Methyl 1-cyclohexenyl ketoxime IVb was prepared from 1-acetylcyclohexene[15] by a well-known procedure[16] with a yield of 73%.[17]

Compound IVb (128 mg, 0.92 m mol) was dissolved in 25 ml of 95% ethanol, and 20 mg of 10% palladium on carbon was added. The mixture was placed under 1 atm of hydrogen and stirred magnetically as hydrogen was absorbed. After an induction period of 12 min, 1 mol of hydrogen was taken up in 24 min and 2 mol at a distinctly slower rate in 2.5 hr. The hydrogen uptake stopped and the catalyst was removed. Removal of the solvent on a rotary evaporator left 80 mg of an oil which absorbed CO_2 from the air overnight to give a fine powder. Treatment with aqueous sodium hydroxide gave back the oil, and treatment with hydrochloric acid on another portion gave the hydrochloride of α-aminoethylcyclohexane. Recrystallization from ethanol–ethyl acetate gave the pure hydrochloride, mp 241.5° dec (lit.[18] mp 239–240°). An authentic sample of α-aminoethylcyclohexane hydrochloride (below) did not depress the melting point of this compound and gave identical infrared spectra.

An attempted hydrogenation of 130 mg of methyl cyclohexyl ketoxime, mp 60–61.5°,[19] with 19 mg of 10% palladium on carbon under the same conditions as described for compound IVb (above) resulted in an uptake of less than 0.5 mol in 16 hr. The partially reduced product was not further identified.

The authentic sample of α-aminoethylcyclohexane was prepared from 300 mg of methyl cyclohexyl ketoxime. The ketoxime was dissolved in 30 ml of absolute ethanol, and 5 g of sodium was added in pieces at a rate to keep the alcohol refluxing. Water was finally added and the amine was steam distilled. The hydrochloride (150 mg, 43%) was isolated and recrystallized from ethanol–ethyl acetate, mp 242–243° dec.

Methyl 2-(3-Bromo-1-cyclohexenyl) Ketoxime (VIb).—To a solution of 3.0 g (0.01 mol) of Vb[17] in 100 ml of carbon tetrachloride was added 1.02 g (0.01 mol) of triethylamine dropwise. Immediately, triethylamine hydrobromide was precipitated. The carbon tetrachloride solution was filtered. After reducing the volume of the filtrate to 25 ml using a rotating evaporator without heating, part of the solution was removed for an nmr spectrum of VIb. The low-field hydrogen on oxygen remained, and there was evidence of a trace amount of triethylamine from the easily identifiable ethyl hydrogens. The vinylic proton appeared at δ 5.66 and the allylic proton at δ 4.24. When the solvent was removed completely, an almost colorless glass of 2.10 g remained. The glassy solid was not as soluble in carbon tetrachloride as the starting compound. The nmr spectrum, as just described, was quite different from that of Vb or VIIb (Table I). However, profound decomposition occurred when an attempt was made to distil the glassy solid.

3-Methyl-$\Delta^{2,3a(4)}$-tetrahydro-1,2-benzisoxazole (VIIb).—In 100 ml of carbon tetrachloride 8.0 g (0.0268 mol) of Vb was dissolved, and to the solution was added 4.5 g of sodium hydroxide pellets. The heterogeneous reaction mixture was stirred for 1 hr, and then the precipitate and excess sodium hydroxide were removed by filtration. The filtrate was washed twice with 50 ml of water and dried over anhydrous sodium sulfate. The dried carbon tetrachloride yielded 2.85 g, 65%, of 3-methyl-$\Delta^{2,3a(4)}$-tetrahydro-1,2-benzisoxazole. The analytical sample was distilled at reduced pressure: bp 54–55° (0.12 mm), $n^{25}D$ 1.5174, d^{25}_4 1.0453.

When 2.0 g of VIb was suspended in carbon tetrachloride and treated with 4.5 g of sodium hydroxide pellets, as just described, 1.0 g of VIIb (identical ir and nmr spectra) was obtained.

Registry No.—Ia, 20936-78-1; Ib, 24010-91-1; Ic, 24010-92-2; IIIb, 24010-93-3; IIIc, 24010-94-4; IVa, 23042-97-9; IVb, 23042-98-0; IVc, 23042-99-1; Va, 24010-49-9; Vb, 24010-50-2; Vc, 24010-51-3; VIb, 24010-98-8; VIIb, 24010-99-9; VIIc, 24011-00-5.

(15) R. E. Christ and R. C. Fuson, *J. Amer. Chem. Soc.*, **59**, 893 (1937).
(16) R. L. Shriner, R. C. Fuson, and D. Y. Curtin, "Systematic Identification of Organic Compounds," 5th Ed., John Wiley & Sons, Inc., New York, N. Y., 1964.
(17) C. Shiue, K. P. Park, and L. B. Clapp, *J. Org. Chem.*, **35**, 2063 (1970).
(18) M. Freifelder and G. R. Stone, *J. Amer. Chem. Soc.*, **80**, 5270 (1958).
(19) M. Godchot, *C. R. Acad. Sci., Paris*, **151**, 1131 (1910), reported mp 60°.

Elimination of Methyl Mercaptan from N-Substituted N′-Cyano-S-methylisothioureas. Evidence for N-Cyanocarbodiimides[1a,b]

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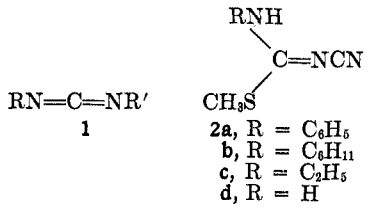
Although carbodiimides with a wide variety of substituents (R and R′ in **1**) have been prepared and characterized,[2] to our knowledge there is little, if any, recorded information on N-cyanocarbodiimides (R or R′ being CN in **1**). We report here evidence for the existence of N-cyanocarbodiimides in solutions resulting from the thermal or metal ion assisted elimination of methyl mercaptan from a series of N-substituted N′-cyano-S-methylisothioureas (**2a–2d**).

During the preparation of several compounds of the general formula **2** for another study,[3] it was found that they readily lose methyl mercaptan at their temperature of melting to yield viscous red oils or red glasses. The elimination of mercaptans from isothioureas was reported as early as 1881 by Will[4] and has been used by Ferris and Schutz[5] for the *in situ* generation of carbodiimides in solution. Ferris and Schutz facilitated the elimination by using a heavy metal ion to effect precipitation of an insoluble metal mercaptide and a base to serve as an acid acceptor. Their technique has been adopted in the present study.



Compounds **2a–2d** were conveniently prepared by the reaction of ammonia or the appropriate amine with dimethylcyanodithioimidocarbonate (**3**) which, in turn, was prepared by the method of Hantzsch and Wolvekamp.[6] The formulation of the isothioureas as shown in **2a–2d** is supported by their elemental analyses and spectral properties, some of which are summarized in Table I. Worthy of comment is the

TABLE I
INFRARED SPECTRA OF ISOTHIOUREAS 2a–2d

Compd	ν, cm⁻¹ (KBr) NH	C=N	C≡N
2a	3210	1520	2160, 2180
2b	3290	1550	2180
2c	3290	1550	2180
2d	3120, 3310	1530	2180, 2200

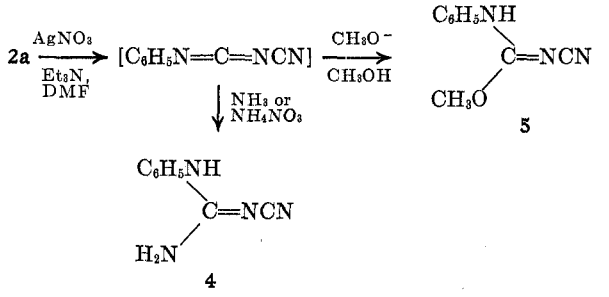
(1) (a) Support in part by NASA Grant NsG(T)-21 is gratefully acknowledged. (b) Abstracted from the M.S. Thesis of J. E. Parkinson and the Ph.D. Thesis of D. M. Wieland, West Virginia University, 1969. (c) NASA Trainee, 1965–1968.
(2) F. Kurzer and K. Douraghi-Zadeh, *Chem. Rev.*, **67**, 107 (1967).
(3) C. G. McCarty and D. M. Wieland, *Tetrahedron Lett.*, 1787 (1969).
(4) W. Will, *Chem. Ber.*, **14**, 1485 (1881).
(5) A. F. Ferris and B. A. Schutz, *J. Org. Chem.*, **28**, 71 (1963).
(6) A. Hantzsch and M. Wolvekamp, *Justus Liebigs Ann. Chem.*, **331**, 265 (1904).

nitrile absorption in the ir spectra of **2a** and **2d**. The observation of a shoulder on the main peak in **2a** and a sharp doublet of equal intensity in **2d** is consistent with the conclusion that *syn–anti* isomerism about the C=N bond is possible in these compounds.[3] For **2b** and **2c** either only one isomer is preferred in the crystalline state or the difference in absorption frequencies must be small or nonexistent.

$$\underset{\mathbf{3}}{(CH_3S)_2C{=}NCN} + RNH_2 \xrightarrow{C_2H_5OH} \mathbf{2a\text{–}2d}$$

Each of the compounds **2a–2d**, when taken to its melting point in a vial or capillary tube, gives off methyl mercaptan. As the mercaptan is being evolved, a red, viscous oil forms which becomes quite hard upon cooling. In the case of **2a** analysis of the resulting red glass showed sulfur to be absent.

A variety of procedures was employed to prepare and trap the N-cyanocarbodiimides from **2a–2d**. The salts found to be most useful for these studies were silver nitrate and mercuric chloride. Both are soluble in a fair number of organic solvents and give mercaptide salts insoluble in the same solvents. Triethylamine was used as a proton acceptor in all cases. In a typical experiment, the elimination reaction was carried out by adding a solution of the metal salt to a stirred solution of **2** and triethylamine in the same solvent at room temperature. The metal mercaptide usually started precipitating instantly in finely divided form and was essentially completely formed in 0.5 hr, although stirring was continued, at room temperature, for 1 hr before the red solution was cooled and the solid was collected and weighed. After removal of the precipitate, the desired "trapping" reagent was added to the filtrate to convert the intermediate into a guanidine or isourea derivative. The reactions carried out with **2a**, for example, are shown in the following scheme.



Some of the results of these elimination and trapping reactions for **2a** and the other isothioureas are summarized in Table II. The derivatives isolated were identified by comparisons with authentic samples and by their microanalyses and spectral properties. As can be seen from Table II, the mercaptide formation was usually close to quantitative, suggesting high yields of the reactive intermediate. The lower yields of final products were not unexpected in view of reported yields for similar derivatives from carbodiimides,[5] suspected reactions of the intermediate with itself, and the problems sometimes encountered in the isolation of the products.

Since the same final products could have been obtained by direct reaction of the trapping reagents with the starting isothioureas, it is important to emphasize that in each of these studies of metal ion assisted elimination of mercaptan, the reported yield of mercaptide salt was isolated before the trapping reagent was added to the solution. Indeed, the direct reaction with the isothioureas was tried in some cases for the synthesis of the final products and, in each case, more stringent reaction conditions (higher temperatures, sealed tubes) were required to obtain reasonable yields.

TABLE II

RESULTS OF ELIMINATION AND TRAPPING EXPERIMENTS[a]

Isothiourea	Mercaptide salt (yield, %)[b]	Trapping reagent	Derivative formed (yield, %)
2a	$AgSCH_3$ (100)	NH_3	1-Phenyl-2-cyanoguanidine (52)
2a	$HgClSCH_3$ (87)	CH_3OH–CH_3O^-	N-Phenyl-N′-cyano-O-methylisourea (46)
2b	$AgSCH_3$ (97)	NH_3	1-Cyclohexyl-2-cyanoguanidine (54)
2c	$AgSCH_3$ (86)	NH_3	1-Ethyl-2-cyanoguanidine (22)
2d	$AgSCH_3$ (100)	$C_6H_{11}NH_2$	1-Cyclohexyl-2-cyanoguanidine (23)
2d	$AgSCH_3$ (96)	NH_3	Dicyandiamide (50)

[a] All reactions were in DMF–Et_3N solutions except the second, which was in CH_3OH–Et_3N. [b] All yields are corrected for the triethylamine salt present.

The thermal elimination of methyl mercaptan from **2a** was also investigated. Heating a solution of **2a** in diphenyl ether to 150° while sweeping the gas evolved through two traps containing aqueous silver nitrate resulted, after 2 hr, in an 80% yield of silver mercaptide being collected. Subsequent addition of ammonium nitrate to the diphenyl ether solution led to the formation of **4** in 32% yield.

Although the intermediates in these reactions could not be isolated in monomeric form and characterized, despite numerous attempts to do so,[7] the evidence presented uniquely supports N-cyanocarbodiimides as the reactive species. It is known that many carbodiimides with unsaturated substituents on nitrogen are short-lived in monomeric form.[8] It would appear that N-cyanocarbodiimides are no exception to this, although they may be relatively stable in inert solvents at low concentrations.

Experimental Section

Melting points were determined with a Mel-Temp apparatus and are uncorrected. Elemental analyses were performed by Galbraith Laboratories, Knoxville, Tenn. Nmr spectra were recorded on a Varian HA-60-EL spectrometer using tetramethylsilane as an internal standard (τ 10.0) and solvents as specified. Ir spectra were recorded on Perkin-Elmer Model 137B and Beckman Model IR-8 spectrophotometers.

Synthesis of N-Substituted N′-Cyano-S-methylisothioureas.—The preparations of **2a–2d** were modeled after the procedure reported by Davidson.[9] The products were identified by comparison of melting points with those reported in the literature,[10] by elemental analyses (correct to within ±0.3% for each element

(7) In a few experiments it was possible to obtain ir spectra of the filtrate after removal of the metal mercaptide and some of the DMF solvent. The carbodiimide region (2200–2000 cm^{-1}) showed an absorption band at *ca.* 2150 cm^{-1} which was not due to solvent or C≡N of starting material. This band disappeared as further solvent was removed and was always absent in the red oils or glasses resulting from complete removal of solvent.

(8) H. G. Khorana, *Chem. Rev.*, **53**, 145 (1953).

(9) J. S. Davidson, *Chem. Ind.* (London), **48**, 1977 (1965).

(10) F. H. Curd, J. A. Henry, T. S. Kenny, A. G. Murray, and F. L. Rose, *J. Chem. Soc.*, 1630 (1948).

in each case), and by their ir (Table I) and nmr spectra. The procedure for **2a** is given as a typical example.

N-Phenyl-N'-cyano-S-methylisothiourea (2a).—Dimethyl cyanodithioimidocarbonate[6] (10.0 g, 0.069 mol) was dissolved in 200 ml of ethanol. To the stirred solution was added 10 ml (0.11 mol) of aniline over a period of 30 min. The solution was kept at 80° for 5 hr and then reduced by evaporation to one-fourth the original volume. The white crystals which appeared while the solution was cooled at 0° for 2 hr were collected by filtration. Recrystallization from ethanol gave 11.0 g (83%) of white crystals: mp 194–196° (lit.[10] mp 195–196°); ir (KBr) 3210 (NH), 2160 and 2180 (shoulder) (C≡N), and 1520 cm^{-1} (C=N); nmr (DMSO-d_6) τ 0.05 (s, 1, NH), 2.4–2.9 (m, 5, C_6H_5), and 7.45 (s, 3, CH_3S).

Anal. Calcd for $C_9H_9N_3S$: C, 56.5; H, 4.70; N, 22.0; S, 16.7. Found: C, 56.5; H, 4.65; N, 21.9; S, 16.7.

1-Phenyl-2-cyanoguanidine from 2a. Method A.—A solution of 0.27 g (0.0016 mol) of silver nitrate in 20 ml of DMF was added to a solution of 0.30 g (0.0016 mol) of **2a** and 10 drops of triethylamine in 50 ml of DMF. A yellow precipitate of silver mercaptide formed immediately. After the mixture was stirred for 1 hr at room temperature and then cooled in a Dry Ice–acetone bath, the yellow precipitate was collected by filtration and washed with DMF. After drying it amounted to 0.235 g, a quantitative yield of silver mercaptide. Ammonia was bubbled through the filtrate for 1 hr at 0°. The mixture was then stirred at room temperature for several hours followed by removal of all but 10 ml of the DMF by vacuum distillation. Addition of 100 ml of ether and cooling in a Dry Ice–acetone bath led to the formation of 0.13 g (52%) of 1-phenyl-2-cyanoguanidine, mp 197–199° (lit.[11] mp 195–196°). The ir and nmr spectra were consistent with the proposed product, as was the microanalysis (below).

Anal. Calcd for $C_8H_8N_4$: C, 60.0; H, 5.00; N, 35.0. Found: C, 60.3; H, 5.11; N, 35.2.

Method B.—The thermal elimination of methyl mercaptan from **2a** was effected by heating a solution of 1.00 g(0.0053 mol) of **2a** in 100 ml of diphenyl ether for 2 hr at 150° while nitrogen gas swept the mercaptan into traps containing 5% aqueous silver nitrate solution. The silver mercaptide collected after 2 hr was 0.65 g or 79.5% of the theoretical amount. At this point 1.00 g (0.013 mol) of ammonium nitrate was added to the diphenyl ether solution and the temperature was held at 120° for 12 hr. The solvent was removed by vacuum distillation, leaving a red oil from which a white solid formed after a few hours. Purification of the solid by column chromatography (neutral alumina) afforded 0.27 g (32.2%) of white solid, mp 197–198°, ir and nmr spectra identical with those of the product from method A.

N-Phenyl-N'-cyano-O-methylisourea from 2a.—To a stirred solution of 1.00 g (0.0053 mol) of **2a** and 1 ml of triethylamine in 150 ml of absolute methanol at 50° was added 1.25 g (0.0062 mol) of mercuric chloride. A white precipitate formed immediately. After the reaction mixture was stirred at room temperature for 45 min, the precipitate of $HgClSCH_3$ was collected by filtration, yield 1.29 g (87%). Sodium methoxide (0.070 g, 0.0013 mol) was then added to the colorless filtrate as a catalyst and stirring was continued at 50° for 10 hr. Removal of solvent by distillation gave 0.425 g (46%) of long, white needles: mp 166–167°; nmr (DMSO-d_6) τ −0.3 (s, 1, NH), 2.4–2.7 (m, 5, C_6H_5), and 6.1 (s, 3, CH_3O).

Anal. Calcd for $C_9H_9N_3O$: C, 61.7; H, 5.14; N, 24.0. Found: C, 61.6; H, 5.03; N, 24.1.

1-Cyclohexyl-2-cyanoguanidine from 2b.—To a solution of 0.31 g (0.0016 mol) of **2b** and 1 ml of triethylamine in 50 ml of DMF was added a solution of 0.27 g (0.0016 mol) of silver nitrate in 20 ml of DMF. The yellow precipitate of silver mercaptide formed immediately and was removed by filtration after the solution had been stirred for 2 hr. The yield of silver salt was 0.226 g (97%). Dry ammonia was bubbled through the filtrate for 1 hr at 0° and then the mixture was stirred for 10 hr at room temperature. After the DMF solution was concentrated to 10 ml by vacuum distillation, it was diluted with ether and water and allowed to stand for 2 days. The crystals which formed during this time were collected and found to constitute a 54% yield: mp 157–158° (lit.[11] mp 158–160°); nmr (DMSO-d_6) τ 3.1–3.8 (m, 3, NH_2 and $C_6H_{11}NH$) and 8.0–9.0 (m, 11, C_6H_{11}).

Anal. Calcd for $C_8H_{14}N_4$: C, 57.8; H, 8.44; N, 33.8. Found: C, 58.1; H, 8.42; N, 33.8.

(11) B. C. Redmon and D. E. Nagy, U. S. Patent 2,455,807 (1948).

1-Ethyl-2-cyanoguanidine from 2c.—A solution of 0.255 g (0.0016 mol) of **2c** and 1 ml of triethylamine in 50 ml of DMF was combined with a solution of 0.27 g (0.0016 mol) of silver nitrate in 20 ml of DMF. After the resulting solution was stirred for 1 hr the precipitated silver mercaptide was collected, yield 0.200 g (86%). Dry ammonia was bubbled through the solution for 30 min and then stirring at 40° was maintained for 24 hr. Removal of the solvent by vacuum distillation left a red oil, which was further purified by column chromatography (neutral alumina). Collection of the band eluted with a 1:1 ethyl–cyclohexane mixture yielded a red oil, which could not be induced to crystallize despite repeated attempts. This oil amounted to 0.042 g (22%) and gave spectral and analytical results expected for the desired product: nmr (DMSO-d_6) τ 3.0–3.6 (m, 3, NH_2 and C_2H_5NH), 6.7–7.1 (q, 2, CH_3CH_2), and 8.8–9.1 (t, 3, CH_3CH_2).

Anal. Calcd for $C_4H_8N_4$: C, 42.8; H, 7.20; N, 50.0. Found: C, 42.7; H, 7.26; N, 50.0.

1-Cyclohexyl-2-cyanoguanidine from 2d.—To a stirred solution of 1.00 g (0.0087 mol) of **2d** and 2 ml of triethylamine in 100 ml of DMF was added 1.60 g (0.0094 mol) of silver nitrate in 50 ml of DMF. A light yellow solid precipitated and the solution was stirred for 45 min at 0°. An excess (2 ml) of cyclohexylamine was added to the filtrate after the removal of the silver mercaptide (1.37 g, 100%) and then the mixture was kept at reflux temperature for 6 hr. Vacuum distillation of solvent left a red oil, which was placed on a column of neutral alumina for further purification. The total yield of crystals from the 1:1 ether–chloroform fraction was 0.33 g (23%), mp 157–159° (lit.[11] mp 158–160°). A mixture melting point with the material previously described from **2b** and a consistent ir spectrum were taken as evidence for the product being 1-cyclohexyl-2-cyanoguanidine.

Dicyandiamide from 2d.—A solution of 1.00 g (0.0087 mol) of **2d** and 1 ml of triethylamine in 100 ml of DMF was stirred for 45 min with 1.60 g (0.0094 mol) of silver nitrate. The yellow silver mercaptide (1.3 g, 96%) was removed by filtration and then dry ammonia was passed through the filtrate for 1 hr at 0°. Concentration of the solution to 20 ml by vacuum distillation followed by cooling in a Dry Ice–acetone bath produced 0.46 g of white solid. Recrystallization from ethanol gave 0.40 g (50%) of white crystals, mp 208–209° (lit.[12] mp 209–211°). The ir spectrum matched the recorded spectra of dicyandiamide.[13]

Registry No.—**2a**, 21504-96-1; **2b**, 24010-75-1; **2c**, 5848-25-9; **2d**, 15760-26-6; methyl mercaptan, 74-93-1; N-phenyl-N'-cyano-O-methylisourea, 24010-78-4; 1-cyclohexyl-2-cyanoguanidine, 24010-79-5; 1-ethyl-2-cyanoguanidine, 24010-80-8.

(12) "Handbook of Chemistry and Physics," 46th ed, Chemical Rubber Co., Cleveland, Ohio, p C-954.

(13) "Sadtler Standard Spectra," Sadtler Research Laboratories, Inc., Spectra No. 497 and 13632.

Evidence for an Azomethine Ylide Intermediate in the Carbonyl-Assisted Decarboxylation of Sarcosine. A Novel Synthesis of *dl*-Phenylephrine Hydrochloride

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There is much evidence to indicate that the rate of thermal decarboxylation of α-amino acids is accelerated in the presence of certain aromatic carbonyl compounds.[1] For cases involving amino acids with primary amino groups, the effect has been interpreted mecha-

(1) A. F. Al-Sayyab and A. Lawson, *J. Chem. Soc., C*, 406 (1968), and references cited therein.