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A clean synthesis of bis(indolyl)methane and biscoumarin derivatives using P_4VPy–CuO nanoparticles as a new, efficient and heterogeneous polymeric catalyst

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P_4VPy–CuO nanoparticles as a novel solid catalyst were synthesized using an ultrasound irradiation method and characterized by X-ray diffraction (XRD), scanning electron microscopy (SEM), transmission electron microscopy (TEM) and Fourier Transform Infrared (FT-IR) spectroscopy. The prepared catalyst was applied to the green, simple and highly efficient synthesis of bis(indolyl)methanes and 3,3′-(arylmethylene)bis(4-hydroxycoumarins). This methodology has some advantages such as short reaction times, environmentally friendly conditions, easy work-up, and excellent yields. This catalyst can be easily separated and re-used without any appreciable loss in its activity.

1. Introduction

In recent years, nano-catalysts have been considered as sustainable and competitive alternatives to conventional catalysts. These reagents have a high surface-to-volume ratio that enhances their activity and selectivity and on the other hand, they maintain the intrinsic features of heterogeneous catalysts.[1] During the past decade the synthesis of metal oxide nanoparticles such as those of titanium, zinc, iron and magnesium has attracted the attention of many researchers. Among these metal oxides, CuO nanoparticles have been investigated quite considerably. This oxide is used as an antimicrobial[2] and photothermal and photoconductive agent,[3] in chemical and biological sensing,[4,5] as a promoter in catalytic reactions,[6] in lithium ion batteries[7] and solar cells.[8] In the synthesis of metal oxide nanoparticles, polymers are used to stabilize the aggregation of metal oxides.[9] Poly(vinylpyridine) (PVP) is an attractive polymer for immobilization of nanoparticles because of the strong affinity of the pyridyl group to metals and its ability to undergo hydrogen bonding with polar species. In addition, PVP can interact electrostatically in quaternized or protonated forms with charged surfaces[10,11] and a variety of different PVP-supported reagents have been designed in this context to catalyze a range of organic reactions.

Throughout the past decade different routes have been suggested to fabricate the CuO nanoparticles, including electrochemical method,[12] wet chemical reaction,[13] hydrothermal method,[14] thermal oxidation,[15] microwave irradiation[16] and quick-precipitation.[17] Some of these methods have limitations due to the requirement of high temperatures, expensive instruments and special catalysis. For cost-effectiveness and simplicity of operation, sonochemical method is preferred. On other hand in recent years, ultrasound irradiation has been established as a significant technique in synthetic organic chemistry. Shorter reaction times, simple experimental procedure, high yields, improved selectivity and clean reaction conditions are the main benefits of ultrasound-assisted reactions.[18–21]

Nowadays, synthesis of bis-heterocyclic compounds have received significant attention because they play a vital role in plant growth and in many pharmacological and biological activities.[22] Indoles are very important class of heterocyclic compounds. The indole nucleus as a “privileged structure” is present in many natural products isolated from marine and terrestrial organisms.[23] Among them, bis(indolyl)alkane derivatives have found a great deal of interest because of their applications in pharmaceuticals. For example, they show antitumor,[24] antileishmanial,[25] antihyperlipidemic[26] and anticancer activities.[27] Among various methods which are used for the synthesis of bis(indolyl)methanes, generally, these compounds can be obtained *via* the condensation of indole with aromatic (or aliphatic) aldehydes in the presence of a variety of catalyst. Some of the applied catalysts are I_2,[28] [bmim]BF_4 ionic liquid,[29] sulfated zirconia nanoparticles,[30] PEG–SO_3H,[31] $ZrOCl_2 \cdot 8H_2O$, camphor sulphonic acid,[32] benzyltriphenylphosphonium tribromide[33] and ceric ammonium nitrate.[34]

Coumarins are another important class of heterocyclic compounds. Coumarins have received increasing attention due to their wide range of biological properties such as anti-HIV,[35] anti-bacterial,[36] anti-cancer,[37] anti-coagulant,[38] anti-hepatitis C

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virus,[39] anti-tumor,[40] and spasmolytic[41] activities. Biscoumarins, the bridge substituted dimers of coumarin were also used as anti-inflammatories, antipyretics, antifungals, antiseptics[42] and as urease inhibitors.[43] Biscoumarins are usually synthesized through the Knoevenagel–Michael reactions of aldehydes with 4-hydroxycoumarin. For this purpose, a variety of catalysts including I_2,[44] *p*-dodecylbenzenesulfonic acid/piperidine,[45] nano silica chloride,[46] sodium dodecyl sulfate (SDS)[47] cellulose sulfonic acid[48] and poly(4-vinylpyridine)-supported dual acidic ionic liquid[49] have been reported.

Although the above mentioned procedures provide efficient access to the coumarin and indole structures, most of them suffer from disadvantages such as the use of expensive catalysts, long reaction times, harsh reaction conditions, the use of large excesses of toxic reagents or organic solvents, tedious work-up, low selectivity and un-reusable catalyst. Based on these limitations, introduction of a simple, efficient and clean procedure by use of a re-usable nano-catalyst without any discernible loss in its activity for the development of the synthesis of compounds belonging to these structural classes is still in demand.

2. Experimental

2.1. General

All chemicals were purchased from Merck or Fluka Chemical Companies and used without further purification. All yields refer to the isolated products. Products were characterized by their physical constants, and through a comparison with authentic samples. The reactions were monitored by thin layer chromatography (TLC) using silica gel SIL G/UV 254 TLC plates (Germany).

2.2. Instrumentation

X-ray diffraction (XRD) measurements were performed at room temperature on a D8-Bruker Advanced X-ray powder diffractometer, using Ni filter and Cu-Kα radiation ($k = 1.542$ Å). Scanning electron microscopy (SEM) and energy-dispersive X-ray spectroscopy (EDX) studies were carried out with SEM HITCHI S4160. TEM studies were carried out with PHILIPS CM10. The FT-IR spectra were recorded on a run on a VERTEX 70 Bruker company (Germany) spectrometer. ^{1}H NMR spectra were recorded on a Bruker Avance 400 MHz instrument (Germany) and the ^{13}C NMR data were collected on a Bruker Avance 100 MHz instrument. All the chemical shifts from the NMR spectra have been reported relative to TMS using deuterated solvent. Melting points were recorded on a Büchi B-545 apparatus (Germany) in open capillary tubes. Elf (with a frequency of 50 Hz and a nominal power 200 W) ultrasonic bath was used for ultrasonic irradiation.

2.3. Preparation of P4VPy–CuO nanoparticles (PC-NPs)

A mixture of poly(4-vinylpyrridine) (100 mg) [poly(4-vinylpyridine) cross-linked with 2% DVB ∼60 mesh, MW: 60 000] and bulk copper(II) oxide (35 mg, 0.437 mmol) in ethanol (10 mL) was irradiated by ultrasound for 2 hours. Then, the black solid powder was separated by centrifugation and washed three times with ethanol (3 × 2 mL) and dried at 60 °C (125 mg).

2.4. General procedure for the synthesis of bis(indolyl) methane derivatives

A mixture of aldehyde (1 mmol), indole (2 mmol), and P_4VPy–CuO (20 mg) was heated at 80 °C under solvent-free conditions for the appropriate time. After completion of the reaction (monitored by TLC using a 3 : 7 mixture of EtOAc/*n*-hexane), ethanol (10 mL) was added to the mixture and the catalyst was collected by filtration. Then, water was added and the precipitated product was collected by filtration in high purity.

The spectral data for the new compound are shown below:

Compound 1V. FT-IR (KBr, cm^{-1}): $\nu = 3400$ (NH str.), 3100 (aromatic C–H), 2840 (aliphatic C–H str.), 1679 (aromatic C=C str.), 580 (C–Br); ^{1}H NMR (DMSO-d$_6$, 400 MHz): $\delta = 1.26$ (6H, d, $J = 6.92$ Hz, CH_3), 2.8–2.9 (1H, m, CH), 5.7 (1H, s, Ar–CH), 6.48 (2H, s), 7.18 (2H, d, $J = 8$), 7.22 (2H, d, $J = 8$ Hz), 7.25 (2H, d, $J = 8.2$), 7.28 (2H, d, $J = 8.2$ Hz), 7.76 (2H, s), 9.96 (s, NH); ^{13}C NMR (DMSO-d$_6$, 400 MHz): $\delta = 22.9$, 32.6, 38.4, 111.4, 112.5, 116.1, 121.2, 122.1, 123.8, 125.5, 127.3, 128.6, 133.3, 134.3, 141.6.

Compound 1W. FT-IR (KBr, cm^{-1}): $\nu = 3400$ (NH str.), 3100 (aromatic C–H), 2840 (aliphatic C–H str.), 1681 (aromatic C=C str.), 580 (C–Br); ^{1}H NMR (DMSO-d$_6$, 400 MHz): $\delta = 3.78$ (3H, s, OCH_3), 5.75 (1H, s, Ar–CH), 6.84 (2H, s), 7.12 (2H, d, $J = 8$), 7.38 (2H, d, $J = 8$), 7.64–7.67 (2H, m), 7.83 (2H, s), 9.76 (s, NH); ^{13}C NMR (DMSO-d$_6$, 400 MHz): $\delta = 40.2$, 55.7, 108.7, 111.9, 117.8, 120.3, 123.4, 124.6, 125.9, 128.5, 129.1, 133.2, 134.7, 142.3.

2.5. General procedure for the synthesis of 3,3′-(arylmethylene)-bis-(4-hydroxycoumarins) derivatives

A mixture of aldehyde (1 mmol), 4-hydroxycoumarin (2 mmol) and P_4VPy–CuO (20 mg) in H_2O (5 mL) was stirred at reflux temperature for the appropriate time. The progress of the reaction was monitored by TLC (EtOAc : *n*-hexane; 1 : 4). Upon completion of the reaction the mixture was cooled to room temperature and filtered to separate the catalyst. After evaporation of the solvent the residue was recrystallized from a mixture of EtOH and water (95 : 5) to afford the pure product.

3. Results and discussion

3.1. Catalyst characterization

In order to understand the chemical and structural nature of the synthesized P_4VPy–CuO-NPs, FT-IR analysis was carried out. In Fig. 1(a), which shows the FT-IR of P_4VPy the absorption bands at 1600, 1556, 1498, and 1414 cm^{-1} are assigned to the characteristic vibrations of the pyridine ring. The absorption bands at 1069 and 995 cm^{-1} are assigned to the in-plane and out-of-plane bending of the C–H bonds of the ring, respectively.[50] Metal oxides commonly show absorption bands below 1000 cm^{-1}.[51] In this Fig. 1(b) the absorption bands which are observed at 604 and 504 cm^{-1} are related to bare Cu–O. Fig. 1(c) shows the FT-IR spectrum of the prepared catalyst. In this Fig. the bands related to the pyridine ring are appeared at 1603, 1558, 1499 and 1415 cm^{-1} while their intensities are decreased. The two characteristic bands of CuO were also observed at 608 and 511 cm^{-1}.[52]

The P_4VPy and P_4VPy–CuO-NPs samples were also analyzed by powder X-ray diffraction (XRD) (Fig. 2). All of the peaks in the

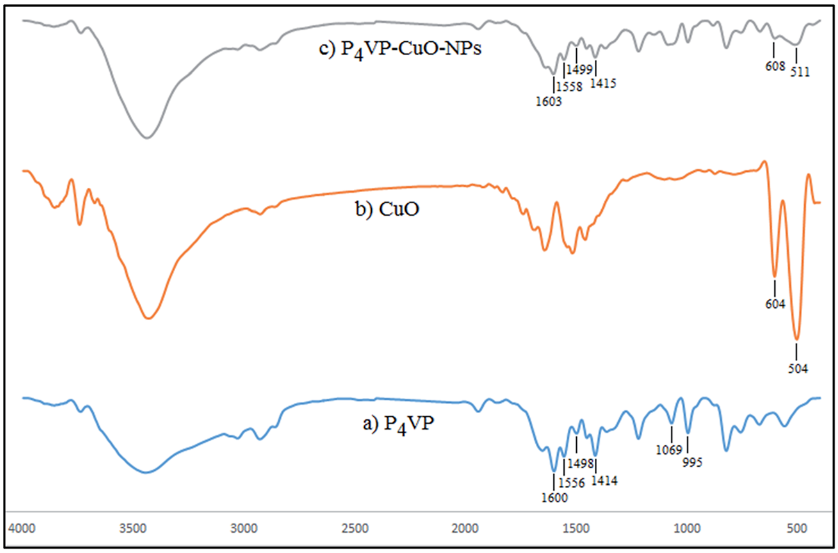


Fig. 1 FT-IR spectra of (a) P_4VPy (b) CuO and P_4VPy–CuO-NPs (c).

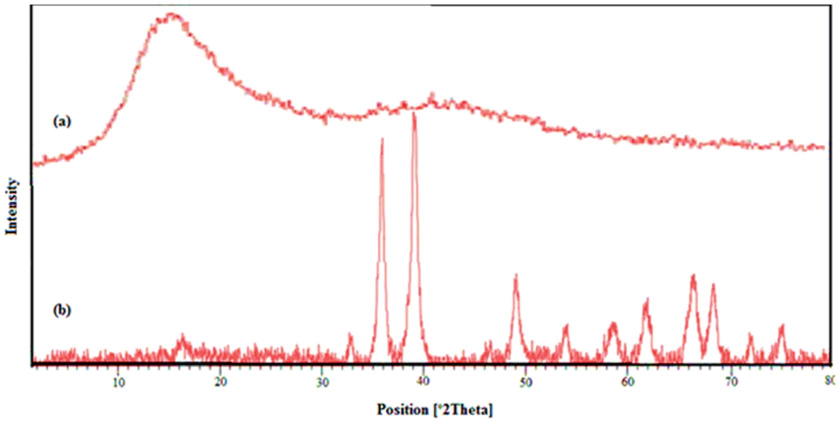


Fig. 2 XRD patterns of (a) P_4VPy and (b) P_4VPy–CuO-NPs.

diffraction diagram could be assigned to the CuO. The peaks at 2θ values of 32.86, 35.89, 39.09, 46.37, 49.04, 54.15, 58.63, 61.88, 66.62, 68.46, 72.58, and 75.34 correspond to the crystal planes of copper oxide 110, 002, 111, 112, 202, 020, 202, 113, 311, 113, 311, and 004, respectively, which are in good agreement with the recent observations.[52] No other peak is observed belonging to the impurities, indicating the high purity of as-obtained samples. These values are consistent with the respective Joint Committee on Powder Diffraction Standard card no. 45-0937.

Scanning electron microscopy (SEM) is used to determine the size of the CuO particles (Fig. 3). This method clarified that these particles are in nano size. On the basis of the obtained results it can be concluded that because of the reduction of the size of the CuO particles which increases its surface area the activity of the prepared reagent in the requested reactions became higher (as described in the next sections).

Typical transmission electron microscopy (TEM) displays the morphologies of the prepared sample. In Fig. 4 nanorod and nanosphere structures can be observed for the prepared reagent.

3.2. Catalyst activity

As we have mentioned previously, CuO is one of the most prominent catalysts and is extensively used in environmental catalysis. CuO nanoparticles typically have higher catalytic activity than their bulk or micro counterparts caused by their large surface area.[53] In addition, CuO on various supporters have also been extensively investigated and is known to be highly active.[54]

In the present study and after preparation and identification of P_4VP–CuO-NPs and in order to solve the previously mentioned drawbacks we were interested to investigate the applicability of this reagent in the promotion of different types of the synthesis of 3,3′-(arylmethylene)bis(4-hydroxycoumarins) and bis(indolyl)methanes.

At first, we focused our attention on the synthesis of bis(indolyl)methanes compounds. For optimization of the reaction conditions, the reaction between 4-chlorobenzaldehyde and indole to give the corresponding product was selected as

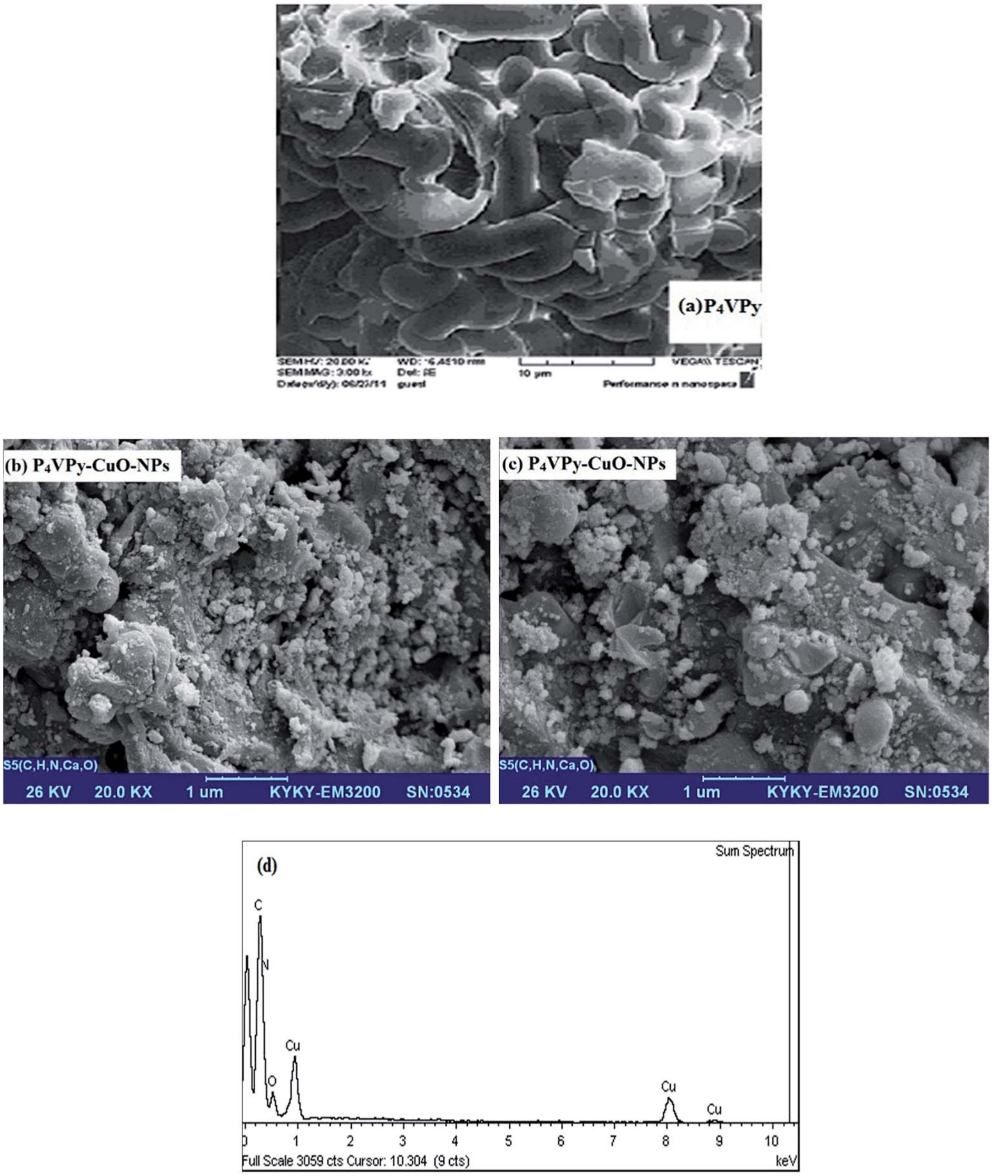


Fig. 3 SEM images of (a) P_4VPy and (b and c) P_4VPy–CuO-NPs and EDX of P_4VPy–CuO-NPs (d).

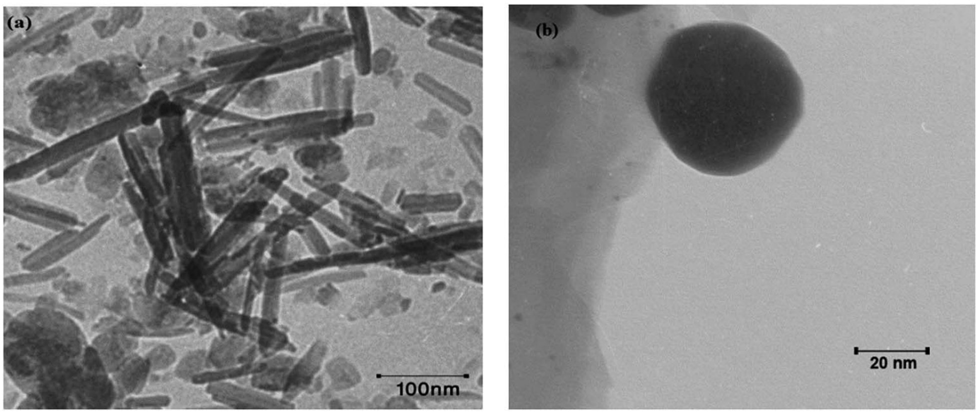
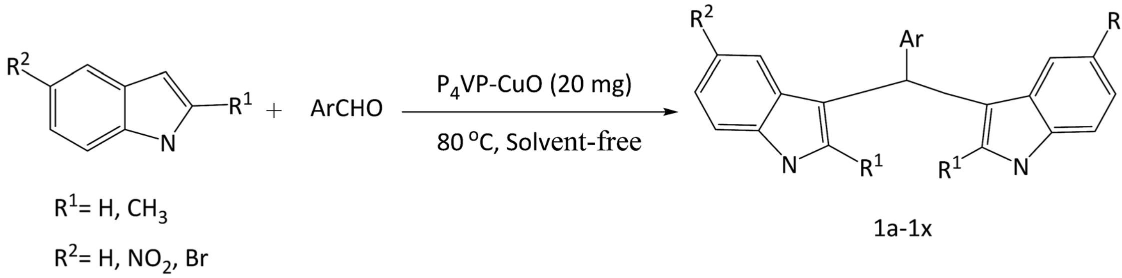


Fig. 4 TEM images of P_4VPy–CuO-NPs.



Scheme 1 Synthesis of bis(indolyl)methane derivatives in the presence of P_4VPy–CuO-NPs.

a model reaction and the various conditions including the amount of catalyst, solvent and temperature were examined. The best result was achieved by carrying out the reaction of the aldehyde (1 mol) and indol (2 mol) in the presence of 20 mg of P_4VPy–CuO at 80 °C under solvent-free conditions, as shown in Scheme 1. Any further increasing in the amount of the catalyst or temperature did not improve the reaction time or yield.

Using these optimized conditions, the reaction of various aldehydes with different indole derivatives, including: indole, 2-methyl indole, 5-nitro indole, and 5-bromo indole was explored (Table 1).

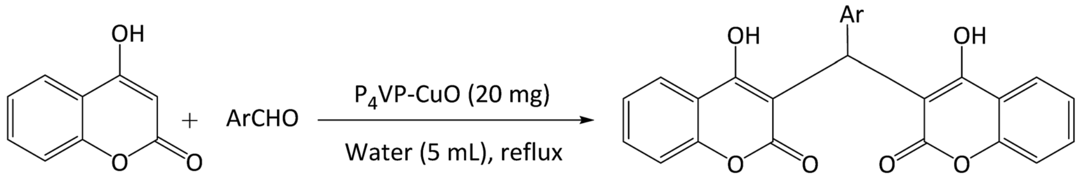
Aromatic aldehydes containing electron-withdrawing (Cl, Br, and NO_2) or electron-donating (CH_3, OCH_3 and OH) groups, as well as α,β-unsaturated (cinnamaldehyde), and heterocyclic (isatin) aldehydes, all reacted smoothly with indole in the presence of the P_4VPy–CuO-NPs to give the corresponding products in high yields (Table 1, entries 1–15). Also, 2-methyl indole, 5-nitro indole and 5-bromo indole, were successfully converted to the corresponding bis(indolyl)methanes under the optimized conditions (Table 1, entries 16–24). The results showed that when 2-methyl indole was used in the reaction, the desired bis(indolyl) methanes were obtained in short reaction times rather than other indoles. For more investigation, acetophenone as a ketones was examined under this conditions. It was seen that no product was obtained which indicates the chemoselectivity of the catalyst. This chemoselectivity can be attributed to the higher electrophilicity of aldehydes in comparison with ketones, aldehydes are more reactive than ketones.

After the successful application of P_4VPy–CuO-NPs as a polymer-supported catalyst in the synthesis of bis(indolyl) methanes, we decided to use it in the condensation of 4-hydroxycoumarin with aldehydes in aqueous medium to form

Table 1 Preparation of bis(indolyl)methane derivatives catalyzed by P_4VPy–CuO-NPs[a]

							Melting point (°C)		
Entry	Ar	R^1	R^2	Product	Time (min)	Yield[b] (%)	Found	Reported	Ref.
1	C_6H_5–	H	H	1a	10	90	126–128	126–127	28
2	2-Cl–C_6H_4–	H	H	1b	8	87	76–78	75–76	55
3	4-Cl–C_6H_4–	H	H	1c	5	92	78–80	78–80	32
4	4-Br–C_6H_4–	H	H	1d	6	90	112–114	116–117	56
5	3-NO_2–C_6H_4–	H	H	1e	4	92	220–222	219–221	55
6	4-NO_2–C_6H_4–	H	H	1f	5	94	221–223	222–224	55
7	4-Me–C_6H_4–	H	H	1g	12	90	90–92	89–91	55
8	3-MeO–C_6H_4–	H	H	1h	15	86	166–168	165	57
9	4-MeO–C_6H_4–	H	H	1i	10	89	184–186	186–187	31
10	4-$(CH_3)_2CH$–C_6H_4–	H	H	1j	10	87	150–152	153–154	58
11	4-$(CH_3)_2N$–C_6H_4	H	H	1k	22	85	172–174	170–172	32
13	4-OH–C_6H_4–	H	H	1l	35	88	122–124	124–126	32
14	C_6H_5–CH=CH–	H	H	1m	10	90	98–100	100–101	32
15	Isatin	H	H	1n	45	79	305–307	>300	34
16	C_6H_5–	CH_3	H	1o	5	90	252–254	250–253	32
17	4-Cl–C_6H_4–	CH_3	H	1p	3	94	244–246	247–248	55
18	4-NO_2–C_6H_4–	CH_3	H	1q	3	95	242–244	241–243	32
19	4-MeO–C_6H_4–	CH_3	H	1r	5	91	102–104	102–103	32
20	4-NO_2–C_6H_4–	H	NO_2	1s	30	92	300–302	304–306	59
21	4-MeO–C_6H_4–	H	NO_2	1t	35	90	316–318	317–319	59
22	C_6H_5–	H	Br	1u	25	83	242–244	246–248	58
23	4-$(CH_3)_2CH$–C_6H_4–	H	Br	1v	35	80	262–264	—	—
24	4-MeO–C_6H_4–	H	Br	1w	15	89	254–256	—	—
25	Acetophenone	H	H	1x	120	—	—	—	—

[a] Reaction conditions: aldehyde (1 mmol), indole (2 mmol), P_4VPy–CuO-NPs (20 mg) at 80 °C under solvent free conditions. [b] Isolated yields.



2a-2s

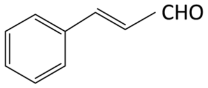
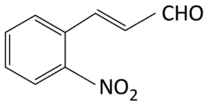
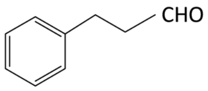
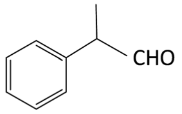
Scheme 2 Synthesis of 3,3′-(arylmethylene)-bis-(4-hydroxycoumarin) derivatives in the presence of P_4VPy–CuO-NPs.

3,3′-(arylmethylene)bis(4-hydroxycoumarins). For this purpose and to obtain the optimum reaction conditions, the reaction between 4-clorobenzaldehyde and 4-hydroxycoumarin was studied as a model reaction in different conditions.

Several different solvents were examined in the model reaction, including ethanol, diethyl ether, dichloromethane and water that gave the best results in terms of the yield and reaction time. Finally, the optimal reaction conditions for this reaction was obtained using 1 mmol aldehyde, 2 mmol 4-hydroxycoumarin and 20 mg P_4VPy–CuO-NPs as the catalyst in 5 mL H_2O at reflux temperature, as shown in Scheme 2.

Subsequently, a broad range of aromatic and aliphatic aldehydes were reacted with 4-hydroxycoumarin under the optimized conditions and the corresponding 3,3′-(arylmethylene)-bis-(4-hydroxycoumarins) were obtained in good to high yields, as shown in Table 2. Various aromatic aldehydes containing electron-withdrawing or electron-donating groups (Cl, Br, NO_2, CH_3, OCH_3, $N(CH_3)_2$, SCH_3 and OH) and also α,β-unsaturated aldehydes (cinnamaldehyde and 2-nitrocinnamaldehyde) were efficiently condensed with 4-hydroxycoumarin in very good yields and times (Table 2, entries 1–17). Furthermore, using this method, 3-phenylpropionaldehyde and 2-phenylpropionaldehyde as aliphatic

Table 2 Preparation of 3,3′-(arylmethylene)-bis-(4-hydroxycoumarins) derivatives catalyzed by P_4VPy–CuO-NPs[a]

					Melting point (°C)		
Entry	Ar	Product	Time (min)	Yield[b] (%)	Found	Reported	Ref.
1	C_6H_5–	2a	20	90	232–234	230–232	47
2	2-Cl–C_6H_4–	2b	55	88	217–219	220–222	48
3	3-Cl–C_6H_4–	2c	35	90	225–227	228–230	47
4	4-Cl–C_6H_4–	2d	15	93	255–257	256–258	47
5	4-Br–C_6H_4–	2e	20	89	268–270	266–268	46
6	2-NO_2–C_6H_4–	2f	20	91	198–200	200–202	60
7	3-NO_2–C_6H_4–	2g	15	94	233–235	235–237	48
8	4-NO_2–C_6H_4–	2h	10	95	230–232	230–232	48
9	2-Me–C_6H_4–	2i	60	85	219–221	221–223	47
10	4-Me–C_6H_4–	2j	25	92	265–267	265–266	48
11	3-MeO–C_6H_4–	2k	25	92	240–242	238	43
12	4-MeO–C_6H_4–	2l	35	89	248–250	246–248	47
13	4-$(CH_3)_2N$–C_6H_4–	2m	30	93	220–222	222–224	47
14	4-MeS–C_6H_4–	2n	25	91	259–261	258–260	59
15	4-OH–C_6H_4–	2o	50	85	228–230	222–224	46
16		2p	25	90	226–228	230–232	44
17		2q	55	88	188–190	190–192	61
18		2r	60	90	196–198	190	43
19		2s	45	80	194–196	198	43

[a] Reaction conditions: 4-hydroxycoumarin (2 mmol), aldehyde (1 mmol), P_4VPy–CuO-NPs (20 mg) and water (5 mL) at reflux temperature. [b] Isolated yields.

Table 3 Comparison of the results obtained from the synthesis of 3,3′-(4-chlorophenylmethylene)-bis-(1*H*-indole) and 3,3′-(4-chlorophenylmethylene)-bis-(4-hydroxycoumarin) in the presence of P_4VPy–CuO-NPs with those obtained using other catalysts

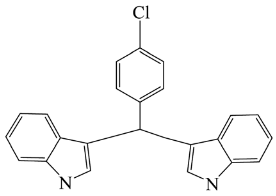
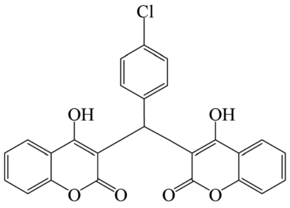
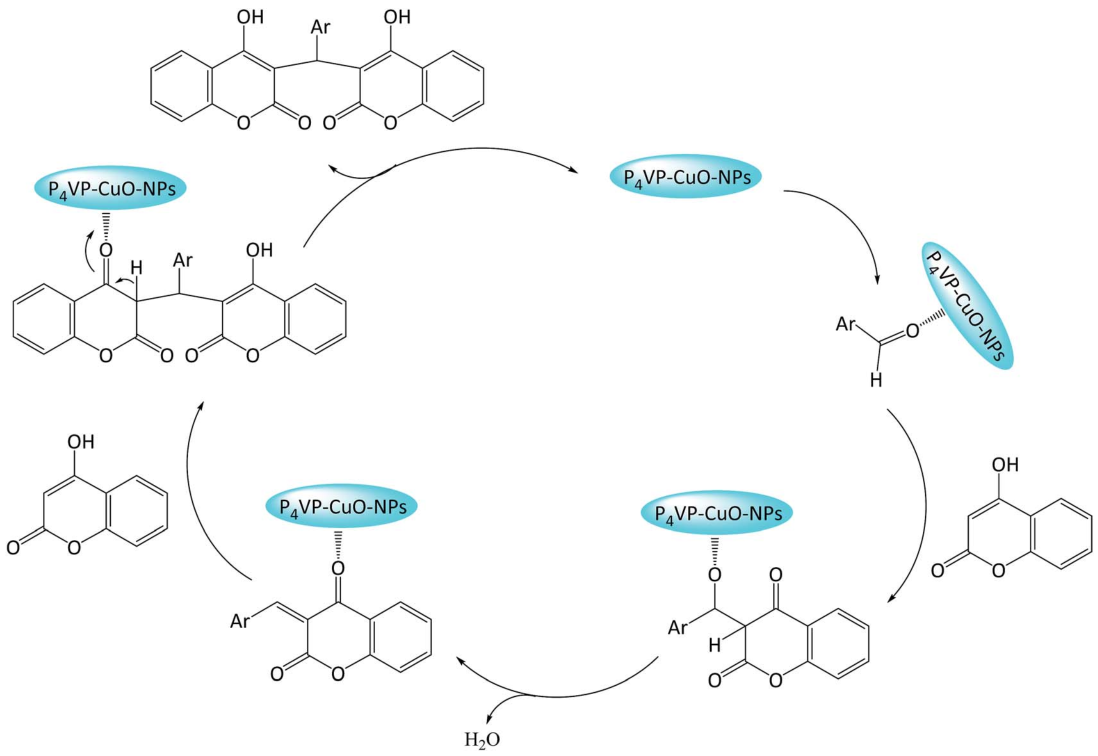
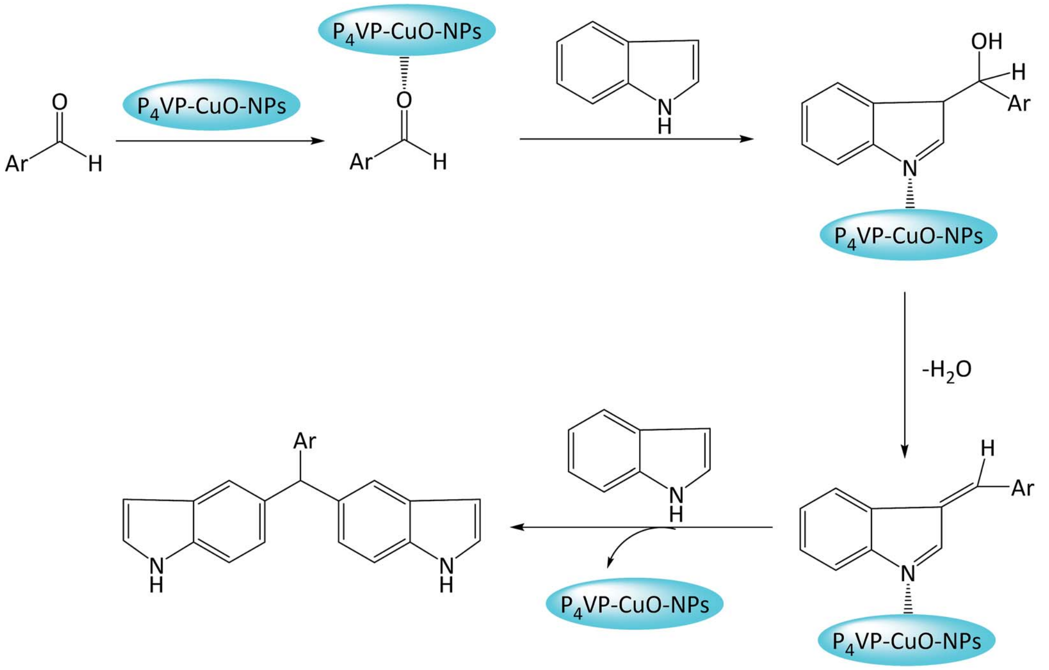
Product	Catalyst (loading)	Reaction conditions	Time (min)	Yield (%)	Ref.
	$FeCl_3$–RiH (150 mg)	80 °C/EtOH	10	96	55
	Ni nanoparticles (10 mol%)	80 °C/solvent-free	100	90	56
	$ZrOCl_2 \cdot 8H_2O$ (5 mol%)	r.t./H_2O–EtOH	540	89	32
	$Mg(HSO_4)_2$ (1 mmol)	r.t./EtOH	450	90	62
	P_4VPy–CuO-NPs (20 mg)	80 °C/solvent free	5	92	(This work)
	Cellulose sulfonic acid (20 mg)	Reflux/H_2O	120	80	48
	[P_4VPy–$BuSO_3H$]HSO_4 (0.1 mmol)	90 °C/toluene	48	94	49
	CuO–CeO_2 nano-composite (50 mg)	Reflux/H_2O	10	93	63
	SDS (20 mol%)	60 °C/H_2O	180	98	47
	P_4VPy–CuO-NPs (20 mg)	Reflux/H_2O	15	93	(This work)

Table 4 Reusability of P_4VPy–CuO-NPs in the synthesis of bisindoles and biscoumarins

	3,3′-(4-Chlorophenylmethylene)-bis-(1*H*-indole)		3,3′-(4-Chlorophenylmethylene)-bis-(4-hydroxycoumarin)	
Run	Time (min)	Yield (%)	Time (min)	Yield (%)
1	5	92	15	93
2	7	90	18	90
3	10	86	23	83



Scheme 3 The possible mechanism for synthesis of biscoumarines in the presence of P_4VP–CuO-NPs.



Scheme 4 The plausible mechanism for synthesis of bisindoles in the presence of P_4VP–CuO-NPs.

Table 5 Comparison of the results obtained from the synthesis of 3,3′-(4-chlorophenylmethylene)-bis-(1*H*-indole) and 3,3′-(4-chlorophenylmethylene)-bis-(4-hydroxycoumarin) in the presence of P_4VPy, bulk CuO and P_4VPy–CuO-NPs

		3,3′-(4-Chlorophenylmethylene)-bis-(1*H*-indole)		3,3′-(4-Chlorophenylmethylene)-bis-(4-hydroxycoumarin)	
Entry	Catalyst	Time (min)	Conversion (%)	Time (min)	Conversion (%)
1	P_4VP	25	100	35	70
2	CuO	30	50	25	80
3	P_4VP–CuO-NPs	5	100	15	100

aldehydes were converted to their corresponding products in good yields (Table 2, entries 18, 19).

In order to show the merit of our newly developed procedures, we have compared our results for the synthesis of 3,3′-(4-chlorophenylmethylene)-bis-(1*H*-indole) and 3,3′-(4-chlorophenylmethylene)-bis-(4-hydroxycoumarin) using the P_4VPy–CuO nanocatalyst with the results of some of the catalysts reported in the literature for the same transformation (Table 3). The P_4VPy–CuO-NPs as a supported catalyst, improved the reaction very effectively and gave the desired products in short reaction times. This catalyst is prepared easily and a very low amount of the catalyst is used for the preparation of the required reactions (Table 4).

The proposed mechanism for the preparation of biscoumarines in the presence of P_4VPy–CuO-NPs as the catalyst, based on the reported pathway in literature,[63] is shown in Scheme 3. At first, the aldehyde is activated by P_4VPy–CuO-NPs. Nucleophilic attack of 4-hydroxycoumarin to activated aldehyde followed by loss of H_2O generates intermediate, which is further activated by P_4VPy–CuO-NPs. The intermediate undergoes a second nucleophilic attack by another 4-hydroxycoumarin to provide the final product.[63]

For synthesis of bisindoles, the condensation reaction probably proceeds through the activation of a carbonyl group by P_4VPy–CuO-NPs. Then, indole attacks to the activated carbonyl group to form intermediate which is subsequently attacks by a second molecule of indole to product bis(indolyl)methanes as shown in Scheme 4.

The reusability of the catalyst was also investigated for both types of the reactions. The model reactions were studied under the optimized reaction conditions. After completion of the reactions, the catalyst was separated by filtration, washed with acetone, dried and used again in the same reaction. This process was repeated for at least three runs for each type of the reactions with good activity.

In the next attempt, the catalytic activity of P_4VPy–CuO nanoparticles was compared with bulk CuO and P_4VPy for the synthesis of 3,3′-(4-chlorophenylmethylene)-bis-(1*H*-indole)

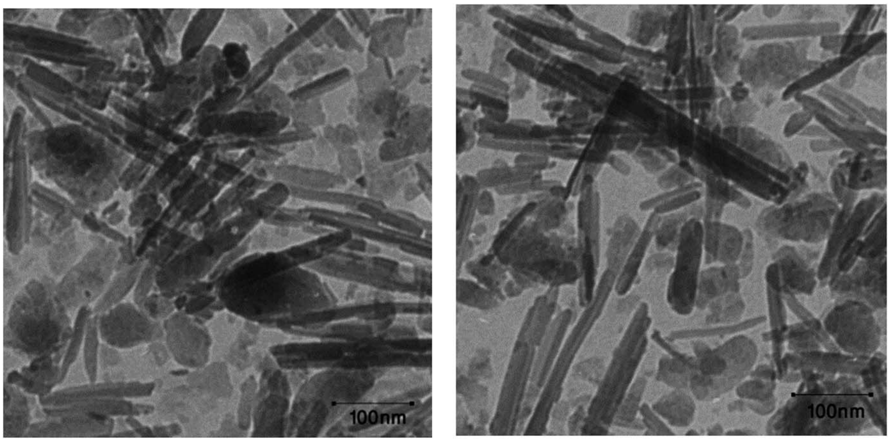


Fig. 5 TEM images of P_4VPy–CuO-NPs by precipitation (left) and reflux (right) method.

and 3,3′-(4-chlorophenylmethylene)-bis-(4-hydroxycoumarin). The results proved the efficiency of the prepared catalyst as shown in Table 5.

During a separate investigation and in order to evaluate the ability of the method used for the preparation of the catalyst, the reagent was also synthesized *via* two other methods, too. In first method, P_4VPy–CuO nanoparticles were synthesized by quick precipitation route. For this purpose, $Cu(NO_3)_2 \cdot 3H_2O$ was added to the suspension of P_4VPy in deionized water and stirred for 15 min. Then, a solution of NaOH 1 M was added to the mixture at 60 °C to form black nanoparticles.[9] In the second method, P_4VPy–CuO nanoparticles were prepared *via* the reaction of CuO and P_4VPy in ethanol at reflux temperature under ambient conditions according the method reported by Albadi *et al.*[64]

The obtained catalysts were characterized by FT-IR and the same FT-IRs clarified that the prepared samples are the same as each other.

The morphology of the catalysts that prepared by two other methods was also characterized by transmission electron microscopy. The TEM images of the catalysts proved that they have nanorod and nanosphere structures as shown in Fig. 5.

After preparation the catalytic activity of these catalysts were examined in the synthesis of 3,3′-(4-chlorophenylmethylene)-bis-(1*H*-indole) and 3,3′-(4-chlorophenylmethylene)-bis-(4-hydroxycoumarin). The results showed that the catalytic activity was not affected by the preparation method used for the synthesis of the reagent, while the ultrasound irradiation assisted the preparation of the catalyst in shorter reaction times and lower temperature.

4. Conclusions

In conclusion, we have prepared and identified P_4VPy–CuO-NPs as a novel reusable nanocatalyst and used it in a green procedure for the synthesis of bis(indolyl) methanes and biscoumarins. The most significant advantages of this method are high yields of products, short reaction times, reusability of the catalyst and easy work-up. Further work to explore this catalyst in other organic transformations is in progress.

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References

1 D. Astruc, *Nanoparticles and Catalysis*, John Wiley & Sons, VCH, Weinheim, 2008.
2 G. Rena, D. Hub, E. W. C. Chengb, M. A. Vargas-Reusc, P. Reipd and R. P. Allaker, *Int. J. Antimicrob. Agents*, 2009, **33**, 587.
3 H. M. Yates, L. A. Brook, I. B. Ditta, P. Evans, H. A. Foster, D. W. Sheel and A. Steele, *J. Photochem. Photobiol., A*, 2008, **197**, 197.
4 X. Wang, C. Hu, H. Liu, G. Du, X. He and Y. Xi, *Sens. Actuators, B*, 2010, **144**, 220.
5 S. Aygun and D. Cann, *Sens. Actuators, B*, 2005, **106**, 837.
6 F. B. Derekaya, C. Kutar and C. Guldur, *Mater. Chem. Phys.*, 2009, **115**, 496.
7 H. Wang, Q. Pan, J. Zhao and W. Chen, *J. Alloys Compd.*, 2009, **476**, 408.
8 H. Zhang and M. Zhang, *Mater. Chem. Phys.*, 2008, **108**, 184.
9 N. A. Ibrahim and M. Shahmiri, *Adv. Sci., Eng. Med.*, 2013, **5**, 193.
10 S. A. Sukhishvili and S. Granic, *Phys. Rev. Lett.*, 1998, **80**, 3646.
11 K. S. Schmitz, *Macromolecules*, 2000, **33**, 2284.
12 G. Q. Yuan, H. F. Jiang, C. Lin and S. J. Liao, *J. Cryst. Growth*, 2007, **303**, 400.
13 Q. Liu, Y. Liang, H. Liu, J. Hong and Z. Xu, *Mater. Chem. Phys.*, 2006, **98**, 519.
14 M. A. Dar, Y. S. Kim, W. B. Kim, J. M. Sohn and H. S. Shin, *Appl. Surf. Sci.*, 2008, **254**, 7477.
15 M. Kaur, K. P. Muthe, S. K. Despande, S. Choudhury, J. B. Singh, N. Verma, S. K. Gupta and J. V. Yakhmi, *J. Cryst. Growth*, 2006, **289**, 670.
16 H. T. Zhu, C. Y. Zhang, Y. M. Tang and J. X. Wang, *J. Phys. Chem. C*, 2007, **111**, 1646.
17 R. Wu, Z. Ma, Z. Gu and Y. Yang, *J. Alloys Compd.*, 2010, **504**, 45.

18 T. J. Mason and J. P. Lorimer, *Sonochemistry: theory, applications and uses of ultrasound in chemistry*, John Wiley and Sons, New York, 1988.
19 K. S. Suslick, *Ultrasound, its physical, biological and chemical effects*, VCH, Weinheim, 1988.
20 A. Gaplovsky, M. Gaplovsky, S. Toma and J. Luche, *J. Org. Chem.*, 2000, **65**, 8444.
21 R. R. Deshmukh, R. Rajagopal and K. V. Srinivasan, *Chem. Commun.*, 2001, **17**, 1544.
22 P. F. Xu, X. W. Sun, L. M. Zhang and Z. Y. Zhang, *J. Chem. Res.*, 1999, **2**, 170.
23 G. Bartoli, R. Dalpozzo and M. Nardi, *Chem. Soc. Rev.*, 2014, **43**, 4728.
24 P. Diana, A. Carbone, P. Barraja, A. Martorana, O. Gia, L. DallaVia and G. Cirrincione, *Bioorg. Med. Chem. Lett.*, 2007, **17**, 6134.
25 S. B. Bharate, J. B. Bharate, S. I. Khan, B. L. Tekwani, M. R. Jacob, R. Mudududdla, R. R. Yadav, B. Singh, P. R. Sharma, S. Maity, B. Singh, I. A. Khan and R. A. Vishwakarma, *Eur. J. Med. Chem.*, 2013, **63**, 435.
26 K. V. Sashidhara, A. Kumar, M. Kumar, A. Srivastava and A. Puri, *Bioorg. Med. Chem. Lett.*, 2010, **20**, 6504.
27 A. Kamal, Y. V. V. Srikanth, M. J. Ramaiah, M. N. A. Khan, M. K. Reddy, M. Ashraf, A. Lavanya, S. N. C. V. L. Pushpavalli and M. Pal-Bhadra, *Bioorg. Med. Chem. Lett.*, 2012, **22**, 571.
28 S. J. Ji, S. Y. Wang, Y. Zhang and T. P. Loh, *Tetrahedron*, 2004, **60**, 2051.
29 J. S. Yadav, B. V. S. Reddy and S. Sunitha, *Adv. Synth. Catal.*, 2003, **345**, 349.
30 G. Chen, C. Y. Guo, H. Qiao, M. Ye, X. Qiu and C. Yue, *Catal. Commun.*, 2013, **41**, 70.
31 A. Hasaninejad, M. Shekouhy, A. Zare, S. M. S. H. Ghattali and N. Golzar, *J. Iran. Chem. Soc.*, 2011, **8**, 411.
32 S. Mishra and R. Ghosh, *Indian J. Chem., Sect. B: Org. Chem. Incl. Med. Chem.*, 2011, **50**, 1630.
33 F. Shirini, M. S. Langroodi and M. Abedini, *Chin. Chem. Lett.*, 2010, **21**, 1342.
34 S. Y. Wang and S. J. Ji, *Tetrahedron*, 2006, **62**, 1527.
35 P. Zhou, Y. Takaishi, H. Duan, B. Chen, G. Honda, M. Itoh, Y. Takeda, O. K. Kodzhimatov and K. Lee, *Phytochemistry*, 2000, **53**, 689.
36 Y. Kong, Y. J. Fu, Y. G. Zu, F. R. Chang, Y. H. Chen, X. L. Liu, J. Stelten and H. M. Schiebel, *Food Chem.*, 2010, **121**, 1150.
37 S. S. Bhattacharyya, S. Paul, S. K. Mandal, A. Banerjee, N. Boujedaini and A. R. Khuda-Bukhsh, *Eur. J. Pharmacol.*, 2009, **614**, 128.
38 I. Manolov, C. Maichle-Moessmer and N. Danchev, *Eur. J. Med. Chem.*, 2006, **41**, 882.
39 J. Neyts, E. D. Clercq, R. Singha, Y. H. Chang, A. R. Das, S. K. Chakraborty, S. C. Hong, S. C. Tsay, M. Hsu and J. R. Hwu, *J. Med. Chem.*, 2009, **52**, 1486.
40 C. Ito, M. Itoigawa, S. Onoda, A. Hosokawa, N. Ruangrungsi, T. Okuda, H. Tokuda, H. Nishino and H. Furukawa, *Phytochemistry*, 2005, **66**, 567.
41 I. Kostava, I. Manolov, I. Nicolova, S. Konstantonov and M. Karaivanova, *Eur. J. Med. Chem.*, 2001, **36**, 339.
42 H. Hussain, J. Hussain, A. Al-Harrasi and K. Krohn, *Tetrahedron*, 2012, **68**, 2553.
43 K. M. Khan, S. Iqbal, M. A. Lodhi, G. M. Maharvi, Z. Ullah, M. I. Choudhary, A. Rahman and S. Perveen, *Bioorg. Med. Chem.*, 2004, **12**, 1963.
44 M. Kidwai, V. Bansal, P. Mothsra, S. Saxena, R. K. Somvanshi, S. Dey and T. P. Singh, *J. Mol. Catal. A: Chem.*, 2007, **268**, 76.
45 A. Kumar, M. K. Gupta and M. Kumar, *Tetrahedron Lett.*, 2011, **52**, 4521.
46 R. Karimian, F. Piri, A. A. Safari and S. J. Davarpanah, *J. Nanostruct. Chem.*, 2013, **3**, 52.
47 H. Mehrabi and H. Abusaidi, *J. Iran. Chem. Soc.*, 2010, **7**, 890.
48 M. Sedighi and N. Montazeri, *Adv. Stu. In Bio*, 2015, **7**, 89.
49 K. P. Boroujeni, P. Ghasemi and Z. Rafienia, *Monatsh. Chem.*, 2014, **145**, 1023.
50 K. H. Wu, Y. R. Wang and W. H. Hwu, *Polym. Degrad. Stab.*, 2003, **79**, 195.
51 C. N. R. Rao, *Chemical applications of infrared spectroscopy*, Academic Press, New York, 1963.
52 M. Shahmiri, N. A. Ibrahim, F. Shayesteh, N. Asim and N. Motallebi, *J. Mater. Res.*, 2013, **28**, 3109.
53 K. Zhou, R. Wang, B. Xu and Y. Li, *Nanotechnology*, 2006, **17**, 3939.
54 F. B. Derekaya, C. Kutar and C. Guldur, *Mater. Chem. Phys.*, 2009, **115**, 496.
55 F. Shirini, S. Akbari-Dadamahaleh and A. Mohammad-Khah, *C. R. Chim.*, 2013, **16**, 945.
56 A. Olyaei, M. Vaziri, R. Razeghi, B. Shams and H. Bagheri, *J. Serb. Chem. Soc.*, 2013, **78**, 463.
57 R. Tayebee, M. M. Amini, F. Nehzat, O. Sadeghi and M. Armaghan, *J. Mol. Catal. A: Chem.*, 2013, **366**, 140.
58 K. Tabatabaeian, M. Mamaghani, N. Mahmoodi and A. Khordishi, *Can. J. Chem.*, 2006, **84**, 1541.
59 F. Shirini, M. Seddighi and M. Mamaghani, *RSC Adv.*, 2013, **3**, 24046.
60 N. Tavakoli-Hoseini, M. M. Heravi, F. F. Bamoharram, A. Davoodnia and M. Ghassemzadeh, *J. Mol. Liq.*, 2011, **163**, 122.
61 K. Tabatabaeian, H. Heidari, A. Khorshidi, M. Mamaghani and N. O. Mahmoodi, *J. Serb. Chem. Soc.*, 2012, **77**, 407.
62 K. Niknam, M. A. Zolfigol, T. Sadabadi and A. Nejati, *J. Iran. Chem. Soc.*, 2006, **3**, 318.
63 J. Albadi, A. Mansournezhad and S. Salehnasab, *Res. Chem. Intermed.*, 2015, **41**, 5713–5721.
64 J. Albadi, N. Iravanian and M. Khoshakhlagh, *Iran. J. Catal.*, 2012, **2**, 85.