A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

# Working with Hazardous Chemicals

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*September 2014: The paragraphs above replace the section "Handling and Disposal of Hazardous Chemicals" in the originally published version of this article. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.*

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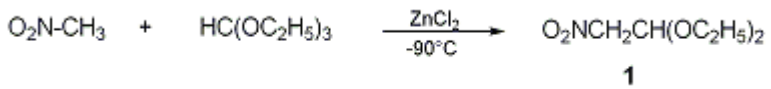
# NITROACETALDEHYDE DIETHYL ACETAL

## [Ethane, 1,1-diethoxy-2-nitro-]




**1**

Submitted by V. Jäger and P. Poggendorf[1].
Checked by E. Jnoff and Leon Ghosez.

## 1. Procedure

*CAUTION! Distillation of nitromethane and reactions using it as a solvent or a reactant at an elevated temperature, as well as reactions of nitroalkanes in general, should be conducted behind a safety shield. In one instance a minor deflagration was observed upon erroneously aerating the distillation residue while it was still hot. The apparatus, therefore, should only be ventilated after cooling to ambient temperature, and nitrogen, not air, is recommended for this purpose.*

A 500-mL, round-bottomed flask, equipped with a magnetic stirring bar, 20-cm Vigreux column, column head, Claisen distilling head, and thermometer, is charged with 89.3 g (602 mmol) of triethyl orthoformate (Note 1), 180 g (2.95 mol) of nitromethane (Note 2), and 5.00 g (36.6 mmol) of anhydrous zinc chloride. The solution is heated to 90°C (oil bath temperature, (Note 3)). After 16 hr (overnight) ca. 30 mL of ethanol is collected (Note 4). The remaining mixture, a brown suspension, is cooled to room temperature, and filtered by suction through a sintered glass funnel. The brown liquid obtained is distilled from a 100-mL, round-bottomed flask through a 20-cm Vigreux column at reduced pressure. First, excess nitromethane is removed (bp ca. 30°C/35 mm), then the fraction boiling at 58–60°C/1 mm (Note 3) is collected to afford 39–41 g (40–42% yield) of nitroacetaldehyde diethyl acetal **1** as a colorless liquid (Note 4), (Note 5).

## 2. Notes

1. All reagents were purchased from Fluka Feinchemikalien GmbH, Neu-Ulm, Germany and used without further purification.
2. Nitromethane, 98% purity, was used.
3. The rate of heating depends on the type of Vigreux column used, in this case a 20-cm, silver-plated Vigreux column with 4-cm outer and 1 1/2-cm inner diameter. The bath temperature should not be raised above 110°C when using this type of column, to avoid co-distillation of nitromethane (bp at 760 mm, 101°C). Ethanol should be distilled off at a rate of about 10 drops/min.
4. The spectroscopic properties of nitroacetaldehyde diethyl acetal are as follows: IR (film) $\nu_{max}$ $cm^{-1}$: 2970 (CH), 2920 (CH), 2880 (CH), 1550 (N=O), 1365 (N=O), 1340, 1120 (C-O), 1060; $^1H$ NMR (250 MHz, $CDCl_3$) δ: 1.15 (t, 6 H, $CH_2CH_3$), 3.56 and 3.67 (2 q, 4 H, J = 7.1, 2 $CH_2CH_3$), 4.44 ("d", 2 H, J = 5.8, $CH_2NO_2$), 5.09 ("t", 1 H, J = 5.8, CH); $^{13}C$ NMR (63 MHz, $CDCl_3$) δ: 15.0 (q, $CH_2CH_3$), 63.3 (t, $CH_2CH_3$), 76.8 (t, $CH_2NO_2$), 98.7 [d, $CH(OEt)_2$].
5. This reaction was carried out in the submitter's group more than 30 times, with yields ranging from 32–41% (lit.[2]: 49%). The purity of this material was repeatedly determined by gas chromatographic analysis to be >98%. GLC analysis: Column PS 086/.30 mm × 20 m glass capillary, 95:5 methyl/phenylsilicone. Program $T_1$, 40°C (1 min), rate 10°C/min; $T_2$, 300°C, 0.4 mm hydrogen pressure; $R_t$ = 9.37 min.

## Waste Disposal Information

All toxic materials were disposed of in accordance with "Prudent Practices in the Laboratory"; National Academy Press; Washington, DC, 1995.

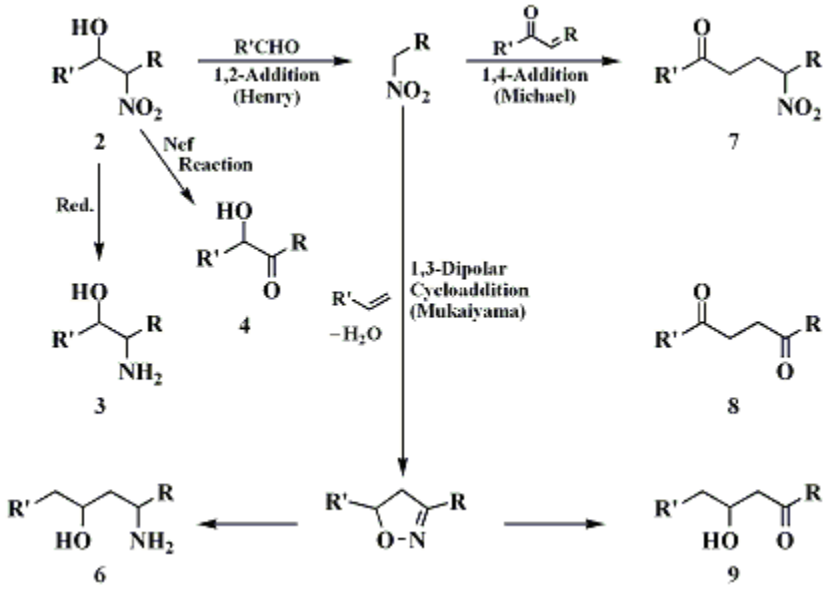
## 3. Discussion

This procedure describes the preparation of nitroacetaldehyde diethyl acetal **1** according to the method of René and Royer.[2]

Two other procedures for the preparation of **1** are known, i.e., by treatment of chloroacetaldehyde diethyl acetal with silver nitrite,[3] and by the reaction of α,α-diethoxymethyltriethylammonium tetrafluoroborate and nitromethane.[4] These alternate methods are less suited and less economic for preparation of **1** on a large scale. The dimethyl acetal has been obtained by treatment of 1-chloro-2-nitroethene with sodium methoxide.[5]

Diethyl acetal **1** has been used to obtain various other acetals by transacetalization,[6,7] such as the dimethyl, the ethyleneglycol, and the neopentylglycol acetal (2,2-dimethyl-1,3-propylidene acetal).

Aliphatic nitro compounds are highly versatile building blocks in organic synthesis[8 9 10 11,12 13] (see Scheme 1). For example, the nitroaldol addition (Henry reaction)[14] leads to the formation of 1,2-nitro alcohols, **2**, which are easily transformed into 1,2-amino alcohols, **3**, by reduction, and into α-hydroxycarbonyl compounds, **4**, by hydrolysis[15] (Nef reaction). The former process, mostly using nitromethane, has been widely employed in carbohydrate chemistry.[16 17 18 19 20 21 22]




Dehydration of primary nitro compounds (Mukaiyama reaction)[23] affords nitrile oxides, which may dimerize to yield furoxans, or otherwise be trapped by suitable dipolarophiles such as double or triple bond systems, leading to the formation of various heterocyclic systems, **5**.[24 25] The latter have been used for further derivatization in the heterocyclic series, or in "return" as precursors of acyclic products after ring cleavage,[11,26 27 7] for example, 1,3-amino alcohols **6** or β-hydroxycarbonyl compounds, **9**.

Both nitroaldol[28 29] and 1,3-dipolar cycloaddition products (e.g., isoxazolines, from alkenes)[24,25,26,27,7] have shown that nitroacetaldehyde diethyl acetal **1** constitutes a versatile $C_2$ building block in organic synthesis, notably what concerns amino sugar target structures. Recent work both on nitroaldol and nitroalkane derived dipolar additions has concentrated on the study and elaboration of stereoselective C-C forming steps with nitroalkanes.

Further uses of nitroalkanes are in 1,4-additions (Michael reaction) to α,β-unsaturated carbonyl compounds and the like. Recent reports deal with transformations of 1,4-nitro ketones, **7**, into 1,4-keto aldehydes, **8**, and cyclization to cyclopentenones.[30 31]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 10, 577

## References and Notes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## Appendix
## Chemical Abstracts Nomenclature (Collective Index Number);

**(Registry Number)**

dimethyl, the ethyleneglycol

neopentylglycol acetal (2,2-dimethyl-1,3-propylidene acetal)

ethanol (64-17-5)

hydrogen (1333-74-0)

nitrogen (7727-37-9)

sodium methoxide (124-41-4)

zinc chloride (7646-85-7)

triethyl orthoformate (122-51-0)

Nitromethane (75-52-5)

silver nitrite (7783-99-5)

chloroacetaldehyde diethyl acetal (621-62-5)

Nitroacetaldehyde diethyl acetal,
Ethane, 1,1-diethoxy-2-nitro- (34560-16-2)

α,α-diethoxymethyltriethylammonium tetrafluoroborate

1-chloro-2-nitroethene