



A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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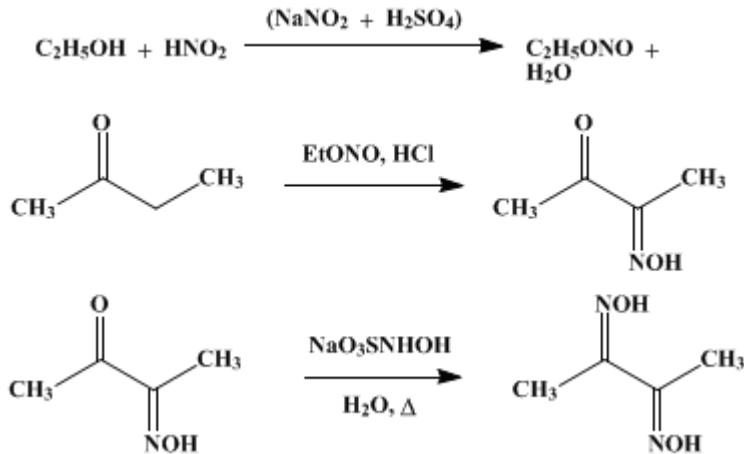
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 2, p.204 (1943); Vol. 10, p.22 (1930).

DIMETHYLGLYOXIME

[Glyoxime, dimethyl-]



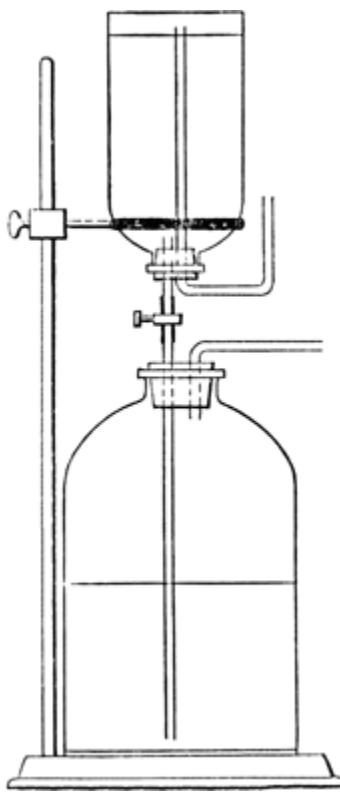
Submitted by W. L. Semon and V. R. Damerell.
Checked by Henry Gilman and R. E. Fothergill.

1. Procedure

(A) *Ethyl Nitrite*.—Two solutions are prepared. Solution I contains 620 g. (9 moles) of sodium nitrite (650 g. of technical 95 per cent quality), 210 g. (4.6 moles) of alcohol (285 cc. of 90 per cent denatured alcohol, or its equivalent), and water to make a total volume of 2.5 l. Solution II contains 440 g. of sulfuric acid (255 cc. of sp. gr. 1.84) and 210 g. of alcohol, diluted with water to 2.5 l. *Ethyl nitrite* may be generated continuously in gaseous form by allowing solution II to flow into solution I.

The gas can be conveniently made by putting solution II in a 2.5-l. bottle fitted with a two-holed rubber stopper (Fig. 7) and provided with glass tubing as indicated in the diagram. The rate of flow of solution II into a 6-l. bottle containing solution I is regulated by a screw clamp. The *ethyl nitrite* generated flows out of the second opening in the stopper of the lower bottle. The stoppers to both bottles should be wired on. A mechanical stirrer in the lower bottle is helpful in securing a steady evolution of the gas (Note 1).

Fig. 7



(B) *Biacetyl Monoxime*.—In a 2-l. three-necked flask provided with a condenser, a thermometer, and an inlet tube for ethyl nitrite, and arranged for external cooling, is placed 620 g. of commercial methyl ethyl ketone which has been dried with, and filtered from, 75 g. of anhydrous copper sulfate. Forty cubic centimeters of hydrochloric acid (sp. gr. 1.19) is added (Note 2) and the temperature raised to 40°. The ethyl nitrite from the preceding preparation is now bubbled in, the temperature being maintained between 40° and 55°. After all the ethyl nitrite has been passed in (Note 3) the crude product may be used in the preparation of dimethylglyoxime by distilling off the alcohol formed in the reaction until the temperature of the liquid reaches 90° (Note 4).

If pure biacetyl monoxime is desired, the crude product is neutralized with about 35 cc. of concentrated aqueous ammonia and diluted with half its volume of water. It is then distilled to remove alcohol, etc., until the distillate is no longer inflammable. The receiver is changed, and the contents are now rapidly distilled, using superheated steam. Almost all the biacetyl monoxime comes over in the first 5 l. of distillate. One to 1.5 kg. of salt is dissolved in the distillate, which is then cooled to 0°. The solid biacetyl monoxime crystallizes and may be filtered. The yield is 480–520 g. The product can be further purified, if desired, by recrystallizing from water (Note 5).

(C) *Sodium Hydroxylamine Monosulfonate*.—In a 12-l. crock are mixed 5 kg. of shaved ice (Note 6) and 569 g. of sodium nitrite (594 g. of the technical 95 per cent quality). Into this is stirred a suspension of sodium bisulfite containing 1.1 kg. of available sulfur dioxide (about 1775 g. of technical bisulfite) in 750 cc. of water. Then, beneath the surface of the solution is added, with constant stirring, 150 cc. of glacial acetic acid (Note 7) followed by a mixture of 550 cc. of concentrated hydrochloric acid (sp. gr. 1.19) with 400 g. of shaved ice (Note 8). The entire solution should always remain below 0°, further ice being added if there is a tendency for the temperature to rise. The solution should now become acid to Congo red paper and contain 6 or more moles of the sodium hydroxylamine disulfonate, which rapidly hydrolyzes to an acid solution of the monosulfonate.

(D) *Dimethylglyoxime*.—The crude biacetyl monoxime remaining after distilling to 90°, and containing about 5 moles of biacetyl monoxime, is added to the sodium hydroxylamine monosulfonate solution (which has been filtered to remove any sediment) and which is contained in a 15-l. flask. It is heated to 70° and allowed to remain warm (with occasional stirring) for several hours (Note 9). The

dimethylglyoxime separates in crystals which can be filtered from the solution as soon as it has become cold (Note 10). The crystals are washed with cold water until free of sulfate. The yield of compound melting at 238–240° is 540–575 g.

Recrystallization is unnecessary since the product is pure white and free from tarry material (Note 5).

(E) **Sodium Dimethylglyoximate**.—To a solution of 75 g. of **sodium hydroxide** in 300 cc. of water is added, with stirring, 100 g. of **dimethylglyoxime** (Note 11). Heat is applied to effect solution (Note 12), and the mixture is filtered from any slight residue. The solution is poured while hot into 500 cc. of 95 per cent **alcohol**. After cooling to 5°, with stirring, the crystals which form are filtered, then suspended in 150 cc. of **alcohol** and again filtered, and finally dried at 25° until the solid has no odor of alcohol (Note 13). The yield is 213–230 g. (81–88 per cent of the theoretical amount) of the octahydrate.

2. Notes

1. If a mechanical stirrer is not used attention is necessary to prevent a layer of solution II from collecting at the bottom of solution I, since, under these conditions, a little shaking produces too violent an evolution of gas.

Because **ethyl nitrite** is harmful if inhaled continuously, the reaction should be run in a hood or out of doors.

2. The **methyl ethyl ketone** should not be allowed to stand any length of time between the addition of the **hydrochloric acid** and the treatment with **ethyl nitrite**, inasmuch as the acid causes a condensation of the ketone with itself, thereby lowering the yield of **biacetyl monoxime**.

3. The **ethyl nitrite** may be passed into the solution as rapidly as possible, provided that the temperature does not exceed 55°. Very complete absorption takes place, and the time of addition is about one and one-half hours.

4. This distillation for the removal of alcohol and excess **methyl ethyl ketone** should not stop before the temperature of the liquid reaches 90° or continue after this temperature is attained. If the distillation is stopped too soon, the alcohol that was not removed later increases the solubility of the **dimethylglyoxime**; too high a temperature causes the formation of tarry products. Both factors reduce the yield.

5. About 70–80 per cent of the **biacetyl monoxime** is recovered on crystallization. Practically all the monoxime left in the mother liquor can be recovered by steam distillation. The recrystallized and dried compound melts at 76.5°. Purification by distillation is not recommended.

Biacetyl monoxime turns brown rapidly after preparation; it must not be allowed to stand before adding it to the hydroxylamine monosulfonate in the preparation of **dimethylglyoxime** if this final product is to be obtained in a colorless condition.

6. Shaved ice is used in place of crushed ice because of more efficient cooling. The use of snow is advised, if it is available.

7. The **acetic acid** helps to buffer the solution and maintain a low hydrogen-ion concentration, which is favorable for a good yield.

8. The acid may be added as rapidly as desired so long as the temperature remains below 0° and no evolution of gas takes place. The entire addition should require not more than fifteen minutes.

9. The mixture is warmed to hasten the hydrolysis of disulfonate to monosulfonate, and also to increase the solubility of the **biacetyl monoxime** in the monosulfonate solution.

10. The **dimethylglyoxime** should not be filtered until the mixture has become perfectly cool, because **dimethylglyoxime** is slightly soluble in a warm acid solution.

11. Crude or discolored **dimethylglyoxime** may be used since the impurities remain in solution in the aqueous alcohol.

12. The solution of **dimethylglyoxime** in **sodium hydroxide** should not be boiled, since prolonged heating causes decomposition.

13. The sodium salt may be further purified if desired by dissolving in water and reprecipitating with alcohol. Large crystals may be secured by crystallizing slowly from water.

Too long drying, or drying at too high a temperature, partially dehydrates the salt, with the result that it dissolves much more slowly in water and is therefore less desirable for making solutions for use in qualitative or quantitative analysis. **Sodium dimethylglyoximate** is extremely soluble in water. A 3 per

cent (0.1 M) aqueous solution is suggested to replace the 1 per cent alcoholic solution now used in analytical work.

3. Discussion

Biacetyl monoxime has been prepared by the action of amyl nitrite on methyl ethyl ketone using sodium hydroxide¹ or hydrochloric acid² as a condensing agent, and by melting nitrosolevulinic acid.³

Dimethylglyoxime has been prepared by the action of hydrochloric acid upon biacetyl monoxime;⁴ by the action of hydroxylamine on biacetyl;⁵ by the action of hydroxylamine on biacetyl monoxime;⁶ and by the action of sodium hydroxylamine monosulfonate on biacetyl monoxime.⁷ It is formed in small amounts, together with ethylnitrolic acid, by the action of oxides of nitrogen upon methyl ethyl ketone.⁸

This preparation is referenced from:

- Org. Syn. Coll. Vol. 5, 1022
- Org. Syn. Coll. Vol. 6, 542

References and Notes

1. Claisen, Ber. **38**, 696 (1905).
 2. Diels and Farkas, ibid. **43**, 1957 (1910); Biltz, Z. anal. Chem. **48**, 164 (1909); Semon and Damerell, J. Am. Chem. Soc. **47**, 2038 (1925).
 3. Thal, Ber. **25**, 1720 (1892).
 4. Schramm, ibid. **16**, 180 (1883); Johlin, J. Am. Chem. Soc. **36**, 1218 (1914).
 5. Fittig, Daimler, and Keller, Ann. **249**, 182 (1888).
 6. Tschugaeff, Ber. **38**, 2520 (1905); Gandarin, J. prakt. Chem. (2) **77**, 414 (1908); Biltz, Z. anal. Chem. **48**, 164 (1909); Adams and Kamm, J. Am. Chem. Soc. **40**, 1281 (1918).
 7. Semon and Damerell, ibid. **46**, 1290 (1924); **47**, 2033 (1925).
 8. Behrend and Tryller, Ann. **283**, 244 (1894).
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Appendix Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

oxides of nitrogen

ethylnitrolic acid

alcohol (64-17-5)

sulfuric acid (7664-93-9)

hydrochloric acid (7647-01-0)

acetic acid (64-19-7)

ammonia (7664-41-7)

sodium hydroxide (1310-73-2)

sulfur dioxide (7446-09-5)

copper sulfate (7758-98-7)

sodium nitrite (7632-00-0)

sodium bisulfite (7631-90-5)

ethyl nitrite (109-95-5)

amyl nitrite (463-04-7)

hydroxylamine (7803-49-8)

sodium hydroxylamine disulfonate

DIMETHYLGlyoxime,
Glyoxime, dimethyl- (95-45-4)

Biacetyl monoxime (57-71-6)

methyl ethyl ketone (78-93-3)

Sodium Hydroxylamine Monosulfonate

Sodium Dimethylglyoximate

nitrosolevulinic acid

biacetyl (431-03-8)