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# A novel and reusable ionically tagged nanomagnetic catalyst: Application for the preparation of 2-amino-6-(2-oxo-2*H*-chromen-3-yl)-4- arylnicotinonitriles *via* vinylogous anomeric based oxidation



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<i>Keywords:</i> 2-Amino-6-(2-oxo-2 <i>H</i> -chromen-3-yl)-4- arylnicotinonitrile Anomeric effect Anomeric based oxidation (ABO)	Herein, we report $Fe_3O_4@O_2PO_2(CH_2)_2NH_3^+CF_3CO_2^-$ as a novel and reusable ionically tagged nanomagnetic catalyst. It was characterized by several techniques including Fourier transform infrared (FT-IR) spectroscopy, thermo gravimetric analysis/differential thermal analysis (TGA/DTA), scanning electron microscopy (SEM), transmission electron microscopy (TEM), vibrating sample magnetometer (VSM) and energy dispersive X-ray (EDX), analysis. The catalytic behaviour of the Fe_O_0C_PO_1(CH_2)NH_2^+CF_1CO_2^- was examined at the
Fe <sub>3</sub> O <sub>4</sub> @O <sub>2</sub> PO <sub>2</sub> (CH <sub>2</sub> ) <sub>2</sub> NH <sub>3</sub> <sup>+</sup> CF <sub>3</sub> CO <sub>2</sub> <sup>-</sup>	(EDX) maryos. The enabled behavior of the respectively defended as the second detailed at the

#### 1. Introduction

Multicomponent reactions

Reusable nanomagnetic catalyst

Vinylogous anomeric based oxidation

Homogeneous catalytic systems holding varied merits including excellent activity, selectivity, high turnover numbers (TON) and turn over frequencies (TOF). However, catalytic applications of homogeneous systems in industrial processes, particularly for the drug and pharmaceutical industries are restricted because the extra purity of the drugs is very important. This limitation comes from obstacles in the step of the isolation and separation of homogeneous catalysts from the desired products. An efficient strategy to overcome the difficulties connected to cumbersome process of isolation and separation of the homogeneous catalysts is their conversion to the corresponding heterogeneous analogous systems. This process creates a heterogeneous catalytic system [1–4]. However, in the case of heterogeneous catalysts due to the lower dimensionality of the interactions between reactant and the surface of catalysts, the active sites are not as approachable as in the case of homogeneous ones, and therefore the activity of the heterogeneous catalysts is reduced. Although, nano-making of heterogeneous catalysts can enhance their activity and selectivity, but making their separation tedious instead. Therefore, magnetization of the heterogeneous catalysts seems to be the most reasonable solution. Magnetic nanocatalysis presents a catalytic system which shows suitable activity, selectivity, easy separation and recovery. This field of chemistry has been extensively reviewed [5-11].

The effective and rapid synthesis of target molecules accompanied with economic and ecological insight which is the paramount goal of one-pot multicomponent reactions. This excellent synthetic tool can be an influential source of molecular diversity. One-pot multicomponent strategy offers procedures with merits such as facile access to high levels of diversity through a time-saving process with high atom and step economy, waste prevention, and energy efficiency. Therefore, it appears that access to "ideal synthesis" through a one-pot multicomponent process is realized for chemists [12–19].

synthesis 2-amino-6-(2-oxo-2H-chromen-3-yl)-4-arylnicotinonitrile derivatives. Experimental data has approved

that the final step of the plausible mechanism proceeded via a vinylogous anomeric based oxidation mechanism.

Described catalys shows excellent potential of recycling and reusing at the described multicomponent reaction.

Coumarin structural kernels have found an important role in pharmaceutical industry as they can serve as antimicrobial, antioxidant, antiamoebic, analgesic, anti-pyretic, and anticancer agents [20–22]. Also, these versatile molecules are applied as additives to food, cosmetics, perfumes, laser dyes, optical brightener, and dispersed fluorescence [23,24].

On the other hand, *N*-heteroaromatic structures particularly pyridine ring systems are ubiquitous in pharmaceutical active molecules and natural products [25,26]. Among the *N*-heteroaromatic molecules, 2-amino-3-cyano pyridine scaffold represent fascinating biological characteristics. These compounds can apply as  $A_{2A}$  adenosine receptor antagonists, IKK- $\beta$  inhibitors, inhibitors of HIV-1 integrase, anti-microbial, anti-tumour, analgesic, anti-inflammatory, and antipyretic agents [27–31]. Although, chromene-linked nicotinonitrile derivatives present excellent biological activities but, only a few procedures

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**Scheme 1.** Anomeric effect leads to bond-breaking in the case of 4-halo-1-azabicyclo[2.2.2]octanes.

reported for their preparation which have desired disadvantages [32–36]. Therefore, exploring newer and greener methods for the synthesis of chromene-linked nicotinonitriles is highly valuable and great demand.

Researches in recent years have demonstrated that the concept of anometic effect is not restricted to chemistry of carbohydrate compounds and its role is observed in various chemical phenomena [37–44]. One of the most important features of anometic effect is the interference in bond-weakening and unusual hydride transfer processes. This effect obviously observed in the reaction mechanism of Cannizzaro reaction and as well as in the case of tricyclic orthoamides [45]. Rapid solvolysis and fragmentation of 4-halo-1-azabicyclo[2.2.2]octanes demonstrated that if the steric arrangement is correct, the bond-weakening effect can be happened through a  $\sigma$ -bond framework. In the case of this compound, the overlap between nitrogen lone pair electrons leads to broken of C–C and C–X bonds respectively (Scheme 1) [46]. Thus the major factor for mentioned fragmentation is anomeric effect and/or negative hyperconjugation. Recently, anomeric based oxidation has been reviewed [47].

In this study, in connection with our previous investigation for the synthesis of biological valuable heterocyclic structures and developing our recently established term entitled "anomeric based oxidation" as a new mechanistic lookout for the oxidative aromatization of a good range of susceptible heterocyclic molecules [45,47], herein, we wish to report a novel functionalized magnetic nanoparticle as an efficient and recoverable catalyst for facile preparation of 2-amino-6-(2-oxo-2*H*-chromen-3-yl)-4-arylnicotinonitrile derivatives *via* vinylogous anomeric based oxidation mechanism (Schemes 2 and 3).

The systematic development of vinylogous anomeric based oxidation on the suitable molecules, allows the design of synthetic methodologies based on anomerically driven stereoselective reactions, or highly biased equilibria among stereoisomers (Scheme 4). Scheme 4 shows that a paramount preference for a reaction which benefits from two lone pairs antiperiplanar to the leaving group, leading to breaking of the endocyclic C–N bond. The other products would derive from a leaving group departure that involves only one lone pair that is antiperiplanar to the departing group. The similar effects have been reported for an enzymatic reaction (Scheme 5).

In the many biological transformations involve oxidation and/or reduction of substrates by NADP<sup>+</sup>/NADPH or NAD<sup>+</sup>/NADH systems, the unusual hydride transfer from carbon atom *via* a vinylogous anomeric based oxidation (ABO) is the major step in the oxidation-reduction mechanism (Scheme 6). Thus systematic investigation of ABO

mechanism leads to designing of task-specific biomimetic reactions in the future.

#### 2. Experimental

## 2.1. General procedure for the construction of nano magnetic catalyst $Fe_3O_4@O_2PO_2(CH_2)NH_3^+CF_3CO_2^-$

Fe<sub>3</sub>O<sub>4</sub> nanoparticles were prepared according to the previously reported method [54] Then, alike to previously reported method [55], Fe<sub>3</sub>O<sub>4</sub>@O<sub>2</sub>PO<sub>2</sub>(CH<sub>2</sub>)<sub>2</sub>NH<sub>2</sub> were synthesized. In the next step, the resulting Fe<sub>3</sub>O<sub>4</sub>@O<sub>2</sub>PO<sub>2</sub>(CH<sub>2</sub>)<sub>2</sub>NH<sub>2</sub> in 20 mL toluene was sonicated for 15 min. Then CF<sub>3</sub>CO<sub>2</sub>H (10 mmol, 1.14 g) was added to the above mentioned mixture and refluxed for 12 h to give desired catalyst Fe<sub>3</sub>O<sub>4</sub>@O<sub>2</sub>PO<sub>2</sub>(CH<sub>2</sub>)<sub>2</sub>NH<sub>3</sub> <sup>+</sup>CF<sub>3</sub>CO<sub>2</sub><sup>-</sup>.

#### 2.2. General procedure for the synthesis of 3-acetylcoumarin derivatives

According to the previously reported procedure [32–36], in a round bottom flask, a mixture of 2-hydroxy benzaldehyde or 2-hydroxy-3methoxy benzaldehyde (20 mmol), ethyl acetoacetate (20 mmol, 2.6 g) and dimethylamine (0.5 mL) in 10 mL distilled water was stirred at room temperature until yellow precipitate was formed. After that, the precipitate filtered off and washed thoroughly with ethanol to give pure 3-acetylcoumarin derivatives.

#### 2.3. General procedure for the synthesis of 2-amino-6-(2-oxo-2H-chromen-3-yl)-4-arylnicotinonitrile derivatives

To the mixture of aromatic aldehydes (1 mmol), 3-acetylcoumarin derivatives (1 mmol), malononitile (1 mmol, 0.066 g), and ammonium acetate (1.5 mmol, 0.116 g) in a round bottom flask,  $Fe_3O_4@O_2PO_2(CH_2)_2NH_3^+CF_3CO_2^-$  (10 mg) was added as a catalyst and the resulting mixture was stirred magnetically under solvent-free conditions at 70 °C in an oil bath for the suitable time (Table 2). After completion of the reaction, as checked out using TLC (*n*-hexane/ethyl acetate (2:1)), hot ethyl acetate was added to the reaction mixture for precipitation of nanomagnetic catalyst and dissolving the desired product and unreacted starting materials. Afterwards,  $Fe_3O_4@O_2PO_2(CH_2)_2NH_3^+CF_3CO_2^-$  was separated from the reaction mixture by using an external magnetic bar. After evaporation of the ethyl acetate, EtOH was added to the mixture for precipitation of the desired products. Finally, recrystallization of the obtained precipitate yielded the pure products.

#### 2.4. Selected spectral data

#### 2.4.1. 3-Acetyl-2H-chromen-2-one Melting point: 119–121 °C.

FT-IR (KBr):  $\nu$  (cm<sup>-1</sup>): 3052, 1724, 1686, 1601, 1557.



Scheme 2. The synthetic pathway for the preparation of  $Fe_3O_4@O_2PO_2(CH_2)_2NH_3^+ CF_3CO_2^-$ .



Scheme 3. Synthesis of 2-amino-6-(2-oxo-2H-chromen-3-yl)-4-arylnicotinonitrile derivatives in the presence a catalytic amount of  $Fe_3O_4(\alpha)$ O<sub>2</sub>PO<sub>2</sub>(CH<sub>2</sub>)<sub>2</sub>NH<sub>3</sub><sup>+</sup>CF<sub>3</sub>CO<sub>2</sub><sup>-</sup>.



Scheme 4. Breaking of the endocyclic C-N bond due to the anomeric effect [48].



Peptidase mimic

Scheme 5. Anomeric effect in an enzymatic reaction [49].



NADH

Scheme 6. Molecular structures of NADH and NADPH [50-53].

 $\delta_{\rm H}$  (300 MHz, DMSO): 8.64 (s, 1H, Coumarin 4-H), 7.96–7.92 (m, 1H, ArH), 7.77-7.71 (m, 1H, ArH), 7.46-7.38 (m, 2H, ArH), 2.59 (s, 3H, COMe).

δ<sub>C</sub> (75 MHz, DMSO): 195.5, 158.9, 155.1, 147.5, 134.9, 131.2, 125.4, 124.8, 118.6, 116.6, 30.5.

#### 2.4.2. 3-Acetyl-8-methoxy-2H-chromen-2-one Melting point: 170-172 °C.

FT-IR (KBr): *ν* (cm<sup>-1</sup>): 3079, 1735, 1685, 1601, 1473.

δ<sub>H</sub> (300 MHz, DMSO): 8.62 (s, 1H, Coumarin 4-H), 7.49-7.34 (m, 3H, ArH), 3.94 (s, 3H, OMe), 2.60 (s, 3H, COMe).

 $\delta_C$  (75 MHz, DMSO): 195.6, 158.6, 147.7, 146.7, 144.4, 125.3, 125.0, 122.1, 119.1, 116.9, 56.7, 30.5.

2.4.3. 2-Amino-4-(4-chlorophenyl)-6-(2-oxo-2H-chromen-3-yl) nicotinonitrile (1b)

Melting point: 243-245 °C.

FT-IR (KBr): ν (cm<sup>-1</sup>): 3470, 3312, 2205, 1732.

δ<sub>H</sub> (300 MHz, DMSO): 8.85 (s, 1H, Coumarin 4-H), 7.91-7.89 (d, J = 6 Hz, 1H, ArH), 7.75–7.66 (m, 5H, ArH and PyrH), 7.56–7.42 (m, 3H, ArH), 7.13 (s, 2H, NH<sub>2</sub>).

δ<sub>c</sub> (75 MHz, DMSO): 160.7, 159.5, 154.1, 154.0, 153.9, 144.3, 136.2, 135.2, 133.7, 130.5, 130.0, 129.5, 125.5, 124.7, 124.1, 119.3, 117.7, 116.9, 116.5, 112.8, 88.6.

2.4.4. 2-Amino-4-(3,5-difluorophenyl)-6-(2-oxo-2H-chromen-3-yl) nicotinonitrile (10)

Melting point: 269-271 °C.

FT-IR (KBr):  $\nu$  (cm<sup>-1</sup>): 3408, 3320, 2206, 1729.

δ<sub>H</sub> (300 MHz, DMSO): 8.85 (s, 1H, Coumarin 4-H), 7.93- 7.91 (d, J = 6 Hz, 1H, ArH), 7.74–7.71 (m, 1H, ArH), 7.65 (s, 1H, Pyr-H), 7.54-7.41 (m, 5H, ArH), 7.22 (s, 2H, NH<sub>2</sub>).

 $δ_C$  (75 MHz, DMSO): 162.8 (d, J = 232.5 Hz), 160.6, 159.5, 154.2, 154.1, 152.7, 147.7, 144.5, 140.8 (d, *J* = 10.5 Hz), 133.8, 130.1, 125.5, 124.1, 119.3, 116.6, 112.6 (d, J = 16.5 Hz), 112.2, 106.6 (t, J = 25.5 Hz), 88.7.

2.4.5. 2-Amino-6-(8-methoxy-2-oxo-2H-chromen-3-yl)-4-(4-

(trifluoromethyl)phenyl) nicotinonitrile (1p)

Melting point: 288-290 °C.

FT-IR (KBr): *ν* (cm<sup>-1</sup>): 3458, 3359, 2213, 1726.

δ<sub>H</sub> (300 MHz, DMSO): 8.84 (s, 1H, Coumarin 4-H), 7.99-7.97 (d,







Fig. 2. EDX analysis of the novel catalyst.



Fig. 3. SEM images of the novel nanomagnetic catalyst.

 $J=6~{\rm Hz}~{\rm 2H},~{\rm ArH}),~7.88{\rm -}7.85~({\rm d},~J=6~{\rm Hz}~{\rm 2H},~{\rm ArH}),~7.69~({\rm s},~1{\rm H},~{\rm Pyr-H}),~7.45{\rm -}7.35({\rm m},~3{\rm H},~{\rm ArH}),~7.22~({\rm s},~2{\rm H},~{\rm NH}_2),~3.96~({\rm s},~3{\rm H},~{\rm OMe}).$ 

 $\delta_C$  (75 MHz, DMSO): 160.7, 159.2, 154.1, 153.8, 146.8, 144.6, 143.4, 141.4, 129.7, 126.3 (q, J= 4.5 Hz), 125.4, 124.1, 121.1, 119.8, 116.8, 115.8, 112.8, 101.3, 88.6, 56.7.

#### 3. Result and discussion

Development of reusable catalysts and their application in the synthesis of target drug candidates are our main interest [56]. With this aim,  $Fe_3O_4@O_2PO_2(CH_2)_2NH_3^+CF_3CO_2^-$  was designed, synthesized, characterized, and applied for synthesis of a good range of 2-amino-6-(2-oxo-2*H*-chromen-3-yl)-4-arylnicotinonitriles. The described reusable nanomagnetic heterogeneous catalyst, namely  $Fe_3O_4@$ 



Fig. 4. TEM images of new nanomagnetic catalyst.



Fig. 5. VSM hysteresis curve of a, b and desired catalyst c.



Fig. 6. TGA and DTG curves of the nanomagnetic catalyst.

 $O_2PO_2(CH_2)_2NH_3^+CF_3CO_2^-$  was synthesized as depicted in Scheme 2. As mentioned above, we probed its catalytic applicability at the formation of 2-amino-6-(2-oxo-2*H*-chromen-3-yl)-4-arylnicotinonitrile derivatives *via* the reaction of various aromatic aldehydes, 3-

acetylcoumarin derivatives, malononitrile, and ammonium acetate, under solvent-free conditions (Scheme 3). It is worthy to mention that 3-acetylcoumarin derivatives were synthesized from the reaction of salicylaldehyde and ethyl acetoacetate in the presence of

#### Table 1

Optimizing of the reaction conditions for the synthesis of 2-amino-6-(2-oxo-2*H*-chromen-3-yl)-4-arylnicotinonitrile derivatives.<sup>a</sup>

Entry	Solvent	Temperature (°C)	Load of catalyst (mg)	Time (min)	Yield (%) <sup>b</sup>
1	-	r.t.	10	180	60
2		50	10	60	75
3 <sup>c</sup>	-	70	10	45	83
4	-	90	10	45	85
5	-	70	15	45	85
6	-	70	5	60	70
7	-	70	-	180	25
8 <sup>d</sup>	-	70	10	60	40
9 <sup>e</sup>	-	70	10	60	45
10	$H_2O$	70	10	180	40
11	$C_2H_5OH$	70	10	180	35
12	$CH_3CN$	Reflux	10	180	30
13	EtOAc	Reflux	10	180	35
14	$CH_2Cl_2$	Reflux	10	180	Trace
15	n-Hexane	Reflux	10	180	Trace

<sup>a</sup> Reaction conditions: benzaldehyde (1 mmol, 0.106 g), 3-acetylcoumarin (1 mmol, 0.188 g), malononitrile (1 mmol, 0.066 g) and ammonium acetate (1.5 mmol, 0.115 g).

<sup>b</sup> Isolated yields.

<sup>c</sup> Data for the model reaction under air, nitrogen and argon atmosphere are similar.

<sup>d</sup> Reaction performed using Fe<sub>3</sub>O<sub>4</sub> nanoparticles as a catalyst.

 $^{e}$  Reaction performed using  $Fe_{3}O_{4}@O_{2}PO_{2}(CH_{2})_{2}NH_{2}$  nanoparticles as a catalyst.

dimethylamine in water.

#### 3.1. Characterization of novel nanomagnetic catalyst

The structure of  $Fe_3O_4@O_2PO_2(CH_2)_2NH_3^+CF_3CO_2^-$  was confirmed using suitable techniques such as FT-IR, EDX, SEM, TEM, TG, DTG, and VSM. Details are discussed below.

The FT-IR spectrum of the novel ionically tagged nanomagnetic heterogeneous catalyst "Fe<sub>3</sub>O<sub>4</sub>@O<sub>2</sub>PO<sub>2</sub>(CH<sub>2</sub>)<sub>2</sub>NH<sub>3</sub><sup>+</sup>CF<sub>3</sub>CO<sub>2</sub><sup>-"</sup> was investigated in the domain of 400–4000 cm<sup>-1</sup> (Fig. 1). The broad peak at about 2600–3600 cm<sup>-1</sup> is related to ammonium moiety of the novel catalyst, uncoated OH groups on to the surface of Fe<sub>3</sub>O<sub>4</sub> and physically absorbed water during the catalyst preparation. Also, the carbonyl group within the structure of the prepared catalyst appeared at 1682 cm<sup>-1</sup>. P=O stretching mode is distinguishable at about 1200 cm<sup>-1</sup>.

For elemental characterization of the prepared nanomagnetic catalyst, energy dispersive X-ray (EDX) analysis was applied. The data from energy dispersive X-ray (EDX) analysis of the new heterogeneous catalyst showed all expected elements including iron, oxygen, phosphorous, carbon, nitrogen, and fluorine atoms as indicated in Fig. 2.

For determination of the size and morphology of the novel catalyst, SEM analysis was used. As can be concluded from Fig. 3, the catalyst particles have a mean diameter of about 26–36 nm with nearly spherical in shape.

Also, an insight to the novel nanomagnetic catalyst was achieved by TEM images. The recorded TEM images were illustrated in Fig. 4. According to the obtained TEM images, the sizes of the catalyst particles are in the nanometer scale.

In a comparative manner VSM analysis was applied to characterize the magnetic properties of the Fe<sub>3</sub>O<sub>4</sub> nanoparticles (a), Fe<sub>3</sub>O<sub>4</sub>@  $O_2PO_2(CH_2)_2NH_2$  (b) and desired catalyst Fe<sub>3</sub>O<sub>4</sub>@  $O_2PO_2(CH_2)_2NH_3^+CF_3CO_2^-$  (c). The obtained hysteresis curves are depicted in Fig. 5. According to the resulting hysteresis curves, the saturation of Fe<sub>3</sub>O<sub>4</sub>@O<sub>2</sub>PO<sub>2</sub>(CH<sub>2</sub>)<sub>2</sub>NH<sub>3</sub><sup>+</sup>CF<sub>3</sub>CO<sub>2</sub><sup>-</sup> as a catalyst reduced from 66.23 emu g<sup>-1</sup> for Fe<sub>3</sub>O<sub>4</sub> nanoparticles to 55.15 emu g<sup>-1</sup>. This reduction in saturation arises from the surface modification of the

 $Fe_3O_4$  nanoparticles with 2-aminoethyl dihydrogen phosphate and  $CF_3CO_2H$  respectively during the preparation of the catalyst.

TGA/DTG analysis was applied to study the thermal stability of  $Fe_3O_4(@O_2PO_2(CH_2)_2NH_3^+CF_3CO_2^-$  and the obtained curves is illustrated in Fig. 6. The weight loss upon heating from room temperature to about 160 °C can be attributed to the evaporation of water or other organic solvents which were employed during the course of catalyst preparation (weight loss of about 3%). Also, the weight loss from 160 to 360 °C can be ascribed to the decomposition of the ionic tags loaded on catalyst (weight loss of about 9.34%). The weight loss from 360 to 590 °C, can be related to decomposition of organic layer connected to Fe<sub>3</sub>O<sub>4</sub> nanoparticles (weight loss of about 7%). Based on obtained results, the presented nanomagnetic catalyst shows proper thermal behavior upon the investigated reaction.

## 3.2. Application of the nanocatalyst in the synthesis of 2-amino-6-(2-oxo-2H-chromen-3-yl)-4-phenylnicotinonitrils

After characterizing, the role of Fe<sub>3</sub>O<sub>4</sub>@ O<sub>2</sub>PO<sub>2</sub>(CH<sub>2</sub>)<sub>2</sub>NH<sub>3</sub><sup>+</sup>CF<sub>3</sub>CO<sub>2</sub><sup>-</sup> as a heterogeneous nanomagnetic catalyst was evaluated at the synthesis of 2-amino-6-(2-oxo-2H-chromen-3-yl)-4-phenylnicotinonitrils. In attempting to test its catalytic performance and in order to find the best operational reaction conditions in terms of amount of nanomagnetic catalyst, solvent and temperature, benzaldehyde, 3-acetylcoumarin, malononitrile, and ammonium acetate were picked up as model substrates. As revealed in Table 1, the best results were achieved when the reaction was performed using 10 mg of nanomagnetic catalyst at 70 °C and under solvent free conditions (Table 1, entry 3). Also, we investigated the optimal reaction conditions under nitrogen and argon atmosphere to present an evidence for the final step of the suggested anomeric based oxidation mechanism for aromatization of target molecules. The obtained results showed that the yield and time for two reactions under air, nitrogen, and argon atmosphere are same. To optimize the reaction temperature, the model reaction was performed at ambient temperature, 50 °C, 70 °C and 90 °C. As reveled in Table 1, 70 °C gives the best results and therefore it is the optimal reaction temperature (Table 1, entry 1-4). Furthermore, the amount of nanomagnetic catalyst was also optimized. The obtained results indicated that 10 mg of Fe<sub>3</sub>O<sub>4</sub>@O<sub>2</sub>PO<sub>2</sub>(CH<sub>2</sub>)<sub>2</sub>NH<sub>3</sub><sup>+</sup>CF<sub>3</sub>CO<sub>2</sub><sup>-</sup> is the optimized amount of the catalyst (Table 1, entry 3). Also, we tested the model reaction in the presence of Fe<sub>3</sub>O<sub>4</sub> and Fe<sub>3</sub>O<sub>4</sub>@O<sub>2</sub>PO<sub>2</sub>(CH<sub>2</sub>)<sub>2</sub>NH<sub>2</sub> but, the obtained data was not satisfactory (Table 1, entries 8 and 9). Also, comparing the achieved results from solvent free condition and different solvents like H2O, C2H5OH, CH3CN, CH3CO2C2H5, CH2Cl2, and *n*-hexane, illustrated that the solvent free condition is the best of choice.

Subsequently of recognizing the optimal reaction parameters, to efficacv and applicability studv the of the Fe<sub>2</sub>O₄@  $O_2PO_2(CH_2)_2NH_3^+CF_3CO_2^-$  as a magnetic nanoparticles catalyst in the preparation of target molecules, varied aryl aldehydes bearing electron withdrawing and electron donating substituents were treated with 3acetylcoumarin derivatives, ammonium acetate, and malononitile to furnish the corresponding 2-amino-6-(2-oxo-2H-chromen-3-yl)-4-phenylnicotinonitril derivatives with high yields and shorten reaction times. The attained data as indexed in the Table 2 disclose that all reactions carried out gently under optimal reaction conditions with good to high yields.

#### 3.3. Catalyst recycling and reusing test

One of the interesting features of nanomagnetic catalysts is their simple separation from the reaction mixture by applying an external magnet bar. The reusability test of the presented nanomagnetic catalyst was investigated upon the condensation reaction between 4-nitrobenzaldehyde, malononitrile, 3-acetylcoumarin and ammonium acetate in 60 min. As mentioned above, after completion of the

#### Table 2

#### Synthesis of target molecules 1a-p in the presence of $Fe_3O_4@O_2PO_2(CH_2)_2NH_3^+CF_3CO_2^{-.a}$

Entry	Х	Y	Product	Structure	Time (min)	Yield (%) <sup>b</sup>	Melting point (°C), [found] [Lit]·
1	Н	Н	1a	N N	45	83	280–282 [258–259] [32]
2	4-Cl	Н	1b	H <sub>2</sub> N CN	45	91	243–245 [245–247] [33]
3	2-Cl	Н	1c	H <sub>2</sub> N CN CI	60	87	230–232 [287–289] [32]
4	4-Br	Н	1d		45	88	285–287 [224–226] [34]
5	3-Br	Н	le	H <sub>2</sub> N CN Br	50	84	280–282 [242–244] [34]
6	4-NO <sub>2</sub>	Н	1f	H <sub>2</sub> N CN Br	60	94	250–252 [252–254] [33]
7	3-NO <sub>2</sub>	Н	1g	H <sub>2</sub> N CN NO <sub>2</sub>	60	95	254–256 [262–264] [32]
8	4-CN	Н	lh		60	92	276–278 [332–334] [ <mark>36</mark> ]
9	4-Me	Н	1i	H <sub>2</sub> N CN CN	60	75	270–272 [271–273] [33]

(continued on next page)

#### Table 2 (continued)

Entry	Х	Y	Product	Structure	Time (min)	Yield (%) <sup>b</sup>	Melting point (°C), [found] [Lit]·
10	4-OMe	Н	1j		60	76	221–223 [268–270] [33]
11	3-OMe	Н	1k	CN OMe	70	75	193–195 [242–244] [36]
12	3,4-OMe <sub>2</sub>	Н	11	H <sub>2</sub> N CN OMe	75	78	278–280 [278–279] [32]
13	4-OH	Н	lm	H <sub>2</sub> N CN OMe	75	76	277–279 [263–264] [35]
14	3-ОН	Н	ln	H <sub>2</sub> N CN OH	75	75	245–247 [238–240] [34]
15	3,5-F <sub>2</sub>	Н	10		40	96	269–271 [New]
16	4-CF <sub>3</sub>	2-OMe	1p	$H_2N + F$ $F$ $H_2N + F$ $F$ $H_2N + F$ $F$ $F$ $F$ $F$ $F$ $F$ $F$ $F$ $F$	45	93	288–290 [New]

<sup>a</sup> Reaction conditions arylaldehyde (1 mmol), 3-acetylcoumarin derivatives (1 mmol), malononitrile (1 mmol, 0.066 g) and ammonium acetate (1.5 mmol, 0115 g). <sup>b</sup> Isolated yields.



Fig. 7. The reusing test of the nano magnetic catalyst.

reaction, hot ethyl acetate was added to the reaction mixture for precipitation of nanomagnetic catalyst and dissolving the desired product and unreacted starting materials. Then, the catalyst was collected using a magnet bar, washed with ethyl acetate, dried and reused for the next runs. From the data depicted in Fig. 7, it is clear that the activity of the investigated catalyst is restored after seven successive runs with a marginal decreasing of its catalytic activity.

A suggested plausible mechanistic route for the synthesis of target molecule **1a** *via* anomeric based oxidation mechanism is demonstrated in Scheme 7. At first, Knoevenagel condensation reaction was carried out between activated malononitrile and benzaldehyde to gives **A**. The in-situ generated ammonia from ammonium acetate, as nitrogen source, attacks to catalytic activated 3-acethylcumarine. The reaction



Scheme 7. Plausible mechanistic process for the synthesis of target molecule 1a via anomeric based oxidation.

was improved by imine-enamine tautomerization. The enamine A reacts with B through Michael condensation to gives intermediate C. After imine to enamine tautomerization and cycloaddition, intermediate D produced. In the next step, intermediate D through tautomerization converted to the related intermediate E. In contrast to the previously reported studies [34,36], that have been proposed an aerobic auto oxidation of intermediate E to target molecule 1a, we believed that, this step might be progress through anomeric based oxidation in the absence of oxygen molecules. In the intermediate E, sharing the electron density from the nitrogens lone pairs to the vacant antibonding  $\sigma^*$  orbital of SP<sup>3</sup> C–H bond through vinylic C=C double bonds support the unusual hydride transfer for releasing the molecular hydrogen (H<sub>2</sub>). Recently, we have been named this phenomenon as an "anomeric based oxidation" (ABO) and its development for various catalytic systems is our main research interest [67-70]. The described "anomeric based oxidation" (ABO) mechanism is in good agreement with the "vinylogous anomeric effect" concept which had introduced by other researchers [57-66]. Finally, after H<sub>2</sub> releasing, the intermediate E converted to the intermediate F which furnished the desired molecule 1a in the presence of the describe nano magnetic catalyst.

#### 4. Conclusions

In summary, we have developed a novel, green and reusable nanomagnetic heterogeneous catalyst, namely  $Fe_3O_4@O_2PO_2(CH_2)_2NH_3^+$  $CF_3CO_2^-$  which was fully characterized by using suitable methods such as FT-IR spectroscopy, SEM, TEM, TG, DTG, VSM, and EDX. The described catalyst was successfully used for synthesis of a good range of 2amino-6-(2-oxo-2*H*-chromen-3-yl)-4-arylnicotinonitrile derivatives *via* the condensation reaction of arylaldehydes, 3-acetylcoumarin derivatives, malononitrile, and ammonium acetate as a source of nitrogen under solvent-free conditions with high yields. The latter step of the mechanistic route for the synthesis of target molecules has proceeded *via* an anomeric based oxidation mechanism. Reusability of catalyst, mildness, generality, easy work-up and short reaction time are the major advantages of the presented method.

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#### Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.mcat.2018.11.009.

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