



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.

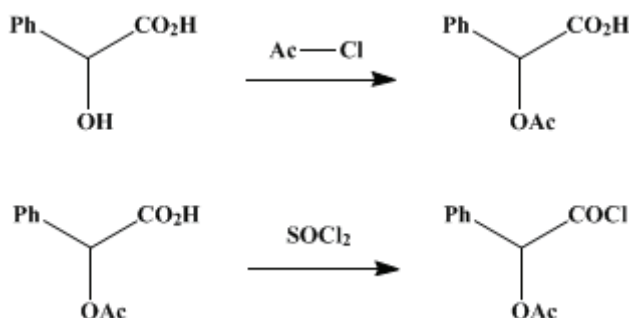
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*These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.*

*Organic Syntheses, Coll. Vol. 1, p.12 (1941); Vol. 4, p.1 (1925).*

## ACETYLMANDELIC ACID and ACETYLMANDELYL CHLORIDE

[(Mandelic acid, acetate) (Mandelyl chloride, acetate)]



Submitted by F. K. Thayer

Checked by Roger Adams and E. E. Dreger.

### 1. Procedure

(A) In a 500-cc. Claisen distilling flask with a low side tube connected to a condenser, are placed 105 g. (0.69 mole) of [mandelic acid](#) (p. 336) (m.p. 118°) and 151 g. (137 cc., 1.92 moles) of [acetyl chloride](#). A reaction sets in without the application of heat ([Note 1](#)). As soon as a clear solution results, the flask is warmed on a water bath and the excess [acetyl chloride](#) is distilled. The last trace of [acetyl chloride](#) may be removed by prolonged drying in a vacuum. The [acetylmandelic acid](#) then crystallizes in large, round, white clusters after one or two days' standing. The yield is 130–133 g. (97–99 per cent of the theoretical amount) ([Note 2](#)).

(B) To the crude [acetylmandelic acid](#) still containing some [acetyl chloride](#) obtained as described above, is added 250 g. (149 cc., 2.1 moles) of [thionyl chloride](#). The reaction starts at once without warming but it is necessary to reflux for four hours to complete the reaction ([Note 3](#)). The excess [thionyl chloride](#) is then distilled and the residue distilled under reduced pressure ([Note 4](#)). The yield is 115–120 g. (79–82 per cent of the theoretical amount) of almost colorless liquid boiling at 125–130°/10 mm. (150–155°/33 mm.).

### 2. Notes

1. Occasionally the application of a little heat is necessary to bring about a more rapid acetylation.
2. The melting points given in the literature range from 39 to 80°. The [acetylmandelic acid](#) is difficult to crystallize but may be purified from [benzene](#) or [chloroform](#), preferably the former. The product thus obtained melts at about 79–80°.
3. Prolonged refluxing of the [acetylmandelic acid](#) with the [thionyl chloride](#) tends to lower the yield.
4. The boiling point of [acetylmandelyl chloride](#) has been reported<sup>1</sup> as 129°/10 mm. The pressure should be reduced as low as possible, to avoid the formation of tar during the distillation.

### 3. Discussion

[Acetylmandelic acid](#) can be prepared by the action of [acetyl chloride](#)<sup>1</sup> or [acetic anhydride](#)<sup>2</sup> on [mandelic acid](#).

[Acetylmandelyl chloride](#) can be prepared by the action of [phosphorus pentachloride](#)<sup>1</sup> or [thionyl chloride](#)<sup>3</sup> on [acetylmandelic acid](#).

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### References and Notes

1. Anschütz and Böcker, Ann. **368**, 57, 59 (1909).
  2. Kaufler and Herzog, Ber. **42**, 3872 (1909).
  3. v. Braun and Müller, Ber. **51**, 244 (1918).
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**Appendix**  
**Chemical Abstracts Nomenclature (Collective Index Number);**  
**(Registry Number)**

[Benzene](#) (71-43-2)

[acetic anhydride](#) (108-24-7)

[phosphorus pentachloride](#) (10026-13-8)

[Acetylmandelic acid](#)

[Acetylmandelyl chloride](#) (1638-63-7)

[Mandelic acid, acetate](#) (5438-68-6)

[Mandelyl chloride, acetate](#)

[Mandelic acid](#) (90-64-2)

[acetyl chloride](#) (75-36-5)

[thionyl chloride](#) (7719-09-7)

[chloroform](#) (67-66-3)