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Plant Coumarins: VIII.* Suzuki Reaction in the Synthesis of 3-Aryl(hetaryl)furocoumarins

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Abstract—Suzuki cross coupling of oreoselone trifluoromethanesulfonate with substituted phenyl- and hetarylboronic acids in the presence of palladium complexes with uni- and bidentate ligands gave the corresponding 3-substituted furocoumarins.

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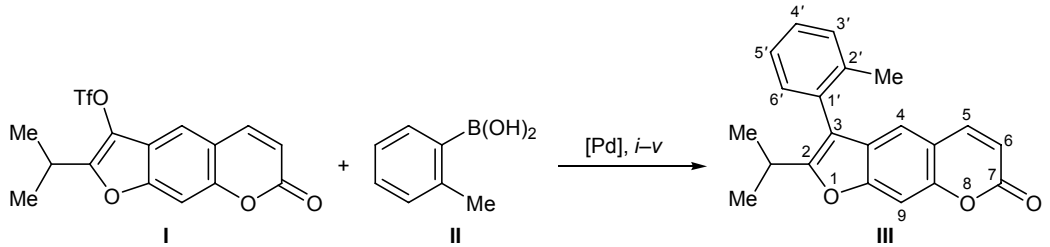
Natural linear furocoumarins such as psoralen and 8-methoxypsoralen are traditionally used as photochemotherapeutic agents in PUVA therapy of skin diseases, in particular of psoriasis, vitiligo, and atopic eczema [2]. However, their application in combination with UV irradiation gives rise to side effects (mutagenic etc.), so that search for new psoralen derivatives is strongly desirable. It was found that application of synthetic derivatives, e.g., of 3-ethoxycarbonylpsoralen, reduces side effects in therapy of skin diseases [3]. Derivatives of 3-alkyl- and 3-aryl-substituted furocoumarins are known as inhibitors of leukotriene LTB_4 biosynthesis, and they may be promising from the viewpoint of design of anti-inflammatory photoactive agents [4]. In addition, extensive search for Kv-1.3 potassium channel blockers is performed in the series of amino-substituted furocoumarins [5]. Garazd et al. [6] synthesized 3-aryl-substituted furocoumarins which exhibited cardiotropic activity [6].

3-Aryl-substituted linear furocoumarins were synthesized according to MacLeod (Williamson reaction of 7-hydroxycoumarins with α-halo ketones in the presence of K_2CO_3 and cyclization in the presence of 1 N NaOH with subsequent acidolysis [4–7]). This approach includes a number of steps and requires the corresponding 7-hydroxycoumarins as starting compounds. In the present work we made an attempt to synthesize furocoumarin derivatives containing an aromatic or heteroaromatic substituent on C^3 by palladium-catalyzed cross-coupling of oreoselone trifluoromethanesulfonate (**I**) with boronic acid (Suzuki reaction). 4-Halo- and 4-trifluoromethylsulfonyloxycoumarins were successfully involved in Suzuki–Miyaura reaction to synthesize 4-aryl(hetaryl or alkynyl)coumarins [8, 9], while analogous reactions with substituted furocoumarins were not reported previously.

Cross-coupling of oreoselone trifluoromethanesulfonate (**I**) with *o*-tolylboronic acid (**II**) was used as

Scheme 1.



I II III

For reaction conditions (*i*–*v*), see table.

* For communication VII, see [1].

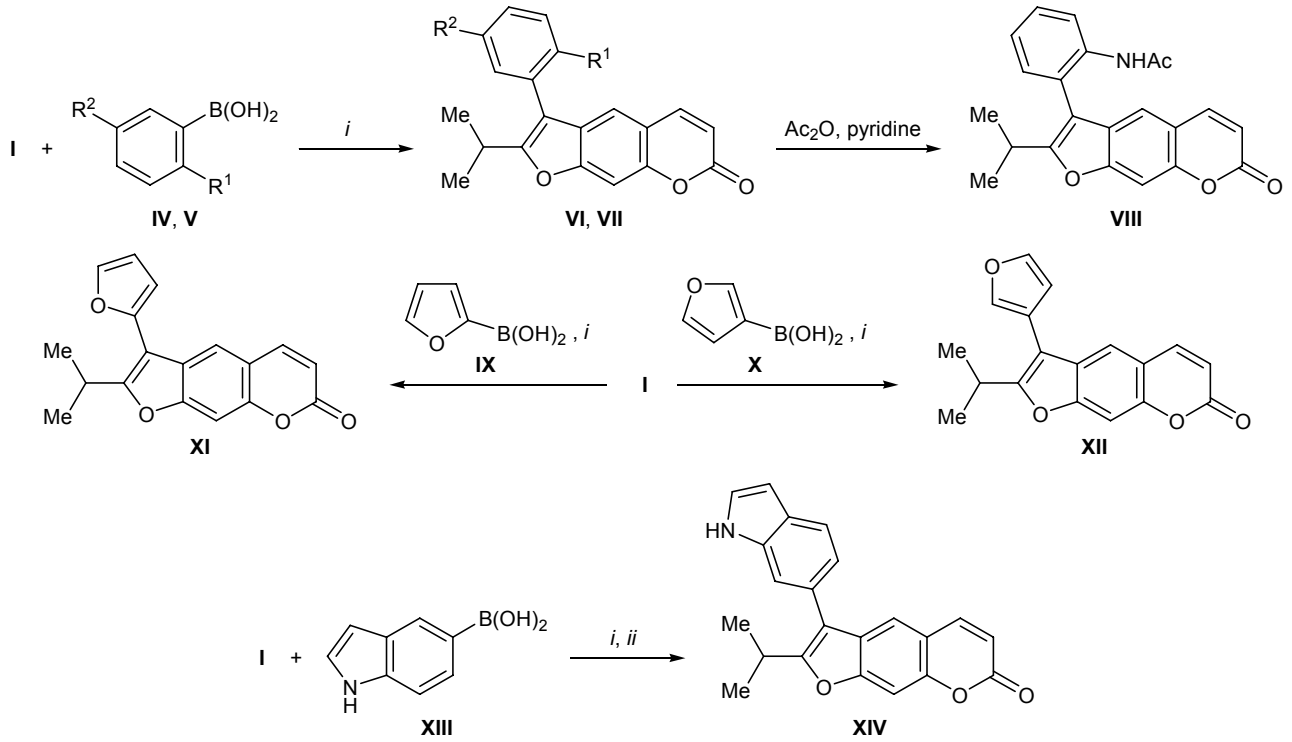
Suzuki reaction of oreoselone trifluoromethanesulfonate (**I**) with *o*-methylphenylboronic acid (**II**)

Conditions	Catalyst	Base	Solvent	Dope	Temperature, °C	Reaction time, h	Yield of **III**, %
i	$PdCl_2(dppf)$	K_3PO_4	MeCN	–	80	6	35
ii	$PdCl_2(dppf)$	K_2CO_3	MeCN	–	80	6	68
iii	$PdCl_2(dppf)$	K_2CO_3	MeCN	$Bu_4N^+Br^-$	80	4.5	75
iv	$PdCl_2(dppf)$	Et_3N	MeCN	–	80	6	55
v	$Pd(PPh_3)_4$	K_2CO_3	Dioxane	$Bu_4N^+Br^-$	100	6	70

model reaction to optimize the conditions (see table, Scheme 1). The reaction in acetonitrile in the presence of $PdCl_2(dppf)$ [dppf is 1,1′-bis(diphenylphosphino)-ferrocene] as catalyst and K_3PO_4 as base was accompanied by considerable tarring, and arylation product **III** was isolated in 35% yield. The process turned out to be sensitive to the nature of the base. Using potassium carbonate we succeeded in isolating compound **III** in 68% yield. It is known that addition of ammonium salts initiates cross coupling with boronic acids [9, 10]. We found that the reaction of oreoselone trifluoromethanesulfonate (**I**) with *o*-tolylboronic acid (**II**) in the presence of $Bu_4N^+Br^-$ (10%) requires shorter time (4.5 h) and ensures increased yield of compound **III** (to 75%). Replacement of K_2CO_3 by NEt_3 was not successful: the yield of arylfurocoumarin **III** was 55%, and 22% of unreacted compound **I** was recovered. The results were not improved to an appreciable extent when the reaction was carried in dioxane in the presence of palladium complex with unidentate ligand, $Pd(PPh_3)_4$, which is often used in Suzuki cross couplings; in this case, 70% of **III** was isolated.

Thus the optimal conditions included the use of 5 mol % of $PdCl_2(dppf)$ as catalyst, 3 equiv of K_2CO_3 as base, 0.1 equiv of $Bu_4N^+Br^-$, and acetonitrile as solvent. Under these conditions we performed cross-couplings of oreoselone trifluoromethanesulfonate (**I**) with 2-chloro-5-trifluoromethylphenylboronic acid (**IV**) and 2-aminophenylboronic acid (**V**). Arylation products **VI** and **VII** were isolated in high yield (71–

Scheme 2.



IV, **VI**, R^1 = Cl, R^2 = CF_3; **V**, **VII**, R^1 = NH_2, R^2 = H; **VIII**, R^1 = AcNH, R^2 = H; *i*: $PdCl_2(dppf)$, K_2CO_3, $Bu_4N^+Br^-$, MeCN, 80°C; *ii*: $Pd(PPh_3)_4$, K_2CO_3, $Bu_4N^+Br^-$, dioxane, 100°C.

72%; Scheme 2). Compound **VII** was converted into the corresponding *N*-acetyl derivative **VIII**. Likewise, compound **I** reacted with 2-furylboronic acid (**IX**) and 3-furylboronic acid (**X**) to give 2-isopropyl-3-(2-furyl)- and 2-isopropyl-3-(3-furyl)psoralens **XI** and **XII** in 58 and 67% yield, respectively. By cross-coupling of trifluoromethanesulfonate **I** with 1*H*-indol-5-ylboronic acid (**XIII**) we obtained 42% of psoralen derivative **XIV** containing an indole fragment. The reaction of **I** with **XIII** in dioxane in the presence of $Pd(PPh_3)_4$ on heating at 100°C afforded only 35% of indolyl-substituted furocoumarin **XIV**.

The structure of the newly synthesized compounds was determined on the basis of their spectral parameters and elemental compositions. Their ^1H and ^{13}C NMR spectra were fully consistent with the assumed structures, and only one set of signals typical of the furocoumarin fragment and the corresponding substituent was present.

To conclude, Suzuki cross-coupling of oreoselone trifluoromethanesulfonate with various aryl(hetaryl)-boronic acids ensures preparation of 3-substituted furocoumarin (peucedanin) derivatives which attract interest as potential pharmacologically active compounds.

EXPERIMENTAL

The NMR spectra were recorded on Bruker AV-300 (300.13 MHz for ^1H and 75.47 MHz for ^{13}C), AV-400 (400.13 MHz for ^1H and 100.78 MHz for ^{13}C), and AV-600 spectrometers [600.30 for ^1H and 150.96 MHz for ^{13}C); the chemical shifts were measured relative to residual proton and carbon signals of the solvent ($CHCl_3$, δ 7.24 ppm; $CDCl_3$, δ_C 76.90 ppm). Multiplicity of signals in the ^{13}C NMR spectra was determined using *J* modulation technique. Signals in the NMR spectra of **VIII**, **XI**, **XII**, and **XIV** were assigned on the basis of carbon–proton shift correlation spectra (COXH, COLOC). The IR spectra were obtained in KBr on a Bruker Vector-22 spectrometer. The UV spectra were recorded on an HP 8453 UV Vis spectrophotometer. The elemental compositions were determined using a Carlo Erba 1106 CHN analyzer.

The products were isolated by column chromatography on silica gel (0.035–0.070 mm, Acros Organics) using chloroform and chloroform–ethanol (50:3) as eluents. The progress of reactions was monitored by TLC on Silufol UV-254 plates; eluent chloroform or chloroform–ethanol (50:2); detection under UV light or by treatment with iodine vapor.

Commercially available palladium complexes $PdCl_2$(dppf) and $Pd(PPh_3)_4$, arylboronic acids **II**, **IV**, and **V**, and hetarylboronic acids **IX**, **X**, and **XIII** (Alfa Aesar) were used. The solvents (acetonitrile, dioxane) and triethylamine were purified by standard procedures and were distilled in a stream of argon just before use. Oreoselone trifluoromethanesulfonate (**I**) was synthesized from natural plant coumarin, peucedanin [11], according to the procedure described in [12].

2-Isopropyl-3-(2-methylphenyl)-7*H*-furo[3,2-*g*]-chromen-7-one (III). *a*. Compound **I**, 200 mg (0.5 mmol), was dissolved in 3 ml of acetonitrile, 690 mg (0.65 mmol, 1.3 equiv) of *o*-tolylboronic acid (**II**), 18 mg (0.025 mmol, 0.05 equiv) of $PdCl_2$(dppf), and 318 mg (1.5 mmol, 3 equiv) of K_3PO_4 were added under argon, and the mixture was stirred for 6 h at 80°C until initial compound **I** disappeared (TLC). The mixture was cooled, diluted with 3 ml of water, and extracted with methylene chloride (4×3 ml), the extracts were combined, dried over magnesium sulfate, and evaporated, and the residue was subjected to column chromatography on silica gel. A fraction containing compound **III** was treated with hexane to isolate 56 mg (35%) of product **III** and a large amount of tars.

b. Compound **I**, 200 mg (0.5 mmol), was dissolved in 3 ml of acetonitrile, 690 mg (0.65 mmol) of *o*-tolylboronic acid (**II**), 18 mg (0.025 mmol) of $PdCl_2$(dppf), and 200 mg (1.5 mmol) of K_2CO_3 were added under argon, and the mixture was stirred for 6 h at 80°C (TLC). The mixture was cooled, diluted with 3 ml of water, and extracted with methylene chloride (4×3 ml), the extracts were combined, dried, and evaporated. The residue was subjected to column chromatography on silica gel, and a fraction containing the product was ground with diethyl ether to isolate 108 mg (68%) of compound **III** and 26 mg (14%) of unreacted oreoselone trifluoromethanesulfonate (**I**).

c. Compound **I**, 200 mg (0.5 mmol), was dissolved in 3 ml of acetonitrile, 690 mg (0.65 mmol) of *o*-tolylboronic acid (**II**), 18 mg (0.025 mmol) of $PdCl_2$(dppf), 200 mg (1.5 mmol) of K_2CO_3, and 11 mg (10 mol %) of $Bu_4N^+Br^-$ were added under argon, and the mixture was stirred for 4.5 h at 80°C until initial compound **I** disappeared (TLC). The mixture was cooled, diluted with 3 ml of water, and extracted with CH_2Cl_2 (4×3 ml), the extracts were combined, washed with water, dried over magnesium sulfate, and evaporated, and the residue was subjected to column chromatography on silica gel. A fraction containing compound **III** was treated with diethyl ether. Yield 119 mg (75%).

d. Compound **I**, 200 mg (0.5 mmol), was dissolved in 3 ml of acetonitrile, 690 mg (0.65 mmol) of *o*-tolylboronic acid (**II**) and 18 mg (0.025 mmol) of

$PdCl_2$(dppf) were added under argon, and 200 mg (2 mmol, 4 equiv) of triethylamine was then added in portions. The mixture was stirred for 6 h at 80°C, cooled, diluted with 3 ml of water, and extracted with methylene chloride (5×6 ml). The extracts were combined, washed with water, dried over $MgSO_4$, and evaporated, and the residue was subjected to column chromatography on silica gel. By treatment of the corresponding fraction with Et_2O we isolated 20 mg (22%) of unreacted initial compound **I** and 67 mg (55%) of cross-coupling product **III**. Conversion 78%.

e. Compound **I**, 200 mg (0.5 mmol), was dissolved in 3 ml of anhydrous dioxane, 690 mg (0.65 mmol) of *o*-tolylboronic acid (**II**), 14 mg (0.025 mmol) of $Pd(PPh_3)_4$, 200 mg (1.5 mmol) of K_2CO_3, and 11 mg (10 mol %) of $Bu_4N^+Br^-$ were added under argon, and the mixture was stirred for 6 h at 100°C until the initial compound disappeared (TLC). The mixture was cooled, diluted with 3 ml of water, and extracted with CH_2Cl_2 (4×3 ml), the extracts were combined, washed with water, dried over $MgSO_4$, and evaporated, and the product was isolated by column chromatography on silica gel, followed by treatment with diethyl ether. Yield 110 mg (70%), mp 181–182°C (from Et_2O). IR spectrum, ν, cm^{-1}: 3059, 3018, 2970, 2927, 2871, 1734, 1687, 1633, 1597, 1576, 1477, 1452, 1388, 1284, 1220, 1165, 1146, 1130, 1113, 1042, 1000, 960, 939, 881, 850, 825, 754, 729, 702. UV spectrum (EtOH), λ_{max}, nm (log ε): 209 (4.44), 253 (4.21), 295 (3.82), 337 (3.53). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.38 d [6H, $(CH_3)_2CH$, *J* = 7], 2.04 s (3H, CH_3), 3.55 m [1H, $CH(CH_3)_2$], 6.23 d (1H, 6-H, *J* = 9.6), 7.12 s (1H, 9-H), 7.34 m (2H, 3′-H, 4′-H), 7.38 s (1H, 4-H), 7.47 m (1H, 5′-H), 7.52 d (1H, 6′-H, *J* = 7.4), 7.68 d (1H, 5-H, *J* = 9.6). ^{13}C NMR spectrum, δ_C, ppm: 20.31 q [$(CH_3)_2CH$], 23.09 q (CH_3), 25.91 d [$CH(CH_3)_2$], 100.54 d (C^9), 115.64 s (C^3), 116.07 s (C^{4a}), 116.65 d (C^6), 120.72 d (C^4), 122.39 s (C^{3a}), 125.24 d ($C^{6'}$), 130.54 d ($C^{5'}$), 131.05 d ($C^{4'}$), 131.11 s ($C^{1'}$), 132.16 d ($C^{3'}$), 133.54 s ($C^{2'}$), 143.65 d (C^5), 146.20 s and 150.82 s (C^{8a}, C^{9a}), 157.20 s (C^2), 160.83 s (C^7). Found, %: C 78.92; H 5.57. *m*/*z* 318.1246 $[M]^+$. $C_{21}H_{18}O_3$. Calculated, %: C 79.22; H 5.70. *M* 318.1251.

3-[2-Chloro-5-(trifluoromethyl)phenyl]-2-isopropyl-7*H*-furo[3,2-*g*]chromen-7-one (VI). Compound **I**, 200 mg (0.5 mmol), was dissolved in 3 ml of acetonitrile, 145 mg (0.65 mmol) of 2-chloro-5-(trifluoromethyl)phenylboronic acid (**IV**), 18 mg (0.025 mmol) of $PdCl_2$(dppf), 200 mg (1.5 mmol) of K_2CO_3, and 11 mg (10 mol %) of $Bu_4N^+Br^-$ were added under argon, and the mixture was stirred for 5 h at 80°C until the initial compound disappeared (TLC). The mixture was cooled, diluted with 3 ml of water, and extracted with methylene chloride (4×5 ml), the extracts were combined, dried over magnesium sulfate, and evaporated, and the residue was subjected to column chromatography on silica gel. A fraction containing the product was treated with diethyl ether. Yield 187 mg (71%), mp 131–133°C (from diethyl ether). IR spectrum, ν, cm^{-1}: 3103, 3066, 3055, 2981, 2936, 2878, 1732, 1685, 1636, 1610, 1578, 1472, 1431, 1369, 1331, 1296, 1248, 1213, 1196, 1138, 1078, 1047, 1038, 930, 870, 837, 820, 764, 748, 678, 648. UV spectrum (EtOH), λ_{max}, nm (log ε): 203 (4.43), 222 (4.18), 250 (4.27), 285 (3.75), 333 (3.62). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.38 d [6H, $(CH_3)_2CH$, *J* = 7], 3.55 m [1H, $CH(CH_3)_2$], 6.24 d (1H, 6-H, *J* = 9.6), 7.11 s (1H, 9-H), 7.46 d (1H, 3′-H, *J* = 8.4), 7.57 s (1H, 6′-H), 7.58 s (1H, 4-H), 7.68 d (1H, 5-H, *J* = 9.6), 7.90 d (1H, 4′-H, *J* = 8.4). ^{13}C NMR spectrum, δ_C, ppm: 20.34 q [$(CH_3)_2CH$], 25.96 d [$CH(CH_3)_2$], 97.81 d (C^9), 105.27 s (C^3), 116.23 s (C^{4a}), 116.64 d (C^6), 119.18 d (C^4), 123.38 s (C^{3a}), 124.20 q (CF_3), 126.34 d ($C^{4'}$), 129.02 d ($C^{6'}$), 130.16 d ($C^{3'}$), 130.82 s ($C^{5'}$), 134.33 s ($C^{2'}$), 136.84 s ($C^{1'}$), 143.66 d (C^5), 151.35 s (C^{8a}, C^{9a}), 157.26 s (C^2), 160.92 s (C^7). Found, %: C 61.82; H 3.21; Cl 18.00; F 13.52. $C_{21}H_{14}ClF_3O_3$. Calculated, %: C 62.00; H 3.47; Cl 18.72; F 14.01.

3-(2-Aminophenyl)-2-isopropyl-7*H*-furo[3,2-*g*]-chromen-7-one (VII). Compound **I**, 200 mg (0.5 mmol), was dissolved in 3 ml of acetonitrile, 89 mg (0.65 mmol) of 2-aminophenylboronic acid (**V**), 18 mg (0.025 mmol) of $PdCl_2$(dppf), 200 mg (1.5 mmol) of K_2CO_3, and 11 mg (10 mol %) of $Bu_4N^+Br^-$ were added under argon, and the mixture was stirred for 4.5 h at 80°C until the initial compound disappeared (TLC), cooled, diluted with 3 ml of water, and extracted with methylene chloride (4×3 ml), and the extract was dried and evaporated. By column chromatography on silica gel using chloroform and chloroform–ethanol (50:2) as eluents we isolated 114 mg (72%) of compound **VII** as an oily substance. IR spectrum, ν, cm^{-1}: 3439, 3396, 3363, 3344, 3047, 3025, 2978, 2937, 2880, 1730, 1690, 1610, 1575, 1499, 1462, 1420, 1384, 1319, 1303, 1288, 1242, 1210, 1142, 1115, 1049, 1020, 860, 763, 756, 680, 654. UV spectrum (EtOH), λ_{max}, nm (log ε): 208 (4.43), 245 (3.96), 304 (3.49), 353 (3.30). ^{1}H NMR spectrum ($CDCl_3$–CD_3OD), δ, ppm (*J*, Hz): 1.42 d [6H, $(CH_3)_2CH$, *J* = 7.0], 3.38 m [1H, $CH(CH_3)_2$], 6.40 d

(1H, 6-H, J = 9.6), 6.78 m (3H, NH_2, 3′-H), 6.90 m (1H, 5′-H), 7.15 m (1H, 4′-H), 7.27 s (1H, 9-H), 7.68 m (1H, 6′-H), 7.89 s (1H, 4-H), 8.03 d (1H, 5-H, J = 9.6). ^{13}C NMR spectrum, δ_C, ppm: 19.88 q [(**C**H_3)$_2$CH], 25.85 d [**C**H(CH$_3$)$_2$], 100.31 d (C^9), 114.96 s (C^3), 115.44 d ($C^{3'}$), 115.78 d (C^6), 116.19 s (C^{4a}), 116.78 s ($C^{1'}$), 119.03 d ($C^{5'}$), 120.02 d (C^4), 121.43 s (C^{3a}), 120.71 d ($C^{6'}$), 128.96 d ($C^{4'}$), 141.99 s ($C^{2'}$), 144.30 d (C^5), 152.01 s (C^{8a}), 153.03 s (C^{9a}), 156.99 s (C^2), 161.25 s (C^7). Found, %: C 74.92; H 5.12; N 4.21. $C_{20}H_{17}NO_3$. Calculated, %: C 75.22; H 5.37; N 4.39.

3-[(2-Acetylamino)phenyl]-2-isopropyl-7*H*-furo-[3,2-*g*]chromen-7-one (VIII). Acetic anhydride, 0.066 ml (0.7 mmol), was added dropwise under stirring to a solution of 150 mg (0.47 mmol) of compound **VII** in 3 ml of pyridine, and the mixture was left to stand for 3 h at room temperature, treated with a solution of ammonia to pH 7–8, and extracted with CH_2Cl_2. The extract was evaporated, the residue was treated with a 10% solution of H_2SO_4 and extracted with CH_2Cl_2 (5×10 ml), and the extracts were combined, washed with water, dried over $MgSO_4$, and evaporated. The product was purified by recrystallization from diethyl ether. Yield 110 mg (65%), mp 123–125°C (from Et_2O). IR spectrum, ν, cm^{-1} : 3436, 3396, 3052, 3022, 2981, 2883, 1730, 1710, 1650, 1610, 1576, 1494, 1464, 1421, 1386, 1319, 1248, 1211, 1142, 1100, 1049, 1000, 960, 866, 822, 760, 700, 656. UV spectrum (EtOH), λ_{max}, nm (logε): 210 (4.58), 245 (4.33), 249 (4.33), 295 (3.83), 320 (3.77). ^{1}H NMR spectrum ($CDCl_3$–CD_3OD), δ, ppm (J, Hz): 1.36 d [6H, (C**H**$_3$)$_2$CH, J = 6.9], 2.09 s ($COCH_3$), 3.25 m [1H, C**H**(CH$_3$)$_2$], 6.40 d (1H, 6-H, J = 9.4), 7.05 m (1H, 5′-H), 7.24 s (1H, 9-H), 7.25 m (1H, 4-H), 7.45 m (2H, 3′-H, 6′-H), 7.63 s (1H, 4-H), 7.90 d (1H, 5-H, J = 9.5). ^{13}C NMR spectrum, δ_C, ppm: 19.60 q [(**C**H_3)$_2$CH], 19.65 q (CO**C**H_3), 22.94 d [**C**H(CH$_3$)$_2$], 100.04 d (C^9), 114.68 s (C^3), 115.68 d (C^6), 116.02 s (C^{4a}), 117.42 d ($C^{3'}$), 118.94 d ($C^{6'}$), 120.33 d (C^4), 119.66 d ($C^{5'}$), 121.19 s (C^{3a}), 123.64 s ($C^{1'}$), 128.25 s ($C^{4'}$), 138.07 s ($C^{2'}$, 143.91 d (C^5), 151.75 s (C^{8a}), 152.94 s (C^{9a}), 156.77 s (C^2), 160.70 s (C^7), 169.76 s (NHC=O). Found, %: C 72.92; H 5.18; N 3.93. $C_{22}H_{19}NO_4$. Calculated, %: C 73.12; H 5.30; N 3.88.

3-(Furan-2-yl)-2-isopropyl-7*H*-furo[3,2-*g*]chromen-7-one (XI). Compound **I**, 200 mg (0.5 mmol), was dissolved in 3 ml of acetonitrile, 76 mg (0.65 mmol) of furan-2-ylboronic acid (**IX**), 18 mg (0.025 mmol) of $PdCl_2$(dppf), 200 mg (1.5 mmol) of K_2CO_3, and 11 mg (10 mol %) of $Bu_4N^+Br^-$ were added under argon, and the mixture was stirred for 5 h at 80°C until the initial compound disappeared (TLC). The mixture was cooled, diluted with 3 ml of water, and extracted with CH_2Cl_2 (4×5 ml). The extract was washed with water, dried over $MgSO_4$, and evaporated, the residue was subjected to column chromatography on silica gel using chloroform and chloroform–ethanol (50:2) as eluents, and a fraction containing the product was treated with diethyl ether. Yield 89 mg (58%), mp 160–163°C (from diethyl ether). IR spectrum, ν, cm^{-1}: 3105, 2981, 2837, 1732, 1635, 1576, 1485, 1429, 1389, 1346, 1311, 1290, 1250, 1195, 1140, 1116, 1084, 1049, 1009, 960, 906, 869, 819, 758, 695, 650. UV spectrum ($CHCl_3$–EtOH, 3:1), λ_{max}, nm (logε): 242 (4.32), 287 (3.77), 297 (3.76), 338 (3.67). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (J, Hz): 1.39 d [6H, (C**H**$_3$)$_2$CH, J = 6.9], 3.54 m [1H, C**H**(CH$_3$)$_2$], 6.20 d.d (1H, 3′-H, J = 3.4, 0.8), 6.25 d (1H, 6-H, J = 9.6), 6.38 d.d (1H, 4′-H, J = 3.4, 1.6), 7.14 s (1H, 4-H), 7.46 d (1H, 5′-H, J = 1.6, 0.8), 7.58 s (1H, 4-H), 7.68 d (1H, 5-H, J = 9.6). ^{13}C NMR spectrum, δ_C, ppm: 20.75 q [(**C**H_3)$_2$CH], 25.87 d [**C**H(CH$_3$)$_2$], 100.38 d (C^9), 103.66 d ($C^{3'}$), 108.92 d ($C^{4'}$), 112.30 s (C^3), 114.55 s (C^{4a}), 114.91 d (C^6), 122.44 s (C^{3a}), 124.85 d (C^4), 142.93 d ($C^{5'}$), 145.19 d (C^5), 151.67 s (C^{8a}), 152.77 s (C^{9a}), 158.51 d ($C^{2'}$), 159.96 s (C^2), 160.86 s (C^7). Found, %: C 72.98; H 4.49. $C_{18}H_{14}O_4$. Calculated, %: C 73.46; H 4.79.

3-(Furan-3-yl)-2-isopropyl-7*H*-furo[3,2-*g*]chromen-7-one (XII). Compound **I**, 200 mg (0.5 mmol), was dissolved in 3 ml of acetonitrile, 76 mg (0.65 mmol) of furan-3-ylboronic acid (**X**), 18 mg (0.025 mmol) of $PdCl_2$(dppf), 200 mg (1.5 mmol) of K_2CO_3, and 11 mg (10 mol %) of $Bu_4N^+Br^-$ were added under argon, and the mixture was stirred for 4.5 h at 80°C until the initial compound disappeared (TLC). The mixture was cooled, diluted with 3 ml of water, and extracted with CH_2Cl_2 (4×5 ml). The extract was washed with water, dried over $MgSO_4$, and evaporated, the residue was subjected to column chromatography on silica gel using chloroform and chloroform–ethanol (50:2) as eluents, and a fraction containing the product was treated with diethyl ether. Yield 102 mg (67%), mp 132–133°C (from Et_2O). IR spectrum, ν, cm^{-1}: 3130, 3067, 3049, 2981, 1732, 1718, 1634, 1564, 1504, 1468, 1431, 1410, 1387, 1371, 1362, 1350, 1288, 1213, 1198, 1140, 1114, 1068, 1047, 1020, 934, 905, 878, 820, 781, 748, 744, 700, 681. UV spectrum ($CHCl_3$–EtOH, 3:1), λ_{max}, nm (logε): 252 (4.26), 288 (3.83), 295 (3.76), 334 (3.63). ^{1}H NMR spectrum ($CDCl_3$–CD_3OD), δ, ppm (J, Hz):

1.39 d [6H, (C**H**$_3$)$_2$CH, J = 6.9], 3.31 m [1H, C**H**(CH$_3$)$_2$], 6.26 d (1H, 6-H, J = 9.6), 6.37 br.s (2H, 9-H, 4′-H), 7.29 br.s (1H, 5′-H), 7.48 s (1H, 4-H), 7.54 br.s (1H, 2′-H), 7.77 d (1H, 5-H, J = 9.6). ^{13}C NMR spectrum, δ_C, ppm: 19.85 q [(**C**H$_3$)$_2$CH], 25.81 d [**C**H(CH$_3$)$_2$], 100.28 d (C^9), 112.71 d (C$^{4'}$), 113.24 s (C^3), 114.95 d (C^6), 116.18 s (C^{4a}), 116.71 d (C^4), 117.27 s (C^{3a}), 126.07 s (C$^{3'}$), 142.35 d (C$^{2'}$), 144.17 d (C^5), 149.76 d (C$^{5'}$), 151.97 s (C^{8a}), 152.97 s (C^{9a}), 156.99 s (C^2), 161.11 s (C^7). Found, %: C 73.28; H 4.92. $C_{18}H_{14}O_4$. Calculated, %: C 73.46; H 4.79.

3-(1*H*-Indol-5-yl)-2-isopropyl-7*H*-furo[3,2-*g*]-chromen-7-one (XIV). *a*. Compound **I**, 200 mg (0.5 mmol), was dissolved in 3 ml of acetonitrile, 104 mg (0.65 mmol) of 1*H*-indol-5-ylboronic acid (**XIII**), 18 mg (0.025 mmol) of $PdCl_2$(dppf), 200 mg (1.5 mmol) of K_2CO_3, and 11 mg (10 mol %) of $Bu_4N^+Br^-$ were added, and the mixture was stirred for 6 h at 80°C until the initial compound disappeared (TLC). The mixture was cooled, diluted with 3 ml of water, and extracted with CH_2Cl_2 (3×4 ml), the extracts were combined, dried over $MgSO_4$, and evaporated, and the product was isolated by column chromatography on silica gel, followed by treatment of the corresponding fraction with Et_2O. Yield 72 mg (42%).

b. Compound **I**, 200 mg (0.5 mmol), was dissolved in 3 ml of anhydrous dioxane, 0.104 g (0.65 mmol) of 1*H*-indol-5-ylboronic acid, 14 mg (0.025 mmol) of $Pd(PPh_3)_4$, 200 mg (1.5 mmol) of K_2CO_3, and 11 mg (10 mol %) of $Bu_4N^+Br^-$ were added under argon, the mixture was stirred for 6 h at 100°C, and the product was isolated as described above in *a*. Yield 60 mg (35%), mp 165–166°C (from diethyl ether). IR spectrum, ν, cm^{-1}: 3392, 3110, 3065, 3047, 3010, 2980, 1732, 1718, 1689, 1634, 1610, 1578, 1514, 1471, 1433, 1412, 1337, 1310, 1248, 1211, 1196, 1136, 1094, 1047, 1029, 980, 902, 892, 870, 820, 735, 679. UV spectrum (EtOH), λ_{max}, nm (log ε): 203 (4.42), 228 (4.72), 250 (4.11), 261 (3.96), 277 (3.92), 281 (3.92), 331 (3.32). ^{1}H NMR spectrum ($CDCl_3$–CD_3OD), δ, ppm (J, Hz): 1.40 d [6H, (C**H**$_3$)$_2$CH, J = 7.0], 3.31 m [1H, C**H**(CH$_3$)$_2$], 6.39 d (1H, 6-H, J = 9.6), 6.46 d (1H, 3′-H, J = 2.6), 7.22 s (1H, 9-H), 7.36 d (1H, 2′-H, J = 2.6), 7.46 d (1H, 7′-H, J = 7.8), 7.54 d (1H, 6′-H, J = 7.8), 7.61 s (1H, 4-H), 7.76 d (1H, 5-H, J = 9.6), 7.82 br.s (1H, 4′-H), 8.01 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 19.85 q [(**C**H$_3$)$_2$CH], 25.73 d [**C**H(CH$_3$)$_2$], 100.13 d (C^9), 101.65 d (C$^{3'}$), 110.22 d (C$^{7'}$), 110.34 s (C^3), 114.75 d (C^6), 115.84 s (C^{4a}), 116.50 d (C^4), 118.80 d (C$^{5'}$), 119.94 s (C^{3a}), 126.24 d (C$^{6'}$), 124.02 d (C$^{2'}$), 126.32 s (C$^{3a'}$), 126.56 s (C$^{7a'}$), 137.32 s (C$^{5'}$), 144.03 d (C^5), 151.78 s (C^{8a}), 152.86 s (C^{9a}), 156.81 s (C^2), 161.14 s (C^7). Found, %: C 76.69; H 5.21; N 4.14. $C_{22}H_{17}NO_3$. Calculated, %: C 76.95; H 4.99; N 4.08.

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