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A mild and expeditious synthesis of amides from aldehydes using bio glycerol-based carbon as a recyclable catalyst

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ABSTRACT

The new bioglycerol-based carbon catalyst acts as an efficient, readily available, and reusable catalyst for the synthesis of amides, when aldehyde and hydroxylamine hydrochloride react in acetonitrile.

Benzamides represent an important class of organic compounds in pharmaceutical chemistry with potential biological activity,[1] playing a crucial role in the context of heterocyclic chemistry. These are important intermediates in organic synthesis,[2] as well as in plastics, lubricants, detergent manufacturing, and in pharma applications.[3] Oxyclozanide (Fig. 1) was developed as an anti helmintic agent effective against *Fasciola hepatica* in the treatment of liver fluke infection.[4] Recently Narasimhan et al. reported the development of useful QSAR (quantitative structure–activity relationship) models for antimicrobial activity,[5] and anti-inflammatory activity.[6] Numerous methods have been reported for the synthesis of substituted benzamides involving catalysts like Ir,[7] Rh,[8] Ru,[9] Ag/Au,[10] Pd[11] compounds, anhydrous oxalic acid,[12] chloral,[13] sulfamic acid,[14] cyanuric chloride/DMF,[15] ethyl chloroformate/boron trifluoride etherate[16], and chlorosulfonic acid.[17] However, the above mentioned methods suffer from one or more disadvantages such as the use of hazardous organic solvents, expensive moisture-sensitive catalysts, tedious work-up conditions, longer reaction times, or large volume of catalyst loadings. In continuation of our efforts toward the development of novel environ friendly methodologies,[18] herein, we report a mild and efficient one-pot protocol for the synthesis of substituted benzamide derivatives for the first time by a two-component reaction involving aldehydes, and hydroxylamine hydrochloride using a novel and recyclable bioglycerol-based carbon catalyst in acetonitrile (Scheme 1). In recent years carbon-based solid acid catalysts[19] have gained prominence due to their significant advantages over homogeneous liquid phase mineral acids such as increased activity, selectivity, longer catalyst life, negligible equipment corrosion, ease of product separation, and reusability. These carbon based catalysts were obtained by incomplete carbonization of sulfo-aromatic polycyclic carbon catalyst from bioglycerol (biodiesel by-product) and also from glycerol-pitch (waste from fat splitting industry) by in situ partial carbonization and sulfonation in a single pot.[20] These carbon catalysts were demonstrated for their effectiveness for the esterification, THP protection and deprotection of alcohols and phenols, respectively. In continuation of exploring the possible applications for the carbon-based solid acid catalyst,[21] herein we report a facile and efficient one-pot synthesis of substituted benzamides for the first time (Scheme 1), catalyzed by bioglycerol derived carbon acid catalyst.

Benzaldehyde and hydroxylamine hydrochloride were used as model substrates to optimize the reaction conditions. Effect of parameters such as bases, solvents, and reaction temperature were studied (Table 2). Several bases namely Cs_2CO_3, KOH, K_2CO_3, and Na_2CO_3 were employed in the reaction. Of these screened bases, Cs_2CO_3 was found to be an excellent base (Table 2, entry 7) to carry forward the reaction in terms of rate of the reaction, and product yield and the corresponding results were shown in Table 2. Later the efficacy of different solvents was investigated toward the optimization. While evaluating the influence of different solvent

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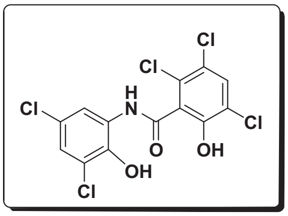
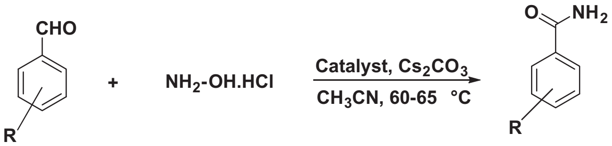


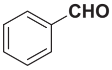
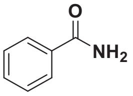
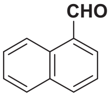
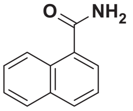
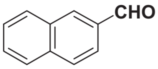
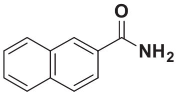
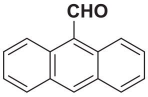
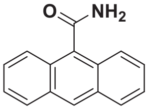
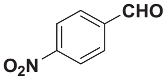
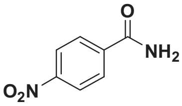
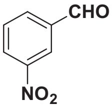
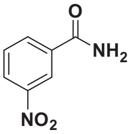
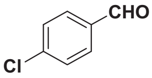
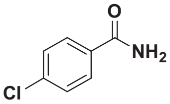
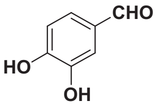
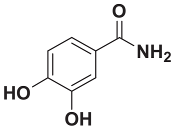
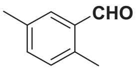
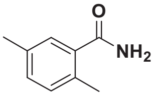
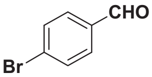
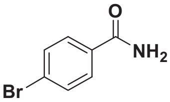
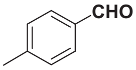
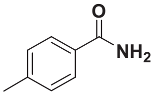
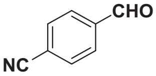
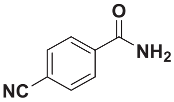
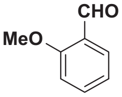
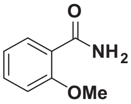
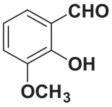
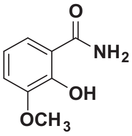
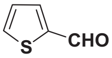
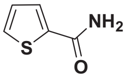
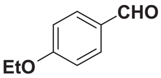
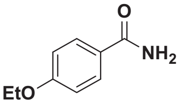
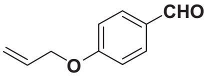
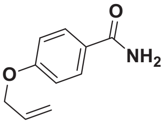
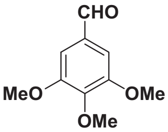
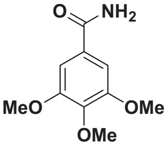
Figure 1. Oxyclozanide.



R = -H, -Cl, -Br, -NO_2, -F, -CH_3, -OCH_3, -CN, -OC_2H_5, -Ph, -o-allyloxy.

Scheme 1. Synthesis of substituted benzamides.

Table 1
Synthesis of substituted benzamides[a]

Entry	Aldehyde	Product	Yield[b] (%)
1			75
2			73
3			74
4			75
5			78
6			76
7			75
8			72
9			73
10			74
11			75
12			77
13			74
14			71
15			73
16			74
17			73
18			71

[a] *Reaction conditions*: aldehydes (1.0 mmol), $NH_2OH{\cdot}HCl$ (1.0 mmol), Cs_2CO_3 (1.0 mmol), catalyst (10 wt %), CH_3CN (10 mL).

[b] Isolated yield.

Table 2
Optimization conditions for the synthesis of substituted benzamides[a]

Entry	Base	Solvent	*T* (°C)	Yield[b] (%)
1	KOH	CH_3CN	60–65	46
2	K_2CO_3	Toluene	70–75	42
3	Na_2CO_3	Ethanol	60–65	40
4	Cs_2CO_3	Methanol	50–55	28
5	Cs_2CO_3	DMSO	80–85	44
6	Cs_2CO_3	CH_3CN	rt	44
7	Cs_2CO_3	CH_3CN	60–65	75

[a] *Reaction conditions*: aldehydes (1.0 mmol), $NH_2OH{\cdot}HCl$ (1.0 mmol), base (1.0 mmol), catalyst (10 wt %), solvent (10 mL).

[b] Isolated yield.

systems for bioglycerol-based carbon catalyzed synthesis of substituted benzamides, such as toluene, ethanol, methanol, DMSO, and CH_3CN (Table 2, entries 2–5 and 7), CH_3CN was observed to be the promising solvent, attaining optimum yields (Table 2, entry 7). In all these reactions bio glycerol-based carbon catalyst can be recovered and reused. After the reaction, the reaction mass was cooled

Table 3
Recyclability of the catalyst

Cycles	Yield (%)	Catalyst recovered (%)
Fresh	75	88
1	73	86
2	72	85
3	71	83

to room temperature and catalyst was filtered and washed with ice-cold methanol and dried. The recovered catalyst was further used in the reaction with the same substrates and checked for the yields and catalytic activity of the recovered catalyst, as shown in Table 3. It was observed that the yields of highly substituted benzamides diminished slightly after two to three recycles. The experimental results are included in Table 1. All the products were characterized[22,23] by ^{1}H, ^{13}C NMR, and mass spectra.

Conclusion

In summary, we have developed a simple, efficient, and eco-friendly protocol for the synthesis of amides from aldehydes. This simple and facile method will be an useful addition to green chemistry with an advantage that the reaction excludes moisture sensitive or hazardous catalysts and elevated reaction temperatures, and utilizes bioglycerol based carbon solid acid heterogeneous recyclable catalyst.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2012.03.051.

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22. *General experimental procedure for the synthesis of substituted benzamide derivatives*: To a stirred solution of acetonitrile (10 mL), aldehyde (1.0 mmol) and bioglycerol-based carbon catalyst (10 wt %) were added and stirred for 10 min. To this $NH_2OH\cdot HCl$ (1.0 mmol) followed by Cs_2CO_3 (1.0 mmol) were added, after which the reaction mixture was heated at 60–65 °C until completion of the reaction as indicated by TLC. The reaction mixture was cooled to room temperature and catalyst was filtered, the solvent was removed by rotary evaporator. The crude residue was extracted with ethyl acetate (3×10 mL). The combined organic layers were extracted with water, saturated brine solution, and dried over anhydrous Na_2SO_4. The organic layers were evaporated under reduced pressure and the resulting crude product was purified by column chromatography using ethyl acetate and hexane (2:8) as eluents to give the corresponding substituted benzamide derivative in (71–78%) yield. The identity and purity of the product were confirmed by ^{1}H, ^{13}C NMR, and mass spectra.
23. *Data for the representative examples of synthesized compounds benzamide* (Table 1, entry 1); ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO, TMS) $\delta = 7.78$ (d, 2H, $J = 6.7$ Hz), 7.53–7.40 (m, 4H), 7.25 (s, 1H); ^{13}C NMR (75 MHz, DMSO,TMS) $\delta = 168.38$, 132.90, 130.40, 127.20, 126.62; EI-MS (m/z): 121 $(M)^+$. *4-Methylbenzamide* (Table 1, entry 11); ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO, TMS) $\delta = 7.43$ (d, 2H, $J = 8.1$ Hz), 7.15 (d, 4H, $J = 7.9$ Hz), 2.37 (s, 3H, $-CH_3$); ^{13}C NMR (75 MHz, DMSO,TMS) $\delta = 150.20$, 140.21, 131.01, 129.44, 126.95, 29.67; EI-MS (m/z): 135 $(M)^+$.