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FULL PAPER

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Facile synthesis of indolizines using layered double hydroxides@poly(*p*-phenylenediamine) as a catalyst with a green tool (neat technology)

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The three-component reaction of phenacyl bromide, dimethyl acetylenedicarboxylate and pyridine is catalyzed by layered double hydroxides@poly(*p*-phenylenediamine) (LDHs@PpPDA), in a one-pot reaction, in order to give the corresponding indolizines in excellent yields.

KEYWORDS

1,3-dipolar cycloaddition, DMAD, indolizine, polymer, pyrazine

1 | INTRODUCTION

Advanced materials that can meet the high demands in the domain of industrial applications (e.g. cosmetics, pharmaceuticals, meteorology and microelectronics) are highly sought.[1] Polymers are regarded as very large molecules, or macromolecules, composed of many repeating subunits.[2] Proteins and nucleic acids in the human body, fibers used in clothing, the starch we eat, foam insulation, dishes, furniture and tubes are all made of polymers.[3,4] Polymers may be organic, inorganic or organometallic. Polymers, depending on how they have been formed, may be artificial or natural.[4] Differences in polymers depend on a variety of chemical details, and due to these dissimilarities, their performances will also vary.

Polyaniline (PANI), which is a nitrogen-doped carbon nanomaterial, is of interest due to its ready availability among heteroatom-doped materials and, in comparison to other polymers, its consistency and ease of preparation.[5,6]

Use of nitrogen-containing reactants (such as NH_3, nitric acid and amines) or direct carbonization of nitrogen-rich carbon precursors (such as polyacrylonitrile, melamine, PANI), which include nitrogen-containing functional groups, gives rise to the production of carbon structures.[7–9] Monoamino polymers, such as PANI, also known as black aniline, are among the earliest reported conductive polymers and are known for their environmental constancy in a conducting form, novel electronics, electrochemistry, optical properties, electromagnetic shielding, reversible redox activity, sensing properties, intrinsic features and high conductivity.[10–12] But nowadays, due to the lack of solubility in most organic solvents and poor processability and rigidity, their application has been limited.[13–16]

Aromatic diamine polymers with free amino group in a duplicate unit of polymer chains can be considered as a suitable substitute for polymers such as PANI.[17,18] Moreover, the high proportion of polymers based on aromatic diamines remaining after thermal treatment led to the use of poly(*p*-phenylenediamine) (PpPDA) as a nitrogen-rich carbon precursor. According to the literature, the preparation of polymer-derived carbon networks using a facile integrated oxidation and catalytic carbonization strategy has been rarely reported. In this sense, we envisage interesting and functional features for a carbon-fiber network structure produced using PpPDA.[5]

Phenylenediamines can be used to make new congestion polymers. They can be synthesized by chemical polymerization.[17,19,20] Chan and Rawat and their respective co-workers reported oxidative and electrochemical polymerization of various aromatic diamines.[21,22] A large classification of two-dimensional anionic clay materials is the layered double hydroxides (LDHs) with the formula $[M^{2+}_{(1-x)}M_x{}^{3+}(OH)_2](A^{n-})_{x/n}{\cdot}zH_2O$.[23,24] LDHs or

hydrotalcite-like compounds, due to their layered and evenly divided structure, extensive surface area, high porosity, controllability of layer intervals and anionic exchange, have been used to absorb colored wastes. In order to enhance the adsorption efficiency, many studies considered chemical modifications or combination of LDHs with other functional materials.[25]

Notwithstanding, LDHs are naturally abundant and can be extracted easily from the environment. LDHs have some specific benefits, including a simple preparation methodology from low-cost and recoverable raw materials, convenient synthesis, environmental coordination, thermal stability, being active catalysts and being recyclable and reusable catalysts. In addition, the formation of LDHs from metal salts as starting materials, as compared to preparation from metals, involves the removal of one phase (the oxidation phase), as a result of which the time and cost of using the material decrease. Outstanding issues regarding LDH compositions and structures involve (a) the range of possible divalent and trivalent ions and (b) the inclusion of various anions and also their rich chemistry which make them good catalysts or catalyst precursors.[26,27]

In the work reported here, we aimed at synthesizing LDHs@PpPDA catalyst (Figure 1) using the emulsion polymerization method and also investigating the formation of indolizine compounds. The importance and strong demand for these heterocycles are because of their versatile photochemical features and biological activities.[28–32] The activation of indolizine in many natural and synthetic pharmaceutically active compounds is considered as a special heterocyclic nucleus.[33,34] Indolizines, as a vital class of N-heterocycles with 10 π-delocalized electrons, have received much attention due to their molecular structure and important biological activities.[35] Indolizine derivatives have many pharmaceutical applications, including as anti-tuberculosis agents, antibacterial agents, anticancer agents, anti-inflammatory agents, antihistaminic agents, phosphatase inhibitors, aromatase inhibitors, etc.[36] Therefore, straightforward and valuable strategies for the synthesis of indolizine derivatives are highly desired.[37]

In a multicomponent reaction (MCR), a chemical reaction, three or more components react to create a product. MCRs are reactions by which more than two reactants mix in a successive order to provide extremely selective products that maintain most of the atoms of the initial material. The development of new MCRs is attracting increasing attention in investigations done by industrial chemistry groups as it introduces a challenge for organic chemists. The movement in the direction of the perfect synthesis takes up the step numbers, preferably only one product and preferably 100%, and has been followed actively from the time scholars started to make molecules.[38,39]

According to the literature, several methods have been suggested for the synthesis of indolizine. In this sense, we aimed at synthesizing indolizines by employing a three-component reaction consisting of acyl bromide, pyridine and acetylene (Scheme 1).

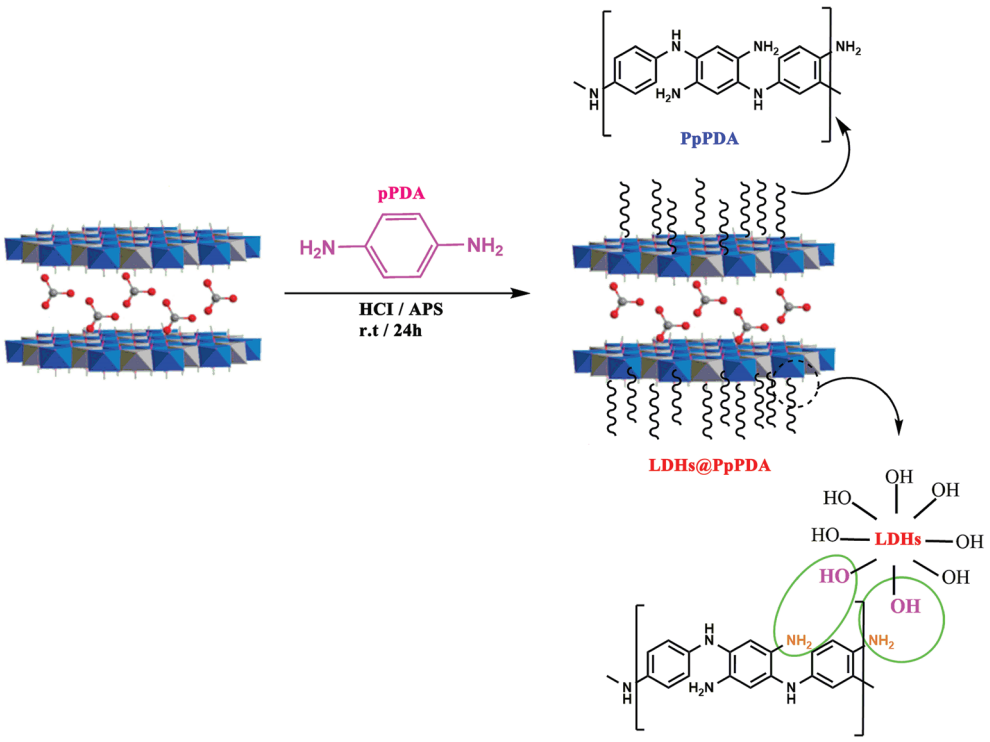
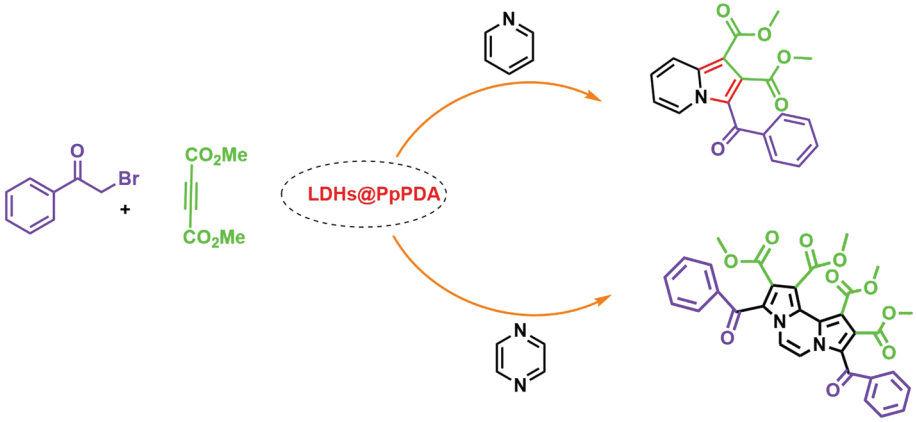


FIGURE 1 Layered double hydroxide@poly(p-phenylenediamine) structure

SCHEME 1 General synthesis of dimethyl 3-(4-nitrobenzoyl)indolizine-1,2-dicarboxylate



2 | EXPERIMENTAL

2.1 | General information and methods

All commercial materials were purchased from Merck and Fluka, and used without further purifications. ^{1}H NMR and ^{13}C NMR spectra were recorded with Bruker BioSpin 400 MHz FT NMR spectrometers. Fourier transform infrared (FT-IR) spectra were recorded with a Shimadzu 435-U-04 FT-IR spectrophotometer from KBr pellets. Melting points were measured with a BUCHI 510 apparatus in open capillary tubes. Scanning electron microscopy (SEM) was performed with an EM3200 instrument operated at an accelerating voltage of 30 kV. The structure of the new LDHs@PpPDA was characterized using X-ray diffraction (XRD), FT-IR spectroscopy, SEM and thermogravimetric analysis (TGA). Wavelength-dispersive X-ray spectroscopy was performed using a TESCAN Mira3. SEM analysis of the prepared catalyst was performed with a FESEM-SIGM (Germany) instrument. TGA was performed with a DuPont 951 (TA Instruments).

2.2 | Synthesis of LDHs

$Zn–CrNO_3^-$ LDH was synthesized using the co-precipitation method. LDHs can be synthesized in base solutions using metal salts containing M^{2+} and M^{3+}. First, $Zn(NO_3)_2{\cdot}6H_2O$ and $Cr(NO_3)_3{\cdot}9H_2O$ in a ratio of 2:1 were dissolved in deionized water, and then, drop by drop, a solution of 2 M NaOH was added at a pH value of 11.5 (LDHs are highly insoluble materials, at least at the relatively high pH used in their preparation). Afterwards, the reaction was set at 65°C for 18 h without being stirred. Then, the resulting green slurry was filtered, washed several times with distilled water and dried at 60°C in an oven for 24 h.[23]

2.3 | Synthesis of LDHs@PpPDA

LDHs@PpPDA, at room temperature, were synthesized by emulsion polymerization as follows. In a routine experiment, 0.75 g of LDHs was poured into a 250 ml flask and 20 ml of chloroform and 30 ml of distilled water were added. Then, the contents were dispersed for about 30 min in an ultrasonic bath at room temperature. Afterwards, a solution containing pPDA monomer (1 g) in 30 ml of HCl (1 M) was added to the aqueous solution. Then, an oxidizing solution prepared with 1.5 g (6.5 mmol) of ammonium persulfate (APS) in 20 ml of deionized water for 30 min at room temperature was added to the reaction mixture. After 24 h, the resulting precipitate was washed several times with deionized water. Finally, the precipitate was dried in a vacuum oven at 50°C for 24 h.

2.4 | General procedure for synthesis of 1-(3-(4-nitrobenzoyl)indolizin-1-yl)ethane-1-one

The process for the preparation of 1-(3-(4-nitrobenzoyl) indolizin-1-yl)ethane-1-one was as follows. A mixture of phenacyl bromide (0.20 g, 1 mmol), pyridine (0.12 ml, 1.5 equiv.), acetylenedicarboxylate (0.15 ml, 1.5 equiv.) and 0.05 g of LDHs@PpPDA catalyst at 50°C was stirred. The reaction was monitored using TLC (*n*-hexane–acetone, 8:2). After the completion of the reaction, the precipitate was filtered. The resulting jelly-like product was then purified with diethyl ether. After adding the diethyl ether and creating scratches or rubbing the surface of the jelly-like product, a pure powder was obtained. The products were characterized using physical and spectroscopic data (Supporting Information Data S1–S4).

2.5 | General procedure for synthesis of tetramethyl-3,8-bis(4-(nitrooxy)benzoyl) dipyrrolo[1,2-*a*:2′,1′-*c*]pyrazine-1,2,9,10-tetracarboxylate

The process for the preparation of tetramethyl-3,-8-bis(4-(nitrooxy)benzoyl)dipyrrolo[1,2-*a*:2′,1′-*c*]pyrazine-1,2,9,10-tetracarboxylate was as follows. A mixture of phenacyl bromide (0.40 g, 2 mmol), pyrazine (0.08 g, 1 mmol), acetylenedicarboxylate (0.3 ml, 3 equiv.) and 0.1 g of LDHs@PpPDA catalyst at 50°C was stirred. The reaction was monitored using TLC (*n*-hexane–acetone, 7:3), and the resulting precipitate was filtered. The resulting jelly-like product was then purified using diethyl ether. After adding the ethyl ether and creating scratches or rubbing the surface of the jelly-like product, a pure powder was obtained. The product was characterized using physical and spectroscopic data (FT-IR, NMR and MS).

2.6 | Analytical data of selected products

2.6.1 | 3-Benzyl-1,2-dimethylindolizine-1,2,3-tricarboxylate (4a)

Light yellow solid; yield: 90%; m.p. 124–129°C. FT-IR (KBr, ν_{max}, cm^{-1}): 2953, 1739, 1618, 1557. ^1H NMR (400 MHz, DMSO-d_6, δ, ppm): 3.72 (s, 6H, OCH_3), 5.23 (s, 2H, CH_2), 6.56–6.60 (m, 1H, ArH), 7.43 (m, 4H, ArH), 7.92 (m, 1H, ArH), 8.40 (d, J = 8 Hz, 1H, ArH), 8.65 (d, J = 8 Hz, 2H, ArH). ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 66.16, 69.2, 127.7, 127.8, 128.6, 128.9, 129.3, 129.6, 131.0, 143.4, 143.5, 144.5, 145.4, 146.3, 190.1. MS: m/z 367. Anal. Calcd for $C_{20}H_{17}NO_6$ (%): C, 65.39; H, 4.66; N, 3.81. Found (%): C, 65.58; H, 4.85; N, 4.01.

2.6.2 | 3,8-Dibenzyl-1,10,2,9-tetramethyldipyrrolo[1,2-*a*:2′,1′-*c*]pyrazine-1,2,3,8,9,10-hexacarboxylate (4b)

Light yellow solid; yield: 89%; m.p. 139–141°C. FT-IR (KBr, ν_{max}, cm^{-1}): 2946, 1740, 1711, 1624, 1609. ^1H NMR (400 MHz, DMSO-d_6, δ, ppm): 3.47 (s, 12H, OCH_3), 6.26 (s, 4H, CH_2), 7.23–7.18 (m, 5H, ArH), 7.66–7.75 (m, 5H, ArH), 8.79 (d, J = 8 Hz, 2H, ArH). ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 66.2, 73.5, 127.7, 127.8, 128.3, 128.4, 128.5, 128.6, 128.9, 129.3, 129.6, 131.0, 143.4, 143.5, 144.4, 145.4, 146.3, 146.4, 186.4, 190.2. MS: m/z 656. Anal. Calcd for $C_{34}H_{28}N_2O_{12}$ (%): C, 62.20; H, 4.30; N, 4.27. Found (%): C, 62.39; H, 4.49; N, 4.46.

2.6.3 | Dimethyl-3-(4-methylbenzoyl) indolizine-1,2-dicarboxylate (4c)

Light yellow solid; yield: 88%; m.p. 121–124°C. FT-IR (KBr, ν_{max}, cm^{-1}): 2949, 1735, 1691, 1634 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6, δ, ppm): 2.45 (s, 3H, CH_3), 3.58 (s, 6H, OCH_3), 6.40–6.48 (m, 1H, ArH), 7.47 (m, 1H, ArH), 8.01 (d, J = 8 Hz, 2H, ArH), 8.29 (d, J = 8 Hz, 20, 2H, ArH), 8.75 (d, J = 8 Hz, 1H, ArH), 9.03 (d, J = 8 Hz, 1H, ArH). ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 21.3, 66.1, 126.6, 127.7, 127.8, 128.3, 128.4, 128.5, 128.6, 128.9, 129.3, 129.6, 131.0, 143.4, 143.5, 144.4, 145.4, 146.3, 146.4, 189.7, 190.2. MS: m/z 351. Anal. Calcd for $C_{20}H_{17}NO_5$ (%): C, 68.37; H, 4.88; N, 3.99. Found (%): C, 68.56; H, 5.07; N, 4.18.

2.6.4 | Tetramethyl-3,8-bis (4-methylbenzoyl)dipyrrolo[1,2-*a*:2′,1′-*c*] pyrazine-1,2,9,10-tetracarboxylate (4d)

Light yellow solid; yield: 92%; m.p. 129–131°C. FT-IR (KBr, ν_{max}, cm^{-1}): 2952, 1735, 1605. ^1H NMR (400 MHz, DMSO-d_6, δ, ppm): 2.51 (s, 6H, CH_3), 3.64 (s, 12H, OCH_3), 7.55 (d, J = 8 Hz, 2H, ArH), 8.03 (d, J = 8 Hz, 2H, ArH), 8.31–8.33 (m, 2H, ArH), 8.73–8.75 (m, 2H, ArH), 8.91 (d, J = 8 Hz, 1H, ArH), 9.06 (d, J = 8 Hz, 1H, ArH). ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 21.3, 30.7, 66.1, 127.8, 128.3, 129.6, 130.9, 145.5, 146.2, 146.3, 190.1. MS: m/z 624. Anal. Calcd for $C_{34}H_{28}N_2O_{10}$ (%): C, 65.38; H, 4.52; N, 4.49. Found (%): C, 65.57; H, 4.71; N, 4.68.

2.6.5 | Dimethyl-3-(2,4,6-trichlorobenzoyl)indolizine-1,2-dicarboxylate (4e)

Light brown solid; yield: 93%; m.p. 120–122°C. FT-IR (KBr, ν_{max}, cm^{-1}): 2951, 1735, 1634, 1582. ^1H NMR (400 MHz, DMSO-d_6, δ, ppm): 4.15 (s, 6H, OCH_3), 7.79 (s, 2H, ArH), 7.97 (d, J = 8 Hz, 1H, ArH), 8.31–8.33 (m, 1H, ArH), 8.70 (d, J = 8 Hz, 1H, ArH), 9.07(d, J = 8 Hz, 1H, ArH). ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 58.7, 127.7, 128.3, 129.6, 131, 145.4, 146.2, 146.3, 184.3, 190.1. Anal. Calcd for $C_{19}H_{12}Cl_3NO_5$ (%): C, 51.79; H, 2.74; N, 3.18. Found (%): C, 51.98; H, 2.93; N, 3.37.

2.6.6 | Tetramethyl-3,8-bis(2,4,6-trichlorobenzoyl)dipyrrolo[1,2-*a*:2′,1′-*c*] pyrazine-1,2,9,10-tetracarboxylate (4f)

Light yellow solid; yield: 95%; m.p. 126–130°C. FT-IR (KBr, ν_{max}, cm^{-1}): 3061, 1706, 1637, 1583. ^1H NMR

(400 MHz, DMSO-d_6, δ, ppm): 4.13 (s, 12H, OCH_3), 8.31 (d, J = 8 Hz, 2H, ArH), 8.48 (d, J = 8 Hz, 2H, ArH), 8.79 (d, J = 8 Hz, 2H, ArH). ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 66.1, 127.7, 128.3, 129.6, 131, 143.7, 145.4, 146.2, 146.3, 184.3, 190.1. Anal. Calcd for $C_{32}H_{18}Cl_6N_2O_{10}$ (%): C, 47.85; H, 2.26; N, 3.49. Found (%): C, 48.04; H, 2.45; N, 3.68.

2.6.7 | Dimethyl-3-(4-nitrobenzoyl) indolizine-1,2-dicarboxylate (4g)

Light yellow solid; yield: 92%; m.p. 126–130°C. FT-IR (KBr, ν_{max}, cm^{-1}): 2942, 1706, 1637, 1602, 1525. ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 4.44 (s, 6H, OCH_3), 8.30–3.32 (m, 1H, ArH), 8.33–8.34 (m, 1H, ArH), 8.48 (d, J = 8 Hz, 2H, ArH), 8.77 (d, J = 8 Hz, 1H, ArH), 9.09 (d, J = 8 Hz, 1H, ArH). ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 66.4, 124.1, 127.9, 129.8, 138.2, 146.3, 146.6, 150.6, 190. MS: m/z 382. Anal. Calcd for $C_{19}H_{14}N_2O_7$ (%): C, 59.69; H, 3.69; N, 7.33. Found (%): C, 59.88; H, 3.88; N, 7.52.

2.6.8 | Tetramethyl-3,8-bis(4-nitrobenzoyl)dipyrrolo[1,2-*a*:2′,1′-*c*] pyrazine-1,2,9,10-tetracarboxylate (4h)

Light yellow solid; yield: 93%; m.p. 130–135°C. FT-IR (KBr, ν_{max}, cm^{-1}): 3020, 1689, 1636, 1524. ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 6.66 (s, 12H, OCH_3), 8.31 (d, J = 8 Hz, 4H, ArH), 8.48 (d, J = 8 Hz, 4H, ArH), 9.08 (d, J = 8 Hz, 2H, ArH). ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 60.3, 127.7, 128.3, 129.6, 130.9, 139.8, 141.8, 145.5, 146.2, 146.3, 185.2, 190.1. MS: m/z 686. Anal. Calcd for $C_{32}H_{22}N_4O_{14}$ (%): C, 59.69; H, 3.69; N, 7.33. Found (%): C, 59.87; H, 3.88; N, 7.51.

2.6.9 | Dimethyl-3-(3-methoxybenzoyl) indolizine-1,2-dicarboxylate (4i)

Light yellow solid; yield: 93%; m.p. 120–122°C. FT-IR (KBr, ν_{max}, cm^{-1}): 2924, 1697, 1637, 1523. ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 3.71 (s, 3H, OCH_3), 3.93 (s, 6H, OCH_3), 6.52 (d, J = 8 Hz, 1H, ArH), 7.42–7.47 (m, 1H, ArH), 7.61 (s, 1H, ArH), 7.62–7.66 (m, 1H, ArH), 7.73 (d, J = 8 Hz, 1H, ArH), 8.30–8.34 (m, 1H, ArH), 8.79 (d, J = 8 Hz, 1H, ArH), 9.04 (d, J = 8 Hz, 1H, ArH). ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 51.3, 55.6, 127.8, 128.3, 129.6, 135.7, 138.5, 146.2, 146.3, 161.42, 164.8, 193.3. Anal. Calcd for $C_{20}H_{17}NO_6$ (%): C, 59.69; H, 3.69; N, 7.33. Found (%): C, 59.88; H, 3.88; N, 7.52.

2.6.10 | Tetramethyl-3,8-bis(3-methoxybenzoyl)dipyrrolo[1,2-*a*:2′,1′-*c*] pyrazine-1,2,9,10-tetracarboxylate (4j)

Light yellow solid; yield: 90%; m.p. 133–135°C. ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 3.77 (s, 6H, OCH_3, 4.02 (s, 12H, OCH_3), 8.32 (d, J = 8 Hz, 4H, ArH), 8.48 (d, J = 8 Hz, 4H, ArH), 9.08 (d, J = 8 Hz, 2H, ArH). ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 51.3, 55.6, 127.8, 128.3, 129.6, 135.7, 138.5, 145.5, 146.2, 146.3, 161.42, 164.8, 193.3. Anal. Calcd for $C_{34}H_{28}N_2O_{12}$ (%): C, 62.20; H, 4.30; N, 4.27. Found (%): C, 62.39; H, 4.49; N, 4.46.

2.6.11 | Dimethyl-3-(4-cyanobenzoyl) indolizine-1,2-dicarboxylate (4k)

Light yellow solid; yield: 93%; m.p. 125–128°C. ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 3.93 (s, 6H, OCH_3), 8.33 (d, J = 8 Hz, 2H, ArH), 8.41–8.47 (m, 2H, ArH), 8.77–8.79 (m, 2H, ArH), 9.08 (d, J = 8 Hz, 2H, ArH). ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 30.8, 109.3, 115.2, 115.2, 116.5, 118.1, 125.6, 129.8, 132.7, 142.8, 152.4, 153.2, 181.3, 197.5.

2.6.12 | Tetramethyl-3,8-bis(4-methoxybenzoyl)dipyrrolo[1,2-*a*:2′,1′-*c*] pyrazine-1,2,9,10-tetracarboxylate (4l)

Light yellow solid; yield: 90%; m.p. 130–133°C. ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 3.38 (s, 6H, OCH_3), 3.82 (s, 12H,$COOCH_3$), 8.29 (d, J = 8 Hz, 4H, ArH), 8.72–8.78 (m, 4H, ArH), 9.08 (d, J = 8 Hz, 2H, ArH). ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 31.6, 46.6, 98.9, 99.7, 100.1, 128.1, 130.2, 131.1, 133.2, 178.3, 184.2, 197.5.

3 | RESULTS AND DISCUSSION

3.1 | Catalyst texture, structure and morphology

FT-IR spectroscopy was utilized to investigate the chemical components of the synthesized samples. The common features of pure PpPDA polymer are well known in the literature. As seen in Figure 2, the symmetric and asymmetric stretching vibrations of N&bond;H bond of NH_2 group of polymeric chains appeared at 3650 and 2961 cm^{-1}. The peaks at about 3371 cm^{-1} are related to the N&bond;H stretching vibration of the secondary amine group.[6] Two broad bands in the regions of 1500

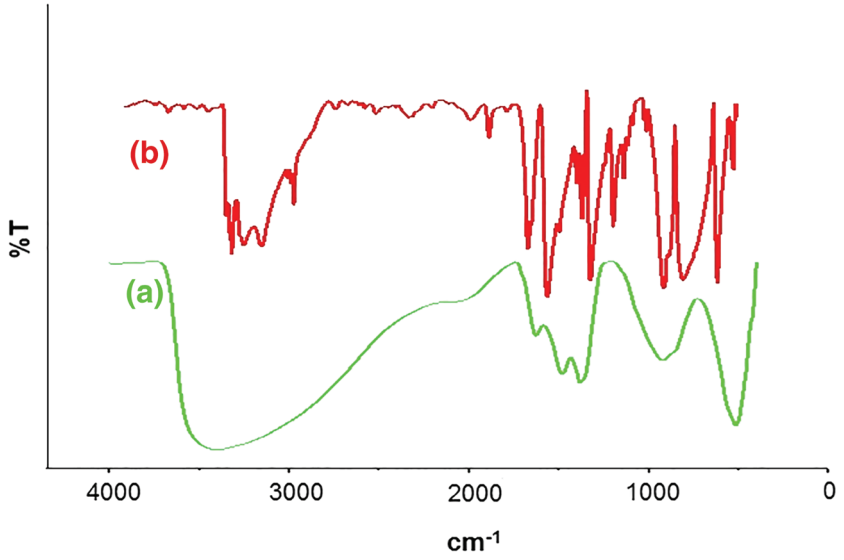


FIGURE 2 FT-IR spectra: a) LDHs, b) LDHs@PpPDA

and 1567 cm^{-1} respectively correspond to the stretching vibrations of C&dbond;C and C&dbond;N in the quinoid and benzenoid rings in the PpPDA polymer structure. Moreover, the peaks at about 1407 and 1261 cm^{-1} are related to the C&bond;N&bond;C stretching vibrations.[16] Frequently, the broad band of hydroxyl groups (OH stretching, 3430 cm^{-1}) is noticeable in the FT-IR spectra of LDH sheets. In short, the absence of OH peaks proved the successful synthesis of the LDHs@PpPDA catalyst.

XRD was used for studying the crystallinity and particle size. The powder XRD patterns of LDHs and LDHs@PpPDA are presented in Figure 3. The XRD patterns of LDHs and LDHs@PpPDA show a series of sharp lines in the regions of 10°, 30° and 40° illustrating the fact that the synthesized polymer samples have high crystallinity and long-range ordering.[40]

The mean diameter of LDHs@PpPDA particles was measured from the Scherer equation.

The EELS elemental mapping technique was applied to record the structural elements of the synthesized composition. As shown in Figure 4, elemental mapping can clearly illustrate the presence of elements such as Zn, Cr, N, O and C.

SEM imaging of LDHs@PpPDA demonstrated that it has a flat surface and hexagonally shaped structure (Figure 5). In addition to the structural morphology, particle size can be estimated using SEM.

In the TGA and differential thermogravimetry curves (Figure 6), the initial mass loss at about 100–200°C shows the evaporation of the entrapped water. On the other hand, the observed decomposition in the range 240–340°C is because of oligomer loss. Finally, the weight loss in the range 300–450°C is related to the dedoping procedure and thermal degradation of PpPDA chains.

3.2 | Catalytic activity

The reaction of 2-bromo-1-(4-nitrophenyl)ethan-1-one (**1**) with acetylenedicarboxylate (**2**) and pyridine was investigated to screen the reaction conditions (Table 1).

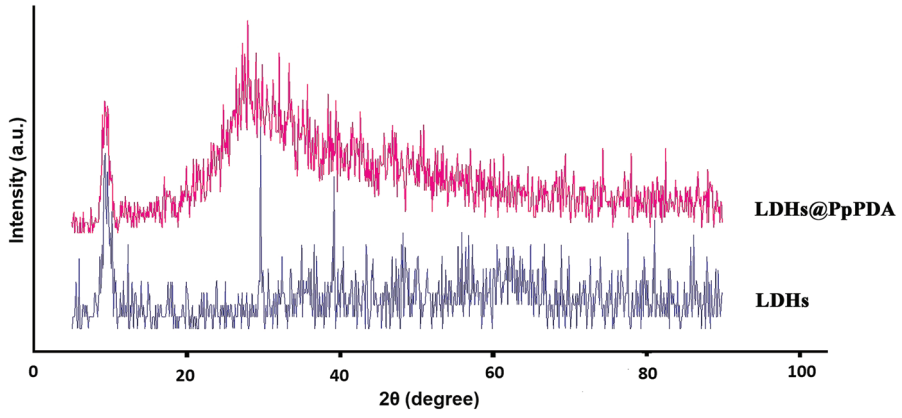


FIGURE 3 XRD patterns: LDHs and LDHs@PpPDA

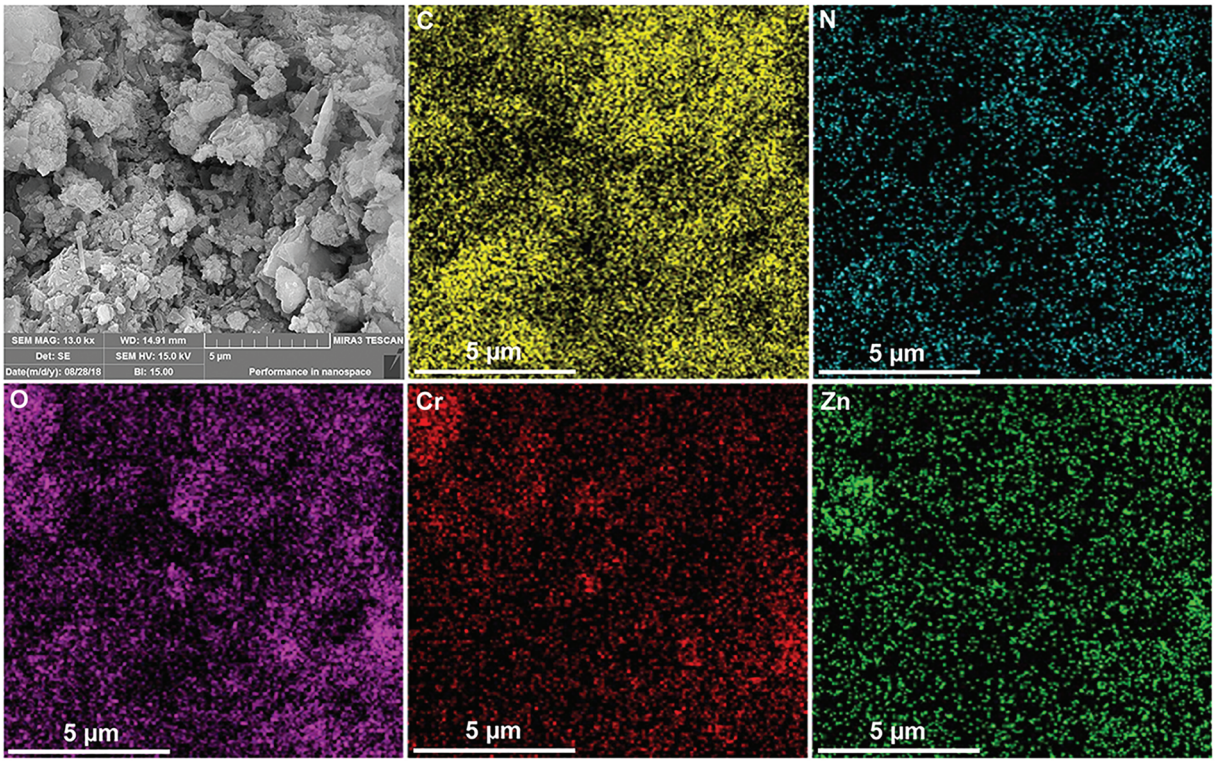


FIGURE 4 WDX images of LDHs@PpPDA

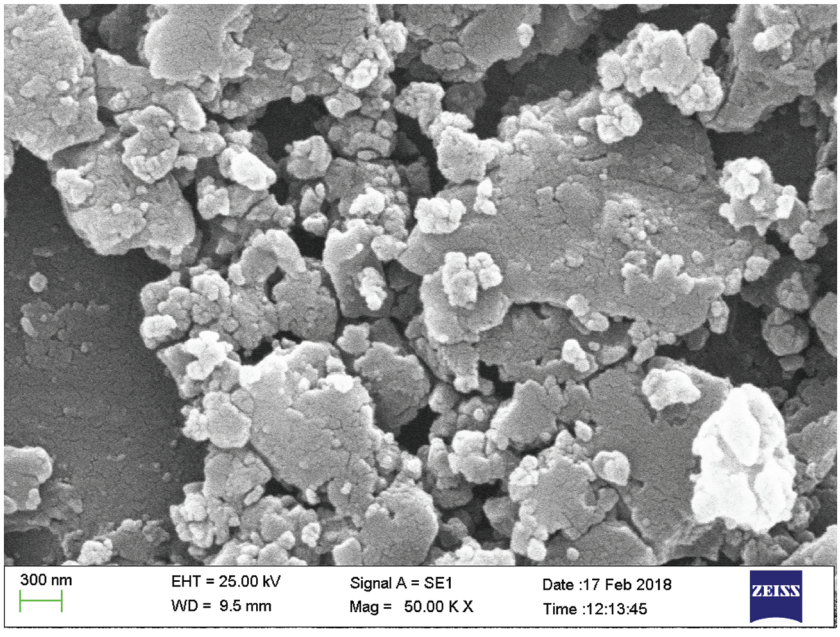


FIGURE 5 Morphology and particle size of LDHs@PpPDA

Compound **1** (1 mmol) was treated with **2** (0.15 ml, 1.5 equiv.) and pyridine (0.12 ml, 1.5 equiv.), in the presence of LDHs@PpPDA (0.05 g) at 50°C for 4 h under neat conditions. The desired product **4g** was obtained in 92% yield (Table 1, entry 3). The structure of **4g** was confirmed by its ^{1}H NMR and ^{13}C NMR spectra and mass spectrum. The catalytic activity of LDHs@PpPDA was crucial for the reaction. As evident from Table 1, the best results were achieved when the reaction was run using 0.05 g of catalyst (Table 1, entry 3). In the absence of the LDHs@PpPDA catalyst, the yield of the reaction was only 20% (entry 7). Examination of the temperature showed that 50° C proved to be the best, affording **4g** in 92% isolated yield. Thus, we determined the optimal

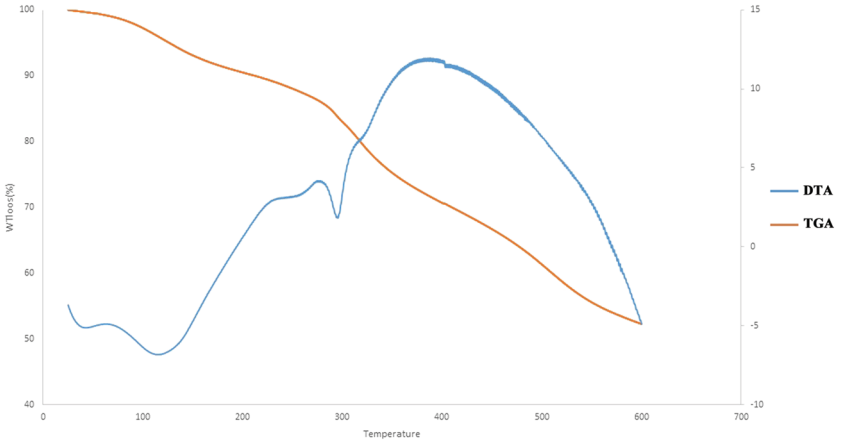


FIGURE 6 TGA curve of LDHs@PpPDA

TABLE 1 Optimization of reaction conditions[a]

Entry	Catalyst (g)	Solvent	Temp. (°C)	Time (min)	Yield (%)[b]
1	0.05	—	100	340	75
2	0.05	—	25	1440	Trace
3	0.05	—	50	100	92
4	0.1	—	50	90	90
5	0.06	—	50	420	89
6	0.025	—	50	1440	60
7	—	—	50	1440	Trace
8	0.05	CH_3COCH_3	56	180	80
9	0.05	H_2O	100	1440	33
10	0.05	C_2H_5OH	90	1440	45

[a]Reaction conditions: 2-bromo-1-(4-nitrophenyl)ethan-1-one (1 mmol), acetylenedicarboxylate (0.15 ml), pyridine (0.12 ml), catalyst, solvent (5 ml).
[bb]Isolated yield.

conditions as in entry 3. Several organic solvents were also screened (entries 8–10). The results obtained show that acetone produces acceptable results as compared to the other solvents, but, as noted above, the lack of solvent (entry 3) reduces the reaction time and increases the reaction efficiency.

With the optimized settings in hand, a series of ethyne and organic bromides were utilized to establish the range and generality of the protocol. All of the reactions proceeded smoothly to afford the desired products in moderate to excellent yields. The use of pyrazine instead of pyridine (Table 2) in the synthesis of indolizine leads to the creation of new structures of indolizine. The mentioned structures have not been synthesized previously, so we were able to synthesize these compounds for the first time.

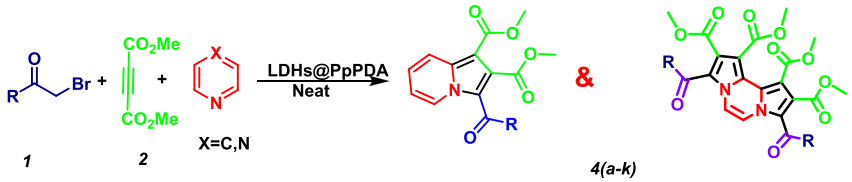
In the present study, our attempt to reach green chemistry or sustainable chemistry has been discussed. Chemical engineering has focused on the design of products and processes that minimize the use and generation of hazardous substances.[41]

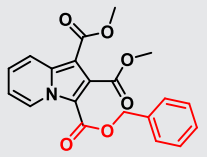
The main benefit of the present results is the use of neat conditions. A neat reaction is a chemical procedure without a solvent minimizing the auxiliary substance (solvent). In addition, the benefits of neat reactions in chemistry are: (a) they are more economic (save costs on solvent), (b) ease of work-up and purification (not necessary to eliminate a solvent post-synthesis), (c) high reaction rate (due to high concentration of reactants) and (d) environmental friendliness (solvent is not needed).[42]

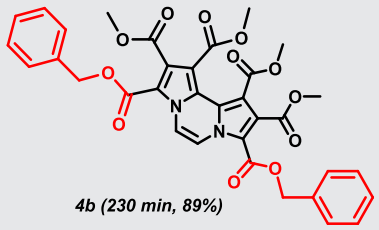
Regarding these benefits, organic reactions without the use of conventional organic solvents have attracted the attention of synthetic organic chemists. Even though a number of so-called modern green solvents, such as fluorous media, ionic liquids and water, have been broadly investigated,[43] "no solvent is the best solvent" is definitely the best.

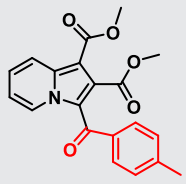
As evident from Table 2, phenacyl bromides with electron-withdrawing groups provided moderate to excellent yields of products (**4e**, **4f**, **4g**, **4h**, **4k**, **4l**), but phenacyl bromides with electron-donating groups gave lower yields in the reaction (**4c**, **4d**, **4i**, **4j**) presumably because

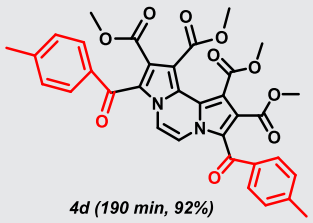
TABLE 2 Substrate scope of dimethyl indolizine-1,2-dicarboxylate

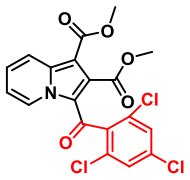


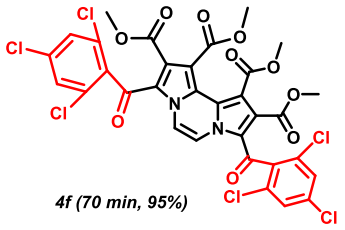

4a (255 min, 90%)

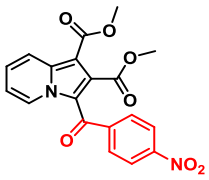

4b (230 min, 89%)

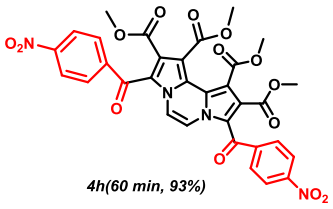

4c (280 min, 88%)


4d (190 min, 92%)


4e (105 min, 93%)


4f (70 min, 95%)


4g (100 min, 92%)


4h(60 min, 93%)

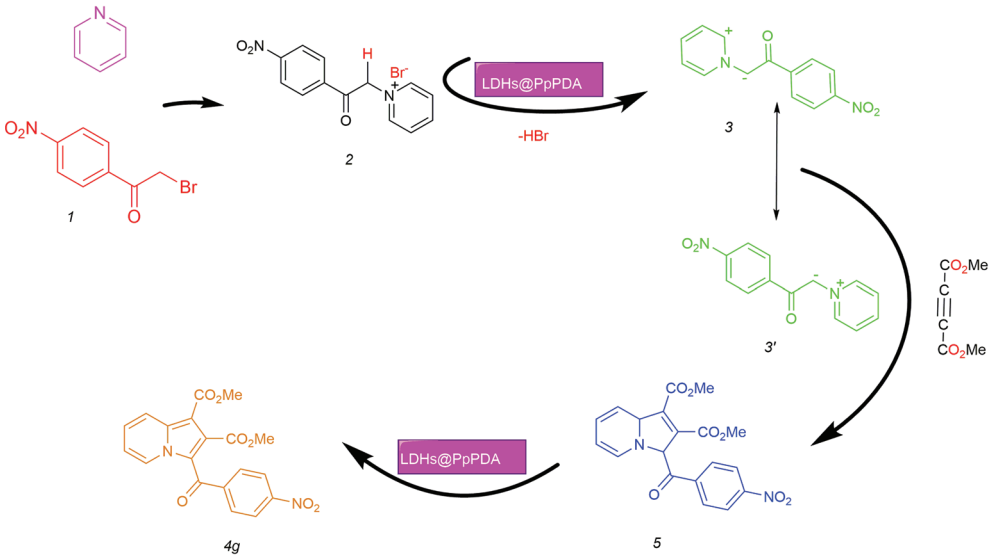
Reaction conditions: phenacyl bromide (1 mmol), acetylenedicarboxylate (0.15 ml), pyridine (0.12 ml) or pyrazine (0.05 mmol), LDHs@PpPDA (0.05 g), 50°C.

of their higher LUMO compared to electron-deficient ones.

In 2016, Wang and co-workers used rhodium(III) as a catalyst. This catalyst allows the synthesis of indolizines at a temperature of over 120°C and a period of 18 h.[32] Benzylated indolizines were synthesized using $Pd_2(dba)_3$ catalyst under reflux conditions with dimethylformamide (DMF) solvent for 16 h.[44] Also, various indolizines have been synthesized through one-pot, two-step 1,3-dipolar cycloadditions in recyclable [Omim]Br with high yields and a broad substrate scope.[45] A palladium-catalyzed direct arylation of 2-arylimidazo[1,2-*a*]pyridines with *o*-dihaloarenes via double C&bond;H activation has been reported. The process afforded benzo[*a*]imidazo[5,1,2-*cd*] indolizine derivatives in DMF and good yields.[46]

The efficiency of LDHs@PpPDA as the catalyst for the synthesis of the model indolizine compounds was compared to that of the best of the well-known data from the literature. It is clear that the previously reported procedures suffer from one or more disadvantages, e.g. longer reaction time, the use of expensive and unattainable materials and the application of high-boiling-point and organic solvents such as DMF. As compared to the other catalysts, not only does LDHs@PpPDA shorten the reaction time, but it also provides thermal stability, convenient synthesis and environmental coordination. Besides, it can be reused several times with no significant loss of its catalytic activity.

Treatment of **1** with pyridine afforded the corresponding pyridinium bromide salt **2** in quantitative yield (Scheme 2). The structure of the isolated bromide salt **2** was confirmed from spectral data as well as chemical transformations (Figure 7). In the next step, the catalyst causes dissociation of the hydrogen identified on the pyridinium salt and forms an intermediate (**3**). Then, the intermediate **3** was treated with dimethyl



SCHEME 2 Suggested mechanism for the synthesis of dimethyl 3-(4-nitrobenzoyl) indolizine-1,2-dicarboxylate catalyzed by LDHs@PpPDA

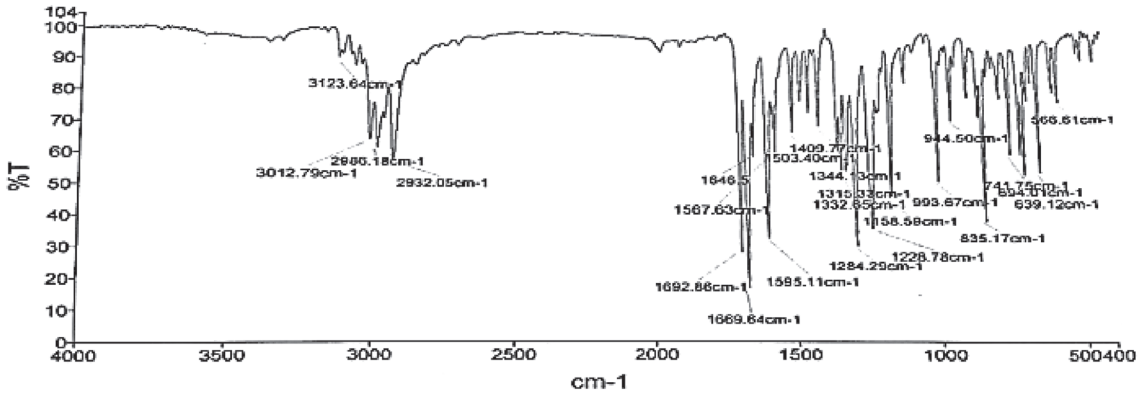


FIGURE 7 FT-IR spectra: Isolated bromide salt

acetylenedicarboxylate (DMAD) as dipolarophile at 50°C, furnishing only one isolable product based on TLC analysis.

The structure of the reaction product was ascertained on the basis of elemental analysis and spectral data as **4g** (Scheme 2). The ^{1}H NMR spectrum of **4g** revealed two singlet signals at 4.42 ppm due to two methyl ester groups. The FT-IR spectrum showed three carbonyl absorptions at 1706, 1637 and 1602 cm^{-1}.

The indolizine derivative **4g** is assumed to be formed via the 1,3-dipolar cycloaddition of DMAD to the nitrogen ylide **3** (which was formed *in situ* through the reaction of the pyridinium salt **2** with LDHs@PpPDA at 50°C) in order to give the nonisolable intermediate **5**. Finally, product **4g** was obtained with the involvement of oxygen and catalyst from the structure **5**. At this point, oxygen causes the oxidation of **5** and the product **4g**.

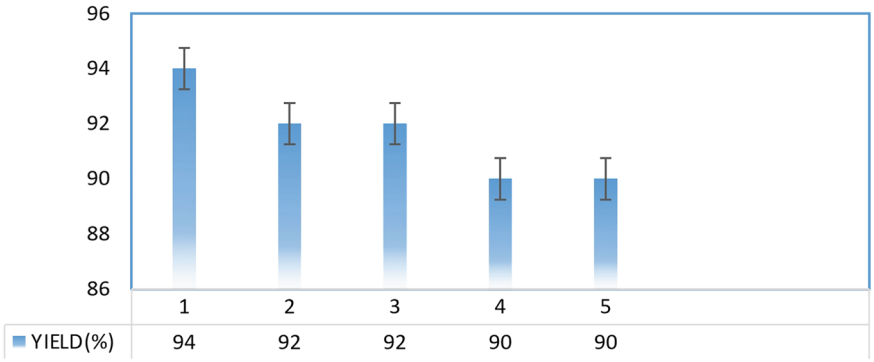


FIGURE 8 Recyclability test of LDHs@PpPDA

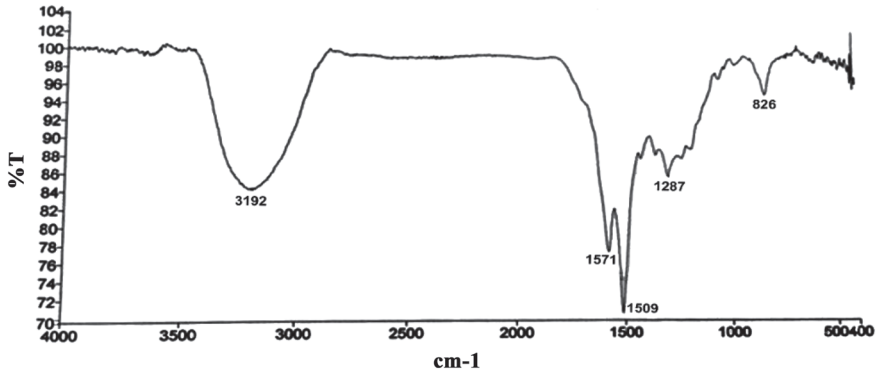


FIGURE 9 IR Spectrum of catalyst after use

Finally, LDHs@PpPDA was separated by simple extraction and reused for the next run. The process could be repeated five times without an obvious change in yields (Figure 8). In the first run, 94% LDHs@PpPDA was recycled, and the pureness and structure of the recovered LDHs@PpPDA remained unchanged on the basis of the FT-IR result (Figure 9).

4 | CONCLUSIONS

Taking everything into account, an effective synthesis of indolizine derivatives catalyzed by LDHs@PpPDA has been described. The initial materials are facilely accessible, and the reactions have a wide substrate range. The reaction overcomes some of the disadvantages of previously reported indolizine synthetic approaches and provides a new effective path to indolizine derivatives. Also, the catalyst can be easily recovered from the reaction and recycled. Also, the reaction rate is increased due to the existence of NH and NH_2 functional groups in the polymer structure of the catalyst.

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