



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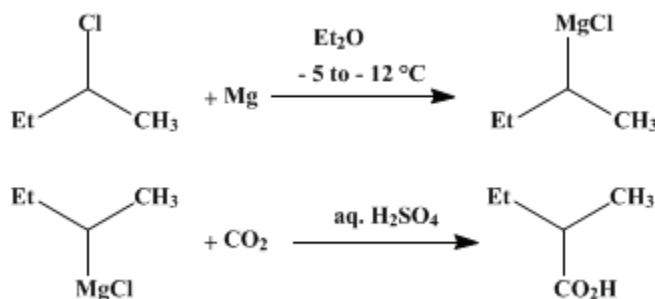
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*These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.*

*Organic Syntheses, Coll. Vol. 1, p.361 (1941); Vol. 5, p.75 (1925).*

## ***dl*-METHYLETHYLACETIC ACID**

### **[Butyric acid, $\alpha$ -methyl-]**



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### **1. Procedure**

In a 1-l. three-necked flask, fitted with a mechanical stirrer, condenser, and 500-cc. separatory funnel, is placed 13.4 g. (0.55 atom) of **magnesium shavings** (Note 1). The shavings are then covered with 50 cc. of anhydrous **ether**. A crystal or two of **iodine** and 3 g. of **sec.-butyl chloride** (Note 2) are added. The reaction is started by warming the flask with a microburner and is then allowed to proceed by its own heat for twenty minutes. A second addition of 50 cc. of anhydrous **ether** is made. A solution of 43 g. (the remainder of 0.5 mole) of **sec.-butyl chloride** in 300 cc. anhydrous **ether** is added over a period of twenty minutes. Vigorous refluxing is avoided by externally cooling the flask with water. The heat from the reaction causes refluxing to continue for twenty minutes after the addition of the halide solution. The reaction mixture is then gently refluxed for one hour with a microburner. The reaction flask is surrounded by an ice and salt mixture and the solution cooled to  $-12^\circ$  in an atmosphere of **nitrogen** (Note 3). The **nitrogen** gas, obtained directly from a cylinder, is dried by passing through two wash bottles containing concentrated **sulfuric acid** and a **phosphorus pentoxide** tower. It is admitted to the flask through an entry tube 10 mm. in diameter at a height of about 60 mm. above the surface of the ether solution. An additional 100 cc. of **ether** is added, and the separatory funnel is replaced by a thermometer.

The cylinder of **nitrogen** is then replaced by a cylinder of **carbon dioxide**. The gas after passing through the drying train enters the reaction flask through the entry tube (Note 4). The rate of flow is regulated so that the temperature of the reaction mixture does not rise above  $-5^\circ$  when rapid stirring is in progress. After one and one-half hours (Note 5) the temperature drops to  $-12^\circ$  and does not rise on increasing the rate of flow of **carbon dioxide**. The drop in temperature is taken as an end-point for the carbonation.

The reaction mixture is then hydrolyzed in the flask with about 500 cc. of 25 per cent **sulfuric acid** (Note 6). Cooling the solution with ice and water permits of rapid hydrolysis without danger of loss of material through too vigorous refluxing. The mixture is transferred to a 1-l. separatory funnel and the ether layer separated. The water layer is extracted with three 50-cc. portions of **ether**. The combined ether extracts are washed with about 150 cc. of 25 per cent **sodium hydroxide** solution until all the organic acid is converted to the salt and thus removed (Note 7) and (Note 8).

The alkaline extract is boiled in a distillation apparatus, to remove ether and other volatile impurities, until its volume is decreased by 10 per cent. It is then acidified with concentrated **hydrochloric acid** and the acid layer separated. The water layer is then distilled from a 1-l. flask until no more oily acid comes over (Note 9). The distillate is saturated with salt and the acid layer separated. This water layer, together with the low-boiling fraction from the acid distillation, is distilled, and the distillate salted out as before.

The combined acid layers are distilled from a 75-cc. flask connected to an air condenser. The product is collected at 173–174°. The yield of acid is 39–44 g. (76–86 per cent of the theoretical amount based on the quantity of *sec.*-butyl chloride used) (Note 10).

## 2. Notes

1. The magnesium shavings must circulate freely through the solution when stirred. Shavings having a width of 5.6 mm., a thickness of 0.36 mm., and a length of 3 to 16 mm. are satisfactory for this purpose.
2. If the *sec.*-butyl chloride is of a good commercial quality it need not be redistilled.
3. The preliminary sweeping with dry nitrogen was used in order to avoid decomposition of the Grignard reagent by the air which is drawn in when the flask and contents are cooled. This procedure may be omitted in some cases because the decrease in yield when nitrogen is not used is only about 3 per cent.
4. Both the nitrogen and carbon dioxide are admitted to the flask through the same entry tube. Troublesome clogging of the tube is avoided by having it above the solution instead of immersed in it.
5. The checkers found it necessary to admit carbon dioxide for two and one-half hours before the noted temperature drop was observed.
6. The reaction product solidifies if it is allowed to stand too long in the reaction flask, thus causing difficulty with the hydrolysis. Time will be saved if the acid is added immediately after the addition of the carbon dioxide is completed. A rather concentrated acid solution is used in order to keep the volume of the water layer as small as possible. For this reason, 250 cc. of 50 per cent sulfuric acid (by weight) might be used in place of the more dilute solution.
7. The products of the reaction cannot be separated smoothly by fractional distillation prior to the extraction with alkali.
8. Considerable heat is evolved in the neutralization of the acid with the sodium hydroxide. The extraction can be effected in less time and without loss if the solution is cooled by the direct addition of ice. Two extractions were used, one with 100 cc. and one with 50 cc. of 25 per cent alkali. It is convenient to test the extracts with phenolphthalein to determine when all the acid has been removed.
9. The methylethylacetic acid may also be obtained by extraction of the acidified solution with ether. This method is not recommended, as small amounts of alcohol, which are invariably present in this solvent, contaminate the product by the formation of ethyl ester.
10. By the same general method, *n*-butyl chloride gives *n*-valeric acid in a 72–73 per cent yield, bromobenzene gives benzoic acid in an 80–85 per cent yield, and cyclohexyl chloride gives cyclohexane-carboxylic acid in an 85 per cent yield.<sup>1</sup>

## 3. Discussion

*dl*-Methylethylacetic acid can be prepared from methylethyl-malonic ester, by hydrolysis and subsequent heating of the methylethylmalonic acid;<sup>2</sup> from methylethylacetoacetic ester;<sup>3</sup> and by the oxidation of the corresponding alcohol or aldehyde.<sup>4</sup> The procedure described is preferred to that which starts with *sec.*-butyl bromide<sup>5</sup> because of the higher yield of acid and the lesser cost of *sec.*-butyl chloride.

This preparation is referenced from:

- Org. Syn. Coll. Vol. 1, 524
- Org. Syn. Coll. Vol. 2, 425
- Org. Syn. Coll. Vol. 3, 541
- Org. Syn. Coll. Vol. 8, 507

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## References and Notes

1. Gilman and Zoellner, J. Am. Chem. Soc. **53**, 1945 (1931).
2. Auwers, Ann. **298**, 167 (1897).
3. Saur, Ann. **188**, 257 (1877).

4. Lieben and Zeisel, *Monatsh.* **7**, 56 (1886).
  5. Gilman and Parker, *Org. Syn.* **5**, 75. Marvel, Blomquist, and Vaughn, *J. Am. Chem. Soc.* **50**, 2810 (1928).
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**Appendix**  
**Chemical Abstracts Nomenclature (Collective Index Number);**  
**(Registry Number)**

alkali

methylethyl-malonic ester

methylethylacetoacetic ester

sulfuric acid (7664-93-9)

hydrochloric acid (7647-01-0)

ether (60-29-7)

sodium hydroxide (1310-73-2)

magnesium shavings (7439-95-4)

sec.-BUTYL BROMIDE (78-76-2)

nitrogen (7727-37-9)

Benzoic acid (65-85-0)

carbon dioxide (124-38-9)

iodine (7553-56-2)

bromobenzene (108-86-1)

n-BUTYL CHLORIDE (109-69-3)

cyclohexyl chloride (542-18-7)

Butyric acid,  $\alpha$ -methyl-,  
methylethylacetic acid,  
DL-Methylethylacetic acid (600-07-7)

phenolphthalein (77-09-8)

cyclohexane-carboxylic acid (98-89-5)

methylethylmalonic acid

phosphorus pentoxide (1314-56-3)

n-valeric acid (109-52-4)

sec.-butyl chloride (78-86-4)

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