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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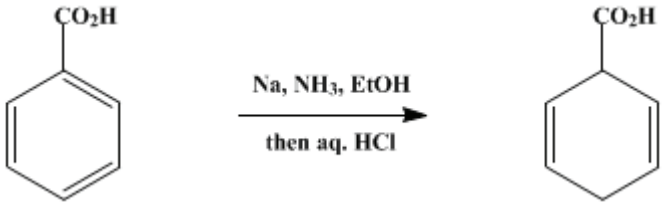
1,4-DIHYDROBENZOIC ACID

[2,5-Cyclohexadiene-1-carboxylic acid]



Submitted by M. E. Kuehne and B. F. Lambert[1].
Checked by Louise Kuda and V. Boekelheide.

1. Procedure

Ten grams (0.082 mole) of benzoic acid is added to 100 ml. of anhydrous ethanol in a 2-l. three-necked flask equipped with a mechanical stirrer and with loose cotton plugs in the side necks. After the benzoic acid has dissolved, 600 ml. of liquid ammonia (Note 1) is added to the stirred solution. Then 6.2 g. (0.27 g. atom) of sodium is added in small pieces. When about one-third of the sodium has been added, the white sodium salt of the acid precipitates, and there is strong foaming of the reaction mixture. After all the sodium has been consumed, as evidenced by the disappearance of the blue color, 14.6 g. (0.27 mole) of ammonium chloride is added cautiously. The mixture is stirred for an additional hour and then allowed to stand until the ammonia has evaporated.

The residue is dissolved in 300 ml. of water. The solution is poured onto 200 g. of ice and acidified to a pH of about 4 by addition of 75 ml. of 10% hydrochloric acid. The resulting mixture is extracted with four 100-ml. portions of peroxide-free ether, and the combined extracts are washed with 50 ml. of a saturated aqueous solution of sodium chloride and dried over 2 g. of anhydrous magnesium sulfate (Note 2). The ether solution is separated from the drying agent and concentrated at room temperature under reduced pressure. The residual oil is distilled from a 25-ml. Claisen flask with an indented neck. 1,4-Dihydrobenzoic acid is obtained as a colorless oil; weight 9.0–9.7 g. (89–95%); b.p. 80–98°/0.01 mm.; n_D^{24} 1.5011. This material is sufficiently pure for most purposes. However, by a careful redistillation, a small fore-run (b.p. 80–90°/0.01 mm.; n_D^{24} 1.5000) can be separated, and the remainder of the material (b.p. 91–97°/0.01 mm.; n_D^{24} 1.5019) solidifies on cooling; m.p. 15–17° (Note 3). It is stored under nitrogen in a closed vessel (Note 4).

2. Notes

1. Arrangements for cooling or condensing the ammonia can be made, but are not necessary. Most simply, the liquid ammonia can be passed directly from a cylinder into the reaction vessel through heavy rubber tubing.
2. 1,4-Dihydrobenzoic acid has a very penetrating, repulsive odor, and care should be taken to avoid contamination of hands or clothing.
3. Samples of the 1,4-dihydrobenzoic acid, after both the first and the second distillations, are transparent in the ultraviolet region between 220 mμ and 300 mμ, indicating the absence of benzoic acid or conjugated dihydrobenzoic acids. The refractive index cited in Reference [2] is in error.
4. In the presence of air, 1,4-dihydrobenzoic acid slowly gives benzoic acid and hydrogen peroxide.[3]

3. Discussion

Apparently, 1,4-dihydrobenzoic acid has been prepared only by the Birch reduction of benzoic acid, as illustrated by the present procedure.[3,2]

4. Merits of the Preparation

This procedure is illustrative of the general method of reduction of aromatic compounds by alkali metals in liquid ammonia known as the Birch reduction. The theoretical and preparative aspects of the Birch reduction have been discussed in excellent reviews,[4,5,6] and there is another example of a Birch reduction in *Organic Syntheses*.[7] Of particular interest in the present procedure is the effect of having a group that forms a stable anion with the alkali metal. For both simple aromatic acids and amides, a Birch reduction gives the corresponding 1,4-dihydro derivative. The same is true when *o*-alkyl or *o*-methoxyl groups are present. However, with *p*-alkyl or *m*-methoxyl substituents, the corresponding tetrahydro derivatives are formed. *p*-Methoxyl or *p*-acetamino groups, which can form stable anionic fragments, are lost during such reductions.

The following examples may be cited to illustrate these generalizations. *p*-Toluic acid under conditions of the Birch reduction essentially as given in this procedure yields mainly 1,2,3,4-tetrahydro-*p*-toluic acid (*cis* and *trans*) plus minor amounts of 1,4-dihydro-*p*-toluic acid (*cis* and *trans*).[2] *o*-Toluic acid gives 1,4-dihydro-*o*-toluic acid in 73% yield;[8] *m*-methoxybenzoic acid gives 1,4,5,6-tetrahydro-3-methoxybenzoic acid in 32% yield;[9] *o*-methoxybenzoic acid gives crude 1,4-dihydro-2-methoxybenzoic acid in 80% yield;[10] 3,4,5-trimethoxybenzoic acid gives 1,4-dihydro-3,5-dimethoxybenzoic acid in 87% yield;[2] 4-acetaminobenzoic acid gives 1,4-dihydrobenzoic acid in 75% yield;[2] benzamide gives 1,4-dihydrobenzamide in 69% yield;[2] *m*-methoxybenzamide gives 1,4-dihydro-3-methoxybenzamide in 30% yield;[2] 3,4,5-trimethoxybenzamide gives 1,4-dihydro-3,5-dimethoxybenzamide in 73% yield;[2] and 3,5-dimethoxybenzamide gives 1,4-dihydro-3,5-dimethoxybenzamide in 59% yield.[2] Thus the present example of the Birch reduction illustrates a useful and general synthetic method for preparing dihydro aromatic derivatives.

References and Notes

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

ethanol (64-17-5)

hydrochloric acid (7647-01-0)

ammonia (7664-41-7)

ammonium chloride (12125-02-9)

sodium chloride (7647-14-5)

nitrogen (7727-37-9)

Benzoic acid (65-85-0)

benzamide (55-21-0)

sodium (13966-32-0)

hydrogen peroxide (7722-84-1)

3,4,5-trimethoxybenzoic acid (118-41-2)

acetamino

magnesium sulfate (7487-88-9)

methoxyl (2143-68-2)

p-Toluic acid (99-94-5)

1,4-Dihydrobenzoic acid,
2,5-Cyclohexadiene-1-carboxylic acid (4794-04-1)

1,4,5,6-tetrahydro-3-methoxybenzoic acid

1,4-dihydro-2-methoxybenzoic acid

1,4-dihydro-3,5-dimethoxybenzoic acid

4-acetaminobenzoic acid (556-08-1)

1,4-dihydrobenzamide

1,4-dihydro-3-methoxybenzamide

3,4,5-trimethoxybenzamide (3086-62-2)

1,4-dihydro-3,5-dimethoxybenzamide

3,5-dimethoxybenzamide (17213-58-0)

o-Toluic acid (118-90-1)

o-methoxybenzoic acid (579-75-9)

m-methoxybenzoic acid (586-38-9)

1,2,3,4-tetrahydro-p-toluic acid

1,4-dihydro-p-toluic acid

1,4-dihydro-o-toluic acid

m-methoxybenzamide (5813-86-5)