



A Publication  
of Reliable Methods  
for the Preparation  
of Organic Compounds

## Working with Hazardous Chemicals

The procedures in *Organic Syntheses* are intended for use only by persons with proper training in experimental organic chemistry. All hazardous materials should be handled using the standard procedures for work with chemicals described in references such as "Prudent Practices in the Laboratory" (The National Academies Press, Washington, D.C., 2011; the full text can be accessed free of charge at [http://www.nap.edu/catalog.php?record\\_id=12654](http://www.nap.edu/catalog.php?record_id=12654)). All chemical waste should be disposed of in accordance with local regulations. For general guidelines for the management of chemical waste, see Chapter 8 of Prudent Practices.

In some articles in *Organic Syntheses*, chemical-specific hazards are highlighted in red "Caution Notes" within a procedure. It is important to recognize that the absence of a caution note does not imply that no significant hazards are associated with the chemicals involved in that procedure. Prior to performing a reaction, a thorough risk assessment should be carried out that includes a review of the potential hazards associated with each chemical and experimental operation on the scale that is planned for the procedure. Guidelines for carrying out a risk assessment and for analyzing the hazards associated with chemicals can be found in Chapter 4 of Prudent Practices.

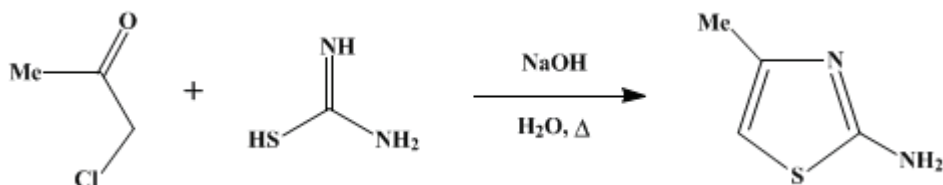
The procedures described in *Organic Syntheses* are provided as published and are conducted at one's own risk. *Organic Syntheses, Inc.*, its Editors, and its Board of Directors do not warrant or guarantee the safety of individuals using these procedures and hereby disclaim any liability for any injuries or damages claimed to have resulted from or related in any way to the procedures herein.

*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.*

*Organic Syntheses, Coll. Vol. 2, p.31 (1943); Vol. 19, p.10 (1939).*

## 2-AMINO-4-METHYLTHIAZOLE

[Thiazole, 2-amino-4-methyl-]



Submitted by J. R. Byers and J. B. Dickey.

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### 1. Procedure

Seventy-six grams (1 mole) of thiourea is suspended in 200 cc. of water (Note 1) in a 500-cc. flask equipped with a reflux condenser, dropping funnel, and mechanical stirrer. The stirrer is started, and 92.5 g. (80 cc., 1 mole) of chloroacetone (Note 2) is run in during thirty minutes. As the reaction proceeds the thiourea dissolves and the temperature rises. The yellow solution is refluxed for two hours and cooled, and, while the mixture is stirred continuously but not so rapidly as to produce a troublesome emulsion, 200 g. of solid sodium hydroxide is added with cooling. The upper, oily layer is separated in a separatory funnel and the aqueous layer is extracted three times with ether, using a total of 300 cc. (Note 3). The dark red oil is combined with the ethereal extract, and the solution is dried over 30 g. of solid sodium hydroxide and filtered by gravity to remove small amounts of tar. The ether is removed by distillation from a steam bath, and the oil is distilled at reduced pressure. After a very small fore-run, 2-amino-4-methylthiazole is collected at 117–120°/8 mm., or 130–133°/18 mm. The yield of material melting at 44–45° is 80–85.5 g. (70–75 per cent of the theoretical amount).

### 2. Notes

1. The reaction may be conducted without this diluent, but it is then likely to become violent.
2. Commercial chloroacetone was distilled and the fraction boiling at 116–122° taken; nearly all of this boiled at 118–120°.
3. If a precipitate is produced and causes an emulsion, add ice and water until it dissolves.

### 3. Discussion

The method given is essentially that of Traumann.<sup>1</sup> 2-Amino-4-methylthiazole has been prepared also from chloroacetone and ammonium thiocyanate;<sup>2</sup> from chloroacetone and ammonium thiocyanate in ammonia water;<sup>3</sup> by the action of ammonium thiocyanate on thiocanoacetone;<sup>3</sup> by saponifying and decarboxylating the cyclic ester from ethyl  $\gamma$ -bromoacetoacetate and thiourea;<sup>4</sup> and from thiocanoacetone and ammonia in absolute ether.<sup>5</sup>

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### References and Notes

1. Traumann, Ann. **249**, 37 (1888).
  2. Hantzsch and Traumann, Ber. **21**, 938 (1888); Hantzsch and Weber, *ibid.* **20**, 3118 (1887).
  3. Tscherniac and Norton, *ibid.* **16**, 345 (1883); Tscherniac, J. Chem. Soc. **115**, 1071 (1919).
  4. Steude, Ann. **261**, 33 (1891).
  5. Hantzsch, Ber. **61**, 1785 (1928).
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**Appendix**  
**Chemical Abstracts Nomenclature (Collective Index Number);**  
**(Registry Number)**

ammonia (7664-41-7)

ether (60-29-7)

ammonium thiocyanate (1762-95-4)

sodium hydroxide (1310-73-2)

2-Amino-4-methylthiazole,  
Thiazole, 2-amino-4-methyl- (1603-91-4)

thiourea (62-56-6)

chloroacetone (78-95-5)

thiocyanoacetone

ethyl  $\gamma$ -bromoacetoacetate