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# An efficient and green synthesis of benzo[4,5]imidazo[1,2-*a*] pyrimidines using highly active and stable poly acrylic acid-supported layered double hydroxides

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ABSTRACT

A facile and efficient method for the synthesis of benzo[4,5]imidazo[1,2-*a*]pyrimidines has been achieved via highly active and reusable heterogeneous poly acrylic acid-supported layered double hydroxides (PAA-*g*-LDHs) catalyst promoted one-pot reaction of 1H-benzo[*d*]imidazol-2-amine, with $\alpha,\beta$-unsaturated carbonyl compounds under solvent-free conditions. PAA-*g*-LDHs catalyst was successfully synthesized via reversible addition-fragmentation chain-transfer polymerization using grafting reaction and was characterized by different analytical techniques. The significant features of this reaction include expedient one-pot process, short reaction time, excellent yields, wide substrate scope and operational simplicity. Also, the catalyst could be reused for several consecutive runs without any apparent loss in its catalytic activity.

## 1. Introduction

Since decades, heterogeneous supported catalysts have attracted much attention due to their inherent advantages, such as ease of handling, greater selectivity, stability, inexpensive, environmental compatibility, and catalysts can be recovered without measurable changes in their catalytic activity and selectivity.[1] Therefore, catalytic system have been obtained enormous significance in pollution preventing processes in the synthetic organic chemistry. Among them, polymer supported catalytic systems have received attracted great attention in synthetic organic chemistry and chemical industries because of they have high catalytic activity with enhanced reaction rates by high surface area, non-flammability with high thermal stability, cleaner product yields with improved product selectivity by decrease waste production, and easy to separation from reaction products for further reusability with regard to the effortlessness of the process and environmental reaction condition.[2]In addition to these merits, small crystal size, hydrophobic cavity, and as good candidates for polymer supporting applications layered double hydroxides (LDHs)[3] are applied for the preparation of various solid-supported reagents[4] and used as heterogeneous supported catalysts in organic synthesis.

Either in pharmaceutical agents or numerous organic materials,[5] which are showing a wide variety of biological activities, such as anti-cancer, antibacterial, anti-inflammatory activities, anti-alzheimer's activity, anti-hypertensive agents, V1b receptor antagonists, anti-TMV, anti-tumor, anti-metabolic and antimalarial agents[6] omnipresent backbone of either naturally or synthetically obtained either one or more nitrogen(s) containing heterocycles. Furthermore, they can be used as dyes, biosensors, for visualization of biomolecules as pH-sensitive fluorescent material, and also in laser technologies.[7] Amongst them, benzo[4,5]imidazo[1,2-*a*]pyrimidines structure bearing two main cores of nitrogen containing heterocycles (a imidazol and a pyrimidine ring) is originated broadly in biologically interesting compounds and natural products. As mentioned above, this core unit have a broad range of

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biological and pharmacological activities include anti-TMV, anti-vascular hypertension, anti-cancer/anti-tumor, anti-inflammatory, anti-metabolic, antimalarial agents and antimicrobial activities.[8] In addition, these derivatives are also played a role of antagonists of the paralyzing action of anti-diabetic activity and are significant core motifs in a wide range of biologically active compounds that are frequently used in pharmaceuticals, agrochemicals and medicinal chemistry.[8,9] Consequently, these structures are significant synthetic targets for bio-organic chemists.

In an ongoing study of design and synthesis of biologically active molecules under heterogeneous catalysis[10] and with the above two significant areas of findings, herein, we prepared a novel poly acrylic acid grafted layered double hydroxides (PAA-g-LDHs) as a recyclable heterogeneous catalyst and it was successfully applied for the construction of benzo[4,5]imidazo[1,2-*a*]pyrimidines (**3**) in one-pot synthesis by coupling of 1*H*-benzo[*d*]imidazol-2-amine (**1**), with *α*,*β*-unsaturated carbonyl compounds (**2**) at 80 °C under solvent-free conditions (Scheme 1).

## 2. Results and discussion

### 2.1. Synthesis of PAA-g-LDHs

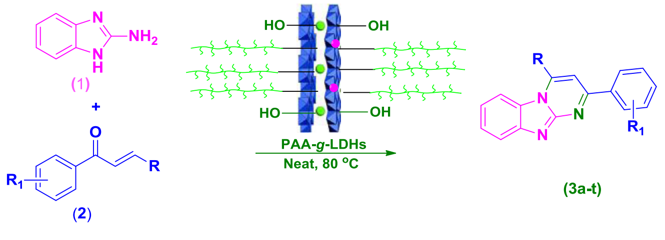
The synthesis of PAA-g-LDHs has been successfully described by an efficient and convenient approach of reversible addition-fragmentation chain-transfer (RAFT) polymerization reaction through the modified reported procedure.[11] Initially surface modification of LDHs (LDHs → LDHs-BTPT) with S′-(3-trimethoxysilyl) propyltrithiocarbonate (BTPT) was performed in first step as prescribed in reported procedure and later followed by 2, 2′-azobis (2-methylpropionitrile) (AIBN) initiated RAFT process using poly acrylic acid (PAA) in the next step was obtained white powder, PAA-g-LDHs (see Scheme 2).

### 2.2. XRD spectra of PAA-g-LDHs

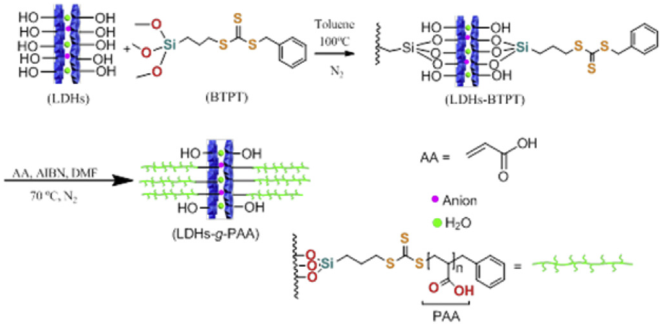
The crystalline nature of the synthesized LDHs, LDHs-BTPT and PAA-g-LDHs were confirmed with the reference LDHs (35-0964) by XRD spectrum (Fig. 1). The newly synthesized LDHs (Fig. 1b), LDHs-BTPT (Fig. 1c) and PAA-g-LDHs (Fig. 2d) peaks are perfectly indexed to tetragonal phase of referenced LDHs (Fig. 1a) with 2θ values of 11.68, 23.47, and 35 respectively with corresponding crystal planes of (003), (006), and (012). These results are revealed that the grafting of polymer did not alter the crystallinity of the LDHs.

### 2.3. TGA analysis of PAA-g-LDHs

In order to know the thermal degradation properties of LDHs, LDHs-BTPT, and PAA-g-LDHs performed a TGA of them and interpreted in Fig. 2. At first, Herein, a closer relationship was observed for LDHs and LDHs-BTPT. But on the other hand, PAA-g-LDHs was shown clear deviation from them and it could be explained as below. At first stage, due to release of absorbed water the LDHs (Fig. 2a) and LDHs-BTPT (Fig. 2b) ware showed a closer decomposition starting at 123.5 °C and lost 12.7% of weight. At 211.76 & 223.3 °C they were showed a second degradation curve due to losing of 21.0% of weight corresponding to the interlayer anions. Finally, the weight loss of 41.2 and 42.8% respectively were shown between 330 and 800 °C since encapsulated organic molecules decamped at high temperature. But on the other hand, the newly prepared PAA-g-LDHs was significantly start degradation at 147 °C



**Scheme 1.** Synthesis of benzo[4,5]imidazo[1,2-*a*]pyrimidines.



**Scheme 2.** Synthesis of PAA-g-LDHs.

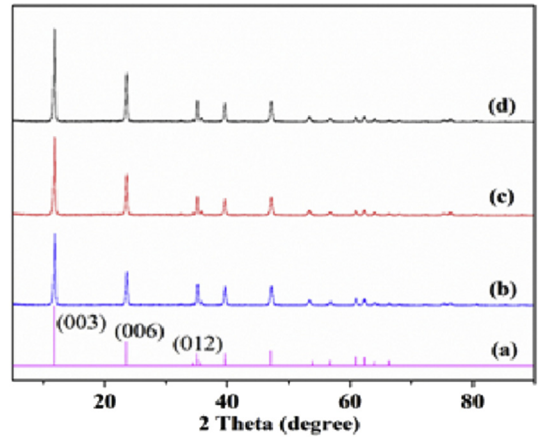


**Fig. 1.** X-ray diffraction patterns of (a) the reference of LDHs (35-0964), (b) synthesized LDHs, (c) LDHs-BTPT, (d) PAA-g-LDHs.

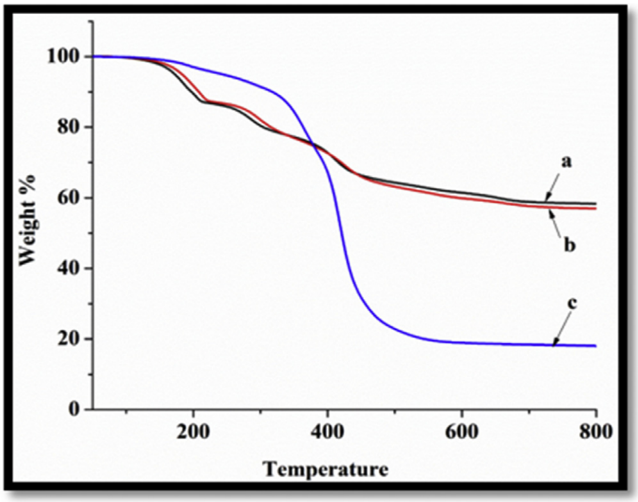


**Fig. 2.** TGA spectra of (a) LDHs, (b) LDHs-BTPT, and (c) PAA-g LDHs.