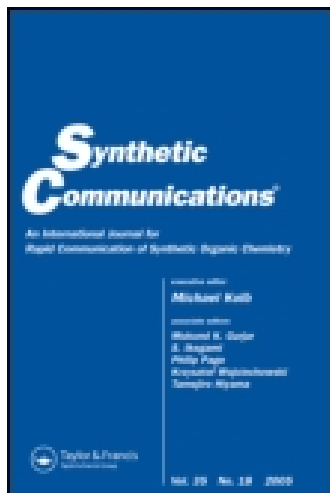


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### A Highly Efficient and Chemoselective Method for Acetalization of Carbonyl Compounds Catalyzed by Solid Superacid

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## A Highly Efficient and Chemoselective Method for Acetalization of Carbonyl Compounds Catalyzed by $\text{TiO}_2/\text{SO}_4^{2-}$ Solid Superacid

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### ABSTRACT

Various types of aldehydes and ketones could be converted to their corresponding diethyl acetals with triethylorthoformate in the presence of  $\text{TiO}_2/\text{SO}_4^{2-}$  solid superacid in good to excellent yield under mild reaction conditions.

*Key Words:* Diethyl acetals; Triethylorthoformate; Acetalization; Carbonyl compound.

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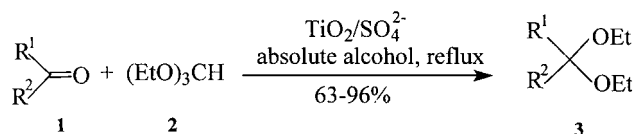


Acetalization of carbonyl compounds as dialkyl acetals is one of most useful method for the protection of carbonyl functions in organic synthesis.<sup>[1]</sup> Acetals have moderate stability and are easily converted into parent compounds. For this reason, acetals have become important tools for the synthesis of pure compounds.<sup>[2]</sup> In this regard, the literature shows that major attention has been paid to the preparation of dimethyl acetals,<sup>[3-5]</sup> and diethyl analogues. Several types of Lewis acid catalysts were introduced previously for this purpose, such as FeCl<sub>3</sub>,<sup>[6]</sup> ZrCl<sub>4</sub>,<sup>[7]</sup> WCl<sub>6</sub>,<sup>[8]</sup> and protic acids such as HCl,<sup>[9]</sup> Amberlyst-15,<sup>[10]</sup> and charcoal bisulfate<sup>[1]</sup> have been used also. Each of the above methods has its merit and some shortcomings. Some of these methods have not been entirely satisfactory as they give low yield, have long reaction times, problems of corrosivity of reagents, harshness of the reaction conditions, tedious workup, and effluent pollution and nonrecoverable catalysts. Consequently, it is desirable to develop alternative methods for the synthesis of diethyl acetals of aldehydes and ketones using mild and environmental friendly conditions.

TiO<sub>2</sub>/SO<sub>4</sub><sup>2-</sup> solid superacid has been used as a catalyst in our studies in recent years.<sup>[11-15]</sup> In continuation of these studies, we now report that TiO<sub>2</sub>/SO<sub>4</sub><sup>2-</sup> efficiently catalyses acetalization of carbonyl compounds with (EtO)<sub>3</sub>CH/EtOH (absolute) at refluxing temperature under mild conditions (Sch. 1).

As summarized in Table 1, when aldehydes and cyclic ketones **1** were treated with triethylorthoformate **2** in the presence of TiO<sub>2</sub>/SO<sub>4</sub><sup>2-</sup>, the corresponding diethyl acetals **3** were obtained in excellent yields in absolute alcohol at refluxing temperature (Entries 1-11). Open chain ketones gave moderate yields under same conditions (Entries 12-14).

We found that absolute alcohol as solvent is necessary in this reaction. For example, 3-chlorobenzaldehyde (Entry 5) provide lower conversion rate (<60%) in refluxing 95% alcohol for 7 h whereas over 95% yield is obtained in refluxing absolute alcohol after 25 min. We also found that cyclic aliphate ketones such as cyclopentanone (Entry 10) and cyclohexanone (Entry 11) undergo acetalization reaction much faster and with higher efficiency than the open chain ketones such as acetophenone



Scheme 1.



## Acetalization of Carbonyl Compounds as Dialkyl Acetals

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**Table 1.** Acetalization of carbonyl compounds using  $\text{TiO}_2/\text{SO}_4^{2-}$  as catalyst.

Entry	$R^1$	$R^2$	Reaction time (min)	Isolated yield (%)
1	$\text{C}_6\text{H}_5$	H	35	96
2	4- $\text{CH}_3\text{C}_6\text{H}_4$	H	35	92
3	4- $\text{CH}_3\text{OC}_6\text{H}_4$	H	35	92
4	3,4-( $\text{OCH}_2\text{O}$ ) $\text{C}_6\text{H}_3$	H	30	90
5	3- $\text{ClC}_6\text{H}_4$	H	25	95
6	4- $\text{ClC}_6\text{H}_4$	H	30	94
7	3- $\text{O}_2\text{NC}_6\text{H}_4$	H	25	96
8	4- $\text{O}_2\text{NC}_6\text{H}_4$	H	25	95
9	$\text{C}_6\text{H}_5\text{CH}=\text{CH}$	H	50	90
10	Cyclopentanone		35	95
11	Cyclohexanone		35	95
12	$\text{C}_6\text{H}_5$	$\text{CH}_3$	180	68
13	4- $\text{ClC}_6\text{H}_4$	$\text{CH}_3$	180	63
14	4- $\text{O}_2\text{NC}_6\text{H}_4$	$\text{CH}_3$	180	63

(Entry 12), 4-chloroacetophenone (Entry 13), and 4-nitroacetophenone (Entry 14).

Selectivity of the synthetic methods is of great importance in organic synthesis. Therefore, several competitive reactions between aldehydes and open chain aromatic ketones and also between cyclic aliphatic ketones and open chain aromatic ketones were conducted successfully with excellent chemoselectivity. The results of a set of competitive experiments are shown in Table 2.

The catalysts need no regeneration and can be reused 10 times for the acetalization of carbonyl compounds without significant loss of activity.

In conclusion, we provide a highly efficient and chemoselective catalyst for acetalization of carbonyl compounds under mild conditions. For this method has operational simplicity, high yield, high chemoselectivity, short reaction time, non-corrosive, non-polluting, and employing a reusable catalyst.

## EXPERIMENTAL

The catalyst  $\text{TiO}_2/\text{SO}_4^{2-}$  solid superacid was prepared according to the Lit.<sup>[11,12]</sup>  $^1\text{H}$ NMR spectra were determined on a Varian VXR-300S spectrometer using  $\text{CDCl}_3$  as solvent and tetramethylsilane



**Table 2.** Selective acetalization of carbonyl compounds using  $\text{TiO}_2/\text{SO}_4^{2-}$  as catalyst.

Entry	Substrate	Reaction time (min)	Isolated yield (%)
15	$\text{C}_6\text{H}_5\text{CHO}$	35	96
	+		
16	$\text{C}_6\text{H}_5\text{COCH}_3$	25	2
	3-Cl $\text{C}_6\text{H}_4\text{CHO}$		95
	+		
17	4-Cl $\text{C}_6\text{H}_4\text{COCH}_3$	35	2
	Cyclohexanone		95
18	+	35	
	$\text{C}_6\text{H}_5\text{COCH}_3$		2
18	Cyclohexanone	35	95
	+		
	4- $\text{O}_2\text{NC}_6\text{H}_4\text{COCH}_3$		2

(TMS) as internal reference. IR spectra were obtained on a Perkin–Elmer 983G spectrometer. The products were characterized by comparison of their melting and boiling points with literature values.

#### General Procedure for Acetalization of Carbonyl Compounds

A mixture of aldehyde or ketone **1** (5 mmol),  $(\text{EtO})_3\text{CH}$  **2** (15 mmol), and  $\text{TiO}_2/\text{SO}_4^{2-}$  (100 mg) was stirred at reflux for the length of time indicated in Table 1. Absolute alcohol (5 mL) was added. The progress of the reaction was monitored by TLC or GC. After completion of the reaction, the catalyst was filtered off and washed with  $\text{Et}_2\text{O}$ . The filtrate was washed with 40%  $\text{NaHSO}_3$  (15 mL) and brine ( $2 \times 15$  mL) successively and dried ( $\text{MgSO}_4$ ). Evaporation of the solvent under reduced pressure gave almost pure product(s). Further purification was proceeded by column chromatography on silica gel (light petroleum-ether as eluent) to afford pure diethyl acetal **3**.

#### Typical Procedure for Selective Acetalization of Benzaldehyde vs. Acetophenone with Triethylorthoformate

To a magnetically stirred solution of benzaldehyde (3 mmol), acetophenone (3 mmol),  $(\text{EtO})_3\text{CH}$  (10 mmol) in absolute alcohol 10 mL of

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reflux was added  $\text{TiO}_2/\text{SO}_4^{2-}$  (100 mg). After completion of the reaction, the catalyst was filtered off and washed with  $\text{Et}_2\text{O}$ , and the filtrate was washed with brine ( $2 \times 15 \text{ mL}$ ) and dried ( $\text{MgSO}_4$ ). The organic layer was concentrated under reduced pressure. The mixture was separated by silical gel column chromatography to afford phenylmethanediol diethyl ether in 96% yield and the acetophenone was almost quantitatively recovered.

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**REFERENCES**

1. Greene, T.W.; Wuts, P.G.M. *Protective Groups in Organic Synthesis*, 2nd Ed.; John Wiley: New York, 1991; 175.
2. Johnson, W.S.; Harbert, C.A.; Stipanovic, R.D. Asymmetric induction of an definic acetal cyclization. *J. Am. Chem. Soc.* **1968**, *90*, 5279.
3. Taylor, E.C.; Chiang, C.S. Trimethylorthoformate absorbed on the montmorillonite clay K-20, an effective reagent for acetal formation. *Synthesis* **1977**, 467.
4. Thurkauf, A.; Jacobson, A.E.; Rice, K.C. An improved procedure for the preparation of acetals from diaryl ketones. *Synthesis* **1988**, 233.
5. Ishihara, K.; Karumi, Y.; Kubota, M.; Yamamoto, H. Scandium trifluoromethane-sulfonimide and scandium trifluoromethanesulfonate as extremely active acetalization catalysts. *Synlett* **1996**, 839.
6. Bornstein, J.; Bedell, S.F.; Drummond, P.E.; Kosloski, C.L. The synthesis of  $\alpha$ -amino-*o*-tolualdehyde diethylacetal and its attempted conversion to pseudoisindole. *J. Am. Chem. Soc.* **1956**, *78*, 83.
7. Firouzabadi, H.; Iranpoor, N.; Karimi, B.  $\text{ZnCl}_4$  catalyzed highly chemoselective and efficient acetalization of carbonyl compounds. *Synlett* **1999**, 321.
8. Firouzabadi, H.; Iranpoor, N.; Karimi, B. Tungsten hexachloride ( $\text{WCl}_6$ ), a highly efficient and chemoselective catalyst for acetalization of carbonyl compounds. *Synth. Commun.* **1999**, *29*, 2255.



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9. Fife, T.H.; Jao, L.K. General acid catalysis of acetal hydrolysis. The hydrolysis of 2-aryloxytetrahydropyrans. *J. Org. Chem.* **1965**, *39*, 1492.
10. Patwardhan, S.A.; Dev, S. Amberlyst-15, a superior catalyst for the preparation of enol. *Synthesis* **1974**, 348.
11. Jin, T.S.; Ma, Y.R.; Liang, D.; Li, T.S. *J. Chem. Research (s)* **2000**, 96.
12. Jin, T.S.; Sun, X.; Li, T.S. *J. Chem. Research (s)* **2000**, 128.
13. Jin, T.S.; Ma, Y.R.; Li, Y.; Sun, X.; Li, T.S. *Synth. Commun.* **2001**, *31*, 2051.
14. Sun, X.; Jin, T.S.; Li, T.S. *Chinese J. Hebei University* **2001**, *21*, 49.
15. Guo, J.J.; Jin, T.S.; Zhang, S.L.; Li, T.S. *Green Chemistry* **2001**, *3*, 193.

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