Iranian Journal of Organic Chemistry Vol. 14, No. 1(2022) 3255-3263

One Pot, Three-Component Synthesis of 2-Amino-4H-Chromenes Catalyzed Using NCTDSS in Water

Azar Purkhosrow[a], Saghar Mowlazadeh Haghighi[b], Ali Khalafi-Nezhad[b], Somayeh Oftadehgan[a,*]

[a]*Department of Pharmacology, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran*
[b]*Department of Chemistry, College of Sciences, Shiraz University, Shiraz, Iran*

Received: November 2021; Revised: December 2021; Accepted: January 2022

Abstract: New derivatives of 2-amino-4*H*-chromenes were prepared using nano-TiO_2 on dodecyl-sulfated silica support (NCTDSS) as a new heterogeneous catalyst in water. The NTDSS catalyst was characterized using different techniques such as TEM, SEM, XRD, ICP, and FT-IR. The catalyst was successfully used for the synthesis of 2-amino-4H-chromenes condensation in water as a green solvent. The high catalytic activity of this catalyst in aqueous medium can be due to the formation of colloidal particles on the surface of the NTDSS catalyst due to the DS parts bonded to the silica surface which acts as a surfactant. In this study, it seems that accelerating the reaction rate in aqueous media is effective due to the production of emulsion droplets containing nano TiO2 on the surface of the catalyst as a reaction reactor. The catalyst was produced by the reaction between sodium dodecyl sulfate (SDS) and silica chloride (SC) and then the addition of $TiCl_4$.

Keywords: Chromene, TiO_2 nanoparticles, Heterogeneous catalyst, Green solvent, Surface area.

Introduction

Chromenes are very important heterocyclic compounds, which frequently exhibit a variety of biological activities [1, 2]. Chromene and their derivatives are known compounds that have biological properties such as antimicrobial, antifungal, antioxidant, antileishmanial, antitumor, hypotensive, antiproliferation, local anesthetic, antiallergenic, central nervous system (CNS) activities and effects as well as treatment of Alzheimer's disease and Schizophrenia disorder. Fused chromene ring systems have platelet antiaggregating, local anesthetic and antihistaminic activities. They also exhibit antidepressant effects, inhibitory effect on influenza virus sialidases, DNA breaking activities, mutagenicity, antiviral activities and act as sex pheromone homologes [3].

*Corresponding author: Tel/Fax: 0098-71-32307591, E-mail: somayeh.oftadegan@gmail.com

Chromenes are important intermediates in the synthesis of many natural products and medicinal agents including flavonoids, coumarin, and derivatives of these compounds [4]. In addition, functional chromones have played an increasing role in synthetic approaches to promising compounds in medicinal chemistry in recent years [5, 6].

Between these compounds, 2-amino-4H-chromene-3-carbonitrile derivatives find applications as pigments and potential biodegradable agrochemicals. Due to their usefulness, the synthesis of these compounds has attracted a lot of interest. Most recently, asymmetric syntheses of some of these 2-amino-4H-Pyran-3-carbonitrile derivatives have also been reported [7, 8]. Moreover, the synthesis of partially saturated 2-amino-4H-chromene-3-carbonitrile derivatives has also been introduced [9-14]. The cyclization reaction between 1,3-dicarbonyl compounds and benzylidene malononitriles in the presence of a suitable base gives 2-amino-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitriles, which have also been demonstrated to

have biological activities [15]. Owing to the wide applications and significance of 2-amino-4H-chromenes in organic synthesis and pharmacology, there is considerable interest in the synthesis of these compounds.

During the recent years, there are several reporting methods to synthesize of 2-amino-4H-chromene derivatives. The best method for synthesis of these compounds involves the three component condensation of malonitrile, aldehyde, and a phenol or naphthol derivatives [16] reagents such as acetyl tri-methylammonium chloride [17], basic alumina [18], nanosized MgO [19] and K_2CO_3 [20] have also been used for this transformation. However, a previously reported articles on the synthesis of 2-amino-4H-chromium requires long reaction times, reagents in stoichiometric amounts, toxic solvents, and mild yields. The development of processes that are facile to carry out in the laboratory without recourse to inert atmosphere or limited solvents especially toxic organic solvents is an important goal in modern synthetic methodology. Therefore, the quest for cheap, environmentally friendly catalysts and mild reaction conditions is still a major challenge [21]. We used NCTDSS (nano-TiO2 on dodecyl-sulfated silica support) as catalysts [22], its catalytic activity is expected to enhance not only because of their increased surface area, but also because of the changes of surface properties. Herein we wish to report a novel procedure for the synthesis of 2-amino-4H-chromenes by a multicomponent condensation of an aldehyde, malononitrile and phenols in water as a green solvent in the presence of NCTDSS as catalyst.

Results and discussion

The synthesis of 2-amino-4H-chromenes in aqueous media is rapidly gaining importance in view of the fact that the use of many toxic and volatile organic solvents. It is highly desirable to develop environmentally benign processes that can be conducted in aqueous media. As we mentioned in previous paper [22], NCTDSS based on Nano TiO_2 is enabled by the use of water as a solvent for organic reactions. For this purpose, sodium dodecyl sulfate (SDS) was reacted with silica chloride (SC), to generate dodecyl sulfated silica (DSS) substrate. Then, addition of $TiCl_4$ to a water solution of DSS substrate, resulted the generation of nanocrystalline TiO_2 on this substrate.

The NCTDSS catalyst was characterized using different techniques such as, scanning electron microscopy (SEM), powder X-ray diffraction (XRD), energy dispersive X-ray spectra (EDX), FT-IR spectroscopy and inductively coupled plasma (ICP) analysis. SEM image of the NCTDSS catalyst shows that the nano TiO_2 particles possess almost cubic morphology with relatively good monodispersity (Figure **1**).

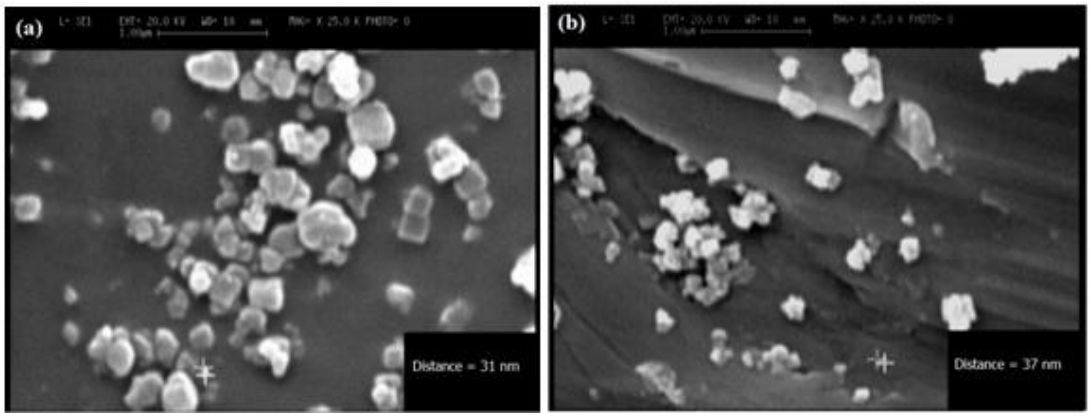


Figure 1. The SEM Image of NCTDSS Catalyst

The average diameter of the TiO2 nanoparticles was ~37 nm. The histogram was proposed according to the results obtained from the SEM image and revealed the size distributions of TiO2 nanoparticles (Figure **1**). The XRD pattern of the NCTDSS catalyst also shows that we have TiO_2 nanoparticles on DSS substrate [Figure **2a**]. The peaks are indexed as the (110), (200), (211) (118) and (220) planes of the TiO2 nanoparticle. TheEDX spectrum was also indicated the presence of Ti in NCTDSS catalyst. The spectrum also shows other

elements such as C, O, S and Si which are exist in the DSS substrate [Figure **2b**][23].

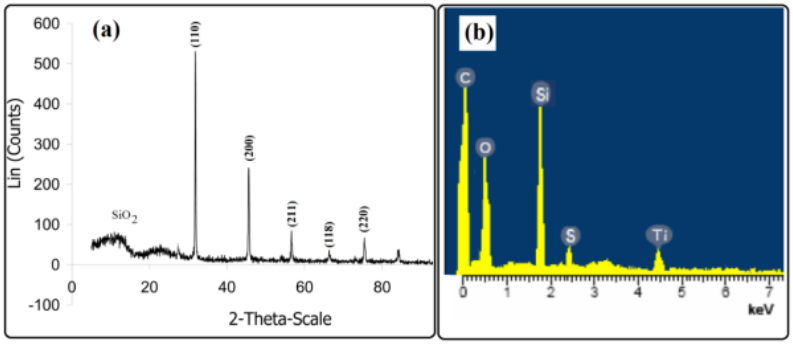


Figure 2. a) The XRD Spectrum of the NCTDSS Catalyst. b) EDX Spectrum of NCTDSS Catalyst

Also, to confirm the TiO_2 content of catalyst it was treated with concentrated HCl and HNO3 to digest the TiO_2 species and then analyzed by ICP analysis. The TiO_2 content was determined to be 73.1 ppm (73.1 mg/L) which was equal to 7.31% w/w. In this study, FT-IR spectroscopy was used as an applicable technique for further characterization of NCTDSS catalyst. In accordance with the FT-IR spectra, the peaks positioned at ~447 and ~470 cm^{-1} are related to the formation of TiO2 nanoparticles [24]. On the basis of the literature, the absorbance bands related to the Ti-O stretching and Ti-O-Ti bending in the structure of TiO2 nanoparticles. The distinguish peaks at ~1635, 933 and 803 cm-1 are to confirm the presence of DS species in the structure of catalyst. Also, the peaks positioned at 933 and 802 cm-1 related to the stretching of the S=O bond [21].The band at 1635 cm-1, belongs to H-O-H bending during the adsorption of water molecules. Additionally, the strong peak at 3379 cm-1 is as a result of the stretching of silica -OH groups caused through the adsorption of H2O molecules. The weak bands at 2924 and 2862 cm-1 is due to the stretching vibration of C–H and C–C bonds (Figure **3**). The reaction between naphthalene-1,6-diol, malonitrile, and 4-chlorobenzaldehyde was selected as simple model reaction to obtain optimum conditions was shown in Table **1**. According to Table **2**, NCTDSS displayed high activity in this reaction. Presumably, the reaction involves the ortho C-alkylation of α-naphthol by the reaction with electrophilic C=C double bond and then, nucleophilic addition of the phenolic OH group to the CN moiety, that producing the final 2-amino-4H-chromene, requires the intervention of the catalyst. As indicated in the Table **2**, wide range of aromatic aldehydes bearing both, electron-donating and electron-withdrawing substituents afforded the corresponding 2-amino-4H-chromenes in good yields. In all cases, the obtained product was purified by recrystallization from ethanol or plate chromatography. The first step in this multicomponent condensation is the Knoevenagel condensation of an aldehyde and malononitrile to produce the corresponding aryl methylene malononitrile. The use of naphthalenediols attracted our attention because the reactions of these compounds with aromatic aldehydes and malonitrile can afford various naphthopyrans, which are of interest for further investigation, and also to our knowledge, the synthesis aspect of such naphthopyrans was only partially exploited [25-27]. Herein, we chose various naphthalenediols. As described in Table **2**, we found that the reaction of 2,3, 1,5- and 1,6-naphthalenediols with 4-chlorobenzaldehyde and malonitrile afforded only benzochromene, regardless of the substrates ratio (1:1:1) (Table **2**, entries **1o-1q**). However, the addition of double amount of 4-chlorobenzaldehyde and malonitrile to 2,7-naphthalenediols yielded benzochromene (Table **2**, entry 1y). We couldn't find any logical reason for formation of products, but it might occur because of formation of center symmetry. It has been shown that 1,6-naphthalenediol reacted with the 4-chlorobenzaldehyde and malonitrile in a molar ratio of 1:2:2 or 1:1:1 to give regioselectively the benzochromene (Table **2**, entry 1q). The ^{1}H-NMR and ^{13}C-NMR spectrum are in good agreement with this structure. To assess the efficiency of NCTDSS as catalyst in inducing these reactions, the reaction of

inactivated phenol, 4-chloro benzaldehyde and malonitrile was also studied. However in this case, phenolreacted smoothly in the presence of NCTDSS to afford the corresponding 2-amino-4H-chromene in moderate yield (Table **2**, entry 1m). Structures of all compounds were suggested for the reaction product based on analytical data and NMR spectra. All the compounds were synthesized as stable colorless to yellowish powders.

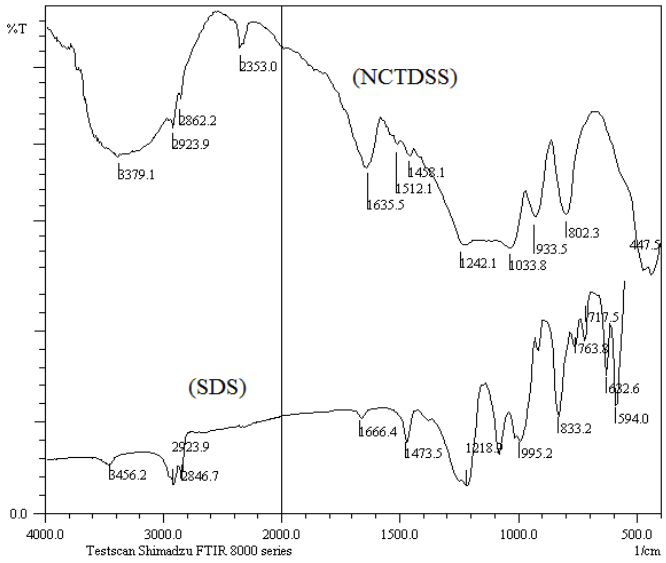
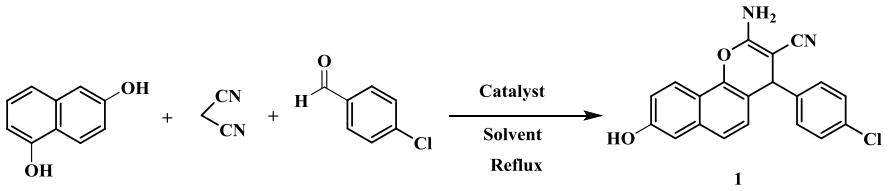


Figure 3. Comparison between the FT-IR Spectra of SDS and NCTDSS Catalyst.

Table 1. One-Pot, Three-Component Condensation Reaction of Naphthalene-1,6-diol, Malonitrile, and 4-Chlorobenzaldehyde in Various Reaction Conditions.



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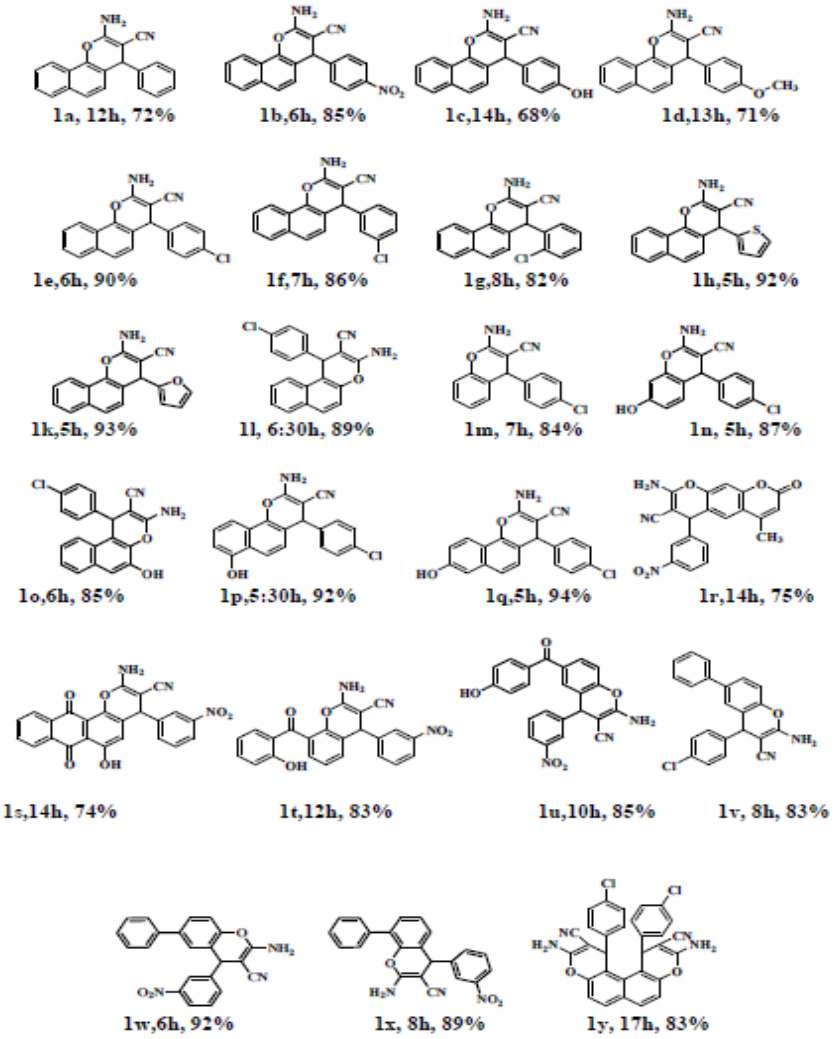
Entry	Catalyst	Solvent	Time (h)	Yield (%)[b]
1	-	H_2O	24	0
2	DABCO	Toluene	24	37
3	DBU	Toluene	24	22
4	K_2CO_3	Toluene	24	15
5	TiO_2	H_2O	24	38
6	Nano-TiO_2	H_2O	24	55
7	**NCTDSS**	**H_2O**	**5**	**94**
8	NCTDSS	EtOH	8	80
9	NCTDSS	Toluene	24	72
10	NCTDSS	H_2O	5	94[c]
11	NCTDSS	H_2O	8	68[d]
12	NCTDSS	H_2O	8	63[e]

[a] Reaction condition: naphthalene-1,6-diol (1 mmol), malononitrile(1 mmol), 4-chloro benzaldehyde (1 mmol), NCTDSS (7.5 mol%) and solvent (5 mL). b Isolated yield. [c] Catalyst: 10 mol%. [d] Catalyst:6 mol%. e Catalyst: 5 mol%.

Table 2. One Pot, Three-Component Condensation of Various Aromatic Aldehydes (1 mmol) with Malonitrile (1 mmol), Phenols (1 mmol) and Catalyst (7.5 mol%) at 100°C in Water.



Conclusion

In conclusion NCTDSS can serve as an efficient catalyst for the synthesis of 2-amino-4H-chromenes as biologically and pharmacologically active compounds. In addition various naphthalenediols can be reacted with aldehydes and malonitrile to produce various naphthopyranes in comparision of other catalysts. Finally, this procedure offers several advantages such as using water as a green an economical solvent, simple reaction set up, easy work up and crystallization of products and good yields.

Experimental

Chemicals were purchased from Fluka and Aldrich chemical companies. For recorded ^{1}H NMR and ^{13}C NMR spectra we used Brucker (250 MHz) Avanc DRX in pure deuterated DMSO-d6 solvent with tetramethylsilane (TMS) as internal standards. Mass spectra were recorded on a FINNIGAN-MAT 8430 mass spectrometer operating at 70 eV. Melting points were determined in open capillary tubes in a Barnstead Electrothermal 9100 BZ circulating oil melting point apparatus. The reaction monitoring was 20 accomplished by thin layer chromatography (TLC) on silica gel Poly Gram SILG/UV254 plates.

General Procedure for Synthesis of 2-Amino-4*H*-Chromenes over NCTDSS

An aromatic aldehyde (1 mmol) was added to a

mixture of NCTDSS (0.075 g, 7.5 mol%), malonitrile (1 mmol) and naphthols or phenols (1 mmol) in 5 mL H_2O. The mixture was heated in an oil bath at 100 ˚C and stirred with a magnetic stirrer. The progress of the reaction was monitored by TLC. After purification by recrystalization (ethyl acetate/*n*-hexane 10:90) or plate chromatography (ethyl acetate/*n*-hexane 20:80) 2-amino-4*H*-chromeneswere obtained.

The spectral data for synthesized compounds

2-Amino-4-phenyl-4-*H*-benzo[*h*]chromene-3-carbonitrile (1a).

Yellow solid. M.p. 200-203 ˚C; Lit.M.p. 210 ˚C [i]. IR (KBr, cm^{-1}): 3420(m), 3310(w), 2201(s), 1650(s).^{1}H-NMR (250 MHz, DMSO-d_6) δ (ppm): 4.72 (s, 2H), 4.86 (s, 1H), 7.00 (d, *J* = 7.5 Hz, 1H), 7.23-7.29 (m, 6H), 7.48-7.53 (m, 2H), 7.76 (d, *J* = 7.5 Hz, 1H), 8.15 (d, *J* = 7.5 Hz, 1H). ^{13}C-NMR (62.9 MHz, DMSO-d_6) δ (ppm): 38.40, 56.19, 107.94, 117.87, 118.25, 120.55, 121.89, 122.69, 123.83, 124.47, 126.17, 126.72, 127.29, 127.60, 128.64, 132.62, 142.67, 145.63, 160.11. Anal. Calcd. for $C_{20}H_{14}N_2O$ (298.11): C 80.52; H 4.73; N 9.39, found: C 80.48; H 4.79; N 9.46.

2-Amino-4-(4-nitrophenyl)-4-*H*-benzo[*h*]chromene-3-carbonitrile (1b).

Yellow solid. M.p. 240-242 ˚C; Lit.M.p. 238-239 ˚C [143]. IR (KBr, cm^{-1}): 3460(br), 3359(w), 1658(s), 2187(s), 1512(m), 1342(m). ^{1}H-NMR (250 MHz, DMSO-d_6,)δ (ppm): 4.80 (s, 2H), 4.94 (s, 1H), 6.86 (dd, *J* = 7.5 Hz, *J* = 5 Hz, 1H),7.17 (d, *J* = 5 Hz, 1H), 7.32-7.35 (m, 3H), 7.46-7.57 (m, 2H), 7.72-7.76 (m, 1H), 8.10-8.24 (m, 2H). ^{13}C-NMR (62.9 MHz, DMSO-d_6) δ (ppm): 55.12, 116.53, 120.12, 120.69, 122.68, 124.00, 124.15, 125.85, 126.77, 126.97, 127.66, 128.96, 132.83, 142.87, 146.42, 152.90, 160.27. Anal. Calcd. for $C_{20}H_{13}N_3O_3$ (343.1): C 69.96; H 3.82; N 12.24, found: C 69.89; H 3.87; N 12.19.

2-Amino-4-(4-hydroxyphenyl)-4-*H*-benzo[*h*] chromene-3-carbonitrile (1c).

Yellow solid, M.p. 246-248 ˚C. IR (KBr, cm^{-1}): 3479(w), 3344(w), 3309(br), 2198(s),1662(s). ^{1}H-NMR (250 MHz, DMSO-d_6)δ (ppm): 4.74 (s, 1H), 6.65-670 (m, 2H), 6.99-7.09 (m, 5H), 7.53-7.62 (m, 3H), 7.86 (t, *J* = 7.5 Hz, 1H), 8.20 (d, J = 7.5 Hz, 1H), 9.32 (s, 1H).^{13}C-NMR (62.9 MHz, DMSO-d_6)δ (ppm): 37.99, 56.64, 115.28, 118.40, 120.58, 122.69, 123.68, 126.28, 126.53, 127.59, 128.61, 132.52, 136.11, 142.47, 156.21, 159.88. Anal. Calcd. for $C_{20}H_{14}N_2O_2$ (314.11): C 76.42; H 4.49; N 8.91, found: C 76.37; H 4.55; N 8.98.

2-Amino-4-(4-methoxyphenyl)-4-*H*-benzo[*h*] chromene-3-carbonitrile (1d).

Yellow solid. M.p. 189-191 ˚C. IR (KBr, cm^{-1}): 3419(br), 3300(m), 2192(s), 1662(s). ^{1}H-NMR (250 MHz, DMSO-d_6)δ (ppm): 3.68 (s, 3H), 4.81 (s, 1H), 6.83-7.25 (m, 7H), 7.51-7.68 (m, 3H), 7.84 (d, *J* = 7.5 Hz, 1H), 8.19 (d, *J* = 7.5 Hz, 1H). ^{13}C-NMR (62.9 MHz, DMSO-d_6) δ (ppm): 38.27, 54.96, 56.48, 113.98, 118.12, 120.52, 120.63, 122.65, 123.78, 126.19, 126.61, 127.59, 128.65, 132.55, 137.75, 142.48, 158.09, 159.94. Anal. Calcd. for $C_{21}H_{16}N_2O_2$ (328.12): C 76.81; H 4.91; N 8.53, found: C 76.76; H 4.98; N 8.48.

2-Amino-4-(4-chlorophenyl)-4-*H*-benzo[*h*] chromene-3-carbonitrile (1e).

Yellow solid. M.p. 230-233 ˚C; Lit. M.p. 232-233 ˚C [143].IR (KBr, cm^{-1}): 3331(m), 2191(s),1668(s). ^{1}H-NMR (250 MHz, DMSO-d_6)δ (ppm): 4.71 (s, 2H), 4.79 (s, 1H), 6.90 (d, *J* = 7.5 Hz, 1H), 7.08-7.23 (m, 4H), 7.43-7.51 (m, 3H), 7.71 (d, *J* = 7.5 Hz, 1H), 8.09 (d, *J* = 7.5 Hz, 1H). ^{13}C-NMR (62.9 MHz, DMSO-d_6)δ (ppm): 55.79, 117.33, 120.30, 120.65, 122.67, 123.95, 126.67, 126.81, 127.63, 128.63, 129.51, 131.49, 132.69, 142.69, 144.59, 160.10. Anal. Calcd. for $C_{20}H_{13}ClN_2O$ (332.07): C 72.18; H 3.94; N 8.42, found: C 72.10; H 4.02; N 8.38.

2-Amino-4-(3-chlorophenyl)-4-*H*-benzo[*h*] chromene-3-carbonitrile (1f).

Yellow solid, M.p. 210-213 ˚C. IR (KBr, cm^{-1}): 3479(m), 3332(m), 2198(s), 1662(s). ^{1}H-NMR (250 MHz, DMSO-d_6) δ (ppm): 4.73 (s, 2H), 4.78 (s, 1H), 6.92 (d, *J* = 7.5 Hz, 1H), 7.10-7.18 (m, 4H), 7.44-7.52 (m, 3H), 7.74 (t, *J* = 7.5 Hz, 1H), 8.52 (d, *J* = 8.09 Hz, 1H). ^{13}C-NMR (62.9 MHz, DMSO-d_6)δ (ppm): 165.47, 153.33, 147.97, 138.46, 137.97, 135.91, 132.90, 132.59, 132.19, 132.10, 131.95, 131.69, 131.21, 129.27, 127.91, 125.92, 125.53, 122.38, 160.81. Anal. Calcd. for $C_{20}H_{13}ClN_2O$ (332.07): C 72.18; H 3.94; N 8.42, found: C 72.12; H 4.03; N 8.39.

2-Amino-4-(2-chlorophenyl)-4-*H*-benzo[*h*] chromene-3-carbonitrile (1g).

Yellow solid, M.p. 247-249 ˚C. IR (KBr, cm^{-1}): 3479(w), 3332(w), 2198(s), 1662(s). ^{1}H-NMR (250 MHz, DMSO-d_6)δ (ppm): 5.38 (s, 1H), 6.96 (d, *J* = 7.5 Hz, 1H), 7.22 (m, 5H), 7.42 (m, 1H), 7.59 (m, 3H), 7.85 (d, *J* = 7.65 Hz, 1H), 8.22 (d, *J* = 7.96 Hz, 1H).^{13}C-NMR (62.9 MHz, DMSO-d_6)δ (ppm): 55.56, 117.12, 120.27, 120.67, 122.66, 124.02, 125.96,

126.44, 126.70, 126.85, 126.94, 127.33, 127.64, 130.66, 132.72, 133.21, 142.71, 148.08, 160.22. Anal. Calcd. for $C_{20}H_{13}ClN_2O$ (332.07): C 72.18; H 3.94; N 8.42, found: C 72.15; H 4.01; N 8.40.

2-Amino-4-(thiophen-2-yl)-4-*H*-benzo[*h*]chromene-3-carbonitrile (1h)

Yellow solid, M.p. 185-187 °C. IR (KBr, cm^{-1}): 3440(w), 3328(w), 2194(s), 1670(s). ^{1}H-NMR (250 MHz, DMSO-d_6)δ (ppm): 4.99 (s, 1H), 6.88 (m, 1H), 7.13-7.57 (m, 8H), 7.85 (m, 1H), 8.19 (m, 1H). ^{13}C-NMR (62.9 MHz, DMSO-d_6)δ (ppm): 36.03, 55.78, 117.60, 120.56, 120.63, 121.40, 122.69, 123.81, 126.04, 126.59, 126.69, 126.83, 126.94, 127.59, 132.64, 142.60, 146.22, 160.26. Anal. Calcd. for $C_{20}H_{13}ClN_2O$ (304.07): C 71.03; H 3.97; N 9.20, found: C 71.00; H 4.05; N 9.14.

2-Amino-4-(furan-2-yl)-4-*H*-benzo[*h*]chromene-3-carbonitrile(1k)

Yellow solid, M.p. 160-162 °C. IR (KBr, cm^{-1}): 3440(m), 3328(m), 2202(s), 1658(s). ^{1}H-NMR (250 MHz, DMSO-d_6)δ (ppm): 5.10 (s, 1H), 6.23-6.43 (m, 2H), 7.27-7.36 (m, 3H), 7.49-7.72 (m, 4H), 7.94 (d, *J* = 7.5 Hz, 1H), 8.28 (d, *J* = 7.5 Hz, 1H).^{13}C-NMR (62.9 MHz, DMSO-d_6)δ (ppm): 34.57, 53.17, 106.08, 110.36, 115.37, 120.21, 120.56, 122.69, 123.81, 125.74, 126.63, 126.80, 127.63, 132.82, 142.64, 143.09, 156.27, 160.80. Anal. Calcd. for $C_{18}H_{12}ClN_2O_2$ (288.09): C 74.99; H 4.20; N 9.72, found: C 74.93; H 4.26; N 9.66.

3-Amino-1-(4chlorophenyl)-1-*H*-benzo[*f*]chromene-2-carbonitrile (1l)

Yellow solid, M.p. 200-202 °C. IR (KBr, cm^{-1}): 3417(w), 3330(m), 2192(s), 1645(s). ^{1}H-NMR (250 MHz, DMSO-d_6)δ (ppm): 5.41 (s, 1H), 7.09 (s, 2H), 7.24-7.53 (m, 7H), 7.84-8.02 (m, 3H).^{13}C-NMR (62.9 MHz, DMSO-d_6)δ (ppm): 57.34, 115.08, 116.73, 120.28, 123.48, 124.95, 127.12, 128.45, 128.64, 128.78, 129.64, 129.98, 130.76, 131.11, 144.62, 146.74, 159.65. Anal. Calcd. for $C_{20}H_{13}ClN_2O$(332.07): C 72.18; H 3.94; N 8.42, found: C 72.13; H 4.00; N 8.37.

2-Amino-4-(4-chlorophenyl)-5-hydroxychromane-3-carbonitrile (1m)

Yellow solid. IR (KBr, cm^{-1}): 3350(s), 2192(s), 1610(s).

2-Amino-4-(4-chlorophenyl)-5-hydroxychromane-3-carbonitrile (1n)

Yellow solid, M.p. 169-171 °C. IR (KBr, cm^{-1}): 3467(w), 3342(m), 3238 (br), 2192 (s). ^{1}H-NMR (250 MHz, DMSO-d_6) δ (ppm): 4.64 (s, 1H), 6.38-6.49 (m, 2H), 6.74 (d, *J* = 10 Hz, 1H), 6.88 (s, 2H), 7.14-7.36 (m, 4H), 9.70 (s, 1H). ^{13}C-NMR (62.9 MHz, DMSO-d_6) δ (ppm): 55.81, 55.94, 102.21, 112.41, 113.18, 121.41, 128.51, 129.16, 129.85, 131.26, 145.09,148.65, 156.87, 160.15. Anal Calcd for $C_{16}H_{11}ClN_2O_2$ (298.08): C 64.33; H 3.71; N 9.38, found: C 64.29; H 3.76; N 9.33.

3-Amino-1-(4-chlorophenyl)-5-hydroxy-1-*H*-benzo[*f*]chromene-2-carbonitrile (1o)

Yellow solid, M.p. 213-215 °C. IR (KBr, cm^{-1}): 3475(m), 3359(w), 3257(s), 2185(s), 1649(s). ^{1}H-NMR (250 MHz, DMSO-d_6) δ (ppm):5.29 (s, 1H), 6.93 (s, 2H), 7.16-7.32 (m, 6H), 7.63-7.71 (m, 2H), 7.93 (d, *J* = 10 Hz, 1H), 10.28 (s, 1H). ^{13}C-NMR (62.9 MHz, DMSO-d_6) δ (ppm):37.49, 57.35, 109.95, 116.68, 120.27, 123.26, 123.71, 124.07, 125.11, 126.40, 128.63, 128.68, 129.66, 130.03, 131.08, 131.20, 132.07, 139.01, 144.57, 160.05. Anal. Calcd. for $C_{20}H_{13}ClN_2O_2$ (348.78): C 68.87; H 3.76; N 8.03, found: C 68.83; H 3.74; N 8.05.MS: *m*/*z* (%) = 348 (M^+), 237 (100), 97 (7), 71 (12), 55 (21).

2-Amino-4- (4-chlorophenyl) -7-hydroxy -4*H*-benzo[*h*]chromene-3-carbonitrile (1p)

Yellow solid, M.p. 220-222 °C. IR (KBr, cm^{-1}): 3508-3208(br), 2200(s), 1660(s). ^{1}H-NMR (250 MHz, DMSO-d_6)δ (ppm): 4.89 (s, 1H), 6.89-7.00 (m, 2H), 7.13-7.39 (m, 7H), 7.63 (m, 1H), 7.77 (d, *J* = 10 Hz, 1H), 10.23 (s, 1H). ^{13}C-NMR (62.9 MHz, DMSO-d_6)δ (ppm): 55.73, 109.20, 111.34, 117.40, 118.30, 120.43, 124.07, 124.39, 127.41, 128.62, 129.40, 131.54, 142.54, 144.50, 153.02, 160.20. Anal. Calcd. for $C_{20}H_{13}ClN_2O_2$ (348.78): C 68.87; H 3.76; N 8.03, found: C 68.82; H 3.73; N 8.10.MS: *m*/*z* (%) =348 (M^+), 237 (100), 191 (13), 164 (12), 127 (5), 83 (5), 57 (10).

3-Amino-1-(4-chlorophenyl)-7-hydroxy-1*H*-benzo[*f*]chromene-2-carbonitrile (1q)

Yellow solid, M.p. 200-202 °C; Lit.M.p. 194-196 °C [143]. IR (KBr, cm^{-1}): 3500-3200(br), 1660(s), 2192(s). ^{1}H-NMR (250 MHz, DMSO-d_6) δ (ppm): 2.47 (s, 2H), 4.83 (s, 1H), 6.47-7.36 (m, 9H), 9.93 (s, 1H). ^{13}C-NMR (62.9 MHz, DMSO-d_6) δ (ppm):55.93, 108.95, 116.94, 118.88, 120.41, 122.40, 126.30, 127.90, 128.57, 129.45, 131.38, 134.60, 142.93, 144.83, 156.11, 160.12. Anal. Calcd. for $C_{20}H_{13}ClN_2O_2$ (348.78): C 68.87; H 3.76; N 8.03, found: C 68.82; H

3.75; N 8.02. MS: *m*/*z* (%) = 348 (M^+), 319 (15), 281 (7), 255 (10), 237 (100), 211 (6), 189 (7), 167 (6), 149 (9), 129 (4), 111 (10), 83 (45), 55 (87).

3-Amino-1-(3-nitrophenyl)-4-methyl-2*H*-chromene-2-one-carbonitrile(1r)

Orange solid, M.p. 150-153 °C. IR (KBr, cm^{-1}): 3315(m), 2189(s), 1640(s). ^{1}H-NMR (250 MHz, DMSO-d_6)δ (ppm): 1.07 (s, 3H), 2.27 (s, 2H), 4.04 (s, 1H), 5.37 (s, 1H), 6.64-6.79 (m, 2H), 7.12-7.19 (m, 4H). ^{13}C-NMR (62.9 MHz, DMSO-d_6)δ (ppm): 19.66, 30.68, 60.02, 84.87, 112.55, 113.60, 114.93, 124.75, 127.86, 128.68, 131.09, 131.96, 135.82, 142.04, 148.61, 143.14, 147.95, 159.21, 161.16, 176.98. Anal. Calcd. for $C_{20}H_{13}N_3O_5$ (375.33): C 64.00; H 3.49; N 11.20, found: C 63.94; H 3.43; N 11.26. MS: *m*/*z* (%) =375 (M^+), 361 (52), 319 (18), 255 (13), 211 (5), 189 (6), 167 (5), 149 (9), 129 (6), 111 (15), 83 (47), 55 (100).

2-Amino-7,12-dihydro-6-hydroxy-4-(3-nitrophenyl)-7,12-dioxo-4*H*-naphtho[2,3-h]chromene-3-carbonitrile (1s)

Orange solid, M.p. 173-175 °C. IR (KBr, cm^{-1}): 3400(br), 2160(s), 1625(s). ^{1}H-NMR (250 MHz, DMSO-d_6, DMSO-d_6)δ (ppm):2.47 (s, 2H), 5.45 (s, 1H), 7.37-8.27 (m, 9H), 12.64 (s, 1H). ^{13}C-NMR (62.9 MHz, DMSO-d_6)δ (ppm):38.08, 84.21, 96.79, 126.63, 129.30, 133.57, 135.04, 135.44, 137.84, 138.66, 139.51, 146.58, 152.68, 153.80, 154.84, 156.63, 156.81, 163.91, 164.61, 184.10. Anal. Calcd. for $C_{24}H_{13}N_3O_6$ (439.38): C 65.61; H 2.98; N 9.56, found: C 65.56; H 3.04; N 9.51.MS: *m*/*z* (%) = 439 (M^+), 413 (13), 309 (17), 255 (15), 149 (14), 129 (7), 111 (15), 83 (47), 57 (100).

3-Amino-1-(3-nitrophenyl)-2-hydroxyphenyl methanone chromene-2-carbonitrile (1t).

Yellow solid, M.p. 190-192 °C. IR (KBr, cm^{-1}): 3398(br), 2200(s), 1615(s). ^{1}H-NMR (250 MHz, DMSO-d_6)δ (ppm): 2.40 (s, 2H), 5.68 (s, 1H), 6.67 (s, 1H), 6.87-7.45 (m, 10H), 10.95 (s, 1H). ^{13}C-NMR (62.9 MHz, DMSO-d_6)δ (ppm): 22.55, 84.87, 108.74, 112.55, 113.60, 114.93, 116.48, 117.36, 120.29, 124.75, 127.86, 128.68, 131.09, 131.96, 132.37, 135.82, 142.61, 143.14, 147.95, 153.48, 159.21, 161.16, 192.98. Anal. Calcd. for $C_{23}H_{15}N_3O_5$ (413.10): C 66.83; H 3.66; N 10.16, found: C 66.78; H 3.71; N 10.11. MS: *m*/*z* (%) =413 (M^+), 387 (27), 293 (29.5), 215 (23.1), 186 (10.3), 121 (100), 93 (24.4), 65 (22.5).

3-Amino-1-(3-nitrophenyl)-4-hydroxyphenyl methanone chromene-2-carbonitrile (1u).

Yellow solid, M.p. 174-176 °C. IR (KBr, cm^{-1}): 3400(s), 2185(s), 1600(s). ^{1}H-NMR (250 MHz, DMSO-d_6) δ (ppm): 2.48 (s, 2H), 5.59 (s, 1H), 6.83 (d, *J* = 7.5 Hz, 1H), 7.55 (d, *J* = 7.5 Hz, 1H), 7.89 (t, *J* = 7.5 Hz, 1H), 8.28-8.48 (m, 8H), 10.27 (s, 1H). ^{13}C-NMR (62.9 MHz, DMSO-d_6)δ (ppm): 27.83, 84.87, 112.55, 113.60, 114.93, 124.75, 126.74, 127.77, 127.86, 128.86, 131.09, 131.96, 132.37, 135.82, 142.04, 142.61, 147.95, 159.21, 161.16, 181.31, 192.98. Anal. Calcd. for $C_{23}H_{15}N_3O_5$ (413.38): C 66.83; H 3.66; N 10.16, found: C 66.79; H 3.70; N 10.12. MS: *m*/*z* (%) = 413.38 (M^+), 215 (23.1), 121 (100), 93 (24.4), 65 (22.5).

2-Amino-4(-4-chlorophenyl) -6-phenyl-4H-chromene-3-carbonitrile (1v)

Yellow solid, M.p. 105-107 °C. IR (KBr, cm^{-1}): 3398(s), 2100(s), 1625(s).^{1}H-NMR (250 MHz, DMSO-d_6)δ (ppm): 2.53 (s, 2H), 5.13 (s, 1H), 6.81 (d, *J* = 7.5 Hz, 1H), 7.23-7.55 (m, 9H), 7.63 (t, *J* = 7.5 Hz, 1H), 7.9 (d, *J* = 7.5 Hz, 1H). ^{13}C-NMR (62.9 MHz, DMSO-d_6)δ (ppm): 27.34, 82.19, 112.94, 113.99, 115.65, 125.87, 126.28, 127.05, 128.72, 129.64, 130.88, 132.07, 138.98, 140.12, 154.00, 157.01, 160.03, 189.30. Anal Calcd for $C_{22}H_{15}ClN_2O$ (358.82): C 73.64; H 4.21; N 7.81, found: C 73.58; H 4.27; N 7.75. MS: *m*/*z* (%) = 358.82 (M^+), 326 (19.2), 237 (12), 129 (10.1), 111 (24.7), 83 (53.5), 57 (100).

2-Amino-4-(-3-nitrophenyl) -6-phenyl-4H-chromene-3-carbonitrile (1w).

Yellow solid, M.p. 111-113 °C. IR (KBr, cm^{-1}): 3401(s), 2112(s), 1630(s). ^{1}H-NMR (250 MHz, DMSO-d_6)δ (ppm): 2.48 (s, 2H), 5.24 (s, 1H), 6.79 (d, *J* = 7.5 Hz, 1H), 7.37-7.54 (m, 2H), 7.86 (t, *J* = 7.5 Hz, 1H), 8.28 (d, *J* = 7.5 Hz, 1H), 8.44-8.75 (m, 7H). ^{13}C-NMR (62.9 MHz, DMSO-d_6)δ (ppm): 31.36, 84.87, 112.55, 113.60, 115.63, 125.86, 126.28, 127.64, 127.86, 128.71, 130.84, 131.05, 131.10, 132.37, 134.85, 135.82, 140.12, 147.95, 159.21, 176.54. Anal. Calcd. for $C_{22}H_{15}N_3O_3$ (369.37): C 71.54; H 4.09; N 11.38, found: C 71.50; H 4.15; N 11.32.

2-Amino-4-(-3-nitrophenyl) -8-phenyl-4H-chromene -3-carbonitrile (1x).

Yellow solid, M.p. 120-123 °C. IR (KBr, cm^{-1}): 3411(s), 2193(s), 1610(s). ^{1}H-NMR (250 MHz, DMSO-d_6)δ (ppm): 2.48 (s, 2H), 5.23 (s, 1H), 7.62-8.34 (m, 12H). ^{13}C-NMR (62.9 MHz, DMSO-d_6)δ (ppm): 31.36, 84.87, 93.37, 112.55, 113.60, 115.63, 124.76, 125.86, 126.28, 127.64, 127.86, 128.71,

131.05, 131.10, 132.37, 135.82, 147.95, 157.02, 159.22, 179.35.

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