



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.

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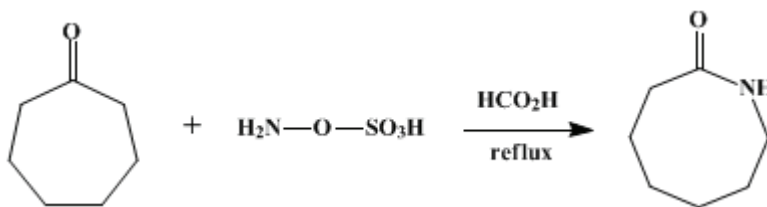
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*These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.*

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## HEXAHYDRO-2-(1*H*)-AZOCINONE

[2(1*H*)-Azocinone, hexahydro-]



Submitted by George A. Olah and Alexander P. Fung<sup>1</sup>.  
 Checked by David Varie and Edwin Vedejs.  
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### 1. Procedure

A 100-mL, three-necked flask is equipped with a magnetic stirring bar, a pressure-equalizing dropping funnel, and a reflux condenser connected to a nitrogen flow line. The system is dried with a heat gun while it is flushed with dry **nitrogen**. The reaction vessel is then cooled in a water bath while a light positive pressure of **nitrogen** is maintained. The flask is charged with **hydroxylamine-*O*-sulfonic acid**<sup>2</sup> (8.48 g, 0.075 mol) (**Note 1**) and 95–97% **formic acid** (45 mL) (**Note 2**). A solution of **cycloheptanone** (5.61 g, 0.05 mol) (**Note 3**) in 15 mL of 95–97% **formic acid** is added with stirring over a 3-min period. After addition is complete, the reaction mixture is heated under reflux for 5 hr and then cooled to room temperature. The reaction mixture is quenched with 75 mL of ice–water. The aqueous solution is slowly neutralized to pH  $\sim$ 7 with 6 *N* **sodium hydroxide** (**Note 4**) and extracted with three 100-mL portions of **chloroform**. The combined organic layers are dried with anhydrous **magnesium sulfate**. After removal of the solvent on a rotary evaporator, the product **hexahydroazocinone** is purified by distillation to give 4.6 g (72%), bp 94–96°C/0.2 mm, (short-path apparatus), lit<sup>3</sup> bp 133–135°C/4 mm (**Note 5**).

### 2. Notes

1. The **hydroxylamine-*O*-sulfonic acid** used by the submitters was purchased from Ventron Corporation and used directly. However, it can be readily prepared in the laboratory.<sup>4,3</sup>
2. **Formic acid** 95–97% was obtained from the Aldrich Chemical Company.
3. Commercial **cycloheptanone** (bp 179°C) obtained from MCB, Inc. was used directly.
4. An external ice–salt bath is used.
5. The product exhibits the following spectra: <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$ : 1.6–1.8 (m, 6 H, CH<sub>2</sub>), 2.40 (3 H, m), 2.57 (m, 2 H, CH<sub>2</sub>CO), 3.31 (m, 2 H, CH<sub>2</sub>-N), 7.16 (br, 1 H, NH); IR (cm<sup>-1</sup>): 3270, 3200, 1650; GLC analysis: 20% SE-30, 60/80 on Chrom-W, 1/8-in  $\times$  20-ft column, 180°C: one peak.

### 3. Discussion

The procedure described here is a one-step conversion of **cycloheptanone** into **hexahydro-2(1*H*)-azocinone**. The method is general and is characterized by good yields, mild conditions, and easy preparation of the product in pure form from readily available starting materials. Several methods are described in the patent literature for simultaneous oximation of ketones and rearrangement of the corresponding oxime, including the use of hydroxylamine and **sulfuric acid**,<sup>5,6</sup> or by employing primary nitroparaffins as a source of hydroxylamine.<sup>7,8</sup> The present method has been shown<sup>9</sup> to be applicable to a wide variety of lactams (C<sub>5</sub>  $\sim$  C<sub>12</sub>). In the specific case of **hexahydroazocinone**, the yield from **cycloheptanone** (60–63%) appears lower than for the conventional two-step method,<sup>10,11</sup> but the latter requires isolation of the intermediate oxime.

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## References and Notes

1. Institute of Hydrocarbon Chemistry and Department of Chemistry, University of Southern California, University Park, Los Angeles, CA 90007.
  2. For a recent review on hydroxylamine-*O*-sulfonic acid, see Wallace, R. G., *Aldrichimica Acta* **1980**, *13*, 3.
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  4. Rathke, M. W.; Millard, A. A. *Org. Synth. Coll. Vol. VI* **1988**, 943.
  5. Novotny, A. U.S. Patent 2579851, 1951; *Chem. Abstr.* **1952**, *46*, 6668.
  6. Barnett, C.; Cohn, I. M.; Lincoln, J. U.S. Patent 2754298, 1956; *Chem. Abstr.* **1957**, *51*, 2853.
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  8. Novotny, A. U.S. Patent 2569114, 1951; *Chem. Abstr.* **1952**, *46*, 5078.
  9. Olah, G. A.; Fung, A. P. *Synthesis* **1979**, 537.
  10. Yields of 97 and 88% are reported for the oximation and Beckmann rearrangement steps, respectively, but no experimental details are given.<sup>11</sup> An earlier publication reports <50% yield in the second step.<sup>3</sup>
  11. McKay, A. F.; Tarlton, E. J.; Petri, S. I.; Steyermark, P. R.; Mosely, M. A. *J. Am. Chem. Soc.* **1958**, *80*, 1510.
  12. Donaruma, L. G.; Heldt, W. Z. *Org. React.* **1960**, *11*, 1.
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## Appendix

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

sulfuric acid (7664-93-9)

sodium hydroxide (1310-73-2)

chloroform (67-66-3)

formic acid (64-18-6)

nitrogen (7727-37-9)

magnesium sulfate (7487-88-9)

Cycloheptanone (502-42-1)

Hydroxylamine-*O*-sulfonic acid (2950-43-8)

hexahydroazocinone (673-66-5)

Hexahydro-2-(1H)-azocinone,  
2(1H)-Azocinone, hexahydro-,  
hexahydro-2(1H)-azocinone (673-66-5)