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β -Cyclodextrin based mesoporous silica as eco-friendly phase transfer catalyst in synthesis of Pyran derivatives

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Abstract: In this research, we report on the synthesis of mesoporous silicas with various quantities of immobilized oligosaccharide groups and different pore ordering degree. The hydrothermal co-condensation of tetraethyl orthosilicate and β-cyclodextrin-containing organosilane in the presence of cetyltrimethylammonium bromide template was employed.. It was prepared several β-cyclodextrin-organosilanes by modification of (3-aminopropyl)triethoxysilane with oligosaccharide. The heterogeneous hybrid nanocomposite, MCM-41-β-CD/NH2, was characterized by SEM, TEM, XRD, TGA, BET and FT-IR. The potential application of this covalently linked basic catalyst was also investigated as an efficient, heterogeneous and recyclable stationary micro-vessel and basic heterogeneous catalyst in synthesis of pyran hetrocycle. High yield, high efficiency and reusability are among the advantages of this environmentally friendly method. The nano catalyst can be easily separated from the reaction mixture and reused after washing for several runs without less in activity.

Keywords: MCM-41-β-CD/NH2, heterogeneous catalyst, β-cyclodextrin (β-CD), Pyran Derivatives.

Introduction

In recent decades, nanomaterials have attracted significant attention in chemistry and material areas due to their unique physical and chemical properties [1-5]. These have a lot of applications in the removal, adsorption and degradation of different pollutants such as dyes and toxic metals [6,7]. MCM-41 consists of hexagonal channels with the surface area around (~1000 m2/g) and have high thermal stability [8-10]. Thus, this nano material has the potential applications in many fields, such as decomposition and absorption, photocatalyst, sensors, nano electronics, encapsulation of enzymes and medicinal properties [11].

Mesoporous silica is more attracted due to advantages of uniform pore size, large surface area, easy functionalization with appropriate practical groups, high pore volume and excellent selectivity [12,13]. The most of latter nanomaterials have a core-shell structure in which magnetic core surrounded by a mesoporous shell. Heterocyclic frameworks have been found in various biologically active natural products, agrochemicals and pharmacological relevance molecules [14,15]. βCD as a one of the phase-transfer catsyst is known as remarkable natural maccrocycle host, having a hydrophpbic cavity which forms inclusion complexes with a large variety of guest molecules. However, this report describes a one-pot multicomponent process for the synthesis of various Pyran derivatives using new nano dual organo-modification MCM-41 as catalyst.

Results and discussion

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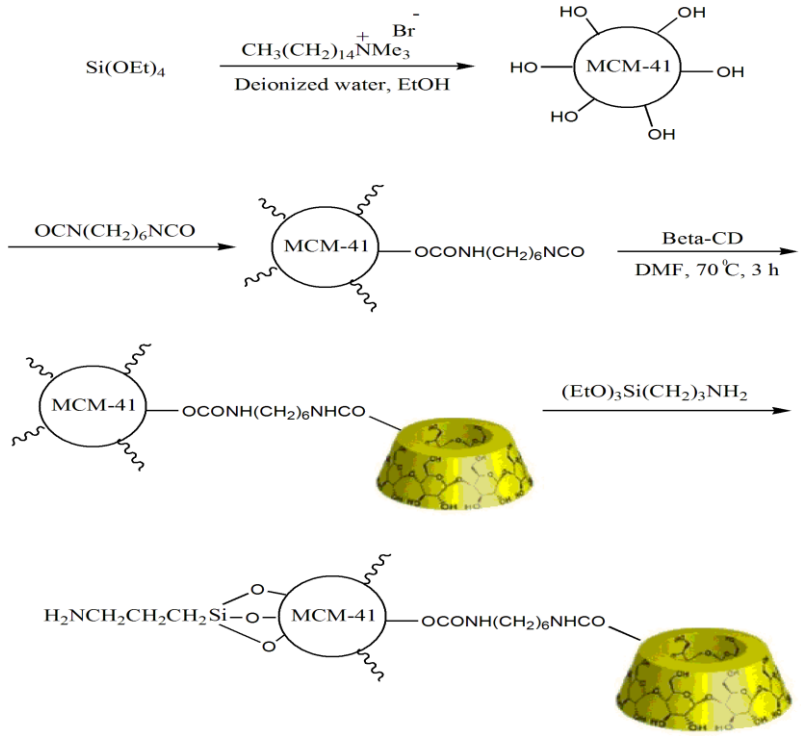
The systematic steps of aminopropyl and β-cyclodextrin grafted mesoporous MCM-41, MCM-41-β-CD.NH2 (Scheme **1**).



Scheme 1. Synthetic procedure of MCM-41-*β*-CD.NH_2

The structures of MCM-41-*β*-CD.NH_2 was confirmed by FT-IR spectra. The typical Si–O–Si bands around 1228, 1063, 794 and 462 cm^{-1} associated with the formation of a condensed silica network are present in the spectra (Figure **1**). The strong peak around 1630 cm^{-1} is mainly from the bending vibration of adsorbed H_2O. The peaks at 2800-3400 cm^{-1} region are attributed to amino groups wich are coverd by O–H vibration located in silica surface and also physically adsorbed water. The bands in the range of 2800–3000 cm^{-1} corresponded to the stretching vibration of C–H bonds of the methylene groups that indicates successful grafting of organic groups to MCM-41.

The morphology and particle size distribution of MCM-41-β-CD/NH_2 was performed by SEM using a Philips XL30 scanning electron microscope. The nanocomposite has spherical shape with nano dimension about 300 nm (Figure **2**). Transmission electron microscopy (TEM) revealed that MCM-41-β-CD/NH2, has an average particle size about 200 nm (Figure **3**). Powder X-ray diffraction (XRD) pattern of MCM-41-β-CD/NH2 through a covalent self assembly process via sol-gel technology (Figure **4**).The broad peak around 2◦ in the XRD pattern is ascribed to amorphous silica. Thermal stability of samples was investigated by Thermal Gravimetric Analysis-Derivative Thermo gravimetric Analysis (TGA-DTG) in which the observed weight loss was associated with the loss of the organic components attached to the MCM-41. The introduction of organic parts, β-CD and amino propyle, in mesoporous MCM-41 network was also confirmed through Thermal Gravimetric Analysis-Derivative Thermo gravimetric Analysis (TGA-DTG). TGA-DTG curve for MCM-41-β-CD/NH_2 was shown in (Figure 5). It shows two distinct steps of weight loss in the combined TG-DTG curves. The curves show that the first weight loss occurs before 200 ^oC, which can be attributed completely to the loss of adsorbed water molecules (11%). The secondary weight losses at about 250 ^oC come from the decomposition of organic substances in MCM-crown composites (24%). Decomposition is complete at about 680 ^oC to form the constituent inorganic oxides. TGA of the samples demonstrated high thermal stability, with decomposition starting at around 250 ^oC under a nitrogen atmosphere.

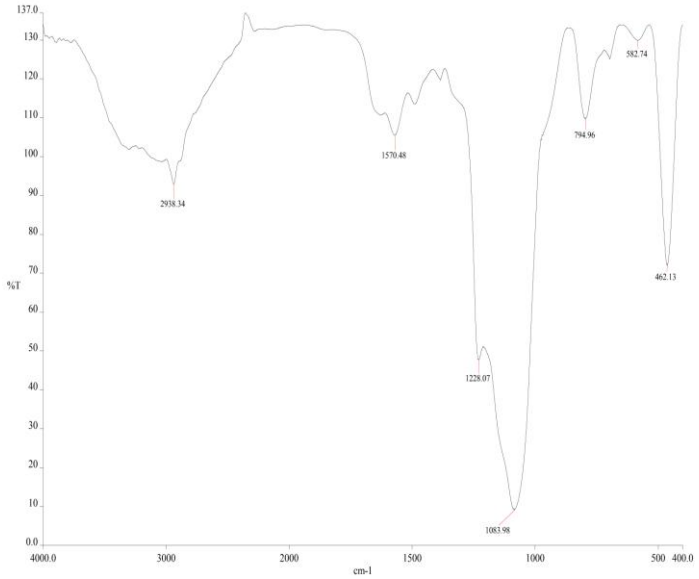


Figure 1. The FT-IR spectra of MCM-41-β-CD/NH_2

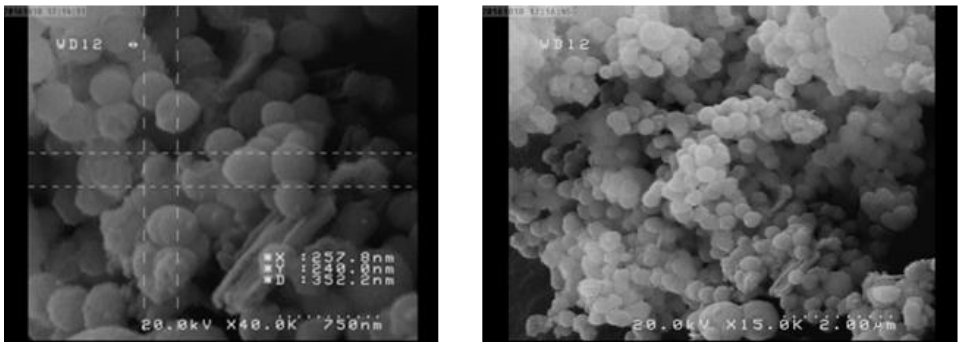


Figure 2. The SEM Images of MCM-41-β-CD/NH_2

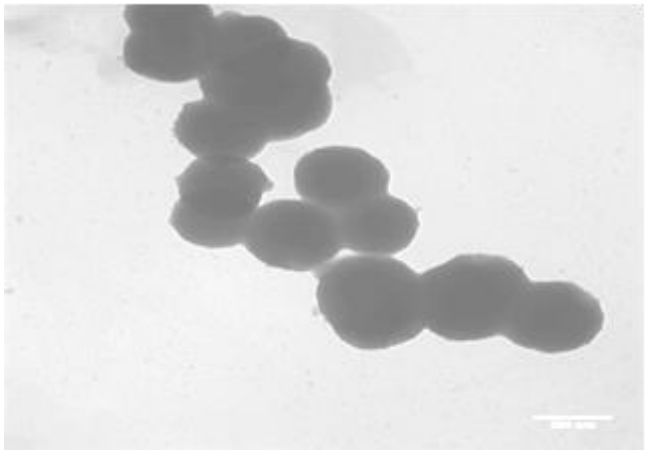


Figure 3. The TEM of MCM-41-β-CD/NH_2

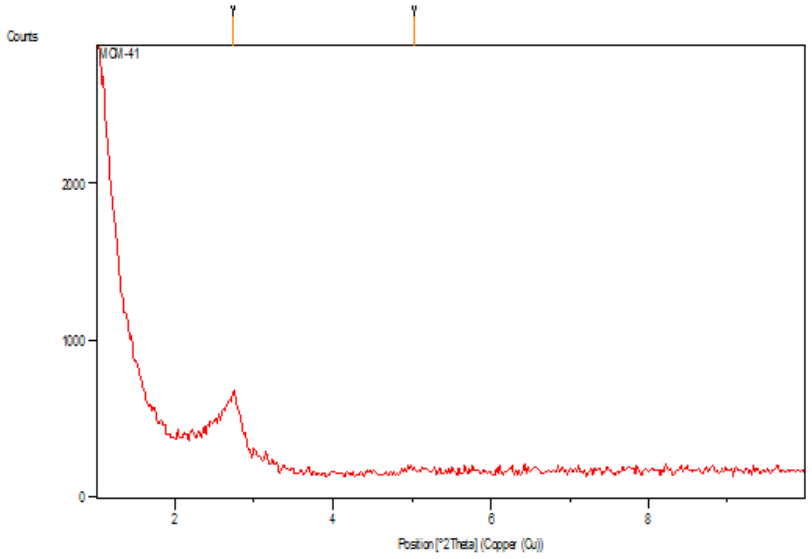


Figure 4. The XRD Analysis of MCM-41-*β*-CD/NH_2

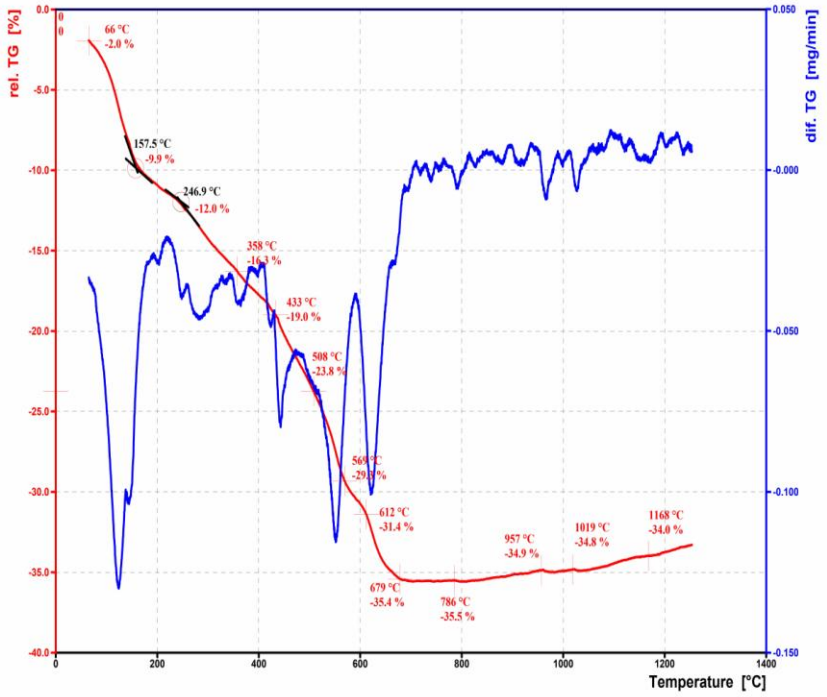


Figure 5. The TGA-DTG of MCM-41-β-CD/NH_2

The specific surface area and the pore size distribution were calculated by Brunauer-Emmett-Teller (BET) method. The pore size distribution was calculated using desorption branches of nitrogen isotherms. The total surface of catalyst is 39.9 m^2/g and the BET surface is 6.981 m^2 (Figure **6**).

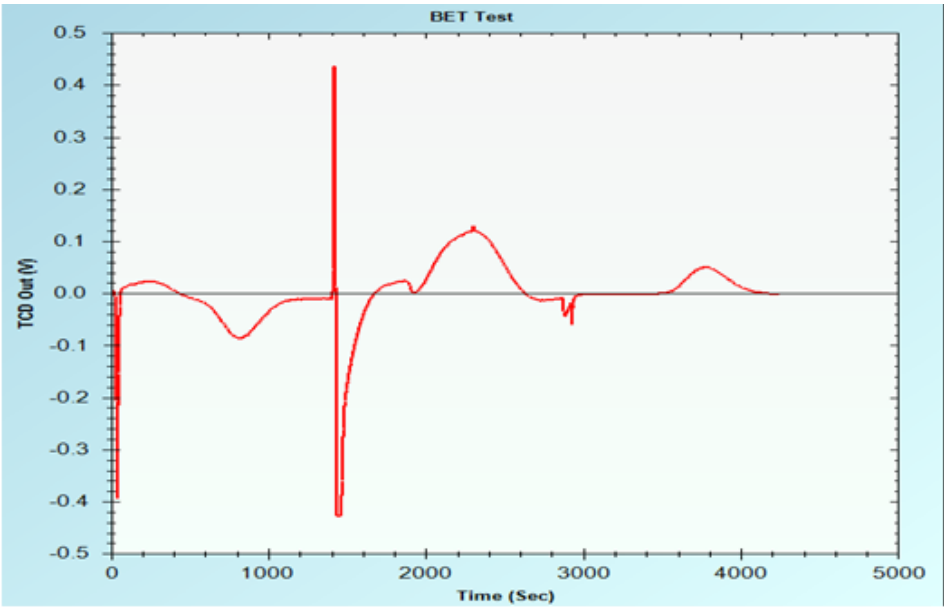


Figure 6. The BET curve of MCM-41- β-CD/NH_2

The catalyst recyclability was confirmed in the Pyran derivatives 2**a** and the results are shown in Figure 7.

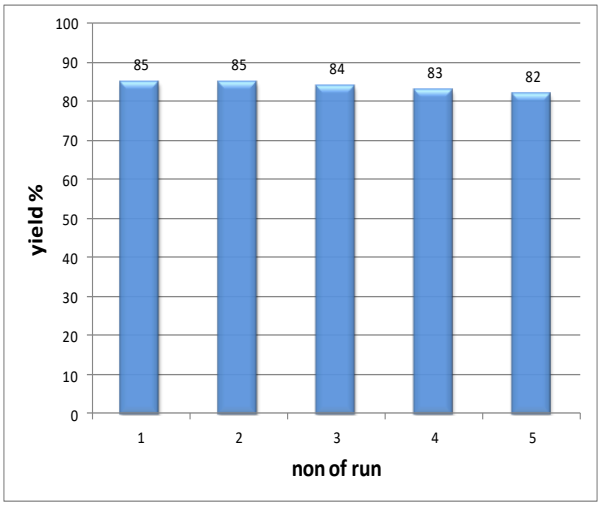
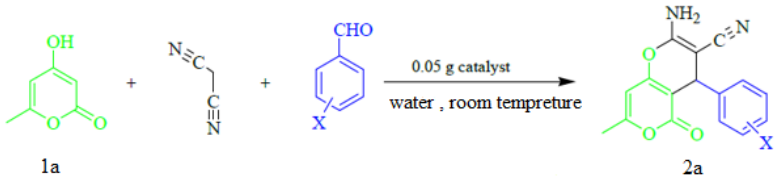


Figure 7. Recyclability of MCM-41-β-CD/NH_2.

We examined the potential application of this covalently linked basic nanocomposite as stationary micro-vessel basic heterogeneous catalyst in Biginelli multicomponent condensation reaction.At first, one pot multicomponents condensation of 1,3-cyclohexadione, benzaldehyde and urea was investigated in the presence of nanocomposite. TLC analysis of the reaction mixture interestingly showed that this catalyst acted very efficiently in CH_3CN, and that 0.15 g of the catalyst was enough to convert 10 mmol of different aromatic aldehydes, carrying electron-donating or withdrawing groups, to their corresponding 4-Aryl-1,3,4,6,7,8-hexahydro quinazolin-2,5(1H,6H) -diones in high yields ((Scheme **2**) Table **1** & **2**).



Scheme 2. MCM-41-*β*-CD/NH_2 catalyzed synthesis of the pyran derivatives (2a)

Table 1. Optimization of reaction conditions in the synthesis of Pyran product (2a) under different conditions.

Comp	catalyst (g)	T (°C)	Solvent	Yield (%) [a]	Time (min) [b]
2a	0.05	r.t.	Solvent free	60	200
2a	0.1	r.t.	H_2O	71	90
2a	0.05	reflux	H_2O	61	110
2a	0.025	r.t.	H_2O	64	165
2a	0.05	r.t.	H_2O	87	120
2a	0.05	r.t.	EtOH	65	160
2a	0.05	r.t.	CH_3CN	61	180
2a	0.05	r.t.	CH_2Cl_2	63	155

a. Isolated Yield; b. Times are given after maximum progress of reaction.

The best condition was achieved using mixture of as aldehyde (10 mmol), malononitrile (12 mmol), 4-hydroxycoumarin (10 mmol)and nano MCM-41-*β*-CD/NH_2 (0.05 g) in water (5 mL) in room tempreture.

The results for the application of aromatic aldehaydes with electron donating and withdrawing groups are shown in Table 2.

Table 2. new nano MCM-41-*β*-CD/NH_2 catalyzed synthesis of some Pyran derivatives 2**a-o**.

Comp.	Ar	Time (min)	Yield%
2**a**	C_6H_5	120	85
2**b**	4-$CH_3C_6H_4$	45	78
2**c**	3-$CH_3C_6H_4$	50	80
2**d**	2-$CH_3C_6H_4$	35	84
2**e**	4-$CH_3OC_6H_4$	45	88
2**f**	3-$CH_3OC_6H_4$	35	83
2**g**	2-$CH_3OC_6H_4$	30	79
2**h**	4-ClC_6H_4	35	81
2**i**	3-ClC_6H_4	40	82
2**j**	2-ClC_6H_4	30	76

2**k**	4-BrC_6H_4	50	79
2**l**	3-BrC_6H_4	45	86
2**m**	2-BrC_6H_4	45	84
2**n**	4-$NO_2C_6H_4$	50	82
2**o**	3-$NO_2C_6H_4$	50	79

Table 2. new nano MCM-41-*β*-CD/NH_2 catalyzed synthesis of new 4-aryl-3,4,6,7,8 hexahydroquinazolin-2,5(1*H*,6*H*)-diones 2a-o

Comp	Ar	Time (min)	Yield%	m.p (˚C)
2a	C_6H_5	45	86	228
2b	4$CH_3C_6H_4$	90	37	192
2c	3$CH_3C_6H_4$	50	44	211
2d	2$CH_3C_6H_4$	50	42	219
2e	4$CH_3OC_6H_4$	60	60	200
2f	3$CH_3OC_6H_4$	70	38	201
2g	2$CH_3OC_6H_4$	45	35	209
2h	4ClC_6H_4	30	88	232
2i	3ClC_6H_4	50	71	219
2j	2ClC_6H_4	30	80	222
2k	4BrC_6H_4	80	64	216
2l	3BrC_6H_4	35	79	215
2m	2BrC_6H_4	30	85	219
2n	4$NO_2C_6H_4$	40	78	225
2o	3$NO_2C_6H_4$	50	71	216

The comparative between phenols in two works (Table **3**) that shown this work has a high yield.

Table 3. Comparative between phenols in two works

comp	Ar	Time (min)	Yield%	m.p (˚C)
This work	C_6H_5	45	86	228
2	C_6H_5	17	55	228

Conclusion

In the present study, a mesoporous MCM-41 having β-CD and amino basic units with pore channels was synthesized via a surfactant-templated sol–gel methodology and a post modification process. The catalytic activity of the basic nanocomposite has been successfully applied for the one-pot three-components reaction malononitrile, aromatic aldehyde and 4-hydroxycoumarin in H2O as solvent. This catalytic system certainly contributes to better environmental and green technology for the facile preparation of the pyran derivatives. The current methodology has the advantages of operational simplicity, short reaction times, good yields and the desired products can be

separated directly from the reaction mixture with high purity.

Experimental

General section

All chemical materials were purchased from Aldrich and Merck Chemical companies. Tetraethyl orthosilicate, (TEOS (98%, Aldrich)) was selected as a source of silica and cetyltrimethyl-ammonium bromide, (CTAB (98%, Aldrich)) was used as the structure directing agent. Deionized water was obtained from a system of two ionic interchange columns, cole–Parmer instruments. Melting points were determined on an electrothermal SI550 apparatus. FT-IR spectra were recorded from KBr discs on a Perkinelemer BX_ll. ^{1}H NMR and ^{13}C NMR spectra were recorded using a Bruker Avance 500 MHz instrument in DMSO-*d6*. Mass spectra were obtained on Platform II spectrometer from Micromass; EI mode at 70 eV. UV/vis spectra (in EtOH) were taken with a CINTRAL 101 spectrophotometer. The surface area and pore size distribution of the support was measured by the nitrogen adsorption–desorption method (ASAP 2000, Micromeritics). Transmission electron microscope (TEM) image was obtained using Zeiss – EM10C –80 kV instrument.

*Synthesis of aminopropyl and β-***cyclodextrin** *grafted mesoporous MCM-41:*

0.5g CTAB was added to 96 mL of deionized H_2O under stirring. After the solution turned clear, 34 mL of ethanol was added to the mixture. Then 10 mL of aqueous ammonia solution was added to mixture and it was allowed to mix for 5 min. After that, 2.0 mL of TEOS was poured into the solution immediately under stirring for 3h at room temperature. The solid product was recovered by filtration and dried at room temperature overnight. The CTAB was removed from the mesoporous MCM-41 by calcining the sample at 540 ˚C for 9h. In the other step, the obtained mesoporous MCM-41 (1g) was dispersed in dry DMF (30 mL) by sonication. Then solution of hexamethylene diisocyanate (HMDI) (3 mL) in 5 mL of dry DMF was added dropwise to the mixture. After mechanically agitation for 3h, the suspended substance was seprated with filtration for removing of unreacted HDMI. To the re-dispersed product in dry DMF (15 mL), *β*-CD (2 mmol) dissolved in 15 mL of dry DMF was added dropwise.The reaction mixture was stirred at 70 °C for 3h. The *β*-cyclodextrin grafted mesoporous MCM-41, MCM-41-*β*-CD, washed with water and acetone several times and dried in vacuum for 24 h. Finally, To the suspension of MCM-41-*β*-CD in 80 mL of toluene, triethoxypropyl silyl amine (2 g) was added and refluxed for 24h at 110 °C. The mesoporous MCM-41-*β*-CD/NH_2 was then filtrate and washed with water and acetone several times and dried under vacuum condition.

General procedure for the synthesis of 4-Aryl-1,3,4,6,7,8-hexahydroquinazolin-2,5(1H,6H)-diones (HHQs) derivatives catalyzed by MCM-41-β-CD/NH₂

To a magnetically stirred mixture of the aldehyde (10 mmol), 1,3-cyclohexadione (10 mmol), urea (12 mmol) in acetonitrile (10 mL), MCM-41-*β*-CD.NH_2 (0.15 g) was added. The resulting mixture was stirred under reflux condition for the appropriate time (30-90 min). After completion of the reaction as indicated by using TLC n-hexane/ethyl acetate (2:1) as an eluent, the insoluble catalyst was filtered off. Then 10 mL water was added to the filtrate and the solid product after filtration recrystallized in ethanol. All these products are characterized by UV/vis, FT-IR, ^{1}H-NMR, ^{13}C-NMR and Ms spectra.

4-phenyl-1,3,4,6,7,8-hexahydroquinazolin-2,5(1H,6H)-diones (2a):

FT-IR (KBr): 3380.25, 2920.93, 1725.05, 1710.01, 1610.17 cm^{-1}. UV/Vis (EtOH): λ_{max} (logε) = 265.66 nm (5.50).

4-(4-methylphenyl)-1,3,4,6,7,8-hexahydroquinazolin-2,5(1H,6H)-diones (2b):

FT-IR (KBr): 3336.85, 2941.02, 1722.08, 1602.37 cm^{-1} ^{1}H NMR (500 MHz, DMSO-d_6): δ= 1.90 (m, *J*=7Hz, 2H, H-8), 2.01 (m, *J*=8.05 Hz, 2H, H-7), 2.19 (m, *J*=6.9 Hz, 2H, H-9), 2.36 (m, *J*=8.35 Hz,3H, CH_3), 2.94 (d, *J*=10.7 Hz, 1H, H-4), 3.90 (d, *J*=9.6 Hz, 1H, NH), 6.83 (s, 1H, NH), 6.94 (m, *J*=7.55 Hz, 2H, Ar-H), 7.08 ppm (m, *J*=7.85 Hz, 2H, Ar-H). ^{13}C NMR (500 MHz, DMSO-*d*6): δ= 20.20, 21.02, 29.05, 32.38, 33.50, 35.41, 37.24, 60.54, 100.45, 101.41, 116.39, 128.08, 128.35, 128.72, 134.02, 134.41, 141.68, 142.60, 195.83, 205.25 ppm. MS (EI, 70 eV): *m/z* (%): 255.1 ($M^{+\cdot}$, $C_{15}H_{15}N_2O_2$), 253.2 ($M^{+\cdot}$ – 2H), 240.1 ($M^{+\cdot}$ – $C_{15}H_{14}NO_2$), 227.2 ($M^{+\cdot}$ – $C_{15}H_{15}O_2$), 164.1 ($M^{+\cdot}$ – C_7H_7), 148.1 ($M^{+\cdot}$ – C_7H_7-CH-NH-CO-NH), 131.1 ($M^{+\cdot}$ – C_7H_7-CH-CH=CH_2), 119.1 ($M^{+\cdot}$ – C_7H_7-CH-NH), 71.1 ($M^{+\cdot}$ – NH-CH=CH-COH), 70.1 ($M^{+\cdot}$ – CH_3-CO-CH=CH_2), 57.1 ($M^{+\cdot}$ – NH-CO-NH), 51.1 ($M^{+\cdot}$ – CH_2=CH-COH), 42.1 ($M^{+\cdot}$ – CH_2-CH_2-CH_2). UV/Vis (EtOH): λ_{max} (logε) = 257.98 nm (5.49).

4-(3-methylphenyl)-1,3,4,6,7,8-hexahydroquinazolin-2,5(1H,6H)-diones (2c):

FT-IR (KBr): 3359.99, 2975.01, 1720.79, 1609.14 cm^{-1}. ^{1}HNMR(500MHz, DMSO-*d*6): δ=1.89 (m, *J*=7.3Hz, 2H, H-8), 2.10 (m, *J*=5.4Hz, 2H, H-7), 2.16 (m, *J*=6.2Hz, 2H, H-9), 2.38 (m, *J*=6.7 Hz, 3H, CH_3), 2.99 (d, *J*=10.65 Hz, 1H, H-4), 3.90 (d, *J*=9.6 Hz, 1H, NH), 6.78 (s, 1H, NH), 6.84 (m, *J*=9.35 Hz, 1H, Ar-H), 6.91 (m, *J*=7.4 Hz, 1H, Ar-H), 7.00 (m, *J*=5.65Hz, 1H, Ar-H), 7.04 (m, *J*=7.45Hz, 1H, Ar-H).^{13}C NMR(500MHz ,DMSO-*d*6): δ=20.40, 21.63, 28.95, 29.09, 32.68, 33.44, 35.39, 37.24, 100.44, 101.39, 111.57, 116.38, 125.43, 126.02, 127.58, 128.79, 129.43, 136.45, 144.74, 145.63, 167.72, 169.47, 189.82, 195.86, 196.27, 205.22, 206.67 ppm.MS (EI, 70 eV): *m/z* (%): 255.2 ($M^{+\cdot}$; $C_{15}H_{15}N_2O_2$), 253.2 ($M^{+\cdot}$ – 2H$_\cdot$), 240.1 ($M^{+\cdot}$ – $C_{15}H_{14}NO_2$), 227.2 ($M^{+\cdot}$ – $C_{15}H_{15}O_2$), 164.1 ($M^{+\cdot}$ –C_7H_7), 148.1 ($M^{+\cdot}$ – C_7H_7-CH-NH-CO-NH), 131.1 ($M^{+\cdot}$ – C_7H_7-CH-CH=CH_2), 119.1 ($M^{+\cdot}$ – C_7H_7-CH-NH), 71.1 ($M^{+\cdot}$ – NH-CH=CH-COH), 70.1 ($M^{+\cdot}$ – CH_3-CO-CH=CH_2), 57.1 ($M^{+\cdot}$ – NH-CO-NH), 51.1 ($M^{+\cdot}$ – CH_2=CH-COH), 42.1 ($M^{+\cdot}$ – CH_2-CH_2-CH_2). UV/Vis(EtOH): λ_{max} (logε)= 268.22 nm (5.50).

4-(2-methylphenyl)-1,3,4,6,7,8-hexahydroquinazolin-2,5(1H,6H)-diones (2d):

FT-IR(KBr): 3314.86, 2936.99, 1712.01, 1617.22 cm^{-1}. ^{1}H NMR(500 MHz ,DMSO-*d*6): δ=1.84 (m, *J*=8.85 Hz, 2H, H-8), 2.08 (m, *J*=4.3 Hz, 2H, H-7), 2.20 (m, *J*=8.65Hz, 2H, H-9), 2.36 (m, *J*=5.65 Hz, 3H, CH_3), 3.15 (d, *J*=10.9 Hz, 1H, H-4), 4.01 (d, *J*=10.65 Hz, 1H, NH), 6.90 (s, 1H, NH), 6.93 (m, *J*=5 Hz, 1H, Ar-H), 6.97 (m, *J*=5 Hz, 1H, Ar-H), 7.02 (m, *J*=5Hz, 2H, Ar-H).^{13}C NMR(500 MHz ,DMSO-*d*6): δ=20.69, 21.35, 28.95, 29.48, 35.98, 37.82, 61.81, 101.07, 101.89, 112.77, 118.22, 125.72, 126.18, 130.13, 135,49, 139.36, 144.54, 167.67, 169.97, 196.42, 206.32 ppm.

MS (EI, 70 eV): *m/z* (%): 255.1($M^{+\cdot}$; $C_{15}H_{15}N_2O_2$), 253.2 (M^{+}. - 2H), 240.1 ($M^{+\cdot}$ – $C_{15}H_{14}NO_2$), 227.2 ($M^{+\cdot}$ – $C_{15}H_{15}O_2$), 164.1 ($M^{+\cdot}$ – C_7H_7), 148.1 ($M^{+\cdot}$ – C_7H_7-CH-NH-CO-NH), 131.1 ($M^{+\cdot}$ – C_7H_7-CH-CH=CH_2), 119.1 ($M^{+\cdot}$ – C_7H_7-CH-NH), 71.1 ($M^{+\cdot}$ – NH-CH=CH-COH), 70.1 ($M^{+\cdot}$ – CH_3-CO-CH=CH_2), 57.1 ($M^{+\cdot}$ – NH-CO-NH), 51.1 ($M^{+\cdot}$ – CH_2=CH-COH), 42.1 ($M^{+\cdot}$ – CH_2-CH_2-CH_2).UV/Vis(EtOH): λ_{max}(logε)= 258.40 nm (5.49).

4-(4-methoxyphenyl)-1,3,4,6,7,8-hexahydroquinazolin -2,5(1H,6H)-diones (2e):

FT-IR(KBr): 3389.23, 2959.93, 1722.04, 1601.58, 1375.17 cm^{-1}. ^{1}H NMR(500 MHz ,DMSO-*d*6): δ=1.86 (m, *J*=5.7 Hz, 2H, H-8), 2.15 (m, *J*=7.8Hz, 2H, H-7), 2.39 (m, *J*=5.75 Hz, 2H, H-9), 3.68 (m, *J*=4.8 Hz, 3H, OCH_3), 2.96 (d, *J*=10.7 Hz, 1H, H-4), 3.88 (d, *J*=10.75 Hz, 1H, NH), 6.84 (s, 1H, NH), 6.75 (m, *J*=6.95 Hz, 2H, Ar-H), 7.10 (m, *J*=6.45 Hz, 2H, Ar-H). ^{13}C NMR (500 MHz, DMSO-*d*6): δ=20.99, 29.07, 31.97, 32.18, 35.41, 37.16, 55.38, 60.58, 100.50, 101.44, 113.71, 116.25, 129.70, 137.51, 157.37, 167.61, 195.87, 205.37 ppm. MS (EI, 70 eV): *m/z* (%): 271.1(M^{+}; $C_{15}H_{15}N_2O_3$), 269.2($M^{+\cdot}$ – 2H), 256.1 ($M^{+\cdot}$ – $C_{15}H_{14}NO_3$), 255.1 ($M^{+\cdot}$ – CH_3), 243.1 ($M^{+\cdot}$ – $C_{15}H_{15}O_3$), 164.1 ($M^{+\cdot}$ – C_7H_7O-CH-NH-CO-NH), 147.1 ($M^{+\cdot}$ – C_7H_7O-CH-CH=CH_2), 135.1 ($M^{+\cdot}$ – C_7H_7O-CH-NH), 107.1 ($M^{+\cdot}$ – C_7H_7O), 71.1 ($M^{+\cdot}$ – NH-CH=CH-COH), 70.1 ($M^{+\cdot}$ – CH_3-CO-CH=CH_2), 57.1 ($M^{+\cdot}$ – NH-CO-NH), 51.1 ($M^{+\cdot}$ – CH_2=CH-COH), 42.1 ($M^{+\cdot}$ – CH_2-CH_2-CH_2). UV/Vis (EtOH): λ_{max}(logε)=265.66 nm (5.50).

4-(3-methoxyphenyl)-1,3,4,6,7,8-hexahydroquinazolin -2,5(1H,6H)-diones (2f):

FT-IR (KBr): 3374.80, 2941.18, 1719.71, 1614.34, 1374.19 cm^{-1}.^{1}H NMR (500 MHz, DMSO-*d*6): δ=1.89 (m, *J*=5.45 Hz, 2H, H-8), 2.16 (m, *J*=5.6Hz, 2H, H-7), 2.39 (m, J=6.65Hz, 2H, H-9), 3.69 (s, 3H, OCH_3), 2.98 (d, *J*=10.7 Hz, 1H, H-4), 3.91 (d, *J*=10.6 Hz, 1H, NH), 6.85 (s, 1H, NH), 6.62 (m, *J*=5.8 Hz, 1H, Ar-H), 6.79 (d, *J*=6.55 Hz, 1H, Ar-H), 7.07 (t, *J*=6.85 Hz, 1H, Ar-H), 6.73 (s, 1H, Ar-H).^{13}CNMR (500 MHz, DMSO-*d*6): δ=20.27, 21.09, 28.98, 29.12, 32.67, 33.47, 35.42, 36.15, .27, 55.22, 59.66, 60.38, 100.48, 101.24, 110.36, 111.54, 114.47, 115.04, 116.00, 120.72, 121.33, 128.64, 146.48, 147.31, 159.11, 167.90, 169.59, 189.83, 195.92, 196.31, 205.29, 206.66 ppm.

MS (EI, 70 eV): *m/z* (%): 271.1 (M^{+} ;$C_{15}H_{15}N_2O_3$), 269.2 (M^{+}. –2H), 256.1 ($M^{+\cdot}$ – $C_{15}H_{14}NO_3$), 255.1 ($M^{+\cdot}$ – CH_3), 243.2 ($M^{+\cdot}$ – $C_{15}H_{15}O_3$), 164.1 ($M^{+\cdot}$ – C_7H_7O-CH-NH-CO-NH), 147.1 ($M^{+\cdot}$ – C_7H_7O-CH-CH=CH_2), 135.1 ($M^{+\cdot}$ – C_7H_7O-CH-NH), 107.1 ($M^{+\cdot}$ – C_7H_7O), 71.1 ($M^{+\cdot}$ – NH-CH=CH-COH), 70.1 ($M^{+\cdot}$ – CH_3-CO-CH=CH_2), 57.1 ($M^{+\cdot}$ – NH-CO-NH), 51.1 ($M^{+\cdot}$ – CH_2=CH-COH), 42.1 ($M^{+\cdot}$ – CH_2-CH_2-CH_2). UV/Vis (EtOH): λ_{max}(logε)=275.12 nm (5.49).

4-(2-methoxyphenyl)-1,3,4,6,7,8-hexahydroquinazolin -2,5(1H,6H)-diones (2g):

FT-IR (KBr): 3260.57, 2955.07, 1710.75, 1611.88, 1383.05 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-*d*6): δ=1.87 (m, *J*=4.65 Hz, 2H, H-8), 2.36 (m, *J*=4.95 Hz, 2H, H-7), 2.38 (m, *J*=5.35 Hz, 2H, H-9), 3.72 (s, 3H, OCH_3),

2.90 (s, 1H, H-4), 4.55 (s, 1H, NH), 6.81 (s, 1H, NH), 7.05 (t, *J*=7.8 Hz, 1H, Ar-H), 6.74 (t, *J*=8.3 Hz, 1H, Ar-H), 6.88 (m, *J*=7.55 Hz, 2H, Ar-H). ^{13}C NMR (500 MHz, DMSO-*d*6): δ=20.50, 20.98, 28.99, 37.26, 55.61, 101.60, 110.41, 111.47, 119.83, 126.55, 129.20, 131.69, 156.54, 169.76, 196.07, 206.42 ppm. MS (EI, 70 eV): *m/z* (%): 271.1 (M^+; $C_{15}H_{15}N_2O_3$), 269.2 (M^+. – 2H), 256.1 ($M^{+\cdot}$ – $C_{15}H_{14}NO_3$), 256.1 ($M^{+\cdot}$ – CH_3), 243.2 ($M^{+\cdot}$ – $C_{15}H_{15}O_3$), 164.1 ($M^{+\cdot}$ – C_7H_7O-CH-NH-CO-NH), 147.1 ($M^{+\cdot}$ – C_7H_7O-CH-CH=CH_2), 135.1 ($M^{+\cdot}$ – C_7H_7O-CH-NH), 107.1 ($M^{+\cdot}$ – C_7H_7O), 71.1 ($M^{+\cdot}$ – NH-CH=CH-COH), 70.1 ($M^{+\cdot}$ – CH_3-CO-CH=CH_2), 57.1 ($M^{+\cdot}$ – NH-CO-NH), 51.1 ($M^{+\cdot}$ – CH_2=CH-COH), 42.1 ($M^{+\cdot}$ – CH_2-CH_2-CH_2)**.** UV/Vis (EtOH): λ_{max} (logε)=267.79 nm (5.50).

4-(4-Chlorophenyl)-1,3,4,6,7,8-hexahydroquinazolin-2,5(1H,6H)-diones (2h):

FT-IR (KBr): 3321.06, 2938.79, 1716.15, 1614.90, 773.18 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-*d*6): δ=1.86 (m, *J*=4.65 Hz, 2H, H-8), 2.04 (m, *J*=6.65 Hz, 2H, H-7), 2.29 (m, *J*=6.3 Hz, 2H, H-9), 3.06 (s, 1H, H-4), 4.64 (s, 1H, NH), 6.93 (s, 1H, NH), 7.12 (d, *J*=7.85 Hz, 2H, Ar-H), 7.30 (d, *J*=7.55 Hz, 2H, Ar-H). ^{13}C NMR (500 MHz, DMSO-*d*6): δ=20.53, 21.01, 28.93, 37.16, 101.55, 110.92, 126.23, 127.34, 128.93, 131.53, 132.50, 141.28, 170.13, 196.22, 205.65 ppm. MS (EI, 70 eV): *m/z* (%): 277.1 ($M^{+\cdot}$;$C_{14}H_{13}N_2ClO_2$), 274.1 (M^+. - 2H), 262.1 ($M^{+\cdot}$ – $C_{14}H_{12}NClO_2$), 249.1 ($M^{+\cdot}$ – $C_{14}H_{13}ClO_2$), 247.1 ($M^{+\cdot}$ – $C_{14}H_{11}ClO_2$), 182.1 ($M^{+\cdot}$ – C_6H_4 Cl -CH-NH-CO-NH), 151.1 ($M^{+\cdot}$ – C_6H_4 Cl -CH-CH=CH_2), 139.1 ($M^{+\cdot}$ – C_6H_4 Cl-CH-NH), 111 ($M^{+\cdot}$ – C_6H_4 Cl), 71.1($M^{+\cdot}$ – NH-CH=CH-COH), 70.1 ($M^{+\cdot}$ – CH_3-CO-CH=CH_2), 57.1 ($M^{+\cdot}$ – NH-CO-NH), 51.1 ($M^{+\cdot}$ – CH_2=CH-COH), 42.1 ($M^{+\cdot}$ – CH_2-CH_2-CH_2).
UV/Vis (EtOH): λ_{max} (logε)=262.24 nm (5.49).

4-(3-Chlorophenyl)-1,3,4,6,7,8-hexahydroquinazolin-2,5(1H,6H)-diones (2i):

FT-IR (KBr): 3074.81, 2984.07, 1718.42, 1603.53, 782.22 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-*d*6): δ=1.89 (m, *J*=4.45 Hz, 2H, H-8), 2.18 (m, *J*=4.8 Hz, 2H, H-7), 2.41 (m, *J*=8.05 Hz, 2H, H-9), 3.04 (d, *J*=10.85 Hz, 1H, H-4), 3.94 (d, *J*=10.8Hz, 1H, NH), 6.94 (s, 1H, NH), 7.21 (d, *J*=8.45 Hz 1H, Ar-H), 7.18 (m, *J*=7.65 Hz, 1H, Ar-H), 7.16 (m, *J*=7.45 Hz, 1H, Ar-H), 7.14 (m, *J*=7.35 Hz, 1H, Ar-H). ^{13}C NMR (500 MHz, DMSO-*d*6): δ=20.43, 20.87, 29.07, 32.95, 35.23, 37.02, 59.76, 100.48, 101.46, 125.71, 127.53, 128.18, 128.90, 129.50, 129.67, 132.33, 132.40, 147.62, 148.20, 168.47, 195.95, 205.40 ppm. MS (EI, 70 eV): *m/z* (%): 277.1 ($M^{+\cdot}$; $C_{14}H_{13}N_2ClO_2$), 274.1 (M^+. –2H), 262.1 ($M^{+\cdot}$ – $C_{14}H_{12}NClO_2$), 249.1 ($M^{+\cdot}$ – $C_{14}H_{13}ClO_2$), 247.1 ($M^{+\cdot}$ – $C_{14}H_{11}ClO_2$), 182.1 ($M^{+\cdot}$ – C_6H_4 Cl -CH-NH-CO-NH), 151.1 ($M^{+\cdot}$ – C_6H_4 Cl -CH-CH=CH_2), 139.1 ($M^{+\cdot}$ – C_6H_4 Cl-CH-NH), 111.1 ($M^{+\cdot}$ – C_6H_4 Cl), 71.1 ($M^{+\cdot}$ – NH-CH=CH-COH), 70.1 ($M^{+\cdot}$ – CH_3-CO-CH=CH_2), 57.1 ($M^{+\cdot}$ – NH-CO-NH), 51.1 ($M^{+\cdot}$ – CH_2=CH-COH), 42.1 ($M^{+\cdot}$ – CH_2-CH_2-CH_2).
UV/Vis (EtOH): λ_{max} (logε)=262.24 nm (5.49).

4-(2-Chlorophenyl)-1,3,4,6,7,8-hexahydroquinazolin-2,5(1H,6H)-diones (2j):

FT-IR (KBr): 3084.82, 2944.99, 1719.08, 1603.92, 796.06cm^{-1}. ^{1}H NMR (500 MHz, DMSO-*d*6): δ=1.89 (m, *J*=4Hz, 2H, H-8), 2.17 (m, *J*=5.95 Hz, 2H, H-7), 2.39 (m, *J*=6.95 Hz, 2H, H-9), 3.01 (d, *J*=10.85 Hz, 1H, H-4), 3.88 (d, *J*=9 Hz, 1H, NH), 6.87 (s, 1H, NH), 7.21 (m, *J*=8.4 Hz, 1H, Ar-H), 7.19 (m, *J*= 2.95 Hz, 2H, Ar-H), 7.07 (d, *J*=8.4 Hz, 1H, Ar-H). ^{13}C NMR (500 MHz, DMSO-*d*6): δ=20.14, 20.87, 29.04, 31.93, 32.55, 35.29, 37.04, 59.92, 100.45, 101.44, 127.71, 129.75, 130.09, 130.15, 130.77, 143.91, 144.63, 168.25, 169.87, 195.91, 196.37, 205.33 ppm. MS (EI, 70 eV): *m/z* (%): 277.1 ($M^{+\cdot}$; $C_{14}H_{13}N_2ClO_2$), 274.1 (M^+. –2H), 262.1 ($M^{+\cdot}$ – $C_{14}H_{12}NClO_2$), 249.1 ($M^{+\cdot}$ – $C_{14}H_{13}ClO_2$), 247.1 ($M^{+\cdot}$ – $C_{14}H_{11}ClO_2$), 182.1 ($M^{+\cdot}$ – C_6H_4 Cl -CH-NH-CO-NH), 151.1 ($M^{+\cdot}$ – C_6H_4 Cl -CH-CH=CH_2), 139.1 ($M^{+\cdot}$ – C_6H_4 Cl-CH-NH), 111.1 ($M^{+\cdot}$ – C_6H_4 Cl), 71.1 ($M^{+\cdot}$ – NH-CH=CH-COH), 70.1 ($M^{+\cdot}$ – CH_3-CO-CH=CH_2), 57.1 ($M^{+\cdot}$ – NH-CO-NH), 51.1 ($M^{+\cdot}$ – CH_2=CH-COH), 42.1 ($M^{+\cdot}$ – CH_2-CH_2-CH_2)**.** UV/Vis (EtOH): λ_{max} (logε)=258.83 nm (5.49)**.**

4-(4-Boromophenyl)-1,3,4,6,7,8-hexahydroquinazolin-2,5(1H,6H)-diones (2k):

FT-IR (KBr): 3174.20, 2945.97, 1720.89, 1603.05 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-*d*6): δ=1.89 (m, *J*=8.95 Hz, 2H, H-8), 2.15 (m, *J*=6.47 Hz, 2H, H-7), 2.40 (m, *J*=4.19 Hz, 2H, H-9), 3.00 (d, *J*=10.87 Hz, 1H, H-4), 3.88 (d, *J*=10.85 Hz, 1H, NH), 6.91 (s, 1H, NH), 7.16 (d, *J*=8.43 Hz, 2H, Ar-H), 7.30 (d, *J*=8.43 Hz, 2H, Ar-H). ^{13}C NMR (500 MHz, DMSO-*d*6): δ= 20.65, 21.06, 28.95, 32.43, 36.71, 37.21, 56.71, 101.63, 111.22, 127.74, 131.90, 132.24, 142.73, 170.16, 196.24, 205.46 ppm. MS (EI, 70 eV): *m/z* (%): 321 ($M^{+\cdot}$; $C_{14}H_{13}N_2BrO_2$), 318 (M^+. –2H), 306 ($M^{+\cdot}$- $C_{14}H_{12}NBrO_2$), 293 ($M^{+\cdot}$- $C_{14}H_{13}BrO_2$), 241 ($M^{+\cdot}$- $C_{14}H_{13}N_2O_2$), 213.1 ($M^{+\cdot}$- C_6H_4 Br -CH-NH-CO-NH), 197 ($M^{+\cdot}$- C_6H_4 Br-CH-CH=CH_2), 185 ($M^{+\cdot}$- C_6H_4 Br-CH-NH), 157 ($M^{+\cdot}$- C_6H_4 Br), 71.1 ($M^{+\cdot}$- NH-CH=CH-COH), 70.1 ($M^{+\cdot}$- CH_3-CO-CH=CH_2), 57.8 ($M^{+\cdot}$- NH-CO-NH), 51.1 ($M^{+\cdot}$- CH_2=CH-COH), 42.1 ($M^{+\cdot}$- CH_2-

CH_2-CH_2). UV/Vis (EtOH): λ_{max} (logε)=255.42 nm (5.48).

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