Synthesis of 8-Bromoflavone and its Buchwald-Hartwig Reaction

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Dedicated to the memory of Prof. Tamás Patonay.

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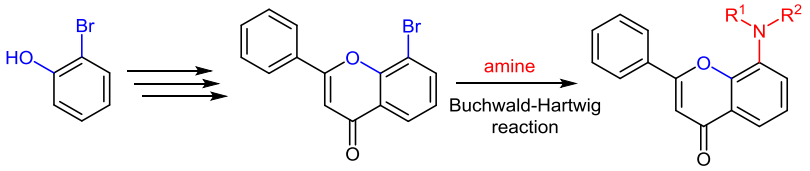

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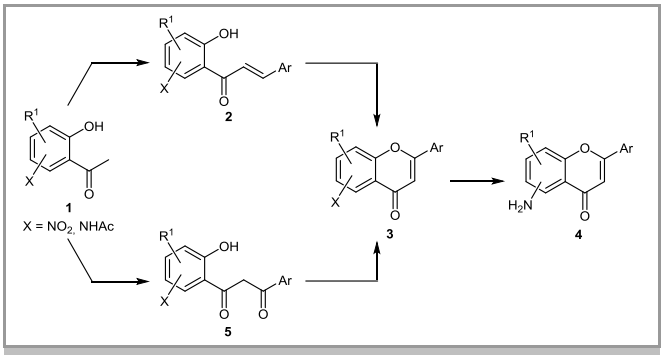
Abstract Simple and convenient synthesis of 8-bromoflavone was achieved, starting from 2-bromophenol through 3'-bromo-2'-hydroxyacetophenone whose preparation was managed to be solved by optimized Fries rearrangement. The Buchwald-Hartwig reaction of 8-bromoflavone with different type of primary and secondary amines was carried out.

Key words palladium, Buchwald-Hartwig reaction, flavones, catalysis, Fries rearrangement

Flavones (2-aryl-4*H*-1-benzopyran-4-ones) are widespread in nature mostly as plant metabolites.[1] Beside their frequent occurrence, flavones also show versatile biological activities, e. g. antioxidant, anti-inflammatory, antimicrobial properties.[2] Noteworthy that many aminoflavone derivatives have considerable enzyme inhibitory effect as α-glucosidase,[3] tyrosin-kinase,[4] cyclin-dependent kinase[5] inhibitors, in addition, antiproliferative,[6] antitumor,[7] cytotoxic effect[8] and central nervous system protective properties[9] were also observed.

Most syntheses of flavones are based on the corresponding chromone (4*H*-1-benzopyran-4-one) core structure by conventional methods. However, synthesis of aminoflavones is suffering from limitations, especially in the case of derivatives linked their amine substituents to Ring A. The most common synthetic methods based on Baker-Venkataraman rearrangement[10,11] or Claisen-Schmidt condensation[12,13] (Scheme 1).

The main problems of these methods are the synthesis of the corresponding acetophenone **1** is limited by the regioselectivity of the acetophenone's nitration and/or the sensitivity of the R^1 substituents under the harsh conditions of nitration. An alternative way is the nitration and reduction of previously prepared flavone moiety but these possibilities are also limited by the regioselectivity and reactivity patterns of the nitration step.[4b,9,14]



Scheme 1 Synthesis of aminoflavone derivatives by conventional methods.

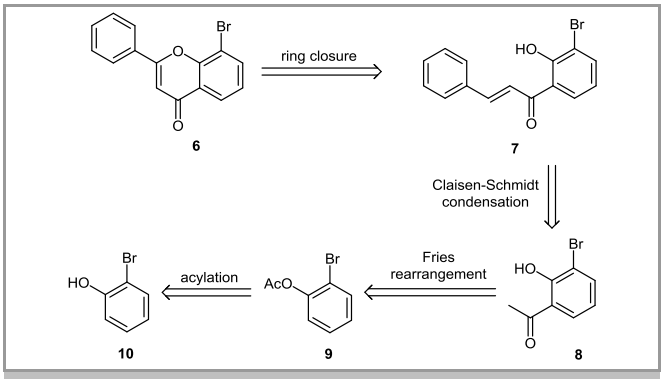
Synthesizing derivatives with alkyl/arylamino or disubstituted amino function represents a much greater challenge than the formation of the amino group. Due to the lack of selectivity, direct alkylation leads to low yields.[6a,c, 15]

In the last decades Buchwald-Hartwig amination of halo substituted aromatic/heteroaromatic systems became useful method for synthesizing alkyl- and arylamino substituted arenes.[16] Nevertheless, in the field of aminoflavone derivatives only sporadic examples have been published. The synthesis of 4'-aminoisoflavone started from its bromide,[8] while 7-amino-5-hydroxyflavone was prepared from the corresponding triflate.[17] Caddick[18] *et al.* used Buchwald-Hartwig reaction for the amination of bromo- or triflyloxy substituted flavones under microwave activation but *only hexylamine* was used as nitrogen source.

Previously our group published the results of the amination of 6- and 7-bromoflavone with different type of primary, secondary amines and aniline derivatives.[19] Although Caddick[18] *et al.* mention the Buchwald-Hartwig amination of 8-bromoflavone (**6**) with *hexylamine*, no other example was presented. Moreover, the synthesis of the 8-bromoflavone substrate is published only in Caddick's paper[18] according to our knowledge.

First, their own initial investigations toward the synthesis of haloflavones have been conducted using protocols based upon the classical Baker-Venkataraman O-acylation approach.[20] However, reactions proved to be relatively low yielding and slow to perform. At the end the synthesis of 8-bromoflavone was performed by the application of a C-acylation methodology described by Cushman[21] for the synthesis of hydroxylated flavones. The method required the utilization of LHMDS at low temperature and 3'-bromo-2'-hydroxyacetophenone (**8**) as a starting material; however the source of compound **8** is not given in their article.

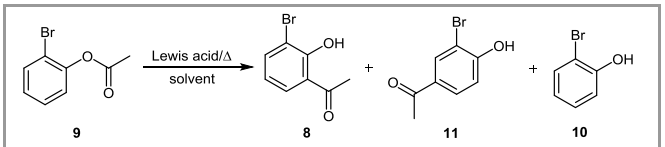
In this paper we represent the synthesis of 8-bromoflavone (**6**) starting from the commercially available 2-bromophenol (**10**) and its Buchwald-Hartwig reaction with some aliphatic and aromatic amine derivatives.



Scheme 2 Retrosynthesis of 8-bromoflavone (**6**).

According to our retrosynthetic analysis the synthesis of 8-bromoflavone (**6**) requires 3'-bromo-2'-hydroxyacetophenone (**8**), as a starting precursor, which can be prepared by Fries rearrangement of ester **9** after the acylation of the commercially available 2-bromophenol (**10**) (Scheme 2). The Claisen-Schmidt condensation of **8** with benzaldehyde results the 2'-hydroxychalcone **7** and its oxidative ring closure could provide 8-bromoflavone (**6**).

The esterification of 2-bromophenol (**10**) with acetyl chloride in the presence of triethyl amine provided 2-bromophenylacetate (**9**) in excellent yield (98%). After the first Fries rearrangement experiment of ester **9**, which was carried out in the usual neat condition, revealed that optimization is required because the reaction resulted exclusively 3'-bromo-4'-hydroxyacetophenone (**11**) and only traces of the desired 3'-bromo-2'-hydroxyacetophenone (**8**) (Scheme 3).



Scheme 3 Fries rearrangement of ester **9**.

Table 1 Synthesis of acetophenone **8** – optimization.

Solvent	Lewis acid	T (°C)	t	Yield of 8 (%)[a]	11[c]	10[c]
neat	$AlCl_3$	100	3 h	trace	+	-
nitrobenzene	$ZnCl_2$	100	3 h	0	-	-
nitrobenzene	$AlCl_3$	100	45 min	0	+	-
1,4-dioxane	$AlCl_3$	100	3 h	0	-	-
carbon disulfide	$AlCl_3$	46	5 h	0	-	-
1,2-dichloroethane	$AlCl_3$	84	48 h	23	+	+
1,2-dichloroethane	$AlCl_3$	84	96 h	29	+	+
chlorobenzene	$AlCl_3$	130	3 h	37[b]	+	+
1,2-dichlorobenzene	$AlCl_3$	140	3 h	62	+	+

[a] Yields refer to pure isolated products
[b] great amount of *p*-acetyl-chlorobenzene was formed
[c] identification with standards by TLC monitoring, not isolated products

In case of nitrobenzene, 1,4-dioxane and carbon disulfide the formation of the desired compound **8** was not detected. The application of $ZnCl_2$ in nitrobenzene did not show even the formation of the *para* substituted acetophenone **11**. Using different halogenated solvents acetophenone **8** was isolated in moderate yield. The rearrangement in *para* position was successfully reduced providing acetophenone **8** by using aluminum trichloride in 1,2-dichlorobenzene at 140°C (Table 1). Under these conditions beside the by-product **11**, the 2-bromophenol (**10**) was also detected in the reaction mixture which could not be separated by using classical chromatographic solvents. The addition of triethyl amine (TEA), as a basic component, to the dichloromethane (dichloromethane : triethyl amine = 20:1) dramatically and solely reduced the retention factor of 2-bromophenol (**10**) (R_f: 0.65→0.15) therefore its separation from compound **8** became possible (Figure 1).

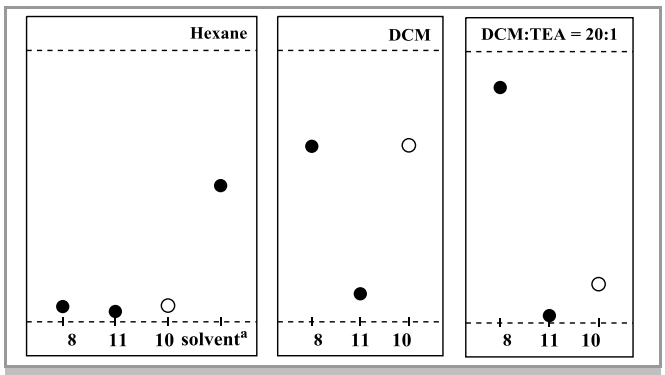
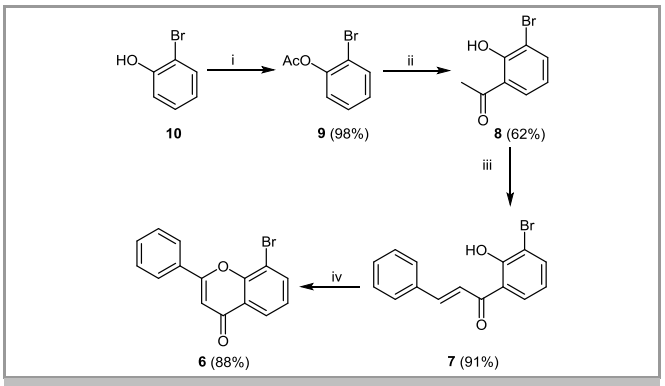


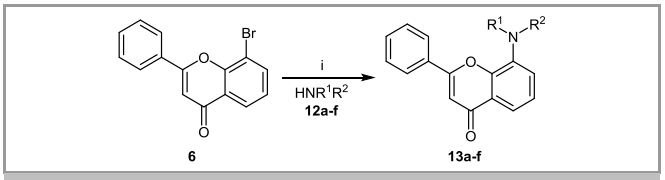
Figure 1 Thin-layer chromatography plates of acetophenone **8**, **11** and phenol **10** in different eluents ([a] 1,2-dichlorobenzene)

In the case of product **8** the retention factor was changed to the higher position, that is, this compound does not behave as a phenolic compound, which phenomenon can be explained by the decreased acidity of the hydroxyl group due to the intramolecular chelate effect of the carbonyl group in compound **8**. The successfully separated 3'-bromo-2'-hydroxy-acetophenone (**8**) was transformed into bromochalcone **7** with benzaldehyde by Claisen-Schmidt condensation. Using catalytic amount of iodine in hot dimethyl sulphoxide[22] the ring-closure of the chalcone derivative **7** provided the desired 8-bromoflavone (**6**) in high yield (Scheme 4).



Scheme 4 Synthesis of **6**. *Reagents and conditions*: (i) **10** (1.0 equiv.), AcCl (1.1 equiv.), TEA (1.1 equiv.), rt, DCM, 1 h; (ii) **9** (1.0 equiv.), $AlCl_3$ (1.5 equiv.), 1,2-dichlorobenzene, 140°C, 3 h; (iii) **8** (1.0 equiv.), PhCHO (1.5 equiv.), KOH in 60% aqueous solution, EtOH, rt, 24 h; (iv) **7** (1.0 equiv.), I_2 (0.08 equiv), DMSO, 180°C, 15 min.

The Buchwald-Hartwig reaction of **6** with amines **12a–f** (1.2 equiv.) results the aminated flavone derivatives **13a–f** in moderate and good yields (Scheme 5, Table 2). The reactions were carried out using $Pd_2(dba)_3$ (5 mol%) as catalyst, BINAP (7.5 mol%) as phosphane and NaOtBu (1.4 equiv.) as base in dry toluene at 110°C.



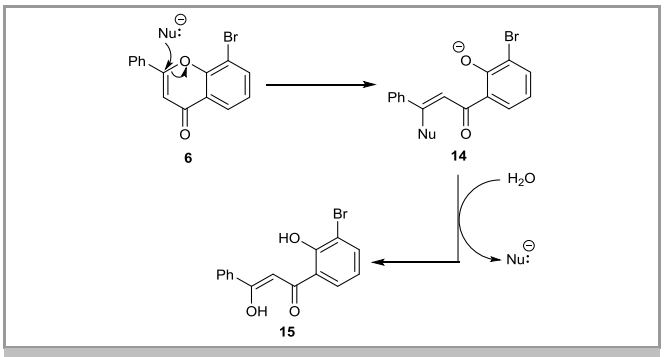
Scheme 5 Synthesis of **13a-f**. *Reagents and conditions*: (i) **6** (1.0 equiv.), $Pd_2(dba)_3$ (5 mol%), BINAP (7.5 mol%), amine **12a-f** (1.2 equiv.), Na*O*t*B*u (1.4 equiv.), dry toluene, 110°C, 3 h.

Table 2 Yields of **13a-f**.

12,13	R^1	R^2	Yields of **13** (%)[a]
a	Bu	H	51
b	Bn	H	66
c	4-Cl-C_6H_4	H	59
d	4-MeO-C_6H_4	H	65
e	$-(CH_2)_2N(CH_3)(CH_2)_2-$		50
f	$-(CH_2)_2O(CH_2)_2-$		47

[a]Yields refer to pure isolated products

Beside the desired product **13a–f** 3'-bromo-2'-hydroxydibenzoylmethane (and its tautomeric form) (**15**) was observed. The appearance of this by-product can be explained by a concurrent ring-opening of the heterocycle under the applied basic condition. As we earlier[19] showed a nucleophilic species e.g. *tert*-butoxide anion attacks the electrophilic C-2 atom of the flavone moiety and the intermediate enol ether **14** hydrolyses during the work-up and the column chromatography on silica as shown by Scheme 6. After the isolation **15** its structure elucidation was achieved by NMR, IR and MS measurements.



Scheme 6 Ring opening reaction of **6**

All products were characterized by spectroscopic methods (NMR, IR, MS). The GC-MS measurements showed high purity which was also proven by the sharp melting points. The yields indicated in the tables refer to pure isolated yields in all cases.

In conclusion, we have demonstrated the synthesis of 8-bromoflavone (**6**) from the commercially available 2-bromophenol through 3'-bromo-2'-hydroxyacetophenone (**8**), as a starting precursor. The synthesis of **8** was optimized and its further transformation to 8-bromoflavone (**6**) requires simple and convenient reaction conditions. Because the starting materials are easily accessible and the reactions give good yields, this new synthetic approach has potential applications in the synthesis of various functionalized flavones, which are of considerable interest as potential biologically active compounds or pharmaceuticals. The Buchwald-Hartwig amination of the prepared 8-bromoflavone (**6**) was studied with different primary and secondary amines. Further studies of the Buchwald-Hartwig reaction with different amino acid derivatives are currently underway in our laboratory.

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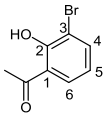
Column chromatography was performed on silica gel (Merck 60, 70-230 mesh), eluents are given at the products. Thin layer chromatography was performed on aluminum backed TLC plates of silica gel 60 F254 (Merck, 0.2 mm) with the indicated eluent. The purity of the compounds was established by GC-MS (Agilent 7890, Agilent 5975 MS detector) with positive EI at 70eV. NMR spectra were recorded on a Bruker AM 360 (360.13 MHz for ^1H, 90.03 MHz for ^{13}C) spectrometer. Chemical shifts (δ) are given from internal $CHCl_3$ signals (δ = 7.26 ppm) for ^1H NMR and (δ = 77.00 ppm) for ^{13}C NMR. Coupling constants (*J* in Hz) are accurate to ±0.2 Hz for ^1H. Melting point data were determined by using Büchi B-540 equipment. Elemental analyses (C, H) were conducted using the Elementar Vario MicroCube instrument. IR spectra were measured in KBr disc with Perkin-Elmer FT-IR 16PC or Jasco FT-IR 4100A equipment.

Synthetic procedure of 3'-bromo-2'-hydroxyacetophenone (8): Commercially available 2-bromophenol (**10**) (10.0 g, 57.8 mmol) was dissolved in 50 mL dry dichloromethane in a round bottom flask, acetyl chloride (5.0 g, 63.6 mmol) and TEA (4.67mL, 63.6 mmol) were added and stirred at room temperature for 1 hour. The solvent was evaporated under reduced pressure to give the pure 2'-bromophenylacetate (**9**) (12.18 g, 56.6 mmol, yield: 98%). The **9** ester was dissolved in 100 mL 1,2-dichlorobenzene, then aluminum chloride (11.3 g, 84.9 mmol) was added. The mixture was heated and stirred at 140°C for 3 hours. Ice and 10% HCl was added till slightly acidic pH. The organic phase was separated in separation funnel, the water phase was extracted with dichloromethane then the combined organic phase was dried on magnesium sulfate, and filtered. The dichloromethane was evaporated under vacuum. The crude residue was treated with hexane (300 mL) and cooled at -20°C when most of the *para* substituted by-product **11** was crystallized and filtered off. The solution was filtered through silica and

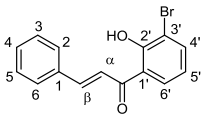
washed with hexane till the 1,2-dichlorobenzene was eluted then the eluent was changed to DCM:TEA = 20:1. After chromatography and evaporation of the eluent the pure product 3'-bromo-2'-hydroxyacetophenone (**8**) was isolated (7.55 g, 35.1 mmol, yield: 62%).



3'-bromo-2'-hydroxyacetophenone (8) : 7.55 g, (62%), oil

^{1}H-NMR($CDCl_3$): δ: 12.97 (s, 1H, O**H**), 7.73 (m, 2H, 4-H, 6-H), 6.82 (t, *J* = 7.9 Hz, 1H, 5-H), 2.66 (s, 3H, C**H$_3$**) **^{13}C-NMR**($CDCl_3$): δ: 204.3 (**C**=O), 158.9 (C-2), 139.6 (C-4),129.9 (C-6), 120.5 (C-1), 119.6 (C-5), 112.0 (C-3), 26.7 (**C**H$_3$) **IR: (ATR) υ/cm^{-1}:** 3008, 2925, 2570, 1643, 1473, 1428, 1364, 1250, 1146, 1071, 968, 836, 775, 738, 627, 595, 523, 437. **MS:** 214 [M$^{+\cdot}$], 216 [M$^{+\cdot}$+2, 100%], 201, 199, 143, 145, 92, 77, 63 **Anal.** Calcd for $C_8H_7BrO_2$: C, 44.68; H, 3.28, Found: C, 44.50; H, 3.19.

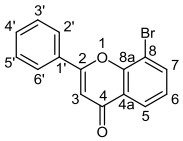
Synthetic procedure of 3'-bromo-2'-hydroxychalcone (7): To the solution of 3'-bromo-2'-hydroxyacetophenone (**8**) (7.55 g, 35.1 mmol) and ethanol (40 mL), benzaldehyde (5.4 mL, 52.6 mmol) and 60% KOH in aqueous solution (45 mL, 0.8 mol, 22 equiv.) was added. The orange solution was stirred for 30 minutes then let it stand for overnight at ambient temperature. At a work-up procedure 10% HCl was added up to pH = 1, the precipitation was filtered and washed with water to give as yellow crystals of **7** (9.68 g, 31.9 mmol, yield: 91%).



3'-bromo-2'-hydroxychalcone (7) : 9.68 g (91%), orange solid, Mp: 116-119°C

^{1}H-NMR($CDCl_3$): δ: 13.61 (s, 1H, O**H**), 7.96 (d, *J* = 15.4 Hz, 1H, β-H), 7.90 (dd, *J* = 8.0, 1.1 Hz, 1H, 5-H), 7.76 (dd, *J* = 7.8, 0.9 Hz, 1H, 7-H), 7.65 (m, 3H, 2,6-H, α-H), 7.45 (m, 3H, 3,5-H, 4-H), 6.86 (t, *J* = 7.9 Hz, 1H, 6-H) **^{13}C-NMR**($CDCl_3$): δ: 193.3 (**C**=O), 160.0 (C-2'), 146.6 (C-β),139.4 (C-4'), 134.3 (C-1), 131.3 (C-4), 129.1 (C-3,5),128.8 (C-2,6, C-6'), 120.8 (C-1'), 119.5 (C-α), 119.4 (C-5'), 112.3 (C-3') **IR: (ATR) υ/cm^{-1}:** 3443, 3063, 2858, 2768, 1948, 1639, 1573, 1472, 1425, 1333, 1226, 1145, 1044, 978, 858, 756, 700, 580. **MS:** 302 [M$^{+\cdot}$], 304 [M$^{+\cdot}$+2], 303 [M+H$^{+\cdot}$, 100%], 305 [M+H$^{+\cdot}$+2], 287, 285, 227, 225, 200, 198, 165, 145, 143, 131, 119, 103, 92, 77, 63, 51 **Anal.** Calcd for $C_{15}H_{11}BrO_2$: C, 59.43; H, 3.66, Found: C, 59.31; H, 3.56.

Synthetic procedure of 8-bromoflavone (6): To the solution of 3'-bromo-2'-hydroxychalcone (**7**) (9.68 g, 31.9 mmol) in dimethyl sulfoxide (60 mL) iodine (650 mg, 2.55 mmol) was added and mildly refluxed for 15 minutes. The mixture was poured into 10 % sodium sulfite aqueous solution (300 mL), and stirred. The solid product **6** was filtered and washed with hexane:acetone = 5:1 eluent (8.46 g, 28.1 mmol, yield: 88%).



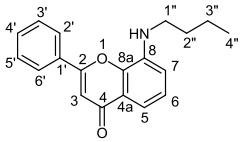
8-bromoflavone (6) : 8.46 g (88%), white solid, Mp: 181.0-182.0°C

^{1}H-NMR($CDCl_3$): δ: 8.14 (m, 3H, 5-H, 2',6'-H), 8.01 (d, *J* = 7.9 Hz 1H, 7-H), 7.62 (m, 3H, 3',5'-H, 4'-H), 7.43 (t, *J* = 7.9 Hz, 1H, 6-H), 7.15 (s, 1H, 3-H) **^{13}C-NMR**($CDCl_3$): δ: 176.6 (C-4), 162.4 (C-2), 152.0 (C-8a), 137.4 (C-7), 132.1 (C-4'), 130.7 (C-1'), 129.2 (C-3',5'), 126.4 (C-5), 126.3 (C-2',6'), 124.7 (C-4a), 124.5 (C-6), 111.5 (C-8), 106.9 (C-3) **IR: (ATR) υ/cm^{-1}:** 3444, 3070, 2309, 1959, 1646, 1472, 1370, 1236, 1103, 1068, 1021, 916, 853, 771, 689, 627, 518, 503, 451, 418. **MS:** 300 [M$^{+\cdot}$], 302 [M$^{+\cdot}$+2, 100%], 274, 272, 200, 198, 172, 170, 137, 135, 119, 102, 82, 63 **Anal.** Calcd for $C_{15}H_9BrO_2$: C, 59.83; H, 3.01, Found: C, 59.78; H, 2.98.

General procedure for 8-alkyl/arylamino-flavone derivatives (13a-f):

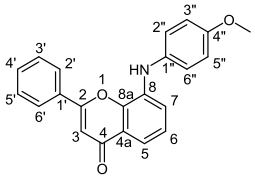
To a mixture of 8-bromoflavone (**5**) (200 mg, 0.66 mmol), NaO*t*Bu (88 mg, 0.92 mmol), BINAP (32 mg, 0.050 mmol) and amine (**12a-f**) (0.80 mmol) in dry toluene (6 mL), $Pd_2(dba)_3$ (30 mg, 0.032 mmol) was added in a dried flask under nitrogen. The reaction mixture was stirred and refluxed at 110°C for 3 hours in oil bath. The crude reaction mixture was filtered on silica with pure acetone, to the filtrated small amount of silica was added then the solvent was removed under reduced pressure. The residue was purified by column chromatography to give the pure cross-coupled product **13a-f** as yellow solid. (The eluent ratio is given at each compound)

Only representative examples are given here, the vast majority of the characterizations are presented in the Supporting Information.



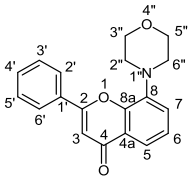
8-(butylamino)flavone (13a) : 99 mg (51%), Mp: 91.5-93.5 °C, Eluent : toluene:ethyl acetate = 8:1

^{1}H-NMR($CDCl_3$): δ: 7.83 (m, 2H, 2',6'-H), 7.54 (m, 3H, 3',5'-H, 4'-H), 7.48 (d, *J* = 7.9 Hz 1H, 5-H), 7.25 (t, *J* = 7.9 Hz, 1H, 6-H), 6.89 (d, *J* = 7.9 Hz, 1H, 7-H), 6.77 (s, 1H, 3-H), 4.45 (s, 1H, N-**H**), 3.28 (m, 2H, 1"-H), 1.74 (p, *J* = 7.2 Hz, 2H, 2"-H), 1.51 (s, *J* = 7.2 Hz, 2H, 3"-H), 1.02 (t, *J* = 7.2 Hz. 2H, 4"-H) **^{13}C-NMR**($CDCl_3$): δ: 178.8 (C-4), 162.4 (C-2), 144.8 (C-8a), 138.1 (C-8), 132.3 (C-1'), 131.4 (C-4'), 129.2 (C-3',5'), 126.2 (C-2',6'), 125.6 (C-6), 123.8 (C-4a), 112.9 (C-7), 111.7 (C-5), 108.0 (C-3), 43.5 (C-1"), 31.5 (C-2"), 20.4 (C-3"), 13.9 (C-4") **IR: (ATR) υ/cm^{-1}:** 3444, 3061, 2961, 2931, 2857, 1904, 1815, 1638, 1590, 1483, 1452, 1375, 1309, 1212, 1149, 1043, 878, 771, 738, 687, 536, 501. **MS:** 293 [M$^{+\cdot}$], 250 (100%), 148, 107, 65 **Anal.** Calcd for $C_{19}H_{19}NO_2$: C, 77.79; H, 6.53; N, 4.77, Found: C, 77.75; H, 6.50; N, 4.73.



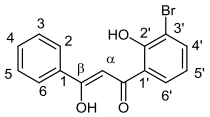
8-[(4-methoxyphenyl)amino]flavone (13d): 148 mg (65%), Mp: 170.0-172.0 °C, Eluent : toluene:ethyl acetate = 8:1

^{1}H-NMR($CDCl_3$): δ: 7.85 (m, 2H, 2',6'-H), 7.60 (dd, *J* = 7.4, 1.8 Hz 1H, 5-H), 7.52 (m, 3H, 3',5'-H, 4'-H), 7.21 (m, 4H, 6-H, 7-H, 2",6"-H), 6.94 (d, 2H, *J* = 8.8 Hz, 3",5"-H), 6.79 (s, 1H, 3-H), 6.16 (s, 1H, N-**H**), 3.83 (s, 3H, OC**H$_3$**) **^{13}C-NMR**($CDCl_3$): δ: 178.6 (C-4), 162.6 (C-2), 156.7 (C-4"), 145.5 (C-8a), 135.9 (C-1"), 133.8 (C-8), 132.1 (C-1'), 131.5 (C-4'), 129.1 (C-3',5'), 126.3 (C-2',6'), 125.2 (C-6), 124.6 (C-2',6'), 124.4 (C-4a), 116.1 (C-7), 115.0 (C-3",5"), 114.4 (C-5), 108.0 (C-3), 55.6 (O**C**H$_3$) **IR: (ATR) υ/cm^{-1}:** 3424, 3298, 3004, 2951, 2830, 2320, 2062, 1633, 1582, 1509, 1379, 1244, 1042, 896, 826, 770, 687, 546, 508, 453. **MS:** 343 [M$^{+\cdot}$, 100%], 328, 226, 170, 142, 120, 77 **Anal.** Calcd for $C_{22}H_{17}NO_3$: C, 76.95; H, 4.99; N, 4.08, Found: C, 76.85; H, 4.94; N, 4.03.



8-Morpholinoflavone (13f): 96 mg (47%), Mp: 200.0-202.0 °C, Eluent : toluene:ethyl acetate = 4:1

^{1}H-NMR(DMSO): δ: 8.06 (m, 2H, 2',6'-H), 7.65 (m, 4H, 5-H, 3',5'-H, 4'-H), 7.41 (m, 2H, 6-H, 7-H), 7.09 (s, 1H, 3-H), 3.90 (m, 2H, 3",5"-H), 3.17 (m, 2H, 2",6"-H) **^{13}C-NMR**(DMSO): δ: 177.5 (C-4), 161.9 (C-2), 149.0 (C-8a), 141.9 (C-8), 131.8 (C-4'), 131.4 (C-1'), 129.3 (C-3',5'), 126.1 (C-2',6'), 125.4 (C-6), 124.3 (C-4a), 122.5 (C-7), 117.7 (C-5), 106.7 (C-3), 66.4 (C-3",5"), 51.4 (C-2",6") **IR: (ATR) υ/cm^{-1}:** 3433, 3059, 2972, 2846, 2830, 2753, 1638, 1576, 1485, 1447, 1376, 1240, 1113, 983, 855, 775, 749, 689, 629, 532, 501, 458, 438. **MS:** 307 [M$^{+\cdot}$, 100%], 276, 249, 231, 165, 147, 119, 92 **Anal.** Calcd for $C_{19}H_{17}NO_3$: C, 74.25; H, 5.58; N, 4.56, Found: C, 74.18; H, 5.50; N, 4.50.



(3-bromo-2-hydroxyphenyl)-3-hydroxy-3-phenylprop-2-en-1-one (15) : Mp 136.0-138.5°C, Eluent : toluene:ethyl acetate = 8:1 This compound was obtained as a by-product from the reaction of amines and 8-bromoflavone.

^{1}H-NMR (CDCl$_3$): δ: 15.34 (s, 1H, β-OH), 12.87 (1H, s, 2'-OH), 7.94 (2H, d, 2,6-H, *J* = 7.6 Hz), 7.74 (m, 3H, 3,5-H, 4-H), 7.50 (m, 2H, 4'-H, 6'-H), 6.83 (m, 2H, 5'-H, α-H) **^{13}C-NMR (CDCl$_3$):** δ: 194.8 (**C**=O), 180.0 (C-β), 158.9 (C-2'), 138.9 (C-4'), 133.3 (C-1), 132.7 (C-4), 128.8 (C-3,5), 127.7 (C-6'), 126.9 (C-2,6), 120.0 (C-1'), 119.7 (C-5'), 112.5 (C-3'), 92.3 (C-α) **IR: (ATR) υ/cm^{-1}:** 3442, 3057, 2923, 2852, 1609, 1576, 1479, 1320, 1240, 1178, 1099, 1057, 884, 756, 706, 681, 623. **MS:** 318 [M$^{+\cdot}$], 320 [M$^{+\cdot}$+2], 121, 199, 105 (100%), 77, 51 **Anal.** Calcd for $C_{15}H_{11}BrO_3$: C, 56.45; H, 3.47, Found: C, 56.38; H, 3.40.

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Financial support from the Hungarian Scientific Research Fund (OTKA) (grant number K75806 and grant number PD 106244) is greatly appreciated.

Supporting Information

YES (this text will be updated with links prior to publication)

Primary Data

NO (this text will be deleted prior to publication)

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