



A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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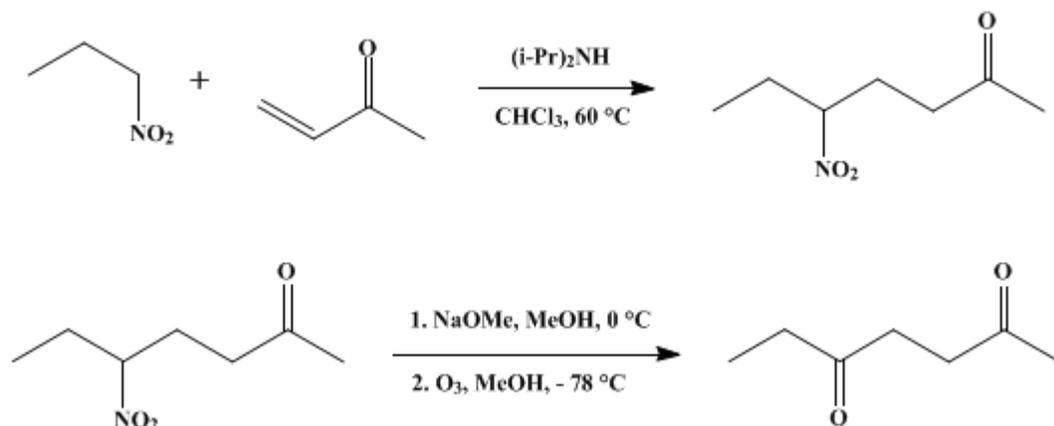
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 6, p.648 (1988); Vol. 56, p.36 (1977).

CONVERSION OF NITRO TO CARBONYL BY OZONOLYSIS OF NITRONATES: 2,5-HEPTANEDIONE



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1. Procedure

Caution! Ozone is extremely toxic and can react explosively with certain oxidizable substances. Ozone also reacts with some compounds to form explosive and shock-sensitive products. Ozone should only be handled by individuals trained in its proper and safe use and all operations should be carried out in a well-ventilated fume hood behind a protective safety shield. [Note added September 2009].

A. *5-Nitroheptan-2-one*. A 500-ml., three-necked flask equipped with a magnetic stirring bar, a 50-ml. addition funnel, and a condenser fitted with a nitrogen-inlet tube is flushed with nitrogen and charged with 36.0 g. (35.7 ml., 0.414 mole) of 1-nitropropane, 14.4 g. (20.0 ml., 0.142 mole) of diisopropylamine (Note 1), and 200 ml. of chloroform. The resulting solution is stirred and heated to 60°, and 28 g. (0.40 mole) of methyl vinyl ketone is added dropwise over a 2-hour period. The reaction mixture is then stirred for another 16 hours at 60°, allowed to cool to room temperature, and transferred to a 500-ml. separatory funnel, where it is washed with two 30-ml. portions of water and 30 ml. of 5% hydrochloric acid. After drying over anhydrous sodium sulfate, the chloroform solution is concentrated with a rotary evaporator. Distillation of the residue under reduced pressure gives 39.1 g. (61%) of 5-nitroheptan-2-one, b.p. 65–70° (0.2 mm.), n_D^{20} 1.4403 (Note 2).

B. *2,5-Heptanedione*. Methanolic sodium methoxide is prepared by cautiously adding small pieces of freshly cut sodium (5.67 g., 0.247 g.-atom) to 200 ml. of cold methanol (Note 3) in a 500-ml., three-necked flask equipped with a mechanical stirrer, a 50-ml. addition funnel, and a condenser fitted with a nitrogen-inlet tube. The resulting solution is stirred and cooled in an ice bath while 38.6 g. (0.243 mole) of 5-nitroheptan-2-one is added over 15 minutes, after which stirring is continued for another 15 minutes at 0°. The ice bath is then replaced with an acetone–dry ice bath, the nitrogen-inlet tube and addition funnel are removed, and a fritted-glass dispersion tube is inserted into the solution. With continued cooling and vigorous stirring, an ozone–oxygen mixture is bubbled through the solution for 5 hours (Note 4) and (Note 5).

After ozone generation has been stopped, pure oxygen is passed through the reaction mixture, removing excess ozone. Dry ice cooling is continued while 21 g. (0.34 mole) of dimethyl sulfide is added in one portion (Note 6), and the mixture is then allowed to come to ambient temperature overnight (18 hours). Methanol is removed with a rotary evaporator, and the residual liquid is dissolved in 250 ml. of diethyl ether. This solution is percolated through a short mat of silica gel (50 g.), removing polar impurities, then concentrated with a rotary evaporator, leaving a residue which is stirred with 30 ml. of 5% hydrochloric acid for 45 minutes (Note 7). Chloroform (40 ml.) is added, the organic layer is separated, and the aqueous phase is further extracted with two 30-ml. portions of chloroform. The organic extracts are combined, washed with saturated aqueous sodium hydrogen carbonate, dried over anhydrous sodium sulfate, filtered, and concentrated with a rotary evaporator. Vacuum distillation of the residue with a Kugelrohr apparatus gives 22.7 g. (73%) of 2,5-heptanedione, b.p. 90° (20 mm.), n_D^{20} 1.4313 (Note 8).

2. Notes

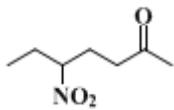
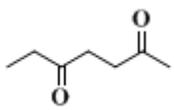
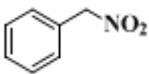
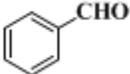
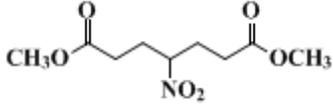
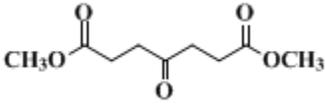
1. Nitropropane from MC and B Manufacturing Chemists and methyl vinyl ketone and diisopropylamine from Aldrich Chemical Company, Inc., were used as supplied.
2. IR (neat) cm^{-1} : 1715, 1545; ^1H NMR (CCl_4), δ (multiplicity, coupling constant J in Hz., number of protons): 0.97 (t, $J = 7$, 3H), 2.13 (s, 3H), 4.38 (m, 1H).
3. By using 300 ml. of methanol at this point, the checkers were able to avoid crust formation on the gas-dispersion tube during ozonolysis (see (Note 5)).
4. Ozone was generated using a Welsbach ozonator, with a total gas flow of 1.0 l. per minute at 115 volts. This corresponds to an ozone flow of 0.104 mole per hour; thus, the time theoretically required to generate one equivalent of ozone in this reaction is 2.3 hours. The use of excess ozone is permissible only for secondary nitronates (see Discussion).
5. The precipitate that forms during ozonolysis sometimes impedes stirring, and in some cases it may be necessary to dilute the slurry with another 100 ml. of methanol after the first hour. Solid can also clog the gas-dispersion tube. The submitters scraped the fritted-glass tip occasionally to maintain a constant flow rate, whereas the checkers prepared a more dilute solution of nitronate anion (Note 3).
6. Dimethyl sulfide is added as a safety precaution, to reduce any highly oxidized and potentially dangerous by-products that might have formed during ozonolysis.
7. Acid treatment hydrolyzes dimethyl ketal by-products, which form to the extent of 5–10% during the reaction.
8. IR (neat) cm^{-1} : 1710; ^1H NMR (CCl_4), δ (multiplicity, coupling constant J in Hz., number of protons): 1.01 (t, $J = 7$, 3H), 2.11 (s, 3H), 2.58 (s, 4H), 3.41 (q, $J = 7$, 2H). GC analysis by the checkers (6.3 mm. by 3 m. column of 20% SE-30 on Chromosorb W, 185° , 60 ml. of helium per minute) showed the presence of two minor impurities with retention times of 1.0 and 2.7 minutes. The major product, 2,5-heptanedione, had a retention time of 2.4 minutes.

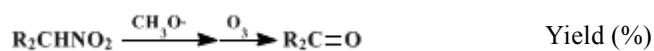
3. Discussion

There are various methods available for transforming a nitro group into a carbonyl group, including the Nef reaction (strongly acidic),² permanganate oxidation of nitronate anions (basic, oxidative),³ persulfate oxidation of nitronates (basic, oxidative),⁴ treatment with a mixture of organic and inorganic nitrite (neutral, oxidative),⁵ and treatment of either a free nitro compound or a nitronate anion with aqueous titanium(III) (neutral, reductive).⁶ Each method is limited, however, by poor yield, inconvenience, or lack of generality.

With the proviso that the substrate not contain a reactive carbon-carbon double bond, the present ozonolysis procedure⁷ appears to provide a convenient and efficient method for carrying out the desired transformation. As can be seen in Table I, both primary and secondary nitronates undergo the reaction. If a primary nitronate is to be used, however, one equivalent of ozone must be slowly metered in since use of an excess leads to overoxidation.

TABLE I

$\text{R}_2\text{CHNO}_2 \xrightarrow{\text{CH}_3\text{O}^-} \xrightarrow{\text{O}_3} \text{R}_2\text{C=O}$		Yield (%)
		73
		68
		65
		88



References and Notes

1. Thimann Laboratories, University of California, Santa Cruz, California 95064. [Present address: Department of Chemistry, Cornell University, Ithaca, New York 14853.]
 2. W. E. Noland, *Chem. Rev.*, **55**, 137 (1955).
 3. H. Shechter and F. T. Williams, *J. Org. Chem.*, **27**, 3699 (1962).
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 6. J. E. McMurry and J. Melton, *J. Org. Chem.*, **38**, 4367 (1973).
 7. J. E. McMurry, J. Melton, and H. Padgett, *J. Org. Chem.*, **39**, 259 (1974). We have recently been informed that ozonolysis of nitronate anions was first reported in a paper by F. Asinger, *Ber. Dtsch. Chem. Ges.*, **77**, 73 (1944).
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Appendix Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

hydrochloric acid (7647-01-0)

methanol (67-56-1)

diethyl ether (60-29-7)

chloroform (67-66-3)

sodium hydrogen carbonate (144-55-8)

sodium sulfate (7757-82-6)

oxygen (7782-44-7)

nitrogen (7727-37-9)

sodium methoxide (124-41-4)

sodium (13966-32-0)

ozone (10028-15-6)

dimethyl sulfide (75-18-3)

methyl vinyl ketone (78-94-4)

helium (7440-59-7)

1-nitropropane,
Nitropropane (108-03-2)

diisopropylamine (108-18-9)

2,5-HEPTANEDIONE (1703-51-1)

5-nitroheptan-2-one (42397-25-1)

nitronate anion

titanium(III)