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ORIGINAL ARTICLE

Nano γ-Al_2O_3: Enhancement of catalytic performance in the synthesis of Bis (Indolyl) Methanes

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Abstract

The synthesis of bis(indolyl)methane derivatives in the reaction between indoles and aldehydes was carried out in a short reaction time (10-20 minutes) with good yield (78-96%) by using 1 mol% of nanoγ-Al_2O_3in H_2O as a green solvent at room temperature. Moreover, we usednanoγ-Al_2O_3 as an effortlessly accessible, less costly, and possible under eco-friendly conditions catalyst in this method. Consequently, this method presented significant benefits containing a low amount of the catalyst, purification of target molecules by non-chromatographic process, use of recyclability of the catalyst, simply efficient, green, and suitable for the synthesis of a broad range of bis(indolyl)methane derivatives. This method achieves to have a numerous scope concerning the difference in the aldehydes and indoles. Moreover, water was the only by-product, which added to its attractiveness. Bis(indolyl)methane derivatives have a varied range of bioactive metabolites of native and marine sources. The hydrothermal and chemical stability of γ-Al_2O_3 is a severe point for catalytic applications. The melting point, FT-IR, and ^{1}H NMR spectra of the selected product showed that these products were synthesized successfully.

Keywords: *Aldehydes; Bis (Indolyl) Methanes; Indoles; Nano γ-Al_2O_3; Water Solvent.*

How to cite this article

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INTRODUCTION

Nanoscience is defined as the investigation of phenomena on a scale of 1-100 nm. Nanometer-sized particles hold great potential for application in chemical, electronic, and mechanical industries, other than in applicable technologies containing magnetic materials, catalysts, superconductors, structural and engineering materials [1]. Metal oxide nanoparticles are interesting remarkable attention as they can change the possible unusual to conformist materials in numerous fields of solid-state chemistry. Metal oxide nanoparticles are being essentially applied as a heterogeneous nanocatalyst in various organic transformations as they enclosed high surface area than their corresponding bulk item [2-3].

Among the several transitions, alumina is recognized, γ-Al_2O_3 is possibly the most important with direct use as a catalyst and catalyst carrier in the automotive and oil sectors. The efficiency of this oxide may be found at a good combination of its textural properties such as the volume of the pores, the distribution of the size of the pores, surface area, and its acid/base characteristics that are primarily related to the local microstructure, surface chemical, and phase composition. However, the hydrothermal and chemical stability of γ-Al_2O_3 is a serious point for catalytic uses [4-6].

The focus on green chemistry using environmentally friendly reagents and reaction conditions is one of the most interesting advances in synthesizing broadly applied organic molecules [7-8]. Particular attention has been given to the use of water as a solvent favourable to organic reactions has received considerable attention

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in the field of organic synthesis as a result of its green identifications [9-13], and organic synthesis in aqueous media, suggesting important benefits for instance rate, improvement, and insolubility of the goal products, which simplifies their isolation by informal filtration [14].

The syntheses and the reactions of indoles have established considerable attention since numerous their derivatives happen in nature and display multipurpose biological activities [15]. Organic chemists are givingconsideration to synthesize several kinds of indole compounds, containingbis(indolyl)methanes [16], *β*-indolylnitro [17], *β*-indolylketone [18], and *β*-indolylalcohols [19]. Bis(indolyl) methanes has engrossed much consideration attention because of their synthetic as well as biological uses [20-22]. The most ubiquitous of the identified bioactive alkaloids are based on the indole tag [23-24]. These compounds are very active cruciferous boilding block employed for developing valuable estrogen metabolism and containing apoptosis in human cancer cells [25]. The most common process and some catalysts have been applied for this transformation containing $AlPW_{12}O_{40}$ [26], [PCBS] and [TCBDA] [27], $Cu_{1.5}PMo_{12}O_{40}$ [28], [Fe(III)(salen)]Cl [29], PEG-supported sulfonic acid [30], TiO_2 nanoparticles [31], PSFSI/SBA-15 [32], {Fe_3O_4@SiO_2@$(CH_2)_3$-Urea-SO_3H/HCl} [33], $[MIMPS]_3PW_{12}O_{40}$ and $[TEAPS]_3PW_{12}O_{40}$ [34] and catalyst-free condition [35].

As part of our continuing program focused on the improvement of facile approaches in organic reactions [36-42], herein we introduce nano*γ*-Al_2O_3 as an efficient and recyclable catalyst for the synthesis of bis(indolyl)methanes in the reaction between indoles with numerous aldehydes (Fig. 1).

MATERIALS AND METHODS

General methods

γ-Al_2O_3 nanoparticles were purchased from commercial centers. All of the chemicals and reagents were purchased from Merck and Aldrich. All reactions were observed by thin-layer chromatography (TLC) and all yields refer to isolated products by using silica gel F_{254} pre-coated sheets and were visualized by using a UV-lamp at a wavelength of 254 nm. Melting points were achieved on the Thermo Scientific apparatus in open capillary tubes and are uncorrected. ^1H was recorded in $CDCl_3$ by using tetramethylsilane (TMS) as the internal reference on a Bruker DRX-400 MHz spectrometer. Infrared spectra (FT-IR) of the reaction products were recorded on a Bruker FT-IR (WQF-510) spectrometer in KBr pellets.

A typical procedure for the synthesis of bis(indolyl) methanes catalyzed by nano γ-Al_2O_3

To a stirred aldehydes (1 mmol) and indoles (2 mmol) in water (3 mL) as a solvent was added 1 mol% catalytic amount of nano*γ*-Al_2O_3. Then, the reaction mixture was stirred at room temperature for an appropriate time (Table 2). The progress of the reaction was detected by TLC (*n*-hexane/ethyl acetate; 4 : 1). After the end of the reaction, the hot ethanol was added to the reaction mixture and the nano*γ*-Al_2O_3 catalyst was recycled for six successive runs without any noteworthy deactivation. At that moment, the reaction mixture was filtered, dried, and recrystallized from hot ethanol to eliminate any remaining reactants and dried, which resulted in precipitation of the desired product.

Spectral data for the selected product 3,3'-((4-Chlorophenyl)methylene)bis(1H-indole)

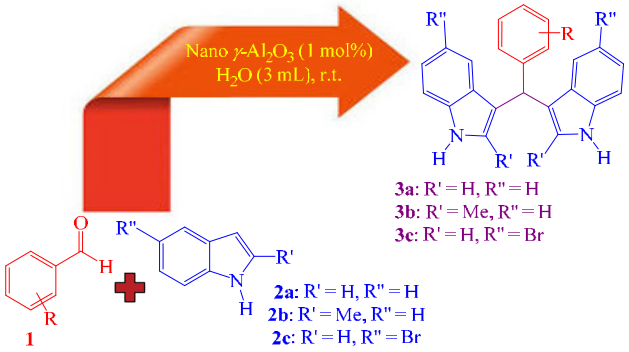


Fig. 1. Synthesis of bis(indolyl)methanes catalyzed by nano *γ*-Al_2O_3.

*(Table 2, **3c**)*: White solid, M.p.: 77-78°C; Yield: 98%; FT-IR (KBr)(υ_{max}, cm^{-1}): 3409, 1500,1462, 1157; ^{1}H NMR (400 MHz, $CDCl_3$): δ_{ppm} = 8.12 (s, 2H, –NH), 7.49-7.50 (d, 2H, *J* = 8.0 Hz, Ar–H), 7.37-7.39 (d, 2H, *J*= 8.0 Hz, Ar–H), 7.14-7.32 (dd, 4H, J_1 = 8.0 Hz and J_2 = 4.0 Hz, Ar–H), 7.14-7.17 (t, 2H, *J*= 6.0 Hz, Ar–H), 6.97-7.00 (t, 2H, *J* = 6.0 Hz, Ar–H), 6.68 (s, 2H, –CH), 5.98 (s, 1H, –CH aliphatic).

RESULTS AND DISCUSSION

To attain the optimum results in terms of yield and reaction time, we studied the effectiveness of several reaction media and catalyst amounts in the condensation reaction of 4-chlorobenzaldehyde and indole as a model. As revealed in Table 1, a substantial improvement of the reaction rate and enhancement of the yield of model product **3c** were detected when 1 mol% of nano*γ*-Al_2O_3 catalyst in water at room temperature was used (Table 1, entry 2). In the absence of nano*γ*-Al_2O_3 catalyst, no formation of the **3c** was identified even after 2 hours. Therefore, to afford the **3c**, the catalyst is required for the reaction under the above reaction conditions. To assess the effect of the catalyst concentration, the reaction was also conducted in the presence of numerous amounts of the catalyst (0.5 and 2 mol%) under similar reaction conditions (Table 1, entries 1 and 3). Decreasing the amount of the catalyst to 0.5 mol%, shrank the yield of the **3c**, whereas increasing the amount of the catalyst to 2 mol% did not increase the yield remarkably.

The model reaction was performed in various solvents such as water, acetonitrile, dichloromethane, ethanol, and ethyl acetate. From this investigation, it was confirmed that water is the best solvent to achieve this synthesis (Table 1, entry 2). Similar results were attained when ethanol was used as a solvent (Table 1, entry 6). Scince focus on green chemistry using mild environmental conditions has been one of the most attractive advances in the synthesis of organic compounds. Water as an optimal solvent for organic reactions has received considerable attention. Water is certainly the least expensive solvent among the many solvents used in organic synthesis. Lack of explosive, flammable, mutagenic and carcinogenic properties are satisfactory aspects of water in researches. In addition, water is confirmed as one of the suitable solvents in terms of environmentally friendly.

We also examined the model reaction at numerous temperatures to find out its influence on the enhancement of the reaction by using the optimized amount of catalyst (1 mol%) in water. The maximum reaction rate was achieved at room temperature as the optimum temperature for the synthesis of **3c**. When the reaction was heated to reflux condition, it did not further enhance the yield and shrinkage time of reaction.

We also assessed the number of necessary reactants in the synthesis of **3c**. It was found that maximum yield (90 %) was attained when the reaction was carried out using a 1:2 molar ratio of aldehydes *vis* indole under optimum reaction conditions.

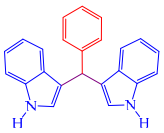
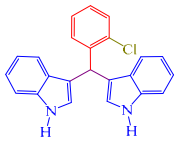
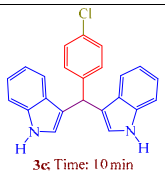
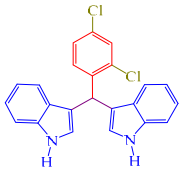
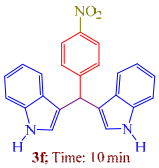
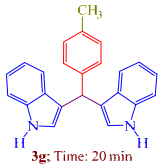
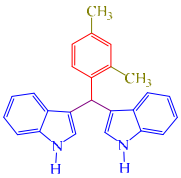
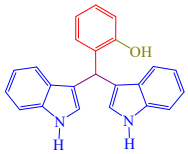
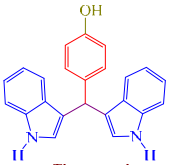
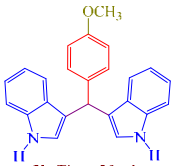
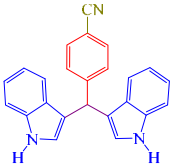
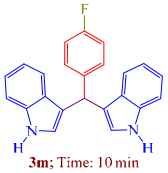
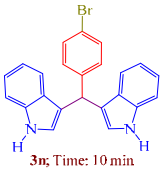
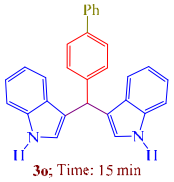
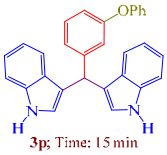
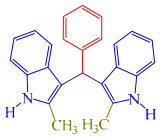
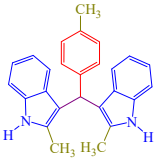
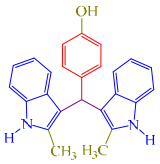
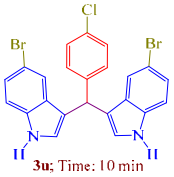
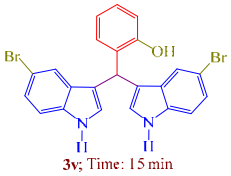
To find the synthetic scope of this reaction, a varied range of structurally numerous aldehydes were studied under this process to provide the corresponding bis(indolyl)methanesin appropriate yields. As revealed in Table 2, it can be established

Table 1. Reaction conditions evaluation for the synthesis of 3c.[a]

Entry	Amount of catalyst (mol%)	Solvent	Time (min)	Yield (%)[b]
1	0.5	H_2O	20	87
2	1	H_2O	10	90
3	2	H_2O	10	90
4	1	CH_3CN	20	89
5	1	CH_2Cl_2	20	87
6	1	C_2H_5OH	15	90
7	1	CH_3CO_2Et	15	88

Reaction condition: [a] 4-chlorobenzaldehyde (1 mmol; 0.140 g), indole (2 mmol; 0.234 g), r.t.; [b] Isolated yield.

Table 2. Synthesis of bis(indolyl)methanesby using nano γ-Al_2O_3 catalyst.[a, b]

 **3a**; Time: 10 min Yield: 93% M.p.: 146-148 °C	 **3b**; Time: 10 min Yield: 94% M.p.: 70-72 °C	 **3c**; Time: 10 min Yield: 90% M.p.: 77-78 °C
 **3d**; Time: 10 min Yield: 88% M.p.: 141-142 °C	 **3e**; Time: 10 min Yield: 96% M.p.: 141-143 °C	 **3f**; Time: 10 min Yield: 90% M.p.: 219-221 °C
 **3g**; Time: 20 min Yield: 80% M.p.: 92-93 °C	 **3h**; Time: 20 min Yield: 78% M.p.: 182-184 °C	 **3i**; Time: 15 min Yield: 85% M.p.: 341-343 °C
 **3j**; Time: 15 min Yield: 88% M.p.: 210-211 °C	 **3k**; Time: 20 min Yield: 82% M.p.: 185-187 °C	 **3l**; Time: 10 min Yield: 92% M.p.: 208-209 °C
 **3m**; Time: 10 min Yield: 92% M.p.: 73-75 °C	 **3n**; Time: 10 min Yield: 88% M.p.: 110-112 °C	 **3o**; Time: 15 min Yield: 90% M.p.: 247-248 °C
 **3p**; Time: 15 min Yield: 88% M.p.: 84-85 °C	 **3q**; Time: 10 min Yield: 95% M.p.: 245-247 °C	 **3r**; Time: 15 min Yield: 78% M.p.: 175-177 °C
 **3s**; Time: 15 min Yield: 88% M.p.: 238-240 °C	 **3t**; Time: 10 min Yield: 92% M.p.: 241-243 °C	 **3u**; Time: 10 min Yield: 95% M.p.: 146-148 °C	 **3v**; Time: 15 min Yield: 88% M.p.: 134-136 °C

Reaction condition: [a] aldehydes (1 mmol), indoles (2 mmol),nanoγ-Al_2O_3 catalyst (1 mol%), H_2O solvent (3 mL) r.t.; [b] Isolated yield.

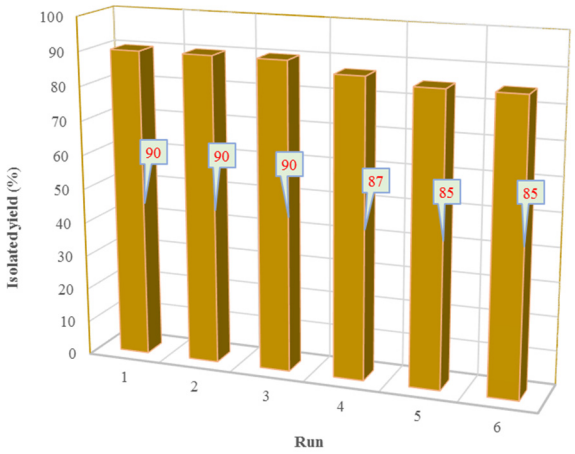


Fig. 2. Reusability studies of nano γ-Al_2O_3 in model reaction after 10 minutes.

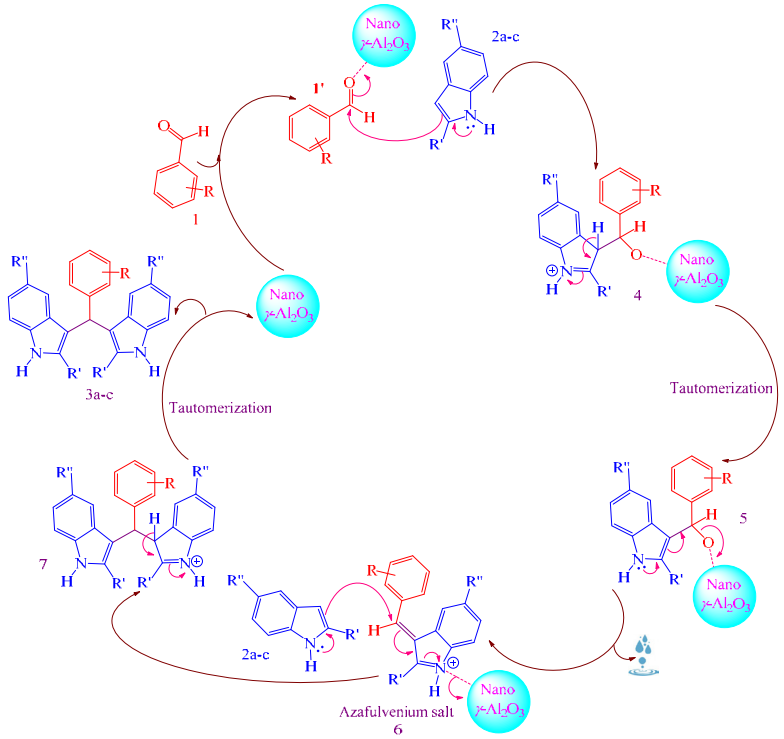
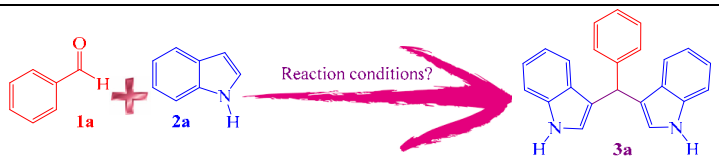


Fig. 3. Proposed mechanism for the synthesis of bis(indolyl)methanescatalyzed by nano γ-Al_2O_3.

that the presence of the electron-withdrawing groups on the aromatic ring can increase the reaction rate and, as a result, the reaction times are decreased and the yields are increased whereas the electron-releasinggroupspossess diverse effects. When 2-methyl indole and 5-bromoindole as a replacement for indole were used in the reaction, the reaction times shrank and the yields increased (Table 2, entries **3q-3v**).

The application of heterogeneous and recyclable catalysts is one of the greenest processes in chemical knowledge. Furthermore, the heterogeneous catalysts should not only be stable and active but also need informal separating and recycling for valuable uses [38]. For this intention, diethyl ether was added to the reaction

Table 3. Comparison of the effectiveness of nano γ-Al_2O_3 in the synthesis of 3a with other reported methods.



Entry	Reaction condition	Time (min)	Yield (%)[b]	Reported reference
1	Nano γ-Al_2O_3 (1 mol%), H_2O, r.t.	10	93	This work
2	Oxalic acid (10 mmol), H_2O, 80 °C	40	96	[44]
3	$AlPW_{12}O_{40}$ (2 mol%), CH_3CN, r.t.	15	92	[26]
4	*p*-sulfonic acid calix[4]arene (1 mol %), H_2O, 80 °C	20	85	[45]
5	$La(PFO)_3$ (5 mol%), C_2H_5OH, r.t.	30	90	[16]
6	HY zeolite (0.5 g), CH_2Cl_2, r.t.	120	80	[46]
7	P_2O_5 (0.86 g), solvent-free, r.t.	30	94	[47]
8	$Zr(DS)_4$ (0.1 mmol), H_2O, r.t.	25	94	[48]
9	SDS (small amount), H_2O, r.t.	150	95	[49]
10	I_2 (2 mmol), solvent-free, r.t.	10	72	[50]
11	Zeokarb-225 (0.5 g), CH_3CN, r.t.	7.5 h	95	[51]

[a]Reaction condition: benzaldehyde (1 mmol; 0.102 mL; 0.106 g), indole (2 mmol; 0.234 g); [b] Isolated yield.

mixture, and the solid catalyst was separated by filtration, washed in ethyl acetate, and dried at 100°C for 120 minutes, and lastly was reused for a similar reaction procedure. It is essential that catalysts could be recovered accurately and recycled, in contrast, shrinkage in the yield of the model product was detected in the course of the first recycle. Additionally, in the sixth run, it was established to be an insignificant shrinkage in the yield of **3c** in the standard reaction (Fig. 2). The small decrease in catalytic activity of nanoγ-Al_2O_3 most probably was due to the loss of catalyst during washing process. Thus, the smaller amount of catalysts was used to the next reaction run. To avoid the such mistake the amount of used reactants should be recalculated to the new mass of reused catalyst.

A suggested route for synthesizing bis(indolyl) methanes **3** catalyzed by nanoγ-Al_2O_3 is offered in Fig. 3. First, nanoγ-Al_2O_3 activates the carbonyl group of aldehydes **1** to afford intermediate **1'**. Then nucleophilic attack of indoles**2** to aldehydes**1'**to provide intermediate **4**. At that point, intermediate **4** tautomerized to intermediate **5** which elimination of one molecule of H_2O from intermediate **5** to give a zafulvenium salt **6**. In the next step, the nucleophilic attack of the second molecule of indole **2** to **6** to afford intermediate **7**, which finally tautomerized to bis(indolyl)methanes **3**.

To display the importance of the current work in comparison with the reported results in the literature, we shortened some of the results for the synthesis of **3a** in Table 3, which illustrations that nanoγ-Al_2O_3 can act as aproper catalyst with concerning the reaction time, temperature and shows broad applicability in terms of yield.

CONCLUSION

In summary, we have established a clean, efficient, and eco-friendly approach for synthesizing bis(indolyl)methanes in up to 96% yields, from aldehydes in combination with indoles in 1 : 2 molar ratios by using readily available nanoγ-Al_2O_3 as a catalyst. This synthetic catalyst process appears facile, worthy yields, workup procedure is informal and provides pure target molecules. We feel that this process is an appropriate addition to the presently reported approaches.

SUPPORTING INFORMATION

The supporting information contains spectral images of FT-IR, ^{1}H NMR, and ^{13}C NMR of selected products.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

[1] Verma P., Kumar Maheshwari S., (2019), Applications of Silver nanoparticles in diverse sectors. *Int. J. Nano Dimens*. 10: 18-36.

[2] Allaedini G., Masrinda Tasirin S., Aminayi P., Yaakob Z., Meor Talib M. Z., (2016), Carbon nanotubes via different catalysts and the important factors that affect their production: A review on catalyst preferences. *Int. J. Nano Dimens.* 7: 186-200.

[3] Sadat Madani S., Zare K., Ghoranneviss M., (2016), Role of growth temperature in CVD synthesis of Carbon nanotubes from Ni-Co bimetallic catalysts. *Int. J. Nano Dimens.* 7: 240-246.

[4] Majedi A., Davar F., Abbasi A. R., (2016), Metal-organic framework materials as nano photocatalyst. *Int. J. Nano Dimens.* 7: 1-14.

[5] Akbari F., Vahdat S. M., Khaksar S., (2021), Aqua mediated SnO_2 nanoparticles: A recyclable and benign catalyst for the synthesis of Quinoxalines. *Int. J. Nano Dimens*. 12: 44-51.

[6] Balakrishnan K., Murugesan N., (2021), Synthesis and characterization of SnO_2 nanoparticles by co-precipitation method. *Int. J. Nano Dimens*. 12: 76-82.

[7] Assi N., Mehrdad Sharif A. A., Manuchehri Naeini Q. S., (2014), Synthesis, characterization and investigation photocatalytic degradation of Nitro Phenol with nano ZnO and ZrO_2. *Int. J. Nano Dimens*. 5: 387-391.

[8] Rahmatinejad B., Abbasgholipour M., Mohammadi Alasti B., (2021), Investigating thermo-physical properties and thermal performance of Al_2O_3 and CuO nanoparticles in Water and Ethylene Glycol based fluids. *Int. J. Nano Dimens*. 12: 252-271.

[9] Qandalee M., Hatami M., Esmaeilzadeh A., Shojaeian A., Biparva P., (2014), Two component reaction for the synthesis of Quinolines in the presence of γ-Al_2O_3 and Cu/ZnO nanoparticles. *Int. J. Nano Dimens*. 5: 505-509.

[10] Montazeri N., (2015), Nano Al_2O_3: An efficient catalyst for the multi-component synthesis of Pyrano [2, 3-d] Pyrimidinone derivatives. *Int. J. Nano Dimens*. 6: 283-287.

[11] Pramod Charpe V., Ragupathi A., Sagadevan A., Chu Hwang K., (2021), Photoredox synthesis of functionalized quinazolines *via* copper-catalyzed aerobic oxidative C_{sp^2}–H annulation of amidines with terminal alkynes. *Green Chem.* 23: 5024-5030.

[12] Tremblay-Parrado K. K., Clara García-Astrain C., Avérous L., (2021), Clickchemistry for the synthesis of biobased polymers and networks derived from vegetable oils. *Green Chem.* 23: 4296-4327.

[13] Cunha I. T., Yang H., Jessop P. G., (2021), High pressure switchable water: An alternative method for separating organic products from water. *Green Chem.* 23: 3996-4007.

[14] Hasaninejed A., Rasekhi Kazerooni M., Zare A., (2013), Room-temperature, catalyst-free, one-pot pseudof-component synthesis of 4, 4-(Arylmethylene)bis(3-methyl-1-phenyl-1H-pyrazol-5-ol)s under ultrasonic irradiation. *ACS Sustain. Chem. Eng.*1: 679-684.

[15] Zhu Y., Zhao J., Luo L., Gao Y., He Bao H., Pengfei Li P.,Zhang H., (2021), Research progress of indole compounds with potential antidiabetic activity. *Eur. J. Med. Chem*. 223: 113665-113668.

[16] Wang L., Han J., Tian H., Sheng J., Fan Z., Tang X., (2005), Rare earth perfluorooctanoate [$RE(PFO)_3$]-catalyzed condensations of indole with carbonyl compounds. *Synlett*. 2: 337-339.

[17] Chakrabarty M., Basak R., Ghosh N., Harigaya Y., (2004), Michael reaction of indoles with 3-(2′-nitrovinyl)indole under solvent-free conditions and in solution. An efficient synthesis of 2, 2-bis(indolyl)nitroethanes and studies on their reduction. *Tetrahedron*. 60: 1941-1949.

[18] Banik B. K., Fernandez M., Clarissa Alvarez C., (2005), Iodine-catalyzed highly efficient michael reaction of indoles under solvent-free condition. *Tetrahedron Lett*. 46: 2479-2482.

[19] Bandini M., Giorgio Cozzi P., Melchiorre P, Umani-Ronchi A., (2004), Kinetic resolution of epoxides by a C-C bond-forming reaction: Highly enantioselective addition of Indoles to *cis*, *trans*, and *meso* aromatic epoxides catalyzed by [Cr(salen)] complexes. *Angew. Chem. Int. Ed.* 43: 84-87.

[20] Osawa T., Namiki M., (1983), Structure elucidation of streptindole, a novel genotoxic metabolite isolated from intestinal bacteria. *Tetrahedron Lett*. 24: 4719-4722.

[21] Porter J. K., Bacon C. W., Robbin J. D., Himmelsbach D. S., Higman H. C., (1977), Indole alkaloids from Balansia epichloe (Weese). *J. Agric. Food. Chem*. 25: 88-93.

[22] Garbe T. R., Kobayashi M., Shimizu N., Takesue N., Ozawa M., Yukawa H., (2000), Indolyl carboxylic acids by condensation of indoles with α-keto acids. *J. Nat. Prod*. 63: 596-598.

[23] Gribble G. W., *In comprehensive Heterocyclic Chemistry*, 2nd ed. (Pergamon Pres: New York, 1996) 202.

[24] Snieckus V., *In The Alkaloids*,(Academic Press: New York, 1998) 11.

[25] Ge X., Yannai S., Rennert G., Gruener N., Fares F. A., (1996) 3, 3′-Diindolylmethane induces apoptosis in human cancer cells. *Biochem. Biophys. Res. Commun.* 228: 153-158.

[26] Firouzabadi H., Iranpoor N., Jafari A. A., (2006), Aluminum dodeca tungstophosphate ($AlPW_{12}O_{40}$), a versatile and a highly water tolerant *green* Lewis acid catalyzes efficient preparation of indole derivatives. *J. Mol. Catal. A Chem*. 244: 168-172.

[27] Ghorbani-Vaghei R., Veisi H., (2010), Poly(N, N′-dichloro-N-ethyl-benzene-1, 3-disulfonamide) and N, N, N′, N′-tetrachlorobenzene-1, 3-disulfonamide as novel catalytic reagents for synthesis of bis-indolyl, tris-indolyl, di(bis-indolyl), tri(bis-indolyl) and tetra(bis-indolyl)methanes under solid-state, solvent and water conditions. *J. Braz. Chem. Soc.* 21: 193-201.

[28] Seyedi N., Khabazzadeh H., Saidi K., (2009), $Cu_{1.5}PMo_{12}O_{40}$ as an efficient, mild and heterogeneous catalyst for the condensation of indole with carbonyl compounds. *Mol. Divers.* 13: 337–342.

[29] Sheikhshoaie I., Khabazzadeh H., Saeid-Nia S., (2009), Iron(III)(salen)Cl as an efficient catalyst for synthesis of bis(indolyl)methanes. *Transition Met. Chem.* 34: 463–466.

[30] Sheng S. R., Wang Q. Y., Ding Y., Liu X. L., Cai M. Z., (2009), Synthesis of Bis(indolyl)methanes using recyclable PEG-supported sulfonic acid as catalyst. *Catal. Lett.* 128: 418-422.

[31] Rahimizadeh M., Bakhtiarpoor Z., Eshghi H., Pordel M., Rajabzadeh G., (2009), TiO_2 nanoparticles: An efficient heterogeneous catalyst for synthesis of bis(indolyl) methanes under solvent-free conditions. *Monatsh Chem.* 140: 1465-1469.

[32] Ma Z. H., Han H. B., Zhou Z. B., Nie J., (2009), SBA-15-supported poly(4-styrenesulfonyl(perfluorobutylsulfo nyl)imide) as heterogeneous Brønsted acid catalyst for synthesis of diindolylmethane derivatives. *J. Mol. Catal. A: Chem.* 311: 46-53.

[33] Zolfigol M. A., Ayazi-Nasrabadi R., Baghery S., (2016), The first urea-based ionic liquid-stabilized magnetic

nanoparticles: An efficient catalyst for the synthesis of bis(indolyl)methanes and pyrano[2, 3-*d*] pyrimidinone derivatives. *Appl. Organometal. Chem.* 30: 273-281.

[34] Vahdat S. M., Khaksar S., Baghery S., (2012), Sulfonated organic heteropolyacid salts: Recyclable green solid catalysts for the highly efficient and green synthesis of bis (indolyl)methanes in Water. *Lett. Org. Chem.* 9: 138-144.

[35] Patil V. D., Dere G. B., Rege P. A., Patil J. J., (2011), Synthesis of Bis(indolyl) methanes in catalyst- and solvent-free reaction. *Synth. Commun.* 41: 736-747.

[36] Vahdat S. M., Ghafouri-Raz S., Baghery S., (2014), Application of nano SnO_2 as a green and recyclable catalyst for the synthesis of 2-aryl or alkylbenzoxazole derivatives under ambient temperature. *J. Chem. Sci.*126: 579-585.

[37] Vahdat S. M., Chekin F., Hatami M., Khavarpour M., Baghery S., Roshan-Kouhi Z., (2013), Synthesis of polyhydroquinoline derivatives via a fourcomponent Hantzsch condensation catalyzed by tin dioxide nanoparticles. *Chin. J. Catal.* 34: 758-763.

[38] Zolfigol M. A., Baghery S., Moosavi-Zare A. R., Vahdat S. M., (2015), Synthesis and characterization of new 1-(α-aminoalkyl)-2-naphtholsusing pyrazine-1,4-diium trinitromethanide{[1,4-DHPyrazine][$C(NO_2)_3$]$_2$} as a novel nano-structured molten saltand catalyst in compared with Ag–TiO_2 nano composite. *J. Mol. Catal. A: Chem.* 409: 216-226.

[39] Maleki B., Baghayeri M., Vahdat S. M., Mohammadzadeh A., Akhoondi S., (2015), Ag@TiO_2 nanocomposite; synthesis, characterization and its application as a novel and recyclable catalyst for the one-pot synthesis of benzoxazole derivatives in aqueous media. *RSC Adv.* 5: 46545-46551.

[40] Chekin F., Vahdat S. M., Asadi M. J., (2016), Green synthesis and characterization of cobalt oxide nanoparticles and its electrocatalytic behavior. *Russ. J. Appl. Chem.* 89: 816-822.

[41] Yazdani S., Hatami M., Vahdat S. M., (2014), The chemistry concerned with the sonochemical-assisted synthesis of CeO_2/poly(amic acid) nanocomposites. *Turk. J. Chem.* 38: 388-401.

[42] Vahdat S. M., Khavarpour M., Mohanazadeh F., (2015), A Facile and highly efficient three component synthesis of pyran and chromene derivatives in the presence of nano SnO_2 as a catalyst. *J. Appl. Chem.* 9: 41-46.

[43] Aminipoya H., Bagheri Ghomi A., Niazi A., (2021), Comparative synthesis of ZrO_2 nanoparticles by green and coprecipitation methods: The effect of template on structure. *Int. J. Nano Dimens*. 12: 59-66.

[44] Nagnnath Kokare N., Sangshetti J. N., Shinde D., (2008), Oxalic acid as a catalyst for efficient synthesis of bis-(indolyl)methanes, and 14-aryl-14H-dibenzo[a,j]xanthenes in water. *Chin. Chem. Lett*. 19: 1186-1189.

[45] Baghbanian S. M., Babajani Y., Tashakorian H., Khaksar S., Farhang M., (2013), *p*-sulfonic acid calix[4]arene: An efficient reusable organocatalyst for the synthesis of bis(indolyl)methanes derivatives in water and under solvent-free conditions. *C. R. Chimie*. 16: 129-134.

[46] Karthik M., Tripathi A. K., Gupta N. M., Palanichamy M., Murugesan V., (2004), Zeolite catalyzed electrophilic substitution reaction of indoles with aldehydes: Synthesis of bis(indolyl)methanes. *Catal. Commun.* 5: 371-375.

[47] Hasaninejad A., Zare A., Sharghi H., Niknam K., Shekouhy M., (2007), P_2O_5/SiO_2 as anefficient, mild, and heterogeneous catalytic system for the condensation of indoles with carbonyl compounds undersolvent-free conditions. *Arkivoc*. xiv: 39-50.

[48] Zolfigol M. A., Salehi P., Shiri M., Tanbakouchian Z. A., (2007), A new catalytic method for the preparation of bis-indolyl and tris-indolyl methanes in aqueous media. *Catal. Commun.* 8: 173-178.

[49] Deb M. L., Bhuyan P. J., (2006), An efficient and clean synthesis of bis(indolyl)methanes in a protic solvent at room temperature. *Tetrahedron Lett*. 47: 1441-1443.

[50] Ji S. J., Wang S. Y., Zhang Y., Loh T. P., (2004), Facile synthesis of bis(indolyl)methanes using catalytic amount of iodine at room temperature under solvent-free conditions. *Tetrahedron.* 60: 2051-2055.

[51] Magesh C. J., Nagarajan R., Karthik M., Perumal P. T., (2004), Synthesis and characterization of bis(indolyl)methanes, tris(indolyl)methanes and newdiindolylcarbazolylmethanes mediated by Zeokarb-225, a novel, recyclable, eco-benign heterogenous catalyst. *Appl. Catal. A: Gen.* 266: 1-10.