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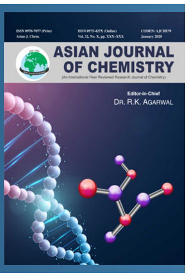

SiO_2:$MgMnO_3$: An Efficient Heterogeneous Catalyst for One Pot Synthesis of 1*H*-Pyrazolo[1,2-*b*]phthalazine-5,10-dione Derivatives

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The present study deals with hydrothermal synthesis of SiO_2 composite $MgMnO_3$ catalyst. The obtained polycrystalline product was analyzed by using physical investigative techniques including XRD, SEM, EDAX, TEM, SAED and BET surface area. The product corresponded to average particle size of 100 nm by TEM images. The BET surface area was found 234.38 cm^2/g for SiO_2 composite $MgMnO_3$ catalyst which indicates a good catalytic property. The synthesized catalyst was applied for the synthesis of 1*H*-pyrazolo[1,2-*b*]-phthalazine-5,10-dione in presence of ethanol as a solvent at 80 ºC. The current procedure and catalyst offers the gains of clean reaction, short reaction time, high yield, easy purification and financial availability of the catalyst.

Keywords: 1*H*-Pyrazolo[1,2-*b*]phthalazine-5,10-dione, Multicomponent reaction, SiO_2:$MgMnO_3$ catalyst, Short reaction time.

INTRODUCTION

Hydrazine heterocyclic components have attracted considerable advertence, because they show enough pharmacological properties and biological activities [1-5]. Phthalazine derivatives are an important group of heterocycles which have been subject to broad study in the past years. Among these phthalazines, 4-substituted phthalazines have been reported as active anticancer [6], antimicrobial [7], antifungal [8], anti-inflammatory [9] and anticonvulsant [10]. Moreover phthalazine derivatives are also found to possess cardiotonic [11] and vasorelaxant [12]. In addition, a number of 2,3-dihydrophthalazine-1,4-dione derivatives are well known to be active as potential anticonvulsant [13]. In view of above mentioned realities and continuation of our research interest for the synthesis of biologically active heterocycles [14].

Multicomponent reactions (MCRs) are one of the most efficient tool for synthesize diverse and complex organic molecule in one pot synthesis. Multicomponent reactions are very significant and contribute to an ideal synthesis, to increase in molecular complexity, high atom efficiency and impressive selectivity within single step in order to avoid time consuming and costly procedures for the purification of various precursors and isolation of intermediate and main products [15,16]. Therefore the development of new procedure for multicomponent reactions is very important in the field of organic and medicinal chemistry.

The synthesis of 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-dione derivatives *via* the three-component coupling of aldehydes, malononitrile or ethyl cyanoacetate and phthalhydrazide has been reported using MCRs in occurrence of diverse catalysts including PTSA/[Bmim]Br [17], Et_3N/EtOH [18], [Bmim]OH/MW [19], (DBU[CH_3COO] [20], AL-KIT-6 [21], $NiCl_2{\cdot}6H_2O$ (ethanol/reflux) [22] $InCl_3$ [23]. But current methodologies are suffered from numerous disadvantages such as longer reaction time, high temperature, harsh reaction condition, use of toxic and expensive catalyst, lack of recyclability of catalyst and so forth. Accordingly, there is a scope to develop another methods for the synthesis of 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-diones under environmentally caring conditions. Heterogeneous catalyst has received remarkable interest, both from a scientific and an industrial viewpoint. Heterogeneous catalysis is leading to a deeper understanding of how chemical reaction takes place at surface [22-24]. Nowadays, nanoparticles have drawn major attention because they connect the gap between bulk materials and atomic or molecular structures.

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Research on composite catalyst has focused on particle size in order to correlating the catalytic activity, many other aspects such as geometry, composition and chemical/physical environment can play a role in determining the catalytic activity. Composite particulate SiO_2:$MgMnO_3$ is one of the most versatile and technologically important materials because of its catalytic behaviour. On account of these properties, as a part of ongoing program on the development of novel methods in organic synthesis, herein, use of SiO_2:$MgMnO_3$ as an efficient catalyst for the synthesis of one pot synthesis 1*H*-pyrazolo[1,2-*b*]phthalazine derivative-5,10-dione by the four-component condensation reaction of phthalic anhydride, hydrazine monohydrate, benzaldehyde and ethyl cyanoacetate in the presence of ethanol as solvent (**Scheme-I**) is reported.

EXPERIMENTAL

All reagents were purchased and used without further purification: silica (SiO_2, Merck, 99.00%), $MgMnO_3$ (synthesized by earlier reported procedure) [25] and sodium hydroxide (NaOH, Merck, 99.90%).

Synthesis of SiO_2:$MgMnO_3$: The silica composite $MgMnO_3$ catalyst was prepared by mixing essential amount of SiO_2 solution (1 mol) with synthesized $MgMnO_3$ powder (1 mol) in presence of buffer solution. The slurry obtained was stirred for 1 h and shifted into steel lined Teflon autoclave and placed in the oven at 120 °C for 24 h. The precipitate obtained was filtered washed with distilled water and dried at 100 °C for 6 h. The polycrystalline product was directly kept in the furnace for calcination at 450 °C for 4 h.

Characterization: The pure products obtained were characterized by various analytical techniques. The XRD pattern obtained was recorded on a multipurpose X-ray diffractometer (Philips-1710 diffractometer with CuK_α, $\lambda = 1.5406$ Å). The surface morphology and chemical stoichiometry of synthesized catalyst were evaluated by scanning electron microscope-JSM-6300 (JEOL) and energy dispersive spectrometer-JED-2300LA (JEOL). The structure and particle size of the synthesized materials were studied using TEM with SAED on CM-200, Phillips microscope. The BET surface area was measured by N_2 adsorption-desorption isotherm and was carried out on Quantachrome Autosorb Automated Gas Sorption System Autosorb-1, NOVA-1200 and Mercury PorosimeterAutosorb-1c.

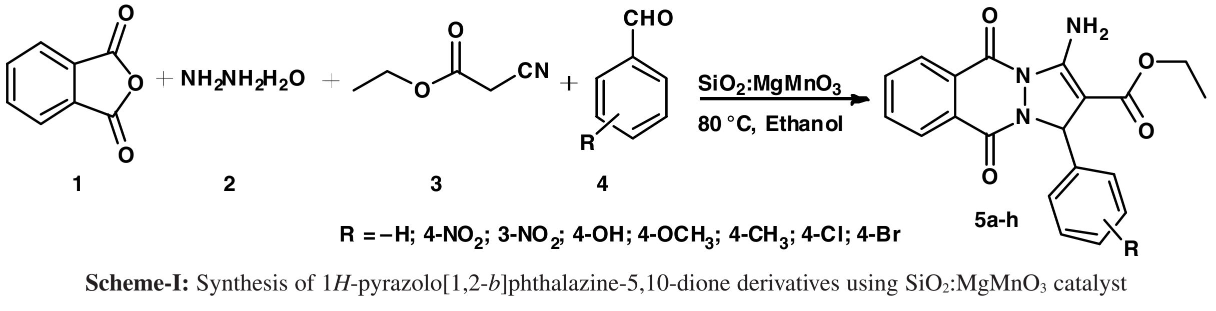
General procedure for the synthesis of 1*H*-pyrazolo-[1,2-*b*]phthalazine-5,10-dione (5a-h): In a 25 mL round-bottom flask, mixture of pthalic anhydride (**1**) (0.57 g, 1 mmol), hydrazine hydrate (**2**) (0.123 g, 1 mmol), ethylcynoacetate (0.34 g, 1 mmol), benzaldehyde (**4**) (0.30 g, 2 mmol) in presence of SiO_2:$MgMnO_3$ catalyst (0.6 mol) were taken. The reaction mixture was heated at 80 ºC in presence of ethanol for 20 min. After completion, the reaction mixture was cooled to room temperature and then poured over crushed ice, stirred for 10-15 min, precipitated product was filtered, washed with water, dried and recrystallized (**Scheme-I**). All the synthesized compounds **(5a-h)** were characterized by IR, ^1H & ^{13}C NMR and LCMS analysis.

Spectral data

Ethyl 3-amino-5,10-dihydro-5,10-dioxo-1-phenyl-1*H*-pyrazolo[1,2-*b*]phthalazine-2-carboxylate (5a): IR (KBr, ν_{max}, cm^{-1}): 3298 ($-NH_2$), 3150 (=C-H), 1698 (C=O), 1653 (C=C), 1554 (C-O), 1211 (C-N); ^1H NMR (300 MHz, DMSO-d_6): 1.23 (3H, t, -$\mathbf{CH_3}$), 2.34 (2H, q, -$\mathbf{CH_2}$), 5.85 (1H, s, -**CH**), 7.19 -7.34 (4H, m, *J* = 7.7 & 2.4Hz, Ar-**H**), 7.76-8.05 (5H, m, *J* = 7.8 & 2.2Hz, Ar-**H**), 10.1 (2H, s, -$\mathbf{NH_2}$) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ 21.9 (-$\mathbf{C}H_3$-), 65.2 (-$\mathbf{C}H_2$-), 98.5 (-CH_3-), 121.0 (Ar-**C**H), 128.7 (Ar-**C**H), 128.8 (Ar-**C**H), 129.2 (Ar-CH), 129.8 (Ar-**C**H), 130.0 (Ar-**C**H), 130.3 (Ar-**C**H), 130.5 (Ar-**C**H), 130.5 (Ar-**C**H), 131.8 (Ar-**C**H), 133.2 (Ar-**C**H), 134.5 (Ar-**C**H), 151.7 (-**C**=O), 157.2 (-**C**=O), 159.6 (-**C**=O); m.f.: $C_{20}H_{17}N_3O_4$; Calculated MS: 363.12; EI-MS (*m/z*): 363.37 (M+1).

Ethyl 3-amino-5,10-dihydro-5,10-dioxo-1-*p*-nitro-1*H*-pyrazolo[1,2-*b*]phthalazine-2-carboxylate (5b): IR (KBr, ν_{max}, cm^{-1}): 3286 ($-NH_2$), 1698 (C=O), 1634 (C=C), 1558 (C=O), 1254 (C-N); ^1H NMR (300 MHz, DMSO-d_6): 1.54 (3H, t, -$\mathbf{CH_3}$), 2.42 (2H, q, -$\mathbf{CH_2}$), 6.01 (1H, s, -C**H**), 7.04-7.45 (4H, m, *J* = 8.0 & 2.1Hz, Ar-**H**), 7.56-7.88 (4H, m, *J* = 7.8 & 2.2Hz, Ar-**H**) 10.8 (2H, s, -$\mathbf{NH_2}$); ^{13}C NMR (75 MHz, DMSO-d_6): δ 19.7 (-$\mathbf{C}H_3$-), 53.9 (-$\mathbf{C}H_2$-), 79.8 (-**C**H-), 110.2 (-**C**-), 119.2 (Ar-**C**H), 126.5 (Ar-**C**H), 129.1 (Ar-**C**H), 131.7 (Ar-**C**H), 132.1 (Ar-**C**H), 132.8 (Ar-**C**H), 134.7 (Ar-**C**H), 134.9 (Ar-**C**H), 137.8 (Ar-**C**H), 137.9 (Ar-**C**H), 140.2 (Ar-**C**H), 140.5 (Ar-**C**H), 156.7 (-**C**=O), 161.1 (-**C**=O), 162.4 (-**C**=O); m.f.: $C_{20}H_{16}N_4O_6$; Calculated MS: 408.1; EI-MS (*m/z*): 408.11 (M+1).

Ethyl 3-amino-5,10-dihydro-5,10-dioxo-1-*m*-nitro-1*H*-pyrazolo[1,2-*b*]phthalazine-2-carboxylate (5c): IR (KBr, ν_{max}, cm^{-1}): 3332 ($-NH_2$), 1693 (C=O), 1634 (C=C), 1540 (C=O), 1345 ($-NO_2$), 1234 (C-N); ^1H NMR (300 MHz, DMSO-d_6): 1.31 (3H, t, -$\mathbf{CH_3}$), 2.39 (2H, q, -$\mathbf{CH_2}$), 5.98 (1H, s, -C**H**), 6.8 (2H, s, -$\mathbf{NH_2}$), 7.07-7.39 (4H, m, *J* = 7.4 & 2.4Hz, Ar-**H**), 7.45-7.89 (4H, m, *J* = 8.0 & 2.2Hz, Ar-**H**); ^{13}C NMR (75 MHz, DMSO-d_6): δ 23.9 (-$\mathbf{C}H_3$-), 51.8 (-$\mathbf{C}H_2$-), 77.2 (-**C**H-), 99.5



Scheme-I: Synthesis of 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-dione derivatives using SiO_2:$MgMnO_3$ catalyst

(-**C**-), 123.2 (Ar-**C**H), 129.9 (Ar-**C**H), 129.9 (Ar-**C**H), 131.6 (Ar-**C**H), 131.8 (Ar-**C**H), 134.3 (Ar-**C**H), 136.4 (Ar-**C**H), 136.5 (Ar-**C**H), 137.5 (Ar-**C**H), 137.8 (Ar-**C**H), 137.9 (Ar-**C**H), 139.7 (Ar-**C**H), 140.5 (Ar-**C**H), 155.7 (-**C**=O), 158.4 (-**C**=O), 159.6 (-**C**=O); m.f.: $C_{20}H_{16}N_4O_6$; Calculated MS: 408.1; EI-MS (*m/z*): 408.11 (M+1).

Ethyl 3-amino-5,10-dihydro-5,10-dioxo-1-*p*-hydroxy-1*H*-pyrazolo[1,2-*b*]phthalazine-2-carboxylate (5d): IR (KBr, ν_{max}, cm^{-1}): 3334 (-NH_2), 3234 (-OH), 1684 (C=O), 1554 (C=C) 1543 (C=O), 1276 (C-N); ^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 1.16 (3H, t, -**CH$_3$**), 2.12 (2H, q, -**CH$_2$**), 5.82 (1H, s, -**CH**), 6.2 (1H, -**OH**), 6.80-7.12 (2H, d, *J* = 7.8 & 2.2Hz, Ar-**H**), 7.32-7.74 (2H, d, *J* = 7.8 & 2.2Hz, Ar-**H**), 7.95-8.24 (4H, m, *J* = 8.1 & 2.1Hz, Ar-**H**), 9.51 (2H, s, -**NH$_2$**); ^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 18.5 (-CH_3-), 61.4 (-CH_2-), 92.6 (-CH-), 115.0 (-**C-**), 116.2 (Ar-**C**H), 126.6 (Ar-**C**H), 127.3 (Ar-**C**H), 128.3 (Ar-**C**H), 128.6 (Ar-**C**H), 128.8 (Ar-**C**H), 133.6 (Ar-**C**H), 134.5 (Ar-**C**H), 150.5 (Ar-**C**H), 153.5 (-**C**=O), 156.6 (-**C**=O), 157.6 (-**C**=O); m.f.: $C_{20}H_{17}N_3O_5$; Calculated MS: 379.21; EI-MS (*m/z*): 379.11 (M+1).

Ethyl 3-amino-5,10-dihydro-5,10-dioxo-1-*p*-methoxy-1*H*-pyrazolo[1,2-*b*]phthalazine-2-carboxylate (5e): IR (KBr, ν_{max}, cm^{-1}): 3361 (-NH_2), 1690 (C=O), 1645 (C=C) 1569 (C=O), 1298 (C-N); ^{1}H NMR (400 MHz, DMSO 34.4 (-**C**H_3-), -d$_6$): δ 1.08 (3H, t, -**CH$_3$**), 2.12 (3H, s, -**CH$_3$**), 3.28 (2H, s, -**CH$_2$**), 5.67 (1H, s, -**CH**), 7.14-7.21 (2H, d, *J* = 7.8 & 2.2Hz, Ar-**H**), 7.34-7.43 (2H, d, *J* = 7.8 & 2.2Hz, Ar-**H**), 7.94-8.25 (4H, dd, *J* = 7.8 & 2.2Hz, Ar-**H**); ^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 20.9 (-**C**H_3-), 34.4 (-**C**H_3-), 55.8 (-**C**H_2-), 82.3 (-**C**H-), 113.1 (-**C**-), 123.4 (Ar-**C**H), 127.4 (Ar-**C**H), 127.6 (Ar-**C**H), 127.9 (Ar-**C**H), 128.1 (Ar-**C**H), 128.7 (Ar-**C**H), 130.2 (Ar-**C**H), 130.8 (Ar-**C**H), 133.3 (Ar-**C**H), 134.6 (Ar-**C**H), 135.0 (Ar-**C**H), 136.5 (Ar-**C**H), 153.0 (-**C**=O), 154.7 (-**C**=O), 157.0 (-**C**=O); m.f.: $C_{21}H_{19}N_3O_5$; Calculated MS: 393; EI-MS (*m/z*): 393.87 (M+1).

Ethyl 3-amino-5,10-dihydro-5,10-dioxo-1-*p*-tolyl-1*H*-pyrazolo[1,2-*b*]phthalazine-2-carboxylate (5f): IR (KBr, ν_{max}, cm^{-1}): 3357 (-NH_2), 1705 (C=O), 1665 (C=C), 1580 (C-O), 1242 (C-N); ^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 1.02 (3H, t, -**CH$_3$**), 1.23 (3H, t, -**CH$_3$**), 2.44 (2H, q, -**CH$_2$**), 5.27 (2H, s, -**CH**), 5.95 (1H, s, -**NH$_2$**), 7.09-7.24 (2H, d, *J* = 7.8 & 2.2Hz, Ar-**H**), 7.34-7.54 (2H, d, *J* = 7.8 & 2.2Hz, Ar-**H**), 7.81-8.46 (4H, dd, *J* = 8.2 & 2.3Hz, Ar-**H**); ^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 16.9 (-**C**H_3-), 24.4 (-**C**H_3-), 61.3 (-**C**H_2-), 93.2 (-**C**H-), 112.1 (**C**-), 122.3 (Ar-**C**H), 127.2 (Ar-**C**H), 127.4 (Ar-**C**H), 127.8 (Ar-**C**H), 128.2 (Ar-**C**H), 128.6 (Ar-**C**H), 128.9 (Ar-**C**H), 131.4 (Ar-**C**H), 134.0 (Ar-**C**H), 134.6 (Ar-**C**H), 135.6 (Ar-**C**H), 136.3 (Ar-**C**H), 154.0 (-**C**=O), 154.5 (-**C**=O), 157.3 (-**C**=O); m.f.: $C_{21}H_{19}N_3O_4$; Calculated MS: 377; EI-MS (*m/z*): 378.21 (M+1).

Ethyl 3-amino-5,10-dihydro-5,10-dioxo-1-*p*-chloro-1*H*-pyrazolo[1,2-*b*]phthalazine-2-carboxylate (5g): IR (KBr, ν_{max}, cm^{-1}): 3245 (-NH_2), 1708 (C=O), 1668 (C=C), 1521 (C-O), 1340 (C-N), 710 (C-Cl); ^{1}H NMR (300 MHz, DMSO-*d*$_6$): 1.09 (3H, t, -**CH$_3$**), 2.21 (2H, q, -**CH$_2$**), 5.43 (1H, s, -**CH**), 7.23-7.58 (4H, dd, *J* = 7.4 & 2.1Hz, Ar-**H**), 7.67-8.01 (4H, dd, *J* = 8.2 & 2.2Hz, Ar-**H**), 9.8 (2H, s, -**NH$_2$**); ^{13}C NMR (75 MHz, DMSO-*d*$_6$): δ 23.5 (-**C**H_3-), 67.3 (-**C**H_2-), 89.3 (-**C**H-), 113.6 (Ar-**C**H), 118.5 (Ar-**C**H), 121.2 (Ar-**C**H), 123.6 (Ar-**C**H), 126.3 (Ar-**C**H), 128.0 (Ar-**C**H), 128.8 (Ar-**C**H), 129.5 (Ar-**C**H), 131.1 (Ar-**C**H), 131.4 (Ar-**C**H), 131.9 (Ar-**C**H), 134.4 (Ar-**C**H), 134.9 (Ar-**C**H), 145.2 (-**C**=O), 147.2 (-**C**=O), 148.6 (-**C**=O); m.f.: $C_{20}H_{16}N_3O_4Cl$; Calculated MS: 397.23; EI-MS (*m/z*): 399.17 (M+1).

Ethyl 3-amino-5,10-dihydro-5,10-dioxo-1-*p*-bromo-1*H*-pyrazolo[1,2-*b*]phthalazine-2-carboxylate (5h): IR (KBr, ν_{max}, cm^{-1}): 3298 (-NH_2), 1703 (C=O), 1645 (C=C), 1590 (C-O), 1234 (C-N), 687 (C-Br); ^{1}H NMR (300 MHz, DMSO-*d*$_6$): 1.14 (3H, t, -**CH$_3$**), 2.56 (2H, q, -**CH$_2$**), 5.63 (1H, s, -**CH**), 7.23-7.56 (4H, dd, *J* = 8.2 & 2.3Hz, Ar-**H**), 7.81-8.11 (4H, dd, *J* = 8.2 & 2.3Hz, Ar-**H**), 10.8 (2H, s, -**NH$_2$**); ^{13}C NMR (75 MHz, DMSO-*d*$_6$): δ 23.7 (-**C**H_3-), 61.2 (-**C**H_2-), 94.7 (-**C**H-), 118.3 (Ar-**C**H), 121.2 (Ar-**C**H), 124.2 (Ar-**C**H), 127.8 (Ar-**C**H), 128.8 (Ar-**C**H), 131.0 (Ar-**C**H), 131.3 (Ar-**C**H), 132.1 (Ar-**C**H), 134.5 (Ar-**C**H), 134.8 (Ar-**C**H), 135.1 (Ar-**C**H), 135.7 (Ar-**C**H), 136.1 (Ar-**C**H), 143.2 (-**C**=O), 147.8 (-**C**=O), 159.9 (-**C**=O); m.f.: $C_{20}H_{16}N_3O_4Br$; Calculated MS: 441.23; EI-MS (*m/z*): 442.17 (M+1).

RESULTS AND DISCUSSION

Fig. 1 shows XRD pattern of SiO_2:$MgMnO_3$ powder formed after heating. The crystal structure of SiO_2:$MgMnO_3$ is cubic in nature and all the *d*-line patterns of $MgMnO_3$ was match with JCPDS data Card No-19-3456. Fig. 1 gives XRD pattern for SiO_2:$MgMnO_3$ having 2θ values with (hkl) plane are 26.3 (111), 32.5 (100), 36.8 (200), 56.2 (202) 56.3 (222), 64.4 (200), 65.85 (100), 77.54 (200). The recorded XRD pattern shows there is no any amorphous phase found and it reveals that product is highly polycrystalline with cubic in nature.

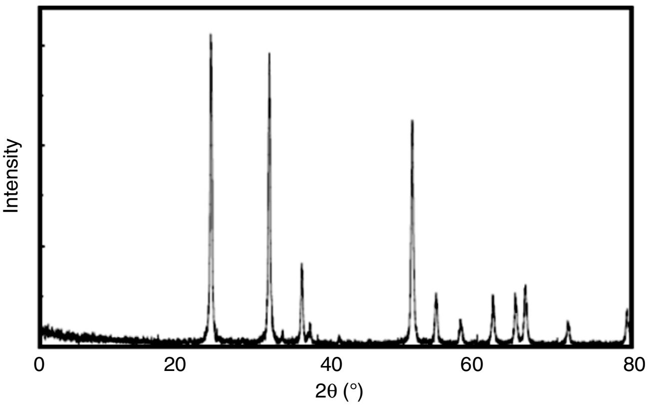


Fig. 1. XRD analysis of SiO_2:$MgMnO_3$ catalyst

The surface morphology and associated chemical composition of the synthesized SiO_2:$MgMnO_3$ catalyst was analyzed by SEM coupled with EDAX as depicted in Fig. 2. Fig. 2 shows that particles are uniformly distributed showing agglomerations. The EDAX data furnishes information about elemental composition associated with the image of SiO_2: $MgMnO_3$ catalyst.

The TEM image along with the selected area of the diffraction pattern (SAED) recorded for the sample corresponding

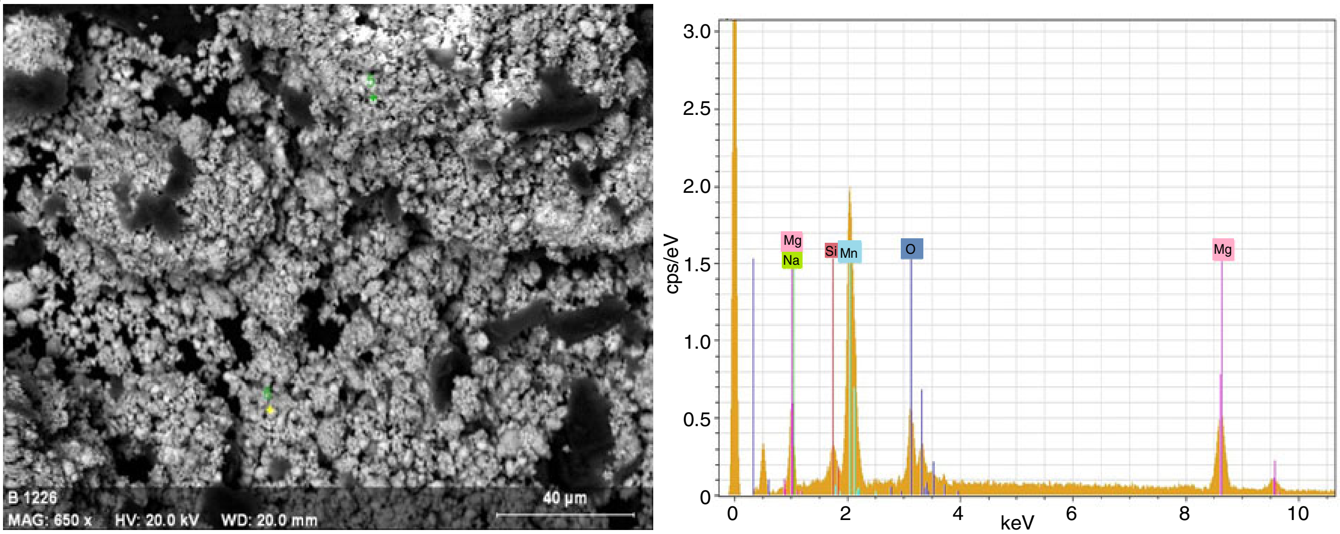


Fig. 2. SEM analysis of SiO_2:$MgMnO_3$ catalyst

to SiO_2:$MgMnO_3$ is given in Fig. 3. The TEM reveals that, the nanoparticles are elongated; however there are several cubic-shaped crystallites. The dark spot in the TEM micrograph can be alluded to SiO_2:$MgMnO_3$ nanoparticles as SAED pattern associated with such spots reveals occurrence of cubic SiO_2: $MgMnO_3$ in total agreement with the XRD data. The average size of the SiO_2:$MgMnO_3$ nanocrystallites were found to be 100 nm.

The detailed information about surface area (BET), mesoporous volume and pore size distribution arises from N_2-adsorption/desorption isotherm method. This method leads to the identification of the isotherm profile as type IV in the BDDT system which is typical for mesoporous material. The BJH pore size distribution demonstrates that all the samples have narrow pore diameter range. Surface area of material plays an important role in catalysis. The BET surface area (S_{BET}), pore volume (Vp), pore diameter (Dp) and other parameters are recorded. In the present investigation the typical nitrogen adsorption/desorption isotherm and BJH pore distribution of synthesized SiO_2:$MgMnO_3$ are depicted in Fig. 4. A careful inspection shows that the surface area for SiO_2:$MgMnO_3$ is 234.38 m^2/g and it founds highest, the average pore volume and diameter are 0.03498 cc/g and 56.87 Å. This clearly gives evidence that the grafting of SiO_2:$MgMnO_3$ shows increase in large surface area.

Our initial experiments were focused on the one pot, four component reactions of ethyl cynoacetate, hydrazine monohydrate, benzaldehyde and phthalic anhydride using different catalysts in presence of ethanol and the results are listed in Table-1. It was found that SiO_2:$MgMnO_3$ showed better catalytic activity than $MgMnO_3$ catalyst. When the reaction was performed in absence of catalyst no product formation takes place.

To get better yield of product the amount of catalyst were optimized for the reaction such as 0.2, 0.4, 0.6, 0.8, 1.0 mol.

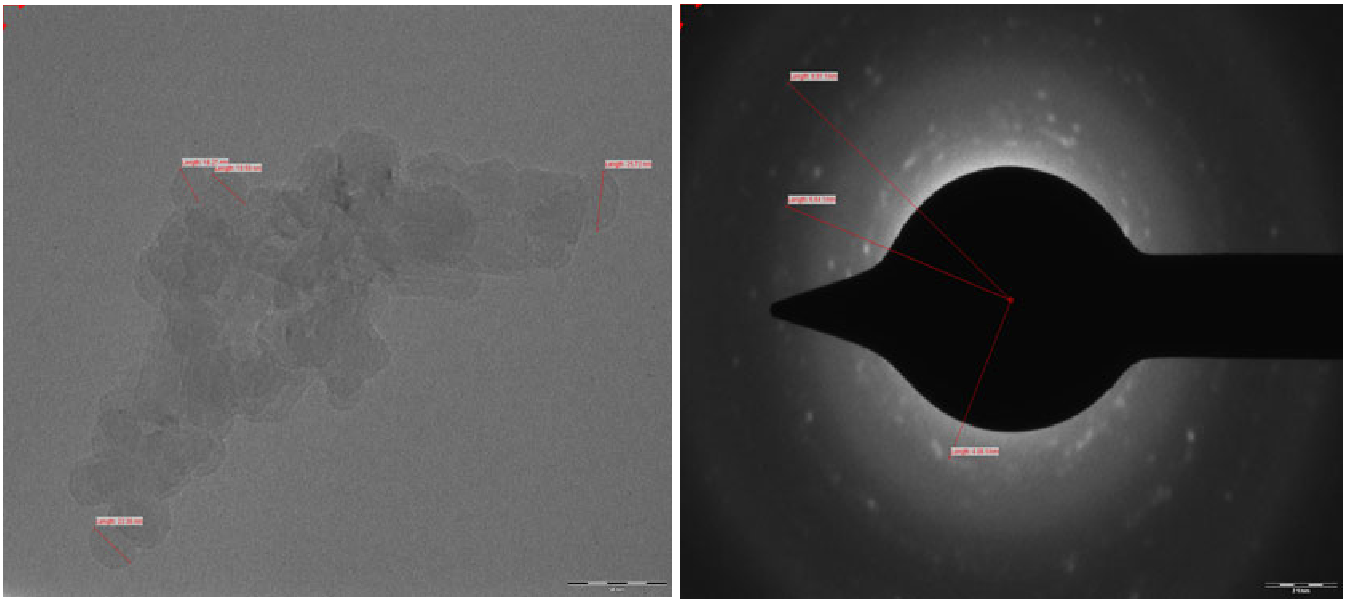


Fig. 3. TEM and SAED analysis of SiO_2:$MgMnO_3$ catalyst

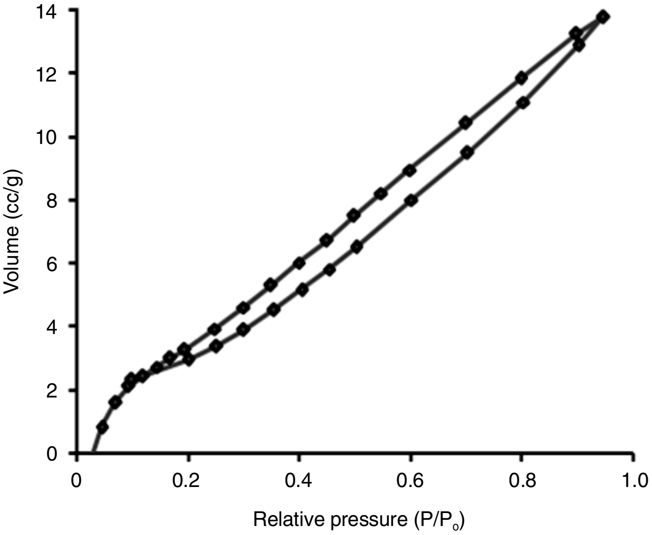


Fig. 4. BET analysis of SiO_2:$MgMnO_3$ catalyst

TABLE-1
CATALYTIC ACTIVITIES OF VARIOUS CATALYSTS

Entry	Catalyst	Time (min)	Yield (%)
1	No catalyst	120	No reaction
2	$MgMnO_3$	60	67
3	SiO_2: $MgMnO_3$	20	93
4	SiO_2	60	57

When 0.6 mol of SiO_2:$MgMnO_3$ was used, the reaction proceeded efficiently and gave the product **5a** with 93% yield (Table-2, entry 3). Moreover, we found that the yields were obviously affected by the amount of SiO_2:$MgMnO_3$ loaded. When 0.2, 0.4, 0.6, 0.8 and 1.0 mol, of SiO_2:$MgMnO_3$ was used, the yields were 58, 76, 93, 92 and 90%, respectively (Table-2, entries 1-5).

TABLE-2
EFFECT OF AMOUNT OF CATALYST ON REACTION

Entry	Catalyst (mol)	Time (min)	Yield (%)
1	0.2	60	58
2	0.4	60	76
3	0.6	20	93
4	0.8	20	92
5	1.0	20	90

Therefore, 0.6 mol of SiO_2:$MgMnO_3$ was sufficient to push the reaction forward and further increasing the amount of SiO_2:$MgMnO_3$ did not increase the yields. In addition, no desired product was detected in the absence of the catalyst (Table-1, entry 1). The above results showed that SiO_2:$MgMnO_3$ was essential in the reaction and the best results were obtained when the reaction was carried out with 0.6 mol of SiO_2:$MgMnO_3$ using ethanol at 80 °C. Then, we examined the effect of solvents for above reaction.

The results of Table-3 indicate that solvents affected the efficiency of the reaction. Poor yields was obtained in presence acetonitrile, DMF, water and solvent free condition (Table-3, entries 1-5). Better yields were obtained in presence of ethanol (Table-3, entry 4).

TABLE-3
OPTIMIZATION OF SOLVENT

Entry	Solvent	Time (min)	Yield (%)
1	No solvent	120	38
2	MeCN	120	58
3	DMF	90	60
4	EtOH	20	93
5	H_2O	120	30

To study the generality of this protocol, we extended our study with different aromatic aldehydes to prepare a series of 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-dione (**5a-h**, Table-4). In case of aromatic aldehydes, products were obtained in good to excellent yields while aliphatic aldehydes results poor yields.

TABLE-4
SYNTHESIS OF 1*H*-PYRAZOLO-[1,2-*b*]PHTHALAZINE-5,10-DIONE

Entry	Compound	-R	Time (min)	Yield (%)
1	**5a**	-H	20	93
2	**5b**	4-NO_2	25	92
3	**5c**	3-NO_2	25	93
4	**5d**	4-OH	25	90
5	**5e**	4-OCH_3	25	93
6	**5f**	4-CH_3	20	89
7	**5g**	4-Cl	25	90
8	**5h**	4-Br	25	87

Conclusion

In the present work, we described an efficient and one-pot synthesis of 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-diones by the four-component condensation reaction of phthalic anhydride, hydrazine monohydrate, benzaldehyde and ethyl cyanoacetate using ethanol at 80 °C with high yields. The benefits offered by this method include, short reaction times, non-toxic, excellent yields, a simple procedure, easy workup, environmentally benign nature make it an attractive process and the employment of a cost-effective catalyst.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

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