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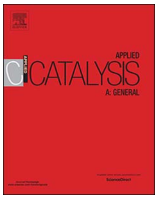

Feature Article

Solvent-free “green” amidation of stearic acid for synthesis of biologically active alkylamides over iron supported heterogeneous catalysts

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ABSTRACT

Stearoyl ethanolamine was synthesized by amidation of stearic acid with ethanolamine in solventless conditions. Iron containing heterogeneous catalysts supported on SiO_2, Al_2O_3, Beta (BEA), ZSM-12 (MTW) and Ferrierite (FER) were used in this work. Sn-modified Ferrierite and H-Ferrierite were also studied for comparison. Fe-modified catalysts synthesized using solid state ion-exchange and evaporation impregnation methods, were thoroughly characterized with X-ray powder diffraction, scanning electron microscope, FTIR with pyridine, nitrogen adsorption, energy dispersive X-ray microanalysis and Mössbauer spectroscopy. The highest conversion was obtained with Fe-H-FER-20 at 140 °C in 1 h giving 61% conversion and 98% selectivity towards the desired amide. The catalytic performance in terms of turnover frequency per mole of iron was achieved with the catalyst exhibiting the largest amount of Fe^{3+} species, optimum acidity and a relatively low Brønsted to Lewis acid site ratio.

1. Introduction

Amidation of fatty acids is an important reaction, in which fatty alkanolamines are formed as products. Applications of these products are related not only to surfactants, but also to high value-added pharmaceuticals exhibiting several biological effects, such anti-carcinogenic ones [1] and activity against the Alzheimer disease [2]. The use of heterogeneous catalysts makes the process more industrially benign and cheaper, avoiding cumbersome catalyst separation.

Fatty acid amides are typically synthesized with homogeneous catalysts, for example by reacting a fatty acid ester with an alkanolamine in the presence offatty acid chlorides [3] or using potassium hydroxideas reagents [4], which are not environmentally benign procedures. Utilization of fatty acids is beneficial from the viewpoint of expanding the feedstock base and typically acidic and metal modified zeolites and mesoporous materials were used as catalysts. Direct amidation of fatty acids with alkanolamines has been scarcely investigated over heterogeneous catalysts [5–8]. These reactions were mainly conducted in the presence of solvents. In some cases, supported iron catalysts have been applied in acetic acid amidation [9,10]. This acid underwent amidation with several phenylamine derivatives over iron on activated carbon catalyst. A high excess of acid was used in this reaction operating at the temperature close to the boiling point of acetic acid yielding 96% of amides within 1- 5 h depending on the reactant [9]. In addition acetic acid was also amidated with aniline using Fe-Beta zeolite with Si/Al ratio of 15 at 117 °C with an excess of acetic acid under microwave irradiation giving 52% conversion of stearic acid in 15 min [10]. Furthermore, cheap alumina balls were used for production of *n*-isopropylheptanamide from heptanoic acid and isopropylamine resulting in 95% yield at 140 °C in 3 h [11]. In this work [11] the alumina balls were calcined prior to the experiment facilitating their function as adsorbents during amidation reaction. The reactant was a relatively short carboxylic acid and the drawback with alumina balls is that they cannot be used in autoclave. When Cu-SiO_2, Cu-Al_2O_3 and Cu-TiO_2 catalysts were studied in α-amidation of cyclic ethers [12], it was observed that the reaction was influenced by the support type and copper dispersion. Application of non-conventional, sustainable, eco-friendly and highly efficient process technology for production of various types of amides is of immense importance. Oxidative amidation of alcohols with amines was carried out using heteropolyanion-based ionic liquids under microwave irradiation and solvent free reaction media [13]. Formation of primary, secondary and tertiary alkyl amides was reported with bifunctional catalysts. Direct amidation of carboxylic acids with amines using ultrasonic irradiation was investigated using

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solid acid sulfonated graphene oxide [14]. Very high yields of amides under shorter reaction time was reported by the authors when sonochemical amidation of carboxylic acid was applied with a reusable solid acid catalyst.

Besides zeolites *per se*, transition and noble metal modified ones have found applications in several industrial processes in the fields of petrochemistry, oil refining, exhaust gas emission abatement, production of specialty and fine chemicals. In the current study besides SiO_2, Al_2O_3 and TiO_2 supports also, Beta (BEA), Ferrierite (FER), and ZSM-12 (MTW) zeolites were modified with Fe using solid state ion-exchange and evaporation impregnation synthesis methods. Sn modified FER was synthesized using evaporation impregnation method. ZSM-12 (MTW) belongs to high silica zeolite group with unidimensional channel systems, 12 membered rings with pore dimensions 0.57 × 0.61 nm. The pore dimensions are slightly larger than for ZSM-5 (MFI) zeolite. ZSM-12 zeolite exhibits shape selectivity and is resistant to coke formation [15,16].

Application of zeolites is not only limited to amidation of carboxylic acids, as they have been used as catalysts for amidation of alcohols [17] and ketones [18]. In the former case for example *sec*-butanol was reacting with acrylonitrile at 160 °C giving 76% selectivity to the corresponding amide with 72% conversion after 8 h [17]. Furthermore, there was an optimum Si/Al ratio observed giving the highest amide selectivity. In the latter case, in the amidation of benzophonene with hydroxylamine hydrochloride the isolated yield of amide using microwave irradiation and HY-zeolite as a catalyst of 94% was achieved in 2 min [18].

The aim in this work was to investigate the possibilities to synthesize stearoyl ethanolamide from stearic acid and ethanolamine in the absence of any volatile solvent and for the first time to use cheap supported iron catalysts in this reaction. The purpose was also to study feasibility of overall technology comprising environmentally benign methods of catalyst preparation by solid state ion exchange and reactions with inexpensive heterogeneous catalysts. The studied catalysts were characterized by several physical-chemical methods, including Mössbauer spectroscopy, gas phase pyridine adsorption desorption, liquid phase adsorption of 2-phenylethylamine, solid state NMR, nitrogen adsorption and SEM. The main parameters were the type of the support and acid sites, concentration of the latter and the oxidation state of iron.

2. Experimental

2.1. Catalyst synthesis

Several commercial zeolites and oxides were used as catalysts and supports. Silica gel 60 (Merck) was sieved with a 90 µm sieve. Titanium (IV) hydroxide granules (Alfa Aesar) were crushed and sieved with ball milling to the size below 90 µm. NH_4-Beta-300, NH_4-Beta-150, NH_4-Beta-25 and NH_4-FER-20, in which the number represents SiO_2 to Al_2O_3 ratio, were purchased from Zeolyst International and calcined in order to get the proton forms. The step calcination procedure was: heating rate of 3.8 °C/min up to 250 °C, holding at this temperature for 40 min, subsequent heating with 2.1 °C/min up to 400 °C, maintaining this temperature for 4 h, thereafter cooling zeolite to 25 °C.

To prepare iron catalysts with 5 wt% by evaporation impregnation method (EIM), 3.6 g ferric nitrate nonahydrate (Fluka) was dissolved in 250 ml of water. The pH was recorded prior and after adding 10 g of the catalyst support. The round bottom flask was put in the rotator evaporator for rotation at 60 °C during 24 h. Thereafter, water was evaporated under vacuum and the catalyst was dried at 100 °C overnight. The catalyst was then calcined in a muffle oven at a rate of 3 °C/min up to 250 °C, maintaining this temperature for 50 min, followed by heating rate of 3.3 °C/min up to 450 °C and holding this temperature for 3 h, thereafter cooling the catalyst to 25 °C. For Fe-SiO_2-50% US-EIM the slurry was first subjected to ultrasound for 2 h, followed by rotation in rotavapor for 24 h. The aqueous solution was finally evaporated, the catalyst was dried for 7 h at 100 °C and calcined in a muffle oven.

For the tin containing catalyst, the same synthesis procedure was applied with 0.905 g of tin sulfate (Fluka, ≥96%) or 1.6976 g of tin chloride (Sigma, 99%). The step calcination procedure was different from iron catalysts: initial heating rate was 2.3 °C/min up to 200 °C, maintaining this temperature for 65 min, heating to 400 °C with 2.9 °C/min, holding at 400 °C for 3 h, thereafter cooling the catalyst to 25 °C.

To prepare iron catalysts of 5 wt% by SSIE, 3.6 g of ferrite nitrate nonahydrate (Fluka) was mixed with 10 g of the catalyst support during ball milling for 6 h. Every 2 h, the equipment was stopped to manually mix and crush the solid mixture. After 6 h of ball milling, the catalyst was dried in an oven at 100 °C overnight. Then, the catalyst was calcined applying the same step calcination procedure as for iron catalysts prepared by EIM.

For the tin catalyst, the same synthesis procedure was applied with 0.905 g of tin sulfate (Fluka, ≥96%).

2.2. Catalyst characterization methods

The specific surface area was determined using nitrogen adsorption with Sorptomatic 1900. The samples were outgassed prior to measurements at 150 °C for 3 h. The specific surface areas were calculated using Dubinin's method [19,20].

XRD measurements were performed to identify the structure of zeolites using Philips X'Pert Pro MPD instrument and monochromated CuKα radiation at 40 kV/50 mA using beam collimation of 0.25° divergence slit and a fixed mask of 20 mm. Philips X'Pert HighScore and MAUD programs were used for analysis.

SEM analyses were performed with a LEO Gemini 1530 scanning electron microscope. Thermo Scientific UltraDry Silicon Detecto (SDD) was used for morphological analysis of samples. The equipment contained both secondary and backscattered electron detectors and an In-Lens detector.

The amounts of Brønsted and Lewis acid sites at bands 1545 cm^{-1} and 1455 cm^{-1}, respectively were quantified with pyridine (Sigma-Aldrich, > 99.5%) adsorption/desorption by FTIR using ATI Mattson instrument and using molar extinction coefficients from Emeis [21].

Adsorption of 2-phenylethylamine on zeolites and metal modified zeolites was investigated using 0.03 M 2-phenylethylamine as an adsorbate in distilled water [22]. Typically 50 mg of the dried catalyst was combined with 3 ml of 2-phenylethylamine (Acros Organics, 99%) solution at 24 °C. The solution was stirred with a magnet for 2 h, which was sufficient to achieve the equilibrium. The supernatant liquid after filtration of the catalyst was analyzed with UV–vis (Shimadzu UV-2550) at 252 nm. The adsorbed amounts of 2-phenylethylamine were calculated by subtracting the amount of 2-phenylethylamine present in the liquid phase from the initial adsorbent concentration. The experimental error in absorbance was 2%.

2.3. Catalyst evaluation for amidation reaction and analytical procedure

Typically the experiments were performed in an autoclave using equimolar amounts of the fatty acid (Sigma Aldrich, 95%) and ethanolamine (0.14 mol, Sigma Aldrich, > 95%) under 20 bar Ar (AGA) under high stirring speed, 1100 rpm to minimize mass transfer limitations using 0.5 g catalyst. External mass transfer was suppressed by applying small catalyst particles, below 90 µm. The liquid volume was 44 ml and the initial concentration of fatty acid was 3.0 M. The samples of reaction mixtures were silylated as follows: the solid sample was dissolved in toluene with the concentration of 1 mg/ml. Thereafter about 1 ml of the sample was silylated with 120 µl of bis(trimethylsilyl) trifluoroacetamide (BSTFA) and 0.4 µl of trimethylchlorosilane (TMCS) at 70 °C for 1 h. The samples were cooled and analyzed with a GC equipped with HP-1 column using the following temperature program: 100 °C (1.5 min) – 12 °C/min – 340 °C (20 min). The injector and