



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.

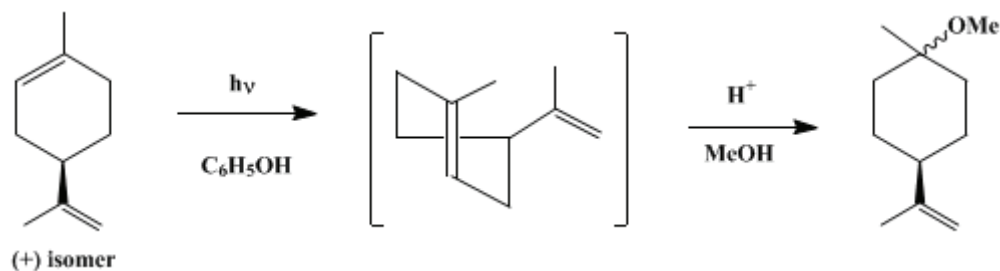
The procedures described in *Organic Syntheses* are provided as published and are conducted at one's own risk. *Organic Syntheses, Inc.*, its Editors, and its Board of Directors do not warrant or guarantee the safety of individuals using these procedures and hereby disclaim any liability for any injuries or damages claimed to have resulted from or related in any way to the procedures herein.

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. 7, p.304 (1990); Vol. 61, p.112 (1983).

PHOTOPROTONATION OF CYCLOALKENES: LIMONENE TO *p*-MENTH-8-EN-1-YL METHYL ETHER

[Cyclohexane, 1-methoxy-1-methyl-4-(1-ethenyl-1-methyl-)]

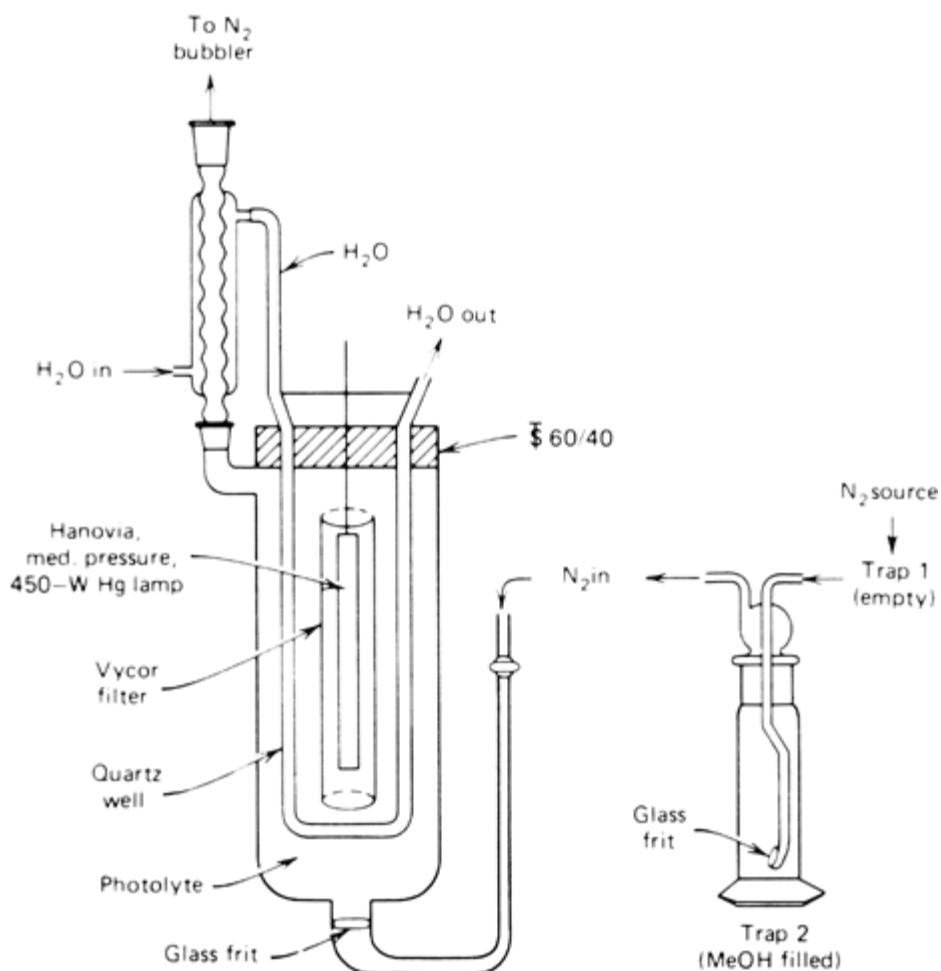


Submitted by F. P. Tise and P. J. Kropp¹.
 Checked by R. L. Amey and R. E. Benson.

1. Procedure

A 250-mL photochemical reactor (see [Figure 1](#)) is fitted with a cylindrical Vycor filter sleeve, a 450-W Hanovia mercury lamp, and a watercooled condenser which is connected to a mineral oil bubbler. Tubing attachments are made so that water is circulated through the condenser and then through the Vycor filter sleeve. The tube leading from the bottom of the reaction vessel and containing the glass frit is connected in series to a trap fitted with a fritted filter stick and then to a trap that is connected to a [nitrogen](#) source. The system is flushed with [nitrogen](#), and sufficient anhydrous [methanol](#) is placed in the trap containing the fritted stick to provide for a methanol-saturated gas stream during the course of the reaction ([Note 1](#)).

Figure 1



The nitrogen-flushed reactor is charged with a solution of 20.0 g (147 mmol) of (+)-limonene (Note 2), 5.0 g (53 mmol) (Note 3) of phenol, and 5 drops of concentrated sulfuric acid in 210 mL (167 g, 5.2 mol) of anhydrous methanol (Note 4). Water flow through the condenser is started (Note 5), and the nitrogen flow is adjusted to provide good agitation of the contents of the vessel. After 15 min, irradiation is started and the reaction followed by GLC (Note 6), with 48 hr being the approximate time needed for essentially complete conversion (Note 7).

The solution is poured into 900 mL of 5% aqueous sodium hydroxide solution containing 125 g of sodium chloride, and the mixture is extracted with two 100-mL portions of ether. The ether layers are combined, washed with 50 mL of saturated sodium chloride solution, and dried over anhydrous sodium sulfate. The drying agent is removed by filtration and the filtrate is concentrated with a Büchi rotary evaporator. After a preliminary distillation to separate the product from a small amount of nonvolatile material, the liquid is distilled at reduced pressure through a Teflon spinning band column (47 cm \times 7 mm). The material that distills at 90–95°C (10 mm) is collected to give 12.8–13.2 g (52–53%) of a mixture of *cis*- and *trans*-*p*-menth-8-en-1-yl methyl ether (Note 8),(Note 9),(Note 10).

2. Notes

1. The submitters used a reactor with a joint that was capped with a rubber septum fitted with two syringe needles, which were attached by means of a Y-tube to a single nitrogen line. To one of these needles is attached a piece of 1.70-mm-o.d. polyethylene tubing of sufficient length to reach to the bottom of the reaction vessel. By use of pinchcocks, nitrogen can be passed through either of the two needles. The solution was stirred with a magnetic stirring bar.
2. (+)-Limonene was obtained from Aldrich Chemical Company, Inc. and distilled before use.
3. The checkers used reagent available from Fisher Scientific Company.

4. The checkers used fresh, acetone-free, absolute [methanol](#) available from Fisher Scientific Company.
5. For best results the cooling water should pass through the condenser first and then through the immersion well. This arrangement lessens evaporation of [methanol](#).
6. The submitters used a 3-m \times 3.2-mm stainless steel column packed with 20% SF-96 on Chromasorb W (60–80 mesh) and a He flow rate of 60 mL/min. With a temperature program of 4 min at 50°C followed by an increase of 10°C/min to a maximum of 200°C, the retention times were 17.9 and 18.7 min.
7. The checkers found that the reaction was impeded by the formation of a yellow film on the immersion well with very little further conversion occurring after 30 hr of irradiation.
8. The checkers used a 2.4-m \times 3.2-mm column packed with 7% SE-30 and 3% Silar on Chromasorb W (60–80 mesh) at 160°C. The retention time was 1.56 min for the trans isomer and 1.81 min for the cis isomer at a He flow rate of 55 mL/min.
9. The spectral properties of the product (approximately 60% cis:40% trans isomers) are as follows: IR (neat) cm^{-1} : 3080 ($=\text{C}-\text{H}$); 2964, 2939, 2860, 2825, ($\text{C}-\text{H}$); 1645 ($\text{C}=\text{C}$); 1464, 1453, and 1442 (overlapping peaks); 1370, 1124, and 1082 ($\text{C}-\text{OC}$); 885 ($=\text{CH}$). ^1H NMR (CDCl_3) δ : 1.10 [s, 3 H, CH_3 (trans)], 1.19 [s, 3 H, CH_3 (cis)], 1.30–2.00 (8 H, $-\text{CH}_2-$), 1.71 [s, 3 H, CH_3 (cis/trans)], 3.14 [s, 3 H, OCH_3 (trans)], 3.21 [s, 3 H, OCH_3 (cis)], 4.69 [s, 2 H, $=\text{CH}_2$ (cis/trans)].
10. The submitters state that similar irradiation of 20.0 g of [cyclohexene](#), 5.0 g of [phenol](#), and 1.5 mL of concentrated [sulfuric acid](#) for 24 hr afforded [cyclohexyl methyl ether](#) in 70% yield.

3. Discussion

Acid-catalyzed, ground-state additions to [limonene](#) generally afford a mixture of products resulting from competing protonation of both double bonds.² In one case in which selective reaction was observed, attack occurred at the acyclic $\text{C}_8\text{-C}_9$ double bond.³

The photoprotonation of cycloalkenes, described in this procedure, is believed to proceed via initial light-induced cis \rightarrow trans isomerization of the alkene.⁴ The resulting highly strained trans isomer undergoes facile protonation. This procedure permits the protonation of cyclohexenes and cycloheptenes under neutral or mildly acidic conditions.⁵ Since the process is irreversible, high levels of conversion to addition products can be achieved.

Photoprotonation is generally specific for cyclohexenes and cycloheptenes. Smaller-ring cycloalkenes are incapable of undergoing cis \rightarrow trans isomerization, and the trans isomers of larger-ring or acyclic analogues have insufficient strain to undergo ready protonation. Thus, in addition to facilitating protonation of cycloalkenes, the procedure affords a means of selectively protonating a double bond contained in a six- or seven-membered ring in the presence of another double bond contained in an acyclic, exocyclic, or larger-ring cyclic environment.⁶ When conducted in non-nucleophilic media, the photoprotonation procedure is also useful for effecting the isomerization of 1-alkylcyclohexenes and -heptenes to their exocyclic isomers.⁴

References and Notes

1. Department of Chemistry, University of North Carolina, Chapel Hill, NC 27599–3290.
2. For a review of the chemistry of limonene, see Verghese, J. *Perfum. Essent. Oil Rec.* **1968**, 59, 439–454.
3. Kuczynski, L.; Kuczynski, H. *Rocz. Chem.* **1951**, 25, 432–453.
4. For reviews of the photochemistry of alkenes see Kropp, P. J. *Mol. Photochem.* **1978**, 9, 39–65; *Organic Photochemistry* **1979**, 4, 1–142.
5. There is a fine balance between the acidity of the alcohol and the basicity of the trans olefin. For example, 1-methylcyclohexenes undergo photoprotonation in methanol whereas cyclohexenes require the addition of small amounts of acid. In the present example, the addition of a small quantity of acid reduces the competing formation of the exocyclic isomer, *p*-mentha-1(7),8-diene.
6. For an earlier report on the photoprotonation of (+)-limonene, see Kropp, P. J. *J. Org. Chem.* **1970**, 35, 2435–2436.

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

sulfuric acid (7664-93-9)

methanol (67-56-1)

ether (60-29-7)

sodium hydroxide (1310-73-2)

phenol (108-95-2)

Cyclohexene (110-83-8)

sodium chloride (7647-14-5)

sodium sulfate (7757-82-6)

nitrogen (7727-37-9)

CYCLOHEXYL METHYL ETHER (931-56-6)

LIMONENE,
(+)-limonene

Cyclohexane, 1-methoxy-1-methyl-4-(1-ethenyl-1-methyl-)

p-Menth-8-en-1-yl methyl ether,
cis- and trans-p-menth-8-en-1-yl methyl ether (24655-71-8)