



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](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.

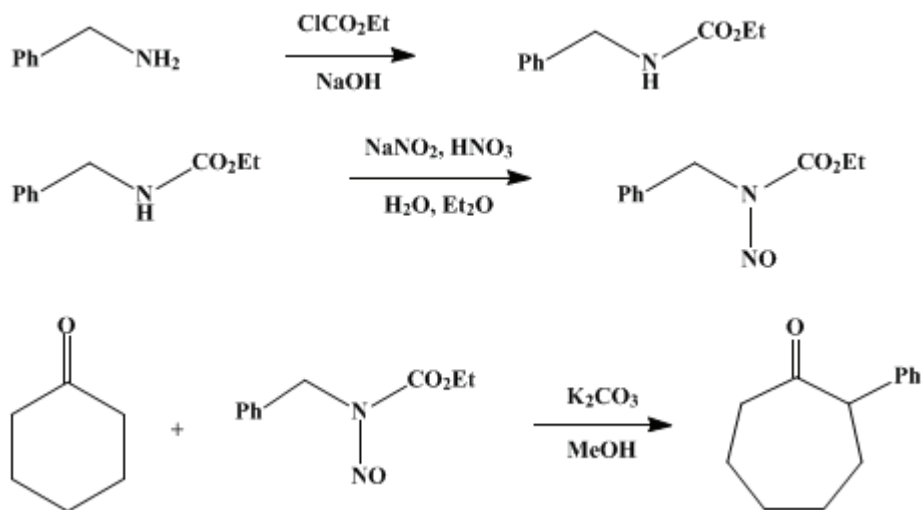
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*These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.*

*Organic Syntheses, Coll. Vol. 4, p.780 (1963); Vol. 35, p.91 (1955).*

## 2-PHENYLCYCLOHEPTANONE

### [Cycloheptanone, 2-phenyl-]



Submitted by C. David Gutsche and Herbert E. Johnson<sup>1</sup>.

Checked by N. J. Leonard and F. P. Hauck, Jr..

### 1. Procedure

A. *Ethyl N-benzylcarbamate*. A 12-l. three-necked flask fitted with a sturdy Hershberg-type stirrer and two 1-l. addition funnels is immersed in an ice bath and charged with 1 kg. (9.33 moles) of benzylamine, 500 ml. of ice water, and 1.5 kg. of chopped ice. To the stirred mixture 525 g. (4.83 moles) of ethyl chloroformate is added dropwise while the temperature is maintained at 10–15° (1.0–1.5 hours) (Note 1). An additional 500 ml. of water and 1 kg. of chopped ice are then added to the flask, and a second 525-g. portion (4.83 moles) of ethyl chloroformate is introduced. Simultaneously with this, an ice-cold solution of 400 g. (10 moles) of sodium hydroxide in 1.3 l. of water is added dropwise at such a rate that equal fractions of the ethyl chloroformate and sodium hydroxide solutions are introduced over equal periods of time, the temperature being maintained throughout at 10–15° (2.5–3.0 hours). The reaction mixture is stirred for an additional 30 minutes and is then filtered through a Büchner funnel. The solid product is washed with copious amounts of cold water and is air-dried to yield 1.6 kg. (96%) of glistening white crystals, m.p. 45–47°.

B. *Ethyl N-nitroso-N-benzylcarbamate* (Note 2). In a 12-l. three-necked flask fitted with a thermometer, a 2-l. addition funnel (Note 3), and a gas outlet tube are placed a solution of 360 g. (2.0 moles) of ethyl N-benzylcarbamate in 2 l. of ether and a solution of 1.2 kg. (17.4 moles) of sodium nitrite in 2 l. of water. A stirrer is not used. The reaction mixture is cooled by means of a water bath to 20° and treated with a solution of 1 l. each of concentrated nitric acid and water, contained in the addition funnel. Enough of this solution is added to impart a permanent green color to the aqueous layer, and the remainder is then added over a period of 5 hours at such a rate as to keep the aqueous phase green (Note 4) and the temperature at 25–30°. The reaction mixture is allowed to stand an additional 30 minutes, and the layers are separated. The ether layer is washed with 200-ml. portions of 10% potassium carbonate solution (Note 5) until the evolution of gas ceases and is then dried over anhydrous potassium carbonate. The ether is removed under vacuum on a water bath kept below 50° (Note 6), a residue of 400–415 g. (95–99%) of a bright orange oil (Note 7) being left.

C. *2-Phenylcycloheptanone*. In a 2-l. three-necked flask fitted with a 500-ml. addition funnel, a sealed Hershberg stirrer, and a reflux condenser (Note 8) are placed 392 g. (4.0 moles) of freshly distilled cyclohexanone, 30 g. of finely powdered potassium carbonate, and 400 ml. of absolute

methanol. To the stirred mixture is added 415 g. (2.0 moles) of ethyl N-nitroso-N-benzylcarbamate over a period of 1.5 hours during which time the reaction temperature is maintained at 25° by means of an ice-water bath. The dark red reaction mixture is then allowed to stand at room temperature until the evolution of nitrogen has ceased (24–28 hours) (Note 9). The solid material is removed by filtration, the lower-boiling materials are removed by evaporation under reduced pressure on the steam bath (Note 10), and the residue is distilled through an efficient column. A fore-run consisting of 30–60 g. of material is discarded or refractionated (Note 10), and the fraction with b.p. 94–96°/0.4 mm. (124–126°/2 mm., 136–138°/4 mm.) is collected. It amounts to 155–177 g. (41–47%) of 2-phenylcycloheptanone,  $n_D^{20}$  1.5395–1.5398, which is pure enough for most purposes, but which may be purified further by recrystallization from petroleum ether (b.p. 30–60°) and obtained as colorless, very long needles; m.p. 21–23° (Note 11).

## 2. Notes

1. During this time ethyl N-benzylcarbamate begins to separate from solution as a white solid.
2. Although the benzyl nitroso compound appears to be a much less active vesicant than the methyl nitroso compound, it is, nevertheless, a wise precaution to wear heavy rubber gloves during the isolation of this product.
3. The stem of the addition funnel should reach to the bottom of the flask.
4. The color may appear yellow green, emerald green, or blue-green, depending upon the size of the run, the amount of nitric acid that has been added, and the room lighting.
5. Seven to nine portions of carbonate solution are sufficient if each portion is shaken very thoroughly with the ether solution. Caution should be observed because of pressure build-up in the separatory funnel!
6. Ethyl N-nitroso-N-benzylcarbamate is heat sensitive and, if the temperature is too high, may detonate violently. The submitters state that attempts to distil the nitroso compound under high vacuum have resulted in explosions.
7. The submitters state that the nitroso compound is stable at low temperature and can be stored in a refrigerator for several months or longer with no signs of deterioration.
8. The reflux condenser is an optional but convenient appendage for the third neck of the flask. To follow the evolution of nitrogen during the reaction, the exit from the condenser can be led either to a eudiometer tube (theoretical nitrogen evolution about 50 l. for the experiment described) or to a bubbler.
9. It is necessary to allow the reaction mixture to stand for a rather prolonged period, since about 40% of the nitrogen is evolved during this time.
10. The lower-boiling material includes methyl benzyl ether, which may be isolated, by careful fractionation through an efficient column, in about 25% yield, b.p. 74–77°/30 mm.
11. In a similar fashion the following 2-arylcycloheptanones have been prepared by the submitters:

	Yield, %Melting Point, or Refractive Index at 25°	
2-( <i>o</i> -Methylphenyl)cycloheptanone	29	1.5348
2-( <i>p</i> -Methylphenyl)cycloheptanone	26	57–58°
2-( <i>o</i> -Methoxyphenyl)cycloheptanone	7	1.5407
2-( <i>m</i> -Methoxyphenyl)cycloheptanone	42	1.5418
2-( <i>p</i> -Methoxyphenyl)cycloheptanone	20	58–59°

## 3. Discussion

Ethyl N-benzylcarbamate and its nitroso compound have been prepared by methods similar to those described for ethyl N-methylcarbamate and its nitroso compound.<sup>2,3</sup> 2-Phenylcycloheptanone has been prepared by the reaction of ethyl N-nitroso-N-benzylcarbamate<sup>4</sup> with cyclohexanone,<sup>5</sup> by the reaction of phenyldiazomethane with cyclohexanone,<sup>6</sup> by the reaction of ethyl N-nitroso-N-methylcarbamate with 2-phenylcyclohexanone,<sup>5</sup> and by the rearrangement of 1-phenyl-2-cyclohexylethylene oxide.<sup>7</sup>

## References and Notes

1. Washington University, St. Louis, Missouri.
  2. *Org. Syntheses Coll. Vol. 2*, 278 (1943).
  3. *Org. Syntheses Coll. Vol. 2*, 464 (1943).
  4. v. Pechmann, *Ber.*, **31**, 2640 (1898).
  5. Gutsche, *J. Am. Chem. Soc.*, **71**, 3513 (1949); Gutsche and Johnson, *J. Am. Chem. Soc.*, **77**, 109 (1955).
  6. Burger, Walter, Bennet, and Turnbull, *Science*, **112**, 306 (1950); Gutsche and Jason, *J. Am. Chem. Soc.*, **78**, 1184 (1956).
  7. Tiffeneau, Weill, Gutmann, and Tchoubar, *Compt. rend.*, **201**, 277 (1935).
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**Appendix**  
**Chemical Abstracts Nomenclature (Collective Index Number);**  
**(Registry Number)**

petroleum ether

potassium carbonate (584-08-7)

methanol (67-56-1)

ether (60-29-7)

sodium hydroxide (1310-73-2)

nitric acid (7697-37-2)

Cyclohexanone (108-94-1)

nitrogen (7727-37-9)

sodium nitrite (7632-00-0)

ethyl chlorocarbonate (541-41-3)

benzylamine (100-46-9)

Ethyl N-methylcarbamate (105-40-8)

ethyl N-nitroso-N-methylcarbamate (615-53-2)

2-Phenylcycloheptanone,  
Cycloheptanone, 2-phenyl- (14996-78-2)

Ethyl N-benzylcarbamate (2621-78-5)

Ethyl N-nitroso-N-benzylcarbamate (6558-76-5)

methyl benzyl ether (538-86-3)

phenyldiazomethane (766-91-6)

2-phenylcyclohexanone (1444-65-1)

1-phenyl-2-cyclohexylethylene oxide

2-(o-Methylphenyl)cycloheptanone

2-(p-Methylphenyl)cycloheptanone

2-(o-Methoxyphenyl)cycloheptanone

2-(m-Methoxyphenyl)cycloheptanone

2-(p-Methoxyphenyl)cycloheptanone