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Synthesis, Characterization and Catalytic Properties of Magnetic Nano Supported Molybdat Sulfuric Acid (Fe_3O_4@MSA NPs) in Base Catalyzed Synthesized of 2-Substituted aryl(amino) and (indolyl) Kojic Acid Derivatives under Solvent-free Conditions

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Abstract Magnetic nanoparticle-supported molybdate sulfuric acid (MNPs-MSA) was synthesized and characterized by X-ray diffraction (XRD), Fourier transform infrared spectroscopy (FT-IR), energy dispersive X-ray spectroscopy (EDX), and scanning electron microscopy (SEM). The catalytic activity of MNPs-MSA was investigated as a recoverable catalyst for the one-pot synthesis of novel 2-substituted aryl (amino) and aryl (indolyl) kojic acid derivatives from the reaction of aldehydes with aniline or indole and kojic acid in high yield at room temperature under solvent-free conditions Abstract should briefly state the purpose of the research, the principal results, and the major conclusions of the study.

Keywords: *magnetic nanoparticle, nanoparticle-supported molybdate sulfuric acid (MNPs-MSA), 2-substituted aryl (amino) kojic acid, 2-substituted aryl (indolyl) kojic acid, One-pot synthesis, solvent-free*

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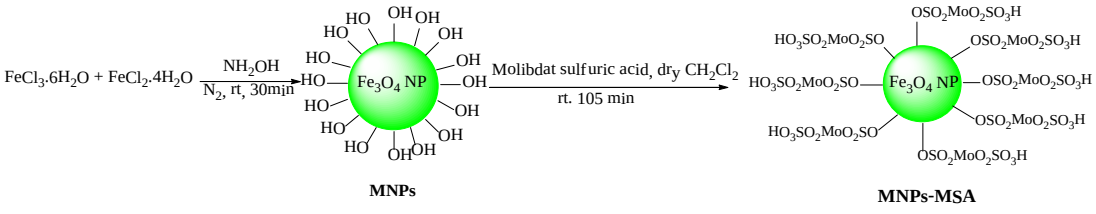
1. Introduction

Magnetic nano particles are efficient, readily available, high-surface-area, resulting in high catalyst loading capacity and outstanding stability heterogeneous supports for catalysts. They show identification and sometimes even higher activity than their corresponding homogeneous analogues [1,2,3]. More important, magnetic separation of the magnetic nano particles is more effective than filtration or centrifugation [4], simple, economical and promising for industrial applications [5]. Among the various magnetic nano particles as the core, magnetic support, Fe_3O_4 nano particles is arguably the most extensively studied [6,7,8].

Kojic acid is a natural pyrone produced by certain filamentous fungi, mainly species of *Aspergillus* and *Penicillium*. It is a common by-product in the fermentation of soy sauce, sake and rice wine, and is widely used as a food additive to prevent oxidative browning or in cosmetics as a depigmenting agent [9]–[11]. Derivatives of kojic acid also have antimicrobial activity against a variety of other fungi and bacteria [12], showing its potential as a polyfunctional backbone for new antimicrobial agents [13]. Therefore, the synthesis and selective functionalization of kojic acids have been the focus of active research over the years [14].

The MNPs–MSA was prepared by the concise route outlined in Scheme 1. Naked magnets Fe_3O_4 nanoparticles were prepared through chemical coprecipitation method, and subsequently were coated with MSA led to the corresponding molybdat sulfuric acid supported on magnetic nanoparticles (MNPs–MSA).



Scheme 1. Synthesis of MNPs-MSA

The XRD pattern of MNPs- MSA is shown in Figure 1. The position and relative intensities of all peaks in the XRD pattern of MNPs-MSA confirms well with the standard XRD pattern of Fe_3O_4 [15].

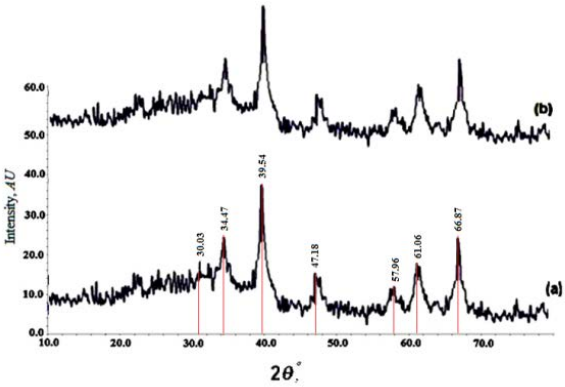


Figure 1. XRD patterns of MNPs (a) and MNPs@MSA (b)

Figure 1 shows the X-ray diffraction pattern of MNPs (Figure 1a) and MNP@MSA (Fig. 1b). The patterns of 2Θ values 30.03, 34.47, 39.54, 47.18, 57.96, 61.06 and 66.87 can be assigned to (220), (311), (400), (422), (511) and (440) crystal planes in Fe_3O_4 cubic lattice which agrees with the standard Fe_3O_4, were also observed for MNP@MSA (Fig. 1b). This revealed that the surface modification of the Fe_3O_4 nano particles does not lead to their phase change. However, the weaker peak intensities in pattern Figure 1b compared to Figure 1a can be attributed to the shielding effect of shell on magnetite.

The IR spectrum of MNPs-MSA shows peaks that are characteristic of a functioned SA group, which clearly differs from that of the unfunctionalized Fe_3O_4 nanomagnets and the MSA-supported magnetic nanoparticles (Figure 2). The FT-IR spectrum for the MNPs alone shows a stretching, vibration at 3420 cm^{-1} which incorporates the contributions from both symmetrical and asymmetrical modes of the O-H bonds which are attached to the surface iron atoms. The bands at low wave numbers (≤700 cm^{-1}) come from vibrations of Fe-O bonds of iron oxide, in which for the bulk Fe_3O_4 samples appear at 570 and 375 cm^{-1} but for Fe_3O_4 nanoparticles at 611 and 577 cm^{-1} as a blue shift, due to the size reduction [18,19]. The FT-IR spectra of MNPs-MSA Fe-O vibrations in the same vicinity, the band at 1221 cm^{-1} assigned to the Fe-O-S stretching vibrations and SO_3H moiety is asserted in 1221 cm^{-1}.

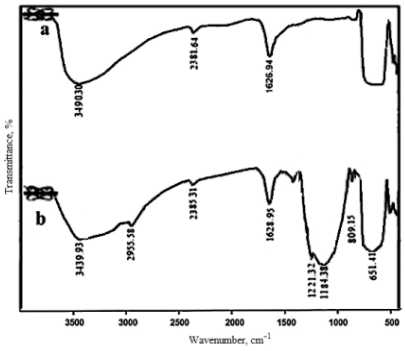


Figure 2. FT-IR spectra of (a) magnetic nanoparticles Fe_3O_4, (b) MNPs-MSA

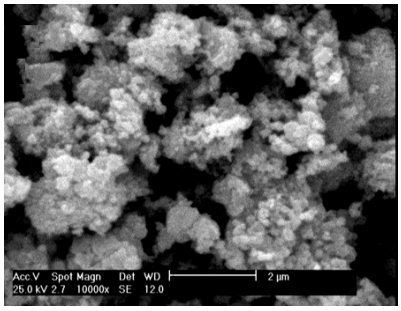


Figure 3. SEM images of MNPs-MSA

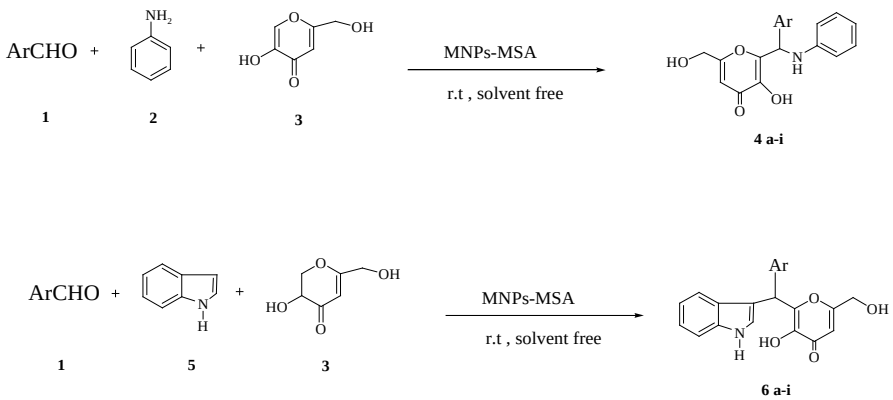
Figure 3 shows the SEM image of the synthesized molybdat sulfuric acid loaded magnetite nanoparticles. It was confirmed that the catalyst was made up of uniform nanometer-sized particles less than 19 nm.

1.1. PH Analysis of MNPs-MSA

To determine the acid amount on the surface, the prepared catalyst (100 mg) was added to an aqueous NaCl solution (1 M, 10 mL) with an initial pH = 5.90. The mixture stirred for 0.7 h, after which the pH of the solution.

2. Results and Discussions

In continuation of our studies on environmentally benign chemical processes [18-24], in the present work we disclose that MNPs- molybdate sulfuric acid can be used as a novel magnetic inter phase nano catalyst for the synthesis of 2-substituted aryl (amino) and aryl (indolyl) kojic acid **(4**a–j**, 6**a-j**)** under solvent-free conditions (Scheme **2**).



Scheme 2. MNPs-MSA catalyzes the preparation of 2-substituted aryl (amino) and aryl (indolyl) kojic acid derivatives.

In order to optimize the reaction conditions, we examined the synthesis of phenyl (amino) and phenyl (indol) kojic acid as a model compound using MNPs-MSA under various reaction conditions in terms of time and product yield (Table 1). As shown in Table 1, the reaction was incomplete in the absence of MNPs-MSA even after 24 h (entries1 and 2). The optimial amount of catalytic (MNPs-MSA) for synthesis of 2-substituted aryl (amino) and aryl (indolyl) kojic acid was 5 mg (0.87 mol %) under solvent-free conditions at room temperature.

Table 1. Optimization of the reaction conditions for synthesis of 2-phenyl amino kojic acid using reaction of aldehydes (1 mmol), aniline (1 mmol) or indole (1 mmol) and kojic acid (1 mmol)

Entry	Catalyst, 5 mg	Aniline / (Indole)	Solvent	Time	Yields, %
1	Catalyst-Free	aniline or (indole)	Solvent-Free	24h	0
2	Fe_3O_4 NP	aniline	Solvent-Free	24 h	21
3	MNPs-MSA	aniline	Solvent-Free	65 min	97
4	MNPs-MSA	aniline	CH_3CN	65 min	75
5	MNPs-MSA	aniline	CH_2Cl_2	65 min	52
6	MNPs-MSA	aniline	EtOH	65 min	35
7	Fe_3O_4 NP	(indole)	Solvent-Free	24 h	25
8	MNPs-MSA	(indole)	Solvent-Free	40 min	96
9	MNPs-MSA	(indole)	CH_3CN	40 min	77
10	MNPs-MSA	(indole)	CH_2Cl_2	40 min	47
11	MNPs-MSA	(indole)	EtOH	40 min	66

Table 2. MNPs-MSA -catalyzed synthesis of 2-substituted aryl (amino) and (indolyl) kojic acid derivatives (4)

Entry	Ar	Time, min	Yields, %[b]	M.P., °C [Ref.]
4a	C_6H_5	65	97	114-116 [23]
4b	4-$OMeC_6H_5$	67	95	127-129 [23]
4c	4-ClC_6H_5	55	96	119-121 [23]
4d	4-BrC_6H_5	58	97	122-125 [23]
4e	2-Naphtyl	64	94	108-110 [23]
4f	4-OHC_6H_5	70	96	99-101 [23]
4g	2-ClC_6H_5	68	97	103-105 [23]
4h	2-BrC_6H_5	67	95	96-98 [23]
4i	2-$OMeC_6H_5$	71	97	87-89 [23]
4j	4-MeC_6H_5	70	94	89-91 [23]
6a	C_6H_5	40	96	76-78 [12]
6b	4-$OMeC_6H_5$	48	92	96-98 [12]
6c	4-ClC_6H_5	37	95	93-95 [12]
6d	4-BrC_6H_5	39	91	91-93 [12]
6e	2-Naphtyl	49	89	86-88 [12]
6f	4-OHC_6H_5	54	90	89-91 [12]
6g	2-ClC_6H_5	42	91	81-83 [12]
6h	CH_3CH_2	57	88	Oil [12]
6i	2-BrC_6H_5	40	93	Oil [12]

[a]) All products were characterized by ^{1}H NMR and ^{13}C NMR [12,23].
[b]) Isolated yields.

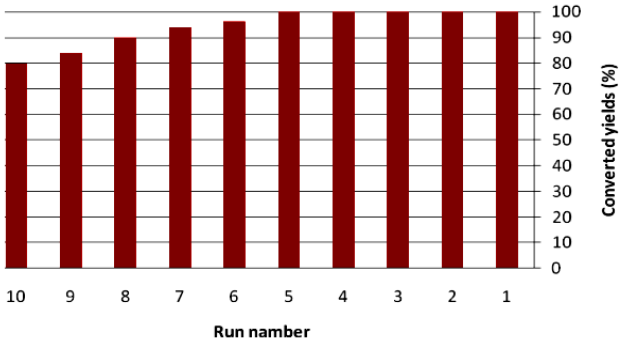


Figure 4. The recycling experiment of MNPs-MSA (5 mg, 0.87 mol %) in synthesis of 2-phenyl (amino) and phenyl (indolyl) kojic acid at room temperature

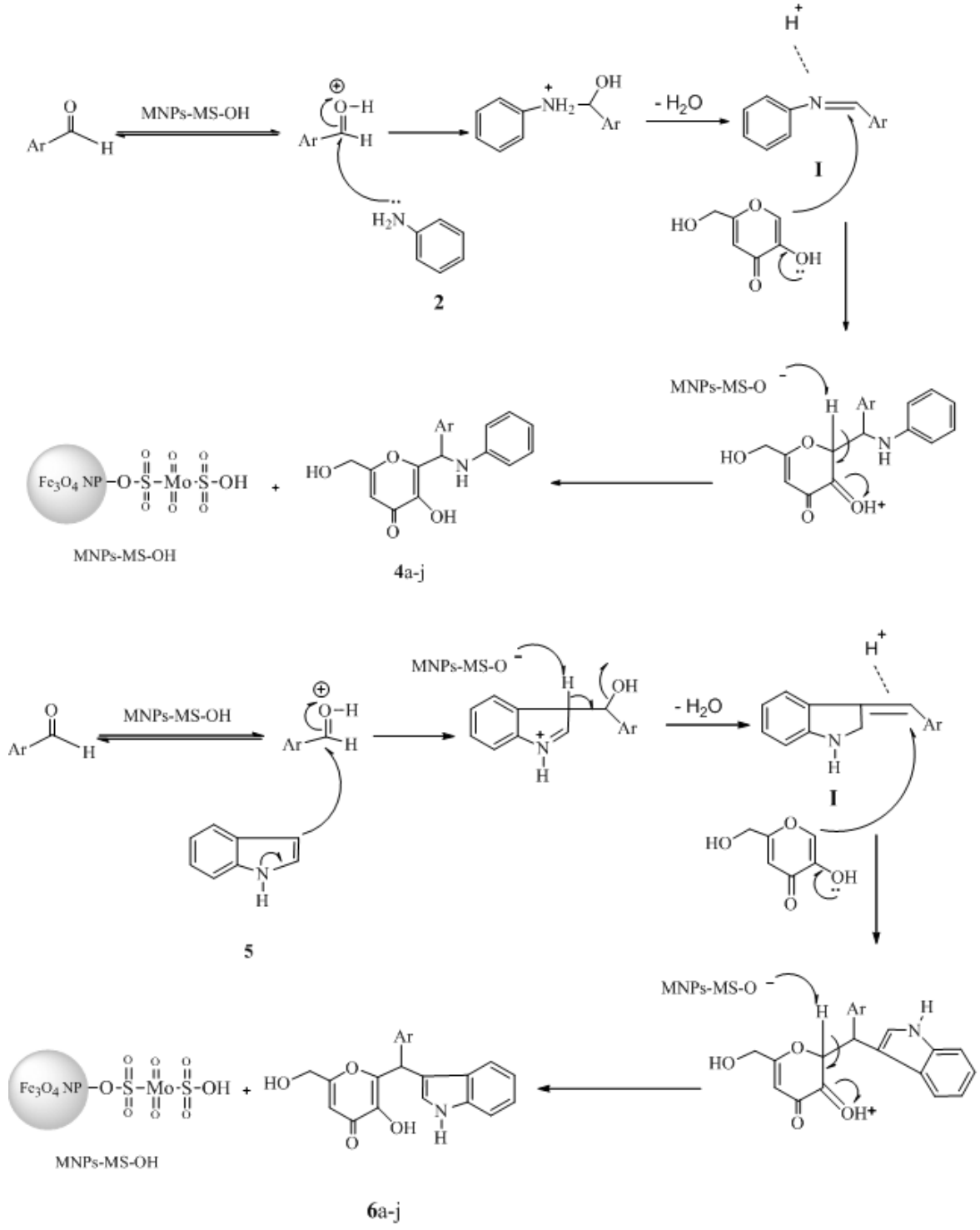
The remaining magnetic nano catalyst was further washed with diethylether to remove residual product. Then, the reaction vessel was charged with fresh substrate and subjected to the next. As shown in Figure 4, the catalyst can be recycled up to 10 runs without any significant loss of activity. In addition, one of the attractive features of this novel catalyst system is the rapid (within 5 s) and efficient separation of the catalyst (100%) by using an appropriate external magnet, which minimizes the loss of catalyst during separation.

For practical purposes, the ability to easily recycle the catalysts is highly desirable. To investigate this issue, the recyclability of the catalyst was examined for the synthesis of 2-substituted aryl (amino) and aryl (indolyl) kojic acid derivatives. We found that this catalyst demonstrated remarkably excellent reusability; after the completion of the reaction, the reaction mixture was diluted with diethyl ether and the catalyst was easy and rapidly separated from the product by exposure to an external magnet and decantation of the reaction solution (Figure 5).

Figure 5. Image showing MNPs-MSA can be separated by applied magnetic field. A reaction mixture in the absence (left) or presence of a magnetic field (right)

Mechanistically, a reasonable pathway for the synthesis of 2-substituted aryl (amino) kojic acid **4**a-j and 2-substituted aryl (indolyl) kojic acid **6**a-j using MNPs-MSA is described in Scheme 2.

We presume that when aniline or indole is treated with aldehyde in the presence of MNPs-MSA, an intermediate (**I**) is formed which is attacked by kojic acid under the influence MNPs-MSA to get the 2-substituted aryl (amino) and aryl (indolyl) kojic acid (Scheme 3).



Scheme 3. Suggested mechanism for the formation of 2-substituted aryl (amino) and aryl (indolyl) kojic acid catalyzed MNPs-MSA

3. Experimental

All reactions were monitored on TLC by comparison with the samples prepared by known procedures. The Infrared spectroscopy (IR) spectra were recorded using a Shimadzu 435-U-04 spectrophotometer (KBr pellets) and ^{1}H and ^{13}C NMR spectra were recorded in DMSO-d_6 with Bruker 300 MHz high resolution NMR spectrometers. The X-ray powder diffraction (XRD) data were collected on an X 'Pert MPD Philips diffractometer. The SEM image was obtained by VEGA TESCAN. All melting points were determined on a Büchi 530 melting point apparatus and are reported uncorrected.

3.1. Preparation of Molybdate Sulfuric Acid-functioned Magnetic Fe_3O_4 Nanoparticles (MNPs-MSA)

The MNPs powder (1.5 g) was dispersed in 100 mL ethanol/water (volume ratio 1:4) solution by stirred for 30 min, and then molybdate sulfuric acid (0.6 g) was added to the mixture. After mechanical stirring under N_2 atmosphere at 40°C for 4 h, the suspended substance was separated with centrifugation (RCF = 13,200 × g for 20 min). Then, the final product was separated by magnetic decantation and washed twice by dry CH_2Cl_2, EtOH and

CH_2Cl_2 respectively to remove the unattached substrates [25,26]. The product stored in a refrigerator to use.

3.2. General Procedure for the Synthesis of 2-substituted aryl (amino) kojic acid derivatives (4a–j)

A mixture of aldehyde derivatives (1 mmol), kojic acid (1 mmol, 0.126 g), aniline (1 mmol, 0.93 g) and MNPs-MSA (5 mg, 0.87 mol %) was added and the mixture was stirred at room temperature for the time specified. The reaction progress was monitored by TLC (EtOAc/hexane, 3:7). After completion of the reaction, Et_2O (2× 5 mL) was added and the catalyst was separated by an external magnet. The combined organics were washed with brine (5 mL) and dried over anhydrous Na_2SO_4.The resulting solution was concentrated under reduced pressure to afford the essentially pure products in most cases. Further purification was achieved by short-column chromatography on silica gel with EtOAc/n-hexane as eluent. The products obtained were fully characterized by spectroscopic methods such as IR, ^{1}H-NMR and ^{13}C-NMR and have been identified by the comparison of the reported spectral data [3].

3-Hydroxy-6-hydroxymethyl-2-(phenyl-phenylamino-methyl)-pyran-4-one (4a): Yield: 97%; ^{13}C-NMR (DMSO-d_6): δ 187.1 (**C**=O), 177.5 ($C_{coj.}$), 143.5, 142.4, 139.0 ($C_{coj.}$), 132.7, 131.2, 130.5, 129.4, 128.7 ($C_{coj.}$), 127.7, 120.3, 119.1, 118.3, 116.9, 112.8, 112.3, 71.3 (**C**H_2), 55.8 (**C**H); ^{1}H-NMR (DMSO + $CDCl_3$, 1:4): δ 8.77 (1H, *s*, O**H**), 6.43–7.14 (10H, *m*, C$\mathbf{H}_{arom.}$), 6.31 (1H, s, =C**H**), 4.59 (1H, *s*, C**H**), 4.25 (1H, s, N**H**), 4.22 (2H, s, C$\mathbf{H}_2$), 3.75 (1H, s, CH_2O**H**); IR (KBr): υ 3331, 2927, 2851, 1712, 1624, 1461, 1208, 747.

3-Hydroxy-6-hydroxymethyl-2-[(4-methoxy-phenyl)-phenylamino-methyl]-pyran-4-one (4b): Yield: 95%; ^{13}C-NMR (DMSO-d_6): δ 187.3 (**C**O), 177.6 ($C_{coj.}$), 143.4, 141.8, 138.5 ($C_{coj.}$), 132.3, 131.5, 130.9, 128.8, 129.2 ($C_{coj.}$), 127.4, 121.0, 119.3, 118.5, 116.7, 112.6, 112.1, 71.5 (**C**H_2), 57.3 (**C**H_3), 55.7 (**C**H); ^{1}H-NMR (DMSO + $CDCl_3$, 1:4): δ 8.93 (1H, *s*, O**H**), 6.52–7.03 (9H, *m*, C$\mathbf{H}_{arom.}$), 6.38 (1H, *s*, =C**H**), 4.61 (1H, *s*, C**H**), 4.03 (1H, *s*, N**H**), 4.20 (2H, *s*, C$\mathbf{H}_2$), 3.73 (3H, *s*, OC$\mathbf{H}_3$), 3.41 (1H, *s*, CH_2O**H**); IR (KBr): υ 3328, 2925, 1701, 1615, 1451, 1317, 1252, 1090, 759, cm^{-1}.

3-Hydroxy-6-hydroxymethyl-2-[(4-chloro-phenyl)-phenylamino-methyl]-pyran-4-one (4c): Yield: 96%; ^{13}C-NMR (DMSO-d_6): δ 186.9 (**C**O), 177.2 ($C_{coj.}$), 143.1, 141.5, 138.4 ($C_{coj.}$), 132.0, 131.2, 130.7, 129.7, 128.4 ($C_{coj.}$), 127.7, 121.6, 119.9, 118.7, 116.9, 113.2, 112.4, 71.6 (**C**H_2), 55.8 (**C**H); ^{1}H-NMR (DMSO + $CDCl_3$, 1:4): δ 8.87 (1H, *s*, O**H**), 6.41–7.15 (9H, *m*, C$\mathbf{H}_{arom.}$), 6.29 (1H, *s*, =C**H**), 4.58 (1H, *s*, C**H**), 4.01 (1H, *s*, N**H**), 4.22 (2H, *s*, C$\mathbf{H}_2$), 3.48 (1H, *s*, CH_2O**H**); IR (KBr): υ 3358, 2932, 1691, 1627, 1488, 1450, 1221, 996, 741 cm^{-1}.

3-Hydroxy-6-hydroxymethyl-2-[(4-bromo-phenyl)-phenylamino-methyl]-pyran-4-one (4d): Yield: 97%; ^{13}C-NMR (DMSO-d_6): δ 186.1 (**C**O), 176.9 ($C_{coj.}$), 144.3, 142.3, 138.3 ($C_{coj.}$), 134.3, 132.8, 130.9, 129.6, 128.5 ($C_{coj.}$), 127.5, 122.1, 119.7, 118.3, 116.8, 114.4, 112.3, 71.7 (**C**H_2), 55.7 (**C**H); ^{1}H-NMR (DMSO + $CDCl_3$, 1:4): δ 8.63 (1H, *s*, O**H**), 6.52–7.19 (9H, *m*, C$\mathbf{H}_{arom.}$), 6.21 (1H, *s*, =C**H**), 4.57 (1H, *s*, C**H**), 4.02 (1H, *s*, N**H**), 4.21 (2H, *s*, C$\mathbf{H}_2$), 3.47 (1H, *s*, CH_2O**H**); IR (KBr): υ 3391, 2924, 1713, 1618, 1509, 1456, 1302, 1179, 1030, 860, 745 cm^{-1}.

3-Hydroxy-6-hydroxymethyl-2-(naphthalen-1-yl-phenylamino-methyl)-pyran-4-one (4e): Yield: 94%; ^{13}C-NMR (DMSO-d_6): δ 185.7 (**C**O), 176.8 ($C_{coj.}$), 144.2, 142.5, 138.1 ($C_{coj.}$), 134.7, 132.5, 131.2, 129.8, 128.5 ($C_{coj.}$), 127.5, 125.5, 125.2, 124.8, 123.3, 122.1, 119.5, 118.7, 116.4, 114.5, 112.2, 71.7 (**C**H_2), 55.6 (**C**H); ^{1}H-NMR (DMSO + $CDCl_3$, 1:4): δ 7.89 (1H, *s*, O**H**), 6.43–7.64 (12H, *m*, C$\mathbf{H}_{arom.}$), 6.30 (1H, *s*, =C**H**), 4.59 (1H, *s*, C**H**), 4.00 (1H, *s*, N**H**), 4.20 (2H, *s*, C$\mathbf{H}_2$), 3.37 (1H, *s*, CH_2O**H**); IR (KBr): υ 3394, 2928, 1705, 1624, 1581, 1455, 1268, 1163, 748 cm^{-1}.

3-Hydroxy-6-hydroxymethyl-2-[(4- hydroxy - phenyl)-phenylamino - methyl]-pyran-4-one (4f): Yield: 96%; ^{13}C-NMR (DMSO-d_6): δ 186.1 (**C**O), 176.9 ($C_{coj.}$), 155.3, 144.5, 142.4, 138.5 ($C_{coj.}$), 134.4, 131.1, 129.2, 128.1 ($C_{coj.}$), 127.4, 122.2, 119.3, 118.5, 116.6, 114.2, 112.5, 71.7 (**C**H_2), 55.6 (**C**H); ^{1}H-NMR (DMSO + $CDCl_3$, 1:4): δ 8.71 (1H, *s*, O**H**), 6.39–7.08 (9H, *m*, C$\mathbf{H}_{arom.}$), 6.22 (1H, *s*, =C**H**), 5.03 (1H, *s*, O**H**), 4.58 (1H, *s*, C**H**), 4.01 (1H, *s*, N**H**), 4.22 (2H, *s*, C$\mathbf{H}_2$), 3.48 (1H, *s*, CH_2O**H**); IR (KBr): υ 3379, 2954, 2705, 1658, 1624, 1514, 1451, 1195, 1020, 747 cm^{-1}.

3-Hydroxy-6-hydroxymethyl-2-[(2-chloro-phenyl)-phenylamino-methyl]-pyran-4-one (4g): Yield: 97%; ^{13}C-NMR (DMSO-d_6): δ 187.5 (**C**O), 177.2 ($C_{coj.}$), 143.2, 141.6, 138.4 ($C_{coj.}$), 132.0, 131.5, 130.7, 129.7, 128.4 ($C_{coj.}$), 127.6, 121.5, 119.9, 118.8, 116.9, 113.3, 112.4, 71.6 (**C**H_2), 55.7 (**C**H); ^{1}H-NMR (DMSO + $CDCl_3$, 1:4): δ 8.93 (1H, *s*, O**H**), 6.72–7.31 (9H, *m*, C$\mathbf{H}_{arom.}$), 6.32 (1H, *s*, =C**H**), 4.59 (1H, *s*, C**H**), 4.02 (1H, *s*, N**H**), 4.23 (2H, *s*, C$\mathbf{H}_2$), 3.47 (1H, *s*, CH_2O**H**); IR (KBr): υ 3387, 2927, 1707, 1650, 1576, 1457, 1310, 1208, 1071, 833, 748 cm^{-1}.

3-Hydroxy-6-hydroxymethyl-2-[(2-bromo-phenyl)-phenylamino-methyl]-pyran-4-one (4h): Yield: 95%; ^{13}C-NMR (DMSO-d_6): δ 187.3 (**C**O), 176.8 ($C_{coj.}$), 144.5, 142.4, 138.3 ($C_{coj.}$), 134.4, 132.8, 131.7, 129.8, 128.5 ($C_{coj.}$), 127.9, 122.2, 119.5, 118.3, 116.7, 114.5, 112.4, 71.7 (**C**H_2), 55.7 (**C**H); ^{1}H-NMR (DMSO + $CDCl_3$, 1:4): δ 8.81 (1H, *s*, O**H**), 6.54–7.23 (9H, *m*, C$\mathbf{H}_{arom.}$), 6.22 (1H, *s*, =C**H**), 4.57 (1H, *s*, C**H**), 4.02 (1H, *s*, N**H**), 4.21 (2H, *s*, C$\mathbf{H}_2$), 3.47 (1H, *s*, CH_2O**H**); IR (KBr): υ 3367, 2923, 1703, 1647, 1453, 1377, 1240, 10514, 989, 753 cm^{-1}.

3-Hydroxy-6-hydroxymethyl-2-[(2-methoxy-phenyl)-phenylamino-methyl]-pyran-4-one (4i): Yield: 97%; ^{13}C-NMR (DMSO-d_6): δ 187.5 (**C**O), 177.6 ($C_{coj.}$), 143.3, 141.1, 138.8 ($C_{coj.}$), 132.2, 131.1, 130.5, 128.7, 129.2 ($C_{coj.}$), 127.4, 121.0, 119.4, 118.5, 116.3, 112.9, 112.2, 71.6 (**C**H_2), 57.4 (**C**H_3), 55.8 (**C**H); ^{1}H-NMR (DMSO + $CDCl_3$, 1:4): δ 8.81 (1H, *s*, O**H**), 6.60–7.11 (9H, *m*, C$\mathbf{H}_{arom.}$), 6.39 (1H, *s*, =C**H**), 4.62 (1H, *s*, C**H**), 4.02 (1H, *s*, N**H**), 4.21 (2H, *s*, C$\mathbf{H}_2$), 3.89 (3H, *s*, OC$\mathbf{H}_3$), 3.42 (1H, *s*, CH_2O**H**); IR (KBr): υ 3310, 2929, 1692, 1621, 1514, 1450, 1248, 1034, 765 cm^{-1}.

3-Hydroxy-6-hydroxymethyl-2-[(4-methyl-phenyl)-phenylamino-methyl]-pyran-4-one (4j): Yield: 94%; ^{13}C-NMR (DMSO-d_6): δ 187.1 (**C**O), 177.5 ($C_{coj.}$), 143.4, 139.4, 138.8 ($C_{coj.}$), 135.7, 131.2, 130.5, 128.7, 129.1 ($C_{coj.}$), 127.5, 121.1, 119.4, 118.5, 116.1, 112.9, 112.2, 71.7 (**C**H_2), 55.7 (**C**H), 20.9 (**C**H_3); ^{1}H-NMR (DMSO + $CDCl_3$, 1:4): δ 8.34 (1H, *s*, O**H**), 6.41–7.05 (9H, *m*, C$\mathbf{H}_{arom.}$), 6.38 (1H, *s*, =C**H**), 4.52 (1H, *s*, C**H**), 4.01 (1H, *s*, N**H**), 4.20 (2H, *s*, C$\mathbf{H}_2$), 3.41 (1H, *s*, CH_2O**H**), 2.31 (3H, *s*,

C**H**$_3$); IR (KBr): υ 3355, 2930, 1621, 1578, 1459, 1249, 1181, 763 cm^{-1}.

3.3. General Procedure for the Synthesis of 2-substituted aryl (indolyl) kojic acid derivatives (6a–i)

A mixture of aldehyde derivatives (1 mmol), kojic acid (1 mmol, 0.126 g), indole (1 mmol, 0.117 g) and MNPs-MSA (5 mg, 0.87 mol %) was stirred at room temperature for a specified time as required to complete the reaction (Table 2). After complete conversion, as indicated by TLC, the reaction mixture was diluted with water and extracted with ethyl acetate (2×10 mL). The combined organic layers were dried over anhydrous Na_2SO_4, concentrated in vacuo and purified by column chromatography on silica gel (Merck, 60–120 mesh, ethyl acetate/hexane, 3:7) to afford the pure substituted aryl (indolyl) kojic acid derivatives. The products obtained were fully characterized by spectroscopic methods such as IR, ^{1}H-NMR and ^{13}C-NMR and have been identified by the comparison of the reported spectral data [12].

2-((1*H*-Indol-3-yl) (phenyl)methyl)-3-hydroxy-6-(hydroxymethyl)-4*H*-pyran-4-one (6a): Yield: 96%; ^{13}C-NMR (DMSO-d_6): δ 174.1 (**C**=O), 166.9 ($C_{coj.}$), 150.3, 141.8, 138.7 ($C_{coj.}$), 135.3, 132.7, 131.2, 130.5, 128.4 ($C_{coj.}$), 127.7, 120.3, 119.1, 118.3, 112.91, 111.1, 109.4, 107.8, 59.7, 38.3, 11.5; ^{1}H-NMR (400 MHz, DMSO + $CDCl_3$, 1:4): δ 10.79 (1H, *s*, N**H**), 8.81 (1H, *s*, O**H**), 7.03–7.19 (3H *m*, C**H**$_{ind.}$), 7.25–7.39 (2H *m*, C**H**$_{ind.}$), 7.41–7.68 (5H, *m*, C**H**$_{arom}$), 6.35 (1H, *s*, =C**H**), 5.97 (1H, *s*, CH_2O**H**), 5.29 (1H, *s*, C**H**), 4.30 (2H, *s*, C**H**$_2$); IR (KBr): υ 3331, 2927, 2851, 1712, 1624, 1461, 1208, 747 cm^{-1}.

2-((1*H*-Indol-3-yl)(4-methoxyphenyl)methyl)-3-hydroxy-6-(hydroxymethyl)- 4*H*-pyran- 4-one (6b): Yield: 92%; ^{13}C-NMR (DMSO-d_6): δ 173.8(**C**=O), 165.5 ($C_{coj.}$), 157.9, 155.6, 152.2, 140.5 ($C_{coj.}$), 136.7, 133.2, 132.8, 130.7, 129.8 ($C_{coj.}$), 126.1, 123.5, 122.7, 118.4, 117.9, 1112, 108.4, 59.4, 53.8, 37.2, 11.8; ^{1}H-NMR (400 MHz, DMSO + $CDCl_3$, 1:4): δ 10.27 (1H, *s*, N**H**), 7.32 (1H, *s*, O**H**), 6.77–7.50 (9H, *m*, C**H**$_{arom}$), 6.58 (1H, *s*, =C**H**), 6.01 (1H, *s*, CH_2O**H**), 5.68 (1H, *s*, C**H**), 4.41 (2H, *s*, C**H**$_2$), 3.63 (3H, *s*, CH_3); IR (KBr): υ 3328, 2925, 1701, 1615, 1512, 1511, 1451, 1317, 1252, 1090, 995, 759, 738cm^{-1}.

2-((1*H*-Indol-3-yl)(4-chlorophenyl)methyl)-3-hydroxy-6-(hydroxymethyl)-4*H*-pyran-4-one (6c): Yield: 95%; ^{13}C-NMR (DMSO-d_6): δ 173.6 (**C**=O), 170.4 ($C_{coj.}$), 167.1, 157.6, 151.5, 141.3, 137.9 ($C_{coj.}$), 133.4, 131.7, 128.7, 127.4 ($C_{coj.}$), 120.0, 118.9, 110.5, 108.8, 59.7, 59.4, 54.9, 20.7, 14.07, 11.8; ^{1}H-NMR (DMSO + $CDCl_3$): δ 10.35 (1H, *s*, N**H**), 7.74 (1H, *s*, O**H**), 6.73–7.48 (9H, *m*, C**H**$_{arom}$), 6.64 (1H, *s*, =C**H**), 6.14 (1H, *s*, CH_2O**H**), 5.67 (1H, *s*, C**H**), 4.48 (2H, *s*, C**H**$_2$); IR (KBr): υ 3391, 2924, 1713, 1618, 1576, 1509, 1456, 1302, 1245, 1179, 1030, 860, 828, 745cm^{-1}.

2-((1*H*-Indol-3-yl)(4-bromophenyl)methyl)-3-hydroxy-6-(hydroxymethyl)- 4*H*-pyran- 4-one (6d): Yield: 91%; ^{13}C NMR (DMSO): δ 174.1 (**C**=O), 170.8 ($C_{coj.}$), 167.5, 157.2, 152.1, 141.4, 138.3($C_{coj.}$), 133.0, 132.1, 128.5 ($C_{coj.}$), 127.1, 120.3, 118.7, 110.6, 108.5, 59.4, 59.1, 55.8, 20.3, 14.05, 11.4; ^{1}H-NMR (DMSO + $CDCl_3$): δ 10.33 (1H, *s*, N**H**), 7.76 (1H, *s*, O**H**), 6.61–7.39 (9H, *m*, C**H**$_{arom}$), (1H, *s*, =C**H**), 6.07 (1H, *s*, CH_2O**H**), 5.66 (1H, *s*, C**H**), 4.47 (2H, *s*, C**H**$_2$); IR (KBr): υ 3394, 2928, 1705, 1624, 1581, 4197, 1455, 1268, 1163, 1072, 748 cm^{-1}.

2-((1*H*-Indol-3-yl)(2-naphtyl)methyl)-3-hydroxy-6-(hydroxymethyl)- 4*H*-pyran- 4-one (6e): Yield: 89%; ^{13}C-NMR (DMSO-d_6): δ 173.5 (**C**=O), 168.3 ($C_{coj.}$), 167.2, 152.0, 147.8, 145.4, 142.3, 139.4, 138.2 ($C_{coj.}$), 133.3, 131.5, 130.7, 127.2 ($C_{coj.}$), 121.8, 120.2, 118.9, 118.4, 115.1, 112.8, 109.5, 108.7, 108.3, 59.6, 55.8, 11.7; ^{1}H-NMR (DMSO + $CDCl_3$): δ 10.27 (1H, *s*, N**H**), 7.90 (1H, *s*, O**H**), 7.18–7.83 (12H, *m*, C**H**$_{arom}$), 6.89 (1H, *s*, =C**H**), 6.10 (1H, *s*, CH_2O**H**), 5.68 (1H, *s*, C**H**), 4.43 (2H, *s*, C**H**$_2$); IR (KBr): υ 3379, 2954, 2705, 1658, 1624, 1575, 1514, 1451, 1195, 1020, 863, 747 cm^{-1}.

2-((1*H*-Indol-3-yl)(4-hydroxyphenyl)methyl)-3-hydroxy-6-(hydroxymethyl)- 4*H*-pyran-4-one (6f): Yield: 90%; ^{13}C-NMR (DMSO-d_6): δ 173.2(**C**=O), 167.4 ($C_{coj.}$), 155.8, 150.5, 141.3, 137.9 ($C_{coj.}$), 135.6, 133.2, 131.0, 129.7, 128.3 ($C_{coj.}$), 127.4, 121.4, 118.8, 118.0, 110.4, 108.3, 107.6, 59.2, 38.5, 11.8; ^{1}H-NMR (DMSO + $CDCl_3$): δ 10.25 (1H, *s*, N**H**), 8.79 (1H, *s*, O**H**), 6.92–7.41 (9H, *m*, C**H**$_{arom}$), 6.89 (1H, *s*, =C**H**), 6.68 (1H, *s*, PhO**H**), 6.12 (1H, *s*, CH_2O**H**), 5.68 (1H, *s*, C**H**), 4.41 (2H, *s*, C**H**$_2$); IR (KBr): υ 3387, 2927, 1707, 1650, 1619, 1576, 1457, 1310, 1208, 1071, 1011, 869, 833, 748 cm^{-1}.

2-((1*H*-Indol-3-yl)(2-chlorophenyl)methyl)-3-hydroxy-6-(hydroxymethyl)- 4*H*-pyran- 4-one (6g): Yield: 91%; ^{13}C-NMR (DMSO-d_6): δ 174.0 (**C**=O), 167.6 ($C_{coj.}$), 151.2, 141.4, 137.5 ($C_{coj.}$), 135.6, 135.3, 133.2, 132.7, 127.8 ($C_{coj.}$), 126.2, 125.1, 120.3, 118.1, 110.4, 108.5, 107.4, 59.3, 20.5, 11.6; ^{1}H-NMR (DMSO + $CDCl_3$): δ 10.26 (1H, *s*, N**H**), 7.95 (1H, *s*, O**H**), 7.15–7.69 (9H, *m*, C**H**$_{arom}$), 6.42 (1H, *s*, =C**H**), 5.79 (1H, *s*, CH_2O**H**), 5.79 (1H, *s*, C**H**), 4.43 (2H, *s*, C**H**$_2$); IR (KBr): υ 3367, 2923, 1703, 1647, 1581, 1453, 1377, 1240, 10514, 989, 822, 753 cm^{-1}.

3-hydroxy-6-hydroxymethyl-2-((1*H*-Indol-3-yl) propyl)- 4*H*-pyran- 4-one (6h): Yield: 88%; ^{13}C-NMR (DMSO-d_6): δ 172.8 (**C**=O), 156.5 ($C_{coj.}$), 149.6, 138.1 ($C_{coj.}$), 132.1, 127.4 ($C_{coj.}$), 126.7, 123.2, 122.7, 112.3, 111.8, 110.2, 107.1, 58.7, 30.4, 18.5, 15.7, 12.3; ^{1}H-NMR (DMSO + $CDCl_3$): δ 10.39 (1H, *s*, N**H**), 7.68 (1H, *s*, O**H**), 7.23–7.56 (5H, *m*, C**H**$_{arom}$), 6.96 (1H, *s*, =C**H**), 5.90 (1H, *s*, CH_2O**H**), 5.18 (1H, *s*, C**H**), 4.50 (2H, *s*, C**H**$_2$), 4.45 (3H, *t*, *J*=7.9 Hz), 1.75 (3H, *q*, 4H); IR (KBr): υ 3310, 2929, 1692, 1621, 1514, 1450, 1248, 1034, 795, 765 cm^{-1}.

2-((1*H*-Indol-3-yl)(2-bromophenyl)methyl)-3-hydroxy-6-(hydroxymethyl)- 4*H*-pyran- 4-one (6i): Yield: 93%; ^{13}C-NMR (DMSO-d_6): δ 174.1(**C**=O), 170.8 ($C_{coj.}$), 167.5, 157.2, 152.1, 141.4, 137.3 ($C_{coj.}$), 133.0, 132.1, 128.5 ($C_{coj.}$), 127.1, 120.3, 118.7, 110.6, 108.5, 59.4, 59.1, 55.8, 20.3, 14.05, 11.4; ^{1}H-NMR (DMSO + $CDCl_3$): δ 10.33 (1H, *s*, N**H**), 7.76 (1H, *s*, O**H**), 6.61–7.39 (9H, *m*, C**H**$_{arom}$), 6.54 (1H, *s*, =C**H**), 6.07 (1H, *s*, CH_2O**H**), 5.66 (1H, *s*, C**H**), 4.47 (2H, *s*, C**H**$_2$); IR (KBr): υ 3394, 2928, 1705, 1624, 1581, 4197, 1455, 1268, 1163, 1072, 748 cm^{-1}.

4. Conclusion

In summary, we have synthesized the first MNPs-MSA for use as a magnetically heterogeneous basic nanocatalyst. The catalyst is easily synthesized and can catalyze the synthesis of 2-substituted aryl (amino) and aryl (indolyl) kojic acid derivatives from kojic acid with different aldehydes and aniline or indole with good to high yields

under solvent-free conditions at room temperature. The characteristic aspects of this catalyst are rapid, simple and efficient separation by using an appropriate external magnet, which minimizes the loss of catalyst during separation and reusable for several times with little loss of activity**.**

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