



A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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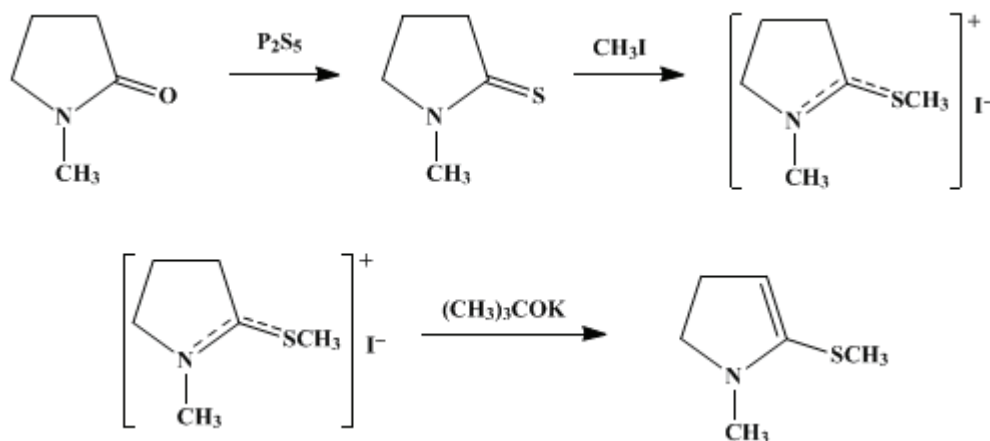
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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2-METHYLMERCAPTO-N-METHYL- Δ^2 -PYRROLINE

[2-Pyrroline, 1-methyl-2-methylthio-]



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1. Procedure

Caution! Hydrogen sulfide is very poisonous. Procedure A should be conducted in a hood.

A. *N-Methyl-2-pyrrolidinethione*. Phosphorus pentasulfide (667 g., 3.00 moles) is suspended in 600 ml. of carbon disulfide in a 2-l. three-necked flask equipped with a mechanical stirrer with a segment-shaped paddle, an efficient reflux condenser, and a dropping funnel. *N-Methyl-2-pyrrolidinone* (300 g., 3.03 moles) is added in large portions from the dropping funnel with vigorous stirring. The reaction mixture warms up considerably and, after addition of about two-thirds of the amide, becomes so viscous that further stirring is impossible. The addition of the remainder is carried out without stirring at a rate such that the solution boils gently. The semisolid, yellow-brown mixture is boiled under reflux on a water bath for a further 10 hours.

The carbon disulfide is decanted, and 200–300 ml. of water is added to the contents of the flask. Initially the mixture reacts slowly, but after some time the reaction becomes so vigorous that it is necessary to pour off the water (Note 1) and (Note 2). The addition of water, followed by its removal when the reaction becomes very vigorous, is repeated until decomposition is complete. The combined aqueous solutions are extracted several times with chloroform, and the combined extracts are dried over anhydrous sodium sulfate. Distillation of the solvent gives a dark brown liquid residue which is distilled under reduced pressure to give 310.3 g. (89%) of the thioamide as a yellow liquid, b.p. 133–135° (12 mm.) (Note 3).

B. *2-Methylmercapto-N-methyl- Δ^2 -pyrrolinium iodide*. *N-Methyl-2-pyrrolidinethione* (310 g., 2.69 moles) is dissolved with stirring in 1.1 l. of anhydrous ether in a 2-l. three-necked flask equipped with a mechanical stirrer, a reflux condenser fitted with a drying tube, and a dropping funnel. To this solution is added ca. 5 g. of the product as seed crystals (Note 4) to prevent initial deposition of the iodide as an oil that suddenly crystallizes with considerable evolution of heat. Methyl iodide (520 g., 3.66 moles) is then added rather rapidly. The solution becomes turbid after a short time, and separation of the salt begins with heat evolution. After 12 hours the hygroscopic, crystalline paste is filtered and dried in a desiccator; yield 663 g. (96%).

This product can be used without further purification. Crystallization from mixtures of acetonitrile

and ether gives colorless, felted needles, m.p. 118–120° (dec.) (Note 5).

C. *2-Methylmercapto-N-methyl- Δ^2 -pyrroline*. 2-Methylmercapto-N-methyl- Δ^1 -pyrrolinium iodide (662 g., 2.57 moles) is suspended in 1.25 l. of anhydrous ether in a 4-l. three-necked flask equipped with a mechanical stirrer and a reflux condenser with a segment-shaped paddle. Potassium *t*-butoxide (448 g., 4.0 moles) is added in one batch to this suspension with vigorous stirring. The mixture warms up a little, and later the solid becomes fine-grained and more mobile as a result of separation of potassium iodide. After being stirred for 1.5 hours at room temperature, the mixture is treated with 1.8 l. of anhydrous ether and boiled under reflux on a water bath for 5 hours.

The flask is cooled in an ice bath, and the precipitate is filtered onto a large Buchner funnel and washed well with ether (Note 6). Ether is distilled from the yellow-brown filtrate at atmospheric pressure, and *t*-butyl alcohol is distilled under reduced pressure at 40°. Distillation of the residue through a 10-cm. Vigreux column at the water aspirator gives, after a small forerun (ca. 20 ml.), the product as a colorless liquid, b.p. 70–73° (10–12 mm.); yield 268 g. (81%) (Note 7), (Note 8), and (Note 9). This becomes brown on standing.

Repeated fractional distillation gives a product of analytical purity (Note 10), b.p. 65–68° (8–10 mm.), n_D^{25} 1.5222 (Note 11); yield 62%. This is an extremely disagreeable, musty liquid which on standing in the atmosphere warms up slightly and immediately turns red.

2. Notes

1. The large amount of hydrogen sulfide produced is destroyed by passage into two wash bottles containing concentrated aqueous potassium hydroxide.
2. It is also possible to moderate the reaction by the addition of chloroform.
3. The checkers, working at quarter scale, obtained 84–87% of product, b.p. 131–133° (11 mm.), 139–142° (14–15 mm.).
4. This can be prepared readily in a test tube by addition of methyl iodide to a solution of the thioamide in ether.
5. *Anal.* Calcd. for C₆H₁₂INS: I, 49.36. Found: 49.34.
6. The precipitate may be so fine-grained that the filtrate is initially turbid; the turbid filtrate is then filtered again through the Buchner funnel containing the precipitate.
7. This fraction is followed by tailings (12 g.), b.p. 74–75° (10–12 mm.).
8. The checkers, working at quarter scale, obtained 75% of product, b.p. 68–71° (13 mm.), followed by tailings, b.p. 71–74° (13 mm.).
9. This product is contaminated with N-methyl-2-pyrrolidinone, which does not impair its usefulness for most further reactions.
10. *Anal.* Calcd. for C₆H₁₁NS: C, 55.76; H, 8.58; N, 10.84; S, 24.82. Found: C, 55.60; H, 9.08; N, 10.84, S, 24.66.
11. The checkers found that the refractive index of the pyrroline increases rapidly on exposure to air, impairing its usefulness as a criterion of purity.

3. Discussion

The method described for the preparation of N-methyl-2-pyrrolidinethione is very similar to that of Peak and Stansfield² for the preparation of 4-thioacetylmorpholine. N-Methyl-2-pyrrolidinethione has also been prepared by the reaction of 2-chloro-N-methyl- Δ^1 -pyrrolinium chloride with hydrogen sulfide [yield 83%; b.p. 144–145° (15 mm.)]³ and by heating N-methyl-2-pyrrolidinone with 2 equivalents of phosphorus pentasulfide in xylene [yield not reported; b.p. 125–132° (10 mm.)].⁴ General procedures for the preparation of N,N-disubstituted thioamides have been reviewed.^{5,6}

The method described for the preparation of 2-methylmercapto-N-methyl- Δ^1 -pyrrolinium iodide is based on the general procedure of several authors.^{2,7,8,9} Its preparation has not been described previously; the corresponding methyl sulfate has been obtained as a noncrystalline, viscous mass.^{4,10}

2-Methylmercapto-N-methyl- Δ^2 -pyrroline has been prepared by the present method only.^{11,12}

4. Merits of the Preparation

The procedure illustrates a general method for the preparation of ketene S,N-acetals via thioamides and their crystalline quaternary iodides; some other examples are shown in Table I. 2,2-Dialkyl-substituted ketene S,N-acetals cannot be prepared by this method because the nature of the products makes rigorous purification impractical. Ketene S,N-acetals are useful starting materials for many syntheses.^{11,13,14,15}

TABLE I PREPARATION OF KETENE S,N-ACETALS

$\text{RCH}=\text{C} \begin{array}{l} \text{SCH}_3 \\ \text{NR}'\text{R}'' \end{array}$			B.P., °C.	Yield of Crude Product, % (Purity, %) ^a
R	R'	R''		
H	CH ₃	CH ₃	$\text{H}_2\text{C}=\text{C} \begin{array}{l} \text{SCH}_3 \\ \text{N}-\text{CH}_3 \\ \text{CH}_3 \end{array}$ 31–32 (11 mm.)	77 (92–96) ^b
H	(CH ₂) ₄		$\text{H}_2\text{C}=\text{C} \begin{array}{l} \text{SCH}_3 \\ \text{N}-(\text{CH}_2)_4 \\ (\text{CH}_2)_4 \end{array}$ 79–81 (10 mm.)	60 (72–88)
CH ₃	CH ₃	CH ₃	$\text{CH}_3\text{CH}=\text{C} \begin{array}{l} \text{SCH}_3 \\ \text{N}-\text{CH}_3 \\ \text{CH}_3 \end{array}$ 38–40 (10 mm.)	68 (88)
C ₂ H ₅	CH ₃	CH ₃	$\text{C}_2\text{H}_5\text{CH}=\text{C} \begin{array}{l} \text{SCH}_3 \\ \text{N}-\text{CH}_3 \\ \text{CH}_3 \end{array}$ 56 (11 mm.)	74 (92)
C ₆ H ₅	(CH ₂) ₂ O (CH ₂) ₂ ^c		$\text{C}_6\text{H}_5\text{CH}=\text{C} \begin{array}{l} \text{SCH}_3 \\ \text{N} \\ \text{O} \end{array}$ 114–120 (10 ⁻³ mm.) ^d	81
(CH ₂) ₃	CH ₃		$\text{CH}=\text{C} \begin{array}{l} \text{SCH}_3 \\ \text{N} \\ \text{CH}_3 \end{array}$ 75–76 (12 mm.)	69–73 (94)
(CH ₂) ₄	CH ₃		$\text{CH}=\text{C} \begin{array}{l} \text{SCH}_3 \\ \text{N} \\ \text{CH}_3 \end{array}$	82 (94)

^a Determined by gas chromatography; products distilled through a spinning-band column were 94–99% pure.

^b Yield of pure product, 52%.

^c M. A. T. Rogers, *J. Chem. Soc.*, 3350 (1950).

^d M.p. 44–45° (ex [ethanol](#)).

References and Notes

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Appendix

Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

2-Methylmercapto-N-methyl- Δ^2 -pyrroline

2-Methylmercapto-N-methyl- Δ^1 -pyrrolinium iodide

2-Methylmercapto-N-methyl- Δ^2 -pyrroline

2-chloro-N-methyl- Δ^1 -pyrrolinium chloride

2-methylmercapto-N-methyl- Δ^1 -pyrrolinium iodide

[ethanol](#) (64-17-5)

[ether](#) (60-29-7)

[acetonitrile](#) (75-05-8)

chloroform (67-66-3)

hydrogen sulfide (7783-06-4)

sodium sulfate (7757-82-6)

potassium iodide (7681-11-0)

potassium hydroxide (1310-58-3)

carbon disulfide (75-15-0)

xylene (106-42-3)

Methyl iodide (74-88-4)

methyl sulfate (75-93-4)

phosphorus pentasulfide

t-butyl alcohol (75-65-0)

PYRROLINE

2-Pyrroline, 1-methyl-2-methylthio- (25355-52-6)

N-Methyl-2-pyrrolidinone (872-50-4)

N-Methyl-2-pyrrolidinethione (10441-57-3)

4-thioacetylmorpholine

potassium t-butoxide (865-47-4)