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$InCl_3$ as an Efficient Catalyst for Cyclotrimerization of Aldehydes: Synthesis of 1,3,5-Trioxane Under Solvent-Free Conditions

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Abstract: 1,3,5-Trioxanes derived from aldehydes were synthesized using indium trichloride as a catalyst. Cyclotrimerization of the aldehydes gave excellent yields under neat conditions within a short span of time.

Keywords: Aldehyde, cyclotrimerization, $InCl_3$, solvent-free, trioxane

INTRODUCTION

1,3,5-Trioxanes have substantial application as flavoring materials;[1] carriers for scents, repellents, and deodorants;[2] insecticides,[3] constituents of a stabilizing solution in color photography; burning regulators in fumigants for potato tuber sprouting inhibition; and the basis for many polymers and copolymers.[4,5] In general, they are formed by cyclotrimerization of aldehydes catalyzed by heteropolyacids,[6] Lewis acids such as zinc chloride,[7] tantalum pentachloride,[8] and other catalysts investigated including zeolites,[9] methylrheniumtrioxide,[10] acetyltriphenylphosphoniumbromide,[11] trimethylsilyl chloride,[12] and $H_3PW_{12}O_{40} \cdot xH_2O$.[13]

The utility of $InCl_3$ is a reagent of choice for many transformations.[14] Here we report yet another application of $InCl_3$ for trimerization of aldehydes (Scheme 1).

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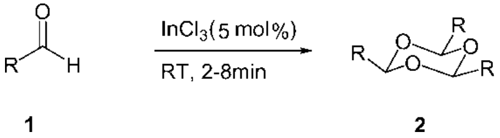
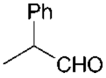
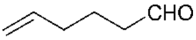
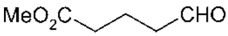
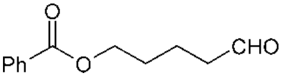
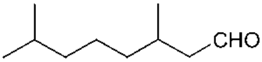
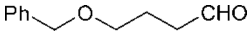
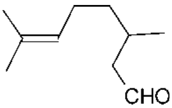


Scheme 1.

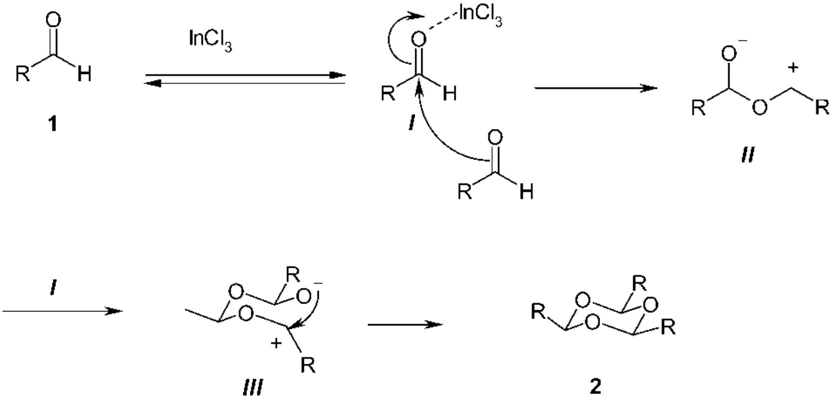
A mixture of isobutrylaldehye and 5 mol% of In(III) chloride for 2 min gave a solid product, which upon recrystalization gave 1,3,5-trioxane (**2**). The ^{1}H NMR spectrum of (**2**) showed a CH proton appearing at 4.5 ppm. The ^{13}C NMR spectrum revealed characteristic carbon resonance at 110 ppm. GC-MS and elemental analysis supported the assigned structure. To reveal the versatility of $InCl_3$, many aldehydes were trimerized (Table 1).

Table 1. 1,3,5-Trioxane synthesis by $InCl_3$ under solvent-free conditions at room temperature

Entry	Aldehyde	Time (min)	Yield (%)[a,b]
1	Me_2CHCHO	2	86
2	Me_3CCHO	5	90
3	$Ph(CH_2)_2CHO$	3	79
4	$MeCH_2CHO$	7	92
5	$MeCHO$	4	78
6	$Me(CH_2)_2CHO$	6	85
7		8	86
8		6	78
9		4	87
10		7	82
11		5	84
12		6	79
13		20	81

[a] All the products were characterized by IR, ^{1}H, ^{13}C NMR, and mass spectroscopy and by comparison with reported data.[8]

[b] Yield is based on recrystalization.



Scheme 2.

The InCl$_3$-catalyzed trioxane formation was attributed to the effective coordination of the catalyst with carbonyl oxygen of aldehyde to form ***I***. Consequently the nucleophilic attack of second molecule of aldehyde to formed ***II***, which combines with another aldehyde molecule and concomitantly cyclized to form **2** (Scheme 2).

In conclusion, InCl$_3$ was found to be an efficient reagent for the cyclotrimerization of aldehydes.

GENERAL EXPERIMENTAL PROCEDURE

A mixture of aldehyde (1 mmol) and InCl$_3$ (5 mol %) was stirred under neat conditions at rt (Table 1). The reaction was monitored by TLC and the mixture was quenched with cold water and extracted with ether. The organic layer was washed with brine and dried over Na$_2$SO$_4$. The solvent was evaporated and the crude product was recrystallized (yield 78–92%).

2,4,6-Tris(2,6-dimethyl-hept-5-enyl)-1,3,5-trioxane. Viscous liquid; ^{1}H NMR (CDCl$_3$, 500 MHz) δ 0.80 (d, $J = 10$ Hz, 9H), 1.28–1.31 (m, 6H), 1.51–1.54 (m, 6H), 1.55 (s, 9H), 1.63 (s, 9H), 1.63–1.67 (m, 3H), 1.72–2.01 (m, 6H), 4.82 (t, $J = 5.35$ Hz, 3H, –OCHO), 5.05 (t, $J = 6.75$ Hz, 3H) ^{13}C NMR (CDCl$_3$, 125 MHz) δ 25.4, 25.6, 27.7, 36.9, 50.9, 102.1, 126.0, 133.2, IR (KBr) 3068, 1642, 1443, 1354 cm^{-1}; MS m/z (relative intensity): 462.9 (M$^+$, 4), 71.1 (100), 137 (77), 109.17 (50.2), 153 (36.6). Anal. calcd. for C$_{30}$H$_{54}$O$_3$: C, 77.80; H, 11.67. Found: C, 77.87; H, 11.65.

Triisopropyl-1,3,5-trioxane. White solid, mp 59–61°C; ^{1}H NMR (CDCl$_3$, 500 MHz) δ 0.94 (d, $J = 6.8$ Hz, 18H, –CH$_3$), 1.83–1.88 (m, 3H), 4.50 (d, $J = 5.5$ Hz, 3H, –OCHO); ^{13}C NMR (CDCl$_3$, 125 MHz) δ 16.7, 32.4, 104.7; IR (KBr) 2958, 1470, 1355, 1263 cm^{-1}; MS m/z (relative intensity): 216 (M^+, 1), 199 (94), 127 (100), 98 (55), 81 (83). Anal. calcd. for $C_{12}H_{24}O_3$: C, 66.63; H, 11.18. Found: C, 66.59; H, 11.14.

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