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Nano-SiO_2: a green, efficient, and reusable heterogeneous catalyst for the synthesis of quinazolinone derivatives

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Abstract A highly efficient and general method is applied for the multicomponent synthesis of quinazolinone derivatives from cyclocondensation of aromatic aldehydes and dimedone with 2-amino benzimidazole or 3-amino-1,2,4-triazole using nano-SiO_2 as a catalyst in acetonitrile at room temperature. In this method, nano-SiO_2 was used as a green and reusable catalyst. This synthetic method provides several advantages including excellent yields, short reaction times, simple workup, mild conditions and inexpensiveness, green, and recyclable.

Keywords Triazoloquinazolinone · Benzimidazoquinazolinone · Nano-SiO_2 · Heterogeneous catalyst · Reusable catalyst

Introduction

The advent of combinatorial chemistry has in the recent past emerged as a powerful tool for the rapid generation, identification and optimization of lead compounds in the drug discovery processes [1–3]. Multi-component reactions (MCRs) [4, 5], reactions in which more than two starting materials all present simultaneously together in one reaction vessel combine to form a final product and have accordingly been used to efficiently generate chemical diversity in the final products in a few reaction steps. Compared with conventional organic reactions, MCRs are profitable in being highly convergent and in requiring the minimum effort to be achieved. One of the important compounds derived from MCRs is nitrogen-containing compounds [6, 7] because nitrogen-containing heterocycles are abundant in nature and exhibit diverse and important biological properties [8–11]. Among such heterocycles, quinazoline and quinazolinone derivatives exhibited interesting pharmacological activities. Diseases of the arterial tree cause more premature deaths than all the other diseases such as cancer and infections combined. Among the major risk factors for arterial diseases, high blood pressure has been identified as the most powerful one [12]. Quinazolines and condensed quinazolines are reported to possess interesting pharmacological activities such as antihypertensive [13–15], analgesic and antiinflammatory [16, 17], antihistaminic [18, 19], anticancer [20], and anti-HIV [21] activities. Also, the quinazolinone derivatives exhibited more potent activity in anesthetized animals [22]. Moreover, many naturally occurring and synthetic compounds containing the benzimidazole and triazole derivative scaffolds possess interesting pharmacological properties [23, 24]. A potent antihypertensive activity has been observed in 1,2,4-triazoloquinazoline derivatives [25]. There are a few methods reported in the literature [26] for the synthesis of triazolo/benzimidazoloquinazolinones derivatives which include a three-component condensation of aromatic aldehydes and dimedone with 2-aminobenzimidazole/3-amino-1,2,4-triazole using $H_6P_2W_{18}O_{62}$•$18H_2O$ [27], microwave [28], molecular iodine (I_2) [29], and refluxing in DMF [30, 31]. However, some of these procedures are lengthy and require expensive and hazardous catalysts and result in poor yields. Synthetic alternatives are many and varied, and have resorted to harsh conditions, for example, requiring refluxing conditions. Therefore, the development of simple, efficient, inexpensive, nontoxic, and readily available reagents

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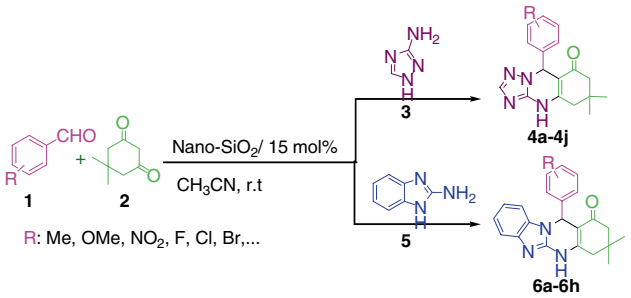


Scheme1 Synthesis of triazoloquinazolinone **4** and benzimidazoquinazolinone **6** derivatives using nano-SiO_2

providing convenient procedures with improved yields is necessary. Herein, we report a simple, rapid and one-pot procedure for the synthesis of triazoloquinazolinones and benzimidazoquinazolinones using nano catalyst. Nanotechnology is a growing and important field in the modern sciences. Nano-sized catalysts continue to attract attention for different research areas due to their different physical and chemical properties when compared to bulk material. The extremely small-sized particles maximized the surface area which was exposed to the reactant, allowing more reactions to occur at the same time, thus speeding up the process. To the best of our knowledge, there is no report of the use of nano materials as catalyst for the synthesis of triazoloquinazolinones and benzimidazoquinazolinones. In view of the importance of heterogeneous solid nano materials as reusable catalysts in organic synthesis [32–35], herein we report the use of nano-SiO_2 as a recyclable green catalyst for the synthesis of triazoloquinazolinones and benzimidazoquinazolinones (Scheme 1).

Experimental

General

The melting point and IR spectra of all compounds were obtained on an Electrothermal 9100 apparatus and a JASCO FT/IR-460 plus spectrometer, respectively. ^{1}H and ^{13}C NMR spectra of compounds were recorded on a Bruker DRX-400 Avance instrument in DMSO at 400 and 100 MHz, respectively. Elemental analyses for the new compounds for C, H, and N were performed using a Heraeus CHN-O-Rapid analyzer. The mass spectra for the new compounds were recorded on an Agilent Technology (HP) mass spectrometer, operating at an ionization potential of 70 eV. All reagents were purchased from Merck (Darmstadt, Germany), Acros (Geel, Belgium) and Fluka (Buchs, Switzerland). Also, nano-SiO_2 was purchased from Canada (MKN-SiO_2-015P).

General procedure for the preparation of triazoloquinazolinones **4** and benzimidazoquinazolinones **6**

To a mixture of dimedone (1 mmol), aldehyde (1 mmol), 2-aminobenzimidazole or 3-amino-1,2,4-triazole (1 mmol) and nano-SiO_2 (15 mol %) in the acetonitrile (5 mL) was stirred for appropriate time (Table 2) at 25–30 °C. After the completion of the reaction as indicated by TLC, dichloromethane (CH_2Cl_2) was added to the solidified mixture and the insoluble catalyst was separated by filtration. Evaporation of the solvent from the filtrate and recrystallization of the solid residue from hot ethanol afforded the pure products in high yields.

6,7-Dihydro-6,6-dimethyl-9-p-tolyl-[1,2,4]triazolo[5,1-b] quinazolin-8(4H,5H,9H)-one (**4d**)

White solid (93 % yield), m.p. = 263–265 °C; IR (KBr, cm^{-1}) 3421, 3036, 2964, 1649, 1578, 1364, 1259, 757; ^{1}H NMR (400 MHz, DMSO) δ = 0.96 (s, 3H, CH_3), 1.04 (s, 3H, CH_3), 2.07 (d, 1H, J = 16.0 Hz, H-5), 2.20 (d, 1H, J = 12.0 Hz, H′-5), 2.28 (s, 3H, CH_3), 2.48–2.59 (m, 2H, H-7), 6.16 (S, 1H, H-9), 7.07 (s, 4H, Ar–H), 7.67 (s, 1H, H-2), 11.09 (s, 1H, NH).

6,7-Dihydro-9-(2,4-dimethoxyphenyl)-6,6-dimethyl-[1,2,4]triazolo[5,1-b]quinazolin-8(4H,5H,9H)-one (**4f**)

White solid (88 % yield); m.p. 208–210 °C; IR (KBr, cm^{-1}): 3150, 3093, 3030, 2959, 2933, 1694, 1652, 1579, 1508, 1416, 1338, 1294, 1183, 1038, 826; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.07 (s, 3H, CH_3), 1.15 (s, 3H, CH_3), 2.22 (d, J = 16.0 Hz, 1H, H-5), 2.29 (d, J = 16.0 Hz, 1H, H′-5), 2.48 (d, J = 16.0 Hz, 1H, H-7), 2.59 (d, J = 16.0 Hz, 1H, H′-7), 3.71 (s, 3H, OCH_3), 3.77 (s, 3H, OCH_3), 6.40 (d, J = 2.4 Hz, 1H, Ar–H), 6.47 (dd, J = 8.0, 4.0 Hz, 1H, Ar–H), 6.56 (s, 1H, H-9), 7.38 (d, J = 8.0 Hz, 1H, Ar–H), 7.64 (s, 1H, H-2), 11.76 (s, 1H, NH).

6,7-Dihydro-6,6-dimethyl-9-(naphthalen-2-yl)-[1,2,4]triazolo[5,1-b]quinazolin-8(4H,5H,9H)-one (**4i**)

White solid (97 % yield); m.p. 268–270 °C; IR (KBr, cm^{-1}): 3416, 3246, 3091, 2963, 2927, 1652, 1574, 1469, 1410, 1364, 1335, 1251, 779; ^{1}H NMR (400 MHz, DMSO): δ = 0.97 (s, 3H, CH_3), 1.05 (s, 3H, CH_3), 2.06 (d, J = 16.0 Hz, 1H, H-5), 2.23 (d, J = 16.0 Hz, 1H, H′-5), 2.58 (dd, J = 16.0, 24.0 Hz, 2H, H-7), 6.38 (S, 1H, H-9), 7.26 (dd, J = 4.0, 8.0 Hz, 1H, Ar–H), 7.48–7.50 (m, 2H, Ar–H), 7.69 (s, 1H, H-2), 7.80 (d, J = 4.0 Hz, 1H, Ar–H), 7.84 (d, J = 8.0 Hz, 2H, Ar–H), 7.90 (t, J = 4.0 Hz, 1H, Ar–H), 11.20 (s, 1H, NH).

9-(2-Bromophenyl)-6,7-dihydro-6,6-dimethyl-[1,2,4]triazolo[5,1-b]quinazolin-8(4H,5H,9H)-one (**4j**)

White solid (98 % yield), m.p. = 278–280 °C; IR (KBr, cm^{-1}) 3143, 3090, 2960, 1644, 1581, 1369, 1257, 753; ^{1}H NMR (400 MHz, DMSO) δ = 1.01 (s, 3H, CH_3), 1.05 (s, 3H, CH_3), 2.05 (d, 1H, J = 16.0 Hz, H-5), 2.20 (d, 1H, J = 16.0 Hz, H′-5), 2.50–2.51 (m, 1H, H-7), 2.55 (d, 1H, J = 16.0 Hz, H′-7), 6.57 (S, 1H, H-9), 7.16–7.18 (m, 1H, Ar–H), 7.29 (d, 1H, J = 8.0 Hz, Ar–H), 7.54 (d, 1H, J = 8.0 Hz, Ar–H), 7.66 (s, 1H, H-2), 8.28 (s, 1H, Ar–H), 11.22 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO) δ = 21.2, 27.4, 28.9, 32.6, 40.0, 50.2, 58.5, 125.9, 128.2, 128.5, 130.1, 133.3, 140.1, 147.2, 150.5, 151.5,193.3; MS (EI, 70 eV): *m/z* (%) = 373 (2) $[M]^+$, 293 (100), 266 (2), 139 (1), 217 (10), 183 (4), 161 (8), 127 (3), 105 (7), 83 (3), 55 (3); Anal. Calcd for $C_{17}H_{17}BrN_4O$: C, 54.70; H, 4.59; N, 15.01. Found: C, 54.85; H, 4.50; N, 15.09 %.

3,3-Dimethyl-12-phenyl-1,2,3,4,5,12-hexahydrobenzo[4,5]imidazo[2,1-b]quinazolin-1-one (**6a**)

White solid (95 % yield), m.p. = >300 °C; IR (KBr, cm^{-1}) 3430, 3093, 2956, 1643, 1615, 1569, 1376, 1257, 750; ^{1}H NMR (400 MHz, DMSO) δ = 0.92 (s, 3H, CH_3), 1.05 (s, 3H, CH_3), 2.05 (d, 1H, J = 16.0 Hz, H-4), 2.26 (d, 1H, J = 16.0 Hz, H′-4), 2.45 (d, 1H, J = 16.0 Hz, H-2), 2.58 (d, 1H, J = 16.0 Hz, H′-2), 6.41 (S, 1H, H-12), 6.95 (t, 1H, J = 8.0 Hz, Ar–H), 7.04 (t, 1H, J = 8.0 Hz, Ar–H), 7.15 (t, 1H, J = 8.0 Hz, Ar–H), 7.24 (t, 1H, J = 8.0 Hz, Ar–H), 7.33 (d, 3H, J = 8.0 Hz, Ar–H), 7.37 (q, 3H, J = 8.0 Hz, Ar–H), 10.18 (s, 1H, NH).

3,3-Dimethyl-12-[2,4]dichlorophenyl-1,2,3,4,5,12-hexahydrobenzo[4,5]imidazo[2,1-b]quinazolin-1-one (**6b**)

White solid (96 % yield); m.p. >300 °C; IR (KBr, cm^{-1}): 3238, 3061, 2963, 2931, 1650, 1615, 1595, 1573, 1563, 1459, 1374, 1270, 737; ^{1}H NMR (400 MHz, DMSO): δ = 0.95 (s, 3H, CH_3), 1.06 (s, 3H, CH_3), 2.04 (d, J = 16.0 Hz, 1H, H-4), 2.24 (d, J = 16.0 Hz, 1H, H′-4), 2.29 (d, J = 12.0 Hz, 1H, H-2), 2.33 (d, J = 16.0 Hz, 1H, H′-2), 6.65 (S, 1H, H-12), 6.96 (t, J = 8.0 Hz, 1H, Ar–H), 7.03 (s, 1H, Ar–H), 7.08-7.12 (m, 1H, Ar–H), 7.38 (s, 1H, Ar–H), 7.40 (s, 1H, Ar–H), 7.48 (d, J = 8.0 Hz, 1H, Ar–H), 11.25 (s, 1H, NH).

3,3-Dimethyl-12-(3-indolyl)-1,2,3,4,5,12-hexahydrobenzo[4,5]imidazo[2,1-b]quinazolin-1-one (**6h**)

Pale yellow solid (94 % yield), m.p. = >300 °C; IR (KBr, cm^{-1}) 3470, 3415, 2925, 1647, 1615, 1570, 1442, 1372, 740; ^{1}H NMR (400 MHz, DMSO) δ = 0.84 (s, 3H, CH_3), 1.04 (s, 3H, CH_3), 1.99 (d, 1H, J = 12.0 Hz, H-4), 2.24 (d, 1H, J = 16.0 Hz, H′-4), 2.55 (d, 1H, J = 8.0 Hz, H-2), 2.66 (d, 1H, J = 8.0 Hz, H′-2), 6.71 (S, 1H, H-12), 6.83 (t, 1H, J = 8.0 Hz, Ar–H), 6.8–6.99 (m, 3H, Ar–H), 7.26 (d, 1H, J = 8.0 Hz, Ar–H), 7.25 (d, 1H, J = 8.0 Hz, Ar–H), 7.30 (d, 1H, J = 8.0 Hz, Ar–H), 7.34 (d, 1H, J = 8.0 Hz, Ar–H), 10.03 (s, 1H, NH), 11.11 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO) δ = 27.0, 29.3, 32.4, 48.3, 50.5, 105.8, 110.5, 112.2, 113.2, 114.7, 117.1, 118.3, 119.2, 120.5, 121.3, 121.9,124.8, 125.6, 132.5, 136.7, 142.5, 146.0, 150.2, 193.2; MS (EI, 70 eV): *m/z* (%) = 382 (7) $[M]^+$, 325 (3), 298 (9), 266 (34), 236 (6), 208 (4), 180 (14), 152 (12), 117 (100), 89 (43), 69 (9), 51 (39); Anal. Calcd for $C_{24}H_{22}N_4O$: C, 75.37; H, 5.80; N, 14.65. Found: C, 75.55; H, 5.95; N, 14.70 %.

Results and discussion

According to literature reports, utilities of the heterogeneous nano materials as new environmentally friendly catalysts for the synthesis of biologically active molecules have increased. Therefore, we describe a simple and efficient method for the synthesis of triazoloquinazolinones and benzimidazoquinazolinones using the environmentally benign and reusable nano-SiO_2 as a catalyst herein. We would like to report the preparation of triazoloquinazolinone and benzimidazoquinazolinone derivatives using reactions involving arylaldehydes, dimedone, and 2-aminobenzimidazole/3-amino-1,2,4-triazole (Scheme 1). We chose the reaction of 4-methyl benzaldehyde **1**, dimedone **2** and **3**-amino-1,2,4-triazole 3 in the presence of nano-SiO_2 in the acetonitrile as a model system for the optimization study. Initially, a series of comparative experiments were performed to compare the effectiveness of different amounts of nano-SiO_2 in the formation of 6,7-dihydro-6,6-dimethyl-9-*p*-tolyl-[1,2,4]triazolo[5,1-b]quinazolin-8(4H,5H,9H)-one **4d**. The results are shown in Table 1 and the best result was obtained in 15 mol % of nano-SiO_2. This amount of catalyst indicates a good yield of product, while increasing the catalyst loading did not further improve the results. The catalyst showed a very good catalytic activity. This might be due to its small particle size, which provides a large surface area for reactant adsorption and accordingly, a high catalytic activity. As shown in Table 1, no product was obtained in the absence of the catalyst (Table 1, entry 1). Also, the reaction did not lead to the desired product under solvent-free conditions (Table 1, entry 8). That might have been due to the lack of effective interaction between reactants and the catalyst in the absence of the solvent.

Moreover, the synthesis of **4d** was separately carried out in different solvents such as tetrahydrofuran (THF),

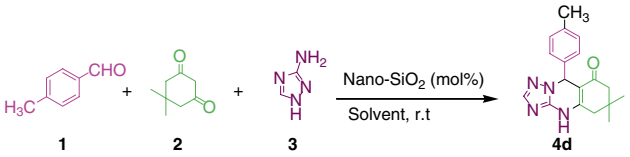
ethanol, dichloromethane, and acetonitrile under the stirring and at room temperature. Among the screened solvent systems, acetonitrile was the solvent of choice, since the reaction proceeded smoothly and afforded the desired adducts in high yields. Also, the performance of bulk SiO_2 was studied on model system and the product was obtained in low yields (20–25 %) and undesired products were produced. Therefore, bulk of SiO_2 cannot be suitable catalyst for this reaction.

In continuation of our research to demonstrate the utility and generality of this method, we used a diverse of aldehydes to investigate these three-component reactions under the optimized conditions. We observed that various aldehydes could be introduced with high efficiency and produced products in high yields. As shown in Table 2, various aromatic aldehydes in the presence of electron-withdrawing or electron-releasing substituents, both of which gave the desired product in excellent yields (Table 2).

We then explored the scope of this procedure in the three-component synthesis of benzimidazoquinazolinone derivatives **6**, via the condensation of aromatic aldehydes **1**, dimedone **2** and 2-aminobenzimidazole **5** under the optimized conditions in Table 1. In all cases, the reaction proceeded smoothly and the desired products were obtained in good yields. The results are summarized in Table 2.

All known products were identified by the comparison of the melting points and the analytical data (IR, NMR) with those reported for authentic samples. The structure of new compounds **4j** and **6h** was deduced on the basis of IR, ^{1}H NMR spectroscopy, ^{13}C NMR spectroscopy, mass spectrometry, and elemental analysis. For example, the mass spectrum of **4j** displayed the molecular ion peak (M^+) at $m/z = 373$, which is consistent with the proposed structure. The ^{1}H NMR spectrum of **4j** exhibited two singlet at $\delta = 1.01$ and 1.05 ppm for the geminal methyl protons. Three doublets and one multiplet were observed at $\delta = 2.05$ ($J = 16.0$ Hz), 2.20 ($J = 16.0$ Hz), 2.55 ($J = 16.0$ Hz) and

Table 1 Condensation reaction of 3-amino-1,2,4-triazole, 4-methyl benzaldehyde and dimedone in the presence of different loadings of the catalyst at ambient conditions



Entry	Solvent/temp	Catalyst (mol %)	Time (min)	Yield (%)[a]
1	CH_3CN/rt	–	180	–
2	CH_3CN/rt	5	30	81
3	CH_3CN/rt	10	20	86
4	**CH_3CN/rt**	**15**	**15**	**93**
5	CH_3CN/rt	20	30	90
6	CH_3CN/rt	25	35	89
7	CH_3CN/rt	30	20	91
8	–/rt	15	180	–

All the reactions were carried out using 1 mmol of 4-methylbenzaldehyde, 1 mmol of dimedone and 1 mmol of 3-amino-1,2,4-triazole with varying amounts of catalyst in CH_3CN (5 mL) at room temperature. Bold shows the best conditions for the reaction during the course of the screening of different loadings of the catalyst

[a] Yield refers to the pure isolated products

Table 2 Synthesis of various triazoloquinazolinones and benzimidazoquinazolinones in the presence of nano-SiO_2

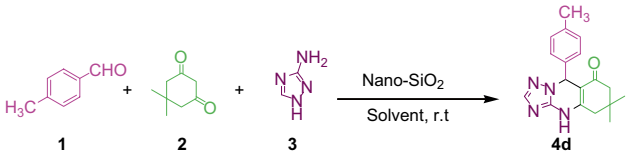
Entry	R	Amine	Product	Time (min)	Yield (%)[a]	Mp (°C)	Lit. mp (°C) [Ref.]
1	H	3	**4a**	30	96	248–250	248–250 [31]
2	4-OH	3	**4b**	45	89	305–306	307–309 [27]
3	4-Cl	3	**4c**	10	94	302–304	304–306 [29]
4	4-Me	3	**4d**	15	93	263–265	264–269 [27]
5	2,4-$(Cl)_2$	3	**4e**	20	97	320–322	323–325 [29]
6	2,4-$(OMe)_2$	3	**4f**	18	85	208–210	210–212 [29]
7	4-F	3	**4 g**	20	90	256–258	258–260 [28]
8	3-NO_2	3	**4 h**	14	98	265–267	266–269 [29]
9	2-Naphthyl-	3	**4i**	20	93	268–270	287–290 [29]
10	2-Br	3	**4j**	15	98	278–280	This work[b]
11	H	5	**6a**	25	95	>300	>300 [27]
12	2,4-Cl_2	5	**6b**	20	97	>300	>300 [29]
13	4-NO_2	5	**6c**	30	98	>300	>300 [30]
14	4-F	5	**6d**	25	87	>300	>300 [28]
15	4-OMe	5	**6e**	15	95	>300	>300 [30]
16	4-Cl	5	**6f**	18	91	>300	>300 [27]
17	4-Br	5	**6 g**	20	95	>300	>300 [27]
18	3-Indole-	5	**6 h**	45	94	>300	This work[b]

Column written in bold indicates the number of product was obtained

[a] Yields refer to the pure isolated products

[b] The new compounds synthesized in this work

Table 3 Reusability of the nano-SiO_2 in the reaction of 3-amino-1,2,4-triazole, 4-methyl benzaldehyde and dimedone for the synthesis of **4d**



Run	Solvent/temp	Time (min)	Yield (%)[a]
1	CH_3CN/rt	15	93
2	CH_3CN/rt	15	92
3	CH_3CN/rt	18	90
4	CH_3CN/rt	24	89
5	CH_3CN/rt	30	87

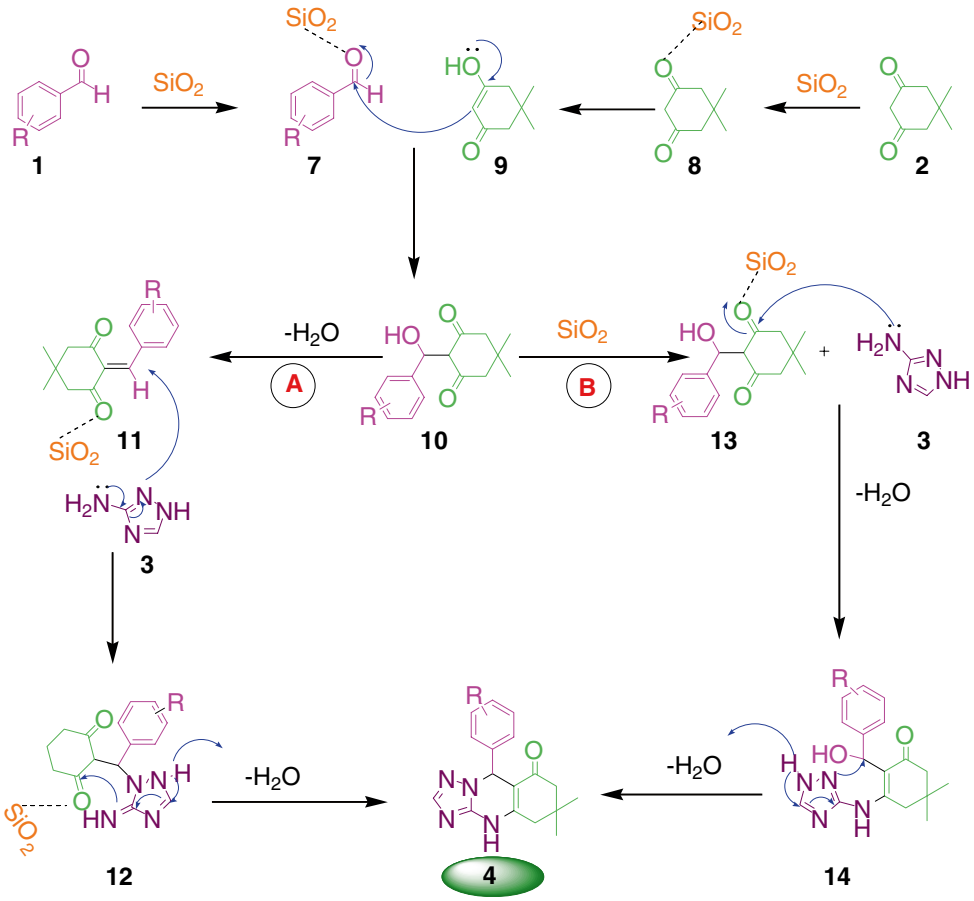
All the reactions were carried out using 1 mmol of 4-methylbenzaldehyde, 1 mmol of dimedone and 1 mmol of 3-amino-1,2,4-triazole with varying amounts of catalyst in CH_3CN (5 mL) at room temperature

[a] Yield refers to the pure isolated products

2.50–2.51 for the diastereotopic methylene protons of H-5, H′-5, H′-7 and H-7, respectively. The methine proton of the central ring (H-9) was observed as a singlet at δ = 6.57 ppm. The aromatic protons resonance was observed as multiplets at δ = 7.16–8.28 ppm. The proton of the NH group was appeared as a singlet at δ = 11.22 ppm.

It is noteworthy that, in our procedure, products were obtained without byproducts in good to high yields with short reaction times and the reaction was carried out at ambient temperature. In organic reactions, when a heterogeneous catalyst is used, the recyclability of the catalyst is very important. To investigate the recyclability of nano-SiO_2, the reuse and recovery of the nano-SiO_2 are highly desirable, and five batches of the experiments were carried out for the preparation of product **4d**. The results are shown in Table 3. The catalyst was filtered off and washed with an excess of dichloromethane and reused in a new reaction.

Based on the obtained results and according to the previous reports on the catalytic synthesis of triazoloquinazolinones **4** and benzimidazoquinazolinones **6**, two plausible mechanisms can be proposed for the synthesis of these compounds in the presence of nano-SiO_2. Therefore, this reaction may occur via Knoevenagel condensation for the formation of α, β-unsaturated carbonyl compounds **11** upon the loss of water molecule (route **A**). Then, via an intermolecular Mannich type reaction α,β-unsaturated carbonyl compounds, undergoing nucleophilic attack by amine, gave



Scheme 2 Plausible mechanisms (**A** and **B**) for the synthesis of quinazolinone derivatives **4a–4j** and **6a–6h**

Table 4 Comparison result of nano-SiO_2 with $H_6P_2W_{18}O_{62}$•$18H_2O$ [27], microwave [28], molecular iodine (I_2) [29], and refluxing in DMF [30, 31] in the synthesis 1,2,4-triazolo/benzimidazolo quinazolinone derivatives

Entry	Compound	Catalyst/conditions	Time (min)	Yield (%)
1	**4a**	$H_6P_2W_{18}O_{62}$•$18H_2O$/CH_3CN, reflux	30	95
		Silica gel/microwave	4	90
		I_2/CH_3CN, reflux	10	81.2
		DMF/reflux	–	76
		Nano-SiO_2/CH_3CN, rt	30	96
2	**4d**	$H_6P_2W_{18}O_{62}$.$18H_2O$/CH_3CN, reflux	40	91
		Silica gel/microwave	–	–
		I_2/CH_3CN, reflux	–	–
		DMF/reflux	–	–
		Nano-SiO_2/CH_3CN, rt	15	95
3	**4g**	$H_6P_2W_{18}O_{62}$•$18H_2O$/CH_3CN, reflux	–	–
		Silica gel/microwave	5	93
		I_2/CH_3CN, reflux	10	82.4
		DMF/reflux	–	–
		Nano-SiO_2/CH_3CN, rt	20	90
4	**4h**	$H_6P_2W_{18}O_{62}$•$18H_2O$/CH_3CN, reflux	30	98
		Silica gel/microwave	5	96
		I_2/CH_3CN, reflux	–	–
		DMF/reflux	–	–
		Nano-SiO_2/CH_3CN, rt	14	98
5	**6a**	$H_6P_2W_{18}O_{62}$•$18H_2O$/CH_3CN, reflux	15	96
		Silica gel/microwave	3	95
		I_2/CH_3CN, reflux	10	84.6
		DMF/reflux	–	65
		Nano-SiO_2/CH_3CN, rt	25	95
6	**6c**	$H_6P_2W_{18}O_{62}$•$18H_2O$/CH_3CN, reflux	10	99
		Silica gel/microwave	3	94
		I_2/CH_3CN, reflux	10	97.1
		DMF/reflux	–	53
		Nano-SiO_2/CH_3CN, rt	20	98
7	**6g**	$H_6P_2W_{18}O_{62}$•$18H_2O$/CH_3CN, reflux	15	94
		Silica gel/microwave	4	92
		I_2/CH_3CN, reflux	10	84.4
		DMF/reflux	–	–
		Nano-SiO_2/CH_3CN, rt	20	95

the intermediate **12**. Further intermediate **12** undergoes intra-molecular cyclization by the loss of water molecule to yield the observed quinazolinones **4** (Scheme 2). The difference between the routes **A** and **B** is in the initial attack of the nitrogen atom (NH_2 or N^2). Similarly, the route **B** was followed by intermediate **10.** The next step, intermediate **10** reacts with amine sources **3** to afford **14** upon the loss of water molecule. Further, the intermediate **14** undergoes intra-molecular cyclization by the loss of water molecule to give the desired products **4**. The mechanism of the route **B** is reported by Puligoundla et al. in the presence of molecular iodine [29]. The proposed mechanism is outlined in Scheme 2.

This paper describes nano-SiO_2 as a heterogeneous, easy to prepare, inexpensive, and efficient catalyst for the synthesis of triazoloquinazolinone and benzimidazoquinazolinones from readily available aromatic aldehydes, dimedone, and 2-aminobenzimidazole/3-amino-1,2,4-triazole. The distinguished advantages of this procedure are no byproducts, operational simplicity, high yields and the ease of isolation; hence, no need to column chromatography. The products were obtained in excellent yields and short reaction times. Also, ambient conditions were significantly kinder and milder than the available methods. The present approach demonstrates a simple and effective method using nano-SiO_2 while a wide range of functional groups can be

tolerated. Also, the above catalyst was recyclable, cost-effective, and environment-friendly as well and could be used in similar reactions.

To show the merit of the this work in comparison with reported results in the literature, we compared results of nano-SiO_2 with $H_6P_2W_{18}O_{62}$•$18H_2O$ [27], microwave [28], molecular iodine (I_2) [29], and refluxing in DMF [30, 31] in the synthesis 1,2,4-triazolo/benzimidazolo quinazolinone derivatives. As shown in Table 4, nano-SiO_2 can act as productive and effective catalyst with respect to reaction times and yields of products.

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References

1. E.M. Gordon, R.W. Barret, W.I. Dower, S.P. Fodor, M.A. Gallop, J. Med. Chem. **37**, 1385 (1994)
2. M.A. Gallop, R.W. Barret, W.J. Dower, S.P. Fodor, E.M. Gordon, J. Med. Chem. **37**, 1233 (1994)
3. A. Golisade, J. Wiesner, C. Herforth, H. Joma, A. Link, Bioorg. Med. Chem. **10**, 769 (2002)
4. C. Hulme, V. Gore, Curr. Med. Chem. **10**, 51 (2003)
5. A. Domling, I. Ugi, Angew. Chem. Int. Ed. **39**, 3168 (2000)
6. A. Shaabani, A. Rahmati, A.H. Rezayan, H.R. Khavasi, J. Iran. Chem. Soc. **8**, 24 (2011)
7. A. Shaabani, A. Rahmati, A.H. Rezayan, M. Darvishi, Z. Badri, A. Sarvari, QSAR Comb. Sci. **26**, 973 (2007)
8. A. Monge, J.A. Palop, J.C.D. Castillo, J.M. Caldero, J. Roca, G. Romero, J.D. Rio, B. Lasheras, J. Med. Chem. **36**, 2745 (1993)
9. K. Toshima, R. Takano, T. Ozawa, S. Matsumara, Chem. Commun. **3**, 212 (2002)
10. B. Dowlati, D. Nematollahi, M.R. Othman, Int. J. Electrochem. Sci. **7**, 5990 (2012)
11. Y.B. Kim, Y.H. Kim, J.Y. Park, S.K. Kim, Bioorg. Med. Chem. Lett. **14**, 541 (2004)
12. P.A.G.M. De Smet, Drugs **54**, 801 (1997)
13. J.D. Garcia, R. Somanathan, I.A. Rivero, G. Aguirre, L.H. Hellberg, Synth. Commun. **30**, 2707 (2000)
14. V.J. Ram, R.C. Srimal, D.S. Kushwaha, L. Mishra, J. Prakt. Chem. **332**, 629 (1990)
15. V. Alagarsamy, V.R. Solomon, G. Vanikavitha, V. Paluchamy, M. Ravichandran, A. Arnaldsujin, A. Thangathirupathy, S. Amuthalakshmi, R. Revathi, Biol. Pharm. Bull. **25**, 1432 (2002)
16. V. Alagarsamy, G. Murugananthan, R. Venkateshperumal, Biol. Pharm. Bull. **26**, 1711 (2003)
17. V. Alagarsamy, R. Venkatesaperumal, S. Vijayakumar, T. Angayarkanni, P. Pounammal, S. Senthilganesh, S. Kandeeban, Pharmazie. **57**, 306 (2002)
18. V. Alagarsamy, Pharmazie **59**, 753 (2004)
19. V. Alagarsamy, V.R. Solomon, M. Murugan, Bioorg. Med. Chem. **15**, 4009 (2007)
20. H. MannJen, H. Li Jiau, K. Sheng Chu, X. Yi Bastow, B. Kenneth, N. Y. Hamel, E. Lee, K. Hsiung, J. Med. Chem. **43,** 4479 (2000)
21. V. Alagarsamy, R. Revathi, S. Meena, K.V. Ramaseshu, S. Rajasekaran, E. De Clercq, Indian J. Pharm. Sci. **66**, 459 (2004)
22. K.-C. Liu, M.-K. Hu, Arch. Pharm. **319**, 188 (1986)
23. T. Eicher, S. Hauptmann, *Chemie der Heterocyclen* (Georg Thieme, Stuttgart, New York, 1994), p. 398
24. V. Haridas, K. Lal, Y.K. Sharma, Tetrahedron Lett. **48**, 4719 (2007)
25. V. Alagarsamy, U.S. Pathak, Bioorg. Med. Chem. **15**, 3457 (2007)
26. A. Shaabani, A. Rahmati, E. Farhangi, A.H. Rezayan, Monatsh. Chem. **138**, 615 (2007)
27. M.M. Heravi, L. Ranjbar, F. Derikvand, B. Alimadadi, H.A. Oskooie, F.F. Bamoharram, Mol. Divers. **12**, 181 (2008)
28. G. Krishnamurthy, K.V. Jagannath, J. Chem. Sci. **125**, 807 (2013)
29. R.G. Puligoundla, S. Karnakanti, R. Bantu, N. Kommu, S.B. Kondra, L. Nagarapu, Tetrahedron Lett. **54**, 2480 (2013)
30. V.V. Lipson, S.M. Desenko, S.V. Shishkina, M.G. Shirobokova, O.V. Shishkin, V.D. Orlov, Chem. Heterocycl. Compd. **39**, 1041 (2003)
31. V.V. Lipson, S.M. Desenko, M.G. Shirobokova, V.V. Borodina, Chem. Heterocycl. Compd. **39**, 1213 (2003)
32. J. Safaei-Ghomi, R. Teymuri, H. Shahbazi-Alavi, A. Ziarati, Chin. Chem. Lett. **24**, 921 (2013)
33. J. Albadi, A. Mansournezhad, Z. Derakhshandeh, Chin. Chem. Lett. **24**, 821 (2013)
34. F.F. Bamoharram, M.M. Heravi, H. Teymouri, M. Zebarjad, A. Ahmadpour, Synth. React. Inorg. Met.-Org. Chem. **41**, 1221 (2011)
35. E. Rafiee, M. Khodayari, M. Kahrizi, R. Tayebee, J. Mol. Catal. A: Chem. **358**, 121 (2012)