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Sulfonated graphene oxide-catalyzed *N*-acetylation of amines with acetonitrile under sonication

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ABSTRACT

Sulfonated reduced graphene oxide (rGO-SO_3H, SRGO) was synthesized by introducing aryl diazonium salt of sulfanilic acid radicals onto chemically modified reduced graphene oxide (rGO) under sonication. SRGO catalyst was characterized by X-ray diffraction (XRD), Raman spectroscopy, solid state ^{13}C MAS NMR (^{13}C SSNMR), scanning electron microscopy (SEM), energy dispersive spectroscopy (EDS), transmission electron spectroscopy (TEM), and X-ray photoelectron spectroscopy (XPS). SRGO was efficiently used as a reusable, metal-free, solid acid catalyst for the direct *N*-acetylation of amines with acetonitrile under sonication into the corresponding amides. Thus, the method could also serve as a novel convenient alternative for the other acetylation reactions under sonication to avoid using toxic substances such as acetic anhydride, acetyl chloride, and acetic acid.

1. Introduction

Amide formation is a very common and essential procedure as a protecting function in organic synthesis [1–4]. The formed amide molecules can be further utilized in wide industrial applications such as pharmaceuticals, agrochemicals, and polymers [4–5]. For amide formation, *N*-acetylation is usually conducted by the reaction of amines with carboxylic acid derivatives, *e.g.* acetic anhydride, acetyl halides, and esters [6–9]. Nevertheless, a number of inherited problems have been encountered in *N*-acetylation [10]: Acyl halides and anhydrides are moisture sensitive and readily reacted with water and alcohols to form the corresponding acids and esters, which leads to the low purity in desired amides [11-15]; The reagents mentioned above are banned in several countries because they could also be used in the synthesis of narcotics; The reactants mostly need basic media like imidazole and pyridine to carry out the reaction [16,17]; The base catalysts are well known for their toxic properties to the environment and humans. The above problems need to be resolved for greener and safer process. *N*-acetylation reactions can be improved by using free acids/thioacids, or via some transamidification [18,19]. Even though good to excellent yields could be achieved from these methodologies, the required reagents have to be manufactured from acid anhydrides and acyl chlorides, which will raise the expense. Besides, most of these reactions are not selective. Therefore, it is very important to develop a new synthetic methodology for the *N*-acetamide formation without using acetic anhydrides, acyl chlorides, and their sources.

There are very few examples in literature for nitriles being used as acyl equivalents [20,21]. Initiated from Garves [22], preparation of aryl and heteroaryl ketones via the transition metal catalyzed insertion of nitriles into arenes/hetero arenes was studied by several research groups [23,24]. In these reactions, an aryl metal complex was reacted with a nitrile functional group to generate a nitrile adduct [25]. The resultant ketimine was subsequently hydrolyzed to produce the ketone. Thus, an attack of aryl metal complex nucleophile onto a comparatively inert nitrile group was enabled by the coordination of transition metal with the nitrogen atom [26]. In some reactions, nucleophilic amines were hired to afford an amide function. However, these methodologies severely suffer from the disadvantages such as necessity of expensive ligands, consumption of costly catalysts (*e.g.* Pt, Ru), and prolongation of reaction time [27,28]. In addition, some of the reported procedures need to use stoichiometric quantities of coupling reagents or highly hazardous reagents and only attain a poor efficiency [20,23,26]. In spite of the above efforts, direct amide formation is still the most important for an industrial process from both environmental and economic viewpoints. To overcome these problems, the use of a cheap and metal free catalyst for *N*-acetylation is desired.

Metal free solid acids are generally considered as environmental-friendly catalysts to replace liquid acids and metal complexes [29]. For example, acidic carbons were adopted

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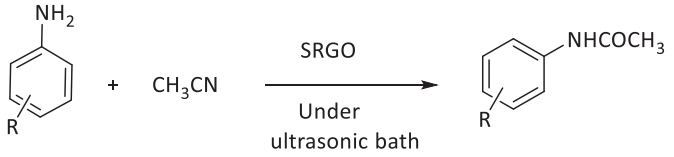

Scheme 1. Sonochemical acetylation of amines with acetonitrile by SRGO.

as highly active protonic and stable acid catalysts for various acid catalyzed reactions [30]. Graphite oxide/graphene oxide (GO) has been efficiently applied in some organic conversions as useful heterogeneous catalysts [31,32]. Moreover, graphite bisulfate was also employed as a solid acid catalyst for organic reaction transformations [33]. In this study, GO was selected as the raw material of a potential catalyst due to its availability and efficiency.

In literature [34–37], ultrasound irradiation was prompted for the chemical modifications of GO and other functionalized GO, *e.g.* the modification of GO with 6-aminoindazole via sonochemical nucleophilic substitutions. With ultrasound method, sulfonated reduced graphene oxide (rGO-SO_3H, SRGO) catalyst was synthesized in our lab by covalently introducing sulfonic acid-containing phenyl radicals onto the 2D-surface of GO. The SRGO product was then employed as the catalyst for the *N*-acetylation of amines with acetonitrile to the corresponding amide compounds under ultrasonic irradiation (Scheme 1) for the first time. The catalytic property of SRGO as a recyclable metal-free solid acid catalyst was also investigated. Although the influence of ultrasound irradiation in organic synthesis is well known [36], we found from a vast survey of literature that there are very few model reactions on this *N*-acetylation reaction [20,21,37].

2. Experimental

2.1. Reagents and analyses

GO (product no.: EW-GO) was purchased from E-Way Technology (Taiwan). All the reagents and solvents were obtained from commercial chemical suppliers (ACROS, TCI, and Sigma) and used without further purification for acetylation reaction. All the experiments were conducted in a 100 mL round-bottomed Pyrex glass flask under N_2 atmosphere with mechanical stirring speed at 600–700 rpm. Flash chromatography had been done on a Merck silica gel 60 (230–400 mesh). Visualization of the progress of the reaction on thin layer chromatography (TLC) was attained by illumination under UV lamp (254 nm).

For the characterization of the prepared catalyst, X-ray diffraction (XRD) was executed on MacScience MXP3 (λCu Kα = 0.154 nm) at 40 kV and 30 mA. The collection interval and scanning rate were 0.02° ($\theta/2\theta$ mode) and 5°/min, respectively. Micro-Raman scattering experiment was operated by using a Dilor X-Y 800 spectrometer with spectral resolution of 0.6 cm^{-1} at room temperature (RT) in air. An argon-ion laser (wavelength of 514.5 nm) with the power of 8 mW and the diameter of 1 µm was used for the excitation over the wavenumber from 200 to 800 cm^{-1}. The spectra were later deconvoluted for defining the suitable peak position. The overall spectra were standardized to the He–Ne laser excitation line. 4 mm CP/MAS DR probe solid state ^{13}C NMR (^{13}C SSNMR) was used at a spinning rate of 10 KHz. For morphology reading and EDS elemental analysis, scanning electron microscope (SEM, model JSM6700F JEOL, Tokyo, Japan) was conducted. The catalyst image was also measured by high resolution transmission electron microscope (HR-TEM, model JEM-2010, JEOL, Tokyo, Japan). In addition, the wide-scan spectrum was recorded via X-ray photoelectron spectroscopy (XPS, PHI 5000 VersaProbe, ULVAC-PHI).

For products, NMR spectra were recorded on a Varian mercury-400 instrument using DMSO-d_6 as solvent. Chemical shifts were reported in parts per million (ppm) with the internal standard tetramethylsilane (TMS). Standard abbreviations specifying multiplicity were used as follows: s = singlet, d = doublet, t = triplet, dd = double doublet, q = quartet, m = multiplet, b = broad. Melting points were determined and reported uncorrected. The mass spectra were examined on a Finnigan LTQ-Orbitrap XL instrument (ESI source).

2.2. Preparation of SRGO catalyst

The chemical modification of GO to SRGO was prepared via grafting of diazonium salt of sulfanilic acid onto GO, similar to the method reported in previous study [37]. The reaction scheme for the synthesis of SRGO is shown in Fig. 1. Firstly, 25 mg of GO nano powder (brown color) was taken into a round bottomed glass flask with 25 mL of deionized water and stirred homogeneously with magnetic stirrer. The resulting mixture was poured into another glass beaker for the sonication in an ultrasonic bath (frequency of 20 kHz and 100% output power). A solution which contains 10 mg of $NaBH_4$ in 15 mL of deionized water was added dropwise into the dispersed GO solution. Later, the whole solution was raised to 60–90 °C for 1 h to obtain a black dispersion mixture. Further, this reaction mixture was washed with deionized water. After centrifugation, the reduced GO (rGO, partially reduced) was achieved. The rGO was then irradiated in 50 mL of ultrasonic bath for 40 min. A diazonium salt was prepared by mixing 50 mg sulfanilic acid and 1 mL of 1 N HCl in 25 mL of deionized water under cooling condition (0–5 °C), monitored by adding 20 mg $NaNO_2$ in 10 mL of deionized water. Subsequently, diazonium solution was poured into the rGO dispersion solution at 0–5 °C and stirred overnight at 30 °C. The resultant mixture was then centrifuged at 5000 rpm for 10–15 min and washed 3 times with deionized water. The consequent black residue was subjected to filtration under vacuum and then dried in an oven at 60 °C for 8 h.

2.3. Direct N-acetylation

The mixture of aniline (3 mmol or 1 equiv) and acetonitrile (3 mmol or 1 equiv) was stirred in a round bottom flask to obtain the homogeneous reaction mixture under sonication bath (frequency of 20 kHz and 100% output power). After the reaction mixture was well stirred, 0.05 g of SRGO was slowly added at 50–60 °C. Reaction was maintained for 15 h to attain dark brown precipitate, which was an indication of reaction completion confirmed by primary analytical technique TLC. Thereafter, the residue was taken into 25 mL of ethyl acetate. The separated and extracted organic layer was dried over anhydrous sodium sulfate. The obtained organic layer was then concentrated under reduced pressure. Eventually, the pure *N*-acylated amine (99%) was gained after the column purification using hexane:ethylacetate (10:1). The procedure has been repeated for the varieties of amines and the obtained compounds were examined with ^1H NMR and ^{13}C NMR (referring to Supplementary Material).

2.4. Spectral data for all the product compounds

***N*-(4-methylbenzyl)-acetamide (3a).** m.p. 127–129 °C, yield 96%. ^1H NMR (400 MHz, DMSO–d_6) δ 10.00 (brs, 1H, CONH), 7.18–7.45 (m, 4H, ArH), 4.25 (s, 2H, NCH_2Ar) 2.6 (s, CH_3, $COCH_3$), 2.3 (s, 3H, Ar-CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) 169.10, 132.00, 130.00, 127.80, 127.00, 126.11, 125.89, 42.45, 24.00, 21.00; FT-IR (KBr, cm^{-1}) 1624, 2990, 3000; HRMS (ESI) calcd for $[C_{10}H_{14}NO]^+$: 164.03. Found: 164.023.

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