



A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

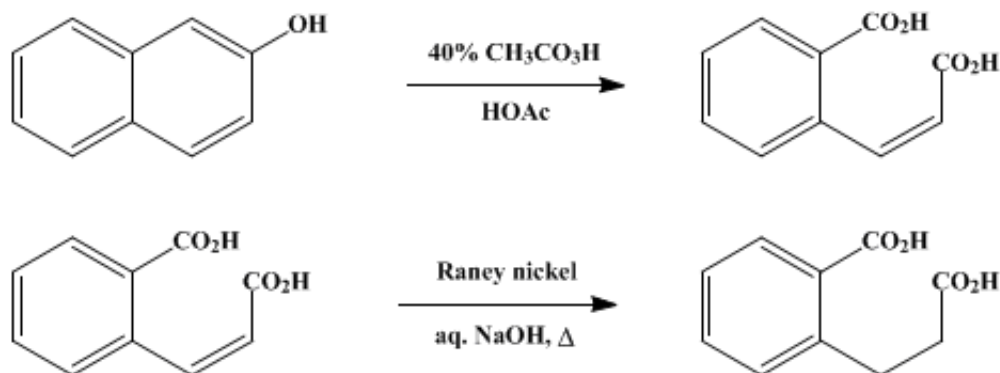
Working with Hazardous Chemicals

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). 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.

β -(*o*-CARBOXYPHENYL)PROPIONIC ACID[Hydrocinnamic acid, *o*-carboxy-]Submitted by G. A. Page and D. S. Tarbell¹.

Checked by William S. Johnson, Shirley Rosenberg, and Robert D. Eberhardt.

1. Procedure

*Caution! Reactions and subsequent operations involving peracids and peroxy compounds should be run behind a safety shield. Peroxy compounds should be added to the organic material, never the reverse. For relatively fast reactions, the rate of addition of the peroxy compound should be slow enough so that it reacts rapidly and no significant unreacted excess is allowed to build up. The reaction mixture should be stirred efficiently while the peroxy compound is being added, and cooling should generally be provided since many reactions of peroxy compounds are exothermic. New or unfamiliar reactions, particularly those run at elevated temperatures, should be run first on a small scale. Reaction products should never be recovered from the final reaction mixture by distillation until all residual active oxygen compounds (including unreacted peroxy compounds) have been destroyed. Decomposition of active oxygen compounds may be accomplished by the procedure described in Korach, M.; Nielsen, D. R.; Rideout, W. H. *Org. Synth.* 1962, 42, 50 (*Org. Synth.* 1973, Coll. Vol. 5, 414). [Note added January 2011].*

A. *o*-Carboxycinnamic acid. Eighty-eight grams (78 ml., 0.46 mole of peracid) of 40% peracetic acid (Note 1) is placed in a 250-ml. Erlenmeyer flask which is immersed in a water bath maintained at 25–30°. A 150-ml. dropping funnel is mounted so that the stem enters the flask to within about 4 cm. of the liquid surface. With mechanical stirring (Note 2), a cold solution of 20 g. (0.14 mole) of β -naphthol (Note 3) in 100 ml. of glacial acetic acid is added dropwise over a period of 4 hours to the peracid. With the appropriate rate of addition, the temperature of the reaction mixture slowly rises to 30–35° and should not exceed 40°. Solid material begins to separate from the orange solution when one-third or more of the naphthol solution is introduced. When the addition is complete, the mixture is stirred for 1 hour and the flask is allowed to stand in the water bath until the exothermic reaction ceases (usually 6–8 hours), then at room temperature for 4 days (Note 4). The solid material is collected by suction filtration and washed on the filter with sufficient (10–20 ml.) acetic acid to remove colored impurities. Drying in the air gives 19.6–20.1 g. of crude *o*-carboxycinnamic acid as a pale yellow crystalline solid (Note 4) and (Note 5).

The crude acid is purified by dissolving in 360–400 ml. of cold 5% sodium bicarbonate solution, filtering, and acidifying the filtrate with sufficient excess of mineral acid to turn Congo red paper blue. The product is separated by suction filtration, washed with water to remove mineral acid, and air-dried. Material thus obtained weighs 17.9–18.7 g. (67–70% yield). It melts generally (Note 6) between 202°

and 205°, and is sufficiently pure (Note 7) for most practical purposes.

B. β -(*o*-Carboxyphenyl)propionic acid. In an open 1-l. wide-mouthed round-bottomed flask are placed 18 g. (0.094 mole) of *o*-carboxycinnamic acid and 550 ml. of 10% sodium hydroxide solution. The mixture is warmed to 90° (Note 8) on a steam bath and stirred mechanically. The steam bath is then removed while 54 g. (Note 9) of nickel-aluminum alloy (Raney catalyst) powder is added through the open neck of the flask in small portions (from the end of a spatula) at frequent intervals (Note 10). When addition of the alloy is complete (about 50 minutes), the mixture is stirred and maintained at 90–95° for 1 hour by warming on a steam bath. Distilled water is added as needed to maintain the total volume at approximately 550 ml. The hot mixture is filtered with suction, and the metallic residue is washed with 50 ml. of hot 10% sodium hydroxide solution and two 50-ml. portions of hot water in such a manner that the solid is always covered with liquid (Note 11). The cooled filtrate and washings are added dropwise with mechanical stirring to 300 ml. of concentrated hydrochloric acid (sp. gr. 1.19) in an open 2-l. beaker at such a rate that the temperature does not exceed 80–85° (Note 12). Separation of crystalline material begins almost immediately and is complete when the beaker contents have cooled to room temperature. The β -(*o*-carboxyphenyl)propionic acid is separated by suction filtration, washed with water, and air-dried (Note 13). The yield is 16.8–17.3 g. (92–95%), m.p. 165.5–167° (Note 14).

2. Notes

1. Commercial 40% (w/w) peracetic acid is available from the Becco Sales Corporation, Buffalo 7, New York. The use of a 3.3 molecular proportion of the peracid results in slightly higher and more consistent yields of product than when the theoretical 3.0 proportion is employed. The procedure gives the same yield (percentage) of product when using proportionately smaller quantities of reactants.
2. The operator should be protected by means of a safety shield. A glass (propeller-blade) stirrer passing through the open neck of the Erlenmeyer flask is convenient; rapid stirring is not essential.
3. β -Naphthol of C.P., U.S.P., or N.F. grade has been used with equal success.
4. After 15 hours' standing, 15.0–16.8 g. of crude *o*-carboxycinnamic acid may be recovered by filtration, washing, and drying.
5. The filtrate, either on concentration under reduced pressure or upon dilution with water, fails to yield more *o*-carboxycinnamic acid, but a crystalline by-product, presumably 4-(*o*-carboxyphenyl)-5,6-benzocoumarin,² may be encountered in small yield.
6. On melting, *o*-carboxycinnamic acid cyclizes to give the lactone of β -hydroxy- β -(*o*-carboxyphenyl)propionic acid (phthalideacetic acid), m.p. 153°. If the melting point is taken too slowly, or if the diacid is not washed completely free of mineral acid, it may therefore melt considerably below 200°. The reduction step (part B), however, proceeds normally with such material.
7. The acid may be recrystallized from aqueous ethanol to give small, white, felted prisms, m.p. 205°.
8. It is advisable to insert a thermometer only at intervals since the alkaline mixture attacks glassware to an appreciable extent on prolonged contact.
9. Using less than 50 g. of the alloy results in the same yield of final product, which, however, contains small amounts of unchanged *o*-carboxycinnamic acid. Equally good results are obtained when proportionately smaller quantities of reactants are used.
10. If excessive foaming is encountered it may be controlled as required by the addition of a few drops of octyl alcohol.
11. The metallic residue may ignite if allowed to dry on the filter. Disposal can be carried out by dissolving the residue in dilute nitric acid. (*Caution! Vigorous reaction.*)
12. With this order of addition, aluminum salts remain in solution, thus simplifying the procedure. External cooling may be applied in order to save time.
13. Extraction of the filtrate with ether gives an additional 0.4–0.5 g. of the crude acid after removal of solvent by distillation. It may be purified by conventional means to give an additional 0.25–0.35 g. of the pure product.
14. β -(*o*-Carboxyphenyl)propionic acid may be recrystallized from hot water (about 20 ml./g.), giving material m.p. 166.5–167.5°.

3. Discussion

o-Carboxycinnamic acid has been prepared by the hydrolysis of *o*-carboxycinnamionitrile,³ by the opening of the lactone ring in phthalideacetic acid,^{4,5} and by the dehydration of metallic salts of β -hydroxy- β -(*o*-carboxyphenyl)propionic acid.⁴ It has also been obtained from β -naphthol by reaction with the following oxidizing agents: potassium permanganate in neutral or alkaline solutions;⁶ 30% hydrogen peroxide in acetic acid;⁷ and peracetic acid in acetic acid.⁸ β -Naphthoquinone may be oxidized to give *o*-carboxycinnamic acid, with 30% hydrogen peroxide⁹ or perbenzoic acid.¹⁰ Naphthalene also yields this acid on oxidation with peracetic acid¹¹ The procedure described here is essentially that of Böeseken and Königsfeldt and of Greenspan.⁸

β -(*o*-Carboxyphenyl)propionic acid has been prepared by the action of reagents (mostly potassium permanganate as an oxidant) upon di- and tetrahydronaphthalenes and their derivatives.¹² *o*-Carboxycinnamic acid has been reduced by means of sodium amalgam,¹³ and cinnam-*o*-hydroxamic acid has been reduced catalytically,¹⁴ to give the propionic acid. The dialdehyde of β -(*o*-carboxyphenyl)propionic acid has been oxidized to the diacid, using potassium permanganate in sodium carbonate solution.¹⁵ The diacid has also been prepared by the action of heat upon *o*-carboxybenzylmalonic acid,¹⁶ and from *o*-cyanohydrocinnamionitrile,¹⁷ β -(*o*-cyanophenyl)propionic acid,¹⁸ and ethyl *o*-cyanobenzylmalonate¹⁹ by procedures involving hydrolysis. Hydrolytic cleavage of bis(1-keto-2-hydrindylidenemethyl)hydroxylamine and of 2-cyanohydrindone-1²⁰ gives β -(*o*-carboxyphenyl)propionic acid. It has been obtained also by the nitric acid oxidation of α -tetralone.²¹ The present procedure has been published²² and is adapted from a general method for reducing cinnamic acids.²³

This preparation is referenced from:

- [Org. Syn. Coll. Vol. 4, 348](#)

References and Notes

1. University of Rochester, Rochester, New York. The submitters wish to thank the National Institutes of Health for a grant under which this work was done.
2. Bader, *J. Am. Chem. Soc.*, **73**, 3731 (1951); Dischendorfer and Danziger, *Monatsh.*, **48**, 325 (1927).
3. Beckmann and Liesche, *Ber.*, **56**, 7 (1923); Edwards, *J. Chem. Soc.*, **1926**, 816.
4. Gabriel and Michael, *Ber.*, **10**, 2203 (1877).
5. Leupold, *Ber.*, **34**, 2834 (1901); Rowe, Haigh, and Peters, *J. Chem. Soc.*, **1936**, 1104; Titley, *J. Chem. Soc.*, **1928**, 2576.
6. Ehrlich and Benedikt, *Monatsh.*, **9**, 528 (1888); Leman and Deremaux, *Bull. soc. chim. France*, **9**, 165 (1942).
7. Raacke-Fels, Wang, Robins, and Christensen, *J. Org. Chem.*, **15**, 627 (1950).
8. Böeseken and Königsfeldt, *Rec. trav. chim.*, **54**, 316 (1935); Greenspan, *Ind. Eng. Chem.*, **39**, 847 (1947).
9. Böeseken, Lichtenbelt, Milo, and van Marlen, *Rec. trav. chim.*, **30**, 146 (1911); Böeseken and Slooff, *Rev. trav. chim.*, **49**, 91 (1930).
10. Karrer and Schneider, *Helv. Chim. Acta*, **30**, 859 (1947).
11. Böeseken and Slooff, *Rec. trav. chim.*, **49**, 100 (1930).
12. Bamberger and Bammann, *Ber.*, **22**, 967 (1889); Bamberger and Helwig, *Ber.*, **22**, 1915 (1889); Bamberger and Kitschelt, *Ber.*, **23**, 1562 (1890); Straus and Ekhard, *Ann.*, **444**, 158 (1925); Straus and Lemmel, *Ber.*, **46**, 239 (1913); Straus and Rohrbacher, *Ber.*, **54**, 66 (1921).
13. Beckmann and Liesche, *Ber.*, **56**, 7 (1923); Gabriel and Michael, *Ber.*, **10**, 2204 (1877).
14. Neunhoeffler and Kölbel, *Ber.*, **68**, 262 (1935).
15. von Braun and Zobel, *Ber.*, **56**, 2140 (1923).

16. Wislicenus, *Ann.*, **242**, 39 (1887).
 17. Snyder and Poos, *J. Am. Chem. Soc.*, **71**, 1395 (1949).
 18. Linstead, Rowe, and Tuey, *J. Chem. Soc.*, **1940**, 1076; Mayer, Philipps, Ruppert, and Schmitt, *Ber.*, **61**, 1971 (1928).
 19. Mitchell and Thorpe, *J. Chem. Soc.*, **1910**, 2271.
 20. Johnson and Shelberg, *J. Am. Chem. Soc.*, **67**, 1757 (1945).
 21. Balaceanu and de Radzitzky (to Institut Français du petrole, des carburants, et lubrifiants), Brit. pat. 778,311 [*C. A.*, **52**, 1245 (1958)]; de Radzitzky and Balaceanu, *Compt. rend. 27^e congr. intern. chim. ind., Brussels*, **1954**, 2; *Ind. chim. belge*, **20**, Spec. No. 182 (1955) [*C. A.*, **50**, 15462 (1956)].
 22. Page and Tarbell, *J. Am. Chem. Soc.*, **75**, 2053 (1953).
 23. Schwenk, Papa, Whitman, and Ginsberg, *J. Org. Chem.*, **9**, 175 (1944).
-

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

peracid

nickel-aluminum alloy (Raney catalyst) powder

lactone of β -hydroxy- β -(o-carboxyphenyl)propionic acid (phthalideacetic acid)

dialdehyde of β -(o-carboxyphenyl)propionic acid

ethanol (64-17-5)

hydrochloric acid (7647-01-0)

acetic acid (64-19-7)

ether (60-29-7)

sodium hydroxide (1310-73-2)

sodium bicarbonate (144-55-8)

nitric acid (7697-37-2)

potassium permanganate (7722-64-7)

sodium carbonate (497-19-8)

naphthol (90-15-3)

β -naphthol (135-19-3)

sodium (13966-32-0)

Naphthalene (91-20-3)

hydrogen peroxide (7722-84-1)

octyl alcohol (111-87-5)

β -naphthoquinone (524-42-5)

α -Tetralone (529-34-0)

peracetic acid (79-21-0)

phthalideacetic acid (4743-58-2)

bis(1-keto-2-hydrindylidenemethyl)hydroxylamine

2-cyanohydrindone-1

Perbenzoic acid (93-59-4)

Hydrocinnamic acid, o-carboxy-,
 β -(o-Carboxyphenyl)propionic acid,
 β -(o-Carboxyphenyl)propionic acid (776-79-4)

o-Carboxycinnamic acid (612-40-8)

4-(o-carboxyphenyl)-5,6-benzocoumarin

o-carboxycinnamitrile

β -hydroxy- β -(o-carboxyphenyl)propionic acid

cinnam-o-hydroxamic acid

o-carboxybenzylmalonic acid

o-cyanohydrocinnamitrile

β -(o-cyanophenyl)propionic acid

ethyl o-cyanobenzylmalonate