



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.

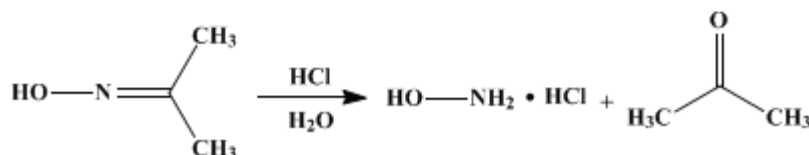
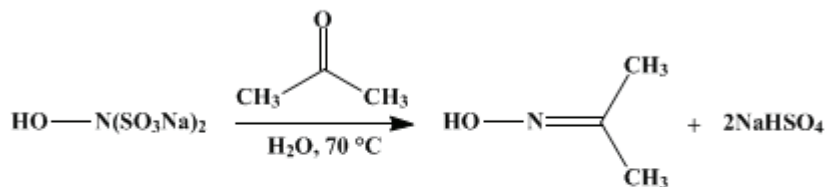
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 1, p.318 (1941); Vol. 3, p.61 (1923).

HYDROXYLAMINE HYDROCHLORIDE and ACETOXIME



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1. Procedure

In a 2-gallon (8-l.) wide-mouthed bottle ([Note 1](#)) packed in ice-salt mixture are placed 630 g. (8.7 moles) of commercial (95 per cent) [sodium nitrite](#) and 5 kg. of chopped ice, and the mixture is well stirred. A cold (0–5°) solution of [sodium bisulfite](#), made by saturating with [sulfur dioxide](#) a solution of 495 g. (4.7 moles) of anhydrous [sodium carbonate](#) in 1500 cc. of water, is now added slowly with hand stirring. When all is in, a sufficiently large quantity of the ice will have melted to allow a mechanical stirrer to be fitted. A stream of [sulfur dioxide](#) is now passed in, with continual stirring, the temperature being kept at 0–2°, until an acid reaction to Congo red paper is obtained and the dark color, which appears just before the reaction is complete, has faded. During the addition of the [sulfur dioxide](#), 500 g. more of ice may be added.

The mixture is now transferred to a 12-l. flask, 495 g. (625 cc., 8.5 moles) of [acetone](#) is added, and the solution is heated on the steam bath to 70°. Heating is then discontinued, the flask wrapped in burlap in order to retard loss of heat, and the mixture allowed to stand overnight. The acid is then neutralized with a concentrated (50 per cent) solution of [sodium hydroxide](#) (about 720 g. of alkali is required), until a distinctly alkaline reaction to litmus is just obtained.

The resulting [acetoxime](#) is now distilled in a current of steam ([Note 2](#)), and the distillation is continued until a 5-cc. sample, shaken with 2 cc. of [ether](#), yields no appreciable residue on evaporating the ether. To the distillate (2–2.5 l.) is added 600 cc. of concentrated [hydrochloric acid](#), and the acid solution is distilled at atmospheric pressure until the distillate is free of [acetone](#) ([Note 3](#)). The residual liquor is then evaporated to dryness on the steam bath, either in an open dish or preferably under reduced pressure. The crude [hydroxylamine hydrochloride](#) so obtained, weighing 296–470 g. (49–77 per cent of the theoretical amount), is suitable for many purposes, but is best purified by recrystallization from half its weight of water. By systematic recrystallization of the product from several batches, the yield of pure product, which crystallizes in long flat needles, melting when dry at 150–154°, may be brought as high as 70 per cent of the theoretical amount ([Note 4](#)).

In order to prepare pure [acetoxime](#) ([Note 5](#)), the procedure is modified in the following way: After neutralizing the solution of [acetoxime](#) formed after the addition of [acetone](#), the oily layer is separated and the aqueous solution shaken with two or three 150-cc. portions of [benzene](#). The oil and [benzene](#) solutions are mixed, the water thereby thrown out is removed, and the oil fractionally distilled with the use of a column, the portion boiling 133–136° being collected as pure [acetoxime](#). This product, which

weighs 420–480 g. (67–76 per cent of the theoretical amount), solidifies in the receiver to colorless needles melting at 60–61°. The foreruns and aqueous liquors are best distilled with steam and the distillate converted into [hydroxylamine hydrochloride](#) as above, whereupon 75–90 g. of pure salt is obtained.

2. Notes

1. The preparation can be run in larger batches than that indicated. Earthenware crocks may suitably replace the glass bottle; but since the external cooling in such vessels is not so efficient, it will be necessary, in case they are used, to add a larger proportion of ice during the reaction in order to maintain the correct temperature. This, however, is no great disadvantage, since the formation of the oxime appears to take place equally well in more dilute solution. Metal cans are entirely satisfactory for the distillation of the faintly alkaline liquids.
2. The [acetoxime](#) may be distilled by direct heating rather than by injection of steam; when the prescribed quantities are taken, however, it will be found that the liquor becomes saturated with [sodium sulfate](#) at a point just before the expulsion of the oxime is complete, so that addition of water during the distillation is necessary. More rapid distillation can be obtained by the use of a current of steam, especially if a condensing receiver (p. 479) is employed. The oxime can also, if desired, be isolated for hydrolysis by separation of the oily layer and extraction with [benzene](#); the resulting crude [hydroxylamine hydrochloride](#) is, however, apt to be dark in color and to contain inorganic salts.
3. By redistillation of the aqueous [acetone](#) with the use of a column, 60 per cent or more of the material taken can readily be recovered and employed in a subsequent batch.
4. The final mother liquors from the recrystallization of the [hydroxylamine hydrochloride](#) contain a high proportion of [ammonium chloride](#). The [hydroxylamine](#) present therein is best recovered by reconversion into [acetoxime](#), which is isolated by steam distillation of the faintly alkaline solution.
5. [Acetoxime](#) can be obtained in long needles by allowing the first portions of the steam distillate (which are saturated with oxime) to cool, and filtering off the crystals which separate; unfortunately, this product cannot be obtained in a perfectly dry condition without considerable loss by volatilization.

3. Discussion

[Hydroxylamine hydrochloride](#) can be prepared technically by the electrolytic reduction of [nitric acid](#)¹ and by the action of [sodium bisulfite](#) on [sodium nitrite](#).² Raschig, who discovered the latter process, suggested the use of [calcium nitrite](#) and bisulfite so that the bulk of the inorganic salts could be removed in the form of [calcium sulfate](#).³ He also showed that [sodium hydroxylamine disulfonate](#) yields [acetoxime](#) on treatment with [acetone](#),⁴ and it has long been known that [acetoxime](#) readily yields [hydroxylamine hydrochloride](#) on treatment with [hydrochloric acid](#);⁵ but apparently these facts in combination were only used advantageously at a later time.⁶ Excellent yields have been reported by the reaction of [acetone](#) and [sodium nitrite](#) with [zinc dust](#).⁷

This preparation is referenced from:

- [Org. Syn. Coll. Vol. 1, 327](#)
- [Org. Syn. Coll. Vol. 2, 67](#)
- [Org. Syn. Coll. Vol. 2, 70](#)
- [Org. Syn. Coll. Vol. 2, 76](#)
- [Org. Syn. Coll. Vol. 2, 313](#)
- [Org. Syn. Coll. Vol. 2, 622](#)
- [Org. Syn. Coll. Vol. 3, 172](#)

References and Notes

1. Tafel, *Z. anorg. Chem.* **31**, 322 (1902); Boehringer and Sons, Ger. pat. 133,457 [*Chem. Zentr.* II, 313 (1902)]; Ger. pat. 137,697 [*Chem. Zentr.* I, 106 (1903)]; Ponzio and Pichetto, *Ann. chim. applicata* **14**, 250 (1924) [*C. A.* **19**, 239 (1925)]; Shcherbakov and Libina, *Z. Elektrochem.* **35**, 70

- (1929) [C. A. **23**, 2372 (1929)].
2. Raschig, Ann. **241**, 161 (1887); Ger. pat. 41,987 [Chem. Zentr. I, 246 (1888)]; Divers and Haga, J. Chem. Soc. **69**, 1665 (1896); **77**, 673 (1900); Adams and Kamm, J. Am. Chem. Soc. **40**, 1281 (1918).
 3. Raschig, Ger. pat. 216,747 [Chem. Zentr. I, 308 (1910)].
 4. Raschig, Ann. **241**, 187 (1887).
 5. Janny, Ber. **16**, 170 (1883).
 6. Semon, J. Am. Chem. Soc. **45**, 188 (1923).
 7. Ogata and Hirano, J. Pharm. Soc. Japan **50**, 555 (1930) [C. A. **24**, 4758 (1930)]
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Appendix
Chemical Abstracts Nomenclature (Collective Index Number);
(Registry Number)

hydrochloric acid (7647-01-0)

Benzene (71-43-2)

ether (60-29-7)

ammonium chloride (12125-02-9)

sodium hydroxide (1310-73-2)

nitric acid (7697-37-2)

sodium carbonate (497-19-8)

sulfur dioxide (7446-09-5)

sodium sulfate (7757-82-6)

sodium nitrite (7632-00-0)

sodium bisulfite (7631-90-5)

calcium sulfate (7778-18-9)

acetone (67-64-1)

zinc (7440-66-6)

Hydroxylamine hydrochloride (5470-11-1)

ACETOXIME

hydroxylamine (7803-49-8)

calcium nitrite

sodium hydroxylamine disulfonate

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