

# Derivatives of Potassium Cyanodithioimidocarbonate. I. Synthesis of 1,4,6,9-Tetrathiaspiro[4.4]nonane and Related Compounds<sup>1</sup>

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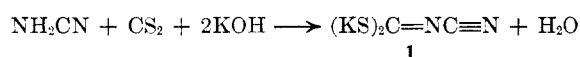
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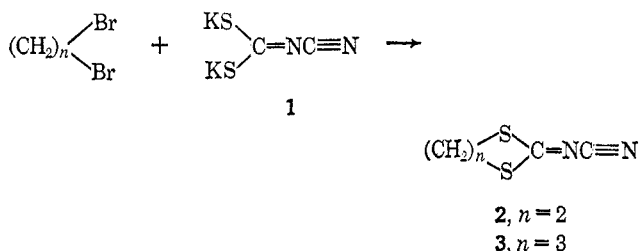
The preparation of 1,4,6,9-tetrathiaspiro[4.4]nonane (6) and 1,4,6,10-tetrathiaspiro[4.5]decane (7) from 2-cyanoimino-1,3-dithiolane (2) and 2-cyanoimino-1,3-dithiocyclohexane (3) with alkyldithiol compounds is described. This novel reaction was also used to prepare 1,5,7,11-tetrathiaspiro[5.5]undecane (5) in good yield. Mechanisms and supporting analytical data are discussed.

Johnston and co-workers<sup>2</sup> reported the synthesis of 1,5,7,11-tetrathiaspiro[5.5]undecane (5) in 33% yield by the reaction of 2,2'-iminodiethanol with trimethylene trithiocarbonate. We now wish to report an improved and novel method for preparation of 5. The utilization of this method furnished the previously unknown 1,4,6,9-tetrathiaspiro[4.4]nonane (6) and 1,4,6,10-tetrathiaspiro[4.5]decane (7).

The key intermediate, potassium cyanodithioimidocarbonate (1), was prepared by the method of Hantzsch<sup>3</sup> as illustrated by the following reaction.



A dilute aqueous solution of 1 with 1,2-dibromoethane or 1,3-dibromopropane furnished 2-cyanoimino-1,3-dithiolane (2) and 2-cyanoimino-1,3-dithiocyclohexane (3) in yields of 83 and 70%, respectively. Analyses,



and infrared and nmr spectra were in agreement for the proposed structures of 2 and 3.

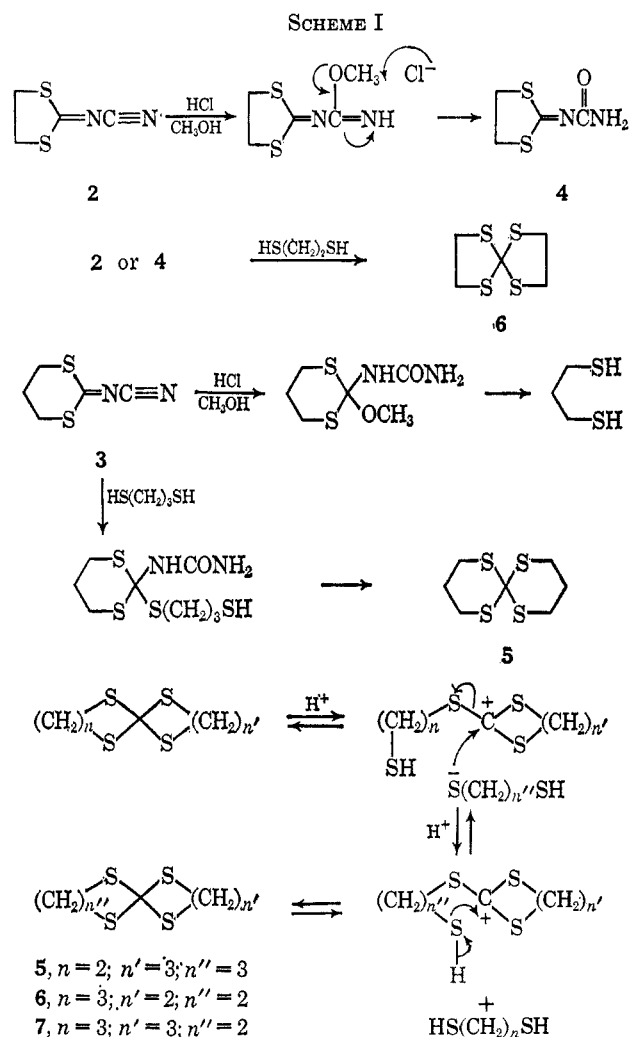
Acid-catalyzed methanolysis of 2 at 25–30° gave 1-(1,3-dithiacyclopentylidene)urea hydrochloride in 77% yield. At reflux temperature, a resinous product was obtained. Neutralization of the hydrochloride with ammonium hydroxide furnished 1-(1,3-dithiacyclopentylidene)urea (4) in 78% over-all yield. The formation of 4 is suggested to occur *via* the *o*-methylurea intermediate (Scheme I).

Under the same conditions, the reaction of 3 with methanolic hydrogen chloride did not lead to the urea, but to another product, C<sub>7</sub>H<sub>12</sub>S<sub>4</sub>, in 58% yield, together with a small amount of 1,3-propanedithiol. The nmr, infrared, and mass spectra suggested that the nitrogen-free product was 1,5,7,11-tetrathiaspiro[5.5]undecane (5). The nmr spectrum showed two band systems of peak urea in a 2:1 ratio in the region expected for methylene proton absorption and the infrared and nmr

(1) Presented at First International Congress of Heterocyclic Chemistry, Albuquerque, N. M., June 1967.

(2) T. P. Johnston, C. R. Strongfellow, Jr., and A. Gallagher, *J. Org. Chem.*, **27**, 4068 (1962).

(3) A. Hantzsch and M. Wolvekamp, *Ann. Chem.*, **331**, 265 (1904).

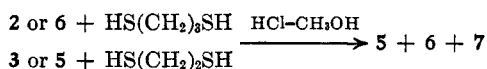


spectra were identical with those reported by Johnston and co-workers for 5.<sup>2</sup> The yield of 5 was increased to 90% by addition of 1,3-propanedithiol to the methanolic hydrogen chloride.

The reaction of 2 with 1,2-ethanedithiol in hydrogen chloride-methyl alcohol at 25–30° furnished 4 and the new 1,4,6,9-tetrathiaspiro[4.4]nonane (6) in yields of 69 and 8%, respectively. However, when the reaction was carried out under reflux, none of 4 was isolated and the yield of 6 was increased to 56%. Proof that 4 was a precursor in the formation of 6 was offered by employing 4 as one of the reactants whereby 6 was obtained in 68% yield. Analysis, molecular weight, infrared, nmr, and mass spectra were in agreement for the structure of 6.

The mechanism offered for the formation of 5 and 6 is illustrated in Scheme I. Since thiols are very good

TABLE I  
ADDITIONAL REACTIONS WITH HS(CH<sub>2</sub>)<sub>n</sub>SH



Reaction no.	Reactants		Temp, °C	Crude product			Yield, %				
	HS-(CH <sub>2</sub> ) <sub>n</sub> SH, n	Heterocyclic compound no.		State	Grams	Mp, °C	5	6	7	HS-(CH <sub>2</sub> ) <sub>2</sub> SH	HS-(CH <sub>2</sub> ) <sub>3</sub> SH
1	3	2	65-70	Liquid	43.0	...	9.6	7.1	33.4	1.6	14.3 <sup>a</sup>
2	2	3	25-30	Liquid	23.0	...	4.2	5.3	9.5	0	10.0
				Solid	28.0	103-110	3.0	27.1	19.6	0	0
	2	3	65-70	Liquid	35.0	...	6.6	9.3	14.9	0.6 <sup>a</sup>	22.8
				Solid	13.0	113-116	2.1	12.3	9.5	0	0
3	2	5	65-70	Liquid	73.8	...	16.6 <sup>a</sup>	14.3	31.8	6.0 <sup>a</sup>	76.9
4	3	6	65-70	Liquid	43.8	...	1.7	17.6 <sup>a</sup>	14.0	15.6	48.0 <sup>a</sup>
				Solid	23.8	124-128	0	29.7 <sup>a</sup>	8.0	0	0

<sup>a</sup> Recovered.

nucleophiles, it seems plausible that as soon as any are formed or added as reactants, they should attack 4 or its six-membered homolog in preference to methyl alcohol. Further confirmation of the mechanism was offered by the isolation of mixtures of 5, 6, and the unknown 1,4,6,10-tetrathiaspiro[4.5]decane (7) from the four reactions listed in Table I. By reviewing the yield data listed in Table I, the following generalizations can be drawn for the reactions 1-4: (a) these reactions proceed by a dithiol-dithiol exchange mechanism; (b) the order of stability of the spiran compounds is 7 or 6 > 5; (c) it appears the sequence of spiran formation in reaction 3 is 5, 7, 6; (d) the yield of 6 or 7 was greater than 5 (this is due to the lower stability of 5 under acidic conditions); and (e) the maximum yield of 7 was obtained in reactions 1 and 3.

#### Experimental Section<sup>4</sup>

**Analytical Methods.**—Vapor phase chromatographic analyses of 5, 6, and 7 were performed with an Aerograph Model 350-B gas chromatograph. A 0.25 in. × 2 ft aluminum column packed with 15% SE-30 and 5% Carbowax 20 M on 100/120 mesh Gas Chrom Z was operated isothermally at 215° with a He flow rate of 60 ml/min. Diphenyl sulfide was used as internal standard and benzene was the diluent for all samples. Vapor phase chromatographic analyses of 1,2-ethanedithiol and 1,3-propanedithiol were performed with the Aerograph Model 350-B gas chromatograph. A 0.25 in. × 4 ft aluminum column packed with 10% SE-52 on 80/100 mesh Gas Chrom Z was operated isothermally at 100° with a He flow rate of 60 ml/min. Benzene was used as diluent and the concentration of dimercaptans was determined by comparison of peak heights with those of standards.

The infrared spectra of all compounds were obtained with a Perkin-Elmer Model 21 spectrophotometer with a sodium chloride prism. The nmr spectra of all compounds were obtained with a Varian A-60 nmr spectrometer. The chemical shifts are reported in  $\delta$  using tetramethylsilane as reference. The mass spectra for 5, 6, and 7 were obtained with an Associated Electrical Industries, Ltd., MS-9 double-focusing mass spectrometer with probe injection with 60-ev electrons and with the ionization chamber at 160°. The percentages in the mass spectral data were determined by dividing the ion current of each single peak by the total ion current of the dominant peaks ( $\Sigma_{26}$ ). We are deeply grateful to Dr. W. H. Urry, University of Chicago, for the mass spectra.

(4) All melting points were taken upon a Fisher-Johns block and are uncorrected.

**Potassium Cyanodithioimidocarbonate (1).**—A modified procedure described by Hantzsch<sup>5</sup> was employed. To a stirred solution containing 84 g (1.0 mole) of 50% aqueous cyanamide,<sup>5</sup> 200 ml of ethanol, and 84 g (1.1 mole) of carbon disulfide, 126 g (2.0 moles) of 90% potassium hydroxide in 500 ml of ethanol was added slowly at 0-15° over a 15-min period. After stirring at 25-30° for 1 hr, the precipitate was collected by filtration, washed with 500 ml of ethanol, and air dried at 45-50°. The product was obtained in 87% yield and was used without any further purification. The infrared spectrum as determined from Nujol and Kel-F mulls contained bands at 2320 (w), 2130 (s) [C=N stretching (st)], 1302 (vs), 1260 (s), and 962 (vs) cm<sup>-1</sup>.

**2-Cyanoimino-1,3-dithiolane (2) and 2-Cyanoimino-1,3-dithiocyclohexane (3).**—To a stirred solution containing 583.2 g (3.0 moles) of 1 in 10.5 l. of water, 3.0 moles of 1,2-dibromoethane or 1,3-dibromopropane was added in one portion. The reaction mixture was stirred at 25-30° for 5 days. The resulting precipitate was collected by filtration, washed with 200 ml of ethyl ether, and air dried at 25-30°. Compound 2, mp 81-82°, was obtained in 83.3% yield. The melting point remained unchanged after recrystallization from ethyl alcohol. The infrared spectrum was determined from 2 to 12  $\mu$  in chloroform and from 12 to 15  $\mu$  in dimethylformamide and contained bands at 2980 (w) and 2910 (w) (C-H st), 2170 (vs) (C≡N st), 1515 (vs) (C=N st), 1425 (m) (CH<sub>2</sub> deformation (def)), 1282 (s), 1153 (m), 973 (s), and 850 (m) cm<sup>-1</sup>. The nmr spectrum in deuteriochloroform had a single peak at  $\delta$  3.83 ppm due to equivalent methylene groups.

*Anal.* Calcd for C<sub>4</sub>H<sub>4</sub>N<sub>2</sub>S<sub>2</sub>: N, 19.43; S, 44.47. Found: N, 19.40; S, 44.16.

Compound 3, mp 95-97°, was obtained in 69.6% yield. After two recrystallizations from ethyl alcohol, it melted at 99-100°. The infrared spectrum was determined from 2 to 12  $\mu$  in chloroform and from 12 to 15  $\mu$  in dimethylformamide and contained bands at 2980 (w) and 2910 (w) (C-H st), 2160 (vs) (C≡N st), 1470 (vs) (C=N st), 1425 (CH<sub>2</sub> def), 1284 (m), 1080 (s), and 967 (m) cm<sup>-1</sup>. The nmr spectrum in deuterated chloroform had a two-band system at 2-2.7 and 3.1-3.5 ppm in the methylene proton region whose areas were in a 1:2 ratio, respectively. The band systems were complex, indicating a higher order spin pattern.

*Anal.* Calcd for C<sub>6</sub>H<sub>6</sub>N<sub>2</sub>S<sub>2</sub>: N, 17.70; S, 40.53. Found: N, 17.46; S, 40.56.

**1-(1,3-Dithiacyclopentylidene)urea Hydrochloride.**—To 363 g (3.63 moles) of 36.5% hydrogen chloride-methanol solution at 5°, 87 g (0.6 mole) of 2 was added in one portion. An exothermic reaction raised the temperature from 8 to 25°. The reaction mixture was stirred at 25-30° for 18 hr. After cooling to 0°, the precipitate was collected by filtration and air dried at 50°. The product, mp 206-207°, was obtained in 76.5% yield. The infrared spectrum as determined from Nujol mull contained bands at 3300-3100 (broad) (NH<sub>3</sub><sup>+</sup> st), 1725 (s) [—C(=O)NH<sub>3</sub><sup>+</sup> st], 1611 (m), 1515 (s), 1010 (s), 844 (s), and 722 (s) cm<sup>-1</sup>.

(5) This compound was kindly supplied by American Cyanamid Co.

*Anal.* Calcd for  $C_4H_6N_2OS_2 \cdot HCl$ : S, 32.28. Found: S, 32.56.

**1-(1,3-Dithiacyclopentylidene)urea (4).**—To 200 g (2.0 moles) of 36.5% hydrogen chloride-methanol solution at 5°, 72.2 g (0.50 mole) of **2** was added in one portion. By means of an ice bath the reaction mixture was maintained below 30° for the first 30 min and stirring continued at 25–30° for 24 hr. After cooling to 0°, 125 ml of water was added dropwise at 0–10° in 15 min. To this stirred reaction mixture, 150 g of concentrated ammonium hydroxide was added dropwise at 0–10° over a 15-min period. After stirring at 0–10° for 1 hr, the precipitate was collected by filtration and air dried at 25–30°. No evidence of the formation of 1,2-ethanedithiol was noted. The product, mp 151–153°, was obtained in 77.7% yield. After recrystallization from ethanol, it melted at 156–157°. The infrared spectrum as determined from Nujol mull contained bands at 3380 (m) and 3180 (m) ( $NH_2$  st-bonded), 1640 (s) [ $-C(=O)N$  st], 1606 (s) (amide II), 1530 (s) ( $C=N$  st), 977 (s), 850 (m), and 793 (m)  $cm^{-1}$ . The nmr spectrum in deuterated dimethyl sulfoxide has a single peak owing to equivalent methylene groups at  $\delta$  3.5 ppm and a broad peak at  $\delta$  7.0 ppm owing to the amide protons. The area ratio for the methylene protons and amide protons was 2:1.

*Anal.* Calcd for  $C_4H_6N_2OS_2$ : N, 17.27; S, 39.53. Found: N, 17.08; S, 39.62.

**Method II (Refluxing Conditions).**—The procedure was the same as described above except the stirred reaction mixture was heated at 65–68° for 22 hr. The product (35 g) obtained under these conditions was insoluble in all common solvents and decomposed to a sticky resinous material upon standing a few hours. No evidence of the formation of 1,2-ethanedithiol was noted.

**1,5,7,11-Tetrathiaspiro[5.5]undecane (5).** **Method I.**—To 240 g (2.4 moles) of 36.5% hydrogen chloride-methanol solution at 5°, 63.5 g (0.4 mole) of **3** was added in one portion. Within a few minutes a solution resulted. The solution was stirred at 25–30° for 18 hr. After cooling the resulting slurry to 0°, 250 ml of cold water was added dropwise at 0–10° over a 15-min period. To the stirred slurry, 164 g of concentrated ammonium hydroxide was added dropwise at 0–10°. After stirring at 25–30° for 1 hr, the precipitate was collected by filtration, washed with water until the washings were neutral to litmus, and air dried at 25–30°. The filtrate contained a small amount of an offensive smelling liquid which was identified as 1,3-propanedithiol. The product, mp 113–116°, was obtained in 58% yield. After recrystallization from ethyl alcohol, it melted at 119–120°. The infrared spectrum was determined from 2 to 12  $\mu$  in chloroform and from 12 to 15  $\mu$  in dimethylformamide and contained bands at 2980 (m) and 2900 (m) ( $C-H$  st), 1422 (s) and 1410 (m) ( $CH_2$  def), 1272 (s), 1002 (m), 910 (m), 882 (m), 774 (s), and 743 (s)  $cm^{-1}$ . The nmr spectrum in  $CDCl_3$  was identical with that reported by Johnston, *et al.*<sup>2</sup> The mass spectrum had molecular ion 224, 2.1%; base peak 46, 12.1%; 150, 2.3%; 119, 1.2%; 106, 6.8%; 76, 4.6%; 74, 2.7%; 71, 1.6%; 64, 1.8%; 58, 59, 1.2%; 47, 2.1%; 45, 8.7%; 44, 2.9%; 42, 3.6%; 41, 10.1%; 40, 1.7%; 39, 1.2%; 38, 2.2%; 37, 1.5%; and 32, 3.2%, all of  $Z_{26}$ .

*Anal.* Calcd for  $C_7H_{12}S_4$ : C, 37.46; H, 5.39; S, 57.15; mol wt, 224.4. Found: C, 37.61; H, 5.24; S, 57.30; mol wt 228.

**Method II (Preferred Method).**—To 70.2 g (0.702 mole) of 36.5% hydrogen chloride-methanol solution at 5°, 37 g (0.234 mole) of **3** and 25.5 g (0.234 mole) of 1,3-propanedithiol were added in one portion. After the removal of ice cooling, an exothermic reaction raised the temperature from 7 to 33° and, in addition, a precipitate resulted. The reaction mixture was stirred at 25–30° for 18 hr. After cooling to 0°, 250 ml of water was added dropwise at 0–10° over a 15-min period. To the stirred reaction mixture, 63 g of concentrated ammonium hydroxide was added dropwise at 0–10°. The remainder of the procedure was identical with that described for method I. The product, mp 116–118°, was obtained in 90.0% yield. After recrystallization from ethyl alcohol, it melted at 119–120°. A mixture melting point with the product obtained from method I was not depressed and the infrared spectra of the two were superimposable.

*Anal.* Calcd for  $C_7H_{12}S_4$ : S, 57.15. Found: S, 57.16.

**1,4,6,9-Tetrathiaspiro[4.4]nonane (6).** **Method I.**—To 100 g (1.0 mole) of 36.5% hydrogen chloride-methanol solution at 5°, 36.1 g (0.25 mole) of **2** and 23.5 g (0.25 mole) of 1,2-ethanedithiol were added in one portion. After the removal of ice cooling, an exothermic reaction raised the temperature from 5 to 55°. The stirred reaction mixture was heated at 65–73° for 22 hr. After

cooling the stirred reaction mixture to 0°, 200 ml of water was added dropwise at 0–10° in 15 min. This was followed by the dropwise addition of 75 g of concentrated ammonium hydroxide at 0–10° over a 15-min period. After the reaction mixture had stirred at 0–10° for 30 min, the precipitate was collected by filtration and air dried at 25–30°. The product, mp 139–141°, was obtained in 46.9% yield. After recrystallization from ethyl acetate, it melted at 142–143°. The infrared spectrum was determined from 2 to 12  $\mu$  in chloroform and from 12 to 15  $\mu$  in dimethylformamide and contained bands at 2980 (m) and 2900 (m) ( $C-H$  st), 1417 (m) ( $CH_2$  def), 1272 (s), 966 (m), 948 (m), 853 (m), 799 (vs), and 758 (s)  $cm^{-1}$ . The nmr spectrum in  $CDCl_3$  had a sharp singlet at  $\delta$  3.43 due to equivalent methylene groups. The mass spectrum had molecular ion 196, 1.9%; base peak 76, 21.2%; 170, 1.3%; 168, 5.5%; 136, 5.1%; 92, 2.1%; 91, 4.4%; 78, 2.1%; 64, 3.6%; 60, 5.9%; 59, 5.1%; 58, 2.5%; 45, 7.8%; 44, 4.7%; 32, 2.8%; 28, 3.2%; 27, 4.7%, and 26, 4.7%, all of  $Z_{26}$ .

*Anal.* Calcd for  $C_8H_8S_4$ : C, 30.58; H, 4.11; S, 65.31; mol wt 196.4. Found: C, 30.40; H, 4.00; S, 65.31; mol wt 196.

The bottom organic layer of the filtrate was separated and dried over sodium sulfate. The crude product (20 g) was an amber liquid. The vapor phase chromatography of this crude product gave 21.1 and 5.3 wt % and 8.6 and 4.5% (recovered) yield of **6** and 1,2-ethanedithiol, respectively.

**Method II.**—The procedure was identical with method I except that 40.6 g (0.25 mole) of **4** was substituted for **2** and a temperature rise from 5 to 30° resulted upon the addition of the reactants. The product, mp 139–141°, was obtained in 59.3% yield. After recrystallization from ethyl alcohol, it melted at 142–143°. A mixture melting point with the product obtained from method I was not depressed and the infrared spectra of the two were superimposable.

*Anal.* Calcd for  $C_8H_8S_4$ : S, 65.31. Found: S, 65.28.

Based on vapor phase chromatography, the crude liquid product (12 g) gave 34.2 and 18.0 wt % and 8.4 and 9.2% yield (recovered) of **6** and 1,2-ethanedithiol, respectively.

**Method III (4 and 6).**—The procedure was identical with method I except the reaction mixture was stirred at 25–30° for 22 hr. The product **4**, mp 148–150°, was obtained in 69% yield. After recrystallization from ethyl alcohol, it melted at 156–157°. A mixture melting point with an authentic sample was not depressed and the infrared spectra of the two were superimposable.

*Anal.* Calcd for  $C_4H_6N_2OS_2$ : N, 17.27; S, 39.53. Found: N, 17.33; S, 39.44.

Based on vapor phase chromatography, the crude liquid product (21 g) gave 19.3 and 34.8 wt % and 8.3 and 31.1% (recovered) yield of **6** and 1,2-ethanedithiol, respectively.

**Compounds 5, 6, and 1,4,6,10-Tetrathiaspiro[4.5]decane (7).**—To 100 g (1.0 mole) of 36.5% hydrogen chloride-methanol solution at 5° was added 0.25 mole of 1,3-propanedithiol and 0.25 mole of **2** or **6** for reactions 1 and 4 (Table I). For reactions 2 and 3, the above reactants were substituted by 1,2-ethanedithiol and **3** or **5**. After removal of ice cooling, an exothermic reaction raised the temperature from 5 to 40° over a 5–10-min period. The stirred reaction mixture was maintained at the temperatures specified in Table I for 22 hr. After cooling to 0°, 200 ml of water was added dropwise at 0–10°. This was followed by the dropwise addition of 75 g of concentrated ammonium hydroxide at 0–10°. The reaction mixture was stirred at 0–10° for 30 min. In cases where no solids were present, the bottom amber liquid of the reaction mixture was separated and dried over sodium sulfate. When the reaction mixture contained solids and an immiscible liquid, the solids were collected by filtration and air dried at 25–30°. The bottom amber liquid of the filtrate was separated and dried over sodium sulfate. The mixtures (liquid or solid) were analyzed by vpc according to methods in the analytical method section. The data are summarized in Table I.

An attempt to separate **5**, **6**, and **7** by recrystallization was not successful. Compound **7** was identified from a mixture of **5**, **6**, and **7**. The mixture was separated by vapor phase chromatography. Each component was trapped at the outlet tube of the chromatograph. The infrared spectra and mixture melting points confirmed that the first and third chromatographic peaks were **6** and **5**, respectively. The infrared spectrum of the compound represented by the second peak (compound **7**, mp 129–130°) had most of the absorption bands common to either **5** or **6** in the  $C-H$  stretching,  $C-H$  deformation, and skeletal regions. In addition, the mass spectrum was in agreement for the proposed structure **7**. Furthermore, the order of elution time from the gas chromatography

graph was consistent with the proposed structures, since a linear relationship of the logarithmic retention time with molecular weight of 5, 6, and 7 was found. The infrared data of 7 are as follows: 2980 (m) and 2900 (m) (C-H st), 1422 (s), 1417 (m) (CH<sub>2</sub> def), 1274 (s), 998 (m), 966 (w), 947 (m), 905 (m), 877 (s), 842 (m) cm<sup>-1</sup>. 7's mass spectrum had molecular ion 210, 0.1%; base peak, 76, 17.1%; 150, 0.5%; 146, 0.5%; 136, 4.1%; 60, 9.5%; 59, 8.3%; 45, 10.2%; 44, 3.4%; 41, 3.7%; and 32, 13.5%, all of Σ<sub>26</sub>.

**Registry No.**—1, 13145-41-0; 2, 10191-72-7; 3, 10191-73-8; 4, 10191-74-9; 4·HCl, 10191-75-0; 5, 180-97-2; 6, 13145-46-5; 7, 13145-47-6.

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## The Kinetics of Cyanoethylation of Methanol in Mixed Methanol-Aprotic Solvents

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The kinetics of the cyanoethylation of methanol catalyzed by alkali metal methoxides was studied in solvent mixtures of methanol and the aprotic solvents dimethyl sulfoxide, dimethylformamide, dimethylformamide-dioxane (1:1), dioxane, tetrahydrofuran, and benzene. The rate of reaction was first order in acrylonitrile, first order in the alkali metal methoxide, and was proportional to  $1/[\text{CH}_3\text{OH}]^n$ ,  $n$  being dependent on the aprotic solvent. It increased with increasing the concentration of the aprotic solvent in the solvent mixture, owing to its participation in the equilibrium reactions leading to desolvation of methanol-solvated methoxide ions. This enhancement was especially pronounced at low methanol concentrations. Depending on the aprotic solvent, the rate of reaction decreased in the order dimethyl sulfoxide > dimethylformamide >> tetrahydrofuran ≈ dioxane > benzene.

Rates of nucleophilic substitution reactions were highly accelerated when carried out in aprotic solvents such as dimethyl sulfoxide (DMSO) and dimethylformamide (DMF) compared with the generally used protic solvents, such as alcohols. This effect of aprotic solvents was studied intensely recently<sup>2-11</sup> and applied synthetically, with great success, to various nucleophilic substitutions.<sup>4-11</sup> The role of aprotic solvents in the analogous base-catalyzed nucleophilic addition to activated carbon-carbon double bonds was very little investigated<sup>12</sup> although the Michael-type addition reaction is one of the most applicable organic reactions.<sup>13</sup> Rates of reaction involving nucleophilic attack on a carbonyl double bond, such as alkaline hydrolysis of esters, were enhanced<sup>14</sup> even to about 10<sup>4</sup> to 10<sup>5</sup> times<sup>15</sup> by substituting aprotic for hydroxylic solvents. Acid-base equilibria were strongly influenced by transfer from methanol to DMF.<sup>16</sup>

It was the purpose of the present work to study kinetically the influence of aprotic solvents on the methoxide-catalyzed cyanoethylation of methanol, the mechanism of which was previously derived when using methanol as sole solvent.<sup>17</sup> In addition, relatively

detailed kinetic results were available for the cyanoethylation of hydroxylic compounds in protic solvents. The kinetics of the KOH-catalyzed cyanoethylation of ethanolamine in water<sup>18</sup> and that of the base-catalyzed cyanoethylation of water and mono- and polyhydric alcohols<sup>19</sup> were studied. It was found for all these systems that the nucleophilic attack on the double bond was the rate-determining step, the reaction being a second-order reaction, first order in each of the concentrations of the basic catalyst and acrylonitrile.

### Results

The rate of the cyanoethylation of methanol in the mixed solvents was followed either dilatometrically or by titrimetric determination of the concentration of acrylonitrile.

**The Order of Reaction in Acrylonitrile.**—This was studied by measuring the rate of cyanoethylation of methanol in mixed solvents of methanol and each of the following aprotic solvents: DMSO, DMF, dioxane, tetrahydrofuran (THF), benzene, DMF-dioxane (1:1). The rate of reaction was first order in acrylonitrile for all types and compositions of the solvent systems used. This was evident from the straight lines obtained on plotting  $\log [\text{AN}]_0/[\text{AN}]_t$  or  $\log (A_t - A_\infty)$  vs. time (Figures 1 and 2) where  $[\text{AN}]_0$  and  $[\text{AN}]_t$  were the initial concentration and concentration at time  $t$  of acrylonitrile, respectively, and  $A_t$  and  $A_\infty$  were the readings of the dilatometer at time  $t = t$  and at  $t = \infty$ . Pseudo-first-order rate constants,  $k_1$ , calculated from the slopes of the straight lines, and their dependence on the composition of the mixed solvents are summarized in Tables I-III.

The cyanoethylation in methanol-benzene mixed solvent gave straight lines on plotting  $\log (A_t - A_\infty)$

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