The Preparation and Chemistry of the Isomeric Monomethyl Derivatives of Perthiocyanic Acid

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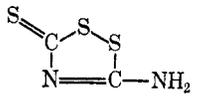
The disodium salt (**5**) of perthiocyanic acid (3,5-dimercapto-1,2,4-thiadiazole) is known to react with 2 mol of an alkylating agent to give dialkyl perthiocyanates. In this study, the course of the monoalkylation of **5** was investigated. The reaction of **5** with 1 mol of methyl iodide gave 27% dimethyl perthiocyanate and 28% 3-methylmercapto-5-mercapto-1,2,4-thiadiazole (**8**); the 5-methyl isomer was not detected. The reaction of **8** with other alkylating agents gave a series of "mixed" perthiocyanates, *e.g.*, 3-methylmercapto-5-benzylmercapto-1,2,4-thiadiazole. The reaction of 3-imino-5-methylmercapto-1,2,4-dithiazole with hydroxide ion resulted both in ring opening and rearrangement to give the salts of S-methyl cyanodithioimidocarbonate and the 5-methyl isomer, 3-mercapto-5-methylmercapto-1,2,4-thiadiazole. The evidence for these products comes from the subsequent methylation of the salts which gave 84% dimethyl cyanodithioimidocarbonate and 7% dimethyl perthiocyanate.

The addition of concentrated hydrochloric acid to an aqueous ammonium thiocyanate solution gives 3-amino-5-thione-1,2,4-dithiazole (**1**), commonly known as isoperthiocyanic acid.[2-5] Earlier work[6,7] with **1** demonstrated or suggested the reaction sequence



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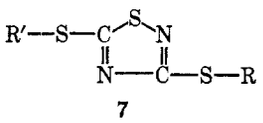
shown in Scheme I. The scheme shown was confirmed (*cf.* Experimental Section), as was the interrelationship of **1**, the cyanodithioimidocarbonate dianion (**2**), and the perthiocyanate dianion (**5**).

Various derivatives (**6**) of **5** were prepared by treating it with 2 equiv of an alkylating agent.[6,8] However, the reaction of **5** with 1 equiv of an alkylating agent has not been studied. It can lead to two isomers, and further reaction with another alkylating agent would result in novel "mixed" perthiocyanates (**7**, R ≠ R′).



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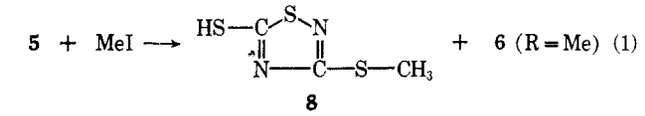
In this study the preparation and chemistry of monomethylated perthiocyanates were investigated.

Results and Discussion

3-Methyl Isomer.—The reaction (eq 1) of sodium perthiocyanate (**5**) with 1 equiv of methyl iodide

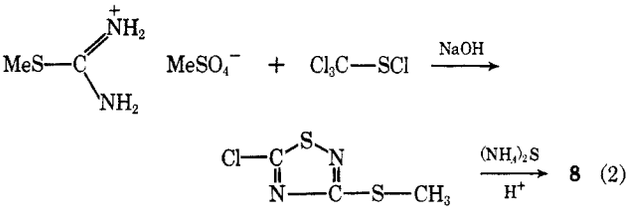


(1)

8

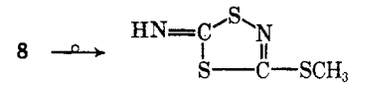
gave a 28% yield of 3-methylmercapto-5-mercapto-1,2,-4-thiadiazole (**8**) and a 27% yield of dimethyl perthiocyanate (**6**, R = Me). The latter compound arose from further methylation of **8**. One factor responsible for the poor material balance was the difficulty in separating **8** from isoperthiocyanic acid (**1**).[9]

The structure of **8** was proven by synthesizing the same compound by the method (eq 2) of Goerdeler and Sperling.[10]



(2)

The possibility of a rearrangement (eq 3), analogous



(3)

to that of **4** to **1**, was ruled out based on the following evidence. The infrared spectrum of **8** shows weak SH absorption at 2560 cm^{-1} and 2670 cm^{-1}. Compound **8** dissolved in 10% aqueous sodium hydroxide without deposition of sulfur. The reaction of **8** with diazomethane gave an 88% yield of dimethyl perthiocyanate (**6**, R = Me). Isoperthiocyanic acid (**1**) gave gummy material, which could not be purified under the same conditions. Thus, the preparation of **6** (R = Me) from **8** under neutral conditions, the smooth formation of the sodium salt of **8**, and the infrared spectrum all indicate that structure **8** is stable and retains the 1,2,4-thiadiazole arrangement.

Various derivatives of **8** were prepared by treating the sodium salt with the appropriate alkylating agent in THF (Table I).

5-Methyl Isomer.—We were unable to isolate or find evidence for the 5-methyl isomer (**7**, R = H; R′ = Me) from the reaction of **5** with 1 equiv of methyl iodide (eq 1). Thus, alternate routes to this compound were investigated.

(1) Geigy Chemical Co., Ardsley, N. Y. 10502

(2) (a) A. Wöhler, *Ann. Phys.*, **69**, 273 (1821); (b) P. Klason, *J. Prakt. Chem.*, (2) **38**, 366 (1888).

(3) L. L. Bambas, "The Chemistry of Heterocyclic Compounds," Vol. 4, Interscience Publishers, Inc., New York, N. Y., 1952, p 35.

(4) A. Hordvik, *Acta Chem. Scand.*, **15**, 1186 (1961).

(5) H. J. Emeléus, A. Haas and N. Sheppard, *J. Chem. Soc.*, 3165 (1963).

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

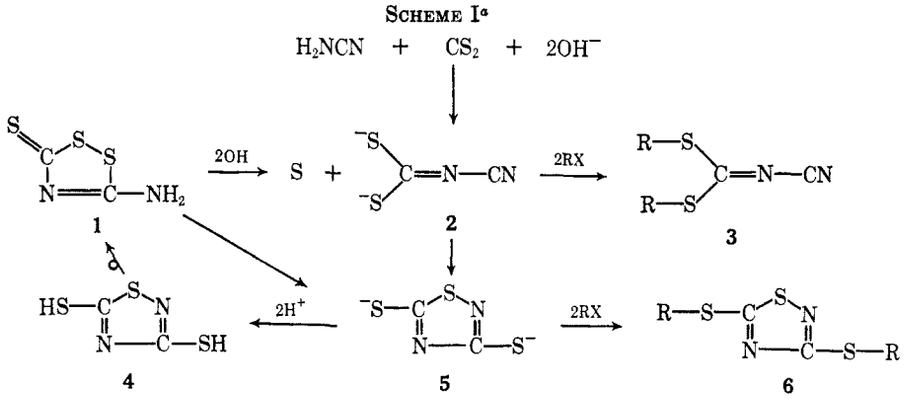
(7) E. Söderback, *Acta Chem. Scand.*, **1**, 529 (1947).

(8) W. H. Hill, U. S. Patent 2,521,570 (1950); E. W. Bousquet, U. S. Patent 2,285,410 (1942).

(9) Isoperthiocyanic acid was obtained from unreacted **5** on acidification.

(10) J. Goerdeler and G. Sperling, *Ber.*, **90**, 892 (1957).

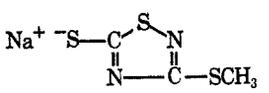
SCHEME I[a]



[a] Treating **1** with 2 mol of hydroxide ion in water gives **2** and sulfur which on subsequent heating gives **5**.[2b,6] Compound **2** can be prepared from cyanamid as shown,[6] and further reaction with sulfur gives **5** (*cf.* Experimental Section). Compound **5** can also be obtained directly from **1** and hydroxide ion in ethanol or ethanol–water[4-7] (*cf.* Experimental Section). The acidification of **5** gives the unstable perthiocyanic acid[4,7] which rearranges to **1**.

TABLE I

PREPARATION OF "MIXED" PERTHIOCYANATES

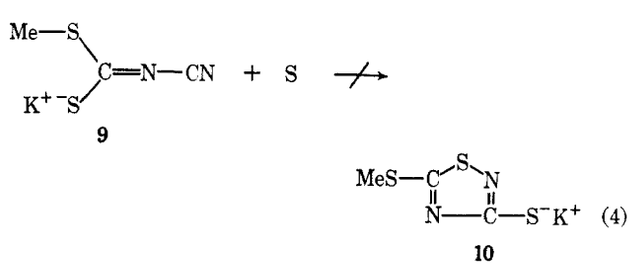


(R = Me)

R′	Yield of **7**, %
Benzyl	71
2,4-Dinitrophenyl	94
Triphenyltin	99
s-Triazinyl[a]	53

[a] This reaction was run using 3 mol of the sodium salt and 1 mol of cyanuric chloride to give the trisubstituted thiocyanurate.

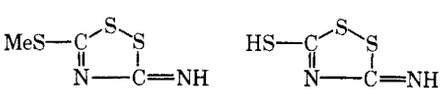
Addition of Sulfur to S-Methyl Potassium Cyanodithioimidocarbonate (9).—The preparation of the 5-methyl isomer *via* the addition of sulfur to **9** (eq 4) was investigated in view of the successful



(4)

addition of sulfur to **2** (*cf.* Experimental Section) and the preparation of 3-chloro-5-methyl-mercapto-1,2,4-thiadiazole from chlorine and **9**.[11] However, no significant amount of sulfur was absorbed under conditions identical with the reaction of **2** with sulfur. Also, neither raising the temperature nor changing the solvent to dimethylformamide increased the reactivity.

Rearrangement of 3-Imino-5-methylmercapto-1,2,4-Dithiazole (11).—The reported preparation[12] of salts of **11** provided a second approach to the 5-methyl isomer. A tautomer (**12**) of isoperthiocyanic acid



is analogous to **11**, and suggested that **11** would undergo a similar rearrangement (eq 5) as that shown

$$11 + OH^- \longrightarrow 10 + H_2O \quad (5)$$

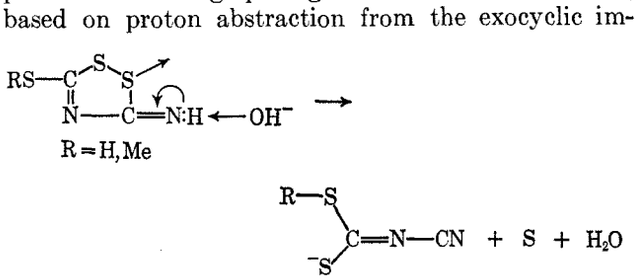
in Scheme I (**1** → **5**). However, the addition of the hydroiodide of **11** to 2 mol of potassium hydroxide in an ethanol–water solution precipitated an 85% yield of sulfur based on eq 6. The sulfur was removed by

$$11 + OH^- \longrightarrow 9 + S + H_2O \quad (6)$$

filtration, and 1 mol of dimethyl sulfate was added to the filtrate. Thus, the subsequent methylation of the filtrate would give dimethyl cyanodithioimidocarbonate (**3**, R = Me) and dimethyl perthiocyanate (**6**, R = Me), diagnostic of **9** and the desired 5-methyl isomer (**10**), respectively. Indeed, after 18 hr at room temperature, gas chromatographic analysis showed an 84% yield of **3** (R = Me) and a 7% yield of **6** (R = Me).

Based on the above correlation between the yield of sulfur and **3**, and the demonstrated addition of sulfur to the cyanodithioimidocarbonate anion (**3**) to form the perthiocyanate anion (**5**), it would be reasonable to suggest that **10** arose from the readdition of the sulfur in solution to **9** (eq 4). However, the demonstrated inertness of sulfur to **9** would indicate that an alternate mechanism is operative.[13]

Finally, the similar reactivity of isoperthiocyanic acid (**1**) and 3-imino-5-methylmercapto-1,2,4-dithiazole (**11**) towards hydroxide ion suggests a similar reaction path for the ring-opening reaction. A mechanism, based on proton abstraction from the exocyclic imino hydrogen, is proposed. Alternate mechanisms, involving the tautomeric hydrogen atom, can be



(11) R. J. Timmons and L. S. Wittenbrook, *J. Org. Chem.*, **32**, 1566 (1967).

(12) R. E. Allen, R. S. Shelton, and M. G. Van Campen, Jr., *J. Amer. Chem. Soc.*, **76**, 1158 (1954).

(13) A referee suggested that **9** arises from **10** and that **10** is an intermediate in the formation of **9** from **11**. This is certainly a possibility, but does not appear to be the case in the analogous transformations involving **1**, **2**, and **5** (Scheme I). Thus, there is no evidence for the formation of **2** from **5**, but **5** can be prepared from **2**.

written for isoperthiocyanic acid (R = H), but are not possible for the methyl derivative (**11**).

Experimental Section

The infrared spectra were determined in Nujol on an IR-8 Beckman spectrophotometer. Gas chromatographic analyses were carried out on an F & M 720 gas chromatograph using a silicone DC 550 column programmed from 120 to 270° at 15 deg min^{-1}.

Preparation of Potassium Perthiocyanate from Dipotassium Cyanodithioimidocarbonate (2)[6] and Sulfur.—To 12.0 g (0.062 mol) of **2** dissolved in 100 ml of a 50% ethanol–water solution was added 1.98 g (0.062 mol) of sulfur. The sulfur dissolved after stirring for 2 hr at room temperature. The solution was filtered and divided in half.

(a) **Methylation to Dimethyl Perthiocyanate.**—To one-half of the solution was added 8.81 g (0.062 mol) of methyl iodide. After 5 hr at room temperature, the reaction mixture was poured onto ice. The white solid was filtered and air dried to give 4.10 g (80%) of dimethyl perthiocyanate, mp 36–38° (lit.[6] mp 42°), mmp with an analytical sample, no depression. The ir spectra of the two samples were identical.

(b) **Acidification to Isoperthiocyanic Acid** (**1**).—The other half of the solution was acidified with 6 *N* HCl to give 4.20 g (90%) of **1**, mp 202° dec, mmp with an analytical sample of **1**, no depression. The ir spectra of the two samples were identical.

5 and Methyl Iodide.—To a solution of 106.6 g (2.66 mol) of sodium hydroxide in 200 ml of water and 800 ml of ethanol was added in portions 200.0 g (1.33 mol) of isoperthiocyanic acid. After solution, 193.0 g (1.33 mol) of methyl iodide was added dropwise, the temperature being kept between 15–25°. The reaction was stirred at room temperature for 24 hr and then poured onto ice. The resulting solid was filtered and air dried to give 62.5 g (27%) of dimethyl perthiocyanate, mp 35–39° (lit.[6] mp 42°), mmp with an authentic sample, no depression. The ir spectra of the 2 samples were identical. The filtrate was acidified dropwise with concentrated HCl; a yellow solid precipitated which was filtered and air dried to give 140.0 g, mp 120–140° (cloudy). Recrystallization from 1500 ml of ethyl acetate gave 61.3 g (28%) of 3-methylmercapto-5-mercapto-1,2,4-thiadiazole (**8**), mp 146–150 dec. An additional recrystallization from acetonitrile gave an analytically pure sample, mp 149–150 dec (lit.[10] mp 150–151° dec), mmp with an analytial sample of **8** prepared by the method of Goerdeler and Sperling, no depression. The ir spectra of the two samples were identical.

Anal. Calcd for $C_3H_4N_2S_3$: N, 17.1; S, 58.6. Found: N, 17.0; S, 58.4.

3-Methylmercapto-5-mercapto-1,2,4-thiadiazole (**8**) was prepared following the procedure of Goerdeler and Sperling,[10] mp 149–150° dec (lit.[10] mp 150–151° dec); **8** dissolved smoothly in 10% aqueous NaOH and was recovered unchanged on acidification with HCl.

Anal. Calcd for $C_3H_4N_2S_3$: N, 17.1; S, 58.6. Found: N, 17.0; S, 58.6.

8 and Diazomethane.—An ethereal solution of diazomethane was prepared using 21.5 g (0.10 mol) of N-methyl-N-nitroso-*p*-toluenesulfonamide. To a solution of 5.00 g (0.031 mol) of **8** in 25 ml of tetrahydrofuran (THF) was added the diazomethane solution. The reaction was allowed to proceed at room temperature until gas evolution ceased. The solvents were allowed to evaporate, and the residue was poured over ice. The mixture was cooled until the product became crystalline. It was filtered and air dried to give 4.80 g (88%) of dimethyl perthiocyanate (**6**, R = Me), mp 30–39°. The ir spectrum was identical with an authentic sample of **6**. Recrystallization from ethanol–water gave 3.01 g, mp 36–39°, mmp with an analytical sample of **6**, no depression.

3-Methylmercapto-5-benzylmercapto-1,2,4-thiadiazole.—The sodium salt of **8** was prepared by adding 22.0 g (0.13 mol) of **8** to a solution of 5.36 g (0.13 mol) of sodium hydroxide in 20 ml of water and 80 ml of methanol. The resulting solution was stripped to dryness. The residue (0.13 mol of the sodium salt) was dissolved in 200 ml of THF, and to it was added a solution of 22.9 g (0.13 mol) of benzyl bromide in 100 ml of THF. Within a few minutes, sodium bromide started to precipitate; after 20 hr at room temperature, the reaction mixture was filtered. The residue amounted to 12.9 g (94%) of sodium bromide. The filtrate was stipped to dryness, leaving 32.2 g of an orange liquid. Distillation gave 3.40 g of a forerun, bp 98–110° (0.50 mm), followed by 23.8 g (71%) of pure 3-methylmercapto-5-benzylmercapto,1,2,4 thiadiazole, bp 148–150° (0.35 mm), $n^{30}D$ 1.6552.

Anal. Calcd for $C_{10}H_{10}N_2S_3$: N, 11.0; S, 37.8. Found: N, 10.8; S, 37.8.

3-Methylmercapto-5-(2′,4′-dinitrophenylmercapto)-1,2,4-thiadiazole.—To a solution of 18.6 g (0.10 mol) of the sodium salt of **8** in 100 ml of THF was added a solution of 20.2 g (0.10 mol) of 1-chloro-2,4-dinitrobenzene in 100 ml of THF. After 19 hr at room temperature (sodium chloride precipitated as the reaction proceeded), the reaction mixture was filtered. The residue amounted to 5.00 g (86%) of sodium chloride. The filtrate was poured over ice to give a yellow solid; the solid was washed free of chloride with water and dried to give 31.0 g (94%) of 3-methylmercapto-5-(2′,4′-dinitrophenylmercapto)-1,2,4-thiadiazole, mp 114–116°. Recrystallization from carbon tetrachloride gave an analytical sample, mp 117–118°.

Anal. Calcd for $C_9H_6N_4O_4S_3$: C, 32.8; H, 1.8; N, 16.9; S, 28.9. Found: C, 32.7; H, 1.8; N, 17.0; S, 28.9.

3-Methylmercapto-5-triphenyltinmercapto-1,2,4-thiadiazole.—To a solution of 0.061 mol of the sodium salt in 100 ml of THF was added a solution of 23.5 g (0.061 mol) of triphenyltin chloride in 75 ml of THF. As the reaction proceeded, sodium chloride precipitated. After 17 hr at room temperature, the reaction mixture was filtered. The residue amounted to 3.30 g (93%) of sodium chloride. The filtrate was stripped to dryness; the residue was triturated with an ethanol–water solution to give 31.0 g (99%) of 3-methylmercapto-5-triphenyltinmercapto-1,2,4-thiadiazole, mp 72–76°. Recrystallization from 95% ethanol gave an analytical sample, mp 75–76°.

Anal. Calcd for $C_{21}H_{18}N_2S_3Sn$: N, 5.5; S, 18.7; Sn, 23.1. Found: N, 5.4; S, 18.6; Sn, 23.0.

Tris(3-methylmercapto-1,2,4-thiadiazole-5)-trithiocyanurate.—To 0.12 mol of the sodium salt dissolved in 100 ml of THF was added 7.26 g (0.04 mol) of cyanuric chloride dissolved in 50 ml of THF. Immediate precipitation occurred, and the temperature rose to 45°. After 1 hr at reflux, the reaction was allowed to stand at room temperature overnight and then filtered. The residue was washed with THF and water and dried (16.5 g). Washing the crude product with boiling dioxane and acetonitrile gave 12.0 g (53%) of tris(3-methylmercapto-1,2,4-thiadiazole-5)-trithiocyanurate, mp 252–254°.

Anal. Calcd for $C_{12}H_9N_9S_9$: C, 25.4; H, 1.6; N, 22.2; S, 50.7; Cl, 0.0. Found: C, 25.7; H, 1.6; N, 21.9; S, 50.1; Cl, 0.1.

3-Imino-5-methylmercapto-1,2,4-dithiazole Hydriodide (**11**) **and Hydroxide Ion.**—To 3.12 g (0.050 mol) of potassium hydroxide dissolved in 100 ml of a 50% ethanol–water solution was added 7.33 g (0.025 mol) of 3-imino-5-methylmercapto-1,2,4-dithiazole hydroiodide.[12] The mixture was stirred at room temperature for 2 hr and then filtered. The residue amounted to 0.68 g of sulfur, mp 90–105°; recrystallization from dimethylformamide gave 0.20 g, mp 117–119°, mmp with authentic sulfur, no depression.

To the filtrate was added 3.16 g (0.025 mol) of dimethyl sulfate. After 18 hr at room temperature, the solution was poured into water and extracted with ether. Drying the ether extract ($MgSO_4$) and then stripping the solvent left 3.40 g of a pale yellow solid. Gc analysis showed 84% dimethyl cyanodithioimidocarbonate and 7% dimethyl perthiocyanate.

Registry No.—**8**, 20069-40-3; 3-methylmercapto-5-benzylmercapto-1,2,4-thiadiazole, 20429-49-6; 3-methylmercapto-5-(2′,4′-dinitrophenylmercapto)-1,2,4-thiadiazole, 20429-50-9; 3-methylmercapto-5-triphenyltinmercapto-1,2,4-thiadiazole, 20429-51-0; Tris-(3-methylmercapto-1,2,4-thiadiazole-5)trithiocyanurate, 20429-52-1.

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