An Efficient Protocol for the Synthesis of Novel 1,2,3-Triazole Substituted 4*H*-Chromene Derivatives

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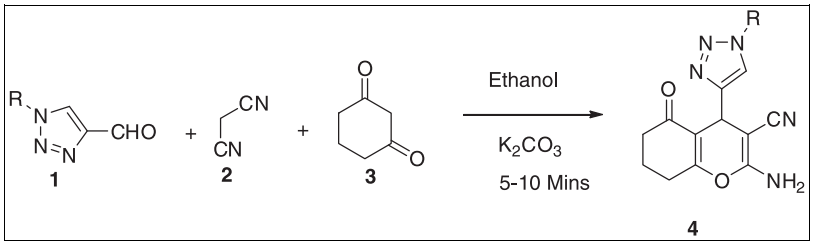

A facile and an efficient protocol has been developed for the synthesis of novel 1,2,3-triazole substituted 4*H*-chromene derivatives **4** in single pot by multicomponent reaction of 1,3-cyclohexanedione, malononitrile and 1-substituted 1,2,3-triazole-5-aldehyde using potassium carbonate as catalyst.

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INTRODUCTION

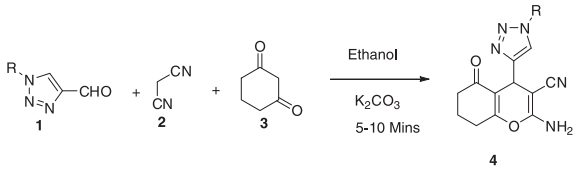
Functionally substituted 4*H*-chromenes have received considerable attention in the area of medicinal chemistry because of their wide range of biological activity. Specifically, these derivatives are known to have antianalgesic [1], antioxidant, spasmolytic, antibacterial [2], antianaphylactic, anti-HIV [3], anticancer [4] and antiallergic activities [5]. The 4*H*-chromenes are also identified in the treatment of neurodegenerative diseases, namely Alzheimer's and Parkinson's diseases [6]. Alternatively, the 1,2,3-triazoles because of their unique chemical and structural properties received much attention over the past decade and found wide applications in medicinal chemistry [7–11]. Recently, multicomponent reactions are developed as efficient synthetic tools that are overriding linear reactions because of their significant advantages in terms of flexible reaction conditions, series of reactions in single step, simplified isolation procedures and thereby atom economy. Earlier synthesis of chromene derivatives was adopted, such as three component condensation of 1,3-diketones, aryl aldehydes and malononitrile using piperidine [12,13], piperidine/ammonium acetate [14], triethylamine [15], electrocatalysis [16] and lipase [17]. On the basis of the importance of chromene derivatives and 1,2,3-triazoles, our attention was attracted toward the synthesis of novel 1,2,3-triazole substituted 4*H*-chromene derivatives. In continuation of our efforts [18–21] in developing new strategies for promising molecules, a new scaffold having both the moieties was designed and we developed an efficient method for the synthesis of novel 1,2,3-triazole substituted 4*H*-chromene derivatives and reported it here for the first time.

RESULTS AND DISCUSSION

Initially, phenyl substituted 1,2,3-triazole-4-aldehyde **1** [22], malononitrile **2** and cyclohexane-1,3-dione **3** were selected as representative substrates and their reactions in ethanol without catalyst at reflux temperature for 10 h were investigated and found to give the corresponding chromene in 46% yield. In order to improve the yield and to find a suitable catalyst, the reaction was performed using different catalysts such as $ZnCl_2$, piperidine, tetrabutyl ammonium bromide (TBAB), L-proline, K_2CO_3 and $CaCO_3$ and by neat grinding. Out of all the catalysts studied, potassium carbonate was considered as the best catalyst that gave product **4** in a high yield of 92%. The reaction was outlined in Scheme 1. The investigation on different catalysts and yields of products **4** formed at different reaction temperatures versus times are tabulated in Table 1.

After identifying potassium carbonate as suitable catalyst for the reaction, the protocol was extended to the multicomponent condensation of diverse substituted 1,2,3-triazol-4-aldehydes with 1,3-cyclohexanedione and malononitrile and diverse substituted 4*H*-chromene derivatives **4** were obtained. The sequence of reaction is mainly a Knoevenagel condensation of malononitrile with 1,2,3-triazol-4-aldehyde to form arylidene malononitrile [23]. Michael addition of 1,3-cyclohexanedione with *in situ* generated electron deficient Knoevenagel adduct followed by intramolecular cyclization resulted product **4**. The details of the mechanism are outlined in the next sections and the products are tabulated in Table 2.

Scheme 1



Mechanism

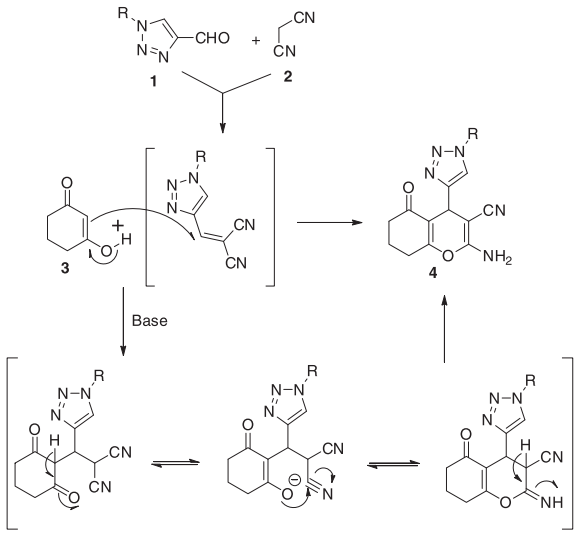


Table 1

Preparation of products **4**.

Entry	Catalyst	Temp (°C)	Time (h.min)	Yield (%)
1	—[a]	78	10.00	46
2	$ZnCl_2$[a]	78	12.00	52
3	TBAB[a]	78	3.00	66
4	L-Proline[a]	78	3.30	65
5	Piperidine[a]	78	2.30	82
6	K_2CO[a]	60	0.10	92
7	K_2CO_3[b]	100	0.30	70
8	$CaCO_3$[a]	78	0.30	75
9	—[c]	27	0.30	56

[a]Reactions were carried out in ethanol.
[b]Reactions were carried out in water.
[c]Reactions were carried out by neat grinding.

CONCLUSION

A series of novel 1,2,3-triazole substituted 4*H*-chromene derivatives were prepared in a single step by multicomponent condensation of 1,3-cyclohexanedione, malononitrile and diverse substituted 1,2,3-triazole-4-aldehydes using potassium carbonate as an inexpensive catalyst. The developed method is quite useful to the synthesis of diverse substituted 4*H*-chromene derivatives.

EXPERIMENTAL

Melting points were recorded in open glass capillaries on Casia-Siamia (VMP-AM) Aldrich (Sigma-Aldrich, St. Louis, MO, USA) and Spectrochem Pvt. Ltd (Mumbai, India) melting point apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer FT-IR 240-C spectrophotometer using KBr optics. ^{1}H NMR spectra were recorded on a Bruker AV 300 MHz in $CDCl_3$ and DMSO-d_6 using TMS as internal standard. ^{13}C NMR spectra were recorded on Bruker AV 75 MHz (Germany) in $CDCl_3$ and DMSO-d_6. Electron impact and chemical ionization mass spectra were recorded on VG 7070 H instrument at 70 eV. All the reactions were monitored by thin-layer chromatography technique on precoated silica gel 60 F_{254} (mesh) plates; spots were visualized with UV light. Merck silica gel (60–120 mesh) was used for column chromatography. CHN analysis was recorded on a Vario EL analyzer.

Synthesis of 2-amino-5-oxo-4-(1-sustituted-1*H*-1,2,3-triazol-4-yl)-5,6,7,8-tetrahydro-4*H*-chromene-3-carbonitrile derivatives (4a–p). ***General procedure.*** A mixture of 1-phenyl-1,2,3-triazol-4-aldehyde **1** (200 mg, 1.08 mmol), malononitrile **2** (72 mg, 1.08 mmol) and K_2CO_3 (15 mg, 0.1 mmol) were taken in ethanol (5 mL). The reaction mixture was heated to 50°C and kept for 4–5 min at the same temperature and white solid was obtained. Then, 1,3-cyclohexanedione (120 mg, 1.08 mmol) was added to the reaction mixture and refluxed for 5 min. As a result, there is a change in color from red to colorless, which indicates completion of reaction. After completion of reaction, the reaction mixture was cooled to room temperature, and the solvent was removed under vacuum. The crude product was purified by letting it pass through a column packed with silica gel using petroleum ether/EtOAc (6:4) as eluent.

2-Amino-5-oxo-4-(1-phenyl-1H-1,2,3-triazol-4-yl)-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (4a). White solid, Yield: 92%, m.p. 208–210°C, IR (KBr, cm^{-1}): 3357, 3311 (—NH_2), 2185 (—CN), 1687 (—C═O), 1653 (N═N); ^{1}H NMR (DMSO-d_6, 300 MHz): δ 2.05 (m, 2H, —CH_2—), 2.39 (t, J = 7.55 Hz, 2H, —CH_2), 2.61 (t, J = 7.58 Hz, 2H, —CH_2), 4.61 (s, 1H, —CH—), 6.61 (br, s, 2H, NH_2), 7.43 (d, J = 7.89 Hz, 1H, Ar—H), 7.51 (t, J = 7.89 Hz, 2H, Ar—H), 7.80 (d, J = 7.94 Hz, 2H, Ar—H), 8.22 (s, 1H, Ar—H); ^{13}C NMR (DMSO-d_6, 75 MHz):191.4, 161.4, 154.2, 146.8, 145.8, 135.5, 132.7, 128.1, 126.7, 125.9, 116.6, 118.4, 115.8, 111.4, 36.4, 28.1, 26.4, 21.2; MS (ESI, 70 eV): *m/z*: 334 (M^+ + H); *Anal.* Calcd for $C_{18}H_{15}N_5O_2$: C, 64.86; H, 4.54; N, 21.01; Found: C, 64.91; H, 4.51; N, 21.12%.

2-Amino-4-(1-(4-fluorophenyl)-1H-1,2,3-triazol-4-yl)-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (4b). White solid, Yield: 89%, m.p. 202–203°C, IR (KBr, cm^{-1}): 3358, 3324 (—NH), 2181 (—CN), 1691 (—C═O), 1642 (N═N); ^{1}H NMR (DMSO-d_6, 300 MHz): δ 2.06 (m, 2H, —CH_2—), 2.36 (t, J = 7.54 Hz, 2H, —CH_2), 2.63 (t, J = 7.59 Hz, 2H, —CH_2), 4.58 (s, 1H, —CH—), 6.66 (br, s, 2H, NH_2), 7.30 (d, J = 8.52 Hz, 2H, Ar—H), 7.85 (d, J = 8.52 Hz, 2H, Ar—H), 8.26 (s, 1H, Ar—H); MS (ESI, 70 eV): *m/z*: 352 (M^+ + H); *Anal.* Calcd for $C_{18}H_{14}FN_5O_2$: C, 61.53; H, 4.02; N, 19.93; Found: C, 61.45; H, 4.05; N, 19.98%.

2-Amino-4-(1-(4-chlorophenyl)-1H-1,2,3-triazol-4-yl)-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (4c). White solid, Yield: 88%, m.p. 190–192°C, IR (KBr, cm^{-1}): 3352, 3321 (—NH), 2183 (—CN), 1671 (—C═O), 1651 (N═N); ^{1}H NMR (DMSO-d_6, 300 MHz): δ 2.08 (m, 2H, —CH_2—), 2.31 (t, J = 7.51 Hz, 2H, —CH_2), 2.65 (t, J = 7.58 Hz, 2H, —CH_2), 4.55 (s, 1H, —CH—), 6.68 (br, s, 2H, NH_2), 7.31 (d, J = 8.42 Hz, 2H,

Table 2

Preparation of 1,2,3-triazole substituted 4*H*-chromene derivatives **4a–p**.

S. No.	Compound	R	Time (min)	Yield (%)	m.p. (°C)
1	**4a**	C_6H_5	4	92	208–210
2	**4b**	4-FC_6H_4	4	89	202–203
3	**4c**	4-ClC_6H_4	4	88	190–192
4	**4d**	3-ClC_6H_4	5	85	188–189
5	**4e**	4-BrC_6H_4	5	85	184–186
6	**4f**	4-$NO_2C_6H_4$	10	81	205–206
7	**4g**	4-$CH_3C_6H_4$	10	84	211–213
8	**4h**	4-$CH_3OC_6H_4$	10	84	185–186
9	**4i**	4-$CF_3C_6H_4$	10	80	216–218
10	**4j**	2,4-$F_2C_6H_3$	10	81	206–208
11	**4k**	2,4-$ClFC_6H_3$	10	80	209–210
12	**4l**	2,4-$ClNO_2C_6H_3$	10	82	218–219
13	**4m**	CH_3—$(CH_2)_6$—CH_2—	10	76	166–167
14	**4n**	CF_3—$(CF_2)_5$—$(CH_2)_2$—	10	72	182–184
15	**4o**	CH_3—$(CH_2)_8$—CH_2—	10	80	188–189
16	**4p**	CF_3—$(CF_2)_7$—$(CH_2)_2$—	10	71	192–194

Ar—H), 7.81 (d, $J = 8.42$ Hz, 2H, Ar—H), 8.31 (s, 1H, Ar—H); MS (ESI, 70 eV): *m/z*: 368 ($M^+ + H$); *Anal*. Calcd for $C_{18}H_{14}ClN_5O_2$: C, 58.78; H, 3.84; N, 19.04; Found: C, 58.71; H, 3.75; N, 19.16%.

2-Amino-4-(1-(3-chlorophenyl)-1H-1,2,3-triazol-4-yl)-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (4d). White solid, Yield: 85%, m.p. 188–189°C, IR (KBr, cm^{-1}): 3345, 3315 (—NH), 2189 (—CN), 1689 (—C═O), 1648 (N═N); ^{1}H NMR (DMSO-d_6, 300 MHz): δ 2.08 (m, 2H, —CH_2—), 2.40 (t, $J = 7.54$ Hz, 2H, —CH_2), 2.64 (t, $J = 7.65$ Hz, 2H, —CH_2), 4.64 (s, 1H, —CH—), 6.34 (br, s, 2H, NH_2), 7.41 (d, $J = 7.41$ Hz, 1H, Ar—H), 7.50 (dd, $J = 7.41$ Hz, $J = 7.48$ Hz, 1H, Ar—H), 7.74 (d, $J = 7.48$ Hz, 1H, Ar—H), 7.85 (s, 1H, Ar—H), 8.21 (s, 1H, Ar—H); MS (ESI, 70 eV): *m/z*: 368 ($M^+ + H$); *Anal*. Calcd for $C_{18}H_{14}ClN_5O_2$: C, 58.78; H, 3.84; N, 19.04; Found: C, 58.86; H, 3.83; N, 19.16%.

2-Amino-4-(1-(4-bromophenyl)-1H-1,2,3-triazol-4-yl)-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (4e). White solid, Yield: 85%, m.p. 184–186°C, IR (KBr, cm^{-1}): 3342, 3323 (—NH), 2179 (—CN), 1693 (—C═O), 1649 (N═N); ^{1}H NMR (DMSO-d_6, 300 MHz): δ 2.11 (m, 2H, —CH_2—), 2.31 (t, $J = 7.67$ Hz, 2H, —CH_2), 2.61 (t, $J = 7.52$ Hz, 2H, —CH_2), 4.54 (s, 1H, —CH—), 6.56 (br, s, 2H, NH_2), 7.38 (d, $J = 8.55$ Hz, 1H, Ar—H), 7.80 (d, $J = 8.55$ Hz, 2H, Ar—H), 8.22 (s, 1H, Ar—H); MS (ESI, 70 eV): *m/z*: 412 ($M^+ + H$); *Anal*. Calcd for $C_{18}H_{14}BrN_5O_2$: C, 52.44; H, 3.42; N, 16.99; Found: C, 52.36; H, 3.44; N, 16.88%.

2-Amino-4-(1-(4-nitrophenyl)-1H-1,2,3-triazol-4-yl)-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (4f). White solid, Yield: 81%, m.p. 205–206°C, IR (KBr, cm^{-1}): 3359, 3317 (—NH), 2188 (—CN), 1687 (—C═O), 1645 (N═N); ^{1}H NMR (DMSO-d_6, 300 MHz): δ 2.08 (m, 2H, —CH_2—), 2.40 (t, $J = 7.56$ Hz, 2H, —CH_2), 2.64 (t, $J = 7.61$ Hz, 2H, —CH_2), 4.68 (s, 1H, —CH—), 6.31 (br, s, 2H, NH_2), 7.66 (d, $J = 8.92$ Hz, 2H, Ar—H), 8.09 (d, $J = 8.92$ Hz, 2H, Ar—H), 8.41 (s, 1H, Ar—H); ^{13}C NMR (DMSO-d_6, 75 MHz):194.6, 163.4, 158.1, 149.3, 147.2, 136.6, 133.6, 129.7, 128.3, 126.9, 118.7, 118.4, 116.8, 111.4, 35.2, 26.1, 25.6, 18.5; MS (ESI, 70 eV): *m/z*: 379 ($M^+ + H$); *Anal*. Calcd for $C_{18}H_{14}N_6O_4$: C, 57.14; H, 3.73; N, 22.21; Found: C, 57.19; H, 3.81; N, 22.29%.

2-Amino-5-oxo-4-(1-(4-methylphenyl)-1H-1,2,3-triazol-4-yl)-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (4g). White solid, Yield: 84%, m.p. 211–213°C, IR (KBr, cm^{-1}): 3354, 3313 (—NH), 2185 (—CN), 1687 (—C═O), 1643 (N═N); ^{1}H NMR (DMSO-d_6, 300 MHz): δ 2.09 (m, 2H, —CH_2—), 2.21 (t, $J = 7.65$ Hz, 2H, —CH_2), 2.43 (s, 3H, —CH_3), 2.63 (t, $J = 7.59$ Hz, 2H, —CH_2), 4.64 (s, 1H, —CH—), 6.61 (br, s, 2H, NH_2), 7.44 (d, $J = 7.84$ Hz, 2H, Ar—H), 7.51 (d, $J = 7.84$ Hz, 2H, Ar—H), 8.22 (s, 1H, Ar—H); MS (ESI, 70 eV): *m/z*: 348 ($M^+ + H$); *Anal*. Calcd for $C_{19}H_{17}N_5O_2$: C, 65.69; H, 4.93; N, 20.16; Found: C, 65.79; H, 4.99; N, 20.28%.

2-Amino-4-(1-(4-methoxyphenyl)-1H-1,2,3-triazol-4-yl)-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (4h). White solid, Yield: 84%, m.p. 185–186°C, IR (KBr, cm^{-1}): 3344, 3315 (—NH), 2177 (—CN), 1687 (—C═O), 1651 (N═N); ^{1}H NMR (DMSO-d_6, 300 MHz): δ 2.05 (m, 2H, —CH_2—), 2.36 (t, $J = 7.55$ Hz, 2H, —CH_2), 2.56 (t, $J = 7.54$ Hz, 2H, —CH_2), 3.62 (s, 3H, —OCH_3), 4.68 (s, 1H, —CH—), 6.68 (br, s, 2H, NH_2), 7.51 (d, $J = 8.12$ Hz, 2H, Ar—H), 7.80 (d, $J = 8.12$ Hz, 2H, Ar—H), 8.28 (s, 1H, Ar—H); MS (ESI, 70 eV): *m/z*: 364 ($M^+ + H$); *Anal*. Calcd for $C_{19}H_{17}N_5O_3$: C, 62.80; H, 4.72; N, 19.27; Found: C, 62.91; H, 4.75; N, 19.19%.

2-Amino-5-oxo-4-(1-(4-(trifluoromethyl)phenyl)-1H-1,2,3-triazol-4-yl)-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (4i). White solid, Yield: 80%, m.p. 216–218°C, IR (KBr, cm^{-1}): 3349, 3321 (—NH), 2188 (—CN), 1681 (—C═O), 1612 (N═N); ^{1}H NMR (DMSO-d_6, 300 MHz): δ 2.11 (m, 2H, —CH_2—), 2.32 (t, $J = 7.62$ Hz, 2H, —CH_2), 2.73 (t, $J = 7.64$ Hz, 2H, —CH_2), 4.73 (s, 1H, —CH—), 6.81 (br, s, 2H, NH_2), 7.72 (d, $J = 8.41$ Hz, 2H, Ar—H), 7.88 (d, $J = 8.41$ Hz, 2H, Ar—H), 8.31 (s, 1H, Ar—H); MS (ESI, 70 eV): *m/z*: 402 ($M^+ + H$); *Anal*. Calcd for $C_{19}H_{14}F_3N_5O_2$: C, 56.86; H, 3.52; N, 17.45; Found: C, 56.88; H, 3.41; N, 17.37%.

2-Amino-4-(1-(2,4-difluorophenyl)-1H-1,2,3-triazol-4-yl)-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (4j). White solid, Yield: 81%, m.p. 206–208°C, IR (KBr, cm^{-1}): 3351, 3312 (—NH), 2191 (—CN), 1698 (—C═O), 1651 (N═N); ^{1}H NMR (DMSO-d_6, 300 MHz): δ 2.12 (m, 2H, —CH_2—), 2.38 (t, $J = 7.54$ Hz, 2H, —CH_2), 2.77 (t, $J = 7.55$ Hz, 2H, —CH_2), 4.89 (s, 1H, —CH—),

6.74 (br, s, 2H, NH_2), 7.72 (d, J = 8.34 Hz, 1H, Ar—H), 7.81 (d, J = 8.34 Hz, 1H, Ar—H), 7.94 (s, 1H, Ar—H), 8.38 (s, 1H, Ar—H); MS (ESI, 70 eV): *m/z*: 370 (M^+ + H); *Anal*. Calcd for $C_{18}H_{13}F_2N_5O_2$: C, 58.54; H, 3.55; N, 18.96; Found: C, 58.65; H, 3.53; N, 18.84%.

2-Amino-4-(1-(3-chloro-4-Fluorophenyl)-1H-1,2,3-triazol-4-yl)-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (4k). White solid, Yield: 80%, m.p. 209–210°C, IR (KBr, cm^{-1}): 3351, 3319 (—NH), 2181 (—CN), 1689 (—C═O), 1641 (N═N); ^{1}H NMR (DMSO-d_6, 300 MHz): δ 2.15 (m, 2H, —CH_2—), 2.43 (t, J = 7.55 Hz, 2H, —CH_2), 2.76 (t, J = 7.59 Hz, 2H, —CH_2), 4.71 (s, 1H, —CH—), 6.83 (br, s, 2H, NH_2), 7.71 (d, J = 8.41 Hz, 1H, Ar—H), 7.79 (d, J = 8.41 Hz, 1H, Ar—H), 7.88 (s, 1H, Ar—H), 8.41 (s, 1H, Ar—H); MS (ESI, 70 eV): *m/z*: 386 (M^+ + H); *Anal*. Calcd for $C_{18}H_{13}ClFN_5O_2$: C, 56.04; H, 3.40; N, 18.15; Found: C, 56.19; H, 3.47; N, 18.27%.

2-Amino-4-(1-(2-chloro-4-nitrophenyl)-1H-1,2,3-triazol-4-yl)-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (4l). White solid, Yield: 82%, m.p. 218–219°C, IR (KBr, cm^{-1}): 3363, 3322 (—NH), 2198 (—CN), 1698 (—C═O), 1634 (N═N); ^{1}H NMR (DMSO-d_6, 300 MHz): δ 2.15 (m, 2H, —CH_2—), 2.39 (t, J = 7.67 Hz, 2H, —CH_2), 2.69 (t, J = 7.51 Hz, 2H, —CH_2), 4.81 (s, 1H, —CH—), 6.82 (br, s, 2H, NH_2), 7.91 (d, J = 8.43 Hz, 1H, Ar—H), 7.98 (d, J = 8.43 Hz, 1H, Ar—H), 8.04 (s, 1H, Ar—H), 8.29 (s, 1H, Ar—H); MS (ESI, 70 eV): *m/z*: 413 (M^+ + H); *Anal*. Calcd for $C_{18}H_{13}ClN_6O_4$: C, 52.37; H, 3.17; N, 20.36; Found: C, 52.48; H, 3.11; N, 20.24%.

2-Amino-5-oxo-4-(1-octyl-1H-1,2,3-triazol-4-yl)-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (4m). White solid, Yield: 76%, m.p. 166–167°C, IR (KBr, cm^{-1}): 3347, 3328 (—NH), 2178 (—CN), 1699 (—C═O), 1653 (N═N); ^{1}H NMR (DMSO-d_6, 300 MHz): δ 0.91 (t, J = 6.58 Hz, 3H, —CH_3), 1.29 (m, 10H, —CH_2), 1.87 (m, 2H, —CH_2—), 2.11 (m, 2H, —CH_2—), 2.41 (t, J = 6.93 Hz, 2H, —CH_2), 2.56 (t, J = 7.11 Hz, 2H, —CH_2), 4.11 (t, J = 6.68 Hz, 2H, —CH_2), 4.76 (s, 1H, —CH—), 6.61 (br, s, 2H, NH_2), 8.32 (s, 1H, Ar—H); MS (ESI, 70 eV): *m/z*: 370 (M^+ + H); *Anal*. Calcd for $C_{20}H_{27}N_5O_2$: C, 65.02; H, 7.37; N, 18.96; Found: C, 65.11; H, 7.38; N, 18.88%.

2-Amino-5-oxo-4-(1-(3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluoro-octyl)-1H-1,2,3-triazol-4-yl)-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (4n). White solid, Yield: 80%, m.p. 182–184°C, IR (KBr, cm^{-1}): 3356, 3313 (—NH), 2175 (—CN), 1681 (—C═O), 1637 (N═N); ^{1}H NMR (DMSO-d_6, 300 MHz): δ 2.08 (m, 2H, —CH_2—), 2.39 (t, J = 6.67 Hz, 2H, —CH_2), 2.61 (m, 2H, —CH_2—), 2.68 (t, J = 7.27 Hz, 2H, —CH_2), 4.11 (t, J = 7.67 Hz, 2H, —CH_2), 4.61 (s, 1H, —CH—), 6.66 (br, s, 2H, NH_2), 8.21 (s, 1H, Ar—H); MS (ESI, 70 eV): *m/z*: 604 (M^+ + H); *Anal*. Calcd for $C_{20}H_{14}F_{13}N_5O_2$: C, 39.81; H, 2.34; N, 11.61; Found: C, 39.73; H, 2.34; N, 11.69%.

2-Amino-5-oxo-4-(1-decyl-1H-1,2,3-triazol-4-yl)-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (4o). White solid, Yield: 72%, m.p. 188–189°C, IR (KBr, cm^{-1}): 3344, 3321 (—NH), 2195 (—CN), 1697 (—C═O), 1643 (N═N); ^{1}H NMR (DMSO-d_6, 300 MHz): δ 0.96 (t, J = 6.52 Hz, 3H, —CH_3), 1.28 (m, 14H, —CH_2), 1.88 (m, 2H, —CH_2), 2.15 (m, 2H, —CH_2—), 2.44 (t, J = 7.23 Hz, 2H, —CH_2), 2.58 (t, J = 7.61 Hz, 2H, —CH_2—), 4.17 (t, J = 7.68 Hz, 2H, —CH_2), 4.76 (s, 1H, —CH—), 6.71 (br, s, 2H, NH_2), 8.28 (s, 1H, Ar—H); MS (ESI, 70 eV): *m/z*: 398 (M^+ + H); *Anal*. Calcd for $C_{22}H_{31}N_5O_2$: C, 66.47; H, 7.86; N, 17.62; Found: C, 66.39; H, 7.77; N, 17.74%.

2-Amino-5-oxo-4-(1-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluoro-decyl)-1H-1,2,3-triazol-4-yl)-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (4p). White solid, Yield: 71%, m.p. 192–194°C, IR (KBr, cm^{-1}): 3351, 3319 (—NH), 2186 (—CN), 1689 (—C═O), 1633 (N═N); ^{1}H NMR (DMSO-d_6, 300 MHz): δ 2.10 (m, 2H, —CH_2—), 2.41 (t, J = 7.68 Hz, 2H, —CH_2), 2.61 (m, 2H, —CH_2—), 2.66 (t, J = 7.63 Hz, 2H, —CH_2), 4.16 (t, J = 7.44 Hz, 2H, —CH_2), 4.51 (s, 1H, —CH—), 6.76 (br, s, 2H, NH_2), 8.29 (s, 1H, Ar—H); MS (ESI, 70 eV): *m/z*: 704 (M^+ + H); *Anal*. Calcd for $C_{22}H_{14}F_{17}N_5O_2$: C, 37.57; H, 2.01; N, 9.96; Found: C, 37.48; H, 2.12; N, 9.89%.

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