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Nano-CoFe₂O₄ supported molybdenum as an efficient and magnetically recoverable catalyst for a one-pot, four-component synthesis of functionalized pyrroles[†]

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A novel magnetic nanoparticle $CoFe_2O_4$ supported Mo ($[CoFe_2O_4@SiO_2-PrNH_2-Mo(acac)_2]$) was prepared and found to be a highly active and efficient catalyst for a one-pot synthesis of polysubstituted pyrroles *via* four-component reaction of aldehydes, amines, 1,3-dicarbonyl compounds and nitromethane. The easy recovery of the catalyst and reusability, broad substrate scopes, short reaction time, high yields of products and solvent-free conditions make this protocol practical, environmentally friendly and economically attractive.

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Introduction

Pyrroles are broadly found as important structural motifs in numerous natural products as well as bioactive compounds such as porphyrins, bile pigments, coenzymes, and alkaloids.¹ They have also tremendous applications in materials science, medicinal chemistry and drug synthesis.² Widespread synthetic utilities coupled with the interesting biological activities have made them attractive synthetic targets. The most common routes for the construction of pyrrole rings are Clauson-Kaas condensation,³ Hantzsch reaction,⁴ the Paal-Knorr synthesis⁵ and various cycloaddition methods.⁶ However, it remains difficult to prepare the structural variety of pyrroles by these methodologies. Consequently, conceptually novel and elegant procedures have been devised for the construction of functionalized pyrroles, for example, (1) tandem one-pot addition and cyclization of the Blaise reaction intermediate and nitroolefins, $^{7}(2)$ dehydrogenative coupling of β -amino alcohols with secondary alcohols,⁸ (3) the intermolecular Wacker-type reaction of unactivated alkenes with amines,⁹ (4) rhodium-catalyzed reaction of furans with N-sulfonyl-1,2,3-triazoles,¹⁰ (5) oxidative annulation of enamides with alkynes,¹¹ (6) the coupling of α -diazoketones with β -enaminoketones and esters,¹² (7) oxidative alkyne annulations with electron-rich enamines,¹³ (8) tandem cyclization of alkynoates with amines,¹⁴ (9) cyclization of propargylic carbonates with β -enamino esters,¹⁵ (10) copper-catalyzed reaction of amine with but-2-ynedioate,¹⁶ (11) reaction of α -azido chalcones and 1,3-dicarbonyl compounds,¹⁷ and (12) *via* the one-pot two-step procedure by the treatments of acetaldehyde, ethyl acetoacetate, sodium carbonate, piperidine, and iodine.¹⁸ In addition, multicomponent reactions have been proven to be efficient methods for the synthesis of highly substituted pyrroles.¹⁹ Despite these achievements, the further development of effective, environmentally benign and practical procedures to synthesize functionalized pyrroles that minimize the use of special reagents, cost, time, and steps from readily available and inexpensive materials is a very important subject.

With the increasing demand for "green chemistry", the design of efficient and recoverable supported heterogeneous catalysts becomes one of the most important topics of research in synthetic organic chemistry, material science, and engineering. The catalyst immobilization enables the efficient recovery of the catalyst from the product without a troublesome separation process. One of the most attractive alternatives to catalyst supports are magnetic nanoparticles (MNPs), which have witnessed increasing popularity due to their high surface areas and improved dispersability in the reaction medium. Specifically, magnetically supported catalysts can be recovered using an external magnet due to the paramagnetic character of the support. This makes the removal and recycling of the catalyst much easier than filtration and centrifugation. Moreover, functionalized MNPs can be easily prepared by appropriate structural surface modification and have been applied in a range of organic transformations.²⁰ Among various MNPs, cobalt ferrite $(CoFe_2O_4)$ with the general formula AB_2O_4 is one of the most versatile magnetic materials as it has high saturation magnetization, chemical stability, low toxicity, readily accessibility,



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inexpensiveness and relatively high permeability.²¹ Meanwhile, multicomponent reactions (MCRs) have been shown to provide efficient access to structurally complex target compounds with fascinating biological properties in a one-pot manner ensuring atom economy, high overall yields and high selectivity, minimizing waste, labor, and manpower, and less time consumption, and obviation of complicated purification processes.²² The combination of the benefits of multicomponent reactions and environmentally compatible catalysts can be considered to result in a highly green synthesis design.

Considering the above subjects and continuing our efforts toward the design of magnetic nanocatalysts²³ and sustainable synthesis development,²⁴ herein, we report on the preparation of a new type of magnetic nanoparticle-supported Mo complex ([CoFe₂O₄@SiO₂-PrNH₂-Mo(acac)₂]) and its application in the synthesis of *N*-protected functionalized pyrroles *via* four-component reactions (4CRs) of amines, aldehydes, 1,3-dicarbonyl compounds and nitromethane (Scheme 1).

Results and discussion

The MNP-supported Mo complex ($[CoFe_2O_4@SiO_2-PrNH_2-Mo(acac)_2]$) was synthesized according to the procedure shown in Scheme 2. At first, $CoFe_2O_4$ nanoparticles were prepared by a chemical co-precipitation technique using $FeCl_3 \cdot 6H_2O$ and $CoCl_2 \cdot 6H_2O$ as precursors according to the method reported in the literature.²⁵ The coating of a layer of silica on the surface of $CoFe_2O_4$ nanoparticles was achieved by sonication of a $CoFe_2O_4$ suspension in an alkaline ethanol-water solution of tetraethyl orthosilicate (TEOS). Particle surfaces were further functionalized with 3-aminopropyltriethoxysilane (APTES) in refluxing toluene to afford aminated- $CoFe_2O_4@SiO_2$ MNPs. The molybdenyl acetylacetonate complex was then anchored to aminated- $CoFe_2O_4@SiO_2$ to yield MNPs supported Mo catalyst ($CoFe_2O_4@SiO_2-PrNH_2-Mo(acac)_2$).

The Mo metal amount of the immobilized catalyst was found to be 2.10 mmol g^{-1} Mo based on inductively coupled plasma



Scheme 2 Synthesis of CoFe₂O₄@SiO₂-NH₂-Mo(acac)₂



Fig. 1 EDS spectrum of CoFe₂O₄@SiO₂-NH₂-Mo(acac)₂.

mass spectrometry (ICP-MS) analysis. The presence of Fe, Co, Si, P, O, C and Mo was observed in the EDX spectrum (Fig. 1).

Fig. 2 shows Fourier transform infrared (FT-IR) spectra of CoFe₂O₄(a)SiO₂, CoFe₂O₄(a)SiO₂-PrNH₂ and CoFe₂O₄(a)SiO₂-PrNH₂-Mo(acac)₂. The bands at 454, 1082, 1619 and 3438 cm⁻¹ are characteristic of SiO₂ absorption, which show evidence of the formation of a silica shell. The presence of Co-O and Fe-O bonds in the magnetic particles is confirmed by the characteristic peak that appear at 597 cm^{-1} . The intense and broad peaks near 1084 and 3300 cm⁻¹ in the three spectra are characteristic absorption bands of the vibration of -OH bands, which are overlapped with the $-NH_2$ stretching vibration. The band at 1559 cm⁻¹ provides direct evidence to support the existence of N-H deformation vibration. The appearance of two new peaks near 948 and 917 cm⁻¹ is due to Mo-O in the CoFe₂O₄(a)SiO₂-PrNH₂-Mo(acac)₂ material, which clearly indicates that $Mo(acac)_2$ has been anchored onto the $CoFe_2O_4(aSiO_2)$. Two bands are present at 2937 and 2857 cm⁻¹, which are assignable to stretching of alkyl C-H bonds.

The XRD pattern of CoFe₂O₄@SiO₂-PrNH₂-Mo(acac)₂ is shown in Fig. 3. A weak broad band ($2\theta = 22$ to 23°) appeared in the MNP-supported Mo complex pattern, which could be assigned to the amorphous silane shell formed around the magnetic cores. Furthermore, the diffraction peaks at 2θ values of 18.2°, 30.1°, 35.5°, 43.1°, 57.0° and 62.6° were also observed, which corresponded to the (111), (220), (311), (400), (511) and (440) reflections, respectively. It is apparent that these diffraction



Fig. 2 IR spectra of the (a) $CoFe_2O_4@SiO_2$, (b) $CoFe_2O_4@SiO_2-NH_2$ and (c) $CoFe_2O_4@SiO_2-NH_2-Mo(acac)_2$.





Fig. 3 XRD pattern of CoFe₂O₄@SiO₂-NH₂-Mo(acac)₂.



Fig. 4 TEM image of CoFe₂O₄@SiO₂-NH₂-Mo(acac)₂.

peaks are consistent with the standard $CoFe_2O_4$ with the cubic spinel structure (JCPDS 22-1086), which revealed that the crystal structure of the $CoFe_2O_4$ core was still well-maintained after functionalization.

The TEM and SEM images of MNP-supported Mo complex are shown in Fig. 4 and 5, respectively. The TEM image of the catalyst shows that magnetic particles are highly aggregated. The average size of these particles is about 20 nm, which shows a close agreement with the values calculated by XRD data. The SEM image of the supported catalyst confirms that these nanoparticles are uneven-sized particles due to deposition of silica on magnetic nanoparticles and most of the particles have a quasi-spherical shape.

The nitrogen absorption–desorption measurements indicated that the catalyst had a specific surface area of 49 m² g⁻¹.

The thermal stability of the magnetic catalyst was determined under N_2 atmosphere by thermogravimetric analysis (TGA) (Fig. 6). The weight loss at temperatures below 200 °C





Fig. 5 SEM image of CoFe₂O₄@SiO₂-PrNH₂-Mo(acac)₂ (a) "fresh" catalyst and (b) "recovered" catalyst after reusing 5 times.



is due to the removal of physically adsorbed solvent and the surface hydroxyl group. Organic groups have been reported to desorb at temperatures above 250 $^{\circ}$ C. The curve shows a weight loss of about 35% from 250 $^{\circ}$ C to 450 $^{\circ}$ C, resulting from the decomposition of the organic spacer grafting onto the MNPs surface.



Fig. 7 Magnetization curves of (a) CoFe_2O_4@SiO_2 and (b) CoFe_2O_4@SiO_2-PrNH_2-Mo(acac)_2.

The magnetic properties of the samples $CoFe_2O_4(@SiO_2 and CoFe_2O_4(@SiO_2-PrNH_2-Mo(acac)_2)$ were evaluated by vibrating sample magnetometery (VSM) at room temperature. The VSM magnetization curves of magnetic nanoparticles, before and after functionalization, exhibit a superparamagnetic character (Fig. 7). The magnetic saturation (M_{sat}) values are 21.0 emu g⁻¹ and 25.0 emu g⁻¹ for CoFe₂O₄(@SiO₂-PrNH₂-Mo(acac)₂ and CoFe₂O₄(@SiO₂. The decrease in M_{sat} for CoFe₂O₄(@SiO₂-PrNH₂-PMo is probably due to the existence of the large amount of non-magnetic material [PrNH₂-Mo(acac)₂] on the surface of the CoFe₂O₄ particles. Even with this reduction in the saturation magnetization, the prepared catalyst could still be efficiently separated from the reaction mixtures with the help of an external magnetic force.

The activity of the prepared catalyst was tested for the reaction of 4-chlorobenzaldehyde (1 mmol), aniline (1 mmol), acetylacetone (1 mmol) and nitromethane (0.5 ml) under solventfree conditions. As shown in Table 1, the reaction proceeded sluggishly in the absence of catalyst and offered only 20% yield of the expected product (Table 1, entry 1). To our delight, heating the mixture at 90 °C led to the formation of product 5v in 86% yield in the presence of CoFe₂O₄@SiO₂-PrNH₂-Mo(acac)₂ (Table 1, entry 20). Moreover, a higher reaction temperature (100 °C) does not make an obvious difference in the yield of the product, but a lower reaction temperature of 80 °C decreased the yield to 84% (Table 1, entry 17). The yield was greatly affected by the amount of catalyst loaded. When 0.5, 1.0 and 1.5 mol% of the catalyst was used, the yield varied from 78, 86 and 87%, respectively. A number of common solvents were examined, but no better yield was obtained. It should be mentioned that the presence of nanoparticles of γ -Fe₂O₃@SiO₂-PW,²⁶ γ -Fe₂O₃@SiO₂-PMo,²⁷ γ-Fe₂O₃@SiO₂-TfOH,^{23a} γ-Fe₂O₃@HAP-SO₃H,^{23c} γ-Fe₂O₃@SiO₂-NHC-Cu(π),^{3b} γ-Fe₂O₃@SiO₂-NHC-Zn(π),^{3b} CoFe₂O₄, CoFe₂O₄@SiO₂ led to a decreased yield of product. Accordingly, performing the reaction in the presence of 1.0 mol% of CoFe2O4@SiO2-PrNH2-Mo(acac)₂ at 90 °C under solvent-free conditions was chosen as optimal.

To demonstrate preparative utility, we also enlarged the reaction scale to 50 mmol for the model reaction, and it was found that the reaction yield reached the same level as when it was performed in a small scale (entry 22).

Table 1 Reaction of 4-chlorobenzaldehyde, aniline, acetylacetone and nitromethane in different conditions^a

Entry	Catalyst	Solvent	Temp (°C)	Yield (%)
1	No	No	90	20
2	γ-Fe ₂ O ₃ @SiO ₂ -PW	No	90	39
3	γ-Fe ₂ O ₃ @SiO ₂ -PMo	No	90	71
1	γ-Fe ₂ O ₃ @SiO ₂ -TfOH	No	90	30
5	γ-Fe ₂ O ₃ @HAP-SO ₃ H	No	90	28
5	γ-Fe ₂ O ₃ @SiO ₂ -NHC-Cu(II)	No	90	41
7	γ -Fe ₂ O ₃ @SiO ₂ -NHC-Zn(II)	No	90	45
3	CoFe ₂ O ₄	No	90	35
Ð	CoFe ₂ O ₄ @SiO ₂	No	90	32
10	CoFe ₂ O ₄ @SiO ₂ -PrNH ₂ -Mo(acac) ₂	H_2O	90	80
11	CoFe ₂ O ₄ @SiO ₂ -PrNH ₂ -Mo(acac) ₂	THF	Reflux	5
12	CoFe ₂ O ₄ @SiO ₂ -PrNH ₂ -Mo(acac) ₂	MeCN	Reflux	12
13	CoFe ₂ O ₄ @SiO ₂ -PrNH ₂ -Mo(acac) ₂	MeOH	Reflux	16
14	CoFe ₂ O ₄ @SiO ₂ -PrNH ₂ -Mo(acac) ₂	Toluene	90	7
15	CoFe ₂ O ₄ @SiO ₂ -PrNH ₂ -Mo(acac) ₂	No	25	30
16	CoFe ₂ O ₄ @SiO ₂ -PrNH ₂ -Mo(acac) ₂	No	70	61
17	CoFe ₂ O ₄ @SiO ₂ -PrNH ₂ -Mo(acac) ₂	No	80	84
18	CoFe ₂ O ₄ @SiO ₂ -PrNH ₂ -Mo(acac) ₂	No	100	82
19	CoFe ₂ O ₄ @SiO ₂ -PrNH ₂ -Mo(acac) ₂	No	90	78
	(0.5 mol%)			
20	CoFe ₂ O ₄ @SiO ₂ -PrNH ₂ -Mo(acac) ₂	No	90	86
21	CoFe ₂ O ₄ @SiO ₂ -PrNH ₂ -Mo(acac) ₂	No	90	86
	(1.5 mol%)			
22^b	CoFe ₂ O ₄ @SiO ₂ -PrNH ₂ -Mo(acac) ₂	No	90	87
	- 、 /-			

 a Reaction condition: 4-chlorobenzaldehyde (1 mmol), aniline (1 mmol), acetylacetone (1 mmol), nitromethane (0.5 ml), catalyst (1.0 mol%), solvent (2 ml), 5 h. b The reaction was carried out in 50 mmol scale.

Under the optimal reaction conditions, the scope and limitation of these 4CRs for the synthesis of pyrrole 5 were evaluated and the selected results are summarized in Table 2. Initially, a range of amines were treated with benzaldehydes, acetylacetone and nitromethane. It was generally observed that high to excellent yields of the products were obtained for aniline bearing electron-rich or weakly electron-poor groups. Strongly electron-poor aromatic amines such as 4-nitroaniline decreased the reactivity and afforded the desired product in moderate yield. An amine with a larger aromatic group, such as naphthyl, was also applicable to this reaction to afford the desired product, albeit in relatively low yield. The reaction was also very effective with 9H-fluoren-2-amine to form 5j in 89% yield (entry 10). Moreover, different kinds of aliphatic amines also worked well in this reaction, leading to high turnover frequencies (TOF) in a relatively short time. It should be noted that although various aliphatic amines were good substrates for this 4CRs in the presence of NiCl₂,^{28a} FeCl₃^{28b} and I₂,^{28c} aromatic amines were not favored reactants and the desired products were obtained in lower yields.

Subsequently, a variety of aldehydes were evaluated in these 4CRs. The substituents on the aromatic ring of benzaldehyde show no significant influence on the reaction times and the yields of the products. Moreover, this reaction works well with heteroaromatic carbaldehydes such as 2-furaldehyde and 2-thiophenealdehyde, (Table 2, entries 26 and 27). 1-Naphth-aldehyde was also a suitable partner and gave the desired product **5ab** in 80% yield (Table 2, entry 28). To our disappointment, aliphatic aldehydes are not appropriate starting materials

						R	4			
		0 0					R ²			
		_	NO	CoFe ₂ O ₄ @SiO ₂	-NH ₂ -Mo(acac)	2				
			31402		90 °C	►	/ \}			
					30 0	R°	`Ņ			
	1 2	3	4			5	I R ¹			
						Time	Viold ^a		TOF	
Entry	Aldehyde	Amine	\mathbf{R}^3	\mathbf{R}^4	Product	(h)	(%)	TON^b	(h^{-1})	mn (°C)
	machyac	Aunne	ĸ	ĸ	Tiouuet	(11)	(70)	1010	(III)	mp (c)
1	PhCHO	$PhNH_2$	Me	Me	5a	4.0	90	90	22.5	106-107
2	PhCHO	$3-OCH_3C_6H_4NH_2$	Me	Me	5b	5.0	86	86	17.2	Oil
3	PhCHO	$4-CH_3C_6H_4NH_2$	Me	Me	5c	4.0	92	92	23	109–111
4	PhCHO	$4-FC_6H_4NH_2$	Me	Me	5 d	5.5	90	90	16.4	130-131
5	PhCHO	$4-ClC_6H_4NH_2$	Me	Me	5e	4.0	80	80	20	127-128
6	PhCHO	$4-BrC_6H_4NH_2$	Me	Me	5f	6.5	82	82	12.6	141-143
7	PhCHO	$4-NO_2C_6H_4NH_2$	Me	Me	5g	48	50	50	1.0	171-172
8	PhCHO	$4 - OCF_3C_6H_4NH_2$	Me	Me	5h	7.0	80	80	11.4	109-110
9	PhCHO	Naphthalen-1-amine	Me	Me	5i	12.0	48	48	4.0	143-144
10	PhCHO	9 <i>H</i> -Fluoren-2-amine	Me	Me	5j	5.5	83	83	15.9	147-149
11	PhCHO	$H_2C = CHCH_2NH_2$	Me	Me	5k	1.0	88	88	88	Oil
12	PhCHO	PhCH ₂ NH ₂	Me	Me	51	0.5	90	90	180	87-88
13	PhCHO	4-CH ₃ C ₆ H ₄ CH ₂ NH ₂	Me	Me	5m	0.5	91	91	182	100-102
14	PhCHO	4-FC ₆ H ₄ CH ₂ NH ₂	Me	Me	5 n	1.0	87	87	87	98-100
15	PhCHO	PhCH ₂ CH ₂ NH ₂	Me	Me	50	0.5	91	91	182	91-92
16	PhCHO	$4-OHC_6H_4(CH_2)_2NH_2$	Me	Ме	5p	1.0	90	90	90	Oil
17	PhCHO	Cyclopropanamine	Me	Ме	5q	0.5	90	90	180	72-74
18	PhCHO	Cyclopentanamine	Me	Me	5r	0.5	86	86	172	74-76
19	4-FC ₆ H ₄ CHO	Propan-1-amine	Me	Me	5s	0.5	90	90	180	Oil
20	4-OCHMe ₂ C ₆ H ₄ CHO	$PhNH_2$	Me	Me	5t	6.0	81	81	13.5	Oil
21	4-FC ₆ H ₄ CHO	PhNH ₂	Me	Me	5u	5.0	87	87	17.4	112-113
22	4-ClC ₆ H ₄ CHO	PhNH ₂	Me	Ме	5 v	4.0	86	86	21.5	105-106
23	4-BrC ₆ H ₄ CHO	PhNH ₂	Me	Ме	5w	5.0	85	85	17	90-93
24	4-NO ₂ C ₆ H ₄ CHO	PhNH ₂	Me	Ме	5x	6.5	83	83	12.8	Oil
25	4-CF ₂ C _c H ₄ CHO	PhNH2	Me	Ме	5v	6.5	85	85	13.1	Oil
26	Furan-2-carbaldehvde	PhNH2	Me	Ме	5z	8.0	60	60	7.5	91-92
27	Thiophene-2-carbaldehvde	PhNH2	Me	Ме	5aa	5.5	71	71	12.9	105-106
28	1-Naphthaldehvde	PhNH2	Me	Ме	5ab	8.0	80	80	10	114-115
29	Thiophene-2-carbaldehyde	4-CH ₂ C ₆ H ₄ CH ₂ NH ₂	Me	Me	5ac	6.0	80	80	13.3	106-108
30	Thiophene-2-carbaldehyde	4-FC ₆ H ₄ NH ₂	Me	Me	5ad	6.5	75	75	11.5	97-99
31	5-Methylthiophene-2-carbaldehyde	4-FC ₆ H ₄ NH ₂	Me	Me	5ae	6.0	78	78	13	78-80
32	5-Methylthiophene-2-carbaldehyde	4-ClC _c H ₄ NH ₂	Me	Me	5af	6.0	70	70	11.7	108-110
33	5-Methylthiophene-2-carbaldehyde	9 <i>H</i> -Fluoren-2-amine	Me	Me	589	6.0	80	80	13.3	Oil
34	Thiophene-2-carbaldehyde	PhCH ₂ NH ₂	Me	Me	5ah	2.0	80	80	40	115-116
35	4-CH ₂ C ₂ H ₂ CHO	PhCH ₂ CH ₂ NH ₂	Me	Me	5ai	1.0	88	88	88	105-106
36	4-FC_H_CHO	PhCH ₂ CH ₂ NH ₂	Me	Me	5ai	1.0	89	89	89	111-112
37	3-CF ₂ C ₂ H ₄ CHO	PhCH ₂ CH ₂ NH ₂	Me	Me	5ak	2.0	85	85	42.5	73-74
38	4-CMe ₂ C ₂ H ₄ CHO	Cyclopropanamine	Me	Me	5al	0.5	88	88	176	Oil
39	PhCHO	PhNH	Me	OMe	5am	5.0	80	80	16	Oil
40	PhCHO	PhNH	Me	OFt	5an	5.0	82	82	16 /	Oil
41	PhCHO	PhNH ₂	Me	OCH CH-OM	520	5.5	80	80	14 5	Oil
42	PhCHO	PhNH ₂	Me	OCH_CH=C	H _a 5an	5.5	78	78	14.5	Oil
43	PhCHO	PhNH ₂	Ft	OMe	112 Jap 590	5.0	20 80	80	14.2	Oil
40	110110	1 111 11 12	ы	ONIC	Jay	5.0	00	00	10	011

^{*a*} Isolated yield. ^{*b*} Turnover numbers were simple calculated according to mol product/mol Mo in each case. ^{*c*} Turnover frequencies [(mol product/mol Mo)/time] were calculated at the time indicated in each case.

under these reaction conditions, a complex mixture was detected and no desired product was isolated.

Stimulated by these results, we then extended the scope of this reaction to several other β -ketoesters, such as methyl acetoacetate, ethyl acetoacetate, 2-methoxyethyl acetoacetate, allyl acetoacetate and methyl 3-oxopentanoate. In general, the present method was also equally effective with β -ketoesters and led to the desired products in high yields (Table 2, entries 39–43). These successful results demonstrate that this procedure is extendable to a wide variety of substrates for construction of structural variations of pyrroles.

Finally, to further extend the high synthetic potential of this new MCR, the synthesis of dipyrrole derivatives was also examined. As shown in Scheme 3, treatment of 4-chloroaniline (2 mmol), acetyl-acetone (2 mmol) and nitromethane (1 ml) with 1,4-phthalaldehyde (1 mmol) under the above optimal conditions led to the formation of the corresponding dipyrrole **6** in 75% yield. Likewise, the reaction of 4-benzaldehyde (2 mmol), benzene-1,4-diamine (1 mmol), acetyl-acetone (2 mmol) and nitromethane (1 ml) proceeded efficiently to furnish the expected dipyrrole **7** in 78% yield.

The structures of the products were identified by their FTIR, ¹H NMR, ¹³C NMR spectra and elemental analysis.



Scheme 3 Synthesis of dipyrroles.



Furthermore, the structure of compound **5h** was unambiguously confirmed by single crystal X-ray analysis (Fig. 8).

A plausible mechanism for the formation of pyrrole derivatives is proposed in Scheme 4. The intermediates (*Z*)-4-(phenylamino)pent-3-en-2-one (A) from aniline and acetylacetone and (*E*)-1-chloro-4-(2-nitrovinyl)benzene (B) from 4-chlorobenzaldehyde and nitromethane could be generated in the presence of a magnetic nanocatalyst and were separated in the reaction process. These two intermediates reacted *via* Michael addition, followed by intramolecular cyclization with the elimination of nitroxyl (HNO) and water to lead to the final product **5v**.

Finally, the catalyst recyclability has been tested in the model reaction. After the completion of reaction, the catalyst was separated magnetically from the reaction mixtures and washed with ethyl acetate. The recovered catalyst was dried to remove residual solvents, and then reused directly in the model reaction for the next round without further purification. In addition, metal leaching in the catalyst was determined and ICP-MS analysis of the clear filtrate indicated that the Mo and Fe contents were 0.10 and 0.15 ppm, respectively. Five runs can be efficiently performed with



Scheme 4 Plausible mechanism for the synthesis of pyrrole derivatives.



the recycled catalyst with essentially no loss of catalytic activity (Fig. 9). Furthermore, SEM images of both fresh and recovered catalysts indicated that no significant change in the shape and size of the support had occurred during the reaction and the recycling stages (Fig. 5). This indicates that MNP-supported Mo catalyst was very high chemical stable and could endure the

Conclusions

employed hydrothermal conditions.

In conclusion, a novel type of magnetically recoverable nanoparticle $CoFe_2O_4$ supported molybdenum catalyst was successfully prepared. The synthesized catalyst was confirmed using XRD, FT-IR, TEM, SEM, TGA, ICP-MS, and VSM techniques. The immobilized Mo complex was shown to be an efficient heterogeneous catalyst for a one-pot four-component coupling reaction of amines, aldehydes, 1,3-dicarbonyl compounds and nitromethane. A wide range of amines, aldehydes, 1,3-dicarbonyl compounds can be tolerated, giving the structural diversity of pyrroles in good to excellent yields. Morever, the catalyst could be easily recovered by simple magnetic decantation and reused five times without significant loss of activity, showing good potential for industrial application.

Experimental section

General methods

All solvents and chemicals were commercially available and were used as purchased. The X-ray diffraction analysis was performed on a PANalytical X'Pert Pro X-ray diffractometer. Surface morphology and particle size were studied using a Hitachi S-4800 SEM instrument. Transmission electron microscope (TEM) observations were carried out using a Hitachi H-7650 microscope at 80 KV. Elemental compositions were determined using a Hitachi S-4800 scanning electron microscope equipped with an INCA 350 energy dispersive spectrometer (SEM-EDS) presenting a 133 eV resolution at 5.9 keV. The molybdenum content was determined using ICP-MS (an X Series 2 spectrometer). Melting points were measured on an X-4 digital melting point apparatus and are uncorrected. IR spectra were obtained as KBr pellets or as liquid films on KBr pellets using a Bruker-TENSOR 27 spectrometer. ¹H NMR (500 MHz) and ¹³C NMR (125 MHz) spectra were recorded on a Bruker DRX-500 spectrometer using CDCl₃ as the solvent and

TMS as an internal standard. Elemental analyses were determined on a Vario EL III CHNOS elemental analyzer.

Preparation of CoFe₂O₄(a)SiO₂-**PrNH**₂-**Mo(acac)**₂ magnetic nanoparticles. CoFe₂O₄ were prepared as reported by our group in a previous work.³⁰ FeCl₃·6H₂O (2.70 g) and CoCl₂·6H₂O (1.19 g) were dissolved in 50 ml distilled water in a three-necked flask equipped with a mechanical stirrer. 25 ml of NaOH (3 mol L⁻¹) solution was added under vigorous stirring. The reaction mixture was then continually stirred under refluxing conditions for 1 h. The reaction mixture was cooled to room temperature. The magnetic CoFe₂O₄ was separated using an external magnet, washed with water followed by ethanol and dried under vacuum at 50 °C for 24 h.

Coating of a layer of silica on the surface of the $CoFe_2O_4$ NPs was achieved by adding distilled water (80 ml) to purified $CoFe_2O_4$ NPs (1 g) which were then heated for 1 h at 40 °C. Then concentrated ammonia solution (1.5 ml) was added and the resulting mixture was stirred at 40 °C for 30 min. Subsequently, tetraethyl orthosilicate (TEOS, 1.0 ml) was charged to the reaction vessel and the mixture was continuously stirred for 24 h. After cooling the solution to room temperature, the silica-coated NPs were collected using a permanent magnet, followed by washing three times with ethanol and diethyl ether and drying at 100 °C in a vacuum for 24 h.

The obtained CoFe₂O₄($@SiO_2$ (1 g) was added to the solution of 3-aminopropyltriethoxysilane (5 mmol) in dry toluene (20 ml) and refluxed for 20 h. The aminated-CoFe₂O₄($@SiO_2$ was separated by a permanent magnet, washed with double-distilled water and anhydrous ethanol, and dried at 100 °C for 5 h to give the surface bound amino group CoFe₂O₄($@SiO_2$ -NH₂.

For the preparation of $CoFe_2O_4$ (2)SiO₂-NH₂-Mo(acac)₂: a mixture of $CoFe_2O_4$ (2)SiO₂-PrNH₂ (0.5 g) and bis(acetylacetonato)dioxomolybdenum (2.0 mmol) was refluxed in dry MeOH (15 ml) for 24 h. The solid was collected using a permanent magnet, followed by washing three times with CH₂Cl₂. Finally, the obtained $CoFe_2O_4$ (2)SiO₂-PrNH₂-Mo(acac)₂ was dried under vacuum at 60 °C for 24 h. The Mo content was determined by ICP-MS and it was found to be 2.10 mmol g⁻¹.

General procedure for the synthesis of functionalized pyrroles 5. The mixture of aldehyde (1 mmol), amine (1 mmol), 1,3-dicarbonyl compound (1 mmol), CH_3NO_2 (0.5 ml) and $CoFe_2O_4(@SiO_2-PrNH_2-Mo(acac)_2$ (1.0 mol%, 0.005 g) was stirred at 90 °C (monitored by TLC). Upon completion of the reaction, the reaction mixture was cooled to room temperature and 5 ml of ethyl acetate was added. The pyrrole derivatives were dissolved in ethyl acetate and the catalyst was separated magnetically, washed with ethyl acetate, and used for subsequent cycles after drying under vacuum. Pure products were obtained by evaporation of the solvent, followed by recrystallization from ethanol or by column chromatography on silica gel using ethyl acetate/hexane as the eluent.

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- 29 Crystallographic data for **5h** have been deposited in the Cambridge Crystallographic Data Centre with the deposition number CCDC 949005. Crystal data for **5h**: Empirical formula C₂₀H₁₆F₃NO₂, white solid, crystal dimensions 0.156 × 0.122 × 0.103 mm, monoclinic, space group *C2/c*, *a* = 27.553(3), *b* = 7.7658(8), *c* = 17.6413(18) Å, *α* = 90, β = 110.441(2), γ = 90°, *T* = 296 K, *V* = 3537.1(6) Å³, *M*_r = 359.3, *Z* = 8, ρ_{calcd} = 1.350 Mg m⁻³, λ = 0.71073 Å, μ (Mo-K*α*) = 0.108 mm⁻¹, *F*(000) = 1488, *R*₁ = 0.0610, w*R*₂ = 0.1761, GOF = 1.045 for *I* > 2*σ*(*I*).
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