



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.

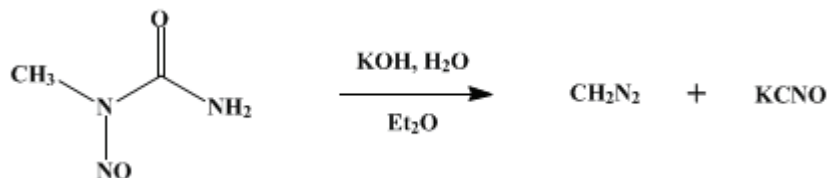
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 2, p.165 (1943); Vol. 15, p.3 (1935).

DIAZOMETHANE

[Methane, diazo-]



Submitted by F. Arndt

Checked by C. R. Noller and I. Bergsteinsson.

1. Procedure

Diazomethane is highly toxic. The utmost care is essential in the preparation and use of this material.

In a 500-cc. round-bottomed flask are placed 60 cc. of 50 per cent aqueous potassium hydroxide solution and 200 cc. of ether. The mixture is cooled to 5°, and 20.6 g. (0.2 mole) of nitrosomethylurea (p. 461) is added with shaking. The flask is fitted with a condenser set for distillation. The lower end of the condenser carries an adapter passing through a two-holed rubber stopper and dipping below the surface of 40 cc. of ether contained in a 300-cc. Erlenmeyer flask and cooled in an ice-salt mixture. The exit gases are passed through a second 40-cc. portion of ether likewise cooled below 0°. The reaction flask is placed in a water bath at 50° and brought to the boiling point of the ether with occasional shaking. The ether is distilled until it comes over colorless, which is usually the case after two-thirds of the ether has been distilled. Under no circumstances should all the ether be distilled. The combined ether solutions in the receiving flasks contain from 5.3 to 5.9 g. of diazomethane (63–70 per cent of the theoretical amount) (Note 1) and (Note 2), which is sufficiently dry for most purposes (Note 3).

If a dry solution of diazomethane is required, the ether solution is allowed to stand for three hours over pellets of pure potassium hydroxide (Note 4). For extremely dry solutions, further drying is effected with sodium wire.

2. Notes

- For analysis an aliquot portion (about one-twentieth) of the solution is allowed to react at 0° with a solution of an accurately weighed sample of about 1.3 g. of pure benzoic acid in 50 cc. of absolute ether. The benzoic acid must be in excess as evidenced by the complete decolorization of the diazomethane solution. The unreacted benzoic acid is titrated with standard 0.2 N alkali.
- The same procedure may be used for preparing two or three times the quantity obtained here.
- The ether solution does not contain ammonia or methyl alcohol. It does contain traces of methylamine, but this is also present when diazomethane is prepared from nitrosomethylurethane. If one does not require a pure, water-free solution, as is frequently the case when carrying out tests with small amounts of material, a simplified procedure may be used. To 100 cc. of ether is added 30 cc. of 40 per cent potassium hydroxide, and the mixture is cooled to 5°. To this, with continued cooling and shaking, is added 10 g. of finely powdered nitrosomethylurea in small portions over a period of one to two minutes. The deep yellow ether layer can be decanted readily; it contains about 2.8 g. of diazomethane, together with some dissolved impurities and water. The water may be removed by drying for three hours over pellets of pure potassium hydroxide. Solutions of diazomethane in benzene and other water-immiscible organic solvents may be prepared in the same way.
- Broken sticks should not be used as the sharp corners facilitate the decomposition of the diazomethane.

3. Discussion

There are four methods of practical importance for the preparation of [diazomethane](#): the action of alcoholic [potassium hydroxide](#)¹ or [sodium](#) dissolved in glycol² on [nitrosomethylurethane](#); heating a mixture of [potassium hydroxide](#), [chloroform](#), [hydrazine hydrate](#), and absolute [alcohol](#);³ the action of [potassium hydroxide](#) on [nitrosomethylurea](#),⁴ the method described above; and the action of alkoxides on the nitroso derivative of β -methylaminoisobutyl methyl ketone.⁵ The choice of a method will usually depend upon the availability of the starting material. Directions for the preparation of the starting materials used in the first three methods are given in this volume; directions for preparing the nitroso derivative of β -methylaminoisobutyl methyl ketone and from it [diazomethane](#) will appear in a forthcoming volume of Organic Syntheses.

Arndt, Loewe, and Avan have discussed the merits of the various methods of preparing [diazomethane](#),⁶ as has Eistert.⁷

This preparation is referenced from:

- [Org. Syn. Coll. Vol. 3, 244](#)
- [Org. Syn. Coll. Vol. 4, 250](#)
- [Org. Syn. Coll. Vol. 5, 231](#)
- [Org. Syn. Coll. Vol. 5, 245](#)
- [Org. Syn. Coll. Vol. 5, 351](#)
- [Org. Syn. Coll. Vol. 5, 877](#)
- [Org. Syn. Coll. Vol. 5, 1099](#)
- [Org. Syn. Coll. Vol. 6, 432](#)
- [Org. Syn. Coll. Vol. 6, 613](#)
- [Org. Syn. Coll. Vol. 8, 196](#)
- [Org. Syn. Coll. Vol. 9, 300](#)

References and Notes

1. v. Pechmann, *Ber.* **27**, 1888 (1894); **28**, 855 (1895).
 2. Meerwein and Burneleit, *ibid.* **61**, 1845 (1928).
 3. Staudinger and Kupfer, *ibid.* **45**, 505 (1912).
 4. Arndt and Amende, *Angew. Chem.* **43**, 444 (1930); Arndt and Scholz, *ibid.* **46**, 47 (1933).
 5. Adamson and Kenner, *J. Chem. Soc.* **1935**, 286; **1937**, 1551.
 6. Arndt, Loewe, and Avan, *Ber.* **73**, 606 (1940).
 7. Eistert, *Angew. Chem.* **54**, 99, 124 (1941).
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Appendix Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

nitroso derivative of β -methylaminoisobutyl methyl ketone

[alcohol](#) (64-17-5)

[ammonia](#) (7664-41-7)

[Benzene](#) (71-43-2)

methyl alcohol (67-56-1)

ether (60-29-7)

chloroform (67-66-3)

Benzoic acid (65-85-0)

potassium hydroxide (1310-58-3)

sodium,
sodium wire (13966-32-0)

hydrazine hydrate (7803-57-8)

methylamine (74-89-5)

Diazomethane,
Methane, diazo- (334-88-3)

Nitrosomethylurea

Nitrosomethylurethane