



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.

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.

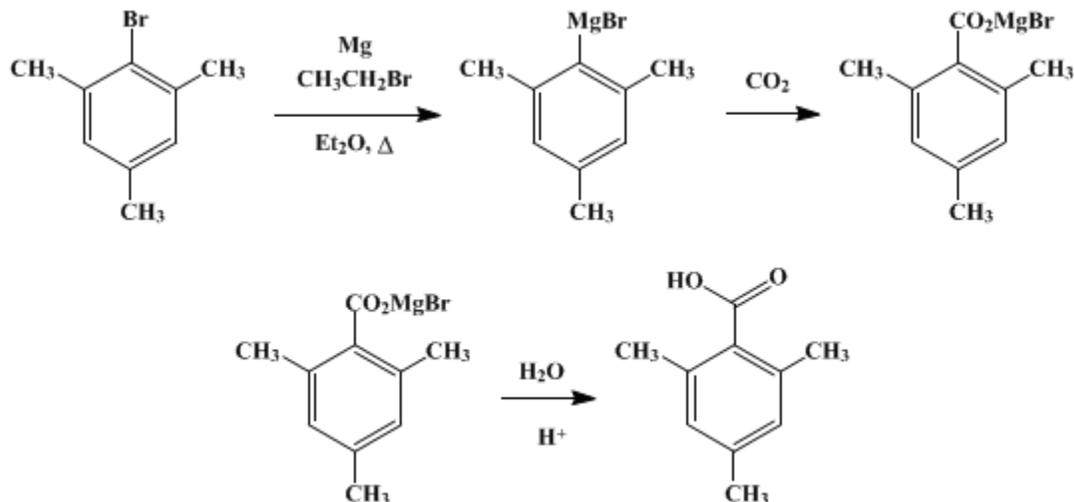
*These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.*

*Organic Syntheses, Coll. Vol. 3, p.553 (1955); Vol. 21, p.77 (1941).*

## MESITOIC ACID

### [ $\beta$ -Isodurylic acid]

#### [I. METHOD A]



Submitted by Douglas M. Bowen  
Checked by H. R. Snyder and John R. Demuth.

### 1. Procedure

In a dry 2-l. three-necked flask, equipped with a sealed wire stirrer, a condenser protected by a drying tube, and a dropping funnel, are placed 85.0 g. (3.5 gram atoms) of **magnesium turnings** and 150 ml. of dry **ether** (Note 1). A solution of 199 g. (1 mole) of carefully fractionated **bromomesitylene** and 218 g. (2 moles) of **ethyl bromide** (Note 2) in 1 l. of dry **ether** (Note 1) is placed in the funnel. Stirring is commenced, and about 25 ml. of the **ether** solution is added; the reaction begins almost at once. The rest of the solution of halides is added during the course of 1.25–1.5 hours to the vigorously refluxing mixture; moderate cooling is necessary to permit addition within the specified period. After completion of the addition, refluxing is maintained by external heating for 30 minutes. The reaction mixture is then cooled, and the solution of alkyl magnesium bromides is decanted slowly from the excess **magnesium** onto 600 g. of Dry Ice which is stirred manually in a 4-l. beaker. The Dry Ice should be in the form of small lumps, and the addition must be slow enough to avoid spattering. The flask is rinsed with two 200-ml. portions of dry **ether**, which are added to the carbonation mixture. When most of the Dry Ice has evaporated, an additional 200-g. portion is added along with 250 ml. of dry **ether**. The viscous is stirred until it becomes largely granular.

When the bulk of the Dry Ice has evaporated, 800 ml. of 20% **hydrochloric acid** and enough ice to keep the mixture cold are added with stirring. After most of the solid has dissolved, the mixture is transferred to a separatory funnel with the addition of ordinary **ether** if the volume of the organic layer is much less than 1 l. After agitation until both layers are clear, the aqueous layer is rejected, and the ethereal layer is washed with three 1-l. portions of cold water to remove **hydrochloric acid** and most of the **propionic acid** formed in the carbonation. The product is extracted by shaking first gently and then vigorously with a 540-ml. (600-g.) portion of *ice-cold* 10% **sodium hydroxide** solution. After agitation for several minutes the aqueous solution should still be strongly basic as shown by testing with a suitable indicator paper. The aqueous layer is separated and acidified with stirring by the slow addition of 250 ml. of 20% **hydrochloric acid**. The suspension is cooled, and the nearly colorless product, consisting of small granules, is collected and washed well with water. The crude acid, amounting to 141–143 g. (86–87%) (Note 3), melting at 152–154° (cor.), is satisfactory for most purposes. A purer

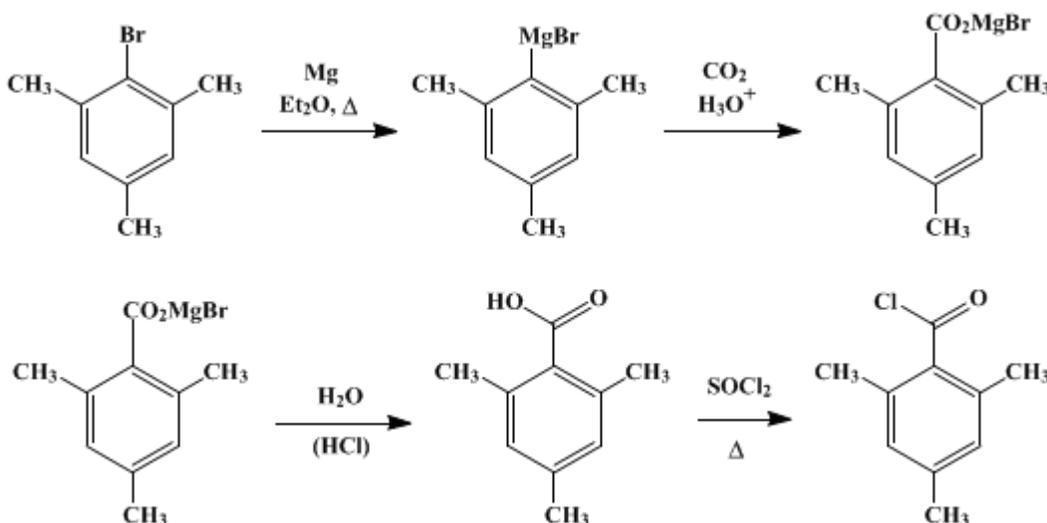
product may be obtained as large, nearly colorless crystals, m.p. 153.4–154.4° (cor.), by crystallization from a solution, saturated at the boiling point, in 45% **methanol**. The yield of the recrystallized acid is 138–141.5 g. (84–86%) (**Note 4**).

## 2. Notes

1. The checkers used commercial anhydrous **ether** which had been stored over sodium wire, and they dried the various pieces of apparatus in an oven before assembly. If the redrying of the **ether** over **sodium** was omitted, the yield was lowered appreciably.
2. When 1 mole of **ethyl bromide** is used with 1 mole of **bromomesitylene**, the yield of crude acid is 81–82%. No appreciable improvement in yield is effected by use of more than 2 equivalents of **ethyl bromide**. If the **ethyl bromide** is omitted entirely, **bromomesitylene** reacts with **magnesium** very slowly and the Grignard reagent obtained affords **mesitoic acid** in 61–66% overall yield. Except in the absence of **ethyl bromide** there is no advantage in the use of an atmosphere of **nitrogen**.
3. This procedure may be conducted on one-fifth the scale without alteration in yield.
4. The checkers employed 20 ml. of a solvent mixture containing 45% of **methanol** by weight for each 10 g. of the crude acid. To avoid the loss of **methanol** from the hot solution the operation was carried out under a reflux condenser, and the clear, nearly colorless solution was cooled rapidly without transferral. If filtration of the hot solution should be desirable a higher concentration of **methanol** would be more convenient.

## [II. METHOD B]

### [MESITOIC ACID AND MESITOYL CHLORIDE]



Submitted by R. P. Barnes

Checked by Nathan L. Drake and Ralph Mozingo.

## 1. Procedure

In a 2-l. three-necked flask, fitted with a condenser protected by a drying tube, a dropping funnel, and a sealed stirrer, are placed 24.3 g. (1 gram atom) of **magnesium turnings**, a small crystal of **iodine**, enough absolute **ether** to cover the **magnesium**, and 10 g. (0.05 mole) of **bromomesitylene**. The bottom of the flask is warmed with the hand or a warm cloth until the reaction begins. The mixture is then stirred gently during the gradual addition of 190 g. (0.95 mole) of **bromomesitylene** dissolved in 500 g. (700 ml.) of absolute **ether**. When all the ethereal solution has been added, the reaction mixture is refluxed for about 2 hours, or until all the **magnesium** has dissolved. A large excess of solid **carbon dioxide** is now added slowly in small pieces with rapid stirring (**Note 1**). The resulting tough addition product is decomposed by pouring, with stirring, into a large volume of finely crushed ice to which has

been added 100 ml. (1.2 moles) of concentrated [hydrochloric acid](#). The [ether](#) is removed by evaporation, and the resulting oily solid is filtered, dissolved in 200–400 ml. of hot [methanol](#), filtered, and thrown out by dilution with 1 l. of ice water. The crude [mesitoic acid](#) melts between 135° and 148° and weighs 110–120 g. The acid is recrystallized from petroleum ether (b.p. 90–100°), about 10 ml. of petroleum ether being used per gram of the crude acid. The product, melting at 150–152° after one recrystallization, weighs 90–100 g. (55–61%) ([Note 2](#)).

A mixture of 90 g. (0.55 mole) of [mesitoic acid](#) and 100 g. (63 ml., 0.84 mole) of [thionyl chloride](#) in a 500-ml. large-mouthed Claisen flask, with the side arm and adjacent neck closed, and with the other neck fitted with a condenser protected by a drying tube, is refluxed gently until the evolution of [sulfur dioxide](#) and [hydrogen chloride](#) ceases ([Note 3](#)). The excess [thionyl chloride](#) is removed by distillation at atmospheric pressure, and the residual acid chloride is distilled at 143–146°/60 mm. ([Note 4](#)). The yield is 90–97 g. (90–97%).

## 2. Notes

1. The Grignard reagent may be carbonated by pouring it slowly over Dry Ice contained in a 2-l. beaker. The yield is unchanged.
2. A small amount of [mesitoic acid](#) can be recovered by concentrating the filtrate to a small volume and cooling it.
3. This requires from 1 to 2 hours. The reaction mixture may also be allowed to stand overnight at room temperature, in which case no heating is necessary.
4. The boiling point varies with the rate of distillation.

## 3. Discussion

[Mesitoic acid](#) has been obtained by hydrolysis of its amide which was prepared from [mesitylene](#), [carbonyl chloride](#), and [aluminum chloride](#) in [carbon disulfide](#).<sup>1</sup> It has been prepared by heating [isodurene](#) with dilute [nitric acid](#),<sup>2,3</sup> in small yields by the distillation of [2,4,6-trimethylmandelic acid](#),<sup>4</sup> by dry distillation of [2,4,6-trimethylphenylglyoxylic acid](#),<sup>4,5</sup> by oxidation of [2,4,6-trimethylphenylglyoxylic acid](#) with [potassium permanganate](#),<sup>6</sup> and by treating [2,4,6-trimethylphenylglyoxylic acid](#) with concentrated [sulfuric acid](#) either with heating<sup>7</sup> or in the cold.<sup>8</sup> The preparation of the acid from [2,4,6-trimethylphenylmagnesium bromide](#) and a stream of [carbon dioxide](#) has been described.<sup>9</sup>

The method for the preparation of the chloride is the general method for preparing aromatic acid chlorides with [thionyl chloride](#),<sup>10</sup> which has been applied to the preparation of [mesitoyl chloride](#).<sup>9</sup>

This preparation is referenced from:

- [Org. Syn. Coll. Vol. 3, 549](#)
- [Org. Syn. Coll. Vol. 5, 706](#)

---

## References and Notes

1. Michael and Oechslin, *Ber.*, **42**, 317 (1909).
2. Jannasch and Weiler, *Ber.*, **27**, 3441 (1894).
3. Jacobsen, *Ber.*, **15**, 1853 (1882).
4. Meyer and Molz, *Ber.*, **30**, 1270 (1897).
5. Feith, *Ber.*, **24**, 3542 (1891).
6. Claus, *J. prakt. Chem.*, (2) **41**, 506 (1890).
7. van Scherpenzeel, *Rec. trav. chim.*, **19**, 377 (1900).
8. Hoogewerff and van Dorp, *Rec. trav. chim.*, **21**, 349 (1902).
9. Kohler and Baltzly, *J. Am. Chem. Soc.*, **54**, 4015 (1932).
10. Meyer, *Monatsh.*, **22**, 415 (1901).

---

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

petroleum ether

$\beta$ -Isodurylic acid

sulfuric acid (7664-93-9)

hydrogen chloride,  
hydrochloric acid (7647-01-0)

methanol (67-56-1)

ether (60-29-7)

sodium hydroxide (1310-73-2)

thionyl chloride (7719-09-7)

magnesium,  
magnesium turnings (7439-95-4)

nitric acid (7697-37-2)

potassium permanganate (7722-64-7)

propionic acid (79-09-4)

sulfur dioxide (7446-09-5)

Ethyl bromide (74-96-4)

nitrogen (7727-37-9)

carbon dioxide (124-38-9)

iodine (7553-56-2)

aluminum chloride (3495-54-3)

sodium (13966-32-0)

carbon disulfide (75-15-0)

Mesitylene (108-67-8)

Bromomesitylene (27129-86-8)

Isodurene (527-53-7)

carbamyl chloride

Mesityl chloride (938-18-1)

2,4,6-trimethylphenylglyoxylic acid (3112-46-7)

2,4,6-trimethylphenylmagnesium bromide

Mesitoic acid (480-63-7)

2,4,6-trimethylmandelic acid