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Original article

Catalytic activity of TiO_2 nanoparticles in the synthesis of some 2,3-disubstituted dihydroquinazolin-4(1*H*)-ones

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ABSTRACT

Green chemistry is playing an important role for synthesizing organic compounds, due to its eco-friendly nature and low cost. In green chemistry, metal nanoparticles exhibited some useful physical and chemical properties (catalytic activity). Due to its diverse properties, nanoparticles can be utilized as a catalyst in various organic reactions. Recent research has been directed towards the utilization of eco-friendly and bio-friendly plant materials in nanoparticles synthesis. In our present work, TiO_2 nanoparticles (TiO_2 NPs) were synthesized using *Annona squamosa* peel extract and their catalytic applications were studied on the 2,3-disubstituted dihydroquinazolin-4(1*H*)-one synthesis. Synthesized compounds were confirmed using FT-IR, ^1H NMR, ^{13}C NMR and GC–MS analyses.

1. Introduction

Nowadays nanoparticles have drawn the attention of scientists, because of their extensive application in the development of new technologies in the areas of electronics, material sciences, catalyst and medicine at the nanoscale [1–3]. The development of green processes using agricultural waste for the synthesis of nanoparticles is evolving into an important branch of nanotechnology [4–6]. The use of environmentally benign materials like plant leaf extract [7], bacteria [8], fungi [9] and enzymes [10] for the synthesis of metal nanoparticles offers numerous benefits such as eco-friendliness and compatibility for pharmaceutical and other biomedical applications as they do not use toxic chemicals in the synthetic protocols. Eco-friendly reagents, catalysts, and reaction medium such as water, supercritical fluids, ionic liquids or solvent-free reactions for green chemical approaches have been studied. In this context, metal oxide nanoparticles are attractive candidates as solid supports for the highly active and recyclable catalytic systems. Due to their large surface area, which can carry a high payload of catalytically active species, nanoparticles exhibit very high catalytic activity and chemical selectivity under mild conditions [11]. In addition, they can be recovered through a centrifugation or filtration process and reused for the next reaction, combining the advantages of both homogeneous and heterogeneous catalysts. Although many synthetic technologies are present, worldwide the researchers are continuously searching suitable bio-methods for the synthesis of desired nanoparticles [12].

Currently, TiO_2 nanoparticles have emerged as an attractive multi-functional material. TiO_2 nanoparticles have unique properties such as high stability, long lasting, safe and broad-spectrum anti-biosis [13]. TiO_2 nanoparticles in particular have been the centre of attention because of their photo-catalytic activities. TiO_2 nanoparticles have been used as a green catalyst in many organic reactions [14]. One-pot multicomponent reactions become increasingly important in organic and medicinal chemistry. The strategies of MCRs offer significant advantages over conventional linear-type syntheses in terms of high degree of atom economy, convergence, and ease of execution [15]. Multicomponent reactions leading to the formation of nitrogen-containing heterocyclic systems such as pyridine and pyrimidine have recently been studied [16,17]. The achievement of making multiple bonds in a one-pot multicomponent coupling reaction provides a sustainable synthetic approach in new molecule discovery [18].

Quinazolin-4(1*H*)-ones are important *N*-heterocyclic compounds having various biological activities [19–24]. However, methods for the selective synthesis of 2,3-dihydroquinazolin-4(1*H*)-ones have not been explored before. Thus, developing versatile approaches to synthesize 2,3-dihydroquinazolin-4(1*H*)-ones still remains a highly desired goal in organic synthesis. In our present work of solvent free synthesis of quinazolinone, we

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utilized bio-inspired TiO_2 NPs as catalyst in the 4(1*H*)-quinazolinone synthesis.

2. Experimental

2.1. Bio-fabricated TiO_2 nanoparticles

Biosynthesis of rutile TiO_2 nanoparticles (TiO_2 NPs) was achieved by a novel, biodegradable and convenient procedure using fruit peel *Annona squamosa* aqueous extract. Rutile TiO_2 NPs were characterized using UV, XRD, SEM and TEM studies [25].

2.2. General procedure for synthesis of 2,3-disubstituted 2,3-dihydroquinazolin-4(1H)-ones, **4a–g**

A mixture of isatoic anhydride, **1** (0.234 g, 2 mmol), methyl amines, **2** (68.7 μL, 2 mmol), benzaldehydes **3a–g** (2 mmol) and TiO_2 NPs (5 mol%) was heated at 70 °C for 30 min. The reaction was monitored by TLC analysis using petroleum ether-ethyl acetate (1:4, v/v). After the completion of the reaction, the reaction mixture was cooled to room temperature. The solid residue was dissolved in hot ethanol and centrifuged to remove the catalyst. Then the filtrate was subjected to column chromatography eluting with petroleum ether-ethyl acetate (1:4, v/v) to isolate the desired compounds. The isolated compounds were confirmed by FTIR, ^{1}H NMR, ^{13}C NMR and GC–MS analyses.

3. Results and discussion

We isolated the 2,3-dihydro-3-methyl-2-phenylquinazolin-4(1*H*)-one analogues, **4a–g** by column chromatography in >90% yield. These products were characterized using FT-IR, ^{1}H NMR, ^{13}C NMR and mass analyses. Analysis results are given in Supporting information. In FT-IR, compound **4a** showed peaks at 3452.58 cm^{-1}, corresponding to –NH stretching, 3265.49 cm^{-1} for $-NCH_3$, and 1622.13 cm^{-1} for the –C=O group. In proton NMR, the singlet at δ 2.88 corresponds to methyl protons ($-CH_3$), the peak at δ 4.48 is corresponding to –NH proton, peak at δ 5.71 is corresponding to –CH proton and peaks at δ 6.52–7.97 belong to aromatic protons. In ^{13}C NMR, the methyl group appears at δ 32, –CH group appears at δ 74, aromatic carbons appears at a δ 114–145 and –C=O appears at δ 163. We optimizeded the reaction with various amount (mol%) of TiO_2 NPs. Catalyst concentration plays a major role in the product yields. It was observed that increasing the loading of the catalyst from 2 to 5 mol% gave an improved yield of 91% of the product (Table 1). Further increase of catalyst loading leads to lower reaction yields because the products tend to be absorbed on the catalyst.

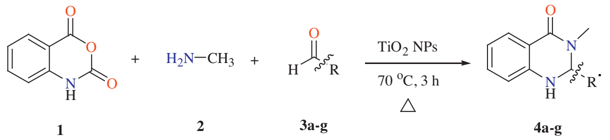
Table 1
Optimization of the amount of TiO_2 NPs in the synthesis of 2,3-dihydro-3-methyl-2-(4-(dimethylamino)phenyl)quinazolin-4(1*H*)one, **4b**.

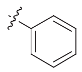
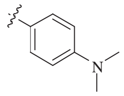
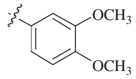
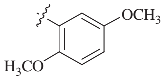
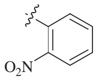
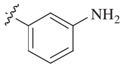
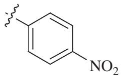
Catalyst (mol%)	2	3	4	5	6
Yield GC–MS (%) **4b**	49.68	54.53	76.42	91.86	89.47

Table 2
Effect of solvent for the synthesis of 2,3-dihydro-3-methyl-2-(4-(dimethylamino)-phenyl)quinazolin-4(1*H*)one, **4b**.

Solvent	Time (min)	Yield GC–MS (%) **4b**
DCM	90	36.76
$CHCl_3$	60	40.54
EtOH	45	73.64
H_2O	30	76.05
Solvent free	30	91.86

Table 3
Synthesis of 2,3-disubstituted 2,3-dihydroquinazolin-4(1*H*)-ones, **4a–g**.



Compounds	R	Yield[a] (%)	Mp (°C)
4a		98	156–158
4b		91	164–166
4c		95	200–202
4d		97	178–180
4e		94	138–140
4f		93	164–165
4g		96	153–155

[a] Isolated yield.

In order to elucidate the role of the solvents, various solvents were used in order to evaluate the scope and limitation of the reaction. After screening different solvents, it was found that TiO_2 NPs catalyzed syntheses of quinazolinone were not only faster, but also resulted in better yields under solvent free conditions (Table 2).

In general, the polar protic solvents (EtOH and water) result in good yields. The aprotic solvents ($CHCl_3$ and DCM) give the lowest yield. The dielectric constant measures the solvent's ability to reduce the field strength of the electric field surrounding a charged particle immersed in it. The protic solvents have higher dielectric constant values compared with aprotic (non-polar) solvents. The protic (polar) solvents that can donate proton easily can form hydrogen bonds with the reactants. These could be the reasons that we are getting better yields in protic solvents than in aprotic solvents. In Table 3, the results of isatoic anhydride, **1** methylamine, **2** with various substituted aromatic aldehydes, **3a–g** under solvent free conditions using TiO_2 NPs are shown. All products were isolated by column chromatography in good yields (>90%).

4. Conclusion

We have successfully synthesized the TiO_2 nanoparticles using aqueous *A. squamosa* peel extract. These synthesized TiO_2 nanoparticles were characterized using UV, XRD and TEM. Synthesized TiO_2 nanopowders were used as a catalyst for 2,3-dihydro-3-methyl-2-phenylquinazolin-4(1*H*)-one analogues,

4a–**g** synthesis. The compounds were purified by column chromatography using petroleum ether-ethyl acetate (75:25, v/v) as eluting solvents.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.cclet.2013.11.040.

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