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ZnO and ZnO-nanoparticles: Efficient and reusable heterogeneous catalysts for one-pot synthesis of *N*-acylsulfonamides and sulfonate esters

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ABSTRACT

Commercially available and preparative ZnO nanoparticles are reported as efficient and reusable catalysts for the chemoselective synthesis of *N*-acylsulfonamides and sulfonate esters. A one-pot sequential sulfonylation and acylation of amines took place to afford the *N*-acylsulfonamides in excellent yields under solvent-free conditions. The ZnO catalyst can be reused for without significant loss of catalytic activity.

1. Introduction

Sulfonylation and acylation of heteroatoms are valuable transformations which resulted in the imide, sulfonimide, amide, sulfonamide, ester and sulfonate ester moieties as building blocks of important biologically active and polyfunctional molecules [2–5]. Sulfonate esters are well-known alkylating agents and cell proliferation inhibitors [6], while sulfonamide derivatives are clinically used as antibacterial and antibiotic medicines [7–11]. Moreover, a number of enzyme inhibitors [12], new therapeutic agents for Alzheimer's disease [13], and hepatitis C virus NS protease inhibitors [14] are derived from *N*-acylsulfonamides.

As a result of wide range of activity and importance, there are several available procedures for the preparation of these compounds. *N*-acylsulfonamides can be prepared by either base-catalyzed acylation of sulfonamides [7–12] or sulfonylation of amides [10]. Due to the less nucleophilicity of amide nitrogen and sensitivity of imide bond, acylation of sulfonamides is often preferred to sulfonylation of amides. Similarly, sulfonate esters and sulfonamides have been prepared through the sulfonylation of alcohols and amines [1–6,15–24] in the presence of basic catalysts like pyridine, triethyl amine and aqueous metal hydroxides. Some of these reactions are together with the formation of undesired side products, use of toxic or corrosive reagents, and tedious processes for purification of products. A good option of catalyst be able to enhance the rate of sulfonylation and acylation reactions via dual activation of S=O, C=O and NH groups. Therefore, searching for one-pot catalytic procedures with less reaction steps is still of interest.

Recently, metal oxides have been used as efficient heterogeneous catalysts in various organic transformations [25–28]. Although metal oxide surfaces exhibit both Lewis acid and base properties, nature of metal cation and surface area of metal oxides have extensively manipulated to their catalytic properties. Zinc oxide is a low-priced metal oxide which as both industrial and nano type has been used as a professional catalyst in various organic transformations [29–33]. In our recent reports [33–36], we have pointed to the raising of carbon-hetero atom bonds activities by coordination to accessible zinc cation of heterogeneous catalysts [33,34]. Accordingly, it was supposed that coordination of S=O and NH bonds to ZnO and nanoZnO could activate these groups, and facilitate their reactions. In the present paper, we report our results on the use of ZnO and ZnO nanoparticles as efficient and reusable catalysts in the one-pot preparation of *N*-acylsulfonamides, sulfonamides and sulfonate esters (Scheme 1).

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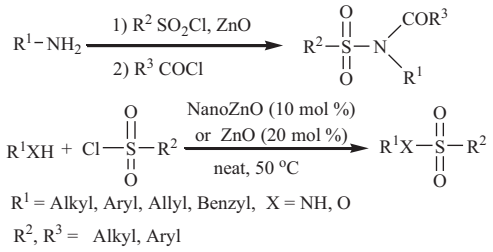

Scheme 1. ZnO-catalyzed sulfonylation and acylation.

2. Experimental

2.1. Preparation of nanocatalysts

2.1.1. Preparation of nanoZnO I [30]

Zinc acetate dihydrate (5.5 g) was dissolved in 50 mL of deionized water and then solid NaOH (16 g) was added slowly into the solution under magnetic stirring at room temperature. A transparent $Zn(OH)_4$ solution was formed. Then 2 mL of ionic liquid 1-butyl-3-methylimidazolium bis (trifluoromethylsulfonyl) imide ([bmim][NTf_2]) was added to 3 mL of the above solution. The suspension was put into a domestic microwave oven (850 W) in air, 30% of the output power of the microwave was used to irradiate the mixture for 5 min (on for 10 s, off for 5 s). The white precipitate was collected by centrifugation, washed with deionized water and ethanol several times, and dried in vacuum oven at 40 °C for 10 h. The mean particle size of these nanoparticles was 47–37 nm [30].

2.1.2. Preparation of nanoZnO II [31]

The ZnO nanoparticles type II was prepared according to the previously reported procedure [31]. In a typical procedure, 0.22 g (1 mmol) of $Zn(CH_3CO_2)_2{\cdot}2H_2O$ was suspended in 120 mL of 2-propanol under vigorous stirring at 50 °C. A NaOH alcoholic solution was prepared by adding 0.08 g (2 mmol) NaOH to 30 mL of 2-propanol under vigorous stirring at 50 °C. The flasks containing $Zn(CH_3CO_2)_2{\cdot}2H_2O$ and NaOH alcoholic solution were cooled in an ice-water bath. The NaOH solution was then added to $Zn(CH_3CO_2)_2{\cdot}2H_2O$ solution under vigorous stirring to give a total volume of 150 mL. Final solution was heated up to 80 °C by microwave irradiation. After 5 min, the transparent solution was obtained. The centrifugation of transparent solution yields white solid which was then calcined at 600 °C for 1 h. The mean particle size of ZnO nanoparticles was reported as 30 nm [31].

2.2. General procedure for the one-pot synthesis of N-acylsulfonamides

Amine (2 mmol) was added to a stirred mixture of ZnO (0.5 mmol) and sulfonylating agent (2 mmol) and the mixture was stirred at ambient temperature for the given times (Table 1). After completion of the sulfonylation reaction (TLC monitoring), acylating agent (2 mmol) was added and the reaction was monitored by TLC again. Then, EtOAc (2 × 10 mL) was added and the precipitated ZnO was filtered off. The resulting organic solution was washed with 10% $NaHCO_3$ and brine, dried over anhydrous Na_2SO_4, and. evaporated to give the desired *N*-acylsulfonamide. The structure of products was assigned by analysis of their IR, ^{1}H NMR, ^{13}C NMR spectra and comparison to authentic samples or elemental analysis. Known products showed physical states; melting points and spectroscopic data in agreement with authentic samples.

2.3. General procedure for sulfonylation of amines and alcohols

Substrate (amine or alcohol) (2 mmol) was added to a stirred mixture of ZnO (0.2 mmol, 20 mol% or nanoZnO type I) and sulfonylating agent (2 mmol). Then, the reaction mixture was stirred at ambient temperature for the given times (Table 2). After completion of the reaction (TLC monitoring), EtOAc (2 × 10 mL) was added and the precipitated ZnO was filtered off. The resulting organic solution was washed with $NaHCO_3$ (10%) and dried over anhydrous Na_2SO_4. Finally, the solvent was removed to give the sulfonylated product in 60–95% yields. No further purification was required for sulfonamides, while sulfonate esters were typically purified by short column chromatography (Hexane, EtOAc).

2.4. Reusability of catalyst

ZnO, nanoZnO type I and nanoZnO type II was regenerated by simple washing with EtOAc and drying under microwave irradiation. Using the recycled catalysts for three consecutive times in both sulfonylation and acylation reactions furnished the product with no significant decreasing in reaction yield.

2.5. Selected spectral data

2.5.1. N-phenyl-N-tosyl acetamide (Table 1, entry 12, compound (*j*))

Colorless needles (EtOH), Mp = 154–156 °C (Lit. 149–150 °C [8]). FT-IR (KBr) ν_{max}: 1700, 1598, 1370, 1267, 1170 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.90 (s, 3H, $COCH_3$), 2.48 (s, 3H, CH_3), 7.26–7.30 (m, 2H, H_{meta} Ph-N), 7.35 (d, 2H, J = 7.8 Hz, H_{ortho} Ph-CH_3), 7.46–7.50 (m, 3H, $H_{ortho,para}$ N-Ph), 7.95 ppm(d, 2H, J = 7.8 Hz, H_{meta} Ph-CH_3). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 21.50, 25.20, 129.10, 129.30, 130.00, 130.50, 136.20, 140.00, 145.00, 170.30 ppm.

2.5.2. N-butyl-N-tosyl acetamide (Table 1, entry 15, compound (*m*))

Thick oil. FT-IR (neat) ν_{max}: 1704, 1596, 1358, 1250, 1168 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) (: 0.90 (t, J = 7.5 Hz, 3H, CH_2CH_3), 1.35 (m, 2H, CH_2CH_3), 1.65 (m, 2H, NCH_2CH_2), 2.28 (s, 3H, CH_3Ph), 2.38 (s, 3H, CH_3CO), 3.80 (t, J = 7.5 Hz, 2H, NCH_2CH_2), 7.30 (d, J = Hz, 2H_{arom}), 7.75 ppm (d, J = 7.8 Hz, 2H_{arom}).

2.5.3. 1-Octyl tosylate (Table 2, entry **2b**)

Thick oil. FT-IR (neat) ν_{max}: 2927, 2857, 1448, 1364, 1188, 1097, 951, 826, 754, 688 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) (: 0.90 (t, J = 7.5 Hz, 3H, CH_2CH_3), 1.25–1.50 (m, 10H, $(CH_2)_5$), 1.60–1.80 (m, 2H, CH_2), 3.00 (s, 3H, CH_3SO_2), 4.20 ppm (t, J = 7.5 Hz, 3H, CH_2O).

2.5.4. Pyridin-2-yl-N-tosylmethanamine (Table 2, entry 10)

White needles (H_2O:EtOH), Mp = 92–94 °C. FT-IR (KBr) ν_{max}: 3210, 3060, 1598, 1441, 1327, 1161, 1111, 1090, 817, 762, 660 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6) δ: 2.37 (s, 3H, CH_3Ph), 4.50 (d, J = 6.30 Hz, CH_2), 7.24 (br t, 1H, $NHSO_2$), 7.35 (m, 3H, 2H_{ortho} to CH_3 and H_3 *pyridyl*, 7.68 (d, J = 6.3 Hz, 2H, H_{ortho} SO_2), 7.26 (td, J = 6.3, 1.5 Hz, H_4 *pyridyl*), 8.16 (t, J = 6.3 Hz, H_5 pyridyl), 8.43 (d, J = 4.20 Hz, H_6 *pyridyl*) ppm. ^{13}C NMR (125 MHz, DMSO-d_6) δ: 21.82, 48.78, 122.48, 123.23, 127.43, 130.43, 137.58, 138.55, 143.50, 149.56, 158.04. Anal. Calcd (%) for $C_{13}H_{14}N_2O_2S$: C, 59.52; H, 5.38; N, 10.68; O, 12.20; S, 12.22; Found C, 59.60; H, 5.48; N, 10.88.

2.5.5. N-glycyl 4-methylbenzenesulfonamide (Table 2, entry **13b**)

White needles (EtOH), Mp = 170 °C. IR (KBr): 3356, 1317, 1149, 918 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6) δ: 2.42 (s, 3H, CH_3), 3.58 (d, J = 6 Hz, 2H, CH_2), 6.71 (br s, 1H, N*H*), 7.26–7.37 (m, 2H, H_{arom}), 7.45–7.73 (m, 2H, H_{arom}), 8.03 (br s,1H, COO*H*) ppm.