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.

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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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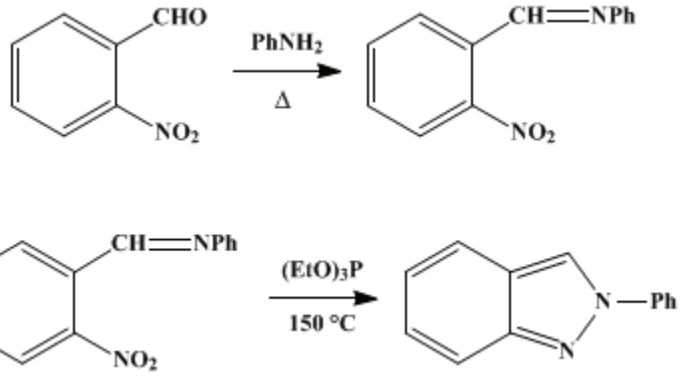
# 2-PHENYLINDAZOLE

## [2*H*-Indazole, 2-phenyl-]




Submitted by J. I. G. Cadogan and R. K. Mackie[1].
Checked by William G. Dauben, Harold B. Morris, and Kent E. Opheim.

## 1. Procedure

A. *o-Nitrobenzalaniline*. A mixture of 14 g. (0.15 mole) of aniline (Note 1) and 22.7 g. (0.15 mole) of *o*-nitrobenzaldehyde (Note 2) is heated in a 100-ml. round-bottomed flask on a water bath for 1 hour, allowed to cool, and dissolved in 100 ml. of ether. The ethereal solution is dried, and the ether is removed by distillation. The residue solidifies on standing (Note 3) and is recrystallized from 55 ml. of water-ethanol (1:8) to yield 29.4–31.8 g. (87–94%) of yellow *o*-nitrobenzalaniline, m.p. 64–66° (Note 4).

B. *2-Phenylindazole*. In a 200-ml. round-bottomed flask fitted with a condenser are mixed 50 g. (0.30 mole) of triethyl phosphite (Note 5) and 22.6 g. (0.10 mole) of *o*-nitrobenzalaniline. The apparatus is sealed from the atmosphere by means of a liquid paraffin bubbler that consists of a U-tube the bend of which is just filled with mineral oil. The apparatus is flushed with nitrogen, and the contents are kept under nitrogen during the reaction. The mixture is heated at 150° in an oil bath for 8 hours and cooled, and the condenser is replaced by a Claisen distillation head. Triethyl phosphite, b.p. 46–48° (10 mm.), and triethyl phosphate, b.p. 90–92° (10 mm.), are removed by distillation under reduced pressure; the volume of distillate is 48–50 ml. On cooling, the black residue solidifies. The flask is filled with glass wool, and the remaining phosphite and phosphate (1–3 g.) are removed by distillation at 30–50° (1 mm.). The residue of crude 2-phenylindazole is distilled at $10^{-4}$ mm.; b.p. 108–112°. The yield is 13–15 g. (67–78%) (Note 6) and (Note 7).

This product is crystallized from 75–100 ml. of ethanol-water (7:3) to yield pale yellow crystals, m.p. 81–82°. Additional material is obtained by dilution of the mother liquor with *ca.* 200 ml. of water and two crystallizations as before. The total yield is 10–12 g. (52–62%).

## 2. Notes

1. Aniline is purified by distillation from zinc dust.
2. The reagent as supplied by British Drug Houses or Eastman Organic Chemicals was used directly.
3. If the product does not solidify at room temperature, it should be cooled with dry ice.
4. *o*-Nitrobenzalaniline is very photosensitive and should be kept away from light as much as possible.
5. The reagent as supplied by Albright and Wilson, Ltd., or Matheson, Coleman and Bell was fractionally distilled from sodium and used within a few days of distillation.
6. A slightly purer sample may be obtained by chromatography on alumina. Elution with chloroform-benzene (1:4) gives a pale yellow solid which is purified further by crystallization from 70% ethanol.
7. The checkers found it more convenient to transfer the crude, black 2-phenylindazole to an apparatus

for simple bulb-to-bulb distillation and not to retain the distillation head.

## 3. Discussion

The procedure given here is essentially that described previously by the submitters[2] and is based on the early work of Knoevenagel.[3] 2-Phenylindazole has been prepared by reduction of N-(*o*-nitrobenzyl) aniline with tin and hydrochloric acid,[4] by reduction of N-(*o*-nitrobenzyl)-N-nitrosoaniline with tin and hydrochloric acid,[5] by dehydration of 2-(phenylazo)benzyl alcohol,[6] by elimination of acetic acid from 2-(phenylazo)benzyl acetate,[7] by dehydrogenation of 3,3a,4,5,6,7-hexahydro-2-phenylindazole with sulfur,[8] and by thermal decomposition of *o*-azidobenzalaniline.[9]

## 4. Merits of the Preparation

Reductive cyclization of nitro compounds by triethyl phosphite is a general method for the preparation of a variety of nitrogen-containing heterocyclic systems. The submitters have synthesized the following ring systems by this method from the starting materials given in parentheses: 2-arylindoles (*o*-nitrostilbenes),[2] 2-arylindazoles (*o*-nitrobenzalanilines),[2] 2-arylbenzotriazoles (*o*-nitroazobenzenes),[2] carbazoles (*o*-nitrobiphenyls),[2] phenothiazines (*o*-nitrodiphenyl sulfides),[10,11] and anthranils (*o*-nitrophenyl ketones).[10]

The products are isolated in good yield in a one-stage synthesis from starting materials that are readily available in the main. An alternative method involves the decomposition of the corresponding azides.[9,12] These compounds are less readily available and are more hazardous to use than are the nitro compounds used in the present synthesis. This synthesis also gives better yields than the cyclization using ferrous oxalate,[12,13] which is performed under much harsher conditions. The present method of synthesis has been reviewed.[14]

## References and Notes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## Appendix
## Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

alumina

chloroform-benzene

o-nitrostilbenes

o-nitrobenzalanilines

o-nitroazobenzenes

o-nitrobiphenyls

o-nitrodiphenyl sulfides

ethanol (64-17-5)

hydrochloric acid (7647-01-0)

acetic acid (64-19-7)

ether (60-29-7)

aniline (62-53-3)

nitrogen (7727-37-9)

tin (7440-31-5)

sulfur (7704-34-9)

zinc (7440-66-6)

sodium (13966-32-0)

o-Nitrobenzaldehyde (552-89-6)

Triethyl phosphite (122-52-1)

triethyl phosphate (78-40-0)

2-PHENYLINDAZOLE,
2H-Indazole, 2-phenyl- (3682-71-1)

water-ethanol

2-(phenylazo)benzyl alcohol

2-(phenylazo)benzyl acetate

3,3a,4,5,6,7-hexahydro-2-phenylindazole

ferrous oxalate (516-03-0)

N-(o-nitrobenzyl)aniline

o-Nitrobenzalaniline (17064-77-6)

N-(o-nitrobenzyl)-N-nitrosoaniline

o-azidobenzalaniline