Research on Chemical Intermediates
https://doi.org/10.1007/s11164-018-3592-9

Synthesis of benzamides through direct condensation of carboxylic acids and amines in the presence of diatomite earth@IL/$ZrCl_4$ under ultrasonic irradiation

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Received: 30 May 2018 / Accepted: 10 September 2018

Abstract

A green, rapid, mild and highly efficient pathway for the preparation of benzamide derivatives is reported. The reaction was performed through direct condensation of benzoic acids and amines under ultrasonic irradiation in the presence of Lewis acidic ionic liquid immobilized on diatomite earth (diatomite earth@IL/$ZrCl_4$). A new, highly efficient and green solid acid catalyst was easily prepared via a two-step procedure and used as an effective reusable catalyst. The prepared catalyst provides active sites for the synthesis of benzamides. The advantages of this method are the use of a superior and recoverable catalyst, low reaction times, simple procedure, high-yielding and eco-friendly process and use of ultrasonic irradiation as a green and powerful technology. Since benzamides are used widely in the pharmaceutical, paper and plastic industries, and also as an intermediate product in the synthesis of therapeutic agents, the presented new synthetic methods for this type of compounds can be of considerable importance.

Keywords Benzamides · Diatomite earth · Solid acid catalyst · Ultrasound irradiation · Diatomite earth@IL/$ZrCl_4$

Introduction

The American Chemical Society's Green Chemistry Institute Pharmaceutical Round Table recently identified that amide formation avoiding poor atom economy reagents is a priority area of research in the pharmaceutical industry [1–3]. As many

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Published online: 20 September 2018

as 65% of drug molecules prepared by pharmaceutical companies are attached to an amide group. Amides are in the structures of potential drug compounds such as loperamide (Imodium AD, antidiarrheal) acetaminophen (analgesic), lidocaine (Xylocaine, local anesthetic), [4, 5] atorvastatin (cholesterol-lowering) [6], lisinopril (inhibitor of angiotensin converting enzyme) [7], valsartan (blockade of angiotensin-II receptors) [8], sorafenib [9] and diltiazem (calcium channel blockers used in the treatment of angina and hypertension) [10], and lipitor [11–13] and vyvanse [14], which have been widely used for the treatment of cancer, hypercholesterolemia, and juvenile hyperactivity, respectively [15]. Amide compounds are also widely used in industries such as paper, plastic and rubber and in agricultural areas [16]. They are also used as an intermediate product in the synthesis of therapeutic agents. Amide derivatives also show antiplatelet activity [17, 18]. These compounds are usually produced from the reaction between carboxylic acids and amines at high temperature (> 180 °C) ,but this is incompatible with most functionalized molecules [19]. Also, activation of carboxylic acids in acid chloride form, anhydrides or esters requires a separate step, and this protocol suffers from low atom economy [20, 21]. On the other hand, various coupling agents have been used for the activation of carboxylic acids such as bis[bis(trimethylsilyl)amino] tin(II) [22], titanium tetrachloride [23], trimethylaluminium [24], tetrazoles [25], Lawesson's reagent [26], benzoxazoles [27], oxalates [28], phosphonium reagents, carbodiimides and uronium reagents [29] in amidation reaction. The limitations of these reagents are stability, hazardous nature, toxicity, cost and the requirement for the removal of byproducts that complicate the isolation of the desired amides.

Recently, a number of researchers have developed efficient boron-based catalysts for this transformation, but there are some drawbacks. Preparation of these catalysts is not trivial, and separation of the products, as well as the homogeneous catalysts, from the reaction mixture can be difficult [30–35]. Also, different catalysts such as Glutaryl-7-ACA acylase [36], Ti, Zr and Al-supported mesoporous silica [37], Montmorillonite K10 [38] and mesoporous silica SBA-15 [39] have been applied for preparation of amides through direct amidation of acids.

Among the recent developments in catalysis, the use of ionic liquids has become an active area of research. Ionic liquids show many advantages including infinitesimally low vapor pressure, high thermal stability, low toxicity, and ease of handling. All of these properties make them alternative "green" reaction media for replacing volatile solvents in various catalytic processes [40–43].

Sonochemistry is increasingly valuable tool in organic chemistry, since it offers a versatile and facile pathway for a large variety of syntheses. Without doubt, compared with conventional thermal heating, the benefits of the sonochemical processing method are substantial decreases of reaction time, enhanced organic reaction rates, environmentally friendly reactions (using small amounts of solvents and generating fewer side products) and in many cases, improved yields and purity of the compounds and selectivity, in addition to lower cost and simplicity in handling and processing.

Ultrasound is a sound wave with a frequency above 20 kHz. Acoustic cavitation and acoustic streaming are the two basic phenomena associated with any ultrasonic

process. Ultrasonic waves consist of compression and expansion cycles. When an ultrasonic wave is passed through a liquid, a positive pressure is exerted on the liquid during the compression cycle and a negative pressure is exerted during the expansion cycle. During the negative pressure, molecules are pulled away from each other, resulting in the formation of cavities in the liquid. Over many cycles, these cavities grow and enlarge. Finally, collapse of the bubbles leads to very high temperatures of more than 5000 K and high pressures of 2000 atmospheres [44–51].

Here, we reported a green and highly efficient synthesis of benzamide derivatives by one-pot condensation of benzoic acids and amines in the presence of a green reusable and highly efficient catalyst (diatomite earth@IL/$ZrCl_4$) under ultrasound irradiation (Scheme 1).

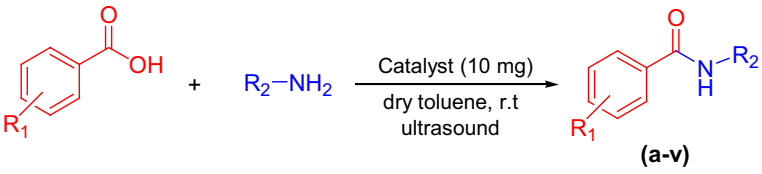
Experimental

Materials and apparatus

All the materials were purchased commercially from Sigma-Aldrich and Merck and were used without further purification. A multiwave ultrasonic generator (Sonicator 3200; Bandelin, MS 73, Germany), equipped with a converter/transducer and titanium oscillator (horn), 12.5 mm in diameter, operating at 20 kHz with a maximum power output of 200 W, was used for the ultrasonic irradiation. The ultrasonic generator automatically adjusted the power level. FT-IR spectra were recorded with KBr disc using a Magna-IR spectrometer 550 Nicolet. NMR spectra were recorded on a Bruker 400 MHz spectrometer with $CDCl_3$ as a solvent and TMS as an internal standard. Elemental analysis (CHN) was carried out on a Carlo ERBA Model EA 1108 analyzer. The thermogravimetric analysis (TGA) curves were carried out using a V5.1A DUPONT 2000. To investigate the morphology of the functionalized diatomite, FE-SEM images and EDS spectrum of the products were visualized by a Sigma ZEISS, Oxford Instruments, Field Emission Scanning Electron Microscope.

Preparation of diatomite earth@IL/ZrCl4

In the first step, ionic liquid was prepared according to the procedure reported by Sasaki et al. [52]. *N*-Methylimidazole (1 mmol) and 3-trimethoxysilylpropyl chloride (1 mmol) were mixed in a dry 50-ml flask under nitrogen flow. The system was evacuated and refilled with nitrogen, and this procedure was repeated



Scheme 1 Synthesis of benzamide derivatives using diatomite earth@IL/$ZrCl_4$

five times, and refluxed for 48 h. Secondly, diatomite earth (2.0 g) was dispersed in dry toluene (50 mL) and ultrasonicated for 30 min. Then, 0.6 mmol of 1-(3 trimethoxysilylpropyl)-3-methyl-imidazolium chloride (IL) was added slowly with continuous stirring during 1 h. After 18 h, 0.18 g of ZrCl4 was added and refluxed overnight under dry N2 atmosphere. Finally, the resultant mixture was cooled and separated by centrifugation and washed with acetone and methanol four times and dried in a vacuum oven at 80 °C for 8 h (Scheme 2).

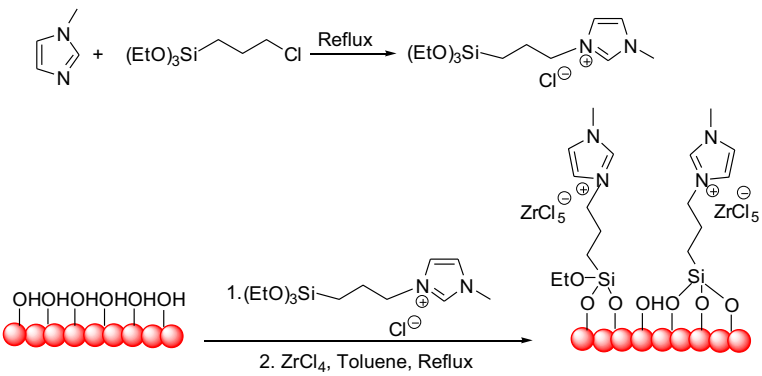
General procedure for the preparation of benzamides

Benzoic acid derivatives (1 mmol) and heterogeneous catalyst (10 mg) were mixed for 5 min in 1 mL of anhydrous toluene. Then, the amine (1.2 mmol) was added and the mixture was reacted under ultrasound for about 15–60 min at room temperature. After completion of the reaction (monitored by TLC), the catalyst was separated through filtration and the solvent was removed in vacuo. The obtained residue was dissolved in chloroform (10 ml) and washed with 10% $NaHCO_3$ (10 ml) and HCl (1 M, 10 ml). The organic layer was extracted and dried over Na_2SO_4 and concentrated under reduced pressure to afford the amide, which was purified by recrystallization or column chromatography.

Representative spectral data

***N*-Methyl benzamide (a)** White solid; mp: 76–78 °C [53]; IR (KBr) (ν_{max}/cm^{-1}): 3276 (NH), 1645 (CO), 1480–1583 (C=C); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8:00 (d, J = 7.0 Hz, 2H; Ar), 7.50 (m, J = 7.0 Hz, 1H; Ar–H), 7.40 (d, J = 7.0 Hz, 2H; Ar–H), 7:00 (s, NH), 2.91 (d, J = 5.6 Hz, 3H).

***N*-Butylbenzamide (b)** Oil; IR (KBr) (ν_{max}/cm^{-1}): 3413 (NH), 1666 cm^{-1} (C=O); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8:00 (d, J = 7.0 Hz, 2H; Ar–H), 7.64 (br s, 1H; NH), 7.5 (m, J = 7.0 Hz, 1H; Ar–H),) 7.4 (d, J = 7.0 Hz, 2H; Ar–H), 2.92 (t, J = 6.4 Hz, 2H), 1.26 (d, J = 9.6, 4H), 0.89 (t, J = 6.4 Hz, 3H).



Scheme 2 Synthesis of diatomite earth@IL/$ZrCl_4$

***N*-Phenylbenzamide (c)** White solid; mp: 160–162 °C [54]; IR (KBr) (ν_{max}/cm^{-1}): 3303 (NH), 1635 (C=O); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) δ 8.80 (s, NH), 7.70 (d, J = 6 Hz, 2 H), 7.51 (t, J = 6.8 Hz, 1 H), 7.42 (t, J = 6.4 Hz, 2H), 7.33 (t, J = 6.8 Hz, 2H), 7.27 (t, J = 8 Hz, 3H).

***N*-(4-Methoxyphenyl)benzamide (d)** White solid; mp: 164–165 °C [54]; IR (KBr) (ν_{max}/cm^{-1}): 3421 (NH), 1637 cm^{-1} (C=O); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.12 (d, J = 7.2 Hz, 2H, Ar–H), 7.62 (d, J = 7.2 Hz, 1H, Ar–H), 7.48 (m, J = 7.6 Hz, 3H, Ar–H), 6.77 (d, J = 8.8 Hz, 2H, Ar–H), 6.72 (d, J = 8.8 Hz, 2H, Ar–H), 6.4 (s, 1H, NH), 3.75 (s, 3H, CH_3).

***N*-(4-Chlorophenyl)benzamide (e)** Colorless crystals; mp: 192–193 °C [37]; IR (KBr) (ν_{max}/cm^{-1}): 3377 (NH), 1640 (C=O); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.86 (d, J = 7.2 Hz, 2H), 7.48–7.59 (m, 6H), 6.67 (s, NH).

***N*-(4-Bromophenyl)benzamide (f)** Colorless crystals; mp: 198–200 °C [54]; IR (KBr) (ν_{max}/cm^{-1}): 3421 (NH), 1646 cm^{-1} (C=O); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 7.86 (d, J = 7.2 Hz, 2H), 7.79 (s, NH), 7.49–7.58 (m, 6H).

***N*-(2-Bromoethyl)benzamide (g)** White solid; mp: 105–106 °C [55]; IR (KBr) (ν_{max}/cm^{-1}): 3303 (NH), 1635 (C=O), 1487–1577 (C=C); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 7.79 (d, J = 7.6 Hz, 2H), 7.52 (t, J = 7.6 Hz, 1H), 7.45 (t, J = 7.6 Hz, 2H), 6.64 (s, NH), 3.9 (q, J = 6 Hz, 2H), 3.6 (t, J = 6 Hz, 2H).

***N*-(3-Bromopropyl)benzamide (h)** White solid; mp: 53–55 °C [56]; IR (KBr) (ν_{max}/cm^{-1}): 3458 (NH), 1661 (C=O), 1488–1521 (C=C); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 7.78 (d, J = 7.2 Hz, 2H), 7.51 (d, J = 7.2 Hz, 1H), 7.44 (d, J = 7.6 Hz, 2H), 6.48 (bs, 1H), 3.62 (q, J = 6.4 Hz, 2H), 3.49 (t, J = 6.4 Hz, 2H), 2.20 (quin, J = 6.4 Hz, 2H).

***N*-(2-Bromoethyl)-2,6-dimethoxybenzamide (i)** White solid; mp: 147–150 °C; IR (KBr) (ν_{max}/cm^{-1}): 3322 (NH), 1648 cm^{-1} (C=O); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.31(t, J = 8.4 Hz, 1H), 6.57 (d, J = 8.4 Hz, 2H), 6.2 (br, NH), 3.88 (dt, J = 17.6 Hz, 6 Hz, 2H), 3.83 (s, 6H), 3.61 (t, J = 6 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 167.6, 159.8, 134.2, 106.7, 105.2, 55.5, 47.4, 31.

***N*-(3-Bromopropyl)-2,6-dimethoxybenzamide (j)** White solid; mp: 112–114 °C. IR (KBr) (ν_{max}/cm^{-1}): 3262 (NH), 1661 (C=O); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 2.19 (q, J = 6.4 Hz, 2H), 3.56(t, J = 6.4 Hz, 4H), 3.81 (s, 6H), 5.9 (br, NH), 6.55(d, J = 8.4 Hz, 2H), 7.26 (t, J = 8.4 Hz, 1H), ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 167.7, 158.9, 134.1, 105.9, 105.7, 56, 39.3, 32.8, 30.8.

***(S)*-*N*-((Ethyl-2-pyrrolidiny1)methyl)-2,6-dimethoxybenzamide (k)** White solid; mp: 102–103 °C [57]; IR (KBr) (ν_{max}/cm^{-1}): 3262 (NH), 166 l (C=O), ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.29 (t, J = 8.5 Hz, 2H), 6.6 (d, J = 8.5 Hz, 1H), 6.30

(br, NH), 3.86 (s, 6H), 3.28 (m, 1H), 3.14 (m, 1H), 2.95 (m, 1H), 2.65 (q, J = 7 Hz, 1H), 2.2 (m, J = 8.5 Hz, 2H), 1.92 (m, 1H), 1.82 (m, 1H), 1.74 (m, 2H), 1.11 (t, J = 7 Hz, 3H).

***N*-((*S*)-1-Hydroxy-3-phenylpropan-2-yl)benzamide (l)** White solid; mp: 174–176 °C [58]; IR (KBr) (ν_{max}/cm^{-1}): 3309 (NH), 1635 (C=O), 1485–1544 (C=C), ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.7 (d, J = 6 Hz, 2H), 7.5 (t, J = 6.8 Hz, 1H), 7.4 (t, J = 6.4 Hz, 2H), 7.33 (t, J = 6.8 Hz, 2H), 7.27 (t, J = 8 Hz, 3H), 6.45 (br, s, NH), 4.39 (s, 1 H, CH), 3.79 (t, CH_2), 3.01 (s, 2H, CH_2).

***N*-((*S*)-1-Hydroxy-3-phenylpropan-2-yl)2,6-dimethoxybenzamide (m)** White solid; mp: 220–222 °C; IR (KBr) (ν_{max}/cm^{-1}): 3412 (NH), 1660 (C=O), 1474–1596 (C=C); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.2–7.3 (m, 6H), 6.56 (d, J = 8.4 Hz 2H), 6.28 (s, NH), 4.63 (m, 1H), 4.36 (t, J = 8 Hz, 1H), 4.14 (t, J = 8 Hz 1H), 3.82 (s, 6H, OCH), 3.28 (dd, J = 14, 5.2 Hz, 1H), 2.8 (dd, J = 14, 9.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 42, 56.27, 66.27, 71.83, 103.88, 107.66, 126.54, 128.7, 129.51, 131.65, 138.41, 159, 160.73, mass spectrum, m/z (relative intensity, %): 315.38 (0, M^+); 206.2 (100), 178.2 (57), 165.1 (20), 91.1 (28), 83 (32), 42.1 (12), 77.1 (8).

***N*-((*S*)-1-Hydroxy-3-phenylpropan-2-yl)-6-chloropyridine-3-carboxamide (n)** White solid; IR (KBr) (ν_{max}/cm^{-1}): 3253 (NH), 1659 (C=O), 1452–1590 (C=C); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.61 (s, 2H), 8.02 (d, J = 8 Hz, 2H), 7.26–7.42 (m, 5H), 6.52 (d, J = 4.8 Hz, NH), 4.45 (m, 1H), 3.82 (m, 2H), 3.04 (d, J = 7.2 Hz, 2H), 1.82 (s, OH).

***N*-Benzylbenzamide (o)** White solid; mp: 104–106 °C [39]; IR (KBr) (ν_{max}/cm^{-1}): 3295 (NH), 1640 (C=O), 1490–1547 (C=C); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.80 (d, J = 7.6 Hz, 2H), 7.51 (d, J = 7.2 Hz, 2H), 7.42 (d, J = 7.6 Hz, 2H), 7.31–7.52 (m, 4H), 6.61 (s, 1H), 4.63 (d, J = 5.2 Hz, 2H).

***N*-Benzyl-4-bromobenzamide (p)** White solid; mp: 155–159 °C [59]; IR (KBr) (ν_{max}/cm^{-1}): 3314 (NH), 1640 (C=O), 1482–1590 (C=C); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.66 (d, J = 8 Hz 2H), 7.55 (d, J = 8.4 Hz, 2H), 7.26–7.36 (m, 5H), 6.49 (s, NH), 4.62 (t, J = 5.6 Hz, 2H).

***N*-Benzyl-3-bromobenzamide (q)** White solid; mp: 112–116 °C [59]; IR (KBr) (ν_{max}/cm^{-1}): 3310 (NH), 1640 (C=O), 1466–1548 (C=C); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.8 (s, 1H), 7.59 (t, J = 7.6 Hz, 2H), 7.26–7.35 (m, 6H), 6.40 (s, NH), 4.64 (t, J = 5.6 Hz, 2H).

***N*-Benzyl-4-methoxybenzamide (r)** White solid; mp: 124–125 °C [60]; IR (KBr) (ν_{max}/cm^{-1}): 3265 (NH), 1632 (C=O), 1506–1607 (C=C); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.76 (d, J = 8.4 Hz, 2H), 7.26–7.36 (m, 5H), 6.92 (d, J = 8.8 Hz, 2H), 6.48 (s, NH), 4.65 (d, J = 5.2 Hz, 2H), 3.85 (s, 3H, OCH_3).

***N*-Benzyl-3,5-dinitrobenzamide (s)** White solid; mp: 202–203 °C [61]; IR (KBr) (ν_{max}/cm^{-1}): 3315 (NH), 1638 (C=O), 1454–1542 (C=C); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 9.12 (s, 1H), 8.93 (s, 2H), 7.24–7.41 (m, 5H), 6.28 (s, NH), 4.7 (d, J = 5.2 Hz, 2H).

***N*-Benzylpropionamide (t)** White solid; mp: 51.2–52.3 °C [62]; IR (KBr) (ν_{max}/cm^{-1}): 3421 (NH), 1637 (C=O), 1488–1548 (C=C); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.28–7.36 (m, 5H), 6.31 (s, NH), 4.64 (d, J = 5.2 Hz, 2H), 2.12 (q, J = 7.2 Hz, 2H), 0.97 (t, J = 7.2 Hz, 3H).

***N*-(4-Methoxyphenyl)propionamide (u)** White solid; mp: 78–85 °C [63]; IR (KBr) (ν_{max}/cm^{-1}): 3421 (NH), 1637 (C=O), 1488–1548 (C=C); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.43 (d, J = 8.4 Hz, 2H), 6.74 (d, J = 8.4 Hz, 2H), 6.16 (s, NH), 3.73 (s, OCH_3, 3H), 2.36 (q, J = 7.2 Hz, 2H), 1.13 (t, J = 7.2 Hz, 3H).

***N*-Benzylacetamide (v)** White solid; mp: 61 °C [64]; IR (KBr) (ν_{max}/cm^{-1}): 3414 (NH), 1639 (C=O), 1483–1571 (C=C); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.19–7.27 (m, 5H), 6.96 (s, NH), 4.32 (d, J = 5 Hz, 2H), 1.92 (s, 3H).

Results and discussion

Structural analysis of diatomite earth@IL/ZrCl4

The FT-IR spectrum of the prepared catalyst was evaluated in order to characterize the surface functionlization. As can be seen in Fig. 1, the broad peaks at about 1089, 794 and 477 cm^{-1} in all the spectra contributed to asymmetric stretching, symmetric stretching and bending vibrations in siloxane (Si–O–Si and Si–OH) respectively. The broad peak at 3421 cm^{-1} was related to the stretching vibration in the structural hydroxyl groups. In FTIR of the catalyst, the presence of a peak around 2900 cm^{-1} (C–H in propyl chain) indicates that the chloropropyl chain is covalently bound on the surface of the diatomite earth. Absorption at 1600 cm^{-1} is related to C=N in the imidazole ring and suggests that ionic liquid (1-methylimidazolium chloride) was successfully loaded on the diatomite earth surfaces. Symmetric stretching and bending vibrations in zirconium tetrachloride (Zr–Cl) cannot be seen in the FT-IR spectrum, because it appears at around 990 cm^{-1} and overlaps with the Si–OH peak.

Figure 2 shows SEM images of natural diatomite earth and the functionalized sample. As can be seen, there has been small changes in the morphology of modified diatomite surfaces showing that functionalization with IL/$ZrCl_4$ has occurred.

EDX as a powerful technique was used for the evaluation of the catalyst content elements. The result confirmed the presence of Si, O, C, N, Cl, and Zr in the catalyst structure (Fig. 3). According to the weight percentage of the catalyst composition, it is clear that about 2.5 wt% of ionic liquid and $ZrCl_4$ were attached on the diatomite earth surfaces.

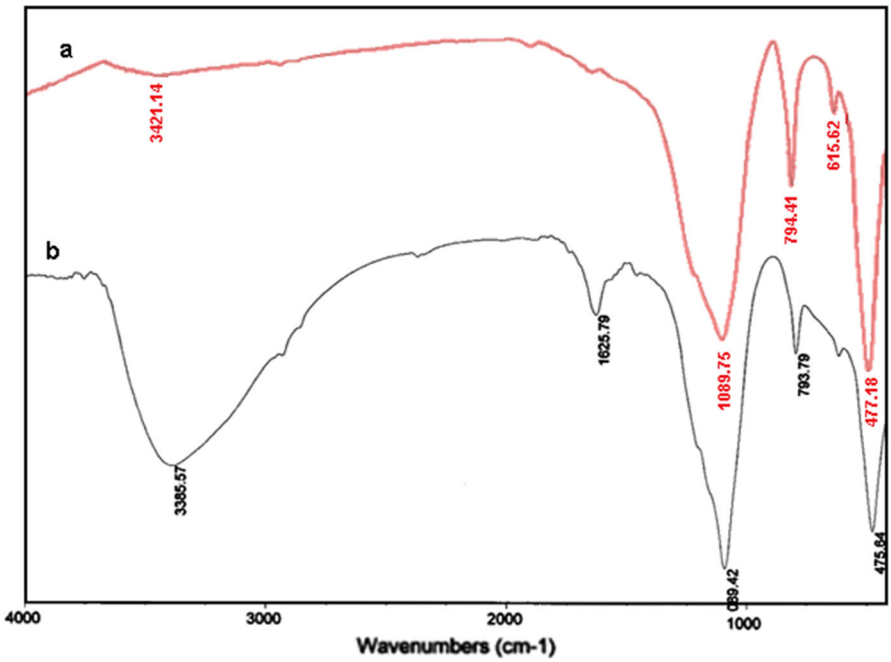


Fig. 1 FT-IR spectra of a diatomite earth (a) and diatomite earth@IL/$ZrCl_4$ (b)

The thermal stability of the diatomite earth and catalyst (diatomite earth@IL/$ZrCl_4$) was evaluated by TGA (Fig. 4). The tGA curves show the mass loss of the catalyst due to decomposition of attached organic groups with an increase in heating. The first mass loss at 100–200 °C contributes to the evaporation of physically adsorbed water. The weight loss at 200–600 °C is related to the thermal decomposition of the ionic liquid and organic spacer covalently bonded to the diatomite earth surfaces.

After the preparation and characterizations of the atalyst, we studied the optimization of different reaction parameters using a model reaction under ultrasonic irradiation. In this way, benzoic acid was reacted with butylamine in dry toluene under ultrasound irradiation for just 15 min in the presence of a series of potential catalysts. The reaction was performed in different solvents. As illustrated in Table 1, the prepared solid acid catalyst showed best activity in toluene compared to other organic solvents. According to the obtained results, 10 mg of catalyst was the best amount with the higher yield. Furthermore, when the amount of the catalyst was increased to 15 mg, the yield was not improved, while the uncatalyzed reaction produced only 10% yield of the product.

When the direct reaction between the acid and the amine was carried out under reflux conditions, a high temperature and long time were required, while ultrasonic conditions led to an excellent yield of products in short reaction times. The probable explanation for the positive association of irradiation is that the ultrasonic irradiation could increase the number of active cavitation bubbles and the size of

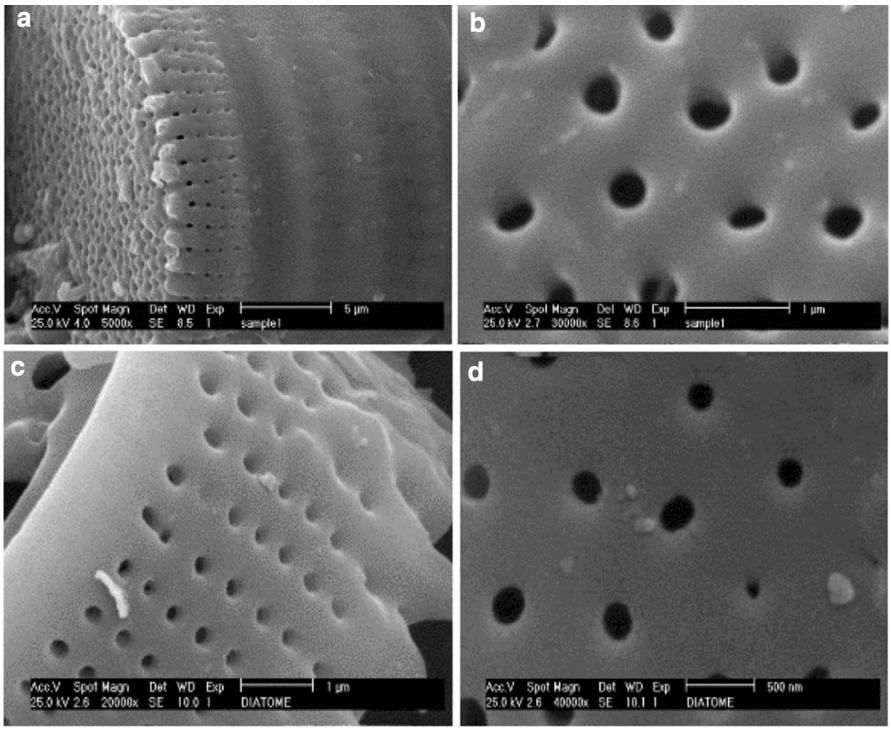


Fig. 2 SEM images of diatomite earth (**a**, **b**) and diatomite earth@IL/$ZrCl_4$ (**c**, **d**)

the individual bubbles, both of which are expected to result in higher maximum collapse temperatures and accelerated respective reactions. In continuation of our investigation, the role of ultrasonic irradiation on the yield and time of the reactions was investigated. A model reaction was employed under various powers of ultrasound irradiation. It was found that the reaction gave satisfactory yields in the presence of 10 mg of diatomite earth@IL/$ZrCl_4$ under ultrasonic irradiation with a power of 60 W (Table 2).

After evaluation of the optimized reaction conditions, the condensation of benzoic acid derivatives and different amines in the presence of solid acid catalysts was studied. As shown in Table 3, reactions proceeded with good yields of products. The system was applicable to aliphatic and aromatic amines with various groups, such as Cl, Br, OCH_3 and OH. Anilines with electron-donating groups on the phenyl ring and aromatic acids with electron-withdrawing groups, showed higher yields of products. Also, aliphatic amines (and aliphatic acids) are more active than aromatic types. On the other hand, the hydroxyl group on amine moiety does not need to be protected (entries 12 and 13) and no side reaction was observed with substrates having an unprotected hydroxyl group.

For estimation of catalyst efficiency, a model reaction was considered and repeated with a recycled catalyst. When the reaction was complete, the catalyst was separated and washed with acetone and methanol four times and dried in a vacuum

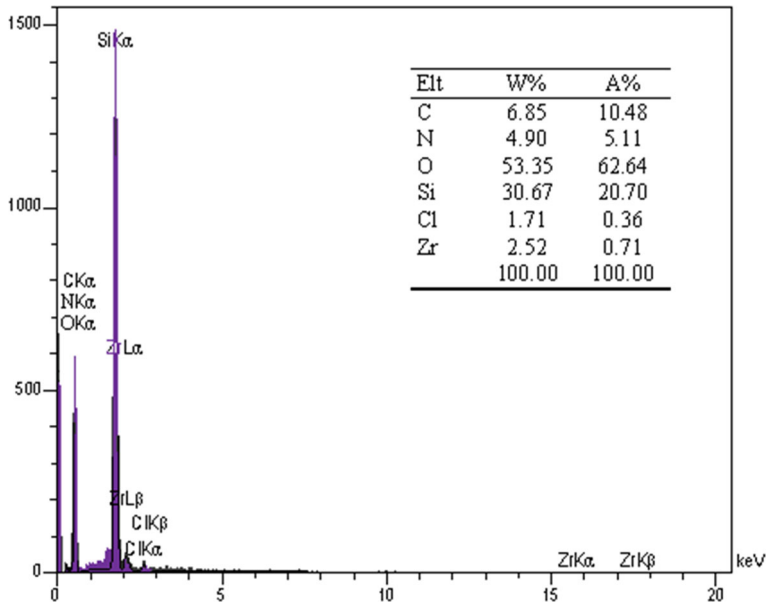


Fig. 3 EDX of diatomite earth@IL/$ZrCl_4$

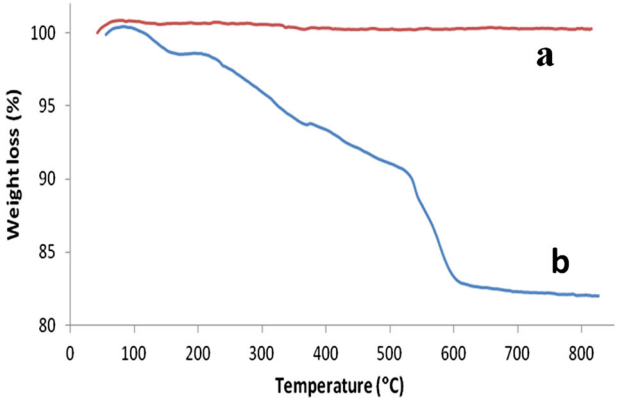
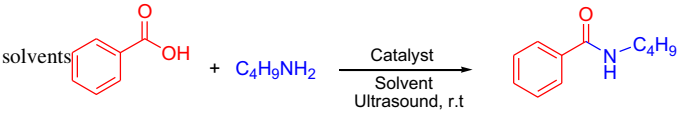


Fig. 4 TGA graphs of a diatomite earth (a) and diatomite earth@IL/$ZrCl_4$ (b)

oven at 80 °C for 8 h. The separated catalyst was reused five times. As shown in Fig. 5, the product yields reduced to a small extent on each cycle (run 1, 87%; run 2, 85%; run 3, 82%; run 4, 78% and run 5, 74%).

In addition, the reversibility of the benzamides was studied. The appropriate secondary amide, *N*-butyl benzamide (0.15 mmol), and water (2 mL) were added to a tube. Toluene (2 mL) and, diatomite earth@IL/$ZrCl_4$ (10 mg) were added and the tube was sealed and heated under ultrasonic irradiation for 1 h (Scheme 3). Then, the solvent was removed on a rotary evaporator and the products were analyzed. The results showed only 3% hydrolysis into benzoic acid and butylamine occurred.

Table 1 Optimization of catalysts and solvents



Entry	Solvent	Catalyst	Yield[a] (%)
1	Toluene	No catalyst	10
2	Toluene	CuO (10 mol%)	27
3	Toluene	$CoFe_2O_4$ (10 mol%)	80
4	Toluene	$ZrCl_4$ (10 mol%)	70
5	CH_2Cl_2	$ZrCl_4$ (10 mol%)	65
6	CH_3CN	$ZrCl_4$ (10 mol%)	58
7	THF	$ZrCl_4$ (10 mol%)	65
8	Toluene	ZrO_2 (10 mol%)	25
9	Toluene	$ZnCl_2$ (10 mol%)	20
10	Toluene	Fe_3O_4 (10 mol%)	75
11	CH_2Cl_2	Diatomite earth@IL/$ZrCl_4$ (10 mg)	80
12	THF	Diatomite earth@IL/$ZrCl_4$ (10 mg)	80
13	CH_3CN	Diatomite earth@IL/$ZrCl_4$ (10 mg)	74
14	Toluene	Diatomite earth@IL/$ZrCl_4$ (10 mg)	78
15	Toluene	Diatomite earth@IL/$ZrCl_4$ (10 mg)	87
16	Toluene	Diatomite earth@IL/$ZrCl_4$ (15 mg)	85

Benzoic acid (1 mmol), butylamine (1.2 mmol), dry toluene (1 ml), catalyst and ultrasound with power of 60 W, 15 min

[a]Isolated yield

Table 2 The effect of ultrasonic irradiation on the formation of benzamides

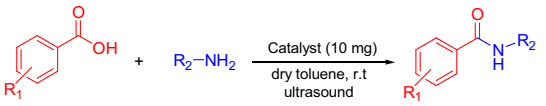
Entry	Power (W)	Yield (%)[a]
1	30	48
2	40	56
3	50	68
4	60	87
5	70	85

Benzoic acid (1 mmol), butylamine (1.2 mmol), dry toluene (1 ml), catalyst (10 mg), ultrasound, 15 min

[a]Isolated yields

To measure the extent of Zr leaching, the hot filtration test was employed. For this, the reaction between benzoic acid and butylamine under optimized conditions was performed. The reaction mixture was filtered after 7.5 min to remove the catalyst. Continuation of the reaction under the same conditions showed 54%

Table 3 Synthesis of benzamide derivatives using diatomite earth@IL/$ZrCl_4$ (10 mg) under ultrasonic irradiation (60 W)



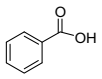
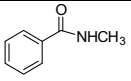
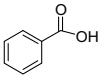
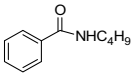
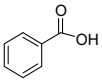
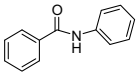
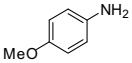
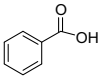
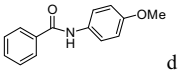
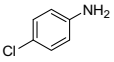
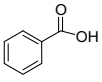
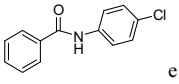
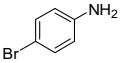
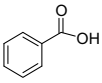
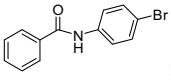
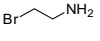
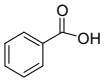
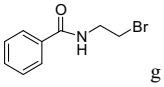
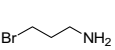
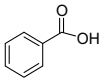
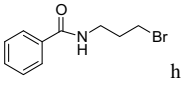
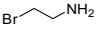
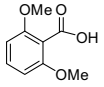
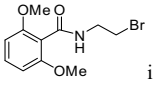
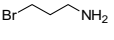
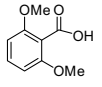
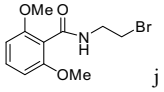
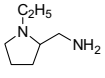
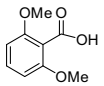
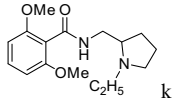
Entry	Amine	Acid	Product	Time (min)	Yield[a] (%)
1			 a	15	78
2			 b	15	87
3			 c	60	70
4			 d	45	72
5			 e	40	70
6			 f	40	71
7			 g	25	77
8			 h	25	77
9			 i	32	70
10			 j	32	73
11			 k	20	80

Table 3 continued

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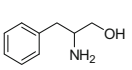
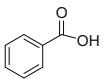
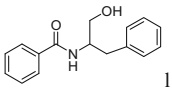
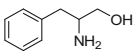
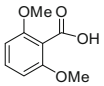
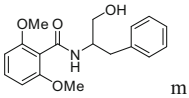
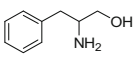
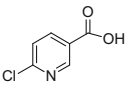
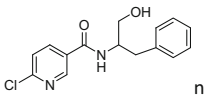
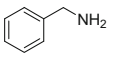
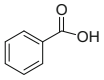
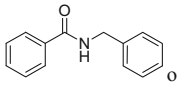
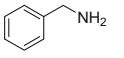
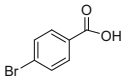
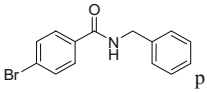
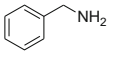
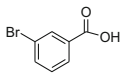
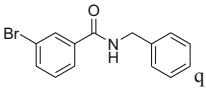
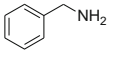
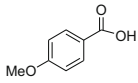
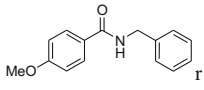
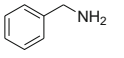
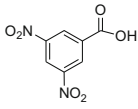
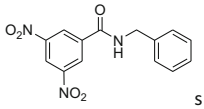
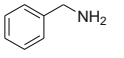
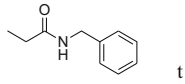
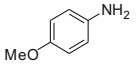
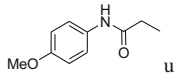
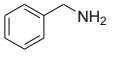
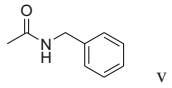
12			 l	35	82
13			 m	40	76
14			 n	42	78
15			 o	20	90
16			 p	20	90
17			 q	20	92
18			 r	35	82
19			 s	18	95
20			 t	10	95
21			 u	20	93
22			 v	15	95

[a]Isolated yield

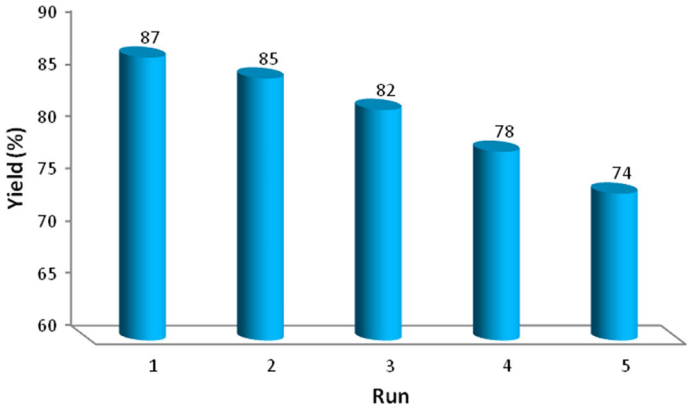
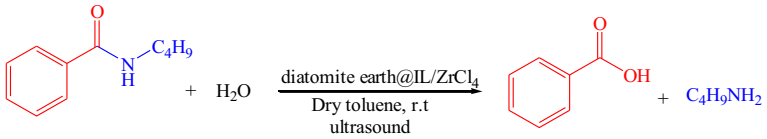


Fig. 5 Reusability of diatomite earth@IL/$ZrCl_4$ as the catalyst for the synthesis of **1b**

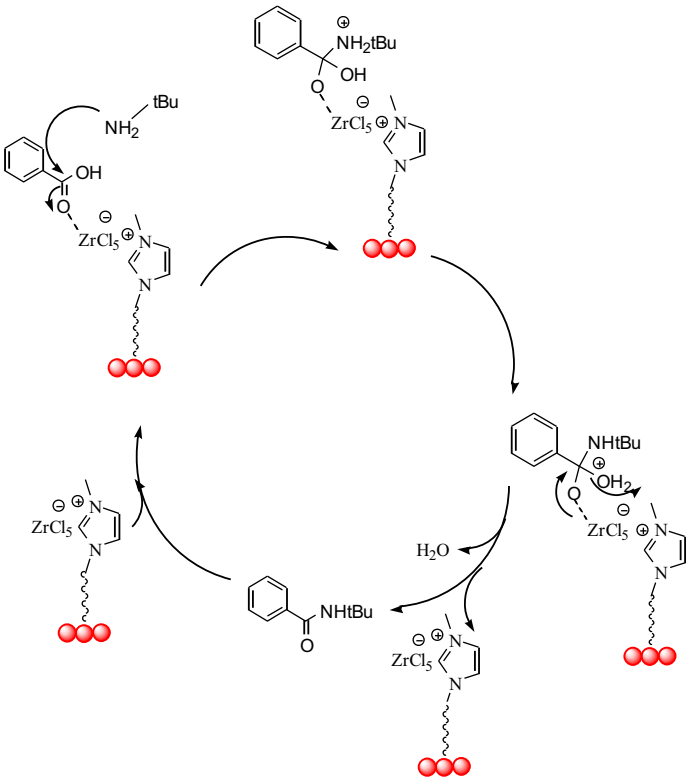


Scheme 3 Reversibility study of *N*-butyl benzamide into benzoic acid and butyl amine

conversion after other 7.5 min. This result shows that the amount of leaching of the catalyst into the reaction mixture should be very low and confirms that the catalyst acts heterogeneously in the reaction.

The reaction mechanism

A proposed mechanism is illustrated in Scheme 4. The activation of the carboxylic acid occurred through the interaction between Zr and the carbonyl group of carboxylic acid followed by the nucleophilic addition of amine. Then, the amide was formed after the removal of a water molecule. In this mechanism, the diatomite earth@IL/ZrCl4 activates the C=O groups for better reactions with nucleophiles. In fact, this green catalyst can be used for other significant organic reactions and transformations.



Scheme 4 Schematic mechanism for the synthesis of benzamides in the presence of diatomite earth@IL/$ZrCl_4$

Conclusions

In conclusion, we have presented an efficient method for the synthesis of benzamides using diatomite earth@IL/$ZrCl_4$ under ultrasonic irradiation. The Lewis acidic ionic liquid immobilization was carried out through the reaction between 1-(3-triethoxysilyl)-propyl-3-methylimidazolium chloride molecules and the hydroxy groups of diatomaceous earth surfaces, followed by the addition of zirconium (IV) chloride. The prepared catalyst provides active sites for the synthesis of benzamides. The advantages of this method are the use of a superior catalyst, the recoverability of the catalyst, low reaction times, simple procedure, a high-yielding and eco-friendly process, and the use of ultrasonic irradiation as a valuable, green and powerful technology.

Acknowledgement The authors are grateful for financial support from the University of Kashan by Grant No. 784946.

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