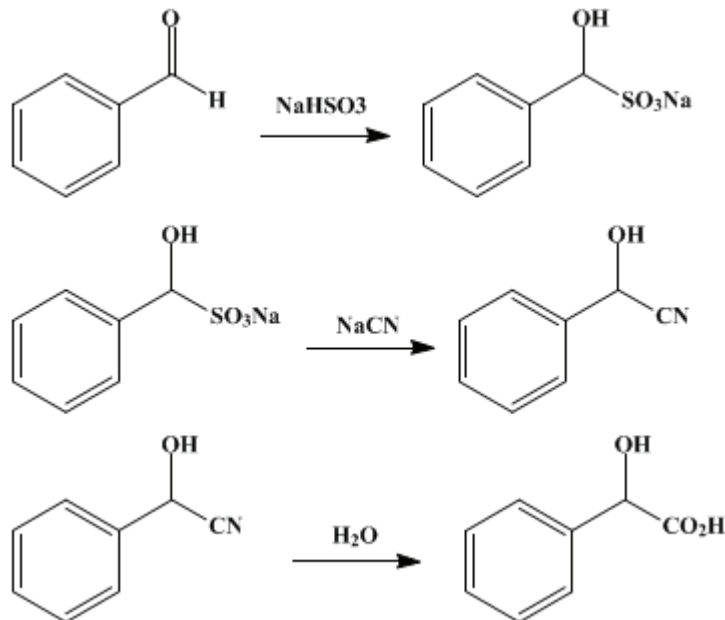


MANDELIC ACID



Submitted by B. B. Corson, Ruth A. Dodge, S. A. Harris, and J. S. Yeaw.
Checked by C. S. Marvel and M. M. Brubaker.

1. Procedure

In a 4-l. wide-mouthed glass jar, fitted with a mechanical stirrer, is placed a solution of 150 g. (3 moles) of sodium cyanide (Note 1) in 500 cc. of water and 318 g. (3 moles) of u.s.p. benzaldehyde. The stirrer is started, and 850 cc. of a saturated solution of sodium bisulfite (Note 2) is added to the mixture, slowly at first and then in a thin stream. The time of addition is ten to fifteen minutes. During the addition of the first half of this solution, 900 g. of cracked ice is added to the reaction mixture, a handful at a time. The layer of mandelonitrile which appears during the addition of the sulfite solution is separated from the water in a separatory funnel. The water is extracted once with about 150 cc. of benzene, the benzene is evaporated, and the residual mandelonitrile is added to the main portion.

The crude nitrile (about 290 cc.) is placed at once (Note 3) in a 25-cm. evaporating dish, and 425 cc. of c.p. concentrated hydrochloric acid (sp. gr. 1.19) is added. The hydrolysis is allowed to proceed in the cold (Note 4) for about twelve hours, after which the mixture is heated on a steam bath to remove the water and excess hydrochloric acid. After heating for five to six hours it is advisable to cool the mixture (Note 5) and filter the ammonium chloride and mandelic acid mixture that separates. The filtrate is then evaporated to dryness. This residue is added to the solid material obtained before. The product is deeply colored and must be dried in the air and light for at least twenty-four hours. The total yield of the crude mandelic acid-ammonium chloride mixture is 370–390 g., depending on the amount of moisture. The mixture of ammonium chloride and mandelic acid is ground in a mortar, transferred to a 2-l. flask, and washed twice with 750-cc. portions of cold benzene (Note 6). The insoluble portion is transferred to a suction funnel and sucked dry.

Either of two methods may be used to extract the mandelic acid from the ammonium chloride.

(A) *Extraction with Benzene.*—The mandelic acid is separated from the ammonium chloride by extraction with hot benzene. This is best done by dividing the solid mixture into ten approximately equal parts (Note 7). One of these portions is placed in a flask with 1 l. of boiling benzene. After a few minutes the hot benzene solution is decanted through a suction funnel (Note 8). The filtrate is cooled in an ice bath and the mandelic acid that crystallizes is filtered with suction. The benzene is returned to the

extraction flask containing the residue from the first extraction, and a new portion of the ammonium chloride-mandelic acid mixture is added and extracted as before. The process is repeated until the mandelic acid is completely removed from the ammonium chloride (Note 9).

The yield of pure white mandelic acid melting at 118° is 229–235 g. (50–52 per cent of the theoretical amount based on benzaldehyde).

(B) *Extraction with Ether* (Note 10).—The solid mixture is transferred to a 2-l. flask and shaken ten minutes with 750 cc. of ether. The ether solution is decanted through a suction filter and the solid thrown onto the filter and pressed dry. The solid is then returned to the flask and shaken with 400 cc. of ether. This mixture is filtered by suction and the solid washed twice on the filter with 250-cc. portions of ether. Each portion is allowed to drain through the filter several times while the solid is kept porous with a spatula. The combined ether filtrate is then filtered through an ordinary funnel (Note 11). The ether solution is placed in a 3-l. round-bottomed flask, and 750 cc. of toluene (Note 12) is added. The mixture is distilled on a steam bath through an efficient fractionating column as long as it distils easily, and about 1100–1400 cc. of distillate is collected. The temperature of the vapor rises to about 70°. The mixture is then heated over a free flame until the temperature in the column is 95°; about 300 cc. distils (Note 13). The residual liquid is poured while still hot into a large beaker immersed in ice water. The liquid (about 900 cc.) is stirred by hand until it has become a thick crystal mush. The cooling is continued for two hours with occasional stirring so as to bring the temperature down to 5–10°. The mixture is filtered with suction and the solid pressed dry. It is then thoroughly washed on the filter with 300 cc. of toluene in several portions (Note 14).

The yield is the same as that obtained by method (A) (Note 15).

2. Notes

1. This reaction and the subsequent hydrolysis should be carried out in a good hood as some hydrogen cyanide is liberated. The sodium cyanide used was the technical "cyan-egg," containing about 92–95 per cent of cyanide.
2. This saturated solution is best prepared by stirring 1500 g. of technical sodium bisulfite (97–100 per cent) with 2 l. of water and filtering to remove the excess salt. The specific gravity of this solution is 1.37–1.39.
3. The mandelonitrile should be mixed with hydrochloric acid as soon as it is separated from the water. This appears necessary in order to avoid a rapid conversion to the acetal of benzaldehyde and mandelonitrile, $C_6H_5CH[OCH(CN)C_6H_5]_2$. Hence if it is allowed to stand long before the hydrolysis, the yield of mandelic acid is reduced.
4. The hydrolysis can be carried out in the hot, but the final product may be deeply colored.
5. It is advisable to stir the mixture during the cooling in order to break up the lumps and thus obtain a product that can be more easily filtered.
6. If the crude product is not first washed with cold benzene the final product is usually colored. Very little mandelic acid is lost by this washing.
7. The entire amount of the ammonium chloride-mandelic acid mixture may be boiled with the benzene, but this gives a supersaturated solution of the acid in the benzene and much difficulty is met in the filtration. The solubility of mandelic acid in hot benzene is approximately 1 g. in 50 cc. It may be better to carry out the extraction in a Soxhlet apparatus or an apparatus of the type described on p. 375.
8. The funnel should be previously heated and have fairly large holes so as not to be clogged by the mandelic acid that begins to crystallize as soon as the solution cools slightly. Only slight suction should be applied during filtration.
9. Usually two or three extractions of the ammonium chloride residues after the addition of the last portion of the crude mixture are necessary in order to obtain all the mandelic acid. On concentrating the benzene used for the extraction, about 5 g. of impure mandelic acid may be obtained. To diminish mechanical losses it is recommended that the same container be used to collect and crystallize the several filtrates.
10. The ether extraction method (B) is quicker, especially when several runs are to be made. Mandelic acid is obtained in the same yield by this method. The benzene extraction may be better for small

preparations, or when a single run is to be made.

11. An occasional water layer should be removed in a separatory funnel.

12. Benzene works almost as well as toluene; xylene can also be used.

13. The temperature in the column is a better guide than the volume of distillate. A few porous chips should be added to prevent bumping. The ether-toluene solution should not stand long before distillation as mandelic acid is apt to separate. The heating with steam and with the free flame should be done quickly since prolonged heating lowers the yield.

14. The mother liquors are worked up for toluene, but it is not profitable to try to recover the small amount of impure mandelic acid which they contain.

15. The following modification is suggested for small-scale operations: When the hydrolysis of mandelonitrile is complete, the mixture is cooled, sufficient water is added to bring the solid matter into solution, and the solution is extracted thoroughly with ether. The ethereal solution is dried with sodium sulfate, the ether is distilled off from a water bath, and the mandelic acid, which does not at once solidify, is taken up in benzene and allowed to crystallize (L. F. Fieser, private communication).

3. Discussion

Mandelic acid can be prepared by the hydrolysis of amygdalin with sulfuric acid¹ or of mandelonitrile with hydrochloric acid.² The mandelonitrile can be prepared by the action of hydrocyanic acid on benzaldehyde,³ and by the action of sodium or potassium cyanide on the sodium bisulfite addition product of benzaldehyde.⁴ The procedure described differs from earlier methods in that the sodium bisulfite addition compound of benzaldehyde is prepared in the presence of sodium cyanide and the nitrile is formed immediately.

This preparation is referenced from:

- Org. Syn. Coll. Vol. 1, 12
- Org. Syn. Coll. Vol. 1, 241
- Org. Syn. Coll. Vol. 3, 538

References and Notes

1. Smith, Ber. **64**, 432 (1931); Winckler, Ann. **4**, 246 (1832).
2. Wood and Lilley, J. Chem. Soc. **127**, 95 (1925).
3. Naquet and Louguinine, Ann. **139**, 299 (1866); Wallach, Ann. **193**, 38 (1878); Spiegel, Ber. **14**, 239 (1881); Ultee, Rec. trav. chim. **28**, 254 (1909); Rule, J. Chem. Soc. **113**, 12 (1918).
4. Meister, Ber. **4**, 980 (1871); Müller, Arch. Pharm. **202**, 385 (1873); Hofmann and Schoetensack, Ger. pat. 85,230 [Fr. **4**, 160 (1894–97)]; Pape, Chem. Ztg. **20**, 90 (1896).

Appendix

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

nitrile

ammonium chloride-mandelic acid

acetal of benzaldehyde

mandelonitrile, C₆H₅CH[OCH(CN)C₆H₅]₂

amygdalin

sodium or potassium cyanide

sulfuric acid (7664-93-9)

hydrochloric acid (7647-01-0)

Benzene (71-43-2)

ether (60-29-7)

ammonium chloride (12125-02-9)

Mandelic acid (90-64-2)

sodium cyanide (143-33-9)

hydrogen cyanide,
hydrocyanic acid (74-90-8)

sodium sulfate (7757-82-6)

cyanide (57-12-5)

sodium bisulfite (7631-90-5)

benzaldehyde (100-52-7)

toluene (108-88-3)

mandelonitrile (532-28-5)

xylene (106-42-3)

mandelic acid-ammonium chloride