



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.

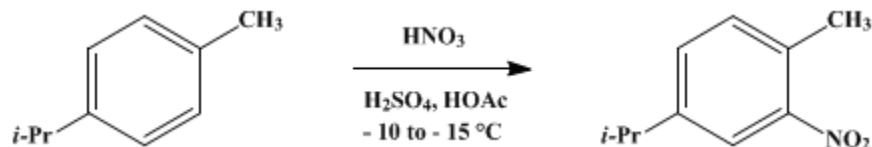
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 3, p.653 (1955); Vol. 21, p.96 (1941).

2-NITRO-*p*-CYMENE

[*p*-Cymene, 2-nitro-]



Submitted by Kenneth A. Kobe and Thomas F. Doumani.

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1. Procedure

A 5-qt. enamel pail or bain-marie jar is fitted with two mechanical stirrers (Note 1) placed off center, a thermometer for reading low temperatures, and a dropping funnel, the lower end of which is placed just over the vortex created by one of the stirrer blades, so that each drop of added liquid is immediately mixed with and diluted by the chilled reaction mixture.

In the pail are placed 1 kg. (544 ml.) of concentrated sulfuric acid and 300 ml. of glacial acetic acid (Note 2), and this mixture is chilled by Dry Ice until the temperature is 0° to -5°. Next, 500 g. (585 ml.) of *p*-cymene (Note 3) is added from the dropping funnel with vigorous stirring, any rise of temperature being prevented by the addition of Dry Ice (Note 4). Concurrently the nitrating mixture is prepared from 369 g. (262 ml.) of nitric acid (sp. gr. 1.42) and 1 kg. (544 ml.) of concentrated sulfuric acid, and cooled to 0-5° by the direct addition of small pieces of Dry Ice (Note 4).

The hydrocarbon emulsion is then cooled to -15° to -10° and the nitrating mixture is admitted dropwise from the dropping funnel over a period of about 2 hours, avoiding any temperature rise (Note 4) and (Note 5). Stirring is continued for 10 minutes, after which the entire contents of the pail are poured, with adequate stirring, into a mixture of 1 kg. of cracked ice and 1 l. of water. Separation into layers occurs after about 2 hours, whereupon the lower acid layer is drawn off by siphoning or by means of a large separatory funnel (Note 6) and extracted twice, using 50-ml. portions of petroleum ether or 500-ml. portions of ether (Note 7). The extracts and crude nitrocymene are combined and washed three times with 300-ml. portions of water (Note 8), and the ether layer is dried by 50 g. of calcium chloride. After the ether is filtered and distilled, the residual liquid is fractionated under reduced pressure, using a 1-l. modified Claisen flask with indented neck. Fractions are collected at 15-17 mm. as follows: up to 125°, 25-30 g. (Note 9); 125-139°, 520-550 g. (78-82%), n_D^{26} 1.5280; tarry residue, 25-30 g. The product is mainly 2-nitro-*p*-cymene but contains about 8% of *p*-nitrotoluene; it is suitable for reduction¹ to 2-amino-*p*-cymene, from which the *p*-toluidine is readily removed. Upon refractionation of the mixed nitro compounds, the last half is essentially pure 2-nitro-*p*-cymene, b.p. 137-139°/17 mm.; 128-131°/12 mm.; 108°/3 mm., n_D^{25} 1.5290. The properties of pure 2-nitro-*p*-cymene are as follows: b.p. 126°/10 mm.; 142°/20 mm.; n_D^{20} 1.5287.

2. Notes

1. It is advisable to use more powerful stirring motors than those usually found in the organic laboratory, since the success of the preparation is largely dependent on the production of a good emulsion. The checkers employed two "Lightnin" stirrers (Model L mixers) having shafts and blades of Monel metal.
2. On mixing the acids, the temperature rises to about 60°.
3. The authors recommended that a technical grade of cymene be used, since the terpenic impurities present facilitated emulsification. The checkers used both a technical product and one free from terpenes; They encountered no difficulties with emulsification and secured a slightly higher yield (3-4%) with the purified grade. Cymene from different sources varies considerably in its composition.
4. The amounts of Dry Ice given are approximate. The actual quantities depend on the initial

temperature and the rapidity of cooling required. Ordinarily 200 g. is required to cool the nitrating mixture, 500 g. to chill the cymene-sulfuric-acetic acid mixture, and 1.5 kg. during the actual nitration. The nitrating acid will solidify if chilled too far. It is extremely important to keep the temperatures indicated to secure the best yields, and Dry Ice should be used freely. The [carbon dioxide](#) evolved aids in mixing.

5. If the mixture is cooled too much, the emulsion is broken.

6. The separation into layers is not sharp; 10–15 g. of product may be lost with the acid layer at this point ([Note 7](#)).

7. The extractions can be omitted with a smaller yield of product. Thus from the first extraction there is obtained approximately 15 g. of nitro compound, and 7 g. from the second.

8. Sometimes an emulsion is formed during washing; this can be broken by the addition of a few milliliters of [sulfuric acid](#) and shaking.

9. The fore-run, on refractionation at atmospheric pressure, yields 4–6 g. of impure *p*-cymene, b.p. 160–165°, and 10–13 g. of nitro compound. This latter amount is included in the total yields given in the procedure.

3. Discussion

[2-Nitro-*p*-cymene](#) has always been secured by the nitration of the hydrocarbon, either by the use of mixed sulfuric and nitric acids with² or without³ the addition of [acetic acid](#), or by fuming [nitric acid](#) in [acetic acid](#).⁴

This preparation is referenced from:

- [Org. Syn. Coll. Vol. 3, 63](#)

References and Notes

1. Doumani and Kobe, *Ind. Eng. Chem.*, **31**, 264 (1939).
2. Söderbaum and Widman, *Ber.*, **21**, 2126 (1888); Andrews, *J. Ind. Eng. Chem.*, **10**, 453 (1918); Wheeler and Smithey, *J. Am. Chem. Soc.*, **43**, 2613 (1921); Phillips, *J. Am. Chem. Soc.*, **44**, 1777 (1922); Demonbreun and Kremers, *J. Am. Pharm. Assoc.*, **12**, 296 (1926) [*C. A.*, **17**, 3906 (1923)]; Kobe and Doumani, *Ind. Eng. Chem.*, **31**, 257 (1939).
3. Andrews, U. S. pat. 1,314,920 [*C. A.*, **13**, 2765 (1919)]; Selden, Brit. pat. 142,226 [*C. A.*, **14**, 2645 (1920)].
4. Schumow, *J. Russ. Phys. Chem. Soc.*, (1) **19**, 119 (1887); *Ber. Ref.*, **20**, 218 (1887).

Appendix

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

petroleum ether

sulfuric and nitric acids

cymene-sulfuric-acetic acid

[calcium chloride](#) (10043-52-4)

[sulfuric acid](#) (7664-93-9)

acetic acid (64-19-7)

ether (60-29-7)

nitric acid (7697-37-2)

carbon dioxide (124-38-9)

cymene,
p-cymene (99-87-6)

2-Amino-p-cymene (2051-53-8)

nitrocymene

p-toluidine (106-49-0)

p-nitrotoluene (99-99-0)

2-Nitro-p-cymene,
p-Cymene, 2-nitro- (943-15-7)