Organic Syntheses

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.

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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.

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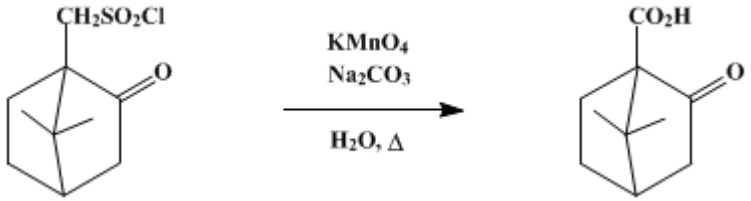
DL-KETOPINIC ACID

[1-Apocamphanecarboxylic acid, 2-oxo-]



Submitted by Paul D. Bartlett and L. H. Knox[1].
Checked by John D. Roberts

1. Procedure

A 4-l. beaker containing a solution of 100 g. (0.95 mole) of anhydrous sodium carbonate in 900 ml. of water is placed on a steam bath, provision being made for efficient mechanical stirring. The stirrer is started and, when the solution is hot, one-third of a solution of 100 g. (0.63 mole) of potassium permanganate in 600 ml. of hot water is added all at once, followed by a 34-g. portion of DL-10-camphorsulfonyl chloride (Note 1). After an interval of 5–10 minutes, half the remaining permanganate is poured in, followed by 33 g. of the chloride. After a similar interval, the remaining permanganate solution and a final 33-g. portion of the chloride are added and heating is continued for an hour.

The excess permanganate is destroyed by adding a few milliliters of an acidified solution of sodium sulfite. The reaction mixture is cooled and made strongly acidic by cautious addition (foaming may occur) of 20% sulfuric acid. The mixture is heated, and the precipitated manganese dioxide is dissolved by stirring in powdered sodium sulfite (usually 70–80 g. is required). The resulting solution is cooled and extracted with one 200-ml., two 150-ml., and one 100-ml. portions of ether. The combined ether extracts are dried over anhydrous sodium sulfate and the bulk of the ether removed by distillation from a steam bath. The residue is evaporated in a crystallizing dish (Note 2). The crude acid (38–45 g.) is recrystallized from hot water. Considerable oiling may occur and 250–400 ml. of water is usually required to give complete solution. The yield of recrystallized acid is 28–32 g. (38–43%), m.p. 233–234° (Note 3).

2. Notes

1. The camphorsulfonyl chloride is the crude product obtained as described on p. 196. If it is not carefully dried, it should be oxidized reasonably promptly after its preparation. The oxidation is conveniently carried out in 100-g. portions. Several reactions can easily be carried out in parallel.
2. The checker found it convenient to use a rotary evaporator at this point.
3. An additional small crop of crystals may be obtained by concentration of the mother liquor. The checker observed m.p. 240–242°.

3. Discussion

DL-Ketopinic acid has been prepared by oxidation of bornyl chloride with nitric acid at 20°[2] or with perbenzoic acid in acetic acid;[3] from 10,10-dinitrocamphan-2-ol[4] or apocamphan-2-ol-1-carboxylic acid[5] with alkaline permanganate; and from the oxidation of 10-camphorchlorosulfoxide, obtained from 10-camphorsulfonyl chloride by the action of pyridine, with potassium permanganate.[6] The present procedure represents a simplification of the latter and gives as high an overall yield.[7]

4. Merits of the Preparation

Ketopinic acid is of interest as a β-keto acid which fails to decarboxylate readily.[8] It may be

converted to apocamphane-1-carboxylic acid.[7]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 5, 196

References and Notes

1. Converse Memorial Laboratory, Harvard University, Cambridge, Massachusetts. Preparation was submitted November 1, 1939.
2. H. E. Armstrong, *J. Chem. Soc.*, **69**, 1397 (1896).
3. G. Gallas and J. M. Montañés, *Anales Soc. Espan. Fis. Quim.*, **28**, 1163 (1930) [*C.A.*, **25**, 506 (1931)].
4. P. Lipp, *Ann.*, **399**, 241 (1913).
5. J. Bredt and R. May, *Chem. Ztg.*, **34**, 65 (1910) [*C.A.*, **4**, 1476 (1910)].
6. E. Wedekind, *Ber.*, **57**, 664 (1924).
7. P. D. Bartlett and L. H. Knox, *J. Am. Chem. Soc.*, **61**, 3184 (1939).
8. For references and discussion, F. S. Fawcett, *Chem. Rev.*, **47**, 219 (1950).

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

DL-Ketopinic acid

D,L-ketopinic acid

ketopinic acid

1-Apocamphanecarboxylic acid, 2-oxo-

apocamphan-2-ol-1-carboxylic acid

10-camphorchlorosulfoxide

apocamphane-1-carboxylic acid

sulfuric acid (7664-93-9)

acetic acid (64-19-7)

ether (60-29-7)

sodium sulfite (7757-83-7)

nitric acid (7697-37-2)

potassium permanganate (7722-64-7)

sodium carbonate (497-19-8)

sodium sulfate (7757-82-6)

pyridine (110-86-1)

manganese dioxide (1313-13-9)

Perbenzoic acid (93-59-4)

10-CAMPHORSULFONYL CHLORIDE,
camphorsulfonyl chloride,
DL-10-Camphorsulfonyl chloride (6994-93-0)

10,10-dinitrocamphan-2-ol

bornyl chloride (464-41-5)

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