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Bismuth Subnitrate as an Efficient Heterogeneous Catalyst for Acetalization and Ketalization of Carbonyl Compounds with Diols

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Abstract Bismuth subnitrate has been found to be an excellent catalyst for acetalization and ketalization of a wide range of aldehydes and ketones with diols under mild conditions. The catalyst remained in solid form throughout the reaction and could be readily reused and recycled without any loss of activity. It is deduced that the excellent performance of bismuth subnitrate may be ascribed to its acidity.

Keywords Bismuth subnitrate · Acetalization · Ketalization · Carbonyl compound · Diol

For the sake of green chemistry and sustainable development, researches have been done on the applications of bismuth compounds because bismuth is the only stable heavy element in nature that is free of toxicity and radioactivity, and some of its compounds have been found to be potentially useful either as catalysts or as reagents for organic synthesis [1–8]. After an extensive literature survey, we found that, besides those of bismuth nitrate and bismuth triflate [7–8], there is no report on the application of bismuth compounds as catalysts for the acetalization and ketalization of carbonyl compounds. The acetalization or ketalization process is widely used in organic synthesis because the dioxolane group is generally stable to bases, Grignard reagents, hydrogenation reagents, metal hydrides, oxidants, bromination and esterification reagents, and is ideal for "protecting" the carbonyl groups of aldehydes and ketones [9–10]. Besides acting as protecting agents in organic synthesis, many acetals (ketals) have found applications in industry such as fragrances, cosmetics, pharmaceuticals, detergents, lacquer, polymers, food and beverage additives, etc. [10]. Recently, Yoshioka et al. reported the $GaCl_3$-catalyzed insertion of isocyanides into a C–O bond of cyclic ketals and acetals [11], and the discovery has widened further the application of acetals and ketals in organic synthesis.

Many compounds have been reported to be catalytically active towards acetalization and ketalization of carbonyl compounds [9–10, 12–41]. The commonly used catalysts (protic acids) are inorganic acids such as sulfuric and phosphoric acid, and problems related to corrosion and catalyst separation are inevitable [9–10]. When organic protic acids were used [12], product yield was not good. Inorganic metal salts (e.g., halides) or complexes were found to show catalytic activity towards these reactions [7–8, 13–18], but their performance is far short of industrial expectation. Recently, researchers employed acidic ionic liquids as catalysts [19–22], but due to the high cost and toxicity of ionic liquids, the approach is not popular. From a standpoint of green chemistry, solid catalysts are preferable because it is easy to separate the catalysts from the reaction media. Molecular sieves (e.g., HZSM-5, Y, MCM-41) [23–29], montmorillonite [26–27, 29–30], sulfonic resin [29, 31], heteropoly acids [32, 33], supported protic acid [34–39], phosphates [40], and others [41] have been evaluated for acetalization and ketalization of carbonyl compounds but found to be unsatisfactory in either activity or selectivity.

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With the aim of developing catalysts suitable for acetalization and ketalization of carbonyl compounds, and as an extension of our work on application of bismuth compounds [6], we evaluated the catalytic performance of a number of inorganic bismuth compounds under relatively mild reaction conditions. In the present study, bismuth subnitrate (abbreviated BSN hereinafter) was found to be the most effective among the tested catalysts, showing high activity, selectivity, stability, and recyclability. We also conducted an investigation on the effects of reaction parameters. Finally, we measured the surface acidity of BSN by means of Hammett indicator method.

The bismuth compounds, montmorillonite K10 clay (surface area 220 m^2/g), and sulfonic resin (Amberlyst 15, surface area 45 m^2/g) were purchased from Aldrich Co. The carbonyl compounds, diols, and other chemicals were purchased from Alfa Aesar Chemical Co. or Hunan Yueming Chemicals, Glass and Machine Trade Co. All the chemicals were used as received with montmorillonite K10 clay being the only exception. For the removal of metal cations, the clay was treated in an aqueous 2 M NH_4NO_3 solution at room temperature (RT) for 3 h, followed by calcination in air at 500 °C for 1 h.

All the reactions were performed in a 100 mL round-bottom glass flask equipped with a magnetic stirrer and a specific distillation condenser with tiny groves on its inner wall. Under these conditions, most of the azeotropically removed water was trapped by the condenser. Typically, a mixture of carbonyl compounds (0.1 mol), diol (0.15 mol), catalyst (0.85 mmol estimated on Bi^{3+}) and cyclohexane (15 mL) were charged into the flask; two layers appeared after a short time of stewing. The progress of reaction was monitored by GC analysis of small aliquots drawn from the reaction mixture. After completion of reaction and stop of stirring, the mixture was cooled to RT. The mixture existed in two layers, and the top layer was decanted for product collection.

The reaction mixture was qualitatively analyzed by a Hewlett-Packard 6890/5793 GC/MS system equipped with a HP-5MS column (30 m × 0.45 mm × 0.8 μm) using helium as carrier gas. The quantitative analysis of extracts was conducted on a Hewlett-Packard GC 5790 apparatus equipped with a thermal conductivity detector and DB-wax capillary column (30 m × 0.45 mm × 0.8 μm). The concentrations of reactants and products were acquired according to peak area calibration over a GC chemstation. The surface acidity of catalyst was determined by means of $^{n}BuNH_2$ titration methods using different Hammett indicators (crystal violet: $pK_a = 0.8$, phenylazodiphenylamine: $pK_a = 1.5$, 2-amino-5-azotoluene: $pK_a = 2.0$, benzeneazo-naphthylamine: $pK_a = 4.0$, neutral red: $pK_a = 6.8$).

For the investigation of catalytic activity of bismuth compounds, we selected cyclohexanone ketalization with ethylene glycol (EG) as model reaction (Table 1). One can see that in a blank run without a catalyst, cyclohexanone conversion at 82 °C is low (15.4%). In the presence of $Bi(NO_3)_3$, BSN, $BiCl_3$, and $BiBr_3$, conversion is above 80%, and the activity of bismuth compounds can be ranked in the order of: $Bi(NO_3)_3 \approx BSN > BiCl_3 > BiBr_3 > Bi_2O_3$. For catalysts such as $La(NO_3)_3$, HZSM-5, Al-MCM-41, montmorillonite K10, and sulfonic resin (Amberlyst-15), they are inferior in performance. Srivastava et al. [7] reported that bismuth nitrate was superior to bismuth triflate as catalyst (for protection of carbonyl compounds as acetal, ketal, mixed ketal and thioketal) but they did not provide information related to catalyst reusability and structure after acetalization. Unlike $La(NO_3)_3$ which dissolves completely in EG and shows good solubility in the product, BSN remains in solid form throughout the reaction. It is known that in the presence of water, $Bi(NO_3)_3$ easily hydrolyzed into $BiONO_3$ and corrosive HNO_3, and bismuth halides into bismuth oxyhalides and hydrogen halide. However, BSN is stable in the presence of water and/or air. In view of commercial availability and relatively low cost of BSN as well as its extremely low solubility in organic solvents, we consider that BSN is a suitable catalyst for cyclohexanone ketalization.

Furthermore, we found that BSN is an excellent catalyst for acetalization and ketalization of a wide range of aldehydes and ketones (Table 2). One can see that reactant conversion is above 90% in all cases, and selectivity to the

Table 1 Results of cyclohexanone ketalization with EG[a]

Entry	Catalyst	Reaction results[b]		
		Conv.%	Sel.%	Yield%
1	None	15.4	100	15.4
2	Bismuth subnitrate	94.5	100	94.5
3	Bismuth nitrate	95.1	100	95.1
4	Bismuth carbonate	88.2	100	88.2
5	Bismuth trichloride	86.8	100	86.8
6	Bismuth tribromide	82.4	100	82.4
7	Bismuth oxide	15.9	100	15.9
8[c]	Lanthanum nitrate	80.4	100	80.4
9[c]	Al-MCM-41	64.5	100	64.5
10[c]	H-ZSM-5	29.3	100	29.3
11[c]	Amberlyst-15	73.9	100	73.9
12[c]	Montmorillonite	37.9	100	37.9

[a] Reaction conditions: catalyst estimated based on Bi^{3+} 0.85 mmol, EG 0.15 mol, cyclohexanone 0.1 mol, temperature 82 °C, time 0.5 h, cyclohexane 15 mL

[b] GC analysis, Conv.: cyclohexanone conversion; Sel.: selectivity of ketal; Yield: Yield of ketal

[c] $La(NO_3)_3$: 0.28 g (0.85 mmol); Al-MCM-41 (Si/Al = 25), HZSM-5 (Si/Al = 25) , Amberlyst-15, Montmorillonite: 0.25 g

Table 2 BSN-catalyzed acetalization or ketalization of carbonyl compounds with diols[a]

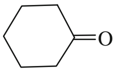
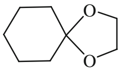
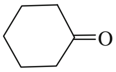
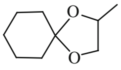
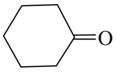
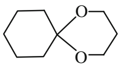
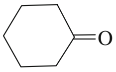
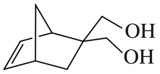
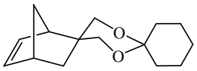
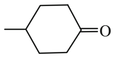
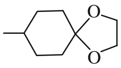
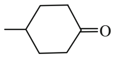
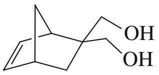
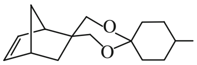
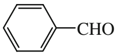
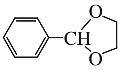
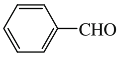
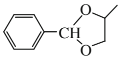
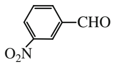
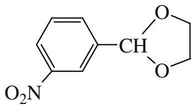
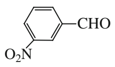
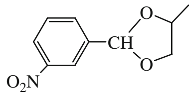
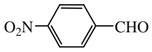
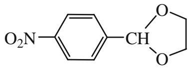
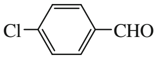
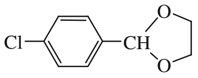
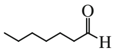
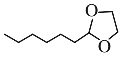
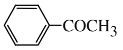
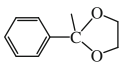
Entry	Reactants		Product	Time (min)	Yield[b] (%)
	Carbonyl compound	Diol			
1		$\mathrm{HOCH_2CH_2OH}$		30	94.5
2		$\mathrm{HOCH_2CH(OH)CH_3}$		30	92.5
3		$\mathrm{HOCH_2CH_2CH_2OH}$		25	92.9
4				40	92.8
5		$\mathrm{HOCH_2CH_2OH}$		30	95.7
6				40	93.9
7		$\mathrm{HOCH_2CH_2OH}$		30	90.3
8		$\mathrm{HOCH_2CH(OH)CH_3}$		30	91.2
9		$\mathrm{HOCH_2CH_2OH}$		30	98.4
10		$\mathrm{HOCH_2CH(OH)CH_3}$		30	96.3
11		$\mathrm{HOCH_2CH_2OH}$		30	96.9

Table 2 continued

Entry	Reactants		Product	Time (min)	Yield[b] (%)
	Carbonyl compound	Diol			
12		$HOCH_2CH_2OH$		30	91.9
13		$HOCH_2CH_2OH$		30	91.3
14		$HOCH_2CH_2OH$		60	90.7

[a] Reaction conditions: bismuth subnitrate 0.25 g, diol 0.15 mol, carbonyl compounds 0.1 mol, temperature 82 °C, cyclohexane 15 mL

[b] GC yield

desired products is 100%. Thus, we have demonstrated that BSN has wide application for dioxolane syntheses from aldehydes and ketones. For catalytic protection of carbonyl compounds, the BSN-catalyzed approach seems to be more practical and convenient than the use of bismuth triflate [7] or bismuth nitrate [8] as catalyst.

Bismuth subnitrate (BSN) shows high activity towards the condensation reaction. It is meaningful to find out the influence of reaction parameters on catalytic performance. We fixed the amount of reactants and solvent and varied the amount of BSN to study the effect of Bi^{3+}/cyclohexanone (molar ratio) on catalytic performance. The results are depicted in Fig. 1. As mentioned, ketalization rate at 82 °C without a catalyst is slow but a small presence of BSN brings about prominent improvement in ketal yield. Moreover, the yield increases with rise of catalyst concentration. Nevertheless, when Bi^{3+}/cyclohexanone is varied from 8.5×10^{-3} to 1.2×10^{-2}, there is little change in ketal yield. We hence take that the optimal Bi^{3+}/cyclohexanone for the target reaction is *ca.* 8.5×10^{-3}.

Water is a reaction product and its accumulation can have adverse effect on the equilibrium reaction, particularly if it is adsorbed on the catalyst. Generally speaking, water can be removed via azeotropic distillation. The commonly employed azeotropic agents are toluene, benzene, hexane, cyclohexane, halogenated hydrocarbons, etc. [33, 36–40]. We investigated the outcomes of using cyclohexane, toluene, hexane, and chloroform as entrainer. It is clear from Fig. 2 that under reflux of equal time, ketal

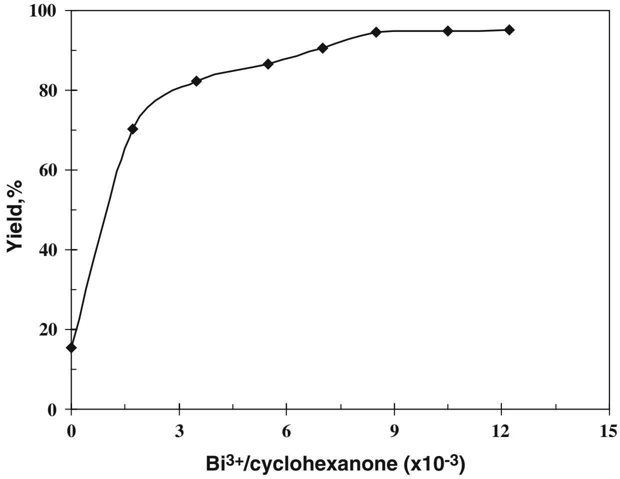


Fig. 1 Effect of catalyst amount on cyclohexanone ketalization with EG over BSN (cyclohexanone 9.81 g, EG 9.31 g, BSN 0.25 g, cyclohexane 15 mL, 82 °C, 30 min)

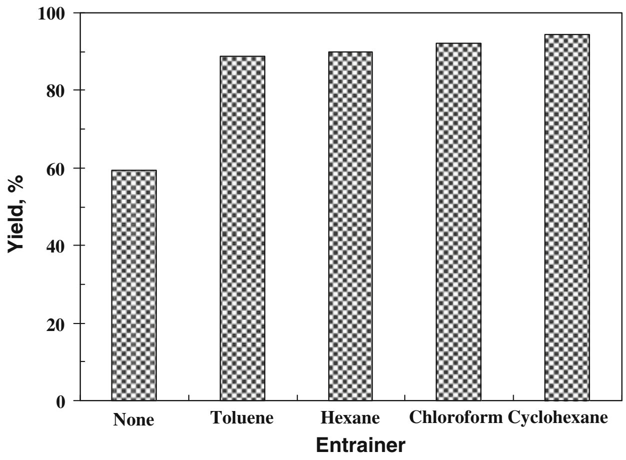


Fig. 2 Effect of azeotropic agent on cyclohexanone ketalization with EG over BSN (cyclohexanone 9.81 g, EG 9.31 g, BSN 0.25 g, azeotropic agent 15 mL, 82 °C, 30 min)

yield can be ranked in the order of: cyclohexane > $CHCl_3$ > hexane > toluene. The result is somewhat unexpected because toluene has boiling point higher than cyclohexane, and an increase of reaction temperature is beneficial for ketalization. Nevertheless, the phenomena can be explained by the fact that cyclohexane is effective for water removal, and the use of cyclohexane as entrainer would promote ketal formation. In addition, cyclohexane is low in toxicity, and we consider that it is a wise choice to use cyclohexane as entrainer.

It was reported that reaction time showed effect on acetalization and ketalization of carbonyl compounds [12, 21, 28, 31, 40]. In our investigation, we observed that there is a remarkable increase in ketal yield in the first 30 min, and the rate of ketal yield declines afterward. After 1 h, cyclohexanone conversion is completed and ketal yield is 100%. Therefore, it goes without saying that for easy separation of product, it is better to adopt a reaction time of 1 h for complete conversion of cyclohexanone. We consider that the optimal conditions for cyclohexanone ketalization with EG are: 82 °C, 1 h, BSN(Bi^{3+})/cyclohexanone 8.5×10^{-3}, and cyclohexane as entrainer.

To examine the reusability and applicability of catalyst, BSN was subject to cycles of reaction. In order to monitor the variation of ketone conversion, we did not adopt the optimal conditions so as to keep conversion below 100%. After the completion of reaction and with the stop of stirring, the mixture separated into two layers. According to the results of GC and GC–MS analyses, the upper layer contains the desired ketal product, entrainer and minute amount of cyclohexanone, while the lower layer contains EG and the suspended catalyst. We observed that BSN settled on the flask bottom after a period of 30 min. It is apparent that at RT BSN does not dissolve in ketal, cyclohexanone, EG or water. Thus, between cycles, it is just a matter of decanting the upper layer and adding fresh cyclohexane, ethylene glycol and cyclohexanone into the flask; there is no loss of catalyst because removal of BSN from the flask is not necessary. That is to say, for each new cycle the amounts of fresh cyclohexanone and cyclohexane added are 9.81 g and 15 mL, respectively, with fresh EG satisfying molar EG/cyclohexanone = 1.5. As shown in Fig. 3, the decline in ketal yield is minimal in a trial of 6 cycles. We also tested the catalyst for 6 cycles in the reaction of cyclohexanone with propan-1,2-diol, and observed similar efficiency.

It has been commonly recognized that the acetalization or ketalization reactions proceed via an acid-catalyzed mechanism [12, 24, 36]. We determined the surface acidity of BSN by using Hammett indicators. It is observed that the acid strength (H_o) of BSN is ≥ 2 and the total acid amount is 15 μmol per gram. A recent report by Shimizu et al. disclosed that high concentration of acid sites is not indispensable for acetalization of carbonyl compounds over functionalized FSM-16 mesoporous silica, whereas a relatively strong acid strength is essential [36]. It is apparent that the excellent catalytic ability of bismuth subnitrate can be ascribed to its acid character. The poor performance of Bi_2O_3 could be due to the poor acidity of the compound. Further work is under way to confirm the nature of active sites and to disclose the mechanistic aspect of the catalytic reaction.

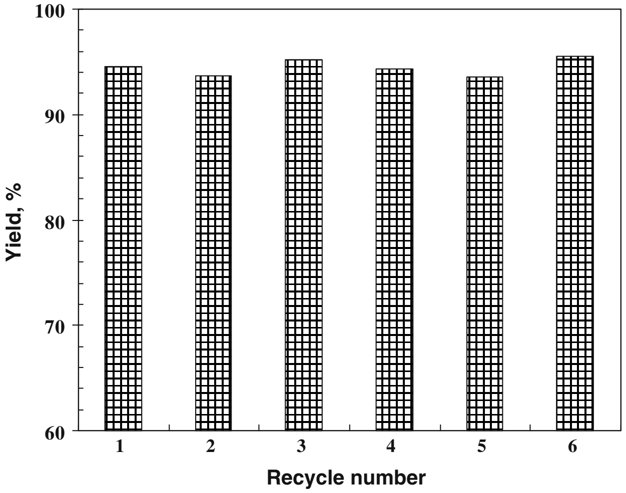


Fig. 3 Catalyst recycling (For each cycle: cyclohexanone 9.81 g, EG 9.31 g, BSN 0.25 g, cyclohexane15 mL, 82 °C, 30 min)

In summary, bismuth subnitrate has been found for the first time to be catalytically effective for the acetalization and ketalization of carbonyl compounds. In the heterogeneous system, activity and selectivity under mild conditions is up to 100%, and the catalyst can be recycled easily. We propose that the excellent performance is related to the acidity nature of bismuth subnitrate. From the viewpoint of industrial application, bismuth subnitrate is a catalyst potentially suitable for the acetalization or ketalization of carbonyl compounds.

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