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Synthesis of new 6-amino substituted flavones using Buchwald coupling reactions

T. Sowjanya[1*], Gogula Thirupathi[2], Y. Jayaprakash Rao[3], N.Y. Sreenivasa Murthy[4]
[1]Department of Chemistry, Jawaharlal Nehru Technological University, Hyderabad-500085, India
[2]Department of Chemistry, University College of science, Osmania University, Hyderabad-500007, India
[3]Department of Chemistry, Telangana University, Nizamabad-503322, India
[4]Department of Chemistry, Anurag group of Institutions, Hyderabad-501301, India
***Corresponding author: E-Mail: sowjitummala7@gmail.com, Tel: +919849384036**

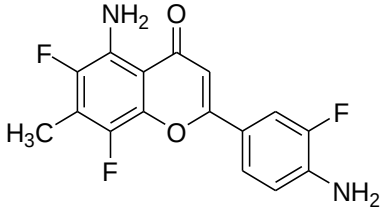
ABSTRACT

Synthesis of a new series of N-substituted flavones from 6-amino flavone and aryl and hetero aryl halides by using palladium catalyzed Buchwald-Hartwig cross coupling reaction reported. These reactions occurred in high yield with 0.05 mol% catalyst loading. All the synthesized products were characterized by IR, ^{1}H NMR, ^{13}C NMR, Mass spectrometry and elemental analysis.

KEY WORDS: Aminoflavone, Buchwald coupling, $Pd_2(dba)_3$, xantphos.

1. INTRODUCTION

In vitro and *in vivo* studies of flavones were showed a wide range of biological and pharmacological activities (Ono, 2009), those are anti-allergic (Matsuo, 1996), antiosteoporotic (Vijayaraghavan, 1991), anti-HIV (Huck, 2000), antiulcer (Beli, 1995), anti-hepatotoxic (Hanghic, 2005), anti-proliferative (Yang, 2001), enzyme-inhibitory effects (Polkowski, 2000), anti-arthritic (Kim, 1999), vasculo-protective (Perez-Vizcanio, 2002), antiviral (Bae, 2000), anti-inflammatory (Landolfi, 1984), antimicrobial (Xu, Lee, 2001), antidiabetic (Havsteen, 1983), anti-oxidant (Daskiewicz, 2005; Gao, 2005), anti-cancer (Han, 1997; Brit, 2001), anti-fungal activities (Nijveldt, 2001). Amino flavones and aminoflavone prodrugs have demonstrated antiproliferactive (Meng, 2006) activity against several renal, breast and ovarian cancer cell lines (Terzuoli, 2010; Mclean, 2008). The amino flavones kill tumor cells without destroying bone marrow and having other toxic effects (Edward, 2002) (Fig-1).



5-amino-2-(4-amino-3-fluorophenyl)-6,8-difluoro-7-methyl-4H-chromen-4-one

Figure.1. Biologically active aminoflavone

Carbon–Nitrogen bond formation is one of the most powerful routes to the synthesis of aryl amine compounds that have diverse range of potential applications (Venkat Reddy, 2008; Buchwald, 2006; Xie, 2006; Harris, 2002; Stauffer, 2000; Tundel, 2006). Pd-catalyzed Buchwald-Hartwig coupling reaction of amines with aryl halides is preferred methodology because of its advantages over the other approaches such as nucleophilic aromatic substitution and reductive amination (Dai & Gao, 2006; Navarro, 2004; Shen, 2008; Parrish, 2001).

2. EXPERIMENTAL METHODS

All used reagents were purchased from Sigma-Aldrich and commercial sources and were used without further purification. Melting points (m.p.) were determined in open capillary tubes on a Buchi 530 melting point apparatus and are uncorrected. Thin layer chromatography (TLC) was performed to monitor progress of the reaction and assess purity of the compounds; spots were detected by their absorption under UV light. IR spectra were recorded with IR prestige-21 (FT-IR, Shimadzu) and mass spectra were recorded using 'Hewlett-Packard' HP GS/MS 5890/5972. ^{1}H NMR spectra were recorded with Bruker DPX operating at 400MHz in $CDCl_3$ or DMSO-d_6 solution, with tetramethylsilane (TMS) as an internal standard. Chemical shifts are shown as d values (ppm), the J values are expressed in Hertz (Hz). Signals are represented as s (singlet), d (doublet), t (triplet), q (quintet), or m (multiplet). Column chromatography was carried out on silica gel (100-200 mesh) using ethyl acetate/hexane (1:9) as eluent.

General procedure for the synthesis of compounds 7a-q: Dried round bottom flask containing a stir bar was charged with of $Pd_2(dba)_3$ (0.02 mmol) and Xantphos (0.02 mmol) ligand. The RB was sealed with a plastic septum and then evacuated and backfilled with Nitrogen; this sequence was repeated two additional times. The 6-amino flavone (0.42 mmol), aryl/hetero aryl halide (0.50 mmol), NaO-*t*-Bu (0.63 mmol), and 1, 4-Dioxane (5ml) were added prior to the evacuation and backfill sequence. Aryl /hetero aryl halides were successively added via syringe. The round bottom flask was submitted to heating (110°C) with stirring until the starting 6-amino flavone had been

completely consumed as judged by TLC analysis. The mixture was cooled to room temperature and then diluted with cool water and ethyl acetate. The organic layers were separated and wash with brine solution, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The crude material was purified by column chromatography on silica gel (eluting with ethyl acetate/hexane mixtures). All the synthesized compounds were confirmed by spectral and analytical data.

2-phenyl-6-(pyridin-2-ylamino)-4H-chromen-4-one (7a): Yield: 85%, m.p: 202-205°C, IR (KBr) cm^{-1}: 3132 (N-H), 1631 (C=O); ^{1}H-NMR (400MHz, $CDCl_3$) δ: 8.26 (1H, d, *J* = 8.75 Hz), 8.08 (1H, d, *J* = 8.74 Hz), 7.95-7.89 (3H, m), 7.58-7.53 (5H, m), 6.91 (1H, d, *J* = 6.79 Hz), 6.82 (2H, d, *J* = 6.75 Hz), 6.67 (1H, s); ^{13}C-NMR (100MHz, $CDCl_3$) δ: 177.2, 162.0, 155.4, 150.1 147.2, 139.4, 137.4, 131.6, 131.4, 129.1, 126.1, 124.9, 123.7, 118.7, 114.9, 111.1, 110.5, 106.2, 79.1; MS: *m/z* = 315 $[M+H]^+$; Anal. Calcd. for $C_{20}H_{14}N_2O_2$: C 76.42; H 4.49; N 8.91; Found: C 76.92; H 4.24; N 8.71.

6-(2,4,6-tris(trifluoromethyl)phenylamino)-2-phenyl-4H-chromen-4-one (7b): Yield: 81%, m.p: 206-208°C, IR (KBr) cm^{-1}: 3135 (N-H), 1651 (C=O). ^{1}H-NMR (400MHz, $CDCl_3$) δ: 7.95 (2H, m), 7.63 (3H, d, *J* = 8.75 Hz), 7.56 (2H, m), 7.39 (2H, s), 6.83 (2H, s), 6.21 (1H, s); ^{13}C-NMR (100MHz, $CDCl_3$) δ: 177.2, 163.7, 152.2, 146.1, 139.4, 132.2, 131.1, 130.7, 126.1, 124.9, 123.9, 120.1, 119.1, 115.2, 112.4, 106.3; MS: *m/z* = 518 $[M+H]^+$; Calcd. for $C_{24}H_{12}F_9NO_2$: C 55.72; H 2.34; N 2.71; Found: C 54.98; H 2.55; N 3.04.

6-(4-nitrobenzylamino)-2-phenyl-4H-chromen-4-one (7c): Yield 75%, m.p: 130-132°C, IR (KBr) cm^{-1}: 3315 (N-H), 1721 (C=O). ^{1}H-NMR (400MHz, $CDCl_3$) δ: 8.20 (3H,m), 8.02 (1H, d, *J* = 8.75 Hz), 7.63-7.50 (3H, m), 7.31-7.23 (3H, m), 7.13 (1H, d, *J* = 8.75 Hz), 6.88 (1H, d, *J* = 8.71 Hz), 6.62 (2H, d, *J* = 6.75 Hz). ^{13}C-NMR (100MHz, $CDCl_3$) δ: 182.2, 163.7, 147.8, 146.4, 145.7, 142.3, 130.4, 128.7, 128.0, 127.8, 126.0, 124.8, 120.2, 118.5, 112.2, 104.5, 46.2; MS: *m/z* = 374 $[M+H]^+$. Anal. Calcd. for $C_{22}H_{16}N_2O_4$: C 70.96; H 4.33; N 7.52; Found: C 70.14; H 4.68; N 7.17.

4-(4-oxo-2-phenyl-4H-chromen-6-ylamino) benzonitrile (7d): Yield 65%, m.p: 100-101°C, IR (KBr) cm^{-1}: 3327 (N-H), 1654 (C=O). ^{1}H-NMR (400MHz, $CDCl_3$) δ: 8.02 (1H, m), 7.70 (9H, m), 7.07 (3H, m), 6.68 (1H, s); ^{13}C-NMR (100MHz, $CDCl_3$) δ: 182.5, 163.0, 146.9, 143.8, 134.3, 133.2, 130.4, 128.7, 128.0, 126.2, 125.6, 124.9, 119.8, 118.5, 117.6, 115.8, 104.2, 102.6. MS: *m/z* = 339 $[M+H]^+$. Anal. Calcd. for $C_{22}H_{14}N_2O_2$: C 78.09; H 4.17; N 8.28; Found: C 77.91; H 4.35; N 8.46.

6-(4-(trifluoromethyl) phenyl amino)-2-phenyl-4H-chromen-4-one (7e): Yield 78%, m.p: 118-120°C, IR (KBr) cm^{-1}: 3327 (N-H), 1651 (C=O). ^{1}H-NMR (400MHz, $CDCl_3$) δ: 7.87 (1H, m), 7.65 (1H, d, *J* = 8.75 Hz), 7.50 (2H, m), 7.35 (2H, m), 7.21 (2H, m), 7.05 (1H, m), 6.97 (1H, m), 6.75 (1H, m), 6.06 (1H, s), 5.97 (1H, s), 5.64 (1H, s); ^{13}C-NMR (100MHz, $CDCl_3$) δ: 162.1, 157.2, 154.5, 150.1, 140.7, 136.8, 135.2, 132.1, 131.0, 130.9, 128.0, 126.2, 123.9, 120.1, 118.5, 115.8, 112.2, 110.6, 106.2, 98.1, 55.8; MS: *m/z* = 382 $[M+H]^+$; Anal. Calcd. for $C_{22}H_{14}F_3NO_2$: C 69.29; H 3.70; N 3.67; Found: C 68.98; H 4.01; N 3.87.

6-(o-tolylamino)-2-phenyl-4H-chromen-4-one (7f): Yield 60%, m.p: 106-108°C, IR (KBr) cm^{-1}: 3327 (N-H), 1654 (C=O). ^{1}H-NMR (400MHz, $CDCl_3$) δ: 7.87 (3H, m), 7.62 (8H, m), 6.83 (6H, m); ^{13}C-NMR (100MHz, $CDCl_3$) δ: 183.1, 164.2, 147.0, 138.6, 134.5, 131.8, 130.2, 128.7, 128.0, 126.7, 125.0, 119.0, 118.2, 104.5, 20.2; MS: *m/z* = 328 $[M+H]^+$; $C_{22}H_{17}NO_2$. Anal. Calcd. for: C 80.71; H 5.43; N 4.28; Found: C 81.71; H 4.58; N 3.63.

2-phenyl-6-(phenyl amino)-4H-chromen-4-one (7g): Yield 82%, m.p: 200-202°C, IR (KBr) cm^{-1}: 3325 (N-H), 1631 (C=O). ^{1}H-NMR (400MHz, $CDCl_3$) δ: 7.93 (2H, m), 7.53 (5H, m), 7.21 (2H, m), 6.83 (4H, m), 6.06 (1H, d, *J* = 6.74 Hz), 5.93 (1H, s); ^{13}C-NMR (100MHz, $CDCl_3$) δ: 182.2, 163.7, 146.8, 139.6, 134.3, 130.4, 129.7, 129.7, 128.7, 128.0, 126.4, 125.6, 124.9, 119.1, 118.6, 118.3, 117.8, 104.5; MS: *m/z* = 314 $[M+H]^+$; Anal. Calcd. for $C_{21}H_{15}NO_2$: C 80.49; H 4.82; N 4.47; Found: C 80.01; H 4.95; N 4.62.

2-phenyl-6-(pyridin-3-ylamino)-4H-chromen-4-one (7h): Yield 83%, m.p: 208-210°C, IR (KBr) cm^{-1}: 3132 (N-H), 1631 (C=O). ^{1}H-NMR (400MHz, $CDCl_3$) δ: 8.43 (1H, d, *J* = 8.75 Hz), 8.40 (1H, d, *J* = 8.74 Hz), 7.94 (3H, m), 7.54 (6H, m), 7.24 (2H, m), 7.05 (1H, m); ^{13}C-NMR (100MHz, $CDCl_3$) δ: 176.7, 162.4, 150.1, 141.6, 140.7, 140.0, 139.3, 131.6, 131.1, 129.1, 128.4, 126.6, 124.3, 123.9, 123.4, 119.9, 108.0, 106.1; MS: *m/z* = 315 $[M+H]^+$; Anal. Calcd. for $C_{20}H_{14}N_2O_2$: C 76.42; H 4.49; N 8.91; Found: C 76.92; H 4.24; N 8.71.

6-(5-nitropyridin-2-ylamino)-2-phenyl-4H-chromen-4-one (7i): Yield 76%, m.p: 182-184°C, IR (KBr) cm^{-1}: 3325 (N-H), 1631 (C=O). ^{1}H-NMR (400MHz, $CDCl_3$) δ: 7.93 (2H, d, *J* = 6.79Hz), 7.81 (1H, s), 7.54 (4H, m), 7.44 (1H, dd, *J* = 7.6 Hz, *J* = 6.7 Hz), 7.33 (2H, m), 7.14 (2H, d, *J* = 6.78 Hz), 7.02 (1H, m); ^{13}C-NMR (100MHz, $CDCl_3$) δ: 163.7, 148.0, 144.9, 137.9, 133.1, 132.9, 130.4, 128.7, 128.0, 126.9, 124.3, 118.0, 115.9, 110.1, 104.4; MS: *m/z* = 360 $[M+H]^+$; Anal. Calcd. for $C_{20}H_{13}N_3O_4$: C 66.85; H 3.65; N 11.69; Found: C 65.98; H 3.82; N 12.11.

6-(isoquinolin-5-ylamino)-2-phenyl-4H-chromen-4-one (7j): Yield 79%, m.p; 126-128°C, IR (KBr) cm^{-1}: 3132 (N-H), 1721 (C=O). ^{1}H-NMR (400MHz, $CDCl_3$) δ: 9.28 (1H, d, *J* = 6.78 Hz), 8.53 (1H, m), 8.00-7.69 (5H, m), 7.60-7.37 (7H, m), 6.81 (1H, d, *J* = 7.78 Hz), 6.27 (1H, s); ^{13}C-NMR (100MHz, $CDCl_3$) δ: 185.5, 164.4, 152.8, 146.9, 140.5, 134.3, 130.9, 129.5, 128.9, 128.0, 127.8, 126.4, 118.5, 117.9, 113.6; MS: *m/z* = 365 $[M+H]^+$; Anal. Calcd. for $C_{24}H_{16}N_2O_2$: C 79.11; H 4.43; N 7.69; Found: C 80.00; H 4.05; N 7.43.

6-(1H-pyrazol-4-ylamino)-2-phenyl-4H-chromen-4-one (7k): Yield 58%, m.p: 121-123°C, IR (KBr) cm^{-1}: 3315 (N-H), 1721 (C=O). ^{1}H-NMR (400MHz, $CDCl_3$) δ: 11.51 (1H, s), 7.95 (1H, s), 7.93 (2H, s), 7.54 (5H, dd, *J* = 7.60 Hz, *J* = 6.70 Hz), 7.08 (1H, s), 6.90 (2H, m), 6.76 (1H, s); ^{13}C-NMR (100MHz, $CDCl_3$) δ: 184.0, 165.9, 147.8, 137.8, 131.1, 130.0, 128.7, 128.0, 126.4, 124.9, 122.8, 118.9, 115.2, 105.2; MS: *m/z* = 304 $[M+H]^+$; Anal. Calcd. for $C_{18}H_{13}N_3O_2$: C 71.28; H 4.32; N 13.85; Found: C 71.85; H 4.55; N 13.28.

2-phenyl-6-(thiophen-3-ylamino)-4H-chromen-4-one (7l): Yield 56%, m.p: 110-112°C, IR (KBr) cm^{-1}: 3325 (N-H), 1631 (C=O). ^{1}H-NMR (400MHz, $CDCl_3$) δ: 7.93 (2H, d, *J* = 7.60 Hz), 7.70 (1H, d, *J* = 7.40 Hz), 7.53 (4H, m), 7.30 (2H, m), 6.97 (1H,d, *J* = 6.78 Hz), 6.86 (1H, s), 6.80 (1H, s), 5.89 (1H, s); ^{13}C-NMR (100MHz, $CDCl_3$) δ: 182.8, 164.2, 147.3, 137.8, 130.4, 128.7, 128.1, 127.4, 126.1, 124.8, 122.1, 121.2, 119.8, 116.2, 105.7; MS: *m/z* = 320 $[M+H]^+$; Anal. Calcd. for $C_{19}H_{13}NO_2S$: C 71.45; H 4.10; N 4.39; Found: C 71.39; H 3.99; N 4.45.

7m: The general procedure using 2-bromo thiophene (82.5 mg, 0.506 m mol) and 6-amino flavone (100 mg, 0.422 m mol) afforded no result.

6-(5-bromopyridin-2-ylamino)-2-phenyl-4H-chromen-4-one (7n): Yield 80%, m.p: 200-202°C, IR (KBr) cm^{-1}: 3315 (N-H), 1719 (C=O); ^{1}H-NMR (400MHz, $CDCl_3$) δ: 9.62 (1H, s), 8.40 (2H, m), 8.09 (3H, m), 7.79 (2H, m), 7.60 (3H, d, *J* = 8.69 Hz), 6.87 (1H, s), 6.85 (1H, d, *J* = 6.78 Hz); ^{13}C-NMR (100MHz, $CDCl_3$) δ: 176.7, 162.2, 150.1, 141.3, 140.7, 139.8, 139.0, 131.6, 131.2, 129.0, 128.5, 126.3, 124.1, 123.8, 123.3, 119.7, 108.0, 106.1; MS: *m/z* = 394 $[M+H]^+$; Anal. Calcd. for $C_{20}H_{13}BrN_2O_2$: C 61.09; H 3.33; N 7.12; Found: C 60.99; H 3.42; N 7.27.

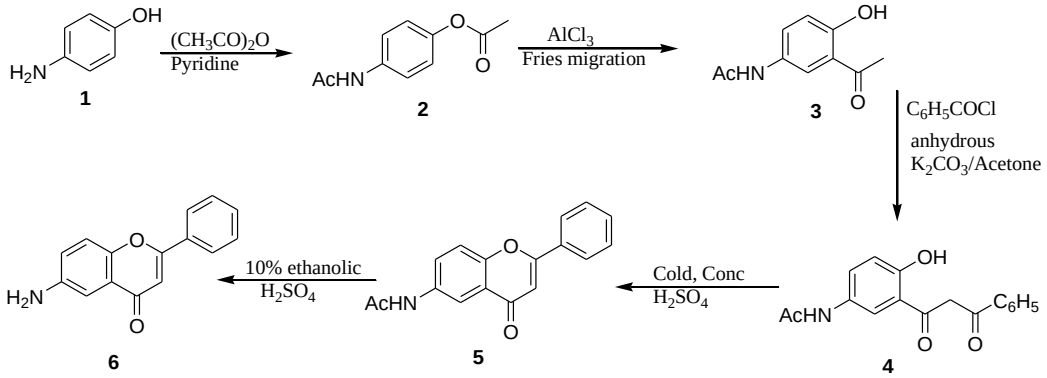
6-(3,5-bis(trifluoromethyl)phenylamino)-2-phenyl-4H-chromen-4-one (7o): Yield 75%, m.p: 191-193°C; IR (KBr) cm^{-1}: 3327 (N-H), 1651 (C=O); ^{1}H-NMR (400MHz, $CDCl_3$) δ: 7.30 (2H, m), 7.21 (2H, m), 7.09 (2H, m), 6.84 (1H, s), 6.71-6.57 (5H, m), 4.50 (1H, s); ^{13}C-NMR (100MHz, $CDCl_3$) δ: 182.3, 163.9, 146.2, 140.3, 134.3, 132.2, 130.5, 128.7, 128.0, 126.4, 125.4, 124.9, 118.2, 112.6; MS: *m/z* = 450 $[M+H]^+$; Anal. Calcd. for $C_{23}H_{13}F_6NO_2$: C 61.48; H 2.92; N 3.12; Found: C 61.68; H 2.67; N 2.85.

6-(3-nitrophenylamino)-2-phenyl-4H-chromen-4-one (7p): Yield 72%, m.p: 133-134°C; IR (KBr) cm^{-1}: 3315 (N-H), 1724 (C=O); ^{1}H-NMR (400MHz, $CDCl_3$) δ: 7.55 (1H, m), 7.35 (5H, m), 7.14-7.21 (3H, m), 6.84 (2H, m), 6.59 (2H, m), 4.8 (1H, s); ^{13}C-NMR (100MHz, $CDCl_3$) δ: 182.9, 162.9 149.3, 146.8, 140.9, 134.8, 130.5, 128.7, 128.0, 126.4, 125.1, 124.7, 118.3, 113.0, 104.9; MS: *m/z* = 359 $[M+H]^+$; Anal. Calcd. for $C_{21}H_{14}N_2O_4$: C 70.39; H 3.94; N 7.82; Found: C 70.20; H 4.12; N 8.01.

6-(4-methoxyphenylamino)-2-phenyl-4H-chromen-4-one (7q): Yield 61%, m.p: 107-108°C; IR (KBr) cm^{-1}: 3325 (N-H), 1631 (C=O); H-NMR (400MHz, $CDCl_3$) δ: 7.30-7.14 (5H, m), 6.84 (2H, m), 6.71 (1H, s), 6.55 (3H, m), 6.35 (2H, m), 4.90 (1H, s), 3.73 (3H, s); ^{13}C-NMR (100MHz, $CDCl_3$) δ: 183.1, 167.0, 150.2, 146.8, 134.3, 131.9, 130.4, 128.7, 128.0, 126.4, 125.6, 120.1, 118.2, 115.2, 104.5, 55.7; MS: *m/z* = 345 $[M+H]^+$; Anal. Calcd. for $C_{22}H_{17}NO_3$: C 76.95; H 4.99; N 4.08; Found: C 77.12; H 4.86; N 3.91.

3. RESULTS AND DISCUSSION

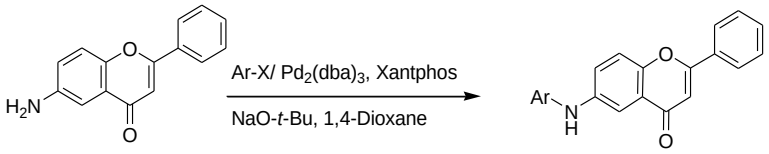
In present study, we have synthesized the novel series of substituted 6- aminoflavone by Buchwald-Hartwig Cross Coupling Reaction. 6-Aminoflavone was prepared using literature procedure (Vijaya Lakshmi, 1972; Palker, 2000), 5-acetamido-2-hydroxy acetophenone 3 was successively condensed with benzoyl chloride in the presence of acetone and anhydrous potassium carbonate medium to obtain the corresponding β-diketone 4. The diketone 4 was cyclized with cold concentrated H_2SO_4 to obtain 6-acetamido flavone 5. Further deacetylated by using 10% ethanolic H_2SO_4 to obtain 6-aminoflavone 6.



Scheme.1. Synthesis of 6-amino flavone

Initially, the compounds of 6-aminoflavone **6** and aryl halide tested in presence of $Pd_2(dba)_3$ and NaO-*t*-Bu base without ligand, reaction was unsuccessful. After that reaction carried out in presence of tetrakis ligand, the reaction did not proceed. Further 6-aminoflavone VI treated with aryl halide and hetero aryl halide in presence of $Pd_2(dba)_3$ and Xantphos ligand using sodium tertiary butoxide base to afford the corresponding aryl amines 7a-q in good yields. The synthesis involves coupling of aryl, heteryl halides with primary amine of 6-amino flavone. In the

case of five membered heterocycles (7k, 7l) the reaction is sluggish, the yields are low. 2-Bromo thiophene is inert even after long time reaction, no product is formed. Interesting observation is coupling at selective position in 2,5-dibromo pyridine (7n), the formation 2-amino-pyridyl derivative (6-(5-bromopyridin-2-ylamino)-2-phenyl-4H-chromen-4-one) is observed

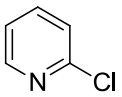
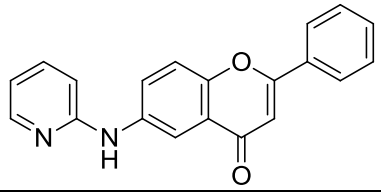
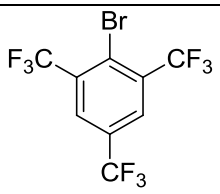
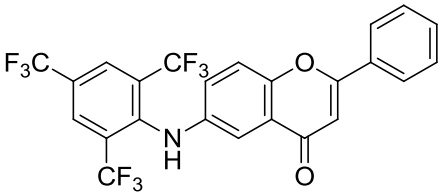
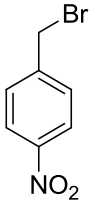
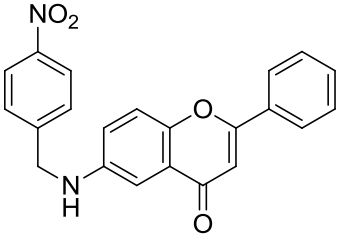
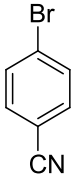
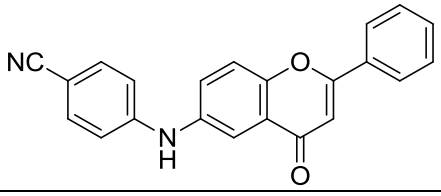
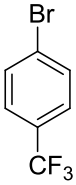
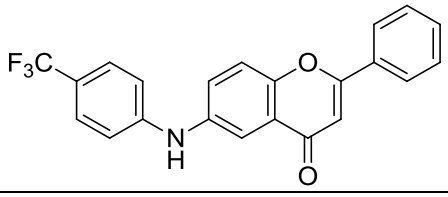
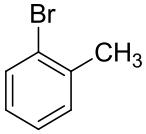
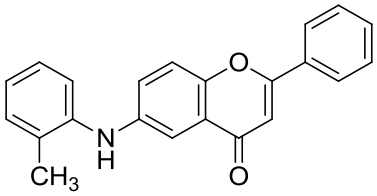


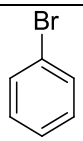
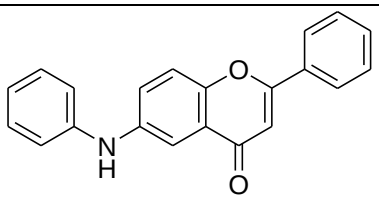
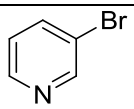
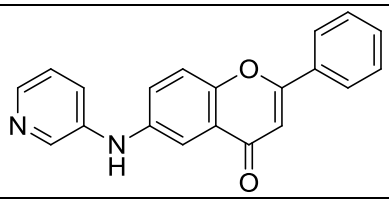
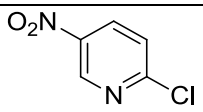
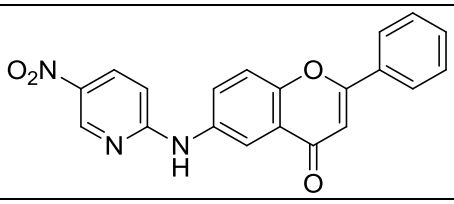
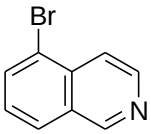
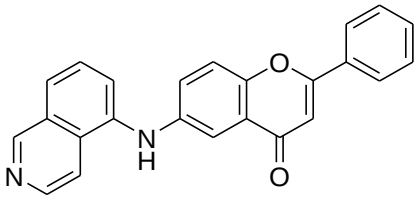
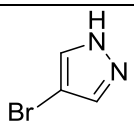
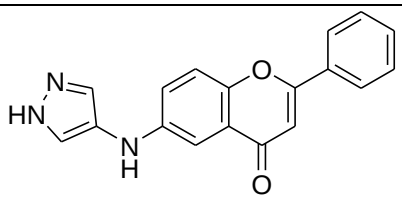
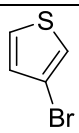
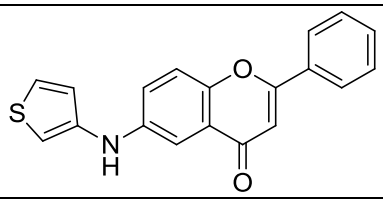
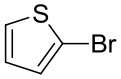
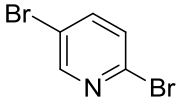
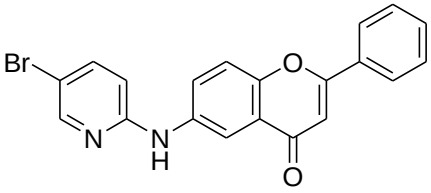
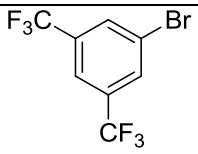
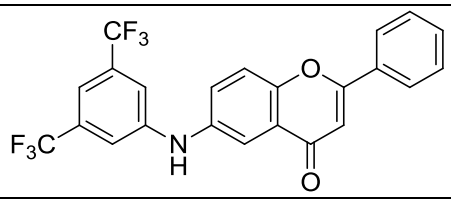
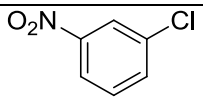
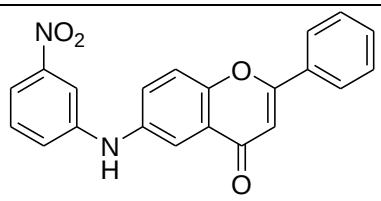
6 7a-q

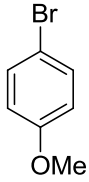
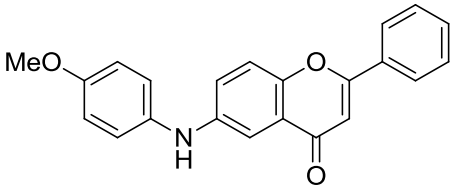
Scheme.2. Synthesis of 6-amino substituted flavones

To the best our knowledge, first report in Buchwald-Hartwig cross coupling is amino flavone with aryl and heteryl halo compounds to develop new synthetic-potential flavone derivatives. All the synthesized compounds were characterized by ^{1}H NMR, ^{13}C NMR, IR and Mass spectral analysis. All compounds were presented in Table.1.

Table.1. Synthesized derivatives of 2-phenyl-6-(aryl amino)-4H-chromene-4-one 7a-q

S.No.	Ar-X	Product	Yield[a] (%)	M.p.(°c)
7a			85	202-205
7b			81	206-208
7c			75	130-132
7d			65	100-101
7e			78	118-120
7f			60	106-108

7g			82	200-202
7h			83	202-210
7i			76	182-184
7j			79	126-128
7k			58	121-123
7l			56	110-112
7m		No reaction	-	-
7n			80	200-202
7o			75	191-193
7p			72	133-134

7q			61	107-108

[a] Isolated product yield

4. CONCLUSION

In view of our interest, we have synthesized novel derivatives of 2-phenyl-6-(aryl amino)-4H-chromene-4-one 7a-q from 6-aminoflavone by using Buchwald- Hartwig coupling reactions as the key steps in excellent yields.

5. ACKNOWLEDGEMENTS

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