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FULL PAPER

Green synthesis of TiO_2 nanoparticles as an efficient heterogeneous catalyst with high reusability for synthesis of 1,2-dihydroquinoline derivatives

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Nano materials find wide applications due to their behavior at nano scale. TiO_2 nanoparticles (TiO_2 NPs) was synthesized using Neem leaf extract. This is simple, rapid, eco-friendly, cheaper and green tools for TiO_2 NPs synthesis using agricultural waste at lower applied temperature. Characterization of the extracted TiO_2 NPs was confirmed by XRD, SEM, EDAX, TEM, HR-TEM, SAED, and FT-IR, respectively. The catalytic activity of TiO_2 NPs was investigated in synthesis of 1,2-dihydroquinoline derivatives with excellent yields and low cost. Purification of the synthesized 1,2-dihydroquinoline derivatives carried out by easy work-up of non-chromatographic methods.

KEYWORDS
1,2-dihydroquinolines, efficient catalyst, neem leaf extract, non-chromatographic, TiO_2 nanoparticles

1 | INTRODUCTION

Modern science highlights on one of the most effective and applicable research which is nanoscience. Recently, nanotechnology is highly progressed technology with inter disciplined research between different branches, e.g. chemistry, physics, biology, material science and medicine. Comparing to bulk materials, nanoparticles (NPs) are more of interest because of their enhanced surface Rayleigh scattering, plasmon resonance, and enhanced surface Raman scattering for fine materials of metal and their corresponding metal oxide. Consequently, medical, catalytic, electronic, optoelectronic, and developed research of different chemical and biochemical sensor depend strongly upon the technology of nanoparticles.[1–3] Fast expansions in research for metal and metal oxide synthesis with strong surface modification as nanoparticle materials are carrying out for many proposals, e.g. biological, medicine, and electronic applications. Owing to toxicity, using chemicals and solvents for nanoparticles synthesis is very limited. New methods for nanoparticle materials synthesis as green, non-toxic and safe ways are rapidly developed.[4] Recent research has been directed towards the utilization of TiO_2 nanoparticles which have emerged as an attractive multi-functional material. So the catalytic potential of TiO_2 nanoparticles is used in a wide range of reactions and syntheses of bioactive heterocycles.[5]

On the other hand, substituted dihydroquinolines are highly of interest due to their high potential and applicability in biology pharmacology.[6–9] dihydroquinoline backbone is key molecular motifs to synthesize various natural organic products, e.g. Pharmaceuticals and synthetic intermediates.[10–12] Different synthetic routes of polysubstituted 1,2-dihydroquinolines were progressed[13–20] within traditional gradual procedures of low yielding and special synthetic precursors.[21] Recently, synthesis of dihydroquinoline derivatives has been developed with more progressed efficient strategies using catalysts. One of the most effective catalysts for such dihydroquinoline derivatives synthesis are transition metals, e.g. palladium,[22] ruthenium,[23,24] silver,[25] and gold.[26] They catalyzed anilines reactions with various reagents, like alkynes, scandium triflate,[27] silicotungstic acid,[28] indium triflate,[29] HNO_3,[30] and zeolite.[31]

Moreover, reactivity of amines towards α-ketoesters was studied catalytically by using indium which mediated allylation of quinolones as catalysts.

Progress to develop more green processes by applying agricultural waste in order to synthesize nanoparticles is blossoming into an effective applicable field of nanotechnology.[32–35] Particularly, TiO_2 nanoparticles are the most of interesting in that field resulted from their photo-catalytic sufficiency. TiO_2 nanoparticles have been involved as an high reactive catalyst in alternative organic synthetic processes.[36,37]

The present work describe highly simple and very good yielding protocol for the synthesis polysubstituted 1,2-dihydroquinolines synthesized by α-ketoesters with arylamines using natural TiO_2 nanoparticles as an eco-friendly heterogeneous and recoverable catalyst.

2 | EXPERIMENTAL

2.1 | Material and methods

The utilized plants in our investigation are Neem healthy leaves, which were collected from India. The collected leaves were washed several times by double distilled water to remove any adhering dust. The leaves were dried for 15 days at 25 °C under clean condition. After that, dried leaves were cut into tiny pieces, grinded and sieved to get the finest powder as soon as possible. Ten grams of the dried leaves were mixed with 100 ml of ethanol and refluxed for 3 hrs. Then, the obtained ethanolic leaf extract was obtained by filtering the mixture. Now, the obtained extract is ready for using in synthesis of titanium dioxide nanoparticles. Titanium (IV) isopropoxide ≥97.0%, TiO_2 commercial (CAS Number 13463-67-7) and ethanol Laboratory Reagent, 96% were purchased from Sigma- Aldrich.

2.2 | Preparing of TiO_2 nanoparticles from the extracted neem leaf

0.5 M of titanium tetraisoproxide in ethanolic containing leaf extract was reacted under stirring at 55 °C in the Erlenmeyer flask. Then of the under steady stirring 5 hr, the formed titanium dioxide nanoparticles was acquired by centrifugation at 20000 rpm for 10 minutes. Then the centrifuged particles were washed with ethanol several times and re-centrifuged. The obtained titanium dioxide nanoparticles were dried and grinded to calcinate at 500 °C in muffle furnace for about 5 hours with heating rate 10 °C/min. The calcined titanium dioxide nanopowder was used for further characterization techniques.

2.3 | Characterization techniques for the prepared titanium dioxide nanoparticles

The phase of the extracted TiO_2 was characterized by X-ray diffraction (XRD) pattern with Cu-Kα line (λ = 1.54 A°) operating at 30 kV and 30 mA in the 2θ range 10° – 80°. Surface morphology of the as prepared s TiO_2 nanopowder was studied by a JEOL SET scanning electron microscopy (SEM) with an accelerating voltage of 15.0 kV in a high vacuum mode to achieve magnification between 100 and 10000 using the gold as a reference. The chemical composition of the synthesized nanostructures was also analyzed using energy dispersive analysis of X-ray (EDAX) unit attached to the FE-SEM. Transmission electron microscopy studies (TEM, HR-TEM, SAED) were performed on a JEOL JEM-2100F model. The calculated histograms were performed using image J for TEM program (Broken symmetry software). FT-IR spectra were recorded by FT-IR spectrophotometer Shimadzu-8400 S (Japan) in KBr tablets.

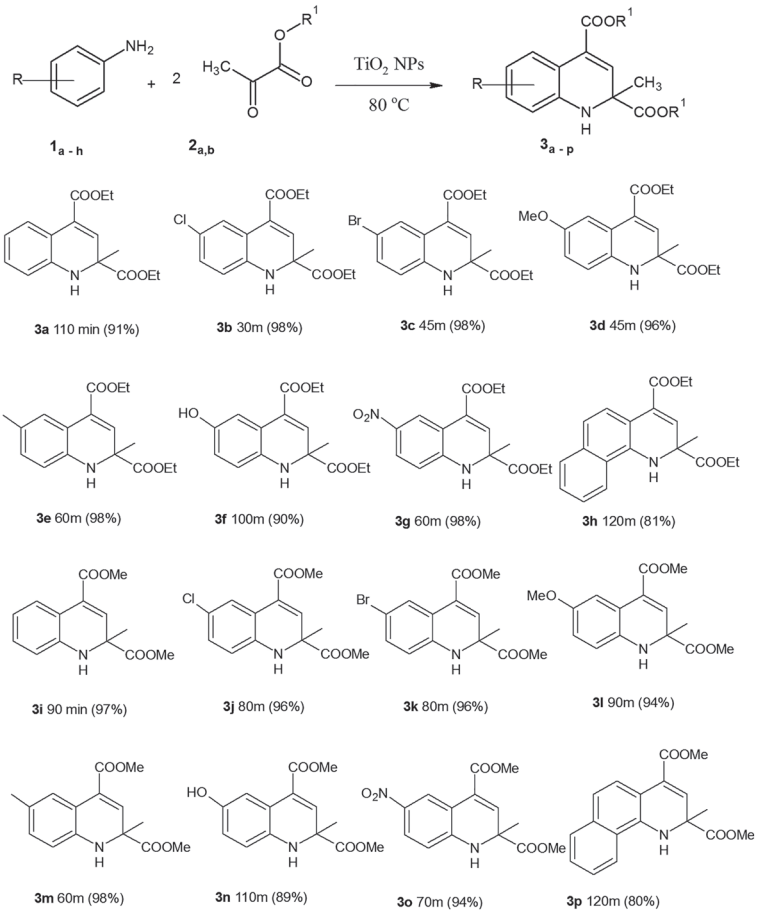
2.4 | General procedure for 1,2-dihydroquinolines ($3_{a\text{-}p}$)

In a two nick 50 ml round flask arylamines (1.0 mmol) was mixed with ethyl or methyl pyruvate (2.0 mmol) in the presence of the suspended TiO_2 nanoparticles (6.0 mol%). The resulted mixture solution was heated at 80 °C for the stipulated period of time (Scheme 1). The reaction progress was followed and monitored by TLC. After the reaction completion, the reaction mixture was cooled to room temperature. The solid residue was dissolved in hot ethanol and centrifuged to remove the catalyst by filtration. The product obtained was purified by TLC and NMR spectroscopy. However, the products were purple further purified by recrystallization from ethanol. All the products reported in literature[23,38] and the data of products were given in supporting information.

IR spectral measurements was achieved as KBr pellets in a Shimadzu DR-8001 spectrometer. ^1H and ^{13}CNMR were recorded on a Bruker DRX-300 or 400 MHz using TMS as an internal reference and $CDCl_3$ as a solvent. All compounds were checked for their purity on TLC plates.

2.5 | Diethyl 2-methyl-1,2-dihydroquinoline-2,4-dicarboxylate, 3a

Yellow oil; FTIR (KBr, cm^{-1}): 3127, 3051, 2930, 1739,1730, 1450; ^1H NMR ($CDCl_3$): δ 1.20 (t, 3H), 1.32 (t, 3H), 1.45 (s, 3H), 4.04–4.19 (m, 2H), 4.21–4.28 (m,



SCHEME 1 Synthesis of 1,2-dihydroquinolines $\mathbf{3}_{\mathbf{a-p}}$ time of reaction (min) and yield (%)

2H), 4.45 (br, 1H), 6.55 (d, 1H), 6.58 (s, 1H), 6.65 (t, 1H), 7.01 (t, 1H), 7.72 (d, 1H); ^{13}C NMR (CDCl3): δ 14.2, 14.2, 27.5, 58.4, 61.01, 61.7, 114.2, 116.4, 118.5, 126.4, 128.4, 129.5, 132.6, 142.7, 165.7, 173.8.

2.6 | Diethyl 6-chloro-2-methyl-1,2-dihydroquinoline-2,4-dicarboxylate, 3b

Yellow oil; FTIR (KBr, cm^{-1}): 3211, 3047, 2898, 1741,1723, 1451; ^{1}H NMR ($CDCl_3$): δ 1.26 (t, 3H), 1.37 (t, 3H), 1.56 (s, 3H), 4.10–4.27 (m,2H), 4.31–4.38 (m, 2H), 4.55 (br, 1H), 6.56 (d,1H), 6.73 (s,1H), 7.03 (dd, 1H), 7.86 (d, 1H); ^{13}C NMR ($CDCl_3$): δ 14.2, 14.1, 27.1, 58.6, 61.1, 62.0, 115.1, 117.7,123.2, 126.2, 127.3, 129.3, 133.8, 141.0, 165.2, 173.7.

2.7 | Diethyl 6-bromo-2-methyl-1,2-dihydroquinoline-2,4-dicarboxylate, 3c

Yellow oil; FTIR (KBr, cm^{-1}): 3169, 3052, 2911, 1740,1729, 1451; ^{1}H NMR ($CDCl_3$): δ 1.25 (t, 3H), 1.37 (t, 3H), 1.55 (s, 3H), 4.11–4.26 (m,2H), 4.30–4.37 (m, 2H), 4.57 (br, 1H), 6.50 (d, 1H), 6.72 (s, 1H), 7.14 (dd, 1H), 8.00 (d, 1H); ^{13}C NMR ($CDCl_3$): δ 14.0, 14.2, 27.3, 58.5, 61.1, 61.7, 110.1, 115.6, 118.1, 127.2, 129.1, 132.0, 133.9, 141.6, 165.1, 173.5.

2.8 | Diethyl 6-methoxy-2-methyl-1,2-dihydroquinoline-2,4-dicarboxylate, 3d

Yellow oil; FTIR (KBr, cm^{-1}): 3147, 3048, 2890, 1742,1729, 1450; ^{1}H NMR ($CDCl_3$): δ 1.25 (t, 3H), 1.37 (t, 3H), 1.55 (s, 3H), 3.76 (s, 1H), 4.10–4.25 (m, 2H), 4.29–4.37 (m, 2H), 4.37 (br, 1H), 6.62 (d, 1H), 6.70 (dd, 1H), 6.75 (s, 1H), 7.50 (d, 1H); ^{13}C NMR ($CDCl_3$): δ 14.2, 14.3, 26.6, 55.6, 58.5, 60.9, 61.8, 111.4, 115.1, 116.2, 117.5, 128.1, 134.1, 136.7, 152.5, 165.7, 174.2.

2.9 | Diethyl 2,6-dimethyl-1,2-dihydroquinoline-2,4-dicarboxylate, 3e

Yellow oil; FTIR (KBr, cm^{-1}): 3138, 3054, 2981, 1738,1720, 1449; ^{1}H NMR ($CDCl_3$): δ 1.25 (t, 3H), 1.38 (t, 3H), 1.54 (s, 3H), 2.21 (s, 3H), 4.11–4.25 (m, 2H),

4.28–4.37 (m, 2H), 4.44 (br, 1H), 6.56 (d, 1H), 6.65 (s, 1H), 6.91 (d, 1H), 7.62 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 14.0, 14.3, 20.7, 27.0, 58.4, 61.0, 61.8, 114.2, 116.6, 126.7, 127.7, 128.5, 130.1, 132.7, 140.3, 165.9, 174.1.

2.10 | Diethyl 6-hydroxy-2-methyl-1,2-dihydroquinoline-2,4-dicarboxylate, 3f

Yellow oil; FTIR (KBr, cm^{-1}): 3437, 3127, 3048, 2911, 1743,1733, 1450; ^{1}H NMR ($CDCl_3$): δ 1.26 (t, 3H), 1.37 (t, 3H), 1.55 (s, 3H), 4.11–4.25 (m, 2H), 4.26–4.34 (m, 2H), 5.68 (br, 1H), 6.55 (d, 1H), 6.64 (dd, 1H), 6.75 (s, 1H), 7.45 (d, 1H); ^{13}C NMR ($CDCl_3$): δ 14.0, 14.2, 26.7, 58.5, 61.2, 61.8, 113.3, 115.2, 116.8, 117.6, 127.9, 134.4, 136.4, 148.5, 165.8, 174.3.

2.11 | Diethyl 2-methyl-6-nitro-1,2-dihydroquinoline-2,4-dicarboxylate, 3 g

Yellow solid; FTIR (KBr, cm^{-1}): 3131, 3051, 2981, 1744,1721, 1451; ^{1}H NMR ($CDCl_3$): δ 1.26 (t, 3H), 1.37 (t, 3H), 1.61 (s, 3H), 4.15–4.29 (m, 2H), 4.30–4.38 (m, 2H), 5.36 (br, 1H), 6.57 (d, 1H), 6.75 (s, 1H), 7.97 (dd, 1H), 8.80 (d, 1H); ^{13}C NMR ($CDCl_3$): δ 14.0, 14.2, 28.3, 59.1, 61.7, 62.4, 113.1, 114.3, 123.4, 126.0, 126.8, 133.2, 138.8, 147.9, 164.7, 172.4.

2.12 | Diethyl 2-methyl-1,2-dihydrobenzo[h]quinoline-2,4-dicarboxylate, 3 h

Reddish brown oil; FTIR (KBr, cm^{-1}): 3126, 3047, 2980, 1742,1727, 1449; ^{1}H NMR ($CDCl_3$): δ 1.27 (t, 3H), 1.42 (t, 3H), 1.60 (s, 3H), 4.14–4.29 (m, 2H), 4.33–4.42 (m, 2H), 5.36 (br, 1H), 6.69 (d, 1H), 7.23 (d, 1H), 7.43–7.48 (m, 2H), 7.73–7.77 (m, 1H), 7.85–7.88 (m, 1H), 7.90 (d, 1H); ^{13}C NMR ($CDCl_3$): δ 14.1, 14.3, 27.3, 58.6, 61.2, 61.8, 111.3, 117.7, 120.0, 122.3, 124.1, 125.1, 126.4, 128.5, 129.3, 130.1, 134.2, 137.8, 166.3, 174.0.

2.13 | Dimethyl 2-methyl-1,2-dihydroquinoline-2,4-dicarboxylate, 3i

Yellow oil; FTIR (KBr, cm^{-1}): 3127, 3048, 2987, 1744, 1729, 1452; ^{1}H NMR ($CDCl^3$): δ 1.54 (s, 3H), 3.71 (s, 3H), 3.86 (s, 3H), 4.57 (br, 1H), 6.61 (d, 1H), 6.67 (s, 1H), 6.70 (t, 1H), 7.07 (t, 1H), 7.78 (dd, 1H); ^{13}C NMR ($CDCl_3$): δ 27.3, 52.2, 52.7, 58.5, 114.4, 116.3, 118.6, 126.4, 128.3, 129.6, 132.7, 142.6, 166.2, 174.3.

2.14 | Dimethyl 6-chloro-2-methyl-1,2-dihydroquinoline-2,4-dicarboxylate, 3j

Yellow oil; FTIR (KBr, cm^{-1}): 3129, 3051, 2983, 1745, 1710, 1450; ^{1}H NMR ($CDCl_3$): δ 1.56 (s, 3H), 3.75 (s, 3H), 3.87 (s, 3H), 4.56 (br, 1H), 6.56 (d, 1H), 6.75 (s, 1H), 7.00 (dd, 1H), 7.87 (d, 1H); ^{13}C NMR ($CDCl_3$): δ 27.2, 52.3, 53.0, 58.6, 115.1, 117.6, 123.3, 126.2, 127.2, 129.3, 134.1, 141.1, 165.5, 174.2.

2.15 | Dimethyl 6-bromo-2-methyl-1,2-dihydroquinoline-2,4-dicarboxylate, 3 k

Yellow solid; FTIR (KBr, cm^{-1}): 3126, 3050, 2990, 1741, 1717, 1450; ^{1}H NMR ($CDCl_3$): δ 1.55 (s, 3H), 3.74 (s, 3H), 3.83 (s, 3H), 4.61 (br, 1H), 6.51 (d, 1H), 6.70 (s, 1H), 7.15 (dd, 1H), 7.98 (d, 1H); ^{13}C NMR ($CDCl_3$): δ 27.2, 52.1, 52.9, 58.6, 110.3, 115.6, 118.0, 127.0, 128.9, 132.2, 134.1, 141.5, 165.5, 174.1.

2.16 | Dimethyl 6-methoxy-2-methyl-1,2-dihydroquinoline-2,4-dicarboxylate, 3 l

Yellow oil; FTIR (KBr, cm^{-1}): 3129, 3053, 2987, 1740, 1722, 1453; ^{1}H NMR ($CDCl_3$): δ 1.54 (s, 3H), 3.74 (s, 3H), 3.75 (s, 3H), 3.87 (s, 3H), 4.35 (br, 1H), 6.57 (d, 1H), 6.71 (dd, 1H), 6.75 (s, 1H), 7.52 (d, 1H); ^{13}C NMR ($CDCl_3$): δ 26.7, 52.1, 52.7, 55.7, 58.5, 111.4, 115.1, 116.2, 117.5, 127.8, 134.3, 136.6, 152.5, 166.1, 174.5.

2.17 | Dimethyl 2,6-dimethyl-1,2-dihydroquinoline-2,4-dicarboxylate, 3 m

Yellow oil; FTIR (KBr, cm^{-1}): 3127, 3050, 2981, 1742, 1720, 1450; ^{1}H NMR ($CDCl_3$): δ 1.55 (s, 3H), 2.24 (s, 3H), 3.72 (s, 3H), 3.86 (s, 3H), 4.44 (br, 1H), 6.56 (d, 1H), 6.67 (s, 1H), 6.91 (dd, 1H), 7.61(s, 1H); ^{13}C NMR ($CDCl_3$): δ 20.6, 27.2, 52.1, 52.7, 58.4, 114.2, 116.4, 126.8, 127.9, 128.2, 130.3, 133.0, 140.2, 166.1, 174.5.

2.18 | Dimethyl 6-hedroxy-2-methyl-1,2-dihydroquinoline-2,4-dicarboxylate, 3n

Yellow oil; FTIR (KBr, cm^{-1}): 3417, 3123, 3050, 2987, 1740, 1723, 1450; ^{1}H NMR ($CDCl_3$): δ 1.52 (s, 3H), 3.73 (s, 3H), 3.85 (s, 3H), 4.60 (br, 1H), 5.75 (s,1H), 6.55 (d,

1H), 6.73 (s, 1H), 6.98 (dd, 1H), 7.72(s, 1H); ^{13}C NMR ($CDCl_3$): δ 27.2, 52.1, 52.8, 58.3, 113.9, 116.7, 123.8, 125.9, 126.2, 130.0, 134.1, 141.1, 165.7, 174.3.

2.19 | Dimethyl 6-nitro-2-methyl-1,2-dihydroquinoline-2,4-dicarboxylate, 3o

Yellow solid; FTIR (KBr, cm^{-1}): 3121, 3053, 2981, 1741, 1720, 1450; ^{1}H NMR ($CDCl_3$): δ 1.51 (s, 3H), 3.65 (s, 3H), 3.84 (s, 3H), 4.61 (br, 1H), 6.54 (d, 1H), 6.72 (s, 1H), 7.15 (dd, 1H), 7.93(s, 1H); ^{13}C NMR ($CDCl_3$): δ 27.1, 52.2, 52.7, 58.2, 110.5, 115.7, 118.8, 127.3, 129.2, 132.10, 134.4, 142.1, 165.0, 174.1.

2.20 | Dimethyl 2-methyl-1,2-dihydrobenzo[h]quinoline-2,4-dicarboxylate, 3p

Reddish brown oil; FTIR (KBr, cm^{-1}): 31271, 3050, 2987, 1743, 1722, 1451; ^{1}H NMR ($CDCl_3$): δ 1.62 (s, 3H), 3.78 (s, 3H), 3.91 (s, 3H), 5.37 (br, 1H), 6.72 (d, 1H), 7.25 (d, 1H), 7.43–7.48 (m, 2H), 7.74–7.78 (m, 1H), 7.86–7.90 (m, 1H), 7.92 (d, 1H); ^{13}C NMR ($CDCl_3$): δ 27.2, 52.1, 52.8, 58.7, 111.1, 117.8,119.8, 122.3, 124.0, 125.2, 126.4, 128.6, 129.0, 130.2, 134.2, 137.9, 166.3, 174.4.

3 | FINDINGS AND DISCUSSION

The structural evolution extracted TiO_2 was investigated by XRD was closely matched with the Joint Committee on powder diffraction standards (JCPDS Card No. 78–2486).[39] It is clearly obtained from the XRD results, which confirm the presence of TiO_2 in the plant extract and this compared with extracted TiO_2 from *Jatropha curcas L.*[40] The TiO_2 peaks in Figure (1) are wide, which means grain size of TiO_2 is rather small. The average size 'd' crystallization in nanometer has been evaluated using Debye Scherrer formula[3,41] and found to be 20 nm.

The images show a narrow size distribution of particles with uniformed spherical structure morphology.

The surface morphology of the extracted TiO_2 are shown in Figure 2(a). The images show a narrow size distribution of particles with uniformed spherical structure morphology. The structural composition was investigated by EDX (Figure 2(b)). Ti and O peaks are only observed in the spectrum, suggesting that the product is composed of Ti and O. A quantitative EDS analysis shows that the atom ratio Ti: O is 24: 51, close to 1: 2, confirming the composition of the extracted product represent TiO_2.

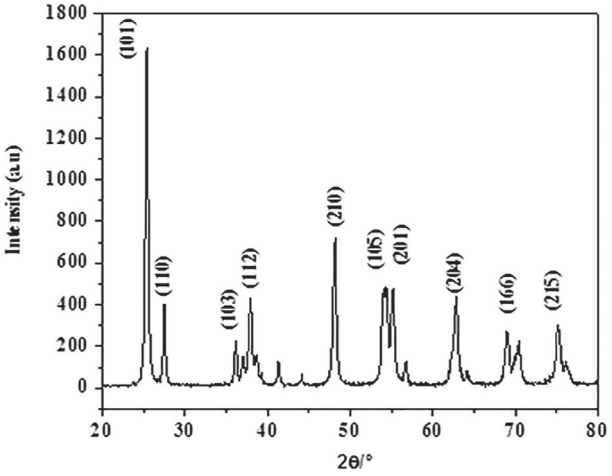


FIGURE 1 Powder x- ray pattern for the extracted TiO_2 nanoparticles

The particle size distribution can be explained on the basis of TEM image for the extracted TiO_2 and the calculated histogram (see Figure 3(a,b)) . It is observed that the major of the particles have the size 19 nm. HRTEM image displayed in Figure 4a for the extracted TiO_2 confirms the high crystalline nature of these nanoparticles. TEM micrograph of a single TiO_2 nanoparticle (Figure 4b) shows the arrangements of atoms within single nanoparticle. The presence of lines also depicts the crystallites of TiO_2 nanoparticles, which were otherwise absent in non-metallic organic molecules. Selected area electron diffraction (SAED) patterns (Figure 5) show that the as-prepared powder is completely crystalline and entirely consists of anatase phase. These are in agreement with XRD results in Figure (1).

3.1 | FTIR of the extracted TiO_2 nanoparticles

FTIR spectrum analysis was performed to specify the biomolecules responsible for capping of the bioreduced TiO_2 NPs synthesized using plant extract (Figure 6). FTIR of Neem leaf plant (see Figure S1) indicates the presence of active functional groups in the synthesized silver nanoparticles. The peaks observed at 3289 cm^{-1} and 2964 cm^{-1} correspond to O–H and C–H stretching frequency, respectively. The assignment at 1642 cm^{-1} corresponds to C=O group. The peak at 1040 might be contributed to the presence of methoxy group. It shows that the extracted TiO_2 NPs has absorption peaks were located at 714 cm^{-1} (Ti–O–O bond), 1076 cm^{-1} (C–N stretch aliphatic amines 1172 cm^{-1} (C–O stretching vibrations in alcoholic groups), 1642 cm^{-1} (N–H bend bond), and 3426 cm^{-1} (O–H stretching due to alcoholic group).

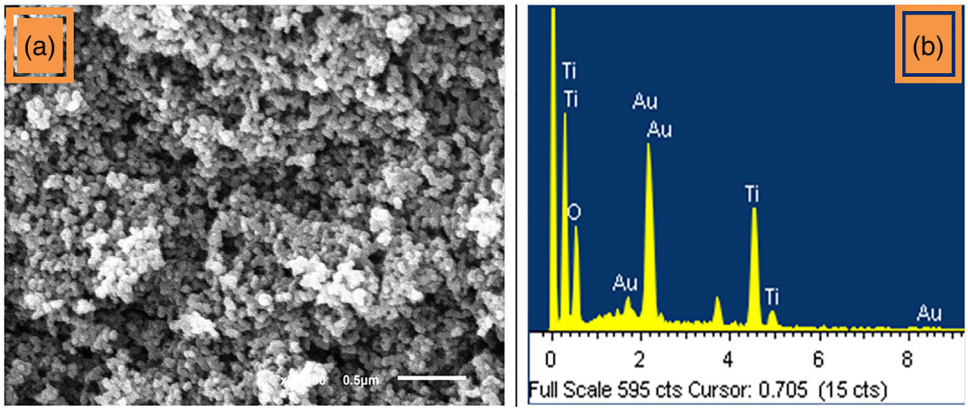


FIGURE 2 (a) SEM image for the extracted TiO_2 nanoparticles. (b): EDS spectrum of the as extracted TiO_2 nanoparticles

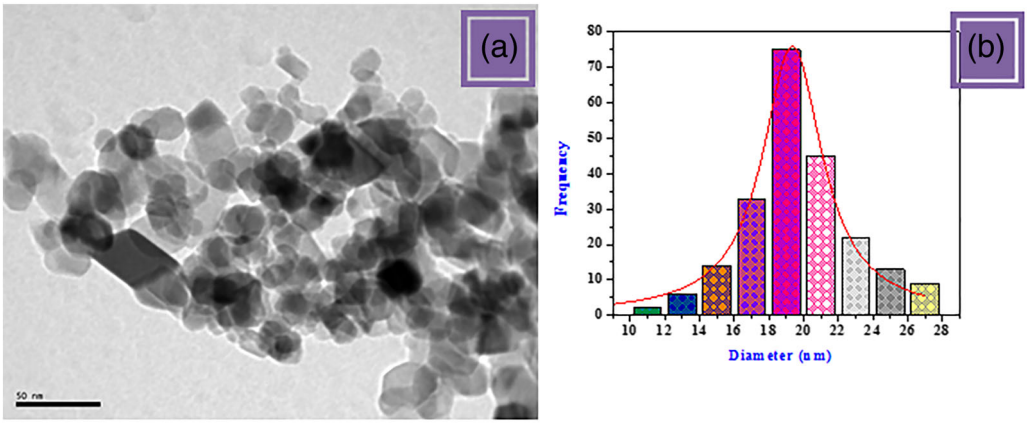


FIGURE 3 (a) Low magnification TEM image for the extracted TiO_2 nanoparticles. (b): Particle size distribution of extracted TiO_2 nanoparticles

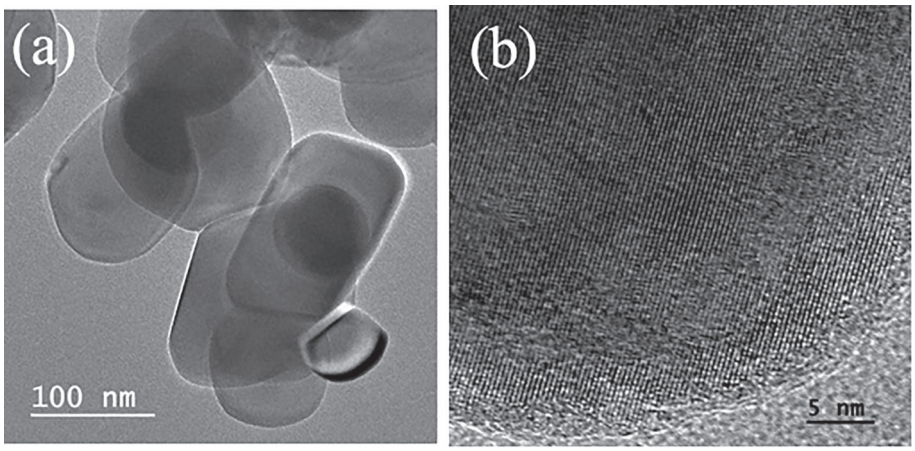


FIGURE 4 (a) HRTEM image for the extracted TiO_2. (b): HR-TEM micrograph of extracted single Ti O_2 nanoparticle

3.2 | Functionalization of the extracted TiO_2 nanoparticles in synthesis of 1,2-dihydroquinolines derivatives

The TiO_2 nanoparticles biosynthesis was progressed Neem leaf extract method as a biodegradable and suitable method. Such method is easily, environmentally friendly and not costed method for the TiO_2 NPs synthesis of at lower temperature form the sources of the agricultural wastes. Their catalytic applications were synthesis of 1,2-dihydroquinolines derivatives $\mathbf{3_{a\text{-}p}}$ in excellent yields.

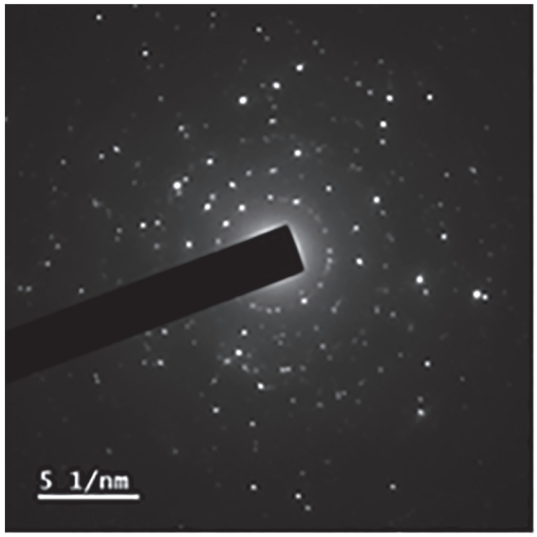


FIGURE 5 Selected area electron diffraction (SAED) patterns for the extracted TiO_2

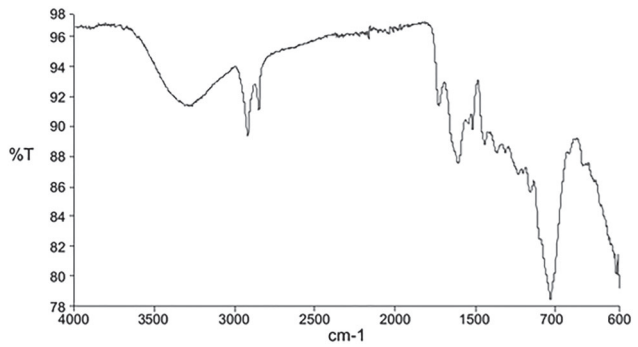


FIGURE 6 FTIR spectra of extracted TiO_2 nanoparticles

When reacted arylamines $\mathbf{1_{a\text{-}h}}$ with 2.0 mmol ethyl or methyl pyruvate $\mathbf{2_{a,b}}$, using TiO_2 nanoparticles as an eco-friendly heterogeneous catalyst gave 1,2-dihydroquinolines derivatives $\mathbf{3_{a\text{-}p}}$ (Scheme 1) .

This protocol offers flexibility in tuning the molecular complexity and diversity. The reactions proceeded to completion almost instantly, and the reaction product was quite pure and did not need to be purified by chromatographic tools, which could be recrystallized only in ethanol.

Optimized conditions for the reaction within different mole amounts of TiO_2 NPs, catalyst concentration has a remarkable role in the product yielding percentages. It was detected that enhancing of the loaded amounts of the catalyst from 2.0 to 6.0 mol% awards higher yield percentages to 98% of the product (Table 1). Further increase of involved amounts of the catalyst more than 6.0 mol% resulted to reduce product yield percentages due to absorption of the products on the catalyst surface. The cascade reaction was carried out 4-chloroaniline and ethyl pyruvate $\mathbf{3_b}$ as a model reaction.

TABLE 1 The yielding amount percentages of TiO_2 NPs in the synthesis of 1,2-dihydroquinolines, $\mathbf{3_b}$

Entry	Catalysts/ mol%	Yield %	Entry	Catalysts/ mol%	Yield[a] %
1	2	62	5	6	98
2	3	75	6	7	98
3	4	85	7	8	96
4	5	92	8	9	92

[a]Isolated Yield.

The reaction could not be proceeded in the absence of the TiO_2 catalyst. Moreover, the catalytic reaction was initiated by using three different types of TiO_2 catalysts, *i.e.*, TiO_2 commercial, TiO_2 nanoparticles fresh (extracted) and recovered TiO_2 nanoparticles. The optimized yielding amount of product was afforded using TiO_2 nanoparticles in the shortest time because of the greater diffusion of TiO_2 nanoparticles in the reaction media. Similarity for the recovered catalyst was resulted to the fresh TiO_2 nanoparticles (Table 2).

To evaluate the effect of the solvents on the catalytic process, various solvents were applied with estimation of the reaction scope and limitation. In particular, it was found that the syntheses of 1,2-dihydroquinolines $\mathbf{3_{a\text{-}p}}$ catalyzed by TiO_2 NPs were not only faster in various solvents, but awarded higher yields under solvent free conditions (Table 3).

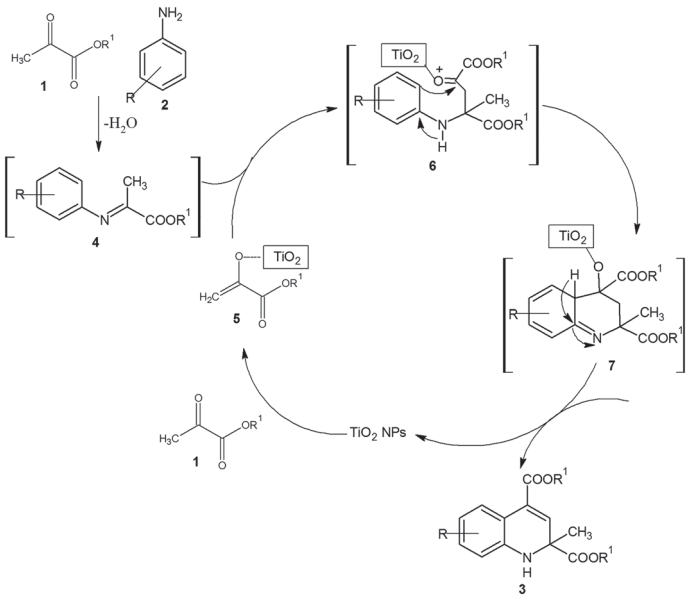
TABLE 2 The effect of different types of TiO_2 in the synthesis of 1,2-dihydroquinolines, $\mathbf{3_b}$

Catalysts	Time	Yield[a] %
TiO_2 commercial	4 hour	72
TiO_2 NPs fresh (extracted)	40 min	98
recovered TiO_2 NPs	40 min	98

[a]Isolated Yield

TABLE 3 Solvent Effect on the synthesis of 1,2-dihydroquinolines ($\mathbf{3_b}$) catalyzed by TiO_2 NPs

Solvent	Tim (min)	Yield (%)
Toluene	190	60
$CHCl_3$	180	63
DCM	160	63
EtOH	90	88
MeOH	90	87
H_2O	60	90
Solvent free	45	98



SCHEME 2 Proposed Reactions Mechanisms of the extracted TiO_2 NPs Catalyzed for Synthesis of 1,2-dihydroquinolines **3**

Particularly, the reaction is more proceeded in polar protic solvents (EtOH, MeOH and water) giving good yields, whereas, in the aprotic solvents, e.g., toluene, $CHCl_3$ and DCM, the catalytic process gives observable low yield. The dielectric constant is a measurement of the polarity of the reaction media, which could be the main factor for the reactivity of the catalytic process to improve the yield of the wanted product, i.e., the protic solvents have larger dielectric constant values compared with aprotic (non-polar) solvents. The protic (polar) solvents those have a high probability to donate proton easily within hydrogen bonds formation with the substrate.

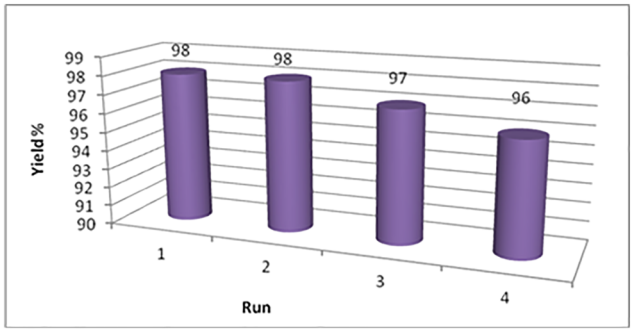


FIGURE 7 Recyclability of TiO_2 NPs in the model reaction

Such mechanistic proposal for the formation of 1,2-dihydroquinoline **3** was reported previously and most likely begins with the generation of an imine from the aniline **2** and the ketoester **1** (Scheme 2), followed by addition of the enolate to the imine. The extracted TiO_2 NPs activated α-ketoesters **5** reacted with imine **4** to give **6** which is a good electrophile.[42] An electron-rich benzene ring could add to the keto ester group **7**, and water elimination followed by proton shift would eventually form the 1,2-dihydroquinoline **3**.

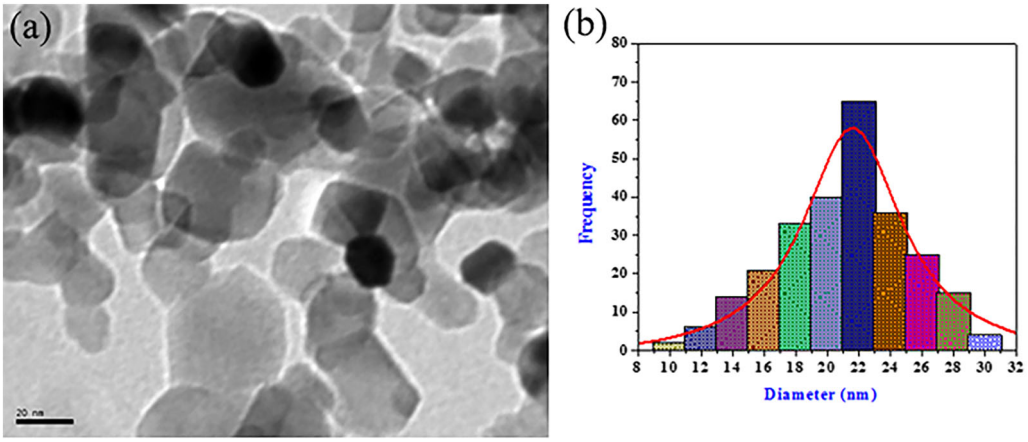


FIGURE 8 (a) TEM image for the recoverable TiO_2 catalyst. (b): Particle size distribution of recoverable TiO_2 catalyst

3.3 | Reusability of the catalyst

The heterogeneous TiO_2 NPs catalyst could be easily reused many times by centrifuged extraction after the reaction completion. The filtered TiO_2 NPs were washed with ethanol and double distilled water. After drying at 90 °C for 3 hr, the catalyst was recycled for another reaction run under the typical reaction condition. The results displayed that the catalytic sufficiency was not affected significantly. Similar conversion and selectivity were obtained when the recovered TiO_2 NPs were reused fourth times (see Figure 7).

Finally, the recoverable catalyst were subjected to TEM analysis and the change in size was found to be negligible (22 nm) (cf. Figure 8 (a,b)) .

4 | CONCLUSION

Green synthesis and characterization of TiO_2 nanoparticles was achieved by a biodegradable and convenient procedure using Neem leaf extract. This is the report simple, rapid, eco-friendly, cheaper and green methods for the synthesis of TiO_2 NPs at lower temperature using agricultural waste. Their catalytic applications first time used for synthesis of 1,2-dihydroquinolines derivatives $\mathbf{3_{a\text{-}p}}$ in excellent yields.

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REFERENCES

[1] T. S. Wong, U. Schwaneberg, *Curr. Opin. Biotechnol.* **2003**, *14*, 590.

[2] a) A. Ramanavicius, A. Kausaite, A. Ramanaviciene, *Biosens. Bioelectron.* **2005**, *20*, 1962; b) M. A. A. El-Remaily, A. M. Abu-Dief, R. M. El-Khatib, *Appl. Organomet. Chem.* **2016**, *30*, 1022. c) L. H. Abdel-Rahman, A. M. Abu-Dief, R. M. El-Khatib, S. M. Abdel-Fatah, *Bioorg. Chem.* **2016**, *69*, 140; d) A. M. Abu-Dief, W. S. Mohamed, *Mater. Res. Express* **2017**, *4*, 035039; e)E. M. M. Ibrahim, L. H. Abdel-Rahman, A. M. Abu-Dief, A. Elshafaie, S. K. Hamdan, A. M. Ahmed, *Mater. Res. Bull.* **2018**, *99*, 103.

[3] a) M. A. A. El-Remaily, *Tetrahedron* **2014**, *70*, 2971; b) M. A. A. El-Remaily, H. A. Hamad, *J. Mol. Catal. A: Chem.* **2015**, *404*, 148; c) M. A. A. El-Remaily, A. M. Abu-Dief, *Tetrahedron* **2015**, *71*, 2579; d) A. A. Marzouk, A. M. Abu-Dief, A. A. Abdelhamid, *Appl. Organomet. Chem.* **2018**, *32*(1), e3794.

[4] a) H. Koopi, F. Buazar, *Ceram. Int.* **2018**, *44*(8), 8940; b) F. Buazar, M. H. Baghlani-Nejazd, M. Badri, M. Kashisaz, A. Khaledi-Nasab, F. Kroushawi, *Starch-Stärke* **2016**, *68*(7–8), 796; c) F. Buazar, M. Bavi, F. Kroushawi, M. Halvani, A. Khaledi-Nasab, S. A. Hossieni, *J. Exp. Nanosci.* **2016**, *11*(3), 175.

[5] J. Joshi, A. Dandia, S. Kumari, *Mini-Rev. Org. Chem.* **2017**, *14*(3), 227.

[6] a) J. V. Johnson, B. S. Rauckman, D. P. Baccanari, B. Roth, *J. Med. Chem.* **1989**, *32*, 1942; b) A. R. Hudson, S. L. Roach, R. I. Higuchi, D. P. Phillips, R. P. Bissonnette, W. W. Lamph, J. Yen, Y. Li, M. E. Adams, L. J. Valdez, A. Vassar, C. Cuervo, E. A. Kallel, C. J. Gharbaoui, D. E. Mais, J. N. Miner, K. B. Marschke, D. Rungta, A. Negro-Vilar, L. Zhi, *J. Med. Chem.* **2007**, *50*, 4699.

[7] a) B. Belleau, R. Martel, G. Lacasse, M. Menard, N. L. Weinberg, Y. G. Perron, *J. Am. Chem. Soc.* **1968**, *90*, 823; b) P. R. Kym, M. E. Kort, M. J. Coghlan, J. L. Moore, R. Tang, J. D. Ratajczyk, D. P. Larson, S. W. Elmore, J. K. Pratt, M. A. Stashko, H. D. Falls, C. W. Lin, M. Nakane, L. Miller, C. M. Tyree, J. N. Miner, P. B. Jacobson, D. M. Wilcox, P. Nguyen, B. C. Lane, *J. Med. Chem.* **2003**, *46*, 1016.

[8] C. L. F. Pooley, J. P. Edwards, M. E. Goldman, M. W. Wang, K. B. Marschke, D. L. Crombie, T. K. Jones, *J. Med. Chem.* **1998**, *41*, 3461.

[9] B. Pedram, A. van Oeveren, D. E. Mais, K. B. Marschke, P. M. Verbost, M. B. Groen, L. Zhi, *J. Med. Chem.* **2008**, *51*, 3696.

[10] A. Balayer, T. Sevenet, H. Schaller, A. Hadi, A. Hamid, A. Chiaroni, C. Riche, M. Pais, *Nat. Prod. Lett.* **1993**, *2*, 61.

[11] J. Parello, *Bull. Soc. Chim. Fr.* **1968**, *3*, 1117.

[12] F. Abe, T. Yamauchi, H. Shibuya, I. Kitagawa, M. Yamashita, *Chem. Pharm. Bull.* **1998**, *46*, 1235.

[13] a) X.-Y. Liu, C.-M. Che, *Angew. Chem. Int. Ed.* **2008**, *47*, 3805; b) S. Kamiguchi, I. Takahashi, H. Kurokawa, H. Miura, T. Chihara, *Appl. Catal. Gen.* **2006**, *309*, 70.

[14] a) G. Lu, J. L. Portscheller, H. C. Malinakova, *Organometallics* **2005**, *24*, 945; b) C. S. Yi, S. Y. Yun, I. A. Guzei, *J. Am. Chem. Soc.* **2005**, *127*, 5782.

[15] a) C. S. Yi, S. Y. Yun, *J. Am. Chem. Soc.* **2005**, *127*, 17000; b) Y. Luo, Z. Li, C. J. Li, *Org. Lett.* **2005**, *7*, 2675.

[16] a) X.-Y. Liu, P. Ding, J. S. Huang, C. M. Che, *Org. Lett.* **2007**, *9*, 2645; b) M.-E. Theoclitou, L. A. Robinson, *Tetrahedron Lett.* **2002**, *43*, 3907.

[17] a) R. Kamakshi, B. S. R. Reddy, *Cat. Com.* **2007**, *8*, 825; b) A. Hegedus, Z. Hell, T. Vargadi, A. Potor, I. Gresits, *Catal.Lett.* **2007**, *117*, 99.

[18] S. H. Lee, Y. S. Park, M. H. Nam, C. M. Yoon, *Org. Biomol. Chem.* **2004**, *22*, 170.

[19] H. Waldmann, G. V. Karunakar, K. Kumar, *Org. Lett.* **2008**, *10*, 2159.

[20] X.-Y. Hu, J.-C. Zhang, W. Wei, J.-X. Ji, *Tetrahedron Lett.* **2011**, *52*, 2903.

[21] R. H. F. Mansake, M. Kulka, *Org. React.* **1953**, *7*, 59.

[22] G. Lu, J. L. Portscheller, H. C. Malinakova, *Organometallics* **2005**, *24*, 945.

[23] C. S. Yi, S. Y. Yun, I. A. Guzei, *J. Am. Chem. Soc.* **2005**, *127*, 5782.

[24] C. S. Yi, S. Y. Yun, *J. Am. Chem. Soc.* **2005**, *127*, 17000.

[25] Y. Luo, Z. Li, C. J. Li, *Org. Lett.* **2005**, *7*, 2675.

[26] X.-Y. Liu, P. Ding, J.-S. Huang, C.-M. Che, *Org. Lett.* **2007**, *9*, 2645.

[27] M.-E. Theoclitou, L. A. Robinson, *Tetrahedron Lett.* **2002**, *43*, 3907.

[28] R. Kamakshi, B. S. R. Reddy, *Cat. Com.* **2007**, *8*, 825.

[29] X.-Y. Hu, J.-C. Zhang, W. Wei, J. X. Ji, *Tetrahedron Lett.* **2011**, *52*, 2903.

[30] J. C. Zhang, J. X. Ji, *ACS Catal.* **2011**, *1*, 1360.

[31] A. Hegedus, Z. Hell, T. Vargadi, A. Potor, I. Gresits, *Catal. Lett.* **2007**, *117*, 99.

[32] R. Kumar, S. M. Roopan, A. Prabhakarn, V. G. Khanna, S. Chakroborty, *Spectrochim. Acta A* **2012**, *90*, 173.

[33] S. M. Roopan, A. Bharathi, R. Kumar, V. G. Khanna, A. Prabhakarn, *Colloids Surf., B* **2012**, *92*, 209.

[34] S. M. Roopan, R. Rohit, G. Madhumitha, A. A. Rahuman, C. Kamaraj, A. Bharathi, T. V. Surendra, *Ind. Crop Prod.* **2013**, *43*, 631.

[35] a) S. M. Roopan, F. R. N. Khan, *Med. Chem. Res.* **2011**, *20*, 732.

[36] Z. N. Tisseh, M. Dabiri, M. Nobahar, A. A. Soorki, A. Bazgir, *Tetrahedron* **2012**, *68*, 3351.

[37] A. Bharathi, S. M. Roopan, A. Kajbafvala, R. D. Padmaja, M. S. Darsana, G. N. Kumari, *Chin. Chem. Lett.* **2014**, *25*, 324.

[38] M. M. Ba-Abbad, A. A. H. Kadhum, A. B. Mohamad, M. S. Takriff, K. Sopian, *Int. J. Electrochem. Sci.* **2012**, *7*, 4871.

[39] J. Chen, L. Zhang, *Mater. Lett.* **2009**, *63*, 1797.

[40] S. P. Goutam, G. Saxena, V. Singh, A. K. Yadav, R. N. Bharagava, K. B. Thapa, *Chem. Eng. J.* **2018**, *336*, 386.

[41] a) E. M. M. Ibrahim, A. M. Abu-Dief, A. Elshafaie, A. M. Ahmed, *Mater. Chem. Phys.* **2017**, *192*, 41; b)W. S. Mohamed, A. M. Abu-Dief, *J. Phys. Chem. Solids* **2018**, *116*, 375.

[42] a) B.-Q. Zhang, Y. Luo, Y.-H. He, Z. Guan, *Tetrahedron* **2014**, *70*, 1961; b) Y.-W. Zhu, J.-L. Qian, W.-B. Yi, C. Cai, *Tetrahedron Lett.* **2013**, *54*, 638.

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