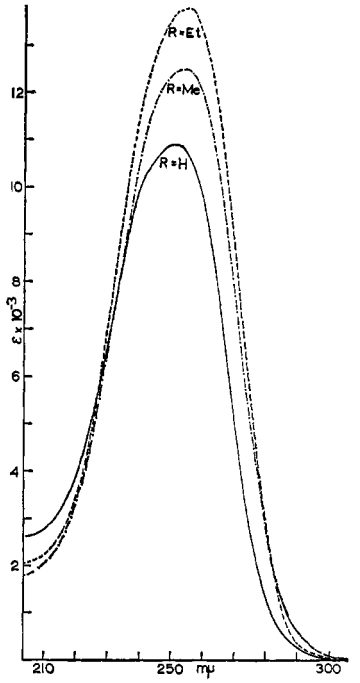
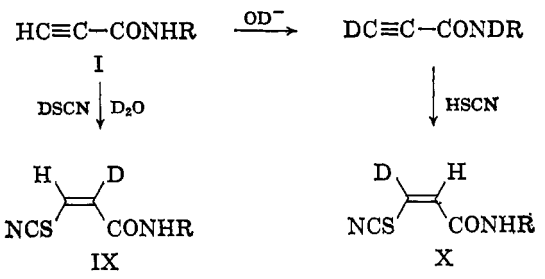


Figure 2.—Ultraviolet absorption spectra of *cis*-3-thiocyanoacrylamides (II) in water, pH 2.0, determined within 20 sec. in solution.

was tentatively indicated also by the recovery of 2-methyl-3-isothiazolone on chloroform extraction of an alkaline solution of *cis*-N-methyl-3-thiocyanoacrylamide and by the conversion of *cis*-3-thiocyanoacrylamide to 3-isothiazolone by recrystallization from acetone in the presence of base.

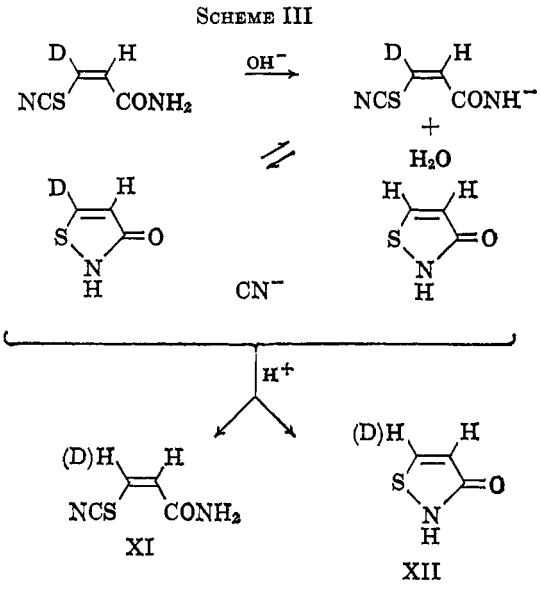
In order to obtain more decisive evidence, an ostensible deuterium-scrambling effect was employed. The deuterated *cis*-3-thiocyanoacrylamides were readily available by the routes shown in Scheme II, the 2-deuterio compound IX by the addition of DSCN to propiolamide and the 3-deuterio isomer X by prior equili-

SCHEME II



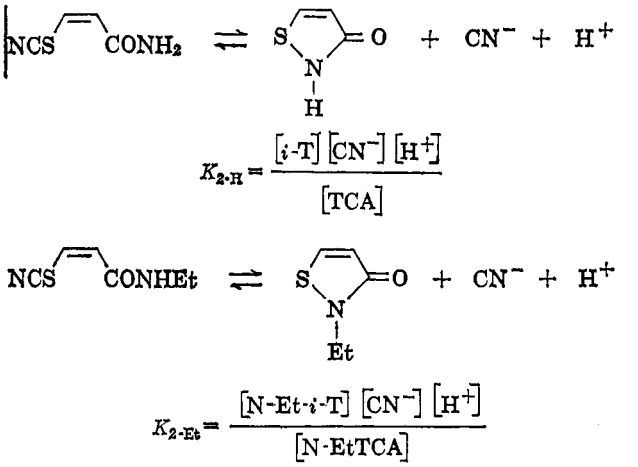
bration of the propiolamide before addition of HSCN. The deuterated isomers did not undergo exchange with the solvent readily either in acid or in alkaline solution. The deuterated isothiazolones showed similar stability. By converting the acrylamide X (R = H) within about 20 sec. to its anion by aqueous sodium hydroxide and adding immediately a molar equivalent of unlabeled 3-isothiazolone, it was possible to show complete scrambling of the 3-deuterium atom—actually, of course, scrambling of the reactant molecules (Scheme III). The D/H ratios in the isolated products XI and XII were equal, and the deuterium content of each was half that in the original *cis*-3-thiocyanoacrylamide-3*d*.

SCHEME III



This finding clearly established the existence of a rapid interchange between the anion of thiocyanoacrylamide and isothiazolone. It also implied that a mixed system, N-alkylisothiazolone (*e.g.*, N-Et-*i*-T) and *cis*-3-thiocyanoacrylamide (TCA), could be used to obtain the ratio of the equilibrium constants involved; see, *e.g.*,

SCHEME IV

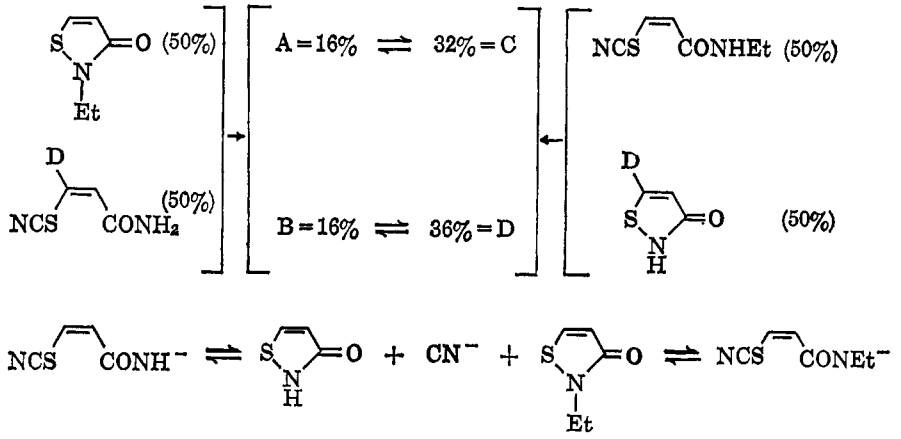


Scheme IV. Since in such a mixture $[CN^-][H^+]$ will of necessity be the same for both systems,

$$K_{2\text{-Et}}/K_{2\text{-H}} = \frac{[\text{N-Et-}i\text{-T}][TCA]}{[\text{N-EtTCA}][i\text{-T}]}$$

Equimolar amounts of *cis*-3-thiocyanoacrylamide-3*d* and 2-ethyl-3-isothiazolone were allowed to equilibrate in 75% DMSO-d_6–25% D_2O at ~25°. The product ratios were determined by analysis of the n.m.r. signals due to the alkyl groups, the acrylic protons, and the heterocyclic protons, using the alkyl groups as an internal integration standard. The equilibrium was also approached from the other side, employing equimolar amounts of *cis*-N-ethyl-3-thiocyanoacrylamide and 3-isothiazolone-5*d*, in order to minimize errors including that due to the loss of hydrogen cyanide. The results of the experiment are shown in Scheme V and indicate the over-all result of cyclization of *cis*-3-thiocyanoacrylamide at the expense of ring fission in

SCHEME V



$K_{2\text{-Et}}/K_{2\text{-H}} = 0.22 \pm 0.05$

2-ethyl-3-isothiazolone. Of possible importance is the fact that 3-isothiazolone can exist in the enol or ionized form ($pK_a = 7.2$), which the N-ethyl derivative cannot.

Preliminary results on the rate of cyclization of *cis*-3-thiocyanoacrylamide which have been obtained indicate an apparent first-order rate constant at pH 5.00. The observed rate constant was lower at pH 4.50 and higher at pH 5.50, as would be expected if the first-order cyclization is that of the anion of *cis*-3-thiocyanoacrylamide (Scheme I, R = H).

Special methods are necessary to obtain a true spectrum of the amide. At pH 2.00 the true spectrum (Figure 2) can be recorded within the first 20 sec. of diluting an ether solution (0.005 *M*) with the required aqueous or alcoholic solvent.

The rate of the reverse reaction has been studied only over a relatively narrow range of pH, owing to experimental difficulties.[18] Within the pH range 5–7, the rate of attack by CN^- on 3-isothiazolone was proportional to $[CN^-]$, but showed no dependence upon $[H^+]$ within the limits of experimental error. Therefore, of the alternate mechanisms for 3-isothiazolone ring opening, A, involving attack on sulfur by cyanide ion, and B, requiring prior N-protonation of the 3-isothiazolone, the evidence is currently in favor of the former. The latter mechanism, involving the necessity of protonation of isothiazolone—a very weak base—prior to attack by cyanide ion cannot, however, be ruled out at lower pH values until more accurate kinetic results are available for this region. It is hoped at a later stage to provide meaningful quantitative figures and more definite evidence for the mechanism postulated. For the present, our study introduces new methods of synthesizing 3-isothiazolones and recognition of the main features of the interconversion of 3-isothiazolones and *cis*-3-thiocyanoacrylamides.

Experimental[19]

N-Alkylpropiolamides.—Methyl propiolate (8.4 g., 0.10 mole) was added gradually with swirling to a solution of the appropriate amine (0.12 mole) in 20 ml. of 50% aqueous methanol cooled in Dry Ice–isopropyl alcohol.[20] After 5–10 min., the solvents were removed on a rotary film evaporator at 0.2 mm., and the residual gum was crystallized or distilled under reduced pressure.

N-Methylpropiolamide crystallized from ether (−20°) as colorless prisms: m.p. 90–91°; yield 76%; ν_{max}^{Nujol} 3270, 3125, 2120, 1660–1845 (br), 1575, 1515, 1305, 1165, 884, 772, 740, and 720 cm.$^{-1}$.

Anal. Calcd. for C_4H_5NO: C, 57.82; H, 6.07; N, 16.86. Found: C, 57.56; H, 6.09; N, 16.63.

N-Ethylpropiolamide was distilled as a colorless oil, b.p. 74–76° (0.8 mm.), yield 72%, which rapidly turned yellow on standing: ν_{max}^{film} 3320, 3120, 2118, 1650 (br), 1550, 1450, 1382, 1360, 1280, 1155, 1060, 925, and 750–650 cm.$^{-1}$ (broad absorption).

Anal. Calcd. for C_5H_7NO: C, 61.84; H, 7.27; N, 14.42. Found: C, 61.34; H, 7.23; N, 13.95.

N,N-Dimethylpropiolamide.—The reaction between dimethylamine and methyl propiolate proceeded with explosive violence at −10°, and it was necessary to cool the amine solution to −78°, with dropwise addition of the ester. The product was contaminated with products of triple-bond addition, which were largely removed by partition between chloroform and 2 *N* HCl. The neutral fraction was sublimed at 50° (0.4 mm.) as colorless prisms, m.p. 75–76°.

Anal. Calcd. for C_5H_7NO: C, 61.84; H, 7.27; N, 14.42. Found: C, 61.46; H, 7.14; N, 14.55.

***cis*- and *trans*-3-Thiocyanocrylamide.**—Propiolamide (0.69 g., 0.01 mole) was added to a solution of ammonium thiocyanate (1.5 g., 0.02 mole) in 10 ml. of 2 *M* sulfuric acid (0.02 mole) at 0°. After 1 hr. at 0° the crude product (1.21 g., 94%) was collected by filtration and washed with a few milliliters of chilled water. It was then triturated under nitrogen with sodium hydroxide (2 *N*, 15 ml.) at 0°, filtered rapidly, and washed with ice–water (5 ml.), and the combined filtrates were neutralized with chilled 5 *N* hydrochloric acid (6 ml.). The *cis* isomer (0.86 g., 71%) crystallized rapidly and was removed by filtration and washed. The *trans* isomer (0.21 g., 17%) did not dissolve in the alkali unless the time of contact was unduly prolonged beyond the necessary minimum. Larger amounts of the mixture were processed batchwise on this account; the *trans* isomer reacts with alkali and cannot then be recovered.

***cis*-3-Thiocyanocrylamide** crystallized from cold dimethyl sulfoxide on dilution with water as pale cream leaflets: m.p. 153–154° dec. (HCN evolved); $\lambda_{max}^{Et_2O}$ 253 mμ (ε 11,160); $\lambda_{max}^{H_2O}$ 253 mμ (ε 10,900); ν_{max}^{Nujol} 3387, 3155, 2163, 1687, 1636, 1596, 1424, 1310, 1200, 799, 778, 725, and 686 cm.$^{-1}$; n.m.r. signals (60 Mc., in DMSO with TMS standard) at τ = 2.22, 2.55 (broad, NH_2),

(18) At low pH it is difficult to obtain a high concentration of cyanide ion; furthermore, the volatility and toxicity of hydrogen cyanide make it difficult to obtain accurate figures for $[CN^-]$, assumed $K_{HCN} = 7.2 \times 10^{-10}$.

(19) All melting points are corrected; boiling points are uncorrected. We are indebted to Mr. Josef Nemeth, Mrs. Mary Rose Kung, and Mrs. Ancilla S. Bay for the microanalyses and to Mr. Dick H. Johnson and Miss Gail Gregory for the n.m.r. spectra, obtained with a Varian Associates Model A-60 n.m.r. spectrometer. We also wish to thank Mr. Johnson for the infrared spectra obtained with a Perkin-Elmer Model 521 spectrophotometer. The ultraviolet spectra were determined using a Cary Model 15 recording spectrometer.

(20) *Caution.* The reaction between methyl propiolate and amines may be violently exothermic. Vigorous cooling (−20 to −70°) is recommended to avoid any accidents. Propiolic acid, its volatile esters (the methyl ester codistils even with dry ether), the amides, and the derived thiocyanoacrylamides are vesicants of dangerous to unpleasant action in the order named. Contact with the skin for only a few seconds can produce intense irritation which may last for several days. The esters may diffuse through surgical gloves.

2.79 (doublet, 3-*H*), and 3.59 p.p.m. (doublet, 2-*H*, $J_{2,3}$ = 9.0 c.p.s.). The assignment was confirmed by preparation of the 2-deuterated isomer (addition of DSCN in D_2O to propiolamide) which showed only a singlet at τ = 2.69 p.p.m. for 3-*H*.

Anal. Calcd. for $C_4H_5N_2OS$: C, 37.50; H, 3.14; N, 21.87. Found: C, 37.41; H, 3.05; N, 21.58.

***trans*-3-Thiocyanoacrylamide** crystallized from water as cream needles: m.p. 193–194° dec. (red melt); $\lambda_{max}^{95\%\ EtOH}$ 242 mμ (ε 13,060); ν_{max}^{Nujol} 3410, 3175, 2162, 1712, 1677, 1645, 1630, 1598, 1405, 1280, 1200, 1118, 958, 940, 933 (sh), 835, 812, 780, 740, and 680 cm.$^{-1}$; n.m.r. signals (60 Mc., in DMSO with TMS standard) at τ = 2.25, 2.75 (broad, NH_2),2.71 (doublet, 3-*H*), and 3.51 p.p.m. (doublet, 2-*H*, $J_{2,3}$ = 14.5 c.p.s.).

Anal. Found: C, 37.20; H, 3.02; N, 21.35.

***cis*-N-Methyl-3-thiocyanoacrylamide.**—N-Methylpropiolamide was treated as described above; the crude product (73% yield) contained no *trans* isomer according to the n.m.r. spectrum, and the alkali-separation process was not required. Crystallization by dilution of a cold saturated chloroform solution with anhydrous ether (2 vol.) and petroleum ether (b.p. 30–60°) to opalescence gave pale cream needles, m.p. 129–130° dec. The compound slowly decomposed on standing. A better sample, m.p. 132–133° dec. (HCN evolved), was obtained by nucleophilic attack of cyanide on 2-methyl-3-isothiazolone (*vide infra*): $\lambda_{max}^{Et_2O}$ 254 mμ (ε 12,680); $\lambda_{max}^{H_2O}$ 254 mμ (12,500); ν_{max}^{Nujol} 3330, 3100, 2168, 1655, 1634, 1595, 1560, 1405, 1262, 1175, 1158, 1058, 802, 793, and 680 cm.$^{-1}$; n.m.r. signals (60 Mc., in DMSO) at τ 1.50 (broad, N*H*) 2.84 (doublet, 3-*H*), and 3.57 (doublet, 2-*H*, $J_{2,3}$ = 9.0 c.p.s.).

Anal. Calcd. for $C_5H_6N_2OS$: C, 42.23; H, 4.25; N, 19.70. Found: C, 42.23; H, 4.35; N, 19.79.

***cis*-N-Ethyl-3-thiocyanoacrylamide.**—N-Ethylpropiolamide was similarly treated, giving only the *cis* isomer (59% yield). Crystallization from cold dimethyl sulfoxide by addition of ice–water gave cream needles: m.p. 144–145°; $\lambda_{max}^{Et_2O}$ 255 mμ (ε 14,030); $\lambda_{max}^{H_2O}$ 255 mμ (13,800); ν_{max}^{Nujol} 3380, 3120, 2180, 1665 (sh), 1648, 1598, 1552, 1340 (w), 1262, 1180, 1075 (w), 980 (w), 918 (w), 827, 797, and 690 cm.$^{-1}$; n.m.r. signals (60 Mc., in DMSO) at τ 1.59 (broad, N*H*), 2.77 (doublet, 3-*H*), and 3.62 (doublet, 2-*H*, $J_{2,3}$ = 9.0 c.p.s.).

Anal. Calcd. for $C_6H_8N_2OS$: C, 46.10; H, 5.17; N, 17.92. Found: C, 46.08; H, 5.17; N, 17.73.

***cis*-N,N-Dimethyl-3-thiocyanoacrylamide.**—N,N-Dimethylpropiolamide was treated similarly to yield 95% crude product, which again contained no *trans* isomer (n.m.r. and infrared spectra). The product was not soluble in alkali, but reacted slowly to give unidentified products. Crystallization from water gave colorless needles: m.p. 108–109°; $\lambda_{max}^{Et_2O}$ 263 mμ (ε 12,900); $\lambda_{max}^{95\%\ EtOH}$ 263 mμ (ε 12,370) (irreversibly altered by addition of alkali); ν_{max}^{Nujol} 3080(w), 2165, 1635, 1610 (sh), 1580 (vw), 1565, 1405, 1321, 1255, 1187, 1162, 1060 (w), 975 (w), 882 (w), 784, and 729 cm.$^{-1}$; n.m.r. signals (60 Mc., in DMSO) at τ 2.53 (doublet, 3-*H*) and 3.02 (doublet, 2-*H*, $J_{2,3}$ = 9.0 c.p.s.).

Anal. Calcd. for $C_6H_8N_2OS$: C, 46.10; H, 5.16; N, 17.92. Found: C, 45.82; H, 5.13; N, 18.25.

3-Isothiazolone. A.—Propiolamide (3.45 g., 0.05 mole) and ammonium thiosulfate (7.5 g., 0.05 mole) in 25 ml. of water at 0° was stirred with a brisk current of nitrogen. Ammonia was evolved, and the pH remained constant at aproximately 9.0. After 4 hr., the solution was divided into two equal portions A and B. Portion A was acidified with 2 ml. of hydrochloric acid and boiled for 10 min., sulfur dioxide being evolved. (No sulfur was precipitated.) Neutralization and continuous extraction with ether gave 3-isothiazolone (1.25 g., 50%), m.p. 74–75° after sublimation at 80° and 0.3 mm.

Portion B was treated with a methanolic solution of iodine (3.18 g., 0.0125 mole), adjusting the pH periodically to neutralize the generated hydriodic acid. After discharging excess iodine (SO_2), the mixture was neutralized and continuously extracted with ether. 3-Isothiazolone (1.51 g., 64%), m.p. 74–76°, was obtained.

B.—*cis*-3-Thiocyanoacrylamide (1.28 g., 0.01 mole) was boiled for 5 min. in sulfuric acid (0.2 *N*, 25 ml.), hydrogen cyanide being evolved (a stream of nitrogen at lower temperatures was also effective). The mixture was cooled and worked up in the usual manner to give 3-isothiazolone (0.64 g., 63%).

C.—*cis*-3-Thiocyanoacrylamide (0.77 g., 0.006 mole) in 0.2 *N* NaOH (30 ml., 0.006 mole) at 0° was stirred with a current of nitrogen and 0.2 *M* ferrous sulfate solution (5 ml., 0.001 mole) was added all at once. A transient orange precipitate was observed, then the solution turned yellow [$Fe(CN)_6^{4-}$ test positive]. Continuous extraction with ether gave 3-isothiazolone (0.55 g., 89%), identified in the usual way. Essentially the same procedure was used with solutions of $CuSO_4$, $FeCl_3$, and $NiSO_4$, quantities being adjusted to fit the stoichiometry of the equation required for the generation of the complex cyanide $Na_xM(CN)_y$. In the case of the ferric salt, precipitation of the very insoluble hydroxide interfered, and, in the case of the copper salt, complex formation between the reactants led to slow and inefficient reaction. Nickel salts led to smooth conversion (83%) to 3-isothiazolone, recrystallized from petroleum ether (b.p. 60–80°) as colorless, flat needles: m.p. 74–75°; $\lambda_{max}^{H_2O}$ 264 mμ (ε 6380) and 275 mμ (ε 6470); at pH >8 this is changed to 275 mμ (ε 6920) and ~273 mμ; $\lambda_{max}^{Et_2O}$ 256 mμ (6570); $\nu_{max}^{CCl_4}$ 3100–2900 (br), 2800, 2700, 2640, 2548 (last four bands were shifted on N-deuteration), 1630 (w), 1577 (sh), 1544, 1522, 1414, 1324, 1234, 1217 (sh), 1088, 983, 863, 828, and 676 cm.$^{-1}$; n.m.r. signals (60 Mc., in $CDCl_3$) at τ −2.63 (N-*H*), 1.58 (doublet, 5-*H*), and 3.43 (doublet, 4-*H*, $J_{4,5}$ = 4.6 c.p.s.). The 4-deuterated derivative, prepared in the usual way, showed a singlet at τ = 1.59 p.p.m.

Anal. Calcd. for C_3H_3NOS: C, 35.63; H, 2.99; N, 13.85. Found: C, 35.69; H, 3.10; N, 13.78.

D.—*cis*-3-Thiocyanoacrylamide (0.64 g., 0.005 mole) was dissolved in the minimum volume of cold acetone containing 1 drop of 2 *N* sodium hydroxide and was allowed to stand in a stoppered vessel. After 48 hr., the solvent was removed under reduced pressure at 40° and 2 ml. of chilled water was added; filtration yielded unchanged starting material (0.35 g., 55%, m.p. 153–154° dec.). Extraction of the filtrates with chloroform afforded 3-isothiazolone (0.17 g., 34%), identified in the usual way.

2-Methyl-3-isothiazolone.—*cis*-N-Methyl-3-thiocyanoacrylamide, on heating with dilute acid as in B above, yielded 2-methyl-3-isothiazolone (80%). Application of method C, using ferrous salts, gave the same product in nearly quantitative (96%) yield. The material was hygroscopic and was therefore purified by sublimation at 50° and 0.5 mm., affording colorless prisms: m.p. 50–51°; $\lambda_{max}^{Et_2O}$ 281 mμ (ε 6550); $\lambda_{max}^{95\%\ EtOH}$ 275 mμ (ε 7250), unaffected by acid or base; $\nu_{max}^{CCl_4}$ 3100, 2960, 1660, 1629, 1512, 1411, 1320, 1280, 1184, 1120, 1052, 920, 710, 688, and 655 cm.$^{-1}$; n.m.r. signals (60 Mc., in $CDCl_3$) at τ 6.63 (N-C*H*$_3$), 1.71 (doublet, 5-*H*), and 3.72 (doublet, 4-*H*, $J_{4,5}$ = 6.5 c.p.s.).

Anal. Calcd. for C_4H_5NOS: C, 41.72; H, 3.37; N, 12.16. Found: C, 41.27; H, 4.44; N, 12.19.

2-Ethyl-3-isothiazolone.—This compound was prepared by cyclization of *cis*-N-ethyl-3-thiocyanoacrylamide with hot dilute acid (88% yield) or by the action of ferrous salts (quantitative). 2-Ethyl-3-isothiazolone sublimed at 50° and 0.5 mm. as colorless prisms: m.p. 61–62°; $\lambda_{max}^{Et_2O}$ 280 mμ (ε 6580); $\lambda_{max}^{95\%\ EtOH}$ 277 mμ (ε 6280), unaffected by acid or alkali; $\nu_{max}^{CCl_4}$ 3100, 2965, 2925, 1653 (br), 1516, 1463, 1451, 1383, 1318, 1250, 1168, 1120, 1083, 1058, 958, 699, 670, and 650 cm.$^{-1}$; n.m.r. signals (60 Mc., in $CDCl_3$) at τ 1.77 (doublet, 5-*H*), 3.72 (doublet, 4-*H*), 6.12 (quartet, CH_2), and 8.67 (triplet, CH_3, $J_{4,5}$ = 6.5 c.p.s.).

Anal. Calcd. for C_5H_7NOS: C, 46.48; H, 5.46; N, 10.84. Found: C, 46.28; H, 5.43; N, 10.82.

Action of Nucleophiles on 3-Isothiazolones. A. Potassium Cyanide.—To 3-isothiazolone (0.505 g., 0.005 mole) in 5 ml. of water was added a solution of potassium cyanide (0.33 g., 0.005 mole) in 2 ml. of water. *cis*-3-Thiocyanoacrylamide (0.140 g., 22%) crystallized immediately and was identified in the usual manner. After 1 min. the solution was acidified (5 ml. of 1 *N* HCl), resulting in rapid crystallization of a further 0.321 g. (50%) of product. The addition of a further 0.005 mole of potassium cyanide and acid resulted in crystallization of a further 0.042 g. (7%) of *cis*-3-thiocyanoacrylamide. The total recovery was 79% (solubility loss *ca.* 10%). The same experiment was repeated, acidifying the isothiazolone solution before addition of cyanide (5 ml. of 2 *N* HCl, 0.01 mole). *cis*-3-Thiocyanoacrylamide (0.511 g., 80%) crystallized slowly over the course of 1.5 hr.

2-Methyl-3-isothiazolone and 2-ethyl-3-isothiazolone were similarly converted to the corresponding *cis*-3-thiocyanoacrylamides in 74 and 86% yield, respectively.

B. Sodium Thiophenolate.—3-Isothiazolone (0.505 g., 0.005 mole) in 5 ml. of water was treated with thiophenol (0.55 g., 0.005 mole) in alkali (2 ml. of 2.5 *M*), followed by acidification (5 ml. of 1 *N* HCl) to complete precipitation. The result was essentially the same if the alkali and acid were omitted. The crude product (0.985 g., 94%) had m.p. 120–124°. Careful dilution of a cold chloroform solution with cold petroleum ether gave colorless plates, m.p. 126–127°, of ***cis*-3-phenyldithioacrylamide:**

$\lambda_{max}^{96\% EtOH}$ 240 mμ (ε 13,000) and 260 mμ (ε 10,000) (sh), shifted to 271 mμ (ε 16,300) by alkali; ν_{max}^{Nujol} 3500, 3210 (NH), 1700 (sh), 1650, 1620, 1580, 1405, 1298, 1180, 803, 769, 741, and 682 cm.$^{-1}$; n.m.r. signals (60 Mc., in DMSO) at τ 2.6 (multiplet, weight 8) containing doublets at τ 2.83 (separation 9.3 c.p.s., weight ~1) and 3.90 (separation 9.2 c.p.s., weight 1).

Anal. Calcd. for $C_9H_9NOS_2$: C, 51.15; H, 4.29; N, 6.63. Found: C, 50.88; H, 4.32; N, 6.52.

If the crude product was recrystallized from aqueous ethanol, only diphenyl disulfide, m.p. 61–62°, was isolated, identified by comparison with an authentic specimen.

C. Sodium *t*-Butyl Mercaptide.—The reaction of *t*-butyl mercaptan with 3-isothiazolone was extremely slow in the absence of alkali. With a molar equivalent of alkali present, as in the case of sodium thiophenolate, ***cis*-3-*t*-butyldithioacrylamide** was obtained and crystallized from dry ether, on addition of petroleum ether, as colorless plates: m.p. 146–147°; ν_{max}^{Nujol} 3500, 3220, 1660, 1645, 1565, 1408, 1356, 1295, 1182, 804, 763, and 687 cm.$^{-1}$; n.m.r. signals (DMSO) at τ 2.53, 2.91 (broad, N*H*), 3.05 (doublet, separation 10 c.p.s.), 4.01 (doublet, separation 10 c.p.s.), and 8.70 (singlet).

Anal. Calcd. for $C_7H_{13}NOS_2$: C 43.94; H, 6.84; N, 7.32. Found: C, 43.81; H, 6.72; N, 7.42.

D. Sulfide.—To 3-isothiazolone (0.250 g., 0.0025 mole) in 1 *M* HCl (5 ml., 0.005 mole) was added sodium sulfide (0.60 g., 0.0025 mole) in 2 ml. of water. There was an immediate precipitate of sulfur (0.06 g., 75% based on sulfide). Extraction of the filtered solution with chloroform gave only a slight residue, but on standing 48 hr. sulfur was deposited as a yellow gum.

E. SCN^-, Cl^-, Br^-, I^-, NO_2^-, $S_2O_3^{2-}$, and SO_3^{2-} Salts.—The absorption at 253 mμ of a 10^{-4} *M* aqueous solution of 3-isothiazolone was unaffected at pH 5.00 by addition of SCN^-, Cl^-, Br^-, I^-, or NO_2^-, indicating the effective absence of nucleophilic attack with ring opening. The addition of SO_3^{2-} led to a rapid rise in the extinction coefficient at 253 mμ, as in the case of CN^-, while the addition of $S_2O_3^{2-}$ led to a much slower increase in the specified absorption.

Deuterium Scrambling in the Thiocyanoacrylamide–3-Isothiazolone System.—*cis*-3-Deuterio-3-thiocyanoacrylamide (0.256 g., 0.002 mole, prepared by exchange of propiolamide in D_2O with a trace of potassium carbonate, followed by the usual procedures) was shown by n.m.r. spectroscopy to contain about 82% deuterium on C-3. Microanalysis showed 22.60 atom % D, equivalent to ~90% D on C-3. The material was dissolved in 2 *N* sodium hydroxide (3 ml., 0.006 mole), and 3-isothiazolone (0.202 g., 0.002 mole) was added rapidly. As soon as solution occurred (5 sec.), 2 *N* hydrochloric acid (3 ml., 0.006 mole) was added and the *cis*-3-thiocyanoacrylamide was recovered by chilling and filtration (total elapsed time *ca.* 1 min.). The recovery was 84%. The 3-isothiazolone was then recovered by repeated extraction with chloroform, and the extracts were evaporated at 20°. The n.m.r. spectrum now showed ~41% deuterium on C-5 in this product (corresponding to C-3 in the thiocyanoacrylamide used), confirming that both compounds pass through a common intermediate in alkaline solution. Examination of the recovered *cis*-3-thiocyanoacrylamide by n.m.r. and microanalysis showed exactly the same pattern, *i.e.*, a 50% drop in the deuterium content at C-3. Microanalysis showed 10.90 atom % D, equivalent to ~43% D on C-3.

Equilibrium in the N-Ethyl-3-thiocyanoacrylamide–3-Isothiazolone System.—All solutions were prepared in DMSO-d_6 containing 25% D_2O. Mixtures of (a) *cis*-N-ethyl-3-thiocyanoacrylamide (0.001 *M*) and 3-isothiazolone-5*d* (0.001 *M*) and (b) 2-ethyl-3-isothiazolone and *cis*-3-thiocyanoacrylamide-3*d* were allowed to equilibrate, the product ratios being determined by n.m.r. analysis, using the alkyl group as an internal integration standard. Results were averaged over both solutions when their compositions were experimentally identical (Table I). The equilibrium was approached from both sides to minimize errors. The deuterated compounds were used to facilitate estimation of otherwise overlapping n.m.r. signals.

TABLE I

Typical run (b)	Initial composition	Final composition
cis-3-Thiocyanoacrylamide-3*d*	0.50	0.16
3-Isothiazolone-5*d*	...	0.32
cis-N-Ethyl-3-thiocyanoacrylamide	...	0.36
2-Ethyl-3-isothiazolone	0.50	0.16

$K_{2\text{-Et}}/K_{2\text{-H}} = 0.22 \pm 0.05$ in 75% DMSO-d_6–25% D_2O at *ca.* 25°.

Preliminary Investigation of the Kinetics of Cyclization and Nucleophilic Attack.—The required solvent ([CN^-], [H^+]) was prepared and an aliquot (1.00 ml., 0.005 *M* solution) was delivered into the appropriate volume of thiocyanoacrylamide solution (49.00 ml., or 49.2 ml. if the aliquot was an ethereal solution) at time zero. Absorption at $\lambda_{253-256}$, depending on the nature of the substituent on nitrogen, was followed on a Cary Model 15 recording spectrophotometer, and ln $(A_t - A_{equil})$ *vs.* *t* was a straight-line plot through 90% of the reaction. The equilibrium value was redetermined several hours after equilibrium had apparently been attained. The concentration of cyanide ion was based on calculations assuming $K_{HCN} = 7.2 \times 10^{-10}$.

Novel Conversion of Diphenylcarbodiimide by Sodium Naphthalene

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The reaction of diphenylcarbodiimide with sodium naphthalenide complex was studied. Several products are formed depending upon experimental conditions, including N,N′,N″,N‴-tetraphenyloxamidine, 1,3-diphenyl-2,4,5-(triphenylimino)imidazolidine, N-(N′,N″-diphenylguanyl)diphenylformamidine, and β-diphenylcarbodiimide. The reaction mechanism evidently involves, as an initial step, the transfer of one or two electrons from sodium naphthalene to the carbodiimide molecule.

It is well known that alkali metals readily combine with some aromatic hydrocarbons in certain basic solvents to form stable colored complexes. Since the earlier work done by Schlenk,[2] several examples of reactions on this kind of organometallic compounds have been reported; for instance, the reaction with carbon dioxide,[3] alkyl halides,[4] and ethers,[5] and the metallation of hydrocarbons[5] and nitriles.[6] Recently they have been used as anionic initiators of polymerization for numerous vinyl compounds.[7] We report here a

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