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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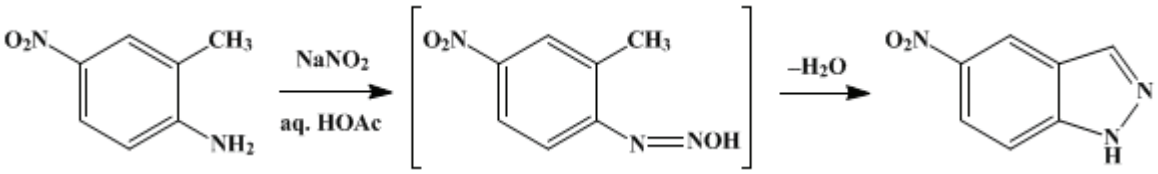
5-NITROINDAZOLE

[Indazole, 5-nitro-]



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1. Procedure

To a solution of 55 g. (0.36 mole) of 2-amino-5-nitrotoluene (m.p. 129–132°) in 2.5 l. of glacial acetic acid in a 5-l. round-bottomed flask, provided with an efficient mechanical stirrer, is added all at once (Note 1) a solution of 25 g. (0.36 mole) of sodium nitrite in 60 ml. of water. During this addition the temperature is not allowed to rise above 25° (Note 2). After the nitrite solution has been added, stirring is continued for 15 minutes to complete the diazotization. Any yellow precipitate formed during the next few hours is filtered and discarded (Note 3).

The solution is allowed to stand for 3 days at room temperature, and is then concentrated on the steam bath under reduced pressure (water pump) until spattering makes further evaporation impossible. Two hundred milliliters of water is added to the residue, and the contents of the flask are washed into a small beaker where they are stirred to a smooth slurry. The product is filtered, washed thoroughly on the funnel with cold water, and dried in an oven at 80–90°. The crude material melts at 204–206° and weighs 47–57 g. (80–96%). It is purified by recrystallization from 650 ml. of boiling methanol using 5 g. of decolorizing charcoal. The recrystallized, pale yellow needles of 5-nitroindazole melt at 208–209°. The yield is 42–47 g. (72–80%) (Note 4). Further recrystallization does not raise the melting point.

2. Notes

1. If the sodium nitrite solution is added slowly, a considerable quantity of a yellow precipitate, presumably the diazoamino compound, is formed.
2. If the solution is cooled in an ice bath to 15–20° before addition of the nitrite solution, the temperature of the mixture will not rise above 25° during the diazotization.
3. This is presumably the diazoamino compound, insoluble in most organic solvents. It melts at about 200°.[1]
4. The unsubstituted *o*-toluidine gives indazole itself, but the yield is very low (3–5%).

3. Discussion

The procedure is essentially that of Noelting.[2]

References and Notes

1. Meunier, *Bull. soc. chim. France*, (3) **31**, 641 (1904).
2. Noelting, *Ber.*, **37**, 2584 (1904).

Appendix

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

acetic acid (64-19-7)

methanol (67-56-1)

sodium nitrite (7632-00-0)

2-amino-5-nitrotoluene (99-52-5)

5-Nitroindazole,
Indazole, 5-nitro- (5401-94-5)

o-toluidine (95-53-4)