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A convenient microwave-assisted 5-amination of flavones

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ABSTRACT

A few examples of 5-aminoflavones' syntheses exist in the literature and for those, which are described, the amino group is introduced before the formation of the flavone skeleton. We describe here an efficient method, which permits the access to 5-aminoflavones by a simple procedure using an SNAr amination under microwaves irradiation.

1. Introduction

Flavones belong to the very important class of natural compounds of the flavonoid group and are widely represented in nature. A great number of biological activities were reported for flavones,[1] such as antiestrogenic,[2] antitumor,[3] antiallergic[4] or anti-inflammatory.[5] These promising properties led to numerous chemical works focusing on the synthesis and the structural modifications of flavones.[6] It is noteworthy that many of the biologically active flavones possess at least one free hydroxyl group on their skeleton.[7] The hydroxyl group is able to bind with various targets acting either as a hydrogen bond acceptor (HBA) or a hydrogen bond donor (HBD). Considering that an amino group is also able to act either as an HBA or an HBD, it has often successfully been employed as a bioisostere of the hydroxyl group in the design of biologically active flavones.[7a,8]

However, very few studies are reported concerning the synthesis of aminoflavones. The amino group is generally introduced before the construction of the chromone moiety limiting thus the diversity and the possibilities of SAR's studies.[7a,8,9] The introduction of an amino group directly on the flavone nucleus is more scarcely reported. Sasaki et al. report the synthesis of 3-aminoflavones from 3-tosyl and 3-mesyloxyflavones, which is supposed to proceed via an aziridine intermediate.[10] Caddick et al. describe Buchwald's aminations from flavone triflates and halides.[11] Amination of the 7-triflyloxyflavone gave only low yields, whereas the 5-isomer was not reactive.

Lemiere et al. report the palladium-catalyzed synthesis of a 7-aminoflavone from a 7-triflyloxyflavone by using the benzophenoneimine as the amino-precursor.[12] Despite the substrate scope for the metal-catalyzed arylamination has been largely extended recently,[13] this reaction always suffers from limitations due to the use of expensive and sensitive catalysts and/or ligands and has not been yet largely applied yet in the synthesis of aminoflavones.

SNAr reaction is another way for the amination of aromatic rings, which most often requires activating substituents, high temperatures, hard bases and/or long reaction times.[14] Recently, aryltriflates were described as good partners for metal-free amination reactions under microwave heating conditions, even in the absence of any activating substituent, to afford regioselectively arylamines with good yields and short reaction times.[15]

We wish to report here our efforts directed to the synthesis of various 5-aminoflavones starting from diosmetin (3′,5,7-trihydroxy-4′-methoxy-2-phenylchromone) by a simple method using a microwave-assisted SNAr reaction.

2. Results and discussion

Diosmetin was first protected with benzyl bromide at room temperature to afford the 3′,7-dibenzylated flavone **1** in 60% yield.[16] Under these conditions, the 5-OH group was not benzylated. The latter was then triflated in 88% yield using the smooth triflating agent *N*-phenylbistriflimide (Scheme 1).

We chose benzylamine to explore the best conditions for the amination of **2**. We investigated the effects of the amine quantity (2, 3 and 4 equiv) and temperature (150 and 200 °C). The reaction was monitored by LC–MS analysis at 5, 10 and 20 min. The results are summarized in Table 1. At 150 °C, the reaction did not go to completion even in increasing the quantity of amine or the reaction time. The best result was obtained with 4 equiv of benzylamine after 20 min. When the temperature was raised to 200 °C, the use of

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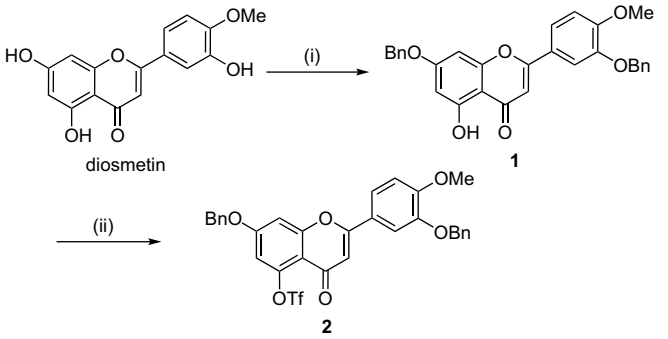


Scheme 1. Reagents and conditions: (i) benzyl bromide, K_2CO_3, DMF, 12 h, rt, 60%; (ii) $PhNTf_2$, NaHMDS, anhydrous THF, 1 h, rt, 88%.

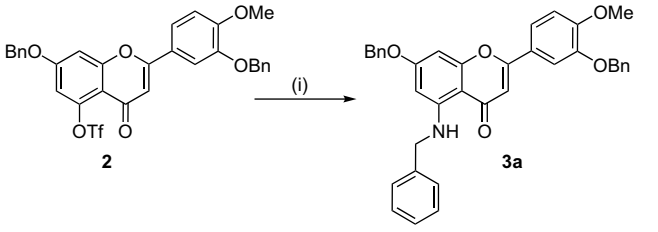
4 equiv of benzylamine permitted the total conversion of **2** after 10 min. The 5-benzylaminoflavone **3a** was isolated in 82% yield. Under classical heating conditions, 1 h was requested for the total conversion of **2**, and **3a** was isolated with a lower 65% yield.

These results prompted us to apply these reaction conditions to other amines (amine: 4 equiv, temperature: 200 °C). In all cases, the reaction was monitored by LC–MS analysis and carried on until all the starting material has disappeared. The results are summarized in Table 2. Using benzylamines (entry **a**–**h**), the reaction was completed within 10–15 min with good isolated yields of 5-benzylaminoflavones (61–92%) except with the bulky trifluoromethoxy group (entry **i**) for which 30 min were necessary for the reaction to be completed. Primary alkylamines (entry **j**–**l**) and cycloalkylamines (entry **m**–**o**) reacted more slowly to afford the corresponding aminoflavones in moderate to good yields.

The reaction appeared to be general with nucleophilic amines and we then tried to apply these conditions to aniline, which is known to be less or non reactive under SNAr conditions. The first attempts did not permit to detect traces of the expected 5-anilinoflavone even after 2 h of microwave heating. So, in order to improve the reactivity of the flavone moiety, we decided to add triethylamine (1 equiv) in the reaction mixture. After 60 min at 200 °C the 5-anilinoflavone **3p** was isolated in a 37% yield. The reaction was repeated with 4-methoxyaniline and 4-fluoroaniline and gave the corresponding derivatives **3q**–**r**, respectively, in 54 and 36% yield. As expected, the more nucleophilic 4-methoxyaniline gave the best result (Table 3).

Finally, we decided to remove the protective benzyl groups by catalytic hydrogenation. Starting from **3a**, the three benzyl groups were easily removed, giving the 5-amino flavone **4a**, whereas the 5-(4-methoxybenzylamino)flavone **3b** only led to the double O-debenzylation to give **4b** (Scheme 2).

Table 1
Results of SN_{Ar} reaction between **2** and benzylamine to give **3a**



Benzylamine (equiv)	Time (min)	150 °C		200 °C	
		2 (%)	**3a**(%)	**2** (%)	**3a** (%)
2	5	71	29	25	75
2	10	57	43	15	85
2	20	45	55	11	89
3	5	55	45	19	81
3	10	54	46	12	88
3	20	31	69	8	92
4	5	45	55	4	96
4	10	32	68		100[a]
4	20	14	86		100

(i) Reagents and conditions: benzylamine, NMP, microwave irradiation.
[a] 1 h at 200 °C under classical heating conditions.

3. Conclusion

We have developed a convenient 5-amination of flavones starting from the corresponding triflates by using an SNAr reaction under microwave heating conditions. The reaction gave good yields with primary and secondary non aromatic amines and has been even successful with anilines in moderate yields. The procedure is very easy and the use of palladium catalysts or ligands and hard bases is not necessary. This methodology allows the synthesis of various 5-aminoflavones and could be used to design new biologically interesting compounds in the flavone series.

4. Experimental

4.1. General

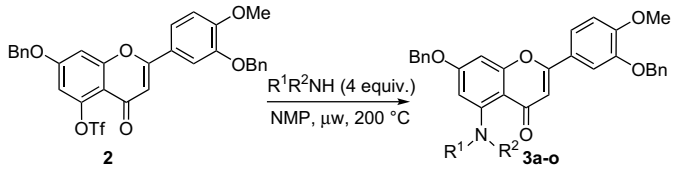
All commercial solvents and reagents were used as-received except THF, which was distilled over Na/benzophenone under Argon. Sodium bis(trimethylsilyl)amide (NaHMDS) was purchased as a 2 M solution in THF.

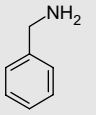
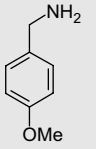
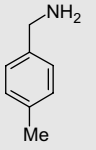
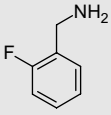
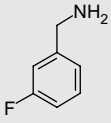
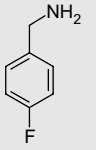
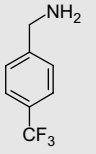
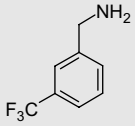
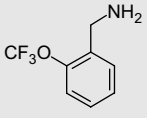
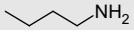
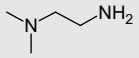
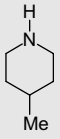
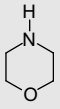
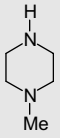
Reactions were monitored by LC/MS and stopped when all the starting material has disappeared. Flash chromatography was realized on silica gel (SDS AAC 60, 70–200) or on neutral alumina gel (Merck 90, 63–200). IR spectra were recorded on KBr disks with a Perkin–Elmer BX FTIR apparatus. ^1H and ^{13}C NMR spectra were recorded, respectively, at 400 and 100 MHz with a Jeol Lambda 400 NMR spectrometer. Chemical shifts δ are reported in parts per million with the solvent resonance as the internal standard; coupling constants J are given in hertz. Multiplicity is given as follows: s (singlet), d (doublet), t (triplet), q (quartet), quint. (quintet), sept. (septet), m (multiplet). The microwave reactions were performed using a Biotage Initiator Microwave oven using 2-5 mL sealed vials. Temperature was measured with an IR-sensor and reaction times are given as hold times. LC/MS (ESI) analyses were realized with a Waters alliance 2695 as separating module using the following gradient: A (95%)/B (5%) to A (5%)/B(95%) in 10 min. This ratio was hold during 3 min before return to initial conditions in 1 min. Initial conditions were then maintained for 5 min (A: H_2O, B: CH_3CN; each containing HCOOH: 0.1%; Column: C18 Xterra MSC 118/2.1×50 mm). MS detection was performed with a Micromass ZMD 2000 by positive ESI. EIMS and HRMS (EI) were performed at 70 eV with a JEOL JMS GCMate. Melting points were determined on Kofler melting point apparatus. Elemental analyses were performed at the 'Institut de Recherche en Chimie Organique Fine' (IRCOF, Rouen-France).

4.2. 7-Benzyloxy-2-(3-benzyloxy-4-methoxyphenyl)-5-hydroxy-4*H*-chromen-4-one (1)

5,7-Dihydroxy-2-(3-hydroxy-4-methoxyphenyl)-4*H*-chromen-4-one (diosmetin) (9 g, 30 mmol), benzyl bromide (7.83 mL, 66 mmol), and potassium carbonate (20.7 g, 150 mmol) were dissolved in DMF (150 mL). The mixture was stirred at room temperature for 4 h and diluted with water (500 mL). The solid was filtrated, washed with water and diethyl ether, dried, and purified by silica gel chromatography with methylene chloride as eluent to give **1** as a yellow solid (8.6 g, 60%); mp: 174 °C, Lit:[16] 176–177 °C; ^1H NMR (400 MHz, $CDCl_3$) δ: 3.97 (s, 3H, OCH_3), 5.15 (s, 2H, CH_2), 5.23 (s, 2H, CH_2), 6.40 (d, J=2.2 Hz, 1H, H_6), 6.50 (s, 1H, H_3), 6.53 (d, J=2.2 Hz,

Table 2
Synthesis of 5-aminoflavones **3a–o** from **2**



Entry	Amine	Time (min)	Yield[a] (%)
a		10 60[b]	82 65
b		15	92
c		15	71
d		15	68
e		10	63
f		15	65
g		15	61
h		15	67
i		30	67
j		30	77
k		60	71
l		45	48
m		60	83
n		90	67
o		30	39

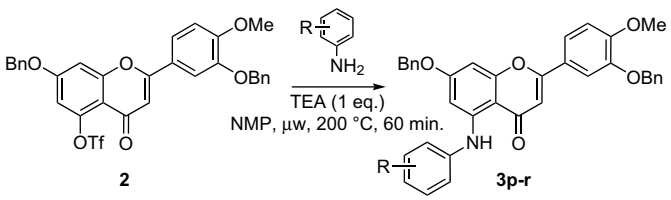
[a] Isolated yields.
[b] Classical heating conditions.

1H, H_8), 6.99 (d, J=8.5 Hz, 1H, $H_{5'}$), 7.34–7.52 (m, 12H), 12.80 (s, 1H, OH). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 56.3, 70.6, 71.6, 93.6, 98.9, 104.7, 105.9, 111.7, 111.9, 120.7, 123.8, 127.6, 127.7, 128.4, 128.6, 128.9, 136.0, 136.6, 148.5, 153.1, 157.8, 162.4, 164.1, 164.7, 182.5. IR (KBr, cm^{-1}): 1665 (C=O). EIMS m/z: 480.0 ($M^{+\bullet}$, 100). Elemental analysis: calcd (%) for $C_{30}H_{24}O_6$: C 47.99, H 5.03; found: C 47.85, H 4.81.

4.3. 7-Benzyloxy-2-(3-benzyloxy-4-methoxyphenyl)-5-trifluoromethanesulfonyloxy-4*H*-chromen-4-one (2)

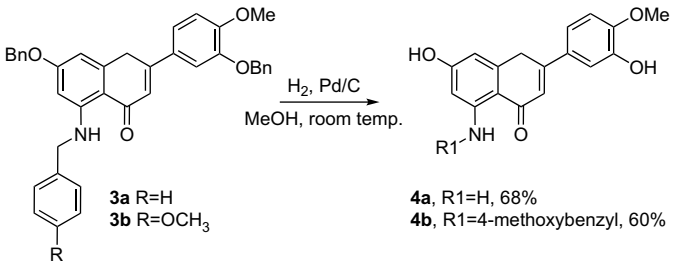
Compound **2** (2 g, 4.17 mmol) was dissolved in dry THF (30 mL). Under N_2, NaHMDS (2 M) in THF (2.5 mL, 5 mmol) was added at room temperature and the mixture was stirred for 15 min. $PhNTf_2$ (1.93 g, 5.42 mmol) was added and the mixture was stirred at room temperature for 1 hour. The solvent was evaporated under reduced pressure. CH_2Cl_2 (50 mL) was added and the resulting solution was washed with water (3×50 mL), dried over $MgSO_4$ and evaporated under reduced pressure. The residue was purified by flash chromatography (SiO_2, CH_2Cl_2) to give **2** as a beige solid (2.24 g, 88%); mp: 174 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.95 (s, 3H, OCH_3), 5.18 (s, 2H, CH_2), 5.22 (s, 2H, CH_2), 6.59 (s, 1H, H_3), 6.84 (d, J=2.2 Hz, 1H, H_8), 6.98 (d, J=8.5 Hz, 1H, $H_{5'}$), 7.03 (d, J=2.2 Hz, 1H, H_6), 7.33–7.59 (m, 12H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 56.1, 71.2, 71.5, 102.1, 107.3, 108.9, 111.7, 111.8, 111.9, 118.2 (q, J=347 Hz), 120.5, 123.2, 127.4, 127.6, 128.2, 128.7, 128.8, 128.9, 134.7, 136.5, 147.9, 148.4, 153.0,

Table 3
Synthesis of 5-anilinoflavones **3p–r**



Compound	R	Yield[a]
3p	H	37
3q	4-MeO	54
3r	4-F	36

[a] Isolated yield.



Scheme 2. Benzyl deprotection of **3a** and **3b**.

158.3, 161.9, 162.2, 175.4. IR (KBr, cm^{-1}): 1651 (C=O). EIMS *m/z*: 612.2 ($M^{+\bullet}$). Elemental analysis: calcd (%) for $C_{31}H_{23}F_3O_8S$: C 60.78, H 3.78; found: C 60.55, H 3.52.

4.4. General procedure for compounds 3a–o

In a 2–5 mL microwave vial, triflate **2** (200 mg, 0.33 mmol) and the amine (1.32 mmol, 4 equiv) were dissolved in *N*-methylpyrrolidin-2-one (2.8 mL). The solution was warmed under microwave heating conditions at 200 °C until all the starting material has disappeared (Controlled by LC–MS analysis, see Table 2 for reaction times). After cooling, the resulting solution was diluted with CH_2Cl_2 (20 mL), washed with water (5×20 mL), dried over $MgSO_4$, and evaporated under reduced pressure. The residue was then purified by flash chromatography (SiO_2, CH_2Cl_2 unless stated otherwise) to afford the corresponding 5-aminoflavones **3a**–**o**.

*4.4.1. 5-Benzylamino-7-benzyloxy-2-(3-benzyloxy-4-methoxyphenyl)-4H-chromen-4-one (**3a**)*

Obtained as a yellow solid (152 mg, 82%); mp: 182 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.95 (s, 3H, OCH_3), 4.42 (d, *J*=5.6 Hz, 2H, CH_2–NH), 5.04 (s, 2H, CH_2), 5.22 (s, 2H, CH_2), 5.95 (d, *J*=2.2 Hz, 1H, H_6), 6.23 (d, *J*=2.2 Hz, 1H, H_8), 6.42 (s, 1H, H_3), 6.97 (d, *J*=8.5 Hz, 1H, $H_{5'}$), 7.31–7.50 (m, 17H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 47.0, 56.1, 70.0, 71.3, 89.2, 92.2, 104.5, 106.3, 111.5, 120.0, 124.1, 127.0, 127.1, 127.5, 128.1, 128.2, 128.7, 136.2, 136.6, 138.4, 148.2, 151.6, 152.3, 159.7, 161.1, 163.9, 180.9. IR (KBr, cm^{-1}): 3234 (N–H), 1644 (C=O). LC–MS (ESI): t_R=13.70 min; *m/z* $[M+H]^+$: 569.81. Elemental analysis: calcd (%) for $C_{37}H_{31}NO_5$: C 78.01, H 5.49, N 2.46; found: C 77.73, H 5.18, N 2.26.

*4.4.2. 7-Benzyloxy-2-(3-benzyloxy-4-methoxyphenyl)-5-(4-methoxylbenzylamino)-4H-chromen-4-one (**3b**)*

Obtained as a yellow solid (180 mg, 92%); mp: 170 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.80 (s, 3H, OCH_3), 3.96 (s, 3H, CH_3O), 4.35 (d, *J*=5.4 Hz, 2H, CH_2–NH), 5.06 (s, 2H, CH_2), 5.23 (s, 2H, CH_2), 5.96 (d, *J*=2.2 Hz, 1H, H_6), 6.23 (d, *J*=2.2 Hz, 1H, H_8), 6.41 (s, 1H, H_3), 6.87 (d, *J*=8.8 Hz, 2H), 6.97 (d, *J*=8.6 Hz, 1H, $H_{5'}$), 7.28 (d, *J*=8.8 Hz, 2H), 7.33–7.50 (m, 12H), 9.68 (t, *J*=5.4 Hz, 1H, NH). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 46.5, 55.3, 56.1, 70.0, 71.4, 89.2, 92.1, 102.3, 106.3, 111.6, 111.7, 114.1, 120.0, 124.1, 127.4, 127.5, 128.1, 128.2, 128.3, 128.4, 128.7, 130.4, 136.3, 136.6, 148.3, 151.6, 152.4, 158.8, 159.7, 161.1, 163.9, 180.9. IR (KBr, cm^{-1}): 3240 (N–H), 1649 (C=O). LC–MS (ESI): t_R=13.55 min; EIMS *m/z*: 599.5 ($M^{+\bullet}$, 100), 508.3 ($M^{+\bullet}-PhCH_2$, 82.5). Elemental analysis: calcd (%) for $C_{38}H_{33}NO_6$: C 76.11, H 5.55, N 2.34; found: C 75.77, H 5.51, N 2.25.

*4.4.3. 7-Benzyloxy-2-(3-benzyloxy-4-methoxyphenyl)-5-(4-methylbenzylamino)-4H-chromen-4-one (**3c**)*

Obtained as a yellow solid (140 mg, 71%); mp: 177 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.34 (s, 3H, CH_3), 3.95 (s, 3H, OCH_3), 4.37 (d, *J*=5.6 Hz, 2H, CH_2–NH), 5.04 (s, 2H, CH_2), 5.21 (s, 2H, CH_2), 5.96 (d, *J*=2.2 Hz, 1H, H_6), 6.22 (d, *J*=2.2 Hz, 1H, H_8), 6.41 (s, 1H, H_3), 6.96 (d, *J*=8.6 Hz, 1H, $H_{5'}$), 7.13 (d, *J*=8.0 Hz, 2H), 7.24–7.49 (m, 14H), 9.72 (t, *J*=5.6 Hz, 1H, NH). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.1, 46.8, 56.1, 70.0, 71.3, 89.1, 92.1, 104.5, 106.3, 111.5, 120.0, 124.1, 127.0, 127.5, 127.6, 128.1, 128.2, 128.6, 128.7, 129.3, 135.3, 136.2, 136.6, 136.7, 148.2, 151.6, 152.3, 159.7, 161.1, 163.9, 180.9. IR (KBr, cm^{-1}): 3269 (N–H), 1654 (C=O). LC–MS (ESI): t_R=14.08 min; *m/z* $[M+H]^+$: 583.79. Elemental analysis: calcd (%) for $C_{38}H_{33}NO_5$: C 78.20, H 5.70, N 2.40; found: C 77.94, H 5.43, N 2.36.

*4.4.4. 7-Benzyloxy-2-(3-benzyloxy-4-methoxyphenyl)-5-(2-fluorobenzylamino)-4H-chromen-4-one (**3d**)*

Obtained as a yellow solid (130 mg, 68%); mp: 194 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.95 (s, 3H, OCH_3), 4.49 (d, *J*=5.8 Hz, 2H, CH_2–NH), 5.06 (s, 2H, CH_2), 5.23 (s, 2H, CH_2), 5.97 (d, *J*=2.2 Hz, 1H, H_6), 6.25 (d, *J*=2.2 Hz, 1H, H_8), 6.43 (s, 1H, H_3), 6.97 (t, *J*=8.6 Hz, 1H, $H_{5'}$), 7.03–7.09 (m, 2H,), 7.22–7.50 (m, 14H), 9.75 (t, *J*=5.8 Hz, 1H, NH). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 40.3 (d, *J*=4.9 Hz), 56.1, 70.1, 71.3, 89.5, 92.0, 104.6, 106.3, 111.5, 111.6, 115.3 (d, *J*=21.4 Hz), 120.0, 124.0, 124.3 (d, *J*=3.3 Hz), 125.3 (d, *J*=14.1 Hz), 127.4, 127.5, 128.1, 128.2, 128.7 (d, *J*=8.0 Hz), 128.7, 128.8, 128.8 (d, *J*=4.1 Hz), 136.2, 136.6, 148.2, 151.5, 152.4, 159.7, 160.7 (d, *J*=245.3 Hz), 161.2, 164.0, 180.9. IR (KBr, cm^{-1}): 3240 (N–H), 1644 (C=O). LC–MS (ESI): t_R=13.80 min; *m/z* $[M+H]^+$: 587.73. Elemental analysis: calcd (%) for $C_{37}H_{30}FNO_5$: C 75.62, H 5.15, N 2.38; found: C 75.29, H 4.84, N 2.19.

*4.4.5. 7-Benzyloxy-2-(3-benzyloxy-4-methoxyphenyl)-5-(3-fluorobenzylamino)-4H-chromen-4-one (**3e**)*

Obtained as a yellow solid (120 mg, 63%); mp: 157 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.95 (s, 3H, OCH_3), 4.42 (d, *J*=5.6 Hz, 2H, CH_2–NH), 5.03 (s, 2H, CH_2), 5.22 (s, 2H, CH_2), 5.88 (d, *J*=2.2 Hz, 1H, H_6), 6.25 (d, *J*=2.2 Hz, 1H, H_8), 6.43 (s, 1H, H_3), 6.94–7.06 (m, 3H), 7.13 (d, *J*=7.6 Hz, 1H), 7.28–7.49 (m, 13H), 9.79 (t, *J*=5.6 Hz, 1H, NH). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 46.5 (d, *J*=2.5 Hz), 56.1, 70.1, 71.3, 89.4, 92.4, 104.6, 106.3, 111.5, 111.6, 113.9 (d, *J*=19.8 Hz), 114.0 (d, *J*=19.8 Hz), 120.1, 122.4 (d, *J*=2.5 Hz), 124.0, 127.5, 127.6, 128.1, 128.2, 128.7, 128.8, 130.2 (d, *J*=8.2 Hz), 136.1, 136.6, 141.2 (d, *J*=6.6 Hz), 148.3, 151.4, 152.4, 159.7, 161.3, 163.1 (d, *J*=245.2 Hz), 163.9, 181.0. IR (KBr, cm^{-1}): 3241 (N–H), 1645 (C=O). LC–MS (ESI): t_R=13.70 min; *m/z* $[M+H]^+$: 587.83. Elemental analysis: calcd (%) for $C_{37}H_{30}FNO_5$: C 75.62, H 5.15, N 2.38; found: C 75.38, H 4.80, N 2.31.

*4.4.6. 7-Benzyloxy-2-(3-benzyloxy-4-methoxyphenyl)-5-(4-fluorobenzylamino)-4H-chromen-4-one (**3f**)*

Obtained as a yellow solid (125 mg, 65%); mp: 179 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.95 (s, 3H, OCH_3), 4.38 (d, *J*=5.6 Hz, 2H, CH_2–NH), 5.05 (s, 2H, CH_2), 5.23 (s, 2H, CH_2), 5.90 (d, *J*=2.2 Hz, 1H, H_6), 6.25 (d, *J*=2.2 Hz, 1H, H_8), 6.42 (s, 1H, H_3), 6.96–7.03 (m, 3H,), 7.26–7.50 (m, 14H), 9.74 (t, *J*=5.6 Hz, 1H, NH). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 46.8, 56.1, 70.0, 71.3, 89.3, 92.3, 104.5, 106.3, 111.4, 111.6, 115.5 (d, *J*=20.7 Hz), 120.0, 124.1, 127.4, 127.5, 128.1, 128.2, 128.5 (d, *J*=8.2 Hz), 128.7, 128.8, 134.0 (d, *J*=3.3 Hz), 136.1, 136.6, 148.2, 151.4, 152.4, 159.7, 161.2, 162.0 (d, *J*=244.5 Hz), 163.9, 180.9. IR (KBr, cm^{-1}): 3257 (N–H), 1652 (C=O). LC–MS (ESI): t_R=13.73 min; *m/z* $[M+H]^+$: 587.87. Elemental analysis: calcd (%) for $C_{37}H_{30}FNO_5$: C 75.62, H 5.15, N 2.38; found: C 75.47, H 4.95, N 2.29.

*4.4.7. 7-Benzyloxy-2-(3-benzyloxy-4-methoxyphenyl)-5-(4-trifluoromethylbenzylamino)-4H-chromen-4-one (**3g**)*

Obtained as a yellow solid (127 mg, 61%); mp: 174 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.95 (s, 3H, OCH_3), 4.48 (d, *J*=5.8 Hz, 2H, CH_2–NH), 5.04 (s, 2H, CH_2), 5.23 (s, 2H, CH_2), 5.84 (d, *J*=2.2 Hz, 1H, H_6), 6.26 (d, *J*=2.2 Hz, 1H, H_8), 6.44 (s, 1H, H_3), 6.97 (d, *J*=8.5 Hz, 1H, $H_{5'}$), 7.33–7.58 (m, 16H), 9.84 (t, *J*=5.8 Hz, 1H, NH). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 46.5, 56.1, 70.1, 71.3, 89.6, 92.4, 104.7, 111.6, 111.7, 120.1, 124.0, 106.3, 125.6 (q, *J*=3.3 Hz), 126.9 (q, *J*=271.8 Hz, CF_3), 127.1, 127.4, 127.5, 128.2, 128.3, 128.7, 128.8, 129.4 (q, *J*=32.2 Hz), 136.1, 136.6, 142.7, 148.3, 151.3, 152.5, 159.8, 161.4, 163.9, 181.0. IR (KBr, cm^{-1}): 3259 (N–H), 1651 (C=O). LC–MS (ESI): t_R=14.08 min. EIMS

m/*z*: 637.0 ($M^{+\bullet}$, 100), 546.0 ($M^{+\bullet}-PhCH_2$, 5.6). Elemental analysis: calcd (%) for $C_{38}H_{30}F_3NO_5$: C 71.58, H 4.74, N 2.20; found: C 71.87, H 4.39, N 2.53.

4.4.8. 7-Benzyloxy-2-(3-benzyloxy-4-methoxyphenyl)-5-(3-trifluoromethylbenzylamino)-4H-chromen-4-one (**3h**)

Obtained as a yellow solid (140 mg, 67%); mp: 171 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.95 (s, 3H, OCH_3), 4.47 (d, *J*=5.6 Hz, 2H, CH_2–NH), 5.04 (s, 2H, CH_2), 5.23 (s, 2H, CH_2), 5.87 (d, *J*=2.2 Hz, 1H, H_6), 6.26 (d, *J*=2.2 Hz, 1H, H_8), 6.44 (s, 1H, H_3), 6.97 (d, *J*=8.6 Hz, 1H, $H_{5'}$), 7.33–7.60 (m, 16H), 9.83 (t, *J*=5.6 Hz, 1H, NH). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 46.5, 56.1, 70.1, 71.4, 89.6, 92.4, 104.7, 106.3, 111.6, 111.7, 120.1, 123.8 (q, *J*=4.1 Hz), 124.0, 124.1 (q, *J*=272.6 Hz), 124.2 (q, *J*=4.1 Hz), 127.4, 127.5, 128.2, 128.3, 128.7, 128.8, 129.2, 130.2, 130.9 (q, *J*=31.3 Hz), 136.1, 136.6, 139.6, 148.3, 151.3, 152.5, 159.8, 161.3, 163.9, 181.0. IR (KBr, cm^{-1}): 3234 (N–H), 1644 (C=O). LC–MS (ESI): t_R=14.02. EIMS *m*/*z*: 637.3 ($M^{+\bullet}$, 100), 546.2 ($M^{+\bullet}-PhCH_2$, 9.0). Elemental analysis: calcd (%) for $C_{38}H_{30}F_3NO_5$: C 71.58, H 4.74, N 2.20; found: C 71.88, H 4.38, N 2.51.

4.4.9. 7-Benzyloxy-2-(3-benzyloxy-4-methoxyphenyl)-5-(2-trifluoromethoxybenzylamino)-4H-chromen-4-one (**3i**)

Obtained as a yellow solid (144 mg, 67%); mp: 153 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.96 (s, 3H, OCH_3), 4.52 (d, *J*=5.6 Hz, 2H, CH_2–NH), 5.04 (s, 2H, CH_2), 5.22 (s, 2H, CH_2), 5.89 (d, *J*=2.2 Hz, 1H, H_6), 6.26 (d, *J*=2.2 Hz, 1H, H_8), 6.44 (s, 1H, H_3), 6.97 (d, *J*=8.6 Hz, 1H, $H_{5'}$), 7.26–7.50 (m, 16H), 9.80 (t, *J*=5.6 Hz, 1H, NH). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 41.2, 56.1, 70.1, 71.3, 89.7, 92.0, 100.5, 104.6, 106.3, 111.4, 111.6, 120.1, 120.7, 122.3 (q, *J*=225.5 Hz), 124.0, 127.2, 127.4, 128.1, 128.2, 128.3, 128.5, 128.7, 128.8, 130.9, 136.1, 136.6, 148.3, 151.5, 152.4, 159.7, 161.0, 161.3, 164.0, 181.0. IR (KBr, cm^{-1}): 3236 (N–H), 1644 (C=O). LC–MS (ESI): t_R=14.17. EIMS *m*/*z*: 562.1 ($M^{+\bullet}-PhCH_2$, 100). Elemental analysis: calcd (%) for $C_{38}H_{30}F_3NO_6$: C 69.83, H 4.63, N 2.14; found: C 69.63, H 4.32, N 1.81.

4.4.10. 7-Benzyloxy-2-(3-benzyloxy-4-methoxyphenyl)-5-isobutylamino-4H-chromen-4-one (**3j**)

Obtained as a yellow solid after chromatography with CH_2Cl_2/MeOH 98:2 (135 mg, 77%); mp: 160 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.02 (d, *J*=6.7 Hz, 6H, $2CH_3$), 1.99 (m, 1H, CH–$(CH_3)_2$), 2.96 (dd, *J*=6.7 Hz and 5.2 Hz, 2H, CH_2–NH), 3.95 (s, 3H, OCH_3), 5.13 (s, 2H, CH_2), 5.22 (s, 2H, CH_2), 5.97 (d, *J*=2.2 Hz, 1H, H_6), 6.20 (d, *J*=2.2 Hz, 1H, H_8), 6.38 (s, 1H, H_3), 6.96 (d, *J*=8.6 Hz, 1H, $H_{5'}$), 7.29–7.49 (m, 12H), 9.38 (t, *J*=5.2 Hz, 1H, NH). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.6, 27.6, 50.8, 56.1, 70.1, 71.3, 88.3, 91.3, 104.3, 106.3, 111.5, 111.6, 120.0, 124.2, 127.5, 127.6, 128.1, 128.2, 128.7, 128.8, 136.4, 136.6, 148.2, 152.0, 152.3, 159.9, 161.0, 164.0, 180.9. IR (KBr, cm^{-1}): 3259 (N–H), 1649 (C=O). LC–MS: t_R=14.22 min; *m*/*z* $[M+H]^+$: 535.78. Elemental analysis: calcd (%) for $C_{34}H_{33}NO_5$: C 76.24, H 6.21, N 2.61; found: C 75.88, H 5.88, N 2.36.

4.4.11. 7-Benzyloxy-2-(3-benzyloxy-4-methoxyphenyl)-5-butylamino-4H-chromen-4-one (**3k**)

Obtained as a yellow solid (124 mg, 71%); mp: 147 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.96 (t, *J*=7.3 Hz, 3H, CH_3), 1.48 (sept., *J*=7.3 Hz, 2H, CH_2–CH_3), 1.66 (quint., *J*=7.3 Hz, 2H, CH_2–CH_2NH), 3.14 (dd, *J*=7.3 Hz and 5.2 Hz, 2H, CH_2NH), 3.95 (s, 3H, OCH_3), 5.13 (s, 2H, CH_2), 5.22 (s, 2H, CH_2), 5.98 (d, *J*=2.2 Hz, 1H, H_6), 6.20 (d, *J*=2.2 Hz, 1H, H_8), 6.38 (s, 1H, H_3), 6.97 (d, *J*=8.6 Hz, 1H, $H_{5'}$), 7.26–7.50 (m, 12H), 9.25 (t, *J*=5.2 Hz, 1H, NH). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 13.9, 20.4, 30.8, 42.7, 56.1, 70.1, 71.3, 88.4, 91.3, 104.3, 106.3, 111.5, 111.6, 119.9, 124.2, 127.4, 127.5, 128.1, 128.2, 128.6, 128.7, 136.3, 136.6, 148.2, 151.9, 152.3, 159.8, 160.9, 164.0, 180.8. IR (KBr, cm^{-1}): 3258 (N–H), 1645 (C=O). LC–MS: t_R=14.08 min; *m*/*z* $[M+H]^+$: 535.84. Elemental analysis: calcd (%) for $C_{34}H_{33}NO_5$: C 76.24, H 6.21, N 2.61; found: C 75.88, H 5.95, N 2.45.

4.4.12. 7-Benzyloxy-2-(3-benzyloxy-4-methoxyphenyl)-5-(2-N,N-dimethylaminoethylamino)-4H-chromen-4-one (**3l**)

Obtained as a yellow solid after flash chromatography on alumina gel with CH_2Cl_2/MeOH 99:1 (87 mg, 48%); mp: 130 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.34 (s, 6H, 2 CH_3), 2.65 (t, *J*=6.6 Hz, 2H, CH_2–$N(CH_3)_2$), 3.29 (dd, *J*=6.6 Hz and 5.1 Hz, 2H, CH_2–NH), 3.95 (s, 3H, OCH_3), 5.14 (s, 2H, CH_2), 5.22 (s, 2H, CH_2), 6.01 (d, *J*=2.2 Hz, 1H, H_6), 6.22 (d, *J*=2.2 Hz, 1H, H_8), 6.39 (s, 1H, H_3), 6.96 (d, *J*=8.6 Hz, 1H, $H_{5'}$), 7.32–7.49 (m, 12H), 9.37 (t, *J*=5.1 Hz, 1H, NH). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 40.9, 45.4, 56.1, 57.7, 70.0, 71.3, 88.7, 91.4, 104.4, 106.3, 111.4, 111.5, 119.9, 124.1, 127.4, 127.5, 128.1, 128.2, 128.6, 128.7, 136.3, 136.6, 148.2, 151.5, 152.3, 159.8, 161.0, 164.0, 180.7. IR (KBr, cm^{-1}): 3248 (N–H), 1648 (C=O). LC–MS (ESI): t_R=9.30 min; *m*/*z* $[M+H]^+$: 550.82. Elemental analysis: calcd (%) for $C_{34}H_{34}N_2O_5$: C 74.16, H 6.22, N 5.09; found: C 73.87, H 6.08, N 4.71.

4.4.13. 7-Benzyloxy-2-(3-benzyloxy-4-methoxyphenyl)-5-(4-methylpiperidin-1-yl)-4H-chromen-4-one (**3m**)

Obtained as a yellow solid after chromatography with CH_2Cl_2/MeOH 94:6 (152 mg, 83%); mp: 164 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.01 (d, *J*=6.4 Hz, 3H, CH_3–CH), 1.69–1.72 (m, 1H, CH–CH_3), 2.63–2.66 (m, 4H, $2CH_2$), 3.43–3.46 (m, 4H, $2CH_2$), 3.95 (s, 3H, OCH_3), 5.14 (s, 2H, CH_2), 5.22 (s, 2H, CH_2), 6.45 (s, 1H, H_3), 6.48 (d, *J*=2.2 Hz, 1H, H_6), 6.87 (d, *J*=8.6 Hz, 1H, H_8), 6.97 (d,=8.6 Hz, 1H, $H_{5'}$), 7.32–7.49 (m, 12H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.9, 30.7, 34.2, 53.6, 56.0, 70.3, 71.3, 94.3, 102.5, 107.6, 111.4, 111.5, 111.6, 120.0, 124.0, 127.4, 127.6, 128.1, 128.3, 128.7, 128.8, 136.0, 136.6, 148.2, 152.2, 154.8, 159.7, 160.7, 162.5, 177.3. IR (KBr, cm^{-1}): 1641 (C=O). LC–MS (ESI): t_R=9.72 min; *m*/*z* $[M+H]^+$: 561.78. Elemental analysis: calcd (%) for $C_{36}H_{35}NO_5$: C 76.98, H 6.28, N 2.49; found: C 76.72, H 6.41, N 2.20.

4.4.14. 7-Benzyloxy-2-(3-benzyloxy-4-methoxyphenyl)-5-(morpholin-4-yl)-4H-chromen-4-one (**3n**)

Obtained as a yellow solid after elution with CH_2Cl_2/triethylamine 98:2 (120 mg, 67%); mp: 202 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.08–3.12 (m, 4H), 3.96 (s, 3H, OCH_3), 3.97–3.99 (m, 4H), 5.15 (s, 2H, CH_2), 5.23 (s, 2H, CH_2), 6.46 (s, 1H, H_3), 6.47 (d, *J*=2.2 Hz, 1H, H_6), 6.63 (d, *J*=8.5 Hz, 1H, H_8), 6.98 (d, *J*=8.6 Hz, 1H, $H_{5'}$), 7.32–7.53 (m, 12H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 53.2, 56.1, 67.1, 70.4, 71.3, 95.1, 102.5, 107.7, 111.4, 111.5, 111.6, 119.9, 123.8, 127.4, 127.6, 128.1, 128.4, 128.7, 128.8, 135.7, 136.6, 148.2, 152.3, 153.9, 160.1, 160.7, 162.6, 177.2. IR (KBr, cm^{-1}): 1642 (C=O). LC–MS (ESI): t_R=11.67 min; *m*/*z* $[M+H]^+$: 549.75. Elemental analysis: calcd (%) for $C_{34}H_{31}NO_6$: C 74.30, H 5.69, N 2.55; found: C 73.95, H 5.36, N 2.38.

4.4.15. 7-Benzyloxy-2-(3-benzyloxy-4-methoxyphenyl)-5-(4-methylpiperazin-1-yl)-4H-chromen-4-one (**3o**)

Obtained as a yellow solid after flash chromatography on alumina gel with CH_2Cl_2/MeOH 99:1 (72 mg, 39%); mp: 181 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.39 (s, 3H, CH_3), 2.78–2.84 (m, 4H), 3.16–3.23 (m, 4H), 3.96 (s, 3H, OCH_3), 5.15 (s, 2H, CH_2), 5.23 (s, 2H, CH_2), 6.45 (s, 1H, H_3), 6.48 (d, *J*=2.2 Hz, 1H, H_6), 6.62 (d, *J*=8.6 Hz, 1H, H_8), 6.98 (d, *J*=8.6 Hz, 1H, $H_{5'}$), 7.33–7.50 (m, 12H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 45.8, 52.2, 55.0, 56.1, 70.3, 71.3, 95.1, 102.7, 107.7, 111.4, 111.5, 111.6, 120.0, 123.9, 127.4, 127.6, 128.1, 128.4, 128.7, 128.8, 135.8, 136.6, 148.2, 152.4, 153.5, 160.0, 160.7, 162.6, 177.2. IR (KBr, cm^{-1}): 1643 (C=O). LC–MS (ESI): t_R=8.98 min; *m*/*z* $[M+H]^+$: 562.81. Elemental analysis: calcd (%) for $C_{35}H_{34}N_2O_5$: C 74.71, H 6.09, N 4.98; found: C 74.57, H 5.91, N 4.58.

4.5. General procedure for compounds 3p–r

In a 2–5 mL microwave vial, triflate **2** (200 mg, 0.33 mmol), aniline (1.32 mmol), and triethylamine (0.12 mL, 0.33 mmol) were dissolved in *N*-methylpyrrolidin-2-one (2.5 mL). The solution was warmed under microwave heating conditions at 200 °C for 1 hour. After cooling, the resulting solution was diluted with CH_2Cl_2

(20 mL), washed with water (5×20 mL), dried over $MgSO_4$, and evaporated under reduced pressure. The residue was then purified by flash chromatography (Al_2O_3, CH_2Cl_2/MeOH 98:2) to afford the corresponding 5-anilinoflavones **3p–r**.

*4.5.1. 7-Benzyloxy-2-(3-benzyloxy-4-methoxyphenyl)-5-(phenylamino)-4H-chromen-4-one (**3p**)*

Obtained as a yellow solid (67 mg, 37%); mp: 172 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.96 (s, 3H, OCH_3), 5.08 (s, 2H, CH_2), 5.24 (s, 2H, CH_2), 6.36 (d, J=2.2 Hz, 1H, H_6), 6.46 (s, 1H, H_3), 6.61 (d, J=2.2 Hz, 1H, H_8), 6.99 (d, J=8.5 Hz, 1H, $H_{5'}$), 7.09–7.52 (m, 17H), 11.16 (s, 1H, NH). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 56.1, 70.1, 71.3, 91.1, 93.7, 104.9, 106.1, 111.5, 111.6, 120.1, 122.9, 123.0, 123.9, 124.0, 127.4, 127.5, 128.1, 128.2, 128.7, 129.4, 136.1, 136.6, 140.2, 148.3, 148.8, 152.5, 159.6, 161.5, 163.6, 180.9. IR (KBr, cm^{-1}): 1644 (C=O). LC–MS (ESI): t_R=14.03 min; m/z $[M+H]^+$: 555.77. Elemental analysis: calcd (%) for $C_{36}H_{29}NO_5$: C 77.82, H 5.26, N 2.52; found: C 77.56, H 4.93, N 2.54.

*4.5.2. 7-Benzyloxy-2-(3-benzyloxy-4-methoxyphenyl)-5-(4-methoxyphenylamino)-4H-chromen-4-one (**3q**)*

Obtained as a yellow solid (104 mg, 54%); mp: 175 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.83 (s, 3H, OCH_3), 3.96 (s, 3H, OCH_3), 5.05 (s, 2H, CH_2), 5.24 (s, 2H, CH_2), 6.30 (d, J=2.2 Hz, 1H, H_6), 6.34 (d, J=2.2 Hz, 1H, H_8), 6.46 (s, 1H, H_3), 6.85 (d, J=8.8 Hz, 2H), 6.98 (d, J=8.6 Hz, 1H), 7.17 (d, J=8.8 Hz, 2H), 7.33–7.51 (m, 12H), 10.88 (s, 1H, NH). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 55.6, 56.1, 70.0, 71.3, 90.4, 93.1, 104.6, 106.1, 111.5, 111.6, 114.7, 120.1, 124.0, 126.0, 127.5, 127.6, 128.1, 128.2, 128.7, 128.8, 132.9, 136.2, 136.6, 148.3, 150.3, 152.4, 156.8, 159.7, 161.3, 163.6, 180.9. IR (KBr, cm^{-1}): 1650 (C=O). LC–MS (ESI): t_R=13.85 min; m/z $[M+H]^+$: 585.74. Elemental analysis: calcd (%) for $C_{37}H_{31}NO_6$: C 75.88, H 5.34, N 2.39; found: C 75.52, H 5.08, N 2.41.

*4.5.3. 7-Benzyloxy-2-(3-benzyloxy-4-methoxyphenyl)-5-(4-fluorophenylamino)-4H-chromen-4-one (**3r**)*

Obtained as a yellow solid (67 mg, 36%); mp: 196 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.96 (s, 3H, OCH_3), 5.07 (s, 2H, CH_2), 5.24 (s, 2H, CH_2), 6.34 (d, J=2.2 Hz, 1H, H_6), 6.40 (d, J=2.2 Hz, 1H, H_8), 6.47 (s, 1H, H_3), 6.98 (d, J=8.5 Hz, 1H, $H_{5'}$), 7.02 (d, J=8.6 Hz, 1H), 7.04 (d, J=8.6 Hz, 1H), 7.17 (d, J=8.6 Hz, 1H), 7.19 (d, J=8.6 Hz, 1H), 7.34–7.52 (m, 12H), 11.01 (s, 1H, NH). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 56.1, 70.1, 71.4, 91.0, 93.1, 104.8, 106.1, 111.5, 116.7 (d, J=22.3 Hz), 120.1, 123.9, 125.0 (d, J=8.2 Hz), 127.5, 128.1, 128.2, 128.7, 136.1, 136.6, 147.6, 148.3, 149.5, 152.5, 159.6, 161.2 (d, J=245.2 Hz), 161.5, 163.6, 181.0. IR (KBr, cm^{-1}): 1645 (C=O). LC–MS (ESI): t_R=13.97 min; m/z $[M+H]^+$: 573.81. Elemental analysis: calcd (%) for $C_{36}H_{28}FNO_5$: C 75.38, H 4.92, N 2.44; found: C 75.01, H 4.57, N 2.34.

4.6. 5-Amino-7-hydroxy-2-(3-hydroxy-4-methoxyphenyl)-4*H*-chromen-4-one (4a)

Compound **3a** (0.37 g, 0.65 mmol) was dissolved in MeOH (50 mL) and the solution was degassed. Pd/C (50 mg) was added and the solution was stirred under H_2 in a Paar apparatus for 5 h. After filtration on Celite, the solvent was removed under reduced pressure and the residue was crystallized in diethyl ether to give **4a** as a yellow solid (0.132 g, 68%); mp: 182 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 3.82 (s, 3H, OCH_3), 5.90 (d, 1H, J=1.9 Hz, H_6), 6.00 (d, 1H, J=1.9 Hz, H_8), 6.40 (s, 1H, H_3), 7.02 (d, 1H, J=8.8 Hz), 7.31–7.40 (m, 4H, 2H_{ar} and 2 OH). ^{13}C NMR (100 MHz, DMSO-d_6) δ: 55.7, 90.6, 96.6, 102.2, 105.0, 112.1, 112.5, 117.8, 123.6, 146.9, 150.5, 152.0, 158.9, 160.3, 163.7, 179.5. IR (KBr, cm^{-1}): 3449, 3330, 1642 (C=O). HRMS (EI): calcd ($M^{+\cdot}$) for $C_{16}H_{13}NO_5$: 299.0793, found: 299.0800.

4.7. 7-Hydroxy-2-(3-hydroxy-4-methoxyphenyl)-5-(4-methoxybenzylamino)-4*H*-chromen-4-one (4b)

Compound **3b** (0.75 g, 1.25 mmol) was dissolved in MeOH (50 mL) and the solution was degassed. Pd/C (50 mg) was added and the solution was stirred under H_2 in a Paar apparatus for 5 h. After filtration on Celite, the solvent was removed under reduced pressure and the residue purified by flash chromatography (SiO_2, CH_2Cl_2/MeOH 98/2) to afford **4b** as a yellow solid (0.313 g, 60%); mp: 245 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 3.73 (s, 3H, OCH_3), 3.83 (s, 3H, OCH_3), 4.29 (d, 2H, J=5.1 Hz, CH_2–NH), 5.82 (d, 1H, J=1.7 Hz, H_6), 6.07 (d, 1H, J=1.7 Hz, H_8), 6.45 (s, 1H, H_3), 6.91 (d, 2H, J=8.3 Hz), 7.04 (d, 1H, J=8.5 Hz, $H_{5'}$), 7.27 (d, 2H, J=8.3 Hz), 7.32 (d, 1H, J=2.2 Hz, $H_{2'}$), 7.44 (dd, 1H, J=8.5 and 2.2 Hz, $H_{6'}$), 9.54 (t, 1H, J=5.1 Hz, NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ: 45.5, 55.0, 55.7, 90.0, 92.4, 102.4, 105.1, 112.2, 112.5, 114.0, 117.9, 123.4, 128.4, 146.7, 150.5, 151.2, 158.4, 159.1, 160.4, 179.5. IR (KBr, cm^{-1}): 3189 (NH), 1637 (C=O). LC–MS (ESI): t_R=9.58 min; m/z $[M+H]^+$: 419.93. HRMS (EI): calcd ($M^{+\cdot}$) for $C_{24}H_{21}NO_6$: 419.1369, found: 419.1375.

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