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Characterization and Application of SO₃H-functionalized Phthalimide (SFP) as an Efficient and Recyclable Catalyst for the Solvent-free Synthesis of 2-Amino-4*H*-chromenes

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In this research, SO₃H-functionalized phthalimide (SFP) has been prepared through simple reaction of phthalimide with chlorosulfonic acid, and characterized using FT-IR, ¹H NMR, ¹³C NMR, SEM (scanning electron microscopy), mass and TG (thermal gravimetric) spectra. Afterward, the solid acid has been utilized as an efficient, green, heterogeneous and recyclable catalyst for the solvent-free synthesis of 2-amino-4*H*-chromenes by the one-pot multi-component reaction of aromatic aldehydes with malononitrile and 1-naphthol under thermal (70 °C) and microwave (540 W) conditions.

Keywords: SO₃H-functionalized phthalimide (SFP), SO₃H-containing solid acid, 2-Amino-4*H*-chromenes, Solvent-free, Microwave

INTRODUCTION

Development of green, heterogeneous and recyclable catalysts for the synthesis of helpful organic compounds is of significance [1-7]. Solid acids, as an important class of these catalysts, have been extensively applied to promote different organic transformations [1-7]; because performing organic reactions using solid acid catalysts are associated with different advantages, such as catalyst efficiency, good agreement with the green chemistry protocols, appropriate thermal stability of catalyst, simple process and product isolation, performing in milder conditions, high reaction selectivity and reducing volume of waste. Among different classes of solid acids, SO₃H-containing ones have been attracted much attention by chemists to catalyze a variety of organic transformations [3-7].

Multi-component reactions (MCRs) have attracted much

attention in modern organic synthesis and medicinal chemistry, because they are one-pot processes bringing together three or more components and show high atom economy and high selectivity [8-14]. On the other hand, the use of many toxic and volatile organic solvents, particularly chlorinated hydrocarbons as the reaction media, contributes pollution to the environment; thus, it is highly desirable to develop environmentally benign processes (such as MCRs) which can be conducted in solvent-free conditions [8-14].

The one-pot multi-component reaction between arylaldehydes, malononitrile and 1-naphthol (or phenols), in the presence of acidic and basic catalysts [15-24], has been used as the best synthetic way toward 2-amino-4*H*-chromenes as biologically and industrially significant compounds. Some biological activities of this class of chromene derivatives include antiviral [25], antitumor [26] and antimicrobial [27] properties. They have also been widely employed as sex pheromone [28], potent biodegradable agrochemicals [29] and cosmetics as well as pigments [30].

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Microwave irradiation (MWI) has been used as a highly efficient technique in organic synthesis. Microwave-assisted synthesis has many advantages compared with synthesis under thermal conditions, since MWI often accelerates reaction rate, and affords products with higher yields and higher purity [31-33]. In the case of conventional heating using an external heat source like an oil bath, the energy transfer depends on the thermal conductivity of the reactants, which is relatively slow. In contrast, the microwave energy is directly transferred to the molecules of the reaction mixture *via* dielectric heating. The heating is largely caused by dipolar polarization and ionic conduction [31-33].

In this work, we report the preparation of a SO₃H-containing solid acid namely SO₃H-functionalized phthalimide (SFP) *via* the reaction of phthalimide with chlorosulfonic acid, and its full identification by studying FT-IR, ¹H NMR, ¹³C NMR, SEM (scanning electron microscopy), Mass, and TG (thermal gravimetric) spectra. Afterward, we report our results on the application of this solid acid as an environmentally benign, heterogeneous, efficient and recyclable catalyst for the synthesis of 2-amino-4*H*-chromenes *via* the one-pot multi-component reaction of aromatic aldehydes with malononitrile and 1-naphthol under conventional thermal (70 °C) and microwave (540 W) conditions in the absence of solvent.

EXPERIMENTAL

General

All chemicals were purchased from Merck or Fluka Chemical Companies. All known compounds were identified by comparing their melting points and spectral data with those reported in the literature. Progress of the reactions was monitored by TLC using silica gel SIL G/UV 254 plates. The ¹H NMR (250 MHz) and ¹³C NMR (62.5 MHz) were run on a Bruker Avance DPX, FT-NMR spectrometer (δ in ppm). Melting points were recorded on a Büchi B-545 apparatus in open capillary tubes. TG was analyzed by a Perkin Elmer apparatus, Model: Pyris 1 (25-500 °C, temperature increase rate of 10 °C min⁻¹, nitrogen

atmosphere).

Procedure for the Preparation of SO₃H-functionalized Phthalimide (SFP)

To a round-bottomed flask (50 ml) containing phthalimide (0.736 g, 5 mmol), was added chlorosulfonic acid (0.594 g, 5.1 mmol) dropwise at 10 °C. After the addition was completed, the reaction mixture was stirred at room temperature for 5 h, and then at 70 °C for 3 h. Then, the residue was washed with CH₂Cl₂ (2 × 10 ml), and dried to give SFP as a white solid in 98% yield.

Spectral data of SFP. IR (KBr): 3350-2950, 1718, 1305, 1287, 1182, 1088, 1070 cm⁻¹. ¹H NMR (250 MHz, DMSO-d₆): δ 7.40-7.55 (m, 4H, aromatic hydrogens), 11.00 (s, 1H, OH of the SO₃H group). ¹³C NMR (62.5 MHz, DMSO-d₆): δ 122.6, 132.0, 134.0, 169.0. Mass (m/z): 227 (M⁺), 228 (M⁺+1), 210 (M⁺-OH), 146 (M⁺-SO₃H), 132 (M⁺-NSO₃H), 104 (M⁺-CONSO₃H) and 76 (M⁺-(CO)₂NSO₃H).

General Procedure for the Preparation of 2-Amino-4*H*-chromenes Catalyzed by SFP under Thermal Conditions

To a mixture of aromatic aldehyde (1 mmol), malononitrile (1 mmol, 0.066 g) and 1-naphthol (1 mmol, 0.144 g) in a test tube, was added SFP (0.05 mmol, 0.0114 g). The resulting mixture was firstly stirred magnetically at 70 °C, and after solidification of the reaction mixture, it was vigorously stirred with a small rod at the same temperature. After completion of the transformation (as indicated by TLC), and cooling the reaction mixture to room temperature, the resulted solid was powdered, ethyl acetate (5 ml) was added to it, stirred for 1 min, and filtered to separate SFP (the products is soluble in ethyl acetate; however, SFP is insoluble in this solvent). Afterward, the solvent of the filtrate was evaporated, and the resulting solid (crude product) was recrystallized from EtOH (96%) to afford the pure product.

General Procedure for the Microwave-assisted Preparation of 2-Amino-4*H*-chromenes Using SFP

A mixture of aromatic aldehyde (1 mmol), malononitrile

(1 mmol, 0.066 g), 1-naphthol (1 mmol, 0.144 g) and SFP (0.025 mmol, 0.0057 g) in a test tube was irradiated in a microwave oven at 540 W. After completion of the reaction (as indicated by TLC), and cooling the reaction mixture to room temperature, the resulted solid was powdered, ethyl acetate (5 ml) was added to it, stirred for 1 min, and filtered to separate SFP (the product is soluble in ethyl acetate; but, SFP is insoluble in this solvent). After that, the solvent of the filtrate was evaporated and the resulting solid (crude product) was recrystallized from EtOH (96%) to afford the pure product.

Selected Spectral Data of 2-Amino-4*H*-chromenes

2-Amino-4-(4-nitrophenyl)-4*H*-benzo[*h*]chromene-3-carbonitrile (3). ¹H NMR (250 MHz, DMSO-*d*₆): δ 5.13 (s, 1H), 7.08 (d, *J* = 8.5 Hz, 1H), 7.31 (s, 1H), 7.50-7.66 (m, 5H), 7.88 (d, *J* = 8.0 Hz, 1H), 8.15-8.26 (m, 3H). ¹³C NMR (62.5 MHz, DMSO-*d*₆): δ 40.1, 55.1, 116.5, 120.1, 120.7, 122.7, 123.9, 124.1, 124.4, 125.8, 126.9, 127.6, 128.9, 132.8, 142.9, 146.4, 152.9, 160.3.

2-Amino-4-(4-chlorophenyl)-4*H*-benzo[*h*]chromene-3-carbonitrile (5). ¹H NMR (250 MHz, DMSO-*d*₆): δ 4.93 (s, 1H), 7.07 (d, *J* = 8.5 Hz, 1H), 7.19-7.27 (m, 6H), 7.52-7.64 (m, 3H), 7.86 (d, *J* = 7.7 Hz, 1H), 8.21 (d, *J* = 8.0 Hz, 1H). ¹³C NMR (62 MHz, DMSO-*d*₆): δ 44.6, 61.0, 122.6, 125.6, 125.9, 127.9, 129.2, 131.3, 131.9, 132.0, 132.9, 133.9, 134.8, 136.7, 137.9, 147.9, 149.8, 165.3.

RESULTS AND DISCUSSION

Preparation and Characterization of the Catalyst

At first, we reacted phthalimide (1 eq.) with

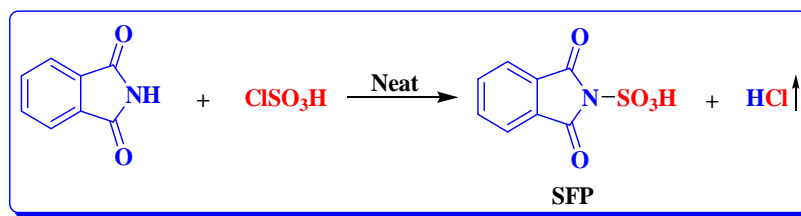
chlorosulfonic acid (1 eq.) according to the mentioned procedure in the experimental section to give SFP (Scheme 1).

In this section, we characterize the catalyst by studying its FT-IR, ¹H NMR, ¹³C NMR, SEM, Mass and TG spectra. The FT-IR spectrum of SFP (Fig. S1) showed a broad peak at 2950-3350 cm⁻¹ related to the OH functional of the SO₃H group. The band at 1070 cm⁻¹ was assigned to SOH bend. The strong peak at 1718 cm⁻¹ corresponds to the carbonyl groups of the catalyst. Moreover, two peaks observed in 1088 cm⁻¹ and 1305 cm⁻¹ correspond to the vibrational modes of N-SO₂ bond. The strong absorptions at 1287 and 1182 cm⁻¹ in the catalyst were assigned to the asymmetric and symmetric stretching and bending for S-O vibrations of the SO₃H.

The ¹H NMR spectrum of SFP (Fig. S2), showed a multiple peak at 7.40-7.55 ppm corresponding to the four aromatic hydrogens of the catalyst. The acidic hydrogen of SO₃H group was observed at 11.00 ppm.

The ¹³C NMR spectrum (Fig. S3) showed three peaks in aromatic region (122.6, 132.0 and 134.0 ppm) related to the four carbon types of the aromatic ring. Furthermore, the peak at 169.0 ppm is related to the carbonyl groups. The SEM image of the catalyst (Fig. 1) indicates the crystal sizes of SFP.

In the mass spectrum of SO₃H-functionalized phthalimide (Fig. S4), the peaks observed at *m/z* = 227 and 228, are related to its molecular mass (*M*⁺) and *M*⁺ + 1. Thermal gravimetric analysis of SFP was also studied at a range of 25-500 °C. The corresponding diagram is shown in Fig. 2. The thermal gravimetric (TG) diagram showed weight losses in two steps, at about 150-220 °C and 275-360 °C.



Scheme 1. The synthesis of SFP

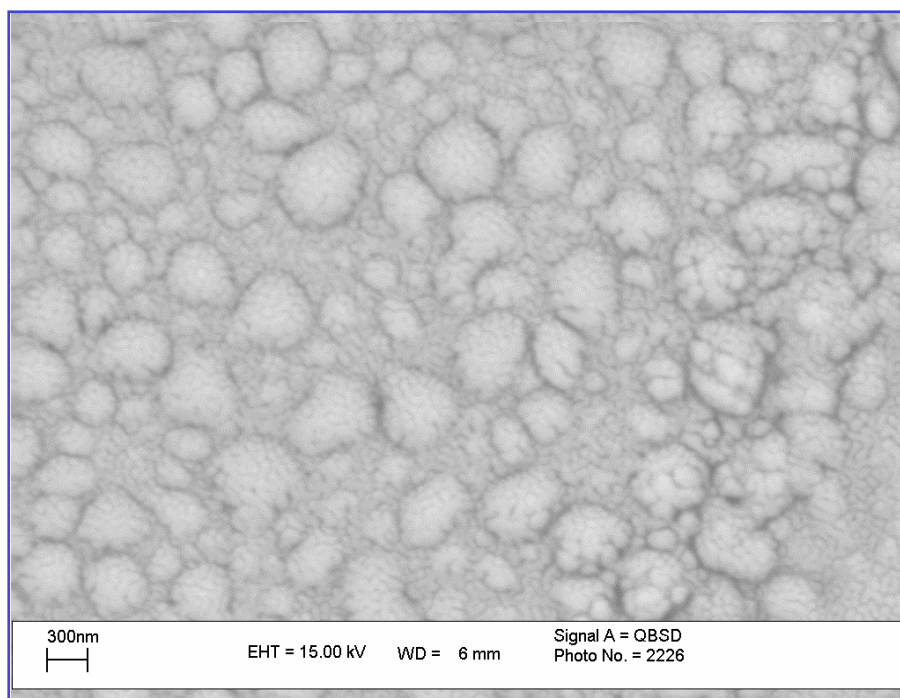


Fig. 1. The SEM image of SFP.

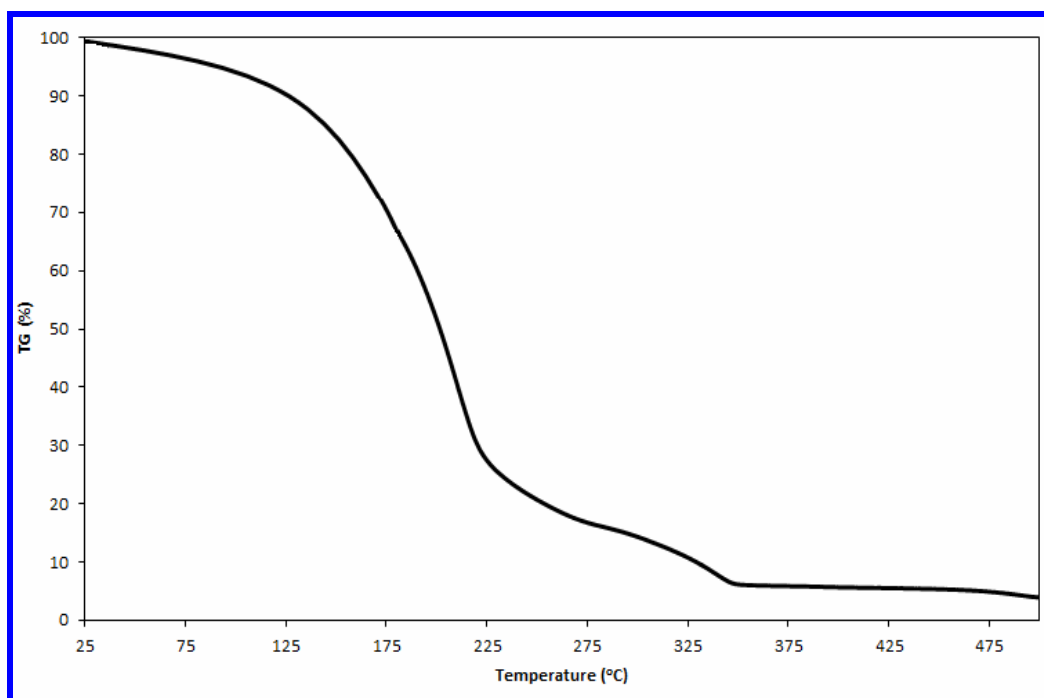
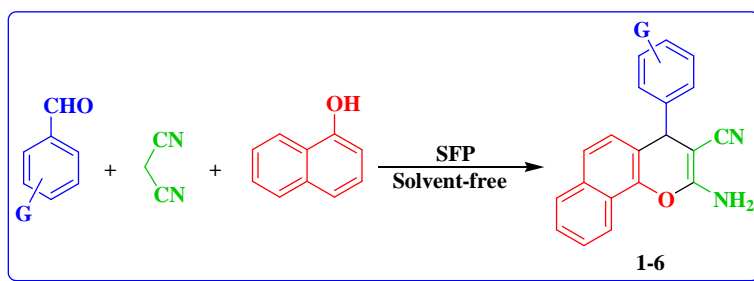


Fig. 2. The TG diagram of SFP.



Scheme 2. The production of 2-amino-4*H*-chromenes using SFP

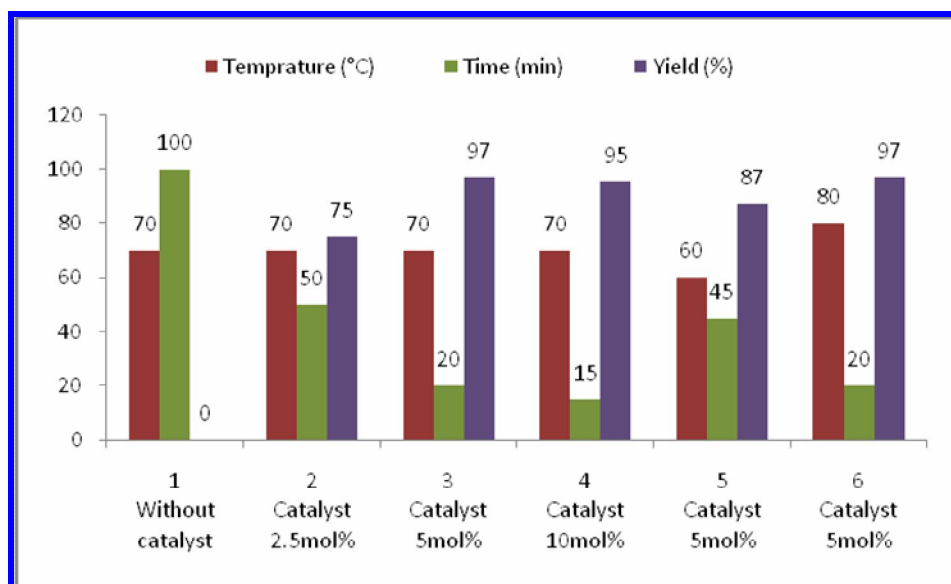


Fig. 3. Optimization of the catalyst amount and temperature on the model reaction.

Table 1. Recyclability of the Catalyst on the Reaction of 3-Nitrobenzaldehyde with Malononitrile and 1-Naphthol

Entry	Cycle	Time (min)	Yield (%) ^a
1	1 (Fresh catalyst)	20	97
2	2	30	97
3	3	30	92

^aIsolated yield.

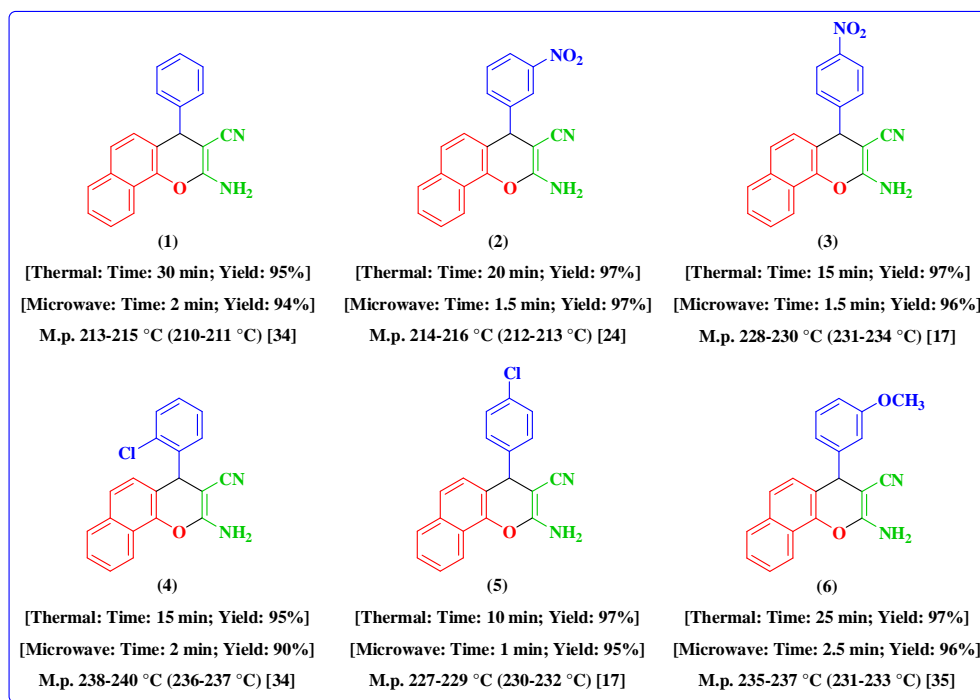


Fig. 4. The solventless preparation of 2-amino-4H-chromenes using SFP under thermal and microwave conditions.

Table 2. Comparison of the Efficacy of SFP with the Reported Catalysts for the Synthesis of 2-Amino-4H-chromenes

Catalyst and conditions	Time (min)	Yield (%)	Ref.
SFP (5 mol%), Solvent-free, 70 °C	20	97	Our work
SFP (2.5 mol%), Solvent-free, MW (540 W)	1.5	97	Our work
Methanesulfonic acid (100 mol%), Reflux in CH ₃ CN	240	90	[15]
Nano MgO (62 mol%), Reflux in CH ₃ OH	60	96	[17]
Nano Fe ₃ O ₄ -guanidine, PEG/H ₂ O (1/1), r.t.	20	90	[18]
<i>p</i> -Toluenesulfonic acid (17 mol%), Reflux in CH ₃ CN	240	90	[21]
K ₃ PO ₄ ·3H ₂ O (10 mol%), Solvent-free, 100 °C	60	77	[24]
Cetyltrimethylammonium bromide (10 mol%), H ₂ O, Ultrasound, r.t.	150	91	[34]
3-Butyl-1-methylimidazolium hexafluorophosphate (solvent and catalyst), 80 °C	120	81	[35]

Examination of Catalytic Activity of SFP to Promote the Synthesis of 2-Amino-4*H*-chromenes

After characterization of SFP, we decided to examine its catalytic activity to promote a useful organic transformation, *i.e.* the synthesis of 2-amino-4*H*-chromene derivatives. To this end, as a model reaction, the solventless condensation of 3-nitrobenzaldehyde (1 mmol) with malononitrile (1 mmol) and 1-naphthol (1 mmol) (Scheme 2) was studied in the presence of different amounts of SFP at various temperatures; the related results are summarized in Fig. 3. As the data in this figure show, the best results are observed when 5 mol% of SFP is used at 70 °C (entry 3). Increasing the amount of SFP and the temperature did not lead to the better results.

Optimizing the reaction, various arylaldehydes were reacted with malononitrile and 1-naphthol in the presence of SFP; the corresponding results are shown in Fig. 4. As clearly shown in this figure, SFP is highly efficient for the preparation of 2-amino-4*H*-chromenes; all functional groups on the arylaldehydes including electron-withdrawing substituent (NO₂), halogen (Cl) and electron-releasing substituent (OCH₃) afforded the respective products in high yields and short reaction times.

Considering the high importance of microwave-assisted synthesis, the synthesis of 2-amino-4*H*-chromenes was also studied under microwave conditions. For this purpose, at first, the reaction of 3-nitrobenzaldehyde (1 mmol), malononitrile (1 mmol) and 1-naphthol (1 mmol) (Scheme 2) was examined in the presence of different amounts of SFP at different microwave powers. The results showed that the best amount of the catalyst and MW power were 2.5 mol% and 540 W, correspondingly. After optimization the reaction conditions under microwave irradiation, the reaction was checked using different arylaldehydes, malononitrile and 1-naphthol in which all reactions proceeded efficiently, and gave the desired products in high yields and short reaction times (Fig. 4).

In another research, recyclability of SFP was tested on the reaction of 3-nitrobenzaldehyde with malononitrile and 1-naphthol under thermal conditions. After completion of the reaction, and cooling the reaction mixture to room

temperature, the resulted solid was powdered, ethyl acetate was added to it, stirred for 1 min, and filtered to separate SFP (the products is soluble in ethyl acetate; however, SFP in insoluble in this solvent). The recycled catalyst was washed by ethyl acetate, dried, and used for the next run. The catalytic activity of SFP was restored for two times recycling. The results are summarized in Table 1.

To compare the efficacy of SFP with the reported catalysts for the synthesis of 2-amino-4*H*-chromenes, the results on the reaction of 3-nitrobenzaldehyde with malononitrile and 1-naphthol promoted by SFP and the previous catalysts, are tabulated in Table 2. As this table indicates, SFP is more efficient compared with the reported catalysts in terms of the yield, reaction time and/or conditions.

CONCLUSIONS

In summary, we have synthesized, identified and applied a novel catalyst namely SO₃H-functionalized phthalimide to promote a useful organic reaction, *i.e.* the preparation of 2-amino-4*H*-chromenes from arylaldehydes, malononitrile and 1-naphthol. The promising points for the presented methodology are high yields, efficiency, short reaction times, cleaner reaction profile, simplicity, ease of the catalyst preparation, reusability of the catalyst and good agreement with the green chemistry protocols.

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