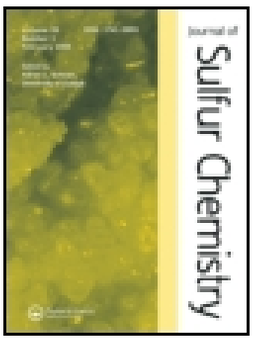

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Crown ether complex cation ionic liquids: synthesis and catalytic applications for the synthesis of tetrahydro-4*H*-chromene and 1,4-dihydropyridine derivatives

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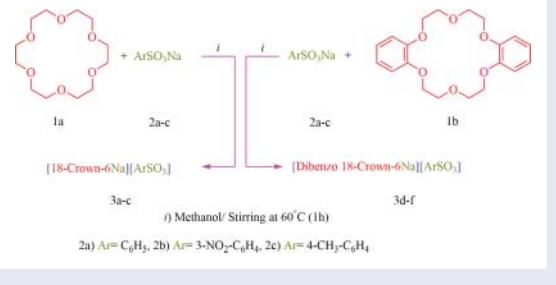
ABSTRACT

A series of crown ether complex cation ionic liquids (CECILs) are synthesized by crown ethers chelated with sodium benzenesulfonates, and used as a green and environmental catalyst, for the synthesis of tetrahydro-4*H*-chromene and 1,4-dihydropyridine derivatives by three-component reactions of aromatic aldehydes and malononitrile with cyclic β-dicarbonyls or cyclic β-enaminoketones respectively, in H_2O/EtOH (1:1), at the reflux condition. CECILs, as a green and environmental catalyst, can be easily obtained and are stable. Furthermore, high conversions, short reaction times, and cleaner reaction profiles are some of the advantages of this method.



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Crown ether complex cation ionic liquids; crown ethers; sodium benzenesulfonates; tetrahydro-4*H*-chromene; 1,4-dihydropyridine

1. Introduction

Ionic liquids (ILs) have attracted significant attention from research groups because of their unique properties and novel applications. ILs exhibit several properties such as low vapor pressure, recyclability, excellent thermal stability and desirable solvating properties [1]. ILs have attracted remarkable attention as new materials for various chemical applications. There are reports on ILs which consist of strong Lewis-acidic metal cations such as lithium ion and potassium ion coordinated by ether-ligands to decrease charge density [2,3]. ILs

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have been used in many organic reactions – for example, S_N2 process [4–8], hydrogenation, oxidation [9–12], three-component reactions [13,14], and carbon–carbon bond-forming reactions, such as Michael addition [15], Henry reaction [16], Knoevenagel condensation and Heck reaction [3,17].

Tetrahydro-4*H*-chromenes, due to their lucrative biological and pharmacological properties, are used as an important class of heterocyclic compounds in the pharmaceutical applications, such as anticancer [18], antimalarial [19], antileishmanial [20], antibacterial [21], antifungal [22], antianaphylactic [23], antiallergenic [24], diuretic [25] and hypotensive [26] agents.

Also, 1,4-dihydropyridines are an important class of compounds with a wide range of biological activities [27]. Due to being pharmacologically active and acting as antitumor [28], calcium channel blocker [29], antitubercular [30], analgesic [31], antithrombotic [32], anti-inflammatory [33], anticonvulsant agents [34], and they are of many interests.

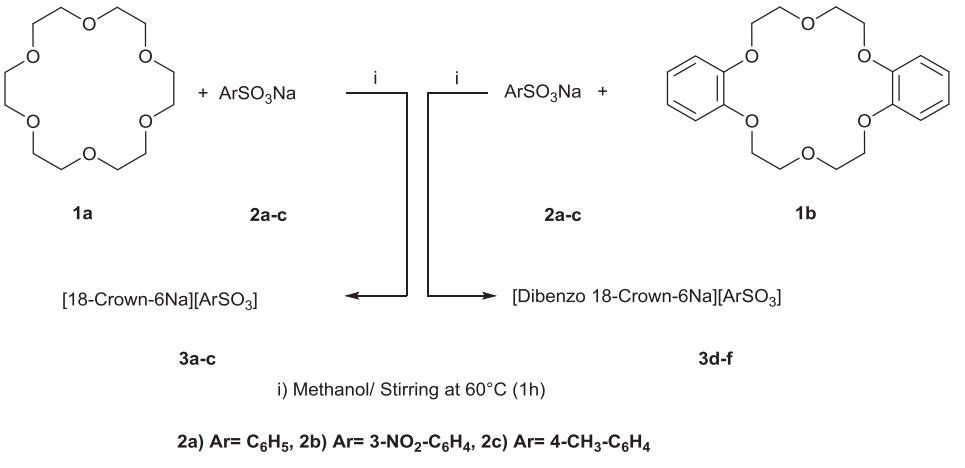
Applications of tetrahydro-4*H*-chromene and 1,4-dihydropyridine derivatives necessitate the advancement in environmental-friendly procedures to synthesize these compounds by three-component reactions of aromatic aldehydes and malononitrile with cyclic β-dicarbonyls or cyclic β-enaminoketones, respectively. There are various catalytic systems for the synthesis of tetrahydro-4*H*-chromene [35–44] and 1,4-dihydropyridine [45–47] derivatives by MCR, but these systems suffer from disadvantages such as the use of toxic organic solvents, costly catalysts, existence of transition metals, difficult work up, time-consuming reactions and low yield. Thus, a simple and green synthesis of tetrahydro-4*H*-chromenes and 1,4-dihydropyridines needs to be carried out without association of these catalytic systems.

Only a few reports are available on the synthesis of crown ether complex cation ionic liquids (CECILs), by crown ethers chelated with alkali metal cations [48–51]. Herein, we synthesize a series of CECILs (CECILs) (**3a–f**) by crown ethers (**1a, 1b**) chelated with sodium benzenesulfonates (**2a–c**), and used as a green and environmental catalyst, for the synthesis of tetrahydro-4*H*-chromene (**7a–v**) and 1,4-dihydropyridine (**10a–p**) derivatives by the three-component reaction of aromatic aldehydes (**4a–j**) and malononitrile (**5**) with cyclic β-dicarbonyls (**6a, b**) or cyclic β-enaminoketone (**9a–d**) respectively, in H_2O/EtOH (1:1), at reflux condition.

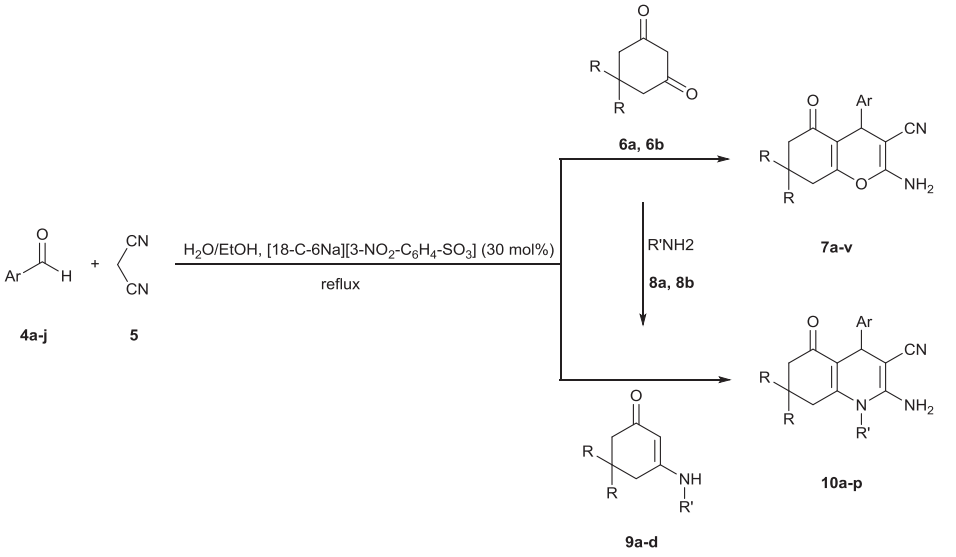
2. Results and discussion

Initially, the 18-crown-6 (**1a**) and sodium benzenesulfonate (**2a**) were mixed and dissolved in water; the desired 18-crown-6 complex cation ionic liquid (CECIL) (**3a**) was not obtained as a clear solution due to the poor solubility of 18-crown-6. Strangely, when the solvent was changed to methanol, a clear solution was obtained after stirring for 1 h at 60°C, and vacuum drying the desired CECIL (**3a**) to generate it in 100% yield. Then, we dissolved the crown ethers (**1a, 1b**) and sodium benzenesulfonates (**2a–c**) in methanol to generate our desirable CECILs (**3a–f**) (Scheme 1). CECILs are very soluble in water, readily soluble in polar solvents, such as methanol, ethanol and acetone, and insoluble in nonpolar solvents, such as alkanes, ethers and aromatic hydrocarbons.

Afterwards, in continuation of our previous works on environmental-friendly multicomponent reactions [52–54], we used CECILs, as a green and environmental catalyst, for



Scheme 1. Synthesis of CECILs (**3a–f**).



Scheme 2. Synthesis of tetrahydro-4*H*-chromene (**7a**–**v**) and 1,4-dihydropyridine (**10a–p**) derivatives.

the synthesis of tetrahydro-4*H*-chromene (**7a**–**v**) and 1,4-dihydropyridine (**10a**–**p**) derivatives by the three-component reaction of aromatic aldehydes (**4a**–**j**) and malononitrile (**5**) with cyclic β-dicarbonyls (**6a, b**) or cyclic β-enaminoketone (**9a**–**d**) respectively, in H_2O/EtOH (1:1), at reflux condition (Scheme 2).

To optimize the reaction conditions, a methodical study considering different variables affecting the reaction time and yield was carried out the three-component reaction of benzaldehyde **4a**, malononitrile **5** and 5,5-dimethylcyclohexane-1,3-dione **6a** in the presence of CECILs as catalysts for preparing compound 2-amino-7,7-dimethyl-5-oxo-4-phenyl-5,6,7,8-tetrahydro-4*H*-chromene-3-carbonitrile **7a** (Scheme 2). The results are shown in Table 1.

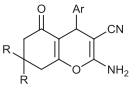
Table 1. Optimization of the model reaction between benzaldehyde **4a**, malononitrile **5** and 5,5-dimethylcyclohexane-1,3-dione **6a**.

Entry	Solvent	Catalyst	Catalyst (mol %)	Time (min)	Yield (%)
1	H_2O/EtOH	[18-C-6Na][C_6H_5-SO_3]	30	25	90
2	H_2O/EtOH	[18-C-6Na][3-NO_2-C_6H_4-SO_3]	30	20	92
3	H_2O/EtOH	[18-C-6Na][4-CH_3-C_6H_4-SO_3]	30	30	87
4	H_2O/EtOH	[Dibenzo 18-C-6Na][C_6H_5-SO_3]	30	35	88
5	H_2O/EtOH	[Dibenzo 18-C-6Na][3-NO_2-C_6H_4-SO_3]	30	25	89
6	H_2O/EtOH	[Dibenzo 18-C-6Na][4-CH_3-C_6H_4-SO_3]	30	40	85
7	H_2O/EtOH	[18-C-6Na][3-NO_2-C_6H_4-SO_3]	20	10	90
8	H_2O/EtOH	[18-C-6Na][3-NO_2-C_6H_4-SO_3]	40	20	92

We used CECILs (**3a**–**f**) in this reaction and the best results in terms of reaction time and yield of the desired product **7a** were obtained when the reaction was conducted in [18-C-6Na][3-NO_2-C_6H_4-SO_3] (Table 1, entries 1–6). We also optimized the quantity of catalysts. The best results were obtained when the reactions were carried out in the presence of 30 mol% [18-C-6Na][3-NO_2-C_6H_4-SO_3] (Table 1, entries 7, 8).

According to our collected data, we decided to apply this method for the synthesis of tetrahydro-4*H*-chromene (**7a**–**v**) and 1,4-dihydropyridine (**10a**–**p**) derivatives by the three-component reaction of aromatic aldehydes (**4a**–**j**) and malononitrile (**5**) with cyclic β-dicarbonyls (**6a, b**) or cyclic β-enaminoketone (**9a**–**d**), respectively, in H_2O/EtOH (1:1), at reflux condition (Scheme 2 and Tables 2 and 3).

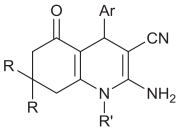
Table 2. Three-component reaction of aromatic aldehydes (**4a**–**j**), malononitrile (**5**) and dimedone (**6a**) or 1,3-cyclohexanedione (**6b**).



7a-v

Compd. No.	R	Ar	Time(min)	Yield (%)	M. P. observed (°C)	M. P. reported (°C)
7a	Me	C_6H_5	8	91	231–232	234–236 [35]
7b	Me	4-Cl-C_6H_4	7	92	215–217	216–218 [35]
7c	Me	2,4-$(Cl)_2$-C_6H_3	7	92	175–178	178–179 [37]
7d	Me	4-Br-C_6H_4	8	92	221–222	222–224 [35]
7e	Me	4-NO_2-C_6H_4	7	93	181–182	180–182 [35]
7f	Me	4-CH_3-C_6H_4	10	89	218–220	219–221 [35]
7g	Me	4-CH_3O-C_6H_4	10	88	200–202	201–203 [35]
7h	Me	4-OH-C_6H_4	12	85	225–228	226–228 [35]
7i	Me	Furan-2-yl	12	88	221–222	220–222 [35]
7j	Me	Thiophen-2-yl	13	87	227–229	226–228 [35]
7k	Me	Pyridin-3-yl	13	86	206–207	206–207 [43]
7l	H	C_6H_5	9	90	230–231	229–231 [37]
7m	H	4-Cl-C_6H_4	8	91	223–226	225–227 [37]
7n	H	2,4-$(Cl)_2$-C_6H_3	7	92	220–222	221–223 [37]
7o	H	4-Br-C_6H_4	8	91	248–250	248–250 [43]
7p	H	4-NO_2-C_6H_4	7	92	234–237	235–237 [37]
7q	H	4-CH_3-C_6H_4	12	89	223–225	224–226 [36]
7r	H	4-CH_3O-C_6H_4	12	87	189–191	190–192 [37]
7s	H	4-OH-C_6H_4	15	85	256–258	257–259 [36]
7t	H	Furan-2-yl	17	86	237–239	237–239 [43]
7u	H	Thiophen-2-yl	17	86	210–211	210–211 [43]
7v	H	Pyridin-3-yl	17	85	229–230	229–230 [43]

Table 3. Three-component reaction of aromatic aldehydes (**4a**–**f**), malononitrile (**5**) and cyclic enaminoketones (**9a**–**d**).



10a-p

Compd. No.	R	R′	Ar	Time (min)	Yield (%)	M. P. observed (°C)	M. P. reported (°C)
10a	Me	H	C_6H_5	15	89	262–264	265–267 [45]
10b	Me	H	4-CH_3O-C_6H_4	18	88	279–281	279–281 [46]
10c	Me	H	4-Br-C_6H_4	12	91	210 (dec.)	210 (dec.)[46]
10d	Me	H	Pyridin-3-yl	16	88	248–250	248–250 [54]
10e	Me	C_6H_5	C_6H_5	12	90	244–245	246–248 [45]
10f	Me	C_6H_5	4-CH_3-C_6H_4	15	90	243–245	243–245 [46]
10g	Me	C_6H_5	4-Br-C_6H_4	10	91	269–271	269–271 [46]
10h	Me	C_6H_5	Pyridin-3-yl	15	89	265–267	265–267 [54]
10i	H	H	C_6H_5	18	87	254 (dec.)	254 (dec.) [46]
10j	H	H	4-CH_3-C_6H_4	20	85	269–271	269–271 [46]
10k	H	H	4-Cl-C_6H_4	15	90	296–298	296–298 [46]
10l	H	H	Pyridin-3-yl	18	87	287–289	287–289 [54]
10m	H	C_6H_5	C_6H_5	15	89	110 (dec.)	110 (dec.) [46]
10n	H	C_6H_5	4-CH_3-C_6H_4	18	87	235 (dec.)	235 (dec.) [46]
10o	H	C_6H_5	4-Cl-C_6H_4	12	91	228–230	228–230 [46]
10p	H	C_6H_5	Pyridin-3-yl	17	88	237–238	237–238 [54]

3. Experimental section

3.1. General methods

Melting points were measured on an Electrothermal-9100 apparatus and are uncorrected. IR spectra were recorded on a Brucker FT-IR Tensor 27 infrared spectrophotometer. ^{1}H NMR spectra were recorded on a Brucker Avance III 400, 300 MHz spectrometer. ^{13}C NMR spectra were recorded on the same instruments at 75 MHz using tetramethylsilane as an internal standard. Elemental analyses were performed using a Heracus CHN-S/O-Rapid analyser.

3.2. General procedure for the synthesis of CECILs (3a–f)

The sodium benzenesulfonates (**2a**–**c**) (2 mmol) with crown ethers (**1a, 1b**) (2 mmol) in 15 mL methanol were stirred for 1 h at 60°C. Then methanol was removed under reduced pressure. The residue was vacuum dried to generate the desired CECIL in 100% yield.

[**18-C-6Na**][**C_6H_5-SO_3**] **(3a).** Liquid; ^{1}H NMR (300 MHz, D_2O) δ_{ppm}: 7.73 (d, 2H, J = 4 Hz, Ar), 7.49–7.43 (m, 3H, Ar), 3.53 (s, 24H, OCH_2); ^{13}C NMR (75 MHz, D_2O) δ_{ppm}: 142.63, 131.48, 128.97, 125.37, 69.33 (OCH_2). Anal. calcd. for $C_{18}H_{29}NaO_9S$: C, 48.64; H, 6.58; S, 7.21%. Found: C, 48.47; H, 6.41; S, 7.05%.

[**18-C-6Na**][**3-NO_2-C_6H_4-SO_3**] **(3b).** Yellow powder; mp 107–109°C; ^{1}H NMR (300 MHz, D_2O) δ_{ppm}: 8.48 (s, 1H, Ar), 8.28 (d, 1H, J = 4 Hz, Ar), 8.07 (d, 1H, J = 4 Hz, Ar), 7.67 (t, 1H, J = 4 Hz, Ar), 3.57 (s, 24H, OCH_2); ^{13}C NMR (75 MHz, D_2O) δ_{ppm}: 147.70, 144.36, 131.82, 130.58, 125.99, 120.64, 69.38 (OCH_2). Anal. calcd. for $C_{18}H_{28}NNaO_{11}S$: C, 44.17; H, 5.77; N, 2.86; S, 6.55%. Found: C, 43.99; H, 5.59; N, 2.69; S, 6.39%.

[**18-C-6Na**][**4-CH_3-C_6H_4-SO_3**] **(3c).** White powder; mp 79–81°C; ^{1}H NMR (300 MHz, D_2O) δ_{ppm}: 7.59 (d, 2H, J = 4 Hz, Ar), 7.25 (d, 2H, J = 4 Hz, Ar), 3.53 (s, 24H, OCH_2), 2.28 (s, 3H, CH_3); ^{13}C NMR (75 MHz, D_2O) δ_{ppm}: 142.26, 139.67, 129.42, 125.36, 69.35 (OCH_2), 20.50 (CH_3). Anal. calcd. for $C_{19}H_{31}NaO_9S$: C, 49.77; H, 6.82; S, 6.99%. Found: C, 49.58; H, 6.65; S, 6.82%.

[**Dibenzo 18-C-6Na**][**C_6H_5-SO_3**] **(3d).** White powder; mp > 300°C; ^{1}H NMR (300 MHz, DMSO-*d*6) δ_{ppm}: 7.69–6.90 (m, 13H, Ar), 4.09 (t, 8H, J = 3 Hz, OCH_2), 3.91 (t, 8H, J = 3 Hz, OCH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ_{ppm}: 148.82, 147.64, 128.91, 128.12, 126.01, 121.13, 111.65, 68.88 (OCH_2), 67.24 (OCH_2). Anal. calcd. for $C_{26}H_{29}NaO_9S$: C, 57.77; H, 5.41; S, 5.93%. Found: C, 57.59; H, 5.25; S, 5.76%.

[**Dibenzo 18-C-6Na**][**3-NO_2-C_6H_4-SO_3**] **(3e).** Yellow powder; mp > 300°C; ^{1}H NMR (300 MHz, DMSO-d_6) δ_{ppm}: 8.42 (s, 1H, Ar), 8.22 (d, 1H, J = 4 Hz, Ar), 8.09 (d, 1H, J = 4 Hz, Ar), 7.68 (t, 1H, J = 4 Hz, Ar), 6.99–6.89 (m, 8H, Ar), 4.10 (t, 8H, J = 3 Hz, OCH_2), 3.93 (t, 8H, J = 3 Hz, OCH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ_{ppm}: 150.41, 147.68, 147.60, 132.51, 130.30, 123.90, 121.11, 111.58, 68.87 (OCH_2), 67.20 (OCH_2). Anal. calcd. for $C_{26}H_{28}NNaO_{11}S$: C, 53.33; H, 4.82; N, 2.39; S, 5.48%. Found: C, 53.16; H, 4.65; N, 2.21; S, 5.31%.

[**Dibenzo 18-C-6Na**][**4-CH_3-C_6H_4-SO_3**] **(3f).** White powder; mp > 300°C; ^{1}H NMR (300 MHz, DMSO-*d*6) δ_{ppm}: 7.56 (d, 2H, J = 4 Hz, Ar), 7.14 (d, 2H, J = 4 Hz, Ar), 7.00–6.90 (m, 8H, Ar), 4.09 (t, 8H, J = 3 Hz, OCH_2), 3.92 (t, 8H, J = 3 Hz, OCH_2), 2.31 (s, 3H, CH_3); ^{13}C NMR (75 MHz, DMSO-*d*6) δ_{ppm}: 147.65, 146.20, 138.15, 128.54, 126.04, 121.12, 111.65, 68.88 (OCH_2), 67.25 (OCH_2), 21.28 (CH_3). Anal. calcd. for $C_{27}H_{31}NaO_9S$: C, 58.48; H, 5.63; S, 5.78%. Found: C, 58.30; H, 5.46; S, 5.61%.

3.2.1. General procedure for the preparation of tetrahydro-4H-chromene (7a–v) and 1,4-dihydropyridine (10a–p) derivatives

A mixture of aromatic aldehydes **4a**–**j** (2 mmol), malononitrile **5** (2 mmol), cyclic β-dicarbonyls **6a, b** or cyclic β-enaminoketones **9a**–**d** (2 mmol) and [18-C-6Na][3-NO_2-C_6H_4-SO_3] (30 mol%) in H_2O/EtOH (1:1) (10 mL) was refluxed for in the reported time in Tables 2 and 3 (the progress of the reaction was monitored by TLC and hexane/ethyl acetate was used as an eluent). After completion of the reaction, the reaction mixture was cooled, and the crude product was filtered and dried. The NMR spectra collected for **7i** and **7j** [35]; **7k**, **7t**, **7u** and **7v** [43]; **10b**, **10g**, **10k** and **10n** [46] are consistent with the previously reported NMR data for these compounds.

2-Amino-4-(furan-2-yl)-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4*H*-chromene-3-carbonitrile (7i). Yellow powder; IR (KBr, ν_{max}/cm^{-1}): 3408, 3328 (NH_2), 2192 (CN), 1680 (C−O), 1600, 1555 (C−C). ^{1}H NMR (400 MHz, DMSO-d_6) δ_{ppm}: 7.46 (d, $^3J_{HH}$ = 4 Hz, CH-Ar), 7.07 (s, 2H, NH_2), 6.30–6.04 (m, 2H, CH-Ar), 4.30 (s, 1H, CH), 2.47 (d, $^2J_{HH}$ = 8 Hz, CH), 2.40 (d, $^2J_{HH}$ = 8 Hz, CH), 2.27 (d, $^2J_{HH}$ = 8 Hz, CH), 2.15 (d, $^2J_{HH}$ = 8 Hz, CH), 1.03 (s, 3H, CH_3), 0.97 (s, 3H, CH_3).

2-Amino-7,7-dimethyl-5-oxo-4-(thiophen-2-yl)-5,6,7,8-tetrahydro-4*H*-chromene-3-carbonitrile (7j). White powder; IR (KBr, ν_{max}/cm^{-1}): 3392, 3328 (NH_2), 2192 (CN), 1673 (C−O), 1596, 1539 (C−C). ^{1}H NMR (400 MHz, DMSO-d_6) δ_{ppm}: 7.30 (d, $^3J_{HH}$ = 4 Hz, CH-Ar), 7.10 (s, 2H, NH_2), 6.88–6.84 (m, 2H, CH-Ar), 4.51 (s, 1H, CH), 2.45 (d, $^2J_{HH}$ = 8 Hz, CH), 2.40 (d, $^2J_{HH}$ = 8 Hz, CH), 2.28 (d, $^2J_{HH}$ = 8 Hz, CH), 2.13 (d, $^2J_{HH}$ = 8 Hz, CH), 1.02 (s, 3H, CH_3), 0.95 (s, 3H, CH_3).

2-Amino-7,7-dimethyl-5-oxo-4-(pyridin-3-yl)-5,6,7,8-tetrahydro-4*H*-chromene-3-carbonitrile (7k). White powder; IR (KBr, ν_{max}/cm^{-1}): 3392, 3312 (NH_2), 2192 (CN), 1680 (C−O), 1596, 1574 (C−C). ^{1}H NMR (400 MHz, DMSO-d_6) δ_{ppm}: 8.37 (s, 2H, NH_2), 7.52–7.10 (m, 4H, CH-Ar), 4.22 (s, 1H, CH), 2.47 (d, $^2J_{HH}$ = 8 Hz, CH), 2.39 (d, $^2J_{HH}$ = 8 Hz, CH), 2.22 (d, $^2J_{HH}$ = 8 Hz, CH), 2.09 (d, $^2J_{HH}$ = 8 Hz, CH), 1.01 (s, 3H, CH_3), 0.92 (s, 3H, CH_3).

2-Amino-4-(furan-2-yl)-5-oxo-5,6,7,8-tetrahydro-4*H*-chromene-3-carbonitrile (7t). Brown powder; IR (KBr, ν_{max}/cm^{-1}): 3408, 3328 (NH_2), 2192 (CN), 1680 (C−O), 1596, 1587 (C−C). ^{1}H NMR (400 MHz, DMSO-d_6) δ_{ppm}: 7.45 (d, $^3J_{HH}$ = 4 Hz, CH-Ar), 7.05 (s, 2H, NH_2), 6.28–6.02 (m, 2H, CH-Ar), 4.30 (s, 1H, CH), 2.47-1.93 (m, 6H, $3CH_2$).

2-Amino-5-oxo-4-(thiophen-2-yl)-5,6,7,8-tetrahydro-4*H*-chromene-3-carbonitrile (7u). White powder; IR (KBr, ν_{max}/cm^{-1}): 3424, 3344 (NH_2), 2192 (CN), 1680 (C−O), 1596, 1580 (C−C). ^{1}H NMR (400 MHz, DMSO-d_6) δ_{ppm}: 7.29 (d, $^3J_{HH}$ = 4 Hz, CH-Ar), 7.11 (s, 2H, NH_2), 6.88-6.83 (m, 2H, CH-Ar), 4.51 (s, 1H, CH), 2.48–1.85 (m, 6H, $3CH_2$).

2-Amino-5-oxo-4-(pyridin-3-yl)-5,6,7,8-tetrahydro-4*H*-chromene-3-carbonitrile (7v). White powder; IR (KBr, ν_{max}/cm^{-1}): 3360, 3312 (NH_2), 2192 (CN), 1664 (C−O), 1580, 1542 (C−C). ^{1}H NMR (400 MHz, DMSO-d_6) δ_{ppm}: 8.38 (s, 2H, NH_2), 7.53–7.09 (m, 2H, CH-Ar), 4.21 (s, 1H, CH), 2.47–1.92 (m, 6H, $3CH_2$).

2-Amino-4-(4-methoxyphenyl)-7,7-dimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carbonitrile (10b) Yellow crystals; IR (KBr, ν_{max}/cm^{-1}): 3392, 3328, 3232 (NH_2, NH), 2192 (CN), 1654 (C−O), 1596 (C−C). ^{1}H NMR (400 MHz, DMSO-d_6): 8.82 (s, 1H, NH), 6.94 (d, 2H, $^3J_{H-H}$ = 4 Hz, CH-Ar), 6.71 (d, 2H, $^3J_{H-H}$ = 4 Hz, CH-Ar), 5.65 (s, 2H, NH_2), 4.16 (s, 1H, CH), 3.61 (s, 3H, OCH_3), 2.32 (d, $^2J_{H-H}$ = 8 Hz, CH), 2.20 (d, $^2J_{H-H}$ = 8 Hz, CH), 2.08 (d, $^2J_{H-H}$ = 8 Hz, CH), 1.89 (d, $^2J_{H-H}$ = 8 Hz, CH), 0.92, 0.81 (s, 6H, $2CH_3$).

2-Amino-4-(4-bromophenyl)-7,7-dimethyl-5-oxo-1-phenyl-1,4,5,6,7,8-hexahydroquinoline-3-carbonitrile (10 g) White crystals; IR (KBr, ν_{max}/cm^{-1}): 3456, 3328 (NH_2), 2160 (CN), 1648 (C−O), 1587 (C−C). ^{1}H NMR (400 MHz, DMSO-d_6): 7.63–7.23 (m, 9H, CH-Ar), 5.71 (s, 2H, NH_2), 4.46 (s, 1H, CH), 2.21 (d, $^2J_{H-H}$ = 4 Hz, CH), 2.17 (d, $^2J_{H-H}$ = 4 Hz, CH), 2.01 (d, $^2J_{H-H}$ = 8 Hz, CH), 1.70 (d, $^2J_{H-H}$ = 8 Hz, CH), 0.88, 0.73 (s, 6H, $2CH_3$).

2-Amino-4-(4-chlorophenyl)-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carbonitrile (10k) Yellow crystals; IR (KBr, ν_{max}/cm^{-1}): 3392, 3328, 3232 (NH_2, NH), 2176 (CN), 1657 (C−O), 1600 (C−C). ^{1}H NMR (400 MHz, DMSO-*d*6): 9.00 (s, 1H, NH), 7.31 (d, 2H, $^3J_{H-H}$ = 4 Hz, CH-Ar), 7.14 (d, 2H, $^3J_{H-H}$ = 4 Hz, CH-Ar), 5.81 (s, 2H, NH_2), 4.35 (s, 1H, CH), 2.28–1.73 (m, 6H, $3CH_2$).

2-Amino-5-oxo-1-phenyl-4-(p-tolyl)-1,4,5,6,7,8-hexahydroquinoline-3-carbonitrile (10n) Yellow crystals; IR (KBr, ν_{max}/cm^{-1}): 3472, 3328 (NH_2), 2192 (CN), 1638 (C−O), 1590 (C−C). ^{1}H NMR (400 MHz, DMSO-*d*6): 7.61–7.11 (m, 9H, CH-Ar), 5.32 (s, 2H, NH_2), 4.46 (s, 1H, CH), 2.27 (s, 3H, CH_3), 2.22–1.56 (m, 6H, $3CH_2$).

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Disclosure statement

No potential conflict of interest was reported by the authors.

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