Ozonolysis of Olefins, VI:[1] Cyanoacetaldehyde by Ozonolysis of (*E*)-1,4-Dicyano-2-butene or Allyl Cyanide

Madhukar Jachak, Martin Mittelbach,* Ulrike Krießmann, Hans Junek
Institute for Organic Chemistry, Karl-Franzens-Universität, Graz, Heinrichstraße 28, A-8010 Graz, Austria

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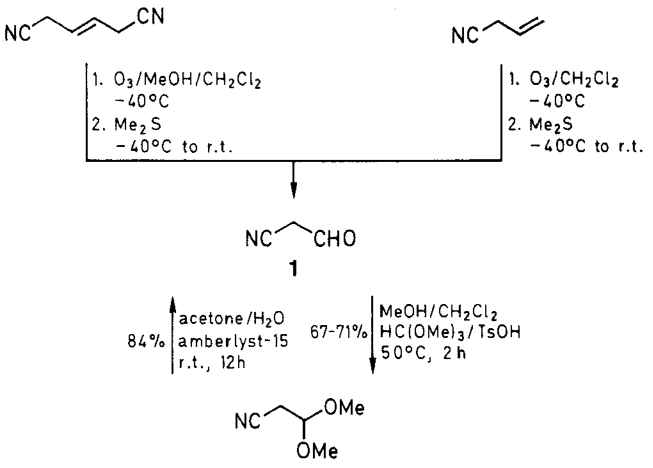
A new route for the preparation of cyanoacetaldehyde (3-oxopropanenitrile, **1**) and its stable dimethyl acetal (3,3-dimethoxypropanenitrile, **2**), which both are valuable intermediates for organic syntheses, is described. It starts from (*E*)-1,4-dicyano-2-butene or allyl cyanide (3-butenenitrile), respectively, which are ozonized at − 40 °C and further treated with dimethyl sulfide to give a solution of **1**. This solution can either be used directly for further reactions or be transformed into the dimethyl acetal **2**. The overall yield of **2** is 67 to 71 %. The acetal can be hydrolyzed again by treatment with Amberlyst-15 to give **1**.

Cyanoacetaldehyde (**1**) or its stable acetal are very useful intermediates for the synthesis of various heterocycles. Compound **1** can be cyclized to pyrazoles and pyridine derivatives,[2,3] and especially in the last years cyanoacetaldehyde diethyl acetal has been used for the synthesis of cytosines[4,5] and precursors for vitamin B_1.[6]

Due to the instability of cyanoacetaldehyde, which can lead to further condensation and polymerization, only the reaction of iodoacetaldehyde and silver cyanide has been described for its synthesis.[7] The alkali salts of **1** can be isolated by treatment of isoxazole with alkali alcoholates,[8] the potassium salt also by reaction of acetonitrile and ethyl formate.[9] Cyanoacetaldehyde diethyl acetal can be synthesized starting either from bromoacetaldehyde dialkyl acetal,[10,11] ethyl acetate and ethyl formate,[12] cyanoacetylene,[13] *β*-chloroacrylnitrile,[14] or acetonitrile.[15] These procedures are either multi-step syntheses or have the disadvantage of requiring not easily available starting materials.



We want to present a new strategy for the synthesis of **1** starting from (*E*)-1,4-dicyano-2-butene and allyl cyanide, respectively, which were ozonized under mild conditions in methanol or dichloromethane and then reduced by dimethyl sulfide to give a solution of **1**, which can be either used directly for further reactions or transformed into the stable dimethyl acetal **2** by reaction with trimethyl orthoformate. The total yield of **2** via this two-step synthesis is 71 %, when starting from (*E*)-1,4-dicyano-2-butene and 67 %, when starting from allyl cyanide. Compound **2** can easily be purified by distillation and, if required, hydrolyzed again in 84 % yield to give **1** by treatment in a suspension of the strong acid ion exchange resin Amberlyst-15.[16]

All reagents were of commercial quality; (*E*)-1,4-dicyano-2-butene and allyl cyanide were purchased from Aldrich Chemical Co., Amberlyst-15 was from Fluka AG. ^1H NMR spectrum (200 MHz) was recorded on Varian XL-200 spectrometer, TMS was used as internal standard. IR spectrum was recorded on Perkin-Elmer 421 spectrometer. GC/MS was performed with Hewlett-Packard MSD; fused-silica capillary column, 30 m × 0.32 mm, 0.25 μm DB-5 (J&W Scientific Inc.); initial temperature: 60 °C (4 min), temperature rate: 5 °C/min, final temperature: 100 °C (7 min). Ozone was generated by using a Fischer instrument, model 503.

Cyanoacetaldehyde (3-Oxopropanenitrile 1); Typical Procedure:
(*E*)-1,4-Dicyano-2-butene (4.0 g, 38.0 mmol) was dissolved in a mixture of CH_2Cl_2 (75 mL) and MeOH (75 mL) and ozonized with a 4–5 vol% O_3/O_2 mixture at −40 °C, until formation of I_2 was observed in a KI solution, which was connected to the reaction vessel. N_2 was passed through the mixture for 5 min, Me_2S (5 mL) was added and the solution was brought slowly to r.t.

Cyanoacetaldehyde (**1**) was identified by GC/MS, the yield (71 %) was determined by further transformation into the dimethyl acetal **2**.

GC/MS: *m*/*z* (%) = 69 (7) [M$^+$], 41 (100), 40 (43), 29 (87).

Similarly, allyl cyanide (4.0 mL, 50.0 mmol) was ozonized in CH_2Cl_2 (100 mL) and MeOH (50 mL) to give **1** in 67 % yield (determined by transformation in **2**); the resulting paraformaldehyde was removed by concentrating the solution under reduced pressure to 50 mL.

Cyanoacetaldehyde Dimethyl Acetal (3,3-Dimethoxypropanenitrile, 2):
To a solution of freshly prepared cyanoacetaldehyde (**1**) by the foregoing procedure, trimethyl orthoformate (16.5 g, 155 mmol) and TsOH (1.5 g, 7.9 mmol) were added and the mixture was stirred at 50 °C for 2 h. Then the solvent was removed under reduced pressure. The oily residue was treated with H_2O and $CHCl_3$ (50 mL), the organic layer was washed with H_2O (25 mL), dried (Na_2SO_4) and the solvent was removed under reduced pressure. The resulting oil was purified by distillation; bp 89 °C/8 mbar (Lit.[13] bp 92.5 °C/30 mbar); yield: 3.9 g.

$C_5H_9NO_2$	calc.	C 52.16	H 7.88	N 12.17
(115.1)	found	52.03	7.99	12.04

IR (KBr): ν = 2250 (CN) cm^{-1}.

^1H NMR ($CDCl_3$): δ = 2.68 (d, J = 6 Hz, 2 H, CH_2), 3.46 (s, 6 H, OCH_3), 4.72 (t, J = 6 Hz, 1 H, CH).

GC/MS: *m*/*z* (%) = 114 (2) [M−H]$^+$, 84 (66) [M−OCH_3]$^+$, 75 (100) [CH(OCH_3)$_2$]$^+$, 56 (53), 29 (51), 15 (66).

Hydrolysis of 2:
To a solution of **2** (1.15 g, 1.0 mmol) in acetone (40 mL) and H_2O (0.6 mL), Amberlyst-15 (0.4 g) was added and the mixture was stirred at r.t. for 12 h. The completeness of the reaction was observed by GC. After filtration of the ion exchange resin the resulting solution could be directly used for further reactions.

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