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Acetalization of Carbonyl Compounds Catalyzed by Bismuth Triflate Under Solvent-Free Conditions

HAMID ALIYAN*, RAZIEH FAZAELI, AHMAD REZA MASSAH, AHMAD REZA MOMENI,
HAMID JAVAHERIAN NAGHASH and BEHZAD MOEINIFARD
Department of Chemistry, Islamic Azad University,
Shahreza Branch, Shahreza, Isfahan-86145-311, Iran
E-mail: aliyan@iaush.ac.ir; hamidaliyan@yahoo.com

Carbonyl compounds were converted to the corresponding 1,3-dioxolanes and 1,3-dioxanes with ethylene glycol and 1,3-propandiol in the presence of bismuth triflate under solvent-free conditions. In addition, high chemoselective protection of aldehydes in the presence of ketones has been achieved.

Key Words: Acetalization, 1,3-Dioxolane, 1,3-Dioxane, Bismuth triflate, Solvent-free.

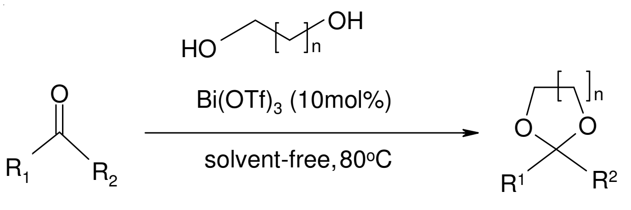
INTRODUCTION

Acetalization is one of the most widely used methods for protecting carbonyl compounds during multistep synthesis in organic, medicinal and drug chemistry[1]. 1,3-Dioxolanes and 1,3-dioxanes is the most popular protecting groups for this purpose.

Preparation of acetals and ketals generally involves reaction of carbonyl compounds with diols in the presence of protic or Lewis acids. Some of these methods employ *p*-toluenesulfonic acid[2], dry HCl[3], Me_3-SiOTf[4], BF_3/etherate[5], $FeCl_3$[6], pyridinium salts[7], $SbCl_3$[8], I_2[9], WCl_6[10], $ZrCl_4$[11], $CoCl_2$[12], $RuCl_3$[13], $Al(HSO_4)_3$[14], P_2O_5/SiO_2[15], DDQ[16], NBS[17], silica sulfuric acid[18], polymer-bound metal complex[19], sulfamic acid[20], envirocat EPZG[21], microwave/ionic liquid[22] and Lewis acidic ionic liquids[23].

The solvent-free organic reactions are important not only for their simplicity, but also as green and sustainable procedures[24]. Bismuth compounds are remarkably non-toxic (for example, LD_{50} Bi_2O_3 = 5 g/Kg, rat, oral) and many bismuth reagents have proven to be versatile catalysts for a variety of organic transformation[25]. Over the past few years, bismuth triflate [$Bi(OTf)_3$] has been reported as a new and efficient catalyst for organic synthesis, which exhibits, in numerous cases, a stronger activity than other known metal triflates, in particular those of transition elements and can be easily prepared in the laboratory in large quantities at relatively low cost[26,27].

In this paper we wish to report a convenient method for the chemoselective acetalization of aldehydes and ketones with diols using bismuth triflate as catalyst under solvent-free conditions (**Scheme-I**).



1 **2,3**

n=1 **2** 1,3-dioxolane
n=2 **3** 1,3-dioxane

Scheme-I

EXPERIMENTAL

General procedure of preparation of 1,3-dioxanes: To a mixture of carbonyl compounds (10 mmol) and $Bi(OTf)_3$ (1 mmol), 1,3-propandiol (10 mmol) was added and stirred at 80 °C for time given in Table-1. The reaction progress was followed by TLC or GC. After completion of the reaction, 10 mL aqueous $NaHCO_3$ (10 %) was added and the mixture was extracted with Et_2O (2 × 15 mL). Evaporation of the solvent afforded crude product. The crude product was purified by silica gel column chromatography using hexane-EtOAc (6:1) as eluent to afford the 1,3-dioxane in good to excellent yields.

RESULTS AND DISCUSSION

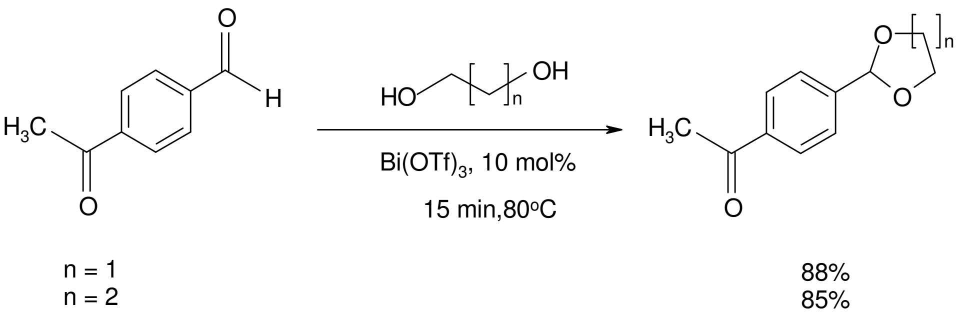
The reaction of 4-nitrobenzaldehyde (1 mmol) with ethylene glycol (1 mmol) in the presence of $Bi(OTf)_3$ (0.1 mmol) at 80 °C afforded the corresponding 1,3-dioxolane derivatives in 88 % yield.

As shown in Table-1 various types of aromatic aldehydes with electron-donating and electron-withdrawing groups and acid-labile substrate such as furfural, cinnamaldehyde and crotonaldehyde were cleanly and rapidly converted to their corresponding dioxolane and dioxane in the presence of $Bi(OTf)_3$ (10 mol %). Aliphatic aldehydes and cyclic ketones were also converted to their corresponding derivatives in good yields. However, aromatic ketones such as acetophenone and benzophenone required prolonged reaction time and moderate to low yields of the desired products were obtained. (Table-1). Because the conversion of aldehydes is faster than aromatic ketones as shown in Table-1, the present method can be used for the chemoselective protection of aldehyde groups in the presence of a ketone in multifunctional 4-acetylbenzaldehyde as substrate (**Scheme-II**).

In conclusion, we have developed a simple and efficient method for acetalization of carbonyl compounds by using $Bi(OTf)_3$ under solvent-free conditions. Furthermore, the high selectivity, good to excellent yields, short reaction times, solvent-free condition, easy procedure and work-up, inexpensive and non-toxic catalyst, make the present method a practical protocol for acetalization processes.

TABLE-1
PREPARATION OF 1,3-DIOXOLANES AND 1,3-DIOXANES: (A) ALL PRODUCTS WERE CHARACTERIZED BY COMPARISON OF THEIR IR, ^{1}H NMR AND ^{13}C NMR WITH THOSE OF AUTHENTHIC SAMPLES. (B) REACTION CONDITIONS: SUBSTRATE (10 mmol), DIOLS (10 mmol), $Bi(OTf)_3$ (1 mmol), 80 °C, SOLVENT-FREE. (c) ISOLATED YIELDS

Entry	Substrate (**1**)	1,3-Dioxolanes (**2**)	1,3-Dioxanes (**3**)
a	Benzaldehyde	15:90	15:87
b	2-Nitrobenzaldehyde	15:80	15:89
c	3-Nitrobenzaldehyde	15:85	1:585
d	4-Nitrobenzaldehyde	15:85	15:85
e	2-Hydroxybenzaldehyde	20:75	15:73
f	4-Hydroxybenzaldehyde	20:78	15:70
g	2-Hydroxy-5-nitrobenzaldehyde	15:80	15:75
h	4-Methylbenzaldehyde	20:78	20:70
i	2-Methoxybenzaldehyde	20:75	20:75
j	3-Methoxybenzaldehyde	20:77	20:73
k	4-Methoxybenzaldehyde	20:75	20:70
l	2-Chlorobenzaldehyde	15:80	15:85
m	4-Chlorobenzaldehyde	15:84	15:87
n	2,4-Dichlorobenzaldehyde	15:82	15:85
o	4-Bromobenzaldehyde	15:85	15:87
p	2-Phenylpropanal	15:88	15:90
q	Cinnamaldehyde	15:80	15:85
r	Furfural	15:85	15:88
s	Crotonaldehyde	15:83	15:90
t	Hexanal	15:90	15:90
u	Cyclohexanone	25:80	35:85
v	Cycloheptanone	30:88	35:87
w	Acetophenone	45:90	45:88
x	4-Bromoacetophenone	50:75	45:65
y	Acetylacetone	35:70	45:68
z	Benzophenone	60:50	60:70



Scheme-II

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