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Green one-pot three-component synthesis of 4H-chromenes in the presence of nano-kaoline/BF_3/Fe_3O_4 as a super paramagnetic nanocatalyst

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KEYWORDS
One-pot three components;
Nano-kaoline/BF_3/Fe_3O_4;
4*H*-chromenes;
Solvent-free condition.

Abstract. Fused benzo-4*H*-pyran, namely 4*H*-chromene moiety, exists in several hetero-cyclic compounds with biological activities such as antioxidant, antibacterial, antiviral, antifungal, hypotensive, diuretic, antiallergenic, antileishmanial, anticoagulant, and antitumor. Herein, one-pot three components of aldehyde, malononitrile, and enolizable compounds in the presence of nano-kaoline/BF_3/Fe_3O_4 catalytic system to improve the 4*H*-chromenes *via* domino Knoevenagel-Michael-cyclization coupling reaction are reported. The advantages of this protocol involve high yield of products, use of solvent-free condition, easy experimental work-up system, low reaction times, recyclable catalyst, and green process, which privilege it as an alternative to other analogous synthetic procedures. The structure of synthesized 4*H*-chromenes was elucidated by FT-IR, ^{1}H NMR, and ^{13}C NMR.

1. Introduction

Environmental pollution is a conductive factor in expanding chemical processes that utilize high efficiency methods, solvents, catalysts, and compatible chemicals. A substantial part of this innovation is that transition metals are not used in chemical processes according to their toxicity. Therefore, a number of researchers have dedicated their efforts to extending green chemistry strategies using alternative methods like nonclassical energy inputs such as microwave and ultrasound irradiations or mechanochemical ball milling technique. Moreover, the toxicity and volatility of organic solvents can be considered two environmentally destructive factors due to their considerable contribution to chemical waste materials. There is great demand for developing manners that support the solvent-free room temperature to reduce the use of volatile organic compounds.

Further, Multi-Component Reactions (MCR) with one-pot reaction, simple purification process, selectivity, immense atom frugality, and high yields can be considered as efficient protocols. Hence, the development of MCRs by academic and industrial research groups results in new operational synthetic protocols for providing several organic molecules such as biologically active heterocyclic compounds.

Fused benzo-4*H*-pyran, namely 4*H*-chromene moiety, exists in several hetero-cyclic natural products

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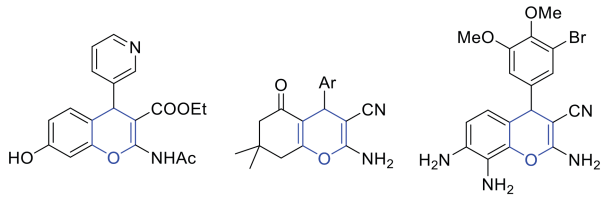


(a) IRAP inhibitor (b) Antibacterial agent (c) Anticancer agent

Figure 1. Selected 4*H*-chromenes scaffold with pharmacological activity.

[1]. Indeed, notable pharmacological and biological efficiencies have been attributed to heterocyclic compounds such as antioxidants and antibacterials [2]. For instance, the derivatives of 2-amino-3-cyano-4*H*-chromene are shown in Figure 1 in the form of (a), (b), and (c), which are insulin-regulated amino peptidase inhibitors for memory and learning ability improvement, anti-bacterial agents, and anticancer, respectively [3].

Thus, the application of different MCR strategies to synthesize 4*H*-chromene scaffold is acceptable. In addition, the derivatives of 2-amino-3-cyano-4*H*-pyran are available through catalytic MCR acting among aldehyde, malononitrile, and diverse enolizable acidic or electron-rich phenolic C–H activated agents. Several protocols that used homogenous and heterogeneous catalysts have been developed to synthesize the derivatives of 2-amino-3-cyano-4*H*-pyran.

A variety of catalytic systems such as UEA [4], sodium selenate [5], potassium flouride [6], Graphene-like boron nitride-modified calcium material [7], nano-sized zeolite clinoptilolite [8], Fe_3O_4@SiO_2-imid-PMAn [9], nanocrystalline $MIIZr_4(PO_4)_6$ ceramics [10], MoO_3H-Fe_3O_4@SiO_2 [11], CuO-CeO_2 [12], Mg/Al hydrotalcite [13], iodine[14], nano silica-bonded 5-N-propyl-octahydro-pyrtmido [1,2–4] azepinium chloride [15], diethylene glycol-bis(3-methylimidazolium) dihydroxide [16], and (H_2O-DMNPs) of γ-Fe_2O_3 [17] have been used for the synthesis of 2-amino-3-cyano-4*H*-pyran derivatives. A number of the related characteristics of the proposed protocol include transition metal usage, immense catalyst loading, reacting at different time intervals, high energy consumption, and volatile solvents. Thus, there is great demand for eco-friendly protocols that are developed by applying safer catalysts, nano-kaoline/BF_3/Fe_3O_4 [18], leading to higher yields.

2. Experimental

2.1. Materials and methods

^{1}H-NMR and ^{13}C-NMR spectra were obtained by (DRX-400 Avance) NMR from Bruker Company. A Magna 550 Nicolet spectrometer was applied in order to get FT-IR spectra.

2.2. General procedure for the synthesis of 4H-chromene catalyzed by nano-kaoline/BF_3/Fe_3O_4

To a mixture of aromatic aldehyde (1.0 mmol), malononitrile (1.0 mmol), and enolizable compound (1.0 mmol) was added 5 mg of nano-kaoline/BF_3/Fe_3O_4. The reaction mixture was stirred mechanically and the progress of reaction was monitored by TLC. Following the completion of reaction, the catalyst was separated using an external magnet and washed repeatedly with warm ethanol. Solid products emerged with the addition of water to residue. Then, the resulting solid product was collected and washed with ethanol to afford the pure product. To ensure further purification, products were recrystallized from ethanol or ethyl acetate to give pure products in high yields.

2.3. Hot filtration test

To a mixture of benzaldehyde (1.0 mmol), malononitrile (1.0 mmol), and dimedone (1.0 mmol) was added 5 mg of nano-kaoline/BF_3/Fe_3O_4. The mixture was mixed at 70°C for 30 min. Then, the catalyst was separated from the mixture using an external magnet. The obtained catalyst-free reaction mixture was heated for 1 hour at 70°C. Any additional promotion of reaction was not observed, meaning that a notable leaching of catalyst did not occur.

2.4. Spectral data

2-amino-7,7-dimethyl-5-oxo-4-phenyl-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (4a):

FT-IR (KBr, $\bar{\upsilon}$ (cm^{-1})): 3395, 3324, 3324, 3251, 3210, 3083, 3028, 2962, 2927, 2882, 2198, 1661, 1602, 1035. ^{1}H-NMR (400 MHz, DMSO-d_6): δ 0.9 (3H, s, CH_3), 1.0 (3H, s, CH_3), 2.1 (2H, CH_2. ABq), 3.3 (2H, s, CH_2), 4.1 (1H, s, CH), 7.0 (2H, br s, NH_2), 7.1 (3H, m, H-Ar), 7.3 (2H, m, H-Ar).

2-amino-4-(4-hydroxy-3-methoxyphenyl)-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (4b):

FT-IR (KBr, $\bar{\upsilon}$ (cm^{-1})): 3497, 3403, 3324, 3254, 3213, 3016, 2962, 2874, 2192, 1654, 1603, 1034. ^{1}H-NMR (400 MHz, DMSO-d_6): δ 0.9 (3H, s, CH_3), 1.0 (3H, s, CH_3), 2.1 (2H, CH_2. ABq), 3.3 (2H, s, CH_2), 3.7 (3H, s, O-CH_3), 4.0 (1H, s, CH), 6.5 (1H, d, $J = 9$ Hz, H-Ar), 6.6.

(2-amino-4-(4-chlorophenyl)-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (4c):

FT-IR (KBr, $\bar{\upsilon}$ (cm^{-1})): 3380, 3323, 3183, 2959, 2889, 2188, 1676, 1603, 1032. ^{1}H-NMR (400 MHz, DMSO-d_6): δ 0.9 (3H, s, CH_3), 1.0 (3H, s, CH_3), 2.1 (2H, CH_2. ABq), 3.3 (2H, s, CH_2), 4.2 (1H, s, CH), 7.0 (2H, br s, NH_2), 7.1 (2H, d, $J = 8.5$ Hz, H-Ar), 7.3 (2H, $J = 8.5$

Hz, H-Ar); 3H, m, H-Ar), 6.9 (2H, br s, NH_2), 8.8 (1H, br s, OH).

2-amino-4-(2,4-dimethoxyphenyl)-7,7-dimethyl- 5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (4d):
FT-IR (KBr, $\bar{\upsilon}$ (cm^{-1})): 3390, 3326, 3256, 3213, 2954, 2836, 2193, 1657, 1604, 1031. ^{1}H-NMR (400 MHz, DMSO-d_6): δ 0.9 (3H, s, CH_3), 1.0 (3H, s, CH_3), 2.1 (2H, CH_2. ABq), 3.6 (6H, s, OCH_3), 4.0 (1H, s, CH), 6.8 (4H, br s, H-Ar, NH_2).

2-amino-7,7-dimethyl-4-(2-nitrophenyl)-5-oxo-5,6,7,8-tetrahydro-4H- chromene-3-carbonitrile (4e):
FT-IR (KBr $\bar{\upsilon}$ (cm^{-1})): 3471, 3332, 3255, 3210, 2960, 2870, 2194, 1688, 1602, 1041. ^{1}H-NMR (400 MHz, DMSO-d_6): δ 0.8 (3H, s, CH_3), 0.9 (3H, s, CH_3), 2.0 (2H, CH_2. ABq), 3.3 (2H, s, CH_2), 4.9 (1H, s, CH), 7.1 (2H, br s, NH_2), 7.3 (1H, d, $J = 9.5$ Hz, -Ar), 7.4 (1H, t, $J = 9$ Hz, H-Ar), 7.6 (1H, t, $J = 9$ Hz, H-Ar), 7.8 (1H, d, $J = 10$ Hz, H-Ar).

2-amino-4-(2-methoxyphenyl)-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (4f):
FT-IR (KBr, $\bar{\upsilon}$ (cm^{-1})): 3396, 3329, 3262, 3219, 2964, 2879, 2189, 1685, 1654, 1036. ^{1}H-NMR (400 MHz, DMSO-d_6): δ 0.9 (3H, s, CH_3), 1.0 (3H, s, CH_3), 2.1 (2H, CH_2. ABq), 3.7 (3H, s, OCH_3), 4.4 (1H, s, CH), 6.8 (2H, br s, NH2), 6.9 (2H, br s, H-Ar), 7.1 (1H, br s, H-Ar).

4,4'-(1,4-Phenylene)bis(2-amino-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile) (4g):
FT-IR (KBr, $\bar{\upsilon}$ (cm^{-1})): 3392, 3325, 3254, 3211, 2963, 2859, 2194, 1686, 1649, 1041. ^{1}H-NMR (400 MHz, DMSO-d_6): δ 0.9 (3H, s, CH_3), 1.0 (3H, s, CH_3), 2.1 (2H, CH_2. ABq), 4.2 (1H, s, CH), 7.0 (2H, br s, NH_2), 7.2 (2H, d, $J = 8$ Hz, H-Ar), 7.8 (2H, d, $J = 8$ Hz, H-Ar).

2-amino-5-oxo-4-(m-tolyl)-4H,5H-pyrano[3,2-c]chromene-3-carbonitrile (4h):
FT-IR (KBr, $\bar{\upsilon}$ (cm^{-1})): 3390, 3321, 3251, 3186, 3052, 3015, 2914, 2879, 2198, 1705, 1674, 1603, 1060. ^{1}H-NMR (400 MHz, DMSO-d_6): δ 2.2 (3H, s, CH_3), 4.4 (1H, s, CH), 7.0 (3H, br s, NH_2, H-Ar), 7.1 (1H, t, $J = 8$ Hz, H-Ar), 7.3 (1H, s, H-Ar), 7.4 (1H, d, $J = 11$ Hz, H-Ar), 7.4 (1H, d, $J = 9.5$ Hz, H-Ar), 7.6 (1H, t, $J = 9.5$ Hz, H-Ar), 7.8 (1H, d, $J = 9.5$ Hz, H-Ar).

2-amino-4-(2-chlorophenyl)-5-oxo-4H,5H-pyrano[3,2-c]chromene-3-carbonitrile (4i):
FT-IR (KBr, $\bar{\upsilon}$ (cm^{-1})): 3398, 3284, 3179, 2199, 1708, 1673, 1603, 1060. ^{1}H-NMR (400 MHz, DMSO-d_6): δ 4.9 (1H, s, CH), 7.2 (3H, m, NH_2, H-Ar), 7.4 (4H, m, H-Ar), 7.7 (1H, t, $J = 9.5$ Hz, H-Ar), 7.8 (1H, d, $J = 9.5$ Hz, H-Ar).

2-amino-5-oxo-4-phenyl-4H,5H-pyrano[3,2-c]chromene-3-carbonitrile (4j):
FT-IR (KBr, $\bar{\upsilon}$ (cm^{-1})): 3377, 3285, 3180, 2887, 2196, 1709, 1673, 1605, 1056. ^{1}H-NMR (400 MHz, DMSO-d_6): δ 4.4 (1H, s, CH), 7.2-7.4 (9H, m, NH_2, H-Ar), 7.6 (1H, br s, H-Ar), 7.8 (1H, d, $J = 6.5$ Hz, H-Ar).

2-amino-4-(4-nitrophenyl)-5-oxo-4H,5H-pyrano[3,2-c]chromene-3-carbonitrile (4k):
FT-IR (KBr, $\bar{\upsilon}$ (cm^{-1})): 3479, 3429, 3367, 3335, 3191310, 3069, 2195, 1718, 1672, 1602, 1054. ^{1}H-NMR (400 MHz, DMSO-d_6): δ 4.6 (1H, s, CH), 7.4-7.5 (4H, m, NH_2, C_{sp^2} H-Ar), 7.7 (1H, t, $J = 10$ Hz, C_{sp^2} H-Ar), 7.9 (1H, d, $J = 10$ Hz, H-Ar), 8.1 (1H, d, $J = 10.5$ Hz, H-Ar).

4,4'-(1,4-phenylene)bis(2-amino-5-oxo-4H,5H-pyrano[3,2-c]chromene-3-carbonitrile) (4m):
FT-IR (KBr, $\bar{\upsilon}$ (cm^{-1})): 3324, 3191, 2196, 1709, 1672, 1604, 1055. ^{1}H-NMR (400 MHz, DMSO-d_6): δ 4.4 (1H, s, CH), 7.1 (2H, br s, NH_2), 7.3-7.4 (4H, m, H-Ar), 7.6 (2H, d, $J = 8$ Hz, H-Ar), 7.8 (2H, d, $J = 9.5$ Hz, H-Ar).

2-amino-4-(4-hydroxy-3-methoxyphenyl)-7-methyl-5-oxo-4H,5H-pyrano[4,3-b]pyran-3-carbonitrile (4n):
FT-IR (KBr, $\bar{\upsilon}$ (cm^{-1})): 3492, 3349, 3094, 2200, 1702, 1673, 1639, 1607, 1034. ^{1}H-NMR (400 MHz, DMSO-d_6): δ 2.2 (3H, s, CH_3), 3.7 (3H, s, OCH_3), 4.1 (1H, s, CH), 6.2 (1H, s, H-pyran), 6.5 (1H, d, $J = 9$ Hz, H-Ar), 6.6 (1H, d, $J = 10.5$ Hz, H-Ar), 6.7 (1H, s, H-Ar), 7.1 (2H, br s, NH_2), 8.9 (1H, br s, OH).

2-amino-7-methyl-4-(3-nitrophenyl)-5-oxo-4H,5H-pyrano[4,3-b]pyran-3 -carbonitrile (4o):
FT-IR (KBr, $\bar{\upsilon}$ (cm^{-1})): 3457, 3360, 3237, 3184, 3118, 3076, 2874, 2195, 1705, 1670, 1639, 1609, 1038. ^{1}H-NMR (400 MHz, DMSO-d_6): δ 2.2 (3H, s, CH_3), 4.5 (1H, s, CH), 6.3 (1H, s, H-pyran), 7.3 (1H, s, H-Ar), 8.0 (2H, s, NH_2), 8.1 (1H, d, $J = 10$, H-Ar).

2-amino-4-(4-ethoxyphenyl)-7-methyl-5-oxo-4H,5H -pyrano[4,3-b]pyran-3-carbonitrile (4p):
FT-IR (KBr, $\bar{\upsilon}$ (cm^{-1})): 3450, 3401, 3209, 3101, 2980, 2929, 2883, 2195, 1702, 1671, 1643, 1610, 1042. ^{1}H-NMR (400 MHz, DMSO-d_6): δ 1.3 (3H, t, $J = 8$, CH_3), 2.2 (3H, s, CH_3), 3.9 (2H, q, $J = 7.5$, CH_2), 4.1 (1H, s, CH), 6.2 (1H, s, H-pyran), 6.8 (2H, d, $J = 10$, H-Ar), 7.0 (2H, d, $J = 10$, H-Ar), 7.1 (2H, br s, NH_2).

4,4'-(1,4-phenylene)bis(2-amino-7-methyl-5-oxo-4H,5H-pyrano[4,3-b]pyran-3-carbonitrile) (4q):

FT-IR (KBr, $\bar{\upsilon}$ (cm^{-1})): 3457, 3374, 3323, 3196, 2891, 2195, 1704, 1677, 1643, 1610, 1039. ^{1}H-NMR (400 MHz, DMSO-d_6): δ 2.2 (3H, s, CH_3), 4.2 (1H, s, CH), 6.3 (1H, s, H-pyran), 7.1 (2H, s, NH_2), 7.2 (1H, s, H-Ar).

3-amino-1-(3-nitrophenyl)-1H-benzo[f]chromene-2-carbonitrile (4r):

FT-IR (KBr, $\bar{\upsilon}$ (cm^{-1})): 3457, 3374, 3323, 3196, 2891, 2195, 1704, 1677, 1643, 1610, 1039. ^{1}H-NMR (400 MHz, DMSO-d_6): δ 2.2 (3H, s, CH_3), 4.2 (1H, s, H-pyran), 6.3 (1H, s, CH), 7.1 (2H, s, NH_2), 7.2 (1H, s, H-Ar).

3-amino-1-(p-tolyl)-1H-benzo[f]chromene-2-carbonitrile (4s):

FT-IR (KBr, $\bar{\upsilon}$ (cm^{-1})): 3426, 3336, 2186, 1643, 1615, 1589, 1035. ^{1}H-NMR (400 MHz, DMSO-d_6): δ 2.2 (3H, s, CH_3), 5.2 (1H, s, CH), 6.3 (1H, s, CH), 6.9 (1H, br s, H-Ar), 7.0 (4H, br s, H-Ar), 7.3-7.4 (8H, m, H-Ar, NH_2), 7.8-7.9 (3H, m, H-Ar).

3. Results and discussion

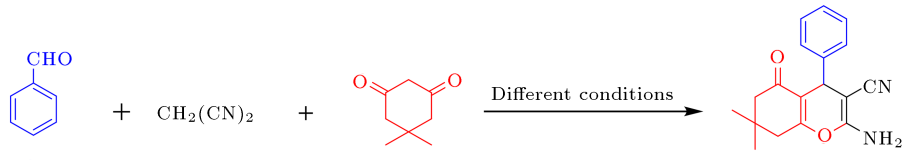
As part of the proposed research programs, the tendency to expand the domain of nano-kaoline/BF_3/Fe_3O_4 [18] as catalyst, this study presents a straightforward and cost-effective procedure in order to provide 2-amino-3-cyano-*4H*-pyran scaffold using MCR protocol.

Herein, this study intends to improve the tetrahydro-4*H*-chromene derivatives via one-pot three-component green condensation of aldehyde, malononitrile, and enolizable compounds in the presence of nano-kaoline/BF_3/Fe_3O_4 catalytic systems. First of all, the synthesis of tetrahydro-4*H*-chromenes was optimized by modifying factors like catalyst amount, solvent presence or solvent freeness, condition and time, which resulted in different yield values. Benzaldehyde (1 mmol), malononitrile (1.1 mmol), and dimedone (1 mmol) were considered in the reaction model. As shown in Table 1 (entries 9, 10, and 11), BF_3 is very active Lewis acid, but is a volatile material with difficult application. Nano-Kaoline-BF_3 is an active catalyst, but is not a magnetic catalyst with simple recovering by external magnet. Nano Kaoline is not an active catalyst. In conclusion, concerning the aim of this study, a high yield of product with simple workup was ensured using nano-kaoline/BF_3/Fe_3O_4 (0.1 g) as a catalyst under a solvent-free condition (Table 1, entry 8).

The achievement in the optimized condition encouraged the current authors to develop the scope of re-action with a variety of aromatic aldehydes and dimedone as an activated C–H acid. The results are summarized in Table 2 (entries 1–7). As shown in Table 2, the nature of the group on the aromatic aldehyde is not effective in yielding desired products, and products are obtained in good to excellent yields in the presence of nano-kaoline/BF_3/Fe_3O_4 nanocomposite as a catalyst.

In the next step, to demonstrate the scope of this efficient nano-catalyst, the optimized reaction conditions were developed to another activated C–H acid, 4-hydroxycoumarin (entries 8–13), 4-hydroxy-6-

Table 1. Synthesis of 2-amino-7,7-dimethyl-5-oxo-4-phenyl-4a,5,6,7,8,8a-hexahydro-4*H*-chromene-3- carbonitrile catalyzed by nano-kaoline/BF_3/Fe_3O_4 under various conditions[a].

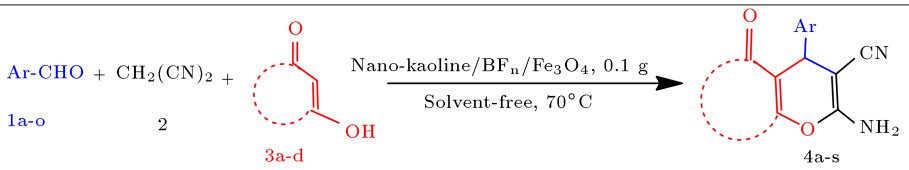


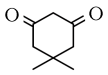
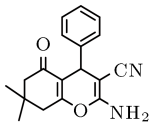
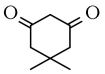
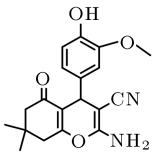
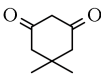
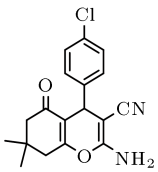
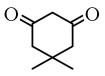
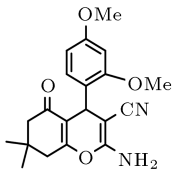
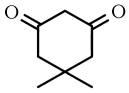
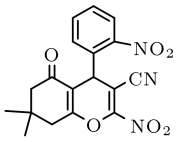
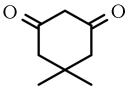
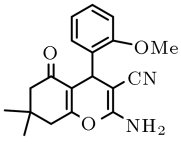
1a 2 3a 4a

Entry	Catalyst (g)	Temperature	Solvent	Time	Yield[b] (%)
1	—	r.t.	—	24 h	Trace
2	—	r.t.	EtOH	24 h	39
3	Nano-kaoline/BF_3/Fe_3O_4 (0.008 g)	r.t.	EtOH	2 h	58
4	Nano-kaoline/BF_3/Fe_3O_4 (0.008 g)	70°C	—	2 h	60
5	Nano-kaoline/BF_3/Fe_3O_4 (0.05 g)	r.t.	EtOH	90 min	67
6	Nano-kaoline/BF_3/Fe_3O_4 (0.05 g)	70°C	—	75 min	79
7	Nano-kaoline/BF_3/Fe_3O_4 (0.1 g)	r.t.	EtOH	60 min	88
8	**Nano-kaoline/BF_3/Fe_3O_4 (0.1 g)**	**70°C**	—	**60 min**	**92**
9	Nano-kaoline/BF_3 (0.08 g)	70°C	—	60 min	95
10	Nano-kaoline (0.1 g)	70°C	—	60 min	55
11	BF_3. OEt_2 (0.05 g)	70°C	—	60 min	96

[a]Reaction conditions: Benzaldehyd (1 mmol), malononitrile (1.1 mmol), dimedone (1 mmol),
[b]Isolated yields.

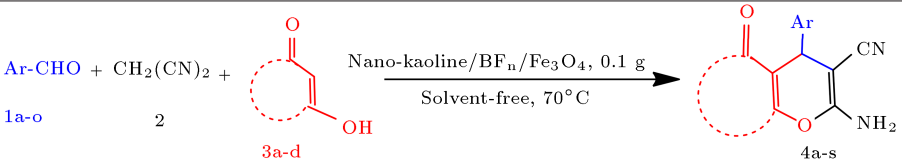
Table 2. Synthesis of tetrahydro-4H-chromenes using nano-kaoline/BF_3/Fe_3O_4[a].

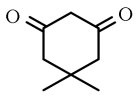
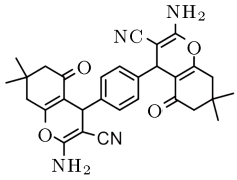
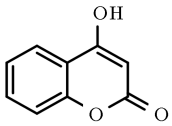
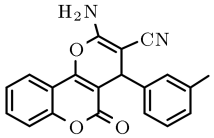
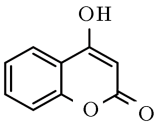
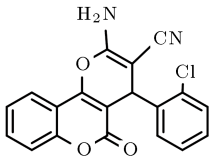
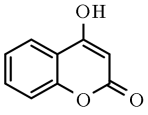
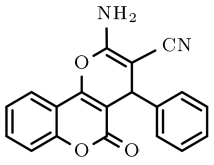
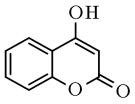
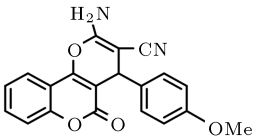
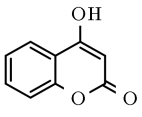
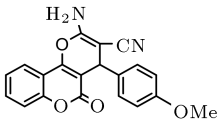


Entry	Ar	Activated C-H acids	Products	Time (min)	Yield[b] (%)	M.P (Obs.)/ M.P (lit.) [Ref.]
1	C_6H_5 1a	 3a	 4a	60	92	238–240 (237–239) [19]
2	4-OH-3-MeO-C_6H_3 1b	 3a	 4b	50	78	230–232 (230–232) [9]
3	4-Cl-C_6H_4 1c	 3a	 4c	45	85	210–212 (213–214) [19]
4	2,4-$(MeO)_2$-C_6H_3 1d	 3a	 4d	45	83	229–231 (227–229) [20]
5	2-NO_2-C_6H_4 1e	 3a	 4e	65	72	236–238 (237–238) [9]
6	2-MeO-C_6H_4 1f	 3a	 4f	55	77	195–197 (196–198) [19]

[a]Reaction conditions: Aldehyde (1 mmol), malononitrile (1.1 mmol), activated C-H acids (1 mmol), and nano-kaoline/BF_n/Fe_3O_4 (0.1 g) at 70°C. [b]Isolated yield.

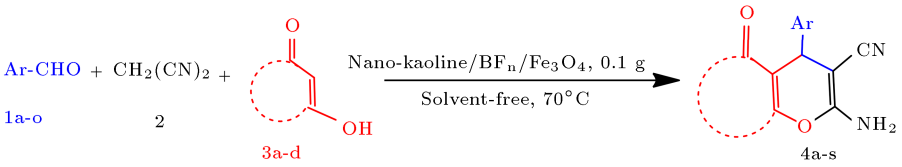
Table 2. Synthesis of tetrahydro-4H-chromenes using nano-kaoline/BF_3/Fe_3O_4[a] (continued).

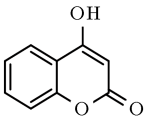
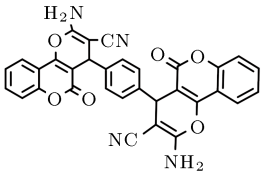
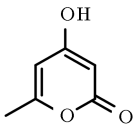
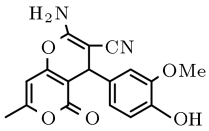
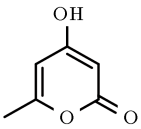
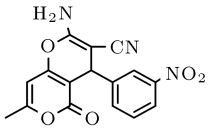
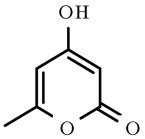
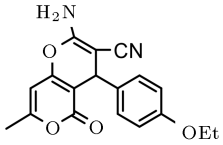
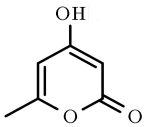
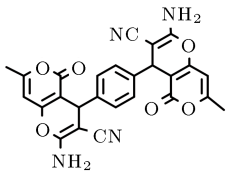
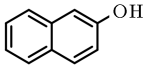
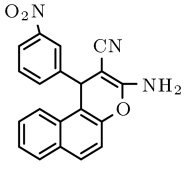


Entry	Ar	Activated C-H acids	Products	Time (min)	Yield[b] (%)	M.P (Obs.)/ M.P (lit.) [Ref.]
7	4-CHO-C_6H_4			60	81	> 280 – [17]
	1g	3a	4g			
8	3-Me-C_6H_4			45	78	253–255 (254–255) [21]
	1h	3b	4h			
9	2-Cl-C_6H_4			48	82	265–267 (267–269) [9]
	1i	3b	4i			
10	C_6H_5			60	80	259–261 (260–261) [9]
	1a	3b	4j			
11	4-NO_2-C_6H_4			42	75	252–254 (252–254) [9]
	1j	3b	4k			
12	4-MeO-C_6H_4			55	77	246–248 (244–246) [9]
	1k	3b	4l			

[a]Reaction conditions: Aldehyde (1 mmol), malononitrile (1.1 mmol), activated C-H acids (1 mmol), and nano-kaoline/BF_n/Fe_3O_4 (0.1 g) at 70°C. [b]Isolated yield.

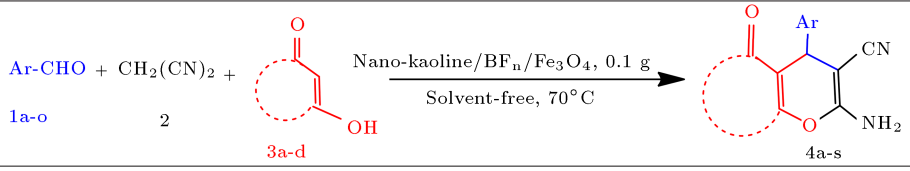
Table 2. Synthesis of tetrahydro-4H-chromenes using nano-kaoline/BF_3/Fe_3O_4[a] (continued).

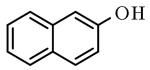
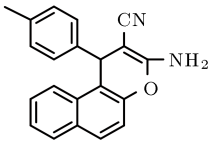


Entry	Ar	Activated C-H acids	Products	Time (min)	Yield[b] (%)	M.P (Obs.)/ M.P (lit.) [Ref.]
13	4-CHO-C_6H_4 1g	 3b	 4m	56	72	> 280 (271–273) [22]
14	4-OH-3-MeO-C_6H_3 1b	 3c	 4n	55	80	260–262 (258–259) [23]
15	3-NO_2-C_6H_4 1m	 3c	 4o	66	79	236–238 (235–237) [24]
16	4-OEt-C_6H_4 1n	 3c	 4p	48	77	230–232 (233–235) [23]
17	4-CHO-C_6H_4 1g	 3c	 4q	56	77	> 280 (305–307) [24]
18	3-NO_2-C_6H_4 1m	 3d	 4r	68	75	238–240 (239–241) [25]

[a]Reaction conditions: Aldehyde (1 mmol), malononitrile (1.1 mmol), activated C-H acids (1 mmol), and nano-kaoline/BF_n/Fe_3O_4 (0.1 g) at 70°C. [b]Isolated yield.

Table 2. Synthesis of tetrahydro-4H-chromenes using nano-kaoline/BF_3/Fe_3O_4[a] (continued).



Entry	Ar	Activated C-H acids	Products	Time (min)	Yield[b] (%)	M.P (Obs.)/ M.P (lit.) [Ref.]
19	4-Me-C_6H_4			55	79	268–270 (255–256) [19]
	1o	3d	4s			

[a]Reaction conditions: Aldehyde (1 mmol), malononitrile (1.1 mmol), activated C-H acids (1 mmol), and nano-kaoline/BF_n/Fe_3O_4 (0.1 g) at 70°C. [b]Isolated yield.

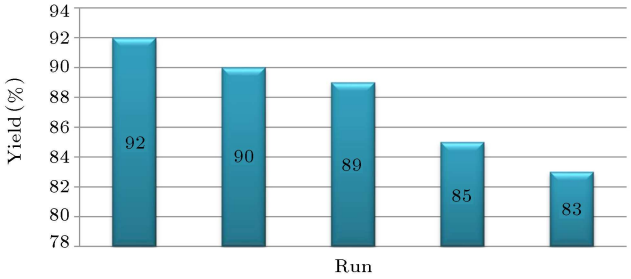


Figure 2. Reusability of the catalyst in the model reaction.

methyl-*2H*-pyran-2-one (entries 14–17), and phenolic compounds (entries 18,19). In addition, the new magnetic nano-catalyst almost fortunately acts very well for preparing a variety of 2-amino-3-cyano-4*H*-chromen derivatives in good to excellent yields.

The reusability of the catalysts is one of the most important benefits that makes them useful for commercial applications. Therefore, this study has investigated the recovery and reusability of nano-kaoline/BF_3/Fe_3O_4 catalyst. The catalyst can be easily separated by magnet and reused after washing with $CHCl_3$ and drying at 60°C. Their reusability was checked in the synthesis of 2-amino-7,7-dimethyl-5-oxo-4-phenyl-5,6,7,8-tetrahydro-4*H*-chromene-3-carbonitr ile by the reaction of benzaldehyde, malononitrile, and dimedone in the presence of nano-kaoline/BF_3/Fe_3O_4. As observed earlier, the catalyst could be used at five successive time intervals at least with an insignificant decrease in its activity (Figure 2).

4. Conclusion

In conclusion, a descriptive and systematic investigation of the heterogeneous water dispersed magnetic nanoparticles of nano-kaoline/BF_3/Fe_3O_4 as a green and reusable catalyst for the synthesis of tetra-hydro-4*H*-chromenes via domino Knoevenagel-Michael-cyclization coupling reactions was presented. The mentioned solvent-free catalytic process can lead to several annulated tetrahydro-4*H*-chromenes under mild conditions. The method characterized by its rapidity, recyclable catalyst, green process is privileged as an alternative to other analogous synthetic procedures. Other advantages of the protocol include preparation of products at high efficiency levels, no use of hazardous solvent, and an easy experimental work-up system.

Acknowledgments

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