



A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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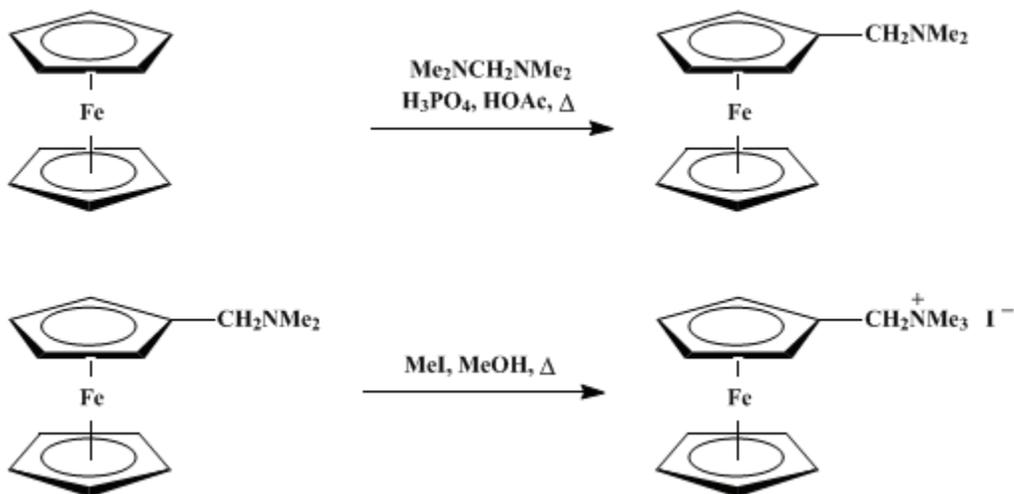
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 5, p.434 (1973); Vol. 40, p.31 (1960).

N,N-DIMETHYLAMINOMETHYLFERROCENE METHIODIDE

[Iron, cyclopentadienyl]((dimethylaminomethyl)cyclopentadienyl)-, methiodid]



Submitted by Daniel Lednicer and Charles R. Hauser¹.

Checked by B. C. McKusick, W. A. Sheppard, R. D. Vest, and H. F. Mower.

1. Procedure

Caution! Bis(dimethylamino) methane is a potent lachrymator, so it should be handled only in a hood.

Ferrocene (46.4 g., 0.250 mole) (Note 1) is added to a well-stirred solution of 43.2 g. (0.422 mole) of bis(dimethylamino)-methane (Note 2) and 43.2 g. of phosphoric acid in 400 ml. of acetic acid in a 2-l. three-necked round-bottomed flask equipped with a condenser, a nitrogen inlet, and a mechanical stirrer (Note 3). The resulting suspension is heated on a steam bath under a slow stream of nitrogen (Note 4) for 5 hours (Note 5). The reaction mixture, a dark-amber solution, is allowed to cool to room temperature and is diluted with 550 ml. of water. The unreacted ferrocene is removed by extracting the solution with three 325-ml. portions of ether. The aqueous solution is then cooled in ice water and made alkaline by the addition of 245 g. of sodium hydroxide pellets. The tertiary amine separates from the alkaline solution as an oil in the presence of some black tar (Note 6). The mixture is extracted with three 500-ml. portions of ether. The organic solution is washed with water and dried over sodium sulfate. Crude dimethylaminomethylferrocene is obtained as a dark-red mobile liquid when the solvent is removed at the water pump (Note 7).

To a gently swirled solution of the crude amine in 54 ml. of methanol is added 54 ml. (123 g., 0.87 mole) of methyl iodide. The solution is heated on a steam bath for 5 minutes and cooled to room temperature, and 800 ml. of ether is added. The methiodide, which separates as an oil, crystallizes on being scratched. The solid is collected on a Büchner funnel, washed with ether, and dried at 20–50 mm. for several hours at room temperature to yield 65–78 g. (68–81%; (Note 8)) of N,N-dimethylaminomethylferrocene methiodide as an orange powder, m.p. 200° (dec.) (Note 9).

2. Notes

1. The ferrocene may be prepared by Wilkinson's procedures² or it may be purchased from Matheson, Coleman and Bell, East Rutherford, New Jersey, and other companies.

2. The amine, under the name N,N,N',N'-tetramethylmethylenediamine, may be purchased from Ames

Laboratories, South Norwalk, Connecticut. The checkers prepared it by the following procedure. A solution of 60.7 g. (0.75 mole) of 37% aqueous formaldehyde solution is placed in an 800-ml. beaker equipped with a mechanical stirrer and thermometer, and cooled in an ice bath. Two hundred seventy-one grams (1.50 moles) of a 25% aqueous solution of dimethylamine is added to this solution at a rate such that the reaction temperature is kept below 15°. The solution is stirred for 30 minutes after the addition is complete, and potassium hydroxide pellets (approximately 150 g.) are added in portions until the reaction mixture separates into two layers. The upper layer is separated, dried over potassium hydroxide pellets overnight, and distilled to give 59–64 g. (77–83%) of bis (dimethylamino) methane, b.p. 83–84°. ³

3. The mixing of the amine and acids is exothermic. It is necessary to add the amine dropwise to the solution of acids with stirring and cooling in an ice bath.

4. Since ferrocene and many of its derivatives are easily oxidized by air in the presence of acids, nitrogen is passed in at a rate sufficient to exclude air from the system.

5. It was found that the reaction is essentially complete after 5 hours. Further heating does not affect the yield.

6. The checkers found that the solution turned into a gel after the addition of sodium hydroxide. They obtained satisfactory results by adding 200 ml. of water to the gel, which made it fluid enough to be extractable with ether.

7. Distillation of the tertiary amine before methiodide formation does not significantly affect the yield or purity of the quaternary salt. The amine boils at 91–92°/0.45 mm.

8. The submitters report yields as high as 89%.

9. The melting point of this compound is ill-defined by reason of considerable darkening and shrinking that start at 175°. The product thus obtained is sufficiently pure for use in further reactions. ⁴

3. Discussion

This procedure is based on the method of Lindsay and Hauser³ as modified slightly by Osgerby and Pauson.⁵ N,N-dimethylaminomethylferrocene methiodide has also been prepared by heating formylferrocene with dimethylamine and hydrogen in the presence of Raney nickel catalyst to give dimethylaminomethylferrocene, which was quaternized with methyl iodide.⁶

Essentially the present procedure converted 1-methylindole to 1-methyl-3-(N,N-dimethylaminomethyl)indole⁷ and α -methylstyrene to α -(N,N-dimethylaminoethyl)styrene.⁸

This preparation is referenced from:

- Org. Syn. Coll. Vol. 5, 578
- Org. Syn. Coll. Vol. 5, 621

References and Notes

1. Department of Chemistry, Duke University, Durham, North Carolina. The work was supported by the Office of Ordnance Research, U. S. Army.
 2. G. Wilkinson, *Org. Syntheses*, Coll. Vol. 4, 473 (1963).
 3. J. K. Lindsay and C. R. Hauser, *J. Org. Chem.*, **22**, 355 (1957).
 4. D. Lednicer, J. K. Lindsay, and C. R. Hauser, *J. Org. Chem.*, **23**, 653 (1958).
 5. J. M. Osgerby and P. L. Pauson, *J. Chem. Soc.*, 656 (1958).
 6. P. J. Graham, K. V. Lindsey, G. W. Parshall, M. L. Peterson, and G. M. Whitman, *J. Am. Chem. Soc.*, **79**, 3416 (1957).
 7. H. R. Snyder and E. L. Eliel, *J. Am. Chem. Soc.*, **70**, 1703 (1948).
 8. G. F. Hennion, C. C. Price, and V. C. Wolff, Jr., *J. Am. Chem. Soc.*, **77**, 4633 (1955); C. J. Schmidle and R. C. Mansfield, *ibid.*, **77**, 4636 (1955).
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Appendix
Chemical Abstracts Nomenclature (Collective Index Number);
(Registry Number)

Ferrocene

N,N-Dimethylaminomethylferrocene methiodide

Iron, cyclopentadienyl[(dimethylaminomethyl)cyclopentadienyl]-, methiodid

dimethylaminomethylferrocene

formylferrocene

acetic acid (64-19-7)

methanol (67-56-1)

ether (60-29-7)

hydrogen (1333-74-0)

sodium hydroxide (1310-73-2)

formaldehyde (50-00-0)

sodium sulfate (7757-82-6)

nitrogen (7727-37-9)

Raney nickel (7440-02-0)

potassium hydroxide (1310-58-3)

phosphoric acid (7664-38-2)

Methyl iodide (74-88-4)

dimethylamine (124-40-3)

Bis(dimethylamino) methane,
bis (dimethylamino) methane,
bis(dimethylamino)-methane,
N,N,N',N'-tetramethylmethylenediamine (51-80-9)

1-Methylindole (603-76-9)

1-methyl-3-(N,N-dimethylaminomethyl)indole

α -(N,N-dimethylaminoethyl)styrene

α -methylstyrene (98-83-9)

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