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A one-pot multi-component synthesis of novel 2((1H-Indole-3yl) (Phenyl) methyl) malononitrile derivative by utilizing recoverable and efficient TiO_2 nanocatalyst

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Abstract: In this research, we have described a facile and user-friendly protocol for the formation of 2((1H-Indole-3yl)(Phenyl)methyl)malononitrile derivatives using a recoverable and efficient TiO_2 nanocatalyst. This protocol is simple and incredibly efficient for the synthesis of novel 2((1H-Indole-3yl)(Phenyl)methyl)malononitrile derivatives. Nanoscale TiO_2 is used as the catalyst. Since TiO_2 has more surface area easily binds with the active site of a reactive molecule and initiates the reaction. At last, TiO_2 also recovered as it acts as a catalyst. This multi-component reaction involves indole, malononitrile, and active aldehyde derivatives in the presence of ethanol as solvent and TiO_2 as a nanocatalyst. The synthetic methodology employed for multi-component reactions produces substituted 2((1H-Indole-3yl)(Phenyl) methyl) malononitrile derivatives with an environmentally friendly protocol under modest reaction conditions. This study shows that the recoverable and environmentally friendly TiO_2 nanocatalyst is an effective material for the synthesis of 2((1H-Indole-3yl) (Phenyl) methyl) malononitrile derivatives with high yields, rapid reaction at room temperature, and effortless product isolation.

Keywords: TiO_2 nanocatalyst; Multicomponent Reaction; 2((1H-Indole-3yl)(Phenyl)methyl) malononitrile; One-pot synthesis; Recoverable.

1. Introduction

A one-pot multi-component reaction is a reaction in which we can add three to four reactants in one pot. Laurent and Gerhardt reported the first multi-component reaction (MCR) in 1838 [1]. Consecutive one-pot reactions are likely different from the systematic multi-step reactions in which the reactants were mixed in every stage of the reaction and give to be less effective than MCRs [2]. In recent decades MCRs have been powerful tools for organic synthesis [3,4]. The advantages of the reaction are highly selective, efficient, low cost, short reaction time, simple separation steps, energy savings, and eco-friendly. This quality inspired us to put sizable effort into designing and implementing MCRs in both commercial and academic for the desired product with less by-product [5]. These reactions have played a vital role in organic heterocyclic reactions such as C-C and C-hetero atom formation using one pot technique [5,6]. Carbon-nitrogen bonds form a primary synthetic phase in organic synthesis to produce various biological active agrochemical and industrial polymers [7]. Nowadays, indole and its derivative contain the compound having more useful in pharmaceutical-appropriate compounds [8], agrochemical [9], and biologically active natural products [10], etc. In the case of indole, the C-3 position plays a vital role in synthesizing active pharmaceutical compounds [11,12].

Consequently, the growth of well-organized and atom-economical approaches for synthesizing indoles from recently presented initial materials is still exciting for this region. We can use commercially available indole derivatives [13,14], active methylene group compounds, and aldehyde derivatives [15]. Indole derivative compounds exhibit anticoagulant [16], anticancer [17], antimicrobial[18], antihypertensive, and vasodilators [19]. O-containing heterocycles moiety such as furan derivative has been shown to be the physiologically most decorative [20] and potent heterocycles that served as active agents such as antioxidants [21], anticancer agents [22], and antimicrobial agents [23], etc. Due to their small size and high surface-to-volume ratio, which alters their chemical and physical properties when compared to bulk materials with similar chemical composition, nanostructure catalysts play significant roles in the synthesis of organic materials. These properties of nanocatalysts also differ from bulk material, including mechanical, biological, and superior catalytic activity, thermal conductivity, electrical

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conductivity, optical absorption, and melting point [2]. Metal oxides are materials found in nature and used in many things, such as pigments [24], catalysts, photo-catalyst [25], energy storage [26], adsorbents [27], and sensors [28]. Metal oxides nanoparticle and their nanocomposite are synthesized as a catalyst in organic synthesis. Some of them are ZnO [29], CuO [7], Fe_3O_4 [30], SiO_2 [31], TiO_2, etc. In recent literature, the metal oxide is used as a nanocatalyst [32], ZnO nanocatalyst used to synthesis of 3,4-dihydropyrimidin-2(1H)-(thio)one derivatives [29], Fe_3O_4@SiO_2@IL nanoparticle used as the synthesis of furans derivatives [30], SiO_2@Im-Fc[OAc] efficient nanocatalyst for synthesis of naphthopyran derivatives [31], $CuFe_2O_4$ Nanoparticles as a Catalyst for the synthesis of 2,3-Benzopyrrole and 1,3-diazole derivative [7]. Among them, TiO_2 nanocatalyst has versatile applications in the physical, inorganic, and organic field. It mostly exhibits Lewis acidic characteristics, acting as an acid catalyst for all reactions and as a photocatalyst for strong redox reactions occurring at low temperatures. The catalytic performance of TiO_2 depends not only on the geometric properties but also on the electronic properties [33]. TiO_2 in Anatase and rutile form are the most studied polymorphs of TiO_2 for solar-driven applications such as photocatalysis, deoxygenation, hydrogenation [34], esterication [35], and visible light-induced organic transformation [36]. In the recent decade, TiO_2 nanocatalyst used in various organic synthesis, hydrogenation of 1,3-butadiene [34] synthesis of new Heterocycles Benzothiazole-Linked Pyrrolidin-2-One [37] synthesis of benzothiazoles bearing substituted pyrrolidine-2-ones [38] synthesis of novel antipyrine based α-amino phosphonates [39]. In this work, we synthesized anatase TiO_2 nanocatalyst by sol-gel method and used it in the synthesis of indole and furan derivatives, a newly desired product investigation under anti-microbial activity. TiO_2 nanocatalysts regenerate after five cycles with near about 60% efficiency.

2. Material and method

2-Propanol $(CH)_2CHOH$, 99%) and Muriatic acid (HCl, 40%) were purchased from CDH. Titanium tetraisopropoxide ($Ti[OCH(CH_3)_2]_4$, 98%) was purchased from Merck. None of the compounds were further purified before usage. The products' melting points were determined using an open capillary's thermal melting point instrument. On an FTIR (Bruker Alpha II) spectrophotometer, KBr pellets were used to generate FT-IR spectra. JEOL Delta□550 spectrometer was used to measure ^{1}HNMR spectra in $CDCl_3$. Nanoparticle SEM data was carried out in the ZEISS instrument. XRD analysis of nanoparticles is done with the help of Bruker D8 Advance diffractometer.

2.1. Preparation of TiO_2 nanoparticles

60 mL of isopropyl alcohol and 15 mL of the precursor titanium isopropoxide (TTIP) were combined and agitated for 45 minutes. After that, 15 mL of a 1:1 solution of deionized water and isopropyl alcohol was carefully added to the TTIP mixture to create a colloidal solution while vigorously stirring. After bringing the acquired colloidal solution's pH level to 3, the TiO_2 nanoparticles were dried in an oven at 110°C for three hours, and the resulting compound was calcined at 500°C for 4hr [40].

2.1.2. Characterization of nanomaterial

2.1.2.1. X-ray diffraction

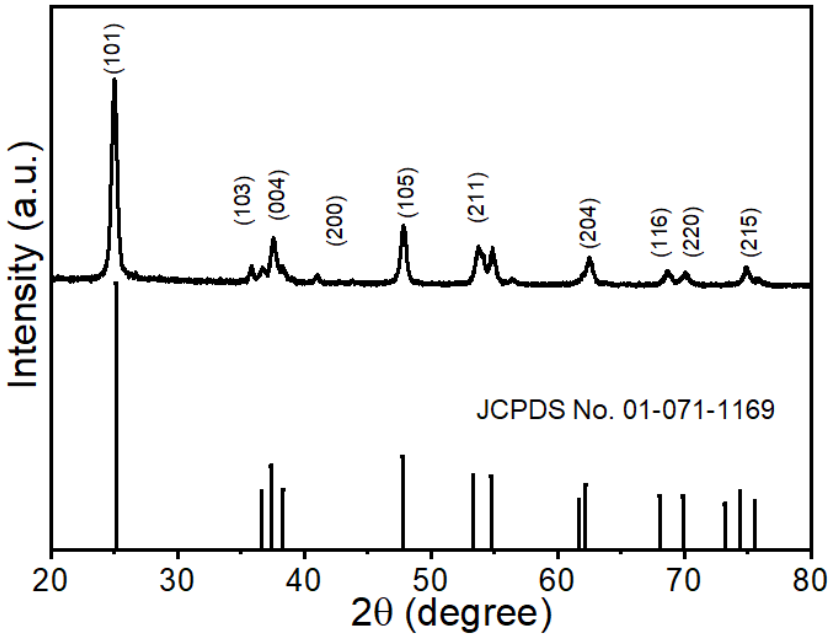


Figure 1. XRD of TiO_2 Nanoparticle

The X-ray diffraction of TiO_2 nanoparticles was carried out to determine structural properties (Figure 1.) The pattern shows peaks at 25.01º (101), 36.56º (103), 37.60º (004), 47.84º (200), 53.84º (105), 54.78º (211),

62.55º, (204), 68.67º (116), 70.20º (220), and 75.03º (215) display the occurrence of tetragonal anatase TiO2 structure [JCPDS No. 01-071-1169] and its decent crystalline nature [41]. The crystallite size (D) was calculated for maximum intensity peak at 2θ=25.01º, (101) Plane by using the Debye–Scherrer equation (D=Kλ/βcosθ), where crystallite size is D (nm), k is a constant (0.94), the wavelength of the X-ray radiation is λ (CuKα=1.54 Å), full width at half maximum is β for most intense peaks, and Bragg's angle is θ. The crystallite size for the (101) plane was 19.49 nm.

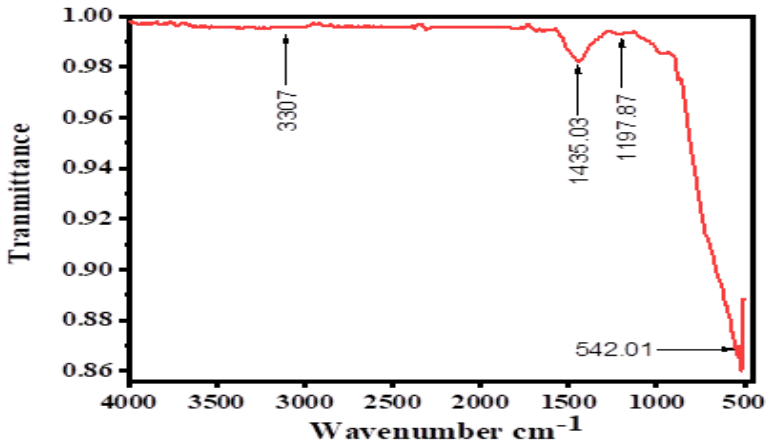


Figure 2. FTIR of TiO_2 Nanoparticle

2.1.2.2. FTIR analyses

The FTIR analyses of TiO_2 nanoparticle was performed (Figure 2) to determine the stretching and bending vibrations of the element present in functional groups. As a result, TiO_2 nanoparticles show the characteristic absorption band at 542.01 cm^{-1}, 1197.60 cm^{-1}, 1435.29 cm^{-1}, and 2307.24 cm^{-1} associated with Ti-O-Ti bond, stretching and bending vibrations of the water molecule, and surface adsorbed hydroxyl groups respectively [42].

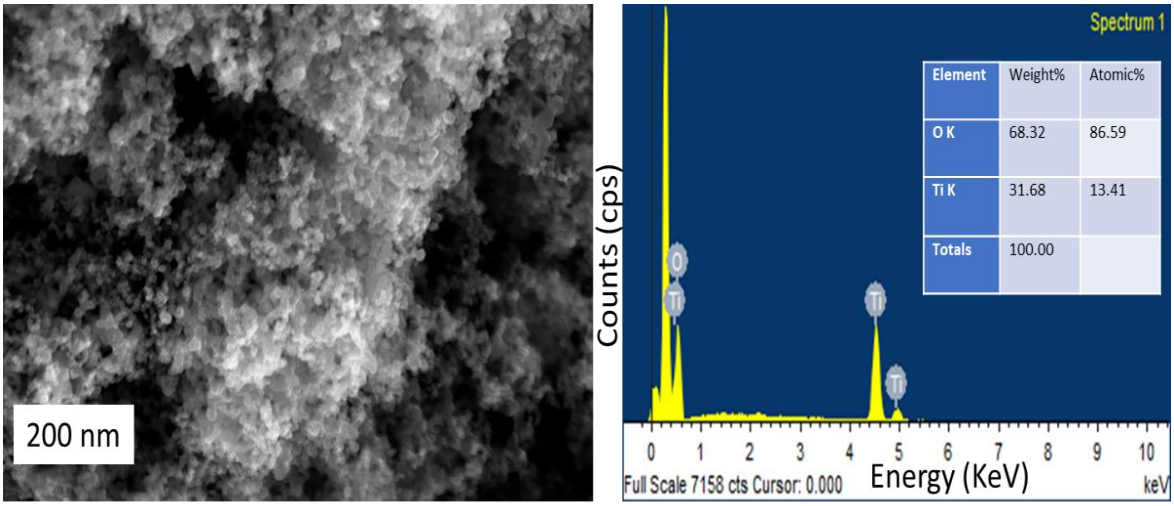


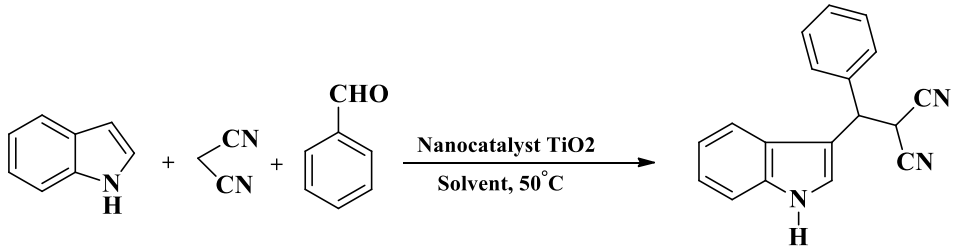
Fig. 3. FESEM and EDX analysis of TiO_2 Nanoparticle

2.1.2.3. FESEM and EDX analysis of nanomaterial

The FESEM was performed (Figure 3) for analysis of the surface morphology of anatase TiO_2 nanoparticle. SEM image of TiO_2 nanoparticle shows agglomerated spherical shape particles [41]. In addition, EDX analysis of TiO_2 nanoparticles was carried out, which exhibits elemental composition Ti (43.41%) and O (56.59%) peaks in the prepared anatase TiO_2 nanoparticle.

2.2. Method of preparation, table, and spectral data of synthesized compound

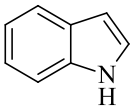
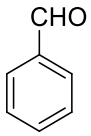
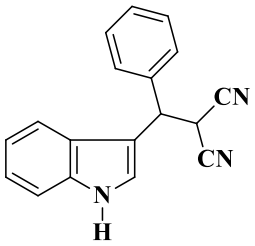
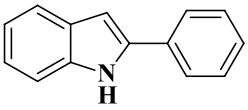
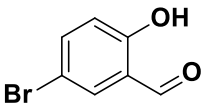
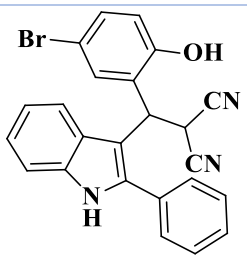
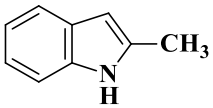
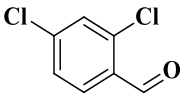
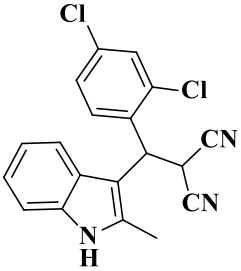
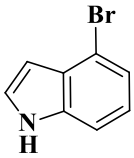
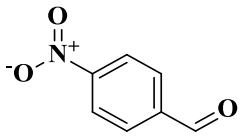
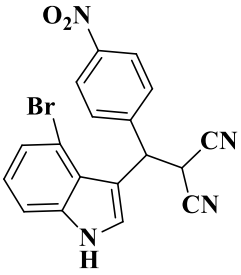
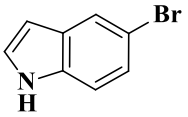
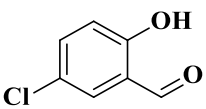
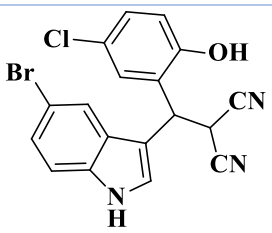
Take 100 ml round bottom flask, and mix 1 mM aldehyde derivative and 1 Mm of malononitrile with ethanol solvent; for 15 minutes at 50^0C. After that, put 1 mM indole derivative in the solution and continue heating and condensation for 1 hr. During the reaction, TLC was done in 15 minutes time intervals. When all the reactants were used up, the reaction was stopped. After the reaction, separate the compound with ethyl acetate and water in a separating funnel. We get two layers: the organic layer containing our product separating the organic layer from water which has the nanoparticle part. As the reaction was finished, all the synthesized compound's spectral data was gathered. After the complete synthesis of the desired compound, a series of Various 2((1H-Indole-3yl)(Phenyl)methyl) malononitrile analogs were produced from different indole and aromatic aldehydes, as shown in Table 1.



2-((1*H*-indol-3-yl)(phenyl)methyl)malononitrile

Scheme 1

Table 1. 2((1H-Indole-3yl) (Phenyl) methyl) malononitrile and its derivatives

S.N.	Indole	Malono-nitrile	Aldehyde	Product	Color	Y %
a					Saffron	92
b	 **2-phenyl-1*H*-indole**		 **5-Bromo salicylaldehyde**		Yellow	90
c	 **2 methyl indole**		 **2,4- dichloro benzaldehyde**		Mustard yellow	89
d	 **4- Bromo indole**		 **4- nitro benzaldehyde**		Dark brown	85
e	 **5- Bromo indole**		 **5- chloro salicylaldehyde**		Brown	83

Y = Yield

Table 2. Optimization of reaction conditions for scheme 1

Sr. No.	Solvent	Catalyst	Time (Hr)	Yield (%)
1	EtOH	TiO_2	1	90
2	EtOH	-	3	70
3	1,4 Dioxane	TiO_2	1.5	75
4	1,4 Dioxane	-	4	60
5	MeOH	TiO_2	2	72
6	MeOH	-	3	60
7	Acetone	TiO_2	2	70
8	Acetone	-	4	65

2.2.1. Spectral data of synthesized compound

a) 2-((1H-Indol-3-yl) (phenyl)methyl)malononitrile

Yield: 92 %; m.p.: 76–780C.
IR (KBr, ν, cm-1): 3345, 3058, 3030, 2881, 2360, 2262.
^{1}H NMR (CDCl3) δH (ppm): d 4.48 (d, J=6.4 Hz, 1H, CH), 4.95 (d, J=6.4Hz, 1H, CH), 7.10 (t, J = 7.2 Hz, 1H), 7.23–7.49 (m, 9H, ArH), 8.30 (s, 1H, NH).
MS: m/z: 271.11 (100.0%), 272.11 (20.6%), 273.12 (1.8%) Calculated analysis for $C_{18}H_{13}N_3$(271.32) C 79.68, H 4.83, N 15.49; Found C 79.80, H 4.66, N 15.54

b) 2-((5-bromo-2-hydroxyphenyl)(2-phenyl-1H-indol-3-yl) methyl) malononitrile

Yield: 90 %; m.p.: 95-97 °C;
IR (KBr, ν, cm-1) 3385, 3159, 3009, 2368, 2199. ^{1}H NMR (500 MHz, CDCl3) δH (ppm): 4.10 (d, J = 6.0 Hz, 1H, CH), 4.27 (d, J = 5.6 Hz, 1H, CH), 5.53 (s J=4.5Hz, 1H) ,6.90–7.92(m, 12H, ArH), 8.38 (s, 1H, NH);
MS: (m/z) 443 (100%). m/z: 271.11 (100.0%), 272.11 (20.6%), 273.12 (1.8%) Calculated analysis for $C_{18}H_{13}N_3$(271.32) C 79.68, H 4.83, N 15.49; Found C 79.80, H 4.66, N 15.54

c) 2-((2,4-dichlorophenyl)(2-methyl-1H-indol-3-yl) methyl) malononitrile

Yield: 89%; m.p.: 158-1610C.
IR (KBr, ν, cm-1): 3411, 3059, 2899, 2256, 2219.
^{1}H NMR (500 MHz, CDCl3): 2.39 (s J=2-3Hz 3H) 4.15 (d, J = 6.0 Hz, 1H, CH), 4.28 (d, J = 5.6 Hz, 1H, CH), 7.10 (t, J = 7.2 Hz, 1H), 7.20–7.62 (m, 7H, ArH), 8.38 (s, 1H, NH) ppm.
MS: (m/z) 354 (100%) 355(81%), 353(20%).
Calculated analysis for $C_{19}H_{13}Cl_2N_3$(354.23) C 64.42, H 3.70, Cl 20.02, N 11.86 Found C 64.45, H 3.77, Cl 20.06, N 11.87.

d) 2-((4-bromo-1H-indol-3-yl)(4-nitrophenyl)methyl)malononitrile

Yield:85%; M.p.: 82–840C;
IR (KBr, ν, cm-1) 3385, 3059, 2880, 2258, 2220.
^{1}H NMR (500 MHz, CDCl3) δH (ppm) d 4.36 (d, J = 6.4 Hz, 1H, CH), 4.94 (d, J= 6.4Hz,1H, CH), 7.12(t, J = 7.2 Hz, 1H), 7.06–8.25 (m, 8H, ArH), 9.91 (s, 1H, NH);
MS: (m/z) 394 (100%).
Calculated analysis for $C_{18}H_{11}BrN_4O_2$(394.01) C 54.70, H 2.81, Br 20.22, N 14.18, O 8.10
Found C 54.71, N 14.18, H 2.85, Br 20.26, O 8.10.

e) 2-((5-bromo-1H-indol-3-yl)(5-chloro-2-hydroxyphenyl)methyl)malononitrile

Yield: 83%; m.p.:94-97 °C;
IR (KBr, ν, cm-1) 3385, 3159, 3009, 2258, 2210.
^{1}H NMR (500 MHz, CDCl3) δH (ppm): d 4.16 (d, J = 6.4 Hz, 1H, CH), 4.29 (d, J = 6.4 Hz, 1H, CH), 5.03 (s J=4.5Hz, 1H) 7.03–8.90 (m, 8H, ArH), 10.01 (s, 1H, NH); MS: (m/z) (%) 398.9 (100%). Calculated analysis for $C_{18}H_{11}BrClN_3O$ (398.98) C 53.96, H 2.77, Br 19.94, Cl 8.85, N 10.49, O 3.99
Found C 53.96, H 2.87, Br 19.98, Cl 8.87 N 10.50, O 3.96

3. Result and Discussion

TiO_2 nanoparticles were synthesized by the reported protocol with some modifications. All the characteristic data of TiO_2 nanoparticles show the high purity of synthesized nanoparticles, and the size of the nanoparticle was determined with the help of FESEM, which shows the nanoscale production of TiO_2 nanoparticles. The EDX spectra show the Ti and O FTIR and XRD spectra confirming the production of TiO_2 nanoparticles. This synthesized TiO_2 was used for the catalysis purpose for the synthesis of 2((1H-Indole-3yl) (Phenyl)methyl) malononitrile derivative as these particles have more surface area they act as efficient catalysts. The reaction time was less than conventional synthesis methods, and the catalysts were recoverable. The catalyst was quickly removed from the reaction mixture and reused again after a simple purification process.

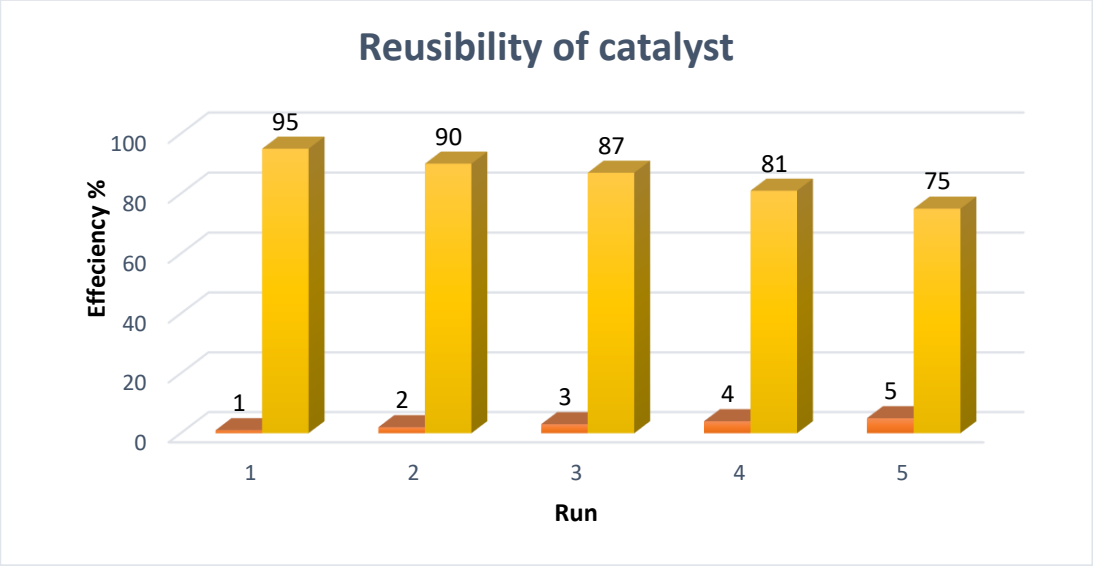


Figure 4. Reusability of TiO_2 Nanocatalyst

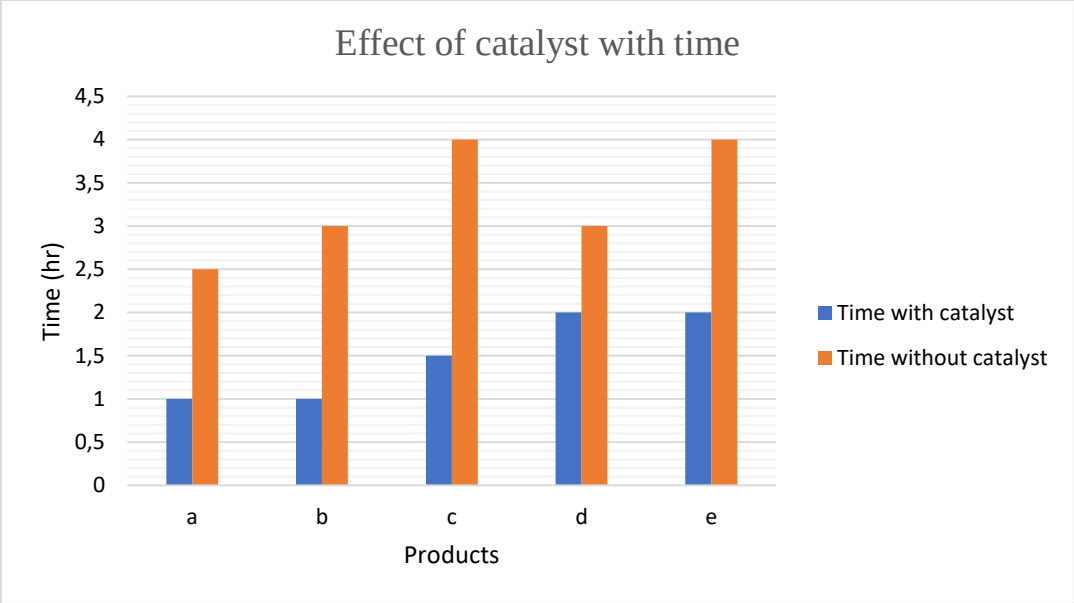


Figure 5. Time with and without TiO_2 Nanocatalyst

In order to prove the reusability of the catalyst, a separation test was performed. The catalyst was separated from the reaction mixture using a separating funnel. The progress of the reaction was monitored after the removal of the catalyst and without the catalyst indicating that the catalyst was stable under the reaction conditions and could be reused without significant loss of its activity. We check the reusability of the catalyst in five consecutive runs and observe only 20% loss in yield percent. Figures 4 and 5 show the reusability of the catalyst and without it.

4. Conclusion

Here we have successfully synthesized 2((1H-Indole-3yl) (Phenyl)methyl)malononitrile derivative by utilizing TiO_2 nanomaterial. Since the reaction conditions were not harsh and the use of less hazardous solvents, thus, this reaction may be classified as a green chemical reaction. The overall enhanced efficacy, higher yield, fast reaction completion, and effortless product isolation reported in this work were all achieved using TiO_2 nanoparticles. TiO_2 nanoparticles used in the reaction have more surface area, helping them to interact with the active site of reagents to accelerate reaction initiation and faster reaction completion. This TiO_2 nano-catalyst can be quickly recovered and reused for future reactions. The characterization of different malononitrile derivatives in this work, done with the help of FT-IR, 1H-NMR, and MS spectroscopy, strongly supports the methodology used and validates the efficacy of vindicated organic synthesis

Acknowledgments

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References

1- P. Phukan, S. Agarwal, K. Deori, D. Sarma, Zinc Oxide Nanoparticles Catalysed One -Pot Three-Component Reaction : A Facile Synthesis of 4-Aryl-NH-1, 2, 3-Triazoles, *Catal. Letters*, **2020**, *150* (8), 2208–2219.

2- M.M. Khodaei, A. Alizadeh, M. Haghipour, Supported 4-Carboxybenzyl Sulfamic Acid on Magnetic Nanoparticles as a Recoverable and Recyclable Catalyst for Synthesis of 3,4,5-Trisubstituted Furan-2(5H)-one derivatives, *J. Organomet. Chem.*, **2018**, *870*, 58–67.

3- A. Chanderiya, A. Roy, R. Das, Synthesis of 3,4-Dihydropyrano[c]Chromene Derivatives Using Porous Copper Oxide as Nanocatalyst and Their Electrochemical Study, *Mediterr. J. Chem.*, **2022**, *12* (2), 201–209.

4- W.H. Zhang, M. N. Chen, Y. Hao, X. Jiang, X.L. Zhou, Z.H. Zhang, Choline Chloride and Lactic Acid: A Natural Deep Eutectic Solvent for One-Pot Rapid Construction of Spiro[Indoline-3,4′-Pyrazolo[3,4-b]Pyridines], *J. Mol. Liq.*, **2019**, *278*, 124–129.

5- N. M. Evdokimov, A.S. Kireev, A.A. Yakovenko, M.Y. Antipin, I.V. Magedov, A. Kornienko, One-Step Synthesis of Heterocyclic Privileged Medicinal Scaffolds by a Multi-component Reaction of Malononitrile with Aldehydes and Thiols, *J. Org. Chem.*, **2007**, *72* (9), 3443–3453.

6- P. Singh, P. Yadav, A. Mishra, S.K. Awasthi, Green and Mechanochemical One-Pot Multi-component Synthesis of Bioactive 2-Amino-4 H-Benzo[b]Pyrans via Highly Efficient Amine-Functionalized SiO_2@Fe_3O_4 Nanoparticles, *ACS Omega*, **2020**, *5* (8), 4223–4232.

7- A.V. Nakhate, G.D. Yadav, Hydrothermal Synthesis of $CuFe_2O_4$ Magnetic Nanoparticles as Active and Robust Catalyst for N-Arylation of Indole and Imidazole with Aryl Halid, *ChemistrySelect*, **2017**, *2* (8), 2395–2405.

8- G. Mohammadi Ziarani, R. Moradi, T. Ahmadi, N. Lashgari, Recent Advances in the Application of Indoles in Multi-component Reactions, *RSC Adv.*, **2018**, *8* (22), 12069–12103.

9- W. Yan, S.S. Zhao, Y.H. Ye, Y.Y.; Zhang, Y. Zhang, J.Y. Xu, S.M. Yin, R.X. Tan, Generation of Indoles with Agrochemical Significance through Biotransformation by Chaetomium Globosum, *J. Nat. Prod.*, **2019**, *82* (8), 2132–2137.

10- M.M. Heravi, Z. Amiri, K. Kafshdarzadeh, V. Zadsirjan, Synthesis of Indole Derivatives as Prevalent Moieties Present in Selected Alkaloids, *RSC Adv.*, **2021**, *11* (53), 33540–33612.

11- T. Shaikh, A. Sharma, H. Kaur, Ultrasonication-Assisted Synthesis of 3-Substituted Indoles in Water Using Polymer Grafted ZnO Nanoparticles as Eco-Friendly Catalyst, *ChemistrySelect*, **2019**, *4* (1), 245–249.

12- T. Lee; F. Rostami, $H_3PW_{12}O_{40}$/SBA-15 for the Solventless Synthesis of 3-Substituted Indoles, *Catalysts*, **2019**, *9* (5), 409.

13- M. Zhang, Y.h. Liu, Z.R. Shang, H.C. Hu, H.Z. Zhang, Supported Molybdenum on Graphene Oxide/Fe_3O_4: An Efficient, Magnetically Separable Catalyst for One-Pot Construction of Spiro-Oxindole Dihydropyridines in Deep Eutectic Solvent under Microwave Irradiation, *Catal. Commun.*, **2017**, *88*, 39–44.

14- N. M. Ghohe, R. Tayebee, M.M. Amini, A. Osatiashtiani, A.M. Isaacs, F.A. Lee, $H_5PW_{10}V_2O_{40}$@VO_x/SBA-15-NH_2 Catalyst for the Solventless Synthesis of 3-Substituted Indoles, *Tetrahedron*, **2017**, *73* (40), 5862–5871.

15- I. Choi, H. Chung, J.W. Park, Y.K. Chung, Active and Recyclable Catalytic Synthesis of Indoles by Reductive Cyclization of 2-(2-Nitroaryl) Acetonitriles in the Presence of Co–Rh Heterobimetallic Nanoparticles with Atmospheric Hydrogen under Mild Conditions, *Org. Lett.*, **2016**, *18* (21), 5508–5511.

16- H. Ramshini, B. Mannini, K. Khodayari, A. Ebrahim-Habibi, A.S. Moghaddasi, R. Tayebee, F. Chiti, Bis(Indolyl)Phenylmethane Derivatives Are Effective Small Molecules for Inhibition of Amyloid Fibril Formation by Hen Lysozyme, *Eur. J. Med. Chem.*, **2016**, *124*, 361–371.

17- M. Esmaeilpour, J. Javidi, F. Dehghani, F.A. Nowroozi Dodeji, Green One-Pot Three-Component Synthesis of Tetrahydrobenzo[b]Pyran and 3,4-Dihydropyrano[c]Chromene Derivatives Using a Fe_3O_4@SiO_2-Imid-PMAn Magnetic Nanocatalyst under Ultrasonic Irradiation or Reflux Conditions, *RSC Adv.*, **2015**, *5* (34), 26625-26633.

18- H.L. Qin, J. Liu, W.Y. Fang, L. Ravindar, K.P. Rakesh, Indole-Based Derivatives as Potential Antibacterial Activity against Methicillin-Resistance Staphylococcus Aureus (MRSA), *Eur. J. Med. Chem.*, **2020**, *194*, 112245.

19- M.A. Ghasemzadeh, R. Bakhshali-Dehkordi, Novel and Green Preparation of Fe_3O_4@TiO_2-Immobilized-ILs Based on DABCO for Highly Efficient Synthesis of Primido[4,5-d]Pyrimidines, *ChemistrySelect*, **2020**, *5* (29), 9097–9104.

20- A. Roy, A.K. Bahe, A.A. Chanderiya, H. Dangi, P. Mishra, A.K. Mishra, R. Das, Synthesis of Nitrogen-and Oxygen-Containing Heterocyclic Compounds Using Nanocatalyst: A Review, *J. Turkish Chem. Soc. Sect. A Chem.*, **2021**, *8* (3), 851–862.

21- M. Shen, F. Zhang, T. Hong, J. Xie, Y. Wang, S. Nie, M. Xie, Comparative Study of the Effects of Antioxidants on Furan Formation during Thermal Processing in Model Systems, *Lwt*, **2017**,

75, 286–292.
22- A.F. Kassem, I.F. Nassar, M.T. Abdel-Aal, M.H. Awad, W.A. El-Sayed, Synthesis and Anticancer Activity of New ((Furan-2-Yl)-1,3,4-Thiadiazolyl)-1,3,4-Oxadiazole Acyclic Sugar Derivatives, *Chem. Pharm. Bull.*, **2019**, *67* (8), 888–895.
23- S. Malladi, R.V. Nadh, K.S. Babu, P.S. Babu, Synthesis and Antibacterial Activity Studies of 2,4-Di Substituted Furan Derivatives, *Beni-Suef Univ. J. Basic Appl. Sci.*, **2017**, *6* (4), 345–353.
24- T.Srichumpong, S. Angkulpipat, S. Prasertwong, S. Thongpun, N.Teanchai, C. Veronesi, P. Suputtamongkol, K. Leonelli, C. Heness, D. Chaysuwan, Effect of the Crystallisation Time and Metal Oxide Pigments on Translucency and the Mechanical and Physical Properties of Mica Glass-Ceramics, *J. Non. Cryst. Solids*, **2020**, *528* (October 2019), 119730.
25- V. Jeyalakshmi, R. Mahalakshmi, K. Ramesh, P.V.C. Rao, V.N. Choudary, K. Thirunavukkarasu, K.R. Krishnamurthy, B. Viswanathan, Metal Oxides as Photo Catalysts: Modified Sodium Tantalate as Catalyst for Photo Reduction of Carbon Dioxide, *Mol. Catal.*, **2018**, *451*, 105–113.
26- S. Fang, D. Bresser, S. Passerini, Transition Metal Oxide Anodes for Electrochemical Energy Storage in Lithium- and Sodium-Ion Batteries, *Adv. Energy Mater.*, **2020**, *10* (1).
27- R.K. Upadhyay, N. Soin, S.S. Roy, Role of Graphene/Metal Oxide Composites as Photocatalysts, Adsorbents and Disinfectants in Water Treatment: A Review, *RSC Adv.*, **2014**, *4* (8), 3823–3851.
28- J.Tang, F. Redl, Y. Zhu, T. Siegrist, L.E. Brus, L.M. Steigerwald, An Organometallic Synthesis of TiO_2 Nanoparticles, *Nano Lett.*, **2005**, *5* (3), 543–548.
29- A. Hassanpour, R.H. Khanmiri, J. Abolhasani, ZnO Nanoparticles as an Efficient, Heterogeneous, Reusable, and Ecofriendly Catalyst for One-Pot, Three-Component Synthesis of 3,4-Dihydropyrimidin-2(1 H)-(Thio)one derivatives in Water, *Synth. Commun.*, **2015**, *45* (6), 727–733.
30- M. Shirzaei, E. Mollashahi, M. Taher Maghsoodlou, M. Lashkari, Novel Synthesis of Silica-Coated Magnetic Nanoparticles Based on Acidic Ionic Liquid, as a Highly Efficient Catalyst for Three Component System Leads to Furans Derivatives, *J. Saudi Chem. Soc.*, **2020**, *24* (2), 216–222.
31- R.T.M. Gholamhosseini-nazari, Novel Ferrocene-Based Ionic Liquid Supported on Silica Nanoparticles as Efficient Catalyst for Synthesis of Naphthopyran Derivatives, *Res. Chem. Intermed.*, **2017**, *43* (12), 7105–7118.
32- R. Tayebee, M.M. Amini, N. Abdollahi, A. Aliakbari, S. Rabiei, H. Ramshini, Magnetic Inorganic-Organic Hybrid Nanomaterial for the Catalytic Preparation of Bis(Indolyl)Arylmethanes under Solvent-Free Conditions: Preparation and Characterization of $H_5PW_{10}V_2O_{40}$/Pyridino-Fe_3O_4 Nanoparticles, *Appl. Catal. A Gen.*, **2013**, *468*, 75–87.
33- M. Boominathan, N. Pugazhenthiran, M. Nagaraj, S. Muthusubramanian, S; Murugesan, N. Bhuvanesh, Nanoporous Titania-Supported Gold Nanoparticle-Catalyzed Green Synthesis of 1,2,3-Triazoles in Aqueous Medium, *ACS Sustain. Chem. Eng.*, **2013**, *1* (11), 1405–1411.
34- X. Jiang, Y. Liu, H. Hao, Y. Xu, J. Huang, D. Sun, Q. Li, Rape Pollen-Templated Synthesis of C,N Self-Doped Hierarchical TiO_2 for Selective Hydrogenation of 1,3-Butadiene, *ACS Sustain. Chem. Eng.*, **2018**, *6* (1), 882–888.
35- Z. Li, R. Wnetrzak, W. Kwapinski, J.J. Leahy, Synthesis and Characterization of Sulfated TiO_2 Nanorods and ZrO_2/TiO_2 Nanocomposites for the Esterification of Biobased Organic Acid. *ACS Appl. Mater. Interfaces* **2012**, *4* (9), 4499-4505.
36- Y. Yamazaki, M. Fujitsuka, S. Yamazaki, Effect of Organic Additives during Hydrothermal Syntheses of Rutile TiO_2 Nanorods for Photocatalytic Applications, *ACS Appl. Nano Mater.*, **2019**, *2* (9), 5890–5899.
37- A. Elsanousi, Y. Riadi, O. Ouerghi, M.H. Geesi, Synthesis, Characterization of TiO_2-Based Nanostructure as Efficient Catalyst for the Synthesis of New Heterocycles Benzothiazole-Linked Pyrrolidin-2-One: Catalytic Performances Are Particle's Size Dependent, *Polycycl. Aromat. Compd.*, **2022**, *0* (0), 1–14.
38- M.H. Geesi, O. Ouerghi, O. Dehbi, Y. Riadi, Metal-Doped TiO2nanocatalysts in an MX_2/Urea Mixture for the Synthesis of Benzothiazoles Bearing Substituted Pyrrolidin-2-Ones: Enhanced Catalytic Performance and Antibacterial Activity, *J. Environ. Chem. Eng.*, **2021**, *9* (4), 105344.
39- S. Shaikh, I. Yellapurkar, M.M.V. Ramana, Ultrasound Assisted One-Pot Synthesis of Novel Antipyrine Based α-Aminophosphonates Using TiO_2/Carbon Nanotubes Nanocomposite as a Heterogeneous Catalyst, *React. Kinet. Mech. Catal.*, **2021**, *134* (2), 917–936.
40- S.S. Al-Taweel, H.R. Saud, New Route for Synthesis of Pure Anatase TiO_2 Nanoparticles via Utrasound-Assisted Sol-Gel Method, *J. Chem. Pharm. Res.*, **2016**, *8* (2), 620–626.
41- M. Chandra Sekhar, B. Purusottam Reddy, S.V. Prabhakar Vattikuti, G. Shanmugam, C.H. Ahn, S.H. Park, Structural, Magnetic, and Catalytic Properties of Mn-doped Titania Nanoparticles Synthesized by aSol–Gel Process, *J. Clust. Sci.*, **2018**, *29* (6), 1255–1267.
42- B. Manikandan, K. Murali, R. John, R. Optical, Morphological and Microstructural Investigation of TiO_2 nanoparticles for Photocatalytic Application, *Iran. J. Catal.*, **2021**, *11* (1), 1–11.