Organic Syntheses

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.

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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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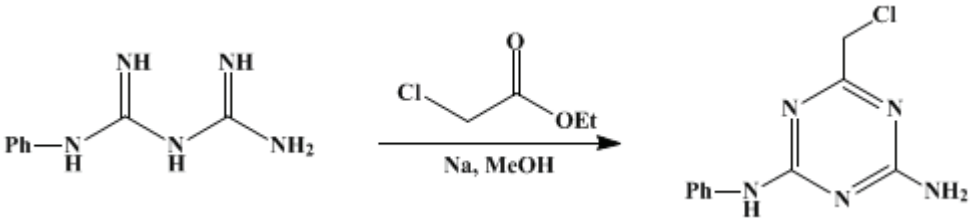
2-AMINO-4-ANILINO-6-(CHLOROMETHYL)-*s*-TRIAZINE

[*s*-Triazine, 2-amino-4-anilino-6-(chloromethyl)-]



Submitted by C. G. Overberger and Francis W. Michelotti[1].
Checked by B. C. McKusick and F. W. Stacey.

1. Procedure

Methanol (225 ml.) is placed in a 500-ml. two-necked flask equipped with a mechanical stirrer and a reflux condenser. Sodium (6.8 g., 0.30 g. atom) in small pieces is dropped down the condenser into the stirred methanol. The resultant solution is cooled to room temperature, and 64 g. (0.30 mole) of 1-phenylbiguanide hydrochloride (Note 1) is added. The mixture is stirred at room temperature for 20 minutes. The sodium chloride that precipitates is separated on a Büchner funnel and washed with 25 ml. of methanol.

The combined filtrates, which contain 1-phenylbiguanide as the free base, are placed in a 500-ml. three-necked flask equipped with a mechanical stirrer, a drying tube containing calcium chloride, and a dropping funnel, and 36.8 g. (0.30 mole) of ethyl chloroacetate (Note 2) is added at room temperature with stirring. The mixture is stirred at room temperature for 14 hours, during which time 2-amino-4-anilino-6-(chloromethyl)-*s*-triazine precipitates as a white solid. After being separated by filtration and air-dried, the triazine weighs 37–40 g. and melts at 138–140°. The methanol filtrate is added to 500 ml. of cold water. The mixture is cooled in an ice bath with stirring for 2 hours and filtered to remove an additional 10–12 g. of gray triazine, m.p. 140–142°. The total yield of crude product is 47–52 g.

The triazine is purified by recrystallizing it from 250 ml. of dioxane, using 2 g. of decolorizing carbon and filtering hot. The recrystallized triazine is dried for 5 hours at 60° (1–5 mm. pressure) in a vacuum oven (Note 3). It then weighs 31–33 g. (44–47%) (Note 4), m.p. 142–143° (Note 5).

2. Notes

1. 1-Phenylbiguanide hydrochloride can be obtained from American Cyanamid Company. If 1-phenylbiguanide itself is available, the triazine can be prepared in the same way by dissolving 53 g. (0.30 mole) of 1-phenylbiguanide in 250 ml. of methanol, adding 36.8 g. of ethyl chloroacetate, and proceeding as before. The same yield is obtained whether one starts with the free base or its hydrochloride.
2. Ethyl chloroacetate from Fisher Scientific Company was used.
3. The checkers found that less rigorous drying failed to remove all the dioxane.
4. An additional 3–5 g. of the triazine, m.p. 141–143°, can be obtained by concentrating the dioxane filtrate to about 60 ml. and cooling the concentrate.
5. 2-Chloromethyl-4,6-diamino-*s*-triazine can be prepared in 82% yield by stirring a mixture of biguanide and ethyl chloroacetate in methanol in the same way.

3. Discussion

2-Amino-4-anilino-6-(chloromethyl)-*s*-triazine has been prepared from 1-phenylbiguanide and ethyl chloroacetate in the presence of methanol[2] or sodium methoxide at −40°.[3]

References and Notes

1. Polytechnic Institute of Brooklyn, Brooklyn, New York.
2. Schuller, U. S. pats. 2,822,364 and 2,848,452 [*C. A.*, **52**, 6807, 19169 (1958)].
3. Shapiro and Overberger, *J. Am. Chem. Soc.*, **76**, 97 (1954).

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

methanol (67-56-1)

sodium chloride (7647-14-5)

sodium methoxide (124-41-4)

carbon (7782-42-5)

sodium (13966-32-0)

Ethyl chloroacetate (105-39-5)

dioxane (123-91-1)

1-phenylbiguanide hydrochloride

1-phenylbiguanide (102-02-3)

triazine (289-96-3)

2-Amino-4-anilino-6-(chloromethyl)-s-triazine,
s-Triazine, 2-amino-4-anilino-6-(chloromethyl)- (30355-60-3)

2-Chloromethyl-4,6-diamino-s-triazine