



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](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.

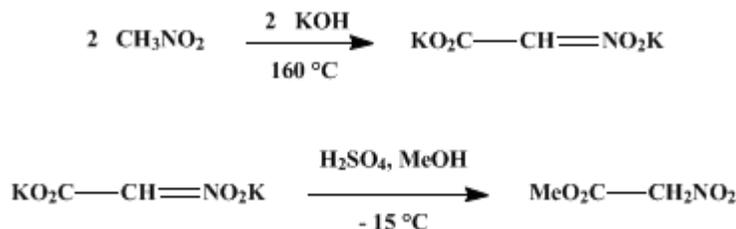
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*These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.*

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## METHYL NITROACETATE

[Acetic acid, nitro-, methyl ester]



Submitted by S. Zen, M. Koyama, and S. Koto<sup>1</sup>.

Checked by M. Ando and G. Büchi.

### 1. Procedure

*Ecwkqp#"Dgp|gpg'j cu'dggp'lf gpwkkf "cu'c'ectekqi gp'cpf 'lj qwf 'dg'j cpf rnf 'kp'c'hw g'j qaf 'y kj 'rt qrgt " r t g e c w k q p u 'v q 'c x q f 'g z r q u m t g O I t k p f k p i 'f t { 'f k q c u u k w o 'p k t q c e g v g 'k u 'r q v g p k e m 'j c | c t f q u i 'c p f " f k a n k r c v k p 'q h o g y { n p k t q c e g v g 'e c p 'd g 'j c | c t f q u i 'h k o r w t k k g u 'c t g 'r t g u g p v O 'V j g u g 'j c | c t f u 'o c { 'd g 'c x q f g f ' d { 'g o r r q { k p i 'j g 'o q f k k g f 'x g t u k q p 'q h i j k u 'r t q e g f w t g 't g r q t v g f 'd { 'L a j p u q p . 'G O E O I w j o " p . 'R O G O Y k p i c t f . 'N O C O 'U c d c v k k 'L O L O R g u e g / T q f t k i w g l . 'T O C O Q t i O R t q e g u i 'T g u O F g x 0 2 0 1 7 . ' 4 3 . ' z z z z z z z z z z " \*DOI: "320243keu0jrtf 0d222; 5+JP qvg'o qf kkgf 'Lvpq."4239\_*

A. *Dipotassium salt of nitroacetic acid.* A 3-l., three-necked, round-bottomed flask equipped with a sealed mechanical stirrer, a condenser fitted with a calcium chloride drying tube, and a pressure-equalizing dropping funnel is charged with a fresh solution of 224 g. of potassium hydroxide in 112 g. of water. From the dropping funnel is added, over 30 minutes (Note 1), 61 g. (1.0 mole) of nitromethane. The reaction mixture is heated to reflux for 1 hour in an oil bath maintained at approximately 160° (Note 2). After cooling to room temperature, the precipitated crystalline product is filtered, washed several times with methanol, and dried in a vacuum desiccator under reduced pressure, yielding 71.5–80.0 g. (79–88%) of the dipotassium salt of nitroacetic acid, m.p. 262° (dec.).

B. *Methyl nitroacetate.* A 2-l., three-necked, round-bottomed flask equipped with a sealed mechanical stirrer, a pressure-equalizing dropping funnel fitted with a calcium chloride drying tube, and a thermometer is charged with 70 g. (0.39 mole) of finely powdered dipotassium salt of nitroacetic acid (Note 4) and 465 ml. (11.6 moles) of methanol.

The reaction mixture is cooled to  $-15^\circ \pm 3^\circ$  and 116 g. (1.16 moles) of concentrated sulfuric acid is added with vigorous stirring over approximately 1 hour at such a rate that the reaction temperature is maintained at  $-15^\circ$ . The reaction mixture is allowed to warm to room temperature over a 4-hour period and stirred for another 4 hours at room temperature. The precipitate is removed by suction filtration, and the filtrate is concentrated on a rotary evaporator at 30–40°. The residual oil is dissolved in benzene and washed with water. The organic layer is dried over anhydrous sodium sulfate, and the benzene is removed by distillation. Further distillation under reduced pressure yields 30–32 g. (66–70%) of methyl nitroacetate, b.p. 80–82° (8 mm.), 111–113° (25 mm.) (Note 5).

### 2. Notes

1. The reaction mixture heats to 60–80° during the addition of nitromethane. The mixture may require external heating to maintain this temperature. The initial, yellowish color begins to turn red-brown and gradually deepens as ammonia gas is liberated.
2. The reaction mixture should not be stirred mechanically during this period in order to avoid decomposition of the product.
3. This crude product is rather pure. It can and should be employed for the esterification step without further purification. Elemental analyses for  $\text{C}_2\text{HO}_4\text{NK}_2$  were as follows; *calculated*: C, 13.26; H, 0.56; N, 7.73; K, 43.16%, *found*: C, 13.27; H, 0.57; N, 7.80; K, 42.68%. This is a hygroscopic crystalline

powder and should be used immediately after drying. There is a report<sup>2</sup> regarding an explosion of the dry dipotassium salt prepared by another method. There is no evidence that this procedure produces the same unstable impurities.

4. This must be ground into a fine powder with a mortar and pestle immediately prior to use.

5. The spectral properties of the product are as follows; IR (neat)  $\text{cm}^{-1}$ : 1776, 1760;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ),  $\delta$  (multiplicity, number of protons, assignment): 3.83 (s, 3H,  $\text{OCH}_3$ ), 5.20 (s, 2H,  $\text{CH}_2$ );  $n_{\text{D}}^{20}$  1.4260.

### 3. Discussion

Methyl nitroacetate has been prepared from nitromethane via the dipotassium salt of nitroacetic acid by the classical Steinkopf method,<sup>3</sup> but in lower yield. The dipotassium salt was obtained in 45% yield. The method has been improved by Matthews and Kubler,<sup>4</sup> but the salt must be recrystallized prior to esterification.

This procedure<sup>5</sup> is an improvement in that the reaction time is reduced and the yield is improved by increasing the concentration of alkali.

The acid-catalyzed esterification has been accomplished with either hydrochloric acid<sup>3</sup> or sulfuric acid;<sup>6</sup> an improvement on the Steinkopf method has been reported,<sup>7</sup> but the procedure lacks the simplicity of the present method.

Application of sulfuric acid as the catalyst is considered more practical for esterification because of its higher boiling point, its incompatibility with benzene, and the stability of nitroacetic acid in the reaction mixture, which allows omission of the final neutralization step.

The ethyl ester can also be prepared from ethyl acetoacetate (ethyl 3-oxobutanoate) by the method of Rodionov<sup>8</sup> as well as via Steinkopf's method.<sup>3</sup> Ethyl nitroacetate can be prepared in >70% yield<sup>5</sup> from the dipotassium salt, ethanol, and sulfuric acid, using anhydrous magnesium sulfate to avoid the Nef reaction.<sup>9</sup> The propyl and 2-propyl esters can also be obtained by this method.

This preparation is referenced from:

- [Org. Syn. Coll. Vol. 6, 503](#)

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### References and Notes

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2. D. A. Little, *Chem. Eng. News*, **27**, 1473 (1949).
3. W. Steinkopf, *Ber. Dtsch. Chem. Ges.*, **42**, 2026, 3925 (1909); *Justus Liebigs Ann. Chem.*, **434**, 21 (1923).
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### Appendix

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

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

sulfuric acid (7664-93-9)

hydrochloric acid (7647-01-0)

ammonia (7664-41-7)

Benzene (71-43-2)

methanol (67-56-1)

sodium sulfate (7757-82-6)

potassium hydroxide (1310-58-3)

Ethyl acetoacetate,  
ethyl 3-oxobutanoate (141-97-9)

Nitromethane (75-52-5)

magnesium sulfate (7487-88-9)

ethyl nitroacetate (626-35-7)

Methyl nitroacetate,  
Acetic acid, nitro-, methyl ester (2483-57-0)

nitroacetic acid

Dipotassium salt of nitroacetic acid