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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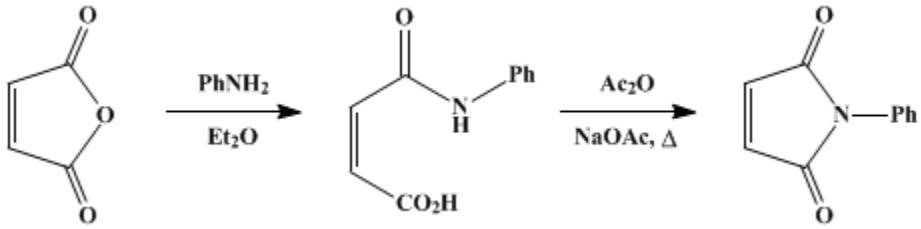
N-PHENYLMALEIMIDE

[Maleimide, N-phenyl-]



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1. Procedure

A. *Maleanilic acid*. In a 5-l. three-necked flask provided with a paddle-type stirrer, a reflux condenser, and a dropping funnel are placed 196 g. (2 moles) of maleic anhydride (Note 1) and 2.5 l. of ethyl ether (Note 2). The stirrer is started and, when all the maleic anhydride has dissolved, a solution of 182 ml. (186 g., 2 moles) of aniline (Note 3) in 200 ml. of ether (Note 2) is run in through the dropping funnel (Note 4). The resulting thick suspension is stirred at room temperature for 1 hour and is then cooled to 15–20° in an ice bath. The product is obtained by suction filtration. It is a fine, cream-colored powder, m.p. 201–202°, suitable for use in the next step without purification. The yield is 371–374 g. (97–98%).

B. *N-Phenylmaleimide*. In a 2-l. Erlenmeyer flask are placed 670 ml. of acetic anhydride (Note 5) and 65 g. of anhydrous sodium acetate. The maleanilic acid (316 g.), obtained as described above, is added, and the resulting suspension is dissolved by swirling and heating on a steam bath for 30 minutes (Note 6). The reaction mixture is cooled almost to room temperature in a cold water bath and is then poured into 1.3 l. of ice water. The precipitated product is removed by suction filtration, washed three times with 500-ml. portions of ice-cold water and once with 500 ml. of petroleum ether (b.p. 30–60°), and dried. The yield of crude N-phenylmaleimide is 214–238 g. (75–80%), m.p. 88–89°. Recrystallization from cyclohexane gives canary-yellow needles, m.p. 89–89.8° (Note 7).

2. Notes

1. Reagent grade maleic anhydride is used without purification.
2. Reagent grade anhydrous ether is used.
3. Reagent grade aniline is used without further purification.
4. The aniline solution may be run in as fast as is possible without flooding the condenser.
5. Carbide and Carbon or Baker's Analyzed technical grade acetic anhydride is used.
6. The sodium acetate fails to dissolve completely.
7. About 500 ml. of the refluxing solvent will dissolve some 58 g. of N-phenylmaleimide. The recovery of recrystallized material is approximately 93%.

3. Discussion

The procedure described here is based on a method outlined in U. S. patent 2,444,536.[2] N-Phenylmaleimide has also been prepared by the dry distillation of the aniline salt of malic acid,[3,4] by treating the aniline salt of malic acid with phosphorus pentoxide,[5] and by treating maleanilic acid with phosphorus trichloride or with phosphorus pentoxide.[6] Ring-substituted N-phenylmaleimides, viz., N-(*p*-methoxyphenyl)-, N-(*p*-ethoxyphenyl)-, and N-(*p*-nitrophenyl)maleimide, have been prepared by treatment of the appropriate maleanilic acids with acetic anhydride and fused potassium acetate.[7]

4. Merits of Preparation

N-Phenylmaleimide is an active dienophile in the Diels-Alder reaction and usually gives crystalline adducts.

This preparation is referenced from:

- Org. Syn. Coll. Vol. 5, 957

References and Notes

1. Chemistry Department, The Ohio State University, Columbus, Ohio.
2. N. E. Searle (to E. I. du Pont de Nemours and Co., Inc.) U.S. pat. 2,444,536 (1948) [*C.A.*, **42**, 7340c (1948)].
3. A. Michael and J. F. Wing. *Am. Chem. J.*, **7**, 278 (1885).
4. R. Anschutz and Q. Wirtz, *Ann.*, **239**, 140, 142 (1887).
5. K. Auwers, *Ann.*, **309**, 346 (1899).
6. A. E. Kretov and N. E. Kul'chitskaya, *Zhur. Obshchei Khim.*, **26**, 208 (1956) [*C.A.*, **50**, 13771g (1956)].
7. W. R. Roderick, *J. Am. Chem. Soc.*, **79**, 1710 (1957).

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

petroleum ether

N-(p-methoxyphenyl

N-(p-ethoxyphenyl

ether,
ethyl ether (60-29-7)

acetic anhydride (108-24-7)

sodium acetate (127-09-3)

aniline (62-53-3)

cyclohexane (110-82-7)

phosphorus trichloride (7719-12-2)

potassium acetate (127-08-2)

maleic anhydride (108-31-6)

N-Phenylmaleimide,
Maleimide, N-phenyl- (941-69-5)

maleanilic acid (555-59-9)

phosphorus pentoxide (1314-56-3)

aniline salt of malic acid

N-(p-nitrophenyl)maleimide (4338-06-1)