



A convenient solvent-free preparation of 1,3,5-trioxanes

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Abstract—In the presence of a small amount of trimethylsilyl chloride, aldehydes gave at room temperature in solvent-free conditions the corresponding 1,3,5-trioxanes with good to excellent yields. © 2002 Elsevier Science Ltd. All rights reserved.

1,3,5-Trioxanes have many applications in various fields, such as stabilizers in colour photography,¹ burning regulators in fumigants,² flavouring materials,³ carriers for scents, repellents, deodorants,⁴ and insecticides.⁵

1,3,5-Trioxanes could be formed by cyclotrimerization of aldehydes catalyzed by protonic acids,⁶ Keggin-type heteropolyacids,⁷ cation-exchange resins⁸ or Lewis acids such as zinc chloride,⁹ tantalum pentachloride,¹⁰ bismuth trichloride,¹¹ titanium or tin tetrachlorides.¹² The Lewis acid-catalyzed equilibrium between the free aldehyde and its trimer is highly temperature-dependent as evidenced by ¹³C NMR spectroscopy.¹³ Other catalysts were investigated including zeolithes,¹⁴ bentonitic earth,¹⁵ methylrhenium trioxide¹⁶ or acetyltriphenylphosphonium bromide.¹⁷ In a stereoselective synthesis of acetal-β,β-diglucosides using trimethylsilyl triflate as the acetalization catalyst, trimerization of the starting aldehydes was observed as a side-reaction.¹⁸ Trimethylsilyl triflate in the presence of bis(trimethylsilyl)-formamide was found to catalyze the trimerization of phenylacetaldehyde.¹⁹ Our own observations concerning the formation of a trimer in reactions where aldehydes were involved with trimethylsilyl chloride led us to investigate more precisely such an occurrence.

In a first experiment 0.1 equiv. of trimethylsilyl chloride was added to neat octanal (Scheme 1). A weakly exothermic reaction occurred during 15 min; the medium was evaporated after 16 h giving 73% of the trioxane and 27% of the free aldehyde as evidenced by

NMR spectroscopy in CDCl₃. We observed that the ratio trioxane/aldehyde decreases to 13:87 after 24 h and to 2:98 after 4 days. This was an indication that an equilibrium between the aldehyde and the trioxane could occur in CDCl₃. When the trimerization of octanal was conducted in THF, a smaller amount of trioxane was obtained, which prompted us to pursue our studies in the environmentally advantageous solvent-free conditions. The amount of trimethylsilyl chloride was found to be a crucial factor with an optimum around 0.4%.

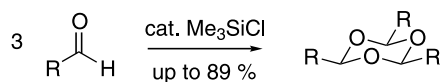
In a typical experiment, 0.004 equiv. of trimethylsilyl chloride was added under stirring to the liquid aldehyde. The mixture was allowed to stand overnight under argon. It was then evaporated to remove TMSCl. The solid residue was eventually recrystallized from ethanol.

TMSCl is efficient as a catalyst for straight and branched-chain aldehydes (entries 1–5 in Table 1) but inefficient for aldehydes, such as benzaldehyde, phenylacetaldehyde and 2-phenylpropanal. For the light aldehydes leading to liquid trioxanes (entries 7 and 8 in Table 1), a simple evaporation of the reaction mixture gave good yields of the corresponding trioxanes. Except in one case (entry 6), the crystalline trioxanes were recrystallized from ethanol. All the products were characterized by ¹H and ¹³C NMR spectroscopy.

The melting points and the spectroscopic data were conform with those reported in the literature.^{7,16,17}

Keywords: trioxanes; trimerization; solvent-free reactions; trimethylsilyl chloride.

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Scheme 1.

Table 1. Cyclotrimerization of aldehydes under solvent-free conditions at room temperature

Entry	Aldehyde	TMSCl (equiv.)	Work-up	Yield (%)	Mp (°C)
1	Me(CH ₂) ₆ CHO	0.004	A	87	34
2	Me ₂ CHCHO	0.004	A	72	53–54
3	C ₆ H ₁₁ CHO	0.004	A	89	195
4	Me ₃ CCHO	0.004	A	81	69
5	Me(CH ₂) ₈ CHO	0.004	A	45	41
6	Ph(CH ₂) ₂ CHO	0.01	B	64	62–63
7	MeCH ₂ CHO	0.004	C	78	
8	MeCHO	0.004	C	70	

Condition A: recrystallization from ethanol. Condition B: silica gel chromatography with cyclohexane/ethyl acetate as the eluent. Condition C: direct evaporation of the reaction mixture.

In summary, our protocol provides a convenient preparation of 1,3,5-trioxanes from aldehydes. The small amount of the catalyst, its easy accessibility and removal, the absence of solvent, along with the mild conditions, are the main advantages of the process.

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