



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). 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.

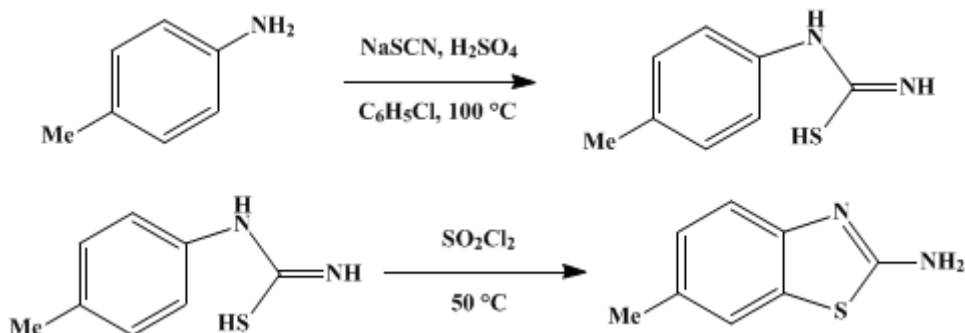
The procedures described in *Organic Syntheses* are provided as published and are conducted at one's own risk. *Organic Syntheses, Inc.*, its Editors, and its Board of Directors do not warrant or guarantee the safety of individuals using these procedures and hereby disclaim any liability for any injuries 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. 3, p.76 (1955); Vol. 22, p.16 (1942).

2-AMINO-6-METHYLBENZOTHAZOLE

[Benzothiazole, 2-amino-6-methyl-]



Submitted by C. F. H. Allen and James VanAllan.
Checked by W. E. Bachmann and N. W. MacNaughton.

1. Procedure

A solution of 107 g. (1 mole) of *p*-toluidine (Note 1) in 700 ml. of chlorobenzene is prepared in a 3-l. three-necked, round-bottom flask fitted with a stirrer, reflux condenser, thermometer, and dropping funnel. Over a period of 5 minutes, 54 g. (29.3 ml., 0.55 mole) of concentrated sulfuric acid is added dropwise. To the finely divided suspension of *p*-toluidine sulfate is added 90 g. (1.1 moles) of sodium thiocyanate, and the mixture is heated for 3 hours at 100° (inside temperature) in an oil bath (Note 2). The solution, which now contains the thiourea, is cooled to 30°, and 180 g. (108 ml., 1.34 moles) of sulfuryl chloride is added over a period of 15 minutes, with care that the temperature does not exceed 50°. The mixture is kept at 50° for 2 hours (no further evolution of hydrogen chloride), after which the chlorobenzene is removed by filtration (Note 3).

The solid residue is then dissolved in 1 l. of hot water, and the remainder of the solvent is removed by a current of steam (Note 4). The solution is filtered from a little solid and is then made alkaline to litmus by the addition of 200 ml. of concentrated ammonium hydroxide (sp. gr. 0.90). The precipitated aminomethylbenzothiazole is filtered and washed with 200 ml. of water. The solid, which melts over the range 123–128°, is dissolved in 300 ml. of hot ethanol (Note 5), 10 g. of Norit is added, and the hot suspension is filtered. The filtrate is diluted with 500 ml. of hot water, and the mixture is vigorously stirred and quickly chilled. After 30 minutes, the pale yellow granular product is filtered and washed with 150 ml. of 30% ethanol. After drying to constant weight, the product weighs 100–105 g. and melts at 135–136°, with preliminary shrinking at 130–131° (Note 6). On the addition of 200 ml. of water to the filtrate, a further 5–8 g. of product is recovered, making the total yield 105–110 g. (64–67%).

2. Notes

- All the chemicals used were from the Eastman Kodak Company. The checkers used the practical grade of *p*-toluidine, which was distilled just before use.
- The *p*-tolylthiourea may be isolated at this point, if desired, by filtering and washing the solid residue with ether. The dried solid (172 g.) is a mixture of the urea and sodium sulfate. It is extracted with 250 ml. of warm (50–60°) water; the residual urea, m.p. 188–189°, is completely soluble in ethanol. The yield is 139 g. (84%).
- The recovery is about 600 ml.; it may be used again without purification.
- Treatment of the solution with Norit at this point does not give a product of any better quality.
- If less ethanol is used, crystallization takes place during filtration.
- The literature gives melting points ranging from 128° to 142°, the higher value being for aminomethylbenzothiazole prepared via the hydrochloride (m.p. 250–253°). The submitters report that the product obtained above is unchanged in melting point after regeneration from the hydrochloride. By

this treatment, however, the color is removed.

3. Discussion

2-Amino-6-methylbenzothiazole has been prepared by the action of cupric thiocyanate,^{1,2,3} or of chloramine and ammonium thiocyanate,⁴ on *p*-toluidine; by the action of chlorine on di-*p*-tolylthiourea;⁵ or of bromine on acetyldi-*p*-tolylthiourea;⁶ by treatment of *p*-tolylthiourea with halogens⁷ or acid halides.^{8,9,10,11,12} 2-Aminobenzothiazole has been prepared in excellent yield by the action of hydroxylamine upon benzothiazole,¹³ and has also been obtained from 2-mercaptobenzothiazole by the action of ammonium bisulfite at 150°. ¹⁴ It has been prepared by the electrolysis of *p*-toluidine in the presence of ammonium thiocyanate.¹⁵ Two German patents report a general method for the preparation of 2-aminobenzothiazoles¹⁶ and 2-aminonaphthothiazoles¹⁷ consisting of the treatment of an aromatic amine with potassium thiocyanate and acetic acid and subsequently with bromine in acetic acid.

Nearly quantitative yields are reported for a process using a modified cupric thiocyanate method.¹⁸

References and Notes

1. Kaufmann, Oehring, and Clauberg, *Arch. Pharm.*, **266**, 197 (1928) [*C. A.*, **22**, 2166 (1928)].
2. Kaufmann and Kuchler, *Ber.*, **67**, 946 (1934).
3. Kaufmann, Ger. pat. 579,818 [*C. A.*, **28**, 1053 (1934)].
4. Likhosherstov and Petrov, *J. Gen. Chem. U.S.S.R.*, **3**, 759 (1933) [*C. A.*, **28**, 2690 (1934)].
5. I. G. Farbenind. A-G., Fr. pat. 688,867 [*C. A.*, **25**, 968 (1931)].
6. Hunter and Jones, *J. Chem. Soc.*, **1930**, 2197.
7. Hunter, *J. Chem. Soc.*, **1926**, 1399.
8. Herz and Schubert, U. S. pat. 2,003,444 [*C. A.*, **29**, 4774 (1935)].
9. I. G. Farbenind. A-G., Brit. pat. 345,735 [*C. A.*, **26**, 1944 (1932)].
10. E. I. du Pont de Nemours and Company, Fr. pat. 727,410 [*C. A.*, **26**, 5103 (1932)].
11. Herz and Schubert, Ger. pat. 537,105 [*Frdl.*, **17**, 615 (1932); *C. A.*, **26**, 1000 (1932)].
12. Schubert and Schütz, Ger. pat. 604,639 [*Frdl.*, **21**, 227 (1934); *C. A.*, **29**, 819 (1935)].
13. Skraup, *Ann.*, **419**, 65 (1919).
14. Ubaldini and Fiorenza, *Gazz. chim. Ital.*, **76**, 215 (1946).
15. Melnikov and Cherkasova, *J. Gen. Chem. U.S.S.R.*, **14**, 113 (1944) [*C. A.*, **39**, 934 (1945)].
16. Ger. pat. 491,223 [*Frdl.*, **16**, 2566 (1927–1929)].
17. Ger. pat. 492,885 [*Frdl.*, **16**, 479 (1927–1929)].
18. Fridman, *Zhur. Obshchei Khim.*, **20**, 1191 (1950) [*C. A.*, **45**, 1579 (1951)].

Appendix

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

2-aminobenzothiazoles

2-aminonaphthothiazoles

ethanol (64-17-5)

sulfuric acid (7664-93-9)

hydrogen chloride (7647-01-0)

acetic acid (64-19-7)

ether (60-29-7)

ammonium thiocyanate (1762-95-4)

bromine (7726-95-6)

sodium sulfate (7757-82-6)

Norit (7782-42-5)

chlorobenzene (108-90-7)

sulfuryl chloride (7791-25-5)

chlorine (7782-50-5)

urea (57-13-6)

ammonium hydroxide (1336-21-6)

potassium thiocyanate (333-20-0)

hydroxylamine (7803-49-8)

thiourea (62-56-6)

sodium thiocyanate (540-72-7)

2-Amino-6-methylbenzothiazole,
Benzothiazole, 2-amino-6-methyl- (2536-91-6)

aminomethylbenzothiazole

cupric thiocyanate (18223-42-2)

chloramine (10599-90-3)

2-Aminobenzothiazole (136-95-8)

benzothiazole (95-16-9)

2-mercaptobenzothiazole (149-30-4)

ammonium bisulfite (10192-30-0)

p-toluidine (106-49-0)

p-toluidine sulfate

p-tolylthiourea (622-52-6)

di-p-tolylthiourea

acetyldi-p-tolylthiourea

Copyright © 1921-2005, Organic Syntheses, Inc. All Rights Reserved