



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.

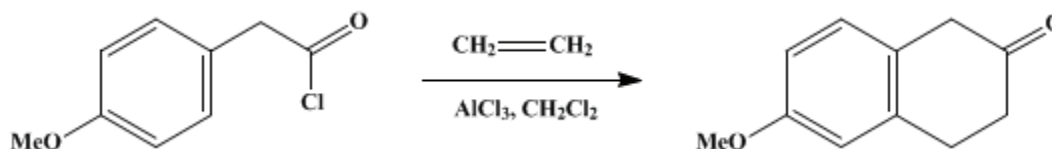
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*These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.*

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## 6-METHOXY- $\beta$ -TETRALONE

[2(1*H*)-Naphthalenone, 3,4-dihydro-6-methoxy-]



Submitted by James J. Sims<sup>1</sup>, L. H. Selman, and M. Cadogan.

Checked by Robert E. Ireland and Ronald I. Trust.

### 1. Procedure

A 2-l., three-necked flask equipped with a mechanical stirrer, a reflux condenser fitted with a calcium chloride drying tube, and a pressure-equalizing dropping funnel is charged with 53.4 g. (0.400 mole) of anhydrous aluminum chloride (Note 1) and 800 ml. of dichloromethane (Note 2). The flask is placed in an acetone-dry ice bath, and the mixture is stirred for a few minutes before slowly adding a solution of 36.9 g. (0.200 mole) of (4-methoxyphenyl)acetyl chloride (Note 3) in 200 ml. of dichloromethane over 45 minutes. When the addition is complete, the funnel is replaced with a gas-inlet tube (Note 4), and ethylene is bubbled vigorously into the flask for about 10 minutes. The gas-inlet tube is replaced with a stopper, the cooling bath is removed, and the reaction mixture is allowed to warm to room temperature, then stirred for 3–3.5 hours (Note 5). The reaction mixture is cooled in an ice bath while 250 ml. of ice water is added carefully (Note 6). The mixture is stirred until all of the solid material is dissolved. The yellow organic layer is separated, washed two times with 150-ml. portions of 5% hydrochloric acid and two times with 150-ml. portions of saturated sodium hydrogen carbonate. The organic layer is dried over magnesium sulfate and filtered. The solvent is distilled with a rotary evaporator, keeping the bath temperature under 60°. Distillation (Note 7) of the yellow residue through a 15-cm. Vigreux column gives 21–24 g. (60–68%) of 6-methoxy- $\beta$ -tetralone, b.p. 114–116° (0.2 mm.), which solidifies to a white solid on standing in the refrigerator, m.p. 33.5–35° (Note 8).

### 2. Notes

1. A 100% molar excess of aluminum chloride is necessary to obtain an acceptable yield in a short time. The reaction of phenylacetyl chloride with ethylene requires only 1 mole of aluminum chloride per mole of acid chloride.
2. Matheson, Coleman and Bell dichloromethane, b.p. 39.5–40.5°, was used without purification. The use of this solvent rather than carbon disulfide is the major improvement of this procedure over the published one.<sup>2</sup>
3. (4-Methoxyphenyl)acetyl chloride is prepared from (4-methoxyphenyl)acetic acid (Aldrich Chemical Company, Inc., m.p. 85–86.5°) by the procedure of Buckles and Cooper.<sup>3</sup> Thionyl chloride (50 ml.) is added to 100 g. (0.603 mole) of (4-methoxyphenyl)acetic acid in a 500-ml. round-bottomed flask containing a few boiling stones and a magnetic stirring bar, and fitted with a calcium chloride drying tube. The contents of the flask are stirred slowly for 24 hours at room temperature. Dry benzene (80 ml.) is added and removed by distillation on a rotary evaporator; the process is then repeated. The yellow-green liquid is transferred to a 200-ml. flask with a small volume of benzene and, after removal of the solvent under vacuum, distillation of the liquid through a 15-cm. Vigreux column affords 102–108 g. (92–97%) of (4-methoxyphenyl)acetyl chloride, b.p. 80–88° (0.5 mm.).
4. A glass tube (6 mm. o.d.), flanged at one end and bent to direct gas bubbles in the direction of stirring is used. A fritted disk will become clogged during the addition and should not be used.
5. This reaction time was found to give the best yield of pure product. The progress of the reaction should be checked by either IR spectroscopy or GC. A small aliquot (1–2 ml.) is worked up in a test tube by quenching with water, separating the organic phase, and drying over magnesium sulfate. The IR spectrum will show a disappearance of the acid chloride carbonyl peak at 1786 cm.<sup>-1</sup> and appearance of

the 6-methoxy- $\beta$ -tetralone carbonyl peak at 1701  $\text{cm}^{-1}$  GC was carried out in a 185 cm.  $\times$  3.2 mm. column packed with 5% by weight SE-30 on Diatoport S (60–80 mesh). The reaction may also be followed visually. The initial yellow suspension changes to green and finally to red-brown with a green cast. The reaction is essentially complete with the precipitation of dark green aluminum salts.

6. Much heat is generated on addition of water to the dark red-brown mixture. The addition should be dropwise until the heat is dissipated.

7. If the distillation is not carried out promptly, the crude product should be placed under nitrogen in a freezer. The tetralone seems to keep well under nitrogen at low temperature in glassware that has been rinsed with ammonium hydroxide and dried in an oven; the distillation flask and column were also routinely treated this way.

8. This material contains a small amount of impurity (2–5%). A higher grade material may be obtained by discarding a 1–2 g. forerun.

### 3. Discussion

This procedure, an improvement over the method of Burckhalter and Campbell,<sup>2</sup> represents the most convenient method of preparing 6-methoxy- $\beta$ -tetralone, a valuable intermediate for the synthesis of natural products, and provides a general method for the synthesis of substituted  $\beta$ -tetralones.<sup>2,4</sup>

6-Methoxy- $\beta$ -tetralone has been synthesized from 6-methoxy-3,4-dihydronaphthalenecarboxylic acid by the Curtius reaction.<sup>5</sup> Other preparations include the Birch reduction of 6-methoxy-2-naphthol,<sup>6,7</sup> oxidation of 6-methoxytetralin,<sup>6,8</sup> and synthesis from 6-methoxy- $\alpha$ -tetralone.<sup>9</sup> The other practical approaches depend upon tedious preparations of naphthalene derivatives.

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### References and Notes

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### Appendix

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

hydrochloric acid (7647-01-0)

Benzene (71-43-2)

thionyl chloride (7719-09-7)

sodium hydrogen carbonate (144-55-8)

nitrogen (7727-37-9)

aluminum chloride (3495-54-3)

carbon disulfide (75-15-0)

ethylene (9002-88-4)

ammonium hydroxide (1336-21-6)

dichloromethane (75-09-2)

magnesium sulfate (7487-88-9)

phenylacetyl chloride (103-80-0)

6-methoxytetralin (1730-48-9)

6-Methoxy-2-naphthol (5111-66-0)

6-Methoxy- $\beta$ -tetralone,  
2(1H)-Naphthalenone, 3,4-dihydro-6-methoxy- (2472-22-2)

6-methoxy- $\alpha$ -tetralone (1078-19-9)

(4-methoxyphenyl)acetyl chloride (4693-91-8)

(4-methoxyphenyl)acetic acid (104-01-8)

6-methoxy-3,4-dihydronaphthalenecarboxylic acid